Copper-catalyzed C-SI bond formation based on SI-B bond activation

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**NANYANG
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**COPPER-CATALYZED C-SI BOND FORMATION
BASED ON SI-B BOND ACTIVATION**

**PENG WANG
SCHOOL OF PHYSICAL AND MATHEMATICAL
SCIENCES
2011**

**COPPER-CATALYZED C-SI BOND FORMATION
BASED ON SI-B BOND ACTIVATION**

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LIST OF ABBREVIATIONS

δ	chemical shift
acac	acetylacetone
Ar	aryl
BINAP	2,2'-diphenylphosphino-1, 1'-binaphthyl
B ₂ pin ₂	bis(pinacolato)diboron
calcd	calculated
Cy	cyclohexyl
d	doublet
DIBAL	diisobutylaluminium hydride
DPPE	1,2-bis(diphenylphosphino)ethane
DPPF	1,1'-Bis(diphenylphosphino)ferrocene
DPEphos	bis(2-diphenylphosphinophenyl)ether
dd	doublet of doublets
DFT	density functional theory
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethyl sulfoxide
dt	doublet of triplets
ee	enantiomeric excess
equiv.	equivalent(s)
ESI	electrospray ionization
FTIR	fourier transform infrared spectrometry
h or hrs	hour(s)
HRMS	high resolution mass spectrometry
IMe	1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene
IAd	1,3-di-(1-adamantyl)imidazole-2-ylidene
I ^t Bu	1,3-di-(1-tert-butyl)imidazole-2-ylidene
SIMe	1,3-bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene
IPr	1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene
SIPr	1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene

Johnphos	(2-biphenyl)di-tert-butylphosphine
m	multiplet
m/z	mass per charge ratio
M ⁺	parent ion peak (mass spectrum)
MOM	methoxymethyl
min	minute(s)
mol%	mole percent
MS	mass spectrometry
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance
Ph	phenyl
ppm	parts per million
q	quartet
R _f	retention factor
rt	room temperature
s	singlet
t	triplet
^t Bu	tert-butyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
UV	ultraviolet
vol	Volume
Xantphos	4,5-bis(diphenylphosphine)-9,9-dimethylxanthene

SUMMARY

This thesis describes copper-catalyzed carbon-silicon bond formations, including 1,4-addition to α,β -unsaturated esters, 1,2-addition to aldehydes and highly regioselective silylcupration of terminal alkynes, based on Si-B bond activation.

Chapter 1.

A brief summary of traditional Si-B bond activation catalyzed by transition metal catalysts is given. Some recent examples of silylboration of terminal alkynes and unsaturated carbonyl compounds are highlighted in this chapter. The mechanisms involving Si-B bond activation of above reactions are also thoroughly discussed.

Chapter 2.

A highly efficient β -silylation of α,β -unsaturated esters catalyzed by an *N*-heterocyclic carbene-copper complex based on Si-B bond activation has been developed. This new method produced highly functionalized products with a wide substrate scope, thus providing an ideal strategy to asymmetric transformations.

Chapter 3.

A new protocol to prepare α -hydroxysilanes using an *N*-heterocyclic carbene copper(I) complex as catalyst has been developed and successfully applied to the addition to various aldehydes in good yields under ambient conditions. This is the first successful example to realize catalytic nucleophilic transfer of silicon to aldehydes through a Cu-Si intermediate based on Si-B bond activation. This protocol opens up an easy and efficient access to a pool of α -hydroxysilanes.

Chapter 4.

Part 1: A highly regioselective synthesis of branched vinylsilanes through silicon-copper addition to terminal aliphatic alkynes catalyzed by copper(I) has been developed using methanol as additive. The corresponding vinylsilanes were obtained in good yields with excellent branched to linear selectivity of up to 99/1.

Part 2: For terminal aromatic alkynes, β -vinylsilanes has been synthesized in good to excellent yields under ambient conditions. The most notable character of this mild reaction system is its perfect anti-Markovnikov regiocontrol.

CHAPTER 1

Transition Metal-Catalyzed Silicon-Boron Bond Activation and Its Applications in Organic Synthesis

Introduction

As the versatility and usefulness of organosilicon compounds become increasingly apparent in both organic synthesis and material science, the importance to develop new methodologies that allow access to various organosilanes increases exponentially. The use of transition metal catalysts stands as the most efficient route to synthesize organosilicon compounds. This is exemplified by the numerous investigations conducted on the addition of various Si-X (X= Si, B, Ge, Sn, C, S etc) to unsaturated organic compounds using transition metals as catalysts in the past decades, to afford structurally defined and functionalized organic molecules directly.¹ Despite the fact that silylboranes had already been discovered in 1960,² they received little attention in organic synthesis. Suginome and Ito et al. began to investigate the synthetic applications of silylboration in the 1990s and managed to develop numerous efficient synthetic methods using group 10 metal complexes as catalysts to give new organometallic compounds containing both silicon and boron.³ These newly introduced organometallic compounds serve as versatile intermediates for various transformations such as Suzuki-Miyaura coupling, oxidation, allylation, conjugate addition and so on.⁴ This chapter serves to briefly summarize some recent examples of the silylboration of alkynes and unsaturated carbonyl compounds which are directly related to this thesis. The

¹ (a) Suginome, M.; Ito, Y. *Chem. Rev.* **2000**, *100*, 3221. (b) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320.

² (a) Seyferth, D.; Kögler, H. P. *J. Inorg. Nucl. Chem.* **1960**, *15*, 99. (b) Cowley, A. H.; Sisler, H. H.; Ryschkewitsch, G. E. *J. Am. Chem. Soc.* **1960**, *82*, 501.

³ Ohmura, T.; Suginome, M. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 29.

⁴ (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suginome, M.; Nakamura, H.; Masuda, T.; Ito, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4248. (c) Suginome, M.; Matsuda, T.; Ito, Y. *Organometallics* **1998**, *17*, 5223. (d) Sasaki, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229.

mechanisms involving Si-B bond activation of above-mentioned reactions will also be discussed thoroughly.

Group 10 Transition Metal-Catalyzed Si-B Bond Addition to Alkynes via Oxidative Addition

In 1996, Suginome and Ito reported silylboration of alkynes catalyzed by the palladium-*tert*-alkyl isonitrile to yield (*Z*)-1-boryl-2-silyl alkenes with nearly complete regio- and stereoselectivity (Scheme 1.1).⁵ The silylboration proceeded via *cis* addition, in which the boryl group added to the terminal carbon, and the silyl group bonded to the internal carbon. With palladium or

Scheme 1.1 Palladium-catalyzed *cis*-silylboration of terminal alkynes

platinum catalysts, several functional groups on aliphatic alkynes such as chloro, cyano, MEMO and hydroxyl groups showed tolerance, and such substituted alkynes underwent addition to afford good yields of alkenes with the use of Ph(Me)₂SiBpin (Scheme 1.2).⁶ Similar reactions with internal alkynes

Scheme 1.2 Silylboration of aliphatic alkynes catalyzed by palladium or platinum

⁵ Suginome, M.; Nakamura, H.; Ito, Y. *Chem. Commun.* **1996**, 2777.

⁶ Suginome, M.; Matsuda, T.; Nakamura, H.; Ito, Y. *Tetrahedron* **1999**, 55, 8787.

also proceeded with high regioselectivity. Ozawa et al. proposed a catalytic cycle for the silylation of terminal alkynes (Scheme 1.3) based on the observations of all the elementary steps in the stoichiometric reaction of silylboranes with a platinum complex.⁷ The catalytic cycle involves oxidative addition of a silylborane to a low-valent metal complex **I** (M = Pd or Pt) to form a borylsilylmetal intermediate **II**, insertion of an alkyne into the M-B bond, and reductive elimination of the resulting alkenysilyl intermediate **III** to afford the silylboration product.

Scheme 1.3 Proposed catalytic cycle for palladium- or platinum-catalyzed *cis* silylboration of terminal alkynes

The synthetic applications of silylboranes among chemists were severely impeded by the lack of efficient methods to synthesize silylboranes. It was only until 2000 that Ito found an easy and practical route to form the diol-derived silylboranes, by the reaction of pinacolborane and dimethylphenylsilyllithium in THF/hexanes (1/1) at 0 °C to room temperature (Scheme 1.4).⁸

⁷ Sagawa, T.; Asano, Y.; Ozawa, F. *Organometallics* **2002**, 21, 5879.

⁸ Suginome, M.; Matsuda, T.; Nakamura, H.; Ito, Y. *Organometallics* **2000**, 19, 4647.

Scheme 1.4 Convenient preparation of silylborane

Reversing the regio- and stereoselectivity of the silylboration of alkynes is an interesting topic. Ohmura, Suginome and coworkers found that the reversal of stereochemistry of the silylboration of terminal alkynes could be attained by controlling stoichiometric ratio between the silylborane and alkyne (Scheme 1.5).⁹ When the reaction was carried out with a slight excess of

Scheme 1.5 Palladium-catalyzed reversal silylboration of terminal alkynes

terminal alkyne ((chlorodimethylsilyl)pinacolborane:1-octyne=1.0:1.2), the *cis*-addition product, *Z* isomer was obtained. In contrast, the *trans*-addition product, *E* isomer was formed when using a small excess of silylborane. More recently, the same group reported an elegant way to control the regioselectivity by the utilization of different phosphine ligands and palladium catalyst (Scheme 1.6).¹⁰

⁹ Ohmura, T.; Oshima, K.; Suginome, M. *Chem. Commun.* **2008**, 1416.

¹⁰ Ohmura, T.; Oshima, K.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2010**, 132, 12194.

Scheme 1.6 Palladium-catalyzed regioselective silylboration via ligand control

In order to rationalize the different outcomes for regioselectivity in the silylboration of terminal alkynes using different phosphine ligands, Suginome et al. proposed the mechanism shown in Scheme 1.7. An alkyne inserts into the B-Pd bond of a borylsilylpalladium intermediate **I** to form intermediate **II**, where the B-C bond formation has taken place at the terminus of the alkyne (path a, Scheme 1.7). Subsequently, the “normal” silylboration product **III** is obtained through reductive elimination. The “inverse” product **V** is obtained through an intermediate **IV**, results from B-C bond formation at the internal carbon of the alkyne (path b, Scheme 1.7). When the ligand on palladium is bulky as Johnphos, intermediate **IV** is favoured over **II** because of less steric repulsion between the ligand and the substituent R-group.

Scheme 1.7 Proposed mechanism of regioselective silylboration via ligand control

Suginome et al. also developed the nickel-catalyzed double insertion of a tethered diyne into the Si-B bond of Ph(Me)₂SiBpin, leading to regio- and stereoselective silylborative cyclization (Scheme 1.8).¹¹ Remarkably, the nickel

Scheme 1.8 Nickel-catalyzed silylborative cyclization of alkynes

catalyst could also catalyze intermolecular silylborative dimerization of 1-hexyne in the presence of 5 mol% Ni(acac)₂ with DIBAH as a reductant (Ni/Al = 1:2) (Scheme 1.9).

Scheme 1.9 Nickel-catalyzed intermolecular dimerization of 1-hexyne

A proposed mechanism of the silylborative dimerization of alkynes catalyzed by nickel is shown below (Scheme 1.10). Initially, Si-B bond undergoes oxidative addition to nickel (0) to form a borylsilynickel **II** intermediate, followed by alkyne insertion into the Ni-B bond to afford an alkenylsilylnickel **III** intermediate. In the presence of an excess alkyne, intermediate **III** may preferentially undergo alkyne insertion into the Ni-Si bond affording a diakenylnickel intermediate **IV**. Finally, reductive elimination of **IV** affords the dimerization product **V**.

¹¹ Suginome, M; Matsuda, T.; Ito, Y. *Organometallics* **1998**, *17*, 5233.

Scheme 1.10 Mechanism of the silylboration dimerization of alkynes catalyzed by Ni

Besides the silylboration of alkynes, Si-B bonds can also undergo addition to various unsaturated compounds such as alkenes, 1,3-dienes, allenes and methylenecyclopropanes in the presence of different transition metal catalysts such as palladium, nickel and platinum catalysts via oxidative addition.¹²

¹² Ohmura, T.; Sugimoto, M. *Bull. Chem. Soc. Jpn.* **2009**, 82, 29.

Rhodium-Catalyzed Si-B Bonds Addition to α,β -Unsaturated Carbonyls Involving Transmetalation

With the success in utilizing group 10 transition metal catalysts such as palladium, nickel and platinum in the silylboration of various unsaturated bonds based on activation of Si-B bond, there has been a need to explore other activation models as the previously reported processes all involve oxidative addition. Oestreich and coworkers designed a new strategy to cleave Si-B bond through transmetalation in the presence of rhodium (Scheme 1.11).¹³ A

Scheme 1.11 Proposed catalytic cycle of conjugate silyl transfer catalyzed by rhodium hydroxorhodium(I) complex **I** undergoes transmetalation with a silylborane via a four-centered transition state **II** to afford a silylrhodium(I) species **III**. Insertion of a Michael acceptor into the Rh-Si bond afforded rhodium enolate **IV**. Finally, protonation of the rhodium enolate with water gives a 1,4-addition product and regenerate **I**. On the basis of the above hypothesis, Oestreich began investigations on the 1,4-silylation of cyclic α,β -unsaturated ketones catalyzed

¹³ Walter, C.; Fröhlich, R.; Oestreich, M. *Tetrahedron* **2009**, 65, 5513.

by a Rh(I) complex.¹⁴ The desired 1,4-addition product was obtained in good yield (76%) when the reaction was conducted using [(dppp)Rh(cod)]ClO₄ (5.0 mol%), dppp (5.0 mol%), Et₃N (1.0 equiv) in 1,4-dioxane and H₂O (10:1) at 50 °C (Table 1.1).

Table 1.1 Optimized conditions of conjugate silylation of 2-cyclohexenone

entry	Rh(I)	ligand	base	<i>T</i>	yield
1	[(dppp)Rh(cod)Cl] ClO ₄	dppp	no	100 °C	8%
2	[(dppp)Rh(cod)Cl] ClO ₄	dppp	KOH	50 °C	65%
3	[(dppp)Rh(cod)Cl] ClO ₄	no	KOH	50 °C	18%
4	[(dppp)Rh(cod)Cl] ClO ₄	dppp	Et ₃ N	50 °C	76%

When the reaction was extended to an α,β -unsaturated ester, a reduced product was unexpectedly obtained in good yield rather than a desired 1,4-addition product (Scheme 1.12).¹⁵ After screening different solvent systems, 1,4-

Scheme 1.12 Unexpected conjugate reduction catalyzed by rhodium

1,4-dioxane/MeOH (10:1) was found to favour conjugate addition to reduction. Subsequently, highly enantioselective 1,4-silylation of (*Z*)- α,β -unsaturated esters was successfully developed (Scheme 1.13). However, the reaction

¹⁴ Walter, C.; Oestreich, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5675.

¹⁵ Walter, C.; Oestreich, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3818.

Scheme 1.14 New strategy to activate Si-B bond catalyzed by copper(I) alkoxide

This will open an entirely new door for the synthetic application of silylboranes. Due to the facile formation of the Cu-Si key intermediate, it could be utilized for building various chiral and non-chiral functionalized organosilicon compounds. In this thesis, we have successfully induced the carbon-silicon bond formation including 1,4-Michael addition to α,β -unsaturated esters, 1,2-addition to aldehydes and highly regioselective silylcupration of terminal alkynes based on Si-B bond activation in the presence of a copper catalyst.

It is important to note here that our investigations into 1,4-silylation of α,β -unsaturated esters were in the final stages of completion when Hoveyda's paper on asymmetric 1,4-silylation using a chiral copper-*N*-heterocyclic carbene catalyst was published (Scheme 1.15).¹⁸

Scheme 1.15 Catalytic cycle for the conjugate additions promoted by a NHC-Cu(I)

¹⁸ Lee, K. -S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 2898.

During the preparation of this thesis, several groups also employed this activation strategy for different categories of organic transformations. For instance, Chatani et al. described the synthesis of 2-boryl- and silylindoles by copper-catalyzed borylative and silylative cyclization of 2-alkenylaryl isocyanides.¹⁹ Riant extended Hoveyda's work to domino silylative aldol reactions leading to stereocontrolled quaternary carbon center.²⁰ Later, Oestreich described branch-selective allylic substitution of linear allylic chloride (Scheme 1.16).²¹

Scheme 1.16 Catalytic cycle for the branched-selective allylic substitution

¹⁹ Tobisu, M.; Fujihara, K.; Chatani, N. *J. Org. Chem.* **2010**, 75, 4841.

²⁰ Welle, A.; Petriguet, J.; Tinant, B.; Riant, O. *Chem. Eur. J.* **2010**, 16, 10980.

²¹ Vyas, D. J.; Oestreich, M. *Angew. Chem. Int. Ed.* **2010**, 49, 8513.

CHAPTER 2

*Copper-Catalyzed β -Silylation of α,β -Unsaturated
Esters under Mild Reaction Conditions*

2.1 Introduction

The conjugate addition of silyl nucleophiles to α,β -unsaturated acceptors delivering functionalized β -silylcarbonyls provides versatile access to useful organosilicon compounds.²² It is well-established that stoichiometric anionic silyl nucleophiles can be generated through transmetalation from lithium to copper (Scheme 2.1)²³ and these protocols have been widely applied in various conjugate additions.²⁴

Scheme 2.1 Silicon-based cuprates stoichiometric in copper

²² (a) Brook, M. A. In *Silicon in Organic, Organometallic and Polymer Chemistry*, Wiley: New York, 2000. (b) Ojima, I.; Li, Z. Y.; Zhu, J. W. In *Chemistry of Organic Silicon Compounds*; Rappoport, Z., Apeloig, Y. Eds.; Wiley: Chichester, 1998; p1687. (b) Fleming, I., *Science of synthesis*; Thieme: Stuttgart, Germany, 2002; Vol. 4; p 927.

²³ (a) Ager, D. J.; Fleming, I. *J. Chem. Soc., Perkin, Trans. 1* **1978**, 177. (b) Fleming, I.; Kindon, N. D. *J. Chem. Soc., Perkin, Trans. 1* **1987**, 1177. (c) Fleming, I.; Newton, T. W. *J. Chem. Soc., Perkin, Trans. 1* **1984**, 1805. (d) Lipshutz, B. H.; Reuter, D. C.; Ellsworth, E. L. *J. Org. Chem.* **1989**, *54*, 4975. (e) Hale, M. R.; Hoveyda, A. H. *J. Org. Chem.* **1994**, *59*, 4370. (f) Palomo, C.; Aizpurua, J. M.; Iturburu, M.; Urchegui, R. *J. Org. Chem.* **1994**, *59*, 240. (g) Dambacher, J.; Bergdahl, M. *Chem. Commun.* **2003**, 144.

²⁴ (a) Permetter, P. *Conjugate Addition Reaction in Organic Synthesis*; Pergamon Press: Oxford, 1992. (b) Ager, D. J.; Fleming, I.; Patel, S. K. *J. Chem. Soc., Perkin, Trans. 1* **1981**, 2520. (c) Crump, R. A. N. C.; Fleming, I.; Urich, C. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 701. (d) Lipshutz, B. H.; Sclafani, J. A.; Takanami, T. *J. Am. Chem. Soc.* **1998**, *120*, 4021. (e) Taylor, R. J. K. *Organocopper Regents: A Practical Approach*; Oxford University Press, 1994. (f) Weickgenannt, A.; Oestreich, M. *Chem. Eur. J.* **2010**, *16*, 402.

