STUDIES ON ENANTIOSELECTIVE DESYMMETRIZING ALKYNE HYDROSILYLATION

By

YAO CHUNG CHANG

Presented to the Faculty of the Graduate School of

The University of Texas at Arlington in Partial Fulfillment

of the Requirements

for the Degree of

MASTER OF SCIENCE IN CHEMISTRY

THE UNIVERSITY OF TEXAS AT ARLINGTON

August 2021

Acknowledgements

First, I would like to thank my research supervisor, Dr. Junha Jeon, for his guidance and support over the past year to help me achieve my first graduate degree. He enthusiastically welcomed me to join this team last year even though I have difficulty planning for my project. He is an excellent teacher who has taught me so much not only about research but also about life. Under his guidance, I have learned plenty of reactions and purification techniques, which are much more than what I can learn from books. I am very thankful to have him as my advisor.

I would also want to give my appreciate to my committee members, Dr. Carl J. Lovely and Dr. He Dong. Moreover, I would also want to thank another organic faculty member, Dr. Frank Foss, and graduate students in the organic division for their advice during my studies.

I would like to give me thanks to Dr. Udaya Sree Dakarapu. She was willing to give me her advice even when she had already left the group for a while. I would like to say a special thanks to our research team member Dr. Hiep Nguyen. I really appreciate him for teaching me to start working in the lab and sharing his experience without any doubt. Also, I really appreciate our other team members, Tahmina Afroz, Suman Das Adhikary, Sabid Ahamed and our undergraduates for their hard work. My heartful thanks to Dr. Brian Edwards and Dr. Roy McDougald for their training and guidance on numerous instruments. I would also want to thank Debbie Cooke and Jill Howard for their support.

July 28, 2021

Abstract

STUDIES ON ENANTIOSELECTIVE DESYMMETRIZING ALKYNE HYDROSILYLATION

Yao Chung Chang, M.S

The University of Texas at Arlington, 2021

Supervising Professor: Junha Jeon

This research focuses on the design and synthesis of enantioselective desymmetrizing α-hydrosilylation of propargyl alcohols to provide α-hydroxy (*E*)-vinylsilanes. Transition metal-catalyzed, regio-and stereoselective intramolecular hydrosilylation of propargylic alcohols with an easily removable acetal directing group has been studied. This project thus far screened 35 chiral ligands with rhodium (I) to achieve enantioselective alkyne hydrosilylation. This strategy consists of sequential hydrosilylation of bis-propargyl formate with iridium catalyst and intramolecular alkyne hydrosilylation with chiral rhodium catalyst. To this end, a variety of chiral phosphine ligands has been tested, yet an enantiomeric excess of the α-hydroxy (*E*)-vinylsilanes has not been fruitful thus far, which was determined by chiral HPLC analysis. However, the result showed that the bulkier chiral ligands generally gave better enantioselectivity. In future, further ligand

screening as well as structural modification of hydrosilane will be performed to achieve the enantioselective intramolecular α-hydrosilylation of propargyl alcohols.

Table of Contents

List of Illustrations

List of Tables

1. Introduction

Organosilanes are commercially available and relatively cheap. Organosilanes also have the advantage of being virtually nontoxic and stable. They are used as important synthetic building blocks to produce bioactive small molecules and useful materials.[1] In organic synthesis, organosilanes also play an important role as a protecting group and a reducing agent.[2] In this role, hydrosilanes that have one or more hydrogen atoms which are attached to a silicon atom can reduce substrates via an ionic or free radical pathway. The resulting vinyl silyl groups can be converted into some useful functional groups which are important. Possible reactions include cycloaddition, oxidation, stereoselective substitution and various organometallic reactions.[3-4]

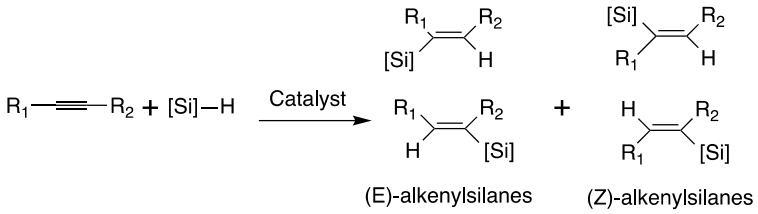
2. Introduction of Alkyne hydrosilylation

Hydrosilylation is described as an addition reaction of silicon-hydrogen bonds across unsaturated bonds, such as alkene, alkyne, and carbonyl, to create various silicon-containing compounds. Alkyne hydrosilylation is one of the most effective pathways to generate organosilane compounds.[5] Many metal catalysts had been used for alkyne hydrosilylation, which includes iron, ruthenium, iridium and rhodium.[6-8] [14-16] Alkyne hydrosilylation can be classified into intermolecular and intramolecular alkyne hydrosilylation.

2a. Intermolecular Alkyne hydrosilylation

Based on the direction of the addition of hydrogen-silicon bond to the triple bond, the intermolecular alkyne hydrosilylation reaction could generate a mixture of four alkenylsilane isomers, which are shown in Scheme 1. (*E*)-Alkenylsilane isomers are generated by addition of

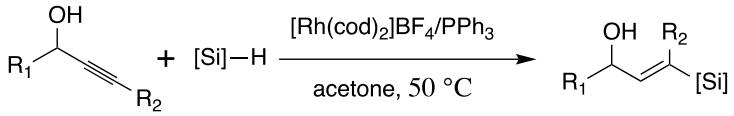
the hydrogen-silicon bond from the same direction of the triple bond, and (Z)-isomers were formed by the opposite approach of two hydrogen-silicon compounds to alkyne.



Scheme 1 Intermolecular alkyne hydrosilylation

2a-1. Takeuchi's intermolecular alkyne hydrosilylation

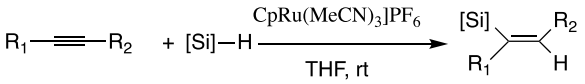
To achieve regio- and stereo selective alkyne hydrosilylation, Takeuchi used $[Rh(COD)_2]BF_4$ as the catalyst to successfully produce (E)-alkenylsilane through a *syn*-addition of hydrosilane to alkyne (Scheme 2). [6]



Scheme 2 Takeuchi's intermolecular alkyne hydrosilylation

2a-2. Trost's intermolecular alkyne hydrosilylation

Trost reported that $CpRu(MeCN)_3PF_6$ catalyst (Cp* = pentamethylcyclopentadiene) facilitates to provide (*Z*)- alkenylsilane as a major product via an *anti*-addition of hydrosilane to alkyne in intermolecular alkyne hydrosilylation (Scheme 3).[7]

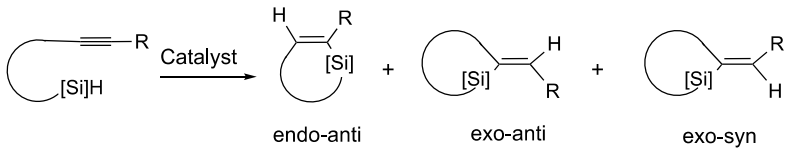


Scheme 3 Trost's intermolecular alkyne hydrosilylation

Although the successful examples described above, hydrosilylation of unsymmetrical alkyne suffers from formation of an inseparable mixture of stereoisomers and regioisomers. To address the regioselectivity, a directing group strategy has been introduced. The proximal selectivity is generally preferred in the presence of a directing group.

