

Palladium(II) Catalyzed Intramolecular Hydroamination of 1,3-dienes

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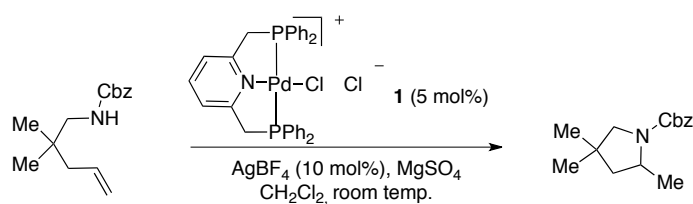
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Introduction

The formation of carbon-nitrogen bonds is of key importance in the synthesis of many industrial chemicals, pharmaceuticals and natural products. Traditional methods for C-N bond formation have limitations associated with them, so new methods for this transformation would prove interesting and valuable.¹ Hydroamination is the addition of an amine to an unsaturated carbon-carbon bond. This is a thermodynamically feasible reaction, yet needs to be promoted because of a significantly high reaction barrier.² One way to promote hydroamination is through the use of transition metal



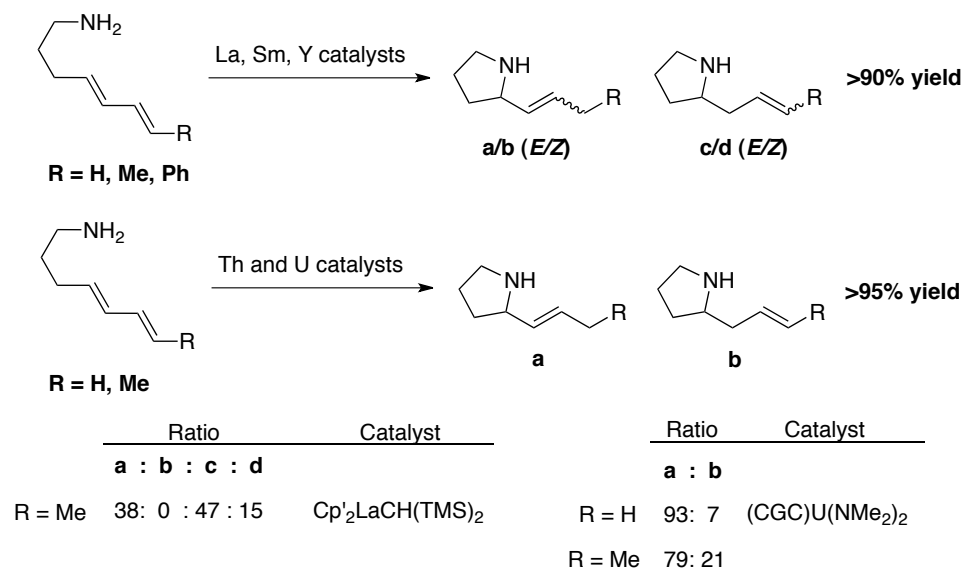
Scheme 1: Michael Hydroamination of Unactivated Alkenes

catalysts. The Michael lab has devised a palladium catalyzed intramolecular hydroamination of unactivated aminoalkenes using a tridentate phosphorous-nitrogen ligand (PNP). The reaction proved to be a great improvement to the field because of short reaction times, low catalyst loading, mild reaction conditions and utilization of a diverse group of amide and carbamate protecting groups.³ With the great success of this hydroamination under the catalytic conditions described by Michael (Scheme 1), new substrates should be explored to highlight its synthetic utility, additionally affording products containing more synthetically useful functionality.

Interest in the hydroamination reaction has greatly increased within the last decade, enabling carbon-nitrogen bond formation across alkenes, alkynes, allenes and dienes using rare earth metals, lanthanides, alkaline earth metals and late transition metals². Many palladium complexes have been used as catalysts for inter- and intramolecular hydroamination of unactivated alkenes, but they often require elevated temperature to achieve practical reaction rates.⁴ In light of palladium's shortcomings for promoting hydroamination, the Michael lab created a variant of the intramolecular palladium catalyzed hydroamination of unactivated alkenes (Scheme 1). Palladium

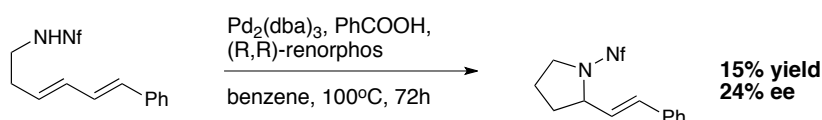
catalyst **1** was able to catalyze the reaction at room temperature while avoiding β -hydride elimination, a common byproduct of palladium catalyzed hydroamination, by using a tridentate ligand to block coordination sites needed for this undesired side reaction. Although the reaction efficiently forms desirable nitrogen heterocycles, the use of alkenes as hydroamination substrates affords products with no reactive handle. Several attempts have been made in our group to expand the substrate scope using the present catalytic system, but only terminal unfunctionalized alkenes showed the desired reactivity. One class of unsaturated aminoalkenes that our lab had not yet explored for the intramolecular hydroamination reaction was 1,3-dienes. Use of 1,3-dienes as substrates for hydroamination are appealing because products still contain an olefin, which could be useful for further functionalization. These substrates have been previously studied in hydroamination reactions, but often suffer selectivity issues when adding nitrogen across the olefin.

It has been shown that rare earth metal complexes, late transition metal complexes and certain Brønsted acids will catalyze the intramolecular hydroamination of dienes to form substituted pyrrolidines and piperidines with pendant alkenyl functionality. Although more synthetically useful products are offered upon diene hydroamination than alkene hydroamination, the allowed substitution patterns on the diene itself are limited (typically terminal or no substitution) and use of these catalytic systems often result in poor selectivity. Furthermore, the complexes themselves are often air and water sensitive.



Scheme 2: Marks Organolanthanide and Actinide Hydroaminations

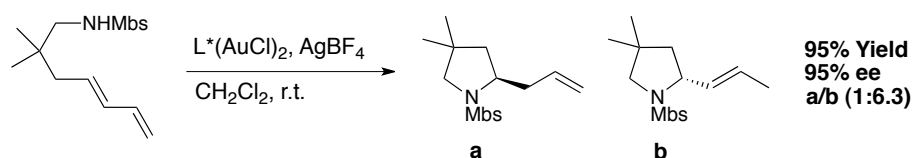
Organolanthanide and actinide complexes that promote the hydroamination of 1,3-dienes have been extensively studied by Marks^{6,7} (Scheme 2). These complexes can be used to hydroaminate unprotected 1,3-dienes with terminal substitution to form a mixture of products. Use of lanthanum, samarium or yttrium catalysts resulted in both poor *E/Z* and 1,2 versus 1,4 addition selectivity, albeit in greater than 90% yield. Thorium and uranium catalysts produced *E* products specifically, but still resulted in poor selectivity between 1,2 and 1,4 addition products.



Scheme 3: Yamamoto Palladium Catalyzed Hydroamination

A palladium catalyzed hydroamination of 1,3-dienes was published by Yamamoto, where he used the catalytic system described in Scheme 3 to enantioselectively hydroaminate a nonafluorobutanesulfonyl protected diene (Scheme 4).⁸ The reaction resulted in 5-endo cyclization of the substrate in a poor 15% yield and 24% enantiomeric excess.

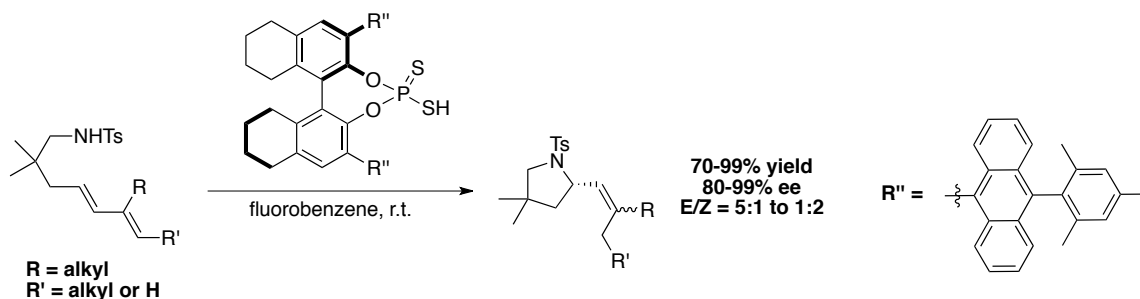
Another transition metal catalyzed hydroamination of 1,3 dienes was recently published by Toste (Scheme 4).⁹ With the use of a chiral gold catalyst and 4-methoxybenzenesulfonyl protected aminodienes, Toste was able to form hydroamination products in excellent yield and enantioselectivity (>85% ee). The reaction forms enantioenriched products under mild reaction conditions and selectivity for 1,2 addition is respectable.



Scheme 4: Toste Gold Catalyzed Hydroamination

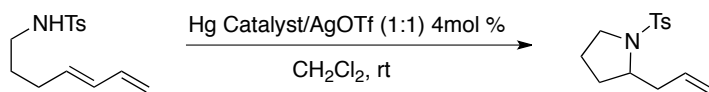
Not only have transition metals been shown to promote the hydroamination of 1,3-

dienes, so have specific Brønsted acids (Scheme 5). One example of a chiral Brønsted acid catalyzed hydroamination was published by Toste, where a chiral dithiophosphoric acid was employed to promote the reaction of tosyl protected aminodienes.¹⁰ Under mild reaction conditions, the hydroamination results in chiral products with excellent yields and enantiomeric excess. Unfortunately, if the product results in $R \neq R'$, a mixture of *E/Z* isomers is formed.



Scheme 5: Toste Hydroamination using Chiral Brønsted Acid

Recently, Yamamoto et. al. have devised a room temperature hydroamination of tosyl protected 1,3-dienes, employing a bulky carboranylmercuric chloride catalyst and silver triflate.¹¹ The reaction produces olefinic nitrogen heterocycles in excellent yields and selectivities with short reaction times, but is limited to tosyl protected amines and utilizes toxic mercury salt catalysts (Scheme 6).



