PALLADIUM(II) CATALYZED ALLYLIC C-H ALKYLATION REACTIONS

BY

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DISSERTATION

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ABSTRACT

The selective formation of new carbon-carbon bonds is a central challenge for organic synthesis; organic molecules are based on carbon scaffolds which must be assembled from simple building blocks. Since Kolbe performed the first organic C-C bond forming reaction in his synthesis of acetic acid in 1845, the growth of organic synthesis has witnessed the proliferation of methods to forge C-C bonds. A recurring theme among these methods is the use of pre-installed, oxidized “functional groups” to enable and control the bond forming reaction. For the past 50 years, however, C-H activation has beckoned to chemists as the synthetic “way of the future.” Rather than relying upon a functional group, C-H activation promises the direct conversion of the inert, ubiquitous C-H bond to the desired C-C bond. This strategy has inspired tremendous excitement and speculation, but only recently has it begun to be reduced to practice in synthetically useful reactions.

This work describes the discovery of the first palladium(II)-catalyzed allylic C-H alkylation reaction. Allylic alkylation has long been performed by palladium(0) catalysis with allylic oxygenate starting materials. In contrast, this method proceeds directly from the readily accessible, chemically robust α-olefin moiety. The development of such a reaction was impeded by the inherent incompatibility of the various steps of the putative catalytic cycle. In order to achieve catalytic turnover, an electrophilic C-H cleavage, a nucleophilic functionalization, and an oxidative Pd(II) regeneration step would all have to operate simultaneously. This series of interlocking compatibility challenges was unraveled with the aid of stoichiometric model studies and mechanistic insights gleaned from previous allylic C-H functionalization reactions. Ultimately, a catalytic allylic C-H alkylation reaction was discovered.

The original allylic C-H alkylation reaction had an olefin scope limited to allylarene
substrates. These substrates could be described as “doubly activated” because the C-H bonds to be cleaved were both allylic and benzylic. Less reactive allylic C-H bonds displayed only very low reactivity under the reported conditions. This substrate limitation was investigated, and it was discovered that the catalytic cycle was inhibited by a necessary cosolvent, dimethylsulfoxide. This solvent was speculated to act as a ligand for palladium, competitively binding to the metal and displacing the ligand required for C-H cleavage. By identifying a more electron-rich C-H cleavage ligand which presumably could better compete with dimethylsulfoxide for binding to palladium, it was possible to overcome the inhibition and restore reactivity to the catalytic system. This allowed the development of an allylic C-H alkylation with a general substrate scope.

The nucleophile scope of the allylic C-H alkylation was explored with the goal of expanding the diversity and complexity of both coupling partners. It was discovered that tertiary carbon nucleophiles, bearing two electron-withdrawing groups to stabilize a carbanion and one aliphatic side chain, could participate in the reaction. The addition of the aliphatic side chain allowed for additional functional groups or rings to be incorporated into the nucleophile, thereby enabling the coupling of two relatively valuable components. This work opened the door to future development of macrocyclization reactions and enantioselective alkylations.
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CHAPTER 1

CATALYTIC INTERMOLECULAR ALLYLIC C-H ALKYLATION

1.1 INTRODUCTION

The construction of new carbon-carbon bonds is a central challenge for organic synthesis. Organic molecules are based upon carbon frameworks, and the assembly of these frameworks from simpler starting materials has inspired the development of a vast library of C-C bond forming reactions. A recurring theme throughout this literature can be described as a “functional group approach,” whereas a more recent movement in the scientific community has championed a “C-H activation approach” (Figure 1).\(^1\)\(^2\)\(^3\) These two strategies provide distinct and frequently complementary approaches to C-C bond formation, and the development of C-H activation into a more versatile approach with broad scope and reliable results is a frontier challenge for chemical methodology in the 21\(^{st}\) century. The emergence of C-H activation as a competitor on equal footing with traditional methodology has the potential to transform the practice of organic synthesis in coming years, the repercussions of which would be felt in all of the fields of scientific research that rely upon small molecules.\(^4\)

*Figure 1: Different approaches to C-C bond formation*

In the functional group approach, two fragments, each bearing a reactive chemical moiety or “functional group” are united to forge a new C-C bond. The functional groups serve as synthetic handles, enabling the bond forming reaction and controlling the site at which the new bond is formed. Some prominent categories of reactions that exemplify the functional group approach include cross-coupling,\(^5\) aldol\(^6\) and olefination\(^7\) reactions (Figure 2). Even biosynthesis typically relies upon functional groups to generate new C-C bonds; for example, polyketides are
assembled from β-keto acid building blocks and terpenes utilize pyrophosphate functional groups. The use of functional groups allows an unprecedented degree of control of chemo-, regio- and stereoselectivity in C-C bond forming reactions. The introduction of new functional groups, for example potassium trifluoroborates for cross-coupling, can result in new or orthogonal reactivity relative to existing methods.

**Figure 2**: Common C-C bond forming reactions from pre-oxidized starting materials.

In the C-H activation approach, a new C-C bond is formed directly from the cleavage of a relatively strong, inert C-H bond. Although there is no universally accepted set of criteria for what constitutes “activation” of a C-H bond versus routine deprotonation, this description is typically applied to C-H bonds which will not react with traditional strong bases such as alkoxides and amides. The C-H cleavage step may occur by several mechanisms, including a radical homolytic cleavage and rebound, a concerted insertion mechanism, or a deprotonation type event. The bond forming event follows directly, thus the process is described as the direct
conversion from C-H to C-C. By definition, this process involves the oxidation of the substrate and therefore an oxidant is required, either in the form of the coupling partner of the reaction or as an external, terminal oxidant.

Comparison of these two approaches reveals several fundamental differences. If, at least in theory, any C-H bond may be considered a potential site of functionalization, the synthetic chemist has a tremendously expanded menu of options. A functional group may install a specific bond at a specific location, but C-H bonds are ubiquitous in organic molecules. However, this ubiquity also leads to the central challenge of C-H activation, the question of how to identify one C-H bond from among many in order to achieve selectivity in the reaction. In addition, C-H activation by definition utilizes a synthetic handle, the C-H bond, which is inert to most traditional chemical reagents. This may greatly simplify synthetic planning because it eliminates the need for protections and deprotections, and functional group manipulations such as oxidation and reduction, associated with the functional group approach to bond formation. However, the inert character of these C-H bonds makes it challenging to develop a reaction which may achieve the desired C-H activation without resorting to conditions that are so harsh as to render the reaction intolerant of other functionality and thus useless in the context of complex molecule synthesis. Finally, C-H activation may provide a significant synthetic advantage by eliminating the need to pre-install a functional group, potentially eliminating multiple steps from a synthetic sequence.

A central challenge for C-H activation is the selection of one C-H bond from among many on any given substrate. Numerous strategies have been developed to control which C-H bond of a substrate molecule is activated, and the strategies for C-H alkylation may generally be divided into three categories (Figure 3). First, the use of a directing group, such as a pyridyl or
carbonyl, may be used to coordinate the transition metal catalyst and approximate it to the bond which will be activated.\textsuperscript{9} Alternatively, C-H activation may be performed on heteroaromatic substrates, which have electronic biases that make some C-H bonds more reactive than others and therefore more susceptible to activation.\textsuperscript{10} Finally, an activating group such as an olefin, \(\alpha\)-heteroatom or an aromatic ring may be used to weaken a specific C-H bond and impart selectivity in the C-H activation step.\textsuperscript{11}

**Figure 3**: Common strategies for selectivity in C-H alkylation

We targeted the development of an allylic C-H alkylation reaction, an exemplar of the activating group category of C-H activation. This transformation had been known in the literature for more than forty years; it was initially reported as a two step process, stoichiometric in palladium, by Tsuji and Trost in the 1960s (Figure 4). An initial C-H cleavage step, effected by an electrophilic palladium(II) salt, generated a \(\pi\)-allyl intermediate which could be trapped and isolated.\textsuperscript{12} The \(\pi\)-allyl was subsequently exposed to attack by a nucleophile, forging the desired allylic C-C bond.\textsuperscript{13} Despite this strong stoichiometric precedent, and despite the early enthusiasm for developing the reactivity into a catalytic cycle, no palladium(II) catalyzed allylic C-H alkylation was ever reported.\textsuperscript{14} We attribute this gap in the literature to the fundamental
challenge of combining these dissimilar steps—electrophilic C-H cleavage, nucleophilic functionalization, and oxidative regeneration of Pd(II)—in one reaction vessel, and identifying conditions and reagents where each step would not interfere with the others.

*Figure 4*: Stoichiometric allylic C-H alkylation

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We believed that previous efforts in our lab in the discovery of allylic C-H esterification\textsuperscript{15,16} and amination reactions\textsuperscript{17,18} had laid a solid groundwork for the development of an allylic C-H alkylation reaction (Figure 5). We had discovered palladium(II)/bis-sulfoxide catalyst 1, capable of performing allylic C-H activation under relatively mild conditions and with superb functional group tolerance. We had studied the mechanism of the reaction and identified the roles of each of the reaction components. And finally, we had previously attempted to develop an alkylation procedure and encountered some of the challenges we would need to

*Figure 5*: Allylic C-H functionalization reactions
overcome in order to achieve a catalytic system.

1.2 RESULTS AND DISCUSSION

The first challenge that we faced was the identification of a nucleophile that would be suitable for allylic alkylation. In order to effect C-H cleavage, a highly electrophilic palladium(II) species must coordinate to the olefin substrate, acidifying the adjacent allylic protons for a soft deprotonation event. Many common nucleophiles would be expected to coordinate to the palladium, thereby attenuating its electrophilicity and inhibiting C-H cleavage. We thus recognized the importance of discovering conditions under which these two species could coexist without detrimental interactions.

We initially explored organometallic reagents, such as vinyl and aryl stannanes, boronates and zins. These nucleophiles have broad and well-precedented functional group tolerance. Furthermore, they do not behave like traditional nucleophiles—their reactivity can be largely limited to transmetallation with the transition metal catalyst. Allylic alkylation might therefore be achieved through a sequence of C-H cleavage followed by transmetallation and reductive elimination. The use of these organometallic nucleophiles to functionalize π-allyl intermediates generated either stoichiometrically or catalytically through displacement of allylic functional groups provided good precedent for their reactivity.19

In stoichiometric model studies, we investigated transmetallation and reductive elimination under our desired reaction conditions. Beginning from pre-formed π-allyl intermediates, we found that vinyl boronic acids and esters were most effective for the desired functionalization reaction (Figure 6). We isolated the 1,4-diene product 4 arising from functionalization at the least hindered terminus of the π-allyl as the major product. Although we were able to detect some trace product formation using aryl nucleophiles or other metals such as
tin and zinc, vinyl boronates such as 3 and 5 were clearly the most effective nucleophiles. We limited our studies to conditions we knew to be suitable for C-H cleavage, specifically, slightly elevated temperatures (typically 45°C) and ethereal or chlorinated solvents. We also did not investigate activators such as fluoride or hydroxide which we expected would inhibit C-H cleavage.

**Figure 6**: Stoichiometric functionalization with vinyl boronates

![Stoichiometric functionalization with vinyl boronates](image)

Although we had demonstrated that vinylboronic acids and esters could functionalize a π-allyl, our efforts to develop a catalytic reaction using these nucleophiles were unsuccessful. We found that under catalytic conditions the reaction consistently generated homocoupled nucleophile and a range of constitutional isomers of the product (Figure 7). These isomers were most likely the result of an unselective oxidative Heck reaction. This reactivity had been previously documented for α-olefin substrates with allylic substitution, where C-H cleavage is not feasible.\(^{20}\) Our results indicated that this competing pathway was simply too fast even for substrates that could undergo C-H cleavage. Transmetallation of the nucleophile with palladium was substantially faster than C-H activation, and the resulting organopalladium species would divert reactivity down the undesired homocoupling and Heck pathways. Consequently, we determined that organometallic nucleophiles were not suitable reagents for our desired allylic C-H alkylation reaction.
We subsequently turned our attention to a series of stabilized soft carbanion nucleophiles. We suspected in particular that the most acidic nucleophiles could be suitable for the proposed alkylation reaction. During previous experimentation in the course of developing allylic C-H esterification and amination reactions, we had observed that highly acidic, weak nucleophiles were most reactive. This seemingly counterintuitive result may be rationalized by acknowledging that the nucleophile is activated in situ via an equilibrium deprotonation process. Therefore, nucleophiles with the lowest $pK_a$ have the highest equilibrium population of deprotonated anion under the reaction conditions, which is presumably the species responsible for functionalization. In practice we found that nucleophiles with $pK_a$ similar to acetic acid, in the range of 3-6, were most effective. Additionally, we hypothesized that the use of weak nucleophiles served to circumvent the challenge of a nucleophile coordinating to the palladium catalyst and attenuating its electrophilicity; a very weak nucleophile would be expected to have only a weak and transient interaction with the electrophilic metal and therefore a negligible effect on its electronics.

We therefore synthesized a series of soft carbanion nucleophiles bearing a variety of electron withdrawing stabilizing groups (Figure 8). The $pK_a$ of the acidic C-H bonds in these molecules ranged from as high as 13 to as low as 5. In order to render the reaction intramolecular and improve the reactivity of the system, we tethered the nucleophiles to the substrate via a homoallylic ester linkage, which would provide $\gamma$-lactones as the desired product.
However, extensive experimentation utilizing these substrates failed to furnish even trace quantities of the desired alkylated products. Reactions typically resulted in low conversions; only small amounts of diene product were observed which were derived from elimination of the homoallylic ester.

Figure 8: Intramolecular stabilized carbanion substrates

In an effort to discern the reasons for the failure of the alkylation reaction, we performed an experiment that provided a valuable insight (Figure 9). The experiment was designed to allow observation of the functionalization of the $\pi$-allyl intermediate in a stoichiometric model system. We generated the $\pi$-allyl in situ by exposing the substrate to one equivalent of palladium(II) trifluoroacetate/bis(phenylsulfinyl)ethane complex. The trifluoroacetate counterions were used in this case in order to stop the reaction at the $\pi$-allyl intermediate and avoid functionalization; the reduced $pK_a$ of trifluoroacetate relative to acetate means that it is not able to deprotonate the nucleophile to initiate its attack on the electrophile. The $\pi$-allyl was observed in situ by $^1$H NMR spectroscopy. Tetrabutylammonium acetate was subsequently added to the reaction mixture in order to deprotonate the nucleophile and effect functionalization. However, analysis of the crude reaction mixture revealed that even from a stoichiometrically formed $\pi$-allyl intermediate, no alkylated product was generated.

This result was particularly notable because an analogous protocol for intramolecular allylic amination resulted in smooth functionalization of the $\pi$-allyl (Figure 9). Because the nitrogen and carbon nucleophiles of these related substrates had similar $pK_a$ and should both be
readily deprotonated by acetate base, we reasoned that allylic alkylation was encountering a unique, previously unidentified obstacle. We speculated that perhaps the attack of the carbanion nucleophile on the π-allyl was inhibited by stereoelectronic constraints. Specifically, the deprotonated nitrogen nucleophile attacks with electrons in a sp$^2$ hybridized orbital perpendicular to the conjugated π orbital system of the carbamate and sulfonyl groups. However, the deprotonated carbon nucleophile would have to attack with electrons that are part of the π system with the nitro and ester groups. Both the π-allyl and the deprotonated nucleophile are locked in a planar conformation by orbital overlap, leaving only two bonds with free rotation. We wondered if the substrate was too constrained in its geometry to reach a conformation where orbital overlap would allow allylic alkylation to occur.

*Figure 9: Stoichiometric comparison of alkylation vs. amination*

Inspired by this theory, we advanced a counterintuitive solution: in order to improve reactivity, the tether between the nucleophile and substrate should be cleaved and the reaction should be rendered intermolecular. The functionalization of a pre-formed π-allyl with methyl nitroacetate was thus found to proceed smoothly with the addition of acetate base to activate the nucleophile (Figure 10).

The success of methyl nitroacetate as a nucleophile, however, engendered another problem in the development of a catalytic alkylation reaction. The product forming steps reduce
palladium(II) to palladium(0), and in order to close the catalytic cycle the metal must be reoxidized. This step was accomplished using 1,4-benzoquinone in our previous allylic C-H esterification and amination reactions. However, benzoquinone is incompatible with soft carbanion nucleophiles, oxidizing them directly in a Michael reaction.\textsuperscript{21} This incompatibility was manifested in our initial efforts to develop a catalytic reaction—only low yields of the desired alkylated product were formed, and conversion of the nucleophile and oxidant was observed.

We concluded that benzoquinone would have to be eliminated from the reaction conditions in order to develop a catalytic reaction. This was a challenging endeavor, however, because benzoquinone has been shown to play several important roles in the allylic C-H functionalization catalytic cycle (Figure 11).\textsuperscript{16} In mechanistic experiments to probe the allylic esterification reaction, it was found that benzoquinone promoted the functionalization of the $\pi$-allyl intermediate. It coordinated the $\pi$-allyl and, acting as a $\pi$-acidic ligand, activated the intermediate to attack by the weakly nucleophilic carboxylate. Additionally, benzoquinone served as the terminal oxidant for the reaction, regenerating palladium(II). In the course of reoxidation it generated two equivalents of acetate which acted as a catalytic source of endogenous base. We realized that these roles were critical to the catalytic cycle and that surrogates would have to be identified if benzoquinone were removed from the reaction.
In search of a suitable surrogate to promote functionalization of the π-allyl, we surveyed a variety of known π-acceptor ligands. Stoichiometric model studies showed that maleic anhydride, dimethyl maleate, dimethyl fumarate, and electron deficient styrene derivatives were all unable to promote functionalization of the π-allyl. Alkylated product was obtained in the presence of phosphine ligands, however, these ligands were unstable to the oxidative reaction conditions. Our studies eventually identified dimethylsulfoxide (DMSO) as an oxidatively stable ligand which could mediate alkylation of a pre-formed π-allyl (Table 1). The use of solvent quantities of DMSO to promote nucleophile addition to a π-allyl was well preceded from

**Table 1:** Stoichiometric allylic alkylation

<table>
<thead>
<tr>
<th>entry</th>
<th>NuH</th>
<th>yield (L+B)</th>
<th>L:B</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhO₂SCH₂CO₂Me, 15</td>
<td>9%</td>
<td>---</td>
</tr>
<tr>
<td>2</td>
<td>NO₂CH₂COPh, 16</td>
<td>82%</td>
<td>8:1</td>
</tr>
<tr>
<td>3</td>
<td>NO₂CH₂SO₂Ph, 17</td>
<td>89%</td>
<td>16:1</td>
</tr>
<tr>
<td>4</td>
<td>NO₂CH₂CO₂Me, 13</td>
<td>86%</td>
<td>4:1</td>
</tr>
<tr>
<td>5</td>
<td>13 (no DMSO)</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

*a* Determined by \(^1\)H NMR analysis of the crude, \(^b\) 0.033M, \(^c\) Dioxane (0.033M).
early studies in organopalladium chemistry.\textsuperscript{23}

A number of previously reported systems for the reoxidation of palladium catalysts were examined to find a successor to benzoquinone in the role of terminal oxidant (Table 2). We found common oxidants such as hypervalent iodine\textsuperscript{24} and copper salts\textsuperscript{25} to be ineffective under our conditions (entries 1, 2). As our use of DMSO as a cosolvent was reminiscent of Larock’s early reports of palladium oxidations involving direct reoxidation with oxygen, we also investigated reactions under oxygen atmosphere.\textsuperscript{26} We found that modest catalyst turnover could be achieved with atmospheric oxygen pressure, and pressurized oxygen reaction conditions performed somewhat better (entries 3, 4). However, we were unable to further optimize these conditions and higher oxygen pressures did not improve turnover. Similarly, catalysts which facilitate the reoxidation of palladium by molecular oxygen were not successful (entries 5, 6). Instead, we returned to quinone oxidants and selected 2,6-dimethylbenzoquinone. This quinone is more sterically hindered than the parent benzoquinone, which we hoped would impair the Michael reaction, but its oxidation potential remains similar.\textsuperscript{27} To our delight, we found that the addition of 2,6-dimethylbenzoquinone did result in efficient reoxidation, providing conditions for

\textit{Table 2}: Catalytic allylic C-H alkylation

<table>
<thead>
<tr>
<th>entry</th>
<th>Pd(II)\textsubscript{L\textsubscript{n}}</th>
<th>oxidant (equiv.)</th>
<th>yield (L+B)\textsuperscript{a}</th>
<th>L:B\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>Ph(OAc)\textsubscript{2} (2.0)</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>Cu(OAc)\textsubscript{2} (2.0)</td>
<td>8%</td>
<td>---</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>O\textsubscript{2} (1 atm.)</td>
<td>27%</td>
<td>4:1</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>O\textsubscript{2} (7 atm.)</td>
<td>35%</td>
<td>4:1</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>O\textsubscript{2} (1 atm.)/HPMV</td>
<td>10%</td>
<td>4:1</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>O\textsubscript{2} (1 atm.)/Cu(OAc)\textsubscript{2}</td>
<td>17%</td>
<td>4:1</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>DMBQ (1.5)\textsuperscript{f}</td>
<td>72%</td>
<td>4:1</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>DMBQ (1.5)\textsuperscript{f}</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>DMBQ (1.5)\textsuperscript{f}</td>
<td>4%</td>
<td>---</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>DMBQ (1.5)\textsuperscript{f}</td>
<td>63%</td>
<td>4:1</td>
</tr>
<tr>
<td>11\textsuperscript{f}</td>
<td>1</td>
<td>DMBQ (1.5)\textsuperscript{f}</td>
<td>83%</td>
<td>4:1</td>
</tr>
</tbody>
</table>

\textsuperscript{f} Determined by \textsuperscript{1}H NMR analysis of crude. \textsuperscript{b} 0.33 M. \textsuperscript{f} DMBQ = 2,6-dimethylbenzoquinone (1.5 equiv.). ACOH (0.5 equiv.). \textsuperscript{f} Pd(trifluoroacetate)\textsubscript{2} / bis(phenylisulfiny1)ethane. \textsuperscript{f} nBu\textsubscript{4}NOAc (1 equiv.). \textsuperscript{f} 13 (3 equiv.).
the first palladium(II) catalyzed allylic C-H alkylation reaction (entries 7, 11). Notably, reactivity was significantly diminished when either adding stoichiometric Bu₄NOAc or omitting all sources of catalytic acetate (entries 8, 9). These results underscore the importance of quinone/AcOH as a source of catalytic acetate base.

The discovery of optimized catalytic conditions allowed us to explore the substrate scope of the reaction (Table 3). Consistent with our observations in the development of allylic esterification and amination reactions, this reaction demonstrated excellent functional group tolerance. A wide variety of both electron-donating (entries 1-3) and electron-withdrawing (entries 5-11) substituents were tolerated on the aryl moiety. Alkylated products were generated in high yields with good regioselectivities and excellent E/Z selectivities (>20:1). Significantly, pure linear compound was readily obtained for all substrates in good yields (50-70%) using standard column chromatography. Functionalities that are unstable to traditional palladium(0)-catalyzed allylic alkylations, such as aryl halides and triflates, were inert to these oxidative conditions (entries 5, 17, 22-23). A variety of pharmacophoric functionalities such as catechol, indanone, phthalide, and salicylate were also well-tolerated (entries 19-23). Notably, heteroaromatic rings including benzotriazole and unprotected indole could be subjected to the reaction conditions (entries 24-25). This functional group tolerance was unexpected given that heteroaromatics are often reactive with and/or attenuate the electrophilicity of palladium(II) catalysts. The reaction was not suitable for substrates containing strongly coordinating functional groups. Basic nitrogen moieties, such as pyridine and unprotected alkyl amines, were not tolerated; no desired product was formed. Similarly, unprotected phenols resulted in somewhat reduced yields of alkylated products. In addition, the reaction conditions were unsuitable for unactivated substrates (see Chapter 2).
**Table 3**: Scope of the allylic C-H alkylation reaction

<table>
<thead>
<tr>
<th>entry</th>
<th>major product</th>
<th>L:B&lt;sup&gt;b&lt;/sup&gt;</th>
<th>isolated yield L&lt;sup&gt;c&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>1</td>
<td>R = OMe, 20</td>
<td>1.7:1</td>
<td>50%</td>
</tr>
<tr>
<td>2</td>
<td>Me, 21</td>
<td>3.1</td>
<td>61%</td>
</tr>
<tr>
<td>3</td>
<td>CH=CH₂, 22</td>
<td>3.1</td>
<td>63%</td>
</tr>
<tr>
<td>4</td>
<td>H, 14</td>
<td>4.1</td>
<td>62%</td>
</tr>
<tr>
<td>5</td>
<td>Br, 23</td>
<td>4.1</td>
<td>60%</td>
</tr>
<tr>
<td>6</td>
<td>NTSMe, 24</td>
<td>4.1</td>
<td>63%</td>
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<tr>
<td>7</td>
<td>F, 25</td>
<td>4.1</td>
<td>65%</td>
</tr>
<tr>
<td>8</td>
<td>CO₂Me, 26</td>
<td>10.1</td>
<td>61%</td>
</tr>
<tr>
<td>9</td>
<td>C(O)Me, 27</td>
<td>10.1</td>
<td>66%</td>
</tr>
<tr>
<td>10</td>
<td>CF₃, 28</td>
<td>10.1</td>
<td>56%</td>
</tr>
<tr>
<td>11</td>
<td>CN, 29</td>
<td>12.1</td>
<td>65%</td>
</tr>
<tr>
<td>12</td>
<td>R = OMe, 30</td>
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<td>58%</td>
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<tr>
<td>13</td>
<td>N=CPh₂, 31</td>
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<td>58%</td>
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<td>15</td>
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<td>&gt;20:1</td>
<td>59%</td>
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<td>16</td>
<td>OTBS, 34</td>
<td>3:1</td>
<td>58%</td>
</tr>
<tr>
<td>17</td>
<td>OTf, 35</td>
<td>15:1</td>
<td>57%</td>
</tr>
<tr>
<td>18</td>
<td>R = OMe, 36</td>
<td>4:1</td>
<td>65%</td>
</tr>
<tr>
<td>19</td>
<td>37</td>
<td>3:1</td>
<td>56%</td>
</tr>
<tr>
<td>20</td>
<td>38</td>
<td>12:1</td>
<td>62%</td>
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<tr>
<td>21</td>
<td>39</td>
<td>15:1</td>
<td>70%</td>
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<tr>
<td>22</td>
<td>40</td>
<td>7:1</td>
<td>63%</td>
</tr>
<tr>
<td>23</td>
<td>41</td>
<td>5:1</td>
<td>64%</td>
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<tr>
<td>24</td>
<td>42</td>
<td>5:1</td>
<td>68%</td>
</tr>
<tr>
<td>25</td>
<td>43</td>
<td>1:5</td>
<td>42%</td>
</tr>
</tbody>
</table>

<sup>a</sup> Olefin (1 equiv.), 13 (3 equiv.), DMBQ (1.5 equiv.), AcOH (0.5 equiv.), 1 (10 mol%), dioxane/DMSO (4:1, 0.33 M). Average of 2 runs at 0.5 mmol. Products isolated as one regio- and olefin isomer. <sup>b</sup> Determined by 1H NMR analysis of the crude.

We noted a strong correlation between the electronic properties of the aryl ring and the regioselectivity of the allylic alkylation reaction. Electron-withdrawing moieties significantly
increased linear isomer ratios (entries 8-11, 20-21), whereas electron-donating moieties eroded linear selectivity (e.g., entries 1-2). In the case of extremely electron-rich 3-allylindole, a complete reversal of selectivity was observed furnishing the branched isomer as the major product (entry 25). A steric influence on regioselectivity was also observed with ortho substitution leading to significant increases in the linear to branched product ratio (entries 14, 15 vs 2, 10). The electronic and steric influences upon selectivity may both derive from modulation of the stability of a high energy palladium π-benzyl intermediate, which would exist in equilibrium with the palladium π-allyl and which might favor alkylation at the internal, branched position (Figure 12).\textsuperscript{28} Features of the substrate that stabilize this intermediate, such as donating groups that increase the electron density of the aromatic ring or para substitution that offers no steric interference, would be expected to increase the proportion of branched isomer produced. These observations coincided with previously reported regioselectivities for functionalization of electronically biased π-allyl intermediates.\textsuperscript{29}

\textit{Figure 12:} Mechanistic rationale for regioselectivity

The scope of nucleophiles that could participate in this alkylation reaction was also briefly surveyed (Table 4). Consistent with the hypothesis that the nucleophile must be activated \textit{in situ} by an equilibrium deprotonation process, the most acidic nucleophiles tested proved to be the most effective coupling partners. Nucleophiles with a higher p$K_a$ value such as 1,3-diketones and methyl (phenylsulfonyl)acetate were simply too sluggish to be useful in the alkylation reaction (entries 1, 2), though slow functionalization could be observed in stoichiometric reactions from the pre-formed π-allyl (see Table 1). More acidic carbon nucleophiles were more
effective coupling partners (entries 3-6). Except in special cases such as Meldrum’s acid, the use of a nitro group was generally necessary—no special interactions were ascribed to this moiety, it was simply used to sufficiently acidify the adjacent methylene. Notably, the (phenylsulfonyl)nitromethane nucleophile 17, despite having a very low pK\(_a\), was very slow to functionalize under standard reaction conditions, perhaps as a consequence of its steric bulk. By switching the catalyst ligand to 1,2-bis(benzylsulfinyl)ethane, complex 49, we were able to restore reactivity, an observation that would prove important in later work. We speculate that further optimization could incrementally expand the nucleophile scope of this methodology. The theoretical upper limit for nucleophile pK\(_a\) is likely close to 10, the pK\(_a\) of dihydroquinone, which acts as the terminal proton acceptor in the reaction.

**Table 4:** Nucleophile scope of the allylic C-H alkylation reaction

<table>
<thead>
<tr>
<th>entry</th>
<th>major product</th>
<th>L:B(^a)</th>
<th>isolated yield L:B(^a) E:Z &gt;20:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>44</td>
<td>---</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>45</td>
<td>---</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>46</td>
<td>---</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>14 4:1</td>
<td>83%</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>47 8:1</td>
<td>74%</td>
</tr>
<tr>
<td>6(^c)</td>
<td></td>
<td>48 16:1</td>
<td>71%</td>
</tr>
</tbody>
</table>

\(^a\) Olefin (1 equiv), 13 (3 equiv), DMBQ (1.5 equiv), AcOH (0.5 equiv), 1 (10 mol%), 1,2-dioxane, DMSO (4:1, 0.33M). Average of 2 runs at 0.5 mmol. Products isolated as one regio- and olefin isomer. \(^b\) Determined by \(^1\)H NMR analysis of the crude. \(^c\) Catalyst 49 = 1,2-bis(benzylsulfinyl)ethane/Pd(OAc)_2 (10 mol%).

Having established the optimized reaction conditions and explored the scope of the
alkylation reaction, we sought to demonstrate the utility of the products as synthetic intermediates by developing strategies for their further elaboration (Figure 13). We found that the action of zinc dust in acidic media would selectively reduce the nitro group in the presence of the olefin and ester, furnishing the α-amino ester 50 in quantitative yield.30 This reduction opens a ready route to unnatural amino acids and amino alcohols. Alternatively, we sought to exploit the latent nucleophilicity of the product by performing a second alkylation. Using the modified cinchona alkaloid catalyst 51, we effected a conjugate addition into β-nitrostyrene.31 The product of this reaction is a precursor to α,α-disubstituted amino acids, which have been shown to introduce conformational bias in peptide chains32 and to resist the activity of protease enzymes.33 The reaction proceeded in high yield and with excellent diastereoselectivity and enantioselectivity. The conjugate addition was also performed using a para-bromo substituted aromatic substrate, which allowed for the unambiguous assignment of both relative and absolute stereochemistry by X-ray crystallography.

Figure 13: Synthetic elaboration of the allylic alkylation products

1.3 CONCLUSIONS

This work resulted in the discovery of the first palladium(II) catalyzed allylic C-H alkylation reaction. The development of such a reaction had first been proposed in the literature nearly four decades prior to our work based on strong stoichiometric precedent, yet no catalytic
system had been reported. Our studies indicated that the major challenge in developing this methodology would be identifying conditions which could simultaneously satisfy the dissimilar requirements of each individual step of the proposed catalytic cycle. We had to address two principal problems: the compatibility of the electrophilic palladium(II) catalyst with the carbon nucleophile, and the compatibility of the nucleophile with the oxidant.

We were able to apply our understanding of the catalytic cycle of allylic C-H functionalization, established in the course of the development of the branched allylic esterification reaction, to guide our experimentation. When a component of the reaction mixture was changed, we used this mechanistic construct to better understand how other parts of the reaction were affected, and to suggest stoichiometric model studies to probe certain steps of the reaction. This approach was important to reduce the complexity of a reaction with many subtleties and many finely balanced equilibria. Consequently, we were able to identify a series of acidic carbon nucleophiles which were compatible with the palladium catalyst, and we replaced benzoquinone with DMSO and 2,6-dimethylbenzoquinone as \( \pi \)-acceptor and oxidant, respectively, to achieve compatibility of nucleophile and oxidant. These insights provided for catalytic conditions for the desired allylic C-H alkylation. The method demonstrated excellent functional group compatibility and good reactivity. It also served as a launching pad for development of more general and more synthetically useful allylic alkylation reactions.

1.4 EXPERIMENTAL SECTION

**General Information:** All commercially obtained reagents for the allylic alkylation reaction were used as received: 2,6-dimethylbenzoquinone, methyl phenylsulfonylacetate, benzoynitromethane, \((\text{phenylsulfonyl})\text{nitromethane}\), allylbenzene, 4-allylanisole, safrole, Pd\([1,2\text{-bis(phenylsulfanyl)ethane}]\text{(OAc)}_2\) “Catalyst 1” (Sigma-Aldrich); glacial acetic acid
Methyl nitroacetate 13 was prepared according to the published procedure. Catalyst 49 was prepared according to the published procedure. Catalyst 51 was prepared according to the published procedure. Catalyst 1 was stored at -20 °C and weighed out in air prior to use. Dioxane and tetrahydrofuran were purified prior to use by passage through a bed of activated alumina (Glass Contour, Laguna Beach, California). Dimethyl sulfoxide was obtained from Fisher Scientific and used as received. All allylic alkylation reactions were run under air with no precautions taken to exclude moisture. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized with UV and potassium permanganate stain. Flash chromatography was performed as described by Still using ZEOprep 60 ECO 43-60 micron silica gel (American International Chemical, Inc.).

1H NMR spectra were recorded on a Varian Unity-400 (400 MHz), Varian Inova-500 (500 MHz), or Varian Unity-500 (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 7.26 ppm). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, b = broad, ap = apparent; coupling constant(s) in Hz; integration. Proton-decoupled 13C NMR spectra were recorded on a Varian Unity-500 (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 77.16 ppm). 19F spectra were recorded on a Varian Unity-500 (470 MHz) spectrometer and are reported in ppm using a CFCl₃ standard referenced to 0 ppm. Regioselectivity of the allylic alkylation reaction was determined by 1H NMR analysis of the crude reaction mixture. IR spectra were recorded as thin films on NaCl plates on a Perkin-Elmer Spectrum BX and are reported in frequency of absorption (cm⁻¹). HPLC analysis was performed on an Agilent Technologies 1100 HPLC system with a model 1100 Quaternary Pump, Diode Array Detector, Thermostat, and Autosampler using a Daicel Chemical Industries Chiralcel OD-H column (0.46 cm x 25 cm). High-resolution mass spectra.
were obtained at the University of Illinois Mass Spectrometry Laboratory. Optical rotations were obtained using a JAS.CO DIP-360 digital polarimeter and a 3.5 x 50 mm cell and are reported as follows: concentration (c = g / 100 mL), solvent.

**General Procedure for the Allylic Alkylation:** To a two-dram (8 mL) borosilicate vial was added Pd[1,2-bis(phenylsulfinyl)ethane](OAc)$_2$ (0.10 equiv, 0.050 mmol) and 2,6-dimethylbenzoquinone (1.5 equiv, 0.75 mmol). Olefin (1 equiv, 0.50 mmol), methyl nitroacetate (3 equiv, 1.50 mmol), and acetic acid (0.50 equiv, 0.25 mmol) in dioxane (1.2 mL); dimethylsulfoxide (0.30 mL); and a stir bar were added sequentially. No precautions were taken to exclude air or moisture. The olefin, nucleophile and acid were weighed out in a ½ dram vial and transferred via dioxane (3 x 0.4 mL). The reaction vial was capped and stirred at 45 °C for 12-24 hours. The allylic alkylation was monitored until complete conversion of the α-olefin starting material was observed by TLC. The vial was cooled to room temperature, and the reaction mixture was diluted with saturated aqueous NH$_4$Cl (40 mL) and extracted with ethyl acetate (3 x 40 mL). The combined organic extracts were dried over MgSO$_4$. The mixture was filtered and concentrated *in vacuo*. Purification by flash chromatography (SiO$_2$, EtOAc/hexanes mixtures) provided the pure linear product. In all cases branched product was readily separated and generally possessed a higher R$_f$ value than linear product.

