

**Studies on New Synthetic Reactions via sp^3C – sp^3C Bond
Cleavage under Transition Metal Catalysis**

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Contents

General Introduction	1
Chapter 1	
Nickel-Catalyzed Borylative Ring Opening Reaction of Vinylcyclopropanes with Bis(pinacolato)diboron Yielding Allylboronates	35
Chapter 2	
Nickel-Catalyzed Borylation of Aryl Cyclopropyl Ketones with Bis(pinacolato)diboron to Synthesize 4-Oxoalkylboronates	49
Chapter 3	
Palladium-Catalyzed Preparation of Silyl Enolates from Cyclopropyl Ketones or α,β -Unsaturated Ketones with Hydrosilanes	67
Chapter 4	
Nickel-Catalyzed Arylative Ring Opening of 3-Methylenecycloalkane-1,1-dicarboxylate	87
Chapter 5	
Rhodium-Catalyzed Allylation of Aldehydes with Homoallyl Alcohols by Retro-Allylation and Isomerization to Saturated Ketones with Conventional or Microwave Heating	105
Chapter 6	
Nickel-Catalyzed Allylation of Allyl Carbonates with Homoallyl Alcohols via Retro-Allylation Providing 1,5-Hexadienes	131
Publication List	153
Acknowledgment	157

Ac	acetyl	i.e.	that is
acac	acetylacetonate	IR	infrared (spectrum)
aq.	aqueous	<i>J</i>	coupling constant (in NMR)
Ar	aryl	Ltd.	limited.
BINAP	2,2'-bis(diphenylphosphino)- 1,1'-binaphthyl	m	multiplet (spectral), meter(s), milli
Bn	benzyl	M	molar (1 M = 1 mol dm ⁻³)
Boc	<i>tert</i> -butoxycarbonyl	Me	methyl
brs	broad singlet (spectral)	μL	microliter
Bu	butyl	mg	milligram(s)
<i>c</i>	cyclo	MHz	megahertz
°C	degrees Celsius	min	minute(s)
ca.	circa	mL	milliliter(s)
calcd	calculated	mm	millimeter(s)
cat.	catalytic	mmol	millimole
cm	centimeter(s)	MS3A	molecular sieves 3A
cod	1,5-cyclooctadiene	<i>n</i>	normal
conc.	concentrated	NMR	nuclear magnetic resonance
Cp	cyclopentadienyl	Np	naphthyl
δ	chemical shift in parts per million downfield from tetramethylsilane	Nu	nucleophile
d	doublet (spectral)	p.	page(s)
dba	dibenzylidene acetone	Ph	phenyl
DCE	dichloro ethane	pin	pinacolato
DIBAL-H	diisobutylaluminum hydride	ppm	parts per million (in NMR)
DME	dimethoxy ethane	Pr	propyl
DMF	<i>N,N</i> -dimethylformamide	q	quartet (spectral)
DMSO	dimethyl sulfoxide	quant.	quantitative
DPPE (dppe)	1,2-bis(diphenylphosphino)ethane	<i>R_f</i>	retention factor (in TLC)
DPPP (dppp)	1,3-bis(diphenylphosphino)propane	RI	index of refraction
DPPB (dppb)	1,4-bis(diphenylphosphino)butane	r.t.	room temperature (25 ± 3 °C)
DPPF	1,1'-bis(diphenylphosphino)ferrocene	s	singlet (spectral)
dr	diastereomer ratio	t	triplet (spectral)
Ed(s).	editor(s)	<i>t</i> (<i>tert</i>)	tertiary
ee	enantiomeric excess	temp.	temperature
eq	equation	Tf	triflate
equiv	equivalent(s)	THF	tetrahydrofuran
Et	ethyl	TIPS	triisopropylsilyl
g	gram(s)	TLC	thin-layer chromatography
h	hour(s)	TMS	trimethylsilyl
Hz	hertz (s ⁻¹)	Torr	1 mmHg, 1/760 atm, 133.322 Pa
<i>i</i>	iso	UV	ultraviolet
		vide infra	see below

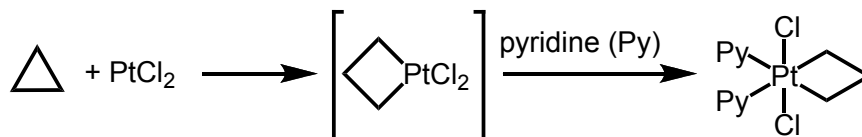
General Introduction

1. sp^3 Carbon– sp^3 Carbon Bond Cleavage of Strained Cycloalkane Under Transition Metal Catalysis

Development of efficient methods for cleavage of C–C bonds catalyzed by transition metal complexes is a new trend and a challenging topic of modern organic chemistry.^{1,2} However, cleavage of sp^3 C– sp^3 C bonds is still difficult due to their stability as well as the high directionality of the σ orbital of an sp^3 C– sp^3 C bond. Transition-metal-catalyzed sp^3 C– sp^3 C bond cleavage is not only interesting but also important in organic synthesis because the cleavage can lead to skeletal rearrangement and new C–C bond formation. Moreover, from the industrial point of view, such processes are important in petroleum refining. For example, catalytic cracking can convert linear hydrocarbons to more useful fuels.

To achieve sp^3 C– sp^3 C bond cleavage, a large number of researchers have utilized strained cycloalkanes, which have relatively low C–C bond energy. The first example of sp^3 C– sp^3 C bond cleavage with a metal complex by using a strained cycloalkane was reported by Tipper in 1955.³ The reaction of PtCl_2 with cyclopropane gave a product formulated as $[\text{PtCl}_2 \cdot \text{C}_3\text{H}_6]_2$. The platinacyclobutane structure was elucidated in 1961 by Chatt, using a combination of NMR and IR studies on the bis(pyridine) adduct.⁴ Mason also confirmed the structure crystallographically (Scheme 1).⁵

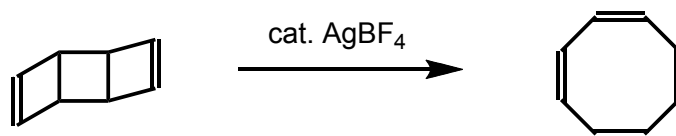
Scheme 1



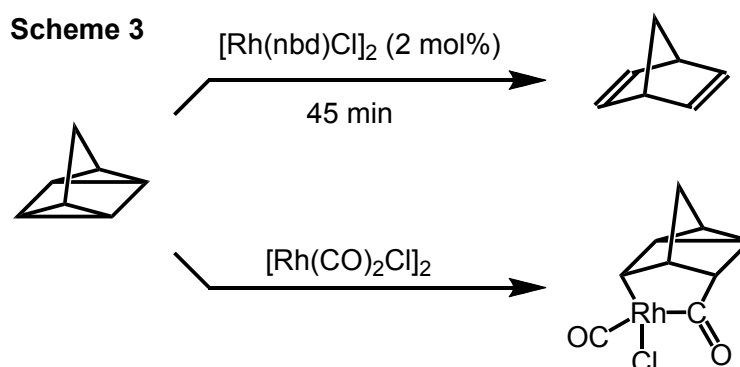
In 1967, Pettit and Mark reported transition-metal-catalyzed ring opening of cyclobutene to butadiene.⁶ In the reported example, *anti*-tricyclooctadiene isomerized to cyclooctatetraene in the presence of silver tetrafluoroborate with a half life of 5 min at 56 °C

(Scheme 2). Besides silver(I), nickel(II), copper(II), platinum(II), and palladium(II) complexes were found to be effective catalysts for similar isomerizations.⁷

Scheme 2



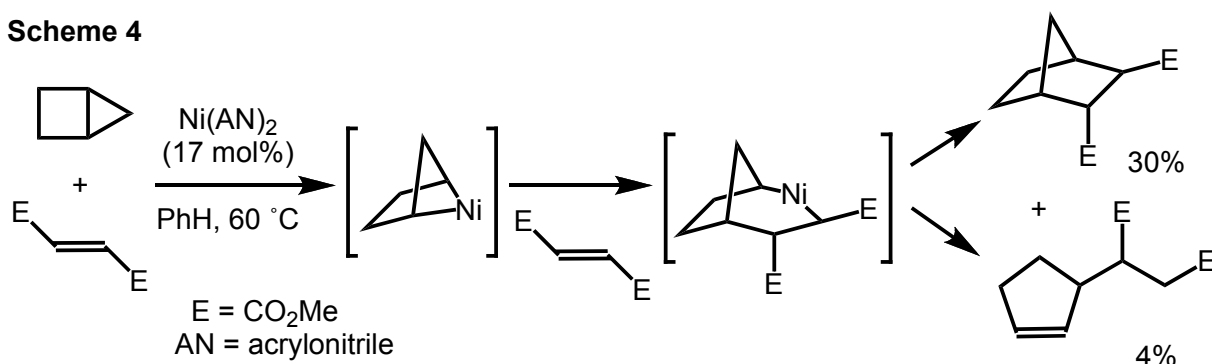
In the same year, Hogeveen and Volger found that low valent transition metal can catalyze rearrangement of quadricyclene to norbornadiene (nbd) (Scheme 3).⁸ The isomerization completed within 45 min at 0 °C when 2 mol% of $[\text{Rh}(\text{nbd})\text{Cl}]_2$ was used as the catalyst. Moreover, in 1970, Manassen isolated a rhodium complex, which suggested a mechanism that oxidative addition of quadricyclene to Rh(I) occurred and was followed by migration of carbon monoxide.⁹ This is the first example to show the evidence that direct oxidative insertion of a low valent transition metal to an $sp^3\text{C}-sp^3\text{C}$ bond occurs.



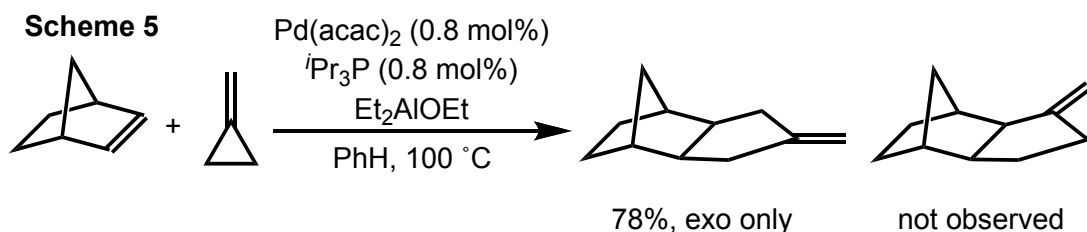
Although many examples of the rearrangement of strained cycloalkanes catalyzed by a Lewis acidic or a low valent transition metal had been reported since Pettit's work,^{6,7} application of $sp^3\text{C}-sp^3\text{C}$ bond cleavage to intermolecular C–C bond formation had not been reported. As a pioneering work, in 1971, Noyori disclosed the reaction utilizing oxidative insertion of a low valent nickel to an $sp^3\text{C}-sp^3\text{C}$ bond.¹⁰ Reaction of dimethyl fumarate with bicyclopentane in the presence of bis(acrylonitrile)nickel(0) $[\text{Ni}(\text{AN})_2]$ afforded a mixture of coupling products (Scheme 4). Although the yields were low, it is noteworthy that the stereochemical mode of the reaction is formally equivalent to that of a thermally forbidden

[2+2] process. Noyori proposed a mechanism in which an oxidative insertion of the nickel into the strained inner bond of bicyclopentane produces the nickelacyclobutane. Dimethyl fumarate then inserts into the nickel-carbon bond. The resulting nickelacycloheptane undergoes reductive elimination to give the bicyclic adduct or is converted to cyclopentene via β -hydride elimination.

Scheme 4



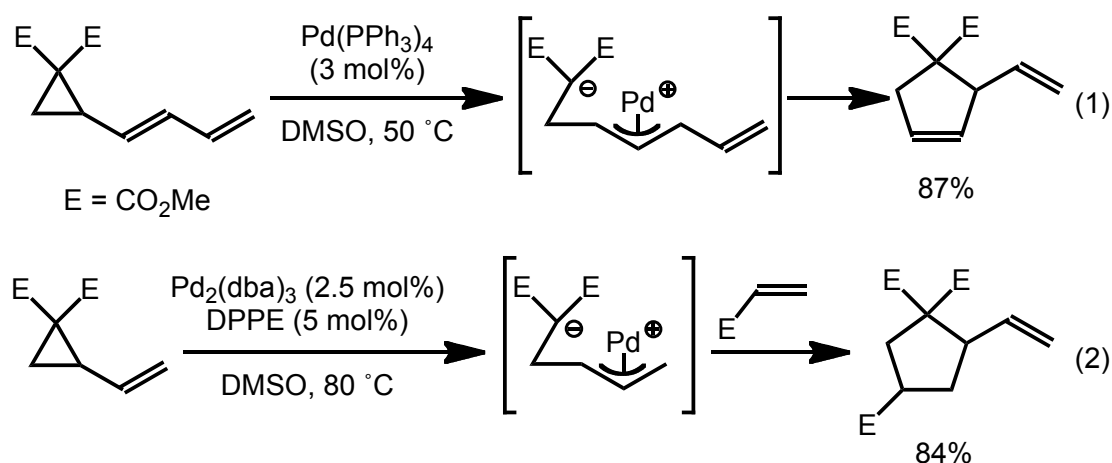
Since then, the reaction via $sp^3\text{C}-sp^3\text{C}$ bond cleavage of a strained alkane catalyzed by transition metal has been extensively investigated. Transition-metal-catalyzed cycloaddition between methylenecyclopropanes and alkenes provided a useful method for the synthesis of methylenecyclopentanes. In 1977, Binger found that palladium catalysts promote the cycloaddition of methylenecyclopropane with electron-rich olefins.¹¹ The reaction occurs exclusively at the distal bond of methylenecyclopropane (Scheme 5). On the other hand, Noyori had also reported cycloaddition by using methylenecyclopropane under nickel catalysis in 1970.¹² The nickel catalyst broke the C-C bond of methylenecyclopropane preferably at the proximal position in the mechanism Noyori proposed.



Two additional pioneering works are the reactions of vinylcyclopropanes having two electron-withdrawing groups in the presence of a palladium catalyst to afford

vinylcyclopentanes. In 1982, Oshima described intramolecular cyclization of dimethyl 2-(1,3-butadienyl)cyclopropane-1,1-dicarboxylate with a catalytic amount of $\text{Pd}(\text{PPh}_3)_4$ to provide vinylcyclopentene derivative (Scheme 6, eq 1).¹³ Furthermore, Tsuji extended this reaction to intermolecular cycloaddition of vinylcyclopropane with electron-deficient olefin (Scheme 6, eq 2).¹⁴ Although zwitterionic π -allylpalladium complexes were known as useful intermediate for 1,3-dipolar cycloaddition, preparation of these complexes were not easy. Oshima and Tsuji provided efficient routes to generate zwitterionic π -allylpalladium complexes from vinylcyclopropanes under mild conditions without a leaving group. The electron-withdrawing substituents are postulated to increase the reactivity for oxidative addition or to stabilize the anionic intermediates that are formed by the oxidative addition.

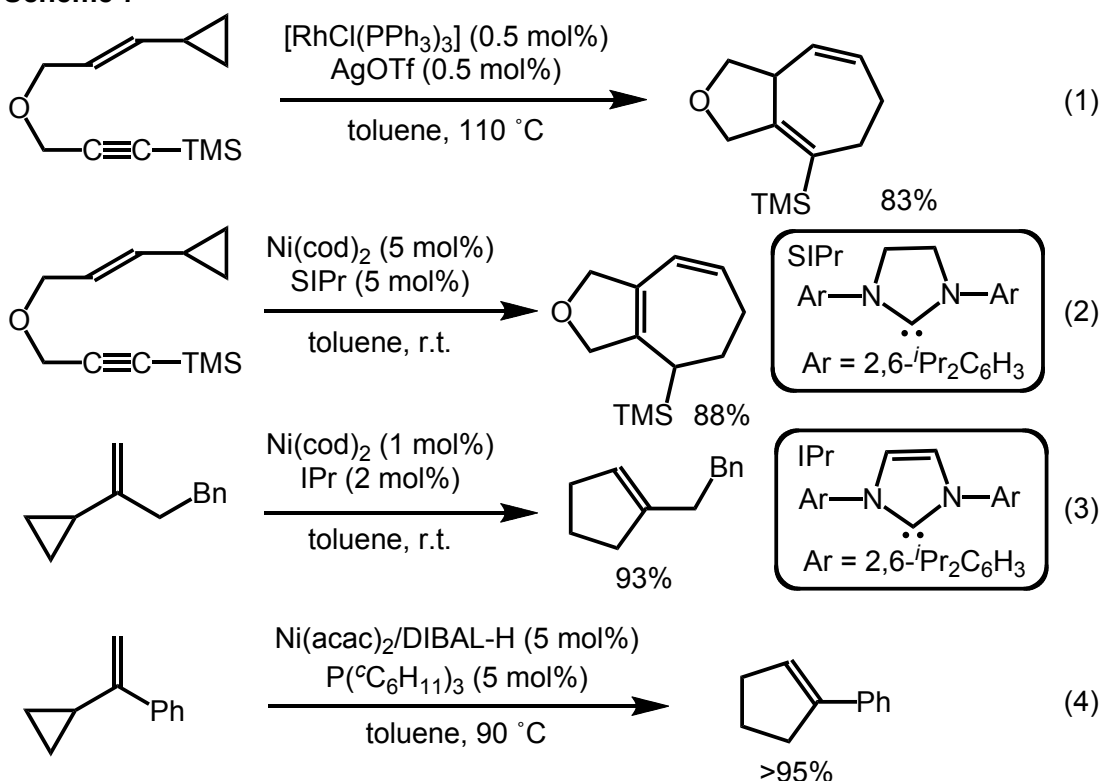
Scheme 6



Other transition metals (Ni, Rh, Cu, Cr, Mo, and Fe) were also reported to catalyze rearrangements of vinylcyclopropane.¹⁵ However, these protocols did not offer significant improvement over the methods described above and were also generally limited to activated vinylcyclopropanes. In 1995, Wender and Witulski reported cationic rhodium-catalyzed intramolecular [5+2] cycloaddition of unactivated vinylcyclopropane tethering an alkynyl moiety to produce cycloheptadiene (Scheme 7, eq 1).¹⁶ Although it was the first example of transition-metal-catalyzed cycloaddition of vinylcyclopropane with alkyne, it generally required high temperatures. Louie reported similar intramolecular [5+2] cycloaddition under conditions milder than the case of rhodium by using a nickel/N-heterocyclic carbene (NHC)

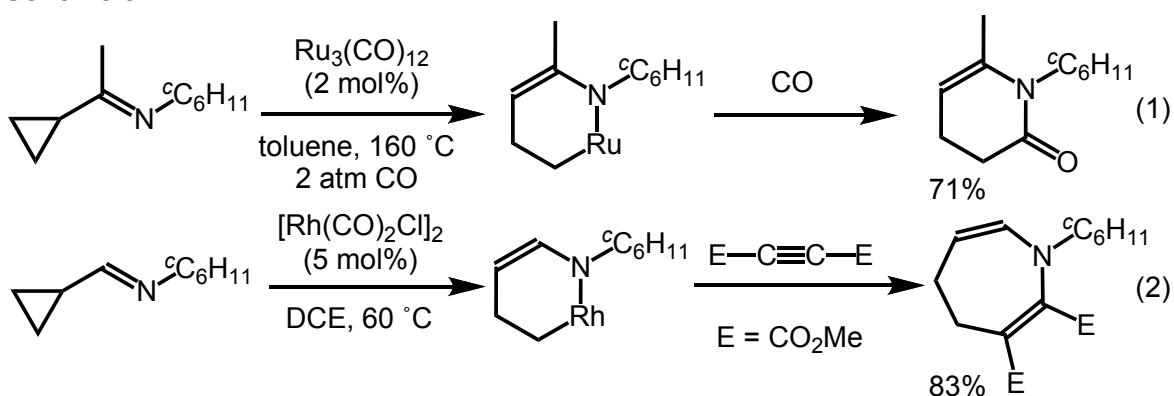
catalytic system (Scheme 7, eq 2).¹⁷ The combination of a nickel complex and a different NHC also promoted simple rearrangement of unactivated vinylcyclopropane to cyclopentene (Scheme 7, eq 3).¹⁸ Although Ito and Sugimoto also reported only one example of rearrangement of unactivated vinylcyclopropane to cyclopentene by means of the combination of $\text{Ni}(\text{acac})_2/\text{DIBAL-H}/\text{P}(\text{C}_6\text{H}_{11})_3$, their system required high temperature (Scheme 7, eq 4).¹⁹ The key to the success of the ring opening reactions might be η^2 -coordination of the unsaturated bond to locate the cyclopropyl ring on a transition metal, which was suggested by a computational study on a rhodium complex given by Houk.²⁰ Very recently, Louie and Tantillo also reported a computational study of simple rearrangement of vinylcyclopropane to cyclopentene catalyzed by a nickel complex and NHC.²¹ Afterwards, various reactions of vinylcyclopropanes with diverse reactants (carbon monoxide, allyl chloride, aldehyde) were reported.²²

Scheme 7



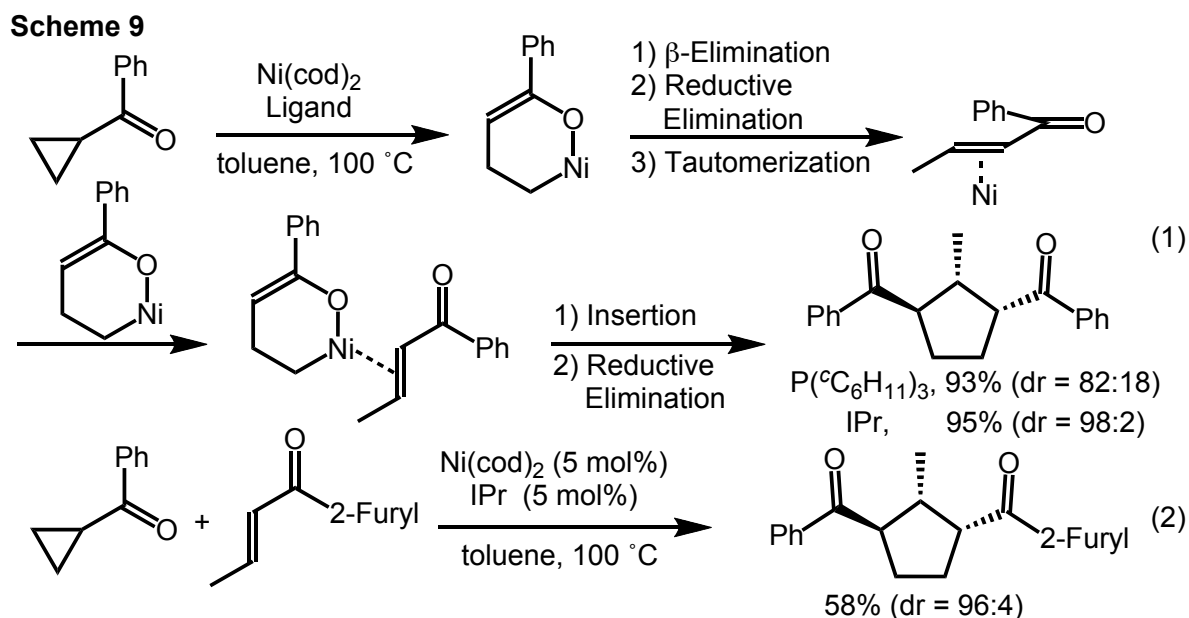
Following these studies on the ring opening reaction of cyclopropane having an unsaturated bond, Chatani, Wender, Ogoshi, and Montgomery illustrated that cyclopropyl imines and cyclopropyl ketones could be good candidates for similar ring opening reaction. In 2000, Chatani reported ruthenium-catalyzed hetero [5 + 1] cycloaddition of cyclopropyl imine with carbon monoxide leading to α,β -unsaturated six-membered lactam derivatives (Scheme 8, eq 1).²³ In 2002, Wender reported rhodium-catalyzed hetero [5 + 2] cycloadditions of cyclopropyl imine with electron-deficient alkyne, providing dihydroazepines (Scheme 8, eq 2).²⁴ They showed that oxidative cyclization of Ru(0) and Rh(I) with cyclopropyl imine easily occurred to form azametalacycle.

Scheme 8



In a related process, Ogoshi and Montgomery showed that oxidative insertion of nickel into cyclopropyl ketones formed a six-membered oxanickelacycle complex. Ogoshi synthesized an oxanickelacycle complex from a nickel complex and cyclopropyl ketones and applied this oxidative cyclization to cycloadditions with another cyclopropyl ketones or enone to produce cyclopentanes (Scheme 9, eq 1).²⁵ In the case of cycloaddition of two molecules of cyclopropyl ketones, the reaction would include β -hydride elimination from oxanickelacycle followed by isomerization to generate α,β -unsaturated ketone. Insertion of α,β -unsaturated ketone to another oxanickelacycle would then occur to eventually afford the product. Although Ogoshi also described the catalytic version of the dimerization reaction of cyclopropyl ketones, no catalytic cross-cycloaddition reaction of cyclopropyl ketones with

enone was shown. Moreover, the diastereoselectivities of the dimerization were unsatisfactory. Montgomery reported the catalytic reaction with enone and improved diastereoselectivities by using an NHC ligand (Scheme 9, eq 2).²⁶

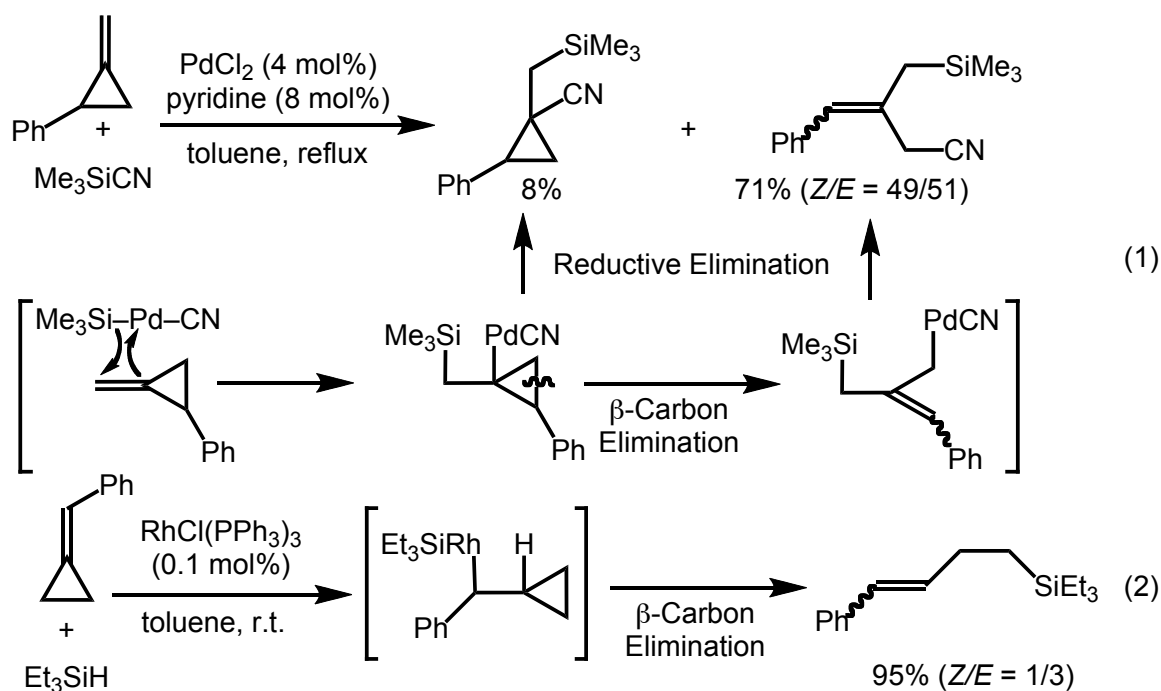


Until Ogoshi provided the evidence suggesting the intermediacy of oxanickelacycle by means of NMR and X ray analysis,^{25b} only computational studies given by Houk and Louie supported metalacycle intermediates which had often been proposed in the reactions of transition metal with cyclopropane having an unsaturated bond (vinylcyclopropane, cyclopropyl imine).^{20,21}

Not only cycloaddition reactions but also ring opening functionalizations of cyclopropanes having an unsaturated bond have been investigated. Transition metal catalysts for the activation of methylenecyclopropanes, vinylcyclopropanes and cyclopropyl ketones allowed σ -bond metathesis or transmetalation with concomitant C–X and C–Y bond formations in the presence of appropriate reactants X–Y such as $\text{R}_3\text{Si–CN}$,²⁷ $\text{R}_3\text{Si–H}$,²⁸ $\text{R}_3\text{Sn–H}$,²⁹ $\text{R}_2\text{N–H}$,³⁰ RO–H ,³¹ RS–H ,³² and $\text{R}_2\text{B–BR}_2$.³³ In particular, silylation and borylation of cyclopropanes having an unsaturated bond are extremely important since the reaction provides synthetically useful products in organic synthesis for further regio- and/or stereoselective functionalization.

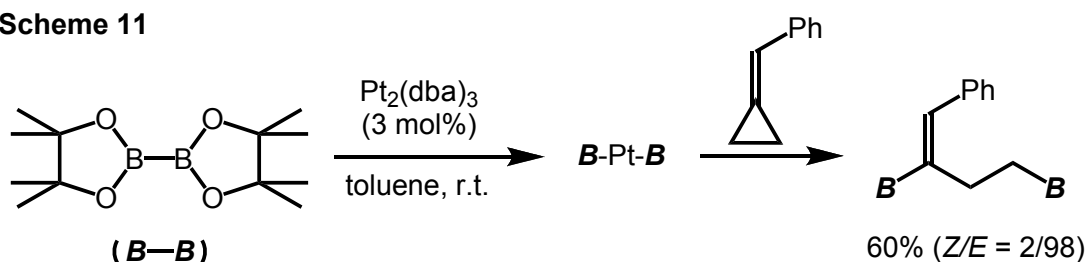
Chatani reported palladium-catalyzed silylcyanation of methylenecyclopropane with silyl cyanide (Scheme 10, eq 1).²⁷ Palladium-catalyzed silylcyanation of methylenecyclopropane gave β -(cyanomethyl)allylsilane and a small amount of cyclopropanecarbonitrile as a byproduct. Observing that the cyclopropane ring could remain intact, Chatani proposed that the reaction would involve oxidative addition of silyl cyanide to palladium, insertion of the olefin, and β -carbon elimination leading to the ring opening. Beletskaya reported the Wilkinson-complex-catalyzed hydrosilylation of methylenecyclopropane with hydrosilane (Scheme 10, eq 2).²⁸ In the reactions of methylenecyclopropane with X–Y such as silyl cyanide and hydrosilane, it is often difficult to figure out the reaction mechanism precisely. Three reaction pathways could be considerable as described below: (a) oxidative insertion of metal to methylenecyclopropane at the distal bond followed by σ -bond metathesis with X–Y, (b) oxidative insertion of metal to methylenecyclopropane at the proximal bond followed by σ -bond metathesis with X–Y, and (c) oxidative addition of X–Y to metal followed by insertion of olefin and β -carbon elimination.

Scheme 10



Miyaura has reported the pioneering works in borylative ring opening reaction of methylenecyclopropane. Among them, he disclosed that platinum-catalyzed diboration of methylenecyclopropane with bis(pinacolato)diboron provided 2,4-bis(boryl)-1-butene derivatives through the cleavage of the proximal bond of the cyclopropane ring (Scheme 11).^{33a} He proposed the catalytic cycle involving oxidative addition of diboron to platinum, regioselective insertion of methylenecyclopropane, β -carbon elimination, and reductive elimination, which is similar to the reaction of methylenecyclopropane with Me_3SiCN or Et_3SiH . The stoichiometric reaction of *cis*-(Ph_3P)₂Pt(Bpin)₂^{33b} with methylenecyclopropane also afforded the corresponding product with the same regioselectivity as that in the catalytic reaction. In addition, a stoichiometric reaction of methylenecyclopropane with $\text{Pt}(\text{PPh}_3)_4$ did not provide any evidence for oxidative cyclization. These results strongly suggest that the reaction is triggered by oxidative addition of bis(pinacolato)diboron to platinum.

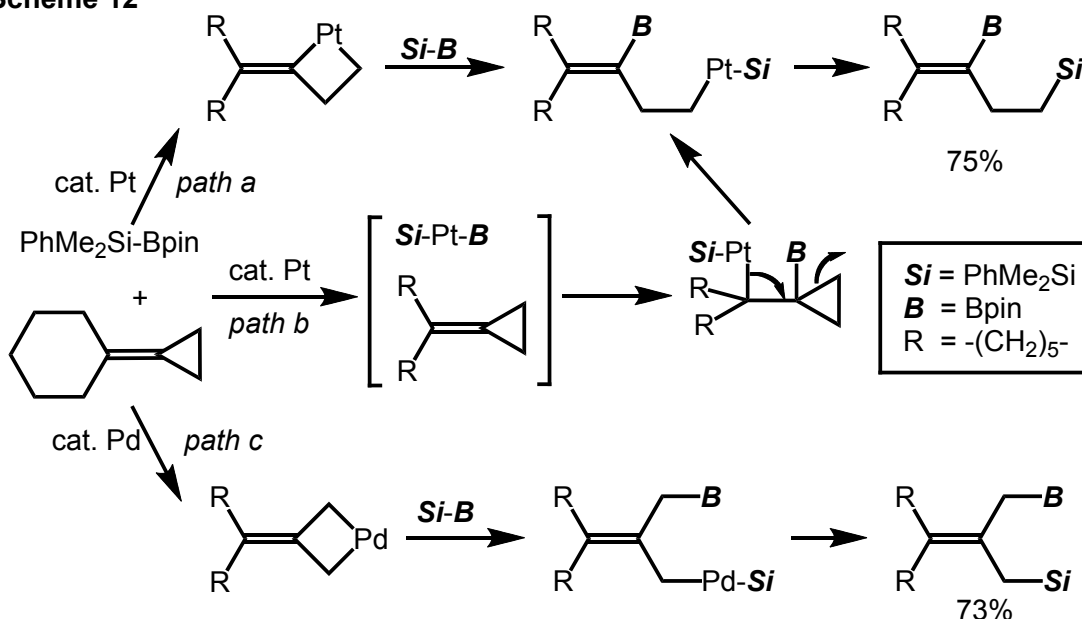
Scheme 11



In 2000, Ito and Suginome developed palladium- and platinum-catalyzed reactions of methylenecyclopropanes with silylborane which accompany ring opening (Scheme 12).³⁴ In these reactions, an appropriate choice of metals and ligands selectively promoted the cleavage of the proximal or the distal bond of methylenecyclopropanes, giving the corresponding silaborylation products regio- and stereoselectively. Methylenecyclopropane which has a tetrasubstituted olefin moiety reacted with silylborane in the presence of $\text{Pt}(\text{CH}_2=\text{CH}_2)(\text{PPh}_3)_2$ catalyst. The platinum-catalyzed reaction selectively gave the product possessing a vinylic boryl group as well as a homoallylic silyl group in the molecule via proximal bond cleavage. On the other hand, the silaborylation product bearing an allylic boryl group was derived

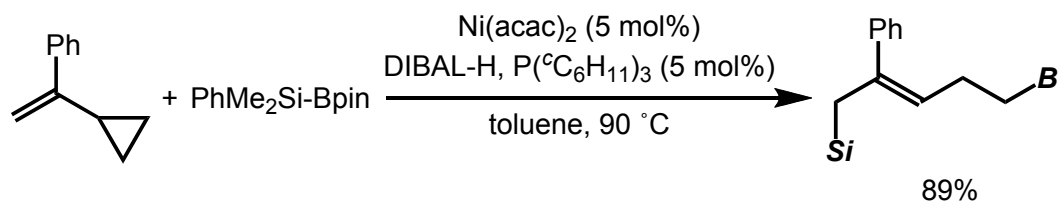
regioselectively from the distal bond cleavage in the presence of a palladium-phosphite catalyst system (Scheme 12, path c). In the case of the reaction catalyzed by platinum, two pathways are possible (Scheme 12, path a and b). According to the fact that the reaction of the platinum complex with methylenecyclopropane gave no evidence for oxidative addition as Miyaura reported, the mechanism which involves oxidative addition of silylborane to platinum (path b) is more reasonable.

Scheme 12



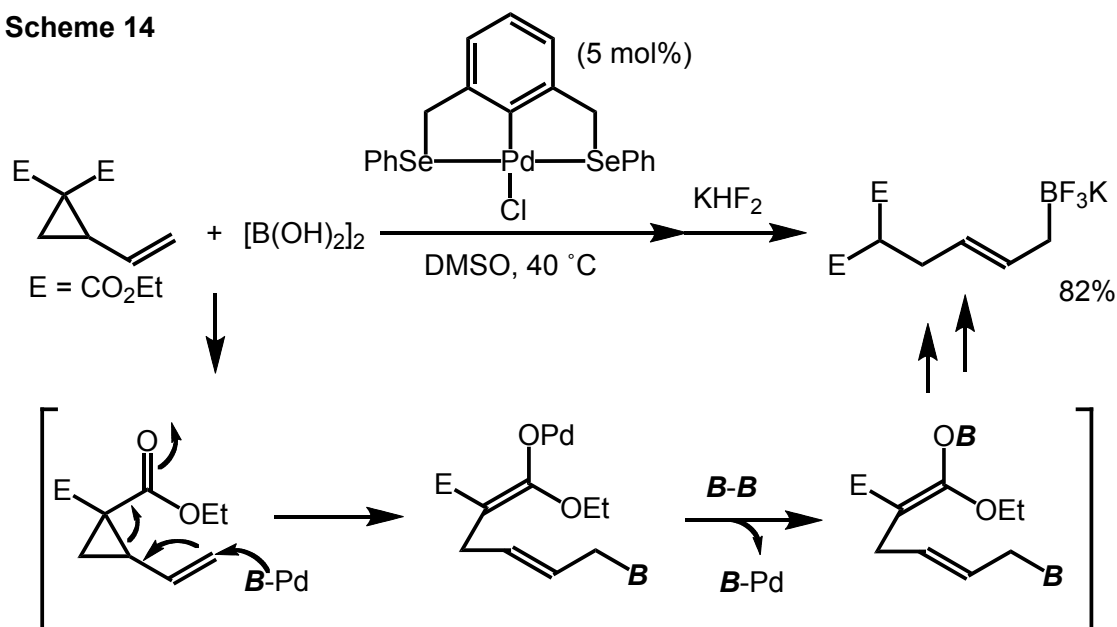
Moreover, Ito and Suginome also reported nickel-catalyzed ring opening silaborylation of vinylcyclopropane (Scheme 13).¹⁹ It is noteworthy that the silaborylation of vinylcyclopropane proceeded with highly selective Si-C and B-C bond formations at the terminal vinyl carbon and at the 2-position of the cyclopropane ring of vinylcyclopropane, respectively. Although they envisaged that a possible mechanism includes oxidative addition of silylborane to nickel to yield a Si-Ni-B complex, the mechanism that starts from oxidative cyclization of vinylcyclopropane with nickel could be considerable, similar to the mechanism of the platinum-catalyzed silaborylation of methylenecyclopropane.

Scheme 13



The reaction of diboron with vinylcyclopropane having two geminal electron-withdrawing groups was also reported (Scheme 14).^{33c} Szabó found that a pincer complex readily catalyzes boryl transfer reactions from tetrahydroxydiboron to vinylcyclopropane. This reaction afforded allylboronic acid, which subsequently reacted with aqueous KHF_2 to yield the corresponding potassium allyl trifluoroborate. In this transformation, Szabó claimed that the catalytic cycle is initiated by transmetalation between $[\text{B}(\text{OH})_2]_2$ and the pincer complex followed by transfer of $\text{B}(\text{OH})_2$ group to vinylcyclopropane in an $\text{S}_{\text{N}}2'$ -type mode. Although the particular palladium complex was required, this catalytic system realized an access to highly functionalized allylic borane from vinylcyclopropane.

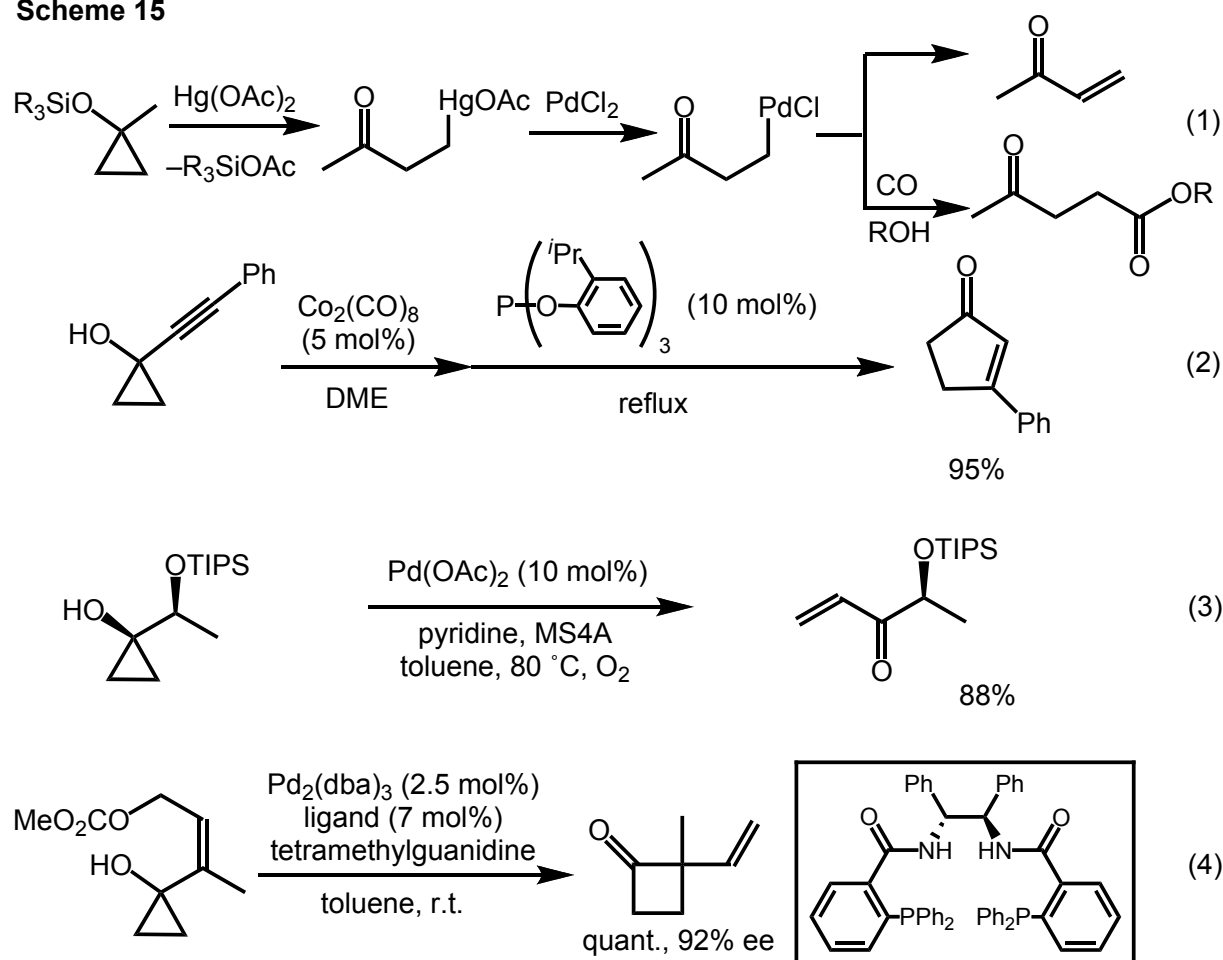
Scheme 14



Additionally, siloxycyclopropanes are also important substrates. Sonoda reported a convenient synthesis of β -mercuri ketones by the reaction of mercuric acetate with siloxycyclopropanes (Scheme 15, eq 1).³⁵ When a metal cation is sufficiently electrophilic to cause the ring opening and the counter anion is capable of removing the silyl group, the

reaction of siloxycyclopropanes with the metal salt should offer a methodology for generating β -metal-substituted ketones. However, no application to catalytic reaction was reported. Alternatively, several reactions of cyclopropanols were reported. Cobalt-catalyzed rearrangement of 1-(1-alkynyl)cyclopropanols to 2-cyclopentenones and palladium-catalyzed ring opening of cyclopropanols to α,β -unsaturated ketones were shown (Scheme 15, eq 2, 3).^{36,37} Trost applied asymmetric allylic alkylation to cyclopropanol having an allyl carbonate moiety to give vinylcyclobutanone (Scheme 15, eq 4).³⁸

Scheme 15

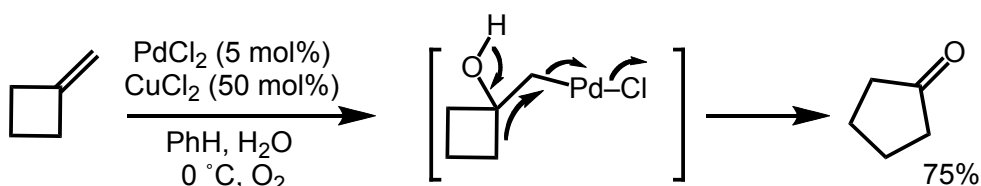


Alkoxycyclopropanes are prone to undergo ring opening.³⁹ Nonetheless, the transition-metal-catalyzed ring opening reaction of alkoxycyclopropane and its application have rarely been reported. On the other hand, various reactions of alkoxycyclobutanes under transition metal catalysis have been reported.

