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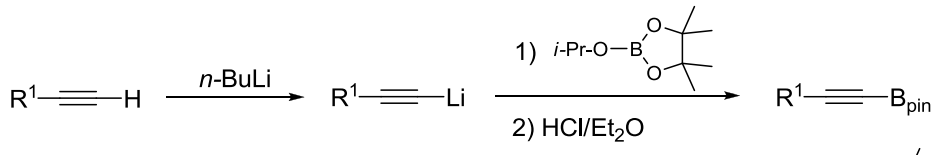
Abstract

Highly regio- and stereoselctive synthesis of multisubstituted olefins presents a particular challenge in organic synthesis. Chemists are still dedicating big efforts to exploit facile, practical, and efficient pathways to synthesize multisubstituted olefins with various functional groups owing to their wide range of application in natural products and pharmaceuticals as well as organic functional materials.

In this PhD Thesis, the Author focuses on the synthesis of multisubstituted olefins from the readily available starting substrates. A series of alkynylmetal species such as alkynylboronates and alkynylsilanes were prepared for transition-metal-catalyzed addition with Si–B and B–B bond-containing inter-element compounds. Highly selective *syn*-dimetalation reactions could offer versatile and suitable multimetalated olefin templates. The subsequent Suzuki-Miyaura cross-couplings were well screened to discriminate the different boron groups and to introduce substituents chemoselectively. The successful transformation of the silicon functionalities to halogen realized a further functionalization to afford multiarylated olefins. This PhD Thesis supplies a good combination of well-documented fundamental reactions, which reads to the synthesis of multisubstituted olefins.

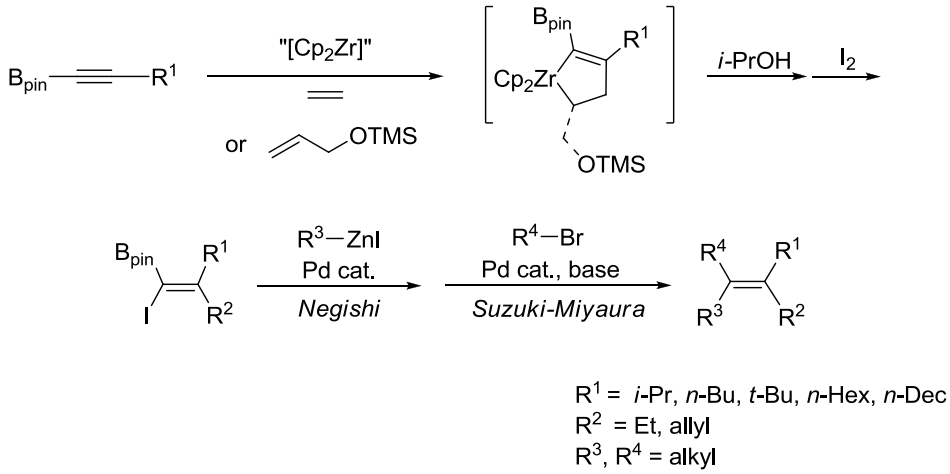
Chapter 2. Synthesis of Alkynylboron Compounds Directed toward Multialkylated Olefins

Alkynylboron compounds are versatile synthetic building blocks for diverse structures in organic synthesis. Owing to their stability, moderate reactivity, and ease of handling, alkynylboronic acid pinacol esters have been most widely used among all the alkynylboron compounds. In this Chapter, the Author successfully synthesized a series of alkynylboronates bearing alkyl and aryl groups, which could be utilized for the synthesis of multialkylated olefins. The simple and general synthetic methods starting from terminal alkynes afforded alkynylboronates in moderate to good yields.



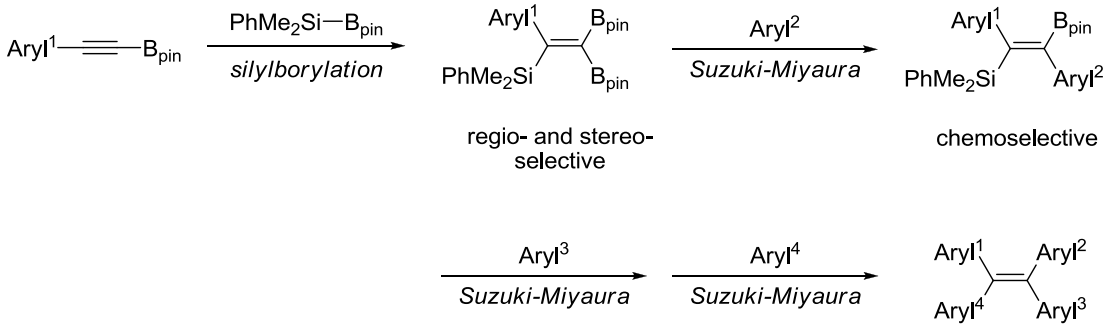
R^1alkyl = *n*-Dec, *n*-Hex, *n*-Bu, *t*-Bu, *i*-Pr;
R^1aryl = Ph, 4-$MeOC_6H_4$, 4-$CF_3C_6H_4$, 4-NCC_6H_4.

The synthesized alkynylboron compounds are subjected to the synthesis of multialkylated olefins, indicating that alkynylboron compounds are versatile and synthetically valuable substrates in organic synthesis.



Chapter 3. Synthesis of Multisubstituted Olefins through Regio- and Stereoselective Silylborylation of an Alkynylboronate/Chemoselective Cross-Coupling Sequences

In this Chapter, the synthesis of multisubstituted olefins, in particular, unsymmetrical tetraarylethenes is reported. Tetraarylethenes, one of significant classes of multisubstituted olefins, owing to their interesting photophysical and redox properties, are valuable synthetic targets in materials science.

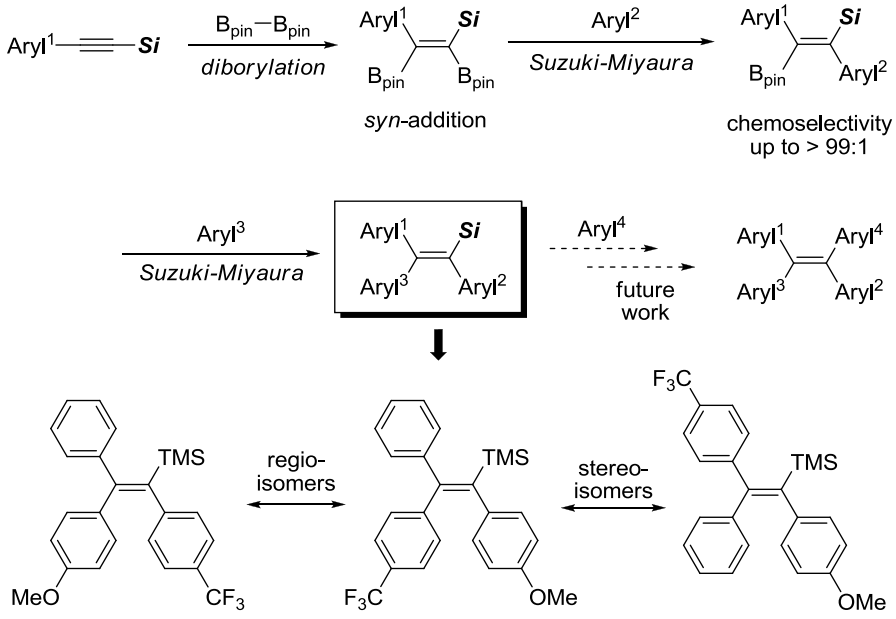


In Chapter 3, a highly regio- and stereoselective silylborylation of an alkynylboronate is disclosed. $PhMe_2Si–B_{pin}$ (B_{pin}: pinacolatoboryl) underwent the $Pd(OAc)_2$/*t*-OctNC-catalyzed *syn*-addition to an alkynylboronate to yield 1-phenyl-1-silyl-2,2-diborylethene with high regioselectivity. The obtained product was

then chemoselectively arylated by Suzuki-Miyaura coupling to afford (*Z*)-1-silyl-2-borylstilbene derivatives whose structure was confirmed by X-ray analysis. By examining various reaction conditions, 5 mol% $PdCl_2$(dppf) was proved to be efficient to yield the desired products with high chemoselectivity. A diversity of aryl iodides and bromides demonstrated good performance to afford (*Z*)-1-silyl-2-borylstilbenes in good yields. The second aryl groups were successively introduced to the remaining boron moiety. The silyl group was also transformed to the aryl group with desilybromination in the presence of Br_2/NaOMe, followed by Suzuki-Miyaura cross-couplings. At last, this approach was extended to the synthesis of a tetraarylated olefin with four different substituents.

Chapter 4. Synthesis of Multisubstituted Olefins through Regio- and Stereoselective Diborylation of Alkynylsilanes/Chemoselective Cross-Coupling Sequences

As the continuous research interests in regio- and stereoselective synthesis of multisubstituted olefins, a more efficient synthetic pathway was reported in this Chapter.



Bis(pinacolato)diboron (B_{2pin2}) underwent the $Pt(PPh_3)_4$-catalyzed *syn*-addition to alkynylsilanes to yield 1-aryl-1-silyl-2,2-diborylethenes in good yields with a perfect stereoselectivity. Sequential chemoselective Suzuki-Miyaura couplings were screened with several palladium catalysts. Among them, $PdCl_2$(dppp) and PEPPSI-IPr performed well to give rise to (*Z*)-1-boryl-silylated stilbene derivatives with a perfect

chemoselectivity up to >99:1. The configuration of the product was unambiguously determined by means of the results obtained in previous work described in Chapter 3. The two boron moieties were perfectly discriminated to render this synthetic strategy more facile and atom economic. A wide range of aryl halides regardless electron-donating, -withdrawing, and reactive functional groups such as –OMe, $–CF_3$, –Cl, $–CO_2Et$, –Ac, –CN, $–NO_2$, *etc*. were examined in the chemoselective Suzuki-Miyaura cross-couplings. The subsequent Suzuki-Miyaura cross-coupling readily introduced the second aryl groups in good yields. Moreover, various regio- and stereoisomers of multisubstituted olefins were successfully synthesized. This protocol would provide an alternative to more efficient and practical synthesis of tetraarylethenes. The further transformations of the silyl groups to the aryl groups more efficiently are now in progress.

CHAPTER 1

General Introduction

1-1 Introduction

Multisubstituted olefins represent one of the most widely occurring and important classes of organic compounds.[1] Multisubstituted olefins reflect their significance in their wide utilization in biologically active substances such as Tamoxifen,[2] Vioxx,[3] natural products such as Nileprost analogues,[4] *epi*-Illudol,[5] insect sex hormones derivatives such as diene I and triene II (Figure 1-1).[6] Moreover, multiarylated olefins and their derivatives are implicated in various materials such as liquid crystals and optoelectronic materials owing to their physical and electronic properties (Figure 1-2).[7]

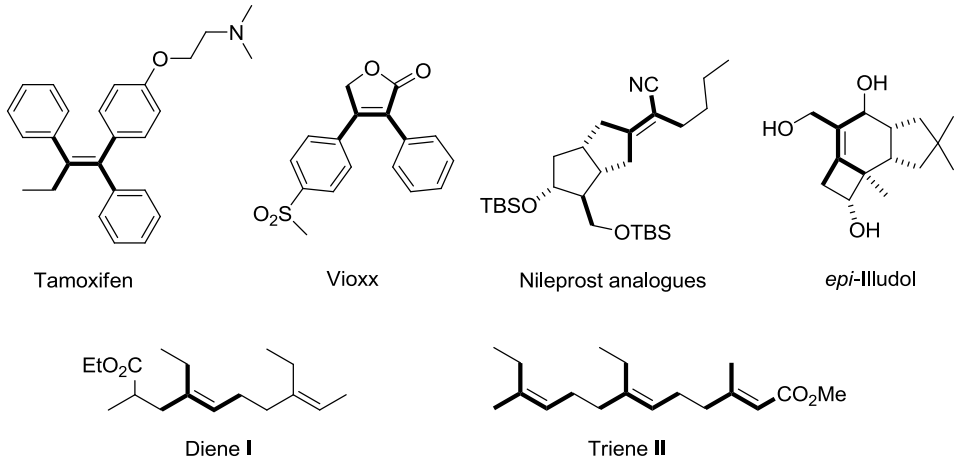


Figure 1-1

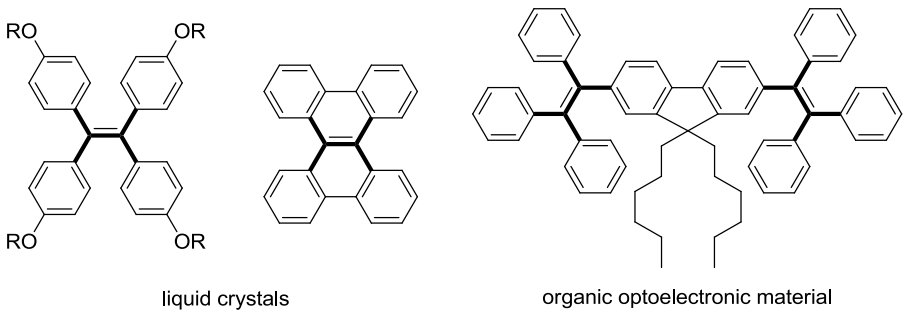


Figure 1-2

The synthesis of mono- and disubstituted olefins has been impressively developed and well established, but the synthesis of multisubstituted (tri- and tetrasubstituted) olefins has still faced many challenges for years.

1-2 Synthesis of Multisubstituted Olefins

There are four representative types of the olefin synthesis, as listed in Scheme 1-1.

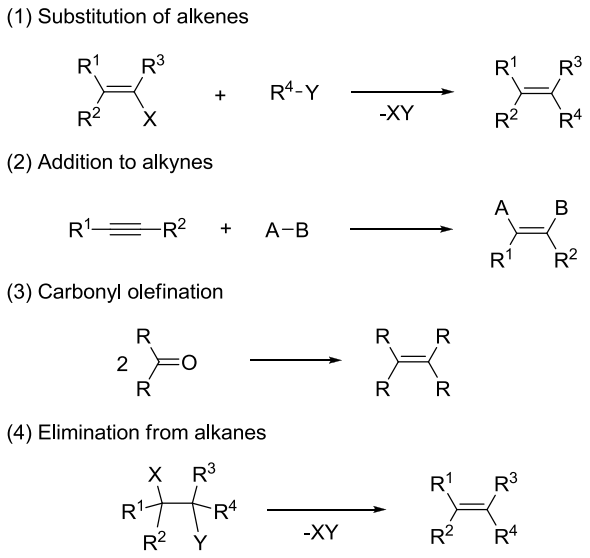
(1) Substitution of alkenes: *e.g.,* transition-metal-catalyzed cross-coupling reactions of suitable coupling partners with C−X, C−M or C−H on a C=C bond.

(2) Addition to alkynes: *e.g*., transition-metal-catalyzed hydrometalation, carbometalation, dimetalation, *etc.*

(3) Carbonyl olefination: *e.g.,* Wittig and Horner-Wadsworth-Emmons reaction, McMurry coupling, Julia-Lythgoe olefination, *etc.*

(4) Elimination from alkanes: *e.g.,* Hofmann elimination, Cope elimination, *β*-elimination from sulfoxide or selenoxide, *etc.*

Scheme 1-1



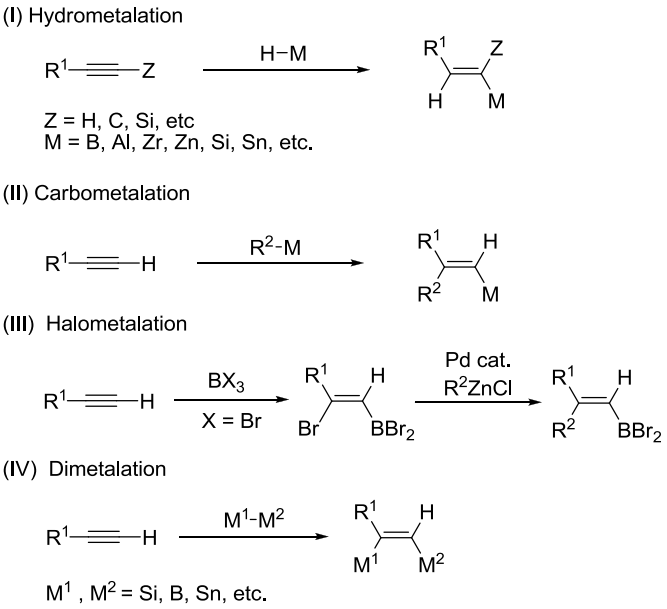
Besides, other synthetic methods such as olefin metathesis are also useful to obtain multisubstituted olefins.

1-2-1 Substitution of Alkenes

The Pd-catalyzed alkenylation has evolved since the mid-1970s into arguably the most general and highly selective method for the synthesis of substituted olefins. The scope of Pd-catalyzed alkenylation is fundamentally limited by an availability of the required alkenyl precursors. It has become critically important to synthesize alkenyl metals or alkenyl halides efficiently and selectively for substituted olefins. Conventional addition reactions to alkynes, such as hydrometalation,[8] carbometalation,[9] halometalation,[10] and

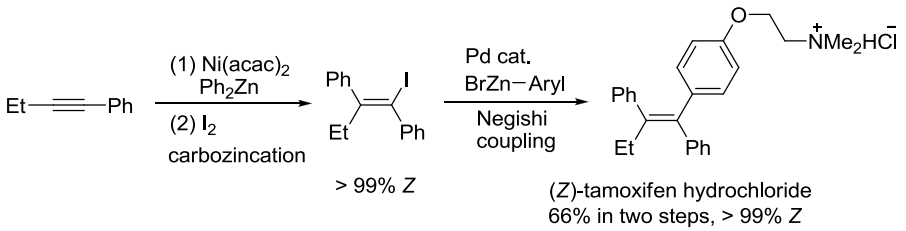
dimetalation[11] provide various alkenyl intermediates for coupling reactions (Scheme 1-2). Nevertheless, these approaches have been extensively developed in the synthesis of di-, and trisubstituted alkenes, but they have limitations in various synthesis of tetrasubstituted olefins.

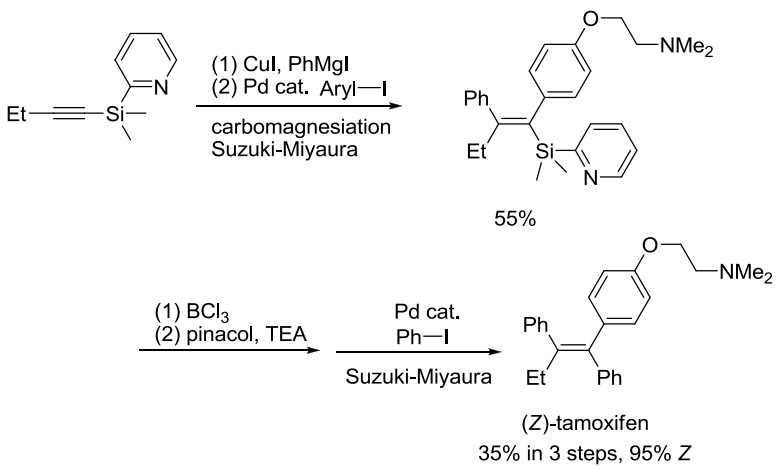
Scheme 1-2



As long as the requisite alkenyl reagents can be obtained, Pd-catalyzed alkenylation would provide a wide range of tetrasubstituted olefins with defined regio- and stereochemistry. As representative examples of the tetrasubstituted olefin synthesis, two following routes to an anticancer agent (*Z*)-tamoxifen are shown in Scheme 1-3: Ni-catalyzed carbozincation/Negishi coupling sequences [12] or Cu-catalyzed carbomagnesiation/Suzuki-Miyaura coupling sequences.[13]

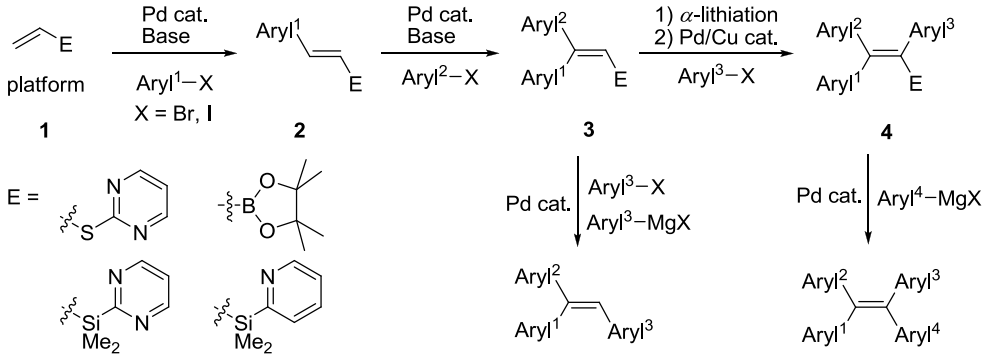
Scheme 1-3





One of the recent successful examples of the multisubstituted olefin synthesis via coupling reactions has been disclosed by Itami and Yoshida *et al.*[14] The synthesis of multisubstituted olefins was developed from vinyl-element compounds as the platform via successive installation of the aryl substituents at the C=C bond.

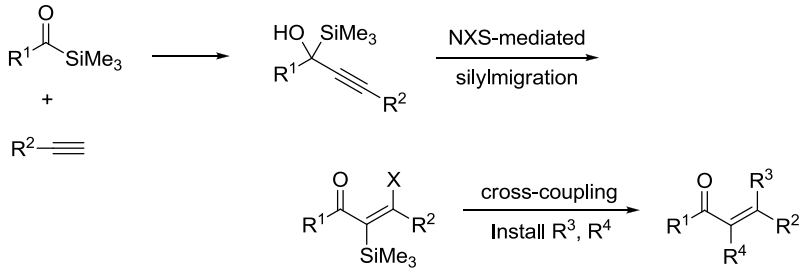
Scheme 1-4



As shown in Scheme 1-4, they utilized Pd-catalyzed double Mizoroki-Heck reactions to install two aryl groups at the two *β*-C−H bonds of **1** in one-pot. The successive installation of the third aryl group in the *α*-C−H bond by *α*-lithiation of **3** with *t*-BuLi and the subsequent cross-coupling reaction with aryl halides in the presence of the $Pd(PPh_3)_4$/CuI catalyst.

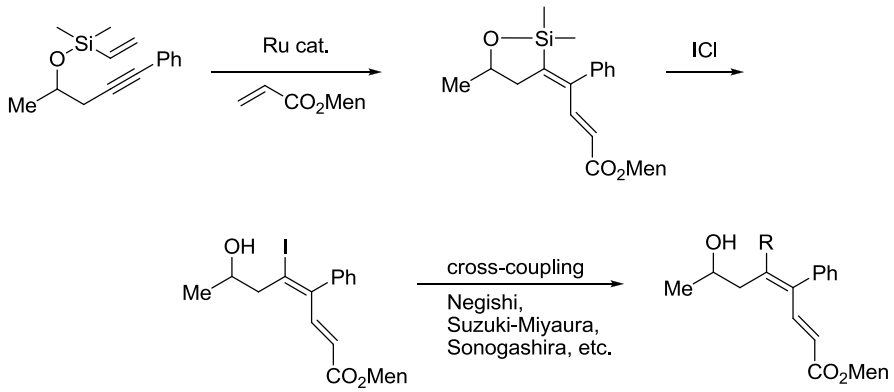
Ferreira *et al.*[15] have developed a stereoselective synthesis of tetrasubstituted olefins through halosilylation of alkynes via migration of the silicon group and sequential cross-couplings installing the carbon substituents to produce tetrasubstituted olefins with a desired geometry exclusively (Scheme 1-5).

Scheme1-5



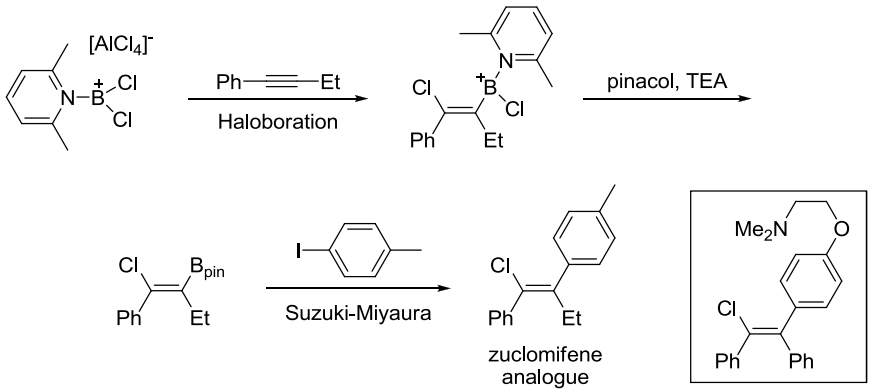
Clark and his coworkers [16] have reported the ruthenium-catalyzed novel *trans*-silylvinylation of internal alkynes, followed by Pd-catalyzed cross-couplings, which afforded tetrasubstituted olefins with high regio- and stereoselectivities (Scheme 1-6).

Scheme 1-6



Very recently, Ingleson used a series of novel boronium and borenium cations for selective haloborylation of internal alkynes. [17] Compared to terminal alkynes, haloborylation of internal alkynes with boron trihalides was difficult to achieve due to their steric hindrance. The stronger Lewis acidic borenium cations demonstrated higher reactivities toward unreactive internal alkynes. The generated vinyl haloboronates were successfully subjected to cross-couplings for the synthesis of tetrasubstituted olefins (Scheme 1-7).

Scheme 1-7



As examples shown above, Pd-catalyzed cross-coupling of alkenes have proved to be most widely used fundamental class of reactions for the synthesis of multisubstituted olefins. Any new and satisfactory methods discovered for the preparation of multisubstituted alkenyl metals and alkenyl halides would automatically and continuously keep expanding the synthetic horizon of the Pd-catalyzed cross-coupling reactions.

1-2-2 Addition to Alkynes

In the aforementioned alkenylation via cross-coupling reactions, before the critical formation of the desired multisubstituted olefins, alkenyl reagents or intermediates are prepared by addition reactions across various alkynes, which have been extensively explored as convenient and readily available methods for the synthesis of multisubstituted olefins. Regio- and stereocontrol are two important issues to achieve the high demanding of regio- and stereointegrity, in particular, when unsymmetrical alkynes were involved.

The regioselectivity can be addressed using the directing groups which have steric and electronic effects, or chelating in nature. For stereoselectivity, addition to alkynes might proceed in two pathways, *e.g.*, in *syn* or *anti* fashion, which might be controlled by nature of metals and catalysts, or reaction conditions.

1-2-2-1 Carbometalation to Alkynes

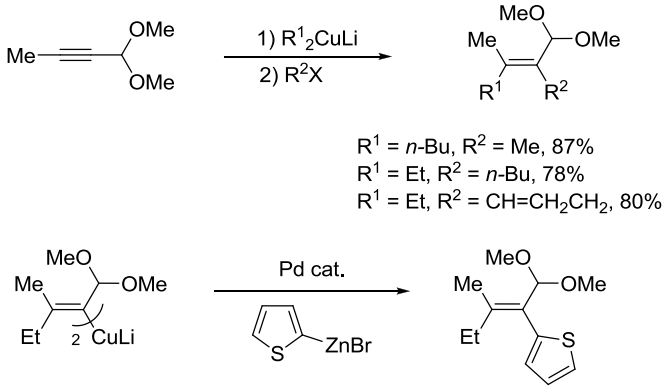
Carbometalation to alkynes has been the most widely used method for the formation of multisubstituted olefins.

(1) Carbocupration

Some of the earliest explored carbometalation involved organocopper reagents, termed as carbocupration. For most carbocupration reactions, *syn*-addition prevails but regioselectivity is usually dependent on the substituents of alkynes.[18]

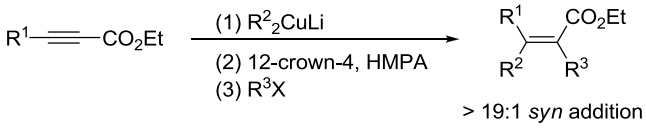
Alexakis *et al.* succeeded an early example of carbocupration of alkynyl acetals with high regio- and stereointegrity at low temperatures.[19] Copper species derived from organolithium reagents were required, and the reactions had to be conducted in THF to avoid a competing elimination pathway forming allenes. The tetrasubstituted olefins could be obtained using electrophilic alkyl halides. Moreover, palladium-mediated cross-couplings were followed by the *in-situ* conversion of cuprates to afford the corresponding zinc species (Scheme1-8).

Scheme 1-8



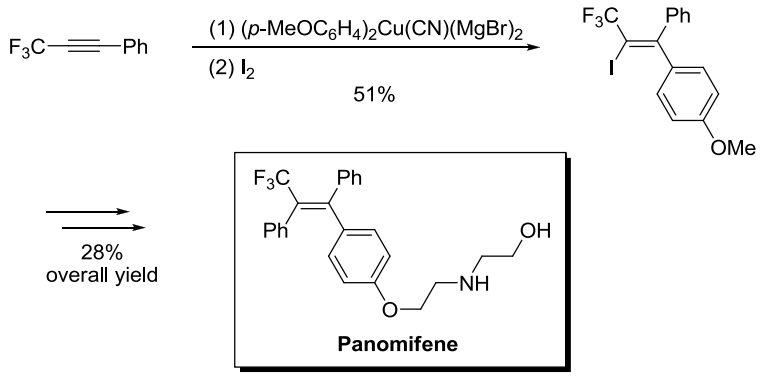
Carbocupration of acetylenic esters was later reported.[20] Stereoisomerization of the generated organocuprate species occurred through enolization of the intermediate copper anion, while excellent regio- and stereoslectivities were achieved recently by using additives such as HMPA and 12-crown-4 to control the extent of allenoate formation (Scheme 1-9).[21]

Scheme 1-9



Konno has reported the highly regio- and stereoselective carbocupration of fluoroalkylated internal alkynes, which were successfully utilized in the short, stereoselective total synthesis of the antiestrogenic drug panomifene (Scheme 1-10).[22]

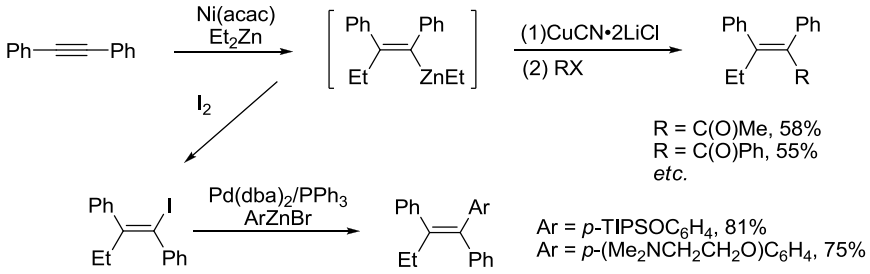
Scheme 1-10



(2) Carbozincation

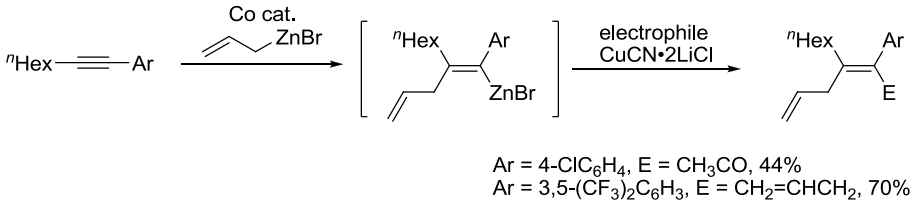
Organozinc reagents have also been used in several instances to prepare tetrasubstituted olefins. For example, carbozincation to alkynes was described in the presence of the nickel catalyst to undergo a *syn*-addition to diphenylacetylene, which afforded vinylzinc intermediates which were captured with different electrophiles (Scheme 1-11).[12]

Scheme 1-11



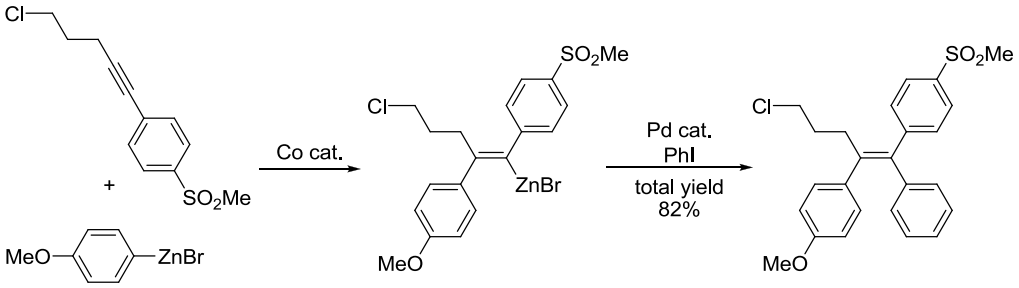
Yorimitsu and Oshima reported that allylzincation of 1-aryl-1-alkynes took place with high regio- and stereoselectivity when the reaction was catalyzed by cobalt (Scheme 1-12).[23]

Scheme 1-12



Recently, Gosmini *et al.* gave another example of carbozincation of internal alkynes using arylzinc reagents with the cobalt catalyst (Scheme 1-13).[24]

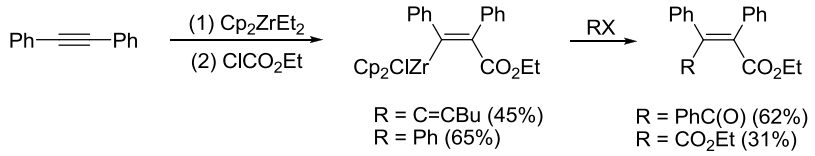
Scheme 1-13



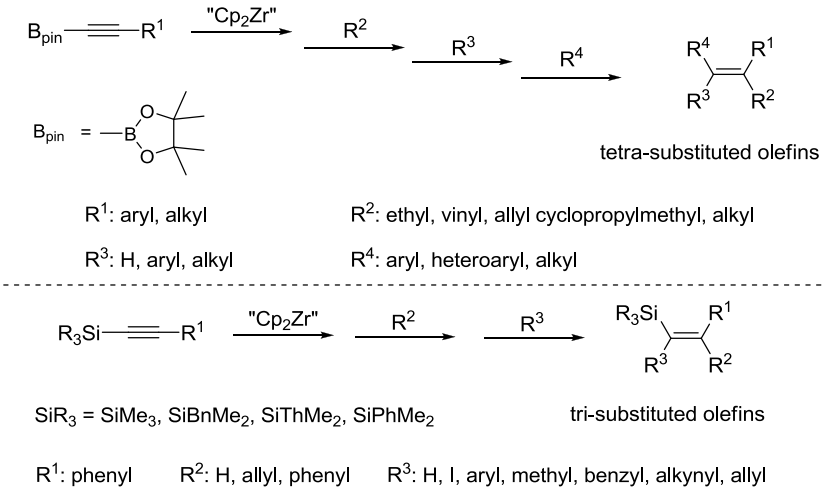
(3) Carbozirconation

Carbozirconation is a highly reliable method to functionalize alkynes, proceeding with a high degree of regio- and stereoselectivity. This reaction, consistently providing *syn*-isomers with regioselectivity, has been extensively studied. These reagents have a significant potential for preparing multsubstituted olefins. Takahashi [25] (Scheme 1-14) and Nishihara[26](Scheme 1-15) described a series of zirconium-based methods to construct multisubstituted olefins.