**Procedure for preparation of Catalyst 1:**
1,2-bis(phenylsulfinyl)ethane: A 50 mL flask was charged with a stir bar, 1,2-bis(phenylthio)ethane (2.0 g, 8.12 mmol, 1 equiv.), and acetic acid (12.2 mL). A solution of H$_2$O$_2$ (50 wt%, 1.10 mL, 16.2 mmol, 2 equiv.) in acetic acid (6.7 mL) was added dropwise at room temperature. After approximately 15 min. the solution became homogeneous and turned a pale yellow. An additional 1.4 mL of acetic acid was then added and the solution was allowed to stir for 24 h at room temperature. The acetic acid was removed with mild heating (45 °C) under high vacuum. The pale yellow solid was emulsified in cold ethanol and cold-filtered to yield a mixture of the meso and racemic 1,2-bis(phenylsulfinyl)ethane (2.088g, 92% yield). Meso-1,2-bis(phenylsulfinyl)ethane $^1$H NMR (500 MHz, CDCl$_3$) δ 7.56-7.52 (m, 10H), 3.05 (s, 4H). $^{13}$C NMR (500 MHz, CDCl$_3$) 142.29, 131.55, 129.63, 124.10, 47.06. IR (neat, cm$^{-1}$) 3049, 2970, 2922, 1442, 1036, 745, 696; racemic-1,2-bis(phenylsulfinyl)ethane $^1$H NMR (500 MHz, CDCl$_3$) δ 7.51-7.48 (m, 10H), 3.40 (m, 2H), 2.74 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) 142.55, 131.53, 129.64, 124.08, 47.94. IR (neat, cm$^{-1}$) 3053, 2911, 1443, 1084, 1043, 749. HRMS (ESI) m/z calculated for C$_{14}$H$_{14}$O$_2$S$_2$Na [M+Na]$^+$: 301.0333, found 301.0320.

Recrystallization of 1,2-bis(phenylsulfinyl)ethane: To a solution of refluxing acetone (~100 ml) was added the crude ligand mixture (~2 g). Acetone was then added slowly to the mixture with reflux until the powder dissolved completely. The mixture was allowed to cool to room temperature. (NOTE: In the event of over-oxidation, the mono- or di-sulfone will recrystallize first as large plates in approximately 6-8 hours. In this case the mixture was filtered, rinsing with minimal cold acetone). The sulfone free mixture was left at room temperature for an hour, then cooled to 4°C over night. IMPORTANT: The meso isomer crystallizes first as small white prisms. Extended time is needed to allow the racemic (long white needles) to crystallize. The
meso crystals were collected via filtration with a Buchner funnel and rinsed with cold acetone to give ~75% yield. Additional crops may be obtained by evaporating the mother liquor and redissolving the white solid in minimal refluxing acetone.

**Recrystallization of Pd(OAc)$_2$:** Pd(OAc)$_2$ (~2 g) was dissolved in minimal refluxing benzene (~25 mL). A black precipitate was removed by hot Acrodisc® filtration. The resulting solution was cooled to room temperature without further manipulation. Amber crystals began to form after ~2 h. After 24 h the slurry was filtered to give the recrystallized Pd(OAc)$_2$. A difference in NMR purity was noted between “old” and recrystallized Pd(OAc)$_2$ samples. Reported hydrogen values are normalized ratios of the smallest peak in the acetate region. “Old” Pd(OAc)$_2$ $^1$H NMR (500 MHz, CDCl$_3$) δ 2.17 (s, 1H), 2.10 (s, 3.6H), 2.07 (s, 6.1H), 2.06 (s, 6.1H), 2.03 (m, 15.3H), 2.00 (m, 95.7H), 1.97 (s, 5.7H), 1.95 (s, 6.3), 1.89 (s, 9.4H). Recrystallized Pd(OAc)$_2$ $^1$H NMR (500 MHz, CDCl$_3$) δ 2.10 (s, 1H), 2.03 (s, 2.8H), 2.00 (s, 40.1H), 1.97 (s, 1.2H), 1.90 (s, 2.3H).

![Catalyst 1: A flame-dried 250 mL flask fitted with a condenser under argon atmosphere was charged with meso-1,2-bis(phenylsulfinyl)ethane (2.53 g, 9.1 mmol), Pd(OAc)$_2$ (2.04 g, 9.1 mmol), and CH$_2$Cl$_2$ (101 mL). The mixture was stirred at 40 °C for 24h. The solution becomes dark red and homogenous during the reaction time. The solution was concentrated in vacuo and dried with a stream of N$_2$ for 6 h to give a dark red solid used without further purification. NOTE: The catalyst must be stored at or below 4 °C. The catalyst slowly decomposes at ambient temperature; however, it may be stored for prolonged periods (months) at reduced temperatures. $^1$H NMR and IR spectra of this catalyst resemble 1,2-](image)
bis(phenylsulfinyl)ethane and Pd(OAc)$_2$. Trace amounts of phenyl vinyl sulfoxide can be observed by $^1$H NMR.

**NOTE:** Commercially available catalyst 1 (Sigma-Aldrich) and homemade catalyst were used interchangeably in the entries of Table 3. While catalyst batch variability is occasionally observed, no significant variability was observed between commercial and homemade catalyst.

**Stoichiometric allylic alkylation**

<table>
<thead>
<tr>
<th>entry</th>
<th>NuH</th>
<th>yield (L+B)$^b$</th>
<th>L:B$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhO$_2$SCH$_2$CO$_2$Me, 15</td>
<td>9%</td>
<td>---</td>
</tr>
<tr>
<td>2</td>
<td>NO$_2$CH$_2$COPh, 16</td>
<td>82%</td>
<td>8:1</td>
</tr>
<tr>
<td>3</td>
<td>NO$_2$CH$_2$SO$_2$Ph, 17</td>
<td>89%</td>
<td>16:1</td>
</tr>
<tr>
<td>4</td>
<td>NO$_2$CH$_2$CO$_2$Me, 13</td>
<td>86%</td>
<td>4:1</td>
</tr>
<tr>
<td>5</td>
<td>13 (no DMSO)$^c$</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

$^a$ Determined by $^1$H NMR analysis of the crude. $^b$ 0.033M. $^c$ Dioxane (0.033M).

bis[chloro(1,2,3-trihapto-allylbenzene)palladium (II)]: A 50 mL flask was charged with allylbenzene (264 μL, 2.0 mmol, 1.0 equiv), catalyst 1 (1.01 g, 2.0 mmol, 1.0 equiv), and a stir bar. To this was added 6 mL dioxane. The solution was allowed to stir for 60 min at room temperature under air, at which time an acetone solution (6 mL) of $n$-Bu$_4$NCl (2.22 g, 8.0 mmol, 4 equiv) was added via syringe. The anion exchange proceeded at room temperature for 60 min. The mixture was filtered over a plug of Celite (to remove metallic Pd), concentrated and purified via column chromatography (10%→50% EtOAc/hexanes gradient) to afford bis[chloro(1,2,3-trihapto-allylbenzene)palladium (II)] as a yellow solid (182 mg, 0.752 mmol, 35% yield). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.50 (d, $J = 7.6$ Hz, 4H), 7.35 (m, 2H), 7.27 (d, $J = 7.6$ Hz, 4H), 5.80 (td, $J = 11.6$, 6.8 Hz, 2H), 4.62 (d, $J = 11.2$ Hz, 2H), 3.97 (d,
\[ J = 6.6 \text{ Hz, 2H}, \ 3.04 \ (d, \ J = 11.7 \text{ Hz, 2H}). \] Spectral data match those of the reported compound.\(^{36}\)

In order to investigate the low isolated yields of bis[chloro(1,2,3-trihapto-allylbenzene)palladium (II)] (vide supra) formation of the product was observed by \(^1\text{H NMR}. \) To a ½ dram borosilicate vial were added allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv). Catalyst 1 (50.3 mg, 0.10 mmol, 1.0 equiv), dioxane-d\(_8\) (300 μL) and a stir bar were added sequentially. No precautions were taken to exclude air or moisture. The vial was capped and stirred for 60 min at 45 °C. The vial was cooled to room temperature and \( n\text{-Bu}_4\text{NCl} \) (111.2 mg, 0.40 mmol, 4.0 equiv) was added in one portion. The anion exchange proceeded at room temperature for 60 min. To the crude reaction mixture was added nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) and the solution was shaken vigorously. A sample was removed for \(^1\text{H NMR} \) analysis and diluted with CDCl\(_3\). Yield was determined by integration of product peaks at 5.80, 4.62, 3.97 ppm relative to nitrobenzene. Run 1 (72% yield); run 2 (74% yield). Average yield: 73%. A low isolated yield may therefore be attributed to streaking during column chromatography rather than to low reactivity of the olefin and catalyst 1.

![bis[acetato(1,2,3-trihapto-allylbenzene)palladium (II)] (12)](image)

A flame-dried 10 mL flask was charged with bis[chloro(1,2,3-trihapto-allylbenzene)palladium (II)] (51.8 mg, 0.20 mmol, 1.0 equiv) and a stir bar. To this was added silver acetate (33.4 mg, 0.20 mmol, 1.0 equiv) dissolved in 2 mL of CHCl\(_3\), followed by a rinse with 1 mL CHCl\(_3\). The reaction was allowed to stir for 60 min at room temperature under Ar atmosphere. The mixture was filtered over a plug of Celite (to remove metallic Pd) and
concentrated in vacuo, and blown dry under a stream of N₂ to afford bis[acetato(1,2,3-trihapto-allylbenzene)palladium (II)] as a yellow oil which solidified when stored at -20 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.6-7.1 (m, 10H), 6.0-5.8 (m, 2H), 4.64 (bd, J = 9.5 Hz, 2H), 3.88 (bd, J = 6.3 Hz, 2H), 2.92 (m, 2H), 2.0-1.2 (m, 6H).

**General stoichiometric screening procedure (see Table 1):** To a 40 mL borosilicate vial were added sequentially bis[acetato(1,2,3-trihapto-allylbenzene)palladium (II)] (28.3 mg, 0.100 mmol, 1.0 equiv) and nucleophile (1.00 mmol, 10 equiv), and a stir bar. Dioxane (2.4 mL) and dimethylsulfoxide (0.60 mL) were added. No precautions were taken to exclude air or moisture. The vial was capped and stirred for 3.5 h at 45 °C. The vial was cooled to room temperature and the reaction mixture was diluted with saturated aqueous NH₄Cl (20 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organics were dried over MgSO₄. The mixture was filtered and concentrated in vacuo. To the crude reaction mixture was added nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv). The crude mixture was dissolved completely in CDCl₃ and a sample was removed for ¹H NMR analysis. Yield was determined by integration of olefinic product peaks relative to nitrobenzene.

**Entry 1:** Bis[acetato(1,2,3-trihapto-allylbenzene)palladium (II)] (14.1 mg, 0.050 mmol, 1.0 equiv), methyl phenylsulfonylacetae (107.1 mg, 0.50 mmol, 10 equiv), and nitrobenzene (4.9 mg, 0.040 mmol, 0.80 equiv) were used. Run 1 (9% yield); run 2 (9% yield). **Average yield:** 9%. Spectral data match those of the reported compound.³⁷
Entry 2: Bis[acetato(1,2,3-trihapto-allylbenzene)palladium (II)] (28.3 mg, 0.10 mmol, 1.0 equiv), benzylnitromethane (165.2 mg, 1.0 mmol, 10 equiv), and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. Run 1 (79% yield, 8.0:1 L:B); run 2 (84% yield, 7.9:1 L:B).

Average yield: 82%.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.99 (m, 2H), 7.67 (m, 1H), 7.54 (m, 2H), 7.30 (m, 4H), 7.24 (m, 1H), 6.56 (d, $J$ = 15.9 Hz, 1H), 6.17 (dd, $J$ = 9.0, 5.1 Hz, 1H), 6.13 (dt, $J$ = 15.7, 7.2 Hz, 1H), 3.26 (dddd, $J$ = 15.1, 8.9, 7.6, 1.3 Hz, 1H), 3.08 (dddd, $J$ = 15.0, 6.8, 5.2, 1.5 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 188.4, 136.4, 135.4, 135.0, 134.0, 129.4, 129.0, 128.8, 128.1, 126.5, 121.7, 89.3, 34.2; IR (film, cm$^{-1}$): 3064, 3027, 2922, 1695, 1559, 1449, 967; HRMS (ESI) m/z calculated for C$_{17}$H$_{15}$NO$_3$Na [M+Na]$^+$: 304.0950, found 304.0941.

Entry 3: Bis[acetato(1,2,3-trihapto-allylbenzene)palladium (II)] (28.3 mg, 0.10 mmol, 1.0 equiv), (phenylsulfonyl)nitromethane (201.2 mg, 1.0 mmol, 10 equiv), and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. Run 1 (87% yield, 17:1 L:B); run 2 (91% yield, 15:1 L:B).

Average yield: 89%.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.93 (m, 2H), 7.80 (m, 1H), 7.65 (m, 2H), 7.29 (m, 4H), 7.24 (m, 1H), 6.54 (d, $J$ = 15.6 Hz, 1H), 5.97 (dd, $J$ = 15.7, 7.8, 6.7 Hz, 1H), 5.59 (dd, $J$ = 11.2, 3.4 Hz, 1H), 3.22 (dddd, $J$ = 14.9, 6.4, 3.5, 1.4 Hz, 1H), 3.12 (dddd, $J$ = 15.0, 11.2, 7.9, 1.1 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 136.4, 135.9, 135.7, 134.0, 130.1, 129.7, 128.7, 128.4, 126.5, 119.0, 101.4, 31.5; IR (film, cm$^{-1}$): 3063, 3031, 2981, 2929, 2258, 1562, 1449, 1342, 1158, 909, 732, 689; HRMS (ESI) m/z calculated for C$_{16}$H$_{15}$NO$_4$SNa [M+Na]$^+$: 340.0620, found 340.0629. Spectral data match those of the reported compound.$^{37}$

Entry 4: Bis[acetato(1,2,3-trihapto-allylbenzene)palladium (II)] (28.3 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (119.1 mg, 1.0 mmol, 10 equiv), and nitrobenzene (4.9 mg, 0.040
mmol, 0.40 equiv) were used. Run 1 (87% yield, 4.1:1 L:B); run 2 (84% yield, 4.3:1 L:B).

**Average yield: 86%.** \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.32 (m, 4H), 7.25 (m, 1H), 6.65 (d, \(J = 15.6\) Hz, 1H), 6.08 (dt, \(J = 15.6, 7.3\) Hz, 1H), 5.23 (dd, \(J = 9.2, 5.5\) Hz, 1H), 3.85 (s, 3H), 3.16 (m, 1H), 3.07 (m, 1H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) 164.6, 136.3, 135.6, 128.7, 128.2, 126.5, 121.1, 87.6, 53.8, 33.9; IR (film, cm\(^{-1}\)): 3028, 2958, 1954, 1884, 1754, 1563, 1495, 1438; HRMS (ESI) \(m/z\) calculated for C\(_{12}\)H\(_{13}\)NO\(_4\)Na [M+Na]\(^+\): 258.0742, found 258.0729. Spectral data match those of the reported compound.\(^{37}\)

**Entry 5:** Bis[acetato(1,2,3-trihapto-allylbenzene)palladium (II)] (28.3 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (119.1 mg, 1.0 mmol, 10 equiv), and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. Dioxane (3.0 mL) used as solvent. Run 1 (<1% yield); run 2 (<1% yield). **Average yield: <1%.**

**Catalytic allylic C-H alkylation**

\[
\text{entry} \quad \text{Pd(II)\textsubscript{catalyst}} \quad \text{oxidant (equiv.)} \quad \text{yield (L+B)}^a \quad \text{L:B}^a
\]

<table>
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<tr>
<th>entry</th>
<th>Pd(II)\textsubscript{catalyst}</th>
<th>oxidant (equiv.)</th>
<th>yield (L+B)(^a)</th>
<th>L:B(^a)</th>
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<td>Phi(OAc)(_2) (2.0)</td>
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</tr>
<tr>
<td>2</td>
<td>1</td>
<td>Cu(OAc)(_2) (2.0)</td>
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<td>O(_2) (7 atm.)</td>
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<td>4:1</td>
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<tr>
<td>5</td>
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<td>O(_2) (1 atm.) HFMV</td>
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<td>O(_2) (1 atm.)</td>
<td>Cu(OAc)(_2) (1 atm.)</td>
<td>17%</td>
</tr>
<tr>
<td>7</td>
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<td>---</td>
<td>---</td>
</tr>
<tr>
<td>9</td>
<td>19(^\text{a})</td>
<td>DMBQ (1.5)(^\text{a})</td>
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<td>---</td>
</tr>
<tr>
<td>10</td>
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<td>Pd(OAc)(_2)</td>
<td>DMBQ (1.5)(^\text{a})</td>
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</tr>
</tbody>
</table>

\(^{a}\) Determined by \(^1\)H NMR analysis of crude. \(^{\text{catalyst}}\) 0.03 mmol, DMBQ = 2,6-dimethylbenzoquinone (1.5 equiv.), Cu(OAc)\(_2\) = 0.5 equiv., Pd(II) = Pd(tetrafluorocarboxylate)\(_2\) / bis(phenylsulfanyl)ethane \(^\text{c}\) nBu\(_4\)NOAc (1 equiv.), \(^\text{d}\) 13 (3 equiv.)

**General catalytic screening procedure (see Table 2):** To a 1/2 dram borosilicate vial were added catalyst 1 (5.0 mg, 0.010 mmol, 0.10 equiv) and dimethylbenzoquinone (20.4 mg, 0.15 mmol, 1.5 equiv). Allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (11.9 mg,
0.10 mmol, 1.0 equiv), and acetic acid (2.9 μL, 0.050 mmol, 0.50 equiv) in dioxane (240 μL); dimethylsulfoxide (60 μL); and a stir bar were added sequentially. No precautions were taken to exclude air or moisture. The olefin, nucleophile and acid were weighed out in a ½ dram vial and transferred via dioxane (2 x 120 μL). The vial was capped and stirred for 24 h at 45°C. The vial was cooled to room temperature and the reaction mixture was diluted with saturated aqueous NH₄Cl (10 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organics were dried over MgSO₄. The mixture was filtered and concentrated in vacuo. To the crude reaction mixture was added nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv). The crude mixture was dissolved completely in CDCl₃ and a sample was removed for ¹H NMR analysis. Yield was determined by integration of olefinic product peaks relative to nitrobenzene.

**Entry 1**: Catalyst 1 (5.0 mg, 0.010 mmol, 0.10 equiv), allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (11.9 mg, 0.10 mmol, 1.0 equiv), (diacetoxyiodo)benzene (48.3 mg, 0.15 mmol, 1.5 equiv) and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. Run 1 (<5% yield); run 2 (<5% yield). **Average yield: <5%**.

**Entry 2**: Catalyst 1 (5.0 mg, 0.010 mmol, 0.10 equiv), allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (11.9 mg, 0.10 mmol, 1.0 equiv), copper(II) acetate (27.2 mg, 0.15 mmol, 1.5 equiv) and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. Run 1 (9% yield); run 2 (7% yield). **Average yield: 8%**.

**Entry 3**: Catalyst 1 (5.0 mg, 0.010 mmol, 0.10 equiv), allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (11.9 mg, 0.10 mmol, 1.0 equiv), and nitrobenzene (4.9 mg, 0.040
mmol, 0.40 equiv) were used. The reaction vial was fitted with a balloon of O₂. Run 1 (26% yield, 4.1:1 L:B); run 2 (28% yield, 4.3:1 L:B). **Average yield: 27%**.

**Entry 4:** Catalyst 1 (5.0 mg, 0.010 mmol, 0.10 equiv), allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (11.9 mg, 0.10 mmol, 1.0 equiv), and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. The reaction vial pressurized with O₂ to 7 atm. Run 1 (35% yield, 4.2:1 L:B); run 2 (34% yield, 4.3:1 L:B). **Average yield: 35%**.

**Entry 5:** Catalyst 1 (5.0 mg, 0.010 mmol, 0.10 equiv), allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (11.9 mg, 0.10 mmol, 1.0 equiv), HPMV (5.0 mg) and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. The reaction vial was fitted with a balloon of O₂. Run 1 (8% yield, 4.0:1 L:B); run 2 (12% yield, 3.9:1 L:B). **Average yield: 10%**.

**Entry 6:** Catalyst 1 (5.0 mg, 0.010 mmol, 0.10 equiv), allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (11.9 mg, 0.10 mmol, 1.0 equiv), copper(II) acetate (1.8 mg, 0.010 mmol, 0.10 equiv) and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. The reaction vial was fitted with a balloon of O₂. Run 1 (15% yield, 4.1:1 L:B); run 2 (19% yield, 4.1:1 L:B). **Average yield: 17%**.

**Entry 7:** Catalyst 1 (5.0 mg, 0.010 mmol, 0.10 equiv), allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (11.9 mg, 0.10 mmol, 1.0 equiv), dimethylbenzoquinone (20.4 mg, 0.15 mmol, 1.5 equiv), acetic acid (2.9 μL, 0.050 mmol, 0.50 equiv), and nitrobenzene (4.9 mg,
0.040 mmol, 0.40 equiv) were used. Run 1 (71% yield, 3.8:1 L:B); run 2 (72% yield, 3.8:1 L:B). 

**Average yield: 72%**.

**Entry 8:** Catalyst 1 (5.0 mg, 0.010 mmol, 0.10 equiv), allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (11.9 mg, 0.10 mmol, 1.0 equiv), tetrabutylammonium acetate (30.2 mg, 0.10 mmol, 1.0 equiv), dimethylbenzoquinone (20.4 mg, 0.15 mmol, 1.5 equiv), acetic acid (2.9 μL, 0.050 mmol, 0.50 equiv), and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. Run 1 (<1% yield); run 2 (<1% yield). **Average yield: <1%**.

**Entry 9:** Pd(TFA)$_2$ (3.3 mg, 0.010 mmol, 0.10 equiv), meso-1,2-bis(phenylsulfinyl)ethane (2.8 mg, 0.010 mmol, 0.10 equiv), allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (11.9 mg, 0.10 mmol, 1.0 equiv), dimethylbenzoquinone (20.4 mg, 0.15 mmol, 1.5 equiv), and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. Run 1 (5% yield); run 2 (4% yield). **Average yield: 4%**.

**Entry 10:** Pd(OAc)$_2$ (2.2 mg, 0.010 mmol, 0.10 equiv), allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (11.9 mg, 0.10 mmol, 1.0 equiv), dimethylbenzoquinone (20.4 mg, 0.15 mmol, 1.5 equiv), acetic acid (2.9 μL, 0.050 mmol, 0.50 equiv), and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. Run 1 (63% yield, 3.7:1 L:B); run 2 (63% yield, 3.9:1 L:B). **Average yield: 63%**.

**Entry 11:** Catalyst 1 (5.0 mg, 0.010 mmol, 0.10 equiv), allylbenzene (11.8 mg, 0.10 mmol, 1.0 equiv), methyl nitroacetate (35.7 mg, 0.30 mmol, 3.0 equiv), dimethylbenzoquinone (20.4 mg,
0.15 mmol, 1.5 equiv), acetic acid (2.9 μL, 0.050 mmol, 0.50 equiv), and nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) were used. Run 1 (84% yield, 3.4:1 L:B); run 2 (82% yield, 3.5:1 L:B).

**Average yield: 83%**. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.32 (m, 4H), 7.25 (m, 1H), 6.65 (d, $J$ = 15.6 Hz, 1H), 6.08 (dt, $J$ = 15.6, 7.3 Hz, 1H), 5.23 (dd, $J$ = 9.2, 5.5 Hz, 1H), 3.85 (s, 3H), 3.16 (m, 1H), 3.07 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) 164.6, 136.3, 135.6, 128.7, 128.2, 126.5, 121.1, 87.6, 53.8, 33.9; IR (film, cm$^{-1}$): 3028, 2958, 1954, 1884, 1754, 1563, 1495, 1438; HRMS (ESI) $m/z$ calculated for C$_{12}$H$_{13}$NO$_4$Na [M+Na]$^+$: 258.0742, found 258.0729. Spectral data match those of the reported compound. This reaction was also run at 0.5 mmol scale, and pure linear product was isolated in 62% yield (vide infra).
## Scope of the allylic C-H alkylation reaction

<table>
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<tr>
<th>entry</th>
<th>major product</th>
<th>L:B&lt;sup&gt;b&lt;/sup&gt;</th>
<th>E:Z &gt;20:1</th>
<th>isolated yield L&lt;sup&gt;a&lt;/sup&gt;</th>
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<tr>
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<td>4</td>
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<td></td>
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<td>42</td>
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<sup>a</sup> Olefin (1 equiv.), 13 (3 equiv.), DMBG (1,5 equiv.), AcOH (0,5 equiv.), 1 (10 mol%).<br>
<sup>b</sup> Determined by 1H NMR analysis of the crude.
(E)-methyl 5-(4-methoxyphenyl)-2-nitropent-4-enoate [20]: 4-allylanisole (74.1 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By \(^1\)H NMR analysis of the crude product, the linear:branched ratio was 1.7:1 and the E/Z isomer ratio was >20:1. Flash chromatography (20% EtOAc/hexanes) yielded pure linear product as a light yellow solid. Run 1 (66.9 mg, 0.252 mmol, 50% yield); run 2 (66.6 mg, 0.251 mmol, 50% yield). **Average yield: 50%**. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.27\) (d, \(J = 8.8\) Hz, 2H), 6.84 (d, \(J = 8.8\) Hz, 2H), 6.49 (d, \(J = 15.6\) Hz, 1H), 5.93 (dt, \(J = 15.8, 7.3\) Hz, 1H), 5.22 (dd, \(J = 9.2, 5.5\) Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 3.13 (m, 1H), 3.04 (m, 1H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) 164.7, 159.6, 135.0, 129.1, 127.7, 118.8, 114.1, 87.8, 55.4, 53.8, 34.0; IR (film, cm\(^{-1}\)): 3033, 3005, 2958, 2839, 1891, 1756, 1608, 1566, 1514, 1250, 1176, 1033, 971; HRMS (ESI) \(m/z\) calculated for C\(_{13}\)H\(_{18}\)NO\(_5\)Na [M+Na]\(^+\): 288.0848, found 288.0848.

(E)-methyl 2-nitro-5-p-tolylpent-4-enoate [21]: 4-allyltoluene (68.6 mg, 96% pure, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By \(^1\)H NMR analysis of the crude product, the linear:branched ratio was 3.3:1 and the E/Z isomer ratio was >20:1. Flash chromatography (15% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (75.5 mg, 0.303 mmol, 61% yield); run 2 (76.8 mg, 0.308 mmol, 62% yield). **Average yield: 61%**. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 7.22\) (d, \(J = 8.1\) Hz, 2H), 7.11 (d, \(J = 8.1\) Hz, 2H), 6.52 (d, \(J = 15.6\) Hz, 1H), 6.02 (dt, \(J = 15.7, 7.2\) Hz, 1H), 5.22 (dd, \(J = 9.2, 5.5\) Hz, 1H), 3.85 (s, 3H), 3.15 (m, 1H), 3.05 (m, 1H), 2.33 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) 164.6, 138.1, 135.4, 133.5, 129.4, 126.4, 120.0, 87.7, 53.8,
(E)-methyl 2-nitro-5-(4-vinylphenyl)pent-4-enoate [22]: 4-allylstyrene (72.1 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 3.3:1 and the E/Z isomer ratio was >20:1. Flash chromatography (15% EtOAc/hexanes) yielded pure linear product as a light yellow solid. Run 1 (77.3 mg, 0.296 mmol, 59% yield); run 2 (84.8 mg, 0.325 mmol, 65% yield); run 3 (22.7 mg, 0.087 mmol, 0.132 mmol scale, 66%). **Average yield: 63%**. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.35 (d, $J$ = 8.4 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 6.69 (dd, $J$ = 17.6, 10.9 Hz, 1H), 6.54 (d, $J$ = 15.9 Hz, 1H), 6.08 (dt, $J$ = 15.7, 7.3 Hz, 1H), 5.75 (d, $J$ = 17.6 Hz, 1H), 5.24 (m, 2H), 3.85 (s, 3H), 3.16 (m, 1H), 3.07 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.6, 137.4, 136.4, 135.8, 135.2, 126.7, 126.6, 121.1, 114.2, 87.6, 53.8, 33.9; IR (film, cm$^{-1}$): 2958, 2927, 2850, 1750, 1627, 1563, 1436, 1218, 978, 914, 814; HRMS (ESI) m/z calculated for C$_{14}$H$_{16}$NO$_4$ [M+H]$^+$: 262.1079, found 262.1066.

(E)-methyl 2-nitro-5-phenylpent-4-enoate [14]: Allylbenzene (59.1 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 4.4:1 and the E/Z isomer ratio was >20:1. Flash chromatography (15% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (73.8 mg, 0.314 mmol, 63% yield); run 2 (71.2 mg, 0.303 mmol, 61% yield). **Average yield: 62%**. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.32 (m, 4H), 7.25 (m, 1H), 6.65 (d, $J$ = 15.6 Hz, 1H), 6.08 (dt, $J$ = 15.6, 7.3 Hz, 1H), 5.23 (dd, $J$ = 9.2, 5.5 Hz, 1H),
3.85 (s, 3H), 3.16 (m, 1H), 3.07 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) 164.6, 136.3, 135.6, 128.7, 128.2, 126.5, 121.1, 87.6, 53.8, 33.9; IR (film, cm$^{-1}$): 3028, 2958, 1954, 1884, 1754, 1563, 1495, 1438; HRMS (ESI) m/z calculated for C$_{12}$H$_{13}$NO$_4$Na [M+Na]$^+$: 258.0742, found 258.0729.

Spectral data match those of the reported compound.$^{36}$

(E)-methyl 5-(4-bromophenyl)-2-nitropent-4-enoate [23]: 4-bromoallylbenzene (98.5 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 4.2:1 and the E/Z isomer ratio was >20:1. Flash chromatography (15% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (86.4 mg, 0.275 mmol, 55% yield); run 2 (85.2 mg, 0.271 mmol, 0.454 mmol scale, 60% yield); run 3 (83.6 mg, 0.266 mmol, 0.400 mmol scale, 67%). **Average yield:** 60%. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.43 (d, $J = 8.4$ Hz, 2H), 7.19 (d, $J = 8.4$ Hz, 2H), 6.49 (d, $J = 15.7$ Hz, 1H), 6.08 (dt, $J = 15.7$, 7.3 Hz, 1H), 5.23 (dd, $J = 9.2$, 5.4 Hz, 1H), 3.85 (s, 3H), 3.15 (m, 1H), 3.05 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.5, 135.2, 134.4, 131.9, 128.1, 122.0, 122.0, 87.4, 53.9, 33.8; IR (film, cm$^{-1}$): 3033, 2960, 1760, 1568, 1488, 1439, 1342, 1224, 1009, 693; HRMS (ESI) m/z calculated for C$_{12}$H$_{12}$NO$_4$BrNa [M+Na]$^+$: 335.9847, found 335.9841.

(E)-methyl 5-(4-(N,4-dimethylphenylsulfonamido)phenyl)-2-nitropent-4-enoate [24]: N-(4-allylphenyl)-N,4-dimethylbenzenesulfonamide (151 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 4.0:1 and the E/Z isomer ratio was >20:1. Flash chromatography (30%
EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (133 mg, 0.318 mmol, 64% yield); run 2 (128 mg, 0.306 mmol, 61% yield). Average yield: 63%. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.42 (d, $J = 8.1$ Hz, 2H), 7.24 (m, 4H), 7.04 (d, $J = 8.6$ Hz, 2H), 6.52 (d, $J = 15.9$ Hz, 1H), 6.07 (dt, $J = 15.8$, 7.2 Hz, 1H), 5.24 (dd, $J = 9.3$, 5.3 1H), 3.86 (s, 3H), 3.16 (m, 1H), 3.13 (s, 3H), 3.07 (m, 1H), 2.42 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.5, 143.8, 141.3, 135.2, 134.5, 133.3, 129.5, 127.9, 126.9, 126.6, 122.0, 87.5, 53.8, 38.0, 33.8, 21.6; IR (film, cm$^{-1}$): 3035, 2959, 2934, 2259, 1921, 1756, 1598, 1563, 1505, 1348, 1172, 911, 729; HRMS (ESI) m/z calculated for C$_{20}$H$_{23}$N$_2$O$_6$S [M+H]$^+$: 419.1277, found 419.1289.

$^{(E)}$-methyl 5-(4-fluorophenyl)-2-nitropent-4-enoate [25]: 4-

Fluoroallylbenzene (68.1 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 4.3:1 and the E/Z isomer ratio was >20:1. Flash chromatography (20% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (84.3 mg, 0.333 mmol, 67% yield); run 2 (80.5 mg, 0.318 mmol, 64% yield). Average yield: 65%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.30 (m, 2H), 7.00 (m, 2H), 6.52 (d, $J = 15.9$ Hz, 1H), 6.00 (dt, $J = 15.6$, 7.3 Hz, 1H), 5.23 (dd, $J = 9.0$, 5.4 Hz, 1H), 3.85 (s, 3H), 3.15 (m, 1H), 3.05 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.4, 162.5 (d, $J_{CF} = 247.7$ Hz), 134.2, 132.3 (d, $J_{CF} = 2.8$ Hz), 127.9 (d, $J_{CF} = 8.3$ Hz), 120.8, 115.5 (d, $J_{CF} = 21.1$ Hz), 87.4, 53.7, 33.7; $^{19}$F NMR (470 MHz, CDCl$_3$) 98.9; IR (film, cm$^{-1}$): 2959, 2924, 2851, 1759, 1602, 1567, 1511, 1228, 970; HRMS (ESI) m/z calculated for C$_{12}$H$_{12}$NO$_4$FNa [M+Na]$^+$: 276.0648, found 276.0646.
(E)-methyl 4-(5-methoxy-4-nitro-5-oxopent-1-enyl)benzoate

[26]: Methyl 4-allylbenzoate (73.6 mg, 95.8% pure, 0.4 mmol, 1.0 equiv) was reacted for 12h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 10.1:1 and the E/Z isomer ratio was >20:1. Flash chromatography (25% EtOAc/hexanes), followed by short silica plug (100% CH$_2$Cl$_2$), followed by flash chromatography (25% EtOAc/hexanes), followed by repeated extractions as necessary to remove methyl nitroacetate (sat. aq. NaHCO$_3$), yielded linear product contaminated by ca. 6% methyl 6-(4-(methoxycarbonyl)phenyl)-5,6-dihydro-4H-1,2-oxazine-3-carboxylate as a light yellow oil. A pure spectroscopic sample was obtained by column chromatography (15% EtOAc/hexanes). Run 1 (76.6 mg, 0.261 mmol, 65% yield); run 2 (79.6 mg, 0.271 mmol, 0.479 mmol scale, 54% yield), run 3 (43.2 mg, 0.147 mmol, 0.234 mmol scale, 63%). **Average yield:** 61%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.98 (d, $J = 8.5$ Hz, 2H), 7.39 (d, $J = 8.3$ Hz, 2H), 6.59 (d, $J = 15.9$ Hz, 1H), 6.21 (dt, $J = 15.7$, 7.3 Hz, 1H), 5.26 (dd, $J = 9.0$, 5.4 Hz, 1H), 3.91 (s, 3H), 3.86 (s, 3H), 3.19 (m, 1H), 3.10 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 166.9, 164.5, 140.6, 134.7, 130.1, 129.6, 126.4, 124.0, 87.3, 53.9, 52.3, 33.9; IR (film, cm$^{-1}$): 3004, 2956, 2849, 1931, 1759, 1716, 1608, 1563, 1438, 1286, 1111, 761; HRMS (ESI) $m/z$ calculated for C$_{14}$H$_{16}$NO$_6$ [M+H]$^+$: 294.0978, found 294.0969.

(E)-methyl 5-(4-acetylphenyl)-2-nitropent-4-enoate

[27]: 4’-allylacetoacetophenone (86.5 mg, 92.6% pure, 0.5 mmol, 1.0 equiv) was reacted for 12h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 10.3:1 and the E/Z isomer ratio was >20:1. Flash chromatography (25→35% EtOAc/hexanes gradient), followed by short silica plug
(100% CH₂Cl₂), followed by flash chromatography (25→35% EtOAc/hexanes gradient) yielded linear product contaminated by ca. 6% methyl 6-(4-acetylphenyl)-5,6-dihydro-4H-1,2-oxazine-3-carboxylate as a light yellow oil. A pure spectroscopic sample was obtained by column chromatography (15% EtOAc/hexanes). Run 1 (96.2 mg, 0.347 mmol, 69% yield); run 2 (71.6 mg, 0.258 mmol, 40% mmol scale, 65% yield), run 3 (88.3 mg, 0.318 mmol, 50.9 mmol scale, 63%). **Average yield: 66%**. 

**1H NMR (400 MHz, CDCl₃)** δ 7.90 (d, J = 8.5 Hz, 2H), 7.41 (d, J = 8.3 Hz, 1H), 6.23 (dt, J = 15.8, 7.3 Hz, 1H), 5.26 (dd, J = 9.3, 5.4 Hz, 1H), 3.86 (s, 3H), 3.20 (m, 1H), 3.10 (m, 1H), 2.59 (s, 3H); 

**13C NMR (125 MHz, CDCl₃)** 197.6, 164.5, 140.8, 136.5, 134.6, 128.9, 126.6, 124.2, 87.3, 53.9, 33.9, 26.8; IR (film, cm⁻¹): 2957, 2926, 2853, 1755, 1679, 1604, 1562, 1360, 1267; HRMS (ESI) m/z calculated for C₁₄H₁₆NO₅ [M+H]⁺: 278.1028, found 278.1017.

(E)-methyl 2-nitro-5-(4-(trifluoromethyl)phenyl)pent-4-enoate [28]: 4-allylbenzotrifluoride (93.1 mg, 0.5 mmol, 1.0 equiv) was reacted for 18h following the general procedure. By ¹H NMR analysis of the crude product, the linear:branched ratio was 10.2:1 and the E/Z isomer ratio was >20:1. Flash chromatography (20% EtOAc/hexanes) yielded linear product contaminated by ca. 5% methyl 6-(4-(trifluoromethyl)phenyl)-5,6-dihydro-4H-1,2-oxazine-3-carboxylate as a light yellow oil. A pure spectroscopic sample was obtained by column chromatography (10% EtOAc/hexanes). Run 1 (83.7 mg, 0.276 mmol, 55% yield); run 2 (87.5 mg, 0.289 mmol, 58% yield). **Average yield: 56%**. 

