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Yuxing Wang Date

EXPANDING THE SCOPE OF DONOR/ACCEPTOR

RHODIUM-CARBENE CHEMISTRY

By

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Master of Science

Chemistry

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EXPANDING THE SCOPE OF DONOR/ACCEPTOR RHODIUM-CARBENE CHEMISTRY

By

Yuxing Wang

M.S., Tsinghua University, 2011

Advisor: Huw M. L. Davies, Ph.D.

An abstract of

A thesis submitted to the Faculty of the

James T. Laney School of Graduate Studies of Emory University

in partial fulfillment of the requirements for the degree of

Master of Science

in Chemistry

2015

Abstract

The reactions of donor/acceptor rhodium carbenoids have been studied extensively in the past several decades. Cyclopropanation was a major early application of rhodium carbenoid chemistry and has been widely used in both academia and the industrial world. Also, C-H insertion by rhodium carbenoids is one of the most promising methodologies for C-H functionalization. This work attempts to expand the scope of existing rhodium carbenoid methodologies as well as develop new methodologies.

The first part of this thesis describes a systematic optimization of catalyst, solvent, reaction temperature, additive, as well as reaction substrates to achieve C-H insertion of Rh(II)-stabilized carbenoids into acetals with high enantioselectivity. Eight substrates were tested under optimized conditions affording C-H insertion product in 25 - 83% yield and 87 - 94% ee. This reaction can be considered as a surrogate for the Claisen condensation.

The second part of the thesis describes the development of the combined C-H functionalization/Cope rearrangement (CHCR) and C-H insertion reaction with triazoles and dihydronaphthalene. However, the reaction scope is very limited, and only a few substrates are compatible with this transformation.

The last part of the thesis describes the development of an asymmetric transformation of propargylic alcohols with donor/acceptor-substituted carbenoids affording 2,5-dihydrofuran derivatives *via* tandem ylide formation/[2,3]-sigmatropic rearrangement/cycloisomerizaion using *S*-xylyl-BINAP$(AuCl)_2$ and $AgSbF_6$ as the catalysts.

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From 2005 I joined THU to now, I spent 10 years in chemistry. I am glad it came to an end. Although I might not doing chemistry any more, I am sure I will benefit from these training and knowledge though my life.

Table of Contents

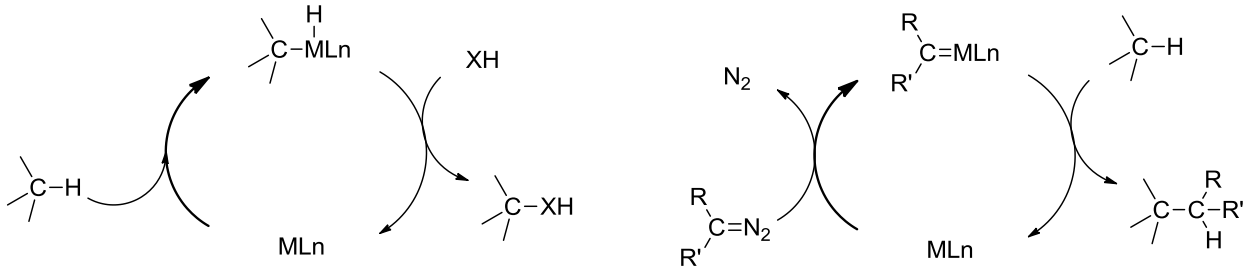
List of Tables

List of Schemes

Chapter 1. Introduction

The development of efficient ways to achieve the construction of complex bioactive compounds and/or natural products has been one of the main foci of organic chemists for centuries. As a novel strategy for organic transformations, functionalization of un-activated C-H bonds offers unique synthetic strategies for the construction complex molecules. [1]

Traditionally, the majority of transition-metal-catalyzed C-H functionalization requires an activation step, that is, the insertion of the metal into the C-H bond (Scheme 1.1, (A)).[2, 3] Alternatively, C-H functionalization can be achieved by insertion of a metal carbenoid into a C-H bond (Scheme 1, (B)).[4, 5] *In situ* generation of the metal carbenoid via decomposition of diazo compounds with chiral transition metals complexes has made asymmetric C-H functionalization an efficient and very promising method in synthetic chemistry.[5]

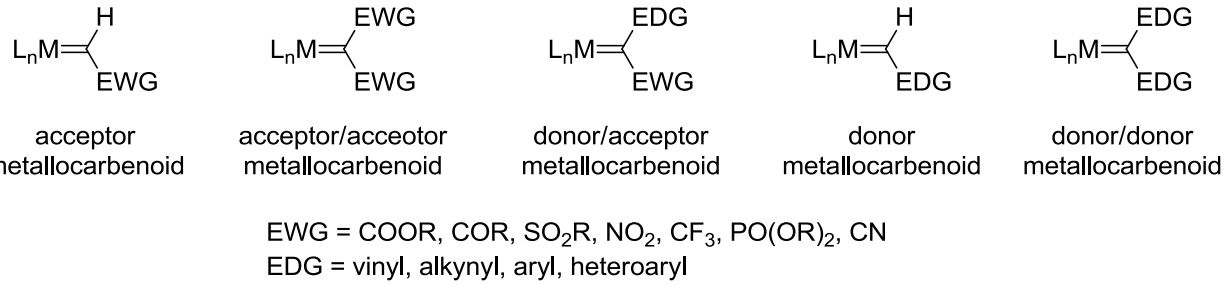


Scheme 1.1 (A) Activation of C-H bond via oxidative addition and (B) C-H activation via metal-carbenoid

1.1 Metallocarbenoid chemistry

The metal-catalyzed decomposition of diazo compounds to generate metal-stabilized carbenoids has been exploited in a variety of useful synthetic transformations.[4, 6] It has been demonstrated that the reactivity profile of metallocarbenes is dependent on the metallocarbene structure.[4, 5, 7] In general, diazo compounds can be classified into five major groups: acceptor[4], acceptor/acceptor[8], donor/acceptor[5], donor[8] and donor/donor[9] based on the electronic profile of their substitution (Figure 1.1). The "acceptor" group, which means electron-withdrawing group,

enhances the electrophilicity of the metallocarbenoid, and thus increases its reactivity. The "donor" group, which means electron-donating group, helps to stabilize the metallocarbenoid through attenuation of its reactivity, and thus enhances selectivity of metallocarbenoid.[5] As a consequence; donor/acceptor-substituted carbenoids are generally more chemoselective than carbonoids that are substituted with only acceptor groups. As a result, even though the discovery of donor/acceptor carbenoids was late relative to that of acceptor and acceptor/acceptor carbenoids, plenty of efficient transformations have been discovered using donor/acceptor carbenoids.

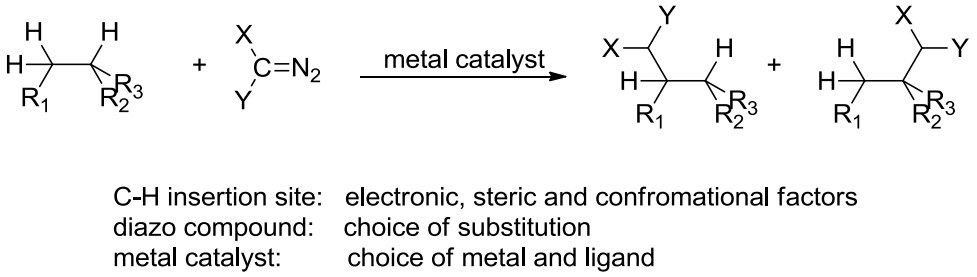


Scheme 1.2 Different types of metallocarbenoids

It has been demonstrated that the reactivity and selectivity of carbenoid intermediates is dependent on their structure (Figure 2).[5] By using a donor/acceptor metallocarbenoid, C-H insertion can be achieved in a highly chemo-, regio-, and stereoselective manner. Generally speaking, acceptors on carbenoids increase the reactivity while donors attenuate the reactivity and at the same time enhance the selectivity. This is expected, since insertion of metal carbenoids into un-activated C-H bond is a process in which the metal carbenoid serves as an electrophile. Furthermore, a recent result from Davies group also demonstrated that different ester substitutions on the acceptor group play an important role in manipulating the selectivity profile of rhodium-catalyzed carbenoid C-H insertions[9].

The nature of the transition metals also influences the reactivity of the carbenoid intermediate.[5] The ideal catalyst is one that can bind to the carbene center through strong σ-bonding, and weak π-bonding donation, which stabilizes the carbene to some extent but still ensures that the carbenoid retains high electrophilicity. Moreover, if the catalyst has electron-withdrawing ligands, the electrophilicity of the carbenoid is further enhanced.

The site selectivity of C-H activation is also influenced by substituents adjacent to the C-H bond.[5] Electron-donating groups, such as alkoxy and vinyl groups adjacent to the site of C-H activation, promote the reaction since there is positive charge build-up on the reacting carbon. Besides electronic effects, steric or even conformational factors also influence the reactivity and selectivity. [5, 10]



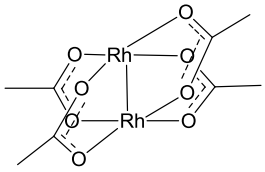
Scheme 1.3 Factors that control the selectivity of C-H functionalization

Besides C-H insertions[4,5], metallocarbenoids can undergo a series of other transformations, such as cyclopropanation[11-13], cycloaddition[14-16] and ylide formation[17-19], generating useful scaffolds and building blocks for further diversification. The reactivity of metal carbenoids has been broadly utilized in the total synthesis of natural products and biologically active compounds.[4, 5, 20]

1.2 Chiral catalysts for the metallocarbenoid chemistry

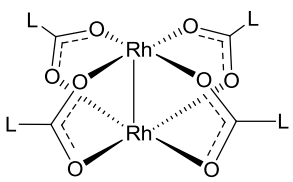
Various metals, including copper, palladium, rhodium, silver, ruthenium and cobalt have been used to generate metal-stabilized carbenoids. Plenty of useful transformations have been achieved utilizing metal carbenoids. [4, 5]

The development of rhodium catalysts for the decomposition of diazo compounds greatly enhanced the scope of transformations by metal carbenoids.[4] Rhodium catalysts used in metal carbenoid chemistry are usually dirhodium complexes. It is suggested that only one of the rhodium atom binds to the carbene center and the second one serves as the electron sink. The Rhodium tetraacetate ($Rh_2(OAc)_4$), which is widely used in the early rhodium carbenoid chemistry, has four bridging acetate ligands positioned symmetrically around the two rhodium atoms to give the dimeric "paddlewheel" complex with an overall D_{4h} symmetry (Figure 3)[5].

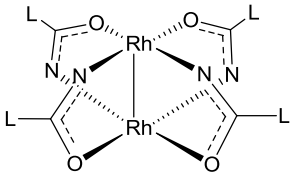


Scheme 1.4 Dirhodium tetraacetate "paddlewheel"

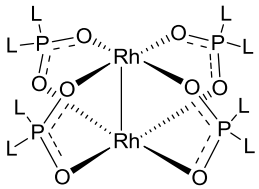
Rhodium (II) catalysts can be classified into four major types according to their structures: rhodium carboxylates, rhodium carboxamidates, rhodium phosphates and *ortho*-metalated aryl phosphine rhodium complexes (Figure 1.4). [5]



Dirhodium (II) Tetracarboxylates



Dirhodium (II) Tetracarboxamidates

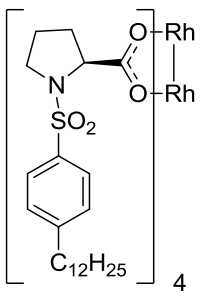


Dirhodium (II) Tetraphosphates

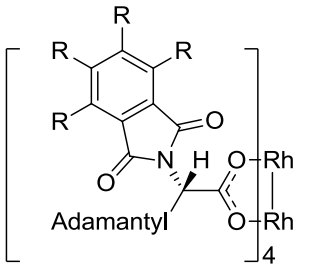
Scheme 1.5 Types of Dirhodium (II) catalysts

Rhodium carboxamidates developed by the Doyle group are also effective catalysts for the decomposition of diazo compounds.[21] Representative ligands in this class of catalysts are pyrrolidinones, oxazolidinones, imidazolidinones and azetidinones.

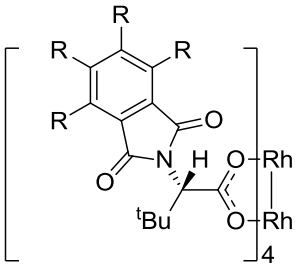
Rhodium (II) carboxylates are very reactive catalysts for the decomposition of diazo compounds[5], among which, *N*-benzenesulfonyl protected *L*-proline derivatives and *N*-phthaloyl - (*S*) - amino acids ligated catalysts (Figure 1.5) have been well developed and investigated. Rh_2(*S*-DOSP)$_4$[22] and Rh_2(*S*-PTAD)$_4$ [5, 14] developed by the Davies group are excellent catalysts for reactions of donor-acceptor carbenoids. Rh_2 (*S*-PTTL)$_4$ developed by the Hashimoto group performed site selective intramolecular C-H insertion reactions of diazo ketoesters, diazo ketones, or *R*-methoxycarbonyldiazoacetamides to give enantioselective 2,3-dihydrobenzofurans[23] and 2-pyrrolidinone[24] derivatives with up to 94%, and 90% ee, respectively. Rh_2(*S*-BTPCP)$_4$ is another generation of chiral rhodium catalyst developed by the Davies group and is very effective for enantioselective reactions of aryl- and styryldiazoacetates.[12, 25] All of these catalysts are also used in rhodium-catalyzed decomposition of triazoles to generate metallocarbenoids.



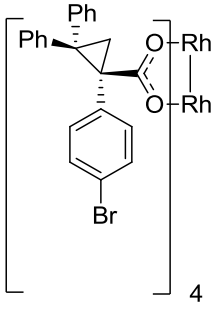
Rh_2(*S*-DOSP)$_4$



R = H: Rh_2(*S*-PTAD)$_4$
R = Cl: Rh_2(*S*-TCPTAD)$_4$



R = H: Rh_2(*S*-PTTL)$_4$
R = Ph: Rh_2(*S*-TPPTTL)$_4$
R = Cl: Rh_2(*S*-TCPTTL)$_4$
R = Br: Rh_2(*S*-TBPTTL)$_4$



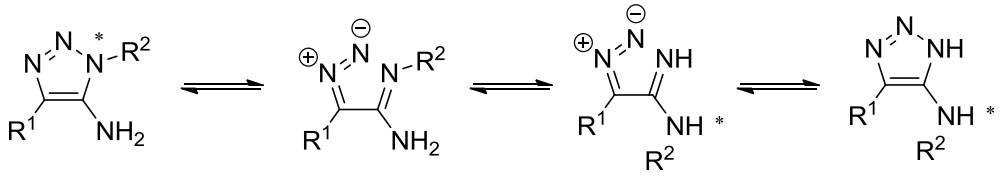
Rh_2(*S*-BTPCP)$_4$

Scheme 1.6 Rhodium (II) carboxylates

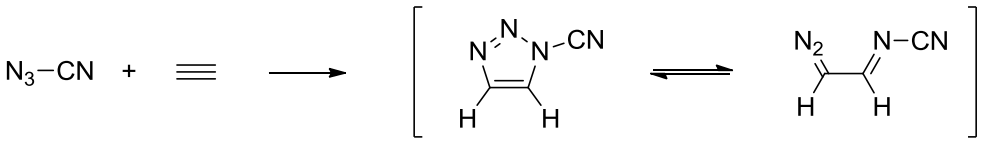
1.3 Use of triazoles as an alternative carbene precursors.

It is well known that 1,2,3-triazoles-4-amines can undergo a rearrangement reaction through a ring-opening, ring-closure sequence to isomeric triazoles. This rearrangement is also known as Dimroth rearrangement (Scheme 1.7).[26] Having a strong electron-withdrawing group at the *N*-1 position, the equilibrium favors the ring-opened imino diazo structure. In 1967, Hermes and Marsh reported that at slightly above room temperature, closed and open-isomer of 1-cyano-1,2,3-triazole exists as a 1:1 isomeric mixture.[27] In 1970, Harmon reported that *N*-sulfonyl-1,2,3-triazoles with an amino group at the C-5 position also existed as an isomeric mixture of open and closed-chain isomers.[28]

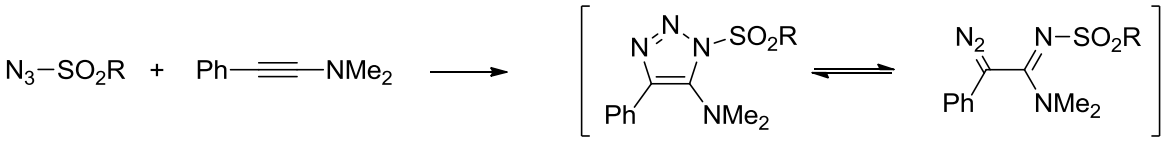
Dimroth Rearrangement[26]



Hermes and Marsh's work[27]



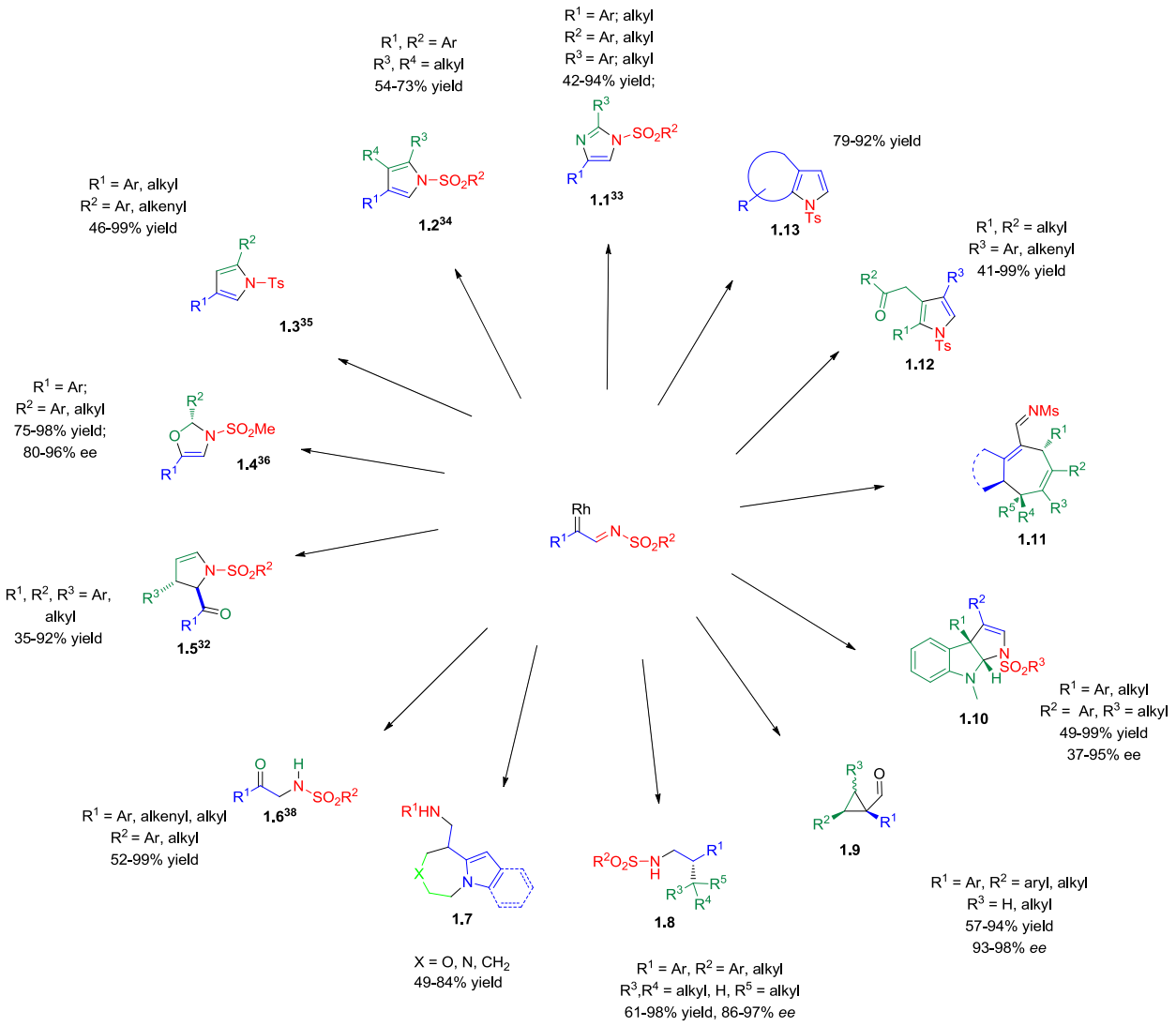
Harmon's work[28]



Scheme 1.7 Triazole rearrangements/ring-chain isomerization.

Recently, 1,2,3-triazoles bearing a strong electron-withdrawing group at the *N*-1 position, which are capable of undergoing a 'ring-to-chain isomerization' to expose the diazo moiety, have been shown to act as masked diazo compounds[29,30]. In 2007, Chuprakov and Gevorgyan reported the first example of rhodium carbenoids generated from triazoles.[29] In this study, 7-chloro-substituted pyridotriazole was decomposed in the presence of a rhodium(II) catalyst to reveal a transient rhodium carbenoid, which was then confirmed by inserting into the Si-H bond of triethylsilane. After this initial report, Gevorgyan and Fokin reported using *N*-sulfonyl-1,2,3-triazoles as convenient precursors to rhodium(II)-stabilized imino carbenes.[30] They reported that in the presence of 1 mol% $Rh_2(OAc)_4$, *N*-sulfonyl triazoles reacted with styrene affording the *trans*-cyclopropane carboxaldehyde after hydrolysis of the sulfonyl imine.

A distinctive feature of using *N*-sulfonyl triazoles is the generation of metallocarbenes with a pendant sulfonyl imine group.[31] The nitrogen atom exhibits a higher nucleophilicity than the oxygen atom in the related α-oxo metallocarbene.[32] Due to this increased nucleophilicity, the α-imino group has the ability to participate in reactions involving zwitterionic intermediates, which can then cyclize to new heterocycles. Numerous studies have demonstrated the application of N-sulfonyltriazoles as viable precursors in both classic and novel rhodium carbenoid reactivities[31]. Some selected transformations are shown in scheme 1.3. A detailed review of transformations with metallocarbenoids derived from *N*-sulfonyl-1,2,3-triazoles has been published by the Davies group.[31]



Scheme 1.8 Selected Rhodium-catalyzed triazole reactions

In 2008, Fokin and Gevorgyan reported that *N*-sulfonyl triazoles reacted with nitriles to generate imidazoles **1.1** (Scheme 1.3).[33] In this transformation, a board scope of nitriles and *N*-sulfonyl triazoles can be used. The following year, Murakami reported a nickel-catalyzed annulation reaction with *N*-sulfonyl triazoles with internal alkynes to form pyrroles **1.2** in moderate yield.[34] However, using unsymmetrical alkynes gave a mixture of regioisomers and

terminal alkynes were not tolerated. Later on, Gevorgyan reported a transformation of *N*-tosyl-triazole with terminal alkynes forming pyrroles **1.3** in good yield with a combination of rhodium and silver dual catalytic system.[35]

Ylide formation followed by sequential rearrangement with rhodium carbenoid generated from triazoles is also established. In 2013, Fokin reported a ylide formation followed by intermolecular cyclization with triazole and aldehydes generating 4-xazolines **1.4** in high yield and excellent enantioselectivity.[36] In the same year, Murakami group reported a similar transformation using α,β-unsaturated aldehydes to generated trans-2,3-disubstituted dihydropyrroles.[32] The mechanism of this transformation is proposed that the reaction first generates 4-oxazolines as Fokin reported[36], under more vigorous conditions, a ring-opening followed by 3,3-sigmatropic rearrangement sequence occurred. In addition to aldehydes, ylide formation of water[37], alcohols[37] and allylic alcohols[38] were reported by Murakami.

