Alkene Amination Reactions Enabled by Organoselenium Catalysis

Derek C. Obenschain

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Reading Committee:

Forrest E. Michael, Chair

Gojko Lalic

Champak Chatterjee

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Abstract

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Derek C. Obenschain

Chair of the Supervisory Committee:
Associate Professor Forrest E. Michael
Department of Chemistry

The discovery of new modes of catalytic reactivity represents the forefront of organic methodology. Many important transformations are catalyzed by expensive transition metal catalysts. Replacing these with cheaper, more abundant alternatives is an important goal. This dissertation explores the development of new catalytic oxidative transformations enabled by organoselenium catalysts. The focus of this work is on using these organoselenium catalysts to enable a variety of amination reactions.

Herein, the development of three oxidative allylic C-H amination reactions enabled by novel organoselenium catalysis is presented: the allylic C-H amination of alkenes using sulfonamides, the expansion of this transformation to utilize carbamates and trifluoroacetamide as nucleophiles, and the direct formation of conjugated sulfonyl imines from alkenes. The development of a 1,2-diamination of alkenes using these same organoselenium catalysts is also discussed.

A novel selenium-catalyzed C-H amination reaction was achieved using either phosphine or imidazolium-based ligands on selenium with diacetoxyiodobenzene as an oxidant and sulfonamides serving as the amine sources. This transformation enabled amination for all alkene substitution patterns with a highly predictable regiochemical outcome. An extensive number of functional groups were tolerated by these reaction conditions and numerous synthetically valuable sulfonamide and sulfamate nucleophiles were found to be suitable coupling partners for this reaction. Pharmaceutical drugs, natural products, and terpenoids were derivatized using this method demonstrating its power for late-stage functionalization.

A direct protocol for the synthesis of conjugated sulfonyl imines from highly substituted alkenes was also developed. This reaction was realized by increasing the oxidizing power of the amination reaction conditions and through the careful optimization of the catalyst and sulfonamide coupling partner. The use of the triarylphosphine selenide catalysts were critical in the development of this reaction by suppressing a competitive diamination reaction. The use of electron rich sulfonamides was found to be important for high yields of the desired imine products. Various novel derivatizations of the imine products were developed including a transimination protocol.

An expansion of the selenium-catalyzed C-H amination reaction described above to incorporate carbamate nucleophiles was also realized. The use of N-tert-butyl imidazolium ligand on selenium proved critical in enabling good yields for this transformation. Numerous synthetically valuable carbamate nucleophiles including benzyl, allyl, and trimethylsilyl ethyl carbamates were found to be competent coupling partners in this reaction. The transformation was

successful for a variety of 1,1-di- and tri-substituted olefins offering unprecedented direct access to allylic carbamates through catalytic C-H activation. Trifluoroacetamide was also shown to be a suitable coupling partner for this reaction. The late stage C-H amination of natural products and terpene derivatives was demonstrated.

A novel selenium catalyzed 1,2-diaddition of alkenes was also demonstrated. Unlike the previous three reports, this transformation proceeds via formation of a seleniranium intermediate. The use of TMSOTf as a fluoride scavenger was critical to prevent the addition/elimination pathway typically observed for oxidative selenium alkene reactions. High yields were enabled for this transformation using phosphoramide ligands on selenium. The diamination reaction was demonstrated on an extensive variety of terminal and 1,2-disubstituted alkenes in high yields.

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LIST OF ABBREVIATIONS

Å:	Angstrom
Ac:	Acetyl
Ar:	Aryl
Bn:	Benzyl
Bz:	Benzoyl
Boc:	*tert*-Butyloxycarbonyl
Cbz:	Carbobenzyloxy
Cy:	Cyclohexyl
DCC:	N,N’-Dicyclohexylcarbodiimide
DCE:	Dichloroethane
DMSO:	Dimethyl sulfoxide
DMAP:	4-Dimethylaminopyridine
dppf:	Bis(diphenylphosphino)ferrocene
ESI MS:	Electrospray Ionization Mass Spectrometry
Et:	Ethyl
GC/MS:	Gas Chromatography/ Mass Spectrometry
hr:	Hour
Hz:	Hertz
IAd:	1,3-Bis(1-adamantal)imidazole-2-ylidine
IBn:	1,3-Di-benzylimidazol-2-ylidine
ICy:	1,3-Di-cyclohexylimidazol-2-ylidine

IMe:	1,3-Di-methylimidazole-2-ylidine
IMes:	1,3-Bis(2,4,6-trimethylphenyl)imidazole-2-ylidine
i-Pr:	*iso*-Propyl
IPr:	1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidine
ItBu:	1,3-Di-*tert*-butylimidazol-2-ylidine
L:	Ligand
Me:	Methyl
Mes:	Mesityl
MHz:	Megahertz
MIDA:	N-Methyliminodiacetate
mp:	Melting Point
Ms:	Mesyl
Nbos:	*ortho*-Nitrobenzenesulfamyl
NHC:	*N*-Heterocyclic carbene
NFBS:	*N*-Fluorobenzenesulfonamide
NMR:	Nuclear Magnetic Resonance

Abbreviations for NMR Splitting:

s:	singlet
d:	doublet
t:	triplet
q:	quartet
quin:	quintet
m:	multiplet

br:	broad
Ns:	4-Nitrobenzenesulfonyl
Nu:	Nucleophile
Ph:	Phenyl
PG:	Protecting Group
PMP:	*para*-Methyoxyphenyl
ppm:	Parts Per Million
rt:	Room Temperature
t-Bu:	*tert*-Butyl
TBDPS:	*tert*-Butyldiphenylsilyl
Tces:	2,2,2-Trichloroethoxysulfonyl
TEMPO:	2,2,6,6-Tetramethylpiperidine 1-oxyl
Tf:	Trifluoromethanesulfonyl
TfO:	Trifluoromethanesulfonate
TMSOTf:	Trimethylsilyl Trifluoromethanesulfonate
Tfes:	2,2,2-Trifluoroethoxysulfonyl
THF:	Tetrahydrofuran
TLC:	Thin Layer Chromatography
TMS:	Tetramethylsilane
TMSOTf:	Trimethylsilyl Trifluoromethanesulfonate
Troc:	2,2,2-Trichloroethoxycarbonyl
Ts:	*para*-Toluenesulfonyl

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I owe the completion of my graduate studies to many people. This section is my attempt to thank them.

First, I would like to thank my advisor, Forrest Michael, for everything he has done to help me succeed in my graduate career. One of my biggest regrets from graduate school was that I never had the opportunity to take a class taught by Forrest. He is perhaps the best teacher I have ever had, and I found his passion for learning organic chemistry truly inspiring. This passion for learning, coupled with his unbelievably amazing memory, made Forrest an invaluable resource for project ideas and solutions. Nearly any problem I encountered, Forrest either had a solution ready or would help find one immediately. His extensive knowledge of the field coupled with his hands-off approach to research management enabled me to develop into a much more self-reliant and creative chemist, knowing that I had him as a safety net if I truly got stuck.

I would like to thank my committee members: Gojko Lalic and Champak Chatterjee. Gojko has been an excellent source of knowledge during my graduate career. We shared joint group meetings with his group and I greatly benefitted from seeing his perspective on chemistry and his approach to research. Champak is an amazing teacher and I really enjoyed running into him in the hallways. He can always put a smile on your face, and I appreciated his insights and reminders to think about the biological applications of my research.

Next, thank you to the members of the Michael Lab. First, there is my best bro, John Tabor. We joined the Michael Lab at the same time and went through the entire journey together. I feel so lucky to have him as a friend. So many of my best memories during this time are thanks to him, from pulling all-nighters working on physical organic exams (with some late night trips to Thai

65), to brewing and drinking great beers with Andy, to belting out some lab classics while we worked. John's positive attitude, his stress-free approach to problem solving, and his willingness to tackle any challenge were inspirational during graduate school and are traits I still try to emulate. Thank you also to Andrew Holtzen and Valerie Lesniak, who joined the lab with us. I really enjoyed getting to know them and sharing classroom and research experiences with them. I need to thank the members who have joined after me: Wei Pin Teh, Tianyi Zhang, Alex Dohoda, Parker Maloney, Janna Berman, Jesse Spillane, and Zach Stein. They made coming into work so much better and I will miss all of them. I also would like to thank the members of Gojko's lab. It was always inspiring getting to watch how quickly they could develop their projects.

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Thank you to my previous chemistry teachers and mentors without whom I would not be here including Stephen Moore, Karl Zachary, and of course, Wade Downey. Thank you for setting me on this path.

Graduate school took me far from my home but thanks to the love and support of my family I never felt alone. I owe so much of my success to my parents, Tina and Todd, my sisters, Ayn and Kir, and my grandmother, Nana. I also need to thank my future mother-in-law, Karen, who took me in during this time and supported me without question. I know my family is also appreciative that she was there to help me.

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For everyone else to whom I owe some of my success, yet failed to specifically thank in this section, thank you.

DEDICATION

To my parents, Todd and Tina,

my sisters, Kir and Ayn,

my grandparents, Nana and Jenny,

and my fiancé Molly.

For everything you have done for me.

Chapter 1. ORGANOSELENIUM CATALYZED ALLYLIC C-H AMINATION OF ALKENES[1]

Section 1: INTRODUCTION

The selective functionalization of specific carbon-hydrogen (C-H) bonds is a powerful tool for synthetic chemists which allows for the rapid functionalization of complex organic molecules. Traditional methods for diversification of complex molecules often require completely unique syntheses for each target variation. Even when a novel synthesis is not required, the installation of an often-sensitive synthetic handle is typically necessary. If this synthetic handle is installed too early, compatibility issues with subsequent steps in the synthesis may arise. On the other hand, late stage installation of the synthetic handle could suffer from regiochemical issues and/or compatibility issues with previously installed functional groups. Furthermore, after the synthetic handle has been successfully installed, an additional synthetic step is required to convert it to the final desired functional group. Late-stage C-H functionalization has emerged as an economically and environmentally advantageous alternative to these traditional synthetic methods. By selectively replacing a specific C-H bond in a complex molecule with a desired functional group, numerous otherwise necessary synthetic steps can be avoided. Beyond shortening the synthetic timeline, this approach has the added benefits of improving the overall atom economy and significantly reducing the chemical waste generated for a target synthesis. Since late-stage C-H functionalization is more efficient, cost-effective, and environmentally benign than traditional synthetic approaches, the development of new methodologies for late-stage C-H functionalization has drawn significant attention from the synthetic community.[2]

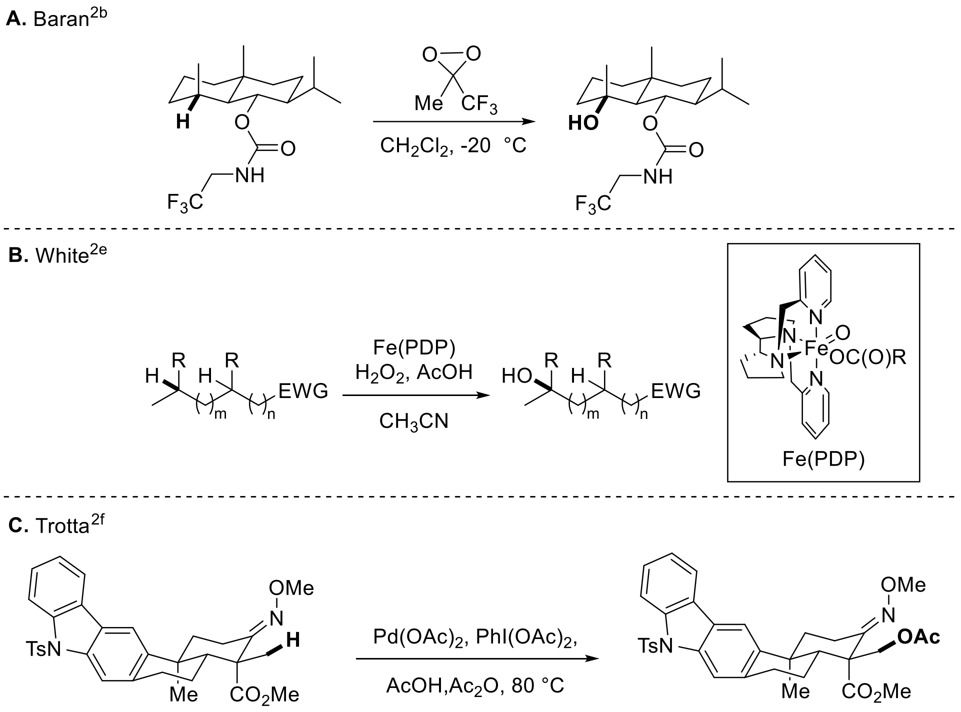


Figure 1.1. Selected examples of late-stage C-O functionalization enabled by C-H activation

Much of this focus has been on the development of new methods for the total synthesis of natural products through the highly specific late stage installation of carbon-oxygen (C-O) bonds through the C-H activation of terpene derivatives (Figure 1.1).[3] These methods have exploited various means to achieve their selectivity such as activating the weakest C-H bonds (often tertiary) (Figure 1.1A and B), developing systems which are highly sensitive to stereoelectronic effects (Figure 1.1B), and/or utilizing directing groups to select for only one position (Figure 1.1A and C). While these methods have been extensively explored, the analogous C-H amination reactions have remained underdeveloped (Figure 1.2). Owing to the known biological activity of amine groups as well as the extensive use of oxidized monoterpenes as flavoring agents, in perfumes, and as synthetic building blocks, the selective C-H amination of terpenes would provide unprecedented access to a complex range of potentially valuable molecules.

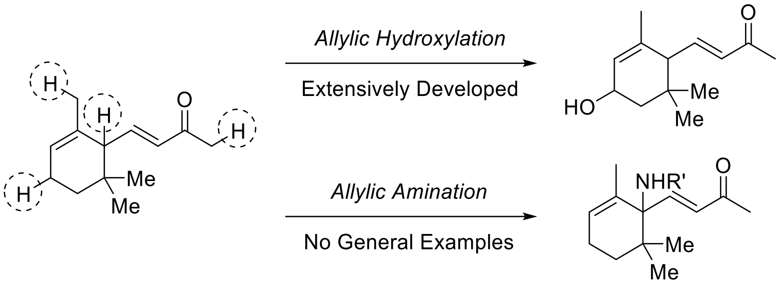


Figure 1.2. Site-selective C-H Allylic Oxidation

Perhaps the most significant obstacle to the development of new C-H functionalization reactions comes from the ubiquitous nature of C-H bonds in organic molecules. This abundance of C-H bonds can make the selective functionalization of just one specific C-H bond a daunting task. We envisioned a highly specific C-H amination reaction of complex molecules could be realized through the functionalization of the comparatively weak allylic C-H bonds found in many terpenoids and their derivatives. Relative to their aliphatic counterparts, allylic C-H bonds are more acidic and have decreased bond strengths due to their proximity to the adjacent π-system. We envisioned that these properties might allow a catalytic system to differentiate between these allylic C-H bonds and other aliphatic C-H bonds thereby selectively functionalizing only the allylic position even in complex natural products. While these allylic groups provide a means to differentiate C-H groups in complex molecules, they also present numerous regio- and chemo-selectivity challenges (Figure 1.3). These selectivity issues have limited the success in employing previously developed C-H amination approaches to the late-stage allylic functionalizations. For instance, currently employed nitrenoid based methods for C-H amination result in competing aziridination and alkene addition reactions when applied to alkenes.[4] Similarly, radical based approaches also suffer from competing aziridination and alkene additions for alkenes but the presence of the radical also commonly results in alkene transposition.[5] This additional complication arises due to the nature of the generated allylic radicals. Without some substrate bias favoring one position over the other (e.g. tethered nucleophiles, stabilized radical species, etc.) the generated allylic radicals can react from either of the end of the allyl radical. Furthermore, both the nitrenoid and radical based approaches can be utilized to functionalize benzylic C-H bonds. While this is an advantage for simple molecules, its presents yet another chemoselectivity issue when trying to selectively functionalize a specific allylic C-H bond in a complex molecule that also contains accessible benzylic positions (Figure 1.3B).

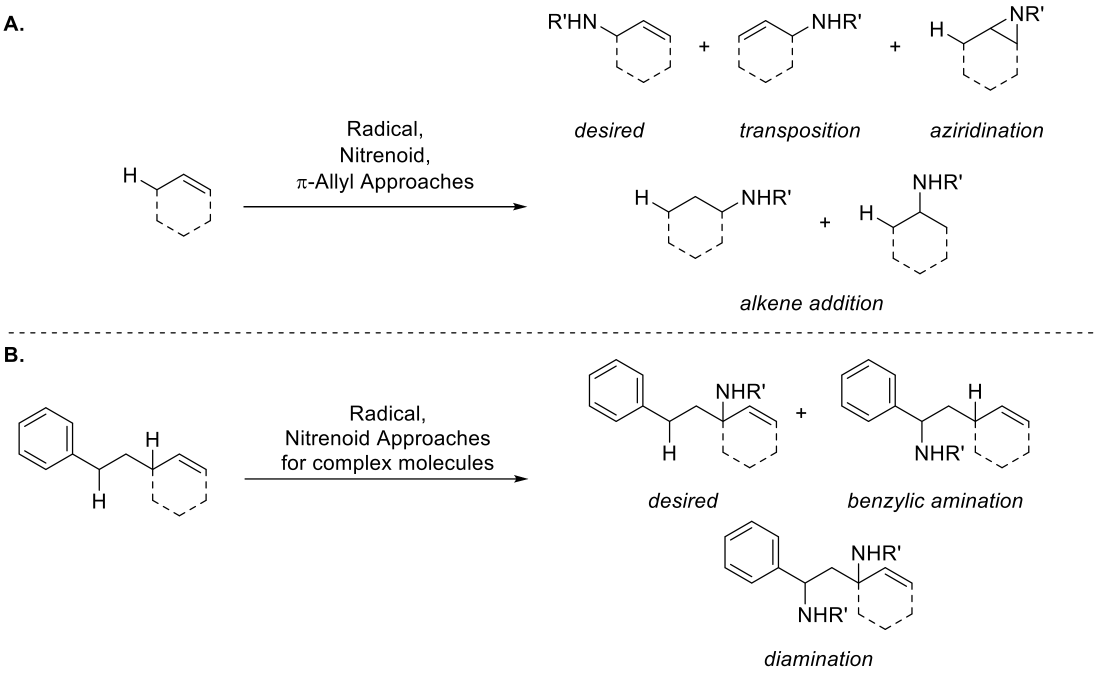


Figure 1.3. Regio- and Chemoselective Issues with C-H Amination Methods

A few methods relying on transition metal catalysis have been developed which avoid the undesired aziridination.[6] Unfortunately, many of these reactions proceed through an intermediate π-allyl complex which often presents its own challenges. Since the generated π-allyl complexes can undergo functionalization at either end, regiochemical isomers and the resulting alkene transposition is a common problem particularly for internal alkenes with little to differentiate one end over the other. These fundamental issues typically limit the substrate scope of these methods to alkenes with clearly differentiated ends for the necessary π-allyl complex (e.g. terminal alkenes, styrenyl alkenes, etc.). Beyond the reduced alkene scope, these approaches are often limited to coupling with just one type of amine source or requiring the use of specially designed preformed amine partners which restricts their utility for rapid incorporation of multiple types of nitrogen functionally.

Despite the recent development of these catalytic methods for C-H allylic amination, the stoichiometric approach by Sharpless and coworkers developed in 1976 remains one of the most selective in terms of product distribution.[7] This method utilized stoichiometric amounts of a putative selenium bis(imido) species derived from N-sodio-N-chlorotoluenesulfonamide (Chloramine T) to install allylic amines in a variety of simple alkene containing compounds. This approach resulted in the formation of only the desired allylic amine with no aziridination, no alkene transposition, and predictable regiochemistry. Unfortunately, the reliance on an explosive nitrogen source, use of stoichiometric amounts of toxic materials, and moderate yields resulted in minimal adaptation of this method.[8]

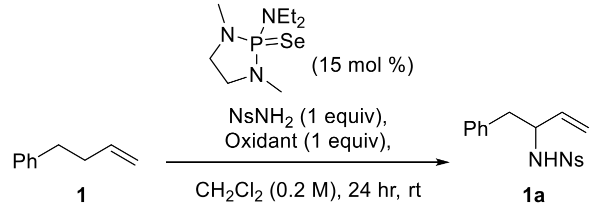
Due to its inherent selectivity, we hypothesized that the catalytic generation of a selenium bis(imido) species *in situ* from safe and convenient nitrogen sources would be an attractive method for the selective C-H allylic amination of complex molecules. We envisioned this would be possible by utilizing diacetoxyiodobenzene with sulfonamide and sulfamate nitrogen sources to oxidize catalytic amounts of selenium and thereby regenerate the active selenium bis(imido) species. This would not only vastly improve the safety of such an approach but generating the selenium bis(imido) species *in situ* would allow for rapid incorporation of an array of functionality simply by varying the nitrogen coupling partners.

Section 2: RESULTS AND DISCUSSION

1.2.1 *Initial Optimization*

The initial optimization on this work was completed by my collaborator Wei Pin Teh and the most important discoveries are included in the following subsection. The preliminary discovery was made by treating 4-phenyl-1-butene (**1**) in the presence of N-nosyl iminoiodinane (PhINNs), 4-nitrobenzene sulfonamide ($NsNH_2$), and a triaminophosphine selenide in dichloromethane resulting in a 32% yield of the allylic amine product (**1a**) (Table 1.1, entry 1).

Table 1.1. Oxidant Screen for Allylic Amination



1 **1a**

Entry	Oxidant	%Yield[a]
1	PhINNs	30
2	$PhI(OAc)_2$	31
3	PhINNs[b]	72
4	$PhI(OAc)_2$[b]	71

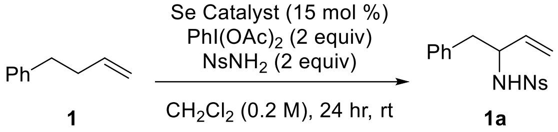
[a] Yield determined using 1,3-dinitrobenzene as an internal standard

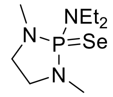
[b] 2 equiv of oxidant and nosyl amide

Increasing the amount of oxidant used to two equivalents resulted in 72% yield of the desired product (Table 1.1, entry 3). Pleasingly, a combination of the sulfonamide and diacetoxyiodobenzene could be used instead of the iodinane resulting in comparable reaction outcomes (Table 1.1, entry 2 and 4). This combination was preferable because it circumvents the need to synthesize these iodinane oxidants which are not commercially available. Furthermore, since the preformation of the iodinane is not required, other nitrogen nucleophiles could readily be incorporated into this chemistry simply by adding them directly to the reaction mixture.

A screen of catalysts revealed that a variety of phosphine selenides could be employed to generate the desired product in moderate yields but that tricyclohexyl phosphine selenide ($SePCy_3$) was the best, affording a nearly quantitative yield of the desired product (Table 1.2, entry 5).

Table 1.2. Catalyst Screen for Allylic Amination



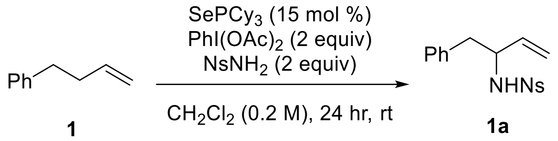
Entry	Catalyst	%Yield[a]
1		71
2	$SeP(NEt_2)_3$	51
3	$SeP(OPh)_3$	75
4	$SePPh_3$	55
5	$SePCy_3$	99 (93)
6	PhSeSePh	NR

[a] Yield determined using 1,3-dinitrobenzene as an internal standard. [b] Parentheses indicate isolated yield

It is worth noting that the most commonly employed organoselenide catalyst, diphenyl diselenide (PhSeSePh), resulted in no desired reactivity (Table 1.2, entry 6).

Having determined the optimal catalyst for this reaction, a survey of reduced catalyst and reagent loading was performed (Table 1.3). It was found that the catalyst could be reduced to 10 mol % with a minimal detrimental effect on the yield (Table 1.3, entry 2). Unfortunately, lowering the catalyst loading further continued to diminish reactivity with 2.5 mol % only affording the product in 27% yield in 24 hours (Table 1.3, entry 4).

Table 1.3. Equivalence Screen for Allylic Amination



Entry	Variation From Ideal	%Yield[a]
1	none	99
2	10 mol % $SePCy_3$	84
3	5 mol % $SePCy_3$	64
4	2.5 mol % $SePCy_3$	27
5	$PhI(OAc)_2$ and $NsNH_2$ (1.2 equiv)	60

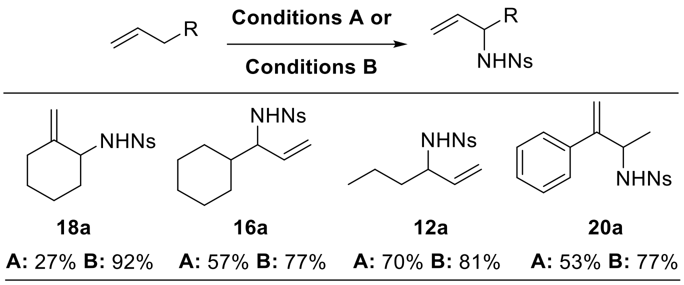
[a] Yield determined using 1,3-dinitrobenzene as an internal standard

It was also found that lowering the amount of oxidant and nucleophile was well tolerated albeit in a somewhat reduced yield of 60% (Table 1.3, entry 5).

1.2.2 *Expansion of the Substrate Scope*

When I joined this project, the previously optimized conditions were working well for many terminal alkene substrates, but numerous substrates were failing to provide the desired products in sufficient yields including several terminal alkenes, as well as more highly substituted substrates such as 1,2-disubstitued alkenes and trisubstituted alkenes. First, we focused on improving the yields for those terminal alkenes that were proving to be less reactive such as allyl cyclohexane (**16**) and methylene cyclohexane (**18**). An extensive catalyst screen was performed on these substrates but unfortunately, we found that $SePCy_3$ was already the optimal catalyst. Fortunately, we found that we could improve the reactivity for these substrates by increasing the reaction temperature. We assumed that at higher temperatures, the oxidant would be too reactive, so the amount of oxidant and amine source were both lowered to 1.5 equivalents. Using these new conditions at 35 °C, the yields of a number of substrates drastically improved (Scheme 1.1).

Scheme 1.1. *Effect of Increasing Temperature for Some Substrates*



18a	**16a**	**12a**	**20a**
A: 27% **B:** 92%	**A:** 57% **B:** 77%	**A:** 70% **B:** 81%	**A:** 53% **B:** 77%

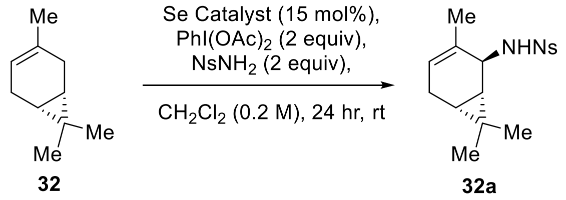
Conditions A: $SePCy_3$ (15 mol %), $PhI(OAc)_2$ (2 equiv), $NsNH_2$ (2 equiv), CH_2Cl_2 (0.2 M), 24 hr, rt

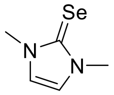
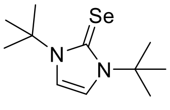
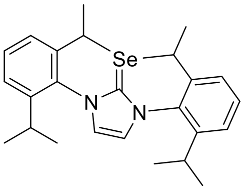
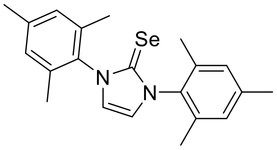
Conditions B: $SePCy_3$ (15 mol %), $PhI(OAc)_2$ (1.5 equiv) $NsNH_2$ (1.5 equiv), CH_2Cl_2 (0.2 M), 24 hr, 35 °C

While we were pleased with this improvement, certain 1,1-disubstitued alkenes were still proving problematic particularly those bearing an exocyclic isoprenyl group such as the carvone derivatives. No combination of heat or oxidant/ sulfonamide loading seemed to improve the yields for this class of substrates.

We then turned our attention to internal alkenes. This substrate class was giving significantly reduced yields of the desired allylic amines under these reaction conditions. In order to improve the yield of the desired product, a survey of ligands was tested on a model internal alkene (Table 1.4).

Table 1.4. Catalyst Screen for Internal Alkenes



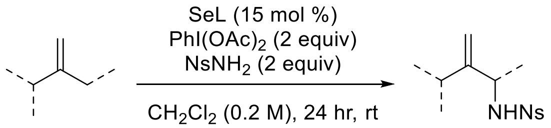
Entry	Catalyst	%Yield[a]
1	$SePCy_3$	16
2	$SeP(NEt_2)_3$	50
3	$SePPh_3$	5
4	$SeP(OPh)_3$	4
5	 "SeIMe"	87
6	 "SeItBu"	65
7	 "SeIPr"	30
8	 "SeIMes"	27

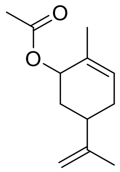
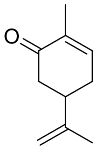
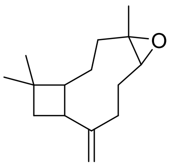
[a] Yield determined using 1,3-dinitrobenzene as an internal standard

The optimal catalyst for terminal alkenes, $SePCy_3$, only gave 16% of the desired product (Table 1.4, entry 1). Other phosphine selenides resulted in similarly low yields this substrate class (Table 1.4, entries 3 and 4). A triamino phosphine afforded an improved 50% of the desired product (Table 1.4, entry 2). Switching from phosphine to N-aryl imidazolium based catalysts provided a moderate improvement to product yield (Table 1.4, entries 7 and 8). Moving to N-alkyl imidazolium catalysts greatly improved the desired reactivity (Table 1.4, entries 5 and 6). The N-methyl imidazolium catalyst (SeIMe) proved to be the best of the catalysts screened, with an 87 % yield of the allylic amine **32a** (Table 1.4, entry 5). Using this SeIMe catalyst, a wide array of internal alkenes was shown to give the desired products in high yields.

When we turned our attention back to 1,1-disubstitued alkenes, we found that some substrates afforded higher yields using SePCy$_3$ while for others, SeIMe proved to be the optimal catalyst. (Table 1.5).

Table 1.5. Catalyst Screen for 1,1-Disubstituted Alkenes



Entry	Substrate	Catalyst	%Yield[a]
1	 **43**	SePCy$_3$ SeIMe	22 78
2	 **42**	SePCy$_3$ SeIMe	59 62
3[b]	 **41**	SePCy$_3$ SeIMe	75 4

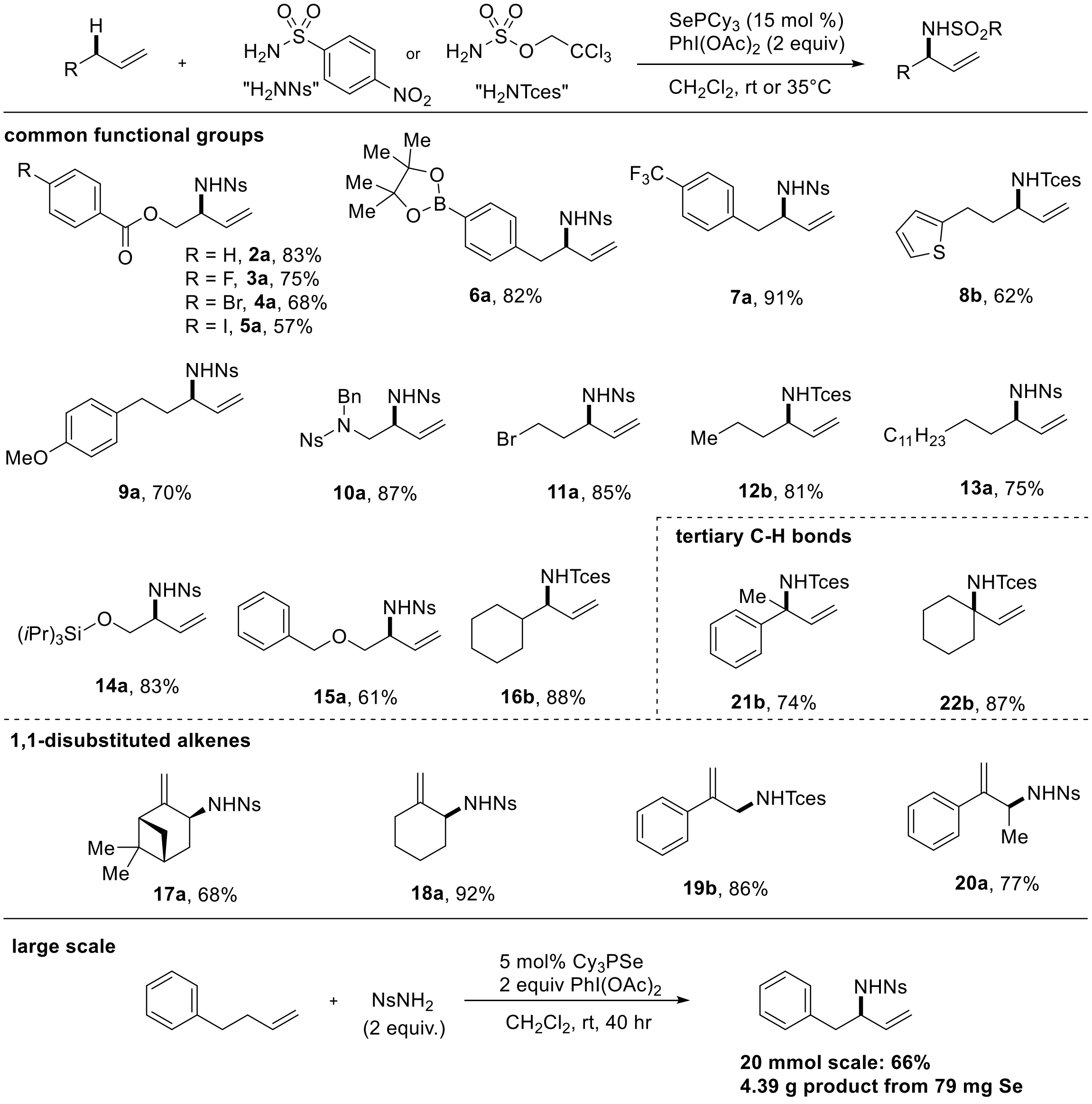
[a] Yield determined using 1,3-dinitrobenzene as an internal standard
[b] Reactions run at 30 °C

Fortunately, reoptimization was found to be unnecessary since we observed sufficient yields for each alkene using one of the two previously optimized catalysts.

1.2.3 *Investigation of the Scope*

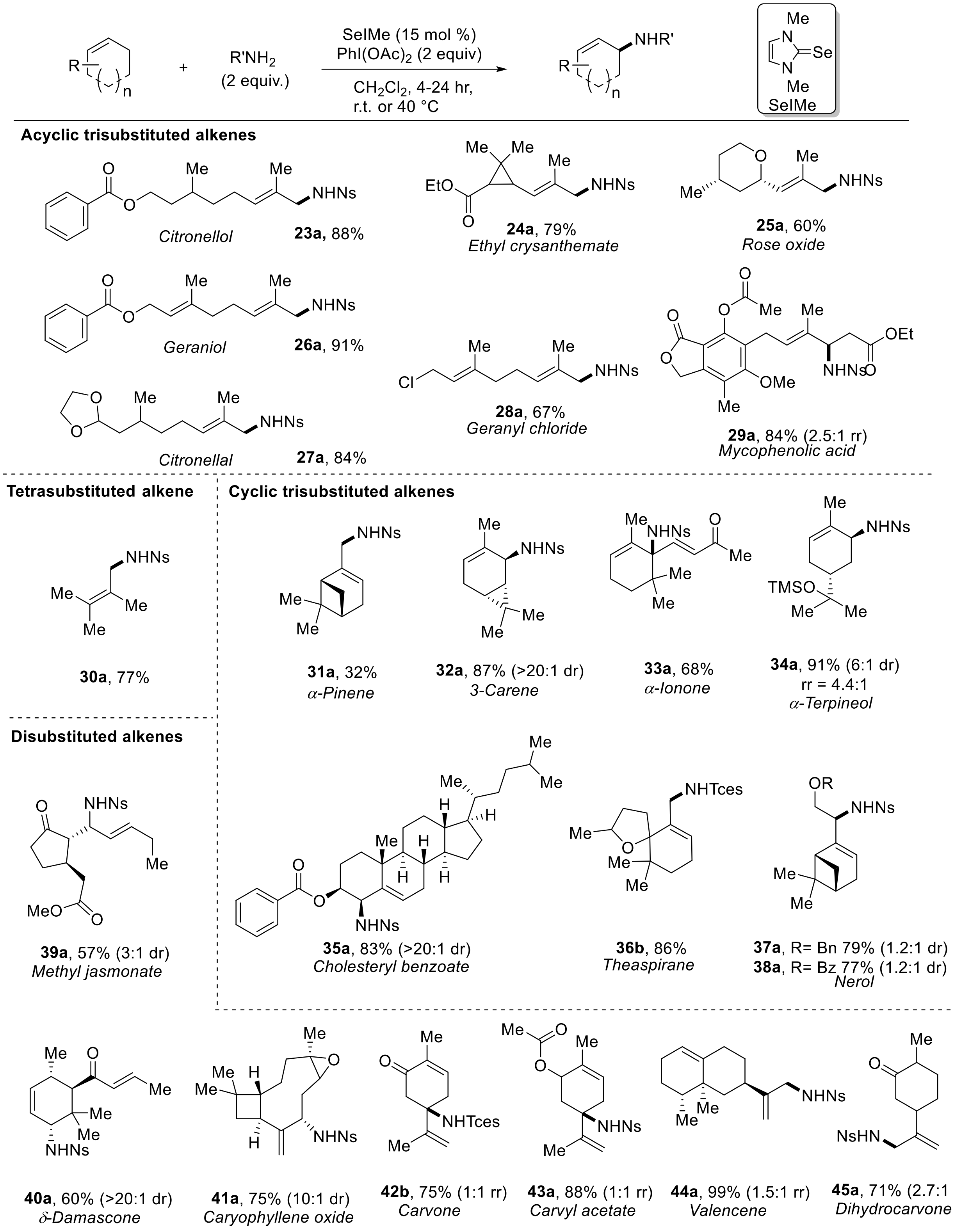
Having developed a set of conditions using either $SePCy_3$ or SeIMe as a catalyst that worked for all substitution classes of alkenes, we turned our attention to the substrate scope. Using $SePCy_3$ as the catalyst, a vast array of terminal and some 1,1-disubstituted alkenes were shown to give the desired allylic amines in high yields (Table 1.6). A large variety of functional groups were tolerated including esters (**2a – 5a**), ethers (**15a**), silyl ethers (**14a**), protected amines (**10a**), and even alkyl bromides (**11a**). Pleasingly, these reaction conditions were compatible with oxidizable aromatic groups such as anisole (**9a**) and thiophene (**8b**). This reaction offers orthogonal reactivity to transition metal methods for allylic amination by tolerating aryl boronic esters (**6a**) and numerous aryl halides (**4a**, **5a**). This reaction also facilitated the synthesis of tertiary allylic amines (**21b**, **22b**), a longstanding limitation of allylic amination methods. We found this method to be amenable to large scale synthesis of allylic amines and a significantly reduced catalyst loading was well tolerated on this scale. Using only 80 mg of elemental selenium we could obtain 4.39 grams of the desired product. This result was particularly encouraging since previous attempts at lowering the catalyst loading to 5 mol % for the small scale reaction resulted in diminished product yield (Table 1.3, entry 3).

Table 1.6. Terminal Alkene Scope



Utilizing SeIMe as a catalyst provided access to allylic amines from the remaining 1,1-disubstituted and internal alkenes (Table 1.7). Specifically, this catalyst facilitated the late stage allylic amination of an array of biologically active molecules and terpene derivatives. Further expansion of functional group tolerance was observed including epoxides (**41a**), allylic halides (**28 a**), ketones (**33a**, **39a**, **42b**, **45a**) and protected aldehydes (**27a**). We typically observed very high regioselectivity for these substrates. For substrates with multiple alkenes, we observed allylic amination exclusively at the most electron rich alkene (**26a**, **28a**, **40a**, **42b**, **43a**). We observed very high regioselectivity for allylic amination of acyclic trisubstituted alkenes with functionalization exclusively on the carbon trans to the third substituent even in the presence of comparably weaker allylic C-H bonds (**23a** – **29a**). For example, mycophenolic acid (**29a**) preferentially reacted in this trans position despite having neighboring allylic/benzylic C-H bonds. In the case of cyclic trisubstituted alkenes, we observed selectivity for endocyclic amination (**32a** – **34a**). High diasteroselectivity was typically observed for cyclic substrates with amination occurring selectively at the axial C-H bond (**32a**, **34a**, **35a**, **40a**, **41a**). In cases where there were no axial endocyclic allylic CH bonds, we observed exocyclic amination products in high yields (**31a**, **36a-38a**). This includes cyclic substrates **31a**, **37a**, and **38a**, where exocyclic amination was the exclusive product despite these substrates bearing equatorial C-H bonds at bridgehead carbons. For disubstituted alkenes we observed a reactivity trend where CH_2 groups reacted preferentially to CH groups (**40a**, **41a**). We also found that one CH_2 could be aminated over another when an electronic bias was present with methyl jasmonate selectively aminating on the side of the alkene with the γ-ketone rather than at the more sterically accessible side (**39a**). Regioselectivity issues were observed for alkenes bearing a CH and a CH_3 group such as cyclic terpene derivatives bearing an exocyclic isoprenyl group (**42b** – **45a**). For these substrates we typically observed a 1:1 mixture of regioisomers but the combined yields for these products were still very high.

Table 1.7. Allylic C – H amination of Terpenes



Acyclic trisubstituted alkenes

Citronellol **23a,** 88%

24a, 79% *Ethyl crysanthemate*

25a, 60% *Rose oxide*

Geraniol **26a**, 91%

28a, 67% *Geranyl chloride*

29a, 84% (2.5:1 rr) *Mycophenolic acid*

Citronellal **27a**, 84%

Tetrasubstituted alkene

30a, 77%

Cyclic trisubstituted alkenes

31a, 32% *α-Pinene*

32a, 87% (>20:1 dr) *3-Carene*

33a, 68% *α-Ionone*

34a, 91% (6:1 dr) rr = 4.4:1 *α-Terpineol*

Disubstituted alkenes

39a, 57% (3:1 dr) *Methyl jasmonate*

35a, 83% (>20:1 dr) *Cholesteryl benzoate*

36b, 86% *Theaspirane*

37a, R= Bn 79% (1.2:1 dr)
38a, R= Bz 77% (1.2:1 dr) *Nerol*

40a, 60% (>20:1 dr) *δ-Damascone*

41a, 75% (10:1 dr) *Caryophyllene oxide*

42b, 75% (1:1 rr) *Carvone*

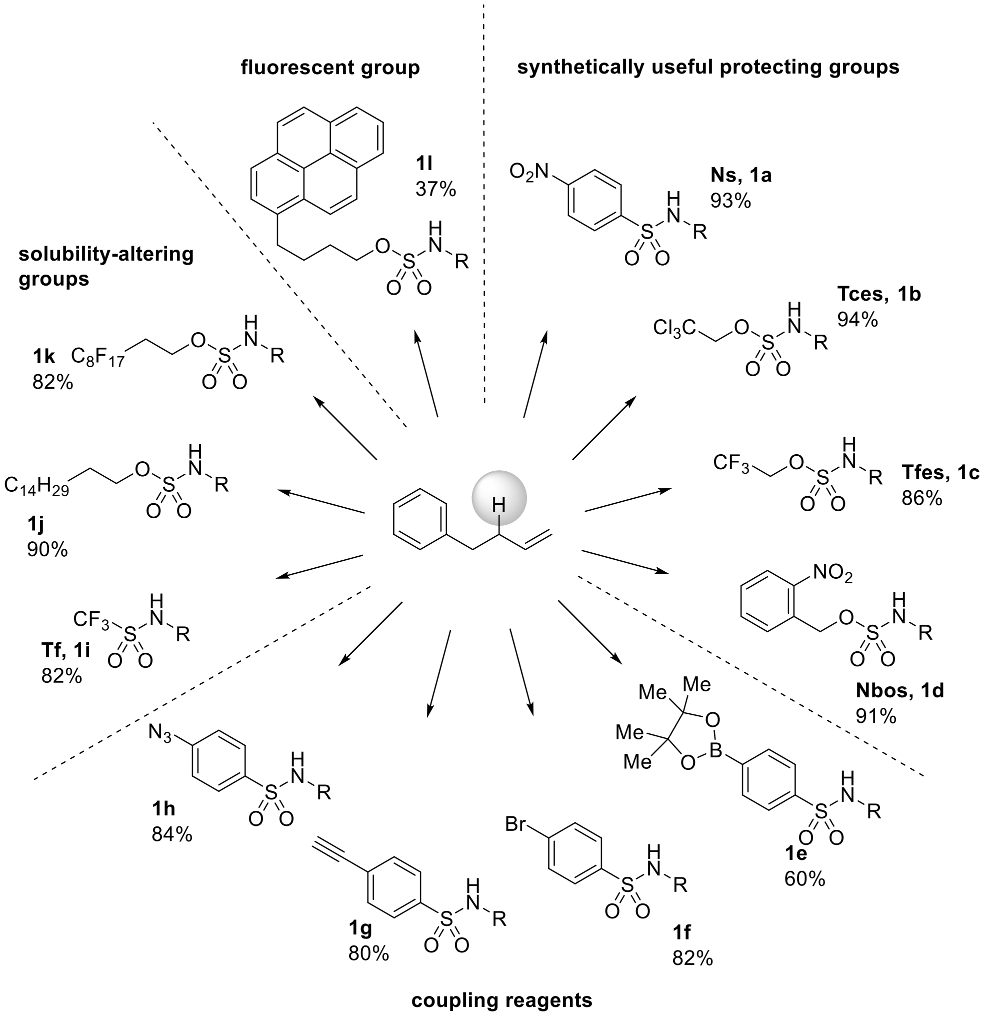
43a, 88% (1:1 rr) *Carvyl acetate*

44a, 99% (1.5:1 rr) *Valencene*

45a, 71% (2.7:1 rr) *Dihydrocarvone*

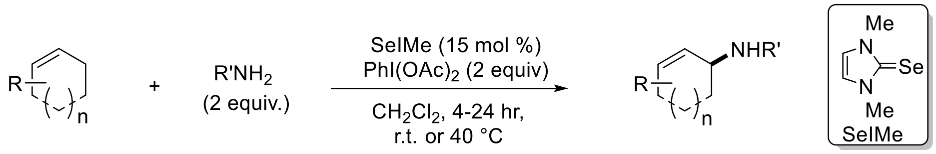
To demonstrate the utility of this reaction as a method for introducing functionality via the amine coupling partner, an assortment of synthetically useful sulfonamides and sulfamates were coupled to our model terminal alkene (Table 1.8). A variety of amines bearing synthetically useful protecting groups could be utilized including those that could be deprotected through nucleophilic substitution (**Ns**, **1a**), zinc reduction (**Tces**, **1b**), hydrolysis (**Tfes**, **1c**), and photolytic cleavage (**Nbos**, **1d**). Sulfonamides bearing synthetic handles for further functionalization could also be utilized such as those bearing aryl boronic esters (**1e**) or aryl halides (**1f**) for cross couplings and those with pendant alkynes (**1g**) or azides (**1h**) for copper catalyzed click chemistry. We also found that we could utilize a sulfonamide containing a fluorescent group (**1l**) as a coupling partner demonstrating this procedure as a method for fluorescent labeling. Finally, we found that we could incorporate amines into the final products in order to facilitate separation including those that would provide an acidic handle for acid/base extraction (**Tf**, **1i**) or by increasing the hydrophobicity (**1j**) or fluorophilicity (**1k**) of the final molecule.

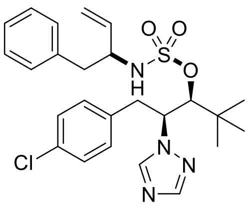
Table 1.8. Sulfonamide and Sulfamate Scope



To demonstrate the full extent of the late stage coupling power of this reaction, numerous alkenes of varied complexity were coupled with sulfonamides and sulfamates derived from drug molecules (Table 1.9). Celecoxib, bearing an aryl sulfonamide, coupled readily to a terpenoid under our conditions (**50**). Drug molecules bearing free alcohols were readily converted into the corresponding sulfamates and coupled with ease to a variety of alkene substitution patterns in good to excellent yields (**46** – **49**). We also demonstrated that we could couple the fluorescent dye dansyl amide (**51**), bearing a free sulfonamide, to natural product scaffolds in good yields.

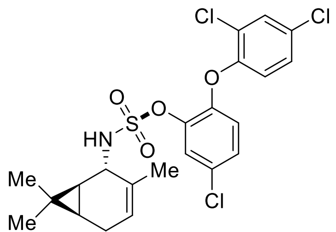
Table 1.9. Allylic C – H Amination Using Drug Derived Nucleophiles





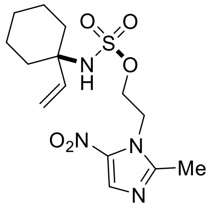
Paclobutrazol

46, 53%



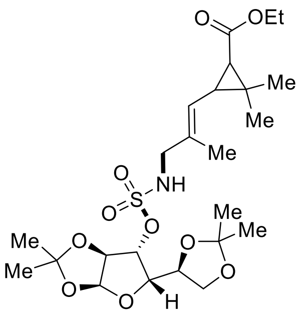
Triclosan

47, 94%



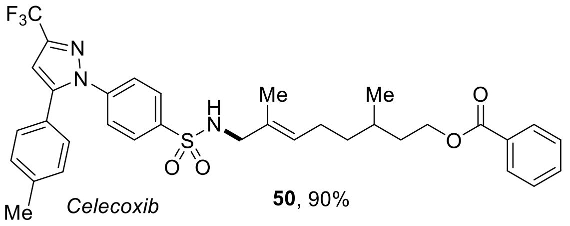
Metronidazole

48, 63%



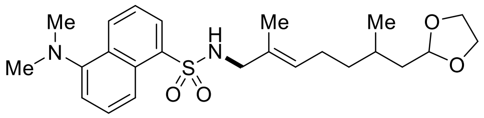
Glucofuranose

49, 72%



Celecoxib

50, 90%



Dansyl amide

51, 49%

1.2.4 *Mechanistic Investigation*

Much of our mechanistic proposal is based on early work done by Sharpless and coworkers to elucidate the mechanism of selenium dioxide oxidation of alkenes. One significant aspect of this selenium dioxide oxidation is that the allylic alcohol products retain the original regiochemistry of the starting alkene. This selectivity suggests that carbocation formation is unlikely. To explain the selective regiochemistry without the generation of carbocation intermediates, Sharpless and coworkers proposed that selenium dioxide could undergo an ene reaction with alkenes resulting in an oxidized allylic selenide species which could then undergo a

[2,3]-sigmatropic rearrangement leading to the seleninic acid and eventually, exclusively the allylic alcohol product with net retention of the original alkene (Figure 1.4).

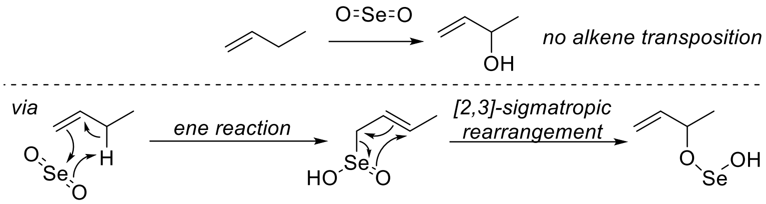


Figure 1.4. Proposed Mechanism for Selenium Dioxide Oxidation of Alkenes

Sharpless and coworkers set out to support each proposed elementary step in an effort to support their hypothesis (Figure 1.5). To demonstrate the possibility that oxidized allylic selenides could undergo a [2,3]-sigmatropic rearrangement, Sharpless and coworkers treated an allylic selenide with hydrogen peroxide using methanol as the solvent (Figure 1.5 A).[9] . They observed exclusive formation of the transposed allylic alcohol. If this mechanism involved a carbocation, it might be expected that either the allylic alcohol regioisomer or the two potential allylic ethers (resulting from reaction with the alcohol solvent) might be observed. The formation of only the transposed allylic alcohol product suggests that a [2,3]-sigmatropic rearrangement is the most likely reaction pathway.

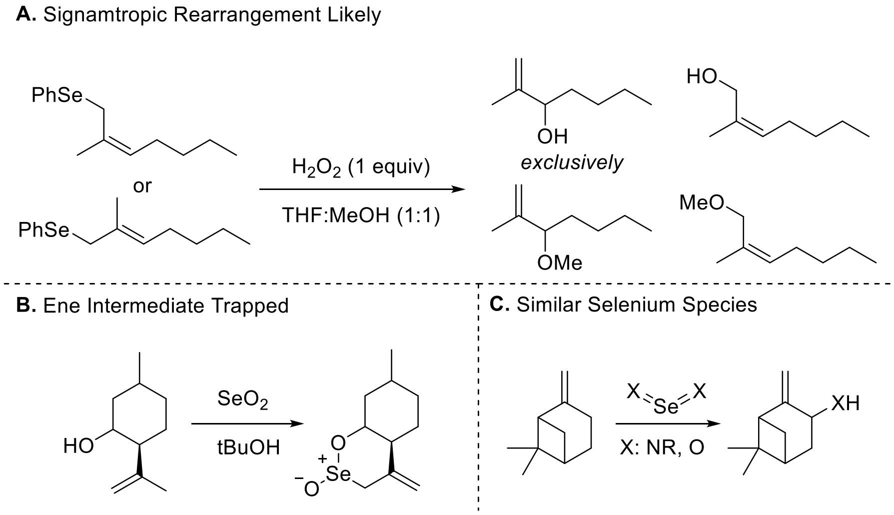


Figure 1.5. Previous Work by Sharpless and Coworkers

Having supported that oxidized allylic selenides can undergo [2,3]-sigmatropic rearrangements, Sharpless and coworkers turned to supporting the initial ene reaction which would lead to those proposed intermediates. Since the reactive nature of these suggested intermediates would prevent their isolation (they should rapidly undergo the [2,3]-sigmatropic rearrangement as previously demonstrated), Sharpless and coworkers decided to engineer a system that might trap the oxidized allylic selenide after the ene reaction, but before the resulting [2,3]-sigmatropic rearrangement could occur. They did this by treating an alkene bearing a pendant alcohol with selenium dioxide (Figure 1.5B).[10]. This pendant alcohol could coordinate to the allylic selenide species resulting from the ene reaction thereby stabilizing the intermediate as a selenolactone and preventing the subsequent [2,3]-sigmatropic rearrangement from occurring. This strategy proved successful with the isolation of the selenolactone species strongly supporting that selenium dioxide can undergo ene reactions with alkenes leading to oxidized allylic selenides.

Together, these experiments supported that the selenium dioxide oxidation of alkenes likely does proceed through an ene reaction followed by a [2,3]-sigmatropic rearrangement leading to allylic alcohols with net retention of the original alkene regiochemistry. Later, Sharpless and coworkers were working with what they believed to be *in situ* generated selenium bis(imido) species (the nitrogen analogue to selenium dioxide) in the presence of alkenes. They found that these species reacted in a similar fashion to selenium dioxide resulting in the exclusive formation of allylic amine products which retained the original regiochemistry of the starting alkene. Due to the isoelectronic nature of the two species and the similar reaction outcomes, Sharpless and coworkers proposed that selenium bis(imido) species reacted with alkenes in an analogous mechanism to that of selenium dioxide (Figure 1.5C).[7b]

Our reaction provides the same products as Sharpless' stoichiometric allylic amination of alkenes and is under similar conditions so it is plausible that it too is proceeding through the generation of a selenium bis(imido) species (**I**) which could be generated from oxidation of our selenide precatalysts. In accordance with that hypothesis we propose the following mechanism. Oxidation of the phosphine selenide precatalyst affords the selenium bis(imido) species (**I**). This species could undergo an ene reaction with the alkenes to afford allylic selenium species **II**. This oxidized species could undergo a [2,3]-sigmatropic rearrangement to afford the allylic selenium protected amine **III**. Protonolysis and oxidation affords the desired allylic amine and regenerates the selenium bis(imido) species (**I**).

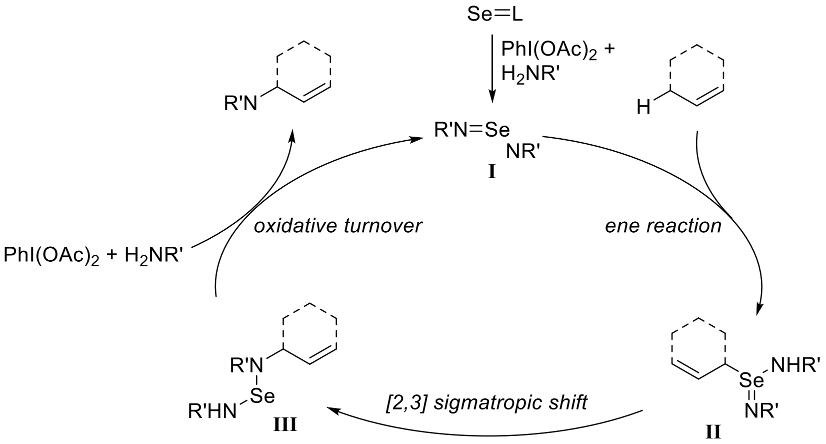
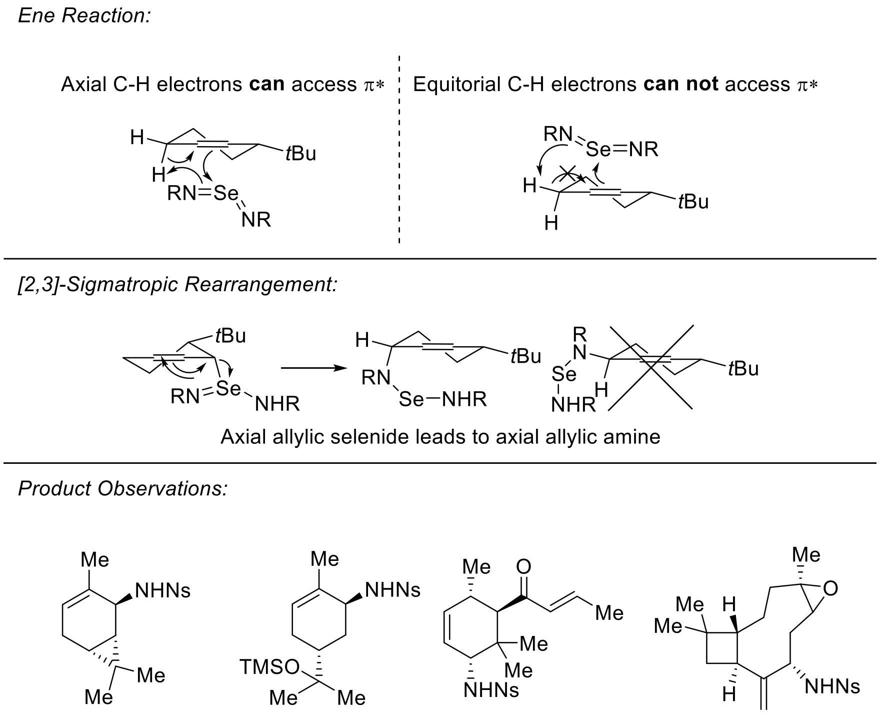


Figure 1.6. Proposed Catalytic Cycle

The observed substrate scope and regiochemical outcomes for this reaction are consistent with this mechanistic proposal. Most notably, the observation of high diastereoselectivity caused by axial amination can be readily explained by this mechanism (Figure 1.7). During the initial ene reaction, only the axial C-H electrons can interact with the neighboring π* orbital of the alkene since the equatorial C-H bond is out of plane. This leads to the preferential formation of the axial allylic selenide. The subsequent [2,3]-sigmatropic rearrangement of this allylic selenide must lead to the axial allylic amine due to the constricted bond angles of the cyclic system.



32a, 87% (>20:1 dr)
3-Carene

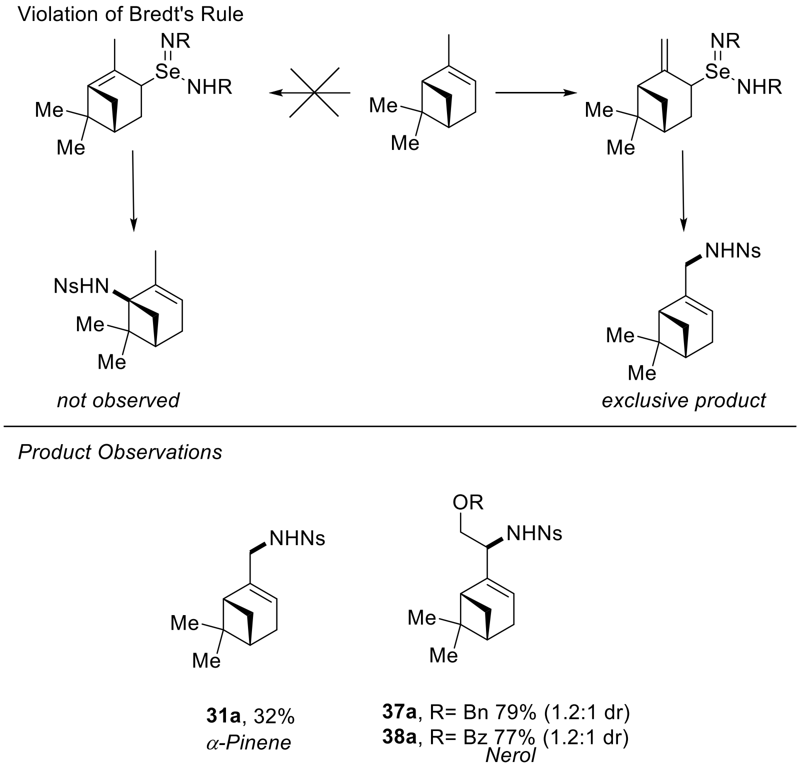
34a, 91% (6:1 dr)
rr = 4.4:1
α-Terpineol

40a, 60% (>20:1 dr)
δ-Damascone

41a, 75% (10:1 dr)
Caryophyllene oxide

Figure 1.7. Diastereoselectivity for cyclic substrates is consistent with mechanistic proposal

Similarly, this mechanistic proposal can explain why alkenes bearing equatorial C-H bonds at bridgehead carbons were found to give exclusively exocyclic amination despite the inherent preference for endocyclic reactivity (Figure 1.8). For these substrates, endocyclic amination would have to proceed through an allylic selenide where the newly formed alkene would be placed at the bridgehead position. Following Bredt's Rule, the substrates were found to instead prefer amination at the exocyclic positions despite the inherent selectivity for endocyclic amination.



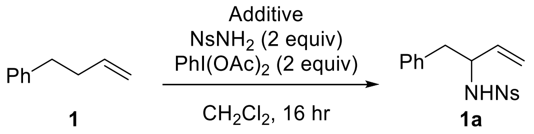
31a, 32%
α-Pinene

37a, R= Bn 79% (1.2:1 dr)
38a, R= Bz 77% (1.2:1 dr)
Nerol

Figure 1.8. Lack of allylic amination for bridgehead C-H is consistent with Bredt's Rule

Despite the similarities to Sharpless' stoichiometric allylic amination, this reaction provides the same products in 20-40 % higher yields using only catalytic amounts of selenium. Therefore, initial investigations to elucidate the role of phosphine ligand in this reaction were undertaken (Table 1.10)

Table 1.10. Equivalence Screen for Allylic Amination



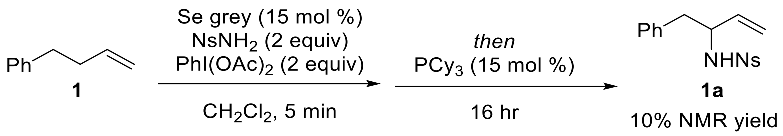
Entry	Additive	%Yield[a]
1	$SePCy_3$ (15 mol %)	99
2	none	0
3	Se grey (15 mol %)	0
4	Se grey (100 mol %)	0
5	Se grey (15 mol %) PCy_3 (15 mol %)	97[b]
6	Se grey (15 mol %) $O{=}PCy_3$ (15 mol %)	0

[a] Yield determined using 1,3-dinitrobenzene as an internal standard

[b] Everything stirred for 5 minutes before oxidant was added

With the phosphine selenide, there is quantitative product formation (Table 1.10, entry 1). Using selenium grey in catalytic or stoichiometric amounts without the addition of a ligand resulted in no product formation (Table 1.10, entries 3 and 4). However, adding catalytic amounts selenium grey and phosphine together before addition of the oxidant resulted in comparable product yields to the experiment using the preformed phosphine selenide indicating that the catalyst can be generated *in situ* (Table 1.10, entry 5). These experiments demonstrate that the phosphine is essential for the reactivity of this system. Interestingly, catalytic phosphine oxide was not able to generate the desired reactivity when combined with selenium grey (Table 1.10, entry 6). This result suggests that the phosphine might strongly coordinate to the selenium species, at least initially, since we have observed rapid oxidation of free phosphine under these reaction conditions. To further confirm that suspicion, another experiment was performed using catalytic amounts of selenium grey (Scheme 1.2). After allowing this reaction to stir for 5 minutes, a catalytic amount of phosphine was added.

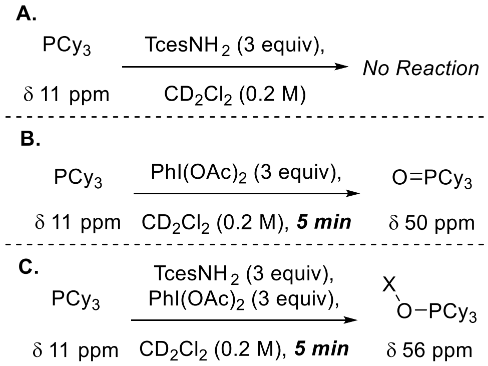
Scheme 1.2. *Changing the Order of Addition Changes Reactivity.*



Indeed, this order of addition significantly reduced the amount of product formed. It is likely that most of the free phosphine oxidized before it could coordinate to the selenium resulting in the reduced yields. These two results taken together indicate that either: a) the phosphine remains coordinated to the selenium species during the course of the entire reaction or b) the phosphine is required initially to convert the inactive selenium species to the active catalytic species and may no longer be required after that.

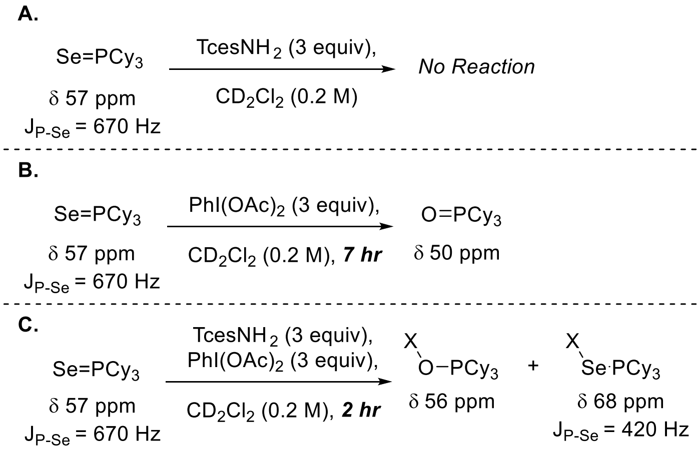
To gain further insight into the role of the phosphine ligands, some preliminary attempts were made to observe the reaction by ^{31}P NMR. We began by running control studies to observe what happens to free phosphine under our reaction conditions (Scheme 1.3).

Scheme 1.3. *Free Phosphine Under Reaction Conditions*



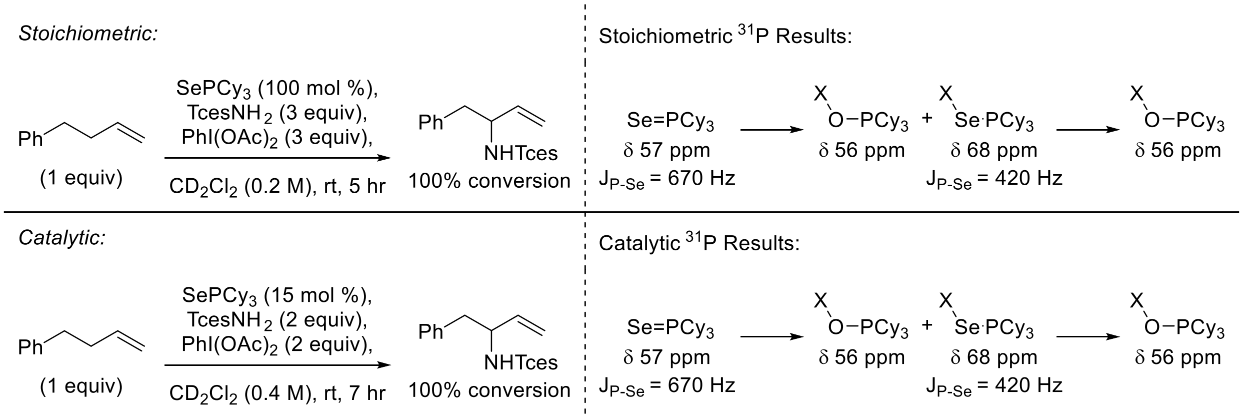
No change was observed for the phosphine when treated with the sulfamate nucleophile (Scheme 1.3A). As expected, treating the free phosphine with oxidant resulted in immediate conversion to the phosphine oxide (Scheme 1.3B). This result was not surprising given that electron-rich phosphines rapidly oxidize in air and PhI(OAc)$_2$ is a relatively strong oxidant. Interestingly, treating the phosphine with nucleophile and oxidant resulted in conversion to a clear new phosphine resonance about 6 ppm down field from the phosphine oxide (50 vs 56 ppm) (Scheme 1.3C). Using an authentic sample of phosphine oxide for independent and doping experiments revealed this new species to be phosphine oxide with the downfield shift being consistent with coordination of the oxygen to a Lewis acid or a hydrogen bond donor.[11] An identical set of control experiments was run for the phosphine selenide catalyst (Scheme 1.4).

Scheme 1.4. *Phosphine Selenide Under Reaction Conditions*



Treating the phosphine selenide with sulfamate nucleophile resulted in no change in the phosphorous signal (Scheme 1.4A). Adding oxidant to the phosphine selenide resulted in slow conversion to the phosphine oxide over 7 hours (Scheme 1.4B). Interestingly, adding both the oxidant and the nucleophile to the phosphine selenide resulted in the rapid conversion to the downshifted phosphine oxide species at 56 ppm as well as a new phosphorous species at 68 ppm with clear selenium satellites ($J_{P\text{-}Se}$ ~420 Hz) within 2 hours (Scheme 1.4C). The downfield shift and reduced coupling constant of this species relative to the phosphine selenide precatalyst (57 ppm, $J_{P\text{-}Se}$ 680 Hz) are both consistent with substantial weakening of the Se-P perhaps through coordination at Se. Similar values have been observed for metal complexes of $SePCy_3$.[11b] We hypothesized that this new phosphine selenide species might be catalytically relevant so we analyzed the stoichiometric and catalytic reactions by phosphorous NMR as well (Scheme 1.5).

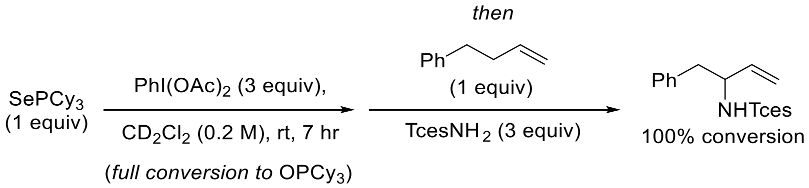
Scheme 1.5. *Allylic Amination Reactions Monitored by Phosphorous NMR*



Indeed, both the catalytic and stoichiometric reactions resulted in rapid conversion of the phosphine selenide into this new phosphine selenide species as well as some downshifted phosphine oxide in a roughly 1:1 ratio. In both the stoichiometric and catalytic experiments, we observed a slow disappearance of the new phosphine selenide species eventually resulting in complete conversion to the downshifted phosphine oxide species.

