Development of Cooperative Catalytic Systems and Bimetallic Catalysts for Organic Synthesis

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A dissertation submitted to the faculty of Brigham Young University in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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ABSTRACT

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The development of new catalysts for organic synthesis is an important pursuit that enables the discovery of new and more efficient reactions and the identification of new reaction mechanisms. Cooperative catalytic systems and bimetallic catalysts represent unique approaches to catalyst development that achieve reactivity that cannot be obtained with a single catalyst or metal. These types of catalysts can activate substrates in unique ways, facilitate reactions under mild conditions, increase substrate scope, and provide access to completely new transformations. The first part of this work describes the development of a cooperative nickel-titanium-catalyzed amination of allylic alcohols. The cooperative effects of the two metals allow for mild reaction conditions that tolerate a larger substrate scope. A unique tandem cyclization amination is also shown that only takes place using both metals. Additionally, the benefits of using boron tethers are shown in the boron templated dimerization of allylic alcohols. This dimerization forms boron-protected 1,3-diols. Derivatization studies were performed that show the synthetic utility of this new transformation.

The second portion of this work focuses on the development of a novel bimetallic rhodium complex and its use in organic synthesis. Using a 2-phosphinoimidazole ligand in the presence of carbon monoxide, a bimetallic Rh(II) complex is formed and purified in high yield. This complex shows versatile reactivity and performs reactions that are traditionally catalyzed by both Rh(I) and Rh(II) complexes. An X-ray crystal structure and DFT calculations confirm the bimetallic nature of this catalyst. Our catalyst shows a unique ability to perform reductive eliminations with weak nucleophiles where other rhodium catalysts perform β-hydrogen elimination. The utility of this catalyst is shown in the intramolecular hydroamination of allenes to form small and medium sized nitrogen heterocycles. We also describe the development of a bimetallic trifluoroacetoxylation of allenes. This reaction only occurs with our bimetallic catalyst and over 30 examples are shown.

Keywords: bimetallic, rhodium, catalyst, nickel, titanium, cooperative catalysis, boron templated reaction
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Chapter 1 Introduction to Cooperative Catalytic Systems and Bimetallic Catalyst

1.1 Cooperative catalytic systems

Cooperative catalysis involves the use of multiple catalysts in the same reaction that work in concert to activate substrates and forge new bonds. One approach to cooperative catalysis uses two different catalysts to activate both the electrophile and nucleophile to form a new bond (Figure 1.1). While traditional catalysts may activate either the nucleophile or the electrophile (nucleophile shown in example), cooperative catalysis activates both and may use two different mechanisms to accomplish the activation or each substrate. There is some confusion when it comes to cooperative catalysis because multiple metals are used in many catalytic systems. Additionally, cooperative catalysis has been called by many names including synergistic catalysis, cooperative dual catalysis, and contemporaneous dual catalysis. Bifunctional catalysis also involves activation of both the electrophile and nucleophile, however, this is done using a single catalyst (Figure 1.2a). Some reactions use multiple catalysts that both activate the electrophile or nucleophile but not both (Figure 1.2b). Gold is commonly used to activate olefins in the presence of another catalyst that also binds to the olefin. Cascade reactions also use multiple catalysts, but this is done by performing a transformation of the substrate followed another transformation using a separate catalyst (Figure 1.2c).
Macmillan and others have gained insight into how cooperative catalysis is used in nature.\(^1\) Enzymes may have more than one activation sight where they can activate both the electrophile and nucleophile. The production of tetrahydrofolate is a good example of this, where the electrophile, an imine in dihydrofolate, is activated by dihydrofolate reductase. The nucleophile, a hydride, is also activated by coenzyme NADP\(^+\). Cooperative catalysts have many advantages including more catalyst turnover, reactivity under mild condition, expanded substrate scope of known reactions, and new catalytic activity. In this review, we will focus on cooperative catalytic systems that rely on the use of two metals, or bimetallic complexes to enable new reactivity and cooperative or bimetallic mechanisms.

While there are significant examples of cooperative organocatalysts and transition metal/organocatalyst cooperative systems,\(^7\) our lab is interested in the benefits of cooperative catalysis using two transition metal catalysts. This introduction will focus on cooperative catalysis with two metals. An early example of metal cooperative catalysis is the Sonogashira reaction (Figure 1.3).\(^8\) In this reaction, the palladium performs oxidative addition into the aryl halide bond and copper activates the alkyne for deprotonation. The organocopper complex then undergoes transmetallation of the alkyne to the palladium and reductive elimination at palladium.

\[ \text{Figure 1.3 Mechanism of copper palladium cooperative catalysis in the Sonogashira reaction} \]

gives the product. The cooperative catalysis activates substrates to the degree that very mild conditions can be used; the reaction can be run at room temperature, in aqueous media and using
a mild base. This cross-coupling has been used frequently to form new carbon-carbon bond and has shown good utility in total synthesis.9

Another reaction that shows good utility of cooperative catalysis is work done by Ito and coworkers (Figure 1.4).10 Ito developed an enantioselective allyl insertion into $\alpha$-cyano carbonyls to give $\alpha$-allyl-$\alpha$-cyano-carbonyls. In this transformation, the Pd catalyst reacts with an allylic carbonate to generate and electrophilic pi allyl complex and the rhodium acts as a Lewis acid to facilitate deprotonation of the nucleophile. This reaction gives excellent ee and yield with substrates containing esters, amides, and phosphonates. It is important to note that when palladium is not present, no conversion takes place. Under Tsuji-Trost conditions, using only palladium, reaction rates are significantly lower and using chiral Pd gives no enantioselectivity.

Cooperative catalysis with first row transition metals offers additional benefits because these metal catalysts have lower cost and through cooperative mechanisms, new transformations can be achieved that typically work with more expensive noble metal catalysts. Semba and Nakao
used a cooperative palladium copper reaction for the aryl borylation of alkenes (Figure 1.5). In the proposed reaction mechanism the copper alkoxide reacts with the $\text{B}_2(\text{pin})_2$ to generate the borylcopper compound. The borylcopper reacts with styrene to give the $\beta$-borylalkylcopper which can undergo transmetallation to place the substrate on palladium. Reductive elimination gives the final product. Consistent with benefits seen in other cooperative catalysis systems, this reaction tolerates a wide variety of substrates including, electron rich and poor aryl bromides and styrenes. Additionally, sensitive groups including tertiary amines, nitriles and esters work well in the reaction.

While these cooperative catalysts demonstrate unique mechanistic insight, metals can also simply bind to substrates to activate them. As shown in the examples above, copper and gold have been shown to activate alkenes and alkynes for a variety of reactions. Lewis acidic metals can also have a strong effect in the activation of alcohols and other electron rich substrates.

Figure 1.5 Work by Semba and Nakao, cooperative palladium copper arylborylation of styrenes
The Trost Lab has shown these benefits using a vanadium and palladium catalyst to form \( \alpha \)-allylated \( \alpha, \beta \)-unsaturated ketones (Figure 1.6).\(^{22}\) This process proceeds as vanadium catalyzes the propargylic rearrangement by coordinating to the oxygen. This activates the substrate to add to the palladium allyl. Trost refers to this as a “contemporaneous dual catalysis by coupling highly transient nucleophilic and electrophilic Intermediates”. Essentially the vanadium activates the allyl by coordinating to the oxygen facilitating faster formation of the allene.

![Figure 1.6 Vanadium palladium catalysis and catalytic intermediates](image)

In a similar approach, the Michaelis laboratory has used titanium as a Lewis acid to activate late transition metals toward nucleophilic addition. (Figure 1.7). Using a platinum titanium catalyst (Figure 1.7a) the titanium activated the platinum for increased bonding affinity to the alkyne.\(^{11}\) In a separate study, large synergistic effects were seen when the Michaelis group investigated the mechanism of a Pd–Ti mediated allylic amination reaction (Figure 1.7b).\(^{12}\) Their computational studies showed that the palladium is activated by the titanium to lower the energy for the rate limiting reductive amination step. The benefits were apparent as the catalyst turn over numbers were increased by \( \sim 10^5 \). While these studies were primarily focused the metal-metal interactions, we are very interested in using the synergy that could be present with a Lewis acidic metal in activating the substrate in a similar fashion to how the Trost group used vanadium.

As described, many benefits come from the development of cooperative catalysis systems. However, many challenges arise in the development of these types of systems. One of the most apparent issues relates to the concentration of catalyst-activated substrates in the system, which influences reaction kinetics. A cooperative catalytic system relies on reaction
between the activated nucleophile and activated electrophile, which each exist in low (catalytic) concentrations. This means that while these substrates are activated for faster coupling, they must overcome the lower rate from low concentrations. This is illustrated in equation 1, (rate law for product formation) where \([A']\) is the concentration of activated electrophile and \([B']\) is the concentration of activated nucleophile.

\[
\frac{dc}{dt} = k \times [A'] \times [B']
\]  

(1-1)

Another obstacle with cooperative catalysis can be an increase in background reactions. The addition of a new catalyst that activates an additional substrate inherently increases the amount of background reactions that can take place. Each activated starting material may react with an inactivated one allowing for potential loss. In addition to reactants combining in undesirable ways, each catalyst can also undergo decomposition, slowing reaction rates. Complexation of a Lewis acid and base or a redox interaction are among the potential ways that catalyst can deactivate each other.\(^1\) Cooperative catalysts is a growing area in organic synthesis. These cooperative catalysts allow for new chemical transformations that proceed with increased substrate scopes and under mild conditions. Work in cooperative catalysis has shown significant advancements in understanding these systems and the complications with using them.

1.2  Bimetallic catalytic systems

---

\(\text{Figure 1.7} \) Past work in the Michaelis lab using titanium metal activation.
Both transition metal cooperative catalysis systems and bimetallic catalysts use two metals to achieve novel mechanistic effects. Bimetallic catalysts, however, contain both metals on the same complex, which provides several advantages. As discussed above using two distinct catalysts to activate two substrates can lead to more background reactions, lower rates of product formation due to low concentrations, and possible self-quenching/decomposition of catalysts. By placing both metals in one complex, unfavorable interactions can often be avoided. Bimetallic catalysts can also undergo unique coordination to substrates, binuclear mechanisms, and additional activation of substrates as seen in cooperative catalysis.

Binuclear mechanisms are of interest because in addition to opening new reaction pathways they also increase our understanding of how metals can work together. Typically, only two factors can be optimized in homogenous catalyst design: 1) the identity of the metal and 2) the electronics and steric present in the ligands. Using two metals allows for more fine-tuned optimization where the two different metals may interact synergistically and even the spacing between the metals can be tuned to achieve reactivity similar to what occurs in an enzyme active site. Dobbek and coworkers have proposed an interesting binuclear activation of carbon dioxide in the nickel iron clusters found in carbon monoxide dehydrogenase (Figure 1.8a). Crystal structures of the intermediates indicate the nickel and iron both bind to the carbon dioxide. The Lalic group has also shown some unique binuclear activity with copper in the hydroalkylation of alkynes (Figure 1.8b). The believe that two copper atoms are necessary to activate the alkyne and enable the reaction. Interestingly, this reaction proceeds without concomitant side reactions while using highly reactive alkyl triflates. This gives further evidence of some of the benefits of bimetallic reactions over cooperative catalysis. Mankad has also proposed a binuclear oxidative addition and binuclear reductive elimination with an Fe–Cu complex in his work with a photochemical C-H borylation (Figure 1.8c). These studies provide evidence of the potential new reactivity that

![Figure 1.8 Binuclear mechanism intermediates](image_url)
can be obtained when using bimetallic complexes in catalysis. While binuclear mechanisms are of interest it can be difficult to know if a reaction is proceeding through a bimetallic pathway. In addition, only limited examples mechanistic studies have been reported that really tease out the role of two metals in a bimetallic catalyst. One effect of bimetallic catalysis that is easier to observe is the unique coordination of substrates to bimetallic catalysts. Uyeda has shown some of these coordination benefits in the cyclotrimerization of alkynes catalyzed by a dinickel complex (Figure 1.9).\textsuperscript{17} Both nickels are involved in coordinating to the alkynes during the mechanism, as shown in crystal structures, which allows for increased reaction rates and mild conditions. Full conversion was reached in the majority of substrates after 15 minutes, at room temperature, with 1\% catalyst loading. The unique coordination of these nickel complexes also leads to differences in the products formed. Typically, mono nickel complexes convert terminal alkynes into a mixture of cyclic (arene and cyclooctatetraene) and acyclic products.\textsuperscript{18} The specificity of this reaction to form only the 1,2,4 substituted arenes is likely strongly related to the coordination of both nickels.

Figure 1.9 Work by Uyeda in the cyclotrimerization of alkynes using binuclear coordination to substrates.
Another factor in bimetallic catalysis is the electronic effects of the metal-metal bond. Metal-metal bonds are seen in nature in the nickel iron hydrogenase (Figure 1.10a) and may be present in other cofactors of enzymes including CO dehydrogenase and acetyl-CoA synthase. As discussed above, past work in the Michaelis lab has utilized Lewis acidic titanium to remove electron density and facilitate faster reductions (Figure 1.10c). A similar approach has been used with zirconium (Figure 1.10b). The development of new catalytically active bimetallic complexes is a growing area of interest, and the Cambridge Structural Database contains well over 40000 examples of multinuclear complexes with strong metal-metal interactions. In addition to the polarity of the metal-metal bond, the bond order can also have an impact on the reactivity of the complex and is a factor to consider when designing bimetallic complexes. The formation metal-metal multiple bonds can bring two metals closer together and enhance the reactivity of the two metals. Heterobimetallic complexes that contain an electron rich and an electron poor metal can contain bond lengths as short as 1.73 Å. Some metal-metal interactions may also be as weak as a hydrogen bond, as seen in the Au-Au bond interactions in Figure 1.10e. The ability to change the metal interactions by changing the identity of each metal in bimetallic catalysts is part of what creates such large potential for the discovery of new reactions and mechanisms with bimetallic complexes.

In previous studies from our laboratory, we reported the synthesis of 2-phosphinoimidazole-derived homobimetallic Pd(I) and Pd(II) complexes (Figure 1.11a, b). These complexes are catalytically active in Buchwald-Hartwig type amination reactions and in aminocarbonylations of aryl halides. In addition, we discovered a new method for naphthalene synthesis that only
proceeds with our bimetallic complexes; monometallic Pd complexes are generally inactive. Our mechanistic and computational studies on this new transformation indicate that the unique structure of the bimetallic Pd(II) complex enables access to dimeric Pd(III) intermediates during catalysis to facilitate a ketone alpha-arylation step under oxidizing conditions starting with a Pd(II) catalyst.

```latex
\begin{figure}
\centering
\includegraphics[width=\textwidth]{bimetallic_complexes.png}
\caption{Past bimetallic complexes synthesized in the Michaelis lab and commercially available bimetallic rhodium complexes}
\end{figure}
```

Based on our success in developing bimetallic Pd complexes on the 2-phosphinoimidazole ligand scaffold, we have also sought the development of other bimetallic complexes, including bimetallic Rh catalysts. Bimetallic Rh complexes have seen widespread application in metal carbene and nitrene chemistry, including for cyclopropanations, aziridinations, and C-H amination and alkylation reactions. Common rhodium dimers used in this chemistry are shown in Figure 1.11c, e-f). These catalysts share similar backbone structures with rhodium tetraacetate, all possessing four carboxylate anions that hold the two Rh(II) centers in close proximity. Rhodium has a tendency to form bridged dimer species, such as with [Rh(cod)Cl]$_2$ or complex d, however these precatalysts are generally thought to break up into monometallic species upon addition of ligands and during catalysis. Importantly dirhodium tetracarboxylate catalysts are known to catalyze processes that mono-metallic rhodium complexes do not.$^{32-45}$
Rhodium dimers are known to facilitate many reactions. In particular, rhodium tetraacetate derivatives are known for the decomposition of diazo compounds to form carbenes. These carbenes can be used in a variety of reactions including C-H insertions (Figure 1.12a), and cycloadditions (Figure 1.12b). One of the reasons these complexes may be able to form carbenes more readily than other rhodium complexes may be due to the Rh-Rh bond. This bond allows the rhodium being oxidized or reduced to distribute that electronic burden over both rhodium centers. This is one of the reasons rhodium tetraacetate complexes are commonly used to form metal carbenes, as they form a more stable carbene than other metal complexes. The lower reactivity allows for more control in influencing the selectivity of the reaction.

Another area of intense interest using rhodium is C-H functionalization reactions. These reactions are typically done with rhodium (III) catalysts (Figure 1.13a). These rhodium (III) complexes like [Rh(cod)Cl]₂ contain bridging chloride ligands and while they are still rhodium dimers, do not contain a Rh-Rh bond. These rhodium (II) dimers with bridging X type ligands have been used in a wide variety of reactions including hydrogenation of prochiral olefins, ketones, CO₂, and polynuclear heteroaromatic compounds; the ring opening of oxa- and azabicyclic alkenes; the addition of carboxylic acids to alkynes; CO-gas-free...
hydroformylation (Figure 1.13b)\textsuperscript{38} and carbonylations;\textsuperscript{39} Pauson–Khand-type reactions;\textsuperscript{40} olefin isomerization;\textsuperscript{41} cycloadditions;\textsuperscript{42} the coupling of aldehydes and allenes (Figure 1.13c);\textsuperscript{43} and 1,4-addition of organoboronic acids,\textsuperscript{44} to mention only a few. Rhodium dimers remain an area of interest as they show great activity in a diverse range of reactions and many possible rhodium complexes have not been explored.

The discovery of bimetallic Rh complexes by our group that depart from the typical rhodium tetracarboxylate framework provides new opportunities for us to explore reactivity across two metals with rhodium (Figure 1.14). Our 2-phosphinoimidazole-based bimetallic Rh complexes contain a metal-metal bond while at the same time maintaining open coordination sites and have coordination structures similar to those observed with monometallic Rh(I) complexes. Thus, we believe that our new dirhodium catalyst have the potential to display reactivity similar to both Rh(I) and dirhodium(II) complexes (discussed in chapters 4-5).

In conclusion, the development of cooperative transition metal catalytic systems and bimetallic catalysts provide many opportunities and challenges in developing new and useful
chemistry. One of the challenges associated with bimetallic catalysis is that synthesizing these complexes can be difficult and often requires the use of sterically hindered ligands that may limit applications in catalysis. It can be difficult to find low coordinate systems that still favor the formation of the metal-metal bond. Additionally, after forming a reactive bimetallic complex it can be difficult to identify and discover if it proceeds through a bimetallic pathway. Computational studies are often needed, and intermediates can be difficult to trap to obtain crystal structures. Bimetallic catalysis is an increasing area of interest and the ability to control more factors than traditional mono metallic complexes has promoted recent excitement.

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Chapter 2  C-N Bond Formation from Allylic Alcohols via Cooperative Nickel and Titanium Catalysis

Contributions: Personal contributions to this project include the substrate scope of amines, alcohols, and substrates scope in the tandem amination/cyclization.

2.1 Introduction

Tandem catalysis involves the use of two separate catalysts in a reaction to facilitate activation of multiple reaction partners. For example, tandem catalysis can be used to activate both the electrophile and nucleophile in a reaction to enable more facile coupling reactions. There are four core benefits to using cooperative catalysis: (i) new chemical reactions can be achieved that are unattainable without the activation of both reagents, (ii) improved yields and catalytic efficiency can often be observed, (iii) stochiometric activation of starting materials is not required, and (iv) Tandem catalysis can enable the development or improvement of enantioselective and diastereoselective reactions. There are many examples of catalysts working synergistically together to achieve some of these benefits. These examples include both organo-catalysts and organometallic catalysts.

The catalytic activation of alcohols to improve their leaving group ability is an attractive method in synthesis because it precludes the need to stoichiometrically activate the alcohol as a tosylate or halide. Previous examples have demonstrated that catalytic activation of alcohols can be used in tandem with transition metal catalysis. Kimura et al. used Lewis acidic triethyl borane to activate allylic alcohols and facilitate the oxidative insertion of palladium into the allylic C-O bond. Kimura and others have used this Lewis acid approach to activate allylic alcohols for a variety of reactions. Using these results as precedent, we sought to develop an efficient method for conversion of simple allylic alcohols to amines via

\[
\text{Figure 2.1 Past examples of allylic amination of alcohols}
\]
catalytic activation of an allylic alcohol substrate.

The transition metal-catalyzed allylic amination reaction is a highly versatile approach to C–N bond formation that takes advantage of the high reactivity of allylic leaving groups. Allylic aminations with simple allylic alcohols, however, are quite limited because alcohols are poor leaving groups and the acidic OH limits reactions using basic reagents. Thus, the substrate scope of allylic amination reactions with unprotected alcohols is quite limited with published catalysts (Figure 2.1). These reactions require high temperatures to achieve improved yields. Recent advances have involved using additives such as tetrabutylammonium acetate (Figure 2.1a), which help the reaction proceed under milder conditions and with lower catalyst loadings. Tandem catalysis has also been shown using Lewis acidic boronic esters with a palladium catalyst. Kinmura and Onodera have shown that use of a boron-containing ligand can facilitate activation of the alcohol near the Pd center to enable faster oxidative addition to the C–O bond (Figure 2.1b). While these processes show good utility in functionalizing allylic alcohols, expanding the use of less expensive first row transition metals in the tandem catalysis of allylic alcohols is an area of interest.

We previously reported the use of bimetallic Pd–Ti complexes to enable the addition of hindered nitrogen nucleophiles to allyl chloride substrates. Our hypothesis was that the presence of a Ti atom in the complex activated the Pd center, making it more electrophilic and thus accelerating the reductive addition step in the allylic amination. The Pd–Ti complex increased reaction rates in allylic aminations by ~10^5. Building on these results, we wondered a) R
\[\text{OH} \quad \text{HN} \quad R_1 \quad R_2 \]

b) R
\[\text{HO} \quad \text{HN} \quad R_1 \quad R_2 \]

Figure 2.2 a) Cooperative Ni/Ti catalysis b) tandem cyclization amination reaction
whether we could use titanium to activate allylic alcohols as leaving groups for allylic amination reactions. Our initial efforts in this area focused on the use of nickel catalysts because they are less expensive than Pd catalysts and are more environmentally friendly. Our work described in this chapter highlights the development of this system and the unique chemistry enabled by using tandem nickel-titanium catalysis.

As seen in Figure 2.2, catalytic amounts of both nickel and titanium are used in the allylic amination of alcohols to create allylic amines. The titanium activates the oxygen, enabling faster oxidative addition of the nickel into the C-O bond, generating the metal allyl intermediate. The mechanism then proceeds through a nucleophilic attack by the amine on the least hindered carbon of the metal allyl intermediate. In addition to enabling lower reaction temperatures and lower catalyst loadings, our catalyst demonstrates unique reactivity that is not observed in single catalyst systems. In the presence of a diene, we observe a distinctive cyclization and amination reaction that is only achieved under our catalytic conditions and is not observed with other known catalytic systems. This expanded use of cooperative catalysis represents a viable option in synthetic chemistry to form allylic amines from alcohols under low temperatures and low catalyst loads.

![Figure 2.3 Plausible mechanism for cooperative Ni/Ti amination of alcohols](image-url)
2.2 Results and discussion

Past work in our lab using palladium-titanium complexes had demonstrated the affinity titanium has to activate alcohols. There is also significant literature supporting titanium tetraiodosopropoxide (TiOiPr)₄, undergoing trans-alkoxylation with alcohols. Applying these principles to the hydroamination of allylic alcohols we envisioned a mechanism facilitated by the (TiOiPr)₄-mediated activation of the alcohol (Figure 2.3). This cooperative mechanism proceeds starting with the activation of the alcohol by (TiOiPr)₄ to create the titanium ether. The titanium-activated intermediate enables the rapid oxidative addition into the C-O bond to create the metal allyl. The metal allyl is then attacked on the least hindered carbon by the amine nucleophile to generate the product. Titanium oxide is produced as a byproduct. We hypothesized that

![Chemical structure of the reaction]

**Table 2.1 Optimization of cooperative catalysis system**

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<th>entry</th>
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<th>conv. (%)</th>
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<td>2</td>
<td>99 (96)</td>
</tr>
</tbody>
</table>

a) Reaction run with 1.6 mmol of alcohol, 2.4 mmol of amine (1.5 equiv) in solvent (4 M). b) Conversion measured by 1H NMR analysis of the crude reaction. c) With 10% of Ti(O-i-Pr)₄. d) With 50% of Ti(O-i-Pr)₄. e) With 100% of Ti(O-i-Pr)₄
activation of the allylic alcohol as a titanium alkoxide would allow for lower temperature reactions with lower catalyst loadings.

To optimize this reaction, we used morpholine and cinnamyl alcohol as test substrates, which are commonly used in allylic amination reactions (Table 2.1). In the presence of Ni(cod)2 and bis(diphenylphosphino)-ferrocene (dppf) low yields were obtained (Table 2.1, entry 1). Upon adding a catalytic amount of titanium isopropoxide (30%), the yield and reaction rate were significantly increased (entry 2). Importantly, the reaction proceeds to full conversion in the presence of titanium in just 12 hours at room temperature. Further optimization revealed that lower amounts of titanium gave slower reaction times (entry 4) and increased amounts of Ti(O-i-Pr)4 could reduce the reaction time, even down to two hours with 100 mol% Ti(O-i-Pr)4 (entries 18 and 19). No conversion was obtained without the nickel catalyst (entry 3). Other common

Figure 2.4 Amination of primary and secondary alcohol substrates. (a) Reaction run with 2 mol% of Ni and 0.5 eq of Ti(O-iPr)4. (b) Reaction run with 5 mol% of Ni and 1 eq of Ti(O-iPr)4
Lewis acidic additives such as tetrabutylammonium acetate (TBAA), TiCl₄, BF₃, or AlCl₃, all gave reduced yields (entries 5-8). The use of other phosphine ligands gave moderate to high conversions however all were lower than dppf (entries 9-13). Acetonitrile is important to obtain good conversion, other solvents gave substantially reduced yields (entries 14-17).

To further analyze the role of titanium in the mechanism of this reaction, titanium tetraisopropoxide was added to cinnamyl alcohol in the presence of morpholine. Shifts in the ¹H NMR spectra indicate that the alcohol is coordinated to the Lewis acidic titanium (experimental section). When adding the titanium tetraisopropoxide to the nickel dppf catalyst no shifts occur in the NMR spectra, indicating that the prominent role of the titanium is that of activating the alcohol and not as a ligand/activator of the nickel catalyst.

After optimizing reaction conditions, we investigated the tolerance of our reaction and catalyst for different allylic alcohol substrates (Figure 2.4). Electron withdrawing or donating groups on the aryl portion of the cinnamyl alcohol had little effect on the yield of the reaction (2d–2h). The reaction tolerated a variety of mono and unsubstituted allyl alcohols giving high yields (2a-2c, 2i). Secondary alcohols also gave good to excellent yields including sp³ and sp²

![Chemical structure](image)

**Figure 2.5** Substrate scope for amine nucleophiles. (a) Reaction run with 2 mol% of Ni and 1 eq of Ti(O-iPr)₄. (b) Reaction run with 0.5 mol% of Ni and 1 eq of Ti(O-iPr)₄
carbons alpha to the alcohol (2i-2m). This reaction also tolerated alcohols containing a thiophene ring in high yield. Lower yields were observed for trisubstituted alkenes and Bailis-Hillman adduct (2o, 2p). It should be noted that in most cases a catalytic amount of Ti(O-iPr)4 (30%) was used with the majority of the substrates. However, substrates 2i, 2k, 2m, 2n, and 2p required stochiometric amounts of titanium to achieve full reaction conversion.

We next investigated the scope of the amine nucleophile in the reaction (Figure 2.5). Secondary amines including dialkylamines (3a, 3b, 3d, 3e, 3f), nitrogen heterocycles (3g-3i) and diaryl amines (3c) gave good to excellent yields. Slightly lower yields were obtained for primary amines (3j-3k). Secondary alcohols (3l, 3m) gave improved yields to primary amines suggesting that over alkylation of the amine may be the cause of low yields. Very hindered secondary amines nucleophiles also gave reduced yield (3n).

One of the unique attributes of this cooperative reaction is the ability to perform a tandem reaction.

Figure 2.6 Plausible mechanism for cooperative Ni/Ti tandem cyclization amination of alcohols
cyclization amination reaction. This process allows for the concerted creation of complex structures. In the presence of a diene, the nickel catalyst promptly inserts into the diene after oxidative insertion to form the kinetically favored five-member intermediate (Figure 2.6). The second nickel allyl intermediate can then undergo attack by the amine nucleophile to give the final product. To determine if this tandem cyclization process was unique to our catalytic system, the conditions developed by Mashima\(^\text{11}\) were also explored. When tetrabutylammonium acetate was used as an additive, amination was detected but no cyclized product was observed. Our catalyst creates the cyclized product as the major product in good yield while forming two stereocenters with good diastereoselectivity.

This new tandem reaction gives moderate to excellent yield for a variety of amine nucleophiles (Figure 2.7). Aryl amines (4a, 4b) and benzylic amines (4c) gave good yields. Simple heterocyclic amines also gave moderate to good yields. More complex heterocycles (4f, 4g) with multiple heteroatoms gave moderate to high yields. The diastereoselectivity of these reactions varied but was generally high (from 3.5:1 to 8.8:1). This reaction could be valuable in the synthesis of complex alkaloids because it demonstrates the ability to place a diverse group of functional groups in a single step.
reactive functional groups in a dense arrangement. In conclusion, this work shows the cooperative catalysis of titanium and nickel for the amination of allylic alcohols. The use of titanium greatly enhances the reaction rate and yield of the reaction. The reaction tolerates a variety of amines and allylic alcohols. Importantly, this catalytic system also shows unique chemistry not seen with other cooperative amination catalysts. The tandem cyclization/amination generates a highly functionalized product with good diastereoselectivity and in good yield.

2.3 Supporting Information

2.3.1 General Information

All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring, unless otherwise indicated. Solvents were dried by J. C. Meyer’s Solvent Purification System. The substrates were prepared by literature procedures or as described below. All other reagents were used as obtained unless otherwise noted. Flash Chromatography was performed with EM Science silica gel (0.040-0.063µm grade). Analytical thin-layer chromatography was performed with 0.25 mm coated commercial silica gel plates (E. Merck, DC-Plastikfolien, kieselgel 60 F254). Proton nuclear magnetic resonance (1H-NMR) data were acquired on a Mercury 400 (400 MHz) or on a Varian Unity Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in delta (δ) units, in parts per million (ppm) downfield from tetramethylsilane or from DMSO (2.54 ppm). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; p, pentet, m, multiplet, br, broad. Carbon-13 nuclear magnetic resonance (13C-NMR) data were acquired at 100 MHz on a Mercury 400 or at 125 MHz on a Varian Unity Inova 500 spectrometer. Chemical shifts are reported in ppm relative to the center line of a triplet at 77.23 ppm for chloroform-\(d\) or from the center line of DMSO-\(d_4\) 40.45 ppm. Infrared (IR) data were recorded as films on sodium chloride plates on a Thermo Scientific
Nicolet IR100 FT-IR spectrometer. Absorbance frequencies are reported in reciprocal centimeters (cm⁻¹). Chiral HPLC analyses were performed on a Thermo Separation Products Spectra Series P-100 or 200 and UV100 (254 nm) using Chiralcel® columns (OD-H, OB-H, OJ, AD, AS, OC, IA, IB or IC) eluting with heptane / iso-propanol mixtures indicated. Optical rotations were measured on a Jasco P-2000 digital polarimeter using 5 cm cells and the sodium D line (589 nm) at ambient temperature in the solvent and concentration indicated. Gas Chromatograms were obtained on a Hewitt Packard 6890 series GC system.

Synthesis of the substrates

Substrates 2i-2k were synthesized according to previously reported procedures.

diethyl 2-((E)-4-hydroxybut-2-en-1-y1)-2-((E)-penta-2,4-dien-1-y1)malonate (4):

To a solution of diethyl (E)-2-(penta-2,4-dien-1-y1)malonate⁶b (L₁, 550 mgr, 2.43 mmol, 1eq) in THF was added sodium hydride (60% dispersion in mineral oil, 146 mgr, 3.64 mmol, 1.5 eq) at 0°C and stirred at room temperature for 30 minutes. A solution of (E)- tert-butyl((4-chlorobut-2-en-1-yl)oxy)dimethylsilane⁶c (L₂, 642 mgr, 2.91 mmol, 1.2 eq) in DMSO(2ml) was added and the mixture stirred overnight. The reaction mixture diluted with ethyl acetate and washed with NAHCO₃(aq), dried over magnesium sulfate, and concentrated in vacuum. Purification on column using EtOAc/Hex(1% to 2.5%) gave the product as a yellowish liquid(900 mgr, 76%). H NMR (500 MHz, CDCl₃) δ 6.19-6.35 (m, 1H), 6.02-6.13 (m, 1H), 5.41-5.68 (m, 3H), 5.08 (d, J=16.91 Hz, 1H), 5.0 (d, J= 10.55 Hz,1H), 4.17 (q, J=14.23 Hz, 4H), 4.10 (d, J=4.66 Hz, 2H),2.63 (t, J= 7.82 Hz, 4H), 1.23 (t, J=7.12 Hz, 6H), 0.9 (s, 9H), 0.055 (s, 6H) ; 13C NMR  (75 MHz, CDCl₃) δ 170.79, 136.68, 135.01, 134.08, 128.03, 123.90, 116.27, 63.55, 61.32, 57.66, 35.75, 35.48, 25.95, 14.18, -5.09; IR (film) νmax 2929, 2856, 1736, 1462, 1256, 1133; HRMS(EI) calcd. for C₃₀H₂₉N₃P, [M+H]+, 463.2172; found, 463.2175.

To a solution of the product (1 gr, 2.5 mmol, 1eq) in THF was added tetra butyl ammoniumfluoride (1M in THF, 6 ml, 6mmol, 2eq) at 0°C. The reaction mixture warmed up and stirred at room temperature overnight. The mixture was diluted with EtOAc and washed with water. Organics were dried on sodium sulfate, concentrated, and purified on column chromatography using Hex/EtOAc(0 to25%) gave the product as a colorless liquid( 600 mgr, 82%). H NMR (500 MHz, CDCl₃) δ 6.22-6.32 (m, 1H), 6.05-6.13 (m, 1H), 5.68-5.77 (m, 1H), 5.47-5.59 (m, 2H), 5.12 (d, J= 17.34 Hz,1H), 5.01 (d, J=10.42 Hz, 1H), 4.18(q, J=14.31 Hz, 4H), 4.08 (t, J=5.39 Hz, 2H),2.64 (dd, J= 7.96,11.23 Hz, 4H), 1.24 (t, J=7.18 Hz, 6H); 13C NMR (75
MHz, CDCl3) δ 170.68, 136.60, 135.06, 133.80, 127.86, 126.06, 116.45, 63.35, 61.35, 57.61, 35.80, 35.40, 14.19; IR (film)νmax 3465, 2980, 1732, 1456, 1202; HRMS(EI) calcd. for C30H29N3P, [M+H]+, 463.2172; found, 463.2175.

2.3.2 General Procedure for Nickel Catalyzed Cross Coupling of Allylic Alcohols with Amines

Inside a glove box and in a 3 ml dram vial were placed Ni (COD)2 (2.2 mg, 0.008 mmol, 0.005 eq) and dppf (9 mg, 0.016 mmol, 0.01 eq) in acetonitrile (300 µl). The mixture stirred for 5 minutes, and after addition of the allylic alcohol (1.6 mmol, 1 eq), the amine (2.4 mmol, 1.5 eq), and Ti(O-iPr)4 (0.1 mL, 0.3 eq, 4.879 M solution in toluene), the vial was sealed, and the reaction mixture stirred for 12 hours. All the volatiles were removed on the rotovap, and the crude mixture was purified on column using EtOAc and Hexane as eluent.

Optimization Studies:

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<th>Entry</th>
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<td>MeCN</td>
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N,N-dibenzyl prop-2-en-1-amine (2a): prepared following the general procedure using Ni(COD)$_2$(2.2 mgr, 0.008 mml, 0.005eq), dppf( 9 mgr, 0.016 mmol, 0.01eq), allyl alcohol (93 mgr, 1.6 mmol, 1 eq), dibenzyl amine( 473 mgr, 2.4 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.1 ml, 0.3 eq, 4.879 M solution in toluene) in acetonitrile (300 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (368mg, 97%). Spectral data is in accordance with the reported values$^{17}$.

(E)-N,N-dibenzylbut-2-en-1-amine (2b): prepared following the general procedure using Ni(COD)$_2$(2.2 mgr, 0.008 mml, 0.005eq), dppf( 9 mgr, 0.016 mmol, 0.01eq), E-2-butene-1-ol(115 mgr, 1.6 mmol, 1 eq), dibenzyl amine( 473 mgr, 2.4 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.1 ml, 0.3 eq, 4.879 M solution in toluene) in acetonitrile (300 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (369mg, 92%). Spectral data is in accordance with the reported values$^{17}$.

N,N-dibenzyl 2-methyl prop-2-en-1-amine (2c): prepared following the general procedure using Ni(COD)$_2$(2.2 mgr, 0.008 mml, 0.005eq), dppf( 9 mgr, 0.016 mmol, 0.01eq), 2-methyl-2-propene-1-ol(115 mgr, 1.6 mmol, 1 eq), dibenzyl amine( 473 mgr, 2.4 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.1 ml, 0.3 eq, 4.879 M solution in toluene) in acetonitrile (300 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (361mg, 90%). Spectral data is in accordance with the reported values$^{12}$. 
4-cinnamylmorpholine (2d): prepared following the general procedure using Ni(COD)\(_2\)(2.2 mgr, 0.008 mmol, 0.005eq), dppf( 9 mgr, 0.016 mmol, 0.01eq), cinnamyl alcohol (214 mgr, 1.6 mmol, 1 eq), morpholine( 236 mgr, 2.4 mmol, 1.5 eq), and Ti(O-ipr)\(_4\)(0.1 ml, 0.3 eq, 4.879 M solution in toluene) in acetonitrile (300 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (277mg, 86%). Spectral data is in accordance with the reported values\(^{12}\).

\[\text{---Diagram---}\]

(E)-4-(3-(4-methoxyphenyl)allyl)morpholine (2e): prepared following the general procedure using Ni(COD)\(_2\)(1.1 mgr, 0.004 mmol, 0.005eq), dppf( 9 mgr, 0.008 mmol, 0.01eq), (E)-3-(4-methoxyphenyl)prop-2-en-1-ol (132mgr, 0.8mmol, 1 eq), morpholine( 140 mgr, 1.2 mmol, 1.5 eq), and Ti(O-ipr)\(_4\)(0.05 ml, 0.3 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (90.5mg, 97%). Spectral data is in accordance with the reported values\(^{12}\).

\[\text{---Diagram---}\]

(E)-4-(3-(p-tolyl)allyl)morpholine (2f): prepared following the general procedure using Ni(COD)\(_2\)(1.1 mgr, 0.008 mmol, 0.005eq), dppf( 9 mgr, 0.008 mmol, 0.01eq), (E)-3-(p-tolyl)prop-2-en-1-ol ( 120 mgr, 0.8mmol, 1 eq), morpholine( 140mgr, 1.2 mmol, 1.5 eq), and Ti(O-ipr)\(_4\)(0.05 ml, 0.3 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (85mg, 98%). Spectral data is in accordance with the reported values\(^{18}\).

\[\text{---Diagram---}\]

(E)-4-(3-(4-chlorophenyl)allyl)morpholine (2g): prepared following the general procedure using Ni(COD)\(_2\)(2.2 mgr, 0.008 mmol, 0.02eq), dppf( 9 mgr, 0.016 mmol, 0.04eq), (E)-3-(4-chlorophenyl)prop-2-en-1-ol ( 68 mgr, 0.4mmol, 1 eq), morpholine( 70 mgr, 0.6 mmol,
1.5 eq), and Ti(O-ipr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (79mg, 83%). H NMR (500 MHz, CDCl$_3$) δ 7.22-7.36 (m, 4H), 6.48 (d, J=16.33 Hz, 1H), 6.16-6.28 (m, 1H), 3.73 (t, J=4.62 Hz, 4H), 3.13 (dd, J=1.38, 6.74 Hz, 2H), 2.49 (t, J=4.64 Hz,4H); 13C NMR (75 MHz, CDCl$_3$) δ 132.05, 128.74, 127.52, 126.92, 67.00, 61.35, 53.73; IR (film)νmax 2856, 2464, 1492, 1452, 1119; HRMS(EI) calcd. for C$_{13}$H$_{16}$ClNO, [M+H]$^+$, 239.0891; found, 239.0897.

(E)-4-(3-(4-(trifluoromethyl)phenyl)allyl)morpholine(2h): prepared following the general procedure using Ni(COD)$_2$(2.2 mgr, 0.008 mmol, 0.02eq), dppf( 9 mgr, 0.016 mmol, 0.04eq), (E)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-ol (80 mgr, 0.4mmol, 1 eq), morpholine(70 mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (101.5mg, 94%). H NMR (500 MHz, CDCl$_3$) δ 7.38- 7.63 (m, 4H), 6.57 (d, J=15.68 Hz, 1H), 6.27-6.45 (m, 1H), 3.73 (t, J=4.62 Hz, 4H), 3.13 (dd, J=1.38, 6.74 Hz, 2H), 2.49 (t, J=4.64 Hz,4H); 13C NMR (75 MHz, CDCl$_3$) δ 131.88, 129.11, 126.47, 125.57, 66.97, 61.25, 53.73; IR (film)νmax 2958, 2806, 1615, 1325, 1117; HRMS(EI) calcd. for C$_{14}$H$_{16}$F$_3$NO, [M+H]$^+$, 272.1218; found, 272.1212.