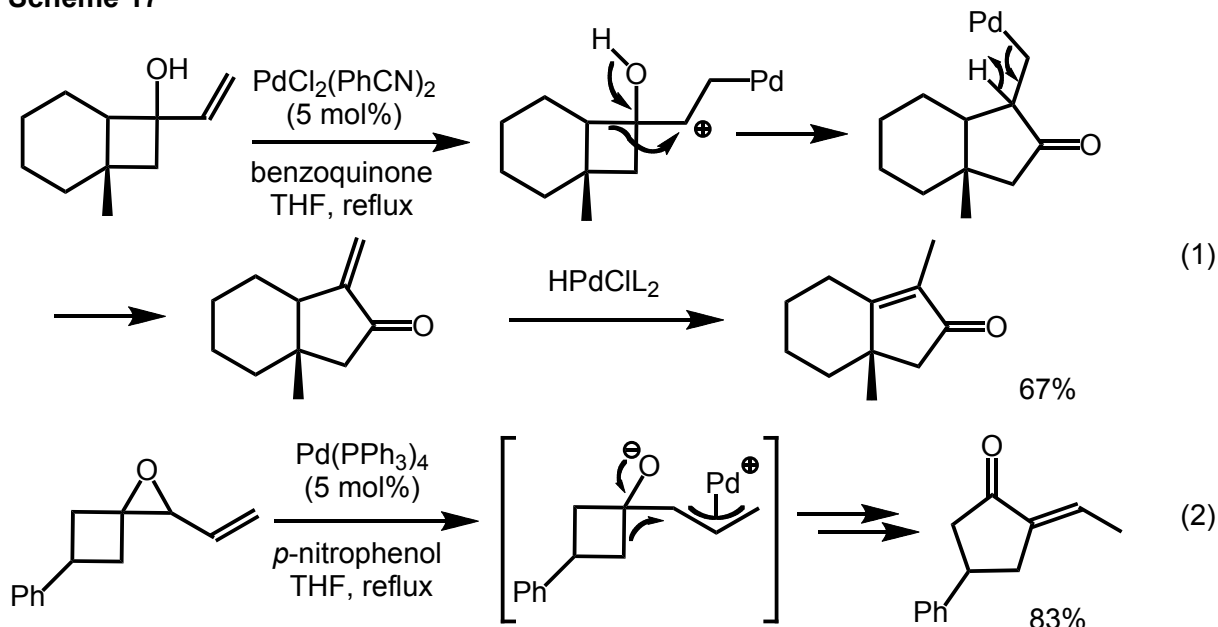
In 1977, Boontanonda observed palladium-catalyzed oxidative rearrangement of methylenecyclobutane to cyclopentanone which proceeds through the Wacker process (Scheme 16).⁴⁰ In the reaction pathway, the methylene moiety undergoes hydroxypalladation under Wacker conditions to form 1-(2-palladamethyl)cyclobutanol. The cyclobutanol can be rearranged to cyclopentanone under release of the ring strain.

Since Boontanonda's report, diverse reactions of alkoxy-cyclobutane under palladium catalysis have been studied. Clark reported the ring expansion of vinylcyclobutanol to cyclopentenone (Scheme 17, eq 1).⁴¹ Kim reported palladium-catalyzed ring expansion of vinyl oxaspirohexane to afford methylene cyclopentanone (Scheme 17, eq 2).⁴² Both of the reactions utilized palladium-mediated Wagner-Meerwein shift as well as ring strain.

Scheme 16



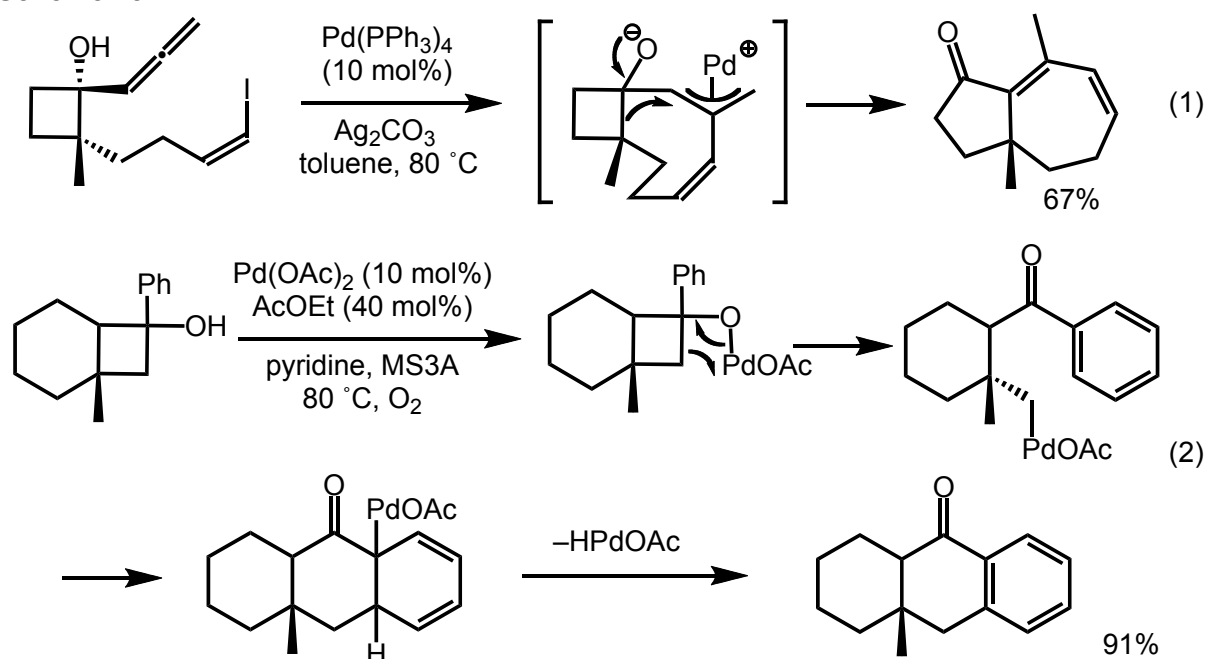
Scheme 17



According to this concept, Nemoto and Uemura developed unique transformations of cyclobutanols. Nemoto reported that the cascade carbopalladation-ring expansion reaction of

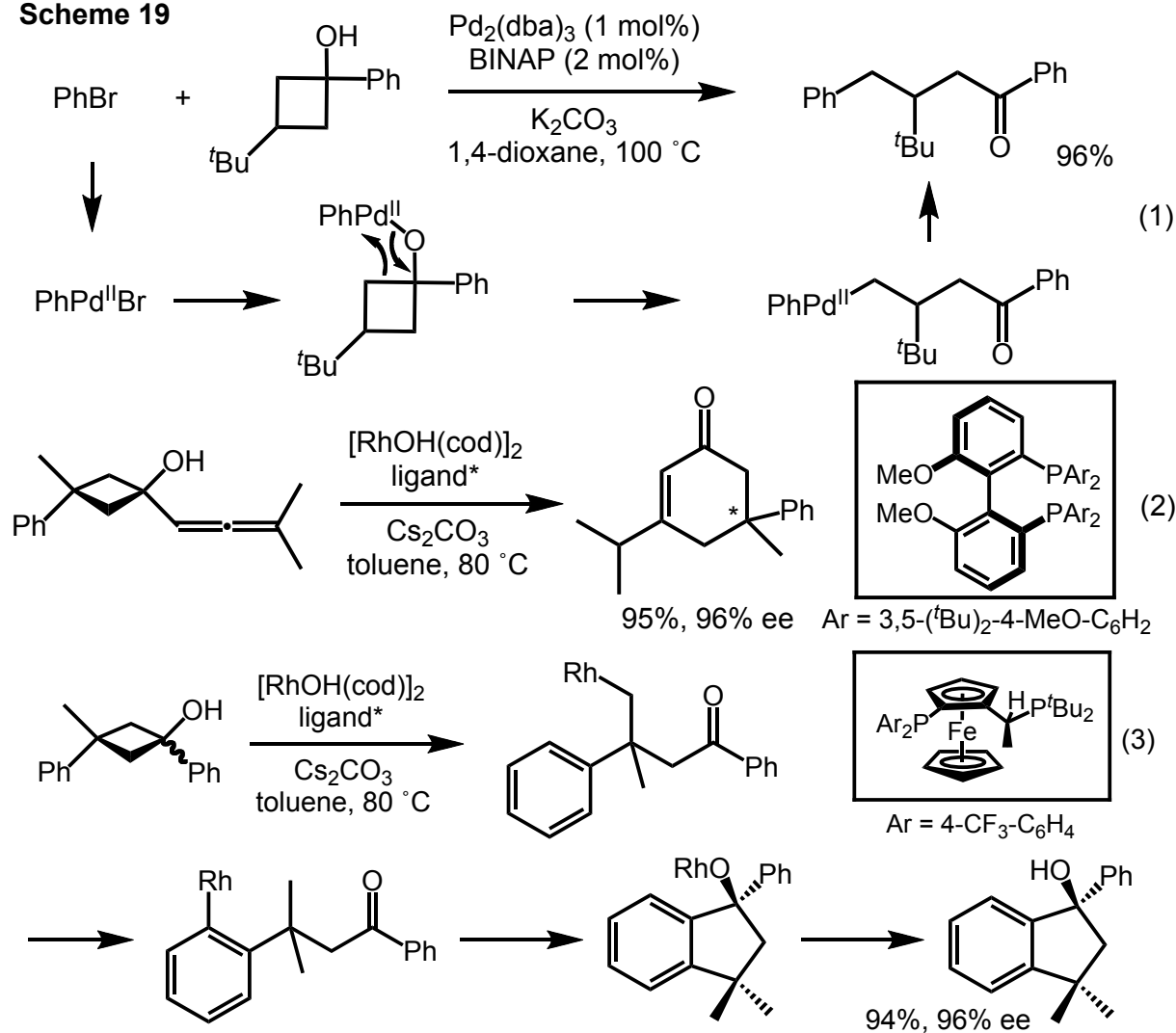
allenylcyclobutanols bearing an alkenyl iodide moiety affords β -substituted cyclopentenones (Scheme 18, eq 1).⁴³ Uemura described palladium-catalyzed formation of anthracenone as shown in Scheme 18, eq 2.⁴⁴ Uemura supposed that these catalytic reactions proceed via the sequence of the formation of a Pd(II)-alcoholate species, β -carbon elimination, and intramolecular cyclization onto the phenyl ring, β -hydrogen elimination to afford the product.

Scheme 18



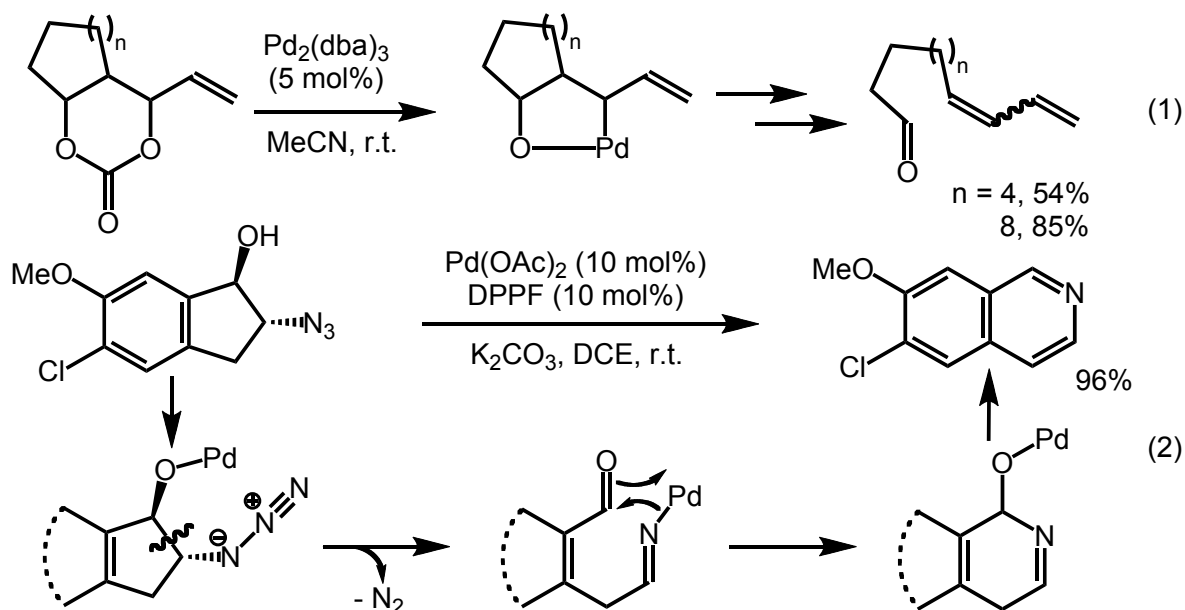
Uemura reported that treatment of aryl halide with tertiary cyclobutanols afforded arylated product via β -carbon elimination (Scheme 19, eq 1).⁴⁵ The ring opening arylation was extended to asymmetric transformation by using an appropriate chiral ligand. In terms of enantioselective reaction, Cramer reported that rhodium also represented potent reactivity towards cyclobutanol (Scheme 19, eq 2, 3).⁴⁶

Scheme 19



Carbon–carbon bond cleavage of metal cycloalkoxide of normal size was also reported. Tamaru demonstrated that dienals were obtained from the ring opening of bi- and tricyclic carbonate under palladium catalysis (Scheme 20, eq 1).⁴⁷ Chiba reported palladium(II)-catalyzed ring expansion of cyclic 2-azidoalcohols, which involves C–C bond cleavage and C–N bond formation to provide azaheterocycles (Scheme 20, eq 2).⁴⁸

Scheme 20

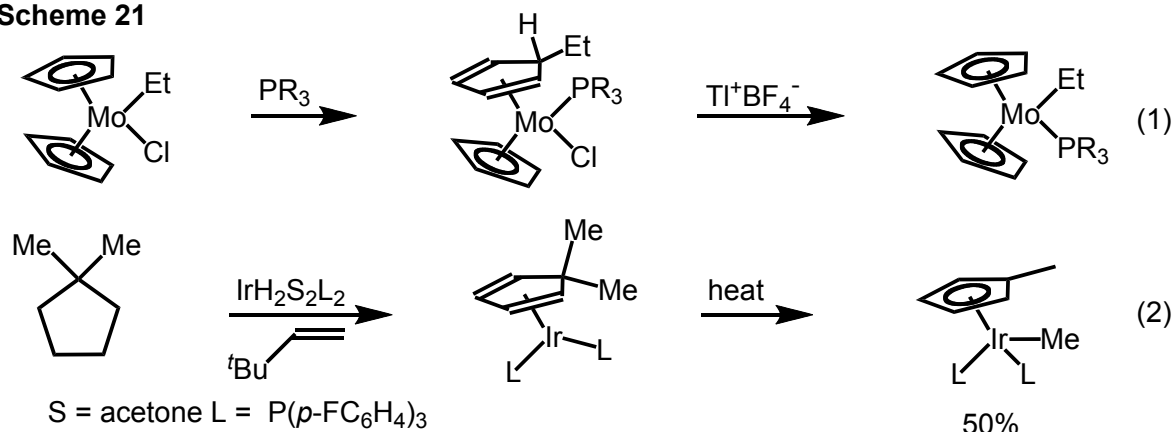


2. Allyl Transfer via Unstrained sp^3 Carbon– sp^3 Carbon Bond Cleavage Under Transition Metal Catalysis

As mentioned in Section 1, transition-metal-catalyzed C–C bond cleavage has been a long pursued process of considerable theoretical and practical interest. In general, it can be facilitated by the presence of an activating group and driven by a decrease of steric strain. The ultimate goal in the area of C–C bond cleavage is to achieve the selective cleavage of unstrained and unactivated $sp^3\text{C}$ – $sp^3\text{C}$ bonds.

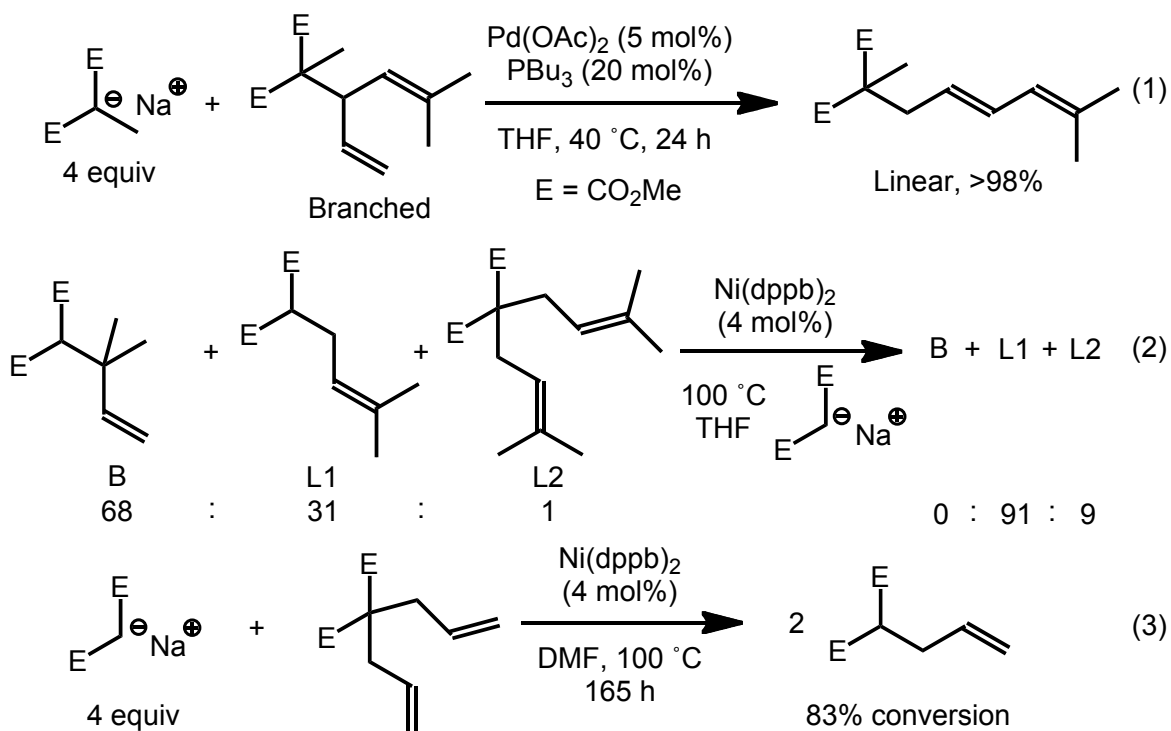
As a stoichiometric reaction, Green observed an interesting reversible rearrangement of a molybdenum complex in which an ethyl group migrates from the metal center to the cyclopentadienyl ring (Scheme 21, eq 1).⁴⁹ Moreover, Crabtree reported iridium-mediated reaction sequence which led to indirect C–C bond cleavage in an unstrained alkane by combining alkane dehydrogenation (Scheme 21, eq 2).⁵⁰ Although these several examples of migration of an alkyl group to metal via unstrained $sp^3\text{C}$ – $sp^3\text{C}$ bond cleavages were observed in organometallic chemistry, there were few examples of catalytic reactions.

Scheme 21



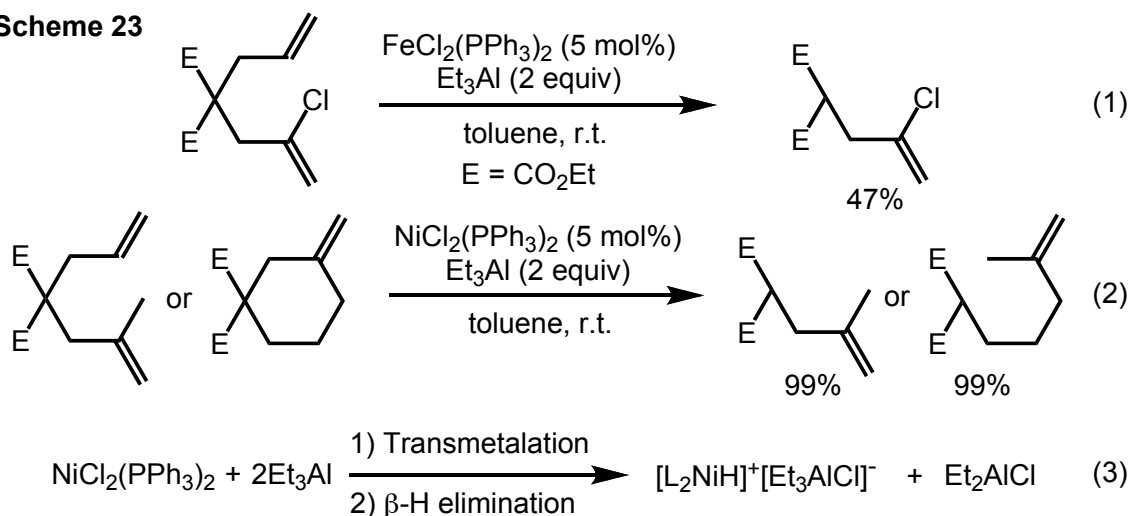
Usually, carbon-centered anions do not serve as leaving groups, especially in nucleophilic substitution reactions, due to the generally unpolarized C–C bond and the normally high instability of the resultant carbanions. In 1993, during the course of study on palladium-catalyzed alkylation of allyl electrophiles, Bäckvall observed isomerization of allylmalonate derivatives.⁵¹ The reaction of dienyl(methyl)malonate with nucleophile in the presence of a palladium catalyst resulted in the isomerization to give the linear isomer as the major product (Scheme 22, eq 1). Control experiments showed that the reaction in the absence of the catalyst did not lead to any detectable isomerization. This observation strongly indicated that the palladium(0) catalyst generated in situ is capable of cleaving the allylic C–C bond to give a π -allyl complex, which results in the reversible alkylation. In addition, Mortreux reported nickel-catalyzed isomerization of a mixture of branched and linear allylmalonate derivatives to the linear isomer exclusively (Scheme 22, eq 2).⁵² Mortreux also described the synthesis of dimethyl allylmalonate via the nickel-catalyzed synproportionation between dimethyl diallylmalonate and anion of dimethyl malonate (Scheme 22, eq 3).⁵² So far, the alkylation of stabilized malonate anion was usually considered to be irreversible. However, they demonstrated the reversibility of the C–C bond forming step at higher temperatures and longer reaction time. Under these conditions, mono- and diallylmalonate derivatives were converted to thermodynamically more stable regioisomers.

Scheme 22



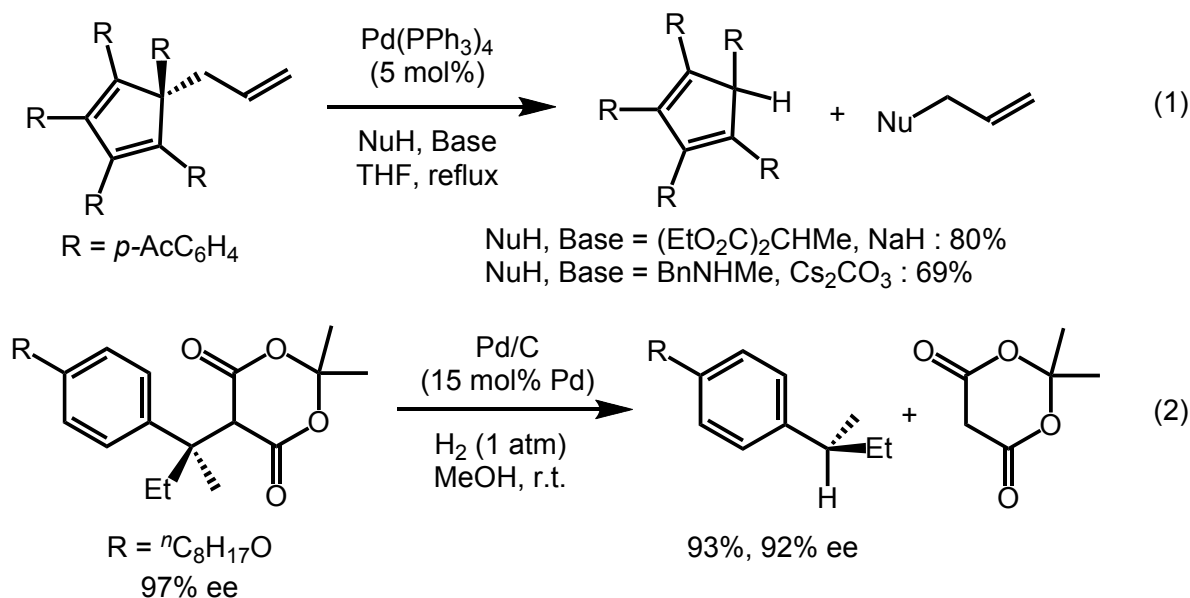
After a decade, Kotora observed iron-catalyzed deallylation of diallylmalonate with triethylaluminium under milder conditions (Scheme 23, eq 1).⁵³ Although the yield of desired product was only 47%, it is noteworthy that the unactivated C–C bond was cleaved and that the more reactive C–Cl bond remained intact. Kotora also showed that methylenecycloalkanes were also feasible in this reaction (Scheme 23, eq 2).⁵⁴ Although this process was catalyzed by a number of transition metal complexes (Fe, Ru, Co, Rh, Ni, and Pd), the highest catalytic activity and wide generality were achieved by a combination of $\text{NiCl}_2(\text{PPh}_3)_2$ complex and triethylaluminium.

Scheme 23

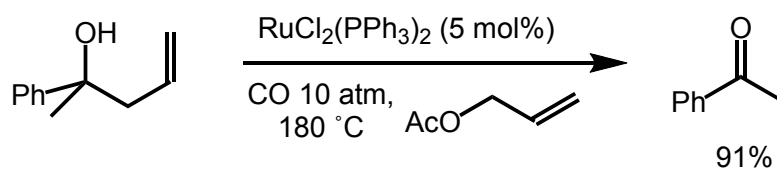


Kotora assumed that the reaction mechanism includes generation of a cationic nickel hydride from Et_3Al and nickel complex as an active catalyst (Scheme 23, eq 3). Hydronickelation to less substituted olefin followed by β -carbon elimination gives the product.

Lambert exploited the stability of cyclopentadienyl anion for oxidative addition of allylpentaarylcyclopentadiene to palladium via C–C bond cleavage. Lambert developed allylation of malonate anions and amines with the allylpentaarylcyclopentadiene (Scheme 24, eq 1).⁵⁵ In a related process, Fillion described palladium-catalyzed reductive cleavage of an unstrained C–C bond. The hydrogenolysis of benzyl Meldrum's acids bearing an benzylic quaternary center furnished Meldrum's acid and aromatics bearing a tertiary benzylic stereocenter. The reaction of enantioenriched substrates resulted in complete inversion of configuration (Scheme 24, eq 2).⁵⁶

Scheme 24

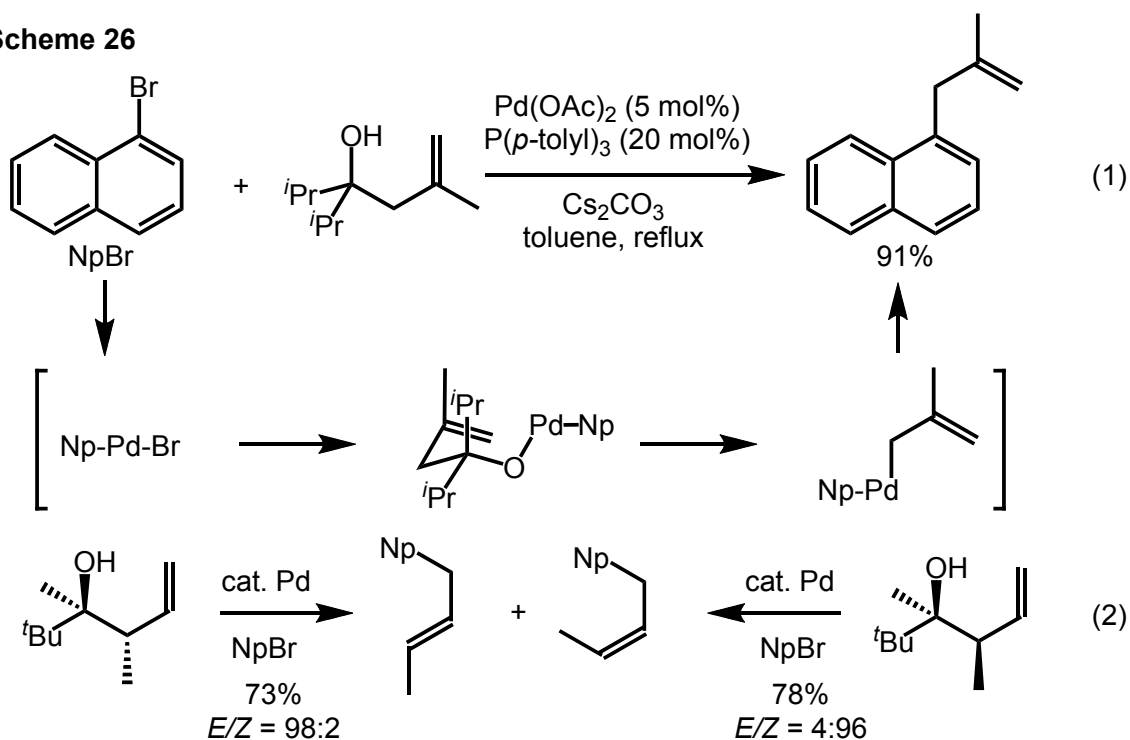
On another front, Mitsudo and Kondo reported in 1998 ruthenium-catalyzed retro-allylation of tertiary homoallyl alcohols via selective cleavage of a C–C bond to afford the corresponding ketones (Scheme 25).⁵⁷ Although it is well known that allylations of carbonyl compounds with stoichiometric allylmethyl reagents (Li, Mg, Ti, Zn) are reversible, there had been no examples of catalytic retro-allylation so far. Unfortunately, no application of the allylruthenium species, which should be generated in the reaction flask, to C–C bond formation was reported.

Scheme 25

Oshima applied this type of C–C bond cleavage to allylation of aryl halides with tertiary homoallyl alcohols under palladium catalysis. Since the palladium-catalyzed retro-allylation would proceed in a concerted fashion through a conformationally regulated six-membered cyclic transition state, the reaction gave the allylated product with high stereo- and

regioselectivity (Scheme 26, eq 1 and 2).⁵⁸ A possible mechanism of palladium-catalyzed retro-allylation begins with oxidative addition of aryl halides to palladium to form arylpalladium. Then, base-mediated ligand exchange between arylpalladium halide and homoallyl alcohol would take place to give palladium alkoxide, which could be followed by retro-allylation to afford allyl(aryl)palladium. Finally, reductive elimination produces the allylated product.

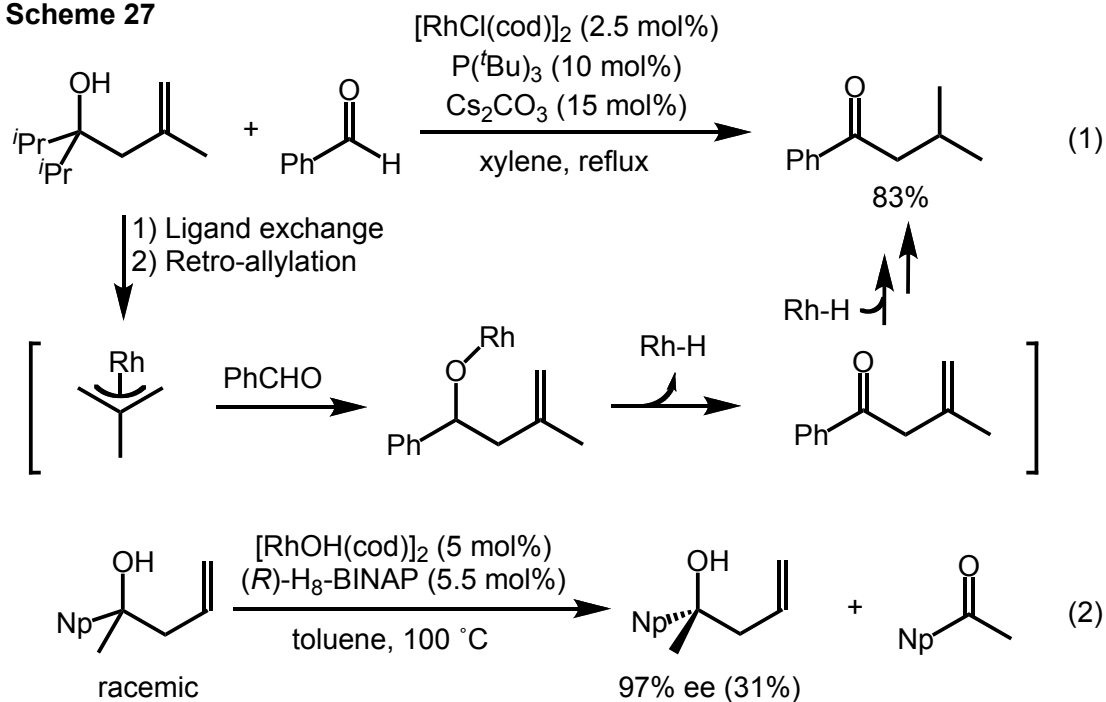
Scheme 26



Rhodium is also effective for retro-allylation of tertiary homoallyl alcohols and enabled allylation of aldehydes (Scheme 27, eq 1).⁵⁹ In the case of rhodium, ligand exchange occurs at first and then retro-allylation takes place to generate nucleophilic allylrhodium. Subsequent allylation of aldehyde with the allylrhodium affords secondary alkoxyrhodium. Isomerization through iterative β -H elimination-hydorrhodation provides the corresponding saturated ketones. Although it is well known that allylmetal reagents are basically difficult to handle due to their high reactivity, transition-metal-catalyzed retro-allylation solved the problem. Moreover, Hayashi focused on utilizing rhodium-catalyzed retro-allylation for

kinetic resolution of tertiary homoallyl alcohols and provided a facile access to chiral tertiary homoallyl alcohols (Scheme 27, eq 2).⁶⁰

Scheme 27



3. Overview of This Thesis

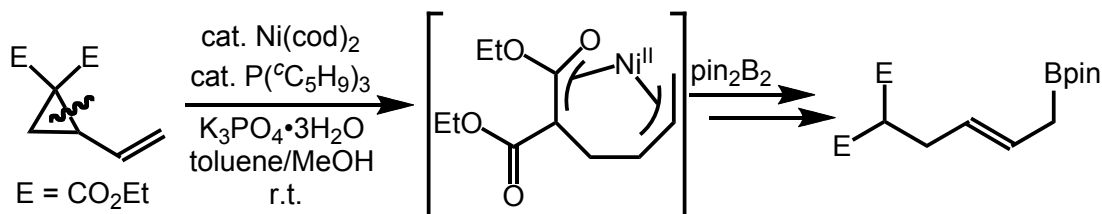
The author focused on the cleavage of $sp^3\text{C}-sp^3\text{C}$ bonds of strained cyclopropanes, allylmalonates, and homoallyl alcohols catalyzed by low valent 9 or 10 group complexes and applied the cleavage to develop some new C–C bond forming reactions. In Chapters 1 and 2, nickel-catalyzed borylative ring opening reactions of cyclopropane derivatives with bis(pinacolato)diboron are described. In Chapter 3, palladium-catalyzed synthesis of silyl enolate from cyclopropyl ketone and hydrosilane is mentioned. Chapter 4 describes nickel-catalyzed allylation of arylzinc reagents with dialkyl allylmalonate derivatives via deallylation from the allylmalonate derivatives. In Chapters 5 and 6, rhodium- or nickel-catalyzed allylation of aldehydes or allyl carbonates via retro-allylation of tertiary homoallyl alcohols are represented. Overview of this thesis is described below.

3.1. Nickel-Catalyzed Borylative Ring Opening Reaction of Cyclopropane Derivatives: Vinylcyclopropane and Cyclopropyl Ketone (Chapters 1 and 2)

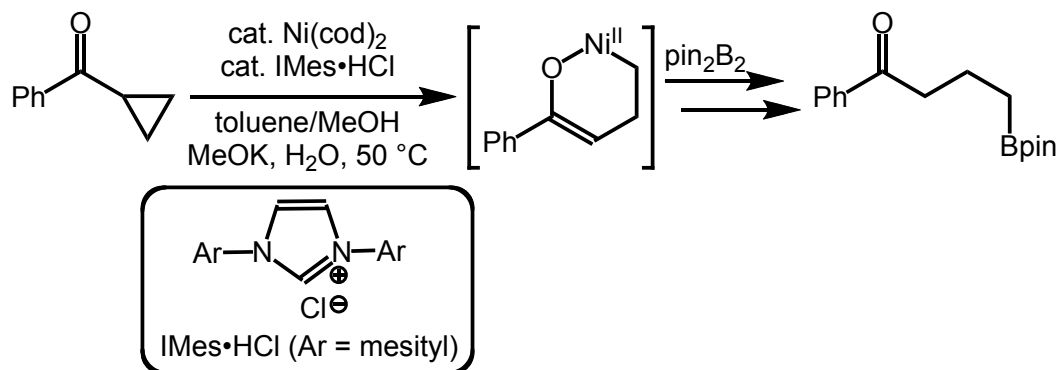
Organoboron compounds are extremely important reagents in organic synthesis. Transition-metal-catalyzed borylation of unsaturated C–C bonds is one of the most powerful methods to synthesize organoboron reagents. Although Pd, Pt, Rh, Cu, and Au are known to catalyze such borylation,⁶¹ there are few examples of borylation catalyzed by a nickel complex.⁶²

In Chapter 1, the author describes borylative ring opening reactions of vinylcyclopropanes along with releasing the ring strain to give functionalized allylboronates in the presence of a catalytic amount of a nickel complex and tricyclopentylphosphine (Scheme 28). He assumed that this reaction starts with oxidative cyclization of vinylcyclopropane with a low valent nickel complex to give allyl(oxaallyl)nickel intermediate.

Scheme 28



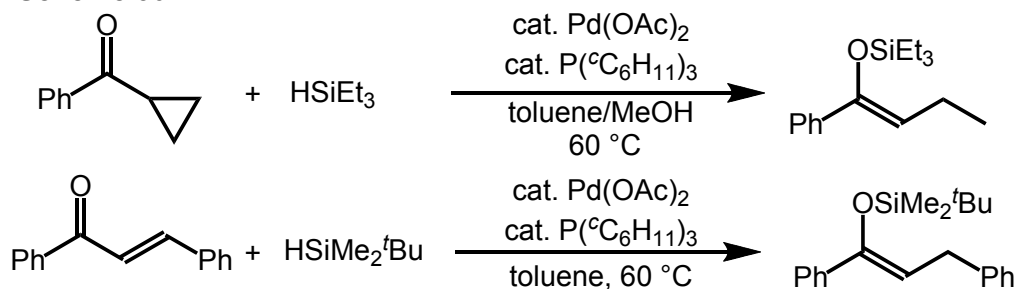
Therefore, he envisioned that cyclopropyl ketones could be applied to borylative ring opening reactions, since oxidative cyclization of cyclopropyl ketones with a nickel complex has been reported (Scheme 29).²⁵ In Chapter 2, the author discloses borylative ring opening reactions of cyclopropyl ketones with diboron to give 4-oxoalkylboronates under nickel catalysis.

Scheme 29

3.2. Palladium-Catalyzed Preparation of Silyl Enolates from the Reactions of Cyclopropyl Ketones or α,β -Unsaturated Ketones with Hydrosilanes (Chapter 3)

Nowadays, transition-metal-catalyzed 1,4-hydrosilylation of α,β -unsaturated carbonyl compounds is recognized as a powerful method to synthesize silyl enolates. Although some examples are known, the stereoselectivities are unsatisfactory in the cases of acyclic enones. Moreover, 1,2-hydrosilylation competes in some cases.⁶³

In Chapter 3, the author describes synthesis of silyl enolates with high *Z* selectivity from cyclopropyl ketones and hydrosilane in the presence of a palladium catalyst (Scheme 30). The reaction might proceed through generation of α,β -unsaturated ketones in situ from cyclopropyl ketones followed by 1,4-hydrosilylation of the resulting α,β -unsaturated ketones to afford the product. Hence, he applied this reaction to α,β -unsaturated ketones and indeed obtained various silyl enolates with high *Z* selectivities.

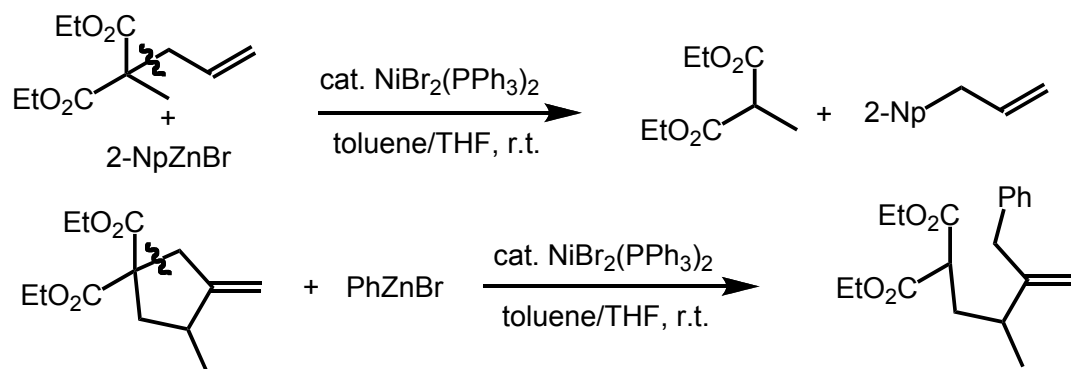
Scheme 30

3.3. Use of Allylmalonate as Allyl Cation Equivalent by Nickel-Catalyzed C–C Bond Cleavage (Chapter 4)

Functionalization or modification of sp^3 -hybridized carbon centers by cleavage of unstrained C–C bond remains unexplored to date. Although several examples of unstrained sp^3C – sp^3C bond cleavage have been reported,^{47,49–54,56,57} its applications to new C–C bond formation have not been well studied.^{48,55}

In Chapter 4, the author describes the reaction of arylzinc reagents with dialkyl allylmalonate derivatives to give allylarenes (Scheme 31). He proposed the reaction mechanism which begins with oxidative addition of the allylic C–C bond to a nickel complex to form allylnickel species. Arylation of the allyl moiety would then occur to afford zinc enolate, which is protonated to yield the product and regenerate zerovalent nickel catalyst.

