Vanadium-Catalyzed Selenide Oxidation with *in situ* [2,3] Sigmatropic Rearrangement: Scope and Asymmetric Applications.

A Thesis

Presented for the

Master of Science

Degree

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DEDICATION

To my future bride Chrissy Castrichini

and my grandparents Tommie and Walter Bourland

ACKNOWLEDGEMENTS

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ABSTRACT

Allylic alcohols are vital cogs in organic synthesis. This functionality provides a platform for the synthesis of key intermediates for complex structures such as natural products. Selenides have proven useful in introducing key functionalities into complex organic compounds. One particular use is the oxidation of selenium to the reactive selenoxides. These selenoxides can be used as a platform for *syn* elimination to give an alkene, or [2,3] sigmatropic rearrangement to produce an allylic alcohol.

This research is the development of a vanadium-catalzyed selenide oxidation with *in situ* [2,3] sigmatropic rearrangement to produce allylic alcohols. A racemic system was optimized to show the utility of this methodology. Next, a ligand-based approach was incorporated in an attempt to obtain asymmetric oxidation. Finally, a chiral-auxiliary-based system was utilized to understand the nature of chiral induction of selenoxides.

It was concluded that asymmetric selenide oxidation with *in situ* [2,3] sigmatropic or ASOS reaction was a useful way to access chiral allylic alcohols.

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acac	acetylacetonate
AcOH	acetic acid
ASOS	asymmetric selenide oxidation with *in situ* [2,3] sigmatropic rearrangement
Bu	butyl
CHP	cumene hydrogenperoxide
DAST	diethylaminosulfurtrifluoride
d.e.	diastereomeric excess
DET	diethyl tartrate
d.s.	diastereomeric selectivity
DIBAL-H	diisobutylaluminum hydride
DMAP	4-(*N*, *N*-dimethylamino)-pyridine
E	entgegen
equiv	equivalent
Et	ethyl
EtOAc	ethyl acetate
i	iso
KHMDS	potassium *bis*-(trimethylsilyl)-amide
LA	Lewis Acid
m	multiplet
M	molar
m-CPBA	3-chloroperbenzoic acid

Me	methyl
min	minutes
m.p.	melting point
NaHMDS	sodium *bis*-(trimethylsilyl)-amide
NMO	*N*-methyl morpholine *N*-oxide
NMR	nuclear magnetic resonance
Nu	nucleophile
P	protecting group
Ph	phenyl
ppm	parts per million
py	pyridine
r.t.	room temperature
s	singlet
SAE	Sharpless Asymmetric Epoxidation
SOS	selenide oxidation with *in situ* [2,3] sigmatropic rearrangement
t	triplet
t	tert
TBAF	tetrabutylammonium fluoride
TBHP	*tert*-butyl hydroperoxide
TBS	*tert*-butyldimethylsilyl
Tf	trifluoromethanesulfonate
TFA	trifluoroacetic acid
TIPS	triisopropylsilyl

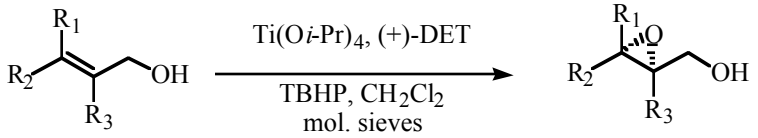
Ts	4-toluenesulfonyl
Z	zusammen

I. INTRODUCTION INTO THE SYNTHESIS AND UTILITY OF ALLYLIC ALCOHOLS

Allylic alcohols are vital cogs in organic synthesis. This functionality provides a platform for the synthesis of key intermediates for complex structures such as natural products.[1] Because of the importance of allylic alcohols as synthons, many chemists have explored a variety of pathways for constructing this intricate subunit. Furthermore, chemists have presented ways to exploit chiral and achiral allylic alcohols to create other useful precursors including epoxides,[2] cyclopropanes,[3] and unsaturated diols.[4]

The achiral allylic alcohol is a useful precursor for the production of asymmetric substrates. K. Barry Sharpless introduced a powerful reagent-controlled asymmetric epoxidation[5] transformation in the early 1980's utilizing a simple allylic alcohol **1** to give an epoxy alcohol product **2** with a high level of enantiomeric excess (e.e.) (Scheme 1). Reagents include a chiral diethyl tartrate species [(+)- or (-)-DET], titanium (IV) iso-propoxide [Ti(O*i*-Pr)$_4$], and *tert*-butyl hydroperoxide (TBHP). The hydroxyl group on the allylic alcohol **1** is crucial in directing facial selectivity for the tartrate-titanium complex to approach the double bond for the epoxidation. This reaction generally occurs in high yield (70-90%) with outstanding enantioselectivity (up to 99% e.e.) The Sharpless asymmetric epoxidation (SAE) has proven to be one of the most versatile reactions in synthetic chemistry.[6]

Scheme 1: Sharpless Asymmetric Epoxidation (SAE Reaction).



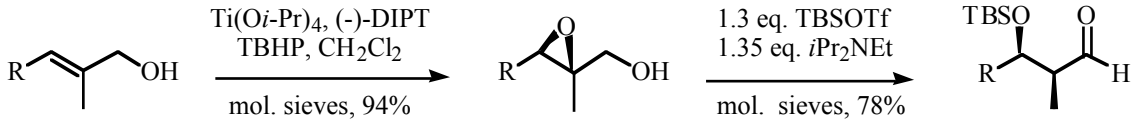
up to 99% e.e.

1 **2**

Achiral allylic alcohols can also be used to produce chiral aldol products without using aldol chemistry (Scheme 2).[7] Traditionally, chiral auxiliaries[8] were necessary to

access the desired aldol products; however, the Jung group has developed a novel methodology to bypass this established route. Absolute stereochemistry was introduced by Sharpless[9] asymmetric epoxidation of the achiral starting material **3**. The epoxide **4** was then opened regiospecifically by an intramolecular hydride transfer from an adjacent silyl ether group. The geometry of the olefin and the chirality of the tartrate species determine the configuration of the final product, thereby providing access to any of the four diastereomers.

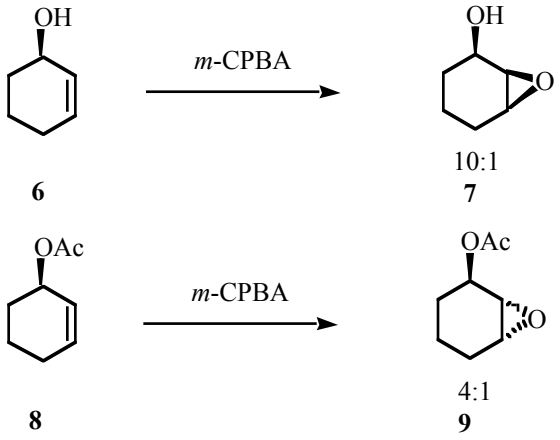
Scheme 2: Jung's Non-Aldol Aldol Reaction.



3 **4** **5**

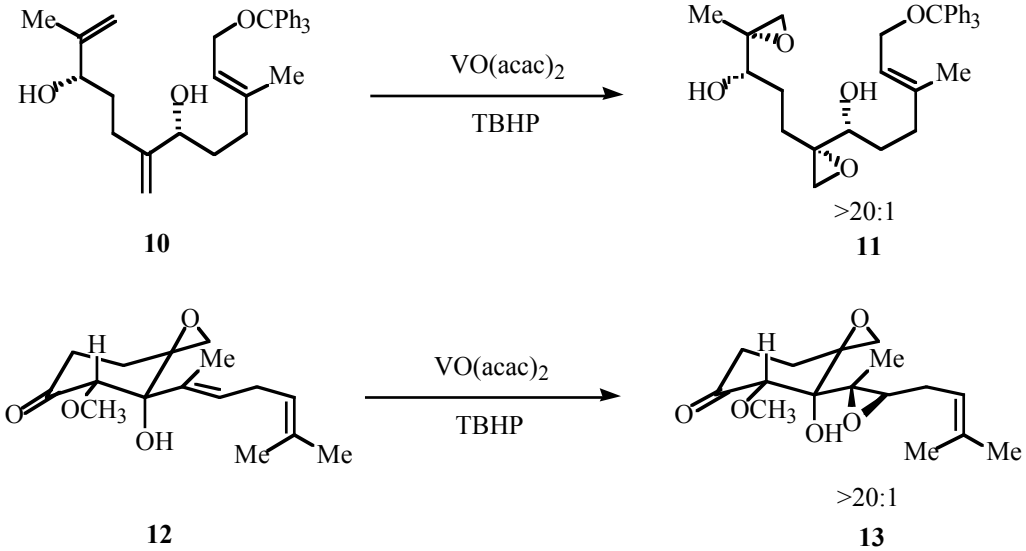
Chiral allylic alcohols have proven equally effective as the achiral precursor in producing diastereoslective epoxide products (Scheme 3). For example, a chiral 2° allylic alcohol can act as a director in stereoselective epoxidation reactions.[10] Henbest and Wilson first explored this phenomenon in the late 1950's by treating chiral cyclic allylic alcohols, such as the cyclohexenol **6**, with the peracid *m*-CPBA.[11] The result was the *syn*-epoxy alcohol **7** with 10:1 diastereoselectivity. It is interesting to note when the hydroxyl functionality is protected with an acetate group **8**, the subsequent oxidant yields an *anti*-epoxy alcohol **9** with 4:1 selectivity. The difference in stereochemistry is rationalized by a "butterfly" transition state proposed by Bartlett.[12]

Scheme 3: Selected Examples of Hydroxyl-Directed Epoxidations.



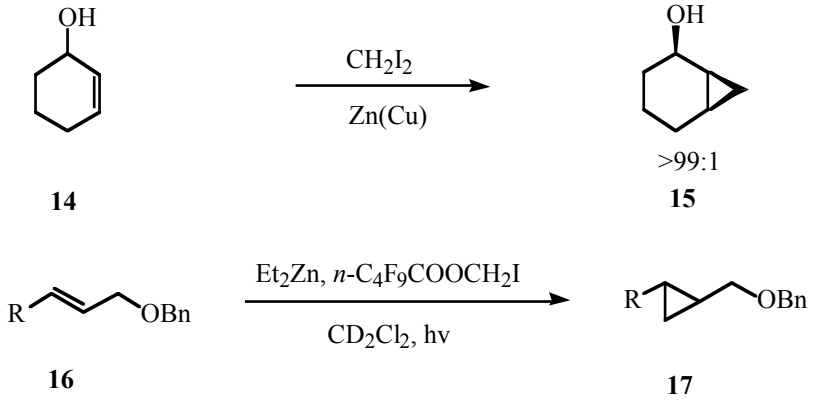
The controlling effect of a chiral 2° allylic alcohol is not limited to peracid epoxidations (Scheme 4).[13] A key step in the synthesis of the juvenile hormone *dl*-C_{18}*Cecropia* illustrates regio- and stereocontrol of a vanadium-catalyzed epoxidation to give the product **11** in greater than 95% diastereoselectivity.[14] Likewise, in the total synthesis of the natural product (±) ovalicin, Corey elegantly uses the chiral tertiary allylic alcohol **12** to obtain >20:1 diastereoselection in a vanadium-catalyzed epoxidation.[15]

Scheme 4: Selected Examples of Metal-Catalyzed, Hydroxyl-Directed Epoxidations.



Allylic alcohols are not limited to epoxidations. Interesting chemistry has been developed utilizing the allylic alcohol to form another significant intermediate: cyclopropane (Scheme 5). The cylcopropane functionality is known to have potent biological activity[16] and has also been demonstrated to be a key synthetic intermediate.[17] In 1958, Simmons and Smith developed one of the first cyclopropanation reactions of an olefin by treatment with zinc-copper and iodomethyl iodide.[18] Winstein and co-workers applied this transformation to 2° allylic alcohols and consequently discovered a specificity for the *syn*-cyclopropyl alcohol **15** with >99:1 selectivity on cyclic systems.[19] The hydroxyl group is a key director in forming the stereoselective product. Similarly, Charette and co-workers have developed an acyloxymethyl zinc reaction,[20] which produces the desired cyclopropane on many unfunctionalized substrates. One specific example uses a benzylated cinnamyl alcohol precursor **16**, which produces the desired cylcopropane **17**.

Scheme 5: Selected Examples of Metal-Catalyzed, Hydroxyl-Directed Cyclopropanations.

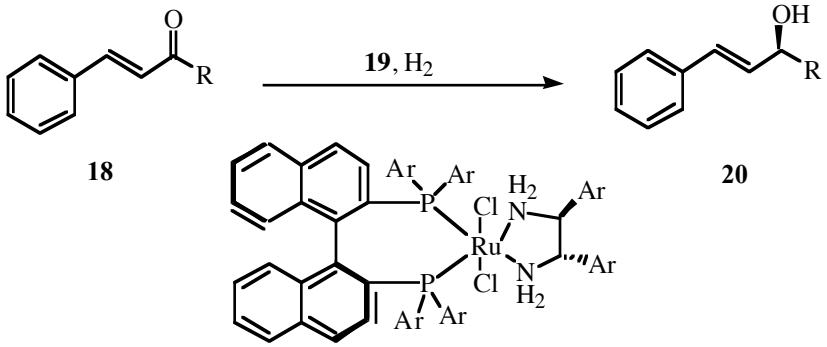


Due to the importance of the allyl alcohol group in synthesis, chiral and achiral methods are needed for the creation of this functionality (Scheme 6). Several methods do exist for accomplishing this important goal. For example, the Noyori group employs a ruthenium catalyst with a binapthyl ligand **19** to selectively hydrogenate (reduce) an

unsaturated ketone to an alcohol in high yield with <99% e.e.[21] Numerous groups have developed methods for the asymmetric addition of dialkyl zinc species to α,β-unsaturated aldehydes, such as **21**.[22] Despite important accomplishments, this further innovation is required in the synthesis of chiral allylic alcohols.

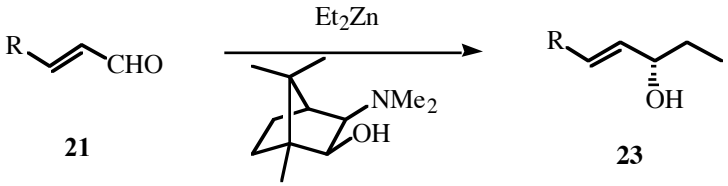
Scheme 6: Selected Examples of Methods for the Construction of Chiral Allylic Alcohols.

Asymmetric Reductions



19

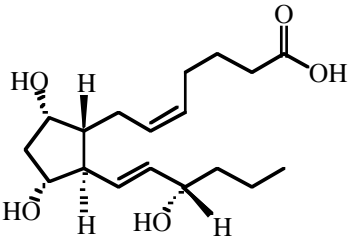
Asymmetric Zinc Additions



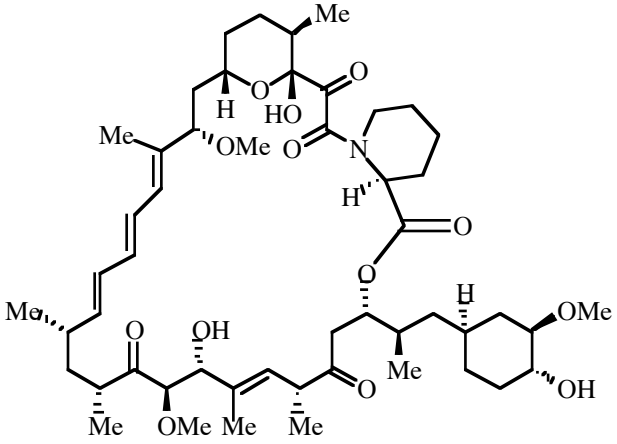
21 **22** **23**

A myriad of natural products exists (Figure 1) that contain chiral secondary and tertiary allylic alcohols. Some specific examples include the prostaglandins,[23] such as compound **24**, and rapamycin (**25**).[24] Due to the presence of the allylic alcohol moiety in such a variety and abundance of natural products, in consort with its use as a precursor in important synthetic pathways, novel concepts are necessary for the creation and utilization of this particular functionality.

Figure 1: Selected Natural Products Containing Chiral Allylic Alcohols.



24



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[1] Nicolaou, K. C.; Sorenson, E. J. *Classiscs in Total Synthesis* 1996 VCH press, pp. 295.
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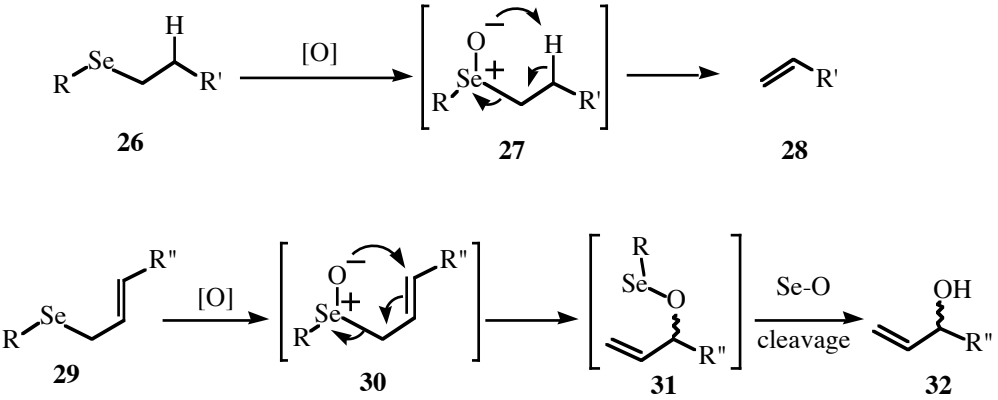
II. VANADIUM-CATALYZED SOS REACTION

2.1 Introduction.

Selenides have proven useful in introducing key functionalities in complex organic compounds. One particular use is the oxidation of selenium to the reactive selenoxides **27** and **30** (Scheme 7)**.** These selenoxides **27** and **30** can be used as a platform for *syn* elimination or to give the alkene **28** or [2,3] sigmatropic rearrangement to produce an allylic alcohol **32** respectively.[1] For the latter transformation, the allylic alcohol **32** is produced in good yield by the oxidation of the allylic selenide **29** to the reactive allylic selenoxide **30**, followed by the hydrolysis of the intermediate selenenate **31** after rearrangement. This route has proven effective and versatile in the production of primary, secondary, and tertiary allylic alcohols.[2]

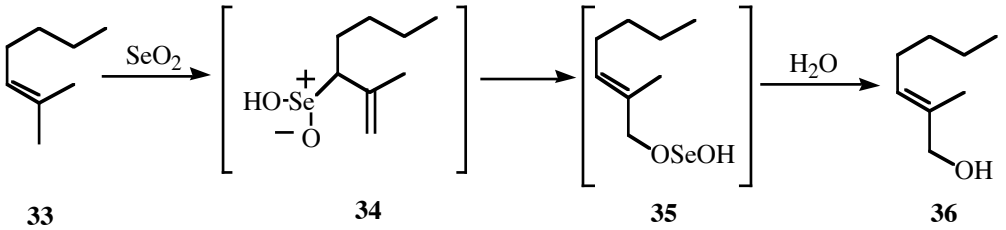
Scheme 7: Selected Examples of Useful Transformations Involving Selenides.



Oxidation of selenide **26** to the corresponding selenoxide **27** has been known since the early part of the 20th century;[3] however, not until 1972 did the selenoxides in allylic systems become applicable in synthesis. Sharpless and co-workers, using selenium dioxide for the oxidation of olefins, first commented on the [2,3] sigmatropic rearrangement of a selenoxide to the allylic alcohol[4] to explain an unexpected product emitted from this oxidation (Scheme 8). Sharpless not only noted that the reaction was a facile process, but also the advantage of the selenoxide intermediate compared to the

more widely studied sulfoxide intermediate.[5] Sharpless' proposal of this reaction mechanism laid the groundwork for further development of this transformation.

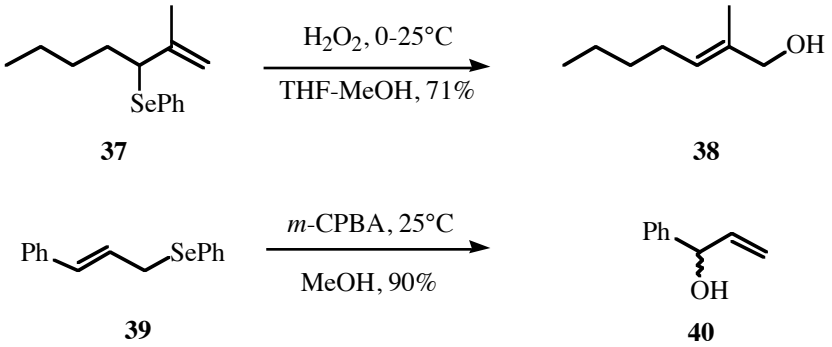
Scheme 8: The Sharpless' SeO_2 Oxidation.



33 **34** **35** **36**

Other laboratories have further explored the oxidation of allylic selenides to selenoxides with [2,3] sigmatropic rearrangement to produce allylic alcohols (Scheme 9). Early methods to convert the selenide to the corresponding selenoxide included the use of H_2O_2 and peracetic acid.[6] Despite the success of traditional oxidants in selenium oxidations with [2,3] sigmatropic rearrangement (SOS reaction), little effort has been put forth towards a metal-catalyzed system.

Scheme 9: Selected Examples of Selenide Oxidation with [2,3] Sigmatropic Rearrangement (SOS Reaction).



37 **38**

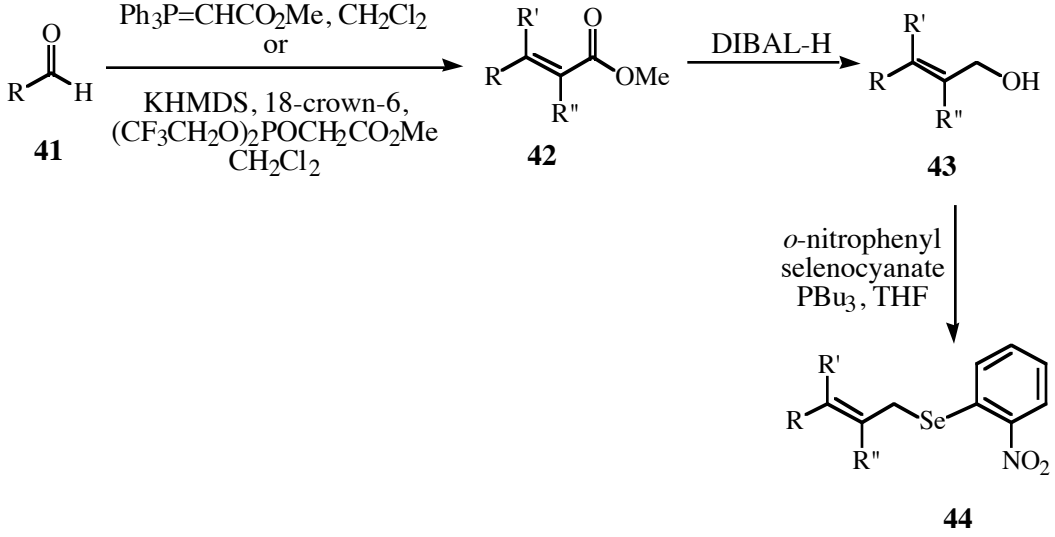
39 **40**

2.2 Synthesis of Aryl Allylic Selenides.

Aryl allylic selenides are readily accessible from the corresponding allylic alcohols. A Mitsonubo-type conversion of the allylic alcohol **43** is completed in the presence of tributyl phosphine and the commercially available selenocyanate (Scheme 10). The required allylic alcohol precursors **43** are constructed using a Wittig olefination

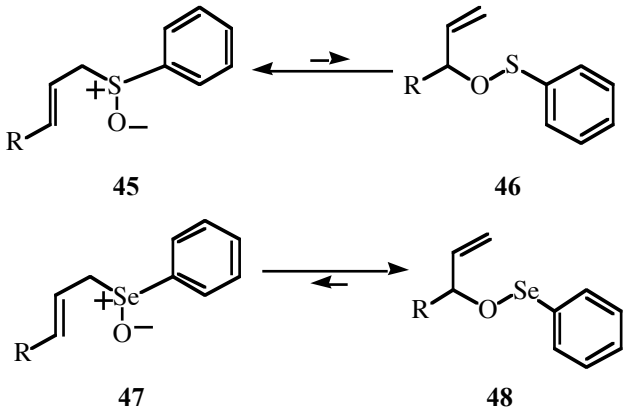
to access the (*E*)-alkene or a Gennari-Still olefination to produce the (*Z*)-alkene, followed by reduction.

Scheme 10: General Protocol for the Synthesis of the Aryl Allylic Selenides.



Similar sulfide systems can undergo a metal-catalyzed oxidation to produce a sulfoxide intermediate, which, in allylic systems, can rearrange to give an allylic alcohol. It was surprising that a similar methodology was not developed for selenium-based systems, since the selenoxide intermediate is notably more efficient at rearrangement compared to the sulfoxide.[7] Reich and co-workers reported a detailed kinetic and thermodynamic study of selenoxides **47** versus sulfoxides **45** in [2,3] sigmatropic rearrangement (Scheme 11).[8]

Scheme 11: Proposed Equilibrium of Sulfur and Selenium Compounds.

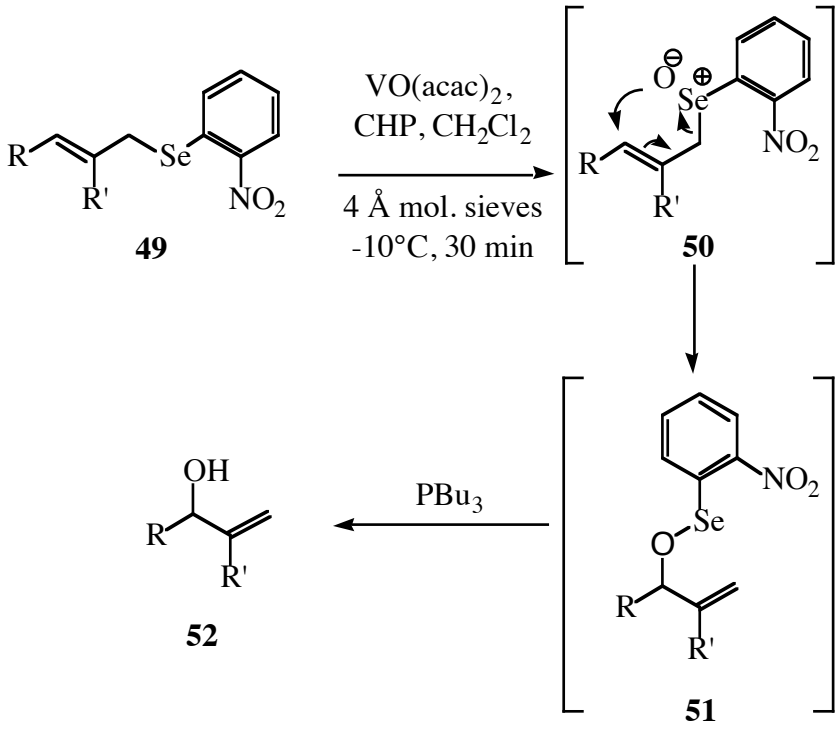


2.3. Development of the Vanadium-Catalyzed SOS Reaction.

While isolated reports of stoichiometric, titanium-based system for the oxidation of selenides have been published,[9] no methods have been disclosed for the use of a metal in a sub-stoichiometric sense. Our preliminary investigations with the titanium conditions led us to conclude that the titanium systems proceed slowly and the metal species cannot be lowered below stoichiometric levels without sacrificing conversion of the selenide **47**. These disappointing results with titanium-based systems led us to develop a truly catalytic system for the SOS reaction.

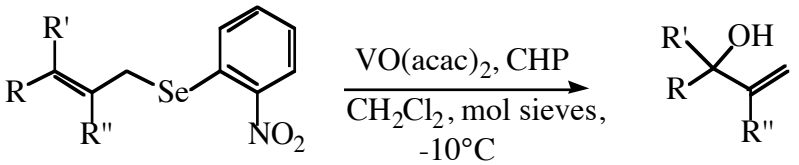
Before attempts could be made for asymmetric induction of selenoxides, a well established racemic oxidation was necessary. Vanadyl (IV) acetylacetonate [$VO(acac)_2$] appeared to be an ideal candidate, considering its success with the corresponding sulfide oxidation (Scheme 5).[10] Our laboratory was gratified to find that $VO(acac)_2$ can be used to effect selenide oxidation in the presence of a peroxide co-oxidant cumene (CHP) or *tert*-butyl hydroperoxide (TBHP) The advantages of the vanadyl system include mild reaction conditions and the requirement of only 10 mol % of the metal for full conversion of the selenide. Standard reaction conditions involved a 0.3 M solution of selenide **47** in CH_2Cl_2, with $VO(acac)_2$ (10 mol%) in the prescence of 4 Å mol. sieves (Scheme 12). This green solution was then cooled to –10°C and CHP or TBHP was added to the stirred solution. The reactions were typically complete within 30 minutes. Conversion of the selenenate **51** to the allylic alcohol **52** was best facilitated using PBu_3. Early attempts using traditional methods[11] (Py/H_2O or PPh_3) proved cumbersome and slow. Finally, it is important to note that a control experiment without $VO(acac)_2$ resulted in less than 5% conversion upon extended reaction times.

Scheme 12: Vanadium-catalzyed SOS reaction.

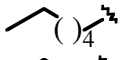
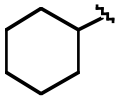
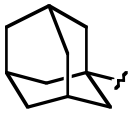
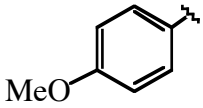
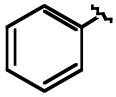
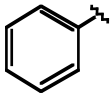
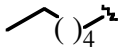
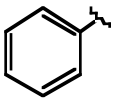


The optimized conditions of the vanadium-catalyzed SOS reaction were quite successful on a variety of substrates (Table 1). This reaction occurred rapidly regardless of steric environment located at the product's allylic position. In addition, the conditions are equally effective in aryl-conjugated and non-conjugated systems.

Table 1: Selected Examples of Vanadium-Catalyzed SOS Reaction.



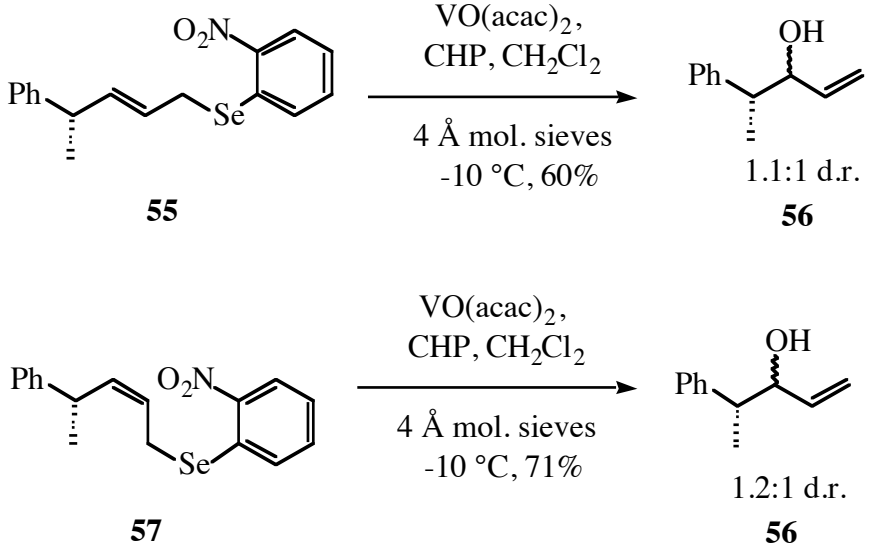
53 **54**

Entry	R	R'	R"	Yield
a		H	H	85%
b		H	H	75%
c		H	H	84%
d		H	H	80%
e		H	H	65%
f		H	CH_3	70%
g	H		H	63%
h	H		H	86%

Perhaps the most notable result is the lack of influence of a stereocenter located adjacent to the product's allylic position as shown in selenides **55** and **57** (Scheme 13).[12] The reaction provided essentially a 1:1 diastereomeric mixture of the rearranged alcohol regardless of olefin geometry. This result is in good agreement with Davis and co-workers who have shown that the stereochemistry of the resultant alcohol from acyclic substrates appears to be determined by the oxidation of the selenide.[13] It is important to note, however, that this result is in stark contrast to the Cram chelation and Felkin-Ahn

models of addition to aldehydes and ketones where a neighboring stereogenic center can have a significant effect on the diastereomeric outcome of the transformation.[14]

Scheme 13: Effect of a Stereogenic Center in the SOS Reaction.



The protocol and the scope have been explored for the vanadium-catalyzed SOS reaction in the racemic series. This methodology appears to be generally applicable to a wide variety of substrates and can be performed in a rapid and straightforward manner. It is clear that this methodology will see significant application to current synthetic problems.

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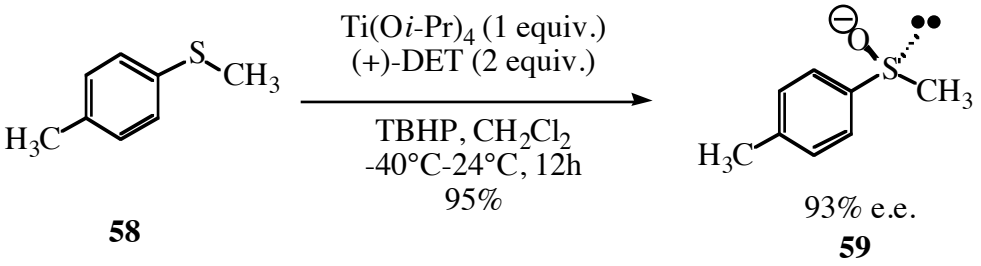
III. VANDIUM-CATALYZED, LIGAND-BASED ASOS REACTION

3.1 Introduction.

Asymmetric oxidation is a useful transformation to the synthetic chemist for the construction of complex natural products. These transformations have proven valuable in converting achiral functional groups to the desired chiral product, but more importantly, asymmetric oxidants have been used on a broad spectrum of substrates. Kagan and co-workers utilized a modification of the well-known Sharpless conditions to oxidize prochiral sulfides to the corresponding sulfoxides with enantiomeric excess (e.e.) up to 93 % e.e. on selected substrates (Scheme 14).[1] This work was important as it showed that chiral induction could be achieved from a titanium-tartrate complex during oxidation, hence laying the foundation for future asymmetric oxidations of sulfides to sulfoxides utilizing metal-ligand complexes.

