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

Yuto Sumida
2010
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General Introduction

1. **sp³ Carbon–sp³ 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. However, cleavage of \( sp^3 \text{C–}sp^3 \text{C } \) bonds is still difficult due to their stability as well as the high directionality of the \( \sigma \) orbital of an \( sp^3 \text{C–}sp^3 \text{C } \) bond. Transition-metal-catalyzed \( sp^3 \text{C–}sp^3 \text{C } \) 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 \( sp^3 \text{C–}sp^3 \text{C } \) bond cleavage, a large number of researchers have utilized strained cycloalkanes, which have relatively low C–C bond energy. The first example of \( sp^3 \text{C–}sp^3 \text{C } \) bond cleavage with a metal complex by using a strained cycloalkane was reported by Tipper in 1955. The reaction of \( \text{PtCl}_2 \) 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. Mason also confirmed the structure crystallographically (Scheme 1).

\[
\begin{align*}
\text{Scheme 1} & \\
\text{\( \Delta + \text{PtCl}_2 \rightarrow \left[ \begin{array}{c} \text{PtCl}_2 \\ \text{pyridine (Py)} \end{array} \right] \rightarrow \text{Py} \quad \text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{Cl} \end{align*}
\]

In 1967, Pettit and Mark reported transition-metal-catalyzed ring opening of cyclobutene to butadiene. 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.\textsuperscript{7}

\textbf{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).\textsuperscript{8} The isomerization completed within 45 min at 0 °C when 2 mol% of [Rh(nbd)Cl]\textsubscript{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.\textsuperscript{9} This is the first example to show the evidence that direct oxidative insertion of a low valent transition metal to an \textit{sp}^3–\textit{sp}^3 bond occurs.

\textbf{Scheme 3} \quad [\text{Rh(nbd)Cl}]\textsubscript{2} (2 mol%)

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,\textsuperscript{6,7} application of \textit{sp}^3–\textit{sp}^3 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 \textit{sp}^3–\textit{sp}^3 bond.\textsuperscript{10} Reaction of dimethyl fumarate with bicyclopentane in the presence of bis(acrylonitrile)nickel(0) [Ni(AN)\textsubscript{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 $sp^3C$–$sp^3C$ 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. 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. The nickel catalyst broke the C–C bond of methylenecyclopropane preferably at the proximal position in the mechanism Noyori proposed.

Scheme 5

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 Pd(PPh₃)₄ to provide vinylcyclopentene derivative (Scheme 6, eq 1). Furthermore, Tsuji extended this reaction to intermolecular cycloaddition of vinylcyclopropane with electron-deficient olefin (Scheme 6, eq 2). 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. 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). 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). The combination of a nickel complex and a different NHC also promoted simple rearrangement of unactivated vinylcyclopropane to cyclopentene (Scheme 7, eq 3). Although Ito and Suginome also reported only one example of rearrangement of unactivated vinylcyclopropane to cyclopentene by means of the combination of Ni(acac)₂/DIBAL–H/P(C₆H₉), their system required high temperature (Scheme 7, eq 4).

The key to the success of the ring opening reactions might be η²-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. Very recently, Louie and Tantillo also reported a computational study of simple rearrangement of vinylcyclopropane to cyclopentene catalyzed by a nickel complex and NHC. Afterwards, various reactions of vinylcyclopropanes with diverse reactants (carbon monoxide, allyl chloride, aldehyde) were reported.
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 oxanickelacycl 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

**Scheme 9**

![Scheme 9 Diagram]

Until Ogoshi provided the evidence suggesting the intermediacy of oxanickelacycle by means of NMR and X ray analysis,25 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 R₃Si–CN,27 R₃Si–H,28 R₃Sn–H,29 R₂N–H,30 RO–H,31 RS–H,32 and R₂B–BR₂.33 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). 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). 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 pathway 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.
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).\textsuperscript{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\textsubscript{3}SiCN or Et\textsubscript{3}SiH. The stoichiometric reaction of cis-(Ph\textsubscript{3}P)\textsubscript{2}Pt(Bpin)\textsubscript{2} 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 Pt(PPh\textsubscript{3})\textsubscript{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](image)

In 2000, Ito and Suginome developed palladium- and platinum-catalyzed reactions of methylenecyclopropanes with silylborane which accompany ring opening (Scheme 12).\textsuperscript{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 Pt(CH\textsubscript{2}=CH\textsubscript{2})(PPh\textsubscript{3})\textsubscript{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.

Moreover, Ito and Suginome also reported nickel-catalyzed ring opening silaborylation of vinylcyclopropane (Scheme 13). 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.
The reaction of diboron with vinylcyclopropane having two geminal electron-withdrawing groups was also reported (Scheme 14). 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 [B(OH)$_2$]$_2$ and the pincer complex followed by transfer of B(OH)$_2$ group to vinylcyclopropane in an S$_{N}$2'-type mode. Although the particular palladium complex was required, this catalytic system realized an access to highly functionalized allylic borane from vinylcyclopropane.

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). 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). Trost applied asymmetric allylic alkylation to cyclopropanol having an allyl carbonate moiety to give vinylcyclobutanone (Scheme 15, eq 4).

Scheme 15

Alkoxycyclopropanes are prone to undergo ring opening. 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 alkoxycyclobutane 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**

\[
\text{Scheme 17}
\]

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).  Uemura described palladium-catalyzed formation of anthracenone as shown in Scheme 18, eq 2.  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).  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).
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). 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).
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 \( sp^3 \)C–\( sp^3 \)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 \( sp^3 \)C–\( sp^3 \)C bond cleavages were observed in organometallic chemistry, there were few examples of catalytic reactions.
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). 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). 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 NiCl₂(PPh₃)₂ complex and triethylaluminium.
Kotora assumed that the reaction mechanism includes generation of a cationic nickel hydride from Et₃Al 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). 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).
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). Although it is well known that allylations of carbonyl compounds with stoichiometric allylmetal 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.

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). 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.

Rhodium is also effective for retro-allylation of tertiary homoallyl alcohols and enabled allylation of aldehydes (Scheme 27, eq 1). 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-hydorhodation 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).

**Scheme 27**

\[
\begin{align*}
\text{Np} & \xrightarrow{[\text{RhOH(cod)}]_2 (5 \text{ mol\%})} \text{PhCO} + \text{PhCHO} \\
\text{racemic} & \xrightarrow{[\text{RhCl(cod)}]_2 (2.5 \text{ mol\%})} \xrightarrow{\text{P(Bu)}_3 (10 \text{ mol\%})} \xrightarrow{\text{Cs}_2\text{CO}_3 (15 \text{ mol\%})} \xrightarrow{\text{xylene, reflux}} \text{Np}^\prime \quad 97\% \text{ ee (31\%)}
\end{align*}
\]

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,\textsuperscript{61} there are few examples of borylation catalyzed by a nickel complex.\textsuperscript{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.

\textbf{Scheme 28}

\[
\begin{align*}
\text{E} & \quad \text{E} \\
\text{E} = \text{CO}_2\text{Et} \\
\text{cat. Ni(cod)}_2 & \quad \text{cat. P(C}_5\text{H}_9)_3 \\
\text{K}_3\text{PO}_4 \cdot 3\text{H}_2\text{O} & \quad \text{toluene/MeOH} \\
& \quad \text{r.t.}
\end{align*}
\]

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).\textsuperscript{25} In Chapter 2, the author discloses borylative ring opening reactions of cyclopropyl ketones with diboron to give 4-oxoalkylboronates under nickel catalysis.
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.
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 \(sp^3\)C–\(sp^3\)C 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](image)

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). 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**

\[
\begin{align*}
\text{Ph} & \quad \text{OBoc} + \quad \begin{array}{c}
\text{OH} \\
\text{R}
\end{array} \\
\text{R} & = \text{SiR’₃, Ar}
\end{align*}
\]

toluene, reflux

Linear only
References and Notes


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).\(^4-6\)

\[ \text{Scheme 1.} \]

\[ \begin{array}{c}
\text{E}^1 \quad \text{E}^2 \\
\text{O} \quad \text{B} \quad \text{O} \\
\text{O} \quad \text{O}
\end{array} \]
\[ \stackrel{\text{cat. Ni(cod)}_2}{\text{cat. P(C}_5\text{H}_9)_3} \]
\[ \text{K}_3\text{PO}_4 \cdot 3\text{H}_2\text{O} \]
\[ \text{toluene/Methanol} \]
\[ \text{r.t.} \]

Results and Discussion

Treatment of bis(ethoxycarbonyl)-substituted vinylcyclopropane \(1\text{a}\) 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 \(3\text{a}\) (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,\(^6,c,7\) the reaction required base, which would activate boron species. The addition of methanol was essential for smooth protonation of the boron enolate\(^6,c,7\) (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 \(1\text{d}\) reacted with 2 to provide \(3\text{d}\) with moderate stereoselectivity (entry 4). Diacetyl-substituted vinylcyclopropane \(1\text{e}\) was converted to desired
product 3e in only 20% yield, along with furan derivative 4 as a byproduct (entry 5).\textsuperscript{5f}

Table 1. Scope of Vinylcyclopropanes

<table>
<thead>
<tr>
<th>entry</th>
<th>$E^1$</th>
<th>$E^2$</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Yield(%)\textsuperscript{a}</th>
<th>$E:Z$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CO$_2$Et</td>
<td>CO$_2$Et</td>
<td>1a</td>
<td>5</td>
<td>3a</td>
<td>84(98)</td>
<td>94:6</td>
</tr>
<tr>
<td>2</td>
<td>CO$_2$Me</td>
<td>CO$_2$Me</td>
<td>1b</td>
<td>2</td>
<td>3b</td>
<td>73(80)</td>
<td>91:9</td>
</tr>
<tr>
<td>3</td>
<td>CO$_2$\textsuperscript{t}Bu</td>
<td>CO$_2$\textsuperscript{t}Bu</td>
<td>1c</td>
<td>7.5</td>
<td>3c</td>
<td>66(84)</td>
<td>95:5</td>
</tr>
<tr>
<td>4</td>
<td>CO$_2$Et</td>
<td>Ac</td>
<td>1d</td>
<td>2</td>
<td>3d</td>
<td>57(75)</td>
<td>80:20</td>
</tr>
<tr>
<td>5</td>
<td>Ac</td>
<td>Ac</td>
<td>1e</td>
<td>2</td>
<td>3e</td>
<td>(20)\textsuperscript{b}</td>
<td>N.D.\textsuperscript{c}</td>
</tr>
<tr>
<td>6</td>
<td>CO$_2$\textsuperscript{t}Bu</td>
<td>H</td>
<td>1f\textsuperscript{d}</td>
<td>5</td>
<td>3f</td>
<td>85</td>
<td>91:9</td>
</tr>
<tr>
<td>7</td>
<td>H</td>
<td>CO$_2$\textsuperscript{t}Bu</td>
<td>1g</td>
<td>5</td>
<td>3f</td>
<td>44</td>
<td>85:15</td>
</tr>
</tbody>
</table>

\textsuperscript{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. \textsuperscript{b} Furan derivative 4 was obtained in 6% yield. \textsuperscript{c} Not determined. \textsuperscript{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
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 ($E = \text{CO}_2\text{Et}$)

![Scheme 2](image)

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 $\pi$-allyl(oxa-$\pi$-allyl)nickel$^{10}$ I. Transmetalation then occurs to yield $\pi$-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 H$_2$O are not clear at this point according to this mechanism.
Another mechanism (path B) that involves a formation of alkoxy nickel 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).