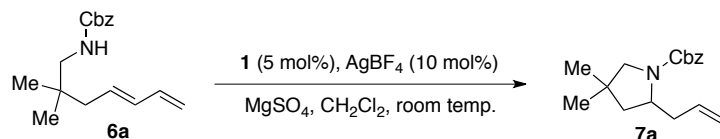
Scheme 6: Yamamoto Hydroamination using Mercury Catalyst

From the previously reviewed literature on 1,3-diene hydroamination, it can be determined that improvements can be made to this reaction. Rare earth metal, gold and Brønsted acid catalysts discussed result in poor *E/Z* selectivity or 1,2 and 1,4 addition selectivity. Furthermore, protecting group compatibility is not diverse for any of these systems and many substitution patterns on the dienes themselves are yet to be explored. With the use of the catalytic palladium system developed by our lab, we hope these issues may be addressed.

Section 1: Results and Discussion

1.1 Substrate Scope and Functional Group Tolerance

Hydroamination conditions were carried out on aminodiene **6a** and resulted in the formation of only the 5-exo, 1,4 addition product **7a** in 95% yield (Scheme 7). Delighted



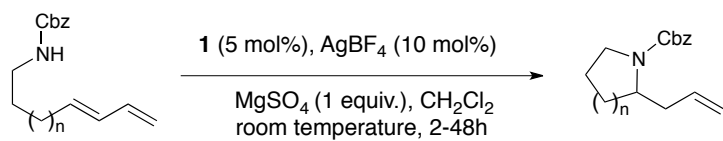
Scheme 7: Initial Reaction of 1,3-diene with Catalytic System

by this result, since this perfect regiochemistry has only been observed by Yamamoto's mercury catalyzed hydroamination, we explored more substrates containing 1,3 dienes with an array of substitution patterns and protecting groups. Unlike all other previously reported hydroaminations of 1,3-dienes, our conditions allowed for a much larger assortment of nitrogen protecting groups (Table 1). Several useful amide and carbamate protecting groups tolerated hydroamination conditions, resulting in excellent yields of the cyclized product (**3a-d**). Furthermore, sulfonamide protected dienes **2e-g** also cyclized under standard hydroamination conditions, albeit with longer reaction times and slightly diminished yields. This was surprising, considering that hydroamination of alkenes under

The general reaction scheme shows the hydroamination of aminodiene **2a-g** to form the cyclized product **3a-g**. The starting material **2a-g** is a 1,3-diene with a PG-protected secondary amine. The reaction conditions are: **1** (5 mol%), AgBF₄ (10 mol%), MgSO₄, CH₂Cl₂, room temp. The product **3a-g** is a 5-membered ring with a PG-protected nitrogen and a terminal vinyl group. The reaction is labeled (3).

PG	diene	product	%yield (isolated)
Cbz	2a	3a	>99%
Boc	2b	3b	76%
<i>p</i> -toluoyl	2c	3c	86%
Ac	2d	3d	>99%
Ts	2e	3e	73%
4-Ns	2f	3f	97%
SES	2g	3g	73%

Table 1: Effect of Protecting Groups



Entry	Substrate	Product	% Yield
1	 6a	 7a, 95%	95%
2	 8a	 9a, 95%	95%
3	 10a	 11a, 95%	95%
4	 12a	 13a, 95%	95%
5	 14a	 15a, 90%	90%
6	 16a	 17a, >99%	>99%
7	 18a	 19a, 18%	18%

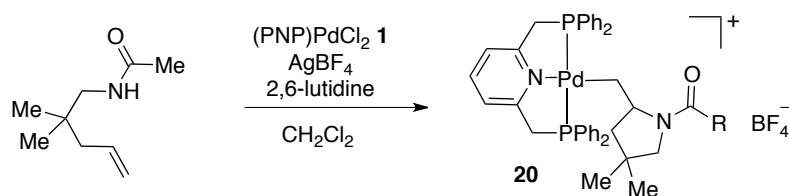
Table 2: Substrate Scope

these conditions does not work. Finally, Table 1 displays the use of an unsubstituted backbone, confirming that Thorpe-Ingold effect is not necessary for cyclization.

In exploring the hydroamination of 1,3-dienes using our catalytic system, we investigated the tolerance of a very diverse set of substrates. In previous hydroaminations of 1,3-dienes, substitution patterns on the olefinic moiety were rarely explored except for terminal substitution. We decided to explore internal diene substitution patterns to understand the full utility of our catalytic system. Our investigation of substrate scope began by reacting terminally substituted diene **8a**, which formed the cyclized product in 95% isolated yield. More substitution patterns on the olefinic moiety were explored in substrates **10a** and **12a**, with the olefin bearing an alkyl substituent at the 1 and 3 positions, respectively. Both of these substrates formed the desired nitrogen heterocycles in nearly quantitative yields. Product **11a** was particularly exciting, because no other hydroamination of 1,3-dienes has been shown to cyclize to form a sterically hindered tetrasubstituted carbon center. Other substrates explored under the reaction conditions were **14a**, which cyclized to form the six-membered heterocyclic ring, and substrate **16a**, which cyclized to form morpholine product **17a** in quantitative yield. Interestingly, when the terminally disubstituted substrate **18a** was subject to hydroamination conditions, 6-endo cyclization product **19a** was obtained instead of the expected 5-exo product.

1.2 Isolation of Palladium Allyl Complex

In a mechanistic study of the palladium catalyzed hydroamination of unactivated alkenes by Michael and Cochran⁵, a key step in understanding the catalytic system was the isolation of a stable monocationic palladium alkyl complex **20** (Scheme 8). Isolation of the complex was achieved by the addition of 2,6-lutidine to the reaction with stoichiometric (PNP)PdCl₂. The base was able to sequester protons and stop the catalytic cycle at the turnover-limiting protonolysis step.



Scheme 8: Synthesis of Palladium Alkyl Complex

Isolation of the terminally bound palladium alkyl complex by Michael made us question whether hydroamination of 1,3-dienes went through a similar intermediate. More interestingly, if they did form a similar intermediate, would palladium be bound to the substrate internally, **21**, or externally, **22**, after cyclization? To investigate these questions, an array of bases was screened in an attempt to isolate a complex. It was found

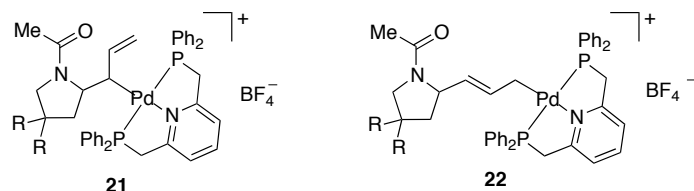
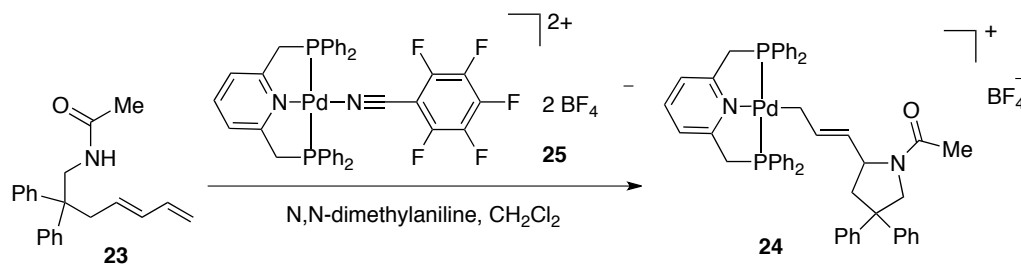


Figure 1: Possible Palladium Allyl Complexes

that bases used to isolate complex **20** were not strong enough to stop protonolysis of the allyl complex or were not sterically hindered enough and would simply coordinate to palladium rendering the catalyst useless. Two bases were found to solve both of these problems, 4-methyl-2,6-ditertbutylpyridine and *N,N*-dimethylaniline. Of these two bases, *N,N*-dimethylaniline was more effective at stopping protonolysis from occurring once the palladium allyl complex was formed.

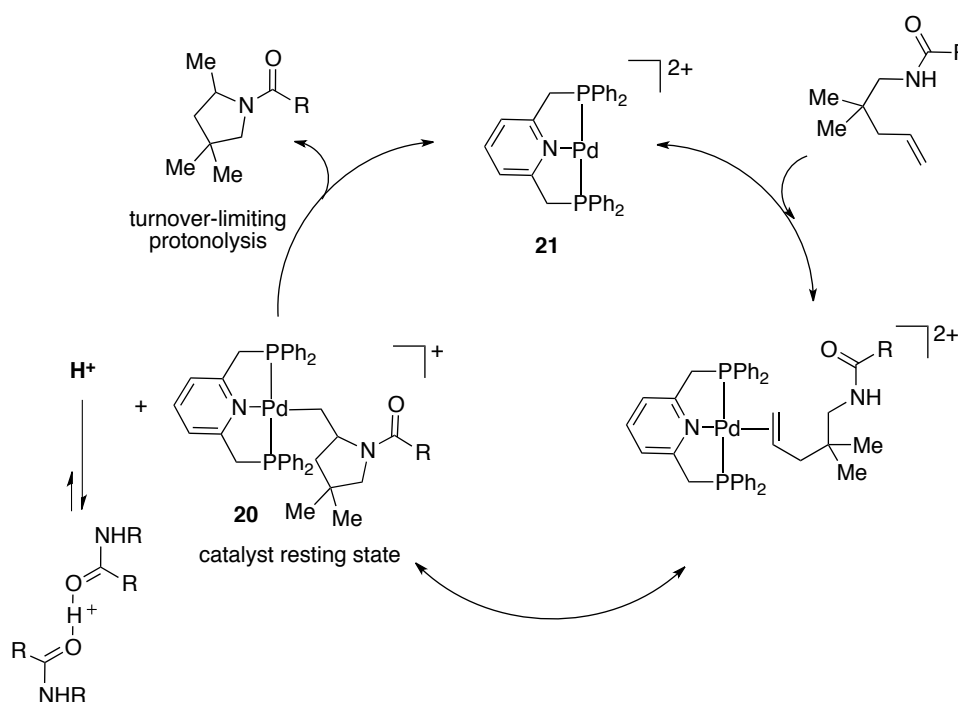
When acetyl protected aminodiene **23** was reacted with stoichiometric catalyst and *N,N*-dimethylaniline, palladium allyl complex **24** was isolated as a yellow solid in 70% yield. Spectroscopic data confirmed that palladium was bound to the terminal end of the former diene moiety, leading to one of two conclusions. Either palladium coordinates to the terminal double bond and cyclization occurs, or palladium coordinates to the internal double bond, and after cyclization palladium shifts to the terminal position via η^3 π -allyl species. It is possible that terminal palladium allyl species is the only species isolated because it is less sterically hindered than the internal species.



