Development of New Carbon–Carbon Bond Forming Reactions Catalyzed by Palladium and Nickel

Naoki Ishida

2008

Preface

The studies described in this thesis have been carried out under the direction of Professor Masahiro Murakami from April 2002 to March 2008. These studies concern with novel carbon–carbon forming reactions catalyzed by palladium and nickel.

This thesis is completed with the aid of so many people such as a supervisor, collaborators and colleagues. The author would like to show his appreciation them.

First of all, the author would like to express his sincerest gratitude to Supervisor Professor Masahiro Murakami for providing an opportunity to study state-of-the-art organic chemistry. All the works in this thesis could be achieved with his constant supervisions.

The author also would like to acknowledge to:

Associate professor Ryoichi Kuwano and Assistant professor Tomoya Miura for their directions covered from guidance of the project to experimental procedures.

Professor Michinori Suginome, Assistant professor Takanori Matsuda, and Assistant professor Toshimichi Ohmura for helpful discussions and advises.

Dr. Yoshiyuki Miyake, Dr. Yuichiro Mutoh, Mr. Hideyuki Igawa, Dr. Akihiko Yamamoto, Dr. Sho Kadowaki, Dr. Munehiro Hasegawa, Dr Hiroyoshi Noguchi for their kind directions.

the collaborators, Yusuke Takahashi, Tatsuo Shinmoto, and Mizuna Narumi for their support on the research. Their patience and earnest lead to the results described herein.

Dr. Masahiko Shimada, Masaomi Makino, Tomoaki Hasui, Atsushi Fujimoto, Shinji Ashida, Hiroshi Shimizu, Ippei Usui, Taisuke Sasaki, Motonori Koyabu, Miki Terayama, Masanori Shigeno, Motoshi Yamauchi, Tatsuro Harumashi, Hiroki Nakazawa, Soichiro Konno, Tsuyoshi Goya, Tomoya Tsuboi, Yoshiyuki Yamaguchi, Yoshiteru Ito, Tomohiro Tamai, Yohei Maruyama, Taisaku Moriya, Keita Ueda, Tomohiro Igarashi, Dr. Lars Uehlin, Dr. Markus Hoffman, Dr. Atsushi Seki, Sung-Yu Ku, Dr. Markus Mosimann, Karl Deutsche, Dr. Peter Brüchner for their friendliness.

Ms. Chiyo Nagae and Mrs. Yuki Hasegawa for their help on the laboratory life.

The author also thanks to Horomi Yoshida, Keiko Kuwata, and Haruo Fujita for the help on the measurement of mass and NMR spectra.

The author acknowledges to the Japan Society of the Promotion of Science for Young Scientist for the financial support.

Finally, the author would like to express his appreciation to his parents, Mr. Eiichi

Ishida and Mrs. Yoko Ishida for their constant assistance.

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March, 2008

Contents

General Introduction

Transition metal-catalysis has attracted ever-increasing attention in organic synthesis because it provides unique transformations which are otherwise difficult to achieve.[1] For example, construction of C_{sp2}–C_{sp2} bonds, which are often seen in pharmaceuticals and optoelectronic materials, can be executed by palladium- or nickel-catalyzed cross-coupling reactions.[2] Therefore, these catalysts plays a crucial role in drug discovery and development of functional materials. Olefin metathesis reactions catalyzed by ruthenium and molybdenum complexes enable to form cyclic structures between two olefin moieties in the presence of many functional groups, causing a paradigm shift in the retrosynthesis of cyclic compounds including macrocyclic natural products.[3] These transformations became feasible by means of transition metal catalysts, exemplifying the usefulness of transition metals for innovations.

In this thesis, the author would like to describe novel transition metal-catalyzed or -mediated reactions which are directed towards the following issues;

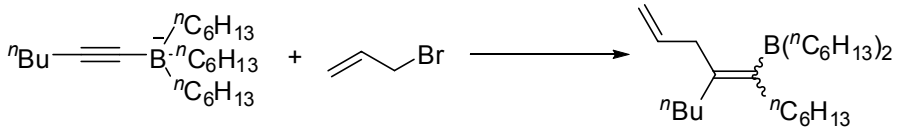
(1) Stereoselective synthesis of trisubstituted alkenylboranes

(2) Enantioselective construction of a chiral quaternary carbon center

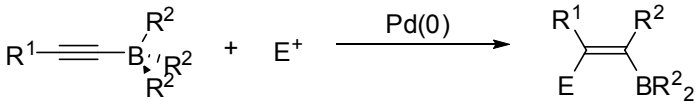
(3) Utilization of carbon dioxide as carbon resources

(1) Stereoselective synthesis of trisubstituted alkenylboranes

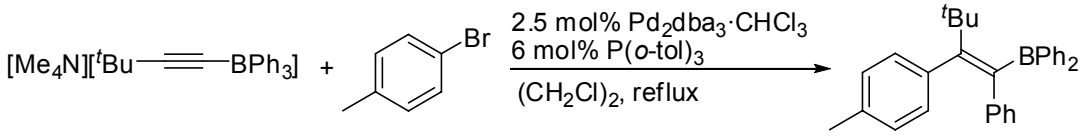
Organoboron compounds have received ever-increasing attention because of their interesting photophysical properties[4] as well as facile reactivities.[5] Representative optoelectronic materials based on organoboranes are light-emitting diodes,[6] fluorescent sensors,[7] non-linear optics,[8] and two-photon emitters.[9] So far, such organoboron-based materials have been synthesized by two conventional methods; a hydroboration reaction of terminal alkynes and a substitution reaction of halo- and alkoxyboranes with organometallic reagents.[5b] Alternative pathway is available starting from alkynyltriorganylborates, which react with a variety of electrophiles[10] such as a proton,[11] organic halides,[12,13] carbon dioxide,[14] oxiranes,[15] chlorophosphanes,[16] sulfenyl chlorides,[17] and metal halides.[18] An electrophile attacks the alkynyl carbon β to boron, inducing 1,2-migration of an organyl group from boron to the α-carbon to give alkenylboranes. For example, a reaction of hexyn-1-yltrihexylborate with allyl bromide afforded a 1,4-dienylborane.[12a] Allyl and hexyl groups were installed across the boron-substituted carbon–carbon double bond.



This class of reactions provides a valuable method to prepare di- and trisubstituted alkenylboranes which are difficult to synthesize through the other conventional methods mentioned above. However, it is difficult to control the stereoselectivity. It is hardly affected by solvent, temperature and other reaction parameters except for the structure of substrates including electrophiles. In this regards, the use of transition metal catalysis is intriguing because organometallic intermediates can work as electrophiles and interact with alkynylborates in a different way from usual electrophiles, affording an additional possibility to control the stereoselectivity as well as to expand the reaction scope. In this thesis, the author focused on the palladium-catalysis because it can catalyze a variety of reactions including Heck reaction, allylation reaction, and hydrogenation reaction.[19]

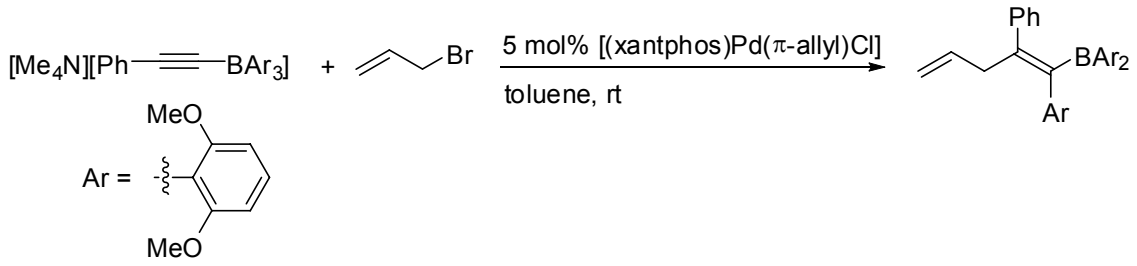


In chapter 1, the author deals with a palladium-catalyzed reaction of alkynyltriarylborates with aryl halides. In the presence of Pd(0) and P(*o*-tol)$_3$, alkynyltriarylborates reacted with aryl halides to give trisubstituted alkenylboranes stereoselectively. Two different aryl groups were installed across carbon–carbon double bond in a *cis* arrangement. The reaction would proceed through oxidative addition of aryl halides to palladium(0), carbopalladation across the carbon–carbon triple bond, migration of an aryl group on boron to palladium (intramolecular transmetalation), and reductive elimination.

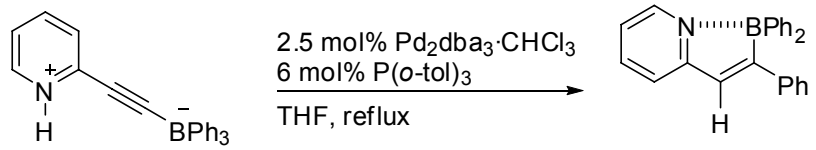


In chapter 2, a palladium-catalyzed allylation reaction of alkynyltriarylborates is described. In the presence of palladium(0) ligated by xantphos, alkynyltriarylborates reacted with allyl bromide to give trisubstituted alkenylboranes. When

2,6-dimethoxyphenyl group was employed as substituents on boron, air-stable organoborane was obtained stereoselectively.

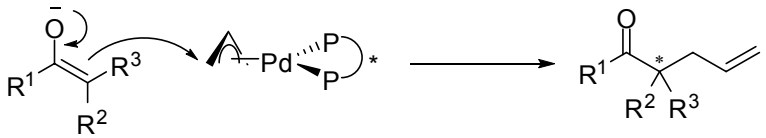


In chapter 3, a palladium-catalyzed rearrangement reaction of ammonioalkynyltriarylborates is described. In the presence of a palladium catalyst, alkynyltriarylborates having tethered tertiary ammonium moiety were rearranged to afford amine–borane intramolecular complexes in a stereoselective manner. Instead of the tertiary ammonium moiety, anilinium and pyridinium groups also participated in the reaction, affording the corresponding intramolecular B–N adducts. Some products exhibited strong fluorescence.



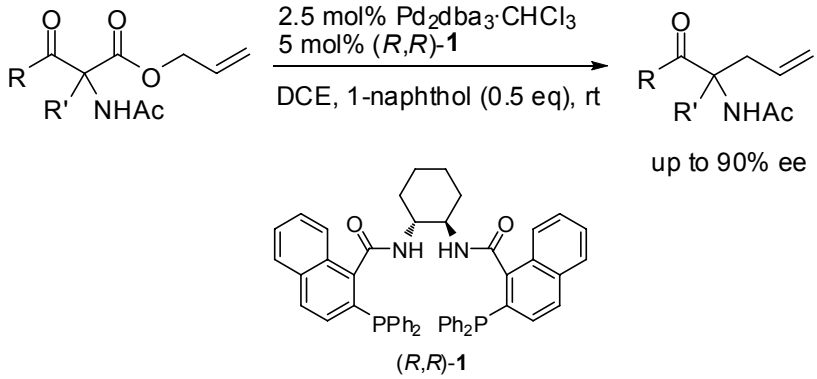
(2) Enantioselective construction of a chiral quaternary carbon center

The enantioselective construction of a chiral quaternary carbon center is an active research area in organic synthesis because chiral quaternary carbon centers are often seen in natural products.[20] Catalytic asymmetric allylation through a chiral π-allylpalladium complex has been intensively studied for the purpose.[21] Most of the successful examples introduce a chiral center on an allylic substrate, whereas the enantioselective electrophilic attack to a prochiral nucleophile is difficult to be controlled by a chiral ligand on the palladium atom because the ligand is located at the opposite side of the π-allyl carbon structure from the approaching nucleophile.[22]



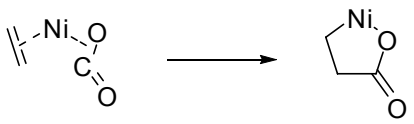
In chapter 4, a palladium-catalyzed asymmetric allylation reaction of prochiral

nucleophiles is depicted.[23,24] In the presence of a palladium catalyst modified with a chiral phosphine ligand, allyl α-acetamido-β-ketoesters were decarboxylated to give α-aminoketones having a quaternary carbon center. The reaction proceeded through oxidative addition of allyl carboxylate to palladium, decarboxylation to generate an enolate, nucleophilic attack of the enolate to the chiral π-allylpalladium.[25] The use of chiral ligand **1** and an addition of phenol derivatives is crucial for high enantioselectivity, affording the product with up to 90% ee.



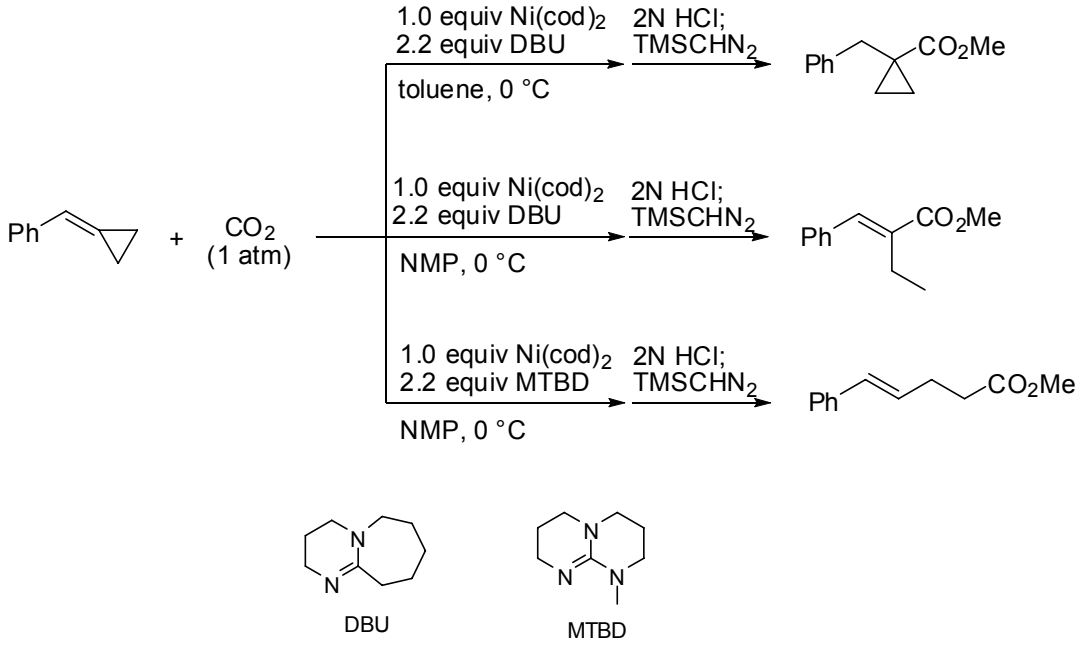
(3) Utilization of carbon dioxide as carbon resources

There is an increased recognition by the world's scientific, industrial, and political communities that the concentrations of greenhouse effect gases including carbon dioxide on the earth are increasing and causing a serious climate change.[26] Many attempts to decrease the emission of carbon dioxide have been executed, however, it is still difficult to utilize carbon dioxide as carbon resources because of the high stability. A nickel(0) complex is potentially useful to convert carbon dioxide into carboxylic acids.[27,28] Unsaturated hydrocarbons and carbon dioxide are reductively coupled on a nickel(0) complex to give five-membered nickelalactones. The nickelalactone has a reactive carbon–nickel bond, which can be utilized for subsequent transformations.[29]

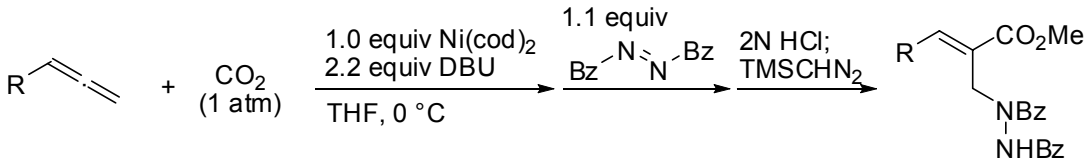


In chapter 5, nickel-mediated carboxylation reactions of methylenecyclopropanes is described. Methylenecyclopropanes were coupled with carbon dioxide on an amine-ligated nickel(0) complexes to give nickelalactones, which lead to various carboxylic acids depending on the reaction conditions. When DBU was employed as an

amine, oxidative cyclization occurred under atmospheric pressure of carbon dioxide to generate nickelalactones with a cyclopropane moiety. In a nonpolar solvent, cyclopropane carboxylic acids were obtained after acidic hydrolysis. Meanwhile in a polar solvent, acrylic acid derivatives were produced probably through β-carbon elimination of the generated nickelalactone. On the other hand, the use of MTBD as an amine altered the reaction course, affording γ,δ-unsaturated carboxylic acids.



In chapter 6, the author mentions about a nickel(0)-mediated sequential addition reaction of carbon dioxide and a diazene onto unsaturated hydrocarbons. A nickelalactone generated from carbon dioxide and an allene reacts with a diazene to furnish a hydrazine. Other unsaturated hydrocarbons such as alkynes and methylenecyclopropanes participated in the reaction, resulting in carboxylic acids having a β-hydrazino moiety. Treatment of SmI_2 with the hydrazines reductively cleaved the nitrogen–nitrogen bond, affording β-amino acid derivatives.



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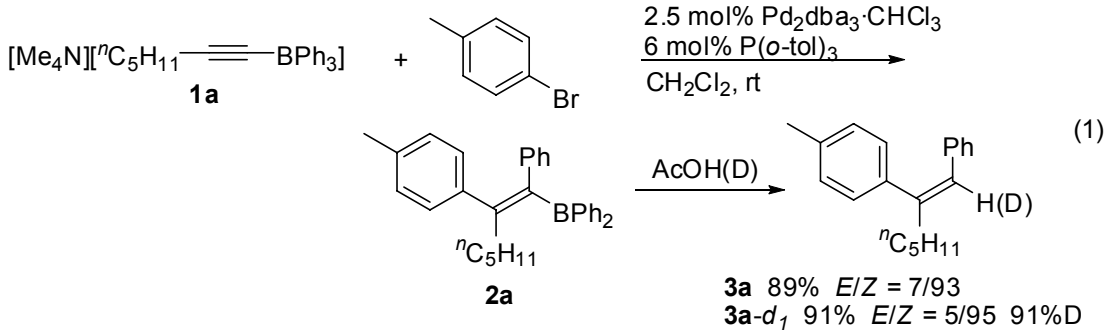
Chapter 1

Stereoselective Synthesis of Trisubstituted Alkenylboranes by Palladium-Catalyzed Reaction of Alkynyltriarylborates with Aryl Halides

Abstract: The palladium-catalyzed reaction of alkynyltriarylborates with aryl halides afforded trisubstituted alkenylboranes, in which two different aryl groups were installed across the carbon–carbon double bond in a *cis* arrangement.

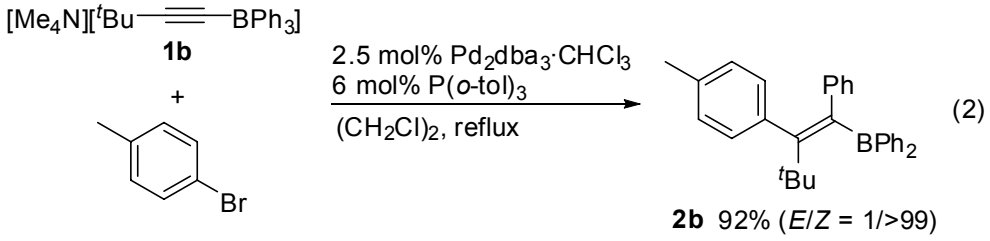
Organoboron compounds are valuable reagents in organic synthesis, especially for carbon–carbon bond forming reactions such as Suzuki-Miyaura coupling reaction.[1] In addition, recent studies on boron-containing compounds have demonstrated their potential as functional materials.[2] Therefore, efficient methods to prepare organoboranes in a stereo-defined form are of significant interest.[3] Di- and trisubstituted alkenylboranes can be synthesized by the reaction of alkynyltriorganylborates with electrophiles,[4] such as a proton,[5] alkyl halides,[6] acyl halides,[7] (π-ally)palladium species,[8] carbon dioxide,[9] oxiranes,[10] chlorophosphanes,[11] sulfenyl chlorides[12] and metal halides,[5a,13] which attack the β-position of the alkynyl group to induce 1,2-migration of the organyl group from boron to the α-position. However, an analogous reaction using aryl halides or pseudohalides has not been reported, although such an arylative reaction would significantly reinforce the potential of the 1,2-migration protocol for the synthesis of π-conjugated organic materials. Herein, the author report the palladium-catalyzed reaction of alkynyltriarylborates with aryl halides, which affords trisubstituted alkenylboranes in a highly stereoselective manner.

Alkynytriarylborate **1a**[14] (1.0 equiv) was reacted with 4-bromotoluene (1.0 equiv) for 3 h at room temperature in the presence of a catalyst generated from $Pd_2dba_3{\cdot}CHCl_3$ and P(*o*-tol)$_3$. Subsequent treatment of the reaction mixture with acetic acid afforded trisubstituted alkene **3a** in 89% yield (*E*/*Z* = 7/93, eq 1).[15] The ^{1}H NMR spectrum of the reaction mixture showed that no 4-(hept-1-ynyl)toluene was formed[16] and that only a trace amount (less than 5%) of 4-methylbiphenyl was produced.



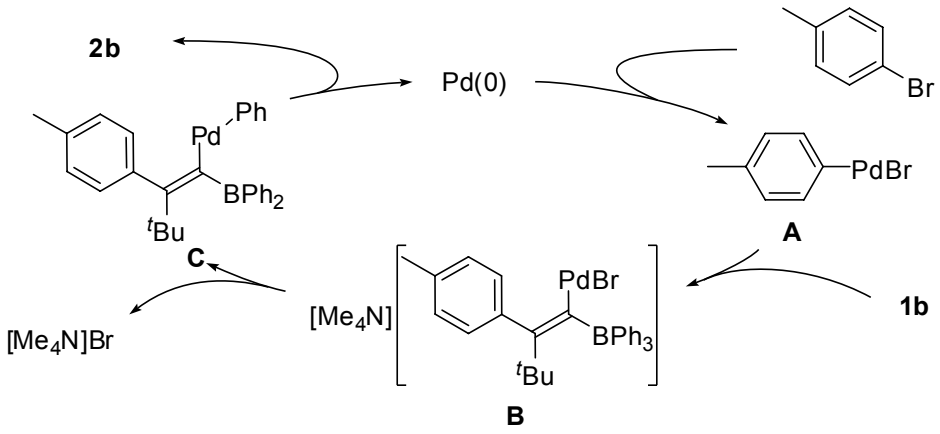
When deuterated acetic acid was employed for hydrolysis, **3a**-d_1 was obtained in 91% yield (91% incorporation of D), indicating that the alkenylborane **2a** was likely the precursor to **3a**. Although attempts to isolate **2a** failed due to the lability of the carbon–boron linkage, the alkenylborane **2b** (*E*/*Z* = 1/>99), generated from **1b** at reflux in 1,2-dichloroethane, was stable enough to be isolated by column chromatography on silica

gel (eq 2). The tertiary butyl group located *cis* to boron may have provided steric protection for the labile carbon–boron linkage.



A possible mechanism for the formation of **2b** from **1b** is shown in Scheme 1. Initially, oxidative addition of 4-bromotoluene to palladium(0) occurs, giving *p*-tolylpalladium species **A**. Regioselective carbopalladation across the carbon–carbon triple bond of **1b** forms the intermediate **B**. Then, a phenyl group migrates from boron to palladium, replacing the bromide anion. Finally, the alkenylborane **2b** is released by reductive elimination with regeneration of palladium(0).[17]

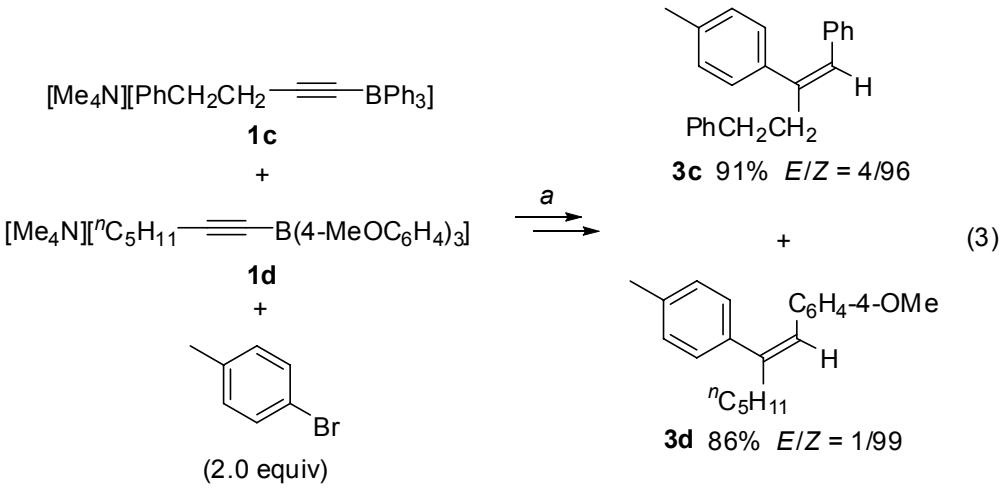
Scheme 1. Proposed mechanism



A minor pathway leading to the formation of (*E*)-**3a** from **1a** may arise from 1,2-phenyl migration from boron to the α-carbon, displacing palladium(0) and the bromide anion. Such a substitutive 1,2-phenyl migration can occur with inversion of the α-carbon stereochemistry.[18]

Intramolecular transfer of the aryl group on boron was confirmed by a crossover experiment (eq 3). When a mixture of **1c** and **1d** was subjected to the reaction with

4-bromotoluene (2.0 equiv), **3c** and **3d** were obtained in 91 and 86% yield, respectively. No crossover products were detected by ^{1}H NMR and GC-MS.



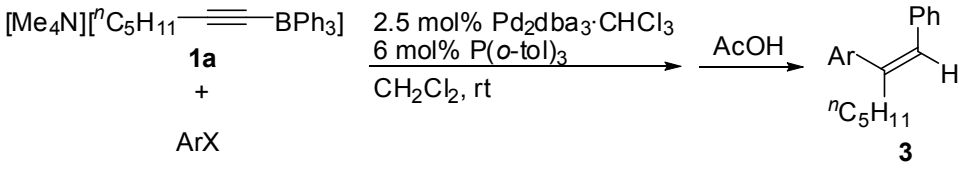
(3)

[a] 5.0 mol% $Pd_2dba_3{\cdot}CHCl_3$, 12 mol% P(*o*-tol)$_3$, CH_2Cl_2, rt, 3 h; then AcOH, rt, 3 h.

Trisubstituted alkenes **3** were synthesized by the reaction of **1a** with various aryl halides (Table 1). The reaction of 4-iodotoluene was complete within 1 h, yielding the product **3a** stereoselectively in 89% yield (entry 1). The corresponding chloride and triflate gave only a trace amount of the product. Aryl bromides having electron-donating and -withdrawing groups at the 4-positions both successfully participated in the reaction (entries 3 and 4). Ester, phthalimide and chloro groups remained intact under the reaction conditions (entries 5-7). Although 3-bromotoluene reacted smoothly (entry 8), the reaction with 2-bromotoluene was sluggish, probably due to steric reasons.

The use of other alkynyltriarylborates in the reaction with 4-bromotoluene was also examined (Table 2). Alkynylborates possessing a primary alkyl group as the R substituent gave **3l** and **3m** in good yield with high selectivities (entries 1 and 2). In the case where R = isopropyl, (*Z*)-**3n** was formed exclusively (entry 3). Both electron-donating and -withdrawing groups were tolerated as the substituents on the aryl group on boron (entries 4-6, eq 3). Furthermore, a 2-thienyl group was efficiently transferred onto the α-carbon (entry 7). In contrast, no or only a trace amount of the corresponding trisubstituted alkenes were obtained when triphenyl(2-phenylethynyl)borate **1l** and triethyl(hept-1-ynyl)borate **1m** were subjected to the reaction with 4-bromotoluene (Chart 1). Alkynylborates derived from phenyl boronic esters such as **1n** failed to give the corresponding trisubstituted alkenyl boronic esters either.[19]

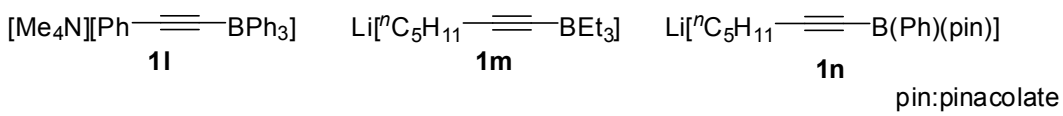
Table 1. Reaction of 1a with various aryl halides[a]



entry	aryl halide	product	yield / %[b]	*E*/*Z*[c]
1[d]	4-MeC_6H_4I	**3a**	89	7/93
2	PhBr	**3e**	88	5/95
3	4-$MeOC_6H_4Br$	**3f**	93	7/93
4	4-$CF_3C_6H_4Br$	**3g**	90	4/96
5	4-$EtO_2CC_6H_4Br$	**3h**	93	7/93
6	4-$PhthNC_6H_4Br$	**3i**	84	6/94
7	4-ClC_6H_4Br	**3j**	88	5/95
8	3-MeC_6H_4Br	**3k**	93	5/95

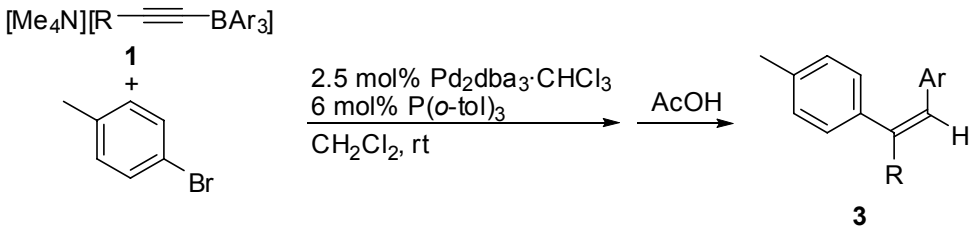
[a] Reaction conditions: 1.0 equiv 1a, 1.0 equiv aryl halide, 2.5 mol% $Pd_2dba_3·CHCl_3$, 6 mol% P(*o*-tol)$_3$, CH_2Cl_2, rt, 3 h; then AcOH, rt, 3 h. [b] Isolated yield. [c] Determined by ^{1}H NMR. [d] Reaction time: 1 h.

Chart 1. Other alkynylborates



The synthetic potential of the reaction was demonstrated by the one-pot procedures shown in Scheme 2. The Suzuki-Miyaura coupling reaction was consecutively executed by simply adding aryl iodide **4** and NaOH to a reaction mixture containing the alkenylborane **2s**. (*E*)-Tamoxifen (**5**) was stereoselectively obtained in 79% yield (*E*/*Z* = 97/3).[20] Stereospecific iodination was accomplished by treatment of the ammonia complex of **2s** with NIS, giving the alkenyl iodide **6** in 59% yield (*E*/*Z* = 96/4). An oxidation reaction with trimethylamine *N*-oxide produced the ketone **7** in 91% yield.

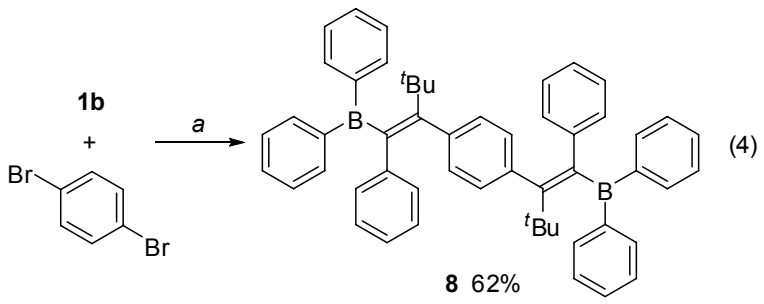
Table 2. Reaction of various alkynylborates **1** with 4-bromotoluene[a]



entry	[Me$_4$N][R—≡—BAr$_3$] **1** (R, Ar)	product	yield / %[b]	*E*/*Z*[c]
1	**1e** (Et, Ph)	3l	85	6/94
2	**1f** (^{i}Bu, Ph)	3m	86	6/94
3	**1g** (^{i}Pr, Ph)	3n	74	1/>99
4	**1h** (^{n}C$_5$H$_{11}$, 4-MeC$_6$H$_4$)	3o	88	6/94
5	**1i** (^{n}C$_5$H$_{11}$, 3-MeC$_6$H$_4$)	3p	89	4/96
6	**1j** (^{n}C$_5$H$_{11}$, 4-FC$_6$H$_4$)	3q	86	6/94
7	**1k** (^{n}C$_5$H$_{11}$, 2-thienyl)	3r	82	9/91

[a] Reaction conditions: 1.0 equiv **1**, 1.0 equiv 4-bromotoluene, 2.5 mol% $Pd_2dba_3{\cdot}CHCl_3$, 6 mol% P(*o*-tol)$_3$, CH_2Cl_2, rt, 3 h; then AcOH, rt, 3 h. [b] Isolated yield. [c] Determined by ^{1}H NMR.

Installation of two aryl groups in juxtaposition across a boron-substituted alkene is attractive in terms of the synthesis of boron-containing π-conjugated materials. Thus, the reaction was successfully applied to the construction of diboranyl compound **8** (eq 4).

