Catalytic Addition of Functionalities across Carbon-Carbon Multiple Bonds with Carbon Dioxide and Related Electrophiles

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2015

Abbreviations

Ac	acetyl
acac	acetylacetonato
Anal.	elemental analysis
APCI	atmospheric pressure chemical ioniation
Ar	aryl
BINAP	2,2´-bis(diphenylphosphino)-1,1´-binaphthyl
bpy	bipyridine
calcd	calculated
cod	1,5-cyclooctadiene
Cy	cyclohexyl
d.r.	diastereomeric ratio
DABCO	1,4-diazabicyclo[2,2,2]octane
dba	dibenzylideneacetone, 1,5-diphenyl-1,4-pentadien-3-one
DBU	1,8-diazabicyclo[5,4,0]undec-7-ene
DG	directing group
DIAD	diisopropyl azodicarboxylate
DMAP	*N*,*N*-dimethyl-4-aminopyridine
DMF	dimethylformamide
DMI	1,3-dimethyl-2-imidazolidinone
DMSO	dimethylsulfoxide
dppb	1,4-bis(diphenylphosphino)butane
dppBz	1,2-diphenylphosphinobenzene
dppe	1,2-bis(diphenylphosphino)-ethane
dtbpy	4,4'-di-*tert*-butyl-2,2'-bipyridyl
ee	enantiomeric excess
EI	electron impact
eq	equation
equiv	equivalent(s)
ESI	electrospray ionization
GC	gas chromatography
h	hour(s)
IMes	1,3-bis-(2,4,6-trimethylphenyl)-imidazol-2-ylidene
IPr	1,3-bis-(2,6-diisopropylphenyl)-imidazol-2-ylidene
IR	infrared
Johnphos	2-(di-*tert*-butylphosphino)biphenyl
L	ligand
m.p.	melting point
Me-DuPhos	1,2-bis(*trans*-2,5-dimethylphospholan-1-yl)benzene
min	minute(s)
MS	mass spectrometer
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
PCy_3	tricyclohexylphosphine
phen	1,10-phenanthroline
HB(pin)	pinacolborane
PMHS	poly(methylhydrosiloxane)
TBAF	tetrabutylammonium fluoride
TBDPS	*tert*-butyldiphenylsilyl
TBS	*tert*-butyldimethylsilyl
THF	tetrahydrofuran
tmeda	*N,N,N′,N′*-tetramethylethylenediamine
TMS	trimethylsilyl
tol	tolyl
Ts	tosyl, *p*-toluenesulfonyl
Xantphos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene

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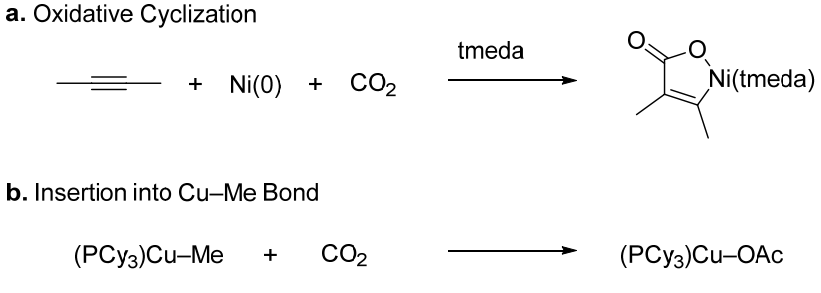
General Introduction

Carbon dioxide in organic synthesis. Carbon dioxide (CO_2) is a nontoxic, abundant, and renewable C1 molecule, whose transformation has been the subject of research over the ages.[1] In particular, C–C bond-forming reaction with CO_2 straightforwardly affords carboxylic acids. Carboxylic acids are ubiquitous motifs found in nature and artificial molecules, hence the development of carboxylation with CO_2 has been a central challenge in synthetic organic chemistry. However, thermodynamically and kinetically stable nature of CO_2 has limited the application toward industrial processes and fine organic syntheses.[2] Reactions often require high temperature and pressure, or the use of highly reactive organometallic reagents (e.g. organolithium or Grignard reagents). The Kolbe-Schmitt reaction, originally reported by Kolbe in 1860 and improved by Schmitt in 1885, is one of the few industrialized processes. The reaction produces a salt of salicylic acid from phenol and CO_2 in the presence of an alkali metal alkoxide at high temperature and pressure (typically around 100–200 °C and 10–20 atm).

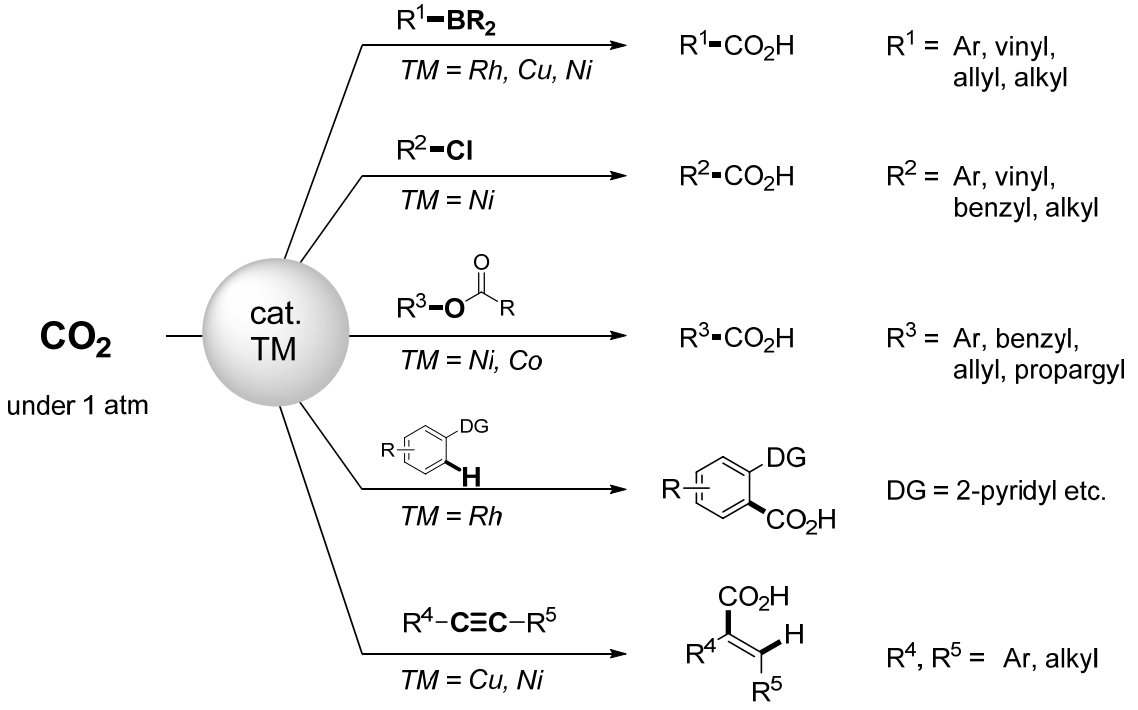
Transition metals can activate this relatively inert, small molecule. In 1975, Aresta reported the first stable CO_2 complex coordinated to a transition metal: $(PCy_3)_2Ni(CO_2)$.[3] During the 1980s, oxidative cyclization reactions of alkenes or alkynes with CO_2 and nickel complexes were reported by Hoberg (Scheme 1a).[4] Another early example of a stoichiometric C–C bond formation with CO_2 is an insertion reaction of CO_2 into Cu–C bond of $(PCy_3)CuMe$ reported by Yamamoto and Ikariya in 1974 (Scheme 1b).[5] It is worth mentioning that all these reactions were proceeded at room temperature or below.

Scheme 1. Early Examples of Transition Metal-Promoted Carboxylation Employing CO_2



In recent years, transition metal-catalyzed carboxylation gains much attentions.[6] Until now, efficient catalytic carboxylation reactions using less nucleophilic organometallic (B,[7,8a,b] Zn,[9] Sn[8]) reagents, organohalides,[10] C–O bonds,[11] C(sp^2)–H bonds,[12] or C–C multiple bonds under 1 atm of CO_2 have been reported (Scheme 2). Some applications in the total synthesis of natural products have also been demonstrated.[13]

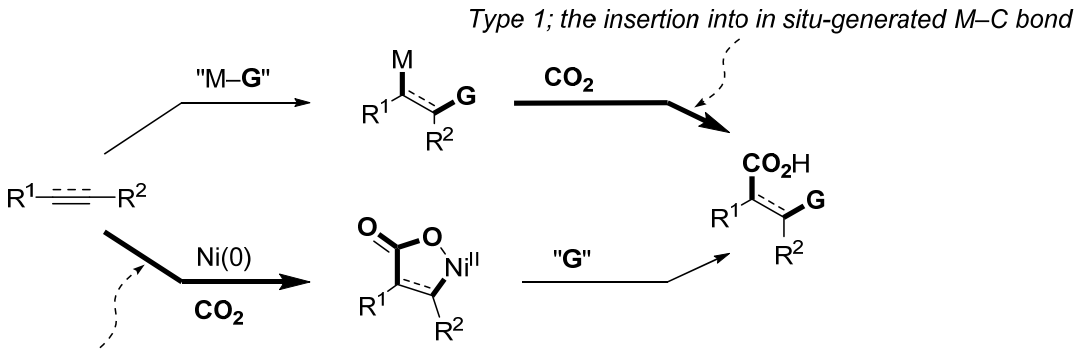
Scheme 2. Representative Transition Metal-Catalyzed Carboxylation Employing CO_2



Among the above-mentioned carboxylations, the addition-type reactions to C–C multiple bonds can install carboxyl group and an additional functionality simultaneously. The author focuses on this feature, and explores the catalytic CO_2 utilization in the functionalization of C–C multiple bonds. To address the progress and existing problems in this area, the author devotes the following section to the detailed backgrounds. Then, he describes the overview of his works on the catalytic addition of functionalities across C–C multiple bonds with CO_2 and related electrophiles.

Catalytic carboxylation of C–C multiple bonds. After the first report by Inoue et al. in 1976 describing the Pd-catalyzed cycloaddition of CO_2 and two molecules of 1,3-butadiene,[14] the early development in this field mainly relied on intramolecular reactions (e.g. CO_2 with *bis*-1,3-dienes[15] or *di*-ynes[16,17]). While these reactions induce skeletal transformations constructing carbo- and heterocycles, specific substrates must be designed and synthesized in multi-steps. Therefore, the diversity of the reactions is limited. Nowadays, the latest catalysts enable carboxylations of more simple and easily available substrates such as alkynes,[18] styrenes,[19] and dienes.[20] These reactions can be roughly classified according to the mode of CO_2 fixation; Type 1 involves the insertion into metal–carbon bond generated by the addition of transition metal species (M–G) across substrates (Scheme 3, top); Type 2 involves the oxidative cyclization of Ni(0), CO_2, and substrates (Scheme 3, bottom).

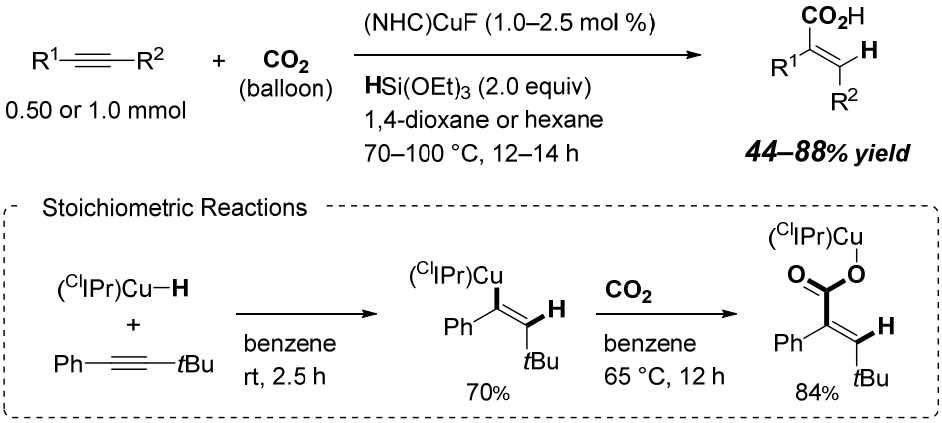
Scheme 3. Catalytic Carboxylation of C–C Multiple Bonds; a Classification



The Type 1 reaction (Scheme 3, top) has a feature that a substituent (G) derived from M–G is introduced to the products. So far, most of the reactions categorized in this class is hydrocarboxylation (G = H).[18a,19,20] If a carbon- or a heteroatom-substituent would be installed, highly functionalized and complex carboxylic acids are rapidly synthesized. In particular, introduction of heteroatom functionalities that can be transformed later on (G = Si, B, halides etc.) is ideal in terms of the diversity of products. Altering G for each targeted molecules (e.g. G = variously-substituted aryl ring) may be troublesome, because it will affect not only reactivity but also regioselectivity of the addition reaction.

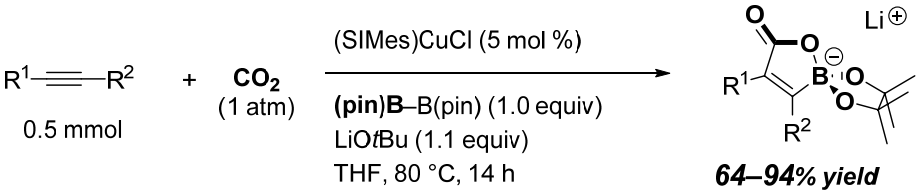
Cu(I) catalyst is a promising candidate for this strategy. Addition reactions of copper species across C–C multiple bonds have been explored (vide infra), and Cu(I)–C bonds are known to react with CO_2.[21] One of the seminal reports is the Cu–H-catalyzed hydrocarboxylation of alkynes by Tsuji et al. (Scheme 4).[18a] They carried out the stoichiometric reactions of copper complexes, confirming the addition/carboxylation mechanism.

Scheme 4. Cu-Catalyzed Hydrocarboxylation of Alkynes

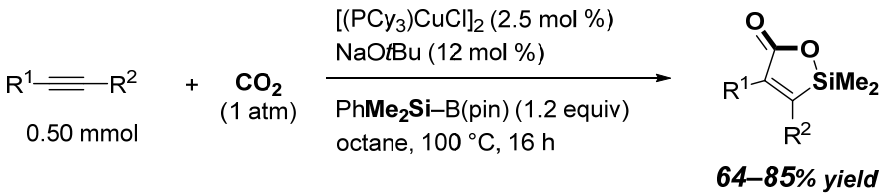


Nonetheless, when the author embarked on the project described in Chapters 1 and 2, no catalytic heterocarboxylation (G = heteroatom functionality) was reported. Since then, intensive efforts have been devoted to this subject (Scheme 5–8). In 2012, Hou et al. reported the Cu-catalyzed boracarboxylation (G = B) of alkynes (Scheme 5)[22]. The author reported the Cu-catalyzed silacarboxylation (G = Si) of alkynes as described in Chapter 1 (Scheme 6). Ma et al. reported intramolecular aminocarboxylation (G = N) of *N*-tosyl-*o*-alkynylanilines catalyzed by a copper catalyst (Scheme 7),[23] while Kobayashi et al. reported Cu-catalyzed alkynylcarboxylation of arynes with terminal alkynes leading to isocoumarins under 15 atm of CO_2 (Scheme 8).[24]

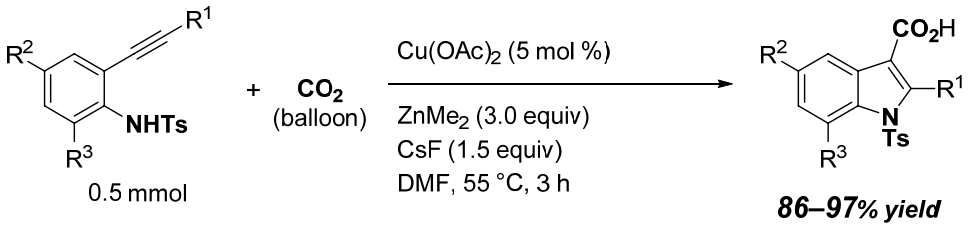
Scheme 5. Cu-Catalyzed Boracarboxylation of Alkynes Employing $B_2(pin)_2$



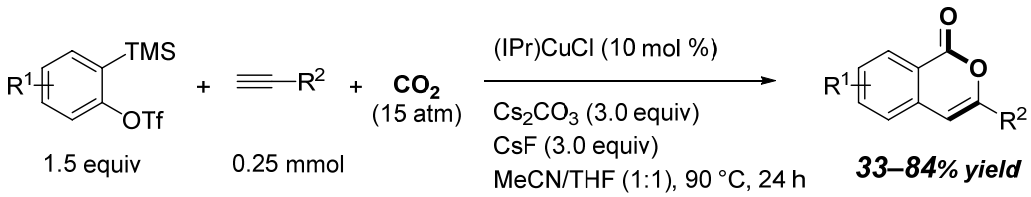
Scheme 6. Cu-Catalyzed Silacarboxylation of Alkynes



Scheme 7. Cu-Catalyzed Intramolecular Aminocarboxylation of Alkynes

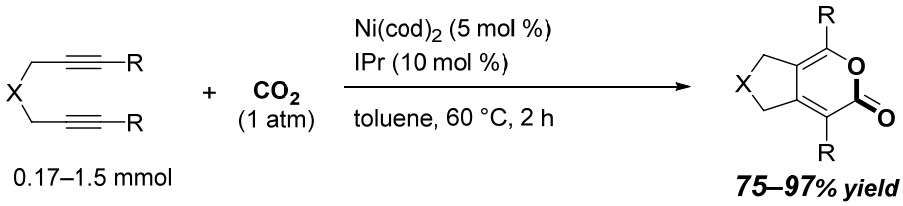


Scheme 8. Cu-Catalyzed Alkynylcarboxylation of Arynes

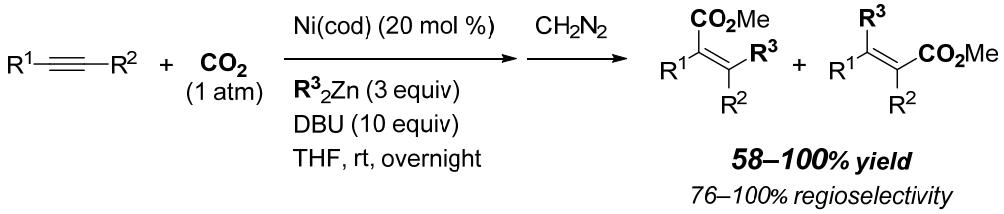


The Type 2 CO_2 fixation (Scheme 3, bottom; oxidative cyclization of Ni, CO_2 and substrates) forms a nickelalactone, containing Ni–C bond for further *in situ* bond-forming events. Taking advantage of this feature as well as the feasibility of the oxidative cyclization, a variety of stoichiometric reactions have been developed.[25] However, there are only two precedents for the catalytic reactions. One is the [2+2+2]-type cycloaddition of CO_2 with two C–C triple bonds to afford pyrones,[16,17] firstly reported by Inoue. Although diynes show good reactivity under 1 atm of CO_2 (Scheme 9),[17] intermolecular variant[16a] requires high pressure of CO_2 (50 atm). The other is the carboxylation of internal alkynes wherein carbon-substituents derived from organozinc reagents are incorporated along with CO_2 (Scheme 10).[26] Unfortunately, this pioneering reaction suffers from regioselectivity problems. In addition, it requires high catalyst loading (20 mol %) as well as large excess of ligand (DBU, 10 equiv) and pyrophoric organozinc reagents (3.0 equiv or more).

Scheme 9. Ni-Catalyzed [2+2+2]-Type Cycloaddition of Diyne with CO_2



Scheme 10. Ni-Catalyzed Alkylative Carboxylation of Alkynes

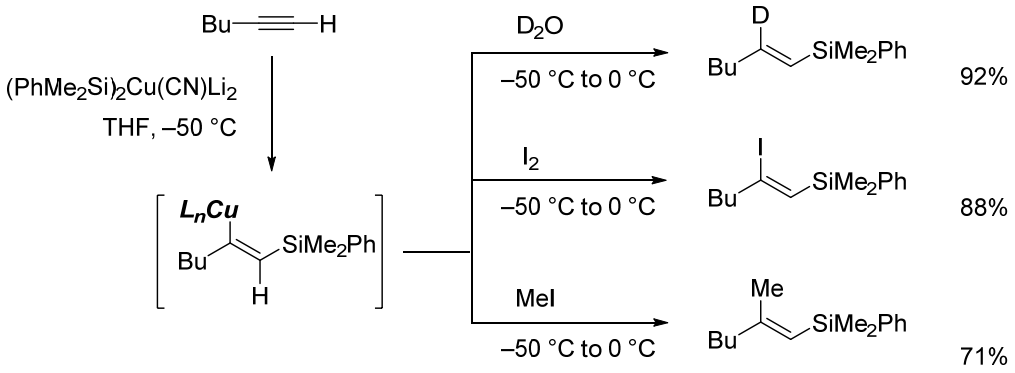


On the basis of these presidents and considerations, the author approaches the above-mentioned challenges through the following strategies: the catalytic addition of silyl-copper species, and the activation of the nickelalactone by $MgBr_2$ and a metal reducing agent. Some fundamentals and ideas of these strategies are summarized below.

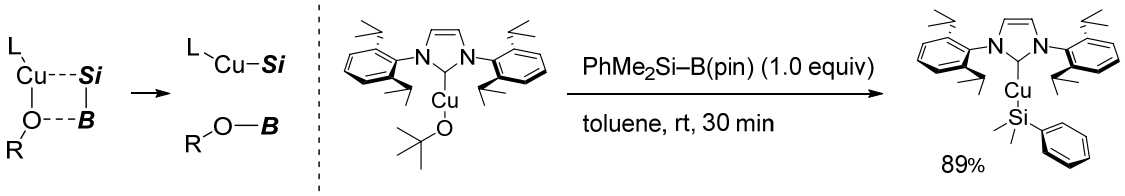
Silylcupration in organic synthesis. Silylcupration (i.e. the addition of Si–Cu bonds) across C–C multiple bonds is a reliable and powerful process that forms both C–Si and C–Cu bonds, with the latter amenable to further *in situ* C–C bond-forming events. Conventionally, a stoichiometric amount of silylcuprate such as $(PhMe_2Si)_2Cu(CN)Li_2$ is used in the reaction (Scheme 11).[27] Those reagents must be prepared just before use by mixing copper salts with one or two equiv of silyllithium reagents. On the other hand, the generation of a silylcopper species by the reaction of a copper alkoxide and a silylborane[28] gains much attentions in the last few years (Scheme 12).[29,30] The catalytic in situ generation of a silylcopper followed by silylcuprations have been postulated in the Cu-catalyzed hydrosilylations of alkynes (Scheme 13)[31] and allenes (Scheme 14).[32] However, utilization of the resulting C–Cu bonds in subsequent C–C bond formation has remained mostly unexplored. Until now, except for the author's works in Chapters 1–3, the only

example is the silylative allylation of aldehydes reported by Procter et al (Scheme 15).[32b] The silylcupration across C=O bonds are also known in catalytic silylations.[33,34] In particular, Kleeberg et al. reported the addition of a silylcopper complex across C=O bond of CO_2 to give CO as a product.[34] Therefore, there are two keys to utilize silylcupration in catalytic carboxylations. One is regio- and chemoselective silylcupration (across C–C multiple bonds, not across CO_2). The other is the generation of sufficiently reactive Cu–C bond toward CO_2.

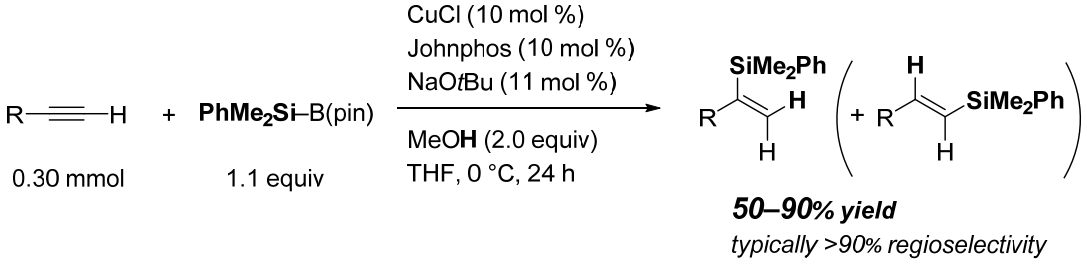
Scheme 11. Representative Stoichiometric Reactions of Silylcuprates



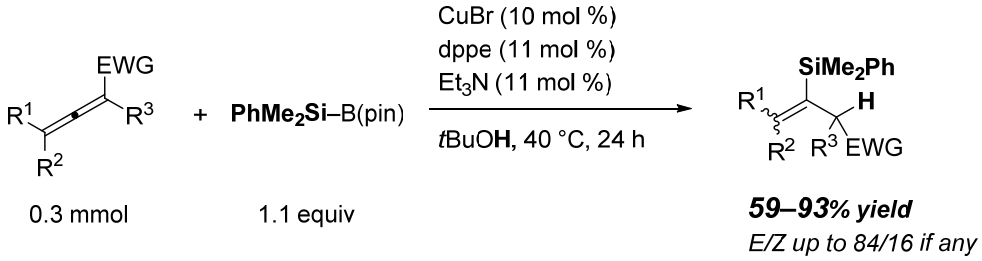
Scheme 12. Generation of a Silylcopper Species from a Copper Alkoxide and a Silylborane; Schematic Representation and a Stoichiometric Reaction



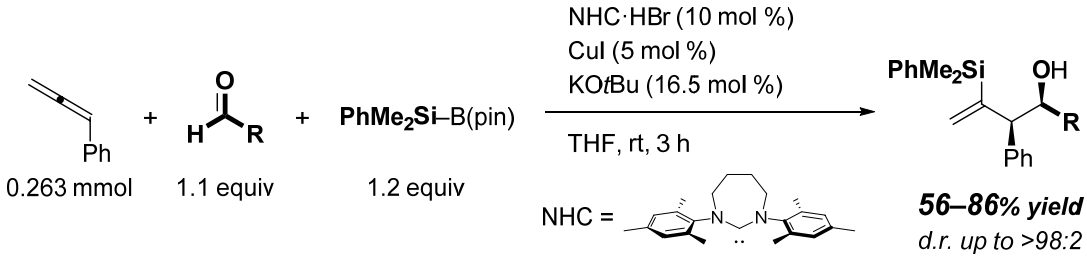
Scheme 13. Catalytic Hydrosilylation of Terminal Alkynes with a Silylborane and Methanol Reported by Loh et al.



Scheme 14. Catalytic Hydrosilylation of Allenes Bearing Electron Withdrawing Substituents with a Silylborane and *t*BuOH Reported by Loh et al.

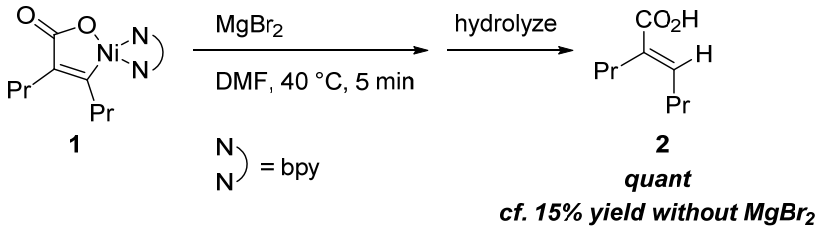


Scheme 15. Catalytic Silylative Allylation of Aldehydes Reported by Procter et al.

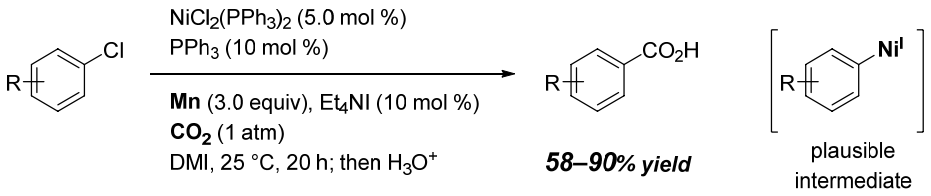


Activation of nickelalactones. Nickelalactone **1** is a relatively stable complex, as Duñah et al. mentioned that the protonation of Ni–C bond required the reaction with 2 M sulfuric acid at 50 °C for 48 h.[35] In contrast, they found that **2** was quantitatively obtained by treating **1** with $MgBr_2$ in DMF at 40 °C for 15 min followed by hydrolysis. In the absence of $MgBr_2$, the yield was less than 15% (Scheme 16). These results indicated that $MgBr_2$ has an ability to activate **1**. A related effect was reported with $ZnCl_2$.[36] On the other hand, the reductive activation of Ni(II) species to Ni(I) by using a metal powder has gained much attentions. In the area of catalytic carboxylation, Tsuji et al. reported the Ni-catalyzed carboxylation of aryl chlorides utilizing Mn powder as a reducing agent (Scheme 17).[10b] The mechanism involving one-electron reduction from Ni(II) to Ni(I) was supported both experimentally and theoretically.[10b,37] These two findings prompt the author to explore the transformation through the cooperative activation of a nickelalactone utilizing $MgBr_2$ and a metal reducing agent.

Scheme 16. Effect of $MgBr_2$ in the Protonation of **1**



Scheme 17. Ni-Catalyzed Carboxylation of Aryl Chlorides

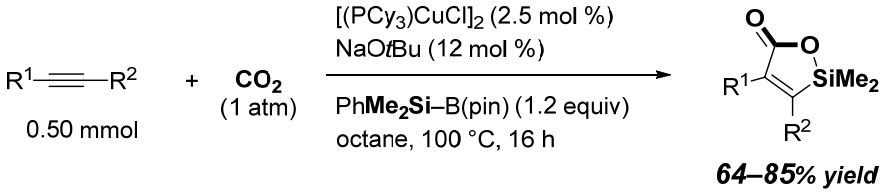


Overview of the present thesis. As described above, carboxylation of C–C multiple bonds has a great potential for the synthesis of highly functionalized and complex carboxylic acids, since the reaction assembles *three* components (i.e. C–C multiple bonds, CO_2 and one more substituent). However, known processes could not fully exploit the advantage. They are largely limited to hydrocarboxylations, intramolecular reactions, and those with low efficiency (e.g. high CO_2 pressure, high catalyst loading, and/or large excess of the reagents). Therefore, the author focused on the efficient catalytic fixation of CO_2 across C–C multiple bonds in an unprecedented mode of functionalization. Described in Chapters 1–3 is catalytic silacarboxylations and a related silylative allylation utilizing highly regioselective silylcupration across alkynes and 1,2-dienes (allenes). Chapter 4 is devoted to a Cu-catalyzed reaction of allenes with CO_2 in the presence of a hydrosilane affording homoallylic alcohols. Chapter 5 includes a development and mechanistic studies on a Ni-catalyzed doublecarboxylation of alkynes.

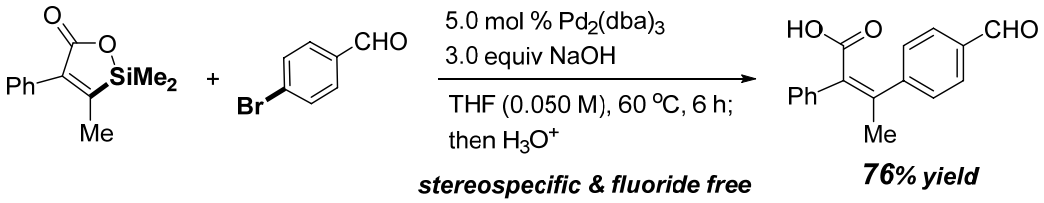
In Chapter 1, the author describes a copper-catalyzed silacarboxylation of internal alkynes with silylboranes under 1 atm of CO_2 (Scheme 18).[38] A PCy_3-ligated copper complex efficiently catalyzed the reaction in combination with a silylborane. The products were silalactones, a cyclic ester containing a silicon atom. This result indicated the

Si–Ph bond of the starting silylborane was cleaved during the reaction. In addition, he clearly demonstrates the synthetic utility of silalactones through Hiyama coupling, which afforded α,β-unsaturated carboxylic acid bearing tetrasubstituted olefin in a setereospecific manner (Scheme 19). The work is the first example of the catalytic silacarboxylation of alkynes.

Scheme 18. Cu-Catalyzed Silacarboxylation of Alkynes (reproduction of Scheme 5)

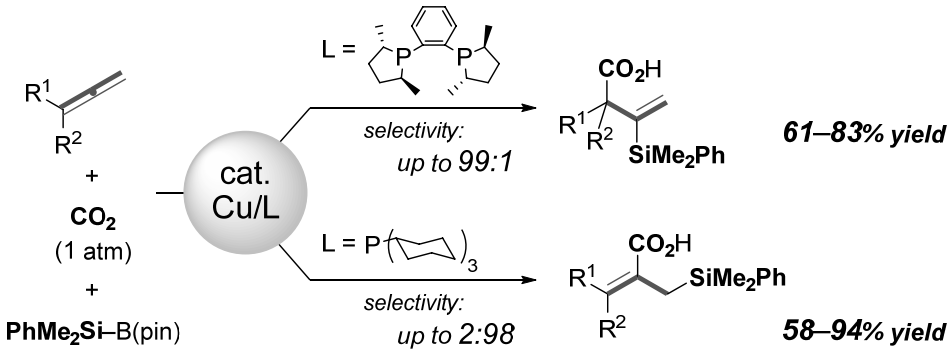


Scheme 19. Hiyama Coupling of a Silalactone with *p*-Bromobenzaldehyde



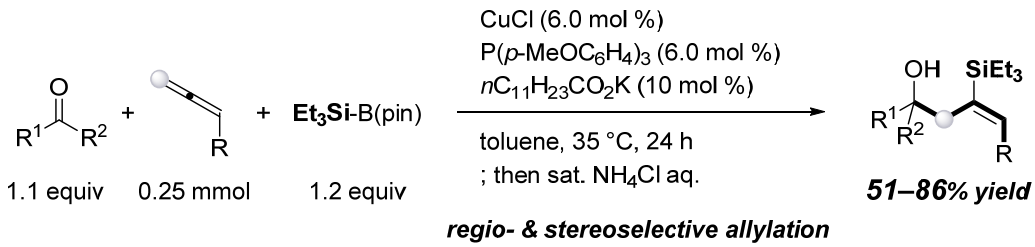
Among a range of C–C multiple bonds, allenes are known to exhibit a variety of reactivity. When two different substituents are incorporated to monosubstituted allenes, we may obtain up to 6 isomers of products. Control of the selectivities is challenging, but once it is achieved, a structurally diverse array of the products become accessible.[39] In Chapter 2, the author discloses a catalytic *regiodivergent* silacarboxylation of allenes (Scheme 20).[40] Two different carboxylated silanes were selectively and regiodivergently synthesized from a single allene substrate. The regioselectivity of the reaction was successfully reversed by the proper choice of ligand; carboxylated vinylsilanes were obtained with *rac*-Me-DuPhos as the ligand, whereas the use of PCy_3 afforded carboxylated allylsilanes.

Scheme 20. Cu-Catalyzed Regiodivergent Silacarboxylation of Allenes



On the basis of the findings in Chapter 2, the author next focused on the catalytic silylative allylation of ketones and aldehydes. The allylation of carbonyl compounds is an important class of carbon–carbon bond-forming reactions because of the versatility of homoallylic alcohols in organic synthesis.[41] In Chapter 3, the author reports that a copper complex with a monophosphine ligand catalyzed the silylative allylation of ketones and aldehydes, affording a distinct regioisomer from the related previous works[32b] (Scheme 21).[42] Homoallylic alcohols bearing internal (*E*)-vinylsilane moieties, which derived from the C–C bond formation between 3-position of allenes with carbonyl carbon, were obtained selectively.

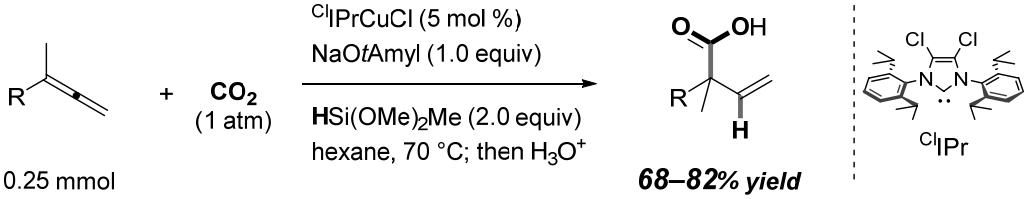
Scheme 21. Cu-Catalyzed Silylative Allylation of Ketones and Aldehydes



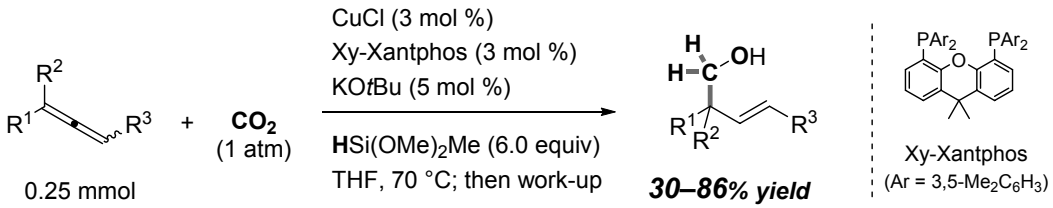
CO_2 fixation catalyzed by transition metal–hydride usually leads to the formation of carboxylic acids (hydrocarboxylation; C–C bond formation)[18a,19,20] or reduced C1 chemicals such as methanol (C–H bond formation).[43] The author succeeded in developing the Cu–H-catalyzed hydrocarboxylation of allenes employing a hydrosilane as a reducing

agent (Scheme 22). Moreover, during the course of this work, he found that a homoallylic alcohol was formed under some reaction conditions. There has been no report on the catalytic conversion of CO_2 into homoallylic alcohols, where *both* C–C and C–H bond are formed with CO_2. Thus, in Chapter 4, the author uncovers a Cu-catalyzed fixation of CO_2 to allenes with a hydrosilane giving homoallylic alcohols, namely, a hydro-hydroxymethylation of allenes (Scheme 23).[44] Noteworthy is that a wide variety of ester functionalities has remained unchanged during the reaction.

Scheme 22. Cu-Catalyzed Hydrocarboxylation of Allenes



Scheme 23. Cu-Catalyzed Reductive Fixation of CO_2 as Homoallylic Alcohols

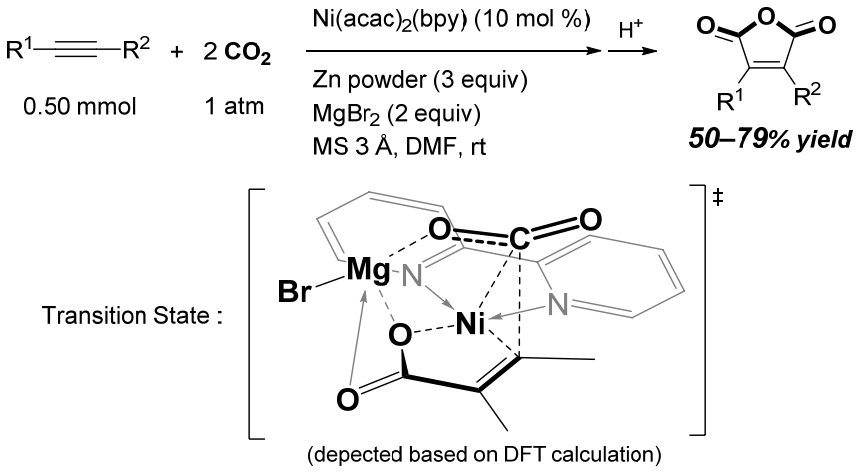


regioselective C–C & C–H bond-formation

As shown above, the addition of copper species across C–C multiple bonds is a versatile strategy for the catalytic carboxylation reactions. Nevertheless, most of the carboxylation reactions are one-to-one couplings of CO_2 and a substrate. On the other hand, doublecarboxylation, which incorporates two molecules of CO_2 to one molecule of a substrate, must be a promising method to synthesize dicarboxylic acids. To realize this transformation, the author focused on the other approach involving the oxidative cyclization of Ni(0), CO_2 and a substrate to form a nickelalactone. He envisioned a cooperative activation of the nickelalactone by $MgBr_2$ and a metal reducing agent. Disclosed in Chapter 5 is a Ni-catalyzed doublecarboxylation of alkynes under CO_2 employing $MgBr_2$ and Zn powder (Scheme 24).[45] Mechanistic studies were carried out both experimentally and

theoretically, and crucial roles of $MgBr_2$ and Zn concerning the second CO_2 insertion have been revealed by DFT calculation.

Scheme 24. Ni-Catalyzed Doublecarboxylation of Alkynes and Calculated Transition State for the Second CO_2 Insertion



The major progress achieved through the present thesis is: (1) the development of a ligand-controlled catalytic silylcupration strategy for highly regioselective silylative difunctionalizations (silacarboxylation and silylative allylation; Chapters 1–3), (2) the development of a novel CO_2 conversion to homoallylic alcohol through a Cu-catalyzed hydro-hydroxymethylation of allenes with CO_2 and a hydrosilane (Chapter 4), and (3) the development of a new method for activating nickelalactone employing $MgBr_2$ and Zn powder toward Ni-catalyzed doublecarboxylation of alkynes (Chapter 5). The author believes that these findings lead to further development of the transition metal-catalyzed transformation, especially in the chemistry of CO_2 utilization.

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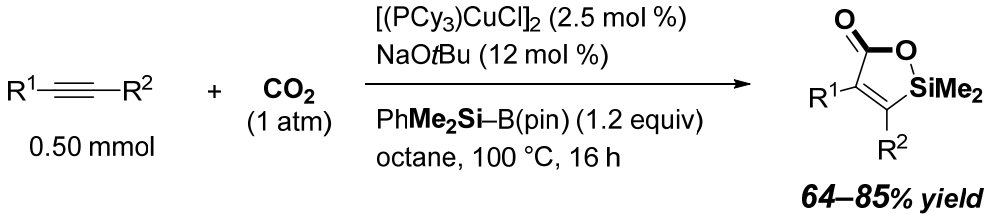
Chapter 1

Copper-Catalyzed Silacarboxylation of Internal Alkynes by Employing Carbon Dioxide and Silylboranes

The copper-catalyzed silacarboxylation of internal alkynes by employing silylboranes as the silicone source under an atmospheric pressure of carbon dioxide has been achieved. The reaction afforded silalactones in good to high yields.

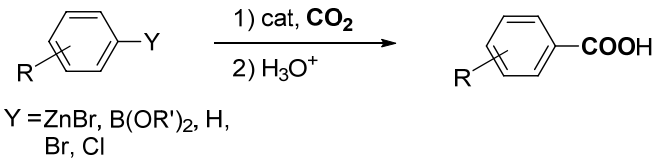


1-1. Introduction

CO_2 is a nontoxic, abundant, and renewable carbon source.[1] The utilization of this environmentally friendly raw material in *carbon–carbon bond-forming reactions* is one of the most important challenges in homogeneous transition-metal catalysis.[2] To date, two types of catalytic transformations using CO_2 with C–C bond formation have been investigated intensively: (a) the substitution of Ar–Y with CO_2 (Scheme 1-1a) and (b) the hydrocarboxylation of C–C unsaturates (Scheme 1-1b). The former reactions involve the carboxylations of organozinc[3a,b] and organoborane[3c-f] compounds, C–H bonds,[3g-j] and bromoarenes[3k] (Scheme 1-1a). Recently, Tsuji et al. reported the Ni-catalyzed carboxylation of *chloro*arenes with CO_2 in the presence of Mn powder under ambient conditions.[4a] As for the hydrocarboxylation (Scheme 1-1b), the reactions of dienes,[5a,b] alkenes,[5c] and alkynes[5d] have been reported. However, in all these cases, highly reactive and pyrophoric Et_3Al[5a,b] or Et_2Zn[5a,c,d] must be used as hydride sources. Tsuji et al. recently reported the hydrocarboxylation of alkynes employing stable and easy-to-handle hydrosilanes as the hydride source.[4b]

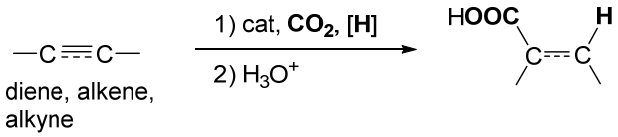
Scheme 1-1. Typical Transformations Using CO_2 with C–C Bond-Formations

(a) Substitution of Ar–Y with CO_2



Y = ZnBr, $B(OR')_2$, H, Br, Cl

(b) Hydrocarboxylation of C–C Unsaturates



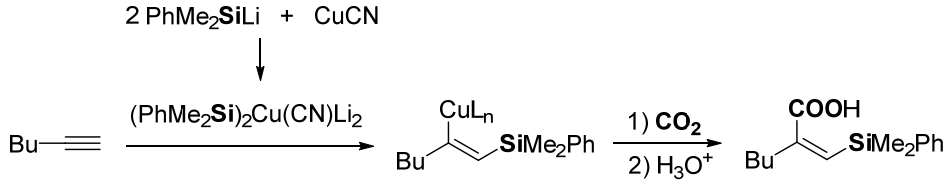
diene, alkene, alkyne

Besides these reactions, catalytic *hetero*carboxylation, in which the heteroatom functionality and CO_2 are simultaneously and catalytically incorporated into unsaturated substrates, is extremely useful, since the reaction will provide a valuable synthetic route employing CO_2 for the formation of highly functionalized carboxylic acid derivatives.

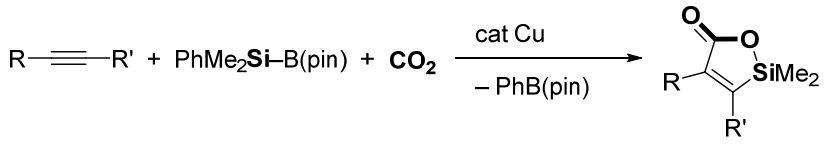
For the *sila*carboxylation of alkynes, the only precedent is the *stoichiometric* reaction of 1-hexyne reported by Fleming et al., who carried out the reaction of 1-hexyne with a stoichiometric amount of $(PhMe_2Si)_2Cu(CN)Li_2$ followed by trapping of the resulting Cu species with CO_2 (Scheme 1-2a).[6] Here, the author reports the copper-catalyzed silacarboxylation of internal alkynes employing CO_2 and silylborane (Scheme 1-2b). The reaction afforded silalactone products regioselectively in good to high yields.

Scheme 1-2. Silacarboxylation of Alkynes

(a) *Previous Work* (Stoichiometric Reaction of 1-Hexyne)



(b) *This Work* (Catalytic Reaction Using a Silylborane)

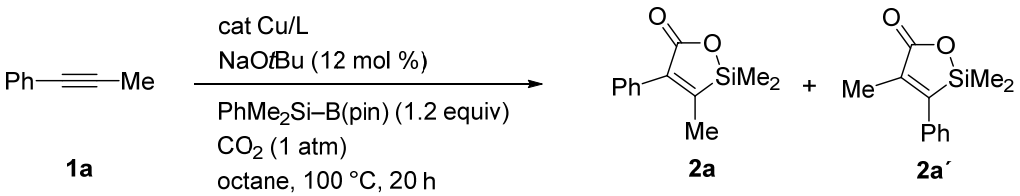


1-2. Results and Discussion

First, the silacarboxylation of 1-phenyl-1-propyne (**1a**) was carried out using the readily available $PhMe_2Si–B(pin)$[7] as the silicon source in the presence of a copper catalyst in octane at 100 ºC under an atmospheric pressure of CO_2 (Table 1-1).[8] A mixture of CuCl and PCy_3 (P/Cu = 1) was employed as the catalyst, and silalactones[9] were afforded in 97% yield with high regioselectivity (**2a**/**2a'** = 97/3, entry 1). P*t*Bu$_3$ is also an efficient ligand and the products were obtained regioselectively in high yield (entry 2). On the other hand, PBu_3, PPh_3, Xantphos, *rac*-BINAP and dppBz were not effective ligands affording **2a** and **2a'** in quite low yields (entries 3–7). [(IMes)CuCl][10a] bearing IMes, an NHC ligand, gave **2** in high yield, but with slightly lower regioselectivity (**2a**/**2a'** = 88/12) (entry 8). [(IPr)CuCl][10b] bearing the sterically demanding IPr ligand gave the considerably lower yield (entry 9). $[(PCy_3)CuCl]_2$[10c] prepared from CuCl and PCy_3 was the best catalyst giving **2** in a quantitative yield while maintaining high regioselectivity

(entry 10). Through simple recrystallization, the major regioisomer **2a** was isolated in 81% yield in pure form (entry 10). The structure of **2a** was confirmed by X-ray crystallographic analysis[8] (Figure 1-1) as well as 2D NMR measurements. In toluene or 1,4-dioxane as the solvent, the products were obtained in 98% and 84% yields, respectively (entries 11 and 12), while acetonitrile and DMF did not afford the product at all.

Table 1-1. Copper-Catalyzed Silacarboxylation of **1a** with CO_2 Employing $PhMe_2Si$–B(pin)[a]



entry	Cu catalyst	ligand	total yield of **2a**+**2a´** (%)[b]	ratio of **2a**/**2a´**[b]
1	CuCl	PCy_3	97	97/3
2	CuCl	P*t*Bu$_3$	90	97/3
3	CuCl	PBu_3	15	90/10
4	CuCl	PPh_3	28	74/26
5	CuCl	Xantphos	0	–
6	CuCl	*rac*-BINAP	7	–
7	CuCl	dppBz	0	–
8	[(IMes)CuCl]	–	96	88/12
9	[(IPr)CuCl]	–	18	77/23
10	$[(PCy_3)CuCl]_2$[c]	–	99 (81)[d]	96/4
11[e]	$[(PCy_3)CuCl]_2$[c]	–	98	95/5
12[f]	$[(PCy_3)CuCl]_2$[c]	–	84	94/6

[a] Reaction conditions; 1-phenyl-1-propyne (**1a**, 0.50 mmol), copper catalyst (15 μmol, 3.0 mol %), ligand (15 μmol, 3 mol %), NaO*t*Bu (60 μmol, 12 mol %), $PhMe_2Si$–B(pin) (0.60 mmol, 1.2 equiv), under CO_2 (1 atm) in octane (0.50 mL), at 100 ºC for 20 h. [b] Determined by GC analysis. [c] $[(PCy_3)CuCl]_2$ (12.5 μmol, 2.5 mol %) was used as the catalyst. [d] Isolated yield of **2a**. [e] Toluene was used as the solvent. [f] 1,4-Dioxane was used as the solvent.

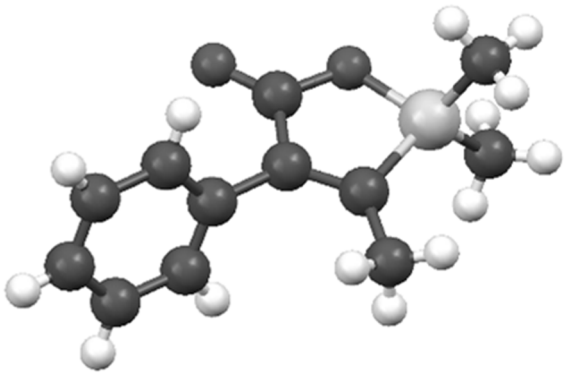
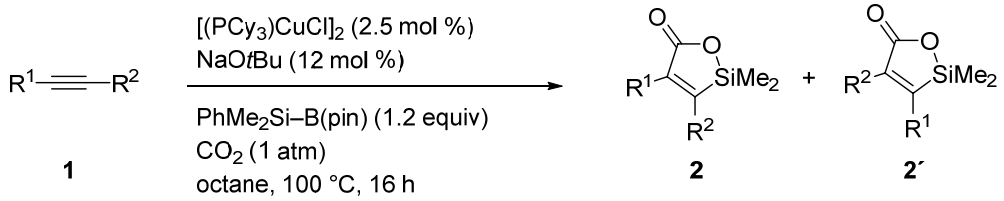


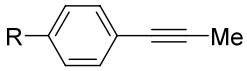
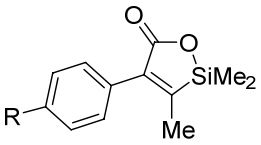
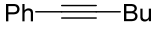
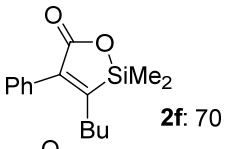
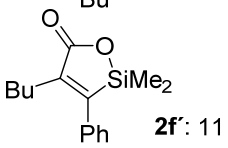
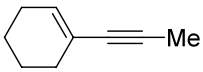
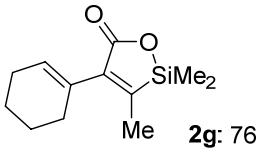
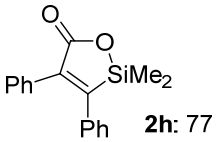
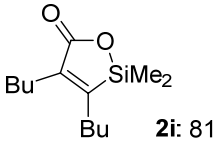
Figure 1-1. X-ray crystal structure of **2a**.