**¹H NMR (500 MHz, CDCl₃)** δ 7.56 (d, J = 8.1 Hz, 2H), 7.43 (d, J = 8.3 Hz, 2H), 6.59 (d, J = 15.9 Hz, 1H), 6.20 (dt, J = 15.8, 7.3 Hz, 1H), 5.25 (dd, J = 9.3, 5.4 1H), 3.86 (s, 3H), 3.19 (m, 1H), 3.10 (m, 1H); **¹³C NMR (125 MHz, CDCl₃)** 164.5, 139.7, 134.3, 130.0 (q, J₉CF = 32.2 Hz),
126.7, 125.7 (q, $J_{CF} = 3.7$ Hz), 124.2 (q, $J_{CF} = 271.6$ Hz), 124.0, 87.3, 53.9, 33.8; $^{19}$F NMR (470 MHz, CDCl$_3$) -62.8; IR (film, cm$^{-1}$): 3047, 3012, 2961, 2936, 2854, 1921, 1760, 1616, 1564, 1439, 1330, 1167, 1122, 1068, 733; HRMS (ESI) $m/z$ calculated for $C_{13}H_{12}NO_4F_3Na$ [M+Na]$^+$: 326.0616, found 326.0631.

(E)-methyl 5-(4-cyanophenyl)-2-nitropent-4-enoate [29]: 4-allylbenzonitrile (72.6 mg, 98.6% pure, 0.5 mmol, 1.0 equiv) was reacted for 12h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 12:1 and the E/Z isomer ratio was >20:1. Flash chromatography (30% EtOAc/hexanes), followed by short silica plug (100% CH$_2$Cl$_2$), followed by flash chromatography (25→35% EtOAc/hexanes gradient) yielded linear product contaminated by ca. 11% methyl 6-(4-cyanophenyl)-5,6-dihydro-4$H$-1,2-oxazine-3-carboxylate as a light yellow oil. A pure spectroscopic sample was obtained by column chromatography (15% EtOAc/hexanes). Run 1 (83.7 mg, 0.322 mmol, 64% yield); run 2 (84.6 mg, 0.325 mmol, 65% yield). **Average yield: 65%**. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.60 (d, $J = 8.3$ Hz, 2H), 7.41 (d, $J = 8.3$ Hz, 2H), 6.57 (d, $J = 15.6$ Hz, 1H), 6.24 (dt, $J = 15.6, 7.3$ Hz, 1H), 5.26 (dd, $J = 9.2, 5.2$ Hz, 1H), 3.86 (s, 3H), 3.19 (m, 1H), 3.11 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.3, 140.6, 134.0, 132.6, 127.1, 125.4, 118.9, 111.5, 87.1, 54.0, 33.8; IR (film, cm$^{-1}$): 3063, 2959, 2929, 2853, 2227, 1756, 1606, 1567, 1439, 1267, 972, 738; HRMS (ESI) $m/z$ calculated for $C_{13}H_{13}N_2O_4$ [M+H]$^+$: 261.0875, found 261.0876.
(E)-methyl 5-(3-methoxyphenyl)-2-nitropent-4-enoate [30]: 3-allylanisole (74.1 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By 1H NMR analysis of the crude product, the linear:branched ratio was 4.5:1 and the E/Z isomer ratio was >20:1. Flash chromatography (20% EtOAc/hexanes) yielded pure linear product as a light yellow solid. Run 1 (77.6 mg, 0.293 mmol, 59% yield); run 2 (61.8 mg, 0.233 mmol, 0.400 mmol scale, 58% yield). **Average yield:** 58%. 1H NMR (500 MHz, CDCl3) δ 7.22 (t, J = 7.9 Hz, 1H), 6.93 (bd, J = 7.6 Hz, 1H), 6.86 (m, 1H), 6.81 (m, 1H), 6.53 (d, J = 15.9 Hz, 1H), 6.08 (dt, J = 15.8, 7.3 Hz, 1H), 5.23 (dd, J = 9.2, 5.5 Hz, 1H), 3.85 (s, 3H), 3.81 (s, 3H), 3.16 (m, 1H), 3.06 (m, 1H); 13C NMR (125 MHz, CDCl3) 164.6, 159.9, 137.7, 135.5, 129.7, 121.5, 119.1, 113.7, 111.9, 87.5, 55.3, 53.8, 33.8; IR (film, cm⁻¹): 3006, 2959, 2838, 1761, 1568, 1436, 1264, 1046, 971, 777, 689; HRMS (ESI) m/z calculated for C₁₃H₁₆NO₅[M+H]⁺: 266.1028, found 266.1024.

(E)-methyl 5-(3-(diphenylmethyleneamino)phenyl)-2-nitropent-4-enoate [31]: 3-allyl-N-(diphenylmethylen)aniline (149 mg, 91% pure, 0.456 mmol, 1.0 equiv) was reacted for 48h following the general procedure. By 1H NMR analysis of the crude product, the linear:branched ratio was 8.6:1 and the E/Z isomer ratio was >20:1. Flash chromatography (20% EtOAc/hexanes) yielded pure linear product as a light yellow solid. Run 1 (119.8 mg, 0.289 mmol, 64% yield); run 2 (108.5 mg, 0.262 mmol, 57% yield); run 3 (61.1 mg, 0.147 mmol, 0.274 mmol scale, 54% yield). **Average yield:** 58%. 1H NMR (500 MHz, CDCl3) δ 7.74 (m, 2H), 7.48 (m, 1H), 7.41 (m, 2H), 7.27 (m, 3H), 7.11 (m, 2H), 7.07 (t, J = 7.8 Hz, 1H), 6.88 (bd, J = 7.8 Hz, 1H), 6.76 (m, 1H), 6.57 (m, 1H), 6.42 (d, J = 15.9 Hz, 1H), 5.90 (dt, J = 15.7, 7.2 Hz, 1H), 5.18 (dd, J = 9.2, 5.5 Hz, 1H),
3.85 (s, 3H), 3.10 (m, 1H), 3.01 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 168.7, 164.6, 151.5, 139.7, 136.6, 136.2, 135.5, 130.9, 129.6, 129.4, 128.8, 128.8, 128.3, 128.1, 121.7, 121.1, 120.8, 119.2, 87.6, 53.8, 33.8; IR (film, cm$^{-1}$): 3060, 3030, 2956, 1758, 1563, 1447, 1267, 910, 735, 698; HRMS (ESI) $m/z$ calculated for C$_{25}$H$_{23}$N$_2$O$_4$ [M+H]$^+$: 415.1658, found 415.1668.

(E)-methyl 2-nitro-5-o-tolypent-4-enoate [32]: 2-allyltoluene (69.5 mg, 95% pure, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 4.7:1 and the E/Z isomer ratio was >20:1. Flash chromatography (15% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (73.5 mg, 0.295 mmol, 59% yield); run 2 (64.5 mg, 0.258 mmol, 0.400 mmol scale, 65% yield); run 3 (63.5 mg, 0.255 mmol, 0.400 mmol scale, 64% yield). **Average yield:** 62%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.35 (m, 1H), 7.16 (m, 3H), 6.77 (d, $J = 15.6$ Hz, 1H), 5.95 (dt, $J = 15.5$, 7.3 Hz, 1H), 5.25 (dd, $J = 9.0$, 5.6 Hz, 1H), 3.86 (s, 3H), 3.18 (m, 1H), 3.09 (m, 1H), 2.31 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.6, 135.6, 135.6, 133.7, 130.4, 128.0, 126.3, 125.9, 122.6, 87.7, 53.8, 34.1, 19.8; IR (film, cm$^{-1}$): 3020, 2957, 2859, 1962, 1919, 1756, 1568, 1439, 1264, 1217, 969, 911, 751; HRMS (ESI) $m/z$ calculated for C$_{13}$H$_{15}$NO$_4$Na [M+Na]$^+$: 272.0899, found 272.0898.

(E)-methyl 2-nitro-5-(2-(trifluoromethyl)phenyl)pent-4-enoate [33]: 1-allyl-2-(trifluoromethyl)benzene (93.1 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was >20:1 and the E/Z isomer ratio was >20:1. Flash chromatography (15% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (91.1 mg, 0.300 mmol,
60% yield); run 2 (88.3 mg, 0.291 mmol, 58% yield). **Average yield: 59%.** $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.62 (bd, $J = 8.1$ Hz, 1H), 7.51 (m, 2H), 7.36 (m, 1H), 6.94 (d, $J = 15.6$ Hz, 1H), 6.07 (dt, $J = 15.2$, 7.5 Hz, 1H), 5.26 (dd, $J = 8.8$, 5.9 Hz, 1H), 3.86 (s, 3H), 3.20 (m, 1H), 3.12 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.5, 135.5, 132.1, 131.7, 127.9, 127.8, 127.5 (q, $J_{CF} = 29.9$ Hz), 125.9 (q, $J_{CF} = 5.8$ Hz), 125.7, 125.3 (q, $J_{CF} = 273.7$ Hz), 87.2, 53.8, 33.8; $^{19}$F NMR (470 MHz, CDCl$_3$) -59.8; IR (film, cm$^{-1}$): 2961, 2930, 2852, 1755, 1568, 1439, 1318, 1165, 1124, 1036, 970, 767; HRMS (ESI) m/z calculated for C$_{13}$H$_{12}$NO$_4$F$_3$Na [M+Na]$^+$: 326.0616, found 326.0607.

![Chemical structure](image)

(E)-methyl 5-(2-(tert-butyldimethylsilyloxy)phenyl)-2-nitropent-4-enoate [34]: (2-allylphenoxy)(tert-butyl)dimethylsilane (124.2 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 2.7:1 and the E/Z isomer ratio was >20:1. Flash chromatography (10% CH$_2$Cl$_2$/toluene) followed by flash chromatography (15% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (93.5 mg, 0.256 mmol, 51% yield); run 2 (111.7 mg, 0.306 mmol, 61% yield); run 3 (67.4 mg, 0.184 mmol, 0.300 mmol scale, 61% yield). **Average yield: 58%.** $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.37 (dd, $J = 7.8$, 1.7 Hz, 1H), 7.13 (m, 1H), 6.89 (m, 2H), 6.78 (dd, $J = 8.2$, 1.1 Hz, 1H), 6.01 (dt, $J = 15.9$, 7.2 Hz, 1H), 5.22 (dd, $J = 9.3$, 5.4 Hz, 1H), 3.85 (s, 3H), 3.16 (m, 1H), 3.06 (m, 1H), 1.02 (s, 9H), 0.21 (s, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.7, 153.0, 130.9, 129.0, 127.8, 126.6, 121.5, 120.9, 119.7, 87.7, 53.8, 34.4, 25.9, 18.5, -4.1, -4.1; IR (film, cm$^{-1}$): 3035, 2957, 2931, 2859, 1756, 1566, 1485, 1261, 914, 838, 783, 734; HRMS (ESI) m/z calculated for C$_{18}$H$_{27}$NO$_5$SiNa [M+Na]$^+$: 388.1556, found 388.1556.

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(E)-methyl 2-nitro-5-(2-(trifluoromethylsulfonyloxy)phenyl)pent-4-enoate [35]: 2-allylphenyl trifluoromethanesulfonate (133.1 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 15:1 and the E/Z isomer ratio was >20:1. Flash chromatography (20% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (98.9 mg, 0.258 mmol, 52% yield); run 2 (70.7 mg, 0.184 mmol, 0.300 mmol scale, 61% yield); run 3 (68.3 mg, 0.178 mmol, 0.300 mmol scale, 59% yield). **Average yield: 57%**. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.54 (m, 1H), 7.34 (m, 2H), 7.26 (m, 1H), 6.76 (d, $J = 15.9$ Hz, 1H), 6.21 (dt, $J = 15.8$, 7.2 Hz, 1H), 5.26 (dd, $J = 8.9$, 5.5 Hz, 1H), 3.87 (s, 3H), 3.21 (m, 1H), 3.14 (m, 1H); C NMR (125 MHz, CDCl$_3$) 164.4, 146.8, 146.6, 130.0, 129.7, 128.7, 127.9, 127.6, 126.5, 121.9, 118.7 (q, $J_{CF} = 320.1$ Hz), 87.1, 53.9, 33.9; $^{19}$F NMR (470 MHz, CDCl$_3$) -73.8; IR (film, cm$^{-1}$): 3061, 2963, 2930, 2857, 1761, 1564, 1485, 1419, 1140, 1075, 970, 894, 737; HRMS (ESI) $m/z$ calculated for C$_{13}$H$_{12}$NO$_7$SF$_3$Na [M+Na]$^+$: 406.0184, found 406.0178.

(E)-methyl 5-(naphthalen-2-yl)-2-nitropent-4-enoate [36]: 2-allylnaphthalene (84.1 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 4.2:1 and the E/Z isomer ratio was >20:1. Flash chromatography (20% EtOAc/hexanes) yielded pure linear product as a light yellow solid. Run 1 (91.0 mg, 0.319 mmol, 64% yield); run 2 (76.0 mg, 0.266 mmol, 0.400 mmol scale, 67% yield). **Average yield:** 65%. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.79 (m, 3H), 7.70 (bs, 1H), 7.53 (dd, $J = 8.6$, 1.7 Hz, 1H), 7.46 (m, 2H), 6.72 (d, $J = 15.9$ Hz, 1H), 6.21 (dt, $J = 15.7$, 7.3 Hz, 1H), 5.28 (dd, $J = 9.2$, 5.6 Hz,
1H), 3.87 (s, 3H), 3.22 (m, 1H), 3.13 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.6, 135.6, 133.7, 133.6, 133.2, 128.4, 128.1, 127.8, 126.7, 126.5, 126.2, 123.4, 121.5, 87.6, 53.8, 34.0; IR (film, cm$^{-1}$): 3057, 2960, 2925, 2852, 1756, 1564, 1438, 1267, 1215, 811, 749; HRMS (ESI) m/z calculated for C$_{16}$H$_{15}$NO$_4$Na [M+Na]$^+$: 308.0899, found 308.0896.

(E)-methyl 5-(benzo[d][1,3]dioxol-5-yl)-2-nitropent-4-enoate [37]: Safrole (81.1 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 3.0:1 and the E/Z isomer ratio was >20:1. Flash chromatography (20% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (80.2 mg, 0.287 mmol, 57% yield); run 2 (77.1 mg, 0.276 mmol, 55% yield). **Average yield: 56%**. $^1$H NMR (500 MHz, CDCl$_3$) δ 6.86 (d, $J = 1.5$ Hz, 1H), 6.75 (m, 2H), 6.46 (d, $J = 15.9$ Hz, 1H), 5.95 (s, 2H), 5.90 (dt, $J = 15.7$, 7.3 Hz, 1H), 5.21 (dd, $J = 9.2$, 5.4 Hz, 1H), 3.85 (s, 3H), 3.12 (m, 1H), 3.03 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.6, 148.2, 147.7, 135.1, 130.8, 121.4, 119.2, 108.4, 105.7, 101.3, 87.7, 53.8, 33.9; IR (film, cm$^{-1}$): 2959, 2901, 2782, 1756, 1671, 1607, 1557, 1504, 1447, 1040, 927, 734; HRMS (ESI) m/z calculated for C$_{13}$H$_{14}$NO$_6$ [M+H]$^+$: 280.0821, found 280.0822.

(E)-methyl 2-nitro-5-(1-oxo-2,3-dihydro-1H-inden-5-yl)pent-4-enoate [38]: 5-allylindanone (110.5 mg, 77.9% pure, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 12:1 and the E/Z isomer ratio was >20:1. Flash chromatography (0.8% MeOH/CH$_2$Cl$_2$), followed by flash chromatography
(30→45% EtOAc/hexanes gradient) yielded linear product contaminated by ca. 6% methyl 6-(1-oxo-2,3-dihydro-1H-inden-5-yl)-5,6-dihydro-4H-1,2-oxazine-3-carboxylate as a light yellow oil. A pure spectroscopic sample was obtained by column chromatography (20% EtOAc/hexanes). Run 1 (82.6 mg, 0.286 mmol, 57% yield); run 2 (55.0 mg, 0.190 mmol, 0.300 mmol scale, 63% yield); run 3 (24.4 mg, 0.0843 mmol, 0.127 mmol scale, 66%). **Average yield: 62%.**

**1H NMR** (500 MHz, CDCl₃) δ 7.69 (d, J = 8.1 Hz, 1H), 7.41 (s, 1H), 7.34 (d, J = 7.8 Hz, 1H), 6.62 (d, J = 15.9 Hz, 1H), 6.26 (dt, J = 15.8, 7.3 Hz, 1H), 5.26 (dd, J = 9.0, 5.4 Hz, 1H), 3.87 (s, 3H), 3.20 (m, 1H), 3.11 (m, 3H), 2.70 (m, 2H); **13C NMR** (125 MHz, CDCl₃) 206.5, 164.4, 155.9, 142.5, 136.8, 134.9, 125.9, 124.7, 124.5, 124.1, 87.3, 53.9, 36.6, 33.9, 25.8; IR (film, cm⁻¹): 2959, 2928, 2851, 1758, 1704, 1608, 1571, 1439, 1277, 1032, 973; HRMS (ESI) m/z calculated for C₁₅H₁₆NO₅ [M+H]^+: 290.1028, found 290.1016.

**Scheme 1: (E)-methyl 2-nitro-5-(1-oxo-1,3-dihydroisobenzofuran-5-yl)pent-4-enoate [39]:** 5-allylphthalide (113.1 mg, 77.0% pure, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. [**NOTE:** The substrate contained 23% 5-(prop-1-enyl)phthalide, which was inert under standard alkylation conditions. In run 1 this material was re-isolated following the reaction (25.8 mg, 99%).] By **1H NMR** analysis of the crude product, the linear:branched ratio was 15:1 and the E/Z isomer ratio was >20:1. Flash chromatography (1% MeOH/CH₂Cl₂), followed by flash chromatography (40% EtOAc/hexanes) yielded linear product contaminated by ca. 8% methyl 6-(1-oxo-1,3-dihydroisobenzofuran-5-yl)-5,6-dihydro-4H-1,2-oxazine-3-carboxylate as a light yellow oil. A pure spectroscopic sample was obtained by column chromatography (25%
EtOAc/hexanes). Run 1 (94.5 mg, 0.324 mmol, 65% yield); run 2 (104.4 mg, 0.358 mmol, 72% yield); run 3 (38.7 mg, 0.133 mmol, 0.180 mmol scale, 74% yield). **Average yield: 70%**. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.86 (d, \(J = 8.1\) Hz, 1H), 7.49 (d, \(J = 7.8\) Hz, 1H), 7.42 (s, 1H), 6.66 (d, \(J = 15.9\) Hz, 1H), 6.29 (dt, \(J = 15.7, 7.3\) Hz, 1H), 5.30 (s, 2H), 5.27 (dd, \(J = 9.3, 5.4\) Hz, 1H), 3.87 (s, 3H), 3.21 (m, 1H), 3.12 (m, 1H); \(^13\)C NMR (125 MHz, CDCl\(_3\)) 170.8, 164.3, 147.4, 142.2, 134.4, 127.6, 126.2, 125.5, 125.3, 119.8, 87.2, 69.6, 54.0, 33.8; IR (film, cm\(^{-1}\)): 2961, 2921, 2852, 1755, 1746, 1618, 1562, 1438, 1211, 1047, 1005; HRMS (ESI) \(m/z\) calculated for \(C_{14}H_{14}NO_6\) [M+H]+: 292.0821, found 292.0816.

\[(E)-\text{methyl 3-methoxy-5-(5-methoxy-4-nitro-5-oxopent-1-enyl)-2-(trifluoromethylsulfonyloxy)benzoate [40]}\]: Methyl 5-allyl-3-methoxy-2-(trifluoromethylsulfonyloxy)benzoate (177.2 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By \(^1\)H NMR analysis of the crude product, the linear:branched ratio was 7.2:1 and the E/Z isomer ratio was >20:1. Flash chromatography (32% EtOAc/hexanes) yielded linear product contaminated by ca. 8% methyl 6-(3-methoxy-5-(methoxycarbonyl)-4-(trifluoromethylsulfonyloxy)phenyl)-5,6-dihydro-4\(H\)-1,2-oxazine-3-carboxylate as a light yellow oil. A pure spectroscopic sample was obtained by column chromatography (20% EtOAc/hexanes). Run 1 (146.3 mg, 0.310 mmol, 62% yield); run 2 (149.5 mg, 0.317 mmol, 63% yield). **Average yield: 63%**. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.53 (d, \(J = 2.2\) Hz, 1H), 7.10 (d, \(J = 2.0\) Hz, 1H), 6.54 (d, \(J = 15.6\) Hz, 1H), 6.19 (dt, \(J = 15.8, 7.3\) Hz, 1H), 5.25 (dd, \(J = 9.3, 5.4\) Hz, 1H), 3.95 (s, 3H), 3.93 (s, 3H), 3.87 (s, 3H), 3.19 (m, 1H), 3.10 (m, 1H); \(^13\)C NMR (125 MHz, CDCl\(_3\)) 164.4, 164.3, 152.0, 137.0, 136.9, 133.4, 125.8, 124.7, 121.2, 118.8 (q, \(J_{CF} = 320.8\) Hz), 114.2, 87.2, 56.6, 54.0, 52.9, 33.7; \(^19\)F NMR (470
MHz, CDCl$_3$) -73.8; IR (film, cm$^{-1}$): 3017, 2958, 2851, 2260, 1758, 1732, 1564, 1425, 1219, 1136, 1067, 911, 878, 735; HRMS (ESI) $m/z$ calculated for C$_{16}$H$_{17}$NO$_{10}$SF$_3$ [M+H]$^+$: 472.0525, found 472.0533.

(E)-methyl 5-(3-methoxy-4-(trifluoromethylsulfonyloxy)phenyl)-2-nitropent-4-enoate [41]:
eugenol trifluoromethanesulfonate (88.9 mg, 0.3 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 4.8:1 and the E/Z isomer ratio was >20:1. Flash chromatography (30% EtOAc/hexanes), followed by flash chromatography (10% CH$_2$Cl$_2$/toluene), followed by flash chromatography (15→40% EtOAc/hexanes gradient) yielded pure linear product as a light yellow oil. Run 1 (78.3 mg, 0.189 mmol, 63% yield); run 2 (81.3 mg, 0.197 mmol, 66% yield). **Average yield: 64%**. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.15 (d, $J = 8.4$ Hz, 1H), 6.94 (m, 2H), 6.53 (d, $J = 15.9$ Hz, 1H), 6.11 (dt, $J = 15.7$, 7.3 Hz, 1H), 5.26 (dd, $J = 9.2$, 5.1 Hz, 1H), 3.92 (s, 3H), 3.86 (s, 3H), 3.17 (m, 1H), 3.08 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.4, 151.6, 138.4, 137.7, 134.2, 123.5, 122.7, 119.1, 118.8 (q, $J_{CF} = 306.6$ Hz), 110.9, 87.3, 56.3, 53.9, 33.7; $^{19}$F NMR (470 MHz, CDCl$_3$) –74.1; IR (film, cm$^{-1}$): 3017, 2960, 2850, 1759, 1602, 1567, 1423, 1212, 1139, 1108, 884, 740; HRMS (ESI) $m/z$ calculated for C$_{14}$H$_{14}$NO$_{8}$SF$_3$Na [M+Na]$^+$: 436.0290, found 436.0284.
methylphenyl)-2H-benzo[d][1,2,3]triazole (151.1 mg, 0.3 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 5.5:1 and the E/Z isomer ratio was $>20:1$. Flash chromatography (15% EtOAc/hexanes) yielded pure linear product as a light yellow solid. Run 1 (129.3 mg, 0.208 mmol, 69% yield); run 2 (123.1 mg, 0.198 mmol, 66% yield). **Average yield: 68%**. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.60 (m, 2H), 7.46 (m, 4H), 7.33 (m, 5H), 7.20 (m, 5H), 6.80 (d, $J = 15.9$ Hz, 1H), 5.70 (dt, $J = 15.8$, 7.1 Hz, 1H), 4.78 (dd, $J = 9.0$, 5.6 Hz, 1H), 3.83 (s, 3H), 2.72 (m, 1H), 2.60 (m, 1H), 2.31 (s, 3H), 0.72 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.5, 144.9, 144.7, 135.1, 132.4, 132.2, 132.1, 131.5, 130.1, 129.8, 128.8, 127.7, 127.5, 126.7, 122.9, 118.3, 87.2, 53.8, 33.6, 26.1, 20.5, 20.0; IR (film, cm$^{-1}$): 3073, 2957, 2933, 2858, 1962, 1906, 1758, 1564, 1478, 1429, 1272, 1114, 911, 736; HRMS (ESI) $m/z$ calculated for C$_{35}$H$_{37}$N$_4$O$_5$Si [M+H]$^+$: 621.2533, found 621.2521.

**Methyl 3-(1H-indol-3-yl)-2-nitropent-4-enoate [43]**: 3-allylindole (78.6 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 1:4.7. Flash chromatography (25% EtOAc/hexanes), followed by repeated extractions as necessary to remove methyl nitroacetate (sat. aq. NaHCO$_3$), yielded pure branched product as a dark yellow oil as a 1.2:1 mixture of diastereomers. Spectroscopic samples of each diastereomer were obtained by flash chromatography (20% EtOAc/hexanes). Run 1 (59.2 mg, 0.216 mmol, 43% yield); run 2 (54.7 mg, 0.199 mmol, 40% yield). **Average yield: 42%**. *Nonpolar diastereomer*: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.12 (bs, 1H), 7.63 (d, $J = 7.9$ Hz, 1H), 7.37 (d, $J = 8.1$ Hz, 1H), 7.22 (m, 1H), 7.15 (m, 2H), 6.13 (dd, $J = 17.1$, 10.1, 8.1 Hz, 1H), 5.62 (d, $J = 10.1$ Hz, 1H), 5.29 (d, $J =$ 
16.9 Hz, 1H), 5.22 (d, J = 10.1 Hz, 1H), 4.73 (ap t, J = 9.1 Hz, 1H), 3.82 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) 164.0, 136.4, 133.8, 125.9, 122.8, 122.6, 120.2, 119.1, 119.0, 111.7 (2C), 90.8, 53.6, 43.4; IR (film, cm$^{-1}$): 3420, 3058, 2956, 2926, 2855, 1756, 1567, 1458, 1365, 1266, 1173, 933, 741; HRMS (ESI) m/z calculated for C$_{14}$H$_{15}$N$_2$O$_4$ [M+H]$^+$: 275.1032, found 275.1021.

**Polar diastereomer**: $^1$H NMR (400 MHz, CDCl$_3$) δ 8.14 (bs, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.38 (d, J = 7.8 Hz, 1H), 7.23 (m, 1H), 7.17 (m, 1H), 7.12 (d, J = 2.4 Hz, 1H), 6.20 (ddd, J = 17.0, 10.2, 8.1 Hz, 1H), 5.59 (d, J = 9.5 Hz, 1H), 5.30 (d, J = 17.1 Hz, 1H), 5.23 (d, J = 10.0 Hz, 1H), 4.71 (ap t, J = 8.9 Hz, 1H), 3.56 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) 163.8, 136.3, 134.3, 125.9, 122.9, 122.8, 120.2, 118.9, 118.7, 111.6, 111.1, 91.2, 53.5, 42.7; IR (film, cm$^{-1}$): 3419, 3056, 2930, 2851, 1751, 1557, 1458, 1368, 1173, 744; HRMS (ESI) m/z calculated for C$_{14}$H$_{15}$N$_2$O$_4$ [M+H]$^+$: 275.1032, found 275.1028.

*By correlating the $^1$H NMR chemical shift of the methyl ester to previously reported data, it can be suggested that the configuration of the nonpolar diastereomer is anti (R,R) + (S,S) and the polar diastereomer is syn (R,S) + (S,R). See: a) Sui, Y.; Liu, L.; Zhao, J.-L.; Wang, D.; Chen, Y.-J. *Tetrahedron*, 2007, 63, 5173. b) Behforouz, M.; Zarrinmayeh, H.; Ogle, M. E.; Riehle, T. J.; Bell, F. W. *J. Heterocyclic Chem.* 1988, 25, 1627.

**Methyl 3-(4-methoxyphenyl)-2-nitropent-4-enoate**: 4-allylanisole (74.1 mg, 0.5 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 1.7:1. Flash chromatography (20% EtOAc/hexanes) yielded pure branched product as a yellow oil as a 1.2:1 mixture of diastereomers. Run 1 (45.4 mg, 0.171 mmol, 34% yield). $^1$H NMR (500 MHz, CDCl$_3$) Major diastereomer: δ 7.16 (m, 2H), 6.86 (m, 2H), 6.04 (ddd, J = 17.0,
Methyl 3-(3-(2H-benzo[d][1,2,3]triazol-2-yl)-2-(tert-butyldiphenylsilyloxy)-5-methylphenyl)-2-nitropent-4-enoate: 2-(3-allyl-2-(tert-butyldiphenylsilyloxy)-5-methylphenyl)-2H-benzo[d][1,2,3]triazole (151.1 mg, 0.3 mmol, 1.0 equiv) was reacted for 24h following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 5.5:1 and the E/Z isomer ratio was >20:1. Flash chromatography (15% EtOAc/hexanes) yielded pure branched product as a light yellow oil as a 1.4:1 mixture of diastereomers. $^1$H NMR (500 MHz, CDCl$_3$) Major diastereomer: $\delta$ 7.53 (m, 2H), 7.38-7.03 (m, 14H), 6.07 (m, 1H), 5.51 (d, $J = 6.8$ Hz, 1H), 5.34 (m, 1H), 5.30 (m, 1H), 5.16 (m, 1H), 3.76 (s, 3H), 2.32 (s, 3H), 0.94 (s, 9H); Diagnostic peaks for minor diastereomer: $\delta$ 7.47 (m, 2H), 5.53 (d, $J = 7.6$ Hz, 1H), 5.49 (m, 1H), 3.84 (s, 3H);$^{13}$C NMR (125 MHz, CDCl$_3$) Mixture of diastereomers: 163.6, 144.7, 144.6, 135.3, 134.8, 134.4, 134.3, 134.1, 133.7, 131.8, 131.7, 131.5, 130.7, 129.6, 129.5, 129.4, 129.3, 127.9, 127.3, 127.2, 127.1, 126.5, 126.3, 120.1, 119.4, 118.2, 118.2, 91.3, 90.3, 53.8, 42.5, 42.4, 26.5, 26.4, 20.6, 20.3; IR (film, cm$^{-1}$): 3073, 2963,
2930, 2857, 1889, 1758, 1486, 1116, 913, 702; HRMS (ESI) \( m/z \) calculated for \( C_{35}H_{37}N_4O_5Si \) [M+H]+: 621.2533, found 621.2530.

**Nucleophile scope of the allylic C-H alkylation reaction**

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<th>Isolated yield</th>
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</table>

\( ^a \) Oligin (1 equiv), 13 (3 equiv), DMBQ (1.5 equiv), AcOH (0.5 equiv), 1 (10 mol%), dioxane DMF (4:1, 0.33 M). Average of 2 runs at 0.5 mmol. Products isolated as one regio- and olefin isomer. \( ^b \) Determined by \( ^1H \) NMR analysis of the crude. \( ^c \) Catalyst 49 = 1,2-bis(benzylsulfonyl)ethanePd(OAc)\(_2\) (10 mol%).

\((E)-2\text{-nitro-1,5-diphenylpent-4-en-1-one}\) [47]: Allylbenzene (355 mg, 3.0 mmol, 1.0 equiv) and benzoylnitromethane (1.49 g, 9.0 mmol, 3.0 equiv) were reacted for 24h following the general procedure. By \( ^1H \) NMR analysis of the crude product, the linear:branched ratio was 7:1 and the E/Z isomer ratio was >20:1. Flash chromatography (15% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (526 mg, 1.87 mmol, 62% yield). \( ^1H \) NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.99 (m, 2H), 7.67 (m, 1H), 7.54 (m, 2H), 7.30 (m, 4H), 7.24 (m, 1H), 6.56 (d, \( J = 15.9 \) Hz, 1H), 6.17 (dd, \( J = 9.0, 5.1 \) Hz,
1H), 6.13 (dt, J = 15.7, 7.2 Hz, 1H), 3.26 (dddd, J = 15.1, 8.9, 7.6, 1.3 Hz, 1H), 3.08 (dddd, J = 15.0, 6.8, 5.2, 1.5 Hz, 1H); 13C NMR (125 MHz, CDCl3) 188.4, 136.4, 135.4, 135.0, 134.0, 129.4, 129.0, 128.8, 128.1, 126.5, 121.7, 89.3, 34.2; IR (film, cm⁻¹): 3064, 3027, 2922, 1695, 1559, 1449, 967; HRMS (ESI) m/z calculated for C₁₇H₁₅NO₃Na [M+Na]⁺: 304.0950, found 304.0941.

(E)-(4-nitro-4-(phenylsulfonyl)but-1-enyl)benzene [48]:

![Chemical Structure](image)

Allylbenzene (59.1 mg, 0.5 mmol, 1.0 equiv), (phenylsulfonyl)nitromethane (301.8 mg, 1.5 mmol, 3.0 equiv) and 1,2-bis(benzylysulfinyl)ethane/Pd(OAc)₂ 49 (26.5 mg, 0.05 mmol, 0.1 equiv) were reacted for 24h following the general procedure. By 1H NMR analysis of the crude product, the linear:branched ratio was 13:1 and the E/Z isomer ratio was >20:1. Flash chromatography (20% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (101.0 mg, 0.318 mmol, 64% yield). 1H NMR (500 MHz, CDCl₃) δ 7.93 (m, 2H), 7.80 (m, 1H), 7.65 (m, 2H), 7.29 (m, 4H), 7.24 (m, 1H), 6.54 (d, J = 15.6 Hz, 1H), 5.97 (ddd, J = 15.7, 7.8, 6.7 Hz, 1H), 5.59 (dd, J = 11.2, 3.4 Hz, 1H), 3.22 (ddddd, J = 14.9, 6.4, 3.5, 1.4 Hz, 1H), 3.12 (ddddd, J = 15.0, 11.2, 7.9, 1.1 Hz, 1H); 13C NMR (125 MHz, CDCl₃) 136.6, 135.9, 135.7, 134.0, 130.1, 129.7, 128.7, 128.4, 126.5, 119.0, 101.4, 31.5; IR (film, cm⁻¹): 3063, 3031, 2981, 2929, 2258, 1562, 1449, 1342, 1158, 909, 732, 689; HRMS (ESI) m/z calculated for C₁₆H₁₅NO₄SNa [M+Na]⁺: 340.0620, found 340.0629.
(E)-methyl 2-amino-5-phenylpent-4-enoate [50]: A 2 dram borosilicate vial was charged with (E)-methyl 2-nitro-5-phenylpent-4-enoate (47.0 mg, 0.2 mmol, 1.0 equiv) and a stir bar. To the vial was added MeOH (2.0 mL, 0.10M) and concentrated HCl (392 μL, 4.0 mmol, 20 equiv). The vial was placed in a 20°C water bath and zinc dust (524 mg, 8.0 mmol, 40 equiv) was added slowly with vigorous stirring. The reaction vial was capped and stirred for 20 min at room temperature. The reaction was diluted with saturated aqueous NaHCO₃ (40 mL—CAUTION: gas evolves) and extracted with ethyl acetate (3 x 30 mL). The combined organics were dried over MgSO₄. The mixture was filtered and concentrated in vacuo. Purification by flash chromatography (SiO₂, 1% MeOH, 0.5% NH₄OH/CH₂Cl₂) provided the pure product. Run 1 (40.6 mg, 0.198 mmol, 99%); run 2 (40.9 mg, 0.199 mmol, 99%). **Average yield: 99%.** ¹H NMR (500 MHz, CDCl₃) δ 7.36 (m, 2H), 7.30 (m, 2H), 7.22 (m, 1H), 6.50 (d, J = 15.9 Hz, 1H), 6.14 (dt, J = 15.7, 7.4 Hz, 1H), 3.75 (s, 3H), 3.63 (dd, J = 7.2, 5.2 Hz, 1H), 2.66 (m, 1H), 2.55 (m, 1H) 1.57 (bs, 2H); ¹³C NMR (125 MHz, CDCl₃) 175.8, 137.1, 133.8, 128.6, 127.5, 126.3, 124.9, 54.4, 52.2, 38.6; IR (film, cm⁻¹): 3381, 3059, 3027, 2951, 2848, 1745, 1438, 1201, 968, 744, 695; HRMS (ESI) m/z calculated for C₁₂H₁₆NO₂ [M+H]⁺: 206.1181, found 206.1176.
(+)-(S,E)-methyl 2-nitro-2-((S)-2-nitro-1-phenylethyl)-5-phenylpent-4-enoate [52]: A ½ dram borosilicate vial was charged with (E)-methyl 2-nitro-5-phenylpent-4-enoate (37.9 mg, 0.161 mmol, 1.0 equiv), catalyst 51 (6.4 mg, 0.0161 mmol, 0.10 equiv), and a stir bar. To the vial was added THF (161μL, 1.0M). The flask was stirred for 5 min at -20°C, at which point trans-β-nitrostyrene was added (48.1 mg, 0.322 mmol, 2.0 equiv). The reaction vial was capped and stirred for 72 h at -20°C. By 1H NMR analysis of the crude product, the diastereomeric ratio was 12:1. The reaction solution was transferred with Et₂O to a flask and evaporated in vacuo. Flash chromatography (9% EtOAc/hexanes) yielded a white solid. By HPLC analysis of the purified product (vide infra), the enantiomeric excess was 95% (Chiralcel OD-H, 90:10 hexanes:2-propanol, t_R(major) = 10.59 min., t_R(minor) = 16.45 min.). Run 1 (54.6 mg, 0.142 mmol, 88% yield); run 2 (53.8 mg, 0.140 mmol, 87% yield). **Average yield: 88%**. 1H NMR (500 MHz, CDCl₃) δ 7.37 (m, 3H), 7.33 (m, 4H), 7.28 (m, 1H), 7.14 (m, 2H), 6.44 (d, J = 15.6 Hz, 1H), 5.98 (ddd, J = 15.5, 8.7, 6.5 Hz, 1H), 5.17 (dd, J = 13.9, 2.7 Hz, 1H), 5.02 (dd, J = 13.9, 10.7 Hz, 1H), 4.48 (dd, J = 10.7, 2.9 Hz, 1H), 3.84 (s, 3H), 2.95 (ddd, J = 14.5, 6.2, 1.6 Hz, 1H), 2.67 (ddd, J = 14.6, 8.5, 1.0 Hz, 1H); 13C NMR (125 MHz, CDCl₃) 166.0, 136.7, 136.2, 132.3, 129.7, 129.6, 128.9, 128.9, 128.4, 126.6, 120.0, 97.1, 77.7, 54.1, 47.7, 38.9; IR (film, cm⁻¹): 3030, 2959, 2926, 1752, 1556, 1378, 1216, 970, 742, 703; HRMS (ESI) m/z calculated for C₂₀H₂₀N₂O₆Na [M+Na]⁺: 407.1219, found 407.1219; [α]D²⁴ = +114.3° (c = 1.0, CHCl₃).