Scheme 9: Synthesis of Palladium Allyl Complex

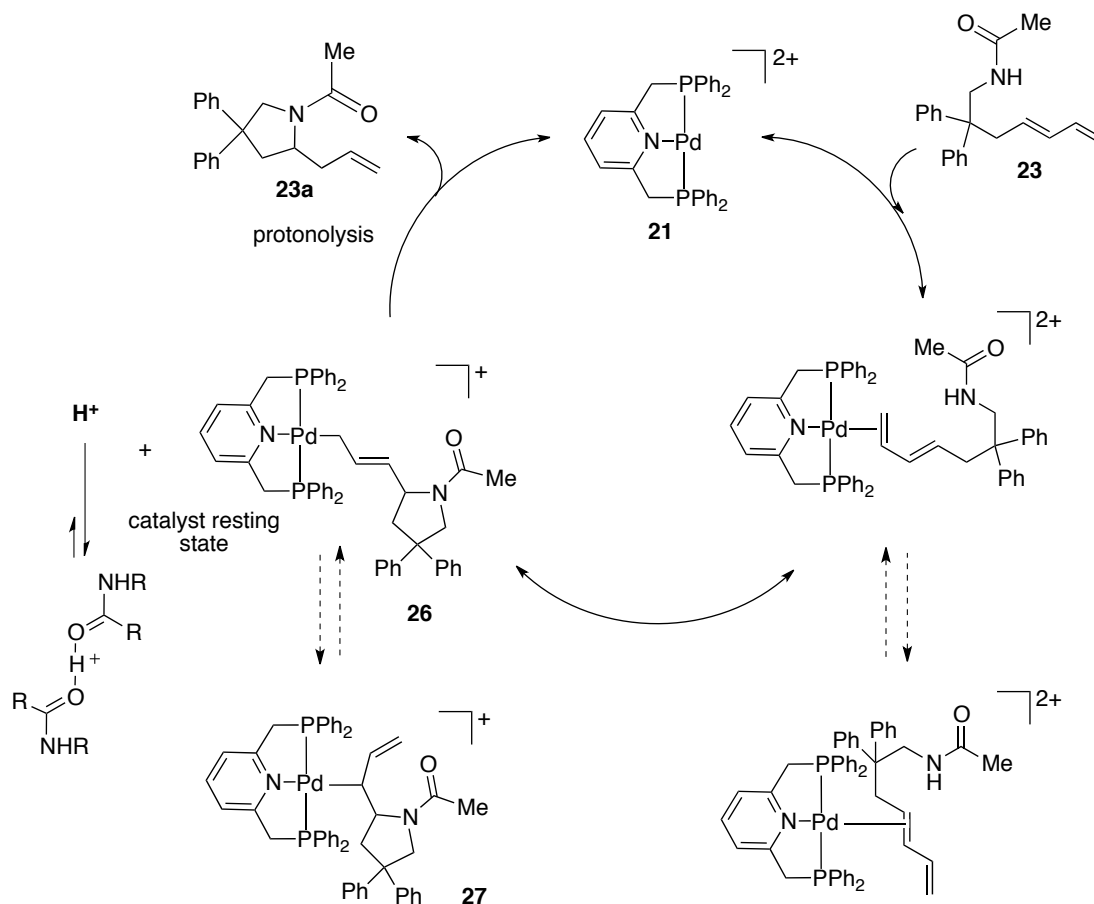
1.3 Proposed Mechanism

With the isolation of palladium allyl complex **24**, a catalytic cycle can be proposed similar to the one proposed by Michael for the hydroamination of unactivated alkenes (Scheme 10). The catalytic cycle begins with coordination of dicationic (PNP)Pd complex **21** to the alkene, followed by reversible cyclization to form the palladium alkyl species **20**. Turnover limiting protonolysis releases the hydroamination product and the dicationic palladium species re-enters the catalytic cycle.



Scheme 10: Proposed Catalytic Cycle for Alkene Hydroamination

Similar to the mechanism proposed by Michael for the hydroamination of unactivated alkenes, dicationic (PNP)Pd **21** coordinates to the diene at either the terminal or internal alkene. Nucleophilic attack of nitrogen leads to the catalyst resting state **26**, which could readily exchange through a palladium η^3 π -allyl species to form internally bound palladium allyl species **27**. Turnover limiting protonolysis to generate the hydroamination product could occur from either palladium allyl intermediate through either an S_E2 or S_E2' mechanism from complexes **27** and **26**, respectively.



Scheme 11: Proposed Catalytic Cycle of 1,3-diene Hydroamination

Section 2: Conclusion

The room temperature palladium catalyzed hydroamination of 1,3-dienes was explored and resulted in the formation of useful olefinic nitrogen heterocycles as well as being highly selective for 1,2 addition over 1,4 addition across the diene. A wide array of aminodienes was successfully cyclized under the described hydroamination conditions, including various substitution patterns and nitrogen protecting groups. Finally, a palladium allyl complex was isolated, giving insight into reaction mechanism.

Section 3: Synthesis and Analytical Data

3.1 General Procedures

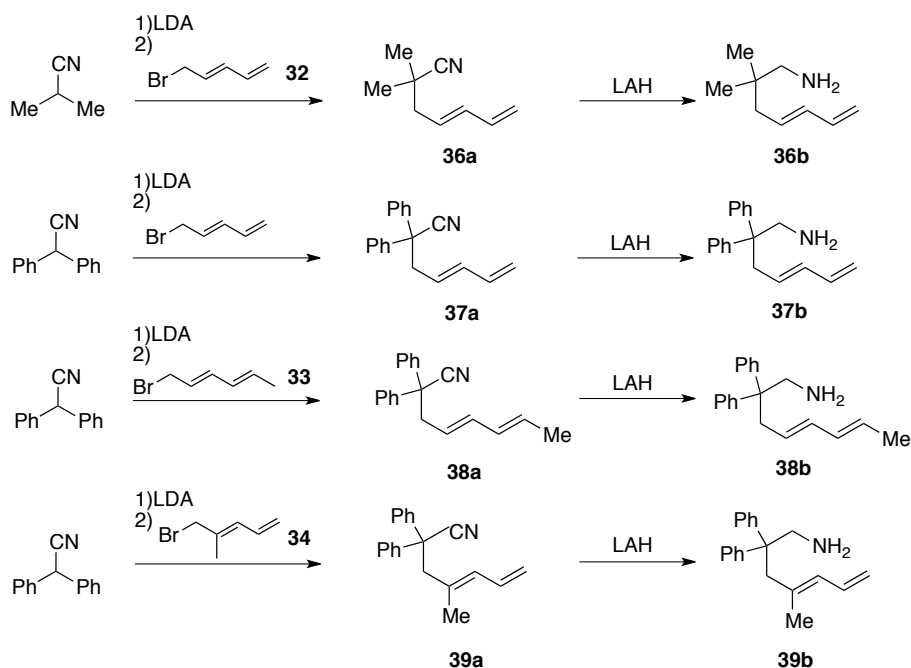
All reactions were performed under a nitrogen atmosphere using flame-dried glassware. NMR spectra were recorded on a Bruker Advance 300 MHz, 301 MHz or 500 MHz spectrometer. ^1H NMR chemical shifts (δ) are reported in parts per million (ppm) downfield of TMS and are referenced relative to residual protiated chloroform (CHCl_3) at 7.26 ppm. Flash chromatography was performed using silica gel (Sorbent Technologies, 60 Å, 230-400 mesh).

3.2 Materials

Dichloromethane, acetonitrile, diethyl ether, and tetrahydrofuran were degassed with nitrogen and dried by passing through a column of neutral alumina. Toluene was degassed with nitrogen and dried by passing through a column of neutral alumina and a column of Q5 reactant. 3A and 4A molecular sieves were powdered and activated under vacuum at ~ 200 °C for 14 h and stored in a glove box or in an oven at 150 °C. Palladium chloride and silver tetrafluoroborate were purchased from Strem Chemicals and used without further purification. Anhydrous magnesium sulfate, benzyl chloroformate, di-*t*-butyldicarboxylate, *p*-toluoyl chloride, acetic anhydride, 3-methyl-2-butenal, sorbyl alcohol and (4-Bromobutyl)triphenylphosphonium bromide were purchased from Aldrich and used without further purification. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and were used without further purification.

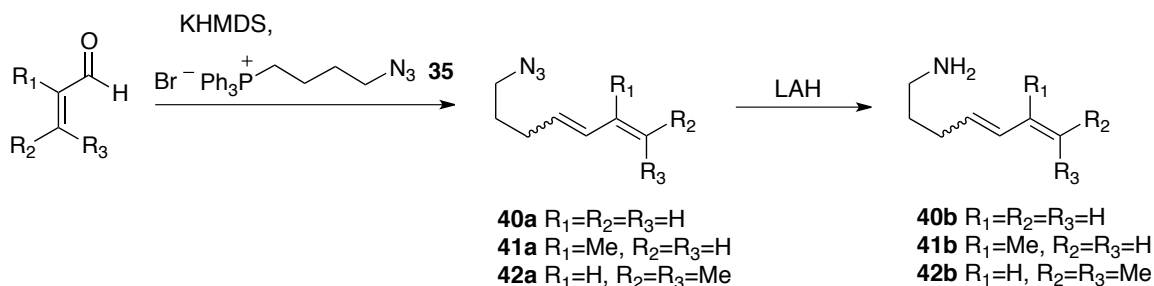
3.3 Synthesis of Substrates

Synthesis of Aminodienes

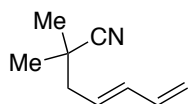


Dienyl bromides (**32**)¹², (**33**)¹², (**34**) were synthesized in a fashion analogous to previously reported methods.