2b. Intramolecular alkyne hydrosilyaltion

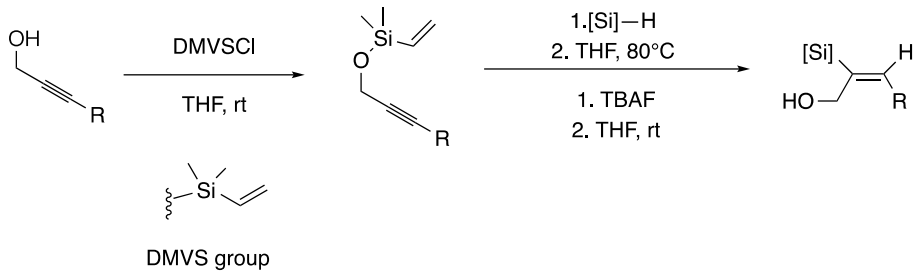
In intramolecular alkyne hydrosilyaltion, based on the way of the addition of hydrogen-silicon bond to the triple bond, the reaction would generate a mixture of maximum of three alkenylsilane isomers (Scheme 4). Two alkenylsilane isomers would be an anti-addition with *endo-anti* alkenylsilanes and *exo-anti* alkenylsilanes. The last product can be formed through a syn addition with *exo-syn* fashion.



Scheme 4 Intramolecular alkyne hydrosilylation

2b-1. Kawasaki's intermolecular alkyne hydrosilyaltion

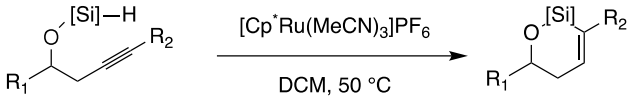
Kawasaki reported that use of DMVS (dimethylvinylsilyl) group is an effective directing group to give α-selective hydrosilylation of propargyl alcohols (Scheme 5).[8] Karstedt's catalyst was used as metal catalyst to facilitate α- and *syn*-selective hydrosilylation of propargyl alcohols with good yield.



Scheme 5 Kawasaki's intermolecular alkyne hydrosilylation

2b-2. Trost's intramolecular alkyne hydrosilylation

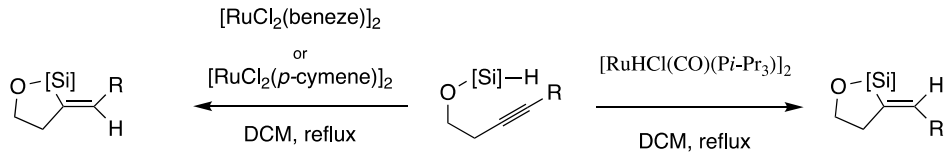
Trost reported the intramolecular hydrosilylation with internal alkynes by using [{$Cp^*Ru(MeCN)_3$}PF_6] as the catalyst.[9] β and *endo-dig* selective hydrosilylation products were obtained (Scheme 6).



Scheme 6 Trost's intramolecular alkyne hydrosilylation

2b-3. Denmark's intramolecular alkyne hydrosilylation

Denmark addressed the regioselectivity issue with a two-atom disiloxane ether directing group to produce a six-membered disiloxane (Scheme 7).[10] Reaction of alkynyl silyl ether with different ruthenium catalysts, $[RuCl_2(C_6H_6)_2]_2$ and $[RuHCl(CO)(P\textit{i}\text{-}Pr_3)]_2$, provided two isomers selectively. *Exo*- and *anti*-alkyne hydrosilylation products were produced with $[RuCl_2(C_6H_6)_2]_2$, and *exo*- and *syn*-alkyne hydrosilylation product were produced with $[RuHCl(CO)(P\textit{i}\text{-}Pr_3)]_2$.



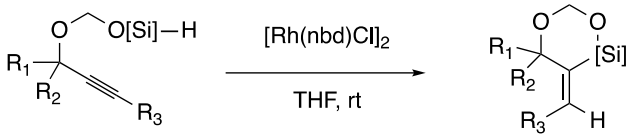
Scheme 7 Denmark's intramolecular alkyne hydrosilylation

3. Acetal-directed intramolecular alkyne hydrosilylation

The alkyne groups would undergo an intramolecular hydrosilylation with $[Rh(nbd)Cl]_2$ and phosphous ligands to form cyclic silylactals, which would create a new chiral center. However, the enantioselective desymmetrizing intramolecular alkyne hydrosilylation is still unknown.

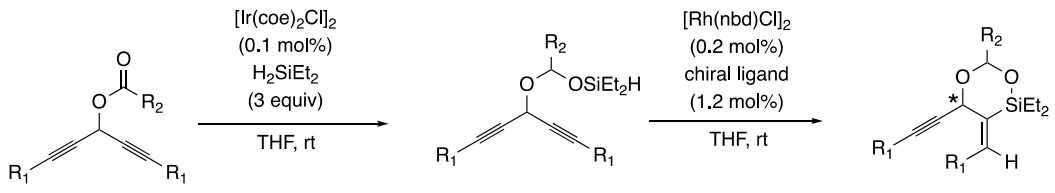
4. Jeon group's intramolecular alkyne hydrosilylation

Jeon group reported hydrosilylation of propargylic esters with traceless acetal directing group by using $[Rh(nbd)Cl]_2$ (Scheme 8). An α- and *exo-syn* selective hydrosilylation of propargyl esters provided the cyclic α-(*E*)-vinylsilanes, dioxasilinanes. The acetal directing group is widely available, easily installable, and does not require purification. The directing group can be removed to get α-hydroxy (*E*)- vinylsilanes.



Scheme 8 Our group's intramolecular alkyne hydrosilylation

The bis-alkyne group undergoes an intramolecular hydrosilylation with $[Rh(nbd)Cl]_2$ and phosphine ligand to form cyclic silylactals with the intramolecular hydrosilylation, which would create a new chiral center (Scheme 9). However, the enantioselective intramolecular alkyne hydrosilylation is still unknown.