Scheme 31

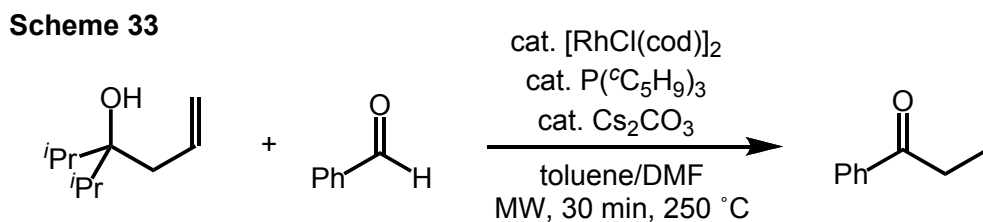
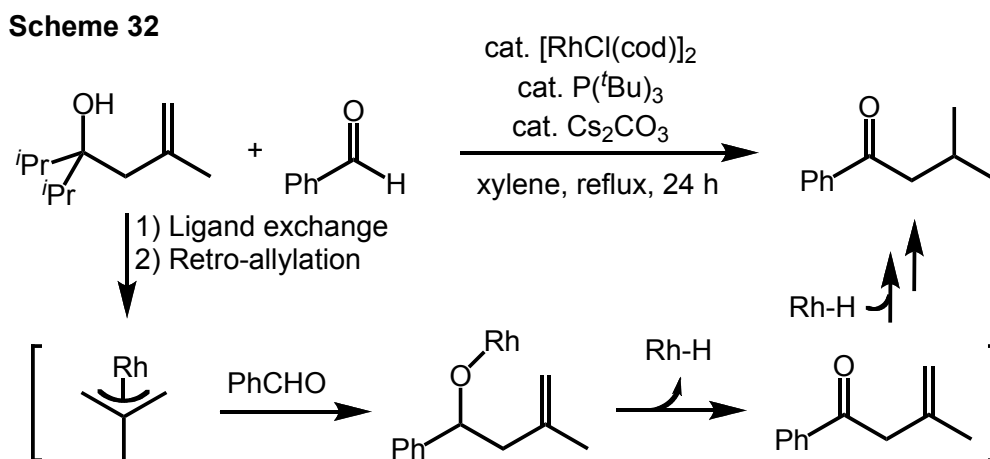


3.4. Rhodium- or Nickel-Catalyzed Allylation of Aldehyde or Allyl Carbonate via Retro-Allylation of Tertiary Homoallyl Alcohols (Chapters 5 and 6)

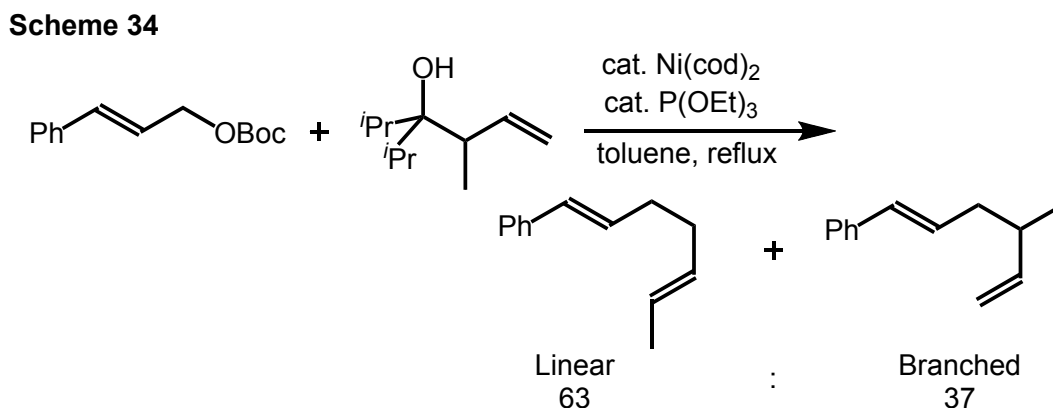
Transition-metal-catalyzed cross-coupling allylation of aryl halides with allylmetal reagents ranks as one of the most attractive allylation reactions.⁶⁴ Recently, transition-metal-catalyzed retro-allylation becomes a powerful method for generation of allylmetal species.

In Chapter 5, the author shows that rhodium-catalyzed retro-allylation gives allylrhodium species which was found to allylate carbonyl compounds to afford saturated

ketones via isomerization (Scheme 32).^{59,60} Moreover, he succeeded to decrease the reaction time in the rhodium-catalyzed allylation of aldehydes by using microwave heating at 250 °C (Scheme 33).



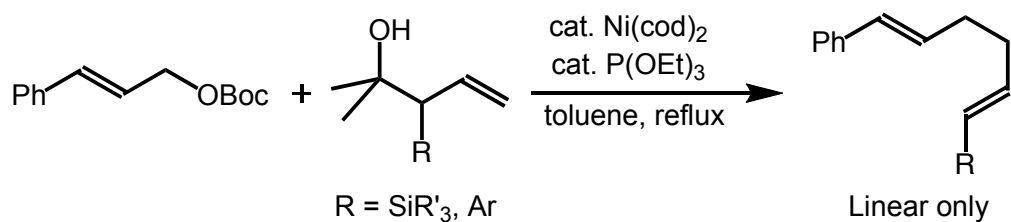
In Chapter 6, the author describes nickel-catalyzed allylation of allyl carbonate by retro-allylation of homoallyl alcohol to yield 1,5-hexadiene (Scheme 34). So far, efficient methods for the synthesis of 1,5-hexadienes from allylmetals and allyl electrophiles are rare.



Although the reaction afforded the corresponding coupling products in high yields, the products were obtained as mixtures of linear and branched isomers. When homoallyl alcohol

bearing a bulky moiety at the allylic position, such as SiR'_3 , and Ar, was used, the linear isomer was obtained exclusively in excellent yield (Scheme 35).

Scheme 35



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Chapter 1

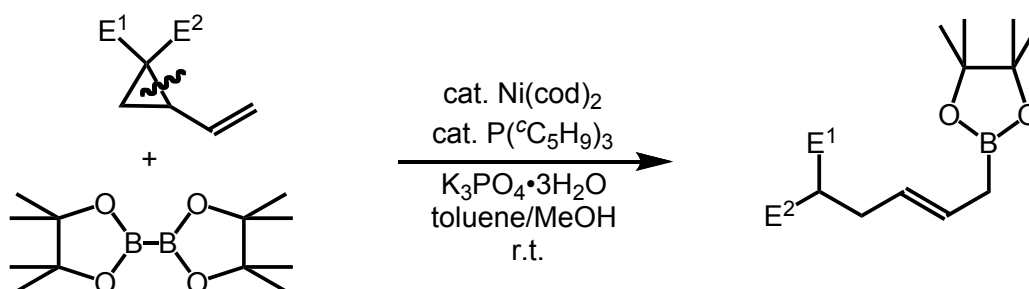
Nickel-Catalyzed Borylative Ring Opening Reaction of Vinylcyclopropanes with Bis(pinacolato)diboron Yielding Allylboronates

Vinylcyclopropanes bearing one or two electron-withdrawing groups on the cyclopropane ring undergo nickel-catalyzed borylative ring opening with bis(pinacolato)diboron to yield allylboronates with high *E* selectivity. The reaction proceeds via oxidative cyclization of a nickel complex and vinylcyclopropane to form oxanickelacycle as a key intermediate.

Introduction

Allylic boron reagents are among the most important reagents in organic synthesis.¹ Modern organic synthesis requires more complex and functionalized allylic boron reagents than ever for synthesis of a wider variety of biologically intriguing compounds. However, functionalized allylic boron reagents are not always easy to synthesize, and development of new methods for the synthesis of allylic boron reagents is expected.^{2,3} In Chapter 1, the author describes nickel-catalyzed borylative ring opening reactions of vinylcyclopropanes with bis(pinacolato)diboron which provide allylic boron reagents (Scheme 1).⁴⁻⁶

Scheme 1.



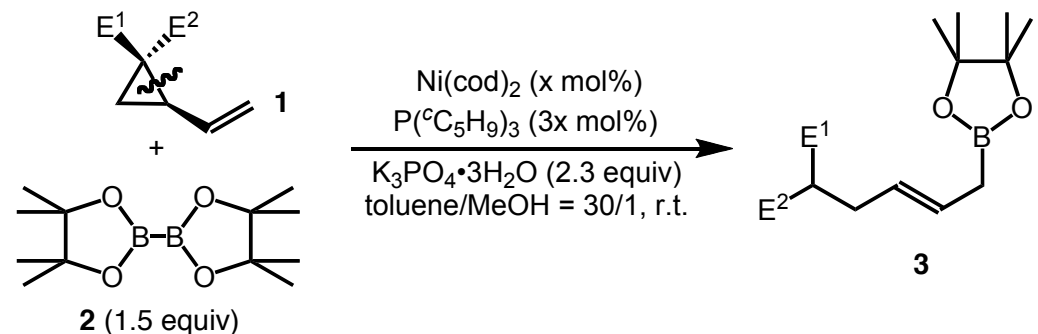
Results and Discussion

Treatment of bis(ethoxycarbonyl)-substituted vinylcyclopropane **1a** with bis(pinacolato)diboron (**2**) in the presence of potassium phosphate trihydrate and catalytic amounts of Ni(cod)₂ and tricyclopentylphosphine in toluene/methanol afforded allyl boronate **3a** (Table 1, entry 1). The reaction was high yielding and proceeded with high *E* selectivity. Analogous to the previous reports on nickel-catalyzed reactions with boron reagents,^{6c,7} the reaction required base, which would activate boron species. The addition of methanol was essential for smooth protonation of the boron enolate^{6c,7c} (vide infra).

As the size of electron-withdrawing groups on the cyclopropane ring become larger, the reactions required higher catalyst loadings to attain high yields and the *E/Z* ratios were slightly improved (entries 1–3). Acetyl-substituted **1d** reacted with **2** to provide **3d** with moderate stereoselectivity (entry 4). Diacetyl-substituted vinylcyclopropane **1e** was converted to desired

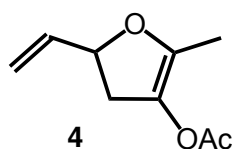
product **3e** in only 20% yield, along with furan derivative **4** as a byproduct (entry 5).^{5f}

Table 1. Scope of Vinylcyclopropanes



entry	E^1	E^2	1	x	3	Yield(%) ^a	$E:Z$
1	CO_2Et	CO_2Et	1a	5	3a	84(98)	94:6
2	CO_2Me	CO_2Me	1b	2	3b	73(80)	91:9
3	CO_2^tBu	CO_2^tBu	1c	7.5	3c	66(84)	95:5
4	CO_2Et	Ac	1d	2	3d	57(75)	80:20
5	Ac	Ac	1e	2	3e	(20) ^b	N.D. ^c
6	CO_2^tBu	H	1f^d	5	3f	85	91:9
7	H	CO_2^tBu	1g	5	3f	44	85:15

^a Isolated yields. NMR yields are in parenthesis. The lower isolated yields would be attributed to partial decomposition of **3** during silica gel column purification. ^b Furan derivative **4** was obtained in 6% yield.



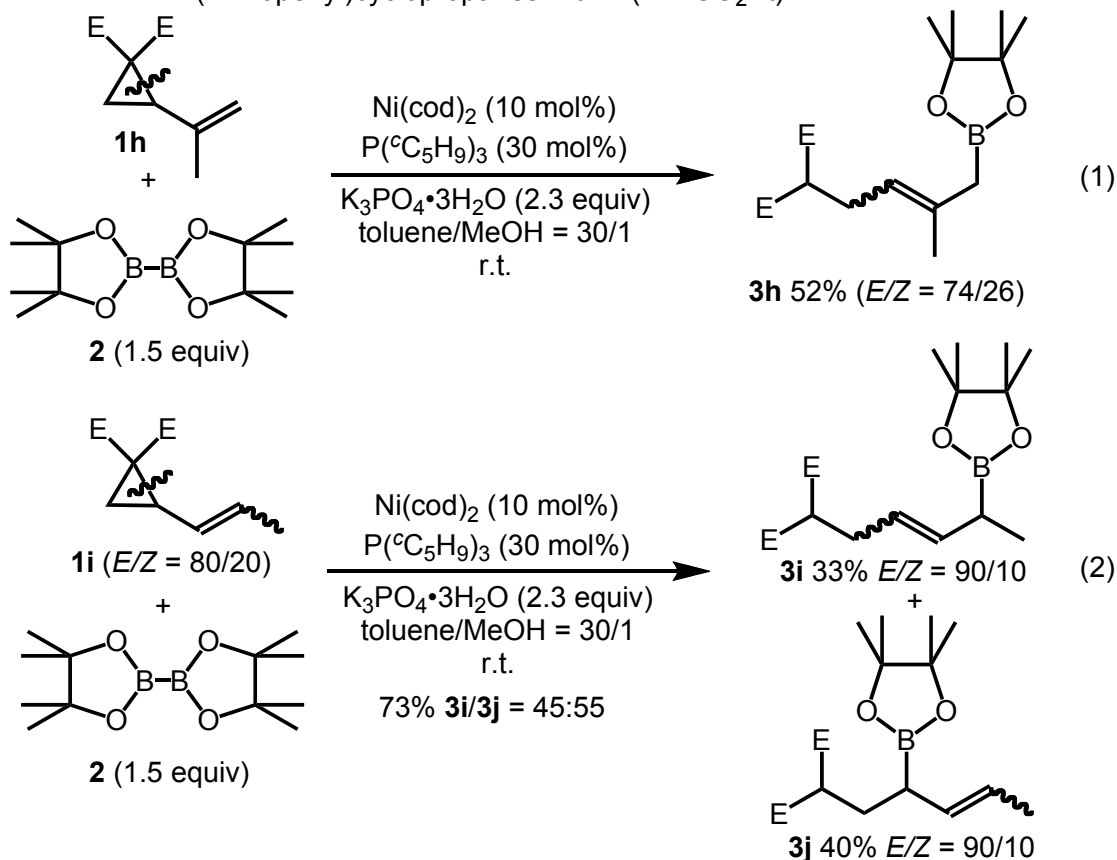
^c Not determined. ^d A mixture of *cis* and *trans* isomers (**1f**/**1g** = 84/16) was used.

Vinylcyclopropane **1f** having only one *tert*-butoxycarbonyl group at the *cis* position underwent efficient borylative ring opening (entry 6). In contrast, the nickel-catalyzed reaction of **1g**, the *trans* isomer of **1f**, led to the formation of **3f** in only 44% yield, in addition to a mixture of unidentified byproducts (entry 7). These results are informative in considering the reaction mechanism (*vide infra*).

Cyclopropanes having a substituted vinyl group also participated in the borylation reaction

(Scheme 2). Isopropenylcyclopropane **1h** underwent the reaction with low stereoselectivity (eq 1). When (1-propenyl)cyclopropane **1i** was employed, a mixture of regioisomers **3i** and **3j** was obtained with high *E* selectivity (eq 2).

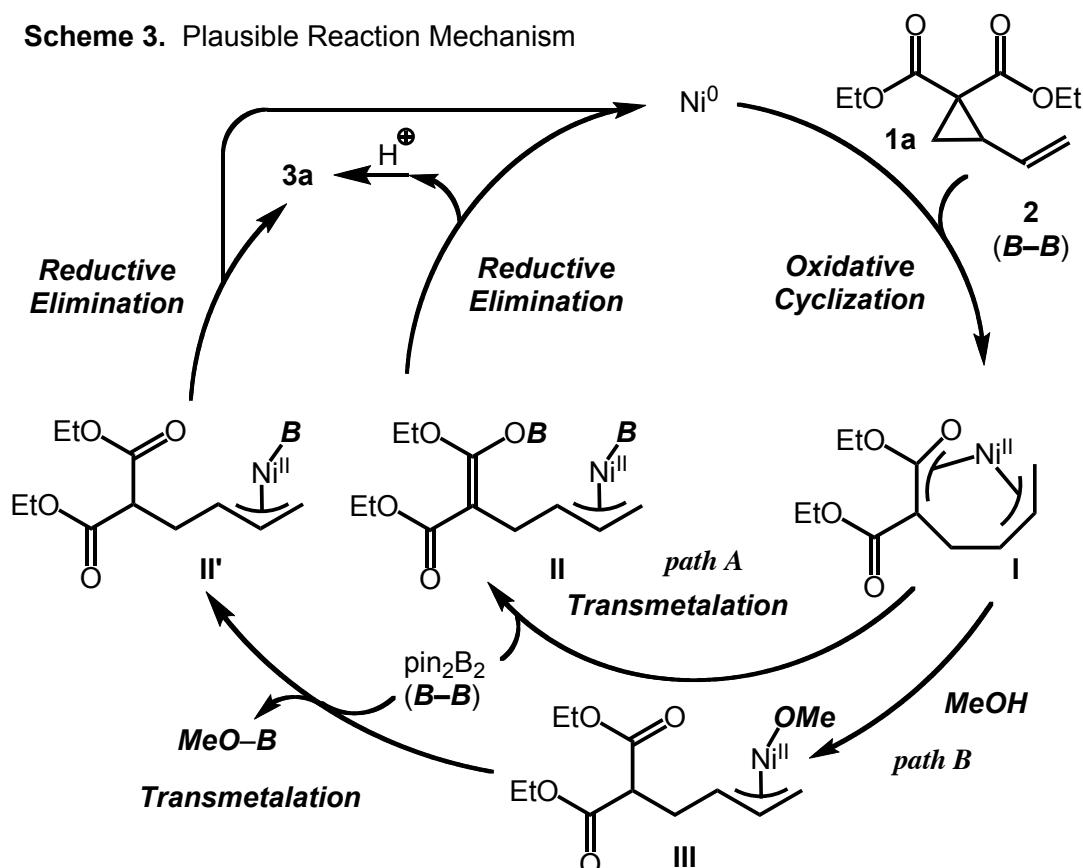
Scheme 2 . Nickel-Catalyzed Reactions of Isopropenyl- and 2(1-Propenyl)cyclopropanes with **2** (E = CO₂Et)



On the basis of these results as well as previous reports,^{6c,7} the author assumes the reaction mechanism as follows (Scheme 3). Cyclopropane **1a** is activated by Lewis acid **2**, and the activated **1a** undergoes oxidative addition to a Ni(0) complex^{6c,7-9} to afford π -allyl(oxa- π -allyl)nickel¹⁰ **I**. Transmetalation then occurs to yield π -allylnickel **II** bearing a boron enolate moiety (path A). Reductive elimination provides the boron enolate of **3a**, which is protonated in situ to afford **3a**, with concomitant formation of the initial Ni(0) complex. The reaction required base, which would activate the boron species. The roles of MeOH and H₂O are not clear at this point according to this mechanism.

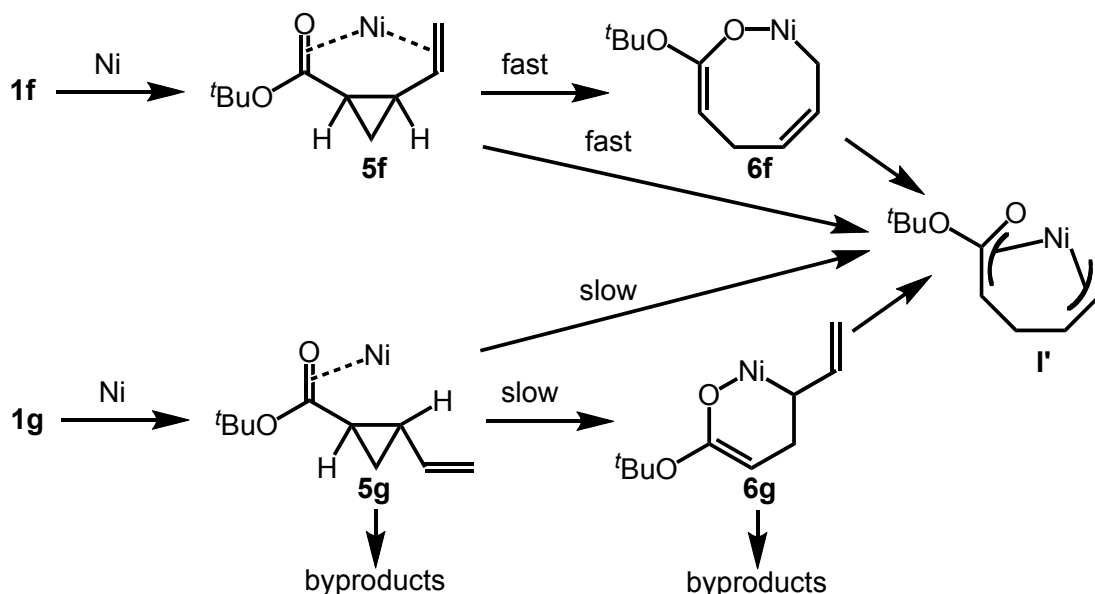
Another mechanism (path B) that involves a formation of alkoxynickel intermediate **III** by protonolysis of **I** with MeOH may operate. In this mechanism, transmetalation between **III** and diboron **2** easily occurs to provide allylnickel intermediate **II'** (path B).

Scheme 3. Plausible Reaction Mechanism



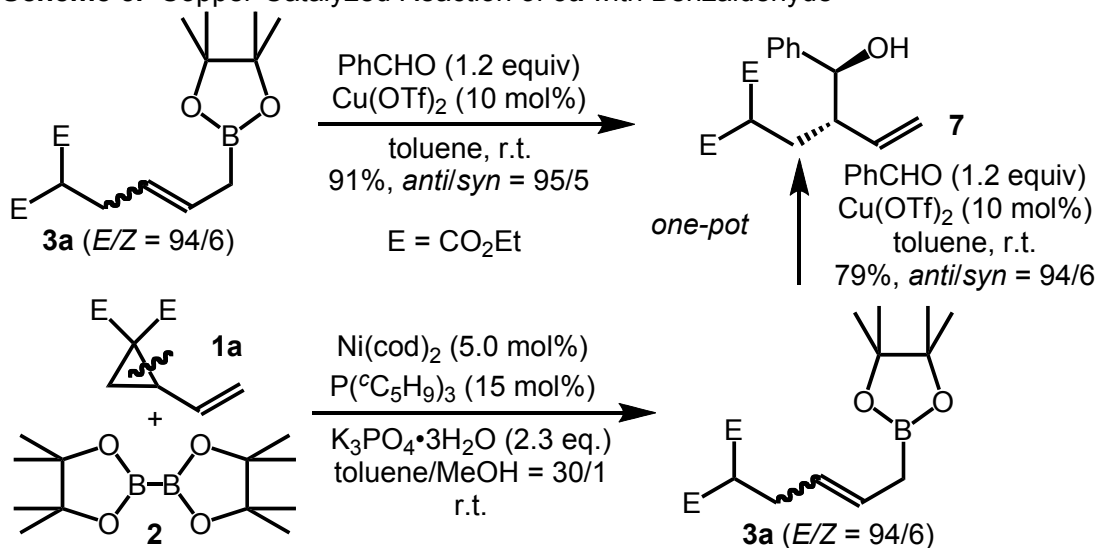
The difference of the reactivities of **1f** and **1g** suggests that oxidative addition of **1f** would be more favorable than that of **1g** (Scheme 4). The *cis* configuration of **1f** would allow for bidentate coordination to nickel to form **5f**, which would undergo smooth oxidative addition, yielding **I'** directly or via oxanickelacyclooctadiene **6f**. Similarly, **1g** would be transformed to **5g**. In contrast to the case of **5f**, the subsequent oxidative addition that yields **I'** directly or oxanickelacyclohexene **6g**^{10,11} would be slow, thereby competing with side reactions.

Scheme 4. Plausible Detailed Mechanism of Oxidative Addition



Finally, the reaction of allylboronate **3a** with benzaldehyde was examined (Scheme 5). Isolated **3a** reacted with benzaldehyde smoothly in the presence of 10 mol% of $\text{Cu}(\text{OTf})_2$ ^{1e,12} in toluene to afford the corresponding homoallyl alcohol **7** in 91% yield with high *anti* selectivity. Notably, one-pot sequential borylative ring opening/allylation reactions also provided **7** in high yield with similar diastereoselectivity.

Scheme 5. Copper-Catalyzed Reaction of **3a** with Benzaldehyde



Experimental Section

Instrumentation and Chemicals

^1H NMR (500 MHz) and ^{13}C NMR (125.7 MHz) spectra were taken on a Varian UNITY INOVA 500 spectrometer and were recorded in CDCl_3 . Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for ^1H and relative to CDCl_3 at 77.0 ppm for ^{13}C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F₂₅₄. Mass spectra (EI unless otherwise noted) were determined on a JEOL Mstation 700 spectrometer. Silica gel 60 N (spherical neutral, obtained from Kanto Chemical) was used for column chromatography. The analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Toluene was dried over slices of sodium and degassed before use. Tricyclopentylphosphine was obtained from TCI and was diluted to prepare 0.5 M hexane solutions, which was stored strictly under argon. Bis(1,5-cyclooctadiene)nickel and bis(pinacolato)diboron were available from Strem.

Syntheses of starting compounds: Starting compounds **1a–1e** are prepared in conventional ways according to the literature.^{5f} Starting compounds **1f–1i** are prepared from the corresponding aldehyde or ketone under Wittig conditions.

Typical Procedure for the Nickel-Catalyzed Borylative Ring Opening Reaction of Vinylcyclopropanes

Synthesis of **3a**

$\text{Ni}(\text{cod})_2$ (2.8 mg, 0.010 mmol) and $\text{K}_3\text{PO}_4 \cdot 3\text{H}_2\text{O}$ (120 mg, 0.45 mmol) were placed in a 20-mL reaction flask under argon. Toluene (1.0 mL) and tricyclopentylphosphine (0.50 M toluene solution, 0.06 mL, 0.03 mmol) were added. The resulting suspension was stirred for 10

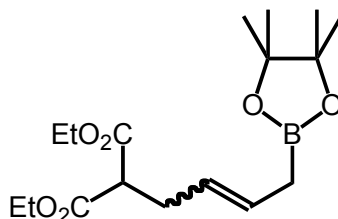
min at 0 °C. Vinylcyclopropane **1a** (42 mg, 0.20 mmol) and bis(pinacolato)diboron (**2**, 76 mg, 0.30 mmol) in toluene (2.0 mL) were then added. Methanol (0.10 mL) was added, and the mixture was allowed to warm to 25 °C and stirred for 10 h. The reaction was quenched with water (3.0 mL). Extraction followed by concentration in vacuo afforded an oil. The crude oil was purified on silica gel (hexane/ethyl acetate = 10/1) by using a dry ice/acetone-jacketed chromatographic column to yield **3a** (57 mg, 0.17 mmol, *E/Z* = 94/6) in 84% yield.

One Pot Procedure for Synthesis of **7** from **1a**

After completion of borylative ring opening reaction, Cu(OTf)₂ (7.2 mg, 0.020 mmol) and PhCHO (24 µL, 0.24 mmol) in toluene (2.0 mL) were added to the reaction mixture at 0 °C. The mixture was allowed to warm to 25 °C and stirred for 20 h. The reaction was quenched with water (3.0 mL). Extraction followed by concentration in vacuo afforded an oil. The crude oil was purified on silica gel (hexane/ethyl acetate = 3/1) to yield **7** (53 mg, 0.16 mmol, *anti/syn* = 94/6) in 79% yield.

Characterization Data

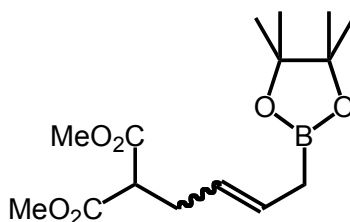
Ethyl 2-ethoxycarbonyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-hexenoate (3a**, a mixture of stereoisomers, *E/Z* = 94/6)**



IR (neat) 2981, 2936, 1717, 1436, 968, 852, 675 cm⁻¹; ¹H NMR (CDCl₃) δ 1.21 (s, 12H), 1.23 (t, *J* = 6.0 Hz, 6H), 1.60 (d, *J* = 7.5 Hz, 0.94×2H), 1.68 (d, *J* = 8.0 Hz, 0.06×2H), 2.53 (dd, *J* = 8.0, 7.0 Hz, 0.94×2H), 2.60 (dd, *J* = 7.5, 7.5 Hz, 0.06×2H), 3.32 (t, *J* = 8.0 Hz, 1H), 4.11–4.20 (m, 4H), 5.32 (dt, *J* = 15.5, 7.0 Hz, 1H), 5.55 (dt, *J* = 15.5, 7.5 Hz, 1H); ¹³C NMR (CDCl₃) for major isomer, δ 14.04, 24.69, 31.94, 52.33, 61.16, 83.14, 125.68, 128.56, 169.02. The signal for

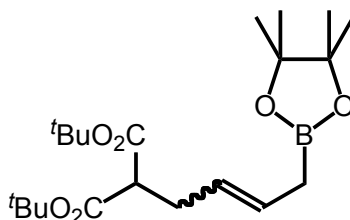
the carbon which is attached to the boron atom was not observed. Found: C, 60.02; H, 8.59%. Calcd for C₁₇H₂₉O₆B: C, 60.17; H, 8.38%.

Methyl 2-methoxycarbonyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-hexenoate (3b, a mixture of stereoisomers, *E/Z* = 91/9)



IR (neat) 2935, 1733, 1436, 1336, 1150, 983, 852, 675 cm⁻¹; ¹H NMR (CDCl₃) δ 1.23 (s, 12H), 1.62 (d, *J* = 7.5 Hz, 0.91×2H), 1.70 (d, *J* = 7.5 Hz, 0.09×2H), 2.57 (dd, *J* = 8.0, 7.0 Hz, 0.91×2H), 2.64 (dd, *J* = 7.5, 6.5 Hz, 0.09×2H), 3.40 (t, *J* = 8.0 Hz, 1H), 3.72 (s, 6H), 5.33 (dt, *J* = 15.5, 7.0 Hz, 1H), 5.58 (dt, *J* = 15.5, 7.5 Hz, 1H); ¹³C NMR (CDCl₃) for major isomer, δ 24.75, 32.05, 52.11, 52.38, 83.22, 125.50, 128.86, 169.45. The signal for the carbon which is attached to the boron atom was not observed. Found: C, 57.71; H, 8.07%. Calcd for C₁₅H₂₅O₆B: C, 57.98; H, 7.96%.

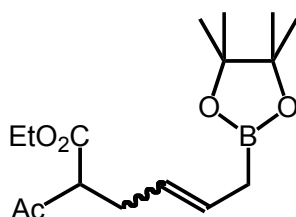
***tert*-Butyl 2-*tert*-butoxycarbonyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-hexenoate (3c, a mixture of stereoisomers, *E/Z* = 95/5)**



IR (neat) 2979, 2934, 1729, 1370, 1330, 1148, 851, 675 cm⁻¹; ¹H NMR (CDCl₃) δ 1.22 (s, 12H), 1.43 (s, 18H), 1.62 (d, *J* = 7.5 Hz, 0.95×2H), 1.70 (d, *J* = 7.5 Hz, 0.05×2H), 2.47 (dd, *J* = 8.0, 7.0 Hz, 0.95×2H), 2.52 (dd, *J* = 8.5, 7.5 Hz, 0.05×2H), 3.13 (t, *J* = 7.5 Hz, 1H), 5.33 (dt, *J* = 15.5, 7.0

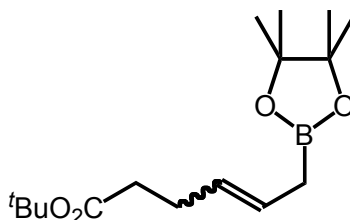
Hz, 1H), 5.54 (dt, $J = 15.5, 8.0$ Hz, 1H); ^{13}C NMR (CDCl_3) for major isomer, δ 24.75, 27.93, 31.97, 54.17, 81.14, 83.16, 126.30, 127.89, 168.50. The signal for the carbon which is attached to the boron atom was not observed. Found: C, 63.64; H, 9.41%. Calcd for $\text{C}_{21}\text{H}_{37}\text{O}_6\text{B}$: C, 63.58; H, 9.58%.

Ethyl 2-acetyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-hexenoate (3d, a mixture of stereoisomers, $E/Z = 80/20$)



IR (neat) 2980, 2935, 2360, 1718, 1456, 1331, 1146, 969, 851 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.22 (s, 12H), 1.25 (t, $J = 7.0$ Hz, 3H), 1.61 (d, $J = 7.0$ Hz, 0.80 $\times$ 2H), 1.69 (dd, $J = 6.5, 6.0$ Hz, 0.20 $\times$ 2H), 2.20 (s, 0.80 $\times$ 3H), 2.22 (s, 0.20 $\times$ 3H), 2.50–2.54 (m, 2H), 3.44 (t, $J = 7.0$ Hz, 1H), 4.17 (q, $J = 7.0$ Hz, 2H), 5.30 (dt, $J = 15.0, 7.5$ Hz, 1H), 5.55 (dt, $J = 15.0, 7.0$ Hz, 1H); ^{13}C NMR (CDCl_3) for major isomer, δ 14.10, 24.75, 29.08, 31.43, 59.94, 61.23, 83.21, 125.73, 128.62, 169.41, 203.03. The signal for the carbon which is attached to the boron atom was not observed. Found: C, 61.95; H, 8.77%. Calcd for $\text{C}_{16}\text{H}_{27}\text{O}_5\text{B}$: C, 61.74; H, 8.94%.

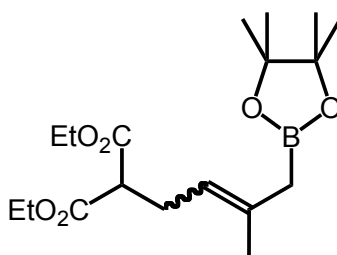
***tert*-Butyl 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-hexenoate (3f, a mixture of stereoisomers, $E/Z = 91/9$)**



IR (neat) 2979, 2933, 1733, 1368, 1328, 1147, 968, 849 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.24 (s, 12H), 1.43 (s, 9H), 1.63 (d, $J = 7.0$ Hz, 0.91 $\times$ 2H), 1.64 (d, $J = 8.0$ Hz, 0.09 $\times$ 2H), 2.24–2.26 (m, 4H),

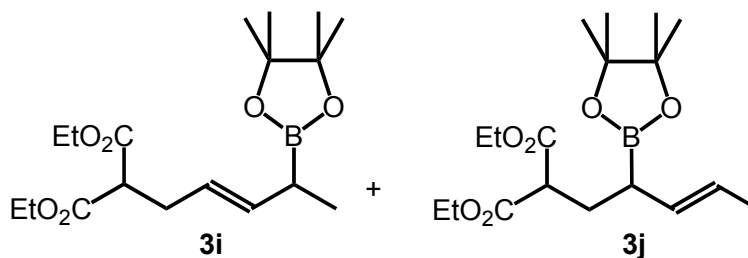
5.35–5.40 (m, 1H), 5.48 (dt, $J = 15.0, 7.0$ Hz, 1H); ^{13}C NMR (CDCl_3) for major isomer, δ 24.75, 28.11, 28.28, 35.66, 79.96, 83.16, 125.98, 128.82, 172.70. The signal for the carbon which is attached to the boron atom was not observed. Found: C, 64.88; H, 9.87%. Calcd for $\text{C}_{16}\text{H}_{29}\text{O}_4\text{B}$: C, 64.96; H, 9.60%.

Ethyl 2-ethoxycarbonyl-5-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-hexenoate (3h, a mixture of stereoisomers, $E/Z = 76/24$)



IR (neat) 2980, 2934, 1733, 1436, 1336, 1149, 983, 852, 675 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.23 (s, 12H), 1.25 (t, $J = 7.5$ Hz, 6H), 1.65 (s, $0.76 \times 2\text{H}$), 1.67 (s, $0.76 \times 3\text{H}$), 1.69 (s, $0.24 \times 2\text{H}$), 1.71 (s, $0.24 \times 3\text{H}$), 2.59 (dd, $J = 7.5, 7.0$ Hz, 2H), 3.32 (t, $J = 7.5$ Hz, $0.76 \times 1\text{H}$), 3.37 (t, $J = 8.0$ Hz, $0.24 \times 1\text{H}$), 4.17 (q, $J = 7.5$ Hz, 4H), 5.04 (t, $J = 7.0$ Hz, 1H); ^{13}C NMR (CDCl_3) for major isomer, δ 14.07, 18.00, 24.72, 27.75, 52.37, 61.21, 83.14, 119.31, 135.33, 169.29. The signal for the carbon which is attached to the boron atom was not observed. HRMS (FAB) Found 355.2285 $[\text{M}+\text{H}]^+$; Calcd for $\text{C}_{18}\text{H}_{32}\text{O}_6\text{B}$: 355.2292.

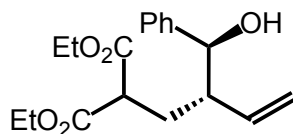
Ethyl 2-ethoxycarbonyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-heptenoate (3i) and ethyl 2-ethoxycarbonyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-heptenoate (3j) (a mixture of isomers, 3i/3j = 45/55)



IR (neat) 2979, 2935, 1733, 1448, 1145, 1038, 969, 852, 669 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.02 (d,

$J = 8.0$ Hz, $0.45 \times 3H$), 1.21 (s, $0.45 \times 12H$), 1.25 (s, $0.55 \times 12H$), 1.23–1.27 (m, 6H), 1.64 (dd, $J = 6.0, 1.0$ Hz, $0.55 \times 3H$), 1.73 (dt, $J = 11.5, 6.0$ Hz, $0.55 \times 1H$), 1.80 (dq, $J = 8.0, 7.5$ Hz, $0.45 \times 1H$), 1.92–1.98 (m, $0.55 \times 1H$), 2.08–2.14 (m, $0.55 \times 1H$), 2.58 (dd, $J = 7.5, 6.5$ Hz, $0.45 \times 2H$), 3.35 (t, $J = 7.5$ Hz, $0.45 \times 1H$), 3.44 (dd, $J = 8.5, 6.5$ Hz, $0.55 \times 1H$), 4.14–4.20 (m, 4H), 5.25–5.34 (m, 1H), 5.40 (dq, $J = 15.5, 6.0$ Hz, $0.55 \times 1H$), 5.61 (dd, $J = 15.5, 8.0$ Hz, $0.45 \times 1H$); ^{13}C NMR ($CDCl_3$) δ 14.08, 18.13, 24.57, 24.61, 24.66, 24.70, 25.00, 29.40, 32.03, 50.84, 52.49, 61.11, 61.17, 61.20, 83.09, 83.31, 123.26, 126.34, 129.66, 135.81, 169.08, 169.49, 169.90. The signals for the carbons which are attached to the boron atoms were not observed. HRMS (FAB) Found 355.2297 $[M+H]^+$; Calcd for $C_{18}H_{31}O_6B$: 355.2292.

Ethyl (*S)-2-ethoxycarbonyl-4-[(*S**)-hydroxy(phenyl)methyl]-5-hexenoate (7, a mixture of stereoisomers, *S**,*S**/*S**,*R** = 94/6)**



IR (neat) 3448, 2982, 1733, 1455, 1369, 1156, 1029, 921, 702 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.19–1.26 (m, 6H), 1.79 (ddd, $J = 14.0, 11.5, 5.0$ Hz, 1H), 1.91 (ddd, $J = 14.0, 10.0, 3.5$ Hz, 1H), 2.17 (s, 1H), 2.31 (ddd, $J = 14.0, 10.0, 3.5$ Hz, $0.06 \times 1H$), 2.37–2.42 (m, $0.94 \times 1H$), 3.34 (dd, $J = 10.0, 5.0$ Hz, 1H), 4.11–4.16 (m, 4H), 4.50 (d, $J = 6.0$ Hz, $0.94 \times 1H$), 4.62 (d, $J = 6.0$ Hz, $0.06 \times 1H$), 4.99 (d, $J = 17.5$ Hz, $0.06 \times 1H$), 5.09 (d, $J = 10.0$ Hz, $0.06 \times 1H$), 5.15 (d, $J = 17.0$ Hz, $0.94 \times 1H$), 5.27 (d, $J = 10.0$ Hz, $0.94 \times 1H$), 5.51 (ddd, $J = 17.5, 10.5, 10.0$ Hz, $0.06 \times 1H$), 5.64 (ddd, $J = 17.0, 10.0, 9.5$ Hz, $0.94 \times 1H$), 7.27–7.37 (m, 5H); ^{13}C NMR ($CDCl_3$) for major isomer, δ 13.97, 14.00, 29.56, 49.94, 50.33, 61.24, 61.40, 76.60, 120.10, 126.82, 127.87, 128.36, 137.24, 141.73, 169.04, 169.52 Found: C, 67.48; H, 7.55%. Calcd for $C_{18}H_{24}O_5$: C, 67.33; H, 7.57%.

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Chapter 2

Nickel-Catalyzed Borylation of Aryl Cyclopropyl Ketones with Bis(pinacolato)diboron to Synthesize 4-Oxoalkylboronates

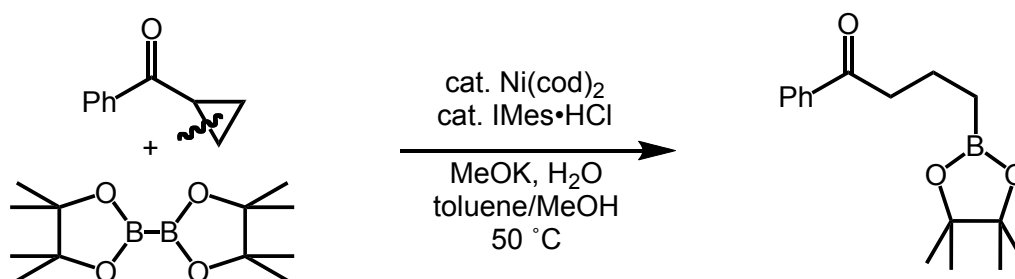
Aryl cyclopropyl ketones undergo nickel-catalyzed borylative ring opening with bis(pinacolato)diboron to yield 4-oxoalkylboronates. The reaction would proceed via oxidative cyclization of a nickel complex and cyclopropyl ketone to form oxanickelacycle as a key intermediate.

Introduction

Transition-metal-catalyzed borylation of unsaturated C–C bonds is one of the most powerful methods to synthesize organoboron reagents.¹ Although many examples of borylation of unsaturated C–C bonds catalyzed by Pt,² Pd,³ Rh,⁴ Cu,⁵ and Au⁶ are known, there are few examples of borylation catalyzed by nickel complexes.⁷

In Chapter 1, the author has described nickel-catalyzed borylative ring opening reaction of vinylcyclopropanes.⁸ In the course of this study, he found another borylative reaction. In Chapter 2, he discloses nickel-catalyzed borylative ring opening reactions of aryl cyclopropyl ketones with bis(pinacolato)diboron yielding synthetically useful 4-oxoalkylboronates (Scheme 1).⁹

Scheme 1.



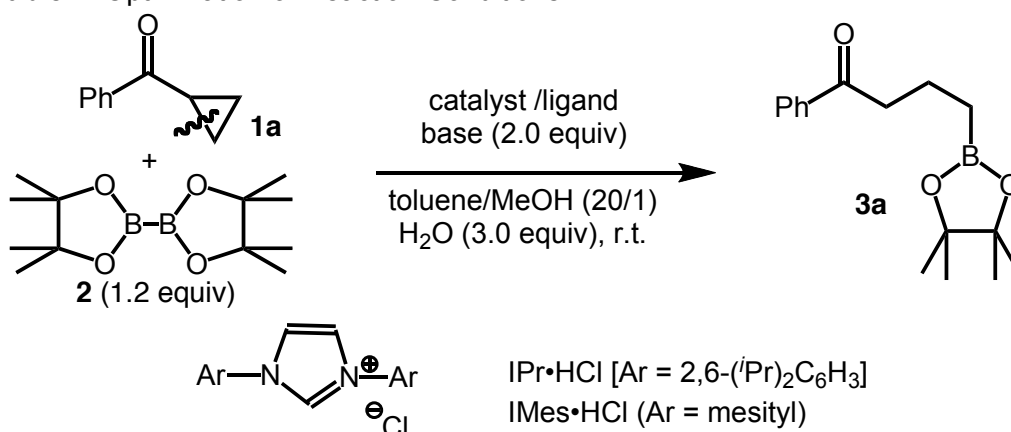
Results and Discussion

The author first attempted the borylative ring opening of cyclopropyl phenyl ketone (**1a**) reaction under the optimized conditions for the reaction of vinylcyclopropane described in chapter 1.⁸ However, the attempt failed to attain high yield. Specifically, treatment of **1a** with bis(pinacolato)diboron (**2**) in the presence of a nickel/tricyclohexylphosphine catalyst, sodium hydroxide, and H₂O in toluene/MeOH afforded the corresponding 4-oxoalkylboronate **3a** in 47% yield (Table 1, entry 1). Tri-*tert*-butylphosphine was inferior to tricyclohexylphosphine (entry 2). When *N*-heterocyclic carbene ligands were applied to this reaction, the results were improved. Among the carbene ligands, IMes•HCl¹⁰ showed the highest activity (entry 4). Interestingly, palladium catalysis also effected the ring opening reaction, albeit in lower yields (entries 5 and 6).

