Diastereoselective Cyclizations of Enantiopure Planar Chiral N-Oxazolidinoyl Diene Iron(0) Tricarbonyl Complexes

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Table of Contents

List of Common Abbreviations 4

Abstract 5

I. Introduction 6
  I.1. Background 6
  I.2. Sulfoxides 8
    I.2.i. Allylations 10
    I.2.ii. Ring-Closing Metathesis 12
    I.2.iii. Intramolecular Pinacol Couplings 15
    I.2.iv. Spiroketalizations and Related Reactions 17
  I.3. New Chiral Auxiliaries 24
  I.4. Oxazolidinones 27
    I.4.i. Early Transformations 27
    I.4.ii. Intramolecular C-H Insertions 29

II. Results and Discussion 32
  II.1. Silyl Ether Cyclopentene 32
  II.2. Indole Cyclopentene 42
  II.3. Diazo Group Installation 46
  II.4. Concluding Remarks 50

III. References 51

Experimental 57

NMR and IR Spectra 108
List of Common Abbreviations

Ac: acetyl
Ar: aryl
BOC: tert-butoxycarbonyl
DME: dimethoxyethane
DMF: dimethylformamide
dr: diastereomeric ratio
EE: ethoxyethyl
MOM: methoxymethyl
MOP: methoxypropyl
Ms: methanesulfonyl ("mesyl")
PG: protecting group
Ph: phenyl
PMB: para-methoxybenzene
TBS: tert-butyldimethylsilyl
TBDPS: tert-butylidiphenylsilyl
TES: triethylsilyl
THF: tetrahydrofuran
THP: tetrahydropyran
TIPS: triisopropylsilyl
TMS: trimethylsilyl
Ts: para-toluenesulfonyl ("tosyl")
Abstract

Iron(0) tricarbonyl diene complexes have long been established as effective stereodirecting groups due to their planar chirality and the steric bulk of the iron fragment. If initial diastereoselective complexation can be achieved, these molecules are therefore capable of acting as scaffolds for the stereoselective synthesis of architecturally complex products. The Paley laboratory uses chiral auxiliaries, most recently oxazolidinones, bound to acyclic dienes to assure diastereoselective complexation, before exploring the potential of diverse diastereomeric chemistry on the diene periphery.

In this work we report progress on the development of an asymmetric, intramolecular rhodium(II)-catalyzed C-H insertion adjacent to the diene to form five-membered carbocycles with two determined stereocenters. In particular, we discuss the synthesis of N-oxazolidinoyl diene iron(0) tricarbonyl complexes containing both protected alcohol and indole functionalities, followed by diastereoselective cyclization to form the corresponding cyclopentenes upon addition of the rhodium catalyst. Additionally, initial steps towards the optimization of these synthetic pathways, including the exploration of alternative methods to install the requisite diazo group, are detailed in this report. It is predicted that these transformations will ultimately enable synthetic access to new classes of natural products.
I. Introduction – History of the Paley Group

1.1. Background

Chirality is the chemical term describing the phenomenon of structures that are non-superimposable with their own mirror image. Chirality can be broadly divided into three forms, reflecting the dimensions of symmetry available in three-dimensional space: central chirality, axial chirality, and planar chirality (Figure 1). Further subdivisions are also possible; while the allene depicted in Figure 1 demonstrates one form of axial chirality, axial stereoisomers that differ by restricted rotation around a single bond are termed atropisomers. 

One of the primary goals of modern organic chemistry is the development of methods with which to enantioselectively and diastereoselectively synthesize target molecules. While simple methodological discovery provides one factor in this motivation, there is a practical factor as well: many natural compounds exist as pure enantiomers or diastereomers, and pharmaceutical development therefore mandates that drugs and therapeutic agents possess similar stereochemical purity to ensure the desired molecular interactions. A particularly infamous example is that of the chiral molecule thalidomide, sold as a drug to counter morning sickness, of which one enantiomer was
found to induce severe birth defects. Central chirality is the predominant form found in nature, although axial and planar chirality exist in specific products as well.

There are several general strategies to control stereochemistry in synthesis, all of which rely on some defined existing source of chirality. The substrate itself can possess existing stereogenic centers that can be exploited in further reactions (substrate control); the stereochemistry can be present on some stoichiometric reagent, and be translated to the substrate (reagent control); the reaction can be conducted in the presence of a chiral catalyst to impart absolute stereochemistry (catalyst control); or a chiral auxiliary unit can be added to the substrate to control reaction stereochemistry, and then removed.

Work in the Paley laboratory has primarily focused on this latter case; particularly, the installation of chiral auxiliaries on acyclic dienes so as to allow for the diastereoselective complexation of iron(0) tricarbonyl fragments. There exists a rich history of these metal complexes: ferrocene is the classic model, but more recent work has led to the availability of complexes bearing an enormous variety of metals that afford different steric and electronic properties.

The iron(0) tricarbonyl group was in fact used primarily to protect 1,3-dienes early in its lifetime, and it is capable of protecting these groups from a huge range of reactions, including additions, oxidations, and reductions. Mild, yet relatively specific oxidizing conditions remove the complex from the diene, enhancing its efficacy as a protecting group. However, it is the ability of the iron fragment to be diastereoselectively complexed that has been exploited by the Paley group. Early examples of such complexations were accomplished through the use of stereodirecting groups that initially
coordinate to the iron (Figure 2). Multiple chiral auxiliaries have also proven capable of inducing this diastereoselectivity.

1.2. Sulfoxides

The Paley group initially chose sulfoxides as a target of investigation. Chiral sulfoxides have been used in asymmetric synthesis for many years; the chiral molecules (S)-(−)-menthyl p-toluene sulfinate and its enantiomer were first isolated in 1925, and, now commercially available, they remain one of the primary synthetic pathways to chiral sulfoxides. This is commonly achieved through the Andersen synthesis (Figure 3), which utilizes Grignard reagents to replace the menthoxide with alkyl or aryl groups, with inversion of stereochemistry. Chiral sulfoxides were chosen due to a range of work reporting their stereodirecting ability in reactions including reductions of β-ketosulfoxides and nucleophilic addition to α,β-unsaturated carboxyls. Additionally, the sulfoxide units were expected to cleave from the body of the molecule easily, or else be converted into relevant functional groups. The ultimate goal of this work, following the diastereoselective complexations, has been to use these planar chiral η⁴ iron(0) tricarbonyl complexes as a means of stereocontrol for the preparation of neighboring

Figure 2. Diastereoselective iron(0) tricarbonyl complexations using stereodirecting groups, accomplished by A) Stephenson et al. and B) Pearson et al.

Figure 3. A general example of the Andersen Synthesis.
steregenic centers, relying on both the steric bulk of the iron fragment and neighboring group participation to direct nearby reactions. It is, to this end, critical to note that the practical utility of any chiral auxiliary is directly related to the ability to either remove it or transform it into a chemically useful moiety.

Before this goal could be truly approached, it was first necessary to determine the ideal substrate, in this case sulfanyl diene, structure to undergo diastereoselective complexation with both high yields and high diastereoselectivity. Following extensive studies placing the sulfoxide at all three possible positions on the diene and alkyl groups at various other positions (Figure 4), it was determined that the highest diastereomeric ratios were obtained using (1Z)-4-alkyl- and (1Z)-3,4-dialkyl-1-sulfanyl dienes. It has since been theorized that the diastereoselectivity of the complexation arises from a minimization of 1,3-allylic strain (Figure 5), and X-ray
crystal structures have confirmed the absolute stereochemistry.\textsuperscript{13,14} At this stage, complexations with diastereomeric ratios greater than 15:1 had been demonstrated, and the resulting $[\eta]^4\,(1Z)$-sulfinyl diene]iron(0) tricarbonyl complexes were ready to attempt the stereodirection of various reactions on the diene periphery.

\textit{1.2.1. Allylations}

The first reaction explored, both as an initial test for the stereodirecting potential of the system and as a means to differentiate between the influence of the iron fragment alone and that of the \textit{cis} configuration of the sulfoxide, was an aldehyde allylation, using allylstannanes. Previous reports had described several diastereoselective nucleophilic additions on the periphery of iron(0) tricarbonyl diene complexes; however, the resultant alcohols were never formed with $\text{dr}$ higher than 85:15, and often significantly below that. However, a simple sequence completed by Paley \textit{et al.}, beginning with one of the complexes (1) described previously, produced the alcohol product 3 with a

\textbf{Scheme 1}
diastereomeric ratio of 95:5 (Scheme 1). This reaction thus proved significantly more diastereoselective than any previously performed allylation adjacent to iron tricarbonyl complexes, implying a significant role of the cis sulfoxide in the stereoselectivity; this role was confirmed by an additional experiment in which the corresponding \( \eta^4-(1E) \)-sulfinyl diene was synthesized, underwent complexation, and was subject to Scheme 1, resulting in only an 80:20 dr.

This reaction was further explored through an investigation of the impact of substituents at the C3 position of the diene (Figure 6). The general model proposed, described more thoroughly in the work of my predecessor, Estroff ’97, is that the reactive conformation of the unsubstituted complex is the s-cis aldehyde, and the introduction of a small group on C3 destabilizes this conformation. However, larger substituents both destabilize the s-trans conformation and render it less reactive by impeding the approach of the nucleophile, leading to a renewed increase in diastereomeric ratio.

Allylations were also accomplished with the initial aldehyde located on the C3 carbon, and the predicted (R) alcohol was obtained with diastereomeric ratios up to 89:11. However, less substrate variety was explored here, and exclusively within the 3,4-
dialkyl diene group of complexes.\textsuperscript{16} Absolute stereochemistry for product alcohols at both diene sites was confirmed by X-ray crystallography.

\textit{I.2.ii. Ring-Closing Metathesis}

Following the synthesis of these allylation products, which notably contained terminal alkenes, the Paley group began considering the possibility of somehow installing a second terminal alkene that could then be used in ring-closing metathesis (RCM).\textsuperscript{17} This investigation was partially motivated by the ubiquity of carbocycles in natural products, and the synthetic difficulty in constructing them enantio- and diastereoselectively. RCM is most frequently catalyzed by Grubbs’ ruthenium carbene catalysts, which allow compatibility with air, water, and many specific functional groups, including alcohols. The metathesis has been demonstrated to occur via a series of [2+2] cycloadditions and cycloreversions (Figure 7).\textsuperscript{18} For this particular attempted

![Chemical structure](image)

\textbf{Figure 7.} The mechanism of the first catalytic cycle of ring-closing metathesis, catalyzed by Grubbs’ ruthenium carbene catalyst.

transformation, carbene 4 was the specific Grubbs’ catalyst used.

The first strategy proposed and successfully implemented for carbocycle formation relied on the Peterson olefination to transform aldehyde 5 into diene 6, which, upon addition of Grubbs’ catalyst, was converted to the six-membered carbocycle 7 with retained stereochemistry (Scheme 2). Initial attempts to extend the chemistry to larger
rings through 
addition of 
vinyl or allyl 
Grignard to 
aldehyde 5 
proved 
unsuccessful or extremely low-yield, but an alternative synthetic pathway was designed based on the work of Roush et al.,\textsuperscript{19} implementing an alkylidene malonate (8) to allow the facile, diastereoselective (98:2) conjugate addition of Grignard reagents and allylstannanes. My predecessor, Gauget '98, was able to accomplish the first such transformation, synthesizing a seven-membered carbocycle with two ring stereocenters (9a).\textsuperscript{20} Slight modifications have since enabled the construction of eight- and nine-membered rings through similar methodology (Scheme 3).

The six- 
through nine- 
membered rings 
were all 
synthesized with 
xcellent yields, 
and the nine- 
membered ring 9c 
was formed with 
a cis/trans ratio

Scheme 2

Scheme 3
of 35:1. The group then turned toward attempts to construct larger rings, following the precedent of Fürstner and Langemann, who demonstrated the ability to use RCM to form macrocycles, provided the substrate was free of conformational restraints. Syntheses were attempted both with and without a fused benzene ring in attempts to form 11- and 12-membered macrocycles, but both were incompatible with RCM (Scheme 4). Liu ’00 argued that the presence of the alkyne is likely at fault, both for imposing conformational restriction and for potentially interacting with the ruthenium catalyst itself.

However, while the construction of carbocycles was seemingly limited to medium sized rings, these ring products 7, 9a-c, are available for further derivatization. These expansions have not been thoroughly explored by the Paley lab, but a single transformation, reported by Newlin ’00, suffices to demonstrate the potential. Beginning with the eight-membered carbocycle 9b, iron was readily decomplexed to yield the diene, before an attempted sulfoxide reduction with SmI2 was found to cleave the C-S bond entirely, leaving triene 10. The substrate, now primed for a Diels-Alder reaction, was thus transformed into the [8,6]-fused ring system 11 with excellent yield.
(although the alcohol was deprotected in some of the product) (Scheme 5). While absolute stereochemistry is still ambiguous, the potential for such cyclooctanoid systems, particularly in natural product syntheses, is clear.

**I.2.iii. Intramolecular Pinacol Couplings**

The Paley laboratory then turned its attention to a new transformation, the intramolecular pinacol coupling, which forms a carbon-carbon bond between two carbonyls while reducing each to an alcohol (Figure 8). This target was motivated by the report of Uemura et al. describing the use of the coupling to diastereoselectively synthesize trans-1,2-diols from η⁶-arene Cr(CO)₃ complexes. These diols, and the formation of the bond between them, are critical elements in several natural product syntheses: the antibiotic graminimycin A₁ (12) was synthesized by Ghiringhelli using a pinacol coupling followed by oxidation to yield the key 1,2-diketone moiety, and the synthesis of anticancer agent sarcophytol B (13) by McMurry et al. required a stereoselective pinacol coupling to form the trans-1,2-diol present in the product (Figure 9).
Methods for inducing this diastereoselectivity remained rare, and relied primarily on substrate control with planar or axial chirality. The Uemura group’s work demonstrated the potential of metal complexes to perform in this context, and thus the reaction was explored with a variety of functionalized sulfanyl iron(0) diene complexes by the Paley group.

The first target approached was a relatively simple aryl system, the trans-1,2-diol synthesized by the pinacol coupling of dialdehyde 14. The coupling was achieved using Pedersen’s conditions and proceeded with good yield and excellent trans selectivity (33:1), although absolute stereochemistry was initially assigned only by precedent and NMR examination (Scheme 6). Given the initial success of this system for the diastereoselective synthesis of 1,2-diols, Sanan ’03 explored derivatizations of the benzene ring, and was successful, again using the vanadium reducing agent to cyclize the methoxy-substituted dialdehyde 16 into another trans-1,2-diol 17, again with good yield and trans selectivity of 27:1. However, while several other substrate variations underwent the intramolecular pinacol coupling to synthesize 1,2-diols, including a 3-formyl-4-(2-formylaryl) substrate 18 and a substituted indole substrate 19 (Scheme 7), further additional functionality led either to failure to synthesize the starting material or pinacol couplings that were essentially stereorandom. In particular, the presence of any group ortho to the aromatic formyl substituent was sufficient to inhibit any diastereoselectivity induced by the iron complex. In fact, in the process of this
investigation, the 1-sulfinyl dienes with 3-aryl groups generally demonstrated atropisomeric properties, realizing a chemical transformation (the complexation) that simultaneously imparted both planar and axial chirality. While the scope of these diastereoselective pinacol couplings is currently modest, the existing substrates have the potential to act as scaffolds for the asymmetric construction of numerous molecules with substantial functional variety.

I.2.iv. Spiroketalizations and Related Reactions

The next target for the Paley group was not a reaction, but a functional group: the spiroketal. The spiroketal is a spirocycle in which the central, quaternary carbon, which has the oxidation state of a ketone, connects two oxane rings (Figure 10a). The groups are named by the ring sizes, and the most common spiroketsals are [6,6], [6,5], and [5,5]. The
spiroketal is a common motif in natural products, such as spiroxabovolid (20), but they are specifically known for their pharmaceutical activity; the immunosuppressant (-)-ushikulide A (21) was the subject of a recent synthesis by Trost and O’Boyle (Figure 10b). However, the stereochemistry of spiroketals is remarkably complex, and requires a careful consideration of several factors to achieve any sort of selective synthesis.