Besides these advancements in the stoichiometric silylating reagents, the development of catalytic silyl conjugate addition to α,β -unsaturated carbonyls is an important and challenging goal. A number of catalytic methods have been reported to prepare β -silyl carbonyls in recent years. In 1998, Lipshutz first reported that $\text{Ph}(\text{Me})_2\text{SiZnMe}_2\text{Li}$ underwent 1,4-addition to various substituted cyclohexenones in the presence of a cyanocuprate $\text{Me}_2\text{CuLi}\cdot\text{LiCN}$ (3 mol%) (Scheme 2.2).²⁵

Scheme 2.2 First copper-catalyzed 1,4-silyl addition

Subsequently, Oestreich et al., inspired by Lipshutz's study, revisited silicon-copper reagent and investigated bis(triorganosilyl)zinc as a mild silicon nucleophile.²⁶ Hosomi disclosed an unprecedented way to introduce a silyl group into α,β -enones by activating Si-Si bond by a catalytic amount of an easily available Cu(I) salt (Scheme 2.3).²⁷

Scheme 2.3 Copper-catalyzed silylation of α,β -unsaturated carbonyl compound

In 2004, Scheidt et al. extended Hosomi's work to disilylation of alkylidene malonates to afford synthetically useful β -silyl diesters (Scheme 2.4).²⁸

²⁵ Lipshutz, B. H.; Sclafani, J. A.; Takanami, T. *J. Am. Chem. Soc.* **1998**, *120*, 4021.

²⁶ (a) Oestreich, M.; Weiner, B. *Synlett* **2004**, 2139. (b) Auer, G.; Weiner, B.; Oestreich, M. *Synthesis* **2006**, 2113.

²⁷ Ito, H.; Ishizuka, T.; Tateiwa, J. -I.; Sonoda, M.; Hosomi, A. *J. Am. Chem. Soc.* **1998**, *120*, 11196.

²⁸ Clark, C. T.; Lake, J. F.; Scheidt, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 84.

Scheme 2.4 Copper-catalyzed disilylation of alkylidene malonates

Hayashi and Ito et al. developed the first enantioselective conjugate carbon-silicon bond formation through β -silylation of α,β -unsaturated ketones catalyzed palladium (Scheme 2.5).²⁹

Scheme 2.5 Palladium-catalyzed asymmetric 1,4-disilylation

Ogoshi and Kurosawa succeeded in the addition of disilanes to enones and enals via the η^3 -siloxyallylpalladium intermediate (Scheme 2.6).³⁰

Scheme 2.6 Palladium-catalyzed 1,4-disilylation via the η^3 -siloxyallylpalladium

Since Hayashi's discovery, the enantioselective 1,4-addition of silicon nucleophiles gained no further attention for almost twenty years. In 2006, Oestreich et al. reported a novel strategy to construct C-Si bond based on Si-B activation by cationic rhodium complexes (Scheme 2.7).³¹ They found that conjugate reduction rather than 1,4-addition took place using acyclic (*E*)- α,β -

²⁹ Hayashi, T.; Matsumoto, Y.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 5579.

³⁰ Ogoshi, S.; Tomiyasu, S.; Morita, M.; Kurosawa, H. *J. Am. Chem. Soc.* **2002**, *124*, 11598.

³¹ Walter, C.; Auer, G.; Oestreich, M. *Angew. Chem. Int. Ed.* **2006**, *45*, 5675.

unsaturated esters as substrates, while the reaction mechanism remaining unclear.³²

Scheme 2.7 Rhodium-catalyzed asymmetric C-Si bond formation

In conclusion, a series of transition metal catalysts have been developed for silyl conjugate addition to α,β -unsaturated carbonyl compounds. In spite of such progress, some drawbacks such as high temperature, long reaction times and narrow substrate scope, of these transformations still exist.

³² (a) Walter, C.; Oestreich, M. *Angew. Chem. Int. Ed.* **2008**, 47, 3818. (b) Walter, C.; Fröhlich, R.; Oestreich, M. *Tetrahedron* **2009**, 65, 5513.

2.2 Copper-Catalyzed β -Silylation of α,β -Unsaturated Esters under Mild Reaction Conditions

Driven by our interest in the development of copper-catalyzed conjugate addition reactions,³³ we extend our research work to develop new and efficient ways to construct C-Si bond through conjugate addition. Here, we report β -silylation of various unsaturated esters with an NHC-copper(I) catalyst under mild reaction conditions (Scheme 2.8).

Scheme 2.8 Designed strategy to furnish catalytic silyl 1,4-addition

2.2.1 Results and Discussion

The initial study was conducted using 4 mol% CuCl as a catalyst and 6 mol% KO^tBu for the reaction of Ph(Me)₂SiBpin with (*E*)-ethyl cinnamate in THF. The desired product was obtained in moderate yield (50% yield; Table 2.1,

³³ (a) Wang, S. Y.; Ji, S. J.; Loh, T. P. *J. Am. Chem. Soc.* **2007**, *129*, 276. (b) Wang, S. Y.; Lum, T. K.; Ji, S. J.; Loh, T. P. *Adv. Synth. Catal.* **2008**, *350*, 673. (c) Lum, T. K.; Wang, S. Y.; Chin, Y. J.; Loh, T. P. *Synthesis* **2009**, 3557. (d) Chin, Y. J.; Wang, S. Y.; Loh, T. P. *Org. Lett.* **2009**, *11*, 3674. (e) Wang, S. Y.; Loh, T. P. *Chem. Commun.* **2010**, *46*, 8694. (f) Wang, S. Y.; Song, P.; Chan, L. Y.; Loh, T. P. *Org. Lett.* **2010**, *12*, 5166.

entry 1). In the search of a suitable copper catalyst to improve the yield, copper *N*-heterocyclic carbene complexes were chosen as they have been widely used in various chemical transformations in the past decade.³⁴ Metal complexes coordinated with NHC ligands are more tolerant to heat, oxygen and moisture allowing for indefinite storage and easy handling.³⁵ Sadighi, when studying the reduction of carbon dioxide to carbon oxide with a copper (I)-carbene complex, reported a reliable and efficient route to synthesize air- and moisture-stable *N*-heterocyclic carbene-copper chloride complex and also demonstrated that the complex could be acted as a precatalyst to react with bis(pinacolato)diboron.³⁶

Inspired by these works, we examined the IMesCuCl³⁷ complex for the silylation reaction. To our delight, the conversion greatly increased to 87% (Table 2.1, entry 2). Encouraged by this result, we screened several other *N*-heterocyclic carbene copper chloride (NHC-Cu-Cl) complexes (entries 2-5). SIPrCuCl emerged as the best catalyst, with which a conversion greater than 98% was achieved under very mild reaction conditions (entry 5). With this promising result in hand, we wondered whether the alcohol additive (MeOH) was critical for this process.³⁸ Unfortunately, the conversion decreased to 59% without MeOH as additive (entry 6). Control experiments demonstrated that both of the copper catalyst and KO^tBu are critical for the reaction (entries 7 and 8).

³⁴ For reviews on *N*-heterocyclic carbene (NHC), see (a) *N-Heterocyclic Carbenes in Transition Metal Catalysis*; Glorius, F., Ed.; Topics in Organometallic Chemistry; Springer: Heidelberg, 2007; vol. 21. (b) *N-Heterocyclic Carbenes in Synthesis*; Nolan, S. P., Ed.; Wiley-VCH: Weinheim, 2006. (c) Herrmann, W. A. *Angew. Chem. Int. Ed.* **2002**, *41*, 1290.

³⁵ Nolan, S. P. *Acc. Chem. Res.* **2011**, *44*, 91.

³⁶ (a) Laitar, D. S.; Müller, P.; Sadighi, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 17196. (b) Mankad, N. P.; Gray, T. G.; Laiar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 1191.

³⁷ Mes: 1,3-Bis(2,4,6-trimethylphenyl)imidazol-2-ylidene; SIMes: 1,3-Bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene; IPr: 1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene; SIPr: 1,3-Bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene.

³⁸ (a) Mun, S.; Lee, J. -E.; Yun, J. *Org. Lett.* **2006**, *8*, 4884. (b) Chen, I. -H.; Yin, L.; Itano, W.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 11664.

Table 2.1 Optimization of conditions for 1,4-silylation of ethyl cinnamate^a

<div><div> </div></div>				
entry	Cu(I)	base	additive	conversion ^b
1	CuCl	KO ^t Bu	MeOH	50%
2		KO ^t Bu	MeOH	87%
3		KO ^t Bu	MeOH	95%
4		KO ^t Bu	MeOH	96%
5		KO ^t Bu	MeOH	> 98%
6		KO ^t Bu	no	59%
7		no	MeOH	no reaction
8	no	KO ^t Bu	MeOH	no reaction

^aAll reactions were performed with ethyl cinnamate (0.3 mmol), Ph(Me)₂SiBpin (0.33 mmol) in THF (1.0 mL) at room temperature for 6 h. ^bDetermined by crude 500 MHz ¹H-NMR spectra.

After establishing the optimized conditions, the scope of the copper-catalyzed 1,4-silylation reactions was examined (Table 2.2). High yields were obtained for β -aryl and alkyl substituted α,β -unsaturated esters. Halogen substituents such as chloride and bromide did not interfere with the reaction. For bulky aliphatic esters, a decrease in yield was observed (entries 2 and 4).

Table 2.2 Copper-catalyzed 1,4-silylation of various α,β -unsaturated esters^{a,b}

^a All reactions were performed in glove box: α,β -unsaturated ester (0.3 mmol, 1.0 equiv), $Ph(Me)_2SiBpin$ (1.1 equiv), $(SiPr)CuCl$ (4 mol%), KO^tBu (6 mol%) and $MeOH$ (2.0 equiv) in THF (1.0 mL) at room temperature for 12 h. ^b Isolated yields.

A plausible catalytic cycle is shown below (Scheme 2.9). We postulate that *N*-heterocyclic carbene copper oxide (NHC-Cu-O^{*i*}Bu) is the initial active catalyst in the 1,4-silylation reaction. It could be easily formed by combining *N*-heterocyclic carbene copper chloride (NHC-Cu-Cl) and KO^{*i*}Bu, which affords a silylcopper intermediate **I** through transmetalation with Ph(Me)₂SiBpin. The intermediate **I** subsequently adds to α,β-unsaturated ester to afford a copper enolate **II**. We speculate the C-enolate **II** is preferred to an O-enolate **III**, because the addition of a proton source, i.e., MeOH greatly improves the reaction.³⁹ Protonation of the intermediate **II** liberates a β-silylester and gives a NHC-Cu-OMe complex **V**. Finally Ph(Me)₂SiBpin undergoes transmetalation with **V** to regenerate the key intermediate **I**.

Scheme 2.9 Proposed catalytic cycle for the 1,4-silylation reaction

³⁹ Similar MeOH effect in Cu-B addition, see: (a) Mun, S.; Lee, J. -E.; Yun, J. *Org. Lett.* **2006**, 8, 4884. (b) Dang, L.; Lin, Z. Y.; Marder, T. B. *Organometallics* **2008**, 27, 4443.

In conclusion, we have successfully developed a method to introduce a silyl group to α,β -unsaturated esters under mild reaction conditions. This new method produces highly functionalized organosilicon compounds with wide substrate scope. Extension to asymmetric 1,4-silylation reaction is in progress in our lab.

2.3 Supporting Information

2.3.1 General Methods

All commercially obtained reagents for the β -silylation reactions were used as received: Ph(Me)₂SiBpin, CuCl, KO^tBu, ethyl crotonate, ethyl cinnamate, methyl cinnamate were purchased from Aldrich or Acros. Unsaturated esters were prepared from the corresponding aldehydes via Horner-Emmons reaction or Wittig-Horner reaction using well established protocols and *N*-heterocyclic carbene copper chloride (NHC-CuCl) complexes were prepared according to the reported references.⁴⁰ All reactions were carried out in oven-dried glassware in a glove box to avoid moisture and oxygen. THF was freshly distilled from Na/benzophenone ketyl and anhydrous MeOH was purchased from Aldrich. Thin-layer chromatography (TLC) was conducted with Merck 60 F254 pre-coated silica gel plate (0.2 mm thickness) and visualized with UV or by ceric acid stain. Flash chromatography was performed using Merck 60 F254 pre-coated silica gel plate with distilled solvents. ¹H-NMR spectra were recorded on a Bruker Avance 300 or 400 NMR spectrometer and are reported in ppm downfield from SiMe₄ (δ 0.0) and relative to the signal of chloroform-d (δ = 7.26, singlet). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ¹³C-NMR spectra were recorded on a Bruker Avance 75 MHz or 100 MHz spectrometer and are reported in ppm using an internal standard (CDCl₃ at 77.0 ppm) as solvent. Conversion of the optimization process was determined by NMR analysis of the crude product. IR

⁴⁰ (a) Laitar, D. S.; Müller, P.; Sadighi, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 17196. (b) Mankad, N. P.; Gray, T. G. ; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 1191. (c) Laitar, D. S. Ph.D. Thesis. Massachusetts Institute of Technology, Cambridge, MA, 2006.

spectra were recorded on a Bio-Rad FTS 165 FTIR spectrometer and were reported in frequency of absorption (cm^{-1}). High resolution mass spectral analysis (HRMS) was performed on Waters Q-ToF Premier Mass Spectrometer using the electrospray ionization (ESI) mode.

2.3.2 Representative experimental procedure

A 4 mL sample vial equipped with a Teflon-coated magnetic stirbar was charged sequentially with (IPr)CuCl (5.9 mg, 0.012 mmol, 4 mol%), KO^tBu (2.0 mg, 0.018 mmol, 6 mol%), THF (1.0 mL) and the mixture was allowed to stir for 0.5 hour. Then Ph(Me)₂SiBpin (90 μ L, 0.33 mmol, 1.1 equiv) was added into the solution using a syringe. After 10 minutes, the starting material ethyl cinnamate (50 μ L, 0.30 mmol, 1.0 equiv) and MeOH (24 μ L, 0.60 mmol, 2.0 equiv) were added into the solution in sequence. The reaction mixture was allowed to stir at room temperature overnight under an argon atmosphere, then diluted with dichloromethane and concentrated *in vacuo*. Purification by silica gel column chromatography (20:1 hexane/ethyl acetate eluent) afforded ethyl-3-(dimethyl(phenyl)silyl)-3-phenylpropanoate as a colourless oil (80 mg, 86% yield).

Ethyl 3-(dimethyl(phenyl)silyl)-3-phenylpropanoate

Yield = 86%. R_f = 0.25 (10:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ (ppm): 7.31-7.40 (m, 5H), 7.16-7.20 (m, 2H), 7.06-7.10 (m, 1H), 6.93-6.95 (m, 2H), 3.86-3.96 (m, 2H), 2.83 (dd, $J_1 = 11.3$ Hz, $J_2 = 4.7$ Hz, 1H), 2.73 (dd, $J_1 = 15.6$ Hz, $J_2 = 11.3$ Hz, 1H), 2.62 (dd, $J_1 = 15.6$, $J_2 = 4.7$ Hz, 1H), 1.03(t, $J = 7.1$ Hz, 3H), 0.25 (s, 3H), 0.21 (s, 3H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ (ppm): 173.0, 141.8, 136.5, 134.2, 129.3, 128.0, 127.7, 127.6, 124.9, 60.3, 34.9, 32.3, 14.0, -4.1, -5.5.

FTIR (neat, cm^{-1}): 2958, 1732, 1599, 1427, 1250, 1165, 1113.

HRMS (ESI) m/z calculated for $\text{C}_{19}\text{H}_{25}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 313.1634, found 313.1624.

Experimental Details of Table 2.2

(Entry 1)

Ethyl 3-(dimethyl(phenyl)silyl)butanoate

The title compound was prepared by the general procedure described above and was obtained as a colourless oil (63 mg).

Yield = 84%. R_f = 0.23 (20:1 hexane/ether).

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ (ppm): 7.48-7.51 (m, 2H), 7.35-7.36 (m, 3H), 4.08 (q, $J = 7.1$ Hz, 2H), 2.38 (dd, $J_1 = 15.2$, $J_2 = 4.0$ Hz, 1H), 2.04 (dd, $J_1 =$

15.2, $J_2 = 11.3$ Hz, 1H), 1.39-1.49 (m, 1H), 1.23 (t, $J = 7.1$ Hz, 3H), 0.97 (d, $J = 7.3$ Hz, 3H), 0.28 (s, 6H).

^{13}C -NMR (100 MHz, CDCl_3) δ (ppm): 174.1, 137.5, 134.1, 129.2, 127.9, 60.3, 37.0, 16.6, 14.6, 14.4, -4.9, -5.2.

FTIR (neat, cm^{-1}): 2957, 1732, 1641, 1414, 1250, 1150, 1111.

HRMS (ESI) m/z calculated for $\text{C}_{14}\text{H}_{23}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 251.1468, found 251.1467.

(Entry 2)

Ethyl 3-(dimethyl(phenyl)silyl)-4-methylpentanoate

The title compound was prepared by the general procedure described above and was obtained as a colourless oil (59 mg).

Yield = 70%. $R_f = 0.29$ (30:1 hexane/ether).

^1H -NMR (400 MHz, CDCl_3) δ (ppm): 7.51-7.54 (m, 2H), 7.34-7.35 (m, 3H), 4.01 (q, $J = 7.1$ Hz, 2H), 2.26-2.38 (m, 2H), 1.88-1.96 (m, 1H), 1.52-1.54 (m, 1H), 1.21 (t, $J = 7.1$ Hz, 3H), 0.91 (d, $J = 6.8$ Hz, 3H), 0.83 (d, $J = 6.8$ Hz, 3H), 0.28 (s, 6H).

^{13}C -NMR (100 MHz, CDCl_3) δ (ppm): 174.7, 138.8, 133.9, 128.9, 127.7, 60.3, 31.8, 29.2, 28.8, 22.8, 20.9, 14.2, -2.6, -3.0.

FTIR (neat, cm^{-1}): 2957, 1734, 1651, 1427, 1249, 1150, 1111.

HRMS (ESI) m/z calculated for $\text{C}_{16}\text{H}_{27}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 279.1780, found 279.1772.

(Entry3)

Ethyl 3-(dimethyl(phenyl)silyl)-4-methylpentanoate

The title compound was prepared by the general procedure described above and was obtained as a colourless oil (79 mg).

Yield = 90%. R_f = 0.26 (30:1 hexane/ether).

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ (ppm): 7.50-7.52 (m, 2H), 7.34-7.36 (m, 3H), 4.01 (q, J = 7.1 Hz, 2H), 2.32 (dd, J_1 = 15.4 Hz, J_2 = 5.9 Hz, 1H), 2.16 (dd, J_1 = 15.4 Hz, J_2 = 7.7 Hz, 1H), 1.48-1.57 (m, 2H), 1.13-1.28 (m, 5H), 0.83 (d, J = 6.5 Hz, 3H), 0.82 (d, J = 6.5 Hz, 3H), 0.29 (s, 6H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ (ppm): 174.4, 138.1, 134.1, 129.1, 127.8, 60.3, 39.9, 35.6, 26.5, 23.4, 21.9, 19.5, 14.3, -4.1, -4.4.

FTIR (neat, cm^{-1}): 2955, 1732, 1589, 1427, 1250, 1152, 1111.