In 2011, Fokin described an enantioselective C-H insertion reaction into unactivated alkanes with rhodium(II) stabilized imino-carbenoid in good yield and high enantioselectivity (Scheme 2).[39] In this reaction, both electron-withdrawing and electron-donating aryl groups were tolerated on the triazole ring and both aryl and alkyl substitution on the sulfonyl group were tolerated.

Davies group has been interested in using 1,2,3-triazoles to expand the scope of donor groups that can be incorporated into donor/acceptor carbene. To this end, The Davies group reported that 4-amido-1-sulfonyl-1,2,3-triazoles can be used to introduce a *N*-phthalimido acceptor group, which enabled an expedited synthesis of cyclopropyl amino acids.[40] Analogously, the Davies group also described a series of transformations N-sulfonyltriazoles as carbenoid precursors, for

instance, formal [3+2] with indole,[41] formal [4+3] with diene[42], formation of trisubstituted pyrrole[43] and formation of 2,3-fused pyrroles and indoles [44].

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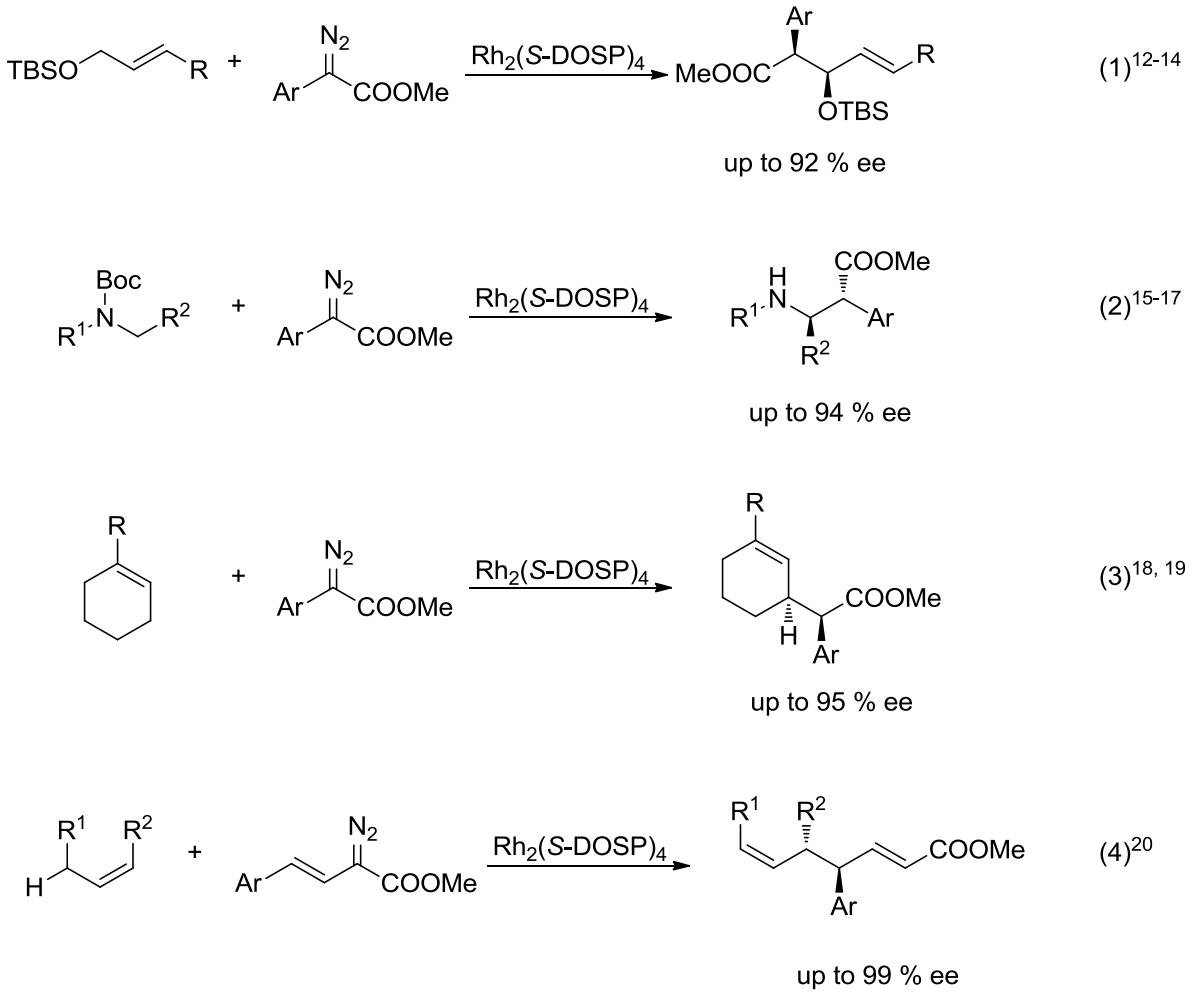
Chapter 2. Asymmetric C-H insertion of Rh(II)-stabilized carbenoids into acetals: a surrogate for Claisen condensation

2.1. Introduction.

The development of new methods for the regio- and stereoselective functionalization of C-H bonds is a challenge in organic methodology studies. Traditionally, the majority of transition-metal-catalyzed C-H functionalization requires an activation step, that is, the insertion of the metal into the C-H bond.[1, 2] Alternatively, C-H functionalization can be achieved by insertion of a metal carbenoid into a C-H bond.[3] Decomposition of diazo compounds with chiral transition metals complexes has made asymmetric C-H functionalization an efficient and very promising method in synthetic chemistry.[3,4]

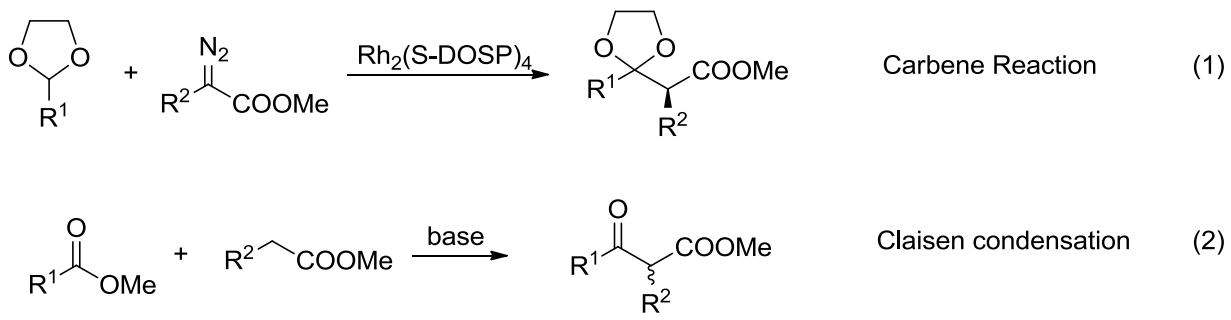
In the past, the efficient and highly enantioselective C-H insertions with carbenoids were limited to intramolecular reactions, as a result of lack of selectivity in the intermolecular reactions.[3] In recent years, however, detailed studies have demonstrated that the carbenoid structure and catalyst system have a great influence on the reactivity profile of carbenoids [4-7]. In the presence of the electron-donating group, normally aryl or vinyl, carbenoids are more stable than the carbenoids, which contains only electron acceptor groups [3, 8]. Furthermore, a recently result of Davies group also demonstrated that different ester substitution on the acceptor group plays an important role on manipulating the selectivity profile of rhodium-catalyzed carbenoid C-H insertions[9]. Moreover, as different type of dirhodium catalysts have been developed, a better control of carbenoid reactivity can be achieved. For instance, with the use of recently developed catalyst Rh_2(*S*-BTPCP)$_4$, the C-H insertion will occur preferentially at a primary C-H bond rather than any other C-H bonds[10].

It has been demonstrated that by using donor/acceptor substituted rhodium carbenoids, a variety of chemo- and stereoselective intermolecular C-H functionalization reactions can be achieved[3, 4, 11]. Some of these reactions can be seen as a complementary carbenoid version of classic synthetic reactions. For example, β-hydroxy esters, products of aldol reaction, can be obtained by C-H insertion α to oxygen[12-14]. Moreover, β-amino esters, which normally can be prepared by Mannich condensation, can be synthesized by C-H insertion α to nitrogen[15-17]. Also, γ,δ-unsaturated esters, which usually are prepared via Claisen rearrangement, can be accessed via allylic C-H insertions[18, 19]. The allylic C-H activation with vinyl carbenoid, which is also known as combined C-H insertion Cope rearrangement reaction, can provide access to complex molecular with at least two adjacent chiral centers in high stero- and entioselectivity[20].



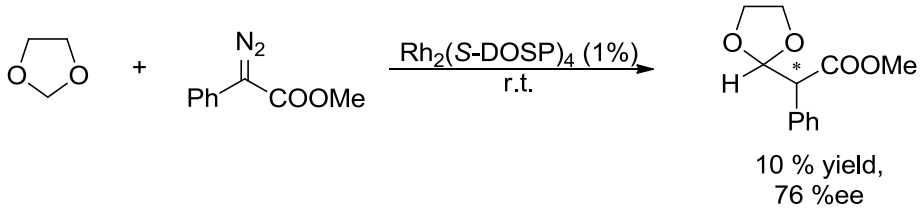
Scheme 2.1 Selected carbene C-H insertion reactions

In 2005, the Davies group published a C-H functionalization methodology of tertiary sites in acetals to form ketal protected β-keto esters in great chemo- and stereoselectivity[21]. This transformation was considered as a surrogate to the Claisen condensation and it has an important advantage compared to Claisen condensation whose stereocontrol is unlikely because in the standard Claisen condensation conditions, that stereo center in unprotected β-keto ester is epimerizable (Scheme 2.2).



Scheme 2.2 Carbene C-H insertion of acetals and Claisen condensation

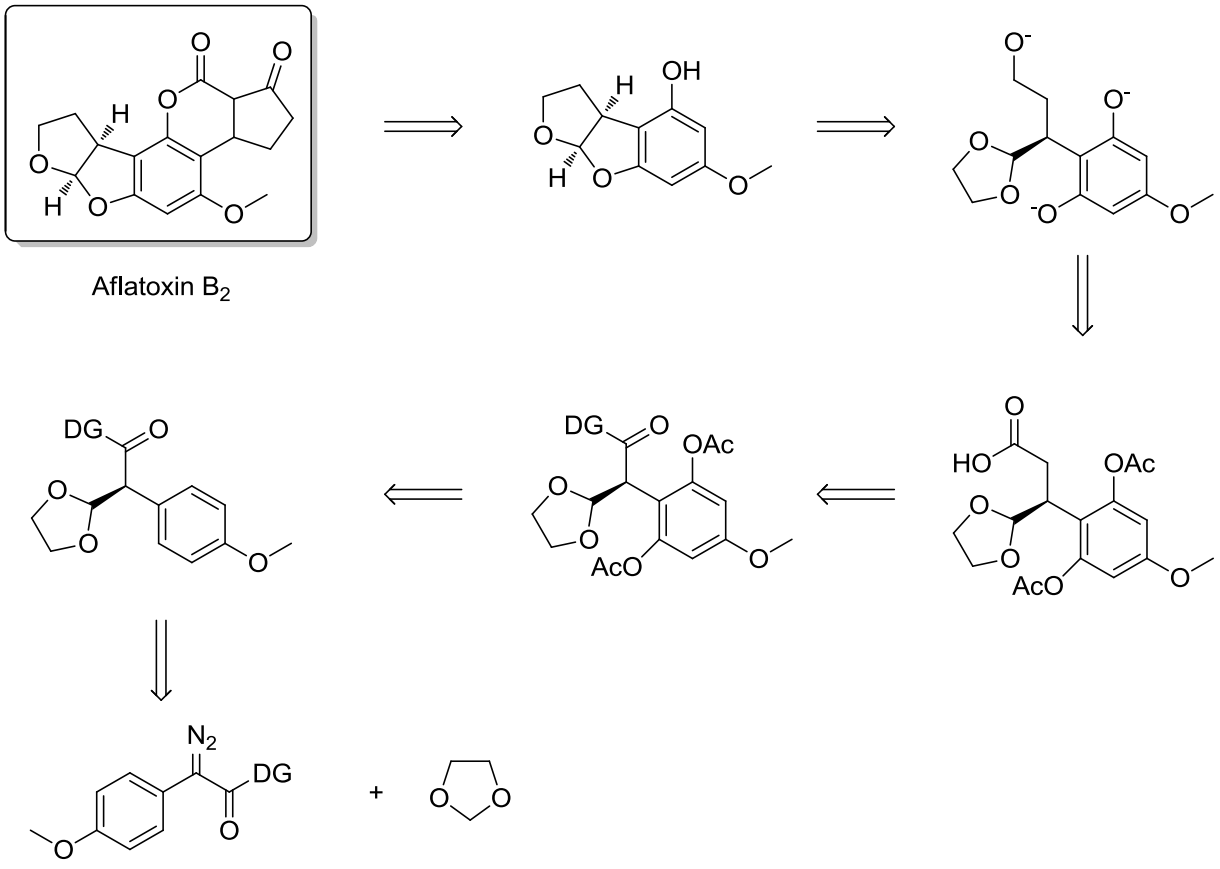
In that study, one of the limitations for that methodology is that the C-H insertion happened on the tertiary site adjacent to a heteroatom. Aryl- or styreneyl- substitution needs to be present in order to achieve a decent yield. The authors did not comment on how non-substituted acetals, for example, dioxalene, would perform under the reaction conditions. The reaction of carbenoid C-H insertion into dioxalene was reported later by J. M. Fraile and coworkers, affording the desired product in only 10% yield and 76%ee (Scheme 2.3) [22].



Scheme 2.3 Carbene C-H insertion of 1,3-dioxalene

Recently, one of our collaborators from Dr. Sorensen's group, Julian West, proposed an interesting route of formal synthesis of Aflatoxin B_2 (Scheme 2.4). The idea for that synthesis is to use enantioselective carbene C-H insertion of dioxalene as the first step, and then use a directed palladium catalyzed C-H activation to introduce two acetoxyl groups into the core. As

the previous methodology only offered a low yielding transformation, I decided to try to develop a new methodology for that particular transformation based on the previous studies.

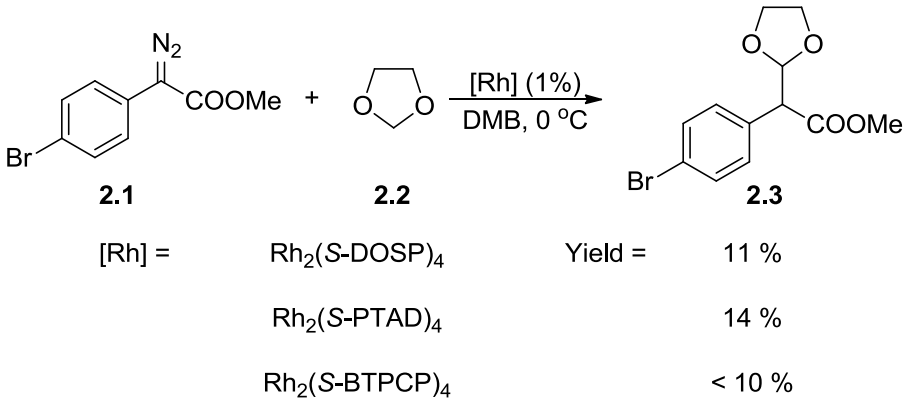


Scheme 2.4 Retrosynthetic analysis of Aflatoxin B_2 by Mr. Julian West

2.1. Results and discussion.

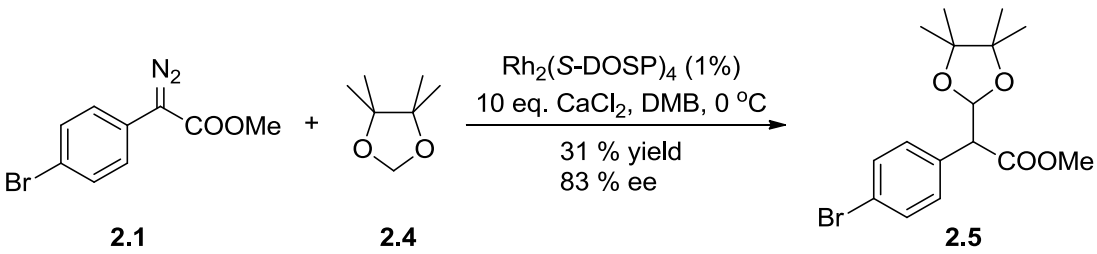
To explore the possibility of C-H insertion of the carbon center adjacent to two heteroatoms, which electronically activate this site, the reaction of dioxalene using different chiral rhodium catalyst was examined. Three representative chiral rhodium catalyst, Rh_2(S-DOSP)$_4$, Rh_2(S-PTAD)$_4$ and Rh_2(S-BTPCP)$_4$,, were explored under the reaction conditions. A complex reaction

mixture was observed in all these cases. The results are consistent with a previous literature report[22].



Scheme 2.5 C-H insertion of 1,3-dioxalene using different Rhodium(II) catalysts

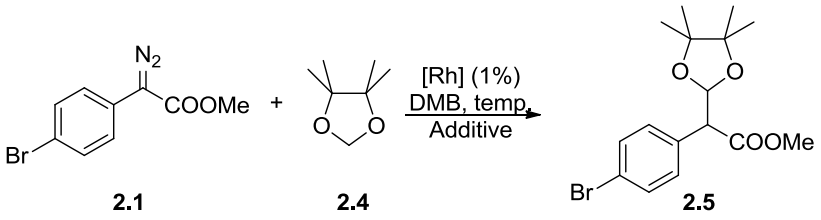
Based on the previous report of C-H insertion into 2-phenyl-1,3-dioxolane[21], I reasoned that the main competing reaction is the ylide formation followed by sequential rearrangement reaction. And also, although less likely, the C-H insertion can also occur at C4 and C5 positions. In order to avoid the undesired ylide formation followed by sequential rearrangement and other possible side products, we decided to introduce more steric hindrance on to the 4,5-positions of the substrate to prevent the undesired ylide formation. To our delight, the C-H insertion into 4,4,5,5-tetramethyl-1,3-dioxalene using Rh_2(S-DOSP)$_4$ as catalyst afforded the desired C-H insertion product in 31% yield and 83 %ee.



Scheme 2.6 C-H insertion of 4,4,5,5-tetramethyl-1,3-dioxalene

Encouraged by this initial result, we decided to explore the effect of the rhodium catalyst, reaction temperature as well as additives. Electron rich catalysts, $Rh_2(Piv)_4$, $Rh_2(TPA)_4$, Rh_2(*S*-BTPCP)$_4$ were tested(Table 2.1, Entries 1-3), none of them afforded the desired product in greater than 5% yield. As we moved to Rh_2(*S*-PTAD)$_4$, Rh_2(*S*-PTTL)$_4$ and Rh_2(*S*-TCPTAD)$_4$ (Table 2.1, Entries 5-7), which are more electron deficient than Rh_2(S-DOSP)$_4$, the yield of C-H insertion product dropped. Using 4Å MS as an additive instead of $CaCl_2$ afforded the product in a similar yield (Table 2.1, Entry 8). Without using any additive, the carbene insertion into water was observed. On increasing the reaction temperature to room temperature, the yield dropped to 19% (Table 2.1, Entry 9). Decreasing the reaction temperature to -50 ^{o}C or -78 ^{o}C was also not beneficial as the yield dropped to 14% (Table 2.1 Entries 10, 11).

Table 2.1 Optimization of C-H insertion of dioxalene



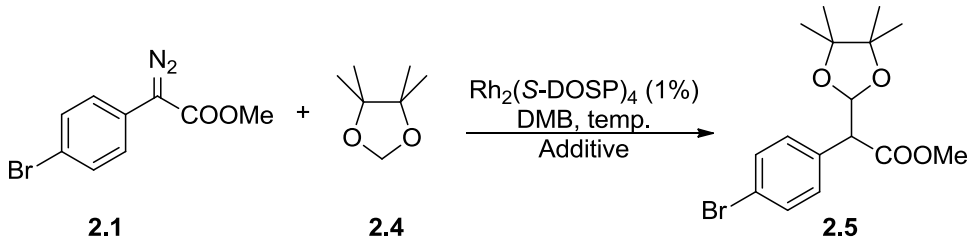
2.1 **2.4** **2.5**

Entry	[Rh] (1%)	temp.	Additive(10 eq.)	Yield[a] (%)	ee (%)
1	$Rh_2(Piv)_4$	0 °C	$CaCl_2$	< 5	--
2	$Rh_2(TPA)_4$	0 °C	$CaCl_2$	< 5	--
3	Rh_2(S-BTPCP)$_4$	0 °C	$CaCl_2$	< 5	ND
4	Rh_2(S-DOSP)$_4$	0 °C	$CaCl_2$	31(28)	83
5	Rh_2(S-PTAD)$_4$	0 °C	$CaCl_2$	14	ND
6	Rh_2(S-PTTL)$_4$	0 °C	$CaCl_2$	12	ND
7	Rh_2(S-TCPTAD)$_4$	0 °C	$CaCl_2$	5	ND
8	Rh_2(S-DOSP)$_4$	0 °C	4A MS	28(25)	83
9	Rh_2(S-DOSP)$_4$	25 °C	$CaCl_2$	19	ND
10	Rh_2(S-DOSP)$_4$	-50 °C	$CaCl_2$	14	ND
11	Rh_2(S-DOSP)$_4$	-78 °C	$CaCl_2$	14	ND

a. Yield was determined by ^{1}H NMR, using 1,3,5-trimethoxylbenzene as internal standard; isolated yield was showed in parenthesis;

In the previous study of C-H insertion into 2-phenyl-1,3-dioxalene we found out that the ratio of diazo compound and trap is crucial for getting decent yield[21]. Based on that study, I decided to test if this is still holds true in the C-H insertion into dioxalene. As shown below, using a ratio of diazo compound to trap 1:4 or 2:1 afforded the product in same yield (Table 2.2, Entries 1, 4). If using dioxalene as solvent, namely 1:40 ratio, the yield dropped to 14% (Table 2.2, Entry 2). If using small excess of dioxalene, namely 1:1.2 ratio, the yield dropped to 26% (Table 2.2, Entry 3).