The first factor relevant to absolute spiroketal stereochemistry is a familiar one, and concerns the substituents on each ring. As with cyclohexane, the oxane rings adopt chair conformations, and substituents are more energetically stable in the equatorial positions than the axial ones, particularly for large substituents. The second factor concerns the relative conformations of the two rings, and is known as the anomeric effect. While the exact cause of the effect is still debated, it is likely that a stabilizing orbital overlap (a stereoelectronic effect) occurs when a heteroatom ring substituent is axial with respect to the primary ring at the anomeric carbon (here, the quaternary carbon). Each oxygen can be either axial or equatorial with respect to the other ring.
leaving four
conformational
possibilities (Figure 11).
The most stable is that in
which both oxygen atoms
are mutually axial to the
other ring, maximizing the
anomeric effect. While each of these effects is well-studied individually, and matched
cases are clear, the stereochemical outcome of mismatched cases can vary considerably.
In addition, external stereodirecting influences can impart a third preference; Iwata et
al.\textsuperscript{34} have used chiral sulfoxides to selectively obtain all four possible diastereomers of a
substituted spiroketal, while Tan et al.\textsuperscript{35} demonstrated spiroketal formation with retention
from diastereoselective epoxidation of cyclic vinyl ethers, again selectively obtaining
desired diastereomers. The Paley group investigated an alternative pathway: the use of a
metal scaffold to influence spiroketal stereochemistry.\textsuperscript{36}

There are several reactions known for the synthesis of spiroketals, but the most
common, and that employed in the Paley laboratory, is the cyclization of
dihydroxyketones (Figure 12). This method, as an acid-catalyzed transformation, offers

![Figure 12. The mechanism for acid-catalyzed cyclization of a dihydroxyketone to form a [6,6]-spiroketal.](image-url)
additional synthetic efficiency, as the alcohol groups may be protected throughout the
preparation of the substrate
before being deprotected and
cyclized in a single step. To
first assess the feasibility of
the iron(0) tricarbonyl
complex as a stereodirecting
unit for spiroketalizations,
simple unsubstituted
spiroketal 23a,b were
prepared from the

![Scheme 8]

corresponding protected dihydroxyketones 22a,b with strong diastereoselectivities
confirmed by X-ray crystallography. In fact, while the Paley group has focused primarily
on 1-sulfinyl dienes, it was demonstrated that 2-sulfinyl dienes could competently direct
the spiroketalization as well, promoting the opposite stereochemical configuration
(Scheme 8).

With these preliminary results in hand, the Paley group turned toward an
expansive examination of the relative impact of these metal scaffolds and ring
substituents on the spiroketal stereochemistry. Through the work of Laupheimer ‘10,37
Ratcliffe ‘11,38 and Wong ‘13,39 methyl groups were placed with regio- and
stereoselectivity at every possible position along the two rings of the 1-sulfinyl-[6,6]-
spiroketals, and the stereochemistry of the products was observed (Figure 13). While the
results were informative, the preference for equatorial positioning of the methyl group
almost universally dominated the preference for the B-ring oxygen to be anti to the iron carbonyl ligands in mismatched cases, limiting the synthetic utility of the metal scaffold for complex molecules. A similar study, with identical conclusions, was conducted with 2-sulfinyl-[6,6]-spiroketal.

<table>
<thead>
<tr>
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<th>Matching</th>
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<th>Dominant</th>
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<td>Eq. Methyl</td>
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<tr>
<td>R₂</td>
<td>Matched</td>
<td>100:1</td>
<td>—</td>
</tr>
<tr>
<td>R₃</td>
<td>Mismatched</td>
<td>1:8:1</td>
<td>~ Equivalent</td>
</tr>
<tr>
<td>R₄</td>
<td>Matched</td>
<td>11.6:1</td>
<td>—</td>
</tr>
<tr>
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<td>Mismatched</td>
<td>4.4:1</td>
<td>Inconclusive</td>
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<td>Matched</td>
<td>4:1</td>
<td>—</td>
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<td>40:1</td>
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<td>—</td>
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<tr>
<td>R₁₂</td>
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![Chemical Structures]

Figure 13. The combined effects of methyl substituents and a metal scaffold on the stereochemistry of synthesized spiroketal. Inconclusiveness of R₅ and R₆ is due to epimerization of the substituted carbon.

21
The principles of this work were extended in several further directions: initially, this directed spiroketalization was used as a method of selective desymmetrization of prochiral carbon centers (Scheme 9). While diastereoselective ratios were not excellent ($\leq 5:1$), the principles of the chemistry were useful, and again demonstrated the directing power of the metal scaffold.

At this stage, targets related to the spiroketal were chosen to explore the scope of the reaction. First chosen were benzannulated spiroketalts and bis-spiroketals, synthetically similar to spiroketalts and themselves common in natural products, such as berkelic acid and salinomycin, respectively (Figure 14). Both motifs were accessible through sulfinyl diene iron(0) tricarbonyl complexes without significant alteration to the methodology discussed above (Scheme 10). The cyclization to monobenzannulated spiroketal 26 proceeded with expected stereochemistry, and was accomplished with a diastereoselective ratio of 20:1. The bis-spiroketal 27, however, was less amenable to

![Scheme 9](image)

![Figure 14](image)
stereochemical direction. The product was recovered with a diastereoselective ratio of 5:5:1:1, indicating that the absolute stereochemistry of the first anomic carbon was controlled by the metal scaffold, albeit modestly, while the second cyclization occurred stereorandomly. Ultimately, this was unsurprising: the myriad factors influencing the conformation of any spiroketal were described previously, and the number only increases upon the addition of a third ring.

The final related synthetic target was the 1-azaspirocycle, which ultimately required the incorporation of several aspects of the Paley group chemistry. As with the spiroketal, the 1-azaspirocycle is common in natural products, such as cocculolidine (Figure 15). It is a common synthetic target, and many methods are known, although again, the stereochemistry of the central carbon is a critical issue. The first attempt in the Paley laboratory at 1-azaspirocycle synthesis, conducted by Wong ’13, followed a pathway conceptually similar to that of the spiroketal, in which imine 28 would be subject to an acid-catalyzed nucleophilic cyclization (see Figure 12 for comparison) to yield the desired azaspirocycle.
However, substantial difficulties were encountered synthesizing the imine, and a 1-azaspirocycle 32 was instead obtained using a variation of previously discussed chemistry: diastereoselective allylation of imine 30 to obtain diene 31, which was then cyclized using ring-closing metathesis to afford the 1-azaspirocycle (Scheme 11). While perhaps less efficient, this method produced a single diastereomer in high yield.

Questions of scope and optimization remain for each of these projects, but the syntheses discussed demonstrate the wide range of applicability of the sulfinyl diene iron(0) tricarbonyl complexes to the asymmetric synthesis of relevant functional groups for natural products and pharmaceuticals.

I.3. New Chiral Auxiliaries

However, although decomplexation was usually simple, removal of the sulfoxide auxiliary from many of these complexes proved inefficient, unpredictable, or downright impossible while maintaining the structural integrity of the rest of the molecule. Given how crucial this ability is for the practical potential of these diastereoselective transformations, the search for alternative chiral auxiliaries has been a recurrent theme of research in the Paley group. The first attempts aimed to mirror the conformational rigidity
enforced by allylic strain in the sulfoxide (Figure 5) with a tetrahedral carbon center. Such auxiliaries initially rendered standard 3,4-disubstituted dienes completely unreactive, leading to the hypothesis that electron-poor dienes (a property previously induced by the sulfoxide) were required for the complexation. Indeed, the construction of dienes with electron-withdrawing esters at the C3 position promoted the complexation, albeit with the necessity of a 20° C temperature increase, and slight diastereoselectivity was observed (Figure 16). The only-moderate diastereoselectivity was attributed, at least partially, to the higher temperature reaction conditions, which allow the carbon chiral

<table>
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</tr>
<tr>
<td>C*</td>
<td></td>
<td></td>
<td></td>
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<td>3.5:1</td>
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Figure 16. The ability of synthesized, carbon-based chiral auxiliaries to induce the diastereoselective complexation of substituted dienes.

auxiliary to more easily rotate and change conformations. Potential existed, but these were not the ideal chiral auxiliaries.

Several years later, inspired by a report from Movassagi et al., Koellhoffer '07 considered the possibility of using a chiral oxazolidinone group to direct the facial selectivity of the iron complexation. Oxazolidinones have been used as chiral auxiliaries in a range of transformations, including 1,3 cycloadditions and Diels-Alder reactions, since Evans first demonstrated their utility in aldol condensations. Although dienes with particularly bulky groups at the C3 position were loath to undergo the complexation at all, an appropriate N-oxazolidinoyl diene 33 was eventually
constructed that was successfully complexed to provide the corresponding iron(0) tricarbonyl complex 34 with 3:1 diastereoselectivity (Scheme 12). No X-ray crystal structure was immediately obtained, so only hypotheses could be offered as to the exact stereochemistry of the product.

Scheme 12

Erskine '10 continued the investigation, successfully synthesizing several further iron complexes (35, 36, 37) with variable diastereoselectivity and yields (Figure 17). The oxazolidinone auxiliary was clearly more fragile than the sulfoxide, as desired, although some additional care was thus required to avoid premature removal or transformation. However, X-ray crystal structures remained elusive until Wong '13 synthesized complex 38, of which both major and minor products were crystallizable. The absolute facial selectivity of the oxazolidinone chiral auxiliary was therefore confirmed.

Figure 17. Several complexes diastereoselectively synthesized from the corresponding oxazolidinone dienes. Absolute stereochemistry of 38 was confirmed by crystal structure.
and a model was developed to justify the preference. The facial distinction likely stems from the isopropyl group, which sterically clashes with any group on C3 (methyl, in 38) to disfavor the minor conformation. The iron then complexes to the same face as the existing carbonyl, in a likely stabilizing electronic effect (Figure 18). Given this stereochemical insight into the chiral oxazolidinone’s impact, as well as the ease of its removal, these groups have become the default chiral auxiliary in the Paley laboratory.

However, work is ongoing in the continued exploration of new possibilities; while none have yet been successful, Dow 18 began an investigation into the use of N-oxazolidinone analogs, such as chiral cyclic sulfonamides and chiral protected cyclic ureas, as potential auxiliaries for future diastereoselective complexations.49

1.4. Oxazolidinones

1.4.1. Early Transformations

The investigation into the stereodirecting capability of these N-oxazolidinoyl diene iron(0) tricarbonyl complexes began by attempting to reproduce several of the diastereoselective reactions previously induced by the sulfoxide chiral auxiliary. Most
prominent was the conjugate addition of various nucleophiles to alkylidene malonate functionality on the diene periphery, in analogy to the first step of the transformations depicted in Scheme 3 (Scheme 13).

While yields were variable, they were largely good to excellent (> 70%); however, more notably, each of these reactions proceeded with perfect diastereoselectivity, producing a single product. These diastereopure products were then available for further transformation.

One such example involved a complex (39) with a previously existing alkyne group on the C3 carbon, which was capable of undergoing enyne metathesis to form a seven-membered carbocycle (40) with defined stereochemistry (Scheme 14).\(^50\) Unfortunately, this reaction proceeded with disappointing yield (12%), so the product was unavailable for further study. Other attempted cyclization reactions, including an intramolecular Diels-Alder\(^51\) and a gold(I)-catalyzed methoxycyclization\(^52\) were either themselves unsuccessful or required substrates that could not be synthesized. However, the stereodirecting capability of the iron complexes seemed unaffected, or

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\(^{50}\) Scheme 13

\(^{51}\) Scheme 14
even heightened, by the shift from sulfoxides to oxazolidinones, prompting the Paley group to attempt diastereoselective control over a new reaction: rhodium(II)-catalyzed intramolecular C-H insertion.

**I.4.ii. Intramolecular C-H Insertions**

The targets chosen by the Paley group, whether reactions or functional groups, have focused primarily on cyclization reactions due to the enormous prevalence of various ring functionalities in natural products. A previously unexplored such transformation is the intramolecular C-H insertion, catalyzed by a transition metal; the reaction begins by the conversion of an α-diazocarbonyl to a metal carbenoid, frequently using rhodium (Figure 19). This methodology allows for the efficient, diastereoselective synthesis of five-membered rings, and has been incorporated in the construction of a huge number of natural products.\(^{33-35}\) Additionally, a report from Jamison *et al.* offered precedent for the potential of accomplishing the insertion in the presence of a metal complex, and in fact the dicobalt hexacarbonyl fragment studied was found to bolster the scope and reactivity of the cyclizations.\(^{56}\) The Paley group predicted a similar impact of
the iron(0) tricarbonyl on the efficacy of C-H insertion reactions, in addition to the
desired stereodirecting influence on the final reaction product.

My predecessor, Choi ’17, was the first to attempt such a synthetic pathway, and
was able to access α-diazooester 41, which was cyclized to cyclopentane 42 upon the
addition of rhodium(II) acetate catalyst (Scheme 15).\(^{57}\) The practical aspects of this
pathway, including yields, stability, and generalizability to other substrates were far from
ideal, and these shortcomings will be detailed in the following sections of this thesis.
However, the product was formed as a single diastereomer, vindicating the hope that the
N-oxazolidinoyl diene iron(0) tricarbonyl complexes would induce significant
stereoselectivity. Initially, crystals were unavailable, and multidimensional NMR was
inconclusive, leading to
the inability to assign
either relative or absolute
stereochemistry to the
cyclopentane 42.
Ultimately, recent
unpublished work by my
colleague Hejna ’19 has confirmed the stereochemical assignment of related structure 43,
which is assumed to be generalizable to all such C-H insertion products. This
methodology remains in its infancy, and its expansion and refinement serve as the
primary goals of this thesis. Already, the observed diastereoselectivity of this
intramolecular C-H insertion represents enormous promise as the latest development in
the overarching goal of the Paley group: using chiral auxiliaries to enforce facial
selectivity in the complexation of an iron(0) tricarbonyl group to a diene, before exploiting that planar chirality to direct the stereochemistry of neighboring transformations, particularly those relevant to the synthesis of complex products.
II. Results and Discussion

The work in this thesis can be broadly divided into three sections: the separate syntheses of cyclopentenes 44 and 45 (Figure 20), and a concurrent investigation into alternative, more effective methods of installing the requisite diazo group for C-H insertion.

![Chemical structures of 44 and 45](image)

Figure 20. The cyclopentane targets of this research. Stereochemistry tentative.

II.1 Silyl Ether Cyclopentene

The effort to access cyclopentene 44 was initially motivated by Choi’s successful synthesis of related complex 42. In fact, complex 42 was the original target of this project. Several practical factors inspired that choice: while Choi’s synthetic pathway (Scheme 16) had ultimately proven successful, several steps, particularly the complexation and the formation of the diazo ester, were quite low-yielding, leading to a desire for optimization and a new approach. Additionally, decomposition was a constant
threat, and when a similar pathway was attempted with a related substrate, complexation failed due to total decomposition of the diene. Therefore, we searched not only for a more efficient, stable pathway, but one that could be generalized as well.

We first tried a pathway in which the requisite homopropargylic alcohol was installed in the first step, the nucleophilic attack of commercially available ethyl propiolate 46 on ethylene oxide to afford alcohol 47 (Scheme 17). While this initial step was successful, as was the subsequent alcohol protection to silyl ether 48, the conditions of the regioselective stannyliccupration that followed induced alcohol deprotection followed by cyclization to yield lactone 50, rather than producing the desired acyclic vinyl stannane 49.58 Thus, we envisaged a new route to the desired cyclopentene. We began by assembling the functionalized Stille partner.

Base-promoted installation of a methyl ester on ether 51 yielded alkyne 52, which then smoothly underwent the same regioselective stannyliccupration as in the previous pathway to afford vinyl stannane 53. At this stage, the ester was reduced to the alcohol (54), followed by iodination of the vinyl stannane using N-iodosuccinimide (NIS), which yielded vinyl iodide 55. The allylic alcohol was then protected as a TBDPS silyl ether.
(56), ideally a stronger protecting group than the THP ether on the other, homoallylic alcohol. In preparation for a one-carbon homologation of that homoallylic alcohol, we attempted to remove the THP protecting group selectively using camphorsulfonic acid (CSA). However, upon TLC examination, the dominant product was more polar than expected, and NMR confirmed that the diol 57 had been formed. In fact, while both singularly unprotected alcohols appeared to be present in small amounts, the second-most prevalent species, which we initially predicted to be starting material due to its low polarity, was a methyl silyl ether byproduct.

However, the more mild acidic conditions of pyridinium p-toluenesulfonate (PPTS), over the course of 60 hours, were capable of cleaving the THP ether selectively, producing alcohol 58 as a singular product.