The silacarboxylation of various alkynes (**1b**–**i**) was carried out (Table 1-2). The reactions of 1-aryl-1-propynes bearing both electron-rich and electron-poor substituents on the aryl ring gave the corresponding silalactones (entries 1–4). The GC and GC-MS analyses of the crude products indicated that these reactions proceeded regioselectively and major regioisomers (**2b**–**e**) were isolated in good to high yields. Gratifyingly, the bromo (entry 3), and ester (entry 4) functionalities remained intact under these reaction conditions. 1-Phenyl-1-hexyne (**1f**) afforded the products in 86% total yield (by GC) with slightly lower regioselectivity (**2f**/**2f'** = 87/13). Pure **2f** and **2f'** were isolated from the reaction mixture by column chromatography in 70% and 11% yields, respectively (entry 5). A conjugated enyne (**1g**) as the substrate gave **2g** and **2g'** in 84% total yield (**2g**/**2g'** = 92/8), from which the major isomer **2g** was isolated in 76% yield in pure form (entry 6). Diphenylacetylene (**1h**) also afforded the corresponding product (**2h**) in good isolated yield with a longer reaction time (entry 7). The reaction of 5-decyne (**1i**) proceeded smoothly at 90 °C for 2 h and **2i** was isolated in 81% yield (entry 8).

Et_3Si–B(pin)[11] (in place of $PhMe_2Si$–B(pin)) was reacted with **1a** under the same reaction conditions as for entry 10 in Table 1-1 (eq 1-1). However, the reaction of Et_3Si–B(pin) was not as clean as that with $PhMe_2Si$–B(pin), and some unidentified byproducts were formed. In the reaction, the corresponding silalactone (**2aE**) was afforded in only trace yield (by GC-MS). Instead, a mixture of two β-silyl-α,β-unsaturated carboxylic acids (**3aE**/**3aE'** = 96/4) was isolated in 64% yield (eq 1-1). Disilanes such as $PhMe_2Si$–$SiMe_2Ph$ could not replace $PhMe_2Si$–B(pin) as the silicon source in the present silacarboxylation reaction, since neither silalactones (**2**) nor β-silyl-α,β-unsaturated

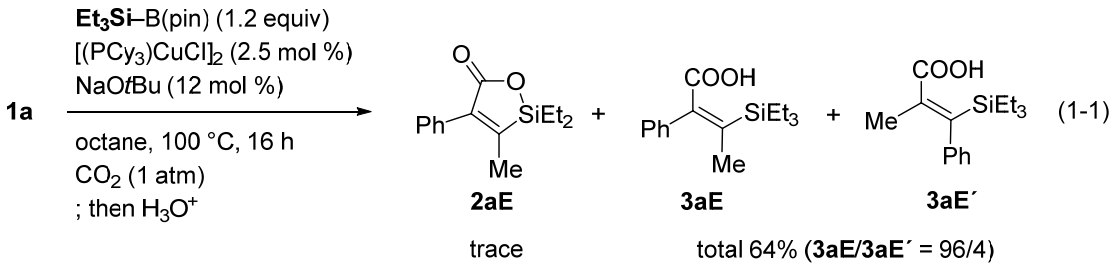
Table 1-2. Copper-Catalyzed Silacarboxylation of Internal Alkynes



entry	substrate	total yield (**2**+**2´**) (%) (regioselevtivity: **2**/**2´**)[b]	isolated yield of major isomer: **2** (%)
			
1	**1b**: R = Me	93 (95/5)	**2b**: 85
2	**1c**: R = MeO	91 (94/6)	**2c**: 84
3	**1d**: R = Br	97 (96/4)	**2d**: 64
4	**1e**: R = CO_2Et	82 (98/2)	**2e**: 80
5	 **1f**	86 (87/13)	 **2f**: 70  **2f´**: 11
6	 **1g**	84 (92/8)	 **2g**: 76
7[c]	 **1h**	92	 **2h**: 77
8[d]	 **1i**	88	 **2i**: 81

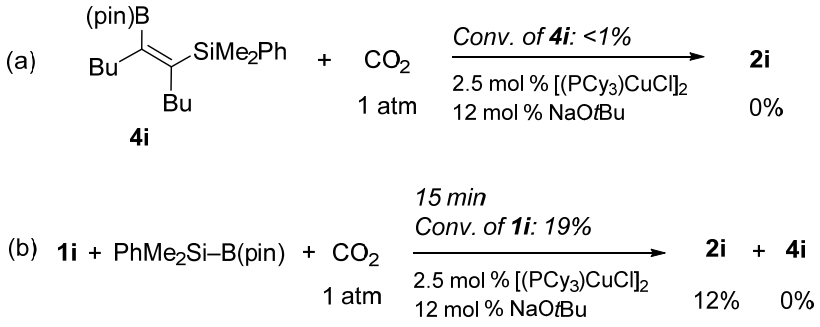
[a] Reaction conditions; alkyne (**1**, 0.50 mmol), $[(PCy_3)CuCl]_2$ (0.0125 mmol, 2.5 mol %), NaO*t*Bu (0.060 mmol, , 12 mol%), $PhMe_2Si$–B(pin) (0.60 mmol, 1.2 equiv), under CO_2 (1 atm) in octane (0.50 mL), at 100 ºC, for 16 h. [b] Determined by GC analysis. [c] For 60 h. [d] At 90 ºC, for 2 h.

carboxylic acids (**3**) were detected in the reaction mixture. Thus, the readily and commercially available $PhMe_2Si$–B(pin) is the best silicon source in this reaction.[12] Regarding the alkynes, terminal alkynes could not be used as the substrates.



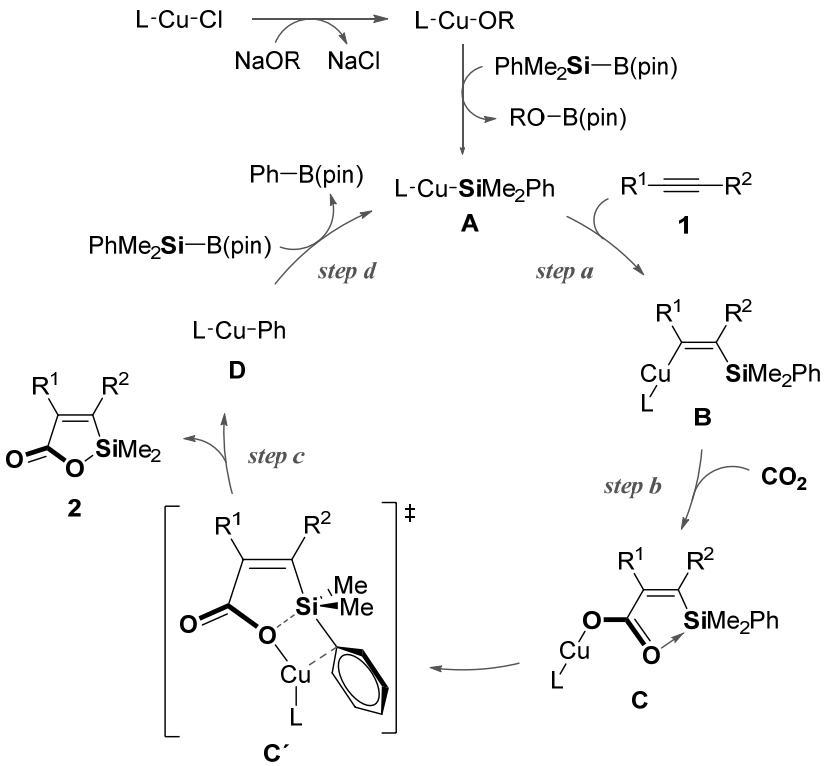
Some control experiments were carried out (Scheme 1-3) to provide an insight into the silacarboxylation mechanism. There is some possibility that the reaction could proceed stepwise via two sequential known reactions, i.e. the silaboration of an alkyne[13] followed by the carboxylation of the resulting vinylboronic esters.[3c-f] Thus, the author first prepared a possible intermediate **4i**[13a] through the silaboration of **1i** with $PhMe_2Si$–B(pin). Then the reaction of **4i** with CO_2 was carried out under the same reaction conditions as for entry 8 in Table 1-2. As a result, **4i** was not converted at all and no **2i** was provided (Scheme 1-3a). Furthermore, **4i** was not detected at all in the reaction mixture at a low conversion of **1i** (reaction time: 15 min, conversion of **1i**: 19%, yield of **2i**: 12%) under otherwise the same reaction conditions as for entry 8 in Table 1-2 (Scheme 1-3b). Thus, in the present catalytic system, the silacarboxylation must proceed in one step, and not via silaboration of the alkyne followed by carboxylation.

Scheme 1-3. Control Experiments Relevant to the Mechanism

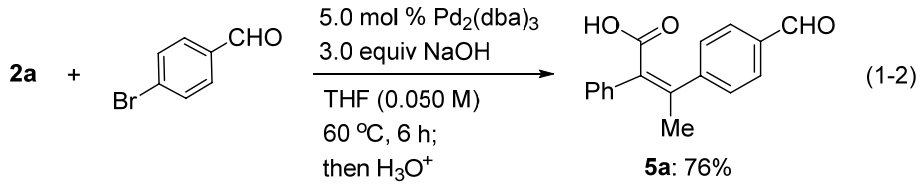


With consideration of these observations, a possible catalytic cycle for the silacarboxylation of alkynes with CO_2 is proposed as shown in Scheme 1-4. First, the reaction of the alkoxocopper species with silylborane affords the silylcopper complex (**A**).[14] *Syn* addition of **A** to the alkyne initiates the catalytic cycle and affords the *β*-silylalkenylcopper intermediate (**B**) (step a). Then, insertion of CO_2 into the Cu–C(vinyl) bond occurs,[4b] providing the corresponding copper carboxylate species (**C**) (step b). Intramolecular cyclization via **C'** affords the phenylcopper species (**D**) extruding the silalactone (**2**) (step c). As shown in eq 1-1, Et_3Si–B(pin) afforded the corresponding silalactone (**2aE**) in only trace yield. Thus, the phenyl moiety on the Si is indispensable for efficient Si–C bond cleavage. Finally, *σ*-bond metathesis of **D** with silylborane provides PhB(pin), and the silylcopper species (**A**) is regenerated (step d). In fact, PhB(pin) was found (86% yield) in the reaction mixture in entry 10 of Table 1-1.

Scheme 1-4. Plausible Reaction Mechanism



The silalactones are good substrates for the Hiyama cross coupling reaction.[9b] Indeed, in the reaction of **2a** with 4-bromobenzaldehyde in the presence of $Pd_2(dba)_3$ as a catalyst, the trisubstituted α,β-unsaturated carboxylic acid (**5a**) was isolated in 76% yield (eq 1-2).



(1-2)

1-3. Conclusion

The first catalytic silacarboxylation of an alkyne has been achieved by utilizing silylborane as the silicon source under atmospheric pressure of CO_2 to afford the silalactone selectively in high yield.

1-4. Experimental Section

1-4-1. General Remarks

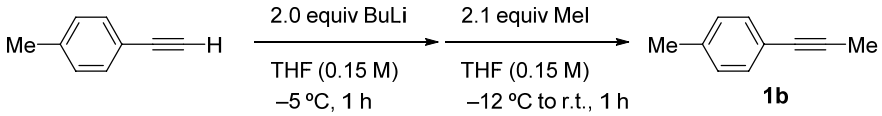
Unless otherwise noted, all reactions were performed under an argon atmosphere using heat-gun-dried glassware on a dual-manifold Schlenk line. ^1H, ^{13}C and ^{29}Si NMR spectra were recorded on a JEOL ECX-400P spectrometer. Chemical shift values (δ) are reported in ppm and calibrated to tetramethylsilane (TMS, 0.00 ppm) for ^1H and ^{29}Si, and to $CDCl_3$ (77.0 ppm) for ^{13}C as an internal standard. IR spectra were recorded on a Jasco FT/IR-4100 spectrometer. EI-MS spectra were recorded on a Shimadzu GCMS-QP5050A. High-resolution mass spectra (ESI-HRMS) were obtained with JEOL JMX-SX 102A spectrometer. Elemental analysis was carried out at the Center for Organic Elemental Microanalysis, Graduate School of Pharmaceutical Science, Kyoto University. GC analysis was carried out using Shimadzu GC-17A equipped with an integrator (C-R8A) with a capillary column (CBP-5, 0.25 mm i.d. × 25 m). TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck Silica gel $60F_{254}$. Column chromatography was carried out on silica gel (Kanto N60, spherical, neutral, 63–210 μm).

Octane and 1,4-dioxane were purified by refluxing over Na/benzophenone followed by distillation under Ar. In the case of octane, a small amount of tetraglyme was added when refluxed. Anhydrous THF, toluene and CH_2Cl_2 were purchased from Kanto Chemical Co., Inc. and further purified by passage through activated alumina under positive argon pressure as described by Grubbs et al.[15] Anhydrous DMF was purchased from Kanto Chemical Co., Inc. and further

distilled under reduced pressure. 1-Phenyl-1-propyne (**1a**) and 5-decyne (**1i**) were purified by distillation under reduced pressure prior to use. PPh_3 was purified by recrystallization prior to use. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Imidazolium salts (IMes·HCl and IPr·HCl),[16] $[(PCy_3)CuCl]_2$,[17] 1-(1-cyclohexenyl)-1-propyne (**1g**)[18] and silylboranes ($PhMe_2Si$–B(pin) and Et_3Si–B(pin))[19,11] were synthesized according to the literatures.

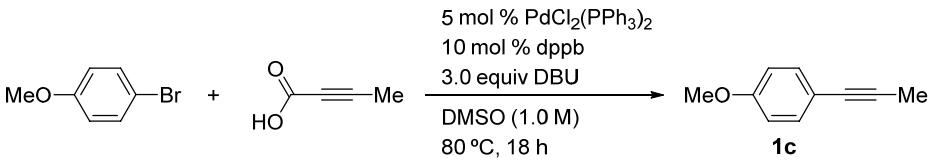
1-4-2. Preparation of Substrates, Reagents and Catalysts

Preparation of 1-(4-tolyl)-1-propyne (1b)



To a dried 200 mL two-neck flask were added 4-ethynyltoluene (1.5 mL, 12 mmol) and THF (80 mL). The flask was placed in an ice water/salt bath and allowed to cool to around –5 °C. Butyllithium (1.63 M in hexane, 15 mL, 25 mmol) was added dropwise and the reaction mixture was stirred for 1 h. Iodomethane (1.6 mL, 26 mmol) was added at –12 °C and the reaction mixture was stirred at room temperature for 1 h. After quenching with a saturated aqueous NH_4Cl solution, the mixture was extracted with CH_2Cl_2 (50 mL × 3). The combined organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by short-path distillation (2 Torr, 55–57 °C) to afford the compound **1b** as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.28 (d, J = 7.7 Hz, 2H), 7.08 (d, J = 7.7 Hz, 2H), 2.33 (s, 3H), 2.04 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 137.5, 131.3, 128.9, 120.9, 84.9, 79.7, 21.4, 4.3. All the resonances in ^{1}H and ^{13}C NMR spectra were in good agreement with literature values.[20]

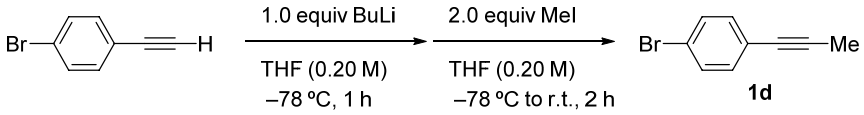
Preparation of 1-(4-methoxyphenyl)-1-propyne (1c)[20]



To a solution of tetrolic acid (420 mg, 5.0 mmol), $PdCl_2(PPh_3)_2$ (175 mg, 0.25 mmol) and dppb (206 mg, 0.50 mmol) in DMSO (5.0 mL) were added 4-bromoanisol (0.75 mL, 5.6 mmol) and DBU (2.2 mL, 15 mmol) in a 100 mL test tube. The mixture was stirred at 80 °C for 18 h, and then cooled to room temperature. The mixture was poured into a saturated aqueous NH_4Cl solution (20 mL), and then extracted with CH_2Cl_2 (20 mL × 3). The combined organic layer was washed with water (10 mL × 5) and dried over $MgSO_4$. After removal of all volatiles under reduced pressure, the residue was purified by column chromatography (eluent: hexane to

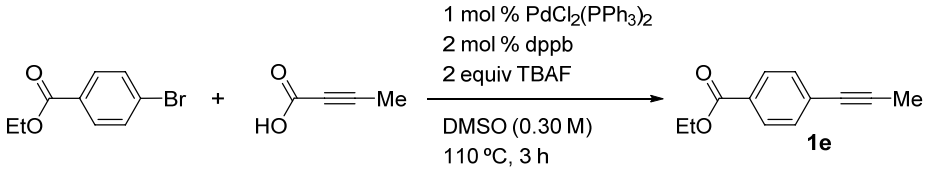
hexane/EtOAc = 30:1). The compound **1c** (230 mg, 31%) was obtained as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.32 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 2.02 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 159.0, 132.8, 116.2, 113.8, 84.1, 79.4, 55.2, 4.2. All the resonances in ^{1}H and ^{13}C NMR spectra were in good agreement with literature values.[20]

Preparation of 1-(4-bromophenyl)-1-propyne (1d)



To a dried 50 mL two-neck flask were added 4-bromophenylacetylene[21] (757 mg, 4.18 mmol) and THF (20 mL). The flask was allowed to cool to around –78 °C. Buthyllithium (1.63 M in hexane, 2.6 mL, 4.24 mmol) was added dropwise and the reaction mixture was stirred for 1 h. To the reaction mixture, iodomethane (0.50 mL, 8.0 mmol) was added dropwise at –80 °C. After the addition, the reaction mixture was stirred at room temperature for 2 h. After quenching with a saturated aqueous NH_4Cl solution (20 mL), the reaction mixture was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography (eluent: hexane) to give the compound **1d** (639 mg, 78%) as a clear and colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.40 (d, 8.6Hz, 2H), 7.24 (d, 8.6Hz, 2H), 2.03 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 132.9, 131.4, 123.0, 121.6, 87.1, 78.7, 4.3. All the resonances in ^{1}H and ^{13}C NMR spectra were in good agreement with the literature values.[22]

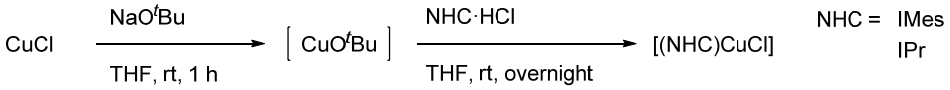
Preparation of 1-(4-ethoxycarbonylphenyl)-1-propyne (1e)



To a solution of ethyl 4-bromobenzoate (1.6 mL, 10 mmol), tetrolic acid (900 mg, 10.7 mmol), $PdCl_2(PPh_3)_2$ (70 mg, 0.10 mmol) and dppb (82 mg, 0.20 mmol) in DMSO (30 mL) was added tetrabutylammonium fluoride (1.0 M solution in THF, 20 mL, 20 mmol) in a 100 mL two-neck flask. The mixture was stirred at 110 °C for 3 h, and then cooled to room temperature. The mixture was poured into a saturated aqueous NH_4Cl solution (60 mL), and then extracted with CH_2Cl_2 (50 mL × 3). The combined organic layer was washed with water (30 mL × 5) and dried over $MgSO_4$. After removal of all volatiles under reduced pressure, the residue was purified by column chromatography (eluent: hexane/CH_2Cl_2 = 2:1) to give the compound **1e** (1.79 g, 95%) as a clear and colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 8.2 Hz,

2H), 4.36 (q, J = 7.2 Hz, 2H), 2.07 (s, 3H), 1.38 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 166.1, 131.3, 129.3, 129.2, 128.7, 89.2, 79.3, 61.0, 14.3, 4.4. All the resonances in ^{1}H and ^{13}C NMR spectra were in good agreement with the literature values.[23]

Typical procedure for the preparation of [(NHC)CuCl]



To a 60 mL flask in a glove box were added copper chloride (638 mg, 6.45 mmol), sodium *tert*-butoxide (591 mg, 6.16 mmol) and THF (50 mL). After the mixture was stirred at room temperature for 2.5 h, IMes·HCl (2.0 g, 5.87 mmol) was added to the resulting suspension. The mixture was stirred overnight at room temperature, and then filtered through a pad of Celite. After all volatiles were removed under reduced pressure, CH_2Cl_2 (50 mL) was added to the residue. Then, the suspension was again filtered through a pad of Celite. The filtrate was poured into hexane to give a white precipitate. The solid was collected by filtration, washed with hexane, and then dried *in vacuo*. [(IMes)CuCl] (2.0 g, 84%) was obtained as a white powder. [(IPr)CuCl] was synthesized in a similar manner. All the resonances in ^{1}H and ^{13}C NMR spectra of the both complexes were in good agreement with those in the literatures.[24]

1-4-3. Experimental Procedure for the Silacarboxylation

Typical procedure for the silacarboxylation of alkynes (Table 1-1, entry 1)

To a dried Schlenk tube was added sodium *tert*-butoxide (5.8 mg, 60 μmol). The Schlenk tube was evacuated and again dried with heating. CuCl (1.5 mg, 15 μmol) and PCy_3 (4.2 mg, 15 μmol) were added to the Schlenk tube, then the tube was evacuated and backfilled with CO_2 three times. To this Schlenk tube were added octane (0.50 mL), 1-phenyl-1-propyne (**1a**) (62 μL, 0.50 mmol) and $PhMe_2Si$–B(pin) (160 μL, 0.59 mmol) in this order. The system was closed, and then the mixture was allowed to stir at 100 °C for 20 h. After cooling to room temperature, the mixture was diluted with acetone (9.5 mL), and tetradecane (50 μL) was added as an internal standard. The mixture was filtered through a pad of Celite and analyzed by GC.

When a commercially available $PhMe_2Si$–B(pin) was used as received, the yield of the product was considerably decreased. Therefore, it must be purified by distillation under high vacuum (3 Pa) before use.

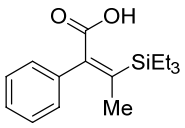
Typical procedure for the silacarboxylation of alkynes (Table 1-2, entry 5)

To a dried Schlenk tube was added sodium *tert*-butoxide (5.8 mg, 60 μmol). The Schlenk tube was evacuated and again dried with heating. $[(PCy_3)CuCl]_2$ (9.5 mg, 12.5 μmol) was added to the Schlenk tube, then the tube was evacuated and backfilled with CO_2 three times. To this Schlenk tube were added octane (0.50 mL, 1.0 M), 1-phenyl-1-butyne (**1f**) (88 μL, 0.50 mmol) and

$PhMe_2Si$–B(pin) (160 μL, 0.59 mmol) in this order. The system was closed, and then the mixture was allowed to stir at 100 °C for 16 h. After cooling to room temperature, the mixture was diluted with acetone (9.5 mL), and tetradecane (50 μL) was added as an internal standard. The mixture was filtered through a pad of Celite, analyzed by GC to determine the total yield and a ratio of **2f** and **2f′**. Then all volatiles were removed under reduced pressure. The residue was purified by column chromatography (eluent: hexane/EtOAc = 20:1 to 10:1). **2f** (91 mg, 70%) and **2f′** (14 mg, 11%) were obtained as white solids.

Procedure for eq 1-1

To a dried Schlenk tube was added sodium *tert*-butoxide (5.8 mg, 60 μmol). The Schlenk tube was evacuated and again dried with heating. $[(PCy_3)CuCl]_2$ (9.5 mg, 12.5 μmol) was added to the Schlenk tube, then the tube was evacuated and backfilled with CO_2 three times. To this Schlenk tube were added octane (0.50 mL), 1-phenyl-1-propyne (**1a**) (62 μL, 0.50 mmol) and Et_3Si–B(pin) (165 μL, 0.61 mmol) in this order. The system was closed, and then the mixture was allowed to stir at 100 °C for 16 h in the dark. After cooling to room temperature, the reaction mixture was quenched with aqueous HCl (1 N, 5 mL) and then extracted with CH_2Cl_2 (5 mL × 5). The combined organic layer was dried over $MgSO_4$, filtered, and evaporated to dryness. The residue was further purified by column chromatography (eluent: hexane/EtOAc = 10:1) to give the mixture of (*E*)-3-triethylsilyl-2-phenyl-2-butenoic acid (**3a-Et**) and (*E*)-3-triethylsilyl-3-phenyl-2-methyl-2-propenoic acid (**3a-Et′**) (88 mg, 64%) as a colorless oil. ^{1}H NMR analysis indicated that the product contained **3a-Et′** in the ratio of 96:4.



^{1}H NMR (400 MHz, $CDCl_3$) δ: 11.38 (brs, 1H), 7.39–7.34 (m, 2H), 7.32–7.27 (m, 1H), 7.16–7.13 (m, 2H), 1.74 (s, 3H), 0.97 (t, J = 7.9 Hz, 9H), 0.78 (q, J = 7.9 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 173.6, 153.0, 143.2, 138.3, 129.2, 128.2, 127.3, 22.4, 7.8, 3.8. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: 4.3. **IR** (neat): 1685.5 cm^{-1}. **EI-MS**: *m*/*z* 247 (100%, $[M–Et]^+$). **ESI-HRMS** (*m*/*z*): $[M–H]^–$ calcd for $C_{16}H_{23}O_2Si$, 275.1473; found, 275.1480.

Procedure for Scheme 1-3a

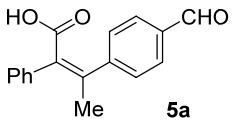
To a dried Schlenk tube was added sodium *tert*-butoxide (5.8 mg, 60 μmol). The Schlenk tube was evacuated and again dried with heating. $[(PCy_3)CuCl]_2$ (9.5 mg, 12.5 μmol) was added to the Schlenk tube, then the tube was evacuated and backfilled with CO_2 three times. To this Schlenk tube was added octane (0.50 mL). Then the mixture was cooled with an ice bath and **4i**[19b] (220 μL, 0.50 mmol) was added to the mixture at 0 °C. The system was closed and the mixture was allowed to stir at 90 °C for 2 h. After cooling to room temperature, the mixture was diluted with Et_2O (9.5 mL) and tetradecane (50 μL) was added as an internal standard. The mixture was filtered through a pad of Celite and analyzed by GC and GC/MS.

Procedure for Scheme 1-3b

To a dried Schlenk tube was added sodium *tert*-butoxide (5.8 mg, 60 μmol). The Schlenk tube was evacuated and again dried with heating. $[(PCy_3)CuCl]_2$ (9.5 mg, 12.5 μmol) was added to the Schlenk tube, then the tube was evacuated and backfilled with CO_2 three times. To this Schlenk tube was added octane (0.50 mL). Then the mixture was cooled with an ice bath and **1i** (90 μL, 0.50 mmol) and $PhMe_2Si$–B(pin) (160 μL, 0.59 mmol) were added in this order. The system was closed, and then the mixture was allowed to stir at 90 °C for 15 min. Then the Schlenk tube was cooled with an ice bath immediately. The mixture was diluted with Et_2O (9.5 mL), and tetradecane (50 μL) was added as an internal standard. After the filtration through a pad of Celite, the mixture was analyzed by GC and GC/MS.

1-4-4. Experimental Procedure for the Hiyama Coupling (Eq. 1-2)

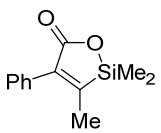
To a dried 20 mL Schlenk tube were added sodium hydroxide (24 mg, 0.60 mmol), **2a** (43.7 mg, 0.20 mmol), 4-bromobenzaldehyde (55.5 mg, 0.30 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (10.4 mg, 10 μmol) and THF (4.0 mL). The resulting mixture was stirred at 60 ºC for 6 h, and then all volatiles were removed under reduced pressure. CH_2Cl_2 (15 mL) and aqueous HCl (1 N, 10 mL) were added to the residue and the mixture was extracted with CH_2Cl_2 (5 mL × 5). The combined organic layer was dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure, and the residue was purified by column chromatography (eluent: CH_2Cl_2 + 3% MeOH + 0.5% AcOH) to give (*E*)-3-(4-formylphenyl)-2-phenyl-2-butenoic acid (**5a**) (40.5 mg, 76%) as a white solid. **m.p.** 154–156 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 10.01 (s, 1H), 7.85 (d, J = 8.6 Hz, 2H), 7.44–7.40 (m, 4H), 7.38–7.33 (m, 1H), 7.32–7.29 (m, 2H), 2.00 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 191.9, 172.5, 149.2, 147.0, 136.4, 135.4, 132.2, 129.8, 129.3, 128.5, 128.0, 127.5, 23.4. **IR** (KBr): 1677.8, 1692.2 cm^{-1}. **ESI-HRMS** (m/z): $[M+H]^+$ calcd for $C_{17}H_{15}O_3$, 267.1016; found, 267.1015.



5a

1-4-5. Characterization of the Silacarboxylation Products

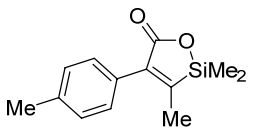
2,2,3-Trimethyl-4-phenyl-2,5-dihyro-1,2-oxasilol-5-one (**2a**)



Isolated by filtration and washing with hexane. White solid (86 mg, 81%): **m.p.** 154–155 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.44–7.40 (m, 2H), 7.37–7.33 (m, 1H), 7.31–7.28 (m, 2H), 2.07 (s, 3H), 0.50 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 168.5, 156.8, 144.9, 132.7, 129.5, 128.1, 128.0, 14.9, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: 23.9. **IR** (KBr): 1718.3 cm^{-1}. **EI-MS**: m/z 218 ($[M]^+$), 159 (100%, $[M–CO_2–Me]^+$). **Anal.** Calcd for $C_{12}H_{14}O_2Si$: C, 66.02; H, 6.46%. Found: C, 65.83; H, 6.33%.

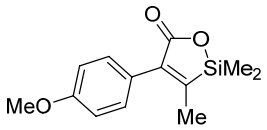
Single crystals of **2a** were obtained by recrystallization from Et_2O solution. The structure was also confirmed by X-ray crystallography.

2,2,3-Trimethyl-4-(4-methylphenyl)-2,5-dihyro-1,2-oxasilol-5-one (**2b**)



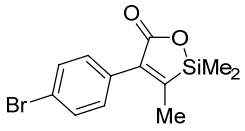
Isolated by column chromatography (eluent: hexane/EtOAc = 20:1 to 10:1). White solid (99 mg, 85%): **m.p.** 140–141 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.24–7.18 (m, 4H), 2.37 (s, 3H), 2.06 (s, 3H), 0.49 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 168.7, 156.2, 144.8, 138.0, 129.8, 129.4, 128.8, 21.3, 14.9, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: 23.7. **IR** (KBr): 1715.4 cm^{-1}. **EI-MS**: *m*/*z* 232 (23%, $[M]^+$), 188 (13%, $[M–CO_2]^+$), 173 (100%, $[M–CO_2–Me]^+$). **Anal.** Calcd for $C_{13}H_{16}O_2Si$: C, 67.20; H, 6.94%. Found: C, 67.48; H, 7.01%.

4-(4-Methoxylphenyl)-2,2,3-trimethyl-2,5-dihyro-1,2-oxasilol-5-one (**2c**)



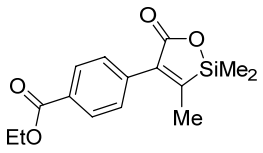
Isolated by column chromatography (eluent: hexane/EtOAc = 10:1). White solid (106 mg, 84%): **m.p.** 111–112 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.28–7.25 (m, 2H), 6.97–6.93 (m, 2H), 3.83 (s, 3H), 2.08 (s, 3H), 0.49 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 168.9, 159.4, 155.5, 144.4, 130.9, 125.1, 113.5, 55.2, 15.0, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ:23.6. **IR** (KBr): 1714.4 cm^{-1}. **EI-MS**: *m*/*z* 248 (40%, $[M]^+$), 204 (10%, $[M–CO_2]^+$), 189 (100%, $[M–CO_2–Me]^+$). **Anal.** Calcd for $C_{13}H_{16}O_3Si$: C, 62.87; H, 6.49%. Found: C, 63.06; H, 6.40%.

4-(4-Bromophenyl)-2,2,3-trimethyl-2,5-dihyro-1,2-oxasilol-5-one (**2d**)



Isolated by column chromatography (eluent: hexane/EtOAc = 10:1 to 4:1). White solid (95 mg, 64%): **m.p.** 125–126 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.57–7.53 (m, 2H), 7.18 (dt, *J* = 8.6, 2.3 Hz, 2H), 2.06 (s, 3H), 0.50 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 168.2, 157.6, 143.8, 131.6, 131.3, 131.2, 122.4, 15.0, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ:24.2. **IR** (KBr): 1714.4 cm^{-1}. **EI-MS**: *m*/*z* 298 (27%, $[M]^+$), 296 (27%, $[M–2]^+$), 254 (29%, $[M–CO_2]^+$), 252 (29%, $[M–CO_2–2]^+$), 239 (87%, $[M–CO_2–Me]^+$), 237 (100%, $[M–CO_2–Me–2]^+$). **Anal.** Calcd for $C_{12}H_{13}BrO_2Si$: C, 48.49; H, 4.41%. Found: C, 48.37; H, 4.53%.

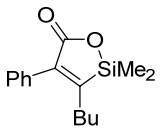
4-(4-Ethoxycarbonylphenyl)-2,2,3-trimethyl-2,5-dihyro-1,2-oxasilol-5-one (**2e**)



Isolated by column chromatography (eluent: hexane/EtOAc = 10:1 to 4:1). White solid (116 mg, 80%): **m.p.** 97–98 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.10 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 4.40 (q, *J* = 7.2 Hz, 2H), 2.08 (s, 3H), 1.40 (t, *J* = 7.2 Hz, 3H), 0.52 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 168.1, 166.3, 158.4, 144.1, 137.3, 130.1, 129.5, 129.3, 61.0, 15.0, 14.3, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ:24.3. **IR** (KBr): 1717.3 cm^{-1}. **EI-MS**: *m*/*z* 290 (45%, $[M]^+$), 246 (59%, $[M–CO_2]^+$), 245 (100%, $[M–OEt]^+$), 231 (68%, $[M–CO_2–Me]^+$). **Anal.** Calcd

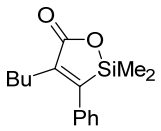
for $C_{15}H_{18}O_4Si$: C, 62.04; H, 6.25%. Found: C, 62.28; H, 6.44%.

3-Butyl-2,2-dimethyl-4-phenyl-2,5-dihyro-1,2-oxasilol-5-one (**2f**)



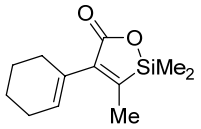
Isolated by column chromatography (eluent: hexane/EtOAc = 20:1 to 10:1). White solid (91 mg, 70%): **m.p.** 59–61 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.43–7.38 (m, 2H), 7.37–7.32 (m, 1H), 7.27–7.24 (m, 2H), 2.50–2.46 (m, 2H), 1.51–1.43 (m, 2H), 1.36–1.26 (m, 2H), 0.87 (t, J = 7.2 Hz, 3H), 0.53 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 168.7, 162.0, 144.5, 133.2, 133.0, 129.3, 128.0, 31.8, 30.0, 22.8, 13.7, –1.7. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: 24.2. **IR** (KBr): 1719.2 cm^{-1}. **EI-MS**: *m*/*z* 261 (22%), 260 (100%, $[M]^+$), 231 (94%, $[M–Et]^+$), 201 (73%, $[M–CO_2–Me]^+$), 174 (49%), 159 (87%, $[M–CO_2–Bu]^+$). **ESI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{16}H_{20}O_2Si$, 261.1305; found, 261.1304.

4-Butyl-2,2-dimethyl-3-phenyl-2,5-dihyro-1,2-oxasilol-5-one (**2f′**)



Isolated by column chromatography (eluent: hexane/EtOAc = 20:1 to 10:1). White solid (14 mg, 11 %): **m.p.** 88–90 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.45–7.41 (m, 2H), 7.36–7.32 (m, 1H), 7.18–7.15 (m, 2H), 2.48–2.44 (m, 2H), 1.56–1.48 (m, 2H), 1.35–1.28 (m, 2H), 0.85 (t, J = 7.5 Hz, 3H), 0.50 (s, 6H) **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 169.7, 156.4, 146.4, 136.4, 128.9, 127.9, 127.1, 31.0, 27.0, 22.8, 13.7, –2.1. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: 22.5. **IR** (KBr): 1731.8 cm^{-1}. **EI-MS**: *m*/*z* 260 (35%, $[M]^+$), 259 (39%, $[M–1]^+$), 245 (3%, $[M–Me]^+$), 231 (17%, $[M–Et]^+$), 218 (30%), 217 (27%), 201 (5%, $[M–CO_2–Me]^+$), 187 (8%), 173 (11%), 159 (34%, $[M–CO_2–Bu]^+$). **Anal.** Calcd for $C_{15}H_{20}O_2Si$: C, 69.19; H, 7.74%. Found: C, 68.92; H, 7.83%.

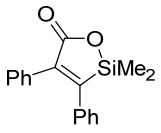
4-(1-Cyclohexenyl)-2,2,3-trimethyl-2,5-dihyro-1,2-oxasilol-5-one (**2g**)



Isolated by column chromatography (eluent: hexane/EtOAc = 20:1 to 10:1). White solid (84 mg, 76%): **m.p.** 127–131 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.55–5.53 (m, 1H), 2.18–2.13 (m, 4H), 1.99 (s, 3H), 1.74–1.63 (m, 4H), 0.42 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 168.5, 154.7, 148.3, 131.6, 129.0, 27.7, 25.2, 22.5, 21.9, 14.5, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: 23.8. **IR** (KBr): 2926.5, 1716.3 cm^{-1}. **EI-MS**: *m*/*z* 222 (83%, $[M]^+$), 181 (27%), 179 (22%), 163 (67%, $[M–CO_2–Me]^+$), 97 (100%, $[M–CO_2–(1\text{-cyclohexenyl})]^+$). **Anal.** Calcd for $C_{12}H_{18}O_2Si$: C, 64.82; H, 8.16%. Found: C, 64.75; H, 7.90%.

2,2-Dimethyl-3,4-diphenyl-2,5-dihyro-1,2-oxasilol-5-one (**2h**)

Isolated by column chromatography (eluent: CH_2Cl_2). White solid (108 mg, 77%): **m.p.** 191–192 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.32–7.29 (m, 3H), 7.28–7.24 (m, 5H), 7.06–7.03 (m, 2H), 0.62 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 168.7, 157.2, 143.1, 135.5, 133.4, 129.8, 128.8,



128.6, 128.4, 128.3, –1.8. Two resonances of phenyl ring were overlapped. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: 23.0. **IR** (KBr): 1731.8 cm^{-1}. **EI-MS**: *m*/*z* 280 (33%, $[M]^+$), 279 (18%), 236 (9%, $[M–CO_2]^+$), 221 (100%, $[M–CO_2–Me]^+$). **Anal.** Calcd for $C_{17}H_{16}O_2Si$: C, 72.82; H, 5.75%. Found: C, 72.62; H, 5.67%.

Single crystals of **2h** were obtained by recrystallization from CH_2Cl_2/Et_2O. The structure was also confirmed by X-ray crystallography (Figure 1-2).

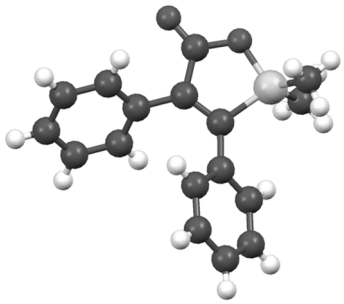
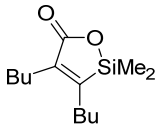


Figure 1-2. Crystal structure of **2h**.

3,4-Dibutyl-2,2-dimethyl-2,5-dihyro-1,2-oxasilol-5-one (**2i**)



Isolated by column chromatography (eluent: hexane to hexane/EtOAc = 40:1 to 20:1). Colorless oil (97 mg, 81%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 2.42 (t, *J* = 7.7 Hz, 2H), 2.36 (t, *J* = 7.5 Hz, 2H), 1.50–1.29 (m, 8H), 0.95 (t, J = 7.2 Hz, 3H), 0.92 (t, *J* = 7.0 Hz, 3H), 0.42 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 169.6, 159.3, 145.6, 31.6, 30.8, 29.1, 26.1, 22.9, 22.6, 13.8, 13.7, –1.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: 23.3. **IR** (neat): 2957.3, 2930.3, 2860.9, 1736.6 cm^{-1}. **EI-MS**: *m*/*z* 240 (33%, $[M]^+$), 211 (100%, $[M–Et]^+$), 197 (35%, $[M–C_3H_7]^+$). **Anal.** Calcd for $C_{13}H_{24}O_2Si$: C, 64.95; H, 10.06%. Found: C, 64.67; H, 9.78%.

1-4-6. X-Ray Diffraction Studies of 2a and 2h

Data were collected on a Rigaku/Saturn70 CCD diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.71070 Å) at 153 K, and processed using CrystalClear (Rigaku). The structure was solved by direct methods (SIR97) and refined by full-matrix least-square refinement on F^2. The non-hydrogen atoms were refined anisotropically. All hydrogen atoms were located on the calculated positions and not refined. All calculations were performed using the CrystalStructure crystallographic software package.

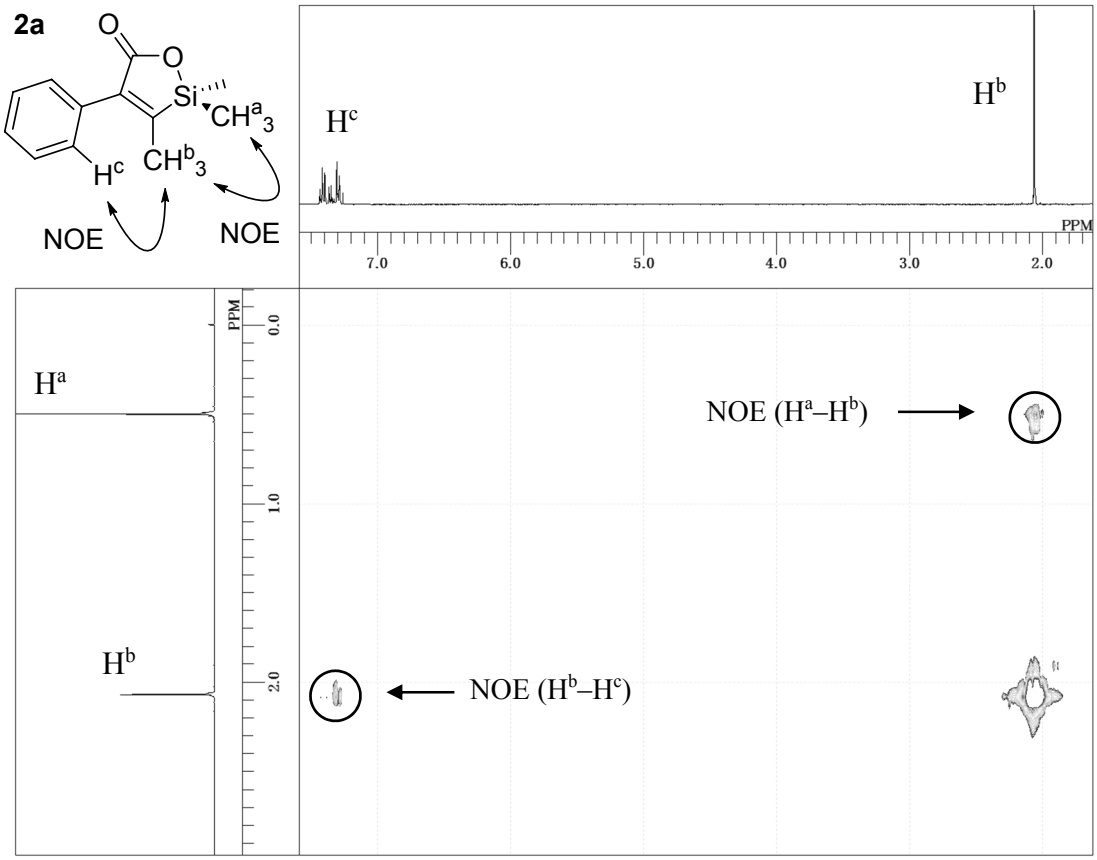
Crystal data for **2a**: $C_{12}H_{14}OSi$, M = 218.33, monoclinic, space group = $C2/c$ (#15), a = 20.544(15) Å, b = 7.027(4) Å, c = 118.474(13) Å, β = 119.378(9)°, V = 2324(3) $Å^3$, Z = 8, density (calc.) = 1.248, unique reflections = 2495 (R_{int} = 0.065), GOF = 1.012. The final $R1$ factor was 0.0713

($I>2\sigma(I)$) ($wR2$ = 0.1759, all data).

Crystal data for **2h**: $C_{17}H_{16}O_2Si$, M = 280.40, monoclinic, space group = $P2_1/n$ (#14), a = 9.996(3) Å, b = 15.381(4) Å, c = 9.880(3) Å, β = 106.586(5)°, V = 1455.9(7) Å^3, Z = 4, density (calc.) = 1.279, unique reflections = 3172 (R_{int} = 0.047), GOF = 1.044. The final $R1$ factor was 0.0359 ($I>2\sigma(I)$) ($wR2$ = 0.0774, all data).

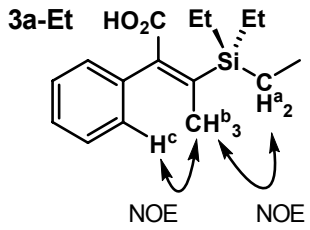
1-4-7. NMR Charts

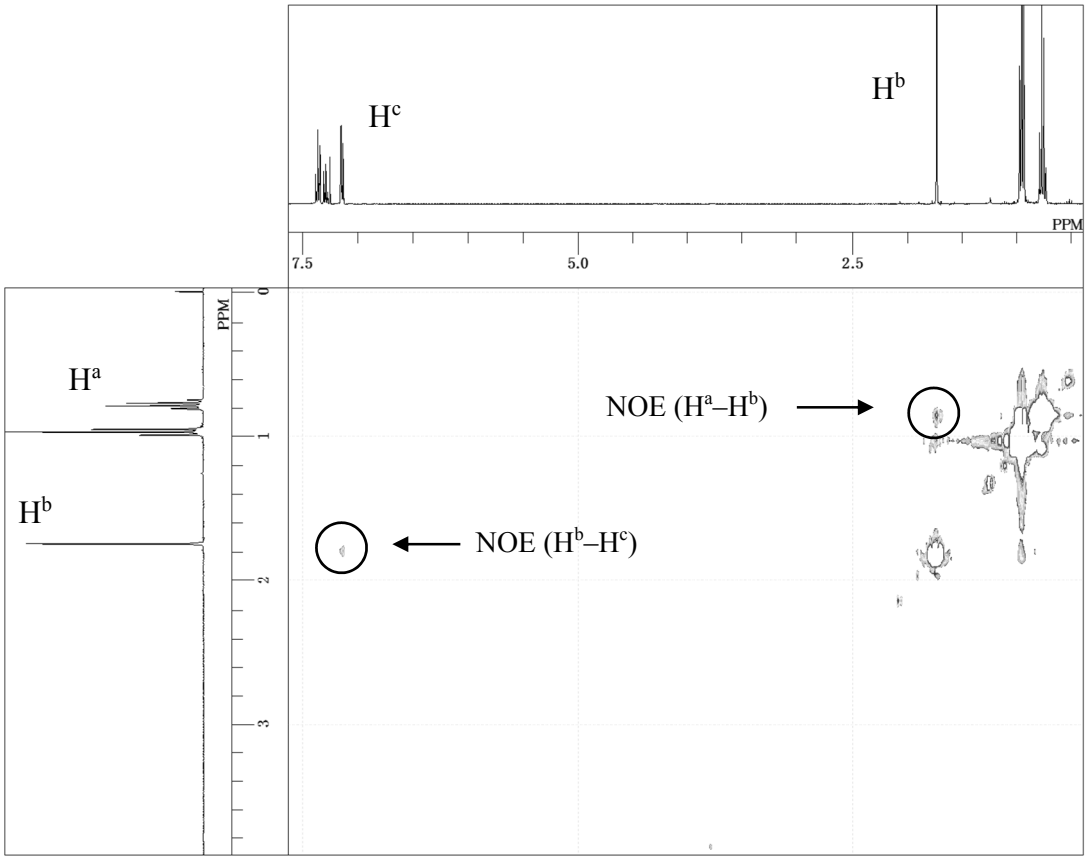
NOESY spectrum of **2a**



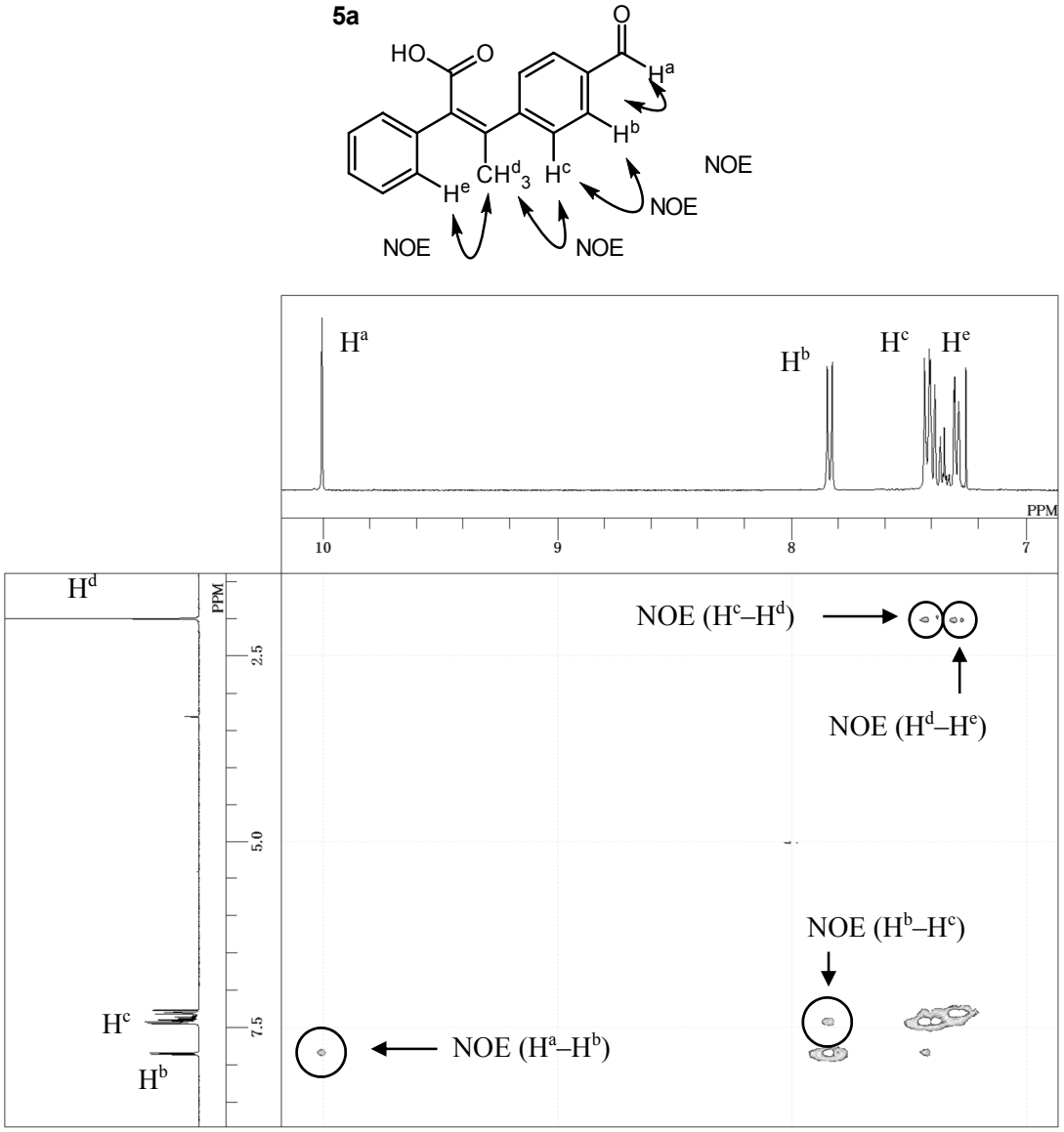
The structures of the other silalactones (**2b**–**2g** and **2f′**) were also confirmed in the same manner.