In order to determine if the new phosphine selenide species (at 68 ppm) was required for this reaction, we treated a stoichiometric amount of phosphine selenide with oxidant until complete conversion to the phosphine oxide was observed and then added the nucleophile and alkene (Scheme 1.6).

Scheme 1.6. *Determining Catalytic Relevance of New Phosphine Selenide Species*



An instantaneous downfield shift in the phosphine oxide to 56 ppm was observed and this species remained the exclusively observed phosphorous species for the remainder of the experiment. Interestingly, this reaction resulted in complete conversion of the alkene to the allylic amine suggesting that the new phosphine selenide species is not required for catalytic reactivity.

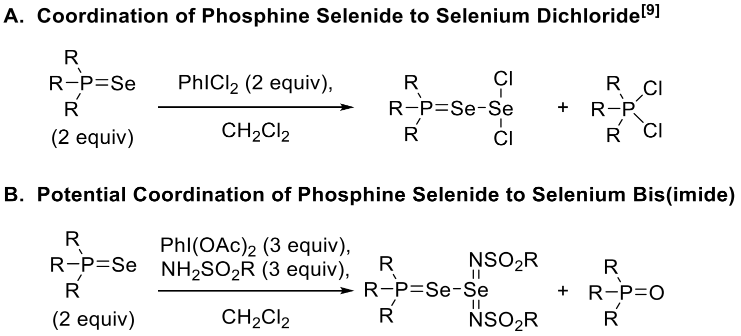


Figure 1.9. Plausible Explanation for New Phosphine Selenide Signal

One potential explanation for this new phosphine selenide peak is that it represents phosphine selenide coordinated to some selenium bis(imide) species resulting from the partial oxidation of the phosphine selenide by $PhI(OAc)_2/RSO_2NH_2$ (Figure 1.9B). Similar species have been observed and characterized for the oxidation of phosphine selenides with chlorine (Figure 1.9A).[12] The stoichiometry of this reaction would also explain the observed roughly 1:1 initial ratio of new phosphine selenide and phosphine oxide. It is possible that this coordination protects the phosphine selenide from oxidation effectively acting to slowly release the catalyst which would explain the progressive erosion of the phosphine selenide peak and eventual total conversion to phosphine oxide. Unfortunately, we currently have little experimental evidence to support this hypothesis, but more work is underway.

Section 3: CONCLUSION

A novel, broadly applicable selenium-catalyzed C-H amination reaction has been developed. Key to the success of this catalytic transformation was the use of ligands on selenium. Simply using either an alkyl phosphine or an alkyl NHC ligand allowed alkenes bearing all substitution patterns to be suitable substrates for this procedure. Amination proceeds with predictable regiochemistry with many complex substrates affording only one of multiple possible isomers. The reaction conditions are tolerant of an extensive number of functional groups. A variety of synthetically useful sulfonamides were found to be suitable coupling partners allowing for alteration of chemical properties, further functionalization, and fluorescent labeling. The procedure was demonstrated to be suitable for late stage functionalization by aminating a variety of natural products and terpene derivatives. Commercial and modified drug compounds were shown to be suitable coupling partners further demonstrating the coupling power of this reaction.

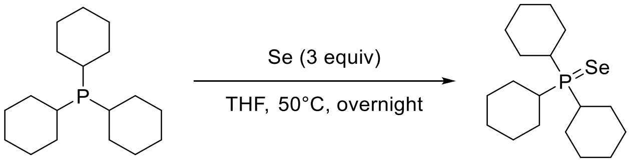
Section 4: EXPERIMENTAL

1.4.1 *General Procedures and Materials*

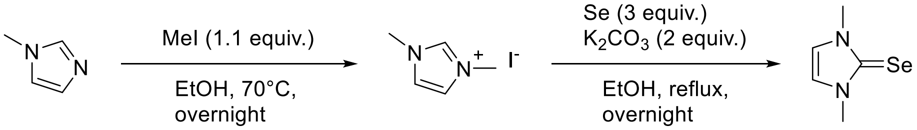
All reactions were performed under a nitrogen atmosphere using oven-dried or flame-dried glassware unless otherwise indicated. Dichloromethane (CH_2Cl_2) and tetrahydrofuran (THF) were degassed and dried by passing through a column of activated neutral alumina. Deuterated solvents ($CDCl_3$, acetone-d^6) were obtained from Cambridge Isotope Laboratories, Inc. and stored over activated 3A molecular sieves. Ethyl acetate (EtOAc), hexanes, and ether (Et_2O) were obtained from Fisher Scientific or Sigma Aldrich and used without further purification. Reagents were purchased from Sigma Aldrich, Tokyo Chemical Industry, Fisher Scientific, Alfa Aesar, Oakwood chemicals and used without further purification unless otherwise indicated. Infrared spectra were acquired using a Perkin Elmer Spectrum RX I spectrometer. Mass spectra were acquired using a Bruker Esquire 1100 Liquid Chromatograph-Ion Trap Mass Spectrometer. Column chromatography was performed using silica gel (Whatman, 60 Å, 230-400 mesh). NMR spectra were recorded on a Bruker AV-300, AV-301, DRX-499, or AV-500 spectrometer. ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) and are referenced relative to TMS (0.00 ppm), $CHCl_3$ (7.26 ppm) or acetone-d^5 (2.06 ppm). ^{13}C NMR chemical shifts (δ) are reported in parts per million (ppm) relative to the carbon resonance of $CDCl_3$ (77.26 ppm) or acetone-d^6 (29.92 ppm). Melting points were taken on a MEL-TEMP melting point apparatus and are uncorrected.

1.4.2 *Synthesis and Characterization of Starting Materials*

General Procedure for Synthesis of Selenium Catalysts.



Tricyclohexylphosphine selenide ($SePCy_3$). A flame-dried round bottom flask equipped with a magnetic stir bar was charged with tricyclohexylphosphine (10 mmol, 1 equiv.) and selenium powder (30 mmol, 3 equiv) in a glove box. The flask was capped with a rubber septum and transferred outside of the glove box. Dry tetrahydrofuran (20 mL, 0.5 M) was added using a syringe and the septum was replaced with a reflux condenser under nitrogen gas. The reaction was heated to 45 °C and allowed to stir overnight. After cooling to room temperature, the mixture was then flushed through Celite with dichloromethane to remove the residual selenium powder. The eluent was then concentrated on a rotary evaporator to afford the crude reaction product. The crude white solid was recrystallized from acetone and cooled in the freezer overnight to afford the product as white needles (3.05 g, 85% yield). The spectroscopic data was consistent with the literature.[13] **^{31}P NMR** (121 MHz, $CDCl_3$) δ 57.65 (d, *J* = 674.5 Hz). **^{79}Se NMR** (57 MHz, $CDCl_3$, 0.4 M) δ -464.45 (d, *J* = 674.9 Hz).

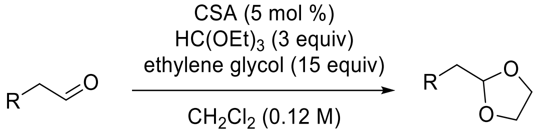


***N,N'*-dimethylimidazole-2-selone (SeIMe).** A flame-dried round bottom flask equipped with a magnetic stir bar was charged with 1-methylimidazole (2 mL, 25.1 mmol, 1 equiv.) and ethanol (50 mL, 0.5 M). Methyl iodide (1.72 mL, 27.6 mmol, 1.1 equiv.) was added to the flask, which was equipped with a water condenser. The reaction was heated to 70 °C and allowed to stir overnight. The reaction mixture was then concentrated on a rotary evaporator to afford the crude imidazolium salt. Potassium carbonate (6.9 g, 50.1 mmol, 2 equiv.), selenium powder (5.9 g, 74.3 mmol, 3 equiv.), and ethanol were added to the flask containing the crude reaction product and refluxed overnight. The reaction mixture was filtered through a pad of Celite and washed with dichloromethane (2 x 100 mL). The filtrate was concentrated on a rotary evaporator and recrystallized to afford the product as pale grey needles (3.25 g, 74%). The spectroscopic data were found to be consistent with reported literature.[14]

General Information for Starting materials.

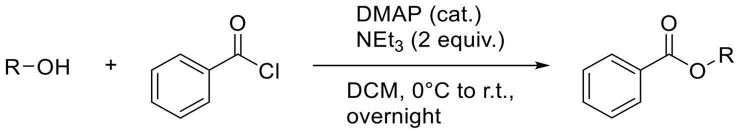
Starting material alkenes and sulfonamides are purchased from commercial sources and used without further purification unless otherwise indicated. Terminal alkenes **2**[15], **3**[16], **4**[16], **5**[17], **6**[18], **7**[19], **8**[20], **9**[21], **10**[22], and **21**[23] were synthesized according to literature procedure and the spectroscopic data were consistent with the reported values. Internal alkenes **23**[24], **26**[25], **27**[26] and were synthesized according to general procedures for acetal/benzoate protection (see below) and the spectroscopic data were consistent with the literature values. Sulfamates **b**[27], **c**[27], **d**[28], **j**[29], **k**[29], **l**, **46**, **47**, and **48** were synthesized according to literature procedure and spectroscopic data of known compounds were consistent with the reported values.

General Procedure for Acetal protection.



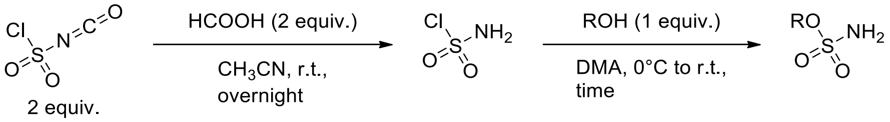
A flame-dried round bottom flask equipped with a magnetic stir bar was charged with ethylene glycol (75 mmol, 15 equiv), triethyl orthoformate (15 mmol, 3.0 equiv), and camphorsulfonic acid (5 mol %) in dichloromethane under nitrogen. The aldehyde was added dropwise (5 mmol, 1.0 equiv) and the mixture was stirred until determined to be completed by TLC. The reaction was quenched with $NaHCO_3$ (20 mL). The aqueous layer was washed with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were washed with brine (20 mL), dried over magnesium sulfate ($MgSO_4$) and concentrated under reduced pressure. Silica gel chromatography was used to purify the crude products.

General Procedure for Benzoate protection.



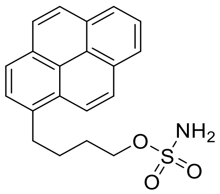
A flame-dried round bottom flask equipped with a magnetic stir bar was charged with alcohol (10 mmol, 1 equiv.) and 4-dimethylaminopyridine (0.2 mmol, 0.02 equiv.). Dry dichloromethane (20 mL, 0.5 M) was added and the reaction mixture was stirred and cooled to 0 ^{o}C. Benzoyl chloride (11 mmol, 1.1 equiv.) was added to the reaction mixture followed by triethylamine (20 mmol, 2 equiv.). The round bottom flask was then allowed to warm to room temperature and stir overnight. The reaction was quenched with water (20 mL) and diluted with ether (30 mL). The organic layer was then washed with saturated sodium bicarbonate (2 x 20 mL) and brine (1 x 20 mL) and dried over sodium sulfate. The solvent was then removed under reduced pressure and silica gel chromatography was used to purify the crude products.

General Procedure for Synthesis of Sulfamates.

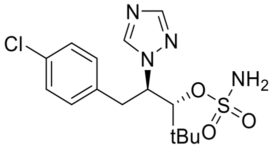


A flame-dried round bottom flask equipped with a magnetic stir bar was charged with a solution of formic acid (26.25 mmol, 3.5 equiv.) in acetonitrile (CH_3CN) (2.5 M). Chlorosulfonyl isocyanate (3 equiv.) in CH_3CN (2.5 M) was added to the reaction mixture over 10 min. The reaction mixture was stirred at room temperature overnight. A solution of alcohol (1 equiv.) in *N*, *N*-dimethylacetamide (0.5 M) was slowly added to the reaction mixture at 0 °C. The reaction was monitored using TLC and quenched with water (~2 mL per 1 mmol of chlorosulfonyl isocyanate) upon completion. Ethyl acetate (3 x amount of water added) was used to extract the aqueous layer and the combined organic layers were further washed with water and brine then dried over sodium sulfate. The solvent was then removed under reduced pressure and purified through silica gel chromatography.

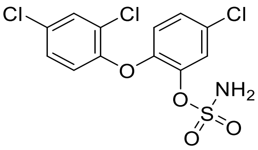
Characterization of Starting Materials.



Pyrenebutanol sulfamate (k). Following the general procedure with 1-pyrenebutanol (1 g, 3.64 mmol) and purified with silica gel chromatography (70:30, hexanes:ethyl acetate) to afford a pale yellow solid (0.62 g, 48% yield). **^{1}H NMR** (300 MHz, Acetone) δ 8.41 (d, *J* = 9.3 Hz, 1H), 8.27 (m, 4H), , 8.12 (d, *J* = 0.8 Hz, 2H), 8.05 (t, *J* = 7.6 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 6.62 (s, 2H), 4.25 (t, *J* = 6.0 Hz, 2H), 3.45 (t, *J* = 7.4 Hz, 2H), 2.03 – 1.80 (m, 4H). **^{13}C NMR** (75 MHz, Acetone) δ 137.69, 132.50, 132.00, 130.92, 129.61, 128.49, 128.41, 128.25, 127.56, 126.96, 125.89, 125.74, 124.46, 70.53, 33.45, 28.85. **IR** (thin film): 3382, 3285, 3040, 2940, 2865, 1602, 1558, 1457, 1363, 1182, 940, 843, 760, 720, 553 cm^{-1}. **MS** (ESI, positive mode): 376.5 (M+Na$^+$) **Melting point** : 113 – 117 °C

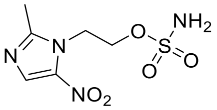


Paclobutrazole sulfamate. Prepared via the general procedure using paclobutrazol (2.93 g, 10 mmol) and purified with silica gel chromatography (50:50, hexanes:ethyl acetate) to afford a white solid (1.26 g, 34% yield). **^{1}H NMR** (500 MHz, Acetone) δ 8.50 (s, 1H), 7.73 (s, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 6.7 Hz, 4H), 5.14 (dd, *J* = 10.7, 4.3 Hz, 1H), 4.77 (s, 1H), 3.57 – 3.44 (m, 1H), 3.39 (dd, *J* = 14.1, 4.4 Hz, 1H), 0.84 (s, 9H). **^{13}C NMR** (75 MHz, Acetone) δ 150.83, 144.69, 137.06, 133.06, 131.63, 129.26, 89.71, 63.05, 40.95, 36.32, 26.57. **IR** (thin film): 3217, 2966, 1706, 1507, 1493, 1366, 1278, 1179, 1138, 1015, 927, 898, 855, 832, 738, 679, 578 cm^{-1}. **MS** (ESI, negative mode): 371.6 (M-H$^+$) **Melting point** : 189– 191 °C



Triclosan sulfamate. Following the general procedure with triclosan (6.41 g, 22 mmol) and purified with silica gel chromatography (70:30, hexanes:ethyl acetate) to afford a pale yellow solid (3.8 g, 47% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50 (s, 2H), 7.32 – 7.16 (m, 3H), 6.89 (d, *J* =

8.8 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 1H), 5.11 (s, 2H) **^{13}C NMR** (75 MHz, Acetone) δ 151.72, 148.87, 141.99, 131.11, 130.50, 129.55, 129.09, 128.50, 127.12, 125.38, 122.81, 120.92. **IR** (thin film): 3407, 3293, 3094, 1580, 1549, 1487, 1474, 1387, 1267, 1197, 1174, 1120, 1100, 923, 870, 804, 768, 750, 692, 584, 538 cm^{-1}. **MS** (ESI, negative mode): 367.4 (M-H$^+$) **Melting point** : 112 – 115 °C



Metronidazole sulfamate. Following the general procedure with metronidazole (1.71 g, 10 mmol) and purified with silica gel chromatography (30:70 hexanes:ethyl acetate) to afford a white solid (1.85 g, 74% yield). **^{1}H NMR** (300 MHz, DMSO) δ 8.04 (s, 1H), 7.58 (s, 2H), 4.62 (t, *J* = 4.8 Hz, 2H), 4.37 (t, *J* = 4.8 Hz, 2H), 2.46 (s, 3H). **^{13}C NMR** (75 MHz, DMSO) δ 151.82, 138.35, 133.06, 67.22, 45.00, 14.01. **IR** (thin film): 3337, 3153, 2967, 1533, 1457, 1387, 1363, 1260, 1185, 1152, 1027, 943, 904, 828, 777, 744, 734, 611, 539, 475 cm^{-1}. **MS** (ESI, negative mode): 249.5 (M-H$^+$) **Melting point** : 165 – 170 °C

1.4.3 *General Procedure for Selenium Catalyzed Allylic Amination*

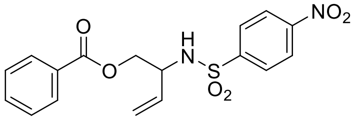
General procedure A: A flame-dried borosilicate glass vial equipped with a magnetic stir bar was charged with $SePCy_3$ (0.03 mmol, 0.15 equiv.), amine (0.4 mmol, 2 equiv.), and alkene (0.2 mmol, 1.0 equiv.). The vial was thoroughly flushed with nitrogen and capped with a Teflon-lined screw cap. Dry dichloromethane (1 mL, 0.2 M) was added, followed by iodobenzene diacetate (0.4 mmol, 2 equiv). The solution was stirred at the specified temperature and the reaction was monitored by TLC. Upon completion, an equal volume of ethyl acetate was added to the reaction and the mixture was flushed through a silica gel plug with ethyl acetate. The eluent was then concentrated on a rotary evaporator to afford the crude reaction product, which was then purified by column chromatography.

General procedure B: A flame-dried borosilicate glass vial equipped with a magnetic stir bar was charged with SeIMe (0.75 mmol, 0.15 equiv.), amine (1 mmol, 2 equiv.), and alkene (0.5 mmol, 1.0 equiv.). The vial was thoroughly flushed with nitrogen and capped with a Teflon-lined screw cap. Dry dichloromethane (0.2 M) was added followed by iodobenzene diacetate (1 mmol, 2 equiv). The solution was stirred at the specified temperature and the reaction was monitored by TLC. Upon completion, an equal volume of ethyl acetate was added to the reaction and the mixture was flushed through a silica gel plug with ethyl acetate. The eluent was then concentrated on a rotary evaporator to afford the crude reaction product, which was then purified by column chromatography.

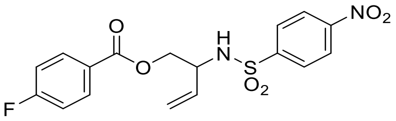
General procedure C: A flame-dried borosilicate glass vial equipped with a magnetic stir bar was charged with SeIMe (0.03 mmol, 0.15 equiv.), amine (0.4 mmol, 2 equiv.), and alkene (0.2 mmol, 1.0 equiv.). The vial was thoroughly flushed with nitrogen and capped with a Teflon-lined screw cap. Dry dichloromethane (1 mL, 0.2 M) was added followed by iodobenzene diacetate (0.4 mmol, 2 equiv). The solution was stirred at specified temperature and the reaction was monitored by TLC. Upon completion, an equal volume of ethyl acetate was added to the reaction and the mixture was flushed through a silica gel plug with ethyl acetate. The eluent was then concentrated on a rotary evaporator to afford the crude reaction product, which was then purified by column chromatography.

Procedure for large scale reaction: A 250 mL flame-dried round bottom flask equipped with a magnetic stir bar was charged with $SePCy_3$ (1 mmol, 0.05 equiv.), amine (40 mmol, 2 equiv.), and alkene (20 mmol, 1.0 equiv.). The round bottom flask was thoroughly flushed with nitrogen and capped with a rubber septum. Dry dichloromethane (100 mL, 0.2 M) was added followed by iodobenzene diacetate (0.4 mmol, 2 equiv). The solution was stirred at room temperature and the reaction was monitored by TLC. Upon completion, the solvent was concentrated and the product purified by silica gel chromatography (95:5 to 80:20, hexanes/ethyl acetate).

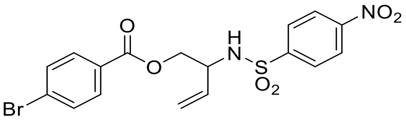
1.4.4 *Characterization of Products*



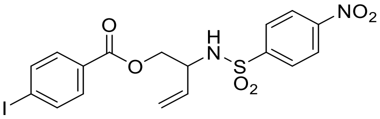
2a. Prepared according to general procedure A and purified by silica gel chromatography (95:5 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (63 mg, 83%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.8 Hz, 2H), 7.95 (d, *J* = 8.8 Hz, 2H), 7.85 – 7.75 (m, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 2H), 5.76 (ddd, *J* = 16.9, 10.4, 5.4 Hz, 1H), 5.48 (d, *J* = 7.5 Hz, 1H), 5.36 (d, *J* = 17.2 Hz, 1H), 5.25 (d, *J* = 10.6 Hz, 1H), 4.37 – 4.31 (m, 2H), 4.24 (dd, *J* = 10.7, 3.2 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.57, 149.87, 146.72, 133.94, 133.44, 129.77, 129.03, 128.64, 128.20, 124.42, 119.07, 65.67, 56.30. **IR** (thin film): 3291, 3106, 1750, 1530, 1350, 1194, 1165, 1093, 934, 854, 738 cm^{-1}. **MS** (ESI, negative mode): 375.8 ($M-H^+$) **Melting point** : 123-125 °C



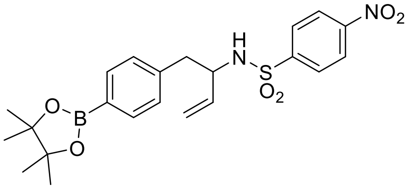
3a. Prepared according to general procedure A and purified by silica gel chromatography (95:5 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (59 mg, 75%). ^{1}**H NMR** (300 MHz, Acetone) δ 8.31 (d, *J* = 8.9 Hz, 2H), 8.11 (d, *J* = 8.9 Hz, 2H), 7.96 (dd, *J* = 8.9, 5.5 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.21 (t, *J* = 8.8 Hz, 2H), 5.87 (ddd, *J* = 16.7, 10.5, 6.0 Hz, 1H), 5.33 (d, *J* = 17.2 Hz, 1H), 5.16 (d, *J* = 10.5 Hz, 1H), 4.50 – 4.39 (m, 1H), 4.40-4.26 (m, 2H). ^{13}**C NMR** (126 MHz, Acetone) δ 166.16 (d, J = 274.7 Hz), 165.25, 150.27, 148.22, 134.80, 132.77, 132.70, 128.67, 126.70, 124.78, 117.94, 115.92 (d, J = 22.2 Hz), 66.41, 56.02. **IR** (thin film): 3280, 3107, 1721, 1698, 1604, 1532, 1508, 1413, 1350, 1307, 1273, 1240, 1167, 1091, 1014, 988, 854, 767, 737, 684 cm^{-1}. **MS** (ESI, negative mode): 393.8 (M-H^{+}) **Melting point** : 116-120 °C



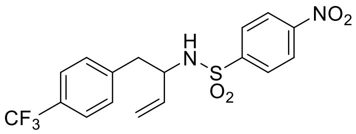
4a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 70:30, hexanes/ethyl acetate) to afford the product as a white solid (62 mg, 68%). ^{1}**H NMR** (300 MHz, Acetone) δ 8.31 (d, *J* = 8.9 Hz, 2H), 8.11 (d, *J* = 8.9 Hz, 2H), 7.81 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 8.6 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 1H), 5.87 (ddd, *J* = 16.9, 10.5, 6.0 Hz, 1H), 5.33 (d, *J* = 17.2 Hz, 1H), 5.16 (d, *J* = 10.5 Hz, 1H), 4.51 – 4.41 (m, 1H), 4.36 (dd, *J* = 11.3, 4.5 Hz, 1H), 4.30 (dd, *J* = 11.3, 7.4 Hz, 1H)..^{13}**C NMR** (126 MHz, Acetone) δ 165.78, 150.74, 148.68, 135.22, 132.67, 132.16, 129.82, 129.12, 128.70, 125.24, 118.42, 66.96, 56.44. **IR** (thin film): 3267, 2924, 2849, 1694, 1515, 1457, 1397, 1340, 1274, 1149, 1089, 850, 758, 733 cm^{-1}. **MS** (ESI, negative mode): 454.3 (M-H^{+}) **Melting point** : 179-181 °C



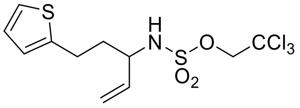
5a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 70:30, hexanes/ethyl acetate) to afford the product as a white solid (57 mg, 57%). **^{1}H NMR** (300 MHz, Acetone) δ 8.23 (d, *J* = 8.9 Hz, 2H), 8.02 (d, *J* = 8.9 Hz, 2H), 7.79 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 1H), 5.79 (ddd, *J* = 16.6, 10.5, 6.0 Hz, 1H), 5.25 (d, *J* = 17.2 Hz, 1H), 5.08 (d, *J* = 10.5 Hz, 1H), 4.41 – 4.32 (m, 1H), 4.27 (dd, *J* = 11.3, 4.4 Hz, 1H), 4.21 (dd, *J* = 11.3, 7.4 Hz, 1H). **^{13}C NMR** (126 MHz, Acetone) δ 166.05, 150.74, 148.69, 138.79, 135.25, 131.93, 130.26, 129.12, 125.25, 118.41, 101.53, 66.92, 56.45. **IR** (thin film): 3286, 2954, 2926, 1725, 1591, 1446, 1399, 1366, 1272, 1186, 1130, 1103, 1070, 1012, 988, 849, 756, 726, 683, 625, 593, 537 cm^{-1}. **MS** (ESI, negative mode): 501.6 (M-H$^+$) **Melting point** : 201-206 °C



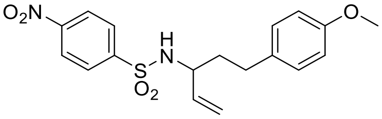
6a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (75 mg, 82%). **^{1}H NMR** (300 MHz, Acetone) δ 8.20 (d, *J* = 8.8 Hz, 2H), 7.82 (d, *J* = 8.8 Hz, 2H), 7.49 (d, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.03 (d, *J* = 8.8 Hz, 1H), 5.86 (ddd, *J* = 16.7, 10.4, 6.0 Hz, 1H), 5.17 (d, *J* = 17.1 Hz, 1H), 5.02 (d, *J* = 10.4 Hz, 1H), 4.28 – 4.13 (m, 1H), 2.92 (dd, *J* = 13.7, 5.6 Hz, 1H), 2.85 – 2.70 (m, 1H), 1.35 (s, 12H). **^{13}C NMR** (126 MHz, Acetone) δ 150.43, 148.56, 141.85, 139.39, 135.37, 129.79, 128.83, 124.86, 115.98, 84.51, 59.11, 42.48, 25.28. **IR** (thin film): 3289, 2981, 2932, 1612, 1532, 1400, 1361, 1273, 1165, 1144, 1091, 1022, 963, 857, 736, 685, 659, 618, 567 cm^{-1}. **MS** (ESI, negative mode): 457.4 (M-H^{+}) **Melting point** : 155-159 °C



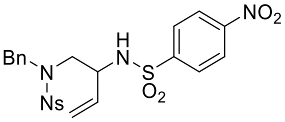
7a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (73 mg, 91%). **^{1}H NMR** (300 MHz, Acetone) δ 8.26 (d, *J* = 8.8 Hz, 2H), 7.89 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.8 Hz, 1H), 5.85 (ddd, *J* = 16.8, 10.4, 6.1 Hz, 1H), 5.16 (d, *J* = 17.2 Hz, 1H), 5.02 (d, *J* = 10.4 Hz, 1H), 4.36 – 4.15 (m, 1H), 3.03 (dd, *J* = 13.7, 5.6 Hz, 1H), 2.87 (dd, *J* = 13.6, 9.1 Hz, 1H). **^{13}C NMR** (126 MHz, Acetone) δ 150.17, 148.16, 142.99, 138.55, 130.75, 128.52, 125.43(q, *J* = 271.2 Hz), 125.41, 124.51, 115.93, 58.51, 41.60. **IR** (thin film): 3280, 2930, 1607, 1531, 1420, 1350, 1325, 1162, 1121, 1093, 1067, 850, 747, 736, 684, 668 cm^{-1}. **MS** (ESI, negative mode): 399.7 (M-H^{+}) **Melting point** : 149-154 °C



8b. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a clear oil (47 mg, 62%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.15 (d, *J* = 5.1 Hz, 1H), 6.93 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.83 (d, *J* = 3.3 Hz, 1H), 5.82 (ddd, *J* = 17.1, 10.3, 6.8 Hz, 1H), 5.40 – 5.27 (m, 2H), 4.67 – 4.62 (m, 1H), 4.61 (s, 2H), 4.17 – 3.94 (m, 1H), 2.96 (t, *J* = 7.7 Hz, 2H), 2.05 (dd, *J* = 7.6, 3.5 Hz, 1H), 2.00 (dd, *J* = 7.3, 3.2 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 143.57, 136.76, 127.27, 125.05, 123.85, 118.27, 93.78, 78.52, 57.44, 37.22, 26.23. **IR** (thin film): 3304, 2946, 2924, 1717, 1649, 1560, 1508, 1441, 1359, 1172, 1083, 1009, 927, 852, 725 cm^{-1}. **MS** (ESI, negative mode): 375.6 (M-H^{+})

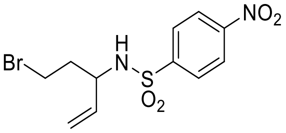


9a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (47 mg, 62%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.8 Hz, 2H), 7.98 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.5 Hz, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 5.64 – 5.43 (m, 1H), 5.01 (d, *J* = 10.2 Hz, 2H), 5.00 (d, *J* = 17.3 Hz, 2H), 4.76 (d, *J* = 8.2 Hz, 1H), 3.87 (quin, *J* = 7.0 Hz, 1H), 3.79 (s, 3H), 2.56 (t, *J* = 7.5 Hz, 2H), 1.80 (q, *J* = 7.2 Hz, 2H) **^{13}C NMR** (126 MHz, Acetone) δ 158.13, 149.92, 148.02, 137.95, 133.21, 129.20, 128.42, 124.15, 115.42, 113.75, 56.40, 54.55, 37.48, 30.59. **IR** (thin film): 3285, 2932, 2858, 1609, 1529, 1215, 1444, 1419, 1349, 1306, 1246, 1163, 1092, 1033, 931, 853, 736, 684 cm^{-1}. **MS** (ESI, negative mode): 375.9 (M-H^{+}) **Melting point** : 71-74 °C

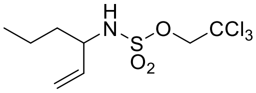


10a. Prepared according to general procedure A and purified by silica gel chromatography (85:15 to 70:30, hexanes/ethyl acetate) to afford the product as a pale yellow solid (95 mg, 87%). **^{1}H NMR** (300 MHz, Acetone) δ 8.43 (d, *J* = 9.0 Hz, 2H), 8.40 (d, *J* = 9.1 Hz, 2H), 8.14 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.8 Hz, 2H), 7.48 – 7.14 (m, 5H), 6.94 (d, *J* = 8.4 Hz, 1H), 5.48 (ddd, *J* = 17.4, 10.4, 7.5 Hz, 1H), 4.85 (d, *J* = 11.5 Hz, 1H), 4.80 (d, *J* = 18.3 Hz, 1H), 4.60 (d, *J* = 15.1 Hz, 1H), 4.42 (d, *J* = 15.1 Hz, 1H), 3.91 (quin, *J* = 7.5 Hz, 1H), 3.52 – 3.23 (m, 2H). **^{13}C NMR** (126

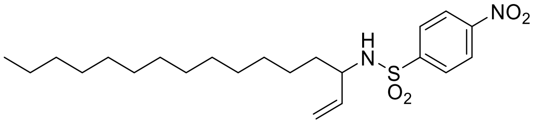
MHz, Acetone) δ 151.29, 151.08, 148.13, 146.63, 136.39, 135.49, 129.87, 129.74, 129.63, 129.49, 129.06, 125.45, 125.22, 118.85, 56.34, 53.47, 52.95. **IR** (thin film): 3293, 3106, 2925, 1606, 1532, 1455, 1402, 1350, 1312, 1164, 1091, 1012, 936, 855, 784, 737, 685 cm^{-1}. **MS** (ESI, negative mode): 545.9 (M-H$^+$) **Melting point** : 153-155 °C



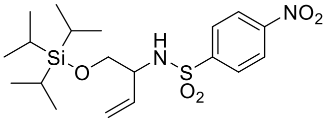
11a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as an off-white solid (59 mg, 85%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.35 (d, *J* = 8.9 Hz, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 5.52 (ddd, *J* = 17.2, 10.3, 6.9 Hz, 1H), 5.13 (d, *J* = 8.6 Hz, 1H), 5.08 (d, *J* = 16.1 Hz, 1H), 5.05 (d, *J* = 9.8 Hz, 1H), 4.18 – 3.98 (m, 1H), 3.49 – 3.22 (m, 2H), 2.12 – 1.97 (m, 2H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 150.32, 146.74, 135.85, 128.71, 124.58, 118.01, 55.58, 38.33, 28.83. **IR** (thin film): 3284, 3106, 2923, 1607, 1530, 1420, 1351, 1311, 1163, 1092, 1054, 934, 854, 737, 685, 616, 564 cm^{-1}. **MS** (ESI, negative mode): 348.6 (M-H$^+$) **Melting point** : 103-106 °C



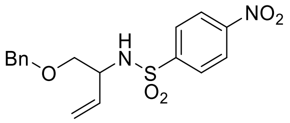
12b. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as an oil (46 mg, 81%). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 5.78 (ddd, *J* = 17.1, 10.3, 6.8 Hz, 1H), 5.30 (d, *J* = 17.1 Hz, 1H), 5.23 (d, *J* = 10.3 Hz, 1H), 4.70 (d, *J* = 8.0 Hz, 1H), 4.61 (s, 2H), 4.08 – 3.94 (m, 1H), 1.69 – 1.56 (m, 2H), 1.49 – 1.35 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 137.70, 117.78, 94.10, 78.77, 58.18, 37.84, 19.21, 14.25. **IR** (thin film): 3301, 2962, 2936, 2875, 1447, 1432, 1363, 1183, 1089, 1048, 1015, 942, 856, 758, 726, 625, 588, 537 cm^{-1}. **MS** (ESI, negative mode): 307.5 (M-H$^+$)



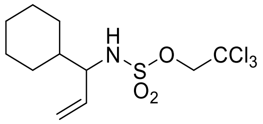
13a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (64 mg, 75%). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.35 (d, *J* = 8.8 Hz, 2H), 8.05 (d, *J* = 8.5 Hz, 2H), 5.48 (ddd, *J* = 17.1, 10.3, 6.9 Hz, 1H), 4.98 (d, *J* = 17.2 Hz, 1H), 4.95 (d, *J* = 10.3 Hz, 1H), 4.92 – 4.90 (m, 1H), 3.85 (quin, *J* = 6.9 Hz, 1H), 1.48 (t, *J* = 6.8 Hz, 2H), 1.35 – 1.03 (m, 22H), 0.88 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 150.22, 147.42, 137.56, 128.73, 124.48, 116.74, 57.30, 36.02, 32.25, 29.97, 29.85, 29.76, 29.68, 29.46, 25.66, 23.01, 14.44. **IR** (thin film): 3276, 2920, 2851, 1682, 1651, 1606, 1529, 1468, 1428, 1347, 1310, 1164, 1091, 1101, 927, 854, 738, 684, 620, 565 cm^{-1}. **MS** (ESI, negative mode): 423.8 (M-H$^+$) **Melting point** : 69-74 °C



14a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a clear film (71 mg, 83%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.32 (d, *J* = 8.9 Hz, 2H), 8.04 (d, *J* = 8.9 Hz, 2H), 5.65 (ddd, *J* = 17.2, 10.3, 6.9 Hz, 1H), 5.23 (d, *J* = 6.3 Hz, 1H), 5.14 (d, *J* = 17.2 Hz, 1H), 5.09 (d, *J* = 10.4 Hz, 1H), 3.92 – 3.81 (m, 1H), 3.70 (dd, *J* = 9.9, 4.3 Hz, 1H), 3.63 (dd, *J* = 9.9, 5.5 Hz, 1H), 1.10 – 1.02 (m, 3H), 1.00 – 0.95 (m, 18H) **^{13}C NMR** (75 MHz, CDCl$_3$) δ 150.19, 146.90, 134.92, 128.70, 124.40, 118.30, 65.91, 58.50, 18.09, 12.02. **IR** (thin film): 3296, 3106, 2944, 2867, 1607, 1532, 1463, 1403, 1349, 1310, 1249, 1168, 1118, 1093, 1069, 1014, 995, 922, 882, 854, 782, 736, 685, 618, 567 cm^{-1}. **MS** (ESI, negative mode): 427.9 (M-H$^+$) **Melting point** : 37-41 °C

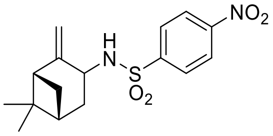


15a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as an off-white wax (44 mg, 61%). **^{1}H NMR** (500 MHz, Acetone) δ 8.30 (d, *J* = 8.4 Hz, 2H), 8.11 (d, *J* = 8.2 Hz, 2H), 7.33 – 7.24 (m, 3H), 7.22 (d, *J* = 7.2 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 1H), 5.80 (ddd, *J* = 16.8, 10.3, 6.1 Hz, 1H), 5.24 (d, *J* = 17.2 Hz, 1H), 5.07 (d, *J* = 10.4 Hz, 1H), 4.39 (s, 2H), 4.20 – 4.13 (m, 1H), 3.55 – 3.39 (m, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 150.06, 146.84, 137.32, 134.67, 128.73, 128.63, 128.34, 128.03, 124.29, 118.28, 73.55, 71.98, 56.52. **IR** (thin film): 3285, 3105, 2864, 1529, 1453, 1402, 1349, 1311, 1166, 1091, 1027, 931, 853, 737, 699, 685 cm^{-1}. **MS** (ESI, negative mode): 361.4 (M-H$^+$)

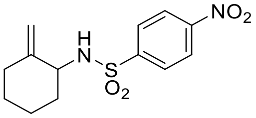


16b. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (61 mg, 88%). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 5.75 (ddd, *J* = 17.3, 10.3, 7.2 Hz, 1H), 5.29 (d, *J* = 17.1 Hz, 1H), 5.26 (d, *J* = 10.3 Hz, 1H), 4.82 (d, *J* = 8.5 Hz, 1H), 4.60 (s, 2H), 3.83 (q, *J* = 7.2 Hz, 1H), 1.88 – 1.63 (m, 5H), 1.59 – 1.46 (m, 1H), 1.31 – 1.15 (m, 3H), 1.13 – 0.92 (m, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 135.85, 118.21, 93.87, 78.45, 63.07, 42.51, 29.17, 29.08, 26.51, 26.27, 26.24. **IR** (thin film):

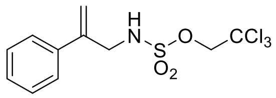
3301, 2929, 2855, 1448, 1363, 1261, 1181, 1089, 1048, 1011, 945, 854, 758, 726, 595, 538 cm^{-1}. **MS** (ESI, negative mode): 347.6 (M-H$^+$) **Melting point** : 77-78 °C



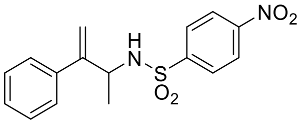
17a. Prepared according to general procedure B and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a yellowish solid (114 mg, 68%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.8 Hz, 2H), 8.11 (d, *J* = 8.8 Hz, 2H), 4.86 (d, *J* = 6.1 Hz, 1H), 4.77 (s, 1H), 4.60 (s, 1H), 4.13 (t, *J* = 6.9 Hz, 1H), 2.59 – 2.37 (m, 2H), 2.36 – 2.16 (m, 1H), 2.03 – 1.83 (m, 2H), 1.28 – 1.17 (m, 4H), 0.66 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 152.49, 150.35, 147.05, 128.76, 124.75, 113.08, 51.35, 49.44, 40.46, 40.31, 35.20, 29.43, 25.97, 22.37. **IR** (thin film): 3276, 3117, 2975, 2921, 1607, 1531, 1348, 1333, 1307, 1167, 1093, 961, 909, 854, 737, 684, 635, 597, 559 cm^{-1}. **MS** (ESI, negative mode): 335.8 (M-H$^+$) **Melting point** : 77-78 °C



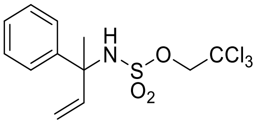
18a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as an off white solid (55 mg, 92%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.6 Hz, 1H), 8.07 (d, *J* = 8.7 Hz, 1H), 5.11 (d, *J* = 8.3 Hz, 1H), 4.66 (s, 1H), 4.65 (s, 1H), 3.99 – 3.77 (m, 1H), 2.34 – 2.16 (m, 1H), 2.03 – 1.90 (m, 1H), 1.90 – 1.79 (m, 1H), 1.78 – 1.56 (m, 2H), 1.53 – 1.29 (m, 3H). **^{13}C NMR** (126 MHz, C_6D_6) δ 149.93, 147.02, 128.26, 124.27, 108.03, 56.64, 35.77, 33.80, 27.17, 24.11. **IR** (thin film): 3290, 3106, 2937, 2859, 1653, 1607, 1530, 1446, 1350, 1308, 1167, 1092, 1013, 969, 909, 854, 736, 685, 616, 562 cm^{-1}. **MS** (ESI, negative mode): 295.4 (M-H$^+$) **Melting point** : 119-122 °C



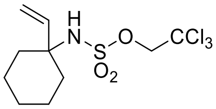
19b. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a clear film (59 mg, 86%). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.49 – 7.31 (m, 5H), 5.54 (s, 1H), 5.39 (s, 1H), 4.75 – 4.64 (m, 1H), 4.54 (s, 2H), 4.29 (d, *J* = 5.2 Hz, 2H). **^{13}C NMR** (126 MHz, C$_6$D$_6$) δ 142.70, 137.75, 129.23, 128.96, 126.53, 116.55, 78.56, 48.32 **IR** (thin film): 3313, 2950, 1428, 1368, 1181, 1087, 1018, 911, 856, 779, 758, 723, 617, 537, 486 cm^{-1}. **MS** (ESI, negative mode): 342.0 (M-H$^+$)



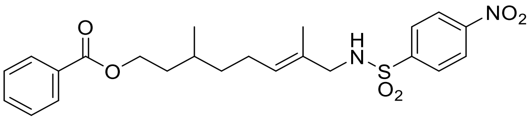
20a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a solid (59 mg, 86%). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.19 (d, *J* = 8.8 Hz, 2H), 7.88 (d, *J* = 8.8 Hz, 2H), 7.29 – 7.13 (m, 3H), 7.09 (dd, *J* = 7.8, 1.5 Hz, 2H), 5.16 (s, 2H), 4.93 (d, *J* = 8.1 Hz, 1H), 4.61 – 4.37 (m, 1H), 1.40 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 150.11, 149.65, 146.81, 139.68, 128.78, 128.47, 128.32, 126.96, 124.42, 114.51, 53.46, 22.50. **IR** (thin film): 3288, 3105, 2981, 2933, 2870, 1607, 1530, 1427, 1350, 1311, 1166, 1089, 979, 911, 854, 779, 736, 685, 621 cm^{-1}. **MS** (ESI, negative mode): 331.8 (M-H$^+$) **Melting point** : 117-121 °C



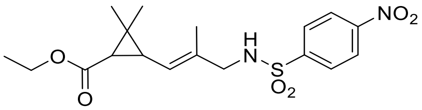
21b. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a clear oil (58 mg, 74%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.54 – 7.46 (m, 2H), 7.45 – 7.32 (m, 3H), 6.25 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.37 (d, *J* = 10.7 Hz, 1H), 5.32 (d, *J* = 17.3 Hz, 1H), 5.17 (s, 1H), 4.53 (d, *J* = 2.4 Hz, 2H), 1.95 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.42, 141.83, 129.04, 128.35, 126.43, 115.69, 93.75, 78.55, 63.74, 25.84. **IR** (thin film): 3297, 3061, 2992, 2948, 1494, 1446, 1410, 1358, 1181, 1124, 1088, 1046, 980, 931, 856, 763, 725, 700, 603, 539 cm^{-1}. **MS** (ESI, negative mode): 355.6 (M-H$^+$)



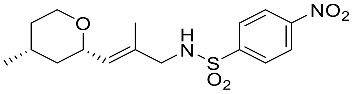
22b. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (59 mg, 87%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.01 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.30 (d, *J* = 17.6 Hz, 1H), 5.27 (d, *J* = 10.8 Hz, 1H), 4.85 (s, 1H), 4.60 (s, 2H), 2.04 – 1.88 (m, 2H), 1.82 – 1.69 (m, 2H), 1.69 – 1.47 (m, 5H), 1.47 – 1.31 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.79, 115.98, 93.90, 78.50, 60.59, 35.78, 25.54, 22.17. **IR** (thin film): 3281, 2934, 2860, 1453, 1428, 1373, 1361, 1345, 1310, 1170, 1142, 1090, 1043, 1023, 996, 933, 903, 857, 763, 721, 593, 524 cm^{-1}. **MS** (ESI, negative mode): 333.5 (M-H$^+$) **Melting point** : 95-97 °C



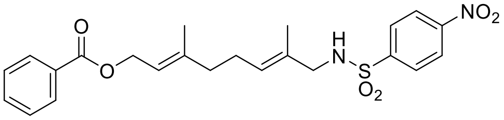
23a. Prepared according to the general procedure B and purified by silica gel chromatography (100:0 to 85:15, hexanes/ethyl acetate) to afford the product as a yellow oil (201 mg, 88% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.8 Hz, 2H), 8.00 (d, *J* = 7.4 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 5.26 (t, *J* = 6.9 Hz, 1H), 5.14 (t, *J* = 6.1 Hz, 1H), 4.32 (m, 2H), 3.51 (d, *J* = 6.1 Hz, 2H), 2.03 – 1.87 (m, 2H), 1.80 – 1.68 (m, 1H), 1.63 – 1.54 (m, 2H), 1.52 (s, 3H), 1.37 – 1.28 (m, 1H), 1.20 – 1.10 (m, 1H), 0.93 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.06, 150.24, 146.63, 133.22, 130.65, 130.01, 129.78, 129.63, 128.66, 128.60, 124.54, 63.69, 51.52, 36.51, 35.69, 29.86, 25.43, 19.80, 14.45. **IR** (thin film): 3433, 1638, 1530, 1348, 1314, 1276, 1164, 1094, 1070, 853, 735, 714, 686, 614 cm^{-1}. **MS** (ESI, negative mode): 459.0 (M-H$^+$)



24a. Prepared according to the general procedure B and purified by silica gel chromatography (100:0 to 85:15, hexanes/ethyl acetate) to afford the product as a yellow oil (157 mg, 79%, 1.4:1 mixture of diastereomers from starting material). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.1 Hz, 3.2H, both), 8.03 (d, *J* = 8.8 Hz, 1.2H, minor), 8.02 (d, *J* = 8.8 Hz, 2H, major), 5.57 (d, *J* = 8.5 Hz, 0.6H, minor), 5.07 (d, *J* = 6.1 Hz, 0.6H, minor), 5.06 (d, *J* = 6.0 Hz, 1H, major), 5.03 (d, *J* = 8.7 Hz, 1H, major), 4.11 (q, *J* = 7.1 Hz, 2H, major), 4.07 – 4.00 (m, 1.2H, minor), 3.56 (d, *J* = 6.1 Hz, 3.2H, both), 1.92 (dd, *J* = 8.4, 5.4 Hz, 1H, major), 1.75 (t, *J* = 8.5 Hz, 0.6H, minor), 1.67 (d, *J* = 8.6 Hz, 0.6H, minor), 1.64 (s, 1.8H, minor), 1.60 (s, 3H, major), 1.34 (d, *J* = 5.4 Hz, 1H, major), 1.24 (t, *J* = 7.1 Hz, 4.8H, both), 1.21 (s, 3H, major), 1.17 (s, 1.8H, minor), 1.14 (s, 1.8H, minor), 1.06 (s, 3H, major). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.15, 171.33, 150.33, 146.63, 146.47, 133.19, 132.67, 128.69, 128.63, 126.41, 124.61, 124.58, 123.79, 60.81, 60.36, 51.54, 51.16, 35.32, 31.87, 31.48, 28.90, 28.83, 26.94, 22.46, 20.58, 15.15, 15.03, 14.95, 14.63, 14.58. **IR** (thin film): 3283, 2981, 2954, 2872, 1717, 1530, 1420, 1378, 1350, 1311, 1197, 1165, 1113, 1094, 1055, 1030, 912, 856, 736, 686, 614, 556 cm^{-1}. **MS** (ESI, negative mode): 395.0 (M-H$^+$)

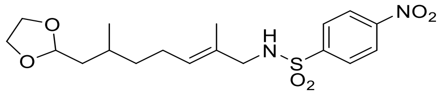


25a. Prepared according to the general procedure B and purified by silica gel chromatography (100:0 to 85:15, hexanes/ethyl acetate) to afford the product as a white solid (106 mg, 60% yield, 10:1 mixture of diastereomers from starting material). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.8 Hz, 2H), 5.24 (d, *J* = 7.8 Hz, 1H), 5.09 (t, *J* = 6.2 Hz, 1H), 3.90 (ddd, *J* = 10.7, 9.2, 2.9 Hz, 2H), 3.54 (d, *J* = 6.1 Hz, 2H), 3.39 (td, *J* = 12.4, 2.0 Hz, 1H), 1.60 (s, 3H), 1.59 – 1.53 (m, 1H), 1.50 (dd, *J* = 13.3, 1.7 Hz, 1H), 1.40 (d, *J* = 13.3 Hz, 1H), 1.15 (qd, *J* = 12.5, 4.6 Hz, 1H), 0.90 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.44, 146.62, 132.61, 130.24, 128.68, 124.68, 74.47, 68.21, 50.92, 40.56, 34.55, 30.33, 22.47, 15.15. **IR** (thin film): 3279, 3106, 2952, 2925, 2869, 1606, 1530, 1456, 1441, 1349, 1311, 1257, 1165, 1091, 913, 854, 736, 686, 613 cm^{-1}. **MS** (ESI, negative mode): 353.0 (M-H$^+$) **Melting Point** : 139 – 144 °C

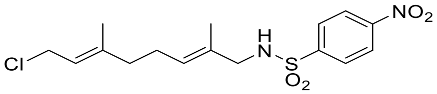


26a. Prepared according to the general procedure B and purified by silica gel chromatography (100:0 to 85:15, hexanes/ethyl acetate) to afford the product as a yellow oil (209 mg, 91% yield).

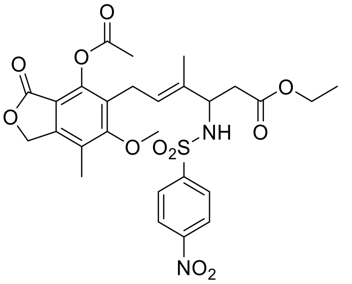
^{1}H NMR (500 MHz, CDCl$_3$) δ 8.32 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.6 Hz, 2H), 8.02 (d, *J* = 6.7 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 5.38 (t, *J* = 6.4 Hz, 1H), 5.23 (t, *J* = 6.6 Hz, 1H), 5.19 (t, *J* = 6.1 Hz, 1H), 4.81 (d, *J* = 6.8 Hz, 2H), 3.50 (d, *J* = 6.1 Hz, 2H), 2.08 (dd, *J* = 14.1, 7.0 Hz, 2H), 2.01 (t, *J* = 7.1 Hz, 2H), 1.71 (s, 3H), 1.52 (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 167.18, 150.27, 146.70, 141.20, 133.30, 130.66, 130.58, 129.90, 128.85, 128.71, 128.62, 124.59, 119.69, 62.31, 51.57, 38.91, 25.96, 16.83, 14.56. **IR** (thin film): 3627, 3280, 3105, 3068, 2922, 1746, 1604, 1585, 1528, 1451, 1349, 1313, 1273, 1165, 1094, 1028, 912, 855, 735, 688, 648, 615, 533 cm^{-1}. **MS** (ESI, negative mode): 457.0 (M-H$^+$)



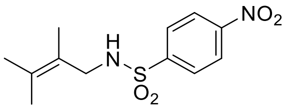
27a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a yellow oil (168 mg, 84%). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.34 (d, *J* = 8.7 Hz, 2H), 8.03 (d, *J* = 8.6 Hz, 2H), 5.25 (t, *J* = 6.7 Hz, 1H), 5.17 (t, *J* = 5.5 Hz, 1H), 4.85 (t, *J* = 4.7 Hz, 1H), 3.94 (s, 2H), 3.81 (s, 2H), 3.51 (d, *J* = 5.7 Hz, 2H), 2.22 – 1.84 (m, 2H), 1.67 – 1.41 (m, 3H), 1.52 (s, 3H), 1.35 – 1.21 (m, 1H), 1.19 – 1.02 (m, 1H), 0.89 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 150.23, 146.55, 129.88, 129.81, 128.59, 124.57, 103.85, 64.98, 64.92, 51.59, 40.90, 36.78, 29.09, 25.30, 20.07, 14.47. **IR** (thin film): 3566, 3285, 3106, 2917, 1717, 1606, 1530, 1435, 1350, 1311, 1227, 1164, 1008, 1093, 1037, 949, 912, 855, 736, 686, 616, 548 cm^{-1}. **MS** (ESI, negative mode): 397.3 (M-H$^+$)



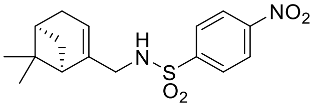
28a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a pale green oil (124 mg, 67%) **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.05 (d, *J* = 8.8 Hz, 2H), 5.38 (t, *J* = 8.0 Hz, 1H), 5.25 (t, *J* = 7.0 Hz, 1H), 4.93 (t, *J* = 5.8 Hz, 1H), 4.08 (d, *J* = 8.0 Hz, 2H), 3.53 (d, *J* = 5.7 Hz, 2H), 2.21 – 1.90 (m, 4H), 1.69 (s, 3H), 1.55 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.32, 146.49, 142.09, 130.63, 128.70, 128.64, 124.62, 121.23, 51.52, 41.39, 38.87, 25.92, 16.23, 14.58. **IR** (thin film): 3630, 3298, 3105, 2925, 2865, 1717, 1662, 1607, 1531, 1437, 1402, 1350, 1312, 1165, 1052, 855, 736, 686, 616, 463 cm^{-1}. **MS** (ESI, negative mode): 371.9 (M-H$^+$)



29a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 70:30, hexanes/ethyl acetate) to afford the product as a white solid (248 mg, 84% yield. 2.5:1 mixture of regioisomers). Major regioisomer (drawn above): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.8 Hz, 2H), 7.92 (d, *J* = 8.8 Hz, 2H), 5.90 (d, J = 7.6 Hz, 1H), 5.20-5.13 (m, 3H), 4.11 (dq, *J* = 14.4, 7.1 Hz, 2H), 4.02 (q, *J* = 7.1 Hz, 2H), 3.67 (s, 3H), 3.18 (d, *J* = 6.9 Hz, 2H), 2.57 (dd, *J* = 15.5, 7.3 Hz, 1H), 2.48 (dd, *J* = 15.3, 5.9 Hz, 1H), 2.37 (s, 3H), 2.19 (s, 3H), , 1.17 (t, *J* = 7.1 Hz, 3H). Minor isomer (amination at methyl group): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.8 Hz, 2H), 8.00 (d, *J* = 8.8 Hz, 2H), 5.32 (t, *J* = 6.2 Hz, 1H), 5.26 (t, *J* = 7.0 Hz, 1H), 3.76 (s, 3H), 3.55 (d, *J* = 6.0 Hz, 2H), 3.35 (d, *J* = 6.9 Hz, 2H), 2.37 (s, 3H), 2.19 (s, 3H), 1.23 (t, *J* = 7.7 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.05, 170.70, 169.50, 169.16, 168.35, 168.31, 162.64, 150.05, 149.84, 146.95, 146.91, 146.67, 146.27, 146.01, 133.91, 133.26, 128.59, 128.44, 127.95, 125.78, 124.39, 124.09, 123.22, 113.62, 68.62, 61.39, 61.28, 61.20, 60.88, 60.52, 57.71, 48.76, 38.98, 32.72, 23.68, 23.30, 20.68, 14.36, 14.18, 12.91, 11.87. **IR** (thin film): 3569, 3277, 3105, 2982, 1762, 1608, 1530, 1473, 1450, 1401, 1350, 1315, 1271, 1165, 1130, 1093, 1071, 1032, 1011, 967, 914, 855, 736, 686, 648, 618, 549 cm^{-1}. **MS** (ESI, negative mode): 588.9 (M-H$^+$) **Melting Point** : 44-51 °C

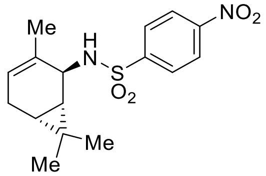


30a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 70:30, hexanes/ethyl acetate) to afford the product as a white solid (44 mg, 77%) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.9 Hz, 2H), 8.05 (d, *J* = 8.9 Hz, 2H), 4.68 (t, *J* = 5.5 Hz, 1H), 3.64 (d, *J* = 5.7 Hz, 2H), 1.61 (s, 3H), 1.57 (s, 3H), 1.52 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 150.28, 146.53, 131.75, 128.54, 124.43, 122.28, 46.37, 20.98, 20.35, 17.09. **IR** (thin film): 3310, 3109, 2322, 1606, 1528, 1346, 1327, 1311, 1155, 1090, 1035, 815, 746, 734, 615, 548 cm^{-1}. **MS** (ESI, negative mode[M – H]$^-$): 283.1 (M-H$^+$) **Melting Point** : 125 – 128 °C

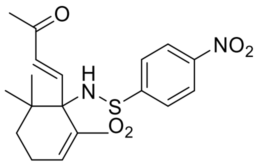


31a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (53 mg, 32%) **^{1}H**

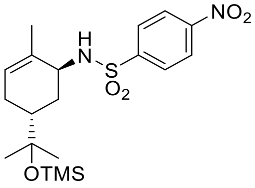
NMR (300 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.6 Hz, 2H), 8.05 (d, *J* = 8.5 Hz, 2H), 5.38 (s, 1H), 4.65 (s, 1H), 3.53 (s, 2H), 2.40 – 2.23 (m, 1H), 2.18 (s, 2H), 2.08 – 1.87 (m, 2H), 1.24 (s, 3H), 0.97 (d, *J* = 8.7 Hz, 1H), 0.75 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.40, 146.45, 142.87, 128.69, 124.70, 121.30, 48.60, 44.19, 40.84, 38.33, 31.77, 31.46, 26.30, 21.34. **IR** (thin film): 3290, 3106, 2919, 1606, 1530, 1428, 1349, 1311, 1165, 1093, 1050, 911, 854, 804, 736, 686, 611, 561, 507 cm^{-1}. **MS** (ESI, negative mode): 335.6 (M-H$^+$) **Melting Point** : 78 – 83 °C



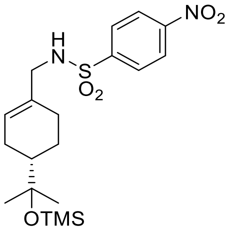
32a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as yellow oil (146 mg, 87%) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.10 (d, *J* = 8.8 Hz, 2H), 5.39 (s, 1H), 4.80 (d, *J* = 9.7 Hz, 1H), 3.66 (d, *J* = 9.5 Hz, 1H), 2.35 (dd, *J* = 19.6, 4.9 Hz, 1H), 1.98 (d, *J* = 19.6 Hz, 1H), 1.51 (s, 3H), 0.82 (s, 3H), 0.79 (s, 3H), 0.64 (t, *J* = 8.2 Hz, 1H), 0.41 (d, *J* = 8.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.22, 147.64, 130.26, 128.62, 126.23, 124.59, 50.58, 28.54, 26.53, 21.30, 21.15, 17.39, 16.16, 13.51. **IR** (thin film): 3284, 3106, 2944, 2873, 1606, 1528, 1433, 1350, 1311, 1165, 1093, 1035, 311, 853, 820, 776, 736, 686, 648, 618, 581, 547 cm^{-1}. **MS** (ESI, negative mode): 335.6 (M-H$^+$)



33a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 70:30, hexanes/ethyl acetate) to afford the product as a white solid (133 mg, 68%) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.8 Hz, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 7.06 (d, *J* = 15.9 Hz, 1H), 6.07 (d, *J* = 15.9 Hz, 1H), 5.65 (s, 1H), 4.91 (s, 1H), 2.29 (s, 3H), 1.92 – 1.82 (m, 2H), 1.52 (s, 3H), 1.39 – 1.31 (m, 1H), 1.31 – 1.21 (m, 1H), 1.01 (s, 3H), 0.81 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.43, 150.23, 148.38, 143.65, 132.83, 131.74, 129.23, 128.82, 124.48, 70.62, 39.27, 32.32, 28.72, 24.84, 23.39, 22.73, 21.70. **IR** (thin film): 3289, 2969, 2927, 1672, 1623, 1531, 1454, 1350, 1256, 1163, 1092, 1056, 1003, 913, 854, 735, 686, 650, 609, 566 cm^{-1}. **MS** (ESI, negative mode): 391.0 ($M-H^{+}$) **Melting Point** : 167-171 °C

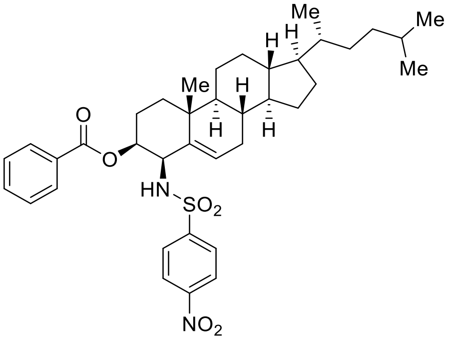


major



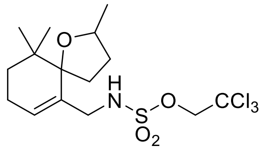
minor

34a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the major regioisomer as clear sticky oil (148 mg, 74%, 6:1 mixture of diastereomers) and the minor regioisomer as a white solid (37 mg, 17%) Major: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.5 Hz, 2.34H, major + minor), 8.10 (d, *J* = 8.5 Hz, 2.34H, major + minor), 5.56 (s, 1.17H, major + minor), 4.93 (d, *J* = 8.7 Hz, 1.17H, major + minor), 3.89 (s, 0.17H, minor), 3.74 (d, *J* = 7.9 Hz, 1H, major), 2.00 (m, 1.17H, major + minor), 1.73 (m, 2.34H, major + minor), 1.52 – 1.41 (m, 3.51H, major + minor), 1.32 (m, 2.34H, major + minor), 1.07 (s, 3.51H, major + minor), 1.05 (s, 3.51H, major + minor), 0.03 (s, 10.53H, major + minor). Major: **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.26, 150.22, 147.66, 147.45, 131.26, 130.99, 128.62, 128.56, 128.50, 128.27, 127.81, 124.68, 74.98, 72.31, 53.82, 53.61, 40.21, 39.25, 33.44, 31.18, 31.16, 27.72, 27.70, 27.63, 26.96, 26.85, 26.71, 26.64, 20.73, 20.69, 2.79. Minor: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.3 Hz, 2H), 8.05 (d, *J* = 8.5 Hz, 2H), 5.58 (s, 1H), 4.79 (t, *J* = 6.0 Hz, 1H), 3.56 (d, *J* = 5.6 Hz, 2H), 2.03 – 1.59 (m, 5H), 1.50 – 1.19 (m, 1H), 1.14 (s, 3H), 1.13 (s, 3H), 1.08 – 0.91 (m, 1H), 0.08 (s, 9H). Minor: **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.34, 146.66, 132.60, 128.74, 126.11, 124.61, 72.75, 49.63, 44.90, 27.67, 27.39, 26.88, 26.75, 23.64, 2.88, 2.27. **IR** (thin film): 3292, 3106, 2970, 1606, 1531, 1449, 1350, 1309, 1249, 1161, 1093, 1061, 1040, 985, 914, 853, 840, 736, 686, 619, 565 cm^{-1}. **MS** (ESI, negative mode): 425.2 (M-H^{+}) **Melting Point** : major: (n/a); minor: 121 – 131 °C

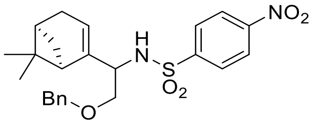


35a. Prepared according to the general procedure B at 40 °C and purified by hot trituration with acetone to afford the product as a white solid (262 mg, 81% yield) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.8 Hz, 2H), 7.87 (d, *J* = 8.8 Hz, 2H), 7.80 (d, *J* = 7.4 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 2H), 5.72 (d, *J* = 2.7 Hz, 1H), 4.98 – 4.84 (m, 2H), 4.24 (t, *J* = 5.0 Hz, 1H), 2.08 (dt, *J* = 18.5, 5.2 Hz, 1H), 2.01 (d, *J* = 12.6 Hz, 1H), 1.94 – 1.79 (m, 4H), 1.64 – 1.49

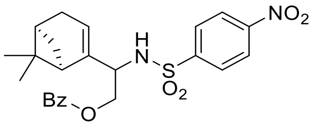
(m, 2H), 1.45 – 1.31 (m, 6H), 1.29 – 1.06 (m, 8H), 1.05 (s, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.64 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.31, 146.32, 137.94, 133.93, 131.58, 129.81, 129.53, 128.80, 128.40, 128.20, 124.29, 73.17, 60.20, 57.05, 56.41, 50.63, 42.56, 39.85, 36.91, 36.51, 36.09, 32.52, 31.95, 28.53, 28.37, 24.59, 24.17, 23.30, 23.17, 22.91, 21.21, 20.61, 19.06, 12.10. **IR** (thin film): 3323, 2942, 2881, 1701, 1519, 1436, 1353, 1316, 1285, 1166, 1117, 738, 717, 687 cm^{-1}. **MS** (ESI, negative mode): 648.1 (M-H$^+$) **Melting Point** : 311-313 °C (decomposition)



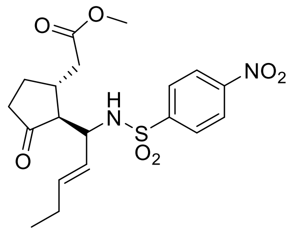
36b. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 70:30, hexanes/ethyl acetate) to afford the major diastereomer as a yellow oil (105 mg, 50%) and the minor diastereomer as a tan oil (79 mg, 36%). Diastereomers came from starting material. Major: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.01 (d, *J* = 8.9 Hz, 1H), 5.67 (s, 1H), 4.67 – 4.55 (m, 2H), 4.22 – 4.06 (m, 1H), 3.83 (d, *J* = 12.8 Hz, 1H), 3.67 (dd, *J* = 12.8, 9.1 Hz, 1H), 2.15 – 2.03 (m, 2H), 2.02 – 1.89 (m, 2H), 1.84 – 1.70 (m, 1H), 1.63 – 1.50 (m, 1H), 1.46 – 1.36 (m, 1H), 1.33 – 1.21 (m, 4H), 0.93 (s, 3H), 0.87 (s, 3H). Major: **^{13}C NMR** (126 MHz, $CDCl_3$) δ 138.08, 128.94, 94.04, 90.20, 78.18, 77.50, 48.05, 36.87, 35.97, 34.77, 34.36, 24.98, 22.96, 21.65, 21.12. Minor: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.91 (d, *J* = 8.9 Hz, 1H), 5.71 (t, *J* = 3.2 Hz, 1H), 4.60 (s, 2H), 4.28 – 4.13 (m, 1H), 3.83 (d, *J* = 12.8 Hz, 1H), 3.69 (dd, *J* = 12.8, 9.2 Hz, 1H), 2.28 – 2.07 (m, 3H), 2.04 – 1.94 (m, 1H), 1.87 – 1.72 (m, 1H), 1.68 – 1.56 (m, 1H), 1.55 – 1.45 (m, 1H), 1.31 (d, *J* = 6.0 Hz, 3H), 1.28 – 1.21 (m, 1H), 0.99 (s, 3H), 0.92 (s, 3H). Minor: **^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.38, 129.28, 94.03, 90.36, 78.21, 78.09, 48.58, 38.08, 35.32, 34.59, 34.02, 25.19, 23.10, 22.68, 21.92. **IR** (thin film): 3307, 2973, 2924, 2874, 1472, 1453, 1411, 1362, 1326, 1260, 1226, 1181, 1085, 1048, 1009, 977, 940, 907, 884, 850, 755, 726, 680, 633, 586, 552, 536 cm^{-1}. **MS** (ESI, negative mode): 419.8 (M-H$^+$)



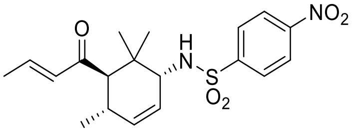
37a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (160 mg 79% yield, 1.2:1 mixture of diastereomers) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.8 Hz, 2H, major), 8.14 (d, *J* = 8.8 Hz, 1.6H, minor), 7.98 (d, *J* = 8.4 Hz, 2H, major), 7.97 (d, *J* = 8.4 Hz, 1.6H, minor), 7.34 – 7.28 (m, 5.4H, both), 7.22 – 7.17 (m, 1.8H, major), 7.17 – 7.12 (m, 1.8H, minor), 5.44 – 5.31 (m, 3.6H, both), 4.36 (d, *J* = 2.9 Hz, 2H, major), 4.32 (s, 1.6H, minor), 3.93 (q, *J* = 6.3 Hz, 1.8H, both), 3.43 (td, *J* = 9.4, 4.4 Hz, 1.6H, minor), 3.34 (ddd, *J* = 16.5, 9.8, 6.8 Hz, 2H, major), 2.35 (dt, *J* = 8.7, 5.6 Hz, .8H, minor), 2.21 (dt, *J* = 8.8, 5.7 Hz, 1H, major), 2.18 (s, 0.8H, minor), 2.14 (s, 2H, major), 2.12 – 2.09 (m, 1H, major), 2.05 (d, *J* = 5.2 Hz, 2H, major), 2.00 (s, 0.8H, minor), 1.24 (s, 2.4H, minor), 1.21 (s, 3H, major), 1.00 (d, *J* = 8.7 Hz, 0.8H, minor), 0.73 (s, 2.4H, minor), 0.70 (s, 3H, major), 0.67 (d, *J* = 8.7 Hz, 1H, major). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.08, 149.98, 147.14, 146.80, 144.37, 144.14, 137.54, 128.77, 128.72, 128.69, 128.60, 128.28, 128.07, 128.02, 124.25, 124.19, 121.57, 120.51, 73.44, 71.37, 70.89, 58.36, 58.13, 44.02, 43.06, 40.94, 40.77, 38.23, 31.98, 31.44, 31.36, 26.37, 26.32, 21.46, 21.40. **IR** (thin film): 3286, 2985, 2918, 1717, 1606, 1528, 1454, 1349, 1312, 1165, 1093, 973, 911, 854, 736, 699, 685, 612, 570 cm^{-1}. **MS** (ESI, negative mode): 455.1 (M-H$^+$) **Melting Point** : 91 - 98 °C