Scheme 9 Jeon group's strategy in hydrosilylation of propargyl alcohols

5. Introduction of enantioselective synthesis

Enantioselective synthesis involves a reaction that one or more new chiral elements is (are) created in the substrate. Enantioselective synthesis has been an important area in organic synthesis and is particularly significant in the biomedical field, because different enantiomers or diastereomers compounds usually have different biological activities. Asymmetric induction can include the chirality transfer by reagents, substrates, catalysts, and even reaction environment. This associates with making the activation energy changes of one enantiomer over other enantiomer. Multiple methods have been known to achieve enantioselective reactions. The most common methods include chiral poor synthesis, chiral auxiliaries, kinetic resolution, and chiral catalyst.

5a. Chiral pool

The chiral pool is one of the oldest, but simplest enantioselective syntheses. An easily accessible chiral starting material would undergo a series reaction, with chiral or achiral reagents to produce a target molecule. This chiral poor is appealing for those molecules which have chirality with relatively inexpensive molecules. However, only a few molecules can undergo this kind of reaction and the pathway of the reactions is limited.

5b. Chiral auxiliary

Chiral auxiliary assists the compounds to undergo an intramolecular asymmetric induction. After the reaction is finished, the chiral auxiliary would be removed without affecting the enantiomeric excess of the resulting chiral compound.[11] Typically, the chiral auxiliary could be recovered after the reaction is completed. A main advantage of chiral auxiliary is that the products

from chiral auxiliary are diastereomers, which can be easily separated by column chromatography and the auxiliary can be removed easily.[11]

5c. Kinetic resolution

Kinetic resolution differentiates two enantiomers in a racemic mixture. Two different enantiomers would have different reaction rates in a reaction with a chiral reagent or catalyst. Compared to chiral resolution, kinetic resolution relies on the different chemical properties of the diastereomeric products instead of the physical properties. Kinetic resolution depends on the reactivity of each enantiomer. Before a full completion of the reaction, an enantiomeric excess of the unreacted starting material would be continuously increased. Therefore, the kinetic resolution is an important technique for the synthesis of enantiomerically enriched products.

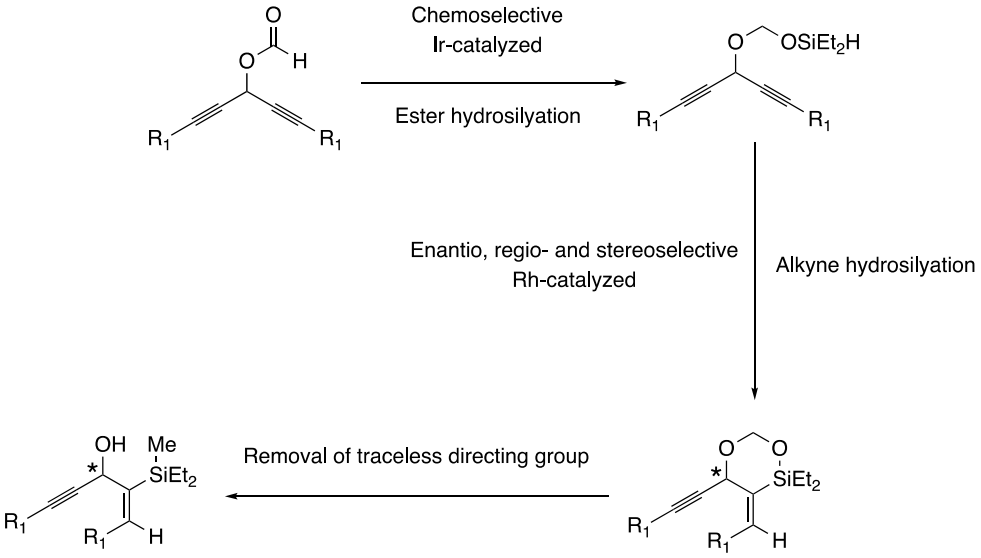
5d. Enantioselective catalysis

Enantioselective catalysis uses chiral catalysts. The chiral metal catalysts are often assembled with transition metal and chiral ligands. A low substrate to catalyst ratio can provide an effective enantioselective reaction.[12] Therefore, it is suitable to use enantioselective catalysis from milligram scale reactions to industrial-scale reactions.

6. Research Design for enantioselective desymmetrizing hydrosilylation of bis-propargyl alcohols with a traceless acetal directing group

We aimed to develop a catalytic system that generates the enantioenriched cyclic α-(*E*)-dioxasilinanes by sequential hydrosilylation of propargyl alcohols (Scheme 10). The pathway consists of one-pot iridium-catalyzed ester hydrosilylation and rhodium-catalyzed alkyne

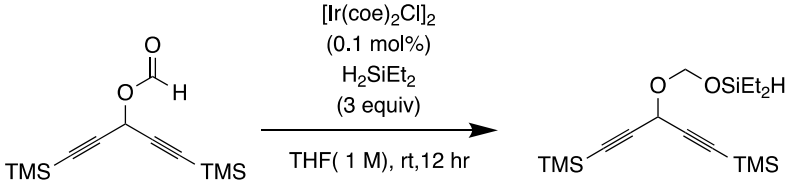
hydrosilylation. During the rhodium-catalyzed cyclization, a new chiral center would be introduced. After the traceless acetal directing group is removed, the enantiomeric excess of α-hydroxy-(*E*)-vinylsilanes can be analyzed by chiral HPLC.



Scheme 10 Proposed design for hydrosilylation of propargyl alcohols

7. Ir-Catalyzed ester hydrosilylation of propargyl alcohols

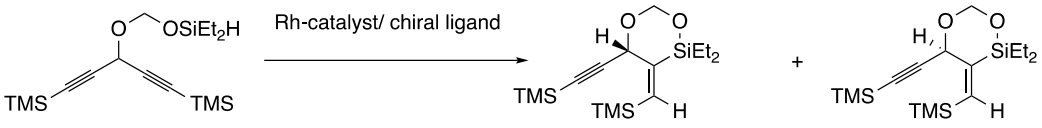
We aimed to develop the chemoselective ester hydrosilylation of bis-propargyl alcohols (Scheme 11). Ester hydrosilylation of symmetrical propargyl ester which can be produced from double addition of a propargyl group to methyl formate has been demonstrated in previous researches.[13-15] In earlier work, ester hydrosilylation would produce a hydrosilylacetal in different substrate classes. In detail, the propargylic ester reacted with diethylsilane with iridium catalyst which generated hydrosilyl acetals in quantitative yield.



Scheme 11 Ir-Catalyzed ester hydrosilylation of propargyl alcohols

8. Rh-Catalyzed alkyne hydrosilylation

The goal of this research is to find out regio-, enantio-, and stereoselective rhodium-catalyzed bis-alkyne hydrosilylation to generate a cyclic enantio-enriched α-(*E*)-vinylsilanes enantiomers.