A higher concentration and an increased amount of diboron enhanced the reaction (entry 7,

77% yield). To optimize this transformation, he next investigated the effects of the bases. After extensive investigations, he found that metal alkoxides were effective. Thus, a high yield was observed with potassium methoxide (entry 8). Moreover, the reaction proceeded smoothly at 50 °C and gave product **3a** in 92% isolated yield, even if an amount of the catalyst was reduced to 5 mol% (entry 9).¹¹

Table 1. Optimization of Reaction Conditions



entry	catalyst (mol%)	ligand (mol%)	base	Yield (%) ^a
1	Ni(cod) ₂ (10)	P(^{<i>c</i>} C ₆ H ₁₁) ₃ (20)	NaOH	47
2	Ni(cod) ₂ (10)	P ^{<i>t</i>} Bu ₃ (20)	NaOH	18
3	Ni(cod) ₂ (10)	IPr•HCl (12)	NaOH	30
4	Ni(cod) ₂ (10)	IMes•HCl (12)	NaOH	49
5	Pd(OAc) (10)	P(^{<i>c</i>} C ₆ H ₁₁) ₃ (20)	NaOH	33 ^b
6	Pd(OAc) (10)	IMes•HCl (12)	NaOH	27 ^b
7	Ni(cod) ₂ (10)	IMes•HCl (12)	NaOH	77 ^c
8	Ni(cod) ₂ (10)	IMes•HCl (12)	MeOK	88 ^c
9	Ni(cod) ₂ (5)	IMes•HCl (6)	MeOK	92 ^{c,d}

^a NMR yields. ^b Toluene/MeOH (30/1) and 1.5 equiv of diboron were used.

^c Toluene/MeOH (15/1) and 1.5 equiv of diboron were used. ^d At 50 °C and isolated yield.

Having optimum conditions in hand, a borylative ring opening reaction was carried out with various aryl cyclopropyl ketones. The reactions of **1b** and **1c** with **2** gave **3b** and **3c** in 79% and

88% yields, respectively (Table 2, entries 1 and 2). The borylation reaction of **1c** required a slightly lower temperature since **3c** was unstable at 50 °C or higher. Fluorine-containing **1d** and 2-naphthyl ketone **1e** were converted to the desired products **3d** and **3e** in 79% and 95% yields, respectively (entries 3 and 4). In addition, heterocyclic compound **1f** can be employed to afford **3f** in moderate yield (entry 5). Probably because the methyl group of **1g** blocks interaction between **1g** and active nickel species, the reaction of **1g** was sluggish to afford **3g** in only 16% yield (entry 6). Unfortunately, the product was not obtained with alkyl cyclopropyl ketones under this catalytic system (vide infra).

Table 2. Scope of Cyclopropyl Ketones

entry	Ar	product	temp. (°C)	Yield (%) ^a
1	4-MeC ₆ H ₄ (1b)	3b	50	79
2	4-MeOC ₆ H ₄ (1c)	3c	40	88
3	4-FC ₆ H ₄ (1d)	3d	50	79
4	2-naphthyl (1e)	3e	50	95
5	2-furyl (1f)	3f	40	54 ^b
6	2-MeC ₆ H ₄ (1g)	3g	70	16 ^{b,c}

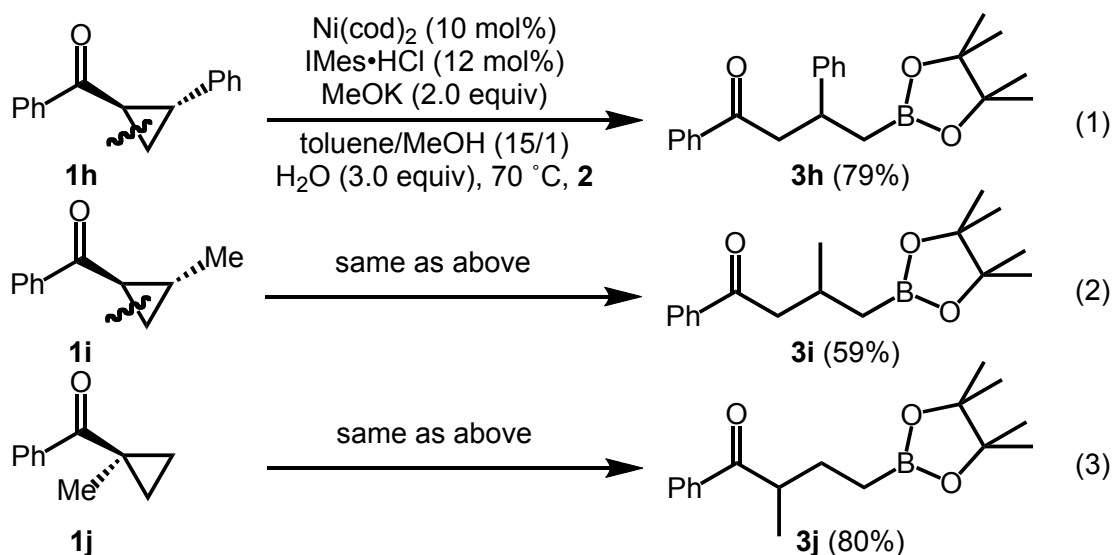
^a Isolated yields. ^b 10 mol% Ni(cod)₂ and 12 mol% IMes·HCl were used.

^c NMR yields.

The author also investigated the borylative reaction of aryl cyclopropyl ketones having an additional substituent on the cyclopropane ring. There are two C–C bonds that may be cleaved in 1,2-disubstituted cyclopropyl ketones **1h** and **1i**. Fortunately, the reactions of *trans*-1-benzoyl-2-phenyl-cyclopropane (**1h**) and *trans*-1-benzoyl-2-methyl-cyclopropane (**1i**) led to **3h** and **3i** as sole products in 79% and 59% yields, respectively (Scheme 1, eqs 1 and 2). The

cleavage of the C–C bond took place selectively on the less sterically hindered side in these reactions. Furthermore, (1-methylcyclopropyl) phenyl ketone (**1j**) also underwent this transformation to give the corresponding product **3j** in high yield (eq 3).

Scheme 2. Reactions of Disubstituted Cyclopropanes

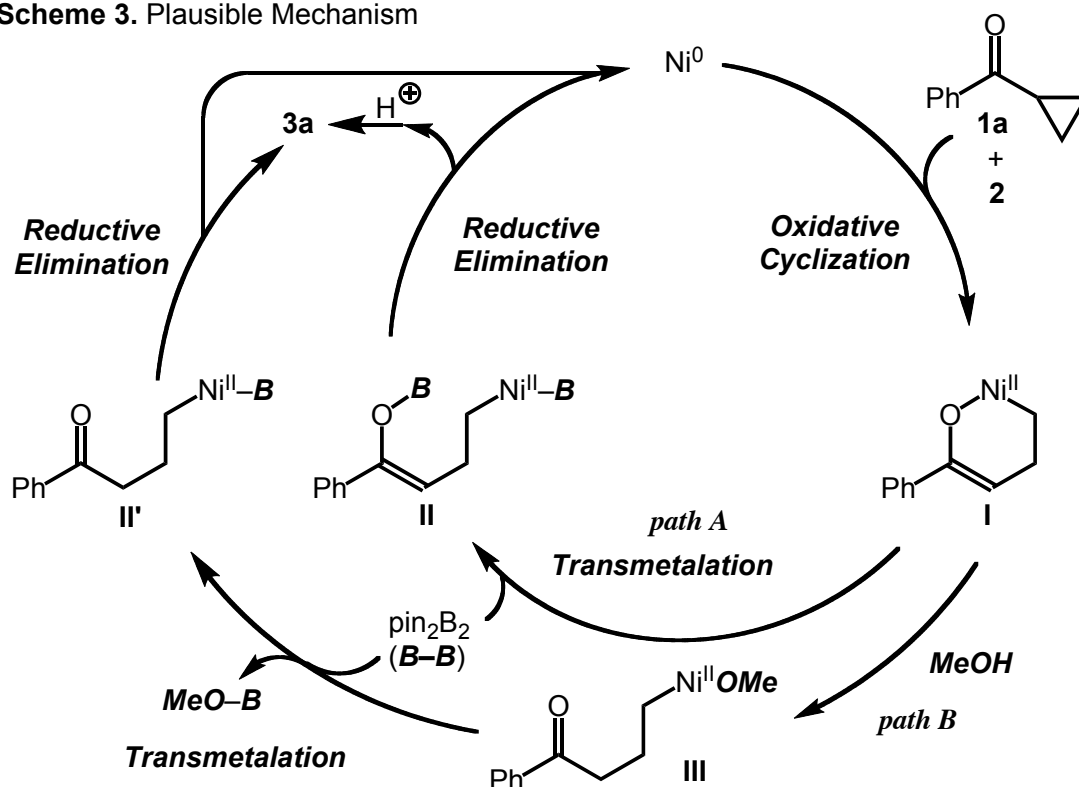


On the basis of the previous studies on nickel-catalyzed borylation of vinylcyclopropanes,⁸ the author assumes the reaction mechanism as follows (Scheme 3). Formation of oxanickelacycle intermediate **4** would occur by oxidative cyclization of cyclopropyl ketone to nickel(0), which was reported by Ogoshi and Kurosawa's¹² and Montgomery's groups.¹³ In this step, bis(pinacolato)diboron might activate the cyclopropyl ketone and promote oxidative cyclization as Lewis acid. Transmetalation would then take place to give alkylnickel intermediate **I** bearing a boron enolate moiety (path A). Reductive elimination produces the boron enolate of **3a**, which is protonated in situ to afford **3a**, with regeneration of the initial nickel(0) complex. The reaction required base, which would activate the boron species.¹⁴ The roles of MeOH and H_2O are not clear at this point.¹⁵

Another mechanism (path B) that involves a formation of alkoxy nickel intermediate **III** by protonolysis of **I** with MeOH may also operate as shown in Chapter 1.¹⁶ In this mechanism, transmetalation between **III** and diboron **2** could easily occur to provide alkylnickel intermediate **II'** (path B).¹⁷

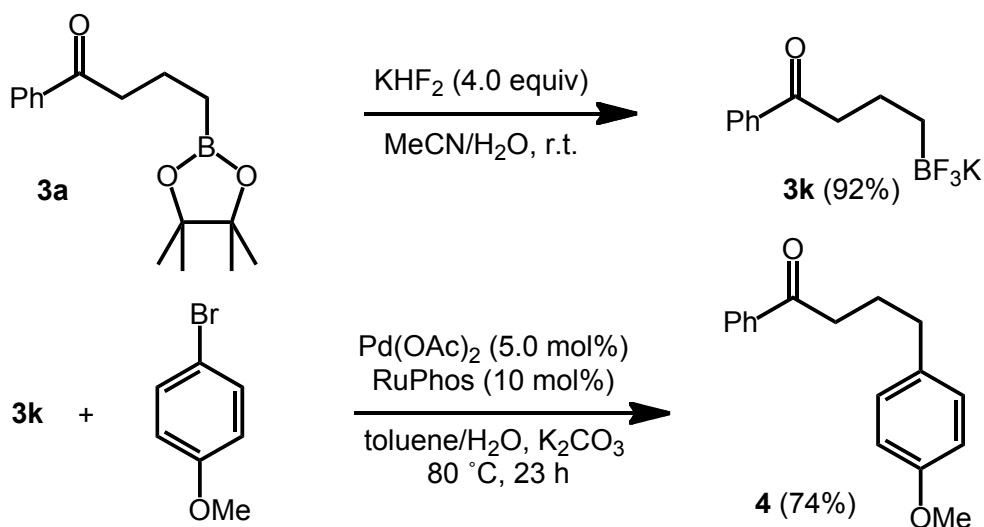
In the cases of alkyl cyclopropyl ketones, oxidative cyclization to nickel(0) would be sluggish, because alkyl cyclopropyl ketones are electron rich compared to aryl cyclopropyl ketones. Furthermore, the amount of oxanickelacycle generated from alkyl cyclopropyl ketone with nickel(0) would be less than that generated from aryl cyclopropyl ketones.

Scheme 3. Plausible Mechanism



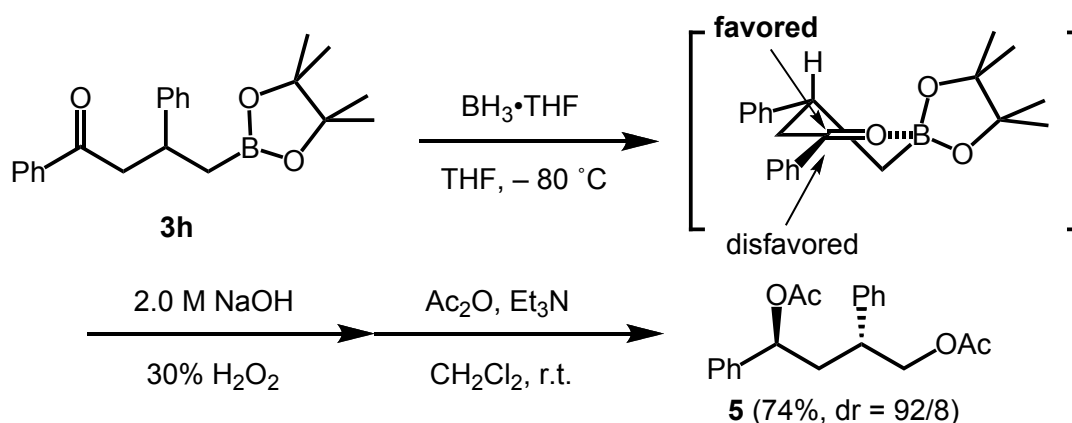
Finally, 4-oxoalkylboronate was subjected to the Suzuki-Miyaura cross coupling reaction (Scheme 3). The boronate **3a** was converted to trifluoroborate **3k** in 92% yield, then **3k** was treated with 4-bromoanisole in the presence of 5 mol% $\text{Pd}(\text{OAc})_2$, 10 mol% RuPhos (2-dicyclohexylphosphino-2',6'-diisopropoxy-1,1'-biphenyl), and K_2CO_3 in toluene/ H_2O at 80°C^{18} to provide the cross-coupling product **4** in 74% yield.

Scheme 4. Application of **3a** to Suzuki-Miyaura Cross Coupling



Molander et al. developed highly diastereoselective reduction of 2-substituted-4-oxoalkyl boronates, wherein intramolecular coordination of the carbonyl oxygen to the boronate ester plays a key role.^{9b} The procedure was applicable to the reduction of **3h**. Treatment of boronate **3h** with $\text{BH}_3\cdot\text{THF}$ as a reductant followed by oxidation and esterification afforded the corresponding diester **5** in 74% yield with high diastereoselectivity (Scheme 5).

Scheme 5. Diastereoselective Reduction of **3h**



Experimental Procedure

Instrumentation and Chemicals

^1H NMR (500 MHz) and ^{13}C NMR (125.7 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and were recorded in CDCl_3 . Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for ^1H and relative to CDCl_3 at 77.0 ppm for ^{13}C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. Mass spectra (EI unless otherwise noted) were determined on a JEOL Mstation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F₂₅₄. Silica gel 60 N (spherical neutral, obtained from Kanto Chemical) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Toluene was dried over slices of sodium and degassed before use. Bis(1,5-cyclooctadiene)nickel, bis(pinacolato)diboron, and tricyclohexylphosphine were available from Strem. Tricyclohexylphosphine was diluted to prepare 1.0 M hexane solutions, which was stored strictly under argon. IMes•HCl and IPr•HCl were prepared in conventional ways according to the literature.^{10a} Potassium methoxide was obtained from Aldrich.

Typical Procedure for Nickel-Catalyzed Borylation of Aryl Cyclopropyl Ketones with Bis(pinacolato)diboron to Synthesize 4-Oxoalkylboronates

Synthesis of 3a

Ni(cod)₂ (2.8 mg, 0.010 mmol), IMes•HCl (8.2 mg, 0.012 mmol), and MeOK (28 mg, 0.4 mmol) were placed in a 20-mL reaction flask under argon. After toluene (0.5 mL) was added, the resulting suspension was stirred for 10 min at room temperature. Cyclopropyl ketone **1a** (29 mg, 0.20 mmol) and bis(pinacolato)diboron (**2**, 76 mg, 0.30 mmol) in toluene (1.0 mL) were then added. Methanol (0.10 mL) and H₂O (10 μL) were added, and the mixture was allowed to warm to 50 °C and stirred for 5 h. The reaction mixture was filtered by alumina (Wako, activated),

followed by concentration in vacuo to afford an oil. The crude oil was purified on silica gel (hexane/ethyl acetate = 5/1) by using a dry ice/acetone-jacketed chromatographic column to yield **3a** (51 mg, 0.18 mmol) in 92% yield.

Synthesis of **3k**

Boronate **3a** (990 mg, 3.5 mmol) was dissolved in acetonitrile (15 mL). Saturated aq. KHF_2 (4.5 M, 3 mL, 14 mmol) was added dropwise via a syringe at room temperature. After the resulting mixture was stirred for 2 h, the mixture was concentrated in vacuo. The dried solids were triturated with hot acetone (10×2 mL) and filtered to remove inorganic salts. The resulting filtrate was concentrated and washed with Et_2O (10×2 mL) to give white solid (**3k**, 820 mg, 3.2 mmol, 92%).

Synthesis of **4**

Potassium (3-benzoylpropyl)trifluoroborate (**3k**, 53 mg, 0.21 mmol), 4-bromoanisole (25 mL, 0.20 mmol), K_2CO_3 (83 mg, 0.60 mmol), $\text{Pd}(\text{OAc})_2$ (2.2 mg, 0.010 mmol), and RuPhos (9.3 mg, 0.020 mmol) were placed in a 20-mL reaction flask under argon. Toluene (0.8 mL) and H_2O (0.1 mL) were added, and the mixture was allowed to warm to 80 °C and stirred for 23 h. After completion, pH 7 buffer (1.5 mL) was added, and the product was extracted with ethyl acetate (3×2 mL). Concentration in vacuo afforded an oil. The crude oil was purified on silica gel (Wakogel 200 mesh, hexane/ethyl acetate = 10/1) to yield **4** (38 mg, 0.15 mmol, 74%).

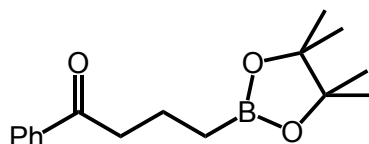
Synthesis of **5**

1,3-Diphenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-butanone (**3h**, 70 mg, 0.20 mmol) was dissolved in THF (1 mL) at -80 °C under argon. $\text{BH}_3 \cdot \text{THF}$ was added dropwise to the solution and the resulting mixture was stirred for 3 h. The reduced boronate was oxidized in situ with a 2 M NaOH aq. (1.0 mL, 2.0 mmol) and a 30% H_2O_2 aq. (0.20 mL, 2.0 mmol). The resulting mixture was extracted with Et_2O (3×2 mL), and the solvent was removed in vacuo to

give an oil. The oil was treated with Ac₂O (0.10 mL, 1.0 mmol) and Et₃N (0.30 mL, 2.0 mmol) in CH₂Cl₂ (2 mL). After the mixture was stirred for 16 h, sat. NH₄Cl aq. was added. The product was extracted with ethyl acetate (3 × 2 mL). Concentration of dried extracts in vacuo afforded an oil. The crude oil was purified on silica gel (hexane/ethyl acetate = 5/1) to yield **5** (a 92/8 mixture of diastereomers, 45 mg, 0.15 mmol, 76%)

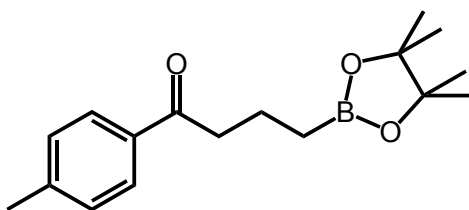
Characterization Data

1-Phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-butanone (**3a**)



IR (neat) 2978, 2935, 1684, 1373, 1317, 1145, 691 cm⁻¹; ¹H NMR (CDCl₃) δ 0.89 (t, *J* = 8.0 Hz, 2H), 1.25 (s, 12H), 1.86 (tt, *J* = 8.0, 7.5 Hz, 2H), 2.98 (t, *J* = 7.5 Hz, 2H), 7.45 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.54 (dd, *J* = 8.0, 7.5 Hz, 1H), 7.97 (dd, *J* = 8.0, 7.5 Hz, 2H); ¹³C NMR (CDCl₃) δ 19.3, 24.8, 40.9, 83.1, 128.1, 128.5, 132.8, 137.1, 200.6. The signal for the carbon which is attached to the boron atom was not observed. Found: C, 70.19; H, 8.65%. Calcd for C₁₆H₂₃O₃B: C, 70.09; H, 8.45%.

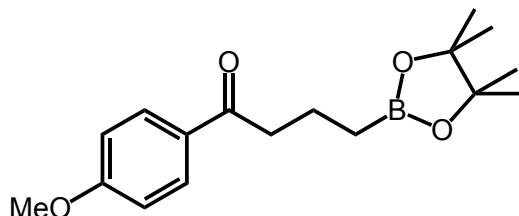
1-(4-Methylphenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-butanone (**3b**)



IR (nujol) 2925, 2897, 2855, 1684, 1456, 1373, 1312, 1146, 847 cm⁻¹; ¹H NMR (CDCl₃) δ 0.87 (t, *J* = 8.0 Hz, 2H), 1.24 (s, 12H), 1.84 (tt, *J* = 8.0, 7.5 Hz, 2H), 2.40 (s, 3H), 2.94 (t, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 8.5 Hz, 2H), 7.87 (d, *J* = 8.5 Hz, 2H); ¹³C NMR (CDCl₃) δ 19.4, 21.6, 24.8, 40.8, 83.0, 128.2, 129.1, 134.6, 143.5, 200.2. The signal for the carbon which is attached to the boron atom was not observed. Found: C, 70.85; H, 8.56%. Calcd for C₁₇H₂₅O₃B: C, 70.85; H,

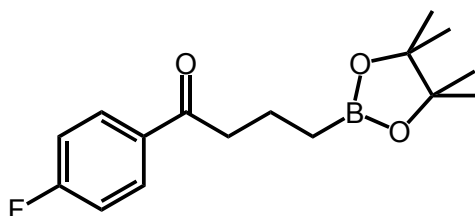
8.74%. Mp: 27–30 °C.

1-(4-Methoxyphenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-butanone (3c)



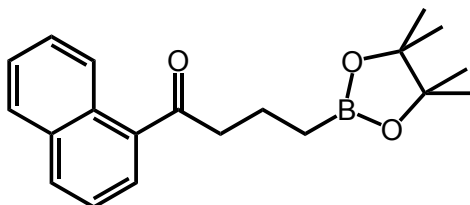
IR (neat) 2977, 2934, 1577, 1459, 1444, 1418, 1171, 1032, 969 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.87 (t, $J = 7.5$ Hz, 2H), 1.24 (s, 12H), 1.84 (tt, $J = 7.5, 7.5$ Hz, 2H), 2.92 (t, $J = 7.5$ Hz, 2H), 3.86 (s, 3H), 6.92 (d, $J = 9.0$ Hz, 2H), 7.95 (d, $J = 9.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 19.5, 24.8, 40.6, 55.4, 83.0, 113.6, 130.2, 130.4, 163.2, 199.2. The signal for the carbon which is attached to the boron atom was not observed. Found: C, 67.10; H, 8.02%. Calcd for $\text{C}_{17}\text{H}_{25}\text{O}_4\text{B}$: C, 67.12; H, 8.28%.

1-(4-Fluorophenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-butanone (3d)



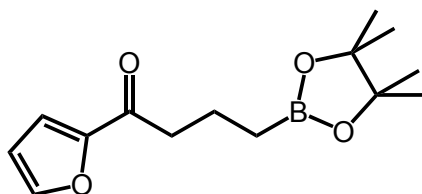
IR (neat) 2978, 2933, 1684, 1500, 1145, 848 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.87 (t, $J = 8.0$ Hz, 2H), 1.24 (s, 12H), 1.84 (tt, $J = 8.0, 7.5$ Hz, 2H), 2.94 (t, $J = 7.5$ Hz, 2H), 7.10 (dd, $J = 9.0, 8.5$ Hz, 2H), 7.99 (dd, $J = 9.0, 5.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 19.3, 24.8, 40.8, 83.1, 115.5 (d, $J = 22.0$ Hz), 130.7 (d, $J = 9.0$ Hz), 133.5 (d, $J = 2.9$ Hz), 165.6 (d, $J = 252.5$ Hz), 198.9. The signal for the carbon which is attached to the boron atom was not observed. Found: C, 65.74; H, 7.55%. Calcd for $\text{C}_{16}\text{H}_{22}\text{O}_3\text{BF}$: C, 65.78; H, 7.59%.

1-(2-Naphthyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-butanone (3e)



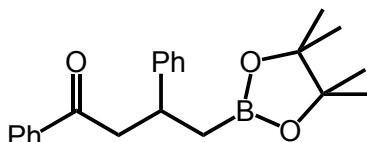
IR (nujol) 2978, 2935, 2855, 1684, 1373, 1317, 1146, 691 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.91 (t, J = 8.0 Hz, 2H), 1.24 (s, 12H), 1.92 (tt, J = 8.0, 7.5 Hz, 2H), 3.07 (t, J = 7.5 Hz, 2H), 7.47–7.59 (m, 3H), 7.85–7.88 (m, 2H), 7.97 (d, J = 8.0 Hz, 1H), 8.55 (d, J = 8.5 Hz, 1H); ^{13}C NMR (CDCl_3) δ 19.5, 24.8, 44.6, 83.1, 124.4, 125.9, 126.3, 127.2, 127.7, 128.3, 130.1, 132.2, 133.9, 136.4, 205.1. The signal for the carbon which is attached to the boron atom was not observed. HRMS (EI) Found 324.1898 $[\text{M}]^+$; Calcd for $\text{C}_{20}\text{H}_{25}\text{O}_3\text{B}$: 324.1897. Mp: 45–47 $^\circ\text{C}$.

1-(2-Furyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-butanone (3f)



IR (neat) 2979, 2933, 1675, 1470, 1373, 1145, 914, 734 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.86 (t, J = 8.0 Hz, 2H), 1.24 (s, 12H), 1.84 (tt, J = 8.0, 7.5 Hz, 2H), 2.82 (t, J = 7.5 Hz, 2H), 6.51 (dd, J = 3.5, 2.0 Hz, 1H), 7.18 (dd, J = 3.5, 0.5 Hz, 1H), 7.56 (dd, J = 2.0, 0.5 Hz, 1H); ^{13}C NMR (CDCl_3) δ 19.3, 24.8, 40.8, 83.1, 112.0, 116.9, 146.1, 152.8, 189.7. The signal for the carbon which is attached to the boron atom was not observed. HRMS (EI) Found 264.1537 $[\text{M}]^+$; Calcd for $\text{C}_{14}\text{H}_{21}\text{O}_4\text{B}$: 264.1533.

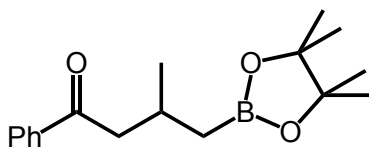
1,3-Diphenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-butanone (3h)



IR (neat) 2978, 2930, 1686, 1322, 1145, 968, 699 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.08 (s, 6H), 1.10 (s, 6H), 1.24 (dd, J = 15.5, 8.5 Hz, 1H), 1.33 (dd, J = 15.5, 7.0 Hz, 1H), 3.24–3.34 (m, 2H),

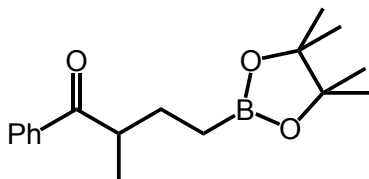
3.59–3.65 (m, 1H), 7.13–7.16 (m, 1H), 7.23–7.28 (m, 4H), 7.42 (dd, $J = 8.0, 7.5$ Hz, 2H), 7.52 (dd, $J = 8.0, 7.5$ Hz, 1H), 7.92 (dd, $J = 8.0, 7.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 24.6, 24.7, 37.3, 47.7, 83.0, 126.1, 127.3, 128.1, 128.2, 128.4, 132.8, 137.2, 146.3, 199.1. Found: C, 75.55; H, 7.74%. The signal for the carbon which is attached to the boron atom was not observed. Calcd for $\text{C}_{22}\text{H}_{27}\text{O}_3\text{B}$: C, 75.44; H, 7.77%.

3-Methyl-1-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-butanone (3i)



IR (neat) 2873, 1683, 1448, 1216, 1144, 971, 691 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.83 (dd, $J = 15.5, 7.5$ Hz, 1H), 0.93 (dd, $J = 15.5, 7.5$ Hz, 1H), 1.00 (d, $J = 6.5$ Hz, 3H), 1.246 (s, 6H), 1.249 (s, 6H), 2.37–2.44 (m, 1H), 2.74 (dd, $J = 15.5, 8.0$ Hz, 1H), 3.05 (dd, $J = 15.5, 5.5$ Hz, 1H), 7.45 (dd, $J = 7.5, 7.5$ Hz, 2H), 7.54 (dd, $J = 7.5, 7.5$ Hz, 1H), 7.98 (dd, $J = 7.5, 7.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 22.6, 24.8, 24.9, 26.7, 47.9, 83.0, 128.3, 128.5, 132.7, 137.4, 200.4. The signal for the carbon which is attached to the boron atom was not observed. HRMS (EI) Found 288.1899 $[\text{M}]^+$; Calcd for $\text{C}_{17}\text{H}_{25}\text{O}_3\text{B}$: 288.1897.

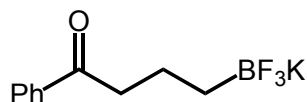
2-Methyl-1-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-butanone (3j)



IR (neat) 2978, 2933, 1684, 1372, 1145, 970, 704 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.82 (t, $J = 7.5$ Hz, 2H), 1.18 (d, $J = 7.0$ Hz, 3H), 1.23 (s, 12H), 1.50–1.57 (m, 1H), 1.89–1.96 (m, 1H), 3.47 (tq, $J = 13.5, 7.0$ Hz, 1H), 7.45 (dd, $J = 8.0, 7.5$ Hz, 1H), 7.54 (dd, $J = 7.5, 7.5$ Hz, 2H), 7.98 (dd, $J = 8.0, 7.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 16.6, 24.8x2, 28.1, 42.3, 83.0, 128.3, 128.5, 132.7, 136.8, 204.6. The signal for the carbon which is attached to the boron atom was not observed.

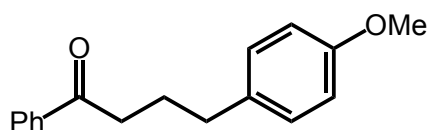
Found: C, 70.87; H, 8.83%. Calcd for C₁₇H₂₅O₃B: C, 70.85; H, 8.74%.

Potassium (3-Benzoylpropyl)trifluoroborate (3k)



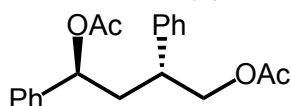
IR (nujol) 2854, 1685, 1448, 1377, 1364, 1015 cm⁻¹; ¹H NMR (DMSO-*d*₆) δ 0.06 (bs, 2H), 1.53 (tt, *J* = 7.5, 7.5 Hz, 2H), 2.89 (t, *J* = 7.5 Hz, 2H), 7.54 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.64 (dd, *J* = 8.0, 7.5 Hz, 1H), 7.95 (dd, *J* = 8.0, 7.5 Hz, 2H); ¹³C NMR (DMSO-*d*₆) δ 22.8, 42.8, 128.8, 129.6, 133.6, 138.0, 202.6. The signal for the carbon which is attached to the boron atom was not observed. Found: C, 47.15; H, 4.31%. Calcd for C₁₀H₁₁OBF₃K: C, 47.27; H, 4.36%. Mp: 193–197 °C.

4-(4-Methoxyphenyl)-1-phenyl-1-butanone (4)



IR (nujol) 2923, 2855, 1684, 1448, 1377, 1245, 1033, 745 cm⁻¹; ¹H NMR (CDCl₃) δ 2.05 (tt, *J* = 7.5, 7.5 Hz, 2H), 2.67 (t, *J* = 7.5 Hz, 2H), 2.97 (t, *J* = 7.5 Hz, 2H), 3.79 (s, 3H), 6.84 (d, *J* = 7.5 Hz, 2H) 7.13 (d, *J* = 8.5 Hz, 2H) 7.45 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.55 (dd, *J* = 8.0, 7.5 Hz, 1H), 7.92 (dd, *J* = 7.5, 7.5 Hz, 2H); ¹³C NMR (CDCl₃) δ 25.9, 34.2, 37.6, 55.2, 113.8, 128.0, 128.5, 129.4, 132.9, 133.7, 137.0, 157.8, 200.2. Found: C, 80.06; H, 7.13%. Calcd for C₁₇H₁₈O₂: C, 80.28; H, 7.13%. Mp: 43–44 °C

(1*R,3*R**)-1,3-Diphenyl-1,4-butanediol diacetate (5, 92:8 mixture of diastereomers)**



IR (neat) 1740, 1496, 1455, 1369, 1236, 1033, 701 cm⁻¹; ¹H NMR (CDCl₃) δ 1.89 (s, 0.08×3H), 1.98 (s, 0.08×3H), 2.01 (s, 0.92×3H), 2.05 (s, 0.92×3H), 2.01–2.09 (m, 1H), 2.21–2.25 (m,

0.08×1H), 2.33–2.39 (m, 0.92×1H), 2.76–2.80 (m, 0.08×1H), 3.07–3.13 (m, 0.92×1H), 4.14 (dd, $J = 9.0, 7.0$ Hz, 0.08×2H), 4.22 (d, $J = 6.5$ Hz, 0.92×2H), 5.50 (dd, $J = 5.0, 4.0$ Hz, 0.92×1H), 5.62 (t, $J = 7.0$ Hz, 0.08×1H), 7.16–7.19 (m, 2H), 7.23–7.35 (m, 8H); ^{13}C NMR (CDCl_3) for major isomer δ 20.9, 21.1, 39.5, 41.6, 68.1, 73.6, 126.1, 127.2, 127.8, 127.9, 128.5, 128.8, 140.5, 140.7, 170.0, 170.9. Found: C, 73.31; H, 6.99%. Calcd for $\text{C}_{20}\text{H}_{22}\text{O}_4$: C, 73.60; H, 6.79%. The relative stereochemistry was assigned according to the literature.^{9b}

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Chapter 3

Palladium-Catalyzed Preparation of Silyl Enolates from Cyclopropyl Ketones or α,β -Unsaturated Ketones with Hydrosilanes

Cyclopropyl ketones undergo palladium-catalyzed hydrosilylation with hydrosilanes to yield (Z)-silyl enolates. The reaction involves formation of α,β -unsaturated ketone from cyclopropyl ketone followed by 1,4-hydrosilylation. Accordingly, the reaction is applicable to various α,β -unsaturated ketones to afford silyl enolates with high Z selectivity.

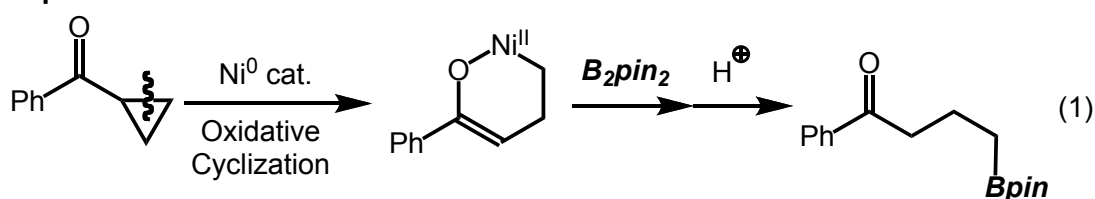
Introduction

Silyl enolates are extremely useful and valuable reagents for C–C bond formation in organic synthesis.¹ Nowadays, transition-metal-catalyzed 1,4-hydrosilylation of α,β -unsaturated carbonyl compounds is one of the most powerful methods to synthesize silyl enolates. Although some examples of 1,4-hydrosilylation of α,β -unsaturated carbonyl compounds catalyzed by Rh,² Pt,³ Cu,⁴ and B(C₆F₅)₃⁵ are known, the stereoselectivities are not satisfactory in the cases of acyclic enones^{2,3} and 1,2-hydrosilylation competes in some cases.^{2,3} Hence, the highly selective synthesis of (*Z*)-silyl enolates remains a challenge.

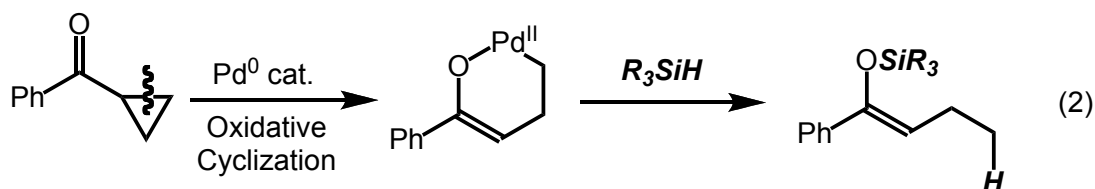
In Chapter 2, the author described a nickel-catalyzed borylative ring opening reaction of aryl cyclopropyl ketones with bis(pinacolato)diboron yielding synthetically useful 4-oxoalkylboronates.⁶ This reaction includes the formation of an oxanickelacycle by oxidative cyclization of cyclopropyl ketone with nickel (Scheme 1, eq 1).⁷ In the course of this study, he found that palladium was also effective for the oxidative cyclization of cyclopropyl ketones. Therefore, he envisioned that the oxapalladacycle intermediate could apply to the reaction of cyclopropyl ketones with hydrosilylanes (eq 2).

Scheme 1. Ring Opening Reaction of Cyclopropyl Ketones

Chapter 2



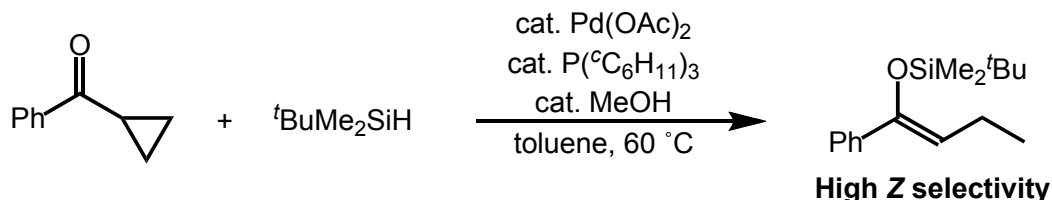
Author's initial hypothesis



In Chapter 3, the author mentions that a combination of palladium acetate and tricyclohexylphosphine is effective for hydrosilylative ring opening of cyclopropyl ketones with

hydrosilanes yielding silyl enolates with high Z selectivity (Scheme 2).

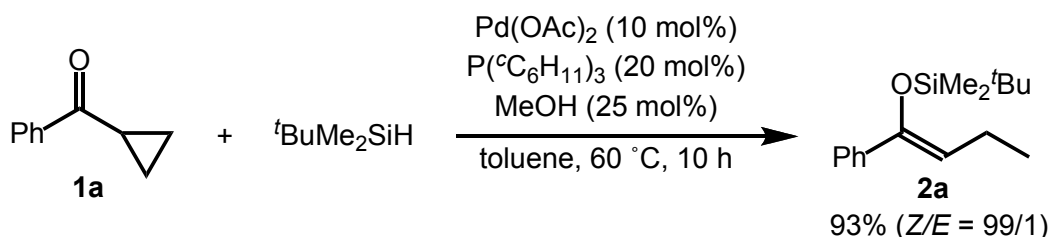
Scheme 2.



Results and Discussion

Treatment of cyclopropyl phenyl ketone (**1a**) with $t\text{BuMe}_2\text{SiH}$ in the presence of a palladium/tricyclohexylphosphine catalyst and a small amount of MeOH as an additive in toluene at $60\text{ }^\circ\text{C}$ afforded the corresponding silyl enolate **2a** in 93% yield with high Z selectivity (Scheme 3).

Scheme 3. Palladium-Catalyzed Reaction of Cyclopropyl Phenyl Ketone with Hydrosilane



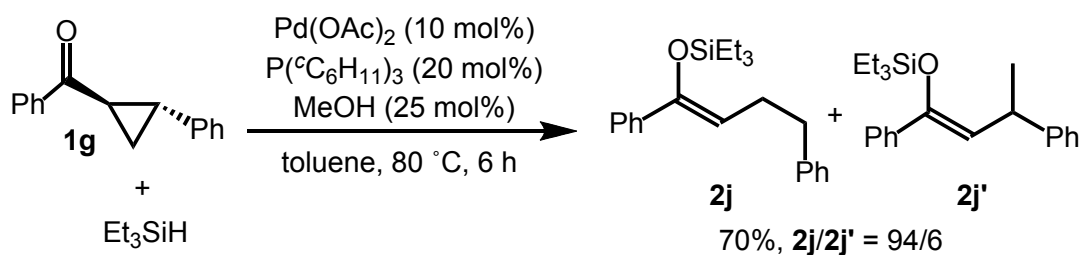
A variety of cyclopropyl ketones were subjected to the reaction, and the results are summarized in Table 1. The reactions of **1b** and **1c** with Et_3SiH gave **2b** and **2c** in 81% and 72% yields, respectively (Table 1, entries 1 and 2). The use of **1d** having an ester group afforded silyl enolate **2d** in 87% yield (entry 3). Treatment of **1a** with Et_3SiH instead of $t\text{BuMe}_2\text{SiH}$ yielded **2e**^{2a,c} with a slightly inferior result (entry 4). Interestingly, alkyl cyclopropyl ketones participated in the hydrosilylation, even though they were unreactive in the nickel-catalyzed borylation (entries 5–8).⁶ In the reactions of alkyl cyclopropyl ketones **1e** and **1f**, $t\text{BuMe}_2\text{SiH}$ was more reactive than Et_3SiH . Benzyl cyclopropyl ketone (**1f**) was transformed to the corresponding enolate **2i**, which is difficult to synthesize by using known methods.⁸ In all cases, silyl enolates were prepared with high Z selectivity.

Table 1. Scope of Cyclopropyl Ketones

entry	R	Si	product	Yield (%) ^a
1	4-MeC ₆ H ₄ (1b)	Et ₃ Si	2b	81 ^b
2	4-MeOC ₆ H ₄ (1c)	Et ₃ Si	2c	72 ^b
3	4-EtO ₂ CC ₆ H ₄ (1d)	Et ₃ Si	2d	87
4	Ph (1a)	Et ₃ Si	2e	81 ^b
5	Me (1e)	Et ₃ Si	2f	(45) ^{c,d}
6	Me (1e)	^t BuMe ₂ Si	2g	79 ^d
7	PhCH ₂ (1f)	Et ₃ Si	2h	(52) ^{c,d}
8	PhCH ₂ (1f)	^t BuMe ₂ Si	2i	85 ^d

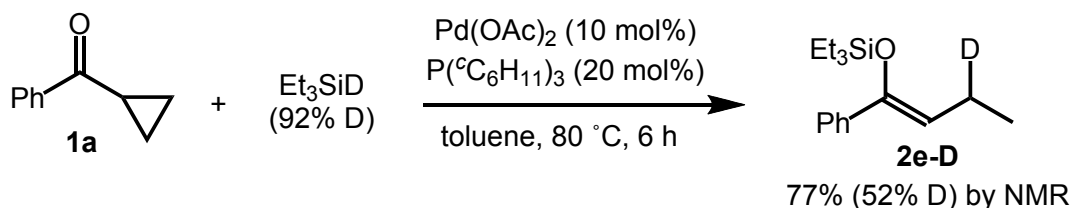
^a Isolated yields. ^b Z/E = 99/1. ^c NMR yields. ^d At 80 °C.

When cyclopropyl ketone **1g** having an additional substituent on the cyclopropane ring was used, the hydrosilylative ring opening reaction of **1g** predominantly gave **2j** through selective cleavage of the most substituted C–C bond (Scheme 4).

Scheme 4. Reaction of Disubstituted Cyclopropane

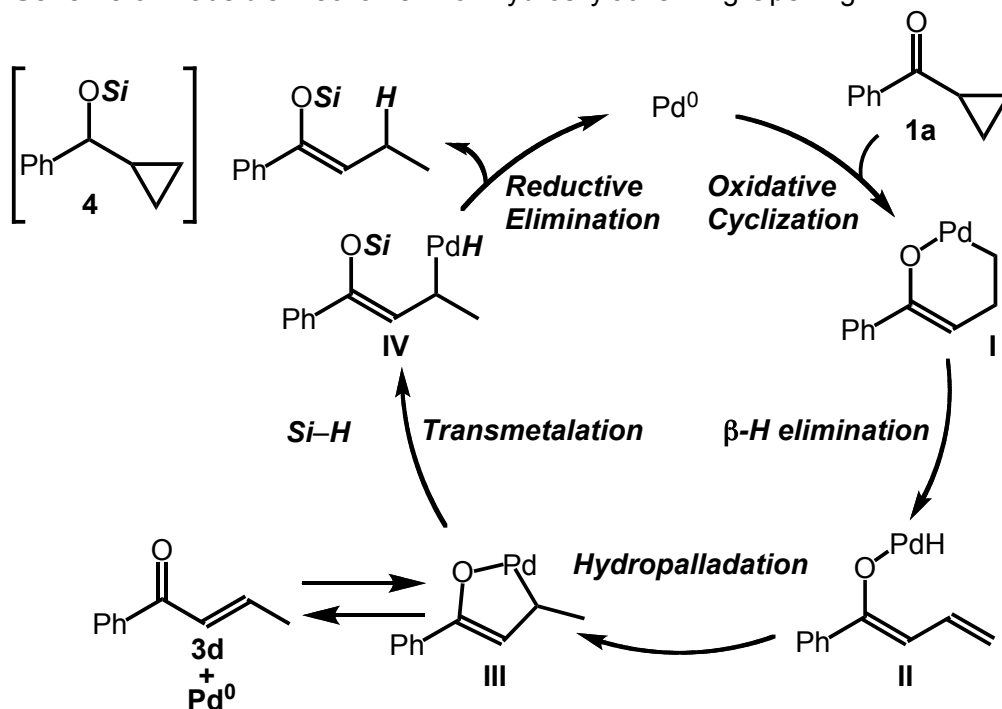
To study the reaction mechanism in detail, the reaction of cyclopropyl phenyl ketone with deuterated silane, Et₃SiD,⁹ was examined. Contrary to the author's expectations (Scheme 1, eq 2), deuterium was introduced into the β-position (Scheme 5).