NOESY spectrum of **3a-Et**





NOESY spectrum of **5a**



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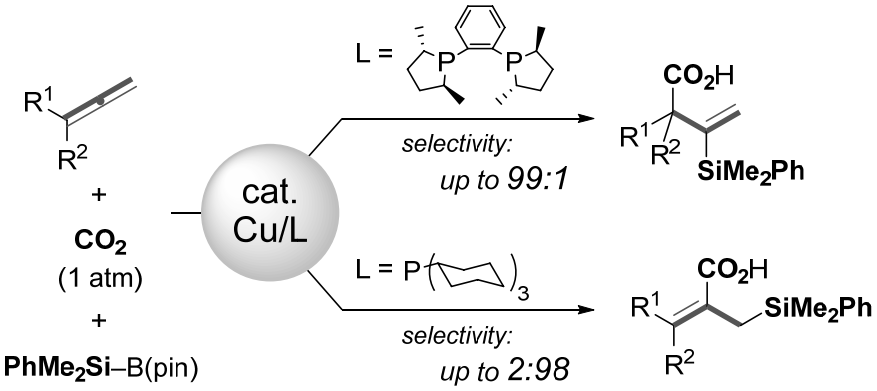
Chapter 2

Copper-Catalyzed Regiodivergent Silacarboxylation of Allenes with Carbon Dioxide and a Silylborane

A regiodivergent silacarboxylation of allenes under a CO_2 atmosphere with $PhMe_2Si$–B(pin) as a silicon source in the presence of a copper catalyst at 70 °C has been developed. The regioselectivity of the reaction is successfully reversed by the proper choice of ligand; carboxylated vinylsilanes are obtained with *rac*-Me-DuPhos as the ligand, whereas the use of PCy_3 affords carboxylated allylsilanes. Thus, two different carboxylated silanes can be selectively and regiodivergently synthesized from a single allene substrate.



2-1. Introduction

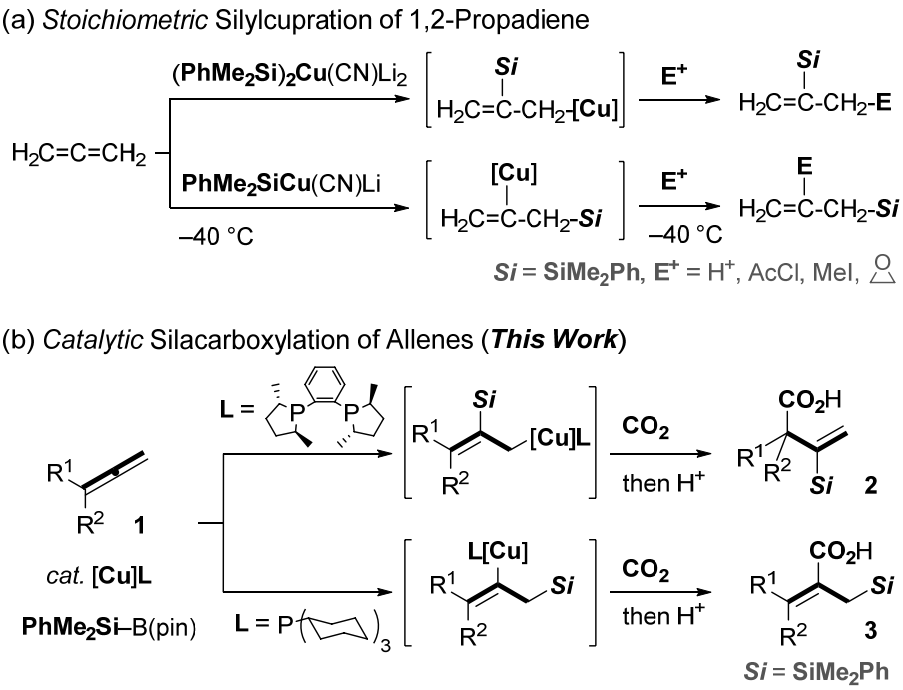
Silylcupration across carbon–carbon multiple bonds[1] is a reliable and powerful process that forms both C–Si and C–Cu bonds, with the latter amenable to further *in situ* C–C bond-forming events. Conventionally, a stoichiometric amount of a silylcuprate such as $(PhMe_2Si)_2Cu(CN)Li_2$ is used in the reaction.[1a-1e] Catalytic silylcuprations employing a silylborane[2] as a silicon source have been postulated in the Cu-catalyzed hydrosilylations of alkynes[1f-1i] and allenes.[1j,1k] However, utilization of the resulting C–Cu bonds in subsequent C–C bond formation has remained mostly unexplored.[1k,1l]

Among unsaturated substrates for silylcupration, allene derivatives are very versatile reaction partners. Addition reactions across allenes often provide many regio- and stereoisomers. Control of the selectivity is challenging, but once it is achieved, a structurally diverse array of the products become accessible.[3] Regioselective silylcuprations of allenes provide vinyl-[4] or allylsilanes,[4a,4d,5] which play indispensable roles in organic synthesis. If a *regiodivergent*[6] allene silylcupration followed by functionalization of the resulting Cu–C moiety could be realized, both the functionalized vinyl- and allylsilanes could be obtained selectively from a single substrate. Pioneering studies by Fleming and Pulido showed that the silylcupration of 1,2-propadiene ($CH_2=C=CH_2$: *unsubstituted* allene) with a stoichiometric amount of a silylcyanocuprate proceeded in a *regiodivergent* manner (Scheme 2-1a).[7] The higher-order silylcyanocuprate afforded vinylsilanes (Scheme 2-1a, top),[7a-7c] whereas the lower-order analogue provided allylsilanes (Scheme 2-1a, bottom).[7d,7e] Unfortunately, substituents on the 1,2-propadiene considerably disturbed the regioselectivity, and thus, the regiodivergence appeared only with $CH_2=C=CH_2$.[7a-7e] Furthermore, the reaction temperature also significantly affected the regiodivergence.[7d,7e]

During studies on catalytic C–C bond-forming reactions using CO_2,[8,9] the author discovered the Cu-catalyzed silacarboxylation of alkynes with a silylborane as described in Chapter 1.[9c] The reaction is highly regioselective but could not be made regiodivergent at all. Among the catalytic carboxylations of allenes using CO_2,[10] there are only two precedents of selective reaction.[11] Mori and Sato reported the selective Ni-catalyzed carboxylation of trimethylsilylallenes.[11a] Iwasawa demonstrated the hydrocarboxylation

of allenes in the presence of a Pd catalyst bearing a PSiP-pincer ligand.[11b] These reactions proceeded with good selectivity, but only one particular regioisomer was afforded. Herein, the author reports a *regiodivergent* silacarboxylation of allenes with CO_2 in the presence of a copper catalyst. The regioselectivity can be highly controlled and even reversed by the proper choice of ligand; both carboxylated vinylsilanes (**2**) and allylsilanes (**3**) can be synthesized regiodivergently from a single substrate (Scheme 2-1b). Notably, there are no reported precedents for the silacarboxylation of allenes or the regiodivergent carboxylation.[12a,b]

Scheme 2-1. Regiodivergent Silylcupration of Allenes



2-2. Results and Discussion

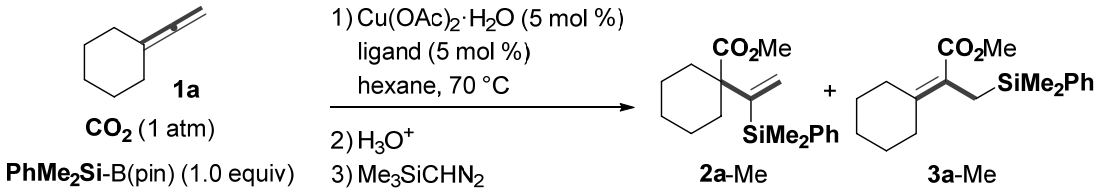
Initially, the author examined the reaction of 1,1-pentamethyleneallene (**1a**) and $PhMe_2Si$–B(pin) under CO_2 (1 atm, closed) with 5 mol % of $Cu(OAc)_2 \cdot H_2O$ and 5 mol % of a ligand at 70 °C (Table 2-1). The carboxylated vinylsilane (**2a**) and allylsilane (**3a**) were obtained, and their yields were determined by GC after conversion to the corresponding methyl esters (**2a**-Me and **3a**-Me) with Me_3SiCHN_2. The nature of the ligands successfully controlled the regioselectivity. The vinylsilane (**2a**) was

regioselectively obtained with *rac*-Me-DuPhos[13] in 72% yield with 93% regioselectivity (i.e., isomeric ratio of **2a**-Me/**3a**-Me; entry 1). When the author used Cu(OAc) as a catalyst precursor, the yield was slightly decreased to 58%, while the regioselectivity remained high (91%, entry 2). Another chelating ligand, dppBz, produced **2a** in good yield (75%), but with slightly decreased regioselectivity (83%, entry 3). Dcpe was not effective at all in terms of yield and regioselectivity (entry 4). In contrast, when the monodentate phosphine PPh_3 was employed as the ligand, the regioselectivity was switched, giving the allylsilane **3a** as the major product (**2a**-Me/**3a**-Me = 16/84), albeit in 24% yield (entry 5). Gratifyingly, tricyclohexylphosphine (PCy_3) as the ligand increased the yield to 64% while maintaining 85% regioselectivity (entry 6). Finally, both the yield and the regioselectivity were significantly improved to 90% and 98%, respectively, with THF as the solvent and a mixture of CuCl/NaOAc as the Cu precursor (entry 8). A use of 10 mol % of PCy_3 decreased both the yield and regioselectivity, suggesting the importance of a vacant coordination site on copper (entry 9). These results clearly indicate that regiodivergent silacarboxylation can be realized simply by tuning the catalyst system with the proper ligand.

After this optimization, regioselective syntheses of carboxylated vinylsilanes **2** were performed using the same catalyst system as in Table 2-1, entry 1, and employing *rac*-Me-DuPhos as the ligand (Conditions A; Table 2-2, left column). From 1,1-disubstituted allenes (**1a–h**), the corresponding vinylsilanes (**2a**–**h**) were afforded regioselectively (**2**/**3** > 95/5) in good yields after silica-gel column chromatography. Functionalities such as ketal (**2b**),[14] alkenyl (**2e**), bromo (**2f**) and ester (**2g**) groups were tolerated during the catalytic reaction. For monosubstituted allenes (**1i**–**l**), the regioselectivity was perfect giving vinylsilanes **2i–l** exclusively in good to high yields.

The regioselectivity switch observed for **1a** in Table 2-1 (entry 1 vs. 8) was quite general for 1,1-disubstituted allenes (**1a**–**h**) using the same catalyst system as in Table 2-1, entry 8 with PCy_3 as the ligand (Conditions B; Table 2-2, right column). The reactions now provided the corresponding allylsilanes (**3a**–**h**) with excellent regioselectivities (**3**/**2** > 98/2, except for **3f**/**2f** = 93/7). Unsymmetrically substituted allenes such as **1c–h** may afford *E*/*Z* mixtures. The present catalyst system distinguished even subtle differences

Table 2-1. Effect of the Ligand on Cu-Catalyzed Silacarboxylation of 1,1-Pentamethyleneallene (**1a**)[a]



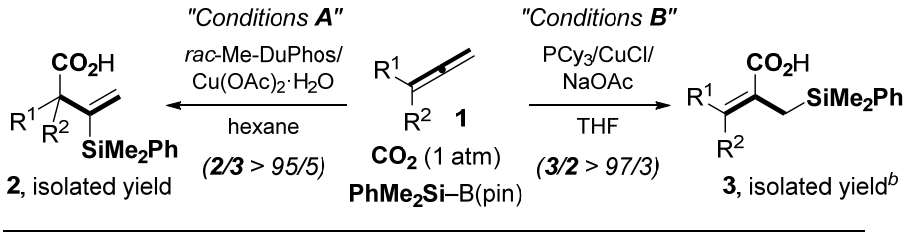
entry	ligand	yield (%)[b]	**2a**-Me/**3a**-Me[c]
1	*rac*-Me-DuPhos	72	93/7
2	*rac*-Me-DuPhos	58	91/9
3	dppBz	75	83/17
4	dcpe	15	50/50
5	PPh_3	24	16/84
6	PCy_3	64	15/85
7	PCy_3	70	6/94
8	PCy_3	90	2/98
9	PCy_3 (10 mol %)	59	11/89

[a]Reaction conditions: **1a** (0.20 mmol), $PhMe_2Si$–B(pin) (1.0 equiv), ligand (5 mol %) and $Cu(OAc)_2·H_2O$ (5 mol %) in hexane (0.40 M) under CO_2 (1 atm, closed) at 70 °C for 16–18 h. [b]Combined yield of **2a**-Me and **3a**-Me determined by GC analysis after esterification using Me_3SiCHN_2. [c]Determined by GC analysis. [d]CuOAc (5 mol %) was used instead of $Cu(OAc)_2·H_2O$. [e]In THF. [f]5 mol % of CuCl and 15 mol % of NaOAc were used instead of $Cu(OAc)_2·H_2O$.

such as between the methyl and the primary alkyl substituents of **1c–g**, affording (*Z*)-isomers preferentially (*Z*/*E* > 80/20) in the crude mixtures. The *Z*/*E* ratios of **3h** was much higher (95/5). Gratifyingly, (*Z*)-**3c–h** were easily isolated by silica-gel column chromatography in good yields with high (*Z*) ratios (*Z*/*E* > 96/4). The structure of (*Z*)-**3h** was further confirmed by X-ray crystallography (Figure 2-1 in the section 2-4). Under Conditions B, ketal (**3b**),[14] alkenyl (**3e**), bromo (**3f**) and ester (**3g**) groups remained intact.[15] The monosubstituted allene bearing a tertiary alkyl substituent (**1i**) afforded the corresponding (*Z*)-allylsilane, (*Z*)-**3i**, with 97% regioselectivity in 92% yield. However, **1j** bearing a secondary alkyl substituent gave (*Z*)-**3j** only preferentially: (*Z*)-**3j**/**2j** = 68/32 in 73% total yield. Furthermore, allenes having a primary alkyl-substituent (**1k** and **1l**)

afforded the two regioisomers in low selectivities: (*Z*)-**3k**/**2k** = 48/52 in 72% total yield and (*Z*)-**3l**/**2l** = 42/58 in 75% total yield. Thus, steric hindrance at the 1-position of allenes

Table 2-2. Regiodivergent Silacarboxylation of Allenes (**1**) to Carboxylated Vinylsilanes (**2**) and Allylsilanes (**3**)[a]



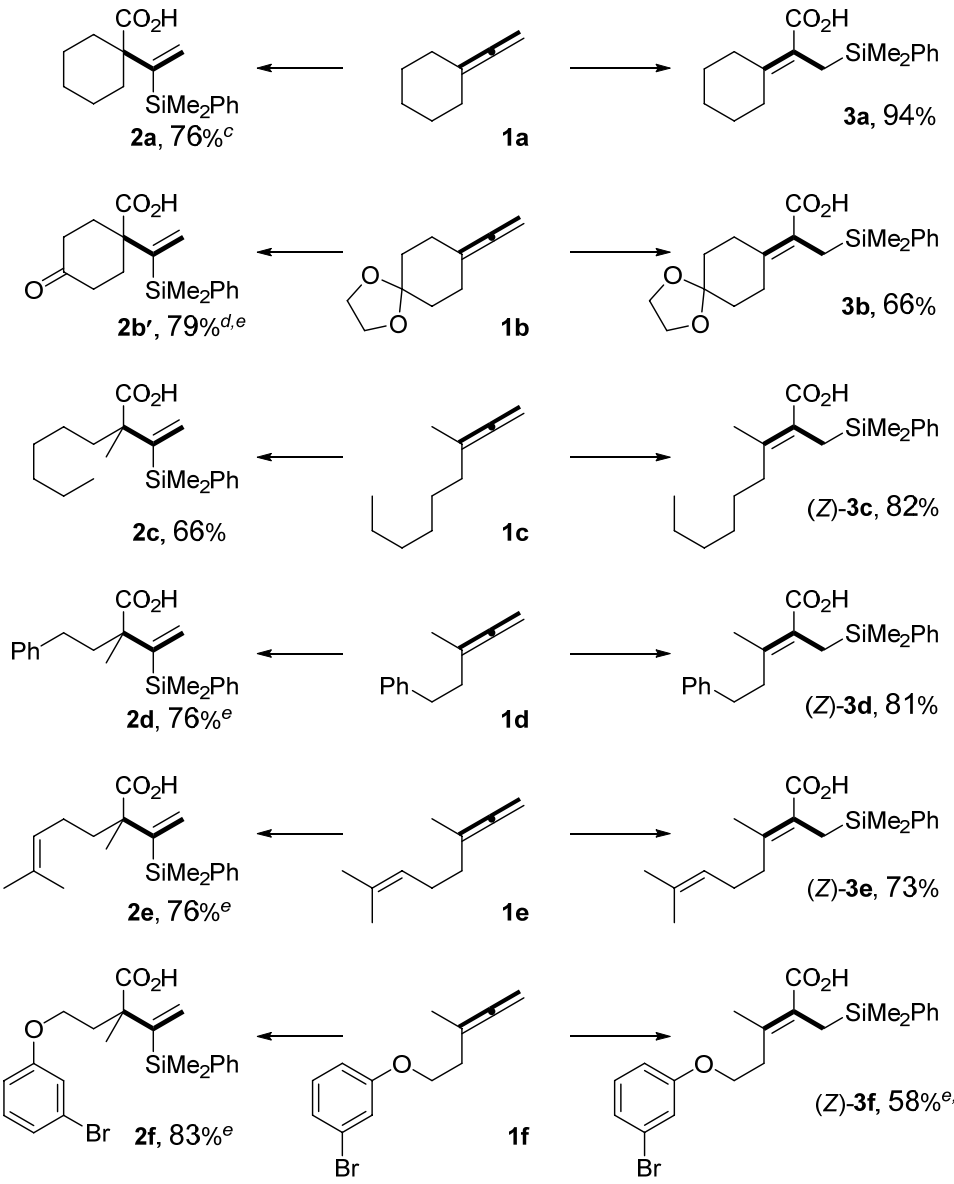
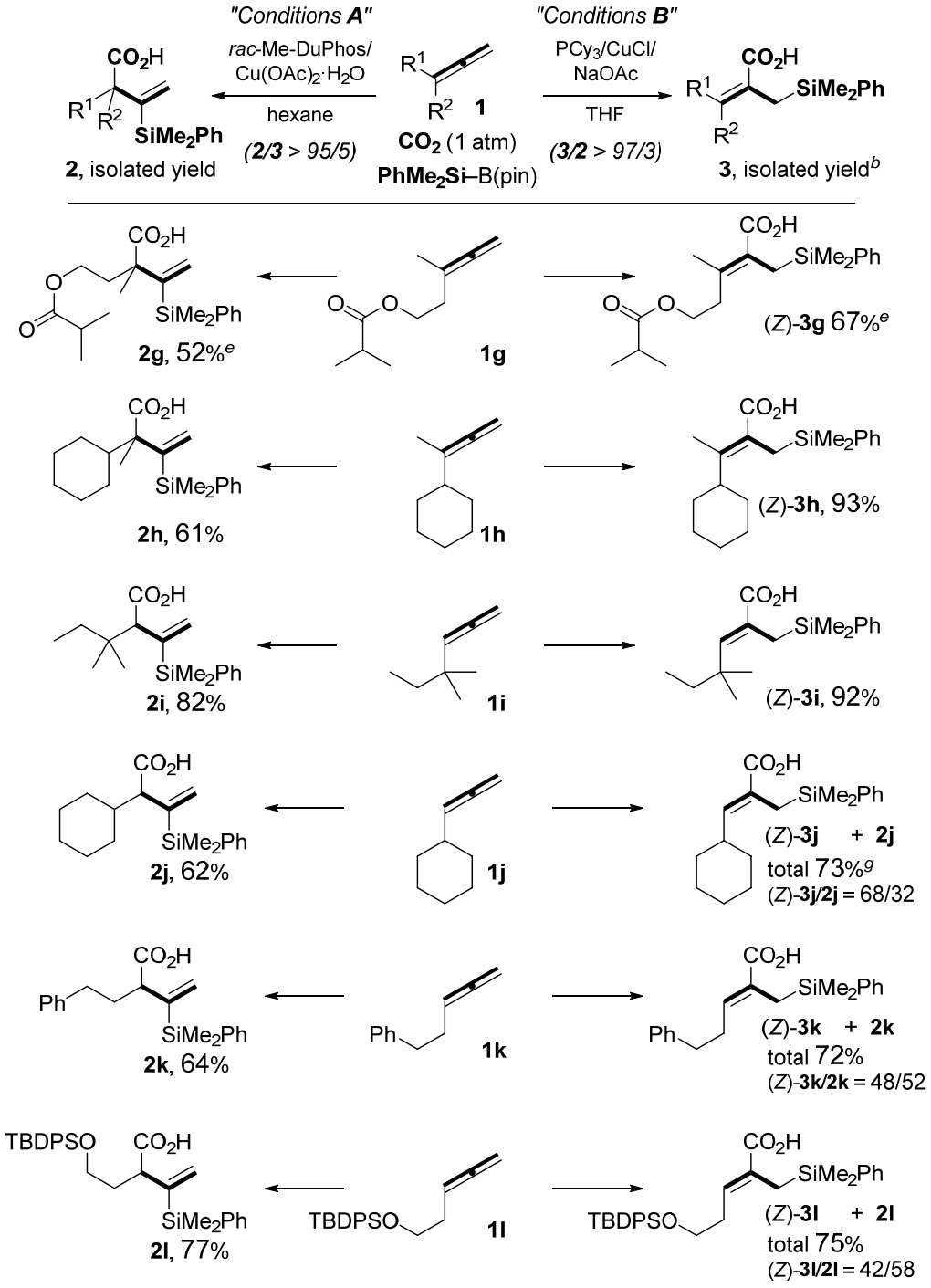


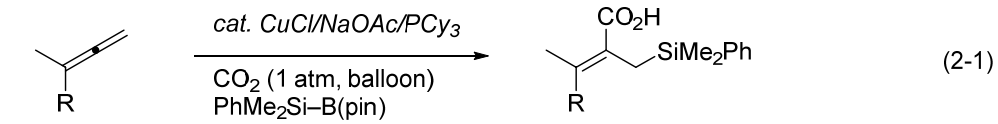
Table 2-2. Regiodivergent Silacarboxylation of Allenes (**1**) to Carboxylated Vinylsilanes (**2**) and Allylsilanes (**3**)[a] (continued)



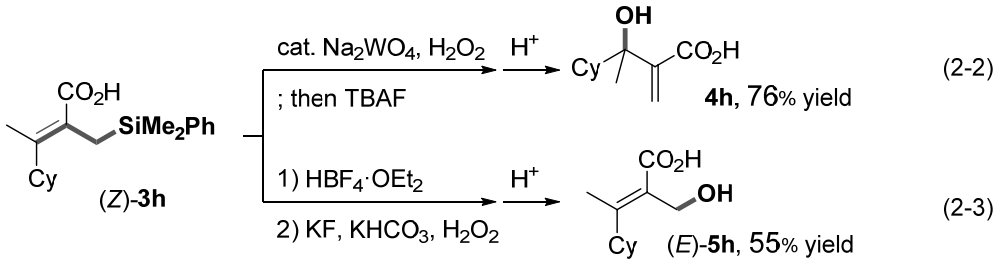
[a]Conditions **A**: *rac*-Me-DuPhos (5 mol %) and $Cu(OAc)_2 \cdot H_2O$ (5 mol %) in hexane (0.40 M). Conditions **B**: PCy_3 (5 mol %), CuCl (5 mol %), and NaOAc (15 mol %) in THF (0.40 M). Under both conditions, **1** (0.20 mmol) and $PhMe_2Si$–B(pin) (1.1 equiv) were reacted under CO_2 (1 atm, closed) at 70 °C for 16–18 h. [b]*Z*/*E* > 96/4 if any. [c]**2a**/**3a** = 93/7. [d]Isolated after acidic work-up.[14] [e]$PhMe_2Si$–B(pin) (1.5 equiv). [f](*Z*)-**3f**/(*E*)-**3f**/**2f** = 90/3/7. [g]PCy_2(*o*-tol) was used instead of PCy_3.

is essential to provide **3** regioselectively. Unfortunately, the reactions using 1-methyl-1-phenylallene, 1-*tert*-butyl-3-(*p*-tolyl)allene, and 1,3-dimethyl-1-(2-phenethyl)-allene were not regiodivergent.

The preparation of **3** could be carried out on gram scale: 1.19 g of (*Z*)-**3c** and 1.05 g of (*Z*)-**3h** were synthesized from **1c** (0.691 g, 5.0 mmol) and **1h** (0.548 g, 4.0 mmol), respectively (eq 2-1). γ-Oxidation of (*Z*)-**3h** through an epoxidation/desilylative ring-opening cascade[16] furnished the tertiary allylic alcohol **4h** in 76% isolated yield (eq 2-2). On the other hand, α-oxidation using the Tamao-Fleming protocol[17] gave primary allylic alcohol (*E*)-**5h** in 55% yield with retention of the olefin configuration (eq 2-3). Usually, the α-oxidation of allylic phenylsilanes by the Tamao-Fleming protocol is unreliable, since allylic C–Si bonds are preferentially cleaved over Ph–Si bonds in the first step.[18] The α-oxidation of **3h** proceeded smoothly, possibly owing to a deactivation of the allylic moiety by conjugation with the carboxylic acid functionality.[18b] Thus, the regiodivergent oxidations (eqs 2-2 and 2-3) and the regiodivergent silacarboxylation (Scheme 2-1b) can provide a wide range of products (**2**, **3**, **4**, and **5**) from a single allene substrate (**1**).



(2-1)



(2-2)

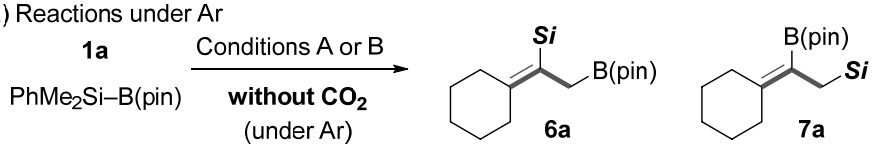
(2-3)

To gain insight into the reaction mechanism, several control experiments were carried out (Scheme 2-2). When the reactions were run in the absence of CO_2 (i.e., under Ar), using the same Conditions A or B as in Table 2-2, the reactions were less clean: the $PhMe_2Si$–B(pin) adducts with **1a** (**6a** and **7a**) were obtained in 25% and 63% yield,

respectively, with different regioselectivities (Scheme 2-2a). Conditions A led to the formation of **6a** with excellent regioselectivity (**6a**/**7a** = 95/5), while Conditions B preferentially afforded **7a** (**6a**/**7a** = 21/79). Subsequent reactions with exchange of the atmosphere in the flask containing **6a** and **7a** from Ar to CO_2 did not convert most of the **6a** and **7a**, and **2a** and **3a** were not detected at all (Scheme 2-2b). These observations, therefore, clearly indicate that **2** and **3** are not generated via **6** and **7**.[19]

Scheme 2-2. Control Experiments in the Absence of CO_2

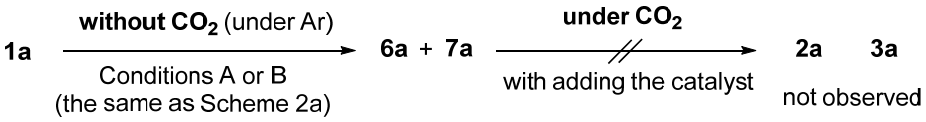
(a) Reactions under Ar



conditions	conversion of **1a**[a,b]	total yield[a,b]	**6a**/**7a**[b]
Conditions A, but without CO_2	>95%	25%	95/5
Conditions B, but without CO_2	>95%	63%	21/79

[a]By ^{1}H NMR. [b]By GC.

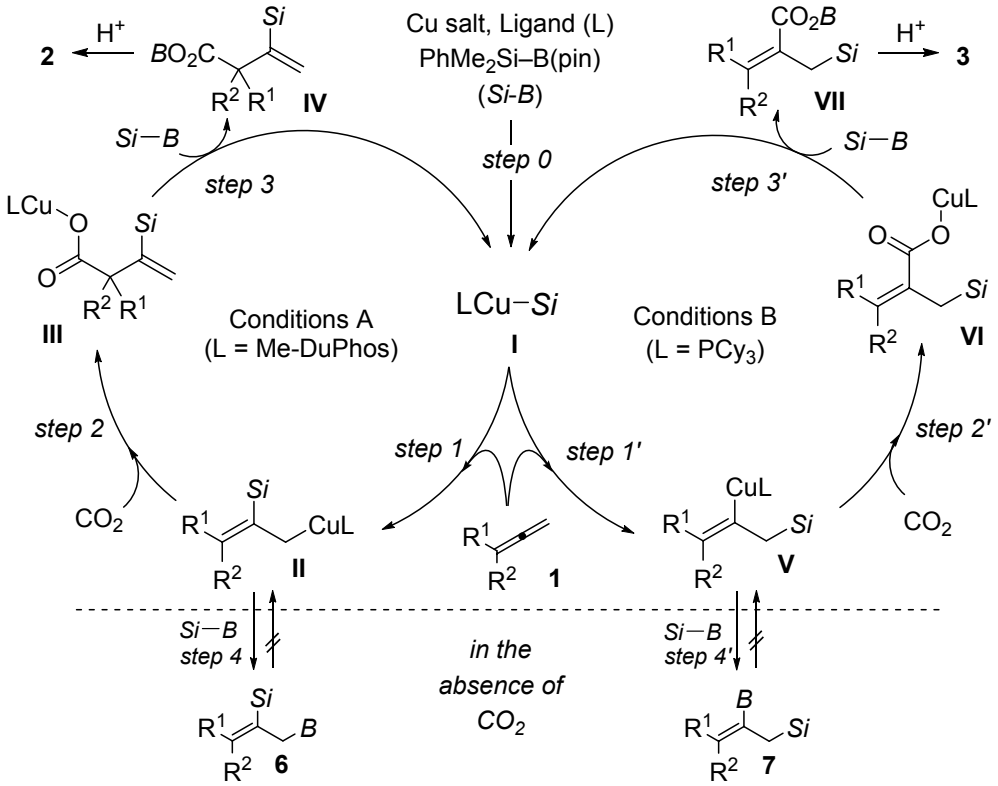
(b) Reactions of **6a** and **7a** with CO_2 in One-pot System



A possible catalytic cycle is shown in Scheme 2-3. The silylcopper species (**I**) is generated *in situ* by the reaction of $PhMe_2Si–B(pin)$ with a Cu precursor (step 0).[20] Next, **I** adds across a terminal double bond of the allene **1** (step 1). Under Conditions A with Me-DuPhos as the ligand, the Cu atom adds at the terminal carbon of **1**, generating allylcopper intermediate (**II**). Then, CO_2 inserts at the γ-position of **II** to provide copper carboxylate species (**III**), possibly via a six-membered ring transition state (step 2). Finally, σ-bond metathesis of **III** with $PhMe_2Si–B(pin)$ affords boron carboxylate (**IV**) and regenerates **I** (step 3). In sharp contrast, under Conditions B using PCy_3 as the ligand, the regioselectivity of the silylcupration is reversed, providing vinylcopper intermediate (**V**) (step 1'). The regioselectivity reversal in steps 1 and 1' might be attributed to the difference in relative steric bulk between the CuL (L = Me-DuPhos or PCy_3) and $SiMe_2Ph$ moieties. The insertion of CO_2 into **V** (step 2') followed by the σ-bond metathesis of **VI**

with $PhMe_2Si$–B(pin) provides boron carboxylate (**VII**) and regenerates **I** (step 3'). In the absence of CO_2, some **II** and **V** could be trapped as **6** and **7** (steps 4 and 4'), suggesting that the regiodivergency occurs at the silylcupration stage (steps 1 and 1').

Scheme 2-3. A Possible Reaction Mechanism



Preliminarily, an enantioselective silacarboxylation of **1d** was carried out with (*R,R*)-Me-DuPhos under Conditions A, and **2d** was obtained in 18% ee (unoptimized).

2-3. Conclusion

In conclusion, the author has developed a regiodivergent silacarboxylation of allenes using $PhMe_2Si$–B(pin) under a CO_2 atmosphere in the presence of a copper catalyst. The regioselectivity is highly controlled by the proper choice of ligand; both the carboxylated vinylsilanes (**2**) and allylsilanes (**3**) can be synthesized regiodivergently from a single substrate. Further studies of the reaction mechanism and optimization of the enantioselective reaction are now in progress.

2-4. Experimental Section

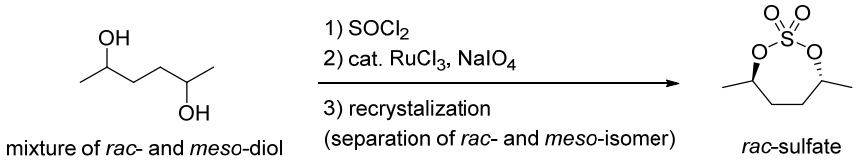
2-4-1. General Remarks

Unless otherwise noted, reactions were performed under an argon atmosphere using heat-gun-dried glassware on a dual-manifold Schlenk line. ^{1}H, ^{13}C, ^{29}Si and ^{31}P NMR spectra were recorded on a JEOL ECX-400P spectrometer or a Bruker AVANCE-500 spectrometer. Chemical shift values (δ) are reported in ppm and calibrated to tetramethylsilane (TMS, 0.00 ppm) or residual solvent (7.26 ppm in $CDCl_3$ or 7.16 ppm in C_6D_6) for ^{1}H, to $CDCl_3$ (77.0 ppm) or C_6D_6 (128.0 ppm) for ^{13}C, to tetramethylsilane (TMS, 0.00 ppm) for ^{29}Si, and to 85% H_3PO_4 (0.00 ppm) as an external standard for ^{31}P. IR spectra were recorded on a Shimadzu IRTracer-100 FT-IR Spectrometer equipped with a Shimadzu MIRacle A (Ge) Single Reflection HATR. EI-MS spectra were recorded on a Shimadzu GCMS-QP2010. High-resolution mass spectra (ESI-HRMS) were obtained with a JEOL JMX-SX 102A spectrometer. Elemental analysis was carried out at the Center for Organic Elemental Microanalysis, Graduate School of Pharmaceutical Science, Kyoto University. GC analysis was carried out using a Shimadzu GC-17A equipped with an integrator (C-R8A) with a capillary column (CBP-5, 0.25 mm i.d. × 25 m). TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck Silica gel $60F_{254}$. Column chromatography was carried out on silica-gel (Kanto N60, spherical, neutral, 63–210 μm). Medium pressure liquid chromatography (MPLC) was performed on a Biotage Isorera One with a silica-gel column (Biotage SNAP Ultra 25 g, HP-Sphere 25μm). Preparative recycling GPC was performed with a SHIMADZU LC-20AP System equipped with a Shodex K-4002.5L column, a SHIMADZU SPD-20A, and a SHIMADZU RID-10A using $CHCl_3$ as the eluent at a flow rate of 14 mL min^{-1}.

Unless otherwise noted, chemicals obtained from commercial suppliers were used without further purification. Hexane was purified by refluxing over Na/benzophenone with a small amount of tetraglyme followed by distillation under Ar. Anhydrous THF, toluene and CH_2Cl_2 were purchased from Kanto Chemical Co., Inc. and further purified by passage through activated alumina under positive argon pressure as described by Grubbs et al.[21] PPh_3 was purified by recrystallization prior to use. Allenes **1b**–**e** and **1i**–**p**, and $PhMe_2Si$–B(pin) were synthesized according to the literatures.[22,23]

2-4-2. Preparation of *rac*-Me-DuPhos[13,24]

Preparation of *rac*-sulfate (*trans*-4,7-dimethyl-1,3,2-dioxathiepane 2,2-dioxide)

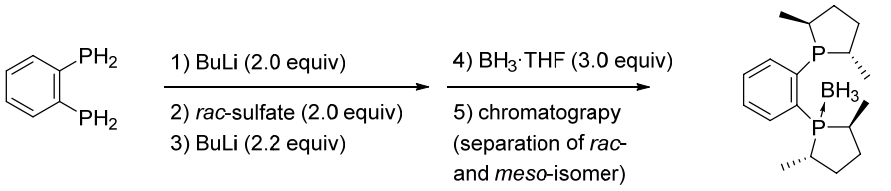


mixture of *rac*- and *meso*-diol

rac-sulfate

To a 500 mL flask containing 2,5-hexanediol (5.9 g, 50 mmol) and CH_2Cl_2 (75 mL) was added dropwise $SOCl_2$ (3.7 mL, 51 mmol) at room temperature. The solution was stirred for 1.5 h, at which point the solvent and $SOCl_2$ were removed on a rotary evaporator. To the residue, CH_2Cl_2 (35 mL), MeCN (35 mL), H_2O (70 mL) and $RuCl_3 \cdot 3H_2O$ (39 mg, 0.15 mmol) were added and the resulting mixture was cooled to 0 °C. Then, $NaIO_4$ (21 g, 100 mmol) was added in two portions. The reaction was allowed to stir at room temperature for 1.5 h and then quenched by adding 250 mL of H_2O. The mixture was extracted with Et_2O (100 mL × 3) and washed with brine (100 mL × 2). After being dried over $MgSO_4$ and filtered through a pad of silica-gel, the solution was concentrated. A colorless crystalline solid formed upon standing at –30 °C was filtered, washed with cold hexane and dried in vacuo. Thus obtained solid (2.69 g, 30%) consisted mostly of *rac*-isomer, and recrystallization from Et_2O yielded diastereomerically pure title compound (2.14 g, 24%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 4.86–4.78 (m, 2H), 2.04–1.85 (m, 4H), 1.44 (d, J = 6.3 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 81.4, 34.5, 21.6. **ESI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_6H_{12}O_4SNa$, 203.0349; found, 203.0344.

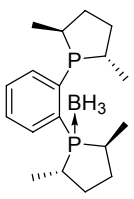
Preparation of *rac*-Me-DuPhos monoborane complex



rac-Me-DuPhos borane complex

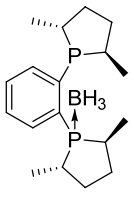
To a 300 mL 2-neck flask containing 1,2-bis(phosphino)benzene (10 wt% solution in hexane, 6.0 g, 4.27 mmol) and THF (100 mL) was added dropwise BuLi (1.6 M in hexane, 5.4 mL, 8.6 mmol) via syringe at room temperature. The yellow solution was stirred for 1 h. To the resulting mixture, *rac*-2,5-hexanediol cyclic sulfate (1.54 g, 8.55 mmol) in THF (10 mL) was added. The white cloudy mixture was stirred for 2 h. Then, BuLi (1.6 M in hexane, 5.9 mL, 9.4 mmol) was added dropwise via syringe to form opaque red solution. The reaction was allowed to stir overnight, then $BH_3 \cdot THF$ (1.0 M in THF, 12.8 mL, 12.8 mmol) was added. The grayish mixture was stirred for 2 h. The reaction was quenched by adding 1N HCl aq. (50 mL), extracted with Et_2O (50 mL × 3), washed with H_2O (50 mL) and brine (50 mL), and dried over $MgSO_4$. The solvents were evaporated and the residue was purified by silica-gel column chromatography (eluent: hexane/Et_2O = 40:1) to give *meso*- (higher R_f, 442 mg, 32%) and *rac*-Me-DuPhos monoborane complex (lower R_f, 477 mg, 35%) as white solids, respectively.

***rac*-Me-DuPhos monoborane complex**; **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.70–7.65 (m, 1H), 7.60–7.53 (m, 1H), 7.49–7.38 (m, 2H), 2.95–2.75 (m, 2H), 2.64–2.48 (m, 2H), 2.44–2.33 (m, 1H), 2.27–2.07 (m, 3H), 1.91–1.80 (m, 1H), 1.67–1.56 (m, 2H), 1.48–1.39 (m, 4H), 1.27 (dd, J = 17.9, 7.0 Hz, 3H), 0.97 (dd, J = 14.0, 7.2 Hz, 3H), 0.86 (dd, J = 9.5, 7.2 Hz, 3H). **^{13}C NMR** (125 MHz,



rac

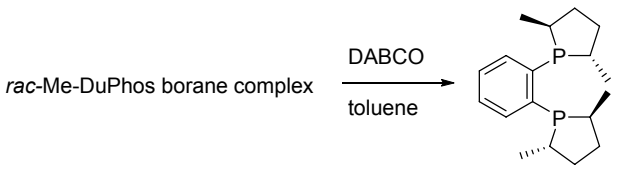
$CDCl_3$) δ: 142.8 (dd, J = 32.4, 11.4 Hz, C_{Ar}–P), 137.5 (dd, J = 43.9, 38.1 Hz, C_{Ar}–P), 135.5 (dd, J = 8.6, 2.9 Hz, $C_{Ar}H$), 132.2 (dd, J = 11.0, 8.1 Hz, $C_{Ar}H$), 129.6 (d, J = 1.9 Hz, $C_{Ar}H$), 129.0 (d, J = 8.6 Hz, $C_{Ar}H$), 38.2 (d, J = 10.5 Hz, *C*H), 37.5 (d, J = 2.9 Hz, CH_2), 36.8 (d, J = 3.8 Hz, CH_2), 35.1 (d, J = 11.4 Hz, *C*H), 33.4 (dd, J = 36.2, 10.5 Hz, *C*H), 32.1–31.9 (m, CH_2 + CH_2), 30.3 (dd, J = 35.3, 4.8 Hz, *C*H), 19.8 (d, J = 34.3 Hz, CH_3), 18.7 (dd, J = 8.1, 6.2 Hz, CH_3), 17.0 (d, J = 3.8 Hz, CH_3), 14.5 (d, J = 2.9 Hz, CH_3). **^{31}P NMR** (200 MHz, $CDCl_3$) δ: 44.5–43.3 (m), 1.4 (d, J = 21.4 Hz). **ESI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{18}H_{32}BP_2$, 321.2067; found, 321.2056. **Anal.** Calcd for $C_{18}H_{31}BP_2$: C, 67.52; H, 9.76%. Found: C, 67.32; H, 9.62%.



meso

***meso*-Me-DuPhos monoborane complex**; **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.16–8.10 (m, 1H), 7.68–7.64 (m, 1H), 7.49–7.40 (m, 2H), 2.75–2.64 (m, 1H), 2.62–2.51 (m, 1H), 2.49–2.05 (m, 6H), 1.79–1.61 (m, 2H), 1.46–1.37 (m, 1H), 1.33 (dd, J = 18.6, 6.8 Hz, 3H), 1.27 (dd, J = 16.1, 7.0 Hz, 3H), 1.05 (dd, J = 14.7, 7.0 Hz, 3H), 0.74 (dd, J = 9.5, 6.8 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 143.1 (dd, J = 33.4, 3.8 Hz, $C_{Ar}H$), 137.6 (dd, J = 18.1, 10.5 Hz, $C_{Ar}H$), 135.4 (dd, J = 7.6, 1.9 Hz, $C_{Ar}H$), 134.8 (dd, J = 38.1, 33.4 Hz, $C_{Ar}H$), 130.2 (d, J = 2.9 Hz, $C_{Ar}H$), 129.0 (d, J = 13.4 Hz, $C_{Ar}H$), 38.6 (d, J = 11.4 Hz, *C*H), 37.4 (d, J = 2.9 Hz, CH_2), 37.0 (d, J = 1.9 Hz, CH_2), 36.2 (dd, J = 34.3, 21.0 Hz, *C*H), 35.4 (d, J = 12.4 Hz, *C*H), 34.9 (dd, J = 38.1, 1.9 Hz, *C*H), 34.8 (d, J = 9.5 Hz, CH_2), 34.0 (dd, J = 10.5, 1.9 Hz, CH_2), 20.2 (d, J = 34.3 Hz, CH_3), 16.2 (d, J = 2.9 Hz, CH_3), 15.6 (dd, J = 6.7, 3.8 Hz, CH_3), 14.2 (dd, J = 3.8, 1.9 Hz, CH_3). **^{31}P NMR** (160 MHz, $CDCl_3$) δ: 47.8–46.3 (m), –1.8 (s). **ESI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{18}H_{31}BP_2Na$, 343.1886; found, 343.1875.

Preparation of *rac*-Me-DuPhos



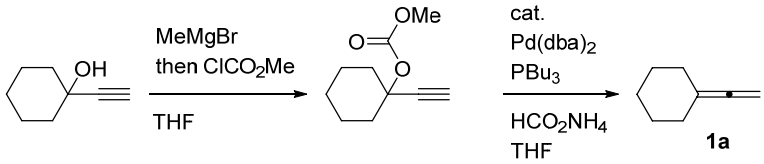
rac-Me-DuPHOS

To a 50 mL Schlenk tube, *rac*-Me-DuPhos monoborane complex (320 mg, 1.0 mmol), DABCO (123 mg, 1.1 mmol) and toluene (10 mL) were added and the mixture was stirred at 50 °C for 15 h. The mixture was cooled to room temperature and filtered through a pad of alumina (deactivated to activity III) that was packed with degassed hexane, and eluted with 150 mL of degassed hexane/Et_2O (10/1). The solution was evaporated and dried in vacuo, yielding *rac*-Me-DuPhos (276 mg, 90%) as a white solid. **^{1}H NMR** (400 MHz, C_6D_6) δ: 7.33–7.28 (m, 2H), 7.14–7.10 (m, 2H), 2.59–2.46 (m, 4H), 2.05–1.94 (m, 2H), 1.92–1.84 (m, 2H), 1.38–1.21 (m,

10H), 1.03–0.99 (m, 6H). **^{13}C NMR** (100 MHz, C_6D_6) δ: 144.4 (d, *J* = 2.9 Hz), 131.5 (t, *J* = 2.4 Hz), 127.9, 36.4, 35.8 (t, *J* = 2.4 Hz), 34.3 (t, *J* = 6.7 Hz), 32.8, 20.7 (t, *J* = 18.1 Hz), 18.7 (t, *J* = 2.9 Hz). **^{31}P NMR** (160 MHz, C_6D_6) δ: 3.3. **ESI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{18}H_{29}P_2$, 307.1739; found, 307.1727.

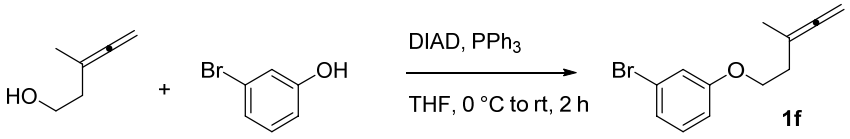
2-4-3. Preparation of substrates 1

Preparation of 1a[22a,25]



To a 300 mL 2-neck flask fitted with dropping funnel were added 1-ethynyl-1-cyclohexanol (10.0 g, 80.5 mmol) and THF (100 mL). The flask was cooled to –60 °C and MeMgBr (3.0 M in Et_2O, 27 mL, 81 mmol) was added dropwise. The mixture was stirred for 1 h while gradually warmed to –10 °C, at which point methyl chloroformate (8.2 mL, 105 mmol) was added. After stirring at room temperature for 13 h, the reaction was quenched by adding sat. NH_4Cl aq. The aqueous phase was extracted with Et_2O (30 mL × 3). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and then evaporated. The residue was filtered through a pad of silica-gel, washed with Et_2O and evaporated to give a carbonate as a yellow oil. The carbonate was mixed with ammonium formate (10 g, 161 mmol) and THF (200 mL) in a 500 mL 2-neck flask, and the flask was evacuated and backfill with Ar three times. To this mixture were added PBu_3 (2.0 mL, 8.1 mmol) and $Pd(dba)_2$ (2.3 g, 4.0 mmol) in this order. After stirring at room temperature for 13 h, the mixture was filtered through a pad of Celite, washed with Et_2O, evaporated and roughly purified by column chromatography (eluent: pentane/Et_2O). The residue was further purified by distillation to give **1a** as a clear colorless liquid (4.9 g, 56% over 2 steps). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 4.55–4.52 (app quintet, *J* = 2.3 Hz, 2H), 2.14–2.10 (m, 4H), 1.61–1.56 (m, 4H), 1.53–1.47 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 203.4, 101.2, 72.5, 31.1, 27.1, 26.1. All the resonances in ^{1}H and ^{13}C NMR spectra were in good agreement with literature values.[25]

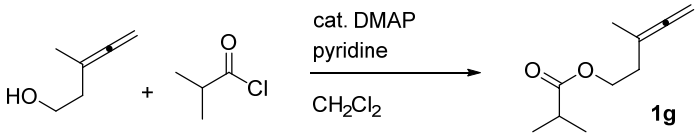
Preparation of allene 1f



To a mixture of allenol[26] (490 mg, 5.0 mmol), *m*-bromophenol (1.3 g, 7.5 mmol) and PPh_3 (2.0 g, 7.5 mmol) in THF (15 mL) was added DIAD (1.9 M in toluene, 3.2 mL, 6.1 mmol)

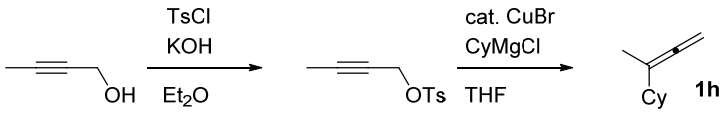
dropwise. Resulting orange solution was stirred at room temperature overnight, and then the solvents were evaporated. The residue was agitated in hexane, then the solid was filtered off and washed with hexane. The solution was evaporated and the residue was purified by MPLC to give **1f** as a clear colorless oil (984 mg, 77%) **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.12 (t, *J* = 7.9 Hz, 1H), 7.08–7.04 (m, 2H), 6.83 (d, *J* = 8.2 Hz, 1H), 4.66–4.63 (m, 2H), 4.04 (t, *J* = 6.6 Hz, 2H), 2.42–2.39 (m, 2H), 1.76 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 206.2, 159.7, 130.5, 123.7, 122.8, 117.8, 113.6, 94.9, 74.9, 66.5, 32.8, 19.1. **ESI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{12}H_{14}BrO$, 253.0223; found, 253.0219.

Preparation of allene 1g



To a 100 mL flask were added allenol (containing small amount of 2-butyn-1-ol as an impurity, 1.55 g, 15.8 mmol), pyridine (1.7 mL, 20.5 mmol), a spatula of DMAP and CH_2Cl_2 (30 mL). The mixture was cooled in an ice bath, and then isobutyryl chloride (2.0 mL, 19.0 mmol) was added dropwise. After resulting solution was stirred at room temperature for 2 h, CH_2Cl_2 (20 mL) and aq. $CuSO_4$ (20 mL) was added and the mixture was further stirred for 30 min. The organic phase was separated, washed with water (30 mL × 1), dried over $MgSO_4$, filtered and the solvents were evaporated. The residue was purified by column chromatography to give **1g** as a clear colorless oil (956 mg, 37%) **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 4.62 (app sextet, *J* = 3.1 Hz, 2H), 4.17 (t, *J* = 6.7 Hz, 2H), 2.53 (sept, *J* = 7.0 Hz, 1H), 2.28–2.25 (m, 2H), 1.72 (t, *J* = 3.2 Hz, 3H), 1.16 (d, *J* = 7.0 Hz, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 206.3, 177.1, 94.7, 74.6, 62.3, 34.0, 32.6, 19.0, 18.8. **EI-HRMS** (*m*/*z*): $[M]^+$ calcd for $C_{10}H_{16}O_2$, 168.1150; found, 168.1145.

Preparation of 1h[22b]



Under air, to a solution of 2-butyn-1-ol (2.8 g, 40 mmol) in Et_2O (80 mL) cooled in an ice-bath were added TsCl (9.1 g, 48 mmol) and crushed KOH (14 g) in this order. The resulting mixture was stirred for 45 min in the ice-bath before being poured into ice water. The mixture was extracted with Et_2O (40 mL × 3), and then combined organic phase was dried over $MgSO_4$, filtered and evaporated to give propargyl tosylate as a slightly yellow oil. To a dried 300 mL 2-neck flask were added this oil, CuBr (574 mg, 4.0 mmol) and THF (80 mL). The mixture was cooled to –40 °C, and then CyMgCl (2.0 M in Et_2O, 22 mL, 44 mmol) was added dropwise over 1 h. The resulting mixture was stirred for 3.5 h before quenched by NH_4Cl aq. (150 mL). The

aqueous layer was extracted with Et_2O (50 mL × 3). Combined organic phase was dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (eluent: pentane) to give **1h** as a colorless liquid (3.38 g, 62% over 2 steps). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 4.59 (app quintet, J = 2.9 Hz, 2H), 1.82–1.62 (m, 9H), 1.31–1.06 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 205.6, 103.5, 74.4, 40.9, 31.7, 26.4, 26.3, 17.1. All the resonances in ^{1}H and ^{13}C NMR spectra were in good agreement with literature values.[27]

2-4-4. Experimental Procedures for the Silacarboxylation of Allenes

Typical procedure for the silacarboxylation of allenes (Table 2-1, entry 1)

To a dried Schlenk tube were added $Cu(OAc)_2 \cdot H_2O$ (2.0 mg, 10 μmol) and *rac*-Me-DuPhos (3.1 mg, 10 μmol). The tube was evacuated and backfilled with CO_2 three times. To this Schlenk tube were added hexane (0.50 mL), **1a** (25 μL, 0.19 mmol) and $PhMe_2Si$–B(pin) (55 μL, 0.20 mmol) in this order. The system was closed, and then the mixture was stirred at 70 °C for 16–18 h. After being cooled to room temperature, the reaction was quenched by adding Et_2O (3.5 mL) and 1N HCl aq. (2 mL), and then tetradecane (30 μL) was added as an internal standard. The resulting mixture was stirred for 20 min. To an aliquot of the organic layer (ca. 1mL) were added methanol (0.2–0.3 mL) and TMS-diazomethane (2.0 M in Et_2O, 0.3 mL) in this order. After 10 min, a few drops of acetic acid were added, and then the solution was filtered through a pad of Celite and analyzed by GC.