38a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (181 mg, 77% yield, 1.2:1 mixture of diastereomers) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.8 Hz, 2H, major), 8.02 (d, *J* = 8.8 Hz, 1.6H, minor), 7.93 (d, *J* = 9.1 Hz, 2H, major), 7.92 (d, *J* = 9.1 Hz, 1.6H, minor), 7.81 (d, *J* = 7.3 Hz, 2H, major), 7.76 (d, *J* = 7.3 Hz, 1.6H, minor), 7.54 (t, *J* = 7.5 Hz, 1H, major), 7.53 (t, *J* = 7.5 Hz, 0.8H, minor), 7.37 (t, *J* = 5.9 Hz, 2H, major), 7.35 (t, *J* = 5.9 Hz, 1.6H, minor), 5.57 (d, *J* = 6.2 Hz, 1.8H, both), 5.32 (d, *J* = 7.6 Hz, 1H, major), 5.28 (d, *J* = 8.2 Hz, 0.8H, minor), 4.33 (d, *J* = 8.8 Hz, 0.8H, minor), 4.31 (d, *J* = 8.6 Hz, 1H, major), 4.21 – 4.16 (m, 3.6H, both), 2.41 (dt, *J* = 8.8, 5.6 Hz, 0.8, minor), 2.33 (dt, *J* = 8.7, 5.6 Hz, 1H, major), 2.25 – 2.20 (m, 2H, both), 2.18 (d, *J* = 5.6 Hz, 1H, major), 2.16 (d, *J* = 5.5 Hz, 1H, major), 2.08 (d, *J* = 16.2 Hz, 1.6H, minor), 1.28 (s, 2.4H, minor), 1.25 (s, 3H, major), 1.06 (d, *J* = 8.8 Hz, 0.8H, minor), 0.84 (d, *J* = 8.8 Hz, 1H, major), 0.77 (s, 2.4H, minor), 0.75 (s, 3H, major). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.44, 166.42, 149.62, 149.53, 146.76, 146.64, 143.34, 143.21, 133.61, 129.56, 129.50, 129.01, 128.97, 128.41, 128.37, 128.05, 127.89, 124.09, 121.67, 121.22, 65.12, 64.56, 58.15, 58.02, 43.61, 43.16, 40.62, 40.53, 38.08, 38.02, 31.75, 31.38, 31.17, 25.99, 21.14. **IR** (thin film): 3432, 2918, 1702, 1654, 1528, 1451, 1431, 1349, 1314, 1273, 1163, 1092, 1027, 981, 853, 736, 713, 685, 616, 566 cm^{-1}. **MS** (ESI, negative mode): 468.9 ($M-H^+$) **Melting Point** : 138-140 °C

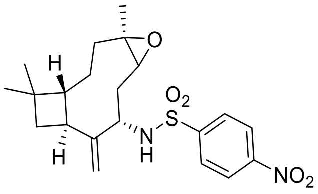


39a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a yellow oil (121 mg, 57%, 3:1 mixture of diastereomers) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.6 Hz, 2H), 8.00 (d, *J* = 8.7 Hz, 2H), 5.74 (t, *J* = 11.6 Hz, 1H), 5.31 – 5.27 (m, 1H), 4.07 – 4.01 (m, 1H), 3.70 (s, 3H), 2.66 (dd, *J* = 15.1, 5.4 Hz, 1H), 2.60 – 2.43 (m, 2H), 2.40 – 2.27 (m, 2H), 2.26 – 2.14 (m, 2H), 2.12 – 2.05 (m, *J* = 14.6, 7.2 Hz, 1H), 1.78 – 1.71 (m, 2H), 1.62 – 1.52 (m, 1H), 0.70 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.26, 172.43, 157.03, 150.29, 150.16, 147.93, 147.10, 138.74, 136.68, 128.91, 128.74, 125.69, 124.38, 124.29, 123.89, 59.58, 58.11, 55.83, 55.64, 52.22, 52.13, 38.85, 38.60, 38.16, 37.98, 35.75, 34.97, 27.41, 27.22, 25.19, 13.25, 13.18. **IR** (thin film): 3450, 3275, 3107, 2963, 1732, 1607, 1529, 1437, 1350, 1311, 1166, 1092, 973, 914, 855, 738, 687, 648, 614 cm^{-1}. **MS** (ESI, negative mode): 423.7 ($M-H^+$)

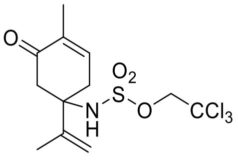


40a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a yellow solid (118 mg, 60%) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.7 Hz, 2H), 8.10 (d, *J* = 8.7 Hz, 2H), 6.88 (dq, *J* = 13.9, 6.9 Hz, 1H), 6.21 (d, *J* = 15.6 Hz, 1H), 5.58 (d, *J* = 9.9 Hz, 1H), 5.17 (d, *J* = 9.6 Hz, 1H), 5.07 (ddd, *J* = 9.7, 5.2, 2.3 Hz, 1H), 3.23 (dd, *J* = 9.5, 5.3 Hz, 1H), 2.58 – 2.49 (m1H), 2.45 (d, *J* = 10.5

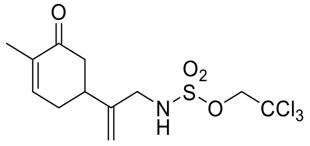
Hz, 1H), 1.88 (d, *J* = 6.8 Hz, 3H), 0.95 (s, 3H), 0.82 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.29, 150.44, 147.39, 143.34, 137.28, 134.52, 128.56, 124.83, 123.33, 59.06, 55.45, 37.35, 31.65, 26.30, 21.53, 19.47, 18.60. **IR** (thin film): 3273, 2968, 2933, 2875, 1734, 1685, 1650, 1623, 1531, 1441, 1349, 1310, 1165, 1093, 1043, 971, 912, 854, 738, 686, 617, 573, 515 cm^{-1}. **MS** (ESI, negative mode): 391.2 (M-H$^+$) **Melting Point** : 149 – 151 °C



41a. Prepared according to the general procedure B using 30% catalyst loading and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a yellow solid (157 mg, 75%, 10:1 mixture of diastereomers). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.5 Hz, 2.22H, major+minor), 8.03 (d, *J* = 8.6 Hz, 0.22H, minor), 7.96 (d, *J* = 8.5 Hz, 2H, major), 5.80 (d, *J* = 6.8 Hz, 0.11H, minor), 5.67 (d, *J* = 7.3 Hz, 1H, major), 5.05 (s, 2H, major), 4.89 (s, 0.11H, minor), 4.83 (s, 0.11H, minor), 4.2-4.12 (m, 0.11H, minor), 3.86 – 3.62 (m, 1H, major), 2.91 (d, *J* = 8.7 Hz, 0.11H, minor), 2.58 (dd, *J* = 8.6, 5.5 Hz, 1H, major), 2.35 – 1.97 (m, 3.33H, major+minor), 1.74 (m, 1.11H, major+minor), 1.65 – 1.45 (m, 3.33H, major+minor), 1.44 – 1.21 (m, 5.55H, major+minor), 1.12 – 0.73 (m, 7.77H, major+minor). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.71, 150.15, 147.23, 128.65, 124.41, 112.83, 59.52, 59.30, 57.37, 57.28, 46.37, 39.80, 38.89, 36.46, 33.01, 29.99, 27.33, 22.61, 16.62. **IR** (thin film): 3272, 3106, 2934, 2862, 1639, 1607, 1530, 1454, 1402, 1385, 1310, 1274, 1260, 1166, 1126, 1093, 1063, 1014, 998, 980, 957, 939, 911, 854, 824, 763, 736, 685, 650, 603, 563, 537 cm^{-1}. **MS** (ESI, negative mode): 419.4 (M-H$^+$) **Melting Point** : 161 – 167 °C

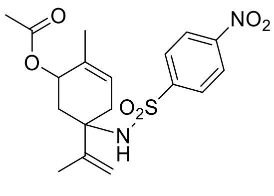


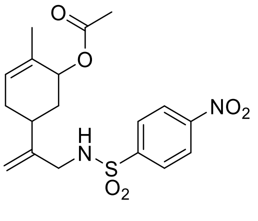
major



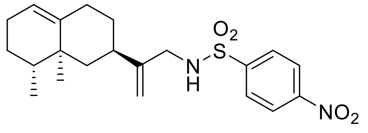
minor

42b. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 70:30, hexanes/ethyl acetate) to afford the major regioisomer as a tan solid (74 mg, 39%) and the minor regioisomer as a tan solid (68 mg, 36%). Major: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.69 (s, 1H), 5.55 (s, 1H), 5.11 (s, 1H), 5.09 (s, 1H), 4.64 – 4.46 (m, 2H), 3.21 – 2.94 (m, 2H), 2.88 (s, 1H), 2.82 (s, 1H) 1.87 (s, 3H), 1.80 (s, 3H). Major: **^{13}C NMR** (126 MHz, $CDCl_3$) δ 196.87, 143.81, 141.31, 136.14, 115.94, 93.70, 78.52, 64.10, 48.00, 34.51, 19.06, 15.67. Minor: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.76 (s, 1H), 5.40 (t, *J* = 5.9 Hz, 1H), 5.21 (s, 1H), 5.06 (s, 1H), 4.64 (s, 2H), 3.87 (d, *J* = 5.8 Hz, 2H), 2.86 (t, *J* = 11.7 Hz, 1H), 2.70-2.50 (m, 2H), 2.49 – 2.19 (m, 2H), 1.78 (s, 3H). Minor: **^{13}C NMR** (126 MHz, $CDCl_3$) δ 199.56, 145.71, 144.67, 136.00, 114.03, 93.80, 78.54, 47.85, 43.25, 38.63, 31.62, 15.96. **IR** (thin film): 3271, 2954, 2925, 1664, 1453, 1369, 1256, 1180, 1113, 1076, 1047, 1017, 987, 913, 855, 755, 727, 648, 572, 536 cm^{-1}. **MS** (ESI, negative mode): 375.8 (M-H^{+}) **Melting Point** : major: 114 – 122 °C; minor: 98 – 106 °C

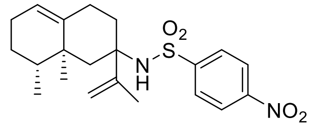




43a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 70:30, hexanes/ethyl acetate) to afford the product as a sticky white oil (173 mg, 88%, 1.1:1 mixture of regioisomers, both regioisomers found as a mixture of diastereomers found in starting material). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.38 – 8.33 (m, 2H, A), 8.32 – 8.26 (m, 2H, B), 8.08 – 8.03 (m, 2H, A), 8.02 – 7.98 (m, 1.4H, B), 7.98 – 7.94 (m, 0.6H, B), 5.66 (dd, *J* = 3.6, 1.7 Hz, 0.7H), 5.52 (d, *J* = 3.8 Hz, 0.3H), 5.46 – 5.36 (m, 1H), 5.35 – 5.25 (m, 2.3H), 5.17 (d, *J* = 12.0 Hz, 1H), 5.09 (t, *J* = 6.3 Hz, 0.7H), 5.06 (s, 0.3H), 5.00 (s, 0.7H), 4.94 (d, *J* = 4.4 Hz, 1H), 4.90 (s, 0.3H), 4.87 (s, 1H), 4.85 (s, 0.7H), 3.74 – 3.53 (m, 2H, A), 2.73 – 2.59 (m, 1H), 2.46 – 2.20 (m, 3.2H), 2.16 (s, 1.3H), 2.07 (s, 2H), 2.05 (s, 2H), 1.95 – 1.68 (m, 3.4H), 1.66 (s, 3.0H), 1.62 – 1.57 (m, 1.3H), 1.56 – 1.52 (m, 2.3H), 1.43 – 1.38 (m, 2.4H), 1.29 – 1.22 (m, 2.1H). **^{13}C NMR** (126 MHz, c) δ 171.40, 171.18, 171.03, 150.30, 149.93, 147.87, 147.65, 147.59, 147.24, 146.22, 144.74, 143.11, 133.28, 133.13, 132.71, 131.46, 129.10, 128.96, 128.64, 128.57, 127.32, 125.47, 124.69, 124.01, 123.90, 123.06, 122.32, 115.99, 114.39, 112.13, 73.12, 70.92, 70.61, 69.57, 61.58, 58.65, 47.47, 47.16, 36.83, 36.45, 35.38, 34.06, 33.95, 32.33, 31.29, 31.19, 29.93, 21.60, 21.38, 21.30, 20.72, 19.94, 19.10, 18.94, 18.48, 18.43. **IR** (thin film): 3441, 3106, 2922, 1731, 1716, 1644, 1607, 1530, 1437, 1371, 1350, 1311, 1242, 1163, 1092, 1060, 1027, 970, 914, 854, 736, 686, 614, 556, 464 cm^{-1}. **MS** (ESI, negative mode): 393.5 $(M\text{-}H^+)$



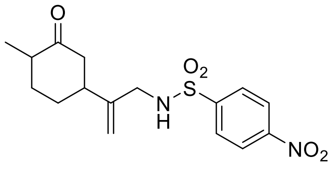
major



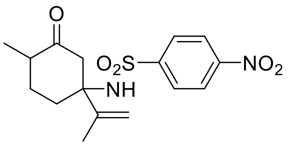
minor

44a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a yellow solid (213 mg, quant, 1.5:1 mixture of regioisomers) **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.7 Hz, 2H, major), 8.29 (d, *J* = 8.7 Hz, 1.32H, minor), 8.07 (d, *J* = 8.7 Hz, 2H, major), 7.99 (d, *J* = 8.7 Hz, 1.32H, minor), 5.29 (s, 1.66H, major+minor), 5.18 (s, 0.66H, minor), 5.14 (t, *J* = 6.2 Hz, 1H, major), 5.07 (s, 0.66H, minor), 4.93 (s, 0.66H, minor), 4.86 (s, 1H, major), 4.82 (s, 1H, major), 3.63 (d, *J* = 6.1

Hz, 2H, major), 2.70 (dq, *J* = 13.4, 2.9 Hz, 0.66H, minor), 2.37 – 2.09 (m, 3.32H, major+minor), 2.09 – 1.82 (m, 4.98H, major+minor), 1.82 – 1.51 (m, 3.32H, major+minor), 1.43 – 1.25 (m, 7.20H, major+minor), 1.16 – 0.97 (m, 1.66H, major+minor), 0.92 – 0.72 (m, 10.96H, major+minor). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.32, 149.88, 149.05, 148.24, 146.37, 142.43, 142.24, 141.82, 129.08, 128.66, 124.66, 123.97, 120.97, 120.90, 116.80, 111.26, 62.91, 47.49, 47.36, 45.19, 41.93, 41.12, 38.67, 38.11, 37.38, 36.66, 33.55, 32.75, 29.90, 27.30, 26.60, 26.08, 25.83, 19.57, 18.53, 18.03, 16.00, 15.87. **IR** (thin film): 3289, 3105, 3037, 2965, 2923, 1644, 1607, 1530, 1435, 1349, 1310, 1163, 1093, 1062, 1010, 910, 854, 736, 686, 616, 561 cm^{-1}. **MS** (ESI, negative mode): 404.3 $(M-H^+)$ **Melting Point** : 104 – 111 °C



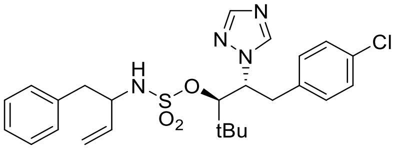
major



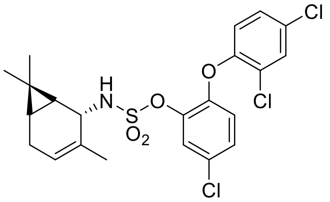
minor

45a. Prepared according to the general procedure B and purified by silica gel chromatography (90:10 to 70:30, hexanes/ethyl acetate) to afford the major regioisomer as a tan solid (75 mg, 43%) and the minor regioisomer as a tan solid (20 mg, 11%) Minor: **^{1}H NMR** (300 MHz, Acetone) δ 8.38 (d, *J* = 8.6 Hz, 2H), 8.05 (d, *J* = 8.6 Hz, 2H), 6.86 (s, 1H), 5.04 (s, 1H), 4.79 (s, 1H), 2.83 – 2.58 (m, 2H), 2.56 – 2.33 (m, 2H), 1.96 (dd, *J* = 19.7, 6.7 Hz, 2H), 1.80 (t, *J* = 11.9 Hz, 1H), 1.35 (s, 3H), 0.96 (d, *J* = 6.5 Hz, 3H). Minor: **^{13}C NMR** (126 MHz, $CDCl_3$) δ 211.06, 150.03, 147.07, 144.07, 129.15, 123.92, 115.25, 66.52, 51.03, 44.77, 32.38, 30.25, 18.30, 14.51. Major: **^{1}H NMR** (300 MHz, Acetone) δ 8.43 (d, *J* = 8.6 Hz, 2H), 8.14 (d, *J* = 8.6 Hz, 2H), 7.04 (s, 1H), 5.04 (s, 1H), 4.93 (s, 1H), 3.71 (d, *J* = 6.1 Hz, 2H), 2.50 – 2.36 (m, 1H), 2.33 (d, *J* = 8.8 Hz, 1H), 2.22 (t, *J* = 10.4 Hz, 1H), 2.14 – 2.07 (m, 1H), 1.89 (d, *J* = 13.9 Hz, 1H), 1.65 (q, *J* = 11.5 Hz, 1H), 1.38 –

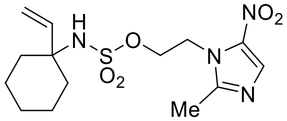
1.15 (m, 2H), 0.92 (d, *J* = 6.5 Hz, 3H). Major: **^{13}C NMR** (126 MHz, CDCl$_3$) δ 212.43, 150.41, 146.81, 146.18, 128.65, 124.76, 112.72, 47.23, 47.03, 45.03, 43.06, 34.98, 31.22, 14.55. **IR** (thin film): 3275, 3106, 2966, 2932, 2864, 1709, 1650, 1606, 1530, 1448, 1402, 1350, 1311, 1220, 1165, 1093, 1055, 1014, 912, 854, 737, 686, 610, 557, 529 cm^{-1}. **MS** (ESI, negative mode): 351.1 (M-H$^+$) **Melting Point** : major: 125 - 129 °C; minor 148 °C decomp



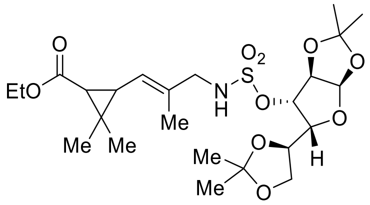
46. Prepared according to the general procedure and purified by silica gel chromatography(80:20 to 50:50, hexanes/ethyl acetate) to afford the product as a yellow oil (53 mg, 53%, 1:1 mixture of diastereomers at newly formed stereocenter) **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.36 (s, 1H, A+B), 7.77 (s, 0.5H, A), 7.72 (s, 0.5H, B), 7.35-7.28 (m,, 2H, A+B), 7.28 – 7.23 (m, 1H, A+B), 7.20 (d, *J* = 8.2 Hz, 4H, A+B), 6.99 (d, *J* = 7.8 Hz, 2H, A+B), 5.87 – 5.74 (m, 1H, A+B), 5.38 – 5.12 (m, 3H, A+B), 5.00 – 4.85 (m, 1H, A+B), 4.55 (s, 0.5H, A), 4.51 (s, 0.5H, B), 4.43 – 4.28 (m, 1H, A+B), 3.35 – 3.26 (m, 2H, A+B), 2.96 (t, *J* = 6.5 Hz, 2H, A+B), 0.77 (s, 4.5H, A), 0.74 (s, 4.5H, B). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 137.04, 136.97, 136.06, 134.77, 133.37, 130.53, 129.88, 129.85, 129.16, 128.98, 128.95, 127.39, 117.68, 117.16, 88.81, 88.15, 62.04, 58.67, 58.51, 42.31, 41.96, 40.46, 35.97, 26.34, 26.23. **IR** (thin film): 3280, 3087, 3029, 2965, 2876, 1601, 1494, 1454, 1353, 1277, 1173, 1136, 1015, 926, 909, 854, 831, 735, 701, 678 cm^{-1}. **MS** (ESI, negative mode): 502.3 (M-H$^+$)



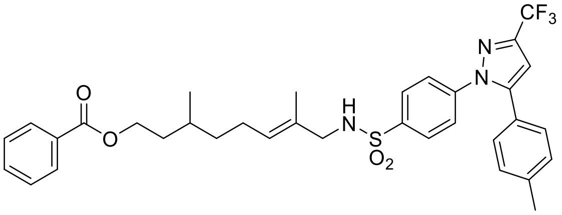
47. Prepared according to the general procedure and purified by silica gel chromatography (80:20 to 70:30, hexanes/ethyl acetate) to afford the product as a white solid (94 mg, 94%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 2.4 Hz, 1H), 7.47 (d, *J* = 2.4 Hz, 1H), 7.21 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.18 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.92 (d, *J* = 8.8 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 5.43 (s, 1H), 4.71 (d, *J* = 9.3 Hz, 1H), 3.92 (d, *J* = 9.2 Hz, 1H), 2.44 – 2.34 (m, 1H), 2.05 (d, *J* = 19.5 Hz, 1H), 1.68 (s, 3H), 0.99 (d, *J* = 8.7 Hz, 1H), 0.92 (s, 3H), 0.80 (s, 3H), 0.66 (t, *J* = 8.0 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 151.10, 147.40, 141.67, 130.76, 130.47, 130.14, 129.64, 128.56, 127.79, 126.36, 126.14, 124.49, 121.03, 120.30, 52.15, 28.71, 25.89, 21.53, 21.03, 17.33, 16.08, 13.37. **IR** (thin film): 3297, 3092, 2943, 2873, 2831, 1588, 1481, 1465, 1457, 1436, 1419, 1405, 1363, 1267, 1192, 1172, 915, 869, 736 cm^{-1}. **MS** (ESI, negative mode): 502.1 ($M-H^+$) **Melting Point** : 121 – 124 °C



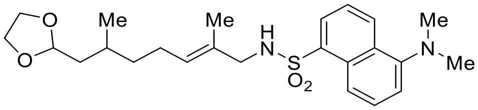
48. Prepared according to the general procedure and purified by silica gel chromatography (80:20 to 70:30, hexanes/ethyl acetate) to afford the product as a white solid (45 mg, 63%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (s, 1H), 5.72 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.18 (d, *J* = 17.6 Hz, 1H), 5.14 (d, *J* = 10.8 Hz, 1H), 4.62 (t, *J* = 4.9 Hz, 2H), 4.60 (s, 1H), 4.41 (t, *J* = 4.9 Hz, 2H), 2.54 (s, 3H), 1.80 – 1.70 (m, 2H), 1.68 – 1.59 (m, 2H), 1.52 – 1.45 (m, 4H), 1.44 – 1.32 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.20, 138.59, 133.64, 115.90,68.10, 59.85, 45.67, 35.61, 25.40, 22.05, 14.75. **IR** (thin film): 3291, 3089, 2936, 2862, 1533, 1471, 1428, 1365, 1262, 1190, 1177, 1148, 1035, 994, 905, 825, 764, 743 cm^{-1}. **MS** (ESI, negative mode): 357.6 (M-H$^+$) **Melting Point** : 98 – 103 °C



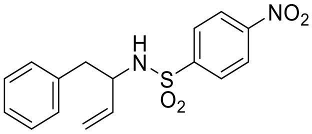
49. Prepared according to the general procedure and purified by silica gel chromatography (80:20, hexanes/ethyl acetate) to afford the product as a transparent oil (77 mg, 72%, mixture of 4 diastereomers from use of racemic and diastereomerically impure chrysanthemic acid). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 5.91 (t, *J* = 5.0 Hz, 1.7H, major + minor), 5.68 (d, *J* = 8.6 Hz, 0.7H, minor), 5.15 (d, *J* = 8.4 Hz, 1H, major), 4.89 (dd, *J* = 6.4, 3.1 Hz, 1.7H major + minor), 4.86 (t, *J* = 3.8 Hz, 1.7H major + minor), 4.80 (t, *J* = 5.6 Hz, 1.2H major + minor), 4.30 – 4.20 (m, 2H, major + minor), 4.17 – 4.00 (m, 6H), 3.77 – 3.72 (m, 1.31H, minor), 3.72 – 3.68 (m, 2H, major), 2.06 (dd, *J* = 8.4, 3.0 Hz, 0.7H, minor), 2.03 (s, 1.8H, major + minor), 1.78 (s, 3H, major), 1.76 (s, 1.8H, minor), 1.71 (d, *J* = 8.6 Hz, 0.8H, minor), 1.50 (s, 3H), 1.45 (dd, *J* = 5.3, 2.4 Hz, 1H, major), 1.43 (s, 1.8H, minor), 1.41 (s, 3H, major), 1.32 (d, *J* = 2.1 Hz, 2H), 1.31 (s, 8H, major + minor), 1.28 – 1.20 (m, 15H, major + minor), 1.14 (s, 3H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 172.26, 172.17, 171.99, 171.17, 133.80, 133.60, 133.29, 133.13, 126.26, 126.19, 125.94, 125.82, 123.71, 123.52, 123.35, 112.79, 109.87, 105.33, 83.39, 83.20, 82.79, 82.63, 82.47, 80.24, 79.27, 72.29, 68.90, 68.73, 68.57, 67.69, 67.63, 64.63, 64.53, 64.25, 60.65, 60.50, 60.22, 52.29, 51.99, 51.73, 51.50, 35.33, 32.07, 31.93, 31.82, 31.62, 31.53, 31.43, 31.06, 29.87, 28.84, 27.10, 26.82, 26.45, 25.53, 25.45, 22.42, 20.55, 15.22, 15.14, 14.93, 14.54. **IR** (thin film): 3265, 2986, 2936, 1722, 1446, 1373, 1257, 1216, 1181, 1076, 1024, 956, 881, 843, 757 cm^{-1}. **MS** (ESI, negative mode): 532.8 (M-H^{+})



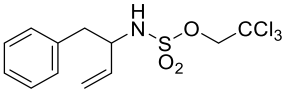
50. Prepared according to the general procedure and purified by silica gel chromatography (80:20 to 70:30, hexanes/ethyl acetate) to afford the product as a transparent oil (113 mg, 89%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.02 (d, *J* = 7.6 Hz, 2H), 7.83 (d, *J* = 8.6 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.48 – 7.39 (m, 4H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.74 (s, 1H), 5.27 (t, *J* = 7.0 Hz, 1H), 4.66 (t, *J* = 6.2 Hz, 1H), 4.43 – 4.26 (m, 2H), 3.44 (d, *J* = 6.1 Hz, 2H), 2.38 (s, 3H), 2.05-1.80 (m, 2H), 1.77 (dt, *J* = 12.2, 4.7 Hz, 1H), 1.64 – 1.55 (m, 1H), 1.54 (s, 3H), 1.44 – 1.32 (m, 1H), 1.25 – 1.15 (m, 1H), 0.96 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 166.91, 145.50, 142.68, 140.08, 140.01, 133.10, 130.71, 130.23, 129.96, 129.75, 129.42, 128.96, 128.58, 128.32, 126.02, 125.71, 121.33 (q, J = 268.9 Hz), 106.49, 63.61, 51.47, 36.53, 35.70, 29.88, 25.42, 21.51, 19.73, 14.44. **IR** (thin film): 3283, 3064, 2958, 2923, 2870, 1717, 1599, 1472, 1275, 1237, 1162, 1136, 1098, 976, 734, 714, 268 cm^{-1}. **MS** (ESI, negative mode): 638.4 (M-H^{+})



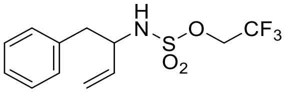
51. Prepared according to the general procedure **B** with 30 mol % catalyst and purified by silica gel chromatography (80:20, hexanes/ethyl acetate) to afford the product as a yellow oil (44 mg, 49%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.53 (d, *J* = 8.4 Hz, 1H), 8.30 (d, *J* = 8.6 Hz, 1H), 8.23 (dd, *J* = 7.3, 1.2 Hz, 1H), 7.61 – 7.48 (m, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 5.14 (t, *J* = 7.1, 1H), 4.85 (t, *J* = 5.0 Hz, 1H), 4.69 (t, *J* = 6.2 Hz, 1H), 3.97 – 3.94 (m, 2H), 3.84 – 3.81 (m, 2H), 3.39 (d, *J* = 6.2 Hz, 2H), 2.89 (s, 6H), 1.93 – 1.78 (m, 2H), 1.65 – 1.54 (m, 2H), 1.47 – 1.43 (m, 1H), 1.41 (s, 3H), 1.30 – 1.20 (m, 2H), 1.12 – 1.00 (m, 1H), 0.89 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 152.23, 135.35, 130.56, 130.37, 130.14, 129.98, 129.91, 129.18, 128.51, 123.41, 119.09, 115.38, 103.92, 64.96, 64.90, 51.54, 45.65, 40.95, 36.80, 29.12, 25.26, 20.09, 14.39 **IR** (thin film): 3288, 2942, 2786, 1588, 1574, 1457, 1408, 1321, 1231, 1201, 1144, 1039, 945, 790, 627, 573 cm^{-1}. **MS** (ESI, negative mode): 445.8 (M-H$^+$)



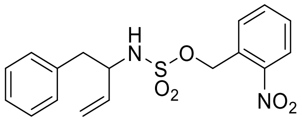
1a. Prepared according to general procedure A and purified by silica gel chromatography (95:5 to 80:20, hexanes/ethyl acetate) to afford the product as pale yellow solid (63 mg, 93%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 9.0 Hz, 2H), 7.78 (d, *J* = 9.0 Hz, 2H), 7.21 – 7.12 (m, 3H), 7.02 (dd, *J* = 6.4, 3.0 Hz, 2H), 5.73 (ddd, *J* = 17.0, 10.4, 6.1 Hz, 1H), 5.13 (d, *J* = 17.2 Hz, 1H), 5.09 (d, *J* = 10.6 Hz, 1H), 4.84 (d, *J* = 7.9 Hz, 1H), 4.09 (quin, *J* = 6.9 Hz, 1H), 2.89 (dd, *J* = 13.9, 5.6 Hz, 1H), 2.70 (dd, *J* = 13.9, 8.2 Hz, 1H). **^{13}C NMR** (126 MHz, Acetone) δ 150.33, 148.38, 138.87, 138.26, 130.10, 128.81, 128.65, 126.93, 124.69, 115.80, 58.95, 42.23. **IR** (thin film): 3292, 3106, 2923, 1529, 1427, 1350, 1311, 1165, 1094, 928, 855, 736, 617, 564 cm^{-1}. **MS** (ESI, negative mode): 332.2 (M-H$^+$) **Melting point** : 104-106°C



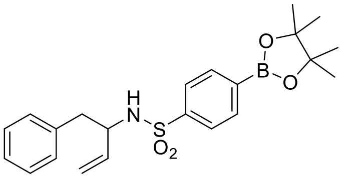
1b. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as clear oil (67 mg, 94%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.42 – 7.19 (m, 5H), 5.88 (ddd, *J* = 17.0, 10.4, 6.4 Hz, 1H), 5.31 (d, *J* = 17.2 Hz, 1H), 5.25 (d, *J* = 10.4 Hz, 1H), 5.23 (d, *J* = 7.9 Hz, 1H), 4.39 (d, *J* = 10.8 Hz, 1H), 4.29 (quin, *J* = 6.0 Hz, 1H), 4.16 (d, *J* = 10.8 Hz, 1H), 3.01 (dd, *J* = 13.8, 6.4 Hz, 1H), 2.92 (dd, *J* = 13.8, 7.3 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 136.73, 136.37, 129.80, 128.95, 127.38, 117.36, 78.16, 58.58, 41.62, 31.08. **IR** (thin film): 3306, 3088, 3066, 3030, 2952, 1497, 1455, 1362, 1266, 1179, 1121, 863, 751 cm^{-1}. **MS** (ESI, negative mode): 358.5 (M-H$^+$)



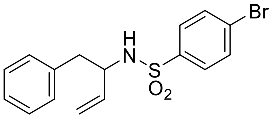
1c. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a clear oil (53 mg, 86%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.20 (d, *J* = 7.4 Hz, 2H), 5.83 (ddd, *J* = 17.0, 10.4, 6.5 Hz, 1H), 5.27 (d, *J* = 18.4 Hz, 1H), 5.24 (d, *J* = 11.5 Hz, 1H), 4.62 (s, 1H), 4.23 (quin, *J* = 6.9 Hz, 1H), 4.14 (dq, *J* = 16.3, 8.0 Hz, 1H), 3.95 (dq, *J* = 16.6, 8.1 Hz, 1H), 2.99 (dd, *J* = 13.8, 6.2 Hz, 1H), 2.86 (dd, *J* = 13.8, 7.4 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 136.57, 136.10, 129.82, 129.09, 127.55, 117.62, 65.18 (q, J = 38.3 Hz), 58.60, 41.68. **IR** (thin film): 3305, 3088, 3030, 2926, 1456, 1419, 1369, 1283, 1183, 1054, 964, 861, 806, 752, 702, 600, 557 cm^{-1}. **MS** (ESI, negative mode): 308.0 (M-H$^+$)



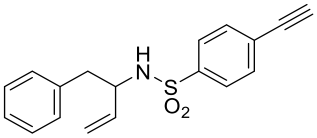
1d. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a yellowish solid (66 mg, 91%). **^{1}H NMR** (500 MHz, Acetone) δ 8.17 (d, *J* = 8.2 Hz, 1H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.27 (d, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 7.4 Hz, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 5.94 (ddd, *J* = 17.1, 10.4, 6.7 Hz, 1H), 5.31 (d, *J* = 14.5 Hz, 1H), 5.25 (d, *J* = 17.1 Hz, 1H), 5.10 (d, *J* = 11.0 Hz, 1H), 5.08 (d, *J* = 13.6 Hz, 1H), 4.22 (quin, *J* = 7.3 Hz, 1H), 2.94 (d, *J* = 7.4 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.99, 139.10, 138.92, 138.71, 135.08, 132.13, 130.44, 130.08, 129.49, 129.14, 127.24, 125.78, 116.51, 68.01, 59.75, 59.61, 42.24. **IR** (thin film): 3314, 1516, 1358, 1340, 1175, 994, 966, 867, 801, 794, 731 cm^{-1}. **MS** (ESI, negative mode): 363.2 (M-H$^+$) **Melting point** : 116 – 120 °C



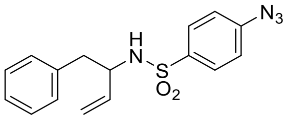
1e. Prepared according to general procedure A and purified by boric acid doped silica gel chromatography (70:30, pentane:ether) to afford the product as a white solid (50 mg, 60%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 8.1 Hz, 2H), 7.23 – 7.17 (m, 3H), 7.05 – 6.99 (m, 2H), 5.65 (ddd, *J* = 16.9, 10.4, 6.2 Hz, 1H), 5.02 (d, *J* = 17.3 Hz, 1H), 5.01 (d, *J* = 10.3 Hz, 1H), 4.61 (d, *J* = 7.4 Hz, 1H), 4.03 (quin, *J* = 6.7 Hz, 1H), 2.81 – 2.72 (m, 2H), 1.36 (s, 12H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.90, 137.26, 136.28, 135.43, 129.72, 128.79, 127.13, 126.24, 116.65, 84.61, 57.19, 42.17, 30.55, 25.12, 25.09. **IR** (thin film): 3280, 3063, 3028, 2979, 2930, 1601, 1392, 1360, 1331, 1271, 1163, 1144, 1099, 1079, 857, 723, 700, 653, 610 cm^{-1}. **MS** (ESI, negative mode): 412.6 (M-H$^+$)**Melting point** : 129-134 °C



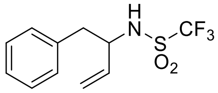
1f. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as an off-white solid (60 mg, 82%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.51 (s, 4H), 7.25 – 7.18 (m, 3H), 7.06 – 6.94 (m, 2H), 5.71 (ddd, *J* = 17.0, 10.3, 6.1 Hz, 1H), 5.09 (d, *J* = 17.1 Hz, 1H), 5.06 (d, *J* = 10.4 Hz, 1H), 4.59 (d, *J* = 7.5 Hz, 1H), 4.02 (quin, *J* = 6.0 Hz, 1H), 2.85 (dd, *J* = 13.8, 6.0 Hz, 1H), 2.71 (dd, *J* = 13.8, 7.6 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 139.75, 137.47, 136.30, 132.36, 129.63, 128.88, 128.77, 127.54, 127.18, 116.66, 57.45, 42.14. **IR** (thin film): 3280, 3086, 3062, 3027, 3924, 3854, 1575, 1472, 1454, 1424, 1389, 1331, 1161, 1092, 1069, 1031, 1010, 927, 821, 739, 700, 668, 614, 567 cm^{-1}. **MS** (ESI, negative mode): 365.4 (M-H$^+$) **Melting point** : 74 – 78 °C



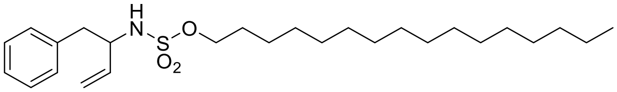
1g. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (50 mg, 80%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.6 Hz, 2H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.24 – 7.18 (m, 3H), 7.02 (dd, *J* = 6.5, 2.9 Hz, 2H), 5.69 (ddd, *J* = 16.7, 10.4, 6.1 Hz, 1H), 5.06 (d, *J* = 17.1 Hz, 1H), 5.04 (d, *J* = 10.2 Hz, 1H), 4.59 (d, *J* = 7.5 Hz, 1H), 4.03 (quin, *J* = 7.4 Hz, 1H), 3.24 (s, 1H), 2.84 (dd, *J* = 13.7, 6.2 Hz, 1H), 2.73 (dd, *J* = 13.7, 7.3 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 140.86, 137.46, 136.35, 132.75, 129.68, 128.88, 127.22, 126.73, 116.66, 82.36, 80.64, 57.41, 42.21. **IR** (thin film): 3269, 3065, 1934, 1313, 1156, 1092, 833, 741, 695, 643, 635, 521 cm^{-1}. **MS** (ESI, negative mode): 310.4 (M-H$^+$) **Melting point** : 134 – 137 °C



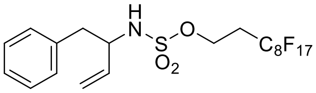
1h. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 70:30, hexanes/ethyl acetate) to afford the product as a yellow oil (55 mg, 82%). **^{1}H NMR** (300 MHz, Acetone) δ 7.72 (d, *J* = 8.7 Hz, 2H), 7.32 – 6.96 (m, 7H), 6.65 (d, *J* = 8.3 Hz, 1H), 5.72 (ddd, *J* = 17.0, 10.4, 6.4 Hz, 1H), 5.02 (d, *J* = 17.2 Hz, 1H), 4.92 (d, *J* = 10.4 Hz, 1H), 4.06 (quin, *J* = 7.2 Hz, 1H), 2.80 (d, *J* = 7.2 Hz, 2H). **^{13}C NMR** (126 MHz, Acetone) δ 144.70, 139.46, 139.01, 138.63, 130.42, 129.70, 129.12, 127.25, 120.20, 116.01, 58.85, 42.75. **IR** (thin film): 3277, 3063, 3028, 2925, 2129, 2099, 1594, 1492, 1325, 1285, 1158, 1129, 1093, 911, 831, 735, 702, 625, 568, 511 cm^{-1}. **MS** (ESI, negative mode): 327.6 (M-H$^+$)



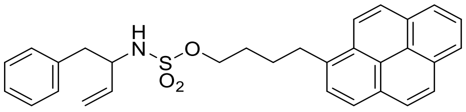
1i. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a clear oil (48 mg, 86%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 3H), 7.22 – 7.15 (m, 2H), 5.83 (ddd, *J* = 17.2, 10.3, 6.0 Hz 1H), 5.23 (dd, *J* = 10.3, 1.2 Hz, 1H), 5.21 (dd, *J* = 17.2, 1.4 Hz, 1H), 4.85 (s, 1H), 4.39 (s, 1H), 2.96 (d, *J* = 6.3 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 136.12, 135.32, 129.97, 129.00, 127.59, 119.6 (q, J = 320.7 Hz), 117.25, 58.60, 42.52. **IR** (thin film): 3307, 3091, 3032, 2927, 1497, 1433, 1374, 1230, 1197, 1146, 1030, 933, 751, 701, 616, 576 cm^{-1}. **MS** (ESI, negative mode): found: 278.3 (M-H$^+$)



1j. Prepared according to general procedure A and purified by silica gel chromatography (95:5, hexanes/ethyl acetate) to afford the product as a white solid (83 mg, 92%). **^{1}H NMR** (500 MHz, $CDCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.3 Hz, 2H), 7.28 – 7.22 (m, 1H), 7.20 (d, *J* = 7.0 Hz, 2H), 5.81 (ddd, *J* = 17.0, 10.4, 6.4 Hz, 1H), 5.23 (d, *J* = 17.2 Hz, 1H), 5.18 (d, *J* = 10.4 Hz, 1H), 4.48 (d, *J* = 7.8 Hz, 1H), 4.17 (quin, *J* = 6.7 Hz, 1H), 3.92 (dt, *J* = 9.4, 6.7 Hz, 1H), 3.81 (dt, *J* = 9.4, 6.6 Hz, 1H), 2.94 (dd, *J* = 13.7, 6.5 Hz, 1H), 2.88 (dd, *J* = 13.7, 6.9 Hz, 1H), 1.63 – 1.54 (m, 2H), 1.35 – 1.20 (m, 28H), 0.88 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 137.29, 136.54, 129.90, 128.88, 127.26, 116.94, 71.10, 58.00, 41.93, 32.16, 29.91, 29.77, 29.68, 29.58, 29.32, 29.02, 25.71, 22.91, 14.32. **IR** (thin film): 3294, 3086, 3029, 2923, 2853, 1466, 1455, 1432, 1357, 1174, 945, 700 cm^{-1}. **MS** (ESI, negative mode): found: 450.8 (M-H$^+$) **Melting point** : 32-36 °C



1k. Prepared according to general procedure A and purified by silica gel chromatography (80:20, hexanes/ethyl acetate) to afford the product as a white solid (110 mg, 82%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.3 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 1H), 7.19 (d, *J* = 7.4 Hz, 2H), 5.81 (ddd, *J* = 17.0, 10.4, 6.4 Hz, 1H), 5.24 (d, *J* = 17.1 Hz, 1H), 5.20 (d, *J* = 10.4 Hz, 1H), 4.55 (d, *J* = 7.9 Hz, 1H), 4.26 – 4.10 (m, 2H), 4.06 – 3.93 (m, 1H), 2.96 (dd, *J* = 13.8, 6.1 Hz, 1H), 2.83 (dd, *J* = 13.8, 7.4 Hz, 1H), 2.53 – 2.29 (m, 2H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 137.09, 136.40, 129.88, 129.01, 127.45, 117.20, 62.03, 58.34, 41.84, 31.21 (t, J = 22.2 Hz). **IR** (thin film): 3299, 3030, 2924, 1456, 1436, 1419, 1360, 1203, 1150, 1056, 998, 753, 703, 667, 656, 601 cm^{-1}. **MS** (ESI, negative mode): 672.5 (M-H$^+$) **Melting point** : 48 – 50 °C



1l. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a yellow film (36 mg, 37%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.15 (d, *J* = 9.2 Hz, 1H), 8.08 (d, *J* = 7.5 Hz, 2H), 8.02 (d, *J* = 7.5 Hz, 2H), 7.94 (s, 2H), 7.91 (t, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.20 (d, *J* = 5.0 Hz, 1H), 7.16 (d, *J* = 7.9 Hz, 1H), 7.15 (d, *J* = 7.2 Hz, 1H), 7.10 (d, *J* = 6.6 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 2H), 5.66 (ddd, *J* = 16.9, 10.3, 6.4 Hz, 1H), 5.10 (d, *J* = 17.1 Hz, 1H), 5.02 (d, *J* = 10.4 Hz, 1H), 4.24 (d, *J* = 7.6 Hz, 1H), 4.06 (quin, *J* = 6.6 Hz, 1H), 3.93 – 3.86 (m, 1H), 3.83 – 3.69 (m, 1H), 3.26 (t, *J* = 7.6 Hz, 2H), 2.80 (dd, *J* = 13.7, 6.3 Hz, 1H), 2.72 (dd, *J* = 13.7, 7.0 Hz, 1H), 1.81 (quin, *J* = 7.6 Hz, 2H), 1.72 – 1.63 (m, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 137.17, 136.38, 136.15, 131.66, 131.11, 130.17, 129.83, 128.87, 128.57, 127.72, 127.61, 127.46, 127.26, 126.96, 126.11, 125.35, 125.24, 125.20, 125.04, 125.02, 123.44, 116.98, 70.72, 57.96, 41.80, 33.04, 28.93, 27.81. **IR** (thin film): 3299, 3028, 2929, 1735, 1602, 1454, 1432, 1357, 1243, 1172, 1030, 939, 847, 818, 752, 720, 700, 602 cm^{-1}. **MS** (ESI, negative mode): 482.8 (M-H$^+$)

1.4.5 *^{31}P NMR Experiments*

General procedure: A flame-dried borosilicate glass vial equipped with a magnetic stir bar was charged with SePCy$_3$ (0.015 mmol, 0.15 equiv.), amine (0.2 mmol, 2 equiv.), and alkene (0.1

mmol, 1.0 equiv.). The vial was thoroughly flushed with nitrogen and capped with a Teflon-lined screw cap. Dry d_2-dichloromethane (0.5 mL, 0.2 M) was added, followed by iodobenzene diacetate (0.2 mmol, 2 equiv). The solution was stirred was stirred at room temperature until the mixture became homogeneous at which point it was transferred to an oven-dried NMR tube. The mixture was analyzed by ^{31}P NMR hourly until completed.

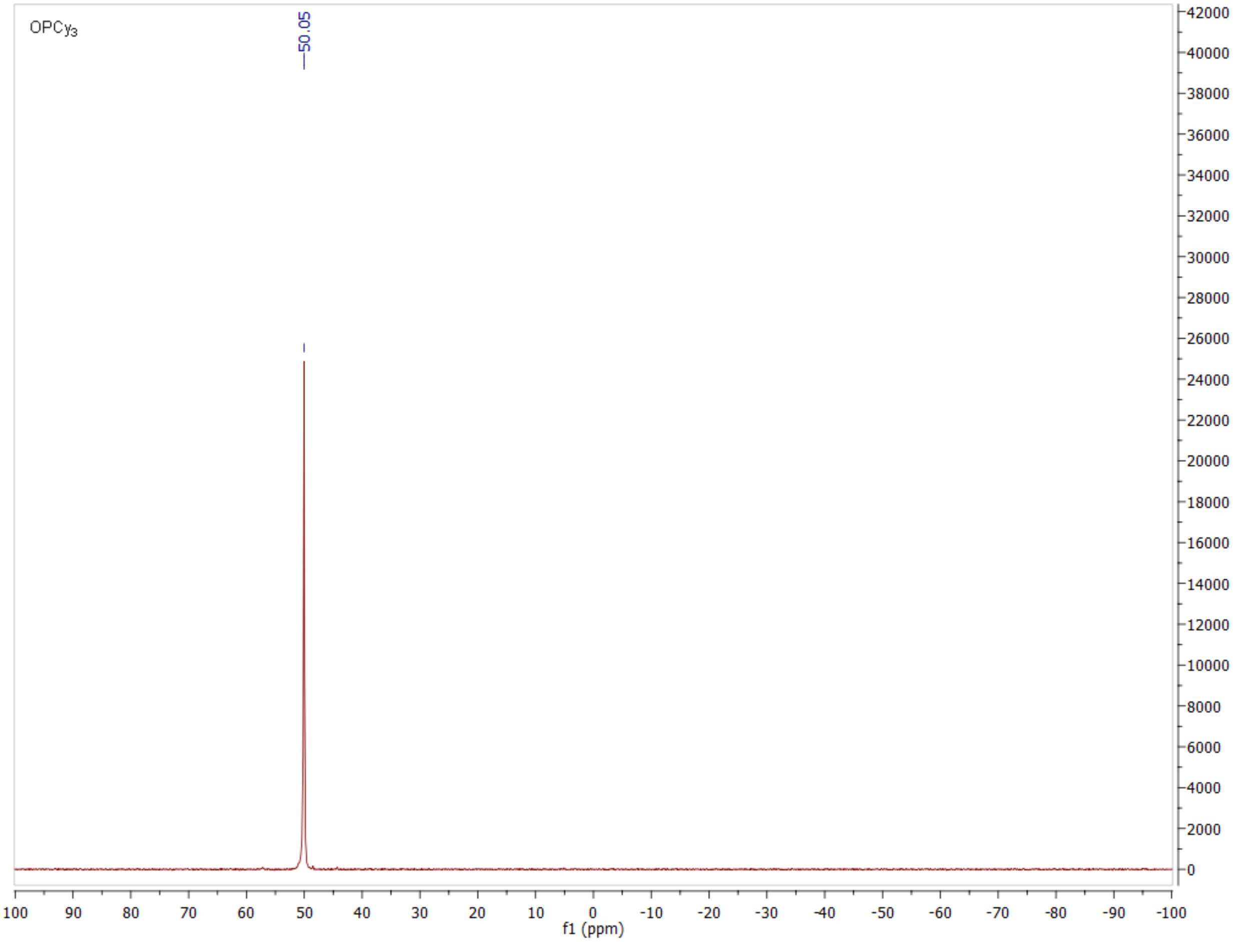


Figure 1.10. Pure Sample of $OPCy_3$ in CD_2Cl_2.

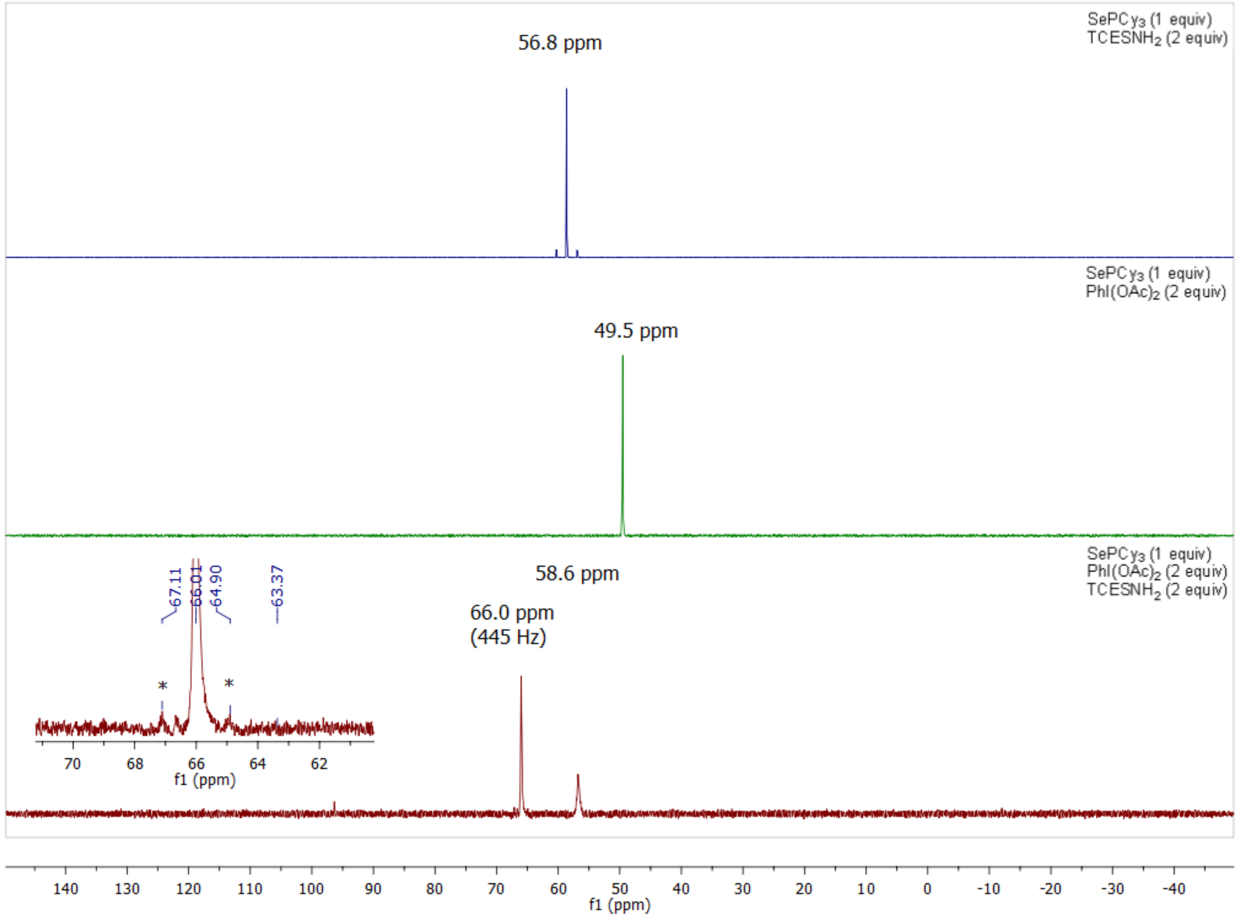


Figure 1.11. ^{31}P NMR of stoichiometric experiments.

(i) 1 equivalent of $SePCy_3$ catalyst with 2 equivalents of trichloroethanesulfamate ($TcesNH_2$) gives no change. (ii) 1 equivalent of $SePCy_3$ catalyst with 2 equivalents of iodobenzene diacetate gives Cy_3PO. (iii) 1 equivalent of $SePCy_3$ with 2 equivalents of iodobenzene diacetate and $TcesNH_2$ gives tricyclohexylphosphine oxide and unknown Cy_3P-Se-X species.

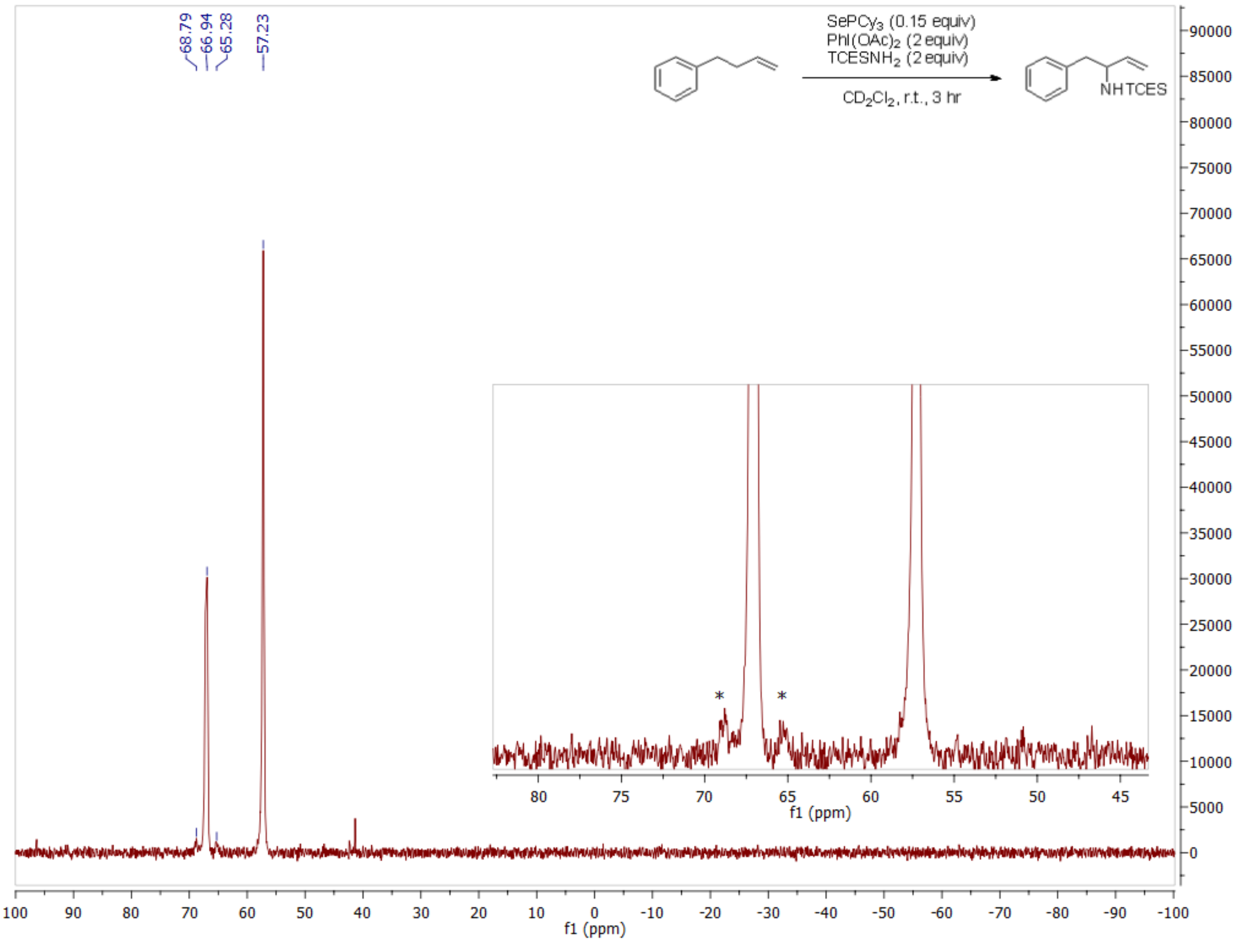


Figure 1.12. ^{31}P NMR spectrum of reaction mixture under standard catalytic reaction conditions

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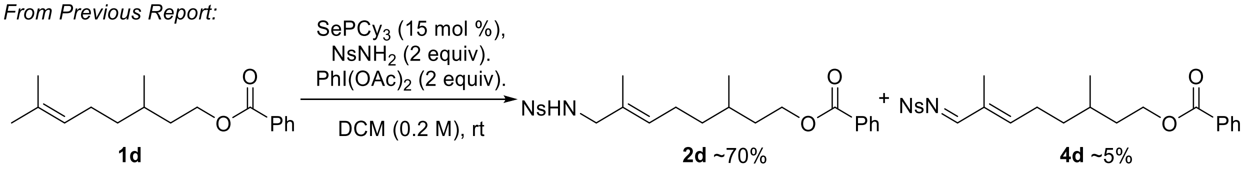
Chapter 2. DIRECT SYNTHESIS OF CONJUGATED SULFONYL IMINES ENABLED BY OXIDATIVE ORANOSELENIUM CATALYSIS

Section 1: INTRODUCTION

Our lab previously demonstrated the oxidative selenium catalyzed allylic amination of alkenes (Chapter 1). Using phosphine and NHC-based selenide catalysts enabled allylic amination of simple alkenes using sulfonamide nucleophiles and diacetoxyiodobenzene as an oxidant. This protocol was operationally simple and worked for all alkene substitution patterns. However, for more highly substituted alkenes, the minor formation of an unknown byproduct at the expense of the desired allylic amine product was occasionally observed. Careful isolation identified this product to be a conjugated sulfonyl imine (Scheme 2.1). This result surprised us because we suspected that these conjugated sulfonyl imines would be highly unstable, yet they could successfully be isolated despite making up only a minor component of the reaction mixture.

Scheme 2.1. *Trace Imine Formation Under Allylic Amination Conditions*



Surveying the literature revealed that these conjugated sulfonyl imines are relatively stable, and have been utilized as substrates in a variety of C-C and C-N bond forming including 1,2-[1] and 1,4-[2] nucleophilic additions, aza-Diels Alder reactions[3], electrocyclizations[4], imino aldol reactions[5], and aza-Fridel Crafts reactions[6] (Figure 2.1).

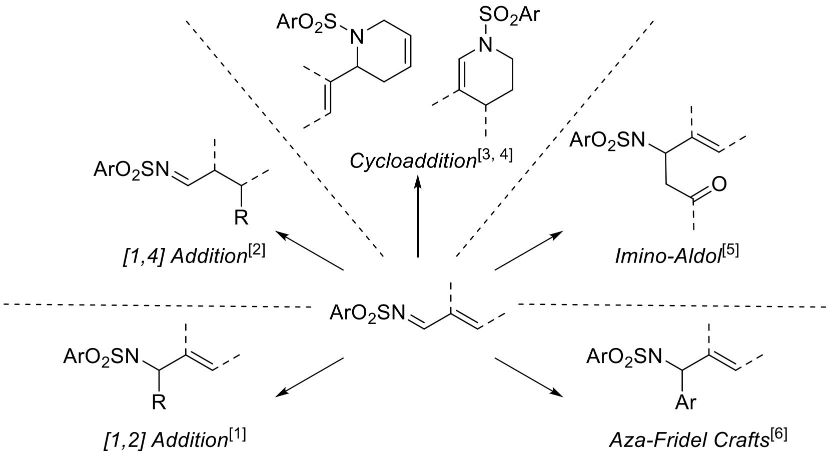


Figure 2.1. Utility of Sulfonyl Imines.

Unfortunately, the preparation of these conjugated sulfonyl imines is surprisingly difficult. Owing to the poor nucleophilicity of the sulfonamide, direct condensation with a carbonyl typically results in low yields. Adding Brønsted acids[7], Lewis acids[3a, 8], or dehydrating agents[9] to these reactions has been shown to help overcome the limited reactivity with certain aryl aldehydes and cinnamaldehyde but other α,β-unsaturated aldehydes have not been suitable substrates for these methods (Figure 2.2 A). The only reliable synthesis of α,β-unsaturated imines is the method developed by Boger and coworkers.[3a] This protocol requires condensation of hydroxyl amine with the α,β-unsaturated aldehyde to form the oxime. Addition of sulfinyl chloride to this substrate results in the O-sulfinyl-oxime, which, upon heating rearranges to the desired α,β-unsaturated imine (Figure 2.2 B).

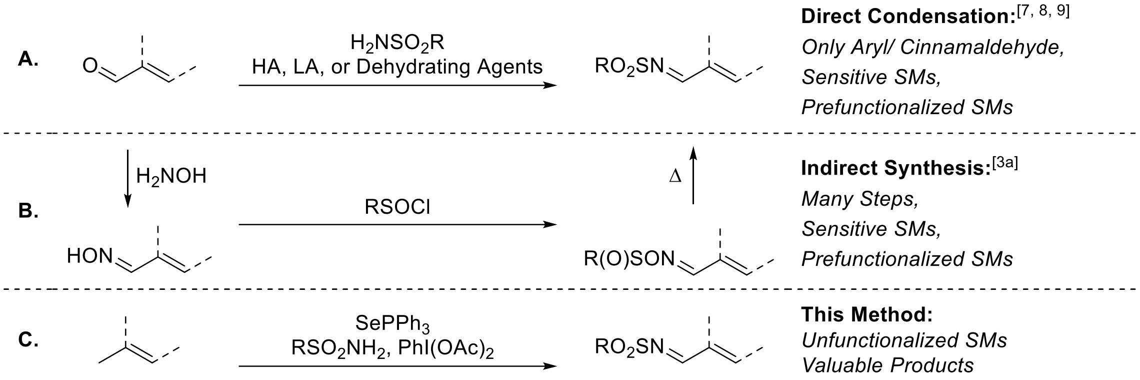


Figure 2.2. Methods for the Synthesis of Imines.

Despite the improvement in scope and yield relative to the direct condensation methods, this protocol requires three synthetic steps and utilizes prefunctionalized α,β-unsaturated aldehydes as substrates. Not only are these extremely sensitive, some are known to be highly toxic[10]. Furthermore, to generate these conjugated sulfonyl imines from simple alkenes, at least one additional oxidation step to the α,β-unsaturated aldehyde would be required adding up to a minimum of 4 synthetic steps. We realized that if we could optimize our reaction conditions to favor the conjugated sulfonyl imine product over the allylic sulfonamide, we could access these substrates from simple alkenes in only one step (Figure 2.2 C). This would represent the first direct method for the generation of conjugated sulfonyl imines as well as the only known protocol for synthesizing imines from simple alkenes.

Section 2: RESULTS AND DISCUSSION

2.2.1 *Mechanistic Investigation*

To optimize the reaction conditions to select for imine products, we sought to gain insight into the mechanism for imine formation. Looking back at our proposed mechanism for the allylic amination of alkenes, we envisioned three potential mechanisms for the allylic amine intermediate to be oxidized into the conjugated imine products shown in Figure 2.3: direct oxidation of the allylic amine by the hypervalent iodine reagent, a second allylic amination and subsequent elimination of the resulting aminal (**IV**), or elimination of either intermediate **II** or intermediate **III** (path b.).

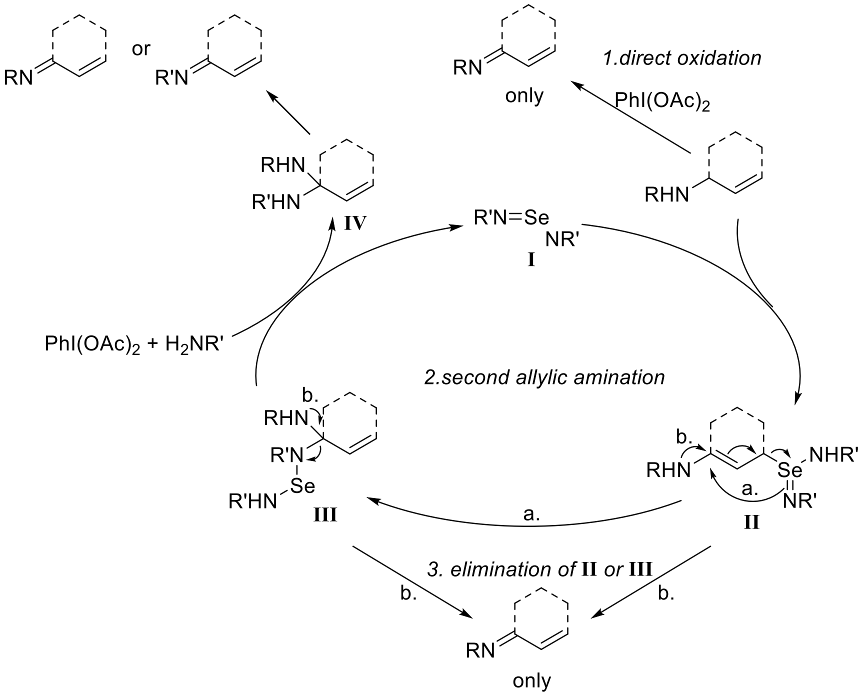
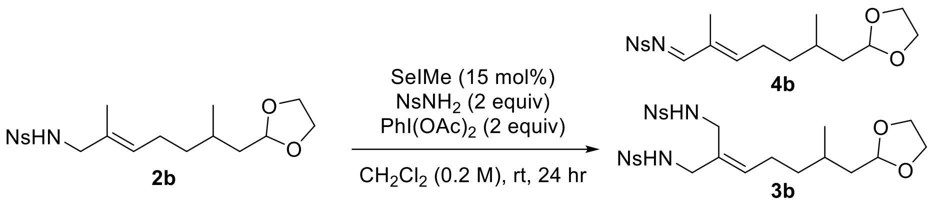


Figure 2.3. Plausible Mechanisms for Imine Formation.

To determine which of these pathways is most likely, we needed to determine which reaction components are required to convert the proposed allylic amine intermediate into the conjugated imine product. A direct oxidation mechanism of the allylic amine to the conjugated imine should only require the presence of oxidant while the other suggested pathways should require the presence of all reaction components. We began this investigation by treating isolated allylic amine (**2b**) to variations of the allylic amination conditions from our previous report (Table 2.1).

Table 2.1. Determining Necessary Reaction Components



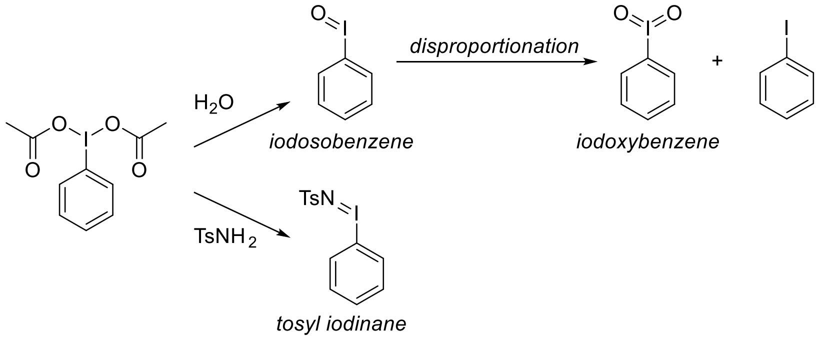
Entry	Change from above conditions	%Conversion
1	no SeIMe and no NsNH$_2$	0
2	no NsNH$_2$	trace
3	no SeIMe	trace
4	none	100[a]

[a] obtained as a 1:1 ratio of imine to diamine

Treating allylic amine (**2b**) with just diacetoxyiodobenzene (PhI(OAc)$_2$) resulted in no conversion to the imine (Table 2.1, entry 1). Additionally, treating the allylic amine (**2b**) with either oxidant and catalyst, entry 2) or oxidant and sulfonamide (Table 2.1, entry 3) resulted in only trace product formation. Only when all reaction components were present did the desired reaction occur. When isolated allylic amine (**2b**) was subjected to the complete reaction conditions from our previous allylic amination report we observed complete conversion to the desired imine product (**4b**) as well as a diamination product (**3b**) in a 1:1 ratio (Table 2.1, entry 4). This result was somewhat surprising since we had previously only observed imine formation as a minor side-product during the allylic amination report (Scheme 2.1) but this may be explained by the increased relative ratio of oxidant and sulfonamide to the allylic amine substrate for this new experiment.

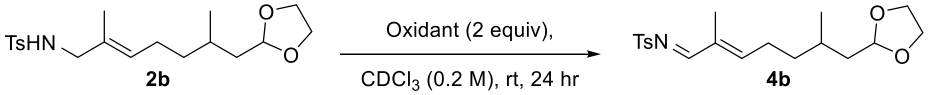
While the previous results implied that the allylic amine cannot be directly oxidized by PhI(OAc)$_2$, there remained a possibility that a different hypervalent iodine reagent generated *in situ* may be doing this oxidation (Scheme 2.2).

Scheme 2.2. *Potential Derivatives of Diacetoxyiodobenzene*



For instance, treating PhI(OAc)$_2$ with a sulfonamide can result in the formation of the respective iminoiodinane (e.g. PhINTs). Additionally, PhI(OAc)$_2$ can be hydrolyzed into iodosobenzene (PhIO) which can then undergo disproportionation to form iodoxybenzene (PhIO$_2$) and iodobenzene. To probe whether any of these derivatives could result in the direct oxidation mechanism, we treated isolated allylic amine (**2b**) with independently synthesized samples of each (Table 2.2).

Table 2.2. Screening Hypervalent Oxidants



Entry	Oxidant	%Starting Material^a	%Yield^a
1	PhI(OAc)$_2$	73	trace
2	PhIO	69	trace
3	PhIO$_2$	60	trace
4	PhINTs	30	trace

^{a}Yield determined using 1,3-dinitrobenzene as an internal standard

Again, we observed that diacetoxyiodobenzene did not oxidize the allylic amine (**2b**) under these reaction conditions (Table 2.2, entry1). Similarly, treating the allylic amine (**2b**) with the potential oxidant derivatives PhIO (Table 2.2, entry 2), PhIO$_2$ (Table 2.2, entry 3), or PhINTs (Table 2.2, entry 4) resulted in no conversion to the desired imine product (**4b**) under these reaction conditions.

Together, these results suggest that a direct oxidation of the allylic amine by the hypervalent iodine species (or some derivative of it, e.g. N-nosyl iminoiodinane) is unlikely, although direct oxidation of the allylic amine by some other oxidant, such as an oxidized selenium species cannot be ruled out. It is worth noting that significant disappearance of the starting material was observed in all cases, particularly when the allylic amine (**2b**) was treated with PhINTs (Table 2.2, entry 4), suggesting that these oxidants are capable of decomposing the starting material in other deleterious side reactions.

Our second proposed mechanism for the oxidation of the allylic amine is a second allylic amination followed by elimination of the resulting aminal species (**IV**). This pathway should result in mixed aminal species if the sulfonamide utilized for the second allylic amination evet is distinct from the one present in the starting allylic amine. This aminal could eliminate either sulfonamide leading to two distinct products (Figure 2.4).