Scheme 5. Reaction of Cyclopropyl Ketone with Et₃SiD



Accordingly, he proposes the reaction mechanism as follows (Scheme 6). Oxidative cyclization of the cyclopropyl ketone to palladium(0) gives six-membered oxapalladacycle intermediate **I**. The subsequent β -hydride elimination generates palladium hydride species **II**. Intramolecular hydropalladation would occur rapidly to afford five-membered oxapalladacycle intermediate **III**.¹⁰ Although the release of **3d** and palladium(0) might be possible, they could be converted smoothly to the five membered oxapalladacycle intermediate **III** reversibly.¹¹ Transmetalation between **III** and the hydrosilane would then take place to give alkylpalladium intermediate **IV** which bears a silyl enolate moiety. Reductive elimination produces the silyl enolate with regeneration of the initial palladium(0) complex. Although oxidative addition of the hydrosilane to palladium(0) can occur competitively,¹² it might be relatively slow.

Scheme 6. Plausible Mechanism for Hydrosilylative Ring Opening



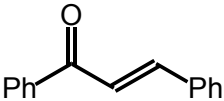
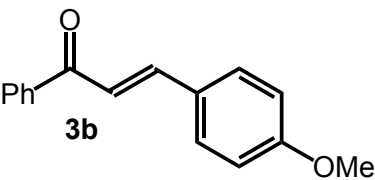
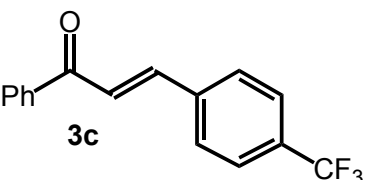
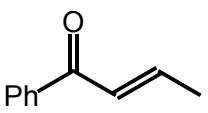
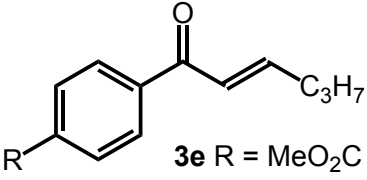
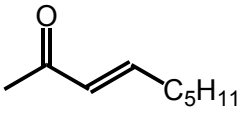
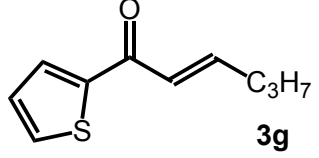
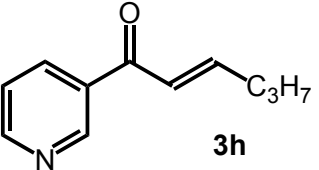
Although the role of MeOH is not clear at this stage, the reaction required MeOH to achieve a high yield. He suspects it may activate hydrosilane species as a Lewis base and promote transmetalation.¹³

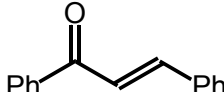
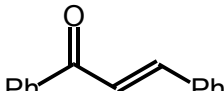
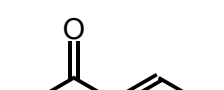
In 1999, Slough et al. reported a rhodium-catalyzed hydrosilylation of cyclopropyl phenyl ketones with Et₃SiH.¹⁴ Since they observed silyl ether **4** (Scheme 6), in addition to *E/Z* mixtures of silyl enolates, they proposed a different mechanism which consisted of oxidative addition of Et₃SiH to rhodium complex and following by 1,2-hydrosilylation of a cyclopropyl ketone. Although no generation of silyl ether **4** was observed in the present case, the mechanism they proposed could not be excluded as an alternative possibility.

The implication of the formation of the α,β -unsaturated ketone in situ promoted the author to investigate the reaction of α,β -unsaturated ketones with hydrosilanes. Indeed, treatment of chalcone (**3a**) with ^tBuMe₂SiH in the presence of a palladium/tricyclohexylphosphine catalyst in toluene at 60 °C afforded (*Z*)-silyl enolate **2k** in 94% yield (Table 2, entry 1). The electronic nature of the aryl group at the β -position had little effect on the yields of **2** (entries 2 and 3). The substituents R and R' are not limited to aryl groups (entries 4–6), and aliphatic α,β -unsaturated ketone **3f** could undergo efficient 1,4-hydrosilylation. Heteroaromatic rings were compatible with the reaction conditions (entries 7 and 8).

He then examined the scope of hydrosilanes. Upon treatment of chalcone with PhMe₂SiH, an excellent yield of the corresponding product **2r** was obtained (entry 9). While the reaction with Et₃SiH gave **2s** smoothly (entry 10), no reaction took place with ⁱPr₃SiH (entry 11).

Table 2. Scope of α,β -Unsaturated Ketones

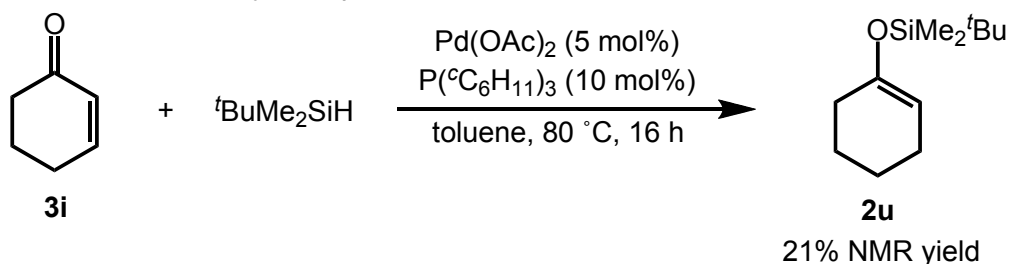
$ \begin{array}{c} \text{R}-\text{C}(=\text{O})-\text{CH}=\text{CH}-\text{R}' \\ \mathbf{3} \end{array} + \text{Si-H} \xrightarrow[\text{toluene, 60 } ^\circ\text{C, 10 h}]{\text{Pd(OAc)}_2 \text{ (5.0 mol\%)} \\ \text{P(C}_6\text{H}_{11})_3 \text{ (10 mol\%)}} \begin{array}{c} \text{R}-\text{C}(\text{OSi})=\text{CH}-\text{CH}_2-\text{R}' \\ \text{(Z)-}\mathbf{2} \end{array} $				
entry	3	Si	2	Yield (%) ^a
1	 3a	^t BuMe ₂ Si	2k	94 ^b
2	 3b	^t BuMe ₂ Si	2l	77
3	 3c	^t BuMe ₂ Si	2m	71
4	 3d	^t BuMe ₂ Si	2a	65
5	 3e R = MeO ₂ C	^t BuMe ₂ Si	2n	95 ^c
6	 3f	^t BuMe ₂ Si	2o	92
7	 3g	^t BuMe ₂ Si	2p	99
8	 3h	^t BuMe ₂ Si	2q	50 ^d

9		3a	PhMe ₂ Si	2r	99
10		3a	Et ₃ Si	2s	68 ^b
11		3a	ⁱ Pr ₃ Si	2t	N.R.

^a Isolated yields. ^b Z/E = 99/1. ^c Z/E = 96/4. ^d Z/E = 94/6.

In contrast to the reactions of acyclic ketones, the reaction of 2-cyclohexenone with ^tBuMe₂SiH gave silyl enolate **2t** in very low yield, even when the reaction temperature was raised to 80 °C (Scheme 7). Unfortunately, the author obtained only trace amounts of the desired products in the cases of enones which have additional substitutions at the α- and β-position.

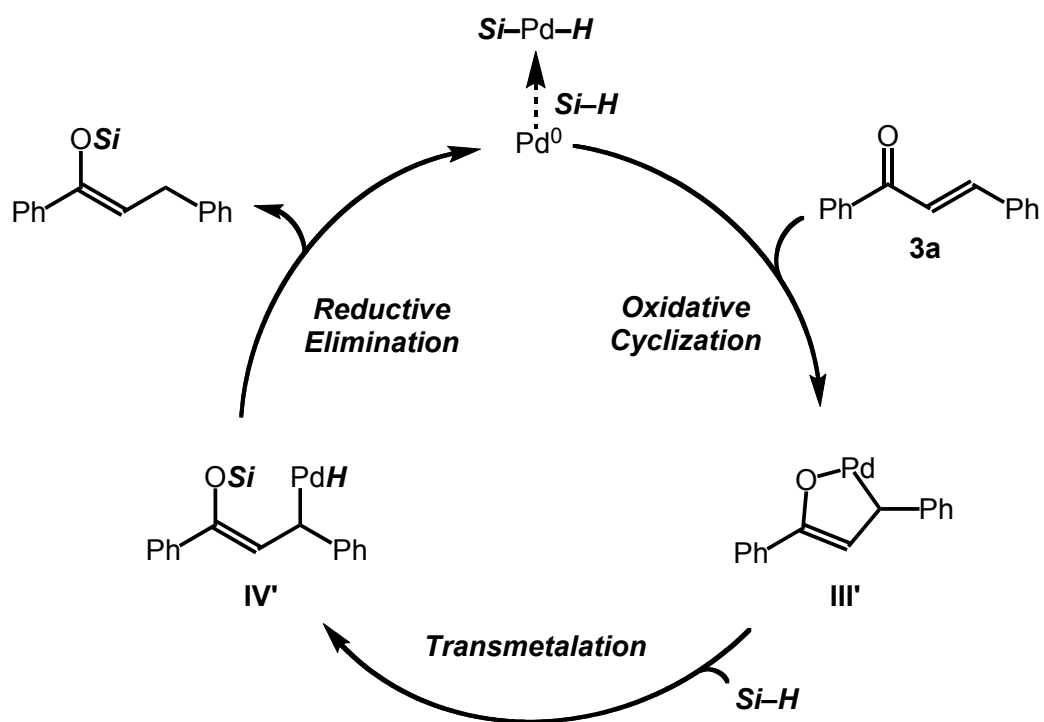
Scheme 7. Reaction of Cyclic α,β-Unsaturated Ketones



On the basis of the study of cyclopropyl ketones and the fact that the reactivities of acyclic enones and cyclohexenone are different, a plausible mechanism is proposed in a manner analogous to the mechanism for cyclopropyl ketone (Scheme 8).

He could not eliminate the pathway which involves oxidative addition of the hydrosilane to palladium(0), 1,4-hydropalladation, and reductive elimination because in the case of cyclic **3i** (Scheme 7) which would be unable to form an oxapalladacycle, a low yield of **2u** was obtained. Consequently, both mechanisms could be in competition in the case of acyclic α,β-unsaturated ketones.

Scheme 8. Plausible Mechanism for Acyclic α,β -Unsaturated Ketones



Experimental Section

Instrumentation and Chemicals

^1H NMR (500 MHz) and ^{13}C NMR (125.7 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and were recorded in CDCl_3 . Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for ^1H and relative to CDCl_3 at 77.0 ppm for ^{13}C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F₂₅₄. Mass spectra (EI unless otherwise noted) were determined on a JEOL Mstation 700 spectrometer. Silica gel 60 N (spherical neutral, obtained from Kanto Kagaku) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Toluene was stored over slices of sodium. Triethylsilane, *tert*-butyldimethylsilane, dimethylphenylsilane, and triisopropylsilane were purchased from Aldrich. Palladium acetate was available from TCI. Tricyclohexylphosphine was obtained from Strem. All reactions were carried out under argon atmosphere.

Typical Procedure for the Palladium-Catalyzed Preparation of Silyl Enolates from α,β -Unsaturated Ketones or Cyclopropyl Ketones with Hydrosilanes

Synthesis of 2a

$\text{Pd}(\text{OAc})_2$ (5.6 mg, 0.025 mmol) and $\text{P}(\text{C}_6\text{H}_{11})_3$ (14 mg, 0.05 mmol) were placed in a 20-mL reaction flask under argon. After toluene (1.5 mL) was added at 0 °C, the resulting solution was stirred for 10 min. Cyclopropyl phenyl ketone (**1a**, 73 mg, 0.50 mmol), $^t\text{BuMe}_2\text{SiH}$ (0.16 mL, 1.0 mmol), and MeOH (50 μL , 0.13 mmol) were then added. The mixture was allowed to warm to 60 °C and stirred for 10 h. The reaction mixture was filtered through a pad of alumina (Wako, activated), and the filtrate was concentrated in vacuo to afford an oil. The crude oil was purified

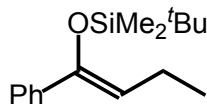
on silica gel (Kanto Chemical, silica gel 60N, hexane) by using a dry ice/acetone-jacketed chromatographic column to yield **2a** (122 mg, 0.47 mmol) in 93% yield.

Synthesis of **2k**

$\text{Pd}(\text{OAc})_2$ (5.6 mg, 0.025 mmol) and $\text{P}(\text{C}_6\text{H}_{11})_3$ (14 mg, 0.05 mmol) were placed in a 20-mL reaction flask under argon. After toluene (1.5 mL) was added at 0 °C, the resulting solution was stirred for 10 min. Chalcone (**3a**, 104 mg, 0.50 mmol) and $t\text{-BuMe}_2\text{SiH}$ (0.16 mL, 1.0 mmol) were then added. The mixture was allowed to warm to 60 °C and stirred for 10 h. The reaction mixture was filtered through a pad of alumina (Wako, activated), and the filtrate was concentrated in vacuo to afford an oil. The crude oil was purified on silica gel (hexane) by using a dry ice/acetone-jacketed chromatographic column to yield **2k** (152 mg, 0.47 mmol) in 94% yield.

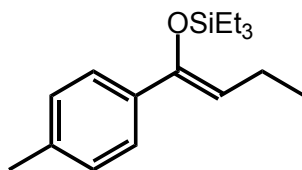
Characterization Data

(*Z*)-1-*tert*-Butyldimethylsiloxy-1-phenyl-1-butene (**2a**)



IR (neat) 2932, 2859, 1680, 1379, 1345, 1295, 1254, 1119, 1050, 1005, 909 cm^{-1} ; ^1H NMR (CDCl_3) δ -0.04 (s, 6H), 0.99 (s, 9H), 1.04 (t, $J = 7.5$ Hz, 3H), 2.23 (dq, $J = 7.5, 7.5$ Hz, 2H), 5.10 (t, $J = 7.5$ Hz, 1H), 7.23 (d, $J = 6.5$ Hz, 1H), 7.29 (dd, $J = 6.5, 7.0$ Hz, 2H), 7.44 (d, $J = 7.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.2, 18.3, 19.5 $\times$ 2, 25.9, 113.8, 125.8, 127.3, 127.9, 139.8, 148.7. Found 262.1754 [M^+]; Calcd for $\text{C}_{16}\text{H}_{26}\text{OSi}$: 262.1753.

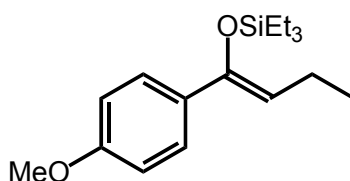
(*Z*)-1-(4-Methylphenyl)-1-triethylsiloxy-1-butene (**2b**)



IR (neat) 2960, 2914, 2877, 1649, 1510, 1458, 1413, 1340, 1278, 876, 813 cm^{-1} ; ^1H NMR

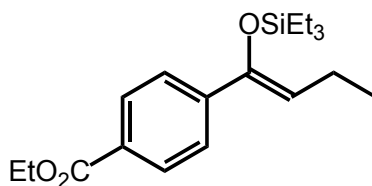
(CDCl₃) δ 0.62 (q, J = 7.5 Hz, 6H), 0.95 (t, J = 7.5 Hz, 9H), 1.04 (t, J = 7.5 Hz, 3H), 2.24 (dq, J = 7.5, 7.5 Hz, 2H), 2.34 (s, 3H), 5.08 (t, J = 7.5 Hz, 1H), 7.10 (d, J = 8.5 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H); ¹³C NMR (CDCl₃) δ 5.3, 6.7, 14.3, 19.4, 21.1, 112.4, 125.4, 128.6, 136.9, 137.0, 148.8. HRMS (EI) Found 276.1906 [M⁺]; Calcd for C₁₇H₂₈OSi: 276.1909.

(Z)-1-(4-Methoxyphenyl)-1-triethylsiloxy-1-butene (2c)



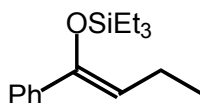
IR (neat) 2836, 1649, 1609, 1459, 1341, 1292, 1174, 909 cm⁻¹; ¹H NMR (CDCl₃) δ 0.61 (q, J = 7.5 Hz, 6H), 0.94 (t, J = 7.5 Hz, 9H), 1.03 (t, J = 7.0 Hz, 3H), 2.22 (dq, J = 7.0, 7.0 Hz, 2H), 3.81 (s, 3H), 5.01 (t, J = 7.0 Hz, 1H), 6.83 (d, J = 9.0 Hz, 2H), 7.38 (d, J = 9.0 Hz, 2H); ¹³C NMR (CDCl₃) δ 5.3, 6.7, 14.3, 19.3, 55.2, 111.7, 113.2, 126.7, 132.4, 148.5, 159.0. HRMS (EI) Found 292.1855 [M⁺]; Calcd for C₁₇H₂₈O₂Si: 292.1859

(Z)-4-(1-Triethylsiloxy-1-butenyl)benzoic acid, ethyl ester (2d)



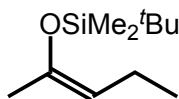
IR (neat) 2878, 1642, 1609, 1459, 1409, 1177, 911, 863, 708 cm⁻¹; ¹H NMR (CDCl₃) δ 0.61 (d, J = 8.0 Hz, 6H), 0.92 (t, J = 8.0 Hz, 9H), 1.05 (t, J = 7.5 Hz, 3H), 1.39 (t, J = 7.0 Hz, 3H), 2.25 (dq, J = 7.5, 7.5 Hz, 2H), 4.37 (q, J = 7.0 Hz, 2H), 5.26 (t, J = 6.5 Hz, 1H), 7.52 (d, J = 8.5 Hz, 2H), 7.97 (d, J = 8.5 Hz, 2H); ¹³C NMR (CDCl₃) δ 5.3, 6.7, 14.1, 14.3, 19.5, 60.9, 115.4, 125.1, 129.1, 129.4, 144.0, 148.1, 166.5. HRMS (EI) Found 334.1958 [M⁺]; Calcd for C₁₉H₃₀O₃Si: 334.1965.

(Z)-1-Phenyl-1-triethylsiloxy-1-butene (2e)



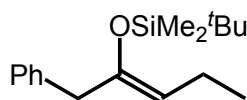
IR (neat) 2960, 2913, 1649, 1341, 1075, 1006, 872, 729 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.62 (q, J = 8.0 Hz, 6H), 0.94 (t, J = 8.0 Hz, 9H), 1.06 (t, J = 7.5 Hz, 3H), 2.25 (dq, J = 7.0, 7.5 Hz, 2H), 5.13 (t, J = 7.0 Hz, 1H), 7.24 (d, J = 7.5 Hz, 1H), 7.30 (dd, J = 6.5, 7.5 Hz, 2H), 7.47 (d, J = 6.5 Hz, 2H); ^{13}C NMR (CDCl_3) δ 5.3, 6.9, 14.2, 19.4, 113.2, 125.5, 127.3, 127.9, 139.7, 148.9. HRMS (EI) Found 262.1754 [M^+]; Calcd for $\text{C}_{16}\text{H}_{26}\text{OSi}$: 262.1753.

(Z)-2-*tert*-Butyldimethylsiloxy-2-pentene (2g)



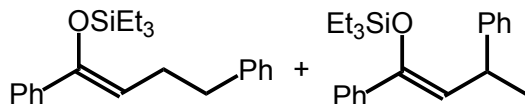
IR (neat) 2931, 2859, 1680, 1379, 1345, 1295, 1253, 1118, 1050, 1005, 909 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.13 (s, 6H), 0.91 (t, J = 8.0 Hz, 3H), 0.95 (s, 9H), 1.76 (s, 3H), 1.97–2.04 (m, 2H), 4.39 (t, J = 8.5 Hz, 1H); ^{13}C NMR (CDCl_3) δ -4.0, 14.4, 18.2, 18.6, 22.7, 25.8, 110.5, 146.1. HRMS (EI) Found 200.1592 [M^+]; Calcd for $\text{C}_{11}\text{H}_{24}\text{OSi}$: 200.1596.

(Z)-2-*tert*-Butyldimethylsiloxy-1-phenyl-2-pentene (2i)



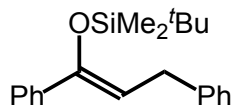
IR (neat) 2857, 1674, 1496, 1362, 1254, 1112, 1074, 1031, 906 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.122 (s, 3H), 0.123 (s, 3H), 0.92 (t, J = 7.5 Hz, 3H), 0.93 (s, 9H), 2.06 (dq, J = 7.0, 7.5 Hz, 2H), 3.35 (s, 2H), 4.34 (t, J = 7.0 Hz, 1H), 7.19–7.24 (m, 3H), 7.28–7.31 (m, 2H); ^{13}C NMR (CDCl_3) δ -3.94, -3.93, 14.4, 18.3, 18.7, 25.8, 42.9, 112.4, 126.1, 128.1, 129.1, 138.6, 148.8. HRMS (EI) Found 276.1908 [M^+]; Calcd for $\text{C}_{17}\text{H}_{28}\text{OSi}$: 276.1910.

(Z)-1,4-Diphenyl-1-triethylsiloxy-1-butene (2j) and (Z)-1,3-Diphenyl-1-triethylsiloxy-1-butene (2j'), (a 94:6 mixture of 2j and 2j')



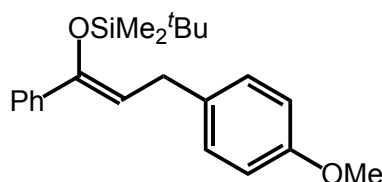
IR (neat) 2877, 2331, 1497, 1447, 1239, 1103, 1075, 1006, 743 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.60 (q, $J = 8.0$ Hz, 6H), 0.93 (t, $J = 8.0$ Hz, 9H), 1.41 (d, $J = 7.0$ Hz, 0.06 $\times$ 3H), 2.56 (dt, $J = 7.5$, 8.5 Hz, 0.94 $\times$ 2H), 2.76 (t, $J = 8.5$ Hz, 0.94 $\times$ 2H), 4.06 (dq, $J = 7.0$, 9.5 Hz, 0.06 $\times$ 1H), 5.17 (t, $J = 7.5$ Hz, 0.94 $\times$ 1H), 5.29 (d, $J = 9.5$ Hz, 0.06 $\times$ 1H), 7.19–7.26 (m, 4H), 7.26–7.33 (m, 4H), 7.45 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR for **2j** (CDCl_3) δ 5.3, 6.7, 27.9, 35.9, 110.3, 125.6, 125.7, 127.5, 127.9, 128.3, 128.4, 139.6, 142.2, 149.9. HRMS (EI) Found 338.2069 [M^+]; Calcd for $\text{C}_{22}\text{H}_{30}\text{OSi}$: 338.2066.

(Z)-1-tert-Butyldimethylsiloxy-1,3-diphenyl-1-propene (2k)



IR (neat) 2930, 2857, 1647, 1493, 1390, 1254, 1006, 939, 668 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.01 (s, 6H), 1.03 (s, 9H), 3.60 (d, $J = 7.5$ Hz, 2H), 5.32 (t, $J = 7.5$ Hz, 1H), 7.20 (t, $J = 6.5$ Hz, 1H), 7.24–7.32 (m, 7H), 7.49 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ -3.9, 18.3, 25.9, 32.3, 110.3, 125.8, 126.0, 127.6, 127.9, 128.3, 128.4, 139.5, 141.6, 150.0. HRMS (EI) Found 324.1911 [M^+]; Calcd for $\text{C}_{21}\text{H}_{28}\text{OSi}$: 324.1909.

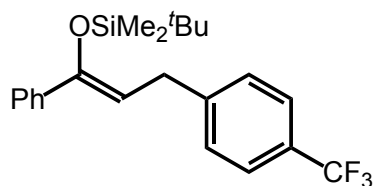
(Z)-1-tert-Butyldimethylsiloxy-3-(4-methoxyphenyl)-1-phenyl-1-propene (2l)



IR (neat) 2930, 2857, 1647, 1512, 1259, 1096, 781 cm^{-1} ; ^1H NMR (CDCl_3) δ -0.01 (s, 6H), 1.02 (s, 9H), 3.53 (d, $J = 7.0$ Hz, 2H), 3.80 (s, 3H), 5.29 (t, $J = 7.0$ Hz, 1H), 6.85 (d, $J = 8.5$ Hz,

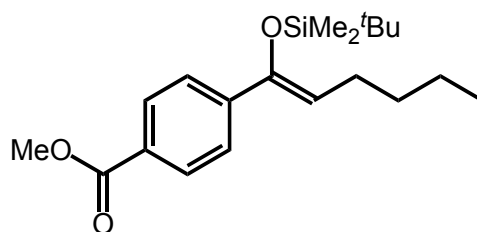
2H), 7.19 (d, $J = 8.5$ Hz, 2H), 7.24–7.31 (m, 3H), 7.49 (d, $J = 7.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ –3.9, 18.4, 25.9, 31.4, 55.3, 110.7, 113.8, 126.0, 127.6, 127.9, 129.3, 133.6, 139.6, 149.8, 157.8. HRMS (EI) Found 354.2015 [M^+]; Calcd for $\text{C}_{22}\text{H}_{30}\text{O}_2\text{Si}$: 354.2015.

(Z)-1-*tert*-Butyldimethylsiloxy-1-phenyl-3-(4-trifluoromethylphenyl)-1-propene (2m)



IR (neat) 2958, 2932, 1648, 1619, 1285, 1164, 1041, 840, 767 cm^{-1} ; ^1H NMR (CDCl_3) δ –0.01 (s, 6H), 1.02 (s, 9H), 3.64 (d, $J = 7.0$ Hz, 2H), 5.27 (t, $J = 7.0$ Hz, 1H), 7.26–7.34 (m, 3H), 7.38 (d, $J = 8.0$ Hz, 2H), 7.49 (d, $J = 7.0$ Hz, 2H), 7.55 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ –3.9, 18.3, 25.9, 32.1, 108.9, 124.4 (q, $J = 270.6$ Hz), 125.3 (q, $J = 1.3$ Hz), 126.1, 127.9, 128.0, 128.2 (q, $J = 32.0$ Hz), 128.7, 139.3, 145.7, 150.9. ^{19}F NMR (CDCl_3) δ 98.8. HRMS (EI) Found 392.1777 [M^+]; Calcd for $\text{C}_{22}\text{H}_{27}\text{OF}_3\text{Si}$: 392.1784.

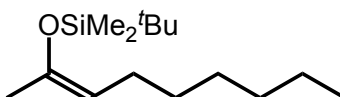
4-(1-*tert*-Butyldimethylsiloxy-1-hexenyl)-benzoic acid, methyl ester (2n, a 96/4 mixture of *Z/E* isomers)



IR (neat) 2931, 2858, 1649, 1463, 1341, 1299, 1258, 1060, 906 cm^{-1} ; ^1H NMR (CDCl_3) δ –0.05 (s, 6H), 0.92 (t, $J = 7.0$ Hz, 3H), 0.98 (s, 9H), 1.33–1.42 (m, 4H), 2.09 (dt, $J = 7.5, 7.5$ Hz, 0.04×2H), 2.22 (dt, $J = 7.5, 7.5$ Hz, 0.96×2H), 3.91 (s, 3H), 5.10 (t, $J = 7.5$ Hz, 0.04×1H), 5.25 (t, $J = 7.5$ Hz, 0.96×1H), 7.45 (d, $J = 9.0$ Hz, 0.04×2H), 7.50 (d, $J = 8.5$ Hz, 0.96×2H), 7.95 (d, $J = 8.5$ Hz, 0.96×2H), 8.00 (d, $J = 9.0$ Hz, 0.04×2H); ^{13}C NMR (CDCl_3) for major isomer δ –4.0,

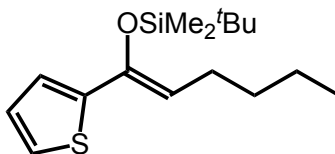
14.0, 18.3, 22.6, 25.8, 26.0, 31.7, 52.0, 114.4, 125.5, 128.8, 129.3, 144.3, 148.3, 167.0. HRMS (EI) Found 348.2128 [M⁺]; Calcd for C₂₀H₃₂O₃Si: 348.2121.

(Z)-2-*tert*-Butyldimethylsiloxy-2-nonene (2o)



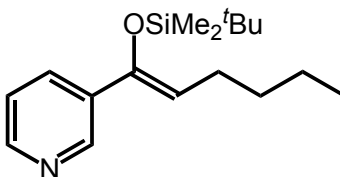
IR (neat) 2929, 2857, 1679, 1463, 1378, 1253, 1004, 940, 809, 778 cm⁻¹; ¹H NMR (CDCl₃) δ 0.13 (s, 6H), 0.88 (t, *J* = 7.0 Hz, 3H), 0.95 (s, 9H), 1.24–1.30 (m, 8H), 1.76 (s, 3H), 1.95–2.01 (m, 2H), 4.40 (t, *J* = 7.5 Hz, 1H); ¹³C NMR (CDCl₃) δ –3.9, 14.1, 18.2, 22.7, 22.8, 25.4, 25.8, 29.2, 29.9, 31.8, 108.8, 146.4. HRMS (EI) Found 256.2231 [M⁺]; Calcd for C₁₅H₃₂OSi: 256.2222.

(Z)-1-*tert*-Butyldimethylsiloxy-1-(2-thienyl)-1-hexene (2p)



IR (neat) 2930, 2858, 1644, 1435, 1340, 1234, 1199, 1005, 977 cm⁻¹; ¹H NMR (CDCl₃) δ 0.078 (s, 3H), 0.079 (s, 3H), 0.93 (t, *J* = 7.0 Hz, 3H), 1.01 (s, 9H), 1.34–1.42 (m, 4H), 2.17 (dt, *J* = 7.0, 7.5 Hz, 2H), 5.17 (t, *J* = 7.0 Hz, 1H), 6.92 (dd, *J* = 3.5, 5.0 Hz, 1H), 7.03 (d, *J* = 3.5 Hz, 1H), 7.11 (d, *J* = 5.0 Hz, 1H); ¹³C NMR (CDCl₃) δ –3.9, 14.0, 18.4, 22.5, 25.8, 25.9, 31.8, 111.8, 123.2, 123.5, 126.8, 143.6, 143.7. HRMS (EI) Found 296.1627 [M⁺]; Calcd for C₁₆H₂₈OSiS: 296.1631.

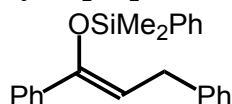
1-*tert*-Butyldimethylsiloxy-1-(3-pyridyl)-1-hexene (2q, a 94/6 mixture of *Z/E* isomers)



IR (neat) 2930, 2858, 1736, 1649, 1567, 1338, 1258, 1005, 875 cm⁻¹; ¹H NMR (CDCl₃) δ –0.05

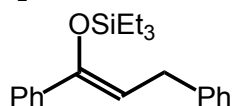
(s, 6H), 0.91 (t, $J = 7.0$ Hz, 3H), 0.97 (s, 9H), 1.33–1.43 (m, 4H), 2.16 (dt, $J = 7.5, 7.5$ Hz, 0.06×2H), 2.20 (dd, $J = 7.0, 7.5$ Hz, 0.94×2H), 5.16 (t, $J = 7.0$ Hz, 0.06×1H), 5.18 (t, $J = 7.0$ Hz, 0.94×1H), 7.16 (dd, $J = 4.5, 7.5$ Hz, 0.06×1H), 7.19 (dd, $J = 5.0, 8.0$ Hz, 0.94×1H), 7.66 (d, $J = 7.5$ Hz, 0.06×1H), 7.70 (d, $J = 8.0$ Hz, 0.94×1H), 8.41 (dd, $J = 1.5, 4.5$ Hz, 0.06×1H), 8.45 (dd, $J = 1.5, 5.0$ Hz, 1H), 8.65 (d, $J = 1.5$ Hz, 0.06×1H), 8.68 (d, $J = 1.5$ Hz, 0.94×1H); ^{13}C NMR (CDCl_3) for major isomer δ –4.0, 13.9, 18.2, 22.5, 25.77, 25.84, 31.7, 113.9, 122.7, 132.9, 135.4, 146.4, 147.2, 148.4. HRMS (EI) Found 291.2021 [M^+]; Calcd for $\text{C}_{17}\text{H}_{29}\text{ONSi}$: 291.2018.

(Z)-1-Dimethylphenylsiloxy-1,3-diphenyl-1-propene (2r)



IR (neat) 3026, 2960, 1647, 1493, 1446, 1253, 1119, 830, 697 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.43 (s, 6H), 3.49 (d, $J = 7.0$ Hz, 2H), 5.42 (t, $J = 7.0$ Hz, 1H), 7.18–7.21 (m, 3H), 7.26–7.31 (m, 5H), 7.37–7.45 (m, 3H), 7.49 (d, $J = 8.5$ Hz, 2H), 7.62 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ –0.9, 32.3, 110.2, 125.7, 125.8, 127.6, 127.7, 127.8, 128.0, 128.3, 128.4, 129.8, 133.4, 138.8, 141.4, 149.6. HRMS (EI) Found 344.1599 [M^+]; Calcd for $\text{C}_{23}\text{H}_{24}\text{OSi}$: 344.1597.

(Z)-1,3-Diphenyl-1-triethylsiloxy-1-propene (2s)



IR (neat) 2956, 2937, 2912, 2877, 1104, 1073, 1006, 731, 697 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.65 (q, $J = 8.0$ Hz, 6H), 0.95 (t, $J = 8.0$ Hz, 9H), 3.60 (d, $J = 7.5$ Hz, 2H), 5.33 (t, $J = 7.5$ Hz, 1H), 7.18–7.21 (m, 1H), 7.24–7.32 (m, 7H), 7.48–7.50 (m, 2H); ^{13}C NMR (CDCl_3) δ 5.4, 6.7, 32.3, 109.7, 125.7, 125.8, 127.6, 128.0, 128.3, 128.4, 139.4, 141.6, 150.2. Found: C, 77.98; H, 8.66%. Calcd for $\text{C}_{21}\text{H}_{28}\text{OSi}$: C, 77.72; H, 8.70%.

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α,β -unsaturated ketone indeed took place although the resulting α,β -unsaturated ketone immediately underwent dimerization in situ as reported previously (ref. 7).

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Chapter 4

Nickel-Catalyzed Arylative Ring Opening of 3-Methylenecycloalkane-1,1-dicarboxylate

The author has developed arylative ring opening reaction of cyclic allylmalonates with arylzinc reagents under nickel catalysis. Upon the ring-opening sp^3C-sp^3C bond cleavage, the allylic moiety serves as an allylic electrophile to react with arylzinc reagents. Simultaneously, the malonate moiety is converted to the corresponding zinc enolate, which can react further with electrophiles. The overall process increases molecular complexity and diversity starting from readily available substrates and will be useful in organic synthesis.

Introduction

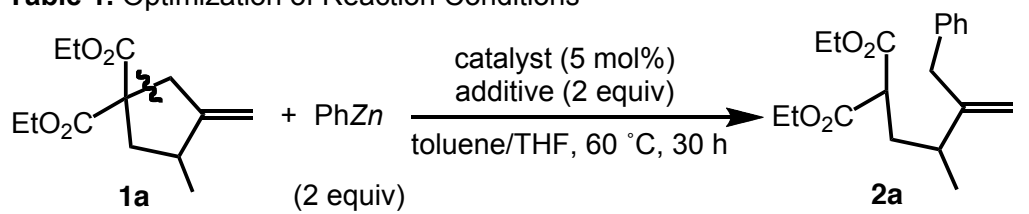
Development of efficient methods for cleavage of C–C bonds catalyzed by transition metal complexes is a new trend and a challenging topic of modern organic chemistry.^{1,2} Having been long pursued, cleavage of unstrained sp^3C – sp^3C bonds is still difficult due to their stability as well as the high directionality of the σ -orbital of an sp^3C – sp^3C bonds. Several noteworthy examples of cleavage of unstrained sp^3C – sp^3C bonds under transition metal catalysis were so far reported. Among them, β -carbon elimination³ and retro-allylation^{1g,4} from metal alkoxides has been well exploited. Another efficient method to cleave sp^3C – sp^3C bonds utilizes highly stabilized carbanions including β -dicarbonyl enolates⁵ and cyclopentadienyl anions⁶ as leaving groups. Transition-metal-catalyzed synproportionation^{5a,b} and deallylation^{5c–f} of allylmalonate derivatives are useful because of the importance of malonate chemistry in organic synthesis. However, the allylic moieties of the malonate derivatives are simply cleaved off^{5c–f} or transferred to another malonate anion^{5a,b} without increasing molecular complexity and diversity. In chapter 4, the author discloses nickel-catalyzed arylative ring opening of cyclic allylmalonate derivatives with arylzinc reagents. The new transformation increases molecular complexity and diversity starting from readily available precursors, utilizing the allylic moieties as allylic electrophiles.

Results and Discussion

Treatment of diethyl 3-methylenecyclopentane-1,1-dicarboxylate (**1a**) with 2 equiv of phenylzinc bromide, which was prepared from zinc bromide and phenyl Grignard reagent in THF, in the presence of 5 mol% of Ni(cod)₂/2PPh₃ in toluene at room temperature afforded a 75% yield of the corresponding product **2a**, and **1a** still remained (Table 1, entry 1). The reaction was completed at 60 °C and gave **2a** in excellent yield (entry 2). Knochel's arylzinc iodide·lithium chloride complex⁷ is easy to prepare from zinc powder and the corresponding aryl iodide in the presence of lithium chloride in THF and allows highly efficient preparation of a broad range of functionalized zinc reagents. Hence, the author applied the phenylzinc iodide·lithium chloride complex to the reaction. However, product **2a** was obtained in only 11% yield (entry 3).

Gratifyingly, addition of magnesium bromide, which was produced in situ in the case of phenylzinc bromide in entries 1 and 2, succeeded in affording the product in 90% yield (entry 4). The author assumes that magnesium bromide promotes the sp^3C-sp^3C bond cleavage by working as a Lewis acid to activate dicarboxylate (vide infra).⁸ Alternatively, it might promote transmetalation between nickel and organozinc complexes.⁹ Divalent nickel complexes, such as $NiBr_2(PPh_3)_2$ and $Ni(acac)_2/2PPh_3$, could serve as well as the expensive zerovalent nickel complex (entries 5 and 6). Other transition metal catalysts were also examined. Low yields of the product were observed when di- or zerovalent palladium complex was used as a catalyst (entries 7 and 8). A cobalt complex failed to catalyze the ring opening reaction (entry 9).

Table 1. Optimization of Reaction Conditions

				
entry	catalyst	PhZn	additive	Yield (%) ^a
1	$Ni(cod)_2/2PPh_3$	$PhZnBr^b$	none	75 ^{c,d}
2	$Ni(cod)_2/2PPh_3$	$PhZnBr^b$	none	96
3	$Ni(cod)_2/2PPh_3$	$PhZnI \cdot LiCl$	none	11 ^d
4	$Ni(cod)_2/2PPh_3$	$PhZnI \cdot LiCl$	$MgBr_2$	90
5	$NiBr_2(PPh_3)_2$	$PhZnI \cdot LiCl$	$MgBr_2$	89
6	$Ni(acac)_2/2PPh_3$	$PhZnI \cdot LiCl$	$MgBr_2$	89
7	$PdCl_2(PPh_3)_2$	$PhZnI \cdot LiCl$	$MgBr_2$	12 ^d
8	$Pd(PPh_3)_4$	$PhZnI \cdot LiCl$	$MgBr_2$	26 ^d
9	$CoCl_2(PPh_3)_2$	$PhZnI \cdot LiCl$	$MgBr_2$	0 ^d

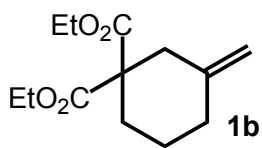
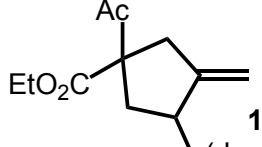
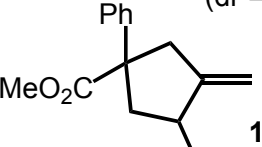
^a Isolated yields. ^b Prepared from $PhMgBr$ and $ZnBr_2$. The ring opening reaction was performed for 8 h. ^c At room temperature. ^d NMR yields.

The arylative ring opening was conducted with a range of methylenecycloalkanes and arylzinc reagents under the optimized conditions (Table 1, entries 2 and 5), and the results are

summarized in Table 2. The reactions of methylenecyclopentane **1a** with 4-methylphenyl- and 4-methoxyphenylzinc reagents occurred to afford the corresponding products in high yields (entries 1 and 2). Although the yield of the reaction with sterically hindered 2-methylphenylzinc iodide·lithium chloride was moderate, high yield was obtained when 2-methylphenylzinc bromide was used (entry 3). The reactions of **1a** with electron-deficient 4-fluorophenyl- and 4-ethoxycarbonylphenylzinc reagents provided the ring opening arylated products in 90% and 59% yields, respectively (entries 4 and 5). An alkenylzinc reagent was also applicable and was converted to the desired product in 66% yield (entry 6). Although the author attempted to alkylate **1a** with benzylzinc bromide, the product was observed in only 28% NMR yield (entry 7). Methylenecyclohexane **1b** also underwent the arylative ring opening smoothly to afford the product in excellent yield (entry 8). Methylenecyclopentane having a β -ketoester part **1c** participated in the reaction with good yield (entry 9). Unfortunately, no reaction occurred when monoester substrate **1d** was used. Thus, the dicarbonyl moieties proved to be essential parts to the reaction.

Table 2. Scope of Methylenecycloalkanes and Organozinc Reagents

entry	1	R'Zn	time (h)	2	Yield (%) ^a
1	 1a	4-MeC ₆ H ₄ ZnI·LiCl	30	2b	82
2	1a	4-MeOC ₆ H ₄ ZnI·LiCl	30	2c	85
3	1a	2-MeC ₆ H ₄ ZnBr ^b	8	2d	93(45 ^c)
4	1a	4-FC ₆ H ₄ ZnI·LiCl	30	2e	90
5	1a	4-EtO ₂ CC ₆ H ₄ ZnI·LiCl	30	2f	59
6	1a	CH ₂ =C(Ph)ZnI·LiCl	30	2g	66

7	1a	PhCH ₂ ZnBr	8	2h	28 ^d
8		PhZnBr ^c	8	2i	95
9	 (dr = 1/1)	PhZnBr ^c	30	2j	78 ^e (dr = 1/1)
10		PhZnBr ^c	8	2k	N.R.

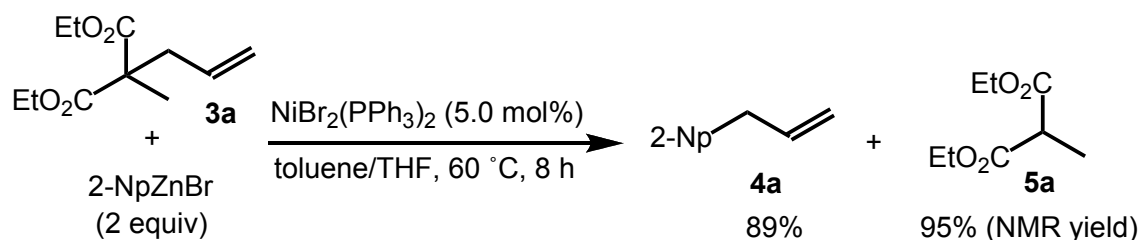
^a Isolated yields. ^b Prepared from ArMgBr and ZnBr₂. No additional MgBr₂ needed.