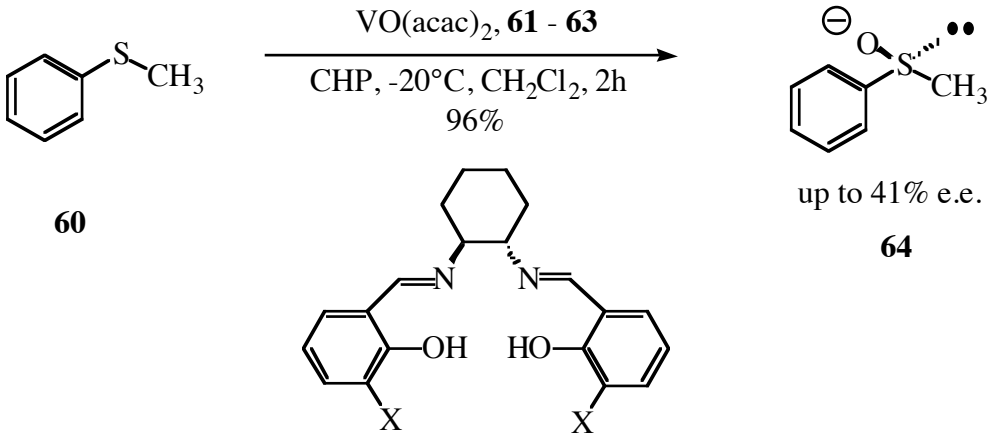
Scheme 14: Kagan's Oxidation of Prochiral Sulfides.



58 **59**

Although useful, Kagan's work was hindered by the requirement of stoichiometric reagents. The Fujita laboratory explored a vanadium-catalyzed asymmetric oxidation of similar sulfides utilizing salen-type ligands **61** - **63** in the presence of peroxides (Scheme 15).[2] The enantioselectivity of Fujita's reaction was significantly less than the Kagan oxidation (up to 41 % e.e.), but only 10 mol % of the chiral vanadium-salen complex was necessary for full conversion.

Scheme 15: Fujita's Vanadium-Salen Complex System.



60

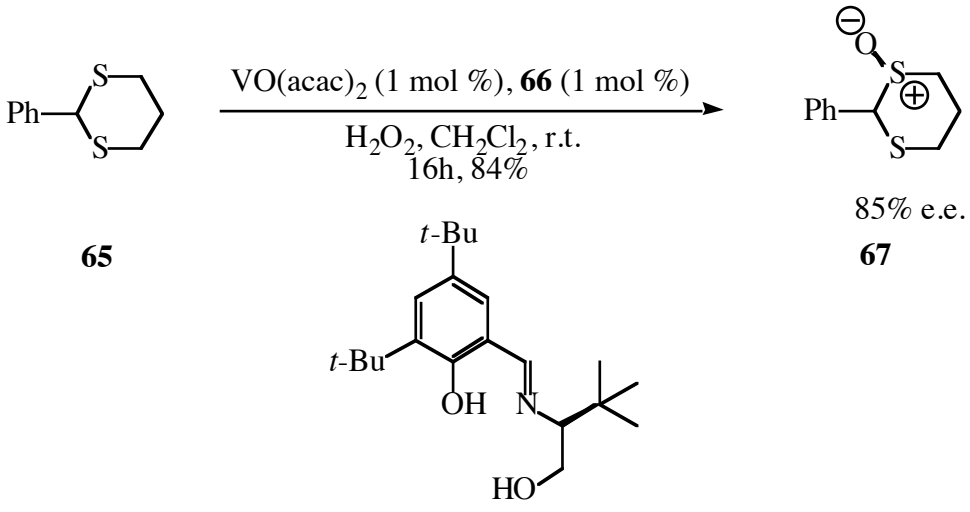
up to 41% e.e.

64

61 X = OMe
62 X = OEt
63 X = *t*-Bu

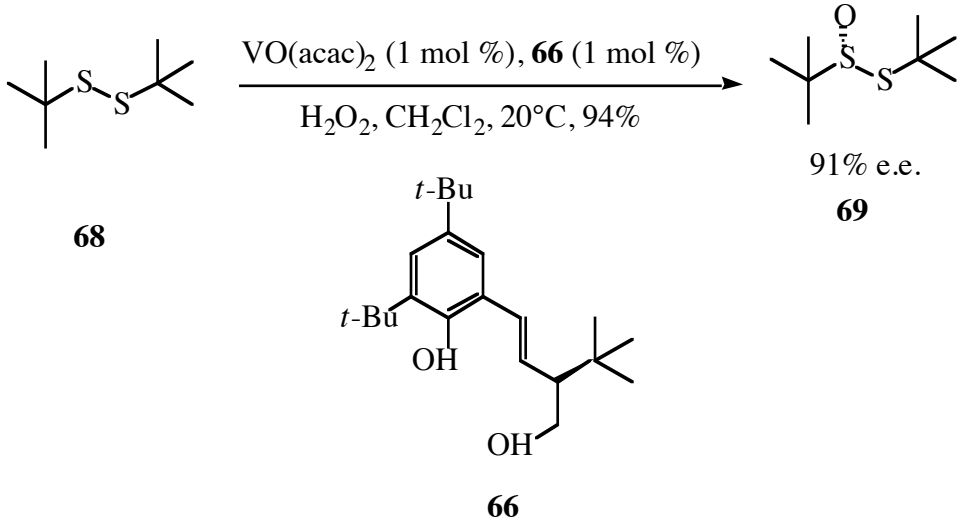
Bolm and co-workers explored a similar vanadium-catalyzed, ligand-based asymmetric oxidation of thioethers to sulfoxides (Scheme 16).[3] The Bolm laboratory enjoyed greater success than the Fujita group, accomplishing selectivities up to 85 % e.e. on certain substrates. This reaction utilized an inexpensive *tert*-leucinol-based ligand **66** complexed with vanadium for chiral induction to the sulfoxide **67**. It should be noted that this protocol required only 1 mol % of the ligand-vanadium complex for full conversion to the sulfoxide **67** in high yield.

Scheme 16: The Bolm Vanadium-Catalyzed Asymmetric Oxidation.



Ellman and co-workers developed a similar system[4] which employed the same chiral ligand to produce an asymmetric vanadium-catalyzed oxidation of the disulfide **68** (Scheme 17). Ellman screened a variety of chiral Schiff-base ligands varying the steric bulk only to find the *tert*-leucinol ligand **66** used by Bolm gave the highest enantioselectivity (91 % e.e.). Ellman also varied solvents, amount of the metal, and temperature to optimize reaction conditions. The optimal conditions used a slight excess of the ligand **66** (1 mol %) compared to the $VO(acac)_2$ (1 mol %) at r.t. with high concentration (1.5 M).

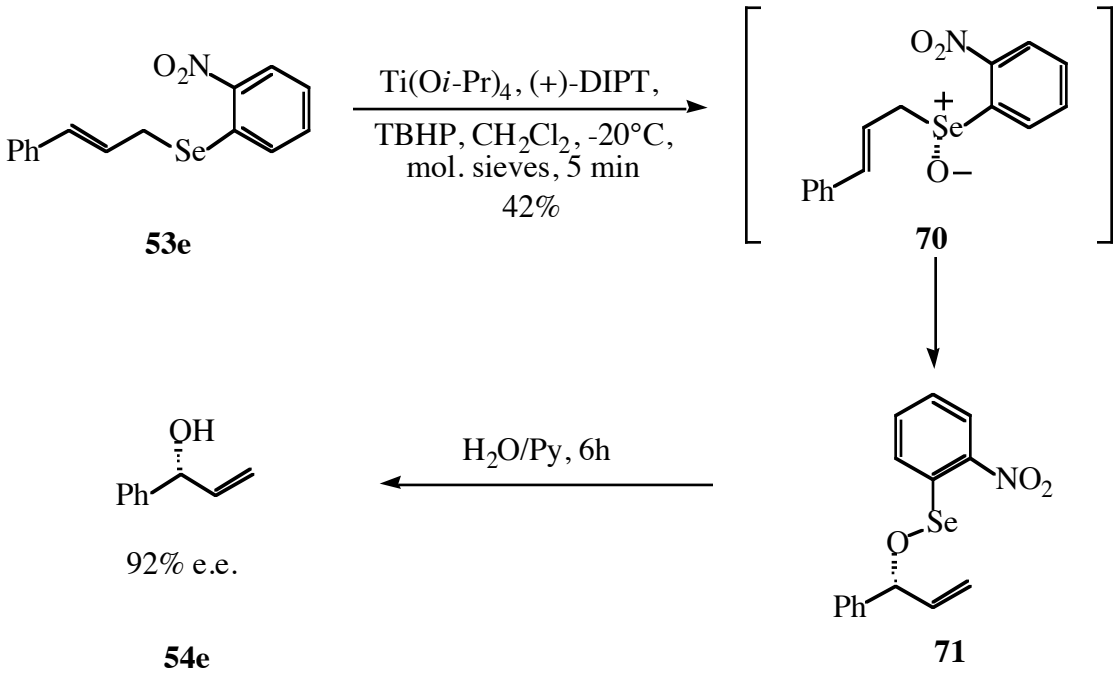
Scheme 17: Ellman's Asymmetric Oxidation of Prochiral Disulfides.



3.2 Prior Work on Metal-Mediated ASOS Reaction.

Despite the success of ligand-based, metal-catalyzed asymmetric oxidations on sulfur systems, little attention has been given towards the corresponding selenides and the ASOS reaction. The Uemura lab group has reported the use of Kagan's conditions in the ASOS reaction (Scheme 18).[5] Once again, Uemura used stoichiometric amounts of the $Ti(O\textit{i}\text{-}Pr)_4$ (1 equiv.) and a tartrate ligand (2 equiv.) to achieve full conversion. Uemura and co-workers reported levels of selectivity varying from 7 % to 92 % e.e. with yields primarily in the 40 % range.

Scheme 18: Uemura's Titanium-catalyzed ASOS Reaction.



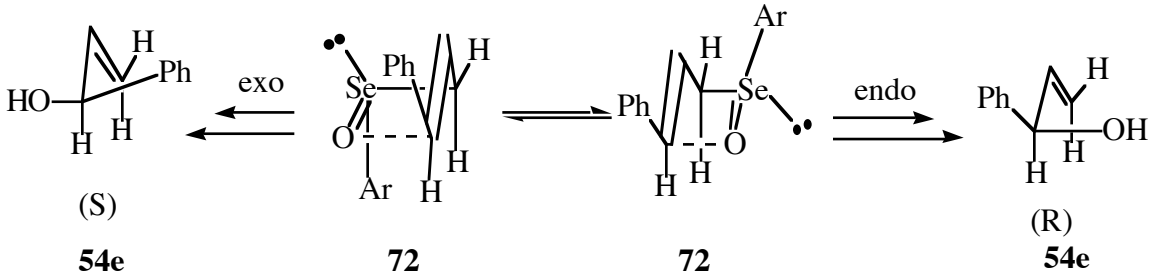
While the Uemura ASOS reaction was initially attractive, several significant problems have hampered the application of this methodology. The poor yields (most were 40 % or lower) of this reaction make these conditions unattractive as a synthetically viable method. The titanium-tartrate complex is stoichiometric requiring *two* equivalents of ligand for full conversion. Furthermore, preliminary studies in the Carter laboratory employing Uemura's protocol yielded poor selectivity (less than 10 % e.e.) and slow reaction times (18 h at –5°C).[6] Further support for the lack of reproducibility of the Uemura system can be found in the fact that no other synthetic laboratory has reported the utilization of this methodology. Finally, the Uemura laboratory appears to have abandoned this strategy entirely by *later* reporting a chiral *auxiliary*-based methodology[7] to achieve the ASOS reaction (using *m*-CPBA as the oxidant). It became apparent that a metal catalyzed, ligand-based ASOS reaction, similar to the successful sulfoxide systems

developed by the Ellman and Bolm laboratories, would prove beneficial to the synthetic community.

3.3. Transition State Model for the [2,3] Sigmatropic Rearrangement.

Reich and Yelm first developed a transition state model to explain the stereochemical outcome of selenoxide rearrangement (Scheme 19).[8] The endocyclic transition state places the aromatic substituent on the selenide on the same side as the bend in the double bond. Conversely, the exocyclic transition state has aromatic selenide group on the opposite side as the bend in the double bond. Davis and co-workers[9] further supported the model of Reich and Yelm by obtaining stereochemical results that predicted the same transition state model. Finally, calculations by Reich and co-workers[10] have determined the *endo* intermediate to be 2 kcal/mol more stable than its *exo* counterpart.[11]

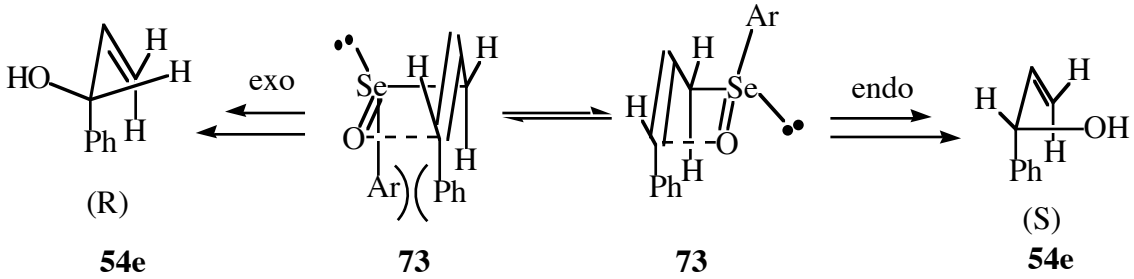
Scheme 19: *Endo* and *Exo* Transition State Models for *E*-Alkene.



(S) **54e** **72** **72** (R) **54e**

Olefin geometry is also thought to play a important role in chiral induction. The Davis laboratory noted the *Z*-olefin geometry to be more efficient for chiral induction[12] Davis reasoned that in the Z configuration, unfavorable 1,4-interaction between the aromatic selenide and the substituent phenyl group in the *exo* configuration makes the *endo* transition state more favorable (Scheme 20). This argument is further supported by Kurose and co-workers who also observed higher selectivity on *Z*-alkene systems.[13,14]

Scheme 20: *Endo* and *Exo* Transition State Models for *Z*-Alkene.

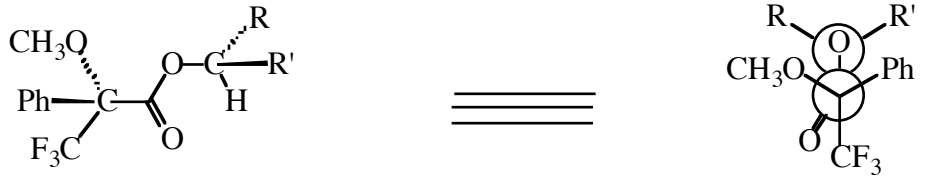


54e **73** **73** **54e**

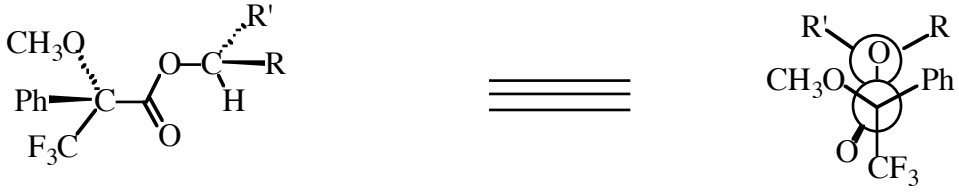
3.4 Determination of Enantiomeric Excess.

In order to study the ASOS reaction, a straightforward and reliable method needed to be employed in order to establish the enantioselectivity of the resultant 2° allylic alcohol. The well-known and reliable Mosher ester method[15] appeared to be ideally suited for this task. The allylic alcohols were condensed with α-methoxy-α-trifluoromethylphenyl acetic acid chloride [(R)-(+)-MTPA-Cl] to yield diastereomeric esters. The two diastereomers are readily differentiated by ^{1}H NMR or ^{19}F NMR. Figure 2 shows a model formulated to account for this result. In the proposed model put forth by Mosher, the α-triflouromethyl group eclipses the carbonyl functionality. A shielding or deshielding effect is observed based on the relationship of R and R' to the methoxy and phenyl substituents.[16]

Figure 2: Model of Diastereomeric Mosher Esters.



(*R*,*R*) diastereomer - **74** **74**

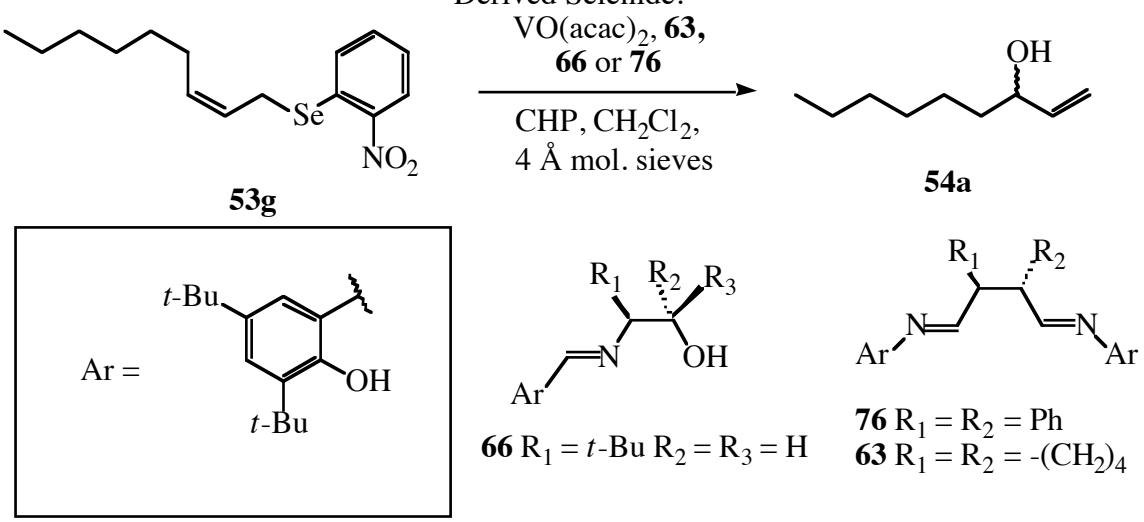


(*S*,*R*) diastereomer - **75** **75**

3.5 Exploration Into a Vanadium-Catalyzed, Ligand-Based ASOS Reaction.

After successfully developing a racemic series of vanadium-catalyzed SOS reactions, a series of ligands were screened with the goal of effecting chiral induction in the ASOS reaction. The ligands chosen were chiral Schiff base systems that were previously successful in asymmetric oxidations of sulfides (See Section 3.1). The selenide **53g** was chosen as the initial substrate for screening (Table 2). The choice of the *Z*-olefin geometry in the allylic selenide was based on precedent by the Davis and Kurose laboratories who have independently shown evidence for improved levels of selectivity versus the corresponding *E*-alkene (See Section 3.3). Multiple variables were tested for optimized conditions, but regardless of temperature[17] or ligand, no chiral induction was observed in this simple alkyl system **53g**. One possible explaination for the poor enantiomeric excess could be found in the lack of steric bulk located on the alkene.

Table 2: Selected Examples of Vanadium-Catalyzed ASOS Reaction Using the *n*-Alkyl Derived Selenide.

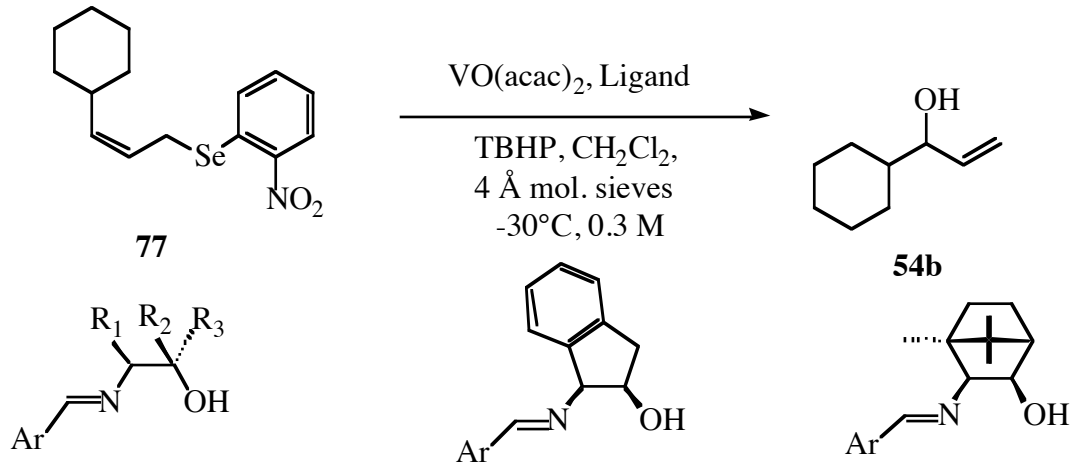


Entry[i]	Ligand	Temperature	Yield	e.e.
a	**66**	-10°C	63%	<2%
b	**66**	-30°C	68%	<2%
c	**66**	-50°C	67%	<2%
d	**76**	-30°C	68%	<2%
e	**63**	-30°C	79%	<2%

i. All reactions were performed at 0.3 M concentration relative to the selenide.

The cyclohexyl selenide **77** was chosen a more sterically demanding substrate; however, only slightly better results were observed. Ligand **63** (Scheme 21) produced the only double digit result of enantiomeric excess in the ligand-based, metal-catalyzed ASOS reaction. It should be noted that a control experiment [omitting $VO(acac)_2$] resulted in less than 5% conversion. Despite the considerable precedent for the corresponding sulfides, only low levels of asymmetric induction (< 10 % e.e.) were observed. It became apparent that the protocols employed for the sulfide systems were not applicable to the selenide series.

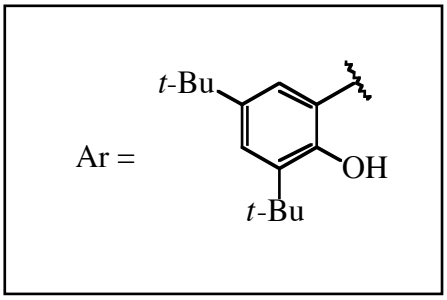
Scheme 21: Selected Examples of Vanadium-catalyzed ASOS Reaction Using the Cyclohexyl-Derived Selenide.

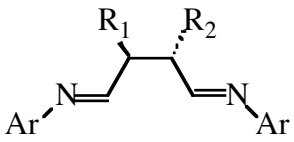


66 R_1 = *t*-Bu, R_2 = R_3 = H (5 % e.e.)
78 R_1 = Ph, R_2 = R_3 = H (< 2 % e.e.)
79 R_1 = *i*-Pr, R_2 = R_3 = H (< 2 % e.e.)
80 R_1 = CH_3, R_2 = Ph, R_3 = H (6 % e.e.)
81 R_1 = R_3 = Ph, R_2 = H (3 % e.e.)

82 (< 2% e.e.)

83 (< 2 % e.e.)





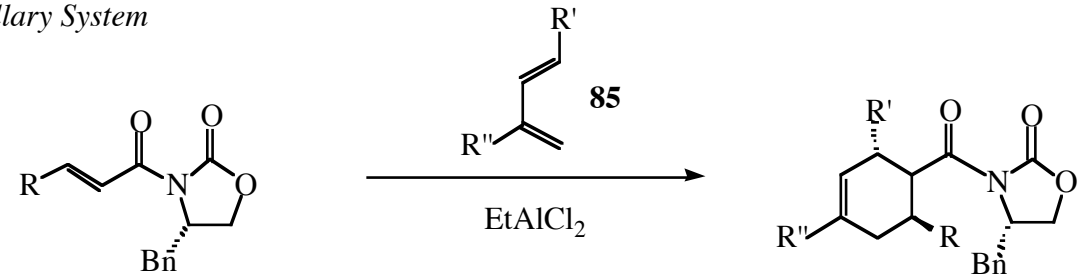
76 R_1 = R_2 = Ph (< 2 % e.e.)
63 R_1 = R_2 = -$(CH_2)_4$ (10 % e.e.)

3.6 Conclusion.

Although a catalytic, ligand-based system should continue to be an attractive, long term goal, a better understanding of the inducing elements appears to be required. An auxiliary-based approach has proven a reliable method for gaining this understanding in other reactions by reduction of the number of potential variables. For example, the Evans auxiliary has proven a powerful tool for asymmetric Diels-Alder[18] reactions (Scheme 22). This important work laid the foundation for the recent successes in asymmetric metal-catalyzed, ligand-based Diels-Alder reactions.[19]

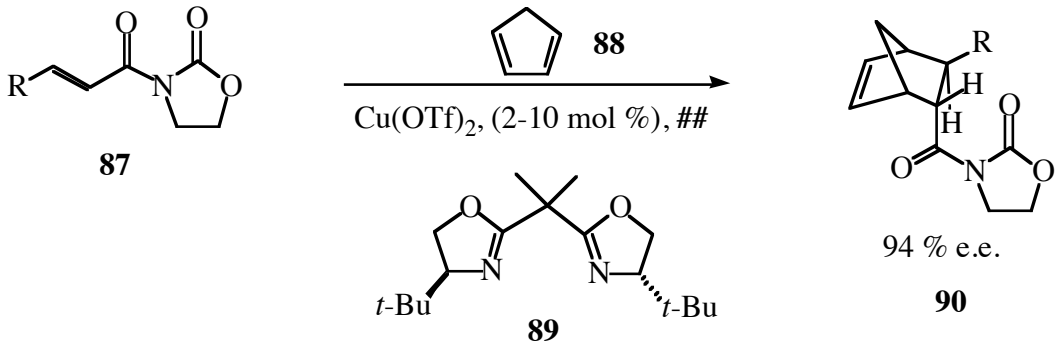
Scheme 22: Ligand and Auxiliary-Based Asymmetric Aldol and Diels Alder Reactions.

Auxillary System



84 **86**

Ligand System



87 **89** **90**

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[6] It is interesting to note that Tingoli and co-workers observe rates and selectivities in agreement with our observations and in stark contrast to Uemura's work. Tiecco, M.; Tingoli, M.; Testaferri, L.; Bartoli, D. *Tett. Lett.* **1987**, *28*, 3849.
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[11] Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 7134. Reich, H. J. *J. Org. Chem.* **1975**, *40*, 2570. Reich, J. J.; Shah, S. K.; Gold, P. M.; Olson, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 3112.
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[13] Kurose,N.; Takahashi, T.; Koizumi, T. *Tetrahedron* **1997**, *53*, 12115.
[14] Uemura and co-workers reported little difference in level of selectivity on their ferrocene-derived selenide system. Nishibayashi, Y.; Singh, J. D.; Fukuzawa, S.; Uemura, S. *J. Org. Chem.* **1995**, *60*, 4114.
[15] Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092.
[16] Juaristi, E. *Introduction to Stereochemical and Conformational Analysis* John Wiley & Sons, Inc.**1991**, pg. 33.
[17] The reaction proceeded unreasonably slow at temperatures below -30°C and the solution was prone to solidification at temperatures below -50°C. For these reasons, –30°C at 0.3 M concentration was optimum for ligand screening.
[18] Oppolozer, W. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 876.

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IV. VANADIUM-CATALYZED, AUXILIARY-BASED ASOS REACTION

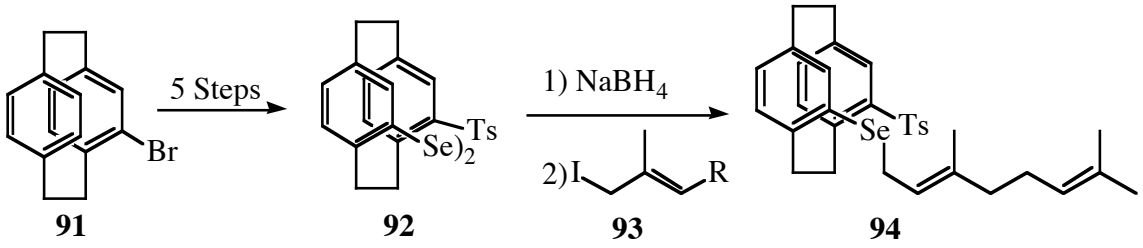
4.1. Introduction.

To better understand the low levels of selectivity observed in the ligand-based system (Chapter 3), a chiral auxiliary-based approach was necessary. Chiral auxiliaries have proven useful in inducing a high level of selectivity in synthesis, but more importantly, the auxiliary systems have unlocked the key components for an enantioselective pathway. Once the true nature of chiral induction in these systems is understood, a catalytic, ligand-based approach might be obtainable.

4.2. Prior Work on the Auxiliary-Based ASOS Reaction.

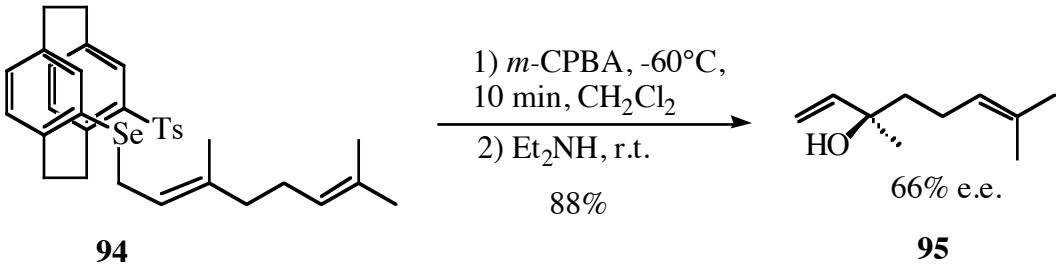
Several routes have been reported utilizing an auxiliary for stereocontrol in ASOS reactions. Reich and Yelm[1] developed the first auxiliary-based approach to synthesize optically active linalool. Reich's auxiliary is a paracylophane derivative that was successfully used by Mori and Toda[2] for selective oxidation of selenides (Scheme 23).

Scheme 23: Synthesis of Reich's Selenide.



ASOS reaction of Reich auxiliary utilized *m*-CPBA as the oxidant at –60°C for 10 min (Scheme 24). A basic work-up produced the (*R*) allylic alcohol in good yield (88 %) with 66 % d.e. Reich's work illustrated the power of the ASOS system to produce a 3° allylic alcohol, which traditionally have been difficult to access in synthesis.

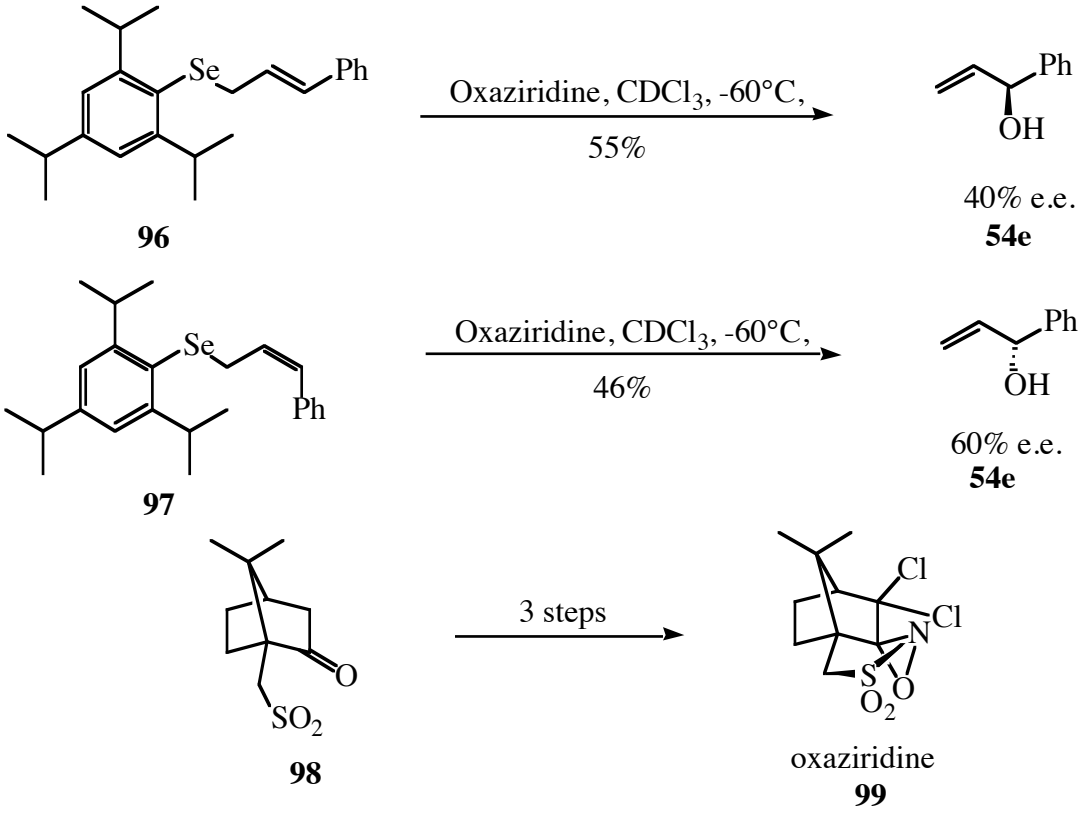
Scheme 24: Reich and Yelm Auxiliary ASOS Reaction.



94 **95**

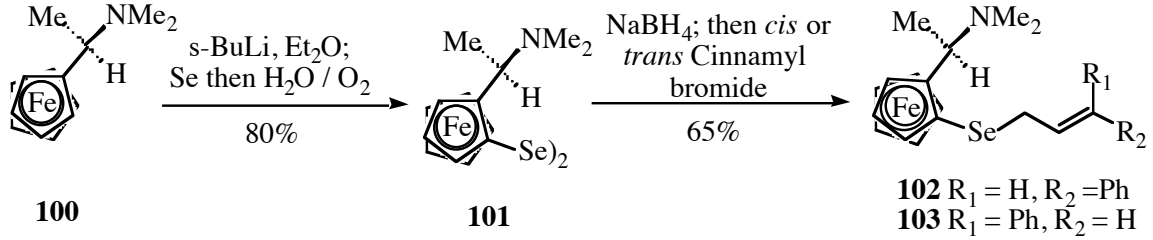
Davis and co-workers[3] utilized an achiral auxiliary in the presence of a chiral oxaziridine in an ASOS reaction to achieve selectivity (Scheme 25). Best results in the Davis system were obtained with isopropyl groups on the achiral auxiliaries **96** and **97**, $CHCl_3$ as the solvent and the temperature at –60°C. These conditions produced the subsequent alcohol in good yield with 40 % e.e.[4] Since the selenoxide in the ASOS reaction is not isolable,[5] Davis and co-workers oxidized several simple, non-allylic selenides in an attempt to ascertain the level of chiral induction from the selenoxide to the selenenate. They were gratified to find that the selenide to selenoxide oxidation occurred in <95% e.e. From these experiments, Davis and co-workers concluded that the chirality transfer from the selenoxide to the allylic alcohol was only 40-60 % efficient. Finally, it should be noted that Davis reported the (*Z*) olefin **97** provided better selectivity (60% e.e.) than its (*E*) counterpart **96** (40% e.e.).

Scheme 25: ASOS Reaction with the Davis Chiral Oxaziridine.



Uemura utilized a ferrocene auxiliary in an ASOS reaction (Scheme 26).[6] The selenide **102** in this reaction was synthesized in two steps from the precursor **100**. While the ferrocene derivative **100** is commercially available, its cost ($320 per gram)[7] make the synthesis of large quantities of **102** unrealistic.