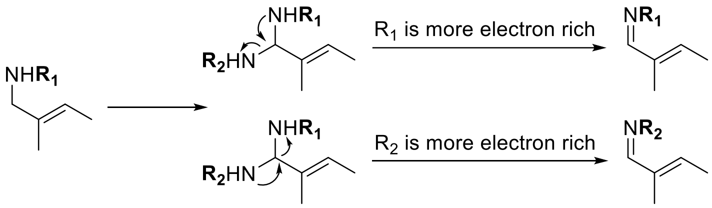
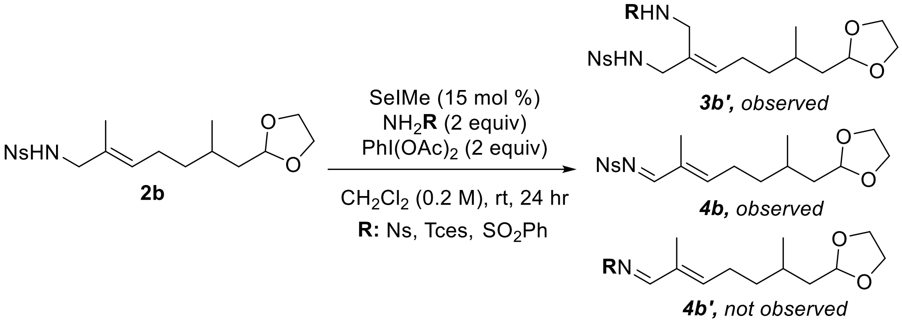


Figure 2.4. Aminal Formation and Decomposition.

The major imine product obtained from this aminal decomposition is likely a result of the more electron rich sulfonamide eliminating the less electron rich sulfonamide. To probe this, isolated nosyl allylic amine (**2b**) was subjected to the reaction conditions with either a more electron rich sulfonamide ($TsNH_2$) for which we might expect formation of the tosyl imine (**4b’**) as the major product, or a less electron rich sulfamate ($TcesNH_2$) for which we might expect formation of the nosyl imine (**4b**) as the major product (Scheme 2.3).

Scheme 2.3. *Only the Starting Amine Goes to the Imine, There is No Mixing.*



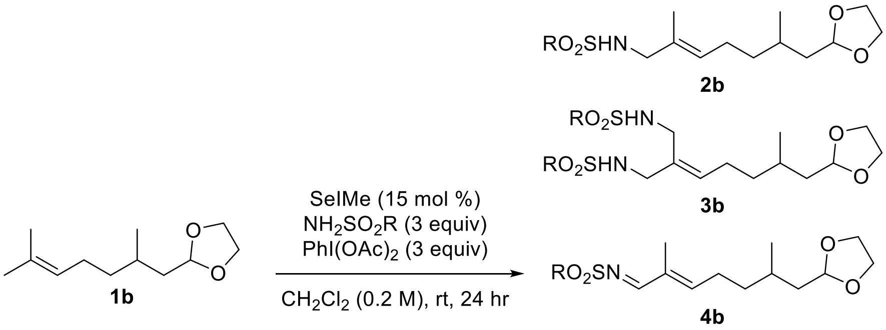
In all cases, only the nosyl imine (**4b**) was observed in addition to the mixed diamine (**3b'**). The presence of the mixed diamine (**3b'**) suggests both that the starting allylic amine (**2b**) is still capable of undergoing a second allylic amination event and that the reaction was not being shut down by some unknown factor. Since no mixed imine (**4b'**) was observed containing either the more electron rich sulfonamide or the less electron rich sulfamate, yet the reaction conditions were still generating the nosyl imine (**4b**) and the mixed diamine (**3b'**), a complete second allylic amination event seems unlikely.

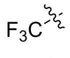
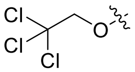
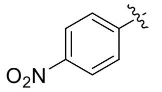
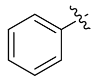
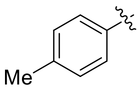
Given these results, we hypothesize that imine formation is likely caused by the elimination of Intermediate **II** or Intermediate **III** (Figure 2.3). This pathway requires all reaction components to be present and would explain why only the nosyl imine was observed when the nosyl allylic amine was subjected to reactions conditions with other sulfonamides/sulfamates. It is worth noting that we cannot rule out an off-cycle selenium catalyzed oxidation of the allylic amine at this time. We also cannot rule out a radical based oxidation. However, radicals can easily undergo addition reactions to alkenes and for these allylic amine substrates, hydrogen atom abstraction could lead to various allylic radicals each of which could lead to a variety of products. Since none of these products were observed, a radical based oxidation seems less likely

2.2.2 *Initial Optimization*

We initially observed the imine as a minor byproduct. We realized that imine formation required additional oxidant to be present and hoped that by adding more oxidant to this reaction, we would increase the conversion to the desired imine products. Pleasingly, increasing the amount of oxidant and nucleophile from two to three equivalents resulted in a significant improvement in imine formation from <5% to 28%. However, we also observed a 30% yield of a diamination product. We decided to probe how the electronic nature of the sulfonamide nucleophile might effect the reaction outcome (Table 2.3).

Table 2.3. Screen of Electronically Varied Sulfonamides



Entry	R	%Yield[a] **2b**	%Yield[a] **3b**	%Yield[a] **4b**
1	 "Tf"	26	14	6
2	 "Tces"	49	-[b]	8
3	 "Ns"	0	30	28
4	 "$PhSO_2$"	0	24	31
5	 "Ts"	0	30	45

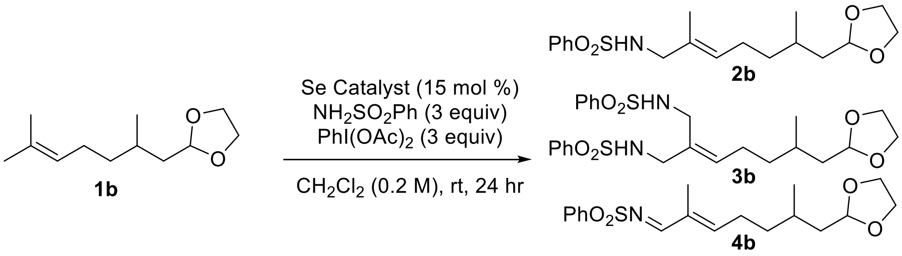
[a] Yield determined using 1,3-dinitrobenzene as an internal standard
[b] Area of the spectrum is too obscured to confidently assign

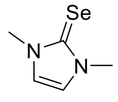
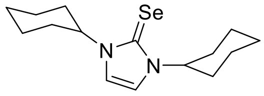
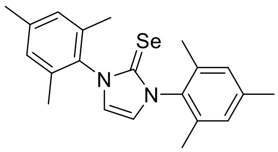
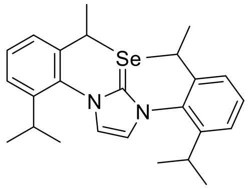
We observed a clear trend where the amount of oxidation depended heavily on the electron richness of the amine source. The more electron poor nucleophiles ($TfNH_2$ and $TcesNH_2$) resulted in reasonable conversion to the allylic amines (**2b**) but gave minimal further oxidation to the diamine (**3b**) or imine (**4b**) products (Table 2.3, entries 1-2). The more electron rich aryl sulfonamides resulted in complete conversion to the more oxidized products (**3b** and **4b**) with no remaining trace of the allylic amine intermediates (**2b**) (Table 2.3, entry 3-5). Despite the clear electronic trend, there was little apparent difference in reaction outcome when using $NsNH_2$ and

$PhSO_2NH_2$ despite the presence of the electron withdrawing NO_2 on the aryl ring of $NsNH_2$ (Table 2.3, entry 3-4). However, the most electron rich sulfonamide tested, $TsNH_2$ with a slightly electron donating methyl group in place of the NO_2 group found in $NsNH_2$, resulted in the greatest amount of oxidation affording the desired imine product (**4b**) in the highest yield (Table 2.3, entry 5).

Despite the improvement in yield using the more electron rich sulfonamide, we wished to improve the selectivity for imine formation over diamination since the formation of this side product was consuming a significant amount of our starting alkene and was greatly limiting the potential yield of the desired imine products. We hoped we could solve this problem by tuning the chemoselectivity of the catalyst through appropriate ligand choice (Table 2.4).

Table 2.4. Ligand Screen with Benzenesulfonamide as the Nucleophile



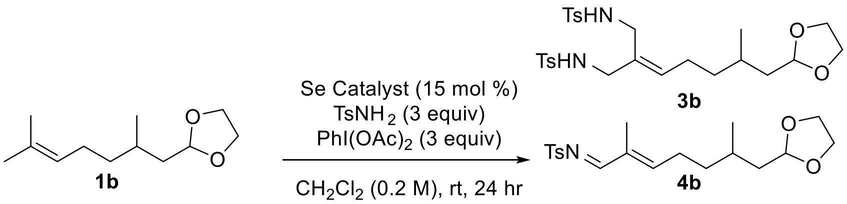
Entry	Catalyst	%Yield^a **2b**	%Yield^a **3b**	%Yield^a **4b**
1	 "SeIMe"	0	28	30
2	 "SeICy"	14	25	33
3	 "SeIMes"	46	0	8
4	 "SeIPr"	50	0	0
5	SePCy$_3$	0	>5	39
6	SePPh$_3$	0	>5	38
7	SePNp$_3$	0	>5	38

^{a}Yield determined using 1,3-dinitrobenzene as an internal standard

Gratifyingly, we found that while the alkyl NHC based catalysts result in significant diamination (Table 2.4, entries 1-2), the phosphine based selenides seem to suppress this byproduct formation while keeping the yield of the desired imine product intact (Table 2.4, entries 5-8). Interestingly, the aryl NHC catalysts afforded no products from a second oxidation and instead resulting in exclusive formation of the allylic amine (**2b**) (Table 2.4, entries 3-4).

Using these phosphine selenides as catalysts with the more electron rich toluenesulfonamide proved to be critical for high yields in the reaction (Table 2.5). Moving from the methyl imidazolium based selenide (Table 2.5, entry 1) to tricyclohexylphosphine selenide improved the yield of the desired imine to 55% and totally suppressed the formation of the undesired diamination product (Table 2.5,entry 2). Switching the catalyst to triphenylphosphine selenide further improved the yield of the desired product to 85% (Table 2.5,entry 3)

Table 2.5. Ligand Screen with Toluenesulfonamide as the Nucleophile



Entry	Catalyst	%Yield^a **3b**	%Yield^a **4b**
1	SeIMe	28	44
2	$SePCy_3$	0	55
3	$SePPh_3$	0	84

^{a}Yield determined using 1,3-dinitrobenzene as an internal standard

With the seemingly optimized conditions in hand, we turned our attention to the scope of this reaction. A variety of highly substituted alkenes gave the desired imine products in high yields. Unfortunately, other less substituted alkene classes failed to deliver the products in acceptable yields and we decided to reoptimize our conditions to include these substrates.

2.2.3 *Other Alkene Substitution Patterns*

We began by examining the imine formation for 4-phenyl-1-butene, in the hopes of utilizing terminal alkenes as substrates. A vast selection of selenium catalysts, various sulfonamides, and additives were screened. Unfortunately, in all cases, only the allylic amination product was formed with no detected imine. We hypothesized that the lack of imine formation for the terminal alkenes was a result of the reduced electron density so we turned our attention to the more electron-rich 1,2-disbstituted alkenes. An extensive screen of reaction conditions was performed on trans-2-octene and again allylic amination was exclusively observed without any desired imine products.   We hypothesized this reduced reactivity may be overcome by increasing the acidity of the allylic protons encouraging the initial ene reaction (Figure 2.5).

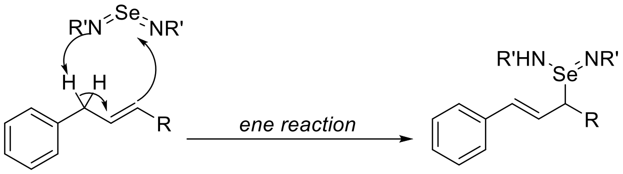
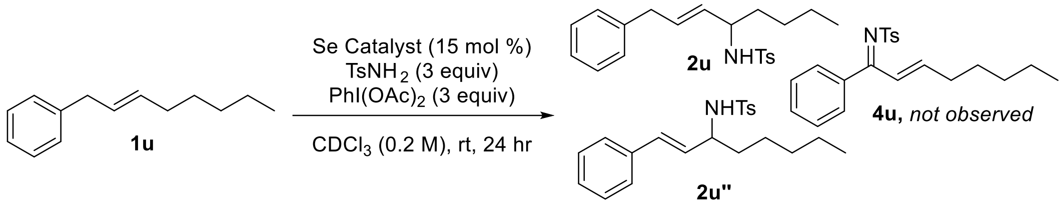
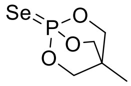
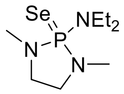
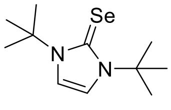


Figure 2.5. Mechanistic Reasoning Behind Substrate Choice

With this in mind, we selected an allylic benzene derivative as the model substrate. We began this investigation with a quick survey of catalysts (Table 2.6). Unfortunately, none of the desired imine was formed for any of the catalysts screened.

Table 2.6. Ligand Screen for Allyl Benzene Derivative

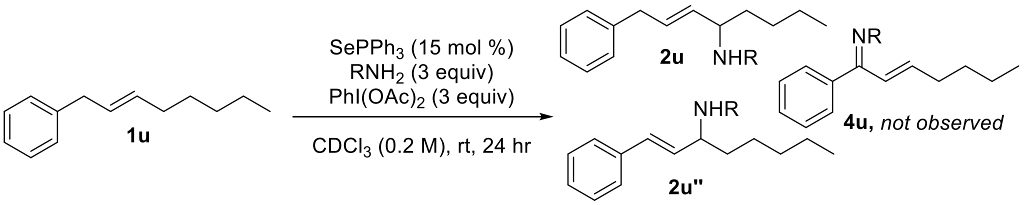


Entry	Catalyst	Starting Material %	%Yield^a **2u**	%Yield^a **2u''**
1	SePPh$_3$	0	14	28
2	SePCy$_3$	0	11	26
3	SeP(OPh)$_3$	0	15	29
4		0	13	26
5		0	13	28
6	 "SeItBu"	91	0	0

^{a} Yield determined using 1,3-dinitrobenzene as an internal standard

Instead of the desired product, we observed the intermediate allylic amine (**2u**) as well as a significant amount of the transposed allylic amine (**2u’’**). We hoped that the proper selection of sulfonamide might avoid the new undesired reaction, so a screen of electronically varied nucleophiles was tested on the model alkene (Table 2.7).

Table 2.7. Sulfonamide Screen for Allyl Benzene Derivative

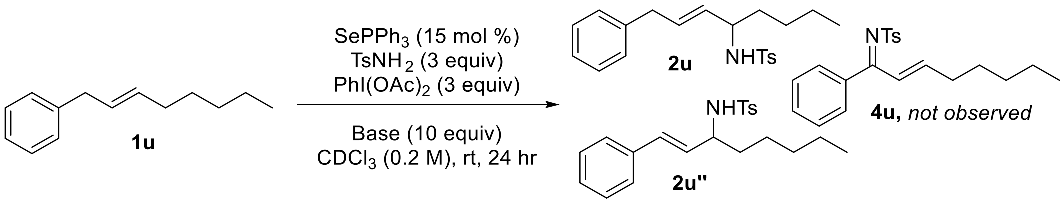


Entry	R	Starting Material (%)	%Yield^a **2u**	%Yield^a **2u"**
1	Ts	0	17	28
2	PhSO2	0	18	28
3	Ns	0	25	28
4	Tces	0	32	25
5	F_3CSO_2	0	31	38
6	$MeSO_2$	0	17	27

[a] Yield determined using 1,3-dinitrobenzene as an internal standard

Again, we observed no desired imine formation and a significant amount of both the intermediate allylic amine (**2u**) and the transposed allylic amine (**2u''**). We noticed that the formation of the transposed product was the highest for the most acidic nucleophile tested (Table 2.7, entry 5). We hypothesized that the alkene isomerization leading to the transposed product could be acid catalyzed. To suppress this side reaction, we screened a variety of base additives (Table 2.8).

Table 2.8. Base Screen for Allyl Benzene Derivative

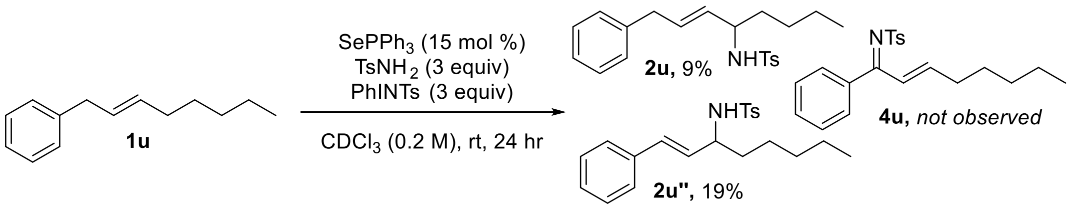


Entry	Base	Starting Material (%)	%Yield[a] **2u**	%Yield[a] **2u''**
1	CaO	59	2	5
2	K_2CO_3	quant	0	0
3	Cs_2CO_3	quant	0	0
4	2,6-lutidine	91	0	0

[a] Yield determined using 1,3-dinitrobenzene as an internal standard

Calcium oxide resulted in minimal reactivity but we still detected the transposed allylic amine (**2u''**) (Table 2.8, entry 1). We observed that both carbonate bases and lutidine resulted in total suppression of amination reactivity (Table 2.8, entries 2 – 4). Since the base additives appeared to shut down all reactivity, we decided to try to avoid the formation of acid entirely. To this end, we tried a reaction using the preformed tosyl iminoiodinane as the oxidant rather than the diacetoxyiodobenzene to prevent acetic acid formation (Scheme 2.4).

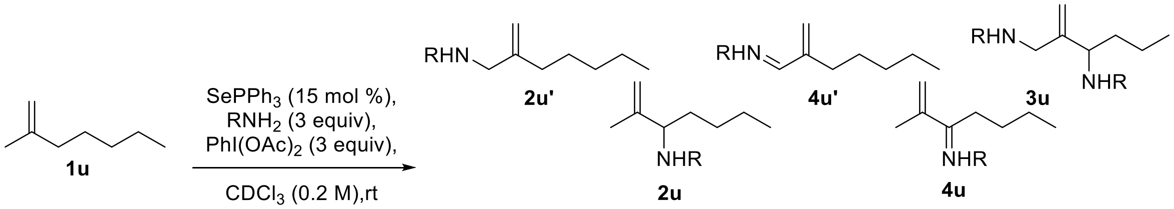
Scheme 2.4. *Using Iminoiodinane as Oxidant Source to Minimize Acid Formation*



Unfortunately, we once again observed no desired product formation and significant amounts of the transposed allylic amine product (**2u''**).

Since 1,2-disubstituted alkenes were not undergoing the desired transformations, we turned our attention to 1,1-disubstituted alkenes. This class of alkenes has improved hyperconjugation and an increased ability to stabilize carbocations at the tertiary carbon resulting in higher nucleophilicity relative to 1,2-disubstituted alkenes. We hoped that this increase in nucleophilicity might result in better reactivity. We selected 2-methyl-1-heptene (**1u**) as the model alkene for this optimization. In addition to the hopefully improved reactivity, we hoped that this substrate might provide insight into how the reaction conditions affect the regiochemical outcome. We knew from the allylic amination chemistry that the secondary position would be favored over the primary and were interested to see if tuning the properties of the sulfonamide/ catalyst might alter this selectivity. We began this investigation with an extensive sulfonamide screen (Table 2.9).

Table 2.9. Sulfonamide Screen for 2-methyl-1-heptene



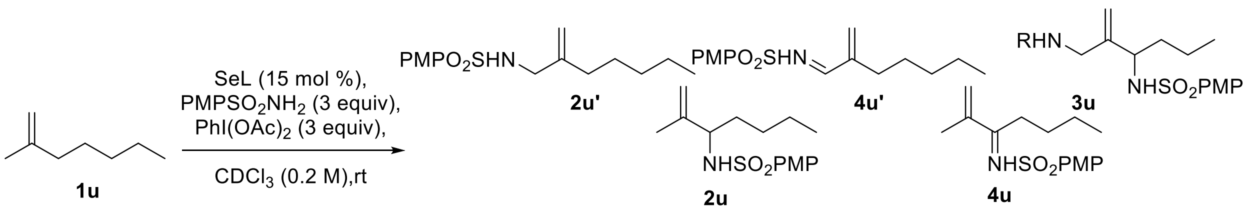
Entry	R	%Yield[a] **2u'**	%Yield[a] **2u**	%Yield[a] **4u'**	%Yield[a] **4u**	%Yield[a] **3u**
1	SO_2Ph	0	20	7	13	12
2	Ts	0	31	11	20	0
3	Ns	11	35	0	0	0
4	SO_2Me	5	27	8	11	15
5	SO_2CF_3	0	13	0	0	25
6	Tces	0	4	0	0	44
7	SO_2tBu	0	0	5	4	0
8	$SO_2CH_2CH_2SiMe_3$	0	13	6	13	0
9	SO_2PMP	0	7	13	30	0

[a] Yields determined using 1,3-dinitrobenzene as an internal standard

We observed a strong electronic effect from the amine source on the product distribution with more electron poor nucleophiles resulting moderate formation of the allylic amine intermediates (**2u** + **2u'**) but no desired imine formation (**4u** + **4u'**) (Table 2.9, entries 3, 5, and 6). Interestingly, the sulfamate TcesNH$_2$ resulted in significant amounts of diamination (**3u**) without any competing imine formation (**4u** + **4u'**) (Table 2.9, entry 6). More electron rich nucleophiles gave higher conversion to the desired imine products (**4u** + **4u'**) and resulted in little to no diamination (**3u**) (Table 2.9, entries 1, 2, 4, 8, and 9). The most electron rich of these nucleophiles gave the best results with para-methoxybenzenesulfonamide affording a 43% yield of the desired product (**4u** + **4u')** as a 3:1 mixture of regioisomers (Table 2.9, entry 9). Interestingly, the isomer of the allylic amine derived from the primary allylic amination (**2u'**) is rarely observed while the other regioisomer (**2u**) was seen in nearly every case. This could indicate that **2u'** might undergo further oxidation reactions either to the diamine or the desired imine product faster than **2u** does.

We then wanted to see what effect catalyst had on this reaction to see if we could improve the yields of the desired imine products. A survey of catalysts was tested on the model alkene using para-methoxybenzenesulfonamide ($PMPSO_2NH_2$) as the nucleophile (Table 2.10).

Table 2.10. Catalyst Screen for 2-methyl-1-heptene



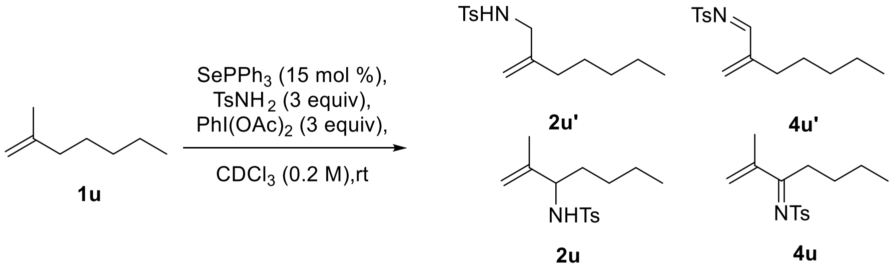
Entry	Ligand	%Yield^a **2u'**	%Yield^a **2u**	%Yield^a **4u'**	%Yield^a **4u**	%Yield^a **3u**
1	PPh_3	0	7	13	30	0
2	PNp_3	0	11	12	28	0
3	PCy_3	0	15	11	26	0
4	$PtBu_3$	0	25	3	7	12
5	P(MeCage)	0	28	8	15	0
6	$P(OPh)_3$	0	24	7	12	3
7	$P(NEt)_3$	0	9	11	17	0
8	IMe	0	6	5	9	25
9	ItBu	0	17	4	12	27
10	IMes	6	65	0	0	0

^{a}Yields determined using 1,3-dinitrobenzene as an internal standard

We once again observed that the alkyl imidazolium catalysts facilitated diamination (**3u**) (Table 2.10, entries 7 and 8) while the phosphine selenides appeared to suppress that mode of reactivity (Table 2.10, entries 1-6). Unfortunately, we discovered that the triphenylphosphine selenide was already the optimal catalyst of the ones screened giving the desired product (**4u** + **4u'**) in 43% yield with minimal intermediate allylic amine (**2u** + **2u')** (Table 2.10, entry 1). Interestingly, the aryl imidazolium failed to give any of the desired oxidation products and instead provided significant conversion to the intermediate allylic amines (**2u** + **2u'**) in 71% combined yield (Table 2.10, entry 9).

Since the formation of the desired product was still limited, we turned to increased temperature and catalyst loading (Table 2.11).

Table 2.11. Temperature and Catalyst Loading Screen for 2-methyl-1-heptene



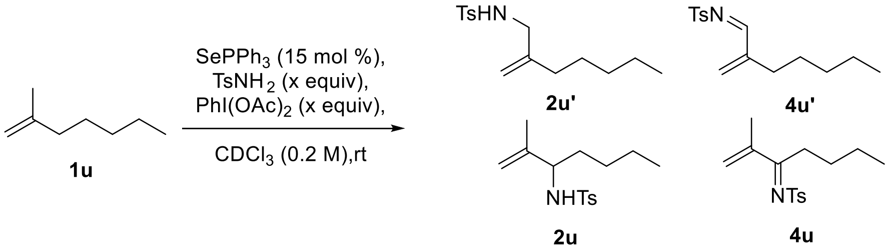
Entry	Change	%Yield^a **2u'**	%Yield^a **2u**	%Yield^a **4u'**	%Yield^a **4u**
1	none	0	34	12	18
2	35 °C	0	26	9	20
3	45 °C	0	14	8	18
4	30 mol %	0	0	15	18

[a]Yields determined using 1,3-dinitrobenzene as an internal standard

We observed a detrimental effect from increased reaction temperature with no improvement in the yield of desired products but a decrease in the amount of intermediate allylic amine (**2u** + **2u'**) (Table 2.11, entries 2 and 3). A similar effect was observed for increasing the catalyst loading with a noted disappearance of the intermediate despite no improvement to the yields of the desired imine products (Table 2.11, entry 4).

In practically every attempt to optimize these substrates, we observed a concerning disappearance of the substrate with no clear indication of what byproducts it was leading to. We hypothesized that the oxidant might be responsible for these mass balance issues. In an effort to minimize the degradation of the starting alkenes, we tried altering the amount of oxidant or nucleophile (Table 2.12).

Table 2.12. Equivalence Screen of Oxidant and Nucleophile for 2-methyl-1-heptene



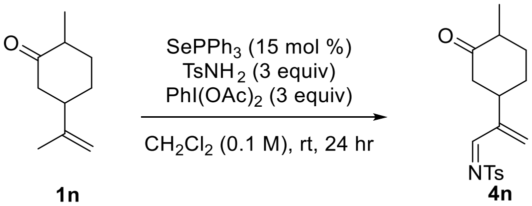
Entry	$TsNH_2$	$IPh(OAc)_2$	%Yield[a] **2u'**	%Yield[a] **2u**	%Yield[a] **4u'**	%Yield[a] **4u**
1	1	2	7	28	11	11
2	1	3	0	21	12	13
3	2	2	0	35	13	15
4	2	3	0	32	12	17
5	3	2	0	36	12	16
6	3	3	0	34	12	18
7	4	4	0	31	13	16

[a] Yields determined using 1,3-dinitrobenzene as an internal standard

Increasing the amount of oxidant and nucleophile from 1 to 4 resulted in very little difference in formation of the desired imine. The only notable difference was that the amount of intermediate allylic amine (**2u**) formed increased in moving from 1 (Table 2.12, entries 1 and 2) to 2 equivalents and up (Table 2.12, entries 3 – 6). We also observed that increasing the amount of oxidant and nucleophile to 4 also did not improve the desired product formation (**4u** + **4u'**) (Table 2.12, entry 7).

We hypothesized that the low mass balance for these reactions may be due to the sensitive nature of the products. To probe this, we selected a different 1,1-disusbtituted alkene with fewer regiochemical concerns and tested a variety of workup conditions to determine the effects on desired product yields (Table 2.13).

Table 2.13. Determining Stability of Products



Entry	Work Up	%Yield^{a}
1	none	52
2	silica plug	44
3	aqueous extraction	33

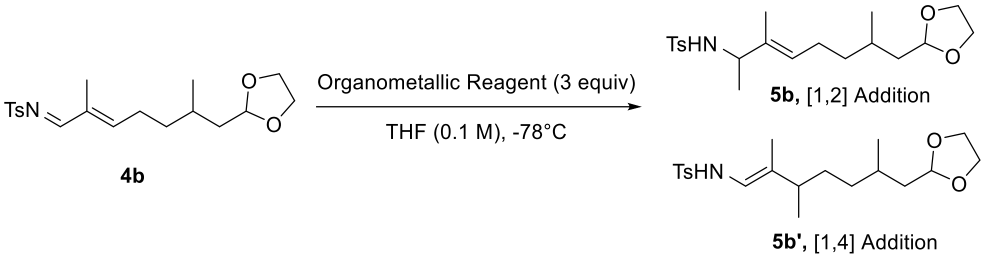
^{a}Yields determined using 1,3-dinitrobenzene as an internal standard

As suspected, we observed a reduction in yield with any workup we attempted with the highest yield obtained associated with no workup (Table 2.13, entry 1). To bypass the reactive nature of the substrates, we hoped to trap the product as a more stable species.

2.2.4 *Trapping of Imine Products*

We decided to turn our attention toward derivatizing these imine products in the hopes of developing an *in situ* method for trapping the products as more stable species. To determine the viability of using organometallic reagents as a trapping method, we took isolated conjugated imines and subjected them to either methyl lithium or methylmagnesium bromide (Table 2.14).

Table 2.14. Organometallic Reagents with Isolated Imine Products



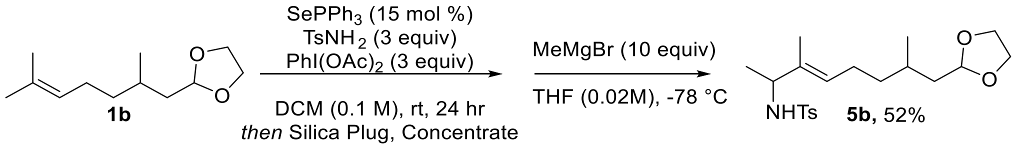
Entry	Organometallic Reagent	**5b** [1,2] Addition[a]	**5b'** [1,4] Addition[a]
1	MeLi	67	33
2	MeMgBr	100	0

[a] Product distributions determined after 100% conversion of Starting Material

In both cases we observed complete conversion of the starting material (**4b**). However, in the case of methyl lithium, we observed a mixture of both [1,2]- (**5b**) and [1,4]- (**5b’**) addition of the nucleophile (Table 2.14, entry 1). Methylmagnesium bromide proved to be far more selective giving exclusively [1,2]-addition (**5b**) (Table 2.14, entry 2). Due to this inherent selectivity, we selected methylmagnesium bromide as a trapping agent.

To utilize this reagent in a trapping protocol, we would need to change the solvent, CH_2Cl_2, and remove the acid generated during the reaction since both can quench organometallic reagents. We hoped that these limitations could be overcome using a minimal work up (Scheme 2.5).

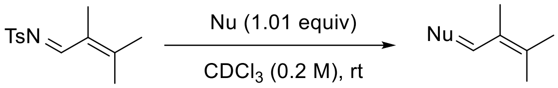
Scheme 2.5. *Grignard Reaction After Minimal Workup*



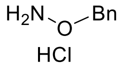
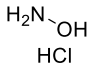
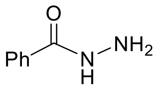
Indeed, by flushing the reaction through a silica plug, concentrating it under reduced pressure, and diluting with THF before adding the Grignard reagent, we could successfully obtain the desired addition product (**5b**), albeit in a reduced yield of 52%. While we were pleased with the ease of this protocol, we determined it was not viable for trapping our products due to the 15% loss of product.

We then turned our attention to trapping the product as an oxime or a hydrazone. We hoped that we could simply add this nucleophile to the reaction mixture and obtain a more stable product. As a preliminary check, we subjected isolated imine to a variety of nucleophiles and monitored the reaction by NMR (Table 2.15).

Table 2.15. Transimination with Various Nucleophiles

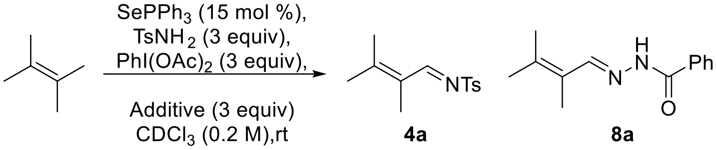


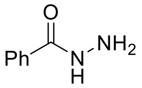
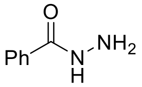
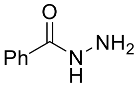
4a **6-8a**

Entry	Nucleophile	Conversion (%) 1 hr	Conversion (%) 24 hr
1	 **6**	0	0
2	 **7**	0	0
3	 **8**	100	100

While we observed no desired reactivity for the hydroxylamine hydrochloride salts (Table 2.15, entries 1 and 2), we observed complete conversion from the sulfonyl imine (**4a**) to the hydrazine (**8a**) within 1 hour using benzhydrazine as the nucleophile (Table 2.15, entry 3). Due to the rapid nature of this reaction, we envisioned it might be a suitable nucleophile for trapping our products. However, one issue we envisioned was the potential instability of the hydrazine under the highly oxidative reaction conditions. Due to these concerns, we screened a variety of trapping protocols (Table 2.16).

Table 2.16. Trapping Protocols for Imine Products



Entry	Additive	Time Added	%Yield[a] **4a**	%Yield[a] **8a**
1	None	-	66	0
2		0 hr	0	0
3		24 hr	0	0
4	DMS (5 equiv)	24 hr	64	0
5	 + DMS (5 equiv)	24 hr	0	50

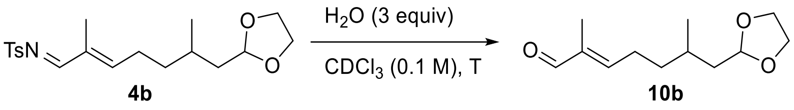
[a] Yield determined using 1,3-dinitrobenzene as an internal standard

With no workup, we obtained 66% of the imine product (**4a**) (Table 2.16, entry 1). Ideally, we would add the trapping nucleophile at the beginning of the reaction. However, we observed violent reactivity between the hydrazine and the oxidant resulting in no desired hydrazine product (**8a**) or imine intermediate (**4a**) when the hydrazine was added at either the beginning of the reaction or after the completion of the reaction (Table 2.16, entries 2 and 3). We envisioned bypassing this issue by quenching the excess oxidant after the completion of the reaction. To do this, we utilized dimethyl sulfide as a reductant. As a control, we tested this quenching method without hydrazine to ensure no deleterious effects on the reaction outcome (Table 2.16, entry 4). Finally, we tried quenching the oxidant and then adding the hydrazine (Table 2.16, entry 5). Unfortunately, while we obtained the desired reactivity, we observed a loss of roughly 15% of the desired product.

2.2.5 *Derivatization of Products*

While developing our *in situ* trapping methods for the imine we became interested in the transamination of these products with other nucleophiles. One obvious transformation is converting the conjugated imines into unsaturated carbonyl groups. We envisioned this would be possible by reacting the products with water.

Scheme 2.6. *Synthesis of Conjugated Carbonyls*

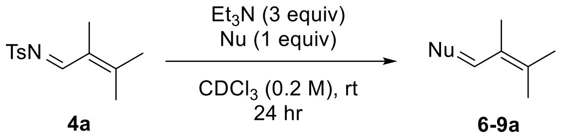


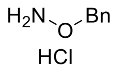
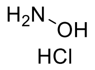
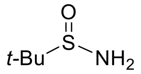
T: rt (0%), 65 °C (25%)

While we observed no desired reactivity at room temperature, we observed some product formation at elevated temperatures. We did not further investigate this mode of reactivity, but there is promise for obtaining the α,β-unsaturated carbonyl groups from this method.

One of the limitations we previously encountered was the lack of reactivity of these imine products with the hydroxylamine hydrochloride salts. We hypothesized this lack of reactivity may be due to the protonated state of the nucleophile, and found that by treating isolated conjugate imine with these nucleophiles in the presence of excess base we could successfully generate the desired oxime products (Table 2.17).

Table 2.17. Transiminations Under Basic Conditions

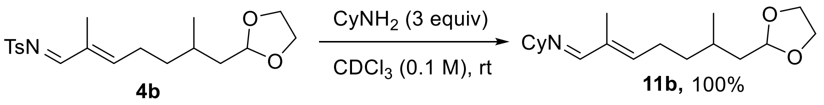


Entry	Nu	Conversion (%)
1	 **6**	100
2	 **7**	100
3	 **9**	0 (0)[a]

[a] Conversion without the addtion of triethylamine

We became inspired by this result and wondered if we could successfully achieve a transamination using a more synthetically valuable amine nucleophile. We had previously demonstrated no desired reactivity when utilizing sulfinyl amines as nucleophiles, but we envisioned the synthesis of sulfinyl imines may be achieved utilizing this transimination reaction. We decided to test our transimination using *tert*-butyl sulfinamide both with and without base additive. Unfortunately, we observed no desired reactivity for these reactions. While we were disappointed by this outcome, we decided to test the transimination using a primary amine which would be more reactive and potentially provide access to a vast array of synthetically useful coupling products. We started this examination by treating isolated tosyl imine (**4b**) with cyclohexylamine which resulted in complete conversion to the new imine product (**11b**) (Scheme 2.7).

Scheme 2.7. *Transimination with Primary Amines*



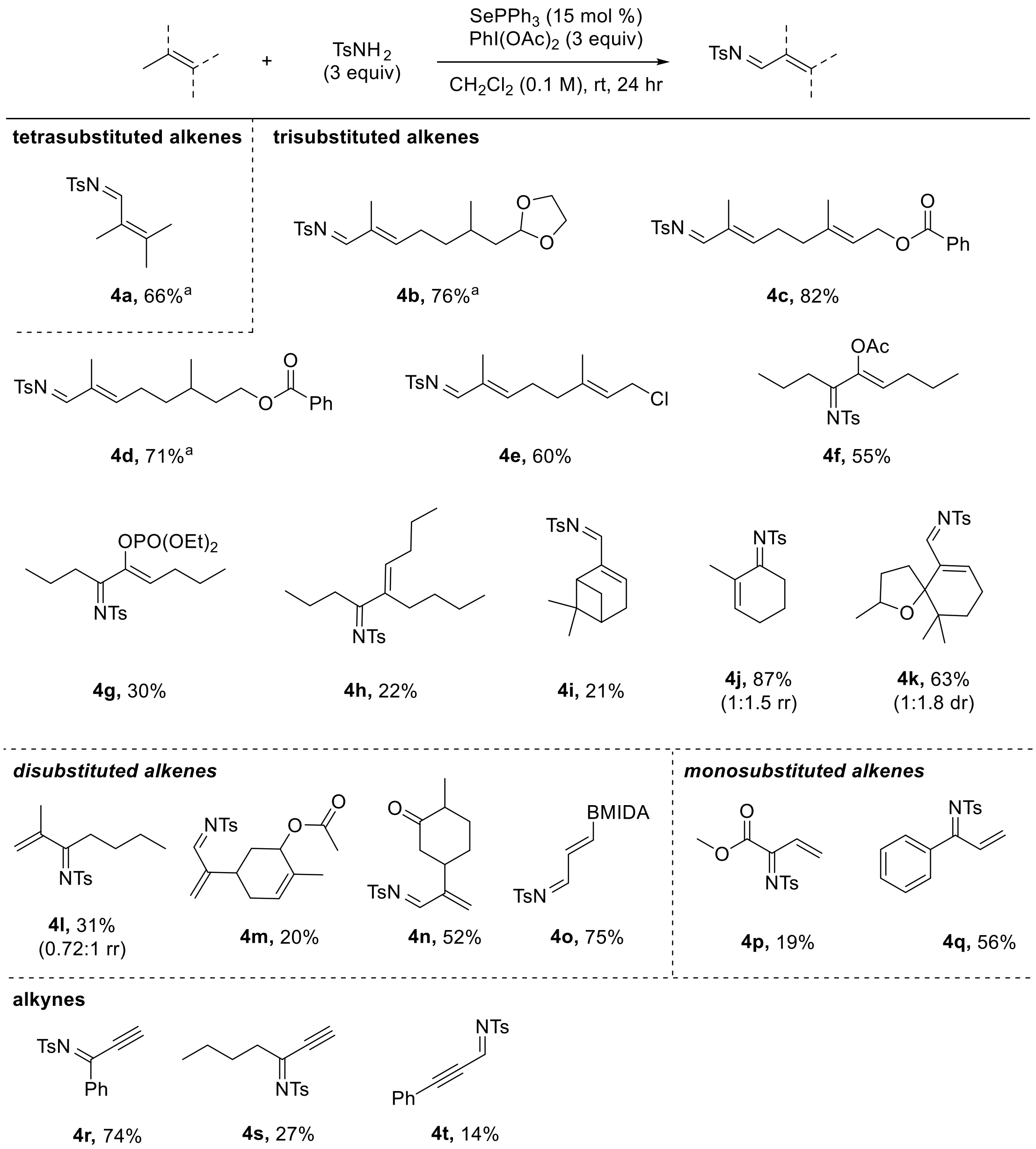
We were particularly excited by this result because we envisioned a modular synthesis where we could take an unfunctionalized alkene and install the sulfonyl imine, transiminate with a synthetically valuable basic amine, and add a Grignard reagent to this intermediate. This would be a highly valuable set of reactions effectively performing a double allylic C-H activation installing any amine and Grignard reagent desired.

2.2.6 *Investigation of the Scope*

We next turned our attention to the scope of this reaction (Table 2.18). The functional group compatibility of this reaction appears to be broad, with esters (**4c**, **4d**, **4f**), ethers (**4k**), and protected aldehydes (**4b**) all being well tolerated. Substrates bearing allylic halides (**4e**) and vinylic boronic esters (**4o**) afforded the desired products in high yields, paving the way for further functionalization. Like the allylic amination reaction, substrates containing multiple alkenes were observed to react exclusively at the more electron rich olefin (**4c**, **4e**, **4m**).

Presently, highly substituted alkenes with the ability to produce conjugated aldimines are the best substrates for this reaction (**4a** – **4e**). Unfortunately, moving to equally electron rich alkenes that would produce ketimines resulted in a significant reduction in yield (**4h**). Cyclic trisubstituted alkenes generally reacted well showing a slight preference for endocyclic imine formation (**4j**), but when this position was blocked, the exocyclic product was formed instead (**4j**, **4k**). Moving to 1,1-disubstituted alkenes generally resulted in a decrease in product yields (**4l – 4n**). The 1,2-disubstituted vinyl boronic ester (**4o**) afforded the product in high yields but other 1,2 disubstitued alkenes, including other vinyl boronic esters, either failed to react entirely or only formed trace amounts of the desired product.

Table 2.18. Current Substrate Scope for Allylic and Propargylic Imine Formation



[a]Isolated Yields

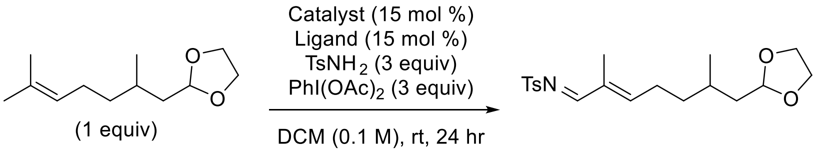
Monosubstituted alkenes also failed to generate any desired product unless an electronic bias was applied. The allylic ester, **1p**, was found to give 19% of the desired product (**4p**) but attempts to increase that yield through alteration of the ester portion proved fruitless. Allylbenzene gave relatively high yields of the desired allylic imine **4q**. Unfortunately, allylbenzene derivatives containing more substitution at the alkene resulted in exclusively allylic amination products (Table

2.6 - Table 2.8). Propargyl benzene was similarly shown to give high yields of the desired imine (**4r**), but other alkenes failed to react as well (**4s**, **4t**). Despite these limitations, the reaction method works for certain classes of alkenes. Further work should be done to expand these substrate classes.

2.2.7 *The Role of Selenium Red*

Throughout the optimization of both the selenium catalyzed allylic amination reaction (Chapter 1) and this selenium catalyzed synthesis of conjugated sulfonyl imines, a red precipitate was often observed. The formation of this insoluble red material typically coincided with the consumption of the starting material and served as a reliable indication that the reaction was complete. We hypothesized that this material was selenium red. Elemental selenium can exist in numerous allotropes. The most stable of these allotropes, and the one we use to make our selenium catalysts, is selenium grey. This structure is composed of long polymeric spiral chains of selenium atoms. Under certain conditions, elemental selenium can exist as cyclic chains consisting of six to eight selenium atoms. Selenium red is the eight membered cyclic selenium allotrope which is known to be highly insoluble in most solvents.[11] Judging by the appearance of the red precipitate, we hypothesized that we might be generating this insoluble selenium red upon completion of our oxidative reactions. Initially, we believed that the appearance of selenium red served as a visual indicator of catalyst decomposition. However, during the early optimization for this project, we commonly observed a flash of red precipitate upon addition of the oxidant to our reaction mixture. This red precipitate was observed to rapidly disappear and the desired reaction would then occur. We hypothesized that this flash of red represented the rapid formation of selenium red followed by its conversion to some more soluble material. This caused us to hypothesize that perhaps selenium red could be catalyzing our reaction. Following a known protocol, we prepared some selenium red from our commercial selenium grey powder and ran some control experiments. It should be noted that this was characterized solely by the red appearance of the resulting powder (Table 2.19).

Table 2.19. Elemental Selenium Catalyzed Synthesis of Conjugated Sulfonyl Imines



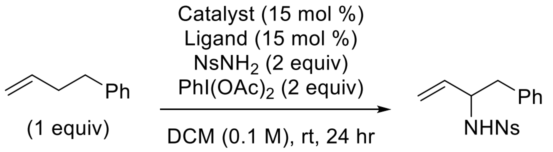
Entry	Catalyst	Ligand	Yield (%)[a]
1	$SePPh_3$	none	81
2	Se grey	none	0
3	Se grey	PPh_3	78
4	Se red	none	70
5	Se red	PPh_3	72

[a]Yield determined by HNMR with dinitrobenzene as an internal standard

Under the standard reaction conditions, we observed 81% yield of the desired conjugated sulfonyl imine (Table 2.19, entry 1). Commercial selenium grey resulted in no desired reactivity (Table 2.19, entry 2). Mixing a phosphine ligand with this elemental selenium before the additional reaction components revived the desired reactivity with a 78% yield of the desired imine revealing that *in situ* generated phosphine selenide is a competent catalyst for this reaction (Table 2.19, entry 3). Interestingly, using our supposed selenium red, we observed 70% yield of the desired product (Table 2.19, entry 4). This surprising result confirmed that selenium red could catalyze our imine reaction and did so nearly as well as the standard phosphine selenide. In fact, we observed little improvement when pre-stirring this selenium red with a phosphine ligand (Table 2.19, entry 5). Together, these results indicate that ligands on selenium are unnecessary for the desired transformation if the proper allotrope of selenium is utilized. However, due to the difficulty in preparation and characterization of selenium red, the phosphine selenides offer a far more practical entrance into this chemistry.

Because selenium red proved to be such a competent catalyst for the synthesis of conjugated sulfonyl imines, we decided to examine whether selenium red could catalyze the allylic amination reaction. To do this, we subjected 4-phenyl-1-butene to a variety of reaction conditions using elemental selenium as a catalyst (Table 2.20).

Table 2.20. Elemental Selenium Catalyzed Allylic Amination



Entry	Catalyst	Ligand	Yield (%)[a]
1	$SePPh_3$	none	86
2	Se grey	none	0
3	Se grey	PPh_3	83
4	Se red	none	79
5	Se red	PPh_3	68

[a]Yield determined by HNMR with dinitrobenzene as an internal standard

Using triphenylphosphine selenide as a catalyst resulted in 86% of the desired allylic amine (Table 2.20, entry 1). Using selenium grey as the catalyst resulted in no desired reactivity (Table 2.20, entry 2). Again, we observed that pre-stirring the selenium grey with the phosphine ligand resulted in similar results to using the preformed phosphine selenide with an 83% yield of the desired product (Table 2.20, entry 3). Interestingly, we observed that selenium red could catalyze this reaction with a 79% yield of the desired allylic amine (Table 2.20, entry 4). Finally, pre-stirring this selenium red with a phosphine ligand was observed to have a slightly detrimental effect on the reaction outcome with a diminished 68% yield of the allylic amine (Table 2.20, entry 5).

The fact that selenium red can catalyze these oxidative amination reactions without the use of ligands raises numerous questions. Do reactions catalyzed by selenium red and the phosphine catalysts go through the same mechanisms? If so, are the phosphine catalysts simply generating selenium red which then undergoes the desired reactions? The observation of a red precipitate at the initial stages of the imine reactions may support this possibility. But then if that is the case, why is there such a pronounce difference in reaction outcome for various ligands? Further work must be undertaken to answer these important mechanistic questions.

Section 3: CONCLUSIONS

A novel, direct protocol for the synthesis of conjugated imines from highly substituted alkenes has been presented. Key to the success of this method was the suppression of competitive diamination reactions through proper catalyst choice. The formation of the desired product was found to be highly dependent on the electron richness of the sulfonamide nucleophiles, with the more electron rich aryl sulfonamides affording the highest yields of the desired products. Numerous novel derivatizations of these highly valuable substrates were demonstrated including a transimination reaction with basic amines. The functional group tolerance of the reaction conditions appears to be very good. Unfortunately, numerous classes of olefins failed to give the desired products in high yields. Further work must be done to expand the substrate scope for this reaction.

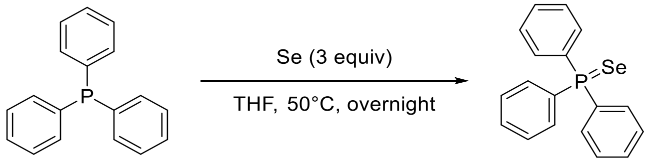
Section 4: EXPERIMENTAL

2.4.1 *General Procedures and Methods*

All reactions were performed under a nitrogen atmosphere using oven-dried or flame-dried glassware unless otherwise indicated. Dichloromethane (CH_2Cl_2) and tetrahydrofuran (THF) were degassed and dried by passing through a column of activated neutral alumina. Deuterated solvents ($CDCl_3$, acetone-d^6) were obtained from Cambridge Isotope Laboratories, Inc. and stored over activated 3A molecular sieves. Ethyl acetate (EtOAc), hexanes, and ether (Et_2O) were obtained from Fisher Scientific or Sigma Aldrich and used without further purification. Reagents were purchased from Sigma Aldrich, Tokyo Chemical Industry, Fisher Scientific, Alfa Aesar, Oakwood chemicals and used without further purification unless otherwise indicated. Infrared spectra were acquired using a Perkin Elmer Spectrum RX I spectrometer. Mass spectra were acquired using a Bruker Esquire 1100 Liquid Chromatograph-Ion Trap Mass Spectrometer. Column chromatography was performed using silica gel (Whatman, 60 Å, 230-400 mesh). NMR spectra were recorded on a Bruker AV-300, AV-301, DRX-499, or AV-500 spectrometer. ^1H NMR chemical shifts (δ) are reported in parts per million (ppm) and are referenced relative to TMS (0.00 ppm), $CHCl_3$ (7.26 ppm) or acetone-d^5 (2.06 ppm). ^{13}C NMR chemical shifts (δ) are reported in parts per million (ppm) relative to the carbon resonance of $CDCl_3$ (77.26 ppm) or acetone-d^6 (29.92 ppm). Melting points were taken on a MEL-TEMP melting point apparatus and are uncorrected.

2.4.2 *Synthesis and Characterization of Starting Materials*

General Procedure for Synthesis of Selenium Catalysts.

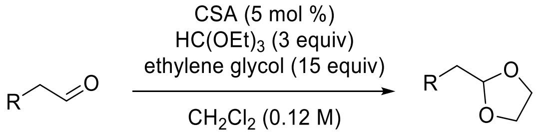


Triphenylphosphine selenide ($SePPh_3$). A flame-dried round bottom flask equipped with a magnetic stir bar was charged with triphenylphosphine (10 mmol, 1 equiv.) and selenium powder (30 mmol, 3 equiv) in a glove box. The flask was capped with a rubber septum and transferred outside of the glove box. Dry THF (20 mL, 0.5 M) was added using a syringe and the septum was replaced with a reflux condenser under nitrogen gas. The reaction was heated to 45 °C and allowed to stir overnight. After cooling to room temperature, the mixture was then flushed through Celite with CH_2Cl_2 to remove the residual selenium powder. The eluent was then concentrated on a rotary evaporator to afford the crude reaction product. The crude white solid was recrystallized from acetone and cooled in the freezer overnight to afford the product as white needles (2.88 g, 84% yield). The spectroscopic data was consistent with the literature.[12] **^{31}P NMR** (121 MHz, $CDCl_3$) δ 35.4 (d, *J* = 742 Hz).

General Information for Starting materials.

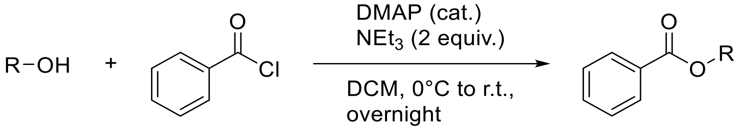
Starting material alkenes and sulfonamides are purchased from commercial sources and used without further purification unless otherwise indicated. Internal alkenes **4b**[13], **4c**[14], and **4d**[15] were synthesized according to the general procedures for acetal/benzoate protection (see below) and the spectroscopic data were consistent with the literature values.

General Procedure for Acetal protection.



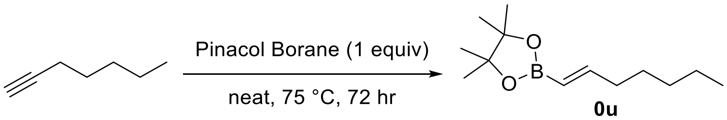
A flame-dried round bottom flask equipped with a magnetic stir bar was charged with ethylene glycol (75 mmol, 15 equiv), triethyl orthoformate (15 mmol, 3.0 equiv), and camphorsulfonic acid (5 mol %) in CH_2Cl_2 under nitrogen. The aldehyde was added dropwise (5 mmol, 1.0 equiv) and the mixture was stirred until determined to be completed by TLC. The reaction was quenched with $NaHCO_3$ (20 mL). The aqueous layer was washed with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were washed with brine (20 mL), dried over magnesium sulfate ($MgSO_4$) and concentrated under reduced pressure. Silica gel chromatography was used to purify the crude products.

General Procedure for Benzoate protection.



A flame-dried round bottom flask equipped with a magnetic stir bar was charged with alcohol (10 mmol, 1 equiv.) and 4-dimethylaminopyridine (0.2 mmol, 0.02 equiv.). Dry dichloromethane (20 mL, 0.5 M) was added and the reaction mixture was stirred and cooled to 0 ^{o}C. Benzoyl chloride (11 mmol, 1.1 equiv.) was added to the reaction mixture followed by triethylamine (20 mmol, 2 equiv.). The round bottom flask was then allowed to warm to room temperature and stir overnight. The reaction was quenched with water (20 mL) and diluted with ether (30 mL). The organic layer was then washed with saturated sodium bicarbonate (2 x 20 mL) and brine (1 x 20 mL) and dried over sodium sulfate. The solvent was then removed under reduced pressure and silica gel chromatography was used to purify the crude products.

Procedure for Synthesis of Allyl Benzene Derivative



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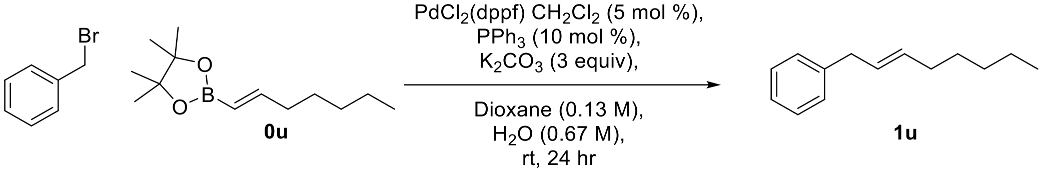
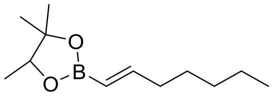
Preparation A: Prepared using a modified literature procedure.[16] A flame-dried vial was charged with alkyne (10 mmol, 1 equiv) and a stir bar. The vial was flushed with N2, then sealed. Pinacolborane (10 mmol, 1 equiv) was added via syringe and the reaction stirred for 7 h at 70 °C.

The reaction was moved to an Erlenmeyer flask, rinsing with THF. The flask was cooled to 0 °C. 1M NaOH was added slowly. The mixture was stirred for 15 min at 0 °C, then the ice-water bath was removed and the reaction stirred for another 15 min. The dark brown mixture was then transferred to a separatory funnel and diluted with Et_2O. After mixing and phase separation, the aqueous phase was extracted with Et_2O. The combined organics were washed with sat. aq. Na_2CO_3 (30mL × 5), brine, dried over $MgSO_4$, filtered and concentrated. The residue was dissolved in EtOAc and precipitated by slow addition of hexanes.

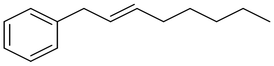


Preparation B: Prepared using a modified literature procedure.[17] A Schlenk tube sealed with a septum, under argon atmosphere, was first charged with Pd(dppf)·CH_2Cl_2 (5 mol %) and PPh_3 (10 mol %), then the boronic ester (11 mmol, 1 equiv) dissolved in dioxane (80 mL), benzyl bromide (11 mmol, 1 equiv), K_2CO_3 (33 mmol, 3 equiv) and H_2O (15 mL) were added. The resulting mixture was stirred at room temperature for 24 h. Brine (40 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 x 40 mL). The combined organic layers were dried over Na_2SO_4, filtered through a pad of Celite, and concentrated *in vacuo*. The residue was purified by flash chromatography over silica gel (n-heptane/EtOAc).

Characterization of Starting Materials



0u. Prepared according to preparation A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.64 (dt, *J* = 17.9, 6.4 Hz, 1H), 5.42 (dt, *J* = 18.0, 1.5 Hz, 1H), 2.14 (dt, *J* = 7.8, 4.1 Hz, 2H), 1.50 – 1.36 (m, 2H), 1.36 – 1.21 (m, 4H), 0.88 (t, *J* = 6.8 Hz, 3H).



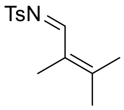
1u. Prepared according to preparation B and purified by silica gel chromatography (99:1, hexanes/ethyl acetate) to afford the product as a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 2H), 7.23 – 7.13 (m, 3H), 5.62 – 5.44 (m, 2H), 3.33 (d, *J* = 5.3 Hz, 2H), 2.02 (dt, *J* = 12.8, 6.7 Hz, 2H), 1.43 – 1.20 (m, 6H), 0.88 (t, *J* = 6.7 Hz, 3H).

2.4.3 *General Procedure for Allylic Imine Formation*

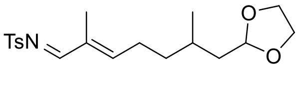
General procedure A: A flame-dried borosilicate glass vial equipped with a magnetic stir bar was charged with $SePPh_3$ (0.03 mmol, 0.15 equiv.), sulfonamide (0.6 mmol, 3 equiv.), and alkene (0.2 mmol, 1.0 equiv.). The vial was thoroughly flushed with nitrogen and capped with a Teflon-lined screw cap. Dry dichloromethane (1 mL, 0.2 M) was added, followed by iodobenzene diacetate (0.6 mmol, 3 equiv). The solution was stirred at the specified temperature and the reaction was monitored by TLC. Upon completion, the solvent was removed under reduced pressure to afford the crude reaction product, which was then purified by column chromatography.

General procedure B: A flame-dried borosilicate glass vial equipped with a magnetic stir bar was charged with $SePPh_3$ (0.03 mmol, 0.15 equiv.), sulfonamide (0.6 mmol, 3 equiv.), and alkene (0.2 mmol, 1.0 equiv.). The vial was thoroughly flushed with nitrogen and capped with a Teflon-lined screw cap. Dry d_2-chloroform (1 mL, 0.2 M) was added, followed by iodobenzene diacetate (0.6 mmol, 3 equiv). The solution was stirred until it became homogenous at which point the sample was transferred to an NMR tube. The reaction was monitored by ^1H NMR spectroscopy. Upon completion, the solvent was removed under reduced pressure to afford the crude reaction product, which was then purified by column chromatography.

2.4.4 *Characterization of Products*

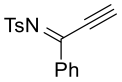


4a. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white solid (32 mg, 64%). ^1H NMR (300 MHz, $CDCl_3$) δ 9.16 (s, 1H), 7.83 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H), 2.15 (d, *J* = 0.7 Hz, 3H), 2.01 (s, 3H), 1.86 (s, 3H).



4b. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a clear film (56 mg, 76%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.83 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 6.52 (t, *J* = 7.3 Hz, 1H), 4.89 (t, *J* = 5.0 Hz, 1H), 4.02 – 3.91 (m, 2H), 3.87 – 3.77 (m, 2H), 2.42 (s, 3H), 2.40 – 2.30

(m, 2H), 1.84 (s, 3H), 1.77 – 1.60 (m, 2H), 1.60 – 1.50 (m, 2H), 1.35 (dt, *J* = 14.0, 8.0 Hz, 1H), 0.98 (d, *J* = 6.6 Hz, 3H).



4r. Prepared according to general procedure A and purified by silica gel chromatography (90:10 to 80:20, hexanes/ethyl acetate) to afford the product as a white film (42 mg, 74%). ^{1}H NMR (300 MHz, CDCl3) δ 8.14 (d, J = 8.0 Hz, 2H), 7.94 (d, J = 8.2 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.7 Hz, 2H), 7.35 (d, J = 8.2 Hz, 2H), 4.28 (s, 1H).

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Chapter 3. SELENIUM CATALYZED C-H ALLYLIC AMINATION USING CARBAMATES AND TRIFLUOROACETAMIDE

Section 1: INTRODUCTION

Allylic amines are highly valuable synthetic targets. These important structural motifs can be found in numerous drug candidates including oryzoxymycin, terbinafine, and flunarizine (Figure 3.1A).[1] Furthermore, manipulation of the amine and alkene moieties makes these substrates indispensable as synthetic intermediates for organic chemists (Figure 3.1B).

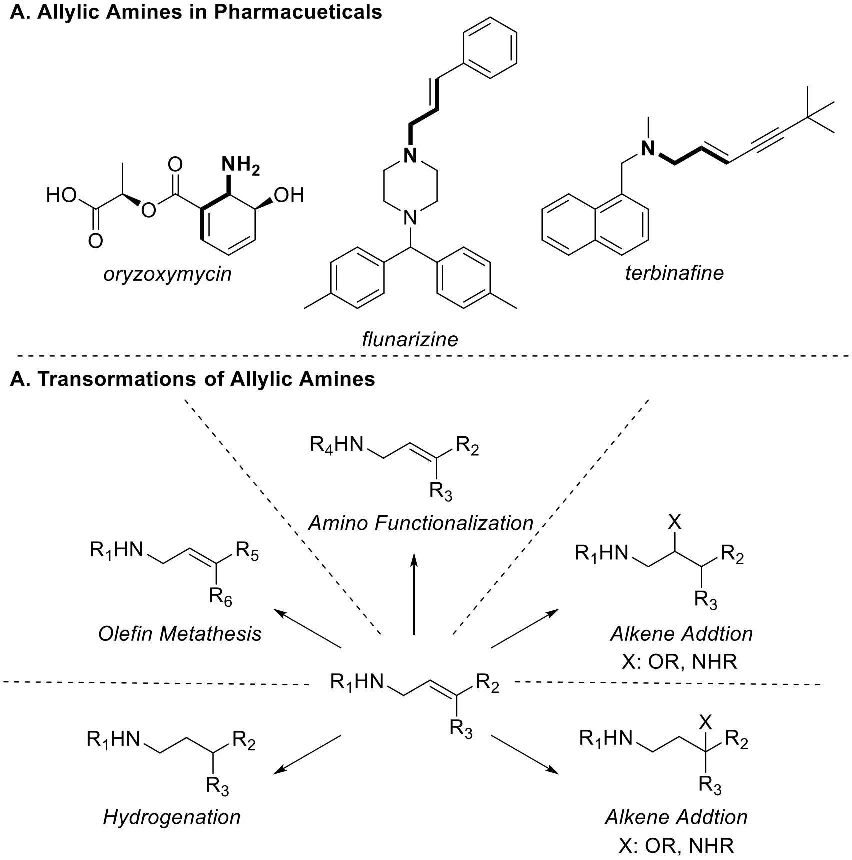


Figure 3.1. Utility of Allylic Amines in Drug Discovery

The most direct route for the synthesis of allylic amines is through the allylic C-H activation of alkenes.[2] Methods utilizing this route facilitate the direct replacement of an allylic hydrogen with a nitrogen nucleophile without having to pre-functionalize the starting alkene. These methods are particularly attractive since they reduce the number of steps required to generate the final products. However, if the target molecule contains the free amine, the nitrogen nucleophiles must be deprotected after addition. Beyond the important role organic carbamates play in medicinal chemistry and drug discovery[3], carbamates are highly valued for their ease of deprotection.[4] Furthermore, this class of nucleophiles offers an opportunity to selectively incorporate a masked free amine during the late stages of synthesis for target prodrugs.[3b]

While significant progress has been made in this area for mono-substituted alkenes[5] more highly substituted alkenes have proven problematic.[6] Furthermore, despite these advances, these methods cannot directly couple with carbamate nucleophiles and being limited to using N-sulfinyl carbamates. One method, developed by Xu and coworkers, has been successfully employed for an allylic C-H amination reaction with carbamate nucleophiles for tri- and tetra-substituted alkenes (Figure 3.2A).[7] While this transformation marked a significant advance, its application is limited to intramolecular reactions and must use N-aryl carbamates. Furthermore, this reaction results in alkene transposition which adds additional complications for total syntheses. To our knowledge, there is no direct method for catalytic C-H amination using carbamate nucleophiles. Furthermore, we are unaware of any method for catalytic intermolecular C-H amination for highly substituted alkenes using any carbamate containing nucleophile.

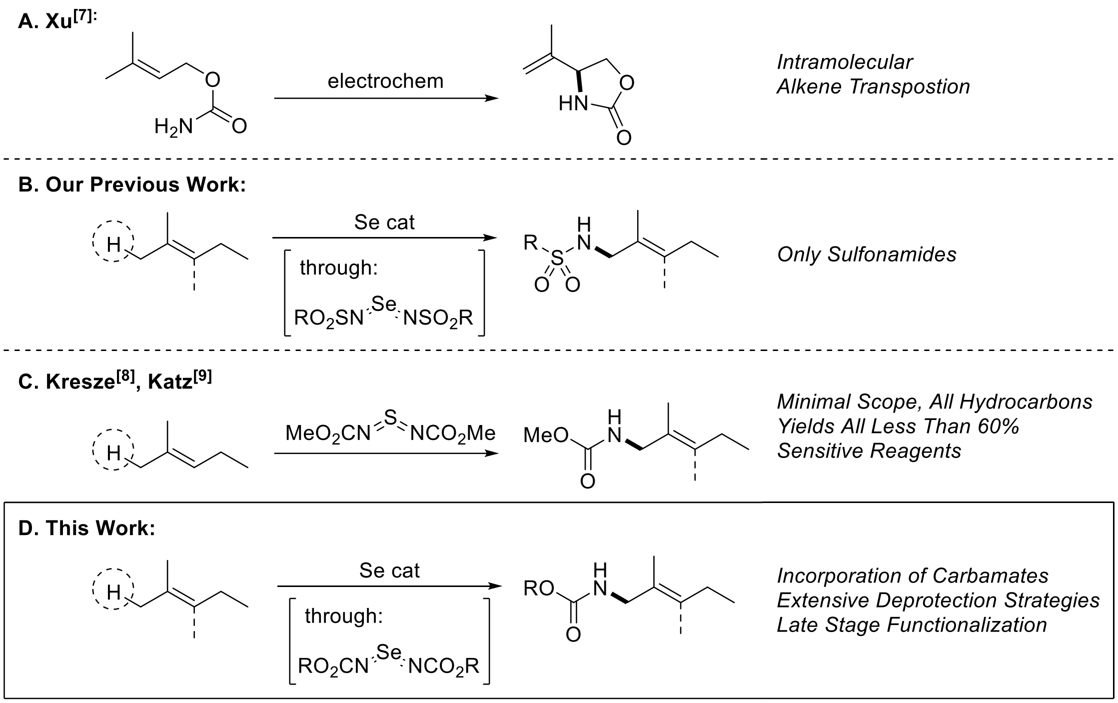


Figure 3.2. Previous Attempts for C-H Allylic Amination for Highly Substituted Alkenes

We previously disclosed our broadly applicable C-H allylic amination protocol with sulfonamides using catalytic selenium (Chapter 1, Figure 3.2B). This protocol was shown to work for more highly substituted alkenes, with amination occurring exclusively on the more substituted side of the alkene. We proposed that this reaction proceeded through the generation of a selenium bis(imido) species formed using the selenium catalyst, the sulfonamide, and the oxidant. We hoped that we could expand upon this work using carbamates as coupling partners (Figure 3.2D). Unfortunately, to achieve this highly desirable reaction, we would have to go through the unprecedented step of generating the selenium bis(imido) species using carbamates.

This approach of using chalcogen based imido carbamates for allylic amination has already been demonstrated stoichiometrically using sulfur in two separate reports (Figure 3.2C). The first was developed in 1983 by Kresze and coworkers which utilized the sulfur diimide synthesized from methyl carbamate for the stoichiometric allylic C-H activation of trisubstituted alkenes.[8] Unfortunately, only a handful of alkenes were shown to react with yields typically around 50%.

Furthermore, the synthesis of the sulfur bis(imido) species required the use of chlorine gas. Later, in 1994, Katz and coworkers improved the synthesis of the sulfur bis(imido) species by generating it from the respective N-sulfinylcarbamate. Unfortunately, the utility of this method was only demonstrated on 2-methyl-2-butene in a 47% yield.[9] The reliance on stoichiometric quantities of sensitive reagents, poor yields, and lack of demonstrated functional group tolerance has prevented the wide adaptation of these methods.

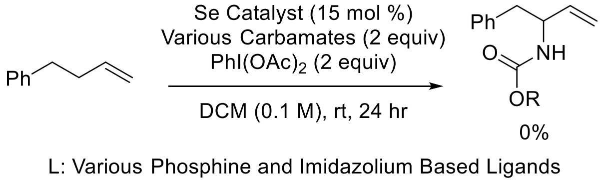
We hoped that by generating the selenium bis(imido) species *in situ*, we might be able to overcome the limitations of the previous allylic amination reports allowing for the catalytic, intermolecular incorporation of carbamates for a wide array of highly substituted alkenes in decent yields (Figure 3.2D). Not only would this complement our previous allylic amination protocol, but we would hopefully provide unfettered access to an exceedingly valuable class of highly substituted allylic amine building blocks.[10]

Section 2: RESULTS AND DISCUSSION

3.2.1 *Optimization for Trisubstituted Alkenes*

Early attempts at incorporating carbamates using the selenium catalysts we developed for our allylic amination protocol using sulfonamides as nitrogen sources proved unsuccessful. Treating 4-phenyl-1-butene with an extensive combination of selenium catalysts and carbamate sources resulted in no desired product formation (Scheme 3.1).