^c The reaction was performed with 2-MeC₆H₄ZnI•LiCl for 30 h.

^d NMR yields. ^e At room temperature.

The author next proceeded to investigate the reaction of acyclic substrates with an arylzinc reagent under nickel catalysis. The catalytic system is also effective for the reaction of diethyl allyl(methyl)malonate (**3a**) with 2-naphthylzinc bromide to yield 2-allylnaphthalene (**4a**) and diethyl methylmalonate (**5a**) as a byproduct (Scheme 1). This result encouraged him to examine the scope of various acyclic allylmalonate derivatives in the reaction, which is summarized in Table 3.

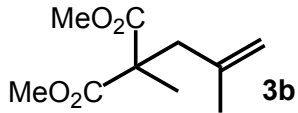
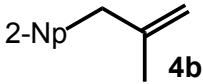
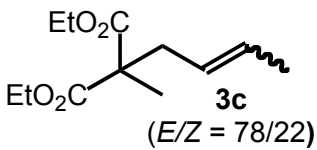
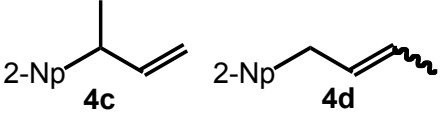
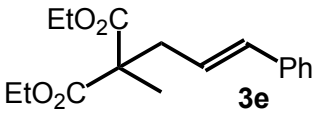
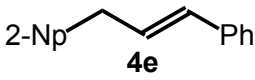
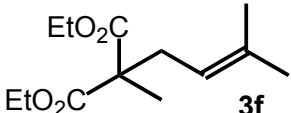
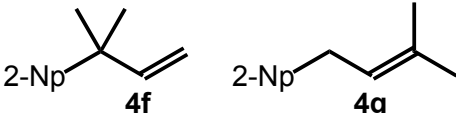
Scheme 1. Reaction of Diethyl Allyl(methyl)malonate with 2-Naphthylzinc Bromide



On treatment of **3b** bearing a methallyl group with 2-naphthylzinc bromide, a high yield of 2-methallylnaphthalene (**4b**) was obtained (Table 3, entry 1). Although the reaction of crotyl-substituted **3c** proceeded successfully, the products were obtained as a mixture of regio- and stereoisomers (entry 2). The lack of regio- and stereoselectivity indicates that the reaction pathway involves a π -allylnickel complex. Meanwhile, **4e** was obtained in quantitative yield as

the sole product when **3e** was used (entry 3). Prenylation of 2-naphthylzinc bromide with **3f** failed due to its steric hindrance (entry 4).

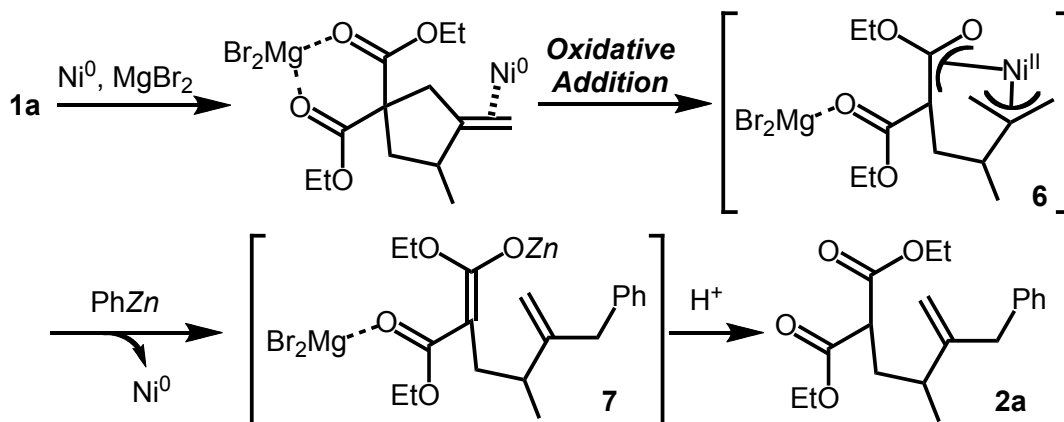
Table 3. Scope of Allylmalonate Derivatives

entry	3	product 4	yield (%) ^a
1			86
2	 (<i>E/Z</i> = 78/22)		88 (4c/4d = 48/52 ^b)
3			quant
4			N.R.

^a Isolated yields. ^b *E/Z* = 71/29.

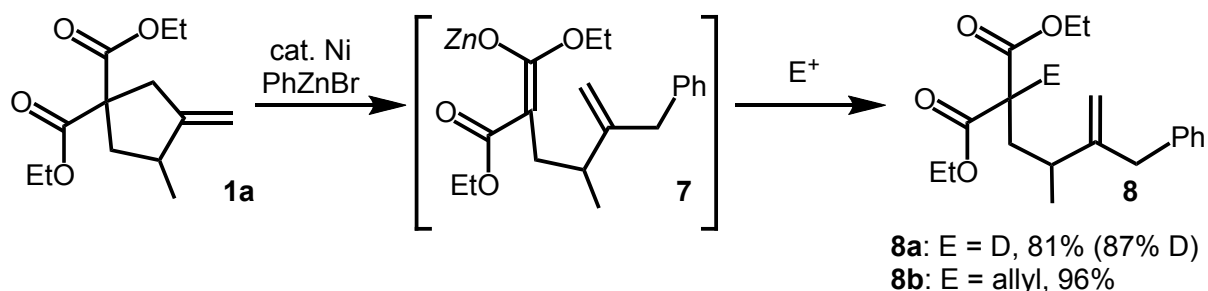
On the basis of these results, the catalytic pathway of the present reaction is proposed as illustrated in Scheme 2. Dicarbonyl compound **1a** coordinates with magnesium bromide. The coordination assists the oxidative addition to zerovalent nickel to cleave the *sp*³C–*sp*³C bond and to form nickel complex **6**. Transmetalation between **6** and phenylzinc reagent followed by reductive elimination¹⁰ gives zinc enolate **7**¹¹ and regenerate the starting nickel complex. Finally, protonolysis of the resulting zinc enolate **7** would provide **2a**.

Scheme 2. Proposed Reaction Mechanism



Intermediate **7** could be trapped with electrophiles (Scheme 3). After finishing the arylative ring opening, treatment of the reaction mixture with $\text{CD}_3\text{CO}_2\text{D}$ gave **8a**. In addition, zinc enolate **7** could be allylated by allyl bromide to yield the corresponding product **8b**.

Scheme 3. Reaction of Zinc Enolate with Electrophiles



Summary

Nickel-catalyzed arylative ring opening reaction of 3-methylenecycloalkane-1,1-dicarboxylate with arylzinc reagents has been developed. The reaction involves nickel-mediated ring-opening $sp^3\text{C}-sp^3\text{C}$ bond cleavage, arylation of allylic moiety, and the formation of the corresponding zinc enolate which is ready for further functionalization.

Experimental Section

Instrumentation and Chemicals

^1H NMR (500 MHz), ^{13}C NMR (125.7 MHz), and ^{19}F NMR (282 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and Mercury 300 spectrometers. Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for ^1H and relative to CDCl_3 at 77.0 ppm for ^{13}C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F₂₅₄. Mass spectra (EI unless otherwise noted) were determined on a JEOL Mstation 700 spectrometer. Silica gel 60 N (spherical neutral, obtained from Kanto Chemical) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Toluene was stored over slices of sodium. Bis(1,5-cyclooctadiene)nickel was available from Strem. $\text{NiBr}_2(\text{PPh}_3)_2$, PPh_3 , zinc powder, and zinc bromide were purchased from Wako Pure Chemical Industries, Ltd. Zinc bromide was stored strictly under argon after drying for 2 h at 170 °C under high vacuum. Magnesium bromide was prepared from ethylmagnesium bromide with allyl bromide and stored under argon.

Typical Procedure for Nickel-Catalyzed Arylative Ring Opening

Reaction of **1a** with Phenylzinc Bromide in the presence of $\text{Ni}(\text{cod})_2/\text{PPh}_3$ (Synthesis of **2a**)

$\text{Ni}(\text{cod})_2$ (6.9 mg, 0.025 mmol) and triphenylphosphine (13 mg, 0.050 mmol) were placed in a 20-mL reaction flask under argon. Toluene (3.0 mL) was added and the resulting suspension was stirred for 10 min at room temperature. Methylene cyclopentane **1a** (120 mg, 0.50 mmol) was then added. To the mixture was added phenylzinc bromide prepared from zinc bromide (230 mg, 1.0 mmol) in dry THF (1.0 mL) and phenylmagnesium bromide (1.0 mL, 1.0 M in THF) at room temperature. The reaction mixture was allowed to warm to 60 °C and stirred for 8 h. The reaction was quenched with saturated NH_4Cl aq. (3.0 mL). Extraction followed by

concentration in vacuo afforded an oil. The crude oil was purified on silica gel (hexane/ethyl acetate = 10/1) to yield **2a** (153 mg, 0.49 mmol) in 96% yield.

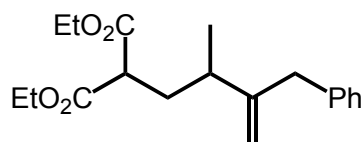
Reaction of **1a** with Phenylzinc iodide•lithium chloride in the presence of $\text{NiBr}_2(\text{PPh}_3)_2$ (Synthesis of **2a**)

To a suspension of $\text{NiBr}_2(\text{PPh}_3)_2$ (19 mg, 0.025 mmol) and methylenecyclopentane **1a** (120 mg, 0.50 mmol) in toluene (3.0 mL), phenylzinc iodide•lithium chloride (1.1 mL, 0.93 M in THF) was added at room temperature under argon. The reaction mixture was allowed to warm to 60 °C and stirred for 30 h. The reaction was quenched with saturated NH_4Cl aq. (3.0 mL). Extraction followed by concentration in vacuo afforded an oil. The crude oil was purified on silica gel (hexane/ethyl acetate = 10/1) to yield **2a** (142 mg, 0.45 mmol) in 89% yield.

Characterization Data

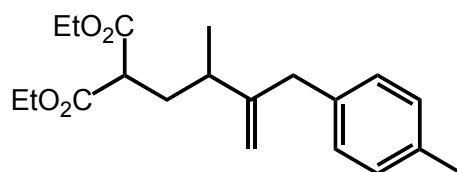
Starting compounds **1a**¹², **1b**¹³, **1c**¹⁴, and **1d**¹² were prepared in conventional ways according to the literature. Products **4a–d**¹⁵ and **4e**¹⁶ are known compounds and showed the identical spectra with those reported in the literature.

Ethyl 2-ethoxycarbonyl-4-methyl-5-methylene-6-phenylhexanoate (**2a**)



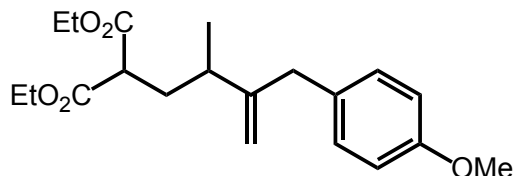
IR (neat) 2978, 1736, 1643, 1450, 1373, 1157, 1034 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.06 (d, J = 7.0 Hz, 3H), 1.24 (d, J = 8.0 Hz, 6H), 1.93–2.08 (m, 1H), 2.02–2.19 (m, 1H), 2.13–2.20 (m, 1H), 3.32 (s, 2H), 3.36 (dd, J = 6.0, 8.5 Hz, 1H), 4.10–4.21 (m, 4H), 4.67–4.68 (m, 1H), 4.86–4.88 (m, 1H), 7.16–7.20 (m, 3H), 7.27 (dd, J = 7.0, 7.8 Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.01, 14.04, 20.1, 34.2, 37.3, 40.6, 50.0, 61.2, 61.3, 111.6, 126.0, 128.2, 124.3, 139.5, 152.2, 169.5, 169.6. Found: C, 71.88; H, 8.09%. Calcd for $\text{C}_{19}\text{H}_{26}\text{O}_4$: C, 71.67; H, 8.23%.

Ethyl 2-ethoxycarbonyl-4-methyl-5-methylene-6-(4-methylphenyl)hexanoate (2b)



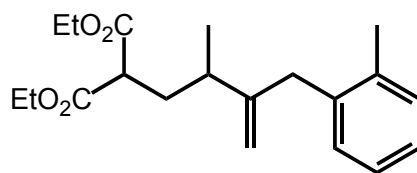
IR (neat) 2978, 1736, 1512, 1450, 1373, 1265, 1157, 1034 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.05 (d, J = 7.0 Hz, 3H), 1.24 (t, J = 7.5 Hz, 3H), 1.25 (t, J = 7.0 Hz, 3H), 1.93–1.98 (m, 1H), 2.02–2.08 (m, 1H), 2.13–2.20 (m, 1H), 2.31 (s, 3H), 3.28 (s, 2H), 3.36 (dd, J = 6.0, 8.5 Hz, 1H), 4.11–4.20 (m, 4H), 4.67–4.69 (m, 1H), 4.84–4.86 (m, 1H), 7.04–7.09 (m, 4H); ^{13}C NMR (CDCl_3) δ 14.01, 14.04, 20.1, 21.0, 34.2, 37.2, 40.2, 50.0, 61.2, 61.3, 111.4, 128.9, 129.2, 135.4, 136.4, 152.3, 169.6, 169.7. Found: C, 72.16; H, 8.62%. Calcd for $\text{C}_{20}\text{H}_{28}\text{O}_4$: C, 72.16; H, 8.49%.

Ethyl 2-ethoxycarbonyl-4-methyl-5-methylene-6-(4-methoxyphenyl)hexanoate (3c)



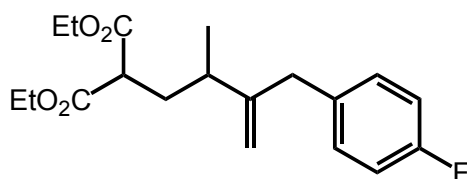
IR (neat) 2981, 2965, 1734, 1371, 1267, 1242, 1176, 1152 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.04 (d, J = 7.0 Hz, 3H), 1.23 (t, J = 7.0 Hz, 3H), 1.25 (t, J = 7.0 Hz, 3H), 1.92–1.98 (m, 1H), 2.01–2.07 (m, 1H), 2.12–2.18 (m, 1H), 3.25 (s, 2H), 3.35 (dd, J = 6.0, 8.5 Hz, 1H), 3.79 (s, 3H), 4.10–4.20 (m, 4H), 4.65–4.67 (m, 1H), 4.84 (brs, 1H), 6.82 (d, J = 8.5 Hz, 2H), 7.08 (d, J = 8.5 Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.02, 14.05, 20.2, 34.2, 37.2, 39.8, 50.0, 55.2, 61.2, 61.3, 111.3, 113.7, 130.2, 131.5, 152.5, 157.9, 169.6, 169.7. Found: C, 69.09; H, 8.14%. Calcd for $\text{C}_{20}\text{H}_{28}\text{O}_5$: C, 68.94; H, 8.10%.

Ethyl 2-ethoxycarbonyl-4-methyl-5-methylene-6-(2-methylphenyl)hexanoate (2d)



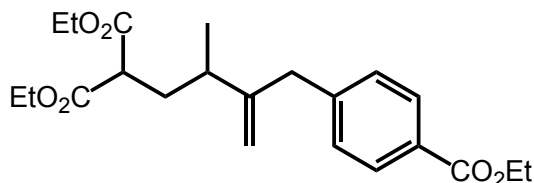
IR (neat) 2978, 1736, 1458, 1373, 1265, 1157, 1034 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.13 (d, $J = 7.5$ Hz, 3H), 1.25 (t, $J = 7.0$ Hz, 3H), 1.27 (t, $J = 6.5$ Hz, 3H), 1.99–2.04 (m, 1H), 2.08–2.14 (m, 1H), 2.22–2.26 (m, 1H), 2.24 (s, 3H), 3.24–3.33 (m, 2H), 3.42 (dd, $J = 6.0, 9.0$ Hz, 1H), 4.14–4.22 (m, 4H), 4.37–4.39 (m, 1H), 4.82 (brs, 1H), 7.08–7.14 (m, 4H); ^{13}C NMR (CDCl_3) δ 14.01, 14.05, 19.2, 20.1, 34.1, 37.5, 38.0, 50.1, 61.2, 61.3, 110.9, 125.8, 126.3, 130.1, 130.4, 136.8, 137.4, 150.9, 169.5, 169.6. Found: C, 72.15; H, 8.67%. Calcd for $\text{C}_{20}\text{H}_{28}\text{O}_4$: C, 72.26; H, 8.49%.

Ethyl 2-ethoxycarbonyl-6-(4-fluorophenyl)-4-methyl-5-methylenehexanoate (2e)



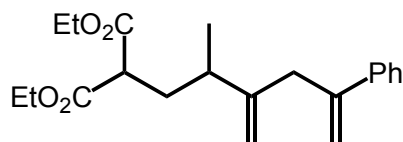
IR (neat) 2978, 1736, 1512, 1458, 1373, 1227, 1157 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.04 (d, $J = 7.0$ Hz, 3H), 1.23 (t, $J = 7.0$ Hz, 3H), 1.24 (t, $J = 7.0$ Hz, 3H), 1.91–1.97 (m, 1H), 2.00–2.06 (m, 1H), 2.09–2.16 (m, 1H), 3.28 (s, 2H), 3.32 (dd, $J = 6.5, 8.5$ Hz, 1H), 4.09–4.19 (m, 4H), 4.65 (brs, 1H), 4.86 (brs, 1H), 6.93–6.97 (m, 2H), 7.10–7.13 (m, 2H); ^{13}C NMR (CDCl_3) δ 13.98, 13.99, 20.1, 34.1, 37.2, 39.8, 50.0, 61.2, 61.3, 111.6, 115.0 (d, $J = 21$ Hz), 130.6 (d, $J = 8.1$ Hz), 135.1 (d, $J = 3.4$ Hz), 152.1, 161.4 (d, $J = 242.5$ Hz), 169.4, 169.6. ^{19}F NMR (CDCl_3) δ 44.0. Found: C, 67.87; H, 7.56%. Calcd for $\text{C}_{19}\text{H}_{25}\text{FO}_4$: C, 67.84; H, 7.49%.

Ethyl 2-ethoxycarbonyl-6-(4-ethoxycarbonylphenyl)-4-methyl-5-methylenehexanoate (2f)



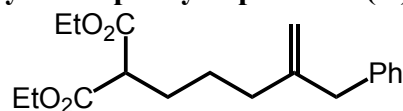
IR (neat) 2978, 1728, 1612, 1458, 1273, 1103 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.05 (d, $J = 7.0$ Hz, 3H), 1.22 (t, $J = 8.0$ Hz, 3H), 1.24 (t, $J = 6.0$ Hz, 3H), 1.38 (t, $J = 7.0$ Hz, 3H), 1.92–1.98 (m, 1H), 2.01–2.06 (m, 1H), 2.11–2.18 (m, 1H), 3.33 (dd, $J = 6.0, 8.5$ Hz, 1H), 3.36 (s, 2H), 4.09–4.21 (m, 4H), 4.36 (q, $J = 7.0$ Hz, 2H), 4.66 (s, 1H), 4.89 (s, 1H), 7.24 (d, $J = 8.5$ Hz, 2H), 7.95 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.00, 14.02, 14.3, 20.1, 34.1, 37.4, 40.5, 50.0, 60.8, 61.29, 61.33, 112.2, 128.4, 129.3, 129.6, 144.9, 151.4, 166.6, 169.5, 169.6. HRMS Found 390.2035 $[\text{M}^+]$; Calcd for $\text{C}_{22}\text{H}_{30}\text{O}_6$: 390.2039.

Ethyl 2-ethoxycarbonyl-4-methyl-5-methylene-7-phenyl-7-octenoate (2g)



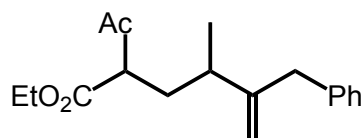
IR (neat) 2978, 1736, 1628, 1450, 1373, 1265, 1157, 1034, 910 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.07 (d, $J = 7.0$ Hz, 3H), 1.25 (t, $J = 7.0$ Hz, 3H), 1.26 (t, $J = 7.0$ Hz, 3H), 1.93–1.98 (m, 1H), 2.03–2.08 (m, 1H), 2.18–2.24 (m, 1H), 3.19–3.21 (m, 2H), 3.32 (dd, $J = 8.5, 9.0$ Hz, 1H), 4.13–4.22 (m, 4H), 4.79–4.82 (m, 1H), 4.83–4.85 (m, 1H), 5.10–5.12 (m, 1H), 5.46–5.48 (m, 1H), 7.22–7.25 (m, 1H), 7.27–7.32 (m, 2H), 7.38–7.42 (m, 2H); ^{13}C NMR (CDCl_3) δ 14.05, 14.07, 19.9, 34.2, 37.6, 39.8, 50.0, 61.26, 61.31, 111.97, 115.1, 126.1, 127.3, 128.2, 140.9, 145.5, 149.9, 169.60, 169.63. Found: C, 73.44; H, 8.00%. Calcd for $\text{C}_{21}\text{H}_{28}\text{O}_4$: C, 73.23; H, 8.19%

Ethyl 2-ethoxycarbonyl-6-methylene-7-phenylheptanoate (2i)



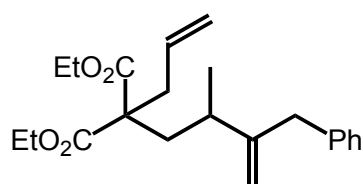
IR (neat) 2932, 1736, 1643, 1450, 1373, 1150, 1026 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.26 (t, $J = 7.0$ Hz, 6H), 1.44–1.51 (m, 2H), 1.84–1.89 (m, 2H), 2.00 (t, $J = 7.5$ Hz, 2H), 3.30 (t, $J = 7.5$ Hz, 1H), 3.32 (s, 2H), 4.15–4.23 (m, 4H), 4.76 (brs, 1H), 4.82 (brs, 1H), 7.16–7.22 (m, 3H), 7.26–7.30 (m, 2H); ^{13}C NMR (CDCl_3) δ 14.1, 25.1, 28.3, 34.8, 42.9, 51.9, 61.3, 111.6, 126.0, 128.3, 128.9, 139.6, 148.0, 169.4. Found: C, 71.67; H, 8.23%. Calcd for $\text{C}_{19}\text{H}_{26}\text{O}_4$: C, 71.84; H, 8.17%

Ethyl 2-acetyl-4-methyl-5-methylene-6-phenylhexanoate (2j, 1:1 mixture of diastereoisomers)



IR (neat) 2963, 1736, 1450, 1366, 1242, 1150, 1026 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.04 (d, $J = 2.5$ Hz, 0.5 $\times$ 3H), 1.06 (d, $J = 2.5$ Hz, 0.5 $\times$ 3H), 1.23 (t, $J = 7.0$ Hz, 0.5 $\times$ 3H), 1.25 (t, $J = 7.0$ Hz, 0.5 $\times$ 3H), 1.92–1.57 (m, 2H), 2.09 (s, 0.5 $\times$ 3H), 2.10 (s, 0.5 $\times$ 3H), 2.03–2.15 (m, 1H), 3.30 (s, 2H), 3.38–3.44 (m, 1H), 4.10–4.19 (m, 2H), 4.69–4.71 (m, 1H), 4.84 (brs, 1H), 7.15–7.21 (m, 3H), 7.26–7.30 (m, 2H); ^{13}C NMR (CDCl_3) δ 14.0, 14.1, 17.7, 17.9, 20.2, 20.5, 33.2, 33.4, 37.1, 37.6, 40.6, 57.3, 57.9, 61.2, 61.3, 111.4, 111.8, 126.09, 126.10, 128.2, 128.29($\times$ 2), 128.3, 129.1, 129.2, 129.3, 139.4, 139.5, 152.1, 152.4, 169.80, 169.82. HRMS (FAB) Found 289.1812 $[\text{M}+\text{H}]^+$; Calcd for $\text{C}_{18}\text{H}_{25}\text{O}_3$: 289.1804.

Ethyl 2-ethoxycarbonyl-4-methyl-5-methylene-6-phenyl-2-(2-propenyl)hexanoate (8b)



IR (neat) 2978, 1728, 1643, 1605, 1450, 1373, 1281, 1219, 1142, 1096 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.98 (d, $J = 7.0$ Hz, 3H), 1.21 (t, $J = 7.0$ Hz, 3H), 1.24 (t, $J = 7.0$ Hz, 3H), 1.96 (dt, $J = 8.0, 8.0$ Hz, 1H), 2.22–2.26 (m, 2H), 2.60–2.68 (m, 1H), 2.69–2.72 (m, 1H), 3.32 (d, $J = 3.5$ Hz, 1H), 3.34 (d, $J = 3.5$ Hz, 1H), 4.03–4.08 (m, 1H), 4.11–4.19 (m, 3H), 4.53–4.55 (m, 1H), 4.87 (brs, 1H), 5.02–5.06 (m, 2H), 5.53–5.62 (m, 1H), 7.16–7.21 (m, 3H), 7.27–7.29 (m, 2H); ^{13}C NMR (CDCl_3) δ 13.96, 14.01, 21.74, 35.0, 36.9, 37.5, 41.0, 56.9, 61.02, 61.09, 110.9, 118.9, 126.0,

128.2, 129.4, 132.6, 139.6, 153.9, 171.2, 171.6. Found: C, 73.45; H, 8.16%. Calcd for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44%.

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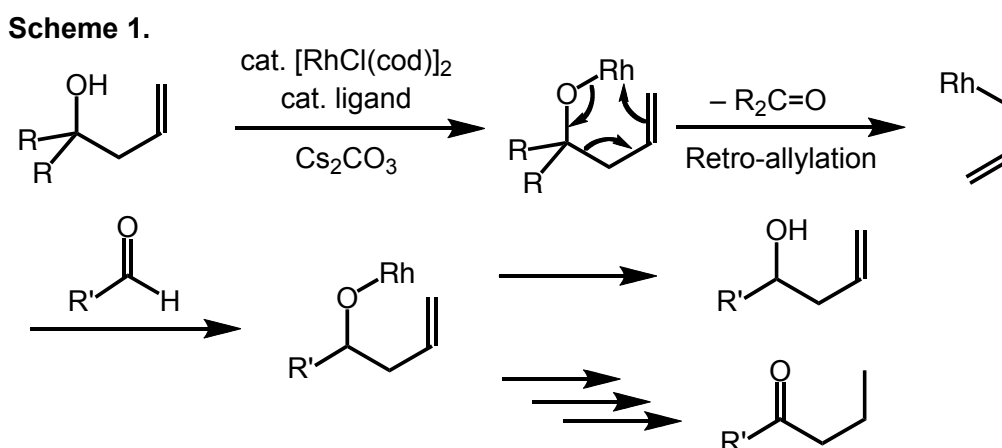
Chapter 5

Rhodium-Catalyzed Allylation of Aldehydes with Homoallyl Alcohols by Retro-Allylation and Isomerization to Saturated Ketones with Conventional or Microwave Heating

Treatment of an aldehyde with a tertiary homoallyl alcohol at 100–250 °C in the presence of cesium carbonate and a rhodium catalyst leads to allyl transfer from the homoallyl alcohol to the aldehyde. The process includes rhodium-mediated retro-allylation to form an allylrhodium species as the key intermediate. The homoallyl alcohol formed initially through the allyl transfer is converted under the reaction conditions into the corresponding saturated ketone when bulky ligands are used. Microwave heating at 250 °C accelerates the reaction significantly.

Introduction

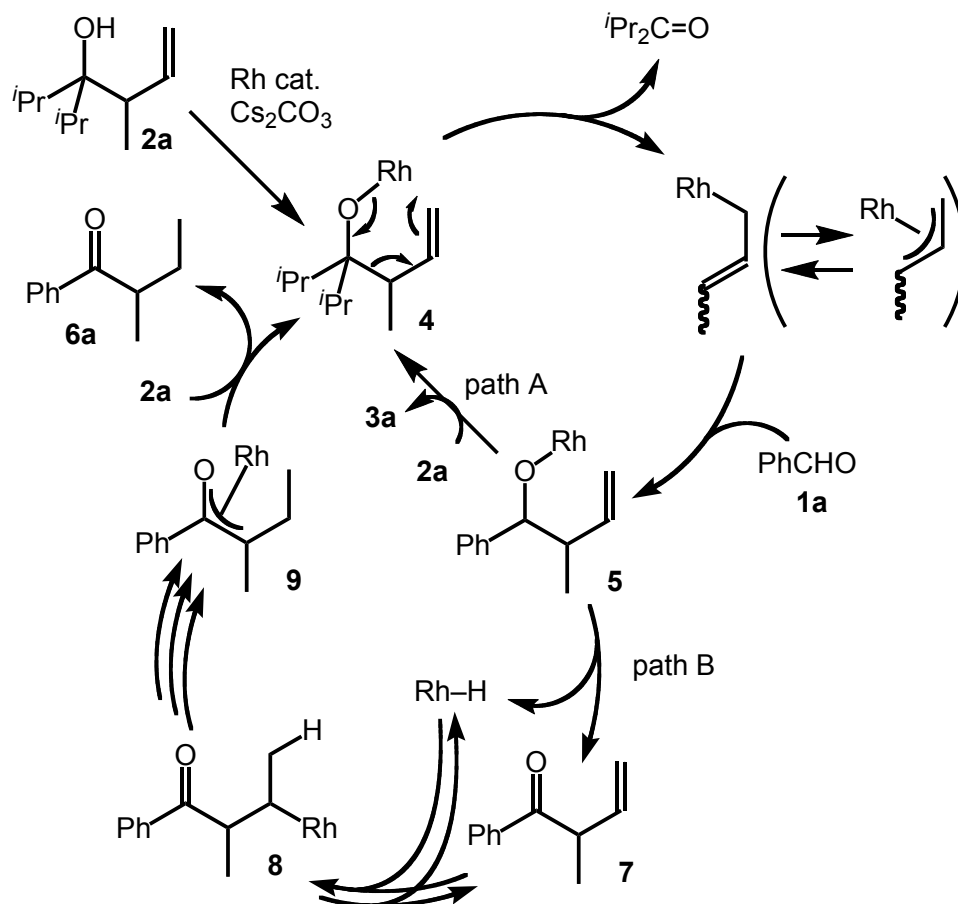
Allylation of carbonyl compounds is among the most important reactions in organic synthesis.¹ Although many allylmatal reagents are used for the allylation, rhodium-mediated carbonyl allylation is quite rare.^{2,3} Recently, the metal-mediated retro-allylation of homoallyl alcohols has been introduced as a useful method for generating allylmatal reagents.⁴ In Chapter 5, the author discloses a method for the generation of allylrhodium reagents from homoallyl alcohols via retro-allylation⁵ and their reaction with carbonyl compounds (Scheme 1).



Results and Discussion

Treatment of benzaldehyde (**1a**, 0.5 mmol) with homoallyl alcohol **2a** (1.0 mmol) in the presence of $[\text{RhCl}(\text{cod})]_2$ (2.5 mol%), PMe_3 (10 mol%), and cesium carbonate (15 mol%) in dioxane (5.0 mL) at reflux for 8 h provided 2-methyl-1-phenyl-3-buten-1-ol (**3a**) in 58% yield (*erythro/threo*⁶ = 49/51, Table 1, entry 1). It is proposed that initial ligand exchange promoted by cesium carbonate between the rhodium catalyst and **2a** provides the intermediate **4** (Scheme 2). The retro-allylation of **4** generates a σ -crotylrhodium species,⁷ which may be in equilibrium with the π -crotylrhodium species under the reaction conditions. The allylrhodium intermediate reacts at the more substituted carbon atom^{2b} with benzaldehyde to yield the rhodium homoallyloxide **5**, which undergoes protonolysis with **2a** to yield **3a** and regenerate **4** (path A).

Scheme 2. Proposed Reaction Mechanism



Moderate to good yields were generally observed for the formation of compounds **3** (Table 1), although the crotylation reaction of electron-rich **1d** gave the product in poorer yield (Table 1, entry 4). The presence of a chloro substituent on the aromatic ring did not prevent the reaction (Table 1, entry 5), and ketone and ester functionalities were compatible with the reaction conditions (Table 1, entries 6 and 7). Unfortunately, no stereoselectivity was observed in any of the reactions.

Table 1. Rhodium-Catalyzed Crotylation of Aromatic Aldehydes with **2a**

entry	Ar	Yield of 3 (%)	<i>erythro</i> / <i>threo</i>
1	Ph (1a)	3a (58)	49/51
2	4-MeC ₆ H ₄ (1b)	3b (49)	54/46
3	4-CF ₃ C ₆ H ₄ (1c)	3c (44)	56/44
4	4-MeOC ₆ H ₄ (1d)	3d (34)	52/48
5	4-ClC ₆ H ₄ (1e)	3e (59)	58/42
6	4-PhCOC ₆ H ₄ (1f)	3f (58)	56/44
7 ^a	4-MeO ₂ CC ₆ H ₄ (1g)	3g (59)	56/44

^a Cs₂CO₃ (30 mol%) was used.

The use of xylene as the solvent and P^tBu₃ as the ligand led to a drastic change in the course of the reaction. Treatment of benzaldehyde (**1a**, 0.5 mmol) with homoallyl alcohol **2a** (1.0 mmol) in the presence of catalytic amounts of [RhCl(cod)]₂, P^tBu₃, and cesium carbonate in xylene at reflux for 24 h provided 2-methyl-1-phenyl-1-butanone (**6a**) in 70% yield (Table 2, entry 1). Both electron-rich (Table 2, entry 4) and electron-deficient aromatic aldehydes (Table 2, entries 3, 6, and 7) were transformed into the corresponding ketones in satisfactory yields.

Table 2. Rhodium-Catalyzed Crotylation of Aromatic Aldehydes with **2a** Followed by Isomerization to Saturated Ketones

entry	Ar	Yield of 6 (%)
1 ^a	Ph (1a)	6a (70) ^b
2	4-MeC ₆ H ₄ (1b)	6b (49)
3 ^c	4-CF ₃ C ₆ H ₄ (1c)	6c (50) ^b
4	4-MeOC ₆ H ₄ (1d)	6d (52) ^b
5	4-ClC ₆ H ₄ (1e)	6e (51) ^b
6	4-PhCOC ₆ H ₄ (1f)	6f (48) ^d
7	4-MeO ₂ CC ₆ H ₄ (1g)	6g (59) ^e

^a Cs₂CO₃ (5 mol%) was used. ^b Yield determined by NMR spectroscopy.

^c The reaction was carried out in toluene at reflux for 24 h.

^d 1-(4-Benzoylphenyl)-1-pentanone was obtained in 3% yield.

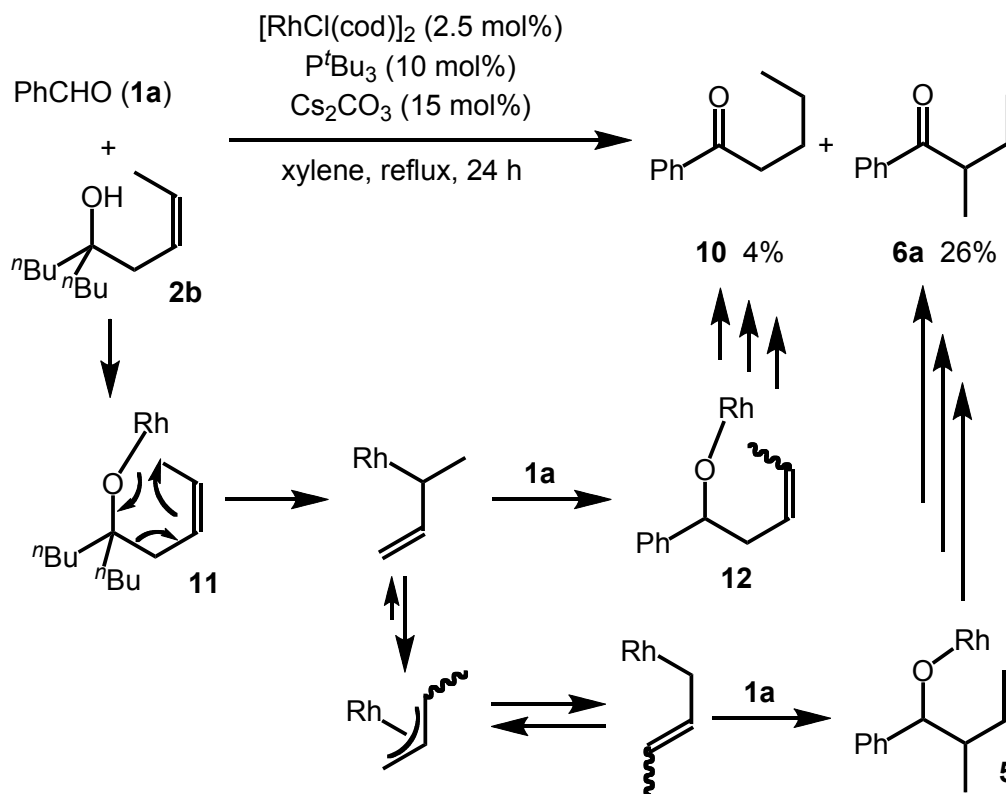
^e 1-(4-Methoxycarbonylphenyl)-1-pentanone was obtained in 3% yield.

The formation of **6a** is rationalized as follows (Scheme 2): Owing to the steric effect of P^tBu₃, the protonolysis of **5** with **2a** (path A) is so slow that β-hydride elimination takes place (path B) to yield **7** with concomitant formation of rhodium hydride. Hydorrhodation of the alkene in **7** then affords **8**, which undergoes iterative β-elimination/hydorrhodation⁸ to yield the oxa-π-allylrhodium intermediate **9**. Protonolysis of **9** with **2a** provides **6a** and **4** to complete the catalytic cycle.

The reaction of homoallyl alcohol **2b** was sluggish and provided **6a** in only 26% yield (Scheme 3). A small amount of **10** was also formed. The formation of **10** was not observed in the reactions in Table 2. These results indicate that the allylrhodium species is formed through a retro-allylation mechanism. The retro-allylation of **11** would yield (1-methyl-2-propenyl)rhodium, some of which would react with **1a** to yield **12** before isomerizing to π- and σ-crotylrhodium. Alkoxide **12** would be converted into **10**. The π- and/or σ-crotylrhodium intermediates would react with **1a** to afford **5** and then **6a**. The

equilibrium between (1-methyl-2-propenyl)rhodium, π -crotylrhodium, and σ -crotylrhodium is probably shifted towards the two crotylrhodium species.

Scheme 3. Plausible Mechanism for the Rhodium-Catalyzed Reaction with **2b**



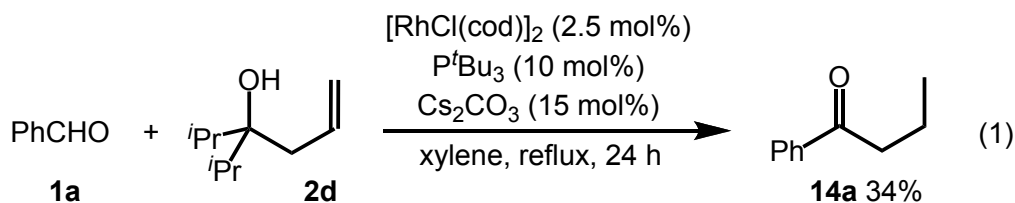
The author studied the sequential methallylation–isomerization of an array of aldehydes with **2c** (Table 3). The generation of methallylrhodium was more facile compared to the formation of crotylrhodium, and products **13** were generally formed in good yields. Both aliphatic and aromatic aldehydes participated in the reaction. Dodecanal (**1h**) was converted into the corresponding saturated ketone **13h** in 70% yield.

Table 3. Rhodium-Catalyzed Methallylation of Aldehydes with **2c** Followed by Isomerization to Saturated Ketones

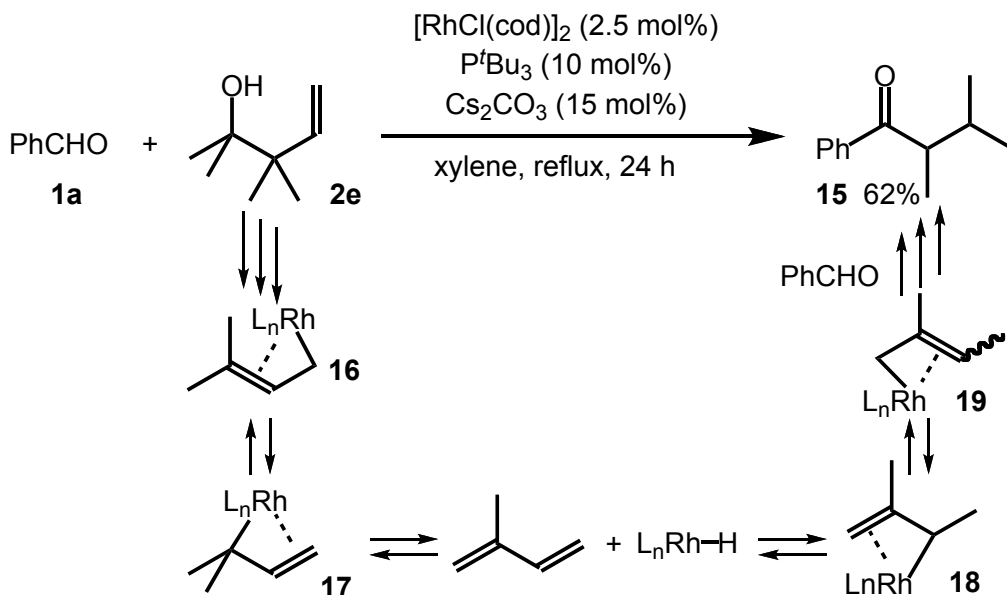
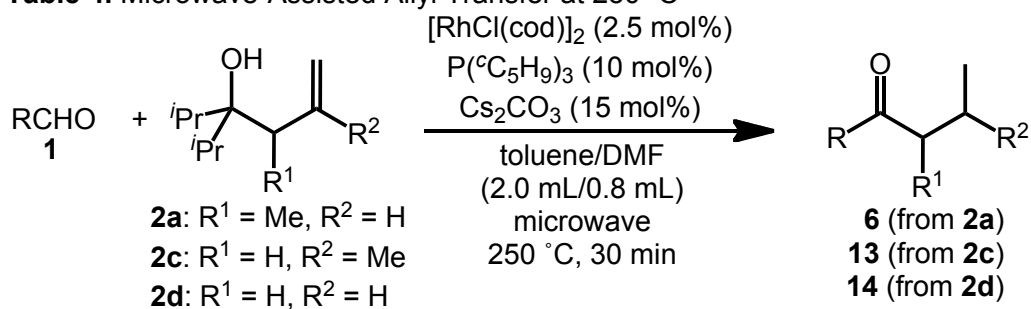
$\text{RCHO} \quad \mathbf{1} + \text{2c} \xrightarrow[\text{xylene, reflux, 24 h}]{\begin{array}{c} [\text{RhCl(cod)}]_2 \text{ (2.5 mol\%)} \\ \text{P}^t\text{Bu}_3 \text{ (10 mol\%)} \\ \text{Cs}_2\text{CO}_3 \text{ (15 mol\%)} \end{array}} \text{13}$		
entry	R	Yield of 13 (%)
1	Ph (1a)	13a (83)
2	4-MeC ₆ H ₄ (1b)	13b (66)
3	4-CF ₃ C ₆ H ₄ (1c)	13c (65)
4	4-MeOC ₆ H ₄ (1d)	13d (77)
5	4-ClC ₆ H ₄ (1e)	13e (54)
6	4-PhCOC ₆ H ₄ (1f)	13f (66)
7	4-MeO ₂ CC ₆ H ₄ (1g)	13g (68)
8	ⁿ C ₁₁ H ₂₃ (1h)	13h (70) ^a

^a NMR yield.

The transfer of the parent allyl group and the prenyl group was also examined. The sequential allylation–isomerization of benzaldehyde (**1a**) with homoallyl alcohol **2d** led to **14a** in low yield (eq 1).



The reaction of **1a** with **2e** provided the unexpected ketone **15** in 62% yield (Scheme 4). The following mechanism is proposed for the formation of **15**: The σ -prenylrhodium intermediate **16** generated by retro-prenylation does not react readily with **1a** as a result of steric repulsion at the highly substituted carbon atom. Accordingly, **16** isomerizes to **17**, from which β -H elimination occurs to give a rhodium hydride and isoprene. Subsequent hydrorhodation of isoprene leads to **18** and **19** and the latter intermediate reacts with **1a** to furnish **15**.