At this stage, we aimed to oxidatively homologate the alcohol to an ester in advance of the Stille coupling. Such oxidative homologations are a common necessity in organic synthesis, and while several strategies exist, they focus primarily on carboxyls.\textsuperscript{59,60} Alcohol homologation is possible, but has typically required a multistep
pathway in which the alcohol is converted to a halide or sulfonate, displaced by cyanide, and hydrolyzed to the carboxylic acid or amide. However, a recent report from Rawal et al. inspired us to attempt the homologation through a Mitsunobu reaction with masked acyl cyanide (MAC) reagents.62

The Mitsunobu reaction, discovered in 1967, has long provided a synthetically simple method by which various nucleophiles can directly perform $S_N2$ substitutions on primary and secondary alcohols.63 The mechanism has been well studied, and is presented in Figure 21.64

![Figure 21. The complete mechanism for a generic Mitsunobu reaction. DIAD may be replaced by another azodicarboxylate.](image)

However, while the reaction tolerates a wide variety of heteroatom nucleophiles, the requirement for the nucleophile to originally bear an acidic proton is largely
prohibitive to the addition of carbon groups. Rawal et al. demonstrated the use of MAC reagents in the Mitsunobu reaction; as acidic, carbon-based pronucleophiles, they are compatible with the methodology, and essentially allow the substitution of an alcohol with an acyl anion equivalent. While the use of the Mitsunobu reaction to form carbon-carbon bonds is itself interesting, this particular method would offer little practical utility if the intermediate MAC-adduct were unable to be “unmasked,” providing the oxidatively homologated product.

Fortunately, Rawal et al. developed and optimized the required conditions to convert this key intermediate into the corresponding esters, amides, or carboxylic acids, accomplishing the initial goal of oxidative homologation (Scheme 19).

To apply this chemistry to the construction of the Stille partner for cyclopentene 42, an initial attempt was made to perform the Mitsunobu with alcohol 58 and a TBS-MAC reagent synthesized from acetylmalonitrile, with the expectation of forming MAC adduct 59. However, multiple attempts produced no clean product, and in fact the report from Rawal et al. indicated similar failure with TBS-MAC and benzyl alcohol. We therefore switched to a MOM-MAC reagent, which reacted with the alcohol to form MAC adduct 60 in good yield. As reported, the adduct was then unmasked by CSA, in a solution of acetic acid and DME, to form the dicyanohydrin intermediate, which was converted successfully to the corresponding ethyl ester (61) after addition of ethanol. These conditions were also sufficient to cleave the silyl ether at the allylic alcohol and
replace it with an acetyl group, but such a transformation was in no way destructive to the synthetic pathway, and the product was therefore continued forward.

To restore the silyl ether, the acetyl group was then removed by base to yield the alcohol (62), which was then reprotected, again as a TBDPS silyl ether (63). This vinyl iodide was thus prepared for a Stille coupling. The vinyl stannane coupling partner bearing the oxazolidinone chiral auxiliary was separately prepared following standard Paley group protocols, beginning with (S)-(−)-4-isopropyl-2-oxazolidinone (64). The auxiliary was first subjected to N-vinylation to compound 65 using vinyl butyl ether with a palladium catalyst. At that stage, tributyltin chloride and base lithium tetramethylpiperidine (LiTMP) were used to regioselectively add a tributyl stannyl group to the vinyl position, producing vinyl stannane 66 as the second Stille coupling partner. The Stille coupling provides a facile, selective method of palladium-catalyzed carbon-carbon bond formation between vinyl (or aryl) iodides and vinyl (or aryl, alkynyl) organostannanes. As one of the first coupling reactions, its mechanism
has been thoroughly investigated, although ligands continue to provide slight alterations to the pathway (Figure 22).

![Stille Reaction Mechanism](image)

Figure 22. The mechanism for a generic Stille coupling between a vinyl (aryl) iodide and a vinyl (aryl) stannane.

The Stille reaction's compatibility with a range of functional groups, along with the ease of formation, purification, and characterization of organostannanes has led to the continued prevalence of the Stille reaction despite the emergence of other coupling reactions and the toxicity of the organostannanes. Additionally, a report from Fürstner et al. provided modified conditions capable of improving the reaction yield and allowing the byproduct to be more easily removed; these conditions are applied to all Stille couplings reported here.\(^{71}\)

To form the diene predecessor (67) to cyclopentene 42, vinyl iodide 63 underwent a Stille coupling with the \(N\)-oxazolidinoyl vinyl stannane 66. The diene was then subjected to complexation with diiron(0) nonacarbonyl to yield product 68 in a pleasing 78% yield, a vindication of this pathway as compared to the 21% yield achieved in the
method previously attempted by Choi. Additionally, the complexation was achieved with
diastereomeric ratio of 11:1, and the minor product was separable by column
chromatography.

However, in a particularly frustrating development, the attempted benzylation of
the iron(0) complex in advance of the diazo transfer resulted in complete destruction of
the complex by a presumed initial allyl elimination that then led to a series of
unidentifiable byproducts. While the modified pathway had allowed higher-yield
preparation of the desired iron(0) tricarbonyl complex, as desired, the conditions then
required to install the diazo group were apparently too harsh for the vulnerable allylic
silyl ether. This setback ended our hopes of exactly recreating cyclopentene 42, but we
hypothesized that the methodological developments involved would be useful in
optimizing synthetic routes to similar complexes.

Scheme 22

Fortunately, the pathway was, as hoped, generalizable to other substrates, and
fellow lab member Hejna was able to synthesize vinyl iodide Stille partner 69, in which
the silyl ether was homoallylic, and thus far less vulnerable, using similar protocols. This
vinyl iodide again underwent Stille coupling with vinyl stannane 66 to produce diene 70,
followed by another successful complexation to 71 with an 89% yield. The complexation was determined by proton NMR to have proceeded with a 12:1 dr; however, the diastereomers were determined to be inseparable, and were thus both carried forward to be separated at a later point.

We then attempted to install the diazo group α to the ester on our new complex. The use of diazo transfer reactions for the synthesis of diazo compounds has long been known, but mechanisms and ideal conditions continue to vary by substrate.72,73 In particular, the methylene typically needs to be in the presence of two electron-withdrawing groups to be reactive. However, numerous reports have detailed temporary activation with formyl, alkoxoyxalyl, and benzoyl groups. We chose to follow the precedent of Taber et al., utilizing titanium tetrachloride (TiCl₄) to promote the initial benzoylation of the diene to α-benzoylated ester 72.74 This was followed by a diazo transfer using 4-acetamidobenzenesulfonyl azide (p-ABSA) as the transfer reagent, along

![Proposed mechanism for diazo transfer with an aryl sulfonyl azide as the transfer reagent and DBU as the base, affording the α-diazoester.](image-url)

Figure 23. Proposed mechanism for diazo transfer with an aryl sulfonyl azide as the transfer reagent and DBU as the base, affording the α-diazoester.
with 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU) as a base. We propose the above mechanism for the transfer (Figure 23).

The transfer successfully produced α-diazoester 73; although the yield was good, the yield of the preceding benzoylation was disappointing at only 38%. This was far below those reported by Taber et al., although the substrates studied in that report were uniformly more simple. However, the direct precursor to our target cyclopentene 44 was now in hand, and ready to be treated with the rhodium(II) catalyst. Upon performing the C-H insertion, two products, presumed to be the major and minor diastereomers, were obtained in a mass ratio of 2.3:1. While we assume that 44 was the major product, matching the configuration of previously crystallized product 43, neither diastereomer was crystallizable, and therefore absolute stereochemical assignments are only tentative. However, multidimensional NMR (NOESY) of the cleaner minor product indicated no spatial interaction between the two protons on stereogenic carbons on the cyclopentene ring, suggesting an anti relationship between those protons, as opposed to the syn relationship proposed in the major product. It seems likely that the last several steps of
this reaction pathway could still be optimized; not only was the benzoylation quite inefficient, the insertion itself produced an unexpected byproduct with the same Rf as the starting material, leading to a likely excessive reaction time. However, the desired cyclopentene was obtained with at least mild diastereoselectivity, again expanding the reported capabilities of our N-oxazolidinoyl diene iron(0) tricarbonyl complexes.

II.2 Indole Cyclopentene

The second project undertaken was a broad attempt to extend the functional group tolerance of the C-H insertion methodology being explored by the Paley group. Indole groups are extremely prevalent in natural products, and indole alkaloids are common synthetic targets. Therefore, we attempted to synthesize cyclopentene 45, containing a protected indole rather than the protected alcohols targeted thus far in the C-H insertion investigation. We began, here, with the aldehyde 74 containing a protected indole, which had been previously prepared for a different project. To convert this material into a vinyl iodide, as would be required for the eventual Stille coupling, the aldehyde needed to be converted to an alkyne. While several methods for such a transformation are known, one of the most commonly applied is the Seyferth-Gilbert homologation; while the original reaction applies only to aryl ketones and uses dimethyl (diazomethyl)phosphonate, the Ohira-Bestmann modification uses dimethyl-1-diazo-2-oxopropylphosphonate instead, and is tolerant of many aldehydes bearing a variety of functional groups.\textsuperscript{75,76} The mechanism, which first involves \textit{in situ} generation of the original Seyferth-Gilbert reagent, has been thoroughly investigated, and is shown below (Figure 24).\textsuperscript{77}

Subjecting aldehyde 74 to the Ohira-Bestmann conditions produced terminal alkyne 75, which then performed nucleophilic attack on ethylene epoxide to afford
homopropargylic alcohol 76. For this compound, the construction of the intermediate vinyl stannane was unnecessary, and instead the alkyne underwent a regioselective hydrozirconation with Schwartz’s reagent before being converted directly to the desired vinyl iodide (77) with N-iodosuccinimide (NIS) in a single flask. At this stage, as with the silyl ether pathway, we hoped to oxidatively homologate the alcohol to an ester before the Stille coupling.

We therefore attempted the same procedure as previously, and we successfully obtained MAC adduct 78 upon performing the Mitsunobu reaction with the alcohol and a MOM-MAC reagent.
However, upon our attempt to unmask the adduct with CSA, in a solution of acetic acid and DME, followed by addition of ethanol to form the ethyl ester, only a series of unidentifiable products was obtained. We hypothesize product formation followed by isomerization, with a possible acetylation of the indole C3.

To bypass this hurdle, we planned to perform the Mitsunobu with a different MAC reagent that could be unmasked under more mild conditions. To that end, we turned to an EE-MAC reagent, which was successfully installed to form MAC adduct 79.

We were pleased to find that, upon treatment with trifluoroacetic acid (TFA) in CH$_2$Cl$_2$, followed again by addition of ethanol, ethyl ester 80 was obtained in good yield (75%). Additionally, the tosyi protecting group remained attached to the indole, so that our vinyl iodide partner was immediately ready for the Stille coupling. To form the desired N-oxazolidinoyl diene (81), this vinyl iodide, bearing the protected indole, was coupled with vinyl stannane 66, identically to our previous compound. This Stille coupling was achieved with an
excellent yield of 82%, and the subsequent complexation with diiron(0) nonacarbonyl proceeded with a 75% yield to produce complex 82. Notably, all complexations using the pathways discussed in this work were accomplished with greater than 70% yield; this represents an enormous improvement over the 21% yield reported by Choi in the first attempt at C-H insertion with an N-oxazolinediylyl diene iron(0) tricarbonyl complex. Additionally, although the diastereomers were again determined to be inseparable at this point in time, proton NMR indicated a dr of 11:1 for the complexation.

The final transformations involved in this pathway were identical to those for the silyl ether complex. The complex was first benzoylated in the presence of TiCl₄ to produce α-benzoylated ester 83, which then underwent a diazo transfer to afford α-diazoester 84. The yield of the benzylation was, unfortunately, no better than for the previous complex, and in this case the diazo transfer was equally inefficient; the overall

Scheme 26
yield over these two steps was just 9%. We were therefore left with less than 15 mg of our cyclopentene precursor. However, we attempted the final C-H insertion, and were indeed able to isolate approximately 4 mg of our presumed product (45). While this mass prohibited the separation of major and minor diastereomers, and therefore any multidimensional NMR analysis, the proton NMR suggested a dr of 9:1, significantly higher than that demonstrated by the silyl ether complex. This improved selectivity seems experimentally unsurprising; as mentioned previously, the α-diazoester 73 was stirred with rh(II) catalyst for nearly 15 hours, while the corresponding complex 84 here reacted for only 3.5 hours, the standard procedure in the Paley laboratory. Given both the minimal yield and the oil-nature of the product, no crystal structures could be obtained; therefore, both absolute and even relative stereochemistry are only tentative. However, we see no reason to hypothesize a different stereoinductive model for this complex than for those previously synthesized, so we propose identical stereochemical assignments.

II.3 Diazo Group Installation

While both of these pathways ultimately led to the formation of the desired cyclopentene complexes, neither could be considered optimized given the low yields obtained; this difficulty was prohibitive to any exploration of post-insertion chemistry. The methodological alterations, as compared to Choi’s original pathway, indeed succeeded in increasing complexation yields, but the diazo transfer steps clearly remain problematic. Therefore, a final, concurrent project aimed to investigate possible alternative methods to construct the diazo group. The general strategy conceived was to synthesize the desired diazo group by cleavage of the corresponding protected hydrazone
diene iron(0) tricarbonyl complex, a common method (Figure 25). The question, therefore, became how to synthesize complex 85.

![Chemical structure](image)

Figure 25. Retrosynthetic analysis for alternative installation of a diazo group from a hydrazine diene complex.

The first potential approach was to install the protected hydrazine directly from the corresponding ketone diene complex. However, previous reports from Franck-Neumann et al. suggest that such reactions, using p-toluenesulfonylhydrazide to form the desired tosylhydrazones, require elevated (reflux) temperatures when the diene C3 is a hydrogen. Given the fragility of our iron complexes at such temperatures, we searched for a different method.

Specifically, we considered installing the hydrazine nearer the beginning of the reaction sequence, before the complexation. Many possibilities arose; theoretically, we could attempt the installation at almost any point in the sequence. However, we were concerned with the compatibility of several reactions, such as alkyne stannylcupration and the subsequent iodination, with the protected hydrazine. Similar questions arose for the key reactions: the Stille coupling and the iron complexation. Given that no precedent for such reactions existed within the Paley group, we embarked upon initial, exploratory attempts.

Morpholine amide 86 had been synthesized for an unrelated project by a predecessor, and it offered the opportunity to make initial feasibility tests. To begin, the amide was reduced to the corresponding ethyl ketone (87) by a cerium(III) chloride-
promoted Grignard addition. At this stage, the ketone was prepared for conversion to the tosyl hydrazone 88, using p-toluenesulfonylhydrazide. We were initially unsure of the optimal conditions for such a transformation; we therefore attempted it simultaneously by two methods, the first using only methanol at 55°C, and the second using PPTS and magnesium sulfate (MgSO₄) at room temperature. While the former was ineffective at installing the hydrazone, the latter conditions yielded 88 in a 74% yield. To our pleasure, a subsequent iodination using NIS appeared to afford vinyl iodide 89. Unfortunately, the scale was now less than 10 mg, so we turned to a new starting material in the hope that the principle established would be applicable to a general pathway.

We therefore began again with alkyne 90, planning to follow a similar strategy as previously. We thus initially installed the morpholine amide group by reacting the terminal alkyne with 4-morpholinecarbonyl chloride to yield 91. The amide then successfully underwent a regioselective stannylcupration to afford vinyl stannane 92 with
75% yield. However, to our surprise and disappointment, four separate attempts to form the ketone, first using ethyl Grignard and later methyl Grignard, appeared to have no impact on the substrate. While our first hypothesis was defective reagent, the failure of multiple Grignard reagents makes this unlikely. Unfortunately, time constraints led to this project being put on hold at this stage; that being said, future work is critical to further explore the possibility of installing a hydrazone early in the reaction sequence, ideally improving the overall yield, and therefore practical applicability, of our C-H insertion pathways.

While other potential pathways exist, further research has led us to doubt the viability of the exploration detailed here. In particular, a report from Neumann et al. has suggested that such iron(0) tricarbonyl α-diazodiene complexes are only stable if an electron-withdrawing group is adjacent to the diazo group, as the electron-rich nature of the complexed diene would otherwise destabilize the diazo functionality. In the current strategy, the adjacent group is installed by a Grignard reaction, therefore prohibiting the
presence of an ester or similar group in that position. Ultimately, this continuing investigation will be complex and require the consideration of many such factors.