Scheme 1-14



Scheme 1-15

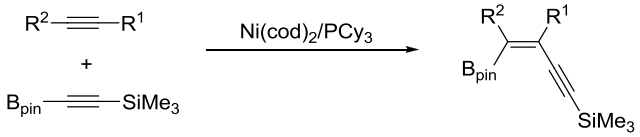


(4) Carboborylation

The use of boron for the carbometalation of alkynes offers significant advantages owing to the low toxicity, mild reactivity of organoboron reagents. Moreover, the synthesized intermediate vinylboron compounds as excellent cross-coupling partners render subsequent functionalization facile.

Suginome *et al*. reported carboborylation, in which a B−C bond in alkynylboranes added to a carbon−carbon triple bond in alkynes. The intermolecular alkynylborylation proceeded in the presence of the phosphine-nickel catalysts to give 1-boryl-enyne derivatives in good yields (Table 1-1).[27]

Table 1-1



entry [a]	R^1	R^2	Yield/% [b]	regioselectivity	*cis/trans*
1	*n*-Pr	*n*-Pr	92 (99)	--	92:8
2	CH_2Ph	CH_2Ph	67 (76)	--	96:4
3	Ph	Me	57 (62)	81:19	90:10
4	Ph	Et	65 (79)	92:8	87:13
5	Ph	*n*-Bu	68 (80)	93:7	89:11
6	*p*-$MeOC_6H_4$	*n*-Bu	71 (99)	93:7	73:27
7	1-Nap	Me	51 (79)	88:12	99:1
8	*p*-$EtO_2CC_6H_4$	*n*-Bu	51 (79)	92:8	93:7
9	Ph	$(CH_2)_2CH=CH_2$	60 (72)	94:6	89:11

[a] A mixture of $Ni(cod)_2$ (5 mol%), and PCy_3 (20 mol%) in toluene at 80 ℃, unless otherwise noted.

[b] Isolated yields, NMR yields in parentheses.

Although a pioneer work by Suginome demonstrated that carboborylation of alkynes occurred via a direct activation of the B−C bond, or three-component couplings with boron electrophiles and carbon nucleophiles,[28] it is still highly desirable to search carboborylation that requires less expensive metals, non-functionalized alkynes, and commercially available boron sources. Recently, the copper-mediated formal

carboborylation reactions of alkynes have been developed by Tortosa[29], (Scheme 1-16) and Yoshida,[30] respectively (Table 1-2).

Scheme 1-16

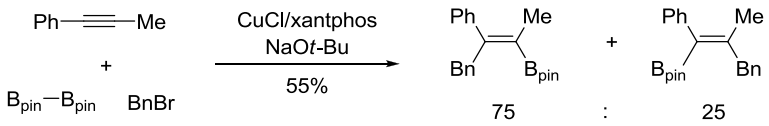
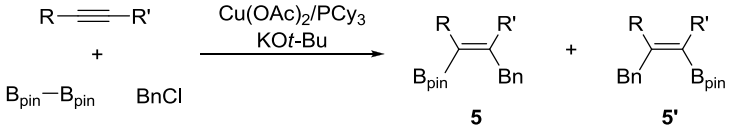


Table 1-2



entry	R	R'	time/h	Yield/%	**5**:**5'**ratio
1	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	54	67	--
2	Ph	*p*-$MeOC_6H_4$	29	84	52:48
3	Ph	4-BrC_6H_4	27	58	51:49
4	Ph	2-Thienyl	27	49	55:45
5	Me	Ph	24	54	>99:1
6	Et	Ph	15	50	>99:1
7	*n*-Pr	*n*-Pr	24	57	--
8	Me	*n*-Pent	8	46	80:20
9	H	Ph	46	44	>99:1
10	H	*n*-Hex	32	51	56:44
11	H	Cyclopent	52	48	55:45

[a] A mixture of alkyne (0.3 mmol), B_2pin_2 (1.3 equiv), BnCl (3 equiv), $Cu(OAc)_2$ (2 mol%) and PCy_3 (7 mol%), KO*t*-Bu (1.5 equiv) in DMF at 50 ℃. [b] Isolated yields.

(5) Other Carbometalation

Carbostannylation,[31] another useful way for multisubstituted olefin preparation has received somewhat less attention than other carbometalation. This synthetic methods using organotin reagents often encounters some problems of toxicity and purification.

Compared to the common *syn*-type carbometalation of alkynes, carbolithiation[32] and carbomagnesiation[13,33] often proceed in a *trans* fashion. Other carbometalation such as carboalumination[34] and carbopalladation[35] were also less studied but offered alternative synthetic routes from unique molecules.

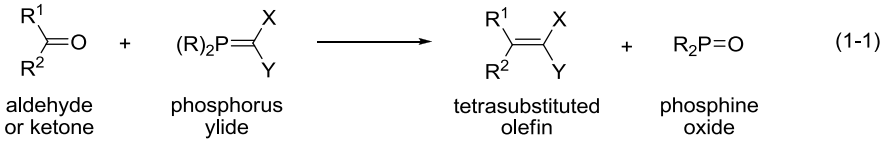
1-2-2-2 Dimetalation

Transition metal–catalyzed dimetalation [36] of unsaturated organic molecules has received much attention in the past two decades after the large emergence of inter-element[37] compounds. Because the low toxic, economical, and maturely synthetic studies of compounds,[38] organic compounds containing Si–Si,[39] B–B,[40] Si–B,[41] Sn–B,[42] and Si–Sn[43] bonds intrigued organic chemists to synthesize borylated or silylated olefins and to obtain more useful bioactive chemicals or functional materials via elaborative bond-forming reactions. The dimetalation of Si–B and B–B across alkynes for the synthesis of multisubstituted olefin will be introduced in Chapters 3 and 4.

1-2-3 Carbonyl Olefination

As another class of synthetic route to multisubstituted olefins, carbonyl olefination processes display serious limitations for the formation of unsymmetrical tetrasubstituted olefins. Most of these methodologies are strongly affected by a steric hindrance. Therefore, the yields of tetrasubstituted olefins are generally low and mixtures of stereoisomers are always obtained. Nevertheless, most of the standard carbonyl olefination have been employed in the synthesis of tetrasubstituted olefins. Wittig and Horner-Wadsworth-Emmons, Julia-Lythgoe, and metal carbene as representative classes of carbonyl olefination are described below.

1-2-3-1 Wittig and Horner-Wadsworth-Emmons Reactions

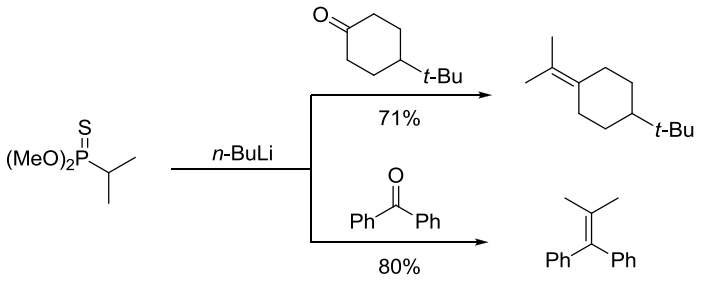


(1-1)

Up to a few decades ago, tetrasubstituted olefins were prepared by carbonyl olefination represented by the phosphorus-based Wittig olefination (eq 1-1) and its variant Horner-Wadsworth-Emmons (HWE) reaction. The early Wittig reactions were employed to synthesize symmetrically substituted alkylidene cyclobutanes[44] and cyclopropanes.[45] Corey and Kwiatkowski found that HWE reaction could be used for tetrasubstituted olefins.[46] The condensation of thiophosphonate with two symmetrical ketones yielded tetrasubstituted olefins, as shown in Scheme 1-17. Although tetrasubstituted olefins can

be obtained by Wittig olefination, reports in recent years still illustrate the difficulty in preparing unsymmetrical tetrasubstituted olefins.

Scheme 1-17



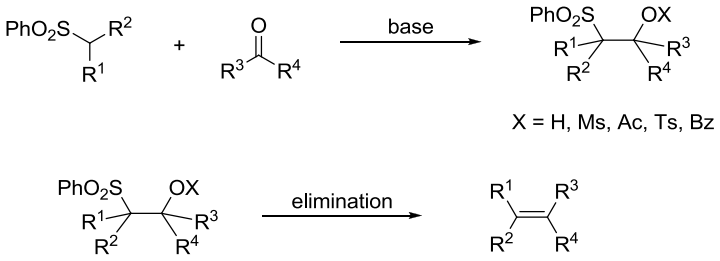
1-2-3-2 McMurry Olefination

The reductive coupling of carbonyl compounds, a range of low-valent titanium-based reactions commonly referred to as the McMurry reaction, constitutes an important method for the formation of tetrasubstituted olefins and has been extensively reviewed.[47] Similar to other carbonyl olefination, a mixture of *E/Z* isomers are generally obtained. But, it has been used to prepare highly strained and sterically hindered tetraarylated olefins.[48]

1-2-3-3 Julia-Lythgoe Olefination

The formation of olefins from sulfone and carbonyl compounds, known as the Julia-Lythgoe olefination, is one of the most powerful tools in modern organic chemistry. The initial reductive elimination of the intermediate *β*-hydroxysulfones using Na-Hg has been gradually superseded by mild, more selective, and less toxic reducing agents such as SmI_2[49] or Mg[50] (Scheme 1-18).

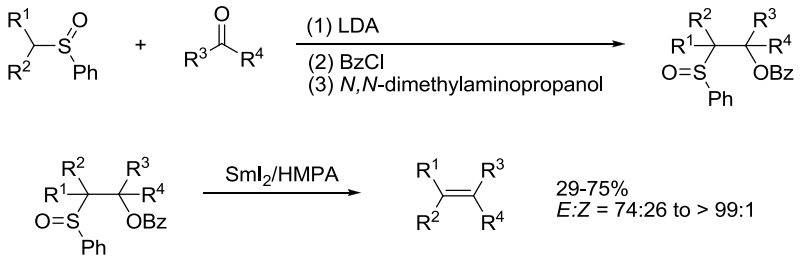
Scheme 1-18



A novel modification of a classical Julia-Lythgoe olefination using sulfoxides instead of sulfones affords 1,2-di-, tri-, and tetrasubstituted olefins in moderate to excellent yields with high *E/Z* selectivity, after the *in situ* benzoylation and SmI_2/HMPA- or

DMPU-mediated reductive elimination.[51] The conditions are mild, and the procedure is broadly applicable (Scheme 1-19).

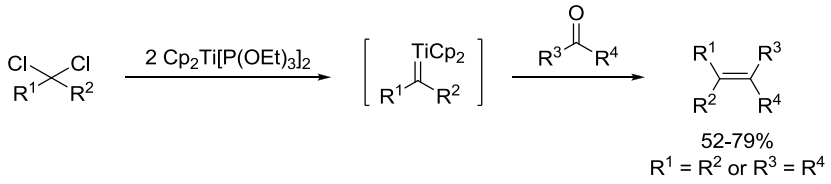
Scheme 1-19



1-2-3-4 Olefination with Metal Carbene Complexes

The reactions of metal carbene complexes with carbonyl compounds are significantly affected by a steric factor, and this process generally cannot form tetrasubstituted olefins. This problem can be partially circumvented by the use of *gem*-dihalides, as illustrated by the Takeda's group (Scheme 1-20).[52]

Scheme 1-20

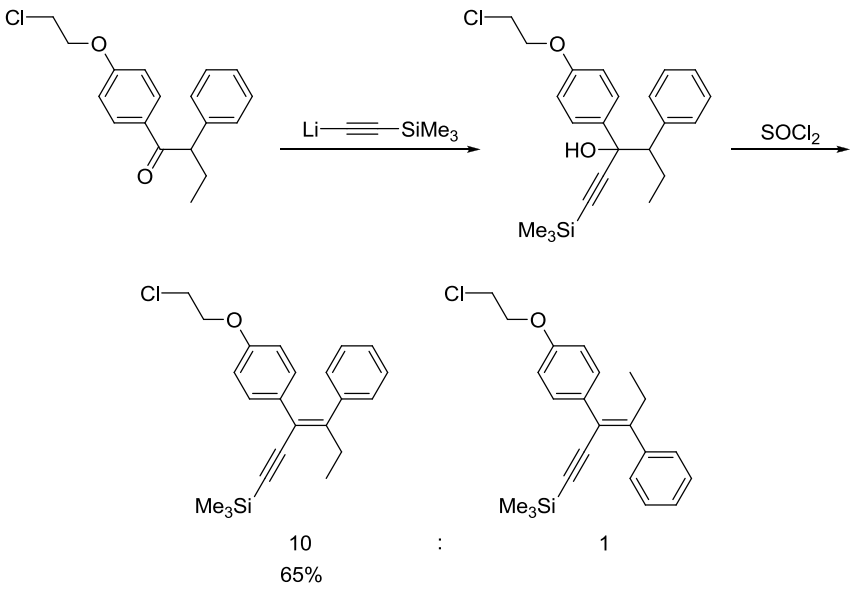


1-2-4 Elimination

Elimination as one of classical pathways in a text book for the synthesis of multisubstituted olefins has less been utilized in recent years. Although E2 reactions always ensure the single isomer of the product, the complicated synthesis of the multisubstituted alkanes by arranging hydrogen and the leaving groups in an antiperiplanar position has a difficulty to achieve.

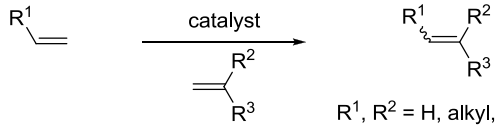
Scheme 1-21 shows an example of the synthesis of tetrasubstituted olefins via elimination. Valliant *et al.* used a base-promoted approach to Tamoxifen analogues.[53] Ketone was treated with lithium (trimethylsilyl)acetylide to give a tertiary alcohol with undefined stereochemistry. The crude alcohol was dehydrated using thionyl chloride to give a mixture of *E* and *Z* alkenes in a 10:1 ratio, with the major isomer being obtained in 65% yield after purification.

Scheme 1-21



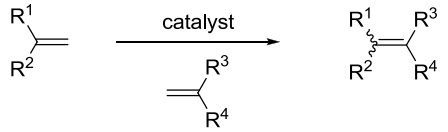
1-2-5 Other method--Olefin metathesis

Di, trisubstituted olefin formation via olefin metathesis



(1-2)

Tetrasubstituted olefin formation via olefin metathesis



(1-3)

As an alternative technology for the olefin generation, olefin metathesis has been focused because of its recent and rapid development.[54] This transformation allows the efficient production of otherwise readily unavailable olefins including heterocycles, carbocycles, trisubstituted olefins, and heteroatom-substituted olefins. Common metathesis pre-catalysts are shown in Chart 1-1, Schrock, Grubbs, and Hoveyda have made a great effort to improve the reactivity and selectivity of these pre-catalyst to the efficient generation of tetrasubstituted olefins.

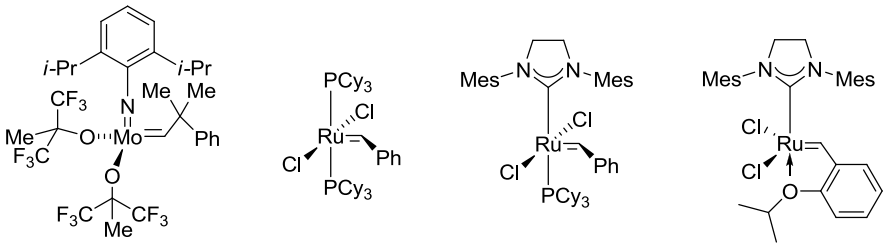
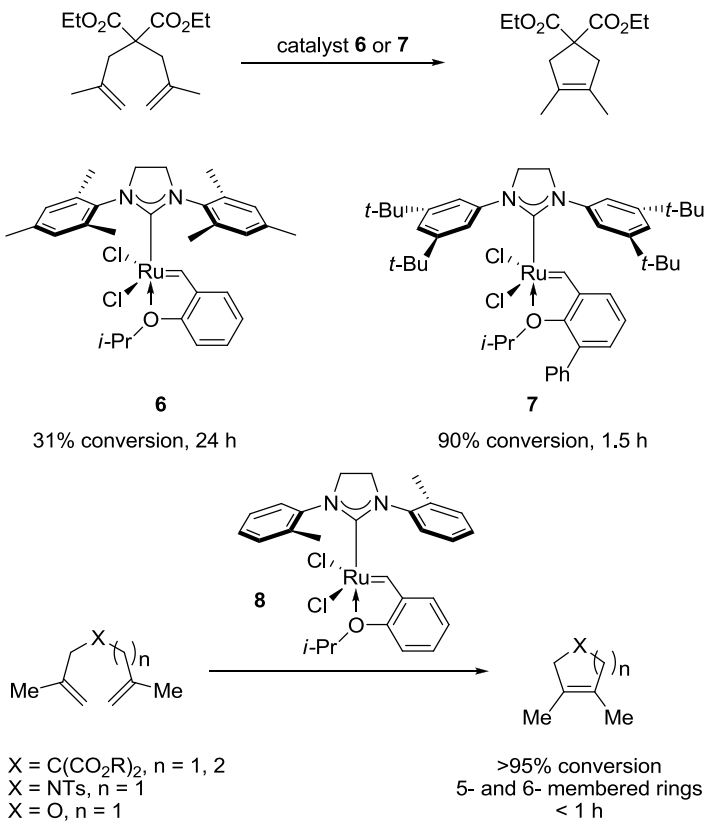


Chart 1-1

Grubbs and Schrodi *et al.*[55] increased an efficiency of the catalysts for ring-closing metathesis to form tetrasubstituted olefins from the challenged substrate diethyl dimethallylmalonate using the ruthenium catalysts ligated *N*-heterocyclic carbene, as shown in Scheme 1-22.

Scheme 1-22



The success of metathesis in tetrasubstituted olefin synthesis depends on the pre-catalyst chosen. Schrock, Grubbs, and Hoveyda's pre-catalysts are the most commonly employed for a direct ring-closing metathesis. The application of olefin metathesis to tetrasubstituted olefins has not yet been realized in industrial production.

1-3 Summary

All the reactions introduced in this chapter have enjoyed widespread applications in organic synthesis. However, all these reactions are far from truly general methods for multisubstituted olefins. A tuning of reaction conditions might result in the selective synthesis of one of the possible isomers, but the synthesis of all possible isomers is almost impossible with these conventional methods.

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CHAPTER 2

Synthesis of Alkynylboron Compounds toward Multialkylated Olefins

2-1 Introduction

Alkynylboron compounds consisting of alkynyl and boron moieties can be categorized according to the substituents on the boron atom, such as alkynylboranes, -boronates, and -borates. In this Chapter, the synthesis and reactions of alkynylboron compounds are systematically introduced. Alkynylpinacolatoboranes and alkynyltrifluoroborates are the most widely utilized classes in organic reactions, owing to their stability and ease of handling. Other alkynylboron compounds have also been developed as convenient substrates for various organic reactions. Thanks to the dedication of many chemists in this field, great advances of a facile synthesis and a wide utilization of alkynylboron compounds have been made with these versatile building blocks for diverse structures in organic synthesis.

Organic chemistry of organoboron compounds has been widely developed because these compounds are readily available, water-stable, and non-toxic. In addition, the inorganic by-products are easily separable after the reactions. Although the research of organoboron compounds bearing sp^2 and sp^3 carbon-boron bonds has been extensively studied, [1] the organoboron compounds bearing the sp carbon-boron bonds have received less attention. The utility of alkynylboron compounds in organic synthesis began to be investigated in the 1970s when they were found to be useful, diversified synthetic intermediates. Brown *et al.* in 1987, succeeded in establishing the most reliable synthetic method of 1-alkynylboronates simply by lithiation of terminal alkynes and the subsequent treatment with triisopropylborate.[2] Because of features of a facile conversion of the boron moieties into other functional groups,[3] alkynylboron compounds proved to be versatile candidates in a series of classical reactions, *e.g.,* coupling, addition, and cycloaddition reactions. Moreover, since alkynylboron compounds bear both alkynyl and boron moieties, when alkynylboron compounds are subjected to organic reactions, they show additionally unique reactivities that neither typical alkynes nor other organoboron compounds possess. In the past two decades, studies on alkynylboron compounds in various organic reactions have been diligently elucidated.

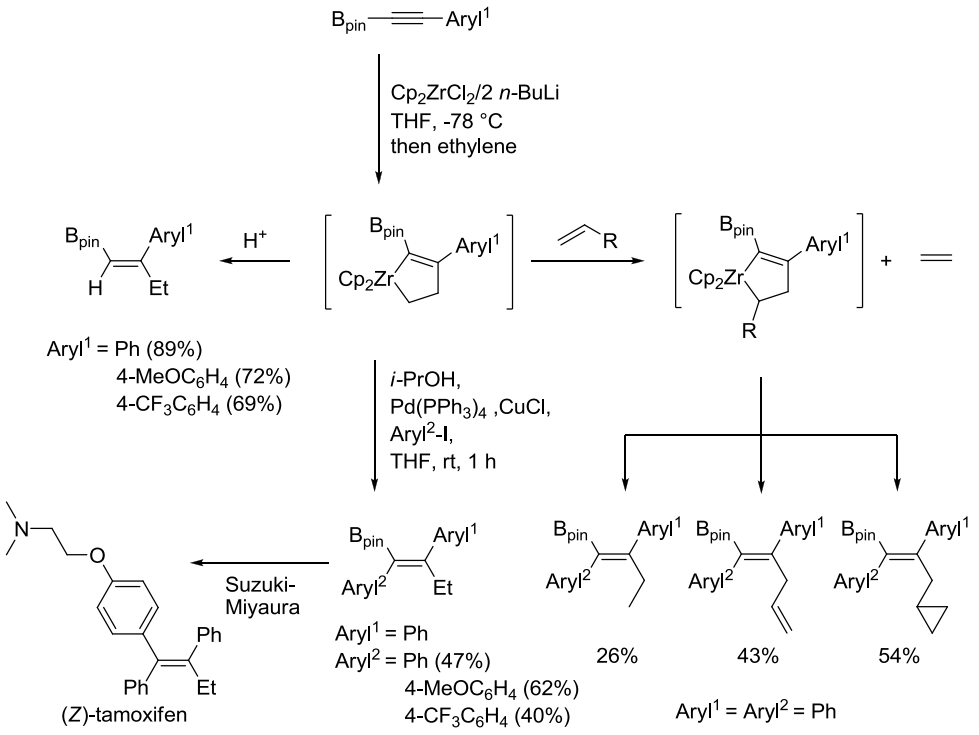
The use of alkynylboron compounds in synthesis of multisubstituted olefins via zirconium chemistry was initially conducted by Srebnik for the synthesis of (*Z*)-1-alkenylboronates that cannot be obtained directly by hydroboration of terminal

alkynes due to the *syn*-addition of hydroboranes to a carbon-carbon triple bond.[4]

The Author's research group succeeded in the utilization of a series of alkynylboronates in conjunction with zirconacycles in synthesizing alkenylboronates. The regio- and stereoselective synthesis of multisubstituted olefins through zirconacycle formation of alkynylboronates were also demonstrated.

In 2007, the versatile and direct synthesis of tetrasubstituted olefins was developed by a regioselective formation of zirconacyclopentenes from aryl-substituted alkynylboronates, followed by a series of functionalizations and Cu/Pd-cocatalyzed arylation with various aryl iodides (Scheme 2-1).[5]

Scheme 2-1. Application of Alkynylboron Compounds for Multisubstituted Olefins.



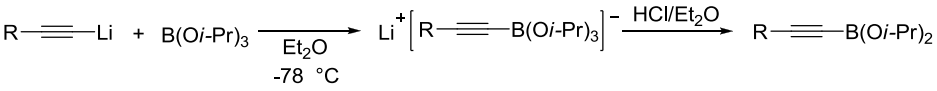
In this Chapter, the Author introduced the synthesis of alkynylboronates as well as the applications of alkyl-substituted alkynylboronates for regio- and stereoselective synthesis of multialkylated olefins.

2-2 Results and Discussion

2-2-1 Synthesis of Alkynylboronates

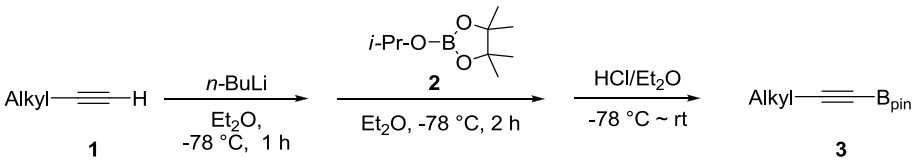
Alkynylboronates, owing to their stability, moderate reactivity, and ease of handling, have been the most widely used among all the alkynylboron compounds. Based on their previous studies in the synthesis of alkyldiisopropylborates,[6] Brown *et al.* have successfully expanded the high-yield synthesis of 1-alkynylboronates with a wide range of substituents in the acetylenic moiety.[2] This simple and general synthetic method, starting from alkynyllithium, triisopropylborate, and hydrogen chloride in diethyl ether, is regarded as a facile pathway toward alkynylboronates (Scheme 2-2).

Scheme 2-2



Based on this method, various alkynylboronates with alkyl and aryl substituents were successfully synthesized.

Table 2-1. Synthesis of Alkyl-substituted Alkynylboronates.[a]



entry[a]	Alkyl—≡—H	Alkyl—≡—B_{pin}	yield[b] (%)
1	*n*-Dec—≡—H	*n*-Dec—≡—B_{pin} **3b**	67
2	*n*-Hex—≡—H	*n*-Hex—≡—B_{pin} **3a**	95
3	*n*-Bu—≡—H	*n*-Bu—≡—B_{pin} **3c**	94
4	*t*-Bu—≡—H	*t*-Bu—≡—B_{pin} **3d**	87
5[c]	*i*-Pr, Br, Br	*i*-Pr—≡—B_{pin} **3e**	86

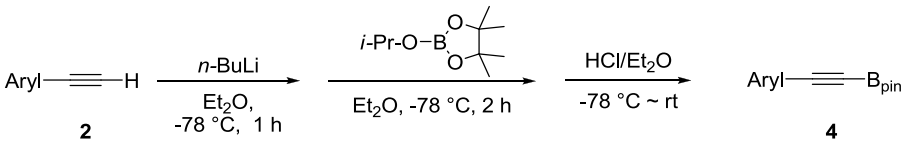
[a] The reactions were carried out using **1** (12 mmol, 1.2 equiv), *n*-BuLi (12 mmol, 1.2 equiv), *i*-PrOBpin (10 mmol). [c] Isolated yields. [b] *n*-BuLi (24 mmol, 2.4 equiv).

As shown in Table 2-1, linear alkyl groups such as *n*-Dec, *n*-Hex, *n*-Bu bearing alkynyllithium was generated from the corresponding alkynes with treatment with *n*-BuLi, to afford **3** in moderate to good yields (Table 2-1, entries 1-3). Alkynyllithium species

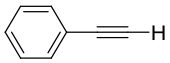
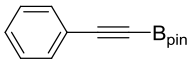
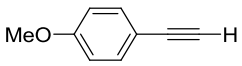
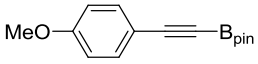
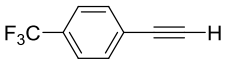
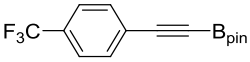
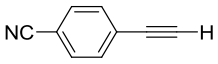
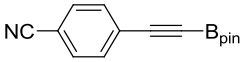
with branched alkyl groups such as *t*-Bu, and *i*-Pr also proceeded well with *i*-PrO–B_{pin} in moderate yields (Table 2-1, entries 4 and 5).

The synthesis of different aryl-substituted alkynylboronates **4** was shown in Table 2-2. The corresponding alkynylboronates bearing substituents with electron-donating and -withdrawing groups were obtained. An electrophilic cyano group was found to be compatible in the presence of alkynyllithium species.

Table 2-2. Synthesis of Aryl-substituted Alkynylboronates [a]



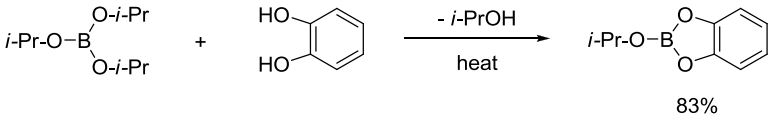
2 **4**

entry [a]	Aryl—≡—H	Aryl—≡—B_{pin}	yield[b] (%)
1		 **4a**	97
2		 **4b**	89
3		 **4c**	66
4		 **4d**	42

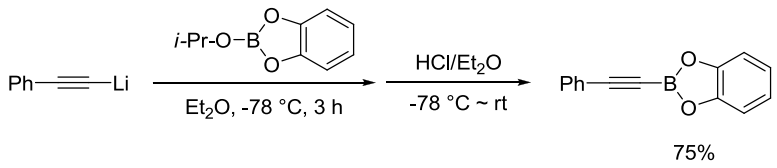
[a] The reactions were carried out using **1** (12 mmol, 1.2 equiv), *n*-BuLi (12 mmol, 1.2 equiv), *i*-PrOB_{pin} (10 mmol). [b] Isolated yield.