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 would be slow, thereby competing with side reactions.
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 Cu(OTf)$_2$ 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

\[
\begin{align*}
3a (E/Z = 94/6) & \quad 1a \\
\text{PhCHO (1.2 equiv)} & \quad \text{Cu(OTf)$_2$ (10 mol$\%$)} \\
\text{toluene, r.t.} & \quad 91\%, \text{anti/syn} = 95/5 \quad E = \text{CO$_2$Et} \\
7 & \quad \text{one-pot} \\
3a (E/Z = 94/6) & \quad \text{PhCHO (1.2 equiv)} \\
& \quad \text{Cu(OTf)$_2$ (10 mol$\%$)} \\
& \quad \text{toluene, r.t.} \\
& \quad 79\%, \text{anti/syn} = 94/6
\end{align*}
\]
Experimental Section

Instrumentation and Chemicals

$^1$H 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 $^1$H 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 60F$_{254}$. 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. 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

Ni(cod)$_2$ (2.8 mg, 0.010 mmol) and K$_3$PO$_4$•3H$_2$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
Vinylcyclopropane \textbf{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 \textbf{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 \textbf{7} (53 mg, 0.16 mmol, antilsyn = 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, $E/Z = 94/6$)

\[
\text{IR (neat) 2981, 2936, 1717, 1436, 968, 852, 675 cm}^{-1}; \quad \text{\textsuperscript{1}H NMR (CDCl$_3$)} \delta 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); \quad \text{\textsuperscript{13}C NMR (CDCl$_3$) for major isomer, } \delta 14.04, 24.69, 31.94, 52.33, 61.16, 83.14, 125.68, 128.56, 169.02. \quad \text{The signal for}
the carbon which is attached to the boron atom was not observed. Found: C, 60.02; H, 8.59%. Calcd for C_{17}H_{20}O_{6}B: 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)**

\[
\begin{align*}
\text{IR (neat) } & 2935, 1733, 1436, 1336, 1150, 983, 852, 675 \text{ cm}^{-1}; \quad ^{1}H \text{ NMR (CDCl}_{3} \text{) } \delta 1.23 (s, 12H), 1.62 (d, J = 7.5 \text{ Hz}, 0.91\times2H), 1.70 (d, J = 7.5 \text{ Hz}, 0.09\times2H), 2.57 (dd, J = 8.0, 7.0 \text{ Hz}, 0.91\times2H), 2.64 (dd, J = 7.5, 6.5 \text{ Hz}, 0.09\times2H), 3.40 (t, J = 8.0 \text{ Hz}, 1H), 3.72 (s, 6H), 5.33 (dt, J = 15.5, 7.0 \text{ Hz}, 1H), 5.58 (dt, J = 15.5, 7.5 \text{ Hz}, 1H); \quad ^{13}C \text{ NMR (CDCl}_{3} \text{) for major isomer, } \delta 24.75, 32.05, 52.11, 52.38, 83.22, 125.50, 128.86, 169.45. \quad \text{The signal for the carbon which is attached to the boron atom was not observed. Found: C, 57.71; H, 8.07%. Calcd for C_{15}H_{25}O_{6}B: C, 57.98; H, 7.96%}.
\end{align*}
\]

**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)

\[
\begin{align*}
\text{IR (neat) } & 2979, 2934, 1729, 1370, 1330, 1148, 851, 675 \text{ cm}^{-1}; \quad ^{1}H \text{ NMR (CDCl}_{3} \text{) } \delta 1.22 (s, 12H), 1.43 (s, 18H), 1.62 (d, J = 7.5 \text{ Hz}, 0.95\times2H), 1.70 (d, J = 7.5 \text{ Hz}, 0.05\times2H), 2.47 (dd, J = 8.0, 7.0 \text{ Hz}, 0.95\times2H), 2.52 (dd, J = 8.5, 7.5 \text{ Hz}, 0.05\times2H), 3.13 (t, J = 7.5 \text{ Hz}, 1H), 5.33 (dt, J = 15.5, 7.0 \text{ Hz}, 1H), 5.58 (dt, J = 15.5, 7.5 \text{ Hz}, 1H); \quad ^{13}C \text{ NMR (CDCl}_{3} \text{) for major isomer, } \delta 24.75, 32.05, 52.11, 52.38, 83.22, 125.50, 128.86, 169.45. \quad \text{The signal for the carbon which is attached to the boron atom was not observed. Found: C, 57.71; H, 8.07%. Calcd for C_{15}H_{25}O_{6}B: C, 57.98; H, 7.96%}.
\end{align*}
\]
Hz, 1H), 5.54 (dt, $J = 15.5, 8.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) for major isomer, $\delta$ 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 C$_{21}$H$_{37}$O$_6$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$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.22 (s, 12H), 1.25 (t, $J = 7.0$ Hz, 3H), 1.61 (d, $J = 7.0$ Hz, 0.80×2H), 1.69 (dd, $J = 6.5, 6.0$ Hz, 0.20×2H), 2.20 (s, 0.80×3H), 2.22 (s, 0.20×3H), 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, $\delta$ 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 C$_{16}$H$_{27}$O$_5$B: C, 61.74; H, 8.94%.

$\text{t}er$t-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$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.24 (s, 12H), 1.43 (s, 9H), 1.63 (d, $J = 7.0$ Hz, 0.91×2H), 1.64 (d, $J = 8.0$ Hz, 0.09×2H), 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 C$_{16}$H$_{29}$O$_4$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)**

![3h](image)

IR (neat) 2980, 2934, 1733, 1436, 1336, 1149, 983, 852, 675 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.23 (s, 12H), 1.25 (t, J = 7.5 Hz, 6H), 1.65 (s, 0.76×2H), 1.67 (s, 0.76×3H), 1.69 (s, 0.24×2H), 1.71 (s, 0.24×3H), 2.59 (dd, J = 7.5, 7.0 Hz, 2H), 3.32 (t, J = 7.5 Hz, 0.76×1H), 3.37 (t, J = 8.0 Hz, 0.24×1H), 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 [M+H]$^+$; Calcd for C$_{18}$H$_{32}$O$_6$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)**

![3i](image) + ![3j](image)

IR (neat) 2979, 2935, 1733, 1448, 1145, 1038, 969, 852, 669 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.02 (d,
J = 8.0 Hz, 0.45×3H), 1.21 (s, 0.45×12H), 1.25 (s, 0.55×12H), 1.23–1.27 (m, 6H), 1.64 (dd, J = 6.0, 1.0 Hz, 0.55×3H), 1.73 (dt, J = 11.5, 6.0 Hz, 0.55×1H), 1.80 (dq, J = 8.0, 7.5 Hz, 0.45×1H), 1.92–1.98 (m, 0.55×1H), 2.08–2.14 (m, 0.55×1H), 2.58 (dd, J = 7.5, 6.5 Hz, 0.45×2H), 3.35 (t, J = 7.5 Hz, 0.45×1H), 3.44 (dd, J = 8.5, 6.5 Hz, 0.55×1H), 4.14–4.20 (m, 4H), 5.25–5.34 (m, 1H), 5.40 (dq, J = 15.5, 6.0 Hz, 0.55×1H), 5.61 (dd, J = 15.5, 8.0 Hz, 0.45×1H); $^{13}$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$_6$B: 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$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.19–1.26 (m, 6H), 1.79 (dd, 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, 0.06×1H), 2.37–2.42 (m, 0.94×1H), 3.34 (dd, J = 10.0, 5.0 Hz, 1H), 4.11–4.16 (m, 4H), 4.50 (d, J = 6.0 Hz, 0.94×1H), 4.62 (d, J = 6.0 Hz, 0.06×1H), 4.99 (d, J = 17.5 Hz, 0.06×1H), 5.09 (d, J = 10.0 Hz, 0.06×1H), 5.15 (d, J = 17.0 Hz, 0.94×1H), 5.27 (d, J = 10.0 Hz, 0.94×1H), 5.51 (ddd, J = 17.5, 10.5, 10.0 Hz, 0.06×1H), 5.64 (ddd, J = 17.0, 10.0, 9.5 Hz, 0.94×1H), 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$_{25}$O$_5$: C, 67.33; H, 7.57%.
References and Notes


(9) In the absence of 2, treatment of 1a under the nickel catalysis at room temperature resulted in recovery of 1a.


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.\textsuperscript{1} Although many examples of borylation of unsaturated C–C bonds catalyzed by Pt,\textsuperscript{2} Pd,\textsuperscript{3} Rh,\textsuperscript{4} Cu,\textsuperscript{5} and Au\textsuperscript{6} are known, there are few examples of borylation catalyzed by nickel complexes.\textsuperscript{7}

In Chapter 1, the author has described nickel-catalyzed borylative ring opening reaction of vinylcyclopropanes.\textsuperscript{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).\textsuperscript{9}

**Scheme 1.**

![Scheme 1](image)

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.\textsuperscript{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 H\textsubscript{2}O in toluene/MeOH afforded the corresponding 4-oxoalkylboronate 3a in 47% yield (Table 1, entry 1). Tri-\textit{tert}-butylphosphine was inferior to tricyclohexylphosphine (entry 2). When \textit{N}-heterocyclic carbene ligands were applied to this reaction, the results were improved. Among the carbene ligands, IMes•HCl\textsuperscript{10} 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).