Typical procedure for Table 2-2, Conditions A (synthesis of 2a)

To a dried Schlenk tube were added $Cu(OAc)_2 \cdot H_2O$ (2.0 mg, 10 μmol) and *rac*-Me-DuPhos (3.1 mg, 10 μmol). The tube was evacuated and backfilled with CO_2 three times. To this Schlenk tube were added hexane (0.50 mL), **1a** (26 μL, 0.20 mmol) and $PhMe_2Si$–B(pin) (60 μL, 0.22 mmol) in this order. The system was closed, and then the mixture was stirred at 70 °C for 16–18 h. After being cooled to room temperature, the reaction was quenched by adding Et_2O (3.5 mL) and 1N HCl aq. (2 mL). The resulting mixture was stirred for 10 min before the phases were separated and the aqueous phase was extracted with Et_2O (3 mL × 5). The combined organic extracts were dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (eluent: hexane/EtOAc = 7:1) to give **2a** (43.4 mg, 76%) as a colorless oil.

Work-up procedure for 2b': After the reaction mixture was cooled to room temperature, all volatiles were removed in vacuo. The residue was dissolved in THF (1.5 mL) and 3N HCl aq. (1.5 mL), and then stirred at room temperature for 5 h. The mixture was diluted with H_2O (3 mL) and Et_2O (8 mL) before the phases were separated. The aqueous phase was extracted with Et_2O (3 mL × 5). The combined organic extracts were dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (eluent: hexane/EtOAc = 2:1 to 1:1) to give **2b'**

(43.3 mg, 72%) as a colorless oil.

Typical procedure for Table 2-2, Conditions B (synthesis of 3a)

To a dried Schlenk tube were added CuCl (1.0 mg, 10 μmol), PCy_3 (2.8 mg, 10 μmol) and NaOAc (2.5 mg, 30 μmol). The tube was evacuated and backfilled with CO_2 three times. To this Schlenk tube were added THF (0.50 mL), **1a** (26 μL, 0.20 mmol) and $PhMe_2Si$–B(pin) (60 μL, 0.22 mmol) in this order. The system was closed, and then the mixture was stirred at 70 °C for 16–18 h. After being cooled to room temperature, the reaction was quenched by adding Et_2O (3.5 mL) and 1N HCl aq. (2 mL). The mixture was stirred for 10 min before the phases were separated and the aqueous phase was extracted with Et_2O (3 mL × 5). The combined organic extracts were dried over $MgSO_4$, filtered through a plug of Celite, and evaporated under reduced pressure. The residue was analyzed by ^1H NMR ($CDCl_3$) to determine a ratio of isomers and yield using fluorene as an internal standard. The crude mixture was further purified by column chromatography to give **3a** (52.0 mg, 94%) as a colorless oil.

E- or *Z*-configurations of the α,β-unsaturated carboxylic acids **3c**–**p** can be easily judged by ^1H NMR. The chemical shifts of allylic methyl protons are typically around 2.0 ppm when they place *cis* to carboxylate group, whereas around 1.6 ppm when *trans*. The configurations were further confirmed by 2D NOE measurements and X-ray crystallography where noted.

Typical procedure for the synthesis of (*Z*)-3 in large scale (eq 2-1)

To a dried Schlenk flask were added CuCl (20 mg, 200 μmol), PCy_3 (56 mg, 200 μmol) and NaOAc (49 mg, 600 μmol). The flask was evacuated and backfilled with CO_2 three times, then fitted with CO_2 balloon. To this Schlenk flask were added THF (10 mL), **1h** (720 μL, 4.02 mmol) and $PhMe_2Si$–B(pin) (1.2 mL, 4.4 mmol) in this order. The mixture was stirred at 70 °C for 18 h. After being cooled to room temperature, the reaction was quenched by adding Et_2O (70 mL) and 1N HCl aq. (40 mL). The mixture was stirred for 10 min before the phases were separated and the aqueous phase was extracted with Et_2O (50 mL × 3). The combined organic extracts were dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude mixture was further purified by column chromatography to give (*Z*)-**3h** (1.05 g, 83%) as a white solid.

2-4-5. Experimental Procedures for the Oxidation

Procedure for eq 2-2

To a dried test tube were added (*Z*)-**3h** (63.3 mg, 0.20 mmol), pyridine (0.75 mL) and a solution of $Na_2WO_4{\cdot}2H_2O$ (9.8 mg, 30 μmol) in H_2O (0.5 mL). The mixture was warmed to 65 °C and then H_2O_2 (30% aq. solution, 100 μL, 0.88 mmol) was added. After the mixture was stirred at 65 °C for 4h, a solution of $Na_2WO_4{\cdot}2H_2O$ (9.8 mg, 30 μmol) in H_2O (100 μL) and H_2O_2 (30% aq. solution, 100 μL, 0.88 mmol) were added. After further stirred at 65 °C for 20 h, H_2O_2 (30%

aq. solution, 100 μL, 0.88 mmol) was added. After the reaction mixture was further stirred for 1 day at 65 °C, TBAF (1.0 M in THF, 1 mL, 1 mmol) was added and the resulting mixture was stirred for 3 days at room temperature. 1N HCl aq. was added and the water phase was extracted with Et_2O (10 mL × 4). The combined organic phase was washed with brine, dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (eluent: hexane/EtOAc = 1:1) to give **4h** as a white solid (30.0 mg, 76%); **m.p.** 113–116 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 6.44 (s, 1H), 5.81 (s, 1H), 1.90 (br d, *J* = 12.5 Hz, 1H), 1.81–1.70 (m, 3H), 1.66 (br d, *J* = 12.5 Hz, 1H), 1.60 (br d, *J* = 12.5 Hz, 1H), 1.35 (s, 3H), 1.26–1.17 (m, 2H), 1.11 (tt, *J* = 12.7, 3.4 Hz, 1H), 1.02 (dq, *J* = 12.6, 3.3 Hz, 1H), 0.93 (dq, *J* = 12.5, 3.5 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 171.7, 143.9, 127.5, 45.8, 28.1, 26.8, 26.6, 26.5, 26.4, 22.2. **IR** (ATR): 985.6, 1018.4, 1244.1, 1506.4, 1541.1, 1558.5, 1683.9, 2854.7, 2926.0, 3649.3 cm^{-1}. **ESI-HRMS**: $[M–H]^+$ calcd for $C_{11}H_{17}O_3$, 197.1183; found, 197.1181.

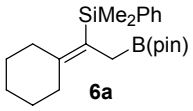
Procedure for eq 2-3

To a dried test tube were added (*Z*)-**3h** (63.3 mg, 0.20 mmol) and CH_2Cl_2 (2.0 mL). The solution was cooled in an ice-bath. $HBF_4{\cdot}OEt_2$ (54 μL, 0.40 mmol) was added and the resulting yellow solution was stirred at room temperature for 2 h. The mixture was diluted with Et_2O (10 mL) and quenched by adding distilled water (5 mL), and then extracted with Et_2O (5 mL × 3). The combined organic layer was dried over $MgSO_4$, filtered, and the solvent was evaporated to give crude fluorosilane. The residue was mixed with KF (23.2 mg, 0.40 mmol), $KHCO_3$ (200 mg, 2.0 mmol), THF (2.0 mL) and MeOH (2.0 mL), and then cooled in an ice-bath. H_2O_2 (300 μL, 2.6 mmol) was added and the resulting mixture was stirred at room temperature for 2.5 h, then cautiously quenched by adding 1N HCl aq. (5 mL) and diluted with Et_2O (10 mL). The organic phase was separated, and the water phase was extracted with Et_2O (10 mL × 3). The combined organic layer was dried over $MgSO_4$, filtered, and the solvent was evaporated. The residue was purified by column chromatography (eluent: hexane/EtOAc = 1:1) to give (*E*)-**5h** as a white solid (21.8 mg, 55%); **m.p.** 103–106 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 4.40 (s, 2H), 2.72 (tt, *J* = 11.4, 3.3 Hz, 1H), 2.06 (s, 3H), 1.79 (br d, *J* = 12.5 Hz, 2H), 1.72 (br d, *J* = 13.1 Hz, 1H), 1.55 (br d, *J* = 12.5 Hz, 2H), 1.44–1.30 (m, 4H), 1.26–1.14 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 174.0, 161.1, 125.6, 58.9, 43.2, 30.5, 26.1, 25.9, 16.9. **IR** (ATR): 707.9, 740.7, 893.0, 970.2, 1068.6, 1112.9, 1197.8, 1240.2, 1456.3, 1541.1, 1618.3, 1683.9, 2935.7 cm^{-1}. **ESI-HRMS**: $[M–H]^+$ calcd for $C_{11}H_{17}O_3$, 197.1183; found, 197.1181. The *E*-configuration of the product was confirmed by ^{1}H NMR as well as 2D NOE measurement as noted in the cases of **3**.

2-4-6. Experimental Procedures for Scheme 2-2

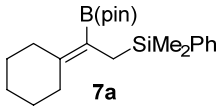
Typical procedure for Scheme 2-2a (Conditions B, but without CO_2)

To a dried Schlenk tube were added CuCl (1.0 mg, 10 μmol), PCy_3 (2.8 mg, 10 μmol) and NaOAc (2.5 mg, 30 μmol) under Ar. To this Schlenk tube were added THF (0.50 mL), **1a** (20 μL, 0.15 mmol) and $PhMe_2Si$–B(pin) (60 μL, 0.22 mmol) in this order. The system was closed, and then the mixture was stirred at 70 °C for 16 h. After being cooled to room temperature, the mixture was diluted with Et_2O (3.5 mL) and filtered through a plug of Celite. After fluorene (15.2 mg) was added as an internal standard, an aliquot of the solution was analyzed by GC and GC/MS. Remaining solution was evaporated under reduced pressure. The residue was analyzed by ^1H NMR ($CDCl_3$) to determine a ratio of isomers and yield.



6a

6a; **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.63–7.60 (m, 2H), 7.31–7.30 (m, 3H), 2.23–2.21 (m, 2H), 2.05–2.02 (m, 2H), 1.82 (s, 2H), 1.56–1.46 (m, 6H), 1.23 (s, 12H), 0.37 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 151.1, 141.4, 133.9, 128.2, 127.3, 122.2, 82.8, 36.5, 31.4, 28.2, 28.0, 26.8, 24.8, –0.2. One resonance in C_{sp3} region could not be found possibly owing to a quadrupole moment of boron atom. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –7.0.



7a

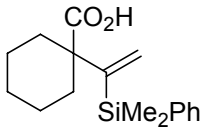
7a; **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.55–7.53 (m, 2H), 7.34–7.31 (m, 3H), 2.49–2.46 (m, 2H), 2.03–2.00 (m, 2H), 1.90 (s, 2H), 1.52–1.49 (m, 4H), 1.42–1.37 (m, 2H), 1.22 (s, 12H), 0.26 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 151.8, 140.1, 133.8, 128.6, 127.5, 82.7, 34.6, 31.4, 29.0, 27.7, 26.9, 24.9, 19.7, –2.6. One resonance in C_{sp2} region could not be found possibly owing to a quadrupole moment of boron atom. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –3.5.

Typical procedure for Scheme 2-2b

To a dried Schlenk tube were added CuCl (1.0 mg, 10 μmol), PCy_3 (2.8 mg, 10 μmol) and NaOAc (2.5 mg, 30 μmol) under Ar. To this Schlenk tube were added THF (0.50 mL), **1a** (20 μL, 0.15 mmol) and $PhMe_2Si$–B(pin) (60 μL, 0.22 mmol) in this order. The system was closed, and then the mixture was stirred at 70 °C for 16 h. After being cooled to room temperature, CuCl (1.0 mg, 10 μmol), PCy_3 (2.8 mg, 10 μmol) and NaOAc (2.5 mg, 30 μmol) were added under Ar. The tube was shortly evacuated and backfilled with CO_2 three times. The system was closed, and then the mixture was stirred at 70 °C for 24 h. After being cooled to room temperature, Et_2O (4 mL) and tetradecane (20 μL) were added. An aliquot of the mixture was filtered through a plug of Celite and analyzed by GC and GC/MS to check the conversion of **6a** and **7a**. To the remaining solution was added 1N HCl aq. (2 mL), then the mixture was stirred for 20 min. To an aliquot of the organic layer (ca. 1mL) were added methanol (0.2–0.3 mL) and trimethylsilyldiazomethane (2.0 M in Et_2O, 0.3 mL) in this order. After 10 min, a few drops of acetic acid were added. The solution was filtered through a plug of Celite and analyzed by GC. Neither carboxylated product **2a** nor **3a** was detected.

2-4-7. Characterization of the Silacarboxylation Products

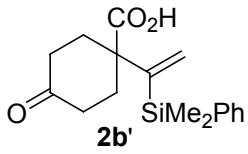
1-(1-(dimethyl(phenyl)silyl)vinyl)cyclohexane-1-carboxylic acid (**2a**)



2a

Purified by column chromatography (eluent: hexane/EtOAc = 7:1). Colorless oil (43.4 mg, 76%, isomeric purity > 93%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.55–7.52 (m, 2H), 7.36–7.33 (m, 3H), 5.99 (d, *J* = 0.9 Hz, 1H), 5.65 (d, *J* = 0.9 Hz, 1H), 2.21–2.12 (m, 2H), 1.59–1.33 (m, 7H), 1.17–1.05 (m, 1H), 0.47 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 181.8, 152.7, 139.1, 133.9, 129.2, 128.9, 127.7, 53.4, 34.4, 25.4, 23.5, –0.4. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –6.7. **IR** (ATR): 733.0, 775.4, 817.8, 850.6, 908.5, 939.3, 1111.0, 1134.1, 1246.0, 1305.8, 1427.3, 1452.4, 1693.5, 2935.7 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{17}H_{23}O_2Si$, 287.1473; found, 287.1474.

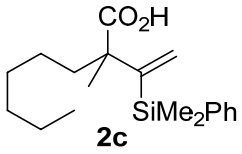
1-(1-(dimethyl(phenyl)silyl)vinyl)-4-oxocyclohexane-1-carboxylic acid (**2b′**)



2b'

Purified by column chromatography (eluent: hexane/EtOAc = 7:1 to 2:1). Colorless oil (47.2 mg, 79%, isomeric purity > 94%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.51–7.49 (m, 2H), 7.35–7.31 (m, 3H), 6.08 (s, 1H), 5.79 (s, 1H), 2.47–2.38 (m, 4H), 2.30–2.24 (m, 2H), 1.93–1.88 (m, 2H), 0.47 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 210.7, 180.0, 150.3, 138.1, 133.7, 130.3, 129.2, 127.9, 52.0, 38.4, 33.7, –0.6. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –6.6. **IR** (ATR): 702.1, 734.9, 777.3, 821.7, 941.3, 1109.1, 1249.9, 1338.6, 1427.3, 1699.3, 1716.7 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{17}H_{21}O_3Si$, 301.1265; found, 301.1267.

3-(dimethyl(phenyl)silyl)-2-hexyl-2-methylbut-3-enoic acid (**2c**)

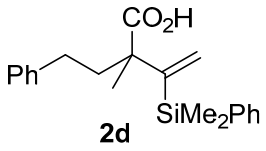


2c

Purified by column chromatography (eluent: hexane/EtOAc = 7:1). Colorless oil (41.7 mg, 66%, isomeric purity > 95%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54–7.51 (m, 2H), 7.34–7.29 (m, 3H), 5.87 (d, *J* = 1.4 Hz, 1H), 5.62 (d, *J* = 1.4 Hz, 1H), 1.83–1.75 (m, 1H), 1.61–1.53 (m, 1H), 1.26–1.08 (m, 11H), 0.85 (t, *J* = 7.0 Hz, 3H), 0.42 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ:183.2, 152.2, 139.0, 134.0, 128.9, 127.9, 127.6, 51.8, 37.4, 31.7, 29.6, 24.3, 22.6, 22.5, 14.1, –0.6, –0.8. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –7.1. **IR** (ATR): 733.0, 775.4, 819.8, 835.2, 935.5, 1111.0, 1249.9, 1427.3, 1558.5, 1697.4, 2858.5, 2929.9, 2955.0 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{19}H_{29}O_2Si$, 317.1942; found, 317.1943.

3-(dimethyl(phenyl)silyl)-2-methyl-2-phenethylbut-3-enoic acid (**2d**)

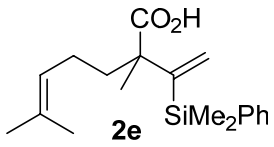
Purified by column chromatography (eluent: hexane/EtOAc = 7:1). Colorless oil (50.6 mg, 76%, isomeric purity > 95%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.55–7.52 (m, 2H), 7.34–7.30 (m, 3H), 7.25–7.22 (m, 2H), 7.15 (t, *J* = 7.3 Hz, 1H), 7.03 (d, *J* = 7.0 Hz, 2H), 5.94 (s, 1H), 5.68 (s, 1H),



2d

2.45 (t, *J* = 8.7 Hz, 2H), 2.15–2.09 (m, 1H), 1.94–1.88 (m, 1H), 1.39 (s, 3H), 0.45 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 182.9, 151.8, 142.0, 138.8, 134.0, 129.0, 128.3, 128.3, 127.7, 125.8, 51.8, 39.5, 30.9, 22.6, –0.5, –0.7. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –7.0. **IR** (ATR): 733.0, 775.4, 817.8, 835.2, 937.4, 1030.0, 1109.1, 1427.3, 1456.3, 1496.8, 1697.4, 2956.9 cm^{-1}. **Anal.** Calcd for $C_{21}H_{26}O_2Si$: C, 74.51; H, 7.74%. Found: C, 74.32; H, 8.00%.

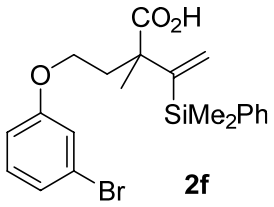
2-(1-(dimethyl(phenyl)silyl)vinyl)-2,6-dimethylhept-5-enoic acid (**2e**)



2e

Purified by column chromatography (eluent: hexane/EtOAc = 7:1). Colorless oil (47.6 mg, 76%, isomeric purity > 96%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.35–7.29 (m, 3H), 5.89 (s, 1H), 5.62 (s, 1H), 4.98–4.96 (m, 1H), 1.86–1.77 (m, 3H), 1.68–1.60 (m, 4H), 1.54 (s, 3H), 1.29 (s, 3H), 0.43 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 183.1, 152.0, 139.0, 134.0, 131.8, 128.9, 128.1, 127.7, 123.8, 51.7, 37.5, 25.6, 23.2, 22.5, 17.6, –0.6, –0.6. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –7.0. **IR** (ATR): 733.0, 775.4, 821.7, 835.2, 935.5, 1111.0, 1284.6, 1377.2, 1427.3, 1697.4 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{19}H_{27}O_2Si$, 315.1786; found, 315.1790.

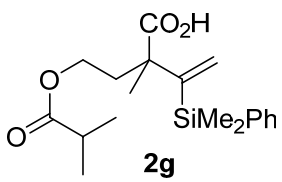
2-(2-(3-bromophenoxy)ethyl)-3-(dimethyl(phenyl)silyl)-2-methylbut-3-enoic acid (**2f**)



2f

Purified by column chromatography (eluent: hexane/EtOAc = 7:1 to 4:1). Colorless oil (74.1 mg, 83%, isomeric purity > 96%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.53–7.51 (m, 2H), 7.32–7.30 (m, 3H), 7.09–7.03 (m, 2H), 6.92–6.91 (m, 1H), 6.71–6.69 (m, 1H), 5.95 (s, 1H), 5.71 (s, 1H), 3.83–3.75 (m, 2H), 2.37–2.31 (m, 1H), 2.12–2.05 (m, 1H), 1.39 (s, 3H), 0.46 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 182.6, 159.4, 151.5, 138.4, 133.9, 130.4, 129.1, 128.8, 127.8, 123.7, 122.7, 117.6, 113.5, 64.8, 50.5, 36.3, 22.9, –0.7, –0.9. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –7.0. **IR** (ATR): 734.9, 775.4, 821.7, 835.2, 939.3, 1024.2, 1064.7, 1109.1, 1157.3, 1226.7, 1247.9, 1282.7, 1427.3, 1471.7, 1573.9, 1589.3, 1697.4 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{21}H_{25}BrO_3Si$, 431.0684; found, 431.0686.

3-(dimethyl(phenyl)silyl)-2-(2-isobutyryloxy)ethyl)-2-methylbut-3-enoic acid (**2g**)

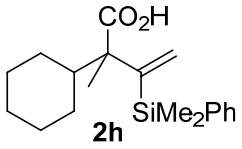


2g

Purified by column chromatography (eluent: hexane/EtOAc = 6:1 + AcOH 4%). Colorless oil (35.6 mg, 52%, isomeric purity > 96%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.53–7.50 (m, 2H), 7.34–7.31 (m, 3H), 5.92 (s, 1H), 5.68 (s, 1H), 3.97 (t, *J* = 7.2 Hz, 2H), 2.46 (sept, *J* = 7.0 Hz, 1H), 2.20–2.14 (m, 1H), 1.98–1.92 (m, 1H), 1.34 (s, 3H), 1.12 (d, *J* = 7.0 Hz, 6H), 0.44 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 181.9, 177.0, 151.2, 138.4, 133.9,

129.0, 128.8, 127.8, 61.1, 50.3, 35.7, 33.9, 22.7, 18.9, –0.7, –0.8. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –7.0. **IR** (ATR): 734.9, 777.3, 819.8, 835.2, 937.4, 1111.0, 1155.4, 1192.0, 1249.9, 1427.3, 1469.8, 1699.3, 1734.0, 2974.2 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{19}H_{27}O_4Si$, 347.1684; found, 347.1687.

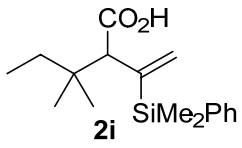
2-cyclohexyl-3-(dimethyl(phenyl)silyl)-2-methylbut-3-enoic acid (**2h**)



2h

Purified by column chromatography (eluent: hexane/EtOAc = 7:1). White solid (37.2 mg, 61%, isomeric purity > 98%); **m.p.** 68–70 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.52–7.48 (m, 2H), 7.32–7.29 (m, 3H), 5.97 (s, 1H), 5.72 (s, 1H), 2.02–1.95 (m, 1H), 1.75–1.54 (m, 5H), 1.26–1.01 (m, 7H), 0.90–0.76 (m, 1H), 0.45 (s, 3H), 0.42 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 182.4, 151.3, 139.4, 133.9, 130.0, 128.7, 127.6, 55.5, 43.2, 29.1, 27.3, 27.0, 26.7, 26.6, 17.1, 0.1, –0.5. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –6.8. **IR** (ATR): 704.0, 734.9, 771.5, 788.9, 821.7, 835.2, 933.6, 1111.0, 1246.0, 1284.6, 1697.4, 2926.0 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{19}H_{27}O_2Si$, 315.1786; found, 315.1789.

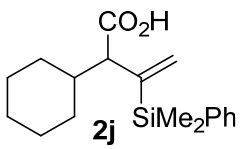
3-(dimethyl(phenyl)silyl)-2-(1,1-dimethylpropyl)but-3-enoic acid (**2i**)



2i

Purified by column chromatography (eluent: hexane/EtOAc = 7:1). White solid (47.3 mg, 82%, isomeric purity > 99%); **m.p.** 48–50 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54–7.52 (m, 2H), 7.36–7.32 (m, 3H), 6.26 (d, *J* = 1.8 Hz, 1H), 5.78 (d, *J* = 1.8 Hz, 1H), 3.20 (s, 1H), 1.37 (dq, *J* = 14.3, 7.1 Hz, 1H), 1.19 (dq, *J* = 14.2, 7.1 Hz, 1H), 0.95 (s, 3H), 0.78 (s, 3H), 0.75 (t, *J* = 7.2 Hz, 3H), 0.43 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 179.2, 144.5, 137.7, 134.2, 133.1, 129.1, 127.7, 55.5, 37.1, 33.5, 24.2, 23.6, 8.2, –2.1, –2.1. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –5.5. **IR** (ATR): 704.0, 719.5, 740.7, 775.4, 792.7, 819.8, 833.3, 941.3, 1112.9, 1165.0, 1238.3, 1458.2, 1699.3, 2962.7 cm^{-1}. **Anal.** Calcd for $C_{17}H_{26}O_2Si$: C, 70.51; H, 9.06%. Found: C, 70.29; H, 9.02%.

3-(dimethyl(phenyl)silyl)-2-cyclohexylbut-3-enoic acid (**2j**)

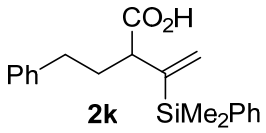


2j

Purified by flash column chromatography (eluent: hexane/EtOAc = 7:1). White solid (37.4 mg, 62%, isomeric purity > 99%); **m.p.** 70–72 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.52–7.49 (m, 2H), 7.35–7.30 (m, 3H), 6.02 (d, *J* = 1.8 Hz, 1H), 5.64 (d, *J* = 2.1 Hz, 1H), 2.84 (d, *J* = 10.7 Hz, 1H), 1.77–1.59 (m, 6H), 1.26–1.17 (m, 1H), 1.12–1.03 (m, 2H), 0.95–0.87 (m, 1H), 0.57–0.51 (m, 2H), 0.41 (s, 3H), 0.41 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 180.2, 146.2, 137.3, 134.1, 130.7, 129.1, 127.7, 56.8, 39.9, 31.6, 30.5, 26.3, 26.1, 26.1, –2.7, –2.8. **^{29}Si NMR** (100 MHz, $CDCl_3$) δ: –7.2. **IR** (ATR): 733.0, 775.4, 819.8, 950.9, 1114.9, 1199.7, 1249.9, 1296.2, 1446.6, 1703.1,

2924.1 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{18}H_{25}O_2Si$, 301.1629; found, 301.1629.

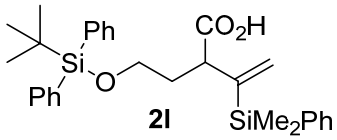
3-(dimethyl(phenyl)silyl)-2-phenethylbut-3-enoic acid (**2k**)



2k

Purified by flash column chromatography (eluent: hexane/EtOAc = 7:1 to 4:1). Colorless oil (39.4 mg, 64%, isomeric purity > 99%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.51-7.49 (m, 2H), 7.37-7.31 (m, 3H), 7.24-7.21 (m, 2H), 7.15 (t, *J* = 7.3 Hz, 1H), 7.03 (d, *J* = 7.0 Hz, 2H), 5.96 (d, *J* = 0.9 Hz, 1H), 5.63 (d, *J* = 1.8 Hz, 1H), 3.15 (dd, *J* = 9.0, 5.6 Hz, 1H), 2.51 (ddd, *J* = 14.0, 10.1, 5.5 Hz, 1H), 2.43 (ddd, *J* = 13.8, 9.5, 6.6 Hz, 1H), 2.08 (dtd, *J* = 13.6, 9.2, 5.5 Hz, 1H), 1.69 (ddt, *J* = 13.5, 10.1, 6.1 Hz, 1H), 0.39 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 180.1, 147.5, 141.3, 137.1, 134.0, 129.2, 129.1, 128.4, 128.3, 127.8, 125.9, 49.1, 34.1, 34.0, –2.9, –3.0. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: –7.1. **IR** (ATR): 734.9, 777.3, 819.8, 939.3, 1111.0, 1249.9, 1701.2 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{20}H_{23}O_2Si$, 323.1473; found, 323.1474.

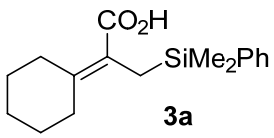
2-(2-(*tert*-butyldiphenylsilyl)oxyethyl)-3-(dimethyl(phenyl)silyl)but-3-enoic acid (**2l**)



2l

Purified by flash column chromatography (eluent: hexane/EtOAc = 7:1). Colorless oil (76.3 mg, 77%, isomeric purity > 99%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.61-7.58 (m, 4H), 7.50-7.48 (m, 2H), 7.42-7.27 (m, 9H), 5.93 (s, 1H), 5.58 (d, *J* = 1.8 Hz, 1H), 3.53 (t, *J* = 6.1 Hz, 2H), 3.49 (dd, *J* = 9.2, 5.2 Hz, 1H), 2.05 (ddt, *J* = 13.8, 9.2, 5.9 Hz, 1H), 1.66 (dtd, *J* = 13.8, 6.5, 5.2 Hz, 1H), 1.00 (s, 9H), 0.42 (d, *J* = 5.2 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 180.0, 147.6, 137.2, 135.5, 135.5, 134.0, 133.7, 133.5, 129.6, 129.5, 129.2, 129.2, 127.8, 127.6, 61.7, 45.8, 35.1, 26.8, 19.1, –2.7, –2.9. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: –3.9, –7.0. **IR** (ATR): 736.8, 777.3, 821.7, 941.3, 1111.0, 1249.9, 1427.3, 1703.1 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{30}H_{37}O_3Si_2$, 501.2287; found, 501.2287.

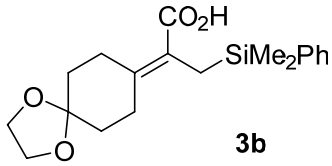
2-cyclohexylidene-3-(dimethyl(phenyl)silyl)propanoic acid (**3a**)



3a

Purified by column chromatography (eluent: hexane/EtOAc = 7:1). Colorless oil (52.0 mg, 94%, isomeric purity > 97%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54–7.50 (m, 2H), 7.35–7.32 (m, 3H), 2.54–2.52 (m, 2H), 2.07 (s, 2H, C*H*$_2$Si), 2.02–1.99 (m, 2H), 1.58–1.48 (m, 4H), 1.43–1.36 (m, 2H), 0.31 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 176.3, 148.3, 138.7, 133.7, 129.0, 127.7, 120.9, 32.5, 32.1, 28.3, 27.5, 26.4, 19.2, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –2.9. **IR** (ATR): 729.1, 831.3, 997.2, 1062.8, 1112.9, 1165.0, 1224.8, 1253.7, 1298.1, 1427.3, 1678.1, 2854.7, 2927.9 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{17}H_{23}O_2Si$, 287.1473; found, 287.1474.

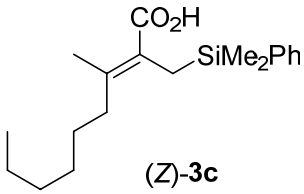
3-(dimethyl(phenyl)silyl)-2-(1,4-dioxaspiro[4.5]decan-8-ylidene)propanoic acid (**3b**)



3b

Purified by column chromatography (eluent: hexane/EtOAc = 2:1 to 1:1). Colorless oil (45.4 mg, 66%, isomeric purity > 97%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.52–7.50 (m, 2H), 7.35–7.32 (m, 3H), 3.94 (s, 4H), 2.70 (t, *J* = 6.3 Hz, 2H), 2.17 (t, *J* = 6.3 Hz, 2H), 2.09 (s, 2H, C*H*$_2$Si), 1.69 (t, *J* = 6.1 Hz, 2H), 1.49 (t, *J* = 6.3 Hz, 2H), 0.31 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 175.6, 145.1, 138.4, 133.6, 129.1, 127.7, 122.5, 108.3, 64.3, 35.5, 34.9, 28.7, 28.7, 19.6, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –2.9. **IR** (ATR): 831.3, 918.1, 1035.8, 1097.5, 1112.9, 1220.9, 1247.9, 1680.0 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{19}H_{25}O_4Si$, 345.1528; found, 315.1528.

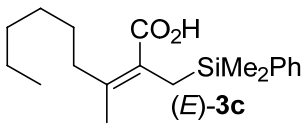
(*Z*)-2-(dimethyl(phenyl)silyl)methyl-3-methylnon-2-enoic acid ((*Z*)-**3c**)



(*Z*)-**3c**

Purified by column chromatography (eluent: hexane/EtOAc = 7:1). Colorless oil (51.7 mg, 82%, isomeric purity > 97%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54–7.50 (m, 2H), 7.35–7.31 (m, 3H), 2.06 (s, 2H, C*H*$_2$Si), 2.01 (s, 3H, C*H*$_3$C=C), 1.89 (t, *J* = 7.7 Hz, 2H), 1.31–1.18 (m, 8H), 0.87 (t, *J* = 7.2 Hz, 3H), 0.31 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 175.5, 147.5, 139.0, 133.6, 128.9, 127.7, 123.3, 36.7, 31.7, 29.5, 27.1, 22.6, 21.1, 19.0, 14.1, –2.7. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –3.0. **IR** (ATR): 723.3, 833.3, 1112.9, 1163.1, 1234.4, 1247.9, 1300.0, 1427.3, 1680.0, 2927.9 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{19}H_{29}O_2Si$, 317.1942; found, 317.1943.

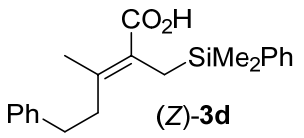
(*E*)-2-(dimethyl(phenyl)silyl)methyl-3-methylnon-2-enoic acid ((*E*)-**3c**)



(*E*)-**3c**

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53–7.51 (m, 2H), 7.34–7.31 (m, 3H), 2.37 (app triplet, *J* = 7.7 Hz, 2H), 2.04 (s, 2H, C*H*$_2$Si), 1.56 (s, 3H, C*H*$_3$C=C), 1.43–1.25 (m, 8H), 0.89 (t, *J* = 6.6 Hz, 3H), 0.31 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 174.4, 147.1, 138.9, 133.6, 129.0, 127.7, 123.5, 36.7, 31.7, 29.4, 28.7, 22.6, 21.3, 19.8, 14.1, –2.8. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: –2.9. The (*E*)-configuration was further confirmed by 2D NOESY measurement.

(*Z*)-2-(dimethyl(phenyl)silyl)methyl-5-phenyl-3-methylpent-2-enoic acid ((*Z*)-**3d**)

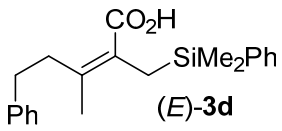


(*Z*)-**3d**

Purified by column chromatography (eluent: hexane/EtOAc = 7:1 then 4:1). White solid (54.0 mg, 81%, isomeric purity > 97%); **m.p.** 44–46 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.52–7.50 (m, 2H), 7.34–7.31 (m, 3H), 7.28–7.22 (m, 2H), 7.20–7.16 (m, 1H), 7.08–7.06 (m, 2H), 2.61–2.57 (m, 2H), 2.23–2.19 (m, 2H), 2.07 (s, 3H, C*H*$_3$C=C), 2.03 (s, 2H, C*H*$_2$Si), 0.31 (s,

6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 175.4, 145.6, 141.5, 138.8, 133.6, 129.0, 128.4, 128.1, 127.7, 126.0, 124.4, 38.6, 33.2, 21.2, 19.1, –2.7 **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –3.0. **IR** (ATR): 723.3, 806.3, 823.6, 1111.0, 1232.5, 1683.9 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{21}H_{25}O_2Si$, 337.1629; found, 337.1634. The (*Z*)-configuration was further confirmed by 2D NOESY measurement.

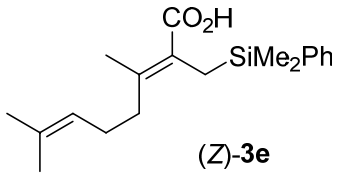
(*E*)-2-(dimethyl(phenyl)silyl)methyl-5-phenyl-3-methylpent-2-enoic acid ((*E*)-**3d**)



(*E*)-**3d**

Colorless oil (9.3 mg, 14%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.54–7.51 (m, 2H), 7.35–7.32 (m, 3H), 7.28–7.21 (m, 5H), 7.19–7.15 (m, 1H), 2.76–2.71 (m, 2H), 2.69–2.64 (m, 2H), 2.07 (s, 2H, C*H*$_2$Si), 1.61 (s, 3H, C*H*$_3$C=C), 0.33 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 174.4, 146.4, 142.2, 138.7, 133.6, 129.0, 128.4, 128.3, 127.7, 125.8, 124.4, 39.3, 35.2, 21.7, 19.8, –2.8.

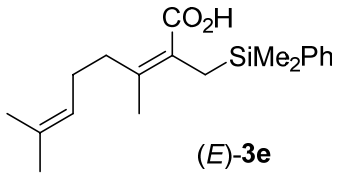
(*Z*)-2-(dimethyl(phenyl)silyl)methyl-3,7-dimethylocta-2,6-dienoic acid ((*Z*)-**3e**)



(*Z*)-**3e**

Purified by column chromatography (eluent: hexane/EtOAc = 7:1 then 4:1). Colorless oil (45.4 mg, 73%, isomeric purity > 97%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54–7.49 (m, 2H), 7.35–7.32 (m, 3H), 5.04–5.00 (m, 1H), 2.07 (s, 2H, C*H*$_2$Si), 2.03–1.92 (m, 7H), 1.67 (s, 3H), 1.57 (s, 3H), 0.30 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 175.7, 146.6, 138.9, 133.6, 132.2, 128.9, 127.7, 123.8, 123.5, 36.7, 25.6, 21.0, 19.0, 17.6, –2.7. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –3.0. **IR** (ATR): 831.3, 1112.9, 1508.3, 1683.9 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{19}H_{27}O_2Si$, 315.1786; found, 315.1791.

(*E*)-2-(dimethyl(phenyl)silyl)methyl-3,7-dimethylocta-2,6-dienoic acid ((*E*)-**3e**)

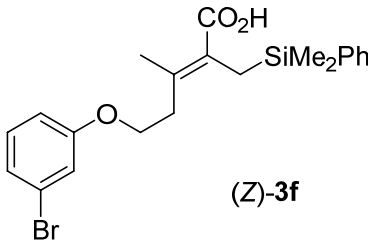


(*E*)-**3e**

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53–7.51 (m, 2H), 7.35–7.32 (m, 3H), 5.14 (tt, *J* = 7.2, 1.4 Hz, 1H), 2.39 (t, *J* = 7.9 Hz, 2H), 2.10 (q, *J* = 7.6 Hz, 2H), 2.04 (s, 2H), 1.69 (s, 3H), 1.62 (s, 3H), 1.58 (s, 3H), 0.31 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 174.2, 146.4, 138.8, 133.6, 131.9, 129.0, 127.7, 124.0, 123.9, 36.8, 27.3, 25.7, 21.3, 19.8, 17.5, –2.8. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –2.9.

(*Z*)-5-(3-bromophenoxy)-2-(dimethyl(phenyl)silyl)methyl-3-methylpent-2-enoic acid ((*Z*)-**3f**)

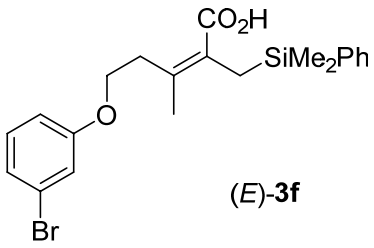
Purified by column chromatography (eluent: hexane/EtOAc = 7:1 to 4:1). Colorless oil (50.1 mg, 58%, isomeric purity > 90%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.52–7.49 (m, 2H), 7.33–7.31 (m, 3H), 7.13–7.05 (m, 2H), 6.95–6.94 (m, 1H), 6.75–6.72 (m, 1H), 3.77 (t, *J* = 7.0 Hz, 2H), 2.36 (t, *J* = 7.0 Hz, 2H), 2.13 (s, 2H, C*H*$_2$Si), 2.06 (s, 3H, C*H*$_3$C=C), 0.34 (s, 6H). **^{13}C NMR** (125 MHz,



(*Z*)-**3f**

$CDCl_3$) δ: 175.1, 159.4, 140.9, 138.3, 133.6, 130.5, 129.2, 127.8, 126.4, 123.9, 122.7, 117.7, 113.6, 65.5, 35.7, 21.2, 19.7, –2.8. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –3.0. **IR** (ATR): 717.5, 775.4, 833.3, 908.5, 991.4, 1031.9, 1112.9, 1157.3, 1242.2, 1282.7, 1425.4, 1469.8, 1573.9, 1589.3, 1681.9 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{21}H_{24}BrO_3Si$, 431.0684; found, 431.0686. The (*Z*)-configuration was further confirmed by 2D NOESY measurement.

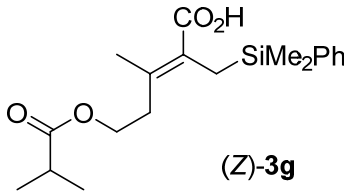
(*E*)-5-(3-bromophenoxy)-2-(dimethyl(phenyl)silyl)methyl-3-methylpent-2-enoic acid ((*E*)-**3f**)



(*E*)-**3f**

Colorless oil (12.6 mg, 15%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.50–7.47 (m, 2H), 7.35–7.27 (m, 3H), 7.13 (t, *J* = 7.9 Hz, 1H), 7.08–7.04 (m, 2H), 6.83 (dd, *J* = 8.1, 2.3 Hz, 1H), 3.99 (t, *J* = 6.7 Hz, 2H), 2.84 (t, *J* = 6.7 Hz, 2H), 2.09 (s, 2H, C*H*$_2$Si), 1.64 (s, 3H, C*H*$_3$C=C), 0.32 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 173.4, 159.4, 141.6, 138.3, 133.6, 130.5, 129.2, 127.7, 127.0, 123.9, 122.8, 117.7, 113.6, 67.2, 36.3, 22.1, 20.3, –2.8. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –2.8.

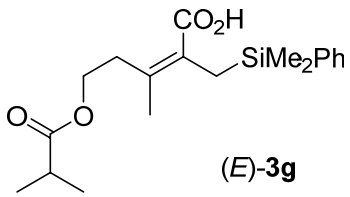
(*Z*)-5-butyryloxy-2-(dimethyl(phenyl)silyl)methyl-3-methylpent-2-enoic acid ((*Z*)-**3g**)



(*Z*)-**3g**

Purified by column chromatography (eluent: hexane/EtOAc = 7:1 to 2:1). Colorless oil (45.9 mg, 67%, isomeric purity > 96%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54–7.50 (m, 2H), 7.35–7.32 (m, 3H), 4.03 (t, *J* = 7.0 Hz, 2H), 2.51 (sept, *J* = 7.0 Hz, 1H), 2.21 (t, *J* = 7.0 Hz, 2H), 2.12 (s, 2H), 2.03 (s, 3H), 1.15 (d, *J* = 6.8 Hz, 6H), 0.33 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 177.0, 175.1, 140.9, 138.4, 133.6, 129.1, 127.7, 126.4, 61.4, 35.1, 33.9, 20.9, 19.5, 18.9, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –3.0. **IR** (ATR): 833.3, 1112.9, 1153.4, 1190.1, 1249.9, 1427.3, 1471.7, 1683.9, 1734.0, 2972.3 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{19}H_{27}O_4Si$, 347.1684; found, 347.1688.

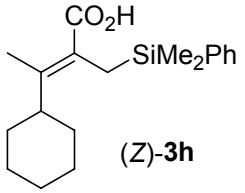
(*E*)-5-butyryloxy-2-(dimethyl(phenyl)silyl)methyl-3-methylpent-2-enoic acid ((*E*)-**3g**)



(*E*)-**3g**

Colorless oil (8.2 mg, 12%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.52–7.49 (m, 2H), 7.35–7.32 (m, 3H), 4.16 (t, *J* = 6.8 Hz, 2H), 2.73 (t, *J* = 6.8 Hz, 2H), 2.53 (sept, *J* = 7.0 Hz, 1H), 2.07 (s, 2H), 1.62 (s, 3H), 1.16 (d, *J* = 7.2 Hz, 6H), 0.32 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 177.1, 173.7, 142.0, 138.4, 133.6, 129.1, 127.7, 126.6, 63.4, 35.7, 34.0, 21.9, 20.2, 19.0, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –2.9. The (*E*)-configuration was further confirmed by 2D NOESY measurement.

(*Z*)-3-cyclohexyl-2-(dimethyl(phenyl)silyl)methylbut-2-enoic acid ((*Z*)-**3h**)



(*Z*)-**3h**

Purified by flash column chromatography (eluent: hexane/EtOAc = 7:1). Colorless solid (57.4 mg, 93%, isomeric purity > 99%); **m.p.** 92–95 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54–7.51 (m, 2H), 7.35–7.32 (m, 3H), 2.18–2.11 (m, 1H), 2.08 (s, 2H, CH_2Si), 1.87 (s, 3H, C=CCH_3), 1.67–1.60 (m, 3H), 1.30–1.16 (m, 4H), 1.11–1.00 (m, 3H), 0.31 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 176.1, 150.2, 138.8, 133.6, 129.0, 127.7, 122.8, 43.0, 29.5, 26.3, 26.0, 18.8, 16.3, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –3.5. **IR** (ATR): 719.5, 831.3, 1111.0, 1247.9, 1674.2, 2924.1 cm^{-1}. **Anal.** Calcd for $C_{19}H_{28}O_2Si$: C, 72.10; H, 8.92. Found: C, 71.91; H, 9.07.

The structure was also confirmed by X-ray crystallography. Single crystals of (*Z*)-**3h** were obtained by recrystallization from Et_2O solution.

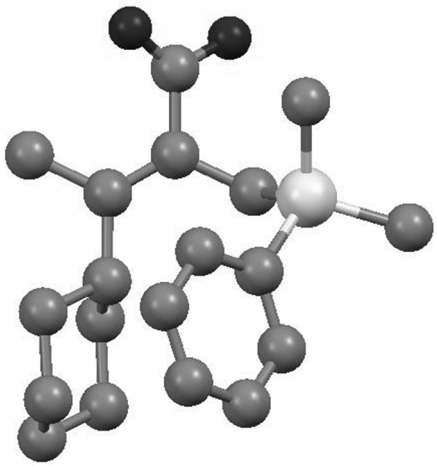
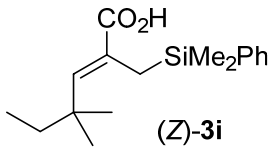


Figure 2-1. X-Ray Crystal Structure of (*Z*)-**3h**.

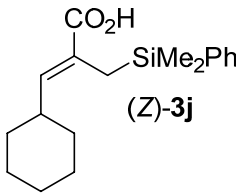
(*Z*)-2-(dimethyl(phenyl)silyl)methyl-4,4-dimethylhex-2-enoic acid ((*Z*)-**3i**)



(*Z*)-**3i**

Purified by flash column chromatography (eluent: hexane/EtOAc = 7:1). Colorless oil (53.0 mg, 92%, isomeric purity > 96%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.55–7.51 (m, 2H), 7.34–7.32 (m, 3H), 6.68 (s, 1H), 2.16 (s, 2H), 1.38 (q, *J* = 7.4 Hz, 2H), 1.02 (s, 6H), 0.79 (t, *J* = 7.5 Hz, 3H), 0.34 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 175.4, 149.3, 139.2, 133.7, 128.9, 128.2, 127.7, 36.7, 36.4, 27.5, 16.9, 9.1, –2.1. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –3.3. **IR** (ATR): 727.2, 831.3, 1070.5, 1112.9, 1166.9, 1280.7, 1622.1, 1680.0, 2962.7 cm^{-1}. **Anal.** Calcd for $C_{17}H_{26}O_2Si$: C, 70.36; H, 8.97%. Found: C, 70.29; H, 9.02%. The (*Z*)-configuration was further confirmed by 2D NOESY measurement.

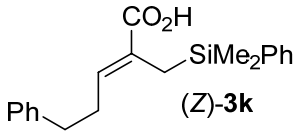
(*Z*)-2-(dimethyl(phenyl)silyl)methyl-3-cyclohexylprop-2-enoic acid ((*Z*)-**3j**)



(*Z*)-**3j**

Purified by flash column chromatography (eluent: hexane/EtOAc = 7:1). Colorless oil (43.9 mg, 73%, (*Z*)-**3j**/**2j** = 68:32). NMR resonance signals assigned to (*Z*)-**3j** are listed below. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: ^{1}H-NMR ($CDCl_3$) δ: 7.54–7.50 (m, 2H), 7.36–7.31 (m, 3H), 6.55 (d, *J* = 10.1 Hz, 1H), 2.01 (s, 2H), 1.98–1.92 (m, 1H), 1.83–1.59 (m, 4H), 1.39–1.34 (m, 2H), 1.14–0.88 (m, 4H), 0.31 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 174.1, 147.0, 138.8, 133.6, 129.0, 127.7, 126.6, 38.2, 31.6, 25.8, 25.5, 16.4, –2.9. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: –3.6. **IR** (ATR): 729.1, 758.0, 821.7, 837.1, 1112.9, 1280.7, 1300.0, 1427.3, 1687.7, 2850.8, 2926.0 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{18}H_{25}O_2Si$, 301.1629; found, 301.1631.

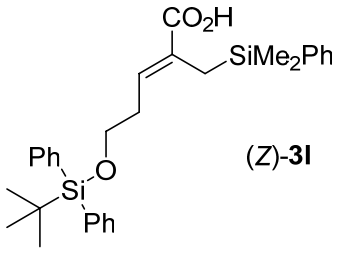
(*Z*)-2-(dimethyl(phenyl)silyl)methyl-3-cyclohexylprop-2-enoic acid ((*Z*)-**3k**)



(*Z*)-**3k**

Purified by flash column chromatography (eluent: hexane/EtOAc = 7:1 to 4:1). Colorless oil (44.5 mg, 72%, (*Z*)-**3k**/**2k** = 48:52). NMR resonance signals assigned to (*Z*)-**3k** are listed below. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.51-7.49 (m, 2H), 7.36-7.32 (m, 3H), 7.28-7.14 (m, 3H), 7.07 (d, *J* = 7.3 Hz, 2H), 6.78 (t, *J* = 7.0 Hz, 1H), 2.59 (t, *J* = 7.8 Hz, 2H), 2.21 (dt, *J* = 7.8, 7.2 Hz, 2H), 1.99 (s, 2H), 0.30 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 173.6, 141.1, 140.9, 138.6, 133.6, 133.0, 129.3, 129.1, 128.3, 127.8, 126.0, 34.6, 31.0, 16.7, –2.8. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: –3.1. **IR** (ATR): 733.0, 777.3, 819.8, 1112.9, 1249.9, 1427.3, 1693.5 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{20}H_{23}O_2Si$, 323.1473; found, 323.1475.

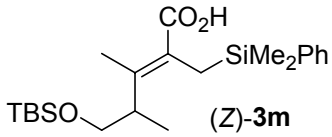
(*Z*)-2-(dimethyl(phenyl)silyl)methyl-3-cyclohexylprop-2-enoic acid ((*Z*)-**3l**)



(*Z*)-**3l**

Purified by flash column chromatography (eluent: hexane/EtOAc = 7:1 to 4:1). Colorless oil (74.2 mg, 75%, (*Z*)-**3l**/**2l** = 42:58). NMR resonance signals assigned to (*Z*)-**3l** are listed below. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.63 (d, *J* = 6.7 Hz, 4H), 7.51-7.47 (m, 4H), 7.42-7.27 (m, 21H), 6.81 (br s, 1H), 3.59 (t, *J* = 6.4 Hz, 2H), 2.16-2.12 (m, 2H), 1.99 (s, 2H), 1.04 (s, 9H), 0.28 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 173.4, 138.6, 138.4, 135.6, 133.7, 133.6, 129.6, 129.1, 127.7, 127.7, 62.4, 32.6, 26.8, 19.1, 16.8. The author was unable to assign other two resonances of (*Z*)-**3l** owing to overlapping. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: –3.1, –3.9. **IR** (ATR): 736.8, 777.3, 821.7, 941.3, 1111.0, 1249.9, 1427.3, 1695.4 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{30}H_{37}O_3Si_2$, 501.2287; found, 501.2288.