This protocol was also proved to be practical for the synthesis of higher reactive alkynylcatecholborane. It can be concluded that the synthesis of alkynylboronates is usually achieved from good nucleophilic alkynyllithium species with boron electrophiles (Scheme 2-3).

Scheme 2-3. Synthesis of Alkynyl Catecholborane.



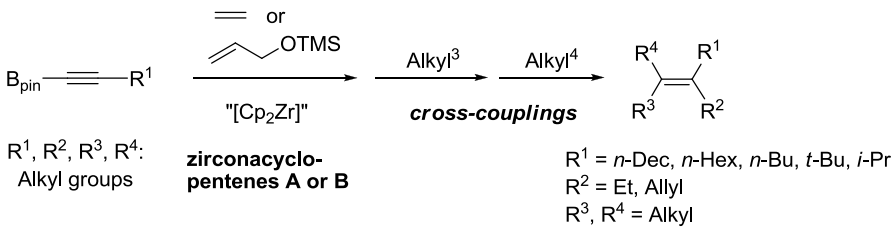
83%



2-2-2 Alkyl-substituted Alkynylboronates in the Synthesis of Multialkylated Olefins

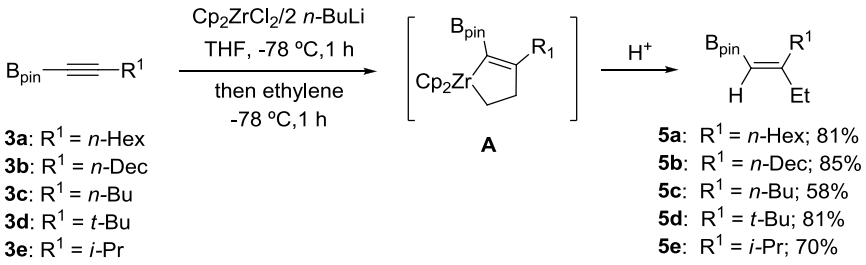
Aryl-substituted alkynylboronate was well investigated in the Author's group for their application in the synthesis of multisubstituted olefins (*vide supra).* Recently, in the application of alkyl-substituted alkynylboronate, unprecedented synthetic methods were developed using alkyl-substituted alkynylboronates to synthesize multialkylated olefins by regioselective formation of zirconacyclopentenes, followed by sequential palladium-catalyzed cross-coupling reactions (Scheme 2-4).[7]

Scheme 2-4. Application of Alkyl-substituted Alkynylboronates for Multialkylated Olefins.



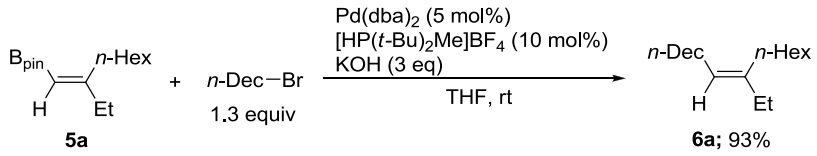
Addition of 1-alkynylboronates **3a**–**3e** to Negishi reagent ($[Cp_2ZrCl_2]$/2 *n*-BuLi)[8] generated *in situ* under an atmosphere of ethylene smoothly produced zirconacyclopentenes **A**,[9] which upon hydrolysis, afforded the corresponding alkenylboronates **5a**–**5e** in moderate to high yields with excellent regioselectivity (Scheme 2-5). The regiochemistry of **5a**–**5e** was confirmed by comparison of their spectroscopic data with those reported for authentic compounds[10] prepared by the reactions of 1-alkynylboronates with Takahashi reagent ($[Cp_2ZrCl_2]$/2 EtMgBr).[11]

Scheme 2-5



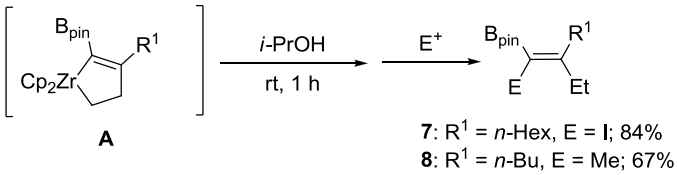
Trialkylated olefins were readily synthesized by a Suzuki-Miyaura coupling of alkenylboronates **5a** with alkyl bromides. To inhibit *β*-hydrogen elimination of alkyl bromides, various milder reaction conditions (Pd catalyst, additive, and solvent) were screened. It was discovered that, under the basic conditions developed by Fu,[12] $[HP(t\text{-}Bu)_2Me]BF_4$ was used as a precursor of the phosphine ligand, the reaction proceeded smoothly at room temperature (Scheme 2-6). This process produced the desired cross-coupled product **6a** in 93% yield and was compatible with a variety of functional groups.

Scheme 2-6



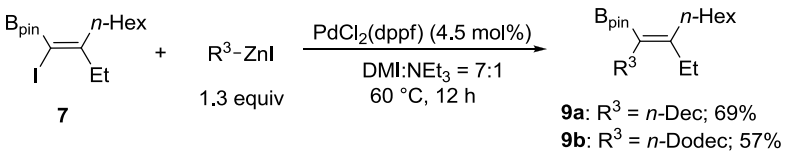
Prior to hydrolysis of zirconacyclopentenes **A** forming **5a-e** (Scheme 2-5), a selective protolysis of Zr-C(sp^3) bond in **A** with isopropyl alcohol, followed by iodolysis[13] afforded the **7** in 84% yield; or a sequential one-pot Pd-catalyzed coupling reaction with iodomethane in the presence of CuCl gave **8** in 67% yield. These approaches served versatile precursors bearing the boron functionality for the synthesis of tetraalkylated olefins (Scheme 2-7).

Scheme 2-7



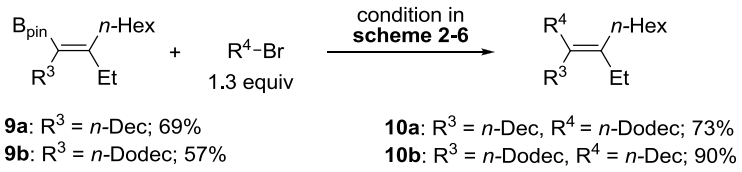
Compound **7** was then subjected to successive Negishi coupling with various alkylzinc reagents having *β*-hydrogens.[14] $PdCl_2(dppf)$[15] was found to be the best catalyst yielding **9a** and **9b** in 69% and 57% yield, respectively, with DMI as the solvent with NEt_3 as the basic additive (7:1).[16] It is noteworthy that the reaction is highly stereoselective (>99:1 as determined by NMR), since isomerization during Negishi coupling was suppressed, which results in a retained configuration. During the reactions, the boron moieties remained intact (Scheme 2-8).

Scheme 2-8



Under the same condition shown in Scheme 2-6, Suzuki-Miyaura cross-coupling of **9a** and **9b** with alkyl bromides smoothly afforded tetraalkylated olefins **10a** and **10b**, respectively, as stereoisomers (Scheme 2-9). In a same manner, compound **8** and 1-bromopropane afforded another tetraalkylated olefin **11** in 64% yield (Scheme 2-10). To the best of her knowledge, this is the first example of a regio- and stereocontrolled synthesis of tetraalkylated olefins bearing four different linear alkyl chains.

Scheme 2-9



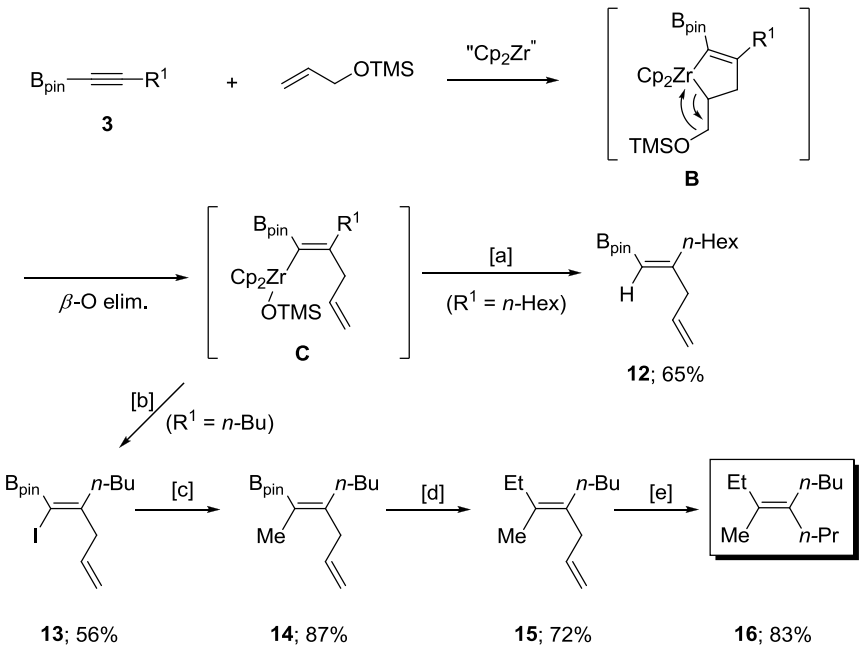
Scheme 2-10

To achieve an introduction of hydrocarbon functionalities other than an ethyl group, a zircono-allylation approach was chosen (Scheme 2-11).[17] Srebnik has reported that the phosphine-stabilized borylzirconacyclopropenes were formed by the reactions of 1-alkynylboronates **3** with Negishi reagent in the presence of tributylphosphine.[18] The added allyloxytrimethylsilane rapidly reacted with the intermediate zirconacyclopropenes to form the zirconacyclopentene **B** regioselectively with the boron moiety in the α-position. The spontaneous β-oxygen elimination resulted in the formation of a transient alkenylzirconocene intermediate **C**. Hydrolysis of the remaining Zr−C bond delivered the trisubstituted alkenylboronate in 65% yield.

Iodo-1-alkenylboronate **13** was then synthesized in 56% yield from **3** with allyloxytrimethylsilane via initial zirconacycle formation with Cp_2ZrCl_2/Mg,[19] followed

by iodonolysis. The Pd-catalyzed alkylation[20] with MeZnBr in the presence of 2 mol % of $Pd(PPh_3)_4$ in THF afforded methylated alkenylboronate **14** in 87% yield with >99% isomeric purity. Compound **14** was subjected to Pd-catalyzed Suzuki-Miyaura coupling with bromoethane to provide **15** in 72% yield. Finally, a selective catalytic hydrogenation of **15** with 10 mol % of Wilkinson's catalyst was performed to deliver **16**, a structural isomer of **11**, in 83% yield with >99% isomeric purity (Scheme 2-11).

Scheme 2-11



[a] Cp_2ZrCl_2 (1.2 equiv), *n*-BuLi (2.4 equiv), $P(n\text{-Bu})_3$ (1.0 equiv), -78 °C, 20 h, then **3a** (1.0 equiv), allyloxytrimethylsilane (1.5 equiv), 50 °C, 1 h, then hydrolysis.
[b] Cp_2ZrCl_2 (1.2 equiv), Mg (2.0 equiv), **3c** (1.2 equiv), allyloxytrimethylsilane (1.0 equiv), 50 °C, 1 h, then I_2 (2.0 equiv), rt, 12 h.
[c] $ZnBr_2$ (1.65 equiv), MeMgBr (1.35 equiv), THF, 0 °C, 30 min, then **13** (1.0 equiv), $Pd(PPh_3)_4$ (2 mol%), rt, 18 h.
[d] **14** (1.0 equiv), bromoethane (1.3 mmol), KOH (3 mmol), $Pd(dba)_2$ (5 mol%), $[HP(t\text{-Bu})_2Me]BF_4$ (15 mol%), THF, 20 °C, 12 h.
[e] $RhCl(PPh_3)_3$ (10 mol%), H_2, benzene, rt, 18 h.

2-3 Summary

In this Chapter, the Author has developed a versatile direct synthesis of multialkylated olefins bearing various alkyl groups by a regioselective formation of zirconacyclopentenes using alkynylboronates, followed by the successive Pd-catalyzed Negishi and Suzuki-Miyaura cross-couplings. The utilization of alkyl substituted alkynylboronates for the synthesis of tetraalkylated olefins indicated that alkynylboron compounds as versatile and synthetically valuable substrates in novel organic reactions contributes to promising perspectives for the synthesis of functional materials and pharmaceuticals.

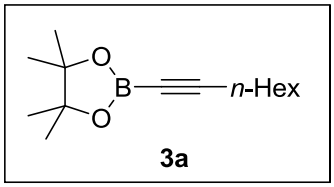
2-4 Experimental Section

2-4-1 General Instrumentation and Chemicals

All the reactions were carried out under an Ar atmosphere using standard Schlenk techniques. Glassware was dried in an oven (130 ℃) and heated under reduced pressure before use. Dehydrated solvent were purchased from Kanto Chemicals Co., Ltd. For thin layer chromatography (TLC) analyses throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. Silica gel column chromatography was carried out using Silica gel 60 N (spherical, neutral, 40-100 μm) from Kanto Chemicals Co., Ltd. NMR spectra (^{1}H, $^{13}C\{^{1}H\}$, and $^{11}B\{^{1}H\}$) were recorded on Varian INOVA-600 (600 MHz) and Mercury-300 (300 MHz) spectrometers. The chemical shifts of the $^{11}B\{^{1}H\}$ NMR spectra were referenced to an external $BF_3 \cdot OEt_2$. Infrared spectra were recorded on a Shimadzu IRPrestige-21 spectrophotometer. GC analyses were performed on a Shimadzu GC-14A equipped with a flame ionization detector using Shimadzu Capillary Column (CBP1-M25-025) and Shimadzu C-R6A-Chromatopac integrator. GC/MS analyses were carried out on a SHIMADZU GC-17A equipped with a SHIMADZU QP-5050 GC-MS system. Elemental analyses were carried out with a Perkin-Elmer 2400 CHN elemental analyzer at Osaka City University.

2-4-2 Experimental Procedures

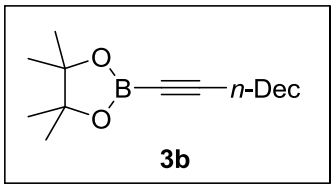
Synthesis of 1-alkynyldioxaborolanes 3 and 4



3a

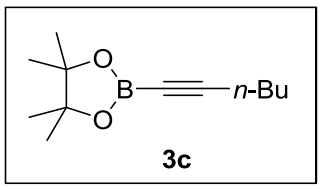
2-(1-Octyn-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3a).[21] To a solution of 1-Octyne (1.8 mL, 12 mmol) in dehydrate Et_2O (30 mL) in a 100 mL of Schlenk tube at -78 ℃ under an Ar atmosphere were added dropwise *n*-BuLi (7.5 mL, 1.6 M hexane solution, 12 mmol). The reaction mixture was stirred for 1 h at -78 ℃. The resulting reaction mixture was then added to a solution of *i*-PrO-Bpin(2.04 mL, 10 mmol) in dehydrate Et_2O (30 mL) -78 ℃. After being stirred for 2 h at -78 ℃, the reaction mixture was quenched with 1.0 M HCl/Et_2O (15.0 mL, 15.0 mmol), and the mixture was

warmed to room temperature with additional 1 h stirring. Filtration and evaporation afforded a pale yellow oil. Bulb to bulb distillation (150 ℃/2 Torr) gave **3b** (2.24 g, 9.5 mmol, 95% yield) as colorless liquid. ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 0.85 (t, J = 6.9 Hz, 3H), 1.17-1.40 (m, 6H), 1.24 (s, 12H), 1.50 (quin, J = 7.5 Hz, 2H), 2.22 (t, J = 7.5 Hz, 2H).



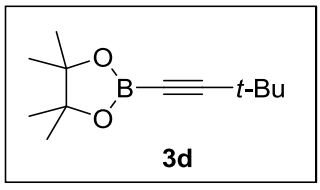
3b

2-(1-Dodecyn-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3b). A colorless liquid. Yield: 67% (1.15 g, 3.9 mmol). Bp. 180 ℃/1.3 Torr. FT-IR (neat, cm^{-1}): 2954 (m), 2927 (s), 1468 (w), 1459 (w), 1386 (m), 1372 (m), 1343 (s), 1313 (m), 1145 (s), 662 (m). ^{1}H NMR ($CDCl_3$, 300 MHz, rt) δ 0.87 (t, J = 6.8 Hz, 3H), 1.26 (s, 12H), 1.26-1.39 (m, 14H), 1.52 (quin, J = 6.9 Hz, 2H), 2.24 (t, J = 6.9 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, rt) δ 14.1, 19.5, 22.7, 24.6, 28.1, 28.9, 29.1, 29.3, 29.4, 29.6, 31.9, 84.0. Two sp carbon signals were not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt) δ 23.4. MS (EI, m/z (relative intensity)): 292 (M^+, 3), 277 (94), 206 (25), 165 (69), 151 (55), 124 (58), 107 (100), 97 (60), 83 (86), 67 (75). Anal. Calcd for $C_{18}H_{33}BO_2$: C, 73.97; H, 11.38%. Found: C, 73.73; H, 11.50%.



3c

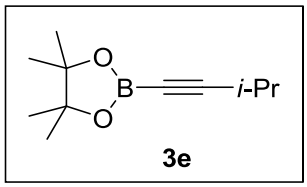
2-(1-Hexyn-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3c).[22] A colorless liquid. Yield: 94% (1.96 g, 9.4 mmol). Bp. 100 ℃/1.3 Torr. ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 0.86 (t, J = 6.8 Hz, 3H), 1.24 (s, 12H), 1.37-1.52 (m, 4H), 2.23 (t, J = 7.2 Hz, 2H).



3d

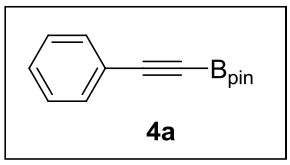
2-(3,3-Dimethyl-1-butyn-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3d).[22] A

white solid. Yield: 87% (1.81 g, 8.7 mmol). Bp. 120 ℃/20 Torr. ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 1.24 (s, 9H), 1.27 (s, 12H).



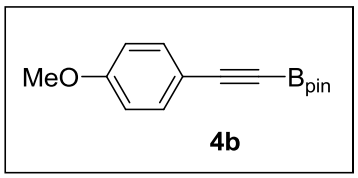
3e

2-(3-Methyl-1-butyn-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3e). [23] A colorless liquid. Yield: 86% (1.67 g, 8.6 mmol). Bp. 125 ℃/30 Torr. ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 1.18 (d, J = 6.6 Hz, 6H), 1.26 (s, 12H), 2.60 (septet, J = 7.2 Hz, 2H).



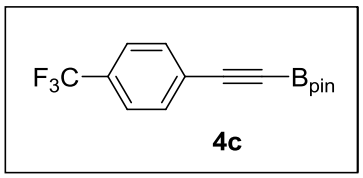
4a

2-[phenyl)ethynyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4a). [24] White solid. Yield 97% (2.22 g, 9.72 mmol). Bp. 150 ℃/2 Torr. ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 1.33 (s, 12H), 7.26-7.36 (m, 3H), 7.51-7.54 (m, 2H).



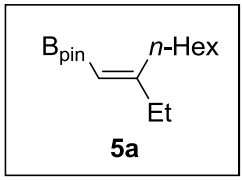
4b

2-[(4-Methoxyphenyl)ethynyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4b).[5] White solid. Yield: 89% (2.29 g, 8.88 mmol). Bp. 190 ℃/2 Torr. ^{1}H NMR (CDCl3, 300 MHz, rt): δ 1.31 (s, 12H), 3.80 (s, 3H), 6.82 (d, J = 9.9, 2H), 7.47 (d, J = 9.9, 2H).



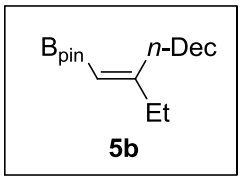
4c

2-[(4-Trifluoromethylphenyl)ethynyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4c).[5] White solid. Yield: 66% (1.96 g, 6.63 mmol). Bp. 150 ℃/2 Torr. ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 1.33 (s, 12H), 7.58 (d, J = 8.4, 2H), 7.63 (d, J = 8.4, 2H).



5a

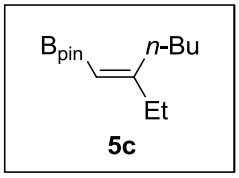
General Procedure for Zirconocene-Mediated Regio- and Stereoselective Synthesis of 2-[(*Z*)-2-Ethyl-1-octen-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5a). To a solution zirconocene dichloride (2.16 g, 7.38 mmol) in THF (36 mL) in a 100 mL of Schlenk tube under an Ar atmosphere was added dropwise *n*-BuLi (9.4 mL, 14.8 mmol, 1.57 M hexane solution) at -78 ℃. After the reaction mixture was stirred for 1 h at -78 ℃, atmospheric ethylene gas was introduced into the vessel for 1 h at -78 ℃. The reaction mixture was warmed to room temperature and 4,4,5,5-tetramethyl-2-(1-octyn-1-yl)-1,3,2-dioxaborolane (**1a**) (1.6 mL, 6.15 mmol) was added. The mixture was stirred for 1 h, quenched with 1 M hydrochloric acid (20 mL), and extracted with diethyl ether (15 mL × 2). The combined ethereal layer was washed with brine and dried over $MgSO_4$. Filtration and evaporation afforded a yellow oil. Bulb to bulb distillation (145 ℃/2 Torr) gave **2a** (1.31 g, 4.93 mmol, 81% yield) as a colorless oil. FT-IR (neat, cm^{-1}): 2977 (s), 2963 (s), 2929 (m), 2859 (m), 1636 (s), 1461 (m), 1379 (s), 1371 (s), 1321 (s), 1269 (m), 1248 (m), 1165 (m), 1146 (m), 1111 (w), 969 (m), 898(w), 865 (m), 852 (m). ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 0.89 (t, J = 7.5 Hz, 3H), 1.04 (t, J = 7.5 Hz, 3H), 1.22-1.42 (m, 20H), 2.11 (dq, J = 1.5, 7.5 Hz, 2H), 2.39 (t, J = 7.5 Hz, 2H), 5.11 (t, J = 1.5 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, rt): δ 12.1, 14.1, 22.6, 24.8, 29.2, 29.6, 31.6, 31.7, 35.0, 82.5, 169.1. The carbon signal adjacent to B was not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt): δ 29.9. MS (EI, m/z (relative intensity)): 266 (M^+, 7), 251 (5), 196 (15), 140 (10), 139 (100), 138 (47), 109 (12), 101 (28), 95 (21), 85 (14), 84 (52), 83 (23), 81 (15), 69 (18), 67 (14). Anal. Calcd for $C_{16}H_{31}BO_2$: C, 72.18; H, 11.74%. Found: C, 72.00; H, 11.52%.



5b

2-[(*Z*)-2-Ethyl-1-dodecen-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5b). A colorless oil. Yield: 85% (824 mg, 2.56 mmol). Bp. 180 ℃/1.1 Torr. FT-IR (neat, cm^{-1}):

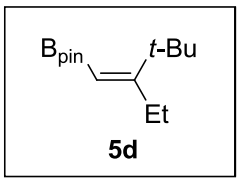
2976 (m), 2964 (m), 2926 (s), 2873 (m), 1636 (m), 1462 (w), 1404 (s), 1388 (m), 1379 (m), 1370 (m), 1321 (s), 1264 (w), 1147 (s). ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 0.88 (t, J = 7.5 Hz, 3H), 1.01 (t, J = 7.5 Hz, 3H), 1.20-1.57 (m, 28H), 2.13 (dq, J = 1.3, 7.5 Hz, 2H), 2.39 (t, J = 7.7 Hz, 2H), 5.13 (t, J = 1.5 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, rt): δ 12.2, 14.1, 22.7, 24.8, 29.4, 29.5, 29.57, 29.64 (×3), 31.6, 31.9, 35.0, 82.4, 169.0. The carbon signal adjacent to B was not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt): δ 29.9. MS (EI, m/z (relative intensity)): 322 (M^+, 3), 196 (12), 139 (100), 101 (21), 95 (14), 84 (46), 81 (11), 69 (14), 67 (11). Anal. Calcd for $C_{20}H_{39}BO_2$: C, 74.52; H, 12.20%. Found: C, 74.48; H, 11.95%.



5c

2-[(*Z*)-2-Ethyl-1-hexen-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2c). A colorless oil. Yield: 58% (412 mg, 1.7 mmol). Bp. 95 ℃/1.3 Torr. ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 0.90 (t, J = 7.2 Hz, 3H), 1.0 (t, J = 7.2 Hz, 3H), 1.25 (s, 12H), 1.25-1.41 (m, 4H), 2.12 (q, J = 7.2 Hz, 2H), 2.39 (t, J = 7.6 Hz, 2H), 5.11 (t, J = 1.5 Hz, 1H).

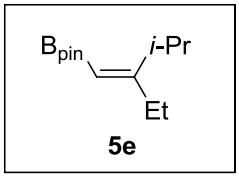
For synthesis of **5d** and **5e**, an excess amount of zirconocene dichloride (702 mg, 2.4 mmol) in THF (36 mL) and *n*-BuLi (2.94 mL, 4.8 mmol, 1.63 M hexane solution) were required, based on **1d** and **1e** (1.0 mmol) to complete the reaction.



5d

2-[(*Z*)-2-Ethyl-1-(3,3-dimethyl-1-buten-1-yl)]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5d). A colorless oil. Yield: 81% (193 mg, 0.81 mmol). R_f = 0.39 (hexane:ethyl acetate = 20:1). FT-IR (neat, cm^{-1}): 2977 (s), 2875 (m), 1640 (m), 1635 (m), 1622 (w), 1482 (m), 1464 (m), 1379 (m), 1370 (s), 1321 (s), 1268 (m), 1146 (s). ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 1.02 (t, J = 7.5 Hz, 3H), 1.04 (s, 9H), 1.26 (s, 12H), 2.10 (dq, J = 1.2, 7.5 Hz, 2H), 5.02 (t, J = 1.5 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, rt): δ 13.9, 24.8, 27.3,

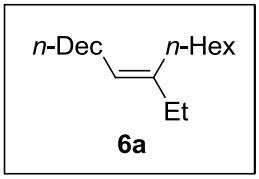
30.0, 37.9, 83.1, 168.0. The carbon signal adjacent to B was not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt): δ 31.1. MS (EI, m/z (relative intensity)): 238 (M^+, 19), 209 (59), 181 (26), 165 (33), 153 (22), 137 (21), 123 (54), 109 (96), 101 (88), 95 (27), 84 (39), 83 (100), 81 (40), 69 (37), 67 (31). Anal. Calcd for $C_{14}H_{27}BO_2$: C, 70.60; H, 11.43%. Found: C, 70.34; H, 11.27%.



5e

2-[(*Z*)-2-Ethyl-1-(3-methyl-1-buten-1-yl)]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5e). A colorless oil. Yield: 70% (156 mg, 0.70 mmol). R_f = 0.38 (hexane:ethyl acetate = 20:1). FT-IR (neat, cm^{-1}): 2977 (s), 2965 (s), 2935 (m), 2873 (m), 1632 (s), 1468 (m), 1403 (m), 1389 (m), 1379 (s), 1371 (s), 1320 (s), 1262 (m), 1146 (s). ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 1.00 (d, J = 7.2 Hz, 6H), 1.02 (t, J = 7.2 Hz, 3H), 1.25 (s, 12H), 2.07 (dq, J = 1.5, 7.2 Hz, 2H), 5.05 (t, J = 1.5 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, rt): δ 12.5, 21.6, 24.6, 24.8, 33.3, 82.5, 173.4. The carbon signal adjacent to B was not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt): δ 29.9. MS (EI, m/z (relative intensity)): 224 (M^+, 19), 167 (52), 125 (36), 124 (90), 123 (49), 109 (30), 101 (100), 96 (21), 95 (39), 85 (34), 84 (78), 83 (86), 69 (36), 67 (32). Anal. Calcd for $C_{13}H_{25}BO_2$: C, 69.66; H, 11.24%. Found: C, 69.27; H, 11.07%.

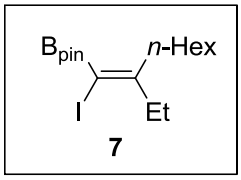
General Procedure for Suzuki-Miyaura Cross-Coupling Reaction of 5 with Alkyl Bromides: (Condition in Scheme 2-7)



6a

(*Z*)-7-Ethyloctadec-7-ene (6a). To a solution of bis(dibenzylidene)palladium ($Pd(dba)_2$) (29 mg, 0.05 mmol, 5 mol %), $[HP(t\text{-}Bu)_2Me]BF_4$ (25.0 mg, 0.10 mmol, 10 mol %), and 2-[(*Z*)-2-ethyl-1-octen-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5a**) (304 μL, 1.0 mmol) in THF (2.5 mL) in a 20 mL of Schlenk tube under an Ar atmosphere were added *n*-decyl bromide (270 μL, 1.32 mmol) and KOH (168 mg, 3.0 mmol) at room

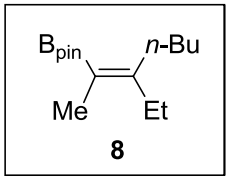
temperature. After being stirred for 24 h at 20 ℃, the reaction mixture was then poured into diethyl ether (30 mL), filtered through a short pad of silica gel with copious washings with diethyl ether (~10 mL),. Evaporation afforded a brown oil. Column chromatography on silica gel gave **6a** (261 mg, 0.93 mmol, 93% yield) as a colorless liquid. R_f = 0.87 (hexane). FT-IR (neat, cm^{-1}): 2958 (s), 2925 (m), 2872 (m), 2855 (m), 1462 (w). ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 0.88 (t, J = 6.9 Hz, 3H), 0.89 (t, J = 6.6 Hz, 3H), 0.97 (t, J = 7.5 Hz, 3H), 1.26-1.38 (m, 24H), 1.95-2.02 (m, 6H), 5.09 (t, J = 7.2 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, rt): δ 12.96, 14.11 (×2), 22.69 (×2), 27.69, 28.53, 29.39, 29.44, 29.53, 29.58, 29.64, 29.68, 29.70, 30.21, 30.23, 31.87, 31.95, 123.51, 141.04. MS (EI, m/z (relative intensity)): 280 (M^+, 17), 125 (28), 111 (68), 97 (75), 83 (66), 70 (100), 69 (82), 67 (24). Anal. Calcd for $C_{20}H_{40}$: C, 85.63; H, 14.37%. Found: C, 85.37; H, 14.19%.



7

2-[(*E*)-2-Ethyl-1-iodo-1-octen-1-yl)]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (7). To a solution zirconocene dichloride (2.10 g, 7.2 mmol) in THF (24 mL) in a 100 mL of Schlenk tube under an Ar atmosphere was added dropwise *n*-BuLi (8.8 mL, 14.4 mmol, 1.64 M hexane solution) at -78 ℃. After the reaction mixture was stirred for 1 h at -78 ℃, atmospheric ethylene gas was introduced into the vessel for 1 h at -78 ℃. The reaction mixture was wormed to room temperature and 4,4,5,5-tetramethyl-2-(1-octyn-1-yl)-1,3,2-dioxaborolane (**1a**) (1.6 mL, 6.0 mmol) was added. After 1 h, *i*-PrOH (367 μL, 4.8 mmol) was added and the reaction mixture was stirred for additional 1 h. Iodine (1.52 g, 6.0 mmol) was added to the mixture and the mixture was stirred overnight at room temperature and quenched with sodium sulfite, and extracted with diethyl ether (10 mL × 2). The combined ethereal layer was washed with brine and dried over $MgSO_4$. Filtration, evaporation, and bulb to bulb distillation (160 ℃/1.6 Torr) gave **5** (1.98 g, 5.0 mmol, 84％ yield) as a yellow liquid. FT-IR (neat, cm^{-1}): 2975 (s), 2930 (s), 2858 (s), 1596 (m), 1462 (s), 1372 (s), 1273 (m), 1144 (m), 908 (s), 853 (s). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 0.87 (t, J = 6.8 Hz, 3H), 1.00 (t, J = 7.5 Hz, 3H), 1.25-1.43 (m, 20H), 2.32-2.43 (m, 4H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, rt): δ 11.5,

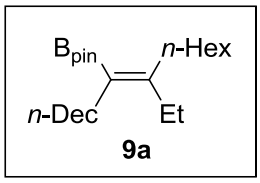
14.0, 22.5, 24.5, 29.1, 29.2, 31.5, 35.1, 35.8, 84.1, 163.5. The carbon signal adjacent to B was not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt): δ 28.6. MS (EI, m/z (relative intensity)): 392 (M^+, 17), 335 (18), 265 (10), 195 (32), 137 (56), 109 (19), 101 (100), 95 (37), 85 (45), 83 (57), 81 (28), 67 (25). Anal. Calcd for $C_{16}H_{30}BIO_2$: C, 49.01; H, 7.71%. Found: C, 49.07; H, 7.74%.