Scheme 3.1. *Initial Attempt at Using Carbamates as Nucleophiles*



Reexamining the start of our proposed mechanism for selenium catalyzed allylic amination, we hypothesized two potential reasons for this failure (Figure 3.3). First, the iminoiodinane and selenium bis(imido) species generated from carbamates[11] are likely more susceptible to Hoffman rearrangements than their sulfonamide[12] counterparts. This could result in decomposition of the amine source before oxidation of the selenium catalyst/alkene could occur. We envisioned fine tuning of the ligand might allow for improved reactivity/stability for the selenium bis(imido) species to hopefully overcome this potential issue.

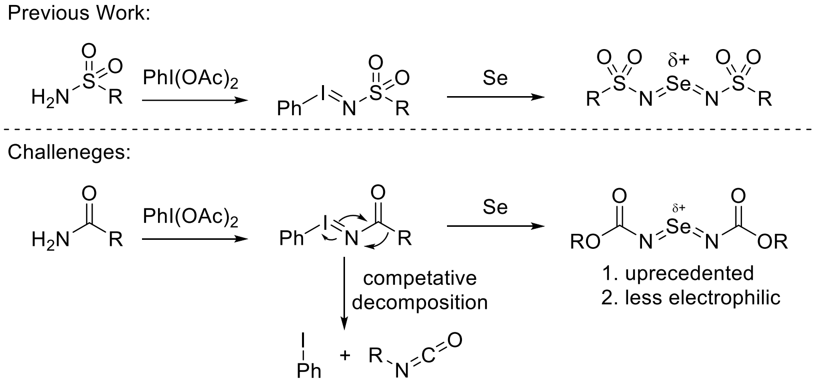
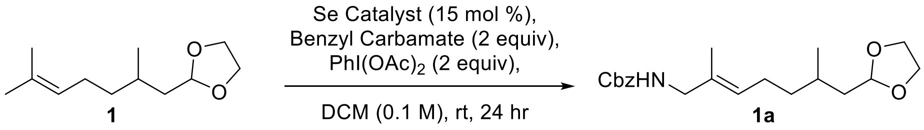


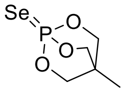
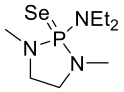
Figure 3.3. Obstacles to Overcome for Allylic Amination with Carbamates Using Selenium

Second, if the selenium bis(imido) species could be formed from carbamates, it would likely be significantly less electrophilic than the one generated from sulfonamides. This would result in a reduced ability to perform the initial ene reaction with electron poor substrates preventing the reaction from proceeding. We hoped that utilizing more electron rich alkenes in concert with proper ligand choice would overcome these challenges and lead to a successful reaction.

We began our optimization by screening a variety of phosphine selenide catalysts on a trisubstituted terpene derived alkene using benzyl carbamate as our nucleophile (Table 3.1).

Table 3.1. Screen of Phopshine Ligands

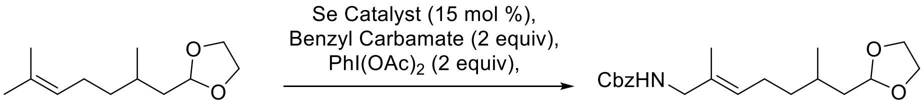


Entry	Catalyst	%Yield[a]
1	SePCy$_3$	19
2	SePPh$_3$	8
3	SePNp$_3$	17
4		6
5	SeP(OPh)$_3$	0
6		11

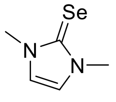
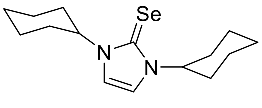
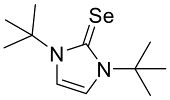
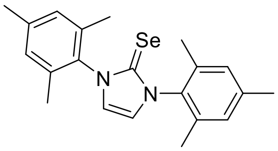
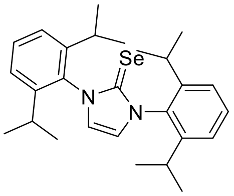
[a] Yield determined by HNMR with dinitrobenzne as IS

Pleasingly, we observed 19% conversion to the desired allylic carbamate utilizing the trialkyl phosphine catalyst from our previous report (Table 3.1, entry 1). Unfortunately, other phosphine ligands resulted in even less product formation (Table 3.1, entries 2-6). We then turned our attention to the NHC based ligands (Table 3.2).

Table 3.2. Screen of NHC Ligands



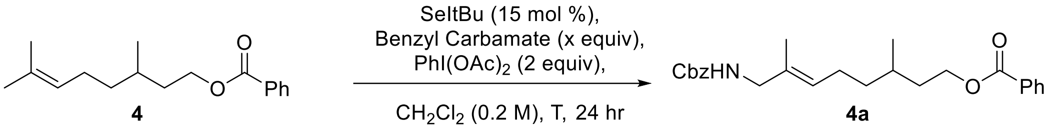
1 → **1a**

Entry	Catalyst	%Yield[a]
1	 "SeIMe"	27
2	 "SeICy"	>5
3	 "SeItBu"	48
4	 "SeIMes"	0
5	 "SeIPr"	17

[a]Yield determined by HNMR with dinitrobenzne as IS

The methyl based NHC ligand (IMe) afforded 27% yield of the desired product (Table 3.2, entry 1). A somewhat bulkier alkyl based NHC ligand, ICy, resulted in trace product formation (Table 3.2, entry 2). However, the bulkiest alkyl ligand (ItBu) resulted in a 48% yield of the desired allylic carbamate (Table 3.2, entry 3). The aryl NHC ligands resulted in less product formation than their alkyl counterparts (Table 3.2, entries 4 and 5). Since the ItBu catalyst provided the desired product in the greatest yield, it was chosen to test the effects of changing the reaction conditions (Table 3.3).

Table 3.3. Temperature and Equivalents Screen for Benzyl Carbamate

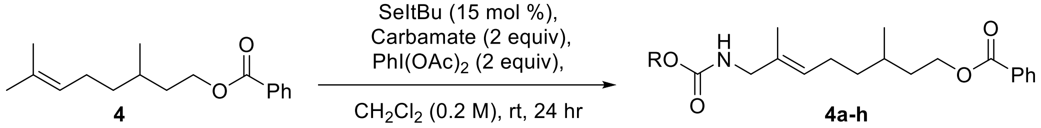


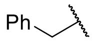
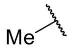
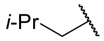
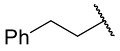
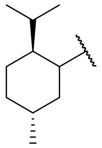
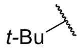
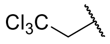
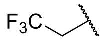
Entry	Temperature (°C)	x equiv	%Yield[a]
1	rt	2	50
2	35	2	63
3	rt	4	74
4	35	4	70
5	45	4	49

[a] Yield determined by HNMR with dinitrobenzne as IS

First, we wanted to see what effect increasing the reaction temperature would have on the reaction outcome. Heating the reaction to 35 ºC resulted in an improved 63% yield of the desired product (Table 3.3, entry 2). We also examined the effects of increasing the amount of nucleophile used. Going from two to four equivalents of benzyl carbamate resulted in an improved 74% yield of the desired product (Table 3.3, entry 3). With four equivalents of nucleophile in the reaction mixture, we observed no improvement when increasing the temperature to 35 ºC (Table 3.3, entry 4) and a significant reduction in yield when heating the reaction mixture to 45 ºC (Table 3.3, entry 5). Having established that both increasing the temperature and increasing the nucleophile amount could improve reactivity, we turned to examine what impact the nature of the carbamate has on the reaction outcome (Table 3.4).

Table 3.4. Carbamate Screen



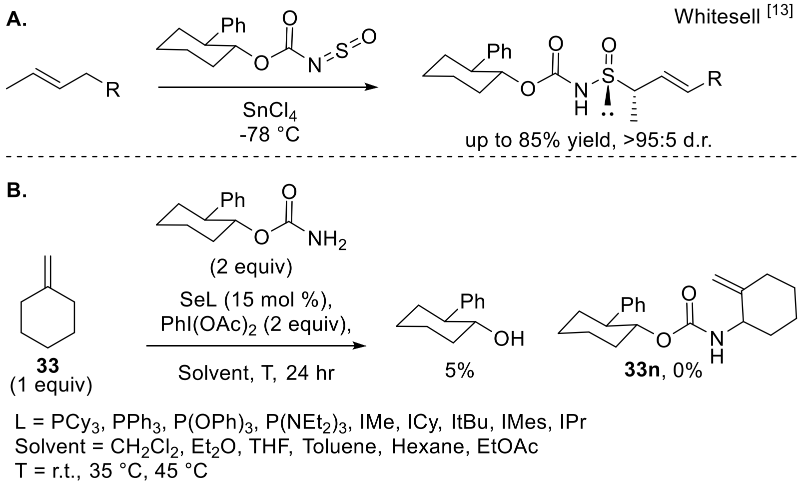
Entry	R	Starting Material (%)	%Yield[a]
1		0	**4a**, 52
2		0	**4b**, 76
3		0	**4c**, 73
4		0	**4d**, 72
5		0	**4e**, 77
6		49	**4f**, 35
7		85	**4g**, 11
8		81	**4h**, 10

[a] Yield determined by HNMR with dinitrobenzne as IS

Using only two equivalents of nucleophile at room temperature, the benzyl carbamate resulted again resulted in roughly 50% yield of the desired allylic carbamate (Table 3.4, entry 1). Switching to alkyl carbamates under these conditions resulted in a significant improvement in product formation (Table 3.4, entries 2-5). Unfortunately, the synthetically valuable t-butyl carbamate proved less reactive perhaps due to the acidic nature of these reaction conditions. Additionally, the trichloro and trifluoro ethyl carbamates resulted in minimal product formation. Numerous attempts were made to improve these yields including screening various catalysts, additives, and reaction conditions. Unfortunately, none of these efforts improved the yields for these carbamates.

One promising result from this carbamate screen was the success of the chiral methyl carbamate in this reaction (Table 3.4, entry 5). Given the success of this nucleophile, we wondered whether we might achieve some diastereoselectivity during our reaction by using a chiral carbamate. This would enable us to control the stereochemistry of the newly generated carbon-nitrogen bond. Examination of the literature revealed one promising candidate to be the carbamate generated from trans-2-phenyl-cyclohexanol. Whitesell and coworkers used the N-sulfinyl version of this carbamate to achieve diastereoselectivity (> 95:5 d.r.) during ene reactions with various alkenes (Scheme 3.2A).[13] Since the first step in our proposed mechanism is an ene reaction, we hoped that by using the carbamate derived from trans-2-phenyl-cyclohexanol we might also obtain diastereoselectivity.

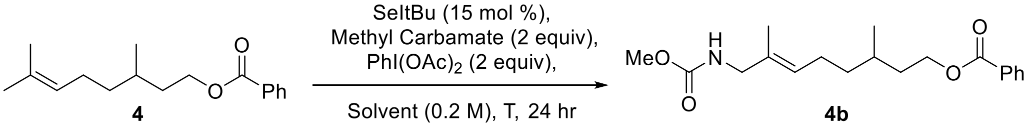
Scheme 3.2. *Initial Attempt at Enantioselectivity*



Unfortunately, despite screening an extensive variety of catalysts, solvents, and reaction conditions, none of the desired product was formed (Scheme 3.2B). Instead, trace amounts of 2-phenyl-cyclohexanol were observed for every reaction. It is likely that the generation of this alcohol through decomposition of the carbamate inhibited the desired reaction. However, because the chiral menthyl carbamate provided the desired product in high yields, this area is still very promising. Further work must be done to ensure the stability of the 2-phenyl-cyclohexanol carbamate and/or to screen other chiral carbamates.

Given the significant improvement obtained by using alkyl carbamates (needing only 2 equivalents and at room temperature), we decided to use methyl carbamate as the nucleophile to screen the effects of solvents on this reaction (Table 3.5).

Table 3.5. Solvent Screen



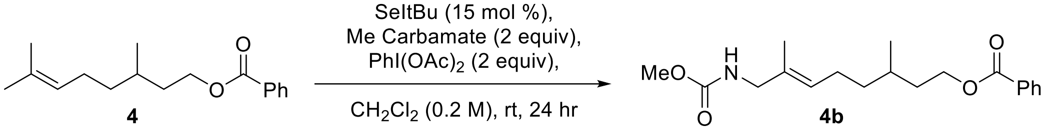
Entry	Solvent	Starting Material (%)	%Yield[a]
1	CH_2Cl_2	0	71
2	EtOAc	60	9
3	MeCN	22	23
4	Et_2O	99	0
5	THF	71	0
6	Toluene	20	56

[a] Yield determined by HNMR with dinitrobenzne as IS

We observed the best reactivity with our dichloromethane (Table 3.5, entry 1). More polar solvents such as ethyl acetate or acetonitrile resulted in a slower reaction with a smaller potential product formation (Table 3.5, entries 2 and 3). Ether solvents resulted in no desired product formation and in the case of THF, only resulted in starting material decomposition (Table 3.5, entries 4 and 5). Interestingly, toluene resulted in significant product formation with minimal loss of starting material (Table 3.5, entry 6). However, the reaction in toluene was significantly slower, so dichloromethane was selected for further investigations.

In our final attempt to improve the reaction, we turned our attention to manipulating the reaction conditions using methyl carbamate as the nucleophile (Table 3.6).

Table 3.6. Temperature and Equivalents Screen for Methyl Carbamate



Entry	Variation	%Yield[a]
1	none	69
2	35 °C	61
3	45 °C	37
4	4 equiv of carbamate	78
5	25 mol % catalyst	71

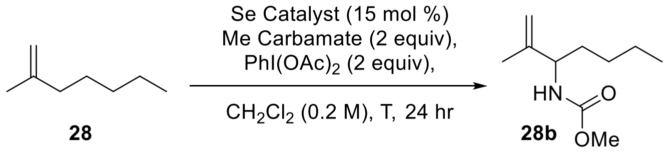
[a]Yield determined by HNMR with dinitrobenzne as IS

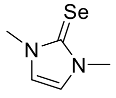
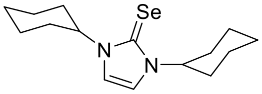
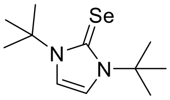
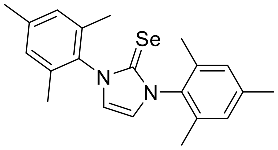
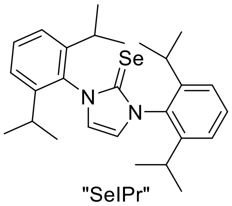
Increasing the reaction temperature to 35 ºC was again found to reduce the desired product formation to 61% (Table 3.6, entry 2). A further reduction in yield to 37% was observed when increasing the reaction temperature to 45 ºC (Table 3.6, entry 3). Increasing the amount of nucleophile from two to four equivalents resulted in an improvement in reaction yield to 78% (Table 3.6, entry 4). Finally, increasing the catalyst loading from 15 to 25 mol % was found to have little effect on reaction outcome (Table 3.6, entry 5).

3.2.2 *Optimization for Disubstituted Alkenes*

Having obtained the desired products for trisubstituted alkenes in significant yields, we turned our attention toward using 1,1-disubstituted alkenes as substrates. We anticipated that these substrates would be similarly reactive to the trisubstituted alkenes. Unfortunately, our initial attempt at subjecting a 1,1-disubstituted alkene to these reaction conditions resulted in only 57% conversion to product. Since we had previously seen such a strong response to catalyst for different substrate classes during the selenium catalyzed allylic amination of alkenes using sulfonamides as nucleophiles (see: Table 1.2 and Table 1.4), we decided to begin our investigation there (Table 3.7).

Table 3.7. Initial Screen of Ligands for Disubstituted Alkenes

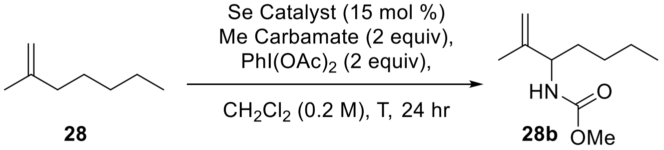


Entry	Catalyst	%Yield[a]
1	$SePCy_3$	33
2	 "SeIMe"	31
3	 "SeICy"	0
4	 "SeItBu"	57
5	 "SeIMes"	0
6	 "SeIPr"	18

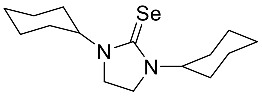
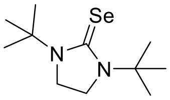
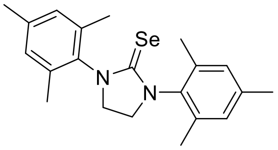
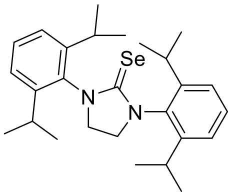
[a] Yield determined by HNMR with dinitrobenzne as IS

Using either the tricyclohexylphosphine (Table 3.7, entry 1) or the IMe (Table 3.7, entry 2) ligands which proved so successful in our sulfonamide allylic amination method resulted in reduced yields of the desired product compared to the ItBu (Table 3.7, entry 4). Other NHC based ligands proved even less effective in this reaction (Table 3.7, entries 3, 5, and 6). In hopes that altering the electronic nature of the NHC ligands might result in improved reactivity of the catalyst, a variety of saturated NHC containing selenide catalysts were synthesized and tested (Table 3.8).

Table 3.8. Screen of Saturated NHC Ligands



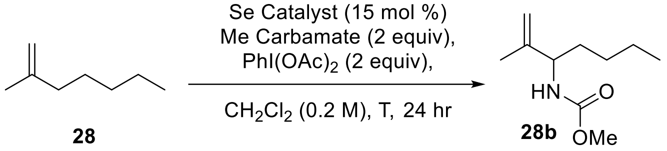
28 **28b**

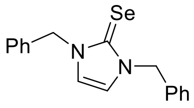
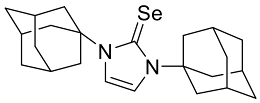
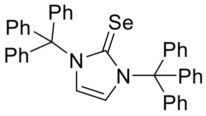
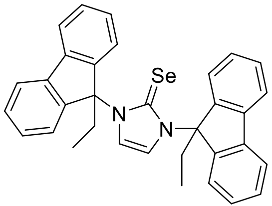
Entry	Catalyst	%Yield[a]
1	 "SeSICy"	17
2	 "SeSItBu"	6
3	 "SeSIMes"	23
4	 "SeSIPr"	0

[a]Yield determined by HNMR with dinitrobenzne as IS

Unfortunately, while a significant difference was observed, no improvement in yield was uncovered. Interestingly, the saturated catalysts SICy and SIMes (Table 3.8, entries 1 and 3) showed improved reactivity compared to their unsaturated counterparts ICy and IMes which had little reactivity before (Table 3.7, entries 3 and 5). In a seemingly opposite trend, the unsaturated catalysts which proved more reactive previously, ItBu and IPr (Table 3.7, entries 4 and 6) showed a significant drop off when converted to their saturated forms, SItBu and SIPr (Table 3.8, entries 2 and 4). Given the observation that the bulkiest unsaturated NHC ligand afforded the best reactivity, we decided to synthesize a variety of other potentially bulkier unsaturated NHC selenides (Table 3.9).

Table 3.9. Screen of Bulky Unsaturated NHC Ligands



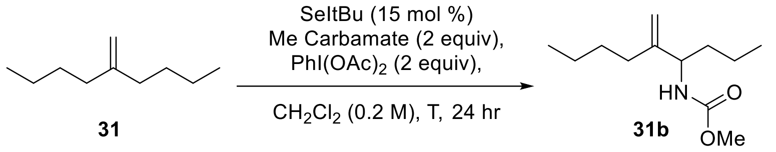
Entry	Catalyst	%Yield^a
1	 "SeIBn"	52
2	 "SeIAd"	54
3	 "SeITrit"	38
4	 "SeIBulk"	57

[a] Yield determined by HNMR with dinitrobenzne as IS

The IBn, IAd, and IBulk ligands all proved to be equally effective to ItBu at generating the desired allylic carbamates (Table 3.9, entries 1,2 and 4). The trityl based NHC, ITrit, afforded the product in slightly reduced yields (Table 3.9, entry 3). Due to the difficulty in synthesis and lack of yield improvement for these new catalysts, SeItBu was determined to be the optimal catalyst.

Since we did not observe an improvement from the catalyst, we decided to examine the reaction conditions for 1,1-disubstituted alkenes (Table 3.10).

Table 3.10. Variation of Reaction Conditions for Disubstituted Alkenes



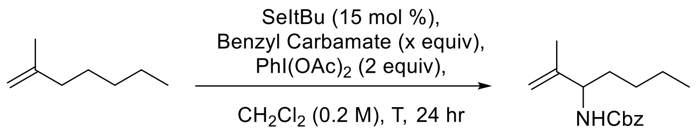
Entry	Change	%Yield[a]
1	none	56
2	10 mol % catalyst	39
3	5 mol % catalyst	9
4	2x concentration	55
5	3 equiv of carbamate	62
6	run under air	57
7	35 °C	70
8	45 °C	70

[a] Yield determined by HNMR with dinitrobenzne as IS

Doubling the concentration of the reaction resulted in no change in reactivity (Table 3.10, entry 4). Increasing the amount of carbamate from two to three equivalents resulted in a slight improvement in yield (Table 3.10, entry 5). Elevating the temperature afforded the best results with reaction temperatures of either 35 ºC or 45 ºC resulting in 70% yield (Table 3.10, entries 7 and 8). Pleasingly, it was observed that the reaction could be run under air with no detriment to reaction outcome (Table 3.10, entry 6). The reaction was found to be rather sensitive to the catalyst loading with a reduction in yield noted when using a reduced 10 or 5 mol % catalyst, 39% and 9% respectively (Table 3.10, entries 2 and 3).

Having seemingly optimized the reaction for methyl carbamate, we turned our attention to benzyl carbamate as a nucleophile due to its improved synthetic utility (Table 3.11).

Table 3.11. Variation Screen for Disubstituted Alkenes with Benzyl Carbamate



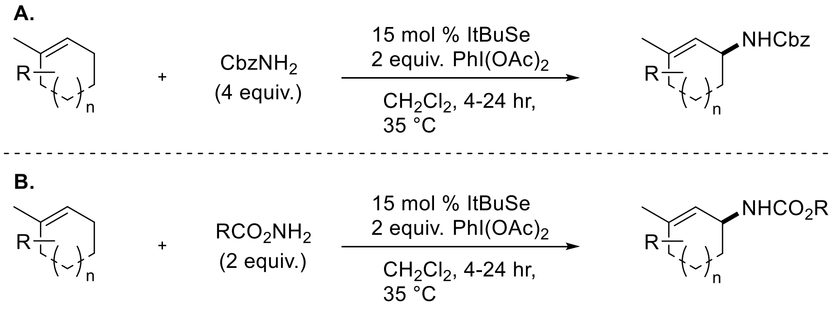
28 **28a**

Entry	Temperature (°C)	x equiv	%Yield[a]
1	rt	2	53
2	35	2	50
3	rt	4	75
4	35	4	80
5	45	4	72

[a]Yield determined by HNMR with dinitrobenzne as IS

Starting with two equivalents of benzyl carbamate resulted in comparable yields to methyl carbamate at room temperature (Table 3.11, entry 1). Unfortunately, for benzyl carbamate increasing the temperature had little effect on the reaction outcome (Table 3.11, entry 2). Pleasingly, increasing the amount of nucleophile used greatly improved the yield of the desired carbamate to 75% (Table 3.11, entry 3). Increasing the temperature to 35 ºC when using four equivalents of nucleophile resulted in a minor improvement in yield to 80% (Table 3.11, entry 4), with a minor reduction in yield to 72% when heating to 45 ºC (Table 3.11, entry 5).

Scheme 3.3. *Optimized Conditions for Trisubstituted Alkenes*

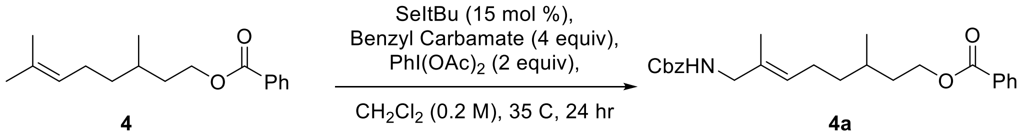


Given all of these results, we settled on two sets of reaction conditions for all substrates (Scheme 3.3). Using the highly valuable Cbz carbamate, we used 4 equivalents of the nucleophile at 35 **°**C since this provided the best yields for the broadest range of alkenes (Scheme 3.3 A). When using other carbamates, we ran the reaction with only two equivalents of nucleophile at 35 °C (Scheme 3.3 B).

3.2.3 *Challenges in Consistency*

During the optimization of these reactions, we observed some inconsistent results for some alkene substrates. Often, we noted a gradual decrease in reaction yields over time when using a newly synthesized alkene. For example, freshly prepared citronellol benzoate afforded the desired product in 74% yield under our optimized reaction conditions (Table 3.12, entry 1)

Table 3.12. Gradual Decrease in Desired Reaction Outcome



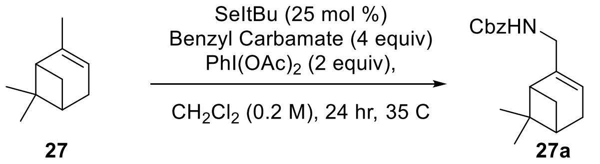
Entry	State of Alkene	%Yield
1	Freshly made	74
2	After two months	38
3	Chromatographed above	41
4	Freshly made again	71

[a]Yield determined by HNMR with dinitrobenzne as IS

Using the same source of alkene for further optimization over the course of two months eventually resulted in a diminished yield of 38% under the optimized conditions (Table 3.12, entry 2) despite ^{1}H NMR revealing no apparent impurity. Attempting to restore the original reactivity by purifying the alkene via column chromatography was typically unsuccessful (Table 3.12, entry 3). Instead, preparing fresh alkene was often required (Table 3.12, entry 4).

Another interesting observation was made when utilizing commercial reagents. Using the purchased reagents directly from the bottle often resulted in lower yields than anticipated. To circumvent this issue, commercial reagents were typically distilled but this often resulted in little improvement. For example, after distilling commercial alpha-pinene, the yield was only 26% (Table 3.13, entry 1).

Table 3.13. Gradual Decrease in Desired Reaction Outcome

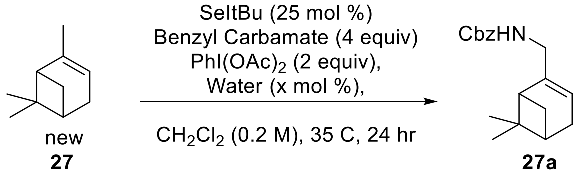


Entry	Source	%Yield
1	Distilled	26
2	Distilled over CaH	62

[a]Yield determined by HNMR with dinitrobenzne as IS

However, distilling the same source of alpha-pinene over calcium hydride resulted in a significantly improved 62% yield of the desired product (Table 3.13, entry 2). Together, these interesting observations led us to believe that this reaction may be highly sensitive to exogenous water. To test this hypothesis, the alpha-pinene distilled over calcium hydride was treated with various amounts of water (Table 3.14).

Table 3.14. Sensitivity of the Reaction to Water



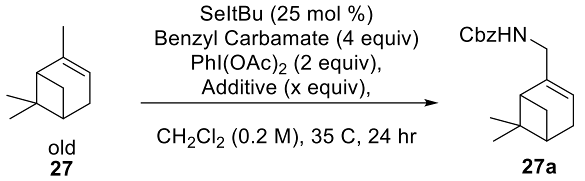
Entry	Water (x mol %)	%Yield
1	0	60
2	1	47
3	10	5
4	25	9
5	50	0

[a]Yield determined by HNMR with dinitrobenzne as IS

Without any additional water, the reaction resulted in a 60% yield of the desired product (Table 3.14, entry 1). Adding as little as 1 mol % of water resulted in a significant reduction of the desired product to 47% (Table 3.14, entry 2). The addition of only 10 mol % of water resulted in the nearly complete shutdown of the desired reactivity (Table 3.14, entry 3).

Having shown how deleterious the effects of water were, we decided to see if we could add a dehydrating reagent to the reaction in order to improve the yields for some of the commercial alkenes without having to distill them over calcium hydride in hopes that this same additive could be added across the board as a safeguard against low yields (Table 3.15).

Table 3.15. Dehydrating Agents as Additives



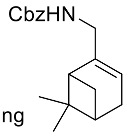
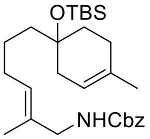
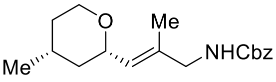
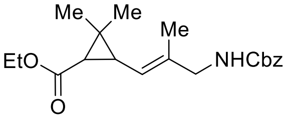
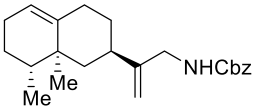
Entry	Additive	%Yield[a]
1	none	30
2	Molecular Sieves (100 mg)	4
3	CaH (0.2 equiv)	15
4	MgO (2 equiv)	2
5	CaO (2 equiv)	6
6	BaO (2 equiv)	0
7	PhCOOH (2 equiv)	3

[a] Yield determined by HNMR with dinitrobenzne as IS

Using the commercial alpha-pinene without any addition of dehydrating reagents resulted in a 30% yield of the desired allylic carbamate (Table 3.15, entry 1). Adding powdered molecular sieves to the reaction resulted in diminished formation of the desired product (Table 3.15, entry 2). Adding calcium hydride as a drying agent similarly resulted in diminished yields (Table 3.15, entry 3). Finally, testing a variety oxide bases as dehydrating agents also hurt the reaction outcome (Table 3.15, entries 4-6). Since the dehydrating bases were hurting the reaction, and because the oxide bases are known to sequester carboxylic acids, we decided to try the addition of benzoic acid to see if that might improve the yield of the desired product (Table 3.15, entry 7). Unfortunately, like the base additives, the benzoic acid was found to nearly shut down the desired reactivity. While we were unable to find an additive that could instantly improve the reaction outcome, distilling alkenes over calcium hydride was observed to improve the yields for a large number of previously difficult substrates.

One additional challenge to overcome was to improve the yield for some of the more complicated substrates. While a variety of catalyst and additive screens were tried, nothing seemed to improve the yields for some substrates. Luckily, we found that by increasing the catalyst loading from 15 mol % to 25 mol %, a variety of underperforming substrates began providing the desired products in sufficient yields (Table 3.16).

Table 3.16. Effect of Increasing Catalyst Loading for Troubling Substrates

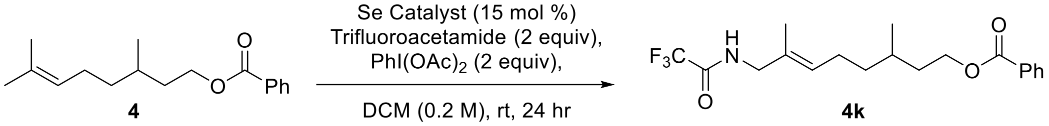
Catalyst Loading					
	27a	**26a**	**25a**	**24a**	**35a**
15 mol %	28%	27%	30%	30%	16%
25 mol %	74%	60%	75%	69%	51%

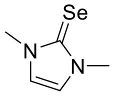
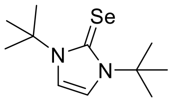
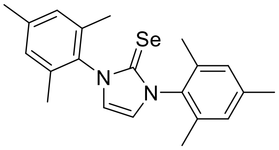
This simple tweak to reaction conditions facilitated amination of several synthetically interesting substrates.

3.2.4 *Optimization for Trifluoroacetamide*

In addition to using carbamates as nucleophiles, we hoped that we may be able to use amides under these reaction conditions. We decided to start this investigation with trifluoroacetamide. As one of the most electron poor amides, we hoped that this nucleophile would result in a more highly electrophilic bis(imido) selenide. We began this investigation with a screen of catalysts (Table 3.17).

Table 3.17. Catalyst Screen Using Trifluoroacetamide for Allylic Amination

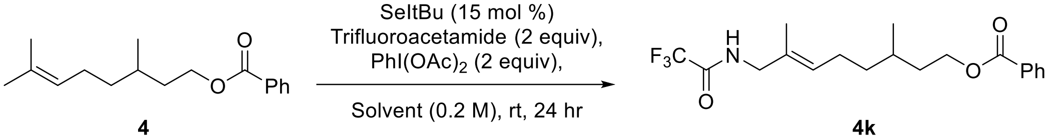


Entry	Catalyst	Starting Material (%)^{a}	%Yield^{a}
1	$SePPh_3$	59	7
2	$SePCy_3$	50	4
3	$SeP(OPh)_3$	47	12
4	$SeP(OEt)_3$	48	8
5	$SeP(NEt_2)_3$	67	6
6	 "SeIMe"	44	13
7	 "SeItBu"	39	14
8	 "SeIMes"	54	2

^{a}Yield determined using 1,3-dinitrobenzene as an internal standard

Significant amounts of starting material were recovered for all catalysts screened. Generally, slightly improved yields were observed for the alkyl NHC based catalysts (Table 3.17, entries 6 and 7) over the phosphine selenides (Table 3.17, entries 1-5). The aryl NHC catalyst was seen to be minimally reactive (Table 3.17, entry 8). Since the ItBu catalyst was found to be one of the most reactive and was the best catalyst for the reaction of carbamates, it was selected for further screening. We next examined the solvent effects for this reaction (Table 3.18).

Table 3.18. Solvent Screen Using Trifluoroacetamide for Allylic Amination

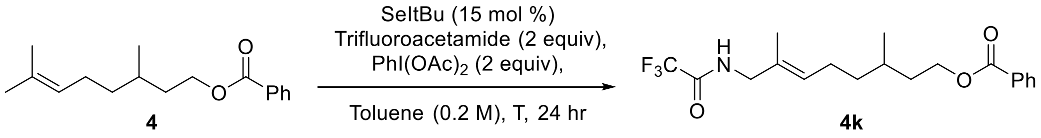


Entry	Solvent	Starting Material (%)[a]	%Yield[a]
1	CH_2Cl_2	40	16
2	EtOAc	28	0
3	MeCN	45	7
4	Et_2O	50	3
5	THF	34	9
6	Toluene	18	38

[a]Yield determined using 1,3-dinitrobenzene as an internal standard

Dichloromethane provided the desired product in 16% yield (Table 3.18, entry 1). More polar solvents such as ethyl acetate (Table 3.18, entry 2) and acetonitrile (Table 3.18, entry 3) were found to hinder the desired reaction. Similarly, ether solvents resulted in little product formation and significant starting material decomposition (Table 3.18, entries 4 and 5). Pleasingly, toluene was found to improve the desired reactivity with a 38% yield of the desired product along with 18% remaining starting material (Table 3.18, entry 6). In an effort to improve the conversion of the starting material to the product, a screen of variations was performed on this reaction using toluene as the solvent (Table 3.19).

Table 3.19. Screen of Reaction Conditions Using Trifluoroacetamide for Allylic Amination

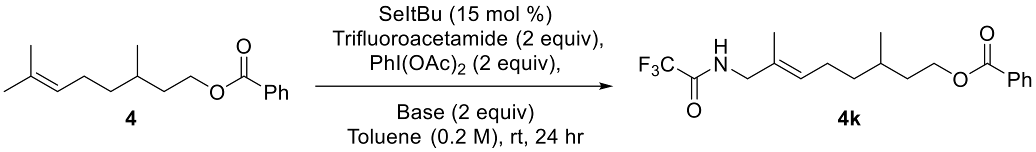


Entry	Difference	Starting Material (%)[a]	%Yield[a]
1	control	24	37
2	3 equiv of nucleophile	31	28
3	40 °C	9	32
4	2 equiv $MgSO_4$	48	2
5	100 mg Molecular Sieves	52	0
6	2 equiv CaO	79	0
7	2 equiv Li_2CO_3	10	53

[a] Yield determined using 1,3-dinitrobenzene as an internal standard

With no change, 37% of the desired product was formed along with a 24% recovery of the starting alkene (Table 3.19, entry 1). Increasing the amount of nucleophile from two to three equivalents was found to have little effect on reaction outcome (Table 3.19, entry 2). Increasing the reaction temperature to 40 ºC resulted in no additional formation of formation but a reduction in the recovery of the starting alkene (Table 3.19, entry 3). We next turned our attention to additives. Realizing the negative impact of water on this chemistry, a few drying agents were screened (Table 3.19, entries 4 and 5). Unfortunately, these seemed to shut down the desired reactivity yet still resulted in starting material decomposition. We then turned toward some basic additives. The addition of calcium oxide was found to completely shut down the desired reaction yet did improve the starting material recovery (Table 3.19, entry 6). Pleasingly, the addition of lithium carbonate was found to greatly enhance the yield of the desired product to 53% with only 10% of starting material remaining (Table 3.19, entry 7). Because of the marked improvement from the base additive, an extensive base screen was performed (Table 3.20).

Table 3.20. Extensive Base Screen Using Trifluoroacetamide for Allylic Amination

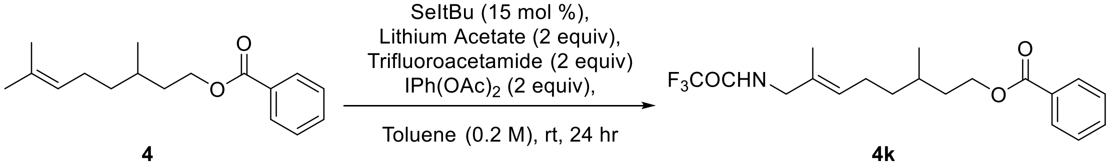


Entry	Base	Starting Material (%)[a]	%Yield[a]
1	Li_2CO_3	6	57
2	Na_2CO_3	81	7
3	K_2CO_3	87	0
4	NaOMe	87	0
5	KOtBu	90	0
6	NaOtBu	94	0
7	$NaHCO_3$	32	33
8	$KHCO_3$	94	0
9	LiOAc	16	65
10	NaOAc	34	36
11	KOAc	78	0
12	CsOAc	98	0
13	LiOAc • H_2O	94	0
14	LiOTFA	36	0

[a] Yield determined using 1,3-dinitrobenzene as an internal standard

Lithium carbonate was found to give the desired product in 57% yield with 6% of starting material remaining (Table 3.20, entry 1). The similar sodium and potassium carbonate bases were found to shut down the desired reactivity (Table 3.20, entries 2 and 3). A variety of alkoxide bases were also screened (Table 3.20, entries 4 - 6). In every case, the desired reaction was suppressed, and nearly quantitative starting material was recovered. Next, we screened some bicarbonate bases. Potassium bicarbonate was found to shut down the desired reaction (Table 3.20, entry 8). Interestingly, sodium bicarbonate did give the desired product in a moderate 33% yield with a starting material recovery of 32%. We then turned our attention to acetate bases. Lithium acetate improved the desired reactivity affording 65% of the desired product along with 16% of the starting material (Table 3.20, entry 9). Sodium acetate performed similarly to sodium bicarbonate with a 36% yield of the desired product and 34% of the starting material remaining (Table 3.20, entry 10). Other acetate bases were found to shut down the desired reaction (Table 3.20, entries 11 and 12). Because lithium acetate provided the best reactivity for this reaction, a couple variations were also screened. Lithium acetate monohydrate was used (Table 3.20, entry 13). This was found to stop the desired reaction, again highlighting the deleterious impact of water on this reaction. The less basic lithium trifluoroacetate was also tested. This resulted in significant decomposition of the starting material with no desired product formation (Table 3.20, entry 14). To confirm that the optimal conditions were found, we screened some variations of these conditions (Table 3.21).

Table 3.21. Screen of Reaction Conditions with Trifluoroacetamide and Lithium Acetate



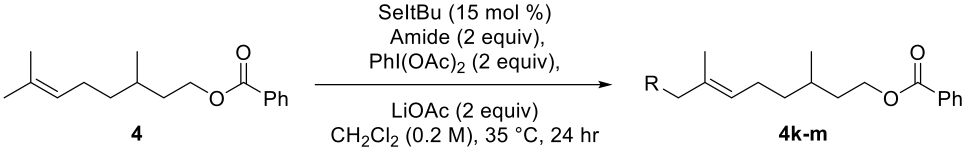
4 **4k**

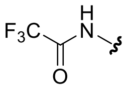
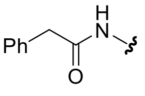
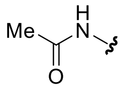
Entry	Variation	%Yield[a]
1	none	64
2	no LiOAc	31
3	CH_2Cl_2 as solvent	66
4	CH_2Cl_2 as solvent, no LiOAc	19
5	SeIMe as catalyst	45
6	$SePCy_3$ as catalyst	58

[a]Yield determined by NMR using 1,3-dinitrobenzene as an internal standard

Standard conditions resulted in 64% yield of the desired product (Table 3.21, entry 1). Switching solvents to dichloromethane provided a comparable yield of the desired product (Table 3.21, entry 3). Leaving out the base from either solvent resulted in significantly diminished yields (Table 3.21, entries 2 and 4). Finally, switching to either SeIMe or $SePCy_3$ each resulted in reduced product formation (Table 3.21, entries 5 and 6). While toluene and dichloromethane resulted in similar product yields, we found that the amination reactions occurred faster in dichloromethane for many substrates (24 hours in CH_2Cl_2 versus 48-72 hours in toluene) so it was selected as the optimal solvent. With these optimized conditions in hand, a few amides were screened as coupling partners (Table 3.22).

Table 3.22. Survey of Amide Coupling Partners for Allylic Amination



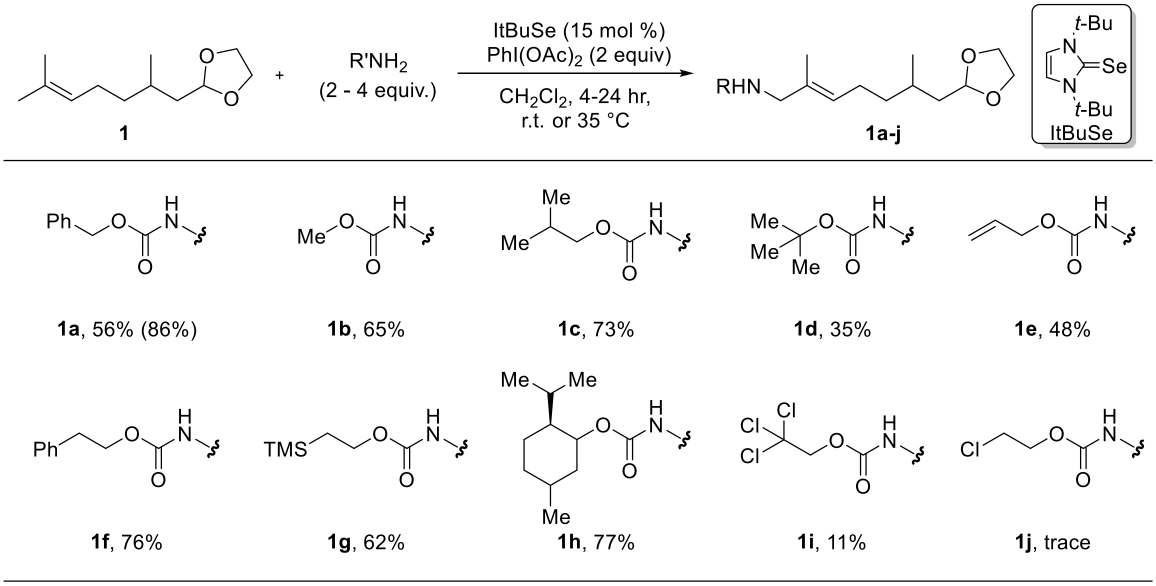
		
66%	0%	0%

Unfortunately, only trifluoroacetamide was found to give the desired product. Both benzamide and acetamide resulted in no desired product formation along with quantitative recovery of the starting alkene.

3.2.5 *Scope*

Having optimized the reaction conditions, we turned our attention to the scope. First, we examined the compatibility with various carbamates. All of the previously examined carbamates worked well under the fully optimized conditions including benzyl (**1a**), methyl (**1b**), phenethyl (**1f**), and menethyl (**1h**) carbamates.

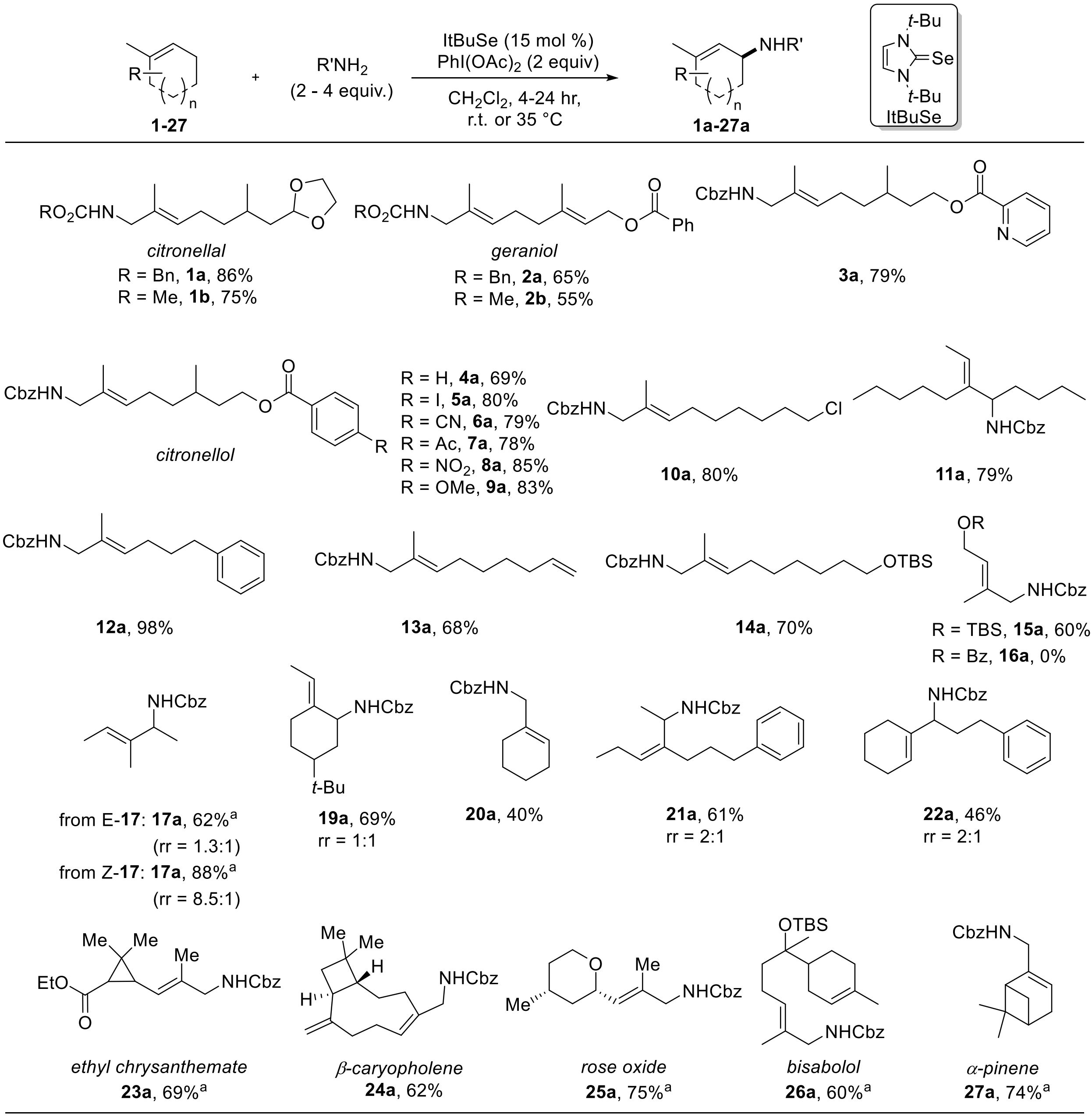
Table 3.23. Carbamate Scope



Pleasingly we observed that allyl (**1d**) and 2-triemthylsilyl-ethyl (**1g**) carbamates were also competent reaction partners providing additional deprotection strategies.

Next, we turned our attention to the scope of this reaction with trisubstituted alkenes (Table 3.24). The functional group tolerance for this reaction proved to be excellent. Esters (**2a**-**9a**, **23a**), ketones (**7a**), ethers (**9a**, **25a**), silyl ethers (**14a**, **15a**, **26a**), nitriles (**6a**), and nitro groups (**8a**) are all well tolerated under these reaction conditions. Pleasingly aryl iodides (**5a**) and alkyl chlorides (**10a**) are tolerated paving the way for further functionalization. We found that heteroarenes (**3a**) can also be tolerated despite the oxidative conditions.

Table 3.24. Scope for Trisubstituted Alkenes

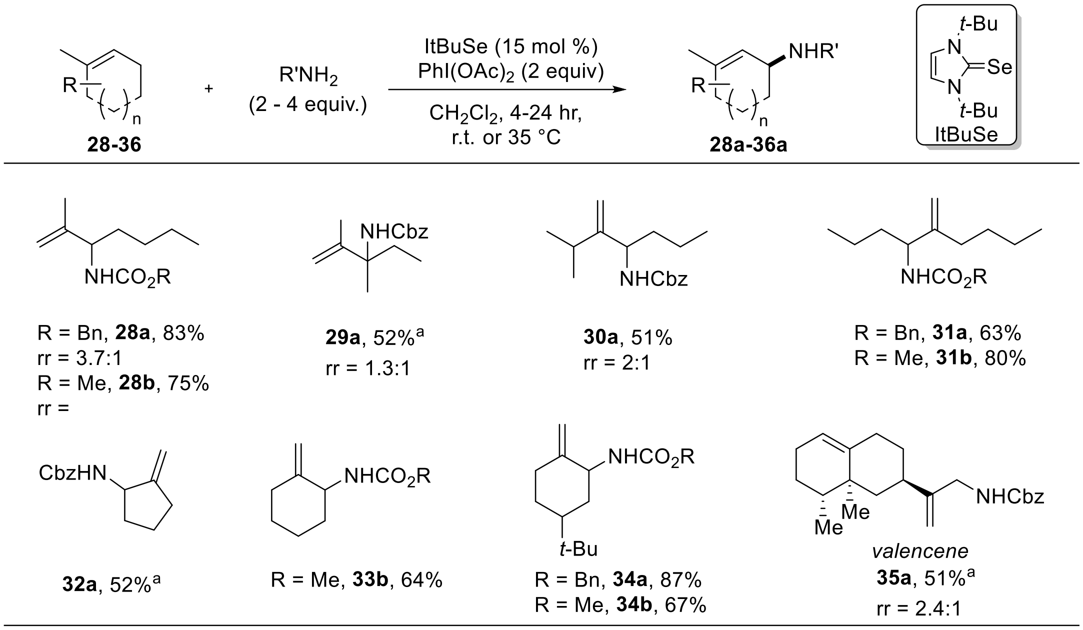


^{a}Standard conditions using 25 mol % catalyst loading, ^{b}Reaction was run for 72 hours

For trisubstituted alkenes, allylic ether groups are well tolerated on the less substituted side of the alkene (**15a**). However, allylic benzoates in this position completely shut down reactivity perhaps due to their stronger electron withdrawing effects (**16a**). For substrates with multiple alkenes, amination occurred exclusively at the more electron rich alkene (**2a**, **13a**, **24a**). Amination was exclusively observed at the more substituted side of the alkene specifically at the alkyl group trans to the third group. There appears to be a preference for amination at secondary positions over primary when a choice is available (**17a**).

A variety of 1,1-disubstituted alkenes were also found to be competent substrates for this reaction (Table 3.25). Both acyclic (**28a**-**31b**, **35a**) and cyclic alkenes (**32a**-**34a**) were well tolerated. Amination was found to occur at 1º, 2º, and even 3º positions.

Table 3.25. Scope for 1,1-Disubstituted Alkenes

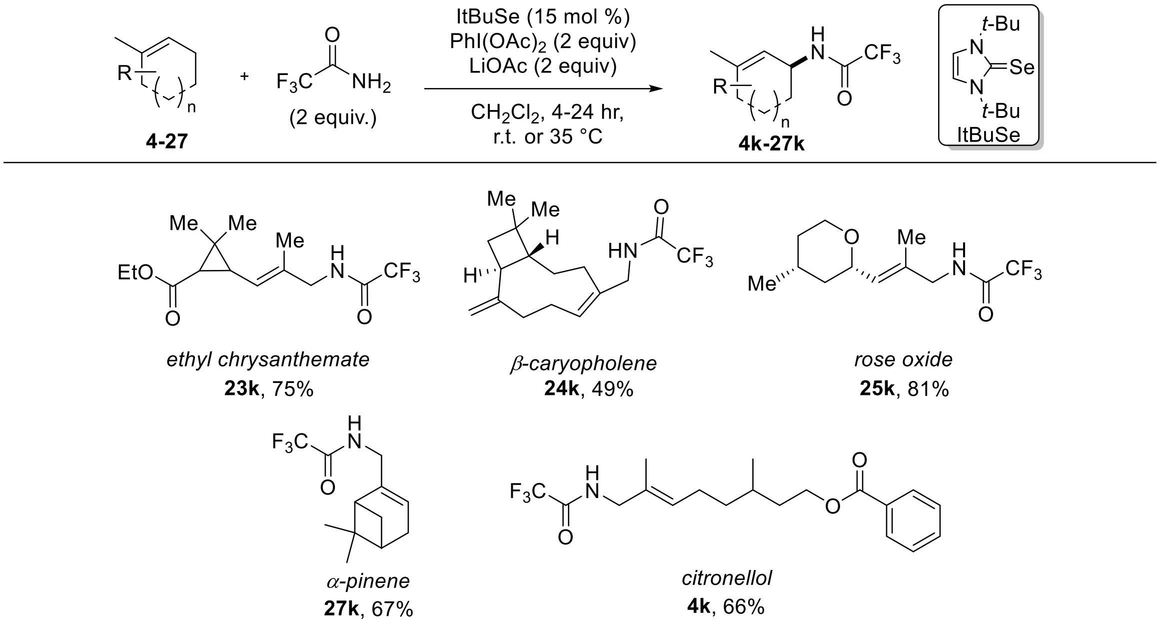


[a]Standard conditions using 25 mol % catalyst loading

The inherent regioselectivity of this reaction for the 1,1-disubstituted alkenes was probed. 2º amination occurs over 1º in a nearly 4 to 1 ratio, (**28a**). Little difference is observed for 1º over 3º with a 1 to 1.3 ratio showing a slight preference for 3º amination, (**29a**). We found that 2º amination was preferred to 3º with a 2:1 ratio, (**30a**).

Finally, we examined scope of this reaction with trifluoroacetamide as a coupling partner (Table 3.26). A handful of terpenes and terpene derivatives were subjected to the reaction conditions using trifluoroacetamide as a nucleophile.

Table 3.26. Alkene Scope with Trifluoroacetamide



ethyl chrysanthemate
23k, 75%

β-caryopholene
24k, 49%

rose oxide
25k, 81%

α-pinene
27k, 67%

citronellol
4k, 66%

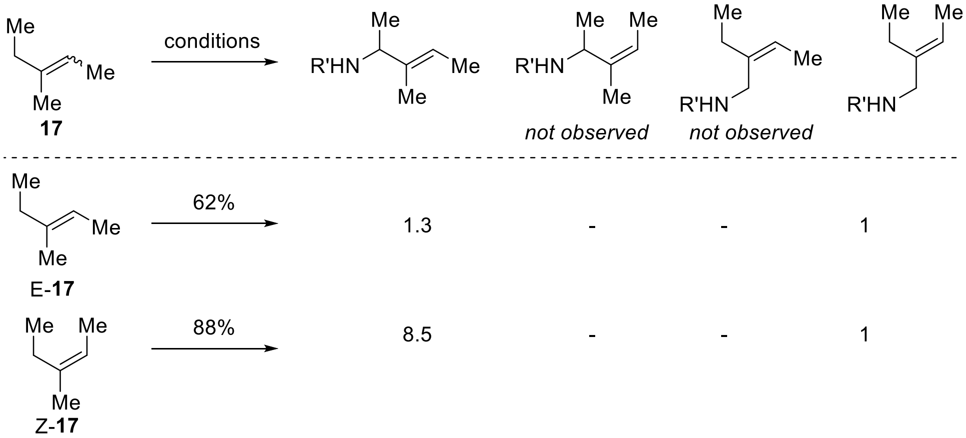
[a] Standard conditions using 25 mol % catalyst loading

Pleasingly, we found that this reaction proceeded well for a variety of trisubstituted terpenes affording the desired products in high yields.

3.2.6 *Mechanistic Considerations*

Examining the results from using 3-methyl-2-pentene (**17**) as a substrate provides numerous mechanistic insights for this reaction. First, we observe only two of the possible four amination products when using this alkene as a substrate (Scheme 3.4). Theoretically, we could obtain two regioisomers, each as a pair of diastereomers differening by the alkene geometry. We only observe the two regioisomers as the E alkenes with the aminated carbon ending up trans to the third alkyl group.

Scheme 3.4. *Potential Products for Differentially Trisubstituted Alkenes*



Both E- and Z-3-methyl-2-pentene result in the formation of the same two products but the ratios are very different with E-3-methyl-2-pentene (E-**17**) affording a 62% yield of the products in a 1.3:1 ratio favoring 2^o amination over 1^o while Z-3-methyl-2-pentene (Z-**17**)resulted in an 88% yield of the amination products in an 8.5:1 ratio favoring 2^o amination over 1^o.

These results can be understood through a careful examination of the mechanism. The generation of only two of the possible four products can be explained by looking at the possible transition states during the [2,3]-sigmatropic rearrangement (Figure 3.4). In the first step of the proposed mechanism, the bis(imido) selenium species undergoes an ene reaction with the alkene which is then followed by the sigmatropic rearrangement. Figure 3.4 depicts the intermediate resulting from the ene reaction at the top face of the alkene but analysis of attack at the bottom face would lead to identical results. The regiochemistry of this initial ene dictates the regiochemistry of the eventual products. In Figure 3.4, if either of the methylene allylic protons (H_a or H_b) participates in the ene reaction, the amination occurs at the 2^o position whereas if the ene reaction occurs with the methyl protons (H_c), the 1^o amination product is obtained. This leads to the two regiochemical products observed for disubstituted and trisubstituted alkenes with an inherent preference for 2^o amination.

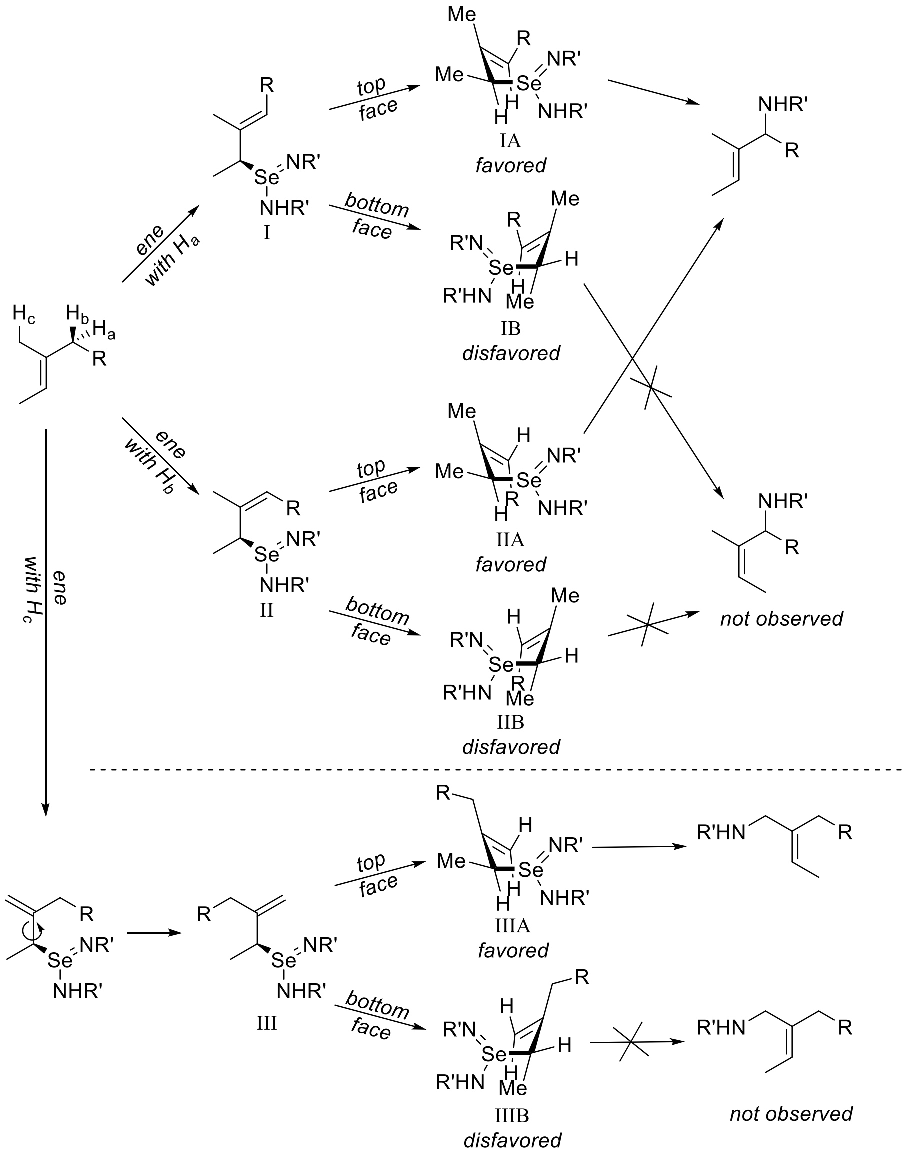


Figure 3.4. Mechanistic Reasoning for Product Distribution for Trisubstituted Alkenes.

Each of these regioisomers could result in a pair of diastereomers differing by the geometry of the resulting alkene. The geometry of this alkene is set in the second step of the proposed mechanism, the [2,3]-sigmatropic rearrangement. This rearrangement occurs through the five-membered transition state with the least $A^{1,3}$ strain. For example, for intermediate I in Figure 3.4, the sigmatropic rearrangement could occur from the top face of the alkene leading to transition state IA or the bottom face leading to transition state IB. Transition state IB has allylic strain between the methyl group and the alkene hydrogen disfavoring the formation of the Z alkene.

Instead, transition state 1A, with the rearrangement occurring from the top face should be favored because the allylic strain is now minimized resulting in the formation of the E alkene. Applying the same analysis to intermediate II leads to the same result. Again, we see that rearrangement from the bottom face of this alkene leads to significant allylic strain, this time between the methyl and the R group of the alkene in transition state IIB. Instead, rearrangement should occur from the top face through transition state IIA leading again to the E alkene.

Finally, applying the same analysis to intermediate III, we see that bottom face attack through transition state IIIB is disfavored due to the strain between the methyl group and the hydrogen of the alkene. Instead, the rearrangement should occur from the top face of the alkene where the allylic strain is minimized and the E alkene is formed. It should be noted that while the products from intermediate I and II result in a net retention of the original alkene geometry, the geometry of the product alkene has been inverted from that of the starting material when going through intermediate III. In each of these cases, the lowest energy transition state results in the aminated carbon ending up trans to the third alkyl group which is why only two of the four possible products are observed.

The sterics of the initial ene reaction can be used to explain how the geometry of the starting alkene effects the regioselectivity of the reaction. The sterics for this reaction for both E- and Z-3-methyl-2-pentene are depicted in Figure 3.5.

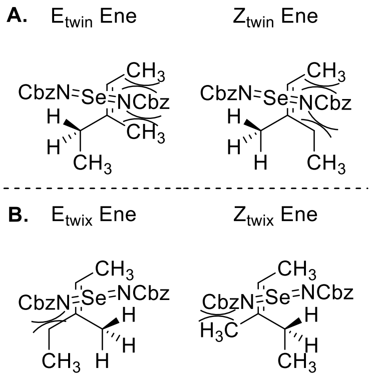
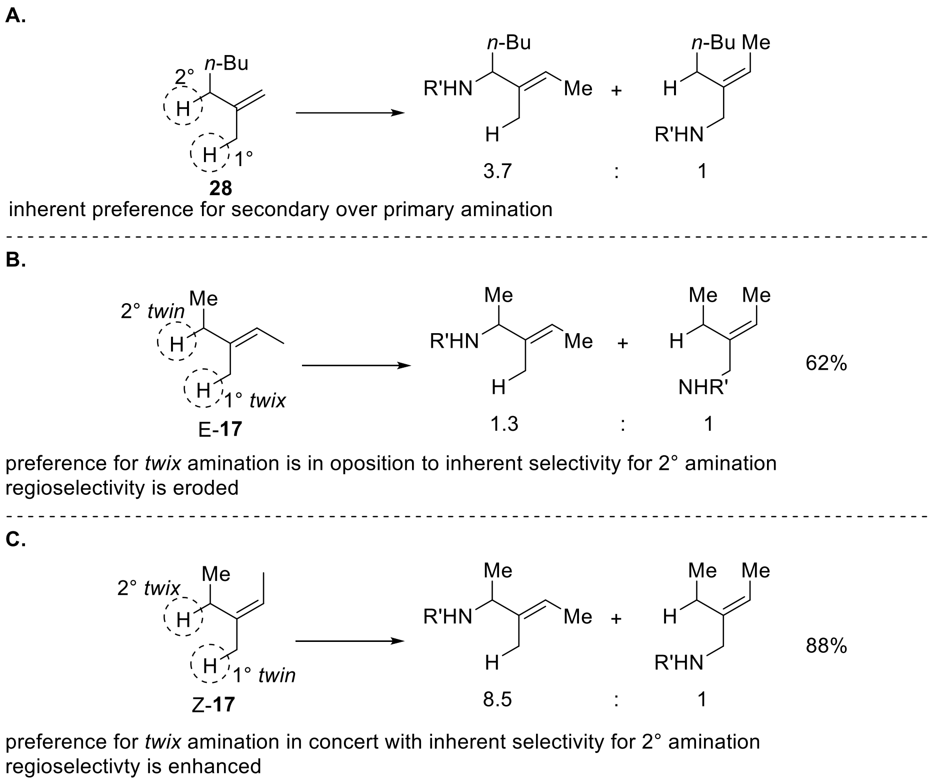


Figure 3.5. Mechanistic Explanation for Regioselectivity During the Ene Reaction.

For the ene reaction to occur at the *twin* position for the E- or Z- alkene, the cbz imido on the catalyst which does not participate sterically clashes with the two other alkene groups. In the case where the ene reaction occurs with one of the *twix* hydrogens, this steric clashing is minimized since now only one alkyl group clashes with the extra cbz imido group (Figure 3.5 B). An analogous explanation has been used for the observed regioselectivity for ene reactions with Nitrosoarenes.[14] Because of this steric effect, we expect a preference for *twix* amination for both the E- and Z- alkenes. Taking a look at 3-methyl-2-pentene (**17**) we can see how this preference for *twix* amination can affect the inherent selectivity based on the nature of the hydrogen observed for the 1,1-disubstituted alkenes (2º > 3º > 1º) (Figure 3.6).



inherent preference for secondary over primary amination

preference for *twix* amination is in oposition to inherent selectivity for 2° amination
regioselectivity is eroded

preference for *twix* amination in concert with inherent selectivity for 2° amination
regioselectivty is enhanced

Figure 3.6. Starting Alkene Geometry Affects Reaction Outcome.

Looking at substrate **28**, we see that with no other factors, the inherent selectivity for 2^o amination over 1^o is 3.7 to 1 (Figure 3.6 A). For E-3-methyl-2-pentene (E-**17**), the preference for *twix* amination is at odds with the inherent regioselectivity where the less favorable 1^o is in the more favorable *twix* position. These clashing forces cause an erosion of regioselectivity to just 1.3:1 for 2^o:1^o amination (Figure 3.6 B). In the case of the Z alkene (Z-**17**), the preference for *twix* amination works in concert with the inherent regioselectivity where the more favorable 2^o is now in the more favorable *twix* position. These synergistic effects work to enhance the regioselectivity to 8:1 for 2^o:1^o amination (Figure 3.6 C). In addition to the improved regioselectivity, the reaction for the Z alkene resulted in a greater yield of 88% compared to 62% for the E Alkene.

Section 3: CONCLUSION

A selenium catalyzed C-H amination reaction using carbamate nucleophiles has been developed. Key to the success of this catalytic transformation was the use of the tert-butyl imidazolium-based ligand on selenium. Numerous regiochemical insights were uncovered for this protocol. The reaction conditions are tolerant of an extensive number of functional groups. A variety of synthetically useful carbamates were found to be suitable coupling partners allowing for an extensive variety of orthogonal deprotection strategies. Additionally, acetamide nucleophiles were shown to be suitable coupling partners for this reaction simply requiring the addition of an acetate base to obtain significant yields. Both procedures were demonstrated to be suitable for late stage functionalization by aminating a variety of natural products and terpene derivatives.

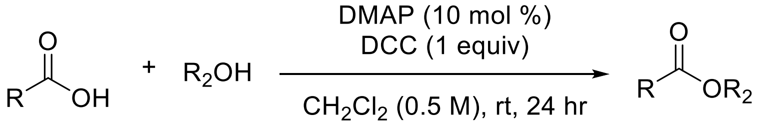
Section 4: EXPERIMENTAL

3.4.1 *General Procedures and Methods*

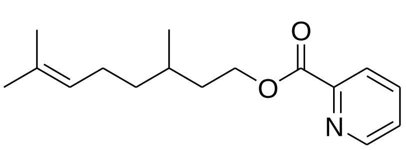
All reactions were performed under a nitrogen atmosphere using oven-dried or flame-dried glassware unless otherwise indicated. Dichloromethane (CH_2Cl_2) and tetrahydrofuran (THF) were degassed and dried by passing through a column of activated neutral alumina. Deuterated solvents ($CDCl_3$, acetone-d^6) were obtained from Cambridge Isotope Laboratories, Inc. and stored over activated 3A molecular sieves. Ethyl acetate (EtOAc), hexanes, and ether (Et_2O) were obtained from Fisher Scientific or Sigma Aldrich and used without further purification. Reagents were purchased from Sigma Aldrich, Tokyo Chemical Industry, Fisher Scientific, Alfa Aesar, Oakwood chemicals and used without further purification unless otherwise indicated. Infrared spectra were acquired using a Perkin Elmer Spectrum RX I spectrometer. Mass spectra were acquired using a Bruker Esquire 1100 Liquid Chromatograph-Ion Trap Mass Spectrometer. Column chromatography was performed using silica gel (Whatman, 60 Å, 230-400 mesh). NMR spectra were recorded on a Bruker AV-300, AV-301, DRX-499, or AV-500 spectrometer. ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) and are referenced relative to TMS (0.00 ppm), $CHCl_3$ (7.26 ppm) or acetone-d^5 (2.06 ppm). ^{13}C NMR chemical shifts (δ) are reported in parts per million (ppm) relative to the carbon resonance of $CDCl_3$ (77.26 ppm) or acetone-d^6 (29.92 ppm). Melting points were taken on a MEL-TEMP melting point apparatus and are uncorrected.

3.4.2 *Synthesis and Characterization of Starting Materials*

General Procedure for Benzoate Protection:

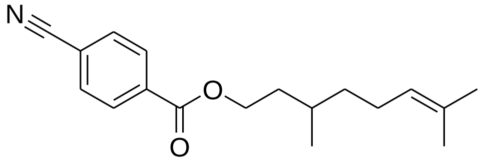


A flame-dried round-bottom flask was charged with a stir bar and placed under an atmosphere of nitrogen. The dichloromethane (0.5 M) was added to the mixture followed by the carboxylic acid (1.0 equiv), the alcohol (1.0 equiv), the DCC (1.0 equiv), and finally the DMAP (0.1 equiv). The mixture was stirred at room temperature for 24 hours. The resulting suspension was filtered and the filtrate was concentrated under reduced pressure. The products were then purified by silica gel chromatography.