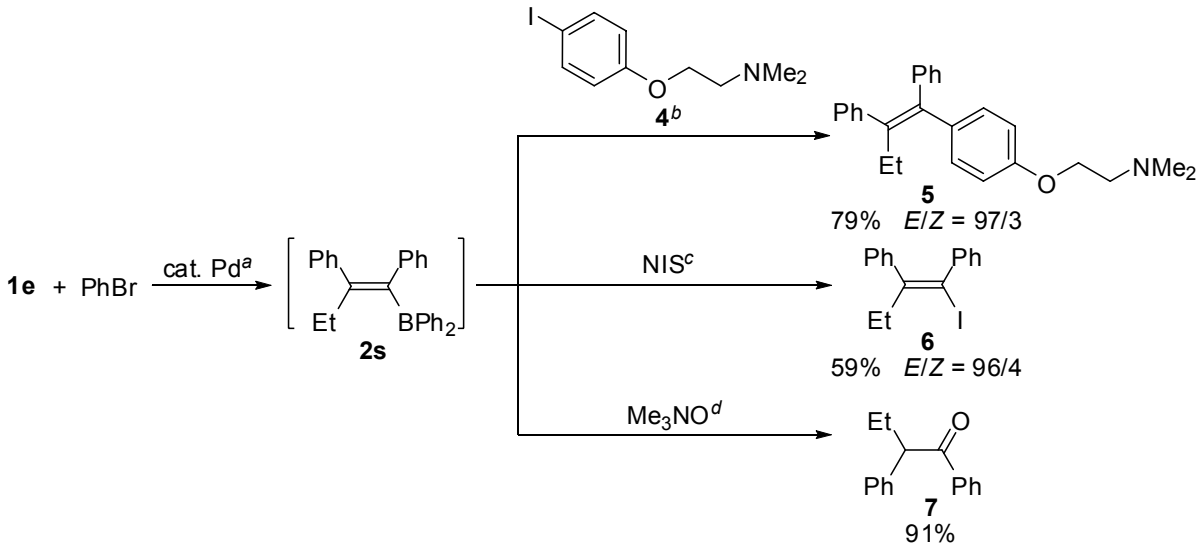


(4)

[a] 2.5 mol% $Pd_2dba_3{\cdot}CHCl_3$, 6 mol% P(*o*-tol)$_3$, $(CH_2Cl)_2$, reflux, 1 h.

In summary, a new method for the stereoselective synthesis of trisubstituted alkenylboranes was developed, in which two different aryl groups were installed across the carbon–carbon double bond in a *cis* arrangement. Application of this method to synthesis of boron-containing functional materials is underway.

Scheme 2. Reactions of alkenylborane **2s**



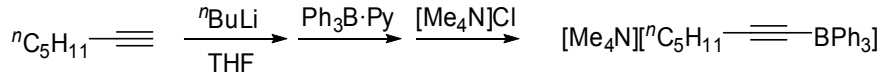
[a] 2.5 mol% $Pd_2dba_3{\cdot}CHCl_3$, 6 mol% P(*o*-tol)$_3$, CH_2Cl_2, rt, 3 h. [b] 3.0 equiv **4**, NaOH, H_2O, rt, 24 h. [c] NH_3 aq.; then 5.0 equiv NIS, acetone, 0 °C, 1 h. [d] 5.0 equiv Me_3NO, rt, 3 h.

Experimental Section

General. NMR spectra were recorded on a Varian Gemini 2000 (^{1}H at 300 MHz and ^{13}C at 75 MHz) or Varian Mercury-400 (^{1}H at 400 MHz and ^{11}B at 128 MHz) spectrometers. Unless otherwise noted, $CDCl_3$ was used as a solvent. Me_4Si (^{1}H, δ = 0.00), residual H of CD_3CN (^{1}H in CD_3CN, δ = 1.94), $CDCl_3$ (^{13}C, δ = 77.0), **C**D_3CN (^{13}C, δ = 1.32), and $BF_3{\cdot}OEt_2$ (^{11}B, δ = 0.00) were used as standard. High-resolution mass spectra were recorded on a JEOL JMS-SX102A spectrometer. All reactions were carried out under an argon atmosphere. Column chromatography was performed with silica gel 60 N (Kanto). Preparative thin-layer chromatography was performed with silica gel 60 PF_{254} (Merck). Gel permeation chromatography (GPC) was carried out with Japan Analytical Industry LC-908.

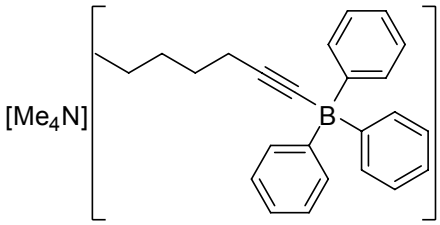
Materials. Unless otherwise noted, all chemicals and anhydrous solvents were obtained from commercial suppliers and used as received. CH_2Cl_2 was purchased from Kanto chemicals. $(CH_2Cl)_2$ was dried over CaH_2. $Pd_2dba_3{\cdot}CHCl_3$ was prepared according to the reported procedures.[21] AcOH and AcOD were degassed by sonication. $Ar_3B{\cdot}Py$ were prepared from thermolysis of $Ar_4B{\cdot}HPy$, which is prepared from ArLi and $BF_3{\cdot}OEt_2$[22] or ArMgBr and $B(OMe)_3$,[23] followed by cation exchange with Py·HCl in water. Aryl iodide **4** was prepared according to reported procedures.[24]

Preparation of alkynyltriarylborate 1a. A typical procedure for the preparation of alkynyltriarylborates.



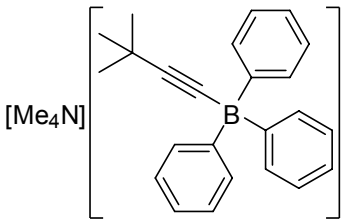
To a stirred solution of hept-1-yne (580 mg, 6.0 mmol) in THF (20 ml) at -78 °C was added *n*-BuLi (1.6 M in hexane, 3.4 ml, 5.5 mmol). After 30 minutes at this temperature, $Ph_3B{\cdot}Py$ (1.61 g, 5.0 mmol) was added and the cooling bath was removed. After being stirred for 1 h at room temperature, the reaction was quenched by adding a small amount of MeOH. Volatile materials were removed under reduced pressure and the residue was dissolved in MeOH. Me_4NCl (1.1 g, 10 mmol) was added with stirring, resulting white solid. It was collected by filtration and was washed with cold MeOH to give alkynyltriarylborate **1a** (1.95 g, 4.7 mmol, 95% yield).

Tetramethylammonium hept-1-ynyltriphenylborate (1a)



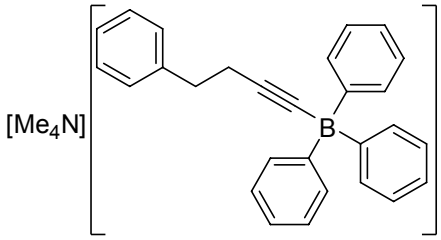
^{1}H NMR (CD_3CN): δ = 0.97 (t, J = 7.2 Hz, 3H), 1.40-1.43 (m, 2H), 1.52-1.59 (m, 4H), 2.28 (t, J = 6.6 Hz, 2H), 2.89-2.95 (m, 12H), 6.89 (t, J = 6.4 Hz, 3H), 7.01-7.05 (m, 6H), 7.41 (br, 6H); ^{13}C NMR (CD_3CN): δ = 14.5, 21.1, 23.1, 31.3, 32.1, 56.0, 94.6, 107.1 (q, J_{B-C} = 65.9 Hz), 123.1, 126.6, 135.4, 162.9 (q, J_{B-C} = 49.8 Hz); ^{11}B NMR (CD_3CN): δ = -7.1; HRMS (FAB) Calcd for $C_{25}H_{26}B$ [M-(NMe_4)]$^-$ 337.2128. Found 337.2123.

Tetramethylammonium (3,3-dimethylbut-1-ynyl)triphenylborate (1b)



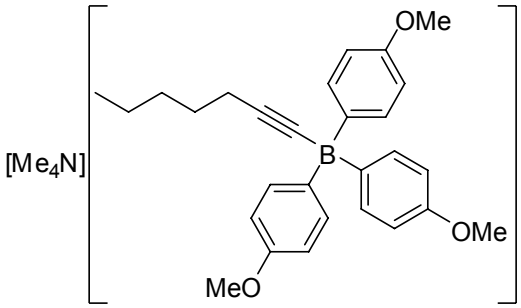
^{1}H NMR (CD_3CN): δ = 1.31 (s, 9H), 2.84-2.87 (m, 12H), 6.89 (t, J = 7.2 Hz, 3H), 7.03 (pseudo t, J = 7.4 Hz, 6H), 7.42 (br, 6H); ^{13}C NMR (CD_3CN): δ = 28.8, 33.1, 55.9, 104.2 (q, J_{B-C} = 64.8 Hz), 104.3, 123.0, 126.5, 135.3, 162.9 (q, J_{B-C} = 49.5 Hz); ^{11}B NMR (CD_3CN): δ = -7.3; HRMS (FAB) Calcd for $C_{24}H_{24}B$ [M-(NMe_4)]$^-$ 323.1971. Found 323.1965.

Tetramethylammonium triphenyl(4-phenylbut-1-ynyl)borate (1c)



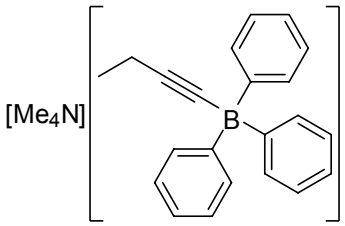
^{1}H NMR (CD_3CN): δ = 2.60 (t, J = 7.4 Hz, 2H), 2.74 (s, 12H), 2.91 (t, J = 7.4 Hz, 2H), 6.93 (tt, J = 7.2, 1.6 Hz, 3H), 7.05-7.09 (m, 6H), 7.24 (tt, J = 7.2, 1.6 Hz, 1H), 7.31-7.35 (m, 2H), 7.39-7.44 (m, 8H); ^{13}C NMR (CD_3CN): δ = 23.6, 37.8, 55.8, 94.1, 107.7 (q, J_{B-C} = 64.1 Hz), 123.1, 126.5, 128.9, 129.6, 135.4, 143.1, 162.6 (q, J_{B-C} = 49.5 Hz); ^{11}B NMR (CD_3CN): δ = -7.0; HRMS (FAB) Calcd for $C_{28}H_{24}B$ [M-(NMe_4)]$^-$ 371.1971. Found 371.1957.

Tetramethylammonium tris(4-methoxyphenyl)hept-1-ynylborate (1d)



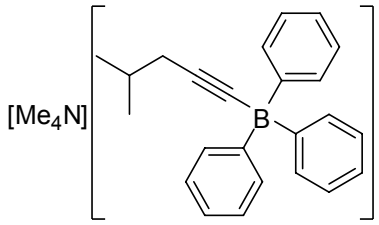
^{1}H NMR (CD_3CN): δ = 0.93 (t, J = 7.2 Hz, 3H), 1.34-1.39 (m, 2H), 1.46-1.54 (m, 4H), 2.22 (t, J = 6.6 Hz, 2H), 2.98-3.00 (m, 12H), 3.68 (s, 9H), 6.60 (d, J = 8.4 Hz, 6H), 7.22 (br d, J = 7.6 Hz, 6H); ^{13}C NMR (CD_3CN): δ = 14.6, 21.2, 23.1, 31.3, 32.1, 55.3, 55.8, 94.4, 107.7 (q, J_{B-C} = 63.6 Hz), 112.2, 135.9, 154.3 (q, J_{B-C} = 48.5 Hz), 156.6; ^{11}B NMR (CD_3CN): δ = -7.9; HRMS (FAB) Calcd for $C_{28}H_{32}BO_3$ $[M-(NMe_4)]^-$ 427.2445. Found 427.2441.

Tetramethylammonium but-1-ynyltriphenylborate (1e)



^{1}H NMR (CD_3CN): δ = 1.18 (t, J = 7.4 Hz, 3H), 2.27 (q, J =7.4 Hz, 2H), 2.92 (s, 12H), 6.87 (tt, J = 7.2, 1.6 Hz, 3H), 7.01 (pseudo t, J = 7.2 Hz, 6H), 7.37 (br, 6H); ^{13}C NMR (CD_3CN): δ = 14.7, 16.5, 55.9, 96.2, 106.2 (q, J_{B-C} = 65.5 Hz), 123.0, 126.5, 135.3, 162.8 (q, J_{B-C} = 49.5 Hz); ^{11}B NMR (CD_3CN): δ = -7.1; HRMS (FAB) Calcd for $C_{22}H_{20}B$ $[M-(NMe_4)]^-$ 295.1658. Found 295.1652.

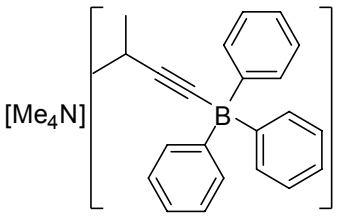
Tetramethylammonium 4-methylpent-1-ynyltriphenylborate (1f)



^{1}H NMR (CD_3CN): δ = 1.05 (d, J = 6.8 Hz, 6H), 1.78 (pseudo sept., J = 6.6 Hz, 1H), 2.14 (d, J = 6.0 Hz, 2H), 2.96-2.99 (br, 12H), 6.83-6.88 (m, 3H), 6.98-7.01 (m, 6H),

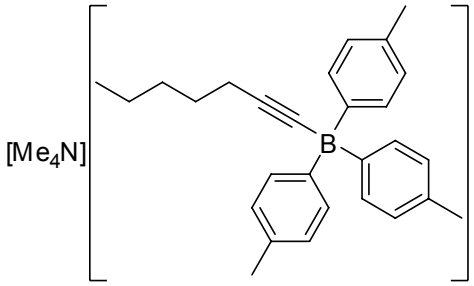
7.36 (br, 6H); ^{13}C NMR (CD_3CN): δ = 22.6, 30.4, 30.7, 56.0, 93.4, 108.0 (q, J_{B-C} = 65.3 Hz), 123.2, 126.7, 135.5, 163.1 (q, J_{B-C} = 50.0 Hz); ^{11}B NMR (CD_3CN): δ = -7.0; HRMS (FAB) Calcd for $C_{24}H_{24}B$ [M-(NMe_4)]$^-$ 323.1971. Found 323.1964.

Tetramethylammonium 3-methylbutyn-1-yltriphenylborate (1g)



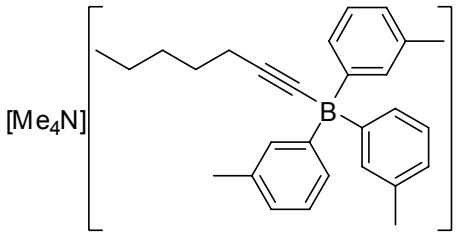
^{1}H NMR (CD_3CN): δ = 1.23 (d, J = 6.8 Hz, 6H), 2.65 (sept., J = 6.8 Hz, 1H), 2.88 (s, 12H), 6.88 (tt, J = 7.2, 1.6 Hz, 3H), 7.00-7.04 (m, 6H), 7.39 (br, 6H); ^{13}C NMR (CD_3CN): δ = 22.7, 25.4, 55.9, 123.0, 126.5, 135.3, 162.8 (q, J_{B-C} = 49.8 Hz); ^{11}B NMR (CD_3CN): δ = -7.2; HRMS (FAB) Calcd for $C_{23}H_{22}B$ [M-(NMe_4)]$^-$ 309.1815. Found 309.1806.

Tetramethylammonium hept-1-ynyltris(4-methylphenyl)borate (1h)



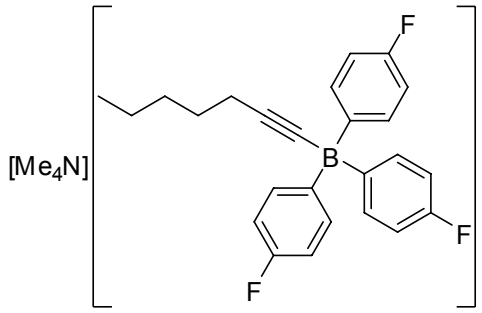
^{1}H NMR (CD_3CN): δ = 0.97 (t, J = 7.2 Hz, 3H), 1.36-1.45 (m, 2H), 1.49-1.59 (m, 4H), 2.23-2.29 (m, 11H), 2.80 (s, 12H), 6.85 (d, J = 7.6 Hz, 6H), 7.27 (d, J = 7.2 Hz, 6H); ^{13}C NMR (CD_3CN): δ = 14.6, 21.2, 23.1, 31.3, 32.1, 55.8, 94.2, 107.6 (q, J_{B-C} = 63.8 Hz), 127.3, 131.5, 135.4, 159.5 (q, J_{B-C} = 49.0 Hz); ^{11}B NMR (CD_3CN): δ = -7.5; HRMS (FAB) Calcd for $C_{28}H_{32}B$ [M-(NMe_4)]$^-$ 379.2597. Found 379.2582.

Tetramethylammonium hept-1-ynyltris(3-methylphenyl)borate (1i)



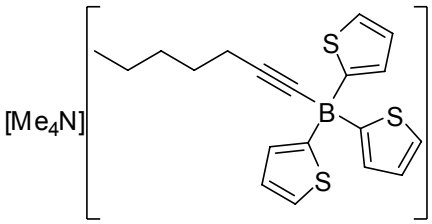
^{1}H NMR (CD_3CN): δ = 0.98 (t, J = 7.4 Hz, 3H), 1.39-1.45 (m, 2H), 1.57-1.58 (m, 4H), 2.22 (s, 9H), 2.28 (m, 2H), 2.80-2.83 (m, 12H), 6.71-6.73 (m, 3H), 6.90-6.94 (m, 3H), 7.16 (br, 3H), 7.28 (br, 3H); ^{13}C NMR (CD_3CN): δ = 14.6, 21.2, 22.0, 23.2, 31.3, 32.1, 55.8, 94.5, 107.5 (q, J_{B-C} = 63.4 Hz), 123.7, 126.4, 132.6, 134.8, 136.3, 162.8 (q, J_{B-C} = 49.0 Hz); ^{11}B NMR (CD_3CN): δ = -7.2; HRMS (FAB) Calcd for $C_{28}H_{32}B$ $[M-(NMe_4)]^-$ 379.2597. Found 379.2600.

Tetramethylammonium tris(4-fluorophenyl)hept-1-ynylborate (1j)



^{1}H NMR (CD_3CN): δ = 0.95 (t, J = 7.2 Hz, 3H), 1.36-1.41 (m, 2H), 1.48-1.58 (m, 4H), 2.26 (t, J = 6.8 Hz, 2H), 2.97 (s, 12H), 6.75-6.81 (m, 6H), 7.32 (br, 6H); ^{13}C NMR (CD_3CN): δ = 14.5, 21.0, 23.1, 31.1, 32.1, 56.0, 95.0, 106.3 (q, J_{B-C} = 64.8 Hz), 112.8 (d, J_{C-F} = 18.2 Hz), 136.2 (d, J_{C-F} = 5.8 Hz), 157.7 (q, J_{B-C} = 50.7 Hz), 160.9 (d, J_{C-F} = 235.1 Hz); ^{11}B NMR (CD_3CN): δ = -7.8; HRMS (FAB) Calcd for $C_{25}H_{23}BF_3$ $[M-(NMe_4)]^-$ 391.1845. Found 391.1828.

Tetramethylammonium hept-1-ynyltri(2-thienyl)borate (1k)

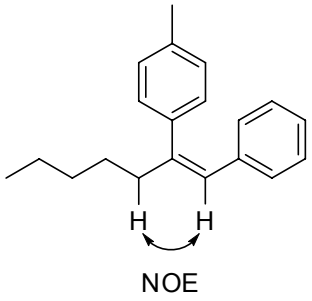


^{1}H NMR (CD_3CN): δ = 0.97 (t, J = 7.2 Hz, 3H), 1.38-1.44 (m, 2H), 1.52-1.62 (m, 4H), 2.25-2.28 (m, 2H), 2.77 (s, 12H), 6.89-6.93 (m, 6H), 7.12 (d, J = 4.4 Hz, 3H); ^{13}C NMR (CD_3CN): δ = 14.5, 20.9, 23.1, 30.8, 32.0, 55.8, 94.5 (q, J_{B-C} = 13.1 Hz), 103.1 (q, J_{B-C} = 68.2 Hz), 124.2, 127.0, 128.3, 164.7 (q, J_{B-C} = 54.6 Hz); ^{11}B NMR (CD_3CN): δ = -12.6; HRMS (FAB) Calcd for $C_{19}H_{20}BS_3$ $[M-(NMe_4)]^-$ 355.0820. Found 355.0819.

Palladium-catalyzed reaction of alkynyltriarylborate 1a with 4-bromotoluene. A typical procedure for the palladium-catalyzed reaction of alkynyltriarylborates with aryl halides.

Under an argon atmosphere, a CH_2Cl_2 solution (0.5 ml) of alkynyltriarylborate **1a** (82.2 mg, 0.20 mmol), $Pd_2dba_3{\cdot}CHCl_3$ (5.2 mg, 2.5 μmol), and P(*o*-tol)$_3$ (3.6 mg, 6.0 μmol) was stirred for 30 minutes at room temperature. To the solution was added 4-bromotoluene (34.2 mg, 0.20 mmol) in CH_2Cl_2 (0.5 ml). After being stirred for 3 h, AcOH (1 ml) was added. After 3 h, the reaction mixture was neutralized with Na_2CO_3 solution. The aqueous layer was extracted with Et_2O (3 times), washed with water (once), brine (once), dried over $MgSO_4$ and concentrated. The residue was purified by preparative thin-layer chromatography on silica gel (hexane) to afford the trisubstituted alkene **3a** with a small amount of impurities. Further purification was performed by GPC, affording the alkene **3a** (46.9 mg, 0.18 mmol, 89% yield, *E*/*Z* = 7/93).

(*Z*)-2-(4-Methylphenyl)-1-phenylhept-1-ene (3a)

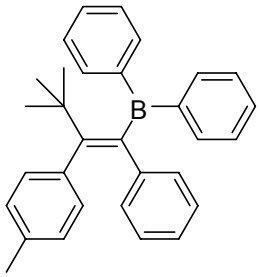


^{1}H NMR: δ = 0.86 (t, *J* = 6.9 Hz, 3H), 1.23-1.43 (m, 6H), 2.33 (s, 3H), 2.45 (t, *J* = 6.9 Hz, 2H), 6.40 (s, 1H), 6.92-6.95 (m, 2H), 7.00-7.21 (m, 7H); ^{13}C NMR: δ = 14.2, 21.3, 22.6, 27.7, 31.5, 40.8, 125.7, 125.8, 127.7, 128.3, 128.8, 129.1, 136.2, 137.6, 138.2, 143.4; HRMS (CI) Calcd for $C_{20}H_{24}$ (M^+) 264.1878. Found 264.1884.

Preparation of trisubstituted alkenylborane 2b

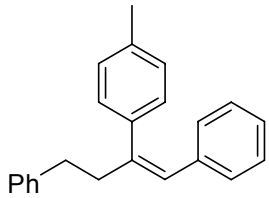
Under an argon atmosphere, a $(CH_2Cl)_2$ solution (0.5 ml) of alkynyltriarylborate **1b** (79.5 mg, 0.20 mmol), $Pd_2dba_3{\cdot}CHCl_3$ (5.1 mg, 2.5 μmol), and P(*o*-tol)$_3$ (3.7 mg, 6.0 μmol) was stirred for 30 minutes at room temperature. To the solution was added 4-bromotoluene (35.0 mg, 0.20 mmol) in $(CH_2Cl)_2$ (0.5 ml). After being stirred at reflux for 3 h, water was added. The aqueous layer was extracted with AcOEt (3 times), washed with water (once), brine (once), dried over $MgSO_4$ and concentrated. The residue was purified by preparative thin-layer chromatography on silica gel (hexane) to afford the trisubstituted alkenylborane **2b** (76.0 mg, 0.18 mmol, 92% yield).

(*Z*)-3,3-Dimethyl-2-(4-methylphenyl)-1-phenyl -1-diphenylborylbut-1-ene (2b)



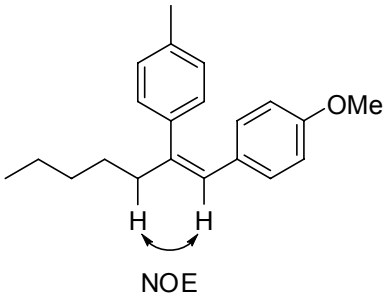
^{1}H NMR: δ = 1.13 (s, 9H), 2.18 (s, 3H), 6.74-6.81 (m, 5H), 6.88 (d, *J* = 8.1 Hz, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 7.43-7.49 (m, 6H) 7.95 (d, *J* = 7.8 Hz, 4H); ^{13}C NMR: δ = 21.1, 31.8, 37.8, 124.7, 127.1, 127.2, 127.5, 130.9, 131.1, 131.4, 134.4, 138.1, 139.0, 140.2, 141.2, 152.7; ^{11}B NMR: δ = 63.7; HRMS (CI) Calcd for $C_{31}H_{31}B$ (M^+) 414.2519. Found 414.2526.

(*Z*)-2-(4-Methylphenyl)-1,4-diphenylbut-1-ene (3c)



^{1}H NMR: δ = 2.35 (s, 3H), 2.68-2.79 (m, 4H), 6.37 (s, 1H), 6.90-6.92 (m, 2H), 7.01-7.30 (m, 12H); ^{13}C NMR: δ = 21.3, 34.6, 42.6, 125.7, 126.0, 126.4, 127.7, 128.2, 128.38, 128.45, 128.9, 129.2, 136.5, 137.4, 137.7, 141.8, 142.1; HRMS (CI) Calcd for $C_{23}H_{22}$ (M^+) 298.1721. Found 298.1720.

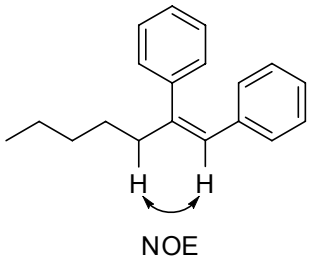
(*Z*)-1-(4-Methoxyphenyl)-2-(4-methylphenyl)hept-1-ene (3d)



^{1}H NMR: δ = 0.86 (t, *J* = 6.9 Hz, 3H), 1.26-1.40 (m, 6H), 2.34 (s, 3H), 2.43 (t, *J* = 7.1 Hz, 2H), 3.71 (s, 3H), 6.33 (s, 1H), 6.63 (d, *J* = 9.0 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 7.04 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR: δ = 14.2, 21.3, 22.6, 27.7,

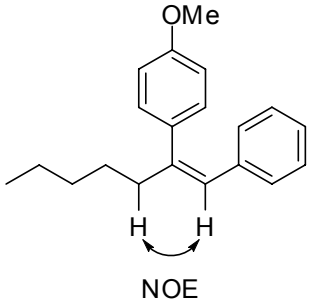
31.5, 40.8, 55.1, 113.1, 125.1, 128.3, 129.1, 129.9, 130.2, 136.1, 138.4, 141.4, 157.6; HRMS (CI) Calcd for $C_{21}H_{26}O$ (M^+) 294.1984. Found 294.1988.

(*Z*)-1,2-Diphenylhept-1-ene (3e)



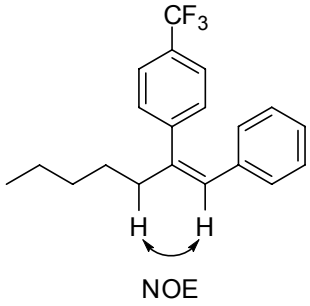
^{1}H NMR: δ = 0.87 (t, *J* = 7.1 Hz, 3H), 1.26-1.45 (m, 6H), 2.48 (t, *J* = 7.1 Hz, 2H), 6.42 (s, 1H), 6.89-6.92 (m, 2H), 7.03-7.32 (m, 8H); ^{13}C NMR: δ = 14.2, 22.6, 27.6, 31.5, 40.7, 125.92, 125.95, 126.7, 127.7, 128.35, 128.43, 128.9, 137.4, 141.3, 143.4; HRMS (CI) Calcd for $C_{19}H_{22}$ (M^+) 250.1721. Found 250.1722.

(*Z*)-2-(4-Methoxyphenyl)-1-phenylhept-1-ene (3f)



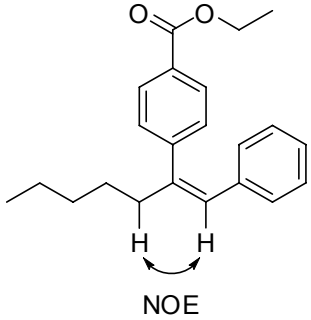
^{1}H NMR: δ = 0.87 (t, *J* = 7.2 Hz, 3H), 1.26-1.41 (m, 6H), 2.45 (t, *J* = 6.9 Hz, 2H), 3.80 (s, 3H), 6.39 (s, 1H), 6.81-6.84 (m, 2H), 6.92-6.96 (m, 2H), 7.03-7.09 (m, 5H); ^{13}C NMR: δ = 14.2, 22.6, 27.7, 31.5, 40.7, 55.1, 113.7, 125.7, 125.8, 127.7, 128.8, 129.5, 133.3, 137.7, 143.0, 158.3; HRMS (CI) Calcd for $C_{20}H_{24}O$ (M^+) 280.1827. Found 280.1823.

(*Z*)-2-(4-Trifluoromethylphenyl)-1-phenylhept-1-ene (3g)



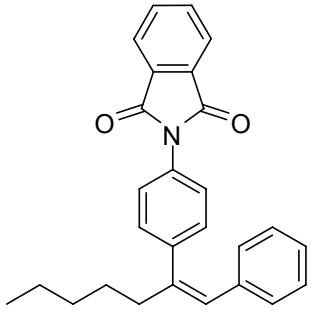
^{1}H NMR: δ = 0.87 (t, *J* = 7.1 Hz, 3H), 1.26-1.43 (m, 6H), 2.49 (t, *J* = 6.9 Hz, 2H), 6.51 (s, 1H), 6.84-6.93 (m, 2H), 7.06-7.14 (m, 3H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.52 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR: δ = 14.2, 22.6, 27.6, 31.4, 40.3, 124.1 (q, $J_{C\text{-}F}$ = 270.2 Hz), 125.3 (q, $J_{C\text{-}F}$ = 3.7 Hz), 126.4, 127.2, 127.9, 128.4 (q, $J_{C\text{-}F}$ = 24.1 Hz), 128.91, 128.93, 136.8, 141.9, 145.2; HRMS (CI) Calcd for $C_{20}H_{21}F_3$ (M^+) 318.1595. Found 318.1597.

(*Z*)-2-(4-Ethoxycarbonylphenyl)-1-phenylhept-1-ene (3h)



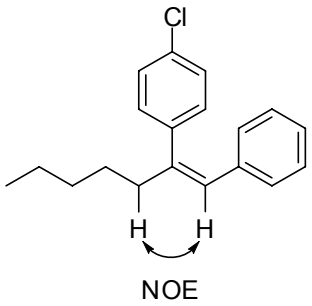
^{1}H NMR: δ = 0.86 (t, *J* = 7.1 Hz, 3H), 1.27-1.43 (m, 9H), 2.49 (t, *J* =7.1 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 6.49 (s, 1H), 6.88-6.91 (m, 2H), 7.05-7.12 (m, 3H), 7.22 (d, *J* = 8.7 Hz, 2H), 7.97 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR: δ = 14.1, 14.4, 22.5, 27.6, 31.4, 40.3, 60.9, 126.2, 126.9, 127.8, 128.6, 128.7, 128.9, 129.6, 136.9, 142.4, 146.3, 166.4; HRMS (CI) Calcd for $C_{22}H_{26}O_2$ (M^+) 322.1933. Found 322.1925.

(*Z*)-1-Phenyl-2-(4-phthalimidophenyl)hept-1-ene (3i)



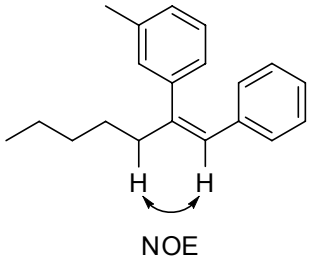
^{1}H NMR: δ = 0.89 (t, *J* = 6.9 Hz, 3H), 1.26-1.47 (m, 6H), 2.50 (t, *J* =7.4 Hz, 2H), 6.48 (s, 1H), 6.96-6.99 (m, 2H), 7.04-7.15 (m, 3H), 7.27-7.31 (m, 2H), 7.38-7.42 (m, 2H), 7.75-7.81 (m, 2H), 7.92-7.98 (m, 2H); ^{13}C NMR: δ = 14.2, 22.5, 27.7, 31.5, 40.5, 123.6, 126.1, 126.7, 127.8, 128.9, 129.1, 130.2, 131.6, 134.3, 137.1, 141.0, 142.3, 167.1; HRMS (CI) Calcd for $C_{27}H_{25}NO_2$ (M^+) 395.1885. Found 395.1884.

(*Z*)-2-(4-Chlorophenyl)-1-phenylhept-1-ene (3j)



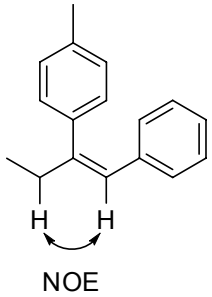
^{1}H NMR: δ = 0.87 (t, *J* = 7.1 Hz, 3H), 1.25-1.39 (m, 6H), 2.45 (t, *J* =7.4 Hz, 2H), 6.44 (s, 1H), 6.91 (m, 2H), 7.07-7.11 (m, 5H), 7.25 (m, 2H); ^{13}C NMR: δ = 14.2, 22.6, 27.6, 31.4, 40.4, 126.2, 126.6, 127.8, 128.6, 128.9, 129.9, 132.4, 137.1, 139.6, 142.0; HRMS (CI) Calcd for $C_{19}H_{21}Cl$ (M^+) 284.1332. Found 284.1328.

(*Z*)-2-(3-Methylphenyl)-1-phenylhept-1-ene (3k)



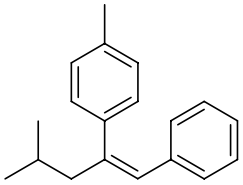
^{1}H NMR: δ = 0.87 (t, *J* = 7.1 Hz, 3H), 1.26-1.42 (m, 6H), 2.30 (s, 3H), 2.45 (t, *J* = 7.4 Hz, 2H), 6.39 (s, 1H), 6.90-7.08 (m, 8H), 7.17 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR: δ = 14.2, 21.6, 22.6, 27.7, 31.5, 40.9, 125.5, 125.7, 125.9, 127.4, 127.7, 128.2, 128.8, 137.4, 137.9, 141.3, 143.6; HRMS (CI) Calcd for $C_{20}H_{24}$ (M^+) 264.1878. Found 264.1879.

(*Z*)-2-(4-Methylphenyl)-1-phenylbut-1-ene (3l)



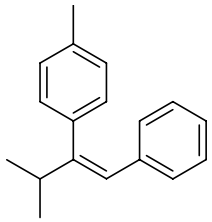
^{1}H NMR: δ = 1.06 (t, *J* = 7.5 Hz, 3H), 2.34 (s, 3H), 2.50 (q, *J* = 7.4 Hz, 2H), 6.40 (s, 1H), 6.91-6.96 (m, 2H), 7.01-7.11 (m, 7H); ^{13}C NMR: δ = 13.0, 21.3, 33.6, 124.7, 125.8, 127.7, 128.3, 128.9, 129.1, 136.3, 137.6, 138.3, 144.8; HRMS (CI) Calcd for $C_{17}H_{18}$ (M^{+}) 222.1409. Found 222.1406.