Scheme 26: Synthesis of Uemura's Selenide with Ferrocene Auxiliary.



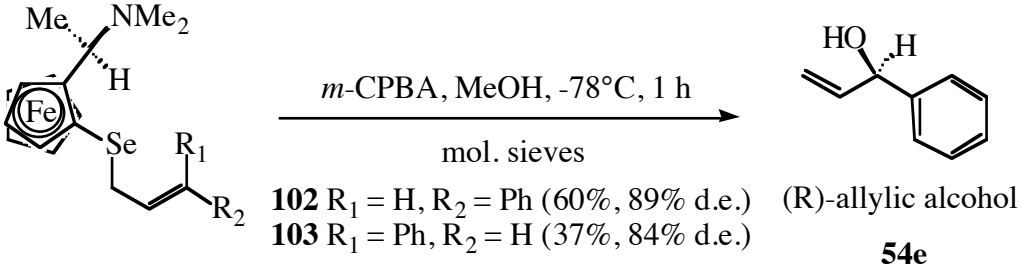
100 **101**

102 R_1 = H, R_2 =Ph
103 R_1 = Ph, R_2 = H

Uemura's ferrocene-based auxiliary ASOS reaction produced the highest selectivity of the known auxiliary systems (Scheme 5). The *trans* selenide **102** was converted to the (*R*)-allylic alcohol **54e** in good yield (60%) with 89% d.e. Interestingly,

the *cis* selenide **103** provided a similar level of selectivity (84% d.e.).[8] Reaction conditions include temperature of –78°C in MeOH and *m*-CPBA as an oxidant (Scheme 27).

Scheme 27: Uemura's ASOS System with Ferrocene Auxiliary.

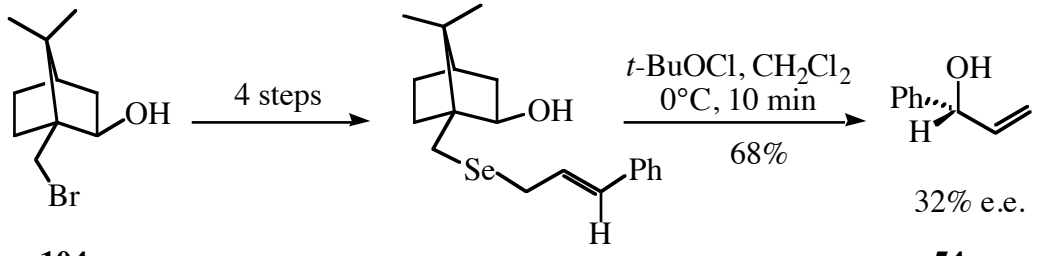


102 R_1 = H, R_2 = Ph (60%, 89% d.e.)
103 R_1 = Ph, R_2 = H (37%, 84% d.e.)

(R)-allylic alcohol
54e

The Koizumi group utilized a borneol-based auxiliary in the ASOS reaction (Scheme 28). The selenide **105** was made from the known (*1S*)-10-bromo-2-*exo*-borneol precursor **104** in 4 steps. Koizumi's ASOS reaction with the borneol-based auxiliary **105** produced the allylic alcohol **54e** in 32% e.e. (68% yield).[9]

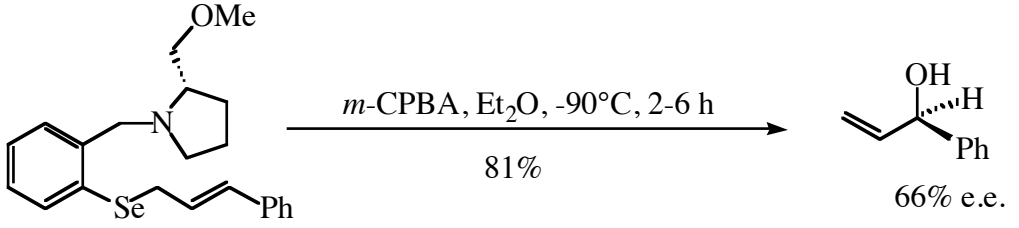
Scheme 28: Koizumi's Borneol-Based Auxiliary in ASOS Reaction.



104 **105** **54e**

The Fujita laboratory[10] also developed an auxiliary-based ASOS reaction (Scheme 29). The auxiliary used was derived from commercially available and economically feasible L-proline (40 cents per gram).[11] The enantiomer D-proline is significantly more costly ($18 per gram). It should also be noted that the selenide takes several steps to make from the amino acid. Fujita found the highest degree of selectivity at –90°C in Et_2O. These particular conditions produced allylic alcohol **54e** in 66% e.e. with a yield of 81%. The oxidant used for this reaction was *m*-CPBA.

Scheme 29: Fujita's L-Proline-Based Auxiliary ASOS.

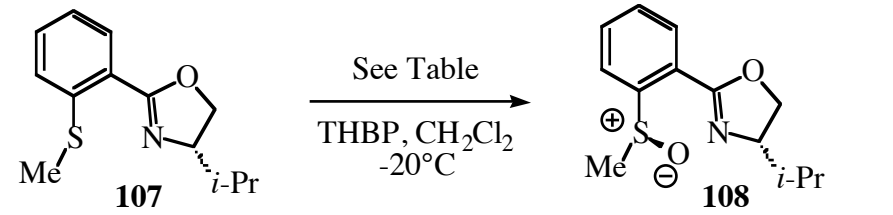


106 **54e**

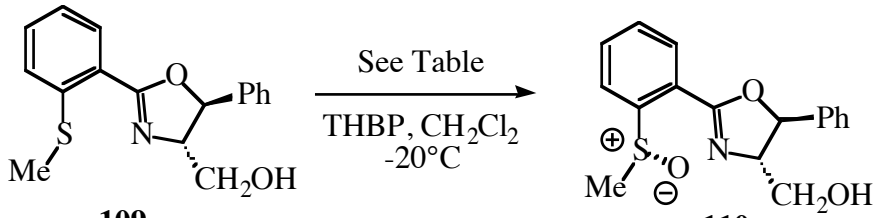
4.3. Vandium-Catalzyzed Asymmetric Oxidation of Sulfides using Oxazole-Based Auxiliaries.

Williams and co-workers used an elegant chiral oxazole-based, metal-catalyzed oxidation to convert prochiral sulfides to chiral sulfoxides (Table 3).[12] The Williams system achieved a net 1,6-asymmetric induction to produce the chiral sulfoxide **108** and **110**. This system appeared ideally suited for application to the corresponding selenide series using a vandium-based system.

Table 3: Williams Oxazole Sulfide System.



107 **108**



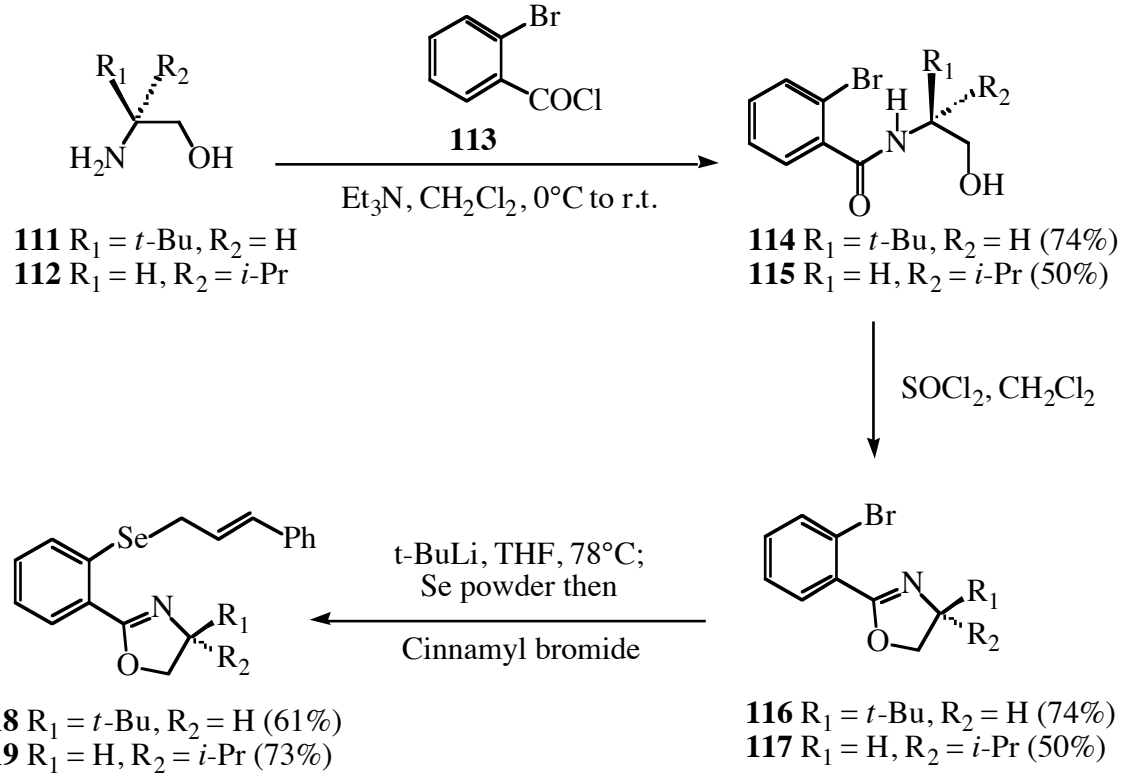
109 **110**

Entry	Oxazole	Metal	Time	Yield	d.s.
a	**107**	$VO(acac)_2$	24 h	77%	70%
b	**109**	$VO(acac)_2$	3 h	85%	74%
c	**109**	$Ti(Oi\text{-}Pr)_4$	4 h	41%	94%

4.4 Monodentate Oxazole Auxiliaries in ASOS Reaction.

Initial exploits in the development of an auxiliary-based, vanadium catalyzed ASOS reaction utilized a monodentate chiral oxazole, similar to Williams' sulfur-containing system **107**. The first series of oxazoles were readily made from commercially available alcohols and condensed with 2-bromobenzoyl chloride **113** to give benzamides **114** and **115** (Scheme 30). The crude benzamides were converted to the oxazole using $SOCl_2$. It should be noted that these oxazoles **116** and **117** are known compounds utilized by the Pfaltz group.[13] The oxazole was then converted to the selenide by way of halogen metal exchange of the bromine with selenium. The selenium nucleophile then proceeded *via* S_N^2 reaction with commercially available trans-cinnamyl bromide to produce the subsequent selenides **118** and **119**.

Scheme 30: Synthesis of the *t*-Butyl and *iso*-Propyl Selenides.



111 R_1 = *t*-Bu, R_2 = H
112 R_1 = H, R_2 = *i*-Pr

114 R_1 = *t*-Bu, R_2 = H (74%)
115 R_1 = H, R_2 = *i*-Pr (50%)

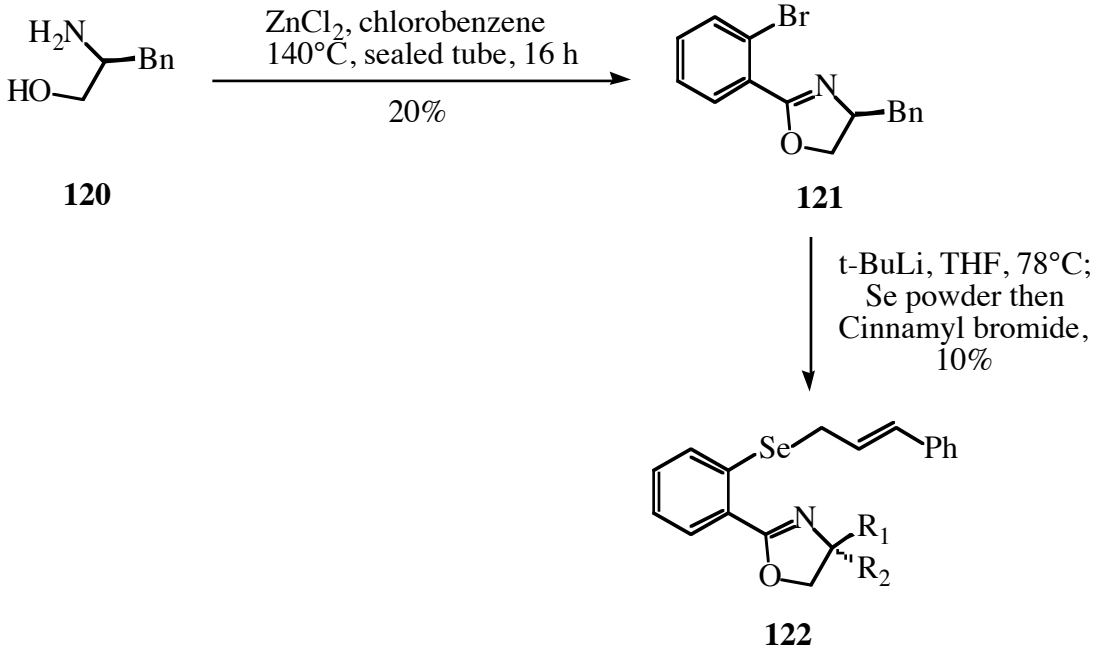
116 R_1 = *t*-Bu, R_2 = H (74%)
117 R_1 = H, R_2 = *i*-Pr (50%)

118 R_1 = *t*-Bu, R_2 = H (61%)
119 R_1 = H, R_2 = *i*-Pr (73%)

A different approach was used to create oxazole **121** in one step from 2-bromobenzylnitrile (Scheme 31). A Lewis acid catalyst ($ZnCl_2$) was employed to create

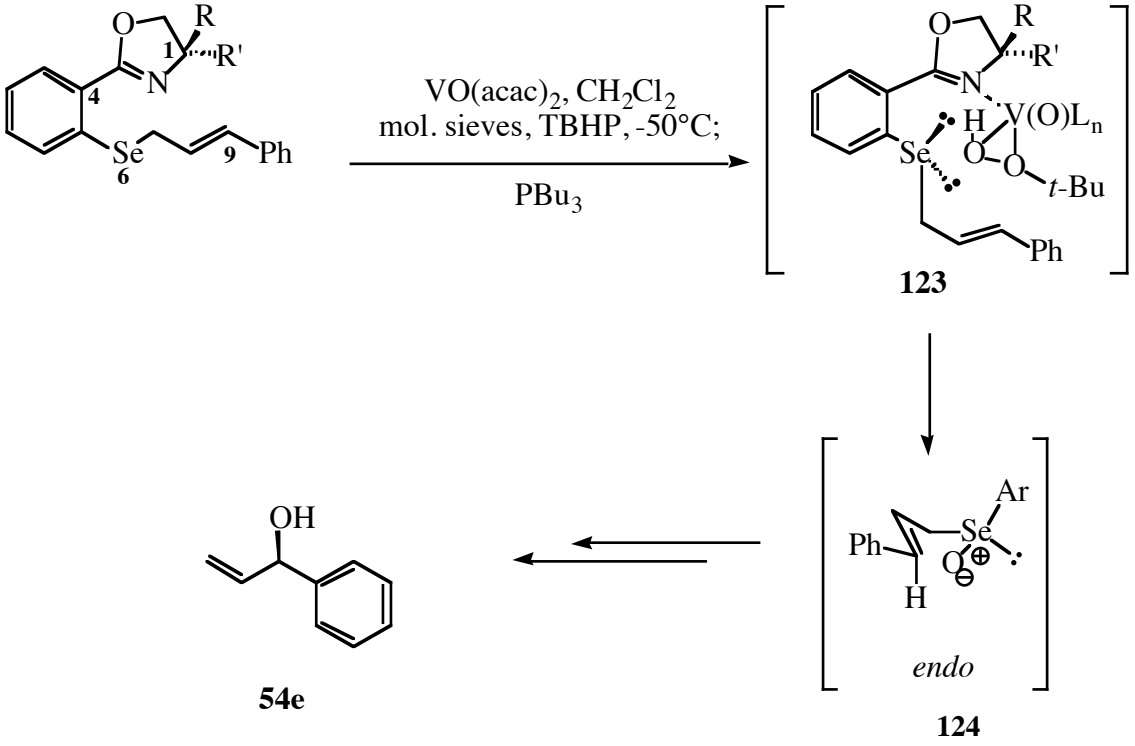
the oxazole ring. Selenide **122** was particularly difficult to construct due to a poor yield in the halogen-metal exchange. Halogen-metal exchanges in the benzylic systems consistently proved problematic in our hands.

Scheme 31: Synthesis of the Benzyl Selenide.



With the oxazole selenides in hand, the ASOS reaction was explored under the standard $VO(acac)_2$ conditions. This series of selenides illustrated that steric bulk was the key in achieving selectivity (Table 4). The (S)-*tert*-leucinol-based oxazole **118** gave the highest amount of selectivity at 40% d.e. Decreased sterics on the oxazole led to a reduction in selectivity. To further explore the steric influence of this reaction, a group of selenides was necessary with more steric bulk than the (S)-*tert*-leucinol-based oxazole **118**.

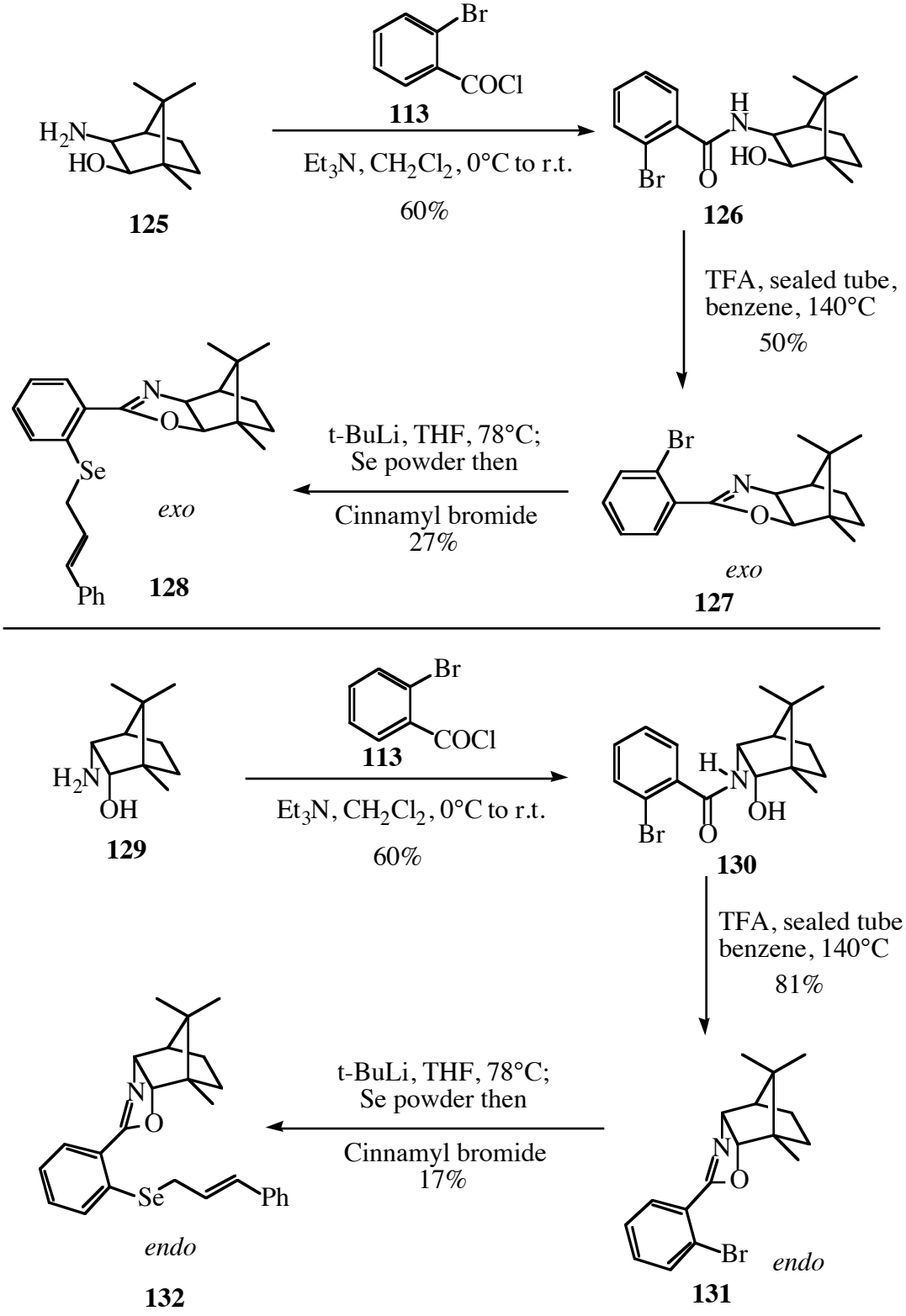
Table 4: Monodentate Oxazoles in ASOS Reaction.



Entry[14]	Selenide	R	R'	d.e.	Temperature	Yield
a	**122**	Bn	H	10% (*R*)	-50°C	78%
b	**119**	H	*i*-Pr	20% (*S*)	-50°C	56%
c	***118***	***t-Bu***	***H***	***40% (R)***	***-50°C***	***52%***

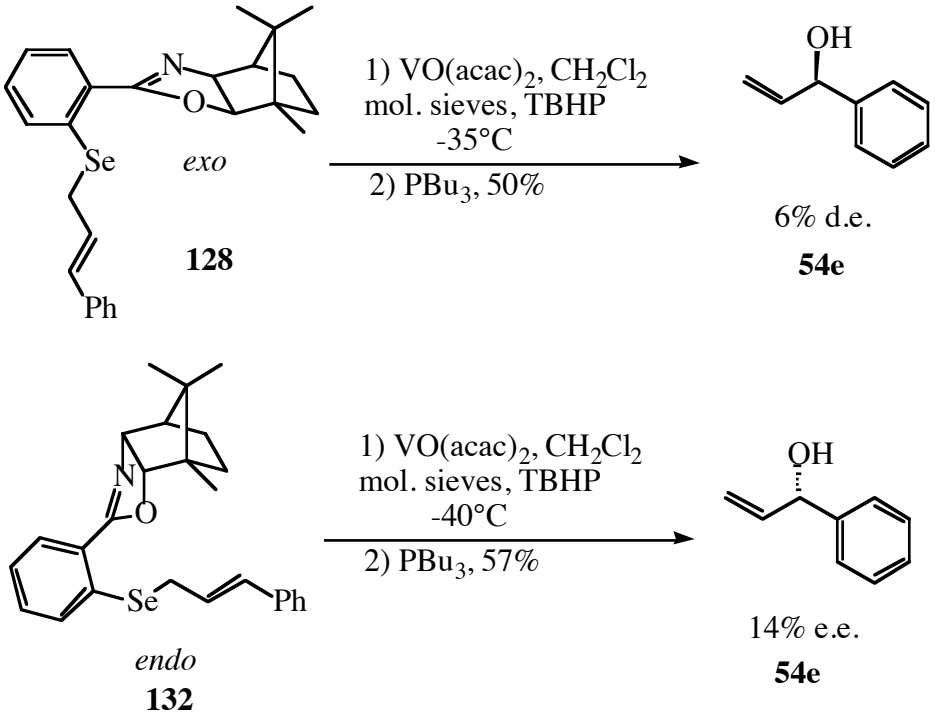
Since sterics seemed to be the key for enhanced levels of chiral induction, the next step was to increase the amount of steric bulk around the selenide to see if selectivity would increase. A camphor-based series of oxazoles was created for this purpose (Scheme 32). These oxazoles were produced similarly to the original amino alcohol series, however, due to the steric bulk present, benzamides **126** and **130** were difficult to convert to the oxazole. In order to form the oxazole ring, benzamides were placed in a sealed tube with catalytic amounts of TFA and heated to 140°C for several hours. The starting *exo* and *endo* amino alcohols **125** and **129** are known compounds.[15]

Scheme 32: Camphor–Based Selenide Synthesis.



The camphor selenides **128** and **132** were subjected to the standard vanadium-catalyzed ASOS reaction (Scheme 33). Despite the apparent increase in steric congestion, both the *endo* and *exo* camphor-based series provided poor levels of diastereomeric excess. One possible hypothesis could involve an alteration of the mechanism, as compared to the previous selenides **118**, **119** and **122**. Due to the increased steric environment near the coordinating oxazole nitrogen, preorganization with the presumed active vanadium species may not be possible. Further support for this hypothesis can be found in significant decrease in reaction rates relative to the selenides **118**, **119** and **122** (which proceeded at -50°C).

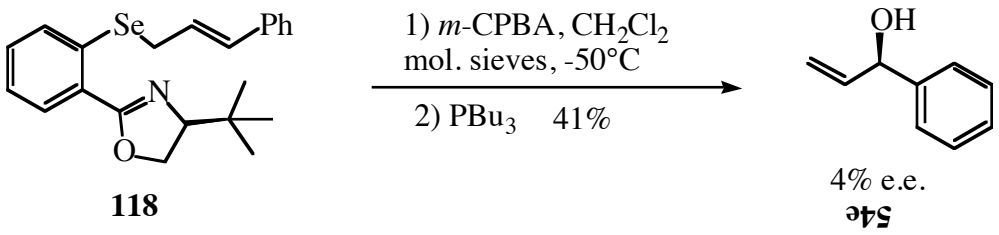
Scheme 33: Camphor-Based Auxiliary ASOS Reaction.



To further support our hypothesis of a precoordinated vanadium species, a simple experiment was done to define the role of the metal-oxidant (Scheme 34). The $VO(acac)_2$/TBHP system was substituted in the ASOS reaction by *m*-CPBA. Using the leucinol-based selenide **118** [which previously provided 40 % d.e. with $VO(acac)_2$], a

nearly complete disappearance of the selectivity was observed (4% d.e.). This result strongly supports the preorganization of the vanadium oxidant to the oxazole prior to oxidation.

Scheme 34: *m*-CPBA as the Oxidant in the ASOS reaction.



118 **54e**

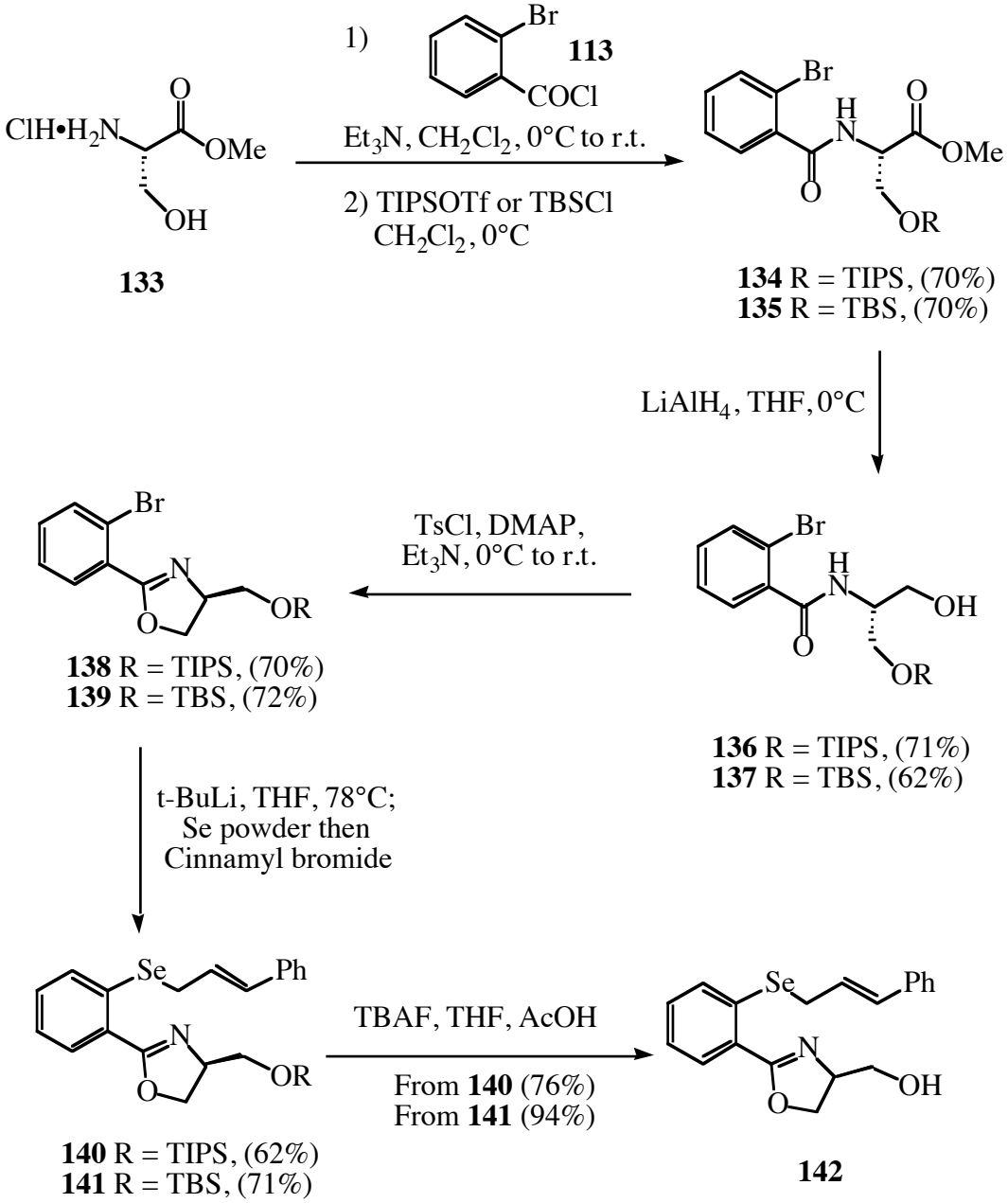
4.5. Bidentate Oxazole Auxiliaries in ASOS Reaction.

The monodentate auxiliary approach in the ASOS reaction did not provide satisfactory levels of selectivity, but this route did yield several key results which called for the development of a bidentate approach. The *m*-CPBA experiment strongly suggested vanadium coordinated with the nitrogen on the oxazole. This "preorganization" of the vanadium and oxazole may be the key for increasing the chiral induction of the selenoxide on the way to the selenenate. It was hoped that an additional coordinating group might increase the level of diastereoselectivity. This proposal led us to develop an oxazole series with a secondary coordination site to test this hypothesis.

The first auxiliary system developed was a serine-derived oxazole **142** (Scheme 35). This oxazole was constructed from inexpensive L-serine methyl ester•HCl (both enatiomers around $3 per gram).[16] Similar to the previous monodentate oxazoles, serine methyl ester was condensed with 2-bromobenzoyl chloride **113** followed by protection of the silyl ethers **134** and **135**. The resulting silyl esters **134** and **135** were reduced to produce the subsequent alcohols **136** and **137**. The alcohols **136** and **137** were then converted to tosyl leaving groups, which were cyclized to the oxazoles *via* an S_N^2

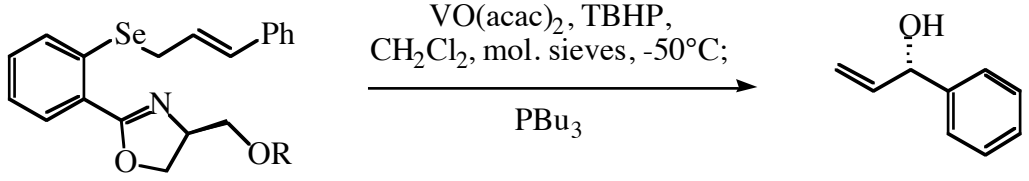
reaction. The selenides **140** and **141** were then produced through the previously established halogen-metal exchange reaction. The resulting silyl-selenides **140** and **141** were deprotected with buffered TBAF to produce hydroxy selenides **142**. It should be noted that oxazole series could be successfully performed on a large scale (25g).

Scheme 35: Synthesis of Serine-Based Selenide.



The protected and deprotected serine-based selenides produced important results upon oxidation with rearrangement (Table 5). The deprotected selenide **142** significantly improved in selectivity (60% e.e.) over our previous highest result (selenide **118**, Table 4, 40% e.e.). As expected, the protected selenide **140** gave essentially no selectivity upon rearrangement. It is generally accepted that silyl ethers do not readily participate in chelation with metal complexes.[17,18] These results support the hypothesis that the free hydroxyl function is coordinated to the metal-oxazole complex, thereby increasing the level of chiral induction.

Table 5: Serine-Based Selenides in the ASOS Reaction.

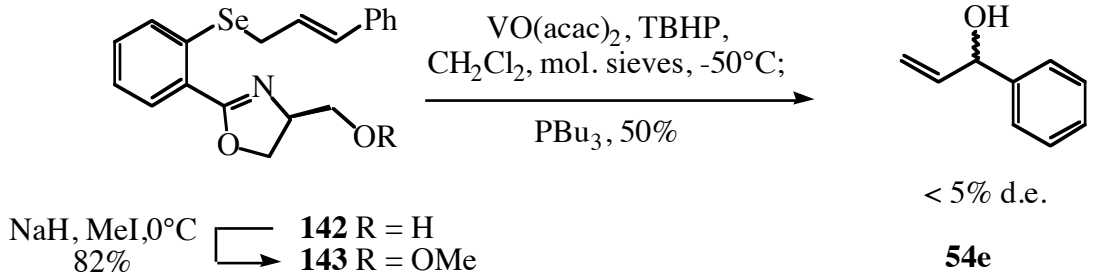


54e

Selenide	R	Yield	d.e. (Configuration)
140	TIPS	52%	<5%
142	*H*	*63%*	*60% (S)*

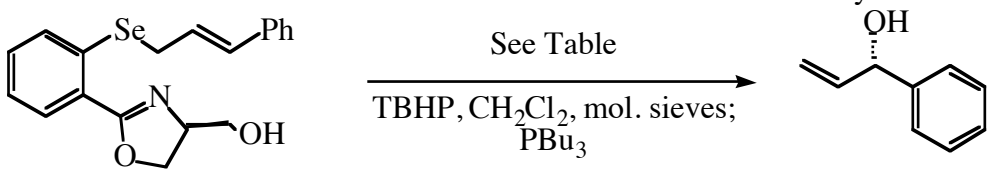
In order to establish if a free hydroxyl function is required (versus another bidentate coordination site) the 1° hydroxyl group was converted to the methyl ether **143** (Scheme 36). Interestingly, the methyoxy selenide showed virtually no selectivity (< 5% d.e.) upon rearrangement. This result strongly supports the requirement of a free hydroxyl function for high levels of chiral induction.

Scheme 36: Methylated Serine Auxiliary ASOS Reaction.



Since the free hydroxyl was key for increasing selectivity, a variety of metal-oxidant complexes were screened to determine if the vanadium system was the most efficient for chiral induction (Table 6). From the results, it is clear that $VO(acac)_2$ (Entry g) provided a significant improvement in selectivity, as compared to other catalytic and stoichiometric systems. It is interesting to note that the $Ti(O\textit{i}\text{-}Pr)_4$ system (Entries **a** and **b**) provided inferior levels of selectivity versus the $VO(acac)_2$ (Entry g). This result is in stark contrast to Williams's work[19] on the sulfide series (Section 4.2), where the titanium series provided superior results.