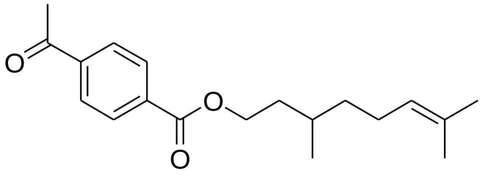
Prepared according to the general benzoate procedure and purified by silica gel chromatography (70:30 to 40:60, hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 8.77 (ddd, *J* = 4.7, 1.6, 0.8 Hz, 1H), 8.12 (dt, *J* = 7.9, 0.9 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.47 (ddd, *J* = 7.6, 4.7, 1.1 Hz, 1H), 5.09 (t, *J* = 7.1 Hz, 1H), 4.51 – 4.41 (m, 2H), 2.04 – 1.92 (m, 2H), 1.92 – 1.83 (m, 1H), 1.69 – 1.66 (m, 3H), 1.66 – 1.61 (m, 2H), 1.60 (s, 3H), 1.43 – 1.35 (m, 1H), 1.31 – 1.23 (m, 1H), 0.97 (d, *J* = 6.3 Hz, 3H).



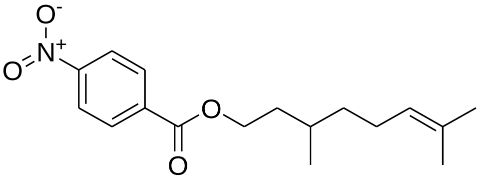
Prepared according to the general benzoate procedure and purified by silica gel chromatography (90:10 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 8.13 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 5.09 (t, *J* = 7.1 Hz, 1H), 4.46 – 4.31 (m, 2H), 2.10 – 1.91 (m, 2H), 1.83 (qd, *J* = 7.1, 4.8 Hz, 1H), 1.67 (s, 3H), 1.66 – 1.61 (m, 2H), 1.60 (s, 3H), 1.46 – 1.34 (m, 1H), 1.32 – 1.19 (m, 1H), 0.97 (d, *J* = 6.5 Hz, 3H).



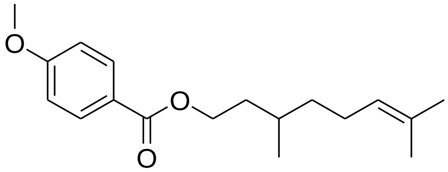
Prepared according to the general benzoate procedure and purified by silica gel chromatography (90:10 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 8.12 (d, *J* = 8.6 Hz, 2H), 8.01 (d, *J* = 8.6 Hz, 2H), 5.10 (ddd, *J* = 7.1, 4.2, 1.3 Hz, 1H), 4.44 – 4.32 (m, 2H), 2.65 (s, 3H), 2.08 – 1.93 (m, 2H), 1.89 – 1.77 (m, 1H), 1.67 (s, 3H), 1.66 – 1.61 (m, 1H), 1.60 (s, 3H), 1.45 – 1.36 (m, 1H), 1.32 – 1.21 (m, 2H), 0.98 (d, *J* = 6.5 Hz, 3H).



Prepared according to the general benzoate procedure and purified by silica gel chromatography (90:10 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil.

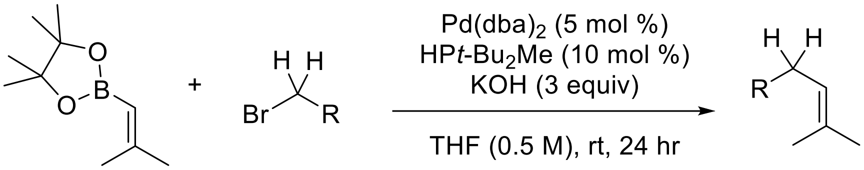
^{1}H NMR (500 MHz, CDCl3) δ 8.29 (d, *J* = 9.0 Hz, 2H), 8.20 (d, *J* = 9.0 Hz, 2H), 5.09 (t, *J* = 7.1 Hz, 1H), 4.46 – 4.35 (m, 2H), 2.08 – 1.93 (m, 2H), 1.90 – 1.78 (m, 1H), 1.68 (s, 3H), 1.66 – 1.61 (m, 1H), 1.60 (s, 3H), 1.48 – 1.36 (m, 1H), 1.34 – 1.20 (m, 2H), 0.98 (d, *J* = 6.4 Hz, 3H).



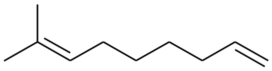
Prepared according to the general benzoate procedure and purified by silica gel chromatography (90:10 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 7.99 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 5.10 (t, *J* = 7.1 Hz, 1H), 4.40 – 4.25 (m, 2H), 3.86 (s, 3H), 2.09 – 1.93 (m, 2H), 1.85 – 1.75 (m, 1H), 1.67 (s, 3H), 1.65 – 1.61 (m, 1H), 1.60 (s, 3H), 1.45 – 1.36 (m, 1H), 1.33 – 1.19 (m, 2H), 0.97 (d, *J* = 6.6 Hz, 3H).

General Procedure for Cross Coupling Reactions:

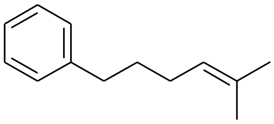


Prepared according to a literature procedure.[15] The $Pd(dba)_2$ (0.05 equiv), [HPt-Bu_2Me]BF_4 (0.10 equiv), and the boronic ester (1.32 equiv) were sequentially added to the THF (0.5 M) in a flame-dried Schlenk tube under nitrogen. The alkyl bromide (1 euqiv) was added followed by the KOH (3 equiv). The mixture was stirred for 24 hours at room temperature. The resulting mixture was poured into diethyl ether. This mixture was filtered, concentrated, and purified using silica gel chromatography.



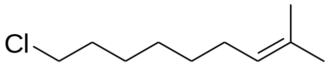
Prepared according to the general cross coupling procedure and purified by silica gel chromatography (99:1, hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 5.88 – 5.73 (m, 1H), 5.11 (t, *J* = 6.9 Hz, 1H), 4.99 (d, *J* = 17.0 Hz, 1H), 4.93 (d, *J* = 10.2 Hz, 1H), 2.05 (q, *J* = 6.7 Hz, 2H), 2.01 – 1.92 (m, 2H), 1.69 (s, 3H), 1.60 (s, 3H), 1.44 – 1.29 (m, 4H).



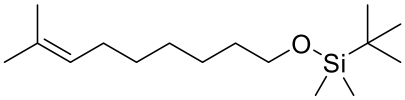
Prepared according to the general cross coupling procedure and purified by silica gel chromatography (99:1, hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 7.31 – 7.24 (m, 2H), 7.17 (t, *J* = 7.5 Hz, 3H), 5.14 (t, *J* = 6.7 Hz, 1H), 2.61 (t, *J* = 7.8 Hz, 2H), 2.02 (q, *J* = 7.3 Hz, 2H), 1.70 (s, 3H), 1.68 – 1.61 (m, 2H), 1.59 (s, 3H).



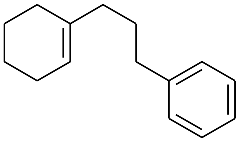
Prepared according to the general cross coupling procedure and purified by silica gel chromatography (95:5, hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 5.10 (t, *J* = 6.9 Hz, 1H), 3.53 (t, *J* = 6.6 Hz, 2H), 2.02 – 1.93 (m, 2H), 1.82 – 1.72 (m, 2H), 1.69 (s, 3H), 1.60 (s, 3H), 1.47 – 1.38 (m, 2H), 1.38 – 1.27 (m, 4H).



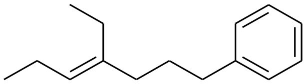
Prepared according to the general cross coupling procedure and purified by silica gel chromatography (90:10 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 5.11 (t, *J* = 6.6 Hz, 1H), 3.60 (t, *J* = 6.6 Hz, 2H), 1.96 (d, *J* = 6.3 Hz, 2H), 1.69 (s, 3H), 1.60 (s, 3H), 1.54 – 1.46 (m, 2H), 1.30 (s, 6H), 0.89 (s, 9H), 0.05 (s, 6H).



Prepared according to the general cross coupling procedure and purified by silica gel chromatography (99:1, hexanes: ethyl acetate) to afford the product as a clear oil.

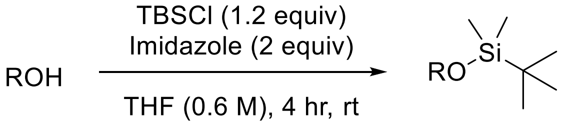
^{1}H NMR (500 MHz, CDCl3) δ 7.31 – 7.23 (m, 2H), 7.18 (d, *J* = 7.5 Hz, 3H), 5.41 (s, 1H), 2.58 (t, *J* = 7.8 Hz, 2H), 2.02 – 1.94 (m, 4H), 1.91 (s, 2H), 1.76 – 1.67 (m, 2H), 1.64 – 1.58 (m, 2H), 1.58 – 1.54 (m, 2H).



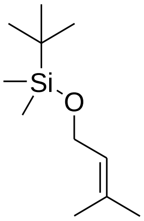
Prepared according to the general cross coupling procedure and purified by silica gel chromatography (99:1 hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 7.31 – 7.26 (m, 2H), 7.22 – 7.14 (m, 3H), 5.10 (t, *J* = 7.1 Hz, 1H), 2.59 (t, *J* = 7.7 Hz, 2H), 2.02 (dd, *J* = 15.6, 7.8 Hz, 6H), 1.80 – 1.64 (m, 2H), 0.95 (t, *J* = 7.5 Hz, 6H).

General Procedure for Silyl Protection:

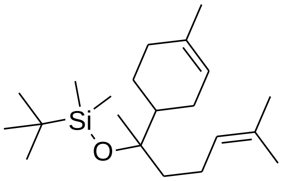


Prepared according to a literature procedure.[16] A flame-dried round-bottom flask was charged with a stir bar and placed under an atmosphere of nitrogen. To this flask was added the imidazole (2 equiv) followed by the THF (0.6 M). The alcohol (1 equiv) and the silyl chloride (1.2 equiv) were added sequentially, and the resulting mixture was stirred for 4 hours. The mixture was diluted with diethyl ether. The organic layer was washed with water and the resulting aqueous layer was washed with diethyl ether three times. The combined organics were dried, concentrated, and purified by column chromatography.



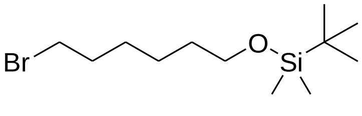
Prepared according to the general silyl protection procedure and purified by silica gel chromatography (95:5 to 90:10, hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 5.30 (t, *J* = 6.5 Hz, 1H), 4.17 (d, *J* = 6.5 Hz, 2H), 1.71 (s, 3H), 1.63 (s, 3H), 0.91 (s, 9H), 0.07 (s, 6H).



Prepared according to the general silyl protection procedure and purified by silica gel chromatography (90:10 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 5.38 (s, 1H), 5.13 – 5.04 (m, 1H), 2.04 – 1.89 (m, 5H), 1.88 – 1.75 (m, 1H), 1.68 (d, *J* = 0.8 Hz, 3H), 1.64 (s, 3H), 1.60 (s, 3H), 1.55 – 1.50 (m, 2H), 1.50 – 1.38 (m, 2H), 1.35 – 1.23 (m, 1H), 1.18 (s, 1.5H), 1.14 (s, 1.5H), 0.89 – 0.85 (m, 9H), 0.07 (d, *J* = 3.6 Hz, 3H), 0.07 (d, *J* = 4.8 Hz, 3H).

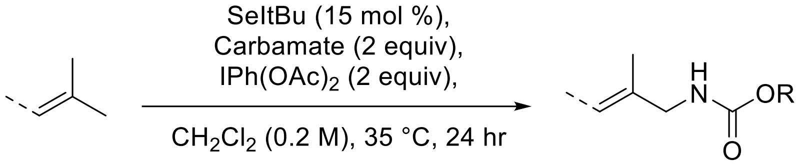


Prepared according to the general silyl protection procedure and purified by silica gel chromatography (90:10 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil.

^{1}H NMR (500 MHz, CDCl3) δ 3.61 (t, *J* = 6.3 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 1.91 – 1.83 (m, 2H), 1.54 – 1.49 (m, 2H), 1.49 – 1.41 (m, 2H), 1.40 – 1.33 (m, 2H), 0.91 – 0.88 (m, 9H), 0.05 (s, 6H).

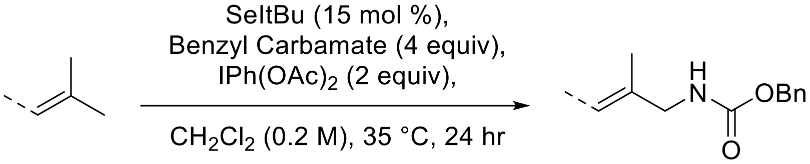
3.4.3 *General Procedure for the Selenium Catalyzed Amination of Highly Substituted Alkenes using Carbamate Nucleophiles*

General Procedure A:



A flame-dried borosilicate glass vial charged with a magnetic stir bar was placed under an atmosphere of nitrogen. To this vial was added the SeItBu (0.03 mmol, 0.15 equiv), dichloromethane (1 mL, 0.2 M), and alkene (0.2 mmol, 1.0 equiv). The carbamate (0.4 mmol, 2 equiv) was added followed by the iodobenzene diacetate (0.4 mmol, 2 equiv). The solution was stirred at 35 ºC and monitored by TLC for the consumption of starting alkene. Upon completion, the mixture was passed through a silica gel plug using ethyl acetate as the eluent. The resulting solution was concentrated under reduced pressure and purified using silica gel chromatography.

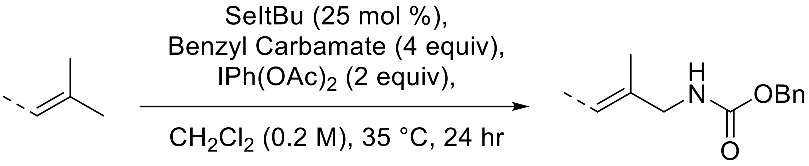
General Procedure B:



A flame-dried borosilicate glass vial charged with a magnetic stir bar was placed under an atmosphere of nitrogen. To this vial was added the SeItBu (0.03 mmol, 0.15 equiv), dichloromethane (1 mL, 0.2 M), and alkene (0.2 mmol, 1.0 equiv). The benzyl carbamate (0.8

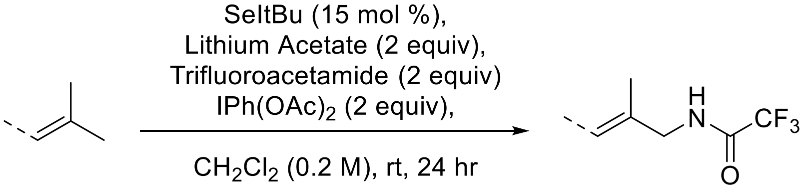
mmol, 4 equiv) was added followed by the iodobenzene diacetate (0.4 mmol, 2 equiv). The solution was stirred at 35 ºC and monitored by TLC for the consumption of starting alkene. Upon completion, the mixture was passed through a silica gel plug using ethyl acetate as the eluent. The resulting solution was concentrated under reduced pressure and purified using silica gel chromatography.

General Procedure C:



A flame-dried borosilicate glass vial charged with a magnetic stir bar was placed under an atmosphere of nitrogen. To this vial was added the SeItBu (0.05 mmol, 0.25 equiv), dichloromethane (1 mL, 0.2 M), and alkene (0.2 mmol, 1.0 equiv). The benzyl carbamate (0.8 mmol, 4 equiv) was added followed by the iodobenzene diacetate (0.4 mmol, 2 equiv). The solution was stirred at 35 ºC and monitored by TLC for the consumption of starting alkene. Upon completion, the mixture was passed through a silica gel plug using ethyl acetate as the eluent. The resulting solution was concentrated under reduced pressure and purified using silica gel chromatography.

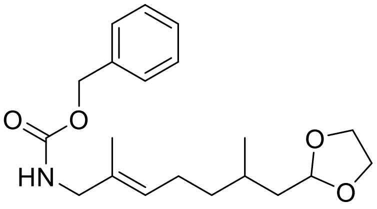
General Procedure D:



A flame-dried borosilicate glass vial charged with a magnetic stir bar was placed under an atmosphere of nitrogen. To this vial was added the SeItBu (0.03 mmol, 0.15 equiv), dichloromethane (1 mL, 0.2 M), and alkene (0.2 mmol, 1.0 equiv). The trifluoroacetamide (0.4

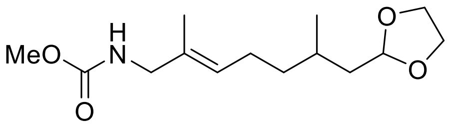
mmol, 2 equiv) was added followed by the lithium acetate (0.4 mmol, 2 equiv) and finally the iodobenzene diacetate (0.4 mmol, 2 equiv). The solution was stirred at 35 ºC and monitored by TLC for the consumption of starting alkene. Upon completion, the mixture was passed through a silica gel plug using ethyl acetate as the eluent. The resulting solution was concentrated under reduced pressure and purified using silica gel chromatography.

3.4.4 *Characterization of Products*



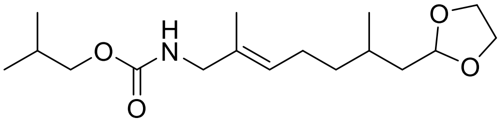
1a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (60 mg, 86%)

^{1}H NMR (500 MHz, CDCl3) δ 7.43 – 7.30 (m, 5H), 5.28 (t, *J* = 7.0 Hz, 1H), 5.11 (s, 2H), 4.88 (t, *J* = 4.9 Hz, 1H), 4.80 (s, 1H), 3.95 (s, 2H), 3.81 (d, *J* = 5.7 Hz, 2H), 3.70 (d, *J* = 5.5 Hz, 2H), 2.08 – 1.89 (m, 2H), 1.72 – 1.63 (m, 2H), 1.61 (s, 3H), 1.53 – 1.45 (m, 1H), 1.43 – 1.33 (m, 1H), 1.26 – 1.15 (m, 1H), 0.95 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.54, 136.78, 131.75, 128.59, 128.17, 127.67, 127.05, 126.91, 103.79, 66.76, 65.36, 64.81, 64.74, 48.77, 40.89, 37.01, 29.11, 25.15, 19.94, 14.42.



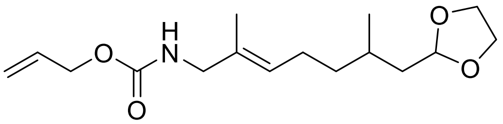
1b. Prepared according to general procedure A and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (35 mg, 65%)

^{1}**H NMR** (500 MHz, CDCl3) δ 5.22 (t, *J* = 7.0 Hz, 1H), 4.82 (t, *J* = 4.8 Hz, 1H), 4.66 (s, 1H), 3.94 – 3.84 (m, 2H), 3.82 – 3.72 (m, 2H), 3.67 – 3.53 (m, 5H), 2.03 – 1.87 (m, 2H), 1.65 – 1.56 (m, 2H), 1.55 (s, 3H), 1.47 – 1.38 (m, 1H), 1.37 – 1.29 (m, 1H), 1.16 (dd, *J* = 17.3, 8.7 Hz, 1H), 0.89 (d, *J* = 6.3 Hz, 3H). ^{13}**C NMR** (126 MHz, CDCl3) δ 157.22, 131.85, 126.79, 103.81, 64.81, 64.74, 52.14, 48.73, 40.89, 37.02, 29.10, 25.14, 19.93, 14.37. **IR** (thin film): 3348, 2954, 2921, 1711, 1534, 1462, 1254, 1193, 1138, 1079, 1034, 947, 778 cm^{-1}



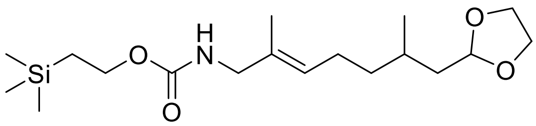
1c. Prepared according to general procedure A and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (46 mg, 73%)

^{1}**H NMR** (500 MHz, CDCl3) δ δ 5.29 (t, *J* = 6.9 Hz, 1H), 4.89 (t, *J* = 4.9 Hz, 1H), 4.69 (s, 1H), 4.00 – 3.91 (m, 2H), 3.89 – 3.79 (m, 4H), 3.69 (d, *J* = 5.2 Hz, 2H), 2.09 – 1.95 (m, 2H), 1.95 – 1.83 (m, 1H), 1.73 – 1.63 (m, 2H), 1.63 (s, 3H), 1.55 – 1.45 (m, 1H), 1.45 – 1.36 (m, 1H), 1.25 – 1.18 (m, 1H), 0.96 (d, *J* = 6.5 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 6H). ^{13}**C NMR** (126 MHz, CDCl3) δ 157.00, 132.00, 126.80, 103.84, 71.11, 64.86, 64.79, 48.71, 40.94, 37.07, 29.16, 28.19, 25.18, 19.96, 19.18, 14.43. **IR** (thin film): 3343, 2958, 2930, 2874, 1721, 1699, 1532, 1471, 1436, 1410, 1380, 1368, 1243, 1137, 1036, 947 cm^{-1}.



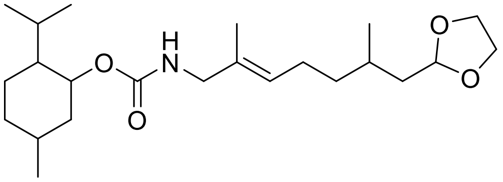
1e. Prepared according to general procedure A and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (29 mg, 48%)

^{1}H NMR (500 MHz, CDCl3) δ 5.93 (m, 1H), 5.36 – 5.25 (m, 2H), 5.21 (dd, *J* = 10.4, 0.9 Hz, 1H), 4.89 (t, *J* = 4.9 Hz, 1H), 4.77 (s, 1H), 4.57 (d, *J* = 5.0 Hz, 2H), 4.02 – 3.91 (m, 2H), 3.89 – 3.78 (m, 2H), 3.70 (d, *J* = 5.5 Hz, 2H), 2.11 – 1.93 (m, 2H), 1.72 – 1.63 (m, 2H), 1.62 (s, 3H), 1.54 – 1.45 (m, 1H), 1.45 – 1.35 (m, 1H), 1.30 – 1.16 (m, 1H), 0.96 (d, *J* = 6.5 Hz, 3H). **IR** (thin film): 3339, 2928, 1711, 1529, 1460, 1410, 1246, 1137, 1035, 992, 938, 777, 509 cm^{-1}.



1g. Prepared according to general procedure A and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (44 mg, 62%)

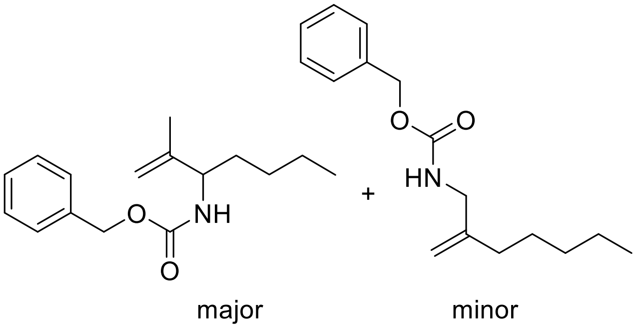
^{1}H NMR (500 MHz, CDCl3) δ 5.27 (t, *J* = 6.9 Hz, 1H), 4.88 (t, *J* = 4.7 Hz, 1H), 4.64 (s, 1H), 4.14 (dd, *J* = 8.5, 8.0 Hz, 2H), 3.95 (s, 2H), 3.82 (s, 2H), 3.69 – 3.58 (m, 2H), 2.08 – 1.92 (m, 2H), 1.72 – 1.62 (m, 2H), 1.60 (s, 3H), 1.52 – 1.44 (m, 1H), 1.43 – 1.33 (m, 1H), 1.30 – 1.16 (m, 1H), 1.05 – 0.89 (m, 5H), 0.02 (s, 9H). **IR** (thin film): 3343, 2953, 2924, 1710, 1527, 1459, 1410, 1250, 1177, 1132, 1039, 945, 860, 838, 769, 695 cm^{-1}.



1h. Prepared according to general procedure A and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (61 mg, 77%)

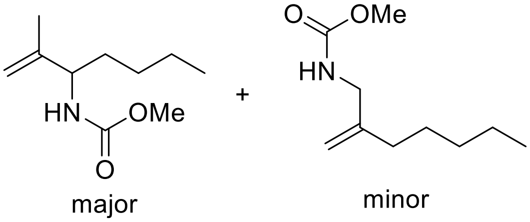
^{1}H NMR (500 MHz, CDCl3) δ 5.27 (t, *J* = 6.7 Hz, 1H), 4.89 (t, *J* = 5.0 Hz, 1H), 4.61 (s, 1H), 4.56 (td, *J* = 10.8, 4.2 Hz, 1H), 4.00 – 3.92 (m, 2H), 3.88 – 3.79 (m, 2H), 3.68 (d, *J* = 4.9 Hz, 2H), 2.10

– 1.97 (m, 3H), 1.97 – 1.88 (m, 1H), 1.71 – 1.63 (m, 5H), 1.61 (s, 3H), 1.53 – 1.45 (m, 2H), 1.43 – 1.35 (m, 1H), 1.30 (t, *J* = 10.9 Hz, 1H), 1.26 – 1.17 (m, 1H), 1.06 (ddd, *J* = 16.3, 13.4, 3.8 Hz, 1H), 0.96 (d, *J* = 6.5 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 7.0 Hz, 3H), 0.87 – 0.82 (m, 1H), 0.79 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.67, 132.15, 126.56, 103.85, 74.57, 64.87, 64.79, 48.62, 47.63, 41.66, 40.95, 37.12, 34.49, 31.51, 29.18, 26.48, 25.19, 23.76, 22.19, 20.93, 19.98, 16.67, 14.40. **IR** (thin film): 3347, 2953, 2927, 2870, 1718, 1522, 1456, 1407, 1387, 1370, 1244, 1180, 1134, 1080, 1039, 985, 972 cm^{-1}.



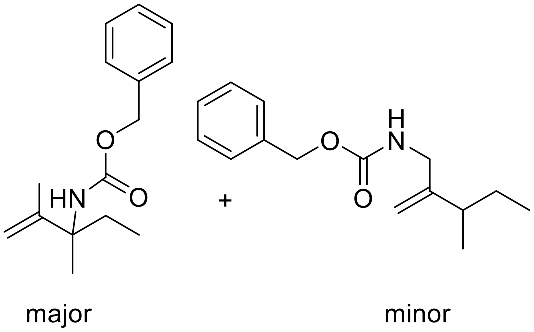
28a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (43 mg, 83%)

^{1}H NMR (500 MHz, CDCl3) δ 7.44 – 7.29 (maj + min, m, 5H), 5.17 – 5.03 (maj + min, m, 2H), 4.89 (maj + min, s, 1H), 4.85 (maj + min, s, 1H), 4.76 (maj + min, s, 1H), 4.08 (maj, d, *J* = 6.3 Hz, 0.8H), 3.77 (min, d, *J* = 5.6 Hz, 0.4H), 2.02 (min, t, *J* = 7.5 Hz, 0.4H), 1.71 (maj, s, 2.4H), 1.61 – 1.52 (maj + min, m, 1H), 1.52 – 1.38 (maj + min, m, 1H), 1.38 – 1.16 (maj + min, m, 4H), 0.89 (t, *J* = 6.7 Hz, 4H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.51, 155.93, 146.52, 145.05, 136.78, 128.64, 128.24, 111.55, 109.89, 66.79, 56.60, 45.78, 34.01, 33.25, 31.65, 29.83, 28.18, 27.44, 22.58, 18.97, 14.08. **IR** (thin film): 3416, 3332, 3066, 3033, 2955, 2930, 2858, 1701, 1650, 1529, 1454, 1331, 1240, 1105, 1047, 1027, 896, 776, 734, 696 cm^{-1}.



28b. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (28 mg, 75%)

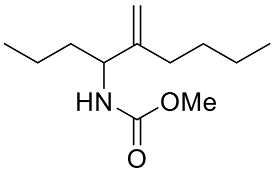
^{1}H NMR (500 MHz, CDCl3) δ 4.88 (maj + min, s, 1H), 4.84 (maj + min, s, 1H), 4.68 (maj + min, s, 1H), 4.05 (maj, s, 0.75H), 3.76 – 3.60 (maj + min, m, 3.5H), 2.02 (min, t, *J* = 7.7 Hz, 0.5H), 1.71 (maj, s, 2.25H), 1.63 – 1.51 (maj + min, m, 1H), 1.51 – 1.39 (maj + min, m, 1H), 1.39 – 1.27 (maj + min, m, 4H), 0.89 (maj + min, t, *J* = 6.6 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 157.19, 156.61, 146.61, 145.19, 111.42, 109.77, 56.54, 52.12, 45.74, 34.00, 33.27, 31.65, 29.83, 28.19, 27.42, 22.61, 22.58, 18.96, 14.13, 14.07. **IR** (thin film): 3327, 2956, 2932, 2859, 1702, 1651, 1536, 1456, 1376, 1256, 1193, 1053, 895 cm^{-1}.



29a. Prepared according to general procedure C and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (27 mg, 58% rr=1.3:1)

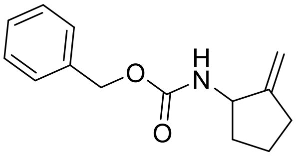
^{1}H NMR (500 MHz, CDCl3) major: δ 7.39 – 7.29 (m, 5H), 5.05 (s, 2H), 4.94 (s, 1H), 4.88 (s, 1H), 4.79 (s, 1H), 1.72 (s, 3H), 1.69 – 1.64 (m, 2H), 1.43 (s, 3H), 0.81 (t, *J* = 7.5 Hz, 3H). minor: δ 6.70

– 6.59 (m, 5H), 4.42 (s, 2H), 4.19 (s, 1H), 4.14 (s, 1H), 4.09 (s, 1H), 3.07 (d, *J* = 5.5 Hz, 2H), 1.41 – 1.30 (m, 1H), 0.82 – 0.71 (m, 1H), 0.66 (dd, *J* = 13.9, 6.4 Hz, 1H), 0.34 (d, *J* = 6.7 Hz, 3H), 0.14 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl3) major: δ 147.60, 136.93, 128.64, 128.24, 128.17, 111.48, 66.29, 59.19, 31.31, 23.53, 19.29, 8.21. minor: 156.51, 150.93, 136.76, 128.67, 128.27, 108.79, 66.91, 44.32, 39.62, 28.32, 19.56, 11.86. **IR** (thin film): major: 3342, 3090, 3066, 3033, 2971, 2939, 2880, 1736, 1720, 1695, 1524, 1505, 1456, 1373, 1243, 1088, 1052, 1029, 893, 778, 736, 696 cm^{-1}. minor: 3337, 3066, 3033, 2962, 2932, 2874, 1703, 1532, 1455, 1248, 1134, 1044, 987, 898, 735, 696 cm^{-1}.



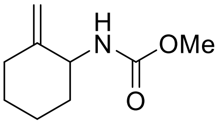
31b. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (34 mg, 80%)

^{1}H NMR (500 MHz, CDCl3) δ 4.84 (s, 1H), 4.77 (s, 1H), 4.59 (s, 1H), 4.01 (s, 1H), 3.59 (s, 3H), 1.93 (dd, *J* = 13.5, 6.5 Hz, 2H), 1.56 – 1.45 (m, 1H), 1.43 – 1.33 (m, 3H), 1.31 – 1.21 (m, 4H), 0.85 (t, *J* = 7.3 Hz, 3H), 0.84 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 170.38, 156.60, 150.10, 109.34, 64.23, 55.37, 52.10, 36.33, 32.86, 30.14, 22.65, 19.39, 14.09, 13.98. **IR** (thin film): 3328, 3083, 2957, 2931, 2872, 1702, 1648, 1536, 1458, 1361, 1255, 1193, 1106, 1061, 895 cm^{-1}.



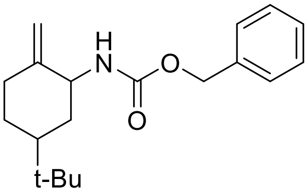
32a. Prepared according to general procedure C and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (24 mg, 52%)

^{1}H NMR (500 MHz, CDCl3) δ 7.39 – 7.29 (m, 5H), 5.12 (s, 2H), 4.99 (d, *J* = 2.0 Hz, 1H), 4.98 (d, *J* = 2.3 Hz, 1H), 4.71 (s, 1H), 4.41 (d, *J* = 8.1 Hz, 1H), 2.43 – 2.25 (m, 2H), 2.22 – 2.13 (m, 1H), 1.73 (ddt, *J* = 15.8, 7.8, 4.0 Hz, 1H), 1.63 – 1.57 (m, 1H), 1.41 (dtd, *J* = 12.2, 9.7, 7.3 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl3) δ 152.39, 136.73, 128.67, 128.26, 106.96, 66.85, 55.53, 34.32, 30.96, 22.20. **IR** (thin film): 3311, 3066, 3032, 2959, 2865, 1694, 1537, 1454, 1344, 1292, 1244, 1044, 1028, 898, 753, 697 cm^{-1}.



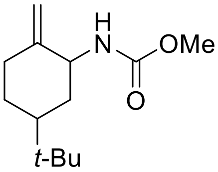
33b. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (22 mg, 64%)

^{1}H NMR (500 MHz, CDCl3) δ 4.84 – 4.59 (m, 3H), 4.17 – 3.86 (m, 1H), 3.67 (s, 3H), 2.38 (d, *J* = 13.6 Hz, 1H), 2.06 (t, *J* = 11.5 Hz, 1H), 2.01 – 1.92 (m, 1H), 1.81 – 1.67 (m, 2H), 1.58 – 1.45 (m, 1H), 1.36 – 1.17 (m, 2H). **^{13}C NMR** (126 MHz, CDCl3) δ 170.39, 156.82, 133.38, 126.29, 64.24, 52.11, 49.47, 30.20, 29.84, 25.27, 25.08, 22.67, 21.03, 18.63, 11.17. **IR** (thin film): 3321, 3083, 2932, 2856, 1702, 1651, 1536, 1447, 1364, 1325, 1299, 1254, 1232, 1193, 1054, 1038, 894 cm^{-1}.



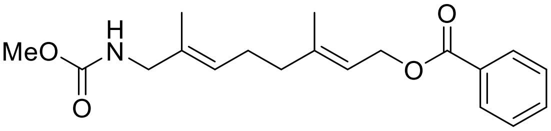
34a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (53 mg, 87%)

^{1}H NMR (500 MHz, CDCl3) δ 7.44 – 7.27 (maj + min m, 5H), 5.22 – 4.99 (maj + min, m, 3H), 4.94 (maj + min, s, 1H), 4.84 – 4.65 (maj + min, m, 1H), 4.36 (maj, s, 0.9H), 4.19 – 4.02 (min, m, 0.1H), 2.46 (min, d, *J* = 13.7 Hz, 0.1H), 2.27 (maj, d, *J* = 13.9 Hz, 0.9H), 2.21 – 2.06 (maj + min, m, 1H), 2.00 (maj + min, d, *J* = 12.4 Hz, 1H), 1.86 (maj + min, d, *J* = 12.2 Hz, 1H), 1.36 (maj + min, t, *J* = 11.5 Hz, 1H), 1.25 (maj + min, m, 1H), 1.09 (maj + min, td, *J* = 12.5, 3.6 Hz, 1H), 0.93 – 0.80 (m, 9H). **^{13}C NMR** (126 MHz, CDCl3) δ 170.34, 147.04, 136.66, 128.65, 128.35, 128.25, 110.75, 66.78, 64.19, 53.81, 47.47, 42.08, 34.66, 33.55, 32.45, 32.31, 30.97, 29.81, 28.55, 27.65, 27.59. **IR** (thin film): 3327, 3068, 3033, 2950, 2865, 1708, 1522, 1498, 1454, 1396, 1365, 1338, 1270, 1231, 1077, 1047, 1027, 982, 902, 777, 735, 697, 460 cm^{-1}.



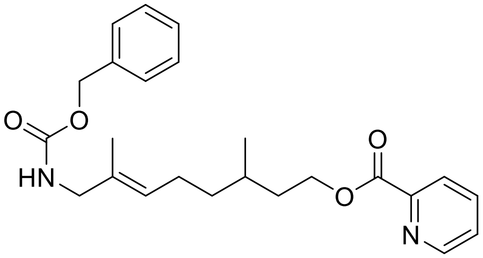
34b. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (30 mg, 67%)

^{1}H NMR (500 MHz, CDCl3) δ 4.92 (s, 2H), 4.77 (s, 1H), 4.33 (s, 1H), 3.67 (s, 3H), 2.26 (dt, *J* = 13.8, 2.9 Hz, 1H), 2.12 (td, *J* = 13.6, 4.4 Hz, 1H), 1.98 (dd, *J* = 13.3, 2.6 Hz, 1H), 1.90 – 1.81 (m, 1H), 1.35 (td, *J* = 13.1, 3.9 Hz, 1H), 1.25 (t, *J* = 12.5 Hz, 1H), 1.08 (ddd, *J* = 25.2, 12.6, 4.1 Hz, 1H), 0.85 (s, 9H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.25, 147.15, 110.64, 64.23, 53.75, 52.07, 42.11, 34.69, 33.62, 32.34, 30.99, 28.56, 27.61. **IR** (thin film): 3325, 3072, 2949, 2866, 1703, 1654, 1529, 1452, 1365, 1337, 1234, 1193, 1083, 1048, 1018, 901, 778, 661, 610 cm^{-1}.



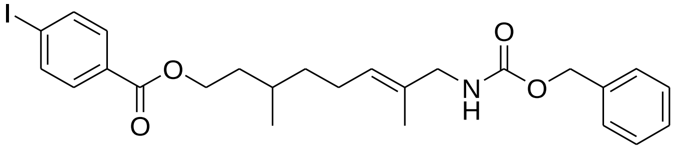
2b. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (43 mg, 65%)

^{1}H NMR (500 MHz, CDCl3) δ 8.04 (d, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 5.45 (t, *J* = 6.9 Hz, 1H), 5.26 (t, *J* = 6.8 Hz, 1H), 4.83 (d, *J* = 7.0 Hz, 2H), 4.75 (s, 1H), 3.71 – 3.63 (m, 5H), 2.16 (dd, *J* = 14.7, 7.3 Hz, 2H), 2.12 – 2.05 (m, 2H), 1.76 (s, 3H), 1.60 (s, 3H). **IR** (thin film): 3380, 2922, 1717, 1525, 1451, 1314, 1272, 1111, 1070, 1026, 713, 588, 510, 485 cm^{-1}.



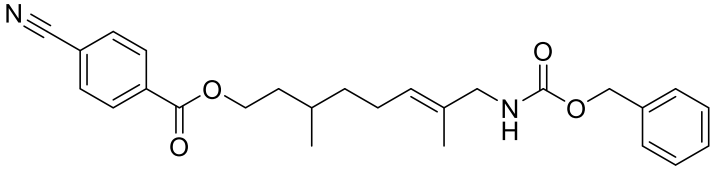
3a. Prepared according to general procedure B and purified by silica gel chromatography (60:40 to 40:60, hexanes: ethyl acetate) to afford the product as a clear oil (65 mg, 79%)

^{1}H NMR (500 MHz, CDCl3) δ 8.76 (s, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.82 (t, *J* = 7.1 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.40 – 7.29 (m, 5H), 5.28 (s, 1H), 5.11 (s, 2H), 4.86 (s, 1H), 4.55 – 4.34 (m, 2H), 3.69 (s, 2H), 2.04 (dd, *J* = 18.0, 12.3 Hz, 2H), 1.86 (d, *J* = 7.4 Hz, 1H), 1.61 (s, 5H), 1.40 (s, 1H), 1.26 (s, 1H), 0.97 (d, *J* = 5.6 Hz, 3H).



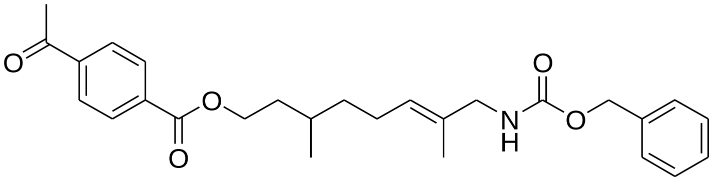
5a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (79 mg, 73%)

^{1}H NMR (500 MHz, CDCl3) δ 7.79 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 8.5 Hz, 2H), 7.38 – 7.29 (m, 5H), 5.28 (t, *J* = 6.7 Hz, 1H), 5.11 (s, 2H), 4.77 (s, 1H), 4.42 – 4.28 (m, 2H), 3.70 (d, *J* = 5.8 Hz, 2H), 2.10 – 1.94 (m, 2H), 1.84 – 1.74 (m, 1H), 1.65 – 1.53 (m, 5H), 1.45 – 1.34 (m, 1H), 1.27 – 1.20 (m, 1H), 0.96 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 166.29, 156.55, 137.85, 136.79, 131.98, 131.12, 130.07, 128.65, 128.24, 126.62, 100.73, 66.83, 63.85, 48.71, 36.70, 35.57, 29.81, 25.24, 19.62, 14.48. **IR** (thin film): 3368, 3064, 3032, 2957, 2923, 1720, 1586, 1519, 1455, 1393, 1307, 1269, 1177, 1115, 1008, 754, 697 cm^{-1}.



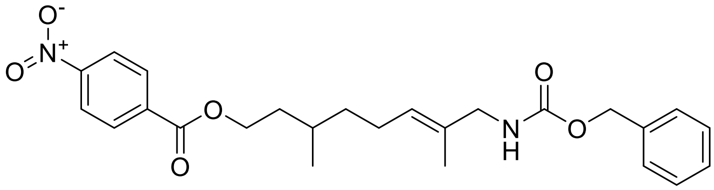
6a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (77 mg, 89%)

^{1}H NMR (500 MHz, CDCl3) δ 8.12 (d, *J* = 8.3 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.38 – 7.31 (m, 5H), 5.28 (t, *J* = 6.6 Hz, 1H), 5.11 (s, 2H), 4.76 (s, 1H), 4.45 – 4.32 (m, 2H), 3.70 (d, *J* = 5.7 Hz, 2H), 2.12 – 1.96 (m, 2H), 1.85 – 1.78 (m, 1H), 1.65 – 1.56 (m, 5H), 1.46 – 1.37 (m, 1H), 1.30 – 1.24 (m, 1H), 0.97 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 165.14, 156.54, 136.78, 134.40, 132.36, 132.04, 130.19, 128.67, 128.26, 126.52, 118.13, 116.49, 66.86, 64.44, 48.70, 36.70, 35.53, 29.81, 25.23, 19.59, 14.49. **IR** (thin film): 3381, 2957, 2923, 2231, 1722, 1716, 1522, 1455, 1310, 1277, 1177, 1107, 1019, 862, 768, 693 cm^{-1}.



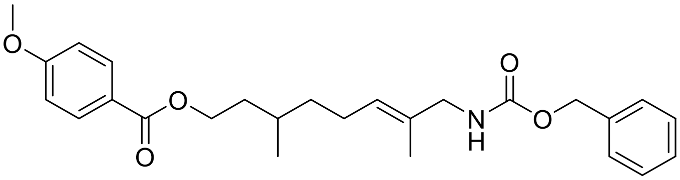
7a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (76 mg, 84%)

^{1}**H NMR** (500 MHz, CDCl3) δ 8.11 (d, *J* = 8.2 Hz, 2H), 8.00 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.32 (m, 5H), 5.28 (t, *J* = 6.6 Hz, 1H), 5.11 (s, 2H), 4.75 (s, 1H), 4.44 – 4.35 (m, 2H), 3.70 (d, *J* = 6.0 Hz, 2H), 2.64 (s, 3H), 2.10 – 1.99 (m, 2H), 1.85 – 1.78 (m, 1H), 1.66 – 1.59 (m, 5H), 1.46 – 1.37 (m, 1H), 1.29 – 1.23 (m, 1H), 0.98 (d, *J* = 6.4 Hz, 3H). ^{13}**C NMR** (126 MHz, CDCl3) δ 197.67, 165.93, 156.55, 140.36, 136.80, 134.37, 132.01, 129.92, 128.66, 128.35, 128.24, 126.63, 66.84, 64.08, 48.74, 36.71, 35.58, 29.82, 27.01, 25.25, 19.63, 14.49. **IR** (thin film): 3366, 2957, 2923, 1719, 1690, 1521, 1455, 1405, 1357, 1263, 1109, 1016, 960, 769, 739, 696, 612 cm^{-1}.



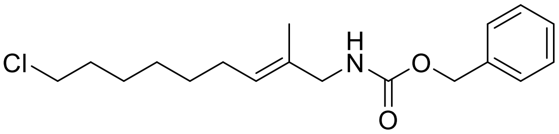
8a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (66 mg, 73%)

^{1}H NMR (500 MHz, CDCl3) δ 8.27 (d, *J* = 8.9 Hz, 2H), 8.19 (d, *J* = 8.9 Hz, 2H), 7.38 – 7.29 (m, 5H), 5.29 (t, *J* = 6.6 Hz, 1H), 5.11 (s, 2H), 4.81 (s, 1H), 4.46 – 4.33 (m, 2H), 3.70 (d, *J* = 5.6 Hz, 2H), 2.13 – 1.96 (m, 2H), 1.88 – 1.77 (m, 1H), 1.65 – 1.57 (m, 5H), 1.46 – 1.36 (m, 1H), 1.32 – 1.21 (m, 1H), 0.98 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 164.84, 156.51, 150.61, 136.74, 135.89, 132.03, 130.74, 128.60, 128.19, 126.42, 123.63, 66.78, 64.54, 48.64, 36.65, 35.47, 29.76, 25.18, 19.55, 14.45. **IR** (thin film): 3345, 3111, 3064, 3032, 2959, 2925, 2871, 1722, 1698, 1608, 1532, 1455, 1410, 1379, 1349, 1320, 1276, 1119, 1103, 1083, 1015, 874, 842, 736, 720, 697 cm^{-1}.



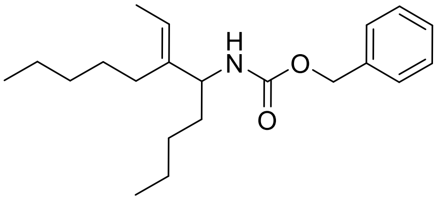
9a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (71 mg, 81%)

^{1}H NMR (500 MHz, CDCl3) δ 7.98 (d, *J* = 8.9 Hz, 2H), 7.38 – 7.29 (m, 5H), 6.91 (d, *J* = 8.9 Hz, 2H), 5.28 (td, *J* = 7.1, 1.1 Hz, 1H), 5.11 (s, 2H), 4.80 (s, 1H), 4.38 – 4.26 (m, 2H), 3.84 (s, 3H), 3.69 (d, *J* = 5.9 Hz, 2H), 2.11 – 1.97 (m, 2H), 1.85 – 1.74 (m, 1H), 1.64 – 1.52 (m, 5H), 1.45 – 1.34 (m, 1H), 1.29 – 1.18 (m, 1H), 0.96 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 166.53, 163.41, 156.55, 136.80, 131.90, 131.63, 128.61, 128.18, 126.71, 123.03, 113.70, 66.77, 63.20, 55.52, 48.71, 36.68, 35.66, 29.77, 25.23, 19.64, 14.44. **IR** (thin film): 3357, 3064, 3033, 2957, 2927, 1720, 1705, 1606, 1538, 1525, 1511, 1455, 1317, 1277, 1258, 1168, 1103, 1029, 848, 771, 697, 614 cm^{-1}.



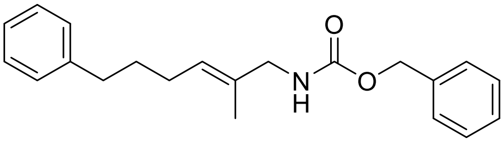
10a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (52 mg, 80%)

^{1}H NMR (500 MHz, CDCl3) δ 7.33 (dd, *J* = 20.9, 4.4 Hz, 5H), 5.28 (t, *J* = 7.2 Hz, 1H), 5.11 (s, 2H), 4.79 (s, 1H), 3.71 (d, *J* = 5.8 Hz, 2H), 3.52 (t, *J* = 6.7 Hz, 2H), 2.00 (q, *J* = 6.9 Hz, 2H), 1.82 – 1.69 (m, 2H), 1.61 (s, 3H), 1.42 (dt, *J* = 14.6, 7.5 Hz, 2H), 1.37 – 1.23 (m, 4H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.51, 136.77, 131.91, 128.60, 128.18, 126.68, 66.76, 48.70, 45.20, 32.66, 29.36, 28.60, 27.64, 26.83, 14.44. **IR** (thin film): 3334, 3089, 3065, 3032, 2931, 2856, 1721, 1717, 1698, 1694, 1537, 1524, 1455, 1346, 1309, 1246, 1138, 1066, 1017, 775, 735, 697, 649 cm^{-1}.



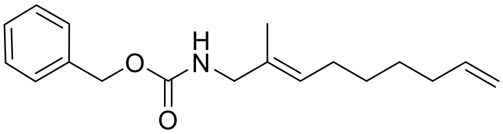
11a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (53 mg, 79%)

^{1}H NMR (500 MHz, CDCl3) δ 7.39 – 7.27 (m, 5H), 5.39 (dd, *J* = 12.9, 6.3 Hz, 1H), 5.08 (s, 2H), 4.68 (d, *J* = 7.8 Hz, 1H), 4.07 – 3.97 (m, 1H), 2.15 – 1.87 (m, 2H), 1.60 (d, *J* = 6.7 Hz, 3H), 1.58 – 1.50 (m, 1H), 1.49 – 1.42 (m, 1H), 1.42 – 1.35 (m, 1H), 1.34 – 1.24 (m, 9H), 0.88 (t, *J* = 6.9 Hz, 6H). **^{13}C NMR** (126 MHz, CDCl3) δ 155.84, 140.68, 136.90, 128.59, 128.19, 128.14, 120.00, 66.63, 56.45, 34.15, 32.30, 28.72, 28.64, 28.51, 22.64, 22.60, 14.17, 14.11, 13.28. **IR** (thin film): 3446, 3328, 3090, 3066, 3033, 2955, 2932, 2859, 1736, 1732, 1694, 1674, 1544, 1540, 1510, 1495, 1467, 1456, 1338, 1251, 1108, 1039, 733, 696 cm^{-1}.



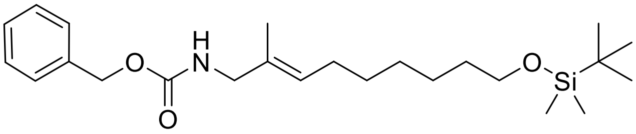
12a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (63 mg, 98%)

^{1}H NMR (500 MHz, CDCl3) δ 7.38 – 7.28 (m, 5H), 7.28 – 7.24 (m, 2H), 7.19 – 7.11 (m, 3H), 5.30 (td, *J* = 7.1, 1.3 Hz, 1H), 5.11 (s, 2H), 4.76 (s, 1H), 3.70 (d, *J* = 5.9 Hz, 2H), 2.59 (t, *J* = 7.8 Hz, 2H), 2.08 – 1.98 (m, 2H), 1.70 – 1.62 (m, 2H), 1.58 (s, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.53, 142.47, 136.77, 132.21, 128.61, 128.52, 128.36, 128.19, 126.42, 125.79, 66.78, 48.68, 35.57, 31.19, 27.37, 14.49. **IR** (thin film): 3415, 3335, 3085, 3063, 3027, 2931, 2857, 1736, 1732, 1722, 1703, 1683, 1674, 1556, 1549, 1537, 1517, 1495, 1455, 1435, 1346, 1247, 1129, 1077, 1058, 1028, 747, 698 cm^{-1}.



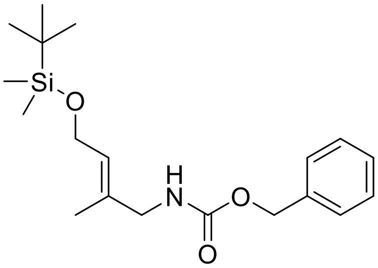
13a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (39 mg, 68%)

^{1}H NMR (500 MHz, CDCl3) δ 7.45 – 7.27 (m, 5H), 5.80 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.29 (td, *J* = 7.2, 1.2 Hz, 1H), 5.11 (s, 2H), 4.99 (ddd, *J* = 17.1, 3.5, 1.6 Hz, 1H), 4.93 (ddt, *J* = 10.2, 2.2, 1.2 Hz, 1H), 4.82 – 4.51 (m, 1H), 3.71 (d, *J* = 5.8 Hz, 2H), 2.04 (dd, *J* = 12.9, 5.9 Hz, 2H), 2.00 (dd, *J* = 13.3, 6.4 Hz, 2H), 1.61 (s, 3H), 1.42 – 1.29 (m, 4H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.54, 139.06, 136.79, 131.85, 128.63, 128.22, 126.86, 114.46, 66.81, 48.76, 33.77, 29.07, 28.67, 27.66, 14.45. **IR** (thin film): 3333, 3066, 3033, 2975, 2927, 2855, 1703, 1640, 1532, 1455, 1346, 1246, 1135, 1063, 993, 909, 776, 752, 735, 697 cm^{-1}.



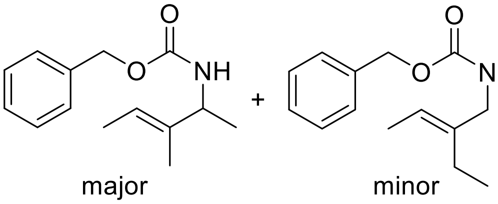
14a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (59 mg, 70%)

^{1}H NMR (500 MHz, CDCl3) δ 7.38 – 7.29 (m, 5H), 5.30 (td, *J* = 7.2, 1.2 Hz, 1H), 5.11 (s, 2H), 4.77 (s, 1H), 3.71 (d, *J* = 5.7 Hz, 2H), 3.60 (t, *J* = 6.6 Hz, 2H), 1.99 (q, *J* = 6.8 Hz, 2H), 1.61 (s, 3H), 1.54 – 1.45 (m, 2H), 1.38 – 1.27 (m, 6H), 0.92 – 0.85 (m, 9H), 0.05 (s, 6H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.54, 136.80, 131.72, 128.62, 128.20, 127.06, 66.79, 63.38, 48.79, 32.95, 29.60, 29.22, 27.77, 26.11, 25.83, 18.49, 14.43, -5.13. **IR** (thin film): 3334, 3066, 3033, 2928, 2856, 1736, 1713, 1683, 1537, 1524, 1471, 1455, 1255, 1101, 1006, 836, 811, 775, 752, 735, 696 cm^{-1}.



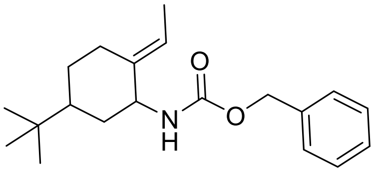
15a. Prepared according to general procedure C and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (46 mg, 66%)

^{1}H NMR (500 MHz, CDCl3) δ 7.38 – 7.30 (m, 5H), 5.46 (td, *J* = 6.2, 1.2 Hz, 1H), 5.11 (s, 2H), 4.80 (s, 1H), 4.20 (d, *J* = 6.1 Hz, 2H), 3.74 (d, *J* = 6.0 Hz, 2H), 1.64 (s, 3H), 0.90 (s, 9H), 0.06 (s, 6H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.55, 136.71, 133.55, 128.67, 128.25, 125.97, 66.92, 60.06, 48.21, 26.13, 18.55, 14.73, -4.99. **IR** (thin film): 3333, 3066, 3033, 2955, 2928, 2885, 2856, 1720, 1703, 1538, 1524, 1474, 1456, 1253, 1111, 1068, 1005, 835, 814, 776, 735, 696 cm^{-1}.



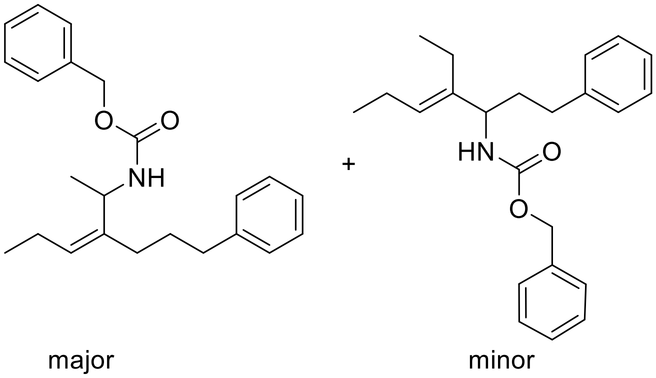
E-17a. Prepared according to general procedure C and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (30 mg, 65%)

^{1}H NMR (500 MHz, CDCl3) δ 7.39 – 7.29 (m, 11H), 5.44 (maj, m, 1.2H), 5.35 (min, q, *J* = 6.8 Hz, 1H), 5.16 – 5.02 (maj + min, m, 4.4H), 4.71 (maj+min, s, 2.2H), 4.17 (maj, s, 1.2H), 3.74 (min, d, *J* = 5.8 Hz, 2H), 2.05 (min, q, *J* = 7.5 Hz, 2H), 1.60 (maj + min, m, 10.2H), 1.21 (maj, d, *J* = 6.8 Hz, 3.6H), 0.98 (min, t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.53, 138.52, 136.82, 128.64, 128.23, 120.67, 119.40, 66.81, 66.71, 53.36, 46.46, 21.48, 20.14, 13.29, 12.97, 12.87. **IR** (thin film): 3329, 3064, 3033, 2968, 2932, 2874, 1703, 1532, 1455, 1325, 1244, 1066, 1028, 776, 736, 696 cm^{-1}.



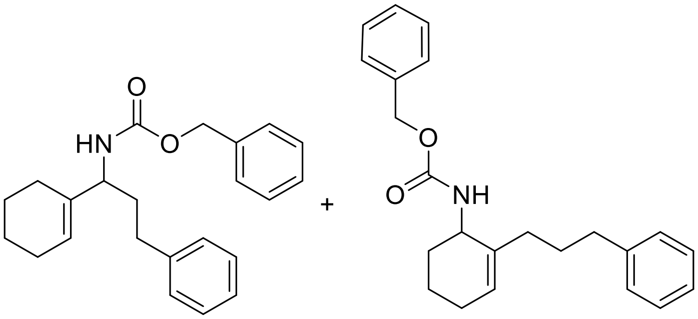
19a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (44 mg, 69%)

^{13}C NMR (126 MHz, CDCl3) δ 155.82, 139.19, 137.61, 136.83, 136.78, 136.72, 128.64, 128.33, 128.29, 128.21, 120.01, 112.25, 66.79, 66.70, 55.69, 54.31, 47.48, 42.68, 37.10, 33.68, 32.46, 32.37, 32.34, 28.81, 27.78, 27.72, 27.66, 27.59, 27.38, 24.13, 12.92, 12.80, 12.57. **IR** (thin film): 3446, 3328, 3089, 3064, 3032, 2952, 2864, 1703, 1524, 1505, 1479, 1455, 1394, 1365, 1337, 1261, 1234, 1085, 1044, 1027, 776, 735, 696 cm^{-1}.



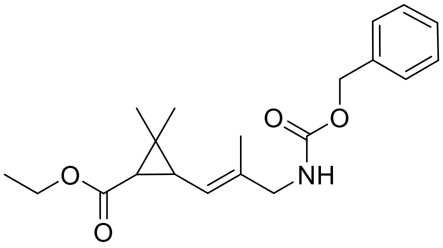
21a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (43 mg, 61%)

^{1}H NMR (500 MHz, CDCl3) δ 7.40 – 7.28 (maj + min, m, 5H), 7.28 – 7.24 (maj + min, m, 2H), 7.17 (maj + min, t, *J* = 6.6 Hz, 3H), 5.36 – 5.26 (maj + min, m, 1H), 5.17 – 5.03 (maj + min, m, 2H), 4.80 – 4.69 (min, m, 0.33H), 4.69 – 4.56 (maj, m, 0.66H), 4.27 – 4.16 (maj, m, 0.66H), 4.16 – 4.05 (min, m, 0.33H), 2.70 – 2.51 (maj + min, m, 2H), 2.12 – 2.00 (maj + min, m, 1H), 1.96 (maj + min, m, 2H), 1.78 – 1.65 (maj + min, m, 2H), 1.21 (maj, d, *J* = 6.6 Hz, 2.4H), 1.03 – 0.91 (maj + min, m, 3.6H). **^{13}C NMR** (126 MHz, CDCl3) δ 155.64, 142.35, 139.86, 136.81, 128.63, 128.53, 128.51, 128.48, 128.40, 128.21, 128.05, 127.43, 126.01, 125.85, 66.69, 51.19, 36.29, 36.22, 32.84, 31.02, 28.66, 21.00, 20.90, 20.65, 14.52, 14.44, 14.13. **IR** (thin film): 3330, 3085, 3063, 3028, 2962, 2932, 2872, 1736, 1721, 1706, 1694, 1544, 1539, 1516, 1498, 1458, 1436, 1404, 1373, 1338, 1238, 1112, 1058, 1028, 775, 748, 698 cm^{-1}.



22a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (32 mg, 46%)

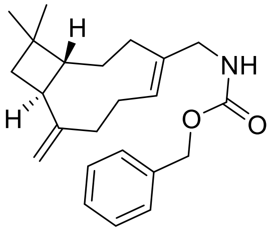
^{1}H NMR (500 MHz, CDCl3) δ 7.40 – 7.29 (maj + min, m, 7.5H), 7.28 – 7.23 (maj + min, m, 3H), 7.20 – 7.12 (maj + min, m, 4.5H), 5.63 (min, s, 0.5H), 5.57 (maj, s, 1H), 5.17 – 5.03 (maj + min, m, 3H), 4.82 – 4.74 (min, m, 0.5H), 4.71 (maj, d, *J* = 9.1 Hz, 1H), 4.21 – 4.13 (maj, m, 1H), 4.11 – 3.98 (min, m, 0.5H), 2.69 – 2.51 (maj + min, m, 3H), 2.14 – 1.41 (m, 15H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.00, 142.55, 136.94, 136.78, 128.65, 128.55, 128.52, 128.49, 128.38, 128.22, 126.07, 126.01, 125.78, 123.54, 66.80, 66.75, 47.79, 35.73, 35.44, 34.08, 32.66, 30.17, 29.73, 25.21, 25.11, 22.79, 22.56, 18.46. **IR** (thin film): 3405, 3325, 3084, 3061, 3027, 2930, 2857, 1701, 1525, 1497, 1453, 1328, 1235, 1119, 1062, 1043, 984, 750, 698 cm^{-1}.



23a. Prepared according to general procedure C and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (48 mg, 69%)

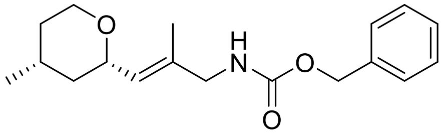
^{1}H NMR (500 MHz, CDCl3) δ 7.39 – 7.28 (maj + min, m, 9H), 5.59 (min, d, *J* = 8.5 Hz, 0.8H), 5.10 (maj + min, s, 3.6H), 5.04 (maj, d, *J* = 7.9 Hz, 1H), 4.85 (maj + min, s, 1.8H), 4.18 – 4.02

(maj + min, m, 3.6H), 3.76 (min, d, *J* = 5.8 Hz, 1.6H), 3.72 (maj, d, *J* = 5.9 Hz, 2H), 2.05 (maj, dd, *J* = 8.1, 5.4 Hz, 1H), 1.85 (min, t, *J* = 8.6 Hz, 1H), 1.73 – 1.68 (maj + min, m, 5.4H), 1.42 (maj, d, *J* = 5.2 Hz, 1H), 1.28 – 1.24 (maj + min, m, 6.9H), 1.25 – 1.19 (maj + min,m, 7.7H) 1.11 (s, 2.4H). ^{13}**C NMR** (126 MHz, CDCl3) δ 172.24, 171.06, 156.58, 156.48, 136.80, 136.70, 135.41, 134.81, 128.60, 128.56, 128.19, 128.12, 127.03, 123.20, 120.87, 66.80, 66.72, 60.39, 59.96, 48.74, 48.34, 35.06, 31.97, 31.56, 31.45, 28.81, 28.64, 26.57, 22.27, 20.43, 15.11, 14.89, 14.80, 14.45, 14.41. **IR** (thin film): 3351, 3065, 3033, 2979, 2951, 1736, 1713, 1694, 1538, 1524, 1455, 1423, 1379, 1237, 1195, 1174, 1143, 1117, 1081, 1064, 1027, 698 cm^{-1}.



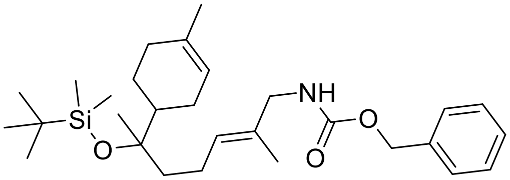
24a. Prepared according to general procedure B and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (44 mg, 62%)

^{1}**H NMR** (500 MHz, CDCl3) δ 7.40 – 7.30 (m, 5H), 5.40 (t, *J* = 8.0 Hz, 1H), 5.11 (s, 2H), 4.82 (s, 1H), 4.74 (s, 1H), 4.69 (s, 1H), 3.75 (dd, *J* = 14.5, 6.1 Hz, 1H), 3.70 (dd, *J* = 14.7, 6.0 Hz, 1H), 2.49 (q, *J* = 9.0 Hz, 1H), 2.33 – 2.25 (m, 2H), 2.25 – 2.12 (m, 2H), 2.09 – 2.02 (m, 1H), 1.85 – 1.76 (m, 1H), 1.75 – 1.66 (m, 1H), 1.62 – 1.51 (m, 2H), 1.50 – 1.40 (m, 1H), 1.32 – 1.20 (m, 1H), 0.98 (d, *J* = 11.9 Hz, 6H). ^{13}**C NMR** (126 MHz, CDCl3) δ 156.53, 155.58, 136.81, 136.74, 128.65, 128.23, 127.32, 110.78, 66.81, 51.98, 46.67, 40.56, 40.27, 35.09, 33.38, 30.10, 29.84, 27.49, 26.49, 25.84, 23.00. **IR** (thin film): 3338, 3066, 3033, 2927, 2859, 1721, 1715, 1524, 1455, 1365, 1328, 1239, 1126, 1043, 1028, 981, 883, 735, 697 cm^{-1}.



25a. Prepared according to general procedure C and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (46 mg, 75%)

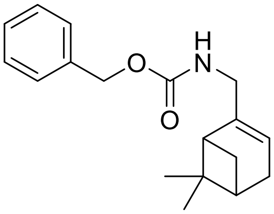
^{1}H NMR (500 MHz, CDCl3) δ 7.40 – 7.28 (maj + min, m, 5.5H), 5.43 (min, d, *J* = 7.7 Hz, 0.1H), 5.31 (maj, d, *J* = 7.9 Hz, 1H), 5.13 – 5.05 (maj + min, m, 2.2H), 4.85 (maj + min, m, 1.1H), 4.38 (min, td, *J* = 8.2, 3.6 Hz, 0.1H), 3.99 (maj, ddd, *J* = 11.3, 9.1, 6.3 Hz, 2H), 3.72 (maj + min, ddd, *J* = 30.8, 15.2, 5.7 Hz, 2.4H), 3.51 – 3.39 (maj, m, 1H), 1.68 (maj + min s, 3.3H), 1.66 – 1.57 (maj + min, m, 1.1H), 1.57 – 1.47 (maj + min, m, 2.2H), 1.20 (maj + min, m, 1.1H), 1.07 – 0.98 (maj + min, m, 1.1H), 0.93 (maj + min, d, *J* = 6.5 Hz, 3.3H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.50, 136.70, 134.95, 128.57, 128.27, 128.20, 128.14, 127.19, 126.37, 125.89, 74.38, 68.92, 67.99, 66.97, 66.80, 48.02, 40.52, 37.96, 34.39, 30.22, 29.78, 24.94, 22.35, 15.04. **IR** (thin film): 3324, 3065, 3033, 2951, 2924, 2868, 2728, 1735, 1732, 1705, 1556, 1541, 1520, 1495, 1458, 1436, 1376, 1330, 1256, 1178, 1168, 1144, 1121, 1087, 1027, 990, 977, 736, 698 cm^{-1}.



26a. Prepared according to general procedure C and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (58 mg, 60%)

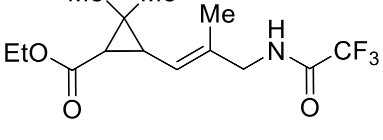
^{1}H NMR (500 MHz, CDCl3) δ 7.39 – 7.29 (m, 5H), 5.38 (s, 1H), 5.26 (s, 1H), 5.16 – 5.01 (m, 2H), 4.77 (d, *J* = 25.6 Hz, 1H), 3.71 (d, *J* = 5.4 Hz, 2H), 2.08 – 1.88 (m, 5H), 1.88 – 1.72 (m, 2H), 1.72 – 1.66 (m, 1H), 1.64 (s, 3H), 1.61 (s, 3H), 1.57 – 1.50 (m, 1H), 1.48 – 1.41 (m, 1H), 1.35 –

1.21 (m, 1H), 1.18 (s, 1.5H), 1.14 (s, 1.5H), 0.87 (s, 9H), 0.08 – 0.05 (m, 6H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.54, 136.79, 134.14, 133.92, 131.64, 128.64, 128.22, 127.11, 127.06, 121.35, 121.08, 66.82, 48.75, 43.45, 42.65, 40.55, 39.73, 31.34, 26.83, 26.71, 26.16, 25.23, 24.72, 23.95, 23.72, 23.49, 22.54, 22.40, 18.63, 18.60, 14.45, -1.67, -1.69, -1.71, -1.74. **IR** (thin film): 3446, 3335, 3066, 3032, 2955, 2927, 2855, 1716, 1698, 1519, 1471, 1455, 1375, 1359, 1254, 1178, 1133, 1049, 1004, 834, 802, 771, 734, 696 cm^{-1}.



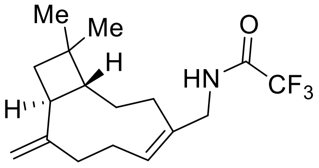
27a. Prepared according to general procedure C and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (42 mg, 74%)

^{1}H NMR (500 MHz, CDCl3) δ 7.39 – 7.27 (m, 5H), 5.39 (s, 1H), 5.10 (s, 2H), 4.71 (s, 1H), 3.70 (d, *J* = 3.7 Hz, 2H), 2.37 (dt, *J* = 8.6, 5.6 Hz, 1H), 2.24 (q, *J* = 17.7 Hz, 2H), 2.12 – 1.98 (m, 2H), 1.27 (s, 3H), 1.14 (d, *J* = 8.6 Hz, 1H), 0.81 (s, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 156.57, 144.79, 136.79, 128.69, 128.64, 128.23, 118.61, 100.11, 67.11, 66.82, 53.55, 46.04, 44.05, 40.92, 38.14, 31.68, 31.23, 26.24, 21.16. **IR** (thin film): 3337, 3065, 3033, 2916, 2832, 1716, 1698, 1694, 1519, 1455, 1331, 1243, 1045, 1029, 736, 697 cm^{-1}.



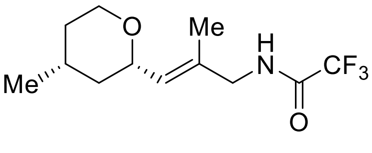
23k. Prepared according to general procedure D and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (46 mg, 75%)

^{1}H NMR (500 MHz, CDCl3) δ 6.44 (min, s, 0.6H), 6.38 (maj, s, 1H), 5.67 (min, d, *J* = 8.5 Hz, 0.6H), 5.13 (maj d, *J* = 8.3 Hz, 1H), 4.19 – 4.05 (maj + min, m, 3.6H), 3.93 (min, t, *J* = 6.9 Hz, 1.2H), 3.90 (maj, d, *J* = 6.0 Hz, 2H), 2.10 – 2.02 (maj, m, 1H), 1.90 – 1.82 (min, m, 0.6H), 1.75 (s, 3H), 1.72 (min, s, 2.4H), 1.47 (maj, d, *J* = 5.7 Hz, 1H), 1.27 (maj + min, m, 7.2H), 1.23 (maj + min, m, 4.8H), 1.15 (maj, s, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 172.05, 171.09, 157.45, 157.16, 132.98, 132.50, 126.00, 123.63, 117.16, 114.87, 60.58, 60.16, 47.44, 47.19, 35.25, 31.81, 31.26, 28.78, 26.80, 22.32, 20.46, 15.15, 14.96, 14.78, 14.50, 14.44.