(*Z*)-4-Methyl-2-(4-methylphenyl)-1-phenylpent-1-ene (3m)



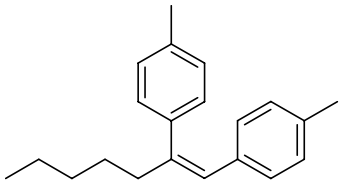
^{1}H NMR: δ = 0.90 (d, *J* = 6.3 Hz, 6H), 1.56 (pseudo sept., *J* = 6.8 Hz, 1H), 2.33-2.36 (m, 5H), 6.38 (s, 1H), 6.93-6.95 (m, 2H), 7.02-7.11 (m, 7H); ^{13}C NMR: δ = 21.3, 22.4, 25.9, 50.5, 125.9, 127.0, 127.7, 128.4, 128.9, 129.1, 136.3, 137.6, 138.0, 142.3; HRMS (CI) Calcd for $C_{19}H_{22}$ (M^{+}) 250.1721. Found 250.1728.

(*Z*)-3-Methyl-2-(4-methylphenyl)-1-phenylbut-1-ene (3n)



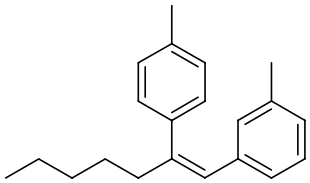
^{1}H NMR: δ = 1.10 (d, *J* = 6.9 Hz, 6H), 2.35 (s, 3H), 2.69 (sept., *J* = 6.8 Hz, 1H), 6.37 (s, 1H), 6.87 (dd, *J* = 8.8, 1.4 Hz, 2H), 7.01-7.12 (m, 7H); ^{13}C NMR: δ = 21.3, 21.9, 37.5, 123.9, 125.8, 127.6, 128.7, 128.9, 129.0, 136.1, 137.6, 138.0, 149.3; HRMS (CI) Calcd for $C_{18}H_{20}$ (M^{+}) 236.1565. Found 236.1562.

(*Z*)-1,2-Bis(4-methylphenyl)hept-1-ene (3o)



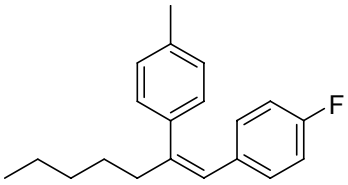
^{1}H NMR: δ = 0.86 (t, *J* = 7.2 Hz, 3H), 1.26-1.43 (m, 6H), 2.22 (s, 3H), 2.34 (s, 3H), 2.44 (t, *J* = 6.8 Hz, 2H), 6.36 (s, 1H), 6.82 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR: δ = 14.2, 21.1, 21.3, 22.6, 27.7, 31.5, 40.8, 125.6, 128.3, 128.4, 128.7, 129.1, 134.7, 135.4, 136.1, 138.4, 142.5; HRMS (CI) Calcd for $C_{21}H_{26}$ (M^+) 278.2034. Found 278.2035.

(*Z*)-1-(3-Methylphenyl)-2-(4-methylphenyl)hept-1-ene (3p)



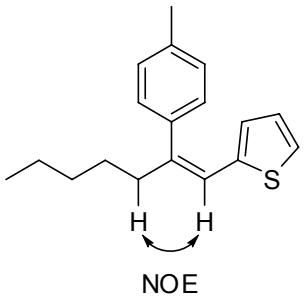
^{1}H NMR: δ = 0.87 (t, *J* = 6.9 Hz, 3H), 1.28-1.43 (m, 6H), 2.12 (s, 3H), 2.33 (s, 3H), 2.45 (t, *J* = 7.4 Hz, 2H), 6.36 (s, 1H), 6.68 (d, *J* = 7.5 Hz, 1H), 6.79 (s, 1H), 6.85 (d, *J* = 7.5 Hz, 1H), 6.94 (dd, *J* = 7.8, 7.2 Hz, 1H), 7.03 (d, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR: δ = 14.2, 21.3, 21.4, 22.6, 27.7, 31.5, 40.8, 125.77, 125.82, 126.6, 127.5, 128.3, 129.0, 129.8, 136.1, 137.1, 137.5, 138.3, 143.2; HRMS (CI) Calcd for $C_{21}H_{26}$ (M^+) 278.2034. Found 278.2042.

(*Z*)-1-(4-Fluorophenyl)-2-(4-methylphenyl)hept-1-ene (3q)



^{1}H NMR: δ = 0.86 (t, *J* = 7.1 Hz, 3H), 1.26-1.43 (m, 6H), 2.34 (s, 3H), 2.44 (t, *J* = 7.2 Hz, 2H), 6.35 (s, 1H), 6.72-6.80 (m, 2H), 6.85-6.91 (m, 2H), 7.01 (d, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR: δ = 14.2, 21.3, 22.6, 27.7, 31.5, 40.7, 114.5 (d, $J_{C\text{-}F}$ = 21.2 Hz), 124.5, 128.3, 129.2, 130.3 (d, $J_{C\text{-}F}$ = 7.3 Hz), 133.6 (d, $J_{C\text{-}F}$ = 2.9 Hz), 136.4, 137.9, 143.2, 160.9 (d, $J_{C\text{-}F}$ = 243.2 Hz); HRMS (CI) Calcd for $C_{20}H_{23}F$ (M^+) 282.1784. Found 282.1776.

(*Z*)-2-(4-Methylphenyl)-1-(2-thienyl)hept-1-ene (3r)



^{1}H NMR: δ = 0.87 (t, *J* = 6.9 Hz, 3H), 1.28-1.45 (m, 6H), 2.36-2.42 (m, 5H), 6.58 (s, 1H), 6.73 (d, *J* = 3.3 Hz, 1H), 6.80 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.92 (d, *J* = 5.1 Hz, 1H), 7.08 (d, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR: δ = 14.2, 21.4, 22.6, 27.5, 31.5, 40.9, 119.5, 124.5, 125.8, 126.6, 128.4, 129.5, 137.0, 137.8, 141.1, 142.2; HRMS (CI) Calcd for $C_{18}H_{22}S$ (M^+) 270.1442. Found 270.1445.

Preparation of (*E*)-Tamoxifen (5)

Under an argon atmosphere, a CH_2Cl_2 solution (0.5 ml) of alkynyltriarylborate **1e** (75.5 mg, 0.20 mmol), $Pd_2dba_3{\cdot}CHCl_3$ (5.2 mg, 2.5 μmol), and P(*o*-tol)$_3$ (3.6 mg, 6.0 μmol) was stirred for 30 minutes at room temperature. To the solution was added bromobenzene (33.0 mg, 0.20 mmol) in CH_2Cl_2 (0.5 ml). After being stirred for 3 h, 4-($Me_2NCH_2CH_2O$)C_6H_4I (**4**, 178 mg, 0.60 mmol) in CH_2Cl_2 (0.5 ml), powdered NaOH (78 mg, 1.8 mmol), and water (100 μl) were added. After 24 h, water was added to the reaction mixture. The aqueous layer was extracted with CH_2Cl_2 (3 times), washed with water (once), brine (once), dried over Na_2SO_4 and concentrated. The residue was purified by preparative thin-layer chromatography on silica gel (benzene:AcOEt:NEt_3 = 100:40:1) to afford Tamoxifen (**5**, 58.4 mg, 0.16 mmol, 79% yield, *E*/*Z* = 97/3). The spectral data was identical to that reported.[20f]

Preparation of alkenyl iodide 6

Under an argon atmosphere, a CH_2Cl_2 solution (0.5 ml) of alkynyltriarylborate **1e** (75.9 mg, 0.20 mmol), $Pd_2dba_3{\cdot}CHCl_3$ (5.2 mg, 2.5 μmol), and P(*o*-tol)$_3$ (3.6 mg, 6.0 μmol) was stirred for 30 minutes at room temperature. To the solution was added bromobenzene (33.2 mg, 0.20 mmol) in CH_2Cl_2 (0.5 ml). After being stirred for 3 h, aqueous ammonia (1 ml) was added. The aqueous layer was extracted with Et_2O (3 times), washed with water (once), brine (once), dried over Na_2SO_4 and concentrated. The residue was dissolved in acetone and treated with NIS (225 mg, 1.0 mmol) at 0 °C for 1 h. The reaction mixture was purified by preparative thin-layer chromatography on

silica gel (hexane), followed by GPC to afford alkenyl iodide **6** (39.2 mg, 0.12 mmol, 59% yield, *E*/*Z* = 96/4). The spectral data was identical to that reported.[20d]

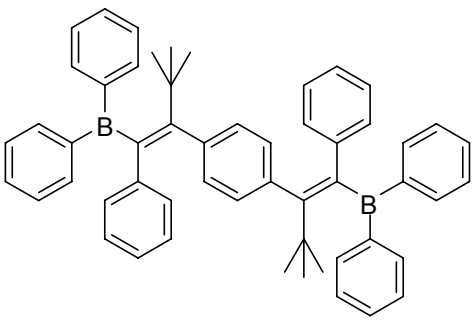
Preparation of ketone 7

Under an argon atmosphere, a CH_2Cl_2 solution (0.5 ml) of alkynyltriarylborate **1e** (75.9 mg, 0.20 mmol), $Pd_2dba_3{\cdot}CHCl_3$ (5.2 mg, 2.5 μmol), and P(*o*-tol)$_3$ (3.6 mg, 6.0 μmol) was stirred for 30 minutes at room temperature. To the solution was added bromobenzene (33.2 mg, 0.20 mmol) in CH_2Cl_2 (0.5 ml). After being stirred for 3 h, trimethylamine-*N*-oxide (75.1 mg, 1.0 mmol) was added. After 3 h, water was added to the reaction mixture. The aqueous layer was extracted with AcOEt (3 times), washed with water (once), brine (once), dried over $MgSO_4$ and concentrated. The residue was purified by preparative thin-layer chromatography on silica gel (hexane:AcOEt = 50:1) to afford ketone **7** (40.8 mg, 0.18 mmol, 91% yield). The spectral data was identical to that reported.[20i]

Preparation of diboranyl compound 8

Under an argon atmosphere, a $(CH_2Cl)_2$ solution (0.5 ml) of alkynyltriarylborate **1b** (79.5 mg, 0.20 mmol), $Pd_2dba_3{\cdot}CHCl_3$ (2.5 mg, 1.2 μmol), and P(*o*-tol)$_3$ (2.9 mg, 3.0 μmol) was stirred for 30 minutes at room temperature. To the solution was added 1,4-dibromobenzene (23.7 mg, 0.10 mmol) in $(CH_2Cl)_2$ (0.5 ml). After being stirred at reflux for 1 h, water was added. The aqueous layer was extracted with AcOEt (3 times), washed with water (once), brine (once), dried over $MgSO_4$ and concentrated. The residue was purified by preparative thin-layer chromatography on silica gel (hexane:AcOEt = 10:1) to afford the diboranyl compound **8** (44.9 mg, 0.062 mmol, 62% yield).

1,4-Bis[(*Z*)-1-*tert*-butyl-2-phenyl-2-(diphenylboryl)ethenyl]benzene (8)



^{1}H NMR: δ = 0.98 (s, 18H), 6.71-6.76 (m, 14H), 7.40-7.48 (m, 12H), 7.91 (d, *J* = 6.8 Hz, 8H); ^{13}C NMR: δ = 31.7, 37.6, 124.6, 127.0, 127.5, 129.5, 130.9, 131.3, 138.1,

139.1, 140.5, 141.3, 143.9, 153.3; ^{11}B NMR: δ = 59.6; HRMS (CI) Calcd for $C_{54}H_{52}B_2$ (M^+) 722.4255. Found 722.4252.

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14. The borate **1a**, isolated as solid, was prepared through cation exchange from the corresponding lithium borate. The direct use of the lithium borate generated *in situ* in THF also gave the product but in lower yield.
15. No reaction occurred in the absence of the palladium catalyst.
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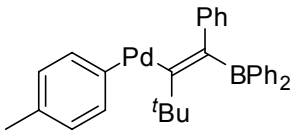
17. An alternative mechanism is also conceivable. The arylpalladium bromide **A** acts as an electrophile like alkyl halides, giving diorganylpalladium **D**. Subsequent reductive elimination affords the alkenylborane **2b** and palladium(0).



D

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19. Other boronic esters including catecholate and ethylene glycolate were also subjected to the reaction conditions. However, no desired alkenylboronic esters were formed, presumably due to the instabilities of the corresponding ate complexes under the reaction conditions.
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Chapter 2

Palladium-Catalyzed Allylation of Alkynyltriarylborates

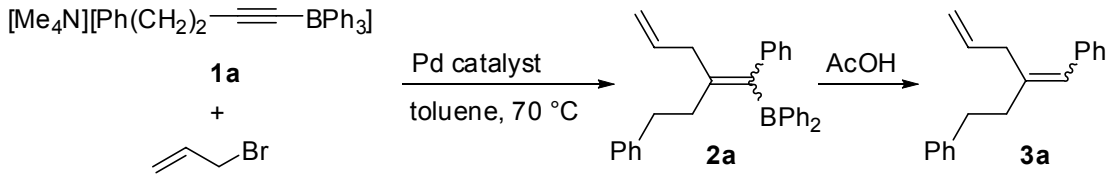
Abstract: In the presence of a palladium catalyst, alkynyltriarylborates reacted with allyl halides to give 1,4-dienylboranes in good yields.

Organoboron compounds have received ever-increasing attention because of their interesting chemical and photophysical properties[1] as well as reactivities. In particular, organoboranes having π-conjugation extended through a vacant p-orbital on boron[2] are attractive in terms of optoelectronic materials such as light-emitting diodes,[3] fluorescent sensors,[4] non-linear optics,[5] and two-photon emitters.[6] Therefore, skeletons containing alkenyl–boron linkages have become a synthetic target of current interest. Palladium-catalyzed as well as non-catalyzed reactions of alkynyltriorganylborates with an allylating agent such as allyl bromide produced trisubstituted alkenylboranes through allylation on the alkynyl carbon β to boron accompanied with 1,2-migration of organyl group on boron.[7] So far, the migrating organyl group was limited to alkyl and alkenyl groups. It would be more attractive in terms of potential as π-conjugated materials if an aryl group is installed by 1,2-migration. In this chapter, the author describes our synthetic study on the palladium-catalyzed reaction of alkynyltriarylborates with allyl halides.

We initially examined a non-catalyzed reaction of alkynyltriphenylborate **1a** with allyl bromide. Alkynyltriphenylborate **1a** was treated with allyl bromide in toluene at 70 °C, and after 15 minutes, the reaction was quenched by addition of acetic acid. Only protonated alkene **4** was obtained in 87% yield, suggesting that allyl bromide was not electrophilic enough to form a carbon–carbon bond with the alkyne carbon. Instead, the proton of acetic acid acted as the electrophile to promote the 1,2-migration reaction of the phenyl group from boron to α-carbon.[8] Thus, it was indicated that alkynyltriarylborates were less reactive than alkynyltrialkylborates. Next, we examined a palladium-catalyzed reaction. In the presence of a catalytic amount of $Pd(PPh_3)_4$, the allylated alkene **3a** was obtained in 11% yield (entry 2). A palladium catalyst modified with P(*o*-tol)$_3$, which was a suitable catalyst for the reaction with aryl halides,[9] gave a complex mixture (entry 3). Although DPPE and DPPF afforded no desired product (entries 4 and 5), BINAP gave **3a** in 42% yield (entry 6). The bidentate phosphine ligand XANTPHOS, possessing a rigid and planar skeleton with a large bite angle of 108 °,[10] gave **3a** in 91% yield as a mixture of geometrical isomers (entry 7, *E*/*Z*=54/46). DPEPHOS, which also has a large bite angle (104 °) but is more flexible than XANTPHOS, gave the product in only 6% yield (entry 8).

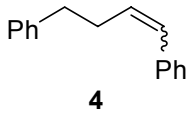
Other allylating reagents were examined (Table 2). Allyl chloride also reacted with **1a** to give the allylated product in 48% yield (entry 2). Allyl acetate and allyl methyl carbonate were ineffective, affording only a small amount of products (entries 3 and 4). Thus allyl bromide gave the best result.

Table 1. Catalyst screening[a]



entry	catalyst (mol%)	yield of **3a** / %[b]	*E*/*Z*[b]
1[c]	-	<1	-
2	$Pd(PPh_3)_4$ (5)	11	72/28
3	$Pd_2dba_3{\cdot}CHCl_3$ (2.5)/ $P(o\text{-tol})_3$ (6)	complex mixture	-
4	$Pd_2dba_3{\cdot}CHCl_3$ (2.5)/ DPPE (6)	<1	-
5	$Pd_2dba_3{\cdot}CHCl_3$ (2.5)/ DPPF (6)	2	-
6	$Pd_2dba_3{\cdot}CHCl_3$ (2.5)/ BINAP (6)	42	29/71
7	$Pd_2dba_3{\cdot}CHCl_3$ (2.5)/ XANTPHOS (6)	91 (90)[d]	54/46
8	$Pd_2dba_3{\cdot}CHCl_3$ (2.5)/ DPEPHOS (6)	6	27/73

[a] Reaction conditions: 1.0 equiv of **1a**, 1.2 equiv of allyl bromide, 5 mol% Pd catalyst, toluene, 70 °C, 15 min. [b] Determined by GC analysis. [c] A protonated product **4** was isolated in 87% yield (*E*/*Z* = 7/93). [d] Isolated yield.

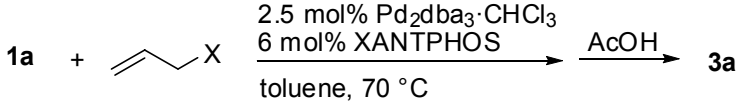


4

The following experiments were carried out in order to support the initial formation of alkenylborane **2a**. When AcOD was employed instead of AcOH for protonolysis, deuterated alkene **3a-*d*$_1$** was isolated in 91% yield (*E*/*Z* = 54/46, *E*: 72% incorporation of D, *Z*: 71% incorporation of D). Successive treatment of the reaction mixture with

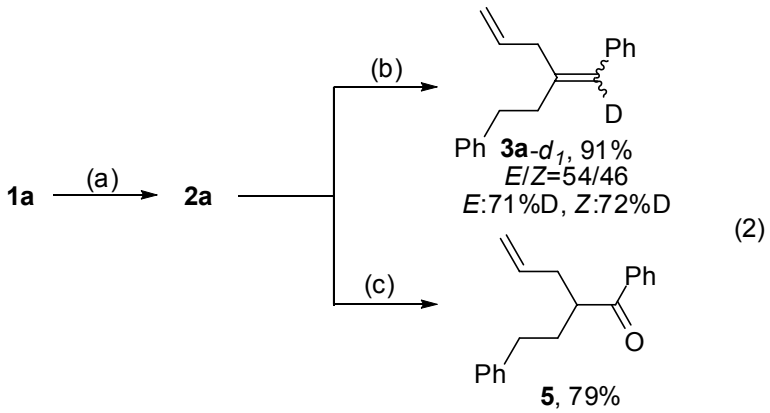
trimethylamine *N*-oxide caused oxidation of the carbon–boron bond to afford the ketone **5** in 79% yield. Thus, the alkenylborane **2a** was initially formed with incorporation of an allyl group on the sp^2 carbon β to boron and a phenyl group on the α sp^2 carbon.

Table 2. Examination on allylating reagents[a]



entry	X	yield of **3a** / %[b]	*E*/*Z*[b]
1	Br	91 (90)[c]	54/46
2	Cl	48	43/57
3	OAc	13	56/44
4	OC(O)OMe	3	52/48

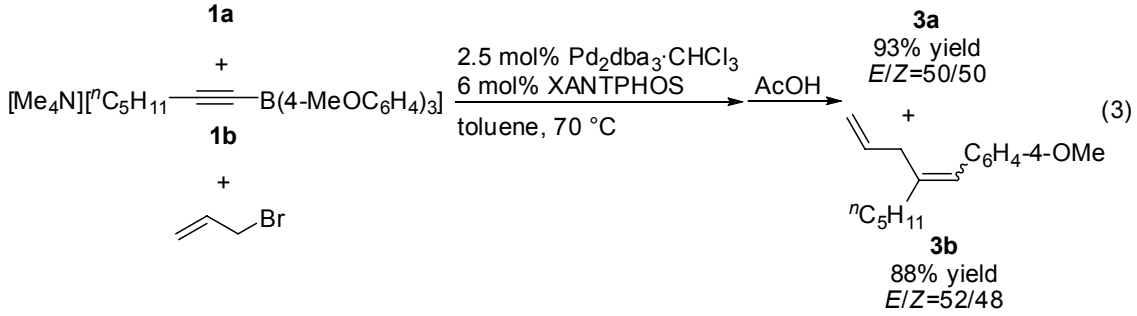
[a] Reaction conditions: 1.0 equiv of **1a**, 1.2 equiv of allylating reagent, 5 mol% Pd catalyst, toluene, 70 °C, 15 min. [b] Determined by GC analysis. [c] Isolated yield.



(2)

(a) 2.5 mol% $Pd_2dba_3·CHCl_3$, 6 mol% P(*o*-tol)$_3$, 1.2 equiv of allyl bromide, toluene, rt, 3 h. (b) AcOD, rt, 3 h. (c) 5 equiv Me_3NO, rt, 3 h.

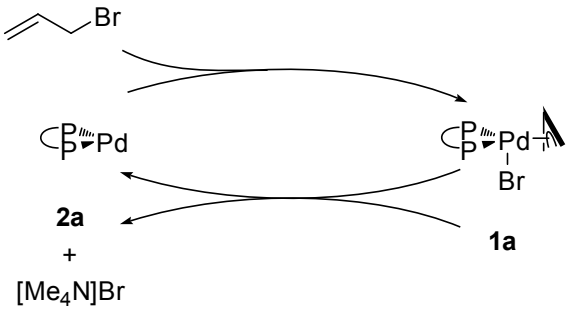
Next, a crossover experiment was carried out (eq 3). When a mixture of **1a** (1.0 equiv.) and **1b** (1.0 equiv.) was subjected to the reaction with 2.4 equiv. of allyl bromide, **3a** and **3b** were obtained in 93% and 88% yield, respectively. No crossover products were detected in the reaction mixture by ^{1}H NMR and GC-MS, suggesting that the 1,2-aryl migration occurred intramolecularly.



(3)

The plausible mechanism is depicted in Scheme 1. Initially, allyl bromide oxidatively adds to palladium(0) to yield π-allylpalladium species ligated by XANTPHOS. The π-allylpalladium species is electrophilic enough to induce a nucleophilic attack of the alkynyltriarylborate anion, which triggers 1,2-phenyl migration from boron to the α-carbon, giving the alkenylborane **2a** and palladium(0).

Scheme 1. Plausible mechanism



Essentially no *E*/*Z* selectivities were observed in the products of the present reaction. This stereochemical outcome stands in contrast to the good stereoselectivities observed in the reaction with aryl halides.[9] Thus, it is inferred that a mechanism different from the arylative variant is operating in the present reaction. We explain the difference in the stereoselectivites is attributed to the nature of π-allylpalladium complex ligated by a bidentate phosphine and σ-arylpalladium complex ligated by a monodentate phosphine. Tetracoordinated $[(\text{xantphos})\text{Pd}(\pi\text{-allyl})]^+$, which would be generated by oxidative addition of allyl bromide, is sterically congested on palladium center, prohibiting the additional coordination of the alkynyl moiety to the palladium. Meanwhile, the side of the allyl ligand opposite to palladium is vulnerable enough to be directly attacked by the alkynyl group. Therefore, the alkynylborate is likely to attack the allyl ligand from the back side of palladium.[11] The 1,2-phenyl migration can occur in both ways, in the *syn*- and *anti-periplanar* directions to the carbon–carbon bond developing at the sp carbon β to boron (Figure 1). On the other hand, tricoordinated

(o-tol)$_3$PPd(aryl)Br, which is generated by oxidative addition of aryl halide to the palladium(0) and is in equilibrium with the dimeric species bridged by bromide ligands, has a vacant site on palladium, allowing the alkynylborate to coordinate.[12] Consequently, it tends to undergo carbopalladation across the carbon–carbon triple bond.

Figure 1. Stereochemistry of 1,2-migration

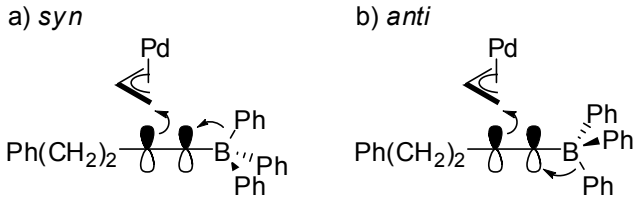
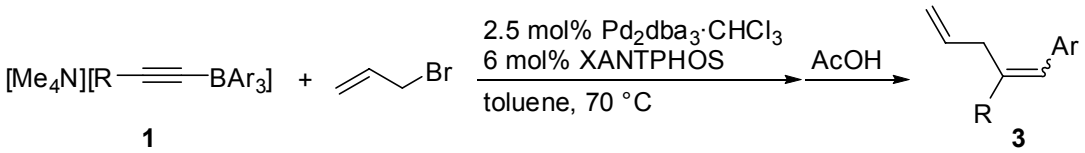


Table 3. Allylation of various alkynyltriarylborates [a]

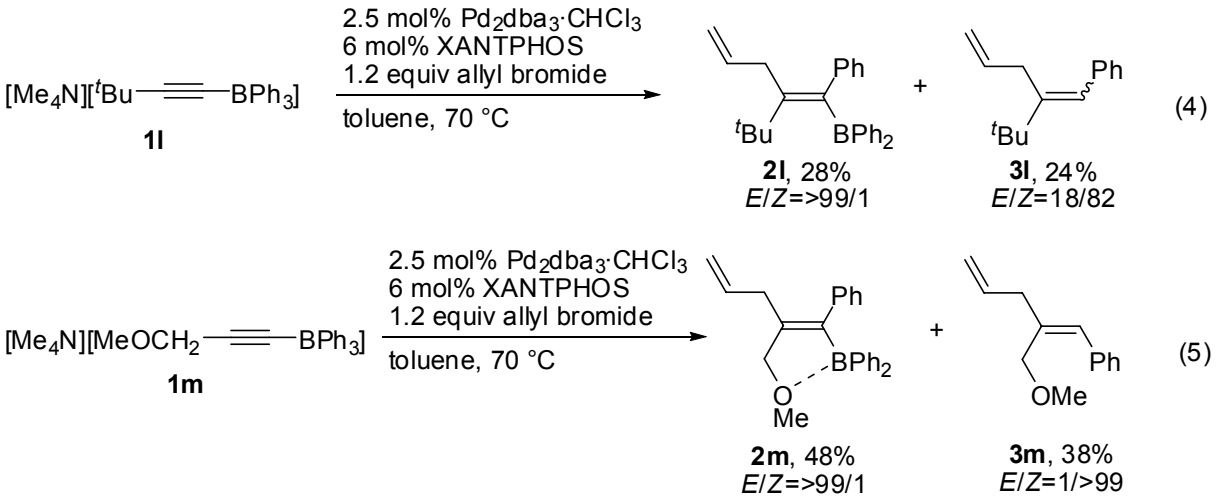


Entry	Alkynyltriarylborate	R	Ar	Yield (%)[b]	E/Z[c]
1	**1c**	$^{n}C_5H_{11}$	Ph	91	54/46
2	**1d**	^{i}Bu	Ph	89	55/45
3	**1e**	^{i}Pr	Ph	72	57/43
4	**1f**	Ph	Ph	24	50/50
5	**1g**	Me_3Si	Ph	n.d.	n.d.
6	**1h**	$^{n}C_5H_{11}$	4-MeC_6H_4	89	47/53
7	**1i**	$^{n}C_5H_{11}$	3-MeC_6H_4	91	48/52
8[d]	**1j**	$^{n}C_5H_{11}$	4-FC_6H_4	83	53/47
9	**1k**	$^{n}C_5H_{11}$	2-thienyl	79	71/29

[a] Reaction conditions: 1.0 equiv. of **1**, 1.2 equiv. of allyl bromide, 2.5 mol% Pd_2dba_3·$CHCl_3$, 6 mol% XANTPHOS, toluene, 70 °C, 15 min. [b] Isolated yield. [c] Determined by ^{1}H NMR analysis. [d] Reaction time: 30 min.

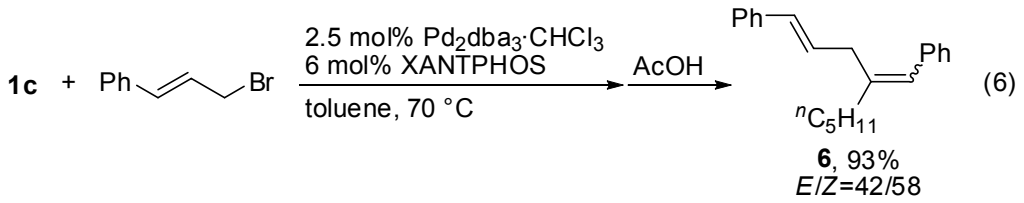
Various alkynylborates were subjected to the palladium-catalyzed allylation reaction conditions (Table 3). Alkynylborates having a primary alkyl substitutent yielded the corresponding 1,4-dienes in high yield (entries 1 and 2). In the case of a secondary alkyl substituent, the yield decreased to 72 % (entry 3). Triphenyl(phenylethynyl)borate (**1f**) was less reactive, giving the product in 24% yield (entry 4). A complex mixture resulted from trimethylsilylethynylborate **1g** (entry 5). As the aryl group on boron, both electron-donating and -withdrawing groups could participated in the reaction (eq 3, entries 6-8). The reaction of alkylnyltriarylborate **1j** (Ar = 4-fluorophenyl) was slower than that of **1c**, requiring 30 minutes to complete, indicating the electron poor borate is less reactive (entry 8). A 2-thienyl group was also migrated to give the corresponding product in 79% yield (entry 9).

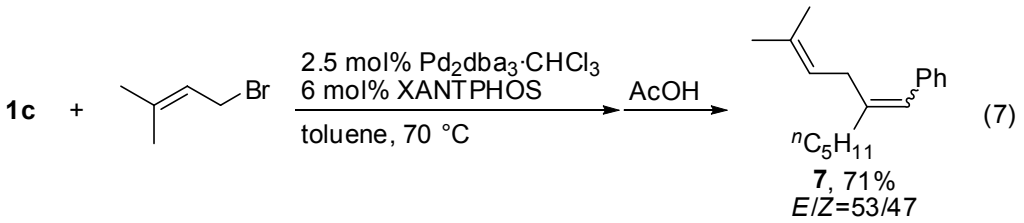
The allylation reaction of alkynylborate **1l** afforded **2l** in 28% yield (eq 4, *E*/*Z* = >99/1) and **3l** in 25% yield (*E*/*Z* = 18/82). The boron–carbon bond of the (*E*)-isomer of **2l** was less labile to protonolysis with acetic acid and oxidation with air owing to the steric protection by the neighboring tertiary butyl group to allow partial isolation of **2l**. The reaction of alkynylborate **1m** equipped with a methoxymethyl substituent gave a mixture of (*E*)-alkenylborane **2m** (eq 5, 48% yield) and (*Z*)-alkene **3m** (38% yield). The (*E*)-alkenylborane **2m** was stabilized by the intramolecular coordination of the oxygen atom, whereas the corresponding (*Z*)-isomer was protonated to **3m**.



We subsequently conducted the reaction with substituted allylic bromides. The reaction of **1c** with cinnamyl bromide afforded the 1,4-diene **6** in 93% yield (eq 6, *E*/*Z*=42/58), while the reaction with crotyl bromide resulted in the mixture of isomers.

Prenyl bromide was selectively incoporated at less hindered position to give **7** in 71% yield (eq 7, *E*/*Z*=53/47).

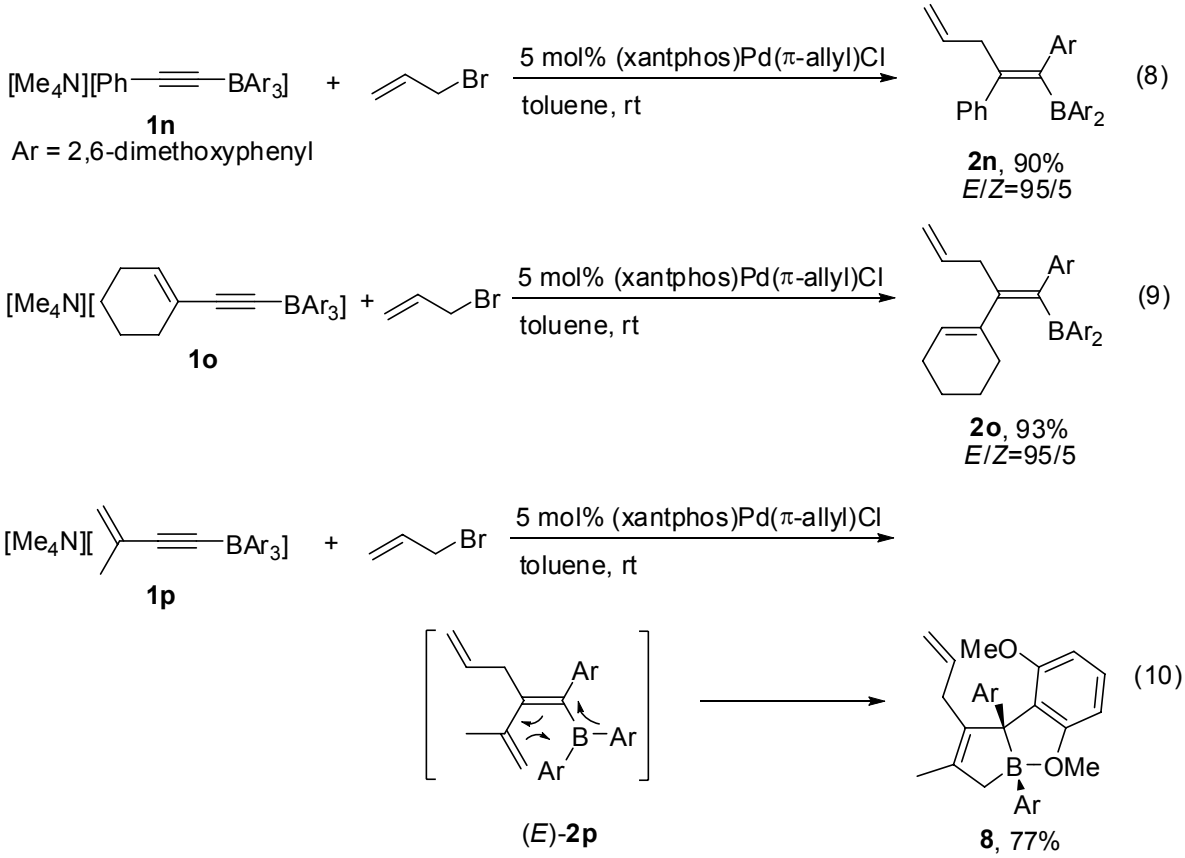




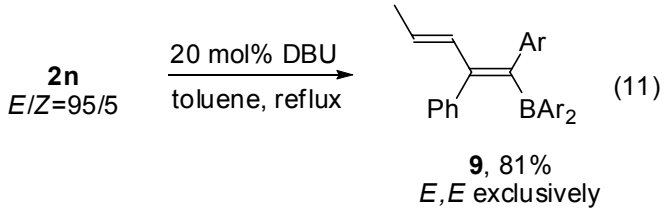
We next tried to make the produced (α-arylalkenyl)diarylboranes less labile by increasing the steric bulkiness of the aryl groups. Our initial attempt to synthesize the borate by the reaction of trimesitylborane[13] with alkynyllithium failed due to the severe steric hindrance around the boron atom. Next, a 2,6-dimethoxyphenyl group was examined as the aryl group on boron, since tris(2,6-dimethoxyphenyl)borane is known as air-stable to form stable complexes with a variety of Lewis bases and nucleophiles.[14] Thus, alkynyllithiums were reacted with tris(2,6-dimethoxyphenyl)borane, and the following treatment with tetramethylammonium chloride afforded the corresponding alkynylborates **1n**, **1o**, and **1p** as air-stable white powders.