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

Table 1. Optimization of Reaction Conditions

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst (mol%)</th>
<th>ligand (mol%)</th>
<th>base</th>
<th>Yield (%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ni(cod)2 (10)</td>
<td>P(oczH11)3 (20)</td>
<td>NaOH</td>
<td>47</td>
</tr>
<tr>
<td>2</td>
<td>Ni(cod)2 (10)</td>
<td>P3Bu3 (20)</td>
<td>NaOH</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>Ni(cod)2 (10)</td>
<td>IPr•HCl (12)</td>
<td>NaOH</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>Ni(cod)2 (10)</td>
<td>IMes•HCl (12)</td>
<td>NaOH</td>
<td>49</td>
</tr>
<tr>
<td>5</td>
<td>Pd(OAc) (10)</td>
<td>P(oczH11)3 (20)</td>
<td>NaOH</td>
<td>33b</td>
</tr>
<tr>
<td>6</td>
<td>Pd(OAc) (10)</td>
<td>IMes•HCl (12)</td>
<td>NaOH</td>
<td>27b</td>
</tr>
<tr>
<td>7</td>
<td>Ni(cod)2 (10)</td>
<td>IMes•HCl (12)</td>
<td>NaOH</td>
<td>77c</td>
</tr>
<tr>
<td>8</td>
<td>Ni(cod)2 (10)</td>
<td>IMes•HCl (12)</td>
<td>MeOK</td>
<td>88c</td>
</tr>
<tr>
<td>9</td>
<td>Ni(cod)2 (5)</td>
<td>IMes•HCl (6)</td>
<td>MeOK</td>
<td>92c,d</td>
</tr>
</tbody>
</table>

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.
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**

<table>
<thead>
<tr>
<th>entry</th>
<th>Ar</th>
<th>product</th>
<th>temp. (°C)</th>
<th>Yield (%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4-MeC₆H₄ (1b)</td>
<td>3b</td>
<td>50</td>
<td>79</td>
</tr>
<tr>
<td>2</td>
<td>4-MeOC₆H₄ (1c)</td>
<td>3c</td>
<td>40</td>
<td>88</td>
</tr>
<tr>
<td>3</td>
<td>4-FC₆H₄ (1d)</td>
<td>3d</td>
<td>50</td>
<td>79</td>
</tr>
<tr>
<td>4</td>
<td>2-naphthyl (1e)</td>
<td>3e</td>
<td>50</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>2-furyl (1f)</td>
<td>3f</td>
<td>40</td>
<td>54b</td>
</tr>
<tr>
<td>6</td>
<td>2-MeC₆H₄ (1g)</td>
<td>3g</td>
<td>70</td>
<td>16bc</td>
</tr>
</tbody>
</table>

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, 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’s and Montgomery’s groups. 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 alkynickel 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. The roles of MeOH and H2O are not clear at this point.

Another mechanism (path B) that involves a formation of alkoxynickel intermediate III by protonolysis of I with MeOH may also operate as shown in Chapter 1. In this mechanism, transmetalation between III and diboron 2 could easily occur to provide alkynickel intermediate II’ (path B).
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% Pd(OAc)$_2$, 10 mol% RuPhos (2-dicyclohexylphosphino-2',6'-diisopropoxy-1,1'-biphenyl), and K$_2$CO$_3$ in toluene/H$_2$O at 80 °C$^{18}$ to provide the cross-coupling product 4 in 74% yield.
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.\textsuperscript{9b} The procedure was applicable to the reduction of 3h. Treatment of boronate 3h with BH\textsubscript{3}•THF as a reductant followed by oxidation and esterification afforded the corresponding diester 5 in 74\% yield with high diastereoselectivity (Scheme 5).

\textbf{Scheme 5. Diastereoselective Reduction of 3h}

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{Ph} & \quad \text{Ph} \\
3\text{h} & \quad \text{BH}_3 \cdot \text{THF} \\
\text{THF, – 80 °C} & \\
\text{2.0 M NaOH} & \quad \text{Ac}_2\text{O}, \text{Et}_3\text{N} \\
30\% \text{H}_2\text{O}_2 & \quad \text{CH}_2\text{Cl}_2, \text{r.t.}
\end{align*}
\]

\[
\begin{array}{c}
\text{favored} \\
\text{disfavored} \\
\end{array}
\]

\[
\begin{align*}
\text{Ph} & \quad \text{OAc} \\
\text{Ph} & \quad \text{Ph} \\
\text{OAc} & \quad \text{OAc} \\
5 \ (74\%, \ dr = 92/8)
\end{align*}
\]
**Experimental Procedure**

**Instrumentation and Chemicals**

$^1$H 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 ($\delta$) are in parts per million relative to tetramethylsilane at 0.00 ppm for $^1$H 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 60F$_{254}$. 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 H$_2$O (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$_2$O (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$_2$CO$_3$ (83 mg, 0.60 mmol), Pd(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$_2$O (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. BH$_3$•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$_2$O$_2$ aq. (0.20 mL, 2.0 mmol). The resulting mixture was extracted with Et$_2$O (3 × 2 mL), and the solvent was removed in vacuo to

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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)

![Diagram of 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)

![Diagram of 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, 8.56%.
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\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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 C\(_{17}\)H\(_{25}\)O\(_4\)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\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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 C\(_{16}\)H\(_{23}\)O\(_3\)FB: 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\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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); \(^1^3\)C NMR (CDCl\(_3\)) \(\delta\) 19.5, 24.8, 44.6, 83.1, 124.4, 125.9, 126.3, 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 [M]+; Calcd for C\(_{20}\)H\(_{25}\)O\(_3\)B: 324.1897. Mp: 45–47 °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\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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); \(^1^3\)C NMR (CDCl\(_3\)) \(\delta\) 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 [M]+; Calcd for C\(_{14}\)H\(_{21}\)O\(_3\)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\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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); 13C NMR (CDCl₃) 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 C₄₂H₂₇O₃B: 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 (CDCl₃) δ 0.83 (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); 13C NMR (CDCl₃) 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. HRMS (EI) Found 288.1899 [M]⁺; Calcd for C₁₇H₂₅O₃B: 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 (CDCl₃) 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); 13C NMR (CDCl₃) 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 C\textsubscript{17}H\textsubscript{25}O\textsubscript{3}B: C, 70.85; H, 8.74%.

**Potassium (3-Benzoylpropyl)trifluoroborate (3k)**

![Chemical Structure](image)

IR (nujol) 2854, 1685, 1448, 1377, 1364, 1015 cm\(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\)) \(\delta\) 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); \(^{13}\)C NMR (DMSO-\(d_6\)) \(\delta\) 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 C\textsubscript{10}H\textsubscript{11}OBF\textsubscript{3}K: C, 47.27; H, 4.36%. Mp: 193–197 °C.

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

![Chemical Structure](image)

IR (nujol) 2923, 2855, 1684, 1448, 1377, 1245, 1033, 745 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 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 C\textsubscript{17}H\textsubscript{18}O\textsubscript{2}: C, 80.28; H, 7.13%. Mp: 43–44 °C.

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

![Chemical Structure](image)

IR (neat) 1740, 1496, 1455, 1369, 1236, 1033, 701 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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 $\delta$ 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 C$_{20}$H$_{22}$O$_4$: C, 73.60; H, 6.79%. The 
relative stereochemistry was assigned according to the literature.$^9b$
References and Notes


(11) A 78% isolated yield of 3a was obtained in larger scale (5 mmol of 1a).


(14) When 10 mol% of MeOK was used to generate carbene ligand, an 11% NMR yield of 3a was observed.

(15) When MeOH was not used, the yield of 3a was only 33% (NMR yield).


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 \(\alpha,\beta\)-unsaturated carbonyl compounds is one of the most powerful methods to synthesize silyl enolates. Although some examples of 1,4-hydrosilylation of \(\alpha,\beta\)-unsaturated carbonyl compounds catalyzed by Rh,\(^2\) Pt,\(^3\) Cu,\(^4\) and B(C\(_6\)F\(_5\))\(_3\)\(^5\) 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 hydrosilylalanes (eq 2).

**Scheme 1. Ring Opening Reaction of Cyclopropyl Ketones**

**Chapter 2**

\[
\begin{align*}
\text{Ni}^0 \text{ cat.} & \quad \xrightarrow{\text{Oxidative Cyclization}} \\
\text{Ni}^{\text{III}} & \quad \xrightarrow{\text{B}_3\text{pin}_2} \\
\text{H} & \quad \xrightarrow{\text{H}^\oplus} \\
\text{Bpin} & \quad (1)
\end{align*}
\]

**Author's initial hypothesis**

\[
\begin{align*}
\text{Pd}^0 \text{ cat.} & \quad \xrightarrow{\text{Oxidative Cyclization}} \\
\text{Pd}^{\text{III}} & \quad \xrightarrow{\text{R}_3\text{SiH}} \\
\text{SiR}_3 & \quad (2)
\end{align*}
\]

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.**

\[
\text{Ph} - \text{C} - \text{H} + \text{BuMe}_2\text{SiH} \xrightarrow{\text{cat. Pd(OAc)}_2, \text{cat. } \text{P}^{(c_6\text{H}_{11})_3} \text{, cat. MeOH}} \text{toulene, 60 °C} \rightarrow \text{OSiMe}_2\text{Bu}
\]

**Results and Discussion**

Treatment of cyclopropyl phenyl ketone (1a) with 'BuMe₂SiH in the presence of a palladium/tricyclohexylphosphine catalyst and a small amount of MeOH as an additive in toluene at 60 °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**

\[
\text{Ph} - \text{C} - \text{H} + \text{BuMe}_2\text{SiH} \xrightarrow{\text{Pd(OAc)}_2 (10 \text{ mol}) \text{, P}^{(c_6\text{H}_{11})_3} (20 \text{ mol}) \text{, MeOH (25 mol)}} \text{toulene, 60 °C, 10 h} \rightarrow \text{OSiMe}_2\text{Bu}
\]

93% (Z/E = 99/1)