8

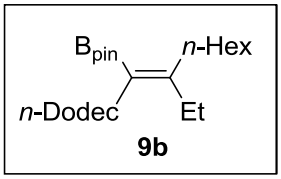
2-[(*Z*)-3-ethyl-2-heptene-2-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (8). To a solution of zirconocene dichloride (175 mg, 0.60 mmol) in THF (3.0 mL) in a 50 mL of Schlenk under an Ar atmosphere were added dropwise *n*-BuLi (0.74 mL, 1.2 mmol, 1.62 M THF solution) at -78 ℃. After the reaction mixture was stirred for 1 h at -78 ℃, atmospheric ethylene gas was introduced into the vessel for 1 h at -78 ℃. The reaction mixture was warmed to room temperature and 2-(1-hexyn-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1c**) (116 μL, 0.5 mmol) was added. After the mixture was stirred for 1 h at room temperature, *i*-PrOH (31 μL, 0.4 mmol) was added and the reaction mixture was stirred for additional 1 h. To the mixture were added CuCl (59.4 mg, 0.60 mol), $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), DMPU (121 μL, 0.90 mmol), and iodomethane (62 μL, 1.00 mmol). The mixture was stirred for 1 h at 50 ℃ and quenched with 1 M hydrochloric acid (10 mL), and extracted with diethyl ether (10 mL × 2). The combined ethereal layer was washed with brine and dried over $MgSO_4$. Filtration, evaporation, and bulb to bulb distillation (130 ℃/2 Torr) gave **4** (86 mg, 0.17 mmol, 68% yield) as a colorless oil. FT-IR (neat, cm^{-1}): 2977 (s), 2964 (s), 2931 (s), 2872 (s), 2861 (s), 1622 (m), 1455 (m), 1356 (s), 1283 (m), 1196 (s), 965 (m), 874 (m), 849 (m). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 0.90 (t, J = 7.2 Hz, 3H), 0.96 (t, J = 7.5 Hz, 3H), 1.23-1.38 (m, 16H), 1.68 (s, 3H), 2.10 (t, J = 7.5 Hz, 2H), 2.30 (t, J = 7.5 Hz, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, rt): δ 12.4, 14.1, 15.9, 23.0, 24.8, 25.5, 32.2, 35.3, 82.6, 157.7. The carbon signal adjacent to B was not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt): δ 30.8. MS (EI, m/z (relative intensity)): 252 (M^+, 22), 210 (24), 195 (49), 153 (100), 123 (23), 109 (23), 101 (97), 95 (26), 84 (58), 83 (54), 81 (31), 69 (35), 67 (25). Anal. Calcd for $C_{15}H_{29}BO_2$: C, 71.44; H, 11.59%. Found: C, 71.39; H, 11.66%.

General Procedure for Preparation of Alkylzinc Reagents. Zinc dust (<10 μm, Aldrich, 98+%, 1.31 g, 20 mmol) was placed in an argon-flushed Schlenk flask and dried using a heat gun under high vacuum. The reaction flask was flushed with argon, and then THF (ca. 0.8 M) was added. 1-Iododecane (2.5 mL, 10 mmol) and Me_3SiCl (9 mol %, 120 μL, heating to ebullition for 15 s) were added at 25 ℃, and the resulting reaction mixture was stirred at 60 ℃ for 3 days. Capillary GC analysis of a hydrolyzed aliquot containing an internal standard showed a concentration of the solution.



9a

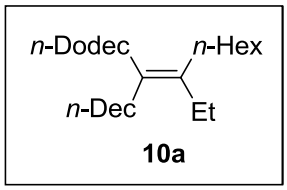
General Procedure for Negishi Cross-Coupling Reaction of 7 with Alkylzinc Reagents: Formation of 2-[(*Z*)-7-Ethyl-7-octadecen-8-yl)]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (9a). To a solution of $PdCl_2$(dppf) (36.5 mg, 0.045 mmol, 4.5 mol %) in DMI (3.5 mL) and NEt_3 (500 μL) in a 20 mL of Schlenk tube under an Ar atmosphere were added n-decylzinc iodide (1.57 M, 960 μL, 1.5 mmol in THF solution) and **7** (324 μL, 1.0 mmol) at room temperature. The reaction mixture was stirred overnight at 60 ℃, quenched with 1.0 M HCl, and extracted with diethyl ether (15 mL × 2). The combined ethereal layer was washed with brine and dried over $MgSO_4$. Filtration and evaporation afforded a brown oil. Column chromatography on silica gel (hexane:ethyl acetate = 20:1) gave **9a** (281 mg, 0.69 mmol, 69% yield) as a colorless liquid. R_f = 0.40 (hexane:ethyl acetate = 20:1). Bp: 180 ℃/1.4 Torr. FT-IR (neat, cm^{-1}): 2974 (s), 2925 (s), 2871 (s), 1616 (m), 1464 (s), 1360 (s), 1286 (m), 1147 (s), 965 (w), 871 (w). ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 0.88 (t, J = 6.6 Hz, 6H), 0.96 (t, J = 7.5 Hz, 3H), 1.20-1.38 (m, 24H), 1.26 (s, 12H), 2.05-2.12 (m, 4H), 2.23 (t, J = 7.5 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, rt): δ 13.4, 14.1 (×2), 22.66, 22.68, 24.8, 29.4, 29.61 (×4), 29.64, 29.8, 30.2, 30.67, 30.72, 31.8, 31.9, 35.6, 82.6, 155.2. The carbon signal adjacent to B was not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt): δ 31.3. MS (EI, m/z (relative intensity)): 406 (M^+, 13), 208 (23), 196 (47), 152 (18), 139 (61), 123 (16), 109 (24), 101 (77), 84 (100), 69 (35), 67 (22). Anal. Calcd for $C_{26}H_{51}BO_2$: C, 76.82; H, 12.65%. Found: C, 76.87; H, 12.80%.



9b

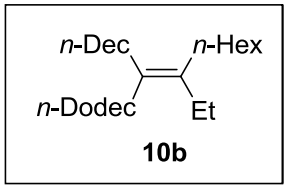
2-[(*Z*)-7-Ethyl-7-icosen-8-yl)]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (9b). A colorless liquid. Isolated yield was 57% (247 mg, 0.57 mmol). R_f = 0.40 (hexane/AcOEt = 20:1). Bp. 205 ℃/1.1 Torr. FT-IR (neat, cm^{-1}): 2974 (s), 2925 (s), 2871 (s), 1616 (m), 1464 (s), 1360 (s), 1286 (m), 1147 (s), 965 (w), 871 (w). ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 0.88 (t, J = 6.6 Hz, 6H), 0.96 (t, J = 7.5 Hz, 3H), 1.20-1.38 (m, 28H), 1.26 (s, 12H), 2.05-2.12 (m, 4H), 2.23 (t, J = 7.5 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, rt): δ 13.4, 14.1 (×2), 22.65, 22.68, 24.8, 29.4, 29.6 (×4), 29.65, 29.68, 29.71, 29.8, 30.2, 30.66, 30.72, 31.8, 31.9, 35.6, 82.6, 155.2. The carbon signal adjacent to B was not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt): δ 31.1. MS (EI, m/z (relative intensity)): 434 (M^+, 10), 196 (43), 139 (59), 101 (75), 95 (30), 85 (54), 84 (100), 83 (66), 69 (35). Anal. Calcd for $C_{28}H_{55}BO_2$: C, 77.39; H, 12.76%. Found: C, 77.23; H, 12.76%.

Preparation of **10a** and **10b** was carried out analogously to **6a.**



10a

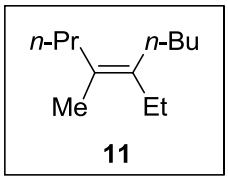
(*Z*)-7-Ethyl-8-decyl-7-icosene (10a). A colorless liquid. Isolated yield was 73% (158 mg, 0.35 mmol). R_f = 0.87 (hexane). FT-IR (neat, cm^{-1}): 2958 (s), 2925 (s), 2854 (m), 1466 (w), 1457 (m). ^{1}H NMR ($CDCl_3$, 300 MHz, rt): δ 0.87-0.95 (m, 12H), 1.27 (s, 44H), 1.93-2.00 (m, 8H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, rt): δ 13.81, 14.12 (×2), 22.72 (×2), 24.44, 29.26 (×2), 29.37, 29.39 (×2), 29.66, 29.67, 29.69 (×3), 29.71 (×3), 29.73 (×2), 30.01, 30.03, 31.22, 31.54, 31.64, 31.90 (×2), 31.94 (×2), 133.08, 134.77. MS (EI, m/z (relative intensity)): 448 (M^+, 46), 125 (38), 111 (67), 97 (100), 85 (45), 84 (47), 83 (90), 71 (56), 69 (93), 67 (22). Anal. Calcd for $C_{32}H_{64}$: C, 85.63; H, 14.37%. Found: C, 85.57; H, 14.60%.



10b

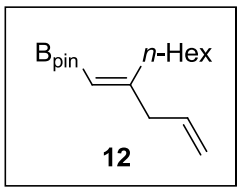
(*E*)-7-Ethyl-8-decyl-7-icosene (10b). A colorless liquid. Isolated yield was 90% (203 mg, 0.45 mmol). R_f = 0.87 (hexane). FT-IR (neat, cm^{-1}): 2958 (s), 2925 (s), 2854 (m), 1467 (w), 1457 (m). ^1H NMR ($CDCl_3$, 300 MHz, rt): δ 0.86-0.95 (m, 12H), 1.26 (s, 44H), 1.92-2.00 (m, 8H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz, rt): δ 13.80, 14.12 (×2), 22.72 (×2), 24.45, 29.27 (×2), 29.37, 29.40 (×2), 29.67, 29.69 (×3), 29.71 (×4), 29.73 (×2), 30.02, 30.04, 31.23, 31.55, 31.66, 31.91 (×2), 31.95 (×2), 133.09, 134.78. MS (EI, m/z (relative intensity)): 448 (M^+, 60), 125 (41), 111 (68), 97 (100), 85 (45), 84 (47), 83 (92), 71 (58), 69 (97), 67 (27). Anal. Calcd for $C_{32}H_{64}$: C, 85.63; H, 14.37%. Found: C, 85.42; H, 14.51%.

Preparation of **11** was carried out analogously to **6a**



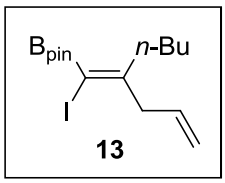
11

(*Z*)-4-Methyl-5-ethyl-4-nonene (11). A colorless liquid. Isolated yield was 74% (125 mg, 0.74 mmol). R_f = 0.85 (hexane). FT-IR (neat, cm^{-1}): 2961 (s), 2931 (s), 2872 (s), 1466 (m), 1457 (m). ^1H NMR (300 MHz, $CDCl_3$, rt): δ 0.88 (t, J = 7.2 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H), 0.93 (t, J = 7.2 Hz, 3H), 1.26-1.44 (m, 6H), 1.61 (s, 3H), 1.94-2.04 (m, 6H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, rt): δ 13.2, 14.1 (×2), 17.6, 21.7, 23.1, 25.2, 31.45, 31.53, 36.2, 127.8, 134.9. MS (EI, m/z (relative intensity)): 168 (M^+, 25), 125 (9), 97 (22), 84 (36), 83 (79), 69 (100), 67 (11). Anal. Calcd for $C_{12}H_{24}$: C, 85.63; H, 14.37%. Found: C, 85.38; H, 14.46%.



12

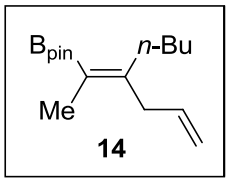
Preparation of 4,4,5,5-Tetramethyl-2-[(*E*)-2-(2-propen-1-yl)-1-octen-1-yl]-1,3,2-dioxaborolane (12). To a solution of zirconocene dichloride (702 mg, 2.4 mmol) in THF (10 mL) in a 50 mL of Schlenk under an Ar atmosphere were added dropwise *n*-BuLi (3.0 mL, 4.8 mmol, 1.6 M THF solution) and tributylphosphine (600 μL, 2.4 mmol) at -78 ℃. The reaction mixture was warmed to room temperature and stirred for 1 h. To the reaction mixture were added 1-alkynylboronate **3a** (527 μL, 2.0 mmol) and allyloxytrimethylsilane (505 μL, 3.0 mmol). After the mixture was stirred for 1 h at 50 ℃, the reaction mixture was quenched with 1.0 M hydrochloric acid (20 mL), and extracted with diethyl ether (25 mL × 2). The combined ethereal layers were washed with brine and dried over $MgSO_4$. Filtration, evaporation and bulb to bulb distillation (155 ℃/1.3 Torr) gave **12** (361 mg, 1.30 mmol, 65% yield) as a colorless liquid. FT-IR (neat, cm^{-1}): 2978 (s), 2959 (s), 2928 (s), 2859 (s), 1635 (s), 1401 (m), 1379 (s), 1319 (s), 1268 (s), 1145 (s), 972 (s), 912 (s), 850 (s). ^1H NMR (300 MHz, $CDCl_3$, rt): δ 0.88 (t, J = 6.6 Hz, 3H), 1.20-1.46 (m, 8H), 1.25 (s, 12H), 2.39 (t, J = 7.8 Hz, 2H), 2.84 (d, J = 7.2 Hz, 2H), 4.94-5.02 (m, 1H), 5.05 (brs, 1H), 5.14 (t, J = 1.2 Hz, 1H), 5.80 (ddt, J = 18.0, 9.0, 7.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, rt): δ 14.1, 22.6, 24.8, 29.1, 29.2, 31.6, 34.7, 43.6, 82.6, 116.5, 136.2, 165.3. The carbon signal adjacent to B was not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt): δ 29.7. MS (EI, m/z (relative intensity)): 278 (M^+, 10), 151 (59), 150 (33), 149 (26), 108 (100), 107 (61), 101 (45), 85 (20), 84 (30), 83 (33), 67 (26). Anal. Calcd for $C_{17}H_{31}BO_2$: C, 73.38; H, 11.23%. Found: C, 73.73; H, 11.50%.



13

Preparation of 2-[(*Z*)-1-Iodo-2-(2-propen-1-yl)-1-hexen-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (13). A 50 mL Schlenk tube under argon was charged with Cp_2ZrCl_2 (361 mg, 1.2 mmol), Mg (turning, 49 mg, 2.0 mmol), and 5 mL of THF. To the mixture were added 2-(1-hexen-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3c**) (279 μL, 1.2 mmol) and allyloxytrimethylsilane (165 μL, 1.0 mmol). After the reaction mixture was heated at 50

℃ for 1 h under argon, iodine (508 mg, 2.0 mmol) was added and the resulting mixture was stirred at room temperature for 12 h. The reaction mixture was quenched with aqueous solution of sodium sulfite, and extracted with ethyl acetate (10 mL x 3). Extract was dried over $MgSO_4$ and concentrated. Purification with bulb to bulb distillation (150 ℃/1.3 Torr) afforded the title compound **10** as a yellow liquid. Isolated yield was 56% (212 mg, 0.56 mmol). FT-IR (neat, cm^{-1}): 2958 (s), 2930 (s), 2928 (s), 1379 (s), 1372 (s), 1334 (s), 1272 (m), 1144 (s), 976 (s), 852 (s). ^1H NMR (300 MHz, $CDCl_3$, rt): δ 0.88 (t, J = 7.2 Hz, 3H), 1.23-1.40 (m, 4H), 1.28 (s, 12H), 2.40 (t, J = 7.5 Hz, 2H), 3.13 (d, J = 6.6 Hz, 2H), 5.05-5.10 (m, 1H), 5.11-5.17 (m, 1H), 5.74 (ddt, J = 17.1, 10.2, 6.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, rt): δ 13.8, 22.5, 24.5, 31.1, 35.8, 46.4, 84.2, 116.8, 133.7, 159.3. The carbon signal adjacent to B was not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt): δ 28.6. MS (EI, m/z (relative intensity)): 376 (M^+, 26), 276 (51), 234 (36), 149 (45), 121 (40), 107 (54), 101 (100), 93 (36), 84 (30), 85 (33), 83 (62), 81 (24), 79 (38), 67 (31). Anal. Calcd for $C_{15}H_{26}BIO_2$: C, 47.91; H, 6.97%. Found: C, 48.11; H, 6.98%.

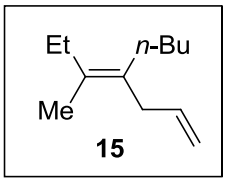


14

Preparation of 4,4,5,5-Tetramethyl-2-[(*Z*)-3-(2-propen-1-yl)-2-hepten-2-yl)]-1,3,2-dioxaborolane (14). Zinc bromide (75 mg, 0.33 mmol) in 20 mL of Schlenk was heated under reduced pressure for 5 min. After THF (0.42 mL) was added, the solution was cooled to 0 ℃. To a solution was added dropwise methylmagnesium bromide (270 μL, 0.27 mmol) at 0 ℃ and the reaction was stirred for 30 min. A solution of $Pd(PPh_3)_4$ (4.6 mg, 0.004 mmol, 2 mol %) and alkenyl iodide **13** (61 μL, 0.2 mmol) in THF (0.2 mL) was added to a cold solution and the mixture was stirred at room temperature for 18 h. The reaction mixture was quenched with 1.0 M HCl and extracted with diethyl ether (5 mL × 3). The combined toluene extracts were washed with $NaHCO_3$ and dried over anhydrous $MgSO_4$. The resulting solution was filtered, and purified by bulb to bulb distillation (130 ℃/1.3 Torr) to give 46 mg (0.17 mmol, 87%) of the title compound **14** as a colorless oil. FT-IR

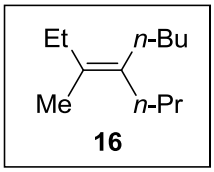
(neat, cm^{-1}): 2978 (s), 2957 (s), 2929 (s), 2872 (m), 1622 (m), 1388 (m), 1357 (s), 1293 (s), 1286 (m), 1147 (s), 1093 (m), 967 (m), 909 (s), 853 (s). ^1H NMR (300 MHz, $CDCl_3$, rt): δ 0.89 (t, J = 7.2 Hz, 3H), 1.21-1.47 (m, 16H), 1.69 (s, 3H), 2.31 (t, J = 7.8 Hz, 2H), 2.87 (d, J = 6.3 Hz, 2H), 4.94-5.06 (m, 2H), 5.67-5.81 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, rt): δ 14.0, 16.2, 22.9, 24.8, 32.0, 35.7, 37.3, 82.7, 115.0, 135.5, 153.0. The carbon signal adjacent to B was not observed due to low intensity; ^{11}B NMR ($CDCl_3$, 96 MHz, rt): δ 30.7. MS (EI, m/z (relative intensity)): 264 (M^+, 5), 136 (20), 121 (39), 107 (16), 101 (19), 84 (23), 83 (22), 81 (17), 67 (16). Anal. Calcd for $C_{16}H_{29}BO_2$: C, 72.73; H, 11.06%. Found: C, 72.52; H, 11.16%.

Preparation of (*E*)-3-Methyl-4-(2-propen-1-yl)-3-octene (15) was carried out analogously to **11**.



15

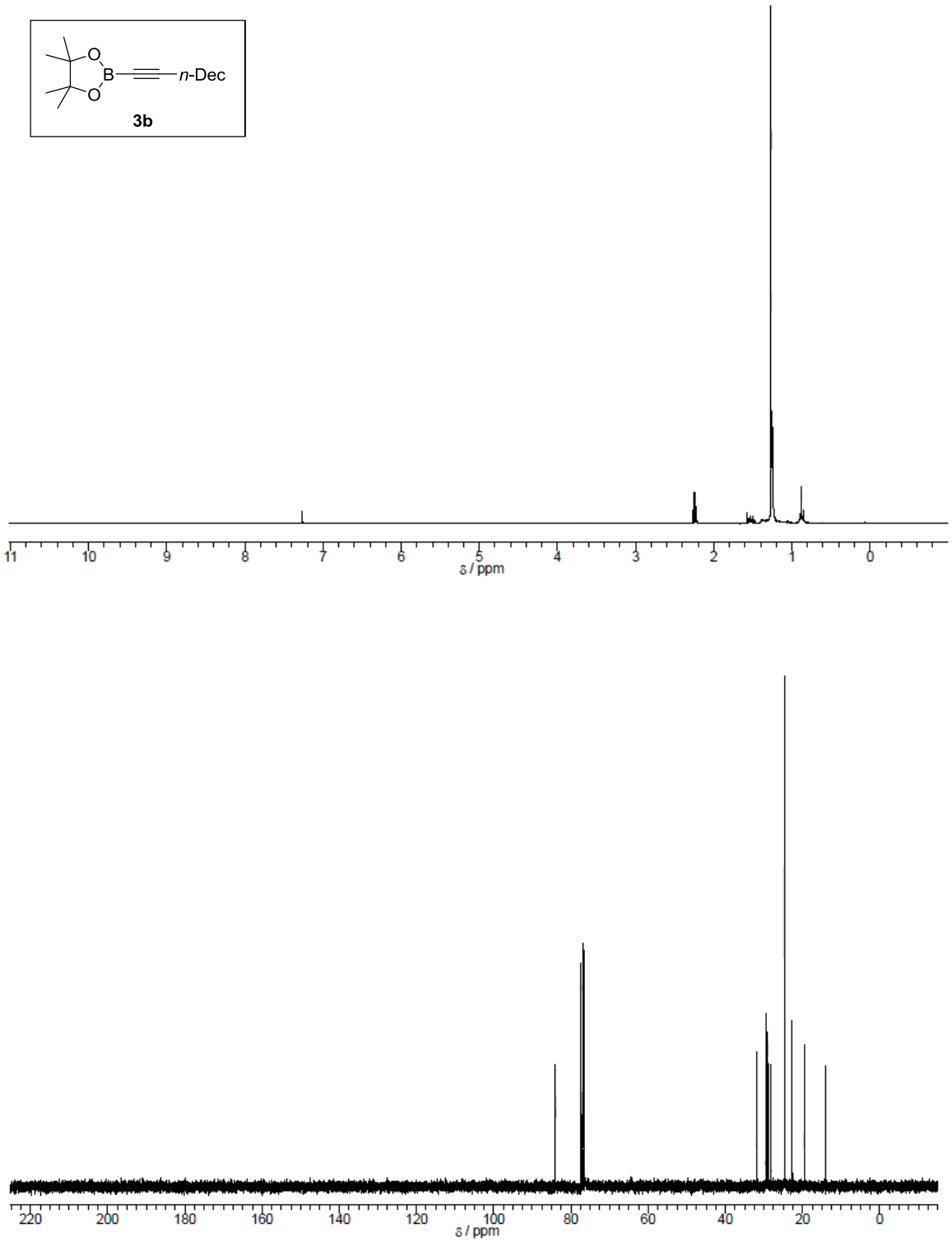
To a solution of bis(dibenzylidene)palladium ($Pd(dba)_2$) (8.6 mg, 0.015 mmol, 5 mol %), $[HP^tBu_2Me]BF_4$ (11.2 mg, 0.045 mmol, 15 mol %), and alkenylboronate **14** (90 μL, 0.30 mmol) in THF (0.75 mL) in a 20 mL of Schlenk tube under an Ar atmosphere were added bromoethane (29 μL, 0.39 mmol) and KOH (50.4 mg, 0.90 mmol) at room temperature. After being stirred for 12 h at 20 ℃, the reaction mixture was then poured into diethyl ether (30 mL), filtered through a short pad of silica gel with copious washings with diethyl ether (~10 mL). Evaporation afforded a brown oil. Column chromatography on silica gel gave **15** (36 mg, 0.216 mmol, 72% yield) as a colorless liquid. R_f = 0.81 (hexane). FT-IR (neat, cm^{-1}): 2960 (s), 2930 (s), 2873 (s), 2860 (s), 1636 (m), 1466 (s), 1456 (s), 1377 (m), 993 (m), 908 (s). ^1H NMR ($CDCl_3$, 300 MHz, rt): δ 0.88-0.92 (m 3H), 0.97 (t, J = 7.8 Hz, 3H), 1.26-1.34 (m, 4H), 1.63 (s, 3H), 1.97-2.01 (m, 4H), 2.75 (d, J = 6.3 Hz, 2H), 4.90-5.06 (m, 2H), 5.74 (ddt, J = 17.1, 10.2, 6.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz, rt): δ 13.3, 14.1, 17.5, 23.0, 27.1, 31.3, 31.8, 36.8, 114.1, 129.7, 131.8, 136.8. MS (EI, m/z (relative intensity)): 166 (M^+, 36), 137 (20), 123 (10), 109 (67), 96 (15), 95 (54), 83 (18), 82 (12), 81 (100), 79 (22), 77 (12), 77 (12), 69 (41), 68 (10), 67 (63). Anal. Calcd for $C_{12}H_{22}$: C, 86.67; H, 13.33%. Found: C, 86.89; H, 13.34%.



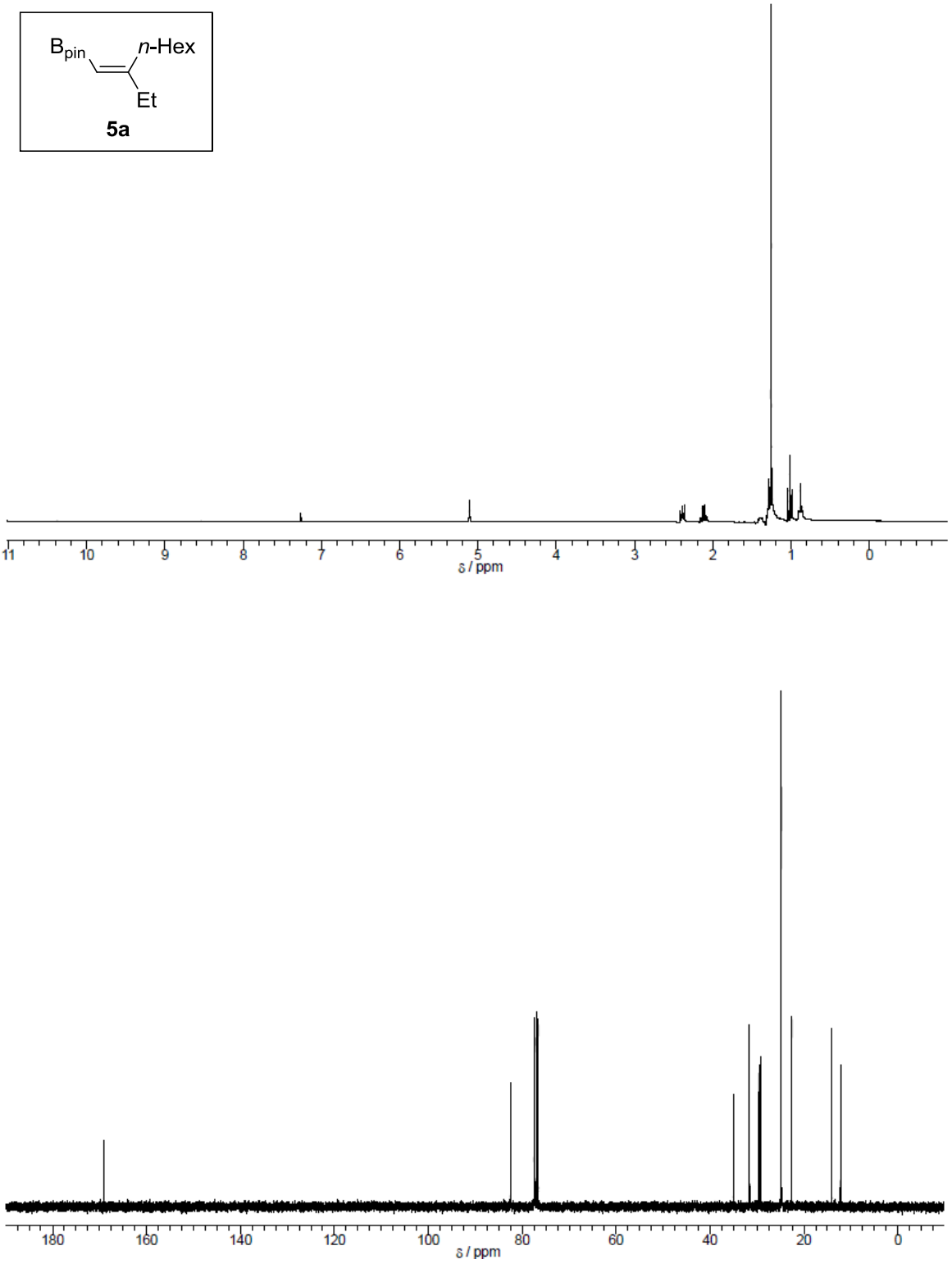
16

Preparation of (*Z*)-3-Methyl-4-propyl-3-octene (16) (Hydrogenation of 15): A two-necked 25 mL Schlenk tube equipped with a septum was placed under hydrogen atmosphere. To a solution of **15** (63 μL; 0.30 mmol) in hydrogen flushed benzene (3 mL) and chlorotris(triphenylphosphine)rhodium(I) (27.8 mg; 0.03 mmol; 10 mol %) were successively introduced, and the resulting brown solution was stirred at room temperature for 18 h, filtered over Celite. The volatiles were removed under reduced pressure. Column chromatography (silica gel; hexane) afforded **16** (421 mg, 0.025 mmol, 83% yield) as a colorless liquid. R_f = 0.85 (hexane). FT-IR (neat, cm^{-1}): 2959 (s), 2931 (s), 2872 (s), 1466 (m), 1458 (m). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 0.89 (t, J = 7.2 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H), 0.95 (t, J = 7.2 Hz, 3H), 1.27-1.40 (m, 6H), 1.62 (s, 3H), 1.93-2.06 (m, 6H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, rt): δ 13.3, 14.1, 14.3, 17.4, 21.9, 23.1, 27.1, 31.67, 31.71, 34.5, 130.1, 132.6. MS (EI, m/z (relative intensity)): 168 (M^+, 27), 125 (7), 97 (41), 84 (39), 83 (57), 69 (100), 67 (10). Anal. Calcd for $C_{12}H_{24}$: C, 85.63; H, 14.37%. Found: C, 85.66; H, 14.34%.