Wittig route to aminodiene



(4-azidobutyl)triphenylphosphonium bromide (**35**) was synthesized in a fashion analogous to previously reported methods.¹⁴

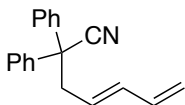


(*E*)-2,2-dimethylhepta-4,6-dienitrile (**36a**)

To a freshly prepared solution of Lithiumdiisopropylamine (5.5mmol, 0.25M in THF) was added isobutyronitrile (1.25mL, 5mmol) dropwise at 0°C over a 5 minute period. The reaction was stirred for 1 hour at this temperature and (*E*)-5-Bromo-1,3-pentadiene **32** was added. The reaction was allowed to stir an additional hour and was quenched with water (20mL). The layers were separated and the aqueous layer was extracted with ether (2x20mL). The combined organic layers were washed with saturated ammonium chloride, brine, dried over MgSO₄, filtered and concentrated. Purification by silica gel chromatography (15:1 Hex:EtOAc) afforded the title compound as a colorless oil (130mg, 19%). ¹H NMR (300 MHz, CDCl₃): δ 6.35 (dt, *J* = 16.8, 10.2 Hz, 1H), 6.16 (dd, *J* = 15.0, 10.2 Hz, 1H), 5.74 (dt, *J* = 15.0, 7.5 Hz, 1H), 5.20 (d, *J* = 16.8 Hz, 1H), 5.09 (d, *J* = 10.2 Hz, 1H), 2.31 (d, *J* = 7.5 Hz, 2H), 1.34 (s, 6H).

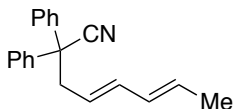
Geminal diphenylnitriles **37a**, **38a** and **39a** were synthesized according to the following procedure. To a flame dried reaction flask under N₂ was added diphenylacetone nitrile (10mmol, 1 equiv.) to a suspension of sodium hydride (60% dispersion in oil, 11mmol, 1.1 equiv.) in dimethylformamide (35mL, 0.25M) at 0°C. Once hydrogen evolution stopped, bromide **32**, **33** or **34** was added dropwise. The reaction was slowly warmed to room temperature and allowed to stir overnight. The reaction was quenched with saturated ammonium chloride (50mL) and extracted with ether (3x75mL). The combined organic layers were washed with a 10% LiCl solution (2x50mL), brine (50mL), dried

over MgSO_4 , filtered and concentrated. Purification by silica gel chromatography (15:1 Hex:EtOAc) afforded pure geminal diphenylnitriles.



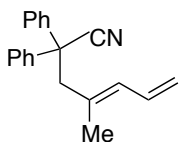
(E)-2,2-diphenylhepta-4,6-dienitrile (37a)

Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.45-7.25 (m, 10H), 6.32-6.05 (m, 2H), 5.56 (dt, $J = 14.2, 7.3$ Hz), 5.19-4.97 (m, 2H), 3.16 (d, $J = 7.3$ Hz, 2H).



(4E,6E)-2,2-diphenylocta-4,6-dienitrile (38a)

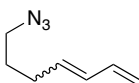
Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.46-7.18 (m, 10H), 6.13 (d, $J = 14.9, 10.9$ Hz, 1H), 6.01-5.88 (m, 1H), 5.76-5.53 (m, 1H), 5.40 (dt, $J = 14.6, 7.2$ Hz, 1H), 3.13 (d, $J = 7.2$ Hz, 2H), 1.71 (d, $J = 5.9$ Hz, 3H).



(E)-4-methyl-2,2-diphenylhepta-4,6-dienitrile (39a)

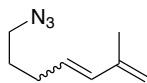
Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.45-7.22 (m, 10H), 6.45 (dt $J = 16.3, 10.3$ Hz, 1H), 5.80 (d, $J = 11.1$ Hz, 1H), 5.12-4.96 (m, 2H), 3.15 (s, 2H), 1.50 (s, 3H).

Dienyl azides **40a**, **41a** and **42a** were synthesized according to the following procedure. To a flame dried reaction flask was added (4-azidobutyl)triphenylphosphonium bromide (5mmol, 1equiv.), and THF (5mL). The reaction mixture was cooled to -78°C and KHMDS (20% w/w in THF, 5mmol, 1equiv.) was added. The reaction was allowed to stir at this temperature for 1 hour and then aldehyde was added (5mmol, 1equiv.) dropwise. The reaction was stirred for another hour and was then warmed to room temperature and quenched with water (5mL). The layers were separated and the aqueous layer was extracted with ether (3x10mL). The organic layer was washed with brine (5mL), dried over MgSO_4 , filtered and condensed. Purification by a short silica gel column (20:1 Pentane:Ether) to remove residual triphenylphosphine oxide afforded pure dieneyl azide.



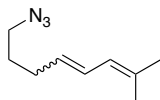
7-azidohepta-1,3-diene (40a)

Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 6.62 (dt, $J = 17.0, 10.3$ Hz, 1H), 6.06 (t, $J = 10.9$ Hz, 1H), 5.41 (dt, $J = 7.7$ Hz, 1H), 5.22 (d, $J = 16.8$ Hz, 1H), 5.14 (d, $J = 10.0$ Hz, 1H), 3.29 (t, $J = 6.7$ Hz, 2H), 2.29 (q, $J = 7.4$ Hz, 2H), 1.69 (p, 7.3 Hz, 2H).



7-azido-2-methylhepta-1,3-diene (41a)

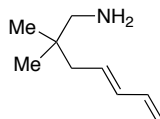
Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 5.89 (d, $J = 11.5$ Hz, 1H), 5.35 (dt, $J = 11.5$, 7.3 Hz, 1H), 4.97 (s, 1H), 4.84 (s, 1H), 3.29 (t, $J = 7.2$ Hz, 2H), 2.36 (dq, $J = 7.4$, 1.4 Hz, 2H), 1.88 (s, 3H), 1.68 (p, $J = 7.0$ Hz, 2H).



8-azido-2-methylocta-2,4-diene (42a)

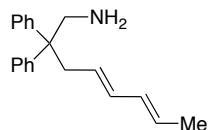
Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 6.22 (t, $J = 11.1$ Hz, 1H), 6.05 (d, $J = 11.8$ Hz, 1H), 5.27 (dt, $J = 11.2$, 7.6 Hz, 1H), 3.29 (t, $J = 7.3$ Hz, 2H), 2.26 (q, $J = 8.1$ Hz, 2H), 1.81 (s, 3H), 1.75 (s, 3H), 1.68 (p, $J = 6.9$ Hz, 2H).

All amines were reduced from the corresponding azide or nitrile according to the following procedure. To a flame dried reaction flask under N_2 was added a solution of azide or nitrile (10mmol, 1 equiv.) in ether (5mL) to a suspension of lithium aluminum hydride (20mmol, 2 equiv.) in ether (25mL) at 0°C . The reaction was allowed to slowly warm to room temperature and stir until starting material was consumed (TLC). The reaction was cooled to 0°C and was quenched by the slow addition of 1M NaOH (~5mL) and was allowed to stir an additional 30 minutes. The white solid was removed by filtration over celite and was washed with ether. The filtrate was dried with MgSO_4 , filtered and concentrated to yield the corresponding amine. The amines were protected with no further purification.



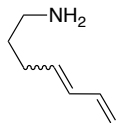
(E)-2,2-dimethylhepta-4,6-dien-1-amine HCl Salt (36b)

Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 8.36 (s, 3H), 6.30 (dt, $J = 10.2$, 16.8 Hz, 1H), 6.14 (dd, $J = 14.7$, 15Hz, 1H), 5.13 (d, $J = 16.5$ Hz, 1H), 5.02 (d, $J = 18.6$ Hz, 1H), 2.79 (d, $J = 5.7$ Hz, 2H), 2.15 (d, $J = 7.8$ Hz, 2H), 1.05 (s, 6H).



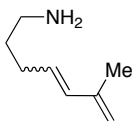
(4E,6E)-2,2-diphenylocta-4,6-dien-1-amine HCl Salt (37b)

Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.84 (s, 3H), 7.31 (m, 11H), 7.16 (d, $J = 6.9$ Hz, 4H), 6.32 (dd, $J = 9.6$, 15.3 Hz, 1H), 5.88 (m, 1H), 5.61 (m, 1H), 4.99 (m, 1H), 3.58 (s, 2H), 3.10 (d, $J = 6.9$ Hz, 2H), 1.69 (d, $J = 6.6$ Hz, 3H).



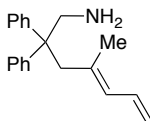
Hepta-4,6-dien-1-amine (40b)

Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): Isolated as a mixture of olefin isomers E/Z = (5:2) δ 6.61 (dt, $J = 10.2, 16.8$ Hz, 1H), 6.31 (dt, $J = 10.2, 17.1$ Hz, 1H), 6.05-6.02 (m, 2H), 5.70 (dt, $J = 7.2, 14.4$ Hz, 1H), 5.45 (dd, $J = 8.1, 18.6$ Hz, 1H), 5.19 (d, $J = 16.8$ Hz, 1H), 5.11-5.08 (m, 2H), 4.97 (d, $J = 10.5$ Hz, 1H), 2.3-2.68 (m, 4H), 2.24 (q, $J = 8.7$ Hz, 2H), 2.20 (q, $J = 6.9$ Hz, 2H), 1.62-1.50 (m, 8H).