N-benzylcyclohex-2-en-1-amine (2i): prepared following the general procedure using Ni(COD)$_2$(5.5mgr, 0.02 mmol, 0.05eq), dppf(18mgr, 0.04 mmol, 0.1eq), cyclohex-2-en-1-ol (40 mgr, 0.4mmol, 1 eq), benzylamine (64 mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.08 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (101.5mg, 94%). Spectral data is in accordance with the reported values$^{19}$.
(E)-4-(4-phenylbut-3-en-2-yl)morpholine (2l): prepared following the general procedure using Ni(COD)$_2$(2.2 mg, 0.008 mmol, 0.02 eq), dppf (9 mg, 0.016 mmol, 0.04 eq), (E)-4-phenylbut-3-en-2-ol (60 mg, 0.4 mmol, 1 eq), morpholine (64 mg, 0.6 mmol, 1.5 eq), and Ti(O-iPr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (84.2 mg, 97%). Spectral data is in accordance with the reported values$^{20}$. 

(E)-4-(1,3-diphenylallyl)morpholine (2m): prepared following the general procedure using Ni(COD)$_2$(5.5 mg, 0.02 mmol, 0.05 eq), dppf (18 mg, 0.04 mmol, 0.1 eq), (E)-1,3-diphenylprop-2-en-1-ol (84 mg, 0.4 mmol, 1 eq), morpholine (64 mg, 0.6 mmol, 1.5 eq), and Ti(O-iPr)$_4$(0.08 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (91 mg, 82%). Spectral data is in accordance with the reported values$^{19}$. 

(E)-4-(3-(thiophen-2-yl)allyl)morpholine (2n): prepared following the general procedure using Ni(COD)$_2$(5.5 mg, 0.02 mmol, 0.05 eq), dppf (18 mg, 0.04 mmol, 0.1 eq), (E)-3-(thiophen-2-yl)prop-2-en-1-ol (56 mg, 0.4 mmol, 1 eq), morpholine (64 mg, 0.6 mmol, 1.5 eq), and Ti(O-iPr)$_4$(0.08 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (73 mg, 87%). Spectral data is in accordance with the reported values$^{21}$. 

![Chemical Structure](image-url)
4-(3,3-diphenylallyl)morpholine (2o): prepared following the general procedure using Ni(COD)₂(5.5 mg, 0.02 mmol, 0.05 eq), dppf(18 mg, 0.04 mmol, 0.1 eq), 3,3-diphenylprop-2-en-1-ol (84 mg, 0.4 mmol, 1 eq), morpholine (64 mg, 0.6 mmol, 1.5 eq), and Ti(O-ipr)₄ (0.08 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (33 mg, 30%). Spectral data is in accordance with the reported values²².

\[
\begin{align*}
\text{methyl (E)-2-(morpholinomethyl)-3-phenylacrylate (2p)}: & \text{ prepared following the general procedure using Ni(COD)₂(5.5 mg, 0.02 mmol, 0.05 eq), dppf(18 mg, 0.04 mmol, 0.1 eq), methyl 2-(hydroxy(phenyl)methyl)acrylate (77 mg, 0.4 mmol, 1 eq), morpholine (64 mg, 0.6 mmol, 1.5 eq), and Ti(O-ipr)₄ (0.08 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (23 mg, 30%). Spectral data is in accordance with the reported values}^{12}.
\end{align*}
\]

\[
\begin{align*}
\text{(E)-N,N-dibenzyl-3-phenylprop-2-en-1-amine (3a):} & \text{ prepared following the general procedure using Ni(COD)₂(2.2 mg, 0.008 mmol, 0.02 eq), dppf(9 mg, 0.016 mmol, 0.04 eq), cinnamyl alcohol (54 mg, 0.4 mmol, 1 eq), dibenzyl amine (118 mg, 0.6 mmol, 1.5 eq), and Ti(O-ipr)₄ (0.08 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (112.5 mg, 90%). Spectral data is in accordance with the reported values}^{23}.
\end{align*}
\]

\[
\begin{align*}
\text{N-cinnamyl-N-methylaniline (3b):} & \text{ prepared following the general procedure using Ni(COD)₂(2.2 mg, 0.008 mmol, 0.02 eq), dppf(9 mg, 0.016 mmol, 0.04 eq), cinnamyl alcohol (54 mg, 0.4 mmol, 1 eq), N-methyl aniline (64 mg, 0.6 mmol, 1.5 eq), and Ti(O-ipr)₄ (0.08 ml,}
\end{align*}
\]
N-cinnamyl-N-phenylaniline (3c): prepared following the general procedure using Ni(COD)$_2$(2.2 mgr, 0.008 mmol, 0.02eq), dppf( 9 mgr, 0.016 mmol, 0.04eq), cinnamyl alcohol (54 mgr, 0.4mmol, 1 eq), diphenyl amine (100mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.08 ml, 1eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (88.5mg, 99%). Spectral data is in accordance with the reported values$^{12}$.

\[
\text{Ph} \quad \text{Ph} \\
\text{N} \\
\text{Ph}
\]

(E)-N,N-diethyl-3-phenylprop-2-en-1-amine(3d): prepared following the general procedure using Ni(COD)$_2$(1.1 mgr, 0.008 mmol, 0.005eq), dppf( 9 mgr, 0.008 mmol, 0.01eq), cinnamyl alcohol (54 mgr, 0.4mmol, 1 eq), diethylamine (44mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (67mg, 89%). Spectral data is in accordance with the reported values$^{25}$.

\[
\text{Ph} \quad \text{N} \\
\text{Me} \quad \text{Me}
\]

(E)-N,N-diisopropyl-3-phenylprop-2-en-1-amine (3e): prepared following the general procedure using Ni(COD)$_2$(2.2 mgr, 0.008 mmol, 0.02eq), dppf( 9 mgr, 0.016 mmol, 0.04eq), cinnamyl alcohol (54 mgr, 0.4mmol, 1 eq), diisopropyl amine (60mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (67mgr, 77%). Spectral data is in accordance with the reported values$^{11}$.

\[
\text{Ph} \quad \text{N} \\
\text{Me} \quad \text{Bn}
\]
(E)-N-benzyl-N-methyl-3-phenylprop-2-en-1-amine (3f): prepared following the general procedure using Ni(COD)$_2$(2.2 mgr, 0.008 mmol, 0.02eq), dppf( 9 mgr, 0.016 mmol, 0.04eq), cinnamyl alcohol (54 mgr, 0.4mmol, 1 eq), N-methyl-1-phenylmethanamine (73mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (91mgr, 96%). Spectral data is in accordance with the reported values$^{26}$.

1-cinnamylpyrrolidine (3g): prepared following the general procedure using Ni(COD)$_2$(2.2 mgr, 0.008 mmol, 0.02eq), dppf( 9 mgr, 0.016 mmol, 0.04eq), cinnamyl alcohol (54 mgr, 0.4mmol, 1 eq), pyrrolidine (43mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (69.6mg, 93%). Spectral data is in accordance with the reported values$^{12}$.

1-cinnamylpiperidine (3h): prepared following the general procedure using Ni(COD)$_2$(2.2 mgr, 0.008 mmol, 0.02eq), dppf( 9 mgr, 0.016 mmol, 0.04eq), cinnamyl alcohol (54 mgr, 0.4mmol, 1 eq), piperidine (51mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (70.4mg, 88%). Spectral data is in accordance with the reported values$^{27}$.

1-cinnamyl-4-methylpiperazine (3i): prepared following the general procedure using Ni(COD)$_2$(2.2 mgr, 0.008 mmol, 0.02eq), dppf( 9 mgr, 0.016 mmol, 0.04eq), cinnamyl alcohol (54 mgr, 0.4mmol, 1 eq), N-methyl piperazine (60mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (82mg, 95%). Spectral data is in accordance with the reported values$^{28}$.
**N-cinnamylaniline (3j):** prepared following the general procedure using Ni(COD)$_2$(2.2 mgr, 0.008 mmol, 0.02eq), dppf( 9 mgr, 0.016 mmol, 0.04eq), cinnamyl alcohol (54 mgr, 0.4mmol, 1 eq), aniline (56mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (63mgr, 76%). Spectral data is in accordance with the reported values$^{29}$.

![N-cinnamylaniline (3j)](image1)

**[(E)-N-(4-phenylbut-3-en-2-yl)decan-1-amine (3k):** prepared following the general procedure using Ni(COD)$_2$(1.1 mgr, 0.008 mmol, 0.005eq), dppf( 9 mgr, 0.008 mmol, 0.01eq), cinnamyl alcohol (54 mgr, 0.4mmol, 1 eq), decylamine (94mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 20% Methanol/EtOAc as eluent (46mgr, 40%). H NMR (500 MHz, CDCl3) $\delta$ 7.38 (d, J=4.04 Hz, 2H), 7.31 (t, J=7.45 Hz, 2H), 7.20-7.25 (m, 1H), 6.52 (d, J= 7.45 Hz, 1H), 6.26-6.35 (m, 1H), 3.29 (d, J= 3.19, 2H), 2.51 (t, J= 7.55 Hz, 1H), 1.48-1.57 (m,1H), 1.19-1.33 (m, 8H), 0.85-0.95 (m, 2H); 13C NMR (75 MHz, CDCl3) $\delta$ 137.18, 134.62, 129.67, 128.52, 127.25, 136.25, 56.37, 47.74, 31.91, 30.36, 29.61, 29.58, 29.34, 27.46, 22.69, 22.12, 14.14; IR (film)$\nu$max 2924, 2359, 1733, 1456, 1273; HRMS(EI) calcd. for C$_{19}$H$_{31}$N, [M+H]$^+$, 274.2490; found, 274.2496.

![[(E)-N-(4-phenylbut-3-en-2-yl)decan-1-amine (3k)]](image2)

**[(E)-3-phenyl-N-(1-phenylethyl)prop-2-en-1-amine(3l):** prepared following the general procedure using Ni(COD)$_2$(1.1 mgr, 0.008 mmol, 0.005eq), dppf( 9 mgr, 0.008 mmol, 0.01eq), cinnamyl alcohol (54 mgr, 0.4mmol, 1 eq), 1-phenylethan-1-amine (73mgr, 0.6 mmol, 1.5 eq), and Ti(O-ipr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (91mgr, 96%). Spectral data is in accordance with the reported values$^{30}$.

![[(E)-3-phenyl-N-(1-phenylethyl)prop-2-en-1-amine(3l)]](image3)
(E)-N-(4-phenylbut-3-en-2-yl)decan-1-amine (3m): prepared following the general procedure using Ni(COD)$_2$(2.2 mg, 0.008 mmol, 0.02 eq), dpff(9 mg, 0.016 mmol, 0.04 eq), (E)-4-phenylbut-3-en-2-ol (60 mg, 0.4 mmol, 1 eq), decylamine (94 mg, 0.6 mmol, 1.5 eq), and Ti(O-iPr)$_4$(0.05 ml, 0.5 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using 20% Methanol/EtOAc as eluent (86 mg, 75%). H NMR (500 MHz, CDCl$_3$) δ 7.39 (d, J=3.7 Hz, 2H), 7.31 (t, J=7.64 Hz, 2H), 7.20-7.25 (m, 1H), 6.47 (d, J=7.96 Hz, 1H), 6.09 (q, J=7.89 Hz, 1H), 3.36 (quin, J=6.68, 1H), 2.61-2.68 (m, 1H), 2.53-2.60 (m, 1H), 1.45-1.55 (m, 2H), 1.23-1.34 (m, 18H), 0.89 (t, J=6.68 Hz, 3H); 13C NMR (75 MHz, CDCl$_3$) δ 137.18, 134.62, 129.67, 128.52, 127.25, 136.25, 56.37, 47.74, 31.91, 30.36, 29.61, 29.58, 29.34, 27.46, 22.69, 22.12, 14.14; IR (film) v max 2924, 2359, 1465, 1136, 964; HRMS(EI) calcd. for C$_{20}$H$_{33}$N, [M+H]$^+$, 288.2647; found, 288.2641.

1-cinnamyl-2,2,6,6-tetramethylpiperidine (3n): prepared following the general procedure using Ni(COD)$_2$(5.5 mg, 0.02 mmol, 0.05 eq), dpff(18 mg, 0.04 mmol, 0.1 eq), cinnamyl alcohol (54 mg, 0.4 mmol, 1 eq), 2,2,6,6-tetramethylpiperidine (85 mg, 0.6 mmol, 1.5 eq), and Ti(O-iPr)$_4$(0.08 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (100 µl). Product was purified on column using pure hexane to 50% EtOAc/Hex as eluent (31 mg, 30%). Spectral data is in accordance with the reported values.$^{30}$

diethyl(E)-3-(3-(dibenzylamino)prop-1-en-1-yl)-4-vinylcyclopentane-1,1 dicarboxylate(4a): prepared following the general procedure using Ni(COD)$_2$(1.5 mg, 0.005 mmol, 0.05 eq), dpff(5.5 mg, 0.01 mmol, 0.1 eq), diethyl 2-((E)-4-hydroxybut-2-en-1-yl)-2-((E)-penta-2,4-dien-1-yl)malonate (30 mg, 0.1 mmol, 1 eq), dibenzylamine (24 mg, 0.12 mmol, 1.2 eq), and Ti(O-iPr)$_4$(0.03 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (50 µl). The
product was obtained as an unseparable mixture of two diastereomers (4.7:1) after purification on column using pure hexane to 70% EtOAc/Hex as eluent (37mg, 78%). H NMR (500 MHz, CDCl3) δ 7.21-7.39 (m, 10H) 5.62-5.78 (m, 1H), 5.48-5.58 (m, 2H), 4.94-5.03 (m, 2H), 4.16-4.24 (m, 4H), 3.56 (s, 4H), 3.01 (2H), 2.74-2.84 (m, 2H), 2.44-2.58 (m, 2H), 2.14-2.26 (m, 2H), 1.20-1.31 (m, 6H); 13C NMR (300 MHz, CDCl3) δ 172.74, 139.81, 138.67, 133.47, 128.84, 128.29, 128.19, 126.79, 115.24, 61.58, 61.52, 59.14, 57.63, 55.29, 50.10, 48.77, 47.31, 46.13, 39.19, 38.71, 14.09; IR (film) vmax 2979, 2793, 1729, 1254, 1104; HRMS(EI) calcd. for C30H37NO4, 476.2756; found, [M+H]+, 476.2753.

\[
\begin{align*}
\text{diethyl(E)-3-(3-(benzyl(methyl)amino)prop-1-en-1-yl)-4-vinylcyclopentane-1,1 dicarboxylate(4b): prepared following the general procedure using Ni(COD)\textsubscript{2}(1.5 mg, 0.005 mmol, 0.05eq), dppf (5.5 mg, 0.01 mmol, 0.1eq), diethyl 2-((E)-4-hydroxybut-2-en-1-yl)-2-((E)-penta-2,4-dien-1-yl)malonate (30 mg, 0.1mmol, 1 eq), N-methyl-1-phenylmethanamine (15mg, 0.12 mmol, 1.2 eq), and Ti(O-ipr)\textsubscript{4}(0.03 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (50 µl). The product was obtained as an unseparable mixture of two diastereomers (8.8:1) after purification on column using pure hexane to 70% EtOAc/Hex as eluent (35mg, 88%). H NMR (500 MHz, CDCl3) δ 5.63-5.78 (m,1H), 5.45-5.55 (m, 2H), 4.94-5.00 (m, 2H), 4.19 (dq, J=7.15, 7.03 Hz, 4H), 3.46 (d, J=2.85 Hz,2H), 2.94-2.97 (m,2H), 2.72-2.84 (m,2H), 2.47 (dd, J=13.89,13.89 2H), 2.16-2.24 (m,2H), 2.15 (s,3H), 1.20-1.28 (m,6H); 13C NMR (75 MHz, CDCl3) δ 172.69, 172.38, 139.06, 138.59, 133.69, 129.13, 128.19, 126.92, 115.21, 61.54, 61.47, 59.46, 59.14, 47.27, 46.06, 42.01, 39.17, 38.71, 29.72, 14.05; IR (film) vmax 2925, 2359, 1730, 1453, 1254; HRMS(EI) calcd. for C24H33NO4, [M+H]+, 400.2443; found, 400.2447
\end{align*}
\]
**diethyl(E)-3-(3-((1-phenylethyl)amino)prop-1-en-1-yl)-4-vinylcyclopentane-1,1 dicarboxylate (4c):** prepared following the general procedure using Ni(COD)$_2$(1.5 mgr, 0.005 mmol, 0.05eq), dppf( 5.5 mgr, 0.01 mmol, 0.1eq), diethyl 2-((E)-4-hydroxybut-2-en-1-yl)-2-((E)-penta-2,4-dien-1-yl)malonate (30 mgr, 0.1mmol, 1 eq), 1-phenylethan-1-amine (15mgr, 0.12 mmol, 1.2 eq), and Ti(O-itr)$_4$(0.03 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (50 µl). The product was obtained as an unseparable mixture of two diastereomers (3.5:1) after purification on column using pure hexane to 70% EtOAc/Hex as eluent (36.3mgr, 91%). H NMR (500 MHz, CDCl$_3$) δ 7.20-7.36 (m, 5H), 5.59-5.75 (m,1H), 5.29-5.55 (m, 2H), 4.92-5.08 (m, 2H), 4.12-4.23 (m, 4H), 3.78 (q, J=6.24 Hz,1H), 2.97-3.09 (m,2H), 2.70-2.79 (m,2H), 2.37-2.56 (m,2H), 2.10-2.23(m, 2H), 1.34 (d, J=6.44 3H), 1.24 (q, J=6.85 6H); 13C NMR (75 MHz, CDCl$_3$) δ 172.68, 172.36, 145.47, 138.56, 138.51, 132.07, 129.47, 129.44, 128.41, 126.88, 126.66, 126.64, 115.33, 61.46, 59.07, 57.23, 49.80, 49.32, 48.39, 47.21, 45.89, 40.25, 39.95, 39.11, 39.04, 38.72, 24.16, 21.79, 21.48, 14.03; IR (film)$\nu_{max}$ 2924, 1728, 1254, 1178; HRMS(EI) calcd. for C$_{24}$H$_{33}$NO$_4$, [M+H]$^+$, 400.2443; found, 400.2448.

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**diethyl(E)-3-(3-(piperidin-1-yl)prop-1-en-1-yl)-4-vinylcyclopentane-1,1 dicarboxylate(4d):** prepared following the general procedure using Ni(COD)$_2$(1.5 mgr, 0.005 mmol, 0.05eq), dppf( 5.5 mgr, 0.01 mmol, 0.1eq), diethyl 2-((E)-4-hydroxybut-2-en-1-yl)-2-((E)-penta-2,4-dien-1-yl)malonate (30 mgr, 0.1mmol, 1 eq), piperidine (11mgr, 0.12 mmol, 1.2 eq), and Ti(O-itr)$_4$(0.03 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (50 µl). The product was obtained as an unseparable mixture of two diastereomers (6:1) after purification on column using pure hexane to 70% EtOAc/Hex as eluent (29mgr, 88%). H NMR (500 MHz, CDCl$_3$) δ 5.65-5.76 (m, 1H), 5.43-5.54 (m, 2H), 4.93-5.03 (m, 2H), 4.19 (q, J=8.02  4H), 2.89-2.93 (m, 2H), 2.71-2.83 (m,2H), 2.46 (q, J= 7.14 Hz, 2H), 2.27-2.40(s, 4H), 2.13-2.24(m, 2H), 1.58 (t, J=5.28, 4H), 1.42 (s, 2H), 1.24 (m, 6H); 13C NMR (75 MHz, CDCl$_3$) δ 172.66, 172.35, 138.57, 133.84, 127.60, 115.11, 114.39, 67.52, 61.51, 59.10, 54.30, 47.74, 47.20, 45.96 48.39, 47.21, 45.89, 39.04, 38.72,
24.21, 21.48, 14.03; IR (film)\(\nu_{\text{max}}\) 2933, 2795, 1730, 1443, 1254; HRMS(EI) calcd. for C\(_{21}\)H\(_{33}\)NO\(_4\), [M+H]\(^+\), 364.2443; found, 364.2449.

diethyl(E)-3-(3-pyrrolidin-1-yl)prop-1-en-1-yl)-4-vinylcyclopentane-1,1-dicarboxylate (4e): prepared following the general procedure using Ni(COD)\(_2\) (1.5 mgr, 0.005 mmol, 0.05eq), dppf (5.5 mgr, 0.01 mmol, 0.1eq), diethyl 2-((E)-4-hydroxybut-2-en-1-yl)-2-((E)-penta-2,4-dien-1-yl)malonate (30 mgr, 0.1 mmol, 1 eq), pyrrolidine (11 mgr, 0.12 mmol, 1.2 eq), and Ti(O-ipr)\(_4\) (0.03 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (50 µl). The product was obtained as an unseparable mixture of two diastereomers (4.8:1) after purification on column using pure hexane to 70% EtOAc/Hex as eluent (21 mgr, 60%). H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 5.63-5.76 (m, 1H), 5.47-5.60 (m, 2H), 4.94-5.07 (m, 2H), 4.19 (q, \(J=\) 7.19 Hz, 4H), 3.06-3.15 (m, 2H), 2.71-2.82 (m, 2H), 2.44 (s, 4H), 2.47 (q, \(J=\) 7.10 Hz, 2H), 2.14-2.24 (m, 2H), 1.78-1.83 (m, 4H), 1.21-1.28 (m, 6H); 13C NMR (300 MHz, CDCl\(_3\)) \(\delta\) 172.38, 138.47, 115.24, 61.55, 59.08, 57.98, 53.72, 47.21, 45.95, 39.07, 38.66, 23.40, 14.03; IR (film)\(\nu_{\text{max}}\) 2925, 2359, 1729, 1255, 1178; HRMS(EI) calcd. for C\(_{20}\)H\(_{31}\)NO\(_4\), 350.2287; found, [M+H]\(^+\), 350.2281.

diethyl (E)-3-(3-morpholinoprop-1-en-1-yl)-4-vinylcyclopentane-1,1-dicarboxylate (4f): prepared following the general procedure using Ni(COD)\(_2\) (3 mgr, 0.01 mmol, 0.05eq), dppf (11
diethyl 2-((E)-4-hydroxybut-2-en-1-yl)-2-((E)-penta-2,4-dien-1-yl)malonate (60 mgr, 0.2 mmol, 1 eq), morpholine (30 mgr, 0.3 mmol, 1.5 eq), and Ti(O-iPr)4 (0.05 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (50 µl). The product was obtained as an unseparable mixture of two diastereomers (4:1) after purification on column using pure hexane to 70% EtOAc/Hex as eluent (33 mgr, 46%). H NMR (500 MHz, CDCl3) δ 5.60-5.74 (m, 1H), 5.40-5.55 (m, 2H), 4.93-5.08 (m, 2H), 4.19 (q, J=7.13 Hz, 4H), 3.70 (t, J= 4.64 Hz, 4H), 2.88-3.02 (m, 2H), 2.71-2.83 (m, 2H), 2.43-2.50 (m, 2H), 2.33-2.54 (m, 6H), 2.11-2.24 (m, 2H), 1.19-1.29 (m, 6H); 13C NMR (75 MHz, CDCl3) δ 172.61, 172.32, 139.33, 138.48, 134.57, 126.77, 115.46, 115.24, 66.96, 61.55, 59.07, 53.66, 53.48, 49.92, 48.51, 47.21, 45.96, 40.21, 39.94, 39.05, 38.66, 29.69, 14.03; IR (film) νmax 2926, 2806, 1729, 1453, 1257, 1118;

HRMS(EI) calcd. for C20H31NO5, [M+H]+, 366.2236; found, 366.2231.

Product (4f) was isolated as the byproduct of the reaction as a brown liquid (30 mgr, 40%) using Methanol/Ethylacetate as eluent. (20%). H NMR (500 MHz, CDCl3) δ 5.52-5.65 (m, 1H), 5.41-5.52 (m, 2H), 5.29-5.41 (m, 2H), 4.16 (q, J= 7.18 Hz, 4H), 3.70 (s, 8H), 2.93 (d, J=6.33 2H), 2.75-2.85 (m, 2H) 2.53-2.65 (m, 4H), 2.30-2.52 (m, 8H), 1.20-1.30 (m, 6H), 1.12 (d, J=6.47 4H); 13C NMR (75 MHz, CDCl3) δ 170.71, 170.66, 136.94, 130.97, 127.90, 125.45, 67.14, 66.94, 62.67, 61.25, 61.05, 57.58, 53.51, 50.55, 35.36, 17.93, 14.14; IR (film) νmax 2958, 2807, 1731, 1453, 1265, 1200,;

HRMS(EI) calcd. for C30H29N3P, [M+H]+, 463.2172; found, 463.2175.

diethyl(E)-3-(3-(4-methylpiperazin-1-yl)prop-1-en-1-yl)-4-vinylcyclopentane-1,1 dicarboxylate (4g): prepared following the general procedure using Ni(COD)2 (1.5 mgr, 0.005 mmol, 0.05 eq), dppf (5.5 mgr, 0.01 mmol, 0.1 eq), diethyl 2-((E)-4-hydroxybut-2-en-1-yl)-2-((E)-penta-2,4-dien-1-yl)malonate (30 mgr, 0.1 mmol, 1 eq), N-methylpiperazine (15 mgr, 0.12 mmol, 1.2 eq), and Ti(O-iPr)4 (0.03 ml, 1 eq, 4.879 M solution in toluene) in acetonitrile (50 µl). The product was obtained as an unseparable mixture of two diastereomers (5.8:1) after purification
on column using 10% MeOH/EtOAC as eluent (36.5mgr, 96%). H NMR (500 MHz, CDCl3) δ
5.60-5.78 (m, 1H), 5.46-5.55 (m, 2H), 4.90-5.06 (m, 2H), 4.19 (q, J= 7.10 Hz, 4H), 2.91-2.98
(m,2H), 2.71-2.85 (m, 2H), 2.37-2.59 (m, 10H), 2.29 (s, 3H), 2.15-2.24 (m, 2H), 1.19-1.30 (m,
6H); 13C NMR (300 MHz, CDCl3) δ 172.37, 138.55, 134.25, 127.25, 115.24, 61.57, 61.51,
60.07, 59.12, 55.11, 53.18, 52.93, 47.24, 46.05, 39.09, 38.71, 14.07 ; IR (film)νmax 2934, 2794,
2359, 1730, 1456, 1256, 1178; HRMS(EI) calcd. for C21H34N2O4, 379.2553; found, [M+H]+,
379.2557.

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Chapter 3  Boron Templated Dimerization of Allylic Alcohols to Form Protected 1,3-Diols via Acid Catalysis

Contributions: (Co-First author) in this project include the reaction discovery, reaction optimization, substrate scope, reaction derivatization

3.1 Introduction

Templated organic transformations represent an important class of reactions that contribute significantly to organic synthesis by enabling highly efficient and selective bond-forming processes. Many different types of catalysts rely on preorganizing substrates into certain conformations and in close proximity to attain selectivity for the desired products in good yield. Enzymes, metal catalysts, porous coordination frameworks such as metal organic frameworks (MOF), and substrates containing removable covalent tethers represent some of the approaches used to achieve substrate preorganization and proximity-induced reactivity.

Recently, Lewis acids have been used to bring substrates into close proximity and selectively control product formation. Ward et al. used a bimetallic zinc and magnesium ligand to bring a diene and dienophile into close proximity for a Diels-Alder reaction (Figure 3.1). Ward's work has been used by K. C. Nicolaou and a variety of other groups in the pursuit of natural product syntheses via this type of templated Diels-Alder reaction. The use of these Lewis acids has resulted in greater selectivity and increased yields for reactions in natural product synthesis. Other Lewis acids such as silicon and boron have been used to create tethers that can selectively form macrocycles or perform dimerization/ trimerizations with a high degree of selectivity.

![Figure 3.1](image-url) Word's work using MgBr and Zinc to bring Diels Alder substrates into close proximity
a) Morgans work on boron tethered Diels-Alder reactions

\[
\begin{align*}
\text{O-BO-} & \quad 1. \text{Quinine} \\
& \quad 2. \text{H}_2\text{O}_2, \text{NaOH}
\end{align*}
\]

b) Smils work on boron tethered radical cyclizations

\[
\begin{align*}
\text{R}_1 \text{B(OH)}_2 & \quad \text{esterification} \\
& \quad \text{exo-trig radical cyclization}
\end{align*}
\]

c) Suginomes work with Ni-Pd and Boron/zirconium lewis acids in carboboration reactions

\[
\begin{align*}
\text{NiPr}_2 & \quad \text{Ni(cod)}_2 \\
\text{Cl} & \quad \text{PPh}_3 \\
\text{Bu} & \quad \text{Toluene, 110 °C, 2h}
\end{align*}
\]

d) Itohs work using boron tethers for the trimerization of alkynes

\[
\begin{align*}
\text{R}' & \quad \text{R} \\
\text{OH} & \quad \text{Cp*RuCl(cod)} \\
\text{R} & \quad \text{PdPCy}_3 \\
\text{ArI} & \quad \text{Toluene, K}_2\text{CO}_3 \\
& \quad 70 °C
\end{align*}
\]

**Figure 3.2** Past work using boron tethers

Boron Lewis acids are also of particular interest because of their ability to dynamically form boron-esters that can be used to activate allylic and benzylic alcohols. Boron has been used to template a variety of reactions (Figure 3.2). Similar to the work by Ward, the Morgan group used a boron-tethered substrate for an enantioselective Diels-Alder reaction (Figure 3.2a). Boron tethers have also been used in radical cyclization reactions. Smils used boron to from boronic esters by coordinating the alkene and halo alcohol partners for an exo-trig radical cyclization
Carboborations of alkenes and alkynes\textsuperscript{13} also benefit from the coordination of boron. For example, Suginomes used two Lewis acids, boron and zirconium, to activate and coordinate their substrates to a nickel-palladium catalyst (Figure 3.2c). Another example worth highlighting is the cyclotrimerizations\textsuperscript{9} of alkynes. Itoh’s work uses boron tethers to bring alkynes together for the ruthenium catalyzed cyclization/trimerization of alkynes (Figure 3.2d). Many of these reactions do not happen without coordination with a boron Lewis acid or yields are significantly diminished in the absence of the tether. In addition to enhancing selectivity and increasing yields, boron tethers are also of particular interest because they are easily removed under basic conditions. Boron carbon bonds are also functionalizable and can be oxidized to new C-O bonds.

This chapter will focus on our recent development of a boron templated selective dimerization of allylic alcohols that relies on the formation of boronic esters in situ under our reaction conditions (Figure 3.3). Herein, we describe the discovery, optimization, reaction substrate scope, mechanism, and derivatization of products for this reaction. It is worth noting that this transformation could be employed to access a core structure in (+)-Wutaianin\textsuperscript{14} and other polyol natural products.

\textbf{Figure 3.3} Boron templated dimerization of allylic alcohol and its application in total synthesis

3.2 Results and Discussion

During the course of our research in nickel titanium cooperative catalysis (See chapter 2), we found that copper(II) triflate enabled what we thought was the addition of phenyl boronic acid across an alkene. Upon further inspection, we found that the actual product of the reaction was a dimerization of the allylic alcohol and that the product contained the boronic acid which had been converted to a boronic ester (Figure 3.4). Copper(II) triflate was found to be essential in the dimerization of the allylic alcohol, which selectively forms a new C-C bond and new C-O bonds.
bond by addition across the alkene of the allylic alcohol substrate. Based in the high regioselectivity of the reaction, we hypothesized that the Boron atom makes an ester with two allylic alcohols and then facilitates a templated cyclization reaction. As seen in previous boron-templated reactions, the boron can easily be removed under basic conditions. The structure of this product was determined by NMR and SC-XRD (Figure 3.5). Through this structural

**Figure 3.4** Boron templated dimerization of allylic alcohol, new bonds shown in blue

**Table 3.1** Optimization of Boron templated dimerization

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>solvent</th>
<th>temp</th>
<th>% yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cu(OTf)2 + dppf</td>
<td>toluene</td>
<td>60 °C</td>
<td>42</td>
</tr>
<tr>
<td>2</td>
<td>CuCl2 + dppf</td>
<td>toluene</td>
<td>60 °C</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>Cu(OAc)2 + dppf</td>
<td>toluene</td>
<td>60 °C</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>CuI + dppf</td>
<td>toluene</td>
<td>60 °C</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>TfOH</td>
<td>toluene</td>
<td>60 °C</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>TfOH</td>
<td>toluene</td>
<td>rt</td>
<td>96</td>
</tr>
<tr>
<td>7</td>
<td>TfOH</td>
<td>DCE</td>
<td>rt</td>
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</tr>
<tr>
<td>9</td>
<td>TfOH</td>
<td>DCE</td>
<td>rt</td>
<td>30</td>
</tr>
<tr>
<td>10</td>
<td>None</td>
<td>DCE</td>
<td>rt</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>TfOH</td>
<td>DCE</td>
<td>rt</td>
<td>0</td>
</tr>
</tbody>
</table>

a) Reactions run with 1 mmol of cinnamyl alcohol, 0.5 mmol of PhB(OH)2, and 10 mol % catalyst in solvent (0.06 M) for 12 h.
b) Isolated yields of 3 (~10:1 dr) after hydrolysis of the boronic ester with aq. KOH. c) After 16 h. d) Reaction run with 5 mol % TfOH e) No PhB(OH)2 added
determination we found that this reaction forms two chiral centers and proceeds with good diastereoselectivity (8:1).

We next set out to optimize this new selective dimerization, and our studies are presented in Table 3.1. Initially, we found that copper triflate gave a modest yield of 42%. Other copper sources such as CuCl₂, Cu(OAc)₂, or CuI gave no product (entries 2–4). This led us to wonder whether the actual catalyst of the reaction was triflic acid, which could be generated in situ by interaction with the allylic alcohol or ambient water. When triflic acid was used instead of Cu(OTf)₂ (entry 5), a much higher yield was obtained and the reaction was able to reach completion at room temperature (entry 6). It was also found that the reaction works well in both dichloroethane and in toluene (entry 7–8). Solvents with hetero atoms; including THF, dioxane, and DMF suppressed the formation of the product. This was likely due to the acid leveling effect of these aprotic solvents.

The mechanism for the dimerization of cinnamyl alcohol likely proceeds first with the esterification of the boron (Figure 3.6). As shown in past studies, Boron has a strong affinity to bind to oxygen and typically forms boronic esters. The addition to two equivalents of the alcohol to the boron generates intermediate B. Intermediate B can be synthesized independently and subjected to the reaction to achieve the same dimerized product. One of the boronic ester oxygens is likely next pronated by the triflic acid to give intermediate C. This generates the activated substrate, which can then undergo attack by the proximal alkene to give the resonance stabilized carbocation on the benzylic carbon (intermediate D). This carbocation is then attacked by the boronic acid oxygen to give the cyclized product. To verify that the mechanism proceeds through this cycle, the doubly esterified boronic ester (Figure 3.6, B) was isolated and subjected to the reaction conditions (TfOH in DCE). It was found that the isolated complex B does indeed cyclize to give the expected dimerized product.

![Figure 3.5 Crystal structure of the dimerization product](image-url)
We next conducted a time-based study to determine if the diastereoselectivity (dr) of the reaction changes over time. A change in dr would indicate a reversible process that is under thermodynamic control. A consistent dr throughout the reaction supports a kinetically controlled product. By measuring the dr by NMR throughout the reaction, we found that the dr remains constant. We propose the following six-member ring structure as the favorable kinetic transition state. This transition state explains the formation of the major diastereomer, where placing groups in the equatorial position of the 6-member chair transition states predicts formation the observed product.

With efficient reaction conditions in hand, and a good understanding of the reaction mechanism, we next set out to explore the substrate scope of our new alcohol dimerization

![Catalytic Cycle Diagram]

**Figure 3.6** Proposed catalytic cycle for the boron templated dimerization
Figure 3.7 Proposed six member transition state

reaction (Figure 3.8). The reaction tolerated a variety of different aromatic allylic alcohols, including substrates substituted with both electron withdrawing and electron donating groups. Strongly electron withdrawing groups such as the trifluoro methyl (2i) gave reduced yields. This is likely due to deactivation of the alkene nucleophile, as well as destabilization of the benzylic carbocation, both of which would slow down the reaction (Figure 3.6 D). Substrates containing

<table>
<thead>
<tr>
<th>% Conversion</th>
<th>D.R.</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>12:1</td>
</tr>
<tr>
<td>20%</td>
<td>13:1</td>
</tr>
<tr>
<td>50%</td>
<td>12:1</td>
</tr>
<tr>
<td>100%</td>
<td>14:1</td>
</tr>
</tbody>
</table>

Figure 3.8 Substrate scope for the boron templated acid catalyzed dimerization of allylic alcohols, d.r. was consistent for all substrates ~10:1
electron donating groups (2c-2e) gave excellent yields, which further supports the proposed catalytic cycle. Substrates with more sterically hindered groups (2f-2g) gave reduced yields. In addition to the various cinnamyl alcohols, the reaction also tolerates other aromatic groups including naphthyl (2n) and a thiophene heterocycle (2r). Non-conjugated trisubstituted alkenes (2s) also gave good yields. To summarize, this reaction works well with a variety of allylic alcohols but suffers lower yields with more electron withdrawing and more sterically hindered groups.

Our final goal with this new transformation was to determine whether the use of a chiral, enantioenriched strong acid or chiral boronic acid could lead to the formation of enantioenriched 1,3 diol products. To test this, (R)-camphorsulfonic acid ((R)-CSA) was used in the reaction. Unfortunately, the reaction only resulted in 33% yield and no enantioselectivity was observed in product formation (Figure 3.9a). Our next strategy was to employ a chiral 2,2'-binaphthyl-derived boronic acid (Figure 3.9b). When this chiral boronic acid was employed, we obtained a high yield (77%) but the product was isolated as a 1:1 mixture of diastereomers, indicating no chirality transfer to the product. After no stereoselectivity was obtained via these two approaches, we decided not to pursue this idea further.

To show the synthetic utility of the products produced from our new alcohol dimerization reaction, we performed derivatization studies with substrate 2a (Figure 3.10). Using Lemieux-Johnson oxidation conditions the alkene was cleaved to provide the aldehyde product (8) in 98% yield. Importantly, the boronic acid protecting group remained intact during the reaction. This

![Figure 3.9 Attempts at stereoinduction of alcohols](image-url)
oxidative cleavage of the alkene allows for the removal of one of the two phenyl groups in the product, which enables further transformations. This result also addresses one of the current limitations of our method, which only enables the dimerization of two of the same alcohols. Hydrogenation of 2a also proceeds in high yield to give saturated product 9 in 91% yield. Using a second generation Hoveyda-Grubbs catalyst, cross metathesis in the presence of ethylene (balloon pressure) gave the terminal alkene 10 in 72% yield. Epoxidation of the alkene also gave good yield generating the epoxide 11 as a 1:1 mixture of diastereomers (71% yield). Importantly, all of these transformations took place without the loss of the boronic ester protecting group. In addition, the boronic acid protecting group could be removed to reveal the 1,3-diol product in high yield.

In conclusion, we have developed a novel boron-templated dimerization of allylic alcohols to form 1,3 diols. This reaction creates a dense arrangement of alcohols and alkenes and two new stereocenters with high diastereoselectivity. The pendent alkene group in the product can be readily functionalized for further applications in organic synthesis. The scope of this reaction shows that it tolerates various aryl groups and trisubstituted olefins. Additionally, this
work also illustrates the potential for using boron tethers to preorganize substrates and facilitate selective intramolecular transformations that proceed in high yield and with high diastereoselectivity.

3.3 Supporting Information

All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring, unless otherwise indicated. Solvents were dried by J. C. Meyer’s Solvent Purification System. Reactions requiring a moisture or oxygen-free environment were done in a nitrogen atmosphere glove box (Innovative Technology, PreLab HE system, double glove box). Flash chromatography was performed with Sorbtech silica gel (0.040-0.063µm grade). Analytical thin-layer chromatography was done with 0.25 mm coated commercial silica gel plates (Merck KGaA, DC silicagel 60 F254). Proton nuclear magnetic resonance (1H NMR) data were acquired on an Inova 300 (300 MHz), Inova-500 (500 MHz) or Bruker (500MHz) spectrometer. Chemical shifts are reported in delta (δ) units relative to the 2H signal of the CDCl3 solvent. Carbon-13 and Boron-11 nuclear magnetic resonance (13C-NMR and 11B-NMR) data were acquired on an Inova 500 at 125 MHz. Signals are reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), qd (quartet of doublets), brs (broad singlet), m (multiplet). Coupling constants are reported in hertz (Hz). Chemical shifts are reported in ppm relative to the center line of a triplet at 77.23 ppm for chloroform-d for 13C-NMR or the singlet at 0 ppm for BF3 · O(Et)2 for 11B-NMR. Infrared (IR) data were recorded as films on sodium chloride plates on a Thermo Scientific Nicolet IR 100 FT-IR spectrometer. Absorbance frequencies are reported in reciprocal centimeters (cm⁻¹). Chiral HPLC analyses were performed on a Thermo Separation Products Spectra Series P-100 or 200 and UV100 using Chiralcel ® columns. Optical rotations were measured on a Jasco P-2000 digital polarimeter using 5 cm cells and the sodium D line (589 nm) at ambient temperature in the solvent and concentration indicated. Mass spectral data were obtained using ESI techniques (Agilent, 6210 TOF).

3.3.1 General Synthesis of Allylic Alcohols

Alcohols were prepared from aldehyde starting material, using a Horner Wadsworth Emmons reaction followed by a DIBAL reduction. An example is shown below.
To a dry flask with dry THF (25 mL) and sodium hydroxide 60% in mineral oil (17.8 mmol) Triethyl phosphonoacetate (17.8 mmol) was added dropwise. After stirring for one hour, 4-ethyl benzaldehyde (17 mmol) was added. The reaction proceeded overnight. After workup with aqueous NaHCO₃, product was purified by column chromatography with 15% ethyl acetate in hexanes as the eluent.