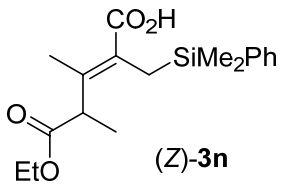
(*Z*)-5-(*tert*-butyldimethylsilyl)oxy-3,4-dimethyl-2-(dimethyl(phenyl)silyl)methylpent-2-enoic acid ((*Z*)-**3m**)



(*Z*)-**3m**

Purified by column chromatography (eluent: hexane/EtOAc = 7:1 then 4:1). Colorless oil (61.8 mg, 76%, isomeric purity > 99%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.55–7.53 (m, 2H), 7.36–7.33 (m, 3H), 3.50–3.41 (m, 2H), 2.78–2.69 (m, 1H, C=CC*H*), 2.23 (d, *J* = 14.5 Hz, 1H, C*H*$_2$Si), 2.11 (d, *J* = 14.5 Hz, 1H, C*H*$_2$Si), 1.87 (s, 3H), 0.89 (s, 9H), 0.80 (d, *J* = 6.8 Hz, 3H), 0.34 (s, 3H, Si*Me*$_2$Ph), 0.32 (s, 3H, Si*Me*$_2$Ph), 0.03 (s, 6H, Si*Me*$_2$*t*Bu). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 175.8, 146.3, 138.8, 133.7, 129.0, 127.7, 125.2, 65.7, 39.8, 25.9, 18.9, 18.2, 15.6, 14.0, –2.7, –3.0, –5.5. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: 19.3, –3.5. **IR** (ATR): 727.2, 775.4, 833.3, 1006.8, 1037.7, 1093.6, 1112.9, 1166.9, 1249.9, 1298.1, 1427.3, 1471.7, 1681.9, 2858.5, 2955.0 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{22}H_{37}O_3Si_2$, 405.2287; found, 405.2285. The (*Z*)-configuration was further confirmed by 2D NOESY measurement.

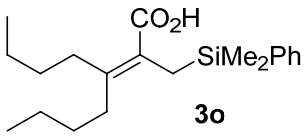
(*Z*)-3,4-dimethyl-2-(dimethyl(phenyl)silyl)methylpent-2-enedioic acid-5-ethyl ester ((*Z*)-**3n**)



(*Z*)-**3n**

Purified by column chromatography (eluent: hexane/EtOAc = 4:1 then 2:1). Colorless oil (46.0 mg, 69%, isomeric purity > 96%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.56–7.50 (m, 2H), 7.37–7.31 (m, 3H), 4.16–4.08 (m, 2H), 3.43 (q, *J* = 7.1 Hz, 1H, C*H*CO_2Et), 2.23 (d, *J* = 14.5 Hz, 1H, C*H*$_2$Si), 2.09 (d, *J* = 14.5 Hz, 1H, C*H*$_2$Si), 1.90 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.05 (d, *J* = 7.2 Hz, 3H), 0.35 (s, 3H), 0.33 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 175.2, 173.3, 142.3, 138.4, 133.6, 129.1, 127.8, 126.5, 60.8, 43.7, 19.4, 16.7, 14.1, 14.1, –2.9, –2.9. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –3.3. **IR** (ATR): 1112.9, 1193.9, 1249.9, 1300.0, 1427.3, 1683.9, 1734.0 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{18}H_{25}O_4Si$, 333.1528; found, 333.1532. The (*Z*)-configuration was further confirmed by 2D NOESY measurement.

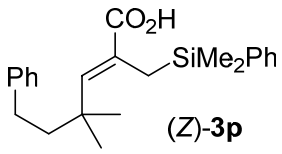
2-(dimethyl(phenyl)silyl)methyl-3-butylhept-2-enoic acid (**3o**)



3o

Purified by flash column chromatography (eluent: hexane/EtOAc = 7:1). Colorless oil (56.2 mg, 86%, isomeric purity > 98%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54–7.50 (m, 2H), 7.35–7.31 (m, 3H), 2.34–2.30 (m, 2H), 2.03 (s, 2H, C*H*$_2$Si), 1.87–1.83 (m, 2H), 1.43–1.22 (m, 8H), 0.91 (t, *J* = 7.0 Hz, 3H), 0.85 (t, *J* = 7.0 Hz, 3H), 0.31 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 175.3, 151.4, 138.9, 133.6, 128.9, 127.7, 123.3, 34.0, 33.9, 31.5, 29.6, 23.1, 23.1, 19.0, 13.9, 13.9, –2.8. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –3.2. **IR** (ATR): 725.2, 833.3, 1112.9, 1249.9, 1681.9, 2956.9 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{20}H_{31}O_2Si$, 331.2099; found, 331.2103.

(*Z*)-2-(dimethyl(phenyl)silyl)methyl-4,4-dimethyl-6-phenylhex-2-enoic acid ((*Z*)-**3p**)



(*Z*)-**3p**

Purified by flash column chromatography (eluent: hexane/EtOAc = 7:1). Colorless oil (65.8 mg, 89%, isomeric purity > 96%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54–7.50 (m, 2H), 7.34–7.31 (m, 3H), 7.28–7.24 (m, 2H), 7.18–7.12 (m, 3H), 6.76 (s, 1H), 2.53–2.49 (m, 2H), 2.20 (s, 2H), 1.68–1.64 (m, 2H), 1.11 (s, 6H), 0.36 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 175.3, 148.7, 142.6, 139.0, 133.7, 129.0, 128.5, 128.3, 128.3, 127.7, 125.7, 46.1, 36.8, 31.4, 28.0, 17.0, –2.1. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: –3.2. **IR** (ATR): 729.1, 827.5, 1112.9, 1166.9, 1207.4, 1280.7, 1456.3, 1680.0, 2958.8 cm^{-1}. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{23}H_{29}O_2Si$, 365.1942; found, 365.1945. The (*Z*)-configuration was further confirmed by 2D NOESY measurement.

2-4-8. X-ray Diffraction Studies of (*Z*)-3h

Data were collected on a Rigaku/Saturn70 CCD diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.71070 Å) at 153 K, and processed using CrystalClear (Rigaku). The structure was solved by direct methods (SIR97) and refined by full-matrix least-square refinement on F^2. The non-hydrogen atoms were refined anisotropically. All hydrogen atoms were located on the calculated positions and not refined. All calculations were performed using the CrystalStructure crystallographic software package.

Crystal data for (*Z*)-**3h**: $C_{19}H_{29}O_2Si$, M = 317.52, triclinic, space group = P-1 (#2), a = 6.799(2) Å, b = 17.085(5) Å, c = 17.516(5) Å, α = 68.123(11)°, β = 83.06(2)°, γ = 77.86(2)°, V = 1843.9(10) Å^3, Z = 4, density (calc.) = 1.325, unique reflections = 8093 (R_{int} = 0.0457), GOF = 1.052. The final $R1$ factor was 0.0795 ($I>2\sigma(I)$) ($wR2$ = 0.2242, all data).

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(15) Besides entries in Tables 2-2, four allenes (**1m**–**p**) including those bearing silyl ether (**1m**) and ester (**1n**) groups also provided the corresponding allylsilanes (**3m**–**p**) selectively in high yields under Conditions B.

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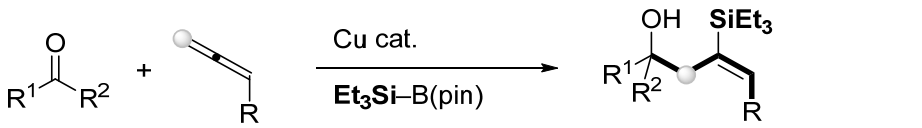
Chapter 3

Copper-Catalyzed Silylative Allylation of Ketones and Aldehydes Employing Allenes and Silylboranes

The copper-catalyzed silylative allylation of ketones with allenes and silylboranes via an in situ generated β-silyl allylcopper intermediate has been developed. Various ketones and allenes were converted to the homoallylic tertiary alcohols bearing internal (*E*)-vinylsilane moieties regio- and stereoselectively in good to high yields. Aldehydes were also employed as electrophiles in the reaction.

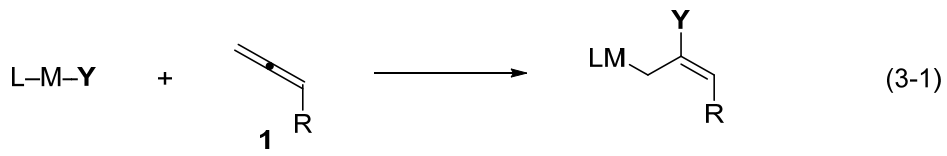


51–86% yield

regio- & stereoselective allylation

3-1. Introduction

The addition of allylic metal reagents (Mg, Zn, B, Si, Sn) to carbonyl compounds is an important class of carbon–carbon bond-forming reactions because of the versatility of homoallylic alcohols in organic synthesis.[1] However, these reagents should be prepared before use. In this regard, much attention has been paid to *catalytic in situ* generation of allylic metal nucleophiles, especially via the addition of transition-metal species (LM–Y) across allenes (eq 3-1). Namely, the catalytic generation of *β*-functionalized allylcopper intermediates and successive use in catalytic transformations have been achieved using a diboron ($B_2(pin)_2$) (M = Cu, Y = B(pin) in eq 3-1)[2,3] or a silylborane ($PhMe_2Si$–B(pin)) (M = Cu, Y = $SiMe_2Ph$ in eq 3-1)[4]. Tsuji et al. have utilized this protocol in the copper-catalyzed hydroboration of allenes,[2a] synthesis of 2-boryl-1,3-butadienes,[2b] and borylative allylation of allylic phosphates.[2c] Recently, the hydrosilylation of electron-deficient allenes employing $PhMe_2Si$–B(pin) and MeOH was reported by Xu and Loh.[4a] In addition, as described in Chapter 2, the author developed the copper-catalyzed regiodivergent silacarboxylation of allenes employing $PhMe_2Si$–B(pin) and CO_2.[4c]

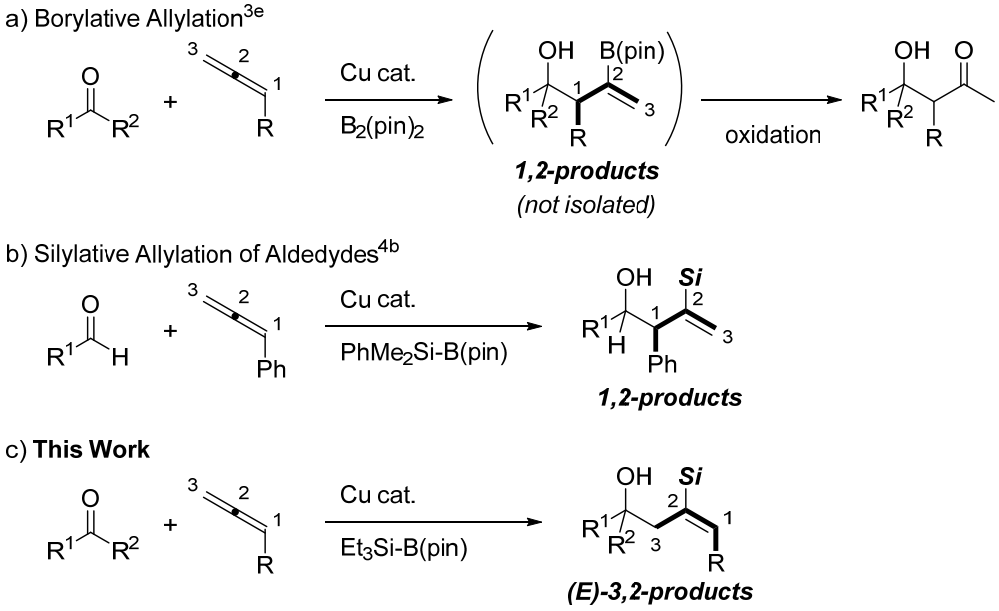


(3-1)

These catalytic generations of *β*-boryl or *β*-silyl allylcopper intermediates have been utilized in the carbonyl allylation reactions. Hoveyda and co-workers reported the copper-catalyzed borylative allylation of aldehydes and ketones.[3e] In the reaction, the vinylboron products were unstable and the products were isolated after oxidation or bromination of the boron moieties (Scheme 3-1a). Procter reported the copper-catalyzed *silylative* allylation of aldehydes using $PhMe_2Si$–B(pin) as a silicon source. However, they employed the only one allene substrate, 1-phenylallene, in the reaction with *aldehydes* as electrophile, and no reactions were carried out with less reactive ketones (Scheme 3-1b).[4b] Importantly, in both the reactions, the electrophiles reacted at the 1-position of allenes, and the boryl or the silyl moieties were incorporated at their 2-position to provide corresponding homoallylic alcohols (1,2-products; Scheme 3-1a and 3-1b).

Herein, the author reports the copper-catalyzed silylative allylation of *ketones* employing allenes and silylboranes (Scheme 3-1c). Unlike the previous cases (Scheme 3-1a and 3-1b), the electrophiles (ketones) reacted at the 3-position of allenes regioselectively to afford various homoallylic alcohols bearing internal (*E*)-vinylsilane moieties[5] ((*E*)-3,2-products; Scheme 3-1c). Aldehydes also reacted at the 3-position of an allene preferentially.

Scheme 3-1. Cu-Catalyzed Bolylative or Silylative Alllylation of Ketones and/or Aldehydes

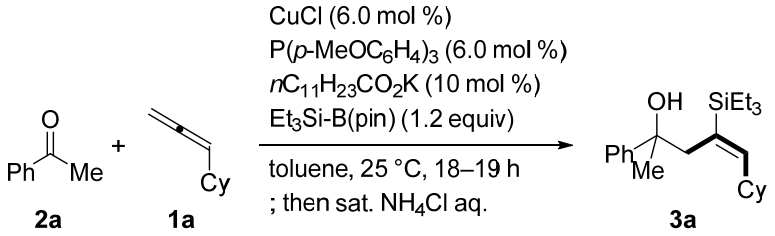


3-2. Results and Discussion

First, the reaction of acetophenone (**2a**) with 1-cyclohexylallene (**1a**) and (triethylsilyl)pinacolborane (Et_3Si–B(pin))[6] was carried out in the presence of a catalytic amount of CuCl (6.0 mol %), a ligand (6.0 mol %) and potassium laurate ($nC_{11}H_{23}COOK$, 10 mol %) in toluene at 25 °C (Table 3-1, entries 1–6). P(*p*-$MeOC_6H_4$)$_3$ was found to be the most effective, affording (*E*)-homoallylic alcohol **3a** in 87% GC yield and in 80% isolated yield (standard reaction conditions: entry 1). Notably, **2a** reacted at the 3-position of **1a**, and any other isomers were not detected at all in the reaction mixture. PPh_3 as the ligand afforded **3a** in 81% yield, while P(*p*-FC_6H_4)$_3$, P(*o*-$MeOC_6H_4$)$_3$ and PCy_3 were not effective (entries 2–5). Bidentate phosphines such as dppp provided the product in

diminished yield (entry 6). When the ligand or potassium laurate was removed from the catalyst system, almost no **3a** was obtained (entries 7 and 8). When potassium acetate was used instead of potassium laurate, **3a** was obtained in lower yield, possibly owing to its poor solubility (entry 9). THF was also a good solvent (entry 10).

Table 3-1. Optimization of Reaction Conditions for the Copper-Catalyzed Silylative Allylation of Acetophenone **2a** with Allene **1a**[a]

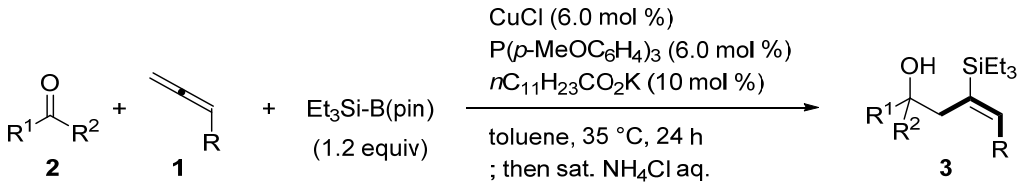


entry	change from the conditions	yield of **3a** (%)[b]
1	none	87 (80)[c]
2	PPh_3 instead of P(*p*-$MeOC_6H_4$)$_3$	81
3	P(*p*-FC_6H_4)$_3$ instead of P(*p*-$MeOC_6H_4$)$_3$	44
4	P(*o*-$MeOC_6H_4$)$_3$ instead of P(*p*-$MeOC_6H_4$)$_3$	49
5	PCy_3 instead of P(*p*-$MeOC_6H_4$)$_3$	13
6	dppp instead of P(*p*-$MeOC_6H_4$)$_3$	37
7	without P(*p*-$MeOC_6H_4$)$_3$	2
8	without *n*$C_{11}H_{23}COOK$	0
9	AcOK instead of *n*$C_{11}H_{23}COOK$	61
10	in THF, not in toluene	86

[a] Conditions: **1a** (0.25 mmol), **2a** (0.28 mmol), Et_3Si–B(pin) (0.30 mmol), CuCl (15 μmol, 6.0 mol %), P(*p*-$MeOC_6H_4$)$_3$ (15 μmol, 6.0 mol %), *n*$C_{11}H_{23}CO_2K$ (25 μmol, 10 mol %), in toluene (0.25 mL) at 25 °C for 18–19 h. [b] Determined by GC. [c] Isolated yield of **3a**.

Next, the reaction of various ketones (**2a**–**j**) and allenes (**1a**–**e**) was performed at 35 °C for 24 h (Table 3-2). Under the conditions, **3a** was isolated in 85% (entry 1; cf. entry 1 in Table 3-1). Acetophenone derivatives with electron-donating (**2b**) and withdrawing (**2c**–**e**) substituents were smoothly reacted with **1a** and the corresponding products (**3b**–**e**) were obtained in good to high yields (entries 2–5). Dialkyl ketones (**2f**, **2g** and **2j**) were

Table 3-2. Copper-Catalyzed Silylative Allylation of Ketones (**2**) Employing Allenes (**1**)[a]



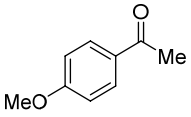
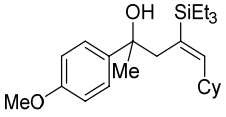
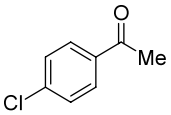
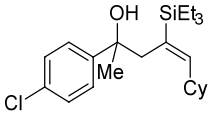
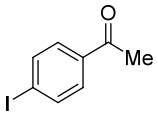
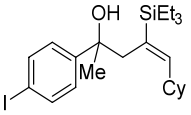
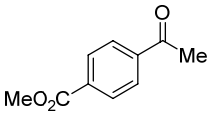
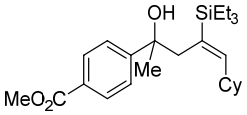
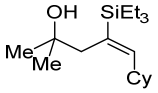
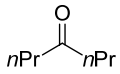
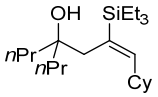
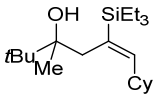
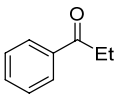
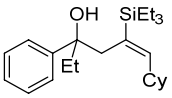
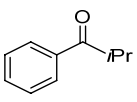
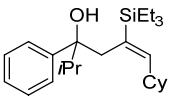
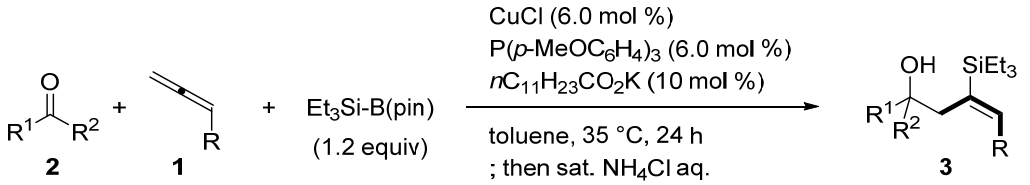
entry	ketone (**2**)		allene (**1**)	product (**3**)		yield (%)[b]
1	**2a**		**1a**	**3a**		85
2		**2b**	**1a**		**3b**	83
3		**2c**	**1a**		**3c**	86
4		**2d**	**1a**		**3d**	66
5		**2e**	**1a**		**3e**	72
6		**2f**	**1a**		**3f**	58
7		**2g**	**1a**		**3g**	66
8		**2h**	**1a**		**3h**	51
9		**2i**	**1a**		**3i**	74
10		**2j**	**1a**		**3j**	66

Table 3-2. Copper-Catalyzed Silylative Allylation of Ketones (**2**) Employing Allenes (**1**)[a] (continued)



entry	ketone (**2**)	allene (**1**)	product (**3**)	yield (%)[b]
11[c]	**2a**	**1b**	**3k**	67
12	**2a**	**1c**	**3l**	66[d]
13[e]	**2a**	**1d**	**3m**	62
14[c]	**2a**	**1e**	**3n**	67

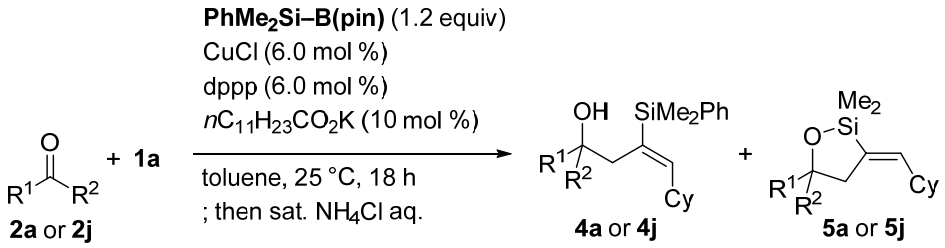
[a]Conditions: **2** (0.28 mmol), **1** (0.25 mmol), Et_3Si–B(pin) (0.30 mmol), CuCl (15 μmol, 6.0 mol %), P(*p*-$MeOC_6H_4)_3$ (15 μmol, 6.0 mol %), *n*$C_{11}H_{23}CO_2K$ (25 μmol, 10 mol %), toluene (0.25 mL), at 35 °C for 24 h. [b]Isolated yield of **3**. [c]At 25 °C. [d]A mixture of ca. 1:1 diastereomers. [e]CuCl (12 mol %), P(*p*-$MeOC_6H_4)_3$ (12 mol %) and *n*$C_{11}H_{23}CO_2K$ (15 mol %) were used.

also converted to the homoallylic alcohols (**3f**, **3g** and **3j**) efficiently (entries 6, 7 and 10). Propiophenone **2h** or more congested ketones (**2i** and **2j**) also provided the homoallylic alcohols (**3h**–**j**) in good yields (entries 8–10). Various 1-monosubstituted allenes (**1b**–**e**) reacted with **2a** or **2j** to provide the corresponding products (**3k**–**n**) in good isolated yields (entries 11–14). Unfortunately, 1-phenylallene, 1,1-*di*-, and 1,3-*di*substituted allenes did not give the desired products selectively.

As for the silylborane, commercially available $PhMe_2Si$–B(pin) was also employed in the reaction (Scheme 3-2). The reaction of **2a** with **1a** smoothly proceeded to give the corresponding homoallylic alcohol (**4a**) in 72% isolated yield with dppp as the ligand

(Scheme 3-2a). In contrast, the reaction of a bulky ketone (**2j**) with **1a** afforded a cyclic silyl ether (**5j**) along with the elimination of the phenyl substituent on the silicon atom (Scheme 3-2b). Similar cyclization extruding the phenyl moiety on the Si has been observed in the copper-catalyzed silacarboxylation of alkynes, giving silalactones as products.[7]

Scheme 3-2. Reaction with $PhMe_2Si$–B(pin) in Place of Et_3Si–B(pin)

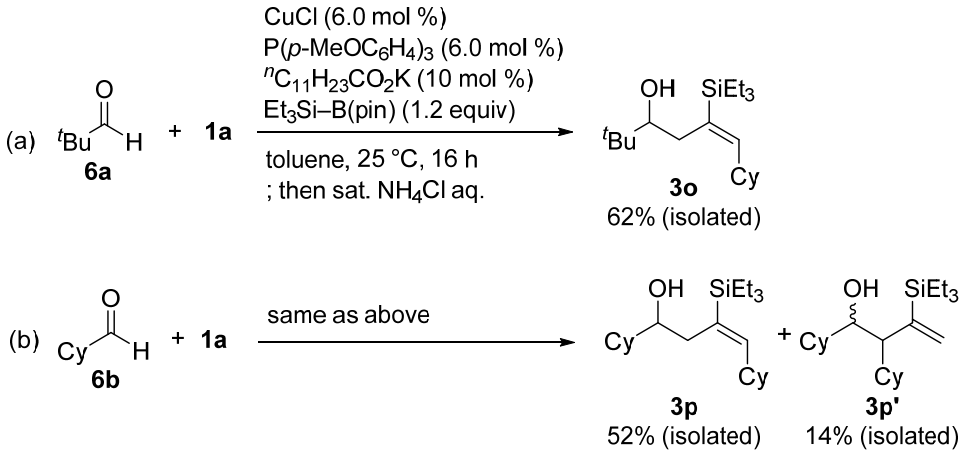


(a) **2a** (R^1 = Ph, R^2 = Me): **4a** (72%) + **5a** (trace)

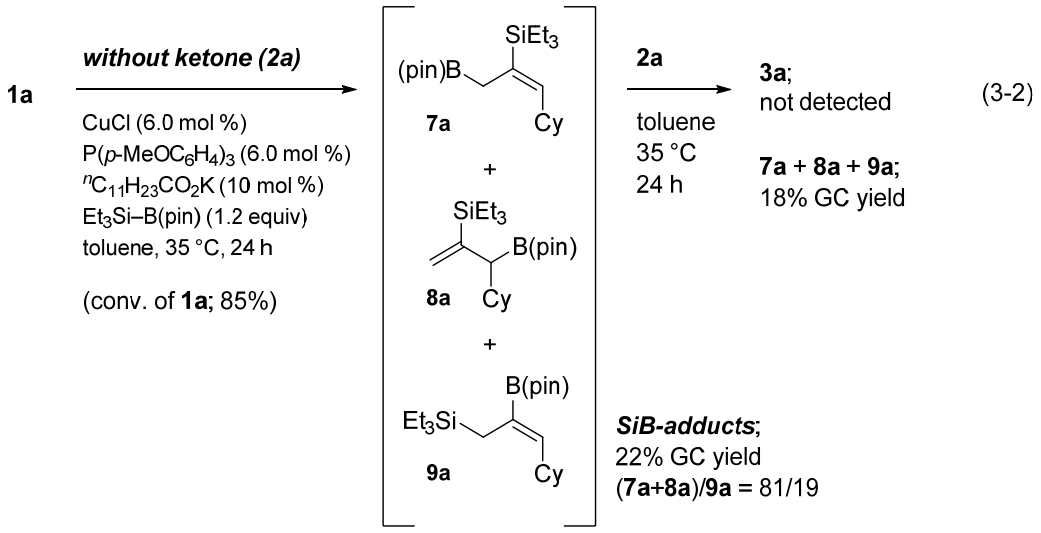
(b) **2j** (R^1 = *t*Bu, R^2 = Me): **4j** (trace) + **5j** (59%)

Besides ketones, aldehydes also afforded the corresponding (*E*)-homoallylic alcohols (Scheme 3-3). The reaction employing a bulky pivalaldehyde (**6a**) afforded the corresponding adduct (**3o**) regioselectively in high isolated yield (Scheme 3-3a). Less congested cyclohexanecarbaldehyde (**6b**) gave a mixture of regioisomers (**3p** and **3p'**). Each isomer was isolated in 52% and 14% yields, respectively (Scheme 3-3b).

Scheme 3-3. Reaction of **1a** with Aldehydes

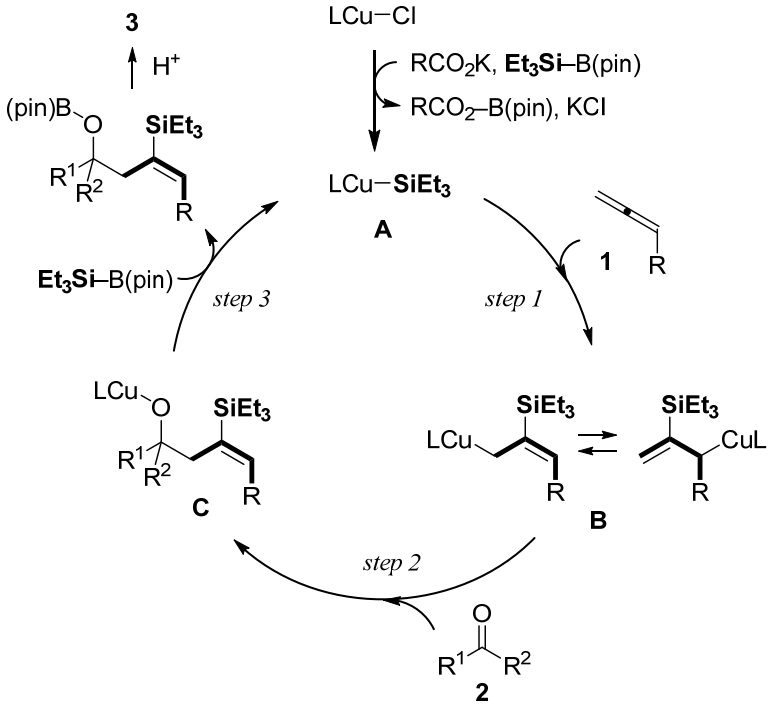


There might be some possibilities that the present silylative allylation of ketones proceeds via silaboration of allenes with silylboranes.[9] Therefore, the reaction of allene **1a** and Et_3Si–B(pin) was carried out without ketone **2a** under otherwise the same conditions as in Table 3-2 (eq 3-2). As a result, the adducts of Et_3Si–B(pin) with **1a** (**7a**, **8a** and **9a**) were afforded as a mixture in only 22% yield (by GC) with (**7a**+**8a**)/**9a** = 81/19 ratio. Moreover, subsequent addition of acetophenone **2a** into the resulting mixture of the adducts **7a**, **8a** and **9a** did not afford **3a** at all, and most of the adducts remained unchanged. Thus, these observations clearly indicate that the silylative allylation of ketones does not proceed via the silaboration of allenes.[9]



A possible catalytic cycle is shown in Scheme 3-4. The silylcopper species (**A**) is generated by the reaction of a silylborane with carboxylatocopper species, which is formed from CuCl, phosphine (L), and potassium laurate.[10] An allene (**1**) reacts with **A** to generate the *β*-silyl allylcopper intermediate (**B**) (step 1). Subsequently, the allylation of a ketone (**2**) with **B** proceeded regio- and stereoselectively, giving the alcoxycopper intermediate **C** (step 2). The formation of the C–C bond at the less sterically hindered site would reflect the bulkiness of the ketone and the internal carbon of allene. Finally, the reaction of **C** with the silylborane provides the borylester of the alcohol (**3**) as the product and regenerates **A** (step 3).

Scheme 3-4. A Possible Catalytic Cycle



3-3. Conclusion

The author developed a copper-catalyzed silylative allylation of ketones with allenes and silylboranes, providing homoallylic alcohols bearing internal (*E*)-vinylsilane moieties. In the reaction, the *β*-silyl allylcopper intermediate is catalytically generated in situ and successfully adds to ketones regio- and stereoselectively.

3-4. Experimental Section

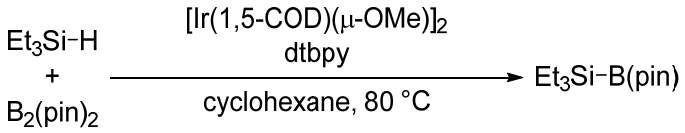
3-4-1. General Remarks

Unless otherwise noted, reactions were performed under an argon atmosphere using heat-gun-dried glassware on a dual-manifold Schlenk line. ^{1}H, ^{13}C and ^{29}Si NMR spectra were recorded on a JEOL ECX-400P spectrometer or a Bruker AVANCE-500 spectrometer. Chemical shift values (δ) are reported in ppm and calibrated to tetramethylsilane (TMS, 0.00 ppm) or residual solvent (7.26 ppm in $CDCl_3$) for ^{1}H, to $CDCl_3$ (77.0 ppm) for ^{13}C, and to tetramethylsilane (TMS, 0.00 ppm) for ^{29}Si. EI-MS spectra were recorded on a Shimadzu GCMS-QP2010. High-resolution mass spectra were obtained with: a Thermo Fischer Scientific EXACTIVE spectrometer for

APCI-HRMS, and a JEOL JMX-SX 102A spectrometer for ESI-HRMS. GC analysis was carried out using a Shimadzu GC-2014 equipped with a capillary column (GL Sciences InertCap 5, 0.25 mm × 30 m). TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck Silica gel $60F_{254}$. Column chromatography was carried out on silica-gel (Kanto N60, spherical, neutral, 63–210 μm). Medium pressure liquid chromatography (MPLC) was performed on a Biotage Isorera One with a silica-gel column (Biotage SNAP Ultra 25 g or 10 g, HP-Sphere 25 μm).

Anhydrous THF and toluene were purchased from Kanto Chemical Co., Inc. and further purified by passage through activated alumina under positive argon pressure as described by Grubbs et al.[10] PPh_3 was purified by recrystallization prior to use. **6b** was purified by distillation. Unless otherwise noted, chemicals obtained from commercial suppliers were used without further purification. Allenes **1a–e** and $PhMe_2Si$–B(pin) were synthesized according to the literatures.[11,12]

3-4-2. Preparation of Triethylsilylboronic Acid Pinacol Ester, Et_3Si-B(pin)[6a]



To a 100 mL 2-neck flask were added $B_2(pin)_2$ (5.08 g, 20.0 mmol), triethylsilane (12.8 mL, 80.0 mmol), $[Ir(1,5\text{-cod})(\mu\text{-OMe})]_2$ (66.3 mg, 0.100 mmol), dtbpy (53.7 mg, 0.200 mmol), and cyclohexane (20.0 mL). The flask was heated to 80 °C and stirred overnight. The mixture was cooled down to room temperature and dried in vacuo. The crude mixture was purified by silica-gel column chromatography (eluent: hexane/EtOAc = 15:1). The crude mixture was distilled to give triethylsilylboronic acid pinacol ester as a clear colorless liquid (3.0 g, 62%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 1.23 (s, 12H), 0.97 (t, J = 7.9 Hz, 9H), 0.59 (q, J = 7.9 Hz, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 82.9, 25.0, 8.3, 2.9. All the resonances in ^{1}H and ^{13}C NMR spectra were in good agreement with literature values.

3-4-3. Experimental Procedures

Typical Procedure for the Copper-Catalyzed Silylative Allylation of Acetophenone with Cyclohexylallene (Table 3-1, entry 1)

To a Schlenk tube filled with Ar was added copper(I) chloride (1.5 mg, 15 μmol), P(*p*-$MeOC_6H_4)_3$ (5.3 mg, 15 μmol), and $nC_{11}H_{23}CO_2K$ (6.0 mg, 25 μmol). The tube was dried, then evacuated and backfilled with Ar three times. To this Schlenk tube was added toluene (0.25 mL), cyclohexylallene (**1a**) (37 μL, 0.25 mmol), acetophenone (**2a**) (32 μL, 0.28 mmol) and Et_3Si–B(pin) (84 μL, 0.30 mmol) in this order. The system was closed, and the mixture was stirred at 25 °C for 19 h. After tridecane (50 μL) was added as an internal standard, the reaction was

quenched by adding hexane (2 mL) and 1N NH_4Cl aq. (2 mL). The resulting mixture was stirred for 1 h. The mixture was diluted with hexane (8 mL), and then an aliquot of the organic phase was filtered through a pad of Celite. The filtrate was analyzed by GC (**3a**: 87% yield). Aqueous phase was extracted with hexane (2 mL × 3), and the combined organic extracts were dried over $MgSO_4$, then filtered and evaporated. The residue was purified by column chromatography (eluent: hexane/EtOAc = 50:1) to give **3a** (71.5 mg, 80%) as a white opaque oil. The stereochemistry of the product **3a** was determined by 2D NMR.

Typical Procedure for Table 3-2

To a Schlenk tube filled with Ar was added copper(I) chloride (1.5 mg, 15 μmol), P(*p*-$MeOC_6H_4)_3$ (5.3 mg, 15 μmol), and $nC_{11}H_{23}CO_2K$ (6.0 mg, 25 μmol). The tube was dried, then evacuated and backfilled with Ar three times. To this Schlenk tube was added toluene (0.25 mL), allene (**1**) (0.25 mmol), ketone (**2a**) (0.28 mmol) and Et_3Si–B(pin) (84 μL, 0.30 mmol) in this order. The system was closed, and then the mixture was stirred at 35 °C for 24 h. After tridecane (50 μL) was added as an internal standard, the reaction was quenched by adding hexane (2 mL) and 1N NH_4Cl aq. (2 mL). The resulting mixture was stirred for 1 h. The mixture was diluted with hexane (8 mL), and then an aliquot of the organic phase was filtered through a pad of Celite. The filtrate was analyzed by GC. Aqueous phase was extracted with hexane (2 mL × 3), and the combined organic extracts were dried over $MgSO_4$ or Na_2SO_4, then filtered and evaporated. The residue was purified by column chromatography or MPLC. The stereochemistry of the products **3b**–**3n** was determined by 2D NMR measurements in a similar manner for **3a**.

Typical Procedure for Scheme 3-2

To a Schlenk tube filled with Ar was added copper(I) chloride (1.5 mg, 15 μmol), dppp (6.2 mg, 15 μmol), and $nC_{11}H_{23}CO_2K$ (6.0 mg, 25 μmol). The tube was dried, then evacuated and backfilled with Ar three times. To this Schlenk tube was added toluene (0.25 mL), cyclohexylallene (**1a**) (37 μL, 0.25 mmol), ketone (**2a** or **2j**) (0.28 mmol) and $PhMe_2Si$–B(pin) (82 μL, 0.30 mmol) in this order. The system was closed, and then the mixture was stirred at 35 °C for 24 h. After tridecane (50 μL) was added as an internal standard, the reaction was quenched by adding hexane (2 mL) and 1N NH_4Cl aq. (2 mL). The resulting mixture was stirred for 1 h. The mixture was diluted with hexane (8 mL), and then an aliquot of the organic phase was filtered through a pad of Celite. The filtrate was analyzed by GC. Aqueous phase was extracted with hexane (2 mL × 3), and the combined organic extracts were dried over Na_2SO_4, then filtered and evaporated. The residue was purified by MPLC. The stereochemistry of the products was determined by 2D NMR measurements.

Typical Procedure for Scheme 3-3

To a Schlenk tube filled with Ar was added copper(I) chloride (1.5 mg, 15 μmol), P(*p*-

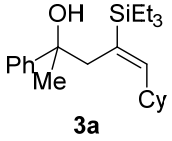
$MeOC_6H_4)_3$ (5.3 mg, 15 μmol), and $nC_{11}H_{23}CO_2K$ (6.0 mg, 25 μmol). The tube was dried, then evacuated and backfilled with Ar three times. To this Schlenk tube was added toluene (0.25 mL), cyclohexylallene (**1**) (37 μL, 0.25 mmol), aldehyde (**6**) (0.28 mmol) and Et_3Si–B(pin) (84 μL, 0.30 mmol) in this order. The system was closed, and the mixture was stirred at 35 °C for 24 h. After tridecane (50 μL) was added as an internal standard, the reaction mixture was quenched by adding hexane (2 mL) and 1N NH_4Cl aq. (2 mL). The resulting mixture was stirred for 1 h. The mixture was diluted with hexane (8 mL), and then an aliquot of the organic phase was filtered through a pad of Celite. The filtrate was analyzed by GC. Aqueous phase was extracted with hexane (2 mL × 3), and the combined organic extracts were dried over Na_2SO_4, then filtered and evaporated. The residue was purified by column chromatography or MPLC. The stereochemistry of the products was determined by 2D NMR measurements in a similar manner for **3a**.

Procedure for eq 3-2.

To a Schlenk tube filled with Ar was added copper(I) chloride (1.5 mg, 15 μmol), P(*p*-$MeOC_6H_4)_3$ (5.3 mg, 15 μmol), and $nC_{11}H_{23}CO_2K$ (6.0 mg, 25 μmol). The tube was dried, then evacuated and backfilled with Ar three times. To this Schlenk tube was added toluene (0.25 mL), cyclohexylallene (**1a**) (37 μL, 0.25 mmol), Et_3Si–B(pin) (84 μL, 0.30 mmol), and tridecane (50 μL) as an internal standard in this order. The system was closed, and then the mixture was stirred at 35 °C for 24 h. A small aliquot (2 μL) was taken out from the reaction mixture at a suitable interval. The sample was diluted with hexane (1.0 mL) and the conversion of **1a** as well as the amount of the silaborated products (**7a**, **8a**, and **9a**) was analyzed by GC and GC-MS. Then, acetophenone (**2a**) (32 μL, 0.28 mmol) was added to the reaction mixture, and further stirred at 35 °C for 24 h. After the reaction mixture was quenched by adding hexane (2 mL) and 1N NH_4Cl aq. (2 mL), the resulting mixture was stirred for 1 h. The mixture was diluted with hexane (8 mL), and then an aliquot of the organic phase was filtered through a pad of Celite. The filtrate was analyzed by GC. The structures of allylsilanes and vinylsilane were determined by ^1H and ^{29}Si NMR measurements.

3-4-4. Characterization of the Homoallylic Alcohols

(*E*)-5-cyclohexyl-2-phenyl-4-(triethylsilyl)pent-4-en-2-ol (**3a**)

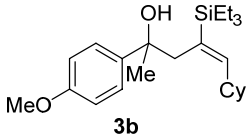


3a

Purified by column chromatography (eluent: hexane/EtOAc = 50:1). White opaque oil (76.1 mg, 85%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.48–7.45 (m, 2H), 7.35–7.30 (m, 2H), 7.24–7.19 (m, 1H), 5.73 (d, *J* = 9.5 Hz, 1H), 2.66 (d, *J* = 13.6 Hz, 1H), 2.60 (d, *J* = 13.6 Hz, 1H), 2.26 (tdt, *J* = 11.3, 9.5, 3.9 Hz, 1H), 1.88 (s, 1H), 1.72–1.50 (m, 7H), 1.30–0.92 (m, 6H), 0.87 (t, *J* = 7.7 Hz, 9H), 0.60–0.43 (m, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 154.2, 149.2, 129.0, 128.0, 126.4, 74.0, 43.9, 38.3, 32.7, 30.4, 26.0, 25.8, 7.4, 3.5. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.5. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for

$C_{23}H_{38}OSi$, 381.2584; found, 381.2569.

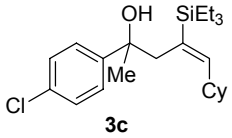
(*E*)-5-cyclohexyl-2-(4-methoxyphenyl)-4-(triethylsilyl)pent-4-en-2-ol (**3b**)



3b

Purified by column chromatography (eluent: hexane/EtOAc = 50:1). Colorless oil (80.3 mg, 83%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.41–7.35 (m, 2H), 6.89–6.83 (m, 2H), 5.72 (d, *J* = 9.5 Hz, 1H), 3.79 (s, 3H), 2.63 (d, *J* = 13.5 Hz, 1H), 2.57 (d, *J* = 13.5 Hz, 1H), 2.23 (tdt, *J* = 11.1, 9.5, 3.7 Hz, 1H), 1.83 (s, 1H), 1.72–1.57 (m, 3H), 1.57–1.48 (m, 4H), 1.32–0.92 (m, 6H), 0.87 (t, *J* = 7.7 Hz, 9H), 0.61–0.45 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 158.2, 154.0, 141.4, 129.1, 126.0, 113.3, 73.8, 55.2, 44.0, 38.2, 32.7, 32.7, 30.4, 26.0, 25.8, 7.4, 3.6. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.5. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{24}H_{40}O_2Si$, 411.2690; found, 411.2681.

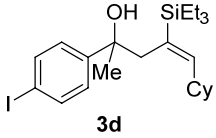
(*E*)-2-(4-chlorophenyl)-5-cyclohexyl-4-(triethylsilyl)pent-4-en-2-ol (**3c**)



3c

Purified by column chromatography (eluent: hexane/EtOAc = 50:1). Colorless oil (81.1 mg, 86%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.41–7.37 (m, 2H), 7.31–7.26 (m, 2H), 5.73 (d, *J* = 9.5 Hz, 1H), 2.62 (d, *J* = 13.6 Hz, 1H), 2.57 (d, *J* = 13.6 Hz, 1H), 2.18 (tdt, *J* = 11.2, 9.5, 3.5 Hz, 1H), 1.88 (s, 1H), 1.74–1.56 (m, 3H), 1.56–1.47 (m, 4H), 1.31–0.91 (m, 6H), 0.87 (t, *J* = 7.7 Hz, 9H), 0.62–0.44 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 154.4, 147.77, 132.3, 128.7, 128.0, 126.5, 73.8, 43.8. 38.4, 32.7, 32.7, 30.5, 26.0, 25.8, 25.8, 7.5, 3.6 . **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.6. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{23}H_{37}ClOSi$, 415.2194; found, 415.2190.

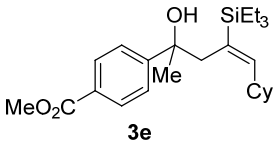
(*E*)-5-cyclohexyl-2-(4-iodophenyl)-4-(triethylsilyl)pent-4-en-2-ol (**3d**)



3d

Purified by MPLC (eluent: hexane/EtOAc = 24:1). Colorless oil (79.5 mg, 66%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.66–7.63 (m, 2H), 7.22–7.20 (m, 2H), 5.71 (d, *J* = 10.0 Hz, 1H), 2.61 (d, *J* = 14.0 Hz, 1H), 2.56 (d, *J* = 13.6 Hz, 1H), 2.15 (tdt, *J* = 10.9, 10.0, 3.5 Hz, 1H), 1.85 (s, 1H), 1.71–1.57 (m, 3H), 1.53–1.46 (m, 4H), 1.24–0.93 (m, 6H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.61–0.45 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 154.4, 148.9, 137.0, 128.6, 127.2, 91.8, 73.9, 43.7, 38.4, 32.7, 32.7, 30.4, 26.0, 25.8, 25.8, 7.4, 3.6. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.6. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{23}H_{37}IOSi$, 507.1551; found, 507.1544.

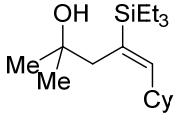
methyl (E)-4-(5-cyclohexyl-2-hydroxy-4-(triethylsilyl)pent-4-en-2-yl)benzoate (**3e**)



3e

Purified by MPLC (eluent: hexane/EtOAc = 24:1 to 19:1). Colorless oil (75.3 mg, 72%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.00 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 5.74 (d, *J* = 9.8 Hz, 1H), 3.91 (s, 3H), 2.67 (d, *J* = 13.4 Hz, 1H), 2.61 (d, *J* = 13.4 Hz, 1H), 2.21 (tdt, *J* = 11.1, 9.8, 3.6 Hz, 1H), 1.99 (s, 1H), 1.69–1.61 (m, 3H), 1.55–1.51 (m, 4H), 1.31–0.90 (m, 6H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.59–0.45 (m, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ:167.0, 154.6, 154.4, 129.4, 128.6, 128.3, 125.0, 74.1, 52.0, 43.6, 38.4, 32.6, 30.5, 25.9, 25.8, 25.7, 7.4, 3.5. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.6. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{25}H_{40}O_3Si$, 439.2639; found, 439.2634.

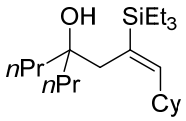
(*E*)-5-cyclohexyl-2-methyl-4-(triethylsilyl)pent-4-en-2-ol (**3f**)



3f

Purified by column chromatography (eluent: hexane/EtOAc = 50:1). Colorless oil (42.9 mg, 58%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.74 (d, *J* = 9.5 Hz, 1H), 2.43 (tdt, *J* = 11.2, 9.5, 3.6 Hz, 1H), 2.33 (s, 2H), 1.75–1.61 (m, 3H), 1.60–1.52 (m, 2H), 1.33 (s, 1H), 1.31–1.22 (m, 2H), 1.21 (s, 6H), 1.19–1.01 (m, 3H), 0.91 (t, *J* = 7.9 Hz, 9H), 0.62 (q, *J* = 7.9 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 153.1, 129.7, 70.9, 42.6, 38.1, 32.8, 30.1, 26.1, 25.8, 7.5, 3.8. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.3. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{18}H_{36}OSi$, 319.2428; found, 319.2424.

(*E*)-1-cyclohexyl-4-propyl-2-(triethylsilyl)hept-1-en-4-ol (**3g**)

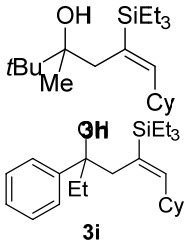


3g

Purified by column chromatography (eluent: hexane/EtOAc = 50:1). Colorless oil (58.0 mg, 66%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.75 (d, *J* = 9.5 Hz, 1H), 2.41 (tdt, *J* = 11.1, 9.5, 3.6 Hz, 1H), 2.29 (s, 2H), 1.76–1.61 (m, 3H), 1.60–1.52 (m, 2H), 1.43–1.00 (m, 14H), 0.93–0.88 (m, 15H), 0.61 (q, *J* = 7.9 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 153.5, 129.5, 74.0, 41.9, 39.6, 38.2, 32.8, 26.1, 25.8, 17.0, 14.7, 7.5, 3.8. **^{29}Si NMR** (79 MHz, $CDCl_3$) δ: 2.4. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{22}H_{44}OSi$, 375.3054; found, 375.3049.

(*E*)-6-cyclohexyl-2,2,3-trimethyl-5-(triethylsilyl)hex-5-en-3-ol (**3h**)

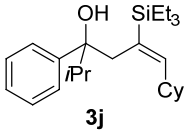
Purified by MPLC (eluent: hexane/EtOAc = 49:1). Colorless oil (43.3 mg, 51%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.75 (d, *J* = 9.5 Hz, 1H), 2.43–2.33 (m, 2H), 2.30 (d, *J* = 13.1 Hz, 1H), 1.69–1.58 (m, 5H), 1.30–1.06 (m, 6H), 1.04 (s, 3H), 1.00 (s, 9H), 0.91 (t, *J* = 7.9 Hz, 9H), 0.66–0.58 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 153.1, 130.4, 76.1, 38.2, 38.1, 35.2, 33.0, 32.6, 26.1, 26.0, 25.9, 25.5, 22.2, 7.5 3.8. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.4. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{21}H_{42}OSi$, 361.2897; found, 361.2891.



(*E*)-6-cyclohexyl-3-phenyl-5-(triethylsilyl)hex-5-en-3-ol (**3i**)

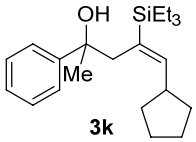
Purified by column chromatography (eluent: hexane/EtOAc = 50:1). Colorless oil (68.5 mg, 74%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.40–7.37 (m, 2H), 7.33–7.29 (m, 2H), 7.19 (tt, *J* = 7.2, 1.5 Hz, 1H), 5.71 (d, *J* = 9.5 Hz, 1H), 2.71 (d, *J* = 13.3 Hz, 1H), 2.63 (d, *J* = 13.3 Hz, 1H), 2.23 (tdt, *J* = 11.3, 9.5, 3.6 Hz, 1H), 1.97–1.87 (m, 2H), 1.81 (td, *J* = 14.2, 7.5 Hz, 1H), 1.71–1.49 (m, 4H), 1.29–0.87 (m, 6H), 0.83 (t, *J* = 7.9 Hz, 9H), 0.71 (t, *J* = 7.5 Hz, 3H), 0.55–0.33 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 154.8, 147.0, 128.6, 127.8, 126.2, 125.5, 76.2, 43.2, 38.3, 35.7, 32.7, 32.6, 26.0, 25.8, 25.8, 24.8, 8.0, 7.4, 3.4. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.6. **ESI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{24}H_{40}OSi$, 395.2741; found, 395.2739.

(*E*)-6-cyclohexyl-2-methyl-3-phenyl-5-(triethylsilyl)hex-5-en-3-ol (**3j**)



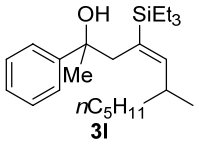
Purified by column chromatography (eluent: hexane/EtOAc = 50:1). Colorless oil (64.1 mg, 66%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.39–7.36 (m, 2H), 7.29–7.25 (m, 2H), 7.19–7.15 (m, 1H), 5.68 (d, *J* = 10.0 Hz, 1H), 2.93 (d, *J* = 13.1 Hz, 1H), 2.66 (d, *J* = 13.1 Hz, 1H), 2.25 (tdt, *J* = 11.0, 10.0, 3.4 Hz, 1H), 2.07 (sept, *J* = 6.8, 1H), 1.95 (s, 1H), 1.75–1.64 (m, 1H), 1.64–1.52 (m, 3H), 1.24–0.83 (m, 9H), 0.76 (t, *J* = 7.9 Hz, 9H), 0.69 (d, *J* = 6.8 Hz, 3H), 0.41–0.30 (m, 3H), 0.23–0.12 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ:155.5, 146.5, 128.6, 127.5, 126.2, 126.2, 77.3, 39.6, 38.9, 38.3, 32.8, 32.5, 26.0, 25.9, 25.8, 17.9, 17.2, 7.4, 3.1. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 3.0. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{25}H_{42}OSi$, 409.2897; found, 409.2893.