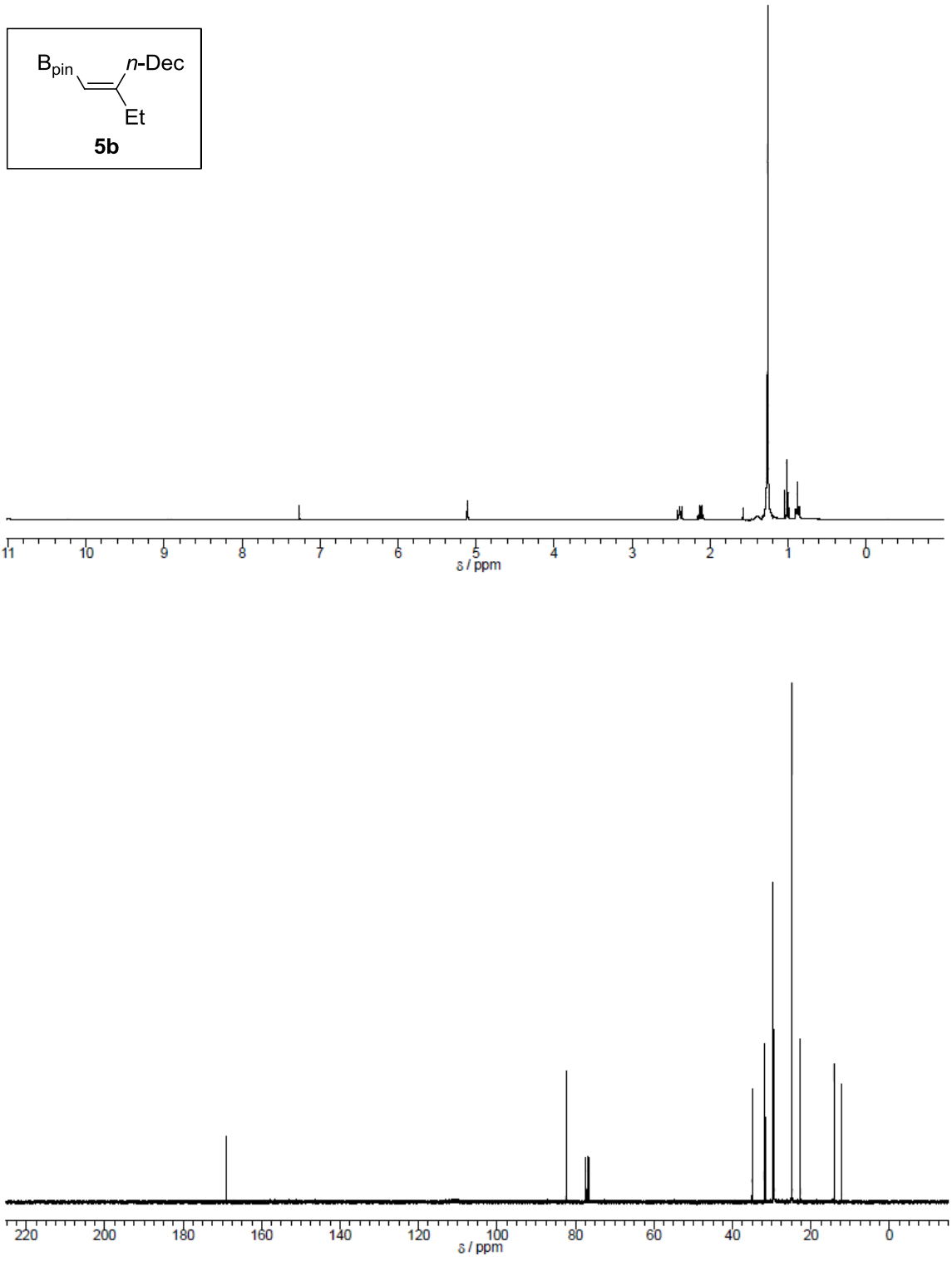
2-4-3 Copies of ^{1}H and $^{13}C\{^{1}H\}$ NMR Charts for the New Compounds.



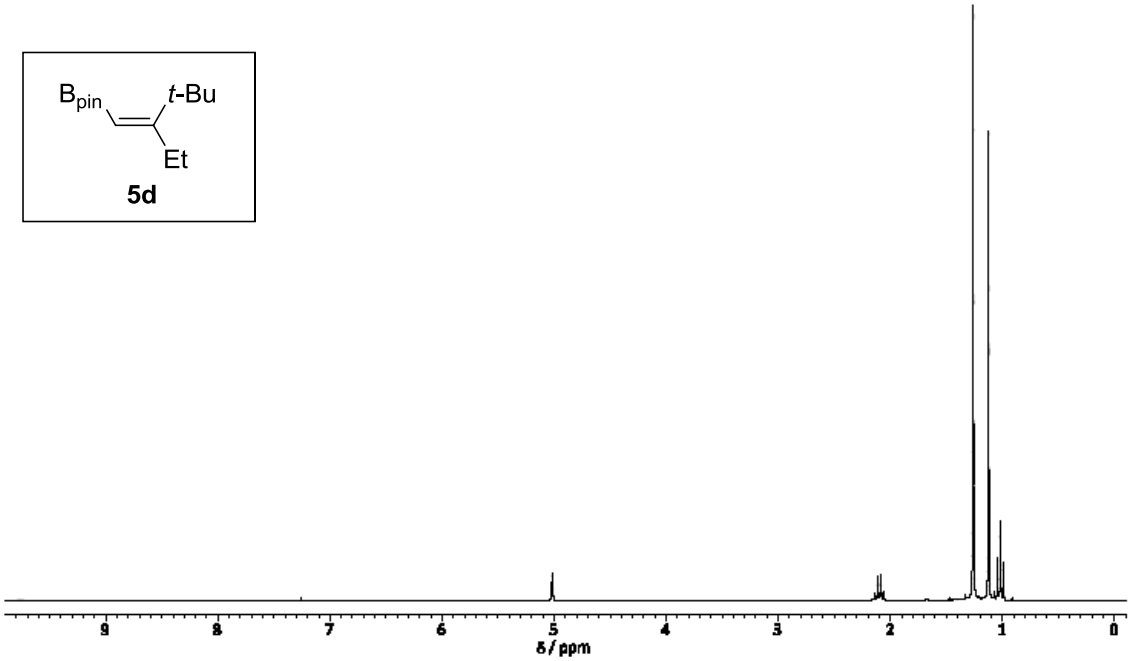
^{1}H NMR (300 MHz) and $^{13}C\{^{1}H\}$ NMR (75 MHz) spectra of **3b** (rt, $CDCl_3$).

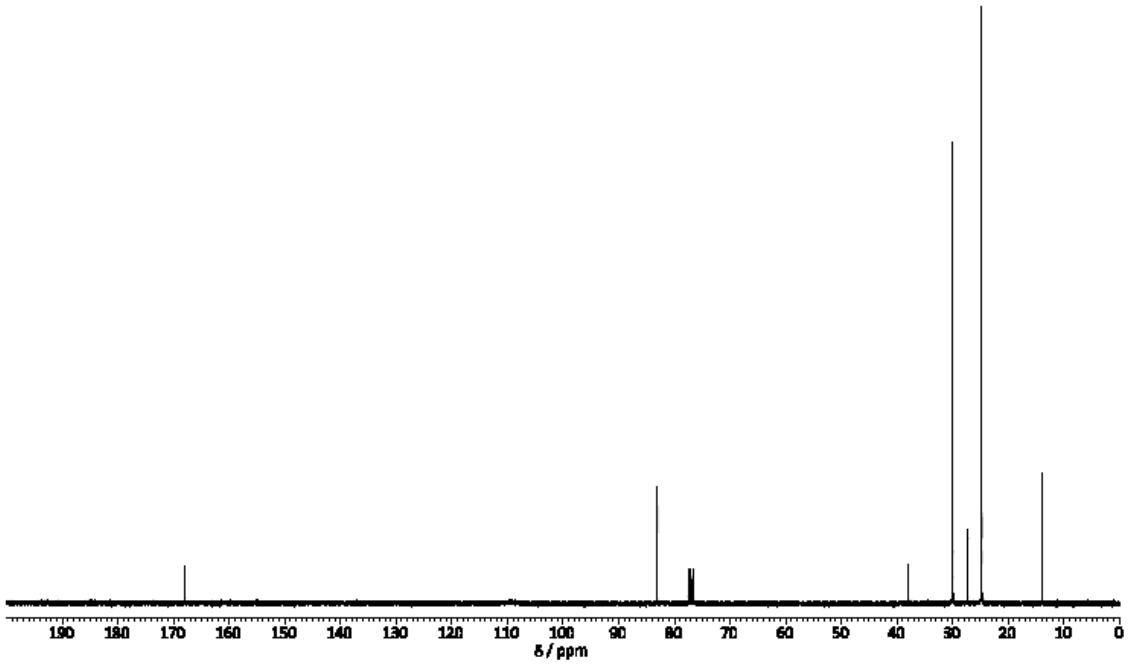


^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **5a** (rt, $CDCl_3$).

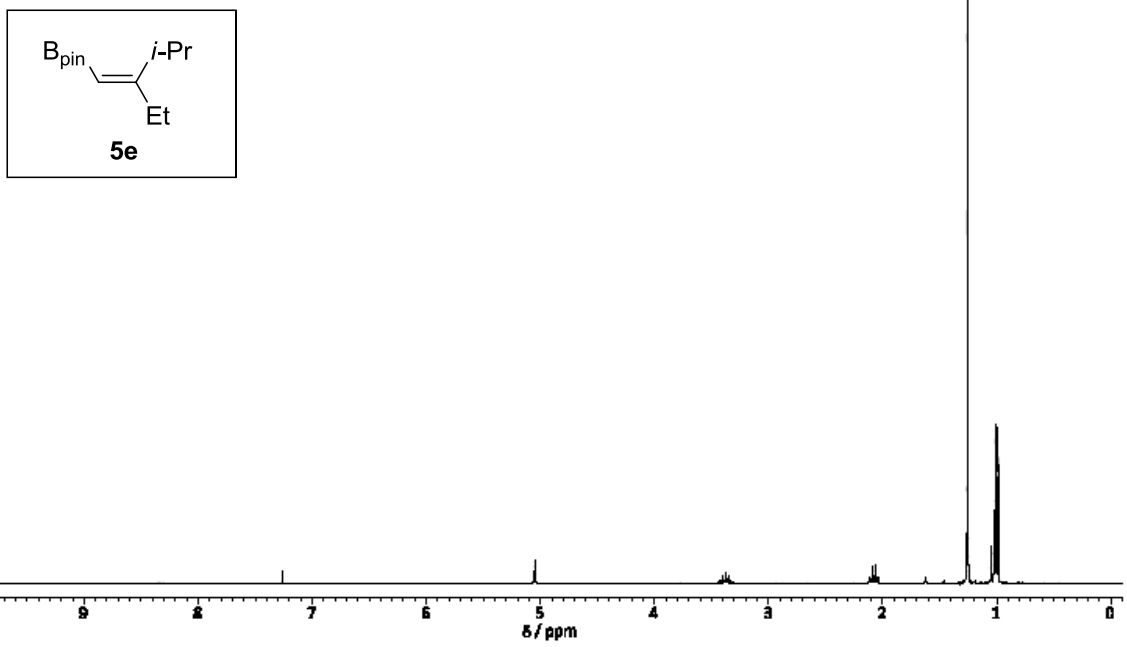


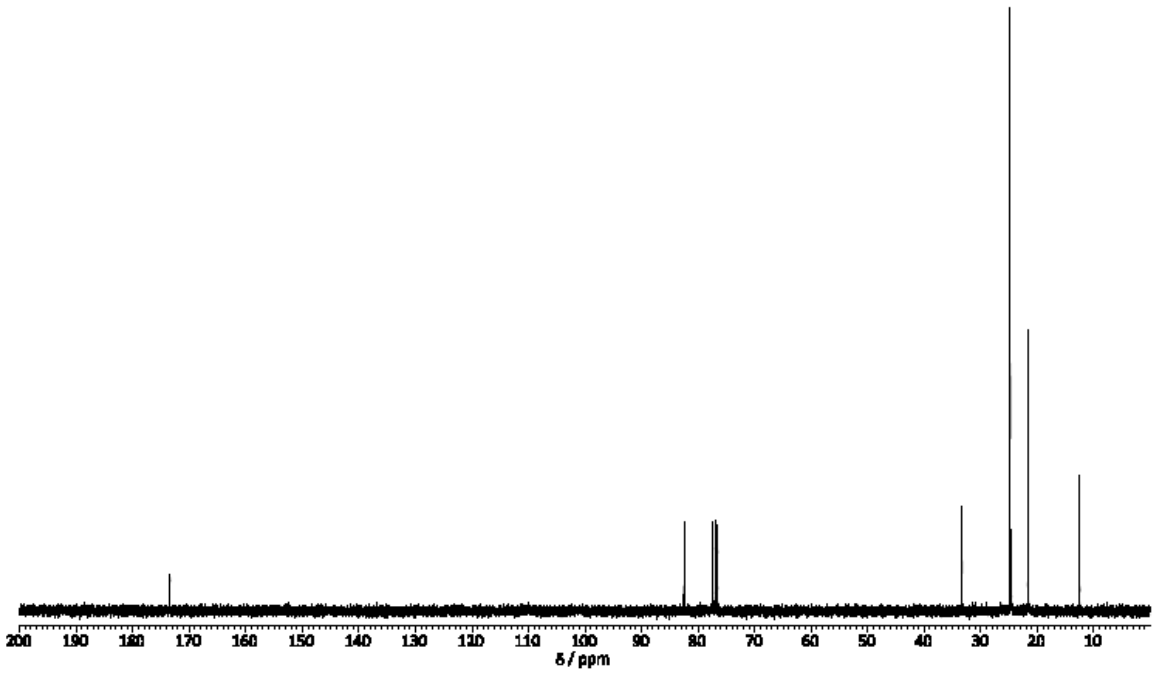
^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **5b** (rt, $CDCl_3$).



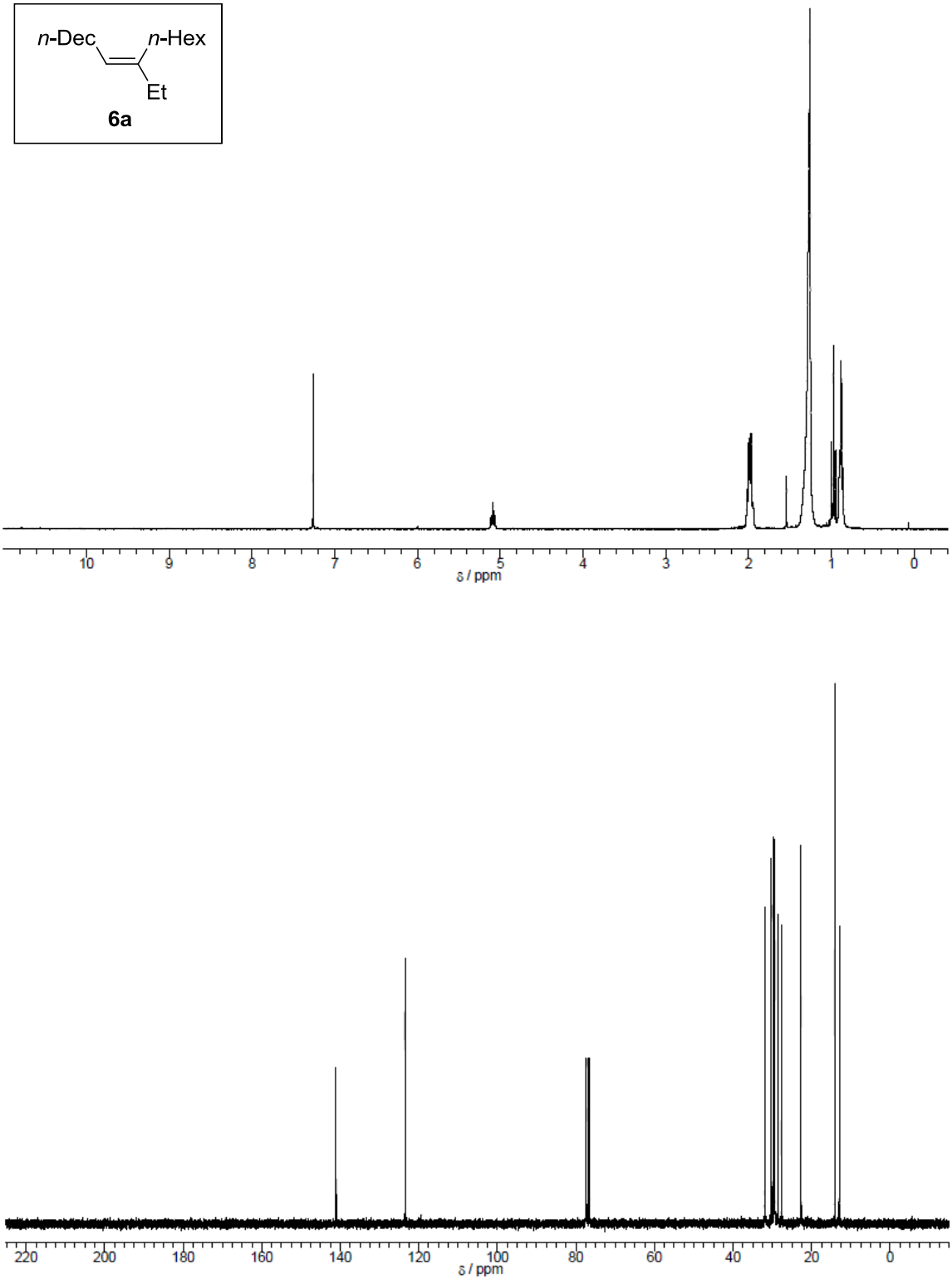


^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **5d** (rt, $CDCl_3$).

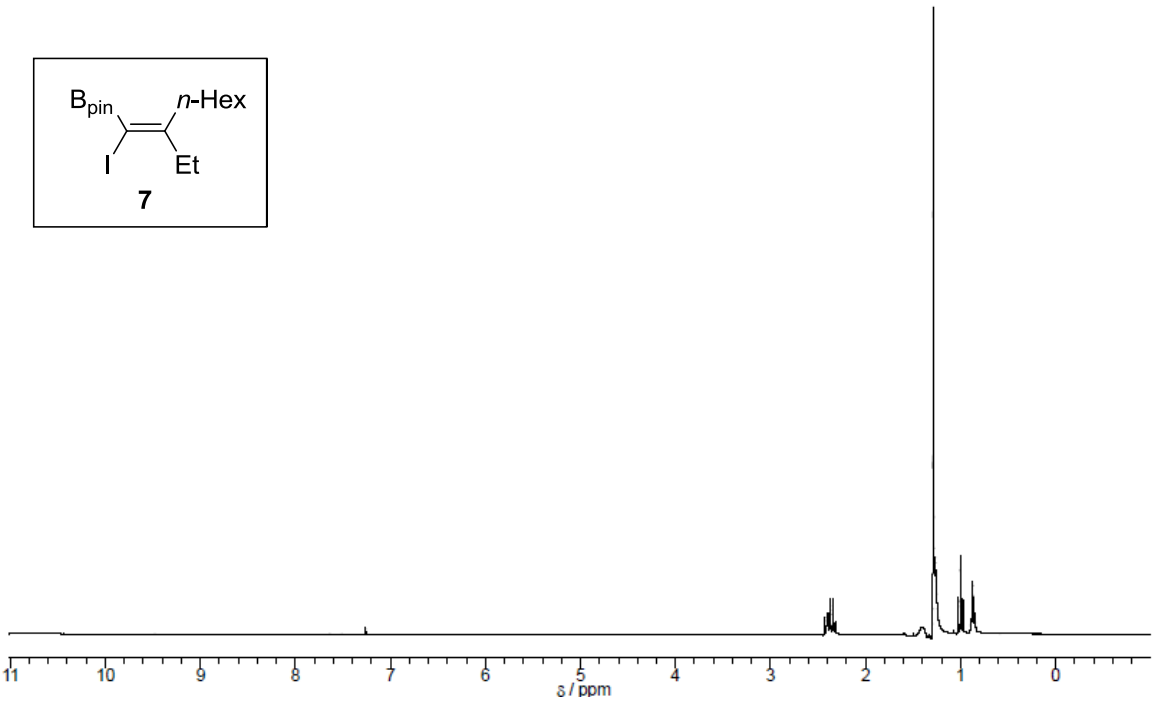


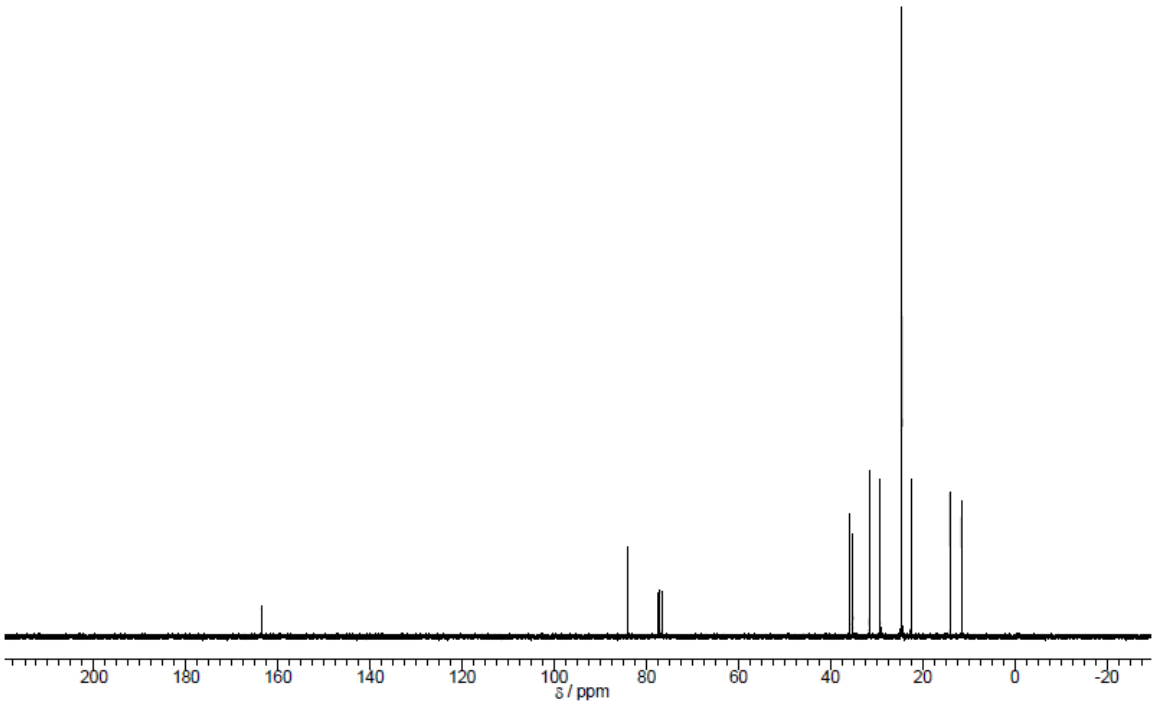


^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **5e** (rt, $CDCl_3$).

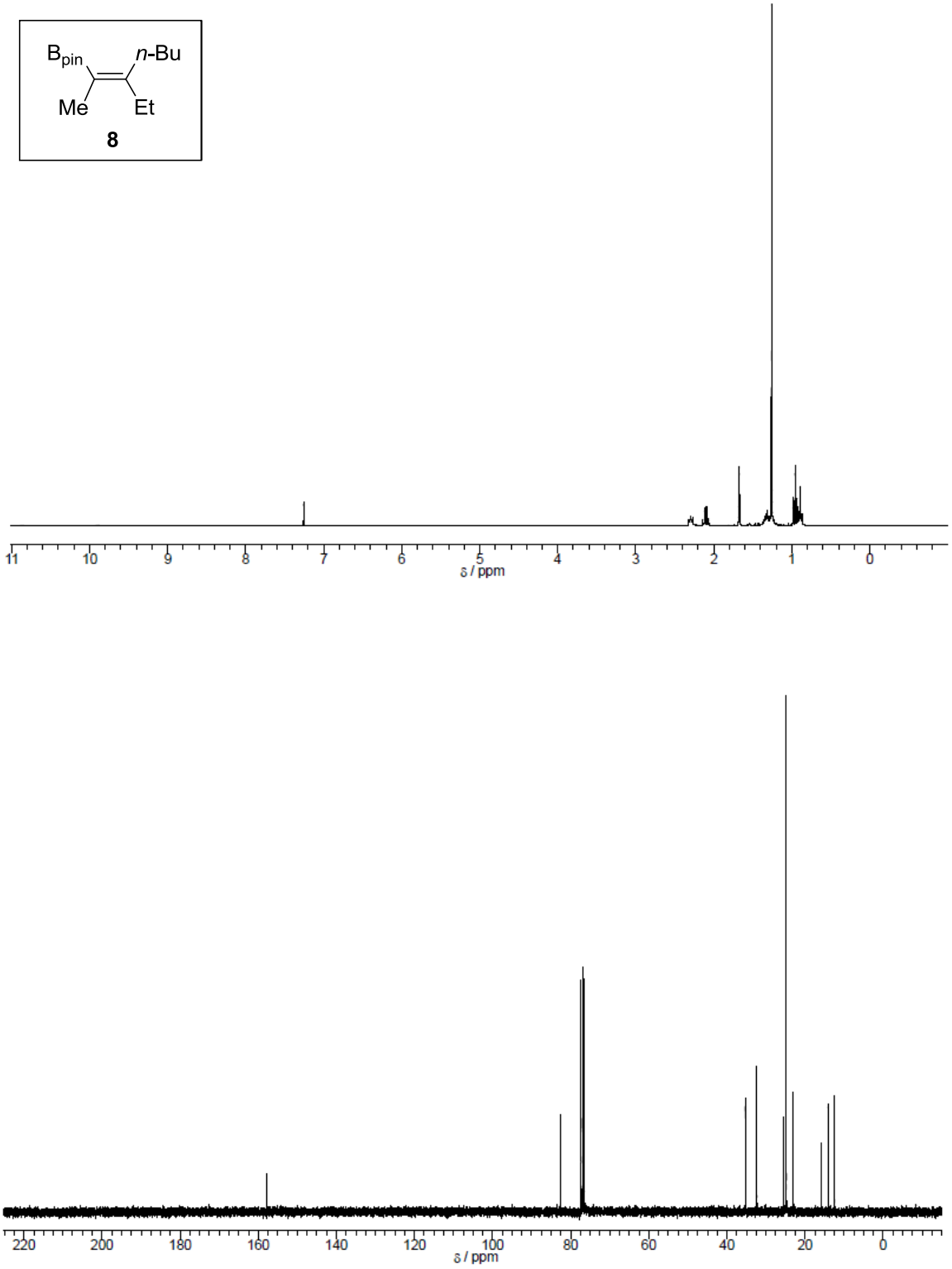


^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **6a** (rt, $CDCl_3$).

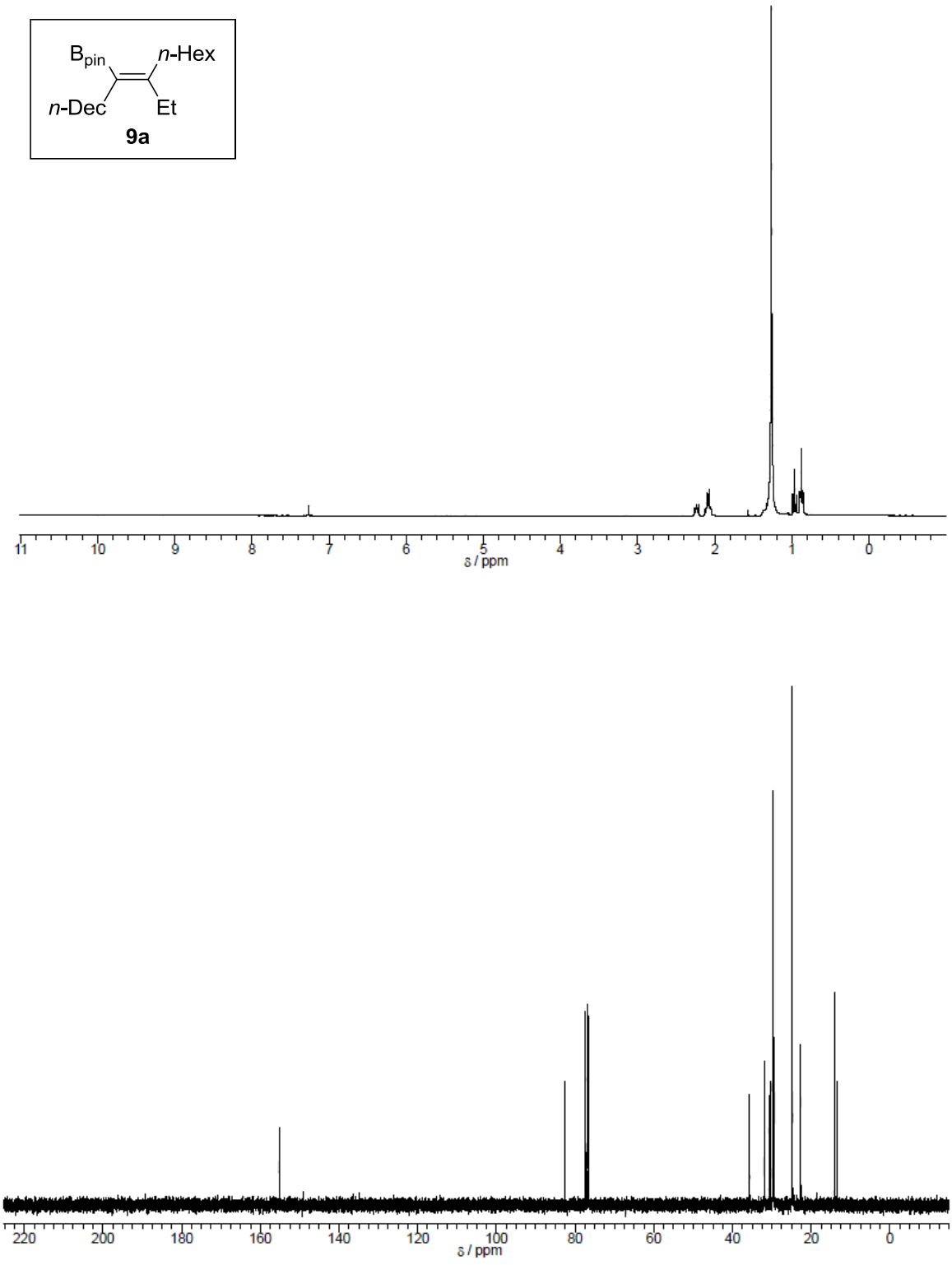




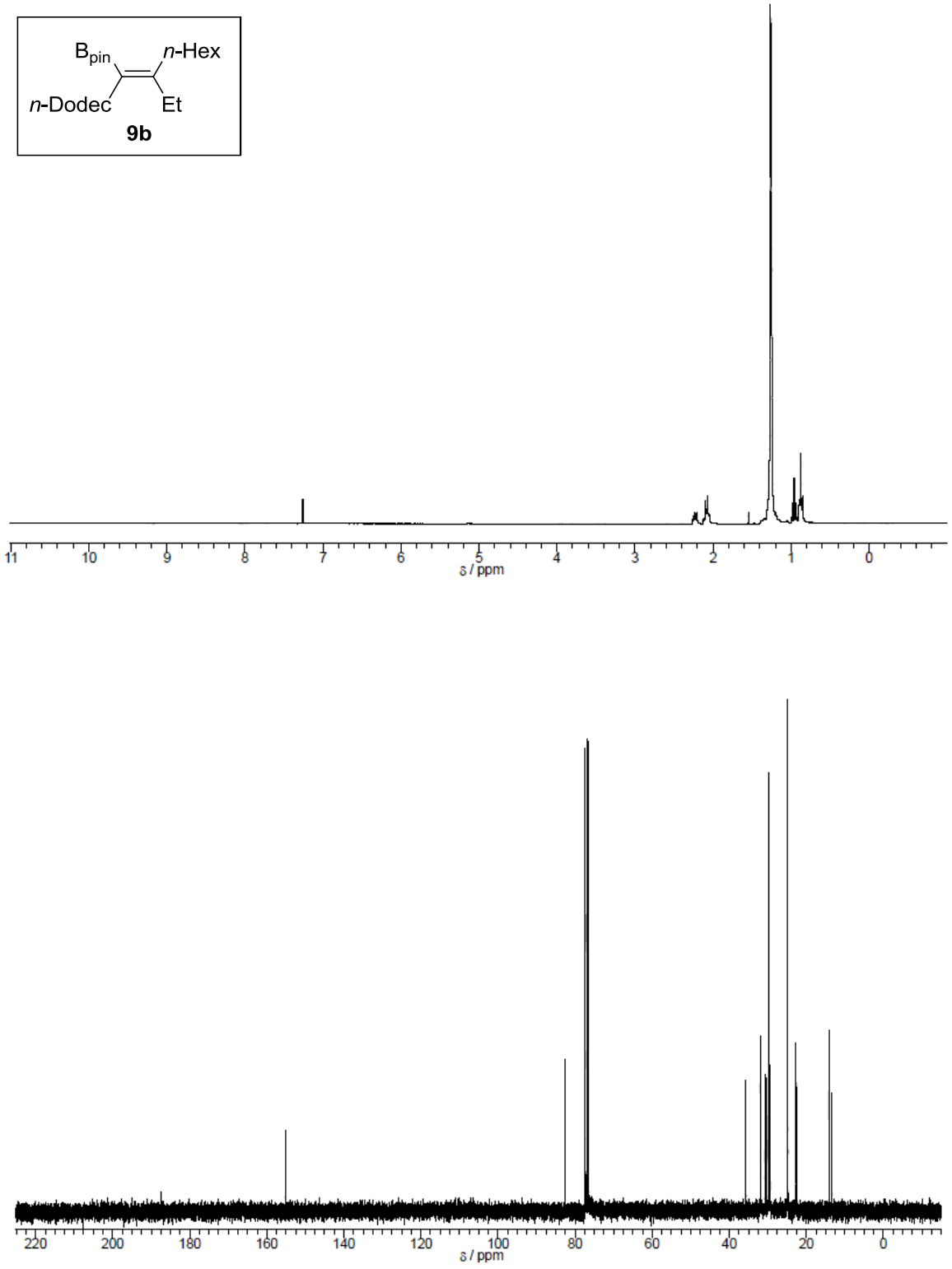
^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **7** (rt, $CDCl_3$).