II.4 Concluding Remarks

The broad goal of this work was to expand the capacity of the Paley group to use N-oxazolidinoyl diene iron(0) tricarbonyl complexes to direct the stereochemistry of transformations on the diene periphery, with a specific aim to investigate the rh(II)-catalyzed intramolecular C-H insertion reaction. We were able to achieve three high-yielding, diastereoselective complexations of dienes bearing privileged functionality: two with carbon chains bearing silyl ethers, and a third bearing a protected indole group. Notably, the novel pathways discussed here led to complexation yields of greater than 70%. Two of these complexes were then successfully carried forward to a C-H insertion reaction, forming cyclopentenes with modest to good diastereoselectivity. However, the currently employed diazo group transfer methodology is an inefficient link in these synthetic pathways, and further exploration of these capabilities should focus on alternative methods to install the diazo group required for the insertion. Future work should also investigate post-insertion chemistry; the versatility of the complexes constructed here will open doors to further diastereoselective transformations, enabling the selective synthesis of multicyclic systems and critical moieties in natural products. Such efforts will require both decomplexation of the iron fragment and removal of the oxazolidinone, but these methods now exist in the Paley group, and will allow general application of the work described in this thesis.
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Experimental

General Experimental Methods

All air- or moisture-sensitive reactions were carried out in inert atmosphere conditions, either on a Schlenk line under argon atmosphere or in a glove box under nitrogen atmosphere. The solvents used in these methods were anhydrous, unless otherwise noted. THF, toluene, and dichloromethane solvents were purchased from J.T. Baker and kept in an anhydrous solvent dispenser. When being utilized, the collection flasks for these solvents were purged with alternating evacuation and argon flow, and the solvents were run through neutral alumina/copper(II) oxide columns to assure that they were anhydrous. All liquids and solutions were measured and transferred using gastight syringes or cannulas, and all solids were weighed using an analytical balance. All air-sensitive reagents were stored under inert nitrogen atmosphere in a glovebox.

All crude products were purified by flash column chromatography using nitrogen-flushed silica gel from Acros Organics, with a mean diameter of 60 Å, as the solid phase, and mixtures of hexanes, ethyl acetate, and sometimes trimethylamine as eluents. Compounds with limited solubility in these solvents were loaded onto the column using either toluene or chloroform.

Thin layer chromatography was carried out using Uniplate 250 micron precoated glass plates purchased from Analtech. Visualization of product spots was achieved using ultraviolet light, vanillin dip, and/or permanganate dip. Products were characterized by NMR using a Bruker Ascend 400 MHz spectrometer, with samples prepared in anhydrous deuterated chloroform. Fourier transform IR spectra were taken using a Thermo Fisher Nicolet iS5 Spectrometer. Rotational analysis was carried out using a
Jasco P-2000 series polarimeter, with samples prepared in chloroform. HRMS was performed by the Mass Spectrometry Facility in the Department of Chemistry at the University of California at Riverside.
Alcohol (47): Ethyl propiolate (46) (300 µL, 2.96 mmol, 1 eq) was dissolved in THF (20 mL) under an Ar atmosphere. Solution was then cooled to -78°C, before n-BuLi (1.302 mL, 3.26 mmol, 1.1 eq) was added dropwise. After 30 minutes of stirring at -78°C, BF₃ • OEt₂ (0.562 mL, 4.44 mmol, 1.5 eq) was added dropwise as well. Ethylene oxide (1.776 mL, 4.44 mmol, 1.5 eq) was added to the flask immediately afterwards, followed by stirring for 3 hrs at -78°C. The solution was then treated with an aqueous saturated NH₄Cl solution (15 mL), the layers were separated, and the aqueous layer was extracted with Et₂O (3 x 15 mL). The combined organic layers were washed with brine, dried (MgSO₄), filtered, and concentrated using a rotary evaporator. A crude NMR indicated the formation of alcohol 47 (assumed 100%), which continued the sequence without purification.

$^1$H NMR (400 MHz) δ 1.33 (t, 3H, J = 7.1 Hz, CO₂CH₂CH₃), 2.23 (s, 1H, CH₃CH₂OH), 2.62 (t, 2H, J = 6.3 Hz, CH₂CH₂OH), 3.82 (t, 2H, J = 6.2 Hz, CH₃CH₂OH), 4.23 (q, 2H, J = 7.1 Hz, CO₂CH₂CH₃).
Silyl ether (48): Alcohol 47 (420 mg, 2.96 mmol, 1 eq), in Schlenk flask, was dissolved in DMF (3 mL). Imidazole (302 mg, 4.44 mmol, 1.5 eq) and TESCl (596 µL, 3.55 mmol, 1.2 eq) were then added in order, before the solution was left to stir at room temperature overnight. Purification of the mixture by column chromatography (silica, 15:1 hexanes/EtOAc) yielded silyl ether 48 (505 mg, 67% - this yield calculated assuming 100% yield in the previous, unpurified reaction).

$^1$H NMR (400 MHz) δ 0.61 (q, 6H, J = 8.0 Hz, Si(CH$_2$CH$_3$)$_3$), 0.96 (t, 9H, J = 7.9 Hz, Si(CH$_2$CH$_3$)$_3$), 1.30 (t, 3H, J = 7.1 Hz, CO$_2$CH$_2$CH$_3$), 2.56 (t, 2H, J = 7.1 Hz, CH$_3$CH$_2$OTES), 3.79 (t, 2H, J = 7.1 Hz, CH$_2$CH$_2$OTES), 4.22 (q, 2H, J = 7.1 Hz, CO$_2$CH$_2$CH$_3$).
Ester (52): Starting alkyne (2-(3-Butyn-1-yloxy)tetrahydro-2H-pyrano) (51) (462 μL, 2.95 mmol, 1 eq) was dissolved in THF (15 mL) and cooled to -78°C. n-BuLi (1.24 mL, 3.10 mmol, 1.05 eq) was added dropwise, and the solution was stirred for 1.5 hrs. To the solution was then added methylchloroformate (240 μL, 3.10 mmol, 1.05 eq) dropwise, and the solution was stirred at -78°C for 2 hrs. The mixture was then capped and left to warm to room temperature (overnight). The solution was then treated with H2O (10 mL), the layers were separated, and the aqueous layer was extracted with Et2O (2 x 100 mL). The combined organic layers were washed with brine (100 mL), dried (MgSO4), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 7:1 hexanes/EtOAc) yielded ester 52 (429 mg, 69%).

1H NMR (400 MHz) δ 1.57 (m, 4H, 4 of OCHOCH2CH2CH2CH2), 1.72 (m, 1H, 1 of OCHOCH2CH2CH2CH2), 1.83 (m, 1H, 1 of OCHOCH2CH2CH2CH2), 2.65 (t, 2H, J = 6.9 Hz, OCH2CH2CCOO2CH3), 3.52 (m, 1H, 1 of OCHOCH2CH2CH2CH2), 3.61 (app. dt, 1H, 1 of OCHOCH2CH2CH2CH2), 3.76 (s, 3H, CO2CH3), 3.88 (m, 2H, OCH2CH2CCOO2CH3), 4.65 (t, 1H, J = 3.4 Hz, OCHOCH2CH2CH2CH2).
Vinyl stannane (53): In a Schlenk flask, Bu₆Sn₂ (2.244 mL, 4.44 mmol, 2.2 eq) was dissolved in THF (10 mL) and cooled to -78°C. n-BuLi (1.696 mL, 4.24 mmol, 2.1 eq) was then added dropwise, the temperature was raised to -40°C, and the solution was stirred for 30 minutes, at which point the mixture was a light yellow. After the 30 minutes, the solution was recooled to -78°C, at which point CuCN (362 mg, 4.04 mmol, 2 eq) was added and the temperature was raised again to -40°C, where the solution was stirred for 45 minutes, now a deep orange color. The temperature was then cooled again to -78°C, and MeOH (123 µL, 3.03 mmol, 1.5 eq) was added. Alkyne 52 (429 mg, 2.02 mmol, 1 eq), dissolved in THF (5 mL), was then added to the original solution via cannula, leaving a red-orange color. The mixture was then stirred at -78°C for 90 minutes, before being raised to -25°C over the course of 10 minutes. The solution was then treated with 9:1 saturated NH₄Cl/NH₄OH (25 mL) and diluted with Et₂O (10 mL), at which point it was allowed to warm to room temperature. The aqueous layer was extracted with Et₂O (2 x 20 mL), before the combined organic layers were washed with 9:1 saturated NH₄Cl/NH₄OH (20 mL) and brine (20 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 15:1 hexanes/EtOAc w/ 0.5% NEt₃ v/v) yielded vinyl stannane 53 (854 mg, 84%).

^1H NMR (400 MHz) δ 0.89 (t, 9H, J = 7.3 Hz, Sn(CH₂CH₂CH₂CH₃)₃), 0.97 (m, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 1.31 (app. sext, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 1.49 (app. m, 10H, Sn(CH₂CH₂CH₂CH₃)₃ and 4 of OCHOCH₂CH₂CH₂CH₂), 1.70 (m, 1H, 1 of
OCHOCH$_2$CH$_2$CH$_3$/CH$_2$), 1.82 (m, 1H, 1 of OCHOCH$_2$CH$_2$CH$_3$/CH$_2$), 3.17 (t w/ Sn
satellites, 2H, J = 6.9 Hz, OCH$_2$CH$_2$CCHCO$_2$CH$_3$), 3.47 (m, 2H,
OCHOCH$_2$CH$_2$CH$_2$CH$_3$/), 3.70 (s, 3H, CO$_2$CH$_3$), 3.83 (m, 2H, OCH$_2$CH$_2$CCHCO$_2$CH$_3$),
4.61 (t, 1H, J = 3.4 Hz, OCHOCH$_2$CH$_2$CH$_2$CH$_2$/), 6.02 (s w/ Sn satellites, 1H,
OCH$_2$CH$_2$CCHCO$_2$CH$_3$).

$^{13}$C NMR (100 MHz) $\delta$ 10.05 (w/ Sn satellites, $J_{\text{Sn-C}}$ = 160 Hz), 13.69, 19.49,
25.50, 27.40 (w/ Sn satellites, $J_{\text{Sn-C}}$ = 29.0 Hz), 28.97 (w/ Sn satellites, $J_{\text{Sn-C}}$ = 10.0 Hz),
30.62, 35.50, 50.92, 62.11, 66.59, 98.59, 129.26, 164.36, 170.35.
Alcohol (54): Ester 53 (852 mg, 1.693 mmol, 1 eq) was dissolved in toluene (17 mL) and cooled to -78 °C. DIBAL (664 µL, 3.724 mmol, 2.2 eq) was then added dropwise, and the solution was stirred at -78 °C for 2.5 hrs, before being warmed to -20 °C over the course of an hour. The solution was then treated with Rochelle salt (12 mL) and stirred for 15 minutes at room temperature, before being diluted with EtOAc (40 mL) and H2O (10 mL). The aqueous layer was extracted with EtOAc (2 x 12 mL) before the combined organic layers were washed with brine (12 mL), dried (MgSO4), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 4:1 hexanes/EtOAc) afforded alcohol 54 (624 mg, 78%).

\[ ^1H \text{NMR (400 MHz)} \delta 0.89 (m, 15H, Sn(CH}_2CH}_2CH}_3)_3, 1.31 (\text{app. sext, 6H, Sn(CH}_2CH}_2CH}_3)_3, 1.51 (\text{app. m, 10H, Sn(CH}_2CH}_2CH}_3)_3 \text{ and 4 of OCHOCH}_2CH}_2CH}_2CH}_2, 1.74 (m, 2H, 2 of OCHOCH}_2CH}_2CH}_2CH}_2, 2.60 (\text{app. t, 2H, J} = 5.9 \text{ Hz, OCH}_2CH}_2CCHCH}_2OH), 2.71 (m, 1H, OCH}_2CH}_2CCHCH}_2OH), 3.33 (m, 1H, 1 of OCHOCH}_2CH}_2CH}_2CH}_2, 3.51 (m, 1H, 1 of OCHOCH}_2CH}_2CH}_2CH}_2, 3.81 (m, 2H, OCH}_2CH}_2CCHCH}_2OH), 4.12 (m, 2H, OCH}_2CH}_2CCHCH}_2OH), 4.60 (t, 1H, J = 3.1 \text{ Hz, OCH}_2CH}_2CH}_2CH}_2, 6.06 (t w/ Sn satellites, 1H, J = 6.6 \text{ Hz, OCH}_2CH}_2CCHCH}_2OH). \]

\[ ^13C \text{NMR (100 MHz)} \delta 9.62 (w/ Sn satellites, J_{Sn-C} = 159 \text{ Hz}), 13.72, 19.27, 25.32, 27.46 (w/ Sn satellites, J_{Sn-C} = 29.0 \text{ Hz}), 29.09 (w/ Sn satellites, J_{Sn-C} = 9.5 \text{ Hz}), 30.18, 33.43, 57.58, 62.01, 66.07, 98.89, 141.56, 146.09. \]
Vinyl iodide (55): Vinyl stannane 54 (624 mg, 1.313 mmol, 1 eq) was dissolved in CH$_2$Cl$_2$ (13 mL) and cooled to 0°C. N-Iodosuccinimide (355 mg, 1.576 mmol, 1.2 eq) was then added, and the solution was stirred for 2.5 hrs at 0°C. The solution was then treated with an aqueous saturated Na$_2$SO$_4$ solution (10 mL) and an aqueous saturated NaHCO$_3$ solution (10 mL), diluted with EtOAc (20 mL), and the organic layer was washed with brine (15 mL), dried (MgSO$_4$), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 3:1 hexanes/EtOAc w/ 0.5% NEt$_3$ v/v) yielded vinyl iodide 55 with slight impurities, so that 100% yield was assumed.

$^1$H NMR (400 MHz) $\delta$ 1.59 (m, 4H, 4 of OCHOCH$_2$CH$_2$CH$_2$CH$_2$), 1.73 (m, 2H, 2 of OCHOCH$_2$CH$_2$CH$_2$CH$_2$), 2.78 (app. t, 1H, J = 6.2 Hz, OCH$_2$CH$_2$CCHCH$_2$OH), 2.84 (m, 2H, OCH$_2$CH$_2$CCHCH$_2$OH), 3.53 (m, 2H, OCHOCH$_2$CH$_2$CH$_2$CH$_2$), 3.87 (m, 2H, OCH$_2$CH$_2$CCHCH$_2$OH), 3.98 (m, 2H, OCH$_2$CH$_2$CCHCH$_2$OH), 4.67 (t, 1H, J = 3.0 Hz, OCHOCH$_2$CH$_2$CH$_2$CH$_2$), 6.72 (t, 1H, J = 7.5 Hz, OCH$_2$CH$_2$CCHCH$_2$OH).

$^{13}$C NMR (100 MHz) $\delta$ 19.26, 25.20, 30.09, 40.13, 59.20, 62.23, 64.23, 99.05, 105.14, 142.30.
Silylether (56): Alcohol 55 (409.8 mg, 1.313 mmol, 1 eq) was dissolved in CH₂Cl₂ (5 mL). Imidazole (268 mg, 3.939 mmol, 3 eq) was then added, the solution was cooled to 0° C, and TBDPSCI (376 µL, 1.445 mmol, 1.1 eq) was added as well. The mixture was then stirred at 0° C for 10 minutes, raised to room temperature, and stirred for a further 30 minutes. The solution was then treated with H₂O (10 mL), the layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (2 x 10 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 19:1 hexanes/EtOAc) afforded silylether 56 (625 mg, 87%), with the impurities of the previous reaction carried through.

\[ ^1\text{H NMR (400 MHz)} \delta 1.04 (s, 9H, OSiPh₂C(\text{CH₃})), 1.42 (m, 3H, 3 of OCHOCH₂CH₂CH₂CH₂), 1.59 (m, 3H, 3 of OCHOCH₂CH₂CH₂CH₂), 2.51 (t, 2H, J = 6.3 Hz, OCH₂CH₂CCHCH₂OTBDPS), 3.40 (m, 2H, OCHOCH₂CH₂CH₂CH₂), 3.72 (m, 2H, OCH₂CH₂CCHCH₂OTBDPS), 4.18 (d, 2H, J = 6.2 Hz, OCH₂CH₂CCHCH₂OTBDPS), 4.51 (t, 1H, J = 3.2 Hz, OCHOCH₂CH₂CH₂CH₂), 6.47 (t, 1H, J = 6.3 Hz, OCH₂CH₂CCHCH₂OTBDPS), 7.41 (m, 6H, 3 each of OSiPh₂C(\text{CH₃})), 7.65 (d, 4H, J = 1.72 Hz, 2 each of OSiPh₂C(\text{CH₃})). \]

\[ ^{13}\text{C NMR (100 MHz)} \delta 19.13, 19.24, 25.35, 26.73, 30.44, 40.10, 61.88, 62.00, 65.38, 98.60, 99.66, 127.71, 129.73, 133.31, 135.56, 142.60. \]

HRMS: (M+Na⁺) calculated for C₂₆H₃₅O₃Si: 550.1400, found 550.1421.
Alcohol (58): Silyl ether 56 (109 mg, 0.198 mmol, 1 eq) was dissolved in methanol (2 mL) under Ar. Pyridinium p-toluesulfonate (PPTS) (9.9 mg, 0.039 mmol, 0.2 eq) was then added, before the solution was stirred at room temperature for approximately 44 hrs. The solution was then diluted with EtOAc (6 mL) and treated with an aqueous saturated NaHCO₃ solution (2 mL), before the layers were separated and the aqueous layer was extracted with EtOAc (2 x 4 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 6:1 hexanes/EtOAc) afforded alcohol 58 (67 mg, 73%).