(*E*)-5-cyclopentyl-2-phenyl-4-(triethylsilyl)pent-4-en-2-ol (**3k**)



Purified by MPLC (eluent: hexane/EtOAc = 1:0 to 33:1). Colorless oil (58.0 mg, 67%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.48–7.45 (m, 2H), 7.34–7.30 (m, 2H), 7.24–7.19 (m, 1H), 5.84 (d, *J* = 9.5 Hz, 1H), 2.79 (tdt, *J* = 16.5, 9.5, 2.1 Hz, 1H), 2.71 (d, *J* = 13.5 Hz, 1H), 2.61 (d, *J* = 13.5 Hz, 1H), 1.92 (s, 1H), 1.79–1.52 (m, 8H), 1.28–0.94 (m, 3H), 0.86 (t, *J* = 7.9 Hz, 9H), 0.57–0.41 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 154.0, 149.2, 129.6, 128.0, 126.4, 124.8, 73.9, 43.8, 40.0, 33.5, 33.4, 30.4, 25.7, 25.6, 7.5, 3.5. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.4. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{22}H_{36}OSi$, 367.2428; found, 367.2424.

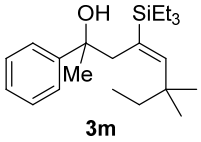
(*E*)-6-methyl-2-phenyl-4-(triethylsilyl)undec-4-en-2-ol (**3l**, diastereomixture)



3l

Purified by column chromatography (eluent: hexane/EtOAc = 50:1). Colorless oil (61.9 mg, 66%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.49–7.44 (m, 2H), 7.35–7.30 (m, 2H), 7.24–7.19 (m, 1H), 5.70 (dd, *J* = 9.5, 7.3 Hz, 1H), 2.76–2.44 (m, 3H), 1.86 (d, *J* = 5.8 Hz, 1H), 1.52 (d, *J* = 9.8 Hz, 3H), 1.30–1.06 (m, 8H), 0.99–0.81 (m, 14H), 0.77–0.72 (m, 1H), 0.63–0.41 (m, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 155.0, 155.0, 149.5, 149.2, 130.1, 129.9, 128.0, 128.0, 126.5, 126.5, 124.8, 124.8, 74.3, 74.1, 44.2, 44.1, 37.4, 37.4, 33.6, 33.5, 32.2, 30.6, 30.2, 27.1, 27.0, 22.6, 20.7, 20.6, 14.1, 7.5, 3.7, 3.5. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.7, 2.6. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{24}H_{42}OSi$, 397.2897; found, 397.2892.

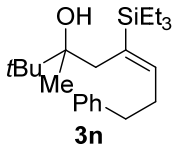
(*E*)-6,6-dimethyl-2-phenyl-4-(triethylsilyl)oct-4-en-2-ol (**3m**)



3m

Purified by MPLC (eluent: hexane/EtOAc = 49:1 to 19:1). Colorless oil (54.1 mg, 62%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.50–7.46 (m, 2H), 7.36–7.30 (m, 2H), 7.25–7.20 (m, 1H), 5.79 (s, 1H), 3.02 (d, *J* = 14.0 Hz, 1H), 2.62 (d, *J* = 14.0 Hz, 1H), 1.89 (s, 1H), 1.53 (s, 3H), 1.40–1.37 (m, 2H), 1.13 (d, *J* = 1.8 Hz, 6H), 0.90–0.81 (m, 12H), 0.60–0.42 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 156.3, 149.9, 131.1, 128.0, 126.5, 124.7, 73.5, 43.1, 39.8, 37.6, 30.6, 28.8, 28.2, 9.3, 7.5, 3.9. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 4.0. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{22}H_{38}OSi$, 369.2584; found, 369.2579.

(*E*)-2,2,3-trimethyl-8-phenyl-5-(triethylsilyl)oct-5-en-3-ol (**3n**)

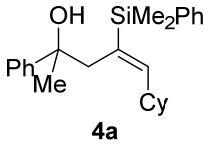


3n

Purified by column chromatography (eluent: hexane/EtOAc = 50:1). Colorless oil (60.3 mg, 67%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.29–7.23 (m, 2H), 7.20–7.14 (m, 3H), 6.00 (t, *J* = 6.8 Hz, 1H), 2.73–2.62 (m, 2H), 2.54–2.37 (m, 2H), 2.31 (d, *J* = 13.3 Hz, 1H), 2.27 (d, *J* = 13.3 Hz, 1H), 1.07 (s, 1H), 1.00 (s, 3H), 0.97 (s, 9H), 0.90 (t, *J* = 7.9 Hz, 9H), 0.66–0.58 (m, 6H).. **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 145.5, 142.0, 135.1, 128.5, 128.3, 125.8, 77.1, 38.3, 35.8, 35.4, 31.6, 25.5, 21.9, 7.5, 3.8 **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: 2.6. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{23}H_{40}OSi$, 383.2741; found, 383.2737.

(*E*)-5-cyclohexyl-4-(dimethylphenylsilyl)-2-phenylpent-4-en-2-ol (**4a**)

Purified by MPLC (eluent: hexane/EtOAc = 49:1 to 19:1). Colorless oil (67.8 mg, 72%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.53–7.47 (m, 2H), 7.36–7.23 (m, 7H), 7.21–7.15 (m, 1H), 5.88 (d, *J* = 9.5 Hz, 1H), 2.70 (d, *J* = 13.1 Hz, 1H), 2.63 (d, *J* = 13.6 Hz, 1H), 2.24 (tdt, *J* = 10.9, 10.0, 3.6 Hz, 1H), 1.74–1.52 (m, 5H), 1.41 (s, 3H), 1.30–0.86 (m, 6H), 0.33 (s, 3H), 0.28 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 154.2, 148.8, 139.8, 134.1, 131.3, 128.7, 127.9, 127.8, 126.3, 124.8, 74.4,

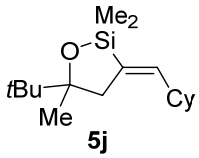


4a

44.0, 38.3, 32.5, 32.5, 30.0, 26.0, 25.8, 25.8, –1.6, –1.7 **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: –7.4. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{25}H_{34}OSi$, 401.2271; found, 401.2263.

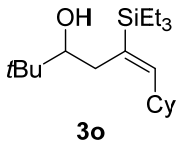
(*E*)-5-(*tert*-butyl)-3-(cyclohexylmethylene)-2,2,5-trimethyl-1,2-oxasilolane (**5j**)

Purified by MPLC (eluent: hexane/EtOAc = 49:1 to 19:1). Colorless oil (41.5 mg, 59%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.61 (ddd, *J* = 8.6, 2.9, 1.8 Hz, 1H), 2.51 (dd, *J* = 15.6, 2.9 Hz, 1H), 2.27–2.11 (m, 2H), 1.76–1.60 (m, 5H), 1.36–1.01 (m, 8H), 0.94 (s, 9H), 0.20 (s, 3H), 0.13 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 143.8, 138.2, 85.4, 39.6, 37.9, 37.7, 32.7, 32.5, 26.1, 25.9, 25.9, 25.4, 24.4, 0.9, 0.0. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 17.8. **APCI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{17}H_{32}OSi$, 281.2295; found, 281.2288.



5j

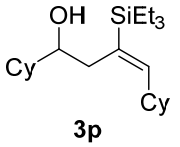
(*E*)-2,2-dimethyl-6-cyclohexyl-5-(triethylsilyl)hex-5-en-3-ol (**3o**)



3o

Purified by MPLC (eluent: hexane/EtOAc = 49:1 to 19:1). Colorless oil (50.7 mg, 62%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 5.78 (d, *J* = 9.5 Hz, 1H), 3.17 (d, *J* = 11.0 Hz, 1H), 2.47–2.35 (m, 2H), 2.15 (dd, *J* = 13.1, 1.5 Hz, 1H), 1.76–1.59 (m, 5H), 1.55 (d, *J* = 13.1 Hz, 1H), 1.34–1.22 (m, 2H), 1.21–1.02 (m, 3H), 0.95 (s, 9H), 0.92 (t, *J* = 7.9 Hz, 9H), 0.67–0.54 (m, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 152.6, 131.5, 77.1, 37.6, 34.7, 33.1, 33.0, 32.0, 26.0, 25.9, 25.8, 7.4, 3.4. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.2. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{20}H_{40}OSi$, 347.2741; found, 347.2737.

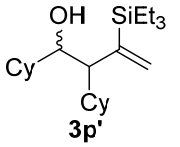
(*E*)-1,6-dicyclohexyl-3-(triethylsilyl)but-3-en-1-ol (**3p**)



3p

Purified by column chromatography (eluent: hexane/CH_2Cl_2 = 10:1 then 5:1). Colorless oil (45.6 mg, 52%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 5.76 (d, *J* = 9.5 Hz, 1H), 3.26 (ddd, *J* = 10.8, 5.9, 3.0 Hz, 1H), 2.44 (tdt, *J* = 11.2, 9.5, 3.5 Hz, 1H), 2.35 (dd, *J* = 13.1, 10.2 Hz, 1H), 2.22 (dd, *J* = 13.1, 3.0 Hz, 1H), 1.93 (d, *J* = 12.8 Hz, 1H), 1.82–1.52 (m, 10H), 1.42–1.01 (m, 11H), 0.91 (t, *J* = 7.8 Hz, 9H), 0.61–0.56 (m, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 152.3, 131.2, 74.2, 43.6, 37.5, 34.9, 33.1, 33.1, 29.1, 28.8, 26.7, 26.4, 26.2, 26.0, 25.9, 25.8, 7.4, 3.4. **^{29}Si NMR** (99 MHz, $CDCl_3$) δ: 2.1. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{22}H_{42}OSi$, 373.2897; found, 373.2891.

(*E*)-1,2-dicyclohexyl-3-(triethylsilyl)but-3-en-1-ol (**3p'**)



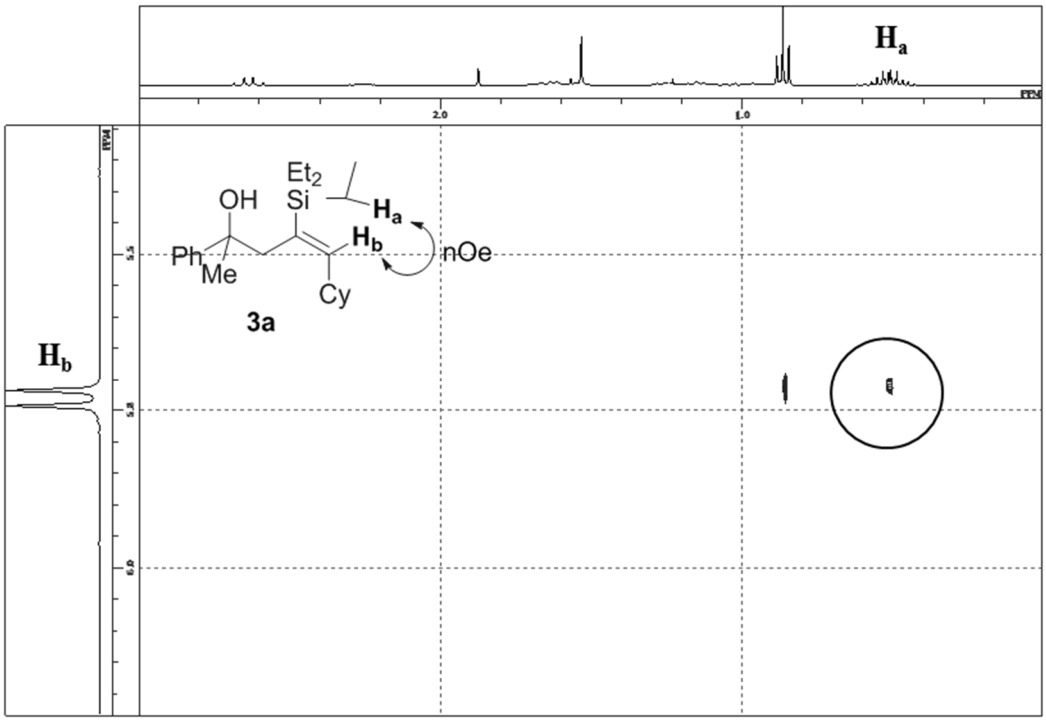
3p'

Purified by column chromatography (eluent: hexane/CH_2Cl_2 = 10:1 then 5:1). Colorless oil (12.5 mg, 14%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 5.86 (d, *J* = 2.4 Hz, 1H), 5.64 (d, *J* = 2.4 Hz, 1H), 3.56 (dd, *J* = 11.1, 5.8 Hz, 1H), 2.28 (dd, *J* = 6.8,

5.8 Hz, 1H), 1.84–1.62 (m, 10H), 1.56–1.48 (m, 1H), 1.43 (d, J = 4.9 Hz, 1H), 1.37–1.28 (m, 1H), 1.27–1.00 (m, 8H), 0.97–0.86 (m, 11H), 0.71–0.57 (m, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 149.4, 129.5, 74.8, 52.4, 40.4, 39.2, 31.5, 31.5, 30.5, 27.2, 26.9, 26.8, 26.7, 26.6, 26.4, 26.2, 7.5, 3.7. **^{29}Si NMR** (79.5 MHz, $CDCl_3$) δ: 1.7. **APCI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{22}H_{42}OSi$, 373.2897; found, 373.2887.

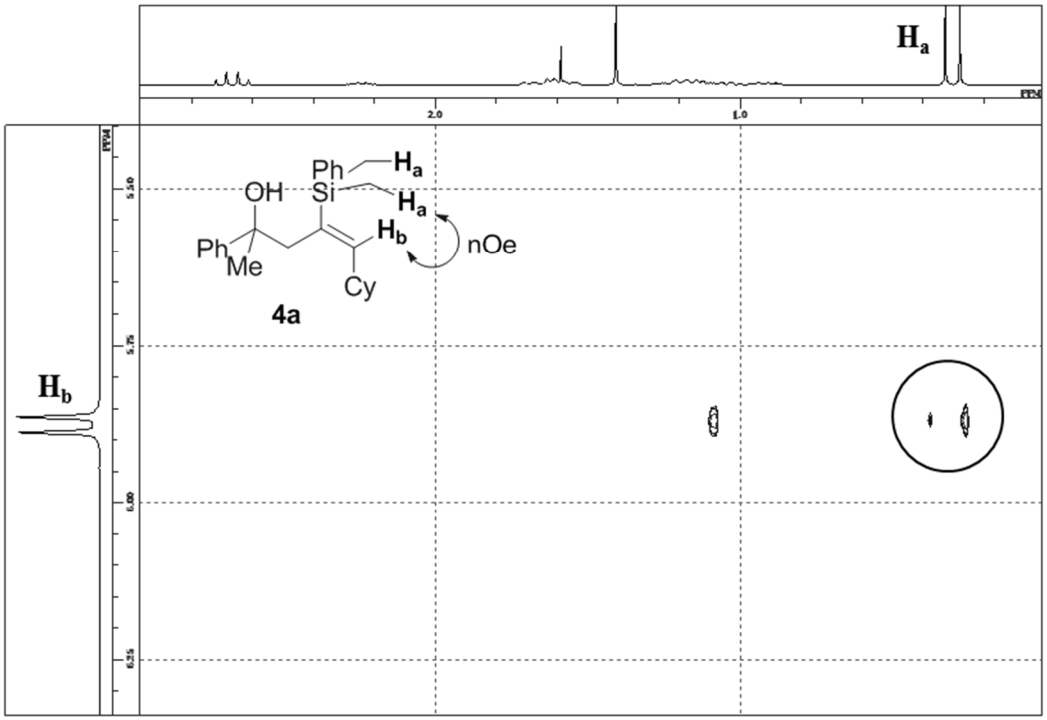
3-4-5. NMR Charts

NOESY spectrum of 3a

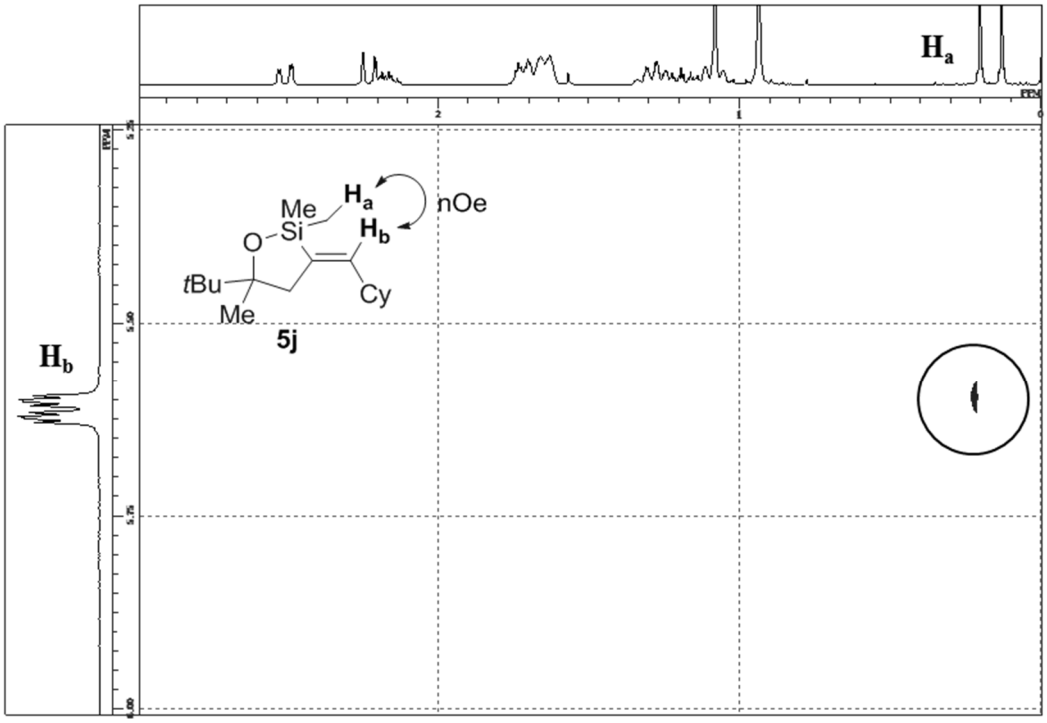


The configurations of double bonds in other γ-Et_3Si-homoallylic alcohols (**3b–3p**) were confirmed to be *E* in a similar manner.

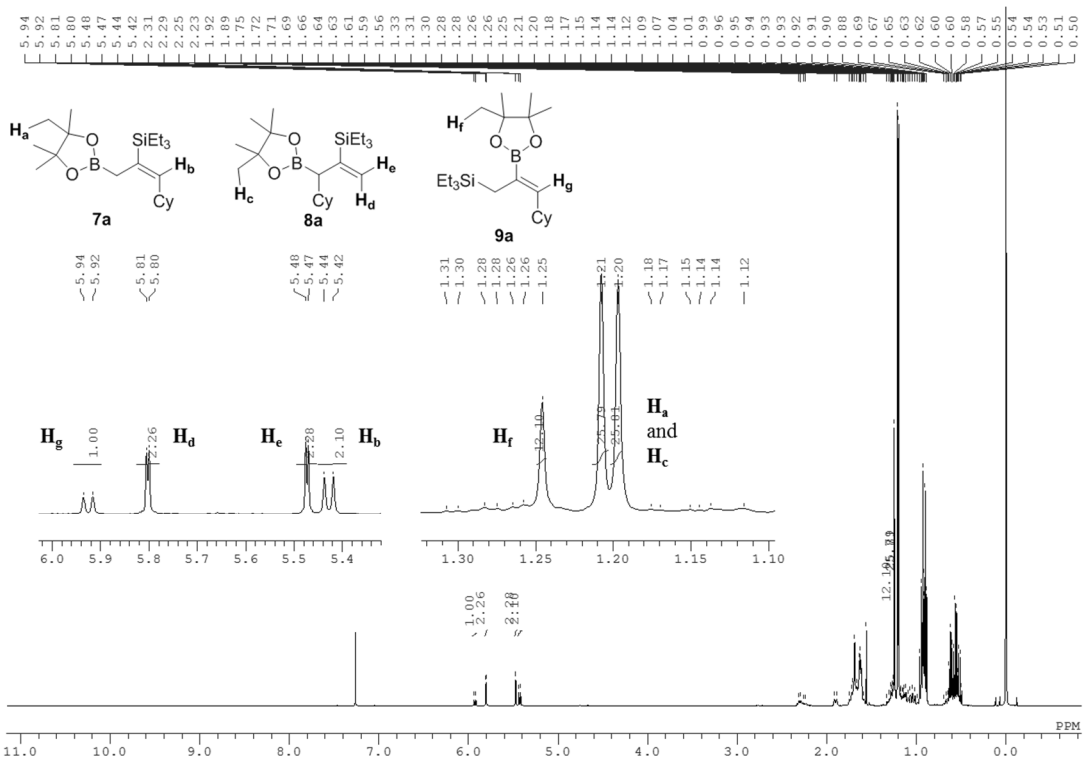
NOESY spectrum of 4a



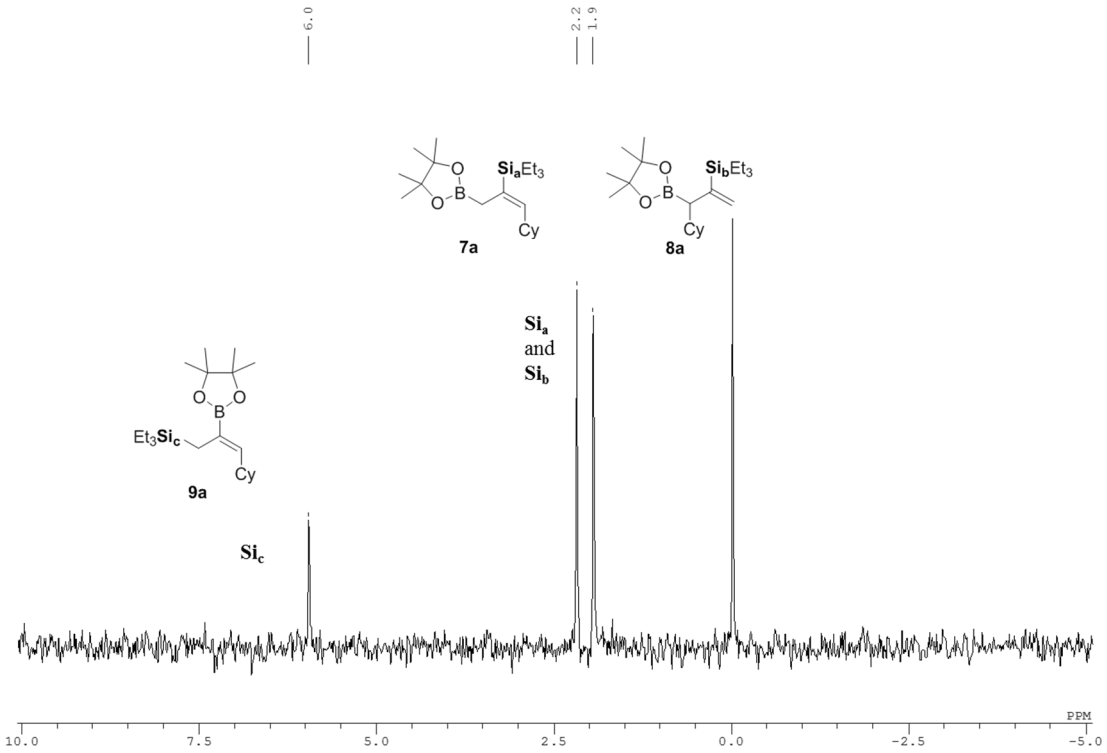
NOESY spectrum of 5j



^{1}H NMR spectrum of the mixture of 7a, 8a and 9a



^{29}Si NMR spectrum of the mixture of 7a, 8a and 9a



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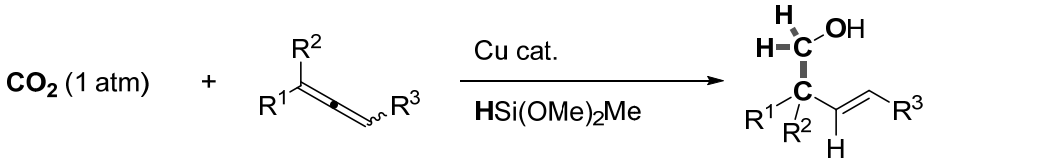
Chapter 4

Copper-Catalyzed Conversion of Carbon Dioxide to Homoallylic Alcohols: Hydro-Hydroxymethylation of Allenes with CO_2 and a Hydrosilane

A copper-catalyzed reaction of allenes with CO_2 and a hydrosilane to give homoallylic alcohols, namely hydro-hydroxymethylation of allenes, has been achieved. The reaction forms one C–C and two C–H bonds with CO_2 under 1 atm. Various allenes are reacted to give the corresponding homoallylic alcohols regioselectively, while a wide range of ester functionalities remains unchanged. This is the first example of a catalytic conversion of CO_2 into homoallylic alcohols. Furthermore, the author also disclosed the copper-catalyzed hydrocarboxylation of allenes giving β,γ-unsaturated carboxylic acids using a stoichiometric amount of a base as an indispensable additive.



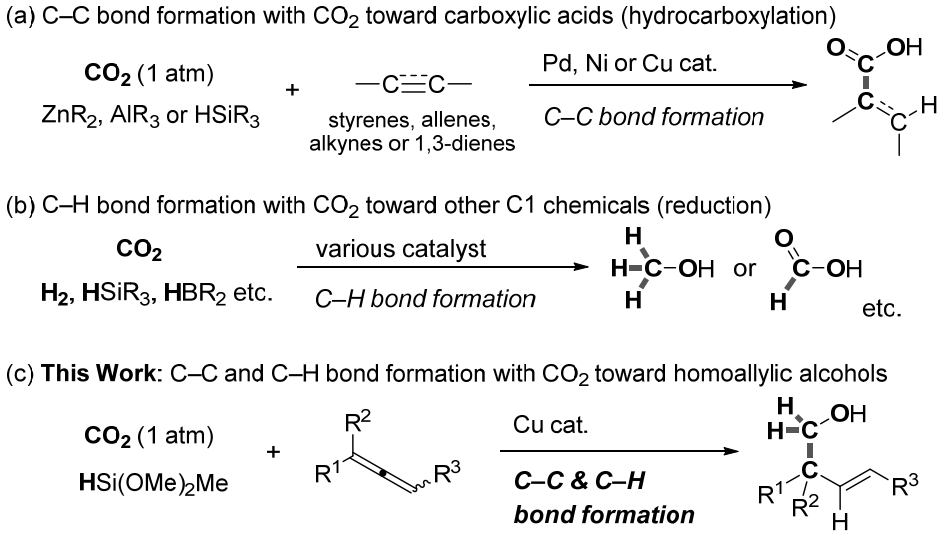
22–86% yields, regioselective

C–C & C–H bond formation with CO_2

4-1. Introduction

Chemical transformation of CO_2, which is an abundant, non-toxic and renewable C1 source, is one of the central challenges in recent organic chemistry.[1] A C–C bond-forming reaction with CO_2 by transition metal catalysts has been investigated as a straightforward route to carboxylic acids.[2] In particular, with the use of a reducing agent as a hydride source, hydrocarboxylation across C–C multiple bonds of styrenes,[3a] allenes,[3b] alkynes[3c,d] and 1,3-dienes[3e] were developed (Scheme 4-1a). On the other hand, direct reductions of CO_2[4] with a hydride source (C–H bond formation) furnish methanol or other reduced C1 chemicals in the presence of a catalyst (Scheme 4-1b). The reduction of CO_2 to CO (deoxygenation) is another well-known process. Sasaki and Tominaga applied this process in a Ru-catalyzed hydroformylation of olefins under H_2 and in situ generated CO, followed by reduction to afford alcohols.[5a] Although the improved catalytic systems were reported, the reaction still required high pressure (total pressure of 60 bar) and temperature (130 °C or more), and suffered from poor regioselectivity.[5b,c] Despite substantial progress in CO_2 transformation, the development of catalytic C–C bond-forming reaction with CO_2 to give alcohols is quite challenging. Herein, the author reports the first catalytic conversion of CO_2 into homoallylic alcohols, where one C–C and two C–H bonds are formed with CO_2 (Scheme 4-1c). Allenes, 1 atm of CO_2 and a hydrosilane were reacted in the presence of a copper catalyst to afford homoallylic alcohols regioselectively.

Scheme 4-1. Catalytic Conversion of CO_2 through C–C and/or C–H Bond Formation



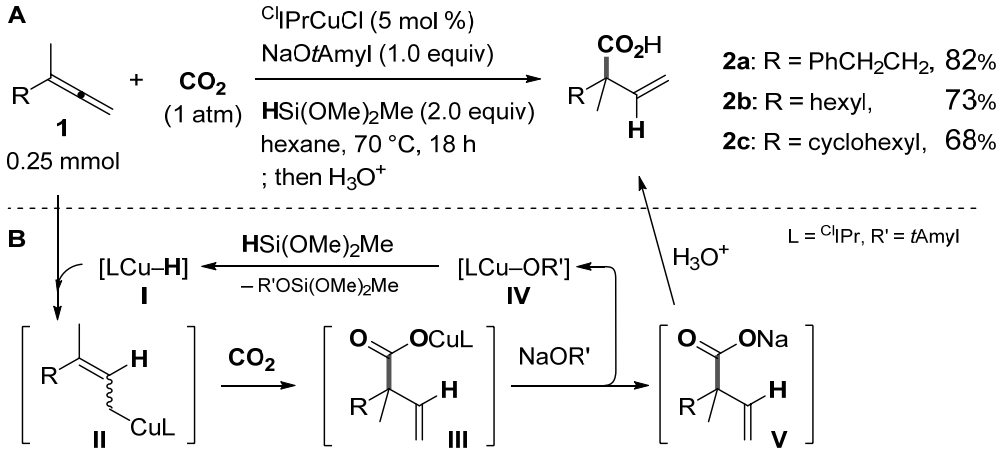
4-2. Results and Discussion

Previously, Tsuji et al. have reported the Cu-catalyzed hydrocarboxylation of alkynes employing a hydrosilane as a mild and easy-to-handle reducing agent.[3c] On the basis of the findings, the author began by expanding the scope of the reaction to allenes. Although Iwasawa reported the Pd-catalyzed hydrocarboxylation of allenes,[3b] the reaction required highly reactive organoaluminiums as a reducing agent.

The reaction of 1-methyl-1-(2-phenethyl)allene (**1a**) with 1 atm of CO_2 and $HSi(OMe)_2Me$ was examined in the presence of a copper catalyst. Gratifyingly, the hydrocarboxylation product (**2a**) was obtained regioselectively in 82% isolated yield by employing ^{Cl}IPrCuCl as the catalyst and 1.0 equiv of NaO*t*Amyl as a base (Scheme 4-2 A). Other allenes (**1b** and **1c**) were also efficiently converted to the corresponding β,γ-unsaturated carboxylic acids (**2b** and **2c**) in good yields. According to the previous work,[3c] the plausible mechanism is presented in Scheme 4-2 B. The catalytic cycle is initiated by the in situ formation of a copper hydride **I**.[6] The addition of **I** across **1** generates an allylcopper intermediate **II**, which then attacks CO_2 to form a copper carboxylate **III**. NaO*t*Amyl might promote the regeneration of **I** by converting **III** to copper alkoxide **IV** and sodium carboxylate **V**. Actually, when the amount of NaO*t*Amyl was reduced to 8 mol % in the reaction of **1a**, the yield of **2a** was dropped to 38%. Moreover, surprisingly, a homoallylic alcohol **3a** was detected from the reaction mixture. Any alcohols derived from CO_2 have not been obtained in previously reported hydrocarboxylation reactions. Encouraged by these results, the author decided to explore this novel reductive fixation of CO_2, namely, hydrohydroxymethylation of allenes (Scheme 4-1 c).

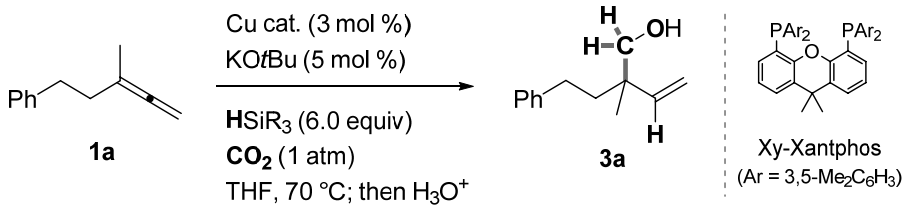
The author revaluated the effects of various copper catalysts and a hydrosilane in the reaction of **1a** with only a catalytic amount of a base. Considering that 3 equiv of a hydride source were required for the conversion to **3a**, the amount of a hydrosilane was increased to 6.0 equiv (Table 4-1). Employing Xy-Xantphos as a ligand and $HSi(OMe)_2Me$ as a hydrosilane, a β-disubstituted homoallylic alcohol **3a** was obtained in 99% GC yield as a sole regioisomer, and in 84% isolated yield after column chromatography (entry 1). Xantphos afforded **3a** in high yield (92%, entry 2), while the yield was decreased with other bidentate ligands such as BINAP and dppp (entries 3 and 4). Bulky NHC ligands

Scheme 4-2. Copper-Catalyzed Hydrocarboxylation of Allenes



IPr and ^{Cl}IPr were also effective, even the yields were moderate (entries 5 and 6). Regarding hydrosilanes, $HSi(OEt)_3$ afforded the product in good yield (entry 7), whereas PMHS was ineffective (entry 8).

Table 4-1. Cu-Catalyzed Hydrohydroxymethylation of **1a**[a]



entry	copper catalyst	hydrosilane	yield of **3a**(%)[b]
1	Xy-Xantphos / CuCl	$HSi(OMe)_2Me$	99 (84)[c]
2	Xantphos / CuCl	$HSi(OMe)_2Me$	92
3	*rac*-BINAP / CuCl	$HSi(OMe)_2Me$	85
4	dppp / CuCl	$HSi(OMe)_2Me$	73
5	IPrCuCl	$HSi(OMe)_2Me$	62
6	^{Cl}IPrCuCl	$HSi(OMe)_2Me$	69
7	Xy-Xantphos / CuCl	$HSi(OEt)_3$	83
8	Xy-Xantphos / CuCl	PMHS	35

[a]Reaction conditions: **1a** (0.25 mmol), hydrosilane (6.0 equiv), copper catalyst (3 mol %), KO*t*Bu (5 mol %) in THF (0.50 mL) under CO_2 (1 atm, closed) at 70 °C for 18 h. [b]Determined by GC analysis. [c]Isolated yield is shown in parenthesis.

With these optimized conditions in hand, the author turned his attention to the substrate scope (Table 4-2). Various 1,1-disubstituted allenes (**1a**–**j**) were converted to the corresponding homoallylic alcohols (**3a**–**j**) in good to high yields (entries 1–9). 2-Phenethyl moiety in **1a** can be replaced with a primary or secondary aliphatic alkyl chains as **3b** and **3c** were obtained in high yield (entries 1 and 2). The reaction of ethyl-substituted allene **1d** gave **3d** in good yield (entry 3). Bromo and ether moieties were well tolerated as **3e** was obtained in 75% yield from **1e** (entry 4). Allene bearing an alkene moiety (**1f**) also affordded **3f** in 72% yield (entry 5), while that bearing the acetamide (**1g**) moiety was less reactive (entry 6). Furthermore, a variety of ester functionalities (**1h**–**j**) was kept intact under the reaction conditions. Thus, homoallylic alcohols bearing primary alkyl acetate (**3h**), isobutyrate (**3i**), and methyl benzoate derivatives (**3j**) were obtained in 62–86% yields. Actually, these ester moieties were hardly reduced under the reaction conditions, since the corresponding diols were not detected by GC, GC/MS or ^{1}H NMR analysis. Considering these chemoselectivity profiles, the current reaction might not proceed through a simple hydrocarboxylation followed by the selective reduction of carboxylates over esters.[7,8] As for mono- and trisubstituted allenes, (2-phenethyl)allene **1k** and 1,3-dimethyl-1-(2-phenethyl)allene **1l** afforded the corresponding homoallylic alcohols (**3k** and **3l**) as a single isomer, albeit in low to moderate yields.

Gratifyingly, as a preliminary result (unoptimized), styrene was converted to 2-phenylpropan-1-ol (**6**) in 18% isolated yield (Scheme 4-3). Attempt to extend the protocol for other C–C multiple bonds including an alkyne and an aliphatic alkene were unsuccessful at this point.

Scheme 4-3. Copper-Catalyzed Hydrohydroxymethylation of Styrene

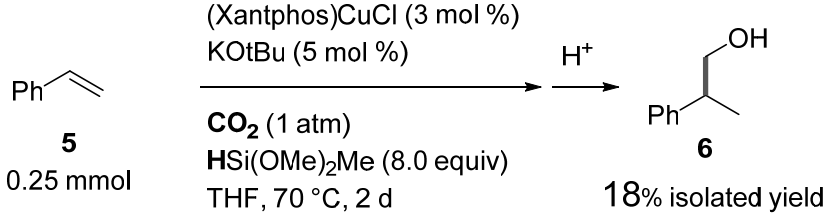
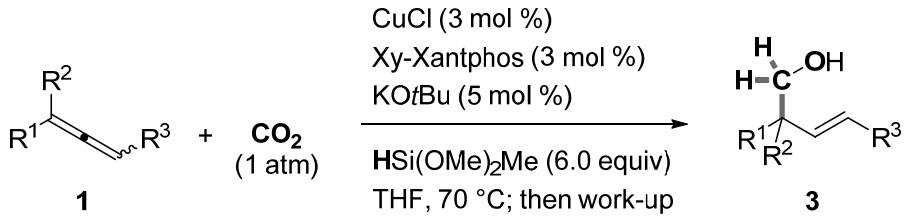
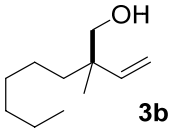
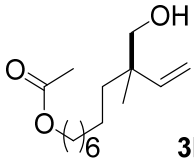
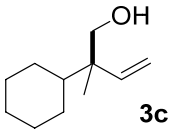
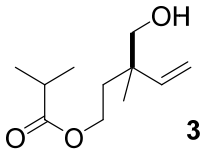
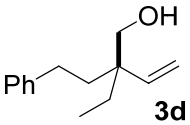
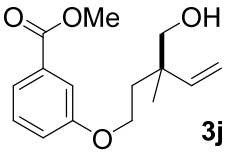
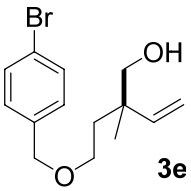
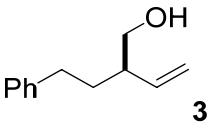
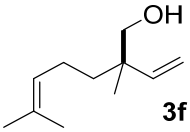
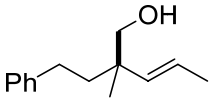
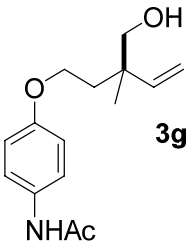


Table 4-2. Cu-Catalyzed Hydrohydroxymethylation of Allenes (**1**)[a]



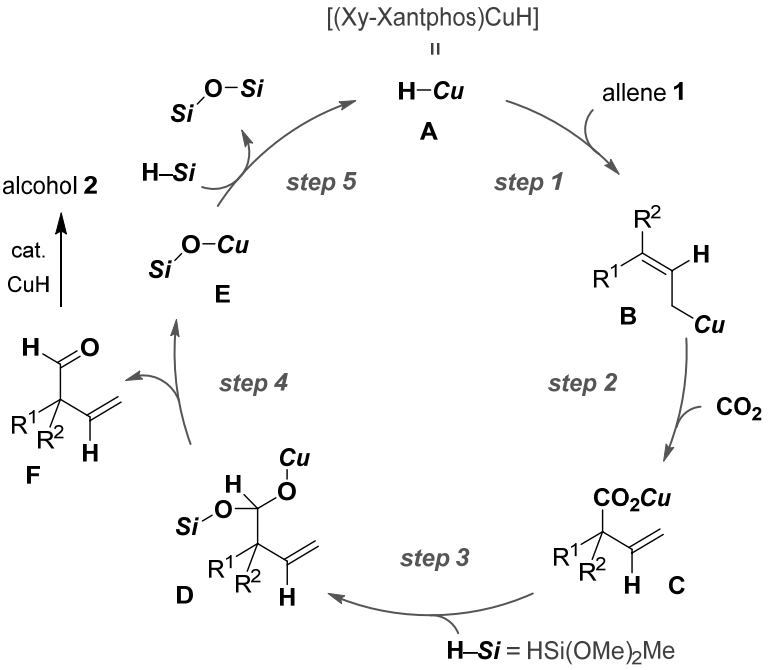
1 **3**

entry	product	yield (%)[b]	entry	product	yield (%)[b]
1	 **3b**	73	7[c]	 **3h**	86
2	 **3c**	68	8[c]	 **3i**	62
3	 **3d**	59	9[c]	 **3j**	75
4	 **3e**	75	10[c,d]	 **3k**	30
5[c]	 **3f**	72	11[c,e]	 **3l**	48
6[c]	 **3g**	22			

[a]Reaction conditions: **1** (0.25 mmol), $HSi(OMe)_2Me$ (6.0 equiv), CuCl (3 mol %), Xy-Xantphos (3 mol %), KO*t*Bu (5 mol %) in THF (0.50 mL) under CO_2 (1 atm, closed) at 70 °C for 18 h. [b]Isolated yield of **3**. [c]$HSi(OMe)_2Me$ (8.0 equiv) was used. [d]DTBM-Xantphos (3 mol %) was used instead of Xy-Xantphos. [e]dppBz (3 mol %) was used instead of Xy-Xantphos.

Although the reaction mechanism is unclear, a tentative reaction pathway is shown in Scheme 4-4. Similar to the hydrocarboxylation (Scheme 4-2), the addition of a diphosphine-coordinated copper hydride **A** across the terminal double bond of **1** generates an allylcopper intermediate **B**. CO_2 reacts with **B** at the γ-position of Cu regioselectively to give a copper carboxylate **C**, which might further react with a hydrosilane to form a tetrahedral intermediate **D**. The elimination of a copper siloxide **E** produces aldehydes **F**, and successive Cu–H-catalyzed reduction of **F** affords **2**. Actually, in some cases, small amounts of aldehydes were detected as side products. Regeneration of **A** from **E** through σ-bond metathesis with a hydrosilane closes the cycle. In the presence of a stoichiometric amount of a base, salt exchange of a copper carboxylate leads to the formation of sodium carboxylate (**V** in Scheme 4-2), prohibiting the reduction to alcohol. An alternative pathway involving hydrosilylaion of CO_2 to a silylformate[9] and successive allylation with **B** to give **D** cannot be excluded.[10]

Scheme 4-4. A Possible Reaction Mechanism



4-3. Conclusion

In conclusion, the author has developed the Cu-catalyzed hydrohydroxymethylation of allenes under 1 atm of CO_2 employing a hydrosilane as the reducing agent. The reaction

afforded homoallylic alcohols regioselectively, making both C–C and C–H bonds with CO_2. This is the first example of a catalytic conversion of CO_2 into homoallylic alcohols. The reaction exhibited intriguing chemoselectivity profiles. While C–H bonds were formed with CO_2, a variety of esters and other reducible functionalities was kept intact. The hydrocarboxylation of allenes has also been developed utilizing a suitable copper catalyst, a hydrosilane, and a stoichiometric amount of a base as a crucial additive. Further studies on the reaction mechanism and optimization of the hydrohydroxymethylation of styrenes, as well as the development of novel approach toward catalytic CO_2 fixation, are now in progress.

4-4. Experimental Section

4-4-1. General Remarks

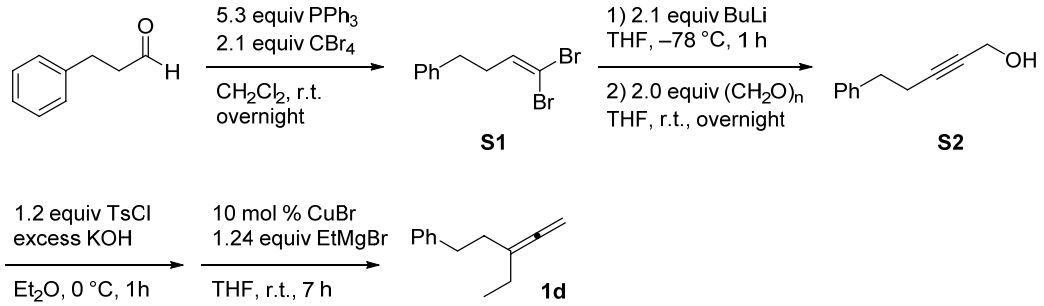
All reactions were performed under an argon atmosphere using standard Schlenk-type glass-wares on a dual-manifold Schlenk line. ^1H and ^{13}C NMR spectra were recorded on a JEOL ECX-400P spectrometer or a Bruker AVANCE-500 spectrometer. Chemical shift values (δ) are reported in ppm and calibrated to tetramethylsilane (TMS, 0.00 ppm) for ^1H and to $CDCl_3$ (77.0 ppm) for ^{13}C as an internal standard. High-resolution mass spectra were obtained with: a Thermo Fischer Scientific EXACTIVE spectrometer for APCI-HRMS, a JEOL JMS-MS700 spectrometer for EI-HRMS and a JEOL JMX-SX 102A spectrometer for ESI-HRMS. Elemental analysis was carried out at the Center for Organic Elemental Microanalysis, Graduate School of Pharmaceutical Science, Kyoto University. GC analysis was carried out using Shimadzu GC-17A equipped with an integrator (C-R8A) with a capillary column (CBP-20, 0.25 mm i.d. × 25 m). TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck Silica gel $60F_{254}$. Column chromatography was carried out on silica gel (Kanto N60, spherical, neutral, 63–210 μm). Preparative recycling GPC was performed with SHIMADZU LC-20AP System equipped with Shodex K-4002.5L column, a SHIMADZU SPD-20A, and SHIMADZU RID-10A using $CHCl_3$ as the eluent at a flow rate of 14 mL min^{-1}.

Hexane was purified by refluxing over Na/benzophenone with a small amount of tetraglyme followed by distillation under Ar. Anhydrous THF, toluene and CH_2Cl_2 were purchased from Kanto Chemical Co., Inc. and further purified by passage through activated alumina under positive argon pressure as described by Grubbs et al.[11] $HSi(OMe)_2Me$, $HSi(OEt)_3$ and styrene were purified by distillation. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Allenes **1a–1c**, **1f**, **1i** and **1k**, (IPr)CuCl, (^{Cl}IPr)CuCl, Xy-

Xantphos, (Xantphos)CuCl and DTBM-Xantphos were synthesized according to the literatures.[3c,12,13]

4-4-2. Preparation of Substrates 1

Preparation of 1-ethyl-1-(2-phenethyl)allene (1d)

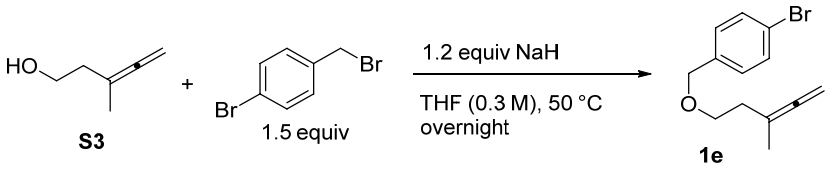


To a dried 300 mL two-necked flask were added PPh_3 (42 g, 160 mmol), CH_2Cl_2 (200 mL) and CBr_4 (20.8 g, 63 mmol). The mixture was stirred for 1 h before 3-phenylpropanal (3.9 mL, 30 mmol) was added. The reaction mixture was stirred at room temperature for 20 h, then filtered through a short pad of silica gel (eluent: hexane). The solvent was removed under reduced pressure to give the compound **S1** (7.0 g, 80%) as a yellow oil.

To a solution of **S1** (6.7 g, 23 mmol) in THF (70 mL) in a 200 mL flask was added *n*BuLi (1.6 M in THF, 30 mL, 50 mmol) dropwise at –78 °C, and the resulting mixture was stirred for 1 h. $(CH_2O)_n$ (1.4 g, 46 mmol) was added and the mixture was stirred at room temperature overnight. After the reaction was quenched with 1 M HCl aq., the aqueous layer was extracted with Et_2O. The combined organic layer was dried over $MgSO_4$, filtered, and evaporated to give the crude **S2**.

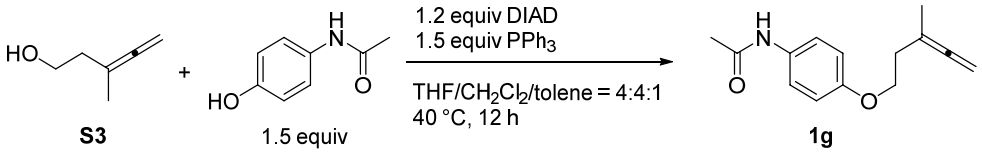
To a solution of **S2** (1.5g, 10.7mmol) and TsCl (2.5 g, 12.8 mmol) in Et_2O (25 mL) in a 100 mL beaker was added KOH (crushed, 3.0 g) at 0 °C. After stirring for 1 h, the reaction was quenched with ice water. The aqueous layer was extracted with Et_2O, and the combined organic layer was dried over $MgSO_4$, filtered and evaporated. The residue, CuBr (153 mg, 1.07 mmol) and THF (20 mL) were added to a dried 100 mL flask. EtMgBr (0.95 M in THF, 27 mL, 25.7 mmol) was added dropwise at room temperature. The reaction mixture was stirred for 8 h, and then the reaction was quenched with 1 M HCl aq. The aqueous layer was extracted with Et_2O. The combined organic layer was dried over $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography (eluent: hexane) to give **1d** (506 mg, 27%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.30–7.26 (m, 2H), 7.21–7.15 (m, 3H), 4.73–4.70 (m, 2H), 2.27–2.21 (m, 2H), 2.01–1.94 (m, 2H), 1.02 (t, J = 7.5 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 205.4, 142.3, 128.4, 128.2, 125.7, 104.7, 76.6, 34.0, 33.9, 25.3, 12.1. **Anal.** calcd for $C_{13}H_{16}$: C, 90.64; H, 9.36%. Found: C, 90.56; H, 9.57%.

Preparation of 1-(2-(4-bromobenzyloxy)ethyl)-1-methylallene (1e)



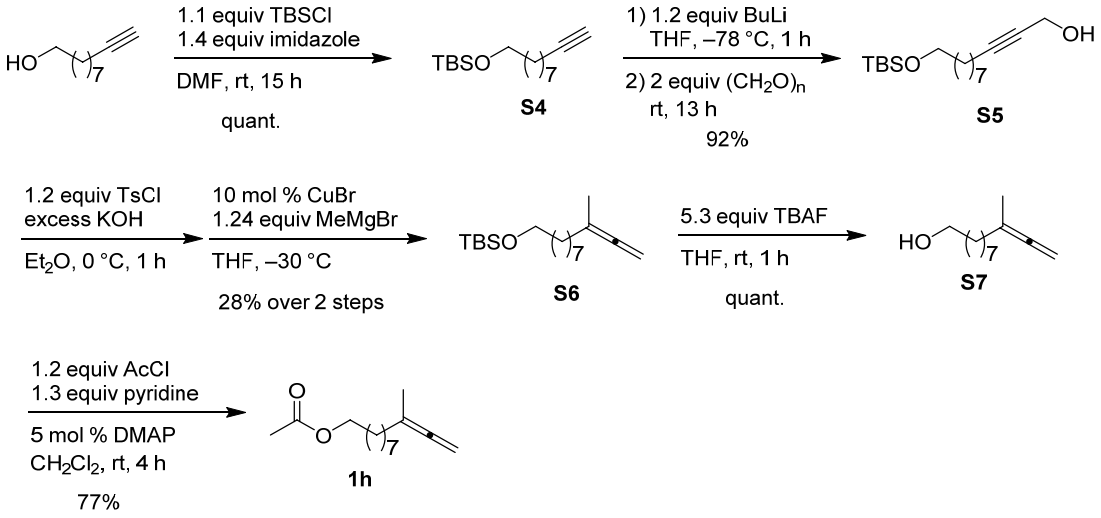
To a dried 50 mL two-neck flask were added NaH (269 mg, 6.7 mmol) and THF (15 mL), and the mixture was cooled to 0 °C. After the **S3**[2c] (547 mg, 5.6 mmol) was added dropwise, the reaction mixture was stirred for 1 h. Then, *p*-bromobenzyl bromide (2.1 g, 8.4 mmol) was added. The reaction mixture was stirred at 50 °C overnight. After the reaction was quenched by adding saturated NH_4Cl aq., the mixture was extracted with Et_2O and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by column chromatography (eluent: hexane/Et_2O = 30:1) to give **1e** (938 mg, 63%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.48–7.44 (m, 2H), 7.23–7.19 (m, 2H), 4.63–4.59 (m, 2H), 4.46 (s, 2H), 3.57 (t, *J* = 7.0 Hz, 2H), 2.28–2.23 (m, 2H), 1.71 (t, *J* = 3.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 206.2, 137.5, 131.4, 129.2, 121.3, 95.4, 74.4, 72.1, 68.6, 33.5, 19.0. **Anal.** calcd for $C_{13}H_{15}BrO$: C, 58.44; H, 5.66%. Found: C, 58.46; H, 5.87%.