Table 6: Serine-Based Selenides with Different Metal Catalysts.



142 **54e**

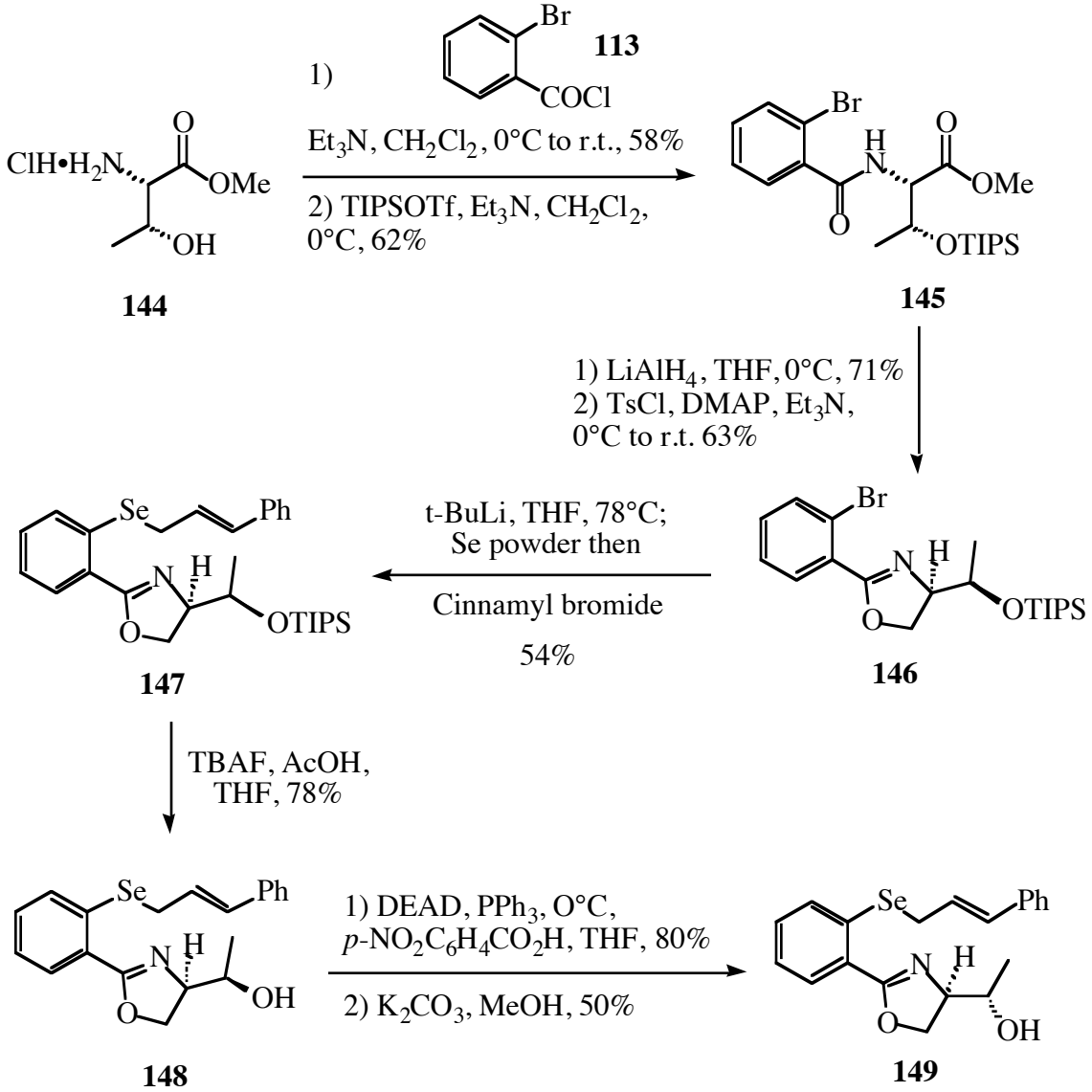
Entry	Metal	Temp.	Yield	d.e.
a	$Ti(Oi\text{-}Pr)_4$ (10 mol %)	-50 to -25°C	47%	30%
b	$Ti(Oi\text{-}Pr)_4$ (100 mol %)	-50°C	60%	30%
c	$MoO_2(acac)_2$ (10 mol %)	-50°C	53%	25%
d	$Zr(acac)_2$ (10 mol %)	-50°C	35%	35%
e	$Mn(acac)_2$ (10 mol %)	-50°C	19%	34%
f[i]	m-CPBA (10 mol %)	-50°C	63%	26%
g	*$VO(acac)_2$ (10 mol %)*	*-50°C*	*63%*	*60%*

i. TBHP was not necessary and therefore omitted in the reaction.

Due to the increased selectivity from the serine-based selenide **142**, we sought to study the effect of a stereogenic center located on the chelating hydroxyl group. Commercially available L-threonine methyl ester[20] ($9 per gram) provided a useful precursor for such the desired system (Scheme 37). Similar conditions to the serine series were used to synthesize the threonine selenides. The hydroxyl epimer of the L-threonine

auxiliary was accessed via Mitsonubu reaction followed by hydrolysis with K_2CO_3/MeOH.

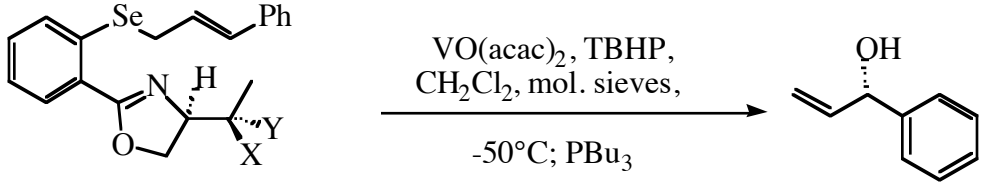
Scheme 37: Synthesis of Threonine-Based Selenides.



The additional stereogenic center on the oxazole appeared to have a significant impact on the level of diastereoselectivity in the ASOS reaction (Table 7). In agreement with the serine series, the silylated threonine selenide **147** produced little selectivity (18 % d.e.) upon rearrangement. Interesting, the threonine selenide **148** provides decreased in diastereoselectivity versus the serine series (50% vs 60% d.e.) whereas the epimeric

threonine selenide **149** gave superior results (66% d.e.). Once again, this supports the idea that an added chelating group enhances chiral induction. Based on these results, exploration into additional steric congestion on the hydroxyl-containing oxazole appears to be warranted.

Table 7: L-Threonine Auxiliary ASOS Reaction.

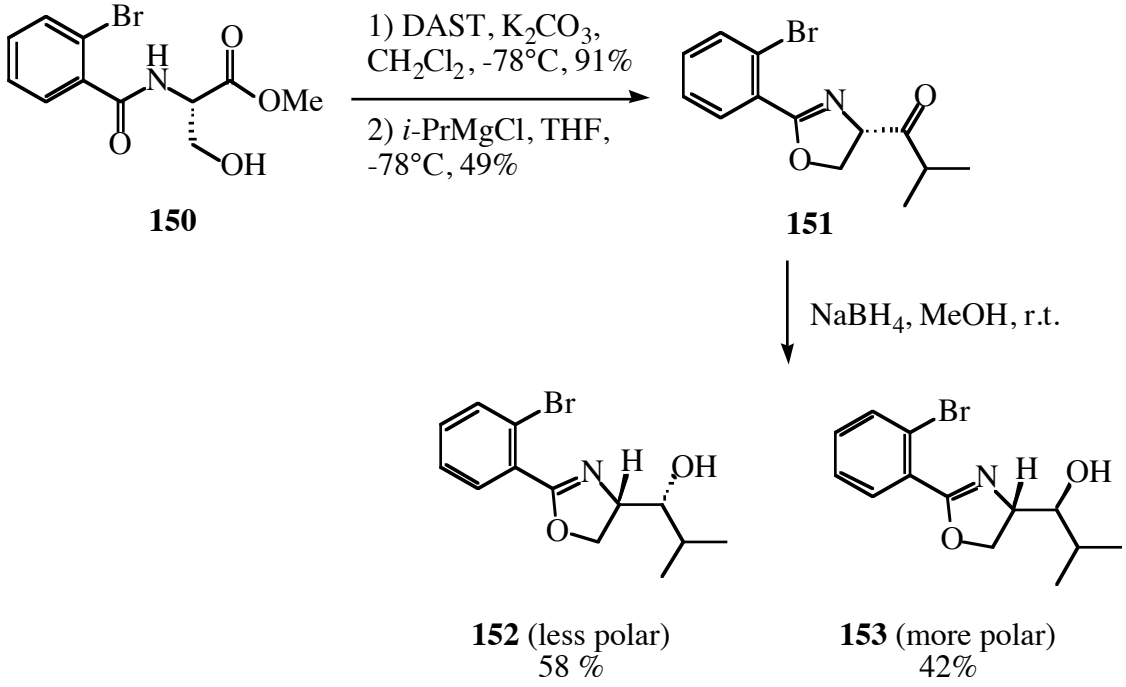


54e

Selenide	X	Y	Yield	d.e. (Configuration)
147	OTIPS	H	69%	15% (R)
148	OH	H	74%	50% (S)
149	*H*	*OH*	*74%*	*66% (S)*

In order to assess the more congested systems, an alternate route to the hydroxyl containing selenides had to be developed (Scheme 38). Starting from the previously described serine-based benzamide 150, the 1° hydroxyl was cyclized followed by selective mono Grignard addition to the ester function producing the ketone **151** (Scheme 37). Subsequent reduction with $NaBH_4$ gave the diastereomeric alcohols **152** and **153**. These alcohols **152** and **153** were easily separable by chromatography.

Scheme 38: Synthesis of Epimeric Selenides.



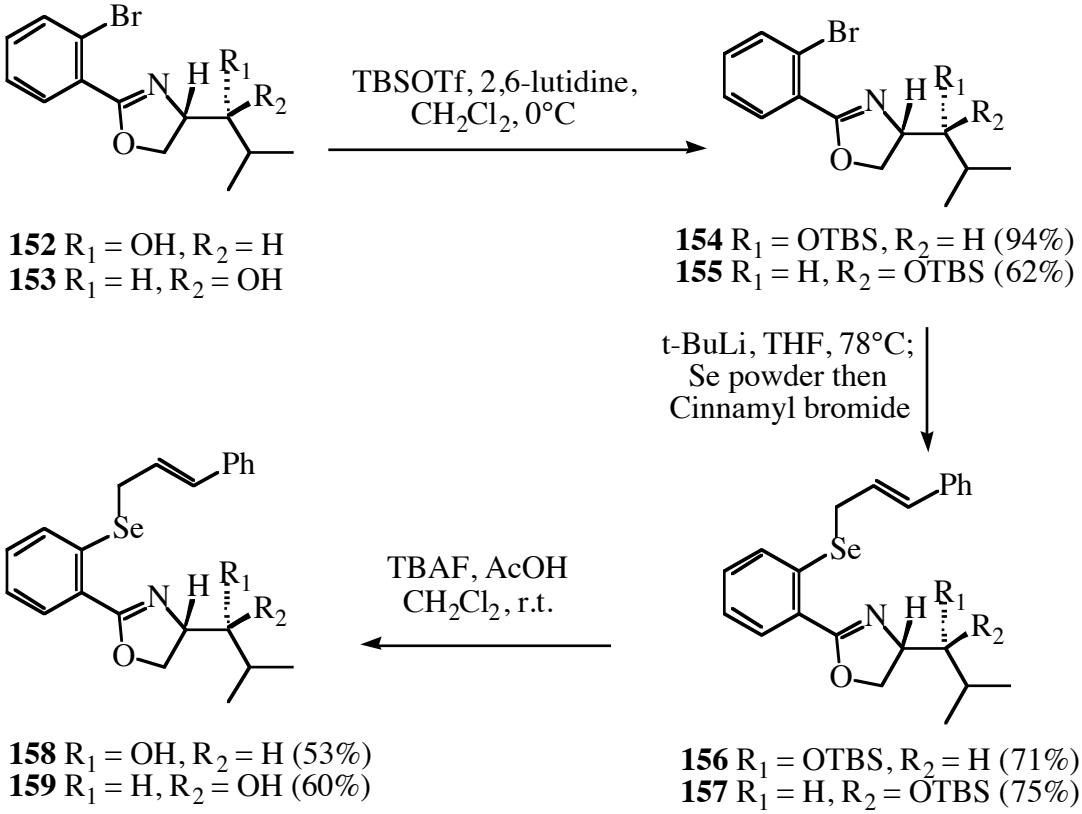
150 **151**

152 (less polar) 58 %

153 (more polar) 42%

Construction of the selenide was possible in 3 steps (Scheme 39). Protection of epimeric alcohols separately provided the silyl ethers **154** and **155**. Subsequent incorporation of the selenide and deprotection proceeded uneventfully to provide the targets **158** and **159**.

Scheme 39: Synthesis of iso-Propyl Derived Selenides.



152 R_1 = OH, R_2 = H
153 R_1 = H, R_2 = OH

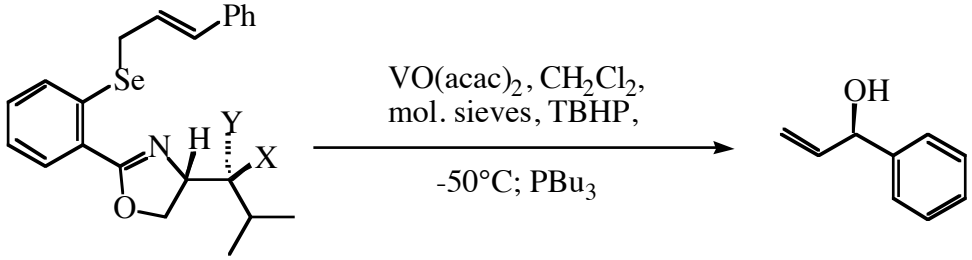
154 R_1 = OTBS, R_2 = H (94%)
155 R_1 = H, R_2 = OTBS (62%)

158 R_1 = OH, R_2 = H (53%)
159 R_1 = H, R_2 = OH (60%)

156 R_1 = OTBS, R_2 = H (71%)
157 R_1 = H, R_2 = OTBS (75%)

ASOS reaction on the iso-propyl containing selenides provided a further, slight increase in selectivity (Table 8). The less polar epimer **158** rearranged to give the allylic alcohol in 70% d.e. while the more polar compound **159** produced the allylic alcohol in 62% d.e. Based on the observed diastereoselectivities and comparison to the threonine selenide series, the stereochemistry of selenides **158** and **159** have been tentatively assigned. Further exploration is underway to determine absolute stereochemistry.

Table 8: ASOS Reaction of Isopropyl Selenides.

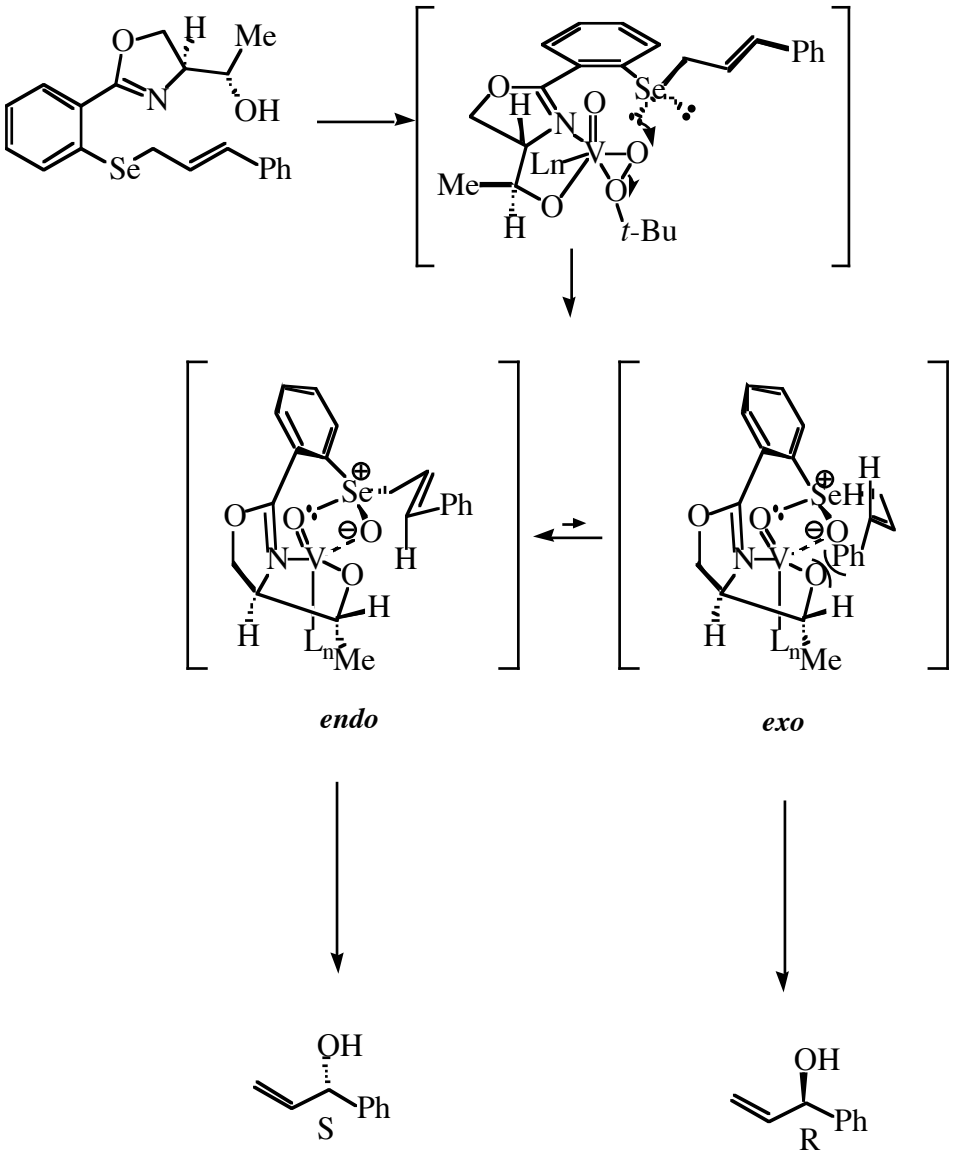


Selenide	X	Y	Yield	d.e. (Configuration)
159	OH	H	61%	62% (R)

158	*H*	*OH*	*71%*	*70% (R)*

Based on our results we developed a working model for the ASOS reaction with the threonine selenide **149** (Scheme **39**). The pathway **161**-*endo* would appear to be favored as the alternate pathway **161**-*exo* appears to have a disruptive interaction between the phenyl and the oxazole. It is important to note two chiral events occur during this transformation, thereby requiring the auxiliary to act in a complementary fashion.

Scheme 40: Possible Mechanistic Cartoon For Matched Threonine Series.



4.6. Conclusion.

Overall, the auxiliary-based selenides have unlocked several key clues in understanding the nature of chiral induction in the metal-catalyzed ASOS reaction. An oxazole-based auxiliary system can produce reasonable selectivity in ASOS reactions (up to 70% d.e.). These results already represent the second highest reported level of induction on comparable trans cinnamyl selenide systems. The level of diastereoselectivity is significantly higher than the theoretical maximum reported by Davis and co-workers (Section 4.1). One possible explanation for the observed level of selectivity has been put forth in which the vanadium / oxazole complex coordinates to the selenoxide in a complementary fashion.

---

[1] Reich, H. J.; Yelm, K. E. *J. Org. Chem.* **1991**, *56*, 5672.
[2] Toda, F.; Mori, K. *J. Chem. Soc. Chem. Comm.* **1986**, 1357.
[3] Davis, F. A.; Reddy, T. R. *J. Org. Chem.* **1992**, *57*, 2599.
[4] Davis, F. A.; Reddy, T. R. *J. Org. Chem.* **1992**, *57*, 2599.
[5] [2,3] sigmatropic rearrangement occurs rapidly, even at -50°C.
[6] Nishibayashi, Y.; Singh, J. D.; Fukazawa, S.; Uemura, S. *J. Org. Chem.* **1995**, *60*, 4114.
[7] Aldrich Chemical Company 2000-2001 Catalog p.656
[8] It should also be noted that both the Z and E alkene produce the same (*R*)-allylic alcohol. No explanation has been provided by the authors for this unusual result.
[9] In certain cis substrates e.e.'s are as high as 80%.
[10] Fujita, K.; Kanakubo, M.; Ushijima, H.; Oishi, A.; Ikeda, Y.; Taguchi, Y. *Synlett* **1998**, 987.
[11] Lancaster Chemical Company 2002-2003 Catalog p.1490
[12] Bower, J. F.; Martin, C. J.; Rawson, D. J.; Slawin, M. Z. A.; Williams, J. M. J. *J. Chem. Soc. Perkin Trans. 1* **1996**, 331.
[13] Zhou, Q.; Pfaltz, A. *Tetrahedron* **1994**, *50*, 4467.
[14] All reactions performed at 0.3 M concentration unless otherwise noted.
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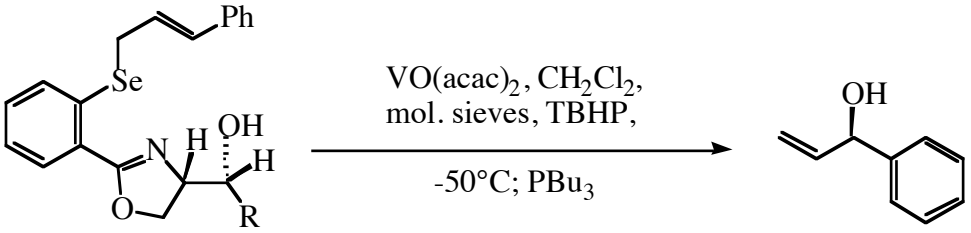
[16] Lancaster chemical Company 2002-2003 catalog p.1533
[17] Keck, G. A. Castellino, S. *Tetrahedron. Lett.* **1987**, *28*, 281. Frye, S. V.; Eliel, E. *Tetrahedron Lett.* **1986**, *27*, 3223.
[18] It should be noted that there have been selected examples reported to the contrary: Willard, P. G. *J. Am. Chem. Soc.* **1987**, *109*, 5539-41. Evans, D. A.; Allison, B. D.; Yang, M. G. *Tetrahedron Lett.* **1999**, *40*, 4457. Evans, D. A.; Halstead, D. P.; Allison, B. D. *Tetrahedron Lett.* **1999**, *40*, 4461.
[19] Bower, J. F.; Martin, C. J.; Rawson, D. J.; Slawin, M. Z. A.; Williams, J. M. J. *J. Chem. Soc. Perkin Trans. 1* **1996**, 331.
[20] Sigma Chemical Company Catalog 2000-2001 p. 955.

V. FUTURE PLANS AND CONCLUSION

Application of the metal-catalyzed ASOS reaction is infinite, yet several variables need to be addressed to ensure the utility of this methodology. The scope of the bidentate system needs to be expanded to further understand chiral induction of the selenoxide. Different groups need to be placed adjacent to the chelating alcohol functionality (Scheme 41) to find the maximum amount of steric bulk that gives the optimal level of chiral induction hence the most selectivity.

Scheme 41: Steric Bulk Adjacent to Chelating Hydroxyl Group.

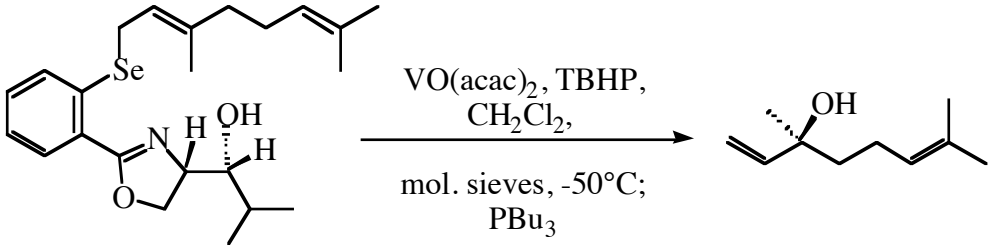


160 R = Ph
161 R = *t*-Bu

54e

To further demonstrate the utility of the ASOS reaction, the current iso-propyl oxazole should be employed in a system that forms an allylic alcohol tertiary center. Tertiary alcohols are prevalent in natural products and have traditionally been difficult to make asymmetrically. A similar system to Reich and Yelm's linalool example would be ideal for screening in our ASOS methodology (scheme 42).

Scheme 42: ASOS Reaction to Create Tertiary Hydroxyl Function.

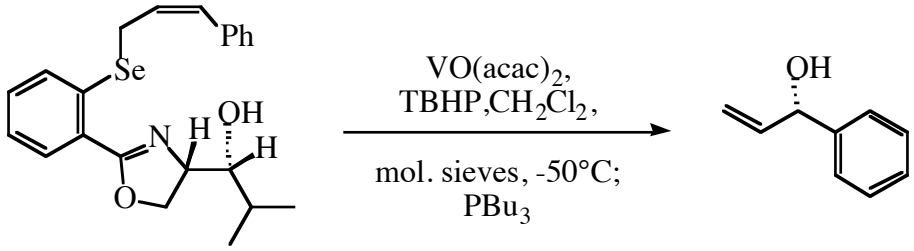


162 **163**

An investigation into the effect of olefin geometry is another future direction to explore (Scheme 43). Davis and co-workers[1] reported the (Z)-olefin geometry gave

higher selectivity (plus the opposite enantiomer) versus the (*E*)-olefin. Their results supported the transition state model which showed the *endo* pathway to be more favored. The vanadium-catalyzed ASOS system should provide interesting and encouraging results in the area.

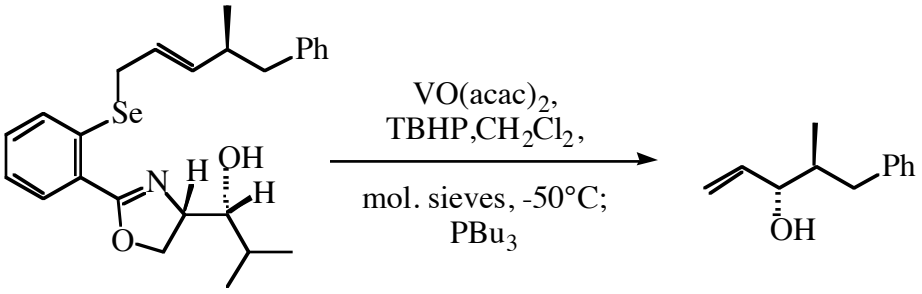
Scheme 43: (*Z*)-Olefin Geometry in ASOS System.



164 **54e**

A stereogenic center located α to the alkene of the allylic selenide should be studied on the current iso-propyl / hydroxyl selenide system (Scheme 44). In our racemic series, an α stereocenter had no effect on chirality of the subsequent allylic alcohol (Chapter 2). It is reasonable to assume that a similar outcome will be observed in the asymmetric series.

Scheme 44: Effect of Adjacent Stereocenter in ASOS Reaction.



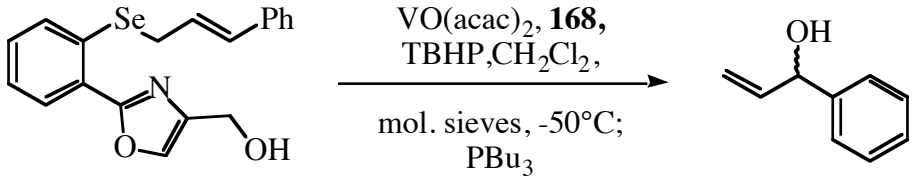
165 **166**

Solvents need to be screened to see if selectivity is enhanced or hindered due to this variable. Uemura and co-workers[2] noticed an increase in selectivity in their ferrocene-based ASOS reaction when the solvent was changed to MeOH. A wide

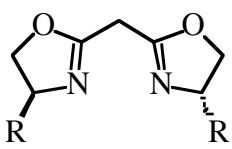
variation of solvents differing in dielectric constants from our standard CH_2Cl_2 should provide informative results.

The ultimate goal of this methodology is a catalytic asymmetric oxidation. The auxillary system provides stoichiometric chirality for asymmetric oxidation; however, truly catalytic chirality is more desirable. Exploration into this area includes the synthesis of an achiral oxazole with a 2° chelating site in the presence of a chiral ligand for the ASOS reaction (Scheme 45).

Scheme 45: Return to the Ligand-Based ASOS Reaction.



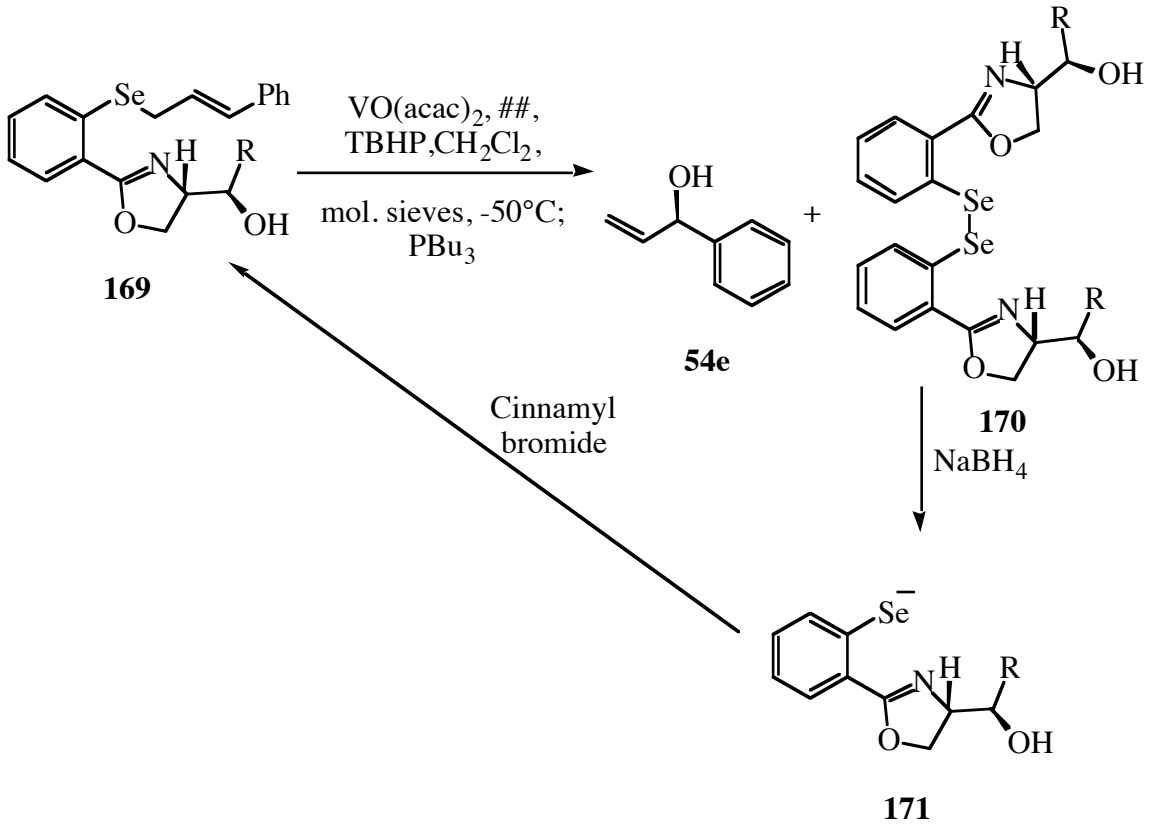
167 **54e**



168

If a ligand-based catalytic system produces disappointing results for the ASOS reaction, a recyclable auxillary could be developed. Koizumi and co-workers[3] illustrated the potential for this concept *via* the diselenide. The deselenide **170** is the biproduct from the ASOS reaction. Treatment of this dimer under mildly reducing condtions ($NaBH_4$) will result in cleavage of the Se-Se bond and reveal the anionic selenium species (scheme 46). Koizumi demonstrated that these species can be alkylated in the presence of unprotected hydroxyl functions.

Scheme 46: Recycling the Auxillary.



The foundation has been laid for the vanadium-catalyzed ASOS reaction based on the first example of a vanadium catalyzed SOS reaction results. With continued exploration into the areas discussed above, the ASOS reaction should develop into a valuable tool for the synthetic community.

---

[1] Davis, F. A.; Reddy, T. R. *J. Org. Chem.* **1992**, *57*, 2599-06
[2] Nishibayashi, Y.; Singh, J. D.; Fukazawa, S.; Uemura, S. *J. Org. Chem.* **1995**, *60*, 4114-20.
[3] Kurose, N.; Takahashi, T.; Koizumi, T. *Tetrahedron* **1997**, *53*, 12115-29.

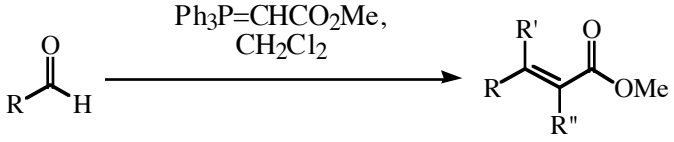
VI. EXPERIMENTAL SECTION

General

Melting points were taken on a Mel-Temp apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer paragon 500 FT-IR spectrophotometer neat unless otherwise indicated. ^{1}H NMR spectra were recorded on a Brüker 300 spectrometer at 300 MHz or a Brüker 500 spectrometer spectrometer at 500 MHz in the indicated solvent and are reported in ppm relative to trimethylsilane and referenced internally to the residually protonated solvent. ^{13}C NMR spectra were recorded on Brüker 300 spectrometer at 75 MHz or a Brüker 500 spectrometer at 100 MHz in the solvent indicated and are reported in ppm relative to trimethylsilane and referenced internally to the residually protonated solvent. Optical rotations were on a Rudolph Research Analytical Autopol III automatic polarimeter using a sodium lamp at 589 nm in $CHCl_3$.

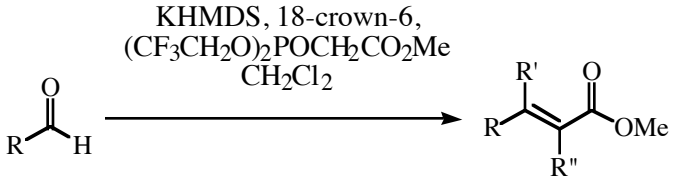
Routine monitoring of reactions was performed using EM Science DC-Alufolien silica gel, aluminum back TLC plates. Flash chromatography was performed with the indicated eluents on Silicycle 230-400 mesh silical gel.

Air and / or moisture sensitive reactions were performed under usual inert atmosphere conditions. Reactions requiring anhydrous conditions were performed under a blanket of argon, in glassware dried ina an oven at 120°C or by a bunsen flame, then cooled under argon. Solvents and commercial reagents were purified in accord with Perrin and Armarego[1] or used without further purification.



41 **42**

General Procedure for Wittig Reaction: To a stirred solution of the aldehyde **41** (0.3M in CH_2Cl_2) was added (carbmethoxymethylene)triphenylphosphorane (1.5 eq.) at r.t. After the reaction was judged to be complete by TLC (2-24 h), the reaction was quenched with aq. sat. NH_4Cl and extracted with Et_2O (3 x). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2-20% ethyl-acetate/hexane.