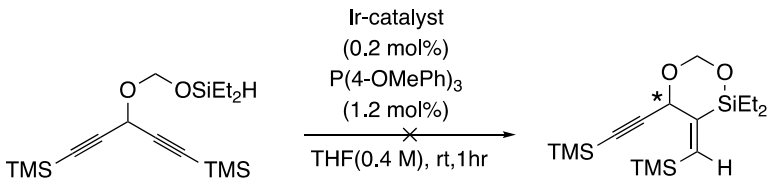


Scheme 12 Rh-Catalyzed alkyne hydrosilylation

9. Initial studies

9a. Initial studies: Survey of metal catalyst

According to Dr. Dakarapu's report, $[Rh(nbd)Cl]_2$ performed well as the catalyst for alkyne hydrosilylation with propargylic acetate to generate the cyclic α-(E)-vinylsilanes. Two other catalysts replaced the $[Rh(nbd)Cl]_2$ to develop catalyst diversity. $[Ir(coe)_2Cl]_2$ and $[Ir(cod)OMe]_2$ (cod = cyclooctadiene) were used with the same amount as $[Rh(nbd)Cl]_2$ (Scheme 13). However, the desired product has not detected at both room temperature and under heating conditions (Table 1). Those iridium-catalysts can only catalyze the ester hydrosilylation instead of the alkyne hydrosilylation.



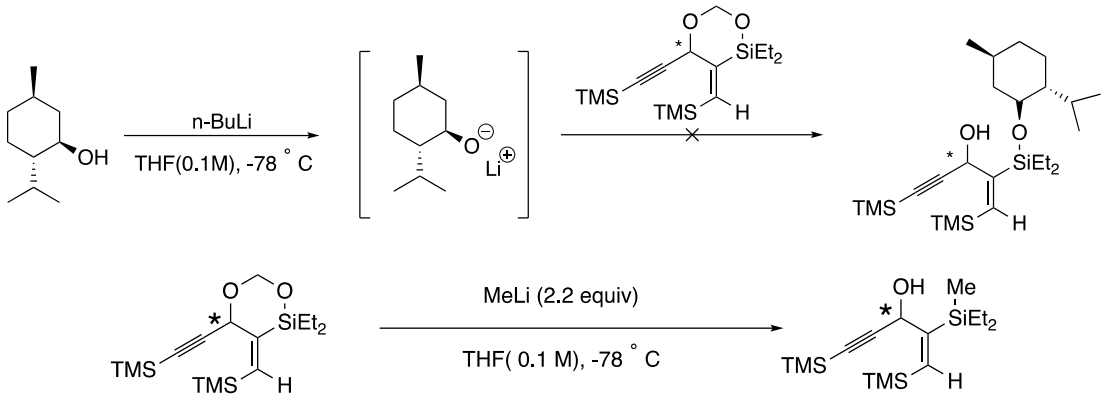
Scheme 13 Initial studies- Ir-Catalyzed alkyne hydrosilylation

Entry	Supporting Catalyst	Temperature	Yield
1	$[Ir(coe)_2Cl]_2$	Room Temperature	Not detected
2	$[Ir(cod)OMe]_2$	Room Temperature	Not detected
3	$[Ir(coe)_2Cl]_2$	100 °C	Not detected
4	$[Ir(cod)OMe]_2$	100 °C	Not detected

Table 1 Initial studies- Ir-Catalyzed alkyne hydrosilylation optimization

9b. Initial studies: Optimization for removing the traceless acetal directing group

The removal of traceless acetal directing group underwent with addition of a nucleophile to (*E*)-dioxasilinanes to generate (*E*)-vinylsilanes. Two different nucleophiles were considered; first, oxygen nucleophiles were tested (Scheme 14). Lithio L-menthol nucleophile was prepared through a reaction of L-menthol reacts with *n*-BuLi. The nucleophilic addition reaction to the silicon center of (*E*)-dioxasilinanes opens the acetal ring and generates the diastereomeric mixture. A benefit of this strategy is that the ratio of diastereomers could be obtained from the NMR spectrum and thus determine enantioselectivity from there. Another strategy is use of carbon nucleophiles. MeLi as the nucleophile removes the acetal group in the same manner as the oxygen nucleophile to generate (*E*)-vinylsilanes. With this strategy, the enantiomeric ratio of the resulting products can be identified by chiral HPLC. Unfortunately, the product of the first strategy was not detected, where desilylation product was mainly observed (Table 2). The addition of MeLi indeed produced (*E*)-Vinylsilanes in an excellent yield (90%) (Table 2).



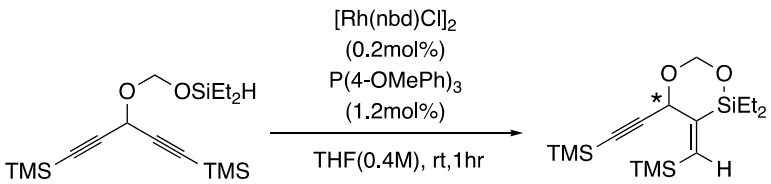
Scheme 14 Initial studies- removal traceless directing group optimization

Entry	Nucleophile	Yield
1	L-menthol	Not detected
2	MeLi	90%

Table 2 Initial studies- removal traceless directing group optimization

9c. Initial studies: Determining the enantiomer excess of the hydrosilylation reaction with racemic phosphine ligand

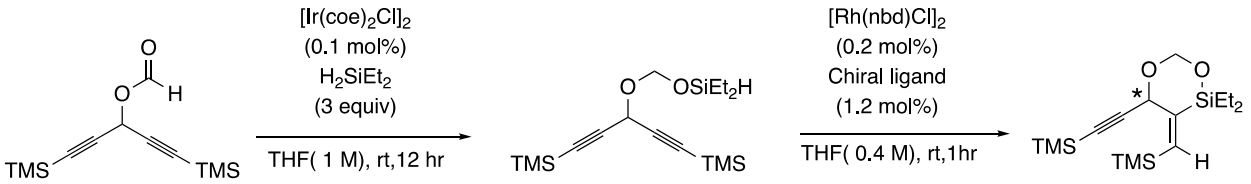
Before starting the chiral ligand screening, the enantiomeric excess from racemic ligand should be determined first. Theoretically, the enantiomers amount should be equal with the racemic ligand from the reaction. With the $P(4\text{-}OMePh)_3$ as the racemic ligand, the yield of the reaction was 84%, and the enantiomer excess was calibrated using Chiralpak chiral column with solvent 100% n-hexane with the flow rate 1mL per minute (Scheme 15).