(+)-(S,E)-methyl 5-(4-bromophenyl)-2-nitro-2-((S)-2-nitro-1-phenylethyl)pent-4-enoate: A ½ dram borosilicate vial was charged with (E)-methyl 5-(4-bromophenyl)-2-nitropent-4-enoate
(48.5 mg, 0.154 mmol, 1.0 equiv), catalyst 51 (6.2 mg, 0.0154 mmol, 0.10 equiv), and a stir bar. To the vial was added THF (154μL, 1.0M). The flask was stirred for 5 min at -20°C, at which point trans-β-nitrostyrene was added (46.1 mg, 0.309 mmol, 2.0 equiv). The reaction vial was capped and stirred for 72 h at -20°C. By 1H NMR analysis of the crude product, the diastereomeric ratio was 11:1. The reaction solution was transferred with Et2O to a flask and evaporated in vacuo. Flash chromatography (9% EtOAc/hexanes) yielded a white solid. By HPLC analysis of the purified product (vide infra), the enantiomeric excess was 81% (Chiralcel OD-H, 90:10 hexanes:2-propanol, t_R(major) = 12.35 min., t_R(minor) = 22.13 min.). Run 1 (51.4 mg, 0.111 mmol, 72% yield). 1H NMR (500 MHz, CDCl3) δ 7.45 (d, J = 8.6 Hz, 2H), 7.37 (m, 3H), 7.19 (d, J = 8.4 Hz, 2H), 7.12 (m, 2H), 6.37 (d, J = 15.9 Hz, 1H), 5.98 (ddd, J = 15.7, 8.6, 6.4 Hz, 1H), 5.15 (dd, J = 13.9, 2.8 Hz, 1H), 5.02 (dd, J = 13.9, 10.7 Hz, 1H), 4.46 (dd, J = 10.7, 2.8 Hz, 1H), 3.83 (s, 3H), 2.92 (ddd, J = 14.8, 6.2, 1.5 Hz, 1H), 2.65 (dd, J = 14.8, 8.6 Hz, 1H); 13C NMR (125 MHz, CDCl3) 166.0, 135.4, 135.1, 132.2, 132.0, 129.8, 129.6, 128.9, 128.0, 122.3, 121.0, 97.1, 77.6, 54.2, 47.9, 38.9; IR (film, cm⁻¹): 2958, 2925, 1753, 1556, 1488, 1378, 1216, 1073, 703; HRMS (ESI) m/z calculated for C₂₀H₁₉N₂O₆BrNa [M+Na]^+: 485.0324, found 485.0314; [α]D²⁴ = +95.6° (c = 1.0, CHCl₃).

Enantiomeric Excess

Enantiopurity of the product 52 was determined by HPLC analysis with a Daicel Chemical Industries, Ltd. Chiralcel OD-H 0.46 cm x 25 cm column. A flow rate of 1.0 mL/min at 25.0°C with 90:10 hexanes:2-propanol with detection at 254 nm gave the major enantiomer at 10.59 min and the
minor enantiomer at 16.45 min. Enantiopurity was determined to be 95%. Relative and absolute stereochemistry of the product was assigned by analogy to (+)-(S,E)-methyl 5-(4-bromophenyl)-2-nitro-2-((S)-2-nitro-1-phenylethyl)pent-4-enoate (vide infra).

Enantiopurity of the product was determined by HPLC analysis with a Daicel Chemical Industries, Ltd. Chiralcel OD-H 0.46 cm x 25 cm column. A flow rate of 1.0 mL/min at 25.0°C with 90:10 hexanes:2-propanol with detection at 260 nm gave the major enantiomer at 12.35 min and the minor enantiomer at 22.13 min. Enantiopurity was determined to be 81%. Relative and absolute stereochemistry of the product was determined by x-ray crystallographic analysis of a single crystal obtained by recrystallization from acetone. The x-ray data crystal was determined to contain the major enantiomer by direct HPLC analysis. The crystal was transferred from the mount to a glass insert (National Scientific, part no. C4010-S630) and dissolved in 15μL 2-propanol. HPLC analysis (vide supra) confirmed the crystal to be the major enantiomer.

Crystal data and structure refinement for ba67bas.

Identification code ba67bas
Empirical formula C20 H19 Br N2 O6
Formula weight 463.28
Temperature 193(2) K
Wavelength 0.71073 Å
Crystal system Orthorhombic
Space group P 21 21 21
Unit cell dimensions a = 6.0498(2) Å, a= 90°.
b = 18.4635(6) Å, b= 90°.
c = 18.5718(5) Å, g = 90°.
Volume 2074.48(11) Å³
Z 4
Density (calculated) 1.483 Mg/m³
Absorption coefficient 2.020 mm⁻¹
F(000) 944
Crystal size 0.50 x 0.06 x 0.06 mm³
Theta range for data collection 1.56 to 25.45°.
Index ranges -7<=h<=7, -22<=k<=22, -22<=l<=21
Reflections collected 25713
Independent reflections 3844 [R(int) = 0.0478]
Completeness to theta = 25.45° 99.8 %
Absorption correction Integration
Max. and min. transmission 0.8933 and 0.4228
Refinement method Full-matrix least-squares on F²
Data / restraints / parameters 3844 / 0 / 319
Goodness-of-fit on F² 1.018
Final R indices [I>2sigma(I)] R1 = 0.0313, wR2 = 0.0583
R indices (all data) R1 = 0.0488, wR2 = 0.0624
Absolute structure parameter -0.003(7)
Largest diff. peak and hole 0.319 and -0.508 e.Å⁻³

Racemic standards:

Major diastereomer was isolated pure following column chromatography (9% EtOAc/hexanes).

Starting Materials

General procedure for allylation of aryl halides:³⁹ An oven-dried 10 mL Schlenk flask under argon atmosphere was charged with Pd(dba)₂ (34.5 mg, 0.060 mmol, 0.03 equiv), PCy₃ (33.7 mg, 0.12 mmol, 0.06 equiv), CsF (668 mg, 4.40 mmol, 2.2 equiv), aryl halide (2.00 mmol, 1 equiv), and a stir bar. Allyltributyltin (644 μL, 2.10 mmol, 1.05 equiv) and dioxane (2 mL, 1.0M)
were added via syringe. The mixture was stirred and heated to 80-100°C. Conversion was monitored by GC. When complete consumption of aryl halide was observed (8-24 h), the reaction was cooled to room temperature. The reaction mixture was diluted with saturated aqueous NH₄Cl (40 mL) and extracted with diethyl ether (2 x 40 mL). The combined organics were dried over MgSO₄. The mixture was filtered and concentrated in vacuo. Purification by flash chromatography (SiO₂, Et₂O/pentane mixtures) provided the pure product.

NOTE: In some cases isomerization was observed, yielding small amounts of internal olefin product [characteristic peaks, ^1H NMR: 6.4 (m, 2H), 1.9 (d, 3H)]. This isomer was generally not separable from the desired allyl compound by column chromatography. However, the internal isomer was unreactive under standard allylic alkylation conditions and could be recovered quantitatively from the reaction mixture.

**Spectral data for known compounds:**

1-allyl-4-fluorobenzene⁴⁰  
N-(4-allylphenyl)-N,4-dimethylbenzenesulfonamide⁴¹  
1-allyl-4-(trifluoromethyl)benzene⁴²  
Methyl 4-allylbenzoate⁴³  
1-allyl-4-methylbenzene⁴⁴  
4-allylbenzonitrile⁴⁵  
1-(4-allylphenyl)ethanone⁴²  
1-allyl-4-bromobenzene⁴⁶  
1-allyl-3-methoxybenzene⁴²  
1-allyl-2-methylbenzene⁴⁷
1-allyl-2-(trifluoromethyl)benzene\textsuperscript{48}

(2-allylphenoxy)(\textit{tert}-butyl)dimethylsilane\textsuperscript{49}

2-allylphenyl trifluoromethanesulfonate\textsuperscript{50}

2-allylnaphthalene\textsuperscript{42}

3-allylindole\textsuperscript{51}

\begin{center}
\textbf{3-allyl-N-(diphenylmethylene)aniline:} \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 7.74 (m, 2H), 7.47 (m, 1H), 7.40 (m, 2H), 7.25 (m, 2H), 7.11 (m, 2H), 7.06 (t, \(J = 7.6\) Hz, 1H), 6.74 (d, \(J = 7.7\) Hz, 1H), 6.57 (m, 2H), 5.80 (ddt, \(J = 16.9,\ 10.2,\ 6.6\) Hz, 1H), 4.95 (dd, \(J = 10.1,\ 1.7\) Hz, 1H), 4.88 (dd, \(J = 17.0,\ 1.8\) Hz, 1H), 3.23 (d, \(J = 6.4\) Hz, 2H); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) 168.3, 151.4, 140.4, 139.8, 137.5, 136.4, 130.8, 129.6, 129.4, 128.6, 128.6, 128.0, 123.7, 121.5, 118.9, 115.7, 40.1; IR (film, cm\textsuperscript{-1}): 3081, 3061, 3039, 3023, 2978, 1621, 1595, 1578, 1447, 1317, 911, 734, 696; HRMS (ESI) \(m/z\) calculated for C\textsubscript{22}H\textsubscript{20}N \([M+H]^+\): 298.1596, found 298.1601.
\end{center}

\begin{center}
\textbf{Methyl 5-allyl-3-methoxy-2-(trifluoromethylsulfonyloxy)benzoate:} \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 7.39 (d, \(J = 2.0\) Hz, 1H), 7.01 (d, \(J = 2.0\) Hz, 1H), 5.93 (ddt, \(J = 16.8,\ 10.2,\ 6.8\) Hz, 1H), 5.15 (m, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 3.42 (d, \(J = 6.5\) Hz, 2H); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) 164.7, 151.7, 141.3, 136.0, 135.7, 125.3, 123.1, 118.8 (q, \(J_{CF} = 320.4\) Hz), 117.6, 117.1, 56.5, 52.8, 39.9; \textsuperscript{19}F NMR (470 MHz, CDCl\textsubscript{3}) –73.9; IR (film, cm\textsuperscript{-1}): 3088, 3015, 2957, 2850, 1731, 1595, 1425, 1339, 1209, 1068, 878, 787; HRMS (ESI) \(m/z\) calculated for C\textsubscript{13}H\textsubscript{14}O\textsubscript{6}F\textsubscript{3}S \([M+H]^+\): 355.0463, found 355.0455.
\end{center}
2-(3-allyl-2-(tert-butyldiphenylsilyloxy)-5-methylphenyl)-2H-benzo[d][1,2,3]triazole: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.47-7.41 (m, 6H), 7.32-7.23 (m, 5H), 7.16 (m, 4H), 7.03 (d, $J = 2.0$ Hz, 1H), 5.73 (ddt, $J = 16.9$, 10.1, 6.6 Hz, 1H), 5.05 (dd, $J = 10.0$, 1.7 Hz, 1H), 4.98 (dd, $J = 17.1$, 1.7 Hz, 1H), 3.34 (d, $J = 6.6$ Hz, 2H), 2.29 (s, 3H), 0.79 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) 144.8, 136.4, 135.0, 132.6, 132.4, 132.0, 131.8, 131.2, 129.6, 127.2, 126.4, 126.2, 118.3, 116.6, 35.2, 26.3, 20.5, 20.1; IR (film, cm$^{-1}$): 3076, 2933, 2859, 1485, 1274, 1115, 910, 718; HRMS (ESI) $m/z$ calculated for C$_{32}$H$_{34}$N$_3$OSi [M+H]$^+$: 504.2471, found 504.2478.

4-allyl-2-methoxyphenyl trifluoromethanesulfonate: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.13 (d, $J = 8.1$ Hz, 1H), 6.85 (d, $J = 1.9$ Hz, 1H), 6.79 (dd, $J = 8.2$, 2.0 Hz, 1H), 5.94 (m, 1H), 5.12 (m, 2H), 3.90 (s, 3H), 3.39 (d, $J = 6.6$ Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) 151.3, 141.9, 137.2, 136.4, 122.3, 120.9, 118.9 (q, $J_{CF} = 320.3$ Hz), 116.9, 113.5, 56.2, 40.1; $^{19}$F NMR (470 MHz, CDCl$_3$) –74.2; IR (film, cm$^{-1}$): 3084, 3018, 2982, 2944, 2920, 2849, 1640, 1607, 1504, 1422, 1211, 1142, 1108, 879, 619; HRMS (EI) $m/z$ calculated for C$_{11}$H$_{11}$F$_3$O$_4$S [M]$^+$: 296.0330, found 296.0331.

5-allyl-2,3-dihydro-1H-inden-1-one: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.69 (d, $J = 7.7$ Hz, 1H), 7.30 (bs, 1H), 7.21 (d, $J = 7.9$ Hz, 1H), 5.96 (m, 1H), 5.12 (m, 2H), 3.47 (d, $J = 6.6$ Hz, 2H), 3.11 (m, 2H), 2.69 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) 206.8, 155.9, 147.8, 136.4, 135.5, 128.3, 126.7, 123.8, 116.9, 40.6, 36.5, 25.8; IR (film, cm$^{-1}$): 3076, 3018, 2928, 2858, 1711, 1608, 1435, 1287, 1031, 917, 756, 733; HRMS (ESI) $m/z$ calculated for C$_{12}$H$_{13}$O [M+H]$^+$: 173.0966, found 173.0960.
5-allylisobenzofuran-1(3H)-one: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.80 (d, $J = 7.8$ Hz, 1H), 7.34 (d, $J = 7.8$ Hz, 1H), 7.30 (bs, 1H), 5.94 (ddt, $J = 16.9$, 10.2, 6.7 Hz, 1H), 5.26 (s, 2H), 5.11 (m, 2H), 3.50 (d, $J = 6.6$ Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) 171.1, 147.4, 147.3, 136.0, 129.9, 125.7, 122.1, 122.1, 117.3, 69.6, 40.4; IR (film, cm$^{-1}$): 3079, 3022, 2979, 2941, 2879, 2254, 1764, 1621, 1440, 1360, 1241, 1121, 1049, 1003, 920, 751; HRMS (ESI) $m/z$ calculated for C$_{11}$H$_{11}$O$_2$ [M+H]$^+$: 175.0759, found 175.0743.

1-allyl-4-vinylbenzene: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.35 (d, $J = 8.1$ Hz, 2H), 7.15 (d, $J = 8.1$ Hz, 2H), 6.70 (dd, $J = 17.6$, 10.7 Hz, 1H), 5.96 (ddt, $J = 16.9$, 10.2, 6.7 Hz, 1H), 5.71 (dd, $J = 17.6$, 1.0 Hz, 1H), 5.20 (dd, $J = 10.8$, 0.9 Hz, 1H), 5.08 (m, 2H), 3.38 (d, $J = 6.8$ Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) 139.9, 137.4, 136.8, 135.7, 128.9, 126.4, 116.0, 113.3, 40.1; IR (film, cm$^{-1}$): 3083, 3007, 2979, 2909, 2852, 1909, 1821, 1639, 1511, 1406, 990, 908, 822; HRMS (EI) $m/z$ calculated for C$_{11}$H$_{12}$ [M]$^+$: 144.0939, found 144.0941.

1.5 REFERENCES


CHAPTER 2

ALLYLIC C-H ALKYLATION OF UNACTIVATED \( \alpha \)-OLEFINS: SERIAL LIGAND CATALYSIS RESUMED

2.1 INTRODUCTION

The allylic alkylation reaction, the development of which was described in Chapter 1, was shown to have excellent functional group tolerance and good yields. However, it was observed in the course of exploring the substrate scope that the reaction was limited to allylarene substrates. Olefins with aliphatic substitution were found to react very slowly under these conditions, with very low conversion of substrate and only about 10% yield of the desired allylic alkylated product recovered after 72 hours of reaction time (Figure 15). This limitation in substrate scope was unexpected because in previous allylic esterification and amination reactions,\textsuperscript{15-18} virtually any \( \alpha \)-olefin substrate could be functionalized in synthetically useful yields.

The two classes of substrate, activated and unactivated olefins, were expected to react at different rates—the allylic C-H bond is cleaved in a heterolytic C-H activation step, and the pK\(_a\) in DMSO of the allylic C-H bonds of allylbenzene is 33,\textsuperscript{52} compared to a pK\(_a\) of 44 for unactivated allylic C-H bonds\textsuperscript{53}—but the difference in overall reactivity was surprising nonetheless. Remarkably, the same effect was observed independently by another team of researchers in their efforts to develop a similar allylic C-H alkylation reaction.\textsuperscript{14b} Shi and coworkers reported a reaction using an earlier version of our palladium(II)/sulfoxide catalyst, complex 49, bearing benzyl substituents in place of phenyl.\textsuperscript{15} The reaction used 1,3-diketone nucleophiles to effect allylic alkylation of \( \alpha \)-olefin substrates (Figure 15). Despite using different reaction conditions (1.4 equiv. nucleophile, 1.3 equiv. benzoquinone, 0.2M toluene,
60°C, 48h) and different nucleophiles, Shi reported that this reaction too was limited to activated allylarene substrates. The attempted alkylation of unactivated substrates resulted in the isolation of methyl ketones from Wacker oxidation rather than the desired allylic functionalization. Intrigued by these results, we wondered if this recurring observation of limited substrate scope indicated a more general problem for the catalytic reaction, and whether we could identify and solve it to discover an allylic C-H alkylation with a truly general substrate scope.\textsuperscript{54}

**Figure 15:** Substrate scope limitation in allylic C-H alkylation reactions

2.2 RESULTS AND DISCUSSION

We initially questioned whether one of the basic product forming steps of the catalytic cycle, either C-H activation or functionalization, was performing poorly in the allylic C-H alkylation. The relative stability and easy isolation of the π-allyl palladium intermediate makes it a convenient tool to probe the individual steps of the catalytic cycle. Stoichiometric model studies demonstrated that C-H cleavage promoted by catalyst 1 proceeded smoothly for both activated and unactivated substrates to form the π-allyl, which was trapped as the chloride dimer for the purposes of purification and characterization. Similarly, beginning from the π-allyl, the
DMSO mediated functionalization step was found to furnish similar yields of both aromatic and aliphatic products (Figure 16). Although these results did not provide insight to the challenges facing the catalytic reaction, they did demonstrate that the basic product forming steps were possible and therefore there was no fundamental reason why unactivated substrates could not undergo the alkylation reaction.

*Figure 16: Stoichiometric studies of unactivated and activated substrates*

Despite the promising foundation of the stoichiometric models, however, we found that our efforts to optimize the catalytic conditions provided only meager returns. After screening various nucleophiles, solvents, quinones and additives we were able to obtain no more than a 25% yield of the desired alkylated product (Figure 17). Analysis of the crude reaction mixture revealed that at the end of the reaction, substantial amounts of substrate, nucleophile and oxidant remained. In addition, palladium metal was observed to precipitate from the reaction mixture and form a mirror in the vial. A more detailed analysis of the time course of the reaction revealed that substrate conversion and product formation essentially ceased after 12 hours, an
unusually short lifespan for a class of reactions that typically continue for 24-72 hours. These results collectively implied that the catalytic cycle was being inhibited by an unidentified source, prematurely deactivating the catalyst and leading to decomposition. We hoped that if we could identify the source of inhibition we might devise a solution to solve the limited substrate scope.

*Figure 17:* Low reactivity under optimized catalytic conditions

Initially, it appeared possible that the reaction was subject to product inhibition. The rate of reaction slowed substantially after approximately the first catalytic turnover, and by the time the ratio of product to catalyst reached 2:1 the reaction had essentially ended. However, product inhibition was conclusively ruled out by catalytic kinetic studies (Figure 18). The reaction was run with known quantities of the product added at time = 0, and the initial rates were measured. The reaction was thus shown to be zero order in product, eliminating product inhibition from consideration.
In search of another hypothesis to explain the observed inhibition of catalysis, we returned to our understanding of the mechanism of the reaction. In the previously reported branched allylic esterification reaction, we had described a rather unusual catalytic cycle we called “serial ligand catalysis” (SLC). This name reflected the fact that the individual steps of the catalytic cycle were each promoted by different ligands which coordinate reversibly to the palladium catalyst. The C-H cleavage step was effected by the bis-sulfoxide ligand and the functionalization and re-oxidation steps were promoted by benzoquinone (Figure 11). Notably, each ligand was only effective for its particular step; neither ligand was capable of promoting the whole catalytic cycle. Unlike palladium(0) reactions in which a strong phosphine ligand may remain bound to the metal throughout the entire cycle, a SLC mechanism relies upon a rapid interchange of ligands at palladium in order to achieve catalytic turnover. Each ligand must coordinate to the metal, promote the desired step, and then dissociate in order to make way for the ligand which will promote the subsequent step.

We hypothesized that the allylic C-H alkylation of unactivated α-olefins could occur via a SLC mechanism (Figure 19). Specifically, the reaction could proceed as follows: 1) catalytic
palladium(II)/bis-sulfoxide-promoted C-H cleavage to furnish a \( \pi \)-allyl intermediate, 2) stoichiometric DMSO-promoted functionalization through ionization of the \( \pi \)-allyl intermediate, and 3) re-oxidation of Pd\(^0\) to Pd\(^{\text{II}}\) with a quinone. In the previously described C-H alkylation of allylarenes we found that the complex formed by Pd(OAc)\(_2\) and DMSO was sufficiently active to cleave the doubly activated allylic/benzylic C-H bond in the absence of bis-sulfoxide ligands, thus obviating the requirement for a SLC mechanism (Table 2, entry 10). However, unactivated allylic C-H bonds may be cleaved only via the much more active Pd/bis-sulfoxide complex.

The SLC mechanism is characterized by multiple kinetically labile ligands exchanging rapidly at palladium in a delicate balance. We wondered if an overly competitive ligand might disrupt the equilibrium required for efficient catalytic turnover. If one ligand bound the metal more strongly than the others, it could potentially disrupt the SLC mechanism by preventing subsequent steps in the cycle. Specifically, we wondered if DMSO, which was present in solvent quantities, was out-competing bis-sulfoxide, present in catalytic quantities, for binding to palladium acetate (Figure 19). This could slow the C-H cleavage step, inhibiting the allylic alkylation and eventually allowing the catalyst to decompose prior to complete conversion of

**Figure 19:** Mechanistic proposal for inhibition of catalysis
If it could be verified, competitive ligand binding would be an intriguing explanation for the observed inhibition, with potential ramifications beyond the immediate context of allylic alkylation. However, it would prove quite challenging to test. Because DMSO was posited to play both a detrimental role in the C-H cleavage step and a productive role in the functionalization step, we found techniques such as catalytic kinetics to be intractably complex. In order to probe this theory it would be preferable to develop a method which could disentangle the positive and negative effects of DMSO on the reaction. The most straightforward way to detect only the detrimental role for DMSO would be to directly observe the ligands coordinating to palladium and to examine how additional DMSO perturbed the equilibrium. This effort was unsuccessful because the binding of palladium(II) acetate/sulfoxide ligand could not be observed by any standard spectroscopic technique (see 2.4 Experimental Section). Infrared, UV-visible and NMR spectra all showed no shifts in peaks between the component spectra and the metal-ligand complex spectra. Lowering the temperature or changing the ratio of metal to ligand did not affect the results. To account for the possibility of competitive ligand binding at another point in the catalytic cycle, we also examined the interaction of the sulfoxides and the \( \pi \)-allyl intermediate, but once again no binding was observed. These results indicated that the interaction between the metal and the ligand was weak and transient, and that the species observed \textit{in situ} was likely not the active catalyst but rather a resting state.

In order to probe the hypothesis of competitive ligand binding, we concluded that a more indirect approach was needed. We proposed to use the previously reported branched allylic C-H esterification and linear allylic amination reactions as chemical reactivity probes.\textsuperscript{16,56} Both of these reactions depended upon the action of the palladium(II)/bis-sulfoxide catalyst to effect
allylic C-H cleavage. However, unlike the allylic alkylation there could be no productive role for DMSO in these reactions, so any inhibition resulting from the addition of DMSO would be readily evident. Thus, in the absence of any additives, both reactions produced the desired functionalized products in good yields (Table 5 entry 1; Table 6 entry 1). Upon the addition of only 1 equivalent of DMSO, a dramatic reduction in reactivity was observed, with diminished yields and low conversion of substrate (entry 2). These results supported the conclusion that DMSO was interfering with coordination of the bis-sulfoxide ligand to the metal and inhibiting C-H cleavage. Notably, in the allylic alkylation reaction reported by Shi and coworkers, the reaction conditions did not include DMSO. However, we suspected that a similar mechanism of inhibition could be at play with a ligand other than DMSO. Shi reported alkylation by 1,3-diketone nucleophiles, which are well known ligands for palladium(II). When 1 equivalent of benzoyleacetone 59 was added to either the allylic amination or esterification reaction conditions, almost complete disruption of the reactivity was observed, which also supported the concept of competitive ligand binding (entry 3).

**Table 5:** Effect of additives on the branched allylic C-H esterification

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>additive</th>
<th>yield (L+B)</th>
<th>L:B</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>---</td>
<td>79%</td>
<td>1:20</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>DMSO (1 equiv)</td>
<td>21%</td>
<td>1:20</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>59 (1 equiv)</td>
<td>6%</td>
<td>---</td>
</tr>
<tr>
<td>4</td>
<td>49</td>
<td>---</td>
<td>47%</td>
<td>1:20</td>
</tr>
<tr>
<td>5</td>
<td>49</td>
<td>DMSO (1 equiv)</td>
<td>35%</td>
<td>1:20</td>
</tr>
<tr>
<td>6</td>
<td>49</td>
<td>59 (1 equiv)</td>
<td>12%</td>
<td>1:19</td>
</tr>
</tbody>
</table>

*53 (1 equiv), 60 (1.5 equiv), 1 or 49 (0.1 equiv), benzoquinone (2 equiv), dioxane (0.33M), 45°C, 72h. *Determined by 1H NMR analysis of crude.*
**Table 6**: Effect of additives on the linear allylic C-H amination

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>additive</th>
<th>yield (L+B)</th>
<th>L:B</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>---</td>
<td>67%</td>
<td>11:1</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>DMSO (1 equiv)</td>
<td>&lt;5%</td>
<td>---</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>59 (1 equiv)</td>
<td>&lt;5%</td>
<td>---</td>
</tr>
<tr>
<td>4</td>
<td>49</td>
<td>---</td>
<td>23%</td>
<td>12:1</td>
</tr>
<tr>
<td>5</td>
<td>49</td>
<td>DMSO (1 equiv)</td>
<td>16%</td>
<td>12:1</td>
</tr>
<tr>
<td>6</td>
<td>49</td>
<td>59 (1 equiv)</td>
<td>8%</td>
<td>---</td>
</tr>
</tbody>
</table>

*a 53 (1 equiv), 63 (2 equiv), 1 or 49 (0.10 equiv), benzoquinone (2 equiv), [P(t-butyl)methyl] (0.06 equiv), t-butyl methyl ether (0.67M), 45°C, 72h. *b Determined by 1H NMR analysis of crude.

The equilibrium exchange of bis-sulfoxide and DMSO ligands at the palladium center was thought to be the underlying cause of inhibition of the catalytic allylic alkylation. We reasoned that, if balance could be restored to the equilibrium, perhaps reactivity could be recovered as well. Therefore, it would be necessary to discover a new ligand for C-H cleavage which could better compete with DMSO for binding to palladium. Inspired by this line of reasoning, we synthesized a series of bis-sulfoxide ligands. The aryl substituents of the parent bis-sulfoxide were replaced by various aliphatic groups. This substitution was motivated by the expectation that more electron rich aliphatic substituents would make the sulfoxide a better σ-donor ligand and therefore better able to compete with DMSO. We were delighted to discover that a range of aliphatic bis-sulfoxide ligands restored good reactivity to the catalytic allylic alkylation (Table 7, entries 5, 8-10). The bis(benzylsulfinyl)ethane ligand was selected for further exploration because its complex with palladium, 49, was the most crystalline and hence most operationally convenient catalyst. When 49 was used as a catalyst for the allylic amination and esterification reactions, it was observed that the addition of DMSO or benzoylecetone diminished the reactivity to a lesser extent than for reactions catalyzed by 1 (Table 5 entries 4-6; Table 6 entries 4-6). We concluded that 49 is relatively insensitive to competitive ligand binding by DMSO or benzoylecetone.
We endeavored to further elucidate the interplay between the two sulfoxide ligands. Consistent with the hypothesis that allylic C-H alkylation of unactivated substrates proceeds through a SLC mechanism, the omission of either sulfoxide ligand dramatically reduced the reactivity (no DMSO, 59% → <5%; no bis-sulfoxide, 59% → 6%; Table 7, entries 4 and 7). Stoichiometric studies demonstrated that catalyst 1 had rates comparable to or faster than 49 for the C-H cleavage and functionalization steps (see 2.4 Experimental Section). However, in contrast to 1, catalyst 49 was active in solution for an extended period of time, presumably because it resisted inhibition and premature catalyst decomposition by DMSO (Figure 20, blue diamond).

Having developed conditions suitable for the allylic alkylation of unactivated α-olefins, we proceeded to examine the substrate scope of the method. In all cases the reaction proceeded with high regioselectivity and excellent E/Z selectivity (>20:1). The alkylation was tolerant of a variety of functionality at the homoallylic position, including carbon, oxygen, and nitrogen (Table 8, entries 2, 3, and 5–8). When branching in the homoallylic position generated a stereocenter, it was not racemized. Similarly, a potentially epimerizable stereocenter alpha to a
Figure 20: Comparison of the allylic alkylation reaction catalyzed by 1 (red squares) or 49 (blue diamonds), and
DMSO

ketone retained its configuration, thus illustrating how this method is orthogonal to traditional carbanion-based C-C bond-forming reactions (entry 4). A trisubstituted olefin was tolerated under the reaction conditions, demonstrating the chemoselectivity of the catalyst for terminal olefins (entry 3). Notably, even an unprotected, allylic secondary alcohol was stable to the oxidative conditions—an unusual example of tolerance for readily oxidized functionality by a palladium(II) reaction (entry 6).

Strategically, the C-H alkylation disconnection provided facile entry to products that were often difficult to access by conventional means (Table 8, entries 5 and 8).\textsuperscript{58} Whereas conventional syntheses require tedious manipulation of oxidized functionality, C-H alkylation uses relatively inert, robust \(\alpha\)-olefins which may be installed at any stage by using versatile, stereoselective allylation methods.\textsuperscript{59}
Table 8: Scope of the allylic C-H alkylation reaction

<table>
<thead>
<tr>
<th>entry</th>
<th>major product</th>
<th>L:B&lt;sup&gt;b&lt;/sup&gt; isolated yield L&lt;sup&gt;a&lt;/sup&gt; E:Z &gt;20:1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>unactivated olefins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>C&lt;sub&gt;9&lt;/sub&gt;H&lt;sub&gt;17&lt;/sub&gt;</td>
<td>57 12:1 56%</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>67 &gt;20:1 61%</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>68 &gt;20:1 49%&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>4&lt;sup&gt;d&lt;/sup&gt;</td>
<td>n-But</td>
<td>69 &gt;20:1 56%&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>5&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td>70 &gt;20:1 63%&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>71 &gt;20:1 58%&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>72 &gt;20:1 53%&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>73 &gt;20:1 66%&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>activated olefins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>R = H, 47 11:1 73%</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>Me, 74 &gt;20:1 54%</td>
</tr>
<tr>
<td>11</td>
<td></td>
<td>75 5:1 63%</td>
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<tr>
<td>12</td>
<td></td>
<td>76 &gt;20:1 60%</td>
</tr>
<tr>
<td>13</td>
<td></td>
<td>77 --- 50%</td>
</tr>
</tbody>
</table>

<sup>a</sup>Olefin (1 equiv.), <sup>b</sup>49 (10 mol%), <sup>c</sup>DMBO (1, 1 equiv.), 1,2-bis(benzyl- sulfanyl)ethane (0.05 equiv.), DCE:DMSO (7:3, 0.67M), 45°C, 72h. Average of 2 runs. Products isolated as one regio- and olefin isomer. <sup>d</sup>Determined by <sup>1</sup>H NMR analysis of the crude <sup>e</sup>d.r. = 1:1 <sup>f</sup>Dioxane:DMSC (7:3, 0.67M).
The C-H alkylation reaction conditions were also suitable for allylbenzene substrates and other classes of activated substrates such as amides and enols, thus providing a general reaction protocol that encompassed both activated and unactivated α-olefin substrates (Table 8, entries 9–13). Because complex 49 is a more robust, long lived catalyst, we also found that the alkylation reaction could be extended to substrates that had previously reacted too sluggishly to reach high conversion. The alkylation of 1-methylallylbenzene was a unique example of C-H activation of a γ-branched olefin (entry 10). The 1,1-disubstituted alkene α-methylstyrene, a representative of a previously unexplored class of olefins, furnished a synthetically useful yield of product 77 (entry 13).

The α-nitroketone subunit installed in this reaction has been demonstrated to be a versatile synthetic handle. A wide variety of transformations have been reported, including selective reductions, exhaustive reduction, and cyclization. In order to complement these strategies for elaboration of the α-nitroketone, we sought to demonstrate the how the motif could be elaborated orthogonally by selectively excising each of the electron-withdrawing moieties (Figure 21). We discovered a novel and extremely mild methanolyisis of the benzoyl group to furnish homoallylic nitroalkane 78 in nearly quantitative yield. Alternatively, we demonstrated the radical de-nitration by AIBN/tributylstannane to produce the γ,δ-unsaturated ketone 79.

Figure 21: Synthetic elaboration of the allylic alkylation products
2.3 CONCLUSIONS

This work resulted in the discovery of the first intermolecular allylic C-H alkylation reaction with a general substrate scope. In previous work, we had discovered a palladium(II) catalyzed allylic C-H alkylation reaction, however its substrate scope was limited to allylarenes. Standard reaction optimization was not successful in improving the substrate scope, and our observations indicated that inhibition of the catalyst was resulting in low conversions and premature deactivation of the catalyst. We endeavored to identify the source of the inhibition by applying our understanding of the catalytic cycle, and to rebalance the reaction conditions to overcome the inhibition and achieve a reaction with general substrate scope.

Our mechanistic studies implicated DMSO as a potential inhibitor under the reaction conditions. Although DMSO plays a vital role in promoting functionalization of the π-allyl intermediate, we suspected that it was also interfering with the formation of the palladium(II)/bis-sulfoxide complex which is necessary for allylic C-H cleavage of unactivated substrates. Due to the complex role played by DMSO and the transient nature of the metal-ligand interaction, we employed indirect methods to test our hypothesis; addition of DMSO to C-H esterification and amination reactions catalyzed by palladium(II)/bis-sulfoxide complexes revealed clear inhibition. This insight inspired the synthesis of stronger σ-donor bis-sulfoxide ligands which could better compete with DMSO for binding to palladium. These new complexes proved to be more robust catalysts which resisted inhibition by DMSO, leading to the discovery of conditions suitable for the allylic C-H alkylation of virtually any α-olefin substrate.