**¹H NMR (400 MHz)** \( \delta \) 1.04 (s, 9H, OSiPh₂C(CH₃)₃), 1.63 (s, 1H, CH₂CH₂OH), 2.53 (t, 2H, J = 5.8 Hz, HOCH₂CH₂CCCH₂OTBDPS), 3.64 (q, 2H, J = 5.7 Hz, HOCH₂CH₂CCCH₂OTBDPS), 4.13 (d, 2H, J = 6.7 Hz, HOCH₂CH₂CCCH₂OTBDPS), 6.55 (t, 1H, J = 6.7 Hz, HOCH₂CH₂CCCH₂OTBDPS), 7.43 (m, 6H, 6 of OSiPh₂C(CH₃)₃), 7.66 (m, 4H, 4 of OSiPh₂C(CH₃)₃).

**¹³C NMR (100 MHz)** \( \delta \) 19.10, 26.70, 42.35, 60.63, 61.40, 101.43, 127.79, 129.85, 133.04, 135.58, 142.90.

**HRMS:** (M+Na⁺) calculated for C₂₁H₂₇O₅Si: 446.0825, found 466.0842.
MOM ether (60): Triphenylphosphine (PPh₃) (41.4 mg, 0.158 mmol, 1.1 eq) was dissolved in THF (0.75 mL) and cooled to 0°C, at which point diisopropyl azodicarboxylate (DIAD) (30.6 µL, 0.158 mmol, 1.1 eq) was added dropwise. This solution was stirred for 40 minutes, and a white precipitate formed after 10 minutes. Alcohol 58 (67.0 mg, 0.144 mmol, 1 eq), dissolved in THF (0.75 mL) was then added to the original mixture via cannula, and stirring was continued for an additional 30 minutes. MOM-MAC (19.9 mg, 0.1580 mmol, 1.1 eq) was added to the solution, which was then left to stir overnight, warming gradually to room temperature. Solvent was removed using a rotary evaporator, then crude product was redissolved in EtOAc and filtered. Column chromatography (silica, 12:1 hexanes/EtOAc) yielded MOM ether 60 (28.8 mg, 35%).

**¹H NMR** (400 MHz) δ 1.04 (s, 9H, OSiPh₂C(CH₃)₃), 2.20 (m, 2H, MOMOC(CN)₂CH₂CH₂C), 2.54 (m, 2H, MOMOC(CN)₂CH₂CH₂C), 3.47 (s, 3H, CH₃OCH₂OC(CN)₂), 4.15 (d, 2H, J = 6.5 Hz, CCH₂COTBDPS), 4.94 (s, 2H, CH₃OCH₂OC(CN)₂), 6.46 (t, 1H, J = 6.5 Hz, CCH₂COTBDPS), 7.43 (m, 6H, 6 of OSiPh₂C(CH₃)₃), 7.65 (m, 4H, 4 of OSiPh₂C(CH₃)₃).

**¹³C NMR** (100 MHz) δ 19.14, 26.71, 33.38, 39.34, 57.39, 61.36, 64.12, 96.18, 98.96, 112.71, 127.84, 129.94, 132.99, 135.59, 142.73.
Ester (61): The MAC adduct 60 (28.8 mg, 0.050 mmol, 1 eq) was dissolved in a 1:1 ratio of AcOH and DME (51 µL/ 51 µL), and camphorsulfonic acid (CSA) (12.8 mg, 0.055 mmol, 1.1 eq) was added. The mixture was then stirred at 60°C for 6 hrs. The solution was then cooled to room temperature, and ethanol (102 µL) was added. The solution was then cooled to -40°C, and a 1:1 mixture of ethanol and triethylamine (144 µL/ 144 µL, 1.022 mmol, 20.4 eq) was added via cannula. The resulting solution was left in the bath to warm gradually to room temperature overnight. The solution was then treated with an aqueous saturated NH₄Cl solution (2 mL) and diluted with EtOAc (4 mL), before the layers were separated and the aqueous layer was extracted with EtOAc (3 x 2 mL). The combined organic layers were washed with brine (3 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 5:1 hexanes/EtOAc) afforded ester 61 (8.2 mg, 56%).

¹H NMR (400 MHz) δ 1.27 (t, 3H, J = 7.1 Hz, CH₂CO₂CH₂CH₃), 2.07 (s, 3H, OCOCH₃), 2.55 (t, 2H, J = 7.4 Hz, CH₂CH₂CO₂Et), 2.78 (t, 2H, J = 7.4 Hz, CH₂CH₂CO₂Et), 4.14 (q, 2H, J = 7.1 Hz, CH₂CO₂CH₂CH₃), 4.57 (d, 2H, J = 7.2 Hz, CHCH₂OAc), 6.38 (t, 1H, J = 7.1 Hz, CHCH₂OAc).

¹³C NMR (100 MHz) δ 14.20, 20.84, 33.84, 34.51, 60.73, 61.05, 107.01, 136.28, 170.60, 171.73.

HRMS: (M+Na⁺) calculated for C₁₀H₁₅O₄I: 326.0015, found 326.0028
Alcohol (62): Dissolve acetate 61 (9.2 mg, 0.0282 mmol, 1 eq) in ethanol (300 µL) under an Ar atmosphere, then add K₂CO₃ (19.5 mg, 0.141 mmol, 5 eq) and stir for 90 minutes at room temperature. The solution was then diluted with H₂O (3 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine (5 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 3:1 hexanes/EtOAc) yielded identifiable amounts of alcohol 62, however, at this scale it was not possible to entirely purify the product.

**¹H NMR** (400 MHz) δ 1.27 (t, 3H, J = 7.1 Hz, CH₂CO₂CH₂CH₃), 2.63 (t, 2H, J = 6.4 Hz, CH₂CH₂CO₂Et), 2.70 (m, 1H, CHCH₂OH), 2.77 (t, 2H, J = 6.4 Hz, CH₂CH₂CO₂Et), 4.14 (m, 4H, CH₂CO₂CH₂CH₃ and CHCH₂OH), 6.54 (t, 1H, J = 7.4 Hz, CHCH₂OH).

**¹³C NMR** (100 MHz) δ 14.19, 33.45, 33.63, 59.95, 61.01, 106.18, 141.60, 172.82.
Silyl ether (63): Alcohol 62 (391 mg, 1.276 mmol, 1 eq) was dissolved in DMF (5 mL), and imidazole (234 mg, 3.44 mmol, 2.5 eq) was added. The mixture was then cooled to 0°C, at which point TBDPSCI (429 µL, 1.65 mmol, 1.2 eq) was added. The mixture was then stirred for 10 minutes, warmed to room temperature, and stirred for an additional 30 minutes. The solution was then treated with an aqueous saturated NH4Cl solution (10 mL), before the layers were separated and the aqueous layer was extracted with Et2O (3 x 15 mL). The combined organic layers were washed with brine (15 mL), dried (MgSO4), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 15:1 hexanes/EtOAc) afforded silyl ether 63 (611 mg, 85%).

1H NMR (400 MHz) δ 1.04 (s, 9H, SiPh2C(CH3)3), 1.21 (t, 3H, J = 7.1 Hz, CO2CH2CH3), 2.38 (m, 2H, CH2CH2CO2Et), 2.50 (t, 2H, J = 7.5 Hz, CH2CH2CO2Et), 4.07 (q, 2H, J = 7.2 Hz, CO2CH2CH3), 4.17 (d, 2H, J = 6.4 Hz, CHCH2OTBDPS), 6.40 (t, 1H, J = 6.3 Hz, CHCH2OTBDPS), 7.41 (m, 6H, 3 each of OSiPh2C(CH3)3), 7.65 (m, 4H, 2 each of OSiPh2C(CH3)3).

13C NMR (100 MHz) δ 14.17, 19.12, 26.73, 33.98, 34.41, 60.56, 61.52, 102.70, 127.75, 129.78, 133.21, 135.57, 141.65, 171.80.

HRMS: (M+Na+) calculated for C24H31O3Si: 522.1087, found 522.1097.
Diene (67): Vinyl stannyl oxazolidinone (66) (519 mg, 1.169 mmol, 1 eq) was dissolved in DMF (8 mL) and transferred to a flask containing vinyl iodide 63 (611 mg, 1.169 mmol, 1 eq) under inert atmosphere. The vial containing oxazolidinone was then rinsed with DMF (2 x 2 mL). Pd(PPh₃)₄ (135 mg, 0.1169 mmol, 0.1 eq) and CuO₂PPh₂ (378 mg, 1.345 mmol, 1.15 eq) were then added to the mixture simultaneously. The flask was then capped and stirred overnight in the glovebox. The mixture was then filtered through a silica gel pad using EtOAc, concentrated, redissolved in Et₂O (100 mL), and extracted with H₂O (2 x 50 mL). The combined organic layers were then washed with brine (50 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 3:1 hexanes/EtOAc) yielded diene 67 (634 mg, 96%).

¹H NMR (400 MHz) δ 0.84 (d, 3H, J = 7.0 Hz, 1 Me of NCO₂CH₂CHCH(CH₃)₂), 0.88 (d, 3H, J = 6.8 Hz, 1 Me of NCO₂CH₂CHCH(CH₃)₂), 1.04 (s, 9H, SiPh₂C(CH₃)₃), 1.20 (t, 3H, J = 7.2 Hz, CO₂CH₂CH₃), 1.89 (broad m, 1H, NCO₂CH₂CHCH(CH₃)₂), 2.19 (m, 2H, CH₂CHCH₂CH₂CO₂Et), 2.47 (m, 2H, CH₂CHCH₂CH₂CO₂Et), 3.74 (m, 1H, 1 of NCO₂CH₂CHCH(CH₃)₂), 4.04 (q, 2H, J = 7.1 Hz, CO₂CH₂CH₃), 4.13 (m, 1H, 1 of NCO₂CH₂CHCH(CH₃)₂), 4.24 (t, 1H, J = 8.9 Hz, NCO₂CH₂CHCH(CH₃)₂), 4.34 (m, 2H, CH₃CHCH₂CH₂CO₂Et), 5.26 (s, 1H, 1 of CHCCH₃), 5.29 (s, 1H, 1 of CHCCH₃), 5.81 (t, 1H, J = 6.1 Hz, CH₃CHCCH₂CH₂CO₂Et), 7.40 (m, 6H, 3 each of OSiPh₂C(CH₃)₃), 7.66 (m, 4H, 2 each of OSiPh₂C(CH₃)₃).
$^{13}$C NMR (100 MHz) δ 14.19, 14.42, 17.82, 19.16, 23.55, 26.77, 29.07, 32.79, 60.15, 60.49, 60.69, 62.68, 112.54, 127.78, 129.82, 131.62, 133.41, 133.52, 134.35, 134.55, 141.17, 156.54, 172.59.

$[\alpha]^{24}_D$: -52.7 (c = 0.59 g/mL)
Iron(0) tricarbonyl complex (68): \( \text{Fe}_2(\text{CO})_9 \) (2.94 g, 8.085 mmol, 7 eq) was placed in a Schlenk flask under inert atmosphere. Diene 67 (634 mg, 1.155 mmol, 1 eq), dissolved in toluene (11.5 mL), was then added to the flask via cannula. The solution was stirred for approximately 20 hrs at 35\(^\circ\) C. The resulting mixture was then filtered through a silica gel pad using EtOAc with 2\% NEt\(_3\), before being concentrated using a rotary evaporator. An initial column was performed, in which 1:1 hexane/CH\(_2\)Cl\(_2\) removed byproduct, before the complex 68 was collected, along with its minor diastereomer, upon addition of EtOAc to the column. A crude NMR was obtained to determine the diastereomeric ratio of complexation. An additional column (silica, 5:1 hexanes/EtOAc) afforded complex 68 (634 mg, 96\%) as a single diastereomer.

\[ {^1}\text{H NMR} \ (400 \text{ MHz}) \delta 0.24 \ (d, 1H, J = 3.4 \text{ Hz}), 0.47 \ (m, 1H), 0.94 \ (dd, 6H, J = 6.8, 1.6 \text{ Hz}), 1.05 \ (s, 9H), 1.24 \ (t, 3H, J = 7.2 \text{ Hz}), 1.73 \ (d, 1H, J = 3.5 \text{ Hz}), 2.35 \ (\text{sex.}, 1H, J = 3.1 \text{ Hz}), 2.56 \ (\text{sex.}, 1H, J = 4.1 \text{ Hz}), 2.87 \ (m, 3H), 3.79 \ (\text{ABX}, 2H), 4.13 \ (m, 4H), 4.40 \ (t, 1H, J = 8.9 \text{ Hz}), 7.40 \ (m, 6H), 7.66 \ (m, 4H). \]

\[ {^{13}}\text{C NMR} \ (100 \text{ MHz}) \delta 13.72, 14.21, 18.06, 19.05, 23.42, 26.76, 29.20, 34.87, 36.14, 56.58, 60.59, 61.90, 62.90, 64.04, 102.23, 127.76, 127.80, 129.82, 133.25, 135.49, 156.75, 172.45. \]

\([\alpha]^2\text{H} : +99.5 \ (c = 0.51 \text{ g/mL}) \]
Diene (70): Vinyl stannyl oxazolidinone (66) (886 mg, 1.995 mmol, 1 eq) was dissolved in DMF (10 mL) and transferred to a flask containing vinyl iodide 69 (1.07 g, 1.995 mmol, 1 eq) under inert atmosphere. The vial containing oxazolidinone was then rinsed with DMF (2 x 5 mL). Pd(PPh₃)₄ (230 mg, 0.199 mmol, 0.1 eq) and CuO₂PPh₂ (644 mg, 2.294 mmol, 1.15 eq) were then added to the mixture simultaneously. The flask was then capped and stirred overnight in the glovebox. The mixture was then filtered through a silica gel pad using EtOAc, concentrated, redissolved in Et₂O (150 mL), and extracted with H₂O (2 x 75 mL). The combined organic layers were then washed with brine (75 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 4:1 hexanes/EtOAc) yielded diene 70 (1.03 g, 92%).

¹H NMR (400 MHz) δ 0.80 (d, 3H, J = 7.0 Hz, 1 Me of NCO₂CH₂CHCH(CH₃)₂), 0.87 (d, 3H, J = 6.8 Hz, 1 Me of NCO₂CH₂CHCH(CH₃)₂), 1.04 (s, 9H, SiPh₂C(CH₃)₃), 1.27 (t, 3H, J = 7.2 Hz, CO₂CH₂CH₃), 1.88 (sex., 1H, J = 3.5 Hz, NCO₂CH₂CHCH(CH₃)₂), 2.48 (m, 5H, CH₂CH₃CHCCH₂CH₂CO₂Et and 1 of CH₂CH₃CHCCH₂CH₂CO₂Et), 2.64 (m, 1H, 1 of CH₂CH₃CHCCH₂CH₂CO₂Et), 3.74 (m, 3H, NCO₂CH₂CHCH(CH₃)₂ and 1 of CH₂CHCCH₂CH₂CO₂Et), 4.12 (m, 3H, CO₂CH₂CH₃ and 1 of CH₂CHCCH₂CH₂CO₂Et), 4.23 (t, 1H, J = 8.9 Hz, NCO₂CH₂CHCH(CH₃)₂), 5.23 (s, 1H, 1 of CHCCH₂), 5.30 (s, 1H, 1 of CHCCH₂), 5.76
(t, 1H, J = 7.2 Hz, CH₂CHCCH₂CH₂CO₂Et), 7.40 (m, 6H, 3 each of OSiPh₂C(CH₃)₃),
7.64 (m, 4H, 2 each of OSiPh₂C(CH₃)₃).

¹³C NMR (100 MHz) δ 14.22, 14.40, 17.78, 19.18, 23.49, 26.81, 29.02, 31.55,
32.95, 60.16, 60.48, 62.65, 63.15, 111.92, 127.70, 129.08, 129.70, 133.58, 133.60,
134.90, 135.50, 141.59, 156.64, 172.87.