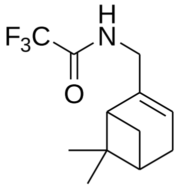
24k. Prepared according to general procedure D and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (31 mg, 49%)

^{1}H NMR (500 MHz, CDCl3) δ 6.21 (s, 1H), 5.46 (t, *J* = 8.1 Hz, 1H), 4.85 (d, *J* = 1.7 Hz, 1H), 4.77 – 4.73 (m, 1H), 3.94 – 3.80 (m, 2H), 2.49 (q, *J* = 9.2 Hz, 1H), 2.38 – 2.15 (m, 5H), 2.05 (ddd, *J* = 13.9, 7.8, 4.2 Hz, 1H), 1.79 (ddd, *J* = 11.8, 9.4, 4.0 Hz, 1H), 1.73 (dd, *J* = 10.8, 8.7 Hz, 1H), 1.63 – 1.54 (m, 2H), 1.53 – 1.41 (m, 1H), 1.00 (s, 3H), 0.98 (s, 3H). **IR** (thin film): 3304, 3074, 2949, 2929, 2862, 1705, 1557, 1455, 1366, 1208, 1183, 1164, 885, 732, 518 cm^{-1}.



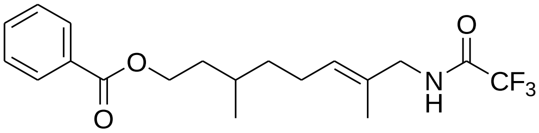
25k. Prepared according to general procedure D and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (43 mg, 81%)

^{1}H NMR (500 MHz, CDCl3) δ 6.57 (maj, s, 1H), 6.40 (min, s, 0.1H), 5.46 (min, d, *J* = 7.8 Hz, 0.1H), 5.34 (maj, d, *J* = 7.9 Hz, 1H), 4.39 (min, t, *J* = 8.3 Hz, 0.1H), 4.08 – 3.95 (maj, m, 2H), 3.90 (maj + min, d, *J* = 5.6 Hz, 2.2H), 3.79 – 3.69 (min, m, 0.2H), 3.47 (maj, t, *J* = 12.0 Hz, 1H), 1.71 (maj + min, s, 3.3H), 1.69 – 1.61 (maj + min, m, 1.1H), 1.61 – 1.50 (maj + min, m, 2.2H), 1.29 – 1.16 (maj + min, m, 1.1H), 1.13– 0.98 (maj + min, m, 1.1H), 0.95 (maj + min, d, *J* = 6.4 Hz, 3.3H). **^{13}C NMR** (126 MHz, CDCl3) δ 157.57, 157.27, 132.86, 129.23, 128.69, 117.15, 114.86, 74.30, 68.88, 68.06, 62.54, 46.85, 46.69, 40.36, 37.80, 34.33, 32.20, 30.19, 28.79, 28.44, 24.92, 22.32, 18.93, 15.12, 15.02. **IR** (thin film): 3298, 3092, 2953, 2927, 2872, 1713, 1557, 1458, 1442, 1376, 1257, 1179, 1075, 1033, 991, 978, 724, 656, 519 cm^{-1}.



27k. Prepared according to general procedure D and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (33 mg, 67%)

^{1}H NMR (500 MHz, CDCl3) δ 6.27 (s, 1H), 5.53 – 5.43 (m, 1H), 3.87 (d, *J* = 5.8 Hz, 2H), 2.42 (dt, *J* = 8.7, 5.6 Hz, 1H), 2.28 (q, *J* = 18.0 Hz, 2H), 2.12 (ddd, *J* = 5.7, 2.9, 1.8 Hz, 1H), 2.05 (td, *J* = 5.6, 1.5 Hz, 1H), 1.29 (s, 3H), 1.17 (d, *J* = 8.8 Hz, 1H), 0.82 (s, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 157.41, 157.12, 142.68, 120.66, 117.19, 114.90, 44.55, 44.18, 40.75, 38.19, 31.62, 31.30, 26.13, 21.14. **IR** (thin film): 3447, 3304, 3100, 2989, 2920, 2835, 1720, 1705, 1561, 1557, 1432, 1367, 1260, 1209, 1184, 1163, 725 cm^{-1}.



4k. Prepared according to general procedure D and purified by silica gel chromatography (95:5 to 80:20, hexanes: ethyl acetate) to afford the product as a clear oil (49 mg, 66%)

^{1}H NMR (500 MHz, CDCl3) δ 8.06 – 8.00 (m, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.44 (dd, *J* = 10.9, 4.8 Hz, 2H), 6.45 (s, 1H), 5.35 (td, *J* = 7.1, 1.2 Hz, 1H), 4.44 – 4.28 (m, 2H), 3.92 – 3.79 (m, 2H), 2.15 – 1.99 (m, 2H), 1.85 – 1.76 (m, 1H), 1.70 – 1.56 (m, 5H), 1.50 – 1.41 (m, 1H), 1.32 – 1.22 (m, 1H), 0.98 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 166.86, 157.47, 157.17, 133.05, 130.54, 129.86, 129.62, 129.04, 128.50, 117.21, 114.92, 63.49, 47.39, 36.43, 35.60, 29.76, 25.33, 19.68, 14.42. **IR** (thin film): 3320, 3092, 2960, 2927, 2873, 1716, 1699, 1555, 1452, 1389, 1363, 1315, 1277, 1208, 1178, 1115, 1071, 1027, 713, 687, 676 cm^{-1}.

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Chapter 4. DIAMINATION OF ALKENES[1]

Section 1: INTRODUCTION

Alkenes are highly valuable chemical feedstocks for the synthesis of biologically active molecules, valuable drug candidates, and useful materials. The difunctionalization of these alkenes is most rapid path for the development of this molecular complexity allowing for the installation of two functionalities at once.[2]

Our lab has taken an interest in the transformation of alkenes enabled by the development of novel catalytic modes of reactivity for selenium. In this vein, we envisioned that we could utilize our understanding of selenium catalysis to realize a novel method for the difunctionalization of alkenes. As a launching point for this ambitious goal we turned to the electrophilicity of seleniranium species generated from selenium and alkenes under oxidative conditions.

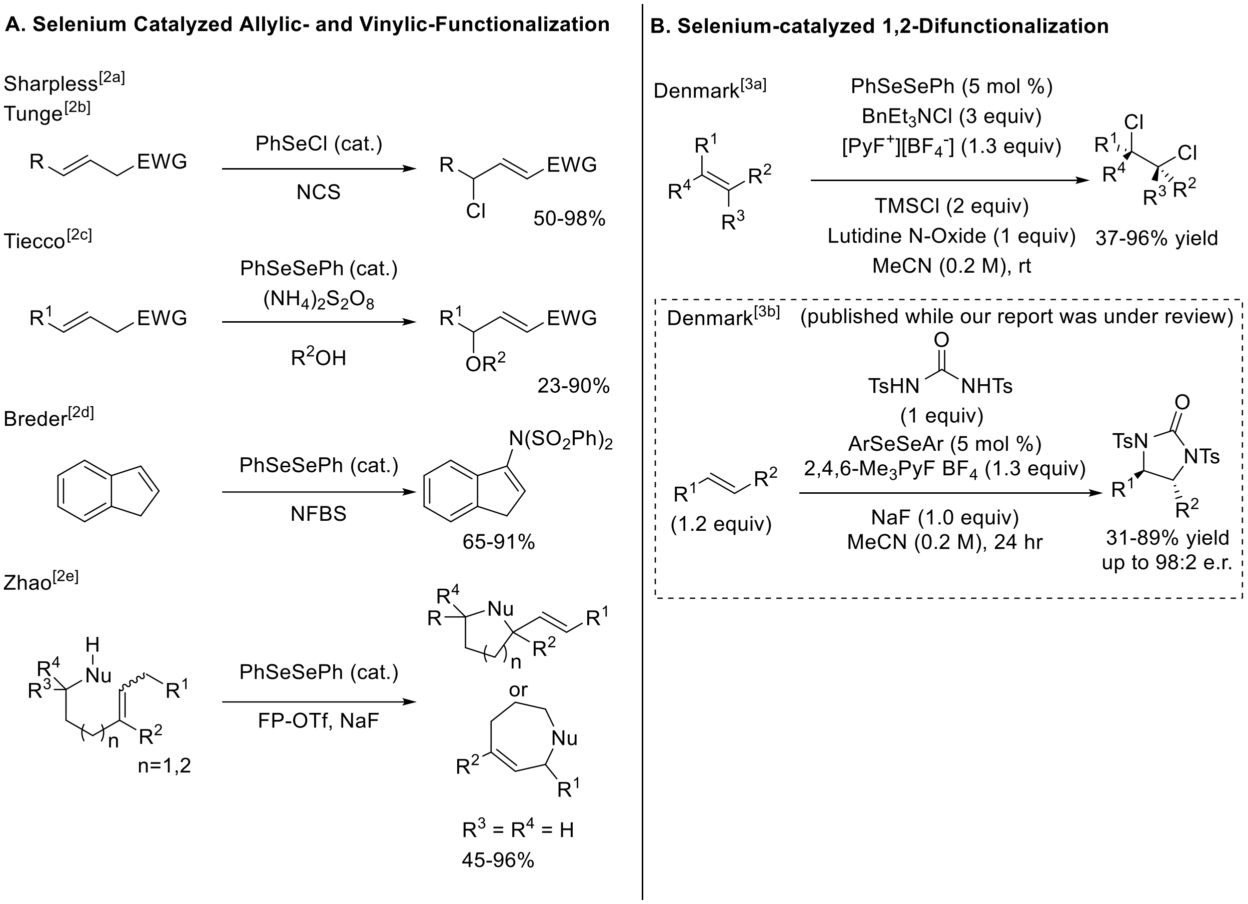


Figure 4.1. Previously reported transformations proceeding through seleniranium ions

Historically, these seleniranium species have been utilized to undergo an addition elimination sequence leading to allylic or vinylic alkene functionalizations. Our group and others have utilized this mode of reactivity to achieve and extensive number of mono-functionalization reactions of alkenes (Figure 4.1A).[3] Despite the advancements in this area, favoring the substitution of the organoselenide intermediate over its elimination has proven elusive. In fact, at the time of our report, the syn dichlorination of alkenes developed by Denmark and coworkers was the only catalytic method in which a nucleophile successfully displaced an organoselenide to achieve a difucntionalization of alkenes (Figure 4.1B).[4]

The main obstacle to achieving difunctionalization reactions in favor of going through the traditional elimination pathway is making the relatively slow intermolecular substitution of the organoselenide intermediate occur faster than the rapid intramolecular elimination. To achieve this goal, we envisioned a two-pronged strategy: utilize a novel class of phosphine selenide catalysts to encourage substitution and simultaneously remove basic reaction components to suppress elimination (Figure 4.2).

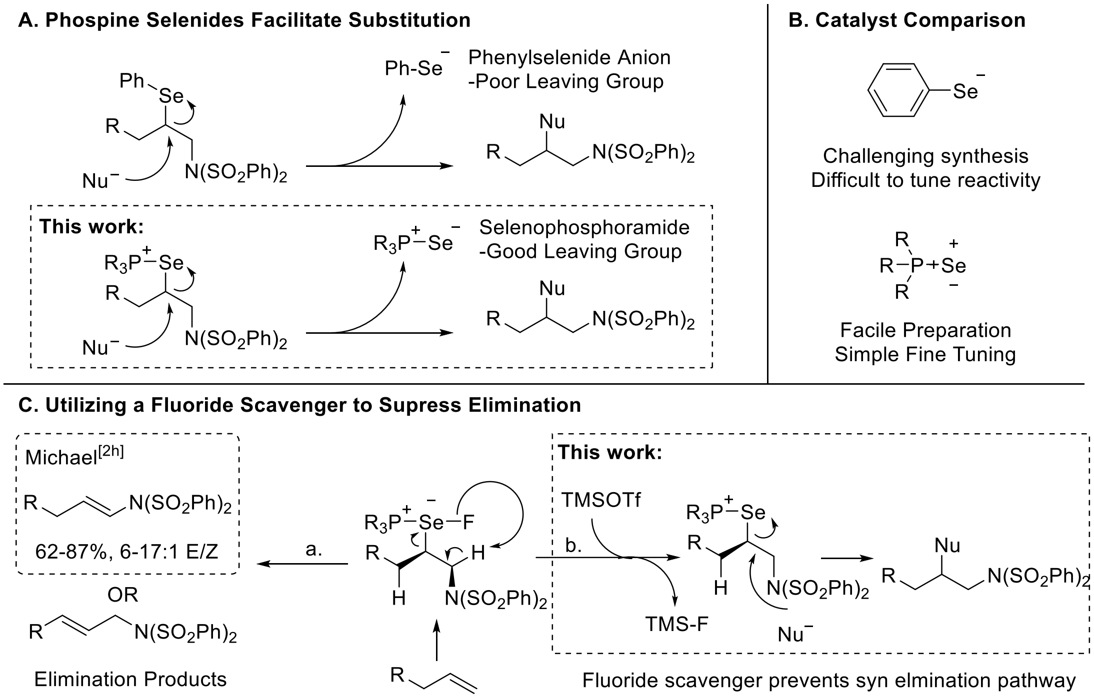


Figure 4.2. Strategy to achieve substitution over elimination

To facilitate substitution, we envisioned utilizing the phosphine selenide catalysts developed in our laboratory. Traditionally, seleniranium reactions utilize diaryl diselenides as catalysts.[3a, 3d-g] In order to achieve a diaddition using these catalysts, substitution of an aryl selenide would be required. Inherently, these are poor leaving groups. Additionally, attempts to alter the chemical properties of these catalysts to improve their leaving group ability are met with a significant synthetic hurdle since any alteration the catalyst must be achieved through functionalization of the aryl moiety (Figure 4.2B). We envisioned that utilizing our phosphine selenides catalysts could bypass both issues: not only are phosphine selenides inherently better leaving groups than aryl selenides (Figure 4.2A), but they are also operationally easy to fine tune since the phosphine component can readily be swapped out (Figure 4.2B).

To suppress the elimination pathway, we envisioned intercepting the basic component responsible for the elimination (Figure 4.2C). We imagined this species would vary depending on the reaction components and decided to investigate a selenium catalyzed vinyl amination reaction previously developed in our lab.[3h] A key mechanistic step in this reaction was the syn-elimination of the selenium-fluorine bond leading to the formation of the vinyl amine products, a step isoelectronic to the well-studied selenoxide elimination.[5] We hypothesized that removing or replacing the fluoride with something less basic might suppress the intramolecular elimination pathway entirely allowing the desired intermolecular substitution to occur.

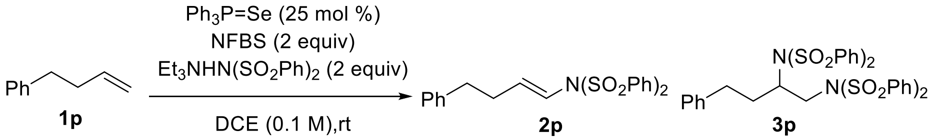
We decided to utilize this strategy to achieve a 1,2-diamination of alkenes. These highly valuable vicinal amine moieties can be found in natural products, drug candidates, materials, and ligands.[6] Despite the widespread use of these products, there are few catalytic fully intermolecular methods for their synthesis from alkenes[7] and most existing methods suffer from limited compatibility or require the use of highly engineered substrates.[8] We decided to pursue a broadly applicable protocol for 1,2-diamines as a demonstration of the potential of this novel mode of catalytic selenium reactivity.

Section 2: RESULTS AND DISCUSSION

4.2.1 *Initial Optimization*

The initial optimization for this reaction was completed by my collaborator John Tabor and the two most important aspects of that optimization will be covered in the following subsection. First, our hypothesis that utilizing a fluoride scavenger would prevent the elimination pathway facilitating a diamination of alkenes was confirmed. Subjecting 4-phenyl-1-butene to catalytic phosphine selenides with N-fluorobenzenesulfonimide as the oxidant in the presence of exogenous benzenesulfonimide nucleophile resulted in significant formation of the vinyl amine product (**2p**) with no observed yield of the desired diamine (**3p**) (Table 4.1, entry 1). However, with the addition trimethylsilyl trifluoromethansulfonate (TMSOTf) as a fluoride scavenger, the fluoride promoted elimination was indeed suppressed and the diamine (**3p**) was obtained in 35% yield and no observed vinyl amination (Table 4.1, entry 2).

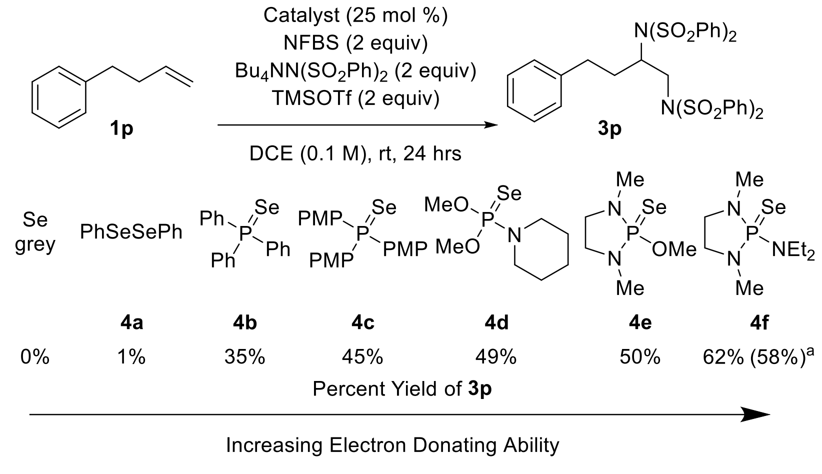
Table 4.1. TMSOTf Suppresses Elimination and Favors Diamination



Entry	TMSOTf (equiv)	%Yield[a] 2p	%Yield[a] 3p
1	0	63	0
2	2	0	35

[a]Yield determined using 1,3-dinitrobenzene as an internal standard

The second major discovery was that while the addition of TMSOTf dictated the chemoselectivity of the reaction, the yields of the desired diamines were highly dependent on the nature of the phosphine selenide catalyst. Desired product formation was improved as the electron donating ability of the phosphine ligand increased with the highly electron donating phosphoramide ligand (**4f**) providing the desired product in the highest yield of those tested (Figure 4.3). Additionally, the catalyst loading for this system could be reduced to 10 mol % minimal impact on the reactivity.



[a]10 mol % catalyst

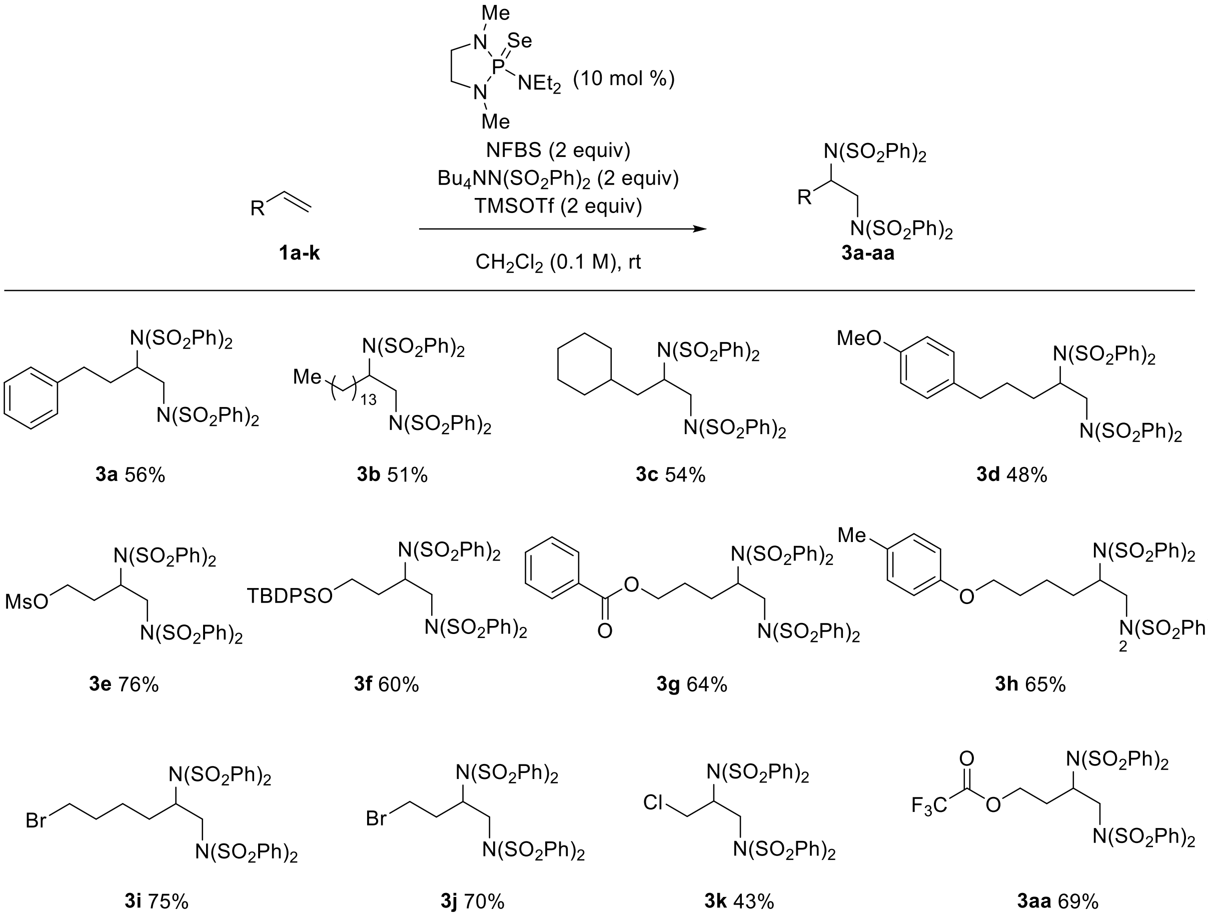
Figure 4.3. Yield of Diamination is Dependent on Phosphine Ligand

To further highlight the important role of the phosphine ligand in this transformation, control reactions were run using commercially available selenium grey and the most utilized organoselenium catalyst, diphenyldiselenide (Ph_2Se_2, **4a**), as catalysts for this reaction in the presence of the fluoride scavenger. Indeed, no meaningful amount of product was observed for either reaction. Further control studies revealed the importance of each reaction component revealing a suppression of desired reactivity when any component was left out of the reaction.

4.2.2 *Investigation of the Scope*

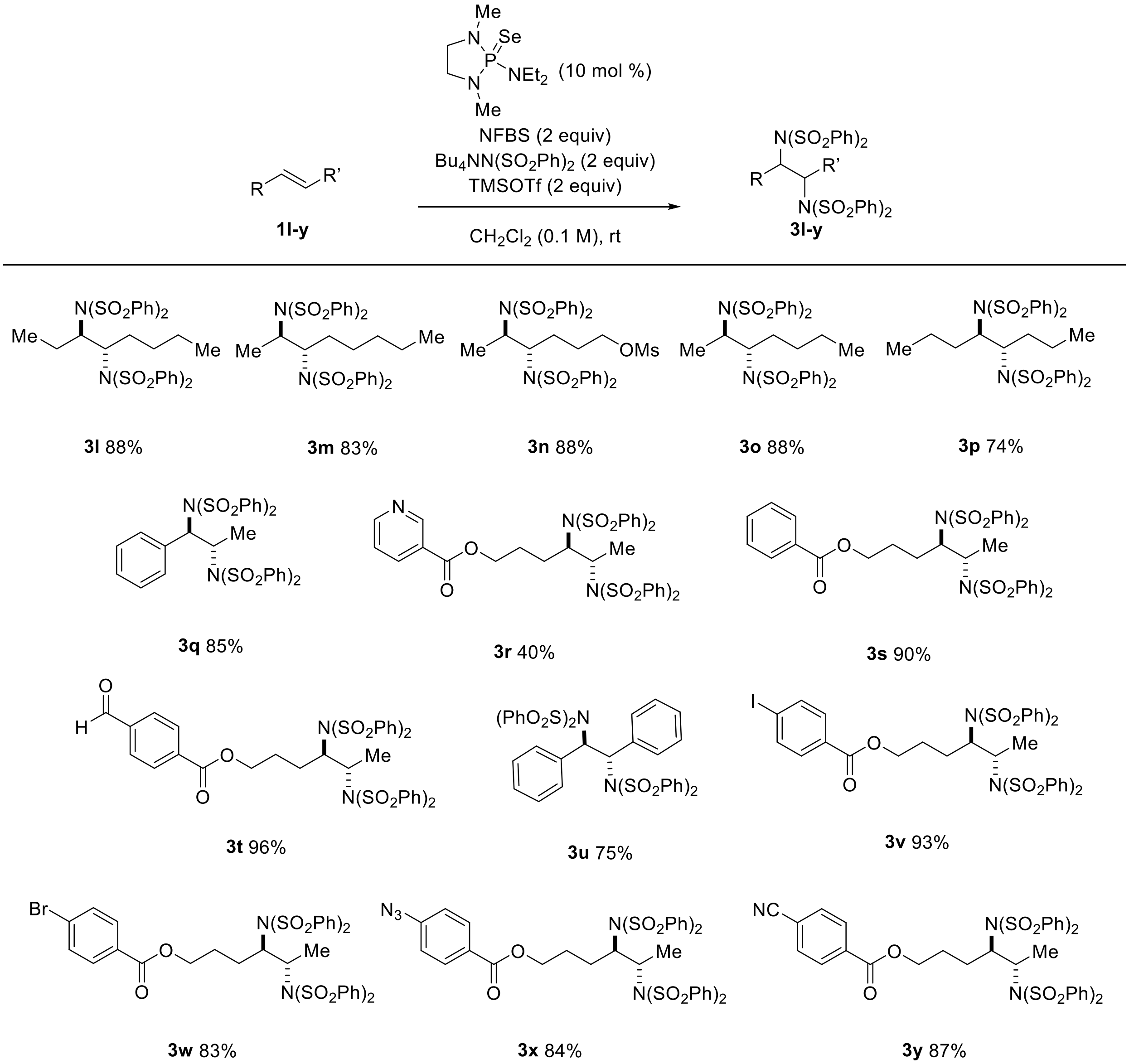
I was initially brought on to this project to help investigate the scope of the reaction. With the optimized conditions in hand, we began by investigating the scope of terminal alkenes. Numerous terminal alkenes were successfully employed in this reaction affording the desired diamines in moderate to good yields (Table 4.2). The reaction conditions were tolerant of numerous functional groups including esters (**3g**), ethers (**3d**, **3h**), silyl ethers (**3f**), sulfonates (**3e**), and alkyl bromides (**3i**, **3j**). It is worth noting that ally chloride (**3k**) could be employed in this reaction offering orthogonality to transition metal catalysis.

Table 4.2. Terminal Alkene Scope



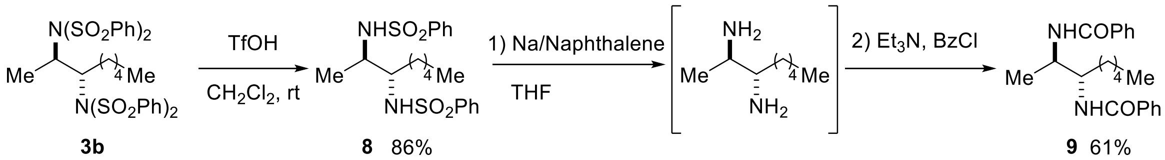
We then began to investigate the reaction on internal alkenes and were pleased to discover that these typically provided improved yields of the desired diamines relative to the terminal substrates (Table 4.3). Unactivated (**3l** – **3p**) and styrenyl (**3q**, **3u**) alkenes provided the products in excellent yields. We observed an expansion of the tolerated functional groups including aldehydes (**3t**), cyano groups (**3y**) and heteroaromatics (**3r**). Pleasingly, substrates containing aryl halides (**3v**, **3w**), and azides (**3x**) were successfully employed offing further orthogonal reactivity to traditional transition metal approaches and paving the way for subsequent functionalization.

Table 4.3. Internal Alkene Scope



In every case where (E)-alkenes were employed we observed excellent diastereoselectivity for trans diamination with no detectable amounts of the syn isomers.[7e] Subjecting (Z)-alkenes to the reaction conditions resulted in successful diamination but a significant reduction in diastereoselectivity. While 1,2-olefins provided high yields of the desired diamines, we found more highly substituted alkenes were incompatible substrates with little to no diamination observed to tri- or tetra- substituted alkenes.

Scheme 4.1. *Stepwise Deprotection of the Diamination Products*



To demonstrate the synthetic utility of this protocol a stepwise deprotection of the sulfonamide groups was performed. Treating an isolated dibenzenesulfonimide product (**3a**) with triflic acid in dichloromethane resulted in the successful mono-deprotection to the desired bis-sulfonamide (**8**).[9] A second, subsequent deprotection could be accomplished utilizing sodium and naphthalene to obtain the free diamine.[7f] This desired diamine was converted to the bis-benzamide (**9)** *in situ* to facilitate isolation and characterization.

4.2.3 *Proposed Mechanism*

Based on literature precedent as well as work previously reported by our lab[3h], we propose the following plausible mechanism for this reaction (Figure 4.4): Oxidative addition of NFBS to the phosphine selenide precatalyst (**I**) and fluoride scavenging by the TMSOTf generates the selenium species, **II**, which can be thought of as a Se (II) species with a coordinated phosphine ligand. Similar species have been isolated and characterized by X-ray crystallography.[10] Dissociation of benzenesulfonaimide anion and concomitant addition of the alkene to this complex results in seleniranium ion, **III**. The seleniranium ion (**III**) is then opened by attack of the benzenesulfonimide anion resulting in the alkyl selenium species, **IV**. The typical elimination of this phosphine selenide to afford the vinyl amine is suppressed by the removal of the basic fluoride anion by TMSOTf allowing for the diaddition pathway to proceed. While the most direct route to the desired product from intermediate, **IV**, would involve displacement of the phosphine selenide by a second equivalent of benzenesulfonimide anion, this route would lead to a net syn addition of sulfonamide for E alkenes. Instead we suggest that the phosphine selenide is displaced from intermediate, **IV**, by one of the sulfonimide oxygens leading to the cyclized intermediate, **V**. This cyclized intermediate is then opened by a second benzenesulfonimide anion leading to the products with the observed trans stereochemistry of addition. A similar intramolecular explanation has been used by Muniz and coworkers to explain their observed trans addition of sulfonimides to alkenes.[7e]

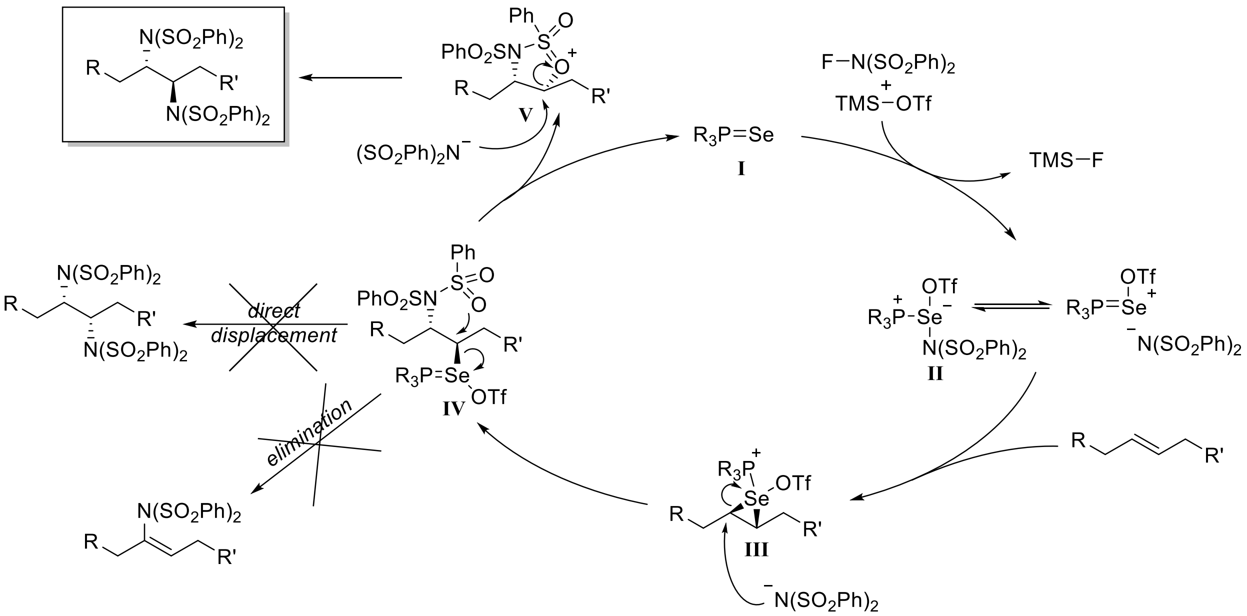


Figure 4.4. Plausible Mechanisms for Selenium Catalyzed Diamination of Alkenes

One of the important aspects of this reaction is the use of TMSOTf to suppress the typical elimination pathway. Leaving out TMSOTf results in exclusively vinyl amination while adding TMSOTf facilitates the diamination. We hypothesize that the TMSOTf acts as a fluoride scavenger preventing the basic fluoride from eliminating the phosphine selenide from complex **IV**, which would lead to the vinyl amination product (Figure 4.2C). We envisioned multiple opportunities where this fluoride scavenging could occur. It is possible that the TMSOTf could directly react with the N-fluorobenzenesulfonimide (NFBS) leading to the formation of N-trifluoromethanesulfonyl benzenesulfonimide (N(OTf)BS) and that this species could oxidize the phosphine selenide precatalyst leading directly to complex **II** (Figure 4.5A). Alternatively, we envisioned that NFBS could oxidize phosphine selenide precatalyst leading to intermediate **II’** and that this complex reacts with the TMSOTf either before or after seleniranium formation (Figure 4.5B).

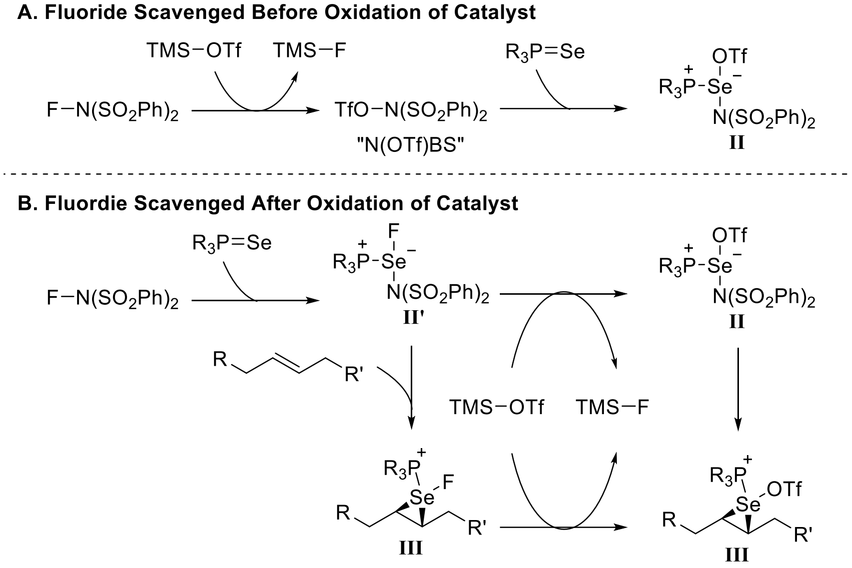


Figure 4.5. Possible Opportunities for Fluoride Scavenging

We attempted to distinguish between these two pathways by independently synthesizing N(OTf)BS and utilizing it as the oxidant in this reaction in place of NFBS. Unfortunately, our attempts to synthesize this reagent revealed it to be highly hygroscopic and too reactive to reliably purify and utilize.

4.2.4 *Rearrangements and Cyclizations*

While we were investigating the scope of this reaction, we became curious what would happen for alkenes with pendant nucleophiles. We subjected homoallylic trifluoro acetate to the reaction conditions and obtained 69% of the typical diamination product **3aa** as well as 16% of a rearranged diamine product **5aa**. In order to explain the formation of this new product, we revisited our proposed mechanism (Figure 4.6).

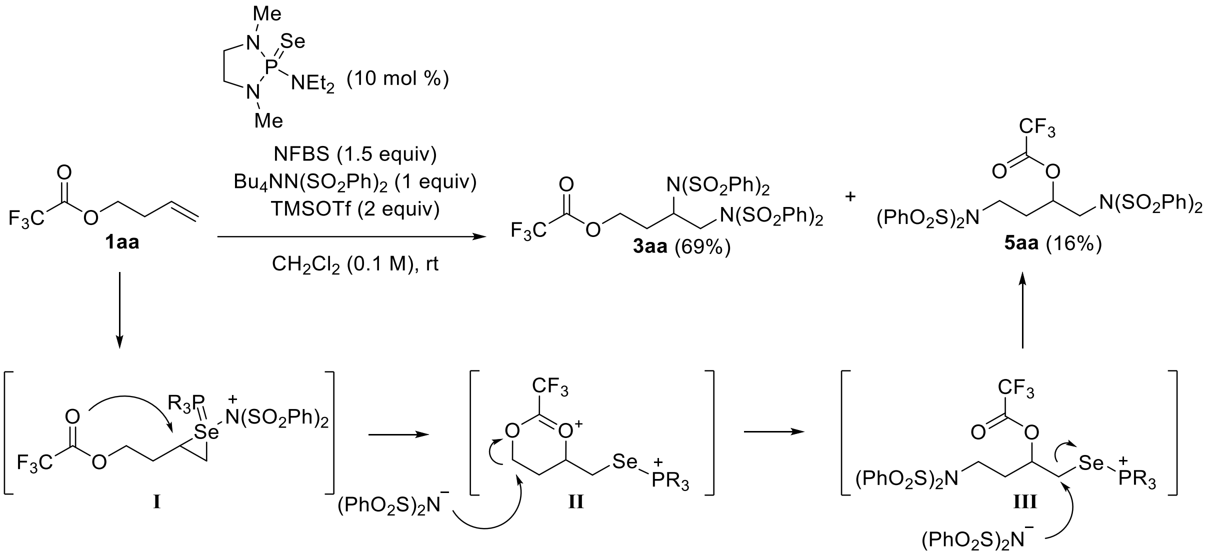
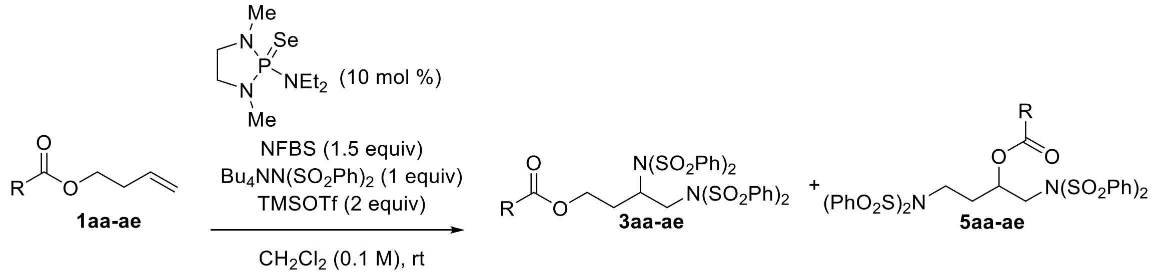


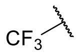
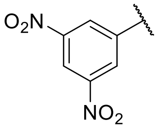
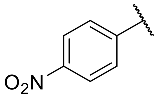
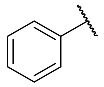
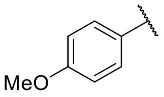
Figure 4.6. Plausible Mechanisms for Ester Rearrangement.

After formation of the seleniranium ion (**I**) by the oxidized selenium catalyst, intramolecular attack of the pendant ester, rather than the previously observed intermolecular attack of a benzenesulfonamide anion, affords cyclized intermediate, **II**. This intermediate is then opened by intermolecular attack of the benzenesulfonamide anion at the less sterically hindered carbon affording alkyl selenide **III**. Finally, nucleophilic substitution of the phosphine selenide affords the rearranged diamine product (**5aa**).

Consistent with our proposed mechanism, we hypothesized increasing the nucleophilicity of the ester would increase the formation of the rearranged product (Figure 4.6). To probe this idea, we subjected a series of electronically varied esters to these reaction conditions (Table 4.4).

Table 4.4. Screen of Electronically Varied Ester Substrates

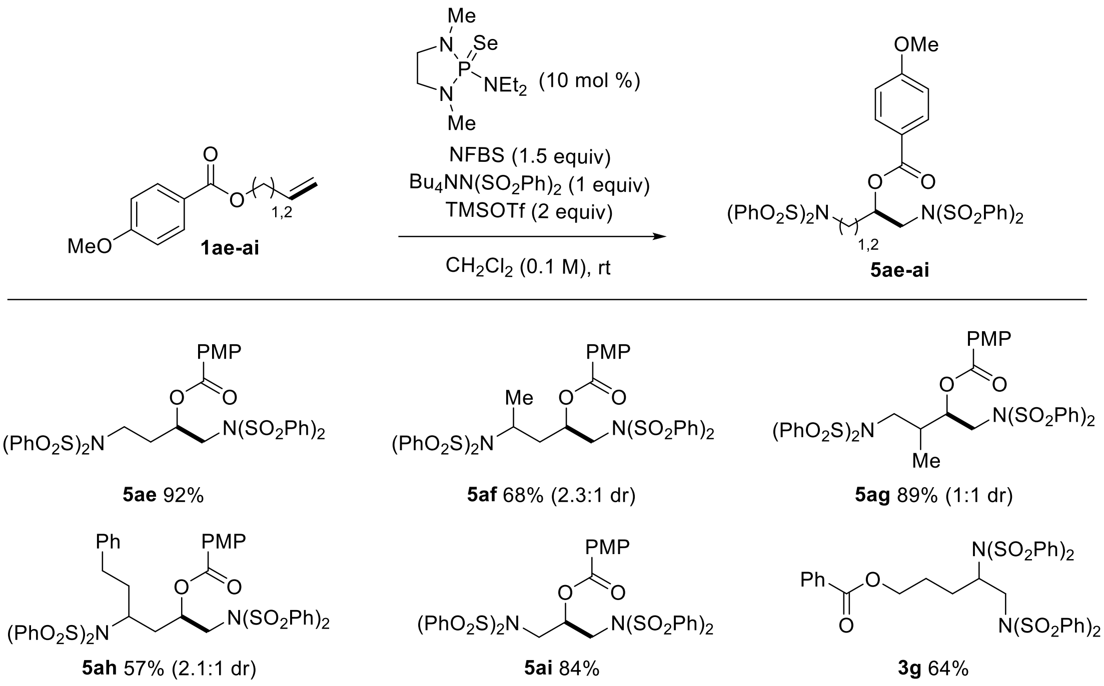


Entry	Starting Material	R =	%Yield[a] Diaddition (**3**)	%Yield[a] Rearrangement (**5**)
1	**1aa**		69	16
2	**1ab**		45	25
3	**1ac**		40	50
4	**1ad**		15	66
5	**1ae**		-	100

[a] Yield determined using 1,3-dinitrobenzene as an internal standard

Indeed, for electronically poor esters (Table 4.4, entries 1 and 2), we observed higher conversion to the standard diamine while electron richer esters afforded significantly more rearrangement (Table 4.4, entries 3-5) with paramethoxybenzoate giving exclusively the rearranged product (Table 4.4, entry 5). We realized this method for rearrangement could be utilized to furnish a variety of highly valuable 1,3-diamino-2-alcohol and 1,4-diamino-2-alcohol derivatives[11] and would serve as a compliment to existing methods for amino alcohol synthesis.[12] To that end, we subjected several homoallylic paramethoxybenzoate esters bearing a variety of substitution patterns to these reaction conditions (Table 4.5).

Table 4.5. Ester Rearrangement Scope



1ae-ai

5ae-ai

5ae 92%

5af 68% (2.3:1 dr)

5ag 89% (1:1 dr)

5ah 57% (2.1:1 dr)

5ai 84%

3g 64%

Isolated Yields.

We obtained the best yields for the unsubstituted homoallylic ester (**5ae**), but we found the reaction was tolerant of both alpha (**5ag**), and beta substitution (**5af**, **5ah**) with respect to the alkene. Next, we decided to probe the effects of the carbon chain length on this reactivity. We observed that the allylic ester readily underwent the expected rearrangement (**5ai**) but that increasing the chain length resulted in exclusive formation of the standard diamine (**3g**).

Inspired by the success of this rearrangement protocol, we decided to subject homoallylic carbonates to these reaction conditions in hopes of obtaining cyclized products via carbonate attack of the seleniranium ion (**I**) and subsequent dealkylation (Figure 4.7).

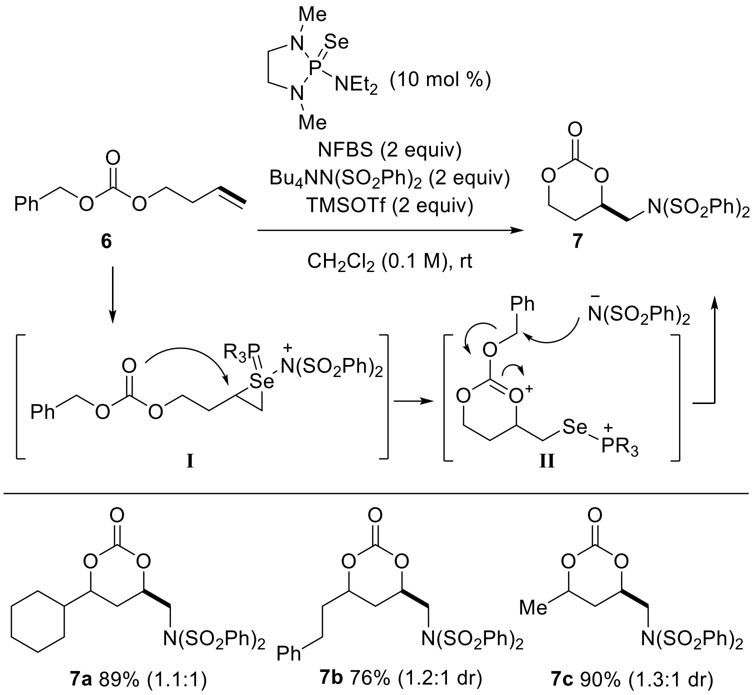


Figure 4.7. Plausible Mechanisms and Scope for Carbamate Cyclizations.

Probing a variety of homoallylic carbonates we observed the highest yields for cyclization utilizing benzyl carbonate. We screened a few homoallylic carbonates bearing this group and obtained high yields for each. We found that the reaction was tolerant of a variety of substituents in the beta position relative to the alkene **(7a – 7c)** including a bulky cyclohexyl group.

Section 3: CONCLUSION

A novel selenium catalyzed 1,2-diaddition of alkenes has been developed. Key to the success of this transformation was the use of TMSOTf as a fluoride scavenger, preventing the addition/elimination pathway typically observed for oxidative selenium alkene reactions. Careful tuning of the electronics of the phosphine ligand of the selenium species proved to be critical for achieving high yields for this transformation with phosphoramide ligands proving the most successful. An extensive variety of terminal and 1,2-disbstituted alkenes underwent the desired diamination reaction in great yields. The products obtained demonstrated exclusively trans-addition of the nucleophiles. The reaction was tolerant of a variety of function groups including those orthogonal to traditional transition metal catalysis. An intramolecular substitution could be achieved for substrates bearing pendant esters and carbamates resulting in rearranged diamines and cyclized oxy amination products respectively. The bis-sulfonimide products could selectively be deprotected to afford either the bis-sulfonamide or the free diamine products further demonstrating the synthetic utility of the products.

Section 4: EXPERIMENTAL

4.4.1 *General Procedures and Materials*

General Procedures. All reactions were performed under a nitrogen atmosphere using flame-dried glassware unless otherwise indicated. Infrared spectra were acquired using a Perkin Elmer Spectrum RX I Spectrometer. Mass spectra were acquired using a Bruker Esquire 1100 Liquid Chromatograph-Ion Trap Mass Spectrometer or a Hewlett Packard 5971A Gas Chromatograph - Mass Spectrometer. Column chromatography was performed using silica gel (Whatman, 60 Å, 230-400 mesh). NMR spectra were recorded on a Bruker AV-300, AV-301, DRX-499 or AV-500 Spectrometer. ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) and are referenced relative to TMS (0.0 ppm), residual CHCl3 (7.26 ppm), CH_2Cl_2 (5.32 ppm) or acetone (2.05 ppm). ^{13}C NMR chemical shifts (δ) are reported in parts per million (ppm) relative to the carbon resonance of CDCl3 (77.16 ppm), CD2Cl2 (53.84 ppm) or acetone-d6 (29.84 ppm). Melting points were taken on a MEL-TEMP melting point apparatus and are uncorrected.

Materials. All commercial reagents were used as received, unless otherwise noted. All solvents were degassed and dried on solvent columns of neutral alumina. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc., stored over 4Å molecular sieves, and were used without further purification. 2-methyl-3-buten-1-ol, 4-phenyl-1-butene, beta-methylstyrene, 6-bromo-1-hexene, 1-hexadecene, allylcyclohexane, 4-octene, 3-octene, 2-octene, 2-heptene, allyl chloride, trans-stilbene, 4-bromo-1-butene and *N*-fluorobenzenesulfonimide were purchased from commercial sources and used without further purification. Trimethylsilyl trifluoromethanesulfonate was purified by vacuum distillation and stored under an atmosphere of nitrogen. 4-[(Tert-butyldiphenylsilyl)oxy]-1-butene[13], 5-(4-methoxyphenyl)-1-pentene[14], 6-(4-methylphenyl)-1-hexene[3h], trans-4-hexenyl benzoate[15], 4-pentenyl benzoate[16], allyl p-methoxybenzoate[17], homoallyl p-methoxybenzoate[18], (2-methyl-3-butenyl)-p-methoxybenzoate[19], 3-butenyl-trifluoroacetate[20], hex-4-enyl methanesulfonate[21], triethylammonium benzenesulfonimide[22], and all phosphine selenide catalysts (unless otherwise noted)[23] were prepared according to previously published procedures and their respective spectroscopic signatures (^{1}H NMR) were found to be consistent with values reported therein.

4.4.2 *Synthesis and Characterization of Starting Materials*

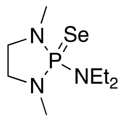
Synthesis of Starting Materials.

General Procedure A: To a flame-dried flask under nitrogen atmosphere, 4-dimethylaminopyridine (DMAP) (776 mg, 12.7 mmol) and triethylamine (3.2 mL, 22.86 mmol) were added to a solution of alcohol (12.7 mmol) in CH_2Cl_2 (63.5 mL, 0.2 M). Next, *p*-methoxybenzoyl chloride (2.4 mL, 17.8 mmol) was slowly added to at 0 °C. The reaction was stirred at room temperature overnight. The resulting mixture was quenched with water (50 mL) and washed with CH_2Cl_2 (3×50 mL). The combined organic layers were washed with 1 M HCl (100 mL), $NaHCO_3$ (sat. aq., 100 mL) and brine (100 mL), dried over magnesium sulfate ($MgSO_4$) and concentrated under reduced pressure. The products were purified by flash chromatography.

General Procedure B: *n*-Butyllithium (12 mL, 2 M in hexanes, 24 mmol) was added dropwise to a solution of alcohol (20 mmol) in THF (20 mL, 1 M) at 0 °C. The reaction mixture was stirred for 2 hours. The reaction was then quenched by pouring onto ice. The aqueous layer was extracted with ether (3x50 mL). The ether layers were combined and washed with brine, then dried over $MgSO_4$. The products were purified by flash chromatography on silica gel.

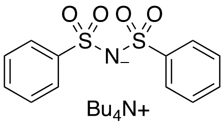
General Procedure C: Carboxylic acid (10 mmol), 4-hexen-1-ol (1.1 mL, 10 mmol), DMAP (122 mg, 1 mmol) and N,N'-dicyclohexylcarbodiimide (DCC) (2 g, 10 mmol) were dissolved in anhydrous CH_2Cl_2 (25 mL, 0.4 M), and the mixture was stirred at room temperature for 24 h. The suspension was filtered, and the filtrate was concentrated *in vacuo*. The products were purified by silica gel chromatography.

Characterization of Starting Materials.



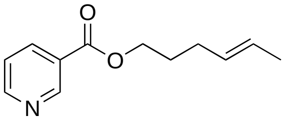
1,3-dimethyl-2-(pentan-3-yl)-1,3,2-diazaphospholidine selenide (4f). To a flame-dried round-bottomed flask under an atmosphere of nitrogen was added ether (200 mL, 0.15 M) followed by phosphorus trichloride (2.6 mL, 30 mmol). This mixture was cooled to -78 °C and *N*,*N*'-dimethylethylenediamine (3.2 mL, 30 mmol) then triethylamine (15 mL, 108 mmol) were added dropwise. The reaction was allowed to warm to room temperature with stirring for 1 hour. The reaction was cooled again to -78 °C and diethylamine (3.1 mL, 30 mmol) was added dropwise. Again, the reaction was allowed to warm to room temperature with stirring overnight. The mixture was filtered over a pad of Celite and the filtrate was concentrated *in vacuo* to give 1,3-dimethyl-

2-(pentan-3-yl)-1,3,2-diazaphospholidine as a yellow oil. The crude triaminophosphine was added to a round bottom flask along with selenium powder (2.8 g, 36 mmol) and CH_2Cl_2 (60 mL, 0.5 M). This mixture was stirred under nitrogen at room temperature overnight. The mixture was then filtered through a pad of silica gel with ethyl acetate and the filtrate was concentrated *in vacuo* to give a beige solid. The solid was recrystallized from ethyl acetate to yield the final product as large colorless crystals. (6.1 g, 76% yield). **Mp:** 59.2-60.7 °C. **^{1}H NMR (300 MHz, $CDCl_3$):** δ 3.33 – 3.10 (m, 6H), 3.10 – 2.88 (m, 2H), 2.47 (d, *J* = 12.8 Hz, 6H), 1.06 (t, *J* = 7.0 Hz, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)**: δ 47.70 (d, *J* = 8.8 Hz), 39.64 (d, *J* = 5.0), 32.11 (d, *J* = 7.6 Hz), 14.65 (d, *J* = 1.3 Hz). **^{31}P NMR (121 MHz, $CDCl_3$):** δ 75.49 ($J^{Se\text{-}P}$ = 791 Hz). **IR (thin film):** 2966.7, 2927.0, 2868.5, 2807.9, 1460.4, 1375.8, 1233.1, 1205.0, 1171.7, 1022.1, 939.7, 786.5, 736.3, 674.0, 525.8 cm^{-1}. **(ESI, positive mode):** 291.9 [M+Na]. **HRMS** (ESI): Calculated for $C_8H_{21}N_3PSe^+$ $[M+H]^+$: 270.0633, Found: 270.0631.

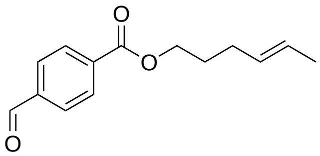


Tetrabutylammonium benzenesulfonimide. To a flame dried 1000 mL round-bottomed flask was added sodium hydride mineral oil dispersion (8.8 g, 220 mmol) and benzenesulfonamide (15.7 g, 100 mmol). THF (400 mL, 0.25 M) was added and the flask was allowed to stir at room temperature for 3 hours, then benzenesulfonyl chloride (15.3 mL, 120 mmol) was added. The cloudy mixture was allowed to stir overnight. Solvent was removed *in vacuo* to give a white solid. Saturated sodium bicarbonate was added and the slurry was filtered with a fritted funnel (to remove any unreactive amide). The filtrate was reacidified with 6 M HCl (until pH = 2), and the product was extracted 3x with ether. The combined ether layers were washed with brine, dried over

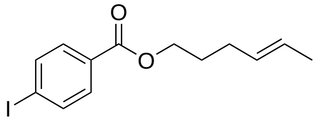
$MgSO_4$, and concentrated *in vacuo* to give a white solid. A minimal amount of 1 M NaOH solution was added slowly to the solid until the solid was dissolved and the pH reached 7-8. (If necessary, the mixture can be filtered to remove undissolved particles.) Next, tetrabutylammonium chloride (27.8 g, 100 mmol) dissolved in a minimum amount of deionized water was pipetted into the mixture and a white solid started to precipitate. The solid continued to precipitate overnight in the fridge. The solid was collected in a fritted funnel, washed with water and dried on the high vac. The resulting solid was recrystallized twice from a minimum amount of ethyl acetate to give large, almost transparent crystals. The crystals were crushed and dried under vacuum at 40 °C overnight. (36 g, 67% yield). **Mp:** 110-113.2 ^{o}C. **^{1}H NMR (300 MHz, $CDCl_3$):** δ 7.71 (d, *J* = 7.6 Hz, 4H), 7.32 – 7.22 (m, 2H), 7.18 (t, *J* = 7.4 Hz, 4H), 3.35 – 3.13 (m, 8H), 1.72 – 1.51 (m, 8H), 1.51 – 1.30 (m, 8H), 0.98 (t, *J* = 7.2 Hz, 12H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 145.60, 129.94, 127.71, 126.77, 58.63, 23.99, 19.68, 13.75. **IR (thin film):** 2960.8, 2874.4, 1478.6, 1444.6, 1381.1, 1279.8, 1155.0, 1132.9, 1086.9, 1054.5, 1023.7, 882.6, 791.1, 751.7, 719.5, 690.8, 593.1, 572.6, 554.0 cm^{-1}. **(ESI, negative mode):** 295.9 [$^-N(SO_2Ph_2)_2$]. **HRMS** (ESI): Calculated for $C_{16}H_{36}N^+$ [Bu_4N]$^+$: 242.2842, Found: 242.2841. Calculated for $C_{12}H_{10}NO_4S_2^-$ [$N(SO_2Ph)_2$]$^-$: 296.0046, Found: 296.001.



(*E*)-hex-4-enyl nicotinate (1g). Prepared according to General Procedure C and purified by silica gel chromatography (10% ethyl acetate/ 90% hexanes) to yield the product as a clear, yellow oil. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 9.23 (s, 1H), 8.86 – 8.66 (m, 1H), 8.39 – 8.19 (m, 1H), 7.51 – 7.33 (m, 1H), 5.60 – 5.36 (m, 2H), 4.36 (td, *J* = 6.6, 1.5 Hz, 2H), 2.15 (m, 2H), 1.92 – 1.78 (m, 2H), 1.65 (d, *J* = 5.8 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 165.42, 153.47, 151.05, 137.12, 129.87, 126.45, 126.22, 123.37, 65.07, 29.06, 28.56, 18.01. **IR (thin film):** 3021, 2958, 2937, 2918, 2854, 1725, 1591, 1450, 1419, 1388, 1327, 1284, 1237, 1193, 1113, 1025, 967, 741, 703 cm^{-1}. **(ESI, positive mode):** 206.0 [M+1]. **HRMS** (ESI): Calculated for $C_{12}H_{16}NO_2^+$ [M+H]$^+$: 206.1176, Found: 206.1174.

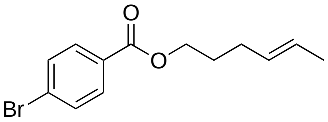


(*E*)-hex-4-enyl 4-formylbenzoate (1i). Prepared according to General Procedure C and purified by silica gel chromatography (5% ethyl acetate/ 95% hexanes) to yield the product as a clear oil. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 10.11 (s, 1H), 8.25 – 8.11 (m, 2H), 8.01 – 7.90 (m, 2H), 5.63 – 5.33 (m, 2H), 4.36 (t, *J* = 6.6 Hz, 2H), 2.15 (dd, *J* = 13.2, 6.8 Hz, 2H), 1.96 – 1.80 (m, 2H), 1.65 (d, *J* = 5.8 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 191.78, 165.72, 139.24, 135.60, 130.29, 129.91, 129.63, 126.21, 65.27, 29.10, 28.58, 18.03. **IR (thin film):** 2958, 2937, 2853, 2733, 1722, 1705, 1699, 1695, 1684, 1386, 1275, 1202, 1117, 1106, 1016, 967, 855, 818, 759, 689 cm^{-1}. **GC-MS (m/z):** 233.1 (1, M+1), 133.0 (671, $C_8H_5O_2^+$), 83.10 (74.04, C_6H11^+), 67.10 (1,250, $C_5H_7^+$). **HRMS** (ESI): Calculated for $C_{14}H_{17}O_3^+$ [M+H]$^+$: 233.1172, Found: 233.1169.

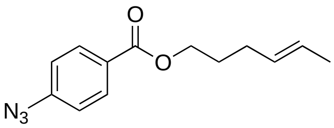


(*E*)-hex-4-enyl 4-iodobenzoate (1k). Prepared according to Genera Procedure C and purified by silica gel chromatography (5% ethyl acetate/ 95% hexanes) to yield the product as a clear oil. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.79 (dd, *J* = 8.4, 1.7 Hz, 2H), 7.74 (dd, *J* = 8.3, 1.6 Hz, 2H), 5.60 –

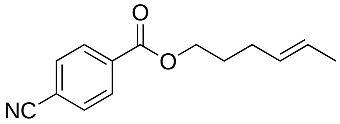
5.31 (m, 2H), 4.30 (td, *J* = 6.6, 1.2 Hz, 2H), 2.13 (m, 2H), 1.93 – 1.72 (m, 2H), 1.65 (d, *J* = 5.6 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 166.23, 137.81, 131.13, 130.09, 129.98, 126.11, 100.69, 64.88, 29.09, 28.60, 18.03. **IR (thin film):** 3020, 2955, 2935, 2851, 1719, 1587, 1482, 1465, 1456, 1448, 1437, 1393, 1306, 1269, 1176, 1115, 1103, 1083, 1008, 966, 845, 753 cm^{-1}. **(ESI, positive mode):** 353.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{13}H_{16}IO_2^+$ $[M+H]^+$: 331.0189, Found: 331.0188.



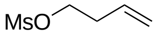
(*E*)-hex-4-enyl 4-bromobenzoate (1l). Prepared according to General Procedure C and purified by silica gel chromatography (5% ethyl acetate/ 95% hexanes) to yield the product as a clear oil. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.90 (dd, *J* = 6.8, 1.8 Hz, 2H), 7.57 (dd, *J* = 8.4, 1.5 Hz, 2H), 5.58 – 5.31 (m, 2H), 4.31 (t, *J* = 6.6 Hz, 2H), 2.13 (m, 2H), 1.88 – 1.74 (m, 2H), 1.65 (d, *J* = 5.5 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 166.02, 131.81, 131.22, 129.99, 129.53, 128.05, 126.13, 64.91, 29.11, 28.61, 18.04. **IR (thin film):** 3020, 2957, 2936, 2853, 1718, 1591, 1398, 1271, 1173, 1116, 1103, 1069, 1012, 966, 847, 756 cm^{-1}. **(ESI, positive mode):** 305.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{13}H_{16}{}^{79}BrO_2^+$ $[M+H]^+$: 283.0328, Found: 283.0325.



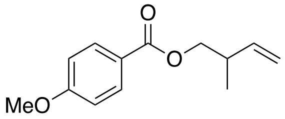
(*E*)-hex-4-enyl 4-azidobenzoate (1m). Prepared according to General Procedure C and purified by silica gel chromatography (5% ethyl acetate/ 95% hexanes) to yield the product as a clear, yellow oil. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.03 (dd, *J* = 6.8, 1.9 Hz, 2H), 7.11 – 6.93 (m, 2H), 5.58 – 5.35 (m, 2H), 4.31 (t, *J* = 6.6 Hz, 2H), 2.14 (m, 2H), 1.90 – 1.76 (m, 2H), 1.65 (d, *J* = 4.7 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 165.93, 144.76, 131.49, 130.04, 127.19, 126.07, 118.92, 64.71, 29.12, 28.66, 18.03. **IR (thin film):** 3020, 2937, 2853, 2413, 2258, 2123, 1719, 1603, 1504, 1274, 1173, 1131, 1109, 1015, 967, 850, 766, 690 cm^{-1}. **(ESI, positive mode):** 268.0 [M+Na].



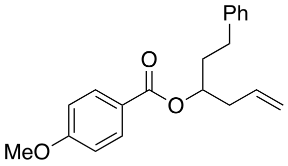
(*E*)-hex-4-enyl 4-cyanobenzoate (1n). Prepared according to General Procedure C and purified by silica gel chromatography (5% ethyl acetate/ 95% hexanes) to yield the product as a clear oil. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.21 – 8.05 (m, 2H), 7.82 – 7.64 (m, 2H), 5.61 – 5.25 (m, 2H), 4.36 (td, *J* = 6.6, 1.2 Hz, 2H), 2.14 (dd, *J* = 13.5, 6.9 Hz, 2H), 1.84 (quin, *J* = 6.6 Hz, 2H), 1.65 (d, *J* = 5.8 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 165.06, 134.40, 132.31, 130.17, 129.80, 126.25, 118.11, 116.42, 65.44, 29.04, 28.51, 18.00. **IR (thin film):** 3098, 3052, 2958, 2937, 2918, 2854, 2231, 1719, 1450, 1405, 1388, 1310, 1275, 1177, 1119, 1108, 1019, 967, 862, 768, 692, 546 cm^{-1}. **(ESI, positive mode):** 252.0 [M+Na]. **HRMS** (ESI): Calculated for $C_{14}H_{16}NO_2^+$ [M+H]$^+$: 230.1176, Found: 230.1172.



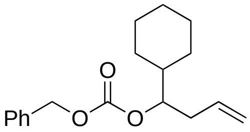
but-3-enyl methanesulfonate (1t). To a flame dried 100 mL round bottom flask was added 3-buten-1-ol (1.72 mL, 20 mmol) and CH_2Cl_2 (20 mL, 1 M). The reaction was cooled to 0 ^{oC} and triethylamine (4.18 mL, 30 mmol) then methanesulfonyl chloride (2.32 mL, 30 mmol) were added dropwise. The reaction was stirred at 0 °C for 1 hour then at room temperature overnight. Saturated ammonium chloride (20 mL) was added and the mixture was extracted with ether (2x50 mL). The combined ether layers were dried over $MgSO_4$ and concentrated *in vacuo* to give a yellow oil. The crude product was purified by silica gel chromatography (5% ethyl acetate/ 95% hexanes) to yield the product as a clear oil. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 5.89 – 5.69 (m, 1H), 5.23 – 5.10 (m, 2H), 4.27 (td, *J* = 6.7, 1.5 Hz, 2H), 3.01 (s, 3H), 2.60 – 2.40 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)**: δ 132.53, 118.59, 68.97, 37.60, 33.52. **IR (thin film):** 3081, 3028, 2984, 2942, 1643, 1353, 1174, 976, 954, 910, 835, 805, 528 cm^{-1}. **(ESI, positive mode):** 172.8 [M+Na]. **HRMS** (ESI): Calculated for $C_5H_{11}O_3S^+$ $[M+H]^+$: 151.0423, Found: 151.0418.



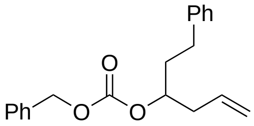
2-methyl-but-3-en-1-yl 4-methoxybenzoate (1ag). Prepared according to General Procedure A and purified by column chromatography (5% EtOAc in hexane) to give the product as a colorless oil (2.3 g, 69%). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.99 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 5.83 (ddd, *J* = 17.3, 10.4, 7.0 Hz, 1H), 5.13 (dd, *J* = 17.3, 1.3 Hz, 1H), 5.07 (dd, *J* = 10.4 Hz, 0.9 Hz, 1H), 4.32 – 4.00 (m, 2H), 3.86 (s, 3H), 2.74 – 2.58 (m, 1H), 1.12 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 166.41, 163.46, 140.30, 131.70, 122.99, 115.11, 113.73, 68.61, 55.55, 37.30, 16.62. **IR (thin film):** 3079, 2966, 2839, 1714, 1607, 1511, 1316, 1276, 1257, 1168, 1114, 1102, 1031, 847, 770, 697, 613 cm^{-1}. **(ESI, positive mode):** 242.9 [M+Na]. **HRMS** (ESI): Calculated for $C_{13}H_{17}O_3^+$ $[M+H]^+$: 221.1172, Found: 221.1169.



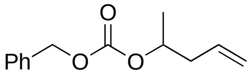
1-phenylhex-5-en-3-yl 4-methoxybenzoate (1ah). Prepared according to General Procedure A and purified by column chromatography (5 % EtOAc, 95% Hexane) to give the product as a colorless oil (2.3 g, 58%). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.00 (d, *J* = 8.8 Hz, 2H), 7.28 – 7.23 (m, 2H), 7.17 (m, 3H), 6.92 (dd, *J* = 8.9, 2.0 Hz, 2H), 5.88 – 5.76 (m, 1H), 5.19 (m, 1H), 5.10 (d, *J* = 17.1 Hz, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 3.86 (s, 3H), 2.83 – 2.61 (m, 2H), 2.47 (t, *J* = 6.5 Hz, 2H), 2.13 – 1.88 (m, 2H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 166.07, 163.46, 141.75, 133.66, 131.72, 128.55, 128.48, 126.04, 123.16, 118.06, 113.73, 73.26, 55.57, 38.91, 35.60, 31.92. **IR (thin film):** 3078, 3025, 3004, 2952, 2839, 1707, 1606, 1511, 1316, 1274, 1256, 1167, 1114, 1102, 1031, 1009, 919, 848, 770, 698, 613 cm^{-1}. **MS (ESI, positive mode):** 310.9 [M+1], 333.0 [M+Na]. **HRMS** (ESI): Calculated for $C_{20}H_{23}O_3^+$ [M+H]$^+$: 331.1642, Found: 311.1642.



benzyl 1-cyclohexylbut-3-enyl carbonate (6a). Prepared according to general procedure B and purified by silica gel chromatography (5% ethyl acetate/ 95% hexanes) to yield the product as a clear oil. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.42 – 7.28 (m, 5H), 5.87 – 5.68 (m, 1H), 5.16 (d, *J* = 12.2 Hz, 1H), 5.12 (d, *J* = 12.2 Hz, 1H), 5.07 (d, *J* = 17.1 Hz, 1H), 5.03 (d, *J* = 10.2 Hz, 1H), 4.61 (m, 1H), 2.44 – 2.26 (m, 2H), 1.82 – 1.60 (m, 5H), 1.60 – 1.47 (m, 1H), 1.27 – 1.09 (m, 3H), 1.09 – 0.95 (m, 2H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 155.36, 135.69, 133.84, 128.66, 128.49, 128.26, 117.87, 81.90, 69.47, 40.94, 35.96, 28.96, 28.04, 26.40, 26.16, 26.04. **IR (thin film):** 3067, 3034, 2929, 2853, 1741, 1643, 1498, 1451, 1385, 1352, 1332, 1258, 1185, 1099, 1081, 1029, 973, 915, 859, 787, 753, 738, 697 cm^{-1}. **(ESI, positive mode):** 311.0 [M+Na]. **HRMS** (ESI): Calculated for $C_{18}H_{25}O_3^+$ $[M+H]^+$: 289.1798, Found: 289.1796.



benzyl 1-phenylhex-5-en-3-yl carbonate (6b). Prepared according to General Procedure B and purified by column chromatography (5% EtOAc in hexane) to give the product as a clear oil (851 mg, 14% yield). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.41 – 7.30 (m, 5H), 7.26 (t, *J* = 8.0 Hz, 2H), 7.21 – 7.09 (m, 3H), 5.84 – 5.67 (m, 1H), 5.16 (s, 2H), 5.12 – 5.00 (m, 2H), 4.86 – 4.68 (m, 1H), 2.75 – 2.66 (m, 1H), 2.66 – 2.56 (m, 1H), 2.40 (t, *J* = 6.4 Hz, 2H), 2.00 – 1.81 (m, 2H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 155.04, 141.43, 135.55, 133.11, 128.72, 128.61, 128.57, 128.48, 128.38, 126.13, 118.41, 77.51, 69.60, 38.76, 35.41, 31.69. **IR (thin film):** 3064, 3028, 2953, 2861, 1740, 1735, 1496, 1454, 1385, 1261, 1029, 994, 916, 859, 789, 750, 698 cm^{-1}. **(ESI, positive mode):** 333.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{20}H_{22}O_3Na^+$ $[M+Na]^+$: 333.1461, Found: 333.1460.