Table 2.2 C-H insertion of dioxalene in different diazo/trap ratio

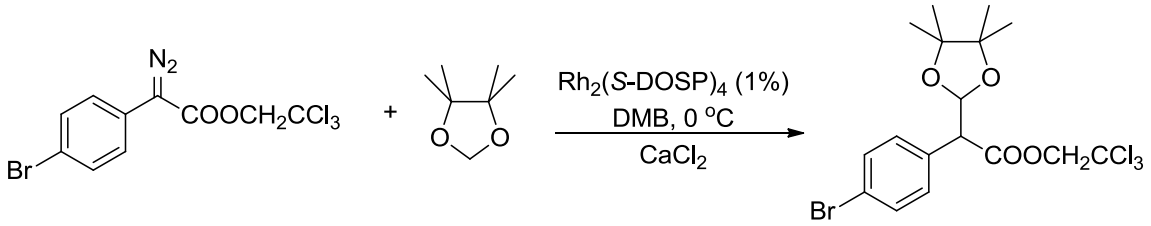


2.1 **2.4** **2.5**

Entry	**1**:**2** ratio	temp.	Additive(10 eq.)	Yield[a] (%)	ee (%)
1	1 : 4	0 °C	$CaCl_2$	31(28)	83
2	1 : 40	0 °C	$CaCl_2$	14	ND
3	1 : 1.2	0 °C	$CaCl_2$	26	ND
4	2 : 1	0 °C	$CaCl_2$	31	83

a. Yield was determined by ^{1}H NMR, using 1,3,5-trimethoxylbenzene as internal standard; isolated yield was showed in parenthesis;

During the same time period, another study in our group showed that using 2,2,2-Trichloroethyl aryldiazoacetates can enhance both reaction yield and enantioselectivity of C–H functionalization of methyl ethers[9]. Thus, we decided to test if that compound can help to improve the C-H insertion of dioxalene. As 1:4 ratio and 2:1 ratio afforded the same overall reaction yield in the methyl ester case, I tried both conditions for 2,2,2-trichloroethyl aryldiazoacetates **2.6**. The reaction of diazo 2,2,2-trichloroethyl aryldiazoacetates **2.6** using an excess dioxalene, namely 1:4 ratio, formed only 10% product. Surprisingly, if using an excess of 2,2,2-trichloroethyl aryldiazoacetates **2.6**, the reaction yield and enantioselectivity were improved to 66% yield and 93% ee (Scheme 2.7).



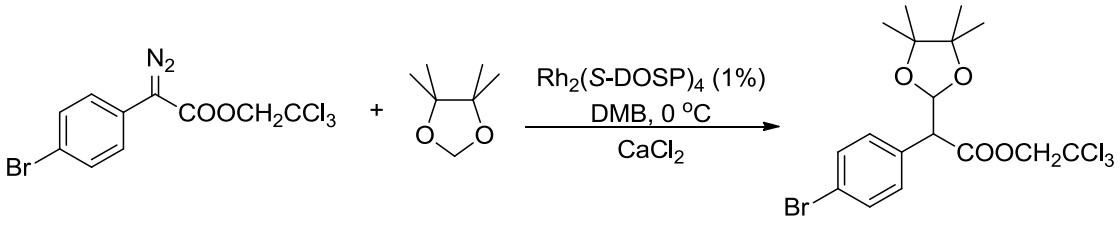
2.6 **2.4** **2.7**

ratio of **2.6 : 2.4**	1 : 4	10 % yield
	2 : 1	66 % yield, 93 %ee

Scheme 2.7 C-H insertion of dioxalene using 2,2,2-Trichloroethyl aryldiazoacetates

Encouraged by this result, different reaction temperatures were tested to further optimize the reaction. The result suggested that increasing the reaction temperature did not improve the reaction yield, in contrast, only it decreased the enantiomeric excess of product (Table 2.3, Entries 2~4).

Table 2.3 C-H insertion of dioxalene in different temperature



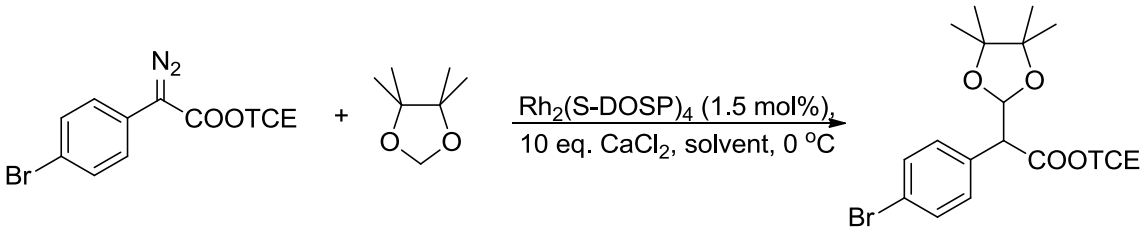
2.6 **2.4** **2.7**

Entry	**2.6:2.4** ratio	temp.	Yield[a] (%)	ee (%)
1	1 : 4	0 °C	10	ND
2	2 : 1	0 °C	66	93
3	2 : 1	25 °C	52	88
4	2 : 1	50 °C	54	83

a. Yield was determined by ^{1}H NMR, using 1,3,5-trimethoxylbenzene as internal standard;

Various solvents were also tested. Using hydrocarbon solvent like hexanes and cyclohexane (Table 2.4, Entries 1, 2), the major side product was C-H insertion into the solvent. Using TFT, however, the desired C-H insertion product was not observed (Table 2.4, Entry 3). It is worth mentioning that when a more polar solvent, DCE, is used, the yield was increased to 77% but the ee was decreased significantly to 28% (Table 2.4, Entry 4). Because the solubility of 2,2,2-Trichloroethyl aryldiazoacetates **2.6** in DMB is relatively low, a large amount of DMB is needed for the reaction, namely, around 40 mL of DMB is needed for 1 mmol scale reaction. This is less practical for total synthesis as DMB is an expensive solvent. Thus, a range of mixed solvents were tested as I hoped by adding a more polar solvent we can reduce the amount of DMB used while not affecting the ee too much. However, none of them could afford decent yield and ee at the same time (Table 2.4, Entries 6~11). Decahydronaphthalene, which is an inert solvent for C-H insertion using diazo methyl ester, was also tested as an alternative solvent for DMB. However, the desired product was observed in only 20% yield, while C-H insertion into decahydronaphthalene was observed as the major side product under reaction condition (Table 2.4, Entry 12).

Table 2.4 C-H insertion of dioxalene in different solvent

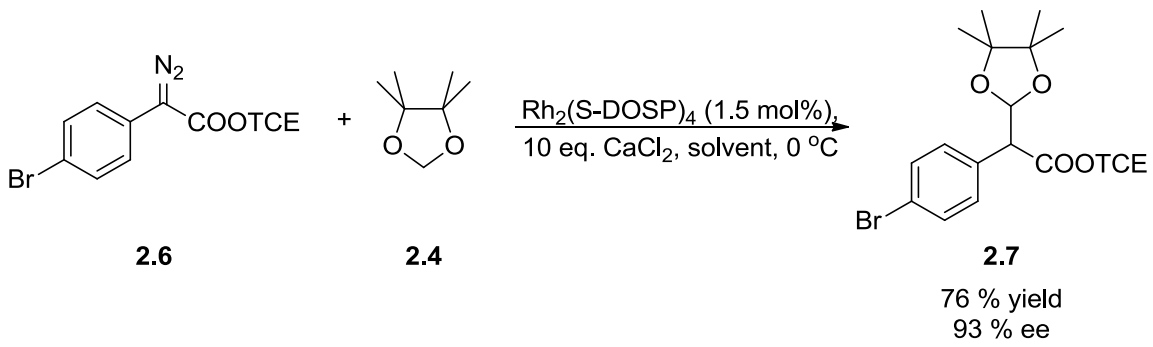


2.6 **2.4** **2.7**

Entry	Solvent	Yield[a] (%)	ee (%)
1	Hexane	< 25[b]	-
2	cyclohexane	< 25[b]	-
3	TFT	Not observed	-
4	DMB	66	93
5	DCE	77	28
6	DMB + DCE (1 : 1)	75	30
7	DMB + DCE (5 : 1)	-	37
8	DMB + DCE (10 : 1)	63	51
9	DMB + TFT (1 : 1)	Not observed	-
10	DMB + TFT (5 : 1)	Not observed	-
11	DMB + TFT (10 : 1)	13	-
12	decahydronaphthalene	< 20[b]	-

a. Yield was determined by 1H NMR, using 1,3,5-trimethoxylbenzene as internal standard;
b. the major is C-H insertion into solvent

As stated before, although 66% yield and 93 % ee is a decent transformation from methodology point of view, the requirement of using large amounts of DMB makes this transformation less practical. Because the C-H bond at C-2 in dioxalene is activated by two heteroatoms, it was hypothesized that the diazo dimer could be avoided if the diazo compound and dioxalene were pre-mixed, which would require less DMB to dissolve all the diazo compound. The result was surprisingly good, as the amount of DMB could be reduced by more than half and the yield of product was increased to 76 % (Scheme 2.8).



2.6 **2.4** **2.7**

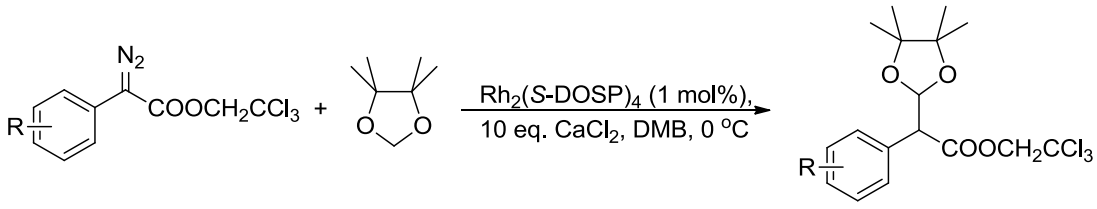
76 % yield
93 % ee

Use non-traditional addition method: $CaCl_2$, diazo were weighted, purged with Ar; dioxalene and DMB were added, cooled to 0 °C, rhodium catalyst was dissolved in DMB, added over 20 min;

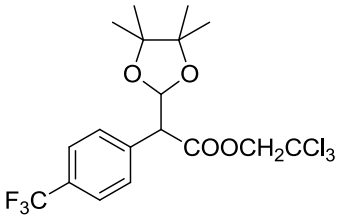
Scheme 2.8 C-H insertion of dioxalene using non-traditional addition method

With the optimized conditions in hand, different diazocompounds were also tested. Most of the *para*-substituents, both electron-donating and electron-withdrawing substitution are tolerated, affording low to good yields and excellent ee (Table 2.5, **2.10**-**2.15**); *meta*-Substitution was also tolerated. 2,2,2-trichloroethyl 2-(3-bromophenyl)-2-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)acetate (**2.16**) was isolated in 45 % yield, 90 %ee. When the substitution is too electro rich, for instance, a methoxyl group, the yield dropped significantly (**2.15**). This compound is the exact compound our collaborator desired for the formal synthesis. With traditional addition method (A), the product was observed in less than 10 % yield. With the new addition method (B), the product was isolated in 25 % yield, 94 % ee. The procedure for making 2,2,2-trichloroethyl *p*-methoxyphenyl-diazoacetate was also modified. Same as making other 2,2,2-trichloroethyl aryldiazoacetates, *o*-NBSA is used as the diazo transfer reagent instead of *p*-ABSA. The major difference is replacing aqueous saturated NH_4Cl work up by a quick silica plug filtration.

Table 2.5 Scope of the C-H insertion of dioxalene with different diazo compounds

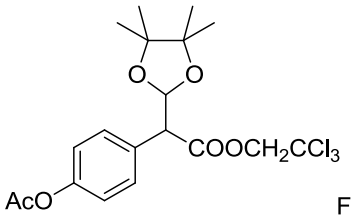


2.8 **2.4** **2.9**



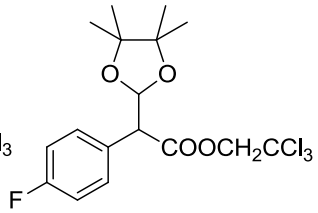
2.10

62 % yield, 87 % ee (A)



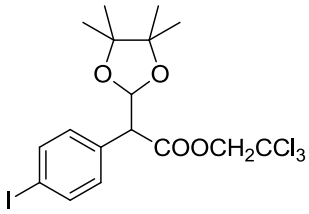
2.11

72 % yield, 93 % ee (A)



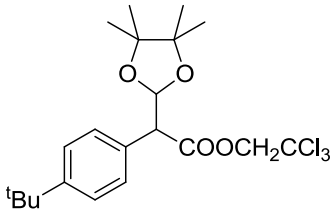
2.12

59 % yield, 92 % ee (A)



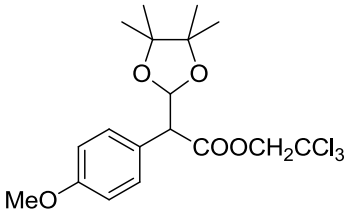
2.13

53 % yield, 88 % ee (A)



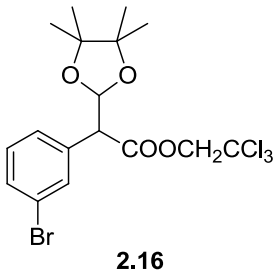
2.14

65 % yield, 88 % ee (A)



2.15

< 10 % yield (A)
25 % yield, 94 % ee (B)



2.16

45 % yield, 90 % ee (A)

A: $CaCl_2$, rhodium catalyst were weighted, purged with Ar; dioxalene and DMB were added, cooled to 0 °C, diazo was dissolved in DMB, added over 2h;
B: $CaCl_2$, diazo were weighted, purged with Ar; dioxalene and DMB were added, cooled to 0 °C, rhodium catalyst was dissolved in DMB, added over 20 min;

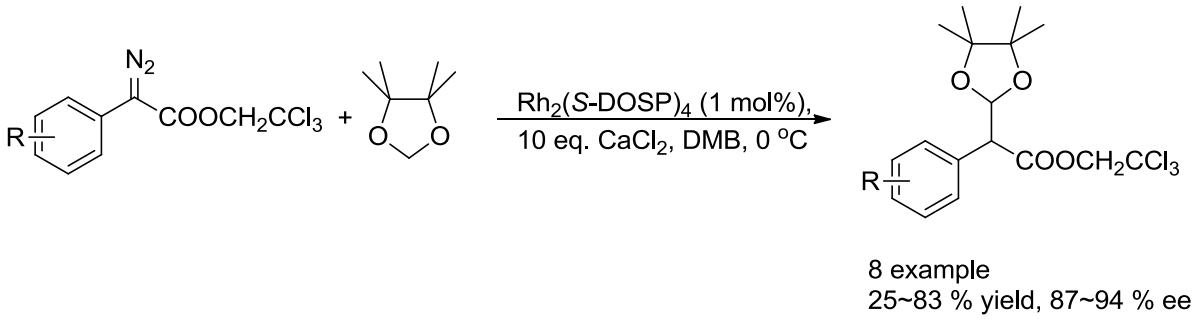
2.3. Future directions

One of the potential problems with this transformation is that the normal method to deprotect acetals might epimerize the enantioenriched product. So the most important thing we needed to do was to find a method to reveal the aldehyde from the acetal without losing the

enantioselectivity of the chiral center. More diazo compounds with different substitution should also be tested to demonstrate the functional group tolerance of this transformation.

2.4. Summary.

After a systematic optimization of catalyst, solvent, reaction temperature, additive, as well as reaction substrates, a C-H insertion of Rh(II)-stabilized carbenoids into acetal was achieved in high enantioselectivity. Eight substrates were tested under optimized condition affording C-H insertion product in 25 - 83% yield, 87 - 94% ee. This reaction can be considered as a surrogate for Claisen condensation.



Scheme 2.9 C-H insertion reaction with dioxalene

Further investigation for deprotection without loss of enatiomeric purity of the chiral center needs to be conducted in the future. This collaborative project showed that the key carbene C-H functionalization step could be achieved. Further studies to apply this methodology to total synthesis are currently under investigation through the NSF Center for Selective C-H Functionalization.

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Chapter 3. Combined C-H Functionalization/Cope Rearrangement Reaction with Triazoles

3.1 Introduction

3.1.1 CHCR reaction

The development of novel and robust methods for catalytic C-H functionalization is a major area of focus for organic chemists and provides new strategies for streamlining the synthesis of natural products and pharmaceutical compounds. There are two major strategies for C-H functionalization. One involves an 'activation' step, in which the transition metal inserts into a C-H bond to form a reactive metal-carbon bond.[1, 2] Alternatively, C-H functionalization can also be achieved by the insertion of a metal carbene into a C-H bond. The Davies group focuses on the latter strategy for C-H stereoselective functionalization.[3,4]

An extensive study has been done in the development of the combined C-H functionalization/ Cope rearrangement (CHCR) reaction which occurs between rhodium stabilized vinylcarbenoid and allylic C-H bonds[5]. Very high levels of asymmetric induction can be achieved with a chiral dirhodiumtetracarboxylate catalyst such as Rh_2(*S*-DOSP)$_4$ or Rh_2(*S*-PTAD)$_4$. This reaction is one of the most stereoselective methods developed for the intermolecular C-H functionalization.[5]

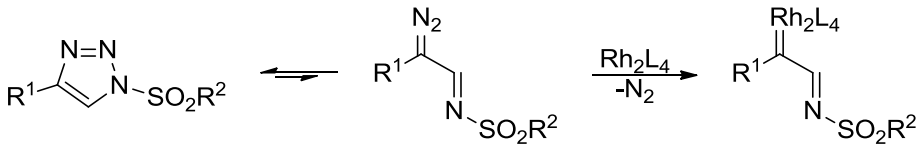
The CHCR reaction also has a broad application in organic synthesis.[5] In collaboration with other groups, the Davies group developed a series of protocols using the CHCR reaction in alternative strategies for some of the classic synthetic strategies including the Michael reaction, the vinylogous Mukaiyama aldol reaction, the tandem Claisen rearrangement/Cope rearrangement, and the tandem aldol reaction/siloxy-Cope rearrangement[5]. Further applications

of CHCR reaction include the total synthesis of several natural products: (-)-colombiasin A, (-)-elisapterosin B, and (+)-elisabrthadione[6]. The key step involved in the combined C-H activation/Cope rearrangement is an enantiodivergent process from a racemic dihydronaphthalene substrate.

In combination with experiments, a detailed computational study was conducted to further understand the mechanism of the CHCR reactions[7]. The study demonstrated that the reaction proceeds through a concerted, but highly asynchronous, hydride-transfer/C-C bond-forming process. The initial hydride transfer event led to the formation of a charged transition state, which could then bifurcate to the CHCR product or direct C-H insertion product.

3.1.2 Using triazole as a mask of donor/acceptor carbenoid

A variety of useful synthetic transformations have been developed with metal-stabilized carbenoids which are generated from the metal-catalyzed decomposition of diazo compounds[8]. More recently, 1,2,3-triazoles bearing a strong electron-withdrawing group at *N*-1 position, which are capable of undergoing a 'ring-to-chain isomerization' to expose diazo moiety, have shown to act as masked diazo compounds.[9, 10] In the presence of a dirhodium tetracarboxylate catalyst, the metal stabilized donor/acceptor carbenoid intermediate was generated from the α-diazo imine which is isomerized from *N*-sulfonyl-1,2,3-triazoles. A number of groups have demonstrated the application of *N*-sulfonyltriazoles as viable precursors in both classic and novel rhodium carbenoid reactivities.[11]

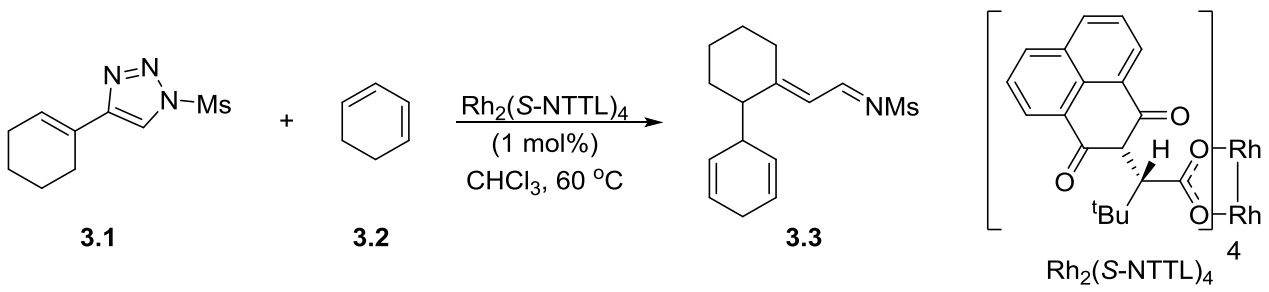


Scheme 3.1 triazole rearrangements/ring-chain isomerization

We have been interested in using 1,2,3-triazoles to expand the scope of donor groups that can be incorporated into donor/acceptor carbenes within the Davies group. To this end, the Davies reported that 4-amido-1-sulfonyl-1,2,3-triazoles can be used to introduce a *N*-phthalimido acceptor group, which enabled an expedited synthesis of cyclopropyl amino acids. The Davies group also described series of transformations using *N*-sulfonyltriazoles as carbenoid precursors, for instance, formal [4+3] with diene[12], formal [3+2] with indole[13], formation of trisubstituted pyrrole[14] and formation of 2,3-fused pyrroles and indoles [15].

In 2011, Fokin described an enantioselective C-H insertion reaction into unactivated alkanes with rhodium(II) stabilized imino-carbenoids in good yields and high enantioselectivities (Scheme 2).[16] In this reaction, both electron-withdrawing and electron-donating aryl group were tolerated on the triazole functionality and both aryl and alkyl substitution on the sulfonyl group were tolerated.

During the study of formal [4+3] cycloadditions conducted by former group member Dr. Brendan T. Parr, a CHCR product was observed. The ratio of the CHCR product to formal [4+3] cycloaddition product is roughly 5:1. The CHCR product was observed as a single diastereoisomer and with 99 % ee. Based on this result, we decided to conduct a systematic study of this transformation using *N*-sulfonyl-1,2,3-triazoles.



Scheme 3.2 CHCR with triazole and 1,3-cyclohexadiene

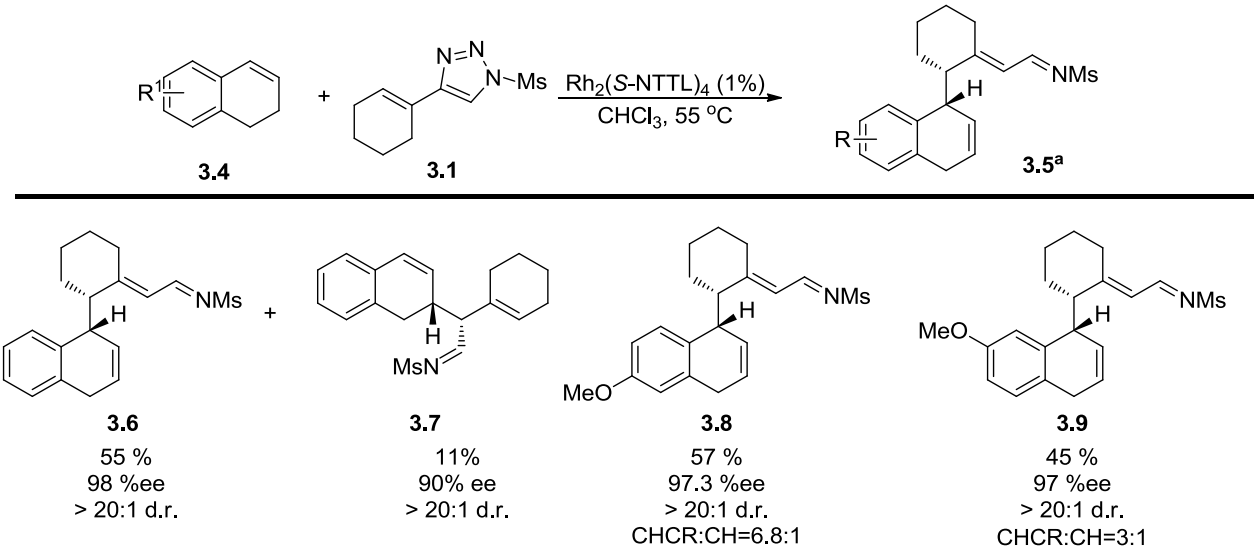
3.2. Result and discussion.