To our delight, the palladium-catalyzed reaction of **1n** and **1o** with allyl bromide proceeded even at room temperature, giving the alkenylborane **2n** and **2o** with high stereoselectivity (eqs 8 and 9, *E*/*Z*=95/5) in 90 and 93% yield, respectively.[15] The alkynylborates **1n** and **1o** were considerably more reactive than triphenyl(phenylethynyl)borate (**1f**). Although it was unclear which steric or electronic factor operated for the stereoselective formation of **2n** and **2o**, The higher reactivity could be attributed to the electron-rich nature of the 2,6-dimethoxyphenyl group, This trend is in agreement with the slower reaction rate observed with tris(4-fluorophenyl)borate **1j**. The organoboranes **2n** and **2o** were so stable that they could be purified by column chromatography on silica gel. The stability can be ascribed either to steric hindrance of the 2,6-dimethoxyphenyl groups or to intramolecular coordination of the methoxy group to boron. In the ^{1}H NMR spetra of **2n** and **2o**, the methoxy signals were observed as equivalent, making the intramolecular coordination unlikely.

The reaction of **1p** furnished a product totally different from that of **1o** (eq 10). 3-Borolene **8** was obtained in 77% yield together with a few percents of (*Z*)-**2p**. The formation of **8** was explained by assuming that (*E*)-**2p**, the major geometrical isomer of the initial product, underwent a cyclization reaction accompanied by 1,2-migration of the 2,6-dimethoxyphenyl group.[16] On the other hand, (*Z*)-**2p**, the minor geometrical isomer, remained as such.



Treatment of 1,4-dienylborane **2n** with a catalytic amount of DBU caused a shift of a carbon–carbon double bond to afford the conjugated (*E,E)*-1,3-dienylborane **9** as a single stereoisomer in 81% yield (eq 11). The steric hindrance around the boron atom would inhibit the complexation with DBU and the π-accepting ability of the boron facilitates isomerization via deprotonation.[17]



Experimental Section

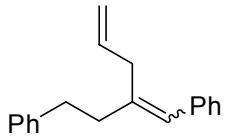
General. NMR spectra were recorded on a Varian Gemini 2000 (^{1}H at 300 MHz and ^{13}C at 75 MHz) or Varian Mercury-400 (^{1}H at 400 MHz and ^{11}B at 128 MHz) spectrometers. Me_4Si (^{1}H, δ=0.00), residual H of CD_3CN (^{1}H in CD_3CN, δ=1.94), $CDCl_3$ (^{13}C, δ=77.0), **C**D_3CN (^{13}C, δ=1.32), and $BF_3{\cdot}OEt_2$ (^{11}B, δ=0.00) were used as standard. High-resolution mass spectra were recorded on a JEOL JMS-SX102A spectrometer. All reactions were carried out under an argon atmosphere. Column chromatography was performed with silica gel 60 N (Kanto). Preparative thin-layer chromatography was performed with silica gel 60 PF_{254} (Merck). Gel permeation chromatography (GPC) was carried out with Japan Analytical Industry LC-908.

Materials. Unless otherwise noted, all chemicals and anhydrous solvents were obtained from commercial suppliers and used as received. CH_2Cl_2 was purchased from Kanto chemicals. Toluene was dried over Na-benzophenone ketyl. AcOH and AcOD were degassed by sonication.

Palladium-catalyzed alkylation of alkynyltriarylborate 1a. A typical procedure.

Under an argon atmosphere, a toluene solution (0.5 ml) of alkynyltriarylborate **1a** (89.0 mg, 0.20 mmol), $Pd_2dba_3{\cdot}CHCl_3$ (5.2 mg, 2.5 μmol), and XANTPHOS (6.9 mg, 6.0 μmol) was stirred for 30 minutes at room temperature. To the solution was added allyl bromide (28.8 mg, 0.24 mmol) in toluene (0.5 ml). After being stirred at 70 °C for 15 minutes, AcOH (1 ml) was added at room temperature. After 3 h, the reaction mixture was neutralized with Na_2CO_3 solution. The aqueous layer was extracted with AcOEt (3 times), washed with water (once), brine (once), dried over $MgSO_4$ and concentrated. The residue was purified by preparative thin-layer chromatography on silica gel (hexane) to afford the trisubstituted alkene **3a** (44.5 mg, 0.18 mmol, 91% yield, *E*/*Z* = 54/46).

(*E*)- and (*Z*)-1-Phenyl-2-(2-phenylethyl)penta-1,4-diene (3a)



A mixture of geometrical isomers (*E*/*Z* = 54/46)

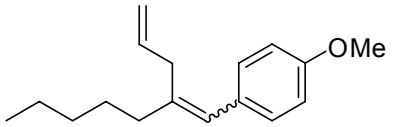
^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.44-2.56 ((*E*)- and (*Z*)-isomer, m, 2H), 2.75-2.85 ((*E*)- and (*Z*)-isomer, m, 2H), 2.96 ((*E*)-isomer, d, *J* = 6.8 Hz, 2H), 3.02 ((*Z*)-isomer, d,

J = 6.0 Hz, 2H), 5.09-5.19 ((*E*)- and (*Z*)-isomer, m, 2H), 5.82-5.97 ((*E*)- and (*Z*)-isomer, m, 1H), 6.34 ((*E*)-isomer, s, 1H), 6.37 ((*Z*)-isomer, s, 1H), 7.13-7.33 ((*E*)- and (*Z*)-isomer, m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ =32.9, 34.4, 34.7, 35.6, 39.1, 42.0, 116.1, 116.5, 125.7, 125.8, 126.08, 126.13, 126.7, 126.8, 128.00, 128.02, 128.19, 128.22, 128.25, 128.37, 128.39, 128.41, 136.0, 136.4, 137.9, 138.0, 139.5, 140.5, 141.8, 141.9; HRMS (EI): Calcd for $C_{19}H_{20}$ (M^+) 248.1565. Found 248.1558.

One-pot oxidation procedure for alkenylborane 2a

Under an argon atmosphere, a toluene solution (0.5 ml) of alkynyltriarylborate **1a** (89.2 mg, 0.20 mmol), Pd_2dba_3·$CHCl_3$ (5.0 mg, 2.5 μmol), and XANTPHOS (7.0 mg, 6.0 μmol) was stirred for 30 minutes at room temperature. To the solution was added allyl bromide (29.0 mg, 0.24 mmol) in toluene (0.5 ml). After being stirred at 70 °C for 15 minutes, Me_3NO (75 mg, 1.0 mmol) was added at room temperature. After 3 h, water was added to the reaction mixture.. The aqueous layer was extracted with AcOEt (3 times), washed with water (once), brine (once), dried over $MgSO_4$ and concentrated. The residue was purified by preparative thin-layer chromatography on silica gel (hexane:AcOEt = 20:1) to afford the ketone **5** (41.8 mg, 0.16 mmol, 79% yield).

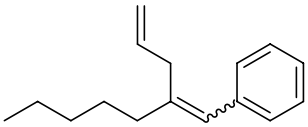
(*E*)- and (*Z*)-1-(4-Methoxyphenyl)-2-pentylpenta-1,4-diene (3b)



A mixture of geometrical isomers (*E*/*Z*=51/49)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86-0.93 ((*E*)- and (*Z*)-isomer, m, 3H), 1.26-1.33 ((*E*)- and (*Z*)-isomer, m, 4H), 1.42-1.54 ((*E*)- and (*Z*)-isomer, m, 2H), 2.11-2.23 ((*E*)- and (*Z*)-isomer, m, 2H), 2.89 ((*E*)-isomer, d, *J* = 6.9 Hz, 2H), 2.97 ((*Z*)-isomer, d, *J* = 6.0 Hz, 2H), 3.81 ((*E*)- and (*Z*)-isomer, s, 3H), 5.06-5.13 ((*E*)- and (*Z*)-isomer, m, 2H), 5.81-5.95 ((*E*)- and (*Z*)-isomer, m, 1H), 6.21 ((*E*)-isomer, s, 1H), 6.31 ((*Z*)-isomer, s, 1H), 6.84-6.87 ((*E*)- and (*Z*)-isomer, m, 2H), 7.16 ((*E*)- and (*Z*)-isomer, pseudo t, *J* = 8.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 14.2, 22.6, 22.7, 27.8, 27.9, 30.8, 31.7, 32.0, 35.4, 37.3, 41.9, 55.2, 113.4, 115.7, 116.0, 125.2, 125.4, 129.5, 129.6, 130.7, 130.9, 136.3, 136.8, 139.2, 140.5, 157.6, 157.7; HRMS (EI): Calcd for $C_{17}H_{24}O$, (M^+) 244.1827. Found 244.1836.

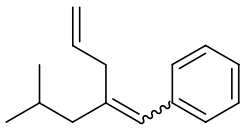
(*E*)- and (*Z*)-2-Pentyl-1-phenylpenta-1,4-diene (3c)



A mixture of geometrical isomers (*E*/*Z*=54/46)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85-0.93 ((*E*)- and (*Z*)-isomer, m, 3H), 1.26-1.34 ((*E*)- and (*Z*)-isomer, m, 4H), 1.43-1.56 ((*E*)- and (*Z*)-isomer, m, 2H), 2.13-2.24 ((*E*)- and (*Z*)-isomer, m, 2H), 2.91 ((*E*)-isomer, d, *J* = 6.6 Hz, 2H), 2.98 ((*Z*)-isomer, d, *J* = 6.0 Hz, 2H), 5.07-5.15 ((*E*)- and (*Z*)-isomer, m, 2H), 5.81-5.95 ((*E*)- and (*Z*)-isomer, m, 1H), 6.28 ((*E*)-isomer, s, 1H), 6.37 ((*Z*)-isomer, s, 1H), 7.16-7.33 ((*E*)- and (*Z*)-isomer, m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 14.2, 22.5, 22.7, 27.8, 27.9, 30.9, 31.7, 32.0, 35.4, 37.2, 41.8, 115.8, 116.2, 125.8, 125.87, 125.92, 126.0, 127.9, 128.0, 128.4, 128.5, 136.2, 136.6, 138.1, 138.3, 140.6, 141.8; HRMS (EI): Calcd for $C_{16}H_{22}$ (M^+) 214.1722. Found 214.1724.

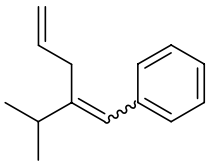
(*E*)- and (*Z*)-2-(2-Methylpropyl)-1-phenylpenta-1,4-diene (3d)



A mixture of geometrical isomers (*E*/*Z*=55/45)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 ((*E*)-isomer, d, *J* = 6.4 Hz, 6H), 0.93 ((*Z*)-isomer, d, *J* = 6.6 Hz, 6H), 1.87 ((*E*)- and (*Z*)-isomer, pseudo sept, *J* = 6.6 Hz, 1H), 2.03 ((*Z*)-isomer, d, *J* = 7.2 Hz, 2H), 2.15 ((*E*)-isomer, d, *J* = 7.2 Hz, 2H), 2.89 ((*E*)-isomer, d, *J* = 6.8 Hz, 2H), 2.95 ((*Z*)-isomer, d, *J* = 6.0 Hz, 2H), 5.05-5.13 ((*E*)- and (*Z*)-isomer, m, 2H), 5.81-5.91 ((*E*)- and (*Z*)-isomer, m, 1H), 6.34 ((*E*)-isomer, s, 1H), 6.35 ((*Z*)-isomer, s, 1H), 7.14-7.30 ((*E*)- and (*Z*)-isomer, m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.56, 22.62, 26.3, 26.4, 35.2, 39.4, 41.7, 46.8, 115.8, 116.2, 125.8, 126.0, 127.0, 127.4, 127.9, 128.0, 128.4, 128.8, 136.2, 136.7, 138.1, 138.5, 139.4, 140.6; HRMS (EI): Calcd for $C_{15}H_{20}$ (M^+) 200.1565. Found 200.1561.

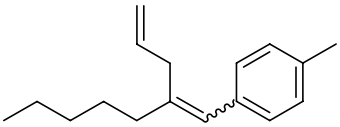
(*E*)- and (*Z*)-2-Isopropyl-1-phenylpenta-1,4-diene (3e)



A mixture of geometrical isomers (*E*/*Z*=43/57)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 ((*Z*)-isomer, d, *J* = 6.9 Hz, 6H), 1.12 ((*E*)-isomer, d, *J* = 6.6 Hz, 6H), 2.42 ((*E*)-isomer, sept, *J* = 6.9 Hz, 1H), 2.87 ((*Z*)-isomer, d, *J* = 6.9 Hz, 2H), 3.01 ((*E*)-isomer, d, *J* = 6.0 Hz, 2H), 3.11 ((*Z*)-isomer, sept, *J* = 6.9 Hz, 1H), 5.05-5.16 ((*E*)- and (*Z*)-isomer, m, 2H), 5.81-5.98 ((*E*)- and (*Z*)-isomer, m, 1H), 6.19 ((*Z*)-isomer, s, 1H), 6.39 ((*E*)-isomer, s, 1H), 7.17-7.33 ((*E*)- and (*Z*)-isomer, m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3, 22.2, 29.2, 29.8, 30.4, 34.3, 34.9, 35.1, 115.7, 116.1, 123.9, 124.6, 125.8, 125.9, 127.9, 128.0, 128.4, 128.6, 136.7, 137.4, 138.3, 138.5, 146.4, 146.6; HRMS (EI): Calcd for $C_{14}H_{18}$ (M^+) 186.1409. Found 186.1406.

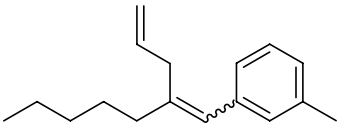
(*E*)- and (*Z*)-1-(4-Metylphenyl)-2-pentylpenta-1,4-diene (3h)



A mixture of geometrical isomers (*E*/*Z*=53/47)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85-0.93 ((*E*)- and (*Z*)-isomer, m, 3H), 1.25-1.39 ((*E*)- and (*Z*)-isomer, m, 4H), 1.43-1.55 ((*E*)- and (*Z*)-isomer, m, 2H), 2.11-2.24 ((*E*)- and (*Z*)-isomer, m, 2H), 2.33 ((*E*)- and (*Z*)-isomer, s, 3H), 2.89 ((*E*)-isomer, d, *J* = 6.9 Hz, 2H), 2.97 ((*Z*)-isomer, d, *J* = 6.0 Hz, 2H), 5.06-5.15 ((*E*)- and (*Z*)-isomer, m, 2H), 5.80-5.95 ((*E*)- and (*Z*)-isomer, m, 1H), 6.24 ((*E*)-isomer, s, 1H), 6.33 ((*Z*)-isomer, s, 1H), 7.08-7.15 ((*E*)- and (*Z*)-isomer, m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 14.2, 21.2, 22.6, 22.7, 27.8, 27.9, 30.9, 31.7, 32.0, 35.5, 37.2, 41.9, 115.7, 116.1, 125.6, 125.8, 128.3, 128.4, 128.7, 135.2, 135.37, 135.42, 135.5, 136.3, 136.7, 139.9, 141.2; HRMS (EI): Calcd for $C_{17}H_{24}$ (M^+) 228.1878. Found 228.1889.

(*E*)- and (*Z*)-1-(3-Metylphenyl)-2-pentylpenta-1,4-diene (3i)

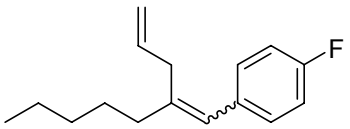


A mixture of geometrical isomers (*E*/*Z*=48/52)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84-0.93 ((*E*)- and (*Z*)-isomers, m, 3H), 1.26-1.39 ((*E*)- and (*Z*)-isomers, m, 4H), 1.43-1.55 ((*E*)- and (*Z*)-isomers, m, 2H), 2.12-2.24 ((*E*)- and (*Z*)-isomers, m, 2H), 2.33 ((*E*)- and (*Z*)-isomers, s, 3H), 2.90 ((*E*)-isomer, d, *J* = 7.1 Hz, 2H), 2.98 ((*Z*)-isomer, d, *J* = 6.3 Hz, 2H), 5.06-5.15 ((*E*)- and (*Z*)-isomers, m, 2H), 5.81-5.95 ((*E*)- and (*Z*)-isomers, m, 1H), 6.25 ((*E*)-isomer, s, 1H), 6.34 ((*Z*)-isomer, s, 1H), 7.00-7.05 ((*E*)- and (*Z*)-isomers, m, 3H), 7.17-7.24 ((*E*)- and (*Z*)-isomers, m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 14.2, 21.5, 22.5, 22.7, 27.8, 27.9, 30.9, 31.7, 32.0,

35.5, 37.2, 41.8, 115.8, 116.1, 125.4, 125.5, 125.8, 126.0, 126.6, 126.7, 127.8, 127.9, 129.2, 129.3, 136.3, 136.7, 137.40, 137.45, 138.1, 138.2, 140.5, 141.7; HRMS (EI): Calcd for $C_{17}H_{24}$ (M^+) 228.1878. Found 228.1889.

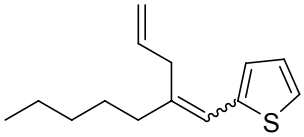
(*E*)- and (*Z*)-1-(4-Fluorophenyl)-2-pentylpenta-1,4-diene (3j)



A mixture of geometrical isomers (*E*/*Z*=53/47)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85-0.93 ((*E*)- and (*Z*)-isomers, m, 3H), 1.19-1.39 ((*E*)- and (*Z*)-isomers, m, 4H), 1.41-1.52 ((*E*)- and (*Z*)-isomers, m, 2H), 2.12-2.20 ((*E*)- and (*Z*)-isomers, m, 2H), 2.89 ((*E*)-isomer, d, *J* = 7.1 Hz, 2H), 2.93 ((*Z*)-isomer, d, *J* = 6.0 Hz, 2H), 5.06-5.15 ((*E*)- and (*Z*)-isomers, m, 2H), 5.79-5.94 ((*E*)- and (*Z*)-isomers, m, 1H), 6.22 ((*E*)-isomer, s, 1H), 6.32 ((*Z*)-isomer, s, 1H), 6.95-7.03 ((*E*)- and (*Z*)-isomers, m, 2H), 7.13-7.21 ((*E*)- and (*Z*)-isomers, m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 14.2, 22.5, 22.7, 27.7, 27.8, 30.8, 31.7, 31.9, 35.3, 37.2, 41.7, 114.8 (d, *J* = 21.2 Hz), 116.1 (d, *J* = 30.6 Hz), 124.6, 124.8, 129.8-130.0 (m), 134.0-134.3 (m), 136.0, 136.5, 140.6, 159.4-152.8 (m); HRMS (EI): Calcd for $C_{16}H_{21}F$ (M^+) 232.1627. Found 232.1629.

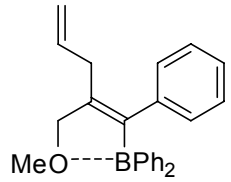
(*E*)- and (*Z*)-2-Pentyl-1-(2-thienyl)penta-1,4-diene (3k)



A mixture of geometrical isomers (*E*/*Z*=71/29)

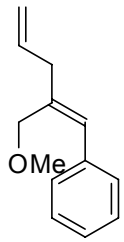
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88-1.19 ((*E*)- and (*Z*)-isomers, m, 3H), 1.27-1.41 ((*E*)- and (*Z*)-isomers, m, 4H), 1.43-1.54 ((*E*)- and (*Z*)-isomers, m, 2H), 2.15 ((*Z*)-isomer, t, *J* = 7.8 Hz, 2H), 2.37 ((*E*)-isomer, m, 2H), 2.90 ((*E*)-isomer, d, *J* = 7.2 Hz, 2H), 3.14 ((*Z*)-isomer, d, *J* = 6.4 Hz, 2H), 5.04-5.14 ((*E*)- and (*Z*)-isomers, m, 2H), 5.78-5.90 ((*E*)- and (*Z*)-isomers, m, 1H), 6.36 ((*E*)-isomer, s, 1H), 6.43 ((*Z*)-isomer, s, 1H), 6.88-6.91 ((*E*)- and (*Z*)-isomers, m, 1H), 6.94-6.97 ((*E*)- and (*Z*)-isomers, m, 1H), 7.15-7.17 ((*E*)- and (*Z*)-isomers, m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 22.63, 22.65, 27.5, 27.8, 31.7, 32.1, 32.2, 36.3, 37.9, 42.6, 115.9, 116.5, 118.7, 118.8, 123.9, 125.9, 126.2, 126.5, 126.7, 135.0, 136.2, 140.1, 140.7, 140.8, 141.0; HRMS (EI): Calcd for $C_{14}H_{20}S$ (M^+) 220.1286. Found 220.1284.

(*E*)-2-Methoxymethyl-1-phenyl-1-diphenylborylpenta-1,4-diene (2m)



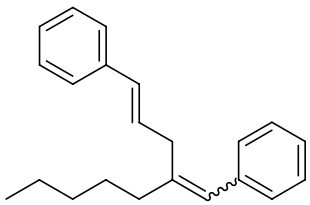
^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.00 (d, *J* = 6.3 Hz, 2H), 3.40 (s, 3H), 4.73 (s, 2H), 5.09-5.21 (m, 2H), 5.83-5.96 (m, 1H), 6.83-6.87 (m, 2H), 7.02-7.13 (m, 3H), 7.22-7.33 (m, 6H), 7.40-7.44 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.0, 59.2, 83.3, 116.0, 125.3, 126.5, 127.0, 127.2, 127.4, 128.0, 133.9, 136.1, 140.0; ^{11}B NMR (128 MHz, $CDCl_3$): δ = 18.5; HRMS (EI): Calcd for $C_{25}H_{25}BO$ (M^+) 352.1998. Found 352.1997.

(*Z*)-2-Methoxymethyl-1-phenylpenta-1,4-diene (3m)



^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.03 (pseudo dt, *J* = 6.9, 1.3 Hz, 2H), 3.31 (s, 3H), 4.02 (s, 2H), 5.10-5.19 (m, 2H), 5.86-6.00 (m, 1H), 7.20-7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 39.8, 58.1, 70.2, 116.5, 126.6, 128.0, 128.7, 129.9, 136.0, 137.1, 137.6; HRMS (EI): Calcd for $C_{13}H_{16}O$ (M^+) 188.1201. Found 188.1199.

(1*E*,4*E*)- and (1*Z*,4*E*)-2-Pentyl-1,5-diphenylpenta-1,4-diene (7)

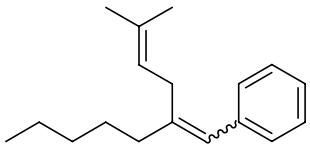


A mixture of geometrical isomers (*E*/*Z*=42/58)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85-0.93 ((*E*)- and (*Z*)-isomers, m, 3H), 1.26-1.38 ((*E*)- and (*Z*)-isomers, m, 4H), 1.47-1.59 ((*E*)- and (*Z*)-isomers, m, 2H), 2.18-2.28 ((*E*)- and (*Z*)-isomers, m, 2H), 3.06 ((*E*)-isomer, d, *J* = 7.2 Hz, 2H), 3.13 ((*E*)-isomer, d, *J* = 6.3 Hz, 2H), 6.21-6.33 ((*E*)- and (*Z*)-isomers, m, 1H), 6.42-6.50 ((*E*)- and (*Z*)-isomers, m, 1H), 7.17-7.40 ((*E*)- and (*Z*)-isomers, m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.07, 14.13, 22.5, 22.6, 27.7, 27.9, 31.0, 31.6, 31.9, 34.5, 37.2, 40.9, 125.99, 126.03, 126.1, 126.2, 127.0, 128.0, 128.1, 128.3, 128.46, 128.49, 128.5, 131.0, 131.5, 137.6,

138.2, 138.3, 140.8, 142.1; HRMS (EI): Calcd for $C_{22}H_{26}$ (M^+) 290.2035. Found 290.2037.

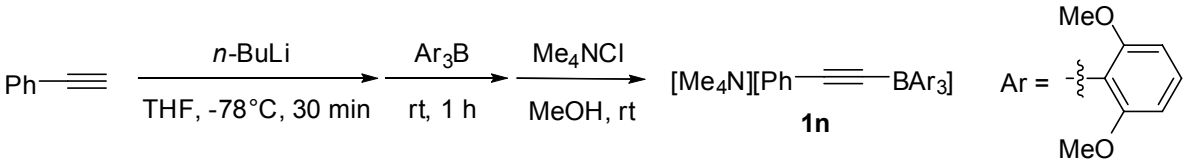
(*E*)- and (*Z*)-5-Methyl-2-pentyl-1-phenylhexa-1,4-diene (8)



A mixture of geometrical isomers (*E*/*Z*=53/47)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85-0.93 ((*E*)- and (*Z*)-isomers, m, 3H), 1.25-1.37 ((*E*)- and (*Z*)-isomers, m, 4H), 1.46-1.59 ((*E*)- and (*Z*)-isomers, m, 2H), 1.60 ((*Z*)-isomer, s, 3H), 1.67 ((*E*)-isomer, s, 3H), 1.72 ((*Z*)-isomer, d, *J* = 1.5 Hz, 3H), 1.76 ((*E*)-isomer, d, *J* = 1.5 Hz, 3H), 2.10-2.22 ((*E*)- and (*Z*)-isomers, m, 2H), 2.84 ((*Z*)-isomer, d, *J* = 7.2 Hz, 2H), 2.91 ((*E*)-isomer, d, *J* = 6.9 Hz, 2H), 5.12-5.18 ((*E*)-isomer, m, 1H), 5.20-5.27 ((*Z*)-isomer, m, 1H), 6.25 ((*Z*)-isomer, s, 1H), 6.28 ((*E*)-isomer, s, 1H), 7.15-7.32 ((*E*)- and (*Z*)-isomers, m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 14.2, 17.8, 18.0, 22.6, 22.7, 25.87, 25.90, 27.8, 28.1, 30.0, 31.1, 31.8, 32.1, 36.0, 37.3, 122.1, 122.4, 124.7, 125.7, 125.8, 127.91, 127.93, 128.5, 128.6, 132.5, 133.0, 138.5, 138.6, 142.8, 143.0; HRMS (EI): Calcd for $C_{18}H_{26}$ (M^+) 242.2035. Found 242.2037.

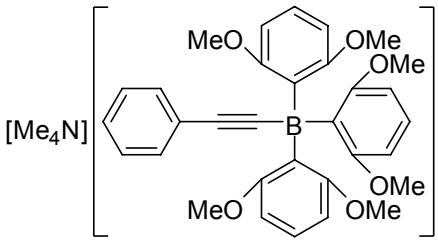
Synthesis of alkynylborates 1n: typical procedure for the preparation of alkynylborates 1n-1p



To an oven-dried, N_2-purged frask were added a solution of phenylacetylene (615 mg, 6.0 mmol) in THF (20 mL) and the mixture was cooled at -78 °C. *n*-BuLi in hexane (1.6 M, 3.4 ml, 5.5 mmol) was added to the solution and the mixture was stirred at this temperature for 30 minutes. Tris(2,6-dimethoxyphenyl)borane (2.1 g, 5.0 mmol) was added, and then the reaction mixture was stirred at room temperature for 1 h. After addition of a small amount of methanol for quenching, the solution was concentrated under high vacuum. The residue was dissolved in methanol and tetramethylammonium chloride (600 mg, 5.5 mmol) was added, resulting in a white precipitate. The precipitate

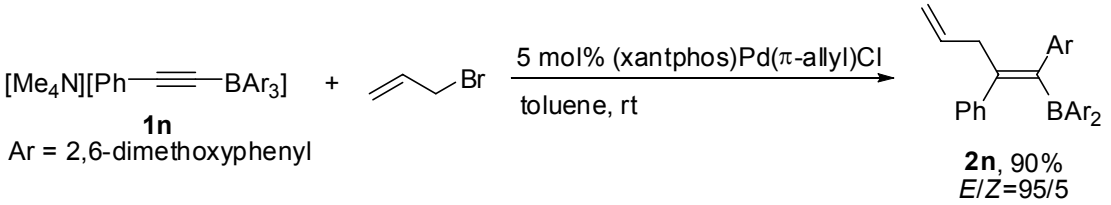
was collected by filtration, washed with cooled methanol, and dried under high vacuum to give the product **1n** (2.6 g, 4.3 mmol, 86% yield).

Tetramethylammonium tris(2,6-dimethoxyphenyl)(phenylethynyl)borate (1n)



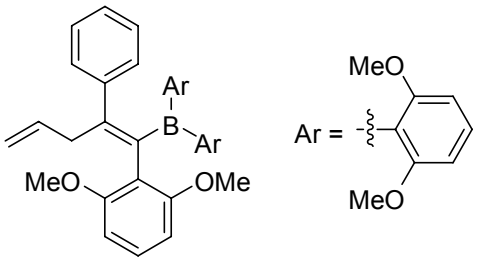
^{1}H NMR (400 MHz, CD_3CN): δ = 2.90 (s, 12H), 3.32 (s, 18H), 6.31 (d, *J* = 8.0 Hz, 6H), 6.77 (t, *J* = 8.0 Hz, 3H), 6.97 (tt, *J* = 6.8, 1.6 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 2H), 7.17 (m, 2H); ^{13}C NMR (75 MHz, CD_3CN): δ = 55.9, 56.7, 106.7, 123.1, 123.9, 128.5, 131.1, 132.5, 141.3 (q, *J* = 52.9 Hz), 165.2; ^{11}B NMR (128 MHz, CD_3CN): δ = -13.9; HRMS (FAB): Calcd for $C_{32}H_{32}BO$ $(M-[Me_4N])^-$ 523.2292. Found 523.2307.

Palladium-catalyzed allylation of alkynylborate 1n. A typical procedure for 1n-1p



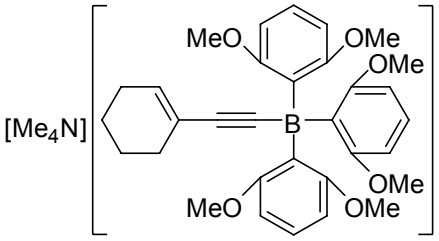
To an oven-dried flask, alkynyltriarylborate **1n** (89.0 mg, 0.20 mmol) and (xantphos)Pd(π-allyl)Cl (5.2 mg, 2.5 μmol) were placed. After purging with Ar, a toluene solution (0.5 ml) containing allyl bromide (14.8 mg, 0.12 mmol) was added and stirred at room temperature. After 15 minutes, water was added to the reaction mixture. The aqueous layer was extracted with AcOEt (3 times), washed with water (once), brine (once), dried over $MgSO_4$ and concentrated. The residue was purified by preparative thin-layer chromatography on silica gel (hexane:AcOEt = 20:1) to afford the alkenylborane **2n** (50.9 mg, 0.090 mmol, 90% yield, *E*/*Z* = 95/5).

(*E*)-1-(2,6-Dimethoxyphenyl)-1-bis(2,6-dimethoxyphenyl)boryl-2-phenylpenta-1,4-diene (2n)



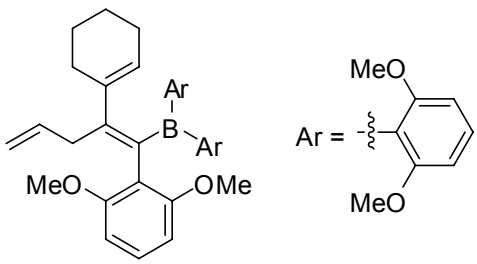
^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.20 (d, *J* = 6.6 Hz, 2H), 3.43 (s, 12H), 3.60 (s, 6H), 4.78-4.82 (m, 1H), 4.89 (dd, *J* = 17.4, 2.1 Hz, 1H), 5.70-5.80 (m, 1H), 6.08 (d, *J* = 7.8 Hz, 4H), 6.29 (d, *J* = 8.1 Hz, 2H), 6.80-6.96 (m, 6H), 7.29-7.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.5, 54.8, 55.1, 102.0, 102.6, 114.3, 123.2, 125.9, 126.1, 126.4, 128.5, 129.1, 138.1, 144.6, 156.7, 157.2, 161.5; ^{11}B NMR (128 MHz, CD_3CN): δ = 68.6; HRMS (EI): Calcd for $C_{35}H_{37}BO_6$ (M^+) 564.2683. Found 564.2686.