To a flame dried flask with dry DCM (15 mL) and ethyl (E)-3-(4-ethylphenyl)acrylate (4 mmol), DIBAL (8.1 mmol) was added dropwise at -78 C. The reaction was allowed to return to room temperature and continued for 2 h. After quenching with water, the product was extracted with ethyl acetate, the organics were dried over Na₂SO₄, the solvent was removed, and the product was purified by column chromatography on silica gel with 25% ethyl acetate in hexanes as the eluent.

<table>
<thead>
<tr>
<th>Cat. (mol%)</th>
<th>Ligand</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>Time (h)</th>
<th>Yield</th>
<th>D.R.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cu(OTf)₂ (10)</td>
<td>Dppf (10)</td>
<td>Toluene</td>
<td>60</td>
<td>16</td>
<td>42</td>
<td>-</td>
</tr>
<tr>
<td>Cu(OTf)₂ (10)</td>
<td>-</td>
<td>Toluene</td>
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3.3.2 Additional Optimization Studies:

3.3.3 Control Studies:

To control for a hydronium effect 4 angstrom molecular sieves were added to soak up the water and reduce the potential hydronium effect. Additional studies were performed with substoichiometric phenyl boronic acid to determine the importance of equal equivalence and the acidifying effect of the phenyl boronic acid. Yields were reported based on the phenyl boronic acid starting material. No reduction in yield was seen to indicate a controlling hydronium effect.

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3.3.4 Synthesis of Dioxaborinanes via Boron Templated Catalysis

**General Procedure:**

In a flame dried flask, allylic alcohol (2 mmol) and phenyl boronic acid (1 mmol) were stirred in toluene (1 mL) for 10 minutes. Triflic acid (0.1 mmol) was added dropwise and the reaction was allowed to proceed for 12 h. At the conclusion of the reaction, the mixture was filtered through a plug of silica gel in a pipet and rinsed through with CH_2Cl_2, the solvent was removed, and the product was loaded directly onto a column of silica gel and eluted with mixtures of ethyl acetate or CH_2Cl_2 and hexanes with 1% triethylamine to deactivate the silica gel. The diastereoselectivity of each transformation was determined by integration of the peaks near 5-5.5 ppm corresponding to the benzylic proton of the dioxaborinane ring.

![5-cinnamyl-2,4-diphenyl-1,3,2-dioxaborinane (2a)]

Synthesized according to the general procedure using cinnamyl alcohol (1.5 g, 11.18 mmol), phenyl boronic acid (0.682 g, 5.59 mmol) and triflic acid (83.8 mg). The reaction was purified by flash chromatography with 70% DCM 30% hexanes as the eluent, 1% triethyl amine.
was added to neutralize the eluent and prevent partial hydrolysis of the boronic ester. The product was isolated as a clear oil (1.9 g, 96% yield, 14:1 DR). Rr: 0.1 in 1:1 DCM:hexanes; $^1$H NMR (500 MHz, CDCl$_3$), δ 7.88 (d, $J$=7.0, 2H); 7.50-7.21 (m, 13H); 6.41 (d, $J$=15.9 Hz, 1H); 6.09 (td, $J$=15.7 Hz, 6.7Hz, 1H); 5.00 (d, $J$=7.3 Hz, 1H); 4.21 (dd, $J$=10.7, 3.1 Hz, 1H); 3.99 (dd, $J$=11.8, 8.0 Hz,1H); 2.39-2.32 (m, 1H); 2.24-2.16 (m, 2H); $^{13}$C NMR (126 MHz, CDCl$_3$), δ 141.4, 137.1, 134.0, 134.0, 132.6, 130.8, 128.5, 128.5, 128.0, 127.6, 127.3, 126.5, 126.4, 126.1, 77.9, 64.5, 43.2, 32.4; $^{11}$B NMR (160 MHz, CDCl$_3$), δ 27.0; IR (film) νmax 3057, 3027, 2903, 1950, 1600, 1312, 1261; Boron removed to gather MS data: HRMS(EI) calculated for C$_{18}$H$_{21}$O$_2$,[M+H]$^+$; 269.1542, found 269.1545

(E)-4-(4-bromophenyl)-5-(3-(4-bromophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane (2b): Synthesized according to the general procedure using 4-bromo cinnamyl alcohol (170.4 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, 0.04 mmol). The reaction was purified by flash chromatography with 70% DCM 30% hexanes as the eluent, 1% Triethyl amine was added to neutralize the eluent and prevent partial hydrolysis of the boronic ester. The product was isolated as a brown oil (204 mg, 56%, 14:1 DR). Rr: 0.7 in DCM; $^1$H NMR (300 MHz, CDCl$_3$), δ 7.87 (d, $J$ = 7.8 Hz, 2H), 7.57 (d, $J$ = 8.4 Hz, 2H), 7.52-7.38 (m, 5H), 7.28 (d, $J$ = 9.0 Hz, 2H), 7.18 (d, $J$ = 8.4 Hz, 2H), 6.34 (d, $J$ = 15.6 Hz, 1H), 6.10-6.00 (m, 1H), 4.96 (d, $J$ = 6.9 Hz, 1H), 4.21 (dd, $J$ = 11.7, 3.3 Hz, 1H), 4.02-3.96 (m, 1H), 2.36-2.28 (m, 1H), 2.25-2.13 (m, 2H); $^{13}$C NMR (126 MHz, CDCl$_3$), δ 140.3, 135.9, 134.0, 131.7, 131.6, 131.0, 128.4, 128.2, 127.7, 127.6, 126.9, 122.0, 121.1, 69.9, 64.5, 43.0, 32.3; $^{11}$B NMR (160 MHz, CDCl$_3$), δ 27.53; IR (film) νmax 3025, 2920, 1900, 1599, 1311, 1259, 641; HRMS(EI) calculated for C$_{24}$H$_{21}$BB$_2$O$_2$Na, [M+Na]$^+$; 534.9873, found 534.9871.

(E)-4-(4-methoxyphenyl)-5-(3-(4-methoxyphenyl)allyl)-2-phenyl-1,3,2-dioxaborinane (2c):
Synthesized according to the general procedure using 4-methoxy cinnamyl alcohol (131.4 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, 0.04 mmol). The reaction was purified by flash chromatography with 100% DCM as the eluent, 1% Triethyl amine was added to neutralize the eluent and prevent partial hydrolysis of the boronic ester. The product was isolated as a yellow oil (153.6 mg, 96 %, 10:1 DR). Rf: 0.6 in DCM; $^1$H NMR (500MHz, CDCl$_3$), δ 7.88 (d, $J$=7.7Hz, 2H); 7.49-7.44 (m, 1H); 7.41-7.36 (m, 2H); 7.31 (d, $J$=8.4 Hz, 2H); 7.28-7.23 (m, 2H) 6.96 (d, $J$=8.4 Hz, 2H); 6.86 (d, $J$=8.4 Hz, 2H); 6.36 (d, $J$=15.5 Hz, 1H); 5.92 (dt, $J$=15.4 Hz, 7.9, 1H); 4.93 (d, $J$=8.5 Hz, 1H); 4.23 (dd, $J$=4.1, 11.88 Hz, 1H); 3.98 (dd, $J$=8.5, 11.2 Hz, 1H); 3.85 (s, 3H); 3.82 (s, 3H); 2.32-2.27 (m, 1H); 2.18-2.10 (m, 2H); $^{13}$C NMR (126 MHz, CDCl$_3$), δ 159.4, 159.0, 134.1, 134.0, 133.6, 131.8, 130.8, 130.0, 127.8, 127.7, 127.6, 127.3, 127.2, 127.1, 124.2, 114.0, 113.9, 113.8, 77.7, 65.0, 55.3, 55.3, 46.1, 43.4, 32.3; $^{11}$B NMR (160 MHz, CDCl$_3$) δ 27.53; IR (film) $\nu$max 3057, 3027, 2903, 1950, 1600, 1312, 1261; Boron removed to gather MS data HRMS(EI) calculated for C$_{20}$H$_{24}$O$_{4}$Na, [M+Na]$^+$; 351.1567, found 351.1570.

(E)-2-phenyl-4-((p-tolyl)-5-(3-(p-tolyl)allyl)-1,3,2-dioxaborinane (2d):

Synthesized according to the general procedure using 4-methyl cinnamyl alcohol (59.2 mg, 0.4 mmol), phenyl boronic acid (24.4 mg, 0.2 mmol) and triflic acid (0.2 uL, 0.02 mmol). The reaction was purified by flash chromatography with 100% DCM as the eluent, 1% Triethyl amine was added to neutralize the eluent and prevent partial hydrolysis of the boronic ester. The product was isolated as a yellow oil (59.2 mg, 90.5 %, 9:1 DR). Rf: 0.8 in DCM; $^1$H NMR (500 MHz, CDCl$_3$), δ 7.90 (d, $J$ = 7.5 Hz, 2H), 7.48 (t, $J$ = 7.5 Hz, 1H), 7.40 (t, $J$ = 7.5 Hz, 2H), 7.29 (t, $J$ = 7.5 Hz, 2H), 7.23 (t, $J$ = 7.5 Hz, 4H), 7.14 (d, $J$ = 8.0 Hz, 2H), 6.38 (d, $J$ = 15.5 Hz, 1H), 6.02 (dt, $J$ = 8.8, 15.7 Hz, 1H), 4.96 (d, $J$ = 7.0 Hz, 1H), 4.23 (dd, $J$ = 11.5, 3.5 Hz, 1H), 4.00-3.97 (m, 1H), 2.41 (s, 3H), 2.36 (s, 3H), 2.39-2.32 (m, 1H), 2.21-2.14 (m, 2H); $^{13}$C NMR (126 MHz, CDCl$_3$), δ 138.5, 137.7, 137.1, 134.4, 134.1, 134.0, 132.3, 130.8, 129.3, 129.2, 129.2, 127.6, 126.5, 126.0, 125.4, 77.9, 64.7, 43.3, 32.4, 21.2; $^{11}$B NMR (160 MHz, CDCl$_3$), δ 27.53;
IR (film) ν\text{max} 3023, 2920, 1901, 1600, 1312, 1260; Boron removed HRMS(EI) calculated for C\text{20}H\text{24}O\text{2}Na, [M+Na]+; 319.1669, found 319.1671.

(E)-4-(4-ethylphenyl)-5-(3-(4-ethylphenyl)allyl)-2-phenyl-1,3,2-dioxaborinane (2e):

Synthesized according to the general procedure using 4-ethylcinnamyl alcohol (129.8 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, 0.04 mmol). The reaction was purified by flash chromatography with 100% DCM as the eluent, 1% Triethyl amine was added to neutralize the eluent and partial hydrolysis of the boronic ester. The product was isolated as a yellow oil (157 mg, 95 %, 11:1 DR). Rr: 0.1 in 1:1 DCM:hexanes \( ^1 \text{H} \text{NMR (500MHz, CDCl}_3 \), δ 7.90 (d, \( J = 7.5 \text{ Hz}, 2 \text{H} \), 7.47 (t, \( J = 7.5 \text{ Hz}, 1 \text{H} \), 7.40 (t, \( J = 7.5 \text{ Hz}, 2 \text{H} \), 7.29 (t, \( J = 7.5 \text{ Hz}, 2 \text{H} \), 7.23 (t, \( J = 7.5 \text{ Hz}, 4 \text{H} \), 7.14 (d, \( J = 8.0 \text{ Hz}, 2 \text{H} \), 6.38 (d, \( J = 15.5 \text{ Hz}, 1 \text{H} \), 6.02 (dt, \( J = 8.8, 15.7 \text{ Hz}, 1 \text{H} \), 4.96 (d, \( J = 7 \text{ Hz}, 1 \text{H} \), 4.23 (dd, \( J = 11.5, 3.5 \text{ Hz}, 1 \text{H} \), 4.00-3.97 (m, 1H), 2.69 (q, \( J = 7.6 \text{ Hz}, 2 \text{H} \), 2.64 (q, \( J = 7.6, 2 \text{H} \) 2.39-2.32 (m, 1H), 2.24-2.16 (m, 2H), 1.28 (t, \( J = 7.5, 3 \text{H} \), 1.24 (t, \( J = 7.6, 3 \text{H} \) ); \( ^{13} \text{C} \text{NMR (126 MHz, CDCl}_3 \), δ 138.5, 137.7, 137.1, 134.4, 134.1, 134.0, 132.3, 130.8, 129.3, 129.2, 129.2, 127.6, 126.5, 126.0, 125.4, 77.9, 64.7, 43.2, 32.4, 21.2, 21.2 \( ^{11} \text{B} \text{NMR (160 MHz, CDCl}_3 \), δ 27.53; IR (film) ν\text{max} 3057, 3027, 2903, 1950, 1600, 1312, 1261; Boron removed for MS. HRMS(EI) calculated For C\text{22}H\text{28}O\text{2}Na, [M+Na]+; 347.1982, found 347.1980 .

(E)-4-(4-pentylphenyl)-5-(3-(4-pentylphenyl)allyl)-2-phenyl-1,3,2-dioxaborinane (2f):

Synthesized according to the general procedure using 4-pentylcinnamyl alcohol (163.4 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, 0.04 mmol). The reaction was purified by flash chromatography with 100% DCM as the eluent, 1% Triethyl amine was added to neutralize the eluent and prevent partial hydrolysis of the boronic ester. The product was isolated as a yellow oil (120.6 mg, 61%, 10:1 DR). Rr: 0.1 in 1:1 DCM:hexanes; \( ^1 \text{H} \text{NMR (500 MHz, CDCl}_3 \), δ 7.87 (d, \( J = 8.0 \text{ Hz}, 2 \text{H} \), 7.48-7.11 (m, 11H), 6.37 (d, \( J = 15.5 \text{ Hz},
1H), 6.04-5.98 (m, 1H), 4.96 (d, \( J = 7.0 \) Hz, 1H), 4.21 (dd, \( J = 11.5, 3.5 \) Hz, 1H), 3.97 (dd, \( J = 11.0, 7.5 \) Hz, 1H), 2.65-2.57 (m, 4H), 2.35-2.30 (m, 1H), 2.20-2.15 (m, 2H), 1.66-1.58 (m, 4H), 1.36-1.32 (m, 8H), 0.93-0.89 (m, 6H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)), \( \delta 142.8, 142.2, 138.6, 134.6, 134.0, 132.3, 130.8, 128.6, 128.5, 127.6, 126.4, 126.2, 126.0, 125.9, 125.7, 125.4, 125.4, 77.9, 64.7, 43.2, 35.7, 35.6, 32.4, 31.6, 31.5, 31.4, 31.3, 31.2, 29.7, 22.6, 22.6, 14.1, 14.0; \(^{11}\)B NMR (160 MHz, CDCl\(_3\)), \( \delta 25.39; \) IR (film) \( \nu_{\text{max}} 3050, 3023, 2930, 2857, 1701, 1605, 1312, 1144; \) HRMS(EI) calculated for C\(_{34}\)H\(_{44}\)BO\(_2\), [M+H]+; 495.3434 found 495.3432.

(E)-4-(4-(tert-butyl)phenyl)-5-(3-(4-(tert-butyl)phenyl)allyl)-2-phenyl-1,3,2-dioxaborinane (2g):

Synthesized according to the general procedure using 4-tert butyl cinnamyl alcohol (152.2 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, .04 mmol). The reaction was purified by flash chromatography with 100% DCM as the eluent, 1% Triethyl amine was added to neutralize the eluent and prevent partial hydrolysis of the boronic ester. The product was isolated as a light yellow solid (87.7 mg, 47%, 19:1 DR). Rf: 0.1 in 1:1 DCM:hexanes; Melting point 86-112 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)), \( \delta 7.87 (d, J = 8.0 \) Hz, 2H), 7.47-7.23 (m, 11H), 6.37 (d, \( J = 16.0 \) Hz, 1H), 6.03-5.97 (m, 1H), 4.96 (d, \( J = 7.0 \)Hz, 1H), 4.20 (dd, \( J = 11.0, 3.5 \) Hz, 1H), 3.96 (dd, \( J = 11.5, 8.0 \) Hz, 1H), 2.37-2.31 (m, 1H), 2.21-2.14 (m, 2H), 1.34 (s, 3H), 1.32 (s, 3H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)), \( \delta 150.9, 150.4, 138.4, 134.4, 134.0, 132.1, 130.8, 127.6, 126.2, 125.8, 125.5, 125.4, 77.9, 69.9, 64.8, 43.2, 34.6, 34.5, 32.5, 31.4, 31.3; \(^{11}\)B NMR (160 MHz, CDCl\(_3\)), \( \delta 26.65; \) IR (film) \( \nu_{\text{max}} 3026, 2962, 2893, 2893, 1714, 1601, 1314, 1268, 1143; \) Boron removed for MS. HRMS(EI) calculated for C\(_{26}\)H\(_{36}\)O\(_2\)Na, [M+Na]+; 403.2608, found 403.2609.

(E)-4-(4-chlorophenyl)-5-(3-(4-chlorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane (2h)
Synthesized according to the general procedure using 4-chloro cinnamyl alcohol (134.89 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol), triflic acid (0.4 uL, 0.04 mmol) and DCE (0.4 mL) at 45 °C. The reaction was purified by flash chromatography with 50% DCM 50% hexanes as the eluent, 1% Triethyl amine was added to neutralize the eluent and prevent partial hydrolysis of the boronic ester. The product was isolated as a light-yellow oil (131 mg, 77%, 8:1 DR). Rr: 0.7 in DCM; 1H NMR (300 MHz, CDCl3), δ 7.87 (d, J = 7.8 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 7.52-7.38 (m, 5H), 7.28 (d, J = 9.0 Hz, 2H), 7.18 (d, J = 8.4 Hz, 2H), 6.34 (d, J = 15.6 Hz, 1H), 6.10-6.00 (m, 1H), 4.96 (d, J = 6.9 Hz, 1H), 4.21 (dd, J = 11.7, 3.3 Hz, 1H), 4.02-3.96 (m, 1H), 2.36-2.28 (m, 1H), 2.25-2.13 (m, 2H); 13C NMR (126 MHz, CDCl3), δ 140.3, 135.9, 134.0, 131.7, 131.6, 131.0, 128.3, 128.2, 127.7, 127.6, 126.9, 122.0, 121.1, 69.9, 64.5, 43.0, 32.3; 11B NMR (160 MHz, CDCl3), δ 27.53; IR (film) νmax 3025, 2920, 1900, 1599, 1311, 1259, 641; boron removed for MS. HRMS(EI) calculated for C18H19Cl2O2, [M+H]+; 337.0757, found 337.0761

(E)-2-phenyl-4-(4-(trifluoromethyl)phenyl)-5-(3-(4-(trifluoromethyl)phenyl)allyl)-1,3,2-dioxaborinane (2i):

Synthesized according to the general procedure using 4-trifluoro methyl cinnamyl alcohol (161.7 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, 0.04 mmol). The reaction was purified by flash chromatography with 100% DCM as the eluent, 1% Triethyl amine was added to neutralize the eluent and prevent partial hydrolysis of the boronic ester. The product was isolated as a yellow oil (33.3 mg, 17%, 10:1 DR). Rr: 0.1 in 1:1 DCM:hexanes; 1H NMR (300 MHz, CDCl3), δ 7.92-7.87 (m, 2H), 7.71 (d, J=8.2 Hz, 2H); 7.61-7.47 (m, 6H); 7.45-7.37 (m, 4H); 6.52-6.40 (m, 1H); 6.16 (dt, J = 7.0 Hz, 15.63, 1H); 5.07 (d, J = 7.3 Hz, 1H); 4.22 (dd, J = 4.1, 12.2 Hz, 1H); 4.07-3.98 (m, 1H); 2.45-2.19 (m, 3H); 13C NMR (75.436 MHz, CDCl3), δ 145.27, 140.29, 134.02, 131.66, 131.13, 130.64, 130.20, 129.12, 128.78, 127.74, 126.93, 126.26, 125.98, 125.64 (J=3.79, 7.38), 125.54 (J=3.66, 7.31), 64.40, 42.98, 32.34; 11B NMR (160 MHz, CDCl3), δ 27.41; IR (film) νmax 3057, 2920, 1900, 1599, 1311, 1259, 641; boron removed for MS. HRMS(EI) calculated for C18H19Cl2O2, [M+H]+; 337.0757, found 337.0761
(E)-2-phenyl-4-(m-tolyl)-5-(3-(m-tolyl)allyl)-1,3,2-dioxaborinane (2j):

Synthesized according to the general procedure using 3-methyl cinnamyl alcohol (118.6 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, .04 mmol). The reaction was purified by flash chromatography with 100% DCM as the eluent, 1% Triethyl amine was added to neutralize the eluent and prevent partial hydrolysis of the boronic ester. The product was isolated as a clear oil (125 g, 82%, 10:1 DR). Rгр: 0.1 in 1:1 DCM:hexanes; \(^1\)H NMR (500 MHz, CDCl\(_3\)), δ 7.90 (d, \(J = 7.5\) Hz, 2H), 7.48 (t, \(J = 7.5\) Hz, 1H), 7.40 (t, \(J = 7.5\) Hz, 2H), 7.29 (t, \(J = 7.5\) Hz, 2H), 7.23 (t, \(J = 7.5\) Hz, 4H), 7.14 (d, \(J = 8\) Hz, 2H), 6.38 (d, \(J = 15.5\) Hz, 1H), 6.02 (dt, \(J = 8.8, 15.7\) Hz, 1H), 4.96 (d, \(J = 7\) Hz, 1H), 4.23 (dd, \(J = 11.5, 3.5\) Hz, 1H), 4.00-3.97 (m, 1H), 2.43 (s, 3H), 2.39 (s, 3H), 2.39-2.32 (m, 1H), 2.26-2.18 (m, 2H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)), δ 138.5, 137.7, 137.1, 134.4, 134.1, 134.0, 132.3, 130.8, 129.3, 129.2, 129.2, 127.6, 125.6, 126.0, 125.4, 77.9, 64.7, 43.2, 32.4, 21.2; \(^{11}\)B NMR (160 MHz, CDCl\(_3\)), δ 27.53; IR (film)νmax 3023, 2920, 1901, 1600, 1312, 1260; Boron removed for MS. HRMS(EI) calculated for C\(_{20}\)H\(_{24}\)O\(_2\)Na, [M+Na]+; 319.1669, found 319.1669.

(E)-4-(3-chlorophenyl)-5-(3-(3-chlorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane (2k)

Synthesized according to the general procedure using 3-chloro cinnamyl alcohol (134.89 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol), triflic acid (0.4 uL, .04 mmol), and DCE (4 mL) at 45 °C. The reaction was purified by flash chromatography with 50% DCM 50% hexanes and 1% triethylamine. The product was isolated as a light-yellow oil (101.5 mg, 60%, 10:1 DR). Rгр: 0.7 in DCM; \(^1\)H NMR (300 MHz, CDCl\(_3\)), δ 7.88 (d, \(J = 7.8\) Hz, 2H), 7.57 (d, \(J = 7.5\) Hz, 2H), 7.25 (dd, \(J = 11.5, 3.5\) Hz, 1H), 4.96 (d, \(J = 7\) Hz, 1H), 4.23 (dd, \(J = 11.5, 3.5\) Hz, 1H), 4.00-3.97 (m, 1H), 2.43 (s, 3H), 2.39 (s, 3H), 2.39-2.32 (m, 1H), 2.26-2.18 (m, 2H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)), δ 138.5, 137.7, 137.1, 134.4, 134.1, 134.0, 132.3, 130.8, 129.3, 129.2, 129.2, 127.6, 126.5, 126.0, 125.4, 77.9, 64.7, 43.2, 32.4, 21.2; \(^{11}\)B NMR (160 MHz, CDCl\(_3\)), δ 27.53; IR (film)νmax 3023, 2920, 1901, 1600, 1312, 1260; Boron removed for MS. HRMS(EI) calculated for C\(_{20}\)H\(_{24}\)O\(_2\)Na, [M+Na]+; 319.1669, found 319.1669.
8.4 Hz, 2H), 7.52-7.38 (m, 5H), 7.28 (d, J = 9.0 Hz, 2H), 7.18 (d, J = 8.4 Hz, 2H), 6.34 (d, J = 15.6 Hz, 1H), 6.10-6.00 (m, 1H), 4.96 (d, J = 6.9 Hz, 1H), 4.21 (dd, J = 11.7, 3.3 Hz, 1H), 4.02-3.96 (m, 1H), 2.36-2.28 (m, 1H), 2.25-2.13 (m, 2H); 13C NMR (126 MHz, CDCl3), δ 140.33, 135.86, 133.98, 131.68, 131.61, 131.01, 128.35, 128.25, 127.69, 127.59, 126.92, 121.98, 121.13, 69.89, 64.53, 43.04, 32.27; 11B NMR (160 MHz, CDCl3), δ 27.53; IR (film) νmax 3025, 2920, 1900, 1599, 1311, 1259, 641; Boron removed for MS. HRMS(EI) calculated for C18H19Cl2O2, [M+H]+; 337.0757, found 337.0760

(E)-2-phenyl-4-(o-tolyl)-5-(3-(o-tolyl)allyl)-1,3,2-dioxaborinane (2l):

Synthesized according to the general procedure using 2-methyl cinnamyl alcohol (118.6 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, 0.04 mmol). The reaction was purified by flash chromatography with 100% DCM and 1% triethylamine. The product was isolated as a clear liquid (149.2 mg, 97.6%, 11:1 DR). Rr: 0.1 in 1:1 DCM:hexanes; 1H NMR (500 MHz, CDCl3), δ 7.97 (d, J = 7.0 Hz, 2H); 7.58-7.18 (m, 11H); 6.71 (d, J = 16.1 Hz, 1H); 6.06 (dt, J = 7.0 Hz, 15.64, 1H); 5.40-5.33 (m, 1H); 4.32 (dd, J = 4.2, 11.98 Hz, 1H); 4.06 (dd, J = 6.6, 11.38 Hz, 1H); 2.49 (s, 3H); 2.39 (s, 3H); 2.468-2.265 (m, 3H); 13C NMR (126 MHz, CDCl3), δ 139.4, 136.4, 135.1, 134.9, 134.1, 130.9, 130.8, 130.7, 130.3, 128.0, 127.7, 127.7, 127.3, 126.4, 126.2, 126.1, 125.6, 64.1, 41.8, 33.0, 20.0, 19.6; 11B NMR (160 MHz, CDCl3), δ 27.53; IR (film) νmax 3057, 3027, 2903, 1950, 1600, 1312, 1261; Boron removed for MS. HRMS(EI) calculated for C20H24O2Na, [M+Na]+; 319.1669, found 319.1670.

(E)-4-(2-methoxyphenyl)-5-(3-(2-methoxyphenyl)allyl)-2-phenyl-1,3,2-dioxaborinane (2m):

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Synthesized according to the general procedure using 2-methoxy cinnamyl alcohol (131.4 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, 0.04 mmol). The reaction was purified by flash chromatography with 100% DCM and 1% triethylamine. The product was isolated as yellow oil (89.5 mg, 54%, 8:1 DR). Rf: 0.1 in 1:1 DCM:hexanes; 1H NMR (500 MHz, CDCl3), δ 7.88 (d, J = 7.7 Hz, 2H); 7.49-7.44 (m, 1H); 7.41-7.36 (m, 2H); 7.31 (d, J = 8.4 Hz, 2H); 7.28-7.23 (m, 2H) 6.96 (d, J = 8.4 Hz, 2H); 6.86 (d, J = 8.4 Hz, 2H); 6.36 (d, J = 15.5 Hz, 1H); 5.92 (dt, J = 7.8, 15.4 Hz, 1H); 4.93 (d, J = 8.5 Hz, 1H); 4.23 (dd, J = 4.1, 11.88 Hz, 1H); 3.98 (dd, J = 8.5, 11.2 Hz, 1H); 3.85 (s, 3H); 3.82 (s, 3H); 2.32-2.37 (m, 1H); 13C NMR (126 MHz, CDCl3), δ 159.4, 159.0, 134.0, 134.0, 133.5, 131.8, 130.8, 130.0, 127.8, 127.7, 127.6, 127.3, 127.2, 127.1, 127.1, 124.2, 114.0, 113.9, 113.8, 77.8, 64.9, 55.3, 46.1, 43.4, 32.4; 11B NMR (160 MHz, CDCl3) δ 27.53; IR (film)νmax 3057, 3027, 2903, 1950, 1600, 1312, 1261; Boron removed for HRMS(EI) calculated for C20H24O2Na, [M+Na]+; 351.1567, found 351.1570.

(E)-4-(naphthalen-2-yl)-5-(3-(naphthalen-2-yl)allyl)-2-phenyl-1,3,2-dioxaborinane (2n):

Synthesized according to the general procedure using 3-(naphthalen-2-yl)prop-2-en-1-ol alcohol (147.4 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, 0.04 mmol). The reaction was purified by flash chromatography with 100% DCM and 1% triethylamine. The product was isolated as a yellow oil (96.3 mg, 53%). Rf: 0.1 in 1:1 DCM:hexanes; 1H NMR (500MHz, CDCl3), δ 7.88 (d, J = 7.0 Hz, 2H); 7.50-7.21 (m, 17H); 6.41 (d, J = 15.9 Hz, 1H); 6.09 (dt, J = 15.7, 6.7 Hz, 1H); 5.00 (d, J = 7.3 Hz, 1H); 4.21 (dd, J = 10.7, 3.1 Hz, 1H); 3.99 (dd, J = 11.8, 8.0 Hz, 1H); 2.39-2.32 (m, 1H); 2.24-2.16 (m, 2H); 13C NMR (126 MHz, CDCl3), δ 141.4, 137.1, 134.0, 134.0, 132.6, 130.8, 128.5, 128.5, 128.0, 127.6, 127.3, 126.5, 126.4, 126.1, 77.9, 64.5, 43.2, 32.4; 11B NMR (160 MHz, CDCl3), δ 27.04; IR (film)νmax 3057, 3027, 2903, 1950, 1600, 1312, 1261; HRMS(EI) calcd. for C32H28BO2, [M+H]+; 455.2177, found 455.2175.
(E/Z)-4-mesityl-5-(3-mesitylallyl)-2-phenyl-1,3,2-dioxaborinane (2o):

Synthesized according to the general procedure using (E)-3-mesitylprop-2-en-1-ol (141.0 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, .04 mmol). The reaction was purified by flash chromatography with 100% DCM and 1% triethylamine. The product was isolated as a yellow oil as a mixture of cis and trans isomers. (144.4 g, 82%, 8:1 DR). Rr: 0.1 in 1:1 DCM:hexanes; 1H NMR (500 MHz, CDCl₃), δ 7.98 (d, J = 7.0 Hz, 2H); 7.58-7.18 (m, 5H); 6.71 (d, J = 16.1 Hz, 1H); 6.06 (dt, J = 15.6, 7.1Hz, 1H); 5.40-5.33 (m, 1H); 4.32 (dd, J = 12.0, 4.2Hz, 1H); 4.06 (dd, J = 11.4, 6.6Hz, 1H); 2.49 (s, 3H); 2.47-2.26 (m, 18H); 13C NMR (126 MHz, CDCl₃), δ 139.4, 136.4, 135.1, 134.9, 134.1, 130.9, 130.8, 130.7, 130.3, 128.0, 127.7, 127.7, 127.3, 126.4, 126.2, 126.1, 125.6, 64.1, 41.8, 33.0, 19.9, 19.6; 11B NMR (160 MHz, CDCl₃), δ 27.53 ; IR (film) νmax 3057, 3027, 2903, 1950, 1600, 1312, 1261; Boron removed for MS. HRMS(EI) calculated For C₂₄H₃₂O₂Na, [M+Na]+; 375.2295, found 375.2293

(E)-4-methyl-2,4-diphenyl-5-(3-phenylbut-2-en-1-yl)-1,3,2-dioxaborinane (2p):

Synthesized according to the general procedure using (E)-3-phenylbut-2-en-1-ol alcohol (118.6 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, .04 mmol). The reaction was purified by flash chromatography with 100% DCM and 1% triethylamine. The product was isolated as a clear oil (61.2 mg, 40%). Rr: 0.1 in 1:1 DCM:hexanes; 1H NMR (500 MHz, CDCl₃), δ 7.95 (d, J = 7.0 Hz, 2H); 7.51-7.23 (m, 13H); 6.71 (d, J = 16.1 Hz, 1H); 6.06 (dt, J = 15.64, 7.0 Hz, 1H); 5.71-5.65 (m, 1H); 4.04-3.95 (m, J = 4.2, 11.98 Hz, 2H); 2.44-2.38 (m, 1H), 2.29-2.23 (m, 2H), 1.96 (s, 3H), 1.76 (s, 3H); 13C NMR (126 MHz, CDCl₃), δ 146.72, 143.58, 137.04, 134.04, 130.80, 128.36, 128.23, 127.70, 127.14, 126.83, 125.64, 125.26, 125.15, 63.01, 46.61, 25.75, 15.97; 11B NMR (160 MHz, CDCl₃), δ ; IR
(E)-4-(3,4-difluorophenyl)-5-(3-(3,4-difluorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane (2q):

Synthesized according to the general procedure using (E)-3-(3,4-difluorophenyl)prop-2-en-1-ol (141 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, 0.04 mmol). The reaction was purified by flash chromatography with 100% DCM and 1% triethylamine. The product was isolated as a clear oil (44.3 mg, 26%, 10:1 DR). Rf: 0.1 in 1:1 DCM:hexanes; 1H NMR (500 MHz, CDCl₃), δ 7.87 (d, J = 7.0 Hz, 2H), 7.47-7.23 (m, 9H), 6.33 (d, J = 6.0 Hz, 1H), 6.05-5.95 (m, 1H), 4.95 (d, J = 7.0 Hz, 1H), 4.21 (dd, J = 11.0, 3.5 Hz, 1H), 3.99 (dd, J = 11.5, 8.0 Hz, 1H), 2.37-2.25 (m, 1H), 2.22-2.14 (m, 2H); 13C NMR (126 MHz, CDCl₃), δ 141.4, 137.1, 134.0, 134.0, 132.6, 130.8, 128.5, 128.0, 127.6, 127.3, 126.5, 126.4, 126.1, 77.9, 64.5, 43.2, 32.4; 11B NMR (160 MHz, CDCl₃), δ 27.04; IR (film)νmax 3057, 3027, 2903, 1950, 1600, 1312, 1261; Boron removed for MS. HRMS(EI) calculated For C₂₀H₂₄O₂Na, [M+Na]+; 319.1669, found 319.1668.

(E)-2-phenyl-4-(thiophen-2-yl)-5-(3-(thiophen-2-yl)allyl)-1,3,2-dioxaborinane (2r):

Synthesized according to the general procedure using (E)-3-(thiophen-2-yl)prop-2-en-1-ol (141 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, 0.04 mmol). The reaction was purified by flash chromatography with 100% DCM and 1% triethylamine. The product was isolated as a yellowish oil (90.8 mg, 62%, 8:1 DR). Rf: 0.1 in 1:1 DCM:hexanes; 1H NMR (500 MHz, CDCl₃), δ 7.86 (d, J = 7.0 Hz, 2H), 7.47-7.23 (m, 4H), 7.2-6.8 (m, 5H) 6.33 (d, J = 6.0 Hz, 1H), 6.05-5.95 (m, 1H), 5.21 (d, J = 7.0 Hz, 1H), 4.21 (dd, J = 11.0, 3.5 Hz, 1H), 3.99 (dd, J = 11.5, 8.0 Hz, 1H), 2.37-2.25 (m, 1H), 2.22-2.14 (m, 2H); 13C NMR (126 MHz, CDCl₃), δ 141.4, 137.1, 134.0, 134.0, 132.6, 130.8, 128.5, 128.0, 127.6, 127.3, 126.5, 126.4, 126.1, 77.9, 64.5, 43.2, 32.4; 11B NMR (160 MHz, CDCl₃), δ 27.04; IR (film)νmax 3057, 3027, 2903, 1950, 1600, 1312, 1261; Boron removed for MS. HRMS(EI) calculated for C₁₈H₁₆F₄O₂Na, [M+Na]+; 363.0979, found 363.0980.
11.0, 3.5 Hz, 1H), 3.99 (dd, J = 11.5, 8.0 Hz, 1H), 2.37-2.25 (m, 1H), 2.22-2.14 (m, 2H); ^13^C NMR (126 MHz, CDCl$_3$), δ 141.4, 137.1, 134.0, 134.0, 132.6, 130.8, 128.5, 128.5, 128.0, 127.6, 127.3, 126.5, 126.4, 126.1, 77.9, 64.5, 43.2, 32.4; ^11^B NMR (160 MHz, CDCl$_3$), δ 27.04; IR (film)ν$_{max}$ 3057, 3027, 2903, 1950, 1600, 1312, 1261; Boron removed for MS. HRMS(EI) calculated for C$_{14}$H$_{16}$O$_2$S$_2$Na, [M+Na]+$^+$; 303.0484, found 303.0485.

4,4-dimethyl-5-(3-methylbut-2-en-1-yl)-2-phenyl-1,3,2-dioxaborinane (2s):

Synthesized according to the general procedure using 3-methylbut-2-en-1-ol (68.9 mg, 0.8 mmol), phenyl boronic acid (48.8 mg, 0.4 mmol) and triflic acid (0.4 uL, .04 mmol). The reaction was purified by flash chromatography with 70% DCM 30% hexanes and 1% triethylamine. The product was isolated as an oil (87.8 mg, 85%, 8:1 DR). R$_f$: 0.1 in 1:1 DCM:hexanes; ^1^H NMR (500 MHz, CDCl$_3$), δ 7.84 (dd, J = 8.1, 1.7 Hz, 2H); 7.51-7.33 (m, 3H); 5.23-5.14 (m, 1H); 4.13 (dd, J = 11.6, 4.3 Hz, 1H); 3.95-3.77 (m, 1H); 2.40-2.33 (m, 1H); 2.22-2.13 (m, 1H); 1.93-1.88 (m, 1H); 1.77 (s, 3H); 1.67 (s, 3H); 1.48 (s, 3H); 1.32 (s, 3H); ^13^C NMR (126 MHz, CDCl$_3$), δ 133.7, 133.5, 130.4, 129.1, 128.2, 127.5, 121.8, 73.9, 63.1, 48.6, 33.9, 29.3, 26.4, 25.8, 23.8, 17.8; ^11^B NMR (160 MHz, CDCl$_3$), δ 25.6; IR (film)ν$_{max}$ 3057, 3027, 2903, 1950, 1600, 1312, 1261; Boron removed for MS. HRMS(EI) calculated for C$_{10}$H$_{20}$O$_2$Na, [M+Na]+$^+$; 195.1356, found 195.1351.

3.3.5 Derivatization Studies

2-cinnamyl-1-phenylpropane-1,3-diol (3)

In a vial 5-cinnamyl-2,4-diphenyl-1,3,2-dioxaborinane (0.4 mmol, 141.7mg) and sodium hydroxide (2 mmol, 80mg) in a 1:1 solution of THF:H$_2$O (8 mL) was stirred at 60 °C for 20 h. The product was then extracted from the mixture with DCM, and the combined organics were dried over sodium sulphate. The product was isolated as an oil (107.3 mg, 100%). R$_f$: 0.1 in 1:1 DCM:hexanes; ^1^H NMR (500 MHz, CDCl$_3$), δ 7.50-7.21 (m, 10 H); 6.41 (d, J=15.9 Hz, 1H); 6.09 (dt, J = 15.7, 6.7 Hz, 1H); 5.00 (d, J =7.3, 1H); 4.21 (dd, J=10.73, 3.12 Hz, 1H); 3.99 (dd, J = 11.77, 7.96 Hz, 1H); 2.393-2.320 (m, 1H); 2.245-2.163 (m, 2H); ^13^C NMR (126 MHz, CDCl$_3$),
δ 141.4, 137.1, 134.0, 132.6, 130.8, 128.5, 128.5, 128.0, 127.6, 127.3, 126.5, 126.4, 126.1, 77.9, 64.5, 43.2, 32.4. 11B NMR (160 MHz, CDCl3): δ 27.04; IR (film) νmax 3057, 3027, 2903, 1950, 1600, 1312, 1261; HRMS(EI) calculated for C18H21O2, [M+H]+: 268.1463, found 268.1725

**Dicinnamyl phenylboronate (4)**

In a dry vial cinnamyl alcohol (0.8 mmol, 107.4 mg) and phenyl boronic acid (0.4 mmol, 48.8 mg) were stirred in toluene (0.4 mL) for 10 min at room temperature. The product was achieved in quantitative yield and used for the following reaction. The product was isolated as a clear oil (141.7 mg, >99%). 1H NMR (500 MHz, CDCl3): δ 7.85 (d, J = 7.2 Hz, 1 H); δ 7.68 (d, J = 5.9 Hz, 1 H); δ 7.43-7.17 (m, 15 H); δ 6.67-6.57 (m, 2 H); δ 6.38-6.26 (m, 2 H); δ 4.71 (d, 4 H) 13C NMR (126 MHz, CDCl3), δ 137.0, 134.8, 133.6, 131.5, 130.7, 130.1, 128.7, 128.1, 128.0, 127.7, 126.6; HRMS(EI) calculated for C24H24BO2, [M+H]+ 355.1864, found 355.1861

**bis(cinnamyloxy)dimethylsilane (5)**

In a dry vial, cinnamyl alcohol (7.5 mmol, 1.026 g) and triethylamine (7.8 mmol, 1.1 mL) were stirred for 5 minutes at room temperature in dichloromethane (8mL). Dimethyl dichlorosilane (3.7 mmol, 0.45 mL) was added slowly and the reaction was stirred for 4 hours at room temperature. The solution was concentrated, washed with pentane, and filtered. The reaction was purified by flash chromatography with 5% methanol in dichloromethane. The product was isolated as an oil (817 mg, 68%). Characterization matched literature by Fleming, (Tet. Lett. 1992, 33, 1013-1016). 1H NMR (500 MHz, CDCl3): δ = 7.38 (d, J = 8.5 Hz, 4 H), 7.31 (t, J = 8.0 Hz, 4 H), 7.25-7.23 (m, 2 H), 6.63-6.59 (m, 2 H), 6.36-6.29 (m, 2 H), 4.45-4.44 (dd, J = 1.5, 5.5 Hz, 3 H), 4.43-4.41 (dd, J = 1.5, 5.5 Hz, 1 H), 0.26 (s, 4 H), 0.20 (s, 2 H).
(2'-phenyl-[1,1'-binaphthalen]-2-yl)boronic acid (6)

Prepared following the procedure by Hisashi (Synthesis, 2017, 49, 175–180). A mixture of 1,1'-binaphthyl-2,2'-diboronic acid (3, 171 mg, 0.5 mmol, 1 equiv), Pd(PPh₃)₄ (14.4 mg, 2.5 mol%), Ba(OH)₂·8H₂O (315.5 mg, 1 mmol, 2 equiv), and iodobenzene (56 μL, 0.5 mmol, 1 equiv) in THF (5 mL) and water (1 mL) was heated at 60 °C for 14 h. The mixture was then allowed to cool down to r.t. The residue was extracted with CH₂Cl₂, washed with brine and dried (Na₂SO₄). After filtration and removal of solvent, the crude product was purified by column chromatography (hexane/EtOAc 4:1) to afford the product (136 mg, 73%) as a white solid. The enantiomeric excess of 6 was determined to be 96.4 percent ee by HPLC (Hexanes/iPrOH 80:20, flow rate = 1.0 mL/min, λ = 254 nm, T = 20 °C). Spectral data matched reported literature.