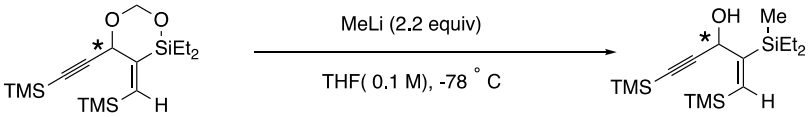
Scheme 15 Initial studies- racemic ligand optimization

10. Scope of various phosphine ligands

Various phosphine supporting ligands were examined, with modulation of electronic and steric capabilities to rhodium (I) metal in the enantioselective alkyne hydrosilylation at room temperature (Scheme 16). After removing the directing group of the acetal group, the enantiomer of α-hydroxy-(*E*)-vinylsilane were separated through the chiral HPLC conditions optimized (Scheme 17). The ligand screening did not show good enantioselectivity. Most of the ligand showed the enantiomer excess of around 0 to 3%, which means the chiral ligand does not affect the enantioselectivity during the cyclization process. Although we did not find the optimal ligand for the enantioselective alkyne hydrosilylation, we gained some insights into the ligand optimization. The more steric the ligand is, the more enantioselective the reaction would be. For example, in the case of BABIBOP ligands (entries 28-31, Table 4) the enantiomeric excess increased as the steric capabilities increase. Some ligands exhibited the inverse selectivity of the reaction with respect of steric hindrance. For instance, in the case of SDP ligands (entries 32-34, Table 4) the enantiomeric excess increased as the steric capabilities decreased. However, most of the results showed that the high enantioselectivity can be obtained through change of the electronic and steric capabilities of the ligands.



Scheme 16 Ligand screening for alkyne hydrosilylation

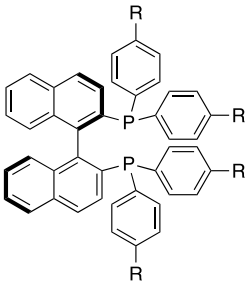


Scheme 17 Removal traceless acetal-directing group

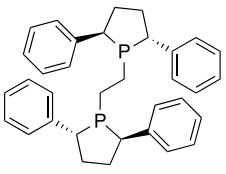
Entry	% ee	% er
1	-0.85	50.08:49.91
2	-0.44	50.30:49.70
3	-0.94	50.04:49.96
4	-0.54	50.25:49.75
5	-0.45	50.29:49.70
6	-1.34	49.85:50.15
7	-0.36	50.34:49.66
8	-1.49	49.77:50.23
9	6.32	53.67: 46.38
10	-0.33	50.35:49.65
11	3.28	52.16:47.84
12	-2.04	49.49:50.51
13	0.39	50.71:49.29
14	-0.56	50.24:49.76
15	-2.36	49.33:50.67
16	-2.02	49.51:50.49
17	0.75	50.89:49.11
18	1.16	51.10:48.90
19	-0.91	50.06:49.94
20	-3.54	48.74:51.26
21	2.40	51.72:48.28

22	2.25	51.64:48.36
23	1.66	51.34:48.36
24	-1.03	50.00:50.00
25	3.78	52.41:47.59
26	1.90	51.47:48.53
27	4.01	52.52:47.48
28	3.97	52.50:47.50
29	5.20	53.11:46.89
30	7.37	54.20:45.80
31	8.51	54.77:45.30
32	5.55	53.27:46.78
33	5.72	53.38:46.62
34	8.22	54.62: 45.38
35	-1.33	49.85:50.15
36	1.25	51.14:48.86
37	2.07	51.55:48.45

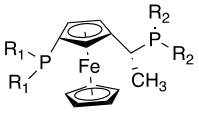
Table 3 Chiral ligand screening



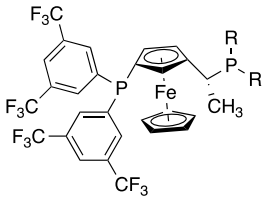
1. R = H
2. R = Me



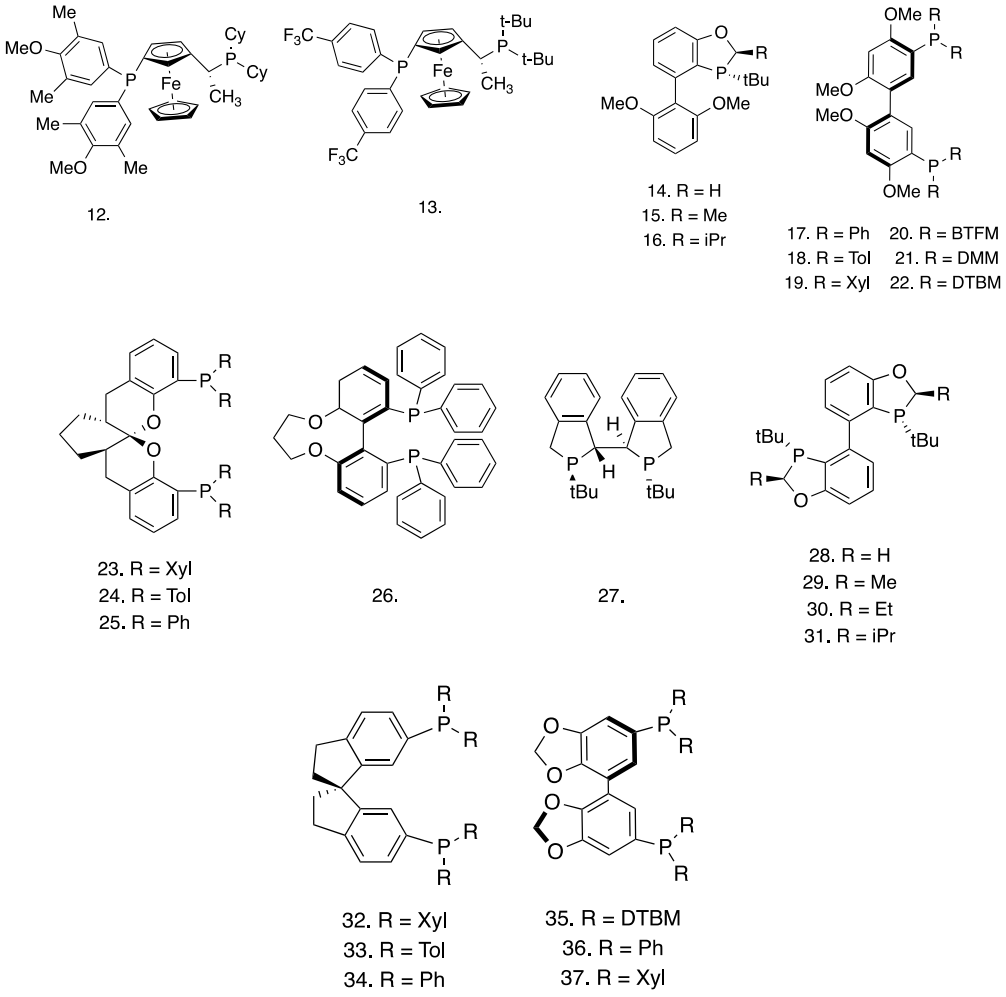
3.