Tetramethylammonium (cyclohex-1-enyl)ethynyltris(2,6-dimethoxyphenyl)borate (1o)



^{1}H NMR (300 MHz, CD_3CN): δ = 1.42-1.59 (m, 4H), 1.92-2.45 (m, 4H), 2.97-2.98 (m, 12H), 3.28 (s, 18H), 5.43-5.49 (m, 1H), 6.26 (d, *J* = 8.1 Hz, 6H), 6.73 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (75 MHz, CD_3CN): δ = 23.2, 24.0, 26.3, 32.1, 56.0, 56.5, 106.6, 122.8, 124.4, 127.6, 165.2; ^{11}B NMR (128 MHz, CD_3CN): δ = -14.1; HRMS (FAB): Calcd for $C_{32}H_{36}BO$ (M-[Me_4N])$^-$ 527.2605. Found 527.2603.

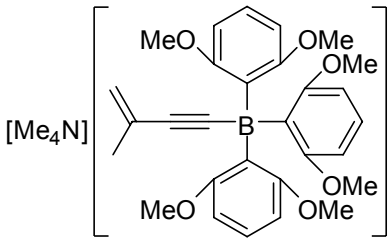
(*E*)-1-(2,6-Dimethoxyphenyl)-1-bis(2,6-dimethoxyphenyl)boryl-2-(cyclohex-1-enyl) penta-1,4-diene (2o)



^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 (br, 4H), 1.64 (br, 2H), 1.83 (br, 2H), 2.88 (d, *J* = 6.6 Hz, 2H), 3.43 (s, 6H), 3.57 (s, 3H), 4.85-4.95 (m, 2H), 5.73-5.87 (m, 1H), 5.95 (br,

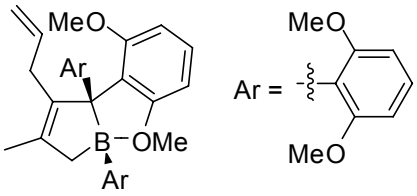
1H), 6.24-6.28 (m, 6H), 6.89 (t, J = 8.3 Hz, 1H), 6.97 (t, J = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8, 22.1, 25.8, 27.2, 38.4, 54.7, 55.1, 55.8, 101.9, 102.9, 113.5, 123.1, 125.8, 127.9, 130.2, 138.4, 142.7, 157.4, 161.0, 161.5; ^{11}B NMR (128 MHz, $CDCl_3$): δ = 67.1; HRMS (EI): Calcd for $C_{35}H_{41}BO_6$ (M^+) 568.2996. Found 568.2994.

Tetramethylammonium 3-methylbut-3-en-1-ynyltris(2,6-dimethoxyphenyl)borate (1p)



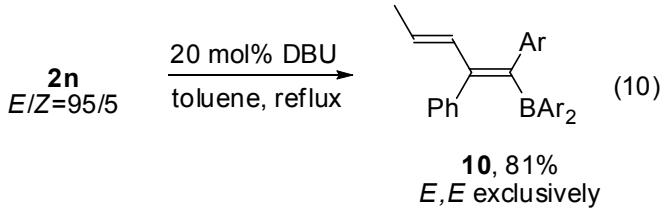
^{1}H NMR (300 MHz, CD_3CN): δ = 1.77 (s, 3H), 2.99 (s, 12H), 3.29 (s, 18H), 4.67 (br, 2H), 6.28 (d, J = 7.8 Hz, 6H), 6.75 (t, J = 8.0 Hz, 3H); ^{13}C NMR (75 MHz, CD_3CN): δ = 25.9, 56.0, 56.5, 106.6, 112.0, 123.0, 134.2, 141.3 (q, J = 52.9 Hz), 165.2; ^{11}B NMR (128 MHz, CD_3CN): δ = -14.0; HRMS (FAB): Calcd for $C_{29}H_{32}$ (M-[Me_4N])$^-$ 487.2292. Found 487.2286.

1,2,2-Tris(2,6-dimethoxyphenyl)-4-methyl-3-(prop-2-enyl)-3-borolene (9)



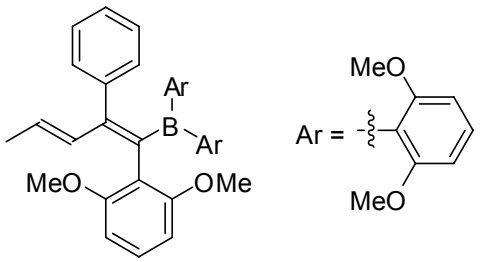
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (d, J =18.3 Hz, 1H), 1.70 (s, 3H), 2.48 (d, J = 18.3 Hz, 1H), 2.71 (s, 3H), 2.93 (dd, J = 16.1, 7.4 Hz, 1H), 3.08 (dd, J = 15.8, 1.4 Hz, 1H), 3.23 (br, 6H), 3.39 (s, 3H), 3.68 (s, 3H), 4.04 (s, 3H), 4.45 (d, J = 10.2 Hz, 1H), 4.55 (d, J = 17.1 Hz, 1H), 4.96-5.10 (m, 1H), 5.91 (d, J = 7.8 Hz, 1H), 6.18 (d, J = 7.5 Hz, 2H), 6.41-6.46 (m, 2H), 6.51 (d, J = 8.1 Hz, 1H), 6.75 (t, J = 8.1 Hz, 1H), 6.89 (t, J = 8.1 Hz, 1H), 6.99 (t, J = 8.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.0, 32.1, 35.1, 53.5, 54.5, 55.4, 56.1, 57.2, 100.1, 102.2, 102.7, 106.2, 106.9, 111.1, 123.1, 123.9, 124.0, 126.3, 128.1, 132.7, 139.2, 139.7, 155.3, 158.0, 158.5, 158.7, 162.2; ^{11}B NMR (128 MHz, $CDCl_3$): δ = 25.2; HRMS (EI): Calcd for $C_{32}H_{37}BO_6$ (M^+) 528.2683. Found 528.2681.

DBU-catalyzed isomerization of 2n



Under Ar atmosphere, a toluene solution (0.5 ml) containing **2n** (56.4 mg, 0.10 mmol) and DBU (3.0 μl, 0.02 mmol) was stirred at reflux. After 24 h, the reaction mixture was cooled to room temperature and water added to the solution. The aqueous layer was extracted with AcOEt (3 times), washed with water (once), brine (once), dried over $MgSO_4$ and concentrated. The residue was purified by preparative thin-layer chromatography on silica gel (hexane:AcOEt = 10:1) to afford the 1,3-dienylborane **10** (45.6 mg, 0.081 mmol, 81% yield).

(*E,E*)-1-(2,6-Dimethoxyphenyl)-1-bis(2,6-dimethoxyphenyl)boryl-2-phenylpenta-1, 3-diene (10)



^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.64 (dd, *J* = 7.4, 1.4 Hz, 3H), 3.42 (s, 12H), 3.60 (s, 6H), 5.27-5.39 (m, 1H), 6.07 (d, *J* = 8.1 Hz, 4H), 6.30 (dd, *J* = 15.5, 1.7 Hz, 1H), 6.32 (d, *J* = 8.1 Hz, 2H), 6.80-6.91 (m, 5H), 6.97 (t, *J* = 8.3 Hz, 1H), 7.20 (dd, *J* = 7.7, 1.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 18.7, 55.06, 55.11, 102.5, 102.6, 122.6, 125.6, 126.2, 126.4, 128.3, 130.6, 131.1, 136.1, 142.1, 155.0, 157.9, 161.3; ^{11}B NMR (128 MHz, CD_3CN): δ = 68.5; HRMS (EI): Calcd for $C_{35}H_{37}BO_6$ (M^+) 564.2683. Found 564.2683.

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10. Johns, A. M.; Utsunomiya, M.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 1828.

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14. Wada, M.; Kanzaki, M.; Ogura, H.; Hayase, S.; Erabi T. *J. Organomet. Chem.* **1995**, *485*, 127.
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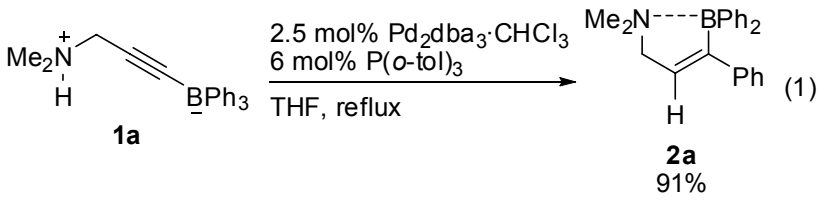
Chapter 3

Synthesis of Amine–Borane Intramolecular Complexes through Palladium-Catalyzed Rearrangement of Ammonioalkynyltriarylborates

Abstract: The palladium-catalyzed rearrangement reaction of alkynyltriarylborates having a tertiary ammonium moiety proceeded stereoselectively to give amine–borane intramolecular complexes, some of which exhibited significantly strong fluorescence.

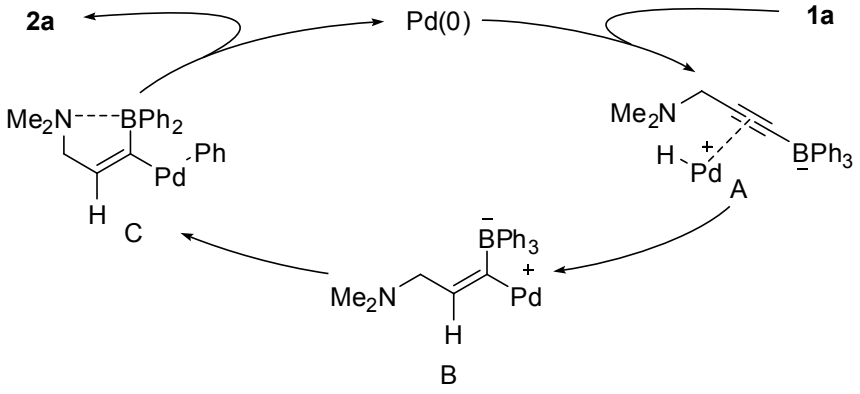
Boron-modified π-conjugated compounds have attracted much attention because they exhibit unique photophysical and electrochemical properties.[1] For example, when a nitrogen-containing π-conjugated skeleton forms an intramolecular complex with a triarylborane moiety suitably positioned within the molecule, it is constrained into a planar structure which leads to considerable lowering of the LUMO level.[2] Thus, this class of compounds has become an intriguing synthetic target with the aim of developing novel electron-transporting materials. We recently reported a palladium-catalyzed reaction of alkynyltriarylborates with aryl halides, which resulted in the stereoselective synthesis of (trisubstituted alkenyl)diarylboranes via a 1,2-migration of an aryl group from boron to the α-carbon.[3] We attempted to employ this reaction for the synthesis of an intramolecular amine-borane complex by using an alkynylborate bearing a tethered amine. However, the reaction failed to proceed, likely due to the strong coordination of the nitrogen atom to palladium. This hypothesis led us to employ an alkynyborate in which the amino group is in the form of an ammonium salt instead of a free amine, in order to mask the coordinating character of the nitrogen atom. Herein, we report the successful application of this strategy to the stereoselective synthesis of amine–borane intramolecular complexes.

Alkynyltriarylborate Thus, zwitterionic alkynyltriarylborate **1a**[4] was treated with a catalytic amount of $Pd_2dba_3{\cdot}CHCl_3$ and P(*o*-tol)$_3$ in refluxing THF. A rearrangement reaction took place, and after 1 h, the cyclic alkenylborane **2a**, in which the unmasked tertiary amino group was coordinated to boron, was isolated by column chromatography on silica gel in 91% yield (eq 1). In this product, the ammonium proton on nitrogen had migrated onto the *sp* carbon β to boron, whereas the phenyl group on boron migrated to the α *sp* carbon. Both the hydrogen atom and phenyl group were incorporated across the carbon–carbon double bond in a *cis* fashion to give the (*E*)-isomer, which was the only stereoisomer detected in the ^{1}H NMR spectrum of the reaction mixture. Of note is that the observed stereochemistry in which hydrogen and boron are vicinally attached across a carbon–carbon double bond in a *trans* fashion is difficult to access by conventional hydroboration reactions. In the absence of a palladium catalyst, **1a** remained unchanged in refluxing THF. On the other hand, a complex mixture resulted when **1a** was treated with Brønsted acids such as acetic acid or methanesulfonic acid.[5]

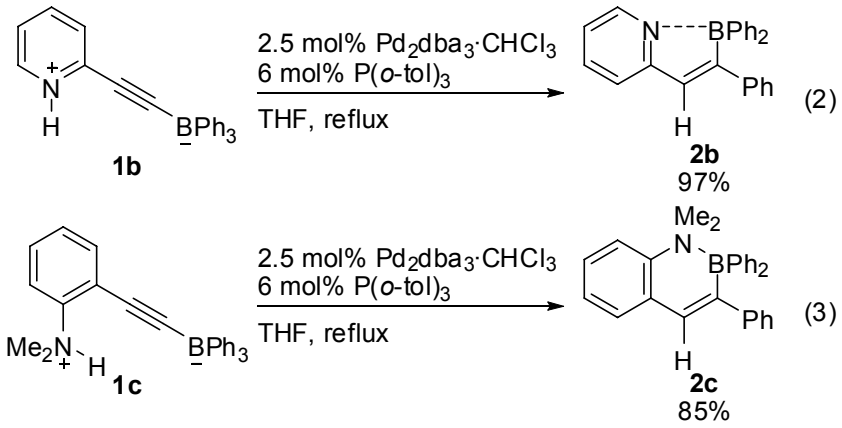


A possible mechanism is depicted in Scheme 1. Transfer of the proton from the tertiary ammonium moiety to palladium(0) takes place initially giving cationic palladium species **A**. Then, regioselective *cis*-hydropalladation across the carbon–carbon triple bond takes place, affording the zwitterionic intermediate **B**. Migration of one of the phenyl groups from boron to palladium takes place, furnishing the triorganylborane, which spontaneously forms a complex with the unmasked tertiary amino group to give diorganopalladium species **C**. Finally, the cyclic amine–borane adduct **2a** is released through reductive elimination with the regeneration of palladium(0).

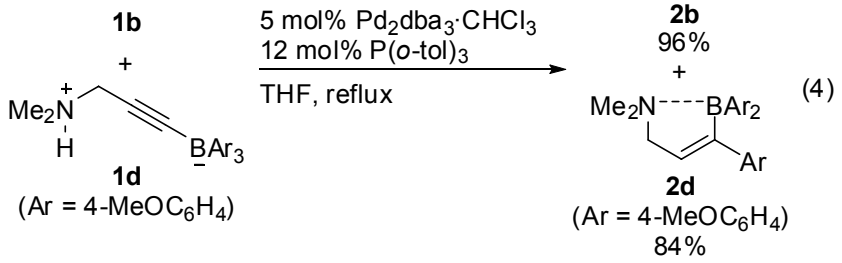
Scheme 1. Possible Mechanism



The sSubstrate **1b** having a pyridinium group and **1c** having an anilinium group underwent analogous reactions. Six-membered ring aniline–borane complex **2c** as well as five-membered ring pyridine–borane complex **2b** were produced in good to excellent yields, respectively (eqs 2 and 3). Interestingly, the pyridine-borane complex **2b** exhibited strong fluorescence (vide infra).



A crossover experiment was carried out as shown in eq 4, and showed definitively that the aryl migration occurs intramolecularly, as with the previous case.[3] A mixture of **1b** and **1d** was treated with the palladium catalyst, resulting in the formation of a mixture of **2b** and **2d** in 96, 84% respectively. No crossover products were observed by ^{1}H NMR analysis of the reaction mixture.

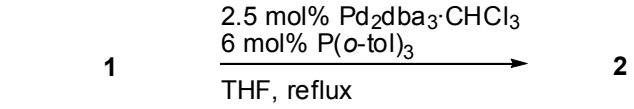


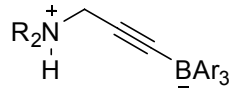
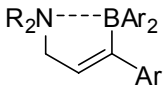
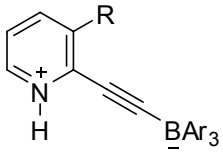
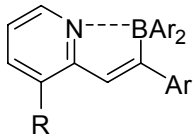
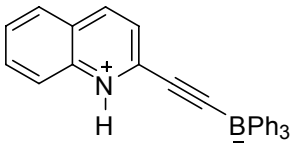
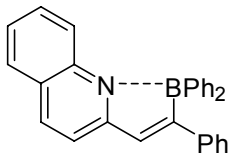
The reactions of structurally modified substrates are summarized in Table 1. Both electron-donating and -withdrawing groups were tolerated as the aryl substituents (entry 1 and eq 4). Chloro substituents remained intact under the reaction conditions (entry 5). A reaction of 2-quinolinium derivative **1j**, whose nitrogen atom was more sterically hindered than **1b**, gave a 96% yield of quinoline-borane complex **2j** (entry 6).

The photophysical properties of compounds **2b**, **2h**, and **2j** are summarized in Table 2. The absorption wavelength of **2b** (λ_{abs} = 356 nm in MeOH) was apparently elongated in comparison with those of non-borylated counterparts such as (*E*)-2-styrylpyridine **3** (λ_{abs} = 309 nm) and (*E*)-*N*-methyl-2-styrylpyridinium iodide **4** (λ_{abs} = 340 nm, Chart 1),[6] probably due to the planar structure enforced by the B–N coordination.[2a] In addition, **2b** exhibited strong purple fluorescence in CH_2Cl_2 solution (λ_{em} = 422 nm, Φ_F = 0.44). The extension of π-conjugation from **2b** to the naphthyl analogue **2h** caused a red shift of the emission maxima by 9 nm, whereas π-extention to

the quinoline derivative **2j** shifted emission maxima by 51 nm. Thus, it seems possible to tune the emission color by simple structural modifications.

Table 1. Reactions of Various Ammonioalkynyltriarylborates[a]



entry	alkynylborate **1**	product **2**	yield / %[b]
1[c]			67
	1e R = Me, Ar = 4-FC_6H_4	**2e**	
2	**1f** R = Bn, Ar = Ph	**2f**	89
3[d]			92
	1g R = Me, Ar = Ph	**2g**	
4	**1h** R = H, Ar = 2-Np	**2h**	98
5	**1i** R = H, Ar = 4-ClC_6H_4	**2i**	96
6			96
	1j	**2j**	

[a] Reaction conditions: 2.5 mol% $Pd_2dba_3·CHCl_3$, 6 mol% P(*o*-tol)$_3$, THF, reflux, 1 h. [b] Isolated yield. [c] Reaction was conducted in refluxing cyclopentyl methyl ether. [d] Reaction was conducted in 1,2-dichloroethane at 70 °C.

Chart 1.

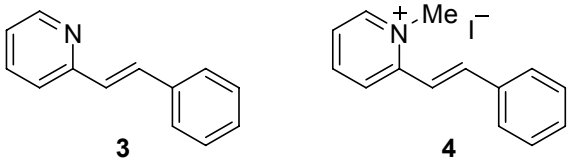


Table 2. Photophysical properties of pyridine-boranes **2**

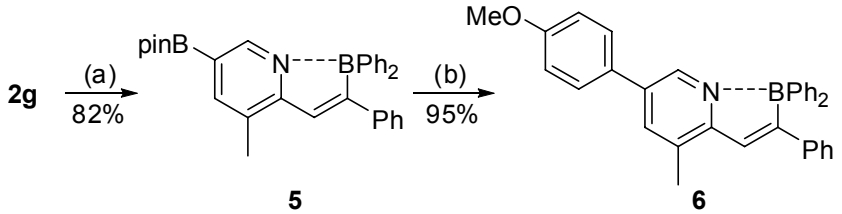
Pyridine-borane	UV-vis absorption[a]		Fluorescence[a,b]	
2	λ_{abs} / nm	log ε	λ_{em} / nm	Φ_F
2b	359 (356)[c]	4.17	422	0.44
2h	372	4.12	431	0.32
2j	395	4.35	473	0.26

[a] Measured in CH_2Cl_2. [b] Determined with reference to 2-aminopyridine in 0.1 N H_2SO_4 and aqueous tryptophan solution (pH = 7.2). Excited at 280 nm. [c] Measured in MeOH.

Finally, we examined further functionalization of the produced amine–borane complex. When the pyridine–borane complex **2g** was subjected to the Ir-catalyzed C–H borylation reaction,[7] the 5-position of the pyridine ring, which is probably most sterically accessible, was selectively borylated to give boronic ester **5** in 82% yield. A subsequent cross-coupling reaction of **5** with 4-bromoanisole proceeded regioselectively on the pyridine ring to afford biaryl **6** in 95% yield with the other B–C bonds remaining unreacted by virtue of the nitrogen coordination. The resulting pyridine–borane **6** showed sky-blue fluorescence with a maximum wavelength of 465 nm (Φ_F = 0.40).

In summary, we have developed a palladium-catalyzed rearrangement reaction of ammonioalkynyltriarylborates. Hydrogen and boron were stereoselectively installed across the resulting carbon–carbon double bond in a *trans* fashion to give intramolecular amine–borane complexes, some of which exhibited significantly strong fluorescence. Further investigations on the photophysical properties of these compounds are in progress.

Scheme 2. Functionalization of **2g**



5
λ_{em} = 432 nm
Φ_F = 0.43

6
λ_{em} = 465 nm
Φ_F = 0.40

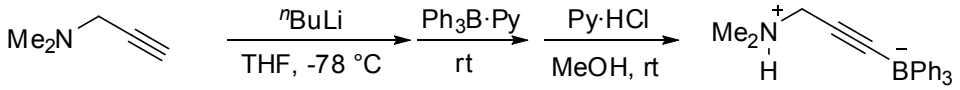
a) 0.5 equiv $(Bpin)_2$, 2.5 mol% $[Ir(OMe)(cod)]_2$, 5 mol% dtbpy, *p*-xylene, 100 °C, 3 h. (b) 1.2 equiv 4-$MeOC_6H_4Br$, 5 mol% $Pd(P^tBu_3)_2$, 3 equiv NaOH, THF, H_2O, 60 °C, 1 h.

Experimental Section

General. NMR spectra were recorded on a Varian Gemini 2000 (^{1}H at 300 MHz and ^{13}C at 75 MHz) or Varian Mercury-400 (^{1}H at 400 MHz and ^{11}B at 128 MHz) spectrometers. Me_4Si (^{1}H, $\delta = 0.00$), residual H of CD_3CN (^{1}H in CD_3CN, $\delta = 1.94$), residual H of DMSO-d_6 (^{1}H in DMSO-d_6, $\delta = 2.50$), $CDCl_3$ (^{13}C, $\delta = 77.0$), **C**D_3CN (^{13}C, $\delta = 1.32$), and $BF_3{\cdot}OEt_2$ (^{11}B, $\delta = 0.00$) were used as standard. High-resolution mass spectra were recorded on a JEOL JMS-SX102A spectrometer. All reactions were carried out under an argon atmosphere. Column chromatography was performed with silica gel 60 N (Kanto). Preparative thin-layer chromatography was performed with silica gel 60 PF_{254} (Merck). Gel permeation chromatography (GPC) was carried out with Japan Analytical Industry LC-908. UV–vis spectra were recorded on Agilent 8453 Spectrophotometer. Fluorescence spectra were recorded on JASCO FP-777.

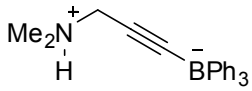
Materials. Unless otherwise noted, all chemicals and anhydrous solvents were obtained from commercial suppliers and used as received. $(CH_2Cl)_2$ was dried over CaH_2. Cyclopentyl methyl ether and *p*-xylene were dried over sodium benzophenone ketyl. $[Ir(OMe)(cod)]_2$,[8] and $Pd(P^tBu_3)_2$[9] were prepared according to the reported procedures.

Preparation of alkynyltriarylborate 1a: A typical procedure for the preparation of alkynyltriarylborates



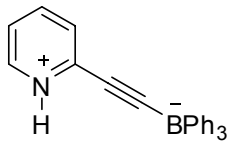
To a stirred solution of 3-(*N*,*N*-dimethylamino)prop-1-yne (500 mg, 6.0 mmol) in THF (20 ml) at -78 °C was added *n*-BuLi (1.6 M in hexane, 3.4 ml, 5.5 mmol). After 30 minutes at this temperature, $Ph_3B{\cdot}Py$ (1.61 g, 5.0 mmol) was added and the cooling bath was removed. After being stirred for 1 h at room temperature, the reaction was quenched by adding a small amount of MeOH. Volatile materials were removed under reduced pressure and the residue was dissolved in MeOH. Py·HCl (1.1g, 10 mmol) was added to the solution with stirring, resulting in white solid. It was collected by filtration and was washed with CH_2Cl_2 to give alkynyltriarylborate **1a** (1.35 g, 4.2 mmol, 83% yield).

3-(*N*,*N*-Dimethylammonio)prop-1-ynyltriphenylborate (1a)



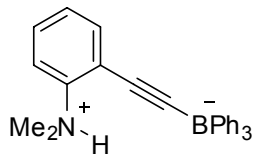
^{1}H NMR (CD_3CN): δ = 2.83 (s, 6H), 3.92 (s, 2H), 6.91-6.97 (m, 3H), 7.05-7.10 (m, 6H), 7.35 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (CD_3CN): δ = 42.5, 50.8, 123.6, 126.9, 135.1; ^{11}B NMR (CD_3CN): δ = -7.0; HRMS (EI) Calcd for $C_{23}H_{24}BN$ $[M]^+$ 325.2002. Found 325.2001.

Triphenyl(2-pyridinioethynyl)borate (1b)



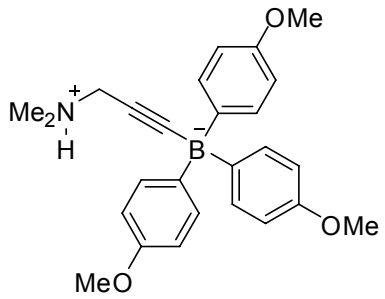
^{1}H NMR (CD_3CN): δ = 6.94-7.00 (m, 3H), 7.08-7.12 (m, 6H), 7.37 (d, *J* = 6.9 Hz, 6H), 7.62-7.67 (m, 1H), 7.82-7.85 (m, 1H), 8.28-8.34 (m, 2H); ^{13}C NMR (CD_3CN): δ = 122.6, 123.9, 127.1, 128.8, 135.2, 142.0, 142.7, 145.9; ^{11}B NMR (CD_3CN): δ = -6.5; HRMS (EI) Calcd for $C_{25}H_{20}BN$ (M^+) 345.1689. Found 345.1692.

{2-(*N*,*N*-Dimethylammonio)phenyl}ethynyltriphenylborate (1c)



^{1}H NMR (CD_3CN): δ = 2.99 (s, 6H), 6.98 (tt, *J* = 7.2, 1.6 Hz, 3H), 7.09-7.14 (m, 6H), 7.36-7.59 (m, 10H); ^{13}C NMR (CD_3CN): δ = 47.0, 120.3, 122.4, 124.3, 127.6, 128.7, 131.4, 132.8, 135.5; ^{11}B NMR (DMSO-d_6): δ = -7.2; HRMS (EI) Calcd for $C_{28}H_{26}BN$ (M^+) 386.2158. Found 387.2152.

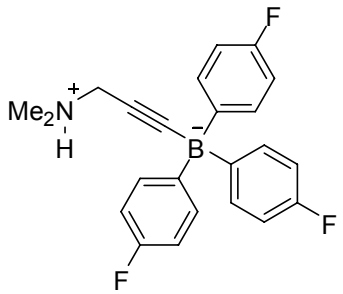
Tris(4-methoxyphenyl){3-(*N*,*N*-dimethylammonio)prop-1-ynyl}borate (1d)



^{1}H NMR (CD_3CN): δ = 2.86 (s, 6H), 3.69 (s, 9H), 3.92 (s, 2H), 6.62-6.67 (m, 6H), 7.18 (d, *J* = 8.4 Hz, 6H); ^{13}C NMR (CD_3CN): δ = 42.6, 50.9, 55.3, 112.5, 135.7, 156.9; ^{11}B

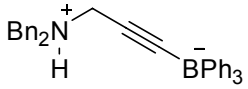
NMR (CD_3CN): δ = -7.8; HRMS (EI) Calcd for $C_{26}H_{30}BNO_3$ (M^+) 415.2319. Found 415.2319.

Tris(4-fluorophenyl){3-(*N*,*N*-dimethylammonio)prop-1-ynyl}borate (1e)



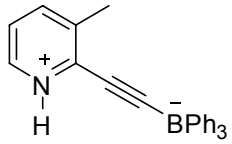
^{1}H NMR (CD_3CN): δ = 2.77 (s, 6H), 3.88 (s, 2H), 6.75-6.83 (m, 6H), 7.26 (pseudo t, *J* = 7.5 Hz, 6H); ^{13}C NMR (CD_3CN): δ = 41.8, 49.5, 113.2 (d, *J* = 18.2 Hz), 136.1 (d, *J* = 6.6 Hz), 161.1 (d, *J* = 235.1 Hz); ^{11}B NMR (CD_3CN): δ = -7.7; HRMS (EI) Calcd for $C_{23}H_{21}BNF_3$ (M^+) 379.1719. Found 379.1715.

3-(*N*,*N*-Dibenzylammonio)prop-1-ynyltriphenylborate (1f)



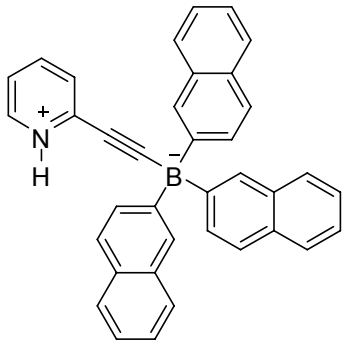
^{1}H NMR (DMSO-d_6): δ =3.58 (s, 2H), 4.25-4.45 (m, 4H), 6.88 (t, *J* = 7.2 Hz, 3H), 7.03 (pseudo t, *J* = 7.2 Hz, 6H), 7.36-7.51 (m, 16H); ^{13}C NMR (DMSO-d_6): δ = 42.3, 55.2, 122.4, 125.7, 128.7, 129.5, 131.1, 134.1; ^{11}B NMR (DMSO-d_6): δ = -7.4; HRMS (EI) Calcd for $C_{35}H_{32}BN$ (M^+) 477.2628. Found 477.2626.

Triphenyl{2-(3-methylpyridinio)ethynyl}borate (1g)



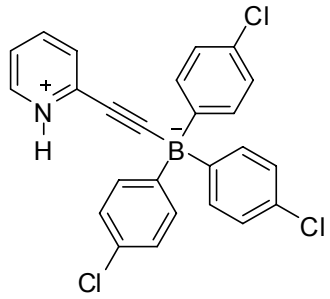
^{1}H NMR (CD_3CN): δ = 2.57 (s, 3H), 6.94-7.00 (m, 3H), 7.07-7.13 (m, 6H), 7.38 (d, *J* = 7.2 Hz, 6H), 7.54 (pseudo t, *J* = 6.8 Hz, 1H), 8.14 (d, *J* = 6.0 Hz, 1H), 8.20-8.24 (m, 1H); ^{13}C NMR (CD_3CN): δ = 19.7, 123.2, 124.0, 127.1, 135.1, 138.3, 140.9, 146.4; ^{11}B NMR (CD_3CN): δ = -6.3; HRMS (EI) Calcd for $C_{26}H_{22}BN$ (M^+) 359.1845. Found 359.1839.

Tris(2-naphthyl)(2-pyridinioethynyl)borate (1h)



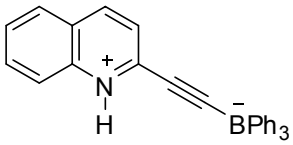
^{1}H NMR (DMSO-d_6): δ = 7.27-7.33 (m, 6H), 7.58-7.81 (m, 16H), 8.01 (d, J = 8.4 Hz, 1H), 8.39 (pseudo t, 7.8 Hz, 1H), 8.62 (d, J = 5.1 Hz, 1H); ^{13}C NMR could not be recorded because of the low solubility; ^{11}B NMR (DMSO-d_6): δ = -7.1; HRMS (EI) Calcd for $C_{37}H_{26}BN$ (M^+) 495.2158. Found 495.2157.

Tris(4-chlorophenyl)(2-pyridinioethynyl)borate (1i)



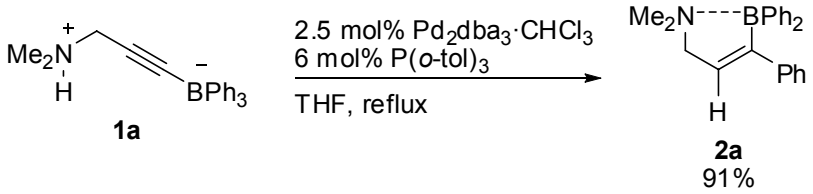
^{1}H NMR (CD_3CN): δ = 7.09-7.14 (m, 6H), 7.30 (d, J = 8.1 Hz, 6H), 7.69 (ddd, J = 7.7, 6.2, 1.4 Hz, 1H), 7.85 (dd, J = 8.6, 1.1 Hz, 1H), 8.31-8.37 (m, 2H); ^{13}C NMR (CD_3CN): δ = 124.1, 127.1, 129.8, 130.6, 136.5, 141.3, 147.0; ^{11}B NMR (CD_3CN): δ = -7.1; HRMS (EI) Calcd for $C_{25}H_{17}BNCl_3$ (M^+) 447.0520. Found 447.0525.

Triphenyl(2-quinolinioethynyl)borate (1j)



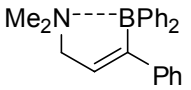
^{1}H NMR (DMSO-d_6): δ = 6.90-6.95 (m, 3H), 7.05 (pseudo t, J = 7.2 Hz, 6H), 7.33 (d, J = 6.6 Hz, 6H), 7.80-7.85 (m, 1H), 7.94 (d, J = 9.0 Hz, 1H), 8.03-8.12 (m, 2H), 8.26 (d, J = 8.7 Hz, 1H), 8.94 (d, J = 8.7 Hz, 1H); ^{13}C NMR (DMSO-d_6): δ = 119.8, 122.9, 125.8, 126.0, 128.5, 128.7, 134.1, 137.8, 140.3, 144.4; ^{11}B NMR (DMSO-d_6): δ = -7.0; HRMS (EI) Calcd for $C_{29}H_{22}BN$ (M^+) 395.1845. Found 395.1847.