The initial studies of CHCR reaction using *N*-sulfonyl-1,2,3-triazoles were quite unsuccessful. The use of simple cyclic alkenes, which are perfect substrates for CHCR reactions of diazo chemistry,[17, 18] did not work well with triazoles. Using cyclohexene as trapping reagent afforded only cyclopropanation product. Using 1-methyl-cyclohexene, intramolecular cyclization of *N*-methylsulfonyl-4-cyclohexenyl-1,2,3-triazole forming 4,5,6,7-tetrahydroindole[13] was observed as major product. When using 1-acetoyxl-cyclohexene or 6-methyl-3,4-dihydro-2H-pyran-2-one as trapping reagent, a complex mixture was observed and therefore, no meaningful product was identified.

As a result, the study was extended to dihydronaphthalene derivatives, which are excellent substrates for CHCR reactions with styryldiazoacetate.[18] The results are summarized in table 3.1. The reaction of *N*-methylsulfonyl-4-cyclohexenyl-1,2,3-triazole **3.1** with 1,2-dihydronaphthalene formed the CHCR and the direct C-H insertion product in roughly 5:1 ratio. CHCR product **3.6** was isolated in 55% yield, over 20:1 d.r., 98 % ee. The direct C-H insertion reaction was also isolated in 11% yield, over 20:1 d.r., 90% ee. Intramolecular cyclization of *N*-

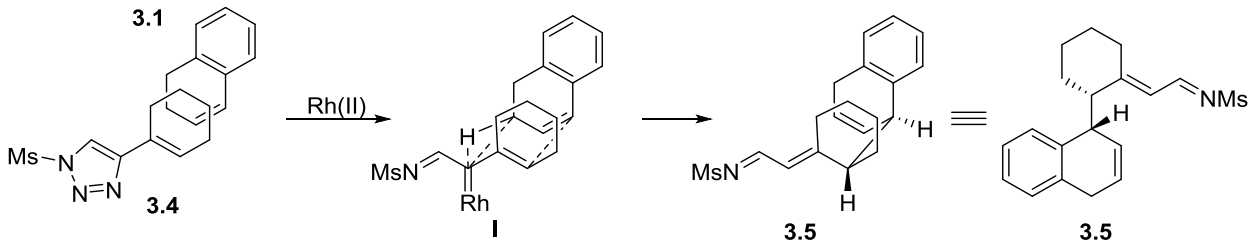
methylsulfonyl-4-cyclohexenyl-1,2,3-triazole was also observed as the major side product. In the reaction with 7-methoxy-1,2-dihydronaphthalene , CHCR product **3.8** and direct C-H insertion product were observed in 6.8:1 ratio. CHCR product **3.8** was isolated as the major product in 57% yield, over 20:1 d.r., 97% ee. Similarly, the reaction with 6-methoxy-1,2-dihydronaphthalene also afforded CHCR product **3.9** as the major product, which was isolated in 45% yield, over 20:1 d.r., 97 % ee. The ratio of CHCR to direct C-H and cyclopropanation was roughly 3:1.

Table 3.1 CHCR reaction of triazoles and dihydronaphthalenes derivatives



a. The relative stereo chemistry is assigned based on analogy of CHCR with styrenyldiazoacetate, the absolute stereo chemistry has not determined.

A possible mechanism of this transformation is shown in Scheme 3, under the presence of the dirhodium catalyst, the triazole substrate underwent a 'chain-ring isomerization', followed by generation the stabilized imino-carbenoid intermediate. The rest of the mechanism is similar with the CHCR using styrenyldiazoacetate; a C-H insertion event was initiated, which was then interrupted by a cope rearrangement, forming the desired CHCR final product.

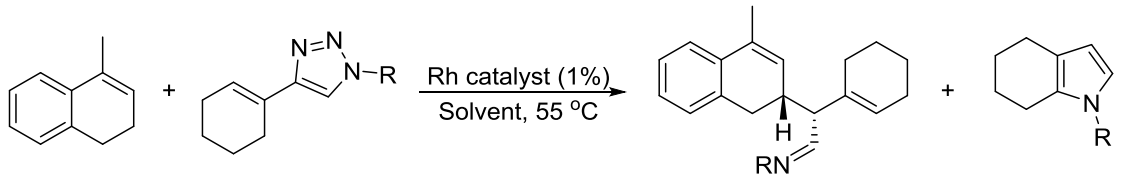


Scheme 3.3 Possible mechanism of CHCR reaction with triazoles

Because direct C-H insertion product was observed for most of the 1,2-dihydronaphthalene substrates as the major side product for CHCR, we wanted to know if we could obtain exclusively direct C-H insertion product by preventing the sequential Cope rearrangement. As expected, direct C-H insertion product **3.13** was observed as well as CHCR product was completely excluded for the reaction with 4-methyl-1,2-dihydronaphthalene **3.10**, simply after introducing a methyl group at the 4-position of 1,2-dihydronaphthalene (table 3.2). A quick optimization was carried out, and results are summarized in table 4.2. Some common solvents that have been utilized for triazole chemistry, such as toluene, DCE, chloroform, were tested (Entries 1-3). The result clearly suggest that increasing the polarity of solvent decreases the formation of the undesired side product tetrahydroindole **3.13** as well as increases the yield of C-H insertion product **3.12**. A short list of chiral rhodium catalysts that are compatible with triazole chemistry were tested (Entry 3-5). Using Rh_2(*S*-NTTL)$_4$ as catalyst, the C-H insertion product **3.12** was observed in 80 % yield, 91.5 % ee (Entry 3), while using Rh_2(*S*-PTAD)$_4$ or Rh_2(*S*-PTTL)$_4$ as the catalyst, C-H insertion product **3.12** was observed in 27% yield, 82.5 % ee (Entry 4) or 32 % yield, 86 % ee (Entry 5), respectively. The choice of *N*-sulfonyl group affected the result significantly. Using *N*-Ts-triazole (Entry 6) instead of *N*-Ms-triazole(Entry 3) resulted in a decrease of C-H insertion product **3.12** to 30 % yield as well as increase of **3.13** to 51 % yield. The result is also consistent with the observation in the 2,3-fused pyrrole study.[13] In that study,

the authors pointed out that using *N*-Ts-triazole afforded the tetrahydroindole in better yield that using *N*-Ms-triazole. With these studies as a guide, the optimal conditions employing Rh_2(S-NTTL)$_4$ as the catalyst and chloroform as the solvent were developed.

Table 3.2 C-H insertion reaction with 4-methly-1,2-dihydronaphthalene and triazoles



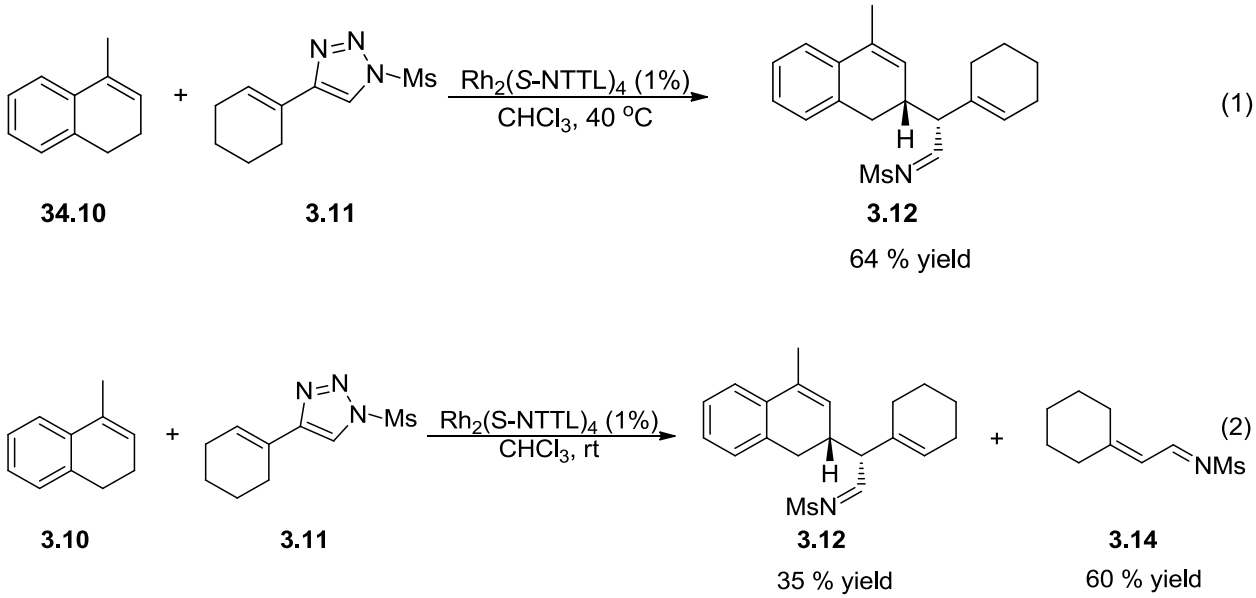
3.10 **3.11** **3.12**[a] **3.13**

Entry	R	Rh catalyst	Solvent	Yield of **3.12** (%)[b]	ee(%)	Yield of **3.13** (%)[c]
1	Ms	Rh_2(*S*-NTTL)$_4$	Toluene	52 (36)	89.5	20 (19)
2	Ms	Rh_2(*S*-NTTL)$_4$	DCE	74	87.4	< 5%
3	Ms	Rh_2(*S*-NTTL)$_4$	$CHCl_3$	80 (73)	91.5	< 5%
4	Ms	Rh_2(*S*-PTAD)$_4$	$CHCl_3$	27	82.5	21
5	Ms	Rh_2(*S*-PTTL)$_4$	$CHCl_3$	32	86	23
6	Ts	Rh_2(*S*-NTTL)$_4$	$CHCl_3$	30	ND	51

a. The relative stereo chemistry is assigned based on analogy of CHCR with styrenyldiazoacetate, the absolute stereo chemistry has not determined;
b. yield was determined by ^{1}H-NMR using CH_2Br_2 as internal standard. Isolated yield shown in parenthesis.
c. yield was determined by ^{1}H-NMR using CH_2Br_2 as internal standard. Isolated yield shown in parenthesis.

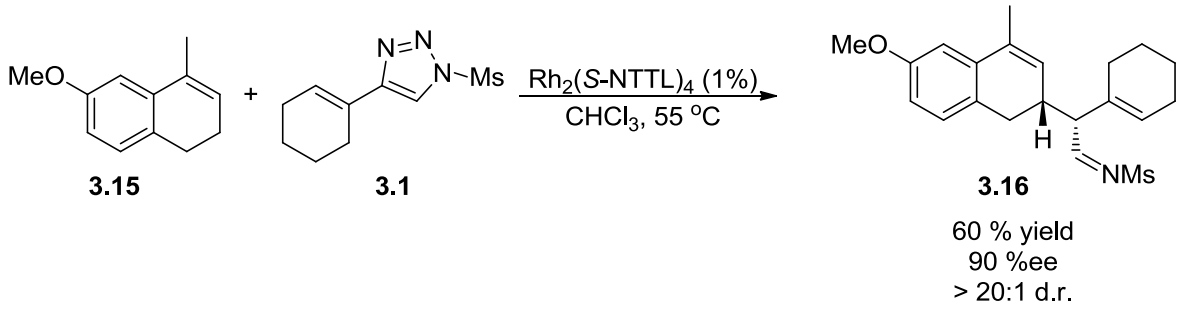
In the study of intramolecular cyclization of tiazoles,[13] the authors also point out that lowering the reaction temperature can also prevent the formation of such product. Although under the optimal conditions the side product **3.13** was observed in very low yield. As it is the only side product observed, tests were conducted to determine if decreasing the reaction temperature can further enhance the yield of the desired transformation. However, when reducing the reaction temperature to 40 °C, although tetrahydroindole was not observed, the yield of direct C-H insertion product was reduced to 64% (Scheme 3.4, (1)). If the reaction temperature is further

reduced to room temperature, the yield was further decreased. *N*-(2-cyclohexylideneethylidene)methanesulfonamide **3.14** was observed as the major product (Scheme 3.4, (2)). Presumably, this is the product formed by fully hydride transfer from the 4-methyl-1,2-dihydranaphthalene.



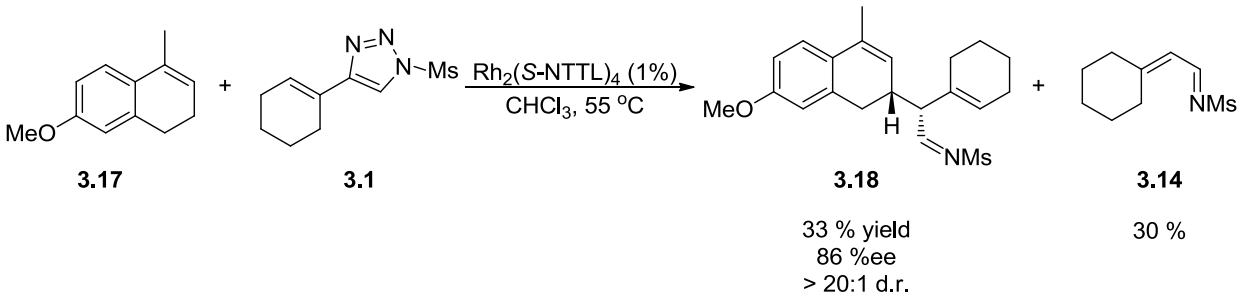
Scheme 3.4 Reaction of triazoles and dihydronaphthalene at different temperatures

With the optimal conditions in hand, different substrates were tested using 6-methoxy-4-methyl-1,2-dihydronaphthalene **3.15** as a trap, the desired C-H insertion product **3.16** was isolated in 60% yield, greater than 20:1 d.r. and 90% ee (Scheme 3.5).



Scheme 3.5 C-H insertion reaction of 6-methoxy-4-methyl-1,2-dihydronaphthalene

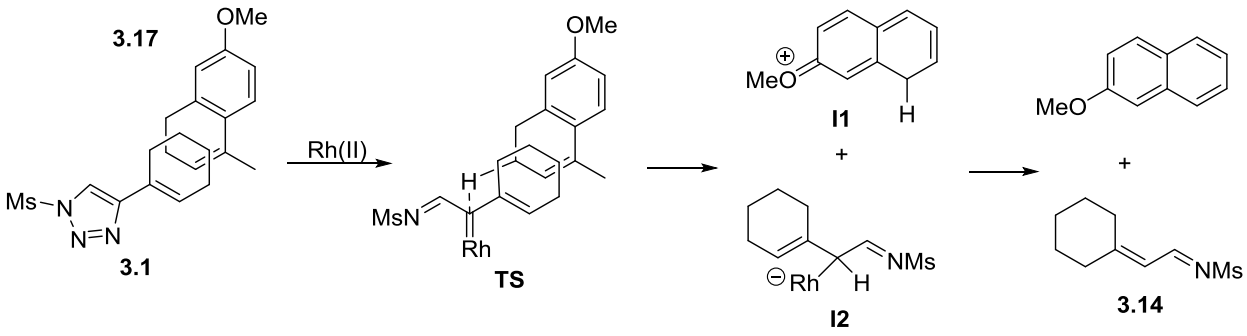
In contrast, using 7-methoxy-4-methyl-1,2-dihydronaphthalene **3.17** as a trap, the desired C-H insertion product **3.18** was only isolated in 23 % yield, greater than 20:1 d.r. and 86 % ee. *N*-(2-cyclohexylideneethylidene)methanesulfonamide **3.14** was isolated in 30% yield as the major side product (Scheme 3.6).



Scheme 3.6 C-H insertion reaction of 7-methoxy-4-methyl-1,2-dihydronaphthalene

In this reaction, 2-methyoxyl-naphthalene was also isolated as the byproduct. A possible mechanism is shown in Scheme 3.7. In the presence of the dirhodium catalyst, the triazole substrate underwent a 'chain-ring isomerization', followed by N_2 exclusion to generate the stabilized imino-carbenoid intermediate **TS**. When 7-methoxy-4-methyl-1,2-dihydronaphthalene **3.18** approaches the rhodium carbenoid, The C-H insertion was initiated. However, instead of being interrupted by the Cope rearrangement as a normal CHCR reaction does, a full hydride transfer event occurred, presumably because the electron rich 7-methoxy-4-methyl-1,2-dihydronaphthalene **3.18** helped stabilized the cation **I1** that is formed. In the end, a proton transfer formed the final product **3.14**. Similar transformations were also observed with other

electron-rich traps like 4-methoxy-1,2-dihydronaphthalene or 4-siloxy-1,2-dihydronaphthalene.



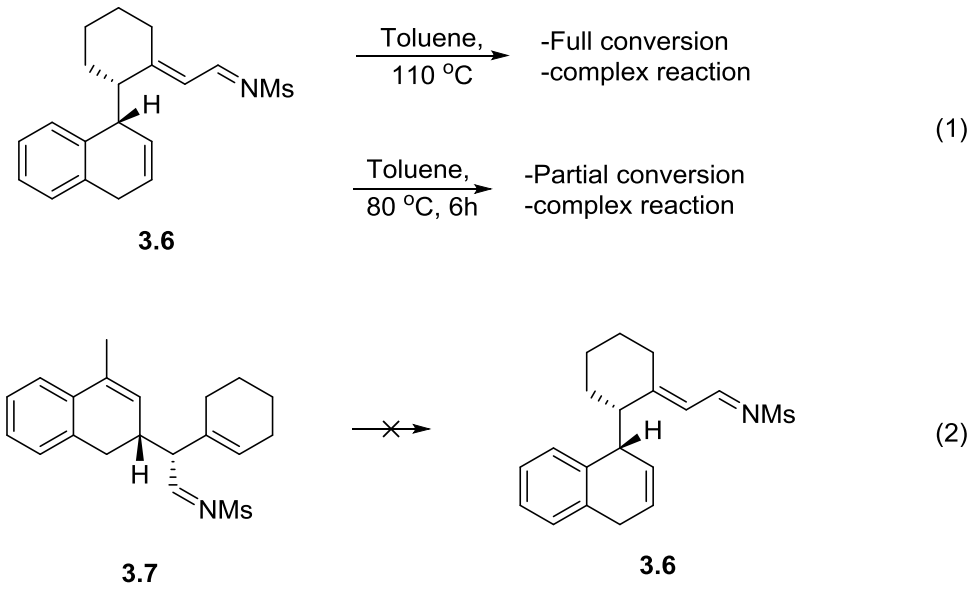
Scheme 3.7 Possible mechanism for formation of the α,β-unsaturated imine

In the CHCR of diazo compounds, the formal C-H insertion product could be generated from the CHCR product by a Cope rearrangement. This rearrangement explains why the formal C-H insertion product was formed in high d.r.[17]

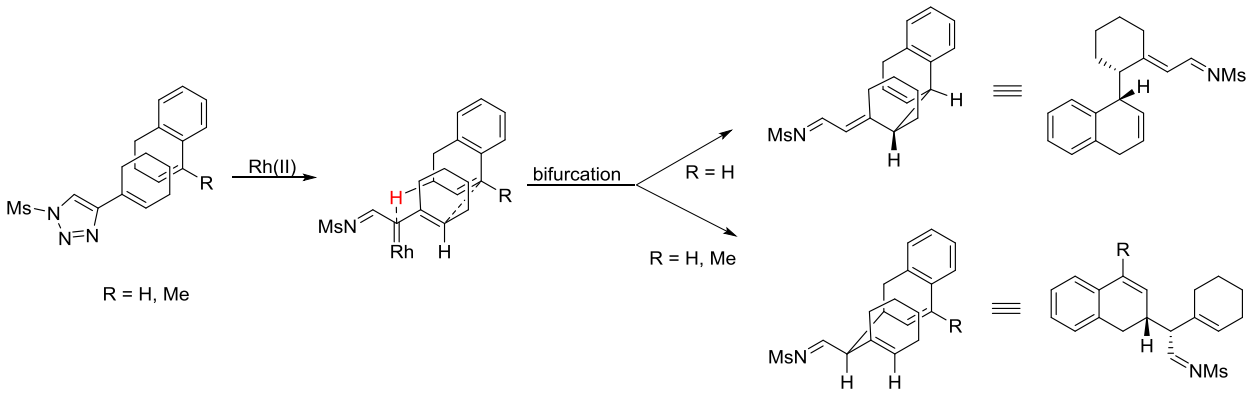
Based on previous experience of CHCR in diazo chemistry, initially we thought the C-H insertion product **3.8** was formed though rearrangement of the CHCR product **3.7**. In order to demonstrate whether *N*-(2-(cyclohex-1-en-1-yl)-2-(1,2-dihydronaphthalen-2-yl)ethylidene)-methanesulfonamide was a direct C-H insertion product or a C-H insertion Cope rearrangement followed by a retro Cope rearrangement, control experiments were carried out. First, the reaction was monitored by ^{1}H NMR at different time points, 1h, 2h, 4h, 8h, 24h. It was found the ratio of **3.6**: **3.7** was always 5:1 (Scheme 3.8). Secondly, *N*-((E)-2-(2-(1,4-dihydronaphthalen-1-yl)cyclohexylidene)ethylidene)methanesulfonamide **3.6** was isolated and heated at elevated temperature (Scheme 3.9, (1)). It does not convert to *N*-(2-(cyclohex-1-en-1-yl)-2-(1,2-dihydronaphthalen-2-yl)ethylidene)methanesulfonamide **3.7**. Also, C-H insertion product **3.**7 could not be converted to CHCR product **3.6** (Scheme 3.9 (2)). These results suggested that the C-H insertion product is not generated by the C-H insertion Cope

rearrangement followed by a retro Cope rearrangement. This is consistent with the computational study of diazo chemistry,[7] which suggested that the initial hydride transfer event formed a charged transition state, which could then bifurcate to the CHCR product or direct C-H insertion product. A revised possible mechanism is shown on scheme 3.10.

Scheme 3.8 Reaction of 1,2-dihyrdonaphthalene and triazole



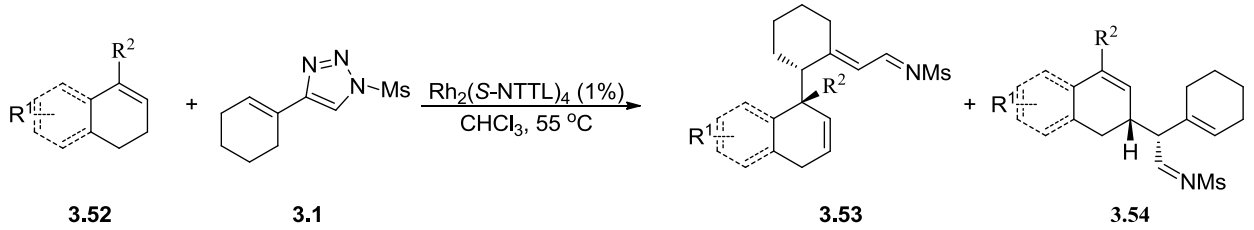
Scheme 3.9 Control reaction



Scheme 3.10 Possible mechanism for CHCR and C-H insertion of triazoles with dihydronaphthalene

3.3. Summary

Based on the initial report of rhodium-catalyzed CHCR with triazoles and cyclohexadiene discovered by Dr. Brendan T. Parr, the reaction of CHCR and C-H insertion with triazoles and dihydronaphthalene was established. Only a limited number of substrates were able to undergo this transformation. To further explore this transformation, additional dihydronaphthalene derivatives need to be tested. Also, different vinyl triazoles need to be explored to broaden the scope of this chemistry.