(4R,5R)-5-cinnamyl-4-phenyl-2-((R)-2'-phenyl-[1,1'-binaphthalen]-2-yl)-1,3,2-
dioxaborinane (7)

In a flame dried vial cinnamyl alcohol (0.748 mmol, 100 mg) and 2'-phenyl-[1,1'-binaphthalen]-2-yl)boronic acid (0.374 mmol, 140 mg) were stirred in toluene (0.4 mL) at room temperature for 10 min. Triflic acid (0.0374 mmol, 5.6 mg) was added and the reaction continued for 8 h. The reaction was purified by flash chromatography with 70% DCM 30% hexanes and 1% triethylamine. The product was isolated as an oil. (162.2 mg, 71.4%, 1.2:1 DR) ¹H NMR (500 MHz, CDCl₃), δ 7.92 (d, J=7.0 Hz, 1H); 7.50-7.21 (m, 23H); 6.41 (d, J=15.9 Hz, 1H); 6.09 (td, J=15.7, 6.7 Hz, 1H); 5.00 (d, J=7.3 Hz, 1H); 4.21 (dd, J=10.7, 3.1 Hz, 1H); 3.99 (dd, J=11.8, 7.9 Hz, 1H); 2.39-2.32 (m, 1H); 2.24-2.16 (m, 2H); ¹³C NMR (126 MHz, CDCl₃), δ 141.4, 137.1, 134.0, 134.0, 132.6, 130.8, 128.5, 128.5, 128.0, 127.6, 127.3, 126.5, 126.4, 126.1, 77.9, 64.5, 43.2, 32.4 ; ¹¹B NMR (160 MHz, CDCl₃), δ 27.04; IR (film)νmax 3057, 3027, 2903,
2-(2,4-diphenyl-1,3,2-dioxaborinan-5-yl)acetaldehyde (8)

In a dry vial 5-cinnamyl-2,4-diphenyl-1,3,2-dioxaborinane (0.28 mmol, 100 mg) and 2.5% wt Osmium tetroxide (0.0043 mmol) were dissolved in 0.6 mL THF:H2O 3:1 solution. Sodium periodate (0.56 mmol, 120 mg) was added slowly and the reaction proceeded stirring at room temperature for two hours. The reaction was quenched with sodium bicarbonate, extracted with CH2Cl2 and then purified by flash chromatography. The product was isolated as an oil (77 mg, 98.2%, 14:1 DR). Rf: 0.1 in 1:1 DCM:hexanes; 1H NMR (500 MHz, CDCl3), δ 9.62 (s, 1H), δ 7.91 (d, J = 7.0 Hz, 2H), 7.47-7.30 (m, 10H), 5.01 (d, J = 7.2 Hz, 1H), 4.20 (dd, J = 11.0, 4.0 Hz, 1H), 3.95-3.90 (m, 1H), 2.73-2.68 (m, 1H), 2.66-2.46 (m, 2H); 13C NMR (126 MHz, CDCl3), δ 199.5, 140.7, 134.2, 131.1, 128.8, 128.3, 127.6, 126.4, 64.2, 43.0, 37.6; 11B NMR (160 MHz, CDCl3), δ 27.04; IR (film)νmax 3057, 3027, 2903, 1950, 1700, 1312, 1261; HRMS(EI) calculated for C17H17O3B, [M+H]+; 280.1271, found 280.1702

2,4-diphenyl-5-(3-phenylpropyl)-1,3,2-dioxaborinane (9)

In a flame dried vial with 5-cinnamyl-2,4-diphenyl-1,3,2-dioxaborinane (0.4235 mmol, 150 mg) and 10% palladium on carbon (20 mg) were stirred in methanol (4 mL) for 7 h while H2 gas was bubbled through. Product was purified by column chromatography. The product was isolated as an oil (137.9 mg, 91%, 14:1 DR). Rf: 0.1 in 1:1 DCM:hexanes; 1H NMR (500 MHz, CDCl3), δ 7.88 (d, J=7.0 Hz, 2H); 7.50-7.21 (m, 15H); 4.93 (d, J=7.29 Hz, 1H); 4.21 (dd, J=10.73, 3.12 Hz, 1H); 3.99 (dd, J=11.8, 8.0 Hz, 1H); 2.39-2.32 (m, 2H); 2.24-2.16 (m, 3H); 13C NMR (126 MHz, CDCl3), δ 141.4, 137.1, 134.0, 134.0, 132.6, 130.8, 128.5, 128.5, 128.0, 127.6, 127.3, 126.5, 126.4, 126.1, 77.9, 64.5, 43.2, 32.4; 11B NMR (160 MHz, CDCl3), δ 27.04; IR (film)νmax 3057, 3027, 2903, 1950, 1600, 1312, 1261; Boron removed HRMS(EI) calculated for C24H25BO2, [M+H]+; 356.1948, found 356.1760
5-allyl-2,4-diphenyl-1,3,2-dioxaborinane (10)

In a flame dry vile with 5-cinnamyl-2,4-diphenyl-1,3,2-dioxaborinane (2a) (0.28 mmol) and Hoveyda Grubbs 2\textsuperscript{nd} generation catalyst (0.02 mmol) in DCE (10 mL) Ethylene gas was bubbled through via a balloon and syringe. After 48 h crude product was purified by column chromatography with 1:1 DCM:hexanes as the eluent. The product was isolated as an oil (56.4 mg, 72%, 14:1 DR). \( R_f \): 0.1 in 1:1 DCM:hexanes; \(^1\text{H} \) NMR (500 MHz, CDCl\(_3\)), \( \delta \) 7.89 (d, \( J=7.0 \) Hz, 2H); 7.50-7.34 (m, 8H); 5.78-5.68 (m, 1H); 5.12-5.05 (m, 2 H); 4.96 (d, \( J=7.4 \) Hz, 1H); 4.18 (dd, \( J=11.9, 4.0 \) Hz, 1H); 3.96-3.91 (m, 1H); 2.25-2.18 (m, 1H); 2.15-2.00 (m, 2H); \(^{13}\text{C} \) NMR (126 MHz, CDCl\(_3\)), \( \delta \) 141.4, 134.7, 134.0, 130.9, 128.5, 127.9, 127.6, 126.5, 117.5, 77.9, 64.6, 42.6, 33.1; \(^{11}\text{B} \) NMR (160 MHz, CDCl\(_3\)), \( \delta \) 27.04; IR (film)\( \nu_{\text{max}} \) 3057, 3027, 2903, 1950, 1600, 1312, 1261; HRMS(EI) calculated. for C\(_{18}\)H\(_{19}\)BO\(_2\), [M+H]+; 278.1478, found 278.2058.

2,4-diphenyl-5-((3-phenyloxiran-2-yl)methyl)-1,3,2-dioxaborinane (11)

Dimethyldioxirane (DMDO) was prepared following the procedure in Org. Synth. 2013, 90, 350-357. In a vial with 5-cinnamyl-2,4-diphenyl-1,3,2-dioxaborinane (100 mg, 0.2823 mmol) and DMDO (0.3105 mmol) in 10 mL acetone was stirred for 16 h at room temperature. Solvent was removed under reduced pressure and purified by chromatography with 70:30 DCM hexane as the eluent. Product was purified as a 1:1 ratio of diastereomers. The product was isolated as an oil (73.6 mg, 71.4%, 14:1 DR). \( R_f \): 0.1 in 1:1 DCM:hexanes; \(^1\text{H} \) NMR (500 MHz, CDCl\(_3\)), \( \delta \) 7.89 (d, \( J=7.0 \) Hz, 2H); 7.50-7.18 (m, 15H); 5.00 (dd, \( J=7.3 \) Hz, 1H); 4.43-4.26 (m, 1H); 4.07 (d, \( J=44.6 \) Hz, 1H); 2.92-2.85 (m, 1H); 2.38-2.29 (m, 1H); 1.95-1.81 (m, 1H); 1.71-1.44(m, 2H); \(^{13}\text{C} \) NMR (126 MHz, CDCl\(_3\)), \( \delta \) 141.4, 137.1, 134.0, 134.0, 132.6, 130.8, 128.5, 128.0, 127.7, 126.6, 126.4, 125.5, 125.4, 78.2, 77.9, 65.2, 64.3, 61.0, 60.5, 59.2, 58.2, 42.1, 40.8, 31.7; \(^{11}\text{B} \) NMR (160 MHz, CDCl\(_3\)), \( \delta \) 27.04; IR (film)\( \nu_{\text{max}} \) 3057, 3027, 2903, 1950, 1600, 1312, 1261; HRMS(EI) calculated. for C\(_{24}\)H\(_{23}\)O\(_3\)B, [M+H]+; 370.1740, found 370.3520

3.3.6 NOE Studies
NOE studies were performed on (tertbutyl substrate with Boron) to confirm the trans stereochemistry of our two substituents. Table X shows the relative intensities of the peaks for hydrogens in question. From the below table, we can see that H₇ sees H₈b but cannot see H₈a, and H₆ can see H₈a but not H₈b. Although we have these results, the intensities do not exactly match expected ratios for a molecule in a chair conformation. However, through process of elimination we know that it cannot be any other arrangement. If H₇ was equatorial, it would not be able to see H₈a or H₈b so it must be axial. Similarly, if H₆ was equatorial it would have to see H₈b much more strongly than it currently does. The odd intensity ratios in our NOE experiments are due to the boron distorting the ring as it strains to move towards a 120° bond angle. The J-coupling values also help to prove this. 1,2 diaxial hydrogens (H₆ and H₇, and H₆ and H₈b) should have coupling values between 8-13 Hz, but here J₇,₆ = 7.0 Hz and J₈b,₆ = 8.0 Hz which are a little low due to the distorted chair shape. Although the coupling between an axial and equatorial hydrogen in a 1,2 relationship is about right (J₈a,₆ = 3.7 Hz), the relationship between geminal hydrogens is also a little lower than what would be expected (J₈a,₈b = 11.5 Hz). We can further confirm the trans nature of our substrates by comparing the NOE studies of (tertbutyl substrate) with the crystal structure taken of (cinnamyl derivative) where the ring substituents come off trans and the bond angle of boron is 123.3°. Thus, we can infer that all of our substrates contain the same stereochemistry.

<table>
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<th></th>
<th>H₄</th>
<th>H₅</th>
<th>H₆</th>
<th>H₇</th>
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<tr>
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<tr>
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<td>2.40%</td>
<td>19%</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3.1. How strongly different hydrogens see each other in (tбу substrate) by NOE experiments.
3.3.7 NMR Data

2a. 5-cinnamyl-2,4-diphenyl-1,3,2-dioxaborinane $^1$H NMR

![1H NMR spectrum of 5-cinnamyl-2,4-diphenyl-1,3,2-dioxaborinane](image)

2a. 5-cinnamyl-2,4-diphenyl-1,3,2-dioxaborinane $^{13}$C NMR

![13C NMR spectrum of 5-cinnamyl-2,4-diphenyl-1,3,2-dioxaborinane](image)
2b. (E)-4-(4-bromophenyl)-5-(3-(4-bromophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane $^1$H NMR

2b. (E)-4-(4-bromophenyl)-5-(3-(4-bromophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane $^{13}$C NMR
2c. (E)-4-(4-methoxyphenyl)-5-(3-(4-methoxyphenyl)allyl)-2-phenyl-1,3,2-dioxaborinane $^1$H NMR

2c. (E)-4-(4-methoxyphenyl)-5-(3-(4-methoxyphenyl)allyl)-2-phenyl-1,3,2-dioxaborinane $^{13}$C NMR
2d. (E)-2-phenyl-4-(p-tolyl)-5-(3-(p-tolyl)allyl)-1,3,2-dioxaborinane $^1$H NMR

2d. (E)-2-phenyl-4-(p-tolyl)-5-(3-(p-tolyl)allyl)-1,3,2-dioxaborinane $^{13}$C NMR
2e. \((E)-4-(4\text{-ethylphenyl})-5-(3-(4\text{-ethylphenyl})\text{allyl})-2\text{-phenyl}-1,3,2\text{-dioxaborinane}\ ^{1}\text{H NMR}

2e. \((E)-4-(4\text{-ethylphenyl})-5-(3-(4\text{-ethylphenyl})\text{allyl})-2\text{-phenyl}-1,3,2\text{-dioxaborinane}\ ^{13}\text{C NMR}
2f. (E)-4-(4-pentylphenyl)-5-(3-(4-pentylphenyl)allyl)-2-phenyl-1,3,2-dioxaborinane $^1$H NMR

2f. (E)-4-(4-pentylphenyl)-5-(3-(4-pentylphenyl)allyl)-2-phenyl-1,3,2-dioxaborinane $^{13}$C NMR
2g. (E)-4-(4-(tert-butyl)phenyl)-5-(3-(4-(tert-butyl)phenyl)allyl)-2-phenyl-1,3,2-dioxaborinane

$^1$H NMR

$^13$C NMR
2h (E)-4-(4-chlorophenyl)-5-(3-(4-chlorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane $^1$H NMR

![NMR spectrum of 2h (E)-4-(4-chlorophenyl)-5-(3-(4-chlorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane]

2h (E)-4-(4-chlorophenyl)-5-(3-(4-chlorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane $^{13}$C NMR

![NMR spectrum of 2h (E)-4-(4-chlorophenyl)-5-(3-(4-chlorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane]
2i. (E)-2-phenyl-4-(4-(trifluoromethyl)phenyl)-5-(3-(4-(trifluoromethyl)phenyl)allyl)-1,3,2-
dioxaborinane $^1$H NMR

![NMR spectrum image]

2i. (E)-2-phenyl-4-(4-(trifluoromethyl)phenyl)-5-(3-(4-(trifluoromethyl)phenyl)allyl)-1,3,2-
dioxaborinane $^{13}$C NMR

![NMR spectrum image]
2j. (E)-2-phenyl-4-(m-tolyl)-5-(3-(m-tolyl)allyl)-1,3,2-dioxaborinane $^1$H NMR

2j. (E)-2-phenyl-4-(m-tolyl)-5-(3-(m-tolyl)allyl)-1,3,2-dioxaborinane $^{13}$C NMR
2k. \((E)-4\)-(3-chlorophenyl)-5-(3-(3-chlorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane \(^1\)H NMR

![NMR spectrum of (E)-4-(3-chlorophenyl)-5-(3-(3-chlorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane](image1)

2k. \((E)-4\)-(3-chlorophenyl)-5-(3-(3-chlorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane \(^1\)C NMR

![NMR spectrum of (E)-4-(3-chlorophenyl)-5-(3-(3-chlorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane](image2)
2l. (E)-2-phenyl-4-((o-tolyl)-5-(3-(o-tolyl)allyl)-1,3,2-dioxaborinane $^1$H NMR

2l. (E)-2-phenyl-4-((o-tolyl)-5-(3-(o-tolyl)allyl)-1,3,2-dioxaborinane $^{13}$C NMR
2m. \((E)-4-(2\text{-methoxyphenyl})-5-(3-(2\text{-methoxyphenyl})\text{allyl})-2\text{-phenyl}-1,3,2\text{-dioxaborinane}\) \(^1\text{H}\) NMR

![1H NMR spectrum]

2m. \((E)-4-(2\text{-methoxyphenyl})-5-(3-(2\text{-methoxyphenyl})\text{allyl})-2\text{-phenyl}-1,3,2\text{-dioxaborinane}\) \(^{13}\text{C}\) NMR

![13C NMR spectrum]
2n. (E)-1-(naphthalen-1-yl)-2-(3-(naphthalen-1-yl)allyl)propane-1,3-diol $^1$H NMR

2n. (E)-1-(naphthalen-1-yl)-2-(3-(naphthalen-1-yl)allyl)propane-1,3-diol $^{13}$C NMR
2o. \((E)-4-(4-(\text{tert-buty}l)\text{phenyl})-5-(3-(4-(\text{tert-buty}l)\text{phenyl})\text{allyl})-2-\text{phenyl}-1,3,2\)-dioxaborinane

\(^1\text{H NMR}\)

\(\text{13C NMR}\)
2p. (E)-3-phenyl-2-(3-phenylbut-2-en-1-yl)butane-1,3-diol $^1$H NMR

\[ \text{Diagram of NMR spectrum} \]

2p. (E)-3-phenyl-2-(3-phenylbut-2-en-1-yl)butane-1,3-diol $^{13}$C NMR

\[ \text{Diagram of NMR spectrum} \]
2q. (E)-4-(3,4-difluorophenyl)-5-(3-(3,4-difluorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane \( ^1 \text{H} \) NMR

2q. (E)-4-(3,4-difluorophenyl)-5-(3-(3,4-difluorophenyl)allyl)-2-phenyl-1,3,2-dioxaborinane \( ^{13} \text{C} \) NMR
2r. (E)-2-phenyl-4-(thiophen-2-yl)-5-(3-(thiophen-2-yl)allyl)-1,3,2-dioxaborinane $^1$H NMR

2r. (E)-2-phenyl-4-(thiophen-2-yl)-5-(3-(thiophen-2-yl)allyl)-1,3,2-dioxaborinane $^{13}$C NMR
2s. 4,4-dimethyl-5-(3-methylbut-2-en-1-yl)-2-phenyl-1,3,2-dioxaborinane $^1$H NMR

![NMR spectrum of 4,4-dimethyl-5-(3-methylbut-2-en-1-yl)-2-phenyl-1,3,2-dioxaborinane](image)

2s. 4,4-dimethyl-5-(3-methylbut-2-en-1-yl)-2-phenyl-1,3,2-dioxaborinane $^{13}$C NMR

![NMR spectrum of 4,4-dimethyl-5-(3-methylbut-2-en-1-yl)-2-phenyl-1,3,2-dioxaborinane](image)
3. 2-cinnamyl-1-phenylpropane-1,3-diol $^1$H NMR

3. 2-cinnamyl-1-phenylpropane-1,3-diol $^{13}$C NMR
4. Dicinnamyl phenylboronate $^1$H NMR

4. Dicinnamyl phenylboronate $^{13}$C NMR
7. (4R,5R)-5-cinnamyl-4-phenyl-2-((R)-2'-phenyl-[1,1'-binaphthalen]-2-yl)-1,3,2-dioxaborinane

$^1$H NMR

$^{13}$C NMR
8. 2-(2,4-diphenyl-1,3,2-dioxaborinan-5-yl)acetaldehyde $^1$H NMR

8. 2-(2,4-diphenyl-1,3,2-dioxaborinan-5-yl)acetaldehyde $^{13}$C NMR
9. 2,4-diphenyl-5-(3-phenylpropyl)-1,3,2-dioxaborinane $^1$H NMR

9. 2,4-diphenyl-5-(3-phenylpropyl)-1,3,2-dioxaborinane $^{13}$C NMR
10. 5-allyl-2,4-diphenyl-1,3,2-dioxaborinane $^1$H NMR

![$^1$H NMR spectrum of 5-allyl-2,4-diphenyl-1,3,2-dioxaborinane](image)

10. 5-allyl-2,4-diphenyl-1,3,2-dioxaborinane $^{13}$C NMR

![$^{13}$C NMR spectrum of 5-allyl-2,4-diphenyl-1,3,2-dioxaborinane](image)
1. 2,4-diphenyl-5-((3-phenyloxiran-2-yl)methyl)-1,3,2-dioxaborinane $^1$H NMR

![NMR spectrum](image1)

11. 2,4-diphenyl-5-((3-phenyloxiran-2-yl)methyl) -1,3,2-dioxaborinane $^{13}$C NMR

![NMR spectrum](image2)
References


Chapter 4  Synthesis and Characterization of a 2-phosphinoimidazole-Derived Bimetallic Rh(II) Complex

4.1 Introduction

Bimetallic transition metal catalysis is a growing field in organometallic chemistry that seeks to take advantage of the unique reactivity that can be achieved when two metals in the same complex work cooperatively together. This type of catalyst has begun to see significant application in organic synthesis and have shown unique reactivity that is not seen when using monometallic catalysts (Figure 4.1). The Mankad group has developed a Fe/Cu catalyst capable of performing C–H Borylation reactions. Their bimetallic catalyst enables unique reactivity in by undergoing binuclear oxidative addition into a B–H bond and binuclear reductive elimination by combination of an iron hydride intermediate with a copper hydride to reform the bimetallic complex.\(^1\) There is also evidence of binuclear bond breaking and bond forming mechanisms with other bimetallic catalysts.\(^2\) A bimetallic complex can also coordinate to reactants in distinct ways, allowing for increased activity. Uyeda has shown that a bimetallic nickel complex can coordinate to and activate aryl groups using both metal centers.\(^3\) Perhaps the most prevalent benefit of using bimetallic catalysts is that electronic communication between two metal centers can facilitate faster oxidative and reductive processes (e.g. oxidative addition). Traditionally, ligand design is used to influence the electron density on a metal and facilitate faster oxidative addition or reductive elimination. Metal–metal bonds can also be made or broken to facilitate these steps in a catalytic cycle. Rhodium tetraacetate is known for its ability to form metal carbenes and to facilitate insertion of diazo compounds into C-H bonds.\(^4\) One reason that dirhodium tetracarboxylates have shown greater activity in these reactions is because the two

![Mankad](image1.png)  
**Mankad**  
*C-H Borylation*

![Uyeda](image2.png)  
**Uyeda**  
*Hydrosilylation/Cyclopropanation*

![Doyle/Davies](image3.png)  
**Doyle/Davies**  
*Cyclopropanation/C-H Insertion*

![Michaelis](image4.png)  
**Michaelis**  
*Amination/Cycloisomerization*

**Figure 4.1** Bimetallic complexes with cooperative activity
metals share a metal–metal bond that allows the rhodium being oxidized or reduced to distribute that electronic burden over both rhodium centers. The Michaelis lab has also observed this type of metal–metal communication using Lewis acidic titanium with palladium. The titanium center was shown to remove electron density form the palladium via formation of a dative bond. This interaction increased the reactivity of the palladium for reductive elimination and increased the turnover of the catalyst by ~10^5. Thus, bimetallic complexes can take advantage of different effects to enable efficient catalysis that cannot occur at a single metal catalysts, including: binuclear mechanisms, bimetallic coordination, and electronic effects. In this chapter, we describe the discovery and characterization of a new bimetallic Rh(II) complex containing a bridging CO ligand. This complex has unique bonding interactions that helps facilitate the unique reactivity observed with this complex in catalysis.

4.2 Results and discussion

The Michaelis laboratory previously reported bimetallic Pd(I) and Pd(II) complexes scaffolded on a 2-phosphinoimidazole ligand (Figure 4.2). These complex shows unique reactivity in the synthesis of naphthalene products and in C–N cross couplings. The bite angle of the 2-phosphinoimidazole ligand prevents it from coordinating both the P and N donors to a single metal, which helps facilitate the formation of bimetallic rather than monometallic complexes. Thus, only bimetallic Pd complexes of the 2-phosphinoimidazole ligand were observed in our previous studies.

The goal of my efforts in bimetallic catalysis focused on the design and synthesis of rhodium-based bimetallic complexes on the same 2-phosphinoimidazole ligands framework. In our initial synthetic studies, we found that the addition of [Rh(cod)Cl]_2 to our phosphinoimidazole

![Figure 4.2 Structure of homobimetallic Palladium Complexes](image-url)
ligand led to the formation of a monometallic Rh(I) complex where only the phosphorous atom is coordinated to the Rh (Figure 4.3a). This complex could be isolated as a through crystallization as a cocrystal with \([\text{Rh(cod)Cl}]_2\). During our crystallization studies, we found that when methanol was used as solvent, a trace amount of a bimetallic rhodium complex containing a bridging CO ligand was formed. This bridging CO ligand likely formed through methanol oxidation. Based on this precedence, we attempted to form the complex under an atmosphere of carbon monoxide and obtained full conversion to the bimetallic complex (Figure 4.3b), which was isolated in 85% yield.

We next performed full characterization of this new bimetallic Rh(II) complex to better understand its bonding and potential reactivity. X-ray quality single crystals of the complex were
grown via slow evaporation and the structure was analyzed. The bimetallic complex shows a Rh–Rh bond distance of 2.6227 Å with a formal shortness ratio of 1.05. This data indicates the presence of a metal-metal bond. We also performed DFT calculations on this complex to investigate the bonding orbitals. The HOMO-3 and the HOMO-4 (Figure 4.4) clearly show significant orbital overlap between the two rhodium centers, providing strong evidence of a metal-metal bond. It should also be noted that the orbitals on the CO show significant back-bonding from the ligand. We believe that the stable bimetallic structure of this new dirhodium(II) complex is made possible via coordination of a bridging CO ligand.

Bridging CO ligands can bond in two different ways in bimetallic and multimetallic complexes. CO ligands may form a 3-center, 2-electron bond with two metals where the 5σ HOMO and a 2π* orbital of CO interact with appropriate metal d orbitals. The CO ligand in this scenario acts as a one-electron donor ligand (neutral bonding, µ-L type, Figure 4.5b). A bridging CO ligand can also bind as a ketone like ligand (µ-X2 type, Figure 4.5a). Over the last 20 years there has been much debate over when each type is assigned. However, a concrete method has been established. If the two metals are thought to use a single d orbital of appropriate symmetry in the overlap with the CO 5σ HOMO, then significant σ-donation occurs. The orbital from the out of phase metal combination of appropriate symmetry will interact with one of the 2π* C–O antibonding orbitals and show significant π-back-bonding. As seen in Figure 4.5 if both bonding and back-bonding are observed then it is a indicator of the ketone like ligand (µ-X2 type). If no back-bonding is observed, then it indicates a neutral µ-L type ligand. The Molecular orbitals for the bimetallic rhodium complex show both bonding and back-bonding interactions, indicating that the CO forms a 2-electron, 3-center bond in our complex. This ketone-like CO ligand results in the formation of two Rh(II) metals and facilitates the formation of a metal-metal bond. Thus, the bridging CO ligand creates a unique bonding situation in our

![Figure 4.4](image)
bimetallic complex, providing it with reactivity that we believe resides somewhere between that of traditional Rh(I) complexes and bimetallic Rh(II) tetraacetate complexes.

Based on the structural analysis of our bimetallic Rh(II) complex presented above, we believe that the two rhodium centers are potentially more electron rich than those in the more common dirhodium(II) tetracarboxylate catalysts. This would suggest that our complex may enable unique reactivity not seen with the tetracarboxylate complexes.

Few bimetallic rhodium complexes have been synthesised that also possess a bridging CO ligand and the reactivity of the few examples that have been reported has not been explored. We set out to determine whether our bimetallic catalyst had reactivity similar to Rh(I) catalysts or more similar to Rh(II) tetracarboxylates. In our initial reactivity studies, we found that our catalyst is reactive in numerous in reactions catalyzed by both Rh(I) and Rh(II) catalysts (Figure 4.6). Our bimetallic Rh complex is active in 4+2-cycloadditions, which have been known to use both

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**Figure 4.5** MOs for a M(μ-CO)M interaction (a) occupied by 4 electrons, giving two 2c–2e bonds and (b) occupied by 2 electrons, giving a 3c–2e bond. For (a), the CO is classified as a μ-X2 donor and contributes one electron to each metal, whereas for (b), the CO is classified as a μ-L donor and contributes a pair of electrons to both metals.
Rh(I)\(^{11}\) and Rh(II)\(^{12}\) complexes (Figure 4.6b). Our catalyst also shows good reactivity for reactions that typically use Rh(II), including cyclopropanations with diazo compounds (Figure 4.6c).\(^{13}\) Arylations of aldehydes with aryl halides (Figure 4.6d) and with phenylboronic acids (Figure 4.6e) also gave excellent yields with our catalyst. We also observed catalytic activity in the hydroamination of allenes,\(^{14}\) which traditionally uses Rh(I) catalysts (Figure 4.6f).

A variety of transition metals have been used in the hydroamination of allenes including Ag, Au, Rh, and Pd catalysts.\(^{15,16}\) The majority of examples of heterocycle-forming intramolecular hydroaminations only report the formation of 5-, and 6-member rings, However, an example of 7-member ring formation with Au catalysts was reported that used aniline substrates for the hydroamination of allenes.\(^{17}\) Hartwig has also reported a copper-catalyzed formation of 7-9-member ring using hydroxylamine derivatives (Figure 4.7b).
Due to the unique structure of our bimetallic Rh(II) catalyst, we wondered whether the hydroamination reaction of allenes could benefit from an expanded coordination sphere capable of coordinating both the allene and amine functional groups. This expanded transition state could lower the energy of the C-N bond forming event. To our delight, the bimetallic rhodium complex formed the 7-member product in excellent to good yield for a small number of substrates (Figure 4.8). Our catalyst is highly efficient at forming 5- and 6-member nitrogen heterocycles via hydroamination of the allene. In addition, aniline substrates undergo rapid cyclization to form the 7-member ring product. In addition, substrates containing an N-phenyl group also cyclize in the reaction to form 7-member rings, a result that has not been demonstrated with other catalysts. This final result is currently being optimized in our laboratory.

During our studies in hydroamination, we also discovered that linear substrates containing an N-tosyl group underwent addition of trifluoroacetic acid to the allene rather than

![Figure 4.7 Methods for the formation of medium sized rings](image)
cyclization. Interestingly, other rhodium catalysts favor the isomerization of the allene to a diene product rather than addition of trifluoroacetic acid (Figure 4.9). The diene isomer is the result of β-hydrogen elimination after forming the metal allyl. The product results from the reductive elimination after forming the metal allyl. We can deduct from this study that our bimetallic rhodium complex favors reductive elimination when other rhodium catalysts undergo beta-hydrogen elimination. The reactivity of our bimetallic Rh(II) complex for allene hydrofunctionalization reactions will be described in detail in chapter 5.

In conclusion, we have discovered a new bimetallic Rh(II) complex containing a bridging CO ligand. This new complex has unique bonding characteristics that we believe make it capable of performing reactions typically catalyzed by both Rh(I) and Rh(II) complexes. Initial reactivity studies demonstrate high reactivity in various systems, which provides ample opportunities to explore the reactivity of these new complexes. In particular, our bimetallic complex is capable of allene hydroamination reactions to form 7-membered heterocycles, and is uniquely active in the addition of trifluoroacetic acid to allenes.
Supporting Information

All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring, unless otherwise indicated. Solvents were dried by J. C. Meyer’s Solvent Purification System. Reactions requiring a moisture or oxygen-free environment were done in a nitrogen atmosphere glove box (Innovative Technology, PreLab HE system, double glove box). Flash chromatography was performed with Sorbtech silica gel (0.040-0.063µm grade). Analytical thin-layer chromatography was done with 0.25 mm coated commercial silica gel plates (Merck KGaA, DC silicagel 60 F254). Proton nuclear magnetic resonance (1H NMR) data were acquired on an Inova 300 (300 MHz), Inova-500 (500 MHz) or Bruker (500MHz) spectrometer. Chemical shifts are reported in delta (δ) units relative to the 2H signal of the CDCl₃ solvent. Carbon-13 nuclear magnetic resonance (13C-NMR) data were acquired on an Inova 500 or Bruker at 125 MHz. Signals are reported as follows: s (singlet), d

Figure 4.9 Rhodium catalysts in the trifluoroacetoxylation of allenes. Each reaction was performed under the standard conditions (shown above). The above rhodium complexes and ligands have been used in the past for hydroamination reactions or have similar characteristics to our catalyst. The ligands 4, 5 were added in 10 mol% with 5% [Rh(cod)Cl]₂.

4.3 Supporting Information

All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring, unless otherwise indicated. Solvents were dried by J. C. Meyer’s Solvent Purification System. Reactions requiring a moisture or oxygen-free environment were done in a nitrogen atmosphere glove box (Innovative Technology, PreLab HE system, double glove box). Flash chromatography was performed with Sorbtech silica gel (0.040-0.063µm grade). Analytical thin-layer chromatography was done with 0.25 mm coated commercial silica gel plates (Merck KGaA, DC silicagel 60 F254). Proton nuclear magnetic resonance (1H NMR) data were acquired on an Inova 300 (300 MHz), Inova-500 (500 MHz) or Bruker (500MHz) spectrometer. Chemical shifts are reported in delta (δ) units relative to the 2H signal of the CDCl₃ solvent. Carbon-13 nuclear magnetic resonance (13C-NMR) data were acquired on an Inova 500 or Bruker at 125 MHz. Signals are reported as follows: s (singlet), d
(doublet), t (triplet), q (quartet), dd (doublet of doublets), qd (quartet of doublets), brs (broad singlet), m (multiplet). Coupling constants are reported in hertz (Hz). Chemical shifts are reported in ppm relative to the center line of a triplet at 77.23 ppm for chloroform-d for $^{13}$C-NMR or the singlet at 0 ppm for BF$_3$ · O(Et)$_2$ for $^{11}$B-NMR. Infrared (IR) data were recorded as films on sodium chloride plates on a Thermo Scientific Nicolet IR 100 FT-IR spectrometer. Absorbance frequencies are reported in reciprocal centimeters (cm$^{-1}$). Mass spectral data were obtained using ESI techniques (Agilent, 6210 TOF).

4.3.1 Synthesis of Bimetallic Rhodium Ligand

![Chemical reaction diagram]

a) 2,6-diisopropylaniline (63.62 mmol, 12 mL, 0.94 g/mL) in methanol (32 mL) was cooled to 0°C and glyoxal (63.62 mmol, 9.23 mL, 40% in H$_2$O, 1 g/mL) was added. The reaction was allowed to warm to room temperature and stirred for 18 h. Ammonium chloride (127.25 mmol, 6.807 g), formaldehyde (127.25 mmol, 3.821 g), and methanol (254 mL) were added and the reaction was refluxed at 95°C for 1 h. Phosphoric acid (152.7 mmol, 8.88 mL, 85% in H$_2$O, 1.685 g/mL) was added dropwise and the reaction continued refluxing for 5 h. After cooling to room temperature, the solvent was removed under reduced pressure, ice water (180 mL) was added, and the reaction was brought to a pH of 9 using KOH. The product was extracted using diethyl ether (3 × 10 mL/mmol) and washed with brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude product was purified by flash chromatography (SiO$_2$, DCM:EtOAc = 1:1) (49% yield). Spectral data matched previously reported values.$^1$

b) 1-(2,6-diisopropylphenyl)-imidazole (4.351 mmol, 993.4 mg) was dissolved in THF (21.8 mL), cooled to -78°C and n-butyllithium (1.91 mL) and TMEDA (4.786 mmol, 0.72 mL, 0.775 g/mL) were added dropwise. After stirring for 1 h, chlorodiphenylphosphine (4.351 mmol, 0.78 mL, 1.23 g/mL) was added, the reaction was allowed to warm to room temperature and the reaction continued for 18 h. The reaction was quenched with H$_2$O, solvent was removed under reduced pressure, and the ligand product was extracted with DCM (3 × 10 mL/mmol). The
organic phases were dried over sodium sulfate, solvent was removed under reduced pressure, and
the crude ligand product was purified by flash chromatography (SiO₂, hexanes:EtOAc = 2:1)
(77% yield). Spectral data matched previously reported values.²

4.3.2 Synthesis of Bimetallic Rhodium Catalyst

In a dry round-bottom flask, 1,5-cyclooctadienerhodium(I) chloride dimer [Rh(COD)Cl]₂
(1.5 mmol, 739.6 mg) and 1-(2,6-diisopropylphenyl)-2-(diphenylphosphaneyl)-1H-imidazole (3
mmol, 1.24 g) were stirred in a 1:1 DCM:Methanol solution (15 mL) for 10 min at 40°C. Carbon
monoxide gas CO(g) was bubbled through the reaction for 10 min. The reaction continued under
CO(g) at 40°C for 18 h. The solvent was removed under reduced pressure leaving a solid crude
product that was dissolved in minimal DCE. Hexanes were added and the resulting precipitate
was isolated and washed using vacuum filtration and hexanes. The completed catalyst was
immediately placed under vacuum and stored a nitrogen atmosphere at 30°C (95% yield).

¹H NMR (500 MHz, CDCl₃), δ 8.24 (s, 2H), 7.50 – 7.46 (t, J = 10.4, 5H), 7.32 – 7.20
(m, 11H), 7.06 – 7.04 (d, J = 7.0, 6H), 6.94 (s, 2H), 6.69 – 6.68 (d, J = 7.1, 2H), 3.37 (s, 2H),
2.06 – 2.01 (m, 2H), 1.63 – 1.57 (m, 2H), 0.80 – 0.77 (q, J = 6.8, 12H), 0.39 – 0.37 (d, J = 6.7,
6H), 0.30 – 0.29 (d, J = 6.7, 6H). ¹³C NMR (126 MHz, CDCl₃), δ 146.6, 145.6, 144.0, 143.6,
132.9, 132.5, 132.4, 131.0, 130.1, 129.7, 127.5, 125.4, 124.9, 74.3, 58.6, 43.5, 28.8, 28.2, 26.8,
26.3, 20.9, 20.5. ³¹P NMR (202 MHz, CDCl₃), δ 42.2, 41.5. HRMS(EI) calculated for
C₅₅H₅₈ClN₄OP₂Rh₂ [M-Cl₂+H] +; 1058.2592, found 1058.2592

4.3.3 Synthesis of Monometallic Rhodium Catalyst

In a dry round-bottom flask, 1,5-cyclooctadienerhodium(I) chloride dimer [Rh(COD)Cl]₂
(1.5 mmol, 739.6 mg) and 1-(2,6-diisopropylphenyl)-2-(diphenylphosphaneyl)-1H-imidazole (3
mmol, 1.24 g) were stirred in a 1:1 dichloromethane (15 mL) at 40°C for 18 h. The solvent was
removed under reduced pressure leaving a solid crude product that was dissolved in minimal DCE. Hexanes were added and the resulting precipitate was isolated and washed using vacuum filtration and hexanes. The reaction was done in situ yielding 80% of the cyclooctadiene (cod) coordinated to the rhodium with the ligand and 20% coordinated to rhodium cod dichloride. This was observed by NMR. The catalyst mixture with Rh(cod)Cl₂ was immediately placed under vacuum and stored a nitrogen atmosphere at 30°C (95% yield).

$$^1$$H NMR (500 MHz, CDCl₃), δ 7.59 – 7.55 (m, 4H), 7.44 (s, 1H), 7.30 (s, 1H), 7.26 – 7.22 (m, 2H), 7.19 – 7.13 (m, 5H), 6.89 – 6.85 (m, 3H), 4.44 (s, 4H), 2.46 (s, 2H), 2.39 (s, 4H), 1.98 (d, J = 8.3, 4H), 0.93 (d, J = 6.7, 6H), ), 0.82 (d, J = 6.3, 6H).$$^{13}$$C NMR (126 MHz, CDCl₃), δ146.0, 140.2, 139.7, 135.4, 135.3, 134.1, 133.8, 133.6, 130.0, 129.9, 129.9, 129.9, 129.9, 128.9, 128.7, 128.4, 127.6, 127.5, 126.8, 123.6, 123.4, 30.9, 28.3, 26.4, 25.7, 22.4, 21.7.$$^{31}$$P NMR (202 MHz, CDCl₃), δ 23.67, 22.91, -35.75. HRMS(EI) calculated for C35H42ClN2PRh [M-Cl+H]⁺; 623.7300, found 623.7290

Excess COD: $$^1$$H NMR (500 MHz, CDCl₃), δ4.23 (s, 1H), 2.19 (s, 1H), 1.75 (s, 1H)

4.3.4 XRD Analysis of Bimetallic Rhodium Catalyst

An orange crystal was harvested under oil in ambient conditions and placed at the tip of a polyimide loop. Low-temperature (100 K) X-ray diffraction data comprising φ- and ω- scans were collected using a Bruker D8 Venture with a kappa goniometer, dual Cu and Mo diamond microfocus X-ray sources, a Bruker Photon-III detector, and an Oxford 800+ low temperature device. Mo Kά radiation (λ = 15.3431 Å) was used for this experiment. The Bruker APEX3 suite was used to process the data; reflection intensities were integrated through the program SAINT, and appropriate absorption corrections were applied to the intensities via a multi-scan method using the program SADABS.¹ The structure was solved using dual-space methods in SHELXT² and refined against $F^2$ on all data by full-matrix least squares with SHELXL-2014³ using established refinement strategies.⁴ All non-hydrogen atoms were refined anisotropically. The positions of all hydrogen atoms calculated geometrically and refined using a riding model.