Palladium-catalyzed rearrangement of 1a: A typical procedure for the rearrangement reaction



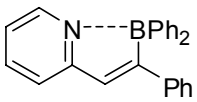
Under Ar atmosphere, a mixture of alkynylborate **1a** (32.4 mg, 0.10 mmol), $Pd_2dba_3{\cdot}CHCl_3$ (2.6 mg, 0.0025 mmol) and P(*o*-tol)$_3$ (1.8 mg, 0.006 mmol) in THF (0.5 ml) was stirred at 70 °C. After 1 h, the reaction mixture was directly subjected to preparative TLC (hexane:DCM = 1:1) to afford **2a** (29.5 mg, 0.091 mmol) in 91% yield.

Dimethyl{(*E*)-3-phenyl-3-diphenylborylprop-2-enyl}amine (2a)



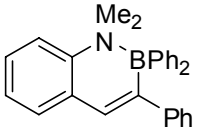
^{1}H NMR ($CDCl_3$): δ = 2.39 (s, 6H), 3.82 (d, *J* = 2.1 Hz, 2H), 6.18 (t, *J* = 2.0 Hz, 1H), 7.06-7.26 (m, 11H), 7.58 (dd, *J* = 8.1, 1.7 Hz, 4H); ^{13}C NMR ($CDCl_3$): δ = 50.1, 70.0, 120.4, 125.8, 125.9, 126.7, 127.2, 127.7, 135.2, 142.2; ^{11}B NMR ($CDCl_3$): δ = 6.6; HRMS (EI) Calcd for $C_{23}H_{24}BN$ (M^+) 325.2002. Found 325.2003.

2-{(*E*)-2-Phenyl-2-diphenylborylethenyl}pyridine (2b)



^{1}H NMR ($CDCl_3$): δ = 7.04 (ddd, *J* = 7.2, 6.1, 1.4 Hz, 1H), 7.11-7.31 (m, 14H), 7.48 (pseudo dt, *J* = 8.4, 1.5 Hz, 1H), 7.58-7.61 (m, 2H), 7.79 (ddd, *J* = 8.3, 7.3, 1.6 Hz, 1H), 8.23 (d, *J* = 5.7 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ =119.32, 119.34, 120.9, 125.7, 127.4, 128.0, 128.2, 128.3, 133.6, 138.5, 139.9, 143.0, 160.1; ^{11}B NMR ($CDCl_3$): δ = 3.5; HRMS (EI) Calcd for $C_{25}H_{20}BN$ (M^+) 345.1689. Found 345.1689.

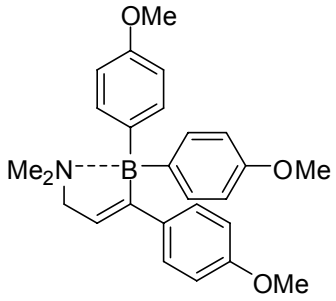
Dimethyl[2-{(*E*)-2-phenyl-2-diphenylborylethenyl}phenyl]amine (2c)



^{1}H NMR ($CDCl_3$): δ = 2.83 (s, 6H), 6.95 (s, 1H), 7.02-7.13 (m, 9H), 7.20-7.24 (m, 3H), 7.31-7.34 (m, 3H), 7.55-7.58 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 48.9, 117.9, 125.6, 125.9, 126.6, 126.8, 127.2, 127.4, 128.0, 128.1, 129.7, 133.4, 136.7, 144.7, 147.1; ^{11}B NMR

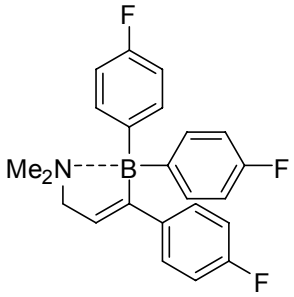
($CDCl_3$): δ = 4.2; HRMS (EI) Calcd for $C_{28}H_{26}BN$ (M^+) 386.2158. Found 387.2161.

(*E*)-3-(4-Methoxyphenyl)-3-bis(4-methoxyphenyl)borylprop-2-enyldimethylamine (2d)



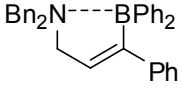
^{1}H NMR ($CDCl_3$): δ = 2.33 (s, 6H), 3.71 (s, 3H), 3.75 (d, *J* = 2.1 Hz, 2H), 3.77 (s, 6H), 6.07 (t, *J* = 2.1 Hz, 1H), 6.67 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 4H), 7.11 (d, *J* = 9.0 Hz, 2H), 7.50 (d, *J* = 8.7 Hz, 4H); ^{13}C NMR ($CDCl_3$): δ = 49.9, 54.9, 55.1, 69.7, 112.7, 113.2, 118.2, 127.9, 134.7, 136.3, 157.8; ^{11}B NMR ($CDCl_3$): δ = 6.4; HRMS (EI) Calcd for $C_{26}H_{30}BNO_3$ (M^+) 415.2319. Found 415.2314.

(*E*)-3-(4-Fluorophenyl)-3-bis(4-fluorophenyl)borylprop-2-enyldimethylamine (2e)



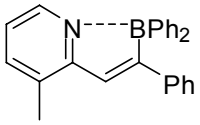
^{1}H NMR ($CDCl_3$): δ = 2.35 (s, 6H), 3.79 (d, *J* = 1.8 Hz, 2H), 6.12 (br, 1H), 6.80 (pseudo t, *J* = 8.9 Hz, 2H), 6.93 (pseudo t, *J* = 9.0 Hz, 4H), 7.07 (dd, *J* = 8.7, 5.7 Hz, 2H), 7.48 (dd, *J* = 8.6, 6.3 Hz, 4H); ^{13}C NMR ($CDCl_3$): δ = 50.1, 69.9, 114.2 (d, *J* = 18.2 Hz), 114.7 (d, *J* = 21.2 Hz), 120.2 (d, *J* = 1.4 Hz), 128.1 (d, *J* = 8.0 Hz), 136.5 (d, *J* = 6.6 Hz), 137.7 (d, *J* =2.9 Hz), 161.5 (d, *J* = 242.5 Hz), 161.8 (d, *J* = 243.2 Hz); ^{11}B NMR ($CDCl_3$): δ = 5.9; HRMS (EI) Calcd for $C_{23}H_{21}BNF_3$ (M^+) 379.1719. Found 379.1722.

Dibenzyl{(*E*)-3-phenyl-3-diphenylborylprop-2-enyl}amine (2f)



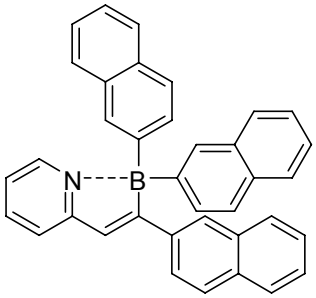
^{1}H NMR ($CDCl_3$): δ = 3.62 (d, *J* = 2.1 Hz, 2H), 3.8-4.4 (br, 4H), 6.01 (t, *J* = 2.0 Hz, 1H), 6.70-6.73 (m, 4H), 7.06-7.31 (m, 17H), 7.71 (dd, *J* = 8.0, 1.7 Hz, 4H); ^{13}C NMR ($CDCl_3$): δ = 59.2, 61.2, 123.0, 125.7, 126.2, 126.6, 127.5, 127.8, 128.1, 128.4, 131.8, 133.4, 135.6, 143.5; ^{11}B NMR ($CDCl_3$): δ = 10.3; HRMS (EI) Calcd for $C_{35}H_{32}BN$ (M^+) 477.2628. Found 477.2626.

3-Methyl-2-{(*E*)-2-phenyl-2-diphenylborylethenyl}pyridine (2g)



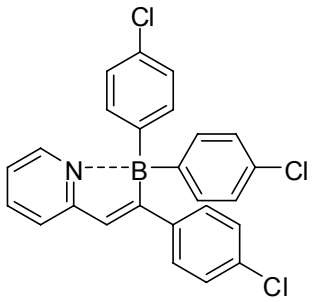
^{1}H NMR ($CDCl_3$): δ =2.55 (s, 3H), 7.00 (pseudo t, *J* = 6.5 Hz, 1H), 7.10-7.30 (m, 14H), 7.58-7.63 (m, 3H), 8.08 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ =18.1, 119.1, 119.2, 125.6, 127.3, 128.0, 128.19, 128.22, 128.8, 133.6, 138.9, 140.3, 140.5, 159.1; ^{11}B NMR ($CDCl_3$): δ = 3.9; HRMS (EI) Calcd for $C_{26}H_{22}BN$ (M^+) 359.1845. Found 359.1845.

2-{(*E*)-2-(2-Naphthyl)-2-bis(2-naphthyl)borylethenyl}pyridine (2h)



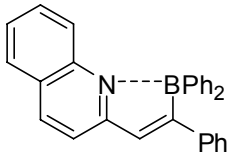
^{1}H NMR ($CDCl_3$): δ = 7.06 (ddd, *J* = 7.5, 6.0, 1.1 Hz, 1H), 7.28-7.38 (m, 7H), 7.49-7.87 (m, 16H), 8.13 (s, 1H), 8.33 (d, *J* = 5.7 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ =119.4, 119.6, 121.7, 124.7, 125.0, 125.7, 126.0, 126.4, 127.30, 127.34, 127.5, 127.7, 128.6, 128.7, 132.0, 132.4, 132.7, 133.2, 133.3, 133.5, 136.0, 140.1, 143.2, 160.3; ^{11}B NMR ($CDCl_3$): δ = 3.9; HRMS (EI) Calcd for $C_{37}H_{26}BN$ (M^+) 495.2158. Found 495.2158.

2-{(*E*)-2-(4-Chlorophenyl)-2-bis(4-chlorophenyl)borylethenyl}pyridine (2i)



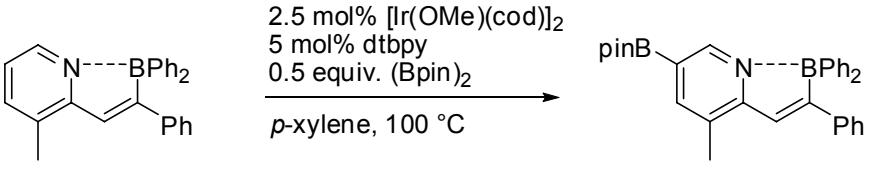
^{1}H NMR ($CDCl_3$): δ = 7.11-7.22 (m, 12H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 1H), 7.88 (pseudo dt, *J* = 7.8, 1.2 Hz, 1H), 8.14 (d, *J* = 5.7 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ =119.8, 119.9, 121.5, 127.7, 128.4, 129.3, 132.0, 134.4, 134.8, 136.5, 140.5, 142.7, 159.9; ^{11}B NMR ($CDCl_3$): δ = 3.1; HRMS (EI) Calcd for $C_{25}H_{17}BNCl_3$ (M^+) 447.0520. Found 447.0517.

2-{(*E*)-2-Phenyl-2-diphenylborylethenyl}quinoline (2j)



^{1}H NMR ($CDCl_3$): δ = 7.07-7.16 (m, 7H), 7.18-7.23 (m, 3H), 7.28-7.32 (m, 4H), 7.36-7.45 (m, 4H), 7.70 (d, *J* = 8.7 Hz, 1H), 7.81- 7.90 (m, 2H), 8.35 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 118.2, 122.1, 123.1, 125.3, 125.7, 126.2, 127.3, 128.0, 128.1, 128.3, 128.5, 131.3, 133.2, 139.3, 141.1, 141.5, 161.9; ^{11}B NMR ($CDCl_3$): δ = 3.9; HRMS (EI) Calcd for $C_{29}H_{22}BN$ (M^+) 395.1845. Found 395.1849.

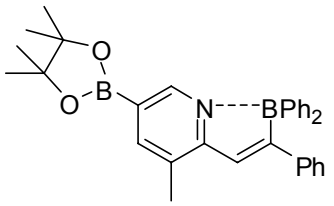
Ir-catalyzed borylation of 2g



2g **5** 82%

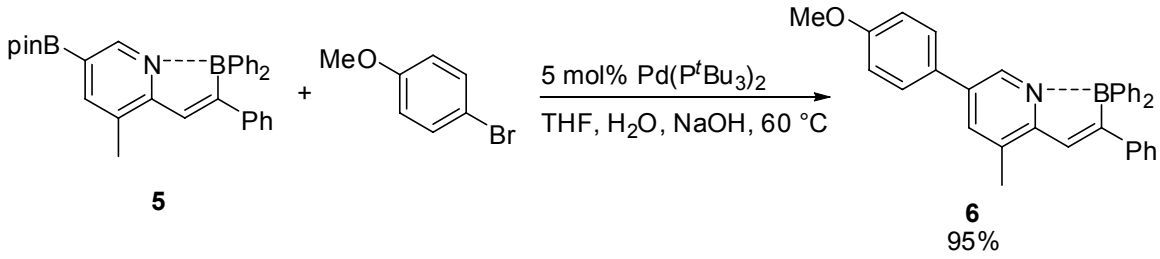
Under Ar atmosphere, a *p*-xylene (1.0 ml) solution containing **2g** (71.8 mg, 0.20 mmol), $(Bpin)_2$ (25.3 mg, 0.10 mmol), $[Ir(OMe)(cod)]_2$ (3.3 mg, 0.005 mmol) and dtbpy (2.7 mg, 0.01 mmol) was stirred at 100 °C for 3 h. After cooling to room temperature, the reaction mixture was passed through a short pad of silica gel. Subsequent purification with GPC afforded pure boronic ester **5** (79.3 mg, 0.16 mmol) in 82% yield.

3-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaboloran-2-yl)-2-{(*E*)-2-phenyl-2-diphen ylborylethenyl}pyridine (5)



^{1}H NMR ($CDCl_3$): δ = 1.27 (s, 12H), 2.53 (s, 3H), 7.11-7.33 (m, 14H), 7.58-7.63 (m, 2H), 7.98 (s, 1H), 8.43 (s, 1H); ^{13}C NMR ($CDCl_3$): δ =17.8, 24.9, 84.4, 119.2, 125.5, 127.3, 127.9, 128.0, 128.3, 128.4, 133.8, 138.7, 146.1, 146.2, 160.8; ^{11}B NMR ($CDCl_3$): δ = 3.5, 30.1; HRMS (EI) Calcd for $C_{32}H_{33}B_2NO_2$ (M^+) 485.2697. Found 485.2691.

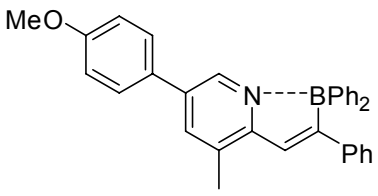
Pd-catalyzed cross-coupling reaction of 5 with 4-bromoanisole



5 **6**
95%

Under Ar atmosphere, a THF solution containing **5** (48.5 mg, 0.10 mmol), *p*-bromoanisole (22.0 mg, 0.12 mmol), Pd(P^{t}Bu$_3$)$_2$ (2.6 mg, 0.005 mmol), NaOH (12.0 mg, 0.30 mmol), and H_2O (5 μl) was stirred at 60 °C for 1 h. After cooling the reaction mixture to room temperature, water was added. The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic phase was washed with water, brine, and dried over $MgSO_4$. Removal of the solvent under reduced pressure and subsequent purification with GPC afforded biaryl **6** (44.0 mg, 0.095 mmol) in 95 % yield.

5-(4-Methoxyphenyl)-3-methyl-2-{(*E*)-2-phenyl-2-diphenylborylethenyl}pyridine (6)



^{1}H NMR ($CDCl_3$): δ = 2.60 (s, 3H), 3.80 (s, 3H), 6.89-6.94 (m, 2H), 7.11-7.26 (m, 10H),

7.31-7.37 (m, 6H), 7.60-7.64 (m, 2H), 7.775-7.784 (m, 1H), 8.26 (d, *J* = 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ =18.2, 55.4, 114.5, 118.9, 125.6, 127.4, 127.8, 128.0, 128.1, 128.2, 128.3, 128.6, 132.8, 133.7, 138.2, 138.4, 138.9, 157.2, 159.8; ^{11}B NMR ($CDCl_3$): δ = 3.9; HRMS (EI) Calcd for $C_{33}H_{28}BN$ (M^+) 465.2264. Found 465.2259.

References

1. Reviews: (a) Entwistle, C. D.; Marder, T. B. *Chem. Mater.* **2004**, *16*, 4574. (b) Yamaguchi, S.; Wakamiya, A. *Pure Appl. Chem.* **2006**, *78*, 1413. (c) Jäkle, F. *Coord. Chem. Rev.* **2006**, *250*, 1107. (d) Loudet, A.; Burgess, K. *Chem. Rev.* **2007**, *107*, 4891.
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3. See Chapter 1.
4. The alkynylborate **1a** was prepared in 83% yield by the reaction of the corresponding lithium acetylide with triphenylborane-pyridine adduct followed by treatment with pyridinium chloride.
5. (a) Miyaura, N.; Yoshinari, T.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* **1974**, *15*, 2961. (b) Pelter, A.; Harrison, C. R.; Subrahmanyam, C.; Kirkpatrick, D. *J. Chem. Soc. Perkin Trans. 1* **1976**, 2435.
6. These values were determined in MeOH solutions. Williams, J. L. R.; Webster, S. K.; Van Allan, J. A. *J. Org. Chem.* **1961**, *26*, 4893.
7. Pyridine ring was preferentially borylated over phenyl C–H bonds. (a) Takagi, J.; Sato, K.; Hartwig, J. F.; Ishiyama T.; Miyaura, N. *Tetrahedron Lett.* **2002**, *43*, 5649. (b) Mkhalid, I. A. I.; Coventry, D. N.; Albesa-Jove, D.; Batsanov, A. S.; Howard, J. A. K.; Perutz, R. N.; Marder, T. B. *Angew. Chem. Int. Ed.* **2006**, *45*, 489.
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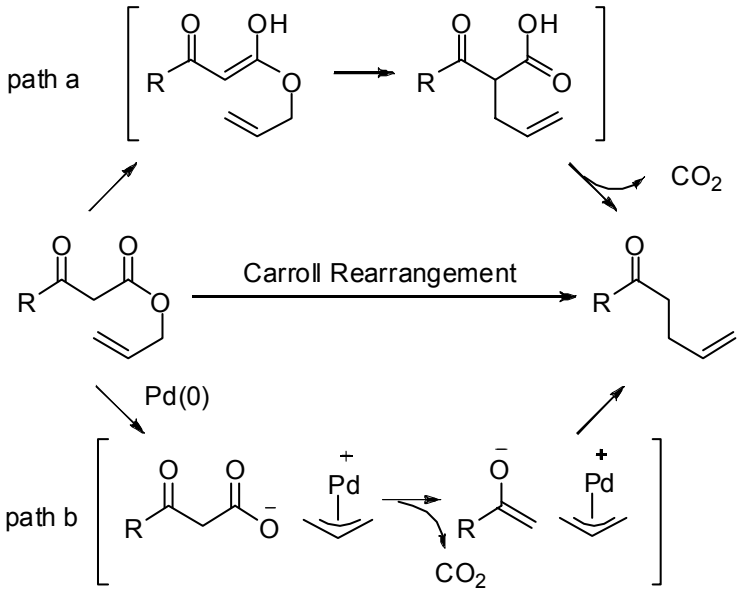
Chapter 4

Asymmetric Carroll Rearrangement of Allyl α-Acetamido-β-ketocarboxylates Catalyzed by a Chiral Palladium Complex

Abstract: Asymmetric decarboxylative rearrangement (Carroll rearrangement) of allyl α-acetamido-β-ketocarboxylates was catalyzed by a palladium complex modified with a chiral phosphine ligand, giving optically active γ,δ-unsaturated α-aminoketones with up to 90% ee.

Carroll rearrangement, a variant of ester Claisen rearrangement, is an efficient carbon–carbon bond forming method to produce γ,δ-unsaturated carbonyl compounds from allylic esters of β-ketocarboxylic acids.[1] Two mechanisms can operate for the decarboxylative rearrangement (Scheme 1). The reaction, occurring at a high temperature or under strongly basic conditions, proceeds by an electrocyclic pathway (*path a*), and has often been used in natural products syntheses.[2] Alternatively, the rearrangement is catalyzed by palladium(0)/phosphine complexes under milder conditions (*path b*).[3] Oxidative addition, decarboxylation, and recombination constitute the catalytic cycle. This catalytic pathway inspired us to explore asymmetric Carroll rearrangement by means of chiral phosphine–palladium complexes. In this chapter, the author describes catalytic asymmetric Carroll rearrangement,[4,5] which affords optically active γ,δ-unsaturated ketones bearing an *N*-substituted quaternary chiral α-carbon with up to 90% ee.

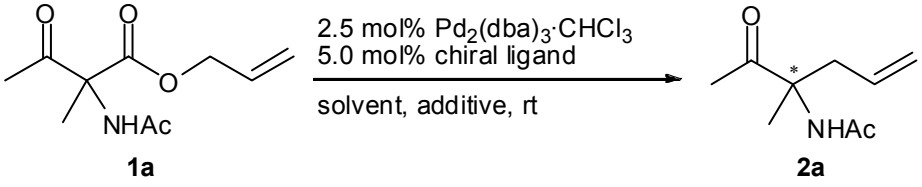
Scheme 1. Carroll rearrangement



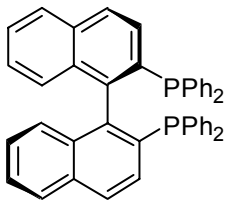
It was reported that a palladium complex modified with BINAP catalyzed a highly enantioselective allylation of α-acetamido-β-ketoesters, whose acetamido group was crucial for the control of stereochemistry.[6] Thus, an allylic esters of α-acetamido-β-ketocarboxylic acids was employed as the substrate for asymmetric Carroll rearrangement. A variety of chiral phosphine ligands were examined in the palladium-catalyzed decarboxylative rearrangement of 2-propenyl 2-(*N*-acetylamino)-2-methyl-3-oxobutanoate (**1**), with the selected results listed in Table 1. Only 25% ee was observed with BINAP, which was the chiral ligand of choice in the

asymmetric allylation reaction previously reported (entry 1).[6] So-called Trost ligand (naphthyl) **3** showed a better enantioselectivity (entry 2).[7,8] Dichloroethane (DCE) was superior to THF as the solvent (entry 3). Finally, it was found that addition of phenol derivatives brought about a dramatic enhancement of the enantioselectivity (entries 4-6). A satisfactory result in terms of both chemical yield and selectivity was obtained when the reaction was carried out in the presence of 0.5 equiv 1-naphthol.[9]

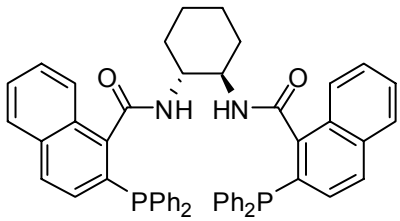
Table 1. Asymmetric Carroll rearrangement of **1**[a]



1a **2a**



(*R*)-BINAP



3

entry	chiral ligand	solvent	additive	yield / %[b]	ee / %[c]
1	(*R*)-BINAP	THF	-	81	25 (-)
2	**3**	THF	-	99	36 (+)
3	**3**	DCE	-	89	51 (+)
4	**3**	DCE	phenol (1 eq)	72	81 (+)
5	**3**	DCE	1-naphthol (1 eq)	70	88 (+)
6	**3**	DCE	1-naphthol (0.5 eq)	79	87 (+)[d]

[a] Reactions were conducted on 0.2 mmol scale at room temperature. [b] Isolated yield. [c] By GC analysis with Chiraldex G-BP. Signs of optical rotation are given in parentheses. [d] $[\alpha]^{20}_{D}$= +7.0 (c 0.50, $CHCl_3$).

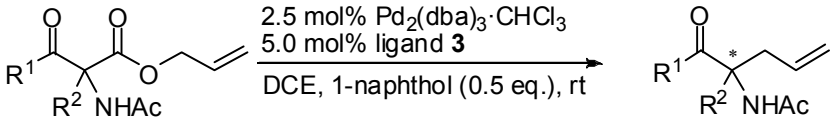
The results of the asymmetric Carroll rearrangement of allyl α-acetamido-β-ketocarboxylates catalyzed by palladium/**3** are summarized in Table 2. A higher enantioselectivity (90% ee) was observed with the substrate having a propanoyl group (entry 1, R^1 = Et). Substrates bearing ethyl and benzyl groups at the α-position gave the corresponding products with 80% ee and 71% ee, respectively (entries 2, 3). Lower reactivities were observed with allylic ester groups other than a 2-propenyl group, like methallyl (low yield), cinnamyl (low yield), crotyl ((*E*)-α-, (*Z*)-α- and diastereomeric

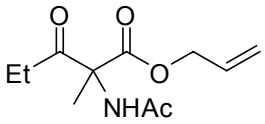
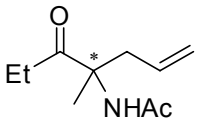
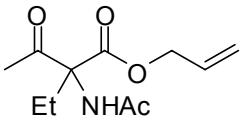
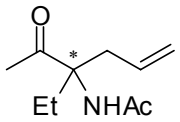
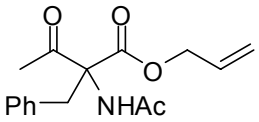
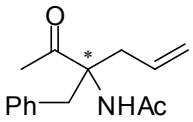
mixture of γ-coupling products), and prenyl (no prenylated product) groups.

For comparison, Carroll rearrangement of allyl β-ketocarboxylates lacking an α-acetamido group was examined (Scheme 2). The reaction of cyclohexanone **4** gave γ,δ-unsaturated ketone **5** with only 14% ee. No asymmetric induction was observed in the reaction of acyclic β-ketoester **6**. These results indicated that the α-acetamido group played a crucial role in enantioface-selection of the enolate generated from β-ketocarboxylate via decarboxylation.

In conclusion, the chiral palladium catalyst generated *in situ* from $Pd_2(dba)_3{\cdot}CHCl_3$ and the optically active bisphosphine ligand **3** accomplished a high degree of asymmetric induction on a *N*-substituted quaternary chiral carbon center (up to 90% ee) in the Carroll rearrangement of allyl α-acetamido-β-ketocarboxylates.

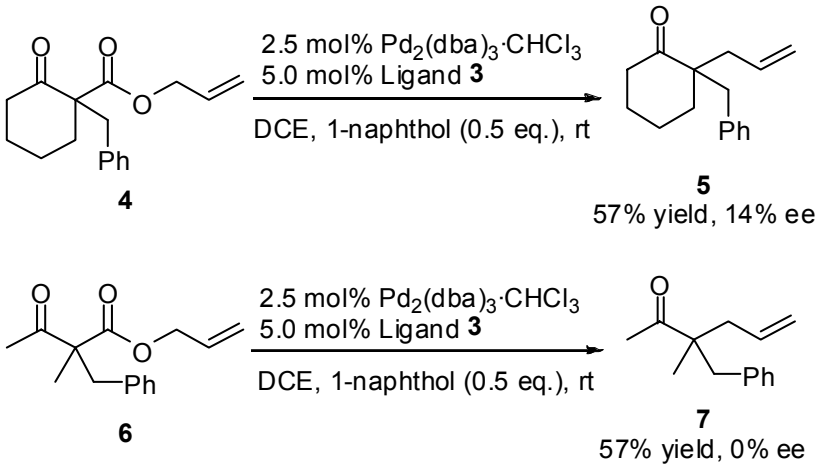
Table 2. Palladium-catalyzed asymmetric Carroll rearrangement of allyl α-acetamido-β-ketocarboxylates[a]



entry	substrate **1**	product **2**	yield / %[b]	ee / %
1	 **1b**	 **2b**	81	90[c]
2	 **1c**	 **2c**	55	80[d]
3	 **1d**	 **2d**	82	71[e]

[a] Reactions were conducted on 0.2 mmol scale at room temperature. [b] Isolated yield. [c] By GC analysis with Chiraldex G-BP. [d] By HPLC analysis with Chiralcel OJ-H. [e] By HPLC analysis with Chiralcel OD-H.

Scheme 2. Carroll rearrangement of allyl β-ketocarboxylates

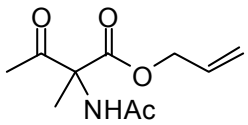


Experimental Section

General. NMR spectra were recorded on a Varian Gemini 2000 (^{1}H at 300 MHz and ^{13}C at 75 MHz) or Varian Mercury-400 (^{1}H at 400 MHz) spectrometers. $CDCl_3$ was used as a solvent. Me_4Si (^{1}H, $\delta = 0.00$), $CDCl_3$ (^{13}C, $\delta = 77.0$) were used as standards. High-resolution mass spectra were recorded on a JEOL JMS-SX102A spectrometer. All reactions were carried out under an argon atmosphere. Column chromatography was performed with silica gel 60 N (Kanto). Preparative thin-layer chromatography was performed with silica gel 60 PF_{254} (Merck).

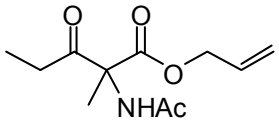
Materials. Unless otherwise noted, all chemicals and anhydrous solvents were obtained from commercial suppliers and used as received. $(CH_2Cl)_2$ was dried over CaH_2.

Prop-2-enyl 2-acetamido-2-methyl-3-oxobutanoate (1a)



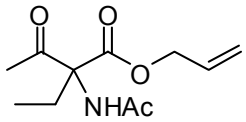
^{1}H NMR (300 MHz): $\delta = 1.74$ (s, 3H), 2.03 (s, 3H), 2.21 (s, 3H), 4.65-4.69 (m, 2H), 5.25-5.36 (m, 2H), 5.81-5.92 (ddd, $J = 17.1, 10.2, 5.7$ Hz, 1H), 7.01 (br, 1H); ^{13}C NMR: $\delta = 20.2, 23.0, 24.1, 66.9, 68.4, 119.4, 131.0, 168.8, 169.1, 200.2$; HRMS (EI): Calcd for $C_{10}H_{15}NO_4$ $(M)^+$ 213.1001. Found 213.1006.

Prop-2-enyl 2-acetamido-2-methyl-3-oxopentanoate (1b)



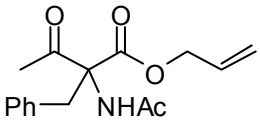
^{1}H NMR (400 MHz): $\delta = 1.08$ (t, $J = 7.2$ Hz, 3H), 1.74 (s, 3H), 2.04 (s, 3H), 2.43-2.63 (m, 2H), 4.63-4.67 (m, 2H), 5.25 (d, $J = 10.4$ Hz, 1H), 5.32 (d, $J = 17.2$ Hz, 1H), 8.86 (ddd, $J = 17.2, 10.4, 5.6$ Hz, 1H), 7.05 (br, 1H); ^{13}C NMR: $\delta = 7.9, 20.3, 23.0, 29.7, 66.8, 68.1, 119.4, 131.1, 169.0, 169.1, 203.4$; HRMS (FAB): Calcd for $C_{11}H_{18}NO_4$ $(M+H)^+$ 228.1236. Found 228.1229.

Prop-2-enyl 2-acetamido-2-ethyl-3-oxobutanoate (1c)



^{1}H NMR (400 MHz): δ = 0.72 (t, *J* = 7.6 Hz, 3H), 2.06 (s, 3H), 2.18 (s, 3H), 2.32 (q, *J* = 7.6 Hz, 1H), 2.50 (q, *J* = 7.6 Hz, 1H), 4.64-4.68 (m, 2H), 5.26 (d, *J* = 10.4 Hz, 1H), 5.32 (d, *J* = 17.2 Hz, 1H), 5.86 (ddd, *J* = 17.2, 10.4, 4.4 Hz, 1H), 6.94 (br, 1H); ^{13}C NMR: δ = 7.5, 23.0, 24.3, 24.6, 66.8, 72.7, 119.5, 131.0, 168.4, 169.1, 200.0; HRMS (FAB): Calcd for $C_{11}H_{18}NO_4$ $(M+H)^+$ 228.1236. Found 228.1236.

Prop-2-enyl 2-acetamido-2-benzyl-3-oxobutanoate (1d)

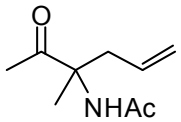


^{1}H NMR (400 MHz): δ = 2.05 (s, 3H), 2.25 (s, 3H), 3.58 (d, *J* = 14.0 Hz, 1H), 3.72 (d, *J* = 14.0 Hz, 1H), 4.69 (d, *J* = 6.0 Hz, 2H), 5.33 (d, *J* = 10.4 Hz, 1H), 5.38 (d, *J* = 17.2 Hz, 1H), 5.88-5.92 (m, 1H), 6.66 (br, 1H), 6.95-6.98 (m, 2H), 7.24-7.27 (m, 3H); ^{13}C NMR: δ = 23.0, 24.7, 37.1, 67.2, 72.7, 120.1, 127.3, 128.4, 129.7, 130.7, 135.2, 167.9, 169.3, 198.7; HRMS (EI): Calcd for $C_{16}H_{19}NO_4$ $(M)^+$ 289.1314. Found 289.1311.

Palladium-catalyzed Carroll rearrangement of 1a: A typical procedure

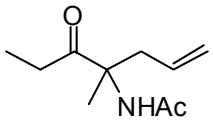
Under nitrogen atmosphere, a CH_2Cl_2 solution (1.0 ml) containing Pd_2dba_3·$CHCl_3$ (5.2 mg, 0.005 mmol), (*R*,*R*)-**3** (8.0 mg, 0.01 mmol), 1-naphthol (14.4 mg, 0.10 mmol) was stirred at room temperature. After 30 minutes, **1a** was added and stirred until the substrate was consumed. The reaction mixture was concentrated and purified with preparative column chromatography (Hexane:AcOEt = 1:1) to afford **2a** (26.7 mg, 0.16 mmol, 79% yield).

4-Acetamido-4-methylhex-1-en-5-one (2a)



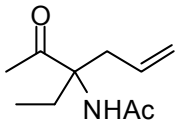
^{1}H NMR (400 MHz): δ = 1.53 (s, 3H), 1.99 (s, 3H), 2.19 (s, 3H), 2.49 (q, *J* = 8.0 Hz, 1H), 3.05 (q, *J* = 8.0 Hz, 1H), 5.08 (m, 1H), 5.12 (m, 1H), 5.51-5.62 (m, 1H), 6.41 (br, 1H); ^{13}C NMR: δ = 21.6, 23.6, 23.7, 39.3, 64.3, 119.2, 132.2, 169.4, 208.0; HRMS (CI): Calcd for $C_9H_{16}NO_2$ $(M+H)^+$ 170.1181, Found 170.1179.