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 Et₃SiH 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 Et₃SiH instead of 'BuMe₂SiH yielded 2e 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). In the reactions of alkyl cyclopropyl ketones 1e and 1f, 'BuMe₂SiH was more reactive than Et₃SiH. Benzyl cyclopropyl ketone (1f) was transformed to the corresponding enolate 2i, which is difficult to synthesize by using known methods. In all cases, silyl enolates were prepared with high Z selectivity.
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).
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. Although the release of 3d and palladium(0) might be possible, they could be converted smoothly to the five membered oxapalladacycle intermediate III reversibly. 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, it might be relatively slow.
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.\textsuperscript{13}

In 1999, Slough et al. reported a rhodium-catalyzed hydrosilylation of cyclopropyl phenyl ketones with Et\textsubscript{3}SiH.\textsuperscript{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 Et\textsubscript{3}SiH 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 \textsuperscript{1}BuMe\textsubscript{2}SiH 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 PhMe\textsubscript{2}SiH, an excellent yield of the corresponding product 2r was obtained (entry 9). While the reaction with Et\textsubscript{3}SiH gave 2s smoothly (entry 10), no reaction took place with Pr\textsubscript{3}SiH (entry 11).
Table 2. Scope of \(\alpha,\beta\)-Unsaturated Ketones

\[
\text{R} \quad \text{C} = \text{O} \quad \text{R}'
\]

\[
\text{3} \quad + \quad \text{Si-H}
\]

\[
\text{Pd(OAc)}_2 (5.0 \text{ mol\%}) \quad \text{P}^{(\text{C}_6\text{H}_{11})}_3 (10 \text{ mol\%})
\]

toluene, 60 °C, 10 h

| entry | 3          | Si           | 2    | Yield (%)
|-------|------------|--------------|------|-----------
| 1     | Ph \quad \text{C} = \text{O} \quad \text{Ph} 3a | \text{tBuMe}_2\text{Si} | 2k   | 94 \(^b\)
| 2     | Ph \quad \text{C} = \text{C} \quad \text{Ph} \quad \text{OMe} \quad \text{3b} | \text{tBuMe}_2\text{Si} | 2l   | 77        
| 3     | Ph \quad \text{C} = \text{O} \quad \text{CF}_3 \quad \text{3c} | \text{tBuMe}_2\text{Si} | 2m   | 71        
| 4     | Ph \quad \text{C} = \text{O} | \text{tBuMe}_2\text{Si} | 2a   | 65        
| 5     | \text{R} \quad \text{C} = \text{C} \quad \text{C}_3\text{H}_7 | \text{tBuMe}_2\text{Si} | 2n   | 95 \(^c\) 
| 6     | \text{C}_5\text{H}_{11} \quad \text{C} = \text{O} | \text{tBuMe}_2\text{Si} | 2o   | 92        
| 7     | \text{CF}_3 \quad \text{C} = \text{O} \quad \text{C}_3\text{H}_7 \quad \text{3g} | \text{tBuMe}_2\text{Si} | 2p   | 99        
| 8     | \text{O} \quad \text{C} = \text{C} \quad \text{C}_3\text{H}_7 \quad \text{3h} | \text{tBuMe}_2\text{Si} | 2q   | 50 \(^d\) 

\(^a\) Isolated yields after chromatography.

\(^b\) Reaction time: 10 h.

\(^c\) Reaction time: 20 h.

\(^d\) Reaction time: 12 h.
In contrast to the reactions of acyclic ketones, the reaction of 2-cyclohexenone with 'BuMe₂SiH 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.

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-hydopalladation, 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

$^1$H 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 $^1$H 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 60F$_{254}$. 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. Triethysilane, 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 $\alpha,\beta$-Unsaturated Ketones or Cyclopropyl Ketones with Hydrosilanes

Synthesis of 2a

Pd(OAc)$_2$ (5.6 mg, 0.025 mmol) and P($^5$C$_{6}$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), $^t$BuMe$_2$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 \textbf{2a} (122 mg, 0.47 mmol) in 93\% yield.

\textbf{Synthesis of 2k}

Pd(OAc)$_2$ (5.6 mg, 0.025 mmol) and P(C$_6$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 \degree C, the resulting solution was stirred for 10 min. Chalcone (3a, 104 mg, 0.50 mmol) and tBuMe$_2$SiH (0.16 mL, 1.0 mmol) were then added. The mixture was allowed to warm to 60 \degree 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 \textbf{2k} (152 mg, 0.47 mmol) in 94\% yield.

\textbf{Characterization Data}

\textbf{(Z)-1-tert-Butyldimethylsiloxy-1-phenyl-1-butene (2a)}

\begin{center}
\begin{tikzpicture}
\draw[thick] (0,0) -- (0.5,0.8) -- (1,0) -- (0.5,-0.8) -- cycle;
\draw[thick] (1,0) -- (1.5,1.2) node[above] {Ph};
\draw[thick] (1,0) -- (1.5,-1.2);\node[above] at (1,0) {\text{O}\text{SiMe}_2\text{Bu}};
\end{tikzpicture}
\end{center}

IR (neat) 2932, 2859, 1680, 1379, 1345, 1295, 1254, 1119, 1050, 1005, 909 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ –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$_3$) $\delta$ 14.2, 18.3, 19.5×2, 25.9, 113.8, 125.8, 127.3, 127.9, 139.8, 148.7. Found 262.1754 [M$^+$]; Calcd for C$_{16}$H$_{30}$OSi: 262.1753.

\textbf{(Z)-1-(4-Methylphenyl)-1-triethylsiloxy-1-butene (2b)}

\begin{center}
\begin{tikzpicture}
\draw[thick] (0,0) -- (0.5,0.8) -- (1,0) -- (0.5,-0.8) -- cycle;
\draw[thick] (1,0) -- (1.5,1.2) node[above] {\text{O}\text{SiEt}_3};
\draw[thick] (1,0) -- (1.5,-1.2);
\end{tikzpicture}
\end{center}

IR (neat) 2960, 2914, 2877, 1649, 1510, 1458, 1413, 1340, 1278, 876, 813 cm$^{-1}$; $^1$H NMR
(CDCl$_3$) 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); $^1$C NMR (CDCl$_3$) δ 5.3, 6.7, 14.3, 19.4, 21.1, 125.4, 128.6, 136.9, 137.0, 148.8. HRMS (EI) Found 276.1906 [M$^+$]; Calcd for C$_{17}$H$_{28}$O: 276.1909.

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

IR (neat) 2836, 1649, 1609, 1459, 1341, 1292, 1174, 909 cm$^{-1}$; $^1$H NMR (CDCl$_3$) 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); $^1$C NMR (CDCl$_3$) 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 C$_{17}$H$_{28}$O$_2$Si: 292.1859

(Z)-4-(1-Triethoxysiloxy-1-butene)benzoic acid, ethyl ester (2d)

IR (neat) 2878, 1642, 1609, 1459, 1409, 1177, 911, 863, 708 cm$^{-1}$; $^1$H NMR (CDCl$_3$) 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); $^1$C NMR (CDCl$_3$) 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 C$_{19}$H$_{30}$O$_3$Si: 334.1965.
(Z)-1-Phenyl-1-triethylsiloxyl-1-butene (2e)

IR (neat) 2960, 2913, 1649, 1341, 1075, 1006, 872, 729 cm⁻¹; ¹H NMR (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₁₆H₂₆O₃Si: 262.1753.

(Z)-2-tert-Butyldimethylsiloxyl-2-pentene (2g)

IR (neat) 2931, 2859, 1680, 1379, 1345, 1295, 1253, 1118, 1050, 1005, 909 cm⁻¹; ¹H NMR (CDCl₃) δ 0.13 (s, 3H), 0.123 (s, 3H), 0.92 (t, J = 7.5 Hz, 3H), 0.95 (s, 9H), 1.76 (s, 3H), 1.97–2.04 (m, 2H), 4.39 (t, J = 8.5 Hz, 1H); ¹³C NMR (CDCl₃) 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 C₁₁H₂₄OSi: 200.1596.

(Z)-2-tert-Butyldimethylsiloxyl-1-phenyl-2-pentene (2i)

IR (neat) 2857, 1674, 1496, 1362, 1254, 1112, 1074, 1031, 906 cm⁻¹; ¹H NMR (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₁₇H₂₈OSi: 276.1910.
(Z)-1,4-Diphenyl-1-triethylsiloxyl-1-butene (2j) and (Z)-1,3-Diphenyl-1-triethylsiloxyl-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 (CDCl₃) δ 0.60 (q, J = 8.0 Hz, 6H), 0.93 (t, J = 8.0 Hz, 9H), 1.41 (d, J = 7.0 Hz, 0.06×3H), 2.56 (dt, J = 7.5, 8.5 Hz, 0.94×2H), 2.76 (t, J = 8.5 Hz, 0.94×2H), 4.06 (dq, J = 7.0, 9.5 Hz, 0.06×1H), 5.17 (t, J = 7.5 Hz, 0.94×1H), 5.29 (d, J = 9.5 Hz, 0.06×1H), 7.19–7.26 (m, 4H), 7.26–7.33 (m, 4H), 7.45 (d, J = 7.5 Hz, 2H); ¹³C NMR for 2j (CDCl₃) 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 C₂₂H₃₀OSi: 338.2066.

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

IR (neat) 2930, 2857, 1647, 1493, 1390, 1254, 1006, 939, 668 cm⁻¹; ¹H NMR (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₂₁H₂₈OSi: 324.1909.

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

IR (neat) 2930, 2857, 1647, 1512, 1259, 1096, 781 cm⁻¹; ¹H NMR (CDCl₃) 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), 7.19–7.33 (m, 7H), 7.48 (d, J = 7.5 Hz, 2H).
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\(_3\)) \(\delta\) –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 C\(_{22}\)H\(_{30}\)O\(_2\)Si: 354.2015.

\((Z)-1\text{-}\text{tert-Butyldimethysiloxy-1-phenyl-3-(4-trifluoromethylphenyl)-1-propene (2m)}\)

![Structural diagram]

IR (neat) 2958, 2932, 1648, 1619, 1285, 1164, 1041, 840, 767 cm\(^{-1}\); \(^{1}\)H NMR (CDCl\(_3\)) \(\delta\) –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\(_3\)) \(\delta\) –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\(_3\)) \(\delta\) 98.8. HRMS (EI) Found 392.1777 [M⁺]; Calcd for C\(_{22}\)H\(_{27}\)OF\(_3\)Si: 392.1784.