4.3.4.1 Discussion points

Details of the crystal structure are listed in Table 1. The target molecule crystallized in the triclinic space group P-1 with the asymmetric unit containing two bimetallic rhodium
complexes. The asymmetric unit contained 3 dichloroethane molecules that were heavily disordered. The program SQUEEZE was used to remove the disordered solvent molecules. The 311 electron counts removed using SQUEEZE correspond well to 3 dichloroethane molecules in the asymmetric unit, 6 in the unit cell. Bond lengths and angles are listed in Table 3. Atomic coordinates and equivalent isotropic displacement parameters for all non-hydrogen atoms are given in Table 2. The full anisotropic displacement parameters are given in Table 4, and the H atom positions, and displacement parameters are given in Table 5.

CCDC deposition number: 2084938

Table 4.1 Crystal data and structure refinement for Rhodium.

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<td>Wavelength</td>
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<td>Space group</td>
<td>P-1</td>
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<tr>
<td></td>
<td>b = 18.0948(12) Å b= 98.764(3)°.</td>
</tr>
<tr>
<td></td>
<td>c = 22.7940(15) Å g = 106.157(2)°.</td>
</tr>
<tr>
<td>Volume</td>
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</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.293 Mg/m³</td>
</tr>
</tbody>
</table>
Absorption coefficient 0.754 mm$^{-1}$
F(000) 2312
Crystal size 0.183 x 0.092 x 0.086 mm$^3$
Theta range for data collection 1.950 to 26.399°.
Index ranges -19<=h<=19, -22<=k<=22, -28<=l<=28
Reflections collected 553975
Independent reflections 23742 [R(int) = 0.0767]
Completeness to theta = 25.242° 99.9 %
Absorption correction Semi-empirical from equivalents
Refinement method Full-matrix least-squares on F$^2$
Data / restraints / parameters 23742 / 1912 / 1209
Goodness-of-fit on F$^2$ 1.068
Final R indices [I>2sigma(I)] R1 = 0.0311, wR2 = 0.0743
R indices (all data) R1 = 0.0408, wR2 = 0.0815
Extinction coefficient n/a
Largest diff. peak and hole 1.209 and -0.806 e.Å$^{-3}$

4.3.5 XRD Analysis of Monometallic Rhodium Catalyst

The catalyst was dissolved in a minimal amount of dichloro ethane for slow evaporation. An orange crystal was harvested under oil in ambient conditions and placed at the tip of a polyimide loop. Low-temperature (100 K) X-ray diffraction data comprising $\phi$- and $\omega$- scans were collected using a Bruker D8 Venture with a kappa goniometer, dual Cu and Mo diamond microfocus X-ray sources, a Bruker-Nonius FR591 Cu rotating anode (Cu $K_\alpha$ radiation, $\lambda = 1.54178$ Å), a MACH3 kappa goniometer, and an ApexII CCD detector. The Bruker APEX3 suite was used to process the data; reflection intensities were integrated using SAINT, and absorption corrections and scaling were applied to the intensities via a multi-scan method using SADABS. The structure was solved using dual-space methods in SHELXT and refined against $F^2$ on all data by full-matrix least squares with SHELXL-2014 using established refinement strategies. The target molecule crystallized in the orthorhombic space group $Pbca$ with the asymmetric unit containing two different Rh complexes and one dichloroethane solvent molecule. All non-hydrogen atoms were refined anisotropically. The positions of all hydrogen
atoms bonded to carbon were calculated geometrically and refined using a riding model. The positions of the hydrogen on the imidazole nitrogen was taken from the difference Fourier synthesis and refined semi-freely with a distance restraint.

Monometallic catalyst was co-crystalized with rhodium cyclooctadiene chloride.

CCDC deposition number: 2113039
4.3.6 Gaussian Computed Orbitals of Bimetallic Rhodium Catalyst

**DFT method** B3LYP/7-31g(d,p)[Rh,lanl2dz]
4.3.7 General Synthesis of Allene Starting Materials

4.3.7.1 General Procedure 1:

\[\text{HO-CH=CH-[C≡C-CH] (1.0 eq)}\rightarrow \text{HO-CH=CH-[C≡C-CH] (1.0 eq)}\rightarrow \text{TsO-CH=CH-[C≡C-CH] (1.0 eq)}\rightarrow \text{Ts-CH=CH-[C≡C-CH] (1.0 eq)}\]

a) Allyne substrate (1.0 eq), copper (I) bromide (0.70 eq), and paraformaldehyde (2.0 eq) were suspended in 1,4-dioxane (0.1 M) at room temperature. The solution was stirred for 30 min and dicyclohexylamine (2.0 eq) was added. The reaction was refluxed at 100°C for 18 h. After cooling to room temperature, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate (3 × 10 mL/mmol) and washed with 1 M HCl and brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude allene product was purified by flash chromatography (SiO₂, hexanes:EtOAc = 3:1).

b) To a solution of p-toluenesulfonyl chloride (1.1 eq) in DCM (0.3 M) at 0°C, the allene substrate (1.0 eq) and triethyl amine (2.0 eq) were added. The reaction was allowed to return to room temperature and stirred for 16 h.

c) Tosylated substrate (1.0 eq), p-toluenesulfonamide (2.0 eq), and potassium carbonate (2.0 eq) were combined in acetonitrile (0.2 M) and refluxed at 100°C for 12 h. After cooling to room temperature, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate (3 × 10 mL/mmol) and washed with 1 M HCl and brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude allene product was purified by flash chromatography (SiO₂, hexanes:EtOAc = 19:1 – 5:1).

4.3.7.2 General Procedure 2:
a) Alkyne substrate (1.0 eq), trimethyl orthoacetate (1.6 eq), and propanoic acid (0.16 eq) were suspended in toluene (0.7 M). Reaction stirred at room temperature for 20 min and then was refluxed at 150ºC with a Dean Stark trap for 16 h. Afterwards, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate (3 × 10 mL/mmol) and washed brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure.

b) To a solution of allene substrate (1 eq) suspended in diethyl ether (0.4 M) at 0ºC, LAH (1.6 eq) was added. The reaction was allowed to return to room temperature and was stirred for 1 h. Afterwards, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate (3 × 10 mL/mmol) and washed brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude allene product was purified by flash chromatography (SiO₂, hexanes:EtOAc = 9:1 – 4:1).

4.3.7.3 General Procedure 3:

Under inert conditions, in an oxygen free environment, the allene substrate (0.2 mmol), Rh-Rh catalyst (0.01 mmol), and Dichloroethane (DCE) (2 mL, 0.1 M) were added to a dry vial and stirred for one minute. Trifluoro acetic acid (TFA) (0.2 mmol) was then added, and the reaction was then heated to 80ºC. Reaction was allowed to run overnight or 18 hours. Product purification and separation from catalyst achieved through flash chromatography.
N-(Octa-6,7-dien-1-yl)aniline (4h): Synthesis began according to GS1a-GS1b. Octa-6,7-dien-1-yl 4-methylbenzenesulfonate (4.23 mmol, 1.2 g) was then combined with aniline (42.3 mmol, 3.94 g), acetonitrile (190.35 mmol, 9.94 mL), and triethyl amine (4.653 mmol, 471 mg) and was refluxed at 83°C for 16 h. After allowing reaction to return to room temperature, sodium bicarbonate was used to neutralize the reaction, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate (3 x 10 mL/mm) and washed with brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude allene product was purified by flash chromatography (SiO2, hexanes:EtOAc:Et3N 90:9:1) to yield the product (0.2043 g, 1.015 mmol, 24%) The product was isolated as an orange oil.

^1H NMR (500 MHz, CDCl3), δ 7.17 (t, J = 7.5, 2H); 6.69 (t, J = 7.3, 2H); 6.61 (d, J = 7.7, 1H); 5.10 (p, J = 6.7, 1H); 4.67 (p, J = 3.4, 2H); 3.59 (s, 1H); 3.11 (t, J = 7.15, 2H); 2.02 (m, 2H); 1.63 (m, 2H); 1.46 (m, 4H); ^13C NMR (126 MHz, CDCl3), δ 148.5, 129.3, 117.1, 112.7, 89.8, 74.4, 43.9, 29.3, 28.8, 26.6, 26.3; IR (film) λmax (3411, 2931, 1955, 1602) HRMS(EI) calculated for C14H20N [M+H]^+; 202.1551, found 202.1571

4-Methyl-N-(2-((5-methylhexa-3,4-dien-1-yl)oxy)phenyl)benzenesulfonamide (4m):
2-((5-methylhexa-3,4-dien-1-yl)oxy)aniline (350 mg, 1.72 mmol) was added to a solution of triethylamine (209 mg, 2.06 mmol), p-toluenesulfonyl chloride (392.7 mg, 2.06 mmol) and dichloromethane (4 mL) at 0°C. The reaction was allowed to return to room temperature and stirred overnight. Solvent was removed, product was washed with brine and extracted with ethyl acetate. The product (0.61 g, 1.7 mmol, 99%) was obtained after flash chromatography (SiO2, hexanes:EtOAc = 20:1).

NMR (500 MHz, CDCl3), δ 7.63 (d, J = 8.4, 2H), 7.54 (dd, J = 8.0 and 1.6, 1H), 7.18 (d, J = 8.0, 2H), 7.01 (td, J = 7.9 and 1.4, 1H), 6.98 (s, 1H), 6.89 (td, J = 7.8 and 1.1, 1H), 6.72 (dd, J = 8.2 and 1.1, 1H), 4.91-4.86 (m, 1H), 3.82 (t, J = 6.7, 2H) 2.35 (s, 3H), 2.27 (q, J = 6.7, 2H), 1.69 (d, J = 2.9, 6H), 1.56 (s, 1H). ^13C NMR (126 MHz, CDCl3), δ 202.5, 148.8, 143.6, 136.3, 129.3, 127.2, 126.0, 125.3, 121.3, 121.0, 111.3, 84.3, 67.9, 29.0, 21.5, 20.6. IR (film) λmax
2-((5-Methylhexa-3,4-dien-1-yl)oxy)aniline (4n): 5-methylhexa-3,4-dien-1-ol was synthesized from 2-methylbut-3-yn-2-ol (1.7g, 20.8mmol) following GS2. Product matched known spectra\textsuperscript{11} (1.935 g, 17.4mmol, 84% yield over 2 steps).

5-methylhexa-3,4-dien-1-ol (0.976 g, 8.7 mmol) and triphenyl phosphine(2.5 g, 9.57 mmol) was added to a solution of 2-nitrophenol (1.33 g, 9.57 mmol) and diisopropyl azodicarboxylate (1.935g, 9.57 mmol) in dichloromethane at 0°C. The reaction was allowed to return to room temperature and stirred overnight (18H). The reaction was washed with brine and extracted with ethyl acetate. The product (0.9 g, 3.86 mmol, 44%) was obtained after flash chromatography (SiO$_2$, hexanes:EtOAc = 98:2). The resulting product (0.9 g, 3.86 mmol) was then placed in a round bottom flask with water (4mL) and ethanol (16 mL). Iron powder (2.15 g, 38.6 mmol) and a catalytic amount of concentrated hydrochloric acid (0.2 mL). The reaction refluxed for 6 hours, the solvent was removed under reduced pressure, and filtered over celite. The product (0.45 g, 2.2 mmol, 57%) was obtained after flash chromatography (SiO$_2$, hexanes:EtOAc = 5:1).

\textsuperscript{1}H NMR (500 MHz, CDCl$_3$), $\delta$ 6.7 (d, $J = 7.9$, 1H), 6.87 (t, $J = 6.2$, 1H), 6.79 (t, $J = 7.6$, 1H), 6.71 (d, $J = 7.8$, 1H), 5.29 (d, $J = 9.5$, 1H), 4.42 – 4.38 (m, 1H), 3.93 (dt, $J = 9.7$, 18.6, 1H), 3.85 – 3.80 (m, 1H), 3.32 (s, 1H), 1.96 – 1.89 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H). \textsuperscript{13}C NMR (126 MHz, CDCl$_3$), $\delta$ 150.31, 140.85, 134.64, 127.03, 123.37, 121.66, 120.97, 119.94, 70.49, 54.47, 38.09, 25.68, 18.32. IR (film) $\lambda_{\text{max}}$ (3151, 2250, 1611, 1454, 1380, 1092). HRMS(EI) calculated for C$_{13}$H$_{18}$NO [M+H] $^+$204.1344, found 204.1368.

5 member ring product
1-tosyl-2-vinylpyrrolidine(7): 1-tosyl-2-vinylpyrrolidine (44mg, 0.176mmol, 88%) was synthesized according to GS3 with N-(hexa-4,5-dien-1-yl)-4-methylbenzenesulfonamide (0.2mmol, 50.2g) used as the starting material. Product was purified by flash chromatography (SiO₂, hexanes:EtOAc = 17:3). NMR matched known spectra.¹⁴

\[
\text{6 Member Ring Product}
\]

1-Tosyl-2-vinylpiperidine (8): 1-tosyl-2-vinylpiperidine (0.176 mmol, 46.7 mg, 88%) was synthesized according to GS3 with N-(hepta-5,6-dien-1-yl)-4-methylbenzenesulfonamide (0.2 mmol, 53.1 mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 9:1). NMR matched known spectra.¹² HRMS(EI) calculated for C₁₄H₂₀NO₂S [M+H]+;266.1215, found 266.1223.

\[
\text{NTs}
\]

1-Phenyl-2-vinylazepane (5h): 1-phenyl-2-vinylazepane (0.122mmol, 24.4mg, 24%) was synthesized according to GS3 with N-(octa-6,7-dien-1-yl)aniline (0.5mmol, 100.65mg) as the starting material and purified by flash chromatography. This compound degrades on the column so it was run in polar conditions (SiO₂, DCM). A few unknown peaks are contained in the NMR so the yield is not perfectly accurate.

\[
\text{NPh}
\]

\[
\begin{align*}
\text{1H NMR (500 MHz, CDCl₃), } & \delta 7.14 – 7.11 (m, 2H), 6.94 (d, J = 4.7, 1H), 6.62 (d, J = 8.4, 2H), 6.57 – 6.53 (m, 1H), 5.78 – 5.71 (m, 1H), 4.99 – 4.91 (m, 2H), 4.05 – 3.98 (m, 1H), \\
& 3.47 (s, 1H), 1.78 – 1.72 (m, 2H), 1.26 – 1.21 (m, 4H), 0.82 – 0.80 (m, 2H); \\
\text{13C NMR (126 MHz, CDCl₃), } & \delta 149.02, 137.58, 129.08, 115.01, 113.35, 110.94, 53.44, 44.04, 35.67, 29.89, 27.83, 25.57; \\
\text{IR (film) } & \lambda_{\text{max}} 3053, 2928, 1640. \text{ HRMS(EI) calculated for C₁₄H₂₀N [M+H]+;202.1596, found 202.1610.}
\end{align*}
\]
4-(2-Methylprop-1-en-1-yl)-5-tosyl-2,3,4,5-tetrahydrobenzo[b][1,4]oxazepine (5m): 4-(2-methylprop-1-en-1-yl)-5-tosyl-2,3,4,5-tetrahydrobenzo[b][1,4]oxazepine (0.166 mmol, 59.2 mg, 83%) was synthesized according to GS3 with N-(2-(hexa-3,4-dien-1-yloxy)phenyl)-4-methylbenzenesulfonamide (0.200 mmol, 71.5 mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 9:1).

\[ {\text{NMR (500 MHz, CDCl₃),}} \]
\[ \delta 7.64 (d, J = 8.3, 2H), 7.31-7.30 (m, 1H), 7.20 (d, J = 8.1, 2H), 6.91 (s, 1H), 6.77-6.73 (m, 2H), 5.00 (d, J = 9.4, 1H), 4.11-4.08 (m, 1H), 3.92 (td, J = 9.8 and 2.6, 1H), 3.57 (q, J = 9.0, 1H), 2.37 (s, 3H), 1.90-1.86 (m, 1H), 1.74 (s, 3H), 1.72 (s, 3H), 1.66-1.59 (m, 1H); \]
\[ {\text{C NMR (126 MHz, CDCl₃),}} \]
\[ \delta 144.6, 143.5, 136.3, 133.0, 129.3, 127.4, 127.1, 125.9, 125.4, 125.0, 119.9, 119.0, 65.3, 33.5, 29.0, 25.8, 21.5, 18.0; HRMS(EI) calculated for C₂₀H₂₄NO₃S [M+H]⁺; 358.1478, found 358.1451. Yellow oil. \]

4-(2-Methylprop-1-en-1-yl)-2,3,4,5-tetrahydrobenzo[b][1,4]oxazepane (5n): was synthesized according to GS3 with 2-((5-methylhexa-3,4-dien-1-yl)oxy)aniline (50 mg, 0.246 mmol) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 19:1) yielding 4-(2-methylprop-1-en-1-yl)-2,3,4,5-tetrahydrobenzo[b][1,4]oxazepane (45.8 mg, 0.225 mmol, 91.7%).

\[ {\text{NMR (500 MHz, CDCl₃),}} \]
\[ \delta 6.95 (dd, J = 7.9 and 1.3, 1H), 6.87 (td, J = 7.5 and 1.3, 1H), 6.79 (td, J = 7.8 and 1.2, 1H), 6.72 (dd, J = 7.7 and 1.4, 1H), 5.29 (d, J = 9.4, 1H), 4.42-4.38 (m, 1H), 3.94 (td, J = 9.7 and 3.2, 1H), 3.84-3.79 (m, 1H), 3.32 (s, 1H), 1.97-1.88 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H); \]
\[ {\text{C NMR (126 MHz, CDCl₃),}} \]
\[ \delta 150.3, 140.8, 134.6, 127.0, 123.4, 121.7, 121.0, 119.9, 70.5, 54.5, 38.1, 25.7, 18.3. HRMS(EI) calculated for C₁₃H₁₈NO [M+H]⁺; 204.1389, found 204.1377. Yellow oil. \]

4.3.8 NMR Data
Bimetallic rhodium complex
Mono metallic rhodium complex (2)
References


7. FSR ref


Chapter 5  Allene Trifluoroacetoxylation with Novel Bimetallic Rh(II) Catalyst

5.1 Introduction

The allene functional group is an important group in organic synthesis because of the inherent reactivity and useful products that result from their functionalization. The synthesis of allenes was first described over 135 years ago, and today allenes can be easily synthesized via homologation of alkynes. However, allenes are among the least studied of all carbon unsaturated functional groups. Recently, allene hydrofunctionalization has become a topic of interest as it creates a highly functional allyl substituted product. Allenes are more reactive than alkenes or alkynes and are an attractive substrate to generate new C-C, C-O and C-N bonds. While some organocatalysts can be used for the hydrofunctionalization of allenes, the use of metal catalysts gives improved efficiency and selectivity to access either the linear or branched addition products. Common metals for the hydrofunctionalization of allenes include

a. Krische: iridium hyrdcarboxylation of allenes

\[
\begin{align*}
\text{R}^1 \equiv \text{Me} + \text{HO} & \quad 1\% [\text{Ir(cod)Cl}]_2 \\
\text{HO} & \quad 2\% \text{BIHPEP} \\
& \quad 2\% \text{Cs}_2\text{CO}_3 \\
& \quad \text{DCE, 60 °C} \\
\rightarrow & \quad \text{MeMe} \quad \text{R} \\
\text{O} & \quad 5 \text{ examples}
\end{align*}
\]

b. Breit: rhodium allene hydrocarboxylation

\[
\begin{align*}
\text{R}^1 \equiv \text{Me} + \text{HO} & \quad 4.5\% [\text{Rh(cod)Cl}]_2 \\
\text{HO} & \quad 9\% (\text{R,R})-\text{DIOP} \\
& \quad 9\% \text{Cs}_2\text{CO}_3 \\
& \quad \text{DCE, 60 °C} \\
\rightarrow & \quad \text{MeMe} \quad \text{R} \\
\text{O} & \quad 17 \text{ examples}
\end{align*}
\]

c. Guo: silver allene hydrocarboxylation

\[
\begin{align*}
\text{N} \equiv \text{Me} + \text{ HO} & \quad \text{Ag}_2\text{CO}_3 \\
\text{HO} & \quad \text{80 °C, 48h} \\
\rightarrow & \quad \text{NMe} \quad \text{R} \\
\text{O} & \quad 5 \text{ examples}
\end{align*}
\]

d. Monnier: copper allene hydrocarboxylation

\[
\begin{align*}
\text{R}^1 \equiv \text{Me} + \text{HO} & \quad 10\% [\text{Cu(CH}_3\text{CN})_4]^+\text{PF}_6^- \\
\text{HO} & \quad 10\% \text{K}_2\text{CO}_3 \\
& \quad \text{THF, 50 °C, 18h} \\
\rightarrow & \quad \text{R}^1 \quad \text{R}^2 \\
\text{O} & \quad 16 \text{ examples}
\end{align*}
\]

**Figure 5.1** Past work in hydrocarboxylation of allenes
Ag, Au, Rh and Pd catalysts. While the scope of these reactions is expanding at an ever-increasing rate, strong nucleophiles like malonates, amines, and alcohols are typically required to achieve high yields. In fact, only a few examples have been reported where electron-deficient nucleophiles, such as carboxylic acids, have been used (hydocarboxylation of allenes). The Krische group has shown the hydrocarboxylation of terminal allenes using an iridium catalyst (Figure 1a). The scope of the allenes was limited to three examples but showed good yields with addition to the most hindered end of the allene. The Breit group also reported a rhodium-catalyzed enantioselective addition to terminal allenes to access the branched product (Figure 1b). Breit then demonstrated its use in the synthesis of Clavolide. In addition to these, silver (Figure 5.1c) and copper (Figure 5.1d) catalysts have been used in hydrocarboxylation with a limited scope. Recently, we discovered that a bimetallic Rh(II) catalyst could enable the addition of trifluoroacetic acid to allenes to generate the branched allylic trifluoroacetate product. This represents the first example of adding a weak nucleophile to an allene under rhodium catalysts. Importantly, other monometallic and bimetallic Rh catalysts do not perform this reaction under our optimized conditions.

Our new Rh-catalyzed addition of weak nucleophiles to allenes represents an attractive method for accessing allylic leaving groups. The addition of a weak nucleophile to an allene to generate an allylic leaving group is of interest because the products can be functionalized through π allyl formation and allylic functionalization. Breit has shown an example of this where he observed an allene TFA insertion intermediate in the addition of carbon nucleophiles to internal allenes (Figure 5.2). Thus, the intermediate allylic trifluoroacetate could react with the Rh catalyst, reforming the π allyl intermediate and facilitating addition of the weak nucleophile.
malonate to form a new C–C bond. In this work, we present the addition of trifluoroacetate groups to allenes and demonstrate that the resulting allyl trifluoroacetate products can be isolated in good yield. In this reaction, the catalyst strongly favors the branched product when our novel bimetallic rhodium catalyst is employed.

5.2 Results and Discussion

a. Previous results in allene hydroamination

\[
\begin{align*}
\text{NHR} & \quad \xrightarrow{5\% \text{ Rh–Rh (2)}} \quad \text{NHTs} \\
\begin{array}{c}
\text{Ts} \\
\text{N} \\
\text{Ph} \\
\text{Ts} \\
\text{N} \\
\text{Ts}
\end{array} & \quad \xrightarrow{40\% \text{ TFA}} \\
\begin{array}{c}
\text{Ts} \\
\text{N} \\
\text{Ph} \\
\text{Ts} \\
\text{N} \\
\text{Ts}
\end{array}
\end{align*}
\]

\[\text{DCE, 80 °C, 18–48 h}\]

88% 88% 24% 83% 92%

b. Bimetallic reactivity in allene functionalization

\[
\begin{align*}
\text{NHTs} & \quad \xrightarrow{5\% \text{ Rh cat.}} \quad \text{NHTs} \\
\begin{array}{c}
\text{N} \\
\text{Ts} \\
\text{N} \\
\text{Ts} \\
\text{N} \\
\text{Ts}
\end{array} & \quad \xrightarrow{60\% \text{ TFA}} \\
\begin{array}{c}
\text{N} \\
\text{Ts} \\
\text{N} \\
\text{Ts} \\
\text{N} \\
\text{Ts}
\end{array}
\end{align*}
\]

\[\text{Bimetallic Rh (2)} \quad \text{Monometallic Rh cats.}\]

TFA it was not unreasonable to have a protonated amine. After performing \(^{19}\text{F} \text{NMR}\) and HMBC studies, we were able to confirm that the product contained a trifluoroacetate (TFA) group and had not cyclized. The quartet pattern in the carbon NMR also became evident. Additionally, the hydrogen peak adjacent to the oxygen was more consistent with the shift of the TFA addition product and not a proton adjacent to a tolsyl amine. TFA is an excellent leaving group and it is common in mass spectroscopy for the substrates to ionize in the mass spectrometer via loss of a good leaving group. These studies taught us that attention to detail is very important when characterizing new products and that we could take more care in performing our characterization studies.

After validating the identity of our product in the allene hydrofunctionalization reaction was indeed the allylic trifluoroacetate product, we set out to optimize this new reaction (Table 5.1). We first determined that both the TFA (entry 1) and the bimetallic rhodium (entry 14) were essential to achieve any conversion in the reaction. Optimal yields were achieved when increasing the catalyst loading to 5% of the bimetallic catalyst at 80 °C with dichloroethane.
(DCE) or toluene as solvent. Lower catalyst loadings gave moderate to low yields (entries 8,9). Other acids were also used but did not give significant amounts of product or decomposed the starting material (entries 11-13). When the percent TFA was increased to 1 equivalent the yield was reduced and a significant hydrogenated biproduct was formed (entry 10). As discussed in chapter 4, a variety of mono and bimetallic rhodium complexes were used in this reaction and none favored the formation of the TFA addition. Many of the other catalyst gave an isomerized diene product or gave no reaction. These studies confirm the unique reactivity of our bimetallic complex, which we believe relies on the presence of the two Rh centers to facilitate catalysis in this system.

Table 5.1 Optimization of rhodium catalyzed trifluoroacetoxylation

<table>
<thead>
<tr>
<th>entry</th>
<th>mol% cat.</th>
<th>temp.</th>
<th>mol% acid</th>
<th>yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>80 ℃</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>80 ℃</td>
<td>15</td>
<td>11%</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>80 ℃</td>
<td>45</td>
<td>43%</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>80 ℃</td>
<td>~60</td>
<td>64%</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>50 ℃</td>
<td>~60</td>
<td>44%</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>23 ℃</td>
<td>~60</td>
<td>17%</td>
</tr>
<tr>
<td>7c</td>
<td>5</td>
<td>80 ℃</td>
<td>~60</td>
<td>59%</td>
</tr>
<tr>
<td>8</td>
<td>2.5</td>
<td>80 ℃</td>
<td>~60</td>
<td>40%</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>80 ℃</td>
<td>~60</td>
<td>11%</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
<td>80 ℃</td>
<td>100</td>
<td>50%</td>
</tr>
<tr>
<td>11</td>
<td>5</td>
<td>80 ℃</td>
<td>45 (TIOH)</td>
<td>0%</td>
</tr>
<tr>
<td>12</td>
<td>5</td>
<td>80 ℃</td>
<td>45 (TsOH)</td>
<td>0%</td>
</tr>
<tr>
<td>13</td>
<td>5</td>
<td>80 ℃</td>
<td>45 (AcOH)</td>
<td>0%</td>
</tr>
<tr>
<td>14</td>
<td>0</td>
<td>80 ℃</td>
<td>45</td>
<td>0%</td>
</tr>
</tbody>
</table>

a) Reaction run on a 0.2 mmol scale of 4 with 5 mol% Rh dimer 3 and 45% TFA in dichloroethane (DCE, 0.2 M) at 80 ℃ for 18 h unless otherwise noted. b) Conversions determined by 1H NMR analysis of the crude reaction mixture. c) Run in toluene.
The scope of our new allene trifluoroacetoxylation reaction was next explored with a variety of substrates containing tethered sulfonamide functional groups (Figure 5.4). Substrates containing tethered sulfonamides between five and 13 all underwent TFA addition and no cyclization products were isolated (4a-4i). While the reaction did tolerate amides and carbamates in addition to sulfonamides (4j-4o), the sulfonamide-protected amine substrates gave the best yields. This may be due to a coordinating effect of the amine with the catalyst, which slows down TFA addition. The reaction works well with anilines (4p, 4q, 4ac, 4ad) and acetamides (4r-4s). Carbamates were among the easiest substrates to synthesize and gave good yields (4t-4ab). This reaction has some limitations; if a hetero atom such as oxygen is allylic to the allene, no product is formed due to deactivation of the allene (4ag). Sterically hindered allenes (4af) also fail to give any product, likely due to steric hindrance in the allene hydrometallation step. While the yields of the TFA addition product are often modest, our
results demonstrate the first general proceed for adding weak nucleophiles such as TFA to allenes to generate allylic leaving groups.

Figure 5.5 Proposed mechanism of trifluoroacteoxylation

Based on these results and the unique nature of the bimetallic catalyst, studies were performed to better understand the mechanism of this reaction (Figure 5.5). The proposed mechanism is consistent with reported mechanisms for allene hydrofunctionalization in the presence of TFA. The rhodium inserts into the OH of the trifluoroacetic acid to give the activated rhodium hydride (A). The rhodium can then reversibly insert into the allene to form the metal allyl (B). Finally reductive elimination of the trifluoroacetate gives the product (C).

While the insertion of rhodium into the OH of the TFA is commonly understood, we wanted to better understand the nature of this catalyst when inserting into the allene. A deuterium labeling study was performed to determine how the Rh facilitated TFA addition (Figure 5.6). After the reaction with the deuterated substrate and deuterated TFA, deuterium was present on all four carbons of the product. This result suggests that during catalysis, the
diene product can be formed by our catalyst via isomerization of the allene. The diene is formed through beta hydrogen elimination from the metal allyl intermediate. As little to no diene is seen in the product, we can deduce that the bimetallic rhodium complex reversibly inserts into the allene and the diene products to generate an allyl intermediate. Only with our bimetallic catalyst is reductive elimination favored to form the allylic TFA product. Interestingly, when other rhodium catalysts are used (see chapter 4) only the isomerized diene product is formed. To understand why this catalyst favors the reductive elimination, computational studies are being performed. Carbonyl ligands are known to favor reductive elimination. However, other Rh catalysts that contain CO ligands still gave the beta hydrogen elimination product. Thus, the bimetallic Rh catalyst has unique reactivity that we believe is enabled by the presence of the Rh–Rh bond in our catalyst.

In conclusion, we discovered a trifluoroacetoxylation of allenes with a novel bimetallic rhodium catalyst. Over 30 allene substrates were shown to react in high yield to give a highly functional allylic leaving group. While the original aim of this work was to create medium and large size rings, our catalyst shows unique reactivity to perform reductive elimination and generate an allylic trifluoroacetate while other similar catalysts perform beta hydrogen elimination and give a diene isomer.

5.3 Supporting Information
All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring, unless otherwise indicated. Solvents were dried by J. C. Meyer’s Solvent Purification System. Reactions requiring a moisture or oxygen-free environment were done in a nitrogen atmosphere glove box (Innovative Technology, PreLab HE system, double glove box). Flash chromatography was performed with Sorbtech silica gel (0.040-0.063µm grade). Analytical thin-layer chromatography was done with 0.25 mm coated commercial silica gel plates (Merck KGaA, DC silicagel 60 F254). Proton nuclear magnetic resonance (1H NMR) data were acquired on an Inova 300 (300 MHz), Inova-500 (500 MHz) or Bruker (500MHz) spectrometer. Chemical shifts are reported in delta (δ) units relative to the 2H signal of the CDCl3 solvent. Carbon-13 nuclear magnetic resonance (13C-NMR) data were acquired on an Inova 500 o r Bruker at 125 MHz. Signals are reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), qd (quartet of doublets), brs (broad singlet), m (multiplet). Coupling constants are reported in hertz (Hz). Chemical shifts are reported in ppm relative to the center line of a triplet at 77.23 ppm for chloroform-d for 13C-NMR or the singlet at 0 ppm for BF₃ · O(Et)₂ for 11B-NMR. Infrared (IR) data were recorded as films on sodium chloride plates on a Thermo Scientific Nicolet IR 100 FT-IR spectrometer. Absorbance frequencies are reported in reciprocal centimeters (cm⁻¹). Mass spectral data were obtained using ESI techniques (Agilent, 6210 TOF).

5.3.1 Other Rhodium Complexes Used in the Reaction

Table 5.2 Use of other rhodium complexes

<table>
<thead>
<tr>
<th>Figure #</th>
<th>Catalyst</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rh-Rh Bimetallic</td>
<td>86% Yield</td>
</tr>
<tr>
<td>2</td>
<td>Rh Mono</td>
<td>Isomerized</td>
</tr>
<tr>
<td>3</td>
<td>[Rh(OAc)₂]₂</td>
<td>No product</td>
</tr>
<tr>
<td>4</td>
<td>[Rh(cod)Cl]₂ + segphos (R) DTBM (10%)</td>
<td>Isomerized</td>
</tr>
<tr>
<td>5</td>
<td>[Rh(cod)Cl]₂ + dpfp (10%)</td>
<td>Isomerized</td>
</tr>
<tr>
<td>6</td>
<td>Rh Doyal complex</td>
<td>No product</td>
</tr>
<tr>
<td>7</td>
<td>Rh Binap complex</td>
<td>Isomerized</td>
</tr>
</tbody>
</table>
Each reaction was performed according to general procedure 3. The above rhodium complexes and ligands have been used in the past for hydroamination reactions or have similar characteristics to our catalyst. The use of the other rhodium catalysts with no formation of product illustrates the uniqueness of this molecule.

5.3.2 General Synthesis of Allene Starting Materials

5.3.2.1 General Procedure 1:

a) Allyne substrate (1.0 eq), copper (I) bromide (0.70 eq), and paraformaldehyde (2.0 eq) were suspended in 1,4-dioxane (0.1 M) at room temperature. The solution was stirred for 30 min and dicyclohexylamine (2.0 eq) was added. The reaction was refluxed at 100°C for 18 h. After cooling to room temperature, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate (3 × 10 mL/mm) and washed with 1 M HCl and brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude allene product was purified by flash chromatography (SiO₂, hexanes:EtOAc = 3:1).

b) To a solution of p-toluenesulfonyl chloride (1.1 eq) in DCM (0.3 M) at 0°C, the allene substrate (1.0 eq) and triethyl amine (2.0 eq) were added. The reaction was allowed to return to room temperature and stirred for 16 h.
c) Tosylated substrate (1.0 eq), p-toluenesulfonylamine (2.0 eq), and potassium carbonate (2.0 eq) were combined in acetonitrile (0.2 M) and refluxed at 100°C for 12 h. After cooling to room temperature, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate (3 × 10 mL/mmol) and washed with 1 M HCl and brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude allene product was purified by flash chromatography (SiO₂, hexanes:EtOAc = 19:1 – 5:1).

5.3.2.2 General Procedure 2:

\[\text{MeO} \quad \text{OMe} \quad \text{OH} \quad \text{R} \quad \text{R} \quad \text{MeO} \quad \text{OMe} \quad \text{OH} \quad \text{R} \quad \text{R} \]

a) Alkyne substrate (1.0 eq), trimethyl orthoacetate (1.6 eq), and propanoic acid (0.16 eq) were suspended in toluene (0.7 M). Reaction stirred at room temperature for 20 min and then was refluxed at 150°C with a Dean Stark trap for 16 h. Afterwards, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate (3 × 10 mL/mmol) and washed with brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure.

b) To a solution of allene substrate (1 eq) suspended in diethyl ether (0.4 M) at 0°C, LAH (1.6 eq) was added. The reaction was allowed to return to room temperature and was stirred for 1 h. Afterwards, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate (3 × 10 mL/mmol) and washed with brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude allene product was purified by flash chromatography (SiO₂, hexanes:EtOAc = 9:1 – 4:1).

5.3.2.3 General Procedure 3:
Under inert conditions, in an oxygen free environment, the allene substrate (0.2 mmol), Rh-Rh catalyst (0.01 mmol), and Dichloroethane (DCE) (2 mL, 0.1 M) were added to a dry vial and stirred for one minute. trifluoro acetic acid (TFA) (~0.12 mmol) was then added, and the reaction was then heated to 80°C. Reaction was allowed to run overnight or 18 hours. Product purification and separation from catalyst achieved through flash chromatography.

4-Methyl-N-(octa-6,7-dien-1-yl)benzenesulfonamide (3a): Synthesis began according to GS1a-GS1b. To a solution of octa-6,7-dien-1-yl 4-methylbenzenesulfonate (14.18 mmol, 3.9758 g), P-toluenesulfonamide (28.36 mmol, 4.8567 g), potassium carbonate (28.36 mmol, 3.9195 g), and acetonitrile (mmol, 70 ml, 0.73 g/mol). The reaction was refluxed at 90°C for 12 hours. Crude product was extracted in ethyl acetate and brine. The product (2.4 g, 8.5 mmol, 86%) was obtained after being purified by flash chromatography (SiO2, hexanes:EtOAc = 19:1 – 5:1). 1H NMR (500 MHz, CDCl3), δ 7.6173 (d, J = 8.1, 2H), 7.1606 (d, J = 8.0, 2H), 4.91-4.86 (m, 1H), 4.79 (t, J = 11.8, 1H), 4.50-4.47 (m, 2H), 2.77 (q, J = 6.7, 2H), 2.28 (s, 3H), 1.79-1.75 (m, 2H), 1.34-1.28 (m, 2H), 1.22-1.11 (m, 4H). 13C NMR (126 MHz, CDCl3), δ 208.4, 143.3, 136.9, 129.7, 127.1, 89.7, 74.8, 43.1, 29.3, 28.4, 27.9, 25.9, 21.5. HRMS(EI) calculated for C15H22NO2S [M+H]+; 280.1327, found 280.1341. IR (film) λmax (3283, 2934, 2858.23, 1954, 1598, 1494, 1431).

N-(Octa-6,7-dien-1-yl)methanesulfonamide (3b): Hept-6-yne-1-yl 4-methylbenzenesulfonate was synthesized from hept-6-yne-1-ol according to GS1b. This product was then used as the starting material to form N-(hept-6-yne-1-yl)naphthalene-2-sulfonamide according to GS1c (substituting the p-toluenesulfonyl chloride with methanesulfonamide and the triethyl amine with potassium carbonate). This was converted into the final product according to GS1a.
4-Nitro-N-(octa-6,7-dien-1-yl)benzenesulfonamide (3c): Synthesized from N-(hept-6-yn-1-yl)-4-nitrobenzenesulfonamide according to GS1a. N-(hept-6-yn-1-yl)-4-nitrobenzenesulfonamide (3.512 mmol, 1.09 g), copper(I) bromide (2.458 mmol, 0.353 g), paraformaldehyde (8.78 mmol, 0.266 g), dicyclohexylamine (8.78 mmol, 1.485 g) were added to a dry round bottom flask with dioxane (0.2M, 20 ml) at room temperature for 30 minutes. Reaction was then refluxed for 18 hours. The product (500 mg, 1.61 mmol, 46%) was obtained after flash chromatography (SiO2, hexanes:EtOAc = 3:1).

Did GS1b to tosylate hept-6-yn-1-ol, then GS1c to exchange OTS with NNosyl. 1H NMR (500 MHz, CDCl3), δ 8.38 (d, J = 8.8, 2H), 8.08 (d, J = 8.8, 2H), 5.06-5.01 (m, 1H), 4.65-4.63 (m, 2H), 3.01 (t, J = 7.1, 2H), 1.97-1.91 (m, 2H), 1.53-1.47 (m, 2H), 1.38-1.29 (m, 4H). 13C NMR (126 MHz, CDCl3), δ 208.5, 150.0, 146.0, 128.3, 124.4, 89.5, 74.9, 43.3, 29.5, 28.3, 27.9, 25.8. IR (film) λmax(3259, 1555, 1460, 1377). HRMS(EI) calculated for C_{14}H_{19}N_{2}O_{4}S [M+H]^+; 311.1021, found 311.1056.

N-(Octa-6,7-dien-1-yl)naphthalene-2-sulfonamide (3d): Hept-6-yn-1-yl 4-methylbenzenesulfonate was synthesized from hept-6-yn-1-ol according to GS1b. This product was then used as the starting material to form N-(hept-6-yn-1-yl)naphthalene-2-sulfonamide according to GS1c (substituting the p-toluenesulfonyl chloride with 2-hydrosulfonylnaphthalene and the triethyl amine with potassium carbonate). This was
N-(Octa-6,7-dien-1-y1)acetamide (3e): octa-6,7-dien-1-yl 4-methylbenzenesulfonylate (0.39 g, 1.39 mmol) was added to a solution of sodium hydride (60% in mineral oil, 0.328 g, 5.564 mmol) and acetamide (0.328 g, 5.564 mmol) in tetrahydrofuran (THF, 10 mL) at 0°C. The reaction then was heated to reflux and allowed to stir overnight. The reaction was then extracted with ethyl acetate and washed with brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The product (0.19 g, 1.136 mmol, 82%) was obtained after flash chromatography (SiO2, hexanes: ethyl acetate = 4:6). 1H NMR (500 MHz, CDCl3), δ 7.3878 (m, J = 3.5, 5H), 5.12 (s, J = 8.1, 2H), 5.08 (p, J = 6.8, 1H), 4.69 (q, J = 6.6, 2H), 3.224 (m, J = 14.6, 2H), 2.01 (m, J = 6.7, 2H), 1.53 (m, J = 7.3, 2H), 1.45 (m, J = 7.6, 2H), 1.37 (m, J = 6.8, 2H); 13C NMR. (126 MHz, CDCl3), δ 208.50, 156.38, 142.92, 137.40, 136.6, 129.61, 128.16, 127.06, 89.80, 74.79, 66.61, 42.00, 29.77, 28.06, 21.51, 14.16; HRMS(EI) calculated for C10H18NO [M+H]+; 167.1385, found 167.1385
Octa-6,7-dien-1-amine (3f-2): 8-azidocta-1,2-diene (1.575g, 10.422mmol), was dissolved in THF (10mL) then Triphenylphosphine (3.554g, 13.548mmol), and water (0.825mL, 45.857mmol) was added. The reaction was then allowed to stir overnight at room temperature. The reaction was then extracted with ethyl acetate and brine. The organic phases were dried over sodium sulfate, and the product was concentrated under reduced pressure and the crude product was taken onto the next step.