4. R_1 = Cy, R_2 = Cy
5. R_1 = Cy, R_2 = t-Bu
6. R_1 = Xyl, R_2 = Furan
7. R_1 = Ph, R_2 = t-Bu
8. R_1 = Ph, R_2 = Cy
9. R_1 = Ph, R_2 = Xyl



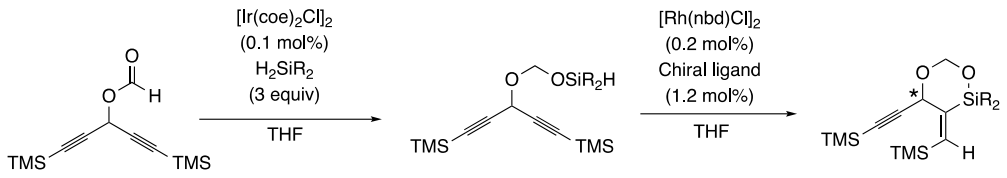
10. R = Cy
11. R = Xyl



Scheme 18 Chiral ligand structure

11. Future work

Although we did not find a suitable chiral ligand to get a reasonable enantiomeric ratio, we did get some insights from the experiment. From the results, we will first introduce a bigger substituent into the silicon group. During the hydrosilylation, we can use other types of hydrosilanes to produce hydrosilyl acetal. Diisopropylsilane, di-tert-butylsilane, and diphenylsilane can be used to improve enantioselectivity in combination with bulkier chiral ligands.



Scheme 19 Alkyne hydrosilylation with different silanes

12. Summary

In summary, the design of the catalytic system for traceless acetal-directing group-directed, enantioselective iridium and rhodium-catalyzed hydrosilylation of propargyl alcohol to produce *(E)*-vinylsilanes through dioxasilinanes has been studied. The result from the ligand screening showed that enantioselectivity is closed related to the electronic and steric capabilities of the ligands. Therefore, the steric and electronic impacts of ligands and hydrosilanes will be studied in future.

Appendix A: List of Abbreviations

δ: chemical shift (ppm)

μL: microliter

Ac: acetate

Bn: benzyl

nBu: n-butyl

*t*Bu: tert-butyl

C: Celsius

calcd: calculated

cat.: catalyst, catalytic amount

coe: cyclooctene

COD: 1,5-cyclooctadiene

Cy: cyclohexyl

DCM: dichloromethane

equiv.: equivalent

Et: ethyl

g: gram

hr: hours

HRMS: high resolution mass spectrometry

Hz: hertz

IR: infrared spectroscopy

J: coupling constant, NMR spectroscopy

M: molar

[M+]: molecular ion

Me: methyl

min: minutes

mg: milligram

MHz: megahertz

mL: milliliter

mmol: millimole

MW: molecular weight

nbd: norbornadiene

ph: phenyl

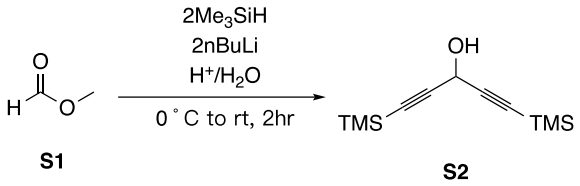
NMR: nuclear magnetic resonance spectroscopy

Appendix B: Experimental Procedures

Materials and Methods

Reactions which required anhydrous conditions were undergoing the nitrogen environment in flame-dried glassware. Anhydrous toluene and dichloromethane (DCM) were distilled from CaH_2. Anhydrous tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium and benzophenone. All reagents and other solvents which purchased from the commercial were used as supplied. ^1H, ^2H, and ^{13}C NMR spectra were recorded on JEOL Eclipse Plus 500 (500 MHz) and JEOL ECX 300 (300 MHz) spectrometers. NMR spectra were recorded by 300 or 500 MHz NMR spectrometer. ^1H NMR chemical shifts are referenced to chloroform-D (7.26 ppm) and benzene-D_6 (7.16 ppm). ^{13}C NMR chemical shifts are referenced to $^{13}CDCl_3$ (77.23 ppm), and benzene-D_6 (128.39ppm). The following abbreviations are used to describe multiplets: s (singlet), d (doublet), t (triplet), q (quartet), pent (pentet), m (multiplet), nfom (non-first- order multiplet), and br (broad). ^1H NMR assignments are indicated by structure environment (e.g., $CH_a\boldsymbol{H}_b$). Infrared (IR) spectra were recorded using neat (for liquid compound) from a concentrated DCM solution. Absorptions are reported in $cm^{-1.}$ Only the most intense and diagnostic peaks are reported. High-resolution mass spectra (HRMS) were recorded in atmospheric-pressure chemical ionization and time-of-flight (APCI/TOF) mode. Samples were introduced as solutions in DCM solution. MPLC refers to medium pressure liquid chromatography (25-200 psi) using hand-packed columns of silica gel (20-45 μm, spherical, 70 Å pore size) with a HPLC pump and a differential refractive index detector. TLC analysis experiments were performed on F254 plate and stained by potassium permanganate solution. HPLC analysis using chiralpal column with 100% n-hexane and flow rate 1mL per minute.

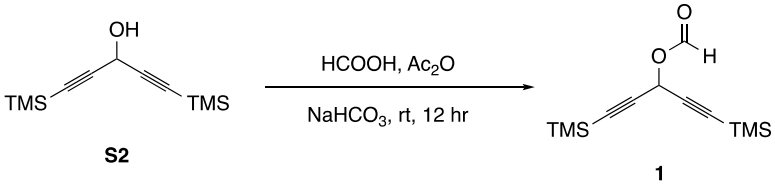
Procedure for propargyl alcohol



S1 **S2**

n-BuLi (30mL, 2 equiv., 60 mmol, 2M in hexane) was added to a solution of trimethylsilylacetylene (8.4 mL, 2 equiv, 60 mmol) in THF (60 mL, 0.5 M) at 0 °C. The colorless mixture was stirred for 15 minutes at 0 °C. Methyl formate **S1** (1.86mL,1 equiv., 30 mmol) was then added dropwise, and the resulting bright yellow mixture was stirred at room temperature for 2 hours. The resulting red mixture was quenched by addition of water. Then the mixture was poured into a separatory funnel containing EtOAc 150 mL and saturated aqueous NH_4Cl 150 mL. The layers were separated and the organic layer was washed with brine 150 mL and then water 150 mL. The organic phase was dried over $MgSO_4$, filtered with a filter paper and concentrated to give a deep red oil. This crude material was purified through flash chromatography (hexanes: EtOAc = 10:1) to give pure alcohol **S2**.