\(4\text{-}(1\text{-}\text{tert-Butyldimethysiloxy-1-hexenyl)-benzoic acid, methyl ester (2n, a 96/4 mixture of Z/E isomers)}\)

![Structural diagram]

IR (neat) 2931, 2858, 1649, 1463, 1341, 1299, 1258, 1060, 906 cm\(^{-1}\); \(^{1}\)H NMR (CDCl\(_3\)) \(\delta\) –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 \(\delta\) –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 $C_{20}H_{32}O_3$Si: 348.2121.

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

\[
\text{IR (neat) 2929, 2857, 1679, 1463, 1378, 1253, 1004, 940, 809, 778 cm^{-1}; } \]
\[
\text{$^1$H NMR (CDCl$_3$) } \delta \text{ 0.13 (s, 6H), 0.88 (t, } J = 7.0 \text{ Hz, 3H), 0.95 (s, 9H), 1.24–1.30 (m, 8H), 1.76 (s, 3H), 1.95–2.01 (m, 2H), 4.40 (t, } J = 7.5 \text{ Hz, 1H); } \]
\[
\text{$^{13}$C NMR (CDCl$_3$) } \delta \text{ -3.9, 14.1, 18.2, 22.7, 22.8, 25.4, 25.8, 29.2, 29.9, 31.8, 108.8, 146.4. } \]
\[
\text{HRMS (EI) Found 256.2231 [M$^+$]; Calcd for } C_{15}H_{30}Si: 256.2222. \]

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

\[
\text{IR (neat) 2930, 2858, 1644, 1435, 1340, 1234, 1199, 1005, 977 cm^{-1}; } \]
\[
\text{$^1$H NMR (CDCl$_3$) } \delta \text{ 0.078 (s, 3H), 0.079 (s, 3H), 0.93 (t, } J = 7.0 \text{ Hz, 3H), 1.01 (s, 9H), 1.34–1.42 (m, 4H), 2.17 (dt, } J = 7.0, 7.5 \text{ Hz, 2H), 5.17 (t, } J = 7.0 \text{ Hz, 1H), 6.92 (dd, } J = 3.5, 5.0 \text{ Hz, 1H), 7.03 (d, } J = 3.5 \text{ Hz, 1H), 7.11 (d, } J = 5.0 \text{ Hz, 1H); } \]
\[
\text{$^{13}$C NMR (CDCl$_3$) } \delta \text{ -3.9, 14.0, 18.4, 22.5, 25.8, 25.9, 31.8, 111.8, 123.2, 123.5, 126.8, 143.6, 143.7. } \]
\[
\text{HRMS (EI) Found 296.1627 [M$^+$]; Calcd for } C_{16}H_{28}OSiS: 296.1631. \]

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

\[
\text{IR (neat) 2930, 2858, 1736, 1649, 1567, 1338, 1258, 1005, 875 cm^{-1}; } \]
\[
\text{$^1$H NMR (CDCl$_3$) } \delta \text{ -0.05 \text{ ppm.} } \]
(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 = 7.6 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); 13C NMR (CDCl3) 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 C17H29O3Si: 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 (CDCl3) 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); 13C NMR (CDCl3) δ = 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 C23H24O3Si: 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 (CDCl3) 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); 13C NMR (CDCl3) 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 C21H24OSi: C, 77.72; H, 8.70%.
References and Notes


(9) Et₃SiD were obtained according to the literature procedure: Caseri, W.; Pregosin, P. S. J. Organomet. Chem. 1988, 356, 259–269.


(11) In the absence of triethylsilane, Pd-catalyzed isomerization of cyclopropyl ketone to
α,β-unsaturated ketone indeed took place although the resulting α,β-unsaturated ketone immediately underwent dimerization in situ as reported previously (ref. 7).


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 $sp^3$C–$sp^3$C 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 \(sp^3\)–\(sp^3\)C bonds is still difficult due to their stability as well as the high directionality of the \(\sigma\)-orbital of an \(sp^3\)–\(sp^3\)C bonds. Several noteworthy examples of cleavage of unstrained \(sp^3\)C–\(sp^3\)C bonds under transition metal catalysis were so far reported. Among them, \(\beta\)-carbon elimination\(^3\) and retro-allylation\(^{1g,4}\) from metal alkoxides has been well exploited. Another efficient method to cleave \(sp^3\)C–\(sp^3\)C bonds utilizes highly stabilized carbanions including \(\beta\)-dicarbonyl enolates\(^5\) and cyclopentadienyl anions\(^6\) 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 arylation 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)\(_2\)/2PPh\(_3\) 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 complex\(^7\) 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 (vid infra).\(^8\) Alternatively, it might promote transmetalation between nickel and organozinc complexes.\(^9\) Divalent nickel complexes, such as \( \text{NiBr}_2(\text{PPh}_3)_2 \) and \( \text{Ni(acac)}_2/2\text{PPPh}_3 \), 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**

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>PhZn</th>
<th>additive</th>
<th>Yield (%)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ni((\text{cod})_2/2\text{PPPh}_3)</td>
<td>PhZn(<del>\text{Br}</del>)</td>
<td>none</td>
<td>75(^c,d)</td>
</tr>
<tr>
<td>2</td>
<td>Ni((\text{cod})_2/2\text{PPPh}_3)</td>
<td>PhZn(<del>\text{Br}</del>)</td>
<td>none</td>
<td>96</td>
</tr>
<tr>
<td>3</td>
<td>Ni((\text{cod})_2/2\text{PPPh}_3)</td>
<td>PhZn(<del>\text{L}</del>\text{iCl}~)</td>
<td>none</td>
<td>11(^d)</td>
</tr>
<tr>
<td>4</td>
<td>Ni((\text{cod})_2/2\text{PPPh}_3)</td>
<td>PhZn(<del>\text{L}</del>\text{iCl}~)</td>
<td>Mg\text{Br}_2</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>( \text{NiBr}_2(\text{PPh}_3)_2 )</td>
<td>PhZn(<del>\text{L}</del>\text{iCl}~)</td>
<td>Mg\text{Br}_2</td>
<td>89</td>
</tr>
<tr>
<td>6</td>
<td>( \text{Ni(acac)}_2/2\text{PPPh}_3 )</td>
<td>PhZn(<del>\text{L}</del>\text{iCl}~)</td>
<td>Mg\text{Br}_2</td>
<td>89</td>
</tr>
<tr>
<td>7</td>
<td>( \text{PdCl}_2(\text{PPh}_3)_2 )</td>
<td>PhZn(<del>\text{L}</del>\text{iCl}~)</td>
<td>Mg\text{Br}_2</td>
<td>12(^d)</td>
</tr>
<tr>
<td>8</td>
<td>( \text{Pd(PPh}_3)_4 )</td>
<td>PhZn(<del>\text{L}</del>\text{iCl}~)</td>
<td>Mg\text{Br}_2</td>
<td>26(^d)</td>
</tr>
<tr>
<td>9</td>
<td>( \text{CoCl}_2(\text{PPh}_3)_2 )</td>
<td>PhZn(<del>\text{L}</del>\text{iCl}~)</td>
<td>Mg\text{Br}_2</td>
<td>0(^d)</td>
</tr>
</tbody>
</table>

\(^a\) Isolated yields. \(^b\) Prepared from Ph\text{MgBr} and Zn\text{Br}_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

<table>
<thead>
<tr>
<th>entry</th>
<th>1</th>
<th>R'Zn</th>
<th>time (h)</th>
<th>2</th>
<th>Yield (%)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>EtO₂C</td>
<td>4-MeC₆H₄Zn⁺LiCl</td>
<td>30</td>
<td>2b</td>
<td>82</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>4-MeOC₆H₄Zn⁺LiCl</td>
<td>30</td>
<td>2c</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>1a</td>
<td>2-MeC₆H₄ZnBrᵇ</td>
<td>8</td>
<td>2d</td>
<td>93(45ᶜ)</td>
</tr>
<tr>
<td>4</td>
<td>1a</td>
<td>4-FC₆H₄Zn⁺LiCl</td>
<td>30</td>
<td>2e</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>1a</td>
<td>4-EtO₂CC₆H₄Zn⁺LiCl</td>
<td>30</td>
<td>2f</td>
<td>59</td>
</tr>
<tr>
<td>6</td>
<td>1a</td>
<td>CH₂=C(Ph)Zn⁺LiCl</td>
<td>30</td>
<td>2g</td>
<td>66</td>
</tr>
</tbody>
</table>
The pathway involves a \( \text{crotyl} \) and stereoisomers (entry 2).

![Table 3]

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 methyImalonate (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**

![Scheme 1 diagram]

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 \( \pi \)-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**

<table>
<thead>
<tr>
<th>entry</th>
<th>3</th>
<th>product 4</th>
<th>yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="Structure 3b" /></td>
<td><img src="image" alt="Structure 4b" /></td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Structure 3c" /></td>
<td><img src="image" alt="Structure 4c" /></td>
<td>88&lt;br&gt;(4c/4d = 48/52&lt;sup&gt;b&lt;/sup&gt;)</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="Structure 3e" /></td>
<td><img src="image" alt="Structure 4e" /></td>
<td>quant</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="Structure 3f" /></td>
<td><img src="image" alt="Structure 4f" /></td>
<td>N.R.</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yields. <sup>b</sup> 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<sup>3</sup>C−sp<sup>3</sup>C bond and to form nickel complex 6. Transmetalation between 6 and phenylzinc reagent followed by reductive elimination<sup>10</sup> gives zinc enolate 7<sup>11</sup> and regenerate the starting nickel complex. Finally, protonolysis of the resulting zinc enolate 7 would provide 2a.
Intermediate 7 could be trapped with electrophiles (Scheme 3). After finishing the arylative ring opening, treatment of the reaction mixture with CD$_3$CO$_2$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**

$8a$: $E = D$, 81% (87% D)
$8b$: $E = $allyl, 96%

**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 $sp^3$C–$sp^3$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

$^1$H 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 $^1$H 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 60F$_{254}$. 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. NiBr$_2$(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 Ni(cod)$_2$/PPh$_3$ (Synthesis of 2a)

Ni(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$_4$Cl 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 NiBr₂(PPh₃)₂ (Synthesis of 2a)**

To a suspension of NiBr₂(PPh₃)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 NH₄Cl 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 1a¹², 1b¹³, 1c¹⁴, and 1d¹² were prepared in conventional ways according to the literature. Products 4a–d¹⁵ and 4e¹⁶ 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 (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₁₉H₂₈O₄: 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 (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₂₀H₂₈O₄: 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 (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₂₀H₂₈O₅: 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$^{-1}$; $^1$H 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 C$_{20}$H$_{28}$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$^{-1}$; $^1$H 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 C$_{19}$H$_{25}$FO$_4$: C, 67.84; H, 7.49%.