Scheme 3.11 Rhodium-catalyzed CHCR and C-H insertion with triazole

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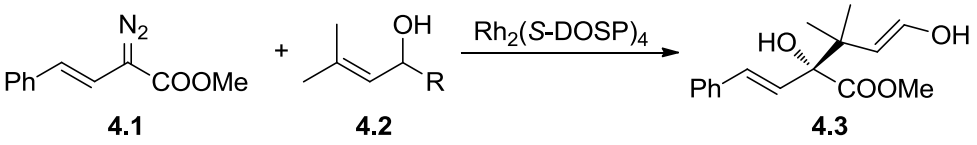
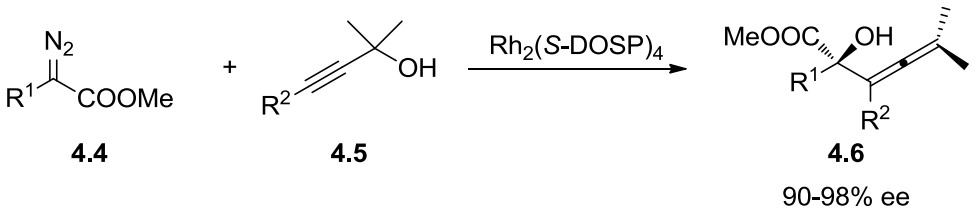
Chapter 4. Asymmetric transformations of propargyl alcohols with donor/acceptor-substituted carbenoids.

4.1 Introduction

The reaction of metal carbenoids with alcohols affording the O-H insertion products has been extensively studied over the past several decades.[1] Recently, Davies and Li reported a transformation involving rhodium carbenoids and allylic alcohols affording α–hydroxycarboxylate derivatives in high enantioselectivity *via* tandem ylide formation/2,3–sigmatropic rearrangement (Scheme 4.1).[2] This reaction is also compatible for propargyl alcohols affording allenic alcohols in high enantioselectivity (Scheme 4.2).[3] In Dr. Zhanjie Li's study, he found that primary and secondary propargyl alcohols, as well as propargyl alcohols with terminal alkynes are less effective. DFT calculations demonstrated that without the two methyl substituent, a significant energy barrier would prevent the formation of the desired2,3-rearrangement product, thus the O-H insertion product would be favored. As our group is interested in expanding the scope of enantioselective gold-catalyzed carbenoid reactions we began to explore whether a similar transformation could be achieved by using gold catalysts.

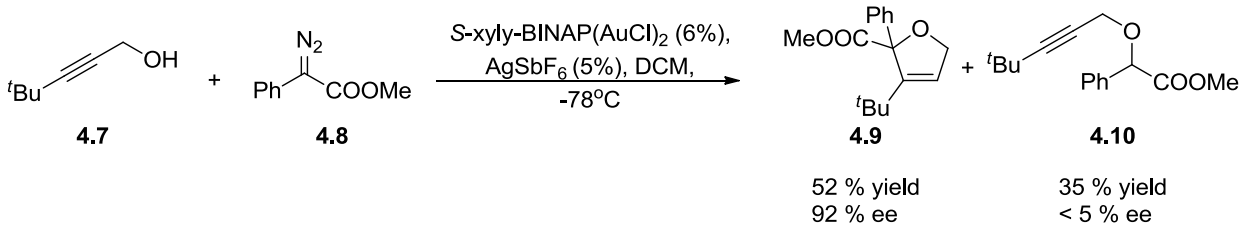


Scheme 4.1 Rhodium-catalyzed tandem ylide formation/[2,3] rearrangement



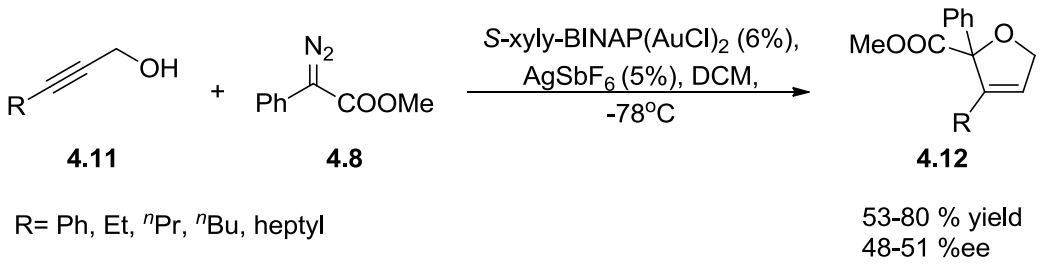
Scheme 4.2 Rhodium-catalyzed tandem ylide formation/[2,3] rearrangement with propargyl alcohols

A promising initial result was reported by Dr. John Frederick Briones.[14] When he treated 4,4-dimethyl-2-pentyn-1-ol with phenyldiazoacetate under Au/Ag catalysis, an unexpected 2,5-dihydrofuran product was formed with high enantioselectivity as the major product, along with the undesired O-H insertion product. This dihydrofuran derivative was envisioned as arising from allenyl carbinol cycloisomerization.



Scheme 4.3 Au/Ag catalyzed formation of dihydrofuran with 3-^{t}Bu-propargyl alcohol

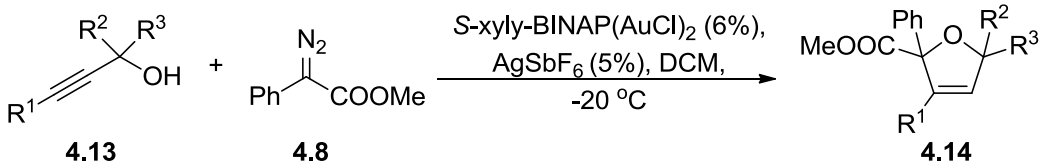
Further studies of the scope of the reaction were conducted using 3-substituded propargyl alcohols. However, only moderate enantioselectivity was achieved using either phenyl or linear alkyl substituents. The O-H insertion product was also formed as a major side product.

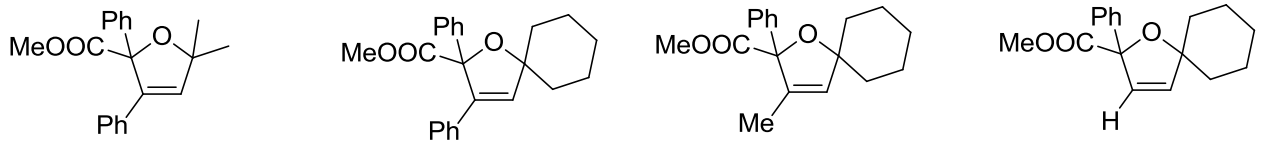


Scheme 4.4 Au/Ag catalyzed formation of dihydrofuran with primary propargyl alcohol

Dr. John Frederick Briones also reported that good-to-excellent levels of enantioselectivity were obtained with tertiary propargylic alcohols (**Table 4.1**).

Table 4.1 Au catalyzed reaction with tertiary propargylic alcohols





4.15	4.16	4.17	4.18
73 % yield 90 % ee	85 % yield 92 % ee	69 % yield 91 % ee	71 % yield 83 % ee

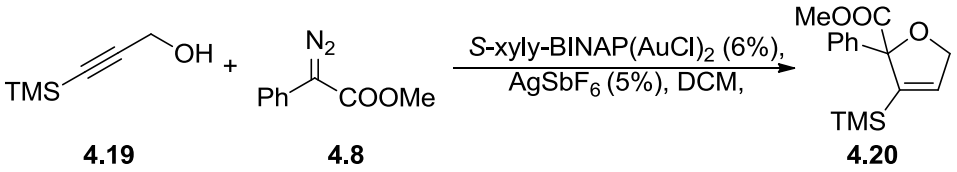
In summary, Dr. John Frederick Briones reported promising initial results that demonstrated a highly enantioselective dihydrofuran derivative could be formed, catalyzed by Au/Ag *via* tandem ylide formation/2,3-sigmatropic rearrangement/cycloisomerizaion. This opened up a great opportunity for Au/Ag catalysts as an important complement for rhodium catalysis. However, there are more aspects to explore about this transformation. A detailed optimization of reaction conditions was required to demonstrate whether we can further improve the enantioselectivity of

this reaction. In addition, the scope and limitations of the reaction has not been fully understood. Thirdly, the structure of the active catalyst was not clear.

4.2 Results and Discussion

With these initial results, we began the study with the optimization of reaction conditions. First, the effect of reaction temperature was tested. By using 3-(trimethylsilyl)-2-propyn-1-ol with methyl phenyldiazoacetate as a model reaction, we found that lowering the reaction temperature resulted in an increase of enantioselectivity, as well as minimal the formation of the undesired side product.

Table 4.2 Reaction of 3-(trimethylsilyl)-2-propyn-1-ol with methyl phenyldiazoacetate in different temperature



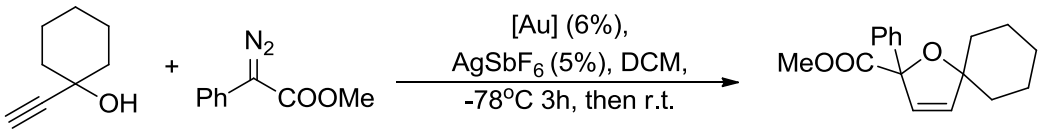
4.19 **4.8** **4.20**

Temperature (°C)	Yield[a] (%)	ee (%)
r.t.	22	82
0	30	89
-78 3h, then r.t.	52	90

a. Yield was determined by ^{1}H NMR using trichloroethylene as internal standard

Other digold complexes were also examined. We tested three BINAP derivatives and the results showed that *S*-xylyl-BINAP(AuCl)$_2$ provided superior levels of enantioselectivity. This probably is due to xylyl-BINAP being the most sterically hindered catalyst in this group.

Table 4.3 Reaction of 1-ethynylcyclohexanol with methyl phenyldiazoacetate



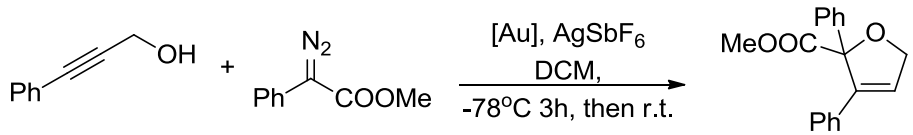
4.19 **4.8** **4.18**

Entry	[Au]	Yield[a] (%)	ee (%)
1	*S*-Ph-BINAP(AuCl)$_2$	47	69
2	*S*-tol-BINAP(AuCl)$_2$	43	73
3	*S*-xyly-BINAP(AuCl)$_2$	68	80

a. Yield was determined by ^{1}H NMR using trichloroethylene as internal standard

Using 3-phenyl-2-propyn-1-ol and methyl phenyldiazaoacetate as a model reaction we also found that (*R*)-SegPhos(AuCl)$_2$ was less effective as a catalyst for this reaction. Decreasing the catalyst loading again resulted in reduced enantioselectivity.

Table 4.4 Reaction of 3-phenyl-2-propyn-1-ol with methyl phenyldiazoacetate



4.20 **4.8** **4.21**

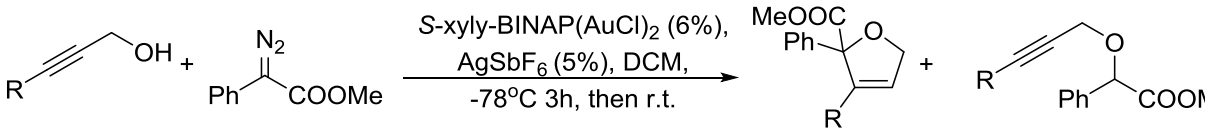
Entry	[Au]	Amount of $AgSbF_6$	Yield[a] (%)	ee (%)
1	*R*-DTBM-SegPhos(AuCl)$_2$(2 %)	1.5 mol%	36	15
2	*S*-xyly-BINAP(AuCl)$_2$(2 %)	1.5 mol%	52	40
3	*S*-xyly-BINAP(AuCl)$_2$(6 %)	5 mol%	57	50

a. Yield was determined by ^{1}H NMR using trichloroethylene as internal standard

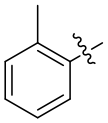
A further scope study was conducted using 3-substituded propargylic alcohols. Simply using 3-(2-methyl-phenyl)-propargyl alcohol, instead of 3-phenyl-propargyl alcohol, the ee of

dihydrofuran product is increased to 66 % (Table 4.5, entries 1-2). This result clearly suggested that the increase in steric demand of the 3-substituded propargyl alcohol could increase the enantioselectivity. We further tested *tert*-butyl (entry 2) and sterically hindered silyl-substituted propargyl alcohols, and all of these afforded the dihydrofuran product with high enantioselectivity (entries 3-6). For all these reactions, the O-H insertion products were still a major side product. A detailed reaction condition study is needed to minimize the undesired O-H insertion reaction. At this point, we are not certain of the structure of the catalyst. Knowing the structure of the active catalyst as well as carbenoid structures would help us to further understand of this reaction and develop a model for asymmetric induction.

Table 4.5 Au-catalyzed reaction with primary propargylic alcohols

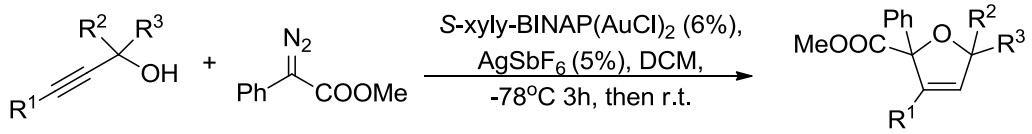


4.11 **4.8** **4.12** **4.22**

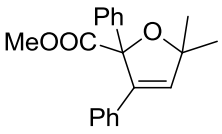
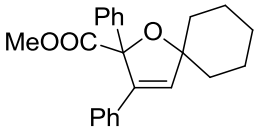
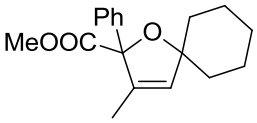
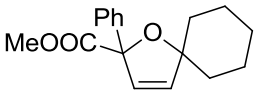
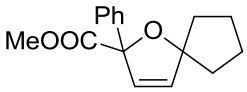
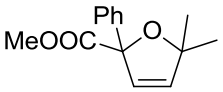
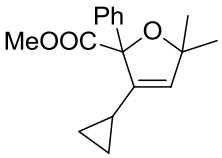
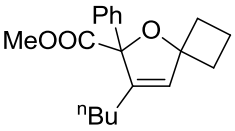
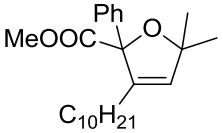
Entry	R	Yield of **4.12**[a] (%)	ee of **4.12** (%)	Yield of **4.22**[b] (%)	ee of **4.22** (%)
1	Ph	56	50	21	<5
2		69	66	14	<5
3	TMS	52	90	16	<5
4	^{t}Bu	59	91	14	<5
5		57	93	23	<5
6	TBS	45	99	42	<5

The reaction was applied to a range of tertiary propargylic alcohols as illustrated in Table 4.6, affording dihydrofurans in moderate-to-excellent enantioselectivity. Only the desired dihydrofuran products were formed and O-H insertion products were minimal in these cases. Both the internal and terminal alkynes were compatible with this reaction and afforded the dihydrofuran products in good enantioselectivity. Generally, 1,1-dimethyl propargyl alcohols afforded products in low yield. Interestingly, the reaction with 1-(1-hexyn-1-yl)cyclobutanol only afforded dihydrofuran product in 55% ee. This is probably due to minimal steric demand of the cyclobutyl moiety.

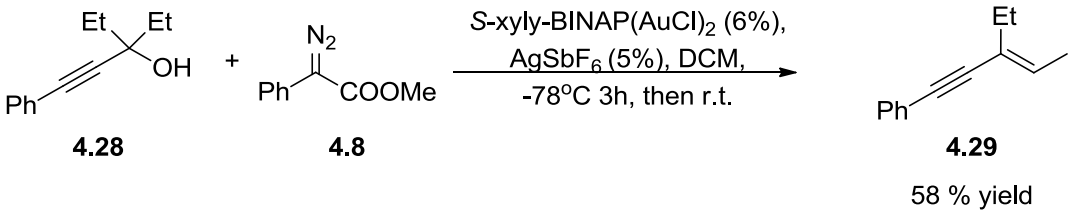
Table 4.6 Au-catalyzed reaction with tertiary propargylic alcohols



4.13 **4.8** **4.14**

		
4.15	**4.16**	**4.17**
28% 85% ee	81 % 88 % ee	83 % 87 % ee
		
4.18	**4.23**	**4.24**
68 % 80 % ee	61 % 75 % ee	39 % 82 % ee
		
4.25	**4.26**	**4.27**
21% 76 % ee	83% 55% ee	17% 81 % ee

Upon treatment with 1,1-diethyl propargyl alcohol with phenyldiazoacetate under the standard reaction conditions, the major product was the elimination product of the alcohol. The dihydrofuran or O-H insertion products were not observed.

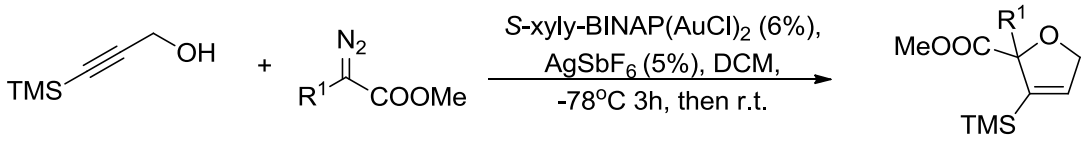


Scheme 4.5 Reaction with 1,1-diethyl propargyl alcohol

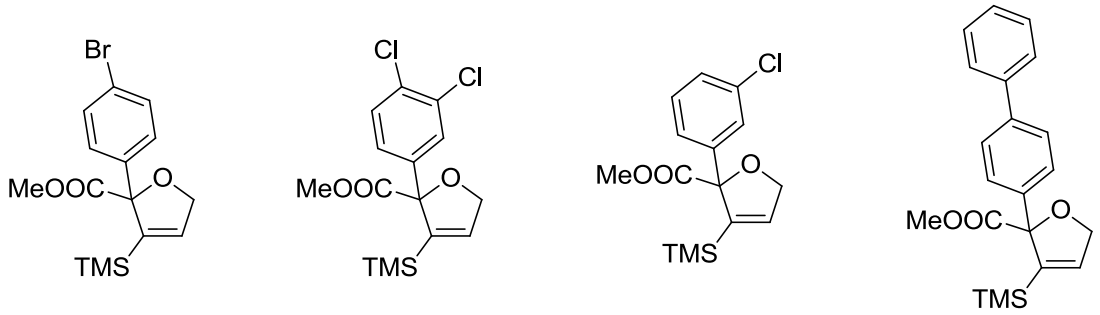
When the 3-substituent on the tertiary propargylic alcohol was a bulky group, such as *t*-butyl, the desired dihydrofuran product was not observed; instead, only O-H insertion product was obtained. This probably due to having steric hinderance on both the 1 and 3 positions of the propargylic alcohol, it is too sterically crowded for the 2,3-rearrangement transition state thus preventing the rearrangement from occuring at a decent rate.

This reaction can also be extended to a series of aryl diazo compounds. Electron withdrawing substituents, such as 4-Br-, 3-Cl and 3,4-dicholoro- were tolerated (Table 4.7). The diazo compound with an electron neutral substituent, methyl 2-([1,1'-biphenyl]-4-yl)-2-diazoacetate, afforded the product with high enantioselectivity.

Table 4.7 Au-catalyzed reaction with different diazo compounds

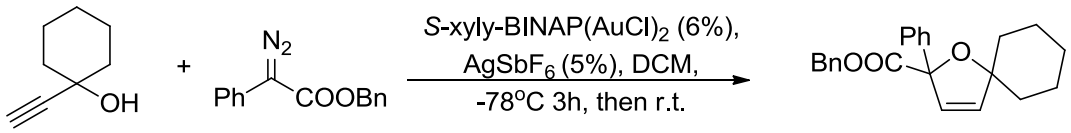


4.19 **4.4** **4.30**



4.31	**4.32**	**4.33**	**4.34**
65%	56%	65%	61%
94 %ee	86%ee	92%ee	92%ee

When benzyl phenyldiazoacetate was used to treat with 1-ethynylcyclohexanol instead of a methyl ester, the ee decreased to 74% (Scheme 2.7). This suggested that the steric bulk on the ester has a negative effect on the enantioselectivity.



4.19 **4.35** **4.36**

73%
74%ee

Scheme 4.6 Reaction with benzyl phenyldiazoacetate

4.3 Summary

We have discovered an asymmetric transformation of propargylic alcohols with donor/acceptor-substituted carbenoids affording 2,5-dihydrofuran derivatives *via* tandem ylide formation/[2,3]-

sigmatropic rearrangement/cycloisomerization using *S*-xyly-BINAP$(AuCl)_2$ and $AgSbF_6$ as catalysts. Depending on the structure of the propargylic alcohols, 2,5-dihydrofuran derivatives can be formed *via* tandem ylide formation/2,3-sigmatropic rearrangement/cycloisomerization in moderate-to-excellent level of enantioselectivity and moderate-to-high yield. The reaction of methyl aryldiazoacetate with 3-bulky-substituented propargylic alcohol proceeded in excellent enantioselectivity and moderate yield. Tertiary propargylic alcohols reacted to yield the productds in moderate-to-high yield and levels of enantioselectivity. Increasing the steric demand on the 3-substituent of the tertiary propargylic alcohol resulted in a shutdown of /2,3-sigmatropic rearrangement reactivity and afforded only O-H insertion product.

References

1. Doyle, M. P.; McKervey, M. A.; Ye, T., *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*. Wiley: 1998.

2. (a) Li, Z.; Parr, B. T.; Davies, H. M. L., *J. Am. Chem. Soc.* **2012,** *134* (26), 10942; (b) Li, Z.; Davies, H. M. L., *J. Am. Chem. Soc.* **2009,** *132* (1), 396.

3. Li, Z.; Boyarskikh, V.; Hansen, J. H.; Autschbach, J.; Musaev, D. G.; Davies, H. M. L., *J. Am. Chem. Soc.* **2012,** *134* (37), 15497.

Experimental Section

General Methods:

^{1}H Nuclear Magnetic Resonance (^{1}H-NMR) and ^{13}C Nuclear Magnetic Resonance (^{13}C-NMR) spectra were recorded on Varian INOVA 400, VNMR 400, INOVA 600 and UNITY 600 MHz. NMR spectra were recorded in deuterated chloroform ($CDCl_3$) at room temperature unless otherwise stated. The NMR data were presented as follows: chemical shift in ppm with tetramethylsilane (TMS, δ = 0.00 ppm) for 1H-NMR and the residual of chloroform (δ = 77.0 ppm) for 13C-NMR as internal standards, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; br. = broad), coupling constant (J/Hz), integration. IR spectra were collected on a Nicolet iS10 from Thermo Scientific and reported in unit of cm-1. Mass spectra were recorded on a Finnigan LTQ FTMS mass spectrometer. Optical rotations were measured on a Jasco P-2000 polarimeter (concentration in g/100mL). Melting points were measured on a MEL-TEMP of Electrothermal (uncorrected). All reactions were performed under argon atmosphere in oven or flame dried glassware. Acetonitrile, dichloromethane and *n*-pentane were dried by a solvent purification system (passed through activated alumina columns). Analytical TLC was performed on silica gel plates using UV light or phosphomolybdic acid (PMA) stain. Flash column chromatography was performed on silica gel 60Å (230-400 mesh) from Sorbent Technologies. Unless otherwise noted, all other chemical reagents were obtained from commercial sources and used as received. Rh_2(*S*-PTTL)$_4$ was prepared via literature procedure.