4-Acetamido-4-methylhept-1-en-5-one (2b)



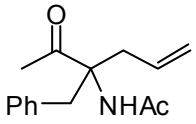
^{1}H NMR (400 MHz): δ = 1.08 (t, *J* = 7.2 Hz, 3H), 1.54 (s, 3H), 2.00 (s, 3H), 2.46-2.61 (m, 3H), 3.06 (q, *J* = 7.2 Hz, 1H), 5.06 (d, *J* = 4.0 Hz, 1H), 5.11 (d, *J* = 3.2 Hz, 1H), 5.50-5.60 (m, 1H), 6.47 (br, 1H); ^{13}C NMR: δ = 7.9, 21.8, 23.8, 28.8, 39.6, 64.2, 119.2, 132.3, 169.4, 210.8; HRMS (EI): Calcd for $C_{10}H_{17}NO_2$ $(M)^+$ 183.1259. Found 183.1259.

4-Acetamido-4-ethylhex-1-en-5-one (2c)



^{1}H NMR (300 MHz): δ = 0.70 (t, *J* = 7.5 Hz, 3H), 1.74 (q, *J* = 7.5 Hz, 1H), 2.02 (s, 3H), 2.17 (s, 3H), 2.42 (dd, *J* = 14.4, 7.5 Hz, 1H), 2.63 (q, *J* = 7.5 Hz, 1H), 3.40 (dd, *J* = 14.4, 7.5 Hz, 1H), 5.02-5.11 (m, 2H), 5.42-5.54 (m, 1H), 6.60 (br, 1H); ^{13}C NMR: δ = 8.0, 23.3, 24.0, 26.9, 38.2, 69.5, 118.6, 132.1, 169.2, 207.8; HRMS (FAB): Calcd for $C_{10}H_{18}NO_2$ $(M+H)^+$ 184.1338. Found 184.1333.

4-Acetamido-4-benzylhex-1-en-5-one (2d)



^{1}H NMR (300 MHz): δ = 1.97 (s, 3H), 2.30 (s, 3H), 2.54 (dd, *J* = 14.4, 7.8 Hz, 1H), 3.11 (d, *J* = 14.4 Hz, 1H), 3.45 (dd, *J* = 14.4, 7.8Hz, 1H), 3.80 (d, *J* = 14.4 Hz, 1H), 5.09 (d, *J* = 8.7 Hz, 1H), 5.13 (d, *J* = 14.4 Hz, 1H), 5.45-5.60 (m, 1H), 6.38 (br, 1H), 7.00-7.03 (m, 2H), 7.21-7.27 (m, 3H); ^{13}C NMR: δ = 24.1, 24.4, 38.3, 39.2, 69.5, 119.1, 127.0, 128.3, 129.6, 131.6, 135.9, 169.6; HRMS (EI): Calcd for $C_{15}H_{19}NO_2$ $(M)^+$ 245.1416. Found 245.1417.

References

1. (a) Carroll, M. F. *J. Chem. Soc.* **1940**, 704. (b) Carroll, M. F. *J. Chem. Soc.* **1940**, 1266. (c) Carroll, M. F. *J. Chem. Soc.* **1941**, 507. (d) Kimel, W.; Cope, A. C. *J. Am. Chem. Soc.* **1943**, *65*, 1992.
2. (a) Echavarren, A. M.; de Mendoza, J.; Prados, P.; Zapata, A. *Tetrahedron Lett.* **1991**, *32*, 6421. (b) Ouvrard, N.; Rodriguez, J.; Santelli, M. *Tetrahedron Lett.* **1993**, *34*, 1149. (c) Hatcher, M. A.; Posner, G. H. *Tetrahedron Lett.* **2002**, *43*, 5009.
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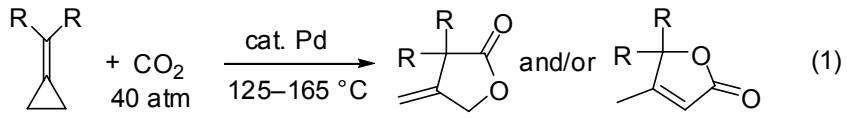
4. For asymmetric Carroll rearrangement by using stoichiometric SAMP or RAMP, see: Enders, D.; Knopp, M. *Tetrahedron* **1996**, *52*, 5805.
5. Recent examples: (a) Trost, B. M.; Xu, J.; Reichle, M. *J. Am. Chem. Soc.* **2007**, *129*, 282. (b) Constant, S.; Tortoioli, S.; Müller, J.; Lacour, J. *Angew. Chem. Int. Ed.* **2007**, *46*, 2082. (c) Schulz, S. R.; Blechert, S. *Angew. Chem. Int. Ed.* **2007**, *46*, 3966. (d) Behenna, D. C.; Stockdill, J. L.; Stoltz, B. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 4077. (e) He, H.; Zheng, X.-J.; Li, Y.; Dai, L.-X.; You, S.-L. *Org. Lett.* **2007**, *9*, 4339.
6. (a) Kuwano, R.; Ito, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3236. (b) Kuwano, R.; Nishio, R.; Ito, Y. *Org. Lett.* **1999**, *1*, 837.
7. Trost, B. M.; Bunt, R. C. *Angew. Chem. Int. Ed.* **1996**, *35*, 99.
8. The chiral ligand **3** is commercially available from Strem Chemicals, Inc.
9. It might be that hydrogen bonding between the protic hydrogens with the amido groups of **3** favors a desired conformation or disfavors undesired amido coordination to palladium. For a similar effect of alcohol addition to improve an enantioselectivity, see: Trost, B. M.; Soldermann, C. P.; Chen, I.; Schroeder, G. M. *J. Am. Chem. Soc.* **2004**, *126*, 4480.

Chapter 5

Solvent and Ligand Partition Reaction Pathways in Nickel-Mediated Carboxylation of Methylenecyclopropanes

Abstract: Methylenecyclopropanes are carboxylated with carbon dioxide in the presence of a stoichiometric amount of a nickel complex. The reaction pathways are significantly influenced by the reaction solvent and the amine ligand.

The incorporation of carbon dioxide into organic compounds presents an important challenge in chemistry, as reduction of greenhouse gases has emerged as a pressing global issue. In addition, due to its abundance as a raw material and innocuous nature, the development of methods to activate intrinsically inert carbon dioxide and to fix it into organic compounds becomes of practical value to synthetic chemists.[1] On the other hand, a number of transition metal-mediated processes involving carbon–carbon bond cleavage of methylenecyclopropanes have been reported.[2] Methylenecyclopropanes are unique in that coordination of their carbon–carbon double bonds to low-valent transition metals triggers cleavage at either the proximal Csp_2–Csp_3 bond or the distal Csp_3–Csp_3 bond of the cyclopropane core.[3] There has been, however, only one example of carboxylation of methylenecyclopropanes with carbon dioxide; a palladium-catalyzed reaction at relatively high temperature forms unsaturated five-membered ring lactones through a sequence involving oxidative addition of the distal carbon–carbon bond to palladium, insertion of carbon dioxide and finally, reductive elimination (eq 1).[4]

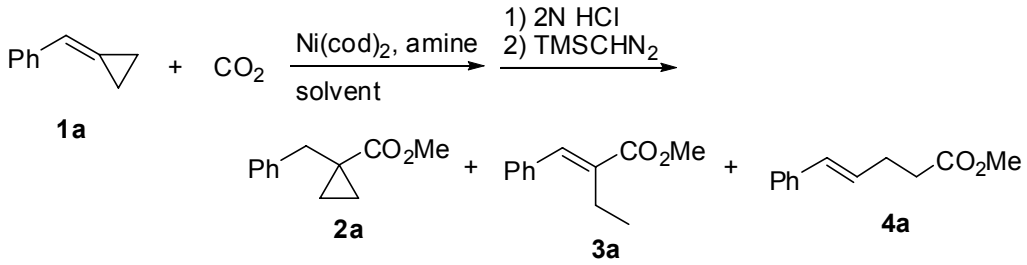


It has been reported recently that low-valent nickel species mediate the coupling of carbon dioxide with various unsaturated hydrocarbons under mild conditions,[5] which encouraged us to explore a new nickel-mediated carboxylation reaction of methylenecyclopropanes. Notably, it was found that diverse reaction pathways are partitioned in response to reaction conditions, such as a reaction solvent and the amine ligand employed, affording products essentially different from those obtained in the palladium case mentioned above.

A solution of benzylidenecyclopropane (**1a**, 1.1 equiv), $Ni(cod)_2$ (1.0 equiv, cod = cycloocta-1,5-diene), and an amine ligand (2.2 equiv) was stirred at 0 °C for 4 h under an atmosphere of carbon dioxide (1 atm). An acidic workup followed by methylation with Me_3SiCHN_2 afforded a mixture of methyl esters of the carboxylated products. The distribution of these products varied significantly as a function of reaction solvent and amine ligand (Table 1). When 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 2.2 equiv) was used as the amine ligand in toluene solvent, cyclopropane derivative **2a** was obtained along with a small amount of the branched α,β-unsaturated ester **3a**[6] (73%, **2a**:**3a**:**4a** = 93:7:0, entry 1). In contrast, the use of more polar solvents favored the formation of **3a** (entries 2–5). In particular, the reaction with DBU in *N*-methyl-2-pyrrolidinone (NMP)

gave **3a** in 78% yield as the major product (**2a**:**3a**:**4a** = 6:94:0). Here, the formation of the linear γ,δ-unsaturated ester **4a** was not observed. However, to our surprise, use of 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD) instead of DBU altered the reaction course to favor production of the linear γ,δ-unsaturated ester **4a**;[7] the reaction with MTBD in NMP gave **4a** in 52% yield exclusively (entry 8). At a higher CO_2 pressure of 5 atm, the yield was improved (67%, **2a**:**3a**:**4a** = 0:1:99, entry 9). Suppression of the formation of **4a** with DBU, and of **2a** and **3a** with MTBD suggests different mechanisms operate with DBU and MTBD (*vide infra*).

Table 1. Nickel-mediated carboxylation of **1a** with CO_2 under various conditions[a]



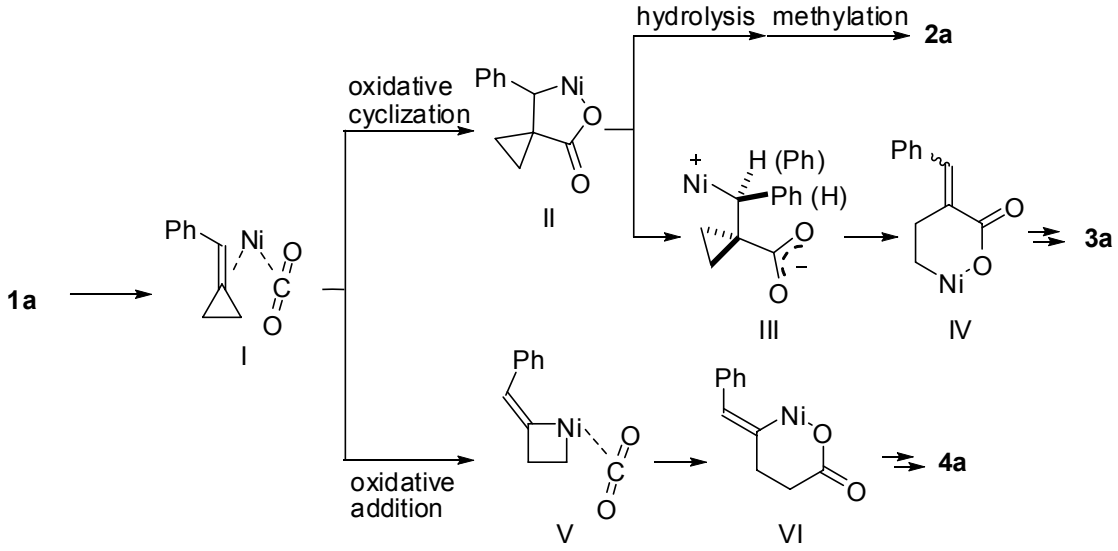
entry	solvent	amine	yield / %[b]	ratio[c] **2a**	**3a**	**4a**
1	toluene	DBU	73	93	7	0
2	THF	DBU	77	40	60	0
3	DMF	DBU	68	23	77	0
4	CH_3CN	DBU	66	4	96	0
5	NMP	DBU	78	6	94[d]	0
6	toluene	MTBD	27	0	0	>99
7	THF	MTBD	40	0	0	>99
8	NMP	MTBD	52	0	0	>99
9	NMP	MTBD	67[e]	0	1	99

[a] Conditions: **1a** (1.1 equiv), CO_2 (1 atm), $Ni(cod)_2$ (1.0 equiv), amine (2.2 equiv), solvent, 0 °C, 4 h; hydrolysis with diluted HCl; then methylation with $TMSCHN_2$, MeOH. [b] Combined yields. [c] Ratio determined by ^1H NMR. [d] *E*:*Z* = 94:6. [e] CO_2 (5 atm).

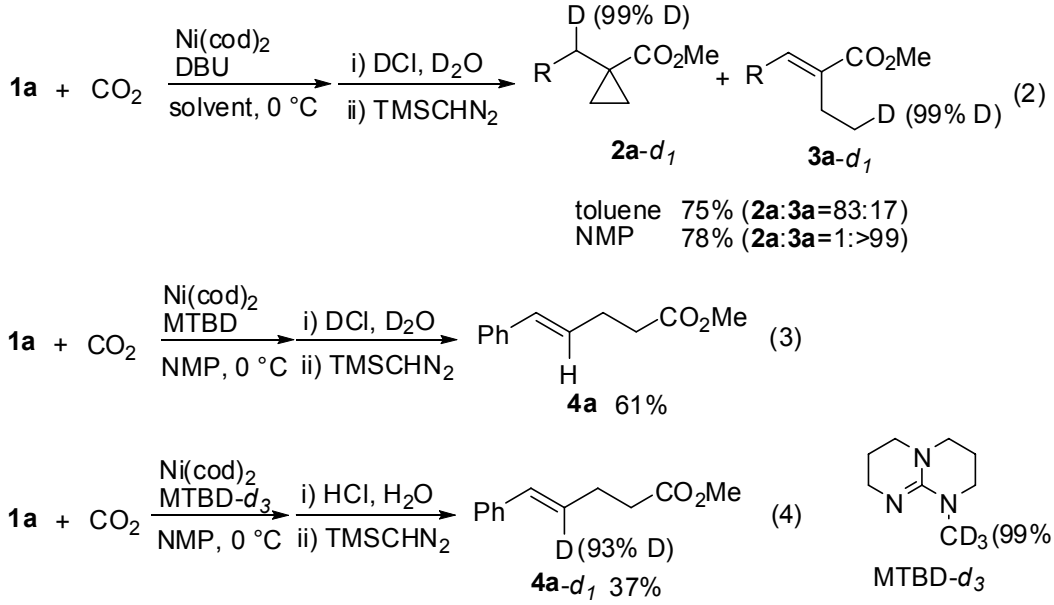
The partitioning of the various reaction pathways can be explained by assuming the mechanism shown in Scheme 1. Initially, nickel(0) forms the π-complex **I** with the carbon–carbon double bond of methylenecyclopropane and carbon–oxygen double bond of carbon dioxide. For the formation of the products **2a** and **3a**, oxidative cyclization occurs to give the nickelacycle **II**.[8] Direct hydrolysis of **II** followed by methylation with

Me_3SiCHN_2 affords **2a**. Alternatively, the intermediate **II** may undergo β-carbon elimination to give the six-membered nickelacycle **IV**, probably through the dissociated zwitterionic complex **III**, which would allow a *syn* (or *synclinal*) conformation of the nickel–carbon linkage with the cleaving carbon–carbon bond.[9] Hydrolysis and methylation then leads to the production of **3a**. We assume that β-carbon elimination occurs more easily with the ionic intermediate **III** than with the nickelacycle **II** and that a polar solvent such as NMP facilitates the formation of the ionic intermediate to favor the formation of **3a**.[10,11] On the other hand, when MTBD is used as the amine ligand, the proximal carbon–carbon bond *cis* to the phenyl group of **1a** undergoes oxidative addition to give the nickelacycle **V**.[12,13] Insertion of carbon dioxide into the nickel–sp^3 carbon linkage affords **VI**. The corresponding *E* product **4a** is selectively produced by subsequent protonolysis and methylation.[14]

Scheme 1. Proposed mechanism for the carboxylation reaction of **1a**



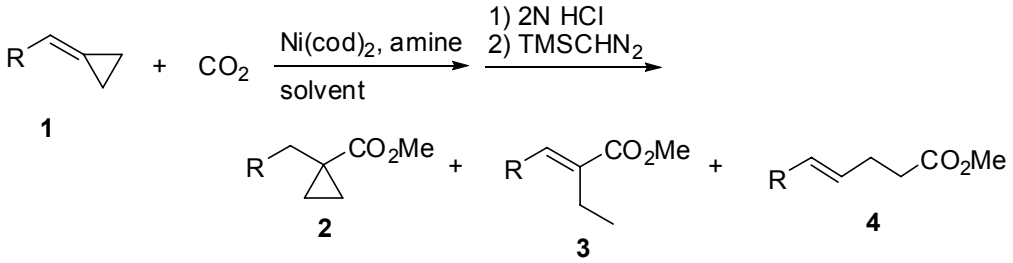
We quenched the reactions with DCl/D_2O (2 M) in order to support the intermediacy of **II**, **IV** and **VI**. With the products **2a** and **3a** obtained, deuterium atoms were incorporated at the expected positions (eq 2), whereas no deuterium incorporation was observed with **4a** (eq 3). On the contrary, when MTBD-d_3 having a CD_3 group on nitrogen, was used as the base, the vinylic position of product **4a** was deuterated (eq 4). These contrasting results shown in eqs 3 and 4 can be explained by assuming that the intermediate nickelacycle **VI** abstracts a proton from the methyl group of MTBD prior to an aqueous workup.



Under the optimized conditions, a structurally diverse set of methylenecyclopropanes **1** was examined (Table 2). The reactions of (arylmethylidene)cyclopropanes **1a**–**1f** in toluene produced the corresponding cyclopropane derivatives **2a**–**2f** with moderate to good selectivities, except in the case of **1d** (entries 1–5). The chlorophenyl moiety of **1f** remained intact in the presence of nickel(0). The alkylidenecyclopropane derivative **1g** gave the ring-opening product **3g** as the major product, even when toluene was used as solvent (entry 6).[15] All the reactions in NMP gave the branched α,β-unsaturated esters **3** selectively (entries 7–12). The use of MTBD as the amine ligand resulted in highly selective formation of the *E* linear γ,δ-unsaturated esters **4**, although the yields were moderate (entries 13–18).

In conclusion, we have described the nickel-mediated carboxylation of methylenecyclopropanes with carbon dioxide. Three types of carboxylated products, which are all different from that obtained by the palladium-catalyzed reaction,[4] are prepared exclusively or preferentially depending on the reaction solvent and the amine ligand employed.

Table 2. Nickel-mediated carboxylation of **1** with CO_2



entry	**1** (R)	conditions[a]	yield / %[b]	ratio[c] **2**	**3** (*E*/*Z*)[d]	**4**
1	**1b** (4-MeC_6H_4)	A	75	78	22	0
2	**1c** (2-MeC_6H_4)	A	77	92	8	0
3	**1d** (4-$MeOC_6H_4$)	A	78	51	49 (91/9)	0
4	**1e** (4-FC_6H_4)	A	79	89	11	0
5	**1f** (4-ClC_6H_4)	A	79	93	7	0
6	**1g** ($PhCH_2CH_2$)	A	70	20	80 (65/35)	0
7	**1b**	B	70	1	99 (93/7)	0
8	**1c**	B	72	3	97 (97/3)	0
9	**1d**	B	79	1	99 (91/9)	0
10	**1e**	B[e]	81	1	99 (93/7)	0
11	**1f**	B[e]	87	8	92 (93/7)	0
12	**1g**	B	68	0	>99 (56/44)	0
13	**1b**	C	58	0	3	97
14	**1c**	C	55	0	4	96
15	**1d**	C	40	0	1	99
16	**1e**	C	66	0	1	99
17	**1f**	C	64	0	0	>99
18	**1g**	C	37	0	6	94

[a] Common conditions: **1** (1.1 equiv), CO_2, $Ni(cod)_2$ (1.0 equiv), amine (2.2 equiv), 0 °C, 4 h; then workup. Conditions A: 1 atm of CO_2, DBU, in toluene; conditions B: 1 atm of CO_2, DBU, in NMP; conditions C: 5 atm of CO_2, MTBD, in NMP. [b] Combined yields. [c] Ratio determined by ^1H NMR. [d] Obtained as a mixture of *E* and *Z* isomers. The ratio given in parenthesis if determined. [e] 6 h.

Experimental Section

General. NMR spectra were recorded on a Varian Gemini 2000 (^{1}H at 300 MHz and ^{13}C at 75 MHz) spectrometers. $CDCl_3$ was used as a solvent. Me_4Si (^{1}H, $\delta = 0.00$), $CDCl_3$ (^{13}C, $\delta = 77.0$) were used as standards. High-resolution mass spectra were recorded on a JEOL JMS-SX102A spectrometer. All reactions were carried out under an argon atmosphere. Column chromatography was performed with silica gel 60 N (Kanto). Preparative thin-layer chromatography was performed with silica gel 60 PF_{254} (Merck).

Materials. Unless otherwise noted, all chemicals and anhydrous solvents were obtained from commercial suppliers and used as received. Toluene was dried over Na-benzophenone ketyl.

Carboxylation of methylencyclopropane 1a: Procedure A.

To a stirred suspension of $Ni(cod)_2$ (82.5 mg, 0.30 mmol) in toluene (3 ml) in a Schlenk-type flask under a nitrogen atmosphere at 0 °C was added DBU (0.66 mmol). The mixture was degassed by a freeze-pump-thaw method, and then carbon dioxide was introduced. Substrate **1a** (0.33 mmol) was added to the resulting pale yellow suspension at 0 °C. After the reaction mixture was stirred at 0 °C for 4 h, diluted HCl aq. (2 M) was added to the reaction mixture. The aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was treated with $TMSCHN_2$ in Et_2O/MeOH. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane:ethyl acetate) to give the product.

Carboxylation of methylencyclopropane 1a: Procedure B.

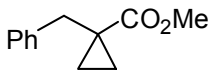
To a stirred suspension of $Ni(cod)_2$ (82.5 mg, 0.30 mmol) in NMP (3 mL) in a Schlenk-type flask under a nitrogen atmosphere at 0 °C was added DBU (0.66 mmol). The mixture was degassed by a freeze-pump-thaw method, and then carbon dioxide was introduced. Substrate **1a** (0.33 mmol) was added to the resulting pale yellow suspension at 0 °C. After the reaction mixture was stirred at 0 °C for 4 h, diluted HCl aq. (2 M) was added to the reaction mixture. The aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was treated with $TMSCHN_2$ in Et_2O/MeOH. The solvent was removed

under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane:ethyl acetate) to give the product.

Carboxylation of methylencyclopropane 1a: Procedure C.

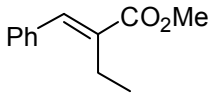
To a stirred suspension of $Ni(cod)_2$ (82.5 mg, 0.30 mmol) in NMP (3 mL) in a Schlenk-type flask under a nitrogen atmosphere at 0 °C was added DBU (0.66 mmol) and the substrate **1a** (0.33 mmol). The mixture was frozen and then pressurized with carbon dioxide (5 atm). After the reaction mixture was stirred at 0 °C for 4 h, the pressure of carbon dioxide was released and diluted HCl aq. (2 M) was added to the reaction mixture. The aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was treated with $TMSCHN_2$ in Et_2O/MeOH. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane:ethyl acetate) to give the product.

Methyl 1-phenylmethylcyclopropane-1-carboxylate (2a)



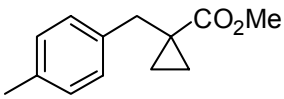
^{1}H NMR: δ = 0.80 (dd, *J* = 7.2, 4.2 Hz, 2H), 1.28 (dd, *J* = 7.2, 4.2 Hz, 2H), 2.99 (s, 2H), 3.62 (s, 3H), 7.16-7.30 (m, 5H); ^{13}C NMR: δ = 15.2, 23.8, 38.3, 51.8, 126.0, 128.0, 128.4, 129.1, 139.3, 175.3;

Methyl (*E*)-2-ethyl-3-phenylprop-1-enoate (3a)



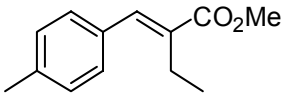
^{1}H NMR: δ = 1.16 (t, *J* = 7.5 Hz, 3H), 2.55 (q, *J* = 7.5 Hz, 2H), 3.82 (s, 3H), 7.20-7.40 (m, 5H), 7.65 (s, 1H); ^{13}C NMR: δ = 14.0, 20.9, 52.0, 128.2, 128.4, 129.1, 134.6, 135.7, 138.5, 168.7;

Methyl 1-(4-methylphenyl)methylcyclopropane-1-carboxylate (2b)



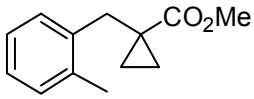
^{1}H NMR: δ = 0.79 (dd, *J* = 6.9, 3.9 Hz, 2H), 1.25 (dd, *J* = 6.9, 3.9 Hz, 2H), 2.31 (s, 3H), 2.95 (s, 2H), 3.62 (s, 3H), 7.06-7.14 (m, 4H); ^{13}C NMR: δ = 15.1, 21.1, 23.8, 37.8, 51.8, 128.7, 129.0 135.5, 136.2, 175.4;

Methyl (*E*)-2-ethyl-3-(4-methylphenyl)prop-1-enoate (3b)



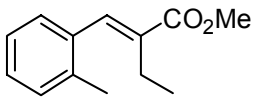
^{1}H NMR: δ = 1.17 (t, *J* =7.5 Hz, 3H), 2.37 (s, 3H), 2.56 (q, *J* = 7.5 Hz, 2H), 3.81 (s, 3H), 7.08-7.30 (m, 4H), 7.62 (s, 1H); ^{13}C NMR: δ = 13.9, 20.9, 21.4, 51.9, 129.1, 129.2, 132.7, 133.7, 138.4, 138.5, 168.8;

Methyl 1-(2-methylphenyl)methylcyclopropane-1-carboxylate (2c)



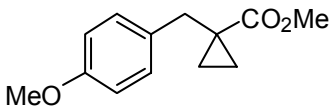
^{1}H NMR: δ = 0.66 (dd, *J* = 6.6, 4.2 Hz, 2H), 1.28 (dd, *J* = 6.6, 4.2 Hz, 2H). 2.26 (s, 3H), 3.05 (s, 2H), 3.64 (s, 3H), 7.09-7.22 (m, 4H); ^{13}C NMR: δ = 14.5, 19.7, 21.9, 34.2, 52.0, 125.6, 126.1, 128.5, 129.8, 136.6, 136.7, 175.7;

Methyl (*E*)-2-ethyl-3-(2-methylphenyl)prop-1-enoate (3c)



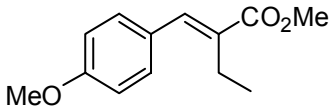
^{1}H NMR: δ = 1.07 (t, *J* = 7.5 Hz, 3H), 2.27 (s, 3H), 2.38 (q, *J* = 7.5 Hz, 2H), 3.83 (s, 3H), 7.17-7.25 (m, 4H), 7.69 (s, 1H); ^{13}C NMR: δ = 14.1, 20.0, 20.9, 51.9, 125.5, 128.0, 128.1, 129.9, 135.1, 135.2, 136.5, 138.1, 168.4;

Methyl 1-(4-methoxyphenyl)methylcyclopropane-1-carboxylate (2d)



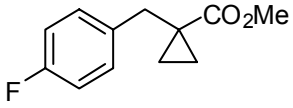
^{1}H NMR: δ = 0.78 (dd, *J* = 6.6, 3.9 Hz, 2H), 1.24 (dd, *J* = 6.6, 3.9 Hz, 2H), 2.92 (s, 2H), 3.62 (s, 3H), 3.77 (s, 3H), 6.78-6.84 (m, 2H), 7.12-7.17 (m, 2H); ^{13}C NMR: δ = 14.9, 24.0, 37.4, 51.8, 55.2, 113.4, 130.0, 131.3, 157.8, 175.4;

Methyl (*E*)-2-ethyl-3-(4-methoxyphenyl)prop-1-enoate (3d)



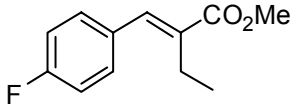
^{1}H NMR: δ = 1.18 (t, *J* =7.5 Hz, 3H), 2.57 (q, *J* = 7.5 Hz, 2H), 3.81 (s, 3H), 3.83 (s, 3H), 6.91-6.95 (m, 2H), 7.33-7.38 (m, 2H), 7.60 (s, 1H); ^{13}C NMR: δ = 13.8, 20.8, 51.9, 55.3, 113.9, 128.1, 130.9, 132.4, 138.1, 159.6, 168.9;

Methyl 1-(4-fluorophenyl)methylcyclopropane-1-carboxylate (2e)



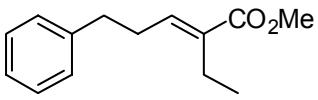
^{1}H NMR: δ = 0.80 (dd, *J* = 7.2, 4.2 Hz, 2H), 1.28 (dd, *J* = 7.2, 4.2 Hz, 2H), 2.94 (s, 2H), 3.62 (s, 2H), 6.91-6.99 (m, 2H), 7.17-7.23, (m, 2H); ^{13}C NMR: δ = 15.1, 37.7, 51.8, 52.0, 114.8 (d, *J* = 21 Hz), 130.3 (d, *J* = 8.0 Hz), 135.0 (d, *J* = 3.7 Hz), 161.3 (d, *J* = 242 Hz), 175.1;

Methyl (*E*)-2-ethyl-3-(4-fluorophenyl)prop-1-enoate (3e)



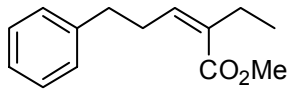
^{1}H NMR: δ = 1.17 (t, *J* = 7.5 Hz, 3H), 2.51 (q, *J* = 7.5 Hz, 2H), 3.82 (s, 3H), 7.04-7.12 (m, 2H), 7.32-7.38 (m, 2H), 7.60 (s, 1H); ^{13}C NMR: δ = 13.8, 20.8, 52.0, 115.2 (d, $^2J_{C–F}$ = 21 Hz), 130.9 (d, $^3J_{C–F}$ = 8.0 Hz), 131.7 (d, $^4J_{C–F}$ = 3.6 Hz), 134.4, 137.3, 162.4 (d, $^1J_{C–F}$ = 247 Hz), 168.5;

(*E*)-Methyl 2-ethyl-5-phenylpent-1-enoate (3g)



^{1}H NMR: δ = 0.94 (t, *J* = 7.5 Hz, 3H), 2.30 (q, *J* = 7.5 Hz, 2H), 2.50 (pseudo q, *J* = 7.5 Hz, 2H), 2.74 (t, *J* = 7.5 Hz, 2H), 3.73 (s, 3H), 6.77 (t, *J* = 7.5 Hz, 1H), 7.18-7.32 (m, 5H); ^{13}C NMR: δ = 13.9, 20.1, 30.4, 35.1, 51.6, 126.0, 128.2, 128.3, 134.4, 140.8, 141.1, 168.1;

(*Z*)-Methyl 2-ethyl-5-phenylpent-1-enoate (3g)



^{1}H NMR: δ = 1.01 (t, *J* = 7.2 Hz, 3H), 2.26 (q, *J* = 7.2 Hz, 2H), 2.72 (s, 2H), 2.74 (s, 2H), 3.73 (s, 3H), 5.90 (m, 1H), 7.16-7.31 (m, 5H); ^{13}C NMR: δ = 13.7, 27.5, 31.3, 35.7, 51.2, 125.8, 128.2, 128.4, 133.9, 139.4, 141.4, 168.4;

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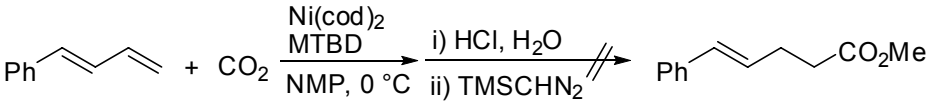
1. Reviews: (a) Yin, X.; Moss, J. R. *Coord. Chem. Rev.* **1999**, *181*, 27. (b) Walther, D.; Ruben, M.; Rau, S. *Coord. Chem. Rev.* **1999**, *182*, 67. (c) Arakawa, H.; Aresta, M; Armor, J. N.; Barteau, M. A.; Beckman, E. J.; Bell, A. T.; Bercaw, J. E.; Creutz, C.; Dinjus, E.; Dixon, D. A.; Domen, K.; Dubois, D. L.; Eckert, J.; Fujita, E.; Gibson, D. H.; Goddard, W. A.; Goodman, D. W.; Keller, J.; Kubas, G. J.; Kung, H. H.; Lyons, J. E.; Manzer, L. E.; Marks, T. J.; Morokuma, K.; Nicholas, K. M.; Periana, R.; Que, L.; Rostrup-Nielson, J.; Sachtler, W. M. H.; Schmidt, L. D.; Sen, A.; Somorjai, G. A.; Stair, P. C.; Stults, B. R.; Tumas, W. *Chem. Rev.* **2001**, *101*, 953.
2. Reviews: (a) Binger, P.; Büch, H. M.; *Top. Curr. Chem.* **1987**, *135*, 77. (b) Ohta, T.; Takaya, H. in *Comprehensive Organic Synthesis*, eds. Trost, B. M.; Fleming, I. Pergamon Press, Oxford, 1991, Vol. 5, pp. 1185–1205. (c) Nakamura, I.; Yamamoto, Y. *Adv. Synth. Catal.* **2002**, *344*, 111.
3. For an example of regiochemical control of the site of cleavage by reaction conditions, see: Suginome, M.; Matsuda, T.; Ito, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11015.
4. (a) Inoue, Y.; Hibi, T.; Satake, M.; Hashimoto, H. *J. Chem. Soc. Chem. Comm.* **1979**, 982. (b) Binger, P.; Weintz, H.-J. *Chem. Ber.* **1984**, *117*, 654.
5. (a) Hoberg, H.; Peres, Y.; Milchereit, A. *J. Organomet. Chem.* **1986**, *307*, C38. (b) Saito, S.; Nakagawa, S.; Koizumi, T.; Hirayama, K.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 3975. (c) Louie, J.; Gibby, J. E.; Farnworth, M. V.; Tekavec, T. N. *J. Am. Chem. Soc.* **2002**, *124*, 15188. (d) Aoki, M.; Kaneko, M.; Izumi, S.; Ukai, K.; Iwasawa, N. *Chem. Comm.* **2004**, 2568. (e) Takimoto, M.; Mizuno, T.; Sato, Y.; Mori, M. *Tetrahedron Lett.* **2005**, *46*, 5173, and references therein.
6. A mixture of stereoisomers.
7. Production of **4a** was not observed with other amines like DBN, TMEDA, 2,2'-bipyridyl, 1,2-dimethylimidazole and 2-methyl-2-oxazoline.
8. For an example of the nickel-mediated oxidative cyclization on ethylene, see: Hoberg, H.; Peres, Y.; Krüger, C.; Tsay, Y.-H. *Angew. Chem. Int. Ed.* **1987**, *26*, 771.
9. For examples of β-carbon elimination with cyclopropylmethyl–nickel species, see: (a) Binger, P. *Angew. Chem. Int. Ed.* **1972**, *11*, 309. (b) Saito, S.; Masuda, M.; Komagawa, S. *J. Am. Chem. Soc.* **2004**, *126*, 10540.