Scheme 4. Attempted Prenylation**Table 4.** Microwave-Assisted Allyl Transfer at 250 °C

entry	R	2	product	yield (%)
1	Ph (1a)	2a	6a	90 ^a
2	4-MeC ₆ H ₄ (1b)	2a	6b	72 ^a
3	4-CF ₃ C ₆ H ₄ (1c)	2a	6c	67 ^a
4	4-MeOC ₆ H ₄ (1d)	2a	6d	87 ^a
5	4-ClC ₆ H ₄ (1e)	2a	6e	55 ^a
6	4-(4-MeC ₆ H ₄ CO)C ₆ H ₄ (1i)	2a	6f	58 ^a
7	4-MeO ₂ CC ₆ H ₄ (1g)	2a	6g	41 ^a
8	ⁿ C ₁₁ H ₂₃ (1h)	2a	6h	64 ^a
9	Ph (1a)	2c	13a	91
10	4-MeC ₆ H ₄ (1b)	2c	13b	86
11	4-CF ₃ C ₆ H ₄ (1c)	2c	13c	64
12	4-MeOC ₆ H ₄ (1d)	2c	13d	74

13	4-ClC ₆ H ₄ (1e)	2c	13e	84
14	4-(4-MeC ₆ H ₄ CO)C ₆ H ₄ (1i)	2c	13i	48
15	4-MeO ₂ CC ₆ H ₄ (1g)	2c	13g	40
16	ⁿ C ₁₁ H ₂₃ (1h)	2c	13h	67
17	^c C ₆ H ₁₁ (1j)	2c	13j	68
18	^t Bu (1k)	2c	13k	<5 ^b
19	Ph (1a)	2d	14a	87
20	4-MeC ₆ H ₄ (1b)	2d	14b	90
21	4-CF ₃ C ₆ H ₄ (1c)	2d	14c	77
22	4-MeOC ₆ H ₄ (1d)	2d	14d	75
23	4-ClC ₆ H ₄ (1e)	2d	14e	68
24	4-(4-MeC ₆ H ₄ CO)C ₆ H ₄ (1i)	2d	14i	66
25	4-MeO ₂ CC ₆ H ₄ (1g)	2d	14g	55
26	ⁿ C ₁₁ H ₂₃ (1h)	2d	14h	58

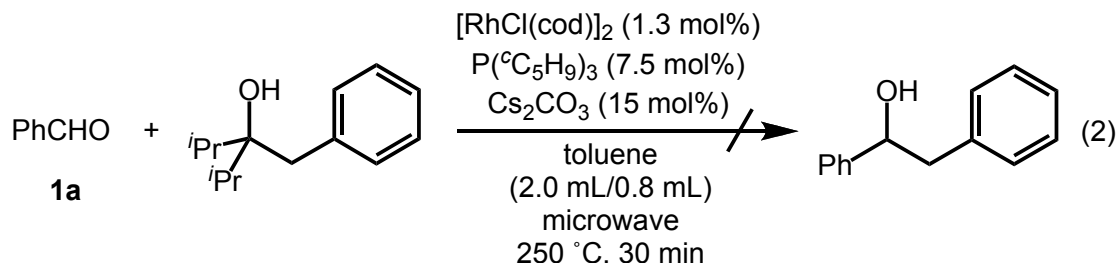
^a The corresponding linear product, RCOⁿBu, was obtained in 3–9% yield.

^b The product is volatile.

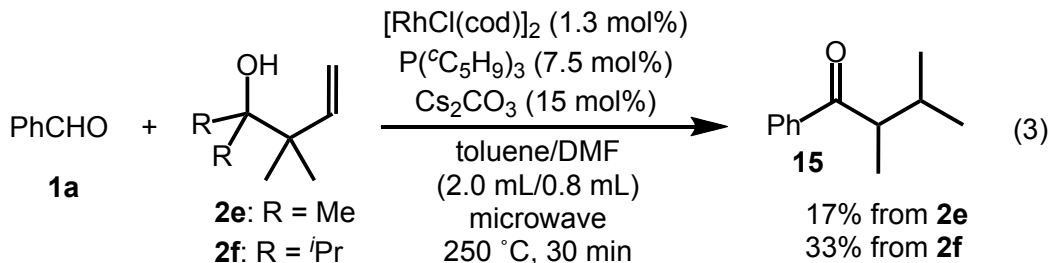
It is well-known that microwave heating accelerates organic reactions.⁹ Such an effect was observed for the allyl transfer reaction (Table 4). Under microwave irradiation, the reactions were complete within 30 min to afford the corresponding ketones in comparable yields to those observed with conventional heating. Tricyclopentylphosphine proved to be the best ligand in the microwave-assisted reactions.

The higher reaction temperature led to poorer regioselectivity (Table 4, entries 1–8). In each case, a small amount of the corresponding linear product, equivalent to **10**, was detected. The linear products were not detected in the reactions in Table 2. The reactions with **2c** were facile (Table 4, entries 9–18). Cyclohexanecarbaldehyde (**1j**) reacted smoothly (Table 4, entry 17); however, the reaction of pivalaldehyde (**1k**) was sluggish (Table 4, entry 18). Allylations with **2d** gave the desired products in good yields under the microwave-assisted conditions (Table 4, entries 19–26), although the equivalent reaction with conventional heating was not efficient (eq 1). Microwave heating at 250 °C may promote the retro-allylation process, which is probably the rate-determining step. The author's

attempts to carry out a benzyl-transfer reaction with derivatives of 2-phenylethanol were unsuccessful (eq 2).



The attempted prenylation of benzaldehyde with **2e** under microwave irradiation also provided **15**, but in only 17% yield. Under these conditions, the isopropyl-substituted homoallylic alcohol **2f** proved to be a better reagent compared to **2e**, and afforded **15** in 33% yield (eq 3). The lower yields observed for the formation of **15** under the conditions of microwave irradiation would result from an increase of side reactions during the transformation of **16** into **19**.



The effect of the ligand on the sequential methallylation–isomerization reaction is summarized in Table 5. Trialkyl phosphine ligands generally gave higher yields of the products compared to triaryl phosphines. It was reported that (π -allyl)bis(triphenylphosphine)rhodium did not react with benzaldehyde at room temperature.¹⁰ In contrast, owing to the strong σ -donor character of trialkyl phosphines, (π -allyl)bis(trialkylphosphine)rhodium complexes could be nucleophilic enough to react with benzaldehyde. However, tri-*tert*-butylphosphine is probably too bulky to promote the reaction (Table 5, entry 4). Bidentate ligands, such as BINAP, were not effective (Table 5, entries 6–8).

c1ccccc1C=O (**1a**) + CC(C)(C)C(C)(C)C(=O)C (**2c**) $\xrightarrow[\text{toluene/DMF (2.0 mL/0.8 mL), microwave, 250 }^\circ\text{C, 30 min}]{\text{[RhCl(cod)]}_2 \text{ (x mol\%), ligand (y mol\%), Cs}_2\text{CO}_3 \text{ (15 mol\%)}}$ CC(C)C(=O)C(=O)c1ccccc1 (**13a**)

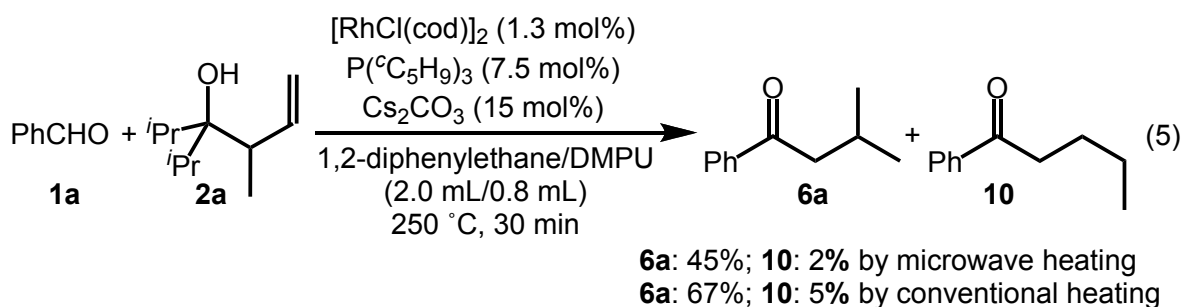
entry	ligand	x	y	Yield (%)
1	P(^c C ₅ H ₉) ₃	1.3	7.5	91
2	PMe ₃	2.5	15	83
3	P(^c C ₆ H ₁₁) ₃	2.5	15	72
4	P ^t Bu ₃	2.5	15	29
5	PPh ₃	1.3	7.5	26
6	BINAP	1.3	4	<1
7	DPPE	1.3	4	21
8	DPPF	1.3	4	9

c1ccccc1C=O (**1a**) + CC(C)(O)CC=C (**2c**) $\xrightarrow[\text{1,2-diphenylethane/DMPU (2.0 mL/0.8 mL), 250 }^\circ\text{C, 30 min}]{\begin{array}{c} [\text{RhCl(cod)}]_2 \text{ (1.3 mol\%)} \\ \text{P}(\text{C}_5\text{H}_9)_3 \text{ (7.5 mol\%)} \\ \text{Cs}_2\text{CO}_3 \text{ (15 mol\%)} \end{array}}$ CC(C)CC(=O)c1ccccc1 (**13a**) (4)

79% by microwave heating
 73% by conventional heating

115

regioselective (Table 4, entries 1–8). To investigate whether the lower regioselectivity was due to a nonthermal microwave effect or to the high temperature, benzaldehyde was treated with **2a** in the presence of the same catalyst system at 250 °C with conventional heating and under microwave irradiation (eq 5). The regioselectivity of the two reactions was similar. Thus, the lower regioselectivity appears to be due to the high temperature.



Conclusion

The author has developed an allyl-transfer reaction of homoallyl alcohols to aldehydes. A retro-allylation reaction is a key process for a carbon–carbon bond cleavage which is catalyzed by rhodium complex. The primary product, homoallyl alcohol could be converted into saturated ketones in one pot, by changing the solvent and phosphine ligand. Microwave heating at 250 °C accelerates the reaction.

Experimental Section

Instrumentation and Chemicals

All microwave-assisted reactions were carried out with a focused microwave unit (Biotage Initiator) with a maximum irradiation power of 400 W. Each reaction was run in a 5-mL glass pressure vial, which is a commercially available special vial for the Biotage Initiator. After the indicated temperature was reached (it took 6 min to reach 250 °C), controlled microwave irradiation was started and was continued for 30 min, during which the temperature of the reaction mixture was kept constant. For classical heating at 250 °C [for the reaction in Equations (4) and (5)], glass ware containing the reaction mixture was heated in a sand bath. ¹H NMR (500 MHz), ¹³C NMR (125.7 MHz), and ¹⁹F NMR (282 MHz) spectra were taken on Varian UNITY INOVA 500 and Mercury 300 spectrometers. Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for ¹H and relative to CDCl₃ at 77.0 ppm for ¹³C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F₂₅₄. Mass spectra (EI unless otherwise noted) were determined on a JEOL Mstation 700 spectrometer. Silica gel (Wakogel 200 mesh) was used for column chromatography. The elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Xylene and dioxane were dried over slices of sodium. Chloro(1,5-cyclooctadiene)rhodium dimer and trimethylphosphine were purchased from Aldrich. P^tBu₃ and tricyclopentylphosphine were obtained from Wako Pure Chemicals and TCI, respectively, and were diluted to 1.0 M in hexane.

Typical Procedure for Crotylation of Aromatic Aldehydes

Synthesis of 3a

[RhCl(cod)]₂ (6 mg, 0.0125 mmol) and Cs₂CO₃ (24 mg, 0.075 mmol) were placed in a

reaction flask. Dioxane (3.0 mL) and PMe_3 (1.0 M in toluene, 0.05 mL, 0.05 mmol) were added dropwise, and the resulting suspension was stirred for 10 min at room temperature. A solution of **2a** (170 mg, 1.0 mmol) in dioxane (2.0 mL) and **1a** (53 mg, 0.5 mmol) were then added, and the mixture was heated at reflux for 8 h. The reaction was then quenched with water (10 mL). Extraction followed by purification provided **3a** (48 mg, 0.29 mmol, 58%, *erythro/threo* = 49/51).

Typical Procedure for Sequential Methallylation of Aldehydes and Isomerization of the Primary Products

Synthesis of **13d**

$[\text{RhCl}(\text{cod})]_2$ (6 mg, 0.0125 mmol) and Cs_2CO_3 (24 mg, 0.075 mmol) were placed in a reaction flask. Dioxane (3.0 mL) and P^tBu_3 (1.0 M in toluene, 0.05 mL, 0.05 mmol) were added dropwise, and the resulting suspension was stirred for 10 min at room temperature. A solution of **2c** (170 mg, 1.0 mmol) in xylene (2.0 mL) and **1d** (69 mg, 0.5 mmol) were then added, and the mixture was heated at reflux for 24 h. The resulting mixture was poured into water (10 mL). Extraction with hexane/ethyl acetate (5/1) followed by purification by silica gel column chromatography afforded **13d** (75 mg, 0.39 mmol, 77% yield).

Typical Procedure for Microwave-Assisted Reaction

Synthesis of **13a**

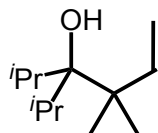
$[\text{RhCl}(\text{cod})]_2$ (3 mg, 0.006 mmol) and Cs_2CO_3 (24 mg, 0.075 mmol) were placed in a 5-mL glass pressure vial. The vial was flushed with argon and sealed with a polytetrafluoroethylene–silicone septum. Toluene (0.5 mL) and $\text{P}(\text{C}_5\text{H}_9)_3$ (1.0 M in hexane, 0.038 mL, 0.038 mmol) were added, and the suspension was stirred for 10 min at room temperature. A solution of **2c** (170 mg, 1.0 mmol) in toluene (1.5 mL), benzaldehyde (**1a**, 53 mg, 0.50 mmol), and DMF (0.80 mL) were added, and the resulting mixture was heated at 250 °C with stirring for 30 min in the microwave reactor. The mixture was then cooled to

room temperature, and the reaction was quenched with water (3 mL). Extraction with hexane/ethyl acetate (10/1) followed by purification by silica gel column chromatography afforded 3-methyl-1-phenyl-1-butanone (**13a**, 74 mg, 0.45 mmol, 91%).

Characterization Data

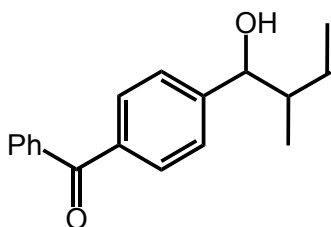
The spectra of compounds **1f**,¹³ **1i**,¹⁴ **2a–e**,¹⁵ **3a**,¹⁶ **3b**,¹⁷ **3c**,¹⁸ **3d**,¹⁹ **3e**,¹⁹ **3g**,¹⁹ **6a**,²⁰ **6b**,²¹ **6d**,¹⁵ **6e**,¹⁵ **13a**,²⁰ **13b**,²¹ **13d**,²² **13e**,²³ **13i**,²⁴ **13j**,²⁵ and **14c**²⁶ were identical to those reported in the literature.

3-Isopropyl-2,4,4-trimethyl-5-hexen-3-ol (**2f**)



IR (neat) 3569, 3082, 1632, 1477, 1383, 1281, 1121, 989; ¹H NMR (CDCl₃) δ 1.08 (d, *J* = 7.0 Hz, 6H), 1.12 (d, *J* = 7.0 Hz, 6H), 1.17 (s, 6H), 2.16 (sept, *J* = 7.0 Hz, 2H), 4.99 (dd, *J* = 11.0, 1.5 Hz, 1H), 5.01 (dd, *J* = 17.5, 1.5 Hz, 1H), 6.22 (dd, *J* = 17.5, 11.0 Hz, 1H); the signal for the OH hydrogen atom was not observed; ¹³C NMR (CDCl₃) δ = 20.7, 21.1, 24.7, 35.6, 47.3, 79.5, 111.7, 148.0. Found: C 78.33, H 13.38. Calcd for C₁₂H₂₄O: C 78.20, H 13.12%.

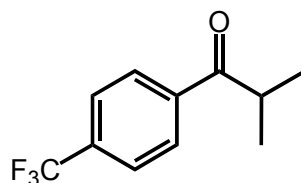
4-(1-Hydroxy-2-methyl-3-butenyl)phenyl phenyl ketone (**3f**) (Mixture of *erythro* and *threo* isomers)



IR (neat) 3446, 2973, 2874, 1645, 1599, 1579, 1448, 1413, 1280, 1178, 1150, 1100, 1001, 924, 844, 749, 702 cm⁻¹; ¹H NMR (CDCl₃) For *erythro* isomer δ 1.02 (d, *J* = 7.0 Hz, 3H), 2.06 (d, *J* = 3.5 Hz, 1H), 2.65 (septet, *J* = 7.0 Hz, 1H), 4.76 (t, *J* = 3.5 Hz, 1H), 5.10–5.15 (m, 2H),

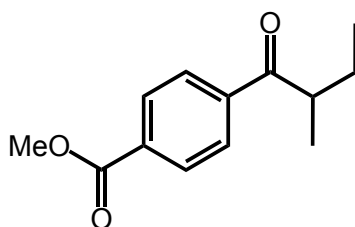
5.77–5.85 (m, 1H), 7.44–7.47 (m, 2H), 7.48–7.52 (m, 2H), 7.61 (tt, $J = 7.0, 1.0$ Hz, 1H), 7.80–7.82 (m, 4H); For *threo* isomer δ 0.95 (d, $J = 7.0$ Hz, 3H), 2.28 (d, $J = 2.5$ Hz, 1H), 2.53 (septet, $J = 7.0$ Hz, 1H), 4.48 (dd, $J = 7.0, 2.5$ Hz, 1H), 5.23–5.26 (m, 2H), 5.77–5.85 (m, 1H), 7.44–7.57 (m, 2H), 7.48–7.52 (m, 2H), 7.61 (tt, $J = 7.0, 1.0$ Hz, 1H), 7.80–7.82 (m, 4H); ^{13}C NMR (CDCl_3) For mixture δ 13.51, 14.12, 16.44, 22.65, 30.95, 31.58, 44.56, 46.41, 76.59, 77.33, 116.23, 117.60, 126.34, 126.74, 128.26, 129.98, 130.01, 130.03, 130.11, 130.33, 132.37, 132.40, 136.54, 136.88, 137.62, 137.65, 139.80, 139.92, 147.05, 147.20, 196.49. Found: C, 81.45; H, 6.88%. Calcd for $\text{C}_{18}\text{H}_{18}\text{O}_2$: C, 81.17; H, 6.81%.

1-(4-Trifluoromethylphenyl)-2-methyl-1-butanone (6c)



IR (neat) 2971, 2937, 2880, 1692, 1463, 1410, 1326, 1268, 1217, 1170, 1132, 1114, 1068, 1017, 974, 857, 592 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.94 (t, $J = 7.5$ Hz, 3H), 1.22 (d, $J = 7.0$ Hz, 3H), 1.48–1.56 (m, 1H), 1.81–1.89 (m, 1H), 3.37–3.44 (m, 1H), 7.75 (d, $J = 8.0$ Hz, 2H), 8.06 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 11.67, 16.49, 26.46, 42.52, 123.62 (q, $J = 272.5$ Hz), 125.68 (q, $J = 3.8$ Hz), 128.53, 134.1 (q, $J = 32.7$ Hz), 139.49, 203.44; ^{19}F NMR (CDCl_3) δ -63.65. Found: C, 62.36; H, 5.39%. Calcd for $\text{C}_{12}\text{H}_{13}\text{F}_3\text{O}$: C, 62.60; H, 5.69%.

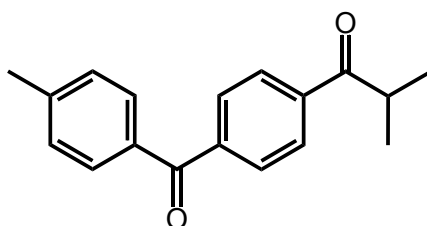
Methyl 4-(2-methyl-1-oxobutyl)benzoate (6g)



IR (neat) 2936, 2877, 1729, 1683, 1572, 1504, 1436, 1407, 1373, 1280, 1215, 1182, 1109,

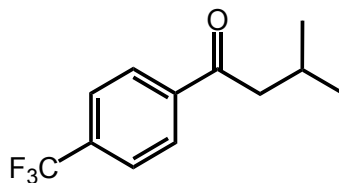
1006, 956, 870, 826, 788, 722 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.93 (t, $J = 7.5$ Hz, 3H), 1.21 (d, $J = 7.0$ Hz, 3H), 1.47–1.55 (m, 1H), 1.80–1.88 (m, 1H), 3.41 (septet, $J = 7.0$ Hz, 1H), 3.96 (s, 3H), 8.00 (dt, $J = 8.5, 2.0$ Hz, 2H), 8.13 (dt, $J = 8.5, 2.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 11.67, 16.52, 26.48, 42.53, 52.44, 128.10, 129.83, 133.55, 140.09, 166.27, 203.98. Found: C, 70.77; H, 7.25%. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3$: C, 70.89; H, 7.32%.

1-[4-(4-Methylbenzoyl)phenyl]-2-methyl-1-butanone (6i)



IR (neat) 2966, 2937, 2876, 1683, 1659, 1404, 1279, 930 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.94 (t, $J = 7.0$ Hz, 3H), 1.22 (d, $J = 6.5$ Hz, 3H), 1.82–1.91 (m, 1H), 2.45 (s, 3H), 3.40–3.47 (m, 2H), 7.30 (dd, $J = 8.5, 1.0$ Hz, 2H), 7.72–7.74 (dm, $J = 8.0$ Hz, 2H), 7.84–7.86 (dm, $J = 8.5$ Hz, 2H), 8.03–8.05 (dm, $J = 8.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 11.95, 16.83, 21.94, 26.79, 42.78, 128.27, 129.40, 130.18, 130.57, 134.52, 139.51, 141.69, 144.13, 195.92, 204.19; Found: C, 81.15; H, 7.19%. Calcd for $\text{C}_{19}\text{H}_{20}\text{O}_2$: C, 81.40; H, 7.19%.

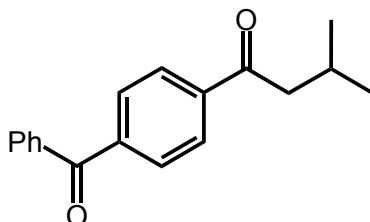
1-(4-Trifluoromethylphenyl)-3-methyl-1-butanone (13c)



IR (neat) 2958, 1684, 1662, 1598, 1448, 1404, 1367, 1277, 1211, 938, 926, 743, 718, 699, 655 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.02 (d, $J = 7.0$ Hz, 6H), 2.27–2.35 (m, 1H), 2.87 (d, $J = 7.0$ Hz, 2H), 7.74 (d, $J = 8.0$ Hz, 2H), 8.06 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 22.69, 25.00, 47.72, 125.63 (q, $J = 3.65$ Hz, 1C), 128.39, 130.23, 134.04, 139.93, 199.19; ^{19}F NMR

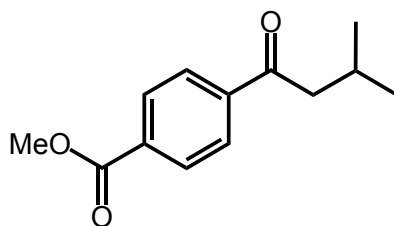
(CDCl₃) δ -63.65. Found: C, 62.85; H, 5.61%. Calcd for C₁₂H₁₃F₃O: C, 62.60; H, 5.69%.

1-(4-Benzoylphenyl)-3-methyl-1-butanone (13f)



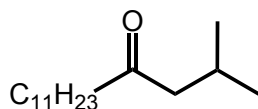
IR (neat) 2958, 1684, 1662, 1598, 1448, 1404, 1367, 1277, 1211, 938, 926, 743, 718, 699, 655 cm⁻¹; ¹H NMR (CDCl₃) δ 1.03 (d, J = 6.5 Hz, 6H), 2.29–2.38 (m, 1H), 2.90 (d, J = 6.5 Hz, 2H), 7.52 (tt, J = 7.5, 1.5 Hz, 2H), 7.64 (tt, J = 7.5, 1.5 Hz, 1H), 7.82 (dt, J = 8.0, 1.5 Hz, 2H), 7.87 (dt, J = 8.0, 1.5 Hz, 2H), 8.06 (dt, J = 8.0, 1.5 Hz, 2H); ¹³C NMR (CDCl₃) δ 22.73, 25.09, 47.82, 127.93, 128.45, 130.04, 130.10, 132.96, 136.91, 139.86, 141.06, 196.03, 199.74. Found: C, 81.05; H, 6.84%. Calcd for C₁₈H₁₈O₂: C, 81.17; H, 6.81%.

Methyl 4-(3-methyl-1-oxobutyl)benzoate (13g)



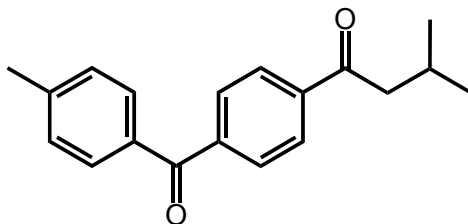
IR (neat) 3674, 2956, 1722, 1683, 1504, 1436, 1407, 1365, 1279, 1198, 1109, 763, 695 cm⁻¹; ¹H NMR (CDCl₃) δ 1.01 (d, J = 6.5 Hz, 6H), 2.27–2.35 (m, 1H), 2.88 (d, J = 7.0 Hz, 2H), 3.96 (s, 3H), 8.01 (d, J = 8.5 Hz, 2H), 8.13 (d, J = 8.5 Hz, 2H); ¹³C NMR (CDCl₃) δ 22.72, 25.01, 47.80, 52.46, 127.97, 129.79, 133.63, 140.54, 166.28, 199.72. Found: C, 71.00; H, 7.53%. Calcd for C₁₃H₁₆O₃: C, 70.89; H, 7.32%.

2-Methyl-4-pentadecanone (13h)



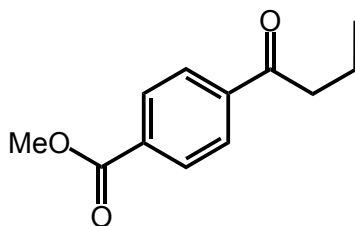
IR (neat) 2927, 2855, 1717, 1468, 1410, 1367, 1287, 1144, 1040, 721 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.89 (t, $J = 7.0$ Hz, 3H), 0.92 (d, $J = 6.5$ Hz, 6H), 1.26–1.31 (m, 16H), 1.55–1.59 (m, 2H), 2.15 (septet, $J = 6.5$ Hz, 1H), 2.28 (d, $J = 7.5$ Hz, 2H), 2.37 (t, $J = 7.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.12, 18.24, 22.60, 22.68, 23.78, 24.59, 29.25, 29.32, 29.42, 29.47, 29.60, 31.90, 43.38, 51.81, 211.39. Found: C, 79.96; H, 13.52%. Calcd for $C_{16}H_{32}O$: C, 79.93; H, 13.41%.

1-[4-(4-Methylbenzoyl)phenyl]-3-methyl-1-butanone (13i)



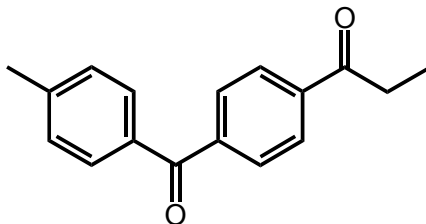
IR (nujol) 2966, 2933, 2876, 1684, 1659, 1607, 1278, 930 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.02 (d, $J = 6.5$ Hz, 6H), 2.32 (triplet of septet, $J = 7.0, 6.5$ Hz, 1H), 2.45 (s, 3H), 2.88 (d, $J = 7.0$ Hz, 2H), 7.30 (d, $J = 8.0$ Hz, 2H), 7.72 (d, $J = 8.0$ Hz, 2H), 7.83 (d, $J = 8.5$ Hz, 2H), 8.03 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 21.69, 22.73, 25.10, 47.81, 127.88, 129.15, 129.89, 130.32, 134.27, 139.71, 141.51, 143.90, 195.71, 199.74. Found: C, 81.24; H, 7.31%. Calcd for $C_{19}H_{20}O_3$: C, 81.40; H, 7.19%. m.p.: 63 $^{\circ}\text{C}$.

Methyl 4-(1-oxobutyl)benzoate (14g)



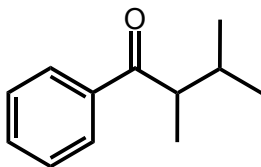
IR (nujol) 2924, 2854, 1722, 1675, 1456, 1285, 1112, 745 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.01 (t, $J = 7.5$ Hz, 3H), 1.78 (tq, $J = 7.5, 7.0$ Hz, 2H), 2.97 (t, $J = 7.0$ Hz, 2H), 3.98 (s, 3H), 8.00 (dt, $J = 8.5, 2.0$ Hz, 2H), 8.11 (dt, $J = 8.5, 2.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.05, 17.82, 41.10, 52.68, 128.17, 130.05, 133.93, 140.55, 166.52, 200.11; Found: C, 69.64; H, 6.80%. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_3$: C, 69.89; H, 6.84%. m.p.: 84 °C.

1-[4-(4-Methylbenzoyl)phenyl]-1-butanone (14i)



IR (nujol) 2966, 2933, 2876, 1684, 1659, 1607, 1313, 1278, 1216, 930 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.03 (t, $J = 7.5$ Hz, 3H), 1.80 (tq, $J = 7.5, 7.5$ Hz, 2H), 2.43 (s, 3H), 3.00 (t, $J = 7.5$ Hz, 2H), 7.29 (d, $J = 8.0$ Hz, 2H), 7.71 (d, $J = 8.0$ Hz, 2H), 7.84 (d, $J = 8.0$ Hz, 2H), 8.05 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 13.83, 17.64, 21.69, 40.85, 127.82, 129.15, 129.89, 130.32, 134.28, 139.43, 141.52, 143.90, 195.71, 199.89. Found: C, 81.17; H, 6.81%. Calcd for $\text{C}_{18}\text{H}_{18}\text{O}_2$: C, 81.18; H, 6.91%. m.p.: 66 °C.

2,3-Dimethyl-1-phenyl-1-butanone (15)



IR (neat) 2963, 2934, 2875, 1683, 1448, 1217, 969 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.89 (d, $J = 7.0$ Hz, 3H), 0.94 (d, $J = 7.0$ Hz, 3H), 1.13 (d, $J = 7.0$ Hz, 3H), 2.09 (doublet of septet, $J = 7.0$, 7.0 Hz, 1H), 3.28 (dq, $J = 7.0$, 7.0 Hz, 1H), 7.44–7.47 (m, 2H), 7.53–7.56 (m, 1H), 7.93–7.95 (m, 2H); ^{13}C NMR (CDCl_3) δ 13.62, 18.86, 21.83, 30.93, 47.10, 128.44, 128.82, 132.97, 137.55, 205.06. Found: C, 81.89; H, 9.17%. Calcd for $\text{C}_{12}\text{H}_{16}\text{O}$: C, 81.77; H, 9.15%.

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Chapter 6

Nickel-Catalyzed Allylation of Allyl Carbonates with Homoallyl Alcohols via Retro-Allylation Providing 1,5-Hexadienes

A highly efficient and mild method for the synthesis of 1,5-hexadienes, nickel-catalyzed reactions of Boc-protected allyl alcohols with homoallyl alcohols, has been developed. Nickel-mediated retro-allylation allows for the use of homoallyl alcohols as allylmetal equivalents in the synthesis of 1,5-hexadienes.

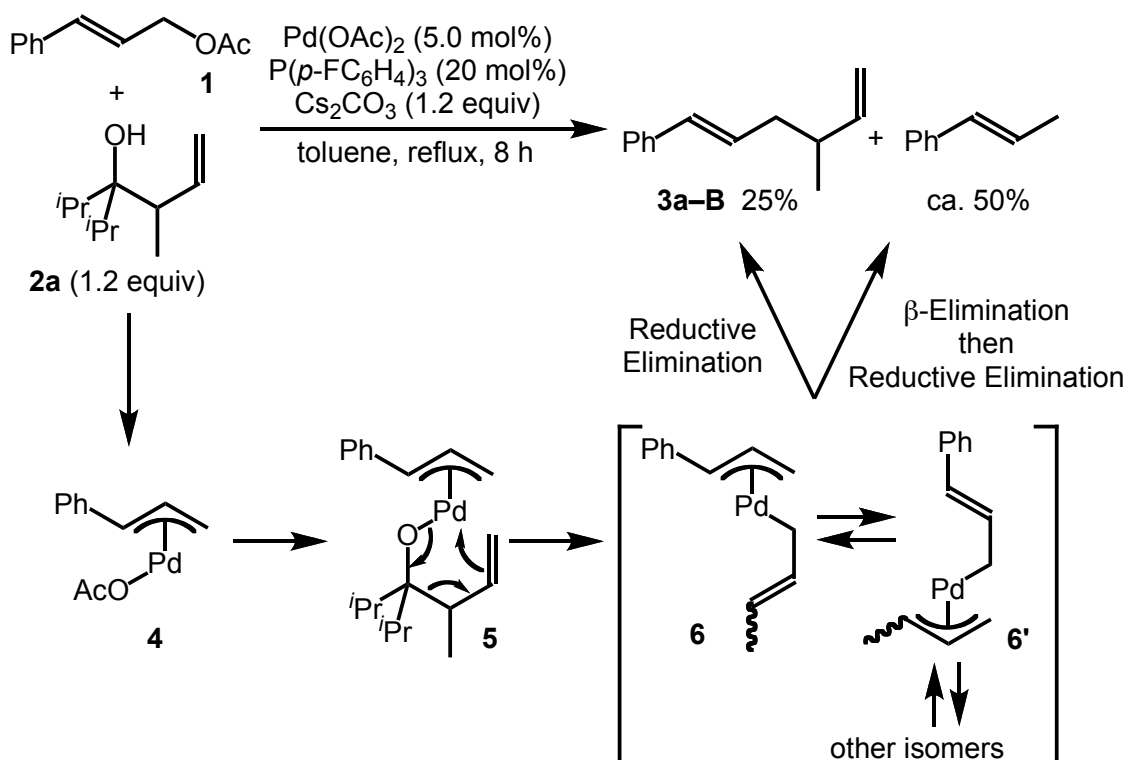
Introduction

Palladium-catalyzed cross-coupling reactions of allyl electrophiles with allylmetals are potentially useful for the synthesis of 1,5-hexadienes.¹⁻⁵ Despite its seeming simplicity, the reactions usually suffer from low yields because of β -hydride elimination from (substituted-allyl)palladium intermediates such as crotylpalladium⁶ and concomitant formation of undesired homo-coupling products.⁷ In most cases, allylstannanes were used as the allylmetal, which required a troublesome purification procedure.³ Thus, efficient methods for the synthesis of 1,5-hexadienes from allylmetals and allyl electrophiles are rare and should be developed.

Results and Discussion

Palladium-catalyzed allylation reactions of aryl halides with homoallyl alcohols as allylmetal equivalents by taking advantage of palladium-mediated retro-allylation have been recently reported.^{8,9} Pursuing a new efficient method for the synthesis of 1,5-hexadienes, the author attempted to apply the retro-allylation-based methodology to the palladium-catalyzed reaction of cinnamyl acetate (**1**) with homoallyl alcohol (**2a**) (Scheme 1). However, the reaction was unsatisfactory, highlighting the difficulty in achieving efficient synthesis of 1,5-hexadienes: branched-coupling product **3a-B** was obtained in only 25% yield, and β -methylstyrene was mainly formed. The formation of β -methylstyrene would result from predominant β -hydride elimination from intermediate **6'** or other isomers⁶ over productive reductive elimination from **6**. Many attempts to find suitable reaction conditions for the palladium-catalyzed allylation reaction of **1** with **2a** failed.

Scheme 1. Palladium-Catalyzed Allylation of Cinnamyl Acetate (**1**) with Homoallyl Alcohol **2a**



He then turned his attention to nickel catalysis, although little is known about the nickel-catalyzed cross-coupling reaction of allylmetals with allyl electrophiles¹⁰ and no information about nickel-mediated retro-allylation was reported. After screening reaction conditions, a combination of 5 mol% of $\text{Ni}(\text{cod})_2$ and 10 mol% of triethyl phosphite proved to catalyze the allylation reaction of Boc-protected cinnamyl alcohol **7a** (Boc = *t*-butoxycarbonyl) with **2a** in the absence of base in refluxing toluene (Table 1, entry 1). The reaction afforded the corresponding coupling products **3a-B** and **3a-L** in high yield in a ratio of **3a-B**/**3a-L** = 37/63. Unfortunately, the ligand effect on the isomer ratio was almost negligible as far as he examined.

Electronic as well as steric factors of the aryl groups of **7** had little influence on this allylation reaction (Table 1, entries 2–4). Replacement of the methyl group in **2a** ($\text{R}^2 = \text{Me}$) with a heptyl group ($\text{R}^2 = \text{C}_7\text{H}_{15}$) slightly improved the regioselectivity (entry 5). Cyclohexyl-substituted homoallyl alcohol **2c** reacted with **7a** to yield the corresponding 1,5-hexadiene in a higher branched/linear ratio of 9/91 (entry 6). The highest branched/linear ratio was observed in the

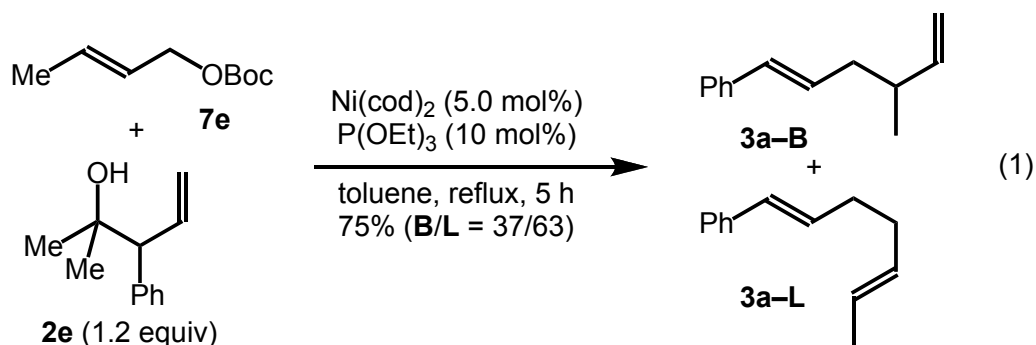
reaction of **7a** with *tert*-butyl-substituted homoallyl alcohol **2d** (3/97, entry 7).

Table 1. Nickel-Catalyzed Allylation of Boc-Protected Cinnamyl Alcohols **7** with Branched Homoallyl Alcohols **2**

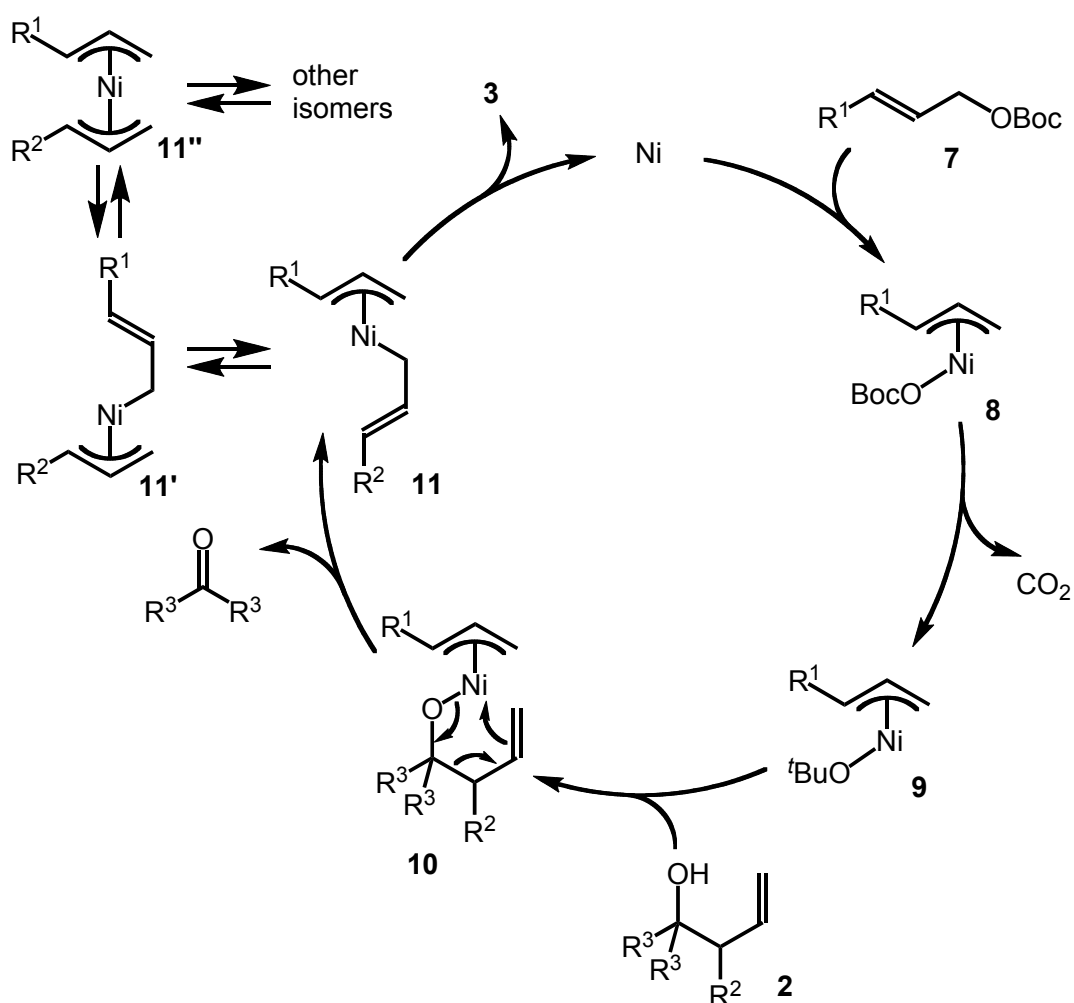
Reaction scheme: Boc-protected cinnamyl alcohol **7** (R¹-CH=CH-CH₂-OBoc) reacts with branched homoallyl alcohol **2** (R²-CH(R³)-CH₂-CH=CH₂) in the presence of Ni(cod)₂ (5.0 mol%) and P(OEt)₃ (10 mol%) in toluene at reflux for 5 h to yield a mixture of branched (**3-B**) and linear (**3-L**) allylated products.

entry	R ¹	7	R ²	R ³	2	3	Yield (%)	B/L
1	Ph	7a	Me	<i>i</i> Pr	2a	3a	91	37/63
2	4-MeOC ₆ H ₄	7b	Me	<i>i</i> Pr	2a	3b	70	40/60
3	4-CF ₃ C ₆ H ₄	7c	Me	<i>i</i> Pr	2a	3c	78	33/67
4	2-MeC ₆ H ₄	7d	Me	<i>i</i> Pr	2a	3d	86	37/63
5	Ph	7a	ⁿ C ₇ H ₁₅	Me	2b	3e	60	26/74
6	Ph	7a	^c C ₆ H ₁₁	Me	2c	3f	77	9/91
7	Ph	7a	^t Bu	Me	2d	3g	79	3/97

It is worth noting that the reaction of Boc-protected crotyl alcohol **7e** with phenyl-substituted alcohol **2e** (eq 1) yielded **3a** in the same branched/linear ratio as the ratio shown in entry 1 of Table 1. The same branched/linear ratio strongly suggests that the reactions proceed via the same diallylnickel intermediate. Based on this fact, a plausible mechanism is proposed in Scheme 2. Oxidative addition of **7** to a nickel catalyst followed by decarboxylation would afford alkoxy(π -allyl)nickel intermediate **9**. Ligand exchange with **2** would yield **10**. Retro-allylation¹¹ would then take place to afford **11** with concomitant formation of ketone R³C=O. Here the configurations and modes of coordination of the allyl ligands R¹CHCHCH₂ and R²CHCHCH₂ would be completely scrambled to yield a mixture of several diallylnickel intermediates such as **11**, **11'**, and **11''**. Reductive elimination prior to β -hydride elimination would afford product **3** and regenerate the initial zero valent nickel catalyst.