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

IR (neat) 2978, 1736, 1458, 1373, 1265, 1157, 1034 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 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).
IR (neat) 2978, 1728, 1612, 1458, 1273, 1103 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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 [M\(^+\)]; Calcd for C\(_{22}\)H\(_{30}\)O\(_6\): 390.2039.

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

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

IR (neat) 2932, 1736, 1643, 1450, 1373, 1150, 1026 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.26 (t, \(J = 7.0\) Hz, 3H), 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\(_3\)) \(\delta\) 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 C\(_{19}\)H\(_{28}\)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\(^{-1}\); \(^1\)H NMR (CD\(_2\)Cl\(_2\)) \(\delta\) 1.04 (d, \(J = 2.5\) Hz, 0.5×3H), 1.06 (d, \(J = 2.5\) Hz, 0.5×3H), 1.23 (t, \(J = 7.0\) Hz, 0.5×3H), 1.25 (t, \(J = 7.0\) Hz, 0.5×3H), 1.92–1.57 (m, 2H), 2.09 (s, 0.5×3H), 2.10 (s, 0.5×3H), 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); \(^1\)C NMR (CD\(_2\)Cl\(_2\)) \(\delta\) 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, 128.29×2, 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 [M+H]\(^+\); Calcd for C\(_{19}\)H\(_{25}\)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\(^{-1}\); \(^1\)H NMR (CD\(_2\)Cl\(_2\)) \(\delta\) 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); \(^1\)C NMR (CD\(_2\)Cl\(_2\)) \(\delta\) 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_{36}O_4: C, 73.71; H, 8.44%.
References and Notes


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. Although many allylmetal reagents are used for the allylation, rhodium-mediated carbonyl allylation is quite rare. Recently, the metal-mediated retro-allylation of homoallyl alcohols has been introduced as a useful method for generating allylmetal reagents. In Chapter 5, the author discloses a method for the generation of allylrhodium reagents from homoallyl alcohols via retro-allylation 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 [RhCl(cod)]2 (2.5 mol%), PMe3 (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 = 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, which may be in equilibrium with the π-crotylrhodium species under the reaction conditions. The allylrhodium intermediate reacts at the more substituted carbon atom with benzaldehyde to yield the rhodium homoallylooxide 5, which undergoes protonolysis with 2a to yield 3a and regenerate 4 (path A).
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.
The use of xylene as the solvent and P\textsubscript{t}Bu\textsubscript{3} as the ligand led to a drastic change in the course of the reaction. Treatment of benzaldehyde (1\textsubscript{a}, 0.5 mmol) with homoallyl alcohol 2\textsubscript{a} (1.0 mmol) in the presence of catalytic amounts of [RhCl(cod)]\textsubscript{2}, P\textsubscript{t}Bu\textsubscript{3}, and cesium carbonate in xylene at reflux for 24 h provided 2-methyl-1-phenyl-1-butanone (6\textsubscript{a}) 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>
<thead>
<tr>
<th>entry</th>
<th>Ar</th>
<th>Yield of 3 (%)</th>
<th>erythro/threo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph (1\textsubscript{a})</td>
<td>3\textsubscript{a} (58)</td>
<td>49/51</td>
</tr>
<tr>
<td>2</td>
<td>4-MeC\textsubscript{6}H\textsubscript{4} (1\textsubscript{b})</td>
<td>3\textsubscript{b} (49)</td>
<td>54/46</td>
</tr>
<tr>
<td>3</td>
<td>4-CF\textsubscript{3}C\textsubscript{6}H\textsubscript{4} (1\textsubscript{c})</td>
<td>3\textsubscript{c} (44)</td>
<td>56/44</td>
</tr>
<tr>
<td>4</td>
<td>4-MeOC\textsubscript{6}H\textsubscript{4} (1\textsubscript{d})</td>
<td>3\textsubscript{d} (34)</td>
<td>52/48</td>
</tr>
<tr>
<td>5</td>
<td>4-ClC\textsubscript{6}H\textsubscript{4} (1\textsubscript{e})</td>
<td>3\textsubscript{e} (59)</td>
<td>58/42</td>
</tr>
<tr>
<td>6</td>
<td>4-PhCOC\textsubscript{6}H\textsubscript{4} (1\textsubscript{f})</td>
<td>3\textsubscript{f} (58)</td>
<td>56/44</td>
</tr>
<tr>
<td>7\textsuperscript{a}</td>
<td>4-MeO\textsubscript{2}CC\textsubscript{6}H\textsubscript{4} (1\textsubscript{g})</td>
<td>3\textsubscript{g} (59)</td>
<td>56/44</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Cs\textsubscript{2}CO\textsubscript{3} (30 mol%) was used.

Table 1. Rhodium-Catalyzed Crotylation of Aromatic Aldehydes with 2\textsubscript{a}
Table 2. Rhodium-Catalyzed Crotylation of Aromatic Aldehydes with 2a Followed by Isomerization to Saturated Ketones

<table>
<thead>
<tr>
<th>entry</th>
<th>Ar</th>
<th>Yield of 6 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>Ph (1a)</td>
<td>6a (70)b</td>
</tr>
<tr>
<td>2</td>
<td>4-MeC₆H₄ (1b)</td>
<td>6b (49)</td>
</tr>
<tr>
<td>3c</td>
<td>4-CF₃C₆H₄ (1c)</td>
<td>6c (50)b</td>
</tr>
<tr>
<td>4</td>
<td>4-MeOC₆H₄ (1d)</td>
<td>6d (52)b</td>
</tr>
<tr>
<td>5</td>
<td>4-ClC₆H₄ (1e)</td>
<td>6e (51)b</td>
</tr>
<tr>
<td>6</td>
<td>4-PhCOC₆H₄ (1f)</td>
<td>6f (48)d</td>
</tr>
<tr>
<td>7</td>
<td>4-MeO₂CC₆H₄ (1g)</td>
<td>6g (59)e</td>
</tr>
</tbody>
</table>

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′Bu₃, 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. Hydorhodation of the alkene in 7 then affords 8, which undergoes iterative β-elimination/hydorhodation 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, \(\pi\)-crotylrhodium, and \(\sigma\)-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.
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

\[
\begin{align*}
\text{PhCHO} + \begin{array}{c}
\text{OH} \\
\text{2e}
\end{array} & \rightarrow \text{L}_2\text{Rh} \\
\text{16} & \rightarrow \text{L}_2\text{Rh} \\
\text{17} & \rightarrow \text{PhCHO} + \text{L}_n\text{Rh-H} \\
\end{align*}
\]

Table 4. Microwave-Assisted Allyl Transfer at 250 °C

<table>
<thead>
<tr>
<th>Entry</th>
<th>R CHO</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph (1a)</td>
<td>2a</td>
<td>6a</td>
<td>90(^a)</td>
</tr>
<tr>
<td>2</td>
<td>4-MeC(_6)H(_4) (1b)</td>
<td>2a</td>
<td>6b</td>
<td>72(^a)</td>
</tr>
<tr>
<td>3</td>
<td>4-CF(_3)C(_6)H(_4) (1c)</td>
<td>2a</td>
<td>6c</td>
<td>67(^a)</td>
</tr>
<tr>
<td>4</td>
<td>4-MeOC(_6)H(_4) (1d)</td>
<td>2a</td>
<td>6d</td>
<td>87(^a)</td>
</tr>
<tr>
<td>5</td>
<td>4-ClC(_6)H(_4) (1e)</td>
<td>2a</td>
<td>6e</td>
<td>55(^a)</td>
</tr>
<tr>
<td>6</td>
<td>4-(4-MeC(_6)H(_4)CO)C(_6)H(_4) (1i)</td>
<td>2a</td>
<td>6f</td>
<td>58(^a)</td>
</tr>
<tr>
<td>7</td>
<td>4-MeO(_2)C(_6)H(_4) (1g)</td>
<td>2a</td>
<td>6g</td>
<td>41(^a)</td>
</tr>
<tr>
<td>8</td>
<td>(^\circ)C(_11)H(_23) (1h)</td>
<td>2a</td>
<td>6h</td>
<td>64(^a)</td>
</tr>
<tr>
<td>9</td>
<td>Ph (1a)</td>
<td>2c</td>
<td>13a</td>
<td>91</td>
</tr>
<tr>
<td>10</td>
<td>4-MeC(_6)H(_4) (1b)</td>
<td>2c</td>
<td>13b</td>
<td>86</td>
</tr>
<tr>
<td>11</td>
<td>4-CF(_3)C(_6)H(_4) (1c)</td>
<td>2c</td>
<td>13c</td>
<td>64</td>
</tr>
<tr>
<td>12</td>
<td>4-MeOC(_6)H(_4) (1d)</td>
<td>2c</td>
<td>13d</td>
<td>74</td>
</tr>
</tbody>
</table>
It is well-known that microwave heating accelerates organic reactions. 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).

\[
\begin{align*}
\text{PhCHO} & \quad \text{OH} \\
1a & \quad \text{Pr} \\
\text{PhCHO} + \quad \text{OH} \\
1a & \quad \text{Pr}
\end{align*}
\]

\[
\text{[RhCl(cod)]_2} (1.3 \text{ mol\%}) \\
P(C_{5}H_{9})_{3} (7.5 \text{ mol\%}) \\
Cs_{2}CO_{3} (15 \text{ mol\%}) \\
toluene \ (2.0 \text{ mL}/0.8 \text{ mL}) \\
microwave \ 250 ^\circ \text{C}, 30 \text{ min}
\]

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.