[α]²⁴: -51.0 (c = 0.54 g/mL)
Iron(0) tricarbonyl complex (71): Fe$_2$(CO)$_9$ (4.64 g, 12.763 mmol, 7 eq) was placed in a Schlenk flask under inert atmosphere. Diene 70 (1.03 g, 1.823 mmol, 1 eq), dissolved in toluene (18.2 mL), was then added to the flask via cannula. The solution was stirred for approximately 20 hrs at 35°C. The resulting mixture was then filtered through a silica gel pad using EtOAc with 2% NEt$_3$, before being concentrated using a rotary evaporator. An initial column was performed, in which 1:1 hexane/CH$_2$Cl$_2$ removed byproduct, before the complex 71 was collected, along with its minor diastereomer, upon addition of EtOAc to the column. A crude NMR was obtained to determine the diastereomeric ratio of complexation. The diastereomers were determined inseparable, and were collected together (1.138 g, 89%)

$^1$H NMR (400 MHz) $\delta$ 0.14 (d, 1H, J = 3.4 Hz), 0.68 (m, 1H), 0.95 (dd, 6H, J = 11.56, 6.8 Hz), 1.05 (s, 9H), 1.26 (t, 3H, J = 7.1 Hz), 1.65 (d, 1H, 3.5 Hz), 1.72 (m, 1H), 2.21 (m, 1H), 2.33 (m, 1H), 2.57 (m, 3H), 2.94 (m, 1H), 3.80 (m, 2H), 3.94 (m, 1H), 4.14 (m, 3H), 4.38 (t, 1H, J = 8.9 Hz), 7.41 (m, 6H), 7.67 (m, 4H).

$^{13}$C NMR (100 MHz) $\delta$ 13.74, 14.22, 18.04, 18.92, 19.19, 21.07, 23.84, 26.87, 29.11, 33.86, 34.02, 35.15, 60.41, 60.78, 61.95, 64.01, 64.70, 127.69, 129.69, 133.59, 133.65, 135.49, 135.56, 172.18.

$[\alpha]^{25}_{D}$: +68.7 (c = 0.54 g/mL)
α-benzoylated ester (72): Ester 71 (1.138 g, 1.618 mmol, 1 eq) was dissolved in CH₂Cl₂ (16.2 mL), before N-methylimidazole (155 µL, 1.942 mmol, 1.2 eq) and benzoyl chloride (188 µL, 1.618 mmol, 1 eq) were added. The mixture was then cooled to -45°C, where TiCl₄ (5.66 mL 1M in CH₂Cl₂, 5.663 mmol, 3.5 eq) was added dropwise, followed immediately by NBu₃ (1.54 mL, 6.472 mmol, 4 eq). The solution was then stirred at -45°C for 90 minutes. The solution was then treated with an aqueous saturated NaHCO₃ solution (18 mL) and diluted with EtOAc (60 mL), before the layers were separated and the aqueous layer was extracted with EtOAc (2 x 18 mL). The combined organic layers were washed with brine (20 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 4:1 hexanes/EtOAc) afforded α-benzoylated ester 72 (496 mg, 38%). Note that all benzoylation products synthesized produced extremely messy NMR spectra; the following values are approximate.

_H NMR (400 MHz) δ 0.90 (m, 15H), 1.05 (s, 9H), 1.14 (q, 3H, J = 7.2 Hz), 1.28 (sex., 7H, J = 7.2 Hz), 1.41 (m, 6H), 2.39 (t, 6H, J = 7.6 Hz), 2.87 (dd, 1H, J = 15.1, 4.1 Hz), 3.46 (m, 1H), 3.75 (m, 1H), 3.91 (m, 1H), 4.13 (m, 3H), 4.51 (m, 1H), 7.39 (m, 8H), 7.63 (m, 5H), 7.94 (d, 2H, J = 7.5 Hz).

_C NMR (100 MHz) δ 13.48, 13.90, 13.97, 14.13, 18.02, 18.12, 19.16, 19.20, 20.81, 26.81, 26.86, 27.85, 29.17, 29.50, 34.54, 53.90, 61.77, 61.97, 65.06, 127.65,
127.68, 127.70, 128.46, 128.85, 128.94, 129.65, 129.69, 133.66, 133.83, 133.88, 135.48, 135.50, 135.55, 136.21, 168.77, 169.21, 194.20.

\[ \alpha^{23} : +5.04 \ (c = 0.44 \text{ g/mL}) \]
α-diazoeester (73): β-ketooester 72 (496 mg, 0.614 mmol, 1 eq) was dissolved in acetonitrile (6.2 mL) and cooled to 0°C. 4-acetamidobenzenesulfonyl azide (p-ABSA) (177 mg, 0.737 mmol, 1.2 eq) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (220.5 µL, 1.474 mmol, 2.4 eq) were then added, and the solution was stirred and allowed to warm to room temperature over 3 hrs. The solution was then treated with H₂O (15 mL) and diluted with EtOAc (20 mL), before the layers were separated and the organic layer was extracted with H₂O (15 mL). The combined aqueous layers were then extracted with EtOAc (2 x 15 mL). The combined organic layers were then washed with brine (15 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 4:1 hexanes/EtOAc) afforded α-diazoeester 73 (329 mg, 73%).

1H NMR (400 MHz) δ 0.15 (d, 1H, J = 3.4 Hz), 0.65 (dd, 1H, J = 9.6, 3.5 Hz), 0.92 (t, 6H, J = 7.5 Hz), 1.04 (s, 9H), 1.29 (t, 3H, J = 7.1 Hz), 1.62 (m, 1H), 1.74 (d, 1H, J = 3.4 Hz), 2.18 (sex., 1H, J = 3.6 Hz), 2.37 (sex., 1H, J = 3.2 Hz), 3.14 (d, 1H, J = 16.0 Hz), 3.6 (d, 1H, J = 16.0 Hz), 3.77 (m, 1H), 3.84 (m, 1H), 4.01 (m, 1H), 4.14 (m, 1H), 4.24 (q, 2H, J = 7.1 Hz), 4.38 (t, 1H, J = 8.6 Hz), 7.40 (m, 6H), 7.67 (m, 4H).

13C NMR (100 MHz) δ 13.61, 14.54, 18.03, 19.19, 22.74, 26.84, 29.12, 34.52, 36.48, 55.08, 61.19, 61.74, 64.16, 64.70, 102.09, 127.69, 129.68, 133.61, 133.68, 135.47, 135.54, 156.39, 166.60.

[α]D23: +10.1 (c = 0.23 g/mL)
Cyclopentene (44): α-diazoester 73 (329 mg, 0.4509 mmol, 1 eq) was dissolved in \( \text{CH}_2\text{Cl}_2 \) (4.5 mL) and cooled to 0°C. The \( \text{Rh}_2(\text{OAc})_4 \) catalyst (4.0 mg, 9.02 µmol, 0.02 eq) was added, and the mixture was stirred for 3.5 hrs. The crude product was then filtered through silica gel and concentrated using a rotary evaporator, and a crude NMR was taken to determine the diastereomeric ratio. Column chromatography (silica, 7:1 hexanes/EtOAc w/ 0.5% NEt₃ v/v) afforded cyclopentene 44 (116.7 mg, 37%) and minor diastereomer 44a (50.9 mg, 16%). Impurities were present in both products, obscuring NMR data.

**Major Diastereomer (44)**

\( ^1\text{H NMR (400 MHz)} \delta \): -0.28 (d, 1H, \( J = 2.6 \) Hz), 0.82 - 1.08 (m, 18H), 1.12 - 1.26 (m, 6H), 1.59 (m, 1H), 2.08 (d, 1H, \( J = 2.9 \) Hz), 2.32 (m, 1H), 2.71 (m, 1H), 2.91 (m, 1H) 3.28 (m, 2H), 3.59 (m, 1H), 3.76 (m, 1H), 4.02 - 4.21 (m, 4H), 4.31 (t, 1H, \( J = 8.5 \) Hz), 7.39 (m, 6H), 7.60 (4H).

\( ^{13}\text{C NMR (100 MHz)} \delta \): 13.89, 14.06, 14.12, 17.86, 19.16, 26.78, 26.82, 28.59, 32.57, 33.09, 33.98, 43.92, 47.81, 60.80, 61.59, 61.69, 63.02, 65.16, 100.01, 110.26, 127.54, 127.66, 127.70, 129.83, 129.93, 133.06, 133.25, 135.55, 135.64, 135.67, 135.77, 155.57, 172.47, 210.35.

**Minor Diastereomer (44a)**
\textbf{\textsuperscript{1}H NMR} (400 MHz) \( \delta \) -0.10 (d, 1H, \( J = 4.0 \) Hz), 0.74 (t, 1H, \( J = 6.7 \) Hz), 0.85 (d, 3H, \( J = 6.9 \) Hz), 1.01 (d, 3H, \( J = 6.8 \) Hz), 1.05 (s, 9H), 1.26 (t, 3H, \( J = 7.2 \) Hz), 1.33 (t, 3H, \( J = 7.2 \) Hz), 1.89 (m, 1H), 2.28 (m, 2H), 3.29 (m, 1H), 3.49 (d, 1H, \( J = 4.0 \) Hz), 3.24 (m, 1H), 3.33 (m, 1H), 4.09 - 4.27 (m, 3H), 4.52 (d, 1H, \( J = 10.2 \) Hz), 4.61 (d, 1H, \( J = 10.2 \) Hz), 7.41 (m, 6H), 7.67 (m, 4H).

\textbf{\textsuperscript{13}C NMR} (100 MHz) \( \delta \) 14.02, 16.18, 16.71, 19.22, 24.63, 26.75, 26.89, 29.92, 33.88, 46.01, 54.59, 61.75, 64.66, 64.68, 68.13, 90.96, 107.88, 127.72, 129.71, 133.62, 135.52, 135.54, 153.26, 170.64.

\([\alpha]^{22}\) -8.84 (c = 0.18 g/mL)
Alkyne (75): The aldehyde (74) (255 mg, 0.778 mmol, 1 eq) was dissolved in methanol (3.2 mL) under an Ar atmosphere. K$_2$CO$_3$ (215 mg, 1.557 mmol, 2 eq) was then added, and the mixture was cooled to 0°C and stirred for 15 minutes. The Ohira-Bestmann reagent (129 µL, 0.856 mmol, 1.1 eq) was then added dropwise, and the cooling bath was removed. The solution was stirred at room temperature for approximately 4 hrs, before being filtered through celite and concentrated using a rotary evaporator. Column chromatography (silica, 6:1 hexanes/EtOAc) afforded alkyne 75 (176 mg, 70%).

$^1$H NMR (400 MHz) $\delta$ 2.00 (t, 1H, $J = 2.6$, CH$_2$CH$_2$CCH), 2.33 (s, 3H, CH$_2$C$_6$H$_4$SO$_2$), 2.68 (m, 2H, CH$_2$CH$_2$CCH), 3.25 (m, 2H, CH$_2$CH$_2$CCH), 6.50 (d, 1H, $J = 0.7$ Hz, C3 of indole), 7.24 (m, 4H, 2 of CH$_3$C$_6$H$_4$SO$_2$ and 2 of indole benzene), 7.43 (d, 1H, $J = 7.0$ Hz, 1 of indole benzene), 7.62 (d, 2H, $J = 8.4$ Hz, 2 of CH$_3$C$_6$H$_4$SO$_2$), 8.15 (d, 1H, $J = 7.7$ Hz, 1 of indole benzene).

$^{13}$C NMR (100 MHz) $\delta$ 18.53, 21.55, 28.46, 69.41, 83.16, 109.83, 114.82, 120.37, 123.59, 124.19, 126.24, 129.58, 129.85, 135.91, 137.19, 139.68, 144.78.

HRMS: (M+H$^+$) calculated for C$_{19}$H$_{17}$NO$_2$S: 323.0980, found 323.0999.
Alcohol (76): Terminal alkyne 75 (176.4 mg, 0.545 mmol, 1 eq) was dissolved in THF (6 mL) under an Ar atmosphere. Solution was then cooled to -78°C, before n-BuLi (240 µL, 0.599 mmol, 1.1 eq) was added dropwise. After 30 minutes of stirring at -78°C, BF₃ • OEt₂ (104 µL, 0.817 mmol, 1.5 eq) was added dropwise as well. Ethylene oxide (327 µL, 0.817 mmol, 1.5 eq) was added to the flask immediately afterwards, followed by stirring for 3 hrs at -78°C. The solution was then treated with an aqueous saturated NH₄Cl solution (4 mL), the layers were separated, and the aqueous layer was extracted with Et₂O (3 x 5 mL). The combined organic layers were washed with brine (5 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 1:1 hexanes/EtOAc) yielded alcohol 76 (157 mg, 78%).

¹H NMR (400 MHz) δ 1.72 (s, 1H, CH₂CH₂OH), 2.33 (s, 3H, CH₃C₆H₄SO₂), 2.41 (m, 2H, CH₃CH₂OH), 2.66 (m, 2H, CH₂CH₂CCCH₂CH₂OH), 3.22 (t, 2H, J = 6.9 Hz, CH₂CH₂CCCH₂CH₂OH), 3.63 (app. t, 2H, J = 6.1 Hz, CH₂CH₂OH), 6.47 (d, 1H, J = 0.7 Hz, C3 of indole), 7.22 (m, 4H, 2 of CH₃C₆H₄SO₂ and 2 of indole benzene), 7.43 (d, 1H, J = 7.4 Hz, 1 of indole benzene), 7.61 (d, 2H, J = 6.8 Hz, 2 of CH₃C₆H₄SO₂), 8.15 (d, 1H, J = 7.8 Hz, 1 of indole benzene).

¹³C NMR (100 MHz) δ 18.96, 21.56, 23.18, 28.91, 61.24, 77.82, 81.19, 109.74, 114.84, 120.29, 123.63, 124.17, 126.23, 129.59, 129.84, 135.90, 137.17, 140.13, 144.77.

HRMS: (M+H⁺) calculated for C₂₁H₂₁NO₃S: 367.1242, found 267.1224.
Vinyl iodide (77): Schwartz’s Reagent (Cp₂ZrHCl) (331 mg, 1.283 mmol, 3 eq) was suspended in DCM (25 mL), before alkyne 76 (157 mg, 0.427 mmol, 1 eq), dissolved in DCM (3 mL), was added via cannula. The mixture was stirred for 3.5 hrs in the dark, at room temperature, before being cooled to 0° C. NIS (192 mg, 0.855 mmol, 2 eq), dissolved in THF (1 mL), was then added to the original solution over the course of 5 minutes. The bath was then removed, and the mixture was stirred for 30 minutes.

The solution was then treated with an aqueous saturated Na₂SO₃ solution (7 mL) and an aqueous saturated NaHCO₃ solution (7 mL), before being diluted with Et₂O. The layers were then separated, and the aqueous layer was extracted with Et₂O (2 x 9 mL). The combined organic layers were washed with brine (7 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 4:1 hexanes/EtOAc) yielded vinyl iodide 77 (137 mg, 65%).

^1H NMR (400 MHz) δ 1.62 (t, 1H, J = 6.2 Hz, CH₂CH₂OH), 2.33 (s, 3H, CH₃C₆H₄SO₂), 2.57 (q, 2H, J = 7.8 Hz, CH₂CH₂CHC(l)CH₂CH₂OH), 2.69 (t, 2H, J = 5.9 Hz, CH₂CH₂OH), 3.06 (t, 2H, J = 7.7 Hz, CH₂CH₂CHC(l)CH₂CH₂OH), 3.76 (q, 2H, J = 6.0 Hz, CH₂CH₂OH), 6.42 (m, 2H, CH₂CH₂CHC(l)CH₂CH₂OH and C3 of indole), 7.21 (m, 4H, 2 of CH₃C₆H₄SO₂ and 2 of indole benzene), 7.40 (d, 1H, J = 7.1 Hz, 1 of indole benzene), 7.61 (d, 2H, J = 8.4 Hz, 2 of CH₃C₆H₄SO₂), 8.15 (d, 1H, J = 8.3 Hz, 1 of indole benzene).
$^{13}$C NMR (100 MHz) $\delta$ 21.55, 28.76, 31.24, 41.58, 61.26, 99.60, 109.85, 114.94, 120.28, 123.71, 124.20, 126.22, 129.70, 129.87, 135.87, 137.29, 140.50, 142.51, 144.83.
MOM ether (78): Triphenylphosphine (PPh₃) (79.8 mg, 0.304 mmol, 1.1 eq) was dissolved in THF (1.4 mL) and cooled to 0°C, at which point diisopropyl azodicarboxylate (DIAD) (59 µL, 0.304 mmol, 1.1 eq) was added dropwise. This solution was stirred for 40 minutes, and a white precipitate formed after 10 minutes. Alcohol 77 (137 mg, 0.2768 mmol, 1 eq), dissolved in THF (1.4 mL) was then added to the original mixture via cannula, and stirring was continued for an additional 30 minutes. MOM-MAC (38 mg, 0.304 mmol, 1.1 eq) was then added to the solution, which was then left to stir overnight, warming gradually to room temperature. Solvent was removed using a rotary evaporator, then crude product was redissolved in EtOAc and filtered. Column chromatography (silica, 7:1 hexanes/EtOAc) yielded product MOM ether 78 with MOM-MAC present, so that 100% yield was assumed.