Procedure for propargyl ester

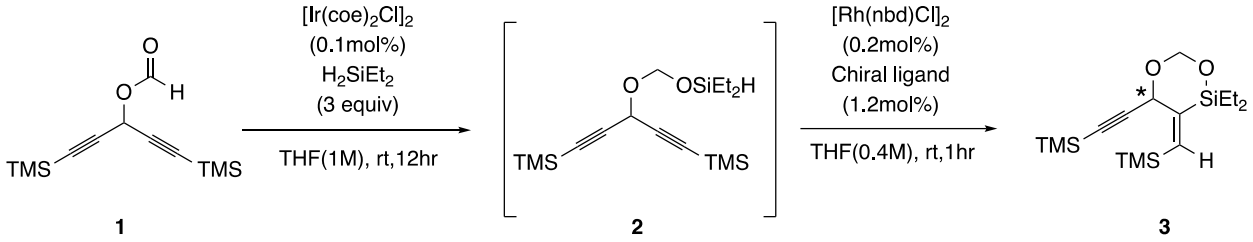


S2 **1**

Formic acid (10.8 mL, 10.6 equiv., 286.2 mmol) and acetic anhydride (21.6 mL, 8.3equiv., 224.1mmol) were added into a flame-dired flask at 0 °C. The solution was heated up to 60 °C by a sand bath and stirred for 30 minutes. The resulting mixture was cooled to room temperature, and propargyl alcohol **S2**(6.1 g, 1 equiv., 27 mmol) and $NaHCO_3$ (4.86 g, 2.1 equiv, 56.7 mmol) were added into the solution and stirred overnight. The resulting deep red mixture was quenched by

addition of water. Then the mixture was poured into a separatory funnel containing Et_2O 150 mL and 150 mL saturated NH_4Cl solution. The layers were separated and the organic layer was washed with 150 mL brine and then 150 mL water. The organic phase was dried over Na_2SO_4, filtered, and concentrated to provide a deep red oil. This crude material was purified through flash chromatography (hexanes: EtOAc = 20: 1) to provide pure ester **1**.

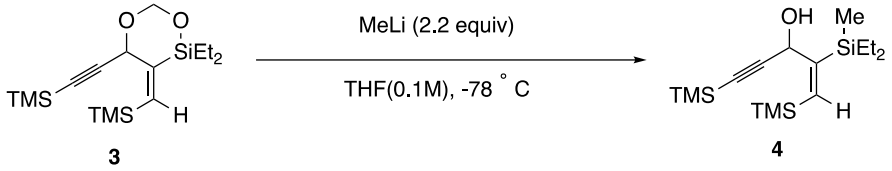
Procedure for Propargyl ester to Prepare Dioxasilinanes



$[Ir(coe)_2Cl]_2$ (0.18mg, 0.1mol%) and propargyl ester **1**(50 μL,1 equiv., 0.2 mmol) under the N_2 atmosphere, THF (0.2 ml, 1 M) were added to a flame-dried flask. Diethylsilane (0.1 mL, 3 equiv., 3mmol) was added to the mixture. The septum on the vial was replaced by a screw cap with a Teflon liner. The reaction mixture was kept at room temperature and stirred for 12 hours. The volatiles were removed *in vacuo* to afford the silyl acetal **2**, which were directly used for subsequent reactions without further purification.

The crude diethylhydrosilyl acetal **2** were dissolved in THF (0.5 mL, 0.4 M) and $[Rh(nbd)Cl]_2$ (0.18mg, 0.2 mol%) and a ligand (1.2 mol%) were added into the vial. The septum on the vial was replaced by a screw cap with a Teflon liner. The reaction mixture is kept at room temperature and stirred for 1.5 hours. The volatiles were removed *in vacuo,* and the resulting mixture was dissolved with pentane, filtered through a pad of Celite® and concentrated under vacuum to give crude cyclic α-(E)-vinylsilanes **3**, with was purified by MPLC (hexanes: ethyl acetate = 40: 1) to afford as a bright yellow oil.

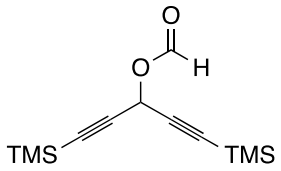
Procedure for Nucleophilic Ring opening of Dioxasilinanes



Dioxasilolane **2**(34 mg, 1 equiv.,0.1 mmol) in THF (1 mL, 0.1 M) was added and mixture cooled to –78 °C. MeLi (0.06mL, 2 equiv., 0.2mmol, 3M in Et_2O) was added slowly to the reaction mixture. After being stirred for 30 minutes at –78 °C, the reaction mixture was quenched with water and extracted with Et_2O. The volatiles were removed to afford crude material, which was purified by MPLC (hexanes: EtOAc = 20:1) to afford as a bright yellow oil.

Appendix C: Spectral data of the compounds

1,5-Bis(trimethylsilyl)penta-1,4-diyn-3-yl formate (1)



Yield: 5.5 g, 80%

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.09 (s, 1H, *H*C=O), 6.13(s, 1H, O-C*H*), and 0.20 [s, 18H, Si(CH_3)$_3$].

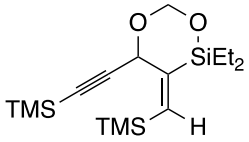
^{13}C NMR ($CDCl_3$, 125 MHz): δ 158.9, 97.3, 91.6, 53.3 and -0.4

IR (neat): 2961 (w), 2185 (m), 1735 (s), 1411 (s), 1250 (s), 990 (s), 836 (s), 758 (s) cm^{-1}.

TLC: R_f = 0.5 in 20:1 hexanes: EtOAc.

HRMS (**APCI/TOF**): Calcd for $(M+H)^+$ $(C_{12}H_{21}O_2Si_2)^+$: 253.2080. Found: 253.2049.

(*E*)-2,2-Diethyl-4-((trimethylsilyl)ethynyl)-3-((trimethylsilyl)methylene)-1,5,2-dioxasilinane (2)



Yield: 65.1 mg, 90%

^{1}H NMR (C_6D_6, 500 MHz): δ 5.98 (d, *J* = 1.5 Hz, 1H, C=C*H*TMS), 5.81 (d, *J* = 6.12 Hz, 1H, OC*Ha*HbO), 5.60 (d, *J* = 1.5 Hz, 1H, O-C*H*), 5.12 (d, *J* = 6.12 Hz, 1H, OCHa*Hb*O), 1.13 (dd, *J* = 7.8, 1.2 Hz, 3H, SiCH$_2$CH_3), 1.08 (dd, *J* = 7.8, 1.3 Hz, 3H, SiCH$_2$CH_3), 0.83-0.62 (m, 4H, SiCH_2CH$_3$), and 0.13 [s, 9H, Si(CH_3)$_3$] and 0.09 [s, 9H, Si(CH_3)$_3$].