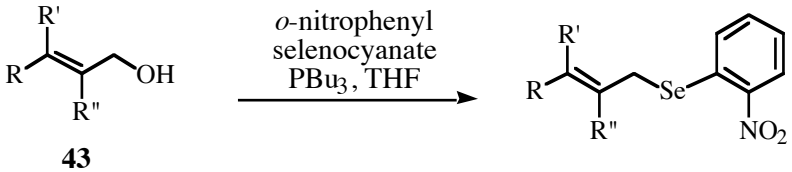


41 **42**

General Procedure for Wadsworth-Emmons Olefination 42: To a stirred solution of 18-Crown-6 (5 equiv), bis(2,2,2-trifluoroethyl)(methoxycarbonylmethyl)-phosphonate (1.15eq) in THF (0.1M) at –78°C was added KHMDS dropwise. After 30 minutes, the aldehyde **41** was added dropwise. After the reaction was judged to be complete, the reaction was quenched with sat. aq. NH_4Cl and extracted with Et_2O (3x). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2-20% ethyl-acetate/hexane.

42 **43**

General Procedure for DIBAL-H reduction 43: To a stirred solution of the ester **42** in CH_2Cl_2 (0.2 M) at –78°C was added DIBAL-H (2.4 eq, 1.0 M in CH_2Cl_2) dropwise over 20 min. After 1 hour, the reaction was warmed to 0°C. After 10 min, the reaction was recooled to –78°C and quenched with methanol followed by an aq. solution of sodium tartrate (10%). After 8-12 hours at r.t., the aqueous layer was extracted with Et_2O (3x). The dried ($MgSO_4$) extract was concentrated *in vacuo*.



43 **53**

Typical experimental procedure for synthesis of selenides 53: To a stirred solution of the alcohol **43** (0.3 M in THF) was added *o*-nitrophenyl selenocyanate (1.2 equiv.) followed by PBu_3 (1.1 equiv.) dropwise over 5 minutes. After 4 - 12 h, the reaction was quenched with aqueous NaOH (1 M) and extracted with EtOAc (3 X). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2-20% ethyl-acetate/hexane.

53a: Purified by column chromatography over silica gel, eluting with 5 - 20% EtOAc / hexanes, to give **53a** (86%):

IR (neat) 2924, 1504, 1130, 728, cm^{-1};

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (d of d, J = 1.1, 7.6 Hz, 1H), 7.50 - 7.56 (m, 2H), 7.27 - 7.34 (m, 1H), 5.78 (d of t, J = 7.2, 15.1 Hz, 1 H), 5.57 (d of t, J = 7.6, 15.1 Hz, 1 H), 3.58 (d, J = 7.2 Hz, 2H), 1.99 - 2.06 (m, 2H), 1.24 - 1.35 (m, 8H),□0.87 (t, J = 6.9 Hz, 3H);

^{13} C NMR (75 MHz, $CDCl_3$) δ 146.9, 136.5, 134.4, 133.7, 129.6, 126.5, 125.6, 123.5, 32.6, 31.9, 29.3, 29.0, 28.9, 22.8, 14.3.

53b: Purified by column chromatography over silica gel, eluting with 5 - 20% EtOAc / hexanes, to give **53b** (75%):

IR (neat) 2922, 2849, 1590, 1565, 1504;

^{1}H NMR (300 MHz, $CDCl_3$) δ 8 .29 (d of d, J = 1.1, 8.5 Hz, 1H), 7.49 - 7.55 (m, 2H), 7.28 - 7.33 (m, 1H), 5.70 (d of d, J = 6.8, 15.2 Hz, 1 H), 5.52 (d of t, J = 7.3, 15.2 Hz, 1 H), 3.57 (d, J = 7.3 Hz, 2H), 1.94 - 1.97 (m, 1H), 1.58 - 1.73 (m, 4H), 1.01 - 1.27 (m, 6H);

^{13} C NMR (75 MHz, $CDCl_3$) δ 146.9, 142.2, 134.3, 133.6, 129.8, 126.5, 121.0, 40.8, 33.4, 32.9, 29.1, 26.3, 26.1.

53c Purified by column chromatography over silica gel, eluting with 5 - 20% EtOAc / hexanes, to give **53c** (92%):

IR (neat) 2900, 2845, 1513, 1330, 729 cm^{-1};

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (d of d, J = 1.1, 6.9 Hz, 1H), 7.49 - 7.54 (m, 2H), 7.33 (d of d, J = 6.9, 8.0 Hz, 1H), 5.62 (d, J = 15.5 Hz, 1 H),□5.41 (d of t, J = 7.2, 15.5 Hz, 1 H), 3.59 (d, J = 7.2 Hz, 2H), 1.97 (bs, 3H), 1.54 - 1.73 (m, 12H);

^{13} C NMR (75 MHz, $CDCl_3$) δ 147.7, 146.9, 134.3, 133.6, 129.8, 126.4, 125.6, 118.4, 42.2, 36.9, 35.2, 29.4, 28.5.

53d: Purified by chromatography over silica gel, eluting with 5 - 30 % EtOAc / petroleum ether, to give **53d** (85%):

IR (neat) 2940, 1596, 1506; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d of d, J = 0.9, 8.3 Hz, 1H), 7.50 - 7.61 (m, 2H), 7.27 - 7.35 (m, 3H) 6.87 (d, J = 7.4 Hz, 2H), 6.61 (d, J = 15.7 Hz, 1H), 6.20 (d of t, J = 7.5, 15.7 Hz, 1H), 3.81 (s, 3H), 3.79 (d, J = 7.5 Hz, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 146.9, 134.2, 134.0, 133.9, 129.6, 129.4, 127.8, 126.6, 125.8, 121.1, 114.2, 55.5, 29.4.

53e: Purified by chromatography over silica gel, eluting with 5 - 10 % EtOAc / petroleum ether, to give **53e** (66%):

IR (neat) 2982, 1562, 1507 cm^{-1};

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d of d, J = 1.0, 8.1 Hz, 1H), 7.64 (d, 8.1 Hz, 1H), 7.53 (d of d of d, J = 1.0, 7.3, 7.9 Hz, 1H), 7.21 - 7.37 (m, 6H), 6.64 (s, 1H), 3.82 (s, 2H), 2.07 (s, 3H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2, 137.5, 134.3, 133.7, 132.9, 129.9, 129.8, 129.0, 128.4, 126.9, 126.5, 125.8, 37.8, 18.3.

55: Purified by chromatography over silica gel, eluting with 10 -20 % EtOAc / hexanes, to give **55** (81%):

IR (neat) 2919, 1560, 1503 cm^{-1};

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d of d, J = 1.0, 8.1 Hz, 1H), 7.48 - 7.51 (m, 2H), 7.09 - 7.35 (m, 6H), 5.71 (d of d, J = 6.7, 15.1 Hz, 1H), 5.49 (d of t, J = 7.3 Hz, 15.1 Hz), 3.55 (d, J = 7.3 Hz), 2.42 - 2.65 (m, 3H), 0.97 (d, J = 6.2 Hz, 3H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 141.1, 140.5, 134.3, 133.6, 129.6, 129.4, 128.3, 126.5, 126.1, 125.6, 122.3, 43.5, 38.6, 28.7, 20.0.

Typical experimental for synthesis of rearranged alcohols: To a stirred solution of the selenide in CH_2Cl_2 (0.3 M) with powdered 4Å molecular sieves (1g per mmol) was added $VO(acac)_2$ (10 mol %). After 10 -15 min, the green solution was cooled to -10°C in an ice / acetone bath and cumene hydrogen peroxide (1.8 equiv.) was added. After 30 min, the deep red solution was quenched with PBu_3 (1.2 equiv.). After an additional 5 min, saturated aqueous NH_4Cl was added and extracted with Et_2O (3 X). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified.

54a: Purified by column chromatography over silica gel, eluting with 0.5% - 1% MeOH / CH_2Cl_2 , to give **54a** (70%):

IR (neat) 3351, 2928, 2857, 1644;

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (d of d of d, J = 6.3, 10.5, 17.2 Hz, 1H), 5.21 (d of d, J =, 1.4, 17.2 Hz, 1H), 5.10 (d of d, J =, 1.4, 10.5 Hz, 1H), 4.08 - 4.10 (m, 1H),1.25 - 1.63 (m, 10H), 0.88 (t, J = 6.8 Hz, 3H);

^{13} C NMR (75 MHz, $CDCl_3$) δ 141.5, 114.7, 73.5, 37.2, 31.9, 29.4, 25.4, 22.8, 14.2.

54b: Purified by column chromatography over silica gel, eluting with 0.5% - 1% MeOH / CH_2Cl_2, to give **54b** (75%):

IR (neat) 3398, 2924, 2852, 1643;

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.85 (d of d of d, J = 6.4, 10.4, 17.1 Hz, 1H), □5.20 (d of d, J = 1.6, 17.1 Hz, 1H), 5.14 (d of d, J = 1.6, 10.4 Hz, 1H), 3.80 (d of d, J = 6.3, 6.4 Hz, 1H),□1.60 - 1.95 (m, 5H), 0.96 - 1.50 (m, 6H);

^{13} C NMR (75 MHz, $CDCl_3$) δ 139.9, 115.7, 43.6, 28.9, 28.5, 26.7, 26.2.

54c Purified by column chromatography over silica gel, eluting with 2-20% EtOAc / hexanes, to give **54c** (84%):

IR (neat) 3368, 2902, 2847 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.94 (d of d of d, J = 6.9, 10.9, 17.4 Hz, 1H), 5.17 - 5.23 (m, 2H), 3.57 (d, J = 6.9 Hz, 1H), 1.98 (bs, 3H), 1.40-1.90 (m, 12H);

^{13} C NMR (75 MHz, $CDCl_3$) δ 139.1, 116.7, 81.7, 38.2, 37.3, 37.0, 28.5.

54d: Purified by chromatography over silica gel, eluting with 2 - 25 % Et_2O / pentane, to give **54d** (66%):

IR (neat) 3400, 3076, 3003, 2956, 1610, 1513 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, J = 6.8 Hz, 2H), 6.89 (d, J = 6.8 Hz, 2H), 6.04 (d of d of d, J = 5.6, 10.3, 17.0 Hz), 5.33 (d of d, J = 1.1, 17.0 Hz, 1H), 5.15 - 5.21 (m, 2H), 3.80 (s, 3H), 2.16 (bs, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 140.6, 135.1, 127.9, 115.0, 114.1, 75.1, 55.5.

54f: Purified by chromatography over silica gel, eluting with 2 - 15 % Et_2O / petroleum ether, to give **54f** (70%):

IR (neat) 3383, 2972, 1651, 1492, 1450 cm^{-1};

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 - 7.40 (m, 5H), 5.22 (s, 1H), 5.13 (s, 1H), 4.97 (s, 1H), 2.15 - 2.25 (bs, 1H) 1.62 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 142.2, 128.6, 127.9, 126.7, 111.4, 78.0, 18.5.

55: Purified by chromatography over silica gel, eluting with 2 - 20 % Et_2O / pentane, to give **55** (60%):

IR (neat) 3386, 3082, 3025, 2962, 2927, 1602.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 - 7.31 (m, 5H), 5.86 - 5.93 (m, 1H),□5.17 - 5.30 (m, 2H), 4.06 (bs, 1H of a diastereomer), 3.99 (bs, 1H of a diastereomer),□2.84 - 2.92 (m, 1H),□2.33 - 2.44 (m, 1H),□1.91 - 1.94 (m, 1H), 1.75 (bs, 1H), 0.87 (d, J = 6.9 Hz, 3H of a diastereomer), 0.84 (d, J = 6.9 Hz, 3H of a diastereomer).

^{13} C NMR (75 MHz, $CDCl_3$) δ 141.2, 141.0, 139.9, 139.2, 129.5, 129.4, 128.5, 128.4, 126.1, 116.5, 115.5, 77.6, 75.7, 40.84, 40.80, 39.4, 38.9, 29.9, 15.0, 14.0.

53g: Purified by column chromatography over silica gel, eluting with 5-20% EtOAc / hexanes, to give **53g** (86%):

IR 2924, 1504, 1130, 728, cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (d, J = 8.1 Hz, 1H), 7.50 - 7.56 (m, 2H), 7.27 - 7.34 (m, 1H),□5.57 - 5.69 (m, 2H), 3.64 (d, J = 6.8 Hz, 2H), 2.13 - 2.20 (m, 2H), 1.29 - 1.45 (m, 8 H), 0.89 (t, J = 6.9 Hz, 3H); ^{13} C NMR (75 MHz, $CDCl_3$); 146.7, 135.9, 135.0, 133.8, 129.5, 126.5, 125.5, 122.5, 31.9, 29.6, 29.2, 27.5, 23.8, 22.8, 14.3.

53h: Purified by chromatography over silica gel, eluting with 2 - 20 % EtOAc / petroleum ether, to give **53h** (70%): IR (neat) 3079, 3056, 2927, 1589, 1565, 1513 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (d of d, J = 1.6, 8.1 Hz, 1H), 7.24 - 7.41 (m, 8H), 6.64 (d, J = 11.5 Hz, 1H), 6.20 (d of t, J = 8.0, 11.5 Hz, 1H), 3.86 (d, J = 8.0 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) □ 146.7, 136.5, 133.9, 133.8, 133.3, 129.6, 129.0, 128.8, 127.7, 126.6, 125.8, 125.7, 25.0.

57 Purified by column chromatography over silica gel, eluting with 2 - 20% EtOAc / hexanes, to give **57** (60%):

IR (neat) 3024, 2957, 2923, 1589, 1565, 1512 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (d, J = 8.1Hz, 1H), 7.48 (d of d, J = 6.8, 7.8 Hz, 1H), 7.15 - 7.40 (m, 7 H), 5.43 - 5.57 (m, 2H), 3.41 (d of d, J = 7.3, 10.8 Hz, 1H), 3.26 (d of d, J = 6.2, 10.8 Hz, 1H), 2.79 - 2.87 (m, 1H), 2.54 - 2.74 (m, 2H), 1.07 (d, J = 6.7 Hz, 3Hz).

^{13}C NMR (75 MHz, $CDCl_3$) 146.2, 140.6, 134.9, 133.8, 129.5, 129.4, 128.6, 128.4, 126.6, 126.3, 125.5, 121.8, 43.8, 24.7, 23.7, 21.1.

54g purified by column chromatography over silica gel, eluting with 0.5%-1% MeOH / CH_2Cl_2, to give **54g** (89%): IR (neat) 3351, 2928, 2857, 1644.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (d of d of d, J = 6.3, 10.5, 17.2 Hz, 1H), 5.21 (d of d, J = 1.4, 17.2 Hz, 1H), 5.10 (d of d, J =, 1.4, 10.5 Hz, 1H), 08 - 4.10 (m, 1H),□1.25 - 1.63 (m, 10H),□0.88 (t, J = 6.8 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 141.5, 114.7, 73.5, 37.2, 31.9, 29.4, 25.4, 22.8, 14.2.

54h: Purified by chromatography over silica gel, eluting with 2 - 15 % Et_2O / petroleum ether, to give **54h**(70%):

IR (neat) 3364, 3071, 2862, 1501 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.26 - 7.43 (m, 5H), 6.06 (d of d of d, J = 6.0, 10.3, 17.0 Hz, 1H), 5. 36 (d, J = 17.0 Hz, 1H), 5.19 - 5.23 (m, 2H), 2.16 (bs, 1H).

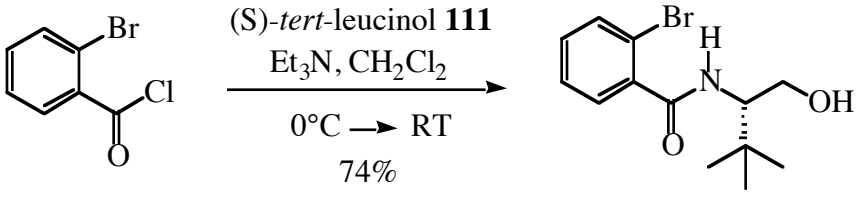
^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8, 140.4, 128.7, 128.0, 126.5, 115.3, 75.6.

56 Purified by column chromatography over silica gel, eluting with 2-20% EtOAc / hexanes, to give **56** (71%):

IR (neat) 3386, 3082, 3025, 2962, 2927, 1602.

^1H NMR (300 MHz, $CDCl_3$) δ 7.17 - 7.31 (m, 5H), 5.86 - 5.93 (m, 1H),□5.17 - 5.30 (m, 2H), 4.06 (bs, 1H of a diastereomer), 3.99 (bs, 1H of a diastereomer), 2.84 - 2.92 (m, 1H), 2.33 - 2.44 (m, 1H), 1.91 - 1.94 (m, 1H), 1.75 (bs, 1H), 0.87 (d, J = 6.9 Hz, 3H of a diastereomer), 0.84 (d, J = 6.9 Hz, 3H of a diastereomer).

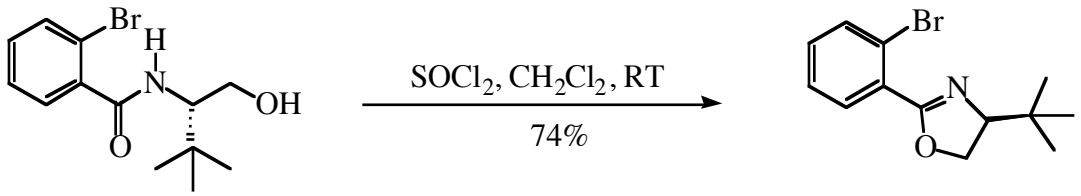
^{13} C NMR (75 MHz, $CDCl_3$) δ 141.2, 141.0, 139.9, 139.2, 129.5, 129.4, 128.5, 128.4, 126.1, 116.5, 115.5, 77.6, 75.7, 40.84, 40.80, 39.4, 38.9, 29.9, 15.0, 14.0.



113 **114**

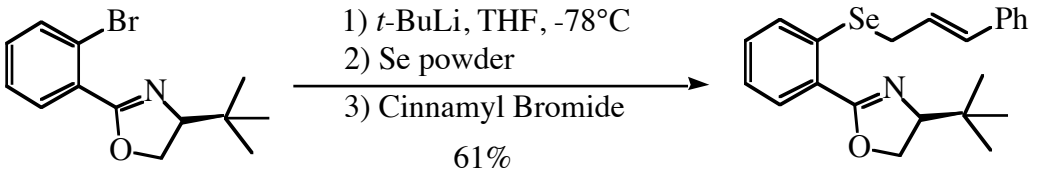
2-bromo-*N*-(1-hydroxymethyl-2,2-(S)-dimethyl-propyl)-benzamide (114):[2] To a stirred solution (*S*)-*tert*-leucinol **111** (515 mg, 4.40 mmol) in CH_2Cl_2 (7.4 mL) at 0°C was

added Et_3N (526 mg, 0.723 mL, 5.20 mmol). After 10 min, a solution of 2-bromobenzoylchloride **113** (876 mg, 0.46 mL, 4.00 mmol) in CH_2Cl_2 (4 mL) was added dropwise to the leucinol solution *via* syringe pump over a period of 20 min. Next, the solution was warmed to r.t. After 2 h, the reaction mixture was quenched with aq. HCl (25 mL, 5%) and extracted with Et_2O (3 x 75 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (25 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* to yield **114** (882 mg, 74%) as a pink oil which was immediately used in the following step.



114 **116**

2-(2-Bromophenyl)-4(*S*)-tert-butyl-2-oxazoline (116):[2] To a stirred solution of **114** (882 mg, 4.0 mmol) in CH_2Cl_2 (11 mL) at 0°C was added $SOCl_2$ (952 mg, 0.58 mL, 8.0 mmol). After 2 h, the reaction was quenched with sat. aq. $NaHCO_3$ (15 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and purified by chromatography on silica gel, eluting with 0.5-1% MeOH/CH_2Cl_2 to give **116** (832 mg, 74%) as a white solid.



116 **118**

4-(S)-*tert*-butyl-2-[2-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydrooxzole (118): To a stirred solution of oxazole **116** (122 mg, 0.43 mmol) in THF (6.5 mL) at –78°C was added *t*-BuLi (0.4 mL, 0.65 mmol, 1.7 M in pentane) dropwise over 20 min resulting in an orange color. After 1 h, Se powder (34.2 mg 0.43 mmol) was added in 1 portion under an inverse argon funnel and warmed to 0°C. After 1 h or until the slurry was homogenous, cinnamyl bromide (85 mg, 53μL, 0.43 mmol) was added. After an additional 1 h, the reaction was quenched with sat. aq. NH_4Cl (5 mL) and the product was extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel eluting with 2-20% EtOAc/hexane. The final product was recrystallized in hexane to yield **118** (105 mg, 61%) as a white solid:

m.p. 138-141°C.

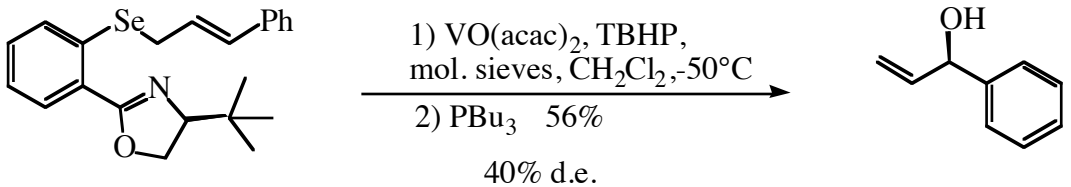
$[\alpha]_D^{23}$ –77.9 (c 1.00, $CHCl_3$).

IR (neat) 2959, 1644, 1353, 957 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 7.7 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.17-7.37 (m, 7H), 6.83 (d, J = 15.7 Hz, 1H), 6.42 (dt, J = 7.4, 15.7 Hz, 1H), 4.28-4.34 (m, 1H), 3.71 (d, J = 7.2 Hz, 2H), 0.99 (s, 9H).

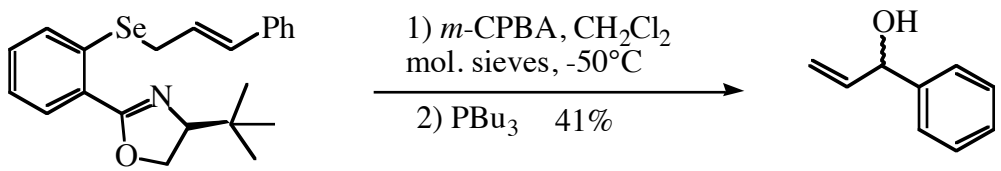
^{13}C NMR (75 MHz, $CDCl_3$) δ 162.7, 137.2, 136.8, 133.1, 130.9, 130.3, 128.7, 128.1, 127.6, 126.7, 126.5, 125.5, 124.7, 76.8, 68.4, 34.2, 28.8, 26.2.

HRMS (FAB) calcd. for $C_{22}H_{25}NOSe$ ($M+H^+$) 399.1101. Found 400.1172.



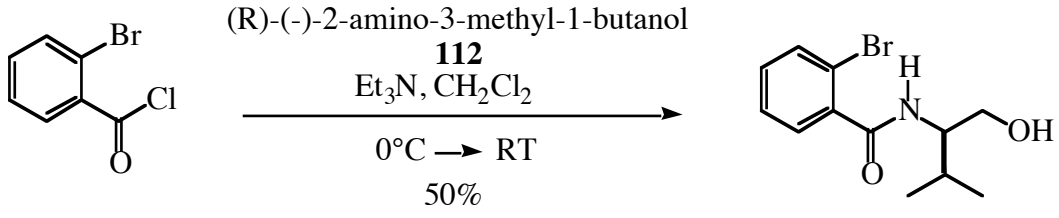
118 **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **118** (87.2 mg, 0.218 mmol) CH_2Cl_2 (0.75 mL) was added $VO(acac)_2$ (6.3 mg, 0.022 mmol) and 4 Å powdered mol. sieves (25 mg) at r.t. After 20 min, the reaction was cooled to –50°C and TBHP (43 μL, 0.24 mmol, 5.5 M in decane) was added. After 20 h, the slurry was quenched with PBu_3 (49.3 mg, 60 μL, 0.239 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (16.7 mg, 56%) as a pale yellow oil. The diastereomeric excess of 40% was determined *via* conversion to the Mosher ester.



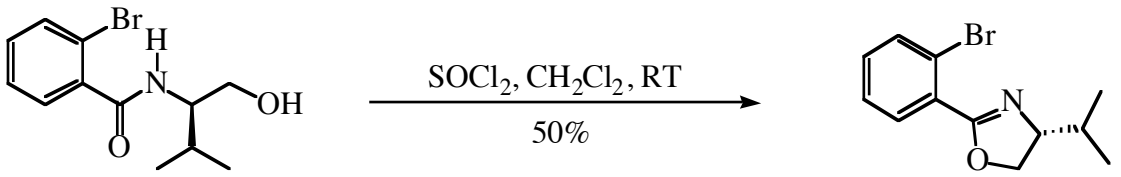
118 **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **118** (62.9 mg, 0.158 mmol) and 4 Å powdered mol. sieves (50 mg) in CH_2Cl_2 (0.55 mL) at –78°C, was added *m*-CPBA (27 mg, 0.158 mmol). After 11 h, the reaction was quenched with PBu_3 (35 mg, 43 μL, 0.174 mmol). After 10 minutes, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 30 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (9.0 mg, 41%) as a pale yellow oil. The diastereomeric excess of 4% was determined *via* conversion to the Mosher ester.



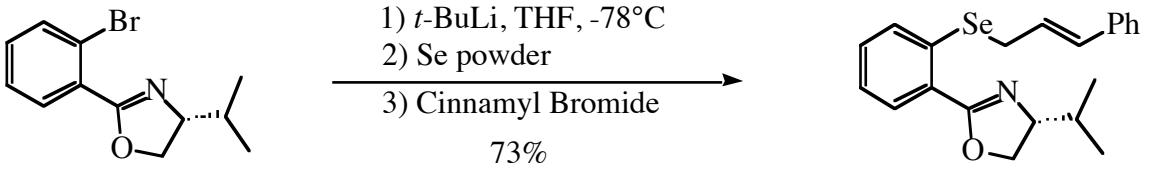
113 **115**

2-Bromo-*N*-(1-hydroxymethyl-2-methyl-propyl)-benzamide (115):[3] To a stirred solution of **112** (*R*)-(-)-2-amino-3-methyl-1-butanol (970 mg, 9.42 mmol) in CH_2Cl_2 (18 mL) at 0°C was added Et_3N (1.18 g, 1.62 mL, 11.66 mmol). After 10 min, a solution of 2-bromobenzoylchloride **113** (1.80 g, 1.18 mL, 8.97 mmol) in CH_2Cl_2 (8.9 mL) was added dropwise *via* syringe pump over 20 min and then warmed to r.t. After 2 h, the reaction was quenched with sat. aq. NH_4Cl (20 mL) and extracted with Et_2O (3 x 75 mL). The organic layer was sequentially washed with aq. HCl (20 mL, 5%) and sat. aq. $NaHCO_3$ (25 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* to yield **115** (1.28 g, 50%) as a light pink oil.



115 **117**

2-(2-Bromo-phenyl)-4-isopropyl-4,5-dihydro-oxazole (117): To a stirred solution of benzamide **115** (2.5 g, 8.97 mmol) in CH_2Cl_2 (28 mL) was added $SOCl_2$ (2.1 g, 1.3 mL, 17.9 mmol) dropwise *via* syringe pump over 20 min. After 2 h, the reaction was quenched with sat. aq. $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue purified by chromatography on silica gel, eluting with 0.5-1% MeOH/CH_2Cl_2 to give **117** (1.72 g, 50%) as light pink solid.



117 **119**

4-Isopropyl-2-[2-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazole (119): To a stirred solution of *t*-BuLi (4.12 mL, 7.0 mmol, 1.7 M in pentane) in THF (21 mL) at –78°C was added benzamide **117** (0.94 g, 3.50 mmol) in THF (11 mL) dropwise *via* syringe pump over 30 min resulting in an orange solution. The benzamide conical vial was further rinsed with an additional amount THF (2 mL). After 1 h, Se powder (290 mg, 3.7 mmol) was added under an inverse argon funnel and the reaction was then warmed to 0°C. After 1 h or until the solution was homogenous, was added cinnamyl bromide (723 mg, 0.53 mL, 3.70 mmol). After 1 h, the reaction was quenched with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane. The final product was recrystallized in hexane to give **119** (981 mg, 73%) as a white solid:

m.p. 122-125 °C.

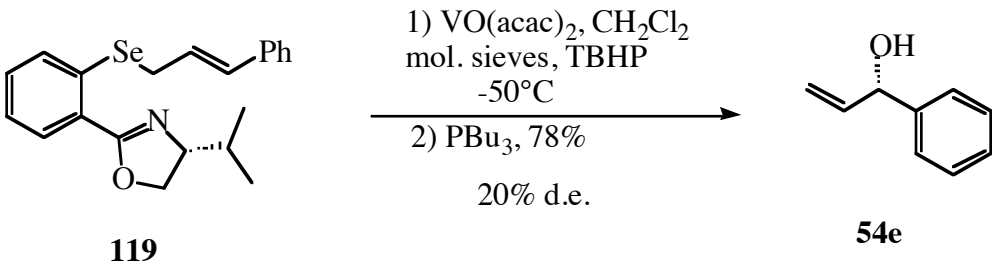
$[\alpha]_D^{23}$ –77.9 (c 1.00, $CHCl_3$).

IR (neat) 2955, 1645, 1363, 1251 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (dd, J = 1.6, 7.8 Hz, 1H), 7.48 (d, J = 8.1 Hz, 1H), 7.18-7.37 (m, 7H), 6.61 (d, J = 15.7 Hz, 1H), 6.40 (dt, J = 7.4, 15.7 Hz, 1H), 4.39 (dd, J = 7.8, 8.9 Hz, 1H), 4.20 (dd, J = 7.8, 14.7 Hz, 1H), 4.10 (dd, J = 7.6, 15.3 Hz, 1H), 3.71 (d, J = 7.5 Hz, 2H), 1.80-1.84 (m, 1H), 1.08 (d, J = 6.7 Hz, 3H), 0.97 (d, J = 6.7 Hz, 3H).

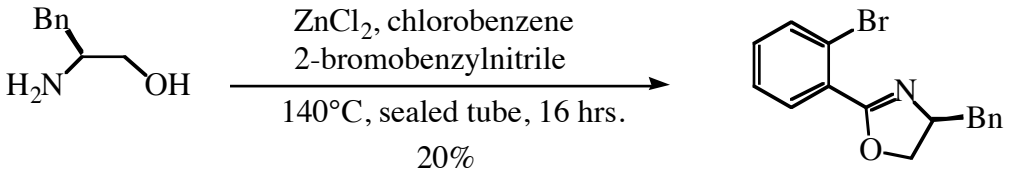
^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 137.1, 136.5, 133.1, 130.9, 130.2, 128.7, 128.1, 127.6, 126.4, 125.4, 124.7, 77.2, 73.6, 70.2, 33.4, 28.8, 19.3, 18.8.

HRMS (FAB) calcd. for $C_{21}H_{23}NOSe$ ($M+H^+$) 385.0945. Found 386.1023.



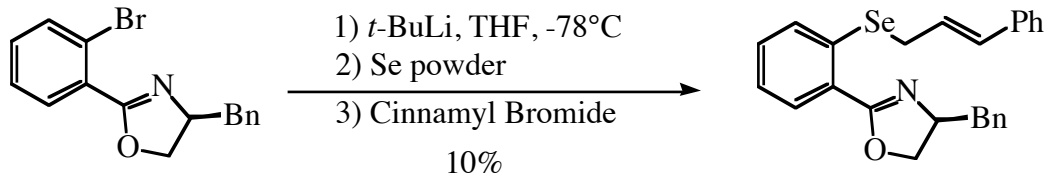
119 **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **119** (101.9 mg, 0.270 mmol) in CH_2Cl_2 (0.9 mL) at r.t. was added $VO(acac)_2$ (6.5 mg, 0.027 mmol) and powdered 4 Å molecular sieves (100 mg). After 20 min, the reaction was cooled to –50°C and TBHP (54 μL, 0.30 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (61 mg, 74 μL, 0.300 mmol). After an additional 10 min, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (31 mg, 78%) as a pale yellow oil. The diastereomeric excess of 20% was determined *via* conversion to the Mosher ester.



120 **121**

4-(S)-Benzyl-2-(2-bromo-phenyl)-4,5-dihydro-oxazole (121):[4] To a stirred solution of 2-bromobenzonitrile (998 mg, 5.49 mmol) and the amino alcohol **120** (829 mg, 5.48 mmol) in chlorobenzene (3.1 mL) at r.t. was added and $ZnCl_2$ (28 mg, 0.21 mmol). After 10 min, the reaction was heated to 140°C in a sealed tube. After 16 h, the reaction was cooled and quenched with sat. aq. NH_4Cl (10 mL) and extracted with Et_2O (3 x 20 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-40% EtOAc/hexane to give **121** (345 mg, 20%) as a light pink oil.

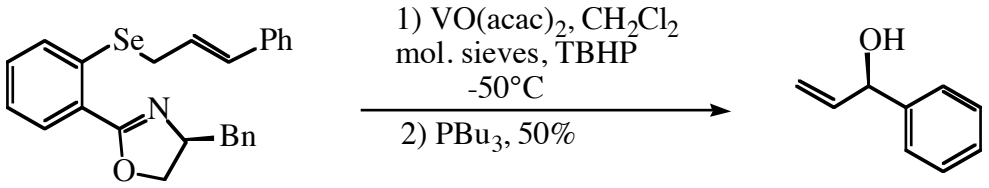


121 **122**

4-(S)-benzyl-2-[2-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazole (122): To a stirred solution of *t*-BuLi (1.18 mL, 2.00 mmol, 1.7 M in pentane) in THF (6 mL) at –78°C was added a solution of benzamide **121** (311 mg, 1.00 mmol) in THF (3 mL) dropwise *via* syringe pump over 20 min resulting in an orange solution. After 1 h, Se powder (79 mg, 1.00 mmol) was added under an inverse argon funnel and the reaction was warmed to 0°C. After 1 h or until the mixture was homogeneous, cinnamyl bromide (196.7 mg, 0.15 mL, 1 mmol) was added. After an additional 1 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted with Et_2O (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to yield **122** (46.3 mg, 10%) as a pale yellow oil:

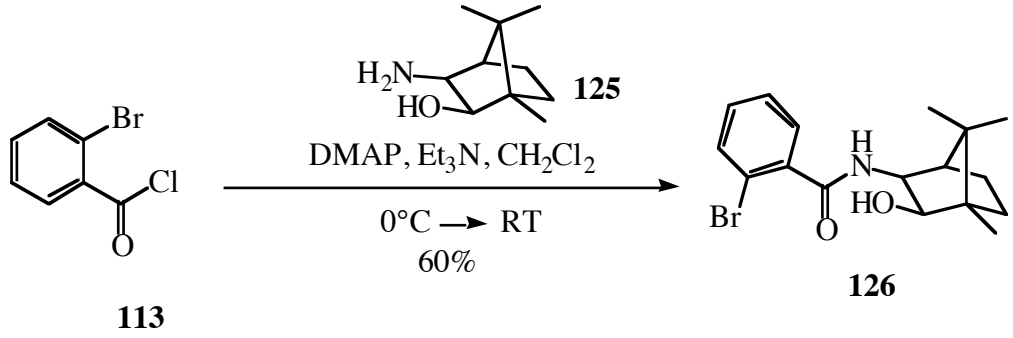
IR (neat) 2959, 1643; 1589 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) δ 7.80 (d, J = 7.8 Hz, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.18-7.37 (m, 12H), 6.62 (d, J = 15.6 Hz, 1H), 6.42 (dt, J = 7.4, 15.2 Hz, 1H), 4.68 (m, 1H), 4.31 (dd, J = 8.7, 8.7 Hz, 1H), 4.10 (m, 1H), 3.73 (d, J = 7.3 Hz, 2H), 3.29 (dd, J = 5.4, 13.7 Hz, 1H), 2.78 (dd, J = 8.6, 13.6 Hz, 1H).