^1H NMR (400 MHz) δ 2.29 (m, 2H, CH₂CH₂CHC(I)CH₂CH₂C(CN)₂OMOM), 2.35 (s, 3H, CH₃C₆H₄SO₂), 2.57 (q, 2H, J = 7.5 Hz, CH₂CH₂CHC(I)CH₂CH₂C(CN)₂OMOM), 2.74 (m, 2H, CH₂CH₂CHC(I)CH₂CH₂C(CN)₂OMOM), 3.08 (t, 2H, J = 7.3 Hz, CH₂CH₂CHC(I)CH₂CH₂C(CN)₂OMOM), 3.54 (s, 3H, OCH₂OCH₃), 5.04 (s, 2H, OCH₂OCH₃), 6.34 (t, 1H, J = 7.6 Hz, CH₂CH₂CHC(I)CH₂CH₂C(CN)₂OMOM), 6.39 (d, 1H, J = 0.5 Hz, C3 of indole), 7.21 (m, 4H, 2 of CH₃C₆H₄SO₂ and 2 of indole benzene),
7.42 (d, 1H, $J = 6.9$ Hz, 1 of indole benzene), 7.58 (d, 2H, $J = 8.4$ Hz, 2 of CH$_3$C$_6$H$_4$SO$_2$),
8.14 (d, 1H, $J = 8.4$ Hz, 1 of indole benzene).
EE Ether (79): Triphenylphosphone (PPh₃) (178 mg, 0.678 mmol, 1.1 eq) was dissolved in THF (2.5 mL) and cooled to 0° C, at which point diisopropyl azodicarboxylate (DIAD) (131 µL, 0.678 mmol, 1.1 eq) was added dropwise. This solution was stirred for 40 minutes, and a white precipitate formed after 10 minutes. Alcohol 77 (305 mg, 0.617 mmol, 1 eq), dissolved in THF (2.5 mL) was then added to the original mixture via cannula, and stirring was continued for an additional 30 minutes. EE-MAC (124 mg, 0.8017 mmol, 1.3 eq), dissolved in THF (1.3 mL) was added to the solution via cannula, which was then left to stir overnight, warming gradually to room temperature. Solvent was removed using a rotary evaporator, then crude product was redissolved in EtOAc and filtered. Column chromatography (silica, 7:1 hexanes/EtOAc) yielded likely product EE ether 79 (301 mg, 77%), with significant impurity carried over from synthesis of the EE-MAC reagent, prohibiting full characterization.
Ester (80): MAC adduct 79 (301 mg, 0.477 mmol, 1 eq) was dissolved in DCM (2.5 mL) and cooled to 0°C. TFA (106 µL, 1.431 mmol, 3 eq) was then added dropwise, the solution was stirred for 10 minutes, and cooled further to -25°C. A mixture of ethanol and triethylamine (500 µL/333 µL, 2.385 mmol, 5 eq) was then added via cannula, and the solution was stirred for 1 hr at -25°C. The solution was then treated with an aqueous saturated NH₄Cl solution (5 mL) and diluted with EtOAc (10 mL), before the layers were separated and the aqueous layer was extracted with EtOAc (3 x 6 mL). The combined organic layers were washed with brine (10 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 7:1 hexanes/EtOAc) afforded ester 80 (196 mg, 75%).

$^1$H NMR (400 MHz) δ 1.26 (t, 3H, J = 7.1 Hz, CO₂CH₂CH₃), 2.33 (s, 3H, CH₃C₆H₄SO₂), 2.49 (t, 2H, J = 7.5 Hz, CH₂CH₂CO₂Et), 2.57 (q, 2H, J = 7.6 Hz, CH₂CH₂CH(CH₃)CO₂Et), 2.71 (t, 2H, J = 7.5 Hz, CH₂CH₂CO₂Et), 3.06 (t, 2H, J = 7.6 Hz, CH₂CH₂CH(CH₃)CO₂Et), 4.13 (q, 2H, J = 7.1 Hz, CO₂CH₂CH₃), 6.27 (t, 1H, J = 7.4 Hz, CH₂CH₂CH(CH₃)CH₂CH₂CO₂Et), 6.40 (s, 1H, C₃ of indole), 7.21 (m, 4H, 2 of CH₃C₆H₄SO₂ and 2 of indole benzene), 7.42 (d, 1H, J = 7.6 Hz, 1 of indole benzene), 7.60 (d, 2H, J = 8.3 Hz, 2 of CH₃C₆H₄SO₂), 8.16 (d, 1H, J = 8.3 Hz, 1 of indole benzene).
\(^{13}\text{C NMR (100 MHz)}} \delta 14.25, 21.58, 28.47, 30.46, 33.92, 34.07, 60.64, 101.67, 109.57, 114.90, 120.26, 123.64, 124.15, 126.23, 129.67, 129.88, 136.00, 137.27, 140.47, 141.10, 144.78, 172.04.

**HRMS:** (M+H') calculated for C\(_{24}\)H\(_{28}\)NO\(_4\)Si: 551.0627, found 551.0640.
Diene (81): Vinyl stannyl oxazolidinone (66) (158 mg, 0.356 mmol, 1 eq) was dissolved in DMF (2 mL) and transferred to a flask containing vinyl iodide 47 (196 mg, 0.356 mmol, 1 eq) under inert atmosphere. The vial containing oxazolidinone was then rinsed with DMF (2 x 0.75 mL). Pd(PPh₃)₄ (41 mg, 0.0356 mmol, 0.1 eq) and CuO₂PPh₂ (115 mg, 0.409 mmol, 1.15 eq) were then added to the mixture simultaneously. The flask was then capped and stirred overnight in the glovebox. The mixture was then filtered through a silica gel pad using EtOAc, concentrated, redissolved in Et₂O (30 mL), and extracted with H₂O (2 x 15 mL). The combined organic layers were then washed with brine (15 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 1:5:1 hexanes/EtOAc) yielded diene 81 (170 mg, 82%).

¹H NMR (400 MHz) δ 0.74 (d, 3H, J = 7.0 Hz, 1 Me of NCO₂CH₂CHCH(CH₃)₂), 0.83 (d, 3H, J = 6.8 Hz, 1 Me of NCO₂CH₂CHCH(CH₃)₂), 1.25 (m, 3H, CO₂CH₂CH₃), 1.82 (broad m, 1H, NCO₂CH₂CHCH(CH₃)₂), 2.36 (m, 6H, CH₃C₆H₄SO₂ and 3 of (CH₂CH₂CHCH₂CH₂CO₂Et, CH₂CH₂CHCH₂CH₂CO₂Et, and CH₂CH₂CHCH₂CH₂CO₂Et)), 2.69 (m, 3H, 3 of (CH₂CH₂CHCH₂CH₂CO₂Et, CH₂CH₂CHCH₂CH₂CO₂Et, and CH₂CH₂CHCH₂CH₂CO₂Et)), 3.12 (t, 2H, J = 7.2 Hz, CH₃CH₂CHCH₂CH₂CO₂Et), 3.67 (t, 1H, J = 4.2 Hz, 1 of NCO₂CH₂CHCH(CH₃)₂), 4.12 (m, 4H, 1 of NCO₂CH₂CHCH(CH₃)₂, NCO₂CH₂CHCH(CH₃)₂, and CO₂CH₂CH₃), 5.21 (s, 1H, 1 of CHCH₂), 5.28 (s, 1H, CHCCH₂), 5.68 (t, 1H, J = 7.1 Hz,
CH₃CH₂CH₃CH₂CH₂CO₂Et, 6.40 (s, 1H, C3 of indole), 7.20 (m, 4H, 2 of CH₃C₆H₄SO₂ and 2 of indole benzene), 7.39 (d, 1H, J = 7.7 Hz, 1 of indole benzene), 7.60 (d, 2H, J = 8.3 Hz, 2 of CH₃C₆H₄SO₂), 8.15 (d, 1H, J = 8.3 Hz, 1 of indole benzene).

¹³C NMR (100 MHz) δ 14.22, 14.34, 17.71, 21.56, 23.49, 27.66, 28.79, 28.92, 32.82, 60.14, 60.53, 62.64, 109.79, 111.81, 114.95, 120.14, 123.69, 124.15, 126.21, 129.62, 129.84, 130.86, 134.49, 135.82, 137.25, 140.90, 141.48, 144.84, 156.63, 172.82.

[α]²³: -39.7 (c = 0.60 g/mL)
Iron(0) tricarbonyl complex (82): Fe$_2$(CO)$_3$ (747 mg, 2.054 mmol, 7 eq) was placed in a Schlenk flask under inert atmosphere. Diene 81 (170 gg, 0.2934 mmol, 1 eq), dissolved in toluene (3 mL), was then added to the flask via cannula. The solution was stirred for approximately 20 hrs at 35° C. The resulting mixture was then filtered through a silica gel pad using EtOAc with 2% NEt$_3$, before being concentrated using a rotary evaporator. An initial column was performed, in which 1:1 hexane/CH$_2$Cl$_2$ removed byproduct, before the complex 82 was collected, along with its minor diastereomer, upon addition of EtOAc to the column. A crude NMR was obtained to determine the diastereomeric ratio of complexation. The diastereomers were determined inseparable, and were collected together (158 mg, 75%)

$^1$H NMR (400 MHz) δ 0.22 (d, 1H, J = 3.4 Hz), 0.59 (m, 1H), 0.95 (t, 6H, J = 7.8 Hz), 1.35 (m, 3H), 1.73 (d, 1H, J = 3.5 Hz), 1.92 (m, 1H), 2.33 (s, 3H), 2.39−2.66 (m, 4H), 2.98 (m, 1H), 3.20 (t, 2H, J = 7.8 Hz), 3.98 (m, 1H), 4.19 (m, 3H), 4.40 (t, 1H, J = 9.0 Hz), 6.44 (s, 1H), 7.21 (m, 4H), 7.41 (d, 1H, J = 7.5 Hz), 7.63 (d, 2H, J = 8.3 Hz), 8.18 (d, 1H, J = 8.3 Hz).

$^{13}$C NMR (100 MHz) δ 13.73, 14.20, 18.04, 21.55, 23.78, 29.15, 31.02, 31.47, 33.85, 35.53, 58.91, 60.86, 61.92, 64.12, 102.19, 109.54, 114.90, 120.24, 123.65, 124.16, 126.22, 129.62, 129.87, 135.87, 137.22, 140.82, 144.84, 156.82, 172.12.

$[^\alpha]^{24}$: $+103.8 \text{ (c = 0.50 g/mL)}$
α-benzoylated ester (83): Ester 82 (158 mg, 0.2204 mmol, 1 eq) was dissolved in
CH$_2$Cl$_2$ (2.2 mL) before N-methylimidazole (21 µL, 0.2645 mmol, 1.2 eq) and benzoyl
chloride (26 µL, 0.2204 mmol, 1 eq) were added. The mixture was then cooled to -45°C,
where TiCl$_4$ (772 µL 1M in CH$_2$Cl$_2$, 0.7715 mmol, 3.5 eq) was added dropwise, followed
immediately by NBu$_3$ (210 µL, 0.8818 mmol, 4 eq). The solution was then stirred at -45°C
for 90 minutes. The solution was then treated with an aqueous saturated NaHCO$_3$
solution (5 mL) and diluted with EtOAc (10 mL), before the layers were separated and
the aqueous layer was extracted with EtOAc (2 x 5 mL). The combined organic layers
were washed with brine (5 mL), dried (MgSO$_4$), filtered, and concentrated using a rotary
evaporator. Column chromatography (silica, 3:1 hexanes/EtOAc) afforded α-benzoylated
ester 83 (47.6 mg, 26%). Again, all benzylation products synthesized produced
extremely messy NMR spectra; the following values are approximate.

$^1$H NMR (400 MHz) δ 0.38 – 0.53 (m, 1H), 0.82 – 0.99 (m, 13H), 1.08 – 1.17 (dt,
3H, J = 22.8, 7.2 Hz), 1.28 (m, 6H), 1.43 (m, 3H), 2.24 – 2.45 (m, 7H), 2.92 (dd, 1H, J =
14.5, 3.7 Hz), 3.11 – 3.42 (m, 3H), 3.51 (m, 1H), 3.91 (d, 1H, J = 8.2 Hz), 4.09 – 4.23 (m,
3H), 4.36 – 4.73 (m, 2H), 6.47 (s, 1H), 7.19 (m, 4H), 7.33 – 7.68 (m, 7H), 7.97 (d, 1H, J
= 7.4 Hz), 8.18 (m, 1H).
$^{13}$C NMR (100 MHz) $\delta$ 13.52, 13.86, 14.11, 18.05, 18.14, 20.79, 21.57, 27.87, 61.86, 62.05, 109.68, 114.90, 120.26, 120.34, 123.70, 124.20, 126.27, 128.54, 128.91, 129.04, 129.70, 129.92, 133.86, 133.93, 140.91.

[$\alpha$]$^\mathrm{25}$: $+27.1$ (c = 0.47 g/mL)
α-diazoester (84): β-ketoester 83 (47.6 mg, 0.0578 mmol, 1 eq) was dissolved in acetonitrile (600 µL) and cooled to 0°C. 4-acetamidobenzenesulfonyl azide (p-ASB) (16.7 mg, 0.0694 mmol, 1.2 eq) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (20.8 µL, 0.1388 mmol, 2.4 eq) were then added, and the solution was stirred and allowed to warm to room temperature over 3 hrs. The solution was then treated with H₂O (3 mL) and diluted with EtOAc (3 mL), before the layers were separated and the organic layer was extracted with H₂O (3 mL). The combined aqueous layers were then extracted with EtOAc (2 x 3 mL). The combined organic layers were then washed with brine (5 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 4:1 hexanes/EtOAc) afforded α-diazoester 84 (13.6 mg, 34%).

\[ \text{H NMR (400 MHz) } \delta 0.23 (d, 1H, J = 3.4 Hz), 0.58 (dd, 1H, J = 9.4, 3.5 Hz), 0.93 (t, 6H, J = 6.7 Hz), 1.28 (t, 3H, J = 7.1 Hz), 1.81 (d, 1H, J = 3.5 Hz), 1.86 (m, 1H), 2.34 (s, 3H), 2.39 (m, 1H), 2.48 (m, 1H), 3.21 (m, 3H), 3.71 (d, 1H, J = 16.1 Hz), 4.04 (m, 1H), 4.15 (m, 1H), 4.24 (q, 2H, J = 7.1 Hz), 4.41 (t, 1H, J = 8.7 Hz), 6.41 (s, 1H), 7.23 (m, 4H), 7.41 (d, 1H, J = 7.1 Hz), 7.64 (d, 2H, J = 8.4 Hz), 8.18 (d, 1H, J = 8.2 Hz).

\[ ^{13}\text{C NMR (100 MHz) } \delta 13.63, 14.50, 18.04, 21.55, 29.18, 31.03, 31.44, 36.78, 58.52, 61.26, 61.81, 64.24, 102.24, 109.21, 114.88, 120.25, 123.59, 124.15, 126.25, 129.59, 129.86, 135.99, 137.25, 140.74, 144.81. \]

\[ [\alpha]^{23} +126.2 \text{ (c = 0.70 g/mL)} \]
Cyclopentene (45): α-diazo ester 84 (13.6 mg, 0.0183 mmol, 1 eq) was dissolved in CH₂Cl₂ (200 µL) and cooled to 0°C. The Rh₂(OAc)₄ catalyst (0.16 mg, 0.4 µmol, 0.02 eq) was added, and the mixture was stirred for 3.5 hrs. The crude product was then filtered through silica gel and concentrated using a rotary evaporator, and a crude NMR was taken to determine the diastereomeric ratio. Column chromatography (silica, 4:1 hexanes/EtOAc w/ 0.5% NEt₃ v/v) afforded cyclopentene 45 (3.9 mg, 29%), along with the minor diastereomer, although significant impurities were also present.

**¹H NMR (400 MHz)** δ -0.28 (d, 1H, J = 3.1 Hz), 0.79 – 0.98 (m, 10H), 1.16 – 1.32 (m, 11H), 1.92 (d, 1H, J = 3.2 Hz), 2.33 (s, 3H), 2.95 – 3.19 (m, 4H), 3.24 (m, 1H), 3.36 (m, 1H), 3.96 – 4.22 (m, 5H), 4.34 (t, 1H, J = 8.2 Hz), 6.48 (s, 1H), 7.21 (m, 4H), 7.44 (d, 1H, J = 7.2 Hz), 7.56 (d, 2H, J = 8.3 Hz), 8.13 (d, 1H, J = 8.3 Hz).