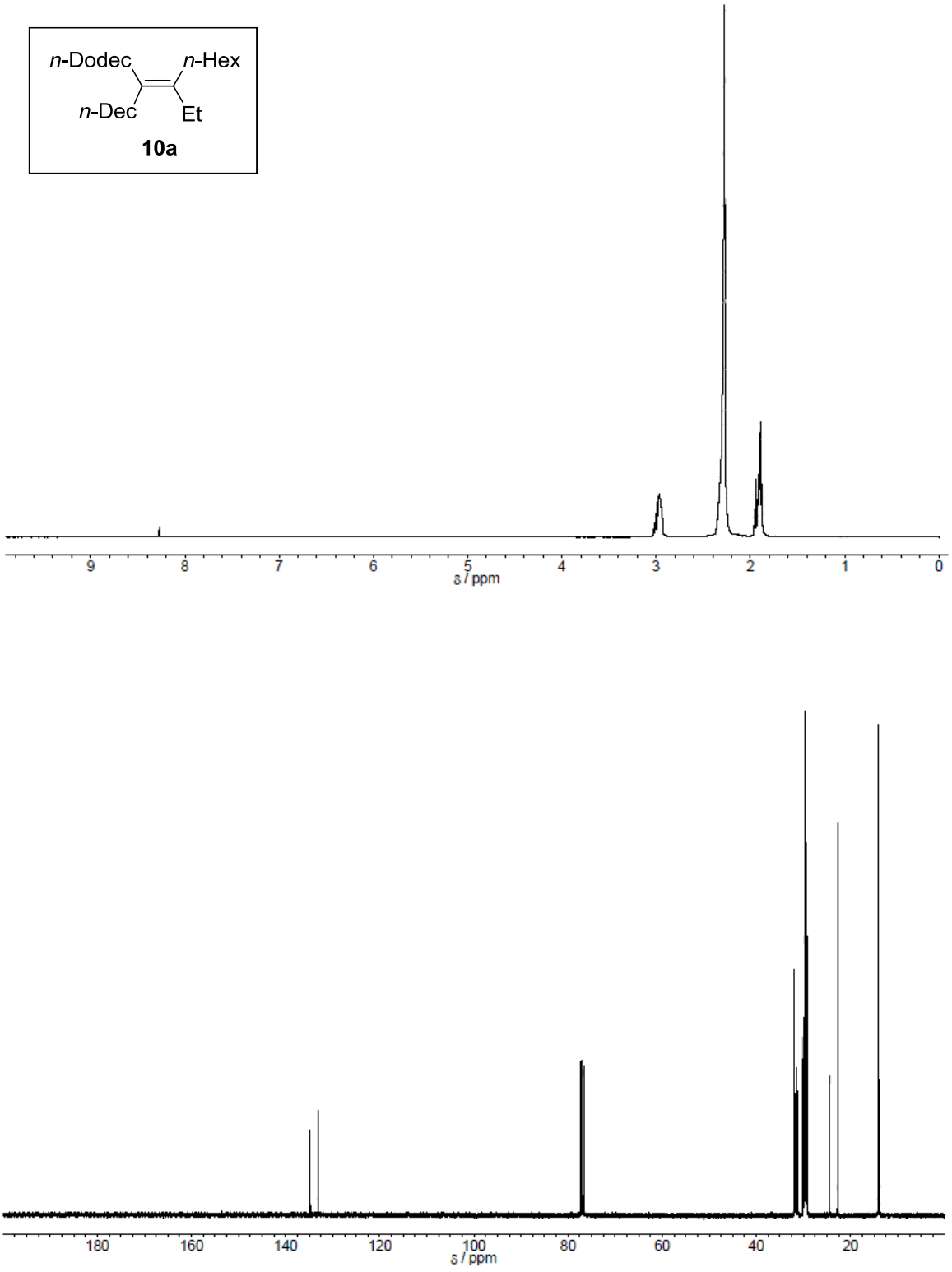
^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **8** (rt, $CDCl_3$).



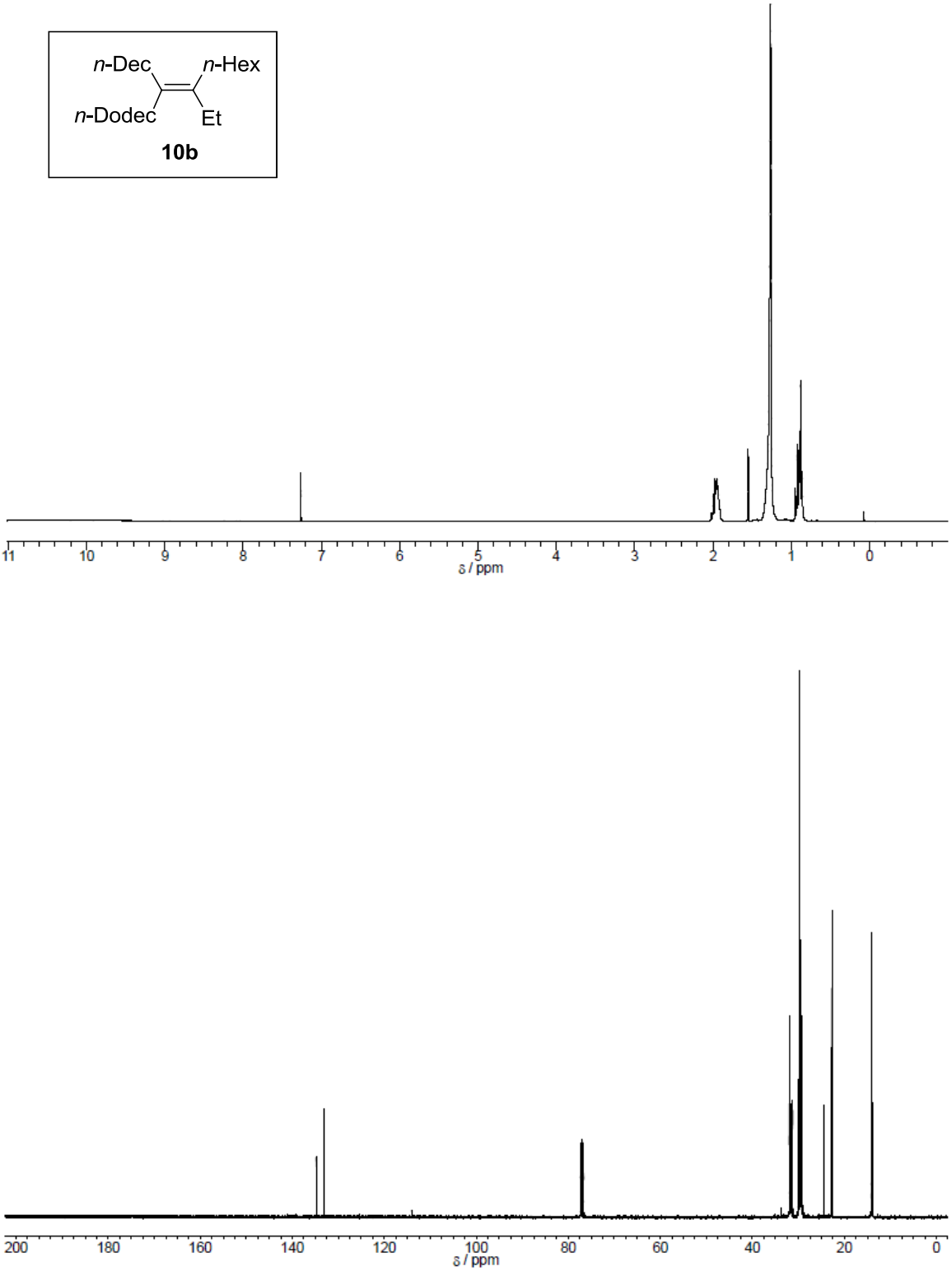
^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **9a** (rt, $CDCl_3$).



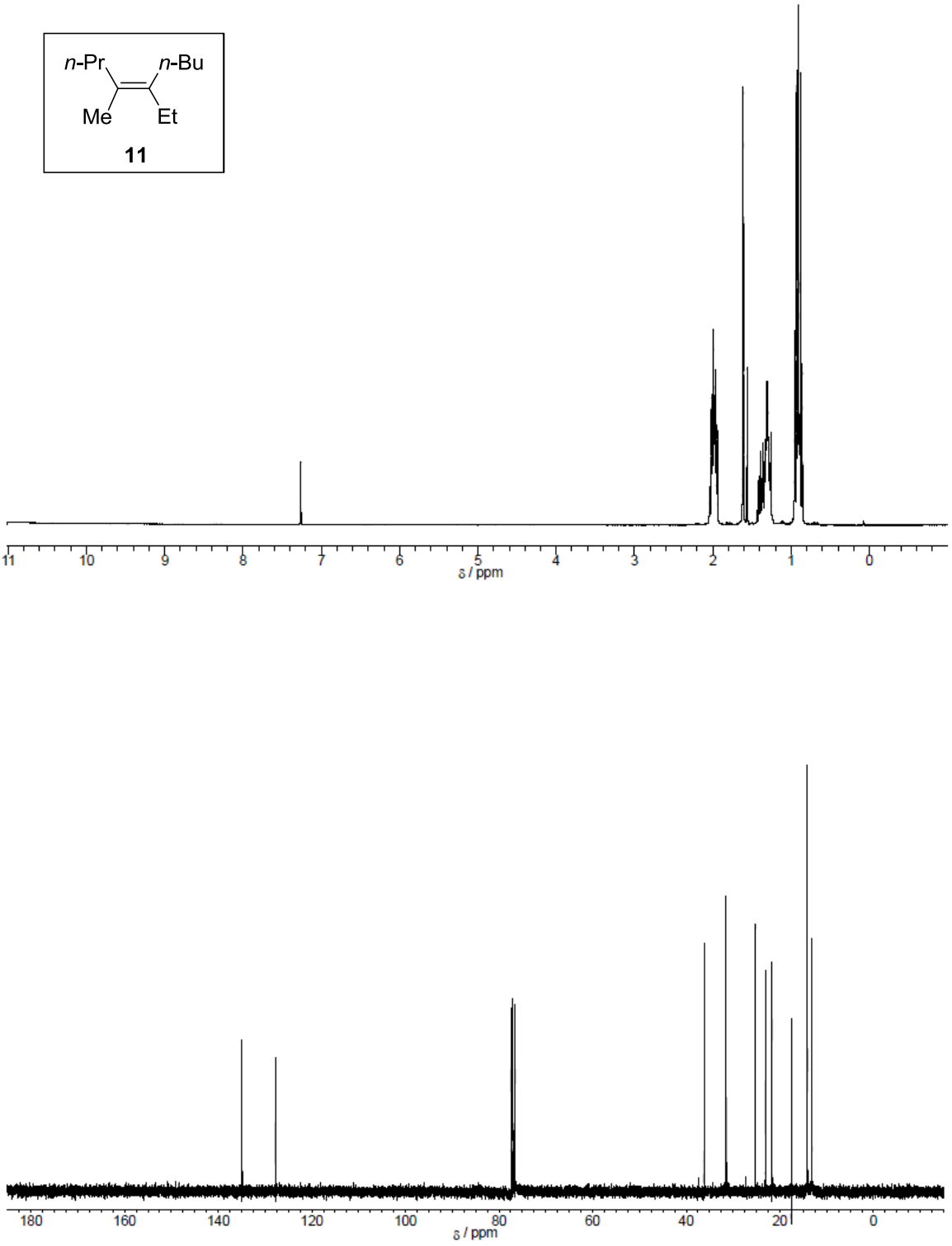
^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **9b** (rt, $CDCl_3$).



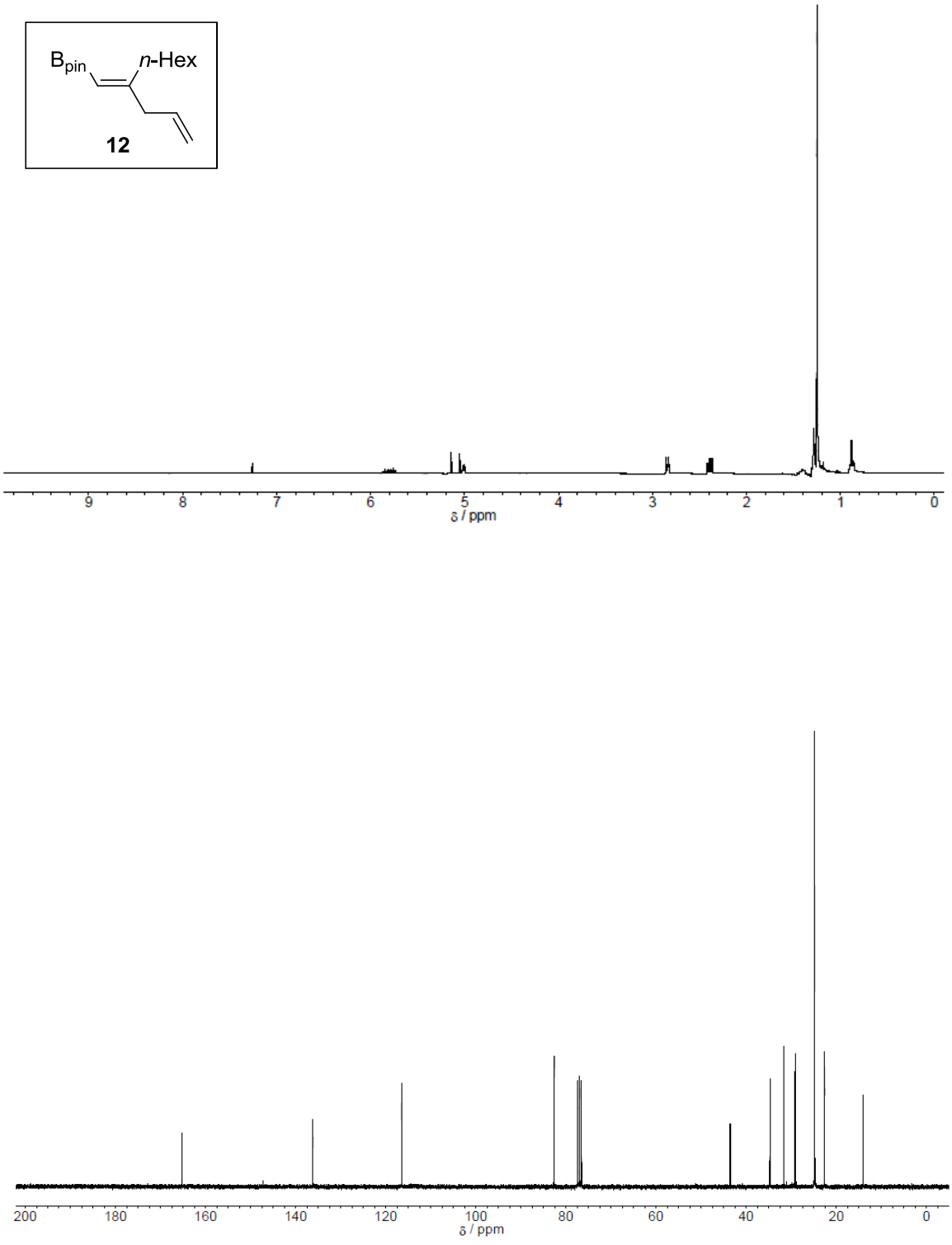
^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **10a** (rt, $CDCl_3$).



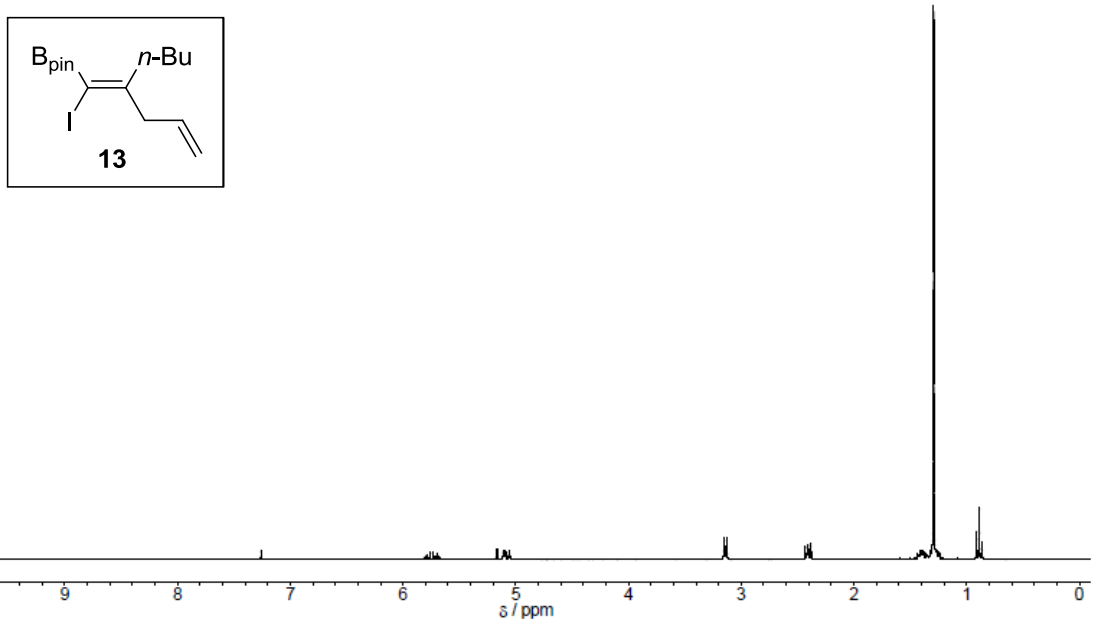
^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **10b** (rt, $CDCl_3$).

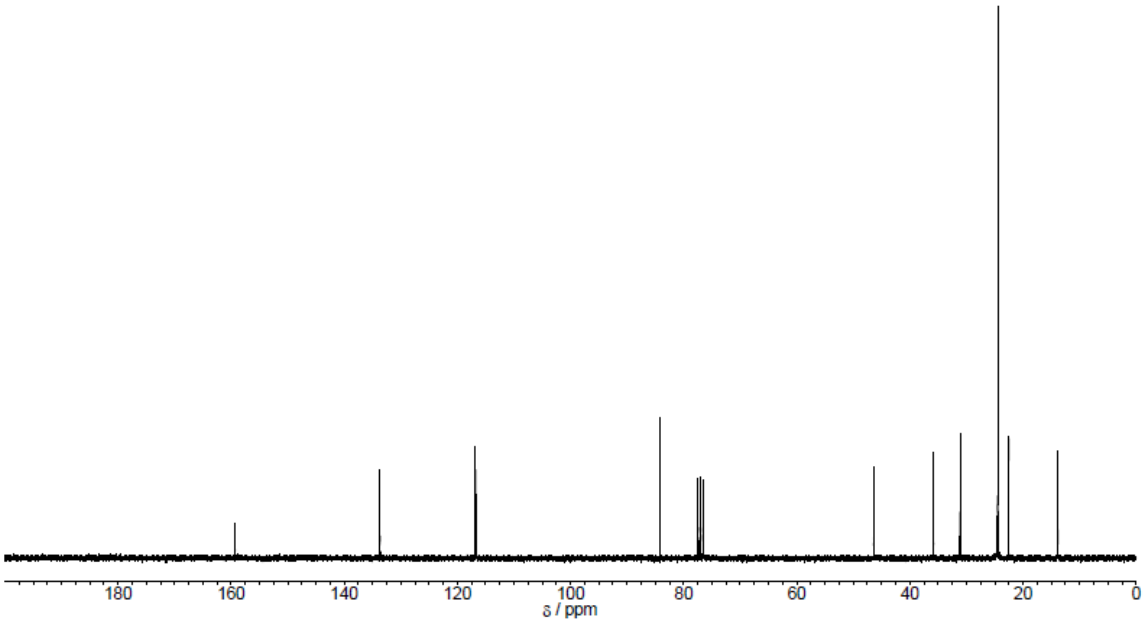


^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **11** (rt, $CDCl_3$).

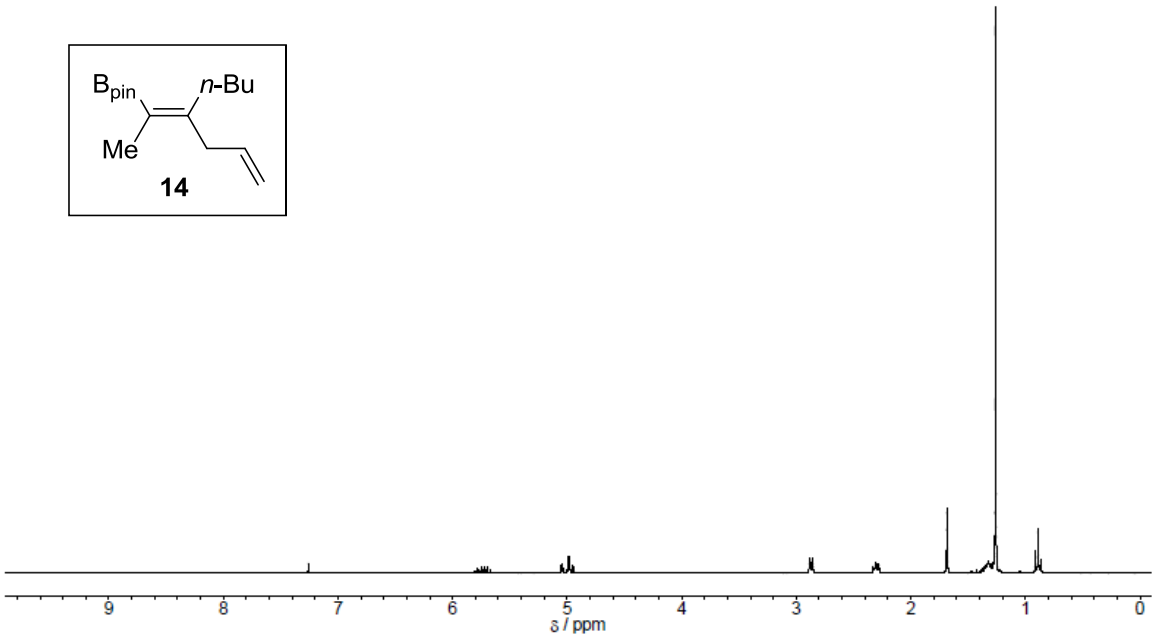


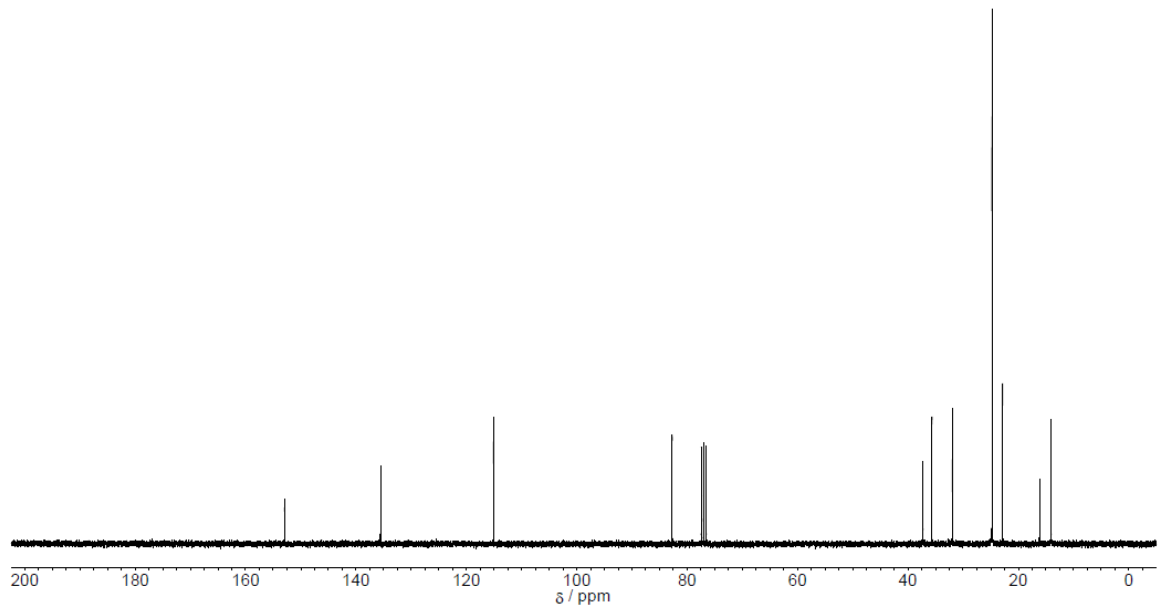
^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **12** (rt, $CDCl_3$).



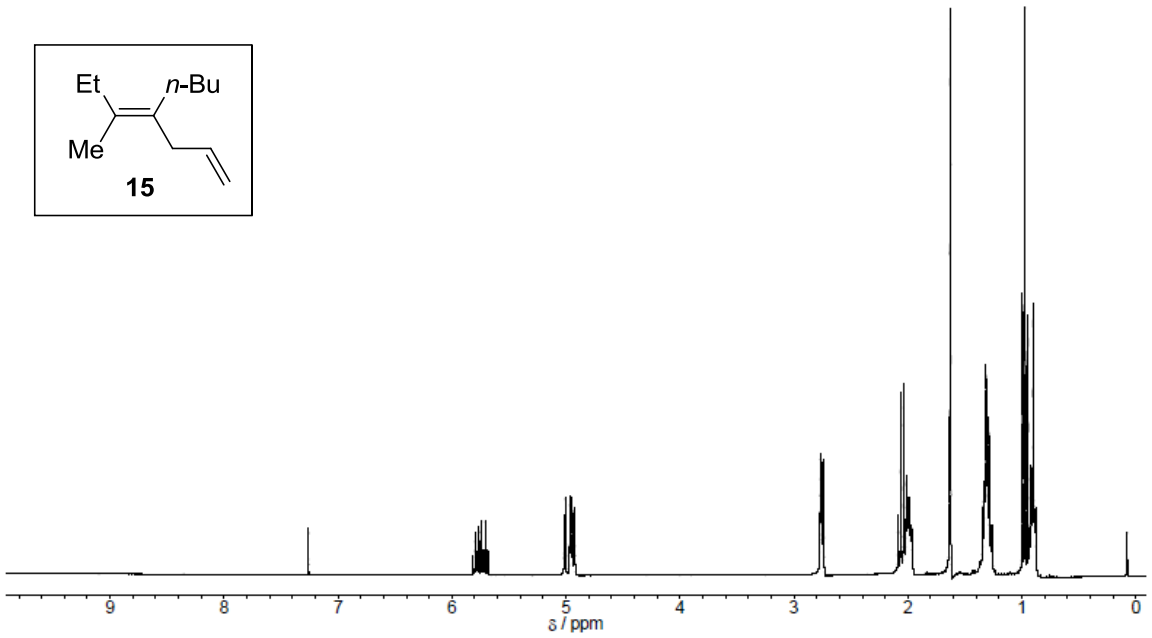


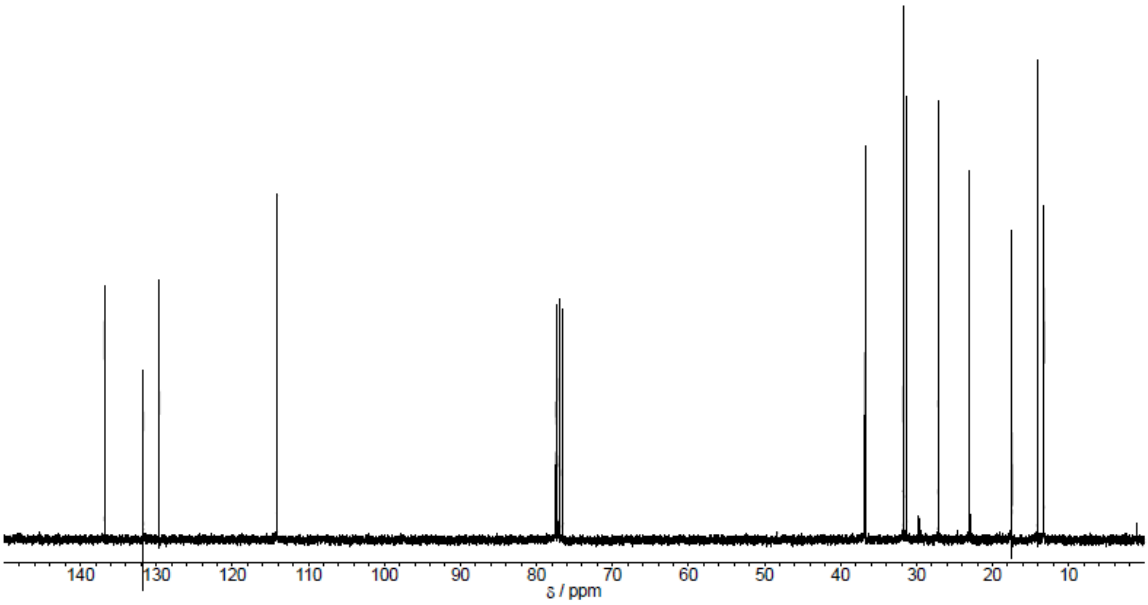
^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **13** (rt, $CDCl_3$)。



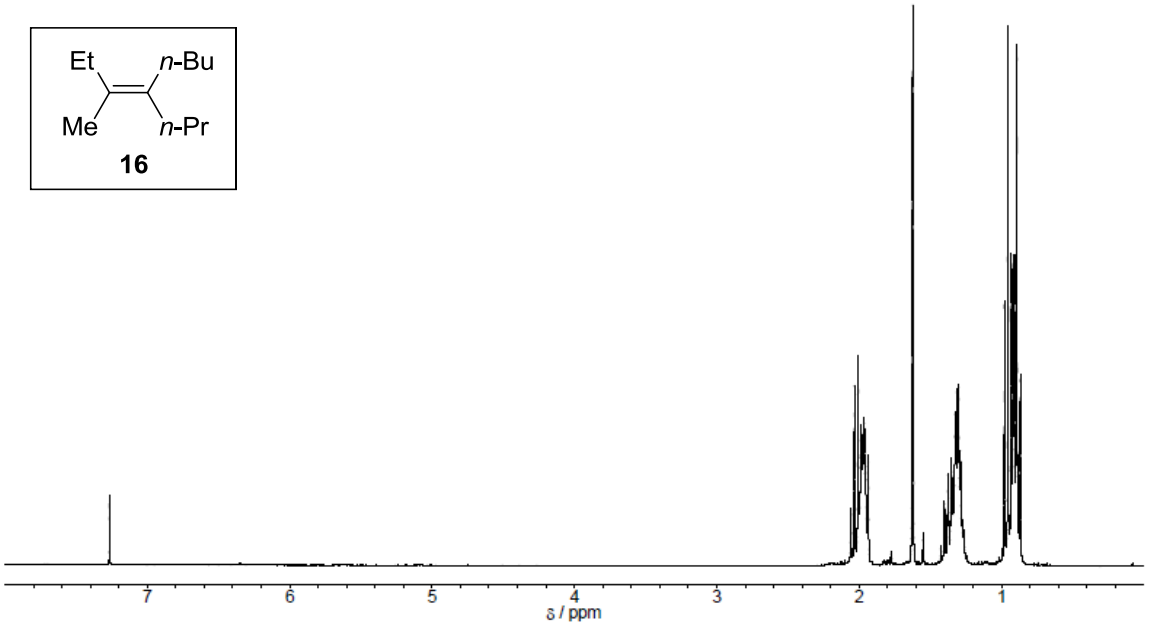


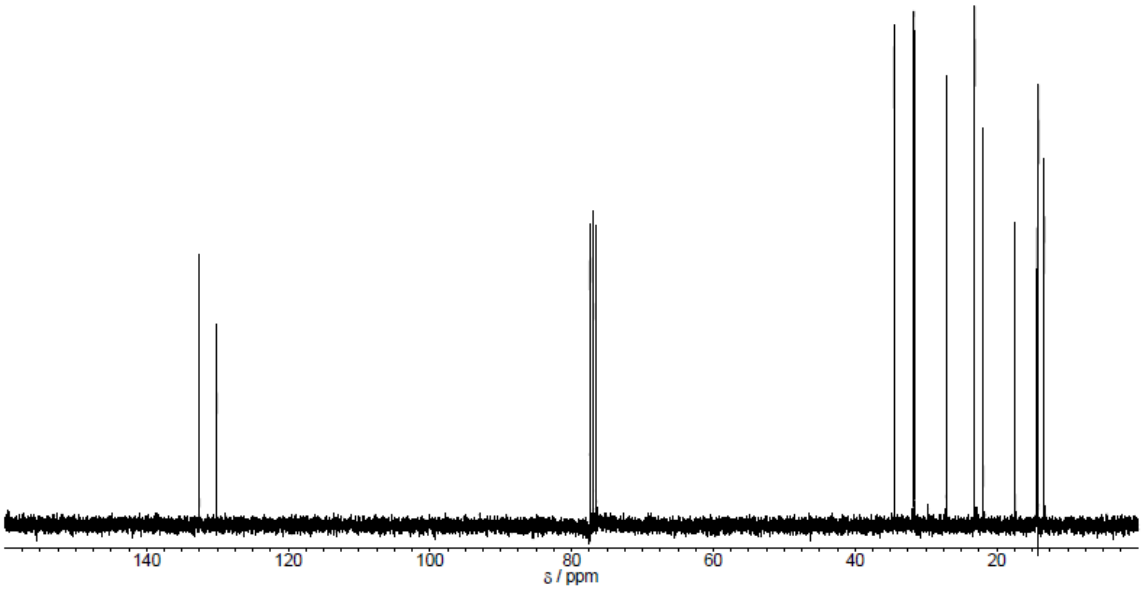
^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **14** (rt, $CDCl_3$).