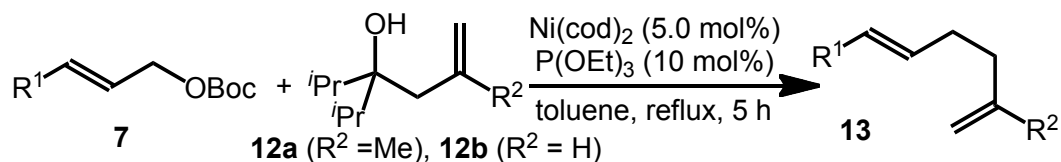
Scheme 2. Plausible Reaction Mechanism



Methallylation of various Boc-protected allyl alcohols **7** proceeded smoothly by using **12a** (Table 2, entries 1–8). Furyl- and thienyl-substituted **7g** and **7h** also participated in the reaction. Interestingly, the reaction of **7i** having a methyldiphenylsilyl group with **12a** afforded 5-methyl-1,5-hexadienylsilane **13h** as the sole product in high yield. Allylation with **12b** also

proceeded smoothly (entries 9–15), although a higher temperature was necessary to attain high yields in some cases (entries 10, 11, and 15).

Table 2. Nickel-Catalyzed Allylation of Boc-Protected Cinnamyl Alcohols **7** with Homoallyl Alcohols **12a** and **12b**



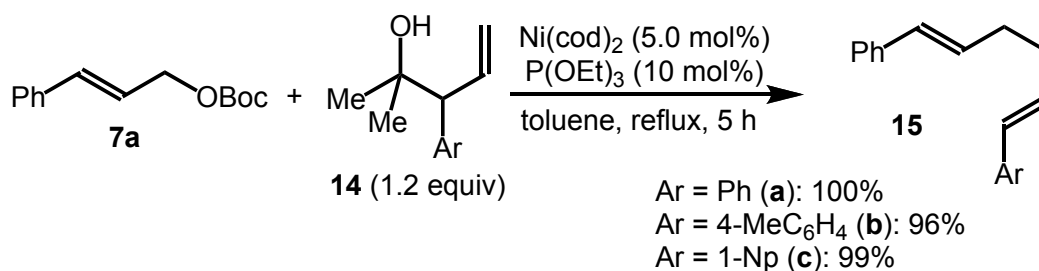
entry	R ¹	7	12	13	Yield (%)
1	Ph	7a	12a	13a	99
2	4-MeOC ₆ H ₄	7b	12a	13b	71
3	4-CF ₃ C ₆ H ₄	7c	12a	13c	94
4	2-MeC ₆ H ₄	7d	12a	13d	84
5	4-MeC ₆ H ₄	7f	12a	13e	100
6	2-furyl	7g	12a	13f	76
7	2-thienyl	7h	12a	13g	76
8	MePh ₂ Si	7i	12a	13h	82
9	Ph	7a	12b	13i	96
10	4-MeOC ₆ H ₄	7b	12b	13j	81 ^a
11	4-CF ₃ C ₆ H ₄	7c	12b	13k	80 ^a
12	2-MeC ₆ H ₄	7d	12b	13l	84
13	4-MeC ₆ H ₄	7f	12b	13m	88
14	2-thienyl	7h	12b	13n	62
15	MePh ₂ Si	7i	12b	13o	89 ^a

^a Xylene was used instead of toluene.

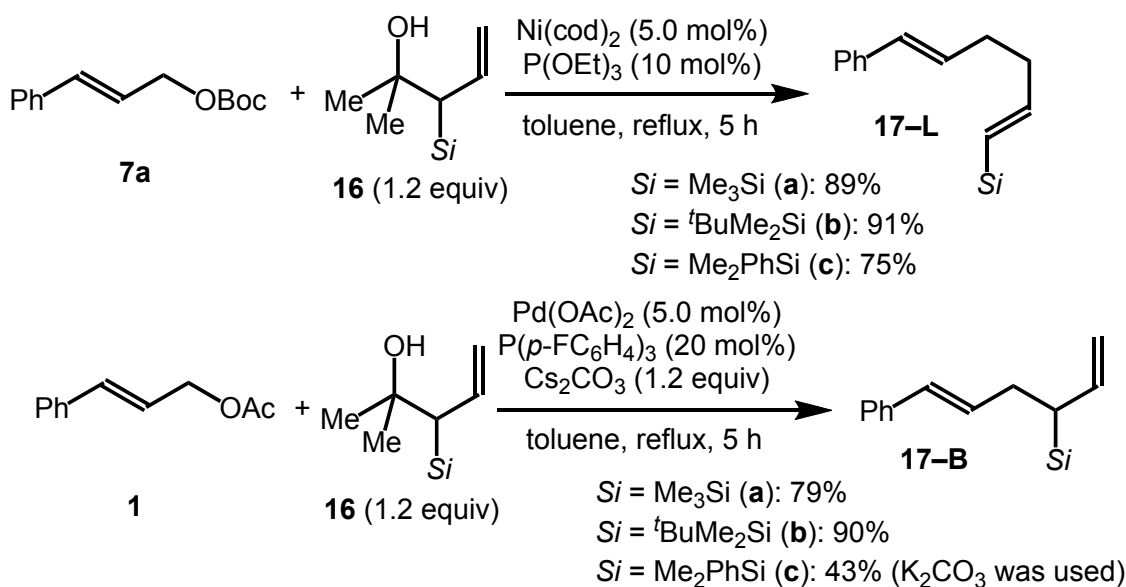
The reactions of **7a** with aryl-substituted homoallyl alcohols **14** afforded the corresponding cross-coupling products 1,6-diaryl-1,5-hexadienes **15** exclusively in excellent yields (Scheme 3). None of the homo-coupling products were observed in the reactions that yielded **15b** and **15c**.

The nickel-catalyzed reactions of **7a** with silyl-substituted homoallyl alcohols **16** yielded the corresponding linear cross-coupling products **17–L** in high yields (Scheme 4). Interestingly, the sense of the regioselectivity was opposite when a palladium catalyst was used. The palladium-catalyzed reactions of **1** with **16** afforded branched allylsilanes **17–B** exclusively.

Scheme 3. Synthesis of 1,6-Diaryl-1,5-hexadienes (**14a** = **2e**)

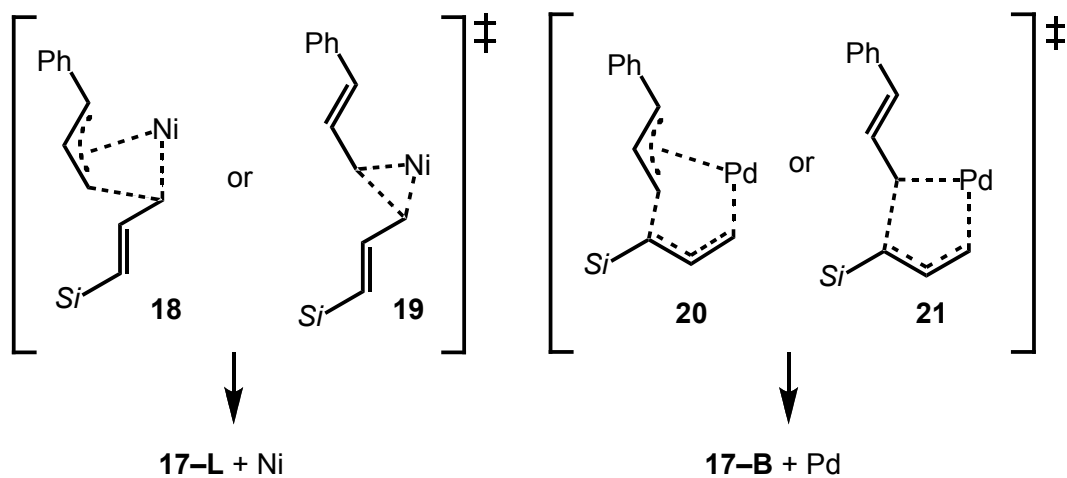


Scheme 4. Selective Preparation of Vinylsilanes and Allylsilanes under Nickel and Palladium Catalysis



The reason for the different regiochemical outcomes is not clear at this stage. The mode of reductive elimination from diallynickel species would be different from that of diallylpalladium (Scheme 5). In the case of nickel, the C–C formation would take place between the less substituted carbons of the allyl moieties on the nickel via a transition state **18** or **19**. In contrast, the C–C formation from diallylpalladium would take place with allylic rearrangement via a transition state **20** or **21**.^{3e}

Scheme 5. Plausible Transition States for Reductive Elimination



Conclusion

The author has developed an efficient method for the synthesis of 1,5-hexadienes, nickel-catalyzed reactions of Boc-protected allyl alcohols with homoallyl alcohols. Nickel-mediated retro-allylation allows for the use of homoallyl alcohols as allylmetal equivalents in the synthesis of 1,5-hexadienes.

Experimental Section

Instrumentation and Materials

^1H NMR (500 MHz), ^{13}C NMR (125.7 MHz), and ^{19}F NMR (282 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and Mercury 300 spectrometers. Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for ^1H and relative to CDCl_3 at 77.0 ppm for ^{13}C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F₂₅₄. Mass spectra (EI unless otherwise noted) were determined on a JEOL Mstation 700 spectrometer. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Toluene and xylene were purchased from Wako Pure Chemical Co. and stored over slices of sodium. Triethyl phosphite and $\text{Ni}(\text{cod})_2$ were purchased from Wako Pure Chemical Co. and Strem, respectively. Boc-protected allyl alcohols **7** were prepared from the corresponding alcohols and Boc_2O in the presence of tetrabutylammonium hydrogensulfate in dichloromethane/30% aqueous NaOH.¹² Homoallyl alcohols **2**, **12**, **14**, and **16** were readily prepared in one step according to the literature.⁸

Typical Procedure for Nickel-Catalyzed Allylation of Allyl Carbonates with Homoallyl Alcohols via Retro-Allylation Providing 1,5-Hexadiene

Synthesis of **3a-L** and **3a-B**

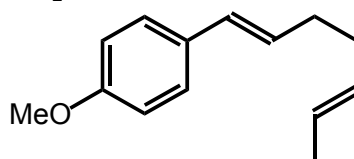
$\text{Ni}(\text{cod})_2$ (3.4 mg, 0.0125 mmol) was placed in a 20-mL reaction flask. Toluene (1.0 mL) and $\text{P}(\text{OEt})_3$ (4 μL , 0.025 mmol) were added, and the resulting suspension was stirred for 10 min at room temperature. Carbonate **7a** (59 mg, 0.25 mmol) and homoallyl alcohol **2a** (51 mg, 0.30 mmol) were then added, and the mixture was heated at reflux for 5 h. The reaction was then quenched with water (2 mL). Extraction followed by purification on silica gel provided a

mixture of (*E*)-1-phenyl-1,5-heptadiene (**3a-L**) and 4-methyl-1-phenyl-1,5-hexadiene (**3a-B**) in 91% combined yield (39 mg, 0.23 mmol, **B/L** = 37/63).

Characterization Data

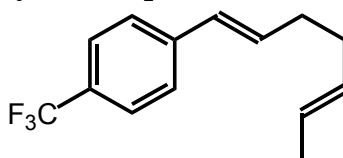
Products **3a-L**¹³ and **13a**¹⁴ showed the identical spectra with those described in the literature. Product **13i** and **15a** were well known compounds.

(1*E*,5*E*)-1-(4-Methoxyphenyl)-1,5-heptadiene (**3b-L**)



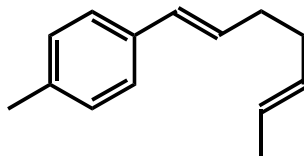
IR (neat) 2961, 1609, 1511, 1249, 1175, 1037, 965, 804 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.67 (d, J = 5.0 Hz, 3H), 2.14–2.17 (m, 2H), 2.23–2.27 (m, 2H), 3.81 (s, 3H), 5.50–5.53 (m, 2H), 6.10 (dt, J = 16.0, 6.5 Hz, 1H), 6.35 (d, J = 16.0 Hz, 1H), 6.85 (d, J = 8.5 Hz, 2H), 7.28 (d, J = 8.5 Hz, 2H); ^{13}C NMR (CDCl_3) δ 17.92, 32.57, 33.09, 126.97, 127.02, 128.31, 129.25, 130.43, 130.66, 158.60. HRMS (EI) Found 202.1360 [M^+]; Calcd for $\text{C}_{14}\text{H}_{18}\text{O}$: 202.1358.

(1*E*,5*E*)-1-(4-Trifluoromethylphenyl)-1,5-heptadiene (**3c-L**)



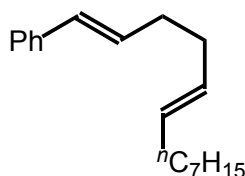
IR (neat) 2933, 1718, 1616, 1419, 1326, 1177, 1166, 1068, 1017, 967, 837 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.66 (dt, J = 4.5, 1.5 Hz, 3H), 2.15–2.19 (m, 2H), 2.26–2.32 (m, 2H), 5.43–5.52 (m, 2H), 6.33 (dt, J = 16.0, 6.5 Hz, 1H), 6.42 (d, J = 16.0 Hz, 1H), 7.42 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.5 Hz, 2H); ^{13}C NMR (CDCl_3) δ 17.92, 32.18, 40.12, 123.96 (q, J = 216.1 Hz), 125.41 (q, J = 3.0 Hz), 125.68, 128.58 (q, J = 25.9 Hz), 126.04, 126.08, 128.85, 130.25, 133.37. ^{19}F NMR (CDCl_3) δ -63.10. Found: C, 69.71; H, 6.51%. Calcd for $\text{C}_{14}\text{H}_{15}\text{F}_3$: C, 69.98; H, 6.29%

(1*E*,5*E*)-1-(2-Methylphenyl)-1,5-heptadiene (3d-L)



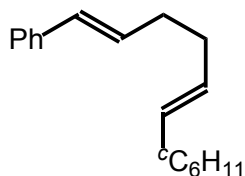
IR (neat) 3022, 2925, 1639, 1485, 1460, 1436, 1419, 1373, 993, 965, 911, 744 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.70 (dm, $J = 3.5$ Hz, 3H), 2.28–2.36 (m, 4H), 2.36 (s, 3H), 5.48–5.56 (m, 2H), 6.12 (dt, $J = 15.5, 6.5$ Hz, 1H), 6.60 (d, $J = 15.5$ Hz, 1H), 7.14–7.16 (m, 3H), 7.43 (d, $J = 7.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 19.80, 32.51, 33.35, 40.41, 125.38, 125.45, 125.96, 126.75, 127.88, 129.10, 130.10, 130.60, 131.82, 134.89. HRMS (EI) Found 186.1405 [M^+]; Calcd for $\text{C}_{14}\text{H}_{18}$: 186.1408.

(1*E*,5*E*)-1-Phenyl-1,5-tridecadiene (3e-L)



IR (neat) 3026, 2956, 2925, 2853, 1496, 1469, 1448, 1437, 963 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.89 (t, $J = 7.0$ Hz, 3H), 1.27–1.36 (m, 10H), 1.98–2.01 (m, 2H), 2.15–2.19 (m, 2H), 2.26–2.30 (m, 2H), 5.41–5.50 (m, 2H), 6.22 (dt, $J = 15.5, 6.5$ Hz, 1H), 6.39 (d, $J = 15.5$ Hz, 1H), 7.18–7.21 (m, 1H), 7.27–7.35 (m, 4H); ^{13}C NMR (CDCl_3) δ 14.09, 22.68, 29.11, 29.20, 29.60, 31.86, 32.45, 32.59, 33.16, 114.28, 125.93, 126.79, 128.45, 129.26, 129.98, 130.53, 131.23. Found: C, 88.99%; H, 11.01%. Calcd for $\text{C}_{19}\text{H}_{28}$: C, 88.73%; H, 11.06%.

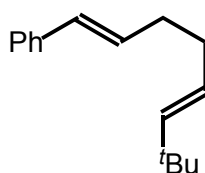
(1*E*,5*E*)-6-Cyclohexyl-1-phenyl-1,5-hexadiene (3f-L)



IR (neat) 3025, 2923, 2850, 1495, 1448, 963 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.02–1.31 (m, 5H),

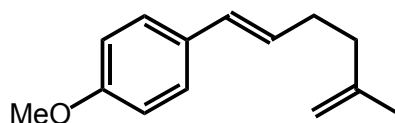
1.62–1.74 (m, 5H), 1.89–1.94 (m, 1H), 2.14–2.18 (m, 2H), 2.23–2.29 (m, 2H), 5.38–5.45 (m, 2H), 6.23 (dt, $J = 15.5, 6.5$ Hz, 1H), 6.39 (d, $J = 15.5$ Hz, 1H), 7.18–7.21 (m, 1H), 7.28–7.35 (m, 4H); ^{13}C NMR (CDCl_3) δ 26.09, 26.20, 32.50, 33.20 (2C overlap), 40.69, 125.90, 125.93, 126.66, 126.77, 128.45, 129.90, 130.54, 137.18. Found: C, 89.94; H, 10.06%. Calcd for $\text{C}_{18}\text{H}_{24}$: C, 90.07; H, 10.31%.

(1*E*,5*E*)-7,7-Dimethyl-1-phenyl-1,5-octadiene (3g-L)



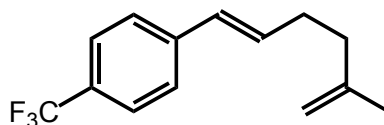
IR (neat) 3025, 2958, 2928, 2904, 1448, 1363, 963 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.00 (s, 9H), 2.14–2.18 (m, 2H), 2.25–2.30 (m, 2H), 5.36 (dt, $J = 15.5, 6.5$ Hz, 1H), 5.50 (dt, $J = 15.5, 1.5$ Hz, 1H), 6.23 (dt, $J = 15.5, 7.0$ Hz, 1H), 6.39 (d, $J = 15.5$ Hz, 1H), 7.18–7.21 (m, 1H), 7.26–7.35 (m, 4H); ^{13}C NMR (CDCl_3) δ 29.76, 32.51, 32.79, 33.26, 123.74, 125.90, 126.77, 128.45, 129.92, 130.55, 137.87, 142.25. Found: C, 89.65; H, 10.35%. Calcd for $\text{C}_{16}\text{H}_{22}$: C, 89.59; H, 10.35%.

(*E*)-5-methyl-1-(4-methoxyphenyl)-1,5-hexadiene (13b)



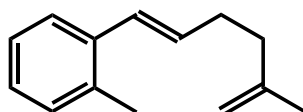
IR (neat) 2935, 1653, 1608, 1511, 1465, 1457, 1249, 1175, 1038 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.78 (s, 3H), 2.20 (t, $J = 7.5$ Hz, 2H), 2.36 (dt, $J = 7.5, 7.0$ Hz, 2H), 3.81 (s, 3H), 4.74 (br s, 1H), 4.77 (br s, 1H), 6.10 (dt, $J = 16.0, 7.0$ Hz, 1H), 6.37 (d, $J = 16.0$ Hz, 1H), 6.85 (d, $J = 7.0$ Hz, 2H), 7.29 (d, $J = 7.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 22.48, 31.17, 37.64, 55.22, 110.16, 113.88, 126.99, 128.19, 129.27, 130.65, 145.28, 158.66. Found: C, 82.75; H, 9.01%. Calcd for $\text{C}_{14}\text{H}_{18}\text{O}$: C, 83.12; H, 8.97%.

(*E*)-5-methyl-1-(4-trifluoromethylphenyl)-1,5-hexadiene (13c)



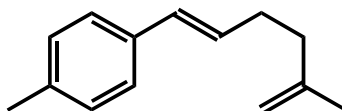
IR (neat) 2882, 2865, 1656, 1620, 1418, 1327, 1165, 1125, 1086, 1015, 966 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.79 (s, 3H), 2.22 (t, $J = 7.5$ Hz, 2H), 2.44 (dt, $J = 7.5, 6.5$ Hz, 2H), 4.76 (m, 1H), 4.80 (m, 1H), 6.35 (dt, $J = 16.0, 6.5$ Hz, 1H), 6.45 (d, $J = 16.0$ Hz, 1H), 7.43 (d, $J = 8.0$ Hz, 2H), 7.55 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 22.41, 31.15, 37.22, 110.46, 124.30 (q, $J = 270.6$ Hz), 125.41 (q, $J = 3.9$ Hz), 126.06, 128.71 (q, $J = 32.4$ Hz), 128.84, 133.24, 141.30, 144.87; ^{19}F NMR (CDCl_3) δ -62.70. Found: C, 69.98; H, 6.52%. Calcd for $\text{C}_{14}\text{H}_{15}\text{F}_3$: C, 69.99; H, 6.29%.

(*E*)-5-methyl-1-(2-methylphenyl)-1,5-hexadiene (13d)



IR (neat) 3072, 3022, 2932, 2851, 2360, 1649, 1513, 1484, 1447, 1374 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.78 (s, 3H), 2.21 (t, $J = 7.5$ Hz, 2H), 2.34 (s, 3H), 2.39 (dt, $J = 7.5, 7.0$ Hz, 2H), 4.73 (m, 1H), 4.75 (m, 1H), 6.10 (dt, $J = 15.5, 7.0$ Hz, 1H), 6.61 (d, $J = 15.5$ Hz, 1H), 7.12–7.16 (m, 3H), 7.41 (d, $J = 7.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 19.81, 22.48, 31.43, 37.59, 110.28, 125.48, 125.98, 126.79, 127.84, 130.11, 131.72, 134.91, 136.96, 145.21. Found: C, 90.04; H, 9.80%. Calcd for $\text{C}_{14}\text{H}_{18}$: C, 90.26; H, 9.74%.

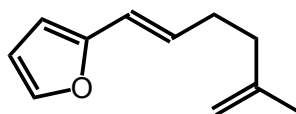
(*E*)-5-methyl-1-(4-methylphenyl)-1,5-hexadiene (13e)



IR (neat) 2921, 1649, 1613, 1446, 1374, 965, 887, 793, 665 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.76 (s, 3H), 2.18 (t, $J = 7.5$ Hz, 2H), 2.33 (s, 3H), 2.35 (dt, $J = 7.5, 7.0$ Hz, 2H), 4.74 (m, 1H), 4.76 (m,

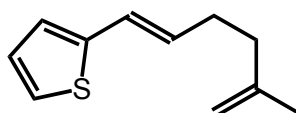
1H), 6.17 (dt, $J = 16.0, 7.0$ Hz, 1H), 6.38 (d, $J = 16.0$ Hz, 1H), 7.10 (d, $J = 8.5$ Hz, 2H), 7.24 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 21.12, 22.50, 31.19, 37.56, 110.19, 125.82, 129.15, 129.34, 129.74, 135.07, 136.53, 145.30. Found: C, 90.39; H, 9.90%. Calcd for $\text{C}_{14}\text{H}_{18}$: C, 90.26; H, 9.74%.

(*E*)-1-(2-Furyl)-5-methyl-1,5-hexadiene (13f)



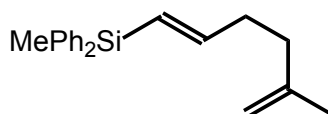
IR (neat) 2969, 2934, 2850, 1676, 1649, 1491, 1448, 1375, 1254, 1151, 1013 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.75 (s, 3H), 2.17 (t, $J = 7.5$ Hz, 2H), 2.33 (dt, $J = 7.5, 6.5$ Hz, 2H), 4.74 (m, 1H), 4.76 (m, 1H), 6.17 (dt, $J = 16.0, 6.5$ Hz, 1H), 6.20–6.26 (m, 2H), 6.34 (dd, $J = 8.0, 2.0$ Hz, 1H), 7.31 (d, $J = 2.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 22.48, 30.93, 37.29, 106.05, 110.27, 111.05, 118.67, 129.38, 141.24, 145.08, 153.21. HRMS (EI) Found 162.1042 [M^+]; Calcd for $\text{C}_{11}\text{H}_{14}\text{O}$: 162.1045.

(*E*)-5-Methyl-1-(2-thienyl)-1,5-hexadiene (13g)



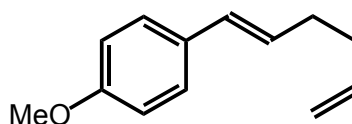
IR (neat) 2968, 2933, 1675, 1652, 1436, 1419, 953, 889, 853, 693 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.76 (s, 3H), 2.18 (t, $J = 7.5$ Hz, 2H), 2.34 (dt, $J = 7.5, 7.0$ Hz, 2H), 4.73 (m, 1H), 4.75 (m, 1H), 6.08 (dt, $J = 16.0, 7.0$ Hz, 1H), 6.54 (ddt, $J = 16.0, 1.5, 1.5$ Hz, 1H), 6.87 (d, $J = 3.5$ Hz, 1H), 6.94 (dd, $J = 5.0, 3.5$ Hz, 1H), 7.09 (d, $J = 5.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 22.49, 31.00, 37.31, 110.30, 123.11, 123.19, 124.24, 127.17, 130.35, 143.00, 145.05. Found: C, 74.23; H, 8.11%. Calcd for $\text{C}_{11}\text{H}_{14}\text{S}$: C, 74.10; H, 7.91%.

(*E*)-1-(Diphenylmethylsilyl)-5-methyl-1,5-hexadiene (13h)



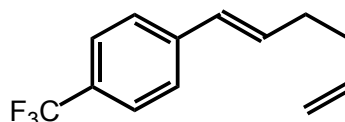
IR (neat) 3069, 2935, 1617, 1428, 1251, 1113, 992, 888 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.66 (s, 3H), 1.78 (s, 3H), 2.20 (t, $J = 8.0$ Hz, 2H), 2.39 (dt, $J = 8.0, 6.0$ Hz, 2H), 4.75 (m, 1H), 4.78 (m, 1H), 6.03 (d, $J = 18.5$ Hz, 1H), 6.22 (dt, $J = 18.5, 6.0$ Hz, 1H), 7.38–7.44 (m, 6H), 7.57–7.59 (m, 4H); ^{13}C NMR (CDCl_3) δ –3.70, 22.47, 34.96, 36.72, 110.19, 125.47, 127.73, 129.11, 134.81, 136.98, 145.18, 150.76. HRMS (EI) Found 292.1640 [M^+]; Calcd for $\text{C}_{20}\text{H}_{24}\text{Si}$: 292.1647.

(*E*)-1-(4-Methoxyphenyl)-1,5-hexadiene (13j)



IR (neat) 2934, 2837, 1701, 1608, 1513, 1250, 1175, 1035 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.21–2.26 (m, 2H), 2.28–2.33 (m, 2H), 3.81 (s, 3H), 5.01 (dm, $J = 12.0$ Hz, 1H), 5.08 (dm, $J = 17.0$ Hz, 1H), 5.84–5.92 (m, 1H), 6.10 (dt, $J = 16.0, 6.5$ Hz, 1H), 6.36 (d, $J = 16.0$ Hz, 1H), 6.85 (d, $J = 9.0$ Hz, 2H), 7.29 (d, $J = 9.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 32.39, 33.68, 55.23, 113.88, 114.79, 127.00, 127.91, 129.50, 130.58, 138.19, 158.68. HRMS (EI) Found 188.1201 [M^+]; Calcd for $\text{C}_{13}\text{H}_{16}\text{O}$: 188.1201.

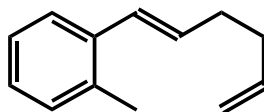
(*E*)-1-(4-Trifluoromethylphenyl)-1,5-hexadiene (13k)



IR (neat) 2981, 2927, 2848, 1653, 1642, 1616, 1415, 1327, 1165, 1125, 1069 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.24–2.29 (m, 2H), 2.33–2.38 (m, 2H), 5.02 (dm, $J = 10.5$ Hz, 1H), 5.08 (dm, $J = 17.0$ Hz, 1H), 5.83–5.91 (m, 1H), 6.34 (dt, $J = 16.0, 6.5$ Hz, 1H), 6.44 (d, $J = 16.0$ Hz, 1H), 7.42 (d, J

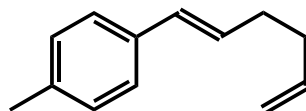
= 8.0 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H); ^{13}C NMR (CDCl_3) δ 32.33, 33.21, 115.11, 124.24 (q, J = 270.1 Hz), 125.40 (q, J = 4.3 Hz), 126.02, 128.67 (q, J = 32.0 Hz), 129.02, 132.92, 137.72, 141.17; ^{19}F NMR (CDCl_3) δ -62.81. Found: C, 68.98; H, 5.90%. Calcd for $\text{C}_{13}\text{H}_{13}\text{F}_3$: C, 69.02; H, 5.79%.

(*E*)-1-(2-Methylphenyl)-1,5-hexadiene (13l)



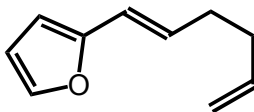
IR (neat) 2925, 1457, 1437, 965, 912 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.24–2.29 (m, 2H), 2.34–2.38 (m, 2H), 2.35 (s, 3H), 5.02 (dm, J = 10.5 Hz, 1H), 5.09 (dm, J = 17.0 Hz, 1H), 5.84–5.94 (m, 1H), 6.11 (dt, J = 16.0, 7.0 Hz, 1H), 6.61 (d, J = 16.0 Hz, 1H), 7.13–7.18 (m, 3H), 7.42 (d, J = 7.0 Hz, 1H); ^{13}C NMR (CDCl_3) δ 19.81, 32.67, 33.64, 114.90, 125.64, 125.98, 126.82, 128.08, 130.12, 131.44, 134.92, 136.90, 138.11. Found: C, 90.64; H, 9.50%. Calcd for $\text{C}_{13}\text{H}_{16}$: C, 90.64; H, 9.36%.

(*E*)-1-(4-Methylphenyl)-1,5-hexadiene (13m)



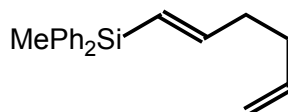
IR (neat) 2923, 2846, 1640, 1514, 1437, 966 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.22–2.26 (m, 2H), 2.30–2.32 (m, 2H), 2.34 (s, 3H), 5.01 (dm, J = 10.0 Hz, 1H), 5.07 (dm, J = 17.0 Hz, 1H), 5.84–5.92 (m, 1H), 6.19 (dt, J = 16.0, 7.0 Hz, 1H), 6.39 (d, J = 16.0 Hz, 1H), 7.11 (d, J = 7.5 Hz, 2H), 7.25 (d, J = 7.5 Hz, 2H); ^{13}C NMR (CDCl_3) δ 21.11, 32.42, 33.61, 114.84, 125.84, 129.06, 129.16, 130.00, 134.97, 136.56, 138.17. Found: C, 90.72; H, 9.52%. Calcd for $\text{C}_{13}\text{H}_{16}$: C, 90.64; H, 9.36%.

(*E*)-1-(2-Thienyl)-1,5-hexadiene (13n)



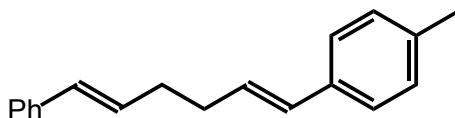
IR (neat) 3076, 2978, 2924, 2843, 1640, 1436, 1204, 955, 913 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.22–2.25 (m, 2H), 2.27–2.31 (m, 2H), 5.01 (dm, $J = 10.5$ Hz, 1H), 5.06 (dm, $J = 17.0$ Hz, 1H), 5.82–5.89 (m, 1H), 6.08 (dt, $J = 15.5, 7.0$ Hz, 1H), 6.54 (d, $J = 15.5$ Hz, 1H), 6.87 (d, $J = 4.5$ Hz, 1H), 6.94 (dd, $J = 5.0, 4.5$ Hz, 1H), 7.09 (d, $J = 5.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 32.22, 33.37, 115.00, 123.15, 123.43, 124.31, 127.18, 130.06, 137.92, 142.94. Found: C, 73.31; H, 7.42%. Calcd for $\text{C}_{10}\text{H}_{12}\text{S}$: C, 73.12; H, 7.36%.

(*E*)-1-(Diphenylmethylsilyl)-1,5-hexadiene (13o)



IR (neat) 3068, 1616, 1428, 1250, 1113, 992 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.62 (s, 3H), 2.21–2.25 (m, 2H), 2.31–2.35 (m, 2H), 5.01 (dm, $J = 10.5$ Hz, 1H), 5.06 (dm, $J = 17.5$ Hz, 1H), 5.82–5.90 (m, 1H), 6.01 (d, $J = 18.5$ Hz, 1H), 6.20 (dt, $J = 18.5, 6.5$ Hz, 1H), 7.36–7.42 (m, 6H), 7.55–7.57 (m, 4H); ^{13}C NMR (CDCl_3) δ –3.68, 32.77, 36.07, 114.79, 125.79, 127.74, 129.13, 134.81, 136.98, 138.07, 150.46. Found: C, 81.85; H, 8.06%. Calcd for $\text{C}_{14}\text{H}_{22}\text{Si}$: C, 81.95; H, 7.96%.

(1*E*,5*E*)-1-(4-Methylphenyl)-6-phenyl-1,5-hexadiene (15b)

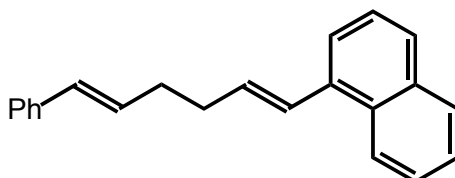


IR (nujol) 2923, 2854, 1458, 1377, 963 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.35 (s, 3H), 2.41–2.42 (m, 4H), 6.22–6.33 (m, 2H), 6.44 (d, $J = 15.0$ Hz, 1H), 6.46 (d, $J = 15.0$ Hz, 1H), 7.13 (d, $J = 8.0$ Hz, 2H), 7.21–7.34 (m, 5H), 7.38 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 21.10, 32.88, 32.96,

125.86, 125.96, 126.88, 128.46, 128.91, 129.16, 130.05, 130.18, 130.30, 134.92, 136.60, 137.72.

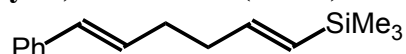
HRMS (EI) Found 248.1562 [M^+]; Calcd for $C_{19}H_{20}$: 248.1565. Mp: 83–84 °C.

(1*E*,5*E*)-1-Naphthyl-6-phenyl-1,5-hexadiene (15c)



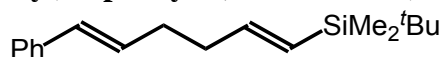
IR (neat) 2923, 2854, 1457, 1377, 963 cm^{-1} ; 1H NMR ($CDCl_3$) δ 2.49–2.58 (m, 4H), 6.31 (dt, J = 15.5, 7.0 Hz, 1H), 6.36 (dt, J = 15.5, 6.5 Hz, 1H), 6.53 (d, J = 15.5 Hz, 1H), 7.21 (d, J = 15.5 Hz, 1H), 7.23–7.27 (m, 1H) 7.35 (t, J = 7.0 Hz, 2H) 7.42 (d, J = 7.5 Hz, 2H), 7.45–7.53 (m, 3H), 7.59 (d, J = 7.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 8.15 (d, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 32.88, 33.22, 123.59, 123.97, 125.63, 125.62, 125.79, 126.00, 126.93, 127.32, 127.74, 128.42, 128.49, 129.97, 130.51, 131.11, 133.25, 133.56, 135.58, 137.69. HRMS (EI) Found 284.1564 [M^+]; Calcd for $C_{22}H_{20}$: 284.1565.

(1*E*,5*E*)-1-Phenyl-6-trimethylsilyl-1,5-hexadiene (17a-L)



IR (neat) 2955, 1617, 1248, 989, 963, 866, 838 cm^{-1} ; 1H NMR ($CDCl_3$) δ 0.07 (s, 9H), 2.27–2.35 (m, 4H), 5.70 (d, J = 18.5 Hz, 1H), 6.08 (dt, J = 18.5, 5.0 Hz, 1H), 6.23 (dt, J = 16.0, 6.5 Hz, 1H), 6.41 (d, J = 16.0 Hz, 1H), 7.20 (t, J = 7.0 Hz, 1H), 7.28–7.35 (m, 4H); ^{13}C NMR ($CDCl_3$) δ –1.18, 32.19, 36.36, 125.92, 126.83, 128.46, 130.07, 130.25, 130.45, 137.80, 146.08. Found: C, 78.16; H, 9.78%. Calcd for $C_{15}H_{22}Si$: C, 78.19, H, 9.62%.

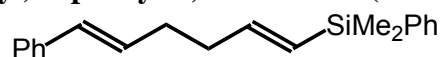
(1*E*,5*E*)-6-(*tert*-Butyldimethylsilyl)-1-phenyl-1,5-hexadiene (17b-L)



IR (neat) 2952, 2926, 2883, 2855, 1616, 1471, 1247, 962 cm^{-1} ; 1H NMR ($CDCl_3$) δ 0.01 (s, 6H), 0.86 (s, 9H), 2.28–2.35 (m, 4H), 5.68 (d, J = 18.0 Hz, 1H), 6.07 (dt, J = 18.0, 7.0 Hz, 1H),

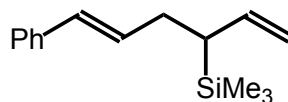
6.22 (dt, $J = 16.0, 6.5$ Hz, 1H), 6.39 (d, $J = 16.0$ Hz, 1H), 7.18–7.21 (m, 1H), 7.27–7.34 (m, 4H); ^{13}C NMR (CDCl_3) δ –6.09, 16.46, 26.40, 32.29, 36.55, 125.92, 126.82, 127.58, 128.44, 130.11, 130.21, 137.79, 147.45. Found: C, 79.14; H, 10.11%. Calcd for $\text{C}_{18}\text{H}_{28}\text{Si}$: C, 79.34, H, 10.36%.

(1*E*,5*E*)-6-(Dimethylphenylsilyl)-1-phenyl-1,5-hexadiene (17c-L)



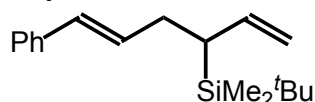
IR (neat) 3024, 2956, 2904, 1616, 1427, 1247, 1113, 963 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.34 (s, 6H), 2.34–2.37 (m, 4H), 5.84 (d, $J = 17.0$ Hz, 1H), 6.14–6.26 (m, 2H), 6.41 (d, $J = 16.0$ Hz, 1H), 7.19–7.22 (m, 1H), 7.27–7.35 (m, 7H), 7.52–7.54 (m, 2H); ^{13}C NMR (CDCl_3) δ –2.49, 32.06, 36.41, 125.94, 126.85, 127.69, 128.24, 128.46, 128.81, 130.10, 130.21, 133.81, 137.75, 139.16, 148.13. Found: C, 82.36; H, 8.41%. Calcd for $\text{C}_{20}\text{H}_{24}\text{Si}$: C, 82.13, H, 8.27%.

(*E*)-1-Phenyl-4-trimethylsilyl-1,5-hexadiene (17a-B)



IR (neat) 2956, 1248, 963, 895, 859, 837 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.03 (s, 9H), 1.69–1.73 (m, 1H), 2.30–2.43 (m, 2H), 4.86 (dm, $J = 17.5$ Hz, 1H), 4.92 (dm, $J = 9.5$ Hz, 1H), 5.68–5.76 (m, 1H), 6.24 (dt, $J = 16.0, 6.0$ Hz, 1H), 6.38 (d, $J = 16.0$ Hz, 1H), 7.17–7.20 (m, 1H), 7.27–7.34 (m, 4H); ^{13}C NMR (CDCl_3) δ –3.14, 32.21, 35.02, 112.21, 125.94, 126.74, 128.43, 129.82, 131.06, 137.85, 139.52. Found: C, 78.39; H, 9.72%. Calcd for $\text{C}_{15}\text{H}_{22}\text{Si}$: C, 78.19, H, 9.62%.

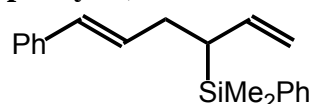
(*E*)-4-(*tert*-Butyldimethylsilyl)-1-phenyl-1,5-hexadiene (17b-B)



IR (neat) 2956, 2928, 2856, 1256, 1249, 963, 832, 824 cm^{-1} ; ^1H NMR (CDCl_3) δ –0.01 (s, 3H), 0.02 (s, 3H), 0.95 (s, 9H), 1.86 (dt, $J = 11.5, 3.0$ Hz, 1H), 2.23–2.26 (m, 1H), 2.44–2.49 (m, 1H), 4.89 (dm, $J = 17.0$ Hz, 1H), 4.93 (dm, $J = 10.5$ Hz, 1H), 5.75 (dt, $J = 17.0, 10.5$ Hz, 1H), 6.24 (dt,

$J = 15.5, 6.5$ Hz, 1H), 6.35 (d, $J = 15.5$ Hz, 1H), 7.17–7.20 (m, 1H), 7.27–7.34 (m, 4H); ^{13}C NMR (CDCl_3) δ –7.02, –6.97, 17.78, 27.35, 32.95, 33.22, 112.72, 125.95, 126.73, 128.43, 129.73, 131.15, 137.87, 140.08. HRMS (EI) Found 272.1961 [M^+]; Calcd for $\text{C}_{18}\text{H}_{28}\text{Si}$: 272.1960.

(1*E*,5*E*)-4-(Dimethylphenylsilyl)-1-phenyl-1,5-hexadiene (17c-B)



IR (neat) 3024, 2959, 1427, 1248, 1114, 964, 830 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.32 (s, 3H), 0.33 (s, 3H), 1.95 (dt, $J = 9.5, 4.0$ Hz, 1H), 2.26–2.40 (m, 2H), 4.87 (dd, $J = 17.5, 1.0$ Hz, 1H), 4.95 (dd, $J = 9.5, 1.0$ Hz, 1H), 5.70 (dt, $J = 17.5, 9.5$ Hz, 1H), 6.16 (dt, $J = 16.0, 6.5$ Hz, 1H), 6.29 (d, $J = 16.0$ Hz, 1H), 7.16–7.18 (m, 1H), 7.26 (d, $J = 4.5$ Hz, 2H), 7.34–7.39 (m, 4H), 7.52–7.56 (m, 3H); ^{13}C NMR (CDCl_3) δ 0.84, 32.25, 34.54, 112.90, 125.93, 126.72, 127.69, 128.39, 129.03, 129.23, 129.92, 130.78, 132.98, 134.07, 139.00. HRMS (EI) Found 292.1652 [M^+]; Calcd for $\text{C}_{20}\text{H}_{24}\text{Si}$: 292.1647.

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Publication List

I. Parts of the present thesis have been published in the following journals.

- Chapter 1 Nickel-Catalyzed Borylative Ring Opening Reaction of Vinylcyclopropanes with Bis(pinacolato)diboron Yielding Allylboronates
Yuto Sumida, Hideki Yorimitsu, and Koichiro Oshima
Org. Lett. **2008**, 10, 4677–4679.
- Chapter 2 Nickel-Catalyzed Borylation of Aryl Cyclopropyl Ketones with Bis(pinacolato)diboron to Synthesize 4-Oxoalkylboronates
Yuto Sumida, Hideki Yorimitsu, and Koichiro Oshima
J. Org. Chem. **2009**, 74, 3196–3198.
- Chapter 3 Palladium-Catalyzed Preparation of Silyl Enolates from Cyclopropyl Ketones or α,β -Unsaturated Ketones with Hydrosilanes
Yuto Sumida, Hideki Yorimitsu, and Koichiro Oshima
J. Org. Chem. **2009**, 74, 7986–7989.
- Chapter 4 Nickel-Catalyzed Arylative Ring Opening of 3-Methylenecycloalkane-1,1-dicarboxylate
Yuto Sumida, Hideki Yorimitsu, and Koichiro Oshima
To be submitted.
- Chapter 5 Rhodium-Catalyzed Allylation of Aldehydes with Homoallyl Alcohols via Retro-Allylation Followed by Isomerization into Saturated Ketones with Conventional or Microwave Heating
Yuto Sumida, Yuko Takada, Sayuri Hayashi, Koji Hirano, Hideki Yorimitsu, and Koichiro Oshima
Chem. Asian J. **2008**, 3, 119–125.

Chapter 6 Nickel-Catalyzed Allylation of Allyl Carbonates with Homoallyl Alcohols via Retro-Allylation Providing 1,5-Hexadienes

Yuto Sumida, Sayuri Hayashi, Koji Hirano, Hideki Yorimitsu, and Koichiro Oshima *Org. Lett.* **2008**, 10, 1629–1632.

II. Other Publications not included in this thesis.

- (1) Discrepancy of the spectral data between adunctin E and the synthetic one.

Masayuki Yamashita, Navnath Dnyanoba Yadav, Yuto Sumida, Ikuo Kawasaki, Ai Kurume, and Shunsaku Ohta

Tetrahedron **2007**, 62, 3523–3535.

- (2) Radical Addition of Polyhaloalkanes to 2-Ethynyl-4,4,5,5-tetramethyl-1,3,2-dioxaboronate.

Tatsuya Wada, Yuto Sumida, Azusa Kondoh, Hideki Yorimitsu, and Koichiro Oshima

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