Experimental Section for Chapter 2: Asymmetric C-H insertion of Rh(II) stabilized carbenoids into acetals: a surrogate for the Claisen condensation

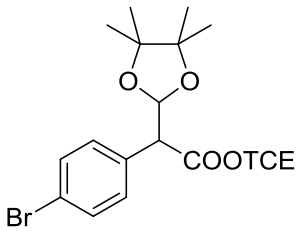
I. General procedure for C-H insertion into dioxalene.

Rh_2(*S*-DOSP)$_4$ (1 mol%), 222 mg $CaCl_2$ (10 eq.) were weighed into a oven dried flask, purged with Ar. Dioxalene and 2 mL DMB were added, purged with Ar, then the reaction mixture was cooled to 0 ^oC. The diazo compound (0.5 mmol) was dissolved in 10 mL DMB, added in 2h at 0 ^oC. The ice bath was allowed to warm up to room temperature. The reaction mixture was stirred overnight.

The solvent of crude mixture was evaporated under reduced pressure. A crude ^{1}H-NMR was carried out. The products were isolated by pretreated silica gel chromatography. TLC was stained by PMA.

II. Experimental Data

2,2,2-trichloroethyl 2-(4-bromo-phenyl)-2-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)acetate (2.7)



Rh_2(*S*-DOSP)$_4$ (3.8 mg, 0.002 mmol), $CaCl_2$ (222 mg, 2 mmol) were weighed into an oven dried flask, purged with Ar. 4,4,5,5-tetramethyl-1,3-dioxolane (26 mg, 0.2 mmol) and 2 mL DMB were added, purged with Ar, then the reaction mixture was cooled to 0 ^oC. 2,2,2-trichloroethyl 2-(4-bromophenyl)-2-diazoacetate (148 mg, 0.4 mmol) was dissolved in 10 mL DMB, added in 2 h

at 0 ^{o}C. The ice bath was allowed to warm up to room temperature. The reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 10:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Rf = 0.5.

IR (neat): 2980, 1754, 1509, 1369, 1147, 1119, 1096, 1057, 1017, 717.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (dd, *J* = 1.9,1.9 Hz, 1H), 7.44 (ddd, *J* = 8.0, 1.9, 1.1 Hz, 1H), 7.31 (ddd, *J* = 7.8, 1.9, 1.1 Hz, 1H), 7.22 (dd, *J* = 7.8, 7.8 Hz, 1H), 5.48 (d, *J* = 7.4 Hz, 1H), 4.57 (, *J* = 12.7, 8.4 Hz, 1H), 4.44 (dq, *J* = 12.7, 8.4 Hz, 1H), 3.73 (d, *J* = 7.4 Hz, 1H), 1.20 (s, 3H), 1.17 (s, 6H), 1.16 (s, 3H).

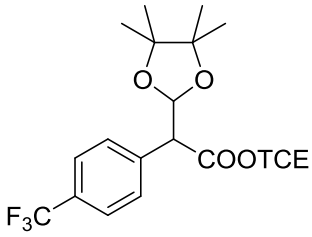
^{13}C NMR (101 MHz, $CDCl_3$): δ 169.05, 132.61, 131.76, 130.74, 122.27, 100.86, 83.06, 82.82, 74.16, 57.85, 24.01, 23.88, 22.20, 22.06.

HRMS (ESI): *m/z* calcd for $C_{17}H_{21}O_4BrCl_3$, 472.9683, found 472.9696 $[M+H]^+$.

HPLC: ADH, 1 % iPrOH/hexane, 1 mL/min, UV 230 nm, t: 5.96 min (minor), 6.86 min (major), 93% ee;

$[\alpha]^{23}_{D}$ = -67.02 (*c* 0.51, $CHCl_3$).

2,2,2-trichloroethyl 2-(4-triflouromethyl-phenyl)-2-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)acetate (2.10)



Rh_2(*S*-DOSP)$_4$ (3.8 mg, 0.002 mmol), $CaCl_2$ (222 mg, 2 mmol) were weighed into an oven dried flask, purged with Ar. 4,4,5,5-tetramethyl-1,3-dioxolane (26 mg, 0.2 mmol) and 2 mL DMB were added, purged with Ar, then the reaction mixture was cooled to 0 ^oC. 2,2,2-trichloroethyl 2-diazo-2-(4-(trifluoromethyl)phenyl)acetate (139 mg, 0.4 mg) was dissolved in 10 mL DMB, added in 2 h at 0 ^oC. The ice bath was allowed to warm up to room temperature. The reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 10:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Rf = 0.41.

IR (neat): 2980, 1756, 1570, 1430, 1283, 1271, 1151,1094.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 5.59 (d, *J* = 7.4 Hz, 1H), 4.81 (d, *J* = 11.9 Hz, 1H), 4.75 (d, *J* = 11.9 Hz, 1H), 3.88 (d, *J* = 7.3 Hz, 1H), 1.20 (s, 3H), 1.18 (s, 6H), 1.16 (s, 3H).

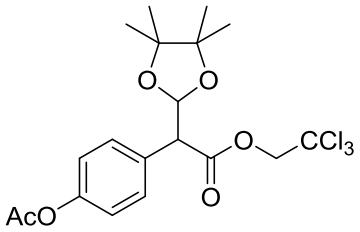
^{13}C NMR (101 MHz, $CDCl_3$): δ 168.90, 137.56, 137.55, 130.22, 129.55, 125.63, 125.60, 100.92, 94.67, 83.24, 82.96, 74.30, 58.30, 24.01, 23.92, 22.24, 22.10.

HRMS (ESI): *m/z* calcd for $C_{18}H_{20}O_4Cl_3F_3Na$, 485.0272, found 475.0277 $[M+Na]^+$.

HPLC: ADH, 1 % iPrOH/hexane, 1 mL/min, UV 230 nm, t: 4.59 min (minor), 5.50 min (major), 87% ee;

$[\alpha]^{23}_{D}$ = -37.12 (*c* 0.71, $CHCl_3$).

2,2,2-trichloroethyl 2-(4-acetoxyl-2-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)acetate (2.11)



Rh_2(*S*-DOSP)$_4$ (3.8 mg, 0.002 mmol), $CaCl_2$ (222 mg, 2 mmol) were weighed into an oven dried flask, purged with Ar. 4,4,5,5-tetramethyl-1,3-dioxolane (26 mg, 0.2 mmol) and 2 mL DMB were added, purged with Ar, then the reaction mixture was cooled to 0 ^{o}C. 2,2,2-trichloroethyl 2-(4-acetoxyphenyl)-2-diazoacetate (155 mg, 0.4 mg) was dissolved in 10 mL DMB, added in 2 h at 0 ^{o}C. The ice bath was allowed to warm up to room temperature. The reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 10:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Rf = 0.31.

IR (neat): 2981, 1756, 1507, 1273, 1200, 1149, 1015.

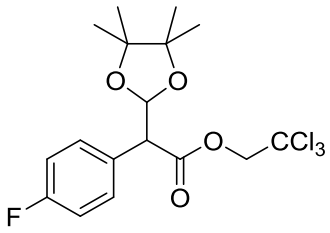
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.6 Hz, 2H), 7.07 (d, *J* = 8.6 Hz, 2H), 5.49 (d, *J* = 7.4 Hz, 1H), 4.57 (dq, *J* = 12.5, 8.4 Hz, 1H), 4.41 (dq, *J* = 12.5, 8.4 Hz, 1H), 3.76 (d, *J* = 7.4 Hz, 1H), 2.29 (s, 3H), 1.19 (s, 3H), 1.18 (s, 3H), 1.17 (s, 3H), 1.15 (s, 3cH).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.50, 150.52, 131.05, 129.96, 122.23, 121.83, 101.14, 83.07, 82.81, 60.83, 60.64, 57.60, 23.95, 23.84, 22.17, 22.05, 21.24

HPLC: ADH, 1 % iPrOH/hexane, 0.8 mL/min, UV 230 nm, t: 11.64 min (minor), 12.66 min (major), 90% ee;

$[\alpha]^{23}_{D}$ = -47.12 (*c* 0.65, $CHCl_3$).

2,2,2-trichloroethyl 2-(4-fluorophenyl)-2-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)acetate (2.12)



Rh_2(*S*-DOSP)$_4$ (3.8 mg, 0.002 mmol), $CaCl_2$ (222 mg, 2 mmol) were weighed into an oven dried flask, purged with Ar. 4,4,5,5-tetramethyl-1,3-dioxolane (26 mg, 0.2 mmol) and 2 mL DMB were added, purged with Ar, then the reaction mixture was cooled to 0 ^{o}C. 2,2,2-trichloroethyl 2-diazo-2-(4-fluorophenyl)acetate (112 mg, 0.4 mmol) was dissolved in 10 mL DMB, added in 2 h at 0 ^{o}C. The ice bath was allowed to warm up to room temperature. The reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 1:1 hexane/ethyl acetate solvent system) to isolate the product as acolorless oil. Rf = 0.37.

IR (neat): 2980, 1754, 1509, 1369, 1147, 1119, 1096, 1057, 1017, 717.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42 – 7.37 (m, 2H), 7.06 – 7.00 (m, 2H), 5.55 (d, *J* = 7.3 Hz, 1H), 4.78 (d, *J* = 12.0 Hz, 1H), 4.75 (d, *J* = 12.0 Hz, 1H), 3.79 (d, *J* = 7.3 Hz, 1H), 1.20 (s, 3H), 1.17 (s, 3H), 1.17 (s, 3H), 1.16 (s, 3H).

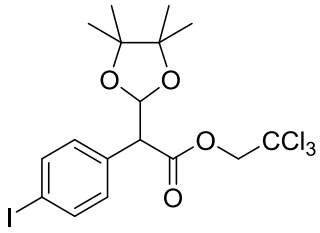
^{13}C NMR (101 MHz, $CDCl_3$): δ 169.45, 162.64 ($J_{C\text{-}F}$ = 245 Hz) 130.73 ($J_{C\text{-}F}$ = 8 Hz) 129.42 ($J_{C\text{-}F}$ = 3 Hz), 115.62 ($J_{C\text{-}F}$ = 22 Hz) 101.02, 94.77, 83.07, 82.82, 74.17, 57.65, 24.04, 23.92, 22.25, 22.11.

HRMS (ESI): *m/z* calcd for $C_{17}H_{20}O_4Cl_3FNa$, 435.0303, found 435.0306 $[M+Na]^+$.

HPLC: ADH, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 5.56 min (minor), 6.29 min (major), 92% ee;

$[\alpha]^{23}_D$ = -35.31 (*c* 0.58, $CHCl_3$).

2,2,2-trichloroethyl 2-(4-iodophenyl)-2-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)acetate (2.13)



Rh_2(*S*-DOSP)$_4$ (3.8 mg, 0.002 mmol), $CaCl_2$ (222 mg, 2 mmol) were weighed into an oven dried flask, purged with Ar. 4,4,5,5-tetramethyl-1,3-dioxolane (26 mg, 0.2 mmol) and 2 mL DMB were added, purged with Ar, then the reaction mixture was cooled to 0 ^{o}C. 2,2,2-trichloroethyl 2-diazo-2-(4-iodophenyl)acetate (128 mg, 0.4 mmol) was dissolved in 10 mL DMB, added in 2 h

at 0 ^{o}C. The ice bath was allowed to warm up to room temperature. The reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 10:1 hexane/ethyl acetate solvent system) to isolate the product as acolorless oil. Rf = 0.55.

IR (neat): 2980, 1758, 1296, 1140, 998.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 5.46 (d, *J* = 7.4 Hz, 1H), 4.59 – 4.49 (dq, *J* = 12.5, 8.3 Hz, 1H), 4.44 (dq, *J* = 12.5, 8.3 Hz, 1H), 3.71 (d, *J* = 7.4 Hz, 1H), 1.19 (s, 3H), 1.17 (s, 3H), 1.17 (s, 3H), 1.15 (s, 3H).

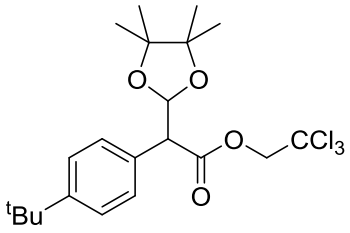
^{13}C NMR (100 MHz, $CDCl_3$): δ 169.28, 137.88, 133.19, 130.81, 100.96, 83.14, 82.29, 60.87, 60.51, 57.73, 23.95, 23.88, 22.19, 22.08.

HRMS (ESI): *m/z* calcd for $C_{17}H_{20}O_4Cl_3FNa$, 435.0303, found 435.0306 $[M+Na]^+$.

HPLC: SS_WHELK, 0.7 % iPrOH/hexane, 0.5 mL/min, UV 230 nm, t: 9.67 (minor), 11.05 min (major), 88% ee;

$[\alpha]^{23}_D$ = -45.12 (*c* 0.83, $CHCl_3$).

2,2,2-trichloroethyl 2-(4-(tert-butyl)phenyl)-2-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)acetate (2.14)



Rh_2(*S*-DOSP)$_4$ (3.8 mg, 0.002 mmol), $CaCl_2$ (222 mg, 2 mmol) were weighed into an oven dried flask, purged with Ar. 4,4,5,5-tetramethyl-1,3-dioxolane (26 mg, 0.2 mmol) and 2 mL DMB were added, purged with Ar, then the reaction mixture was cooled to 0 ^{o}C. 2,2,2-trichloroethyl 2-(4-*tert*-butylphenyl)-2-diazoacetate (128 mg, 0.4 mmol) was dissolved in 10 mL DMB, added in 2 h at 0 ^{o}C. The ice bath was allowed to warm up to room temperature. The reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 10:1 hexane/ethyl acetate solvent system) to isolate the product as acolorless oil. Rf = 0.6.

IR (neat): 2963, 1754, 1367, 1150, 1106, 1057, 1021, 721.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35 (s, 4H), 5.59 (d, *J* = 7.9 Hz, 1H), 4.82 (d, *J* = 11.7 Hz, 1H), 4.68 (d, *J* = 12.0 Hz, 1H), 3.78 (d, *J* = 7.6 Hz, 1H), 1.29 (s, 9H), 1.21 (s, 6H), 1.20 (s, 3H), 1.16 (s, 3H).

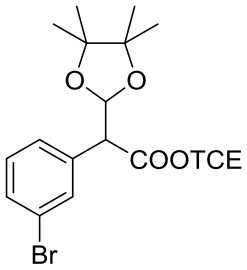
^{13}C NMR (100 MHz, $CDCl_3$): δ 169.28, 137.88, 133.19, 130.81, 100.96, 83.14, 82.29, 60.87, 60.51, 57.73, 23.95, 23.88, 22.19, 22.08.

HRMS (ESI): *m/z* calcd for $C_{21}H_{29}O_4Cl_3Na$, 473.1024, found 473.1030 $[M+Na]^+$.

HPLC: SS_WHELK, 0.7 % iPrOH/hexane, 0.5 mL/min, UV 230 nm, t: 8.03 (minor), 8.94 min (major), 88% ee;

$[\alpha]^{23}_{D}$ = -55.02 (*c* 0.53, $CHCl_3$).

2,2,2-trichloroethyl 2-(4-bromo-phenyl)-2-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)acetate (2.16)



Rh_2(*S*-DOSP)$_4$ (3.8 mg, 0.002 mmol), $CaCl_2$ (222 mg, 2 mmol) were weighed into an oven dried flask, purged with Ar. 4,4,5,5-tetramethyl-1,3-dioxolane (26 mg, 0.2 mmol) and 2 mL DMB were added, purged with Ar, then the reaction mixture was cooled to 0 ^{o}C. 2,2,2-trichloroethyl 2-(4-bromophenyl)-2-diazoacetate (148 mg, 0.4 mmol) was dissolved in 10 mL DMB, added in 2 h at 0 ^{o}C. The ice bath was allowed to warm up to room temperature. The reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 10:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Rf = 0.5.

IR (neat): 2964, 1758, 1513, 1147, 1017, 717.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (dd, *J* = 1.9,1.9 Hz, 1H), 7.44 (ddd, *J* = 8.0, 1.9, 1.1 Hz, 1H), 7.31 (ddd, *J* = 7.8, 1.9, 1.1 Hz, 1H), 7.22 (dd, *J* = 7.8, 7.8 Hz, 1H), 5.48 (d, *J* = 7.4 Hz, 1H), 4.57 (, *J* = 12.7, 8.4 Hz, 1H), 4.44 (dq, *J* = 12.7, 8.4 Hz, 1H), 3.73 (d, *J* = 7.4 Hz, 1H), 1.20 (s, 3H), 1.17 (s, 6H), 1.16 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.05, 132.61, 131.76, 130.74, 122.27, 100.86, 83.06, 82.82, 74.16, 57.85, 24.01, 23.88, 22.20, 22.06.

HRMS (ESI): *m/z* calcd for $C_{17}H_{21}O_4BrCl_3$, 472.9683, found 472.9690 $[M+H]^+$.

HPLC: ADH, 1 % iPrOH/hexane, 0.8 mL/min, UV 230 nm, t: 11.64 min (minor), 12.66 min (major), 90% ee;

$[\alpha]^{23}_D$ = -29.02 (*c* 0.33, $CHCl_3$).

Experimental Section for Chapter 3: Combined C-H Functionalization/Cope Rearrange Reaction with Triazoles

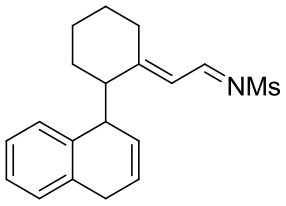
I. General procedure for Combined C-H Functionalization/Cope Rearrange Reaction with Triazoles

Rh_2(*S*-NTTL)$_4$ (0.005 mmol, 1 mol%) and triazole (0.5 mmol, 1 eq.) were weighed into an oven-dried round bottom flask. Then the flask was connected to the vacuum, and then back filled with Ar. This procedure was repeated thrice. The dihydronaphthalene derivative (2mmol, 4 eq) and chloroform (1.5 mL, stabilized with amylene) were added via syringe. Then the flask was heated under Ar at 55 ^{o}C for 8 h.

The solvent of crude mixture was evaporated under reduced pressure. A crude ^{1}HNMR was carried out. The products were isolated by pretreated silica gel chromatography. TLC was stained by PMA.

II. Experimental Data

_N_-((_E_)-2-(2-(1,4-dihydronaphthalen-1-yl)cyclohexylidene)ethylidene)methanesulfonamide (3.6)



Rh_2(*S*-NTTL)$_4$ (0.005 mmol, 9.5 mg, 1 mol%) and the 4-(cyclohex-1-en-1-yl)-1-(methylsulfonyl)-1H-1,2,3-triazole (0.5 mmol, 113.5 mg, 1 eq.) were weighed into an oven-dried round bottom flask. Then the flask was connected to the vacuum, and then back filled with Ar.

This procedure was repeated thrice. The dihydronaphthalene (2 mmol, 260 mg, 4 eq) and chloroform (1.5 mL, stabilized with amylene) were added via syringe. Then the flask was heated under Ar at 55 ^{o}C for 8 h.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) as colorless oil. (90mg, 55% yield). Isolated with compound **3.7** in the same reaction.

IR (neat): 2925, 2854, 1731, 1250, 1055, 908, 731, 697;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.26 (m, 5H), 5.62 (t, *J* = 1.6Hz, 1H), 3.77 (s, 3H), 2.30 (m, 1H), 1.83 (m, 1H), 1.45 (s, 3H), 1.40 (s, 3H), 1.30-1.20 (m, 18H), 0.87 (t, *J* = 6.4 Hz, 3H);

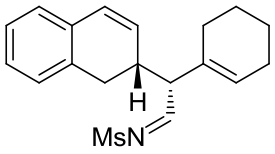
^{13}C NMR (100 MHz, $CDCl_3$): δ 173.20 , 141.21 , 140.16 , 131.01 , 128.41 , 128.04 , 126.20 , 94.83 , 88.18 , 52.49 , 32.11 , 29.78 , 29.75 , 29.69 , 29.59 , 29.53 , 28.82 , 28.14 , 27.99 , 27.00 , 22.89 , 14.32 ;

HRMS (ESI): *m/z* calcd for $C_{19}H_{24}O_2NS$, 330.1535, found 330.1534 $[M+H]^+$.

HPLC: ADH, 10 % iPrOH/hexane, UV 254 nm, t: 13.12 (major), 17.93 min (min), 98% ee with Rh_2(*S*-NTTL)$_4$

$[\alpha]^{23}_{D}$ = -46.32 (*c* 0.58, $CHCl_3$).

_N_-(2-(cyclohex-1-en-1-yl)-2-(1,2-dihydronaphthalen-2-yl)ethylidene)methanesulfonamide (3.7)



Rh_2(*S*-NTTL)$_4$ (0.005 mmol, 9.5 mg, 1 mol%) and 4-(cyclohex-1-en-1-yl)-1-(methylsulfonyl)-1H-1,2,3-triazole (0.5 mmol, 113.5 mg, 1 eq.) were weighed into an oven-dried round bottom flask. Then the flask was connected to the vacuum, and then back filled with Ar. This procedure was repeated thrice. The dihydronaphthalene derivative (2mmol, 260 mg, 4 eq) and chloroform (1.5 mL, stabilized with amylene) were added via syringe. Then the flask was heated under Ar at 55 ^{o}C for 8 h.

Purification by silica gel chromatography with pentane/ether (3:1) to isolate the product as acolorless oil. Isolated with compound **3.6** in the same reaction.

IR (neat): 2937, 2844, 1751, 1055, 958, 776, 685;

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.42 (d, *J* = 5.8 Hz, 1H), 7.20 – 7.09 (m, 4H), 7.07 (dd, *J* = 22.8, 13.6 Hz, 2H), 6.51 (d, *J* = 9.7 Hz, 1H), 5.99 (dd, *J* = 9.6, 4.5 Hz, 1H), 5.59 (s, 1H), 2.97 (s, 3H), 2.95 – 2.82 (m, 3H), 2.08 (t, *J* = 22.8 Hz, 3H), 1.62 (m, 6H).

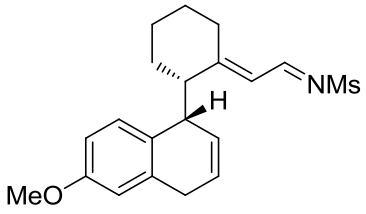
^{13}C NMR (100 MHz, $CDCl_3$): δ 173.20 , 141.21 , 140.16 , 131.01 , 128.41 , 128.04 , 126.20 , 94.83 , 88.18 , 52.49 , 32.11 , 29.78 , 29.75 , 29.69 , 29.59 , 29.53 , 28.82 , 28.14 , 27.99 , 27.00 , 22.89 , 14.32 ;

HRMS (ESI): *m/z* calcd for $C_{19}H_{24}O_2NS$, 330.1535, found 330.1528 $[M+H]^+$.

HPLC: ADH, 10 % iPrOH/hexane, UV 254 nm, t: 13.12 (major), 17.93 min (min), 90% ee with Rh_2(*S*-NTTL)$_4$

$[\alpha]^{23}_{D}$ = -31.22 (*c* 0.78, $CHCl_3$).