^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NM R (75 MHz) spectra of **15** (rt, $CDCl_3$).





^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra of **16** (rt, $CDCl_3$).

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16. Notes: NEt_3 alone (42%), THF: NEt_3 = 7:1 (61%), and DMF: NEt_3 = 7:1 (65%).

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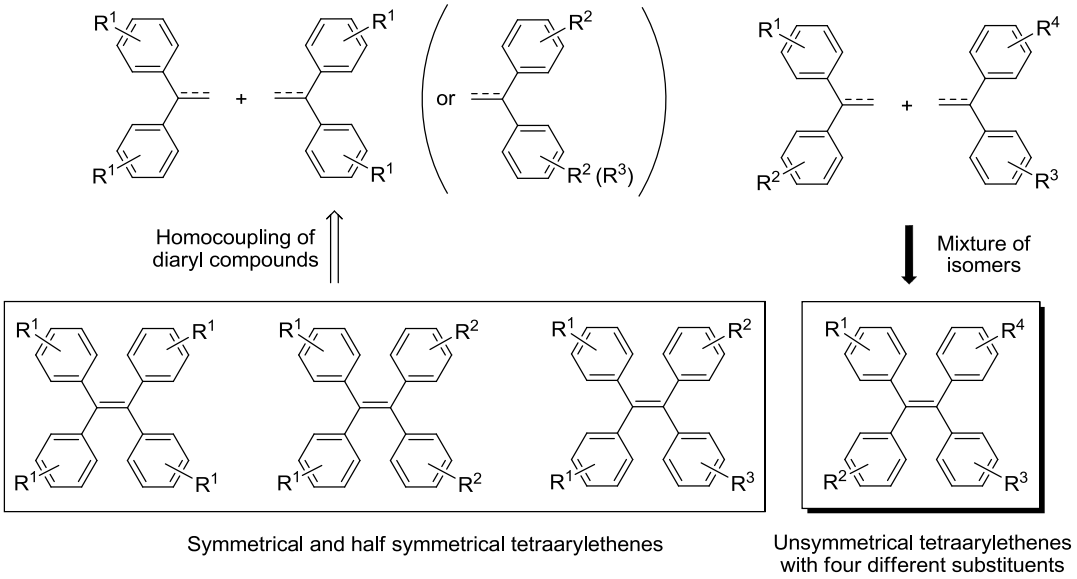
CHAPTER 3

Synthesis of Multisubstituted Olefins through Regio- and Stereoselective Silylborylation of an Alkynylboronate/Chemoselective Cross-Coupling Sequences

3-1 Introduction

As mentioned in Chapter 1, the regio- and stereodefined synthesis of multisubstituted olefins is one of the most challenging goals in synthetic organic chemistry. Tetraarylethenes, as a significant class of multisubstituted olefins, owing to their interesting photophysical and redox properties, are interesting functional materials and their ring-substituted analogues are valuable synthetic targets in materials science.[1] The rigidity and the steric hindrance of tetraarylethene molecules render their synthesis difficult to construct. Moreover, since the reported procedures are, in the main, limited to the preparation of symmetrical tetraarylethenes via homocoupling reactions of diaryldiazomethanes,[2] diaryldichloromethanes,[3] diaryl thioketones,[4] (Scheme 3-1) and diaryl ketones,[5] development of general methods for the synthesis of unsymmetrically substituted tetraarylated olefins, preferably with four different aryl groups, has been a valuable target to organic chemists.[6]

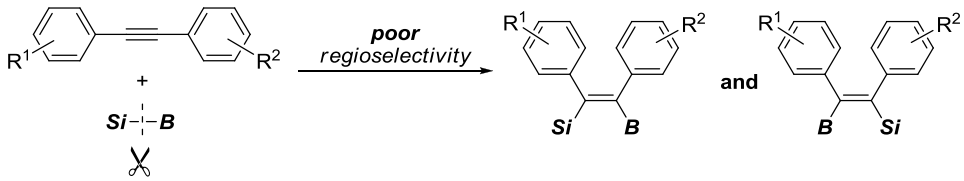
Scheme 3-1



The Author envisaged that a combination of transition-metal-catalyzed silylborylation[7,8,9] of unsymmetrical internal alkynes with cross-coupling reactions could provide a straightforward synthetic entry for various tetraarylethenes. However, silylborylation of unsymmetrical internal alkynes, *e.g.*, 1-phenyl-1-propyne, was reported

to show a low regioselectivity obviously, while the use of unsymmetrical diarylethynes[10] as the substrates are readily anticipated to form a mixture of the regioisomers, which limits a diversity of regio- and stereospecific silylborylated olefins (Scheme 3-2).[7d]

Scheme 3-2



In this Chapter, the Author reports a novel synthetic protocol for the preparation of tetrasubstituted olefins, particularly for a tetraarylated variant with four different aryl groups, by the palladium-catalyzed silylborylation of alkynylboronates,[11] yielding 1-silyl-1-phenyl-2,2-diborylated olefins with perfect regio- and stereoselectivities and sequential chemoselective Suzuki-Miyaura coupling,[12] delivering (*Z*)-1-silyl-2-borylstilbenes. Because the reagents are readily available and the operations are simple, this synthetic strategy proves more selective and tolerant than those previously reported.

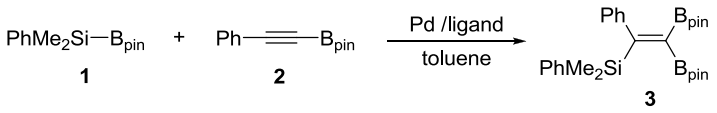
3-2 Results and Discussion

3-2-1 Regio- and Stereoselective Silylborylation

Initial trials of silylborylation of silylborane **1** (B_{pin} is pinacolatoboryl) with the alkynylboronate **2** were conducted according to a report in 1999,[7d] in the presence of the *in situ* generated palladium(0)-isonitrile complex. Reaction of **1** with **2** took place in the presence of a catalytic amount of $Pd(OAc)_2$ and 1,1,3,3-tetramethylbutyl isonitrile (*t*-OctNC) as the ligand. The results are shown in Table 3-1. It is noticed that using 5 mol % of $Pd(OAc)_2$ and 30 mol % of *t*-OctNC, silylborylation product **3** was formed in 53% yield as a sole stereoisomer (Table 3-1, entry 1). Optimal conditions using less palladium catalyst (2 mol %) gave the improved yield when the reaction time was prolonged (Table 3-1, entry 2). It was shown that the reaction did not proceed smoothly at lower temperatures or with a less amount of *t*-OctNC, which decreased yields obviously (Table 3-1, entries 3 and 4). Likewise, $Pd(OAc)_2$ in conjunction with cyclohexyl isonitrile (CyNC) gave a poor yield (19%) (Table 3-1, entry 5). In addition, phosphine and

phosphite ligands could not generate an efficient Pd catalyst for the reaction (Table 3-1, entries 6 and 7).

Table 3-1. Screening silylborylation of alkynylboronate **2** with silylborane **1**. [a]



entry [a]	Pd cat. (mol %)	ligand (mol %)	temp (℃)	time (h)	yield[b] (%)
1	$Pd(OAc)_2$ (5)	*t*-OctNC (30)	110	2	53
2	**$Pd(OAc)_2$ (2)**	***t*-OctNC (30)**	**110**	**12**	**60**
3	$Pd(OAc)_2$ (2)	*t*-OctNC (30)	50	4	17
4	$Pd(OAc)_2$ (1)	*t*-OctNC (20)	110	12	30
5	$Pd(OAc)_2$ (2)	CyNC (30)	110	12	19[c]
6	Pd_2dba_3•$CHCl_3$ (2)	$P(OEt)_3$ (20)	110	2	<1
7	$PdCl_2(PPh_3)_2$ (2)	none	110	2	<1

[a] The reactions were carried out using **1** (1.5 mmol) and **2** (1.0 mmol) . [b] Isolated yields after column and recrystallization. [c]Two stereoisomers were detected.

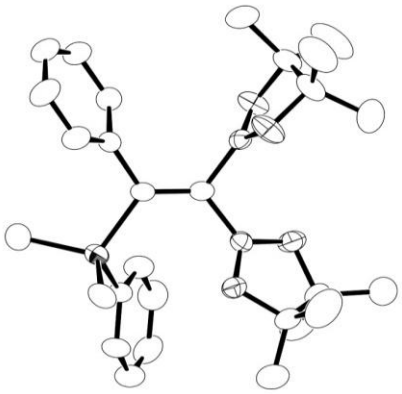
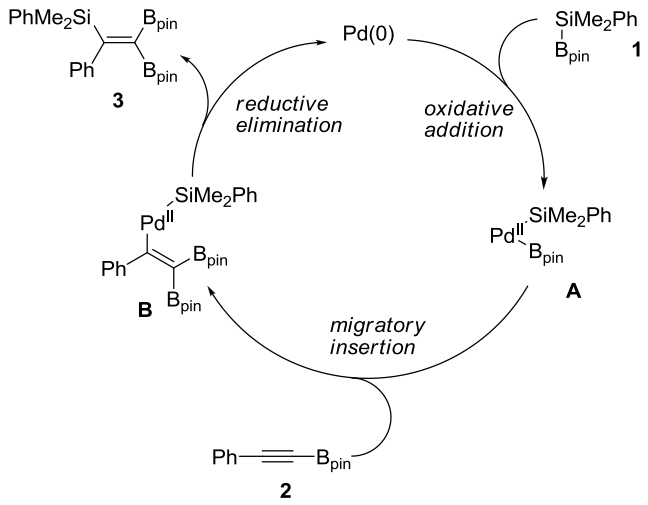


Figure 3-1. An ORTEP Drawing of **3**.

The regio- and stereochemistry of the adduct **3** was confirmed by X-ray crystallographic analysis (Figure 3-1). Thus, silylborylation was found to take place regio- and stereoselectively with the silyl moiety geminal to a phenyl group. Although the similar 1,1-diboryl-1-alkenes have been prepared by *gem*-diborylation of 1,1-dibromo-1-alkenes with *n*-BuLi/bis(pinacolato)diboron [13] or ketone addition of

tris(pinacolato)borylmethyllithium,[14] to the best of her knowledge, there are no precedent examples of the silylated 1,1-diboryl-1-alkenes that are difficult to be synthesized under basic conditions due to an occurrence of desilylation. A possible catalytic cycle forming **3** is proposed to explain the observed regioselectivity. This proposed cycle is presented in Scheme 3-3.

Scheme 3-3. A Plausible Mechanism.



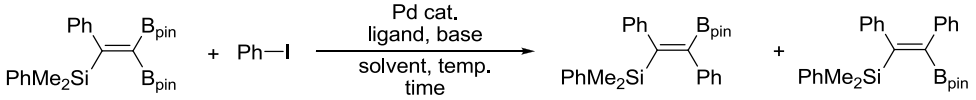
It was proposed that silylborane **1** oxidatively adds to the Pd(0) catalyst to generate the Pd(II) species **A**. Intermediate **A** then undergoes migratory insertion, wherein alkynylboronate **2** inserts into a Pd–B bond (borylpalladation) to form **B**. Although the borylpalladation mechanism has been proposed as the result of theoretical studies,[8c,15] another possibility, silylpalladation, cannot be neglected. This selectivity is opposite to that observed in the analogous process with organozirconium species.[16] Finally, the adduct **3** is produced by reductive elimination, regenerating the Pd catalyst.

3-2-2 Chemoselective Suzuki-Miyaura Coupling of the Silylborylated Compound

Since functional materials, natural products, and bioactive pharmaceuticals have all been synthesized with 1,1-diborylated olefins,[17,18] to further test the utility of this building block, compound **3** was successively subjected to Suzuki-Miyaura coupling with an equimolar of iodobenzene (**4a**) to ascertain whether the first coupling would be chemoselective. Various palladium catalysts and ligands were tested and the results

obtained are listed in Table 3-2. A combination of $Pd(dba)_2$ with $[HP(t\text{-}Bu)Me_2]BF_4$ salt, which had proven the best catalyst for Suzuki-Miyaura coupling reaction of alkenylboronates with alkyl bromides,[12b] was found to be sub-optimal for the present reaction due to desilylation of **3**. $Pd(PPh_3)_4$ also showed a lower reactivity (Table 3-2, entries 2 and 3). PEPPSI-IPr[19] and Pd_2dba_3•$CHCl_3$/P(*t*-Bu)$_3$ proved more reactive and afforded relatively higher yields, albeit with reduced chemoselectivity (Table 3-2, entries 4 and 5). An initial survey demonstrated that aqueous KOH accelerated the reaction.

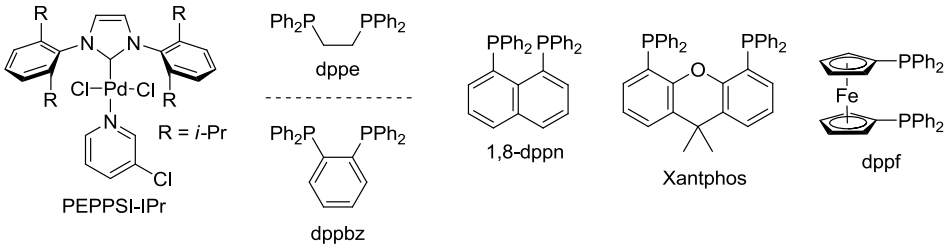
Table 3-2. Screening the Optimal Condition of Chemoselective Suzuki-Miyaura Coupling.



3 **4a** *(Z)*-**5a** *(E)*-**5a**

entry	Pd cat. (mol %)	ligand (mol %)	base	solvent	temp. (℃)	time (h)	yield/% (*Z*:*E*)[b]
1	$Pd(dba)_2$ (5)	$[HP(t\text{-}Bu)Me_2]BF_4$ (20)	KOH	THF	rt	12	0
2	$Pd(PPh_3)_4$ (10)	--	KOH aq.	dioxane	70	12	24 (96:4)
3	$Pd(PPh_3)_4$ (20)	--	KOH aq.	THF	rt	12	38 (92:8)
4	PEPPSI-IPr (5)	--	KOH aq.	toluene	50	12	55 (92:8)
5	PEPPSI-IPr (10)	--	KOH aq.	THF	rt	3	59 (75:25)
6	Pd_2dba_3•$CHCl_3$ (5)	P(*t*-Bu)$_3$ (20)	KOH aq.	THF	rt	3	76 (75:25)
7	Pd_2dba_3•$CHCl_3$ (5)	P(*t*-Bu)$_3$ (20)	Cs_2CO_3 aq.	THF	rt	12	64 (92:8)
8	$PdCl_2(NCPh)$ (10)	dppe (20)	KOH aq.	THF	rt	12	60 (86:14)
9	$PdCl_2(NCPh)$ (10)	dppbz (20)	KOH aq.	THF	rt	12	27 (>99:1)
10	$PdCl_2(NCPh)$ (10)	1,8-dppn (20)	KOH aq.	THF	rt	12	64 (85:15)
11	$PdCl_2(NCPh)$ (10)	Xantphos (20)	KOH aq.	THF	rt	12	41 (86:14)
12	**$PdCl_2$(dppf) (5)**	**--**	**KOH aq.**	**THF**	**rt**	**3**	**85 (88:12)**

[a] Reaction conditions: **3** (0.1 mmol), **4a** (0.1 mmol), Pd cat./ligand, base (0.3 mmol, 3 equiv), solvent (1 mL). [b] Isolated yields of the isomeric mixture, the *Z*:*E* ratios were determined by the ^{1}H NMR spectra.



Palladium catalysts with monodentate ligands were not particularly efficient. Therefore, several representative bidentate ligands were examined (Table 3-2, entries 8-12). It was delighted to find that $PdCl_2(dppf)$[20] gave much improved performance (Table 3-2, entry 12). Although all the examined catalysts gave rise to the coupled product **5a** as a mixture of stereoisomers, the isomeric mixture was separated by silica gel column chromatography. A *Z*-geometry of the major isomer of the product **5a** was confirmed by X-ray crystallographic analysis (Figure 3-2).

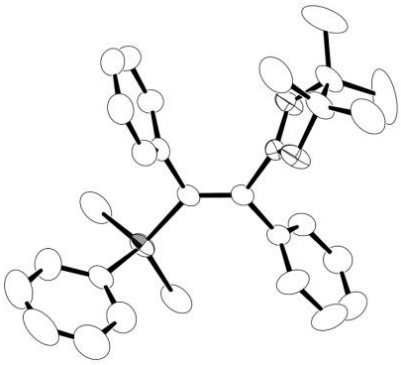
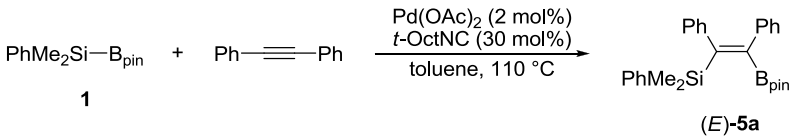


Figure 3-2. An ORTEP Drawing of **3**.

An authentic (*E*)-**5a** was synthesized by silylborylation of diphenylethyne[7d] to provide comparitor NMR data and this was indeed distinct to that of (*Z*)-**5a** (Scheme 3-4). Moreover, the *Z:E* ratios were precisely calculated by the ^{1}H NMR spectra to determine the chemoselectivity, utilizing proton signals on $SiMe_2Ph$ as the references (Figure 3-3, 3-4, 3-5).

Scheme 3-4. Synthesis of Authentic (*E*)-**5a.**



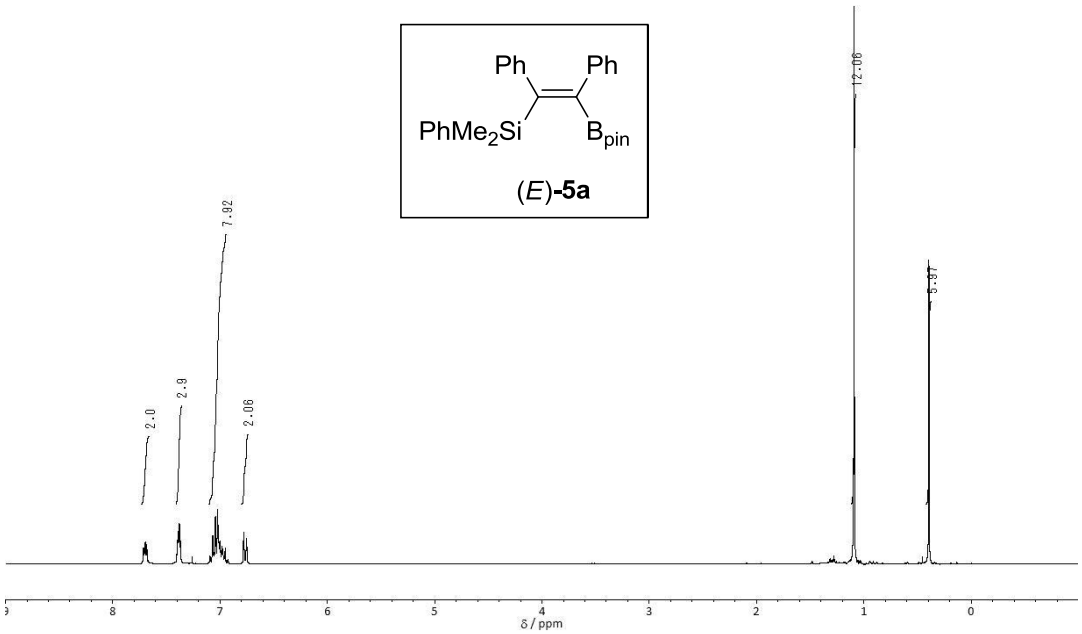


Figure 3-3. The ^{1}H NMR spectrum of (*E*)-**5a.**

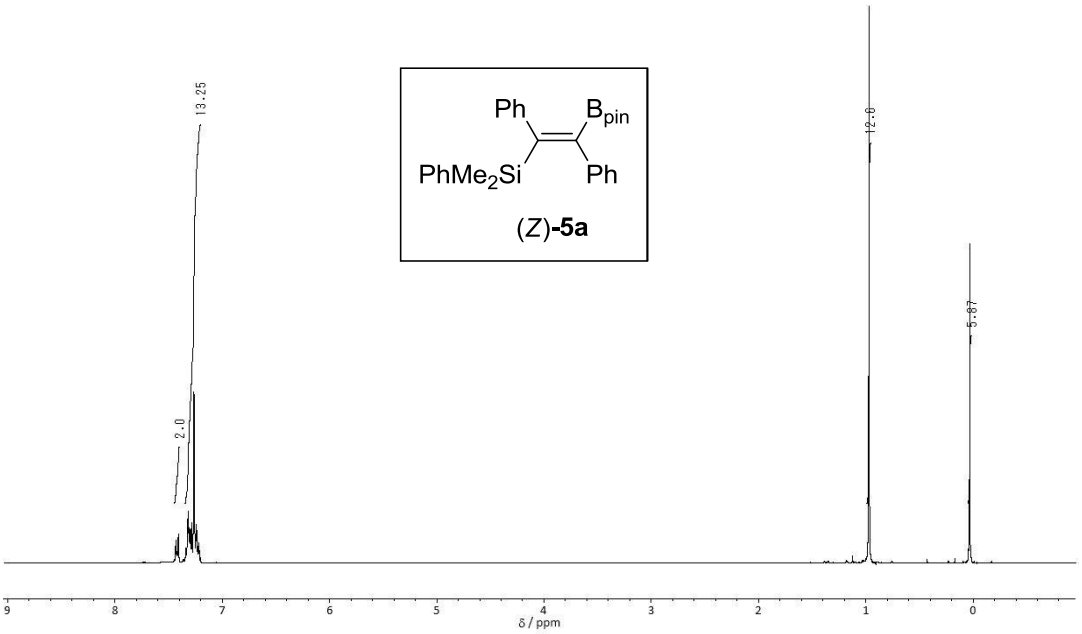


Figure 3-4. The ^{1}H NMR spectrum of synthesized (***Z***)-**5a.**

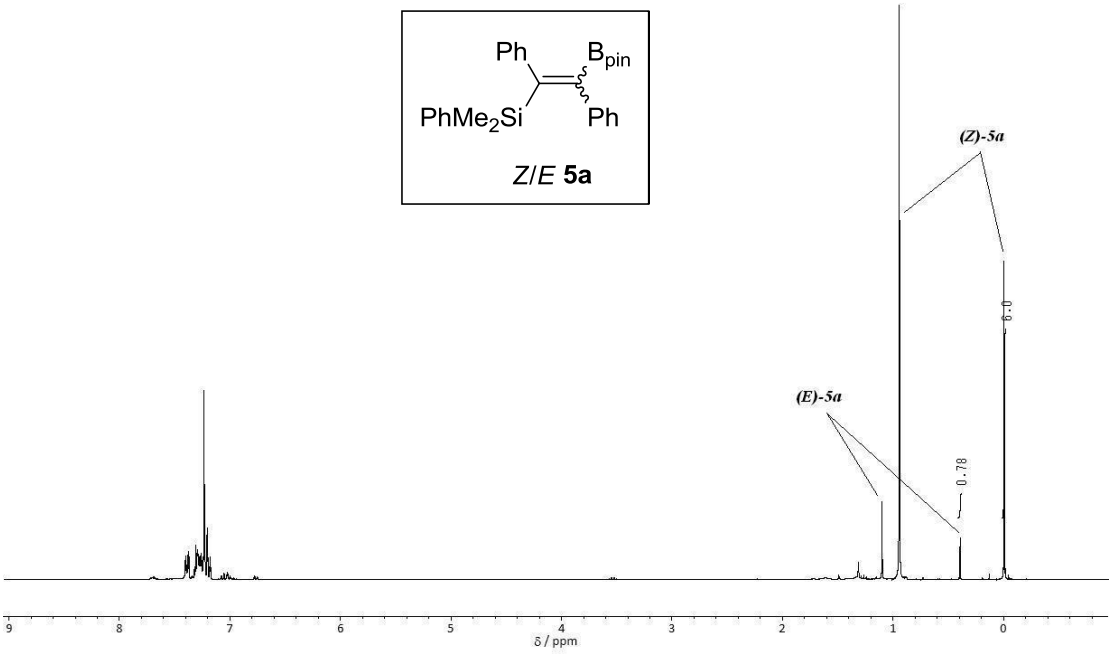


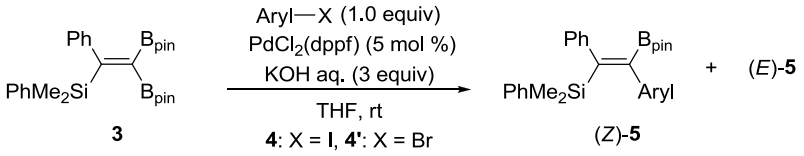
Figure 3-5 Determination of a *Z*/*E* Ratio of **5a** by the ^{1}H NMR Spectrum.

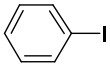
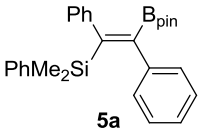
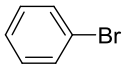
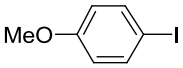
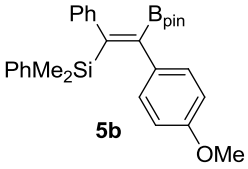
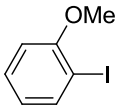
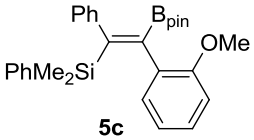
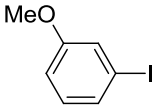
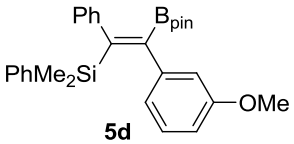
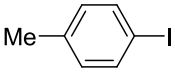
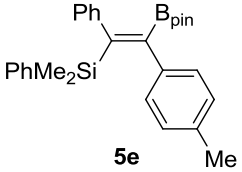
The observed chemoselectivity is consistent with that reported by Shimizu and Hiyama:[17a] the C–C bond formation at the cis position of the alkyl groups was observed in the reaction of 1,1-diboryl-1-alkene with aryl iodides. The C–C bond at the cis position of the $SiMe_2Ph$ group was formed with a discrimination of two geminal boryl groups in **3**. Considering conformational energies (A-values) of the Ph (2.8) and $SiMe_2Ph$ (2.5-2.8) groups,[21] the chemoselectivity cannot be explained simply by a steric effect. From the viewpoint of electronic demands, the ^{11}B NMR spectrum of **3** showed an overlapped signal at 29.9 ppm, indicating that the two boryl groups are electronically similar. Thus, at present, the reason why the two boryl groups in **3** are discriminated remains unclear.

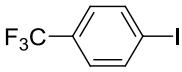
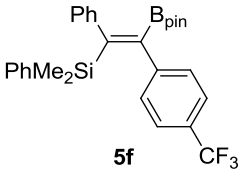
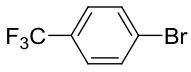
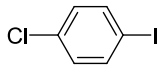
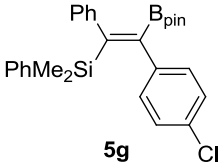
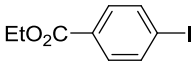
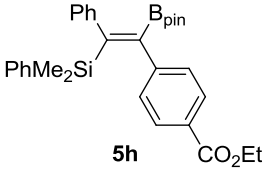
After optimizing the reaction conditions for the chemoselective Suzuki-Miyaura coupling of **3**, a series of aryl iodides **4** were subjected to survey the reaction scope. 2-Iodoanisole (**4c**) afforded the desired product **5c** in a moderate yield due to a steric effect (Table 3-3, entry 4). As shown in Table 2, it is noteworthy that some aryl bromides **4'** also gave **5** in moderate to good yields when the reaction time was extended to 18 h (Table 3-3, entries 2 and 8). It is also notable that a chloro group in the substrate **4g** remained intact during the reaction with no trace of side product observed. Synthesis

of compounds **5** would be impracticable via *anti*-silylborylation[7k] of unsymmetrical diarylethynes because regioselectivity of addition would not be controllable.

Table 3-3. Chemoselective Suzuki-Miyaura Coupling of **3** with Aryl Iodides **4** or Aryl Bromides **4'**.[a]



entry	Ar–X	(*Z*)-5	yield (*Z*:*E*)[b]
1	 (**4a**)	 **5a**	85 (88:12)
2[c]	 (**4a'**)	**5a**	78 (87:13)
3	 (**4b**)	 **5b**	87 (89:11)
4	 (**4c**)	 **5c**	57 (92:8)
5	 (**4d**)	 **5d**	83 (89:11)
6	 (**4e**)	 **5e**	92 (88:12)

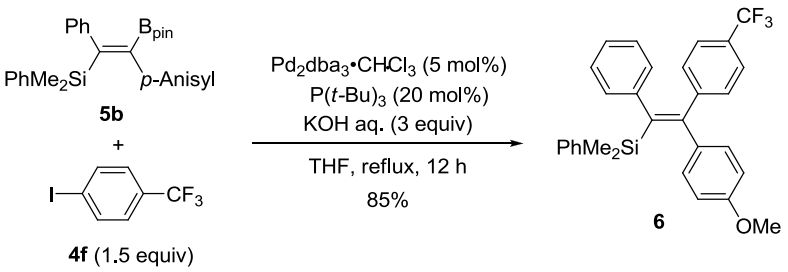
7	 (**4f**)	 **5f**	57 (87:13)
8[c]	 (**4f'**)	**5f**	59 (85:15)
9	 (**4g**)	 **5g**	92 (88:12)
10	 (**4h**)	 **5h**	70 (86:14)

[a] Reaction condition: **3** (245 mg, 0.5 mmol), **4** or **4'** (0.5 mmol), $PdCl_2$(dppf) (18 mg, 5 mol %), 3 M KOH solution (1.5 mmol, 0.5 mL) in THF (5 mL). [b] Isolated yields after silica gel column chromatography, *Z:E* ratios were determined by the ^{1}H NMR spectra. [c] The reaction time was 18 h.