122 10 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **122** (46.0 mg, 0.11 mmol) in CH_2Cl_2 (0.5 mL) at r.t. was added $VO(acac)_2$ (2.9 mg, 0.01 mmol) and powdered 4 Å mol. sieves (50 mg). After 20 min, the reaction cooled to –50°C and TBHP (22 μL, 0.12 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (24 mg, 30 μL, 0.12 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (25 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (7 mg, 50%) as a yellow oil. The diastereomeric excess of 10% was determined *via* conversion to the Mosher ester.



2-bromo-*N*-(3-hydroxy-4,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-benzamide (126): To a stirred solution of amino alcohol **125** (808.0 mg, 4.78 mmol) in CH_2Cl_2 (9 mL) at 0°C was sequentially added DMAP (146.0 mg, 1.20 mmol) and Et_3N (627.1 mg, 0.86 mL). After 10 min, a solution of 2-bromobenzoylchloride **113** (1.05 g, 0.63 mL, 4.00 mmol) in CH_2Cl_2 (4.8 mL) was added dropwise *via* syringe pump over 20 min. After an additional 30 min, the reaction was warmed to r.t. After 2 h, the reaction was quenched with sat. aq. NH_4Cl (25 mL) and extracted with Et_2O (3 x 75 mL). The organic layer was sequentially washed with aq. HCl (5%, 50 mL) and sat. aq. $NaHCO_3$ (100 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-40% EtOAc/hexane to give **126** (842 mg, 60%) as a light pink solid:

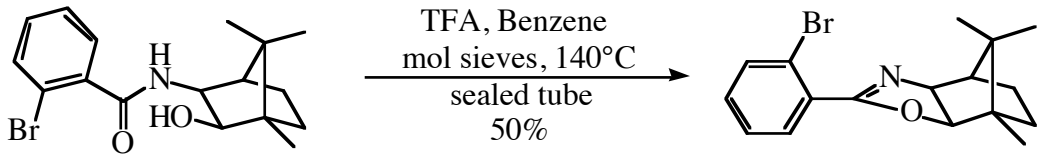
m.p. 169-170°C.

$[\alpha]_D^{23}$ –3.1 (c 0.72, $CHCl_3$).

IR (neat) 3381; 1651, 1506 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, J = 7.9 Hz, 1H), 7.52 (dd, J = 1.5, 7.7 Hz, 1H), 7.23-7.37 (m, 2H), 6.67 (bs, 1H), 4.00 (dd, J = 6.8, 13.4 Hz, 1H), 3.91 (dd, J = 7.6, 4.14 Hz, 1H), 2.17 (bs, 1H), 1.99 (d, J = 4.4 Hz, 1H), 1.27-1.57 (m, 4H), 1.23 (s, 3H), 1.21 (s, 3H), 1.15 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 133.6, 131.3, 129.6, 127.6, 119.6, 80.1, 58.6, 50.4, 49.4, 47.1, 33.4, 26.4, 21.7, 21.4, 11.5.



126 **127**

4-(2-bromo-phenyl)-1, 10, 10-trimethyl-3-oxa-5-aza-tricyclo[5.2.1.0]dec-4-ene (127): To a stirred solution of amino alcohol **126** (137.9 mg, 0.393 mmol) in benzene (1.1 mL) was added TFA (9.1 mg, 6.0 μL, 0.08 mmol) and powdered 4 Å mol. sieves (50 mg). After 10 min, the reaction heated to 140°C in a sealed tube. After 8 h, the reaction was cooled to r.t. and quenched with sat. aq. $NaHCO_3$ (10 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-25% EtOAc/hexane to give **127** (65 mg, 50%) as a white solid:

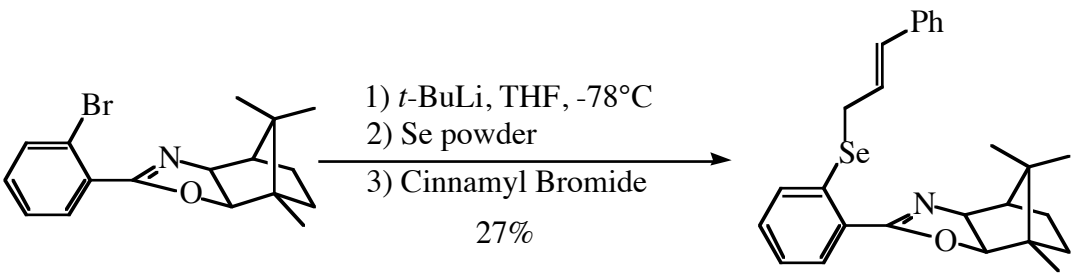
m.p. 142°C.

$[\alpha]_D^{23}$ +10.9 (c 1.3, $CHCl_3$).

IR (neat) 2950; 1651, 1506 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.58-7.80 (m, 2H), 7.26-7.38 (m, 2H), 4.43 (d, J = 8.6 Hz, 1H), 4.24 (d, J = 8.6 Hz, 1H), 2.20 (d, J = 4.5 Hz, 1H) 1.65-1.85 (m, 1H), 1.45-1.60 (m, 1H), 0.95-1.10 (m, 1H), 1.07 (s, 3H), 1.01 (s, 3H), 0.87 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1, 134.4, 131.7, 131.5, 129.9, 127.2, 122.0, 91.7, 77.0, 49.0, 48.9, 47.3, 32.3, 26.2, 23.6, 19.0, 11.6.



127 **128**

1,10,10-trimethyl-4-[2-(3-phenyl-allylselanyl)-phenyl]-3-oxa-5-aza-tricyclo[5.2.1.0]dec-4-ene (128): To a stirred solution of *t*-BuLi (1.18 mL, 2.00 mmol, 1.7 M in pentane) in THF (6.3 mL) at –78°C was added a solution of benzamide **127** (328 mg, 0.99 mmol) in THF (3 mL) dropwise *via* syringe pump over 10 min. The benzamide conical vial was further rinsed with an additional amount of THF (1.5 mL). After 1 h, Se powder (79 mg, 1.00 mmol) was added under an inverse argon funnel and the reaction was warmed to 0°C. After 1 h or until solution was homogeneous, cinnamyl bromide (200 mg, 0.15 mL, 1.00 mmol) was added to the reaction. After 1 h, the reaction was quenched with sat. aq. NH_4Cl (15 mL) and extracted with Et_2O (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane. The final product was recrystallized in hexane to give **128** (122 mg, 27%) as a pale yellow solid:

m.p. 155-160°C.

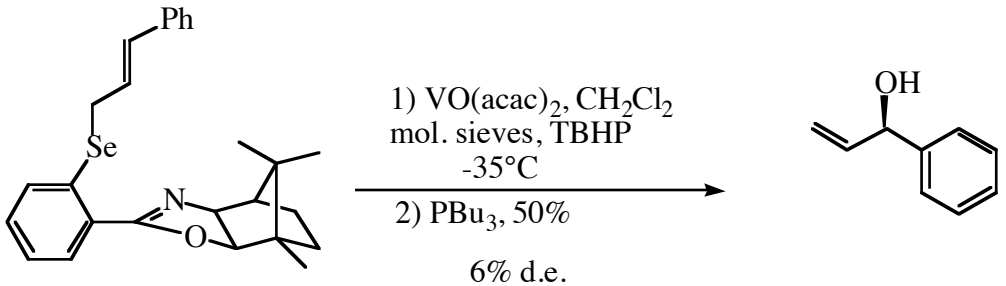
$[\alpha]_D^{23}$ +5.9 (c 2.76, $CHCl_3$).

IR (neat) 2955, 1641 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (dd, J = 1.1, 7.7 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.17-7.36 (m, 7H), 6.61 (d, J = 15.7 Hz, 1H), 6.41 (dt, J = 7.5, 15.7 Hz, 1H), 4.37 (d, J = 8.4 Hz, 1H), 4.31 (d, J = 8.4 Hz, 1H), 3.71 (d, J = 7.4 Hz, 2H), 2.20 (d, J = 4.5 Hz, 1H),

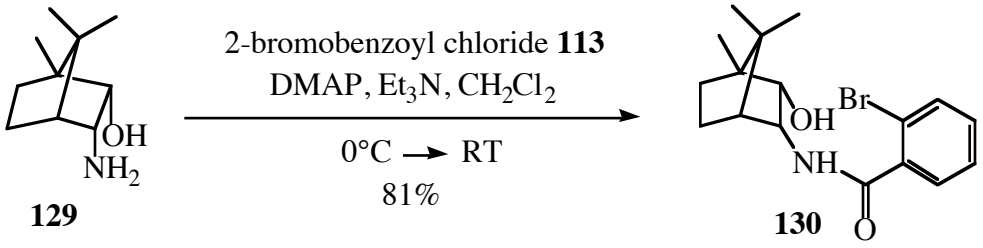
1.70-1.90 (m, 1H), 1.50-1.65 (m, 1H), 0.95-1.10 (m, 2H), 1.11 (s, 3H), 1.09 (s, 3H), 0.89 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 137.1, 136.6, 133.2, 131.0, 130.5, 128.7, 128.0, 127.6, 127.0, 126.4, 125.1, 124.7, 91.0, 77.0, 49.2, 48.8, 47.2, 32.3, 28.7, 26.2, 23.7, 18.9, 11.7.



128 **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **128** (95.0 mg, 0.21 mmol) in CH_2Cl_2 (0.7 mL) at r.t. was added $VO(acac)_2$ (5.6 mg, 0.021 mmol) and powdered 4 Å mol. sieves (50 mg). After 20 min, the reaction was cooled to –35°C and TBHP (42 μL, 0.23 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (47 mg, 58 μL, 0.23 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (25 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (14.2 mg, 50%) as a yellow oil. The diastereomeric excess of 6% was determined *via* conversion to the Mosher ester.



2-bromo-*N*-(3-hydroxy-4,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-benzamide (130): To a stirred solution the amino alcohol **129** (890.1 mg, 5.23 mmol) in CH_2Cl_2 (10 mL) at 0°C was added Et_3N (700 mg, 0.951 mL, 6.85 mmol) and DMAP (160 mg, 1.30 mmol). After 10 min, a solution of 2-bromobenzoylchloride **113** (1.25 g, 0.69 mL, 5.30 mmol) in CH_2Cl_2 (5 mL) was added dropwise *via* syringe pump over a period of 20 min and warmed to r.t. After 2 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) extracted with Et_2O (3 x 75 mL). The organic layer was sequentially washed with aq. HCl (50 mL, 5%) and sat. aq. $NaHCO_3$ (100 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 3-40% EtOAc/hexane to give **130** (1.53 g, 81%) as a white solid:

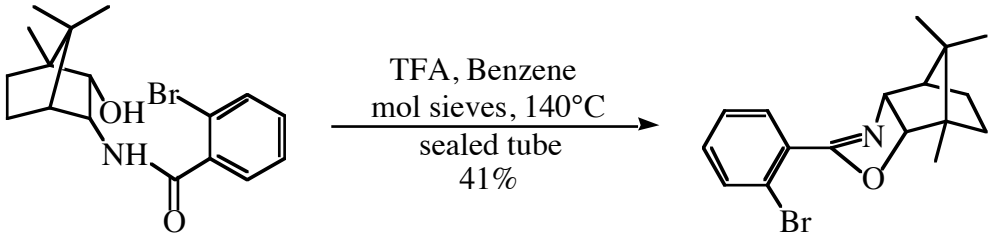
m.p. 92-95 °C.

$[\alpha]_D^{23}$ –10.4 (c 1.29, $CHCl_3$).

IR (neat) 3381; 1651, 1506 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.23-7.59 (m, 4H), 6.79 (bs, 1H), 6.49 (bs, 1H) 4.0 (dd, J = 6.8, 13.4 Hz, 1H), 3.91 (dd, J = 4.14, 7.6 Hz, 1H), 2.17 (bs, 1H), 1.27-1.57 (m, 5H), 1.23 (s, 3H), 1.21 (s, 3H), 1.15 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 133.6, 131.3, 129.6, 127.6, 119.6, 80.1, 58.6, 50.4, 49.4, 47.1, 33.4, 26.4, 21.7, 21.4, 11.5.



130 **131**

4-(2-bromo-phenyl)-1,10,10-trimethyl-3-oxa-5-aza-tricyclo[5.2.1.$0^{255.255}$]dec-4-ene (131): To a stirred solution of amide alcohol (**130**) (1.50 g, 4.32 mmol) in benzene (12 mL) at r.t. was added TFA (90 mg, 66 μL, 0.85 mmol) and powdered 4 Å mol. sieves (200 mg). After 10 min, the reaction was heated to 140°C in a sealed tube. After 24 h, the reaction was cooled to r.t. and quenched with sat. aq. $NaHCO_3$ (40 mL) and extracted with Et_2O (3 x 100 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-25% EtOAc/hexane to give **131** (587 mg, 41%) as a white solid:

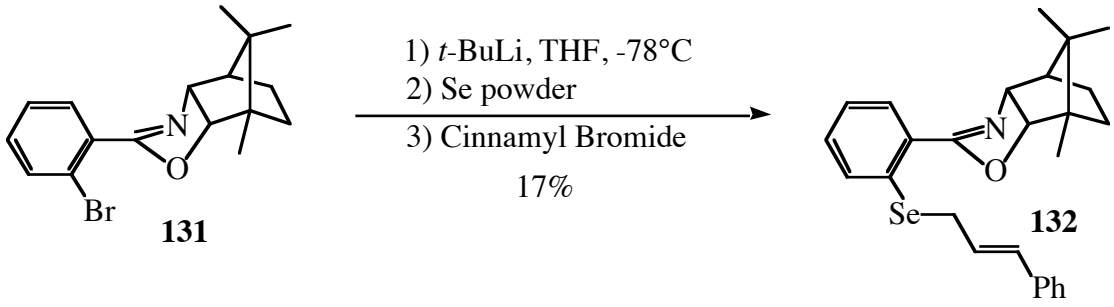
m.p. 110 °C.

$[\alpha]_D^{23}$ –6.9 (c 0.85, $CHCl_3$).

IR (neat) 2950; 1651, 1506 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (dd, J = 1.2, 7.7 Hz, 1H), 7.66 (dd, J = 1.2, 7.9 Hz, 1H), 7.26-7.38 (m, 2H), 4.77 (dd, J = 4.8, 9.8 Hz, 1H), 4.68 (dd, J = 1.5, 9.9 Hz, 1H), 2.19 (t, J = 4.2 Hz, 1H) 1.51-1.69 (m, 2H), 1.00 (s. 3H), 0.99 (s, 3H), 0.98 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.0, 134.2, 131.7, 131.6, 130.3, 127.2, 121.9, 89.4, 72.3, 49.7, 49.5, 49.4, 27.4, 20.9, 20.0, 18.6, 15.2.



1,10,10-trimethyl-4-[2-(3-phenyl-allylselanyl)-phenyl]-3-oxa-5-aza-tricyclo[5.2.1.0$^{255.255}$]dec-4-ene (132): To a stirred solution of *t*-BuLi (3.33 mL, 5.64 mmol, 1.7 M in pentane) in THF (18 mL) at –78°C, was added a solution of benzamide (**131**) (938 mg, 2.82 mmol) in THF (8.5 mL) dropwise over 20 min resulting in an orange solution. The benzamide conical vial was further rinsed with an additional amount of THF (2 mL). After 1 h, Se powder (223 mg, 2.82 mmol) was added under an inverse argon funnel and the reaction was then warmed to 0°C. After 1 h or until the solution was homogeneous, cinnamyl bromide (800 mg, 0.43 mL, 2.9 mmol) was added. After 1 h, the reaction was quenched sat. aq. NH_4Cl (20 mL) and extracted with Et_2O (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane. The final product was recrystallized in hexane to give **132** (215 mg, 17%) of a white solid:

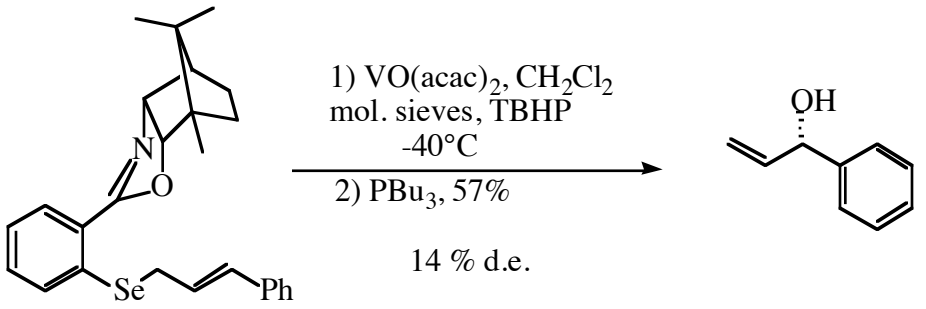
m.p. 154-155°C.

$[\alpha]_D^{23}$ –12.4 (c 1.19, $CHCl_3$).

IR (neat) 2949, 1635 cm^{-1}.

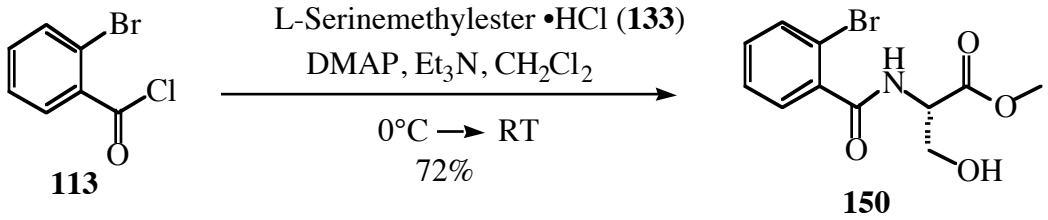
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (dd, J = 1.4, 7.7 Hz, 1H), 7.47 (d. J = 7.7 Hz, 1H), 7.20-7.38 (m, 7H), 6.61 (d, J = 15.7 Hz, 1H), 6.41 (dt, J = 7.5, 15.2 Hz, 1H), 4.81 (dd, J = 4.7, 9.7 Hz, 1H), 4.64 (dd, J = 1.6, 9.8 Hz, 1H), 3.71 (d, J = 7.4 Hz, 2H), 2.19 (t, J = 4.3 Hz, 1H), 1.40-1.60 (m, 3H), 1.10-1.35 (m, 1H), 1.0 (s, 6H), 0.96 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.2, 137.1, 136.5, 133.2, 130.9, 130.4, 128.7, 128.1, 127.6, 127.2, 126.4, 125.2, 124.7, 88.5, 72.4, 49.7, 49.5, 49.3, 28.8, 27.3, 21.0, 20.1, 18.6, 15.2.



132 **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **132** (128 mg, 0.28 mmol) in CH_2Cl_2 (1 mL) at r.t. was added $VO(acac)_2$ (7.5 mg, 0.028 mmol) and powdered 4 Å mol. sieves (50 mg). After 20 min, the reaction was cooled to –40°C and TBHP (57 μL, 0.31 mmol, 5.5 M in decane) was added. After 16 h, the reaction was quenched with PBu_3 (63 mg, 78 μL, 0.31 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (25 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give (20 mg, 57%) as a yellow oil (**54e**). The diastereomeric excess of 14% was determined *via* conversion to the Mosher ester.



113 **150**

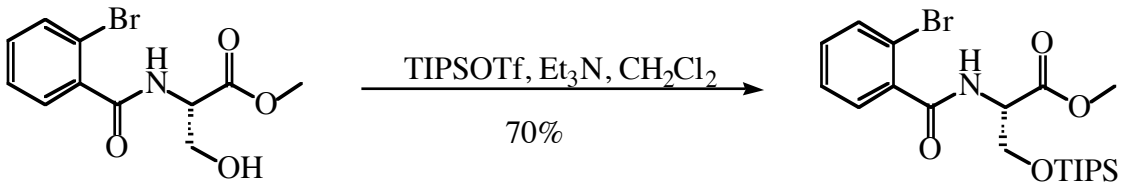
2(S)-(2-bromo-benzoylamino)-3-hydroxy-propionic acid methyl ester (150): To a stirred of L-serine methyl ester hydrochloride **133** (2.11 g, 13.56 mmol) in CH_2Cl_2 (26 mL) at 0°C, was added Et_3N (3.2 g, 4.34 mL, 31.2 mmol) and DMAP (0.331 g, 2.71 mmol). After 10 min, a solution of 2-bromobenzoylchloride **113** (3.30 g, 1.85 mL, 14.9 mmol) in CH_2Cl_2 (15 mL) was added dropwise to the amino alcohol solution *via* syringe pump over a period of 20 min. Next, the solution was warmed to r.t. After 2 h, the reaction mixture was quenched with sat. aq. NH_4Cl (50 mL) and extracted with Et_2O (3 x 75 mL). The organic layer was sequentially washed with aq. HCl (50 mL, 5%) and sat. aq. $NaHCO_3$ (100 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and purified by chromatography on silica gel, eluting with 2-100% EtOAc/hexane to give **150** (2.94 g, 72%) as a clear oil:

$[\alpha]_D^{23}$ +21.2 (c 2.67, $CHCl_3$).

IR (neat) 3335, 1734, 1652 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.54-7.61 (m, 2H), 7.25-7.38 (m, 2H), 7.00 (d, J = 6.8 Hz, 1H), 4.80-4.90 (m, 1H), 4.06-4.14 (m, 2H), 3.83 (s, 3H), 1.24 (t, J = 7.0, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 168.3, 137.0, 133.4, 131.6, 129.4, 127.5, 119.5, 62.4, 55.2, 52.7.



150 **134**

2-(2-bromo-benzoylamino)-3-(S)-triisopropylsilanyloxy-propionic acid methyl ester (134): To a stirred solution of amino alcohol methyl ester **150** (2.68 g, 8.90 mmol) in CH_2Cl_2 (25 mL) at 0°C, was added Et_3N (2.07 g, 2.85 mL, 20.5 mmol). After 10 min, TIPSOTf (3.25 g, 2.9 mL, 10.6 mmol) was added. After 2 h, the reaction was quenched with sat. aq. NH_4Cl (50 mL) and extracted with Et_2O (3 x 100 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **134** (3.11 g, 70%) as a yellow oil:

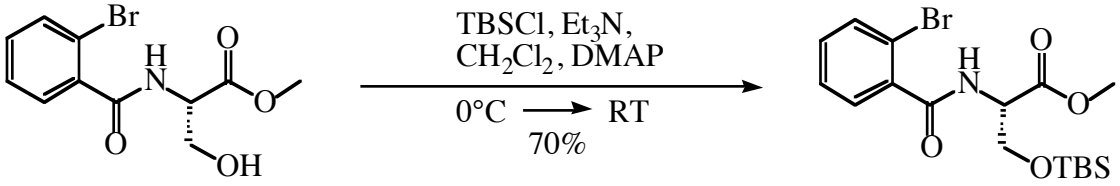
$[\alpha]_D^{23}$ +50.8 (c 0.86, $CHCl_3$).

IR (neat) 2942, 1748, 1652 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.58-7.63 (m, 2H), 7.21-7.34 (m, 2H), 6.97 (d, J = 8.0 Hz, 1H), 4.91 (dt, J = 2.8, 8.1 Hz, 1H), 4.28 (dd, J = 2.5, 9.9 Hz, 1H), 4.12 (dd, J = 2.9, 9.8 Hz, 1H), 3.79 (s, 3H), 1.00-1.10 (m, 21H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 167.2, 137.2, 133.7, 131.7, 129.9, 127.7, 119.6, 64.1, 55.1, 52.6, 18.0, 12.0.

HRMS (FAB) calcd. for $C_{20}H_{32}SiBrNO_4$ (M+H$^+$) 457.1284. Found 458.1362.



150 **135**

2(S)-(2-bromo-benzoylamino)-3-(*tert*-butyl-dimethyl-silanyloxy)-propionic-acid methyl ester (135): To a stirred solution of amino alcohol methyl ester **150** (1.60 g, 5.32 mmol) in CH_2Cl_2 (11 mL) at 0°C was added Et_3N (1.13 g, 1.55 mL, 20.5 mmol) and DMAP (0.129 g, 1.06 mmol). After 10 min, TBSCl (1.20 g, 8.02 mmol) was added and warmed to r.t. After 2 h, the reaction was quenched with sat. aq. NH_4Cl (50 mL) and extracted with Et_2O (3 x 100 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 1-20% EtOAc/hexane to give **135** (1.55 g, 70%) as a yellow oil:

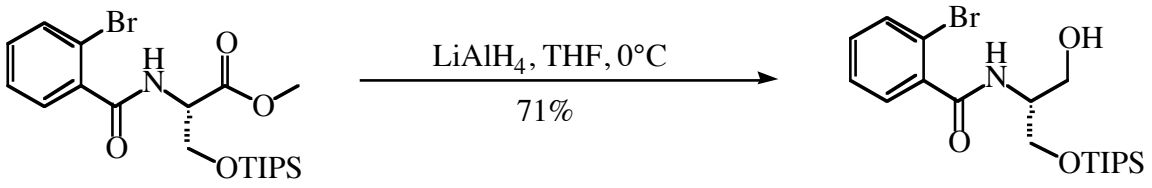
$[\alpha]_D^{23}$ +26.3 (c 0.50, $CHCl_3$).

IR (neat) 2360, 1748, 1652, 1506 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58-7.63 (m, 2H), 7.21-7.34 (m, 2H), 6.97 (d, J = 7.8 Hz, 1H), 4.91 (dt, J = 2.8, 8.1 Hz, 1H), 4.18 (dd, J = 2.8, 10.2 Hz, 1H), 4.00 (dd, J = 2.7, 10.3 Hz, 1H), 3.79 (s, 3H), 0.87 (s, 9H), 0.04 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 167.2, 137.2, 133.7, 131.7, 130.0, 127.7, 119.6, 63.6, 55.0, 52.6, 25.8, 18.3, -5.2,-5.4.

HRMS (FAB) calcd. for $C_{17}H_{26}BrSiNO_4$ (M+H$^+$) 415.0814. Found 416.0893.



134 **136**

2-bromo-*N*(2-hydroxy-1(S)-(triisopropyl-silanyloxymethyl)-ethyl-benzamide (136): To a stirred solution of $LiAlH_4$ (3.5 mL, 3.5 mmol, 1 M in Et_2O) in THF (26 mL) at 0°C was added a solution of benzamide 134 (1.50 g, 3.19 mmol) in THF (17.4 mL) dropwise *via* syringe pump over 30 min. The benzamide flask was rinsed with an additional amount of THF (2 mL). After 2 h, the reaction was quenched with a 1:1 mixture of EtOAc/H_2O (20 mL) and extracted with EtOAc (3 x $_7$5 mL). The dried *(Mg*SO4) organic layer was concentrated in vacuo and the residue was purifed by chromatography on silica gel, eluting with 2-50% EtOAc/hexane to give **136** (1.01 g, 71%) as a light pink oil.

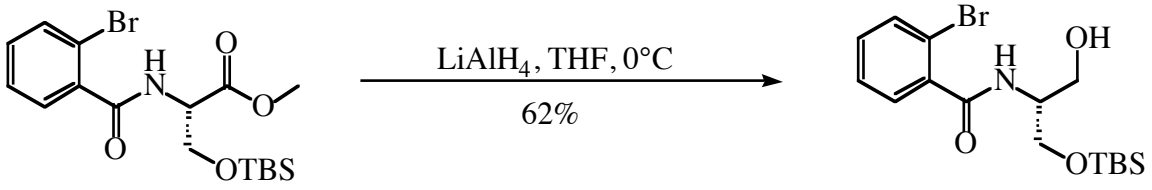
$[\alpha]_D^{23}$ +10.0 (c 4.48, $CHCl_3$).

IR (neat) 3419, 2942, 2865, 1651, 1635, 1539 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55-7.61 (m, 2H), 7.26-7.39 (m, 2H), 6.78 (d, J = 7.3 Hz, 1H), 4.15-4.30 (m, 1H), 4.00 (d, J = 3.6 Hz, 2H), 3.98-4.00 (m, 1H) 3.84-3.90 (m, 1H), 2.9 (bs, 1H), 1.00-1.10 (m, 21H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 137.6, 133.6, 131.5, 129.8, 127.7, 119.4, 64.5, 63.9, 52.6, 18.1, 11.9.

HRMS (FAB) calcd. for $C_{19}H_{32}BrNO_3Si$ ($M+H^+$) 429.1335. Found 430.1413.



135 **137**

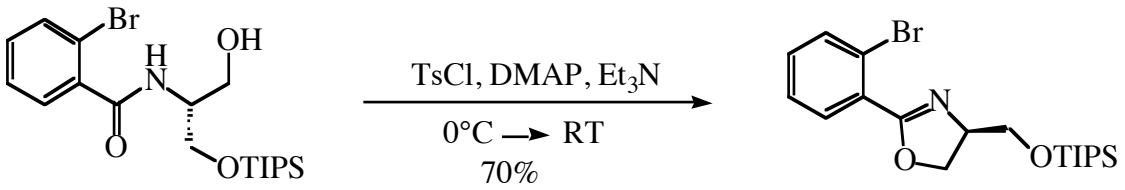
2-bromo-*N*[1-(*tert*butyl-dimethyl-silanyloxymethyl)-2-hydroxy-ethyl]-benzamide (137): To a stirred solution of $LiAlH_4$ (19.8 mL, 19.8 mmol, 1 M in Et_2O) in THF (150 mL) at 0°C was added a solution of benzamide 135 (7.45 g, 18.04 mmol) in THF (100 mL) dropwise *via* syringe pump over 30 min. The benzamide flask was rinsed with an additional amount of THF (5 mL). After 2 h, the reaction was quenched with a 1:1 mixture of EtOAc/H_2O (100 mL) and extracted with EtOAc (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-80% EtOAc/hexane to give **137** (4.62 g, 62%) as a pink oil:

$[\alpha]_D^{23}$ +15.7 (c 0.50, $CHCl_3$).

IR (neat) 3419, 2953, 1652, 1635, 1540 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.55-7.61 (m, 2H), 7.26-7.39 (m, 2H), 6.78 (bd, J = 7.3 Hz, 1H), 4.15-4.25 (m, 1H), 3.90-4.00 (m, 1H), 3.95 (d, J = 6.6 Hz, 2H), 3.80-3.90 (m, 1H), 2.85-3.95 (m, 1H), 1.26 (t, J = 6.5 Hz, 1H), 0.89 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 137.6, 133.6, 131.6, 129.9, 127.7, 119.4, 64.1, 63.9, 52.4, 26.0, 18.3, -5.2, -5.3.



136 **138**

2-(2-bromo-phenyl)-4-(triisopropyl-silanyloxymethyl)-4,5-dihydro-oxazole (138): To a stirred solution of benzamide **136** (1.29 g, 3.01 mmol) in CH_2Cl_2 (10.3 mL) at 0°C, was sequentially added DMAP (74 mg, 0.6 mmol) and Et_3N (0.46 g, 0.63 mL, 4.58 mmol). After 10 min, TsCl (68 mg, 3.6 mmol) was added and the reaction was warmed to r.t. After 12 h, the reaction was quenched with sat. aq. NH_4Cl (50 mL) and extracted with Et_2O (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **138** (997 mg, 70%) as a light pink oil:

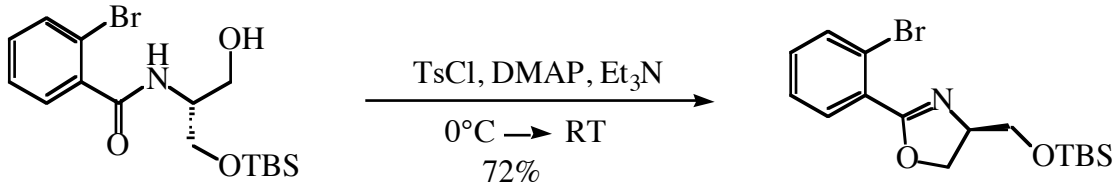
$[\alpha]_D^{23}$ –26.5 (c 1.87, $CHCl_3$).

IR (neat) 2941, 1648, 1465 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (dd, J = 1.9, 7.6 Hz, 1H), 7.65 (dd, J = 1.5, 7.5 Hz, 1H), 7.25-7.36 (m, 2H), 4.45-4.55 (m, 3H), 4.00-4.10 (m, 1H), 3.75-3.85 (m, 1H), 1.00-1.10 (m, 21H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 134.0, 131.7, 131.5, 130.1, 127.2, 121.9, 70.7, 68.8, 65.3, 18.1, 12.1.

HRMS (FAB) calcd. for $C_{19}H_{30}NO_2BrSi$ ($M+H^+$) 411.1229. Found 412.1307.



137 **139**

2-(2-bromo-phenyl)-4(R)-(*tert*-butyl-dimethyl-silanyloxymethyl)-4,5-dihydro-oxazole (139): To a stirred solution of benzamide **137** (4.49 g, 11.6 mmol) in CH_2Cl_2 (22 mL) at 0°C, was added DMAP (283 mg, 2.3 mmol) and Et_3N (2.47 g, 3.4 mL, 24.4 mmol). After 10 min, TsCl (2.41 g, 12.8 mmol) was added and the reaction was warmed to r.t. After 12 h, the reaction was quenched with aqueous NH_4Cl (50 mL) and extracted with Et_2O (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **139** (3.42 g, 72%) as a light pink oil:

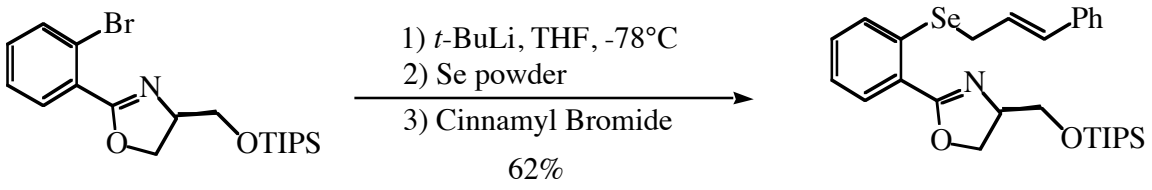
$[\alpha]_D^{23}$ –27.7 (c 1.00, $CHCl_3$).