(9H-Fluoren-9-yl)methyl octa-6,7-dien-1-ylcarbamate (3f): octa-6,7-dien-1-amine (2g, 15.968 mmol) was dissolved in 1,4 dioxane (40mL). Triethyl amine (15.968 mmol, 4.131 g) was then added and the reaction was then cooled to 0℃. 9-Fluorenylmethyl chloroformate was dissolved in 1,4 dioxane (10mL) then added dropwise to the reaction mixture. The reaction was then warmed to 25℃ and stirred for four hours. The solvent was then removed under reduced pressure, and the product (2.15g, 6.188mmol, 39%) was obtained after flash chromatography (SiO2, hexanes:EtOAc = 6:1). 1H NMR (500 MHz, CDCl3), δ 7.69 (d, J = 2H), 7.51 (d, J = 2H), 7.32 (md J = 2H), 7.24 (d, J = 2H), 5.01 (p, J = 1H), 4.58 (q, J = 2H), 4.34 (d, J = 2H), 3.12 (m, J = 3.5, 5H), 1.97 (q, J = 2H), 1.44 (m, J = 2H) 1.35 (m, J = 2H), 1.28 (m, J = 2H); 13C NMR. (126MHz, CDCL), δ 208.51, 156.42, 144.03, 141.39, 129.63, 127.83, 127.61, 127.03, 125.05, 124.94, 119.99, 89.82, 74.81, 66.93, 60.44, 47.48, 41.02, 37.99, 29.78, 28.66, 28.07, 26.13; HRMS(EI) calculated for C23H25NO2 [M+H]+; 347.1885, 347.1855 found.

Benzyl octa-6,7-dien-1-ylcarbamate (3g): octa-6,7-dien-1-amine (2g, 15.968mmol) and sodium carbonate (2.65g, 15.973mmol) was dissolved in 1:1 THF:H2O (20mL). The reaction was then cooled to 0℃, followed by the addition of benzyl chloroformate (2.99g, 17.569mmol). The reaction then was brought to 25℃ and allowed to stir overnight. The reaction was then extracted with ether and brine. The organic phases were dried over sodium
sulfate, and the product was concentrated under reduced pressure and the product (90mg, 0.347mmol, 2.2%) was obtained after flash chromatography (SiO₂, 100% DCM). ¹H NMR (500 MHz, CDCl₃), δ 7.3878 (m, J = 3.5, 5H) 5.12 (s, J = 8.1, 2H), 5.08 (p, J = 6.8, 1H), 4.69 (q, J = 6.6, 2H), 3.22 4 (m, J = 14.6, 2H), 2.01 (m, J = 6.7, 2H), 1.53 (m, J = 7.3, 2H), 1.45 (m, J = 7.6, 2H); 13C NMR (126MHz, CDCL), δ 208.50, 156.38, 142.92, 137.40, 136.6, 129.61, 128.16, 127.06, 89.80, 74.79, 66.61, 42.00, 29.77, 28.06, 21.51, 14.16; HRMS(EI) calculated for C₁₆H₂₁NO₂ [M+H]+; 259.1572, found 259.1568.

N-(Octa-6,7-dien-1-yl)aniline (3h): Synthesis began according to GS1a-GS1b. Octa-6,7-dien-1-yl 4-methylbenzenesulfonate (4.23mmol, 1.2g) was then combined with aniline (42.3mmol, 3.94g), acetonitrile (190.35mmol, 9.94mL), and triethyl amine (4.653mmol, 471mg) and was refluxed at 83°C for 16 h. After allowing reaction to return to room temperature, sodium bicarbonate was used to neutralize the reaction, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate (3 × 10mL/mmoll) and washed with brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude allene product was purified by flash chromatography (SiO₂, hexanes:EtOAc:Et₃N 90:9:1) to yield the product (0.2043g, 1.015mmol, 24%) The product was isolated as an orange oil.

¹H NMR (500 MHz, CDCl₃), δ 7.17 (t, J = 7.5, 2H); 6.69 (t, J = 7.3, 2H); 6.61 (d, J = 7.7, 1H); 5.10 (p, J = 6.7, 1H); 4.67 (p, J = 3.4, 2H); 3.59 (s, 1H); 3.11 (t, J = 7.15, 2H); 2.02 (m, 2H); 1.63 (m, 2H); 1.46 (m, 4H); ¹³C NMR (126 MHz, CDCl₃), δ 148.5, 129.3, 117.1, 112.7, 89.8, 74.4, 43.9, 29.3, 28.8, 26.6, 26.3; IR (film) λmax (3411, 2931, 1955, 1602) HRMS(EI) calculated for C₁₄H₂₀N [M+H]+; 202.1551, found 202.1571

N-Butylocta-6,7-dien-1-amine (3i): Synthesis began according to GS1a and GS1b. To a solution of octa-6,7-dien-1-yl 4-methylbenzenesulfonate (3.57 mmol, 1 g) in acetonitrile (214.2
mmol, 11.2 mL, 0.786 g/mL) was added butylamine (35.7 mmol, 3.53 mL, 0.740 g/mL) and
triethyl amine (3.93 mmol, 0.54 mL, 0.73 g/mol). The reaction was brought to reflux and
stirred 16 h. The reaction was quenched with sodium bicarbonate, the solvent was removed
under reduced pressure, and the product was extracted with ethyl acetate (3 × 10 mL/mmol)
and washed brine. The organic phases were dried over sodium sulfate and concentrated under
reduced pressure. The product (132.3 mg, 0.730 mmol, 20.4%) was obtained after flash
chromatography (SiO₂, hexanes: DCM = 99:1 – 19:1, 1% Et₃N). ¹H NMR (500 MHz,
CDCl₃), δ 5.12-5.06 (m, 1H), 4.66- 4.64 (m, 2H), 2.59 (t, J = 7.3, 4H), 2.02-1.99 (m, 2), 1.52-
1.41 (m, 7H), 1.38-1.32 (m, 4H), 0.92 (t, J = 7.3, 3H). ¹³C NMR (126 MHz, CDCl₃), δ 208.5,
90.0, 74.6, 50.1, 49.9, 32.4, 30.0, 29.0, 28.2, 26.9, 20.6, 14.1. HRMS(EI) calculated for
C₁₂H₂₄N [M+H]+;182.1864, found 182.1859, IR (film) λmax (3281, 2930, 2856, 1952, 1596,
1492, 1430).

4-Methyl-N-(6-methylocta-6,7-dien-1-yl)benzenesulfonamide (3j):
To (0.2M) tetrahydrofuran at -78 º C, copper(I)cyanide (47.0 mmol, 4.2g), lithium chloride
(66.4 mmol, 3g) and methyllithium (45.0mmol, 45ml) were added dropwise and stirred for 1 h.
8-((tert-butyldimethylsilyl)oxy)oct-2-yn-1-ylmethanesulfonate (11.1mmol, 3.7g) was then
added at room temperature and stirred for another 1 h. Reaction was then extracted with sat.
ammonium chloride(aq) and ethyl acetate and purified by flash chromatography (SiO₂,
hexanes:EtOAc = 19:1) to obtain tert-butyldimethyl((6-methylocta-6,7-dien-1-yl)oxy)silane as
the product.
This product was added to (1.2 eq) HCl and (.2M) methanol and stirred at room temperature 1
h. Reaction was neutralized with Na₂Co₃ (aq) and then extracted with ethyl acetate and brine
to obtain 6-methylocta-6,7-dien-1-ol. NMR data matched known spectra⁹.
6-methylocta-6,7-dien-1-ol was then used as the starting material to synthesize 6-methylocta-
6,7-dien-1-ylmethanesulfonate according to GS1b, methanesulfonyl chloride was substituted
for p-toluenesulfonyl chloride (1.1 eq) at -78 °C and stirred 3 h. This was converted into the
final product according to GS1c, dimethyl fumarate was substituted for acetonitrile and ran for
18h. Then reaction was washed with brine and extracted with ethyl acetate. The product
(500mg, 1.61mmol, 46%) was obtained after flash chromatography (SiO2, hexanes:EtOAc = 3:1).

\[ \text{1H NMR (500 MHz, CDCl3), } \delta \text{ 7.75 (d, } J = 8.3, \text{ 2H), 7.31 (d, } J = 8.0, \text{ 2H), 4.58-4.55 (m, 2H), 4.37 (s, 1H, 2.93 (q, } J = 6.7\text{, 2H), 2.43 (s, 3H), 1.88-2.84 (m, 2H), 1.64 (t, } J = 3.1, \text{ 3H), 1.49-1.43 (m, 2H), 1.39-1.33 (m, 2H), 1.30-1.24 (m, 2H).} \]

\[ \text{13C NMR (126 MHz, CDCl3), } \delta \text{ 206.0, 143.4, 136.9, 129.7, 127.1, 198.1, 74.1, 43.2, 33.1, 29.4, 26.7, 26.0, 21.5, 18.7.} \]

\[ \text{IR (film) } \lambda_{\text{max}} \text{ (3283, 2934, 2858.23, 1954, 1598, 1494, 1431). HRMS(EI) calculated for C16H23NO2S [M+H]+, 294.1528, found 294.15219.} \]

4-Methyl-N-(2-(penta-3,4-dien-1-yloxy)phenyl)benzenesulfonamide (3k): 2-(penta-3,4-dien-1-yloxy)aniline (0.5g, 2.85mmol) was added to a solution of triethyl amine (346mg, 3.42mmol), p-toluenesulfonyl chloride (652mg, 3.42mmol) and dichloromethane (6.8mL) at 0°C. The reaction was allowed to return to room temperature and stirred overnight. Solvent was removed, product was washed with brine and extracted with ethyl acetate. The product (400mg, 1.21mmol, 42.6%) was obtained after flash chromatography (SiO2, hexanes:EtOAc = 9:1).

\[ \text{1H NMR (500 MHz, CDCl3), } \delta \text{ 7.54 (d, } J = 7.3, \text{ 2H), 7.09 (d, } J = 8.0, \text{ 2H), 6.95 – 6.92 (m, 2H), 6.83 – 6.80 (m, 1H), 6.64 (d, } J = 7.1, \text{ 1H), 5.00 – 4.94 (m, 1H), 4.70 – 4.68 (m, 2H), 3.76 (t, } J = 6.5, \text{ 2H), 2.26 (s, 3H), 2.26 – 2.22 (m, 2H).} \]

\[ \text{13C NMR (126 MHz, CDCl3), } \delta \text{ 209.13, 148.74, 143.68, 136.29, 129.40, 127.21, 125.39, 121.18, 111.55, 85.90, 76.85, 75.69, 67.52, 28.11, 21.53. IR(film) } \lambda_{\text{max}} \text{ (3331, 3063, 3030, 2950, 2852, 1955, 1698, 1605). HRMS(EI) calculated for C18H20NO3S [M+H]+, 330.1165, found 330.1161} \]

2-(Penta-3,4-dien-1-yloxy)aniline (3l): penta-3,4-dien-1-ol(40.4mmol, 3.4g, 70.8%) was synthesized from 3-butynyl-1-ol(57mmol, 4g) following GS1a, product matched known spectra.10
penta-3,4-dien-1-ol (3.4g, 40.4mmol) and triphenyl phosphine(10.59g, 40.4mmol) was added
to a solution of 2-nitrophenol(5.56 g, 40 mmol) and diisopropyl azodicarboxylate (8.169g,
40.4mmol) in dichloromethane(134mL) at 0°C. The reaction was allowed to return to room
temperature and stirred overnight (18H). The reaction was washed with brine and extracted
with ethyl acetate. The product (2.91g, 14.18mmol, 35%) was obtained after flash
chromatography (SiO₂, hexanes:EtOAc = 5:1). The resulting product (2.91g, 14.18mmol) was
then placed in a round bottom flask with water (14mL) and ethanol (59mL). Iron powder
(7.91g, 141.8mmol) and a catalytic amount of concentrated hydrochloric acid (0.71mL,
0.05mmol). The reaction refluxed for 6 hours, the solvent was removed under reduced
pressure, and filtered over celite. The product (1.36g, 7.8mmol, 55%) was obtained after flash
chromatography (SiO₂, hexanes:EtOAc = 5:1).

\[ ^1H \text{ NMR (500 MHz, CDCl}_3, \delta 7.84 (d, J = 6.4, 1H), 7.55 - 7.52 (m, 1H), 7.10 (d, J = 7.7, 1H), 7.04 (t, J = 7.8, 1H), 6.82 - 6.80 (m, 1H), 6.76 - 6.73 (m, 1H), 5.27 - 5.23 (m, 1H), 4.76 - 4.74 (m, 2H), 4.20 (t, J = 6.7, 2H), 4.09 (t, J = 6.6, 1H), 3.83 (s, 1H), 2.59 - 2.52 (m, 2H); ^13C \text{ NMR (126 MHz, CDCl}_3, \delta 209.11, 152.21, 146.47, 136.43, 129.51, 125.59, 120.34, 118.42, 114.56, 68.82, 67.47. IR (film) \lambda_{max} (3331, 3063, 3030, 2950, 2852, 1955, 1698, 1605). HRMS(EI) calculated for C_{11}H_{13}NO [M+H]^+, 176.1076, found 176.1064 \]

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\text{N}
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4-Methyl-N-(2-((5-methylhexa-3,4-dien-1-yl)oxy)phenyl)benzenesulfonamide (3m):
2-((5-methylhexa-3,4-dien-1-yl)oxy)aniline (350 mg, 1.72 mmol) was added to a solution of
triethylamine (209 mg, 2.06 mmol), p-toluenesulfonyl chloride (392.7 mg, 2.06 mmol) and
dichloromethane (4mL) at 0°C. The reaction was allowed to return to room temperature and
stirred overnight. Solvent was removed, product was washed with brine and extracted with
ethyl acetate. The product (0.61 g, 1.7 mmol, 99%) was obtained after flash chromatography
(SiO₂, hexanes:EtOAc = 20:1).

\[ ^1H \text{ NMR (500 MHz, CDCl}_3, \delta 7.63 (d, J = 8.4, 2H), 7.54 (dd, J = 8.0 and 1.6, 1H), 7.18 (d, J = 8.0, 2H), 7.01 (td, J = 7.9 and 1.4, 1H), 6.98 (s, 1H), 6.89 (td, J = 7.8 and 1.1, 1H), 6.72 (dd, J = \]
= 8.2 and 1.1, 1H), 4.91-4.86 (m, 1H), 3.82 (t, $J = 6.7$, 2H) 2.35 (s, 3H), 2.27 (q, $J = 6.7$, 2H), 1.69 (d, $J = 2.9$, 6H), 1.56 (s, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$), $\delta$ 202.5, 148.8, 143.6, 136.3, 129.3, 127.2, 126.0, 125.3, 121.3, 121.0, 111.3, 84.3, 67.9, 29.0, 21.5, 20.6. IR (film) $\lambda_{\text{max}}$ (3155, 2253, 1613, 1456, 1382, 1096). HRMS(EI) calculated for C$_{20}$H$_{24}$NO$_3$S [M+H]$^+$ 358.1432, found 358.1473.

![Structural formula](image)

2-((5-Methylhexa-3,4-dien-1-yl)oxy)aniline (3n): 5-methylhexa-3,4-dien-1-ol was synthesized from 2-methylbut-3-yn-2-ol (1.7g, 20.8mmol) following GS2. Product matched known spectra$^1$ (1.935 g, 17.4mmol, 84% yield over 2 steps).

5-methylhexa-3,4-dien-1-ol (0.976 g, 8.7 mmol) and triphenyl phosphine(2.5 g, 9.57 mmol) was added to a solution of 2-nitrophenol(1.33 g, 9.57 mmol) and diisopropyl azodicarboxylate (1.935g, 9.57 mmol) in dichloromethane at 0°C. The reaction was allowed to return to room temperature and stirred overnight (18H). The reaction was washed with brine and extracted with ethyl acetate. The product (0.9 g, 3.86 mmol, 44%) was obtained after flash chromatography (SiO$_2$, hexanes:EtOAc = 98:2). The resulting product (0.9 g, 3.86 mmol) was then placed in a round bottom flask with water (4mL) and ethanol (16 mL). Iron powder (2.15 g, 38.6 mmol) and a catalytic amount of concentrated hydrochloric acid (0.2 mL). The reaction refluxed for 6 hours, the solvent was removed under reduced pressure, and filtered over celite. The product (0.45 g, 2.2 mmol, 57%) was obtained after flash chromatography (SiO$_2$, hexanes:EtOAc = 5:1).

$^1$H NMR (500 MHz, CDCl$_3$), $\delta$ 6.7 (d, $J = 7.9$, 1H), 6.87 (t, $J = 6.2$, 1H), 6.79 (t, $J = 7.6$, 1H), 6.71 (d, $J = 7.8$, 1H), 5.29 (d, $J = 9.5$, 1H), 4.42 – 4.38 (m, 1H), 3.93 (dt, $J = 9.7$, 18.6, 1H), 3.85 – 3.80 (m, 1H), 3.32 (s, 1H), 1.96 – 1.89 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$), $\delta$ 150.31, 140.85, 134.64, 127.03, 123.37, 121.66, 120.97, 119.94, 70.49, 54.47, 38.09, 25.68, 18.32. IR (film) $\lambda_{\text{max}}$ (3151, 2250, 1611, 1454, 1380, 1092). HRMS(EI) calculated for C$_{13}$H$_{18}$NO [M+H]$^+$+204.1344, found 204.1368.
2-(Penta-3,4-dien-1-yloxy)-N-tosylacetamide (3t): To a suspension of sodium hydride(60% by weight in mineral oil, 44mg, 1.1mmol) in THF (25mL), was added 2-(penta-3,4-dien-1-yloxy)acetamide (140mg, 0.992mmol). The reaction was refluxed at 70°C for 2 hours, then cooled to 0°C and p-toluene sulfonyl chloride (1mmol, 190.6mg) was added. Reaction was then refluxed for an additional 2 hours. 2-(penta-3,4-dien-1-yloxy)-N-tosylacetamide (88.8mg, 0.3mmol, 30.3%) was purified by flash chromatography (SiO₂, hexanes:EtOAc = 5:1).

\[
\text{H NMR (500 MHz, CDCl₃), } \delta \text{ 8.91 (s, 1H), 7.90 (d, J = 10, 2H), 7.27 (d, J = 10, 2H), 5.07 - 5.01 (p, J = 15, 1H), 4.70 - 4.68 (p, J = 5, 1H), 3.85 (s, 2H), 3.52 - 3.49 (t, J = 15), 2.27 (s, 3H), 2.25 - 2.20 (m, 2H); C NMR (126 MHz, CDCl₃), } \delta \text{ 209.1, 167.6, 167.6, 145.3, 135.4, 129.6, 128.5, 75.7, 71.0, 69.8, 28.2, 21.7; HRMS(EI) calculated for C}_{14}H_{18}NO₄S [M+H]^+, 296.0957, found, 296.0957.}
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2-((4-Cyclohexylidenebut-3-en-1-yloxy)-N-tosylacetamide (3u): Was synthesized from the materials shown below.

To a solution of sodium hydride in THF was added 4-cyclohexylidenebut-3-en-1-ol (synthesized according to GS2) and cooled to 0 °C. Tertbutyl bromoacetate (1.2 eq) was added dropwise and the reaction was allowed to warm to room temperature and stirred overnight. The solvent was removed under reduced pressure and taken directly to the next step.
tert-butyl 2-((4-cyclohexylidenebut-3-en-1-yl)oxy)acetate was placed into Methanol Ammonia mixture and stirred for 1 hour. Solvent was removed under reduced pressure, rinsed with Methanol, and concentrated again. Purified with flash column chromatography on silica gel (1:1 Hexanes: Ethyl Acetate) yielding 2-((4-cyclohexylidenebut-3-en-1-yl)oxy)acetamide (0.172mmol, 87mg 6% yield over two steps).

To a suspension of sodium hydride (60% by weight in mineral oil, 18.3mg, 0.457mmol) in THF (10.4mL), was added 2-((4-cyclohexylidenebut-3-en-1-yl)oxy)acetamide (87mg, 0.416mmol). The reaction was refluxed at 70°C for 2 hours, then cooled to 0°C and p-toluene sulfonyl chloride (0.457mmol, 87mg) was added. Reaction was then refluxed for an additional 2 hours. 2-((4-cyclohexylidenebut-3-en-1-yl)oxy)-N-tosylacetamide (9.2mg, 0.025mmol, 6%) was purified by flash chromatography (SiO2, hexanes:EtOAc = 5:1).

1H NMR (500 MHz, CDCl3), δ 8.85 (s, 1H), 7.91 – 7.90 (d, J = 7.0, 2H), 7.28 – 7.26 (d, J = 8.1, 2H), 4.88 – 4.85 (m, 1H), 3.84 (s, 2H), 3.49 – 3.47 (m, 2H), 2.37 (s, 3H), 2.18 – 2.17 (m, 2H), 2.01 – 2.00 (m, 4H), 1.51 – 1.43(m, 8H). 13C NMR (126 MHz, CDCl3), δ 199.2, 167.6, 145.3, 135.5, 129.6, 128.5, 103.4, 84.3, 71.4, 69.7, 31.6, 29.4, 27.4, 26.1, 21.7. HRMS(EI) calculated for C19H26NO4S [M+H]+;364.1583, found 364.1538.

Hexa-4,5-dien-1-yl tosylcarbamate (3v): To a solution of 4,5-Hexadien-1-ol (4.659mmol, 0.4573g) in dry dichloromethane (47mL) was added triethylamine (5.125mmol, 0.5186g) and tosyl isocyanate (5.125mmol, 1.01g, 0.78mL). After 2 hours stirring at room temperature, the solvent was removed under reduced pressure. The crude product was then extracted with ethyl acetate and washed with brine and 1 M HCl. The solvent was removed under reduced pressure, the residue was purified by flash column chromatography (EtOAc/Hexanes, 1:4) to give hexa-4,5-dien-1-yl tosylcarbamate (1.147g, 83%).

1H NMR (500 MHz, CDCl3), δ 7.92 (d, J = 8.4, 2H), 7.45 (s, 1H), 7.35 (d, J = 8.1, 2H), 5.07-5.02 (m, 1H), 4.69-4.66 (m, 2H), 4.12 (t, J = 6.5, 2H), 2.45 (s, 3H), 2.00-1.95 (m, 2H), 1.73-1.68 (m, 2H). 13C NMR (126 MHz, CDCl3), δ 208.5, 150.3, 145.1, 135.4, 129.6, 128.4, 88.6,
75.6, 66.4, 27.5, 24.1, 21.7. IR (film) $\lambda_{\text{max}}$ (3534, 3241, 2923, 1955, 1748, 1597). HRMS(EI) calculated for C$_{14}$H$_{18}$NO$_{4}$S [M+H] + 296.0957, found 296.0957.

**Hexa-4,5-dien-1-yl cyclohexylcarbamate (3w):** 4,5-hexadiene-1-ol (1g, 10.19mmol) was added to a solution of cyclohexyl isocyanate (1.401g, 11.2mmol), triethyl amine(1.133g, 11.2mmol), and dichloromethane (100mL). The reaction stirred at room temperature for two hours. Solvent was removed under reduced pressure. The product was washed with a one molar solution of hydrochloric acid and extracted with ethyl acetate. The product (670 mg, 3.0 mmol, 29%) was obtained after flash chromatography (SiO$_2$, hexanes:EtOAc = 20:3)

$^{1}$H NMR (500 MHz, CDCl$_3$), $\delta$ 5.16-5.11 (m, 1H), 4.72-4.69 (m, 2H), 4.55 (s, 1H), 4.15-4.08 (m, 2H), 3.49 (s, 1H), 2.089 (s, 2H), 1.95 (d, $J$ = 10.0, 2H), 1.83-1.71 (m, 6H), 1.40-1.32 (m, 3H), 1.21-1.10 (m, 4H). $^{13}$C NMR (126 MHz, CDCl$_3$), $\delta$ 208.5, 89.2, 75.3, 63.9, 54.9,49.7, 33.5, 31.9, 28.4, 26.5, 25.7, 25.5, 24.8, 24.6. IR (film) $\lambda_{\text{max}}$ ( 3334, 3055, 2930, 2853, 2260, 1955, 1693, 1530). HRMS(EI) calculated for C$_{13}$H$_{22}$NO$_{2}$ [M+H]+;224.1606, found 224.1603.

**Hexa-4,5-dien-1-yl phenylcarbamate (3x):** 4,5-hexadiene-1-ol (1g, 10.19mmol) was added to a solution of phenyl isocyanate (1.335g, 11.2mmol), triethyl amine(1.133g, 11.2mmol), and dichloromethane (100mL). The reaction stirred at room temperature for two hours. Solvent was removed under reduced pressure. The product was washed with a one molar solution of hydrochloric acid and extracted with ethyl acetate. The product (1.0g, 4.6mmol, 45%) was obtained after flash chromatography (SiO$_2$, hexanes:EtOAc = 9:1)

Exists as a mixture of two rotamers.

Rotamer 1, $^{1}$H NMR (500 MHz, CDCl$_3$), $\delta$ 7.49 (dd, $J$ = 59.8, $J$ = 8.0, 1H), 7.35 – 7.32 (m, 2H), 7.31 (t, $J$ = 8.0, 2H), 7.11 – 7.05 (m, 1H), 6.58 (s, 1H), 5.14 (p, $J$ = 6.7, 1H), 4.72 – 4.66 (m, 2H), 4.21 (t, $J$ = 6.5, 2H), 2.14 – 2.10 (m, 2H), 1.85 – 1.80 (m, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$), $\delta$ 208.54, 129.06, 128.99, 119.90, 88.98, 75.41, 66.49, 31.90, 28.16, 26.41, 24.47.
Rotamer 2, $^1$H NMR (500 MHz, CDCl₃), $\delta$ 7.40 – 7.27 (m, 2H), 7.22 (d, $J = 7.5$, 2H), 7.01 – 6.98 (m, 1H), 6.25 (s, 1H), 4.97 (p, $J = 6.7$), 4.68 – 4.65 (m, 2H), 4.20 – 4.18 (m, 2H), 1.78 – 1.74 (m, 2H), 1.68 – 1.64 (m, 2H). $^{13}$C NMR (126 MHz, CDCl₃), $\delta$ 208.54, 128.99, 128.82, 128.30, 119.55, 88.49, 64.55, 55.41, 27.51, 25.54, 24.10. IR (film) $\lambda_{max}$ (3327.98, 2725.62, 1955.31, 1736.10, 1597.15, 1376.84). HRMS(EI) calculated for C₁₃H₁₆NO₂ [M+H]+; 218.1136, found 218.1143.

Hexa-4,5-dien-1-yl benzylcarbamate (3y): 4,5-hexadiene-1-ol (1g, 10.19mmol) was added to a solution of benzyl isocyanate (1.491g, 11.2mmol), triethyl amine(1.133g, 11.2mmol), and dichloromethane (100mL). The reaction stirred at room temperature for two hours. Solvent was removed under reduced pressure. The product was washed with a one molar solution of hydrochloric acid and extracted with ethyl acetate. The product (1.0g, 4.6mmol, 45%) was obtained after flash chromatography (SiO₂, hexanes:EtOAc = 20:3)

$^1$H NMR (500 MHz, CDCl₃), $\delta$ 7.35-7.26 (m, 5H), 5.14-5.09 (m, 1H), 4.97 (s, 1H), 4.70-4.67 (m, 2H), 4.37 (d, $J = 5.8$, 2H), 4.13 (t, $J = 6.4$, 2H), 2.07 (s, 2H), 1.78-1.73 (m, 2H). $^{13}$C NMR (126 MHz, CDCl₃), $\delta$ 208.5, 138.5, 128.7, 127.5, 89.1, 75.3, 64.4, 45.0, 28.3, 24.5. IR (film) $\lambda_{max}$ (3331, 3063, 3030, 2950, 2852, 1955, 1698, 1605). HRMS(EI) calculated for C₁₄H₁₈NO₂ [M+H]+; 232.1293, found 232.1325.

Hexa-4,5-dien-1-yl carbamate (3z): Hexa-4,5-dien-1-ol (0.567g, 5.78mmol) was added to a solution of Potassium Isocyanate (0.938g, 11.56mmol), and dichloromethane (10mL). Trifluoroacetic acid (1.384g, 12.141mmol) was then diluted with dichloromethane (10mL), and added dropwise to the solution. The reaction stirred at room temperature for five hours. The product (0.356g, 2.522 mmol, 44%) was then extracted with dichloromethane, and purified with flash chromatography (SiO₂, hexanes:EtOAc = 1:1)
**N-(3-(buta-2,3-dien-1-yloxy)propyl)-4-methylbenzenesulfonamide (4aa):** 4aa was synthesized following the figure shown above and GS1a. To a solution of propane-1,3-diyl bis(4-methylbenzenesulfonate) (5g, 13mmol) in DMF(40mL) in a round bottom flask was added potassium hydroxide (0.7296g, 13mmol) and p-Toluenesulfonamide (2.225g, 13mmol). The reaction refluxed over night then was washed with brine (3x 20mL) and ether. The product (1.2 g, 3.12mmol, 24%) was obtained after flash chromatography (SiO₂, hexanes:EtOAc = 5:1) NMR data matched known spectra. The product (1.2g, 3.13mmol) was then placed in a dry round bottom flask with propargyl alcohol (263.1mg, 4.69mmol) and potassium carbonate (648.7mg, 4.69mmol) in dry DMF/THF (5mL/25mL). The reaction stirred at 80° C overnight (12 H). The product (150mg, 0.56mmol, 18%) was obtained after flash chromatography (SiO₂, hexanes:EtOAc = 5:1)

(3-(buta-2,3-dien-1-yloxy)propyl)(tosyl)-l2-azane was synthesized from (3 -(prop-2-yn-1-yloxy)propyl)(tosyl)-l2-azane following GS1a. The product was extracted with ethyl acetate and 1M HCl. The product (50mg, 0.178mmol, 33%) was obtained after flash chromatography (SiO₂, hexanes:EtOAc = 5:1)

1H NMR (500 MHz, CDCl₃), δ 7.75 (d, J = 8.0, 2H), 7.31 (d, J = 8.0, 2H), 5.18 (t, J = 6.5, 1H), 5.13 (s, 1H), 4.84 – 4.82 (m, 2H), 3.96 – 3.93 (m, 2H), 3.49 (t, J = 5.5, 2H), 3.28 (t, J = 6.0, 2H), 2.44 (s, 3H), 1.76 – 1.71 (m, 2H). 13C NMR (126 MHz, CDCl₃), δ 208.98, 143.189, 137.106, 129.75, 129.63, 128.33, 127.11, 127.05, 87.56, 77.27, 77.02, 76.22, 68.89, 68.49, 46.98, 42.17, 30.19, 28.82, 21.51. IR (film) λmax (3287, 2936, 2861, 1957, 1599, 1431). HRMS(EI) calculated for C₁₄H₁₈NO₃S [M+H]+; 282.1119, 282.1119.
8-(Trimethylsilyl)oct-7-yn-1-yl-4-methylbenzenesulfonate (6a1): Trimethylsilyl acetylene (6.5 mmol, 0.95 mL, 0.690 g/mL) was dissolved in 1,4-dioxane (0.1 M, 11 mL) then cooled to 0°C. n-butyllithium (2.5 M in hexanes, 2.6 mL) was added dropwise over ten minutes. Hexane-1,6-diyl bis(4-methylbenzenesulfonate) (4.68 mmol, 2 g), was then added, and the reaction was stirred at 110°C for 24 hours. After the reaction was cooled to room temperature, the mixture was diluted with ammonium chloride, extracted with ethyl acetate, and washed again with saturated ammonium chloride, water, and brine. The organic phases were dried over sodium sulfate, and the product was concentrated under reduced pressure. The product (0.455 g, 1.29 mmol, 27.6%) was purified by flash chromatography (SiO2, hexanes:EtOAc = 6:1). NMR matched known spectra.12

1H NMR (500 MHz, CDCl3), δ 7.65 (d, J = 8.2, 2H), 7.21 (d, J = 8.0, 2H), 3.88 (t, J = 6.4, 2H), 2.31 (s, 3H), 2.03 (t, J = 7.1, 2H), 1.51 (t, J = 6.9, 2H), 1.31 (t, J = 3.5, 2H), 1.17 (t, J = 3.6, 4H); 13C NMR (126 MHz, CDCl3), δ 144.5, 132.9, 129.6, 127.7, 107.1, 84.3, 77.1, 76.8, 76.6, 70.3, 28.5, 28.1, 27.9, 24.7, 21.4, 19.5, 0.0; IR (film) λmax (2939, 2861, 2172, 1598).

4-Methyl-N-(oct-7-yn-1-yl)benzenesulfonamide (6a2): To a solution of potassium carbonate (9.98 mmol, 1.38 g), p-toluenesulfonamide (5.24 mmol, 0.897 g), and dimethylformamide (0.2 M, 24.95 mL) was added. 8-(trimethylsilyl)oct-7-yn-1-yl-4-methylbenzenesulfonate (4.99 mmol, 1.76 g). The reaction was heated to 85°C and stirred overnight. The product was extracted with ethyl acetate and washed with water and brine. The organic phase was dried over sodium sulfate, then concentrated under reduced pressure. The concentrated product was added to a solution of potassium carbonate (9.98 mmol, 1.38 g) and methanol (10 mL). The reaction was stirred at room temperature overnight. After stirring overnight, the reaction was extracted with ethyl acetate and washed with water and brine. The organic phase was dried over sodium sulfate and concentrated under reduced pressure. The product (0.320 g, 1.145 mmol, 23.0% yield) was purified by silica gel chromatography (SiO2, hexanes:EtOAc = 6:1). NMR matched known spectra.13

1H NMR (500 MHz, CDCl3), δ 7.74 (d, J = 8.2, 2H), 7.31 (d, J = 8.0, 2H), 4.38 (s, 1H), 2.96-2.91 (q, J = 6.8, 2H), 2.43 (s, 3H), 2.15-2.13. (p, J = 3.5, 2H), 1.93 (s, 1H), 1.46 (p, J = 7.27, 4H), 1.28-1.24. (m, 4H).
4-Methyl-N-(nona-7,8-dien-1-yl)benzenesulfonamide (6a): To a solution of 1,4-dioxane (.1M, 2 mL), paraformaldehyde (2.29 mmol, .069 g), and copper (I) bromide (.802 mmol, .115 g), 4-methyl-N-(oct-7-yne-1-yl)benzenesulfonamide (1.145 mmol, .320 g) was added at room temperature. Dicyclohexylamide (2.29 mmol, .378 mL, .912 g/mL) was then added, and the reaction was sealed with parafilm and stirred at 100° C for 24 hours. After cooling to room temperature, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate and washed with 1 M HCl and brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude allene product (.280 g, .955 mmol, 83.3%) was purified by flash chromatography (SiO2, hexanes:EtOAc = 10:1).

1H NMR (500 MHz, CDCl3), 7.74 (d, J = 8.2, 2H), 7.30 (d, J = 8.03, 2H), 5.06 (t, J = 13.5, 1H), 4.66-4.63 (p, J = 6.5, 2H), 4.30 (s, 1H), 2.93 (q, J = 10.2, 2H), 2.43 (s, 3H), 1.98-1.92 (m, 2H), 1.45 (t, J = 13.6, 2H), 1.35-1.24 (m, 6H); 13C NMR (126 MHz, CDCl3), δ 208.4, 143.3, 136.9, 129.6, 127.1, 89.8, 77.0, 43.1, 28.4, 26.2, 21.5, 14.1; IR (film) λmax (3283, 2930, 2856, 1954, 1598, 1495). HRMS(EI) calculated for C16H24NO2S [M+H] 294.1528, found 294.1514.

N-(2-(Hexa-4,5-dien-1-yloxy)phenyl)-4-methylbenzenesulfonamide (6b): hexa-4,5-dien-1-ol was synthesized from 4-pentyne-1-ol following GS1a, product matched known spectra (3.4g, 70.8% yield).

hexa-4,5-dien-1-ol (1.326g, 13.5mmol) and triphenyl phosphine (3.53g, 13.5mmol) was added to a solution of 2-nitrophenol (1.87g, 13.5mmol) and diisopropyl azodicarboxylate (2.729g, 13.5mmol) in dichloromethane (45mL) at 0°C. The reaction was allowed to return to room temperature and stirred overnight (18H). The reaction was washed with brine and extracted with ethyl acetate. The product (1.03g, 4.72mmol, 35%) was obtained after flash chromatography (SiO2, hexanes:EtOAc = 5:1). The resulting product (1.03g, 4.72mmol) was then placed in a round bottom flask with water (4.7mL) and ethanol (19.6mL). Iron powder
(2.66g, 47.72mmol) and a catalytic amount of concentrated hydrochloric acid (0.4mL). The reaction refluxed for 6 hours, the solvent was removed under reduced pressure, and filtered over celite. The product (0.5g, 2.6mmol, 55%) was obtained after flash chromatography (SiO₂, hexanes:EtOAc = 5:1).

2-(hexa-4,5-dien-1-yloxy)aniline (0.5g, 2.64mmol) was added to a solution of triethyl amine (320 mg, 3.17 mmol), p-toluenesulfonyl chloride (604mg, 3.17mmol) and dichloromethane (6.3mL) at 0°C. The reaction was allowed to return to room temperature and stirred overnight. Solvent was removed, product was washed with brine and extracted with ethyl acetate. The product (743mg, 2.16mmol, 82%) was obtained after flash chromatography (SiO₂, hexanes:EtOAc = 9:1).

1H NMR (500 MHz, CDCl₃), δ 7.64 (d, J = 8.3, 2H), 7.57 (dd, J = 6.4, 1.6 ,1H), 7.20 (d, J = 8.1, 2H), 7.04 (td, J = 7.6, 1.6, 1H), 6.97, (s, 1H), 6.92 (td, J = 7.8, 1.1, 1H), 6.74 (d, J = 8.2, 1H), 5.12 (p, J = 6.7, 1H), 4.76 – 4.73 (m, 2H), 3.84 (t, J = 6.4, 2H), 2.38 (s, 3H), 2.07 – 2.01 (m, 2H), 1.79 (p, J = 7.4, 2H). 13C NMR (126 MHz, CDCl₃), δ 208.51, 148.86, 143.64, 136.34, 129.41, 127.18, 125.95, 125.37, 121.50, 121.00, 111.27, 88.94, 75.56, 67.64, 28.15, 24.44, 21.54. IR (film) λmax (3155, 2253, 1613, 1456, 1382, 1096). HRMS(EI) calculated for C₁₉H₂₂NO₃S [M+H] 344.1321, found 344.1319.

Hepta-5,6-dien-1-yl carbamate (6c): hepta-5,6-dien-1-ol was synthesized from 5-hexyne-1-ol according to GS1. To a solution of hepta-5,6-dien-1-ol (4.659mmol, 0.526g) in dry dichloromethane (47mL) was added triethylamine (5.125mmol, 0.5186g) and isocyanc acid (5.125mmol, 1.01g, 0.78mL). After 2 hours stirring at room temperature, the solvent was removed under reduced pressure. The crude product was then extracted with ethyl acetate and washed with brine and 1 M HCl. The solvent was removed under reduced pressure, the residue was purified by flash column chromatography (EtOAc/Hexanes, 1:4) to give hepta-5,6-dien-1-yl carbamate (0.600g, 3.87mmol, 83%).
\(^{1}\)H NMR (500 MHz, CDCl\(_{3}\)), \(\delta\) 5.11 (p, \(J = 6.8\), 1H), 4.71 – 4.68 (m, 2H), 4.61 (s, 2H), 4.09 (t, \(J = 6.7\) 2H), 2.09 – 2.03 (m, 2H), 1.69 (p, \(J = 8.3\), 2H), 1.52 (p, \(J = 7.7\), 2H). \(^{13}\)C NMR (126 MHz, CDCl\(_{3}\)), \(\delta\) 208.55, 156.97, 89.59, 74.95, 65.11, 28.32, 27.81, 25.30. IR (film) \(\lambda_{\text{max}}\) (3534, 3241, 2923, 1955, 1748, 1597). HRMS calculated for C\(_8\)H\(_{14}\)NO\(_2\) [M+H]+ 156.0980, 156.0980 found.

Hepta-5,6-dien-1-ol (6d): Title compound was synthesized from 5-hexyne-1-ol according to GS1. To a solution of hepta-5,6-dien-1-ol (4.659mmol, 0.526g) in dry dichloromethane (47mL) was added triethylamine (5.125mmol, 0.5186g) and tosyl isocyanate (5.125mmol, 1.01g, 0.78mL). After 2 hours stirring at room temperature, the solvent was removed under reduced pressure. The crude product was then extracted with ethyl acetate and washed with brine and 1 M HCl. The solvent was removed under reduced pressure, the residue was purified by flash column chromatography (EtOAc/Hexanes, 1:4) to give hepta-5,6-dien-1-yl tosylcarbamate.

\(^{1}\)H NMR (500 MHz, CDCl\(_{3}\)), \(\delta\) 7.93 (d, \(J = 8.3\), 2H), (d, \(J = 8.2\), 2H), 5.11 - 5.07 (m, 1H), 4.69 - 4.66 (m, 2H), 4.56 (s, 1H), 2.05 (s, 3H), 1.70 - 1.64 (m, 2H), 1.52 - 1.48 (m, 2H), 1.28 (t, \(J = 10\));\(^{13}\)C NMR (126 MHz, CDCl\(_{3}\)), \(\delta\) 208.5, 146.8, 141.7, 130.2, 127.1, 89.6, 74.9, 65.1, 60.4, 28.3, 25.3, 21.8, 14.2. HRMS(EI) calculated for C\(_{15}\)H\(_{20}\)NO\(_4\)S [M+H]+310.1114, found 310.1109.