2.4 EXPERIMENTAL SECTION

General Information: All commercially obtained reagents for the allylic alkylation reaction were used as received: 2,6-dimethylbenzoquinone, benzoylnitromethane, 1-undecene, 1-decene,
allylcyclohexane, allylbenzene (Sigma-Aldrich); benzoynitromethane (Acros Organics). Catalyst 1 was prepared according to the published procedure.\textsuperscript{14a} Catalysts 49, 64-66 were prepared as described below. Catalysts were stored at 4°C and weighed out in air prior to use. Dioxane and benzene were purified prior to use by passage through a bed of activated alumina (Glass Contour, Laguna Beach, California). Dimethyl sulfoxide (DMSO) and methanol were obtained from Fisher Scientific and used as received. 1,2-dichloroethane (DCE) was obtained from Sigma-Aldrich and used as received. All allylic alkylation reactions were run under air with no precautions taken to exclude moisture. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized with UV and potassium permanganate stain. Flash chromatography was performed as described by Still using ZEOprep 60 ECO 43-60 micron silica gel (American International Chemical, Inc.).\textsuperscript{35} Medium pressure liquid chromatography was performed on a Teledyne Isco CombiFlash Rf machine using pre-packed RediSep columns (12g C18) at a rate of 30 mL/min. \textsuperscript{1}H NMR spectra were recorded on a Varian Unity-400 (400 MHz), Varian Inova-500 (500 MHz), or Varian Unity-500 (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl\textsubscript{3} at 7.26 ppm). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, b = broad, ap = apparent; coupling constant(s) in Hz; integration. Proton-decoupled \textsuperscript{13}C NMR spectra were recorded on a Varian Unity-500 (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl\textsubscript{3} at 77.16 ppm). Regioselectivity of the allylic alkylation reaction was determined by \textsuperscript{1}H NMR analysis of the crude reaction mixture. IR spectra were recorded as thin films on NaCl plates on a Perkin-Elmer Spectrum BX FT-IR and are reported in frequency of absorption (cm\textsuperscript{-1}). Chiral high pressure liquid chromatographic (HPLC) analysis was performed on an Agilent Technologies 1100 HPLC system with a model 1100 Quaternary
Pump, Diode Array Detector, Thermostat, and Autosampler using a Daicel Chemical Industries Chiralcel OD-H column (0.46 cm x 25 cm). Chiral gas chromatographic (GC) analysis was performed on an Agilent Technologies 5890A Series instrument equipped with an FID detector using a J&W Scientific β-cyclodextrin column (30m, 0.25mm, 0.25μm). High-resolution mass spectra were obtained at the University of Illinois Mass Spectrometry Laboratory. Optical rotations were obtained using a JAS.CO DIP-360 digital polarimeter and a 3.5 x 50 mm cell and are reported as follows: concentration (c = g / 100 mL), solvent.

**General Procedure for the Allylic Alkylation:** A one dram (4 mL) borosilicate vial was charged with Pd[1,2-bis(benzylsulfinyl)ethane](OAc)₂ 49 (0.10 equiv, 0.030 mmol), 2,6-dimethylbenzoquinone 58 (1.1 equiv, 0.33 mmol), benzoynitromethane 16 (4.0 equiv, 1.20 mmol), and 1,2-bis(benzylsulfinyl)ethane (0.05 equiv, 0.015 mmol). The olefin (1 equiv, 0.30 mmol) was weighed out in a ½ dram vial and transferred via 1,2-dichloroethane (3 x 0.105 mL); dimethylsulfoxide (0.135 mL); and a stir bar were added sequentially to the reaction vial. No precautions were taken to exclude air or moisture. The reaction vial was capped and stirred at 45°C for 72 hours. The vial was cooled to room temperature, and the reaction mixture was diluted with saturated aqueous NH₄Cl (40 mL) and extracted with ethyl acetate (3 x 30 mL). For products of polarity similar to benzoynitromethane, the combined organics were washed with 5% aqueous K₂CO₃ (3 x 20 mL). The combined organics were dried over MgSO₄. The mixture was filtered and concentrated in vacuo. Purification by flash chromatography (SiO₂, EtOAc/hexanes mixtures) provided the pure linear product. In cases where branched product was observed, it was readily separated and generally possessed a higher Rₜ value than linear product. 

**NOTE:** The allylic alkylation products were observed to be slightly unstable on silica gel. While
they may be purified by column chromatography, care should be taken to avoid prolonged exposure to silica.

**Procedure for preparation of Catalyst 49, 64-66:**

![Chemical reaction diagram]

Catalyst 49 was prepared as previously reported, with two modifications to the procedure. First, Pd(OAc)$_2$ was recrystallized from benzene 3 times prior to complexation with bis-sulfoxide. Second, the time of complexation was reduced to 12 hours from 22 hours to reduce decomposition of bis-sulfoxide ligand. Some catalyst batch variability was observed, specifically during observation of initial reaction rates, however overall reactivity was reproducible between batches.

Catalyst 64 was prepared by the procedure described for catalyst 49. The ligand was prepared as a mixture of sulfoxide diastereomers.

![Chemical reaction diagram]

Catalyst 65 was prepared by the procedure above. The ligand was prepared as a mixture of sulfoxide diastereomers.

Catalyst 66 was prepared by the procedure described for catalyst 65. The ligand was prepared as a mixture of sulfoxide diastereomers.
Stoichiometric studies of unactivated and activated substrates

**I. C-H Activation**

To a ½ dram borosilicate vial were added allylbenzene 18 (11.8 mg, 0.10 mmol, 1.0 equiv). Catalyst 1 (50.3 mg, 0.10 mmol, 1.0 equiv), dioxane-d₈ (300 μL) and a stir bar were added sequentially. No precautions were taken to exclude air or moisture. The vial was capped and stirred for 60 min at 45°C. The vial was cooled to room temperature and n-Bu₄NCl (111.2 mg, 0.40 mmol, 4.0 equiv) was added in one portion. The anion exchange proceeded at room temperature for 60 min. To the crude reaction mixture was added nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) and the solution was shaken vigorously. A sample was removed for ¹H NMR analysis and diluted with CDCl₃. Yield was determined by integration of product peaks at 5.80, 4.62, 3.97 ppm relative to nitrobenzene. Run 1 (72% yield); run 2 (74% yield). **Average yield:** 73%.

**II. Functionalization**

bis[chloro(1,2,3-trihapto-allylbenzene)palladium (II)] [54]: To a ½ dram borosilicate vial were added allylbenzene 18 (11.8 mg, 0.10 mmol, 1.0 equiv). Catalyst 1 (50.3 mg, 0.10 mmol, 1.0 equiv), dioxane-d₈ (300 μL) and a stir bar were added sequentially. No precautions were taken to exclude air or moisture. The vial was capped and stirred for 60 min at 45°C. The vial was cooled to room temperature and n-Bu₄NCl (111.2 mg, 0.40 mmol, 4.0 equiv) was added in one portion. The anion exchange proceeded at room temperature for 60 min. To the crude reaction mixture was added nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv) and the solution was shaken vigorously. A sample was removed for ¹H NMR analysis and diluted with CDCl₃. Yield was determined by integration of product peaks at 5.80, 4.62, 3.97 ppm relative to nitrobenzene. Run 1 (72% yield); run 2 (74% yield). **Average yield:** 73%.

¹H NMR (500 MHz, CDCl₃) δ 7.50 (d, J = 7.6 Hz, 4H), 7.35 (m, 2H), 7.27 (d, J = 7.6 Hz,
bis[chloro(1,2,3-trihapto-undecene)palladium (II)] [55]: A 2 dram (8 mL) borosilicate vial was charged with catalyst 1 (101 mg, 0.20 mmol, 1.0 equiv), benzoylnitromethane 16 (330 mg, 2.0 mmol, 10 equiv), and a stir bar. To this was added 3 mL dioxane and 1-undecene 53 (411 μL, 2.0 mmol, 10 equiv). The reaction was allowed to stir for 60 min at 45°C under air, at which time an acetone solution (1 mL) of n-Bu₄NCl (222 mg, 0.80 mmol, 4 equiv) was added via syringe. The anion exchange proceeded at room temperature for 60 min. The mixture was filtered over a plug of Celite (to remove metallic Pd), concentrated and purified via column chromatography (0%→15% EtOAc/hexanes gradient) to afford bis[chloro(1,2,3-trihapto-undecene)palladium (II)] as a bright yellow solid. Run 1 (46.5 mg, 0.0788 mmol, 79% yield), run 2 (45.5 mg, 0.0771 mmol, 77% yield). **Average yield: 78%**. 

1H NMR (500 MHz, CDCl₃) δ 5.26 (td, J = 11.6, 6.8 Hz, 2H), 3.88 (d, J = 6.8 Hz, 2H), 3.85 (m, 2H), 2.82 (d, J = 11.6 Hz, 2H), 1.8-1.2 (m, 28 H), 0.88 (t, J = 7.2 Hz, 6H). Spectral data match those of the reported compound.¹⁶

(E)-methyl 2-nitro-5-phenylpent-4-enooate [14]: To a 40 mL borosilicate vial were added sequentially bis[acetato(1,2,3-trihaptoallylbenzene)palladium (II)] (28.3 mg, 0.100 mmol, 1.0 equiv), methyl nitroacetate (119.1 mg, 1.0 mmol, 10 equiv), and a stir bar. Dioxane (2.4 mL) and dimethylsulfoxide (0.60 mL) were added. No precautions were taken to exclude air or moisture. The vial was capped and stirred for 3.5 h at 45°C. The vial was cooled to room temperature and the reaction mixture was diluted
with saturated aqueous NH₄Cl (20 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organics were dried over MgSO₄. The mixture was filtered and concentrated in vacuo. To the crude reaction mixture was added nitrobenzene (4.9 mg, 0.040 mmol, 0.40 equiv). The crude mixture was dissolved completely in CDCl₃ and a sample was removed for ¹H NMR analysis. Yield was determined by integration of olefinic product peaks relative to nitrobenzene. Run 1 (87% yield, 4.1:1 L:B); run 2 (84% yield, 4.3:1 L:B). Average yield: 86%. ¹H NMR (500 MHz, CDCl₃) δ 7.32 (m, 4H), 7.25 (m, 1H), 6.65 (d, J = 15.6 Hz, 1H), 6.08 (dt, J = 15.6, 7.3 Hz, 1H), 5.23 (dd, J = 9.2, 5.5 Hz, 1H), 3.85 (s, 3H), 3.16 (m, 1H), 3.07 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) 164.6, 136.3, 135.6, 128.7, 128.2, 126.5, 121.1, 87.6, 53.8, 33.9; IR (film, cm⁻¹): 3028, 2958, 1954, 1884, 1754, 1563, 1495, 1438; HRMS (ESI) m/z calculated for C₁₂H₁₃NO₄Na [M+Na]⁺: 258.0742, found 258.0729. Spectral data match those of the reported compound.³⁷

(E)-2-nitro-1-phenyltridec-4-en-1-one [56]: A 1 dram (4 mL) borosilicate vial was charged with bis[acetato(1,2,3-trihapto-undecene)palladium (II)] 2 (15.9 mg, 0.025 mmol, 1.0 equiv), benzoylnitromethane 16 (82.6 mg, 0.50 mmol, 10 equiv), and a stir bar. To this was added dioxane (525 μL) and DMSO (225 μL). The reaction vial was capped and stirred at 45°C for 4 hours. The vial was cooled to room temperature, and the reaction mixture was diluted with saturated aqueous NH₄Cl (15 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organics were dried over MgSO₄. The mixture was filtered and concentrated in vacuo. To the crude reaction mixture was added 1,4-dimethoxybenzene (2.1 mg, 0.015 mmol, 0.30 equiv) as a stock solution in CDCl₃. The crude mixture was dissolved completely in additional CDCl₃ and a sample was removed for ¹H NMR analysis. Yield was determined by integration of olefinic product peaks relative to 1,4-
dimethoxybenzene. Run 1 (74% yield, 12:1 L:B), run 2 (69% yield, 13:1 L:B), run 3 (71% yield, 12:1 L:B). **Average yield: 71%**. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.95 (ap. d, $J = 7.3$ Hz, 2H), 7.66 (ap. t, $J = 7.4$ Hz, 1H), 7.53 (ap. t, $J = 7.9$ Hz, 2H), 6.06 (dd, $J = 9.2$, 5.0 Hz, 1H), 5.63 (m, 1H), 5.37 (m, 1H), 3.03 (m, 1H), 2.85 (m, 1H), 1.96 (q, $J = 7.0$ Hz, 2H), 1.33-1.18 (m, 12H), 0.88 (t, $J = 7.1$ Hz, 3H). This reaction was also run at 0.2 mmol scale, and pure linear product was isolated in 62% yield.

Catalytic allylic C-H alkylation of unactivated $\alpha$-olefins

![Reaction Scheme]

<table>
<thead>
<tr>
<th>entry$^a$</th>
<th>catalyst</th>
<th>additive</th>
<th>yield (L+B)$^b$</th>
<th>L:B$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R = Ph 1</td>
<td>---</td>
<td>&lt;5%</td>
<td>---</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>DMSO (30 vol%)$^c$</td>
<td>25%</td>
<td>12:1</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>59 (1 equiv)</td>
<td>&lt;5%</td>
<td>---</td>
</tr>
<tr>
<td>4</td>
<td>R = Bn 49</td>
<td>---</td>
<td>&lt;5%</td>
<td>---</td>
</tr>
<tr>
<td>5</td>
<td>49</td>
<td>DMSO (30 vol%)</td>
<td>59%</td>
<td>12:1</td>
</tr>
<tr>
<td>6</td>
<td>49</td>
<td>59 (1 equiv)</td>
<td>&lt;5%</td>
<td>---</td>
</tr>
<tr>
<td>7</td>
<td>Pd(OAc)$_2$</td>
<td>DMSO (30 vol%)</td>
<td>6%</td>
<td>---</td>
</tr>
<tr>
<td>8</td>
<td>R = nPr 64</td>
<td>DMSO (30 vol%)</td>
<td>62%</td>
<td>11:1</td>
</tr>
<tr>
<td>9</td>
<td>R = Cy 65</td>
<td>DMSO (30 vol%)</td>
<td>57%</td>
<td>12:1</td>
</tr>
<tr>
<td>10</td>
<td>R = tBu 66</td>
<td>DMSO (30 vol%)</td>
<td>40%</td>
<td>10:1</td>
</tr>
</tbody>
</table>

$^a$53 (1 equiv), 16 (4 equiv), catalyst (0.1 equiv), 2,6-dimethylbenzoquinone (1 equiv), 1,2-dichloroethane (0.67M), 45°C, 72h. $^b$Determined by $^1$H NMR analysis of crude. $^c$30 vol% = 6.3 equiv.

Table 7: Allylic C-H alkylation screening procedure: A ½ dram borosilicate vial was charged with catalyst (0.010 mmol, 0.1 equiv), benzylnitromethane 16 (66.1 mg, 0.40 mmol, 4 equiv) and dimethylbenzoquinone 58 (15.0 mg, 0.11 mmol, 1.1 equiv), 1,2-dichloroethane (105 μL), dimethylsulfoxide (45 μL), undecene 53 (20.5 μL, 0.10 mmol, 1 equiv), and a stir bar were added sequentially. No precautions were taken to exclude air or moisture. The vial was capped and stirred for 72 h at 45°C. The vial was cooled to room temperature and the reaction mixture was diluted with ethyl acetate (10 mL) and washed sequentially with saturated aqueous NH$_4$Cl (10 mL) and 5% aqueous K$_2$CO$_3$ (10 mL). The organic layer was dried over MgSO$_4$. The mixture was filtered and concentrated *in vacuo*. To the crude reaction mixture was added 1,4-
dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) as a stock solution in CDCl₃. The crude mixture was dissolved completely in additional CDCl₃ and a sample was removed for ¹H NMR analysis. Yield was determined by integration of olefinic product peaks relative to 1,4-dimethoxybenzene.

**Entry 1**: Catalyst 1 (5.0 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzylnitromethane (66.1 mg, 0.40 mmol, 4.0 equiv), DCE (150 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (<5% yield); run 2 (<5% yield). **Average yield: <5%**.

**Entry 2**: Catalyst 1 (5.0 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzylnitromethane (66.1 mg, 0.40 mmol, 4.0 equiv), DCE (105 μL), DMSO (45 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (25% yield, 12:1 L:B); run 2 (24% yield, 13:1 L:B). **Average yield: 25%**.

**Entry 3**: Catalyst 1 (5.0 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzylnitromethane (66.1 mg, 0.40 mmol, 4.0 equiv), benzoylacetone (16.2 mg, 0.10 mmol, 1.0 equiv), DCE (150 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (<5% yield); run 2 (<5% yield). **Average yield: <5%**.

**Entry 4**: Catalyst 49 (5.3 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzylnitromethane (66.1 mg, 0.40 mmol, 4.0 equiv), DCE (150 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (<5% yield); run 2 (<5% yield).
Entry 5: Catalyst 49 (5.3 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzoynitromethane (66.1 mg, 0.40 mmol, 4.0 equiv), DCE (105 μL), DMSO (45 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (59% yield, 12:1 L:B); run 2 (58% yield, 13:1 L:B); run 3 (58% yield, 12:1 L:B). Average yield: 59%.

Entry 6: Catalyst 49 (5.3 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzoynitromethane (66.1 mg, 0.40 mmol, 4.0 equiv), benzyloacetone (16.2 mg, 0.10 mmol, 1.0 equiv), DCE (150 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (<5% yield); run 2 (<5% yield). Average yield: <5%.

Entry 7: Pd(OAc)$_2$ (2.2 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzoynitromethane (66.1 mg, 0.40 mmol, 4.0 equiv), DCE (105 μL), DMSO (45 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (6% yield); run 2 (6% yield). Average yield: 6%.

Entry 8: Catalyst 64 (4.3 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzoynitromethane (66.1 mg, 0.40 mmol, 4.0 equiv), DCE (105 μL), DMSO (45 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (63% yield, 10:1 L:B); run 2 (62% yield, 11:1 L:B). Average yield: 62%.

Entry 9: Catalyst 65 (5.1 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv),
benzoylnitromethane (66.1 mg, 0.40 mmol, 4.0 equiv), DCE (105 μL), DMSO (45 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (57% yield, 11:1 L:B); run 2 (57% yield, 11:1 L:B). **Average yield: 57%.**

**Entry 10:** Catalyst 66 (4.6 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzoylnitromethane (66.1 mg, 0.40 mmol, 4.0 equiv), DCE (105 μL), DMSO (45 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (40% yield, 9:1 L:B); run 2 (39% yield, 10:1 L:B). **Average yield: 40%.**

Effect of additives on the branched allylic C-H esterification

<table>
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<td>79%</td>
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<tr>
<td>6</td>
<td>49</td>
<td>59 (1 equiv)</td>
<td>12%</td>
<td>1:19</td>
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</table>

*53 (1 equiv), 60 (1.5 equiv), 1 or 49 (0.10 equiv), benzoquinone (2 equiv), dioxane (0.33M), 45°C, 72h. *6 Determined by H NMR analysis of crude.

Table 5: Allylic C-H esterification screening procedure: A ½ dram borosilicate vial was charged with catalyst 1 or 49 (0.010 mmol, 0.1 equiv), benzoic acid 60 (18.3 mg, 0.15 mmol, 1.5 equiv) and benzoquinone (21.6 mg, 0.2 mmol, 2 equiv). Dioxane (300 μL), undecene (20.5 μL, 0.10 mmol, 1 equiv), and a stir bar were added sequentially. No precautions were taken to exclude air or moisture. The vial was capped and stirred for 72 h at 45°C. The vial was cooled to room temperature and the reaction mixture was diluted with hexanes (10 mL) and washed sequentially with saturated aqueous NaHSO₃ (10 mL) and 5% aqueous K₂CO₃ (3×10 mL). The
combined aqueous layers were extracted with hexanes (2x10 mL). The combined organic layers were dried over MgSO₄. The mixture was filtered and concentrated in vacuo. To the crude reaction mixture was added 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) as a stock solution in CDCl₃. The crude mixture was dissolved completely in additional CDCl₃ and a sample was removed for ¹H NMR analysis. Yield was determined by integration of olefinic product peaks relative to 1,4-dimethoxybenzene.

**Entry 1:** Catalyst 1 (5.0 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzoic acid (18.3 mg, 0.15 mmol, 1.5 equiv), dioxane (300 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (78% yield, 1:>20 L:B); run 2 (80% yield, 1:>20 L:B). **Average yield: 79%**.

**Entry 2:** Catalyst 1 (5.0 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzoic acid (18.3 mg, 0.15 mmol, 1.5 equiv), dioxane (285 μL), DMSO (7.1 μL, 0.1 mmol, 1 equiv), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (19% yield, 1:>20 L:B); run 2 (22% yield, 1:>20 L:B). **Average yield: 21%**.

**Entry 3:** Catalyst 1 (5.0 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzoic acid (18.3 mg, 0.15 mmol, 1.5 equiv), benzoylectone (16.2 mg, 0.10 mmol, 1.0 equiv), dioxane (300 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (6% yield); run 2 (6% yield). **Average yield: 6%**.

**Entry 4:** Catalyst 49 (5.3 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv),
benzoic acid (18.3 mg, 0.15 mmol, 1.5 equiv), dioxane (300 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (46% yield, 1:>20 L:B); run 2 (47% yield, 1:>20 L:B). **Average yield: 47%**.

**Entry 5**: Catalyst 49 (5.3 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzoic acid (18.3 mg, 0.15 mmol, 1.5 equiv), dioxane (285 μL), DMSO (7.1 μL, 0.1 mmol, 1 equiv), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (34% yield, 1:>20 L:B); run 2 (37% yield, 1:>20 L:B); run 3 (33% yield, 1:>20 L:B). **Average yield: 35%**.

**Entry 6**: Catalyst 49 (5.3 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), benzoic acid (18.3 mg, 0.15 mmol, 1.5 equiv), benzoylacetone (16.2 mg, 0.10 mmol, 1.0 equiv), dioxane (300 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (9% yield, 1:16 L:B); run 2 (14% yield, 1:20 L:B); run 3 (15% yield, 1:16 L:B), run 4 (14% yield, 1:>20 L:B). **Average yield: 12%**.

Effect of additives on the linear allylic C-H amination
Table 6: Allylic C-H amination screening procedure: A ½ dram borosilicate vial was charged with catalyst 1 or 49 (0.010 mmol, 0.1 equiv), methyl N-tosylcarbamate 62 (45.9 mg, 0.2 mmol, 2 equiv) and benzoquinone (21.6 mg, 0.2 mmol, 2 equiv). N,N-Diisopropylethylamine (1.0 μL, 0.006 mmol, 0.06 equiv) in tert-butyl methyl ether (150 μL), undecene (20.5 μL, 0.10 mmol, 1 equiv), and a stir bar were added sequentially. No precautions were taken to exclude air or moisture. The vial was capped and stirred for 72 h at 45°C. The vial was cooled to room temperature and the reaction mixture was diluted with diethyl ether (10 mL) and washed sequentially with 5% aqueous K₂CO₃ (3x10 mL). The combined aqueous layers were extracted with diethyl ether (2x10 mL). The combined organic layers were dried over MgSO₄. The mixture was filtered and concentrated in vacuo. To the crude reaction mixture was added 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) as a stock solution in CDCl₃. The crude mixture was dissolved completely in additional CDCl₃ and a sample was removed for ¹H NMR analysis. Yield was determined by integration of olefinic product peaks relative to 1,4-dimethoxybenzene.

Entry 1: Catalyst 1 (5.0 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), methyl N-tosylcarbamate (45.9 mg, 0.2 mmol, 2 equiv), N,N-diisopropylethylamine (1.0 μL, 0.006 mmol, 0.06 equiv) in tert-butyl methyl ether (150 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (69% yield, 12:1 L:B); run 2 (65% yield, 11:1 L:B). Average yield: 67%.

Entry 2: Catalyst 1 (5.0 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), methyl N-tosylcarbamate (45.9 mg, 0.2 mmol, 2 equiv), N,N-diisopropylethylamine (1.0 μL, 0.006 mmol, 0.06 equiv) in tert-butyl methyl ether (150 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (69% yield, 12:1 L:B); run 2 (65% yield, 11:1 L:B). Average yield: 67%.
0.006 mmol, 0.06 equiv) in tert-butyl methyl ether (143 μL), DMSO (7.5 μL, 0.1 mmol, 1 equiv), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (<5% yield); run 2 (<5% yield). **Average yield: <5%**.

**Entry 3**: Catalyst 1 (5.0 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), methyl N-tosylcarbamate (45.9 mg, 0.2 mmol, 2 equiv), benzoylacetone (16.2 mg, 0.10 mmol, 1.0 equiv), N,N-diisopropylethylamine (1.0 μL, 0.006 mmol, 0.06 equiv) in tert-butyl methyl ether (150 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (<5% yield); run 2 (<5% yield). **Average yield: <5%**.

**Entry 4**: Catalyst 49 (5.3 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), methyl N-tosylcarbamate (45.9 mg, 0.2 mmol, 2 equiv), N,N-diisopropylethylamine (1.0 μL, 0.006 mmol, 0.06 equiv) in tert-butyl methyl ether (150 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (21% yield, 12:1 L:B); run 2 (25% yield, 12:1 L:B). **Average yield: 23%**.

**Entry 5**: Catalyst 49 (5.3 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv), methyl N-tosylcarbamate (45.9 mg, 0.2 mmol, 2 equiv), N,N-diisopropylethylamine (1.0 μL, 0.006 mmol, 0.06 equiv) in tert-butyl methyl ether (143 μL), DMSO (7.5 μL, 0.1 mmol, 1 equiv), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (15% yield, 11:1 L:B); run 2 (16% yield, 13:1 L:B). **Average yield: 16%**.

**Entry 6**: Catalyst 49 (5.3 mg, 0.10 mmol, 1.0 equiv), undecene (20.5 μL, 0.10 mmol, 1.0 equiv),
methyl N-tosylcarbamate (45.9 mg, 0.2 mmol, 2 equiv), benzoylacetonate (16.2 mg, 0.10 mmol, 1.0 equiv), N,N-diisopropylethylamine (1.0 μL, 0.006 mmol, 0.06 equiv) in tert-butyl methyl ether (150 μL), and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (7% yield); run 2 (8% yield). **Average yield: 8%**.

Comparison of the allylic alkylation reaction catalyzed by 1 (red squares) or 49 (blue diamonds), and DMSO

**Figure 20:** A ½ dram borosilicate vial was charged with catalyst 1 (5.0 mg, 0.010 mmol, 0.1 equiv) or catalyst 49 (5.3 mg, 0.010 mmol, 0.1 equiv), benzoylnitromethane 16 (66.1 mg, 0.40 mmol, 4 equiv), 2,6-dimethylbenzoquinone 58 (15.0 mg, 0.110 mmol, 1.1 equiv) and a stir bar. To this was added 1-undecene 53 (20.5 μL, 0.10 mmol, 1 equiv) and 4-nitroanisole (4.6 mg, 0.030 mmol, 0.3 equiv, internal standard) as a stock solution in DCE (105 μL) and DMSO (45 μL). The vial was fitted with a cap with a septum and the reaction was allowed to stir for 24 hours at 45°C under air. Reaction aliquots (7 μL) were periodically removed via syringe and
filtered through a silica plug using $^3\text{PrOH}$:hexanes (1:4) solvent. The crude samples were analyzed by HPLC with Agilent Technologies, Inc. Zorbax CN 0.46 cm x 25 cm column. A flow rate of 1.5 mL/min at 35.0°C with 99:1 hexanes:2-propanol with detection at 214 nm gave the 4-nitroanisole standard at 5.12 min and the linear product at 5.42 min. Yield was determined by comparison to a standard curve (see Figure 24). Yields are reported as the average of 3 runs, with error bars representing standard deviation.
Scope of the allylic C-H alkylation reaction

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<sup>a</sup> Olefin (1 equiv.), <sup>b</sup> 49 (10 mol%), <sup>c</sup> DMBQ 58 (1.1 equiv.), 1,2-bis(phenylazidomethyl)ethane (0.05 equiv.), DCE:DMSO (7:3, 0.87 M), 45 °C, 72 h. Average of 2 runs. Products isolated as one regio- and olefin isomer. <sup>d</sup> Determined by 'H NMR analysis of the crude. <sup>e</sup> d.r. = 1:1. <sup>f</sup> Dioxane:DMSO (7:3, 0.87 M).
(E)-2-nitro-1-phenyltridec-4-en-1-one [57]: 1-undecene (46.3 mg, 0.3 mmol, 1.0 equiv) was reacted following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 12:1 and the E/Z isomer ratio was >20:1. Flash chromatography (5% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (54.6 mg, 0.172 mmol, 57% yield); run 2 (51.6 mg, 0.163 mmol, 54% yield); run 3 (52.3 mg, 0.165 mmol, 55% yield). 

**Average yield:** 56%.

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.95 (ap. d, $J = 7.3$ Hz, 2H), 7.66 (ap. t, $J = 7.4$ Hz, 1H), 7.53 (ap. t, $J = 7.9$ Hz, 2H), 6.06 (dd, $J = 9.2$, 5.0 Hz, 1H), 5.63 (m, 1H), 5.37 (m, 1H), 3.03 (m, 1H), 2.85 (m, 1H), 1.96 (q, $J = 7.0$ Hz, 2H), 1.33-1.18 (m, 12H), 0.88 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) 188.7, 137.1, 134.8, 134.2, 129.3, 129.0, 121.8, 89.7, 33.9, 32.6, 32.0, 29.5, 29.4, 29.2, 29.1, 22.8, 14.3; IR (film, cm$^{-1}$): 3064, 2926, 2854, 1697, 1562, 1450, 1255, 972, 688; HRMS (ESI) $m/z$ calculated for C$_{19}$H$_{27}$NO$_3$Na [M+Na]$^+$: 340.1889, found 340.1879.

(E)-5-cyclohexyl-2-nitro-1-phenylpent-4-en-1-one [67]: Allylcyclohexane (37.3 mg, 0.3 mmol, 1.0 equiv) was reacted following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was >20:1 and the E/Z isomer ratio was >20:1. Flash chromatography (5% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (57.3 mg, 0.199 mmol, 66% yield); run 2 (48.5 mg, 0.169 mmol, 56% yield); run 3 (43.4 mg, 0.151 mmol, 0.250 mmol scale, 60% yield). 

**Average yield:** 61%.

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.95 (ap. d, $J = 7.1$ Hz, 2H), 7.66 (ap. t, $J = 7.4$ Hz, 1H), 7.53 (ap. t, $J = 7.8$ Hz, 2H), 6.05 (dd, $J = 9.0$, 5.1 Hz, 1H), 5.56 (dd, $J = 15.4$, 6.8 Hz, 1H), 5.32 (m, 1H), 3.01 (m, 1H), 2.84 (m, 1H), 1.89 (m, 1H), 1.71-1.58 (m, 5H), 1.22 (m, 2H), 1.11 (m, 1H), 0.98 (qd, $J = 12.2$, 3.1 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) 188.8, 142.8,
134.8, 134.2, 129.3, 129.0, 119.4, 89.7, 40.7, 33.9, 32.7, 26.2, 26.0; IR (film, cm\(^{-1}\)): 3062, 2924, 2852, 1969, 1907, 1693, 1564, 1448, 1255, 1228, 972, 910, 735, 688; HRMS (ESI) \(m/z\) calculated for C\(_{17}\)H\(_{21}\)NO\(_3\)Na [M+Na]\(^+\): 310.1419, found 310.1411.

(6\(^S\),\(E\))-6,10-dimethyl-2-nitro-1-phenylenicosa-4,9-dien-1-one [68]: (\(S\))-4,8-dimethylnona-1,7-diene (45.7 mg, 0.3 mmol, 1.0 equiv) was reacted following the general procedure. By \(^1\)H NMR analysis of the crude product, the linear:branched ratio was >20:1 and the E/Z isomer ratio was >20:1. By \(^{13}\)C NMR the diastereomeric ratio was 1:1.\(^{67}\) Flash chromatography (8% EtOAc/hexanes) yielded linear product contaminated by ca. 5 wt% (6\(^S\),\(E\))-4,8-dimethyl-2-nitro-1-phenylenicosa-4,10-dien-1-one as a light yellow oil. A pure spectroscopic sample was obtained by medium pressure liquid chromatography (SP: 15% AgNO\(_3\)/SiO\(_2\); MP: 0%→10% EtOAc/hexanes). Run 1 (46.8 mg, 0.148 mmol, 49% yield); run 2 (46.2 mg, 0.146 mmol, 49% yield). **Average yield: 49%.** \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.95 (ap. d, \(J = 7.3\) Hz, 2H), 7.66 (ap. t, \(J = 7.4\) Hz, 1H), 7.53 (ap. t, \(J = 7.8\) Hz, 2H), 6.06 (dd, \(J = 9.0, 5.1\) Hz, 1H), 5.50 (ddd, \(J = 15.3, 7.8, 4.0\) Hz, 1H), 5.34 (m, 1H), 5.04 (m, 1H), 3.03 (m, 1H), 2.86 (m, 1H), 2.07 (septet, \(J = 6.9\) Hz, 1H), 1.86 (m, 2H), 1.67 (s, 3H), 1.57 (m, 3H), 1.24 (m, 2H), 0.91 (d, \(J = 6.3\) Hz, 3H, *diastereomer A*), 0.89 (d, \(J = 6.6\) Hz, 3H, *diastereomer B*); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) *Mixture of diastereomers* 188.8, 188.7, 142.8, 142.7, 134.8, 134.2, 131.6, 131.6, 129.3, 129.0, 124.5, 120.2, 89.6, 36.9, 36.8, 36.5, 36.4, 33.9, 33.8, 25.9, 25.8, 20.4, 17.8; IR (film, cm\(^{-1}\)): 3062, 2962, 2924, 2854, 1967, 1907, 1695, 1562, 1450, 1373, 1255, 1227, 974, 735, 688; HRMS (ESI) \(m/z\) calculated for C\(_{19}\)H\(_{25}\)NO\(_3\)Na [M+Na]\(^+\): 338.1732, found 338.1737.
(7R,E)-7-methyl-2-nitro-1-phenyldodec-4-ene-1,8-dione [69]: (R)-6-methyldec-9-en-5-one (67.3 mg, 0.4 mmol, 1.0 equiv) was reacted following the general procedure. Dioxane was used in place of DCE as a cosolvent. By $^1$H NMR analysis of the crude product, the linear:branched ratio was >20:1 and the E/Z isomer ratio was >20:1. By $^{13}$C NMR the diastereomeric ratio was 1:1. $^{67}$ Flash chromatography (12% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (83.8 mg, 0.253 mmol, 63% yield); run 2 (72.4 mg, 0.218 mmol, 55% yield); run 3 (42.7 mg, 0.129 mmol, 0.250 mmol scale, 52% yield. **Average yield: 56%**. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.95 (ap. d, $J = 7.3$ Hz, 2H), 7.67 (ap. t, $J = 7.4$ Hz, 1H), 7.53 (ap. t, $J = 7.8$ Hz, 2H), 6.04 (m, 1H), 5.55 (m, 1H), 5.43 (m, 1H), 3.02 (m, 1H), 2.84 (m, 1H), 2.51 (septet, $J = 6.8$ Hz, 1H), 2.45-2.29 (m, 3H), 2.01 (m, 1H), 1.51 (m, 2H), 1.28 (m, 2H), 1.02 (d, $J = 7.1$ Hz, 3H, **diastereomer A**), 1.01 (d, $J = 6.3$ Hz, 3H, **diastereomer B**), 0.90 (m, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) *Mixture of diastereomers* 214.1, 214.0, 188.5, 188.4, 134.9, 134.0, 134.0, 133.9, 133.8, 129.4, 128.9, 124.4, 124.4, 89.5, 89.3, 45.9, 41.3, 41.2, 35.7, 35.6, 33.8, 33.7, 25.8, 22.5, 16.3, 16.3, 14.0; IR (film, cm$^{-1}$): 3064, 2960, 2931, 2873, 1695, 1554, 1450, 1371, 1257, 974, 733, 688; HRMS (ESI) $m/z$ calculated for C$_{19}$H$_{26}$NO$_4$ [M+H]$^+$: 332.1862, found 332.1855.

(6R,E)-6-(benzylloxy)-6-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-nitro-1-phenylhex-4-en-1-one [70]: (R)-4-((R)-1-(benzylloxy)but-3-en-1-yl)-2,2-dimethyl-1,3-dioxolane (65.6 mg, 0.25 mmol, 1.0 equiv) was reacted following the general procedure, including K$_2$CO$_3$ washes during workup. Dioxane was used in place of DCE as a cosolvent. By $^1$H NMR
analysis of the crude product, the linear:branched ratio was >20:1, the E/Z isomer ratio was >20:1, and the diastereomeric ratio was 1:1. Flash chromatography (25% EtOAc/hexanes) yielded linear product contaminated by ca. 3 wt% 4-(1-(benzyloxy)-5-nitropent-2-en-1-yl)-2,2-dimethyl-1,3-dioxolane as a light yellow oil. A pure spectroscopic sample was obtained by reverse phase medium pressure liquid chromatography (SP: C18; MP: 50→90% MeCN/H2O).

Run 1 (67.3 mg, 0.158 mmol, 63% yield); run 2 (66.4 mg, 0.156 mmol, 62% yield); run 3 (67.2 mg, 0.158 mmol, 63%). **Average yield: 63%**. 1H NMR (500 MHz, CDCl3) δ 7.97 (m, 2H), 7.67 (ap. t, J = 7.6 Hz, 1H), 7.53 (ap. t, J = 7.8 Hz, 2H), 7.33 (m, 2H), 7.27 (m, 3H), 6.13 (dd, J = 9.3, 4.9 Hz, 1H, diastereomer A), 6.09 (dd, J = 8.8, 5.4 Hz, 1H, diastereomer B), 5.77-5.60 (m, 2H), 4.52 (d, J = 11.7 Hz, 1H), 4.33 (d, J = 12.0 Hz, 1H, diastereomer A), 4.30 (d, J = 11.7 Hz, 1H, diastereomer B), 4.02 (m, 2H), 3.80 (ddd, J = 12.4, 7.6, 4.8 Hz, 1H), 3.69 (ap. q, J = 6.0 Hz, 1H), 3.15 (m, 1H), 2.99 (m, 1H), 1.35 (m, 6H); 13C NMR (125 MHz, CDCl3) Mixture of diastereomers 188.3, 188.2, 138.0, 137.9, 135.0, 134.0, 133.9, 133.3, 133.1, 129.4, 129.0, 128.9, 128.5, 128.0, 127.9, 127.6, 127.2, 109.7, 89.1, 88.8, 79.8, 77.6, 77.5, 70.8, 70.6, 66.8, 66.8, 33.7, 33.5, 26.7, 26.6, 25.4, 25.3; IR (film, cm−1): 3064, 2989, 2931, 1693, 1554, 1452, 1371, 1213, 1153, 1091, 849, 752; HRMS (ESI) m/z calculated for C24H28NO6 [M+H]+: 426.1917, found 426.1905.