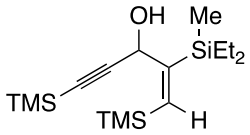
^{13}C NMR (C_6D_6, 125 MHz): δ 158.2, 142.0, 102.3, 95.2, 86.7, 72.5, 6.8, 6.7, 6.6(2), –0.4 and –0.6

IR (neat): 3051 (w), 2942 (m), 2876 (m), 1372 (m), 1241 (m), 1204 (s), 762(s), and 428 (s) cm^{-1}.

TLC: R_f = 0.4 in 40:1 hexanes: EtOAc.

HRMS (**APCI/TOF**): Calcd for $(M+Na)^+$ $(C_{16}H_{32}NaO_2Si_3)^+$: 363.1608. Found: 363.1658.

(*E*)-2-(Diethyl(methoxy)silyl)-1,5-bis(trimethylsilyl)pent-1-en-4-yn-3-ol (3)



Yield: 54.9 mg, 84%

^{1}H NMR (C_6D_6, 500 MHz): δ 6.23 (s, 1H, C=C*H*TMS), 5.15(s, 1H, O-C*H*), 0.95 (dd, *J* = 7.5, 2.3 Hz, 6H, $SiCH_2CH_3$), 0.86-0.72 (m, 4H, $SiCH_2CH_3$), 0.28 [s, 9H, $Si(CH_3)_3$], 0.23 [s, 9H, $Si(CH_3)_3$)] and 0.11 (s, 3H, $SiCH_3$).

^{13}C NMR (C_6D_6, 125 MHz): δ 161.5, 144.3, 107.3, 90.5, 66.8, 7.6, 7.5, 6.3(2), 0.3, -0.5 and -4.8.

IR (neat): 3460 (br), 2954 (w), 1248 (m), 1029 (s), 863 (s), and 439 (m) cm^{-1}.

TLC: R_f = 0.5 in 20:1 hexanes: EtOAc.

HRMS (**APCI/TOF**): Calcd for $(M+H)^+$ $(C_{16}H_{34}OSi_3)^+$: 327.1996. Found: 327.1989.

Reference:

1. Fleming, I.; Barbero, A.; Walter, D. Stereochemical Control in Organic Synthesis Using Silicon-Containing Compounds. *Chem. Rev.* **1997,** *97*, 2063-2192.
2. Tamao, K.; Yao, H.; Tsutsumi, Y.; Abe, H.; Hayashi, T.; Ito, Y. Ortho lithiation directed by amino groups on silicon in phenylsilane derivatives *Tetrahedron Lett.* **1990**, *31*, 2925-2928.
3. Young, D. G. J.; Gomez-Bengoa, E.; Hoveyda, A. H., Diastereoselective Intramolecular Cycloaddition of Vinylsilanes and Silyl Nitronates. Effective Control of Remote Acyclic Asymmetry. *The Journal of Organic Chemistry* **1999,** *64*, 692-693.
4. Han, Y.-K.; Paquette, L. A. Vinylsilane mediated stereoselective total synthesis of (.+-.)-gymnomitrol. *J. Org. Chem.* **1979,** *44*, 3731-3733.
5. Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I. Eds.; Pergamon: Oxford, **1991**; Vol 8, pp. 763-792.
6. Takeuchi, R.; Nitta, S.; Watanabe, D. Complex-Catalyzed Hydrosilylation of 1-Alkynes and Tandem Hydrosilylation/Isomerization Reaction of Propargylic Alcohols to .beta.-Silyl Ketones. *J. Org. Chem*. **1995**, *60*, 3047.
7. Trost, B. M.; Ball, Z. T. Alkyne Hydrosilylation Catalyzed by a Cationic Ruthenium Complex: Efficient and General Trans Addition. *Journal of the American Chemical Society* **2005**, *127*, 17644-17655.
8. Kawasaki, Y.; Ishikawa, Y.; Igawa, K.; Tamooka, K. Directing Group-Controlled Hydrosilylation: Regioselective Functionalization of Alkyne. *Journal of the American Chemical Society* **2011**, *133*, 20712-20715.
9. Trost, B. M.; Ball, Z. T. Intramolecular endo-dig hydrosilylation catalyzed by ruthenium: evidence for a new mechanistic pathway. *Journal of the American Chemical Society* **2003**, *125*, 30-31.

10. Denmark, S.; Pan, W.; Intramolecular Anti-Hydrosilylation and Silicon-Assisted Cross-Coupling: Highly Regio- and Stereoselective Synthesis of Trisubstituted Homoallylic Alcohols. *Org. Lett.* **2002**, *4*, 4163-4166.

11. Glorius, F.; Gnas, Y., Chiral Auxiliaries – Principles and Recent Applications *Synthesis* **2006**, 12,1899–1930.

12. Heitbaum, M., Glorius, F. and Escher, I. (2006) Asymmetric Heterogeneous Catalysis. Angewandte Chemie International Edition, 45, 4732-4762.

13. Hua, Y., Asgari, P., Dakarapu, U. S., Jeon, J. Reductive arene ortho-silanolization of aromatic esters with hydridosilyl acetals. *Chem. Commun.* **2015**, *51*(18), 3778-3781.

14. Dakarapu, U. S.; Bokka, A.; Asgari, P.; Trog, G., Hua, Y.; Nguyen, H. H.; Rahman, N.; Jeon, J. Lewis Base Activation of Silyl Acetals: Iridium –Catalyzed Reductive Horner-Wadsworth-Emmons Olefination. *Org. Lett*. **2015,** *17*, 5792-5795.

15. Asgari, P., Dakarapu, U. S., Nguyen, H. H & Jeon, J. Aryne cycloaddition reactions of benzodioxasilines as aryne precursors generated by catalytic reductive ortho-C-H silylation of phenols with traceless acetal directing groups. *Tetrahedron.* **2017**, *73*(29), 4052-4061.

Biographical Information

Yao Chung Chang was born and raised in Taiwan. He obtained his B.S in Biological science from National Sun Yat-sen University, Taiwan in 2018. He obtained an M.S in organic chemistry from the University of Texas at Arlington in 2021. During his graduate studies, he started working with Dr. Jeon Junha in the field of organic chemistry and metal catalysis. Yao Chung Chang is mainly focused on developing a new strategy for enantioselective of alkyne hydrosilylation. He is intending to continue his graduate studies at the University of Texas at Arlington.