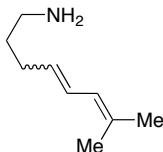
(E)-6-methylhepta-4,6-dien-1-amine (41b)

Colorless oil $^1\text{H NMR}$ (300 MHz, CDCl_3): Isolated as a mixture of olefin isomers E/Z = (3:2) δ 6.03-5.95 (m, 1H), 5.70 (d, $J = 11.7$ Hz, 1H), 5.52-5.47 (m, 1H), 5.92-5.16 (m, 2H), 4.80-4.69 (m, 4H), 2.56 (t, $J = 7.2$ Hz, 4H), 2.17-2.15 (m, 4H), 1.7 (s, 6H), 1.42-1.40 (m, 8H).



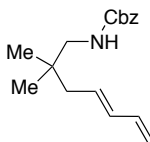
(E)-4-methyl-2,2-diphenylhepta-4,6-dien-1-amine (39b)

Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.38-7.17 (m, 10H), 6.48 (dt, $J = 10.5, 16.8$ Hz, 1H), 5.76 (d, $J = 11.1$ Hz, 1H), 5.08-4.97 (m, 2H), 3.36 (s, 2H), 2.97 (s, 1H), 1.08 (s, 3H), 0.87 (s, 2H).



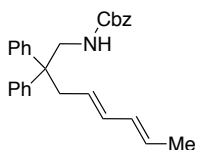
7-methylocta-4,6-dien-1-amine (42b)

Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 6.20 (t, $J = 11.4$ Hz, 1H), 6.11-6.07 (m, 1H), 5.38-5.30 (m, 1H), 2.73 (t, $J = 6.9$ Hz, 2H), 2.23 (q, $J = 7.2$ Hz, 2H), 1.82 (s, 3H), 1.77 (s, 3H), 1.57 (qn, $J = 7.5$ Hz, 2H), 1.48 (s, 2H).



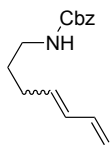
(E)-Benzyl 2,2-dimethylhepta-4,6-dienylcarbamate(6a)

To a reaction flask was added (E)-2,2-dimethylhepta-4,6-dien-1-amine HCl Salt (0.142g, 0.8mmol), CH₂Cl₂ (2mL), triethylamine (0.28mL, 2.0mmol) and placed under a nitrogen atmosphere. The mixture was cooled to 0°C and allowed to stir for one hour. To the mixture was added benzyl chloroformate (0.14mL, 1.0 mmol) dropwise over a period of 5 minutes. The reaction was allowed to slowly warm to room temperature and stir overnight. The reaction quenched with water (1mL) and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (1x2mL) and combined organic layers were dried over MgSO₄, filtered and condensed. Purification by flash chromatography (10:1 Hex:EtOAc) afforded (E)-benzyl 2,2-dimethylhepta-4,6-dienylcarbamate as a colorless oil (0.056g, 25%). ¹H NMR (300 MHz, CDCl₃): δ 7.37-7.33 (m, 5H), 6.32 (dt, *J* = 10.2, 16.8 Hz, 1H), 6.05 (dd, *J* = 10.5, 15.3 Hz, 1H), 5.70 (dt, *J* = 7.5, 15.0 Hz, 1H), 5.13-5.07 (m, 3H), 4.99 (d, *J* = 10.2 Hz, 1H), 4.77 (s, 1H), 3.04 (d, *J* = 6.6 Hz, 2H), 1.99 (d, *J* = 7.5 Hz, 2H), 0.89 (s, 6H).



Benzyl (4E,6E)-2,2-diphenylocta-4,6-dienylcarbamate(8a)

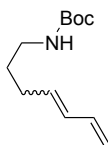
To a reaction flask was added (4E,6E)-2,2-diphenylocta-4,6-dien-1-amine HCl Salt (0.333g, 1.1mmol), CH₂Cl₂ (10mL), triethylamine (0.44mL, 3.2mmol) and placed under a nitrogen atmosphere. The mixture was cooled to 0°C and allowed to stir for 15 minutes. To the mixture was added benzyl chloroformate (0.14mL, 1.0 mmol) dropwise over a period of 10 minutes. The reaction was allowed to slowly warm to room temperature and stir overnight. The reaction quenched with water (4mL) and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (1x10mL) and combined organic layers were dried over MgSO₄, filtered and condensed. Purification by flash chromatography (8:1 Hex:EtOAc) afforded benzyl (4E,6E)-2,2-diphenylocta-4,6-dienylcarbamate as a colorless oil (0.312g, 72%). ¹H NMR (300 MHz, CDCl₃): δ 7.34-7.17 (m, 15H), 5.93-5.89 (m, 2H), 5.57-5.52 (m, 1H), 5.20-5.06 (m, 3H), 4.38 (s, 1H), 3.93 (d, *J* = 6.0 Hz, 2H), 2.88 (d, *J* = 6.3 Hz, 2H), 1.70 (d, *J* = 6.3 Hz, 3H).



Benzyl hepta-4,6-dienylcarbamate(2a)

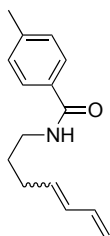
To a reaction flask was added hepta-4,6-dien-1-amine (0.129g, 1.2mmol), CH₂Cl₂ (11mL), triethylamine (0.19mL, 1.4mmol) and placed under a nitrogen atmosphere. The mixture was cooled to 0°C to the mixture was added benzyl chloroformate (0.14mL, 1.0 mmol) dropwise over the period of 10 minutes. The reaction was allowed to slowly warm to room temperature and stir overnight. The reaction quenched with 0.5M citric acid (4mL) and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (1x10mL) and combined organic layers were washed with saturated NaHCO₃, brine, dried over MgSO₄, filtered and condensed. Purification by flash chromatography (8:1 Hex:EtOAc) afforded benzyl hepta-4,6-dienylcarbamate as a colorless oil (0.182g, 64%).

^1H NMR (300 MHz, CDCl_3): Isolated as a mixture of olefin isomers E/Z = (5:2) δ 7.40-7.31 (m, 10H), 6.62 (dt, $J = 10.8, 17.4$ Hz, 1H), 6.32 (dt, $J = 10.2, 18.2$ Hz, 1H), 6.07 (t, $J = 10.8$ Hz, 1H), 5.75-5.65 (m, 1H), 5.45 (dd, $J = 7.5, 18.3$ Hz, 1H), 5.22 (d, $J = 16.8$ Hz, 1H), 5.25-5.10 (m, 6H), 5.00 (d, $J = 9.6$ Hz, 1H), 4.77 (s, 2H), 3.27-3.20 (m, 4H), 2.25 (q, $J = 6.9$ Hz, 2H), 2.15 (q, $J = 7.2$ Hz, 2H), 1.69-1.59 (m, 4H).



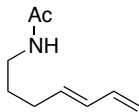
Tert-butyl hepta-4,6-dienylcarbamate(2b)

To a reaction flask was added hepta-4,6-dien-1-amine (0.129g, 1.2mmol) and CH_2Cl_2 (4mL). To the solution was added a mixture of di-tert-butyl dicarbonate (0.252mg, 1.2mmol) in CH_2Cl_2 (0.5mL) and the reaction was allowed to stir at r.t overnight. Reaction was immediately concentrated and the remaining oil was purified by flash chromatography (10:1 Hex:EtOAc). To afford tert-butyl hepta-4,6-dienylcarbamate as a colorless oil (0.146mg, 60%). ^1H NMR (300 MHz, CDCl_3): Isolated as a mixture of olefin isomers E/Z = (5:2) δ 6.63 (dt, $J = 11.1, 16.8$ Hz, 1H), 6.34-6.30 (m, 1H), 6.05-6.03 (m, 1H), 5.72-5.68 (m, 1H), 5.47-5.43 (m, 1H), 5.24-5.11 (m, 3H), 4.99 (d, $J = 9.6$ Hz, 1H), 4.57 (s, 2H), 3.18-3.12 (m, 4H), 2.24 (q, $J = 7.5$ Hz, 2H), 2.14 (q, $J = 7.2$ Hz, 2H), 1.65-1.46 (m, 23H). ^{13}C NMR (75 MHz, CDCl_3): δ 25.0, 28.4, 29.5, 29.7, 29.9, 40.1, 78.9, 115.1, 117.3, 129.9, 131.4, 131.6, 131.9, 134.0, 137.0, 156.0



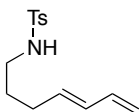
N-(hepta-4,6-dienyl)-4-methylbenzamide(2c)

To a reaction flask was added hepta-4,6-dien-1-amine (0.129g, 1.2mmol), triethylamine (0.18mL, 1.3mmol) and CH_2Cl_2 (4mL). The reaction was cooled to 0 deg C and p-toluoyl chloride (0.168mL, 1.3mmol) was added dropwise. The reaction was warmed to r.t and allowed to stir overnight. Reaction was quenched with 1M HCl and the layers were separated. The aqueous later was extracted once with ether and the combined organic layers were dried over MgSO_4 , filtered and condensed. Purification by flash chromatography (4:1 Hex:EtOAc) afforded N-(hepta-4,6-dienyl)-4-methylbenzamide as a colorless oil (0.201g, 76%). ^1H NMR (300 MHz, CDCl_3): Isolated as a mixture of olefin isomers E/Z = (5:2) δ 7.69-7.66 (m, 4H), 7.29-7.24 (m, 4H), 6.66 (dt, $J = 10.8, 16.8$ Hz, 1H), 6.21-6.05 (m, 5H), 5.77-5.75 (m, 1H), 5.50 (dd, $J = 8.4, 17.7$ Hz, 1H), 5.29 (d, $J = 17.1$ Hz, 1H), 5.17-5.13 (m, 2H), 5.02 (d, $J = 9.6$ Hz, 1H). 3.53-3.47 (m, 4H), 2.42 (s, 6H), 2.33 (q, $J = 7.5$ Hz, 2H), 2.23 (q, $J = 7.5$ Hz, 2H), 1.81-1.60 (m, 4H). ^{13}C NMR (75 MHz, CDCl_3): δ 21.4, 25.3, 29.1, 29.4, 30.1, 39.7, 115.2, 117.4, 127.1, 129.1, 129.9, 131.5, 131.6, 131.8, 132.0, 134.1, 137.1, 141.6, 167.7



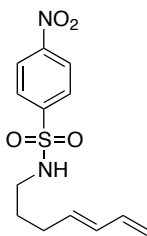
(E)-N-(hepta-4,6-dienyl)acetamide (2d)

To a reaction flask was added acetic anhydride (0.57mL, 6.0mmol), and CH₂Cl₂ (5mL). Hepta-4,6-dien-1-amine (0.555g, 5.0mmol) was added dropwise at room temperature and the reaction was allowed to stir for 5 hours. Reaction was quenched with 1M NaOH (5mL) and the layers were separated. The organic layer was dried over MgSO₄, filtered and concentrated. Purification by flash chromatography (1:1 Hex:EtOAc) afforded the title compound as a colorless oil (0.625g, 82%). ¹H NMR (300 MHz, CDCl₃): δ 6.60 (dt, *J* = 17.1, 10.6 Hz, 1H), 6.02 (t, *J* = 10.9 Hz, 1H), 5.59 (s, 1H), 5.42 (dd, 18.0, 8.1 Hz, 1H), 5.20 (d, *J* = 16.9 Hz, 1H), 5.11 (d, *J* = 10.1 Hz, 1H), 3.23 (q, 7.0 Hz, 2H), 2.22 (q, 7.4 Hz, 2H), 1.96 (s, 3H), 1.60 (quin, 7.6 Hz, 2H).