9-(Trimethylsilyl)non-8-yn-1-yl 4-methylbenzenesulfonate (7a1): Trimethylsilyl acetylene (22.7mmol, 3.23mL, .690g/mL) was added to a solution of 1,4-dioxane (25 mL) under argon, then placed in an ice bath. n-Butyllithium (22.7mmol, 9.08mL, 2.5M in hexanes) was added dropwise over ten minutes. The reaction was brought to room temperature before hexane-1,6-diyl bis(4-methylbenzenesulfonate) (11.35mmol, 5g) was added. The reaction was stirred at 110° C under reflux for 24 hours. The reaction was washed with ammonium chloride, and the
product was extracted with ethyl acetate and washed with brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The product (2.00g, 5.67mmol, 48.1% yield) was obtained after flash chromatography (SiO₂, hexanes:EtOAc = 6:1).

1H NMR (500 MHz, CDCl₃), δ 7.64 (d, J = 8.2, 2H), 7.20 (d, J = 8.1, 2H), 3.87 (t, J = 6.4, 2H), 2.31 (s, 3H), 2.04 (t, J = 7.1, 2H), 1.51-1.30 (m, 6H), 0.74 (t, J = 6.9, 2H), 0.00 (s, 9H); 13C NMR (126 MHz, CDCl₃), δ 144.4, 132.9, 129.6, 127.7, 107.2, 84.2, 76.8, 70.4, 60.2, 34.3, 31.4, 28.3, 22.4, 19.5, 13.9, 0.00; IR (film) λmax (2935, 2858, 2172). HRMS(EI) calculated for C₁₆H₂₆O₃NS [M+NH₄]+ 384.2070, found 384.200.

4-Methyl-N-(non-8-yn-1-yl)benzenesulfonamide (7a2): 9-(trimethylsilyl)non-8-yn-1-yl 4-methylbenzenesulfonyl chloride (3.07 mmol, 1.124 g) was added to a solution of p-toluenesulfonamide (3.22 mmol, .551 g), potassium carbonate (6.132 mmol, .847 g), and dimethylformamide (2 M, 20 mL, .944 g/mL). The reaction was heated to 85°C and stirred for 16 hours. After cooling to room temperature, the product was extracted with ethyl acetate and washed with water and brine. The organic phases were dried over sodium sulfate, and the product was concentrated under reduced pressure. The crude product was then added to a solution of potassium carbonate (6.132 mmol, .847 g) and methanol (15 mL) and stirred at room temperature overnight. The solvent was removed under reduced pressure, and the product was extracted with ethyl acetate and washed with water and brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The product (.31 g, 1.056 mmol, 34.4%) was purified by flash chromatography (SiO₂, hexanes:EtOAc = 6:1). 1H NMR (500 MHz, CDCl₃), δ 7.67 (d, J=8.3, 2H), 7.23 (d, J = 7.99, 2H), 4.16 (s, 1H), 2.85 (q, J = 6.8, 2H), 2.35 (s, 3H), 2.07 (m, 2H), 1.96 (s, 1H), 1.41-1.16 (m, 12H); 13C NMR (126 MHz, CDCl₃), δ 143.3, 136.9, 129.6, 127.1, 84.5, 77.2, 77.0, 76.7, 68.2, 43.1, 34.6, 31.5, 29.4, 28.4, 28.2, 22.6, 21.5, 18.3, 14.1; IR (film) λmax (3289, 2931, 2857, 2115). HRMS(EI) calculated for C₁₆H₂₄NO₂S [M+H]+ 294.1528, found 294.1523.
**N-(Deca-8,9-dien-1-yl)-4-methylbenzenesulfonamide (7a):** To a solution of copper (I) bromide (.739 mmol, .106 g), paraformaldehyde (2.11 mmol, .063 g) and 1,4-dioxane (.1 M, 1.5 mL), 4-methyl-N-(non-8-yn-1-yl)benzenesulfonamide (1.056 mmol, .31 g) was added. Dicyclohexylamide (2.11 mmol, .348 mL, .912 g/mL) was purged over calcium hydride before being added to the reaction. The reaction was then sealed with parafilm, heated and stirred at 100° C for 24 hours. After cooling to room temperature, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate and washed with 1 M HCl and brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude allene product (.262 g, .852 mmol, 80.6%) was purified by flash chromatography (SiO2, hexanes:EtOAc = 6:1).

^1H NMR (500 MHz, CDCl3), δ 7.74 (d, J = 8.2, 2H), 7.31 (d, J = 8.1, 2H), 5.06 (t, J = 6.7, 2H), 4.65-4.63 (m, 2H), 4.38 (s, 1H), 2.92 (t, J = 6.6, 2H), 2.43 (s, 3H), 1.95 (q, J = 3.4, 2H), 1.44-1.23 (m, 8H); ^13C NMR (126 MHz, CDCl3), δ 208.4, 143.3, 136.9, 129.6, 127.1, 89.9, 77.0, 74.6, 43.2, 29.5, 28.8, 28.1, 26.4, 21.5; IR (film) λmax (3230, 2980, 2870, 1980).

HRMS(EI) calculated for C17H25O3S [M+H]+ 309.1525, found 309.1524.

**Octa-6,7-dien-1-yl tosylcarbamate (7b):** hepta-5,6-dien-1-ol was synthesized from 5-hexyne-1-ol according to GS1. To a solution of hepta-5,6-dien-1-ol (4.659mmol, 0.526g) in dry dichloromethane (47 mL) was added triethylamine (5.125mmol, 0.5186g) and tosyl isocyanate (5.125mmol, 1.01g, 0.78mL). After 2 hours stirring at room temperature, the solvent was removed under reduced pressure. The crude product was then extracted with ethyl acetate and washed with brine and 1M HCl. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography (EtOAc/Hexanes, 1:4) to give hepta-5,6-dien-1-yl tosylcarbamate.

^1H NMR (500 MHz, CDCl3), δ 7.95 - 7.94 (d, J = 8.3, 2H), 7.38 - 7.36 (d, J = 8.2, 2H), 5.10 - 5.07 (m, 1H), 4.68 - 4.67 (m, 2H), 4.11 - 4.08 (t, J = 6.7, 2H), 2.47 (s, 3H), 2.00 - 1.97 (m, 2H), 1.62 - 1.58 (m, 2H), 1.41 - 1.39 (m, 2H), 1.32 - 1.31 (m, 2H); ^13C NMR (126 MHz, CDCl3), δ 208.5, 150.3, 145.1, 135.5, 129.6, 128.4, 128.4, 89.6, 74.9, 67.1, 28.5, 28.2, 28.0, 25.0, 21.7.

HRMS(EI) calculated for C16H22NO4S [M+H]+ 324.1270 found, 324.1238.
2-(Hepta-5,6-dien-1-yloxy)-N-tosylacetamide (7c): To a suspension of sodium hydride (60% by weight in mineral oil, 20.5 mg, 0.513 mmol) in THF (11.7 mL), was added 2-(hepta-5,6-dien-1-yloxy)acetamide (79 mg, 0.467 mmol). The reaction was refluxed at 70°C for 2 hours, then cooled to 0°C and p-toluene sulfonyl chloride (0.513 mmol, 97.8 mg) was added. Reaction was then refluxed for an additional 2 hours. 2-(hepta-5,6-dien-1-yloxy)-N-tosylacetamide (6 mg, 0.0396 mmol, 4%) was purified by flash chromatography (SiO2, hexanes:EtOAc = 5:1)

1H NMR (500 MHz, CDCl3), δ 8.86 (s, 1H), 7.99 - 7.98 (d, J = 8.3, 2H), 7.36 - 7.34 (d, J = 8.3, 2H), 5.13 - 5.07 (m, 1H), 4.70 - 4.69 (m, 2H), 3.89 (s, 2H), 3.51 - 3.48 (t, J = 6.6), 2.46 (s, 3H), 2.04 - 2.03 (m, 2H), 1.66 - 1.63 (m, 2H), 1.49 - 1.47 (m, 2H). 13C NMR (126 MHz, CDCl3), δ 208.6, 167.5, 145.3, 135.4, 129.6, 128.5, 89.4, 75.1, 72.0, 69.8, 29.7, 28.6, 27.7, 25.2, 21.7. HRMS(EI) calculated for C19H26NO4S [M+H]+ 324.1270, found 324.1248.

2-(Hepta-5,6-dien-1-yloxy)aniline (7d): 1-(hepta-5,6-dien-yloxy)-5-nitrobenzene (1.381g, 5.918mmol) was placed in a round bottom flask with water (6mL) and ethanol (24mL). Iron powder (3.305g, 59.18mmol) and a catalytic amount of concentrated hydrochloric acid (0.3mL). The reaction refluxed for 6 hours, the solvent was removed under reduced pressure, and filtered over celite. The product (0.786g, 2.2mmol, 57%) was obtained after flash chromatography (SiO2, hexanes:EtOAc = 5:1).

1H NMR (500MHz, CDCl3), δ 6.80 (m, J=12.8, 2H), 6.76 (m, J=13.1, 2H), 5.14 (m, J=6.8, 1H), 4.70 (d, J=13.2, 2H), 4.02 (t, J=9.4, 2H), 2.10 (t, J=10.8, 2H), 1.88 (m, J=7, 2H), 1.64 (p, J=7.7, 2H), 13C NMR. (126MHz, CDCl3), δ 208.58, 146.70, 136.22, 130.22, 124.29, 118.49, 111.40, 89.70, 74.97, 67.92, 28.78, 25.61; IR (film) vmax (3471, 3377, 2938, 1505). HRMS(EI) calculated for C10H24NO3S [M+H]+ 358.1478, found 358.1476.

10 member ring starting materials
10-(Trimethylsilyl)dec-9-yn-1-yl 4-methylbenzenesulfonate (8a1): Trimethylsilyl acetylene (16.50 mmol, 2.35 mL, 0.71 g/mL) was added to 1,4-dioxane (.1 M, 25 mL) and placed in an ice bath. n-butyllithium (16.50 mmol, 6.6 mL, 0.2 M in hexanes) was added dropwise over ten minutes. After reaching room temperature, octane-1,8-diyl bis(4-methylbenzenesulfonate) (10.99 mmol, 5 g) was added, and the reaction was heated to 110° C and stirred for 24 hours. After cooling to room temperature, the reaction was diluted with concentrated ammonium chloride, and the product was extracted with ethyl acetate and washed with concentrated ammonium chloride again, followed by water and brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The product (1.00 g, 2.627 mmol, 23.9%) was purified by flash chromatography (SiO2, hexanes:EtOAc = 8:1).

1H NMR (500 MHz, CDCl3), δ 7.64 (d, J = 8.1, 2H), 7.20 (d, J = 8.0, 2H), 3.87 (t, J = 6.5, 2H), 2.31 (s, 3H), 2.05 (t, J = 7.1, 2H), 1.48 (t, J = 7.2, 2H), 1.50-1.32 (m, 6H), 0.82-0.72 (m, 4H), 0.00 (s, 9H); 13C NMR. (126 MHz, CDCl3), δ 144.4, 133.0, 129.6, 127.7, 107.4, 84.1, 77.0, 70.4, 60.2, 34.4, 31.4, 28.6, 22.4, 13.9, 0.0; IR (film) λmax (2932, 2857, 2172, 1598).

HRMS(EI) calculated for C20H33O3SSi [M+H]+ 381.1920 found 381.1923.

N-(Dec-9-yn-1-yl)-4-methylbenzenesulfonamide (8a2): To a solution of p-toluenesulfonamide (2.76 mmol, 0.472 g), potassium carbonate (5.25 mmol, 0.726 g), and dimethylformamide (0.2 M, 13.1 mL), 10-(trimethylsilyl)dec-9-yn-1-yl-4-methylbenzenesulfonate (2.627 mmol, 1.00 g) was added. The reaction was heated and stirred at 85° C for 16 hours. After cooling to room temperature, the product was extracted with ethyl acetate and was washed with water and brine. The organic phases were dried over sodium sulfate and concentrated under reduced pressure. The crude product was added to a solution of potassium carbonate (5.25 mmol, .726 g) and methanol (15 mL). The reaction was stirred at room temperature for 16 hours. Solvent was removed under reduced pressure, and the product was extracted with ethyl acetate and washed with water and brine. The organic phases were
dried over sodium sulfate and concentrated under reduced pressure. The product was purified by flash chromatography (SiO₂, hexanes:EtOAc = 8:1).

\(^1\)H NMR (500 MHz, CDCl₃), δ 7.74 (d, J = 8.2, 2H), 7.31 (d, J = 7.9, 2H), 4.23 (s, 1H), 2.93 (q, J = 6.8, 2H), 2.43 (s, 3H), 2.18-2.15 (m, 2H), 2.04 (s, 1H), 1.55-1.23 (m, 12H); \(^{13}\)C NMR (126 MHz, CDCl₃), δ 143.3, 136.9, 129.6, 127.1, 84.6, 77.0, 68.1, 60.4, 43.1, 28.5, 26.4, 18.3, 14.2; IR (film) λmax (3287, 2929, 2856, 2115, 1918, 1734), HRMS (EI) calculated for C₁₇H₂₆NO₂S [M+H]+ 308.1685 found 308.1686.

**4-Methyl-N-(undeca-9,10-dien-1-yl)benzenesulfonamide (8a):** Copper (I) bromide (1.867mmol, 0.268g), paraformaldehyde (5.33mmol, 0.160g), and N-(dec-9-yn-1-yl)-4-methylbenzenesulfonamide (2.67mmol, .820g) were added to a round bottom flask with 1,4-dioxane (.1M, 4mL). Dicyclohexylamine (5.33mmol, .88mL, .912g/mL) was then purged with calcium hydride before being added to the reaction. The reaction was sealed with parafilm, then heated to 100°C and stirred for 24 hours. After cooling to room temperature, the solvent was removed under reduced pressure, and the product was extracted with ethyl acetate and washed with 1 M HCl, water, and brine. The product (.807g, 2.51mmol, 94.1%) was concentrated under reduced pressure and purified by flash chromatography (SiO₂, hexanes:EtOAc = 6:1)

\(^1\)H NMR (500 MHz, CDCl₃), δ 7.75 (d, J = , 2H), 7.30 (d, J = , 2H), 5.10 (1H), 4.65 (2H), 3.64 (2H), 2.18-2.15 (m, 2H), 2.04 (s, 1H), 1.55-1.23 (m, 12H); \(^{13}\)C NMR (126 MHz, CDCl₃), δ 208.48, 143.34, 137.02, 129.69, 127.11, 90.07, 90.02, 74.59, 63.09, 43.22, 32.80, 29.09, 29.00, 28.24, 28.20, 26.47, 25.71, 21.52 IR (film) λmax (3230, 2980, 2870, 1980), HRMS (EI) calculated for C₁₈H₂₈NO₂S [M+H]+ 322.1841 found 322.1834.

**2-(Octa-6,7-dien-1-yloxy)-N-tosylacetamide (8b):** To a suspension of sodium hydride (60% by weight in mineral oil, 31.6mg, 0.786mmol) in THF (17 mL), was added 2-(octa-6,7-dien-1-yloxy)acetamide (131mg, 0.7148mmol). The reaction was refluxed at 70°C for 2 hours, then cooled to 0°C and p-toluene sulfonyl chloride (0.786mmol, 149.9mg) was added. Reaction was
then refluxed for an additional 2 hours. 2-(octa-6,7-dien-1-yloxy)-N-tosylacetamide (39.5mg, 0.117mmol, 16%) was purified by flash chromatography (SiO2, hexanes:EtOAc = 5:1).

$^1$H NMR (500 MHz, CDCl3), δ 8.92 (s, 1H), 7.99 - 7.97 (d, J = 8.3, 2H), 7.35 - 7.34 (d, J = 8.2, 2H), 5.11 - 5.08 (m, 1H), 4.68 - 4.65 (m, 2H), 3.89 (s, 2H), 3.50 - 3.47 (t, J = 6.7, 2H), 2.44 (s, 3H), 2.05 - 1.99 (m, 2H), 1.62 - 1.59 (m, 2H), 1.46 - 1.37 (m, 5H); $^{13}$C NMR (126 MHz, CDCl3), δ 208.5, 167.3, 145.3, 135.4, 129.6, 128.5, 89.7, 77.3, 77.1, 76.8, 74.8, 72.1, 69.8, 29.0, 28.7, 28.0, 25.3, 21.7. HRMS (EI) calculated for C$_{17}$H$_{24}$NO$_2$S [M+H]$^+$ 338.1427 found 338.1413.

Nona-7,8-dien-1-yl tosylcarbamate (8c): nona-7,8-dien-1-ol was synthesized from 7-octyne-1-ol according to GS1. To a solution of nona-7,8-dien-1-ol (4.659mmol, 0.6533g) in dry dichloromethane (47mL) was added triethylamine (5.125mmol, 0.5186g) and tosyl isocyanate (5.125mmol, 1.01g, 0.78mL). After 2 hours stirring at room temperature, the solvent was removed under reduced pressure. The crude product was then extracted with ethyl acetate and washed with brine and 1 M HCl. The solvent was removed under reduced pressure, the residue was purified by flash column chromatography (EtOAc/Hexanes, 1:4) to give nona-7,8-dien-1-yl tosylcarbamate.

$^1$H NMR (500 MHz, CDCl3), δ 7.92 (d, J=8.4, 2H), 7.35 (d, J=8.4, 2H), 5.09 - 5.06 (p, J=2.35, 1H), 4.65 (q, J=6.7, 3H), 4.07 (t, J=6.7, 2H), 2.45 (s, 3H), 1.99 - 1.96 (m, 2H), 1.60 - 1.55 (m, 2H), 1.40 - 1.37 (m, 4H); $^{13}$C NMR (126 MHz, CDCl3), δ 208.5, 150.4, 145.1, 135.5, 129.6, 128.4, 89.8, 74.8, 67.2, 28.8, 28.5, 28.4, 28.0, 25.4, 21.7. HRMS (EI) calculated for C$_{18}$H$_{28}$NO$_2$S [M+H]$^+$ 338.1427 found 338.1408.

N-(Dodeca-10,11-dien-1-yl)-4-methylbenzenesulfonamide (13): In a dry round bottom flask 4-methylbenzenesulfonamide (9.519mmol, 1.63g) and potassium carbonate (9.515mmol, 1.316g) were combined in acetonitrile (40mL). Dodeca-10,11-dien-1-yl 4-methylbenzenesulfonate (4.759 mmol, 1.6g) was then added and refluxed for 12 hours at 90°C. After cooling to room temperature, the mixture was diluted with ethyl acetate and extracted
with 1N HCl. The organic phase was washed with 1N HCl and then brine. The organic phase was then dried over sodium sulfate and concentrated under reduced pressure. The product (3.28mm, 1.1g, 69%) was purified by flash chromatography (SiO2, Hexane:EtOAc = 4:1).

NMR (500 MHz, CDCl3), δ 7.76 - 7.74 (d, J = 8.3, 2H), 7.32 - 7.30 (d, J = 8.0, 2H), 5.10 - 5.07 (m, 1H), 4.66 - 4.63 (m, 2H), 4.39 (s, 1H), 3.95 - 3.90 (q, J = 6.9, 2H), 2.43 s, (3H), 1.99 - 1.97 (m, 2H), 1.45 - 1.35 (m, 4H); 13C NMR (126 MHz, CDCl3), δ 208.5, 143.3, 137.0, 129.7, 127.1, 90.1, 74.6, 43.2, 29.5, 29.4, 29.2, 29.1, 29.0, 28.9, 28.2, 26.5, 21.5. HRMS(EI) calculated for C19H30NO2S [M+H]+ 336.1998, 336.1992 found.

4-Methyl-N-(trideca-11,12-dien-1-yl)benzenesulfonamide (14):

In a dry round bottom flask 4-methylbenzenesulfonamide (8.386mmol, 1.44g) and potassium carbonate (8.386mmol, 1.16g) were combined in acetonitrile (40mL). Trideca-11,12-dien-1-yl 4-methylbenzenesulfonate (4.193mmol, 1.46g) was then added and refluxed for 12 hours at 90°C. After cooling to room temperature, the mixture was diluted with ethyl acetate and extracted with 1M HCl. The organic phase was washed with 1M HCl and then brine. The organic phase was then dried over sodium sulfate and concentrated under reduced pressure. The product (3.35mm, 1.17g, 80%) was purified by flash chromatography (SiO2, Hexane:EtOAc = 4:1).

1H NMR (500 MHz, CDCl3), δ 7.92 (d, J = 10, 2H), 7.67 (s, 1H), 7.35 (d, J = 5, 2H), 5.09 - 5.06 (m, 1H), 4.66 - 4.64 (m, 2H), 4.15 - 4.06 (m, 2H), 2.45 (s, 3H), 1.98 - 1.96 (m, 2H), 1.58 - 1.55 (m, 2H), 1.28 - 1.25 (m, 10H); 13C NMR (126 MHz, CDCl3), δ 208.6, 150.5, 145.0, 135.5, 129.6, 128.4, 89.8, 74.4, 67.1, 60.4, 28.8, 28.5, 28.4, 28.0, 25.4, 21.7, 21.1, 14.2; HRMS(EI) calculated for C20H32NO2S [M+H]+ 350.2154, 350.2151 found.

Undecane-1,11-diyl bis(4-methylbenzenesulfonate): P-toluenesulfonyl chloride (55.76mmol, 10.63g) and triethylamine (79.65mmol, 11.10mL) were added to a round bottom flask with
dichloromethane (90 mL). The mixture was then stirred for 10 minutes under argon, and then cooled to 0°C. Undecane-1,11-diol (26.55mmol, 5g) was added slowly, and reaction was warmed to room temperature and stirred overnight under argon. The reaction was then cooled to 0°C and water (90mL) was added, and the organic phase was separated. After washing with water and extracting with ethyl acetate, the organic phase was dried over sodium sulfate and concentrated under reduced pressure. The product (10.80g, 21.74mmol, 82%) was purified by flash chromatography (SiO2, DCM:Hexanes = 1:1).

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\text{H NMR (500 MHz, CDCl}_3, \delta \ 7.79 \ (d, J = 10.0, \ 4H), 7.35 \ (d, J = 5.0, \ 4H), 4.03 - 4.00 \ (m, \ 4H), 2.45 \ (s, \ 6H), 1.65 - 1.60 \ (m, \ 3H), 1.30 - 1.10 \ (m, \ 15H); 1^3\text{C NMR (126 MHz, CDCl}_3, \delta \ 144.6, 133.2, 129.8, 127.9, 70.7, 32.8, 29.5, 29.4, 29.3, 28.9, 28.8, 25.7, 25.3, 21.7; IR. (film) \lambda_{max} \ (3944, 3694, 3054, 2987, 2929, 2856, 2685, 2305, 1599). HRMS(EI) calculated for C_{25}H_{37}O_6S_2 [M+H]^+ 497.2032, found 497.2007.}
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13-(Trimethylsilyl)tridec-12-yn-1-yl 4-methylbenzenesulfonate: In a round bottom flask TMS Acetylene (9.06 mmol, 1.30 mL) was added to 1,4-Dioxane (0.1M, 21 mL). The mixture was then cooled to 0°C to which N-BuLi (9.06 mmol, 3.62 mL) was added dropwise over 10 minutes and then stirred for 10 minutes. Undecane-1,11-diyl bis(4-methylbenzenesulfonate) (6.04 mmol, 3 g) was added and the reaction mixture was heated to 110°C under reflux for 24 hours. After cooling to room temperature, the reaction was diluted with ethyl acetate and saturated ammonium chloride. After washing with saturated ammonium chloride and brine, the organic phase was dried over sodium sulfate and concentrated under reduced pressure. The product (0.857g, 2.03 mmol, 34%) was purified by flash chromatography (SiO2, Hexane:EtOAc = 5:1).

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\text{H NMR (500 MHz, CDCl}_3, \delta \ 7.65 \ (d, J = 10.0, \ 2H), 7.20 \ (d, J = 10.0, \ 2H), 3.87 \ (t, J = 5.0, \ 2H), 2.31 \ (s, \ 3H), 1.37-1.34 \ (m, \ 2H), 1.33-1.32 \ (m, \ 18H); 3^1\text{C NMR (126 MHz, CDCl}_3, \delta \ 144.4, 133.0, 129.6, 127.7, 107.6, 84.1, 70.5, 34.5, 31.4, 29.2, 29.1, 28.9, 28.7, 28.6, 28.6, 28.4, 25.1, 22.5, 21.5, 19.7, 13.9; IR. (film) \lambda_{max} \ (2926, 2854). HRMS(EI) calculated for C_{23}H_{39}O_3SSi [M+H]^+ 423.2390, found 423.2393.}
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4-Methyl-N-(tridec-12-yn-1-yl)benzenesulfonamide: 13-(trimethylsilyl)tridec-12-yn-1-yl 4-methylbenzenesulfonate (2.03 mmol, 0.857 g), P-toluenesulfonamide (2.13 mmol, 0.365 g), and potassium carbonate (4.06 mmol, 0.561 g) were added to a round bottom flask in DMF (12 mL). The reaction was stirred at 85°C overnight under argon. The organic phase was extracted with ethyl acetate and washed with water and brine. After drying over sodium sulfate and being concentrated under reduced pressure, the intermediate was added with potassium carbonate (4.06 mmol, 0.561 g) in MeOH (12 mL) into a round bottom flask and was stirred at room temperature overnight. The solvent was then removed under reduced pressure and the crude product was dilute with ethyl acetate. The organic phase was washed with water and brine and was then dried over sodium sulfate and concentrated under reduced pressure. The product (0.278 g, 0.795 mmol, 39%) was purified by flash chromatography (SiO2, Hexane:EtOAc = 6:1). 1H NMR (500 MHz, CDCl3), δ 7.74 (d, J = 8.3, 2H), 7.31 (d, J = 8.0, 2H), 4.14-4.10 (m, 1H), 2.95-2.91 (m, 2H), 2.43 (m, 2H), 1.53-1.50 (m, 2H), 1.33-1.32 (m, 14H); 13C NMR (126 MHz, CDCl3), δ 143.4, 137.0, 129.7, 127.1, 68.1, 43.2, 30.0, 29.4, 29.4, 29.1, 29.0, 28.7, 28.5, 26.5, 21.5, 18.4; IR. (film) λmax (3154, 2928, 2860, 2253, 1710, 1599). HRMS(EI) calculated for C20H32NO2S [M+H]+ 350.2154, found 350.2164.

4-Methyl-N-(trideca-11,12-dien-1-yl)benzenesulfonamide: In a round bottom flask, 4-methyl-N-(tridec-12-yn-1-yl)benzenesulfonamide (.795 mmol, .278 g), Copper (I) Bromide (.557 mmol, .080 g), and paraformaldehyde (1.59 mmol, .048 g) were added and purged with argon for 5 minutes. Degassed 1,4-dioxane (1.2 mL) and dicyclohexylamine (1.59 mmol, .32 mL) were then added and the reaction mixture was stirred at 90°C for 18 hours. After cooling to room temperature, the mixture was diluted with ethyl acetate and extracted with 1N HCl. The organic phase was washed with 1N HCl and then brine. The organic phase was then dried over sodium sulfate and concentrated under reduced pressure. The product (.149 g, .426 mmol, 54%) was purified by flash chromatography (SiO2, Hexane:EtOAc = 6:1). 1H NMR (500 MHz, CDCl3), δ 7.74 (d, J = 8.3, 2H), 7.31 (d, J = 8.0, 2H), 5.09 (m, 1H), 4.65 (m, 2H), 2.93
(m, 2H), 2.43 (s, 3H), 1.20-1.99 (m, 2H), 1.44-1.23 (m, 2H), 1.25-1.23 (m, 14H); $^{13}$C NMR (126 MHz, CDCl$_3$), δ 208.5, 143.3, 136.9, 129.7, 127.1, 90.1, 74.5, 43.2, 29.6, 29.4, 29.5, 29.4, 29.1, 29.1, 26.5, 21.5; IR (film) λmax (3155, 2958, 2254, 1793). HRMS(EI) calculated for C$_{20}$H$_{32}$NO$_2$S [M+H$^+$] 350.2154 found 350.2198.

**Dodecane-1,12-diyl bis(4-methylbenzenesulfonate):** P-toluenesulfonyl chloride (51.89 mmol, 9.89 g) and triethylamine (74.13 mmol, 10.33 mL) were added to a round bottom flask with dichloromethane (135 mL). The mixture was then stirred for 10 minutes under argon, and then cooled to 0°C. 1,12-Dodecanediol (24.71 mmol, 5 g) was added slowly, and reaction was warmed to room temperature and stirred overnight under argon. The reaction was then cooled to 0°C and water (83 ml) was added, and the organic phase was separated. After washing with water and extracting with ethyl acetate, the organic phase was dried over sodium sulfate and concentrated under reduced pressure. The product (9.56 g, 18.72 mmol, 76%) was purified by flash chromatography (SiO$_2$, DCM:Hexanes = 1:1). $^1$H NMR (500 MHz, CDCl$_3$), δ 7.79 (d, J = 10.0, 4H), 7.35 (d, J = 5.0, 4H), 4.03 - 4.00 (m, 4H), 2.45 (s, 6H) 1.64 – 1.61 (m, 4H), 1.30 - 1.20 (m, 17H); $^{13}$C NMR (126 MHz, CDCl$_3$), δ 144.6, 133.2, 129.8, 127.9, 70.7, 32.8, 29.5, 29.4, 29.3, 28.9, 28.8, 25.7, 25.3, 21.7; IR. (film) λmax (3944, 3693, 3054, 2987, 2685, 2410, 2305, 1712, 1599). HRMS(EI) calculated for C$_{26}$H$_{39}$O$_6$S$_2$ [M+H$^+$] 511.2189, found 511.2146.

**14-(Trimethylsilyl)tetradec-13-yn-1-yl 4-methylbenzenesulfonate:** In a round bottom flask TMS Acetylene (8.81mmol, 1.26mL) was added to 1,4-Dioxane (0.1M, 20 mL). The mixture was then cooled to 0°C to which N-BuLi (8.81mmol, 3.52mL) was added dropwise over 10 minutes and then stirred for 10 minutes. Dodecane-1,12-diyl bis(4-methylbenzenesulfonate) (5.87mmol, 3g) was added and the reaction mixture was heated to 110°C under reflux for 24 hours. After cooling to room temperature, the reaction was diluted with ethyl acetate and saturated ammonium chloride. After washing with saturated ammonium chloride and brine, the organic phase was dried over sodium sulfate and concentrated under reduced pressure. The
product (2.057g, 4.71mmol, 80%) was purified by flash chromatography (SiO₂, Hexane:EtOAc = 5:1).

¹H NMR (500 MHz, CDCl₃), δ 7.65 (d, J = 10.0, 2H), 7.21 (d, J = 5.0, 2H), 3.87 (t, J = 5.0 2H), 2.31 (s, 3H), 2.06 (t, J = 10.0, 2H), 1.38 – 1.35 (m, 2H), 1.13 – 1.07 (m, 24H); ¹³C NMR
(126 MHz, CDCl₃), δ 144.4, 133.0, 129.6, 127.7, 107.6, 84.0, 70.5, 34.5, 31.4, 29.3, 29.3, 29.3,
HRMS(EI) calculated for C₂₄H₄₁O₃SSi [M+H]+ 437.2546, found 437.2545.

4-Methyl-N-(tetradec-13-yn-1-yl)benzenesulfonamide: 14-(trimethylsilyl)tetradec-13-yn-1-yl 4-methylbenzenesulfonate (2.03mmol, 0.857g), P-toluenesulfonamide (4.95mmol, 0.848g),
and potassium carbonate (9.42mmol, 1.302g) were added to a round bottom flask in DMF
(28mL). The reaction was stirred at 85°C overnight under argon. The organic phase was
extracted with ethyl acetate and washed with water and brine. After drying over sodium sulfate
and being concentrated under reduced pressure, the intermediate was added with potassium
carbonate (9.42mmol, 1.302g) in MeOH (28mL) into a round bottom flask and was stirred at
room temperature overnight. The solvent was then removed under reduced pressure and the
 crude product was diluted with ethyl acetate. The organic phase was washed with water and
brine, and was then dried over sodium sulfate and concentrated under reduced pressure. The
product (0.441g, 1.21mmol, 58%) was purified by flash chromatography (SiO₂, Hexane:EtOAc
= 6:1).

¹H NMR (500 MHz, CDCl₃), δ 7.75 (d, J = 5.0, 2H), 7.31 (d, J = 10.0, 2H), 2.96 – 2.89 (m, 2H), 2.43 (s, 3H), 2.20 – 2.16 (m, 2H), 1.95 – 1.93 (t, J = 5.0, 1H), 1.40 – 1.37 (m, 2H), 1.27 –
1.21 (m, 19H); ¹³C NMR (126 MHz, CDCl₃), δ 143.4, 137.0, 129.7, 127.1, 84.8, 68.1, 43.2,
31.6, 29.5, 29.5, 29.4, 29.1, 29.1, 28.8, 28.5, 26.5, 22.7, 22.4, 14.2; IR. (film) λmax
(3154, 2928, 2857, 2254, 1795, 1729, 1600). HRMS(EI) calculated for C₂₃H₃₄NO₂S [M+H]+
364.2311, found 364.2318.
N-(Dodeca-10,11-dien-1-yl)-4-methylbenzenesulfonamide: In a round bottom flask, 4-methyl-N-(tetradec-13-yn-1-yl)benzenesulfonamide (1.21mmol, 0.441g), Copper (I) Bromide (0.847mmol, 0.121g), and paraformaldehyde (2.42mmol, 0.073 g) were added and purged with argon for 5 minutes. Degassed 1,4-dioxane (1.8mL) and dicyclohexylamine (2.42mmol, 0.48mL) were then added and the reaction mixture was stirred at 90°C for 18 hours. After cooling to room temperature, the mixture was diluted with ethyl acetate and extracted with 1M HCl. The organic phase was washed with 1M HCl and then brine. The organic phase was then dried over sodium sulfate and concentrated under reduced pressure. The product (0.173g, 0.476mmol, 39%) was purified by flash chromatography (SiO₂, Hexane:EtOAc = 6:1).

1H NMR (500 MHz, CDCl₃), δ 7.74 (d, J = 8.3, 2H), 7.31 (d, J = 8.1, 2H), 5.08 (p, 1H), 4.63 (p, 2H), 2.93 (m, 2H), 1.57 (s, 3H), 2.00-1.98 (m, 2H), 1.46-1.41 (m, 2H), 1.26-1.21 (m, 16H); 13C NMR (126 MHz, CDCl₃), δ 208.5, 143.3, 136.9, 129.7, 127.1, 90.1, 74.5, 43.2, 29.6, 29.5, 29.4, 29.1, 28.3, 26.5, 21.5, 18.5; IR (film) λ max (3155, 2929, 2857, 2254, 1793).

HRMS(EI) calculated for C₂₁H₃₄NO₂S [M+H]+ 364.2311, found 364.2288.

Tridecane-1,13-diyl bis(4-methylbenzenesulfonate): P-toluenesulfonyl chloride (48.51mmol, 9.25g) and triethylamine (69.30mmol, 9.66mL) were added to a round bottom flask with dichloromethane (78mL). The mixture was then stirred for 10 minutes under argon, and then cooled to 0°C. Tridecane-1,13-diol (23.10mmol, 5g) was added slowly, and reaction was warmed to room temperature and stirred overnight under argon. The reaction was then cooled to 0°C and water (78 ml) was added, and the organic phase was separated. After washing with water and extracting with ethyl acetate, the organic phase was dried over sodium sulfate and concentrated under reduced pressure. The product (9.94g, 18.94mmol, 82%) was purified by flash chromatography (SiO₂, DCM:Hexanes = 1:1).

1H NMR (500 MHz, CDCl₃), δ 7.79 (d, J = 10.0, 4H), 7.35 (d, J = 5.0, 4H), 4.03 - 4.00 (m, 4H), 2.45 (s, 6H), 1.64 – 1.61 (m, 4H), 1.30 - 1.20 (m, 22H); 13C NMR (126 MHz, CDCl₃), δ 144.6, 133.2, 130.0, 127.9, 70.7, 32.8, 29.5, 29.4, 29.4, 29.3, 29.0, 28.8, 25.3, 21.6; IR.(film) λ max (3944, 3694, 3054, 2986, 2927, 2855, 2685, 1711, 1599). HRMS(EI) calculated for C₂₇H₄₁O₆S₂ [M+H]+ 524.2345, found 525.2299.
15-(Trimethylsilyl)pentadec-14-yn-1-yl 4-methylbenzenesulfonate: In a round bottom flask TMS Acetylene (8.58 mmol, 1.23 mL) was added to 1,4-Dioxane (.1M, 20 mL). The mixture was then cooled to 0°C to which N-BuLi (8.58 mmol, 3.43 mL) was added dropwise over 10 minutes and then stirred for 10 minutes. Tridecane-1,13-diyl bis(4-methylbenzenesulfonate) (5.72 mmol, 3 g) was added and the reaction mixture was heated to 110°C under reflux for 24 hours. After cooling to room temperature, the reaction was diluted with ethyl acetate and saturated ammonium chloride. After washing with saturated ammonium chloride and brine, the organic phase was dried over sodium sulfate and concentrated under reduced pressure. The product (.871g, 1.93 mmol, 34%) was purified by flash chromatography (SiO2, Hexane:EtOAc = 5:1).

\[ \text{TsO} \quad \text{TMS} \]

1H NMR (500 MHz, CDCl3), δ 7.65 (d, \( J = 10.0 \), 2H), 7.20 (d, \( J = 5.0 \), 2H), 3.88 – 3.86 (m, 2H), 2.31 (s, 3H), 2.08 – 2.05 (m, 2H), 1.38 - 1.35 (m, 2H), 1.12 – 1.06 (m, 24H); 13C NMR (126 MHz, CDCl3), δ 144.4, 133.0, 129.6, 127.7, 107.6, 84.0, 70.5, 34.5, 31.4, 29.4, 29.4, 29.3, 29.3, 29.2, 28.9, 28.7, 28.6, 28.4, 25.1, 22.5, 21.5, 19.7, 13.9 IR. (film) \( \lambda \) max (2926, 2854, 2173, 1598). HRMS(EI) calculated for C_{25}H_{43}O_{3}SSi \([M+H]^+\) 451.2703, found 451.2708.

4-Methyl-N-(pentadec-14-yn-1-yl)benzenesulfonamide: 15-(trimethylsilyl)pentadec-14-yn-1-yl 4-methylbenzenesulfonate (1.93mmol, 0.871g), P-toluenesulfonamide (2.03mmol, 0.348g), and potassium carbonate (3.86mmol, 0.533g) were added to a round bottom flask in DMF (12 mL). The reaction was stirred at 85°C overnight under argon. The organic phase was extracted with ethyl acetate and washed with water and brine. After drying over sodium sulfate and being concentrated under reduced pressure, the intermediate was added with potassium carbonate (3.86mmol, 0.533g) in MeOH (12mL) into a round bottom flask and was stirred at room temperature overnight. The solvent was then removed under reduced pressure and the crude product was diluted with ethyl acetate. The organic phase was washed with water and brine, and was then dried over sodium sulfate and concentrated under reduced pressure. The product (0.324g, 0.858mmol, 44%) was purified by flash chromatography (SiO2, Hexane:EtOAc = 6:1). 1H NMR (500 MHz, CDCl3), δ 7.75 (d, \( J = 5.0 \), 2H), 7.31 (d, \( J = 10.0 \),
2H), 2.95 – 2.91 (m, 2H), 2.43 (s, 3H), 2.20 – 2.16 (m, 2H), 1.54 – 1.49 (m, 4H), 1.26 - 1.21 (m, 18H); 13C NMR (126 MHz, CDCl₃), δ 143.3, 137.0, 129.7, 127.1, 84.8, 68.0, 43.2, 29.6, 29.5, 29.4, 29.1, 28.8, 28.5, 26.5, 21.5, 18.4 IR. (film) λmax (3154, 2927, 2253). HRMS(EI) calculated for C₂₂H₃₆NO₂S [M+H]+ 378.2468, found 378.2487.

**4-Methyl-N-(pentadeca-13,14-dien-1-yl)benzenesulfonamide:** In a round bottom flask, 4-methyl-N-(pentadec-14-yn-1-yl)benzenesulfonamide (0.858 mmol, 0.324 g), Copper (I) Bromide (0.601 mmol, 0.086 g), and paraformaldehyde (1.72 mmol, 0.052 g) were added and purged with argon for 5 minutes. Degassed 1,4-dioxane (1.3 mL) and dicyclohexylamine (1.72 mmol, 0.34 mL) were then added and the reaction mixture was stirred at 90°C for 18 hours. After cooling to room temperature, the mixture was diluted with ethyl acetate and extracted with 1M HCl. The organic phase was washed with 1M HCl and then brine. The organic phase was then dried over sodium sulfate and concentrated under reduced pressure. The product (0.156 g, 0.413 mmol, 48%) was purified by flash chromatography (SiO₂, Hexane:EtOAc = 6:1).

¹H NMR (500 MHz, CDCl₃), δ 7.74 (d, J = 8.3, 2H), 7.31 (d, J = 8.0, 2H), 5.09 (m, 1H), 4.65 (m, 2H), 2.95-2.91 (m, 2H), 2.43 (s, 3H), 2.01-1.98 (m, 2H), 1.46-1.39 (m, 2H), 1.26-1.21 (m, 18H); 13C NMR (126 MHz, CDCl₃), δ 208.5, 143.3, 136.9, 129.7, 127.1, 90.1, 74.5, 59.5, 43.2, 29.6, 29.6, 29.5, 29.4, 29.4, 29.1, 29.1, 28.3, 21.5, 18.5; IR (film) λmax (3154, 2929, 2254, 1793). HRMS(EI) calculated for C₂₂H₃₆NO₂S [M+H]+ 378.2468, found 378.2449.