***N*-((*E*)-2-(2-(6-methoxy-1,4-dihydronaphthalen-1-yl)cyclohexylidene)ethylidene)methanesulfonamide (3.8)**



Rh_2(*S*-NTTL)$_4$ (0.005 mmol, 9.5 mg, 1 mol%) and 4-(cyclohex-1-en-1-yl)-1-(methylsulfonyl)-1H-1,2,3-triazole (0.5 mmol, 113.5 mg, 1 eq.) were weighed into an oven-dried round bottom flask. Then the flask was connected to the vacuum, and then back filled with Ar. This procedure was repeated thrice. The dihydronaphthalene 7-methoxy-1,2-dihydronaphthalene (2mmol, 320 mg, 4 eq) and chloroform (1.5 mL, stabilized with amylene) were added via syringe. Then the flask was heated under Ar at 55 ^{o}C for 8 h.

Purified by silica gel chromatography (using 5:1 hexane/ethyl acetate solvent system) as colorless oil.

IR (neat): 2933, 2859, 1710, 1250, 1617, 1576, 1237, 1142, 813;

^{1}H NMR (600 MHz, $CDCl_3$): δ 9.03 (d, *J* = 10.0 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.69 (d, *J* = 8.1 Hz, 1H), 6.64 (s, 1H), 6.13 (d, *J* = 10.0 Hz, 1H), 6.03 (dd, *J* = 39.3, 10.1 Hz, 2H), 3.84 (s, 1H), 3.76 (s, 3H), 3.31 (q, *J* = 21.2 Hz, 2H), 3.03 (s, 3H), 2.92 (dd, *J* = 13.3, 6.9 Hz, 1H), 2.53 – 2.37 (m, 2H), 1.75-1.73 (m, 2H), 1.70 – 1.60 (m, 2H), 1.54 – 1.37 (m, 2H).

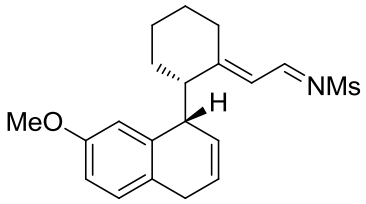
^{13}C NMR (100 MHz, $CDCl_3$): δ 173.71, 167.79, 158.00, 136.68, 129.75, 128.91, 127.44, 126.58, 120.88, 112.99, 112.48, 55.40, 54.05, 40.50, 39.86, 30.65, 29.98, 29.11, 28.39, 24.03;

HRMS (ESI): *m/z* calcd for $C_{20}H_{26}O_3NS$, 360.1635, found 360.1628 $[M+H]^+$.

HPLC: ADH, 10 % iPrOH/hexane, UV 254 nm, t: 15.12 (major), 19.39 min (min), 97.3% ee with Rh_2(*S*-NTTL)$_4$;

$[\alpha]^{23}_D$ = 12.52 (*c* 0.75, $CHCl_3$).

_N_-((_E_)-2-(2-(7-methoxy-1,4-dihydronaphthalen-1-yl)cyclohexylidene)ethylidene)methanesulfonamide (3.9)



Rh_2(*S*-NTTL)$_4$ (0.005 mmol, 9.5 mg, 1 mol%) and 4-(cyclohex-1-en-1-yl)-1-(methylsulfonyl)-1H-1,2,3-triazole (0.5 mmol, 113.5 mg, 1 eq.) were weighed into an oven-dried round bottom flask. Then the flask was connected to the vacuum, and then back filled with Ar. This procedure was repeated thrice . The 7-methoxy-1,2-dihydronaphthalene (2mmol, 320 mg, 4 eq) and chloroform (1.5 mL, stabilized with amylene) were added via syringe. Then the flask was heated under Ar at 55 ^{o}C for 8 h.

Purification by silica gel chromatography with pentane/ether (3:1) to isolate the product as colorless oil.

IR (neat): 3028, 2933, 2859, 1619, 1575, 1311, 1143, 964, 812;

^{1}H NMR (600 MHz, $CDCl_3$): δ 9.06 (d, *J* = 9.9 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.75 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.56 (d, *J* = 2.5 Hz, 1H), 6.21 (d, *J* = 9.9 Hz, 1H), 6.13 – 6.06 (m, 1H), 6.03 – 5.93 (m, 1H), 3.92 – 3.82 (m, 1H), 3.76 (s, 3H), 3.37 – 3.22 (m, 2H), 3.04 (s, 3H), 2.98 (dd, *J* = 14.0, 6.3 Hz, 1H), 2.56 (dt, *J* = 9.1, 4.7 Hz, 1H), 2.50 – 2.38 (m, 1H), 1.83 – 1.68 (m, 2H), 1.67 – 1.54 (m, 3H), 1.53 – 1.36 (m, 2H).

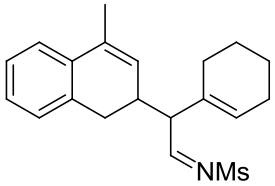
^{13}C NMR (151 MHz, $CDCl_3$): δ 173.44, 167.83, 158.02, 138.75, 129.27, 128.15, 127.69, 125.69, 120.73, 113.17, 112.26, 55.50, 53.86, 40.94, 40.46, 30.16, 29.60, 28.89, 28.23, 24.20;

HRMS (ESI): *m/z* calcd for $C_{20}H_{25}O_3NNaS$, 382.1447, found 382.1456 $[M+Na]^+$.

HPLC: ADH, 10 % iPrOH/hexane, 1.0 mL/min, UV 254 nm, t: 14.96 (major), 20.33 min (minor), 96.6% ee

$[\alpha]^{23}_D$ = 61.48 (*c* 0.82, $CHCl_3$).

_N_-(2-(cyclohex-1-en-1-yl)-2-(4-methyl-1,2-dihydronaphthalen-2-yl)ethylidene)methanesulfonamide (3.12)



Rh_2(*S*-NTTL)$_4$ (0.005 mmol, 9.5 mg, 1 mol%) and 4-(cyclohex-1-en-1-yl)-1-(methylsulfonyl)-1H-1,2,3-triazole (0.5 mmol, 113.5 mg, 1 eq.) were weighed into an oven-dried round bottom

flask. Then the flask was connected to the vacuum, and then back filled with Ar. This procedure was repeated thrice. The 4-methyl-1,2-dihydronaphthalene (2 mmol, 288 mg, 4 eq) and chloroform (1.5 mL, stabilized with amylene) were added via syringe. Then the flask was heated under Ar at 55 ^{o}C for 8h.

Purified by silica gel chromatography (using 4:1 hexane/ethyl acetate solvent system) to isolate the product as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, *J* = 5.9 Hz, 1H), 7.23-7.15 (m, 4H), 6. 5.8780 (s, 1H), 5.58 (s, 1H), 3.1 (s, 3H), 2.90 – 2.81 (m, 2H), 2.61 (dd, *J* = 14.9, 6.2 Hz, 1H), 2.13-2.02 (m, 6H), 1.95-1.83 (m, 2H), 1.63-1.51 (m, 4H).

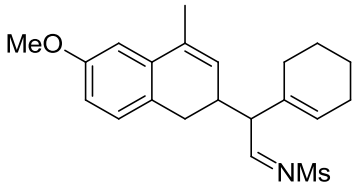
^{13}C NMR (100 MHz, $CDCl_3$): δ 179.53, 135.20, 134.34, 133.68, 132.34, 129.05, 128.05, 127.39, 126.81, 126.28, 123.20, 56.49, 40.01, 32.91, 32.12, 26.86, 25.67, 22.82, 22.23, 19.56;

HRMS (ESI): *m/z* calcd for $C_{20}H_{26}O_2NS$, 344.1638, found 344.1638 $[M+H]^+$.

HPLC: P6, 5 % iPrOH/hexane, 1.0 mL/min, t: 14.96 (minor), 16.3618.92 min (major), 91% ee with Rh_2(*S*-NTTL)$_4$;

$[\alpha]^{23}_D$ = -70.24 (*c* 2.06, $CHCl_3$).

_N_-(2-(cyclohex-1-en-1-yl)-2-(6-methoxy-4-methyl-1,2-dihydronaphthalen-2-yl)ethylidene)methanesulfonamide (3.16)



Rh_2(*S*-NTTL)$_4$ (0.005 mmol, 9.5 mg, 1 mol%) and 4-(cyclohex-1-en-1-yl)-1-(methylsulfonyl)-1H-1,2,3-triazole (0.5 mmol, 113.5 mg, 1 eq.) were weighed into an oven-dried round bottom flask. Then the flask was connected to the vacuum, and then back filled with Ar. This procedure was repeated thrice. The 7-methoxy-4-methyl-1,2-dihydronaphthalene (2 mmol, 348 mg, 4 eq) and chloroform (1.5 mL, stabilized with amylene) were added via syringe. Then the flask was heated under Ar at 55 ^{o}C for 8 h.

Purified by silica gel chromatography (using 5:1 hexane/ethyl acetate solvent system) to isolate the product as colorless oil.

IR (neat): 2928, 2836, 1640, 1362, 1142, 813;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, *J* = 5.9 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 1H), 6.81 (d, *J* = 2.6 Hz, 1H), 6.71 (dd, *J* = 8.2, 2.6 Hz, 1H), 5.80 (s, 1H), 5.57 (s, 1H), 3.81 (s, 3H), 3.08 – 2.90 (m, 4H), 2.90 – 2.68 (m, 2H), 2.57 (dd, *J* = 14.9, 6.2 Hz, 1H), 2.18-1.96 (m, 4H), 1.93-1.74 (m, 2H), 1.61-1.51 (m, 2H).

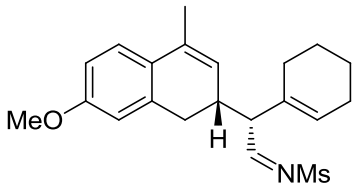
^{13}C NMR (100 MHz, $CDCl_3$): δ 179.67, 158.77, 136.42, 133.73, 132.45, 129.20, 129.17, 128.77, 127.11, 127.06, 126.55, 111.85, 109.99, 56.56, 55.54, 40.18, 40.13, 33.28,31.29, 26.95, 25.78, 22.93, 22.34, 19.59;

HRMS (ESI): *m/z* calcd for $C_{21}H_{28}O_3NS$, 374.1782, found 374.1784 $[M+H]^+$.

HPLC: ADH, 5 % iPrOH/hexane, 1.0 mL/min, t: 14.76 (minor), 16.36 min (major), 86% ee with Rh_2(*S*-NTTL)$_4$;

$[\alpha]^{23}_D$ = -87.02 (*c* 0.51, $CHCl_3$).

_N_-(2-(cyclohex-1-en-1-yl)-2-(7-methoxy-4-methyl-1,2-dihydronaphthalen-2-yl)ethylidene)methanesulfonamide (3.18)



Rh_2(*S*-NTTL)$_4$ (0.005 mmol, 9.5 mg, 1 mol%) and 4-(cyclohex-1-en-1-yl)-1-(methylsulfonyl)-1H-1,2,3-triazole (0.5 mmol, 113.5 mg, 1 eq.) were weighed into an oven-dried round bottom flask. Then the flask was connected to the vacuum, and then back filled with Ar. This procedure was repeated thrice. The dihydronaphthalene derivative (2 mmol, 348 mg, 4 eq) and chloroform (1.5 mL, stabilized with amylene) were added via syringe. Then the flask was heated under Ar at 55 ^oC for 8 h.

Purified by silica gel chromatography (using 5:1 hexane/ethyl acetate solvent system) to isolate the product as colorless oil.

IR (neat): 2932, 2835, 1623, 1608, 1317, 1251, 1151, 801;

^1H NMR (600 MHz, $CDCl_3$): δ 8.41 (d, *J* = 6.1 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 6.74 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.66 (d, *J* = 2.5 Hz, 1H), 5.65 (s, 1H), 5.58 (s, 1H), 3.80 (s, 3H), 2.99 – 2.95 (m,

4H), 2.86 (dd, *J* = 21.6, 8.3 Hz, 2H), 2.66 – 2.56 (m, 1H), 2.13 – 2.04 (m, 2H), 1.97 – 1.86 (m, 2H), 1.72 – 1.55 (m, 6H).

^{13}C NMR (150 MHz, $CDCl_3$): δ 179.80, 159.05, 136.32, 133.49, 132.55, 129.07, 128.57, 124.54, 123.85, 114.55, 111.20, 56.72, 55.47, 40.13, 33.15, 32.73, 27.08, 25.77, 22.95, 22.36, 19.72;

HRMS (ESI): *m/z* calcd for $C_{21}H_{28}O_3NS$, 374.1789, found 374.1784 $[M+H]^+$.

HPLC: ADH, 5 % iPrOH/hexane, 1.0 mL/min, UV 254 nm, t: 12.22 (major), 13.75 min (min), 90% ee with Rh_2(*S*-NTTL)$_4$;

$[\alpha]^{23}_D$ = -60.04 (*c* 0.33, $CHCl_3$).

Experimental Section for Chapter 4: Asymmetric transformations of propargyl alcohols with donor/acceptor-substituted carbenoids

I. General procedure for substituted propargyl alcohol.

To a solution of alkyne in THF butyl lithium in hexane (2.5 M, 1.1 eq.) was added at -78 ^{o}C, then the bath was allowed to warm up. The mixture was stirred at 0 ^{o}C for 2 hours then ketone or formaldehyde was added afterwards. The mixture was stirred for additional 4 h. The reaction was quenched with saturated aq NH_4Cl, extracted with Et_2O three times. The organic layers were combined, washed with saturated aq NaCl, dried over $MgSO_4$ and concentrated. The residue was purified by silica gel flash chromatography using hexane/ethyl acetate as solvent system.

II. General procedure for 3-silyl-substituted propargyl alcohol.

To a 1-(tetrahydropyranoxy)-2-propyne solution in THF *n*-BuLi in hexane (1.2 equiv, 2.5 M) was added at -78 ^{o}C. After 2 h, a solution of the trialkylchlorosilane in THF (1.3 equiv) was added dropwise and the reaction was allowed to warm up to room temperature and stirred for 3-5 h. The reaction was quenched with an aqueous saturated NH_4Cl solution, extracted with ether three times. The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered and concentrated to obtain the crude silylated THP-protected alcohols. The crudematerial was added to a PPTS (0.1–0.2 equiv) solution in MeOH. The mixture was stirred at room temperature for 18–24 h and monitored by TLC. Upon completion, the reaction mixture was concentrated and then purified by silica gel flash chromatography using hexane/ethyl acetate as solvent system.

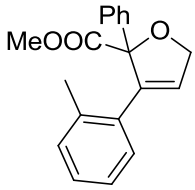
III**. General method for gold catalyzed reactions with propargyl alcohols and aryldiazoacetates**

A mixture of chiral digold catalyst (0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and propargyl alcohol(0.75 mmol) was dissolved in 3 mL of DCM in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Aryldiazoacetate (0.5 mmol) was dissolved in 9 mL of DCE, then added to former solution in 3h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

The solvent of the crude mixture was evaporated under reduced pressure. A crude ^{1}HNMR was carried out. The products were isolated by pretreated silica gel chromatography. TLC was stained by PMA.

IV. Experimental Data

methyl 2-phenyl-3-(*o*-tolyl)-2,5-dihydrofuran-2-carboxylate (4.12b):



A mixture of *(S)*-xylyl-BINAP(AuCl)$_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 3-(o-tolyl)prop-2-yn-1-ol (110 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was

dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Isolated with compound **4.22b** in same reaction.

IR (neat): 2951, 1735, 1249, 1218, 1072, 1011, 762;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.20 (m, 5H), 7.17 (t, J = 7.4 Hz, 1H), 7.13 – 7.01 (m, 2H), 6.82 (d, J = 7.7 Hz, 1H), 5.94 (s, 1H), 5.16 – 5.02 (m, 2H), 3.78 (s, 3H), 1.77 (s, 3H).

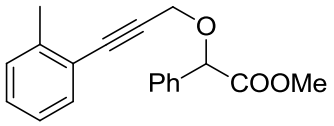
^{13}C NMR (100 MHz, $CDCl_3$): δ 171.71, 141.36, 139.00, 137.78, 133.14, 130.06, 129.66, 128.02, 127.99, 127.85, 126.20, 124.99, 95.33, 75.70, 52.76, 19.71;

HRMS (ESI): *m/z* calcd for $C_{19}H_{19}O_3$, 295.1329, found 295.1331 $[M+H]^+$,

HPLC: ODR, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 9.16 (minor), 12.01 min (major), 66% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = -33.41 (*c* 0.8, $CHCl_3$).

methyl 2-phenyl-2-((3-(*o*-tolyl)prop-2-yn-1-yl)oxy)acetate (4.22b):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 3-(o-tolyl)prop-2-yn-1-ol (110 mg, 0.75 mmol) was mixed in 3 mL of DCE in

an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Isolated with compound **4.12b** in same reaction.

IR (neat): 2951, 2213, 1748, 1208, 1095, 1072, 1021, 757, 731, 697;

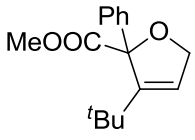
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 – 7.18 (m, 9H), 5.34 (s, 1H), 4.59 (d, *J* = 16.1 Hz, 1H), 4.42 (d, *J* = 16.1 Hz, 1H), 3.73 (s, 3H), 2.44 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.71, 141.36, 139.00, 137.78, 133.14, 130.06, 129.66, 128.02, 127.99, 127.85, 126.20, 124.99, 95.33, 75.70, 52.76, 19.71;

HRMS (ESI): *m/z* calcd for $C_{19}H_{19}O_3$, 295.1329, found 295.13310$[M+H]^+$;

HPLC: ODH, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm. t: 11.93, 14.02 min. less than 5% ee.

methyl 3-(*tert*-butyl)-2-phenyl-2,5-dihydrofuran-2-carboxylate (4.12d):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 4,4-dimethylpent-2-yn-1-ol (84 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then

the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Isolated with compound **4.22d** in same reaction.

IR (neat): 2971, 1736, 1253, 1218, 1087, 1001, 753;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.27 (m, 3H), 7.24 – 7.20 (m, 2H), 6.46 (t, J = 1.5 Hz, 1H), 4.84 (dd, *J* = 13.8, 1.6 Hz, 1H), 4.81 (dd, *J* = 13.8, 1.5 Hz, 1H), 3.79 (s, 3H), 1.02 (s, 9H).

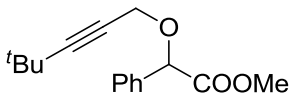
^{13}C NMR (101 MHz, $CDCl_3$): δ 172.22, 151.5, 140.61, 128.14, 128.00, 127.93, 124.59, 94.68, 74.43, 52.51, 33.06, 31.13;

HRMS (ESI): *m/z* calcd for $C_{16}H_{19}O_3$, 295.1329, found 295.1328 $[M-H]^+$;

HPLC: ODH, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 9.70 (major), 13.78 min (major), 91% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;.

$[\alpha]^{23}_{D}$ = -31.56 (*c* 1.2, $CHCl_3$).

methyl 2-((4,4-dimethylpent-2-yn-1-yl)oxy)-2-phenylacetate (4.22d):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and and 4,4-dimethylpent-2-yn-1-ol (84 mg, 0.75 mmol) was mixed in 3 mL of

DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Isolated with compound **4.12d** in same reaction.

IR (neat): 2968, 2866, 2215, 1749, 1454, 1263, 1206, 1098, 1014, 730, 697;

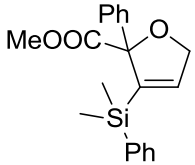
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.30 (m, 5H), 5.21 (s, 1H), 4.29 (d, *J* = 15.6 Hz, 1H), 4.14 (d, *J* = 15.6 Hz, 1H), 3.73 (s, 3H), 1.23 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.27, 136.00, 129.04, 128.88, 127.81, 96.86, 78.51, 77.55, 77.23, 76.91, 73.26, 57.13, 52.56, 31.06, 27.68;

HRMS (ESI): *m/z* calcd for $C_{16}H_{19}O_3$, 295.1329, found 295.1328 $[M-H]^+$;

HPLC: P6, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 4.77, 5.01 min. less than 5% ee.

methyl 3-(dimethyl(phenyl)silyl)-2-phenyl-2,5-dihydrofuran-2-carboxylate (4.12e):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 3-(dimethyl(phenyl)silyl)prop-2-yn-1-ol (142 mg, 0.75 mmol) was mixed in 3

mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Isolated with compound **4.22e** in same reaction.

IR (neat): 2951, 2848, 1750, 1731, 1250, 1088, 1065, 697;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.40 (m, 2H), 7.34 – 7.27 (m, 6H), 7.25 – 7.20 (m, 2H), 6.41 (t, *J* = 1.6 Hz, 1H), 4.84 (d, *J* = 1.5 Hz, 2H), 3.53 (s, 3H), 0.23 (s, 3H), 0.19 (s, 3H).

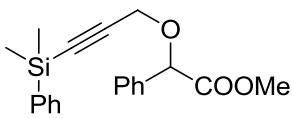
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.27, 142.56, 142.20, 140.62, 138.25, 133.79, 129.17, 128.39, 127.91, 126.87, 99.17, 76.85, 52.10, -1.20, -2.42 ;

HRMS (ESI): *m/z* calcd for $C_{20}H_{23}O_3{}^{28}Si$, 339.1414, found 339.1411 $[M+H]^+$.

HPLC: 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 17.86 (major), 20.49 min (minor), 93% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = -31.18 (*c* 1.74, $CHCl_3$).

methyl 2-((3-(dimethyl(phenyl)silyl)prop-2-yn-1-yl)oxy)-2-phenylacetate(4.22e):



A mixture of *(S)*-xylyl-BINAP($AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 3-(dimethyl(phenyl)silyl)prop-2-yn-1-ol (142 mg, 0.75 mmol) was mixed in 3 mL DCE of in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^oC. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Isolated with compound **4.12e** in same reaction.

IR (neat): 3069, 2955, 2175, 1750, 1250, 1114, 818;

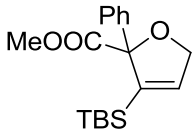
^1H NMR (400 MHz, $CDCl_3$): δ 7.67 – 7.59 (m, 2H), 7.46 – 7.33 (m, 8H), 5.24 (s, 1H), 4.36 (d, J = 16.3 Hz, 1H), 4.21 (d, J = 16.3 Hz, 1H), 3.72 (s, 3H), 0.44 (s, 3H), 0.44 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.01, 136.62, 135.66, 133.87, 129.77, 129.19, 128.95, 128.13, 127.86, 102.04, 91.22, 78.81, 57.33, 52.62, -0.84;

HRMS (ESI): *m/z* calcd for $C_{20}H_{23}O_3{}^{28}Si$, 339.1413, found 339.1411 $[M+H]^+$.

HPLC: ODH, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 7.90, 8.17 min. less than 5% ee.

methyl 3-(*tert*-butyldimethylsilyl)-2-phenyl-2,5-dihydrofuran-2-carboxylate (4.12f):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 3-(tert-butyldimethylsilyl)prop-2-yn-1-ol (128 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Isolated with compound **4.22f** in same reaction.

IR (neat): 2954, 2928, 2884, 2854, 1732, 1250, 1216, 1065;

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33 – 7.27 (m, 3H), 7.24 – 7.20 (m, 2H), 6.46 (t, J = 1.5 Hz, 1H), 4.84 (dd, *J* = 13.8, 1.6 Hz, 1H), 4.81 (dd, *J* = 13.8, 1.5 Hz, 1H), 3.79 (s, 3H), 0.78 (s, 9H), -0.07 (s, 3H), -0.13 (s, 3H).