HRMS (ESI) m/z calculated for $\text{C}_{17}\text{H}_{29}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 293.1928, found 293.1937.

(Entry 4)

Ethyl 3-cyclohexyl-3-(dimethyl(phenyl)silyl)propanoate

This compound was prepared by the general procedure described above and was obtained as a colorless oil (72 mg).

Yield = 75%. R_f = 0.26 (20:1 hexane/ether).

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ (ppm): 7.50-7.52 (m, 2H), 7.33-7.34 (m, 3H), 4.01 (q, $J = 7.1$ Hz, 2H), 2.34 (dd, $J_1 = 15.9$ Hz, $J_2 = 7.6$ Hz, 1H), 2.28 (dd, $J_1 = 15.9$ Hz, $J_2 = 5.4$ Hz, 1H), 1.47-1.67 (m, 6H), 1.01-1.25 (m, 9H), 0.33 (s, 3H), 0.32 (s, 3H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ (ppm): 174.7, 139.0, 133.9, 128.8, 127.7, 60.2, 39.5, 33.2, 32.3, 31.5, 28.7, 27.0, 26.9, 26.3, 14.2, -2.3, -3.0.

FTIR (neat, cm^{-1}): 2951, 1734, 1589, 1369, 1250, 1157, 1111.

HRMS (ESI) m/z calculated for $\text{C}_{19}\text{H}_{31}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 319.2079, found 319.2093.

(Entry 5)

Ethyl 3-(dimethylphenylsilyl)-5-phenylpentanoate

This compound was prepared by the general procedure described above and was obtained as a colorless oil (84 mg).

Yield = 82%. $R_f = 0.21$ (30:1 hexane/ether).

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ (ppm): 7.50-7.52 (m, 2H), 7.36-7.37 (m, 3H), 7.23-7.27 (m, 2H), 7.15-7.18 (m, 1H), 7.07-7.09 (m, 2H), 4.07 (q, $J = 7.1$ Hz, 2H), 2.47-2.67 (m, 2H), 2.43 (dd, $J_1 = 15.5$ Hz, $J_2 = 5.3$ Hz, 1H), 2.30 (dd, $J_1 = 15.5$, $J_2 = 8.4$ Hz, 1H), 1.77-1.79 (m, 1H), 1.49-1.63 (m, 2H), 1.24 (t, $J = 7.1$ Hz, 3H), 0.33 (s, 3H), 0.32 (s, 3H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ (ppm): 174.1, 142.5, 137.7, 134.0, 129.1, 128.3, 127.8, 125.7, 60.4, 35.3, 35.1, 32.6, 21.9, 14.2, -4.2.

FTIR (neat, cm^{-1}): 2953, 1732, 1603, 1427, 1250, 1153, 1111.

HRMS (ESI) m/z calculated for $\text{C}_{21}\text{H}_{29}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 341.1944, found 341.1937.

(Entry 6)

Methyl 3-(dimethyl(phenyl)silyl)-5-phenylpentanoate

This compound was prepared by the general procedure described above and was obtained as a colorless oil (83 mg).

Yield = 85%. R_f = 0.15 (20:1 hexane/ether).

^1H -NMR (400 MHz, CDCl_3) δ (ppm): 7.49-7.51 (m, 2H), 7.35-7.37 (m, 3H), 7.23-7.27 (m, 2H), 7.15-7.18 (m, 1H), 7.07-7.08 (m, 2H), 3.60 (s, 3H), 2.58-2.67 (m, 1H), 2.41-2.53 (m, 2H), 2.32 (dd, J_1 = 15.6 Hz, J_2 = 8.3 Hz, 1H), 1.79-1.84 (m, 1H), 1.48-1.61 (m, 2H), 0.32 (s, 3H), 0.31 (s, 3H).

^{13}C -NMR (100 MHz, CDCl_3) δ (ppm): 174.5, 142.4, 137.6, 134.0, 129.1, 128.3, 127.8, 125.7, 51.5, 35.3, 34.8, 32.5, 32.0, 22.0, -4.3.

FTIR (neat, cm^{-1}): 2949, 1736, 1589, 1427, 1250, 1155, 1111.

HRMS (ESI) m/z calculated for $\text{C}_{20}\text{H}_{27}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 327.1776, found 327.1780.

(Entry 7)

Methyl 3-(dimethyl(phenyl)silyl)-3-phenylpropanoate

This compound was prepared by the general procedure described above and was obtained as a colorless oil (88 mg).

Yield = 98%. R_f = 0.29 (10:1 hexane/ether).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.34-7.41 (m, 5H), 7.18-7.22 (m, 2H), 7.08-7.12 (m, 1H), 6.94-6.96 (m, 2H), 3.47 (s, 3H), 2.85 (dd, $J_1 = 11.0$, $J_2 = 4.6$ Hz, 1H), 2.76 (dd, $J_1 = 15.6$ Hz, $J_2 = 11.0$ Hz, 1H), 2.64 (dd, $J_1 = 15.6$ Hz, $J_2 = 4.6$ Hz, 1H), 0.26 (s, 3H), 0.22 (s, 3H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ (ppm): 173.5, 141.8, 136.5, 134.2, 129.3, 128.1, 127.8, 127.5, 51.5, 34.7, 32.2, -4.1, -5.5.

FTIR (neat, cm^{-1}): 2953, 1738, 1599, 1427, 1250, 1165, 1113.

HRMS (ESI) m/z calculated for $\text{C}_{18}\text{H}_{23}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 299.1462, found 299.1467.

(Entry 8)

Ethyl 3-(dimethyl(phenyl)silyl)-3-*p*-tolylpropanoate

This compound was prepared by the general procedure described above and was obtained as a colorless oil (93 mg).

Yield = 95%. R_f = 0.33 (20:1 hexane/ether).

^1H -NMR (300 MHz, CDCl_3) δ (ppm): 7.33-7.42 (m, 5H), 7.00 (d, J = 7.7 Hz, 2H), 6.83 (d, J = 7.7 Hz, 2H), 3.88-3.92 (m, 2H), 2.79 (dd, J_1 = 11.2, J_2 = 4.6 Hz, 1H), 2.70 (dd, J_1 = 15.1, J_2 = 11.2 Hz, 1H), 2.59 (dd, J_1 = 15.1 Hz, J_2 = 4.6 Hz, 1H), 2.28 (s, 3H), 1.05 (t, J = 7.1 Hz, 3H), 0.23 (s, 3H), 0.20 (s, 3H).

^{13}C -NMR (75 MHz, CDCl_3) δ (ppm): 173.1, 138.5, 136.7, 134.2, 129.2, 128.8, 127.7, 127.5, 60.2, 35.0, 31.7, 21.0, 14.1, -4.0, -5.5.

FTIR (neat, cm^{-1}): 2957, 1734, 1638, 1250, 1163, 1113.

HRMS (ESI) m/z calculated for $\text{C}_{20}\text{H}_{27}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 327.1788, found 327.1780.

(Entry 9)

Ethyl 3-(dimethyl(phenyl)silyl)-3-(4-methoxyphenyl)propanoate

This compound was prepared by the general procedure described above and was obtained as a colorless oil (82 mg).

Yield = 80%. R_f = 0.22 (10:1 hexane/ether).

^1H -NMR (400 MHz, CDCl_3) δ (ppm): 7.34-7.41 (m, 5H), 6.86 (d, J = 8.6 Hz, 2H), 6.75 (d, J = 8.6 Hz, 2H), 3.88-3.96 (m, 2H), 3.77 (s, 3H), 2.77 (dd, J_1 = 11.1 Hz, J_2 = 5.0 Hz, 1H), 2.59-2.72 (m, 2H), 1.05 (t, J = 7.1 Hz, 3H), 0.25 (s, 3H), 0.22 (s, 3H).

^{13}C -NMR (100 MHz, CDCl_3) δ (ppm): 173.1, 157.1, 136.7, 134.2, 133.6, 129.3, 128.5, 127.7, 113.5, 60.2, 55.2, 35.2, 31.3, 14.1, -4.1, -5.4.

FTIR (neat, cm^{-1}): 2955, 1732, 1580, 1248, 1163, 1113.

HRMS (ESI) m/z calculated for $\text{C}_{20}\text{H}_{27}\text{O}_3\text{Si}$ $[\text{M}+\text{H}]^+$: 343.1724, found 343.1729.

(Entry 10)

Ethyl 3-(4-chlorophenyl)-3-(dimethyl(phenyl)silyl)propanoate

This compound was prepared by the general procedure described above and was obtained as a colorless oil (94 mg).

Yield = 90%. R_f = 0.20 (20:1 hexane/ether).

^1H -NMR (400 MHz, CDCl_3) δ (ppm): 7.34-7.39 (m, 5H), 7.15 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 3.89-3.97 (m, 2H), 2.81 (dd, J_1 = 10.9 Hz, J_2 = 5.1 Hz, 1H), 2.59-2.72 (m, 2H), 1.06 (t, J = 7.1 Hz, 3H), 0.25 (s, 3H), 0.23 (s, 3H).

^{13}C -NMR (100 MHz, CDCl_3) δ (ppm): 172.8, 140.4, 136.0, 134.1, 130.5, 129.5, 128.8, 128.2, 127.8, 60.4, 34.8, 32.0, 14.1, -4.3, -5.4.

FTIR (neat, cm^{-1}): 2959, 1732, 1641, 1427, 1250, 1163, 1113.

HRMS (ESI) m/z calculated for $\text{C}_{19}\text{H}_{24}\text{ClO}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 347.1243, found 347.1234.

(Entry 11)

Ethyl 3-(4-bromophenyl)-3-(dimethyl(phenyl)silyl)propanoate

This compound was prepared by the General Procedure described above and was obtained as a colorless oil (100 mg).

Yield = 85%. R_f = 0.27 (10:1 hexane/ether).

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ (ppm): 7.29-7.39 (m, 7H), 6.80 (d, J = 8.3 Hz, 2H), 3.89-3.96 (m, 2H), 2.80 (dd, J_1 = 11.0 Hz, J_2 = 5.1 Hz, 1H), 2.59-2.72 (m, 2H), 1.06 (t, J = 7.1 Hz, 3H), 0.25 (s, 3H), 0.23 (s, 3H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ (ppm): 172.7, 141.0, 135.9, 134.1, 131.1, 129.5, 129.2, 127.8, 118.5, 60.4, 34.7, 32.1, 14.1, -4.3, -5.4.

FTIR (neat, cm^{-1}): 2959, 1732, 1487, 1250, 1165, 1113.

HRMS (ESI) m/z calculated for $\text{C}_{19}\text{H}_{24}\text{BrO}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 391.0731, found 391.0729.

(Entry 12)

Ethyl 3-(dimethyl(phenyl)silyl)-3-(furan-2-yl)propanoate

This compound was prepared by the general procedure described above and was obtained as a pale yellow oil (80 mg).

Yield = 88%. R_f = 0.20 (20:1 hexane/ether).

^1H -NMR (300 MHz, CDCl_3) δ (ppm): 7.43-7.46 (m, 2H), 7.32-7.38 (m, 3H), 7.25-7.36 (m, 1H), 6.23-6.25 (m, 1H), 5.81-5.82 (m, 1H), 3.99 (q, $J = 7.1$ Hz, 2H), 2.96 (dd, $J_1 = 13.8$, $J_2 = 4.4$ Hz, 1H), 2.64 (dd, $J_1 = 16.0$, $J_2 = 11.4$ Hz, 1H), 2.48 (dd, $J_1 = 16.0$ Hz, $J_2 = 4.4$ Hz, 1H), 1.12 (t, $J = 7.1$ Hz, 3H), 0.31 (s, 3H), 0.28 (s, 3H).

^{13}C -NMR (75 MHz, CDCl_3) δ 172.9, 156.1, 140.4, 136.4, 134.0, 129.4, 127.8, 110.3, 104.1, 60.4, 33.7, 25.6, 14.1, -3.9, -5.1.

FTIR (neat, cm^{-1}): 2959, 1732, 1584, 1427, 1252, 1157, 1115.

HRMS (ESI) m/z calculated for $\text{C}_{17}\text{H}_{23}\text{O}_3\text{Si}$ $[\text{M}+\text{H}]^+$: 303.1419, found 303.1416.

(SIPr)CuCl and (SIPr)CuO^tBu complexes was prepared by following the reference.⁴¹

Synthesis of (SIPr)CuCl

[1,3-Bis(2,6-diisopropylphenyl)imidazolin-2-ylidene]copper(I) chloride

In a glovebox, a round-bottomed flask was charged with CuCl (1.30 g, 13.13 mmol) and NaO^tBu (1.20 g, 12.5 mmol). THF (100 mL) was added, and the mixture was stirred for 2 hours. 1,3-Bis-(2,6-diisopropylphenyl)imidazolinium (5.0 g, 12 mmol) was added, and the mixture was stirred for an additional 12 hours. In the air, the mixture was filtered through a pad of Celite, washed with dichloromethane, and concentrated *in vacuo* to give an off-white solid (5.44 g, 95%).

¹H-NMR (400 MHz, CD₂Cl₂) δ (ppm): 7.45 (t, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 7.6 Hz, 4H), 4.03 (s, 4H), 3.08 (sept, *J* = 6.9 Hz, 9H), 1.35 (d, *J* = 7.0 Hz, 24 H).

¹³C-NMR (100 MHz, CD₂Cl₂) δ (ppm): 203.3, 147.4, 135.0, 130.3, 125.0, 54.3, 29.4, 25.7, 24.1.

Synthesis of (SIPr)CuO^tBu

[1,3-Bis(2,6-diisopropylphenyl)imidazolin-2-ylidene]copper(I)tert-butoxide

⁴¹Laitar, D. S. Ph.D. Thesis. Massachusetts Institute of Technology, Cambridge, MA, 2006.

In a glovebox, a round-bottomed flask was charged with (SIPr)CuCl (3.04 g, 6.31 mmol) and NaO^tBu (0.606 g, 6.31 mmol). THF (80 mL) was added, and the mixture was stirred for 1 hour, filtered through a pad of Celite, and concentrated *in vacuo* to give an off-white solid (3.12 g, 94%).

¹H-NMR (400 MHz, C₆D₆) δ (ppm): 7.20 (t, *J* = 7.8 Hz, 2H), 7.07 (d, *J* = 7.6 Hz, 4H), 3.18(s, 4H), 2.99 (sept, *J* = 6.9 Hz, 4H), 1.50 (d, *J* = 6.7 Hz, 12H), 1.28 (s, 9H), 1.19 (d, *J* = 7.0 Hz, 12H).

¹³C-NMR (100 MHz, C₆D₆) δ (ppm): 206.4, 147.2, 136.0, 130.1, 125.0, 53.6, 37.5, 29.4, 25.9, 24.5.

CHAPTER 3

*Catalytic Silicon-Copper Addition to Aldehydes
Based on Si-B Bond Activation*

3.1 Introduction

Organosilicon compounds have served as versatile building blocks for organic synthesis.⁴² As such, significant effort has been devoted to exploration of new methodologies for the preparation of these derivatives. α -Hydroxysilanes are among the most useful organosilicon compounds, which can be utilized for stereocontrolled C-C bond and rearrangement reactions.⁴³ Despite the evident importance of α -hydroxysilanes, there are only a few reported procedures that are currently available for their efficient synthesis.

Of these reported procedures, transfer of silyl groups to carbonyl groups has provided a direct way to prepare α -hydroxysilanes. In 1954, Gilman pioneerly reported that suspensions of triphenylsilylpotassium in ether, serving as silyl anion, reacted with gaseous formaldehyde to give triphenylsilylmethanol (Scheme 3.1).⁴⁴ Subsequently, as a continuation of his previous work, Gilman probed the reactions of organosilylpotassium compounds in THF with aliphatic ketones to afford α -hydroxysilanes as normal addition products.⁴⁵ However, the same reaction with aromatic aldehydes or ketones (e.g., benzophenone) yielded alkoxysilanes as abnormal addition products (Scheme 3.2).⁴⁶

Scheme 3.1 Reaction of triphenylsilylpotassium with formaldehyde

⁴² (a) Brook, M. A. *In Silicon in Organic, Organometallic and Polymer Chemistry*, Wiley: New York, 2000. (b) Ojima, I.; Li, Z. Y.; Zhu, J. W. *In Chemistry of Organic Silicon Compounds*; Rappoport, Z., Apeloig, Y. Eds.; Wiley: Chichester, 1998; p1687.

⁴³ (a) Fleming, I.; Barhero, A.; Waler, D. *Chem. Rev.* **1997**, 97, 2063. (b) Cirillo, P. F.; Panek, J. S. *Org. Prep. Proced. Int.* **1992**, 24, 533.

⁴⁴ Gilman, H.; Wu, T. C. *J. Am. Chem. Soc.* **1954**, 76, 2502.

⁴⁵ Gilman, H.; Lichtenwalter, G. D. *J. Am. Chem. Soc.* **1958**, 80, 2680.

⁴⁶ (a) Wittenberg, D.; Wu, T. C.; Gilman, H. *J. Org. Chem.* **1959**, 24, 1349. (b) Gilman, H.; Wu, T. C. *J. Am. Chem. Soc.* **1953**, 75, 2935.

Scheme 3.2 Reaction of triphenylsilylpotassium with benzophenone

At that time, no information was available on the the origin of this abnormal product. Later on, Brook revealed that this abnormal addition was due to the rearrangement of a silylcarbinol, in the presence of a small amount of active metal, organometallic reagent or base (Scheme 3.3).⁴⁷ Barret found that

Scheme 3.3 Mechanism of Brook rearrangement

dimethylphenylsilyllithium, unlike triphenylsilylpotassium, added readily to a series of aldehydes at -78°C and the corresponding α -hydroxysilanes were obtained in excellent yields.⁴⁸

In contrast to the alkali-metal silyl reagents used by Gilman, there have been few studies for the silyl “Grignard” addition reactions.⁴⁹ Reich et al. elegantly realized highly diastereoselective addition of $\text{Ph}(\text{Me})_2\text{SiMgBr}$ to a ketone affording the expected α -hydroxysilane through the chelation-control strategy (Scheme 3.4).⁵⁰

Scheme 3.4 Nucleophilic silylation of carbonyl groups using silylmagnesium

⁴⁷ (a) Brook, A. G.; *Acc. Chem. Res.* **1974**, 7, 77. (b) Brook, A. G.; Warner, C. M.; McGriskin, M. E.; *J. Am. Chem. Soc.* **1959**, 81, 981.

⁴⁸ Barret, A. G.; Hill, J. M.; Wallace, E. M. *J. Org. Chem.* **1992**, 57, 386.

⁴⁹ Lickiss, P. D.; Smith, C. M. *Coord. Chem. Rev.* **1995**, 145, 75.

⁵⁰ Reich, H. J.; Holtan, R. C.; Bolm, C. *J. Am. Chem. Soc.* **1990**, 112, 5609.