\[
\begin{align*}
\text{PhCHO} & \quad \text{OH} \\
1a & \quad \text{R} \\
\text{PhCHO} + \quad \text{OH} \\
1a & \quad \text{R} \\
2e: & \quad \text{R} = \text{Me} \\
2f: & \quad \text{R} = \text{Pr}
\end{align*}
\]

\[
\text{[RhCl(cod)]_2} (1.3 \text{ mol\%}) \\
P(C_{5}H_{9})_{3} (7.5 \text{ mol\%}) \\
Cs_{2}CO_{3} (15 \text{ mol\%}) \\
toluene/DMF \ (2.0 \text{ mL}/0.8 \text{ mL}) \\
microwave \ 250 ^\circ \text{C}, 30 \text{ min}
\]

17% from 2e \\
33% from 2f

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 \((\pi\text{-allyl})\text{bis(triphenylphosphine)}\text{rhodium} did not react with benzaldehyde at room temperature.\text{10} In contrast, owing to the strong \(\sigma\)-donor character of trialkyl phosphines, \((\pi\text{–allyl})\text{bis(trialkylphosphine)}\text{rhodium complexes could be nucleophilic enough to react with benzaldehyde. However, tri-}\text{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).}
Table 5. Effect of Ligand on Methallylation–Isomerization Reaction

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>x</th>
<th>y</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>P(\text{C}_5\text{H}_9)_3</td>
<td>1.3</td>
<td>7.5</td>
<td>91</td>
</tr>
<tr>
<td>2</td>
<td>PMe_3</td>
<td>2.5</td>
<td>15</td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>P(\text{C}<em>6\text{H}</em>{11})_3</td>
<td>2.5</td>
<td>15</td>
<td>72</td>
</tr>
<tr>
<td>4</td>
<td>PPr_3</td>
<td>2.5</td>
<td>15</td>
<td>29</td>
</tr>
<tr>
<td>5</td>
<td>PPh_3</td>
<td>1.3</td>
<td>7.5</td>
<td>26</td>
</tr>
<tr>
<td>6</td>
<td>BINAP</td>
<td>1.3</td>
<td>4</td>
<td>&lt;1</td>
</tr>
<tr>
<td>7</td>
<td>DPPE</td>
<td>1.3</td>
<td>4</td>
<td>21</td>
</tr>
<tr>
<td>8</td>
<td>DPPF</td>
<td>1.3</td>
<td>4</td>
<td>9</td>
</tr>
</tbody>
</table>

Microwave heating is different from conventional external heating in principle and can have so-called nonthermal microwave effects. The author investigated whether such effects were in operation (eq 4). The reaction of 1a with 2c was complete within 30 min in the solvent mixture 1,2-diphenyl-ethane (b.p.: 284 °C)/N,N’-dimethylpropylene urea (DMPU; b.p.: 146 °C at 44 mmHg) at 250 °C when the reaction mixture was heated under microwave irradiation or in a sand bath. No significant differences were observed. These observations were consistent with Kappe’s work.

Under the microwave-assisted conditions at 250 °C, the reactions with 2a were not
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.

![Chemical structure and reaction equation]

**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)], glassware containing the reaction mixture was heated in a sand bath. $^1$H NMR (500 MHz), $^{13}$C NMR (125.7 MHz), and $^{19}$F 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 $^1$H 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 60F$_{254}$. 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$^3$Bu$_3$ 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 Cs$_2$CO$_3$ (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

[RhCl(cod)$_2$ (6 mg, 0.0125 mmol) and Cs$_2$CO$_3$ (24 mg, 0.075 mmol) were placed in a reaction flask. Dioxane (3.0 mL) and PBr$_3$ (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

[RhCl(cod)$_2$ (3 mg, 0.006 mmol) and Cs$_2$CO$_3$ (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 P(C$_5$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, 1 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-butane (13a, 74 mg, 0.45 mmol, 91%).

Characterization Data

The spectra of compounds 1f, 1i, 2a–e, 3a, 3b, 3c, 3d, 3e, 3g, 6a, 6b, 6d, 6e, 13a, 13b, 13d, 13e, 13i, 13j, and 14c 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), 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 \textit{threo} isomer \( \delta \) 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 \( \delta \) 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 C\(_{18}\)H\(_{18}\)O\(_2\): C, 81.17; H, 6.81\%.

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

\[
\text{IR (neat) 2971, 2937, 2880, 1692, 1463, 1410, 1326, 1268, 1217, 1170, 1132, 1114, 1068, 1017, 974, 857, 592 \text{ cm}^{-1};}  
\]
\[
\text{\( ^1 \)H NMR (CDCl\(_3\)) \( \delta \) 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);}  
\]
\[
\text{\( ^{13} \)C NMR (CDCl\(_3\)) \( \delta \) 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;}  
\]
\[
\text{\( ^{19} \)F NMR (CDCl\(_3\)) \( \delta \) –63.65.}  
\]
Found: C, 62.36; H, 5.39\%.  Calcd for C\(_{12}\)H\(_{13}\)F\(_3\)O: C, 62.60; H, 5.69\%.

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

\[
\text{IR (neat) 2936, 2877, 1729, 1683, 1572, 1504, 1436, 1407, 1373, 1280, 1215, 1182, 1109,}  
\]
1006, 956, 870, 788, 722 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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 C\(_{13}\)H\(_{16}\)O\(_3\): C, 70.89; H, 7.32%.

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

IR (neat) 2966, 2937, 2876, 1683, 1659, 1404, 1279, 930 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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 C\(_{19}\)H\(_{20}\)O\(_2\): C, 81.40; H, 7.19%.

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

IR (neat) 2958, 1684, 1662, 1598, 1448, 1404, 1367, 1277, 1211, 938, 926, 743, 718, 699, 655 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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 (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₁₆H₃₂O: 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 (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₁₉H₂₃O₃: C, 81.40; H, 7.19%. m.p.: 63 °C.
Methyl 4-(1-oxobutyl)benzoate (14g)

IR (nujol) 2924, 2854, 1722, 1675, 1456, 1285, 1112, 745 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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 C\(_{12}\)H\(_{14}\)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\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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 C\(_{18}\)H\(_{18}\)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 (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₁₂H₁₆O: C, 81.77; H, 9.15%.
References and Notes


(7) For convenience, throughout the manuscript, crotylation, methallylation, and prenylation are defined as introductions of the 1-methyl-2-propenyl, 2-methyl-2-propenyl, and 1,1-dimethyl-2-propenyl groups, respectively, into a carbonyl group. On the other hand, the crotyl, methallyl, and prenyl groups are denoted herein as the 2-butenyl, 2-methyl-2-propenyl, and 3-methyl-2-butenyl groups, respectively.


(9) Reviews for microwave-assisted organic reactions: (a) *Microwave Assisted Organic


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.\textsuperscript{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 crotylpalladium\textsuperscript{6} and concomitant formation of undesired homo-coupling products.\textsuperscript{7} In most cases, allylstannanes were used as the allylmetal, which required a troublesome purification procedure.\textsuperscript{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.\textsuperscript{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 isomers\textsuperscript{6} over productive reductive elimination from 6. Many attempts to find suitable reaction conditions for the palladium-catalyzed allylation reaction of 1 with 2a failed.
He then turned his attention to nickel catalysis, although little is known about the nickel-catalyzed cross-coupling reaction of allylmetals with allyl electrophiles\(^\text{10}\) and no information about nickel-mediated retro-allylation was reported. After screening reaction conditions, a combination of 5 mol% of Ni(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 \(2a\) (\(R^2 = \text{Me}\)) with a heptyl group (\(R^2 = \text{C}_7\text{H}_{15}\)) 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

<table>
<thead>
<tr>
<th>entry</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>7</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>R&lt;sup&gt;3&lt;/sup&gt;</th>
<th>2</th>
<th>3</th>
<th>Yield (%)</th>
<th>B/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>7a</td>
<td>Me</td>
<td>iPr</td>
<td>2a</td>
<td>3a</td>
<td>91</td>
<td>37/63</td>
</tr>
<tr>
<td>2</td>
<td>4-MeOC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7b</td>
<td>Me</td>
<td>iPr</td>
<td>2a</td>
<td>3b</td>
<td>70</td>
<td>40/60</td>
</tr>
<tr>
<td>3</td>
<td>4-CF&lt;sub&gt;3&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7c</td>
<td>Me</td>
<td>iPr</td>
<td>2a</td>
<td>3c</td>
<td>78</td>
<td>33/67</td>
</tr>
<tr>
<td>4</td>
<td>2-MeC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7d</td>
<td>Me</td>
<td>iPr</td>
<td>2a</td>
<td>3d</td>
<td>86</td>
<td>37/63</td>
</tr>
<tr>
<td>5</td>
<td>Ph</td>
<td>7a</td>
<td>oC&lt;sub&gt;7&lt;/sub&gt;H&lt;sub&gt;15&lt;/sub&gt;</td>
<td>Me</td>
<td>2b</td>
<td>3e</td>
<td>60</td>
<td>26/74</td>
</tr>
<tr>
<td>6</td>
<td>Ph</td>
<td>7a</td>
<td>oC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;11&lt;/sub&gt;</td>
<td>Me</td>
<td>2c</td>
<td>3f</td>
<td>77</td>
<td>9/91</td>
</tr>
<tr>
<td>7</td>
<td>Ph</td>
<td>7a</td>
<td>iBu</td>
<td>Me</td>
<td>2d</td>
<td>3g</td>
<td>79</td>
<td>3/97</td>
</tr>
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</table>

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-allylation<sup>11</sup> would then take place to afford 11 with concomitant formation of ketone R<sup>3</sup>C=O. Here the configurations and modes of coordination of the allyl ligands R<sup>1</sup>CHCHCH<sub>2</sub> and R<sup>2</sup>CHCHCH<sub>2</sub> would be completely scrambled to yield a mixture of several diallylnickel intermediates such as 11, 11<sup>′</sup>, and 11<sup>″</sup>. Reductive elimination prior to β-hydride elimination would afford product 3 and regenerate the initial zero valent nickel catalyst.
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-hexadienysilane 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