Preparation of 1-(2-(*N*-acetaminophenoxy)ethyl)-1-methylallene (1g)



To a mixture of **S3** (1.67 g, 11.9 mmol), *N*-(4-hydroxyphenyl)acetamide (2.7 g, 17.9 mmol) and PPh_3 (4.68 g, 17.9 mmol) in THF (30 mL) and CH_2Cl_2 (30 mL) was added DIAD (1.9 M in toluene, 7.5 mL, 14.3 mmol) dropwise. Resulting orange solution was stirred at 40 °C overnight, and then the solvents were evaporated. $MgCl_2$ and toluene were added to the residue and stirred for 1 h. Then the solid was filtered off and washed with hexane. The filtrate was dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (eluent: hexane/EtOAc = 2:1 to 0:1) and preparative recycle GPC to give **1g** (250 mg 11%) as a white powder. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.37 (d, *J* = 8.9 Hz, 2H), 7.03 (br s, 1H), 6.86 (d, *J* = 8.9 Hz, 2H), 4.65–4.62 (m, 2H), 4.04 (t, *J* = 6.9 Hz, 2H), 2.42–2.38 (m, 2H), 2.15 (s, 3H), 1.77–1.75 (m, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 206.2, 168.2, 155.8, 131.0, 121.9, 114.9, 95.1, 74.8, 66.6, 32.9, 24.3, 19.1. **ESI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{14}H_{18}NO_2$, 232.1332; found, 232.1328.

Preparation of 1-(8-acetoxyoctyl)-1-methylallene (1h)



To a dried 100 mL two-necked flask were added TBSCl (5.3 g, 35.2 mmol), imidazole (3.0 g, 44.8 mmol), DMF (35 mL) and 9-decyn-1-ol (5.0 g, 32 mmol). The reaction mixture was stirred at room temperature for 15 h. The mixture was diluted with EtOAc and quenched with saturated $NaHCO_3$ aq. The organic layer was washed with water and Brine, dried over $MgSO_4$, and filtered through a short pad of silica gel (eluent: EtOAc) to give **S4** (8.6 g, quant) as a colorless oil.

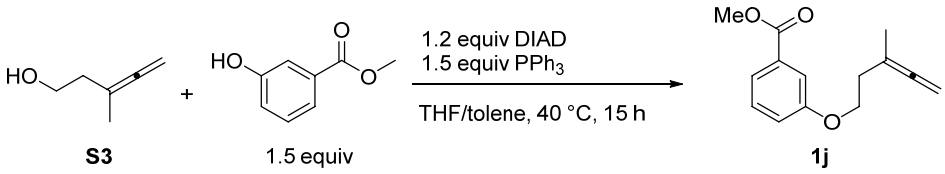
To a solution of **S4** (8.6 g, 32 mmol) and THF (70 mL) in 200 mL flask was added *n*BuLi (1.6 M in THF, 24 mL, 38 mmol) dropwise at –78 °C, and the resulting mixture was stirred for 1 h. $(CH_2O)_n$ (1.9 g, 64 mmol) was added and the mixture was stirred at room temperature for 13 h. After the reaction was quenched with 1 M HCl aq., the aqueous layer was extracted with Et_2O. The combined extracts were dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (eluent: hexane/EtOAc = 8:1) to give **S5** (8.8 g, 92%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 4.26–4.23 (m, 2H), 3.59 (t, J = 6.6 Hz, 2H), 2.23–2.17 (m, 2H), 1.65–1.59 (m, 2H), 1.54–1.46 (m, 4H), 1.40–1.27 (m, 9H), 0.89 (s, 10H), 0.04 (s, 6H).

To a solution of **S5** (8.4 g, 28 mmol) and TsCl (6.6 g, 35 mmol) in Et_2O (25 mL) in 100 mL beaker was added KOH (crushed, 6.0 g) at 0 °C. After the mixture being stirred for 1.5 h, the reaction was quenched with ice water. The aqueous layer was extracted with Et_2O, and the combined organic layer was dried over $MgSO_4$, filtered and evaporated. The residue, CuBr (402 mg, 2.8 mmol) and THF (50 mL) were added to a dried 200 mL flask. MeMgBr (3.0 M in Et_2O, 11.5 mL, 35 mmol) was added dropwise at –30 °C. After the mixture being stirred for 1 h, the reaction was quenched with 1 M HCl aq. and the aqueous layer was extracted with Et_2O. The combined organic layer was dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (eluent: hexane) to give **S6** (2.3 g, 28%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 4.59–4.55 (m, 2H), 3.59 (t, J = 6.8 Hz, 2H), 1.95–1.89 (m, 2H), 1.67 (t, J = 3.2 Hz, 3H), 1.53–1.37 (m, 4H), 1.32–1.27 (m, 8H), 0.89 (s, 9H), 0.05 (s, 6H).

TBAF (1.0 M in THF, 31 mL, 31 mmol) was added to a solution of **S6** (2.3 g, 7.7 mmol) in THF (5 mL) in a 100 mL two-necked flask. After the mixture being stirred for 1 h, TBAF (1.0 M in THF, 10 mL, 10 mmol) was added. After 1 h, the reaction was quenched with water. The aqueous layer was extracted with Et_2O, and the combined organic layer was dried over $MgSO_4$, filtered through a short pad of silica gel and washed with EtOAc to give **S7** (1.4 g, quant).

To a solution of **S7** (1.3 g, 7.5 mmol) and DMAP (46 mg, 0.38 mmol) in CH_2Cl_2 (25 mL) in 100 mL two-necked flask were added pyridine (787 μL, 9.8 mmol) and acetyl chloride (642 μL, 9.0 mmol). After the mixture being stirred for 4 h, the reaction was quenched with water and the organic layer was washed with $CuSO_4$ aq. Then the solvent was removed under reduced pressure, and the residue was purified by column chromatography (eluent: hexane/EtOAc = 6:1) to give **1h** (1.3 g, 77%) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 4.59–4.55 (m, 2H), 4.05 (t, J = 6.7 Hz, 2H), 2.05 (s, 3H), 1.94–1.90 (m, 2H), 1.68–1.66 (m, 3H), 1.64–1.58 (m, 2H), 1.44–1.39 (m, 2H), 1.36–1.28 (m, 8H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 206.2, 171.2, 98.4, 98.4, 73.8, 64.7, 33.5, 29.3, 29.2, 29.1, 28.6, 27.3, 25.9, 21.0, 18.7. **ESI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{14}H_{24}O_2Na$, 247.1669; found, 247.1664.

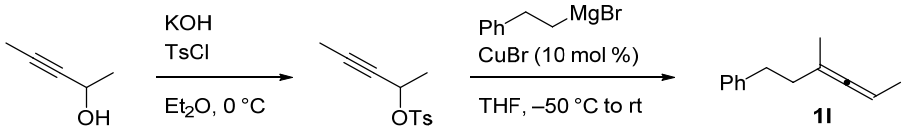
Preparation of 1-(2-(3-methoxycarbonylphenoxy)ethyl)-1-methylallene (1j)



S3 1.5 equiv **1j**

To a mixture of **S3** (530 mg, 5.4 mmol), methyl 3-hydroxybenzoate (1.23 g, 8.1 mmol) and PPh_3 (2.12 g, 8.1 mmol) in THF (16 mL) was added DIAD (1.9 M in toluene, 3.4 mL, 6.5 mmol) dropwise. Resulting orange solution was stirred at room temperature overnight, and then the solvents were evaporated. The residue was agitated in hexane, then the solid was filtered off and washed with hexane. The solvents were removed under reduced pressure. The residue was purified by column chromatography (eluent: hexane/EtOAc = 40:1 to 10:1) to give **1j** (637 mg 51%) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.62 (d, J = 7.6 Hz, 1H), 7.56 (t, J = 2.0 Hz, 1H), 7.32 (t, J = 7.9 Hz, 1H), 7.09 (dd, J = 8.2, 2.7 Hz, 1H), 4.66–4.63 (m, 2H), 4.11 (t, J = 6.9 Hz, 2H), 3.91 (s, 3H), 2.45–2.41 (m, 2H), 1.77 (t, J = 3.2 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 206.2, 166.9, 158.9, 131.4, 129.3, 121.9, 119.9, 114.8, 95.0, 74.8, 66.4, 52.1, 32.9, 19.0. **ESI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{14}H_{17}O_3$, 233.1172; found, 233.1169.

Preparation of 1,3-dimethyl-1-(2-phenethyl)allene (1l)



1l

3-pentyn-2-ol (2.5 g, 30 mmol) and TsCl (6.9 g, 36 mmol) were dissolved in Et_2O (50 mL) under air and cooled to 0 °C. To this stirred solution was added KOH (crushed, 8.5 g) portionwise. The resulting mixture was stirred further for 1 h at this temperature, and then poured into ice water. The phase was separated, and the water phase was extracted with Et_2O (50 mL × 3). The combined organic phase was dried over $MgSO_4$, filtered, and evaporated to give propargyl tosylate. This crude tosylate were mixed with THF (60 mL) and CuBr (431 mg, 3.0 mmol) under Ar and cooled to –50 °C. To this solution was added 2-phenethylmagnesium bromide (ca. 1.0 M in THF, 40 mL, prepared from 2-phenethyl bromide and Mg turning) dropwise over 30 min. The resulting mixture was stirred overnight while it was gradually warmed up to room temperature. The reaction was quenched by adding NH_4Cl aq. (100 mL) and Et_2O (100 mL). The phase was separated and the water phase was extracted with Et_2O (50 mL × 3). Combined organic phase was washed with brine (50 mL), dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (eluent: hexane) to give **1l** as a colorless oil (3.0 g, 58% over 2 steps). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.28–7.25 (m, 2H), 7.20–7.15 (m, 3H), 5.02–4.96 (m, 1H), 2.72 (t, J = 7.8 Hz, 2H), 2.23 (t, J = 7.6 Hz, 2H), 1.69 (s, 3H), 1.56 (d, J = 6.7 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 202.2, 142.3, 128.4, 128.2, 125.6, 98.2, 85.4, 35.7, 34.0, 19.4, 14.8. **EI-HRMS** (*m*/*z*): $[M]^+$ calcd for $C_{13}H_{16}$, 172.1252; found, 172.1256.

4-4-3. Experimental Procedure for the Hydrohydroxymethylation

Typical procedure for the hydrohydroxymethylation of allenes (Table 4-1, entry 1)

To a dried Schlenk tube was added CuCl (0.74 mg, 7.5 μmol) and Xy-Xantphos (5.2 mg, 7.5 μmol), then the tube was evacuated and backfilled with CO_2 three times. To this Schlenk tube were added THF (0.50 mL), 1 M KO*t*Bu in THF, (12.5 μL, 12.5 μmol), $HSi(OMe)_2Me$ (186 μL, 1.50 mmol) and **1a** (44 μL, 0.25 mmol) in this order. The mixture was allowed to stir at 70 °C for 18 h. After being cooled to room temperature, the reaction was quenched with 2 M HCl/MeOH (1 mL), and tetradecane (50 μL) was added as an internal standard. The mixture was stirred for 30 min, and then diluted with water (1 mL) and Et_2O (9 mL). Finally, an aliquot of the mixture was analyzed by GC.

General procedure for the hydrohydroxymethylation (Table 4-2 and Scheme 4-3)

To a dried Schlenk tube was added CuCl (0.74 mg, 7.5 μmol) and Xy-Xantphos (5.2 mg, 7.5 μmol), then the tube was evacuated and backfilled with CO_2 three times. To this Schlenk tube were added THF (0.50 mL), 1 M KO*t*Bu in THF, (12.5 μL, 12.5 μmol), $HSi(OMe)_2Me$ (186 μL, 1.50 mmol) and **1** (0.25 mmol) in this order. The mixture was allowed to stir at 70 °C for 18 h. After being cooled to room temperature, the reaction mixture was worked up as follows:

Work-up procedure A: the reaction was quenched with 2M HCl/MeOH (1 mL). The resulting

mixture was stirred for 30 min, and then diluted with water (1 mL). The aqueous layer was extracted with Et_2O, and the combined organic layer was dried over $MgSO_4$, filtered, and evaporated. Finally, the residue was purified by column chromatography (KF-silica as a stationary phase[14]).

Work-up procedure B: to the reaction mixture was added Et_2O and HF·pyridine (2.0 mL). The resulting mixture was stirred for 1 h, and then diluted with saturated aqueous NH_4Cl solution (1 mL) and water (1 mL). The aqueous layer was extracted with Et_2O, and the combined organic layer was washed with $CuSO_4$ aq. and Brine, dried over $MgSO_4$, filtered, and evaporated. Finally, the residue was purified by column chromatography.

Work-up procedure C: to the reaction mixture was added Et_2O and TBAF (1.0 M in THF, 2.5 mL, 2.5 mmol). The resulting mixture was stirred for 1 h, and then with 1 M HCl aq. (1 mL) was added. The aqueous layer was extracted with Et_2O, and the combined organic layer was dried over $MgSO_4$, filtered, and evaporated. Finally, the residue was purified by column chromatography.

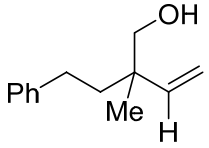
Work-up procedure D: the residue obtained after procedure B was stirred with 3M HCl aq. in acetone. After the aqueous layer was extracted with Et_2O, the combined organic layer was dried over $MgSO_4$, filtered, and evaporated. Finally, the residue was purified by column chromatography.

4-4-4. Typical Procedure for the Hydrocarboxylation of Allenes (Scheme 4-2)

To a dried Schlenk tube was added (^{Cl}IPr)CuCl (4.2 mg, 7.5 μmol) and NaO*t*Amyl (27.5 mg, 0.25 mmol), then the tube was evacuated and backfilled with CO_2 three times. To this Schlenk tube were added hexane (0.50 mL), $HSi(OMe)_2Me$ (62 μL, 0.50 mmol) and **1a** (44 μL, 0.25 mmol) in this order. The mixture was allowed to stir at 70 °C for 4 h. After being cooled to room temperature, the reaction mixture was worked up with 1 mL conc. HCl aq. After the mixture being stirred for 4 h, the aqueous layer was extracted with Et_2O. The combined organic layer was extracted with 1 M NaOH aq. The aqueous layer was acidified by conc. HCl aq. and extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and evaporated. Finally, the residue was purified by column chromatography (eluent: hexane/EtOAc = 4:1 to 0:1).

4-4-5. Characterization of the Hydrohydroxymethylation Products

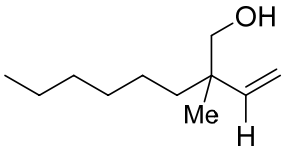
2-methyl-2-(2-phenethyl)but-3-en-1-ol (**3a**)



Work-up with procedure A (eluent: hexane/EtOAc = 6:1). Colorless oil (40 mg, 84%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.29–7.26 (m, 2H), 7.19–7.15 (m, 3H), 5.78 (dd, *J* = 17.7, 10.9 Hz, 1H), 5.23 (dd, *J* = 10.9, 0.9 Hz, 1H), 5.12 (dd, *J* = 17.7, 1.4 Hz, 1H), 3.47–3.37 (m, 2H), 2.62–2.49 (m, 2H), 1.64 (t, *J* = 8.4 Hz, 2H), 1.39–1.34 (m, 1H), 1.11 (s, 3H). **^{13}C NMR** (400 MHz, $CDCl_3$) δ: 143.7, 142.8, 128.4,

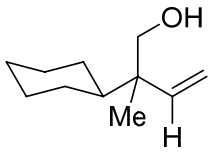
128.3, 125.7, 115.1, 70.1, 42.5, 39.3, 30.3, 19.6. **APCI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{13}H_{19}O$, 191.1430; found, 191.1428.

2-hexyl-2-methylbut-3-en-1-ol (**3b**)



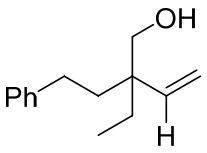
Work-up with procedure A (eluent: hexane/EtOAc = 6:1). Colorless oil (31 mg, 73%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.71 (dd, *J* = 17.7, 10.9 Hz, 1H), 5.15 (dd, *J* = 10.9, 1.4 Hz, 1H), 5.04 (dd, *J* = 17.7, 1.4 Hz, 1H), 3.38 (d, *J* = 10.9 Hz, 1H), 3.33 (d, *J* = 10.9 Hz, 1H), 1.36–1.16 (m, 10H), 1.00 (s, 3H), 0.88 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 144.3, 114.5, 70.2, 42.3, 37.2, 31.8, 30.1, 23.7, 22.6, 19.6, 14.1. Since HRMS of the alcohol **3b** did not obtained, **3b** was acetylated by mixing acetic anhydride, pyridine, and DMAP in CH_2Cl_2. The corresponding ester was obtained after column chromatography. Colorless oil (11 mg, 44%): **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 5.73 (dd, *J* = 17.7, 11.0 Hz, 1H), 5.06 (d, *J* = 11.0 Hz, 1H), 4.99 (d, *J* = 17.7 Hz, 1H), 3.92 (d, *J* = 10.7 Hz, 1H), 3.86 (d, *J* = 10.7 Hz, 1H), 2.05 (s, 3H), 1.36-1.17 (m, 10H), 1.02 (s, 3H), 0.88 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 171.2, 143.6, 113.3, 71.1, 40.1, 37.5, 31.8, 30.0, 23.7, 22.6, 21.0, 20.6, 14.1. **ESI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{13}H_{24}O_2$+Na, 235.1669; found, 235.1664.

2-cyclohexyl-2-methylbut-3-en-1-ol (**3c**)



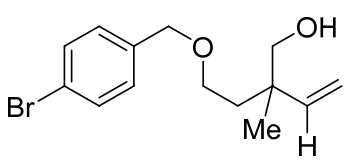
Work-up with procedure A (eluent: hexane/EtOAc = 6:1). Colorless oil (29 mg, 68%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.72 (dd, *J* = 17.7, 10.9 Hz, 1H), 5.20 (dd, *J* = 11.1, 1.6 Hz, 1H), 5.04 (dd, *J* = 17.7, 1.4 Hz, 1H), 3.44 (d, *J* = 6.3 Hz, 2H), 1.79–1.62 (m, 5H), 1.34–0.97 (m, 6H), 0.96 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 143.9, 115.0, 68.5, 45.1, 43.5, 27.7, 27.1, 27.0, 26.9, 26.7, 16.0. **APCI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{11}H_{21}O$, 169.1587; found, 169.1587.

2-ethyl-2-(2-phenethyl)but-3-en-1-ol (**3d**)



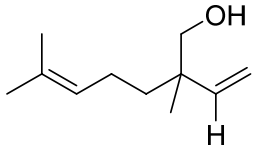
Work-up with procedure A (eluent: hexane/EtOAc = 6:1). Colorless oil (30 mg, 59%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.30–7.25 (m, 2H), 7.20–7.15 (m, 3H), 5.71 (dd, *J* = 17.7, 10.9 Hz, 1H), 5.26 (dd, *J* = 11.3, 1.4 Hz, 1H), 5.09 (dd, *J* = 17.7, 1.4 Hz, 1H), 3.49 (d, *J* = 6.3 Hz, 2H), 2.59–2.47 (m, 2H), 1.75–1.40 (m, 4H), 1.29 (t, *J* = 6.3 Hz, 1H), 0.89 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 143.6, 143.0, 128.4, 128.3, 125.7, 115.3, 66.3, 44.9, 35.0, 29.9, 25.3, 7.7. **APCI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{11}H_{21}O$, 205.1587; found, 205.1585.

2-(2-(4-bromobenzyloxy)ethyl)-2-methylbut-3-en-1-ol (**3e**)



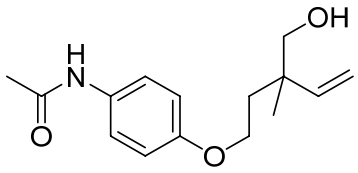
Work-up with procedure A (eluent: hexane/EtOAc = 2:1). Colorless oil (56 mg, 75%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.47 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 5.79 (dd, *J* = 17.7, 10.9 Hz, 1H), 5.10 (dd, *J* = 10.9, 1.4 Hz, 1H), 5.04 (dd, *J* = 17.7, 1.4 Hz, 1H), 4.45 (s, 2H), 3.53 (t, *J* = 6.1 Hz, 2H), 3.45–3.34 (m, 2H), 2.47 (t, *J* = 6.8 Hz, 1H), 1.77–1.66 (m, 2H), 1.02 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 144.1, 136.9, 131.6, 129.4, 121.7, 113.6, 72.5, 69.6, 67.1, 41.3, 37.1, 21.5. **Anal.** Calcd. for $C_{14}H_{19}BrO_2$: C, 56.20; H, 6.40. Found: C, 56.43; H, 6.51.

2-ethenyl-2,6-dimethylhept-5-en-1-ol (**3f**)



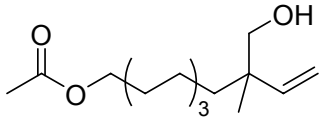
Work-up with procedure C (eluent: hexane/ EtOAc = 4:1). Colorless oil (30 mg, 72%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 5.72 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.18 (dd, *J* = 10.8, 1.4 Hz, 1H), 5.11–5.07 (m, 1H), 5.06 (dd, *J* = 17.7, 1.2 Hz, 1H), 3.39 (d, *J* = 10.7 Hz, 2H), 3.34 (d, *J* = 10.7 Hz, 2H), 1.98–1.85 (m, 2H), 1.67 (s, 3H), 1.59 (s, 3H), 1.36–1.32 (m, 3H), 1.03 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 144.0, 131.5, 124.7, 114.7, 70.1, 42.3, 37.2, 25.7, 22.5, 19.6, 17.6. **EI-HRMS** (*m*/*z*): $[M–H]^+$ calcd for $C_{11}H_{19}O$, 167.1436; found, 167.1433.

N-(4-(3-ethenyl-4-hydroxy-3-methylbutoxy)phenyl)acetamide (**3g**)



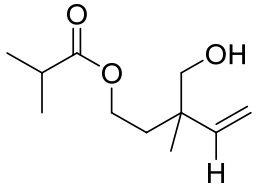
Work-up with procedure D (eluent: hexane/ EtOAc = 1:2 to 0:1). Colorless oil (14.5 mg, 22%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.37 (d, *J* = 8.9 Hz, 2H), 7.23 (br s, 1H), 6.83 (d, *J* = 8.9 Hz, 2H), 5.81 (dd, *J* = 17.7, 11.0 Hz, 1H), 5.17 (d, *J* = 11.0 Hz, 1H), 5.09 (d, *J* = 17.7 Hz, 1H), 4.00 (t, *J* = 6.4 Hz, 2H), 3.49xx–3.42 (m, 2H), 2.14 (s, 3H), 1.87 (t, *J* = 6.6 Hz, 2H), 1.10 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 168.23, 155.42, 143.58, 131.15, 121.93, 114.81, 114.44, 69.80, 65.03, 41.35, 36.09, 24.35, 21.02. **ESI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{15}H_{21}NO_3$+H, 264.1594; found, 264.1589.

9-ethenyl-10-hydroxy-9-methyldecyl acetate (**3h**)



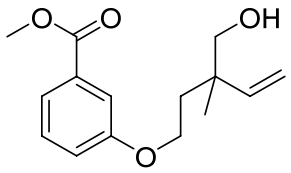
Work-up with procedure B (eluent: hexane/EtOAc = 7:1). Colorless oil (55 mg, 86%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.70 (dd, *J* = 17.7, 10.9 Hz, 1H), 5.16 (d, *J* = 10.9 Hz, 1H), 5.04 (d, *J* = 17.7 Hz, 1H), 4.05 (t, *J* = 6.8 Hz, 2H), 3.40–3.30 (m, 2H), 2.05 (s, 3H), 1.66–1.57 (m, 2H), 1.39–1.20 (m, 12H), 1.00 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 171.3, 144.3, 114.5, 70.2, 64.6, 42.3, 37.2, 30.3, 29.5, 29.2, 28.6, 25.9, 23.7, 21.0, 19.7. **ESI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{28}O_3$+Na, 279.1936; found, 279.1923.

3-ethenyl-4-hydroxy-3-methylbutyl 2-methylpropanoate (**3i**)



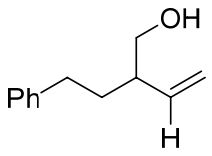
Work-up with procedure B (eluent: hexane/EtOAc = 9:1 to 5:1). Colorless oil (31 mg, 62%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.75 (dd, *J* = 17.7, 10.9 Hz, 1H), 5.18 (d, *J* = 10.9 Hz, 1H), 5.09 (d, *J* = 17.7 Hz, 1H), 4.11 (t, *J* = 7.2 Hz, 2H), 3.41 (d, *J* = 5.9 Hz, 2H), 2.57–2.47 (m, 1H), 1.79–1.67 (m, 2H), 1.59 (t, *J* = 6.1 Hz, 1H), 1.16 (d, *J* = 7.2 Hz, 6H), 1.07 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 177.1, 143.0, 114.9, 70.0, 61.2, 41.2, 35.3, 34.0, 20.2, 18.9. **APCI-HRMS** (*m*/*z*): $[M+H]^+$ calcd for $C_{11}H_{21}O_3$, 201.1485; found, 201.1484.

methyl 3-(3-ethenyl-4-hydroxy-3-methylbutoxy)benzoate (**3j**)



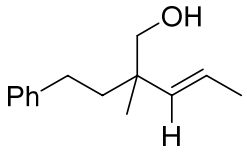
Work-up with procedure B (eluent: hexane/EtOAc = 4:1). Colorless oil (49 mg, 75%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.63 (d, *J* = 7.6 Hz, 1H), 7.54 (s, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 7.08 (dd, *J* = 8.4, 2.6 Hz, 1H), 5.82 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.19 (d, *J* = 11.0 Hz, 1H), 5.11 (d, *J* = 17.7 Hz, 1H), 4.07 (t, *J* = 6.6 Hz, 2H), 3.91 (s, 3H), 3.50–3.44 (m, 2H), 1.96–1.87 (m, 2H), 1.77 (t, *J* = 6.6 Hz, 1H), 1.56 (s, 2H), 1.12 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 167.0, 158.6, 143.4, 131.5, 129.4, 122.1, 119.9, 114.7, 114.6, 69.9, 65.0, 52.2, 41.4, 36.0, 20.9. **ESI-HRMS** (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{20}O_4$+Na, 287.1259; found, 287.1247.

2-(2-phenylethyl)but-3-en-1-ol (**3k**)



Work-up with procedure B (eluent: hexane/ EtOAc = 4:1) and preparative recycle GPC. Colorless oil (13 mg, 30%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.29–7.26 (m, 2H), 7.19–7.15 (m, 3H), 5.65 (ddd, *J* = 18.1, 9.4, 7.9 Hz, 1H), 5.23 (dd, *J* = 10.4, 1.8 Hz, 1H), 5.18 (dd, *J* = 17.1, 1.5 Hz, 1H), 3.58 (dd, *J* = 10.5, 5.0 Hz, 1H), 3.46 (dd, *J* = 10.7, 7.9 Hz, 1H), 2.73–2.66 (m, 1H), 2.60–2.53 (m, 1H), 2.30–2.23 (m, 1H), 1.79–1.72 (m, 1H), 1.62–1.54 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 142.2, 139.6, 128.4, 128.4, 125.8, 118.0, 65.6, 46.5, 33.3, 32.4. **EI-HRMS** (*m*/*z*): $[M]^+$ calcd for $C_{12}H_{16}O$, 176.1201; found, 176.1206.

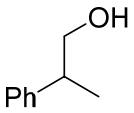
(*E*)-2-methyl-2-(2-phenylethyl)pent-3-en-1-ol (**3l**)



Work-up with procedure D (eluent: hexane/ EtOAc = 4:1). Colorless oil (24 mg, 48%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.28–7.25 (m, 2H), 7.18–7.15 (m, 3H), 5.54 (dq, *J* = 15.7, 6.4 Hz, 1H), 5.37 (d, *J* = 15.9 Hz, 1H), 3.41–3.33 (m, 2H), 2.60–2.49 (m, 2H), 1.75 (d, *J* = 6.1 Hz, 3H), 1.61 (t, *J* = 8.7 Hz, 2H), 1.08 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 143.0, 136.3, 128.3, 128.3, 125.7,

125.6, 70.6, 41.7, 39.8, 30.4, 20.4, 18.4. **EI-HRMS** (*m*/*z*): $[M]^+$ calcd for $C_{15}H_{28}O_3$+Na, 204.1514; found, 204.1513.

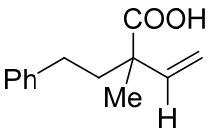
2-phenylpropan-1-ol (**6**)



Work-up with procedure B (eluent: hexane/ EtOAc = 6:1) and preparative recycle GPC. Colorless oil (6 mg, 18%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.35–7.32 (m, 2H), 7.25–7.22 (m, 3H), 3.71 (d, *J* = 6.7 Hz, 2H), 3.00–2.92 (m, 1H), 1.32 (br s, 1H), 1.28 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 143.65, 128.66, 127.49, 126.70, 68.73, 42.45, 17.58. All the resonances in ^{1}H and ^{13}C NMR spectra were in good agreement with literature values.[15]

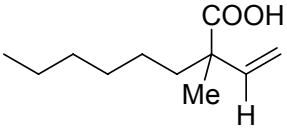
4-4-6. Characterization of the Hydrocarboxylation Products

2-methyl-2-(2-phenylethyl)but-3-enoic acid (**2a**)



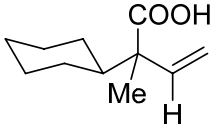
Colorless oil (38 mg, 75%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.29–7.24 (m, 2H), 7.19–7.15 (m, 3H), 6.09 (dd, *J* = 17.4, 10.6 Hz, 1H), 5.21 (d, *J* = 10.4 Hz, 1H), 5.21 (d, *J* = 17.7 Hz, 1H), 2.66–2.53 (m, 2H), 2.10–2.02 (m, 1H), 1.96–1.88 (m, 1H), 1.39 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 182.5, 141.9, 140.7, 128.4, 128.3, 125.9, 114.6, 48.5, 40.9, 31.0, 20.4. All the resonances in ^{1}H and ^{13}C NMR spectra were in good agreement with literature values.[3b]

2-ethenyl-2-methyloctanoic acid (**2b**)



Colorless oil (29 mg, 64%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 6.03 (dd, *J* = 17.4, 11.1 Hz, 1H), 5.14 (d, *J* = 10.9 Hz, 1H), 5.13 (d, *J* = 17.2 Hz, 1H), 1.77–1.68 (m, 1H), 1.62–1.52 (m, 1H), 1.33–1.22 (br m, 11H), 0.87 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 182.4, 141.2, 114.0, 48.4, 39.1, 31.6, 29.7, 24.4, 22.6, 20.2, 14.0. **ESI-HRMS** (*m*/*z*): $[M–H]^-$ calcd for $C_{11}H_{19}O_2$, 183.1391; found, 183.1388.

2-ethenyl-2-methyloctanoic acid (**2c**)



Colorless oil (30 mg, 65%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 6.01 (dd, *J* = 17.7, 10.9 Hz, 1H), 5.18 (dd, *J* = 10.9, 0.9 Hz, 1H), 5.10 (dd, *J* = 17.7, 0.9 Hz, 1H), 1.80–1.72 (m, 3H), 1.68–1.55 (m, 3H), 1.32–0.89 (m, 8H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 182.7, 140.5, 114.9, 52.4, 45.1, 28.0, 27.3, 26.8, 26.7, 26.4, 14.8. All the resonances in ^{1}H and ^{13}C NMR spectra were in good agreement with literature values.[16]

References and Notes

(1) (a) *Carbon Dioxide as Chemical Feedstock*; Aresta, M., Ed.; Wiley-VCH: Weinheim, 2010. (b) Sakakura, T.; Choi, J.-C.; Yasuda, H. *Chem. Rev.* **2007**, *107*, 2365.

(2) For reviews on transition metal-catalyzed C–C bond-forming reaction with CO_2, see: (a) Tsuji, Y.; Fujihara, T. *Chem. Commun.* **2012**, *48*, 9956. (b) Zang, L.; Hou, Z. *Chem. Sci.* **2013**, *4*, 3395. (c) Huang, K.; Sun, C.-L.; Shi, Z.-J. *Chem. Soc. Rev.* **2011**, *40*, 2435. (d) Cokoja, M.; Bruckmeier, C.; Rieger, B.; Herrmann, W. A.; Kühn, F. E. *Angew. Chem., Int. Ed.* **2011**, *50*, 8510.

(3) (a) Williams, C. M.; Johnson, J. B.; Rovis, T. *J. Am. Chem. Soc.* **2008**, *130*, 14936. (b) Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2008**, *130*, 15254. (c) Fujihara, T.; Xu, T.; Semba, K.; Terao, J.; Tsuji, Y. *Angew. Chem., Int. Ed.* **2011**, *50*, 523. (d) Li, S.; Yuan, W.; Ma, S. *Angew. Chem., Int. Ed.* **2011**, *50*, 2578. (e) Takaya, J.; Sasano, K.; Iwasawa, N. *Org. Lett.* **2011**, *13*, 1698.

(4) For reviews on the reduction of CO_2, see: (a) Wang, W.; Wang, S.; Ma, X.; Gong, J. *Chem. Soc. Rev.* **2011**, *40*, 3703. (b) Benson, E. E.; Kubiak, C. P.; Sathrum, A. J.; Smieja, J. M. *Chem. Soc. Rev.* **2009**, *38*, 89.

(5) (a) Tominaga, K.-i.; Sasaki, Y. *Catal. Commun.* **2000**, *1*, 1. (b) Tominaga, K.-i.; Sasaki, Y. *J. Mol. Catal. A* **2004**, *220*, 159. (c) Liu, Q.; Wu, L.; Fleischer, I.; Selent, D.; Franke, R.; Jackstell, R.; Beller, M. *Chem. Eur. J.* **2014**, *20*, 6888.

(6) Successive reaction of ^{Cl}IPrCuCl (**I** in Scheme 4-2) with NaO*t*Bu and then with PMHS was reported to afford ^{Cl}IPrCuH. See: Semba, K.; Fujihara, T.; Xu, T.; Terao, J.; Tsuji, Y. *Adv. Synth. Catal.* **2012**, *354*, 1542.

(7) A cationic bis(NHC)copper complex was reported to catalyze the hydrosilylation of ethyl phenylacetate and other carbonyl compounds. See: Díez-González, S.; Scott, N. M.; Nolan, S. P. *Organometallics* **2006**, *25*, 2355.

(8) The chemoselective reduction of carboxylic acids, carboxylate salts or silyl carboxylates using a hydrosilane as a reducing agent is scarcely found in the literature, especially in the presence of esters. For only and excellent example as long as the author is aware, see: Fernández-Salas, J. A.; Manzini, S.; Nolan, S. P. *Adv. Synth. Catal.* **2014**, *356*, 308.

(9) Copper-catalyzed hydrosilylation and hydroboration of CO_2 to silyl- and borylformate have been reported, see: (a) Motokura, K.; Kashiwame, D.; Miyaji, A.; Baba, T. *Org. Lett.* **2012**, *14*, 2642. (b) Zhang, L.; Cheng, J.; Hou. Z. *Chem. Commun.* **2013**, *49*, 4782. (c) Shintani, R.; Nozaki, K. *Organometallics* **2013**, *32*, 2459.

(10) In the reaction vessel, ca. 2 mmol of CO_2 (8 equiv to an allene) is presented. If the

hydrosilylation of CO_2 is operative and much faster than the hydrocupration of an allene (step 1 in Scheme 4-4), all the hydrosilane would be converted to the silylformate. On the other hand, if the hydrocupration of an allene is much faster, the allylcopper **B** (Scheme 4-4) would be a dead end, otherwise the hydrocarboxylation products should be observed. However, this is not the case. Therefore, if the reaction proceeds via two steps, i.e. the catalytic hydrosilylation of CO_2 with the hydrosilane and the following catalytic allylation of thus formed silylformate with an allene and the hydrosilane, these two catalytic reactions must proceed at a comparable rate.

(11) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

(12) (a) For **1a**, **1f** and **1k**, see ref 3b. (b) For **1b** and **1c**, see: Tani, Y.; Fujihara, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2014**, *136*, 17706. (c) For **S3**, see: Xu, D.; Lu, Z.; Li, Z.; Ma, S. *Tetrahedron*, **2004**, *60*, 11879.

(13) (a) Semba, K.; Fujihara, T.; Xu, T.; Terao, J.; Tsuji, Y. *Adv. Synth. Catal*. **2012**, *354*, 1542. (b) Semba, K.; Shinomiya, M.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. Eur. J*. **2013**, *19*, 7125.

(14) Harrowven, D. C.; Guy, I. L. *Chem. Commun.* **2004**, 1968.

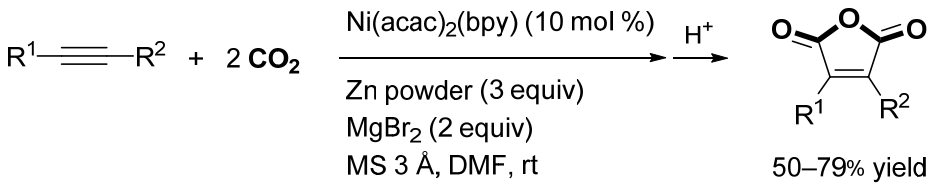
(15) Cheung, L. L. W.; Vasapollo, G.; Alper, H. *Adv. Synth. Catal.* **2012**, *354*, 2019.

(16) Brun, E. M.; Gil, S.; Mestres, R.; Parra, M. *Synthesis* **2000**, *8*, 1160.

Chapter 5

Nickel-Catalyzed Double Carboxylation of Alkynes Employing Carbon Dioxide

The nickel-catalyzed double carboxylation of internal alkynes employing carbon dioxide (CO_2) has been developed. The reactions proceed under CO_2 (1 atm) at room temperature in the presence of a nickel catalyst, Zn powder as a reducing reagent, and $MgBr_2$ as an indispensable additive. Various internal alkynes could be converted to the corresponding maleic anhydrides in good to high yields. DFT calculations disclosed the indispensable role of $MgBr_2$ in the second CO_2 insertion.

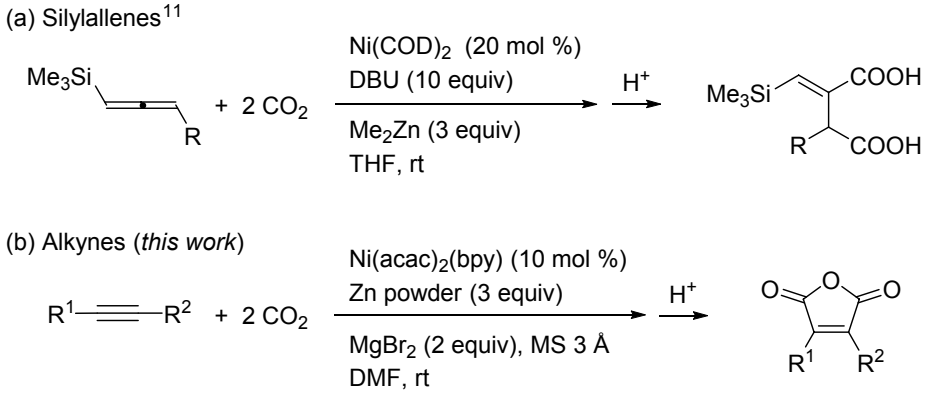


5-1. Introduction

CO_2 is a readily available, nontoxic, and renewable carbon source.[1] Its environmental impact due to its overabundance makes it especially attractive as a raw material in *carbon–carbon bond-forming reactions*.[2] Recently, the highly efficient transition-metal catalyzed carboxylations of arylboranes,[3a-d] organozincs,[3e,f] organic halides,[4] esters,[5] and C–H bonds,[6] as well as hydro-carboxylation of styrenes,[7a] allenes,[7b] alkynes,[7c,d] and 1,3-dienes[7e] using CO_2 have been reported. Furthermore, as described in Chapters 1 and 2, the author established the sila-carboxylation of alkynes[8a] and allenes.[8b] Bora-carboxylation of alkynes[8c] has also been explored. In all these reactions, only *one* CO_2 was incorporated into the unsaturated substrates.

By extension, *double* carboxylation, in which *two* CO_2 molecules are introduced simultaneously into a substrate, would be very promising for the efficient synthesis of dicarboxylic acids. However, to date, such methods have not been extensively developed. Electrochemical double carboxylation was reported,[9] but disappointingly, it was not efficient at all in terms of applicable substrates and/or product selectivity. Other than the electrochemical reactions, stoichiometric Ni complexes have been used to facilitate the double carboxylation of 1,3-butadienes, although the reaction did not proceed catalytically.[10] The single reported catalytic double carboxylation used 1-(trimethylsilyl)-3-alkyl-substituted allenes as substrates (Scheme 5-1a).[11] Unfortunately, the substrate scope was limited and the trimethylsilyl moiety was necessary for the double carboxylation. Herein, the auther reports the Ni-catalyzed double carboxylation of internal alkynes with

Scheme 5-1. Catalytic Double Carboxylation Using CO_2

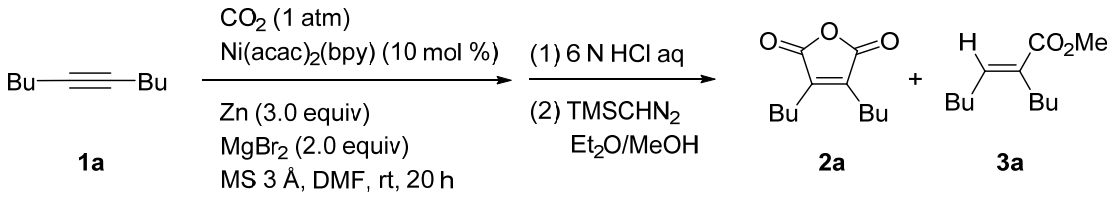


CO_2, affording highly versatile maleic anhydrides[12] as products (Scheme 5-1b). The reactions proceed selectively under 1 atm of CO_2 at room temperature in the presence of Zn powder as a reducing reagent and $MgBr_2$ as an indispensable additive.

5-2. Results and Discussion

Initially, the reaction of 5-decyne (**1a**) was surveyed with $Ni(acac)_2(bpy)$ (10 mol %) as a catalyst, zinc powder (3.0 equiv) as a reducing reagent, and $MgBr_2$ (2.0 equiv) as an additive, in the presence of molecular sieves 3Å (MS 3 Å, powder) in DMF at room temperature under a CO_2 pressure of 1 atm (Table 5-1). The yield of the double-carboxylated product (**2a**) was determined by GC after acidification. Under these conditions, the double-carboxylated product **2a** was obtained in 74% yield (entry 1). A small amount of a hydrocarboxylated product (**3a**), which was analyzed by GC after derivatization to the corresponding methyl ester, was also detected. With $Ni(acac)_2$ as the catalyst (i.e., without the bpy ligand), the reaction did not proceed (entry 2). In the absence of $MgBr_2$, **2a** was not detected (entry 3). The Zn powder was indispensable for the reaction (entry 4). Without MS 3 Å, the yield of **2a** was slightly reduced while that of **3a** increased (entry 5). Employing $MgCl_2$[4c] in place of $MgBr_2$, the yield of **2a** considerably decreased and **3a** was obtained in 23% yield (entry 6). $ZnBr_2$ and $ZnCl_2$ in place of $MgBr_2$ suppressed the double carboxylation (entries 7 and 8). The use of other ligands such as 4,4'-dimethoxybipyridine (MeO-bpy) and phen in place of bpy decreased the yield of **2a** (entries 9 and 10). Regarding the ligand, PPh_3, PCy_3, and dppe were not effective. Full details of the effects of ligands are summarized in Table 5-2. Other reducing agents such as Mn powder or Mg turnings gave the product in moderate or low yields (entries 11 and 12). In DMI as the solvent in place of DMF, **2a** was obtained in 52% yield, whereas THF and toluene were not good solvents, giving trace amounts of **2a**. Under the optimal reaction conditions, **2a** was obtained in 78% GC yield and in 71% isolated yield as shown in entry 13.

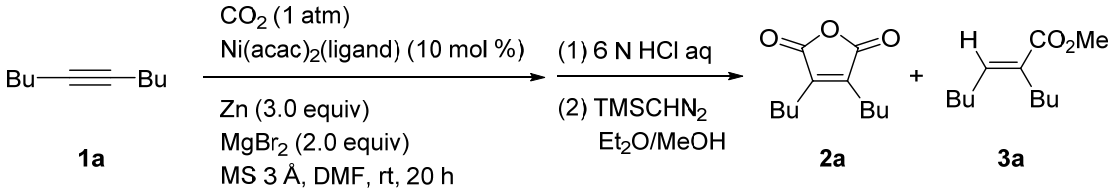
Table 5-1. Optimization of Reaction Conditions on the Nickel-Catalyzed Double Carboxylation of 5-Decyne (**1a**)[a]



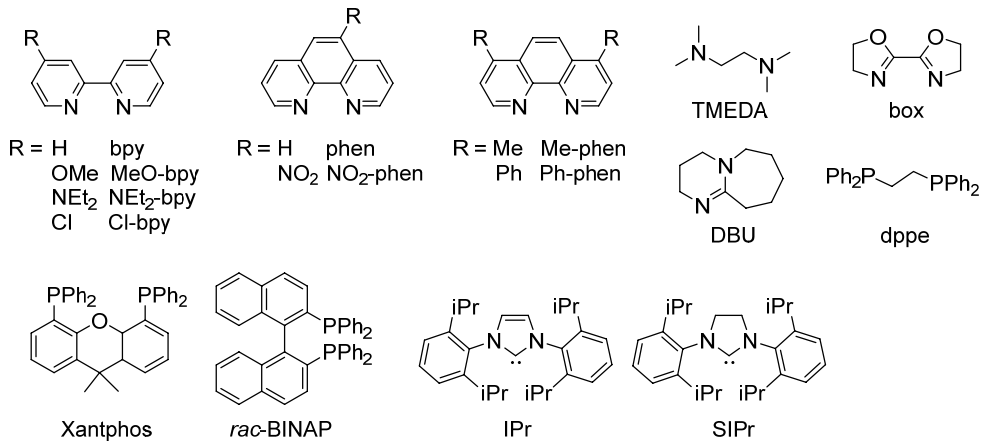
entry	catalyst system: alternation from the reaction conditions	yield of **2a** (%)[b]	yield of **3a** (%)[b]
1	without any change	74	3
2	without bpy	0	0
3	without $MgBr_2$	0	0
4	without Zn powder	0	0
5	without MS 3 Å	62	6
6	$MgCl_2$ in place of $MgBr_2$	24	23
7	$ZnBr_2$ in place of $MgBr_2$	0	0
8	$ZnCl_2$ in place of $MgBr_2$	0	0
9	MeO-bpy in place of bpy	37	2
10	phen in place of bpy	48	trace
11	Mn in place of Zn	66	2
12	Mg in place of Zn	4	trace
13	$MgBr_2$ (3.0 equiv), DMF (2.0 mL)	78 (71)[c]	2

[a] Reaction conditions: 5-Decyne (**1a**, 0.50 mmol), $Ni(acac)_2(bpy)$ (0.050 mmol, 10 mol %), Zn powder (1.5 mmol, 3.0 equiv), $MgBr_2$ (1.0 mmol, 2.0 equiv), molecular sieves 3 Å (MS 3 Å, powder, 100 mg), under CO_2 (1 atm), in DMF (2.5 mL), at room temperature for 20 h. [b] Determined by GC analysis. [c]Isolated yield of **2a**.

Table 5-2. Effects of Ligands[a]



entry	ligand	GC yield (%)		entry	ligand	GC yield (%)	
		2a	**3a**			**2a**	**3a**
1	none	0	0	11	box	0	0
2	bpy	74	3	12[b]	pyridine	0	0
3	MeO-bpy	37	2	13[b]	DBU	0	0
4	NEt_2-bpy	0	4	14	PPh_3	0	0
5	Cl-bpy	0	0	15[b]	PCy_3	0	0
6	Phen	48	trace	16	dppe	0	0
7	Me-phen	52	2	17	Xantphos	0	0
8	Ph-phen	8	7	18	*rac*-BINAP	0	0
9	NO_2-phen	0	0	19[b]	IPr	0	0
10[b]	TMEDA	0	0	20[b]	SIPr	0	0



[a] Reaction conditions: 5-Decyne (**1a**, 0.50 mmol), $Ni(acac)_2$(ligand) (0.050 mmol, 10 mol %), Zn powder (1.5 mmol, 3.0 equiv), $MgBr_2$ (1.0 mmol, 2.0 equiv), molecular sieves 3 Å (MS 3 Å, powder, 100 mg), under CO_2 (1 atm), in DMF (2.5 mL), at room temperature for 16 h. [b] $Ni(acac)_2$ (10 mol %) and Ligand (10 mol %) was used.

The double carboxylations of various internal alkynes (**1b–i**) were carried out (Table 5-3). With 3-hexyne (**1b**) and 2,9-dimethyl-5-decyne (**1c**) as substrates, the corresponding products (**2b** and **2c**) were obtained in good isolated yields (entries 1 and 2). 2-Octyne (**1d**) and 5-phenyl-2-pentyne (**1e**) reacted smoothly, giving the corresponding products (entries 3 and 4). Alkynes with secondary alkyl groups on the sp-carbons (**1f** and **1g**) also provided the double-carboxylated products in good yields (entries 5 and 6). An alkyne having an olefin substituent (**1h**) was converted to the corresponding product with the C=C bond intact (entry 7). A cyclic internal alkyne (**1i**) also took part in the reaction, giving the corresponding product in 79% yield (entry 8). In Table 5-3, **1b-i** were fully converted, but side products other than a small amount of monocarboxylated products were not detected by GC and GC-MS analyses. Unfortunately, terminal alkynes and aromatic internal alkynes did not afford the corresponding double carboxylated products.