On the other hand, the use of milder silyl nucleophiles, such as transition metal silyl derivatives (M-Si), has received less attention even though it would possibly offer another attractive system for selective silylation. Generally, there exist two pathways for transfer of a silyl group from a silyl-transition metal species to a carbonyl group (Scheme 3.5).⁵¹

Scheme 3.5 Two pathways of addition of transition metal silyl derivatives to carbonyl groups

An electron-rich transition metal silyl derivative undergoes the attack of benzaldehyde oxygen upon the trimethyl group, forming an α -siloxyalkylmetal complex (Path a, Scheme 3.5). Gladysz conducted a thorough investigation into the reactivity of transition metal trialkylsilanes complexes and their stoichiometric insertion reactions involving manganese and iron silyl derivatives (Scheme 3.6).⁵²

Scheme 3.6 Stoichiometric manganese and iron silyls additions with benzaldehyde

In contrast to the silylmanganese and iron derivatives, silylmetal derivatives of d^0 metal transfer the silyl groups to carbon center yielding α -silylalkoxides (Path b,

⁵¹ Arnold, J.; Tilley, T. D. *J. Am. Chem. Soc.* **1987**, *109*, 3318.

⁵² (a) Gladysz, J. A. *Acc. Chem. Res.* **1984**, *17*, 326. (b) Johnson, D. L.; Gladysz, J. A. *J. Am. Chem. Soc.* **1979**, *101*, 6433. (c) Johnson, D. L.; Gladysz, J. A. *Inorg. Chem.* **1981**, *20*, 2508.

Scheme 3.5). In 1987, Tilley reported the first example of stoichiometric transfer of a silyl group from a transition-metal to a carbonyl carbon atom using $\text{Cp}^*\text{Cl}_3\text{TaSiMe}_3$ as a nucleophilic silyl source (Scheme 3.7).⁵³

Scheme 3.7 Insertion of organic carbonyl into the Ta-Si bond

Although rare studies of catalytic transition metal silyl derivatives (M-Si) addition to carbonyl groups have been done,⁵⁴ catalytic Cu-B addition to aldehydes and ketones has been disclosed in detail. For example, in 2006, Sadighi and co-workers at MIT reported the first addition of an aldehyde C=O group into a Cu-B bond leading to the formation of a copper carbon σ -bond (Scheme 3.8) and the diboration of aldehydes catalyzed by *N*-heterocyclic carbene ligated copper boryl complexes, (NHC)Cu(boryl) (Scheme 3.9).⁵⁵

Scheme 3.8 Insertion of mesitaldehyde into Cu-B bond

Scheme 3.9 Copper-catalyzed diboration of aldehydes

⁵³ Arnold, J.; Tilley, T. D. *J. Am. Chem. Soc.* **1987**, *109*, 3318.

⁵⁴ Williams, N. A.; Uchamaru, Y.; Tanaka, M. *Dalton Trans.*, **2003**, 236.

⁵⁵ Laitar, D. S.; Tsui, E. Y.; Sadighi, J. P. *J. Am. Chem. Soc.* **2006**, *128*, 11036.

Based on Sadighi's work, Marder and Lin investigated the mechanism of the diboration of aldehydes in detail with the aid of DFT calculation.⁵⁶ The results showed that this copper-catalyzed diboration occurs through aldehyde addition to a borylcopper species **I** to give a Cu-O-C(boryl) species **III**, followed by σ -bond metathesis with a diboron reagent (Scheme 3.10). The results of Marder and Lin's calculation also revealed that the insertion intermediate Cu-O-C(boryl) **III** isomerized to the thermodynamically favored Cu-C-O(boryl) **IV** isomer via a boryl migration to the metal-bonded oxygen.

Scheme 3.10 Mechanism of the diboration of aldehydes catalyzed by Cu(I)

More recently, following the studies by Sadighi et al., Clark reported the diboration of ketones for facile synthesis of tertiary α -hydroxyboronate esters (Scheme 3.11).⁵⁷

⁵⁶ Zhao, H.; Dang, L.; Marder, T. B.; Lin, Z. *J. Am. Chem. Soc.* **2008**, *130*, 5586.

⁵⁷ McIntosh, M. L.; Moor, C. M.; Clark, T. B. *Org. Lett.* **2010**, *12*, 1996.

Scheme 3.11 Copper-catalyzed diboration of ketones

In conclusion, a catalytic borylcopper species generated from a Cu-NHC complex and a diboron has been successfully used in addition reactions to various aldehydes and ketones. On the other hand, the stoichiometric addition reaction of the Ta-Si complex is the example of nucleophilic silyl transfer from a transition metal-silyl derivative to a carbonyl compound.

3.2 Our Strategy

In chapter 2, we have successfully realized the silicon-copper addition to α,β -unsaturated esters using an *N*-heterocyclic carbene copper(I) complex as a catalyst. In view of easy formation of Cu-Si intermediate based on Si-B bond activation, we intend to explore the 1,2-silylation of aldehydes to synthesize α -hydroxysilanes, due to their importance as critical organic building blocks, in this chapter (Scheme 3.12). Inspired by the Cu-B addition to carbonyl groups, herein, we developed a new protocol to produce α -hydroxysilanes in good yields under mild conditions.

Scheme 3.12 Designed strategy for silicon-copper addition to aldehyde

3.3 Catalytic Silicon-Copper Addition to Aldehydes Based on Si-B Activation

3.3.1 Results and Discussion

Optimization of Reaction Conditions for Silicon-Copper Addition.

In our initial experiment, we tested the silicon-copper addition to 1 equivalent of 2-naphthaldehyde by employing 1.1 equivalent Ph(Me)₂SiBpin as a silicon source in the presence of a catalytic amount of a copper salt, NaO^tBu in THF at room temperature (Table 3.1). With CuCl as a copper (I) source, the

Table 3.1 Optimization of conditions for silicon-copper addition to 2-naphthaldehyde^a

entry	Cu(I)	base	additive	conversion ^b
1	CuCl	NaO ^t Bu	MeOH	25%
2		NaO ^t Bu	MeOH	> 98% (81%) ^c
3		NaO ^t Bu	no	< 10%
4		no	MeOH	no reaction
5	no	NaO ^t Bu	MeOH	no reaction

^a Reactions were conducted with 1 equiv of 2-naphthaldehyde, 1.1 equiv of Ph(Me)₂SiBpin at room temperature in the presence of MeOH under argon atmosphere. ^b Conversion was determined by 500 MHz ¹H NMR of the crude mixtures. ^c Separated yield.

desired α -hydroxysilane was obtained with only 25% conversion (Table 3.1, entry 1). To our delight, when SIPrCuCl (SIPr = 1,3-bis-(2,6-diisopropylphenyl)imidazoline-2-ylidene) complex was used as the catalyst, the conversion dramatically increased to more than 98% within 3 hours (entry 2). This result indicates that the highly σ -donating SIPr ligand has increased the catalytic ability to a large extent. Subsequently some control experiments were performed. In the absence of MeOH, the reaction decreased to less than 10% conversion (entry 3). Without the base or copper source, the reaction did not take place at all (entries 4 and 5).

Scope of the Silicon-Copper Addition to Aldehydes. Under the optimized conditions (Table 3.1, entry 2), the scope of the reaction was investigated (Table 3.2). The reactions of Ph(Me)₂SiBpin and various aldehydes proceeded in good to excellent yields. Aromatic aldehydes bearing electron-donating (entries 2 and 3) and electron-withdrawing (entries 4 and 11) groups smoothly participated in the reaction. Compared to *para*-tolualdehyde, *para*-methoxybenzaldehyde reacted with Ph(Me)₂SiBpin in lower yield (entry 3). Heteroaromatic aldehydes such as 3-pyridinecarboxaldehyde and 2-furancarboxaldehyde also afforded the desired addition products in good yields (entries 5 and 6). Aliphatic aldehydes bearing primary and secondary substituents also reacted in high yields (entries 7-9). The low yield for the reaction of *para*-cyano benzaldehyde (entry 10) is due to loss in the purification step (¹H NMR of the crude product showed high conversion of the starting material).

Table 3.2 Copper-catalyzed silicon-copper addition to various aldehydes^{a, b}

^a Conditions: unless otherwise stated, 5 mol% (SIPr)CuCl, 6 mol% NaO^tBu, 0.3 mmol aldehyde, 0.33 mmol Ph(Me)₂SiBpin and 2.0 equiv MeOH in THF at room temperature under argon atmosphere. ^b Isolated yield.

A Proposed Mechanism of Silicon-Copper Addition Reaction. On the basis of the experimental results, a proposed mechanism for the silicon-copper addition to aldehydes is shown in Scheme 3.13. Initially, NHC-CuCl complex reacts with NaO^tBu to form NHC-CuO^tBu, which undergoes σ -bond metathesis with Ph(Me)₂SiBpin to give a Cu-Si intermediate **I**. Then the aldehydes C=O inserts into the Cu-Si bond of **I**, forming α -silylalkoxides **II**. Subsequently **II** undergoes protonolysis with MeOH to give α -hydroxysilane

III and an NHC-CuOMe complex **IV**. The complex **IV** reacts with $\text{Ph}(\text{Me})_2\text{SiBpin}$ to regenerate **I**.

Scheme 3.13 Proposed catalytic cycle of silicon-copper addition to aldehydes

3.3.2 Conclusion

In summary, a new protocol for the preparation of α -hydroxysilanes via NHC-Cu-catalyzed addition of a silyborane to aldehydes has been developed. The reaction affords a variety of α -hydroxysilanes in good yields under mild condition. To the best of our knowledge, this is the first example of catalytic nucleophilic silyl transfer from a silyborane to an aldehydes through a Cu-Si intermediate. This protocol will open up an easy and efficient access to a pool of highly functionalized α -hydroxysilanes.

3.4 Supporting Information

3.4.1 General Methods

All synthetic manipulations were carried out using standard Schlenk techniques under an argon atmosphere. The following commercially available reagents were used as received: Ph(Me)₂SiBpin, CuCl, NaO^tBu were purchased from Aldrich or Acros. All aldehydes were purified by distillation or flash chromatography. THF was freshly distilled from Na/benzophenone ketyl and anhydrous MeOH were purchased from Aldrich.

Thin-layer chromatography (TLC) was conducted with Merck 60 F254 precoated silica gel plate (0.2 mm thickness) and visualized under UV or by potassium permanganate stain. Flash chromatography was performed using Merck silica gel 60 with distilled solvents. ¹H-NMR spectra were recorded on a Bruker Avance 300 or 500 NMR spectrometer and reported in ppm downfield from SiMe₄ (δ 0.0) and relative to the signal of chloroform-d (δ = 7.26, singlet). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ¹³C-NMR spectras were recorded on a Bruker Avance 300 or 500 spectrometer and reported in ppm using solvent as an internal standard (CDCl₃ at 77.0 ppm). Conversion of the addition product was determined by ¹H-NMR analysis of the crude product. IR spectras were recorded on a Bio-Rad FTS 165 FTIR spectrometer and were reported in frequency of absorption (cm⁻¹). High Resolution Mass Spectral (HRMS) analysis was performed on Waters Q-ToF Premier Mass Spectrometer.

3.4.2 Representative experimental procedure of silicon-copper addition

A 10 mL Schlenk flask, equipped with a Teflon-coated magnetic stirbar, was charged sequentially with SIPrCuCl (7.3 mg, 0.015 mmol, 5 mol%), NaO^tBu (1.7 mg, 0.018 mmol, 6 mol%), THF (1.0 mL) and the mixture was left to stir for 15 minutes. Then Ph(Me)₂SiBpin (90 μ L, 0.33 mmol, 1.1 equiv) was injected into the reaction mixture and left to stir for 15 minutes. The starting material 2-naphthaldehyde (46.8 mg, 0.30 mmol, 1.0 equiv) and MeOH (24 μ L, 0.60 mmol, 2.0 equiv) were subsequently added into the solution via syringe. It was allowed to stir at room temperature for 5 hours under an argon atmosphere. Then the reaction solution was diluted with dichloromethane and concentrated *in vacuo*. Purification by silica gel column chromatography (10:1 hexane/ethyl acetate eluent) afforded (dimethyl(phenyl)silyl)(naphthalen-2-yl)methanol as a colourless oil (71 mg, 81%).

(Dimethylphenylsilyl)(naphthalen-2-yl)methanol

Yield = 81%. R_f = 0.30 (10:1 hexane/ethyl acetate).

¹H-NMR (500 MHz, CDCl₃) δ (ppm): 7.83 (d, J = 7.8 Hz, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.59 (s, 1H), 7.53-7.54 (m, 2H), 7.43-7.50 (m, 3H), 7.37-7.40 (m, 2H), 7.20 (dd, J_1 = 8.5 Hz, J_2 = 1.4 Hz, 1H), 4.91 (s, 1H), 0.36 (s, 3H), 0.32 (s, 3H).

¹³C-NMR (125 MHz, CDCl₃) δ (ppm): 141.2, 135.9, 134.4, 133.5, 132.2, 129.6, 127.8, 127.7, 127.5, 126.0, 125.2, 124.3, 123.0, 70.2, -5.3, -6.2.

FTIR (neat, cm⁻¹): 3418, 3051, 3021, 2959, 2899, 1595, 1506, 1427, 1248, 858,

833, 818.

HRMS (ESI) m/z Calcd for $C_{19}H_{21}OSi$ $[M + H]^+$: 293.1362, Found 293.1358.

Experimental Details of Table 3.2

(Entry 1)

(Dimethyl(phenyl)silyl)(phenyl)methanol

The title compound was prepared by the general procedure described above and was obtained as a pale yellow oil (62 mg).

Yield = 85%. R_f = 0.46 (10:1 hexane/ethyl acetate).

1H -NMR (500 MHz, $CDCl_3$) δ (ppm): 7.48-7.50 (m, 2H), 7.35-7.41 (m, 3H), 7.25-7.28 (m, 2H), 7.18 (m, 1H), 7.08-7.10 (m, 2H), 4.72 (s, 1H), 0.31 (s, 3H), 0.28 (s, 3H).

^{13}C -NMR (125 MHz, $CDCl_3$) δ (ppm): 143.5, 136.0, 134.4, 129.5, 128.1, 127.8, 125.9, 125.2, 70.0, -5.4, -6.3.

FTIR (neat, cm^{-1}): 3424, 3068, 3024, 2959, 1697, 1598, 1427, 1248, 833, 790.

HRMS (ESI) m/z Calcd for $C_{15}H_{19}OSi$ $[M + H]^+$: 243.1205, Found 243.1203.

(Entry 2)

(Dimethyl(phenyl)silyl)(*p*-tolyl)methanol

The title compound was prepared by the general procedure described above and was obtained as colorless oil (73 mg).

Yield = 95%. R_f = 0.41 (10:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.49-7.52 (m, 2H), 7.33-7.40 (m, 3H), 7.07 (d, J = 8.0 Hz, 2H), 6.98 (d, J = 8.0 Hz, 2H), 4.67 (s, 1H), 2.32 (s, 3H), 0.42 (s, 3H), 0.25 (s, 3H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ (ppm): 140.4, 136.2, 135.4, 134.4, 129.4, 128.8, 127.8, 125.2, 69.9, 21.1, -5.3, -6.3.

FTIR (neat, cm^{-1}): 3445, 3049, 2961, 1699, 1508, 1427, 1265, 833, 812.

HRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{21}\text{OSi}$ $[\text{M} + \text{H}]^+$: 257.1362. Found 257.1366.

(Entry 3)

(Dimethyl(phenyl)silyl)(4-methoxyphenyl)methanol

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (57 mg).

Yield = 70%. R_f = 0.27 (5:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.47-7.50 (m, 2H), 7.35-7.40 (m, 3H), 7.00 (d, $J = 8.7$ Hz, 2H), 6.81 (d, $J = 8.7$ Hz, 2H), 4.65(s, 1H), 3.79 (s, 3H), 0.30 (s, 3H), 0.26 (s, 3H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ (ppm): 158.0, 136.1, 135.5, 134.4, 129.4, 127.8, 126.4, 113.6, 69.5, 55.3, -5.3, -6.2.

FTIR (cm^{-1}): 3431, 3049, 2957, 1684, 1508, 1427, 1246, 833, 810.

HRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{21}\text{O}_2\text{Si}$ $[\text{M} + \text{H}]^+$: 273.1311 Found 273. 1311.

(Entry 4)

(4-Bromophenyl)(dimethyl(phenyl)silyl)methanol

The title compound was prepared by the general procedure described above and was obtained as an off-white solid (91 mg).

Yield = 95%. M.p. = 67-68 °C. R_f = 0.28 (10:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): δ 7.45-7.47 (m, 2H), 7.34-7.45 (m, 5H), 6.94 (d, $J = 8.3$ Hz, 2H), 4.66 (s, 1H), 0.29 (s, 3H), 0.27 (s, 3H)

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 142.6, 135.4, 134.4, 131.1, 129.7, 127.9, 126.8, 119.4, 69.5, -5.6, -6.3.

FTIR (CH_2Cl_2 , cm^{-1}): 3420, 3048, 2959, 1589, 1485, 1427, 1248, 1115, 1070, 835.

HRMS (ESI) m/z Calcd for $\text{C}_{15}\text{H}_{18}\text{BrOSi}$ $[\text{M} + \text{H}]^+$: 321.0310. Found 321.0321.

(Entry 5)

(Dimethyl(phenyl)silyl)(pyridin-3-yl)methanol

The title compound was prepared by the general procedure described above and was obtained as a pale yellow oil (51 mg).

Yield = 70%. R_f = 0.22 (1:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ (ppm): 8.18-8.26 (m, 2H), 7.40-7.45 (m, 2H), 7.34-7.37 (m, 4H), 7.14 (m, 1H), 4.65 (s, 1H), 0.31 (s, 3H), 0.28 (s, 3H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ (ppm): 147.1, 146.7, 139.2, 135.0, 134.3, 132.8, 129.8, 127.9, 123.0, 67.1, -5.8, -6.2.

FTIR (neat, cm^{-1}): 3393, 3048, 2959, 1653, 1589, 1576, 1427, 1248, 833, 816.

HRMS (ESI) m/z Calcd for $\text{C}_{14}\text{H}_{18}\text{NOSi}$ $[\text{M} + \text{H}]^+$: 244.1158. Found 244.1163.

(Entry 6)

(Dimethyl(phenyl)silyl)(furan-2-yl)methanol

The title compound was prepared by the general procedure described above and was obtained as a pale yellow oil (60 mg).

Yield = 86%. R_f = 0.35 (4:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.55-7.56 (m, 2H), 7.36-7.40 (m, 4H), 6.32 (d, J = 1.8 Hz, 1H), 6.09 (d, J = 2.7 Hz, 1H), 4.64 (s, 1H), 0.44 (s, 3H), 0.37 (s, 3H).

^{13}C -NMR (125 MHz, CDCl_3) δ (ppm): 156.5, 141.7, 135.9, 134.2, 129.6, 127.9, 110.4, 106.1, 62.8, -4.9, -5.5.

FTIR (neat, cm^{-1}): 3482, 3069, 2957, 1589, 1499, 1456, 1427, 1254, 831.

HRMS (ESI) m/z Calcd for $\text{C}_{13}\text{H}_{17}\text{OSi}$ $[\text{M} + \text{H}]^+$: 233.0998. Found 233.1004.

(Entry 7)

1-(Dimethyl(phenyl)silyl)-3-phenylpropan-1-ol

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (73 mg).

Yield = 90 %. R_f = 0.24 (10:1 hexane/ethyl acetate).

^1H -NMR (500 MHz, CDCl_3) δ (ppm): 7.56-7.58 (m, 2H), 7.39-7.42 (m, 3H), 7.28-7.31 (m, 2H), 7.19-7.22 (m, 3H), 3.56 (m, 1H), 2.93 (m, 1H), 2.64 (m, 1H), 1.84-1.88 (m, 2H), 0.37 (s, 3H), 0.36 (s, 3H).