(E)-N-(hepta-4,6-dienyl)-4-methylbenzenesulfonamide (2e)

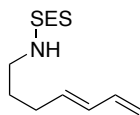
To a reaction flask was added hepta-4,6-dien-1-amine (0.111g, 1.0mmol), triethylamine (0.35mL, 2.5mmol) and CH₂Cl₂ (5mL). The reaction was cooled to 0°C and p-toluene sulfonylchloride (.210g, 1.1mmol) was added. The reaction was warmed to room temperature and stir an additional 30 minutes. The reaction was quenched with 0.1M citric acid (5mL) and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (1x5mL) and the combined organic layers were washed with 1M NaOH (5mL), brine (5mL) dried over MgSO₄, filtered and concentrated. Purification by flash chromatography (6:1 Hex:EtOAc) afforded the title compound as a colorless oil (.109g, 41%). ¹H NMR (300 MHz, CDCl₃): δ 7.60 (d, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 6.37 (dt, *J* = 15.7, 10.5 Hz, 1H), 5.81 (t, *J* = 10.5 Hz, 1H), 5.20-5.12 (m, 1H), 5.01 (d, 16.7Hz, 1H), 4.97-4.87 (m, 2H), 2.81-2.71 (m, 2H), 2.26 (s, 3H), 2.05-1.96 (m, 2H), 1.44-1.34 (m, 2H).



(E)-N-(hepta-4,6-dienyl)-4-nitrobenzenesulfonamide (2f)

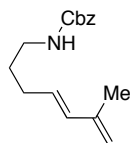
To a reaction flask was added hepta-4,6-dien-1-amine (0.111g, 1.0mmol), triethylamine (0.28mL, 2.0mmol) and CH₂Cl₂ (2mL). The reaction was cooled to 0°C and 4-nitrobenzene sulfonylchloride (.221g, 1.0mmol) was added. The reaction was warmed to room temperature and stir an additional 24 hours. The reaction was diluted with CH₂Cl₂ (5mL) and washed with 1M HCl (2x5mL). The organic layer was then dried with MgSO₄, filtered and concentrated. Purification by silica gel chromatography (4:1 Hex:EtOAc) afforded the title compound as a white solid (.202g, 68%). ¹H NMR (300

MHz, CDCl₃): δ 8.36 (dt, $J = 8.7, 1.7$ Hz, 2H), 8.04 (dt, $J = 8.9, 2.2$ Hz, 2H), 6.51 (dt, $J = 17.0, 10.3$ Hz, 1H), 6.01 (t, $J = 10.8$ Hz, 1H), 5.32 (dd, $J = 18.1, 7.5$ Hz, 1H), 5.20 (d, $J = 17.0$ Hz, 1H), 5.11 (d, $J = 10.1$ Hz, 1H), 4.73 (t, $J = 6.0$ Hz, 1H), 3.03 (q, $J = 7.0$ Hz, 2H), 2.20 (q, $J = 7.2$ Hz, 2H), 1.61 (quin, $J = 7.0$ Hz, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 24.8, 29.6, 43.1, 118.1, 124.7, 128.6, 130.6, 130.7, 131.9, 146.0, 150.3



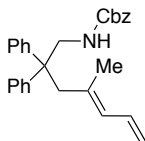
(E)-N-(hepta-4,6-dienyl)-2-(trimethylsilyl)ethanesulfonamide (2g)

To a reaction flask was added hepta-4,6-dien-1-amine (0.111g, 1.0mmol), triethylamine (0.28mL, 2.0mmol) and CH₂Cl₂ (2mL). The reaction was cooled to 0°C and 2-(Trimethylsilyl)ethanesulfonyl chloride (.189g, 1.0mmol) was added. The reaction was warmed to room temperature and stir an additional 24 hours. The reaction was diluted with CH₂Cl₂ (5mL) and washed with 1M HCl (2x5mL). The organic layer was then dried with MgSO₄, filtered and concentrated. Purification by silica gel chromatography (4:1 Hex:EtOAc) to afford the title compound as a pale yellow oil (.109g, 40%). ¹H NMR (300 MHz, CDCl₃): δ 6.60 (dt, $J = 16.9, 10.2$ Hz, 1H), 6.03 (t, $J = 10.8$ Hz, 1H), 5.40 (dd, $J = 17.8, 7.6$ Hz, 1H), 5.20 (d, $J = 16.8$ Hz, 1H), 5.11 (d, $J = 9.8$ Hz, 1H), 4.54 (t, $J = 5.7$ Hz, 1H), 3.09 (q, $J = 6.8$ Hz, 2H), 2.96-2.85 (m, 2H), 2.26 (q, $J = 7.3$ Hz, 2H), 1.65 (quin, $J = 7.3$ Hz, 2H), 1.03-0.93 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 0.0, 12.5, 26.7, 32.2, 44.7, 50.5, 119.7, 132.3, 132.8, 133.9



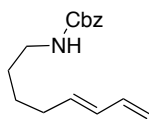
(E)-Benzyl 6-methylhepta-4,6-dienylcarbamate(19)

To a reaction flask was added (*E*)-6-methylhepta-4,6-dien-1-amine (0.142g, 1.1mmol), CH₂Cl₂ (10mL), triethylamine (0.17mL, 1.2mmol) and placed under a nitrogen atmosphere. The mixture was cooled to 0°C and to the mixture was added benzyl chloroformate (0.18mL, 1.3 mmol) dropwise over a period of 5 minutes. The reaction was allowed to slowly warm to room temperature and stir overnight. The reaction quenched with water (10mL) and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (2x20mL) and combined organic layers were washed with 0.5M citric acid, saturated NaHCO₃, dried over MgSO₄, filtered and condensed. Purification by flash chromatography (8:1 Hex:EtOAc) afforded (*E*)-benzyl 6-methylhepta-4,6-dienylcarbamate as a colorless oil (0.052g, 18%). ¹H NMR (300 MHz, CDCl₃): Isolated as a mixture of olefin isomers E/Z = (3:2) δ 7.37-7.31 (m, 10H), 6.18-6.09 (m, 1H), 5.86 (d, $J = 10.8$ Hz, 1H), 5.64-5.60 (m, 1H), 5.42-5.32 (m, 3H), 5.11-5.09 (m, 4H), 4.95 (s, 1H), 4.87 (s, 1H), 4.82 (s, 1H), 4.74 (s, 2H), 3.25-3.18 (m, 4H), 2.30 (q, $J = 6.3$ Hz, 2H), 2.16-2.14 (m, 2H), 1.86 (s, 3H), 1.82 (s, 3H), 1.65-1.52 (m, 4H).



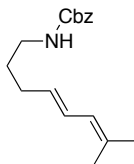
(E)-Benzyl 4-methyl-2,2-diphenylhepta-4,6-dienylcarbamate(21)

To a reaction flask was added (*E*)-4-methyl-2,2-diphenylhepta-4,6-dien-1-amine (0.595g, 2.1mmol), CH₂Cl₂ (21mL), triethylamine (0.36mL, 2.6mmol) and placed under a nitrogen atmosphere. The mixture was cooled to 0°C and to the mixture was added benzyl chloroformate (0.34mL, 2.4mmol) dropwise over a period of 5 minutes. The reaction was allowed to slowly warm to room temperature and stir overnight. The reaction quenched with 0.5M citric acid (10mL) and the layers were separated. The aqueous layer was extracted with ether (2x10mL) and combined organic layers were washed with, saturated NaHCO₃, brine, dried over MgSO₄, filtered and condensed. Purification by flash chromatography (12:1 Hex:EtOAc) afforded (*E*)-benzyl 4-methyl-2,2-diphenylhepta-4,6-dienylcarbamate as a white solid (0.560g, 63%). ¹H NMR (300 MHz, CDCl₃): δ 7.33-7.17 (m, 15H), 6.45 (dt, *J* = 10.2, 16.5 Hz, 1H), 5.73 (d, *J* = 10.8 Hz 1H), 5.06-4.99 (m, 4H), 4.32 (s, 1H), 3.98 (d, *J* = 5.4 Hz, 2H), 2.87 (s, 2H), 1.09 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 18.7, 47.4, 47.6, 50.8, 67.0, 116.3, 126.9, 128.4, 128.5, 128.6, 128.8, 133.3, 146.0, 156.4