(±)-(E)-6-hydroxy-2-nitro-1-phenyltridec-4-en-1-one [71]: 1-undecen-4-ol (51.1 mg, 0.3 mmol, 1.0 equiv) was reacted following the general procedure, including K2CO3 washes during workup. By 1H NMR analysis of the crude product, the linear:branched ratio was >20:1 and the E/Z isomer ratio was >20:1. By 13C NMR the diastereomeric ratio was 1:1. Flash chromatography (30%
EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (78.1 mg, 0.234 mmol, 0.400 mmol scale, 59% yield); run 2 (57.2 mg, 0.172 mmol, 57% yield), run 3 (58.4 mg, 0.175 mmol, 58% yield). **Average yield: 58%**. 

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.96 (ap. d, $J = 8.3$ Hz, 2H), 7.67 (ap. t, $J = 7.4$ Hz, 1H), 7.54 (ap. t, $J = 7.1$ Hz, 1H), 6.09 (dd, $J = 9.2$, 5.0 Hz, 1H), 5.66 (m, 2H), 4.05 (1, $J = 6.0$ Hz, 1H), 3.08 (m, 1H), 2.91 (m, 1H), 1.44 (m, 2H), 1.26 (m, 10H), 0.88 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) *Mixture of diastereomers* 188.5, 139.1, 139.1, 134.9, 134.0, 129.4, 129.0, 122.8, 122.6, 89.2, 89.0, 72.3, 72.3, 37.2, 33.4, 33.3, 31.9, 29.6, 29.3, 25.4, 22.8, 14.2; IR (film, cm$^{-1}$): 3392, 3066, 2927, 2858, 1969, 1905, 1693, 1564, 1450, 1369, 1257, 1227, 974, 910, 733, 688; HRMS (ESI) $m/z$ calculated for C$_{19}$H$_{27}$NO$_4$Na [M+Na]$^+$: 356.1838, found 356.1844.

(±)-(E)-**tert-butyl (2-methyl-7-nitro-8-oxo-8-phenyloct-4-en-3-yl)carbamate** [72]: tert-butyl (2-methylhex-5-en-3-yl)carbamate (53.3 mg, 0.25 mmol, 1.0 equiv) was reacted following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was >20:1 and the E/Z isomer ratio was >20:1. By HPLC the diastereomeric ratio was 1:1. Flash chromatography (20% EtOAc/hexanes) yielded pure linear product as a white solid. Run 1 (50.7 mg, 0.135 mmol, 54% yield); run 2 (49.7 mg, 0.132 mmol, 53% yield). **Average yield: 53%**. 

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.95 (ap. d, $J = 8.3$ Hz, 2H), 7.67 (ap. t, $J = 7.4$ Hz, 1H), 7.54 (ap. t, $J = 7.1$ Hz, 1H), 6.09 (dd, $J = 9.3$, 4.9 Hz, 1H), 5.55 (m, 2H), 4.44 (m, 1H), 3.91 (br. s, 1H), 3.08 (m, 1H), 2.91 (m, 1H), 1.69 (m, 1H), 1.44 (s, 9H, *diastereomer A*), 1.42 (s, 9H, *diastereomer B*), 0.83 (m, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$) *Mixture of diastereomers* 188.4, 155.5, 135.6, 135.4, 134.9, 133.9, 129.4, 129.0, 123.4, 123.0, 89.2, 89.1, 79.5, 57.5, 57.2, 33.6, 32.4, 32.3, 28.5, 18.7,
18.3, 18.1; IR (film, cm$^{-1}$): 3415, 3064, 2964, 2927, 2873, 2735, 2556, 1367, 1252, 1171, 1039, 974, 688; HRMS (ESI) $m/z$ calculated for C$_{20}$H$_{29}$N$_2$O$_5$ [M+H]$^+$: 377.2076, found 377.2085.

(E)-2-nitro-1-phenyl-5-((R)-1-tosylpiperidin-2-yl)pent-4-en-1-one

[73]: (R)-2-allyl-1-tosylpiperidines (69.9 mg, 0.25 mmol, 1.0 equiv) was reacted following the general procedure, including K$_2$CO$_3$ washes during workup. By $^1$H NMR analysis of the crude product, the linear:branched ratio was >20:1, the E/Z isomer ratio was >20:1, and the diastereomeric ratio was 1:1. Flash chromatography (25% EtOAc/hexanes) yielded linear product contaminated by ca. 3 wt% 2-(4-nitrobut-1-en-1-yl)-1-tosylpiperidine as a light yellow oil. A pure spectroscopic sample was obtained by reverse phase medium pressure liquid chromatography (SP: C18; MP: 50→90% MeCN/H$_2$O). Run 1 (71.4 mg, 0.161 mmol, 65% yield); run 2 (75.1 mg, 0.170 mmol, 68% yield). **Average yield: 66%**. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.94 (ap. t, $J = 7.3$ Hz, 2H), 7.66 (m, 3H), 7.54 (ap. t, $J = 7.8$ Hz, 2H), 7.27 (d, $J = 8.3$ Hz, 2H), 6.04 (dd, $J = 9.0$, 5.1 Hz, 1H, diastereomer A), 6.00 (dd, $J = 9.3$, 4.6 Hz, 1H, diastereomer B), 5.55 (m, 2H), 4.52 (m, 1H), 3.61 (m, 1H), 3.06-2.78 (m, 3H), 2.41 (s, 3H, diastereomer A), 2.40 (s, 3H, diastereomer B), 1.64-1.41 (m, 4H), 1.40-1.24 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) Mixture of diastereomers 188.4, 143.2, 137.8, 137.6, 135.0, 135.0, 133.9, 133.8, 133.6, 133.5, 129.7, 129.6, 129.4, 129.4, 128.9, 128.9, 127.3, 127.2, 124.7, 124.7, 88.9, 88.8, 54.4, 54.0, 41.9, 41.7, 33.6, 33.6, 30.1, 29.8, 24.9, 24.8, 21.6, 19.1, 19.1; IR (film, cm$^{-1}$): 3026, 2941, 2860, 1919, 1693, 1562, 1336, 1153, 1093, 935, 752, 660; HRMS (ESI) $m/z$ calculated for C$_{23}$H$_{27}$N$_2$O$_5$S [M+H]$^+$: 443.1641, found 443.1645.
(E)-N,N-diethyl-5-nitro-6-oxo-6-phenylhex-2-enamide [74]: N,N-diethylbut-3-enamide (35.3 mg, 0.25 mmol, 1.0 equiv) was reacted following the general procedure. By $^1$H NMR analysis of the crude product, the linear:branched ratio was >20:1 and the E/Z isomer ratio was >20:1. A short silica plug (100% CH$_2$Cl$_2$; 5% MeOH/CH$_2$Cl$_2$), followed by flash chromatography (60% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (46.7 mg, 0.153 mmol, 61% yield); run 2 (27.9 mg, 0.0917 mmol, 0.156 mmol scale, 59 % yield). **Average yield: 60%**. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.98 (ap. d, $J = 7.3$ Hz, 2H), 7.68 (ap. t, $J = 7.4$ Hz, 1H), 7.55 (ap. t, $J = 7.9$ Hz, 2H), 6.79 (ddd, $J = 14.9, 8.2, 6.6$ Hz, 1H), 6.38 (dt, $J = 15.1, 1.3$Hz, 1H), 6.18 (dd, $J = 9.2, 5.0$ Hz, 1H), 3.41 (q, $J = 7.1$ Hz, 2H), 3.32 (q, $J = 7.0$ Hz, 2H), 3.27 (m, 1H), 3.07 (m, 1H), 1.16 (t, $J = 7.1$ Hz, 3H), 1.13 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) 187.9, 164.7, 136.3, 135.1, 133.7, 129.5, 129.1, 126.0, 87.9, 42.4, 41.0, 33.2, 15.0, 13.2; IR (film, cm$^{-1}$): 3440, 3064, 2978, 2935, 1693, 1662, 1610, 1562, 1450, 1362, 1265, 1146, 943, 781, 692; HRMS (ESI) $m/z$ calculated for C$_{16}$H$_{21}$N$_2$O$_4$ [M+H]$^+$: 305.1501, found 305.1498.

(E)-2-(4-nitro-5-oxo-5-phenylpent-1-en-1-yl)cyclohex-1-en-1-yl acetate [75]: 2-allylcyclohex-1-en-1-yl acetate (54.1 mg, 0.3 mmol, 1.0 equiv) was reacted following the general procedure, including K$_2$CO$_3$ washes during workup. By $^1$H NMR analysis of the crude product, the linear:branched ratio was 5.2:1 and the E/Z isomer ratio was >20:1. Flash chromatography (20% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (63.7 mg, 0.186 mmol, 62% yield); run 2 (62.8 mg, 0.183 mmol, 0.286 mmol scale, 64% yield). **Average yield: 63%**.
\( {^1}H \text{ NMR (500 MHz, CDCl}_3 \) \( \delta \) 7.95 (ap. d, \( J = 7.3 \text{ Hz, 2H)\), 7.67 (ap. t, \( J = 7.4 \text{ Hz, 1H)\), 7.53 (ap. t, \( J = 7.8 \text{ Hz, 2H)\), 6.41 (d, \( J = 15.6 \text{ Hz, 1H)\), 6.07 (dd, \( J = 9.0, 5.1 \text{ Hz, 1H)\), 5.51 (dt, \( J = 15.2, 7.5 \text{ Hz, 1H)\), 3.15 (m, 1H), 2.96 (m, 1H), 2.20 (m, 2H), 2.17 (s, 3H), 2.14 (m, 2H), 1.70 (m, 2H), 1.64 (m, 2H); \( ^{13}C \text{ NMR (125 MHz, CDCl}_3 \) \( \delta \) 188.5, 169.1, 146.6, 134.9, 134.1, 129.6, 129.4, 129.0, 121.2, 120.3, 89.3, 34.3, 27.9, 24.3, 22.6, 22.0, 21.0; IR (film, cm\(^{-1}\))): 3064, 2941, 2864, 1815, 1747, 1693, 1554, 1450, 1371, 1211, 1134, 970, 914, 733; HRMS (ESI) \( m/z \) calculated for \( C_{19}H_{22}NO_5 \) [M+H]\(^{+}\): 344.1498, found 344.1499.

(E)-2-nitro-1,5-diphenylpent-4-en-1-one [47]: Allylbenzene (29.5 mg, 0.25 mmol, 1.0 equiv) was reacted following the general procedure. By \(^1\)H NMR analysis of the crude product, the linear:branched ratio was 11:1 and the E/Z isomer ratio was >20:1. Flash chromatography (12\% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (48.3 mg, 0.172 mmol, 69\% yield); run 2 (53.1 mg, 0.189 mmol, 76\% yield), run 3 (63.7 mg, 0.226 mmol, 0.300 mmol scale, 75\% yield). **Average yield:** 73\%. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.99 (m, 2H), 7.67 (m, 1H), 7.54 (m, 2H), 7.30 (m, 4H), 7.24 (m, 1H), 6.56 (d, \( J = 15.9 \text{ Hz, 1H)\), 6.17 (dd, \( J = 9.0, 5.1 \text{ Hz, 1H)\), 6.13 (dt, \( J = 15.7, 7.2 \text{ Hz, 1H)\), 3.26 (dddd, \( J = 15.1, 8.9, 7.6, 1.3 \text{ Hz, 1H)\), 3.08 (dddd, \( J = 15.0, 6.8, 5.2, 1.5 \text{ Hz, 1H)\); \( ^{13}C \text{ NMR (125 MHz, CDCl}_3 \) \( \delta \) 188.4, 136.4, 135.4, 135.0, 134.0, 129.4, 129.0, 128.8, 128.1, 126.5, 121.7, 89.3, 34.2; IR (film, cm\(^{-1}\))): 3064, 3027, 2922, 1695, 1559, 1449, 967; HRMS (ESI) \( m/z \) calculated for \( C_{17}H_{15}NO_3\)Na [M+Na]\(^{+}\): 304.0950, found 304.0941.
(E)-2-nitro-1,5-diphenylhex-4-en-1-one [76]: But-3-en-2-yl benzene (39.7 mg, 0.3 mmol, 1.0 equiv) was reacted following the general procedure. By \(^1\)H NMR analysis of the crude product, the linear:branched ratio was >20:1 and the E/Z isomer ratio was >20:1. Flash chromatography (15% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (48.0 mg, 0.163 mmol, 54% yield); run 2 (38.8 mg, 0.131 mmol, 0.250 mmol scale, 53% yield). **Average yield: 54%**. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.99 (ap. d, \(J = 7.3\) Hz, 2H), 7.67 (ap. t, \(J = 7.4\) Hz, 1H), 7.54 (ap. t, \(J = 7.8\) Hz, 2H), 7.28 (m, 5H), 6.15 (dd, \(J = 8.8, 5.4\) Hz, 1H), 5.66 (ap. t, \(J = 7.4\) Hz, 1H), 3.30 (m, 1H), 3.08 (m, 1H), 2.06 (s, 3H); \(^1\)C NMR (125 MHz, CDCl\(_3\)) 188.8, 142.9, 140.7, 134.9, 134.1, 129.4, 129.0, 128.4, 127.5, 125.9, 119.5, 89.0, 30.3, 16.4; IR (film, cm\(^{-1}\)): 3059, 2924, 2856, 1693, 1554, 1448, 1371, 1255, 1184, 696; HRMS (ESI) \(m/z\) calculated for C\(_{18}\)H\(_{17}\)NO\(_3\)Na\([M+Na]^+\): 318.1106, found 318.1106. 1D NOE experiments (500 MHz, CDCl\(_3\)): Irradiation of the H-6 resonance at \(\delta\) 2.06 showed NOEs to H-3a at \(\delta\) 3.08, to H-3b at \(\delta\) 3.30, and to H-2’ at \(\delta\) 7.28. Irradiation of the H-3a resonance at \(\delta\) 3.08 showed NOEs to H-6 at \(\delta\) 2.06, to H-3b at \(\delta\) 3.30, to H-4 at \(\delta\) 5.66, to H-2 at \(\delta\) 6.15, and to H-2” at \(\delta\) 7.99. Irradiation of the H-4 resonance at \(\delta\) 5.66 showed NOEs to H-2’ at \(\delta\) 7.28, to H-3a at \(\delta\) 3.08, to H-3b at \(\delta\) 3.30, and to H-2 at \(\delta\) 6.15.

2-nitro-1,4-diphenylpent-4-en-1-one [77]: \(\alpha\)-Methylstyrene (39.0 \(\mu\)L, 0.30 mmol, 1.0 equiv) was reacted following the general procedure. Flash chromatography (5% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (41.8 mg, 0.149 mmol, 50% yield). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.82 (d, \(J = 7.6\) Hz, 2H), 7.64 (t, \(J = 7.5\) Hz, 1H), 7.47 (t, \(J = 7.8\) Hz, 2H), 7.42 – 7.30 (m, 5H), 6.09 (dd, \(J = 9.2, 5.0\))
Hz, 1H), 5.37 (s, 1H), 5.23 (s, 1H), 3.53 (dd, J = 15.3, 9.2 Hz, 1H), 3.40 (ddd, J = 15.3, 5.1, 1.3 Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 188.77, 141.91, 139.08, 134.82, 134.05, 129.22, 128.94, 128.91, 128.53, 126.51, 117.53, 87.92, 36.68.

Synthetic elaboration of the allylic alkylation products

(\textit{E})-5-cyclohexyl-1-phenylpent-4-en-1-one [79]: Prior to use, tributyltin hydride was vacuum distilled and $\alpha,\alpha'$-azoisobutyronitrile (AIBN) was recrystallized from acetone. \textit{NOTE}: The substrate must also be carefully purified, as trace quinone impurities were observed to catalyze undesired cleavage of the phenyl ketone to yield products such as 79. A 10 mL flame dried round bottom flask fitted with a water cooled condenser under argon atmosphere was charged with (\textit{E})-5-cyclohexyl-2-nitro-1-phenylpent-4-en-1-one 67 (57.5 mg, 0.2 mmol, 1.0 equiv) dissolved in benzene (1.5 mL) and a stir bar. To the flask was added AIBN (6.6 mg, 0.04 mmol, 0.20 equiv) dissolved in benzene (0.5 mL) and tributyltin hydride (106 $\mu$L, 0.4 mmol, 2.0 equiv). The reaction was refluxed for 8 h. The crude reaction mixture was filtered through a plug of silica and concentrated \textit{in vacuo}. Purification by flash chromatography (0→5% EtOAc/hexanes gradient) provided the pure product. Run 1 (31.3 mg, 0.129 mmol, 65%); run 2 (31.8 mg, 0.131 mmol, 66%). \textbf{Average yield: 66\%}. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.96 (ap. d, J = 7.1 Hz, 2H), 7.55 (ap. t, J = 7.3 Hz, 1H), 7.46 (ap. t, J = 7.7 Hz, 1H, 3.53 (dd, J = 15.3, 9.2 Hz, 1H), 3.40 (ddd, J = 15.3, 5.1, 1.3 Hz, 1H).
2H), 5.43 (m, 2H), 3.02 (ap. t, J = 7.4 Hz, 2H), 2.42 (m, 2H), 1.89 (m, 1H), 1.72-1.60 (m, 5H), 1.24 (m, 2H), 1.13 (m, 1H), 1.03 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) 200.0, 137.7, 137.2, 133.0, 128.7, 128.2, 126.0, 40.7, 38.8, 33.2, 27.5, 26.3, 26.2; IR (film, cm$^{-1}$): 3060, 3024, 2924, 2850, 1687, 1448, 1201, 968, 742, 690; HRMS (ESI) m/z calculated for C$_{17}$H$_{22}$ONa [M+Na]$^+$: 265.1568, found 265.1564.

(E)-1-nitrododec-3-ene [78]: A 50 mL round bottom flask was charged with (E)-2-nitro-1-phenyltridec-4-en-1-one 57 (47.6 mg, 0.15 mmol, 1.0 equiv) and a stir bar. To the flask was added silica gel (1.5 g) and MeOH (15 mL, 0.01M). The reaction vial was capped and stirred for 12 h at room temperature. The crude reaction mixture was filtered and concentrated in vacuo. Purification by flash chromatography (3% Et$_2$O/pet. ether) provided the pure product. Run 1 (29.6 mg, 0.139 mmol, 93%); run 2 (20.1 mg, 0.094 mmol, 0.100 mmol scale, 94%). **Average yield: 94%**. $^1$H NMR (500 MHz, CDCl$_3$) δ 5.58 (m, 1H), 5.34 (m, 1H), 4.39 (t, $J$ = 7.0 Hz, 2H), 2.68 (qd, $J$ = 7.0, 0.9 Hz, 2H), 1.99 (q, $J$ = 6.8 Hz, 2H), 1.36-1.22 (m, 12H), 0.88 (t, $J$ = 7.0 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) 135.8, 123.0, 75.6, 32.6, 32.0, 30.7, 29.6, 29.4, 29.3, 29.2, 22.8, 14.3; IR (film, cm$^{-1}$): 2956, 2926, 2854, 1554, 1433, 1379, 970; HRMS (Cl) m/z calculated for C$_{12}$H$_{24}$NO$_2$ [M+H]$^+$: 214.1807, found 214.1797.
Stoichiometric Kinetic Studies

**Figure 22:** Stoichiometric allylic C-H cleavage

![Stoichiometric allylic C-H cleavage](image)

**Figure 22:** A ½ dram borosilicate vial was charged with catalyst 1 (10.1 mg, 0.020 mmol, 1.0 equiv) or catalyst 49 (10.6 mg, 0.020 mmol, 1.0 equiv) and a stir bar. To this was added 1-undecene 53 (3.1 mg, 0.020 mmol, 1 equiv) as a stock solution in dioxane (300 μL). The reaction was allowed to stir for the desired interval at 45°C under air, at which time an acetone solution (250 μL) of n-Bu₄NCl (22.2 mg, 0.080 mmol, 4 equiv) was added via syringe. The anion exchange proceeded at room temperature for 60 min. The mixture was filtered over a plug of Celite (to remove metallic Pd) and concentrated in vacuo. To the crude reaction mixture was added 1,4-dimethoxybenzene (0.8 mg, 0.0060 mmol, 0.30 equiv) as a stock solution in CDCl₃. The crude mixture was dissolved completely in additional CDCl₃ and a sample was removed for
1H NMR analysis. Yield was determined by integration of olefinic product peaks relative to 1,4-dimethoxybenzene. Yields are reported as the average of 3 runs, with error bars representing standard deviation.

**Figure 23:** Stoichiometric π-allyl functionalization

**Figure 23:** A 1 dram (4 mL) borosilicate vial was charged with 1,2-bis(phenylsulfinyl)ethane L1 (20.9 mg, 0.075 mmol, 1.5 equiv) or 1,2-bis(benzylsulfinyl)ethane L2 (23.0 mg, 0.075 mmol, 1.5 equiv), bis[acetato(1,2,3-triaphato-undecene)palladium (II)] 2 (15.9 mg, 0.025 mmol, 1.0 equiv), benzylnitromethane 16 (82.6 mg, 0.50 mmol, 10 equiv), and a stir bar. To this was added dioxane (525 μL) and DMSO (225 μL). The reaction vial was capped and stirred at 45°C for the desired interval. The vial was cooled to room temperature, and the reaction mixture was diluted
with saturated aqueous NH₄Cl (15 mL) and extracted with diethyl ether (10 mL). The organic layer was washed with 5% aqueous K₂CO₃ (15 mL). The combined aqueous layers were extracted with diethyl ether (2 x 10 mL). The combined organics were dried over MgSO₄. The mixture was filtered and concentrated in vacuo. To the crude reaction mixture was added 1,4-dimethoxybenzene (2.1 mg, 0.015 mmol, 0.30 equiv) as a stock solution in CDCl₃. The crude mixture was dissolved completely in additional CDCl₃ and a sample was removed for ¹H NMR analysis. Yield was determined by integration of olefinic product peaks relative to 1,4-dimethoxybenzene. Yields are reported as the average of 2 runs.

Catalytic Kinetic Studies

Catalytic kinetics rule out product inhibition

\[ y = -0.00001x + 0.269 \]

\[
\begin{align*}
k_{\text{obs}} / \\
\text{mM-min}^{-1} & \\
0 & 0.1 & 0.2 & 0.3 & 0.4 & 0.5 & 0.6 & 0.7 & 0.8 & 0.9 & 1 \\
0 & 50 & 100 & 150 & 200 & 
\end{align*}
\]

\[ [\text{Product}]_0 / \text{mM} \]
Figure 18: A ½ dram borosilicate vial was charged with catalyst 1 (5.0 mg, 0.010 mmol, 0.1 equiv), benzylnitromethane 16 (66.1 mg, 0.40 mmol, 4 equiv), dimethylbenzoquinone 58 (15.0 mg, 0.11 mmol, 1.1 equiv), product 57 (varied equivalents) and a stir bar. To this was added 1-undecene 53 (20.5 μL, 0.10 mmol, 1 equiv) and 4-nitrophenetole (5.0 mg, 0.030 mmol, 0.3 equiv, internal standard) as a stock solution in DCE (105 μL) and DMSO (45 μL). The vial was fitted with a cap with a septum and the reaction was allowed to stir for 2 hours at 45°C under air. Reaction aliquots (10 μL) were periodically removed via syringe and filtered through a silica plug using iPrOH:hexanes (1:4) solvent. The crude samples were analyzed by HPLC with Agilent Technologies, Inc. Zorbax CN 0.46 cm x 25 cm column. A flow rate of 1.5 mL/min at 35.0°C with 99:1 hexanes:2-propanol with detection at 214 nm gave the 4-nitrophenetole standard at 4.53 min and the linear product at 5.47 min. Yield was determined by comparison to a standard curve (see Figure 24). Initial rate was determined from a plot of yield versus time (see Figure 25 for example). Rates are reported as the average of 3 runs, with error bars representing standard deviation.
Figure 24: HPLC calibration curve for \((E)-2\text{-nitro-1-phenyldodec-4-en-1-one}\) versus nitrophenetole standard

\[ y = 0.3162x \]

\[ R^2 = 1 \]

Figure 25: Sample plot for initial rates with varied DMSO equivalents

\[ y = 0.0061x - 0.0003 \]

\[ R^2 = 0.9999 \]

\[ y = 0.0088x - 0.0003 \]

\[ R^2 = 0.9997 \]

\[ y = 0.0174x - 0.0022 \]

\[ R^2 = 0.9991 \]

\[ y = 0.0312x - 0.0048 \]

\[ R^2 = 0.9993 \]

\[ y = 0.0484x - 0.0079 \]

\[ R^2 = 0.9996 \]
Enantiomeric Excess

Retention of configuration at the C6 stereocenter was determined by NMR analysis of a bis-Mosher ester derivative of the product. Comparison of the $^1$H NMR spectrum to the reported spectra$^{68}$ revealed only one diastereomer at S/N >200:1, confirming retention of configuration at the stereocenter.

Retention of configuration at the C7 stereocenter was determined by chiral GC analysis of a derivative of the product using a J&W Scientific β-cyclodextrin column (30m, 0.25mm, 0.25μm). Using an isothermal method at 105°C gave the major enantiomer at 249.1 min and the minor enantiomer at 254.6 min. Enantiopurity was determined to be 92%.

Enantiopurity of (R)-6-methyldec-9-en-5-one was determined by chiral GC analysis using a J&W Scientific β-cyclodextrin column (30m, 0.25mm, 0.25μm). Using an isothermal method at 60°C gave the major enantiomer at 40.71 min and the minor enantiomer at 41.70 min. Enantiopurity was determined to be 92%.
Retention of configuration at the C2’ stereocenter was determined by chiral HPLC analysis of a derivative of the product using a Daicel Chemical Industries, Ltd. Chiralcel OJ-H 0.46 cm x 25 cm column. Using the reported conditions, a flow rate of 1.0 mL/min at 30.0°C with 80:20 hexanes:2-propanol with detection at 260 nm gave the major enantiomer at 9.86 min and the minor enantiomer at 10.64 min. Enantiopurity was determined to be 89%.

Enantiopurity of (R)-2-allyl-1-tosylpiperidine was determined by HPLC analysis using a Daicel Chemical Industries, Ltd. Chiralcel OD-H 0.46 cm x 25 cm column. Using the reported conditions, a flow rate of 0.5 mL/min at 25.0°C with 98:2 hexanes:2-propanol with detection at 260 nm gave the major enantiomer at 18.08 min and the minor enantiomer at 20.83 min. Enantiopurity was determined to be 89%.

Starting Materials

Spectral data for known compounds:

(S)-4,8-dimethylnona-1,7-diene

(R)-4-((R)-1-(benzyloxy)but-3-en-1-yl)-2,2-dimethyl-1,3-dioxolane

1-undecen-4-ol

tert-butyl (2-methylhex-5-en-3-yl)carbamate

2-allyl-1-tosylpiperidine

N,N-diethylbut-3-enamide

2-allylcyclohex-1-en-1-yl acetate
but-3-en-2-ylbenzene

(R)-6-methyldec-9-en-5-one: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.77 (ddt, $J = 17.1, 10.3, 6.7$ Hz, 1H), 5.01 (m, 1H), 4.96 (m, 1H), 2.54 (sextet, $J = 6.9$ Hz, 1H), 2.43 (m, 2H), 2.02 (m, 2H), 1.77 (m, 1H), 1.54 (m, 2H), 1.40 (m, 1H), 1.30 (sextet, $J = 7.4$ Hz, 2H), 1.07 (d, $J = 7.1$ Hz, 3H), 0.91 (t, $J = 7.3$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) 214.9, 138.3, 115.1, 45.6, 41.2, 32.1, 31.6, 25.9, 22.5, 16.6, 14.0; IR (film, cm$^{-1}$): 3078, 2960, 2933, 2873, 1712, 1460, 1377, 910; HRMS (ESI) m/z calculated for C$_{11}$H$_{21}$O [M+H]$^+$: 169.1592, found 169.1594; [$\alpha$]$_D^{23}$ = -17.9° (c=1.0, CHCl$_3$).

1,2-bis(cyclohexylsulfinyl)ethane: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 3.17 (m, 2H), 3.01 (m, 2H), 2.66 (m, 2H), 2.15 (m, 2H), 1.91 (m, 6H), 1.72 (m, 2H), 1.54-1.26 (m, 10H); $^{13}$C NMR (125 MHz, CDCl$_3$) Mixture of diastereomers 60.5, 59.8, 42.6, 41.5, 26.3, 26.2, 25.6, 25.6, 25.5, 25.4, 25.4, 25.3, 25.2, 25.2; IR (film, cm$^{-1}$): 2916, 2850, 1446, 1128, 1113, 1020, 800, 592; HRMS (ESI) m/z calculated for C$_{14}$H$_{27}$O$_2$S$_2$ [M+H]$^+$: 291.1452, found 291.1451.

1,2-bis(tert-butylsulfinyl)ethane: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 2.98 (m, 2H), 2.92 (m, 1H), 2.81 (m, 1H), 1.29 (s, 18H); $^{13}$C NMR (125 MHz, CDCl$_3$) Mixture of diastereomers 54.3, 53.9 40.5, 39.4, 22.9, 22.9; IR (film, cm$^{-1}$): 2960, 2929, 2870, 1468, 1180, 1099, 1039, 812, 584; HRMS (ESI) m/z calculated for C$_{10}$H$_{23}$O$_2$S$_2$ [M+H]$^+$: 239.1139, found 239.1139.
**1,2-bis(propylsulfinyl)ethane:** \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ 3.21 (m, 2H), 3.02 (m, 2H), 2.83 (m, 2H), 2.69 (m, 2H), 1.84 (sextet, \(J = 7.5\) Hz, 4H), 1.10 (t, \(J = 7.4\) Hz, 6H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) *Mixture of diastereomers* 55.2, 54.8, 45.0, 44.4, 16.5, 16.4, 13.4; IR (film, cm\(^{-1}\)): 2960, 2922, 2873, 1425, 1321, 1136, 1011, 740; HRMS (ESI) \(m/z\) calculated for C\(_8\)H\(_{18}\)O\(_2\)S\(_2\)Na [M+Na]\(^+\): 233.0646, found 233.0648.

**Spectroscopic Studies**

**Infrared Spectroscopy:** Spectra were collected on a Perkin-Elmer Spectrum BX FT-IR instrument with a resolution of 1.0 cm\(^{-1}\) using an International Crystal Labs model SL-4 0.2 mm NaCl solution cell. Solution phase samples were prepared by dissolving 0.01 mmol substrate in 1 mL CH\(_2\)Cl\(_2\) and waiting 30 min for equilibration. Solid phase samples were prepared by grinding 0.01 mmol substrate with ca. 500 mg KBr and producing a solid disk using a manual press.

**UV-Visible Spectroscopy:** Spectra were collected on a Shimadzu Pharma-Spec UV-1700 instrument with a sampling frequency of 0.5 nm using a 10.00 mm quartz cuvette. Samples were prepared by dissolving 0.01 mmol substrate in 1 mL CH\(_2\)Cl\(_2\) and waiting 30 min for equilibration, from which an aliquot of 10 μL was removed and diluted with 0.6 mL CH\(_2\)Cl\(_2\).

\(^1\)H NMR Spectroscopy: Spectra were collected on a Varian Unity-500 (500 MHz) spectrometer equipped with variable temperature control. Samples were prepared by dissolving 0.01 mmol substrate in 0.7 mL CDCl\(_3\) and waiting 30 min for equilibration. Spectra were collected at +20°C and -60°C.
Notes: No association between Pd(OAc)$_2$ and bis-sulfoxide ligand can be observed by standard spectroscopic techniques (IR, UV-Vis, NMR), as judged by a lack of new peaks and no significant shifts in existing peaks. Most samples were allowed 30 min for equilibration; however, spectra were unchanged after 24 h equilibration. Similarly, catalyst 1 (complexed 24 h in refluxing CH$_2$Cl$_2$) was spectroscopically indistinguishable from mixed Pd(OAc)$_2$+bis-sulfoxide. Attempts to crystallize the catalyst result in isolation of separate Pd(OAc)$_2$ trimer and bis-sulfoxide crystals.\textsuperscript{78} Previously characterized complexes with Pd-sulfoxide coordination exhibit large shifts in spectra from non-complexed materials.\textsuperscript{79} McDonald and Stahl reported observation of Pd(TFA)$_2$/DMSO association by NMR and IR, however under identical conditions no association of Pd(OAc)$_2$/DMSO was observed (data not shown).\textsuperscript{80} In the absence of any observable association of metal and ligand, it is impractical to attempt to monitor ligand exchange to provide evidence for alkyl sulfoxides competing with DMSO.

**Pd(OAc)$_2$:** $^1$H NMR (500 MHz, CDCl$_3$, 23°C) δ 2.00 (s, 6H); $^1$H NMR (500 MHz, CDCl$_3$, -60°C) δ 2.04 (s, 6H); IR (CH$_2$Cl$_2$, cm$^{-1}$): 1614, 1434, 1354; UV-Vis (CH$_2$Cl$_2$, $\lambda_{\text{max}}$, nm) 397.

**1,2-bis(phenylsulfinyl)ethane** (meso diastereomer): $^1$H NMR (500 MHz, CDCl$_3$, 23°C) δ 7.55 (m, 10H), 3.05 (s, 4H); $^1$H NMR (500 MHz, CDCl$_3$, -60°C) δ 7.54 (m, 10H), 3.03 (s, 4H); IR (CH$_2$Cl$_2$, cm$^{-1}$): 1478, 1444, 1412, 1085, 1070, 1046, 1022, 999; UV-Vis (CH$_2$Cl$_2$, $\lambda_{\text{max}}$, nm) 250.
**1,2-bis(benzylsulfinyl)ethane** (mixture of diastereomers): $^1$H NMR (500 MHz, CDCl$_3$, 23°C) δ 7.37 (m, 6H), 7.27 (m, 4H), 4.03 (m, 4H), 3.06-2.82 (m, 4H); $^1$H NMR (500 MHz, CDCl$_3$, -60°C) δ 7.38 (m, 6H), 7.26 (m, 4H), 4.07 (m, 4H), 3.03-2.79 (m, 4H); IR (CH$_2$Cl$_2$, cm$^{-1}$): 1497, 1456, 1070, 1047, 1031; UV-Vis (CH$_2$Cl$_2$, $\lambda_{max}$, nm) N/A.

**Pd(OAc)$_2$ + 1 equiv 1,2-bis(phenylsulfinyl)ethane** [1]: $^1$H NMR (500 MHz, CDCl$_3$, 23°C) δ 7.56 (m, 10H), 3.05 (s, 4H), 2.00 (s, 6H); $^1$H NMR (500 MHz, CDCl$_3$, -60°C) δ 7.55 (m, 10H), 3.03 (s, 4H), 2.05 (s, 6H); IR (CH$_2$Cl$_2$, cm$^{-1}$): 1614, 1478, 1444, 1439, 1435, 1432, 1428, 1424, 1084, 1070, 1046, 1023, 999; UV-Vis (CH$_2$Cl$_2$, $\lambda_{max}$, nm) 392, 247.

**Pd(OAc)$_2$ + 1 equiv 1,2-bis(benzylsulfinyl)ethane** [49]: $^1$H NMR (500 MHz, CDCl$_3$, 23°C) δ 7.37 (m, 6H), 7.27 (m, 4H), 4.04 (m, 4H), 3.04-2.81 (m, 4H), 2.00 (s, 6H); $^1$H NMR (500 MHz, CDCl$_3$, -60°C) δ 7.37 (m, 6H), 7.25 (m, 4H), 4.07 (m, 4H), 3.03-2.79 (m, 4H), 2.05 (s, 6H); IR (CH$_2$Cl$_2$, cm$^{-1}$): 1614, 1497, 1455, 1439, 1432, 1354, 1070, 1046, 1031; UV-Vis (CH$_2$Cl$_2$, $\lambda_{max}$, nm) 394.