^{13}C -NMR (125 MHz, CDCl_3) δ (ppm): 142.2, 136.5, 134.2, 129.5, 128.6, 128.4, 128.0, 125.8, 64.9, 35.5, 33.3, -5.4, -5.6.

FTIR (neat, cm^{-1}): 3426, 3067, 3024, 2959, 1603, 1589, 1454, 1427, 829, 812.

HRMS (ESI) m/z Calcd for $\text{C}_{17}\text{H}_{23}\text{OSi}$ $[\text{M} + \text{H}]^+$: 271.1518. Found 271.1510

(Entry 8)

Cyclohexyl(dimethyl(phenyl)silyl)methanol

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (60 mg).

Yield = 80%. R_f = 0.27 (5:1 hexane/ethyl acetate).

¹H-NMR (300 MHz, CDCl₃) δ (ppm): 7.56-7.61 (m, 2H), 7.36-7.39 (m, 3H), 3.35 (d, J = 5.7 Hz, 1H), 1.49-1.87 (m, 6H), 0.85-1.29 (m, 5H), 0.39 (s, 3H), 0.38(s, 3H).

¹³C-NMR (75 MHz, CDCl₃) δ (ppm): 137.8, 134.1, 129.2, 127.9, 71.0, 42.1, 30.8, 29.6, 26.5, 26.4, 26.3, -3.8, -4.3.

FTIR (neat, cm⁻¹): 3447, 3069, 3049, 2926, 2851, 1630, 1427, 1250, 833.

HRMS (ESI) m/z Calcd for C₁₅H₂₅OSi [M + H]⁺ : 249.1675. Found 249.1669.

(Entry 9)

1-(Dimethyl(phenyl)silyl)octan-1-ol

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (74 mg).

Yield = 94%. R_f = 0.49 (10:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.56-7.59 (m, 2H), 7.37-7.40 (m, 3H), 3.52 (m, 1H), 1.50-1.55 (m, 3H), 1.13-1.28 (m, 9H), 0.89 (t, $J = 6.8$ Hz, 3H), 0.36 (s, 3H), 0.35 (s, 3H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ (ppm): 136.9, 134.1, 129.3, 127.9, 65.5, 33.5, 31.5, 29.5, 29.3, 22.7, 14.1, -5.3, -5.6.

FTIR (neat, cm^{-1}): 3443, 3053, 2989, 2926, 2855, 1636, 1422, 1265, 895, 814.

HRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{29}\text{OSi}$ $[\text{M} + \text{H}]^+$: 265.1988. Found 265.1980.

(Entry 10)

4-((Dimethyl(phenyl)silyl)(hydroxy)methyl)benzonitrile

The title compound was prepared by the general procedure described above and was obtained as a white solid (45 mg).

Yield = 56%. M.p. = 100-102 $^{\circ}\text{C}$. R_f = 0.21 (10:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.51 (d, $J = 8.3$ Hz, 2H), 7.29-7.43 (m, 5H), 7.13 (d, $J = 8.3$ Hz, 2H), 4.76 (s, 1H), 0.31 (s, 3H), 0.29 (s, 3H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ (ppm): 149.4, 134.7, 134.3, 131.8, 129.9, 128.0, 125.4, 119.2, 109.2, 69.9, -5.8, -6.2.

FTIR (CH_2Cl_2 , cm^{-1}): 3420, 3069, 3022, 2959, 2226, 1605, 1427, 1250, 851.

HRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{18}\text{NOSi}$ $[\text{M} + \text{H}]^+$: 268.1158. Found 268.1167.

(Entry 11)

(4-Chlorophenyl)(dimethyl(phenyl)silyl)methanol

The title compound was prepared by the general procedure described above and was obtained as a white solid (81 mg).

Yield = 98%. M.p. = 80-81°C. R_f = 0.36 (5:1 hexane/ether).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.44-7.47 (m, 2H), 7.35-7.40 (m, 3H), 7.21 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 4.68 (s, 1H), 0.29 (s, 3H), 0.26 (s, 3H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ (ppm): 142.0, 135.5, 134.4, 131.4, 129.7, 128.1, 127.9, 126.4, 69.4, -5.6, -6.2.

FTIR (CH_2Cl_2 , cm^{-1}): 3443, 3053, 2986, 1605, 1427, 1250, 1115, 1092, 839.

HRMS (ESI) m/z Calcd for $\text{C}_{15}\text{H}_{18}\text{ClOSi}$ $[\text{M} + \text{H}]^+$: 277.0815. Found: 277.0814.

CHAPTER 4

Highly Regioselective Copper-Catalyzed Silylcupration of Terminal Alkynes

4.1 Introduction

Organosilanes serve as versatile building blocks in both organic synthesis and material science.⁵⁸ The low toxicity and ease of handling of vinylsilanes make them particularly useful among organosilanes. In addition, their compatibility with various organic reagents has been widely used in various organic transformations such as Tamao-Fleming oxidation, olefin metathesis, Pd-catalyzed cross-coupling, protodesilylation and cycloaddition.⁵⁹ Hydrosilylation of terminal alkynes offers a straightforward and atom-economic way for the preparation of vinylsilanes.⁶⁰ Besides the hydrosilylation strategy, the silylmatalation of alkynes offers an alternative and attractive route for the efficient synthesis of stereodefined vinylsilanes.⁶¹ However, difficulties in accessing regio- and stereodefined isomers has hampered the widespread use of vinylsilanes.

4.1.1 Transition Metal Catalyzed Hydrosilylation of Terminal Alkynes

The hydrosilylation of a terminal alkyne is commonly catalyzed by transition metal complexes. In such reactions, the use of terminal alkynes as

⁵⁸ (a) Brook, M. A. In *Silicon in Organic, Organometallic and Polymer Chemistry*, Wiley: New York, 2000. (b) Ojima, I.; Li, Z. Y.; Zhu, J. W. In *Chemistry of Organic Silicon Compounds*; Rappoport, Z., Apeloig, Y. Eds.; Wiley: Chichester, 1998; p1687.

⁵⁹ (a) Blumenkopf, T. A.; Overman, L. E. *Chem. Rev.* **1986**, 86, 857. (b) Hiyama, T. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F.; Stang, P. J. Eds.; Wiley-VCH: Weinheim, Germany, 1998; p 421. (c) Denmark, S. E.; Sweis, R. F. In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; de Meijere, A.; Diederich, F. Eds.; Wiley-VCH: Weinheim, Germany, 2004, p 163. (d) Fleming, I.; Maeda, K. *Chem. Commun.* **1984**, 29, 30. (e) Tamao, K.; Maeda, K. *Tetrahedron Lett.* **1986**, 27, 65. (f) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, 52, 7599.

⁶⁰ For recent reviews on hydrosilylation, see: (a) Marciniak, B. In *Hydrosilylation: A Comprehensive Review on Recent Advance (Advance in Silicon Science)*, Springer: Berlin, 2009. (b) Trost, B. M.; Ball, Z. T. *Synthesis* **2005**, 853. (c) Brunner, H. *Angew.Chem. Int. Ed.* **2004**, 43, 2749.

⁶¹ For reviews of silylmatalation reactions of multiple bonds, see: (a) Horn, K. A. *Chem. Rev.* **1995**, 95, 1317. (b) Beletskaya, I.; Moberg, C. *Chem. Rev.* **1999**, 99, 3435. (c) Ito, Y. *J. Organomet. Chem.* **1999**, 576, 300. (d) Sugimoto, M.; Ito, Y. *Chem. Rev.* **2000**, 86, 3221.

substrates potentially lead to a mixture of three isomers: α -vinylsilanes, β -*trans* vinylsilanes and β -*cis* vinylsilanes (Scheme 4.1). The utility of stereodefined vinylsilanes in synthetic organic chemistry has driven research on efficient catalytic systems for the highly selective formation of each of these isomers.

Scheme 4.1 Isomers in the hydrosilylation of terminal alkynes

The traditional platinum catalysts, such as Speier's catalyst H_2PtCl_6 and Karstedt's catalyst, offer low or imperfect regio- and stereoselectivities in hydrosilylation of alkynes with various hydrosilanes (Table 4.1).⁶²

Table 4.1 Alkyne hydrosilylation in the presence of Karstedt's catalyst

Alkyne	Silane R_3SiH	β - <i>trans</i> / β - <i>cis</i> / α
$\text{CH}_3(\text{CH}_2)_2\text{CCH}$	Et_3SiH	89/0/11
	PhMe_2SiH	70/5/25
	$(\text{EtO})_3\text{SiH}$	56/6/38

On the other hand, platinum complexes bearing bulky trialkylphosphines show good regioselectivity. Hiyama disclosed that the use of Karstedt's catalyst in combination with P^tBu_3 resulted in higher β -*trans*-selectivities for a variety of terminal alkynes.⁶³ Denmark used the same catalytic system to achieve

⁶² (a) Speier, J. L. *Adv. Organomet. Chem.* **1979**, *17*, 407. (b) Lewis, N. L.; Sy, K. G.; Bryant, G. L.; Donahue, G. L. *Organometallics* **1991**, *10*, 3750.

⁶³ Takahashi, K.; Minami, T.; Ohara, Y.; Hiyama, T. *Tetrahedron Lett.* **1993**, *34*, 8263.

excellent β -*trans*-regioselectivities in the synthesis of vinylsilanes and sequential hydrosilylation-Hiyama coupling (Scheme 4.2).⁶⁴

Scheme 4.2 One pot hydrosilylation-Hiyama coupling of alkynes with aryl iodides

In the presence an air-stable bulky biaryldicyclohexylphosphine ligand, highly β -*trans*-selective hydrosilylation of functionalized terminal arylalkynes was also successfully achieved (Scheme 4.3).⁶⁵

Scheme 4.3 PtCl_2 catalyzed regioselective hydrosilylation with aromatic alkynes

More recently, a highly regioselective β -*trans*-hydrosilylation reaction of terminal alkynes catalyzed by an *N*-heterocyclic carbene (NHC) platinum(0) complex was reported by Markó et al (Scheme 4.4).⁶⁶ This reaction allows, with a low catalyst loading (0.05 to 0.1 mol%), near exclusive formation of β -*trans*-hydrosilylation products.

⁶⁴ Denmark, S. E.; Wang, Z. G. *Org. Lett.* **2001**, 3, 1073.

⁶⁵ Hamze, A.; Provot, O.; Brion, J. D.; Alami, M. *Tetrahedron Lett.*, **2008**, 49, 2429.

⁶⁶ (a) De Bo, G.; Berthon-Gelloz, G.; Tinant, B.; Markó, I. E. *Organometallics* **2006**, 25, 1881.
(b) Berthon-Gelloz, G.; De Bo, G.; Schumers, J.; Markó, I. E. *J. Org. Chem.* **2008**, 73, 4190.

Scheme 4.4 NHC-Pt complex catalyzed regioselective hydrosilylation

While the Pt complexes afford excellent regio- and stereoselectivity for β -*trans*-vinylsilanes, neutral rhodium complexes catalyze the hydrosilylation of terminal alkynes giving the thermodynamically less favorable β -*cis*-vinylsilanes as the major products (Scheme 4.5).⁶⁷

Scheme 4.5 Hydrosilylation of 1-hexyne in the presence of Rh complex

Interestingly, the stereoselectivity of the Rh-catalyzed hydrosilylation can be changed by the choice of the solvents and the ligands. For example, Takeuchi discovered that (*Z*)-1-silyl-1-hexene was obtained in the process of the hydrosilylation of 1-hexyne with Et_3SiH catalyzed by $[\text{RhCl}(\text{cod})]_2$ in DMF, whereas (*E*)-1-silyl-1-hexene was obtained using 2 equivalents of PPh_3 as the ligand and acetonitrile as the solvent (Scheme 4.6).⁶⁸

⁶⁷ (a) Ojima, I.; Clos, N.; Donovan, R. J.; Ingallina, P. *Organometallics* **1990**, 9, 3127. (b) Doyle, M. P.; High, K. G.; Nesloney, C. L.; Clayton, J. W., Jr.; Lin, J. *Organometallics* **1991**, 10, 1225. (c) Mori, A.; Takahisa, E.; Yamamura, Y.; Kato, T.; Mudalige, A.P.; Kajiro, H.; Hirabayashi, K.; Nishihara, Y.; Hiyama, T. *Organometallics* **2004**, 23, 1755.

⁶⁸ Takeuchi, R.; Tanouchi, N. *J. Chem. Soc., Chem. Commun.* **1993**, 1319.

Scheme 4.6 Reverse regioselective hydrosilylation catalyzed by Rh complex

Although a large number of catalytic systems have been developed for the hydrosilylation of terminal alkynes to produce linear vinylsilanes (β -*trans*- and β -*cis*-vinylsilanes), a procedure for the regioselective syntheses of α -vinylsilanes is underdeveloped. Chang et al. found that Ru-catalyzed hydrosilylation of alkynes having a hydroxyl group at the β -position to the triple bond affords α -vinylsilanes with excellent regioselectivity using catalytic Ru complex (Scheme 4.7).⁶⁹

Scheme 4.7 Hydroxyl group directed hydrosilylation of alkynes

To overcome the shortcoming of pre-installing directing group, Trost reported the α -isomer can be obtained in high yield by a [Cp*Ru]-based catalyst with a variety of functional groups in the alkynes (Scheme 4.8).⁷⁰ In order to understand the *anti*-addition stereochemistry and Markovnikov regiochemistry of the hydrosilylation catalyzed by cationic cyclopentadienyl-ruthenium complexes,

⁶⁹ Na, Y.; Chang, S. *Org. Lett.* **2000**, *4*, 1887.

⁷⁰ Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2001**, *123*, 12726.

Scheme 4.8 Hydrosilylation of terminal alkynes to afford Markovnikov selectivity

Wu and Trost carried out DFT calculations.⁷¹ Their studies demonstrated that hydride insertion is much more favorable than silyl insertion. Following the hydride insertion, the $C_{\alpha}\text{-}C_{\beta}$ bond of a η^2 -vinylruthenium or metallacyclopentene intermediate undergoes a stereospecific counterclockwise rotation. Finally, a facile α -silyl migration yields a *trans*-addition product through a metallacyclopentene-like transition structure.

Yamamoto et al. also found that a ruthenium catalyst bearing a bulky and electron-donating pentamethylcyclopentadienyl (Cp^*) ligand, typically $\text{Cp}^*\text{RuH}_3(\text{PPh}_3)$, is effective for the hydrosilylation of terminal alkynes leading to α -vinylsilanes with good regioselectivity (Scheme 4.9).⁷²

Scheme 4.9 Ru(II)-catalyzed α -selective hydrosilylation of terminal alkynes

⁷¹ Chung, L. W.; Wu, Y. D.; Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2003**, *125*, 11578.

⁷² Kawanami, Y.; Sonoda, Y.; Mori, T.; Yamamoto, Y. *Org. Lett.* **2002**, *4*, 2825.

Later Cossy achieved highly α -selective hydrosilylation of terminal alkynes with the 1st generation Grubbs catalyst (Scheme 4.10).⁷³

Scheme 4.10 Grubbs catalyst-mediated Markovnikov hydrosilylation

In conclusion, a variety of catalytic systems have been developed for hydrosilylation of terminal alkynes. Appropriate choices of the transition metal catalyst and other factors (e.g., substrate, solvent, ligand) allow one to control the regio- and stereoselectivities.

⁷³ Menozzi, C.; Dalko, P.; Cossy, J. *J. Org. Chem.* **2005**, *70*, 10717.

4.1.2 The Silylmetalation of Terminal Alkynes

One of the most attractive strategies for the efficient synthesis of organosilanes is the silylmetalation of multiple bonds.⁷⁴ In particular, the silylcupration of acetylene, which allows the introduction of two different metals (Si and Cu) across a C-C triple bond, provides an easy access to the synthesis of vinylsilanes.⁷⁵ Fleming et al. extensively studied the stoichiometric silylcupration $[(R_3Si)_2CuLi \cdot LiCN]$ to terminal alkynes.⁷⁶ For example, the silylcopper reagent, prepared by mixing two equivalents of dimethylphenylsilyl lithium and one equivalent of CuCN reacted with 1-hexyne to give exclusively a β -*trans*-vinylsilane in high regioselectivity (Scheme 4.11).

Scheme 4.11 Stoichiometric silylcupration of terminal alkynes

Silylcupration also proceeded with 1-aminoalkynes⁷⁷ and propargylamines,⁷⁸ the latter being used for the synthesis of saturated γ -silyl- α -amino acids (Scheme 4.12).

Scheme 4.12 Stoichiometric silylcupration of propargylamines

⁷⁴ For reviews of silylmetalation reactions of multiple bonds, see: (a) Horn, K. A. *Chem. Rev.* **1995**, 95, 1317. (b) Beletskaya, I.; Moberg, C. *Chem. Rev.* **1999**, 99, 3435. (c) Ito, Y. *J. Organomet. Chem.* **1999**, 576, 300. (d) Sugimoto, M.; Ito, Y. *Chem. Rev.* **2000**, 86, 3221.

⁷⁵ For recent reviews, see: (a) Barbero, A.; Pulido, F. J. *Acc. Chem. Chem.* **2004**, 37, 817. (b) Weickgenannt, A.; Oestreich, M. *Chem. Eur. J.* **2010**, 16, 402.

⁷⁶ (a) Fleming, I.; Roessler, F. *J. Chem. Soc., Chem. Commun.* **1980**, 276. (b) Fleming, I.; Newton, T. W.; Roessler, F. *J. Chem. Soc., Perkin Trans. 1*, **1981**, 2527. (c) Fleming, I.; Martínez de Marigortar, E. *J. Chem. Soc., Perkin Trans. 1*, **1999**, 889.

⁷⁷ Capella, L.; Capperucci, G.; Curotto, G.; Lazzari, D.; Dembech, P.; Reginato, G.; Ricc, A. *Tetrahedron Lett.* **1993**, 34, 3311.

⁷⁸ Reginato, G.; Mordini, A.; Valacchi, M.; Grandini, E. *J. Org. Chem.* **1999**, 64, 9211.

Despite the many methods for the stoichiometric silylcupration of acetylenes, there remains a need for catalytic silylcupration in view of atom-economy. Oshima et al. disclosed that $\text{Ph}(\text{Me})_2\text{SiMgMe}$ reacted easily with terminal alkynes in the presence of a catalytic amount copper iodide with high β -*trans*-regioselectivity (Scheme 4.13).⁷⁹

Scheme 4.13 Transition metal catalyzed silylmatalaion of terminal alkynes

In contrast, it is difficult to obtain α -vinylsilanes with high regioselectivity using the method described previously. Later, Oshima and co-workers solved the problem with ate complexes such as lithium di-*tert*-butyl(dimethylphenylsilyl) zincate, which afford α -addition products in the presence of a catalytic amount of CuCN (Scheme 4.14).⁸⁰ However, only a few substrates were examined, and the scope of this reaction remains unclear.

Scheme 4.14 CuCN-catalyzed α -selective silylmatalaion of terminal alkynes

About 20 years later from Oshima's work, Uchiyama et al. employed a bulky zincate (SiBNOL-Zn-ate) to achieve the chemo- and regioselective

⁷⁹ (a) Hayami, H.; Sato, M.; Kanemoto, S.; Morizawa, Y.; Oshima, K.; Nozaki, H. *J. Am. Chem. Soc.* **1983**, *105*, 4491. (b) Okuda, Y.; Morizawa, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1984**, *25*, 2483. (c) Okuda, Y.; Wakamatsu, W.; Tückmantel, K.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26*, 4629.