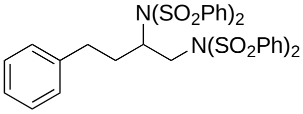
benzyl pent-4-en-2-yl carbonate (6c). Prepared according to General Procedure B and purified by silica gel chromatography (5% ethyl acetate/ 95% hexanes) to yield the product as a clear oil. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.41 – 7.29 (m, 5H), 5.86 – 5.62 (m, 1H), 5.14 (s, 2H), 5.13 – 5.05 (m, 2H), 4.91 – 4.74 (m, 1H), 2.46 – 2.36 (m, 1H), 2.36 – 2.22 (m, 1H), 1.28 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 154.83, 135.54, 133.34, 128.70, 128.58, 128.41, 118.25, 74.69, 69.49, 40.35, 19.55. **IR (thin film):** 3068, 3034, 2980, 2935, 1743, 1456, 1382, 1350, 1262, 1128, 1051, 994, 913, 791, 753, 697 cm^{-1}. **(ESI, positive mode):** 242.9 [M+Na]. **HRMS** (ESI): Calculated for $C_{13}H_{17}O_3^+$ [M+H]$^+$: 221.1172, Found: 221.1169.

4.4.3 *General Procedure for 1,2-Diamination and Oxyamination of Olefins*

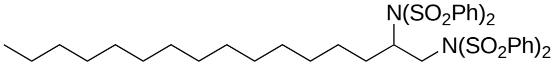
Standard Conditions A: A flame-dried 1-dram vial was allowed to cool under positive pressure of nitrogen. To the vial was added phosphine selenide catalyst (5.4 mg, 0.02 mmol) and tetrabutylammonium benzenesulfonimide (215.5 mg, 0.4 mmol). Next, CH_2Cl_2 (2 mL, 0.1 M), alkene (0.2 mmol), TMSOTf (72.4 µL, 0.4 mmol) and NFBS (126.1 mg, 0.4 mmol) were added in that order. The vial was flushed with nitrogen, capped with a Teflon-lined cap and allowed to stir at room temperature for 24 hours. After 24 hours, dimethyl sulfide (60 µL) and water (0.5 mL) were added and the vial was capped and shaken. The mixture was diluted with CH_2Cl_2 (2 mL) followed by ether (30 mL). The organic layer was washed 1 M citric acid (30 mL), saturated sodium bicarbonate (30 mL) and brine (30 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Standard Conditions B: A flame-dried 1-dram vial was allowed to cool under positive pressure of nitrogen. To the vial was added phosphine selenide catalyst (5.4 mg, 0.02 mmol) and tetrabutylammonium benzenesulfonimide (107.8 mg, 0.2 mmol). Next, CH_2Cl_2 (2 mL, 0.1 M), alkene (0.2 mmol), TMSOTf (72.4 µL, 0.4 mmol) and NFBS (94.6 mg, 0.3 mmol) were added in that order. The vial was flushed with nitrogen, capped with a Teflon-lined cap and allowed to stir at room temperature for 24 hours. After 24 hours, dimethyl sulfide (60 µL) and water (0.5 mL) were added and the vial was capped and shaken. The mixture was diluted with CH_2Cl_2 (2 mL) followed by ether (30 mL). The organic layer was washed 1 M citric acid (30 mL), saturated sodium bicarbonate (30 mL) and brine (30 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*.

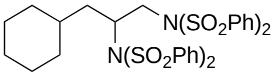
4.4.4 *Characterization of Products*



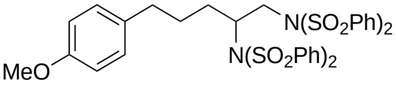
***N*,*N*'-(4-phenylbutane-1,2-diyl)bis(benzenesulfonimide) (3a).** Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as an off-white solid (79.8 mg, 56% yield). **Mp:** 189.5-199.2 ^{o}C. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.18 (dd, *J* = 11.8, 7.9 Hz, 4H), 8.05 (d, *J* = 7.7 Hz, 4H), 7.69 – 7.46 (m, 12H), 7.14 (t, *J* = 7.3 Hz, 3H), 6.60 (d, *J* = 6.5 Hz, 2H), 4.99 – 4.85 (m, 1H), 4.77 (dd, *J* = 14.4, 11.5 Hz, 1H), 3.74 (dd, *J* = 14.5, 3.8 Hz, 1H), 2.18 – 1.98 (m, 2H), 1.95 – 1.84 (m, 1H), 1.78 (dt, *J* = 19.0, 4.8 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 141.09, 140.55, 139.72, 139.35, 134.30, 134.27, 134.10, 129.34, 129.30, 129.19, 129.05, 128.97, 128.63, 128.26, 128.18, 126.02, 62.15, 51.47, 32.41, 30.27. **IR (thin film):** 3065, 3028, 2942, 1448, 1379, 1358, 1170, 1084, 911, 895, 860, 795, 753, 735, 720, 686, 651, 281, 554 cm^{-1}. **MS (ESI, positive mode):** 747.2 [M+Na]. **HRMS** (ESI): Calculated for $C_{34}H_{32}N_2O_8S_4Na^+$ [M+Na]$^+$: 747.0934, Found: 747.0939.



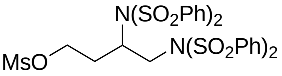
***N*,*N*'-(hexadecane-1,2-diyl)bis(benzenesulfonimide) (3b).** Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as a tan oil (82.4 mg, 51% yield). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.16 (d, *J* = 7.4 Hz, 4H), 8.06 (d, *J* = 7.4 Hz, 4H), 7.68 – 7.59 (m, 4H), 7.54 (td, *J* = 7.9, 5.0 Hz, 8H), 4.78 (tt, *J* = 11.3, 3.3 Hz, 1H), 4.70 (dd, *J* = 14.0, 11.5 Hz, 1H), 3.71 (dd, *J* = 14.1, 3.5 Hz, 1H), 1.85 – 1.69 (m, 1H), 1.47 – 1.36 (m, 1H), 1.36 – 1.19 (m, 15H), 1.19 – 1.11 (m, 2H), 1.08 – 0.97 (m, 2H), 0.89 (t, *J* = 6.9 Hz, 3H), 0.85 – 0.73 (m, 2H), 0.73 – 0.57 (m, 2H), 0.57 – 0.42 (m, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 140.95, 139.98, 139.48, 134.21, 134.09, 133.98, 129.30, 129.19, 128.96, 128.94, 128.88, 128.58, 127.92, 62.11, 51.64, 32.05, 29.84, 29.83, 29.80, 29.78, 29.69, 29.57, 29.50, 29.45, 29.17, 28.67, 26.36, 22.82, 14.25. **IR (thin film):** 3067, 2924, 2856, 1448, 1379, 1359, 1170, 1084, 753, 731, 720, 686, 585, 555 cm^{-1}. **MS (ESI, positive mode):** 834.4 [M+NH$_4$], 839.3 [M+Na]. **HRMS** (ESI): Calculated for $C_{40}H_{52}N_2O_8S_4Na^+$ [M+Na]$^+$: 839.2499, Found: 839.2505.



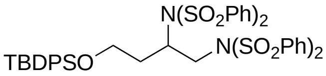
***N,N*'-(3-cyclohexylpropane-1,2-diyl)bis(benzenesulfonimide) (3c).** Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as white solid (79.4 mg, 54% yield). **Mp:** 210.8-213.8 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.20 (d, *J* = 7.4 Hz, 2H), 8.19 (d, *J* = 7.4 Hz, 2H), 8.03 (d, *J* = 7.5 Hz, 4H), 7.72 – 7.60 (m, 4H), 7.60 – 7.47 (m, 8H), 4.99 – 4.84 (m, 1H), 4.64 (dd, *J* = 14.7, 11.1 Hz, 1H), 3.77 (dd, *J* = 14.7, 3.6 Hz, 1H), 1.75 (t, *J* = 12.8 Hz, 1H), 1.55 (d, *J* = 12.0 Hz, 1H), 1.49 – 1.36 (m, 3H), 1.36 – 1.19 (m, 1H), 0.97 – 0.78 (m, 3H), 0.78 – 0.58 (m, 2H), 0.58 – 0.44 (m, 1H), 0.16 (dd, *J* = 21.0, 10.0 Hz, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 141.17, 140.37, 139.43, 134.22, 134.02, 133.96, 129.28, 129.19, 129.01, 128.98, 128.91, 128.72, 59.63, 52.09, 35.84, 33.66, 33.51, 31.73, 26.36, 26.22, 25.78. **IR (thin film):** 3067, 2924, 2851, 1448, 1378, 1170, 1084, 911, 883, 867, 825, 796, 753, 732, 720, 686, 652, 586, 553 cm^{-1}. **MS (ESI, positive mode):** 739.3 [M+Na]. **HRMS** (ESI): Calculated for $C_{33}H_{36}N_2O_8S_4Na^+$ [M+Na]$^+$: 739.1247, Found: 739.1251.



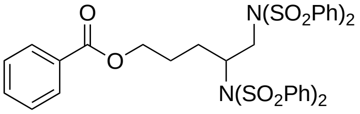
***N,N'*-(5-(4-methoxyphenyl)pentane-1,2-diyl)bis(benzenesulfonimide) (3d).** Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as a yellow resin (75.8 mg, 48% yield). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.15 (d, *J* = 7.4 Hz, 2H), 8.14 (d, *J* = 6.2 Hz, 2H), 8.04 (d, *J* = 7.4 Hz, 4H), 7.67 – 7.46 (m, 12H), 6.75 (d, *J* = 2.2 Hz, 4H), 4.79 (tt, *J* = 11.2, 3.3 Hz, 1H), 4.71 (dd, *J* = 14.0, 11.4 Hz, 1H), 3.78 (s, 3H), 3.72 (dd, *J* = 14.0, 3.5 Hz, 1H), 2.10 – 2.00 (m, 1H), 1.98 – 1.85 (m, 2H), 1.59 – 1.48 (m, 1H), 1.01 – 0.88 (m, 1H), 0.88 – 0.73 (m, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 157.81, 140.95, 139.85, 139.42, 134.25, 134.15, 134.08, 133.86, 129.32, 129.21, 129.05, 128.98, 128.85, 128.55, 113.73, 61.79, 55.40, 51.60, 34.52, 28.60, 28.55. **IR (thin film):** 3067, 3006, 2935, 2860, 1512, 1448, 1378, 1358, 1246, 1170, 1084, 908, 753, 731, 720, 686, 585, 554 cm^{-1}. **MS (ESI, positive mode):** 786.2 [M+NH$_4$], 791.2 [M+Na]. **HRMS** (ESI): Calculated for $C_{36}H_{36}N_2O_9S_4Na^+$ [M+Na]$^+$: 791.1196, Found: 791.1202.



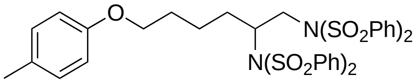
3,4-bis(benzenesulfonimido)butyl methanesulfonate (3e). Prepared according to Standard Conditions A and purified by silica gel chromatography (100% CH$_2$Cl$_2$) to yield the product as a white solid (114.6 mg, 76% yield). **Mp:** 175.8-184.7 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.14 – 8.07 (m, 4H), 8.01 (d, *J* = 7.4 Hz, 4H), 7.75 – 7.63 (m, 4H), 7.60 (t, *J* = 7.7 Hz, 6H), 7.55 (t, *J* = 7.9 Hz, 2H), 5.06 (tt, *J* = 11.5, 3.6 Hz, 1H), 4.62 (dd, *J* = 14.7, 11.3 Hz, 1H), 3.90 (dt, *J* = 10.0, 5.1 Hz, 1H), 3.65 (dd, *J* = 14.6, 4.0 Hz, 1H), 3.58 (td, *J* = 9.6, 4.5 Hz, 1H), 2.91 (s, 3H), 2.47 (ddt, *J* = 16.0, 11.6, 4.5 Hz, 1H), 2.33 – 2.21 (m, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 140.38, 139.12, 138.69, 134.62, 134.59, 129.52, 129.44, 129.38, 128.95, 128.82, 128.75, 66.27, 58.13, 50.21, 37.20, 28.51. **IR (thin film):** 3067, 3032, 2939, 1583, 1449, 1376, 1359, 1083, 950, 909, 859, 754, 732, 720, 686, 650, 586, 554 cm^{-1}. **MS (ESI, positive mode):** 760.2 [M+NH$_4$], 765.2 [M+Na]. **HRMS** (ESI): Calculated for $C_{29}H_{30}N_2O_{11}S_5Na^+$ [M+Na]$^+$: 765.0345, Found: 765.0348.



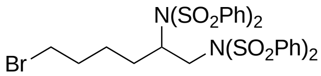
***N*,*N*'-(4-(*tert*-butyldiphenylsilyloxy)butane-1,2-diyl)bis(benzenesulfonimide) (3f).** Prepared according to Standard Conditions A and purified by silica gel chromatography (30% ethyl acetate/ 70% hexanes) to yield the product as a yellow resin (109 mg, 60% yield). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.09 (d, *J* = 7.5 Hz, 2H), 8.02 (m, 6H), 7.59 – 7.49 (m, 6H), 7.47 – 7.31 (m, 16H), 5.00 (tt, *J* = 11.5, 3.8 Hz, 1H), 4.69 (dd, *J* = 14.7, 11.2 Hz, 1H), 3.69 (dd, *J* = 14.7, 4.2 Hz, 1H), 3.24 (td, *J* = 10.1, 4.0 Hz, 1H), 2.89 (dd, *J* = 17.9, 7.7 Hz, 1H), 2.32 (dddd, *J* = 15.5, 11.7, 7.6, 4.1 Hz, 1H), 2.02 (dtd, *J* = 11.6, 8.0, 3.5 Hz, 1H), 0.96 (s, 9H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 140.87, 139.33, 138.86, 135.60, 135.57, 134.27, 134.13, 133.99, 133.94, 133.59, 129.70, 129.23, 129.14, 129.01, 128.87, 128.83, 128.81, 127.84, 127.78, 60.44, 59.02, 50.55, 31.93, 26.98, 19.30. **IR (thin film):** 3070, 2957, 2930, 2857, 1584, 1448, 1378, 1360, 1171, 1111, 1084, 909, 856, 785, 753, 731, 720, 704, 686, 650, 585, 555 cm^{-1}. **MS (ESI, positive mode):** 925.2 [M+Na]. **HRMS** (ESI): Calculated for $C_{44}H_{46}N_2O_9S_4SiNa^+$ [M+X]$^+$: 925.1748, Found: 925.1757.



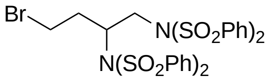
4,5-bis(benzenesulfonimido)pentyl benzoate (3g). Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as a clear oil (99.8 mg, 64% yield). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.20 – 8.13 (m, 4H), 8.03 (d, *J* = 7.9 Hz, 4H), 7.93 (d, *J* = 7.9 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 2H), 7.61 – 7.50 (m, 7H), 7.50 – 7.38 (m, 6H), 4.83 (t, *J* = 11.4 Hz, 1H), 4.79 – 4.70 (m, 1H), 3.85 (dt, *J* = 11.3, 5.8 Hz, 1H), 3.76 – 3.68 (m, 2H), 2.03 – 1.89 (m, 1H), 1.78 – 1.67 (m, 1H), 1.21 – 1.11 (m, 1H), 1.11 – 0.99 (m, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 166.28, 140.80, 139.59, 139.33, 134.30, 134.27, 134.24, 133.05, 130.30, 129.70, 129.29, 129.10, 128.92, 128.84, 128.52, 128.49, 128.28, 63.74, 61.65, 51.44, 25.67, 25.35. **IR (thin film):** 3166, 3067, 3007, 2959, 2894, 1717, 1602, 1584, 1449, 1379, 1 358, 1314m 1275, 1170, 1084, 908, 754, 732, 686, 651, 584, 555 cm^{-1}. **MS (ESI, positive mode):** 805.2 [M+Na]. **HRMS** (ESI): Calculated for $C_{36}H_{34}N_2O_{10}S_4Na^+$ [M+Na]$^+$: 805.0988, Found: 805.0944.



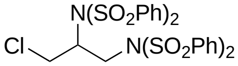
***N*,*N*'-(6-(*p*-tolyloxy)hexane-1,2-diyl)bis(benzenesulfonimide) (3h).** Prepared according to Standard Conditions A and purified by silica gel chromatography (30% ethyl acetate/ 70% hexanes) to yield the product as a tan solid (101.5 mg, 65% yield). **Mp:** 68.4-74.2 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.16 (d, *J* = 8.8 Hz, 2H), 8.14 (d, *J* = 7.8 Hz, 2H), 8.05 (d, *J* = 7.4 Hz, 4H), 7.65 – 7.55 (m, 4H), 7.55 – 7.46 (m, 6H), 7.08 (d, *J* = 8.3 Hz, 2H), 6.69 (d, *J* = 8.5 Hz, 2H), 4.83 – 4.76 (m, 1H), 4.76 – 4.67 (m, 1H), 3.72 (dd, *J* = 13.7, 3.2 Hz, 1H), 3.56 – 3.40 (m, 2H), 2.30 (s, 3H), 1.98 – 1.76 (m, 1H), 1.58 – 1.42 (m, 1H), 1.32 – 1.21 (m, 1H), 1.21 – 1.09 (m, 1H), 0.88 – 0.75 (m, 1H), 0.73 – 0.59 (m, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 156.87, 140.87, 139.72, 139.37, 134.28, 134.18, 134.09, 129.94, 129.79, 129.32, 129.22, 129.02, 128.97, 128.92, 128.86, 128.54, 114.41, 67.45, 61.89, 51.51, 28.76, 28.49, 22.97, 20.59. **IR (thin film):** 3066, 3032, 3006, 2925, 2869, 1612, 1584, 1511, 1488, 1378, 1358, 1243, 1170, 1084, 1043, 999, 910, 890, 851, 793, 753, 720, 686, 651, 585, 555 cm^{-1}. **MS (ESI, positive mode):** 800.3 [M+NH_4], 805.2 [M+Na]. **HRMS** (ESI): Calculated for $C_{37}H_{38}N_2O_9S_4Na$ [M+Na]$^+$: 805.1352, Found: 805.1360.



***N*,*N*'-(6-bromohexane-1,2-diyl)bis(benzenesulfonimide) (3i).** Prepared according to Standard Conditions A and purified by silica gel chromatography (30% ethyl acetate/ 70% hexanes) to yield the product as an off-white solid (111.4 mg, 75% yield). **Mp:** 63.4-71.2 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.15 (d, *J* = 9.3 Hz, 2H), 8.14 (d, *J* = 8.4 Hz, 2H), 8.04 (d, *J* = 7.9 Hz, 4H), 7.66 (dt, *J* = 10.3, 7.3 Hz, 4H), 7.55 (dd, *J* = 14.2, 7.3 Hz, 6H), 4.76 (tt, *J* = 11.0, 3.0 Hz, 1H), 4.73 – 4.66 (m, 1H), 3.72 (dd, *J* = 13.9, 3.2 Hz, 1H), 3.04 – 2.87 (m, 2H), 1.84 (dtd, *J* = 15.4, 11.4, 4.2 Hz, 1H), 1.50 – 1.40 (m, 1H), 1.40 – 1.30 (m, 1H), 1.30 – 1.18 (m, 1H), 0.86 – 0.74 (m, 1H), 0.72 – 0.59 (m, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 140.96, 139.66, 139.37, 134.34, 134.25, 134.14, 129.36, 129.28, 129.08, 128.92, 128.87, 128.57, 61.72, 51.47, 32.93, 32.29, 27.96, 25.01. **IR (thin film):** 3067, 2959, 1584, 1448, 1378, 1358, 1171, 1084, 907, 754, 731, 720, 686, 584, 554 cm^{-1}. **MS (ESI, positive mode):** 777.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{30}H_{31}BrN_2O_8S_4Na^+$ [M+Na]$^+$: 777.0039, Found: 777.0043.

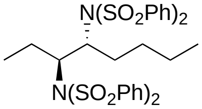


_N,N_'-(4-bromobutane-1,2-diyl)bis(benzenesulfonimide) (3j). Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as an off-white resin (114.7 mg, 70% yield). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.17 – 8.11 (m, 4H), 8.02 (dd, *J* = 7.5, 1.0 Hz, 4H), 7.72 – 7.63 (m, 4H), 7.63 – 7.51 (m, 8H), 4.82 (t, *J* = 11.3 Hz, 1H), 4.68 (dd, *J* = 14.6, 11.3 Hz, 1H), 3.62 (dd, *J* = 14.6, 4.0 Hz, 1H), 2.73 (td, *J* = 10.1, 4.4 Hz, 1H), 2.63 (m, 1H), 2.59 – 2.43 (m, 1H), 2.16 – 2.00 (m, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 140.44, 139.36, 139.01, 134.50, 134.45, 129.44, 129.42, 129.37, 128.91, 128.85, 128.70, 60.53, 50.77, 32.62, 27.79. **IR (thin film):** 3067, 2927, 1448, 1378, 1171, 1084, 753, 731, 720, 685, 583, 554 cm^{-1}. **MS (ESI, positive mode):** 749.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{28}H_{27}{}^{79}BrN_2O_8S_4Na^+$ [M+Na]$^+$: 748.9726, Found: 748.9733.

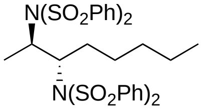


_N,N_'-(3-chloropropane-1,2-diyl)bis(benzenesulfonimide) (3k). Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as an off-white solid (57.5 mg, 43% yield). **Mp:** 196.8-204.9 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.17 (d, *J* = 7.9 Hz, 2H), 7.99 (d, *J* = 7.9 Hz, 6H), 7.69 (t, *J* = 7.5 Hz, 3H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.61 – 7.54 (m, 6H), 7.51 (t, *J* = 7.8 Hz, 2H), 4.99 (tt, *J* = 11.0, 4.1 Hz, 1H), 4.62 (dd, *J* = 14.9, 11.4 Hz, 1H), 4.05 (dd, *J* = 12.6, 11.1 Hz, 1H), 3.89 (dd, *J* = 14.9, 4.4 Hz, 1H), 3.67 (dd, *J* = 12.7, 3.9 Hz, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 140.17, 138.65, 138.53, 134.61, 134.49, 134.34, 129.51, 129.40, 129.21, 129.15, 129.14, 128.99, 128.93, 128.67, 62.38, 49.56, 41.39. **IR (thin film):** 3067, 2927, 1449, 1378, 1360, 1170, 1084, 753, 732, 720, 685, 583, 554 cm^{-1}. **MS**

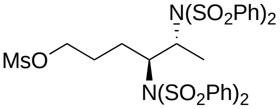
(ESI, positive mode): 691.0 [M+Na]. **HRMS** (ESI): Calculated for $C_{27}H_5ClN_2O_8S_4Na$ $[M+Na]^+$: 691.0074, Found: 691.0079.



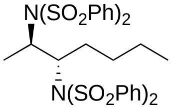
***N*,*N*'-(octane-3,4-diyl)bis(benzenesulfonimide) (3l).** Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as an off-white solid (122.5 mg, 88% yield). **Mp:** 174.1-177.6 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.24 – 7.92 (m, 8H), 7.67 – 7.59 (m, 4H), 7.59 – 7.46 (m, 8H), 5.14 – 4.59 (m, 2H), 1.74 – 1.61 (m, 1H), 1.57 – 1.46 (m, 1H), 1.46 – 1.34 (m, 1H), 1.34 – 1.23 (m, 1H), 0.66 – 0.45 (m, 4H), 0.42 (t, *J* = 7.0 Hz, 3H), 0.35 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 141.27, 141.09, 139.18, 139.13, 134.27, 133.98, 129.74, 129.68, 129.29, 129.17, 128.91, 128.85, 128.83, 67.86, 67.36, 30.86, 28.40, 23.68, 22.38, 13.81, 10.85. **IR (thin film):** 3103, 3067, 2958, 2931, 2872, 1584, 1448, 1366, 1170, 1082, 993, 910, 845, 753, 730, 719, 686, 654, 592, 583, 555 cm^{-1}. **MS (ESI, positive mode):** 727.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{32}H_{36}N_2O_8S_4Na^+$ $[M+Na]^+$: 727.1247, Found: 727.1253.



***N*,*N*'-(octane-2,3-diyl)bis(benzenesulfonimide) (3m).** Prepared according to Standard Conditions A and purified by silica gel chromatography (15% ethyl acetate/ 85% hexanes) to yield the product as a tan solid (114.7 mg, 83% yield). **Mp:** 176.8-177.9 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.19 (d, *J* = 8.8 Hz, 2H), 8.17 (d, *J* = 8.1 Hz, 2H), 8.08 (d, *J* = 7.5 Hz, 2H), 8.00 (d, *J* = 7.4 Hz, 2H), 7.69 – 7.47 (m, 12H), 5.11 (td, *J* = 11.2, 3.4 Hz, 1H), 4.90 (dq, *J* = 10.3, 7.0 Hz, 1H), 1.77 – 1.55 (m, 2H), 1.09 – 0.83 (m, 4H), 0.83 – 0.69 (m, 8H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 141.46, 141.08, 139.05, 138.52, 134.28, 133.99, 133.94, 129.77, 129.31, 129.23, 129.00, 128.92, 128.88, 128.82, 128.67, 65.60, 62.68, 31.68, 30.25, 26.23, 22.52, 16.94, 14.16. **IR (thin film):** 3164, 3101, 3067, 2955, 2929, 2871, 1583, 1448, 1367, 1170, 1083, 911, 861, 753, 732, 721, 686, 652, 586, 555 cm^{-1}. **MS (ESI, positive mode):** 727.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{32}H_{36}N_2O_8S_4Na^+$ [M+Na]$^+$: 727.1247, Found: 727.1255.



4,5-bis(benzenesulfonimido)hexyl methanesulfonate (3n). Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as an off-white solid (142.7 mg, 88% yield). **Mp:** 145-147 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.16 (d, *J* = 7.7 Hz, 4H), 8.03 (d, *J* = 8.2 Hz, 2H), 7.93 (d, *J* = 8.2 Hz, 2H), 7.74 – 7.57 (m, 8H), 7.53 (t, *J* = 7.7 Hz, 4H), 5.13 (td, *J* = 10.4, 3.8 Hz, 1H), 4.97 – 4.87 (m, 1H), 3.86 (t, *J* = 5.8 Hz, 2H), 2.89 (s, 3H), 1.94 – 1.72 (m, 2H), 1.61 – 1.42 (m, 1H), 1.38 – 1.16 (m, 1H), 0.73 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 141.16, 140.75, 138.60, 138.05, 134.57, 134.39, 134.22, 129.70, 129.44, 129.21, 129.19, 129.14, 129.03, 128.84, 128.62, 69.49, 64.72, 62.18, 37.45, 26.47, 26.28, 16.54. **IR (thin film):** 3069, 2926, 2854, 1583, 1449, 1367, 1169, 1083, 961, 912, 860, 732, 722, 686, 651, 587, 555 cm^{-1}. **MS (ESI, positive mode):** 788.0 [M+NH$_4$], 793.0 [M+Na]. **HRMS** (ESI): Calculated for $C_{31}H_{34}N_2O_{11}S_5Na^+$ [M+Na]$^+$: 793.0658, Found: 793.0665.



***N,N'*-(heptane-2,3-diyl)bis(benzenesulfonimide) (3o).** Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as a white solid (110.3 mg, 88% yield). **Mp:** 190.2-199.1 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.18 (m, 4H), 8.08 (dd, *J* = 8.4, 1.0 Hz, 2H), 8.00 (dd, *J* = 8.4, 1.0 Hz, 2H), 7.70 – 7.45 (m, 12H), 5.11 (td, *J* = 11.1, 3.5 Hz, 1H), 4.90 (dq, *J* = 10.3, 7.0 Hz, 1H), 1.80 – 1.49 (m, 2H), 1.06 – 0.77 (m, 4H), 0.75 (d, *J* = 7.0 Hz, 3H), 0.61 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 141.46, 141.06, 139.05, 138.52, 134.29, 134.01, 133.95, 129.78, 129.32, 129.24, 129.01, 128.92, 128.89, 128.81, 128.67, 65.57, 62.69, 29.97, 28.59, 22.53, 16.91, 13.97. **IR (thin film):** 3067, 3029, 2956, 2871, 1583, 1448, 1367, 1170, 1083, 1045, 859, 753, 731, 720, 686, 652, 585, 554 cm^{-1}. **MS (ESI, positive mode):** 713.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{31}H_{34}N_2O_8S_4Na^+$ [M+Na]$^+$: 713.1090, Found: 713.1096.

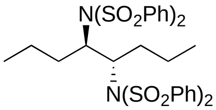
In order to determine the relative stereochemistry of the products derived from internal olefins, the above product (**3o**) was compared to the analogous diaddition products, **8d** (trans) and **8k'** (cis), from Muniz's paper.[7e] These products contain p-toluenesulfonimide groups instead of benzenesulfonimide groups, but are in all other ways identical to **3o**. The alkene resonances of **3o** for both ^{1}H and ^{13}C NMR are consistent with a trans-1,2-diamination product.

3d: ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.11 (td, *J* = 11.1, 3.5 Hz, 1H), 4.90 (dq, *J* = 10.3, 7.0 Hz, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 65.57, 62.69.

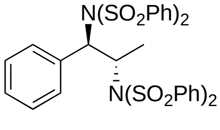
8d: ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.0 – 5.1 (m, 1H), 4.85 (dq, *J* = 10.3, 7.0 Hz, 1H). **^{13}C NMR (125 MHz, CDCl$_3$):** δ 65.4, 62.5.

8k’: ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.2 – 5.3 (m, 2H). **^{13}C NMR (125 MHz, CDCl$_3$):** δ 69.5, 64.8.

The stereochemistry for all other products derived from trans-1,2-olefins was assigned on the same basis.

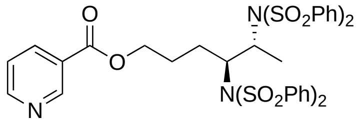


***N,N'*-(octane-4,5-diyl)bis(benzenesulfonimide) (3p).** Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 70% hexanes) to yield the product as a tan solid (100.8 mg, 74% yield). **Mp:** 204.5-206.4 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.15 (d, *J* = 7.5 Hz, 2H), 8.13 (d, *J* = 8.3 Hz, 2H), 7.68 – 7.61 (m, 4H), 7.55 (t, *J* = 7.7 Hz, 8H), 5.03 – 4.93 (m, 2H), 1.46 – 1.31 (m, 2H), 1.29 – 1.16 (m, 2H), 0.82 – 0.57 (m, 4H), 0.29 (t, *J* = 7.3 Hz, 6H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 141.18, 139.16, 134.28, 133.97, 129.72, 129.14, 128.94, 128.80, 66.93, 32.78, 19.60, 13.65. **IR (thin film):** 2963, 2872, 1449, 1366, 1169, 1082, 1058, 1020, 972, 913, 884, 843, 730, 719, 685, 667, 653, 594, 572, 553 cm^{-1}. **MS (ESI, positive mode):** 727.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{32}H_{36}N_2O_8S_4Na^+$ [M+Na]$^+$: 727.1247, Found: 727.1254.

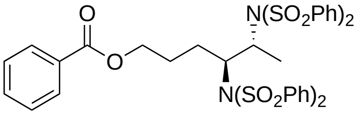


***N,N'*-(1-phenylpropane-1,2-diyl)bis(benzenesulfonimide) (3q).** Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as an off-white solid (114.8 mg, 85% yield). **Mp:** 173.5-181.5 °C.

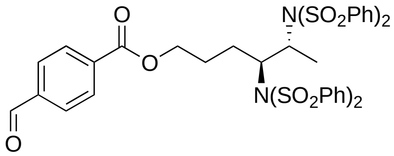
^{1}H NMR (500 MHz, Acetone): δ 8.23 – 8.17 (m, 2H), 8.05 – 8.02 (m, 2H), 7.85 – 7.76 (m, 4H), 7.74 – 7.66 (m, 4H), 7.60 – 7.50 (m, 4H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.38 – 7.28 (m, 6H), 7.22 – 7.16 (m, 2H), 6.48 (d, *J* = 10.9 Hz, 1H), 6.00 (dq, *J* = 11.0, 6.9 Hz, 1H), 0.86 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (126 MHz, Acetone):** δ 206.11, 142.29, 142.27, 139.96, 139.66, 135.77, 135.61, 135.26, 134.56, 134.38, 132.04, 130.39, 130.32, 130.15, 130.04, 129.74, 129.62, 129.21, 128.72, 128.34, 66.61, 60.35, 29.99, 29.84, 29.69, 17.63. **IR (thin film):** 2918, 2849, 1448, 1371, 1352, 1168, 1082, 846, 752, 733, 721, 684, 578, 554 cm^{-1}. **MS (ESI, positive mode):** 733.0 [M+Na]. **HRMS** (ESI): Calculated for $C_{33}H_{30}N_2O_8S_4Na^+$ [M+Na]$^+$: 733.0777, Found: 733.0776.



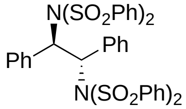
4,5-bis(benzenesulfonimido)hexyl nicotinate (3r). Prepared according to Standard Conditions A and purified by silica gel chromatography (30% ethyl acetate/ 70% hexanes) to yield the product as an off-white solid (63.1 mg, 40% yield). **Mp:** 191.2-196.1 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 9.15 (s, 1H), 8.79 (s, 1H), 8.24 – 8.12 (m, 4H), 8.05 (d, *J* = 8.1 Hz, 2H), 7.99 (d, *J* = 7.5 Hz, 2H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.64 – 7.42 (m, 12H), 7.40 – 7.32 (m, 1H), 5.16 (t, *J* = 10.9 Hz, 1H), 5.06 – 4.79 (m, 1H), 4.13 – 3.92 (m, 1H), 3.92 – 3.71 (m, 1H), 2.01 – 1.88 (m, 1H), 1.88 – 1.75 (m, 1H), 1.61 – 1.45 (m, 1H), 1.33 – 1.14 (m, 1H), 0.82 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 165.06, 153.44, 150.97, 141.32, 141.00, 138.74, 138.37, 137.26, 134.47, 134.36, 134.28, 133.99, 129.71, 129.28, 129.15, 129.02, 128.91, 128.65, 123.51, 65.18, 64.56, 62.37, 26.78, 25.75, 16.95. **IR (thin film):** 3067, 2953, 2894, 1723, 1591, 1448, 1367, 1285, 1169, 1083, 912, 859, 730, 721, 686, 651, 586, 554 cm^{-1}. **MS (ESI, positive mode):** 798.2 [M+H], 800.1 [M+NH$_4$]. **HRMS** (ESI): Calculated for $C_{36}H_{36}N_3O_{10}S_4^+$ [M+H]$^+$: 798.1278, Found: 798.1282.



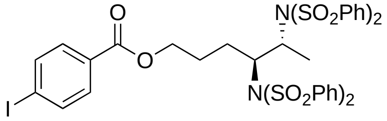
4,5-bis(benzenesulfonimido)hexyl benzoate (3s). Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as a tan solid (142.7 mg, 90% yield). **Mp:** 188.5-191.2 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.21 – 8.15 (m, 4H), 8.09 – 8.05 (m, 2H), 8.01 (dd, *J* = 8.4, 1.1 Hz, 2H), 7.95 – 7.91 (m, 2H), 7.68 – 7.37 (m, 15H), 5.17 (td, *J* = 11.7, 3.1 Hz, 1H), 4.95 (dq, *J* = 10.4, 7.0 Hz, 1H), 4.02 – 3.88 (m, 1H), 3.83 – 3.66 (m, 1H), 2.00 – 1.88 (m, 1H), 1.85 – 1.73 (m, 1H), 1.58 – 1.45 (m, 1H), 1.32 – 1.16 (m, 1H), 0.84 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 166.42, 141.36, 140.95, 138.72, 138.33, 134.45, 134.35, 134.24, 133.94, 133.00, 130.28, 129.72, 129.70, 129.27, 129.12, 129.02, 128.99, 128.98, 128.91, 128.54, 128.49, 65.24, 64.15, 62.42, 26.91, 25.88, 16.95. **IR (thin film):** 3165, 3067, 2954, 2892, 1718, 1449, 1367, 1276, 1170, 1083, 912, 860, 753, 731, 721, 686, 651, 586, 554 cm^{-1}. **MS (ESI, positive mode):** 814.2 [M+NH$_4$], 819.3 [M+Na]. **HRMS** (ESI): Calculated for $C_{37}H_{36}N_2O_{10}S_4Na^+$ [M+Na]$^+$: 819.1145, Found: 819.1150.



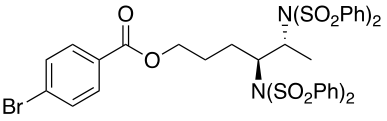
4,5-bis(benzenesulfonimido)hexyl 4-formylbenzoate (3t). Prepared according to Standard Conditions A and purified by silica gel chromatography (30% ethyl acetate/ 70% hexanes) to yield the product as an off-white solid (159.1 mg, 96% yield). **Mp:** 206-201.2 °C. **^{1}H NMR (500 MHz, CD$_2$Cl$_2$):** δ 10.10 (s, 1H), 8.16 (d, *J* = 8.2 Hz, 2H), 8.13 (d, *J* = 8.2 Hz, 2H), 8.10 (d, *J* = 8.0 Hz, 2H), 8.04 (d, *J* = 8.1 Hz, 2H), 7.93 (d, *J* = 9.2 Hz, 2H), 7.92 (d, *J* = 8.7 Hz, 2H), 7.74 – 7.50 (m, 10H), 7.47 (t, *J* = 7.6 Hz, 2H), 5.17 (t, *J* = 10.9 Hz, 1H), 5.04 – 4.86 (m, 1H), 4.11 – 3.97 (m, 1H), 3.87 – 3.76 (m, 1H), 2.03 – 1.91 (m, 1H), 1.86 – 1.73 (m, 1H), 1.63 – 1.48 (m, 1H), 1.34 – 1.17 (m, 1H), 0.84 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 191.83, 165.42, 141.34, 141.00, 139.22, 138.72, 138.33, 135.24, 134.49, 134.37, 134.28, 133.92, 130.36, 129.71, 129.65, 129.29, 129.15, 129.01, 128.90, 128.66, 65.20, 64.68, 62.42, 26.83, 25.78, 16.87. **IR (thin film):** 3067, 2951, 2853, 2738, 1722, 1705, 1610, 1577, 1449, 1367, 1313, 1277, 1202, 1170, 1118, 1083, 1044, 955, 858, 755, 730, 721, 686, 651, 586, 554 cm^{-1}. **MS (ESI, positive mode):** 847.0 [M+Na]. **HRMS** (ESI): Calculated for $C_{38}H_{37}N_2O_{11}S_4^+$ [M+H]$^+$: 825.1275, Found: 825.1281.



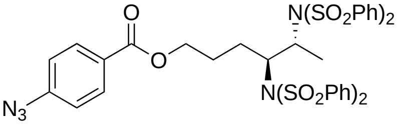
***N*,*N*'-(1,2-diphenylethane-1,2-diyl)bis(benzenesulfonimide) (3u).** Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as a yellow solid (116 mg, 75% yield). **Mp:** 159.5-161.8 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.77 (s, 4H), 7.49 (d, *J* = 7.5 Hz, 4H), 7.40 – 7.30 (m, 4H), 7.21 (s, 2H), 7.14 – 7.06 (m, 14H), 7.01 (t, *J* = 7.4 Hz, 4H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 141.30, 138.69, 135.06, 133.36, 133.07, 128.92, 128.54, 128.51, 128.43, 128.10, 66.60. **IR (thin film):** 3100, 3065, 3034, 1584, 1500, 1448, 1370, 1337, 1166, 1081, 985, 910, 843, 751, 734, 721, 703, 684, 605, 582, 552 cm^{-1}. **MS (ESI, positive mode):** 795.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{38}H_{32}N_2O_8S_4Na^+$ [M+Na]$^+$: 795.0934, Found: 795.0939.



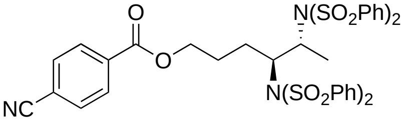
4,5-bis(benzenesulfonimido)hexyl 4-iodobenzoate (3v). Prepared according to Standard Conditions A and purified by silica gel chromatography (100% CH_2Cl_2) to yield the product as a white solid (182.2 mg, 93% yield). **Mp:** 219.5-226.3 °C. **^{1}H NMR (500 MHz, CD_2Cl_2):** δ 8.14 (d, *J* = 8.1 Hz, 2H), 8.11 (d, *J* = 8.2 Hz, 2H), 8.08 (d, *J* = 8.3 Hz, 2H), 7.97 (d, *J* = 8.1 Hz, 2H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.78 – 7.56 (m, 12H), 7.53 (t, *J* = 7.8 Hz, 2H), 5.19 (t, *J* = 11.0 Hz, 1H), 4.99 (m, 1H), 4.10 – 3.95 (m, 1H), 3.87 – 3.71 (m, 1H), 2.06 – 1.88 (m, 1H), 1.88 – 1.69 (m, 1H), 1.68 – 1.43 (m, 1H), 1.40 – 1.18 (m, 1H), 0.88 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (126 MHz, CD_2Cl_2):** δ 166.19, 141.68, 141.38, 139.18, 138.70, 138.35, 135.06, 134.97, 134.83, 134.53, 131.58, 130.45, 130.06, 129.81, 129.52, 129.27, 129.07, 101.05, 65.79, 64.76, 62.76, 27.25, 26.31, 17.23. **IR (thin film):** 3066, 2955, 1719, 1586, 1448, 1367,1280, 1270, 1169, 1083, 860, 753, 685, 585, 554 cm^{-1}. **MS (ESI, positive mode):** 944.9 [M+Na]. **HRMS** (ESI): Calculated for $C_{37}H_{35}IN_2O_{10}S_4Na^+$ [M+Na]$^+$: 945.0111, Found: 945.0121.



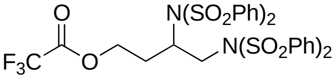
4,5-bis(benzenesulfonimido)hexyl 4-bromobenzoate (3w). Prepared according to Standard Conditions A and purified by silica gel chromatography (100% CH_2Cl_2) to yield the product as a white solid (145.5 mg, 83% yield). **Mp:** 212.9-217.6 °C. **^{1}H NMR (500 MHz, CD_2Cl_2):** δ 8.18 – 8.07 (m, 4H), 8.02 (d, *J* = 7.2 Hz, 2H), 7.91 (d, *J* = 7.5 Hz, 2H), 7.80 (d, *J* = 8.6 Hz, 2H), 7.72 – 7.50 (m, 12H), 7.47 (t, *J* = 7.9 Hz, 2H), 5.18 – 5.07 (m, 1H), 5.00 – 4.85 (m, 1H), 3.98 (dt, *J* = 10.9, 5.5 Hz, 1H), 3.75 (ddd, *J* = 10.9, 8.4, 5.4 Hz, 1H), 1.98 – 1.87 (m, 1H), 1.81 – 1.68 (m, 1H), 1.59 – 1.43 (m, 1H), 1.32 – 1.08 (m, 1H), 0.82 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (126 MHz, CD_2Cl_2):** δ 165.95, 141.68, 141.38, 139.18, 138.70, 135.06, 134.97, 134.83, 134.53, 132.30, 131.70, 130.06, 129.90, 129.81, 129.53, 129.26, 129.08, 128.39, 65.80, 64.78, 62.76, 27.25, 26.31, 17.23. **IR (thin film):** 3068, 2956, 1716, 1590, 1449, 1367, 1273, 1169, 1083, 860, 754, 721, 685, 586, 555 cm^{-1}. **MS (ESI, positive mode):** 897.0 [M+Na]. **HRMS** (ESI): Calculated for $C_{37}H_{35}{}^{79}BrN_2O_{10}S_4Na$ [M+Na]$^+$: 897.0250, Found: 897.0257.



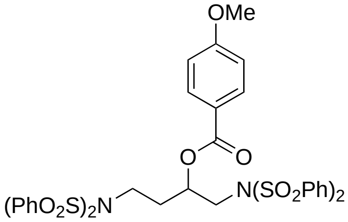
4,5-bis(benzenesulfonimido)hexyl 4-azidobenzoate (3x). Prepared according to Standard Conditions A and purified by silica gel chromatography (30% ethyl acetate/ 70% hexanes) to yield the product as a yellow solid (143 mg, 84% yield). **Mp:** 191.8-194 °C. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.19 (d, *J* = 6.5 Hz, 2H), 8.17 (d, *J* = 7.1 Hz, 2H), 8.06 (d, *J* = 7.6 Hz, 2H), 8.00 (d, *J* = 7.6 Hz, 2H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.70 – 7.39 (m, 12H), 7.03 (d, *J* = 8.5 Hz, 2H), 5.16 (t, *J* = 10.9 Hz, 1H), 5.01 – 4.83 (m, 1H), 4.03 – 3.88 (m, 1H), 3.84 – 3.62 (m, 1H), 1.97 (t, *J* = 13.6 Hz, 1H), 1.88 – 1.70 (m, 1H), 1.62 – 1.38 (m, 1H), 1.35 – 1.14 (m, 1H), 0.83 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 165.59, 144.79, 141.37, 140.97, 138.72, 138.32, 134.45, 134.35, 134.24, 133.91, 131.56, 129.69, 129.27, 129.12, 128.99, 128.90, 128.60, 126.82, 118.96, 65.25, 64.17, 62.40, 26.87, 25.83, 16.90. **IR (thin film):** 3067, 2953, 2124, 1715, 1603, 1448, 1382, 1367, 1275, 1169, 1083, 858, 731, 721, 686, 586, 555 cm^{-1}. **MS (ESI, positive mode):** 838.0 [M+H]. **HRMS** (ESI): Calculated for $C_{37}H_{36}N_5O_{10}S$ [M+H]$^+$: 838.1340, Found: 838.1348.



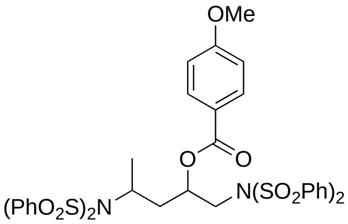
4,5-bis(benzenesulfonimido)hexyl 4-cyanobenzoate (3y). Prepared according to Standard Conditions A and purified by silica gel chromatography (30% ethyl acetate/ 70% hexanes) to yield the product as an off-white solid (141.7 mg, 87% yield). **Mp:** 219.6-223.5 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.28 – 8.10 (m, 4H), 8.10 – 7.90 (m, 6H), 7.79 – 7.38 (m, 14H), 5.23 – 5.09 (m, 1H), 4.94 (dq, *J* = 10.3, 7.0 Hz, 1H), 4.10 (dt, *J* = 10.7, 5.4 Hz, 1H), 3.85 – 3.72 (m, 1H), 2.20 – 2.01 (m, 1H), 1.95 – 1.78 (m, 1H), 1.69 – 1.49 (m, 1H), 1.37 – 1.11 (m, 1H), 0.79 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 164.84, 141.33, 141.04, 138.73, 138.30, 134.51, 134.40, 134.31, 134.10, 133.90, 132.36, 130.28, 129.73, 129.32, 129.17, 129.06, 129.03, 129.01, 128.88, 128.73, 118.16, 116.40, 65.17, 64.81, 62.47, 26.80, 25.79, 16.78. **IR (thin film):** 3067, 2957, 2230, 1724, 1449, 1367, 1277, 1169, 1083, 860, 686, 586, 555 cm^{-1}. **MS (ESI, positive mode):** 844.0 [M+Na]. **HRMS** (ESI): Calculated for $C_{38}H_{35}N_3O_{10}S_4Na^+$ [M+Na]$^+$: 844.1097, Found: 844.1102.



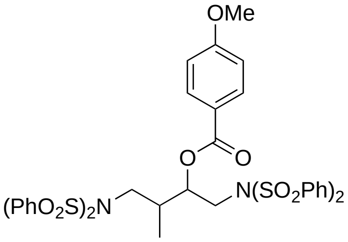
3,4-bis(benzenesulfonimido)butyl 2,2,2-trifluoroacetate (3aa). Prepared according to Standard Conditions A and purified by silica gel chromatography (20% ethyl acetate/ 80% hexanes) to yield the product as a yellow resin (103.6 mg, 68% yield). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.12 (d, *J* = 7.8 Hz, 2H), 8.08 (d, *J* = 7.7 Hz, 2H), 7.99 (d, *J* = 7.7 Hz, 4H), 7.72 – 7.62 (m, 4H), 7.62 – 7.47 (m, 8H), 4.92 (tt, *J* = 11.6, 3.8 Hz, 1H), 4.67 (dd, *J* = 14.7, 11.2 Hz, 1H), 3.91 – 3.75 (m, 2H), 3.59 (dd, *J* = 14.7, 4.3 Hz, 2H), 2.51 – 2.34 (m, 1H), 2.14 (dtd, *J* = 11.5, 8.1, 3.4 Hz, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 156.92 (q, *J* = 42.4 Hz), 140.39, 138.84, 138.68, 134.54, 134.34, 129.45, 129.37, 129.30, 129.10, 128.88, 128.77, 128.70, 114.50 (q, *J* = 285.8 Hz) ,77.36, 64.20, 60.47, 58.15, 50.01, 27.49, 21.14, 14.29. **IR (thin film):** 3167, 3069, 2960, 1789, 1449, 1377, 1361, 1221, 1170, 1083, 911, 879, 818, 780, 753, 733, 721, 686, 651, 584, 554 cm^{-1}. **MS (ESI, positive mode):** 783.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{30}H_7F_3N_2O_{10}S_4Na^+$ [M+Na]$^+$: 783.0393, Found: 783.0396.



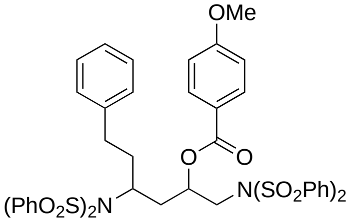
1,4-bis(benzenesulfonimido)butan-2-yl 4-methoxybenzoate (5ae). Prepared according to Standard Conditions B and purified by silica gel chromatography (25% ethyl acetate/ 75% hexanes) to yield the product as a white solid (147.1 mg, 92% yield). **Mp:** 115.7-120.9 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.03 – 7.96 (m, 6H), 7.92 (dd, *J* = 8.4, 1.1 Hz, 4H), 7.64 – 7.54 (m, 4H), 7.47 (m, 8H), 6.96 – 6.87 (m, 2H), 5.36 – 5.18 (m, 1H), 4.12 (dd, *J* = 15.4, 7.5 Hz, 1H), 3.91 – 3.83 (m, 1H), 3.85 (s, 3H), 3.75 (m, 2H), 2.26 – 2.16 (m, 1H), 2.16 – 2.05 (m, 1H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 165.51, 163.80, 139.53, 139.29, 134.13, 134.04, 132.08, 129.27, 129.23, 128.40, 128.23, 121.84, 113.79, 69.79, 55.58, 50.51, 45.39, 32.97. **IR (thin film):** 3067, 3007, 2960, 2934, 2841, 1712, 1606, 1512, 1448, 1374, 1355, 1259, 1170, 1085, 1026, 912, 842, 753, 736, 720, 686, 582, 551 cm^{-1}. **MS (ESI, positive mode):** 816.5 [M+NH$_4$], 821.5 [M+Na]. **HRMS** (ESI): Calculated for $C_{36}H_{34}N_2O_{11}S_4Na^+$ [M+Na]$^+$: 821.0938, Found: 821.0944.



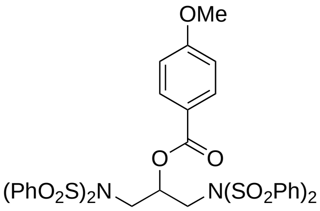
1,4-bis(benzenesulfonimido)pentan-2-yl 4-methoxybenzoate (5af). Prepared according to Standard Conditions B and purified by silica gel chromatography (25% ethyl acetate/ 75% hexanes) to yield the product as a yellow resin (110.8 mg, 68% yield, 2.3:1 dr). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.09 – 7.84 (m, 22H, major+minor), 7.66 – 7.37 (m, 22H, major+minor), 6.95 (d, *J* = 9.0 Hz, 2H, major), 6.90 (d, *J* = 8.9 Hz, 2H, minor), 5.29 – 5.09 (m, 2H, major+minor), 4.39 – 4.28 (m, 1H, minor), 4.28 – 4.18 (m, 1H, major), 4.07 (dd, *J* = 15.4, 7.0 Hz, 1H, major), 4.02 (dd, *J* = 15.9, 7.8 Hz, 1H, minor), 3.92 (dd, *J* = 15.3, 5.0 Hz, 1H, major), 3.87 (s, 3H, major), 3.85 (s, 3H, minor), 3.79 (dd, *J* = 15.9, 3.1 Hz, 1H, minor), 2.71 – 2.61 (m, 1H, major), 2.52 – 2.41 (m, 1H, minor), 2.24 – 2.14 (m, 1H, minor), 2.13 – 2.03 (m, 1H, major), 1.42 (d, *J* = 6.8 Hz, 3H, minor), 1.23 (d, *J* = 6.8 Hz, 3H, major). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 165.76, 165.37, 163.90, 163.70, 139.39, 139.25, 134.14, 134.08, 132.20, 132.03, 129.26, 129.17, 128.47, 128.43, 122.10, 121.75, 113.81, 113.73, 71.63, 69.01, 56.64, 56.16, 55.60, 55.56, 50.91, 50.70, 39.86, 38.70, 29.78, 20.03, 18.42. **IR (thin film):** 3068, 3006, 2935, 2842, 1711, 1606, 1512, 1448, 1370, 1259, 1169, 1085, 1030, 910, 753, 733, 721, 686, 583, 551 cm^{-1}. **MS (ESI, positive mode):** 835.0 [M+Na]. **HRMS** (ESI): Calculated for $C_{37}H_{36}N_2O_{11}S_4Na^+$ $[M+X]^+$: 835.1094, Found: 835.1085.



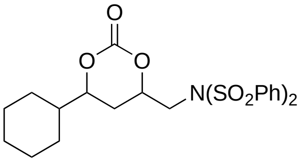
3-methyl-1,4-bis(benzenesulfonimido)butan-2-yl 4-methoxybenzoate (5ag). Prepared according to Standard Conditions B and purified by silica gel chromatography (25% ethyl acetate/ 75% hexanes) to yield the product as a yellow resin (144.1 mg, 89% yield, 1:1 dr). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.05 – 7.96 (m, 14H, A+B), 7.95 (dd, *J* = 8.4, 0.9 Hz, 4H, A+B), 7.89 (dd, *J* = 8.4, 0.9 Hz, 4H, A+B), 7.65 – 7.53 (m, 8H, A+B), 7.53 – 7.39 (m, 14H, A+B), 6.92 (dd, *J* = 8.8, 1.2 Hz, 4H, A+B), 5.40 (m, 2H, A+B), 4.22 (dd, *J* = 15.7, 9.1 Hz, 1H, A), 4.10 (dd, *J* = 15.4, 7.9 Hz, 1H, B), 3.93 (dd, *J* = 15.4, 4.7 Hz, 1H, B), 3.89 – 3.82 (m, 8H, A+B), 3.77 (dd, *J* = 14.6, 4.2 Hz, 2H, A+B), 3.65 (dd, *J* = 14.8, 10.4 Hz, 1H, B), 2.61 – 2.46 (m, 2H, A+B), 1.03 (d, *J* = 7.0 Hz, 3H, A), 0.96 (d, *J* = 7.0 Hz, 3H, B). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 165.42, 165.26, 163.74, 163.71, 139.44, 139.31, 139.27, 134.10, 134.01, 132.18, 132.10, 129.22, 129.20, 129.14, 128.47, 128.41, 128.31, 122.00, 113.77, 113.72, 77.36, 74.00, 72.74, 60.47, 55.57, 51.74, 50.41, 49.80, 48.78, 36.29, 35.18, 29.78, 21.14, 14.30, 13.86, 11.65. **IR (thin film):** 3067, 2971, 2935, 2842, 1712, 1605, 1512, 1448, 1374, 1355, 1259, 1169, 1085, 1031, 912, 794, 782, 753, 738, 720, 686, 583, 551 cm^{-1}. **MS (ESI, positive mode):** 835.3 [M+Na]. **HRMS** (ESI): Calculated for $C_{37}H_{36}N_2O_{11}S_4Na^+$ [M+Na]$^+$: 835.1094, Found: 835.1100.



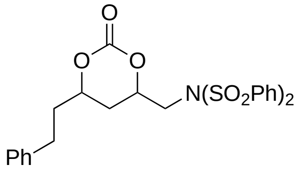
6-phenyl-1,4-bis(benzenesulfonimido)hexan-2-yl 4-methoxybenzoate (5ah). Prepared according to Standard Conditions B and purified by silica gel chromatography (25% ethyl acetate/ 75% hexanes) to yield the product as an off-white resin (102.6 mg, 57% yield, 2.1:1 dr). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.21 – 7.90 (m, 20H, major+minor), 7.80 (d, *J* = 7.8 Hz, 2H, major), 7.69 – 7.31 (m, 22H, major+minor), 7.29 – 7.21 (m, 2H, minor), 7.21 – 7.06 (m, 4H, major+minor), 6.97 (d, *J* = 8.0 Hz, 4H, major), 6.91 (d, *J* = 7.8 Hz, 2H, minor), 6.75 (d, *J* = 7.0 Hz, 2H, minor), 5.36 – 5.29 (m, 1H, minor), 5.29 – 5.18 (m, 1H, major), 4.36 – 4.25 (m, 1H, minor), 4.24 – 4.14 (m, 1H, major), 4.07 (dd, *J* = 15.7, 6.7 Hz, 1H, major), 3.99 – 3.91 (m, 1H, minor), 3.91 – 3.83 (m, 7H, major+minor), 3.78 – 3.68 (m, 1H, minor), 2.64 – 2.52 (m, 1H, major), 2.43 – 2.32 (m, 1H, minor), 2.32 – 2.11 (m, 2H, major+minor), 2.11 – 1.97 (m, 4H, major+minor), 1.94 – 1.76 (m, 4H, major+minor). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 165.79, 165.55, 163.93, 163.74, 141.50, 141.29, 140.86, 139.49, 139.13, 138.83, 134.16, 134.10, 133.80, 132.27, 132.09, 131.77, 129.47, 129.28, 129.21, 129.17, 129.05, 128.85, 128.61, 128.58, 128.51, 128.44, 128.38, 128.35, 128.33, 128.29, 126.04, 122.15, 121.81, 113.86, 113.78, 77.36, 71.59, 68.88, 61.46, 61.25, 60.48, 55.61, 55.59, 51.04, 50.59, 38.64, 36.28, 34.37, 33.57, 32.86, 21.15, 14.30. **IR (thin film):** 3064, 3026, 2935, 2843, 2360, 2340, 1710, 1605, 1448, 1373, 1355, 1259, 1169, 1084, 1026, 910, 753, 732, 720, 686, 582, 551 cm^{-1}. **MS (ESI, positive mode):** 920.2 [M+NH$_4$], 925.2 [M+Na]. **HRMS** (ESI): Calculated for $C_{44}H_{42}N_2O_{11}S_4Na^+$ [M+Na]$^+$: 925.1564, Found: 925.1561.



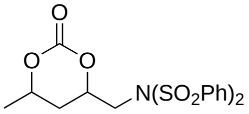
1,3-bis(benzenesulfonimido)propan-2-yl 4-methoxybenzoate (5ai). Prepared according to Standard Conditions B and purified by silica gel chromatography (25% ethyl acetate/ 75% hexanes) to yield the product as a white solid (128.8 mg, 82% yield). **Mp:** 153.7-159.1 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.01 – 7.93 (m, 10H), 7.57 (t, *J* = 7.5 Hz, 4H), 7.45 (t, *J* = 7.9 Hz, 8H), 6.86 (d, *J* = 9.0 Hz, 2H), 5.58 (tt, *J* = 7.3, 4.7 Hz, 1H), 4.21 (dd, *J* = 15.8, 7.3 Hz, 2H), 4.10 (dd, *J* = 15.8, 4.6 Hz, 2H), 3.82 (s, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 165.34, 163.66, 139.08, 134.13, 132.23, 129.20, 128.55, 121.81, 113.65, 69.71, 55.52, 48.96. **IR (thin film):** 3067, 3007, 2936, 2841, 1718, 1605, 1448, 1374, 1259, 1170, 1085, 784, 753, 736, 721, 685, 583, 551 cm^{-1}. **MS (ESI, positive mode):** 802.2 [M+NH$_4$], 807.4 [M+Na]. **HRMS** (ESI): Calculated for $C_{35}H_{32}N_2O_{11}S_4Na^+$ [M+Na]$^+$: 807.0781, Found: 807.0784.



***N*-((6-cyclohexyl-2-oxo-1,3-dioxan-4-yl)methyl)-benzenesulfonimide (7a).** Prepared according to Standard Conditions A and purified by silica gel chromatography (30% ethyl acetate/ 70% hexanes) to yield the product as a tan solid (89 mg, 89% yield, 1.16:1 dr). **Mp:** 68.9-72.5 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.06 (d, *J* = 7.8 Hz, 4H, minor), 8.02 (d, *J* = 7.9 Hz, 4H, major), 7.68 (d, *J* = 6.5 Hz, 2H, minor), 7.67 (d *J* = 6.0 Hz, 2H, minor), 7.56 (t, *J* = 7.8 Hz, 8H, major+minor), 4.82 (quin, *J* = 5.9 Hz, 1H, major), 4.78 – 4.66 (m, 1H, ,minor), 4.23 (q, *J* = 6.5 Hz, 1H, major), 4.11 (m, 3H, major+minor), 3.82 – 3.67 (m, 2H, major+minor), 2.09 – 1.91 (m, 4H, major+minor), 1.91 – 1.46 (m, 10H, major+minor), 1.35 – 1.09 (m, 8H, major+minor), 1.09 – 0.91 (m, 4H, major+minor). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 148.36, 148.26, 138.94, 138.86, 134.44, 134.38, 129.32, 129.28, 128.81, 128.72, 82.75, 80.09, 77.36, 77.12, 74.85, 51.62, 50.56, 42.06, 41.54, 28.30, 27.99, 27.84, 27.75, 26.18, 26.11, 25.74, 25.63, 25.55. **IR (thin film):** 3067, 2930, 2854, 2360, 2341, 1749, 1448, 1375, 1169, 735, 721, 686, 582, 550 cm^{-1}. **MS (ESI, positive mode):** 511.3 [M+NH$_4$], 516.2 [M+Na]. **HRMS** (ESI): Calculated for $C_{23}H_{31}N_2O_7S_2^+$ [M+NH$_4$]$^+$: 511.1567, Found: 511.1570.



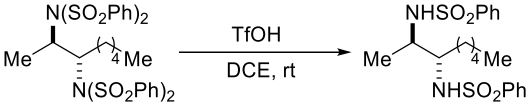
***N*-((2-oxo-6-phenethyl-1,3-dioxan-4-yl)methyl)-benzenesulfonimide (7b).** Prepared according to Standard Conditions A and purified by silica gel chromatography (25% ethyl acetate/ 75% hexanes) to yield the product as a yellow resin (77.9 mg, 76% yield, 1.25:1 dr). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.10 – 7.91 (m, 8H, major+minor), 7.74 – 7.60 (m, 4H, major+minor), 7.55 (t, *J* = 7.6 Hz, 8H, major+minor), 7.38 – 7.14 (m, 10H, major+minor), 4.83 (quin, *J* = 6.1 Hz, 1H, major), 4.78 – 4.69 (m, 1H, minor), 4.54 – 4.44 (m, 1H, major), 4.34 – 4.23 (m, 1H, minor), 4.09 (dd, *J* = 15.8, 6.7 Hz, 2H, major+minor), 3.70 (dt, *J* = 15.6, 6.6 Hz, 2H, major+minor), 2.88 – 2.64 (m, 4H, major+minor), 2.10 – 1.74 (m, 6H, major+minor), 1.70 – 1.54 (m, 2H, major+minor). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 148.04, 147.96, 140.29, 138.73, 134.50, 134.44, 129.35, 129.28, 128.84, 128.73, 128.55, 126.43, 77.46, 77.36, 75.42, 74.55, 51.48, 50.52, 36.86, 36.44, 30.96, 30.61, 30.50, 28.39. **IR (thin film):** 3064, 3027, 2926, 2852, 1749, 1448, 1375, 1355, 1203, 1169, 1130, 1084, 754, 738, 721, 686, 582, 551 cm^{-1}. **MS (ESI, positive mode):** 538.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{25}H_{25}NO_7S_2Na^+$ [M+Na]$^+$: 538.0965, Found: 538.0964.



***N*-((6-methyl-2-oxo-1,3-dioxan-4-yl)methyl)-benzenesulfonimide (7c).** Prepared according to Standard Conditions A and purified by silica gel chromatography (30% ethyl acetate/ 70% hexanes) to yield the product as an off-white solid (77.3 mg, 90% yield, 1.3:1 dr). **Mp:** 58-62.4 °C. **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.04 (d, *J* = 7.4 Hz, 8H, major+minor), 7.67 (t, *J* = 6.7 Hz, 4H, major+minor), 7.56 (t, *J* = 6.1 Hz, 8H, major+minor), 4.90 – 4.82 (m, 1H, major), 4.82 – 4.74 (m, 1H, minor), 4.73 – 4.63 (m, 1H, major), 4.53 – 4.43 (m, 1H, minor), 4.12 (td, *J* = 16.3, 6.8 Hz, 2H, major+minor), 3.73 (td, *J* = 15.6, 5.4 Hz, 2H, major+minor), 2.19 – 2.01 (m, 2H, major+minor), 1.95 – 1.83 (m, 1H, major), 1.59 (m, 1H, minor), 1.36 (d, *J* = 6.2 Hz, 6H, major+minor). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 148.07, 147.96, 138.73, 138.68, 134.48, 134.43, 129.32, 129.26, 128.82, 128.72, 77.26, 75.12, 74.36, 72.79, 51.48, 50.63, 32.18, 29.61, 21.19, 20.64. **IR (thin film):** 3067, 2983, 2935, 1750, 1449, 1373, 1355, 1247, 1203, 1170, 1128, 1084, 913, 822, 755, 736, 721, 686, 583, 551 cm^{-1}. **MS (ESI, positive mode):** 488.1 [M+Na]. **HRMS** (ESI): Calculated for $C_{18}H_9NO_7S_2Na$ [M+Na]$^+$: 448.0495, Found: 448.0492.

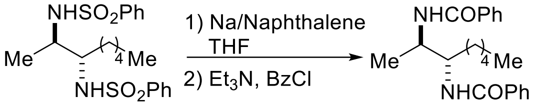
4.4.5 *Procedures for Deprotection*

Monodeprotection



A flame dried round bottom flask equipped with a stir bar and a rubber septum was charged with bis-benzenesulfonimide substrate (956 mg, 1.36 mmol), dichloroethane (DCE) (34 mL, 0.04 M), and triflic acid (480 µL, 5.43 mmol) at 0 °C under nitrogen. The mixture was stirred at room temperature for 43 hours and then quenched with 15 drops of neat ethylenediamine and subsequently diluted with 1.0 M NaOH aq. solution. The resulting biphasic mixture was extracted with CH_2Cl_2 (3x). The combined organic extracts were dried over sodium sulfate (Na_2SO_4), filtered, and then concentrated *in vacuo*. The product was purified via silica gel flash column chromatography (30% pentane/ 70% ether) to yield the product as a yellow resin (496 mg, 86% yield).[9] **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.86 (d, *J* = 7.4 Hz, 2H), 7.80 (d, *J* = 7.4 Hz, 2H), 7.64 – 7.56 (m, 2H), 7.56 – 7.44 (m, 4H), 5.40 (d, *J* = 9.0 Hz, 1H), 4.96 (d, *J* = 8.9 Hz, 1H), 3.34 – 3.19 (m, 1H), 3.00 – 2.87 (m, 1H), 1.24 – 1.15 (m, 1H), 1.12 – 1.05 (m, 1H), 1.05 – 0.96 (m, 2H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.93 – 0.74 (m, 4H), 0.72 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, CDCl$_3$):** δ 140.84, 140.09, 133.00, 132.74, 129.25, 129.24, 127.38, 127.30, 57.84, 52.33, 31.56, 31.08, 25.25, 22.33, 16.59, 13.93. **IR (thin film):** 3278, 3066, 2955, 2931, 2860, 1586, 1448, 1385, 1325, 1263, 1162, 1092, 1024, 905, 801, 756, 721, 690, 597, 559, 457 cm^{-1}. **MS (ESI, positive mode):** 425.1 [M+1], 447.1 [M+Na].

Second Deprotection



An oven dried, two-neck flask was charged with naphthalene (621 mg, 4.85 mmol) in THF (12.13 mL, 0.08 M) and cut-up Na (112 mg, 4.85 mmol) was gradually added. The solution quickly turned dark green and was stirred at room temperature for 4h. The bis-benzenesulfonamide (412 mg, 0.97 mmol) in THF (12.13 mL, 0.08 M) was then added to the above solution via syringe at 0 °C, and the mixture was stirred overnight at room temperature. Water (0.7 mL) was added to quench reaction and the mixture was diluted with EtOAc. The organic layer was dried over $MgSO_4$ and filtered. The organic solution was concentrated and then diluted in CH_2Cl_2 (25 mL) and triethylamine (811 µL, 5.82 mmol) and benzoyl chloride (676 µL, 5.82 mmol) were added. The reaction was allowed to stir for 3 hours then water was added. The mixture was extracted CH_2Cl_2 (3x). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The resulting solid was purified by silica gel flash column chromatography (70% hexane /30% EtOAc) to yield the product as a white solid (209.2 mg, 61% yield).[7f] **Mp:** 228.9-230.8 °C. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.98 (d, *J* = 6.1 Hz, 1H), 7.90 (d, *J* = 7.2 Hz, 2H), 7.85 (d, *J* = 7.4 Hz, 2H), 7.53 (M, 2H), 7.49 – 7.43 (m, 4H), 6.51 (d, *J* = 7.5 Hz, 1H), 4.28 (dd, *J* = 11.9, 5.7 Hz, 2H), 1.75 – 1.62 (m, 1H), 1.62 – 1.51 (m, 1H), 1.51 – 1.39 (m, 2H), 1.38 – 1.29 (m, 4H), 1.26 (d, *J* = 6.6 Hz, 3H), 0.88 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 169.24, 167.15, 134.58, 132.03, 131.47, 128.92, 128.69, 127.28, 127.19, 55.12, 51.27, 32.45, 31.74, 26.39, 22.64, 15.25, 14.12. **IR (thin film):** 3287, 2954, 2924, 2856, 2360, 1630, 1622, 1532, 1479, 1449, 1336, 1155, 696 cm^{-1}. **MS (ESI, positive mode):** 375.2 [M+Na].

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VITA

Derek Obenschain was born and raised in Staunton, Virginia. In 2010, he received his Bachelor of Science majoring in chemistry from the University of Richmond where he worked in Dr. C. Wade Downey’s organic chemistry research laboratory. He attended graduate school at the University of Washington working in Dr. Forrest E. Michael’s synthetic chemistry laboratory. In 2020, he earned a Doctor of Philosophy in Chemistry from the University of Washington.