IR (neat) 2929, 1652 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (dd, J = 1.9, 7.6 Hz, 1H), 7.65 (dd, J = 1.5, 7.5 Hz, 1H), 7.26-7.33 (m, 2 H), 4.40-4.50 (m, 3H), 3.90 (dd, J = 3.4, 9.8 Hz, 1H), 3.70 (dt, J = 3.1, 5.9 Hz, 1H) 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 134.0, 131.8, 131.5, 130.0, 127.2, 121.9, 70.5, 68.7, 64.9, 26.0, 18.4, -5.0, -5.1.

HRMS (FAB) calcd. for $C_{16}H_{24}NO_2BrSi$ ($M+H^+$) 369.0760. Found 370.0838.



138 **140**

2-[2-(3-phenyl-allylselanyl)-phenyl]-4-(triisopropyl-silanyloxymethyl)-4,5-dihydro-oxazole (140): To a stirred solution of *t*-BuLi (1.23 mL, 2.10 mmol, 1.7 M in pentane) in THF (6.6 mL) at –78°C, was added a solution of benzamide **138** (342 mg, 0.84 mmol) in THF (2.7 mL) dropwise *via* syringe pump over 20 min. The benzamide conical vial was further rinsed with an additional amount of THF (0.5 mL). After 1 h, Se powder (66 mg, 0.84 mmol) was added under an inverse argon funnel and the reaction was warmed to 0°C. After 1 h or until the solution was homogeneous, cinnamyl bromide (197 mg, 0.26 mL, 1.0 mmol) was added. After 1 h, the reaction was quenched with sat. aq. NH_4Cl (20 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane. The final product was recrystallized in hexane to give **140** (266 mg, 62%) as a white solid:

m.p. 73 °C.

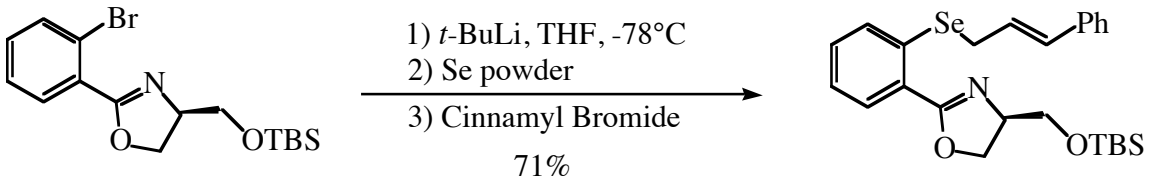
$[\alpha]_D^{23}$ –4.15 (c 3.41, $CHCl_3$).

IR (neat) 2941, 1644, 1469 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 7.6 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.18-7.37 (m, 7H), 6.63 (d, J = 15.7 Hz, 1H), 6.42 (dt, J = 7.3, 15.3 Hz, 1H), 4.50-4.55 (m, 1H), 4.41-4.44 (m, 2H) 4.07 (dd, J = 3.9, 9.7 Hz, 1H), 3.65-3.75 (m, 3H), 1.00-1.10 (m, 21H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 137.0, 136.3, 133.2, 131.0, 130.4, 128.7, 128.3, 127.6, 127.0, 126.4, 125.1, 124.8, 70.3, 69.1, 65.8, 28.8, 18.1, 12.1.

HRMS (FAB) calcd. for $C_{28}H_{39}NO_2SeSi$ ($M+H^+$) 529.1915. Found 530.1994.



139 **141**

4-(*tert*-butyl-dimethyl-silanyloxymethyl)-2-[2-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazole (141): To a stirred solution of oxazole **139** (1.08 g, 2.93 mmol) in THF (27 mL) at –78°C, was added *t*-BuLi (3.45 mL, 5.86 mmol 1.7 M in pentane) dropwise *via* syringe pump over 20 min. After 1 h, Se powder (234 mg, 2.92 mmol) was added under an inverted argon funnel and the reaction was warmed to 0°C. After 1 h or until the solution was homogeneous, cinnamyl bromide (583 mg, 0.44 mL, 2.96 mmol) was added. After 1 h, the reaction was quenched with sat. aq. NH_4Cl (50 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and purified by chromatography on silica gel, eluting with 0-10% Et_2O/hexane to give **141** (1.01 g, 71%) as a white solid:

m.p. 104-106°C.

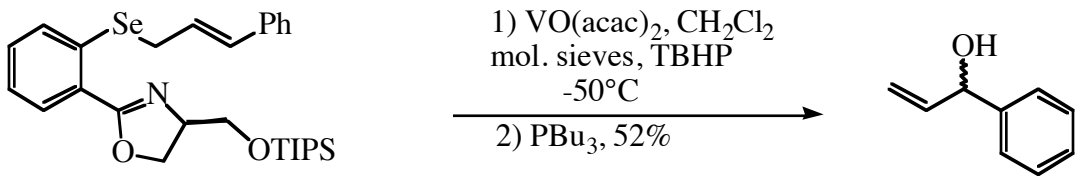
$[\alpha]_D^{23}$ –10.15 (c 1.20, $CHCl_3$).

IR (neat) 2926, 1639, 1469 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.84 (dd, J = 1.6, 7.8 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.18-7.37 (m, 7H), 6.63 (d, J = 15.7 Hz, 1H), 6.42 (dt, J = 7.6, 15.2 Hz, 1H), 4.46-4.53 (m, 1H), 4.40-4.42 (m, 2H), 3.96 (dd, J = 4.0, 10.0 Hz, 1H), 3.73 (d, J = 7.4 Hz, 2H), 3.61 (dd, J = 7.2, 9.8 Hz, 1H), 0.86 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H).

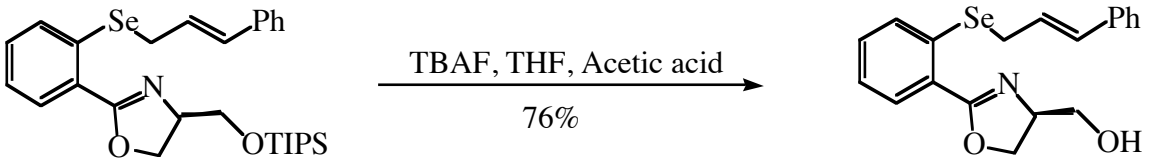
^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 137.0, 136.2, 133.2, 131.0, 130.4, 128.7, 128.3, 127.6, 126.9, 126.4, 125.1, 124.8, 70.1, 68.9, 65.3, 28.8, 26.0, 18.0, -5.0.

HRMS (FAB) calcd. for $C_{25}H_{33}NO_2SiSe$ ($M+H^+$) 487.1446. Found 488.1524.



140 < 5 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **140** (51 mg, 0.10 mmol) in CH_2Cl_2 (0.3 mL) was added $VO(acac)_2$ (3.7 mg, 0.010 mmol), and powdered 4 Å mol. sieves (20 mg). After 20 minutes, the reaction was cooled to –50°C and TBHP (35 μL, 0.19 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (30 mg, 27 μL, 0.11 mmol). After 10 min, at –50°C, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (6.8 mg, 52%) as a yellow oil. The diastereomeric excess of <5% was determined *via* conversion to the Mosher ester.



140 **142**

{2-[2-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazol-4-yl}-methanol (142): To a stirred solution of selenide **140** (97 mg, 0.18 mmol) in THF (1.8 mL) at r.t. was sequentially added acetic acid (33 mg, 32 μL, 0.55 mmol) and TBAF (0.74 mL, 0.74 mmol, 1 M in THF). After 1 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted with EtOAc (3 x 25 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-60% EtOAc/hexane to give **142** (52 mg, 76%) as a white solid.

m.p. 113-115 °C.

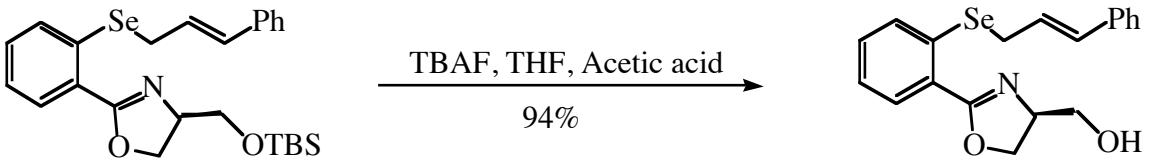
$[\alpha]_D^{23}$ –40.2 (c 1.08, $CHCl_3$).

IR (neat) 3200, 1652 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.81 (dd, J = 1.5, 7.8 Hz, 1H), 7.52 (d, J = 7.9 Hz, 1H), 7.20-7.40 (m, 7H), 6.61 (d, J = 15.6 Hz, 1H), 6.40 (dt, J = 7.5, 15.3 Hz, 1H), 4.53-4.61 (m, 1H), 4.49 (dd, J = 7.9, 9.6 Hz, 1H), 4.34 (dd, J = 7.5, 7.5 Hz, 1H), 4.02 (dd, J = 5.8, 9.3 Hz, 1H), 3.74 (d, J = 7.6 Hz, 2H), 3.64 (dd, J = 3.7, 11.4 Hz, 1H), 2.90 (t, J = 7.5 Hz, 1H).

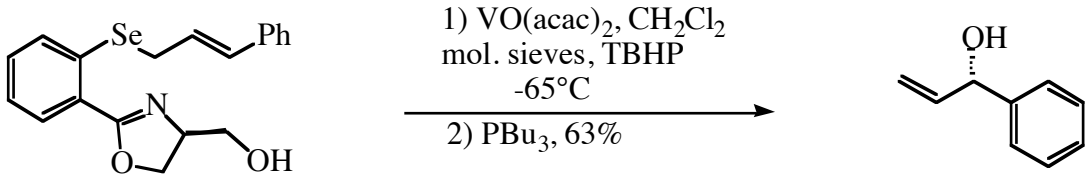
^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 136.9, 136.0, 133.4, 131.3, 130.3, 129.0, 128.7, 127.7, 127.3, 126.5, 125.2, 124.9, 69.2, 68.7, 64.4, 29.4.

HRMS (FAB) calcd. for $C_{19}H_{19}NO_2Se$ ($M+H^+$) 373.0581. Found 374.0659.



141 **142**

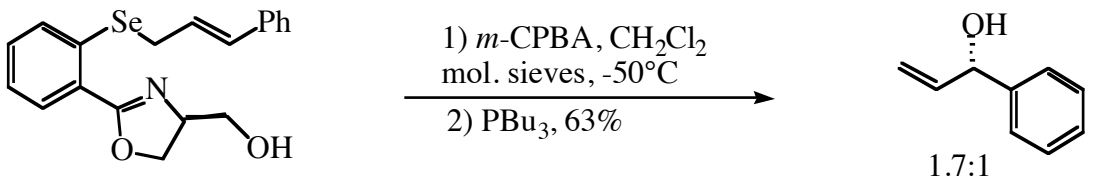
{2-[2-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazol-4-yl}-methanol (142): To a stirred solution of selenide **141** (970 mg, 2.0 mmol) in THF (5 mL) at r.t. was sequentially added acetic acid (314 mg, 0.3 mL, 5.2 mmol) and TBAF (7.6 mL, 7.6 mmol, 1 M in THF). After 1 h, the reaction was quenched with sat. aq. $NaHCO_3$ (20 mL), and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 5-75% EtOAc/hexane to give **142** (700 mg, 94%) as a white solid.



60 % d.e.

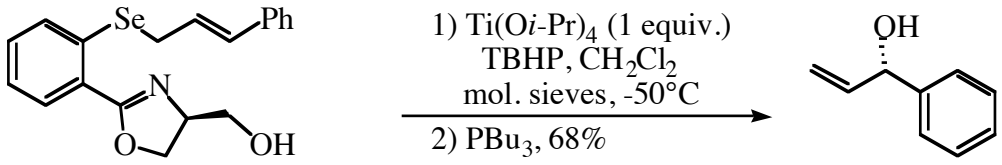
142 **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **142** (53 mg, 0.10 mmol) in CH_2Cl_2 (0.3 mL) at r.t. was added $VO(acac)_2$ (2.7 mg, 0.010 mmol) and powdered 4 Å mol sieves (25 mg). After 20 minutes, the reaction was cooled to –65°C and TBHP (36 μL, 0.20 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (30 mg, 27 μL, 0.11 mmol). After 10 minutes, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (7.6 mg, 63%) as a yellow oil. The diastereomeric excess of 60% was determined *via* conversion to the Mosher ester.



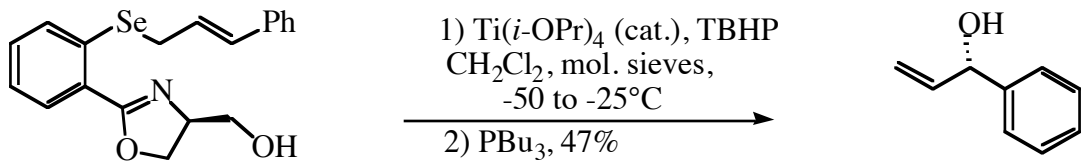
142 26 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **142** (80 mg, 0.22 mmol) and powdered 4 Å mol. sieves (50 mg) in CH_2Cl_2 (0.7 mL) at –50°C was added *m*-CPBA (60 mg, 0.24 mmol). After 11 h, the reaction was quenched with PBu_3 (57 mg, 70 μL, 0.28 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (10 mL) and extracted with Et_2O (3 x 30 mL). The dried organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (17 mg, 63%) as a yellow oil. The diastereomeric excess of 26% was determined *via* conversion to the Mosher ester.



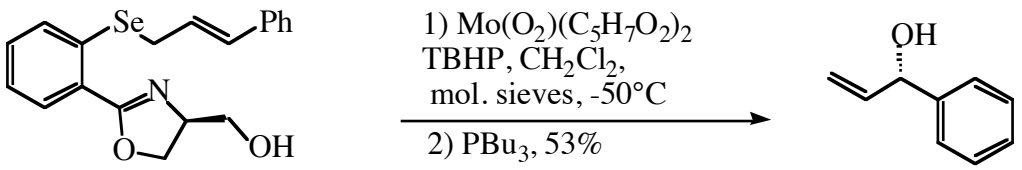
142 30 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **142** (40 mg, 0.11 mmol) in CH_2Cl_2 (0.35 mL) at r.t. was added Ti(*i*OPr)$_4$ (31 mg, 32.1 μL 0.11 mmol) and powdered 4 Å mol. sieves (25 mg). After 20 min. the reaction was cooled to –50°C and TBHP (40 μL, 0.22 mmol, 5.5 M in decane) was added. After 16 h, the reaction was quenched with PBu_3 (33 mg, 30 μL, 0.11 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (10 mg, 68%) as a yellow oil. The diastereomeric excess of 30% was determined *via* conversion to the Mosher ester.



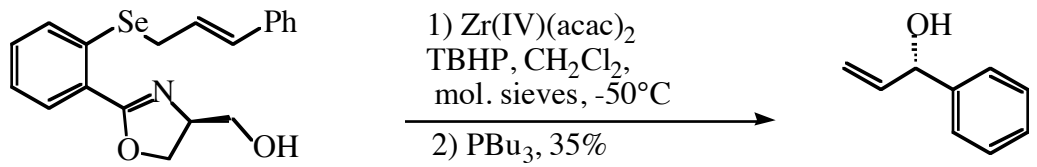
142 30 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **142** (55 mg, 0.150 mmol) in CH_2Cl_2 (0.5 mL), was added Ti(*i*OPr)$_4$ (4.1 mg, 4.4 μL 0.015 mmol) and powdered 4 Å mol. sieves (25 mg). After 20 min, the reaction was cooled to –50°C and TBHP (54 μL, 0.30 mmol, 5.5 M in decane) was added. After 20 min, the reaction was warmed to -25°C. After 24 h, the reaction was quenched with PBu_3 (33 mg, 41 μL, 0.165 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the product residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (47%, 8.9 mg) as a yellow oil. The diastereomeric excess of 30% was determined *via* conversion to the Mosher ester.



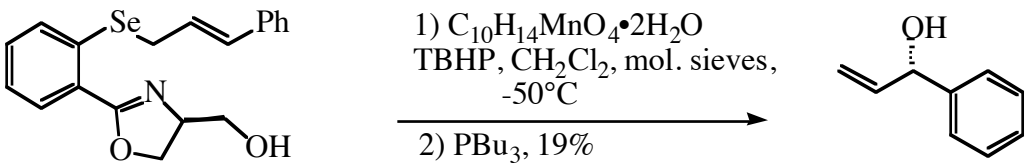
142 25 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **142** (45 mg, 0.12 mmol) in CH_2Cl_2 (0.4 mL) at r.t. was added $Mo(O_2)(acac)_2$ (3.9 mg, 0.12 mmol) and powdered 4 Å mol. sieves (25 mg). After 20 min, the reaction was cooled to –50°C and TBHP (44 μL, 0.24 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (27 mg, 33 μL, 0.13 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (10 mg, 53%) as a yellow oil. The diastereomeric excess of 25% was determined *via* conversion to the Mosher ester.



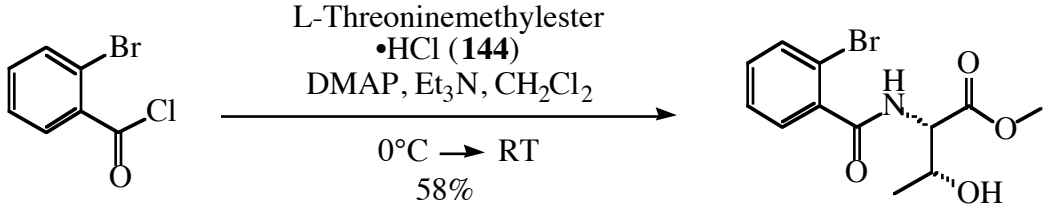
142 35 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **142** (55 mg, 0.150 mmol) in CH_2Cl_2 (0.5 mL), was added Zr(IV)$(acac)_2$ (6.8 mg, 0.015 mmol) and powdered 4 Å molecular sieves (25 mg). The reaction was stirred at room temperature for 20 minutes then cooled to –50°C. After 10 min at –50°C, TBHP (54 μL, 0.30 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (33 mg, 41 μL, 0.165 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (7.0 mg, 35%) as a yellow oil. The diastereomeric excess of 35% was determined *via* conversion to the Mosher ester.



142 34 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **142** (43.0 mg, 0.120 mmol) in CH_2Cl_2 (0.4 mL) at r.t. was added $C_{10}H_{14}MnO_4•2H_2O$ (3.3 mg, 0.012 mmol) and powdered 4 Å mol. sieves (25 mg). After 20 min, the reaction was cooled to –50°C and TBHP (43 μL, 0.24 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (27 mg, 33 μL, 0.132 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (25 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (3.2 mg, 19%) as a yellow oil. The diastereomeric excess of 34% was determined *via* conversion to the Mosher ester.



113 **172**

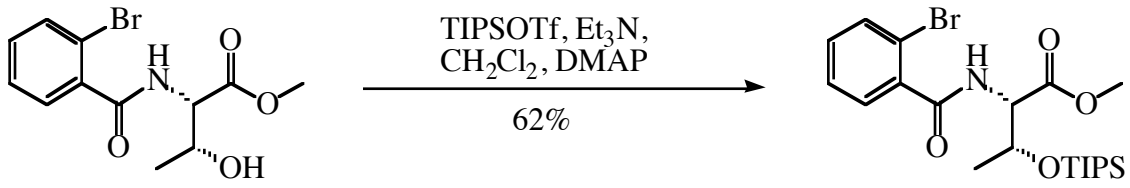
2-(2-bromo-benzoylamino)-3-(S)-hydroxy-butyric acid methyl ester (172): To a stirred of L-threonine methyl ester hydrochloride (**144**) (1.65 g, 9.7 mmol) in CH_2Cl_2 (19 mL) at 0°C was added Et_3N (2.92 g, 4.05 mL, 29.1 mmol) and DMAP (0.297 g, 2.4 mmol). After 10 min, a solution of 2-bromobenzoylchloride (**113**) (2.34 g, 1.4 mL, 14.9 mmol) in CH_2Cl_2 (10 mL) was added dropwise *via* syringe pump over a period of 20 min. Next, the solution was warmed to r.t. After 2 h, the reaction mixture was quenched with sat. aq. NH_4Cl (25 mL) and extracted with Et_2O (3 x 75 mL). The organic layer was sequentially washed with aq. HCl (5%, 50 mL) and sat. aq. $NaHCO_3$ (100 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5-100% EtOAc/hexane to give **172** (1.74 g, 58%) as a white oil:

$[\alpha]_D^{23}$ +1.47 (c 1.91, $CHCl_3$).

IR (neat) 3332, 1744, 1644 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (dd. J = 1.1, 7.9 Hz, 1H), 7.55 (dd, J = 1.8, 7.6 Hz, 1H), 7.26-7.40 (m, 2H), 6.80 (bd, J = 8.1 Hz, 1H), 4.79 (dd, J = 2.2, 8.9 Hz, 1H), 4.44-4.49 (m, 1H), 3.81 (s, 3H), 2.28 (bs, 1H), 1.36 (d, J = 6.4 Hz, 3H),

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 168.1, 137.3, 133.6, 131.7, 129.8, 127.7, 119.5, 68.3, 57.8, 52.9, 20.3.



172 **145**

2-(2-bromo-benzoylamino)-3-(S)-triisopropylsilanyloxy-butyric acid methyl ester (145): To a stirred solution of amino alcohol methyl ester **172** (1.74 g, 5.52 mmol) in CH_2Cl_2 (11 mL) at 0°C was added Et_3N (1.11 g, 1.5 mL, 11 mmol). After 10 min, TIPSOTf (4.9 g, 6 mL, 16 mmol) was added. After 1 h, the reaction was warmed to r.t. After 2 h, the reaction was quenched with sat. aq. NH_4Cl (50 mL) and extracted with Et_2O (3 x 100 mL). The dried filtrate ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2-15% EtOAc/hexane to give **145** (1.60 g, 62%) as a yellow oil:

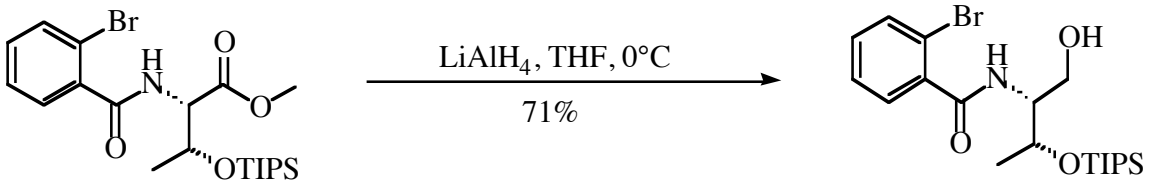
$[\alpha]_D^{23}$ –6.84 (c 1.14, $CHCl_3$).

IR (neat)1744, 1644 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (dd. J = 7.8, 7.9 Hz, 1H), 7.55 (dd, J = 7.8, 7.6 Hz, 1H), 7.26-7.40 (m, 2H), 6.80 (bd, J = 8.1 Hz, 1H), 4.73-4.81 (m, 2H), 3.81 (s, 3H), 1.36 (d, J = 6.4 Hz, 3H), 1.00-1.10(m, 21H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 168.0, 139.0, 133.7, 132.0, 130.1, 128.4, 119.5, 69.5, 59.1, 52.5, 21.2, 18.6, 12.9.

HRMS (FAB) calcd. for $C_{21}H_{34}NO_4BrSi$ ($M+H^+$) 471.1440. Found 472.1519.



145 **173**

2-bromo-*N*-[1-hyrdroxymethyl-2-(S)-(triisopropyl-silanyloxyl)-propyl]-benzamide (173): To a stirred solution of $LiAlH_4$ (3.51 mL, 3.51 mmol, 1.0 M in Et_2O) in THF (26 mL) at 0°C, was added a solution of benzamide **145** (1.50 g, 3.20 mmol) in THF (17.4 mL) dropwise *via* syringe pump over 30 min. The benzamide syringe was rinsed with an additional amount of THF (2 mL). After 30 min the reaction was warmed to r.t. After 2 h, the reaction was quenched with EtOAc/H_2O (100 mL, 1:1) and extracted with ethyl acetate (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-50% EtOAc/hexane to give **173** (1.03 g, 71%) as a light pink oil:

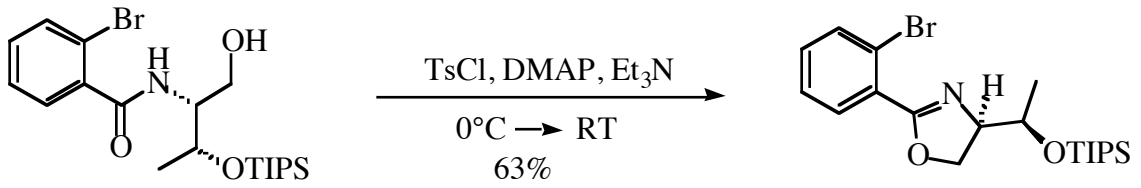
$[\alpha]_D^{23}$ –6.34 (c 1.61, $CHCl_3$).

IR (neat) 2942, 1651, 1506 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (dd, J = 1.7, 4.0 Hz, 1H), 7.60 (dd, J = 1.8, 4.4 Hz, 1H), 7.26-7.40 (m, 2H), 6.80 (bd, J = 9.0 Hz, 1H), 4.43 (dd, J = 4.9, 6.5 Hz, 1H), 4.08-4.10-4.20 (m, 1H), 3.77-3.88 (m, 2H), 2.66 (bs, 1H), 1.36 (d, J = 6.5 Hz, 3H), 1.00-1.10 (m, 21H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 137.5, 133.7, 131.6, 130.2, 127.8, 119.2, 68.1, 64.0, 57.5, 21.7, 18.3, 12.8.

HRMS (FAB) calcd. for $C_{20}H_{34}NO_3BrSi$ ($M+H^+$) 443.1491. Found 444.1569.



173 **146**

2-(2-bromo-phenyl)-4-(S)-(triisopropyl-silanyloxymethyl)-4,5-dihydro-oxazole (146): To a stirred solution of benzamide **173** (750 mg, 1.69 mmol) in CH_2Cl_2 (5 mL) at 0°C, was added DMAP (41 mg, 0.34 mmol) and Et_3N (340 mg, 0.5 mL, 3.38 mmol). After 10 min, TsCl (600 mg, 3.04 mmol) was added and the reaction was warmed to r.t. After 12 h, the reaction was quenched with sat. aq. NH_4Cl (50 mL) and extracted with Et_2O (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **146** (400 mg, 63%) as a light pink oil:

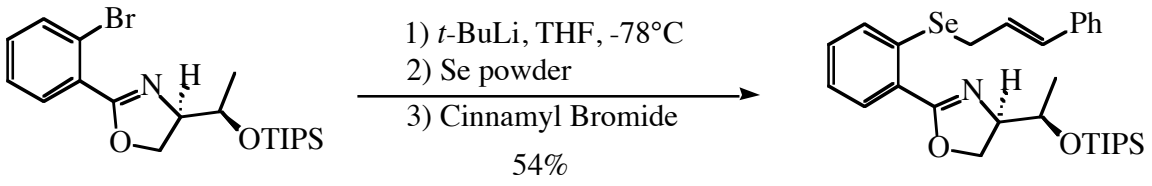
$[\alpha]_D^{23}$ –23.98 (c 1.66, $CHCl_3$).

IR (neat) 2942, 1651, 1463 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.62-7.67 (m, 2H), 7.26-7.37 (m, 2H), 4.54-4.61 (m, 2H), 4.35-4.43 (m, 2H), 1.18 (d, J = 5.5 Hz, 3H), 1.00-1.10 (m, 21H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.2, 133.9, 131.7, 131.4, 130.2, 127.2, 121.8, 72.0, 68.7, 68.4, 17.6, 17.3, 13.0.

HRMS (FAB) calcd. for $C_{20}H_{32}NO_2BrSi$ ($M+H^+$) 425.1386. Found 426.1477.



146 **147**

2-[2-(3-phenyl-allylselanyl)-phenyl]-4-(S)-(triisopropyl-silanyloxymethyl)-4,5-dihydro-oxazole (147): To a stirred solution of *t*-BuLi (1.3 mL, 2.21 mmol, 1.7 M in pentane) in THF (6.7 mL) at –78°C was added a solution of benzamide **146** (434 mg, 1.02 mmol) in THF (3.4 mL) dropwise *via* syringe pump over 20 min resulting in an orange solution. The benzamide conical vial was further rinsed with an additional amount of THF (0.5mL). After 1 h, Se powder (81 mg, 1.02 mmol) was added under an inverse argon funnel and the reaction was warmed to 0°C. After 1 h or until the solution was homogeneous, cinnamyl bromide (220 mg, 0.17 mL, 1.12 mmol) was added. After 1 h, the reaction was quenched with sat. aq. NH_4Cl (20 mL) and extracted with Et_2O (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane. The final product was recrystallized in hexane to give **147** (300 mg, 54%) as a yellow solid:

m.p. 59-63°C.

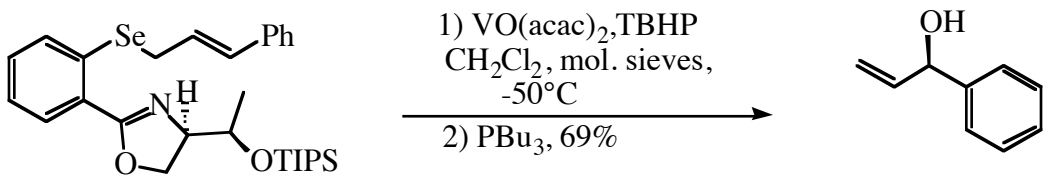
$[\alpha]_D^{23}$ –23.98 (c 1.66, $CHCl_3$).

IR (neat) 2941, 1644, 1464 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (dd, J = 1.6, 7.5 Hz, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.18-7.38 (m, 7H), 6.64 (d, J = 15.6 Hz, 1H), 6.40 (dt, J = 7.5, 15.0 Hz, 1H), 4.67 (dt, J = 4.5, 4.7 Hz, 1H), 4.55 (dd, J = 6.9, 8.6 Hz, 1H), 4.44 (dd, J = 4.5, 6.2 Hz, 1H), 4.35 (dd, J = 8.7, 9.9 Hz, 1H), 3.73 (d, J = 7.5, 2H), 1.18 (d, J = 6.2 Hz, 3H), 1.00-1.10 (m, 21H).

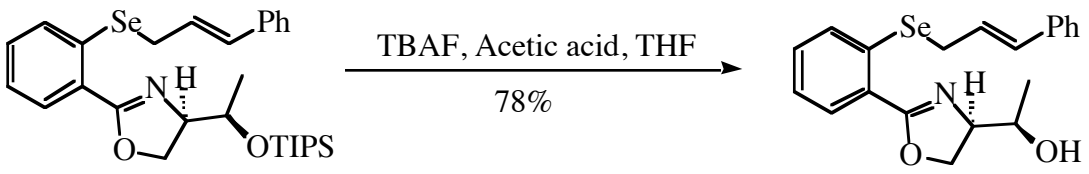
^{13}C NMR (75 MHz, $CDCl_3$) δ 164.0, 137.1, 136.3, 133.2, 131.0, 130.4, 128.7, 128.3, 127.6, 127.0, 126.4, 125.2, 124.8, 72.3, 68.9, 67.7, 28.8, 18.3, 17.7, 12.5.

HRMS (FAB) calcd. for $C_{29}H_{41}NO_2SeSi$ ($M+H^+$) 543.2072. Found 544.2150.



147 18 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **147** (38.0 mg, 0.07 mmol) in CH_2Cl_2 (0.25 mL) at r.t. was added $VO(acac)_2$ (20 mg, 0.0070 mmol), and powdered 4 Å mol. sieves (20 mg). After 20 min, the reaction was cooled to –50°C and TBHP (25 μL, 0.14 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (27 mg, 20 μL, 0.01 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give # (6.5 mg, 69%) as a yellow oil. The diastereomeric excess of 18% was determined *via* conversion to the Mosher ester.



147 **148**

1-{2-[2-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazol-4-yl}-ethanol (148): To a stirred solution of selenide **147** (41 mg, 0.10 mmol) in THF (0.8 mL) at r.t. was added acetic acid (15 mg, 13 μL, 0.2 mmol) and TBAF (1.9 mL, 1.9 mmol, 1 M in THF). After 1 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted with EtOAc (3 x 25 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography over silica gel, eluting with 2-60% EtOAc /hexane to yield **148** (52 mg, 78%) as a white solid:

m.p. 105°C.

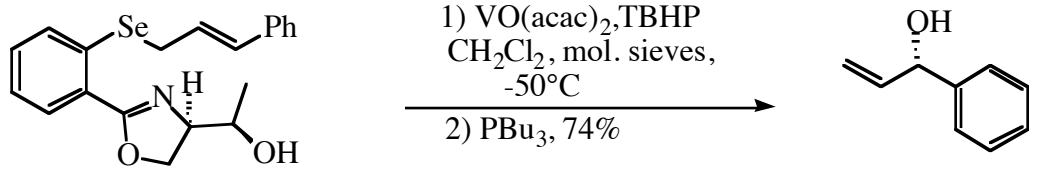
$[\alpha]_D^{23}$ –11.7 (c 0.50, $CHCl_3$).

IR (neat) 3445, 1644, 1472 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.84 (dd, J = 1.5, 7.7 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.20-7.40 (m, 7H), 6.64 (d, J = 15.7 Hz, 1H), 6.43 (dt, J = 7.4, 15.1 Hz, 1H) 4.48 (dd, J = 7.4, 9.3 Hz, 1H), 4.30-4.37 (m, 1H), 4.23 (dd, J = 7.6 Hz, 2H), 3.70 (dd, J = 7.0, 7.9 Hz, 2H), 2.50 (bs, 1H), 1.36 (d, J = 6.5 Hz, 3H).

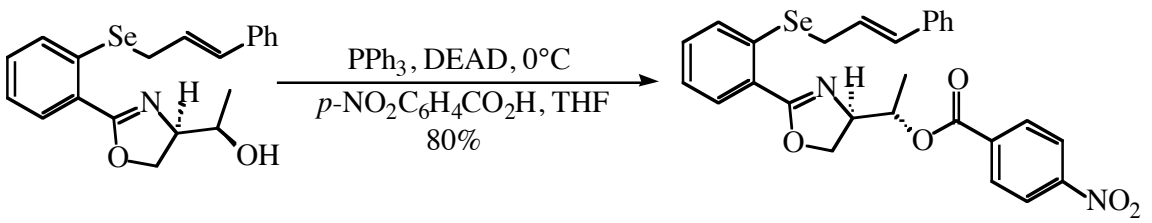
^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 136.9, 136.3, 133.3, 131.3, 130.4, 128.7, 128.7, 127.7, 126.7, 126.5, 125.1, 125.0, 73.4, 70.3, 69.6, 29.3, 20.3.