⁸⁰ Wakamatsu, W.; Nonaka, T.; Okuda, Y.; Tückmantel, K.; Oshima, K.; Utimoto, K.; Nozaki, H. *Tetrahedron* **1986**, *42*, 4227.

silylzincation of terminal alkynes, affording α -vinylsilanes with wide substrate generality in the absence of any catalyst (Scheme 4.15).⁸¹

Scheme 4.15 α -Silylzincation of terminal alkynes with SiBNOL-Zn-ate

In 2006, Oestreich revisited the silylzincation of C-C multiple bond based on Fleming's work and found that the regioselectivity of the silylzincation could be greatly influenced by the reaction temperature (Table 4.2).⁸² At the same time they discovered an unexpected bis-silylation of terminal alkynes with an excess amount of $(\text{Me}_2\text{PhSi})_2\text{Zn}$ (Scheme 4.16).

Table 4.2 Copper-catalyzed silylzincation of terminal alkynes

entry	T / °C	$\beta\text{-trans} / \alpha$	yield
1	-50	78:22	50
2	-78	22:78	85
3	-100	10:90	65

Scheme 4.16 Copper-catalyzed bis-silylation of terminal alkynes

⁸¹ Nakamura, S.; Uchiyama, M.; Ohwada, T. *J. Am. Chem. Soc.* **2004**, 126, 11146.

⁸² Auer, G.; Oestreich, M. *Chem. Commun.* **2006**, 311.

The mechanism of the silylcupration of terminal alkynes has not been well-studied in literature. Bäckvall and co-workers proposed a mechanism involving oxidative addition to give a Cu (III) species followed by reductive elimination to yield the vinylmetal intermediate (Scheme 4.17).⁸³ To the best of our knowledge, this is only one proposed mechanism without direct experimental support.

Scheme 4.17 Catalytic cycle for the formation of a vinylmagnesium intermediate

In summary, silylcupration reactions of terminal alkynes are well established in organic chemistry and have been extensively used in many organic transformations. However, it is still a challenge to achieve high regioselectivity with wide substrate scope through catalytic silylcupration of terminal alkynes. Although transition metal-based catalysts provide powerful protocols to build vinylsilanes via hydrosilylation, silylcupration has the advantage of introducing both the silyl and copper atoms onto the triple bond, which can be transformed into different functional groups subsequently.

⁸³ Liepins, V.; Karström, A. S. E.; Bäckvall, J. –E. *J. Org. Chem.* **2002**, 67, 2136.

4.1.3 Our Strategy

In the previous chapters, our group has successfully realized the silicon-copper 1,4-addition to α , β -unsaturated esters and 1,2-addition to aldehydes based on Si-B bond activation using NHC-copper complexes as catalysts. On the basis of these studies, we envisioned a possibility of catalytic regioselective silylcupration of terminal alkynes. For such transformations to be viable, a ligand must play a critical role in enhancing the reactivity for the Cu-Si intermediate as well as controlling the regioselectivity (Scheme 4.18). In this section, we present a new strategy to access the highly regioselective silylcupration of terminal alkynes based on Si-B activation.

Scheme 4.18 Designed strategy to furnish the catalytic silylcupration of alkynes

4.2 Highly Regioselective Copper-Catalyzed Silylcupration of Terminal Alkynes

Part 1: Cu-Catalyzed α -Selective Silylcupration of Alkyl-Substituted Terminal Alkynes: Synthesis of α -Vinylsilanes

4.2.1 Results and Discussion

The main aim of this part is to study the efficiency, regio- and stereoselectivity in the silylcupration of alkyl-substituted terminal alkynes. Ligand effects on catalytic activity and the stereoselectivity are first studied, followed by exploration of the substrate scope. Finally, a proposed catalytic cycle and the origin of the regioselectivity are discussed.

Ligand Effects on Reactivity and Selectivity. Initially, a family of NHC ligands were screened for a model reaction using 1-octyne **1** and Ph(Me)₂SiBpin **2** (Table 4.3). The silylcupration was performed at -20 °C and the progress of the reaction was monitored by TLC. The structures of the screened NHC salts and their reactivities are summarized in Table 4.3. The bulkiest carbene salts IAd·HBF₄ (1,3-Bis(1-adamantyl)imidazolium tetrafluoroborate) and I'Bu·HCl (1,3-Di-tert-butylimidazolium tetrafluoroborate) yielded the desired silylcupration products with good regioselectivities (B:L 84:16 and 67:33; entries 7 and 8), which suggested that steric effects might be an important factor for regioselectivity. ICy·HBF₄ (1,3-Dicyclohexylimidazolium tetrafluoroborate) was used as ligand and the desired product was obtained in excellent yield with modest linear selectivity (98%; B:L = 43:57; entry 5).

Table 4.3 NHC-copper complex catalyzed silylcupration of terminal alkynes^a

entry	NHC-salt	B / L ^b	yield ^c	entry	NHC-salt	B / L	yield
1	 IMe•HCl	60/40	91%	5	 ICy•HCl	43/57	98%
2	 SiMe•HCl	44/56	83%	6	 iPr•HCl	58/42	66%
3	 iPr•HCl	46/54	81%	7	 tBu•HCl	67/33	95%
4	 SiPr•HCl	53/47	91%	8	 IAd•HBf ₄	84/16	75%

^aReaction conditions unless otherwise specified: 1-octyne (0.3 mmol, 1.0 equiv), Ph(Me)₂SiBpin (1.1 equiv), CuCl (0.1 equiv), NHC-salt (0.1 equiv), NaO^tBu (0.22 equiv) and MeOH (2.0 equiv) in THF (1.0 mL) at -20 °C for 24 h. ^b Determined by ¹H-NMR analysis of the crude mixture. ^c Isolated yields of the mixtures of isomers.

As NHCs ligands have been considered as “phosphine-mimics”,⁸⁴ we examined some phosphine ligands for comparison. Table 4.4 summarizes the representative results for the silylcupration reactions of alkynes with phosphine ligands. The reaction of 1-octyne **1** with Ph(Me)₂SiBpin **2** was carried out in the presence of CuCl (10 mol%) and NaO^tBu (11 mol%) in THF with various phosphine ligands. In the presence of the bidentate ligand DPPE, the product was formed in 47% isolated yield without regioselectivity (B: L 50:50; entry 1). The excellent branched regioselectivity but low reactivity was achieved with

⁸⁴ Huang, J.; Schanz, H. -J.; Stevens, E. D.; Nolan, S. P. *Organometallics* **1999**, *18*, 2370.

(R)-BINAP ligand in the reaction (entry 2). The use of Xantphos and DPPF afforded the vinylsilane in poor yield but with good linear to branched selectivity (entries 3 and 5). Interestingly, the regioselectivity was reversed with monophosphine ligands (entries 6, 7 and 8). For example, the use of PCy₃ led to the formation of the α -vinylsilanes in good yield and regioselectivity (entry 6). Based on these results, we proposed that the utilization of electron-rich and bulky monophosphine ligands might increase both the reactivity and the selectivity.

Table 4.4 Phosphine screening for the silylcupraion of terminal alkynes^a

entry	phosphine	B/L	yield	entry	phosphine	B/L	yield
1		50/50	47%	5		18/82	14%
2		95/5	24%	6		86/14	62%
3		5/95	12%	7		88/12	84%
4		no reaction		8		63/37	35%

^aReaction conditions unless otherwise specified: 1-octyne (0.3 mmol, 1.0 equiv), Ph(Me)₂SiBpin (1.1 equiv), CuCl (0.1 equiv), phosphine (0.1 equiv), NaO^tBu (0.11 equiv) and MeOH (2.0 equiv) in THF (1.0 mL) at -20 °C for 24 h.

Table 4.4 Phosphine screening for the silylcupraion of terminal alkynes^a

entry	phosphine	B/L	yield	entry	phosphine	B/L	yield
9		93/7	70%	12		99 / 1	73%
10		89/11	66%	13		97/3	49%
11		93/7	88%	14		> 99/1	40%

^aReaction conditions unless otherwise specified: 1-octyne (0.3 mmol, 1.0 equiv), Ph(Me)₂SiBpin (1.1 equiv), CuCl (0.1 equiv), phosphine (0.1 equiv), NaO^tBu (0.11 equiv) and MeOH (2.0 equiv) in THF (1.0 mL) at -20 °C for 24 h.

Better yield and regioselectivity were indeed achieved with tri-*tert*-butyl phosphine (entry 9). Gratifying, even better regioselectivity was achieved with Johnphos ligand (entry 12).⁸⁵ Using Johnphos ligand, we began to investigate its activity in the silylcupration at different temperatures in order to improve the yield of the reaction. The yield increased to 80% without decrease in regioselectivity at 0 °C (entry 2). The reaction at ambient temperature gave

⁸⁵ Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 4369.

excellent yield of the product but with a slight deterioration of selectivity (Table 4.5, entry 1).

Table 4.5 Temperature effect for the silylcupration of terminal alkynes^a

entry	T	yield	B/L
1	rt	93%	95/5
2	0 °C	80%	99/1
3	- 20 °C	73%	99/1

^aReaction conditions unless otherwise specified: 1-octyne (0.3 mmol, 1.0 equiv), Ph(Me)₂SiBpin (1.1 equiv), CuCl (0.1 equiv), Johnphos (0.1 equiv), NaO^tBu (0.11 equiv) and MeOH (2.0 equiv) in THF (1.0 mL) for 24 h.

Control Reactions. The control experiments with absence of the copper catalyst or base, resulted in the recovery of the starting materials without detection of any other compounds (Table 4.6, entries 2 and 4). Using CuCl without ligand led to poor levels of reaction efficiency (B:L 63:37, 15% yield; Table 4.6, entry 3).

Table 4.6 Control experiments for the silylcupration of terminal alkynes^a

entry	Cu(I)	ligand	base	yield	B/L
1	CuCl	Johnphos	NaO ^t Bu	80%	99/1
2	no	Johnphos	NaO ^t Bu	no reaction	
3	CuCl	no	NaO ^t Bu	15%	63/37
4	CuCl	Johnphos	no	no reaction	

Scope of the Silylcupration of Terminal Aliphatic Alkynes. With the optimized conditions in hand (Table 4.5, entry 2), we next tested the scope of the reaction using various terminal alkynes. The results are summarized in Table 4.7. Substrates possessing electron-donating (Table 4.7, entries 4, 6 and 12) or electron-withdrawing groups (Table 4.7, entries 2, 3 and 5) smoothly participated in the reaction. A wide range of functional groups, including chloro, cyano, ester, hydroxy and tertiary amino groups were tolerant (entries 2-5 and 12). Terminal alkynes containing alkyl, benzyl, cycloalkyl groups reacted with high branched regioselectivity (entries 1, 7, 8 and 11). It was noteworthy that double bond moiety in the enyne substrate remained intact (entry 10). Another important feature of the reaction was that coordinating groups had no effect on the regioselectivity (entries 6 and 12), though only moderate yields were obtained. When phenylacetylene was employed as a substrate, the regioselectivity decreased dramatically, presumably due to the electron deficient nature of the terminal alkyne carbon (entry 9).

Table 4.7 Highly branch-selective synthesis of vinylsilanes of various terminal alkynes catalyzed by copper^a

entry	reactants	yield ^b	B/L ^c
1	4a	71%	97/3
2	4b	74%	96/4
3	4c	67%	95/5
4	4d	86%	99/1
5	4e	90%	93/7
6	4f	60%	96/4
7	4g	70%	96/4
8	4h	76%	99/1
9	4i	87%	62/38
10	4j	76%	93/7
11	4k	84%	90/10
12	4l	50%	91/9

^a Reaction conditions : **4** (0.3 mmol), Ph(Me)₂SiBpin (0.33 mmol), CuCl (0.03 mmol), Johnphos (0.03 mmol), NaO^tBu (0.03 mmol) and MeOH (2.0 equiv) in THF (1.0 mL), nitrogen, 0 °C for 24 h. ^b Isolated yields of the mixtures of isomers. ^c Determined by ¹HNMR analysis of the crude mixture.

Mechanistic Pathway. Until now the mechanism of the silylcupration of acetylenes has not been well-studied in literature. To the best of our knowledge, there is only one proposed mechanism that is similar to the carbocupration reaction.⁸⁶ It was previously proposed that the carbocupration of alkynes proceeds via direct 1,2-addition fashion via a four-centered transition state and the Cu(I) oxidation state remains unchanged during the reaction.⁸⁷ Later Nakamura et al. deduced through systematic calculations that the carbocupration reaction proceeds via oxidative addition of the alkyne to Cu(I) to give a cuprio(III) cyclopropene intermediate, which undergoes reductive elimination to give the vinyl copper species.⁸⁸ Based on our experimental results, a plausible catalytic cycle is shown in Scheme 4.19. We believe that the LCuCl complex easily reacts with NaO^tBu to form a LCuO^tBu complex, which undergoes formal σ -bond metathesis with Ph(Me)₂SiBpin to generate a silylcopper intermediate **I**. Note that the use of ^tBuOH instead of MeOH under the standard conditions (Table 4.5, entry 2) obtained a similar result (B:L 96:4, 79% yield). This may support our conjecture that a copper-alkoxide is the catalytically active species. Then, the alkyne coordinates to the Cu atom of the intermediate **I** to give a π -complex **II**. Subsequently the C–C triple bond adds to the Cu–Si bond, forming a vinyl copper species **IV**, presumably via a four-centered transition state **III**. Finally the vinylcopper species undergo protonolysis in the presence of methanol to liberate the product **V** and regenerate the catalyst **VI** LCuOMe complex. It should be noted that another

⁸⁶ Liepins, V.; Karström, A. S. E.; Bäckvall, J. –E. *J. Org. Chem.* **2002**, 67, 2136.

⁸⁷ (a) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841. (b) Alexakis, A.; Marek, I.; Mangeney, P.; Normant, J. F. *J. Am. Chem. Soc.* **1990**, 112, 8042.

⁸⁸ (a) Nakamura, E.; Mori, S.; Nakamura, M.; Morokuma, K. *J. Am. Chem. Soc.* **1997**, 119, 4887. (b) Nakamura, E.; Mori, S. *Angew. Chem. Int. Ed.* **2000**, 39, 3750.

mechanistic pathway which involves an oxidative addition and reductive elimination process is also possible and cannot be ruled out.⁸⁹

Scheme 4.19 Proposed catalytic cycle for silicon-copper additions to terminal alkynes

Regioselectivity of Terminal Aliphatic Alkyne Silylcupration. Our catalytic system allows the silylcupration of aliphatic alkynes with up to 99% α -selectivity. The highly Markovnikov selectivity may be rationalized by the four-membered transition state (Scheme 4.20). Both electronic and steric effects should play important roles for this high regioselectivity. The electrophilic metal center interacts preferably with the acetylene β -carbon, which bears larger electron density as compared with the α -carbon (Scheme 4.20, **A**). Meanwhile, in transition state **A** the R¹ group is away from the bulky supporting phosphine ligand on copper, this definitely makes it more favorable than the crowded transition state **B** (Scheme 4.20, **B**).

⁸⁹ Liepins, V.; Karström, A. S. E.; Bäckvall, J. -E. *J. Org. Chem.* **2002**, 67, 2136.

Scheme 4.20 Proposed transition states for the formation of Markovnikov (**A**) and anti-Markovnikov silylcupration product (**B**)

4.2.2 Conclusion

In summary, we have developed a new method to induce highly Markovnikov-selective silylcupration of various terminal aliphatic alkynes based on Si-B bond activation. The reaction is tolerated a wide range of functional groups including chloro, hydroxy, ester, cyano, and amino groups and gives α -vinylsilanes in moderate to good yields with excellent regioselectivities. Extension of the present chemistry to other unsaturated substrates such as allenes, 1, 3-dienes, alkenes is envisioned.

4.3 Part 2: Cu-Catalyzed Anti-Markovnikov Intermolecular Silylcupration of Terminal Aromatic Alkynes: Synthesis of β -Vinylsilanes

4.3.1 Introduction

We described a new α -selective silylcupration of various terminal aliphatic alkynes in the presence of a copper catalyst bearing Johnphos ligand in Part 1. However, when phenylacetylene was employed as a substrate, the regioselectivity decreased drastically. Thus, our interests were directed to efficient switching of the regio- and stereochemistry of the silylcupration of terminal aromatic alkynes. Herein, we report Cu-catalyzed anti-Markovnikov silylcupration of terminal aromatic alkynes for the preparation of trans- β -vinylsilanes based on Si-B bond activation (Scheme 4.21).

Scheme 4.21 Cu-catalyzed anti-Markovnikov silylcupration of aromatic alkynes

4.3.2 Results and Discussions

Ligand Effects on Reactivity and Selectivity. As a model system, the reaction of phenylacetylene **6** and Ph(Me)₂SiBpin was performed with 10 mol% CuCl in the presence of Johnphos ligand at room temperature for 12 hours (Table 4.8). The silylcupration proceeded in excellent yield, but with no observed regioselectivity (98% yield, B:L 50:50; Table 4.8, entry 1). Throughout ligand screening, bidentate ligands emerged as effective ligands for β -selective silylcupration (entries 3-6). The reaction using DPPF as a ligand gave β -vinylsilanes in moderate yield with perfect regioselectivity (B:L 0:100)

(70% yield; Table 4.8, entry 4). Better yields were obtained with DPEphos and Xantphos, with the β -selectivity unaffected (entries 5 and 6). The use of Xantphos led to the best result (88% yield, B:L 0:100; entry 6). Further control reactions revealed that the reaction did not proceed without addition of base or copper (entries 7 and 8).

Table 4.8 Optimization of anti-Markovnikov silylcupration of aromatic alkynes^a

entry	Cu(I)	ligand	base	yield ^b	L/B ^c
1	CuCl	Johnphos	NaO ^t Bu	98%	50/50
2	CuCl	no	NaO ^t Bu	75%	90/10
3	CuCl	DPPE	NaO ^t Bu	96%	> 99/1
4	CuCl	DPPF	NaO ^t Bu	70%	100/0
5	CuCl	DPEphos	NaO ^t Bu	85%	100/0
6	CuCl	Xantphos	NaO^tBu	88%	100/0
7	CuCl	Xantphos	no	no reaction	
8	no	Xantphos	NaO ^t Bu	no reaction	

^aReaction conditions unless otherwise specified: phenylacetylene (0.3 mmol, 1.0 equiv) Ph(Me)₂SiBpin (1.1 equiv), CuCl (0.1 equiv), phosphine (0.1 equiv), NaO^tBu (0.11 equiv) and MeOH (2.0 equiv) in THF (1.0 mL) at room temperature for 12 h. ^b Isolated yield of mixtures of two isomers. ^c Determined by ¹H NMR.

Scope of the Anti-Markovnikov Intermolecular Silylcupration of Terminal Aromatic Alkynes. A variety of aryl- and heteroarylacetylenes were tested for regioselective silylcupration under the optimized conditions. The results are summarized in Table 4.9. Arylacetylenes having electron-withdrawing groups such as Br, Cl, F, CF₃ and CN groups at the *ortho*, *para* or

meta positions, reacted with Ph(Me)₂SiBpin smoothly to afford the corresponding β-vinylsilanes **9a-9f** in high yields with complete regio-control (Table 4.9, entries 1-6). The presence of electron-donating substituents led to decrease in the product yields (entries 7-11). Decreasing the electrophilicity of the acetylene β-carbon atom may have reduced the efficiency of alkyne addition to the Cu-Si bond. 2-Thienylacetylenes reacted with Ph(Me)₂SiBpin to give the product in good yield (Table 4.9, entry 12). 1-Ethynylaphthalene and 4-methoxy substituted 2-ethynylnaphthalene were also converted to the vinylsilanes in moderated yields (entries 13 and 14).