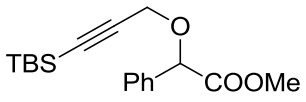
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.67, 141.94, 141.00, 140.91, 128.34, 128.31, 127.16, 99.89, 76.91, 52.40, 26.99, 17.63, -3.73, -4.62;

HRMS (ESI): *m/z* calcd for $C_{18}H_{27}O_3{}^{28}Si$, 319.1724, found 319.1725 $[M+H]^+$.

HPLC: ODH, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 10.54 (major), 11.86 min (minor), 99% ee with (*S*)-xylyl-BINAP$(AuCl)_2$; 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 10.65 (minor), 11.82 min (major), 98.5% ee with (*R*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = 38.41 (*c* 0.99, $CHCl_3$).

methyl 2-((3-(*tert*-butyldimethylsilyl)prop-2-yn-1-yl)oxy)-2-phenylacetate (4.22f):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 3-(tert-butyldimethylsilyl)prop-2-yn-1-ol (128 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil. Isolated with compound **4.12f** in same reaction.

IR (neat): 2951, 1735, 1249, 1218, 1072, 1011, 762;

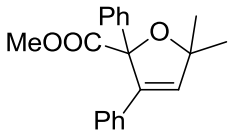
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.40 – 7.34 (m, 3H), 5.26 (s, 1H), 4.33 (d, *J* = 16.3 Hz, 1H), 4.16 (d, *J* = 16.3 Hz, 1H), 3.72 (s, 3H), 0.94 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.01, 135.70, 129.13, 128.90, 127.82, 100.84, 91.47, 78.51, 57.18, 52.54, 26.21, 16.64, -4.54;

HRMS (ESI): *m/z* calcd for $C_{18}H_{27}O_3{}^{28}Si$, 319.1724, found 319.1725 $[M+H]^+$.

HPLC: ODH, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 7.90, 8.17 min. less than 5% ee.

methyl 5,5-dimethyl-2,3-diphenyl-2,5-dihydrofuran-2-carboxylate (4.15):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 2-methyl-4-phenylbut-3-yn-2-ol (120 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) as colorless oil.

IR (neat): 2971, 1736, 1253, 1218, 1087, 1001, 753;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.29 (m, 5H), 7.21-7.19 (m, 5H), 6.30 (s, 1H), 3.77 (s, 3H), 1.52 (s, 3H), 1.49 (s, 3H);

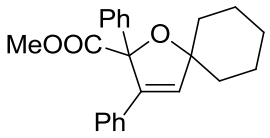
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.96, 140.34, 139.58, 135.41, 133.09, 128.41, 128.39, 128.33, 128.11, 128.01, 127.39, 94.84, 88.24, 52.78, 28.65, 27.97;

HRMS (ESI): *m/z* calcd for $C_{20}H_{20}O_3{}^{23}Na$, 331.1305, found 331.1305 $[M+Na]^+$.

HPLC: SS_WELK, 2 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 10.03 (major), 11.34 min (minor), 86% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = -23.41 (*c* 1.0, $CHCl_3$).

methyl 2,3-diphenyl-1-oxaspiro[4.5]dec-3-ene-2-carboxylate (4.16):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 1-(phenylethynyl)cyclohexan-1-ol (150 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purification by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2931, 2856, 1732, 1246, 1213, 1065, 761, 136, 694;

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35 (dd, *J* = 6.0Hz, 2.4Hz), 7.30-7.28 (m, 3H), 7.20-7.16 (m, 5H), 6.43 (s, 1H), 3.77 (s, 3H), 1.82 (m, 7H), 1.53 (m, 5H);

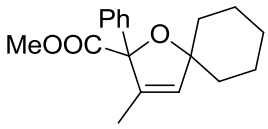
^{13}C NMR (100 MHz, $CDCl_3$): δ 173.20, 140.44, 133.77, 133.52, 128.40, 128.30, 128.26, 128.07, 127.91, 127.39, 94.12, 90.19, 52.68, 38.03, 37.39, 25.57, 23.67 , 23.57;

HRMS (ESI): *m/z* calcd for $C_{23}H_{24}O_3{}^{23}Na$, 371.1618, found 371.1618 $[M+Na]^+$.

HPLC: SS_WHELK, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 9.29 (minor), 10.65 min (major), 88% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_{D}$ = -40.84 (*c* 2.54, $CHCl_3$).

methyl 3-methyl-2-phenyl-1-oxaspiro[4.5]dec-3-ene-2-carboxylate (4.17):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 1-(prop-1-yn-1-yl)cyclohexan-1-ol (104 mg, 0.75 mmol) was mixed in 3 mL of DCM in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purification by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2924, 2856, 1729, 1446, 1235, 1058, 908, 698;

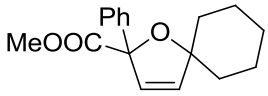
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.64 (dd, J = 8.8, 1.6 Hz, 2H), 7.37-7.26 (m, 3H), 5.74 (d, *J* = 1.6 Hz, 1H), 3.76 (s, 3H), 1.77 (d, *J* = 1.2Hz, 3H), 2.05-1.40 (m, 10H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 173.30, 139.98, 135.88, 132.87, 128.42, 128.02, 126.12, 94.04, 93.34, 52.45, 41.24, 40.36, 29.63, 23.08, 23.00, 13.54;

HRMS (ESI): *m/z* calcd for $C_{23}H_{24}O_3{}^{23}Na$, 371.1618, found 371.1618 $[M+Na]^+$.

HPLC: SS_WHELK, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 5.29 (minor), 5.74 min (major), 54% ee with (*S*)-xylyl-BINAP$(AuCl)_2$.

methyl 2-phenyl-1-oxaspiro[4.5]dec-3-ene-2-carboxylate (4.18):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 1-ethynylcyclohexan-1-ol (93 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2931, 2856, 1751, 1728, 1253, 1228, 1053, 697;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 7.2 Hz 2H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.28 (t, *J* = 7.8 Hz, 1H), 6.15(d, *J* = 6.6Hz, 1H), 6.09 (d, *J* = 6.0 Hz, 1H), 3.72 (s, 3H), 1.86 – 1.44 (m, 10H);

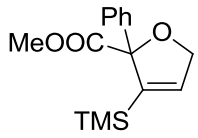
^{13}C NMR (100 MHz, $CDCl_3$): δ 173.33, 141.64, 135.23, 128.57, 128.13, 127.97, 125.45, 92.65, 92.28, 52.74, 37.86, 37.72, 25.53, 23.64, 23.60;

HRMS (ESI): *m/z* calcd for $C_{12}H_{21}O_3$, 273.1486, found 273.1486 $[M+H]^+$;

HPLC: OJH, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 10.36 (major), 15.07 min (minor), 80% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = -0.07 (*c* 1.5 , $CHCl_3$)..

methyl 2-phenyl-3-(trimethylsilyl)-2,5-dihydrofuran-2-carboxylate (4.20):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 3-(trimethylsilyl)prop-2-yn-1-ol (96 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^oC. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2952, 2897, 2848, 1731, 1248, 1086, 1064, 1014, 835, 756, 696;

^1H NMR (400 MHz, $CDCl_3$): δ 7.33–7.27 (m, 3H), 7.24–7.20 (m, 2H), 6.37 (t, J = 1.4 Hz, 1H), 4.88–4.72 (m, 2H), 3.80 (s, 3H), -0.06 (s, 9H).

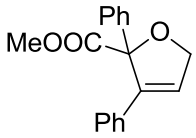
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.64, 144.30, 140.78, 140.11, 128.37, 128.34, 126.77, 99.22, 76.77 , 52.45 , -0.26 ;

HRMS (ESI): *m/z* calcd for $C_{12}H_{21}O_3$, 273.1486, found 273.1486 $[M+H]^+$;

HPLC: ODH, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 11.65 (major), 13.84 min (minor), 90% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = -39.7 (*c* 4.5 , $CHCl_3$).

methyl 2,3-diphenyl-2,5-dihydrofuran-2-carboxylate (4.21):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 3-phenylprop-2-yn-1-ol (99 mg, 0.75 mmol) was mixed in 3 mL of DCM in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^oC. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

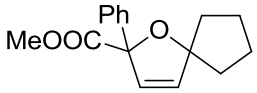
Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

^1H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.29 (m, 5H), 7.28 – 7.17 (m, 5H), 6.51 (t, *J* = 1.7 Hz, 1H), 4.99 (dd, *J* = 13.9, 1.8 Hz, 1H), 4.94 (dd, *J* = 13.9, 1.9 Hz, 1H), 3.80(s, 3H); The ^1H NMR data was consistent with previous report by Dr. John Frederick Briones.

HPLC: SS_WHELK, 3 % iPrOH/hexane, 1.0 mL/min, UV 254 nm, t: 15.08 (minor), 17.16 (major) min 50 % ee with (*S*)-xylyl-BINAP(AuCl)$_2$.

$[\alpha]^{23}_D$ = -43.41 (*c* 2.3, $CHCl_3$).

methyl 2-phenyl-1-oxaspiro[4.4]non-3-ene-2-carboxylate (4.23):



A mixture of *(S)*-xylyl-BINAP(AuCl)$_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 1-ethynylcyclopentan-1-ol (83 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^oC. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purification by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2953, 2872, 1751, 1729, 1227, 1052, 697;

^1H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.0 Hz, 2H), 7.36-7.32 (m, 2H), 7.31 – 7.27 (m, 1H), 6.13 (d, *J* = 5.7 Hz, 1H), 5.92 (d, *J* = 5.8 Hz, 1H), 3.73 (s, 3H), 2.15 – 1.48 (m, 10H).

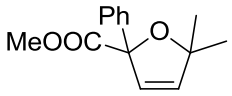
^{13}C NMR (100 MHz, $CDCl_3$): δ 173.15 , 141.30 , 135.22 , 128.56 , 128.01 , 127.69 , 125.59 , 99.96 , 93.01 , 52.74 , 39.38 , 38.95 , 24.94 , 24.81 ;

HRMS (ESI): *m/z* calcd for $C_{16}H_{19}O_3$, 259.1334, found 259.1327 $[M+H]^+$.

HPLC: SS_WHELK, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 7.70 (minor), 9.30 min (major), 75% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = -20.16 (*c* 2.07, $CHCl_3$).

methyl 5,5-dimethyl-2-phenyl-2,5-dihydrofuran-2-carboxylate (4.24):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 2-methylbut-3-yn-2-ol (63 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^oC. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purification by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2932, 2856, 1751, 1728, 1229, 1052, 727, 696;

1H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 2H), 7.31 – 7.27 (m, 1H), 6.12 (d, *J* = 5.8 Hz, 1H), 5.93 (d, *J* = 5.8 Hz, 1H), 3.73 (s, 3H), 1.46 (s, 3H), 1.38 (s, 3H).

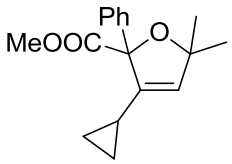
^{13}C NMR (100 MHz, $CDCl_3$): δ 173.14, 141.43, 137.03, 128.64, 128.04, 127.43, 125.50, 93.24, 90.17, 52.76, 28.36;

HRMS (ESI): *m/z* calcd for $C_{14}H_{17}O_3$, 233.1172, found 233.1175 $[M+H]^+$.

HPLC: SS_WHELK, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 8.61 (minor), 10.39 min (major), 82% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = 32.00 (*c* 0.90, $CHCl_3$).

methyl 3-cyclopropyl-5,5-dimethyl-2-phenyl-2,5-dihydrofuran-2-carboxylate (4.25):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 4-cyclopropyl-2-methylbut-3-yn-2-ol (93 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purification by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2974, 1734, 1057, 905,727;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.4 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.30-7.29 (m, 1H), 5.36 (d, *J* = 0.6 Hz, 1H), 3.80 (s, 3H), 1.45-1.42 (m, 1H), 1.39 (d, *J* = 3.0 Hz, 6H), 0.79-0.75 (m, 1H), 0.66-0.62 (m, 1H), 0.53-0.49 (m, 1H), 0.25-0.21 (m, 1H).

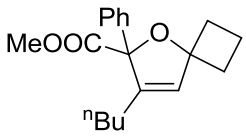
^{13}C NMR (100 MHz, $CDCl_3$): δ 173.22, 143.50, 140.47, 128.31, 128.08, 128.02, 126.47, 74.70, 87.98, 52.62, 28.80, 28.24, 9.04, 8.52, 8.34;

HRMS (ESI): *m/z* calcd for $C_{17}H_{21}O_3$, 273.1485, found 273.1485 $[M+H]^+$.

HPLC: SS_WHELK, 0.5 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 10.80 (minor), 12.66 min (major), 76% ee with (*S*)-xylyl-BINAP$(AuCl)_2$.

$[\alpha]^{23}_D$ = -17.41 (*c* 2.1, $CHCl_3$).

methyl 7-butyl-6-phenyl-5-oxaspiro[3.4]oct-7-ene-6-carboxylate (4.26):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 1-(hex-1-yn-1-yl)cyclobutan-1-ol (114 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purification by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2958, 2934, 2973, 1729, 1245, 1086, 1056, 698 .

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34-7.26 (m, 5H), 5.89 (t, *J* = 1.8 Hz, 1H), 3.78 (s, 3H), 2.59(dq, *J* = 6.6, 3Hz 2H), 2.29-2.23 (m, 2H), 2.20-2.16 (m, 1H), 1.83-1.72 (m, 2H), 1.62-1.48 (m, 2H), 1.44-1.39 (m, 1H), 0.88 (t, J = 7.8Hz, 3H).

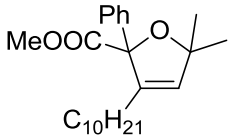
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.36, 141.83, 139.74, 128.42, 128.11, 127.79, 95.10, 90.37, 52.60, 36.69, 36.57, 28.82, 21.13, 14.12, 12.33;

HRMS (ESI): *m/z* calcd for $C_{18}H_{22}O_3{}^{23}Na$, 309.1461, found 309.1462 $[M+Na]^+$.

HPLC: SS_WHELK, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 7.05 (minor), 9.35 min (major), 54% ee with (*S*)-xylyl-BINAP$(AuCl)_2$.

$[\alpha]^{23}_D$ = -14.74 (*c* 1.1, $CHCl_3$).

methyl 3-decyl-5,5-dimethyl-2-phenyl-2,5-dihydrofuran-2-carboxylate (4.27):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 2-methyltetradec-3-yn-2-ol (168 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min.

Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-phenylacetate (88 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purification by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2925, 2854, 1731, 1250, 1055, 908, 731, 697;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.26 (m, 5H), 5.62 (t, *J* = 1.6Hz, 1H), 3.77 (s, 3H), 2.30 (m, 1H), 1.83 (m, 1H), 1.45 (s, 3H), 1.40 (s, 3H), 1.30-1.20 (m, 18H), 0.87 (t, *J* = 6.4 Hz, 3H);

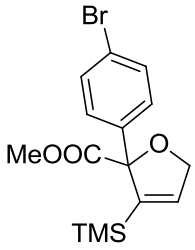
^{13}C NMR (100 MHz, $CDCl_3$): δ 173.20, 141.21, 140.16, 131.01, 128.41, 128.04, 126.20, 94.83, 88.18, 52.49, 32.11, 29.78, 29.75, 29.69, 29.59, 29.53, 28.82, 28.14, 27.99, 27.00, 22.89, 14.32;

HRMS (ESI): *m/z* calcd for $C_{24}H_{37}O_3$, 373.2737, found 373.2736 $[M+H]^+$.

HPLC: SS_WHELK, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 6.24 (minor), 7.61 min (major), 81% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = -46.32 (*c* 0.58, $CHCl_3$).

methyl 2-(4-bromophenyl)-3-(trimethylsilyl)-2,5-dihydrofuran-2-carboxylate (4.31):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 3-(trimethylsilyl)prop-2-yn-1-ol (96 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-(4-bromophenyl)-2-diazoacetate (128 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2953, 2898, 2849, 1732, 1250, 1072, 838, 821.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.7 Hz, 2H), 7.15 (d, *J* = 8.7 Hz, 2H), 6.40 (t, *J* = 1.6 Hz, 1H), 4.82 (d, *J* = 1.6 Hz, 2H), 3.82 (s, 3H), -0.03 (s, 9H).

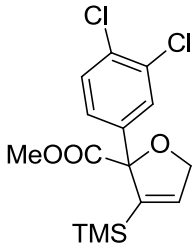
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.20, 144.06, 140.54, 139.94, 131.47, 128.66, 122.41, 98.61, 76.91, 52.56, -0.23;

HRMS (ESI): *m/z* calcd for $C_{15}H_{20}O_3{}^{79}Br^{28}Si$, 355.0360, found 355.0360 $[M+H]^+$.

HPLC: SS_WHELK, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 11.91 (major), 14.17 min (minor), 94% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = -30.32 (*c* 1.65, $CHCl_3$).

methyl 2-(3,4-dichlorophenyl)-3-(trimethylsilyl)-2,5-dihydrofuran-2-carboxylate (4.32):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 3-(trimethylsilyl)prop-2-yn-1-ol (96 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-diazo-2-(3,4-dichlorophenyl)acetate (122 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2953, 2899, 2852, 1733, 1251, 840;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.1, 1H), 7.39 (br, 1H), 7.15 (dd, *J* = 8.4, 2.2, 0.5 Hz, 1H), 6.42 (t, *J* = 1.2 Hz, 1H), 4.83 (d, *J* = 1.2 Hz, 2H), 3.82 (s, 3H), 0.01 (m, 9H).

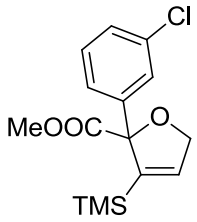
^{13}C NMR (100 MHz, $CDCl_3$): δ 171.83, 143.84, 141.10, 141.04, 132.52, 132.40, 130.29, 129.23, 126.34, 98.05, 77.07, 52.75, -0.22;

HRMS (ESI): *m/z* calcd for $C_{15}H_{19}O_3{}^{35}Cl_2{}^{28}Si$, 345.0480, found 345.0479 $[M+H]^+$;

HPLC: SS_WHELK, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 9.35 (major), 10.30 min (minor), 86% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_{D}$ = -29.86 (*c* 1.66, $CHCl_3$).

methyl 2-(3-chlorophenyl)-3-(trimethylsilyl)-2,5-dihydrofuran-2-carboxylate (4.33):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and methyl 2-diazo-2-(3,4-dichlorophenyl)acetate was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Methyl 2-(3-chlorophenyl)-2-diazoacetate (105 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2952, 2898, 2850, 1732, 1251, 1099, 1076, 840;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 – 7.24 (m, 3H), 7.15 (ddd, *J* = 3.7, 3.8, 2.9 Hz, 1H), 6.39 (t, *J* = 1.6 Hz, 1H), 4.83 (dd, *J* = 13.9, 1.7 Hz, 1H), 4.79 (dd, *J* = 13.9, 1.6 Hz, 1H), 3.81 (s, 3H), -0.03 (s, 8H).

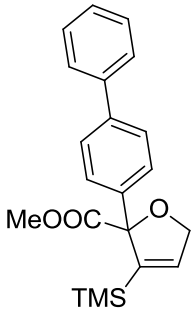
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.10, 144.03, 142.83, 140.67, 134.34, 129.63, 128.50, 127.29, 124.99, 98.59, 76.99, 52.65, -0.24;

HRMS (ESI): *m/z* calcd for $C_{15}H_{20}O_3{}^{35}Cl^{28}Si$, 311.0870, found 311.0869 $[M+H]^+$.

HPLC: SS_WHELK, 1 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 10.93 (major), 12.07 min (minor), 92% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = -28.13(*c* 1.04, $CHCl_3$).

methyl 2-([1,1'-biphenyl]-4-yl)-3-(trimethylsilyl)-2,5-dihydrofuran-2-carboxylate (4.34):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 3-(trimethylsilyl)prop-2-yn-1-ol (96 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^oC. Methyl 2-([1,1'-biphenyl]-4-yl)-2-diazoacetate (126 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2952, 2897, 2847, 1850, 1732, 1251, 1073, 836;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 – 7.54 (m, 5H), 7.47 – 7.40 (m, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 6.43 (t, *J* = 1.6 Hz, 1H), 4.87 (dd, *J* = 13.9, 1.7 Hz, 2H), 4.83 (dd, *J* = 14.1, 1.8 Hz, 2H), 3.86 (s, 3H), 0.01 (s, 9H).

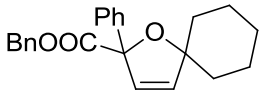
^{13}C NMR (101 MHz, $CDCl_3$): δ 172.60, 144.16, 141.10, 140.72, 140.31, 139.78, 128.91, 127.55, 127.24, 127.05, 98.99, 76.78, 52.45, -0.19;

HRMS (ESI): *m/z* calcd for $C_{21}H_{25}O_3{}^{28}Si$, 353.1573, found 353.1571 $[M+H]^+$.

HPLC: SS_WHELK, 2 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 18.05 (major), 21.56 min (minor), 92% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = -17.15 (*c* 2.88, $CHCl_3$).

benzyl 2-phenyl-1-oxaspiro[4.5]dec-3-ene-2-carboxylate (4.36):



A mixture of *(S)*-xylyl-BINAP$(AuCl)_2$ (36 mg, 0.03 mmol), silver hexafluoroantimonate (8.6 mg, 0.025 mmol) and 1-ethynylcyclohexan-1-ol (93 mg, 0.75 mmol) was mixed in 3 mL of DCE in an oven-dried round-bottom flask covered with aluminum foil, purged with Ar for 20 min. Then the mixture was cooled to -78 ^{o}C. Benzyl 2-diazo-2-phenylacetate (126 mg, 0.5 mmol) was dissolved in 9 mL of DCE then added to former solution in 3 h by syringe pump. After the addition, the bath was allowed to warm up and reaction mixture was stirred overnight.

Purified by silica gel chromatography (using 15:1 hexane/ethyl acetate solvent system) to isolate the product as a colorless oil.

IR (neat): 2931, 2856, 1751, 1726, 1448, 1214, 1051, 754, 728, 686;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (dd, *J* = 7.2, 1.6 Hz, 2H), 7.41 – 7.18 (m, 8H), 6.14 (d, *J* = 5.9 Hz, 1H), 6.05 (d, *J* = 5.9 Hz, 1H), 5.21 (d, *J* = 12.4 Hz, 1H), 5.11 (d, *J* = 12.4 Hz, 1H), 1.91 – 1.34 (m, 10H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.60, 141.48, 135.90, 135.49, 128.58, 128.49, 128.27, 128.11, 127.97, 127.92, 125.52, 92.69, 92.11, 67.03, 37.74, 37.70, 25.49, 23.48, 23.43;

HRMS (ESI): *m/z* calcd for $C_{23}H_{25}O_3$, 349.1804, found 349.1801 $[M+H]^+$. $]^+$.

HPLC: SS_WHELK, 2 % iPrOH/hexane, 1.0 mL/min, UV 230 nm, t: 9.14 (minor), 11.92 min (major), 92% ee with (*S*)-xylyl-BINAP$(AuCl)_2$;

$[\alpha]^{23}_D$ = -12.93 (*c* 2.09, $CHCl_3$).