The present reaction was applied to the fast and highly efficient synthesis of Chaetomellic acid A anhydride, which is isolated from the coelomycete *Chaetomella acutiseta*. The dianionic form of this compound is a potent and selective inhibitor of ras farnesyl protein transferase.[13] As shown in Scheme 5-2, the reaction of commercially available 1-hexadecyne with methyl iodide afforded **1j** quantitatively. The treatment of **1j** under the optimized reaction conditions provided the desired product (**2j**) in 70% isolated yield. To the best of our knowledge, this is the shortest and the most efficient synthetic route to Chaetomellic acid A anhydride among the known procedures.[11,14]

Scheme 5-2. Synthesis of Chaetomellic Acid A Anhydride

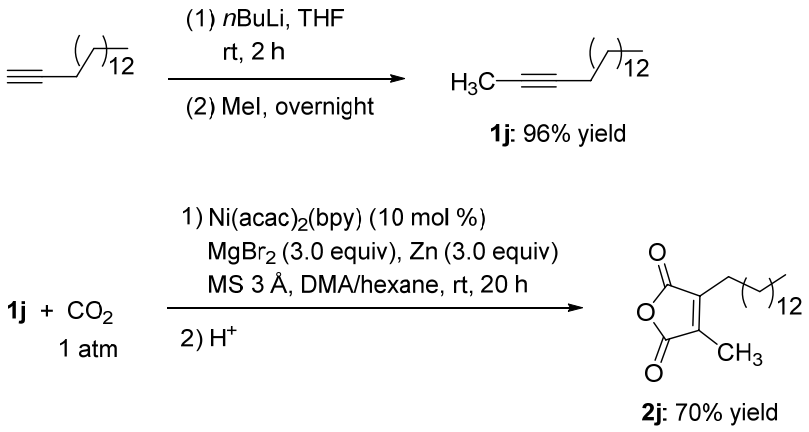
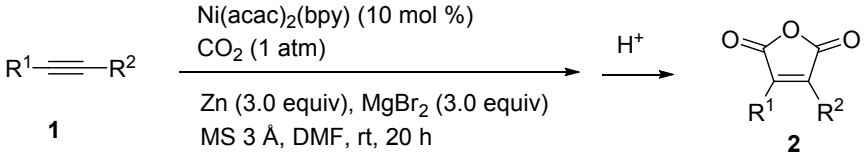


Table 5-3. Nickel-Catalyzed Double Carboxylation of Internal Alkynes[a]



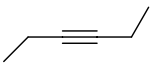
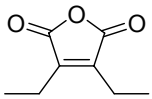
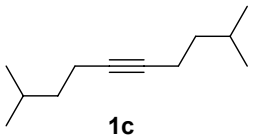
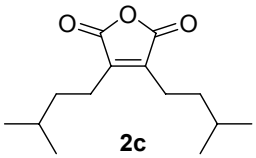
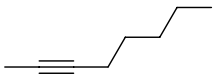
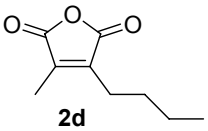
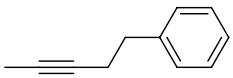
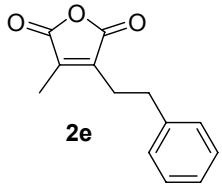
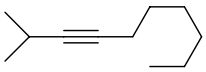
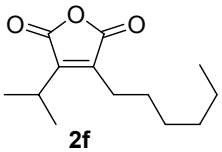
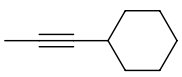
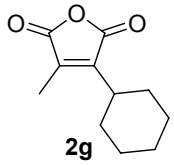
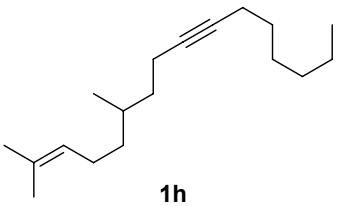
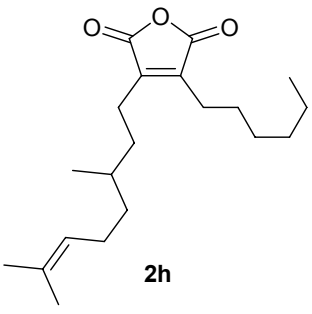
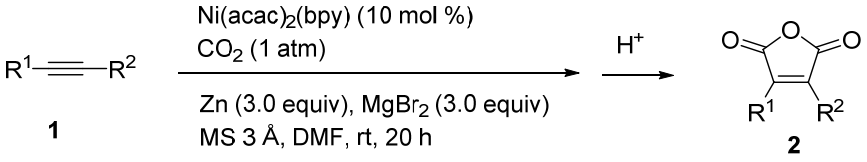
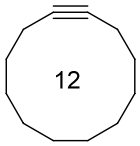
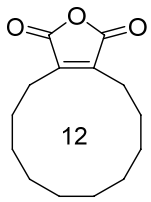
entry	substrate	product	yield (%)[b]
1	 **1b**	 **2b**	60
2	 **1c**	 **2c**	65
3	 **1d**	 **2d**	65
4	 **1e**	 **2e**	50
5	 **1f**	 **2f**	58
6	 **1g**	 **2g**	67
7[c]	 **1h**	 **2h**	69

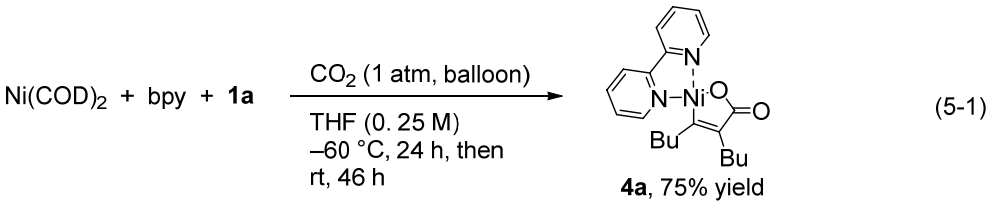
Table 5-3. Nickel-Catalyzed Double Carboxylation of Internal Alkynes[a] (continued)



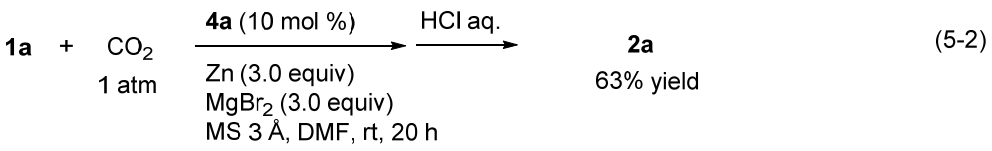
entry	substrate	product	yield (%)[b]
8	 **1i**	 **2i**	79

[a] Reaction conditions: **1** (0.50 mmol), Ni(acac)$_2$(bpy) (0.050 mmol, 10 mol %), $MgBr_2$ (1.5 mmol, 3.0 equiv), Zn powder (1.5 mmol, 3.0 equiv), molecular sieves 3 Å (powder, 100 mg), under CO_2 (1 atm), in DMF (2.0 mL), at 25 ºC for 20 h. [b] Isolated yield. [c] A mixture of DMA/hexane (1.5 mL/0.75 mL) was used as a solvent.

In terms of a mechanism, it is well-known both experimentally[15a,b] and theoretically[15c,d] that the oxidative cyclization of Ni^0, CO_2, and alkynes gives oxanickelacyclopentenones (**4**). Actually, the reaction of **1a** with Ni(COD)$_2$ (COD = 1,5-cyclooctadiene) in the presence of bpy under CO_2 (1 atm) gave the corresponding complex **4a** in 75% yield (eq 5-1).[15b] The double carboxylation of **1a** to **2a** proceeded in the presence of a catalytic amount (10 mol %) of **4a** in 63% yield (eq 5-2). Hence, nickelacycle (**4**) must be involved in the catalytic cycle.



(5-1)



(5-2)

After the formation of nickelacycle (**4**), three possible paths (a–c) may follow for the *second* carboxylation. In path a, direct CO_2 insertion into the Ni^{II}–C bond of **4** occurs without any help by $MgBr_2$. In path b, **4** forms an adduct with $MgBr_2$ followed by the insertion of CO_2 into the Ni^{II}–C bond. Finally, in path c, a one-electron reduction of **4** by Zn in the presence of $MgBr_2$ occurs first to afford a Ni^{I} intermediate, followed by the insertion of CO_2 into the Ni^{I}–C bond.[5b] These three possible paths were examined by density functional theory (DFT) calculations (Figures 5-1–5-4).

Direct CO_2 insertion into the Ni^{II}–C bond of **4b** (**4**: $R^1 = R^2 = CH_3$) proceeds via $\mathbf{TS_{4b\text{-}A1}}$ with a large $\Delta G^{0‡}$ value of 21.9 kcal/mol (path a, Figure 5-1 and 5-2). In path b (Figure 5-3 and 5-4), $MgBr_2$ first interacts with the nickel carboxylate moiety of **4b** to afford **A2**. Then, CO_2 is inserted into the Ni^{II}–C bond of **A2** via $\mathbf{TS_{A2\text{-}A3}}$ to afford **A3** with a $\Delta G^{0‡}$ value of 17.4 kcal/mol. In sharp contrast, in path c (Figure 5-2), after the one-electron reduction of **4b** to **B**, the insertion of CO_2 into the Ni^{I}–C bond of **B1** is quite facile ($\Delta G^{0‡}$ = 5.0 kcal/mol) as compared with paths a and b (cf. 21.9 kcal/mol and 17.4 kcal/mol in Figure 5-1). In the one-electron reduction, $MgBr_2$ plays a crucial role to provide bromide anion to Zn^{2+}. During the CO_2 insertion, the resulting MgBr coordinates with both the carboxylate moiety and the incoming CO_2 in **B1** and $\mathbf{TS_{B1\text{-}C}}$ to facilitate the second carboxylation. Thus, $MgBr_2$ makes the one-electron reduction of **4b** possible and accelerates the CO_2 insertion in **B1**. These crucial roles of $MgBr_2$ have not been previously recognized.

Based on the experimental results (eqs 5-1 and 5-2) and DFT calculations (Figures 5-1–5-4), a plausible catalytic cycle is suggested in Scheme 5-3. The active catalyst species must be Ni^0(bpy)[15d] which is formed via reduction of the Ni^{II} catalyst precursor by Zn (step a). Then, the oxidative cyclization of Ni^0(bpy) with **1** and CO_2 affords the Ni^{II} metallacycle **4** (step b). The reduction of **4** with Zn and $MgBr_2$ provides Ni^{I} species **B** (step c). **B** must be a key intermediate in this double carboxylation, since the carboxylation of **B** to **C** (step d) is much easier due to the higher nucleophilicity of **B** and the coordinative participation of the MgBr moiety (Figure 5-3 and 5-4). Finally, the reduction of **C** affords the double-carboxylated product **D** and regenerates the active Ni^0 catalyst species (step e).

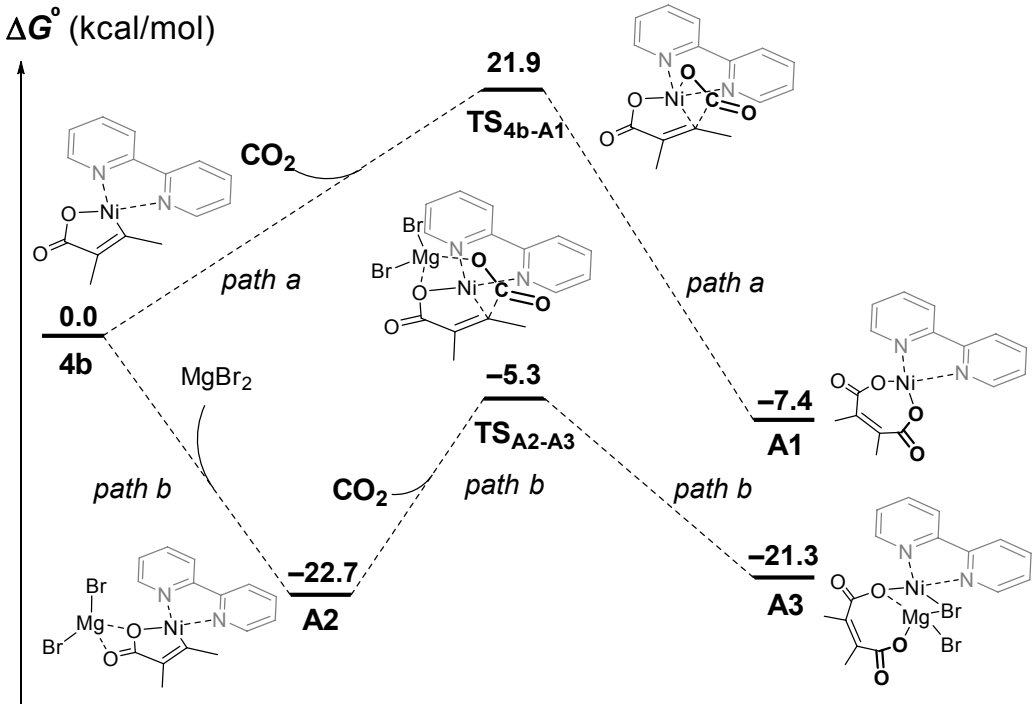


Figure 5-1. The Gibbs energy profile for the second CO_2 insertion (paths a and b).

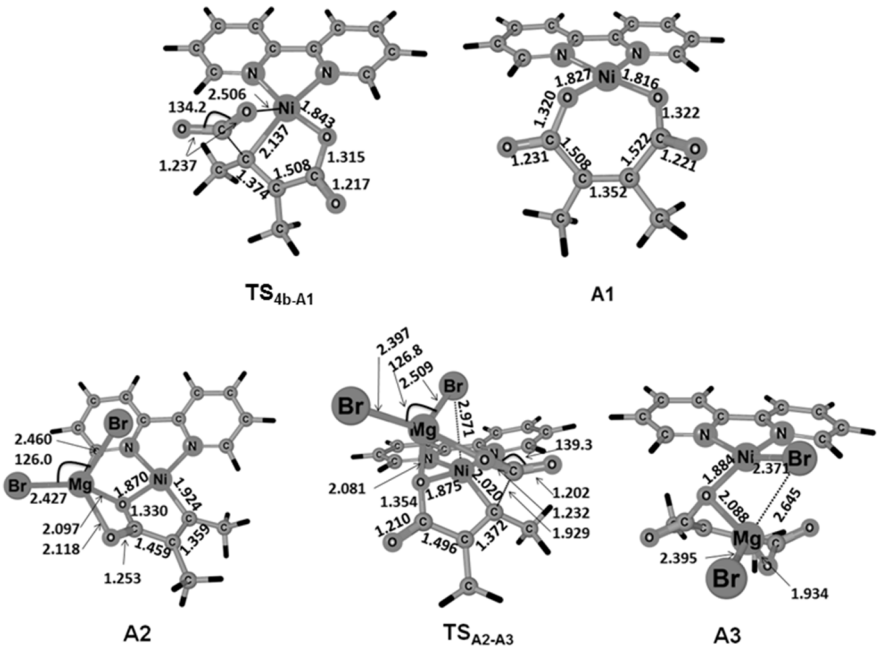


Figure 5-2. Geometries of **TS_{4b-A1}**, **A1**, **A2**, **TS_{A2-A3}** and **A3**. Bond lengths are angstrom units and bond angles in degrees.

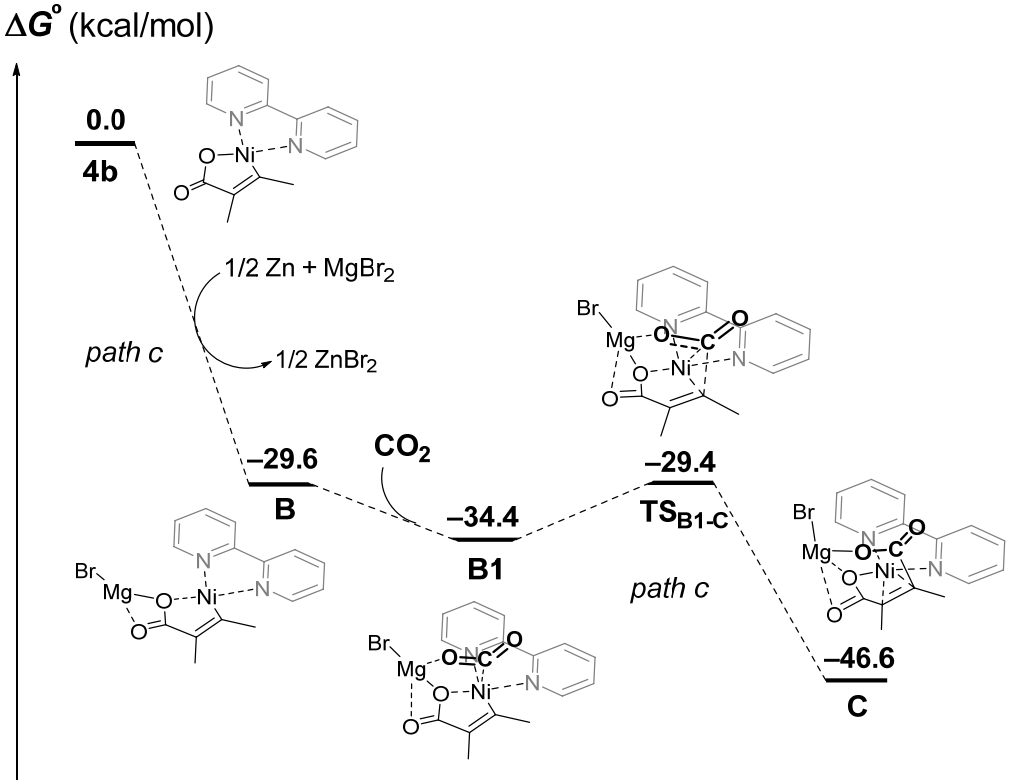


Figure 5-3. The Gibbs energy profile for the second CO_2 insertion (path c).

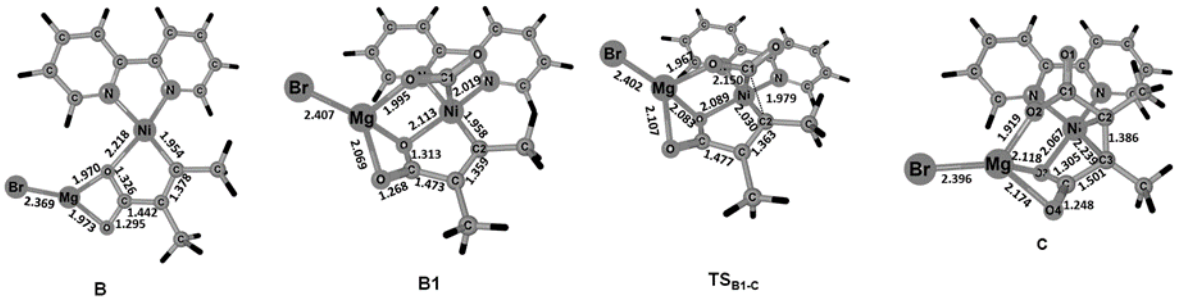
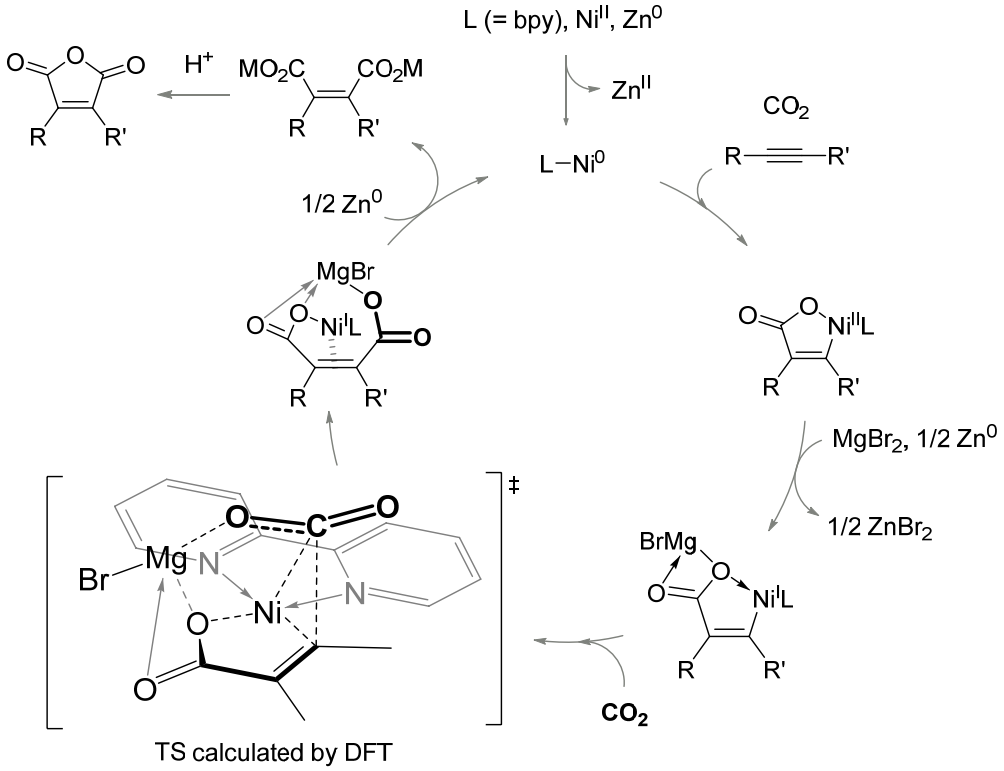


Figure 5-4. Geometries of **B**, **B1**, $\mathbf{TS_{B1\text{-}C}}$ and **C**. Bond lengths are angstrom units and bond angles in degrees.

Scheme 5-3. Plausible Reaction Mechanism



5-3. Conclusion

The author developed a new nickel-catalyzed double carboxylation of alkynes under CO_2 (1 atm) at room temperature to give maleic anhydride derivatives. The key to the success of the present reaction is the generation of the Ni^I metallacycle intermediate and the participation of MgBr in facilitating the second carboxylation. It should be noted that the crucial roles of $MgBr_2$ in the one-electron reduction and the second CO_2 insertion into the Ni^I–C bond are first recognized here.

5-4. Experimental Section

5-4-1. General Remarks

Unless otherwise noted, manipulations were performed under an argon atmosphere using standard Schlenk-type glasswares in a dual-manifold Schlenk line. Unless otherwise noted, reagents and solvents were dried and purified before use by usual procedures. ^1H NMR and ^{13}C NMR spectra were measured with a JEOL ECX-400 spectrometer or a Bruker AVANCE-500 spectrometer. The ^1H NMR chemical shifts are reported relative to tetramethylsilane (TMS, 0.00

ppm) or residual protiated solvent (7.26 ppm) in $CDCl_3$ and residual protiated solvent (2.54 ppm) in DMSO-d_7. The ^{13}C NMR chemical shifts are reported relative to $CDCl_3$ (77.0 ppm) and DMSO-d_7 (40.5 ppm). IR spectra were obtained on a JASCO FT/IR-4100 spectrometer. Elemental analysis was carried out at Center for Organic Elemental Microanalysis, Graduate School of Pharmaceutical Science, Kyoto University. Column chromatography was carried out on silica gel (Kanto N60, spherical, neutral, 63–210 μm). GC analysis was carried out using a Shimadzu GC-17A with a capillary column (CBP-5, 0.25 mm i.d. × 25 m). TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck Silica gel 60F254. Kugelrohr distillation was carried out with SHIBATA Glass Tube Oven GTO-350 RD.

5-4-2. Preparation of Substrates, Reagents and Catalysts

Unless otherwise noted, commercially available chemicals were used as received. Anhydrous THF, toluene and CH_2Cl_2 were purchased from Kanto Chemical and further purified by passage through activated alumina under positive argon pressure as described by Grubbs et al.[16] DMF was distilled under reduced pressure. Alkynes **1a**, **1b**, **1c** and **1d** were purchased from Aldrich, distilled and degassed before use. Alkynes **1e**,[17] **1g**,[18] and **1i**[19] were synthesized according to literature methods, then distilled and degassed before use.

Preparation of $Ni(acac)_2(bpy)$[20]

In a glove box, dried $Ni(acac)_2$ (1.3 mg, 5.0 mmol) and bpy (0.78 g, 5.0 mmol) were added to 300 mL round bottom flask. CH_2Cl_2 (50 mL) was added and the mixture was stirred for 30 min. The mixture was recrystallized by adding hexane (200 mL). The green crystal was filtered off and dried in vacuo.

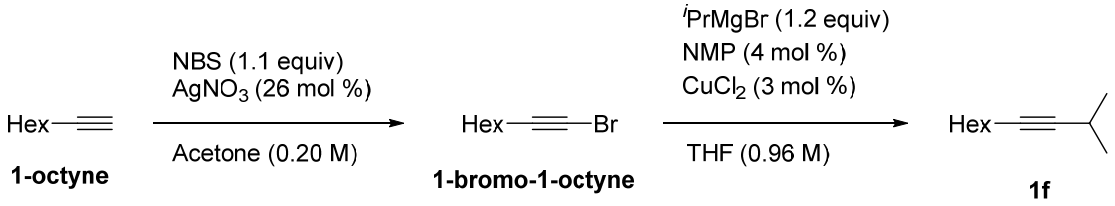
Preparation of dried $MgBr_2$

$MgBr_2 \cdot OEt_2$ (Sigma Aldrich, white powder, 10 g) was added to 100 mL one-necked round bottom flask in a glove box. The powder was heated at 100 °C with a mantle heater for 5 h in vacuo (1 torr). Then, the powder was further heated at 250 °C for 3 days in vacuo (3.0×10^{-3} torr). The white powder was cooled to room temperature and stored in a glove box.

Preparation of dried MS 3Å

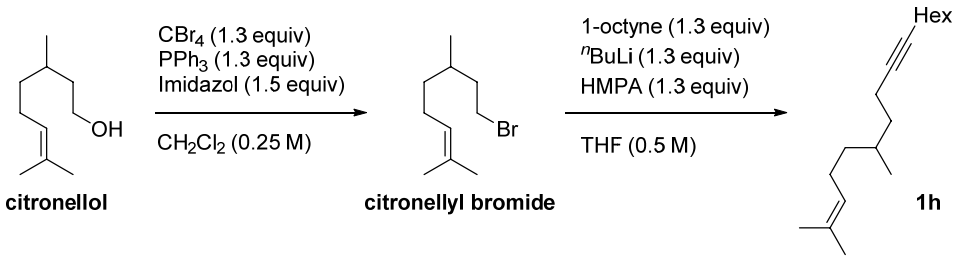
MS 3Å (Sigma Aldrich, white powder, 10 g) was added to 100 mL one-necked round bottom flask in a glove box. MS 3Å was heated at 300 °C with a mantle heater for 3 h in vacuo (1 torr). Then, the powder was further heated at 450 °C for 30 h in vacuo (3.0×10^{-3} torr). White powder was cooled to room temperature and stored in a glove box.

Preparation of 1f



To a dried 200 mL two-neck flask were added 1-octyne (5.0 mL, 34 mmol), NBS (6.7 g, 38 mmol), and acetone (85 mL). After NBS was dissolved, $AgNO_3$ (1.7 g, 10 mmol) was added and the reaction mixture was stirred for 3 h at room temperature. After quenching by adding H_2O, the mixture was filtered and extracted with Et_2O (50 mL × 3). The organic layer was dried over $MgSO_4$. After removal of all volatiles, the product was purified by column chromatography (eluent: Et_2O) to give 1-bromo-1-octyne quantitatively as a yellow oil. Then, to a dried 200 mL two-neck flask were added 1-bromo-1-octyne (7.3 g, 39 mmol), NMP (148 μL, 1.55 mmol), $CuCl_2$ (0.16 g, 1.2 mmol) and THF (40 mL). The flask was allowed to cool to 0 °C. After *i*PrMgBr (63.5 mL in THF, 46 mmol) was added dropwise over 45 min, the mixture was stirred at 0 °C for 30 min. Then, the reaction mixture was quenched with 1 N HCl aq. (20 mL), and extracted with Et_2O (50 mL × 3). The organic layer was dried over $MgSO_4$. After removal of all volatiles, the product was purified by distillation to give the compound **1e** (2.6 g, 44%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.89 (t, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 6H), 1.24–1.40 (m, 6H), 1.43–1.51 (m, 2H), 2.13 (td, *J* = 7.0, 2.0 Hz, 2H), 2.47–2.56 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 14.0, 18.7, 20.5, 22.6, 23.5, 28.5, 29.2, 31.4, 79.4, 86.0. **ESI-HRMS** (*m/z*): $[M+H]^+$ calcd for $C_{11}H_{21}$, 153.1638; found, 153.1635.

Preparation of 1h



To a dried 200 mL two-neck flask were added PPh_3 (11 g, 43 mmol), imidazole (3.4 g, 49 mmol), and CH_2Cl_2 (100 mL). After the mixture was cooled to 0 °C, a solution of CBr_4 (14 g, 4.25 M) in CH_2Cl_2 was added. The mixture was stirred at 0 °C for 5 min, and then a solution of citronellol (5.14 g, 1.4 M) in CH_2Cl_2 was added dropwise and the reaction mixture allowed to warm to room temperature over 30 min. The solvent was removed in vacuo and the residue was triturated with pentane/ether (10:1, 20 mL) in the presence of a small amount (ca. 1 g) of silica gel. The supernatant was filtered through a short plug of silica and concentrated in vacuo to give

a crude oil that was purified by short path distillation to give citronellyl bromide (4.8 g, 67%) as a colorless oil. Then, THF (40 mL) and 1-octyne (2.8 g, 20 mmol) was added to flame dried 200 mL round bottom flask and cooled to –78 °C. *n*BuLi (1.6 M solution in hexane, 16 mL, 26 mL) were slowly added and the mixture was stirred 20 min at 0 °C. HMPA (4.7 mg, 26 mmol) and citronellyl bromide (4.1 g, 14 mmol) were added. After warming to room temperature, the solution was stirred at room temperature overnight. The reaction was quenched with NH_4Cl (30 mL) and extracted with Et_2O (50 mL × 3). The organic layer was dried over $MgSO_4$. After removal of all volatiles, the residue was purified by GPC with $CHCl_3$ as the eluent to give **1h** (2.8 g, 52%) as a colorless oil, which was distilled and degassed before use. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.87 (d, *J* = 6.3 Hz, 3H), 0.89 (t, *J* = 7.0 Hz, 3H), 1.09–1.18 (m, 1H), 1.24–1.41 (m, 8H), 1.44–1.57 (m, 4H), 1.60 (s, 3H), 1.68 (s, 3H), 1.89–2.05 (m, 2H), 2.07–2.23 (m, 4H), 5.07–5.12 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 14.0, 16.5, 17.6, 18.8, 19.1, 22.6, 25.5, 25.7, 28.5, 29.1, 31.4, 31.7, 36.3, 36.8, 80.1, 80.3, 124.9, 131.2. **EI-HRMS** (*m/z*): $[M]^{\bullet+}$ calcd for $C_{18}H_{32}$, 248.2504; found, 248.2497.

5-4-3. Experimental Procedures and Characterization of the Products

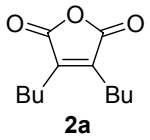
A Typical procedure in Table 5-1 (entry 13)

$Ni(acac)_2(bpy)$ (21 mg, 0.050 mmol), Zn powder (98 mg, 1.5 mmol), $MgBr_2$ (0.18 g, 1.5 mmol) was added to flame dried 50 mL Schlenk flask in a glove box. The flask was evacuated and refilled with CO_2 5 times. Then, DMF (2.5 mL) and 5-decyne (**1a**; 90 μL, 0.50 mmol) were added in this order at 0 °C and the mixture was stirred at room temperature for 20 h. The reaction was quenched with 6 N HCl aq. (4.0 mL) and stirred for 2 h. Then, the mixture was extracted with Et_2O (10 mL). After 2 mL of organic layer was took out, MeOH (0.5 mL) was added. The mixture was dried over $MgSO_4$ followed by addition of $TMSCHN_2$ (100 μL). The yield of the product and by-product was determined by GC analysis relative to an internal standard (tridecane).

General procedure in Table 5-2

$Ni(acac)_2(bpy)$ (21 mg, 0.050 mmol), Zn powder (98 mg, 1.5 mmol), $MgBr_2$ (0.18 g, 1.5 mmol) was added to flame dried 50 mL Schlenk flask in a glove box. The flask was evacuated and refilled with CO_2 5 times. Then, DMF (2.5 mL) and **1** (0.50 mmol) were added in this order at 0 °C and the mixture was stirred at room temperature for 20 h. The reaction was quenched with 6 N HCl aq. (4.0 mL) and stirred for 2 h. Then, the mixture was extracted with Et_2O (10 mL). After removal of volatile, the residue was purified by distillation or silica gel chromatography.

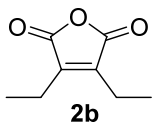
3,4-dibutylfuran-2,5-dione (**2a**)



2a

Isolated by Kugelrohr distillation. Yield 74.6 mg (71%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.95 (t, *J* = 7.2 Hz, 6H), 1.34–1.43 (m, 4H), 1.56 (m, 4H), 2.46 (t, *J* = 7.7 Hz, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 13.6, 22.6, 24.1, 30.0, 144.4, 165.9. **EI-MS** (*m/z*): 210 ($[M]^{\bullet+}$). **Anal.** Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63%. Found: C, 68.31; H, 8.79%.

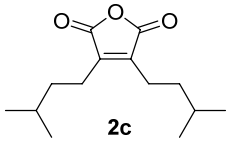
3,4-diethylfuran-2,5-dione (**2b**)



2b

Isolated by Kugelrohr distillation. Yield 46.2 mg (60%).**^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.21 (t, *J* = 7.7 Hz, 6H), 2.50 (q, *J* = 7.7 Hz, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 12.5, 17.7, 145.2, 165.8. **EI-MS** (*m/z*): 154 ($[M]^{\bullet+}$). **Anal.** Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54%. Found: C, 62.26; H, 6.63%.

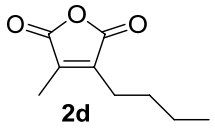
3,4-diisopentylfuran-2,5-dione (**2c**)



2c

Isolated by distillation. Yield 77 mg (65%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.95 (d, *J* = 6.4 Hz, 12H), 1.42–1.46 (m, 4H), 1.61 (sept, *J* = 6.5 Hz, 2H), 2.42–2.46 (m, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 22.2, 22.4, 28.1, 36.9, 144.5, 166.0. **ESI-HRMS** (*m/z*): $[M–H]^-$ calcd for $C_{14}H_{21}O_3$, 237.1496; found, 237.1497.

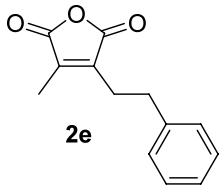
3-butyl-4-methylfuran-2,5-dione (**2d**)



2d

Isolated by Kugelrohr distillation. Yield 59 mg (65%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.91 (t, *J* = 6.6, 3H), 1.30–1.38 (m, 4H), 1.55–1.63 (tt, *J* = 7.7 Hz and *J* = 7.7 Hz, 2H), 2.08 (s, 3H), 2.46 (t, *J* = 7.7 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 9.4, 13.7, 22.2, 24.2, 27.2, 31.4, 140.4, 144.7, 165.8, 166.2. **EI-MS** (*m/z*): 182 ($[M]^+$). **Anal.** Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74%. Found: C, 65.91; H, 8.00%.

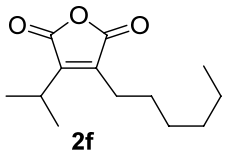
3-methyl-4-phenethylfuran-2,5-dione (**2e**)



2e

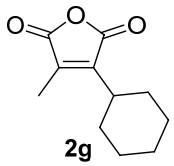
Isolated with column chromatography (eluent: hexane/EtOAc = 9/1). Yield 54 mg (50%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.68 (s, 3H), 2.76 (t, *J* = 7.2 Hz, 2H), 2.90 (t, *J* =7.2 Hz, 2H,), 7.11–7.13 (m, 2H), 7.22–7.31 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 9.03, 26.5, 33.4, 126.7, 128.4, 128.7, 139.4, 141.6, 143.0, 165.7, 166.0. **EI-MS**: *m/z* 216 ($[M]^{\bullet+}$). **Anal.** Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13%. Found: C, 72.74; H, 6.16%.

3-hexyl-4-isopropylfuran-2,5-dione (**2f**)



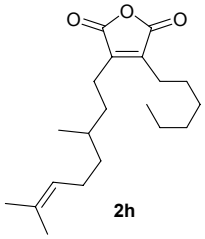
Isolated with column chromatography (eluent: hexane/EtOAc = 9/1). Yield, 65.0 mg, 58%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.89 (t, *J* = 4.0 Hz, 3H), 1.25–1.38 (m, 6H), 1.30 (d, *J* = 7.2 Hz, 6H), 1.51–1.59 (m, 2H), 2.46 (t, *J* = 7.7 Hz, 2H), 2.96 (Sep, *J* = 7.0, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 14.0, 20.3, 22.4, 24.2, 26.2, 28.3, 29.2, 31.3, 143.3, 148.5, 164.8, 166.0. **EI-HRMS** (*m/z*): $[M]^{\bullet+}$ calcd for $C_{13}H_{20}O_3$, 224.1412; found, 224.1411.

3-cyclohexyl-4-methylfuran-2,5-dione (**2g**)



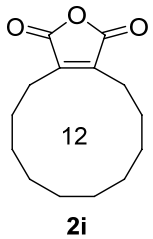
Isolated by Kugelrohr distillation. Yield 69 mg (71%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.29–1.39 (br, 3H), 1.68–1.76 (m, 5H), 1.84–1.87 (m, 2H), 2.10 (s, 3H), 2.58–2.66 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 9.5, 25.4, 25.9, 29.7, 36.2, 139.2, 147.6, 165.1, 166.4. **EI-MS** (*m/z*): 194 ($[M]^{\bullet+}$). **Anal.** Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27%. Found: C, 68.29; H, 7.25%.

3-(3,7-dimethyloct-6-en-1-yl)-4-hexylfuran-2,5-dione (**2h**)



Isolated with column chromatography (eluent: hexane/EtOAc = 9/1). Yield 110 mg (69%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.89 (t, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 1.16–1.60 (m, 13H), 1.61 (s, 3H), 1.69 (d, *J* = 0.9 Hz, 3H), 1.90–2.07 (m, 2H), 2.36–2.50 (m, 4H), 5.06–5.10 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 14.0, 17.6, 19.2, 22.1, 22.4, 24.4, 25.4, 25.7, 27.9, 29.2, 31.3, 32.4, 35.0, 36.5, 124.3, 131.6, 144.2, 144.8, 166.0. **ESI-HRMS** (*m/z*): $[M+H]^+$ calcd for $C_{20}H_{33}O_3$, 321.2424; found, 321.2417.

3,4-decamethylenefuran-2,5-dione (**2i**)



Isolated with column chromatography (eluent: hexane/EtOAc = 9/1). Yield 93 mg (79%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 1.25–1.33 (m, 4H), 1.37–1.44 (m, 8H), 1.75–1.81 (m, 4H), 2.50 (t, *J* = 7.0 Hz, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 21.9, 22.1, 24.2, 25.0, 25.3, 144.9, 165.8. **EI-HRMS** (*m/z*): $[M]^{\bullet+}$ calcd for $C_{14}H_{20}O_3$, 236.1412; found, 236.1407.

Procedure for Scheme 5-2

Preparation of 2-heptadecyne (1j): THF (30 mL) and 1-hexadecyne (2.8 mL, 10 mmol) were added to flame dried 100 mL round bottom flask and cooled to –40 °C. *n*BuLi (1.62 M, 7.5 mL,12 mmol) was added dropwise at –40 °C and the mixture was stirred 1 h at 0 °C. Then, MeI (1.25

mL, 20 mmol) was added dropwise to the reaction mixture. Then, the solution was stirred at room temperature overnight. The reaction was quenched with sat. NH_4Cl aq. (30 mL) and extracted with Et_2O (50 mL × 3). The organic layer was dried over $MgSO_4$ and all volatiles were removed. The product was further purified by distillation. Yield 2.0 g (96%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 0.88 (t, *J* = 6.9 Hz, 3H), 1.24–1.31 (m, 20H), 1.33–1.38 (m, 2H), 1.44–1.49 (m, 2H), 1.78 (t, *J* = 2.4 Hz, 3H), 2.09–2.13 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 3.4, 14.1, 18.7, 22.7, 28.9, 29.1, 29.2, 29.4, 29.5, 29.6, 29.7, 29.7, 29.7, 31.9, 75.3, 79.4. **EI-HRMS** (*m/z*): $[M]^{\bullet+}$ calcd for $C_{17}H_{32}$, 236.2504; found, 236.2506.

Synthesis of Chaetomellic Acid A Anhydride (2j): $Ni(acac)_2(bpy)$ (21 mg, 0.050 mmol), Zn powder (98 mg, 1.5 mmol), $MgBr_2$ (0.18 g, 1.5 mmol) and MS 3Å (100 mg) was added to flame dried 50 mL Schlenk flask in a glove box. After Schlenk tube was brought out, nitrogen was substituted 5 times to CO_2 and the pressure of CO_2 was adjusted to 1 atm. DMA/hexane (1.5 mL / 0.75 mL) and **1j** (0.12 g, 0.50 mmol) were added in this order at 0 °C and the mixture was stirred at room temperature for 20 h. The reaction was quenched with 6 N HCl aq. (4 mL) and stirred for 2 h. Then, the mixture was extracted with Et_2O (10 mL × 4). The solution was dried over $MgSO_4$ and all volatiles was removed. The product was isolated with silica gel column chromatography (eluent: hexane/EtOAc = 30 : 1). Yield 216 mg (70%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.88 (t, *J* = 6.8 Hz, 3H), 1.26 (br, 22H), 1.53–1.61 (m, 2H), 2.07 (s, 3H), 2.45 (t, *J* = 7.7 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 9.4, 14.1, 22.7, 24.4, 27.6, 29.2, 29.3, 29.4, 29.54, 29.59, 29.62, 29.65, 31.9, 140.4, 144.7, 165.9, 166.3 **EI-MS** (*m/z*): 308 ($[M]^{\bullet+}$). All the resonances in ^{1}H and ^{13}C spectrum were consistent with reported values.[13]

Procedure for eq 5-1

$Ni(cod)_2$ (0.83 g 3.0 mmol) and bpy (0.75 g 4.8 mmol) were added to flame dried 50 mL one-necked flask in a glove box. After the flask was brought out, nitrogen was substituted 5 times to CO_2 and the pressure of CO_2 was adjusted to 1 atm. THF (12 mL) was added and the mixture was cooled to –60 °C. Then 5-decyne (0.54 mL, 6.0 mmol) was added to the yellow suspension and the mixture was stirred at –60 °C for 24 h and at room temperature 24 h. During reaction, the color of the mixture was turned to red-orange. The suspension was filtered off. The orange powder was resolved with CH_2Cl_2 (5 mL) and precipitated by adding hexane (50 mL). The orange precipitate was filtered and dried in vacuo. Yield 0.30 g (75%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.78 (t, *J* = 6.8 Hz, 3H), 0.86 (t, *J* = 6.6 Hz, 3H), 1.24 (br, 8H), 1.90 (t, *J* = 7.7 Hz, 2H), 1.97 (t, *J* = 7.0 Hz, 2H), 7.67 (br, 2H) , 8.23 (br, 2H) , 8.40 (br, 2H), 8.56 (br, 2H). **IR** (KBr): 1618, 1606, 1444 cm^{-1}. **MALDI-TOF-MS** (DIT): *m/z* 397 ($[M+H]^+$).

Procedure for eq 5-2

3a (20 mg, 0.050 mmol), Zn powder (98 mg, 1.5 mmol), $MgBr_2$ (184 mg, 1.5 mmol) was

added to flame dried 50 mL Schlenk flask in a glove box. The flask was evacuated and refilled with CO_2 5 times. Then, DMF (2.5 mL) and **1a** (90 μL, 0.50 mmol) were added in this order at 0 °C and the mixture was stirred at room temperature for 20 h. The reaction was quenched with 6 N HCl aq. (4.0 mL) and stirred for 2 h. Then, the mixture was extracted with Et_2O (10 mL). After 2 mL of organic layer was took out, MeOH (0.5 mL) was added. The mixture was dried over $MgSO_4$ followed by addition of $TMSCHN_2$ (100 μL). The yield of **2a** (63%) was determined by GC analysis relative to an internal standard (tridecane).

5-4-4. DFT Calculations

All the geometry optimizations and frequency calculations were performed by the B3LYP-D functional using BS-1 basis set system described below.[21] In BS-1, 6-31G(d) basis sets were employed for H, C, N, O and Mg, 6-31+G(d) for Br, and Lanl2Tz(f) for Ni and Zn with the corresponding effective core potentials (ECPs).[22] Frequency calculations were carried out on all the optimized geometries to ascertain if equilibrium geometry does not have any imaginary frequency and transition state (TS) has only one imaginary frequency. Intrinsic reaction coordinate (IRC)[23] was calculated on all the TSs to validate if the TS connects the corresponding reactant and the product. Conductor-like polarizable continuum model (CPCM)[24] was employed to calculate the solvation effect of DMF using basis set BS-II. In the BS-II, 6-311G(d) basis sets were employed for H, C, N, O and Mg, and 6-311+G(d) for Br, and the basis sets and ECPs by the Stuggart-Dresdon-Bonn group were used for Ni and Zn.[25] The Gibbs energy (ΔG^0) was employed for the discussion, wherein the translational entropy was corrected with the method by Whitesides et al.[26] similar to our previous works.[27] Gaussian 09 package was employed for all these computations.[28]

One electron reduction process

In the experiment, $Ni(acac)_2(bpy)$ was used as the source of nickel catalyst in the presence of Zn and bpy ligand. The $\Delta G_{S1}°$ value for the reduction of $Ni^{II}(acac)_2(bpy)$ to $Ni^0(bpy)$ **5** was calculated, as shown in eq 5-3, where the author used Zn atom as a model of zinc powder like in our previous work.[29] The calculated $\Delta G_{S1}°$ value indicates that this reduction easily occurs.

$$Ni^{II}(acac)_2(bpy) + Zn + \mathbf{2k} + DMF \rightarrow \mathbf{6} + Zn(acac)_2(DMF)_2 \qquad \Delta G_{S1}° = -7.3 \text{ kcal/mol} \quad \text{(5-3)}$$

The second one-electron reduction corresponds to the reduction of the Ni(II) complex **4b** in the presence of $MgBr_2$. Because Suzuki et al.[30] reported that $ZnCl_2$ coordinates with two DMF molecules, the author considered that $ZnBr_2$ is likely to be associated with DMF. This reduction occurs with a substantially negative $\Delta G_{S2}°$ value, indicating that the formation of Ni(I) intermediate **B** occurs easily. Also, it is likely that $MgBr_2$ coordinates with DMF molecules.

Considering this coordination, the author evaluated the $\Delta G_{S3}°$, according to eq 5-5; $\Delta G_{S1}°$ is also considerably negative (–12.2 kcal/mol), indicating that the reduction of **4b** easily occurs under the condition that $MgBr_2$ coordinates with DMF.

4b + $MgBr_2$ + DMF + ½ Zn → **B** + ½ $ZnBr_2(DMF)_2$ $\Delta G_{S2}°$ = –29.6 kcal/mol.....(5-4)

4b + $MgBr_2(DMF)_4$ + ½ Zn
→ **B**$(DMF)_3$ + ½ $ZnBr_2(DMF)_2$ $\Delta G_{S3}°$ = –12.2 kcal/mol.....(5-5)

The final one-electron reduction of **C** generates the double-carboxylated product, as shown in eq 5-6. The calculated $\Delta G_{S4}°$ of –11.5 kcal/mol clearly indicates that this reduction easily occurs.

C + ½ Zn + **2k** → ½ $Zn(O_2CC{=}CCO_2MgBr)_2$ + **6** $\Delta G_{S4}°$ = –11.5 kcal/mol.....(5-6)

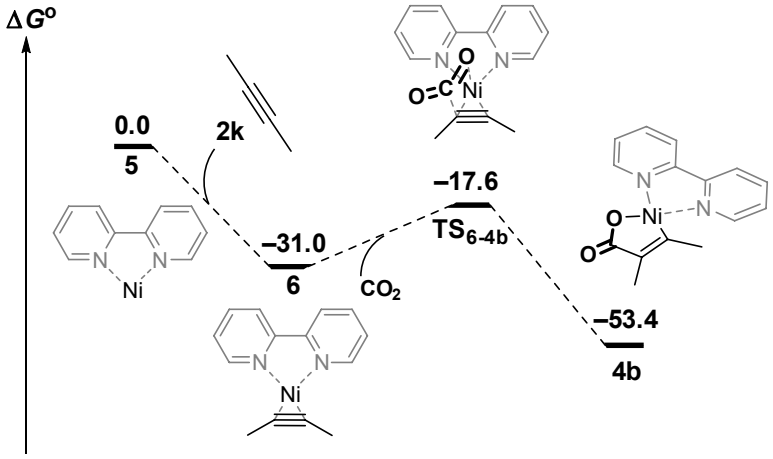


Figure 5-5. The Gibbs energy profile for the oxidative coupling reaction. All the values are in kcal/mol.

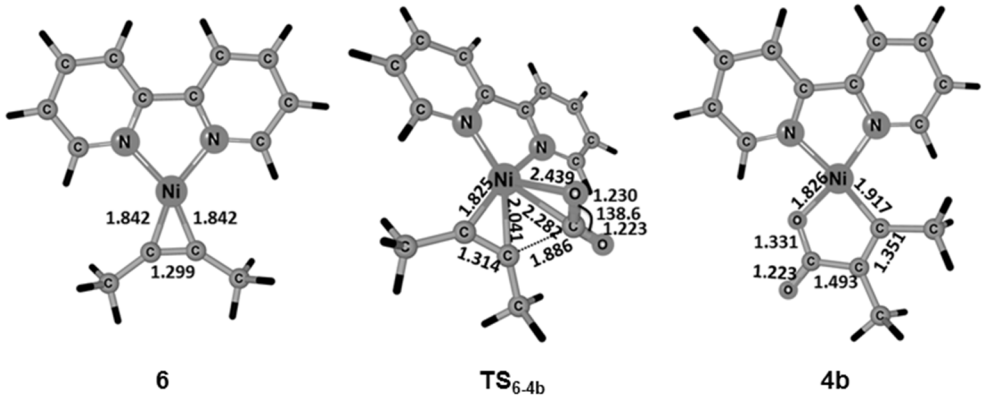


Figure 5-6. Geometries of **6**, **$TS_{6\text{-}4b}$** and **4b**. Bond lengths are angstrom units and bond angles in degrees.

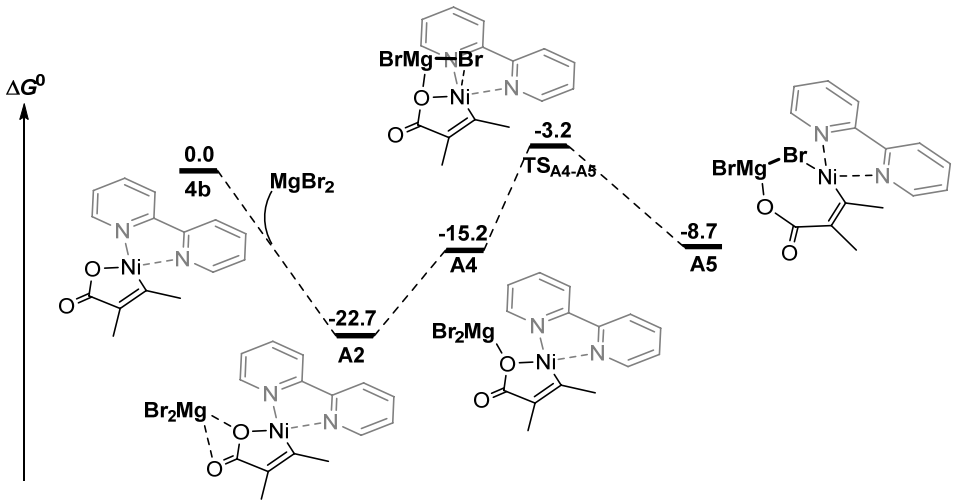


Figure 5-7. Another pathway from **A2** for the formation of Ni(II) complex **A5** by the cleavage of Ni(II)–O bond of **A2**. All the values are in kcal/mol.

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List of Publications

The present Thesis is composed of the following papers.

Chapter 1

(1) Copper-Catalyzed Silacarboxylation of Internal Alkynes by Employing Carbon Dioxide and Silylboranes
Tetsuaki Fujihara, Yosuke Tani, Kazuhiko Semba, Jun Terao, Yasushi Tsuji
Angew. Chem., Int. Ed. **2012**, *51*, 11487–11490.

Chapter 2

(2) Copper-Catalyzed Regiodivergent Silacarboxylation of Allenes with Carbon Dioxide and a Silylborane
Yosuke Tani, Tetsuaki Fujihara, Jun Terao, Yasushi Tsuji
J. Am. Chem. Soc. **2014**, *136*, 17706–17709.

Chapter 3

(3) Copper-Catalyzed Silylative Allylation of Ketones and Aldehydes Employing Allenes and Silylboranes
Yosuke Tani, Tatsuya Yamaguchi, Tetsuaki Fujihara, Jun Terao, Yasushi Tsuji
Chem. Lett. **2015**, *in press*. DOI: 10.1246/cl.141018.

Chapter 4

(4) Copper-Catalyzed Conversion of Carbon Dioxide to Homoallylic Alcohols: Hydro-Hydroxymethylation of Allenes with CO_2 and a Hydrosilane
Yosuke Tani, Kazunari Kuga, Tetsuaki Fujihara, Jun Terao, Yasushi Tsuji
In preparation.

Chapter 5

(5) Nickel-Catalyzed Double Carboxylation of Alkynes Employing Carbon Dioxide
Tetsuaki Fujihara, Yuichiro Horimoto, Taiga Mizoe, Fareed Bhasha Sayyed, Yosuke Tani, Jun Terao, Shigeyoshi Sakaki, Yasushi Tsuji
Org. Lett. **2014**, *16*, 4960–4963.

Acknowledgment

The studies described in this thesis have been carried out under the direction of Professor Yasushi Tsuji from April, 2009 to March, 2015 at the Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University.

The author would like to expresses his sincerest gratitude to Professor Tsuji for giving opportunities to study in his laboratory at Kyoto University (2009–2015) and for his consistent guidance, support, encouragement and enthusiasm throughout his work.

The author deeply appreciates to Professor Jun Terao and Professor Tetsuaki Fujihara at Kyoto University for their daily guidance, hearty advice, helpful discussions and suggestions during the course of this study. He is thankful to Mrs. Aya Uehara and Mrs. Kinuyo Toritani for kind assistance. It is his great pleasure to collaborate with Dr. Kazuhiko Semba, Mr. Yuichiro Horimoto, Mr. Taiga Mizoe, Mr. Kazunari Kuga, and Mr. Tatsuya Yamaguchi for hard and fruitful research. The author greatly wishes to thank all members of Professor Tsuji's group for sharing invaluable moments.

The author is grateful to Professor Shigeyoshi Sakaki and Dr. Fareed Bhasha Sayyed for their collaboration for DFT calculations. He wishes to show his appreciation to Professor Kouichi Ohe and Professor Michinori Suginome for their helpful discussion.

The author would like to give heartfelt thanks to Professor Varinder Kumar Aggarwal for giving him a precious opportunity to join the exciting research group at University of Bristol from June to August, 2013. He is also grateful to Dr. Stefan Roesner and all members of Professor Aggarwal's group for their kind assistance and warm friendship during his stay in Bristol. The Mazume scholarship was indispensable, and the author wishes to acknowledge the founder, Dr. Akira Mazume.

The author is grateful for the financial support of Research Fellowships of the Japan Society for the Promotion of Science (JSPS) for Young Scientists.

Finally, the author wishes to show his sincere appreciation to his parents, Mr. Mamoru Tani and Mrs. Michiyo Tani for their affectionate assistance and encouragement.

Yosuke Tani