**Optimization Studies**

Optimization studies were performed according to general procedure 3 (GS3) using 4-methyl-N-(octa-6,7-dien-1-yl)benzenesulfonamide (0.2 mmol, 55.9 mg) as the starting material. After purifying by flash chromatography (SiO₂, hexanes:EtOAc = 20:3) yields were determined by weight.

**Trifluoro acetate addition products**

![Trifluoro acetate addition product structure](image_url)
8-((4-methylphenyl)sulfonamido)oct-1-en-3-yl 2,2,2-trifluoroacetate (4a): 8-((4-methylphenyl)sulfonamido)oct-1-en-3-yl 2,2,2-trifluoroacetate (0.122mmol, 48.1mg, 61%) was synthesized according to GS3 with 4-methyl-N-(octa-6,7-dien-1-yl)benzenesulfonamide (0.2 mmol, 55.9mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 20:3). A small amount (< 5%) of non separatable isomer was observed in the NMR. This isomer is (E)-4-methyl-N-(octa-5,7-dien-1-yl)benzenesulfonamide (compound 6) and has the same molecular weight as the product therefore the amount was subtracted from the yield.

1H NMR (500 MHz, CDCl₃), δ 7.75(d, J =8.2, 2H), 7.31 (d, J = 8.0, 2H), 5.76 – 5.73, (m, 1H), 5.35 – 5.32 (m, 3H), 2.95 – 2.89 (m, 2H), 2.43 (s, 3H), 1.64 – 1.63 (m, 2H), 1.46 – 1.45 (m, 2H), 1.30 – 1.29 (m, 2H; 13C NMR (126 MHz, CDCl₃), δ 143.4, 141.1, 136.9, 129.7, 127.1, 114.7, 73.0, 43.1, 36.6, 29.5, 26.3, 24.7, 21.5; IR (film) λmax 3285, 3055, 1781, 1711. HRMS(EI) calculated for C₁₅H₂₂NO₂S [M+H]+;279.1372, found 280.1382.

9-((4-methylphenyl)sulfonamido)non-1-en-3-yl 2,2,2-trifluoroacetate (4b): 9-((4-methylphenyl)sulfonamido)non-1-en-3-yl 2,2,2-trifluoroacetate (0.123mmol, 50mg, 61.4%) was synthesized according to GS3 with hexa-4,5-dien-1-yl carbamate (0.2mmol, 58.7mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 20:3).

1H NMR (500 MHz, CDCl₃), δ 7.68 (d, J = 8.2, 2H), 7.24 (d, J = 8.1, 2H), 5.72 – 5.67 (m, 1H), 5.28 – 5.25 (m, 2H), 5.23 (s, 3H), 2.87 – 2.83 (m, 2H), 2.35 (s, 5H); 13C NMR (126 MHz, CDCl₃), δ 143.4, 141.1, 136.9, 134.0, 129.7, 119.3, 114.7, 43.1, 36.7, 33.6, 29.4, 21.5, 18.6 . IR (film) λmax 3055, 2936, 1781, 1711. HRMS(EI) calculated for C₁₆H₂₄NO₂S [M+H]+; 294.1528, found 294.1526.

10-((4-methylphenyl)sulfonamido)dec-1-en-3-yl 2,2,2-trifluoroacetate (4c): 10-((4-methylphenyl)sulfonamido)dec-1-en-3-yl 2,2,2-trifluoroacetate (0.0745mmol, 31.4mg, 57.3%)
was synthesized according to GS3 with N-(deca-8,9-dien-1-yl)-4-methylbenzenesulfonamide (0.13mmol, 40mg) as the starting material and purified by flash chromatography (SiO$_2$, hexanes:EtOAc = 20:3).

$^1$H NMR (500 MHz, CDCl$_3$), $\delta$ 7.76 (d, $J$ = 8.1 ,2H), 7.24 (d, $J$ =8.2, 2H), 5.76 – 5.69 (m,1H), 5.29 – 5.21 (m, 3H), 4.33 – 4.30 (m, 1H), 2.85 (q, $J$ = 6.9, 2H), 2.36 (s,3H), 2.04 – 2.01 (m, 2H), 1.71 – 1.57 (m, 2H), 1.38 – 1.35 (m, 2H), 1.24 – 1.18 (m, 8H).$^{13}$C NMR (500 MHz, CDCl$_3$), $\delta$ 143.38, 134.16, 129.71, 127.12, 127.11, 119.21, 79.78, 43.21, 29.55, 29.17, 29.00, 26.44, 24.71, 21.54, 18.70. HRMS(EI) calculated for C$_{17}$H$_{25}$NO$_2$S $[\text{M+H}]^+$; 308.1685, found 308.1673.

![11-((4-methylphenyl)sulfonamido)undec-1-en-3-yl 2,2,2-trifluoroacetate (4d):](image)

11-((4-methylphenyl)sulfonamido)undec-1-en-3-yl 2,2,2-trifluoroacetate (4d): 11-((4-methylphenyl)sulfonamido)undec-1-en-3-yl 2,2,2-trifluoroacetate (0.0596mmol, 25mg, 44.2%) was synthesized according to GS3 with 4-methyl-N-(undeca-9,10-dien-1-yl)benzenesulfonamide (0.13mmol, 41.8mg) as the starting material and purified by flash chromatography (SiO$_2$, hexanes:EtOAc = 4:1)

$^1$H NMR (500 MHz, CDCl$_3$), $\delta$ 7.67 (d, $J$ = 8.2, 2H), 7.24 (d, $J$ = 8.0, 2H), 5.76 – 5.69 (m, 1H), 5.30 – 5.22 (m, 2H), 4.17 (s, 1H), 2.85 (q, $J$ = 6.7, 2H), 2.36 (s, 3H), 1.49 – 1.36 (m, 2H), 1.24 – 1.21 (m, 2H) 1.21 – 1.36 (m, 10H); $^{13}$C NMR (500 MHz, CDCl$_3$), $\delta$ 143.40, 136.94, 134.16, 129.71, 127.11, 119.22, 79.78, 43.22, 33.71, 29.58, 29.00, 28.91, 26.44, 24.71, 21.55. HRMS(EI) calculated for C$_{18}$H$_{28}$NO$_2$S $[\text{M+H}]^+$; 322.1841, found 322.1825.

![12-((4-methylphenyl)sulfonamido)dodec-1-en-3-yl 2,2,2-trifluoroacetate (4e):](image)

12-((4-methylphenyl)sulfonamido)dodec-1-en-3-yl 2,2,2-trifluoroacetate (4e): 12-((4-methylphenyl)sulfonamido)dodec-1-en-3-yl 2,2,2-trifluoroacetate (0.133mmol, 59.9mg, 66.6%) was synthesized according to GS3 with N-(dodeca-10,11-dien-1-yl)-4-
methylbenzenesulfonamide (0.2mmol, 67.1mg) as the starting material and purified by flash chromatography (SiO2, hexanes:EtOAc = 4:1)

1H NMR (500 MHz, MeOD), δ 7.62 (d, J=8.3, 2H), 7.27 (d, J=8.2, 2H), 5.73–5.80 (m, 1H), (1H), (1H), 2.71 (t, J=7.1, 2H), 2.32 (s, 3H), 1.61–1.68 (m, 2H), 1.13–1.31 (m, 15H); 13C NMR (126 MHz, MeOD), δ 142.8, 137.4, 134.2, 129.0, 126.4, 117.8, 79.6, 42.4, 33.1, 28.9, 28.8, 28.5, 28.5, 26.0, 24.2, 19.8; HRMS(EI) calculated for C19H30NO2S [M+H]+336.1998; found 336.1974.

13-((4-methylphenyl)sulfonamido)tridec-1-en-3-yl 2,2,2-trifluoroacetate (4f): 13-((4-methylphenyl)sulfonamido)tridec-1-en-3-yl 2,2,2-trifluoroacetate (0.0971mmol, 45mg, 58.5%) was synthesized according to GS3 with 4-methyl-N-(trideca-11,12-dien-1-yl)benzenesulfonamide (0.166mmol, 58mg) as the starting material and purified by flash chromatography (SiO2, hexanes:EtOAc = 4:1).

1H NMR (500 MHz, CDCl3), δ 7.74 (d, J=8.3, 2H), 7.31 (d, J=8.1, 2H), 5.77–5.84 (m, 1H), 5.28–5.39 (m, 3H), 4.26 (t, J=6.1, 1H), 2.91–2.95 (m, 2H), 2.43 (s, 3H), 1.65–1.75 (m, 2H), 1.43–1.46 (m, 4H), 1.21–1.25 (m, 12H); 13C NMR (126 MHz, CDCl3), δ 143.4, 137.0, 134.2, 129.7, 127.1, 119.2, 79.8, 43.2, 33.7, 29.6, 29.4, 29.3, 29.3, 29.1, 29.0, 26.5, 24.7, 21.5; HRMS(EI) calculated for C20H32NO2S [M+H]+; 350.2154, found 350.2166.

14-((4-methylphenyl)sulfonamido)tetradec-1-en-3-yl 2,2,2-trifluoroacetate (4g): 14-((4-methylphenyl)sulfonamido)tetradec-1-en-3-yl 2,2,2-trifluoroacetate (0.132 mmol, 65.8%) was synthesized according to GS3 with 4-methyl-N-(tetradeca-12,13-dien-1-yl)benzenesulfonamide (0.2mmol, 72.7mg) as the starting material and purified by flash chromatography (SiO2, Hexanes:EtOAc = 5:1).

1H NMR (500 MHz, CDCl3), δ 7.75 (d, J=10.0, 2H), 7.31 (d, J=10.0, 2H), 5.84 – 5.77 (m, 1H), 5.38 – 5.28 (m, 2H), 4.47 (s, 1H), 2.93 – 2.43 (m, 2H), 2.43 (s, 4H), 1.78 – 1.69 (m, 2H),
1.68 – 1.66 (m, 2H), 1.45 – 1.43 (m, 2H), 1.30 – 1.21 (m, 16H); 13C NMR (126 MHz, CDCl3), δ 143.3, 137.0, 134.2, 129.7, 127.1, 119.1, 79.8, 43.2, 33.7, 29.6, 29.4, 29.4, 29.3, 29.1, 29.1, 26.5, 24.8, 21.5; HRMS(EI) calculated for C21H34NO2S [M+H]+, 364.2311, 364.2318 found.

15-((4-methylphenyl)sulfonamido)pentadec-1-en-3-yl 2,2,2-trifluoroacetate (4h): 15-((4-methylphenyl)sulfonamido)pentadec-1-en-3-yl 2,2,2-trifluoroacetate (0.0705g, .143mmol, 71.4%) was synthesized according to GS3 with 4-methyl-N-(pentadeca-13,14-dien-1-yl)benzenesulfonamide (0.2mmol, 0.0755g) as the starting material and purified by flash chromatography (SiO2, Hexanes:EtoAc = 5:1).

1H NMR (500 MHz, CDCl3), δ 7.75 (d, J = 5.0, 2H), 7.21 (d, J = 10.0), 5.84 – 5.77 (m, 1H), 5.39 – 5.28 (m, 2H), 4.31 – 4.28 (m, 1H), 2.95 – 2.91 (m, 2H), 2.43 (s, 3H) 1.79 – 1.71 (m, 1H), 1.70 – 1.58 (m, 2H), 1.47 – 1.41 (m, 3H), 1.35 – 1.21 (m, 18H); 13C NMR (126 MHz, CDCl3), δ 143.4, 137.0, 134.2, 129.7, 127.1, 119.1, 79.8, 43.2, 33.8, 29.6, 29.5, 29.5, 29.4, 29.4, 29.1, 29.1, 26.5, 24.8, 21.5; HRMS(EI) calculated for C22H36NO2S [M+H]+, 378.2468, 378.2467 found.

16-((4-methylphenyl)sulfonamido)hexadec-1-en-3-yl 2,2,2-trifluoroacetate (4i):

16-((4-methylphenyl)sulfonamido)hexadec-1-en-3-yl 2,2,2-trifluoroacetate (0.038g, 0.0751mmol, 60.1%) was synthesized according to GS3 with N-(hexadeca-14,15-dien-1-yl)-4-methylbenzenesulfonamide (0.125mmol, 0.049g) as the starting material and purified by flash chromatography (SiO2, Hexanes:EtoAc = 5:1).

1H NMR (500 MHz, CDCl3), δ 7.75 (d, J = 10.0, 2H), 7.31 (d, J = 10.0, 2H), 5.84 – 5.77 (m, 1H), 5.39 – 5.28 (m, 3H), 4.46 – 4.44 (m, 1H), 2.94 – 2.90 (m, 2H), 2.43 (s, 3H) 1.77 – 1.65 (m, 2H), 1.45 – 1.43 (m, 4H), 1.34 – 1.30 (m, 6H), 1.25 – 1.20 (m, 18H); 13C NMR (126 MHz, CDCl3), δ 143.4, 137.0, 134.2, 129.7, 127.1, 119.1, 79.8, 43.3, 33.8, 29.7, 29.6, 29.6, 29.5, 29.4,
8-(methylsulfonamido)oct-1-en-3-yl 2,2,2-trifluoroacetate (4j):

8-(methylsulfonamido)oct-1-en-3-yl 2,2,2-trifluoroacetate (0.103 mmol, 32.7 mg, 50%) was synthesized according to GS3 with N-(octa-6,7-dien-1-yl) methanesulfonamide (0.2 mmol, 40.8 mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 4:1). A small amount (< 5%) of non-separable isomer was observed in the NMR. The isomer is (E)-4-nitro-N-(octa-5,7-dien-1-yl)aniline which is the same molecular weight as the product. The amount was subtracted from the yield.

1H NMR (500 MHz, CDCl₃), δ 5.90 - 5.83 (m, 1H), 5.24 - 5.21 (d, J = 17.2, 1H), 5.13 - 5.11 (d, J = 10.4, 1H), 4.40 (s, 2H), 4.13 - 4.09 (m, 1H), 3.14 (s, 5H), 2.96 (s, 3H), 2.15 - 2.00 (m, 2H), 1.49 - 1.39 (m, 2H); 13C NMR (126 MHz, CDCl₃), δ 141.1, 114.8, 73.0, 43.2, 40.3, 36.7, 30.0, 26.4, 24.8, 18.6; IR (film) λmax (3290, 2936, 2861, 1781, 1673). HRMS(EI) calculated for C₉H₁₈NO₂S [M+H]+; 204.1077, found 204.1072.

8-((4-nitrophenyl)sulfonamido)oct-1-en-3-yl 2,2,2-trifluoroacetate (4k):

8-((4-nitrophenyl)sulfonamido)oct-1-en-3-yl 2,2,2-trifluoroacetate (0.0825 mmol, 35.0 mg, 32%) was synthesized according to GS3 with 4-nitro-N-(octa-6,7-dien-1-yl)benzenesulfonamide (0.258 mmol, 80.0 mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 6:1-1:1).

1H NMR (500 MHz, CDCl₃), δ 8.38 (d, J = 8.9, 2H), 8.05 (d, J = 8.9, 2H), 5.82 – 5.74 (m, 1H), 5.37 – 5.29 (m, 3H), 4.65 (t, J = 6.0), 3.01 (q, J = 6.5, 2H), 1.79 - 1.64 (m, 2H), 1.53 – 1.51 (m, 4H); 13C NMR (126 MHz, CDCl₃), 150.1, 145.9, 133.8, 128.3, 124.4, 119.5, 79.4, 43.2, 33.5,
8-(naphthalene-2-sulfonamido)oct-1-en-3-yl 2,2,2-trifluoroacetate (4l): 8-(naphthalene-2-sulfonamido)oct-1-en-3-yl 2,2,2-trifluoroacetate (0.0661 mmol, 28.4 mg, 58%) was synthesized according to GS3 with N-(octa-6,7-dien-1-yl)naphthalene-2-sulfonamide (0.1141 mmol, 35.0 mg) as the starting material and purified by flash chromatography (SiO2, hexanes:EtOAc = 17:3).

1H NMR (500 MHz, CDCl3), δ 7.66 (d, J = 8.2, 2H), 7.20 (d, J = 8.1, 2H), 4.00 – 3.96 (m, 1H), 3.57 – 3.54 (m, 3H), 3.43 – 3.42 (m, 6H), 2.35 (t, J = 7.3, 2H), 2.31 (s, 3H), 1.91 (s, 1H), 1.45 (s, 1H), 1.12 (t, J = 7.2, 3H); 13C NMR (126 MHz, CDCl3), δ 141.1, 136.7, 134.8, 132.2, 129.5, 129.2, 128.8, 128.5, 127.9, 127.6, 122.3, 114.7, 73.0, 43.2, 36.6, 29.5, 26.3, 24.7; IR (film) λmax 3285, 3055, 1672, 1422, 1265 HRMS(EI) calculated for C18H22NO2S [M+H]+; 316.1390, found 316.1362.

8-acetamidoct-1-en-3-yl 2,2,2-trifluoroacetate (4m): 8-acetamidoct-1-en-3-yl 2,2,2-trifluoroacetate (0.1 mmol, 28.4 mg, 50%) was synthesized according to GS3 with N-(octa-6,7-dien-1-yl)acetamide (0.2 mmol, 33.4 mg) as the starting material and purified by flash chromatography (SiO2, hexanes:EtOAc = 1:1). Product was mixed with non-separable isomer (diene isomer, N-(octa-5,7-dien-1-yl)acetamide, (similar to compound 6) in 54:46 mixture. The isomer has the same molecular weight as the product, so the percent isomer was directed subtracted from the yield. Peaks are listed for the major product.

1H NMR (500 MHz, CDCl3), δ 5.76 – 5.27 (m, 1H), 5.24 (s, 1H), 5.22 – 5.01 (m, 1H), 3.20 – 3.15 (m, 2H), 2.08 – 2.05 (m, 2H), 1.91 (s, 3H), 1.71 (s, 2H), 1.45 – 1.41 (m, 3H), 1.40 – 1.31 (m, 2H); 13C NMR (126 MHz, CDCl3), δ 170.1, 134.0, 119.4, 78.9, 39.6, 33.6, 29.5, 29.2, 28.6,
26.4, 26.1, 24.5, 23.4, 18.6, 3.5; HRMS(EI) calculated for C_{10}H_{18}NO \ [M+H]^+; 168.1389, found 168.1388.

8-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)oct-1-en-3-yl 2,2,2-trifluoroacetate (4n): 8-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)oct-1-en-3-yl 2,2,2-trifluoroacetate (0.0293mmol, 13.5mg, 51%) was synthesized according to GS3 with (9H-fluoren-9-yl)methyl octa-6,7-dien-1-ylcarbamate (0.0575mmol, 20mg) as the starting material and purified by flash chromatography (SiO_2, hexanes:EtOAc = 4:1).

1H NMR (500 MHz, CDCl_3), δ 7.70 (d, J = 10, 5H), 7.52 (d, J = 10, 5H), 7.35 - 7.32 (t, J = 15, 5H), 7.26 - 7.23 (t, J = 15, 4H), 5.76 - 5.69 (m, 2H), 5.30 - 5.22 (m, 6H), 4.34 (d, J = 10, 5H), 4.16 - 4.14 (m, 2H), 2.98 (s, 1H), 1.50 - 1.43 (m, 13H), 1.29 (s, 10H), 1.18 (s, 10H); 13C NMR (126 MHz, CDCl_3), δ 144.0, 134.0, 127.7, 127.0, 125.0, 120.0, 119.4, 79.6, 66.5, 47.3, 40.9, 33.7, 29.8, 29.7, 28.3, 26.3, 24.5 HRMS(EI) calculated for C_{23}H_{26}NO_2 \ [M+H]^+; 348.1964, found 348.1961.

8-(((benzyloxy)carbonyl)amino)oct-1-en-3-yl 2,2,2-trifluoroacetate (5o): 8-(((benzyloxy)carbonyl)amino)oct-1-en-3-yl 2,2,2-trifluoroacetate (0.0490mmol, 18.3mg, 32.6%) was synthesized according to GS3 with benzyl octa-6,7-dien-1-ylcarbamate (0.15 mmol, 40 mg) as the starting material and purified by flash chromatography (SiO_2, hexanes:EtOAc = 9:1). 1H NMR (500 MHz, CDCl_3), δ 7.21 – 7.16 (m, 5H), 5.68 – 5.61 (m, 1H), 5.22 – 5.14 (m, 3H), 4.95 (s, 2H), 4.61- 4.59 (m, 1H), 3.04 (q, J = 6.6, 2H), 1.63 – 1.51 (m, 2H), 1.36 – 1.35 (m, 2H), 1.20 (s, 4H); 13C NMR (126 MHz, CDCl_3), δ 156.4, 136.6, 134.0, 128.5, 128.2, 119.4, 79.6, 66.7, 40.9, 33.6, 29.8, 26.3, 24.5; HRMS(EI) calculated for C_{16}H_{21}NO_2 \ [M+H]^+; 260.1651, found 260.1653.
5-(2-((4-methylphenyl)sulfonamido)phenoxy)pent-1-en-3-yl 2,2,2-trifluoroacetate (4p): 5-(2-((4-methylphenyl)sulfonamido)phenoxy)pent-1-en-3-yl 2,2,2-trifluoroacetate (0.101mmol, 45mg, 61.9%) was synthesized according to GS3 with 4-methyl-N-(2-(penta-3,4-dien-1-yloxy)phenyl)benzenesulfonamide (0.164mmol, 54mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 20:3).

1H NMR (500 MHz, CDCl₃), δ 7.55 - 7.53 (d, J = 8.3, 2H), 7.48 - 7.46 (d, J = 9.4, 1H), 7.12 - 7.10 (d, J = 8.1, 2H), 6.98 - 6.94 (t, J = 8.0, 1H), 6.86 - 6.83 (t, J = 7.0, 2H), 6.65 - 6.63 (d, J = 8.1, 1H), 5.77 - 5.71 (m, 1H), 5.37 - 5.30 (m, 2H), 3.74 - 3.71 (t, J = 5.7, 2H), 2.28 (s, 3H), 1.74 - 1.66 (m, 3H). 13C NMR (126 MHz, CDCl₃), δ 148.7, 143.7, 136.4, 133.5, 129.4, 127.2, 125.9, 125.5, 121.7, 120.0, 111.2, 79.1, 67.6, 30.3, 24.5, 21.5; HRMS(EI) calculated for C₁₈H₂₀NO₃S [M+H]⁺; 330.4219 found 330.4107.

5-(2-aminophenoxy)pent-1-en-3-yl 2,2,2-trifluoroacetate (4q): 5-(2-aminophenoxy)pent-1-en-3-yl 2,2,2-trifluoroacetate (0.083mmol, 24mg, 41.5%) was synthesized according to GS3 with 2-(penta-3,4-dien-1-yloxy)aniline (0.2mmol, 35mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 20:3).

1H NMR (500 MHz, CDCl₃), δ 7.80 - 7.78 (d, J = 9.7, 1H), 7.48 - 7.44 (t, J = 8.5, 1H), 7.01 - 6.97 (m, 2H), 5.85 - 5.78 (m, 1H), 5.66 - 5.62 (m, 1H), 5.41 - 5.38 (d, J = 15, 1H), 5.31 - 5.29 (d, J = 10.5, 1H), 5.23 (s, 1H), 4.11 - 4.09 (t, J = 6.2, 2H), 2.27 - 2.22 (m, 2H). 13C NMR (126 MHz, CDCl₃), δ 151.8, 134.2, 133.2, 125.8, 120.9, 120.3, 114.5, 64.9, 53.5, 33.4, 29.7. HRMS(EI) calculated for C₁₁H₁₄NO [M+H]⁺; 176.1076 found 176.1068. Yellow oil.

5-(2-((4-methylphenyl)sulfonamido)-2-oxoethoxy)pent-1-en-3-yl 2,2,2-trifluoroacetate (4r): 5-(2-((4-methylphenyl)sulfonamido)-2-oxoethoxy)pent-1-en-3-yl 2,2,2-trifluoroacetate (0.1307mmol, 38.6mg, 64.1%) was synthesized according to GS3 with 2-(penta-3,4-dien-1-
yloxy)-N-tosylacetamide (0.148mmol, 43.8mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 9:1).

Mixture of rhodimers, major product observed: \(^1\)H NMR (500 MHz, CDCl₃), \(\delta\) 7.82 - 7.79 (d, \(J = 12.6, 2H\)), 7.31 - 7.29 (d, \(J = 7.9, 2H\)), 5.79 - 5.74 (m, 1H), 5.28 - 5.11 (m, 1H), 3.84 (s, 2H), 3.42 - 3.40 (m, 3H), 2.34 (s, 3H), 1.94 - 1.88 (m, 2H). \(^{13}\)C NMR (126 MHz, CDCl₃), \(\delta\) 169.8, 144.9, 140.9, 136.5, 134.0, 129.1, 129.1, 127.9, 127.9, 118.3, 113.3, 76.8, 69.5, 69.4, 69.2, 68.2, 66.7, 36.1, 33.3, 20.1, 19.1. HRMS(EI) calculated for C₄H₁₈NO₄S [M+H]+; 296.0957, found 296.0948.

\[
\text{O} \quad \text{N} \quad \text{O} \\
\text{Ts} \quad \text{O} \\
\text{F₃C} \quad \text{O} \\
\text{H} \\
\text{8-(2-((4-methylphenyl)sulfonamido)-2-oxoethoxy)oct-1-en-3-yl 2,2,2-trifluoroacetate (4s):} \\
\text{8-(2-((4-methylphenyl)sulfonamido)-2-oxoethoxy)oct-1-en-3-yl 2,2,2-trifluoroacetate} \\
(0.0828mmol, 37.4mg, 70.8%) was synthesized according to GS3 with 2-(octa-6,7-dien-1-yloxy)-N-tosylacetamide (0.117mmol, 39.5mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 4:1)
\]

\(^1\)H NMR (500 MHz, CDCl₃), \(\delta\) 7.98 (d, \(J=8, 2H\)), 7.35 (d, \(J=8, 2H\)), 5.85 - 5.78 (m, \(J=6.5, 1H\)), 5.41 - 5.30 (m, 3H), 3.89 (s, 2H), 2.44 (s, 3H), 1.82 - 1.71 (m, 2H), 1.63 - 1.58 (m, 2H), 1.40 - 1.37 (m, 4H); \(^{13}\)C NMR (126 MHz, CDCl₃), \(\delta\) 145.4, 143.7, 138.9, 134.0, 129.6, 128.5, 126.4, 119.4, 33.6, 29.1, 25.5, 24.5, 24.5, 21.7, 21.5. HRMS(EI) calculated for C₁₇H₂₄NO₄S [M+H]+; 338.1427, found 338.1424.

\[
\begin{align*}
\text{O} & \quad \text{N} & \quad \text{Ts} \\
\text{H} & \quad \text{O} & \quad \text{O} \\
\text{F₃C} & \quad \text{O} \\
\text{6-((tosylcarbamoyl)oxy)hex-1-en-3-yl 2,2,2-trifluoroacetate (4t):} \\
\text{6-((tosylcarbamoyl)oxy)hex-1-en-3-yl 2,2,2-trifluoroacetate} \\
(0.0928mmol, 38mg, 54.8%) was synthesized according to GS3 (with the exception that its reaction time was 48 hours) with
\end{align*}
\]
hexa-4,5-dien-1-yl tosylcarbamate (0.1693 mmol, 50 mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 5:1).

1H NMR (500 MHz, CDCl₃), δ 7.92 (d, J = 8.3, 2H), 7.35 (d, J = 8.2, 2H), 5.79-5.72 (m, 1H), 5.37-5.30 (m, 3H), 4.13-4.09 (m, 2H), 2.45 (s, 3H), 1.78-1.62 (m, 4H). 13C NMR (126 MHz, CDCl₃), δ 150.2, 145.2, 135.4, 133.4, 129.7, 128.4, 119.9, 78.8, 66.1, 30.1, 23.9, 21.7.

IR (film) λmax (3245, 2927, 1782, 1751, 1598) HRMS (EI) calculated for C₁₄H₁₈NO₄S [M+H]+; 295.0878, found 296.0931.

6-((cyclohexylcarbamoyl)oxy)hex-1-en-3-yl 2,2,2-trifluoroacetate (4u):

6-((cyclohexylcarbamoyl)oxy)hex-1-en-3-yl 2,2,2-trifluoroacetate (0.0741 mmol, 25 mg, 49.4%) was synthesized according to GS3 with hexa-4,5-dien-1-yl cyclohexylcarbamate (0.15 mmol, 33.5 mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 20:3).

1H NMR (500 MHz, CDCl₃), δ 5.77 – 5.70 (m, 1H), 5.36 – 5.26 (m, 3H), 4.49 (s, 1H), 4.00 (d, J = 5.8, 2H), 3.39 (s, 1H), 1.86 – 1.72 (m, 3H), 1.62 – 1.52 (m, 4H), 1.29 – 1.26 (m, 2H), 1.10 – 1.05 (m, 3H); 13C NMR (126 MHz, CDCl₃), δ 138.5, 133.8, 128.7, 119.6, 89.1, 63.7, 33.4, 31.6, 30.6, 25.5, 24.8, 22.7. λmax (3245, 2927, 1782, 1751, 1598); HRMS (EI) calculated for C₁₃H₂₂NO₂ [M+H]+; 224.1651 found 224.1648.

6-((phenylcarbamoyl)oxy)hex-1-en-3-yl 2,2,2-trifluoroacetate (4v):

6-((phenylcarbamoyl)oxy)hex-1-en-3-yl 2,2,2-trifluoroacetate (0.1344 mmol, 29.2 mg, 44%) was synthesized according to GS3 with hexa-4,5-dien-1-yl phenylcarbamate (0.2 mmol, 43.4 mg) as the starting material and purified by flash chromatography. This compound degrades on the column and was run quickly through a small silica plug (SiO₂, hexanes:DCM = 1:1). A small amount of
starting material remained (<10%). The molecular weight of the starting material is the same as the product and the % starting material was subtracted from the yield.

^1^H NMR (500 MHz, CDCl\textsubscript{3}), δ 7.33 (d, \(J = 7.4\), 2H), 7.26 (t, \(J = 7.5\), 2H), 7.02 (t, \(J = 7.2\), 1H), 6.58 (s, 1H), 5.80-5.73 (m, 1H), 5.41 (q, \(J = 6.4\), 1H), 5.34 (d, \(J = 17.2\), 1H), 5.29 (d, \(J = 10.5\), 1H), 4.18-4.12 (m, 2H), 1.89-1.85 (m, 1H), 1.81-1.77 (m, 1H), 1.73-1.68 (m, 2H), 1.20 (s, 1H).

^13^C NMR (126 MHz, CDCl\textsubscript{3}), δ 156.7, 137.7, 133.7, 129.1, 123.6, 119.7, 79.1, 64.4, 30.6, 28.3, 24.4. IR (film) \(\lambda_{\text{max}}\) 3303, 3059, 2925, 1725, 1642, 1229. HRMS(EI) calculated for C\textsubscript{13}H\textsubscript{16}NO\textsubscript{2} [M+H]+; 218.1182, found 218.1197.

6-((benzylcarbamoyl)oxy)hex-1-en-3-yl 2,2,2-trifluoroacetate (4w): 6-((benzylcarbamoyl)oxy)hex-1-en-3-yl 2,2,2-trifluoroacetate (0.0463mmol, 16mg, 23.2%) was synthesized according to GS3 with hexa-4,5-dien-1-yl benzylcarbamate (0.2mmol, 46.2mg) as the starting material and purified by flash chromatography (SiO\textsubscript{2}, hexanes:EtOAc = 20:3).

^1^H NMR (500 MHz, CDCl\textsubscript{3}), δ 7.39 - 7.30 (m, 5H), 5.85 - 5.78 (m, 1H), 5.30 (s, 2H), 4.27 - 4.17 (m, 3H), 2.05 - 1.85 (m, 2H), 1.78 - 1.75 (m, 2H) ^13^C NMR (126 MHz, CDCl\textsubscript{3}), δ 156.4, 138.4, 133.7, 128.7, 119.6, 79.2, 45.1, 31.6, 30.5, 24.5, 22.7, 14.1. IR (film) (3302, 3059, 2925, 1725, 1642, 1229) HRMS(EI) calculated for C\textsubscript{14}H\textsubscript{18}NO\textsubscript{2} [M+H]+; 232.1338, found 232.1319.

6-(carbamoyloxy)hex-1-en-3-yl 2,2,2-trifluoroacetate (4x): 6-(carbamoyloxy)hex-1-en-3-yl 2,2,2-trifluoroacetate (0.0549mmol, 14mg, 27.4%) was synthesized according to GS3 with hexa-4,5-dien-1-yl carbamate (0.2mmol, 28.2mg) as the starting material and purified by flash chromatography (SiO\textsubscript{2}, hexanes:EtOAc = 20:3).

^1^H NMR (500 MHz, CDCl\textsubscript{3}), δ 7.20 (s, 1H), 5.78 - 5.70 (m, 1H), 5.24 (s, 3H), 4.57 (s, 2H), 4.05 - 4.02 (m, 3H), 1.98 - 1.71 (m, 2H), 1.65 - 1.62 (m, 1H). ^13^C NMR (126 MHz, CDCl\textsubscript{3}), δ
7-((tosylcarbamoyl)oxy)hept-1-en-3-yl 2,2,2-trifluoroacetate (4y): 7-((tosylcarbamoyl)oxy)hept-1-en-3-yl 2,2,2-trifluoroacetate (0.128mmol, 54.4mg, 64%) was synthesized according to GS3 with hepta-5,6-dien-1-yl tosylcarbamate (0.2mmol, 61.9mg) as the starting material and purified by flash chromatography (SiO2, hexanes:EtOAc = 20:3).

$\text{1H NMR (500 MHz, CDCl}_3)$, $\delta$ 7.86 - 7.84 (d, $J = 8.3$, 2H), 7.53 (s, 1H), 7.28 - 7.27 (d, $J = 8.2$, 2H), 5.75 - 5.68 (m, 1H), 5.30 - 5.22 (m, 3H), 4.01 - 3.98 (t, $J = 6.5$, 2H), 2.38 (s, 4H), 1.52 - 1.50 (m, 3H); $\text{13C NMR (126 MHz, CDCl}_3)$, $\delta$ 166.0, 150.4, 145.1, 133.9, 129.6, 128.4, 119.4, 79.5, 66.8, 38.9, 33.5, 28.2, 25.2, 24.3, 21.7, 14.1, 11.1. HRMS(EI) calculated for C$_{15}$H$_{20}$NO$_4$S $[\text{M+H}]^+$; 310.1114, found 310.1109.

7-(carbamoyloxy)hept-1-en-3-yl 2,2,2-trifluoroacetate (4z): 7-(carbamoyloxy)hept-1-en-3-yl 2,2,2-trifluoroacetate (0.109mmol, 29.4mg, 54.6%) was synthesized according to GS3 with hepta-5,6-dien-1-yl carbamate (0.2mmol, 31mg) as the starting material and purified by flash chromatography (SiO2, hexanes:EtOAc = 20:3).

$\text{1H NMR (500 MHz, CDCl}_3)$, $\delta$ 5.84 – 5.77 (m, 1H), 5.41 – 5.31 (m, 3H), 4.59 (s, 2H), 1.82 – 1.73 (m, 2H), 1.68 – 1.64 (m, 2H), 1.47 – 1.41 (m, 2H); $\text{13C NMR (126 MHz, CDCl}_3)$, $\delta$ 156.79, 133.86, 119.49, 79.48, 77.27, 77.22, 77.01, 77.76, 64.65, 33.32, 29.71, 28.40, 28.34, 21.23. HRMS calculated for C$_8$H$_{14}$NO$_2$ $[\text{M+H}]^+$; 156.1025 found 156.0991.

8-((tosylcarbamoyl)oxy)oct-1-en-3-yl 2,2,2-trifluoroacetate (4aa): 8-((tosylcarbamoyl)oxy)oct-1-en-3-yl 2,2,2-trifluoroacetate (0.134mmol, 58.7mg, 67%) was synthesized from GS3.
with octa-6,7-dien-1-yl tosylcarbamate (0.2mmol, 64.7mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 4:1)

¹H NMR (500 MHz, CDCl₃), δ 7.85 (d, J = 8.3, 2H), 7.28 (d, J = 8.1, 2H), 5.73 - 5.68 (m, 2H), 5.29 - 5.22 (m, 3H), 3.99 (t, J = 6.6), 2.37 (s, 3H), 1.53 - 1.48 (m, 2H), 1.27 - 1.22 (m, 3H).

¹³C NMR (500 MHz, CDCl₃), δ 150.62, 145.07, 135.58, 133.92, 129.61, 128.36, 119.44, 79.54, 66.75, 33.54, 28.21, 25.20, 24.31, 21.69. IR (film) νmax 3223.02, 2984.42, 2941.53, 1783.83, 1740.01, 1598.31. HRMS calculated for C₁₇H₂₄NO₄S [M+H]⁺; 324.1225, found 324.1266.

9-((tosylcarbamoyl)oxy)non-1-en-3-yl 2,2,2-trifluoroacetate (4ab): 9-((tosylcarbamoyl)oxy)non-1-en-3-yl 2,2,2-trifluoroacetate (0.0886mmol, 40mg, 44.3%) was synthesized according to GS3 with nona-7,8-dien-1-yl tosylcarbamate (0.2mmol, 67.5mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 4:1)

¹H NMR (500 MHz, CDCl₃), δ 7.91 (d, J=8, 2H), 7.34 (d, J=8, 2H), 5.90 - 5.76 (m, J=6.5, 1H), 5.38 - 5.11 (m, 3H), 4.08 - 4.05 (m, 2H), 2.44 (s, 3H), 1.75 - 1.66 (m, 2H), 1.57 - 1.51 (m, 2H), 1.45 - 1.30 (m, 4H); ¹³C NMR (126 MHz, CDCl₃), 5 150.7, 145.1, 140.8, 135.5, 134.0, 129.6, 128.4, 119.3, 115.1, 67.2, 36.6, 33.6, 28.8, 28.3, 25.5, 24.9, 21.7. HRMS(EI) calculated for C₁₇H₂₄NO₄S [M+H]⁺; 338.1427, found 338.1421.

6-(2-((4-methylphenyl)sulfonamido)phenoxy)hex-1-en-3-yl 2,2,2-trifluoroacetate (4ac):

6-(2-((4-methylphenyl)sulfonamido)phenoxy)hex-1-en-3-yl 2,2,2-trifluoroacetate (0.0711mmol, 32.5mg, 71%) was synthesized according to GS3 with N-(2-(hexa-4,5-dien-1-yloxy)phenyl)-4-methylbenzenesulfonamide (0.1mmol, 34.4mg) as the starting material and purified by flash chromatography (SiO₂, hexanes:EtOAc = 20:3).
$^1$H NMR (500 MHz, CDCl$_3$), $\delta$ 7.54 (d, $J = 8.3$ Hz, 2H), 7.47 (dd, $J = 9.3$, 6.4 Hz, 1H), 7.11(d, $J = 8.1$ Hz, 2H), 6.96 (td, $J = 7.9$, 1.5 Hz, 1H), 6.86 – 6.83 (m, 1H), 6.64 (d, $J = 7.85$ Hz, 1H), 5.78 – 5.73 (m, 1H), 5.37 – 5.30 (m, 3H), 3.73(t, $J = 5.89$, 2H), 2.28 (s, 3H), 1.73 – 1.65 (m, 4H). $^{13}$C NMR (500 MHz, CDCl$_3$), $\delta$ 148.7, 143.7, 136.4, 133.5, 129.4, 127.2, 125.9, 125.5, 121.7, 119.9, 111.2, 79.1, 67.6, 30.3, 24.5, 21.5. IR (film) $\lambda_{max}$ 3266, 2926, 1641, 1164. HRMS(EI) calculated for C$_{19}$H$_{21}$NO$_3$S [M+H]$^+$; 344.1321, found 344.1362.

![Chemical Structure](image.png)

7-(2-((4-methylphenyl)sulfonamido)phenoxy)hept-1-en-3-yl 2,2,2-trifluoroacetate (4ad):

7-(2-((4-methylphenyl)sulfonamido)phenoxy)hept-1-en-3-yl 2,2,2-trifluoroacetate (0.117mmol, 55.0mg, 58%) was synthesized according to GS3 with N-(2-(hepta-5,6-dien-1-yloxy)phenyl)-4-methylbenzenesulfonamide (0.200mmol, 71.5mg) as the starting material and purified by flash chromatography (SiO$_2$, hexanes:EtOAc = 4:1)

$^1$H NMR (500 MHz, CDCl$_3$), $\delta$ 7.63 (d, $J = 8.3$, 2H), 7.53 (dd, $J = 8.0$, 1.5, 1H), 7.2 (d, $J = 8.2$, 2H), 6.99-7.03 (m, 1H), 6.86-6.91 (m, 1H), 6.71 (d, $J = 8.2$, 1H), 5.79-5.86 (m, 1H), 5.34-5.42 (m, 3H), 3.77 (t, $J = 6.5$, 2H), 2.34 (s, 3H), 1.82-1.87 (m, 2H), 1.65-1.81 (m, 2H), 1.26-1.47 (m, 2H); $^{13}$C NMR (126 MHz, CDCl$_3$), $\delta$ 148.7, 143.7, 136.3, 133.8, 129.4, 127.2, 126.0, 125.3, 121.2, 121.1, 119.7, 11.3, 79.4, 68.0, 33.4, 28.6, 21.5, 21.4; HRMS(EI) calculated for C$_{20}$H$_{24}$NO$_3$S [M+H]$^+$, 358.1478 found 358.1456.

5.3.2.4 SI References


4b
TsO

TMS

224

7a2
8c
4h
$\text{O} \quad \text{NH}_2 \quad \text{O} \quad \text{CF}_3$

$\text{O} \quad \text{NH}_2 \quad \text{O} \quad \text{CF}_3$

4r
4t
References