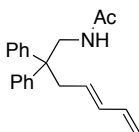
(E)-Benzyl octa-5,7-dienylcarbamate14a

To a reaction flask was added 6,8-nonadienoic acid (0.77mg, 0.5mmol)¹³, triethylamine (.07mL, 0.5mmol) and toluene (1mL). Diphenylphosphoryl azide (0.11mL, 0.5mmol) was added dropwise and then heated to 80°C for 3 hours. The reaction was cooled to room temperature and benzyl alcohol (.08mL, 0.75mmol) was added and allowed to stir for 48 hours. The reaction was condensed, diluted with ether (5mL) and washed with 0.5M citric acid (3mL). The aqueous layer was extracted with ether (3x5mL) and the combined organic layers were washed with saturated NaHCO₃ (5mL), brine (5mL), dried over MgSO₄, filtered and concentrated. Purification by silica gel chromatography (10:1 Hex:EtOAc) yielded the title compound as a colorless oil (63mg, 48%). ¹H NMR (300 MHz, CDCl₃): Isolated as a mixture of olefin isomers E/Z = (4:1) δ 7.40-7.27 (m, 10H), 6.62 (dt, *J* = 16.8 Hz, 10.9 Hz, 1H), 6.30 (dt, *J* = 17.0 Hz, 10.2 Hz, 1H), 6.12-5.92 (m, 2H), 5.71 (dt, *J* = 14.7 Hz, 7.5 Hz, 1H), 5.52-5.30 (m, 2H), 5.26-5.03 (m, 7H), 4.97 (d, *J* = 10.6 Hz, 2H), 4.87 (s, 1H), 4.73 (s, 1H), 3.82-3.07 (m, 4H), 2.28-1.98 (m, 4H), 1.67-1.29 (m, 8H). ¹³C NMR (75 MHz, CDCl₃): δ 26.3, 26.7, 27.3, 29.5, 32.1, 40.9, 66.6, 115.0, 115.2, 117.2, 128.1, 128.2, 128.5, 129.7, 131.4, 132.1, 136.7, 156.4



Benzyl 7-methylocta-4,6-dienylcarbamate(25)

To a reaction flask was added 7-methylocta-4,6-dien-1-amine (0.356g, 2.6mmol), CH_2Cl_2 (25mL), triethylamine (0.43mL, 3.1mmol) and placed under a nitrogen atmosphere. The mixture was cooled to 0°C and to the mixture was added benzyl chloroformate (0.40mL, 2.8mmol) dropwise over a period of 5 minutes. The reaction was allowed to slowly warm to room temperature and stir overnight. The reaction quenched with 0.5M citric acid (10mL) and the layers were separated. The aqueous layer was extracted with ether (2x20mL) and combined organic layers were washed with saturated NaHCO_3 , brine, dried over MgSO_4 , filtered and condensed. Purification by flash chromatography (7:1 Hex:EtOAc) afforded benzyl 7-methylocta-4,6-dienylcarbamate as a colorless oil (0.464g, 66%). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.39-7.33 (m, 5H), 6.22 (dd, $J = 11.4$ Hz, 1H), 6.06 (d, $J = 11.4$ Hz, 1H), 5.31 (dd, $J = 7.8$ Hz, 1H), 5.12 (s, 2H), 4.79 (s, 1H), 3.24 (dd, $J = 6.6$ Hz, 2H), 2.23 (q, $J = 7.5$ Hz, 2H), 1.82 (s, 3H), 1.77 (s, 3H), 1.67-1.58 (m, 2H).



(E)-N-(2,2-diphenylhepta-4,6-dienyl)acetamide (23)

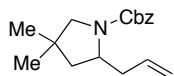
To a reaction flask was added acetic anhydride (0.11mL, 1.2mmol), and CH_2Cl_2 (1mL). (4E,6E)-2,2-diphenylhepta-4,6-dien-1-amine (0.263g, 1.0mmol) was added dropwise at room temperature and the reaction was allowed to stir for 5 hours. Reaction was diluted with CH_2Cl_2 (5mL) quenched with 1M NaOH (5mL) and the layers were separated. The organic layer was dried over MgSO_4 , filtered and concentrated. Purification by flash chromatography (3:1 Hex:EtOAc) afforded the title compound as a colorless oil (0.250g, 82%). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.42-7.13 (m, 10H), 6.17 (dt, $J = 16.5$ Hz, 9.8 Hz, 1H), 5.96 (dd, $J = 15$ Hz, 10.5 Hz, 1H), 5.33 (dt, $J = 14.7$ Hz, 7.3 Hz, 1H), 6.72-6.06 (m, 3H), 3.97 (d, $J = 6.0$ Hz, 2H), 2.89 (d, 7.5 Hz, 2H), 1.87 (s, 3H).

3.4 Hydroamination Reaction and Products

General Hydroamination Conditions and Characterization of Hydroamination Products

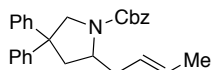
In a glove box, 2,6-bis(diphenylphosphinomethyl)pyridine dichloropalladium (5 mol%), AgBF_4 (0.1 equiv.), and MgSO_4 (1 equiv.) were added to a round-bottomed flask. The flask was capped with a septum, removed from the glove box, placed under an atmosphere of nitrogen, and CH_2Cl_2 (0.5 mL) was added. To the stirring mixture was added a solution of the substrate (1 equiv.) in CH_2Cl_2 (0.5 mL) by syringe. The reaction was stirred for 2 – 16 h while monitoring for the disappearance of diene by TLC. After

complete reaction, the mixture was purified by chromatography (100% CH₂Cl₂) to afford pure product.



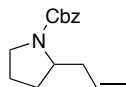
Benzyl 2-allyl-4,4-dimethylpyrrolidine-1-carboxylate(7a)

General Hydroamination Conditions: Colorless oil (0.026g, 95%), ¹H NMR (300 MHz, CDCl₃): Observed as a mixture of rotamers δ 7.37-7.26 (m, 5H), 5.73-5.65 (m, 1H), 5.22-4.98 (m, 4H), 3.96-3.91 (m, 1H), 4.41 (d, *J* = 11.1 Hz, 1H, minor), 3.37 (d, *J* = 10.8 Hz, 1H, minor), 2.98 (d, *J* = 1H), 2.72 (s, 1H, major), 2.54 (s, 1H, minor), 2.30-2.28 (m, 1H), 1.81-1.72 (m, 2H, major + minor), 1.50-1.45 (m, 1H), 1.08 (s, 3H), 0.97 (s, 3H).



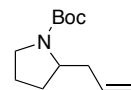
(E)-Benzyl 2-(but-2-enyl)-4,4-diphenylpyrrolidine-1-carboxylate(9a)

General Hydroamination Conditions: Colorless oil (0.026g, 95%), ¹H NMR (300 MHz, CDCl₃): Observed as a mixture of rotamers δ 7.26-7.03 (m, 15H), 5.36-5.19 (m, 3H), 5.19-4.92 (m, 1H), 4.64 (d, *J* = 11.7 Hz, 1H, major), 4.48 (d, *J* = 11.4 Hz, 1H, minor), 3.60-3.62 (m, 1H), 3.49 (t, *J* = 11.4 Hz, 1H), 2.66-2.60 (m, 2H), 2.38 (s, 1H, minor), 2.28-2.19 (m, 1H), 2.14-2.04 (m, 1H), 1.53 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 18.4, 36.8, 37.8, 43.1, 44.0, 52.9, 53.1, 53.7, 57.1, 66.9, 67.1, 126.6, 126.7, 126.8, 127.1, 127.8, 128.1, 128.3, 128.6, 128.7, 128.8, 137.2, 137.4, 146.0, 154.8, 155.6



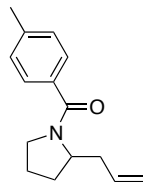
Benzyl 2-allylpyrrolidine-1-carboxylate(3a)

General Hydroamination Conditions: Colorless oil (0.026g, 99%), ¹H NMR (300 MHz, CDCl₃): Observed as a mixture of rotamers δ 7.37-7.27 (m, 5H), 5.78-5.70 (m, 1H), 5.20-4.99 (m, 4H), 3.92 (s, 1H), 3.42 (s, 2H), 2.59 (s, 1H, major), 2.42 (s, 1H, minor), 2.20-2.13 (m, 1H), 1.92-1.71 (m, 4H). ¹³C NMR (75 MHz, CDCl₃): δ 22.9, 23.7, 29.2, 30.0, 38.0, 39.0, 46.5, 46.9, 53.5, 56.8, 57.3, 66.5, 66.7, 117.2, 117.3, 127.8, 127.9, 128.5, 134.9, 135.0, 137.0, 137.2, 154.8



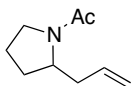
Tert-butyl 2-allylpyrrolidine-1-carboxylate(3b)

General Hydroamination Conditions: Colorless oil (0.026g, 76%), ¹H NMR (300 MHz, CDCl₃): Observed as a mixture of rotamers δ 5.78-5.67 (m, 1H), 5.07-5.01 (m, 2H), 3.84-3.76 (m, 2H, major + minor), 3.30 (s, 2H), 2.52-2.40 (m, 2H, major + minor), 2.51-2.05 (m, 1H), 1.83-1.73 (m, 4H), 1.45 (s, 9H).



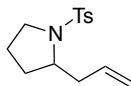
1-(4-methylbenzoyl)-2-allylpyrrolidine (3c)

General Hydroamination Conditions: Colorless oil (0.026g, 86%), ¹H NMR (300 MHz, CDCl₃): Observed as a mixture of rotamers δ 7.34 (d, *J* = , 2H), 7.12 (d, *J* = , 2H), 5.77 (td, *J* = , 5.77), 5.08-5.03 (m, 2H), 4.26 (s, 1H), 3.38-3.43 (m, 2H), 2.59 (s, 1H), 2.34-2.30 (m, 4H), 1.82-1.65 (m, 4H).



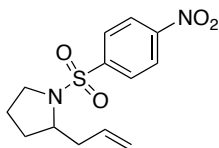
1-(acetyl)-2-allylpyrrolidine (3d)

General Hydroamination Conditions: Colorless oil (0.0151g, 99%), ¹H NMR (300 MHz, CDCl₃): Observed as a mixture of rotamers δ 5.84-5.62 (m, 1H), 5.09 (d, *J* = 15.7, 1H), 5.02 (d, *J* = 8.9 Hz, 1H), 4.18-4.04 (m, 1H, major), 3.94-3.74 (m, 1H, minor), 3.59-3.30 (m, 2H), 2.64-2.47 (m, 1H, major), 2.41-2.26 (m, 1H, minor), 2.17-2.01 (m, 4H, major + minor), 1.98-1.66 (m, 4H).