10. The branched ester **3a** was obtained as the major product (72%, **2a**:**3a**:**4a** = 20:80:0) when the reaction was carried out initially in toluene for 4 h and then CH_3CN was added to the reaction mixture which was further stirred for additional 4 h prior to an aqueous workup.
11. Direct rearrangement of **II** to **IV** cannot be ruled out. See: Binger, P.; Doyle M. J.; Benn, R. *Chem. Ber.* **1983**, *116*, 1.
12. Nickel catalysts generally prefer cleavage of the proximal carbon–carbon bond by insertion whereas palladium catalysts prefer that of the distal one: (a) Noyori, R.; Kumagai, Y.; Umeda, I.; Takaya, H.; *J. Am. Chem. Soc.* **1972**, *94*, 4018. (b) Bapuji, S. A.; Motherwell, W. B.; Shipman, M. *Tetrahedron Lett.* **1989**, *30*, 7107.
13. Regioselective insertion of Zr(II) into the proximal carbon–carbon bond *cis* to the phenyl group of **1a** has been observed: Binger, P.; Müller, P.; Podubrin, S.; Albus, S.; Krüger, C. *J. Organomet. Chem.* **2002**, *656*, 288.
14. Product **4a** can result from carboxylation of 1-phenylbuta-1,3-diene, to which **1a** may possibly isomerise in the presence of nickel(0). The present reaction conditions, however, caused no carboxylation reaction of 1-phenylbuta-1,3-diene prepared independently.



15. The contrasting results obtained with **1g** and (arylmethylidene)cyclopropanes **1a**–**1f** are accounted for by assuming the more stable nature of the nickel–benzylic carbon linkage of **II**.

Chapter 6

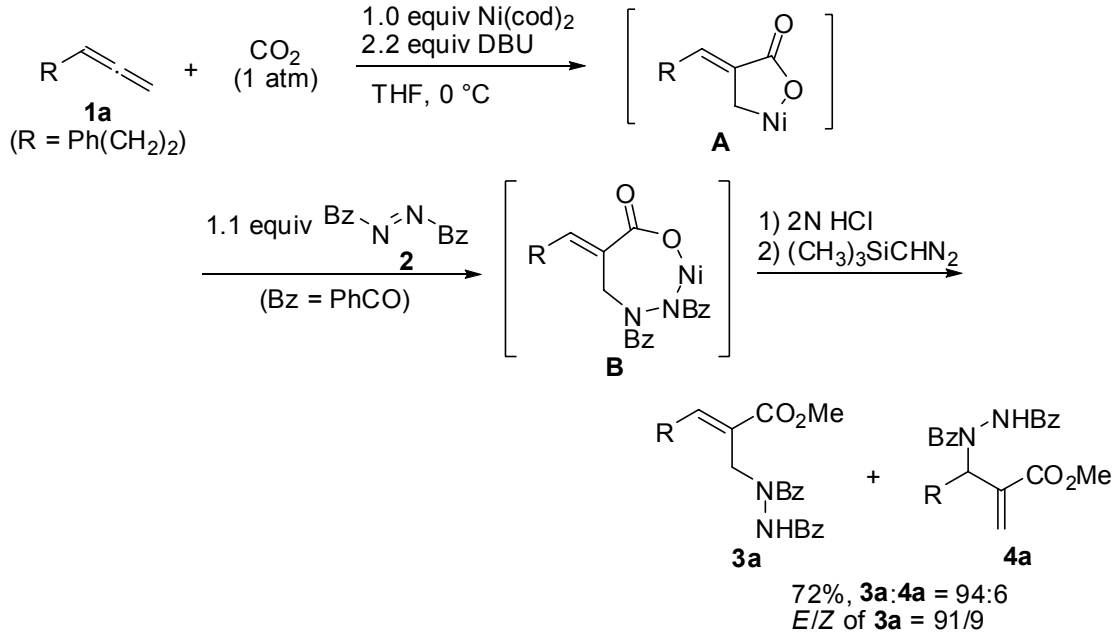
Synthesis of β-Amino Acid Derivatives by Nickel(0)-Mediated Sequential Addition of Carbon Dioxide and Dibenzoyldiazene onto Unsaturated Hydrocarbons

Abstract: A stoichiometric amount of nickel(0) complex mediated the aminative carboxylation of unsaturated hydrocarbons through oxidative cyclization with carbon dioxide followed by insertion of dibenzoyldiazene into the carbon–nickel bond, giving β-amino acid derivatives.

The development of reactions which incorporate carbon dioxide into organic molecules has been an important challenge in chemistry.[1] In recent years, oxidative cyclization on nickel(0) has emerged as an efficient elementary step to activate carbon dioxide[2] which is thermodynamically very stable. Oxanickelacycle intermediates formed by oxidative cyclization of carbon dioxide and unsaturated hydrocarbons can undergo further transformations including oxidation,[2b,g] carbon–carbon bond formation,[2d,f] rearrangement,[3] etc. The nickel(0)-mediated carboxylation reactions possess good functional group compatibility, and thus, provide unique preparative methods of carboxylic acid derivatives. On the other hand, β-amino acid is an intriguing structural motif because it is a valuable constituent of designed peptides and biologically active compounds.[4] It would become a novel synthetic method of amino acids if the carbon–nickel bond of an oxanickelacycle intermediate is transformed into a carbon–nitrogen bond. In this chapter, the author reports the synthesis of β-amino acids via nickel(0)-mediated oxidative cyclization and subsequent amination of the carbon–nickel bond.

Terminal allene **1a** was reacted with bis(1,5-cyclooctadiene)nickel ($Ni(cod)_2$, 1.0 equiv) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 2.2 equiv) at 0 °C in THF under atmospheric pressure of carbon dioxide for 2 h according to the literature procedure.[2f] The resulting reaction mixture containing an oxanickelacycle intermediate was then treated with various nitrogen nucleophiles such as potassium phthalimide and trimethylsilyl azide with the expectation that transmetalation with the nickel carboxylate moiety followed by reductive elimination would form a carbon–nitrogen bond. However, the reactions with nitrogen nucleophiles have all failed so far, which encouraged us to examine electrophilic aminating reagents. To our delight, dibenzoyldiazene (**2**, 1.1 equiv) was successfully incorporated into the oxanickelacycle intermediate.[5,6] Acidic hydrolysis of the nickel carboxylate moiety followed by esterification with $(CH_3)_3SiCHN_2$ afforded β-amino carboxylate **3a** together with a small amount of the regioisomeric aminated product **4a** (72% total yield, **3a**:**4a** = 94:6). The product **3a** in which the terminal allene carbon was aminated predominated over the regioisomeric aminated product **4a**. This regiochemical outcome is in marked contrast to that of the reaction of oxanickelacycles with aldehydes.[2f] The plausible mechanism is shown in Scheme 1. Initially, oxanickelacycle **A** having an allylnickel moiety[7] is formed by oxidative cyclization of carbon dioxide and the allene on nickel(0). Diazene **2** was subsequently inserted into the carbon–nickel bond of **A**, forming the seven-membered nickelacycle **B**. The intermediate **B** is protonated and the resulting acid is esterified with $TMSCHN_2$.

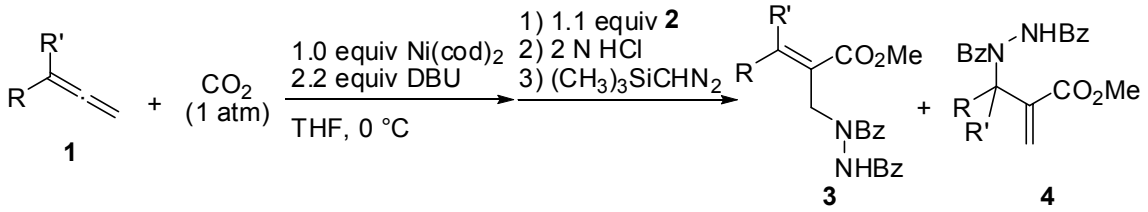
Scheme 1. Sequential addition of carbon dioxide and dibenzoyldiazene (**2**) onto (2-phenylethyl)allene (**1a**)



The results of the nickel(0)-mediated aminative carboxylation of allenes are shown in Table 1. Ether and ester functionalities were tolerated under the reaction conditions (entries 1 and 2). A phtalimide remained intact (entry 3). 1-Methyl-1-phenylallene (**1e**) selectively gave **3e** in 82% yield (entry 4). The lower yield observed with phenylallene (**1f)** can be ascribed to its competitive oligomerization (entry 5).

Next, we examined the use of other unsaturated hydrocarbons (Scheme 2). Terminal alkynes **5a** and **5b**, afforded the corresponding alkenylhydrazine **6a** and **6b** in 47 and 41% yield, respectively. These results indicate that an oxanickellacycle containing a sp^2 carbon–nickel bond can also react with **2**. Methylenecyclopropane **7** yielded the aminative carboxylation product **8** without concomitant cleavage of the cyclopropane ring.[3,8] In contrast to allenes (1,2-dienes), 1,3-dienes such as 1,3-cyclohexadiene and 1-phenyl-1,3-butadiene underwent only carboxylation[2d] but no insertion of **2** occurred, suggesting that the resulting allylic oxanickelacycle intermediate is less reactive than that derived from an allene.

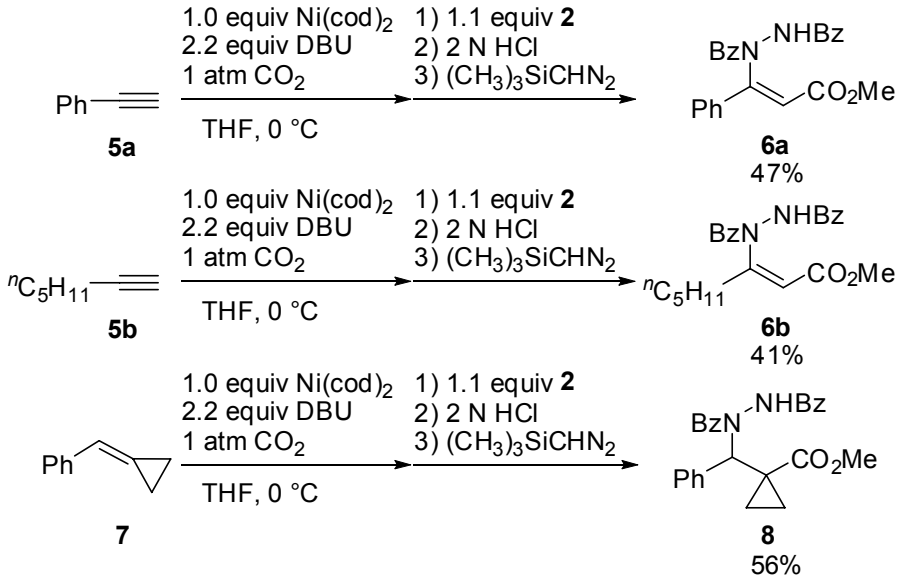
Table 1. Sequential addition of carbon dioxide and **2** onto allenes[a]



entry	substrate (R, R′)	yield (%)[b]	ratio[c] **3**	**4**	*E*/*Z* of **3**[d]
1	**1b** ($BnO(CH_2)_2$, H)	68	92	8	87/13
2	**1c** ($BzO(CH_2)_2$, H)	64	94	6	94/6
3	**1d** ($PhthN(CH_2)_2$, H)	74	94	6	94/6
4	**1e** (Ph, Me)	82	>99	1	>99/1
5	**1f** (Ph, H)	47	94	6	>99/1

[a] For the experimental procedure, see experimental section. [b] Combined yield. [c] Ratio was determined by ^{1}H NMR. [d] The geometry of the olefin was determined by ^{1}H NMR. Phth: phthaloyl.

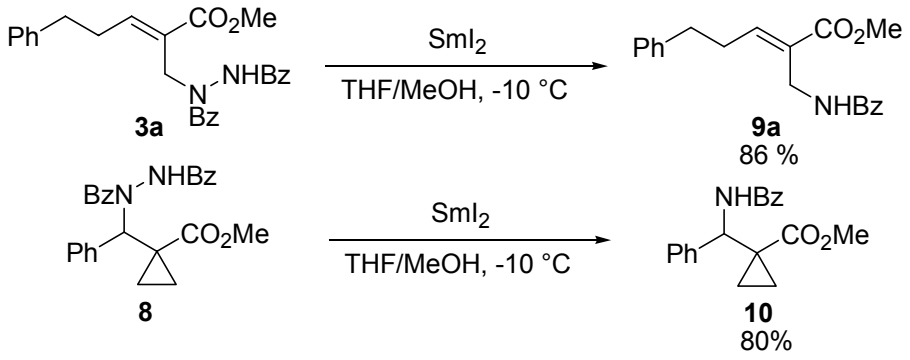
Scheme 2. Reactions with other unsaturated hydrocarbons



Finally, reductive cleavage of the nitrogen–nitrogen bond was performed using SmI_2 (Scheme 3).[9] Treatment of the dibenzoylhydrazine **3a** with SmI_2 in THF/MeOH at

–10 °C gave the benzamide **9a** in 86% yield.[10] The α,β-unsaturated ester group remained at this temperature. The reaction of **8** with SmI_2 was also successful under the same reaction conditions, giving the product **10** in 80% yield.

Scheme 3. Reductive cleavage of the hydrazine moiety



In summary, the author have described the synthesis of β-amino acid derivatives through a nickel(0)-mediated oxidative cyclization reaction of carbon dioxide with unsaturated hydrocarbons followed by an amination reaction with dibenzoyldiazene. Simple unsaturated hydrocarbons such as allenes, alkynes, and methylenecyclopropanes could be employed, giving β-hydrazinocarboxylic acids in one-pot. The present study provides a new example of utilization of carbon dioxide as C1 source.

Experimental Section

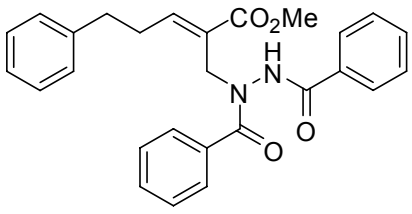
General. NMR spectra were recorded on a Varian Gemini 2000 (^{1}H at 300 MHz and ^{13}C at 75 MHz) spectrometers. $CDCl_3$ was used as a solvent. Me_4Si (^{1}H, $\delta = 0.00$), $CDCl_3$ (^{13}C, $\delta = 77.0$) were used as standards. High-resolution mass spectra were recorded on a JEOL JMS-SX102A spectrometer. All reactions were carried out under an argon atmosphere. Column chromatography was performed with silica gel 60 N (Kanto). Preparative thin-layer chromatography was performed with silica gel 60 PF_{254} (Merck).

Materials. Unless otherwise noted, all chemicals and anhydrous solvents were obtained from commercial suppliers and used as received. Dibenzoyldiazene was prepared according to the reported procedure.[1]

Sequential addition of carbon dioxide and dibenzoyldiazene onto allene 1a: a typical procedure

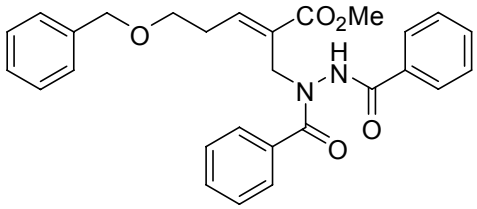
To a stirred suspension of $Ni(cod)_2$ (82.5 mg, 0.30 mmol) in a freshly distilled THF (2.5 mL) in a Schlenk-type flask under a nitrogen atmosphere at 0 °C was added DBU (100 μL, 0.66 mmol). The mixture was degassed by a freeze-pump-thaw method, and then carbon dioxide was introduced. To the resulting pale yellow solution at 0 °C was added a THF solution (0.5 mL) of substrate **1a** (47.6 mg, 0.33 mmol) dropwise (20 μL/min). After the reaction mixture was stirred at 0 °C for 2 h, a THF solution (1 mL) of dibenzoyldiazene (**2**, 79.2 mg, 0.33 mmol) was added. After 2 h, dilute hydrochloric acid (2 N) was added to the reaction mixture. The aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated. The residue was treated with $(CH_3)_3SiCHN_2$ in Et_2O/MeOH. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (dichloromethane:ethyl acetate = 10:1) to give the product (*E*)-**3a**:

(*E*)-Methyl 2-(*N*,*N*'-dibenzoylhydrazinomethyl)-5-phenylpent-2-enoate (3a)



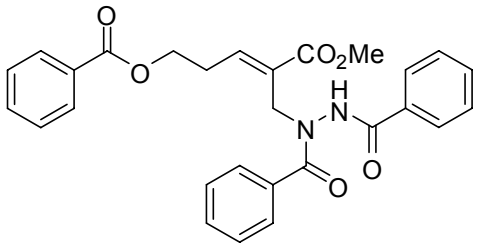
^{1}H NMR: δ = 2.74 (br, 4H), 3.70 (s, 3H), 3.8-5.6 (br, 2H), 7.04 (t, *J* = 6.9 Hz, 1H), 7.1-7.6 (m, 15H), 8.83 (s, 1H); ^{13}C NMR: δ = 30.4, 34.6, 45.8, 52.0, 125.95, 126.01, 126.6, 127.0, 127.8, 128.23, 128.28, 128.31, 128.5, 130.0, 131.8, 132.1, 134.7, 140.5, 148.3, 166.4, 171.9; HRMS (EI): Calcd for $C_{27}H_{26}N_2O_4$ (M^+) 442.1893. Found 442.1895.

(*E*)-Methyl 2-(*N*,*N*'-dibenzoylhydrazinomethyl)-5-benzyloxypent-2-enoate (3b)



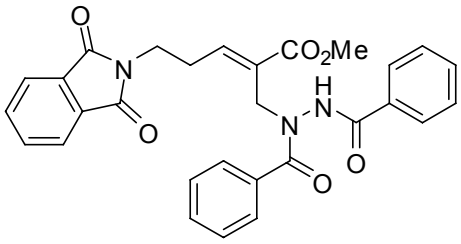
^{1}H NMR: δ = 2.6-3.0 (br, 2H), 3.6 (br, 2H), 3.71 (s, 3H), 3.8-5.5 (br, 2H), 4.45 (s, 2H), 2.74 (br, 4H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.20-7.55 (m, 15H), 8.84 (s, 1H); ^{13}C NMR: δ = 29.4, 45.3, 52.1, 68.6, 73.1, 126.9, 127.0, 127.1, 127.56, 127.61, 127.8, 128.3, 128.5, 129.5, 130.0, 131.9, 132.0, 134.7, 137.6, 146.2, 166.4, 172.0; HRMS (EI): Calcd for $C_{28}H_{28}N_2O_5$ (M^+) 472.1998. Found 472.1987.

(*E*)-Methyl 5-benzoyl-2-(*N*,*N*'-dibenzoylhydrazinomethyl)pent-2-enoate (3c)



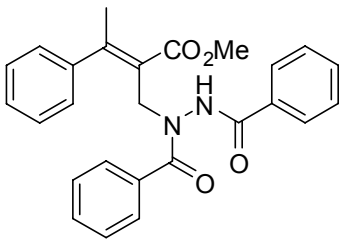
^{1}H NMR: δ = 2.98 (br, 2H), 3.72 (s, 3H), 3.8-5.6 (br, 2H), 4.4 (br, 2H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.27-7.57 (m, 13H), 8.00 (d, *J* = 7.5 Hz, 2H), 9.09 (s, 1H); ^{13}C NMR: δ = 28.3, 46.0, 52.2, 63.1, 127.0, 127.1, 127.8, 128.2, 128.5, 129.4, 129.7, 130.0, 131.7, 132.1, 132.9, 134.5, 144.1, 166.3, 166.4, 172.0; HRMS (EI): Calcd for $C_{28}H_{26}N_2O_6$ (M^+) 486.1791. Found 486.1789.

(*E*)-Methyl 2-(*N*,*N*'-dibenzoylhydrazinomethyl)-5-phtalimidopent-2-enoate (3d)



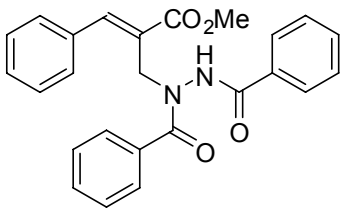
^{1}H NMR: δ = 2.88 (br, 2H), 3.70 (s, 3H), 3.8-5.6 (br, 2H), 3.87 (br, 2H), 7.04 (t, *J* = 7.7 Hz, 1H), 7.2-7.8 (m, 14H), 9.07 (s, 1H); ^{13}C NMR: δ = 28.5, 36.7, 45.7, 52.2, 123.2, 127.0, 127.1, 127.7, 128.5, 130.0, 131.77, 131.79, 132.1, 133.9, 134.4, 144.3, 166.3, 168.1, 171.8; HRMS (EI): Calcd for $C_{29}H_{25}N_3O_6$ (M^+) 511.1743. Found 511.1739.

(*E*)-Methyl 2-(*N*,*N'*-dibenzoylhydrazinomethyl)-3-phenylbut-2-enoate (3e)



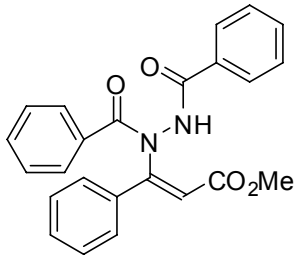
^{1}H NMR: δ = 2.18 (s, 4H), 3.8-5.4 (br, 2H), 3.83 (s, 3H), 6.99 (d, *J* = 2.7 Hz, 2H), 7.25-7.52 (m, 13H), 8.37 (s, 1H); ^{13}C NMR: δ = 23.8, 47.3, 52.1, 124.6, 126.7, 126.9, 127.6, 127.7, 127.8, 128.4, 128.5, 128.6, 130.0, 131.8, 132.1, 134.5, 140.5, 165.7, 169.9, 172.4; HRMS (EI): Calcd for $C_{26}H_{24}N_2O_4$ (M^+) 428.1736. Found 428.1735.

(*E*)-Methyl 2-(*N*,*N'*-dibenzoylhydrazinomethyl)-3-phenylprop-2-enoate (3f)



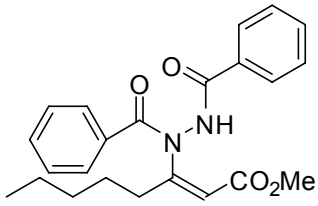
^{1}H NMR: δ = 3.79 (s, 3H), 4.0-5.8 (br, 2H), 7.28-7.53 (m, 15H), 7.91 (s, 1H), 8.80 (s, 1H); ^{13}C NMR: δ = 46.8, 52.4, 126.5, 127.0, 127.1, 127.8, 128.49, 128.53, 129.1, 129.4, 130.0, 131.8, 132.1, 134.0, 134.6, 144.6, 166.4, 168.5, 172.3; HRMS (EI): Calcd for $C_{25}H_{22}N_2O_4$ (M^+) 414.1580. Found 4414.1581.

(*Z*)-Methyl 2-(*N*,*N'*-dibenzoylhydrazino)-2-phenylprop-2-enoate (6a)



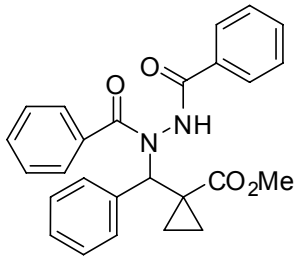
^{1}H NMR: δ = 3.79 (s, 3H), 6.04 (s, 1H), 7.19-7.65 (m, 11H), 7.75 (d, *J* = 6.9 Hz, 2H), 8.09 (br, 2H), 10.1 (br, 1H); ^{13}C NMR: δ = 52.2, 109.8, 127.3, 127.5, 127.7, 127.9, 128.5, 128.6, 130.8, 131.0, 131.8, 132.3, 134.0, 136.4, 157.5, 165.9, 166.3; HRMS (EI): Calcd for $C_{24}H_{20}N_2O_4$ (M^+) 400.1423. Found 400.1423.

(*Z*)-Methyl 2-(*N*,*N'*-dibenzoylhydrazino)hept-2-enoate (6b)



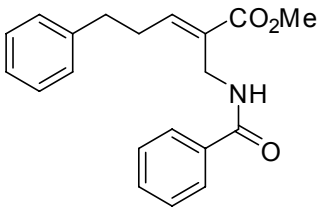
^{1}H NMR: δ = 0.87-0.92 (m, 3H), 1.33-1.35 (m, 4H), 1.63-1.68 (m, 2H), 2.79 (t, *J* = 7.7 Hz, 2H), 3.72 (s, 3H), 5.80 (s, 1H), 7.32-7.50 (m, 6H), 7.60-7.66 (m, 4H), 9.74 (s, 1H); ^{13}C NMR: δ = 14.0, 22.5, 26.8, 31.2, 36.0, 51.9, 112.7, 127.1, 127.2, 128.0, 128.6, 130.7, 131.7, 132.3, 134.1, 161.5, 166.0, 171.0; HRMS (EI): Calcd for $C_{23}H_{26}N_2O_4$ (M^+) 394.1893. Found 394.1892.

Methyl 1-{*N*,*N'*-dibenzoylhydrazino(phenyl)methyl}cyclopropanecarboxylate (8)



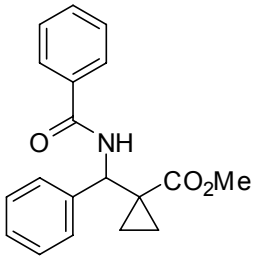
^{1}H NMR: δ = 0.89 (br, 1H), 1.50 (br, 1H), 1.56-1.63 (m, 1H), 1.72 (br, 1H), 3.77 (s, 3H), 5.69 (s, 1H), 7.07-7.64 (m, 15H), 9.59 (s, 1H); ^{13}C NMR: δ = 14.6, 19.6, 26.7, 52.4, 64.1, 126.2, 127.2, 127.4, 127.8, 128.1, 129.5, 129.7, 131.2, 132.5, 134.8, 135.5, 164.9, 171.8, 176.5; HRMS (EI): Calcd for $C_{26}H_{24}N_2O_4$ (M^+) 428.1736. Found 428.1735.

(*E*)-Methyl 2-(benzamidomethyl)-5-phenylpent-2-enoate (9)



^{1}H NMR: δ = 2.80-2.82 (m, 4H), 3.76 (s, 3H), 4.21 (d, *J* = 6.0 Hz, 2H), 6.67 (br t, 1H), 6.92-6.98 (m, 1H), 7.13-7.30 (m, 5H), 7.38-7.52 (m, 3H), 7.69-7.74 (m, 2H); ^{13}C NMR: δ = 30.5, 34.8, 35.8, 52.0, 126.0, 126.8, 128.2, 128.3, 128.37, 128.42, 128.7, 131.3, 134.3, 140.6, 145.4, 166.7, 167.7; HRMS (EI): Calcd for $C_{20}H_{21}NO_3$ (M^+) 323.1521. Found 323.1520.

Methyl 1-{benzamido(phenyl)methyl}cyclopropanecarboxylate (10)



^{1}H NMR: δ = 1.13-1.35 (m, 3H), 1.69-1.76 (m, 1H), 3.64 (s, 3H), 4.93 (d, *J* = 9.3 Hz, 1H), 7.22-7.35 (m, 3H), 7.42-7.56 (m, 5H), 7.86-7.90 (m, 2H), 7.94 (d, *J* = 9.6 Hz, 1H); ^{13}C NMR: δ = 15.3, 16.2, 27.8, 52.0, 56.6, 126.5, 127.0, 127.1, 128.3, 128.5, 131.5, 134.2, 140.2, 166.4, 174.5; HRMS (EI): Calcd for $C_{19}H_{19}NO_3$ (M^+) 309.1365. Found 309.1363.

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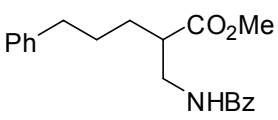
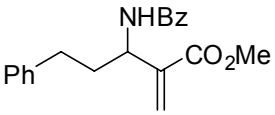
1. Reviews: (a) Yin, X.; Moss, J. R.; *Coord. Chem. Rev.* **1999**, *181*, 27. (b) Walther, D.; Ruben, M.; Rau, S. *Coord. Chem. Rev.* **1999**, *182*, 67. (c) Arakawa, H.; Aresta, M.; Armor, J. N.; Barteau, M. A.; Beckman, E. J.; Bell, A. T.; Bercaw, J. E.; Creutz, C.; Dinjus, E.; Dixon, D. A.; Domen, K.; Dubois, D. L.; Eckert, J.; Fujita, E.; Gibson, D. H.; Goddard, W. A.; Goodman, D. W.; Keller, J.; Kubas, G. J.; Kung, H. H.; Lyons, J. E.; Manzer, L. E.; Marks, T. J.; Morokuma, K.; Nicholas, K. M.; Periana, R.; Que, L.; Rostrup-Nielson, J.; Sachtler, W. M. H.; Schmidt, L. D.; Sen, A.; Somorjai, G. A.; Stair, P. C.; Stults, B. R.; Tumas, W. *Chem. Rev.* **2001**, *101*, 953.
2. (a) Hoberg, H.; Peres, Y.; Milchereit, A. *J. Organomet. Chem.* **1986**, *307*, C38. (b) Hoberg, H.; Ballesteros, A. *J. Organomet. Chem.* **1991**, *411*, C11. (c) Saito, S.; Nakagawa, S.; Koizumi, T.; Hirayama, K.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 3975. (d) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2001**, *123*, 2895. (e) Louie, J.; Gibby, J. E.; Farnworth, M. V.; Tekavec, T. N. *J. Am. Chem. Soc.* **2002**, *124*, 15188. (f) Takimoto, M.; Kawamura, M.; Mori, M. *Org. Lett.* **2003**, *5*, 2599. (g) Aoki, M.; Izumi, A.; Kaneko, M.; Ukai, K.; Takaya, J.; Iwasawa, N. *Org. Lett.* **2007**, *9*, 1251, and references cited therein.
3. See Chapter 2.
4. (a) Cheng, R. P.; Gellman, S. H.; DeGrado, W. F. *Chem. Rev.* **2001**, *101*, 3219. (b) Gnad, F.; Reiser, O. *Chem. Rev.* **2003**, *103*, 1603.
5. For electrophilic amination using azodicarboxylates, see: R. Asukai, D. F. Taber, in *Comprehensive Organic Synthesis*, ed. by Trost, B. M. Pergamon Press, Oxford, **1991**, Vol. 6, 118.
6. Diethyl diazodicarboxylate (DEAD) can be also used for amination. However, **2** was preferred over DEAD for the ease of isolation of the products.
7. Both σ- and π-allyl structures are conceivable.
8. Methylenecyclopropane **7** was consumed and, besides **8**, a complex mixture of various products was obtained. However, it was hardly possible to identify other aminated products such as a cyclopropane opened one.
9. Ding, H.; Friestad, G. K. *Org. Lett.* **2004**, *6*, 637.
10. Because **3a** was contaminated with (*Z*)-isomer and the regioisomer **4a**, the product was obtained with the saturated ester **11a**, which probably resulted from (*Z*)-**3a**, and the regioisomeric ester **12a**.



11a



12a

List of Publications

Chapter 1 Stereoselective Synthesis of Trisubstituted Alkenylboranes by Palladium-Catalyzed Reaction of Alkynyltriarylborates with Aryl Halides
Naoki Ishida, Tomoya Miura, and Masahiro Murakami
Chem. Comm. **2007**, 4381-4383.

Chapter 2 Palladium-Catalyzed Allylation of Alkynyltriarylborates
Naoki Ishida, Tatsuo Shinmoto, Tomoya Miura, and Masahiro Murakami.
In preparation.

Chapter 3 Synthesis of Amine–Borane Intramolecular Complexes through Palladium-Catalyzed Rearrangement of Ammonioalkynyltriarylborates
Naoki Ishida, Mizuna Narumi, and Masahiro Murakami
Org. Lett. **2008**, *10,* 1279-1281.

Chapter 4 Asymmetric Carroll Rearrangement of Allyl α-Acetamido -β-ketocarboxylates Catalyzed by a Chiral Palladium Complex
Ryoichi Kuwano, Naoki Ishida, and Masahiro Murakami
Chem. Comm. **2005**, 3951-3952.

Chapter 5 Solvent and Ligand Partition Reaction Pathways in Nickel-Mediated Carboxylation of Methylenecyclopropanes
Masahiro Murakami, Naoki Ishida, and Tomoya Miura
Chem. Comm. **2006**, 643-645.

Chapter 6 Synthesis of β-Amino Acid Derivatives by Nickel(0)-Mediated Sequential Addition of Carbon Dioxide and Dibenzoyldiazene onto Unsaturated Hydrocarbons
Masahiro Murakami, Naoki Ishida, and Tomoya Miura
Chem. Lett. **2007**, 476-477.