**¹³C NMR (100 MHz)** δ 13.92, 14.11, 17.93, 21.56, 28.86, 29.72, 31.52, 31.77, 33.85, 44.60, 45.97, 61.08, 61.82, 61.93, 63.22, 99.74, 109.87, 110.04, 114.87, 120.34, 123.72, 124.32, 126.29, 129.45, 129.83, 135.98, 137.27, 139.15, 144.83, 155.78, 172.97, 210.23.
Vinyl oxazolidinone (65): Under open-air conditions, the (S)-(−)-4-isopropyl-2-oxazolidinone (64) (1.00 g, 7.74 mmol, 1 eq) added to a flask, before addition of (dpp)Pd(OTFA)$_2$ catalyst (257 mg, 0.387 mmol, 0.05 eq). After addition of butyl vinyl ether (10.0 mL, 77.4 mmol, 10 eq), the mixture was stirred in an oil bath for 4.5 hrs. Purification of the crude mixture by column chromatography (silica, 4:1 hexanes/EtOAc) afforded vinyl oxazolidinone 65 (1.033 g, 86%). As this is a common procedure in the Paley group, no characterization was performed.
Oxazolidinoyl vinyl stannane (66): In a flame-dried Schlenk flask, TMP (1.46 mL, 8.65 mmol, 1.3 eq) was dissolved in THF (7 mL) and cooled to 0°C. n-BuLi (3.33 mL, 8.32 mmol, 1.25 eq) was added dropwise, and the solution was stirred for 30 minutes. In a second Schlenk flask, vinyl oxazolidinone 65 (1.033g, 6.66 mmol, 1 eq) was dissolved in THF (20 mL) and cooled to -78°C. To the second flask was then added Bu₃SnCl (1.97 mL, 7.32 mmol, 1.1 eq), followed by the LiTMP solution by cannula. The resulting mixture was stirred for 15 minutes, before being warmed slowly to room temperature. The solution was then diluted with Et₂O (45 mL) and transferred to a separatory funnel, where the organics were washed with H₂O (2 x 30 mL) and brine (30 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 7:1 hexanes/EtOAc w/ 0.5% NEt₃ v/v) afforded 66 (2.741 g, 93%). As this is a common procedure in the Paley group, no characterization was performed.
Ketone (87): Anhydrous CeCl₃ (220 mg, 0.893 mmol, 2.5 eq) was dissolved, in a Schlenk flask, in THF (5 mL) and stirred vigorously overnight. This solution was then cooled to -78°C, and EtMgBr (238 µL, 0.714 mmol, 2 eq) was added dropwise, before the mixture was stirred for 2 hrs. The amide (86) (215 mg, 0.357 mmol, 1 eq), dissolved in THF (5 mL), was then added via cannula to the original solution, which was then stirred for 1 hr at -78°C, warmed to -40°C, and stirred for a further 30 minutes. The solution was treated with an aqueous saturated NH₄Cl solution (1 mL), allowed to warm to room temperature, and diluted with H₂O (20 mL) and Et₂O (40 mL). The aqueous layer was then washed with Et₂O (20 mL), before the combined organic layers were dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 40:1 hexanes/EtOAc w/ 0.5% NEt₃ v/v) afforded ketone 87 (172 mg, 89%).

¹H NMR (400 MHz) δ 0.01 (app. d, 6H, J = 5.1, OSi(CH₃)₂C(CH₃)₃), 0.88 (m, 27H, OSi(CH₃)₂C(CH₃)₃, Sn(CH₂CH₂CH₂CH₃)₃, and CHCCH(CH₃)CH₂OTBS), 1.05 (t, 3H, J = 7.3 Hz, CHCOCH₂CH₃), 1.29 (app. sext, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 1.45 (m, 6H,Sn(CH₂CH₂CH₂CH₃)₃), 2.45 (q, 2H, J = 7.3 Hz, CHCOCH₂CH₃), 3.41 (app. sext, 2H, J = 7.1 Hz, CHCCH(CH₃)CH₂OTBS), 3.89 (q, 1H, J = 6.8, CHCCH(CH₃)CH₂OTBS), 6.28 (s w/ Sn satellites, 1H, CHCOCH₂CH₃).
Hydrazone (88): Ketone 87 (25.4 mg, 0.0466 mmol, 1 eq) was dissolved in CH₂Cl₂ (1 mL) under open air conditions. To the solution were then added, in order, p-toluene-sulfonylhydrazide (9.6 mg, 0.0513 mmol, 1.1 eq), pyridinium p-toluene sulfonate (0.6 mg, 0.0023 mmol, 0.05 eq), and anhydrous MgSO₄ (28.0 mg, 0.2330 mmol, 5 eq). The resultant mixture was stirred at room temperature for 24 hrs, with reaction progress monitored by TLC. The mixture was then filtered through celite, before being diluted with Et₂O (3 mL) and an aqueous saturated solution of NaHCO₃ (1 mL). The aqueous layer was extracted with Et₂O (3 x 2 mL), before the combined organic layers were washed with brine (2 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Product, unpurified, was confirmed as hydrazone 88 (24.7 mg, 74%).

¹H NMR (400 MHz) δ 0.02 (s, 6H, OSi(CH₃)₂C(CH₃)₃), 0.88 (m, 27H, OSi(CH₃)₂C(CH₃)₃, Sn(CH₂CH₂CH₃CH₃)₃, and CHCCH(CH₃)CH₂OTBS), 1.01 (t, 3H, J = 7.4 Hz, CHCNC(CH₃)₂CH₃), 1.30 (app. sext, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 1.45 (m, 6H, Sn(CH₂CH₂CH₂CH₃)₃), 2.25 (m, 2H, CHCNC(CH₃)₂CH₃), 2.41 (s, 3H, CH₃C₆H₄SO₂), 3.31 (app. sext, 2H, CHCCH(CH₃)CH₂OTBS), 3.75 (s w/ Sn satellites, 1H, CHCCH(CH₃)CH₂OTBS), 5.52 (s w/ Sn satellites, 1H, CHCNC(CH₃)₂CH₃), 7.27 (d, 2H, J = 8.0 Hz, 2 of CH₃C₆H₄SO₂), 7.47 (s, 1H, CNNHSO₂), 7.80 (d, 2H, J = 8.3 Hz, 2 of CH₃C₆H₄SO₂).
Vinyl Iodide (89): Vinyl stannane 88 (24.7 mg, 0.0347 mmol, 1 eq) was dissolved in CH₂Cl₂ (500 µL) and cooled to 0 °C. N-Iodosuccinimide (NIS) (9.4 mg, 0.0416 mmol, 1.2 eq) was then added to the solution, followed by 2.5 hrs stirring at 0 °C. The solution was treated with an aqueous saturated Na₂SO₃ solution (1 mL) and an aqueous saturated NaHCO₃ solution (1 mL), then diluted with EtOAc (2 mL). The organic layer was then washed with brine (2 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 12:1 hexanes/EtOAc) afforded small amounts (<10 mg) of vinyl iodide 89, with slight impurities.

$^1$H NMR (400 MHz) δ 0.12 (d, 6H, J = 4.4 Hz, OSi(CH₃)₂C(CH₃)₃), 0.74 (d, 3H, J = 6.4 Hz, CHCC(CH₃)CH₂OTBS), 0.92 (s, 9H, OSi(CH₃)₂C(CH₃)₃), 1.01 (t, 3H, J = 7.4 Hz, CHCNCH₂CH₃), 1.58 (m, 1H, CHCC(CH₃)CH₂OTBS), 2.25 (app. dq, 2H, CHCNCH₂CH₃), 2.43 (s, 3H, CH₃C₆H₄SO₂), 3.33 (app. d, 2H, CHCC(CH₃)CH₂OTBS), 6.34 (s, 1H, CHCNCH₂CH₃), 7.30 (d, 2H, J = 8.4 Hz, 2 of CH₃C₆H₄SO₂), 7.82 (d, 2H, J = 8.3 Hz, 2 of CH₃C₆H₄SO₂), 8.08 (s, 1H, CNNHSO₂).
Amide (91): Terminal alkyne (90) (915 mg, 2.72 mmol, 1 eq) was dissolved in THF (15 mL) under an Ar atmosphere. Solution was then cooled to -78° C, before n-BuLi (1.142 mL, 2.86 mmol, 1.05 eq) was added dropwise. After 1.5 hours of stirring at -78° C, 4-morpholinecarbonyl chloride (333 µL, 2.86 mmol, 1.05 eq) was equally added dropwise, followed by an additional 2 hours of stirring at the same temperature. The solution was then treated with H₂O (10 mL), the layers were separated, and the aqueous layer was extracted with Et₂O (2 x 80 mL). The combined organic layers were washed with brine (80 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 2:1 hexanes/EtOAc) yielded amide 91 (1.086 g, 89%).

¹H NMR (400 MHz) δ 1.04 (s, 9H, OSiPh₂C(CH₃)₃), 1.68 (m, 4H, TBSOCH₂CH₂CH₂CH₂), 2.38 (t, 2H, J = 6.8, TBSOCH₂CH₂CH₂CH₂), 3.69 (m, 10H, TBSOCH₂CH₂CH₂CH₂ and NC₄H₈O), 7.42 (m, 6H, 6 of OSiPh₂C(CH₃)₃), 7.64 (m, 4H, 4 of OSiPh₂C(CH₃)₃).

¹³C NMR (100 MHz) δ 18.75, 19.21, 24.39, 26.85, 31.65, 41.79, 47.18, 63.09, 66.46, 66.84, 73.39, 94.05, 127.65, 129.63, 133.78, 135.52, 153.30.
Vinyl Stannane (92): In a Schlenk flask, Bu₆Sn₂ (2.684 mL, 5.311 mmol, 2.2 eq) was dissolved in THF (15 mL) and cooled to -78° C. n-BuLi (2.028 mL, 5.069 mmol, 2.1 eq) was then added dropwise, the temperature was raised to -40° C, and the solution was stirred for 30 minutes, at which point the mixture was a light yellow. After the 30 minutes, the solution was recooled to -78° C, at which point CuCN (432 mg, 4.828 mmol, 2 eq) was added and the temperature was raised again to -40° C, where the solution was stirred for 45 minutes, now a deep orange color. The temperature was then cooled again to -78° C, and MeOH (146 µL, 3.62 mmol, 1.5 eq) was added. Alkyne 91 (1.085 g, 2.414 mmol, 1 eq), dissolved in THF (8 mL), was then added to the original solution via cannula, leaving a red-orange color. The mixture was then stirred at -78° C for 90 minutes, before being raised to -25° C over the course of 10 minutes. The solution was then treated with 9:1 saturated NH₄Cl/NH₄OH (25 mL) and diluted with Et₂O (10 mL), at which point it was allowed to warm to room temperature. The aqueous layer was extracted with Et₂O (2 x 20 mL), before the combined organic layers were washed with 9:1 saturated NH₄Cl/NH₄OH (20 mL) and brine (20 mL), dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, gradient eluent: 9:1 \rightarrow 2:1 hexanes/EtOAc w/ 0.5% NEt₃ v/v) yielded vinyl stannane 92 (1.338 g, 75%).
$^1$H NMR (400 MHz) $\delta$ 0.88 (t, 9H, $J = 7.3$ Hz, Sn(CH$_2$CH$_2$CH$_3$)$_3$), 0.94 (m, 6H, Sn(CH$_2$CH$_2$CH$_2$CH$_3$)$_3$), 1.04 (s, 9H, OSiPh$_2$C(CH$_3$)$_3$), 1.30 (app. sext, 6H, $J = 7.4$ Hz, Sn(CH$_2$CH$_2$CH$_2$CH$_3$)$_3$), 1.51 (m, 10H, Sn(CH$_2$CH$_2$CH$_2$CH$_3$)$_3$) and TBSOCH$_2$CH$_2$CH$_2$CH$_2$, 2.43 (t w/ Sn satellites, 2H, $J = 7.8$, TBSOCH$_2$CH$_2$CH$_2$CH$_2$), 3.49 (t, 2H, $J = 4.4$, TBSOCH$_2$CH$_2$CH$_2$CH$_2$), 3.62 (m, 8H, NC$_4$H$_8$O), 6.00 (s w/ Sn satellites, 1H, NCOCHC(Sn), 7.41 (m, 6H, 6 of OSiPh$_2$C(CH$_3$)$_3$), 7.65 (m, 4H, 4 of OSiPh$_2$C(CH$_3$)$_3$).

$^{13}$C NMR (100 MHz) $\delta$ 10.02, 13.71, 19.18, 26.84, 27.37, 29.14, 32.80, 35.85, 41.45, 46.79, 63.74, 66.89, 127.59, 129.52, 131.09, 133.93, 135.54, 158.47, 166.90.
TBS-MAC (93): Under open-air conditions, acetylmalonitrile (0.70 g, 6.47 mmol, 1 eq) was dissolved in H₂O (15 mL) in a Schlenk flask. Peracetic acid (5 mL) was then added to acetic acid (10 mL) and thoroughly mixed before the acid mixture was added dropwise to the original solution, before 2 hrs of stirring at room temperature. The stir bar was then removed, and the solution was distilled until 1-2 mL remained. The resulting residue was stirred under high vacuum for 4 hrs. The remaining material was dissolved in DMF (18 mL) and cooled to 0° C. To this was added TBSCl (1.70 g, 9.70 mmol, 1.5 eq) in a single portion, followed by imidazole (0.66 g, 9.70 mmol, 1.5 eq) in several portions. The solution was stirred for 30 minutes, warmed to room temperature, and stirred for an additional 30 minutes. The solution was then diluted with Et₂O (40 mL) and transferred to a separatory funnel, where the organics were washed with H₂O (30 mL), saturated aqueous NaHCO₃ (20 mL), and brine (20 mL), before being dried (MgSO₄), filtered, and concentrated using a rotary evaporator. Column chromatography (silica, 15:1 hexanes/EtOAc) yielded MAC reagent 93 (935 mg, 74%).

¹H NMR (400 MHz)  δ 0.29 (s, 6H, Si(CH₃)₂(C(CH₃)₃)), 0.94 (s, 9H, Si(CH₃)₂(C(CH₃)₃)), 5.34 (s, 1H, (NC)₂CHOTBS).
NMR and IR Spectra

\begin{align*}
\text{O Et} & \quad \text{O} \\
\text{O Et} & \quad \text{O} \\
\text{OH} & \quad \text{OEt}
\end{align*}

\text{a) n-Bu Li}

\text{b) BF}_3 \cdot \text{O Et, THF}
% Transmittance

Wavenumbers (cm⁻¹)

MeO 53

OTHP

MeO

MeO

SnBu₃

1033.1

1120.8

980.8

869.8

1321.9

1258.9

1358.9

1415.6

1432.1

1591.9

1718.2

1792.5

5354
1.2537
1.2716
1.2894
2.0694
2.5347
2.5530
2.5716
2.7651
2.7836
2.8019
4.1186
4.1364
4.1543
4.1721
4.5626
4.5805
6.3588
6.3767
6.3945
3.09
2.96
2.03
2.05
1.99
2.02
1.00

AcO

a) AcO, DME, CSA, 60° C
b) EtOH, NEt3, -40° to 0°C
61
68
\[ \text{NOEtO}_2\text{Fe( CO)}_3 \text{PhO} \text{TBDSO} \]
\[
\text{Fe(CO)}_3
\]
$\text{N}$

$\text{Fe(CO)}_3$

$\text{TBDSO}$

44a
$\text{Fe( CO)}_3$
\[ \text{Fe(CO)₃} \]

44a
N Ts N

a) n-Bu Li
b) B F 3.O Et,

\[ \text{76} \]
a) n-BuLi
b) B F 3 OEt, THF

[Chemical structure image]
a) T F A, C H 2 Cl 2 , 0° C
b) Et O H, N Et 3 , - 2 5° C
a) TFA, C\text{H}_2\text{Cl}_2, 0{}^\circ \text{C}

b) \text{EtOH}, \text{NEt}_3, -25{}^\circ \text{C}
\[ \text{Fe( CO)}_3 \text{toluene, 35°C} \]
$^{13}$C-NMR (CDCl$_3$, 100.6 MHz) of compound 82:

- ppm values range from 0.0 to 180.

The spectrum shows multiple peaks indicating various chemical shifts, with the highest peak at 2.49 ppm.

Chemical structures include:

- Fe(CO)$_3$,
- PhOCl,
- N,N-dimethylimidazole.

Reactions mentioned:

- TiCl$_4$, Bu$_3$NB, CH$_2$Cl$_2$, -45°C.
Not applicable
Sb Bu3
TBSO

p-toluene-sulfon hydride

PPTS, MgSO4, RT
a) n-BuLi, -78°C

b) 4-morpholine carbonyl chloride, -78°C
a) n-Butyllithium, -78°C
b) 4-morpholinocarbonyl chloride, -78°C
\[ \text{Transmittance} \]
Determining Diastereomeric Ratios

- EtO
- TBPSO
- Fe(CO)₃
- Toluen, 35 °C