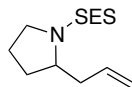
2-allyl-1-tosylpyrrolidine(3e)

General Hydroamination Conditions: Colorless oil (0.019g, 72%), Spectral data of this material matches literature values.¹¹ ¹H NMR (300 MHz, CDCl₃): δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 5.78 (ddt, *J* = 17.2, 10.0, 7.2 Hz, 1H), 5.12-5.03 (m, 2H), 3.65 (dq, *J* = 13.1, 3.8 Hz, 1H), 3.44-3.35 (m, 1H), 3.16 (dt, *J* = 10.3, 7.2 Hz, 1H), 2.65-2.54 (m, 1H), 2.42 (s, 3H), 2.29 (dt, *J* = 14.8, 7.6 Hz, 1H), 1.86-1.70 (m, 1H), 1.70-1.42 (m, 3H).



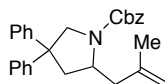
2-allyl-1-(4-nitrophenylsulfonyl)pyrrolidine (3f)

General Hydroamination Conditions: white solid (0.0288g, 97%), ¹H NMR (300 MHz, CDCl₃): δ 8.37 (d, *J* = 8.6 Hz, 2H), 8.03 (d, *J* = 8.7 Hz, 2H), 5.84-5.67 (m, 1H), 5.16-5.04 (m, 2H), 3.71 (dq, 12.7, 3.9 Hz, 1H), (ddd, *J* = 10.3, 7.1, 4.7 Hz, 1H), 3.19 (dt, *J* = 10.1, 7.1 Hz, 1H), 2.65-2.53 (m, 1H), 2.38-2.24 (m, 1H), 1.94-1.77 (m, 1H), 1.77-1.50 (m, 4H).



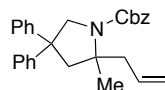
2-allyl-1-(2-(trimethylsilyl)ethylsulfonyl)pyrrolidine (3g)

General Hydroamination Conditions: Colorless oil (0.020g, 73%), ¹H NMR (300 MHz, CDCl₃): δ 5.76 (ddt, *J* = 17.1, 10.2, 7.2 Hz, 1H), 5.12-5.05 (m, 2H), 3.96-3.88 (m, 1H), 3.33-3.28 (m, 1H), 2.90-2.85 (m, 2H), 2.55-2.46 (m, 1H), 2.26-2.15 (m, 1H), 2.00-1.73 (m, 4H), 1.07-0.98 (m, 2H), 0.00 (s, 9H).



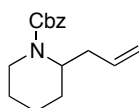
Benzyl 2-(2-methylallyl)-4,4-diphenylpyrrolidine-1-carboxylate(13a)

General Hydroamination Conditions: Colorless oil (0.026g, 75%), ¹H NMR (300 MHz, CDCl₃): Observed as a mixture of rotamers δ 7.39-7.28 (m, 5H), 5.19-5.09 (m, 2H), 4.75 (d, *J* = 10.8 Hz, 1H), 4.67 (d, *J* = 8.7 Hz, 1H), 4.03 (s, 1H), 3.44 (s, 2H), 2.62 (d, *J* = 12.3 Hz, 1H, major), 2.43 (d, *J* = 11.7 Hz, 1H, minor), 2.00-1.65 (m, 8H).



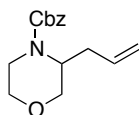
Benzyl 2-allyl-2-methyl-4,4-diphenylpyrrolidine-1-carboxylate(11a)

General Hydroamination Conditions: Colorless oil (0.026g, 95%), ¹H NMR (300 MHz, CDCl₃): Observed as a mixture of rotamers δ 7.37-7.08 (m, 15H), 5.61-5.49 (m, 1H), 5.13-5.09 (m, 2H), 4.59 (d, *J* = 12 Hz, 1H, minor), 4.46 (d, *J* = 11.7, 1H, major), 3.78-3.73 (m, 2H, major + minor), 2.90-2.82 (m, 2H, major + minor), 2.49- 2.52 (m, 3H) 1.04 (s, 3H, major), 0.94 (s, 3H, minor). ¹³C NMR (75 MHz, CDCl₃): δ 25.0, 26.3, 43.3, 44.6, 48.9, 50.9, 56.2, 56.8, 62.6, 63.3, 66.3, 67.1, 126.3, 126.4, 126.6, 126.7, 126.8, 128.0, 128.5, 128.6, 134.1, 145.9, 146.0, 146.2, 153.4, 154.8



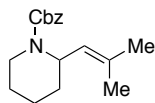
Benzyl 2-allylpiperidine-1-carboxylate (15a)

General Hydroamination Conditions: Colorless oil (0.022g, 90%), ¹H NMR (300 MHz, CDCl₃): Observed as a mixture of rotamers δ 7.43-7.27 (m, 5H), 5.83-5.61 (m, 1H), 5.16-4.95 (m, 4H), 4.45-4.26 (m, 1H), 4.13-3.99 (m, 1H, major + minor), 2.85 (t, *J* = 13.4 Hz, 1H), 2.50-2.36 (m, 1H), 2.32-2.19 (m, 1H), 1.70-1.53 (m, 6H).



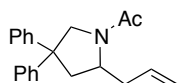
Benzyl 3-allylmorpholine-4-carboxylate (17a)

General Hydroamination Conditions: Colorless oil (0.010g, 96%), $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.42-7.28 (m, 5H), 5.87-5.60 (m, 1H), 5.21-4.97 (m, 4H), 4.14-3.95 (m, 1H), 3.95-3.67 (m, 3H), 3.58-3.33 (m, 3H), 2.49 (t, $J = 7.3$ Hz, 2H).



Benzyl 2-(2-methylprop-1-enyl)piperidine-1-carboxylate(19a)

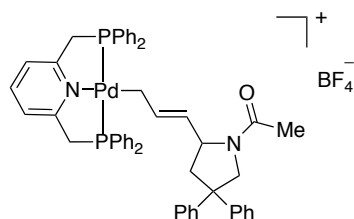
General Hydroamination Conditions: Colorless oil (0.026g, 18%), $^1\text{H NMR}$ (300 MHz, CDCl_3): Observed as a mixture of rotamers δ 7.34-7.25 (m, 5H), 5.48 (d, $J = 8.7$ Hz, 1H), 5.17-5.03 (m, $J = 13.8$ Hz, 3H), 4.04 (s, 1H, minor), 3.99 (s, 1H, major), 2.94 (t, $J = 13.2$ Hz, 1H), 1.71-1.45 (m, 12H).



1-(2-allyl-4,4-diphenylpyrrolidin-1-yl)ethanone (23a)

General Hydroamination Conditions: Colorless oil $^1\text{H NMR}$ (300 MHz, CDCl_3): Observed as a mixture of rotamers δ 7.37-6.94 (m, 10H), 5.78-5.52 (m, 1H), 5.15-4.87 (m, 3H), 4.23 (d, $J = 10.7$ Hz, 1H, major), 4.09-3.95 (m, 1H, minor), 3.84 (d, $J = 10.7$ Hz, 1H, major), 3.81-3.64 (m, 1H, major), 3.47 (d, $J = 12.1$ Hz, 1H, minor), 2.91-2.73 (m, 1H, major + minor), 2.73-2.62 (m, 1H, major), 2.51-2.36 (m, 1H), 2.35-2.14 (m, 3H), 2.04 (s, 1H, major), 1.97 (s, 1H, minor).

3.5 Palladium Allyl Complex



(PNP)palladium allyl complex(24)

In a golvebox was added (PNP)Pd-pentafluorobenzonitrile complex⁵ (0.100mg, 0.12mmol) to a reaction flask. The reaction flask was capped with septum, removed from the box and placed under nitrogen atmosphere. CH_2Cl_2 (2mL) was added to dissolve the catalyst and a solution of (*E*)-*N*-(2,2-diphenylhepta-4,6-dienyl)acetamide (0.36mg, 0.12mmol) and *N,N*-dimethylaniline (.044mL, 0.35mmol) in CH_2Cl_2 (3mL) was then added. The reaction was allowed to stir for 20min and was quenched with citric acid (5mL) and the layers were separated. The organic later was washed with NaHCO_3 , dried over MgSO_4 , filtered and concentrated to give crude product as reddish oil. The oil was dissolved in 1mL CH_2Cl_2 and was precipitated with Et₂O at 0°C. The solvent was decanted off and the solid was washed with ether (3x 2mL). The resulting yellow solid was re-dissolved in CH_2Cl_2 and dried again with MgSO_4 , filtered, concentrated and placed on hi-vac to yield the title compound as a yellow solid. $^1\text{H NMR}$ (500 MHz,

CDCl₃): Observed as a mixture of rotamers 7.94-7.09 (m, 66H, major + minor), 5.46 (dt, $J = 15.0, 7.5$ Hz, 1H, minor), 5.24 (dt, $J = 15.0, 7.5$ Hz, 1H, major), 4.91 (d, $J = 11.5$ Hz, 1H, major), 4.80 (dd, $J = 15.5, 8.0$ Hz, 1H, minor), 4.60 (br s, 1H, minor), 4.51-4.45 (m, 10H, major + minor), 4.26 (d, $J = 10.5$ Hz, 1H, minor), 3.90-3.87 (m, 1H, minor), 3.66 (d, $J = 11.0$ Hz, 1H, minor), 3.39 (q, $J = 8.5$ Hz, 1H, major), 3.21 (d, $J = 12.0$ Hz, 1H, major), 2.73-3.62 (m, 4H, major + minor), 2.54 (dd, $J = 12.0, 6.5$ Hz, 1H, major), 2.44 (dd, $J = 13.0, 6.5$ Hz, 1H, minor), 2.08 (s, 3H, minor), 2.01 (t, $J = 12$ Hz, 1H, major), 1.91 (t, $J = 12$ Hz, 1H, minor), 1.65 (s, 3H, major).

Section 4: References

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