**bis[acetato(1,2,3-trihapto-undecene)palladium (II)]**: $^1$H NMR (500 MHz, CDCl$_3$, 23°C) δ 5.17 (m, 1H), 3.65 (m, 2H), 2.63 (m, 1H), 2.01 (bs, 3H), 1.56-1.16 (m, 14H), 0.88 (t, $J = 6.8$ Hz, 3H); $^1$H NMR (500 MHz, CDCl$_3$, -60°C) δ 5.34-4.97 (m, 1H), 3.89-3.43 (m, 2H), 2.84-2.43 (m, 1H), 2.04 (m, 3H), 1.57-1.25 (m, 14H), 0.82 (m, 3H); IR (CH$_2$Cl$_2$, cm$^{-1}$): 2929, 2859, 1577, 1422, 1217; UV-Vis (CH$_2$Cl$_2$, $\lambda_{max}$, nm) 277.
bis[acetato(1,2,3-trihapto-undecene)palladium (II)] + 1 equiv 1,2-bis(phenylsulfinyl)ethane:

$^1$H NMR (500 MHz, CDCl$_3$, 23°C) δ 7.53 (m, 10H), 5.19 (m, 1H), 3.64 (m, 2H), 2.63 (m, 1H), 3.05 (s, 4H), 2.02 (bs, 3H), 1.53-1.17 (m, 14H), 0.87 (t, $J = 6.8$ Hz, 3H); $^1$H NMR (500 MHz, CDCl$_3$, -60°C) δ 7.54 (m, 10H), 5.33-4.97 (m, 1H), 3.89-3.41 (m, 2H), 3.04 (s, 4H), 2.83-2.43 (m, 1H), 2.04 (m, 3H), 1.60-1.26 (m, 14H), 0.82 (m, 3H); IR (CH$_2$Cl$_2$, cm$^{-1}$): 2926, 2854, 1577, 1478, 1444, 1423, 1085, 1070, 1047, 1022, 999; UV-Vis (CH$_2$Cl$_2$, $\lambda_{max}$, nm) 248.

bis[acetato(1,2,3-trihapto-undecene)palladium (II)] + 1 equiv 1,2-bis(benzylsulfinyl)ethane:

$^1$H NMR (500 MHz, CDCl$_3$, 23°C) δ 7.37 (m, 6H), 7.27 (m, 4H), 5.17 (m, 1H), 4.04 (m, 4H), 3.65 (m, 2H), 3.05-2.82 (m, 4H), 2.63 (m, 1H), 2.00 (bs, 3H), 1.55-1.13 (m, 14H), 0.87 (t, $J = 6.7$ Hz, 3H); $^1$H NMR (500 MHz, CDCl$_3$, -60°C) δ 7.37 (m, 6H), 7.26 (m, 4H), 5.37-4.95 (m, 1H), 4.07 (m, 4H), 3.89-3.43 (m, 2H), 3.03-2.43 (m, 5H), 2.05 (m, 3H), 1.51-1.26 (m, 14H), 0.81 (bs, 3H); IR (CH$_2$Cl$_2$, cm$^{-1}$): 2931, 2856, 1577, 1497, 1455, 1430, 1422, 1072, 1046, 1030, 897; UV-Vis (CH$_2$Cl$_2$, $\lambda_{max}$, nm) N/A.
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CHAPTER 3

ALLYLIC C-H ALKYLATION USING TERTIARY NUCLEOPHILES

3.1 INTRODUCTION

The work discussed in Chapters 1 and 2 described the discovery of an allylic C-H alkylation reaction and the expansion of the substrate scope of this reaction to encompass virtually any α-olefin. However, the reaction remained relatively limited in the scope of nucleophiles that could be appended to the olefin substrate. The nucleophiles which were suitable for this reaction were activated methylene compounds bearing two strongly electron-withdrawing groups. Relatively little variation of the nucleophile was possible beyond interchanging different electron-withdrawing moieties.

While considering the options for future development of the allylic C-H alkylation we concluded that, rather than appending a predefined subunit to a substrate, a reaction that could support variation of each coupling partner would be preferable. This principle is demonstrated in the Pd(0)-catalyzed allylic alkylation literature, for example in the first asymmetric synthesis of strychnine by Overman and coworkers. A palladium(0)-catalyzed alkylation of an allylic oxygenate substrate stereospecifically forges the C14-C21 bond, found in the final product, at an early stage in the sequence (Figure 26). Notably, all of the core carbon atoms of both the electrophile and the nucleophile are included in the final product. This application was possible because both of the coupling partners could be tailored to meet the requirements of the desired

Figure 26: Total synthesis of strychnine using allylic alkylation as a key step
reaction; the nucleophile and the electrophile must each tolerate a degree of modification.

As an initial step toward a more versatile nucleophile coupling partner, we envisioned substituting the parent compound with an aliphatic chain. This activated methine compound would be more sterically hindered, but its $pK_a$ should remain within the desired range. Tertiary nucleophiles are commonly used in palladium(0) catalyzed allylic alkylations;$^{82}$ substitution of the nucleophile prevents overalkylation.$^{83}$ Two allylic C-H alkylation methods have been reported which employ tertiary nucleophiles, however, in both cases the regio- and stereoselectivities are variable and the reaction is constrained to a narrow substrate scope; propene and 1,4 dienes, respectively, are the only reported substrates.$^{14,84}$

If we could develop a more versatile and reliable allylic C-H alkylation with tertiary nucleophiles, we envisioned a number of synthetic applications. By tethering the nucleophile to the substrate through the aliphatic substituent, a macrocyclization protocol could be envisioned (Figure 27). An analogous Pd(0)-catalyzed macrocyclization has been applied repeatedly in total synthesis.$^{85,86}$ Alternatively, we reasoned that a tertiary nucleophile could be well-suited to the development of an asymmetric allylic alkylation. The stereogenic center formed in the reaction would be fully substituted and therefore not susceptible to epimerization, which is a rapid process for enolizable centers under these conditions.$^{87}$

*Figure 27:* Proposed synthetic applications for tertiary nucleophiles

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<thead>
<tr>
<th>I. Macrocyclization</th>
<th>II. Asymmetric alkylation</th>
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</table>

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3.2 RESULTS AND DISCUSSION

Our investigation began with a prototypical tertiary nucleophile, methyl 2-nitropropionate. We were delighted to find that upon reaction with allylbenzene under our reported conditions this nucleophile afforded a 30% yield of the desired product (Table 9, entry 1). Encouragingly, the reaction proceeded with excellent regioselectivity and stereoselectivity (>20:1 linear:branch, >20:1 E:Z). The yield of the process was improved through standard optimization of reaction conditions. A more acidic nucleophile, 2-nitropropiophenone, led to a moderate improvement in yield (entry 2). Consistent with our expectation that tertiary nucleophiles would react more slowly due to their steric bulk, switching from 1 to the more robust and longer-lived catalyst 49 (see Chapter 2) was productive (entry 3). Finally, adjusting the ratio of the cosolvents to 1:4 dioxane:DMSO provided the final improvement to a synthetically useful yield (entry 4).

Table 9: Optimization of the allylic alkylation with tertiary nucleophiles

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>nucleophile</th>
<th>yield</th>
<th>L:B</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>R = OMe, 18</td>
<td>30%</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>R = Ph, 80</td>
<td>32%</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>R = Ph, 81</td>
<td>38%</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>4</td>
<td>49</td>
<td>81</td>
<td>50%</td>
<td>&gt;20:1</td>
</tr>
</tbody>
</table>

We investigated the scope of tertiary nucleophiles suitable for the allylic C–H alkylation reaction (Table 10). A variety of functionalities, including ketone, ester, sulfonyl and nitro moieties were found to be suitable electron withdrawing groups (entries 1, 4, 5). Substitution of the aromatic ring of the nucleophile was tolerated, including an aryl chloride which provided a handle for further derivatization (entries 2, 3). The alkyl substituent of the nucleophile could be
varied to longer chains or a cyclic tetralone derivative (entries 6, 7), and additional non-participating functional groups could be included on the nucleophile (entry 11). Product 92 was notable because the alcohol moiety could potentially be esterified to a carboxylate on the substrate, thereby providing a macrocyclic annulation protocol. For reactions in which the nucleophile coupling partner was particularly valuable, it could be used in limiting quantities with good yields (entry 12).

A nucleophile pKa dependence was noted, consistent with the notion that the nucleophile must undergo facile keto-enol tautomerisation or deprotonation by endogenous acetate base in

### Table 10: Nucleophile scope of the allylic C-H alkylation

<table>
<thead>
<tr>
<th>entry</th>
<th>major product</th>
<th>isolated yield L^a</th>
<th>L:B, E:Z &gt;20:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
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<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

^a Allylbenezene 18 (1 equiv.), nucleophile (2 equiv.), 49 (10 mol%), DMBQ 88 (1.5 equiv.), DMSO/Dioxane (4:1, 0.33M), 45°C, 24h. Average of 2 runs. By 1H NMR analysis of the crude, only one regio- and olefin isomer of the product was observed. ^b Nucleophile (3 equiv.) ^c Allylbenezene 18 (2 equiv.), nucleophile (1 equiv.)
Methyl Meldrum’s acid, a uniquely acidic dicarbonyl compound, was found to be a suitable nucleophile (entry 8). Additionally, other carbonyl compounds were found to effect C-C bond formation provided that all three substituents were electron withdrawing (entries 9, 10).

Our investigation subsequently shifted to an exploration of the scope of $\alpha$-olefin substrates suitable for the reaction (Table 11). We found that a variety of substituted allylbenzenes were readily functionalized, including substrates bearing electron donating and electron withdrawing groups (entries 2, 3). Notably, in all cases high regioselectivity for formation of linear alkylation product was observed. This selectivity, arising from nucleophilic attack at the least hindered terminus of the $\pi$-allyl intermediate, contrasted with our previous observation of variable regioselectivity with less bulky nucleophiles. The reaction was relatively insensitive to steric hindrance of the substrate (entry 6), and functional groups which may be further elaborated via Pd(0) cross-coupling were inert to the reaction conditions (entries 4, 5). A number of activated, non-aromatic compounds were efficiently alkylated (entries 7-9). We found, however, that unactivated $\alpha$-olefin substrates furnished only modest yields of 20-30%. A variety of heterocyclic functionalities which are prevalent in biologically active molecules, such as indole, chromene and diketopiperazine was tolerated (entries 10-12). The xanthene core, important in materials and synthetic applications, was functionalized smoothly (entry 14). This method was also suitable for derivatization of natural products. The common steroid (+)-estrone was elaborated via a short synthetic route (entry 13). Similarly, (-)-maculosin, a naturally occurring diketopiperazine phytotoxin isolated from a fungal pathogen of spotted knapweed, was readily derivatized (entry 12).
**Table 11**: Olefin scope of the allylic C-H alkylation

<table>
<thead>
<tr>
<th>entry</th>
<th>major product</th>
<th>isolated yield $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$L:B, E:Z &gt; 20:1$</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>$X = H, 82$</td>
<td>57%</td>
</tr>
<tr>
<td>4</td>
<td>$X = OMe, 93$</td>
<td>63%</td>
</tr>
<tr>
<td>5</td>
<td>$X = CF_3, 94$</td>
<td>67%</td>
</tr>
<tr>
<td>6</td>
<td>$X = Br, 95$</td>
<td>66%</td>
</tr>
<tr>
<td>7</td>
<td>$X = B(MID)A, 96$</td>
<td>64%$^b$</td>
</tr>
<tr>
<td>8</td>
<td>$X = OTBS, 97$</td>
<td>63%</td>
</tr>
<tr>
<td>9</td>
<td>$X = 98$</td>
<td>51%</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>$X = 99$</td>
<td>62%</td>
</tr>
<tr>
<td>12</td>
<td>$X = 100$</td>
<td>78%</td>
</tr>
<tr>
<td>13</td>
<td>$X = 101$</td>
<td>53%</td>
</tr>
<tr>
<td>14</td>
<td>$X = 102$</td>
<td>60%</td>
</tr>
<tr>
<td>15</td>
<td>$X = 103$</td>
<td>50%$^c$</td>
</tr>
<tr>
<td>16</td>
<td>$X = 104$</td>
<td>61%$^c$</td>
</tr>
<tr>
<td>17</td>
<td>$X = 105$</td>
<td>52%</td>
</tr>
</tbody>
</table>

$^a$ Olefin (1 equiv.), 2-nitropropiophenone 81 (2 equiv.), 49 (10 mol%), DMBQ 98 (1.5 equiv.), DMSO/1,4-dioxane (4:1, 0.33 M), 45 C, 24 h. Average of 2 runs. By $^1$H NMR analysis of the crude, only one regio- and olefin isomer of the product was observed.

$^b$ MIDA = Methyliminodiacetate. $^c$ d.r. = 1:1.
The strategy of C–H activation is often described as a means to rapidly build molecular complexity. It possesses an inherent advantage over traditional methods because it eliminates preactivation of substrates common to many C-C bond forming reactions. We sought to demonstrate this principle by effecting two sequential allylic alkylation reactions, exploiting the divergent reactivities of our previously reported conditions and the present work (Figure 28). Thus, beginning with three simple compounds available in bulk quantities from commercial sources, we first coupled allylcyclohexane and benzoylnitromethane to furnish 67 (see Table 8, entry 2). Taking advantage of the latent nucleophilicity of this product, we subsequently reacted it with allylbenzene to produce the fully substituted compound 107 in only two steps, having incorporated all but four hydrogen atoms of the substrates in the final product. Notably, the sequence proceeded in 56% overall yield. In the second step, the more complex and valuable nucleophile component was used in limiting quantities with good results.

**Figure 28:** Sequential allylic C-H alkylation reactions

3.3 CONCLUSIONS

This work resulted in the development of an intermolecular allylic C-H alkylation reaction using trisubstituted nucleophiles. Modest optimization of the reaction conditions allowed a variety of nucleophiles bearing two electron-withdrawing groups and an aliphatic substituent to participate in the alkylation. The addition of an aliphatic chain opens a window for diversification of the nucleophile coupling partner. A wide variety of nucleophiles was explored,
including examples bearing more elaborate side chains. Future efforts will focus on the
development of a macrocyclization protocol by tethering the nucleophile to the substrate, and an
enantioselective allylic alkylation.

3.4 EXPERIMENTAL SECTION

**General Information:** All commercially obtained reagents for the allylic alkylation reaction
were used as received: 2,6-dimethylbenzoquinone, allylbenzene, estragole, triacetylmethane,
2,2,5-trimethyl-1,3-dioxane-4,6-dione (Sigma-Aldrich); 1-allylcyclohexene (ChemSampCo),
ethyl diacetoacetate (Alfa Aesar). Catalyst 49 was prepared according to the published
procedure.\(^{54}\) Catalysts 49 was stored at 4°C and weighed out in air prior to use. Dioxane was
purified prior to use by passage through a bed of activated alumina (Glass Contour, Laguna
Beach, California). Dimethyl sulfoxide (DMSO) was obtained from Fisher Scientific and stored
under argon. All allylic alkylation reactions were run under air. Thin-layer chromatography
(TLC) was conducted with E. Merck silica gel 60 F254 precoated plates (0.25 mm) and
visualized with UV and potassium permanganate stain. Flash chromatography was performed as
described by Still using ZEOprep 60 ECO 43-60 micron silica gel (American International
Chemical, Inc.).\(^{35}\) Medium pressure liquid chromatography was performed on a Teledyne Isco
CombiFlash Rf machine using pre-packed RediSep columns (12g C18) at a rate of 30 mL/min.

\(^1\)H NMR spectra were recorded on a Varian Unity-400 (400 MHz), Varian Inova-500 (500
MHz), or Varian Unity-500 (500 MHz) spectrometer and are reported in ppm using solvent as an
internal standard (CHCl\(_3\) at 7.26 ppm). Data reported as: s = singlet, d = doublet, t = triplet, q =
quartet, p = pentet, m = multiplet, b = broad, ap = apparent; coupling constant(s) in Hz;
integration. Proton-decoupled \(^{13}\)C NMR spectra were recorded on a Varian Unity-500 (125
MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl\(_3\) at
77.16 ppm). Stereoselectivity of the allylic alkylation reaction was determined by $^1$H NMR analysis of the crude reaction mixture. IR spectra were recorded as thin films on NaCl plates on a Perkin-Elmer Spectrum BX FT-IR and are reported in frequency of absorption (cm$^{-1}$). High-resolution mass spectra were obtained at the University of Illinois Mass Spectrometry Laboratory. Optical rotations were obtained using a JAS.CO DIP-360 digital polarimeter and a 3.5 x 50 mm cell and are reported as follows: concentration (c = g / 100 mL), solvent.

**General Procedure for the Allylic Alkylation:** An oven dried one dram (4 mL) borosilicate vial was charged with Pd[1,2-bis(benzylsulfinyl)ethane](OAc)$_2$ 49 (0.10 equiv, 0.030 mmol) and 2,6-dimethylbenzoquinone (1.5 equiv, 0.45 mmol). The olefin (1 equiv, 0.30 mmol), nucleophile (2.0 equiv, 0.60 mmol), dimethylsulfoxide (0.72 mL), dioxane (0.18 mL) and a stir bar were added sequentially via syringe to the reaction vial. The reaction setup is performed open to the atmosphere. The reaction vial was capped and stirred at 45°C for 24 hours in an oil bath. The vial was cooled to room temperature, and the reaction mixture was diluted with saturated aqueous NH$_4$Cl (40 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organics were dried over MgSO$_4$. The mixture was filtered and concentrated in vacuo. Purification by flash chromatography (SiO$_2$, EtOAc/hexanes mixtures) provided the pure linear product.

Optimization of the allylic alkylation with tertiary nucleophiles

| entry | catalyst | nucleophile | yield | L:B$^b$
|-------|---------|-------------|-------|-------
| 1     | 49      | 81          | 30%   | >20:1 |
| 2     | 49      | 81          | 32%   | >20:1 |
| 3     | 49      | 81          | 38%   | >20:1 |
| 4     | 49      | 81          | 50%   | >20:1 |

$^a$ 18 (1 equiv), nucleophile (2 equiv), 1 or 49 (0.10 equiv), 2,6-dimethylbenzoquinone (1.5 equiv), dioxane/DMSO=4:1 (0.33M), 45°C, 24h. $^b$ Determined by $^1$H NMR analysis of crude.
Table 9: Allylic C-H alkylation screening procedure: A ½ dram oven dried borosilicate vial was charged with catalyst (0.010 mmol, 0.1 equiv) and 2,6-dimethylbenzoquinone 58 (20.4 mg, 0.15 mmol, 1.5 equiv). 1,4-dioxane, dimethylsulfoxide, allylbenzene 18 (13.2 μL, 0.10 mmol, 1 equiv), nucleophile (0.20 mmol, 2 equiv), and a stir bar were added sequentially. No further precautions were taken to exclude air or moisture. The vial was capped and stirred for 24 h at 45°C. The vial was cooled to room temperature and the reaction mixture was quenched with saturated aqueous NH₄Cl (10 mL) and extracted with two 10 mL portions of diethyl ether. The organic extracts were dried over MgSO₄. The mixture was filtered and concentrated in vacuo. To the crude reaction mixture was added 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) as a stock solution in CDCl₃. The crude mixture was dissolved completely in additional CDCl₃ and a sample was removed for ¹H NMR analysis. Yield was determined by integration of olefinic product peaks relative to 1,4-dimethoxybenzene.

Entry 1: Catalyst 1 (5.0 mg, 0.10 mmol, 1.0 equiv), methyl 2-nitropropionate 80 (26.6 mg, 0.20 mmol, 2.0 equiv), dioxane (240 μL), DMSO (60 μL) and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (30% yield); run 2 (30% yield). Average yield: 30%.

Entry 2: Catalyst 1 (5.0 mg, 0.10 mmol, 1.0 equiv), 2-nitropropiophenone 81 (35.8 mg, 0.20 mmol, 2.0 equiv), dioxane (240 μL), DMSO (60 μL) and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (33% yield); run 2 (30% yield). Average yield: 32%.

Entry 3: Catalyst 49 (5.3 mg, 0.10 mmol, 1.0 equiv), 2-nitropropiophenone 81 (26.6 mg, 0.20 mmol, 2.0 equiv), dioxane (240 μL), DMSO (60 μL) and 1,4-dimethoxybenzene (4.1 mg, 0.030
mmol, 0.30 equiv) were used. Run 1 (39% yield); run 2 (36 yield). **Average yield: 38%**.

**Entry 4:** Catalyst 49 (5.3 mg, 0.10 mmol, 1.0 equiv), 2-nitropropiophenone 81 (26.6 mg, 0.20 mmol, 2.0 equiv), dioxane (60 μL), DMSO (240 μL) and 1,4-dimethoxybenzene (4.1 mg, 0.030 mmol, 0.30 equiv) were used. Run 1 (50% yield); run 2 (50% yield). **Average yield: 50%**.

### Nucleophile scope of the allylic C-H alkylation

<table>
<thead>
<tr>
<th>entry</th>
<th>major product</th>
<th>isolated yield</th>
<th>(L:B, E:Z &gt; 20:1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>82</td>
<td>X = H</td>
<td>57%</td>
</tr>
<tr>
<td>2</td>
<td>83</td>
<td>Cl</td>
<td>59%</td>
</tr>
<tr>
<td>3</td>
<td>84</td>
<td>OMe</td>
<td>50%</td>
</tr>
<tr>
<td>4</td>
<td>85</td>
<td></td>
<td>53%</td>
</tr>
<tr>
<td>5</td>
<td>86</td>
<td></td>
<td>67%</td>
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<tr>
<td>6</td>
<td>87</td>
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<td>76%</td>
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<td>62%</td>
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<td>10</td>
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<td>OEt</td>
<td>68%</td>
</tr>
<tr>
<td>11</td>
<td>92</td>
<td></td>
<td>52%</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td>50%</td>
</tr>
</tbody>
</table>

\(^a\) Allylbenzene 18 (1 equiv), nucleophile (2 equiv), 49 (10 mol%). DMBQ 88 (1.5 equiv), DMSO/Dioxane (4:1, 0.33M), 45°C, 24h. Average of 2 runs. By \(^{1}H\) NMR analysis of the crude, only one regio- and olefin isomer of the product was observed.

\(^b\) Nucleophile (3 equiv), \(^c\) Allylbenzene 18 (2 equiv), nucleophile (1 equiv).
(E)-2-methyl-2-nitro-1,5-diphenylpent-4-en-1-one [82] : Allylbenzene (39.7 μL, 0.3 mmol, 1.0 equiv) and 2-nitropropiophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (4% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (52.2 mg, 0.177 mmol, 59% yield); run 2 (49.8 mg, 0.169 mmol, 56% yield). **Average yield: 57%.**

\[
\begin{align*}
\text{\(1^H\) NMR (500 MHz, CDCl\text{\textsubscript{3}}) \delta 7.80 (dd, J = 7.5, 1.6 Hz, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.36 – 7.28 (m, 4H), 7.26 – 7.20 (m, 1H), 6.49 (d, J = 15.6 Hz, 1H), 6.02 (dt, J = 15.5, 7.6 Hz, 1H), 3.26 (dd, J = 14.4, 7.3 Hz, 1H), 3.15 (dd, J = 14.4, 7.9 Hz, 1H), 1.96 (s, 3H);} \\
\text{\(13^C\) NMR (126 MHz, CDCl\text{\textsubscript{3}}) \delta 191.7, 136.5, 136.4, 133.9, 133.5, 129.0, 128.7, 128.6, 128.0, 126.6, 120.8, 95.5, 42.0, 22.5; IR (film, cm\textsuperscript{-1}): 3060, 3028, 2941, 2875, 1967, 1815, 1691, 1597, 1545, 1495, 1448, 1385, 1346, 1255, 972, 744, 692; HRMS (ESI) m/z calculated for C\textsubscript{18}H\textsubscript{18}NO\textsubscript{3} [M+H]\textsuperscript{+}: 296.1287, found 296.1292.}
\end{align*}
\]

(E)-1-(4-chlorophenyl)-2-methyl-2-nitro-5-phenylpent-4-en-1-one [83] : Allylbenzene (39.7 μL, 0.3 mmol, 1.0 equiv) and 4′-chloro-2-nitropropiophenone (128 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (4% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (57.7 mg, 0.175 mmol, 58% yield); run 2 (59.0 mg, 0.179 mmol, 60% yield). **Average yield: 59%.**

\[
\begin{align*}
\text{\(1^H\) NMR (500 MHz, CDCl\text{\textsubscript{3}}) \delta 7.74 (d, J = 8.6 Hz, 2H), 7.43 (d, J = 8.6 Hz, 2H), 7.35 – 7.28 (m, 4H), 7.26 – 7.23 (m, 1H), 6.48 (d, J = 15.7 Hz, 1H), 6.00 (dt, J = 15.5, 7.5 Hz, 1H), 3.24 (dd, J = 14.5, 7.2 Hz, 1H), 3.13 (dd, J = 14.4, 7.9 Hz, 1H), 1.94 (s, 3H);} \\
\text{\(13^C\) NMR (126 MHz, CDCl\text{\textsubscript{3}}) \delta 190.6, 140.5, 136.5, 136.4, 131.8, 130.0, 129.4, 128.7, 128.1, 126.6, 120.5, 95.4, 41.9, 22.5; IR (film, cm\textsuperscript{-1}): 3028, 2924, 1691, 1589, 1543, 1491, 1448, 1385, 1254,}
\end{align*}
\]
1093, 970, 845, 744, 692; HRMS (EI) m/z calculated for C_{18}H_{16}NO_{3}Cl [M]^+: 329.0819, found 329.0810.

\[(E)-1-(4\text{-methoxyphenyl})-2\text{-methyl}-2\text{-nitro-5-phenylpent-4-en-1-one} \text{[84]} :\] Allylbenzene (39.7 µL, 0.3 mmol, 1.0 equiv) and 4′-methoxy-2-nitropropiophenone (188 mg, 0.9 mmol, 3.0 equiv) were reacted following the general procedure. Flash chromatography (5→10% EtOAc/hexanes gradient) yielded pure linear product as a light yellow oil. Run 1 (48.9 mg, 0.150 mmol, 50% yield); run 2 (47.7 mg, 0.147 mmol, 49% yield). **Average yield: 50%**. ¹H NMR (500 MHz, CDCl₃) δ 7.80 (d, J = 9.0 Hz, 2H), 7.36 – 7.27 (m, 4H), 7.24 – 7.20 (m, 1H), 6.92 (d, J = 9.0 Hz, 2H), 6.48 (d, J = 15.6 Hz, 1H), 6.03 (dt, J = 15.4, 7.5 Hz, 1H), 3.87 (s, 3H), 3.24 (dd, J = 14.4, 7.3 Hz, 1H), 3.13 (dd, J = 14.4, 7.9 Hz, 1H), 1.94 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 190.0, 164.1, 136.6, 136.2, 131.2, 128.7, 128.0, 126.6, 126.1, 121.1, 114.3, 95.4, 55.7, 42.1, 22.7; IR (film, cm⁻¹): 3082, 3026, 2939, 2843, 1680, 1601, 1574, 1543, 1512, 1450, 1385, 1315, 1257, 1178, 1144, 1028, 972, 845, 742, 692; HRMS (ESI) m/z calculated for C_{19}H_{19}NO_{4}Na [M+Na]^+: 348.1212, found 348.1214.

\[(E)\text{-methyl 2-methyl-2-nitro-5-phenylpent-4-enoate} \text{[85]} :\] Allylbenzene (39.7 µL, 0.3 mmol, 1.0 equiv) and methyl 2-nitropropanoate (79.9 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (5→10% EtOAc/hexanes gradient) yielded pure linear product as a light yellow oil. Run 1 (39.4 mg, 0.158 mmol, 53% yield); run 2 (38.8 mg, 0.156 mmol, 52% yield). **Average yield: 53%**. ¹H NMR (500 MHz, CDCl₃) δ 7.36 – 7.29 (m, 4H), 7.27 – 7.22 (m, 1H),
6.52 (d, J = 15.7 Hz, 1H), 6.01 (dt, J = 15.4, 7.5 Hz, 1H), 3.83 (s, 3H), 3.16 (ddd, J = 14.3, 7.4, 1.3 Hz, 1H), 3.02 (ddd, J = 14.3, 7.7, 1.3 Hz, 1H), 1.81 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 167.8, 136.5, 136.4, 128.7, 128.1, 126.5, 120.7, 92.4, 53.7, 40.4, 21.4; IR (film, cm$^{-1}$): 3026, 2956, 1955, 1888, 1755, 1552, 1496, 1450, 1387, 1352, 1261, 1215, 972, 741, 694; HRMS (ESI) m/z calculated for C$_{13}$H$_{15}$NO$_4$Na [M+Na]$^+$: 272.0899, found 272.0905.

(E)-(4-nitro-4-(phenylsulfonyl)pent-1-en-1-yl)benzene [86] :

Allylbenzene (39.7 µL, 0.3 mmol, 1.0 equiv) and 1-(phenylsulfonyl)nitroethane (129 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (10→15% EtOAc/hexanes gradient) yielded pure linear product as a light yellow oil. Run 1 (66.4 mg, 0.200 mmol, 67% yield); run 2 (66.9 mg, 0.202 mmol, 67% yield). **Average yield: 67%**. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.90 (d, J = 7.6 Hz, 2H), 7.78 (t, J = 7.4 Hz, 1H), 7.63 (t, J = 7.8 Hz, 2H), 7.33 – 7.28 (m, 4H), 7.28 – 7.24 (m, 1H), 6.54 (d, J = 15.7 Hz, 1H), 5.90 (dt, J = 15.3, 7.4 Hz, 1H), 3.41 (dd, J = 14.4, 6.8 Hz, 1H), 3.05 (dd, J = 14.3, 8.0 Hz, 1H), 1.97 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 137.7, 136.0, 135.5, 132.8, 131.1, 129.4, 128.8, 128.4, 126.5, 118.6, 106.5, 37.2, 17.2; IR (film, cm$^{-1}$): 3062, 3032, 2924, 1552, 1448, 1333, 1155, 1074, 972, 742, 719, 688; HRMS (ESI) m/z calculated for C$_{17}$H$_{17}$SNO$_4$Na [M+Na]$^+$: 354.0776, found 354.0777.

2-cinnamyl-2-nitro-3,4-dihyronaphthalen-1(2H)-one [87] :

Allylbenzene (39.7 µL, 0.3 mmol, 1.0 equiv) and 2-nitro-1-tetralone (115 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (5→10% EtOAc/hexanes gradient) yielded pure linear product as a light yellow
oil. Run 1 (69.8 mg, 0.227 mmol, 76% yield); run 2 (69.0 mg, 0.225 mmol, 75% yield). **Average yield:** 76%. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.12 (d, $J = 7.7$ Hz, 1H), 7.55 (t, $J = 7.6$ Hz, 1H), 7.38 (t, $J = 7.6$ Hz, 1H), 7.36 – 7.20 (m, 6H), 6.57 (d, $J = 15.8$ Hz, 1H), 6.16 (dt, $J = 15.4$, 7.4 Hz, 1H), 3.23 (dd, $J = 14.5$, 7.2 Hz, 1H), 3.16 – 2.93 (m, 4H), 2.50 (dd, $J = 14.2$, 8.9, 4.6 Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 188.1, 142.5, 136.5, 136.1, 134.7, 130.8, 129.1, 128.9, 128.7, 128.1, 127.6, 126.5, 121.7, 94.0, 38.2, 31.8, 25.4; IR (film, cm$^{-1}$): 3068, 3024, 2937, 1693, 1601, 1545, 1454, 1290, 1232, 970, 742, 692; HRMS (ESI) $m/z$ calculated for C$_{19}$H$_{18}$NO$_3$ [M+H]$^+$: 308.1287, found 308.1294.

(\textit{E})-2-ethyl-2-nitro-1,5-diphenylpent-4-en-1-one \textsuperscript{[88]}: Allylbenzene (39.7 µL, 0.3 mmol, 1.0 equiv) and 2-nitrobutylphenone (116 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (3% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (53.9 mg, 0.174 mmol, 58% yield); run 2 (52.7 mg, 0.170 mmol, 57% yield). **Average yield:** 58%. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.80 (d, $J = 7.8$ Hz, 2H), 7.58 (t, $J = 7.4$ Hz, 1H), 7.45 (t, $J = 7.8$ Hz, 2H), 7.33 – 7.27 (m, 4H), 7.25 – 7.20 (m, 1H), 6.45 (d, $J = 15.7$ Hz, 1H), 5.91 (dt, $J = 15.5$, 7.6 Hz, 1H), 3.27 – 3.21 (m, 2H), 2.55 – 2.39 (m, 2H), 0.91 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 191.1, 136.5, 136.0, 134.0, 133.8, 129.0, 128.7, 128.5, 128.0, 126.5, 120.6, 99.0, 38.1, 27.7, 7.9; IR (film, cm$^{-1}$): 3059, 3026, 2980, 2885, 1689, 1597, 1539, 1495, 1448, 1360, 1230, 1186, 968, 746, 692; HRMS (ESI) $m/z$ calculated for C$_{19}$H$_{19}$NO$_3$Na [M+Na]$^+$: 332.1263, found 332.1257.
**5-cinnamyl-2,2,5-trimethyl-1,3-dioxane-4,6-dione [89]**

Alllylbenzene (39.7 µL, 0.3 mmol, 1.0 equiv) and 2,2,5-trimethyl-1,3-dioxane-4,6-dione (94.9 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (10→20% EtOAc/hexanes gradient) yielded pure linear product as a light yellow oil. Run 1 (51.1 mg, 0.186 mmol, 62% yield); run 2 (50.4 mg, 0.184 mmol, 61% yield). **Average yield: 62%.**

**1H NMR (500 MHz, CDCl$_3$)** δ 7.34 – 7.27 (m, 4H), 7.25 – 7.21 (m, 1H), 6.52 (d, $J = 15.7$ Hz, 1H), 6.04 (dt, $J = 15.6$, 7.7 Hz, 1H), 2.91 (d, $J = 7.7$ Hz, 2H), 1.72 (s, 3H), 1.69 (s, 3H), 1.63 (s, 3H); **13C NMR (126 MHz, CDCl$_3$)** δ 170.1, 136.5, 135.9, 128.7, 128.0, 126.5, 122.0, 105.3, 50.5, 43.4, 29.7, 29.0, 24.4; IR (film, cm$^{-1}$): 3030, 2999, 2941, 1778, 1745, 1452, 1381, 1279, 1203, 1146, 1059, 976, 945, 742, 692; HRMS (EI) $m/z$ calculated for C$_{16}$H$_{18}$O$_4$ [M]$^+$: 274.1205, found 274.1198.

**3-acetyl-3-cinnamylpentane-2,4-dione [90]**: Allylbenezene (39.7 µL, 0.3 mmol, 1.0 equiv) and triacetylmethane (80.0 µL, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (10→15% EtOAc/hexanes gradient) yielded pure linear product as a light yellow oil. Run 1 (51.6 mg, 0.200 mmol, 67% yield); run 2 (50.5 mg, 0.196 mmol, 65% yield). **Average yield: 66%.**

**1H NMR (500 MHz, CDCl$_3$)** δ **1H NMR (500 MHz, Chloroform-d)** δ 7.31 – 7.27 (m, 4H), 7.24 – 7.19 (m, 1H), 6.47 (dt, $J = 15.8$, 1.5 Hz, 1H), 6.00 (dt, $J = 15.7$, 7.3 Hz, 1H), 3.06 (dd, $J = 7.3$, 1.4 Hz, 2H), 2.21 (s, 9H); **13C NMR (126 MHz, CDCl$_3$)** δ 203.1, 136.6, 134.4, 128.7, 127.9, 126.5, 123.3, 84.9, 34.9, 28.5; IR (film, cm$^{-1}$): 3026, 2918, 1699, 1495, 1427, 1358, 1201, 1167, 972, 746, 694; HRMS (ESI) $m/z$ calculated for C$_{16}$H$_{18}$O$_3$Na [M+Na]$^+$: 281.1154, found 281.1163.
**(E)-ethyl 2,2-diacyl-5-phenylpent-4-enoate [91]**: Allylbenzene (39.7 μL, 0.3 mmol, 1.0 equiv) and ethyl diacetoacetate (93.6 μL, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (10→20% EtOAc/hexanes gradient) yielded pure linear product as a light yellow oil. Run 1 (59.7 mg, 0.207 mmol, 69% yield); run 2 (57.7 mg, 0.200 mmol, 67% yield). **Average yield: 68%**. \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ 7.33 – 7.27 (m, 4H), 7.24 – 7.18 (m, 1H), 6.45 (d, \(J = 15.8\) Hz, 1H), 6.15 (dt, \(J = 15.7, 7.3\) Hz, 1H), 4.28 (q, \(J = 7.2\) Hz, 2H), 2.99 (dd, \(J = 7.4, 1.4\) Hz, 2H), 2.28 (s, 6H), 1.30 (t, \(J = 7.1\) Hz, 3H); \(^1\)C NMR (126 MHz, CDCl\(_3\)) δ 201.4, 168.1, 136.9, 134.3, 128.6, 127.7, 126.4, 123.9, 77.5, 62.3, 35.9, 28.8, 14.1; IR (film, cm\(^{-1}\)): 3026, 2981, 2929, 1712, 1448, 1427, 1358, 1234, 1173, 1099, 972, 748, 694; HRMS (ESI) \(m/z\) calculated for C\(_{17}\)H\(_{20}\)O\(_4\)Na [M+Na]\(^+\): 311.1259, found 311.1267.