HRMS (FAB) calcd. for $C_{19}H_{30}NO_2BrSi$ ($M+H^+$) 387.0737. Found 388.0824.



148 50 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **148** (38.0 mg, 0.050 mmol) in CH_2Cl_2 (0.25 mL) at r.t. was added $VO(acac)_2$ (1.3 mg, 0.0050 mmol), and powdered 4 Å molecular sieves (20 mg). After 20 min the reaction was cooled to –50°C and TBHP (19 μL, 0.10 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (27 mg, 15 μL, 0.06 mmol). After 10 minutes, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (6.5 mg, 69%) as a yellow oil. The diastereomeric excess of 50% was determined *via* conversion to the Mosher ester.



148 **174**

Seleno-oxazole ester 174: To a stirred solution of selenide **148** (35 mg, 0.087 mmol) in THF (0.72 mL) at –78°C was added PPh_3 (47 mg, 0.18 mmol) and p-NO2C6H4CO2H (30 mg, 0.18 mmol). After 5 min, DEAD (31 mg, 28 □L, 0.18 mmol) was added dropwise to the reaction. Over 2 h, the reaction was warmed slowly from –78°C to r.t. After an additional 5 h at, the reaction was quenched with sat. aq. NH4Cl (5 mL) and extracted with Et2O (3 x 50 mL). The dried (MgSO4) organic layer was concentrated in vacuo and the residue was purified by chromatography on silica gel, eluting with 0.5-10% EtOAc/hexane to yield **174** (39 mg, 80%) as a white solid:

m.p. 97-99°C.

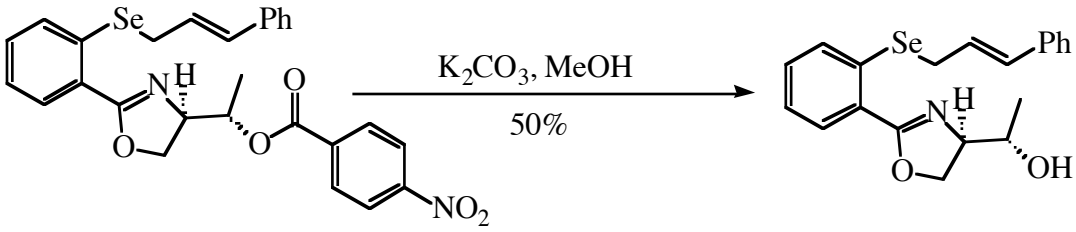
$[\alpha]^{D}_{23}$ +18.4 (c 0.50, CHCl3).

IR (neat) 1723, 1645, 1525, 1272 cm-1.

1H NMR (300 MHz, CDCl3) δ 8.11-8.19 (m, 4H), 7.80-7.83 (dd, J = 1.1, 7.9 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.20-7.37 (m, 7H), 6.58 (d, J = 15.5 Hz, 1H), 6.31 (dt, J = 7.8, 15.5 Hz, 1H), 5.37 (m, 1H), 4.52-4.62 (m, 1H), 4.40-4.50 (dt, J = 8.8, 17.9 Hz, 2H), 3.67 (d, J = 7.4 Hz, 2H), 1.54 (d, J = 6.3 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 164.2, 150.6, 136.9, 136.6, 135.9, 133.2, 131.4, 130.9, 130.4, 128.7, 128.4, 127.7, 126.4, 126.3, 124.9, 123.6, 74.1, 71.0, 68.8, 28.8, 17.2, 14.4.

HRMS (FAB) calcd. for $C_{27}H_{24}N_2O_5Se$ ($M+H^+$) 536.0850. Found 537.0942.



174 **149**

1-{2-[2-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazol-4-yl}-ethanol (149): To a stirred solution of seleno-ester **174** (37 mg, 0.070 mmol) in MeOH (0.3 mL) at r.t. was added K_2CO_3 (2.0 mg, 0.010 mmol). After 30 min, the reaction was quenched with sat. aq. NH_4Cl (3 mL) and extracted with EtOAc (3 x 20 mL), The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue purified by chromatography on silica gel, eluting with 2-40% EtOAc/hexane to give **149** (13 mg, 50%) as a white solid:

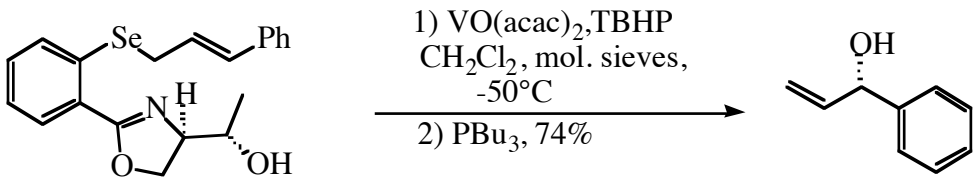
m.p. 100°C.

$[\alpha]_D^{23}$ –5.7 (c 1.20, $CHCl_3$).

IR (neat) 3445, 1644, 1472 cm^{-1}.

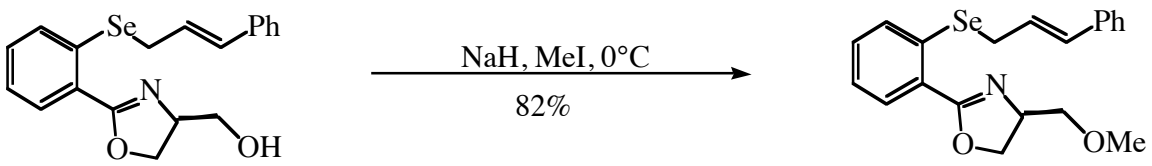
^1H NMR (300 MHz, $CDCl_3$) δ 7.84 (dd, J = 1.5, 7.7 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.20-7.40 (m, 7H), 6.61 (d, J = 15.7 Hz, 1H), 6.41 (dt, J = 7.4, 15.1 Hz, 1H), 4.38-4.42 (m, 3H), 4.11-4.19 (m, 1H), 3.73 (d, J = 7.5 Hz, 2H), 2.05 (bs, 1H), 1.24 (d, J = 6.5 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 136.9, 135.9, 133.3, 131.2, 130.2, 129.0, 128.7, 127.7, 126.5, 125.2, 124.9, 73.0, 68.1, 67.5, 29.4, 18.8, 14.4.



149 66 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of selenide **149** (13 mg, 0.030 mmol) in CH_2Cl_2 (0.11 mL) at r.t. was added $VO(acac)_2$ (1.4 mg, 0.0030 mmol) and powdered 4 Å molecular sieves (20 mg). After 20 min, the reaction was cooled to –50°C and TBHP (12 μL, 0.066 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (20 mg, 14 μL, 0.04 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (3.1 mg, 74%) as a yellow oil. The diastereomeric excess of 66% was determined *via* conversion to the Mosher ester.



142 **143**

4-(S)-methoxymethyl-2-[2-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazole (143): To a stirred solution of NaH (6 mg, 0.148 mmol 60% in mineral oil) and MeI (21 mg, 9.2 μL, 0.15 mmol) in THF (0.4 mL) at 0°C, was added a solution of **142** (50 mg, 0.14 mmol) in THF (0.4 mL) dropwise over 5 min. After 1 h, the reaction was quenched with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 25 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel eluting with 2-20% EtOAc/hexane to yield **143** (41 mg, 82%) as a white solid: m.p. 103-105 °C.

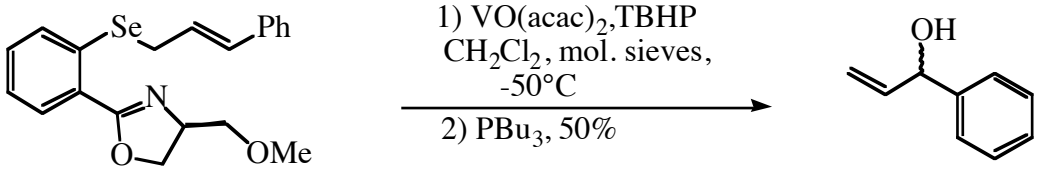
$[\alpha]_D^{23}$ –1.6 (c 1.15, $CHCl_3$).

IR (neat) 2924, 1642, 1471, 1029 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.85 (dd, J = 1.4, 7.8 Hz, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.18-7.37 (m, 7H), 6.63 (d, J = 15.7 Hz, 1H), 6.36 (dt, J = 7.8, 15.7 Hz, 1H), 4.55-4.64 (m, 1H), 4.44 (dd, J = 8.3, 8.3 Hz, 1H), 4.32 (dd, J = 7.5, 7.5 Hz, 1H), 3.71-3.75 (m, 3H), 3.47 (dd, J = 1.9, 7.6 Hz, 1H), 3.41 (s, 3H).

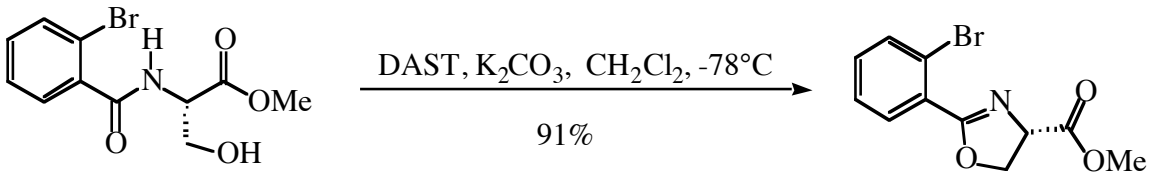
^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 137.0, 136.3, 133.2, 131.2, 130.5, 128.7, 128.4, 127.6, 126.8, 126.4, 125.1, 124.9, 75.0, 70.4, 67.0, 59.5, 28.9.

HRMS (FAB) calcd. for $C_{20}H_{21}NO_2Se$ ($M+H^+$) 387.0737. Found 388.0816.



143 < 5 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of **143** (27 mg, 0.070 mmol) in CH_2Cl_2 (0.25 mL) at r.t. was added $VO(acac)_2$ (1.9 mg, 0.0070 mmol), and powdered 4 Å mol. sieves (20 mg). After 20 min the reaction was cooled to –50°C and TBHP (25 μL, 0.14 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (25 mg, 20 μL, 0.08 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to give **54e** (4.5 mg, 50%) as a yellow oil. The diastereomeric excess of <5% was determined *via* conversion to the Mosher ester.



150 **175**

2-(2-bromo-phenyl)-4,5-dihydro-oxazole-4-(R)-carboxylic acid methyl ester (175): To a stirred solution of **150** (1.24 g, 4.10 mmol) in CH_2Cl_2 (35 mL) at –78°C was added DAST (726 mg, 0.6 mL, 4.50 mmol) dropwise over 15 min. After 1 h, the slurry was quenched with K_2CO_3 (851 mg, 6.20 mmol) and warmed to r.t. After 20 min, sat. aq. $NaHCO_3$ (20 mL) was added and extracted with Et_2O (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silical gel to give **175** (1.06 g, 91%) as a light pink oil:

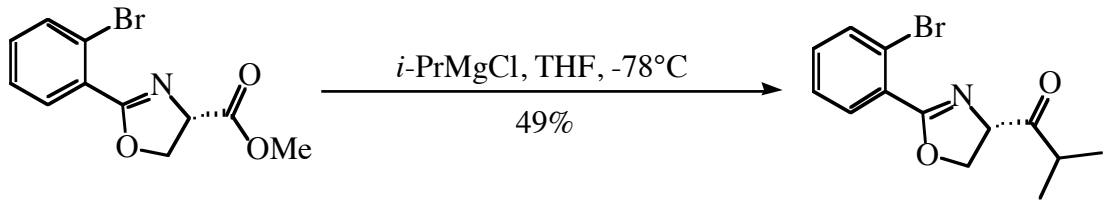
$[\alpha]_D^{23}$ +27.1 (c 1.50, $CHCl_3$).

IR (neat) 2952, 1731, 1651 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (dd, J = 1.9, 6.9 Hz, 1H), 7.62 (dd, J = 1.2, 7.3 Hz, 1H), 7.23-7.34 (m, 2H), 4.99 (dd, J = 8.0, 10.8 Hz, 1H), 4.71 (dd, J = 8.2, 16.9 Hz, 1H), 4.62 (dd, J = 8.6, 10.6 Hz, 1H), 3.78 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 166.0, 134.0, 132.3, 131.8, 128.3, 127.3, 122.0, 69.9, 68.8, 52.9.

HRMS (FAB) calcd. for $C_{11}H_{10}NO_3Br$ ($M+H^+$) 282.9844. Found 283.9922.



175 **151**

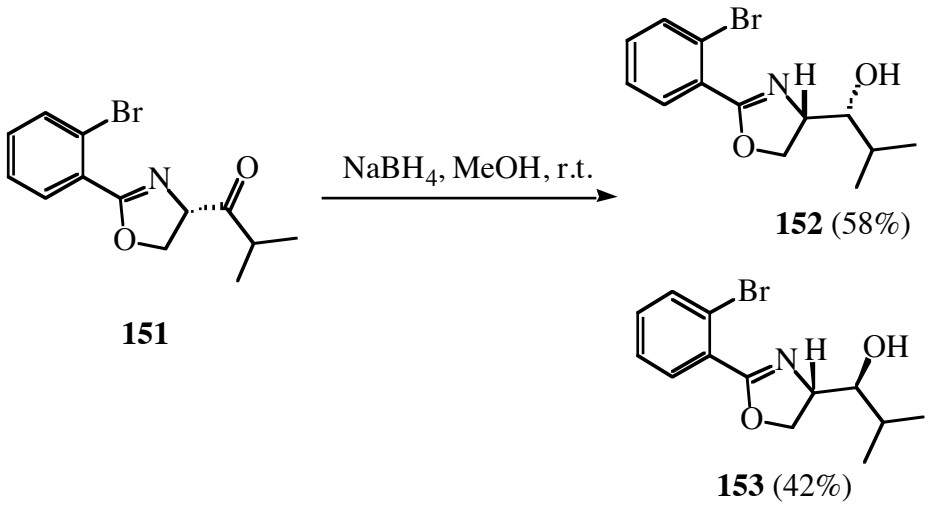
1-[2-(2-bromo-phenyl)-4,5-dihydro-oxazol-4-yl]-2-methyl-propan-1-one (151): To a stirred solution **175** (543 mg, 1.91 mmol) in THF (19 mL) at –78°C was added *i*-PrMgCl (1.1 mL, 2.2 mmol, 2 M in Et_2O) dropwise *via* syringe pump over 20 min. After 1.5 h, the slurry was quenched with NH_4Cl and extracted with Et_2O (3 x 75 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel to give **151** (251 mg, 49%) as a light pink oil:

$[\alpha]_D^{23}$ +10.87 (c 1.26, $CHCl_3$).

IR (neat) 2970, 1715, 1651 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (dd, J = 1.9, 7.3 Hz, 1H) 7.66 (dd, J = 1.4, 7.4 Hz, 1H), 7.26-7.37 (m, 2H), 5.06 (dd, J = 7.4, 10.5 Hz, 1H), 4.82 (dd, J = 7.4, 8.5 Hz, 1H), 4.52 (dd, J = 8.9, 10.9 Hz, 1H), 3.25-3.35 (m, 1H), 1.27 (d, J = 7.2 Hz, 3H), 1.15 (d, J = 6.7 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 211.8, 164.6, 134.2, 132.1, 131.5, 129.2, 127.3, 122.1, 73.8, 68.5, 38.4, 18.8, 17.7.



151

1-[2-(2-bromo-phenyl)-4,5-dihydro-oxazol-4-yl]-2-methyl-propan-1-ol (152 and 153): To a stirred solution of **151** (250 mg, 0.9 mmol) in MeOH (3 mL) at r.t. was added $NaBH_4$ (38 mg, 1 mmol) in portions. After 30 min, the slurry was quenched with sat. aq. NH_4Cl (10 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-30% EtOAc/hexane to give sequentially (S)-(R) **152** (72 mg, 58%) and (S)-(S) **153** (53 mg, 42%) as a light pink oil:

152:

$[\alpha]_D^{23}$ +22.45 (c 0.98, $CHCl_3$).

IR (neat) 3367, 2959 1715, 1654 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.63-7.68 (m, 2H), 7.26-7.37 (m, 2H), 4.50-4.64 (m, 2H), 4.20 (dt, J = 1.0, 10.9 Hz, 1H), 3.25 (dt, J = 4.5, 6.7 Hz, 1H), 2.28 (d, J = 7.1 Hz, 1H), 1.88 (m, 1H), 1.05 (d, J = 6.8 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 133.9, 132.0, 131.3, 129.7, 127.4, 122.1, 79.1, 70.5, 69.6, 31.8, 19.7, 18.2.

153:

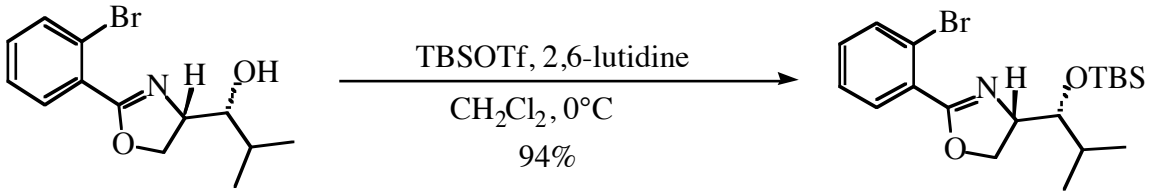
$[\alpha]_D^{23}$ +5.93 (c 1.02, $CHCl_3$).

IR (neat) 3367, 2959 1715, 1654 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.62-7.67 (m, 2H), 7.26-7.37 (m, 2H), 4.39-4.56 (m, 2H), 3.72 (dd, J = 2.8, 7.7 Hz, 2H), 1.85 (bs, 1H), 1.71-1.77 (m, 1H), 1.07 (d, J = 6.5 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 133.9, 131.9, 131.2, 129.9, 127.4, 122.0, 79.0, 69.8, 68.0, 30.6, 19.2, 19.0.

HRMS (FAB) calcd. for $C_{13}H_{16}NO_2Br$ ($M+H^+$) 297.0364. Found 298.0443.



152 **154**

2-(2-bromo-phenyl)-4-[1-(*tert*-butyl-dimethyl-silanyloxy)-2-methyl-propyl]-4,5-dihydro-oxazole (154): To a stirred solution of **152** (70 mg, 0.24 mmol) in CH_2Cl_2 (0.5 mL) at 0°C was sequentially added 2,6-lutidine (39 mg, 42 μL, 0.36 mmol) and TBSOTf (75 mg, 65 μL, 0.28 mmol). After 1 h, the reaction was quenched with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 20 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 1-10% EtOAc/hexane to give **154** (90 mg, 94%) as a pink oil:

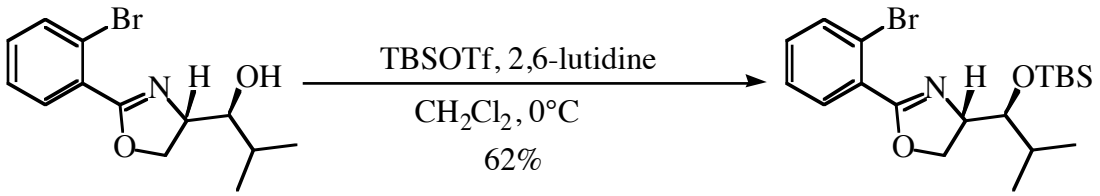
$[\alpha]_D^{23}$ +8.14 (c 0.70, $CHCl_3$).

IR (neat) 2956 1653, 1471 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (dd, J = 2.0, 7.5 Hz, 1H), 7.61 (dd, J = 1.6, 7.8 Hz, 1H), 7.24-7.36 (m, 2H), 4.55-4.60 (m, 1H), 4.36-4.40 (m, 2H), 3.72 (dd, J = 4.0, 5.4 Hz, 1H), 1.00-1.95 (m, 1H), 1.03 (d, J = 6.7 Hz, 3H), 0.97 (d, J = 6.8 Hz, 3H), 0.91 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 134.0, 131.7, 130.3, 127.2, 121.8, 77.9, 70.8, 69.6, 31.0, 26.1, 21.0, 18.5, 17.4, -3.8, -4.2.

HRMS (FAB) calcd. for $C_{18}H_{28}NO_2SiBr$ ($M+H^+$) 397.1073. Found 412.1318.



153 **155**

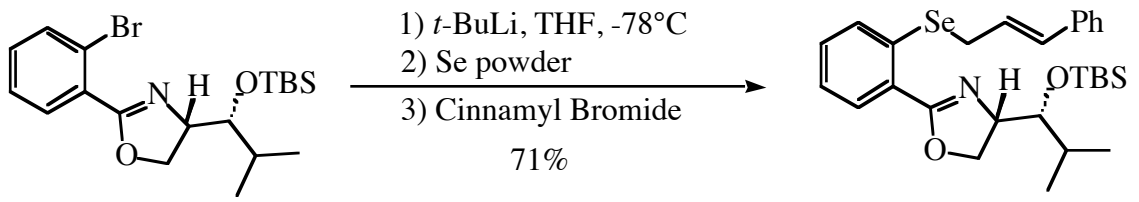
2-(2-bromo-phenyl)-4-[1-(*tert*-butyl-dimethyl-silanyloxy)-2-methyl-propyl]-4,5-dihydro-oxazole (155): To a stirred solution of **153** (57 mg, 0.19 mmol) in CH_2Cl_2 (0.4 mL) at 0°C was sequentially added 2,6-lutidine (32 mg, 27 μL, 0.29 mmol) and TBSOTf (61 mg, 52 μL, 0.23 mmol). After 1 h, the reaction was quenched with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 20 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 1-10% EtOAc/hexane to give **155** (48 mg, 62%) as a light pink oil:

$[\alpha]_D^{23}$ +1.67 (c 0.78, $CHCl_3$).

IR (neat) 2956 1653, 1471 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.76 (dd, J = 2.0, 7.5 Hz, 1H), 7.64 (dd, J = 1.6, 7.8 Hz, 1H), 7.24-7.36 (m, 2H), 4.53 (dd, J = 5.7, 7.0 Hz, 1H), 4.33-46 (m, 2H), 3.99 (dd, J = 2.0, 4.2 Hz, 1H), 1.81-1.87 (m, 1H), 0.96 (d, J = 7.0 Hz, 3H), 0.92 (d, J = 4.3 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 3H), -.015 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 134.0, 131.7, 130.3, 127.2, 121.8, 77.9, 70.8, 69.6, 31.0, 26.1, 21.0, 18.5, 17.4, -3.8, -4.2.



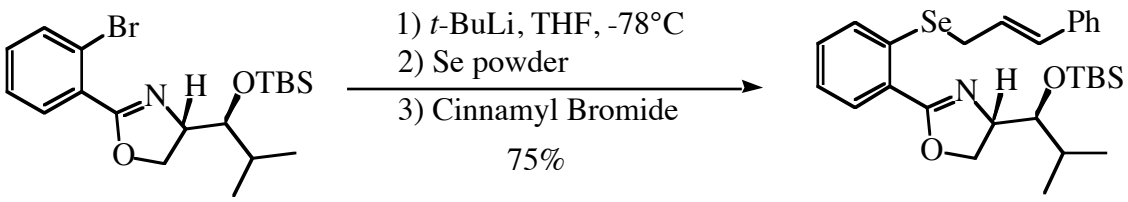
154 **156**

4-[1-(*tert*-butyl-dimethyl-silanyloxy)-2-methyl-propyl]-2-[2-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazole (156): To a stirred solution of **154** (340 mg, 0.82 mmol) in THF (7.2 mL) at –78°C was added *t*-BuLi (1.0 mL, 1.7 mmol, 1.7 M in pentane) dropwise *via* syringe pump over 20 min resulting in an orange solution. After 1 h, Se powder (65 mg, 0.82 mmol) was added to the reaction under an inverse argon funnel and warmed to 0°C. After 2 h, cinnamyl bromide # (162 mg, 0.12 mL, 0.82 mmol) was added. After 1 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and the residue was purified by chromatography on silca gel, eluting with 0-10% EtOAc/hexane to give **156** (300 mg, 71%) as a white solid:

$[\alpha]_D^{23}$ –10.9 (c 1.72, $CHCl_3$).

IR (neat) 2954 1644, 1470 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.84 (dd, J = 1.5, 7.8 Hz, 1H), 7.47 (d, J = 8.1 Hz, 1H), 7.16-7.36 (m, 7H), 6.66 (d, J = 15.7 Hz, 1H), 6.45 (dt, J = 7.7, 15.7 Hz, 1H), 4.60-4.64 (m, 1H), 4.29-4.42 (m, 2H), 3.81 (dd, J = 4.4, 9.1 Hz, 1H), 1.97-1.99 (m, 1H), 1.00 (bs, 21H), 0.25 (s, 3H), 0.16 (s, 3H).



155 **157**

4-[1-(*tert*-butyl-dimethyl-silanyloxy)-2-methyl-propyl]-2-[2-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazole (157): To a stirred solution of selenide **155** (176 mg, 0.43 mmol) in THF (3.8 mL) at –78°C was added *t*-BuLi (0.5 mL, 0.85 mmol, 1.7 M in pentane) dropwise *via* syringe pump over 20 min resulting in an orange solution. After 1 h, Se powder (36 mg, 0.43 mmol) was added to the reaction under an inverse argon funnel and warmed to 0°C. After 2 h, cinnamyl bromide # (63 mg, 63 μL, 0.43 mmol) was added. After 1 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and the residue was purified by chromatography on silca gel, eluting with 0-10% EtOAc/hexane to give **157** (169 mg, 71%) as a white solid:

m.p. 122°C.

$[\alpha]_D^{23}$ –44.2 (c 1.23, $CHCl_3$).

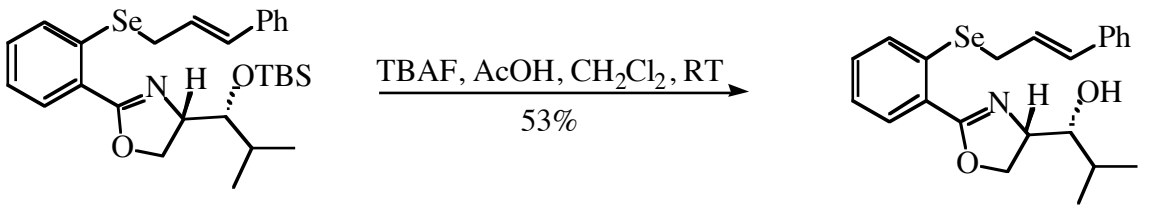
IR (neat) 2954 1644, 1470 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (dd, J = 1.5, 7.8 Hz, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.16-7.36 (m, 7H), 6.62 (d, J = 15.7 Hz, 1H), 6.39 (dt, J = 7.7, 15.7 Hz, 1H), 4.43-4.50 (m, 2H), 4.27-4.33 (m, 1H), 3.92 (dd, J = 2.2, 4.2 Hz, 1H), 3.71 (d, J = 7.4 Hz, 2H), 1.82-1.87 (m, 1H), 0.96 (d, J = 7.0 Hz, 3H), 0.92 (d, J = 6.1 Hz, 3H), 0.88 (s, 9 H), 0.05 (s, 3H), -0.11 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.2, 137.1, 136.4, 133.1, 130.8, 130.4, 128.8, 128.7,

128.1, 127.6, 126.8, 126.5, 125.3, 124.7, 78.3, 70.0, 67.7, 33.5, 26.1, 19.0, 18.5, 18.4, -3.9, -4.0.

HRMS (FAB) calcd. for $C_{28}H_{39}NO_2SiSe$ ($M+H^+$) 529.1915. Found 530.1993.



156 **158**

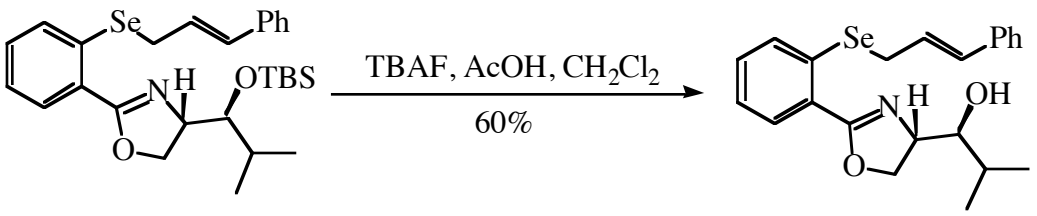
2-methyl-1-{2-[-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazol-4-yl}-propan-1-ol (158): To a stirred solution of selenide **156** (320 mg, 0.6 mmol) in CH_2Cl_2 (1.23 mL) at r.t. was sequentially added acetic acid (78 mg, 70 μL, 1.35 mmol) and TBAF (7.5 mL, 7.5 mmol, 1 M in THF). After 1 h the reaction was quenched with sat. aq. NH_4Cl (20 mL), and extracted with EtOAc (3 x 15 mL). The dried ($MgSO_4$) filtrate was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-30% EtOAc /hexane to yield **158** (134 mg, 53%) of a white solid:

$[\alpha]_D^{23}$ –22.4 (c 2.0, $CHCl_3$).

IR (neat) 3209, 1651, 1449, 1253 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 7.8 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.20-7.39 (m, 7H), 6.59 (d, J = 15.7 Hz, 1H), 6.37 (dt, J = 7.3, 15.4 Hz, 1H), 4.54-4.58 (m, 2H), 4.47 (dd, J = 7.8, 7.8 Hz, 1H), 4.23 (dd, J = 7.7, 7.7 Hz, 1H), 3.72 (d, J = 7.5 Hz, 2H), 3.23 (dd, J = 7.1, 11.8 Hz, 1H), 2.29 (d, J = 7.7 Hz, 1H), 1.90-1.97 (m, 1H), 1.07 (d, J = 6.7 Hz, 3H), 1.06 (d, J = 6.7 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.8, 137.2, 136.4, 133.5, 131.5, 130.5, 129.0, 128.9, 127.9, 127.2, 126.7, 125.3, 79.2, 70.4, 69.9, 32.4, 29.6, 20.0, 18.6.



157 **159**

2-methyl-1-{2-[-(3-phenyl-allylselanyl)-phenyl]-4,5-dihydro-oxazol-4-yl}-propan-1-ol (159): To a stirred solution of selenide **157** (195 mg, 0.38 mmol) in CH_2Cl_2 (1 mL) at r.t. was sequentially added acetic acid (44 mg, 42 μL, 0.74 mmol) and TBAF (2.1 mL, 2.1 mmol, 1 M in THF). After 1 h, the reaction was quenched with sat. aq. NH_4Cl (20 mL) and extracted with EtOAc (3 x 20 mL). The dried ($MgSO_4$) organic layer was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-30% EtOAc /hexane to give **159** (75 mg, 60%) as a white solid:

m.p. 125°C.

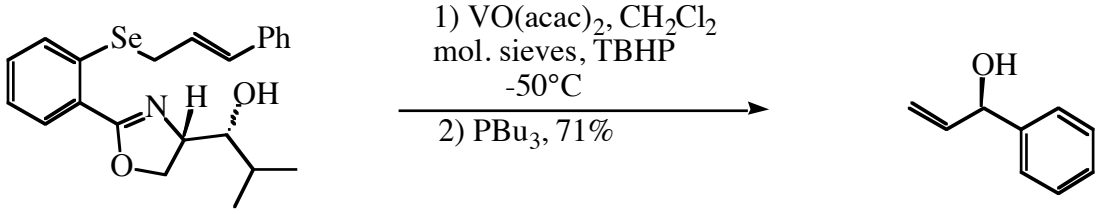
$[\alpha]_D^{23}$ –22.4 (c 2.0, $CHCl_3$).

IR (neat) 3209, 1651, 1449, 1253 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (dd, J = 1.2, 7.60 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.20-7.39 (m, 7H), 6.58 (d, J = 15.7 Hz, 1H), 6.40 (dt, J = 7.3, 15.4 Hz, 1H), 4.56-4.64 (m, 1H), 4.37-4.41 (m, 2H), 3.71-3.76 (m, 3H), 2.12 (bs, 1H), 1.66-1.79 (m, 1H), 1.09 (d, J = 6.6 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H).

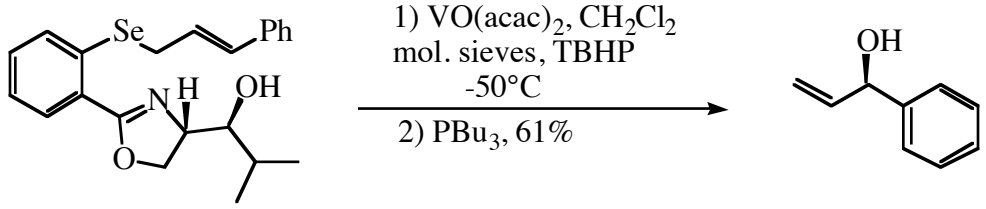
^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 136.9, 135.9, 133.3, 131.2, 130.1, 129.0, 128.7, 127.7, 127.4, 126.5, 125.2, 125.0, 77.7, 70.0, 67.5, 30.6, 29.4, 19.3, 19.2.

HRMS (FAB) calcd. for $C_{22}H_{25}NO_2Se$ ($M-H^+$) 415.1050. Found 414.1136.



158 70 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of **158** (51 mg, 0.12 mmol) in CH_2Cl_2 (0.41 mL) at r.t. was added $VO(acac)_2$ (3 mg, 0.012 mmol) and powdered 4 Å mol. sieves (50 mg). After 20 min, the reaction was cooled to –50°C and TBHP (44 μL, 0.24 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (35 mg, 34 μL, 0.13 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) filtrate was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to yield **54e** (12 mg, 71%) as a yellow oil. The diastereomeric excess of 70% was determined *via* conversion to the Mosher ester.



159 62 % d.e. **54e**

1-Phenyl-prop-2-en-1-ol (54e): To a stirred solution of **159** (48 mg, 0.11 mmol) in CH_2Cl_2 (0.4 mL) at r.t. was added $VO(acac)_2$ (2.9 mg, 0.011 mmol) and powdered 4 Å mol. sieves (50 mg). After 20 min, the reaction was cooled to –50°C and TBHP (42 μL, 0.23 mmol, 5.5 M in decane) was added. After 20 h, the reaction was quenched with PBu_3 (34 mg, 32 μL, 0.12 mmol). After 10 min, the slurry was diluted with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) filtrate was concentrated *in vacuo* and the residue was purified by chromatography on silica gel, eluting with 2-20% EtOAc/hexane to yield **54e** (9.0 mg, 61%) as a yellow oil. The diastereomeric excess of 62% was determined *via* conversion to the Mosher ester.

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[3] Zhou, Q.; Pfaltz, A. *Tetrahedron* **1994**, *50*, 4467-78.
[4] Zhou, Q.; Pfaltz, A. *Tetrahedron* **1994**, *50*, 4467-78.