Table 4.9 Copper-catalyzed anti-Markovnikov intermolecular silylcupration of terminal aromatic alkynes^{a, b}

^aConditions: unless otherwise noted, 10 mol% CuCl, 10 mol% Xantphos, 11 mol% NaO^tBu, 0.3 mmol aromatic alkyne, 0.33 mmol Ph(Me)₂SiBpin and 2 equiv MeOH in THF at room temperature under argon atmosphere. ^bIsolated yield of pure β-vinylsilane.

Regioselectivity of Terminal Aromatic Alkyne Silylcupration. With the Cu-Xantphos catalytic system, silylcupration of terminal aromatic alkynes was achieved with up to 100% β-(*E*)-selectivity. The electronic effect is likely to have overridden the steric effect in the four-centered transition state thus

affording the anti-Markovnikov adducts. In contrast to the aliphatic alkyne, it is the α -carbon of the aromatic alkyne that bears great electron density,⁹⁰ therefore interacts with the metal copper (Scheme 4.22, C). Meanwhile, the nucleophilic silicon atom attacks the β -carbon atom of the aromatic alkyne, which bears partial positive charge.

Scheme 4.22 Proposed transition states for the formation of anti-Markovnikov silylcupration product

4.3.3 Conclusion

In summary, we have successfully developed a copper-catalyzed addition reaction of a silylborane to arylacetylenes to give β -(*E*)-vinylsilanes in good yields with perfect regio- and stereoselectivities. Further elucidation of the reaction mechanism is now underway in our laboratory.

⁹⁰ Yu, D. Y.; Zhang, Y. G. *PNAS*, **2010**, *107*, 20184.

4.4 Supporting Information

Part 1: α -Selective Cu-Catalyzed Silylcupration of Alkyl-Substituted Terminal Alkynes: Synthesis of Vinylsilanes

4.4.1 General Methods

All reagents were commercially purchased and used as received for the reactions: Ph(Me)₂SiBpin, CuCl, NaOtBu, NHC-salts, Johnphos, alkynes were purchased from Aldrich or Acros. All reactions were carried out in oven-dried glassware in a glove box to prevent moisture and oxygen. THF was freshly distilled from Na/benzophenone ketyl and anhydrous MeOH was bought from Aldrich.

Thin-layer chromatography (TLC) was conducted with Merck 60 F254 precoated silica gel plate (0.2 mm thickness) and visualized under UV or by potassium permanganate stain. Flash chromatography was performed using Merck silica gel 60 with distilled solvents. ¹H-NMR spectra were recorded on a Bruker Avance 300, 400 or 500 NMR spectrometer and are reported in ppm downfield from SiMe₄ (δ 0.0) and relative to the signal of chloroform-d (δ = 7.26, singlet). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ¹³C-NMR spectra were recorded on a Bruker Avance 300, 400 or 500 spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 77.0 ppm). Regioselectivity of the silylcupration product was determined by NMR analysis of the crude product. IR spectra were recorded on a Bio-Rad FTS 165 FTIR spectrometer and were reported in frequency of absorption (cm⁻¹). High resolution mass spectral analysis (HRMS) was performed on Waters Q-Tof Premier Mass Spectrometer.

4.4.2 Representative experimental procedure for silylmatalation of terminal aliphatic alkynes

In a glove box, a dry 10 mL glass tube was charged with CuCl (3.0 mg, 0.03 mmol, 10 mol%), NaO^tBu (3.2 mg, 0.033 mmol, 11 mol%), Johnphos (9.0 mg, 0.03 mmol, 10 mol%) and THF (1.0 mL). The resulting mixture was stirred for 20 minutes. Subsequently, Ph(Me)₂SiBpin (86 mg, 90 μ L, 0.33 mmol, 1.1 equiv) was added into the mixture. Then the tube was sealed with a septum and removed from the glove box. The mixture cooled to 0 °C under nitrogen atmosphere in a temperature-controlled colling bath. After stirring for 30 minutes, 1-octyne (33 mg, 45 μ L, 0.3 mmol, 1.0 equiv) and MeOH (24 μ L, 0.60 mmol, 2.0 equiv) were sequentially added to the solution via syringe. The reaction mixture was stirred at 0 °C for 24 hours. Then the reaction solution was diluted with dichloromethane, filtered through a pad of Celite, and concentrated *in vacuo*. Purification by silica gel column chromatography (hexane eluent) afforded a mixture of 2-dimethylphenylsilyl-1-octene and (*E*)-1-dimethylphenylsilyl-1-octene (59 mg, 80%). The regioselectivity was determined to be 99:1 (B/L) by crude ¹HNMR analysis.

A larger scale (0.9 mmol, 1-octyne as reactant) reaction was conducted under the general reaction conditions. Excellent regioselectivity (B/L= 99:1) and high yield (176 mg, 79%) were achieved in consistence with the results of the small scale reaction (0.3 mmol).

2-Dimethylphenylsilyl-1-octene

Colorless oil. $R_f = 0.75$ (hexane).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.51-7.53 (m, 2H), 7.34-7.36 (m, 3H), 5.68-5.69 (m, 1H), 5.39 (d, $J = 3.0$ Hz, 1H), 2.10 (t, $J = 7.6$ Hz, 2H), 1.18-1.35 (m, 8H), 0.85 (t, $J = 7.1$ Hz, 3H), 0.37 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 150.6, 138.5, 133.9, 128.9, 127.7, 125.7, 36.1, 31.8, 29.1, 28.9, 22.6, 14.1, -2.8.

FTIR (neat, cm^{-1}): 3049, 2956, 2926, 1417, 1427, 1247, 1111, 923, 833, 812, 775.

HRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{27}\text{Si}$ $[\text{M}+\text{H}]^+$: 247.1882. Found: 247.1886.

Experimental Details of Table 4.7

(Entry 1)

Following the general procedure, a mixture of **5a** and **5a'** was obtained as a colorless oil (46 mg, 71%).

5a: Hex-1-en-2-yl(dimethyl(phenyl)silane

Colorless oil. $R_f = 0.68$ (hexane).

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ (ppm): 7.53-7.55 (m, 2H), 7.36-7.37 (m, 3H), 5.70-5.71 (m, 1H), 5.41 (d, $J = 2.0$ Hz, 1H), 2.11 (t, $J = 7.2$ Hz, 2H), 1.24-1.39 (m, 4H), 0.85 (t, $J = 7.2$ Hz, 3H), 0.34 (s, 6H).

^{13}C -NMR (100 MHz, CDCl_3) δ (ppm): 150.6, 138.5, 133.9, 128.9, 127.7, 125.7, 35.7, 31.1, 22.5, 14.0, -2.8.

FTIR (neat, cm^{-1}): 3053, 2958, 2930, 1427, 1265, 928, 835, 818, 741.

HRMS (ESI) m/z Calcd for $\text{C}_{14}\text{H}_{22}\text{NaSi}$ $[\text{M}+\text{Na}]^+$: 241.1388. Found: 241.1378.

(Entry 2)

Following the general procedure, a mixture of **5b** and **5b'** was obtained as a colorless oil (53 mg, 74%).

5b: (5-Chloropent-1-en-2-yl)dimethyl(phenyl)silane

Colorless oil. R_f = 0.48 (hexane).

^1H -NMR (400 MHz, CDCl_3) δ (ppm): 7.49-7.51 (m, 2H), 7.34-7.36 (m, 3H), 5.71-5.72 (m, 1H), 5.46 (d, J = 2.1 Hz, 1H), 3.43 (t, J = 6.6 Hz, 2H), 2.25 (t, J = 7.5 Hz, 2H), 1.76-1.83 (m, 2H), 0.38 (s, 6H).

^{13}C -NMR (100 MHz, CDCl_3) δ (ppm): 148.8, 138.0, 133.9, 129.1, 127.8, 126.8, 44.6, 32.9, 31.6, -3.0.

FTIR (neat, cm^{-1}): 3068, 3051, 1427, 1265, 1111, 835, 817, 777, 739.

HRMS (ESI) m/z Calcd for $\text{C}_{13}\text{H}_{20}\text{ClSi}$ $[\text{M}+\text{H}]^+$: 239.1023. Found: 239.1030.

(Entry 3)

Following the general procedure, a mixture of **5c** and **5c'** was obtained as a colorless oil (46 mg, 67%).

5c: 5-(Dimethyl(phenyl)silyl)hex-5-enenitrile

Colorless oil. $R_f = 0.45$ (10:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.49-7.51 (m, 2H), 7.34-7.37 (m, 3H), 5.72 (m, 1H), 5.50 (d, $J = 2.4$ Hz, 1H), 2.25 (t, $J = 7.5$ Hz, 2H), 2.20 (t, $J = 7.2$ Hz, 2H), 1.63-1.69 (m, 2H), 0.38 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 148.2, 137.7, 133.8, 129.2, 127.9, 127.5, 119.6, 34.7, 24.4, 16.4, -3.1.

FTIR (neat, cm^{-1}): 3051, 2957, 2247, 1587, 1427, 1265, 1250, 1111, 934, 833, 818, 777, 741.

HRMS (ESI) m/z Calcd for $\text{C}_{14}\text{H}_{20}\text{NSi}$ $[\text{M}+\text{H}]^+$: 230.1365. Found: 230.1367.

(Entry 4)

Following the general procedure, a mixture of **5d** and **5d'** was obtained as a colorless oil (60 mg, 86%).

5d: 5-(Dimethyl(phenyl)silyl)hex-5-en-1-ol

Colorless oil. $R_f = 0.23$ (5:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.50-7.52 (m, 2H), 7.33-7.35 (m, 3H), 5.68-5.69 (m, 1H), 5.42 (d, $J = 2.4$ Hz, 1H), 3.52 (t, $J = 6.4$ Hz, 2H), 2.13 (t, $J = 7.6$ Hz, 2H), 1.36-1.50 (m, 4H), 1.22 (bs, 1H), 0.37 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 150.1, 138.4, 133.9, 129.0, 127.8, 126.0, 62.8, 35.7, 32.4, 24.9, -2.9.

FTIR (neat, cm^{-1}): 3612, 3368, 3051, 2937, 1427, 1265, 1111, 930, 835, 817, 777, 740.

HRMS (ESI) m/z Calcd for $C_{14}H_{23}OSi$ $[M+H]^+$: 235.1518. Found: 235.1511.

(Entry 5)

Following the general procedure, a mixture of **5e** and **5e'** was obtained as a colorless oil (71 mg, 90%).

5e : Ethyl 4-(dimethyl(phenyl)silyl)pent-4-enoate

Colorless oil. R_f = 0.55 (10:1 hexane/ethyl acetate).

1H -NMR (500 MHz, $CDCl_3$) δ (ppm): 7.49-7.51 (m, 2H), 7.35-7.36 (m, 3H), 5.68 (d, J = 1.6 Hz, 1H), 5.43 (s, 1H), 4.09 (q, J = 7.1 Hz, 2H), 2.35-2.45 (m, 4H), 1.22 (t, J = 7.1 Hz, 3H), 0.38 (s, 6H).

^{13}C -NMR (125 MHz, $CDCl_3$) δ (ppm): 173.3, 148.6, 137.8, 133.9, 129.1, 127.8, 125.9, 60.3, 33.4, 30.4, 14.2, -3.1.

FTIR (neat, cm^{-1}): 3053, 2983, 2959, 1730, 1427, 1371, 1265, 1111, 931, 835, 820, 702.

HRMS (ESI) m/z Calcd for $C_{15}H_{23}O_2Si$ $[M+H]^+$: 263.1467. Found: 263.1463.

(Entry 6)

Following the general procedure, a mixture of **5f** and **5f'** was obtained as a colorless oil (53 mg, 60%).

5f: (4-(Benzyloxy)but-1-en-2-yl)dimethyl(phenyl)silane

Colorless oil. R_f = 0.6 (10:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.48-7.50 (m, 2H), 7.26-7.35 (m, 8H), 5.74-5.75 (m, 1H), 5.47 (d, $J = 2.6$ Hz, 1H), 4.39 (s, 2H), 3.43 (t, $J = 7.3$ Hz, 2H), 2.44 (t, $J = 7.3$ Hz, 2H), 0.35 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 146.8, 138.5, 138.0, 133.9, 129.0, 128.3, 127.8, 127.8, 127.7, 127.5, 72.8, 69.8, 35.9, -3.0.

FTIR (neat, cm^{-1}): 3053, 2858, 1454, 1265, 1111, 933, 895, 818, 777, 740.

HRMS (ESI) m/z Calcd for $\text{C}_{19}\text{H}_{25}\text{OSi}$ $[\text{M}+\text{H}]^+$: 297.1675. Found: 297.1687.

(Entry 7)

Following the general procedure, a mixture of **5g** and **5g'** was obtained as a colorless oil (56 mg, 70%).

5g: Dimethyl(phenyl)(4-phenylbut-1-en-2-yl)silane

Colorless oil. $R_f = 0.35$ (hexane).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ (ppm): 7.50-7.51 (m, 2H), 7.34-7.36 (m, 3H), 7.07-7.26 (m, 5H), 5.74-5.75 (m, 1H), 5.46-5.47 (m, 1H), 2.61-2.67 (m, 2H), 2.37-2.42 (m, 2H), 0.39 (s, 6H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ (ppm): 149.9, 142.4, 138.2, 134.0, 129.0, 128.4, 128.3, 127.8, 126.1, 125.7, 37.7, 35.5, -3.0.

FTIR (neat, cm^{-1}): 3064, 2957, 1603, 1454, 1427, 1265, 1248, 1111, 925, 833, 816, 737.

HRMS (ESI) m/z Calcd for $\text{C}_{18}\text{H}_{23}\text{Si}$ $[\text{M}+\text{H}]^+$: 267.1569. Found: 267.1561.

(Entry 8)

Following the general procedure, a mixture of **5h** and **5h'** was obtained as a colorless oil (57 mg, 76%).

5h: Dimethyl(phenyl)(3-phenylprop-1-en-2-yl)silane

Colorless oil. $R_f = 0.45$ (hexane).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.45-7.47 (m, 2H), 7.32-7.35 (m, 3H), 7.21-7.24 (m, 2H), 7.14-7.16 (m, 1H), 7.04-7.06 (m, 2H), 5.55 (s, 1H), 5.48 (d, $J = 1.3$ Hz, 1H), 3.41 (s, 2H), 0.25 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 149.7, 139.9, 138.0, 134.0, 129.4, 129.0, 128.2, 127.8, 127.8, 125.9, 42.6, -2.9.

FTIR (neat, cm^{-1}): 3051, 2959, 1600, 1452, 1427, 1265, 1250, 1111, 934, 835, 818, 740.

HRMS (ESI) m/z Calcd for $\text{C}_{17}\text{H}_{21}\text{Si}$ $[\text{M}+\text{H}]^+$: 253.1413. Found: 253.1407.

(Entry 10)

Following the general procedure, a mixture of **5j** and **5j'** was obtained as a colorless oil (55 mg, 76%).

5j: (1-(Cyclohex-1-en-1-yl)vinyl)dimethyl(phenyl)silane

Colorless oil. $R_f = 0.63$ (hexane).

^1H -NMR (500 MHz, CDCl_3) δ (ppm): 7.51-7.53 (m, 2H), 7.32-7.34 (m, 3H), 5.80 (d, $J = 2.4$ Hz, 1H), 5.61 (m, 1H), 5.36 (d, $J = 2.4$ Hz, 1H), 2.09-2.12 (m, 2H), 2.00-2.01 (m, 2H), 1.60-1.64 (m, 2H), 1.49-1.54 (m, 2H), 0.40 (s, 6H).

^{13}C -NMR (125 MHz, CDCl_3) δ (ppm): 151.0, 139.4, 138.9, 133.9, 128.7, 127.7, 127.1, 124.3, 27.1, 25.9, 23.0, 22.3, -1.5.

FTIR (neat, cm^{-1}): 3051, 2931, 1427, 1265, 1109, 920, 837, 821, 741.

HRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{23}\text{Si}$ $[\text{M}+\text{H}]^+$: 243.1569. Found: 243.1571.

(Entry 11)

Following the general procedure, a mixture of **5k** and **5k'** was obtained as a colorless oil (51 mg, 84%).

5k: (1-Cyclopropylvinyl)dimethyl(phenyl)silane

Colorless oil. $R_f = 0.63$ (hexane).

^1H -NMR (500 MHz, CDCl_3) δ (ppm): 7.54-7.56 (m, 2H), 7.33-7.35 (m, 3H), 5.45-5.47 (m, 1H), 5.24 (d, $J = 2.4$ Hz, 1H), 1.33-1.39 (m, 1H), 0.58-0.62 (m, 2H), 0.40 (m, 8H).

^{13}C -NMR (125 MHz, CDCl_3) δ (ppm): 151.8, 138.4, 133.9, 129.0, 128.9, 121.7, 15.5, 7.0, -2.9.

FTIR (neat, cm^{-1}): 3051, 3000, 2957, 1427, 1265, 1248, 1109, 920, 839, 822, 739.

HRMS (ESI) m/z Calcd for $\text{C}_{13}\text{H}_{19}\text{Si}$ $[\text{M}+\text{H}]^+$: 203.1256. Found: 203.1263.

(Entry 12)

Following the general procedure, a mixture of **5I** and **5I'** was obtained as a colorless oil (33 mg, 50%).

5I: 2-(Dimethyl(phenyl)silyl)-N,N-dimethylprop-2-en-1-amine

Colorless oil. R_f = 0.45 (10:1 hexane/ethyl acetate).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.54-7.56 (m, 2H), 7.33-7.34 (m, 3H), 5.77 (m, 1H), 5.40 (d, J = 3.0 Hz, 1H), 2.89 (s, 2H), 2.08 (s, 6H), 0.39 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 148.9, 138.6, 134.1, 128.8, 127.6, 127.3, 66.5, 45.4, -2.8.

FTIR (neat, cm^{-1}): 3051, 1427, 1265, 1248, 1172, 1113, 1013, 839, 822, 741.

HRMS (ESI) m/z Calcd for $\text{C}_{13}\text{H}_{22}\text{NSi}$ $[\text{M}+\text{H}]^+$: 220.1522. Found: 220.1530.

Part 2: Cu-Catalyzed Anti-Markovnikov Intermolecular Silylcupration of Terminal Aromatic Alkynes: Synthesis of β -Vinylsilanes

4.4.3 General Methods

All reagents were commercially purchased and were used as received for the reactions: Ph(Me)₂SiBpin, CuCl, NaO^tBu, Xantphos, alkynes were purchased from Aldrich or Acros. All reactions were carried out in oven-dried glassware in glove box to prevent moisture and oxygen. THF was freshly distilled from Na/benzophenone ketyl and anhydrous MeOH was bought from Aldrich.