**(E)-5-benzoyl-5-nitro-8-phenyloct-7-en-1-yl benzoate [92]**: Allylbenzene (26.5 μL, 0.2 mmol, 1.0 equiv) and 5-nitro-6-oxo-6-phenylhexyl benzoate (137 mg, 0.4 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (5→10% EtOAc/hexanes gradient) yielded pure linear product as a light yellow oil. Run 1 (47.0 mg, 0.103 mmol, 51% yield); run 2 (47.7 mg, 0.104 mmol, 52% yield). **Average yield: 52%**. **Alternate stoichiometry**: Allylbenzene (53.0 μL, 0.4 mmol, 2.0 equiv) and 5-nitro-6-oxo-6-phenylhexyl benzoate (68.3 mg, 0.2 mmol, 1.0 equiv) were reacted following the general procedure. Flash chromatography (5→10% EtOAc/hexanes gradient) yielded pure linear product as a light yellow oil. Run 1 (72.7 mg, 0.159 mmol, 80% yield); run 2 (72.2 mg, 0.158 mmol, 79% yield). **Average yield: 80%**. \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ 7.96 (d, \(J = 7.6\) Hz, 2H), 7.78 (d, \(J = 7.8\) Hz, 2H),
7.60 – 7.52 (m, 2H), 7.42 (ap. t, \( J = 7.7 \) Hz, 4H), 7.31 – 7.19 (m, 5H), 6.44 (d, \( J = 15.7 \) Hz, 1H), 5.91 (dt, \( J = 15.4, 7.6 \) Hz, 1H), 4.28 (t, \( J = 6.3 \) Hz, 2H), 3.31 – 3.19 (m, 2H), 2.57 – 2.42 (m, 2H), 1.85 – 1.73 (m, 2H), 1.51 – 1.41 (m, 1H), 1.40 – 1.31 (m, 1H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \( \delta \) 190.9, 166.5, 136.4, 136.2, 133.9, 133.8, 133.1, 130.2, 129.6, 129.0, 128.7, 128.5, 128.4, 128.0, 126.5, 120.4, 98.3, 64.0, 38.7, 33.9, 28.6, 20.0; IR (film, cm\(^{-1}\)): 3062, 3032, 2953, 2873, 1718, 1689, 1599, 1543, 1450, 1315, 1275, 1115, 968, 714, 692; HRMS (ESI) \( m/z \) calculated for C\(_{19}\)H\(_{27}\)NO\(_3\)Na [M+Na]: 458.1967, found 458.1977.
### Olefin scope of the allylic C-H alkylation

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<sup>a</sup> Olefin (1 equiv.), 2-nitropropiophenone 81 (2 equiv.), DMBQ 98 (1.5 equiv.), DMSO/Dioxans (4:1, 0.33M), 45 C, 24h. Average of 2 runs. By H NMR analysis of the crude, only one regio- and olefin isomer of the product was observed.

<sup>b</sup> MIDA = Methyliminodiacetate.  
<sup>c</sup> d.r. = 1:1
**(E)-5-(4-methoxyphenyl)-2-methyl-2-nitro-1-phenylpent-4-en-1-one** [93] : Estragole (46.1 μL, 0.3 mmol, 1.0 equiv) and 2-nitropropiophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (10% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (62.1 mg, 0.191 mmol, 64% yield); run 2 (59.3 mg, 0.182 mmol, 61% yield).

**Average yield:** 63%.

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.79 (d, $J = 8.0$ Hz, 2H), 7.58 (t, $J = 7.4$ Hz, 1H), 7.45 (t, $J = 7.8$ Hz, 2H), 7.26 (d, $J = 8.7$ Hz, 2H), 6.84 (d, $J = 8.7$ Hz, 2H), 6.42 (d, $J = 15.7$ Hz, 1H), 5.87 (dt, $J = 15.4$, 7.6 Hz, 1H), 3.80 (s, 3H), 3.23 (dd, $J = 14.4$, 7.3 Hz, 1H), 3.12 (dd, $J = 14.4$, 7.9 Hz, 1H), 1.95 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 191.9, 159.6, 135.8, 133.8, 133.6, 129.4, 129.0, 128.6, 127.8, 118.5, 114.1, 95.6, 55.5, 42.0, 22.6; IR (film, cm$^{-1}$): 3033, 3005, 2927, 2837, 1691, 1606, 1537, 1512, 1448, 1385, 1346, 1300, 1248, 1176, 1034, 972, 808, 700; HRMS (ESI) m/z calculated for C$_{19}$H$_{19}$NO$_4$Na [M+Na]$^+$: 348.1212, found 348.1219.

**(E)-2-methyl-2-nitro-1-phenyl-5-(4-(trifluoromethyl)phenyl)pent-4-en-1-one** [94] : 4-allylbenzotrifluoride (55.9 mg, 0.3 mmol, 1.0 equiv) and 2-nitropropiophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (5% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (73.1 mg, 0.201 mmol, 67% yield); run 2 (71.6 mg, 0.197 mmol, 66% yield). Average yield: 67%.

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.83 – 7.77 (m, 2H), 7.60 (t, $J = 7.4$ Hz, 1H), 7.55 (d, $J = 8.2$ Hz, 2H), 7.46 (t, $J = 7.9$ Hz, 2H), 7.42 (d, $J = 8.1$ Hz, 2H), 6.52 (d, $J = 15.8$ Hz, 1H), 6.15 (dt, $J = 15.5$, 7.6 Hz, 1H), 3.29 (dd, $J = 14.5$, 7.1 Hz, 1H), 3.15 (dd, $J = 14.4$, 7.9 Hz, 1H), 1.97 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 191.5, 139.9, 135.0, 134.0, 133.4, 129.9 (q, $J_{CF} = 32.6$ Hz), 129.1, 128.6, 126.8, 125.7
(q, $J_{CF} = 3.8$ Hz), 124.2 (q, $J_{CF} = 271.8$ Hz), 123.9, 95.4, 42.0, 22.6; IR (film, cm$^{-1}$): 3068, 3012, 2943, 2875, 1923, 1691, 1616, 1599, 1545, 1448, 1416, 1387, 1327, 1255, 1165, 1124, 1068, 974, 862, 700; HRMS (ESI) $m/z$ calculated for C$_{19}$H$_{16}$NO$_3$F$_3$Na [M+Na]$^+$: 386.0980, found 386.0986.

(E)-5-(3-bromophenyl)-2-methyl-2-nitro-1-phenylpent-4-en-1-one [95]: 1-allyl-3-bromobenzene (59.1 mg, 0.3 mmol, 1.0 equiv) and 2-nitropropiophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (5% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (75.5 mg, 0.202 mmol, 67% yield); run 2 (72.3 mg, 0.193 mmol, 64% yield). **Average yield:** 66%. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.79 (d, $J = 8.0$ Hz, 2H), 7.59 (t, $J = 7.4$ Hz, 1H), 7.49 – 7.42 (m, 3H), 7.37 (d, $J = 7.8$ Hz, 1H), 7.23 (d, $J = 7.8$ Hz, 1H), 7.17 (t, $J = 7.8$ Hz, 1H), 6.41 (d, $J = 15.7$ Hz, 1H), 6.05 (dt, $J = 15.5$, 7.6 Hz, 1H), 3.26 (dd, $J = 14.4$, 7.2 Hz, 1H), 3.13 (dd, $J = 14.4$, 7.9 Hz, 1H), 1.96 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 191.6, 138.6, 134.9, 134.0, 133.4, 130.9, 130.2, 129.4, 129.1, 128.6, 125.3, 122.9, 122.7, 95.4, 41.9, 22.6; IR (film, cm$^{-1}$): 3060, 3010, 2924, 1691, 1595, 1543, 1473, 1448, 1385, 1346, 1257, 1072, 976, 850, 777; HRMS (ESI) $m/z$ calculated for C$_{18}$H$_{16}$NO$_3$BrNa [M+Na]$^+$: 396.0211, found 396.0230.

(E)-6-methyl-2-(3-(4-methyl-4-nitro-5-oxo-5-phenylpent-1-en-1-yl)phenyl)-1,3,6,2-dioxazaborocane-4,8-dione [96]: 2-(3-allylphenyl)-6-methyl-1,3,6,2-dioxazaborocane-4,8-dione (81.9 mg, 0.3 mmol, 1.0 equiv) and 2-nitropropiophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (20→30% acetone/Et$_2$O gradient),
followed by flash chromatography (2% MeOH/CH₂Cl₂) yielded pure linear product as a white solid. Run 1 (87.4 mg, 0.194 mmol, 65% yield); run 2 (85.1 mg, 0.189 mmol, 63% yield). 

**Average yield: 64%.** ¹H NMR (500 MHz, CDCl₃) δ 7.82 – 7.77 (m, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.49 – 7.30 (m, 6H), 6.48 (d, J = 15.8 Hz, 1H), 6.06 (dt, J = 15.4, 7.6 Hz, 1H), 3.92 (d, J = 16.4 Hz, 2H), 3.78 (dd, J = 16.4, 1.6 Hz, 2H), 3.26 (dd, J = 14.4, 7.4 Hz, 1H), 3.13 (dd, J = 14.4, 7.6 Hz, 1H), 2.57 (s, 3H), 1.97 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 191.8, 168.1, 136.5, 136.3, 133.9, 133.5, 132.0, 130.8, 129.1, 128.8, 128.6, 127.8, 121.3, 95.7, 62.1, 47.9, 42.1, 22.5 (NOTE: The C-B signal is not visible due to quadrupolar relaxation by ¹¹B); IR (film, cm⁻¹): 3018, 2947, 2924, 1768, 1693, 1543, 1450, 1336, 1288, 1255, 1184, 1039, 1003, 706; HRMS (ESI) m/z calculated for C₂₃H₂₄N₂O₇B [M+H]⁺: 451.1677, found 451.1676.

(E)-5-(2-((tert-butyldimethylsilyl)oxy)phenyl)-2-methyl-2-nitro-1-phenylpent-4-en-1-one  [97] : (2-allylphenoxy)(tert-butyldimethylsilane (74.5 mg, 0.3 mmol, 1.0 equiv) and 2-nitropropiophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (3% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (79.3 mg, 0.186 mmol, 62% yield); run 2 (80.3 mg, 0.189 mmol, 63% yield). 

**Average yield: 63%.** ¹H NMR (500 MHz, CDCl₃) δ 7.83 – 7.77 (m, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 7.9 Hz, 2H), 7.39 (dd, J = 7.7, 1.8 Hz, 1H), 7.12 (td, J = 7.7, 1.8 Hz, 1H), 6.90 (t, J = 7.6 Hz, 1H), 6.82 (d, J = 15.9 Hz, 1H), 6.77 (dd, J = 8.2, 1.2 Hz, 1H), 5.93 (dt, J = 15.4, 7.5 Hz, 1H), 3.26 (ddd, J = 14.3, 7.2, 1.4 Hz, 1H), 3.15 (ddd, J = 14.3, 7.8, 1.3 Hz, 1H), 1.95 (s, 3H), 0.99 (s, 9H), 0.19 (s, 3H), 0.19 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 191.8, 152.9, 133.8, 133.6, 131.7, 129.0, 128.9, 128.6, 128.0, 126.7, 121.5, 120.4, 119.7, 95.5, 42.4, 25.9, 22.6, 18.4,
-4.06, -4.08; IR (film, cm⁻¹): 3066, 3030, 2951, 2931, 2860, 1693, 1597, 1545, 1485, 1452, 1385, 1346, 1255, 976, 914, 837, 783, 758, 700, 665; HRMS (ESI) m/z calculated for C_{24}H_{32}NO_{4}Si [M+H]^+: 426.2101, found 426.2097.

(E)-2-(4-methyl-4-nitro-5-oxo-5-phenylpent-1-en-1-yl)cyclohex-1-en-1-yl acetate [98] : 2-allylcyclohex-1-en-1-yl acetate (54.1 mg, 0.3 mmol, 1.0 equiv) and 2-nitropropiophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (7→12% EtOAc/hexanes gradient) yielded pure linear product as a light yellow oil. Run 1 (56.6 mg, 0.158 mmol, 53% yield); run 2 (52.9 mg, 0.148 mmol, 49% yield). **Average yield: 51%**. ^1^H NMR (500 MHz, CDCl₃) δ 7.79 – 7.73 (m, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 7.9 Hz, 2H), 6.32 (d, J = 15.7 Hz, 1H), 5.39 (dt, J = 15.3, 7.5 Hz, 1H), 3.14 (dd, J = 14.4, 7.1 Hz, 1H), 3.03 (dd, J = 14.4, 8.0 Hz, 1H), 2.24 – 2.16 (m, 4H), 2.16 (s, 3H), 1.88 (s, 3H), 1.74 – 1.62 (m, 4H); ^1^C NMR (126 MHz, CDCl₃) δ 191.8, 169.1, 146.4, 133.8, 133.6, 130.7, 129.0, 128.6, 121.4, 119.3, 95.5, 42.0, 27.9, 24.4, 22.6, 22.5, 22.0, 21.0; IR (film, cm⁻¹): 3045, 2933, 2862, 1753, 1691, 1664, 1597, 1545, 1448, 1360, 1215, 1134, 974, 706; HRMS (ESI) m/z calculated for C_{20}H_{24}NO₅ [M+H]^+: 358.1654, found 358.1658.

(E)-5-(cyclohex-1-en-1-yl)-2-methyl-2-nitro-1-phenylpent-4-en-1-one [99] : 1-allylcyclohexene (36.7 mg, 0.3 mmol, 1.0 equiv) and 2-nitropropiophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (3% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (55.5 mg, 0.185 mmol, 62% yield); run 2 (55.9 mg, 0.187 mmol, 62% yield).
Average yield: 62%. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.81 – 7.74 (m, 2H), 7.57 (t, $J = 7.3$ Hz, 1H), 7.44 (t, $J = 7.9$ Hz, 2H), 6.09 (d, $J = 15.5$ Hz, 1H), 5.70 (t, $J = 4.2$ Hz, 1H), 5.29 (dt, $J = 15.4$, 7.5 Hz, 1H), 3.12 (dd, $J = 14.3$, 7.3 Hz, 1H), 3.01 (dd, $J = 14.3$, 7.8 Hz, 1H), 2.14 – 2.03 (m, 4H), 1.89 (s, 3H), 1.69 – 1.53 (m, 4H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 192.0, 140.0, 135.2, 133.8, 133.7, 130.5, 129.0, 128.6, 116.2, 95.7, 41.9, 25.9, 24.6, 22.5, 22.5; IR (film, cm$^{-1}$): 3030, 2929, 2860, 2837, 1691, 1649, 1597, 1545, 1448, 1385, 1346, 1255, 970, 791, 702; HRMS (ESI) $m/z$ calculated for C$_{18}$H$_{21}$NO$_3$Na [M+Na]$^+$: 322.1419, found 322.1422.

(E)-$N,N$-diethyl-5-methyl-5-nitro-6-oxo-6-phenylhex-2-enamide [100]: N,N-diethylbut-3-enamide (42.4 mg, 0.3 mmol, 1.0 equiv) and 2-nitropropiophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. A short silica plug (100% CH$_2$Cl$_2$; 5% MeOH/CH$_2$Cl$_2$), followed by flash chromatography (60% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (73.5 mg, 0.231 mmol, 77% yield); run 2 (74.4 mg, 0.234 mmol, 78% yield). Average yield: 78%. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.77 (d, $J = 7.7$ Hz, 2H), 7.58 (t, $J = 7.4$ Hz, 1H), 7.44 (t, $J = 7.8$ Hz, 2H), 6.73 (dt, $J = 15.2$, 7.8 Hz, 1H), 6.27 (d, $J = 14.9$ Hz, 1H), 3.41 (q, $J = 7.1$ Hz, 2H), 3.30 (q, $J = 7.2$ Hz, 2H), 3.21 (dd, $J = 14.5$, 8.2 Hz, 1H), 3.16 (dd, $J = 14.5$, 7.4 Hz, 1H), 1.96 (s, 3H), 1.18 – 1.10 (m, 6H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 191.2, 164.7, 135.3, 133.9, 133.2, 129.0, 128.5, 127.1, 95.1, 42.3, 41.0, 40.9, 22.2, 14.9, 13.2; IR (film, cm$^{-1}$): 3064, 2978, 2935, 2875, 1691, 1662, 1616, 1543, 1483, 1448, 1433, 1385, 1348, 1277, 1257, 1221, 1149, 978, 694; HRMS (ESI) $m/z$ calculated for C$_{17}$H$_{22}$N$_2$O$_4$ [M+H]$^+$: 319.1658, found 319.1651.
(E)-tert-butyl 3-(4-methyl-4-nitro-5-oxo-5-phenylpent-1-en-1-yl)-1H-indole-1-carboxylate [101]: tert-butyl 3-allyl-1H-indole-1-carboxylate (77.2 mg, 0.3 mmol, 1.0 equiv) and 2-nitropropiophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (5% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (69.0 mg, 0.159 mmol, 53% yield); run 2 (68.2 mg, 0.157 mmol, 52% yield). Average yield: 53%. 1H NMR (500 MHz, CDCl3) δ 8.16 (d, J = 8.3 Hz, 1H), 7.84 – 7.78 (m, 2H), 7.68 (d, J = 7.9 Hz, 1H), 7.63 – 7.56 (m, 2H), 7.46 (t, J = 7.9 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.30 – 7.23 (m, 1H), 6.57 (d, J = 15.8 Hz, 1H), 6.10 (dt, J = 15.5, 7.5 Hz, 1H), 3.30 (dd, J = 14.4, 7.1 Hz, 1H), 3.18 (dd, J = 14.4, 7.8 Hz, 1H), 1.99 (s, 3H), 1.67 (s, 9H); 13C NMR (126 MHz, CDCl3) δ 191.8, 149.6, 136.0, 133.9, 133.6, 129.0, 128.6, 128.6, 127.6, 124.9, 124.3, 123.2, 121.2, 120.0, 118.1, 115.5, 95.6, 84.1, 42.7, 28.3, 22.6; IR (film, cm⁻¹): 3060, 2926, 2860, 1738, 1693, 1599, 1547, 1452, 1371, 1308, 1255, 1157, 1090, 1024, 966, 910, 856, 742; HRMS (EI) m/z calculated for C25H26N2O5 [M]⁺: 434.1842, found 434.1837.

(E)-5-(2,2-dimethyl-2H-chromen-6-yl)-2-methyl-2-nitro-1-phenylpent-4-en-1-one [102]: 6-allyl-2,2-dimethyl-2H-chromene (68.3 mg, 88% pure, 0.3 mmol, 1.0 equiv) and 2-nitropropiophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. [NOTE: The substrate contained 12% (E)-2,2-dimethyl-6-(prop-1-en-1-yl)-2H-chromene, which was inert under standard alkylation conditions.] Flash chromatography (5% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (66.8 mg, 0.177 mmol, 59% yield); run 2 (68.4 mg, 0.181 mmol, 60% yield). Average yield: 60%. 1H NMR (500 MHz, CDCl3) δ 7.79 (d, J = 7.4 Hz, 2H), 7.58
(E)-5-(2,7-di-tert-butyl-9,9-dimethyl-9H-xanthen-4-yl)-2-methyl-2-nitro-1-phenylpent-4-en-1-one [105]: 4-allyl-2,7-di-tert-butyl-9,9-dimethyl-9H-xanthen (72.5 mg, 0.2 mmol, 1.0 equiv) and 2-nitropropiophenone (71.7 mg, 0.4 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (2% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (56.6 mg, 0.105 mmol, 52% yield); run 2 (56.0 mg, 0.104 mmol, 52% yield). **Average yield: 52%**. 

### 1H NMR (500 MHz, CDCl₃) δ 7.83 (d, J = 7.2 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 7.39 (d, J = 2.4 Hz, 1H), 7.33 (d, J = 2.3 Hz, 1H), 7.24 (d, J = 2.3 Hz, 1H), 7.22 (dd, J = 8.5, 2.3 Hz, 1H), 6.98 (d, J = 8.5 Hz, 1H), 6.92 (d, J = 15.8 Hz, 1H), 6.14 (dt, J = 15.5, 7.5 Hz, 1H), 3.33 (dd, J = 14.6, 7.1 Hz, 1H), 3.25 (dd, J = 14.3, 7.9 Hz, 1H), 2.00 (s, 3H), 1.63 (s, 3H), 1.62 (s, 3H), 1.33 (s, 9H), 1.33 (s, 9H); 

### 13C NMR (126 MHz, CDCl₃) δ 192.0, 148.3, 146.0, 145.8, 145.1, 133.8, 133.8, 131.8, 130.1, 129.4, 129.0, 128.6, 124.4, 123.6, 122.6, 122.5, 122.3, 122.0, 115.9, 95.6, 42.5, 34.7, 34.6, 34.6, 32.4, 32.2, 31.7, 31.7, 22.7; IR (film, cm⁻¹): 3010, 2958, 2868, 1693, 1545, 1500, 1458, 1363,
1290, 1269, 1223, 974, 756; HRMS (ESI) m/z calculated for C_{35}H_{42}NO_4 [M+H]^+: 540.3114, found 540.3123.

(8R,9S,13S,14S)-13-methyl-3-((E)-4-methyl-4-nitro-5-oxo-5-phenylpent-1-en-1-yl)-7,8,9,11,12,13,15,16-octahydro-6H-cyclopenta[a]phenanthren-17(14H)-one [104]

(8R,9S,13S,14S)-3-allyl-13-methyl-7,8,9,11,12,13,15,16-octahydro-6H-cyclopenta[a]phenanthren-17(14H)-one (58.9 mg, 0.2 mmol, 1.0 equiv) and 2-nitropropioophenone (71.7 mg, 0.4 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (15→20% EtOAc/hexanes gradient) yielded pure linear product as a light yellow oil. Run 1 (58.1 mg, 0.123 mmol, 62% yield); run 2 (56.9 mg, 0.121 mmol, 60% yield). **Average yield: 61%**. \(^1\)H NMR (500 MHz, CDCl_3) \(\delta\) 7.79 (d, \(J = 7.5\) Hz, 2H), 7.58 (t, \(J = 7.5\) Hz, 1H), 7.49 – 7.41 (m, 2H), 7.24 (d, \(J = 8.2\) Hz, 1H), 7.12 (d, \(J = 8.1\) Hz, 1H), 7.07 (s, 1H), 6.43 (d, \(J = 15.7\) Hz, 1H), 5.98 (dt, \(J = 15.4, 7.6\) Hz, 1H), 3.24 (dd, \(J = 14.4, 7.2\) Hz, 1H), 3.13 (dd, \(J = 14.5, 7.9\) Hz, 1H), 2.93 – 2.87 (m, 2H), 2.51 (dd, \(J = 19.0, 8.7\) Hz, 1H), 2.45 – 2.38 (m, 1H), 2.32 – 2.27 (m, 1H), 2.15 (dt, \(J = 18.5, 8.8\) Hz, 1H), 2.11 – 1.95 (m, 3H), 1.94 (s, 3H), 1.67 – 1.42 (m, 6H), 0.91 (s, 3H); \(^{13}\)C NMR (126 MHz, CDCl_3) Mixture of diastereomers \(\delta\) 220.9, 191.8, 139.8, 136.8, 136.1, 134.1, 133.8, 133.5, 129.0, 128.6, 127.1, 125.7, 124.0, 120.1, 95.5, 50.6, 48.1, 44.5, 42.0, 38.2, 36.0, 31.7, 29.5, 26.6, 25.8, 22.5, 21.7, 13.9; IR (film, cm\(^{-1}\)): 3012, 2927, 2860, 1738, 1691, 1597, 1543, 1498, 1450, 1385, 1344, 1255, 972, 910, 731; HRMS (ESI) m/z calculated for C_{30}H_{34}NO_4 [M+H]^+: 472.2488, found 472.2486.
(3S,8aS)-3-(4-((E)-4-methyl-4-nitro-5-oxo-5-phenylpent-1-en-1-yl)benzyl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione [103]: (3S,8aS)-3-(4-allylbenzyl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (85.3 mg, 0.3 mmol, 1.0 equiv) and 2-nitropropionophenone (108 mg, 0.6 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (2→5% MeOH/CH₂Cl₂ gradient) yielded pure linear product as a light yellow oil. Run 1 (69.6 mg, 0.151 mmol, 50% yield); run 2 (68.6 mg, 0.149 mmol, 50% yield). **Average yield: 50%**. 

**¹H NMR** (500 MHz, CDCl₃) δ 7.79 (d, J = 7.5 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.9 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 7.14 (d, J = 8.1 Hz, 2H), 6.44 (d, J = 15.7 Hz, 1H), 6.08 – 5.98 (m, 1H), 5.96 (s, 1H), 4.22 – 4.14 (m, 1H), 3.64 (dt, J = 12.2, 8.4 Hz, 1H), 3.46 – 3.37 (m, 1H), 3.25 (d, J = 14.4, 7.3 Hz, 1H), 3.19 – 3.02 (m, 4H), 2.28 – 2.18 (m, 1H), 1.96 (s, 3H), 1.95 – 1.90 (m, 1H), 1.89 – 1.68 (m, 2H); **¹³C NMR** (126 MHz, CDCl₃) *Mixture of diastereomers* δ 191.6, 169.5, 164.9, 135.8, 135.6, 135.1, 133.9, 133.4, 130.2, 129.0, 128.6, 126.8, 121.3, 95.4, 59.0, 57.9, 45.3, 42.0, 40.2, 29.1, 22.6, 22.5, 21.8; IR (film, cm⁻¹): 3248, 3053, 2924, 2883, 1915, 1678, 1658, 1597, 1543, 1512, 1448, 1344, 1306, 1254, 1119, 974, 912, 729; HRMS (ESI) m/z calculated for C₂₆H₂₈N₃O₅ [M+H]⁺: 462.2029, found 462.2028.

Sequential allylic C-H alkylation reactions
(E)-5-cyclohexyl-2-nitro-1-phenylpent-4-en-1-one [67] : Allylcyclohexane 106 (37.3 mg, 0.3 mmol, 1.0 equiv) and benzoylnitromethane 16 (198 mg, 1.2 mmol, 4.0 equiv) were reacted and purified following the previously published procedure. Spectral data matched those reported.

(E)-2-cinnamyl-5-cyclohexyl-2-nitro-1-phenylpent-4-en-1-one [107] : (E)-5-cyclohexyl-2-nitro-1-phenylpent-4-en-1-one 67 (57.5 mg, 0.2 mmol, 1.0 equiv) and allylbenzene 18 (53.0 µL, 0.4 mmol, 2.0 equiv) were reacted following the general procedure. Flash chromatography (3% EtOAc/hexanes) yielded pure linear product as a light yellow oil. Run 1 (73.6 mg, 0.182 mmol, 91% yield); run 2 (72.6 mg, 0.180 mmol, 90% yield). **Average yield: 91%.** 

**1H NMR (500 MHz, CDCl₃) δ 7.79 (d, J = 7.9 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.34 – 7.20 (m, 5H), 6.43 (d, J = 15.7 Hz, 1H), 5.90 (dt, J = 15.4, 7.6 Hz, 1H), 5.45 (dd, J = 15.3, 7.0 Hz, 1H), 5.13 (dt, J = 15.1, 7.4 Hz, 1H), 3.25 (dd, J = 14.6, 7.4 Hz, 1H), 3.18 (dd, J = 14.6, 7.7 Hz, 1H), 3.11 – 3.02 (m, 2H), 1.94 – 1.86 (m, 1H), 1.73 – 1.59 (m, 4H), 1.36 – 1.08 (m, 4H), 1.01 (m, 2H); **

**13C NMR (126 MHz, CDCl₃) δ 190.7, 144.1, 136.5, 136.2, 134.1, 133.8, 129.0, 128.7, 128.6, 128.0, 126.5, 120.5, 117.8, 98.0, 40.9, 38.5, 38.1, 32.8, 32.8, 26.1, 26.0; IR (film, cm⁻¹): 3060, 3032, 2927, 2850, 1691, 1597, 1545, 1495, 1448, 1356, 1259, 1186, 970, 692; **

**HRMS (ESI) m/z calculated for C_{26}H_{30}NO_{3} [M+H]^+: 404.2226, found 404.2230.**

**Starting Materials**
**General procedure for preparation of allylarenes:** An oven-dried 10 mL Schlenk flask under argon atmosphere was charged with Pd(dba)$_2$ (34.5 mg, 0.060 mmol, 0.03 equiv), PCy$_3$ (33.7 mg, 0.12 mmol, 0.06 equiv), CsF (668 mg, 4.40 mmol, 2.2 equiv), aryl halide (2.00 mmol, 1 equiv), and a stir bar. Allyltributyltin (644 μL, 2.10 mmol, 1.05 equiv) and dioxane (2 mL, 1.0M) were added via syringe. The mixture was stirred and heated to 80-100°C. Conversion was monitored by GC. When complete consumption of aryl halide was observed (8-24 h), the reaction was cooled to room temperature. The reaction mixture was diluted with saturated aqueous NH$_4$Cl (40 mL) and extracted with diethyl ether (2 x 40 mL). The combined organics were dried over MgSO$_4$. The mixture was filtered and concentrated in vacuo. Purification by flash chromatography (SiO$_2$, Et$_2$O/pentane mixtures) provided the pure product.

*NOTE:* In some cases isomerization was observed, yielding small amounts of internal olefin product [characteristic peaks, $^1$H NMR: 6.4 (m, 2H), 1.9 (d, 3H)]. This isomer was generally not separable from the desired allyl compound by column chromatography. However, the internal isomer was unreactive under standard allylic alkylation conditions and could be recovered quantitatively from the reaction mixture.

**General procedure for preparation of 2-nitro ketones:** An oven-dried 25 mL flask under argon atmosphere was charged with silyl enol ether (2.00 mmol, 1 equiv), CH$_2$Cl$_2$ (8 mL), and a stir bar. The flask was wrapped in aluminum foil to exclude light. Tetranitromethane (263 μL, 2.20 mmol, 1.1 equiv) in CH$_2$Cl$_2$ (2 mL) was added dropwise via syringe. The mixture was stirred at room temperature. Conversion was monitored by GC or TLC. When complete consumption of silyl enol ether was observed (10 min - 24 h), the reaction mixture was diluted with CH$_2$Cl$_2$ (40 mL). The mixture was washed repeatedly with 40 mL portions of H$_2$O until the
washes were no longer colored. The organic layer was dried over MgSO₄. The mixture was filtered and concentrated *in vacuo*. Purification by flash chromatography (SiO₂, EtOAc/hexanes mixtures) provided the pure product.

**Spectral data for known compounds:**

2-nitropropiophenone [81]⁹⁹

4′-chloro-2-nitropropiophenone⁹⁰

4′-methoxy-2-nitropropiophenone⁹¹

methyl 2-nitropropanoate [80]⁹²

1-(phenylsulfonyl)nitroethane⁹³

2-nitro-1-tetralone⁹⁹

2-nitrobutylphenone⁹⁴

4-allylbenzotrifluoride⁹⁵

1-allyl-3-bromobenzene⁹⁶

(2-allylphenoxy)(*tert*-butyl)dimethylsilane⁹⁷

2-allylcyclohex-1-en-1-yl acetate⁷⁶

*N,N*-diethylbut-3-enamide⁷⁵

*tert*-butyl 3-allyl-1*H*-indole-1-carboxylate⁹⁸

5-nitro-6-oxo-6-phenylhexyl benzoate: ¹H NMR (500 MHz, CDCl₃) δ 8.01 (d, *J* = 6.8 Hz, 2H), 7.96 (d, *J* = 7.2 Hz, 2H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.9 Hz, 2H), 7.44 (t, *J* = 7.8 Hz,
2H), 6.08 (dd, J = 9.4, 4.7 Hz, 1H), 4.39 – 4.27 (m, 2H), 2.51 – 2.41 (m, 1H), 2.30 – 2.20 (m, 1H), 1.92 – 1.82 (m, 2H), 1.67 – 1.57 (m, 2H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 188.8, 166.6, 134.9, 133.9, 133.1, 130.2, 129.7, 129.4, 128.9, 128.5, 89.7, 64.2, 30.3, 28.3, 22.8; IR (film, cm$^{-1}$): 3064, 2956, 2872, 1971, 1913, 1712, 1554, 1450, 1275, 1117, 712, 688; HRMS (ESI) m/z calculated for C$_{19}$H$_{20}$NO$_5$ [M+H]$^+$: 342.1341, found 342.1346.

2-(3-allylphenyl)-6-methyl-1,3,6,2-dioxazaborocane-4,8-dione: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.38 – 7.29 (m, 3H), 7.28 – 7.22 (m, 1H), 5.95 (ddt, J = 15.8, 11.2, 6.7 Hz, 1H), 5.08 – 5.01 (m, 2H), 3.92 (d, J = 16.4 Hz, 2H), 3.77 (d, J = 16.3 Hz, 2H), 3.39 (d, J = 6.7 Hz, 2H), 2.56 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 168.3, 140.2, 137.6, 132.6, 130.3, 130.1, 128.6, 116.0, 62.0, 47.8, 40.4 (NOTE: The C-B signal is not visible due to quadrupolar relaxation by $^{11}$B); IR (film, cm$^{-1}$): 3010, 2964, 1766, 1457, 1336, 1292, 1250, 1039, 1005; HRMS (ESI) m/z calculated for C$_{14}$H$_{17}$NO$_4$B [M+H]$^+$: 274.1251, found 274.1252.

6-allyl-2,2-dimethyl-2H-chromene: $^1$H NMR (500 MHz, CDCl$_3$) δ 6.92 (dd, J = 8.2, 2.2 Hz, 1H), 6.79 (d, J = 2.2 Hz, 1H), 6.70 (d, J = 8.1 Hz, 1H), 6.29 (d, J = 9.8 Hz, 1H), 5.94 (ddt, J = 16.8, 10.0, 6.7 Hz, 1H), 5.59 (d, J = 9.8 Hz, 1H), 5.10 – 5.01 (m, 2H), 3.28 (d, J = 6.7 Hz, 2H), 1.42 (s, 6H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 151.3, 138.0, 132.2, 130.9, 129.2, 126.4, 122.5, 121.3, 116.3, 115.6, 76.1, 39.5, 28.1; IR (film, cm$^{-1}$): 3076, 3039, 2976, 2927, 1639, 1491, 1261, 1209, 1151, 962, 914; HRMS (EI) m/z calculated for C$_{14}$H$_{16}$O [M]$^+$: 200.1201, found 200.1207.
**4-allyl-2,7-di-tert-butyl-9,9-dimethyl-9H-xanthene**: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.40 (d, $J = 2.4$ Hz, 1H), 7.28 (d, $J = 2.4$ Hz, 1H), 7.21 (dd, $J = 8.5$, 2.3 Hz, 1H), 7.07 (d, $J = 2.4$ Hz, 1H), 6.98 (d, $J = 8.5$ Hz, 1H), 6.06 (ddt, $J = 16.8$, 10.0, 6.7 Hz, 1H), 5.14 (dq, $J = 17.0$, 1.7 Hz, 1H), 5.05 (dq, $J = 10.0$, 1.5 Hz, 1H), 3.53 (d, $J = 6.7$ Hz, 2H), 1.64 (s, 6H), 1.33 (s, 9H), 1.32 (s, 9H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 148.7, 146.5, 145.6, 145.0, 137.3, 129.6, 129.5, 126.7, 125.0, 124.3, 122.5, 120.7, 115.9, 115.6, 35.0, 34.8, 34.6, 32.4, 31.8, 31.6; IR (film, cm$^{-1}$): 3076, 3043, 2966, 2906, 2873, 1757, 1639, 1579, 1500, 1460, 1408, 1363, 1290, 1269, 1221, 1115, 910, 822, 735; HRMS (EI) m/z calculated for C$_{26}$H$_{34}$O [M]$^+$: 362.2610, found 362.2605.

**8R,9S,13S,14S)-3-allyl-13-methyl-7,8,9,11,12,13,15,16-octahydro-6H-cyclopenta[a]phenanthren-17(14H)-one**: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.23 (d, $J = 8.0$ Hz, 1H), 6.99 (d, $J = 8.0$ Hz, 1H), 6.94 (s, 1H), 5.96 (ddt, $J = 16.9$, 10.0, 6.8 Hz, 1H), 5.10 (dq, $J = 17.0$, 1.7 Hz, 1H), 5.06 (dq, $J = 10.0$, 1.4 Hz, 1H), 3.34 (d, $J = 6.8$ Hz, 2H), 2.94 – 2.87 (m, 2H), 2.50 (dd, $J = 19.0$, 8.7 Hz, 1H), 2.46 – 2.38 (m, 1H), 2.33 – 2.25 (m, 1H), 2.14 (dt, $J = 18.8$, 8.9 Hz, 1H), 2.09 – 1.92 (m, 3H), 1.69 – 1.38 (m, 6H), 0.91 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 221.1, 137.7, 137.7, 137.6, 136.6, 129.3, 126.1, 125.6, 115.8, 50.6, 48.1, 44.4, 39.9, 38.3, 36.0, 31.7, 29.5, 26.7, 25.9, 21.7, 14.0; IR (film, cm$^{-1}$): 3456, 3076, 2929, 2864, 1739, 1637, 1498, 1454, 1435, 1257, 1084, 1053, 1007, 912, 820; HRMS (ESI) m/z calculated for C$_{21}$H$_{27}$O [M+H]$^+$: 295.2062, found 295.2057; $[\alpha]_D^{25}$ = +144.3° (c=1.0, CHCl$_3$).
(3S,8aS)-3-(4-allylbenzyl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.14 (ap. s, 4H), 5.98 (s, 1H), 5.93 (ddt, $J = 16.9$, 10.4, 6.7 Hz, 1H), 5.09 – 5.01 (m, 2H), 4.18 (dt, $J = 6.8$, 4.2 Hz, 1H), 3.63 (dt, $J = 12.1$, 8.4 Hz, 1H), 3.41 (ddd, $J = 12.2$, 9.3, 2.9 Hz, 1H), 3.36 (d, $J = 6.6$ Hz, 2H), 3.13 – 3.01 (m, 3H), 2.24 – 2.16 (m, 1H), 1.99 – 1.90 (m, 1H), 1.86 – 1.76 (m, 1H), 1.75 – 1.66 (m, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 169.8, 165.1, 139.3, 137.3, 132.9, 130.1, 128.9, 115.9, 58.8, 57.7, 45.0, 40.0, 39.7, 28.8, 21.6; IR (film, cm$^{-1}$): 3469, 3236, 3024, 2978, 2927, 2889, 2166, 1666, 1512, 1452, 1302, 1119, 918, 731; HRMS (ESI) m/z calculated for C$_{17}$H$_{21}$N$_2$O$_2$ [M+H]$^+$: 285.1603, found 285.1609; $[\alpha]_D^{26}$ = +1.3° (c=1.0, CHCl$_3$).

3.5 REFERENCES

83 For an example of mono- and dialkylation product mixtures see: Ref. 13.