<table>
<thead>
<tr>
<th>entry</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>7</th>
<th>12a</th>
<th>13a</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>7a</td>
<td>12a</td>
<td>13a</td>
<td>99</td>
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<tr>
<td>2</td>
<td>4-MeOC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7b</td>
<td>12a</td>
<td>13b</td>
<td>71</td>
</tr>
<tr>
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<td>7c</td>
<td>12a</td>
<td>13c</td>
<td>94</td>
</tr>
<tr>
<td>4</td>
<td>2-MeC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
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</tr>
<tr>
<td>5</td>
<td>4-MeC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7f</td>
<td>12a</td>
<td>13e</td>
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<td>2-furyl</td>
<td>7g</td>
<td>12a</td>
<td>13f</td>
<td>76</td>
</tr>
<tr>
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<td>2-thienyl</td>
<td>7h</td>
<td>12a</td>
<td>13g</td>
<td>76</td>
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<tr>
<td>8</td>
<td>MePh&lt;sub&gt;2&lt;/sub&gt;Si</td>
<td>7i</td>
<td>12a</td>
<td>13h</td>
<td>82</td>
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<tr>
<td>9</td>
<td>Ph</td>
<td>7a</td>
<td>12b</td>
<td>13i</td>
<td>96</td>
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<tr>
<td>10</td>
<td>4-MeOC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7b</td>
<td>12b</td>
<td>13j</td>
<td>81&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>11</td>
<td>4-CF&lt;sub&gt;3&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7c</td>
<td>12b</td>
<td>13k</td>
<td>80&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>12</td>
<td>2-MeC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7d</td>
<td>12b</td>
<td>13l</td>
<td>84</td>
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<tr>
<td>13</td>
<td>4-MeC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7f</td>
<td>12b</td>
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<td>MePh&lt;sub&gt;2&lt;/sub&gt;Si</td>
<td>7i</td>
<td>12b</td>
<td>13o</td>
<td>89&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> 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.
The reason for the different regiochemical outcomes is not clear at this stage. The mode of reductive elimination from diallylnickel 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
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

$^1$H 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 $^1$H 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 60F$_{254}$. 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 Ni(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$_2$O 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

Ni(cod)$_2$ (3.4 mg, 0.0125 mmol) was placed in a 20-mL reaction flask. Toluene (1.0 mL) and P(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\textsuperscript{13} and 13a\textsuperscript{14} showed the identical spectra with those described in the literature. Product 13i and 15a were well known compounds.

(1\textsuperscript{E},5\textsuperscript{E})-1-(4-Methoxyphenyl)-1,5-heptadiene (3b-L)

![3b-L](image)

IR (neat) 2961, 1609, 1511, 1249, 1037, 965, 804 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\) 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); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\) 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 C\textsubscript{14}H\textsubscript{18}O: 202.1358.

(1\textsuperscript{E},5\textsuperscript{E})-1-(4-Trifluoromethylphenyl)-1,5-heptadiene (3c-L)

![3c-L](image)

IR (neat) 2933, 1718, 1616, 1419, 1326, 1177, 1166, 1068, 1017, 967, 837 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\) 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); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\) 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. \textsuperscript{19}F NMR (CDCl\textsubscript{3}) \(\delta\) –63.10. Found: C, 69.71; H, 6.51%. Calcd for C\textsubscript{14}H\textsubscript{15}F\textsubscript{3}: C, 69.98; H, 6.29%
(1E,5E)-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 (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₁₄H₁₈: 186.1408.

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

IR (neat) 3026, 2956, 2925, 2853, 1496, 1469, 1448, 1437, 963 cm⁻¹; ¹H NMR (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₁₉H₂₉: C, 88.73; H, 11.06%.

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

IR (neat) 3025, 2923, 2850, 1495, 1448, 963 cm⁻¹; ¹H NMR (CDCl₃) 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 C$_{18}$H$_{24}$: C, 90.07; H, 10.31%.

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

![Structure](image)

IR (neat) 3025, 2958, 2928, 2904, 1448, 1363, 963 cm$^{-1}$; $^1$H 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 C$_{16}$H$_{22}$: C, 89.59; H, 10.35%.

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

![Structure](image)

IR (neat) 2935, 1653, 1608, 1511, 1465, 1457, 1249, 1175, 1038 cm$^{-1}$; $^1$H 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 C$_{14}$H$_{18}$O: C, 83.12; H, 8.97%.

142
(E)-5-methyl-1-(4-trifluoromethylphenyl)-1,5-hexadiene (13c)

IR (neat) 2882, 2865, 1656, 1620, 1418, 1327, 1165, 1125, 1086, 1015, 966 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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$_3$) $\delta$ –62.70. Found: C, 69.98; H, 6.52%. Calcd for C$_{14}$H$_{15}$F$_3$: C, 69.99; H, 6.29%.

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

IR (neat) 3072, 3022, 2932, 2851, 2360, 1649, 1513, 1484, 1447, 1374 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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 C$_{14}$H$_{18}$: C, 90.26; H, 9.74%.

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

IR (neat) 2921, 1649, 1613, 1446. 1374, 965, 887, 793, 665 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 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\(_3\)) \(\delta\) 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 C\(_{14}\)H\(_{18}\): C, 90.26; H, 9.74%.

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

![Structure of 13f](image)

IR (neat) 2969, 2934, 2850, 1676, 1649, 1491, 1448, 1375, 1254, 1151, 1013 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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 C\(_{11}\)H\(_{18}\)O: 162.1045.

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

![Structure of 13g](image)

IR (neat) 2968, 2933, 1675, 1652, 1436, 1419, 953, 889, 853, 693 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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 C\(_{11}\)H\(_{18}\)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 (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₂₀H₂₄Si: 292.1647.

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

IR (neat) 2934, 2837, 1701, 1608, 1513, 1250, 1175, 1035 cm⁻¹; ¹H NMR (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₁₃H₁₆O: 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 (CDCl₃) 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 C\(_{13}\)H\(_{13}\)F\(_3\): C, 69.02; H, 5.79%.

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

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\text{IR (neat) 2925, 1457, 1437, 965, 912 cm}^{-1}; \quad \text{\(^{1}\)H NMR (CDCl}\(_3\)) \delta 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); \quad \text{\(^{13}\)C NMR (CDCl}\(_3\)) \delta 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 C\(_{13}\)H\(_{16}\): C, 90.64; H, 9.36%.

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

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\text{IR (neat) 2923, 2846, 1640, 1514, 1437, 966 cm}^{-1}; \quad \text{\(^{1}\)H NMR (CDCl}\(_3\)) \delta 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); \quad \text{\(^{13}\)C NMR (CDCl}\(_3\)) \delta 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 C\(_{13}\)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\(^{-1}\); \(^1\)H NMR (CD\(_3\)Cl) \(\delta\) 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 (CD\(_3\)Cl) \(\delta\) 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 C\(_{10}\)H\(_{12}\)S: C, 73.12; H, 7.36%.

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

IR (neat) 3068, 1616, 1428, 1250, 1113, 992 cm\(^{-1}\); \(^1\)H NMR (CD\(_3\)Cl) \(\delta\) 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 (CD\(_3\)Cl) \(\delta\) –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 C\(_{14}\)H\(_{22}\)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\(^{-1}\); \(^1\)H NMR (CD\(_3\)Cl) \(\delta\) 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 (CD\(_3\)Cl) \(\delta\) 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 C₁₉H₂₀: 248.1565. Mp: 83–84 °C.

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

IR (neat) 2923, 2854, 1457, 1377, 963 cm⁻¹; ¹H NMR (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₂₂H₂₀: 284.1565.

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

IR (neat) 2955, 1617, 1248, 989, 963, 866, 838 cm⁻¹; ¹H NMR (CDCl₃) 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); ¹³C NMR (CDCl₃) 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 C₁₅H₂₂Si: C, 78.19, H, 9.62%.

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

IR (neat) 2952, 2926, 2883, 2855, 1616, 1471, 1247, 962 cm⁻¹; ¹H NMR (CDCl₃) 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 C$_{18}$H$_{28}$Si: C, 79.34, H, 10.36%.

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

IR (neat) 3024, 2956, 2904, 1616, 1427, 1247, 1113, 963 cm$^{-1}$;  $^1$H 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 C$_{20}$H$_{24}$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$^{-1}$;  $^1$H NMR (CDCl$_3$) δ 0.03 (s, 9H), 0.02 (s, 3H), 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 C$_{15}$H$_{22}$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$^{-1}$;  $^1$H 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,
$J = 15.5, 6.5 \text{ Hz, 1H}$, 6.35 (d, $J = 15.5 \text{ Hz, 1H}$), 7.17–7.20 (m, 1H), 7.27–7.34 (m, 4H); $^{13}$C
NMR (CDCl$_3$) $\delta$ –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 C$_{18}$H$_{28}$Si: 272.1960.

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

IR (neat) 3024, 2959, 1427, 1248, 1114, 964, 830 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 0.32 (s, 3H), 0.33
(s, 3H), 1.95 (dt, $J = 9.5, 4.0 \text{ Hz, 1H}$), 2.26–2.40 (m, 2H), 4.87 (dd, $J = 17.5, 1.0 \text{ Hz, 1H}$), 4.95
(dd, $J = 9.5, 1.0 \text{ Hz, 1H}$), 5.70 (dt, $J = 17.5, 9.5 \text{ Hz, 1H}$), 6.16 (dt, $J = 16.0, 6.5 \text{ Hz, 1H}$), 6.29 (d,
$J = 16.0 \text{ Hz, 1H}$), 7.16–7.18 (m, 1H), 7.26 (d, $J = 4.5 \text{ Hz, 2H}$), 7.34–7.39 (m, 4H), 7.52–7.56 (m,
3H); $^{13}$C NMR (CDCl$_3$) $\delta$ 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
C$_{20}$H$_{28}$Si: 292.1647.
References and Notes


(11) Another plausible path yielding 11 or other isomers is β-carbon elimination from 10. However, *ab initio* calculations revealed that retro-allylation is far more favorable process than β-carbon elimination in the case of ruthenium: Sakaki, S.; Ohki, T.; Takayama, T.; Sugimoto, M.; Kondo, T.; Mitsudo, T. Organometallics **2001**, *20*, 3145–3158.


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

Chapter 2 Nickel-Catalyzed Borylation of Aryl Cyclopropyl Ketones with Bis(pinacolato)diboron to Synthesize 4-Oxoalkylboronates
Yuto Sumida, Hideki Yorimitsu, and Koichiro Oshima

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

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

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

(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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Yuto Sumida