Thin-layer chromatography (TLC) was conducted with Merck 60 F254 precoated silica gel plate (0.2 mm thickness) and visualized under UV or by potassium permanganate stain. Flash chromatography was performed using Merck silica gel 60 with distilled solvents. ¹H NMR spectra were recorded on a Bruker Avance 500 NMR spectrometer and are reported in ppm downfield from SiMe₄ (δ 0.0) and relative to the signal of chloroform-d (δ =7.26, singlet). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ¹³C NMR spectra were recorded on a Bruker Avance 500 spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 77.0 ppm). Regioselectivity of the silylcupration product was determined by NMR analysis of the crude product. IR spectra were recorded on a Bio-Rad FTS 165 FTIR spectrometer and were reported in frequency of absorption (cm⁻¹). High resolution mass spectral analysis (HRMS) was performed on Waters Q-ToF Premier Mass Spectrometer.

4.4.4 Representative experimental procedure for silylmatalation of terminal alkynes

In a glove box, a dry 10 ml glass tube was charged with CuCl (3.0 mg, 0.03 mmol, 10 mol%), NaO^tBu (3.2 mg, 0.033 mmol, 11 mol%), Xantphos (17.3 mg, 0.03 mmol, 10 mol%), and THF (1.0 mL). The resulting mixture was stirred for 20 mins. The solution gradually turned into pale yellow color. Subsequently, Ph(Me)₂SiBpin (86 mg, 90 μ L, 0.33 mmol, 1.1 equiv) was added into the mixture. After stirring for 10 mins, then the tube was sealed with a septum and taken out from the glove box. Ethynylbenzene (31 mg, 34 μ L, 0.3 mmol, 1.0 equiv) and MeOH (24 μ L, 0.60 mmol, 2.0 equiv) were added into the solution in sequence under argon atmosphere. The reaction mixture was stirred at room temperature for 12 hours. Then the reaction solution concentrated *in vacuo* and subjected to silica gel column chromatography (eluent with hexane) to afford (*E*)-dimethyl(phenyl)(styryl)silane as a colorless oil (63 mg).

Yield = 88%. R_f = 0.65 (Hexane).

¹H-NMR (500 MHz, CDCl₃) δ (ppm): 7.56-7.57 (m, 2H), 7.43-7.45 (m, 2H), 7.34-7.37 (m, 3H), 7.31-7.32 (m, 2H), 7.23-7.26 (m, 1H), 6.94 (d, J = 19.1 Hz, 1H), 6.58 (d, J = 19.1 Hz, 1H), 0.43 (s, 6H).

¹³C-NMR (125 MHz, CDCl₃) δ (ppm): 145.3, 138.6, 138.2, 134.0, 129.1, 128.6, 128.2, 127.9, 127.1, 126.5, -2.5.

FTIR (neat, cm⁻¹): 3067, 2955, 1605, 1572, 1427, 1247, 1113, 989, 830, 810, 729.

HRMS (ESI) m/z Calcd for C₁₆H₁₉Si [M+H]⁺: 239.1256. Found: 239.1259.

Experimental Details of Table 4.9

(Entry 1)

9a: (*E*)-(4-fluorostyryl)dimethyl(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (63 mg).

Yield = 82%. R_f = 0.70 (hexane).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.56-7.57 (m, 2H), 7.41 (dd, J_1 = 8.6 Hz, J_2 = 5.5 Hz, 2H), 7.37-7.38 (m, 3H), 7.01 (t, J = 8.6 Hz, 2H), 6.88 (d, J = 19.1 Hz, 1H), 6.49 (d, J = 19.1 Hz, 1H), 0.43 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 162.7 (d, J = 246.0 Hz), 143.9, 138.4, 134.4 (d, J = 3.1 Hz), 133.9, 129.1, 128.0 (d, J = 8.1 Hz), 127.8, 126.8 (d, J = 1.8 Hz), 115.4 (d, J = 21.7 Hz), -2.6.

FTIR (neat, cm^{-1}): 3067, 2957, 1593, 1562, 1427, 1248, 1194, 1113, 986, 843, 808, 733.

HRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{18}\text{FSi}$ $[\text{M}+\text{H}]^+$: 257.1162. Found: 257.1171.

(Entry 2)

9b : (*E*)-dimethyl(phenyl)(4-(trifluoromethyl)styryl)silane

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (78 mg).

Yield = 85%. R_f = 0.70 (hexane).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.52-7.59 (m, 6H), 7.37-7.39 (m, 3H), 6.94 (d, $J = 19.1$ Hz, 1H), 6.70 (d, $J = 19.1$ Hz, 1H), 0.45 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 143.7, 141.4, 137.9, 133.9, 130.8, 130.2, 129.8 (q, $J = 32.2$ Hz), 129.2, 127.9, 126.6, 125.5 (q, $J = 3.5$ Hz), 124.2 (q, $J = 271.3$ Hz), -2.7.

FTIR (neat, cm^{-1}): 3069, 2957, 1614, 1574, 1427, 1323, 1249, 1199, 1165, 1066, 988, 849, 822, 797, 733.

HRMS (ESI) m/z Calcd for $\text{C}_{17}\text{H}_{18}\text{F}_3\text{Si}$ $[\text{M}+\text{H}]^+$: 307.1130. Found: 307.1130.

(Entry 3)

9c: (*E*)-(3-fluorostyryl)dimethyl(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (77 mg).

Yield = 98%. $R_f = 0.43$ (10:1 hexane/ ethyl acetate)).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.61 (d, $J = 8.3$ Hz, 2H), 7.54-7.56 (m, 2H), 7.50 (d, $J = 8.3$ Hz, 2H), 7.38-7.40 (m, 3H), 6.91 (d, $J = 19.1$ Hz, 1H), 6.74 (d, $J = 19.1$ Hz, 1H), 0.45 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 143.2, 142.3, 137.7, 133.9, 132.7, 132.4, 129.4, 128.0, 127.0, 119.0, 111.3, -2.7.

FTIR (neat, cm^{-1}): 3069, 2957, 2226, 1603, 1428, 1113, 1066, 989, 849, 822, 793, 731.

HRMS (ESI) m/z Calcd for $\text{C}_{17}\text{H}_{18}\text{NSi}$ $[\text{M}+\text{H}]^+$: 264.1209. Found: 264.1215.

(Entry 4)

9d: (*E*)-(3-fluorostyryl)dimethyl(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (70 mg).

Yield = 91%. R_f = 0.71 (hexane).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.55-7.57 (m, 2H), 7.37-7.38 (m, 3H), 7.27-7.30 (m, 1H), 7.13-7.20 (m, 2H), 6.93-6.97 (m, 1H), 6.88 (d, J = 19.1 Hz, 1H), 6.60 (d, J = 19.1 Hz, 1H), 0.44 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 163.3 (d, J = 243.8 Hz), 143.9 (d, J = 2.0 Hz), 140.6 (d, J = 7.1 Hz), 138.1, 133.9, 129.9 (d, J = 8.3 Hz), 129.2, 129.0, 127.9, 122.5 (d, J = 2.2 Hz), 114.9 (d, J = 21.5 Hz), 112.8 (d, J = 21.1 Hz), -2.6
FTIR (neat, cm^{-1}): 3067, 2957, 1609, 1593, 1578, 1427, 1250, 1199, 1115, 988, 845, 806, 733.

HRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{18}\text{FSi}$ $[\text{M}+\text{H}]^+$: 257.1162. Found: 257.1150.

(Entry 5)

9e: (*E*)-(3-chlorostyryl)dimethyl(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (60 mg).

Yield = 74%. R_f = 0.70 (hexane).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.55-7.57 (m, 2H), 7.43 (s, 1H), 7.37-7.38 (m, 3H), 7.29 (dt, $J_1 = 7.3$ Hz, $J_2 = 1.5$ Hz, 1H), 7.20-7.26 (m, 2H), 6.85 (d, $J = 19.1$ Hz, 1H), 6.60 (d, $J = 19.1$ Hz, 1H), 0.43 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 143.8, 140.1, 138.2, 134.6, 134.0, 129.8, 129.3, 129.2, 128.1, 127.9, 126.5, 124.8, -2.6.

FTIR (neat, cm^{-1}): 3067, 2957, 1609, 1593, 1562, 1428, 1194, 1113, 986, 843, 830, 808, 733.

HRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{18}\text{ClSi}$ $[\text{M}+\text{H}]^+$: 273.0866. Found: 273.0867.

(Entry 6)

9f: (*E*)-(2-bromostyryl)dimethyl(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (89 mg).

Yield = 94%. R_f = 0.69 (hexane).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.57-7.61 (m, 3H), 7.54 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.1$ Hz, 1H), 7.37-7.38 (m, 3H), 7.31 (d, $J = 19.0$ Hz, 1H), 7.27-7.29 (m, 1H), 7.10 (td, $J_1 = 8.0$ Hz, $J_2 = 1.7$ Hz, 1H), 6.54 (d, $J = 19.0$ Hz, 1H), 0.47 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 143.8, 138.2, 137.9, 133.9, 132.9, 131.0, 129.2, 129.1, 127.9, 127.4, 127.0, 123.8, -2.6

FTIR (neat, cm^{-1}): 3067, 2955, 1595, 1558, 1427, 1248, 1198, 1113, 988, 827, 730.

HRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{18}\text{BrSi}$ $[\text{M}+\text{H}]^+$: 317.0361. Found: 317.0354.

(Entry 7)

9g: (*E*)-dimethyl(4-methylstyryl)(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (60 mg).

Yield = 78%. R_f = 0.66 (hexane).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.56-7.58 (m, 2H), 7.35-7.37 (m, 3H), 7.34 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 6.91 (d, J = 19.1 Hz, 1H), 6.51 (d, J = 19.1 Hz, 1H), 2.34 (s, 3H), 0.42 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 145.2, 138.7, 138.0, 135.5, 133.9, 129.2, 128.9, 127.8, 126.4, 125.6, 21.2, -2.5.

FTIR (neat, cm^{-1}): 3067, 2954, 1605, 1510, 1427, 1247, 1113, 988, 840, 790, 733.

HRMS (ESI) m/z Calcd for $\text{C}_{17}\text{H}_{21}\text{Si}$ $[\text{M}+\text{H}]^+$: 253.1413. Found: 253.1414.

(Entry 8)

9h: (*E*)-dimethyl(4-pentylstyryl)(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (70 mg).

Yield = 76%. R_f = 0.73 (hexane).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.56-7.58 (m, 2H), 7.35-7.37 (m, 5H), 7.14 (d, J = 8.0 Hz, 2H), 6.92 (d, J = 19.1 Hz, 1H), 6.52 (d, J = 19.1 Hz, 1H),

2.58 (t, $J = 7.7$ Hz, 2H), 1.57-1.63 (m, 2H), 1.26-1.37 (m, 4H), 0.88 (t, $J = 7.1$ Hz, 3H), 0.42 (s, 6H).

^{13}C -NMR (125 MHz, CDCl_3) δ (ppm): 145.3, 143.3, 138.8, 135.8, 134.0, 129.1, 128.7, 127.9, 126.5, 125.8, 35.8, 31.5, 31.2, 22.6, 14.1, -2.4.

FTIR (neat, cm^{-1}): 3067, 3047, 2955, 2928, 2857, 1604, 1427, 1246, 1113, 988, 822, 787, 729.

HRMS (ESI) m/z Calcd for $\text{C}_{21}\text{H}_{29}\text{Si}$ $[\text{M}+\text{H}]^+$: 309.2039. Found: 309.2049.

(Entry 9)

9i: (E)-(4-methoxystyryl)dimethyl(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as colorless oil (50 mg).

Yield = 62%. R_f = 0.44 (hexane).

^1H -NMR (500 MHz, CDCl_3) δ (ppm): 7.56-7.57 (m, 2H), 7.35-7.40 (m, 5H), 6.85-6.90 (m, 3H), 6.41 (d, $J = 19.0$ Hz, 1H), 3.80 (s, 3H), 0.42 (s, 6H).

^{13}C -NMR (125 MHz, CDCl_3) δ (ppm): 159.7, 144.7, 138.8, 133.9, 131.1, 128.9, 127.8, 127.7, 124.1, 113.9, 55.2, -2.5.

FTIR (neat, cm^{-1}): 3067, 2955, 2835, 1605, 1508, 1427, 1250, 1171, 1113, 1034, 988, 822, 792, 735.

HRMS (ESI) m/z Calcd for $\text{C}_{17}\text{H}_{21}\text{OSi}$ $[\text{M}+\text{H}]^+$: 269.1362. Found: 269.1358.

(Entry 10)

9j: (E)-dimethyl(2-methylstyryl)(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as colorless oil (60 mg).

Yield = 79%. R_f = 0.66 (hexane).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 7.57-7.59 (m, 2H), 7.53-7.54 (m, 1H), 7.36-7.38 (m, 3H), 7.11-7.21 (m, 4H), 6.49 (d, J = 19.0 Hz, 1H), 2.35 (s, 3H), 0.44 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 143.1, 138.7, 137.5, 135.4, 133.9, 130.3, 129.0, 128.8, 127.9, 127.8, 126.1, 125.4, 19.6, -2.5.

FTIR (neat, cm^{-1}): 3067, 2955, 1597, 1566, 1427, 1248, 1113, 989, 841, 810, 731.

HRMS (ESI) m/z Calcd for $\text{C}_{17}\text{H}_{21}\text{Si}$ $[\text{M}+\text{H}]^+$: 254.1413. Found: 254.1411.

(Entry 11)

9k: (E)-(2-methoxystyryl)dimethyl(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (63 mg).

Yield = 78%. R_f = 0.53 (hexane).

^1H -NMR (500 MHz, CDCl_3) δ (ppm): 7.54-7.59 (m, 3H), 7.35-7.40 (m, 4H), 7.22-7.25 (m, 1H), 6.93 (t, $J = 7.5$ Hz, 1H), 6.87 (d, $J = 7.5$ Hz, 1H), 6.56, (d, $J = 19.1$ Hz, 1H), 3.84 (s, 3H), 0.43 (s, 6H).

^{13}C -NMR (125 MHz, CDCl_3) δ (ppm): 156.7, 139.6, 139.0, 133.9, 129.2, 128.9, 127.7, 127.3, 127.0, 126.3, 120.6, 110.9, 55.4, -2.4.

FTIR (neat, cm^{-1}): 3067, 2955, 2835, 1597, 1485, 1427, 1244, 1161, 1113, 1028, 995, 827, 808, 731.

HRMS (ESI) m/z Calcd for $\text{C}_{17}\text{H}_{21}\text{OSi}$ $[\text{M}+\text{H}]^+$: 269.1362. Found: 269.1373.

(Entry 12)

9l: (*E*)-dimethyl(phenyl)(2-(thiophen-3-yl)vinyl)silane

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (66 mg).

Yield = 90%. R_f = 0.70 (hexane).

^1H -NMR (500 MHz, CDCl_3) δ (ppm): 7.55-7.57 (m, 2H), 7.36-7.37 (m, 3H), 7.20-7.29 (m, 3H), 6.92 (d, $J = 19.0$ Hz, 1H), 6.35 (d, $J = 19.0$ Hz, 1H), 0.41 (s, 6H).

^{13}C -NMR (125 MHz, CDCl_3) δ (ppm): 142.0, 139.2, 138.6, 134.0, 129.1, 127.9, 126.8, 126.0, 125.0, 123.1, -2.4.

FTIR (neat, cm^{-1}): 3067, 2955, 1601, 1508, 1427, 1246, 1198, 1113, 984, 908, 843, 731.

HRMS (ESI) m/z Calcd for $\text{C}_{14}\text{H}_{17}\text{SSi}$ $[\text{M}+\text{H}]^+$: 245.0820. Found: 245.0813.

(Entry 13)

9m: (*E*)-dimethyl(2-(naphthalen-1-yl)vinyl)(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as a colorless oil (67 mg).

Yield = 78%. R_f = 0.68 (hexane).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ (ppm): 8.11 (d, J = 8.1 Hz, 1H), 7.83-7.85 (m, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.74 (d, J = 19.0 Hz, 1H), 7.69 (d, J = 7.1 Hz, 1H), 7.62-7.64 (m, 2H), 7.44-7.53 (m, 3H), 7.39-7.40 (m, 3H), 6.67 (d, J = 19.0 Hz, 1H), 0.51 (s, 6H).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ (ppm): 142.7, 138.7, 136.4, 134.1, 133.8, 131.5, 131.0, 129.3, 128.7, 128.5, 128.0, 126.2, 125.9, 125.7, 123.9, 123.6, -2.2.

FTIR (neat, cm^{-1}): 3065, 2955, 1597, 1427, 1248, 1113, 986, 830, 810, 731.

HRMS (ESI) m/z Calcd for $\text{C}_{20}\text{H}_{21}\text{Si}$ $[\text{M}+\text{H}]^+$: 289.1413. Found: 289.1409.

(Entry 14)

9n: (*E*)-(2-(6-methoxynaphthalen-2-yl)vinyl)dimethyl(phenyl)silane

The title compound was prepared by the general procedure described above and was obtained as a white solid (76 mg).

Yield = 80%. M.p. = 80-82 °C. R_f = 0.43 (10:1 hexane/ ethyl acetate).

^1H -NMR (500 MHz, CDCl_3) δ (ppm): 7.64-7.71 (m, 4H), 7.59-7.61 (m, 2H), 7.37-7.38 (m, 3H), 7.11-7.13 (m, 2H), 7.07 (d, $J = 19.1$ Hz, 1H), 6.64 (d, $J = 19.1$ Hz, 1H), 3.92 (s, 3H), 0.46 (s, 6H).

^{13}C -NMR (125 MHz, CDCl_3) δ (ppm): 157.9, 145.4, 138.7, 134.5, 133.9, 133.6, 129.7, 129.0, 128.9, 127.8, 127.0, 126.7, 126.1, 123.9, 118.9, 105.8, 55.2, -2.5.

FTIR (CH_2Cl_2 , cm^{-1}): 3053, 2985, 1629, 1593, 1481, 1425, 1265, 1174, 1113, 1030, 989, 831, 736 .

HRMS (ESI) m/z Calcd for $\text{C}_{21}\text{H}_{23}\text{OSi}$ $[\text{M}+\text{H}]^+$: 319.1518. Found: 319.1526.

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1. Peng Wang, Xue-Liang Yeo and Teck-Peng Loh*. Copper-Catalyzed Highly Regioselective Silylcupration of Terminal Alkynes to Form α -Vinylsilanes. *J. Am. Chem. Soc.* **2011**, *133*, 1254.
2. Peng Wang, Peng-Fei Koh and Teck-Peng Loh*. Copper-Catalyzed Anti-Markovnikov Intermolecular Silylcupration of Terminal Aromatic Alkynes: Synthesis of β -Vinylsilanes. **2011**, Manuscript in preparation.
3. Peng Wang, Ying-Jie Lim and Teck-Peng Loh*. NHC-Copper-complex Catalyzed Silicon-Copper Addition to Aldehydes Based on Si-B Bond Activation. **2011**, Manuscript in preparation.

Conference papers

4. Peng Wang and Teck-Peng Loh*. Cu(I)-TolBINAP-Catalyzed Asymmetric Synthesis of Chiral Allylic Esters. *International Symposium on Catalysis and Fine Chemicals*, December 16-21, **2007**, Singapore.
5. Peng Wang, Suhaila Siti and Teck-Peng Loh*. New Method to Construct C-Si Bond Based on Si-B Bond Activation Catalyzed by Copper Oxide. *6th Asian-European Symposium on Metal Mediated Efficient Reactions*, June 7-9, **2010**, Singapore.