3-2-3 Synthesis of a Triarylated Olefin

With a diverse range of reagents **5** in hand, a further aryl group was sequentially introduced by Suzuki-Miyaura coupling of the remaining boron moiety. The triarylated alkenylsilane **6** was synthesized successfully by the reaction of **5b** with **4f** in the presence of Pd_2dba_3•$CHCl_3$/P(*t*-Bu)$_3$ as the catalyst (Scheme 3-5).

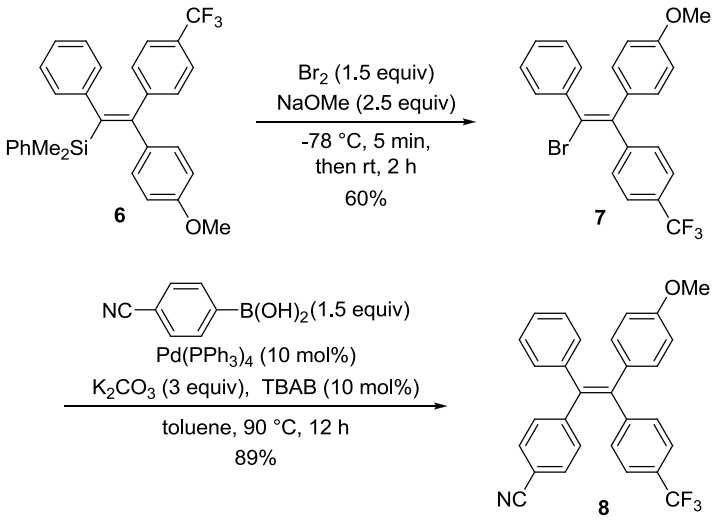
Scheme 3-5. Synthesis of a Triarylated Alkenylsilane **6**.



3-2-4 Synthesis of a Tetraarylated Olefin

Finally, the synthesis of a tetraarylated olefin **8** with four different aryl groups was addressed through sequential cross-couplings by utilizing the remaining silyl moiety. With Br_2 and NaOMe in MeOH,[22] the silyl group in **6** was successfully transformed to the corresponding bromide **7** along an inversion of stereochemistry[23] (Scheme 3-6). Sequential Suzuki-Miyaura coupling of **7** with 4-cyanophenylboronic acid afforded the tetraarylated olefin **8** in 89% yield as a sole product whose structure was unambiguously confirmed by X-ray diffraction (Figure 3-6).

Scheme 3-6. Synthesis of a Tetraarylated Olefin **8.**



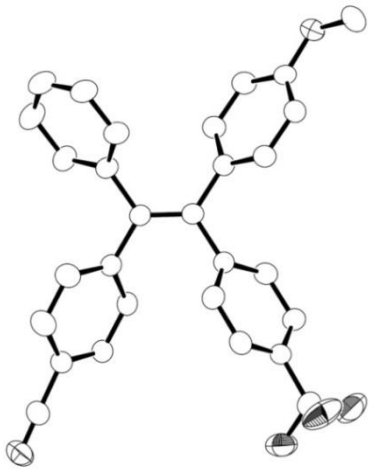


Figure 3-6. An ORTEP Drawing of **8.**

3-3 Summary

The Author has successfully developed the synthesis of tetraarylated olefins featuring a perfectly regio- and stereoselective silylborylation of the alkynylboronate and sequential chemoselective Suzuki-Miyaura couplings. This protocol can be applicable to various aryl moieties bearing a variety of functional groups, including those not compatible with organolithium reagents required in previous approaches. Further studies to clarify the factors for the selectivity and to expand this synthetic method to a more general approach to the complicated π-conjugated molecules are in progress.

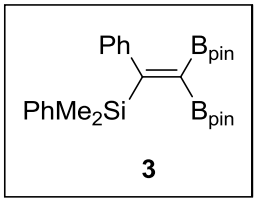
3-4 Experimental Section

3-4-1 General Instrumentation and Chemicals.

All the reactions were carried out under an Ar atmosphere using standard Schlenk techniques. Glassware was dried in an oven (130 ℃) and heated under reduced pressure prior to use. Dehydrated THF, dichloromethane, hexane, and diethyl ether were purchased from Kanto Chemicals Co., Ltd. For thin layer chromatography (TLC) analyses throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. Silica gel column chromatography was carried out using Silica gel 60 N (spherical, 40-100 μm) from Kanto Chemicals Co., Ltd. The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on Mercury-300 (300 MHz) and Varian INOVA-600 (600 MHz) spectrometers. The $^{19}F\{^{1}H\}$ NMR spectra were recorded on Mercury-300 (300 MHz) and chemical shifts were referenced to an external standard ($CFCl_3$). The $^{11}B\{^{1}H\}$ NMR spectra was recorded on Varian INOVA-600 (600 MHz) spectrometers and the chemical shifts were referenced to an external standard ($BF_3 \cdot Et_2O$). Infrared spectra were recorded on a Shimadzu IRPrestige-21 spectrophotometer. GC analyses were performed on a Shimadzu GC-14A equipped with a flame ionization detector using Shimadzu Capillary Column (CBP1-M25-025) and Shimadzu C-R6A-Chromatopac integrator. GC/MS analyses were carried out on a SHIMADZU GC-17A equipped with a SHIMADZU QP-5050 GC-MS system. Elemental analyses were carried out with a Perkin-Elmer 2400 CHN elemental analyzer at Okayama University.

3-4-2 Experimental Procedures

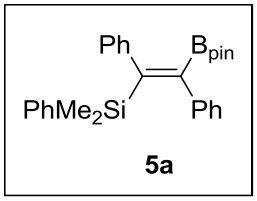
Materials: 2-(Dimethylphenylsilyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1**) was synthesized via the treatment of freshly prepared dimethylphenylsilyllithium with 4,4,5,5-tetramethyl-2-(1-methylethoxy)-1,3,2-dioxaborolane, according to the literature methods. [24] 4,4,5,5-Tetramethyl-2-(phenylethynyl)-1,3,2-dioxaborolane (**2**) were prepared via lithiation of phenylacetylene and sequential treatment with 4,4,5,5-tetramethyl-2-(1-methylethoxy)-1,3,2-dioxaborolane.[15a]



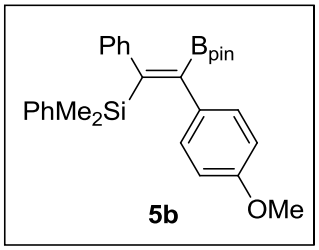
3

Regio- and Stereoselective Silylborylation of 2: Synthesis of 1-Dimethylphenylsilyl-1-phenyl-2,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (3). To palladium(II) acetate (9.0 mg, 0.04 mmol) in a 20 mL of Schlenk tube was added liquid l,1,3,3-tetramethylbutyl isonitrile (105 μL, 0.6 mmol) with stirring at room temperature under an argon atmosphere. The color of the mixture immediately changed to a vivid red, indicating the formation of palladium(0)-isonitrile complex. Toluene (0.5 mL), silylborane **1** (787 mg, 3 mmol), and alkynylboronate **2** (456 mg, 2 mmol) were added, and the reaction mixture was heated at reflux. The cooled reaction mixture was subjected to a short column of silica gel (hexane/ethyl acetate = 20:1), followed by recrystallization in hexane to afford the titled compound **3** (588 mg, 1.2 mmol, 60%) as white solid. Mp = 104-105 ℃. R_f = 0.26 (hexane/ethyl acetate = 20:1). FT-IR (neat, cm^{-1}): 2976 (m), 2929 (m), 1330 (m), 1294 (s), 1269 (s), 1141(s), 848 (s), 700 (s). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 0.27 (s, 6H), 0.95 (s, 12H), 1.06 (s, 12H), 6.97-7.00 (m, 2H), 7.08-7.19 (m, 3H), 7.24-7.27 (m, 3H) 7.52-7.56 (m, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, rt): δ –0.6, 24.3, 24.8, 83.1, 83.3, 125.4, 126.8, 127.31, 127.34, 128.4, 134.2, 139.5, 148.3, 172.3. The carbon signal attached to B was not observed due to low intensity; ^{11}B{^{1}H} NMR (192 MHz, $CDCl_3$, rt): δ 29.9 (brs, overlapped). MS (EI, m/z (relative intensity)): 490 (M^+, 1), 475 (5), 363 (4), 307(11), 135(13), 129 (6), 84 (100), 83 (29), 69 (21). Anal. Calcd for $C_{28}H_{40}SiB_2O_4$: C, 68.59; H, 8.22%. Found: C, 68.20; H, 8.40%.

The authentic sample of **(*E*)-5a** was synthesized according to the procedure above, using diphenylacetylene (356 mg, 2 mmol), as white solid. Yield was 70% (612 mg, 1.39 mmol,). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 0.39 (s, 6H), 1.09 (s, 12H), 1.06 (s, 12H), 6.75-6.78 (q, 2H), 6.78-7.07 (m, 8H), 7.37-7.39 (m, 3H) 7.68-7.71 (m, 2H).

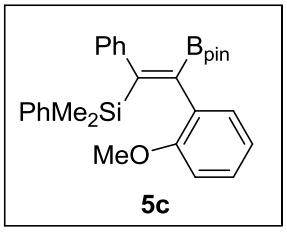


(*Z*)-1-(Dimethylphenylsilyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,2-diphenylethene (5a). To a solution of $PdCl_2$(dppf) (18 mg, 0.025 mmol 5 mol %) in THF (5 mL) as an orange suspension in a 20 mL of Schlenk tube at room temperature under an Ar atmosphere were added **3** (245 mg, 0.5 mmol) and aryl halide **4** (0.5 mmol, 1.0 equiv). After aqueous 3 M KOH solution (1.5 mmol, 0.5 mL) was added, the reaction mixture turned to deep brown solution immediately. The reaction mixture was stirred for 12h at room temperature. After the reaction completed, the reaction mixture was quenched by sat. NH_4Cl solution, then extracted with diethyl ether (20 mL x 2). The combined ethereal layers were washed with brine and dried over $MgSO_4$. Filtration, evaporation and silica gel chromatography (hexane/ethyl acetate = 20:1) gave the pure (*Z*) -**5a**. White solid (164 mg, 0.37 mmol, 75%) from **4a** and (150 mg, 0.34 mmol, 68%) from **4a'**. Mp = 76-78 ℃. R_f = 0.28 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 3068 (m), 2974 (w), 1373 (s), 1336 (s), 1141 (s), 848 (s), 700 (s). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 0.03 (s, 6H), 0.97 (s, 12H), 7.21-7.34 (m, 13H), 7.40-7.43 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, rt): δ –1.3, 24.2, 83.4, 125.7, 126.5, 127.3, 127.5, 127.7, 128.1, 128.4, 128.5, 133.9, 139.4, 142.0, 145.6, 153.8. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.4. MS (EI, m/z (relative intensity)): 440 (M^+, 22), 425 (35), 356 (28), 265 (21), 247 (18), 178 (39), 135 (100), 84 (58), 83 (27), 69 (14). Anal. Calcd for $C_{28}H_{33}SiBO_2$: C, 76.35; H, 7.55%. Found: C, 76.52; H, 7.61%.



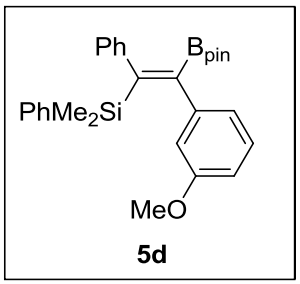
(*Z*)-1-(Dimethylphenylsilyl)-1-phenyl-2-(4-methoxyphenyl)-2-(4,4,5,5-tetramethyl-1

,3,2-dioxaborolan-2-yl)ethene (5b). White solid (182 mg, 0.39 mmol, 77%). Mp = 122-123 ℃. R_f = 0.13 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 3068 (m), 2980 (m), 1602 (m), 1508 (s), 1340 (s), 1298 (s), 1246 (s), 1143 (s), 852(s). ^1H NMR (300 MHz, $CDCl_3$, rt): δ –0.03 (s, 6H), 0.90 (s, 12H), 3.79 (s, 3H), 6.73 (d, J = 8.7 Hz, 2H), 7.10 (d, J = 8.7 Hz, 2H), 7.14-7.19 (m, 3H), 7.22-7.28 (m, 5H), 7.35-7.38 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, rt): δ –1.1, 24.3, 55.1, 83.4, 113.2, 125.6, 127.3, 127.5, 128.4, 128.5, 129.2, 133.9, 134.5, 139.7, 145.7, 153.4, 158.4. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.4. MS (EI, m/z (relative intensity)): 470 (M^+, 67), 455 (31), 386 (49), 295 (18), 227 (24), 208 (48), 135 (100), 84 (24), 83 (32). Anal. Calcd for $C_{29}H_{35}SiBO_3$: C, 74.03; H, 7.50%. Found: C, 74.43; H, 7.48%.



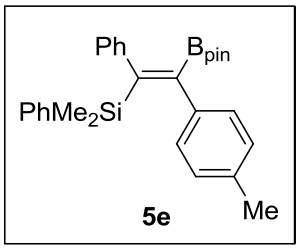
5c

(*Z*)-1-(Dimethylphenylsilyl)-1-phenyl-2-(2-methoxyphenyl)-2-(4,4,5,5-tetramethyl-1 ,3,2-dioxaborolan-2-yl)ethene (5c). White solid (123 mg, 0.26 mmol, 52%). Mp = 95-96 ℃. R_f = 0.19 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2980 (m), 2980 (m), 1456 (m), 1338 (s), 1303 (s), 1242 (m), 1141 (s), 1111 (s), 813 (m), 700 (s). ^1H NMR (300 MHz, $CDCl_3$, rt): δ 0.00 (s, 6H), 0.89 (s, 12H), 3.75 (s, 3H), 6.69 (dd, J = 8.4, 0.6 Hz, 1H), 6.77 (td, J = 7.5, 1.5 Hz, 1H), 7.05 (dd, J = 7.5, 1.5 Hz, 1H), 7.12-7.31 (m, 11H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, rt): δ –1.3, 24.2, 55.0, 83.0, 109.5, 120.0, 125.5, 127.2 (overlapped), 128.2, 128.3, 129.0, 130.9, 132.0, 133.8, 139.7, 145.7, 155.7, 156.7. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.6. MS (EI, m/z (relative intensity)): 470 (M^+, 35), 455 (43), 356 (31), 355 (88), 354 (23), 277 (23), 251 (18), 208 (19), 135 (100), 84 (15), 83 (21). Anal. Calcd for $C_{29}H_{35}SiBO_3$: C, 74.03; H, 7.50%. Found: C, 73.73; H, 7.40%.



5d

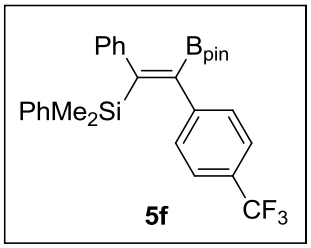
(*Z*)-1-(Dimethylphenylsilyl)-1-phenyl-2-(3-methoxyphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5d). White solid (173 mg, 0.37 mmol, 74%). Mp = 90-91 ℃. R_f = 0.14 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2974 (m), 2929 (w), 1456 (m), 1338 (s), 1305 (s), 1263 (s), 1141 (s), 845 (s), 816 (m), 702 (s). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ –0.02 (s, 6H), 0.91 (s, 12H), 3.58 (s, 3H), 6.70-6.74 (m, 2H), 6.80-6.83 (m, 1H), 7.12 (t, J =7.8 Hz, 1H), 7.17-7.19 (m, 3H), 7.23-7.26 (m, 5H), 7.37-7.40 (m, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, rt): δ –1.2, 24.2, 54.9, 83.4 112.6, 113.3, 120.6, 125.7, 127.4, 127.5, 128.4, 128.5, 128.8, 133.9, 139.7, 143.3, 145.6, 153.6, 159.0. The carbon signal attached to B was not observed due to low intensity; ^{11}B{^{1}H} NMR (192 MHz, $CDCl_3$, rt): δ 29.5. MS (EI, m/z (relative intensity)): 470 (M^+, 20), 455 (40), 386 (29), 295 (18), 277 (23), 277 (23), 208 (42), 135 (100), 84 (39), 83 (38). Anal. Calcd for $C_{29}H_{35}SiBO_3$: C, 74.03; H, 7.50%. Found: C, 73.63; H, 7.59%.



5e

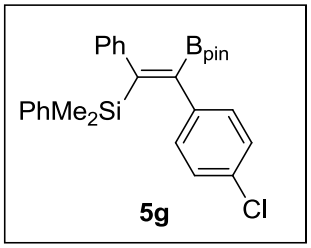
(*Z*)-1-(Dimethylphenylsilyl)-1-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(4-methylphenyl)ethene (5e). White solid (192 mg, 0.42 mmol, 81%). Mp = 83-84 ℃. R_f = 0.27 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2980 (m), 1342 (s), 1305 (m), 1141 (s), 1111 (m), 850 (m), 700 (s). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ –0.05 (s, 6H), 0.89 (s, 12H), 2.31 (s, 3H), 6.97-7.00 (m, 2H), 7.05-7.07 (m, 2H), 7.12-7.17 (m, 3H), 7.20-7.26 (m, 5H), 7.32-7.35 (m, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, rt): δ –1.2, 21.1, 24.2, 83.3, 125.6, 127.3, 127.4, 128.0, 128.3, 128.4, 128.5, 133.9, 136.0, 139.1,

139.5, 145.7, 153.5. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.4. MS (EI, m/z (relative intensity)): 454 (M^+, 37), 439 (31), 370 (33), 279 (21), 261 (24), 192 (59), 135 (100), 84 (47), 83 (39). Anal. Calcd for $C_{29}H_{35}SiBO_2$: C, 76.64; H, 7.76%. Found: C, 76.56; H, 7.60%.



5f

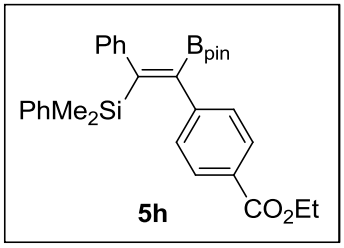
(*Z*)-1-(Dimethylphenylsilyl)-1-phenyl-2-(4-trifluoromethylphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5f). White solid. Isolated in 50% yield (126 mg, 0.25 mmol) from 4-iodobenzotrifluoride (**4f**) and 50% yield (127 mg, 0.26 mmol) from 4-bromobenzotrifluoride (**4f'**), respectively. Mp = 104-105 ℃. R_f = 0.12 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2981 (w), 1348 (m), 1323 (s), 1159 (s), 1141 (s), 1116 (s), 1107 (s), 1064 (s), 702 (m). ^1H NMR (300 MHz, $CDCl_3$, rt): δ 0.01 (s, 6H), 0.89 (s, 12H), 7.15-7.30 (m, 12H), 7.37 (d, J = 8.1 Hz, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ –1.2, 24.2, 83.6, 124.3 (q, $J_{C\text{-}F}$ = 272.2 Hz), 124.6 (q, $J_{C\text{-}F}$ = 3.3 Hz), 126.0, 127.5, 127.7, 128.2, 128.4, 128.5 (q, $J_{C\text{-}F}$ = 32.0 Hz), 128.6, 133.7, 138.6, 145.3, 145.7, 155.8. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.1; $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$, rt): δ –62.8. MS (EI, m/z (relative intensity)): 508 (M^+, 19), 493 (35), 431 (14), 354 (32), 227 (17), 135 (100), 84 (71), 83 (31). Anal. Calcd for $C_{29}H_{32}SiBO_2F_3$: C, 68.50; H, 6.34%. Found: C, 68.49; H, 6.05%.



5g

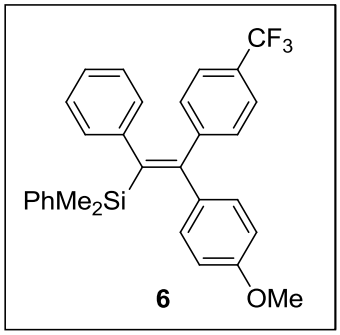
(*Z*)-1-(Dimethylphenylsilyl)-1-phenyl-2-(4-chlorophenyl)-2-(4,4,5,5-tetramethyl-1,3

,2-dioxaborolan-2-yl)ethene (5g). White solid (192 mg, 0.40 mmol, 81%). Mp = 105-106 ℃. R_f = 0.16 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2983 (m), 1489 (m), 1338 (s), 1303 (s), 1141 (s), 1111 (m), 840 (s), 773(m), 702 (s). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 0.00 (s, 6H), 0.90 (s, 12H), 7.03-7.08 (m, 2H), 7.10-7.18 (m, 5H), 7.19-7.32 (m, 7H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, rt): δ –1.2, 24.2, 83.5, 125.8, 127.4, 127.6, 127.8, 128.3, 128.5, 129.5, 132.4, 133.8, 139.0, 140.5, 145.4, 155.0. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.2. MS (EI, m/z (relative intensity)): 474 (M^+, 14), 459 (18), 390 (13), 211 (16), 135 (100), 84 (47), 83 (23). Anal. Calcd for $C_{28}H_{32}SiBO_2Cl$: C, 70.82; H, 6.79%. Found: C, 70.99; H, 6.70%.

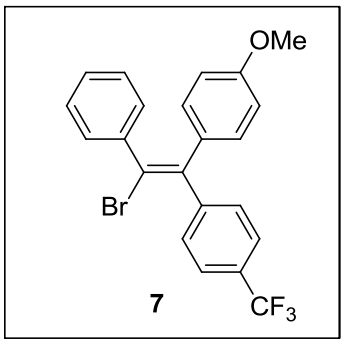


5h

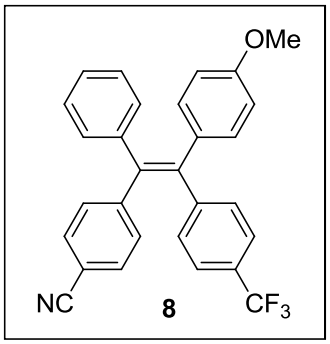
(*Z*)-1-(Dimethylphenylsilyl)-1-phenyl-2-(4-ethoxycarbonylphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5h). White solid (154 mg, 0.30 mmol, 60%). Mp = 91-92 ℃. R_f = 0.27 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2983 (m), 1489 (m), 1338 (s), 1303 (s), 1141 (s), 1111 (m), 840 (s), 773(m), 702 (s). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ –0.03 (s, 6H), 0.88 (s, 12H), 1.40 (t, J = 7.2 Hz, 3H), 4.37 (q, J = 7.2 Hz, 2H), 7.13-7.33 (m, 12H), 7.87 (d, J = 8.7 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, rt): δ –1.2, 14.3, 24.2, 60.8, 83.6, 125.9, 127.4, 127.6, 128.1, 128.2, 128.51, 128.58, 129.1, 133.8, 138.8, 145.3, 147.0, 155.1, 166.6. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 28.6. MS (EI, m/z (relative intensity)): 512 (M^+, 21), 468 (17), 397 (21), 355 (40), 337 (32), 250 (37), 206 (33), 205 (59), 204 (20), 135 (100), 107 (16), 105 (24). Anal. Calcd for $C_{31}H_{37}SiBO_4$: C, 72.65; H, 7.28%. Found: C, 72.55; H, 7.10%.



Suzuki-Miyaura Cross-Coupling of 5b with 4f: Synthesis of (*Z*)-1-(Dimethylphenylsilyl)-1-phenyl-2-(4-trifluoromethylphenyl)-2-(4-methoxyphenyl)ethene (6). To a deep purple solution of Pd_2dba_3 (26 mg, 0.025 mmol, 5 mol %) and P(*t*-Bu)$_3$ (20 mg, 0.1 mmol, 20 mol %) in THF (5 mL) in 20 mL of Schlenk tube were added **5b** (235 mg, 0.5 mmol) and 4-iodobenzotrifluoride (**4f**) (204 mg, 0.75 mmol, 1.5 equiv) at room temperature under an Ar atmosphere. After aqueous 3 M KOH solution (1.5 mmol, 0.5 mL) was added to the reaction mixture, a color of the reaction mixture turned to deep brown solution immediately. The reaction mixture was heated to a reflux temperature and stirred for 12 h. After the reaction completed, the reaction mixture was quenched by sat. NH_4Cl solution, then extracted with diethyl ether (20 mL x 2). The combined ethereal layers were washed with brine and dried over $MgSO_4$. Filtration, evaporation, and silica gel chromatography (hexane: ethyl acetate = 20:1) gave the titled compound **6** (207 mg, 0.42 mmol, 85%) as a colorless viscous oil. R_f = 0.41 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 3068 (w), 1608 (m), 1506 (s), 1325 (s), 1247 (s), 1165 (s), 1122 (m), 1111 (s), 854 (s), 702 (s). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 0.09 (s, 6H), 3.84 (s, 3H), 6.78 (d, J = 8.1 Hz, 2H), 6.96 (d, J = 8.1 Hz, 2H), 7.05-7.10 (m, 5H), 7.13-7.18 (m, 2H) 7.29-7.39 (m, 7H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt): δ –0.8, 55.2, 113.3, 124.1 (q, $J_{C\text{-}F}$ = 272.1 Hz), 124.2 (q, $J_{C\text{-}F}$ = 3.5 Hz), 125.3, 127.5, 127.6, 128.8 (q, $J_{C\text{-}F}$ = 32.6 Hz), 128.6, 129.5, 129.7, 130.8, 133.8, 135.6, 139.8, 143.3, 144.2, 147.1, 153.2, 159.0; ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$, rt): δ –62.8. MS (EI, m/z (relative intensity)): 488 (M^+, 77), 473 (21), 334 (20), 265 (20), 227 (66), 135 (100). Anal. Calcd for $C_{30}H_{27}SiOF_3$: C, 73.74; H, 5.57%. Found: C, 73.78; H, 5.74%.

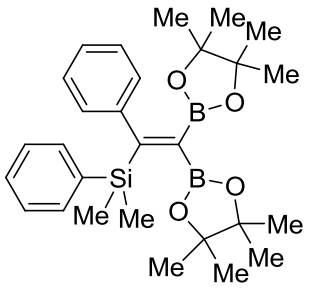


Desilylbromination of 6: Synthesis of (*E*)-1-Bromo-1-phenyl-2-(4-trifluoromethylphenyl)-2-(4-methoxyphenyl)ethene (7). To a solution of **6** (212 mg, 0.43 mmol) in a 20 mL Schlenk tube was added Br_2 (0.64 mL, 0.64 mmol, 1.5 equiv, 1.0 M CH_2Cl_2 solution) at -78 ℃, followed by addition of NaOMe (1.1 mL, 1.1 mmol, 1.0 M MeOH solution). After being stirred for 5 min at -78 ℃, the reaction mixture was allowed to warm slowly to room temperature and stirred for another 2 h. Then the reaction mixture was quenched with H_2O and extracted with Et_2O (10 mL x 2). Evaporation and column chromatography (hexane/ethyl acetate = 20:1) yielded a viscous oil. Recrystallization from Et_2O/hexane afforded the title compound **7** (112 mg, 0.26 mmol, 60%) as white solid. Mp = 97-98 ℃. R_f = 0.30 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 833 (m), 1066 (m), 1122 (s), 1165 (m), 1250 (s), 1327 (s), 1510 (m), 1605 (m). ^{1}H NMR (300 MHz, $CDCl_3$, rt): δ 3.71 (s, 3 H), 6.62 (d, J = 9.0 Hz, 2H), 6.84 (d, J = 9.0 Hz, 2H), 7.20-7.25 (m, 3H), 7.33-7.36 (m, 2H), 7.50 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 8.1 Hz, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt): δ 55.1, 113.4, 122.1, 124.1 (q, $J_{C\text{-}F}$ = 272.1 Hz), 125.2 (q, $J_{C\text{-}F}$ = 3.3 Hz), 128.09, 128.12, 129.4 (q, $J_{C\text{-}F}$ = 32.6 Hz), 130.0, 130.2, 131.6, 132.6, 140.8, 141.8, 147.5, 158.7; ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$, rt): δ –62.9. MS (EI, m/z (relative intensity)): 434 (M^+, 60), 432 (59), 354 (25), 353 (100), 252 (18), 239 (21). Anal. Calcd for $C_{22}H_{16}BrF_3O$: C, 60.99; H, 3.72%. Found: C, 60.87; H, 3.48%.

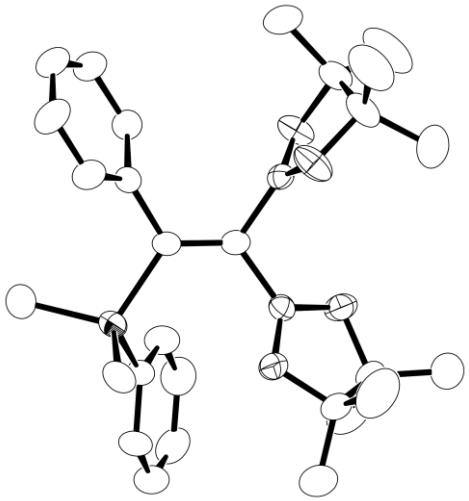


Suzuki-Miyaura Cross-Coupling Reaction of 7 with 4-Cyanophenylboronic Acid: Synthesis of (*E*)-1-(4-Cyanophenyl)-1-phenyl-2-(4-trifluoromethylphenyl)-2-(4-methoxyphenyl)ethene (8). To a yellow solution of $Pd(PPh_3)_4$ (5 mg, 0.004 mmol, 2 mol %) in toluene (2 mL) in a 20 mL of Schlenk tube were added **7** (86 mg, 0.2 mmol), 4-cyanophenylboronic acid (44 mg, 0.3 mmol, 1.5 equiv), tetrabutylammonium bromide (TBAB) (6 mg, 0.02 mmol, 10 mol %), and 2 M K_2CO_3 aqueous solution (0.3 mL, 0.6 mmol, 3 equiv) at room temperature under an Ar atmosphere. The reaction mixture was heated up to 90 ℃ and stirred for 12 h. After the reaction completed, the reaction mixture was quenched by sat. NH_4Cl solution, then extracted with diethyl ether (20 mL x 2). The combined ethereal layers were washed with brine and dried over $MgSO_4$. Filtration, evaporation, and silica gel chromatography (hexane: ethyl acetate = 20:1) gave **8** (81 mg, 0.18 mmol, 89%) as pale yellow fluffy solid. Mp = 135-136 ℃. R_f = 0.18 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 833 (m), 1066 (m), 1126 (s), 1165 (m), 1247 (s), 1323 (s), 1506 (m), 1602 (m), 2227 (w). ^1H NMR (300 MHz, $CDCl_3$, rt): δ 3.75 (s, 3H), 6.67 (d, J = 9.0 Hz, 2H), 6.90 (d, J = 9.0 Hz, 2H), 6.99-7.03 (m, 2H), 7.09-7.19 (m, 7H), 7.40 (d, J = 8.1 Hz, 4H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 55.1, 110.2, 113.3, 118.8, 124.0 (q, $J_{C\text{-}F}$ = 272.1 Hz), 124.9 (q, $J_{C\text{-}F}$ = 3.5 Hz), 127.1, 128.1, 129.0 (q, $J_{C\text{-}F}$ = 32.0 Hz), 131.1, 131.5, 131.6, 131.9, 132.4, 134.4, 139.6, 141.3, 142.4, 146.8, 148.3, 158.7; $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$, rt): δ –62.9. MS (EI, m/z (relative intensity)): 456 (M^+, 33), 455 (100), 436 (2), 353 (2), 278 (3), 277 (3), 266 (3), 264 (3), 239 (3), 218 (2). Anal. Calcd for $C_{29}H_{20}NF_3O$: C, 76.47; H, 4.43; N, 3.08%. Found: C, 76.53; H, 4.35, N, 3.02%.

3-4-3 Structural Determination of Compounds by X-ray Analysis



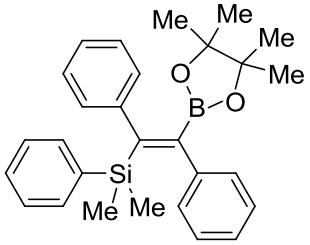
3



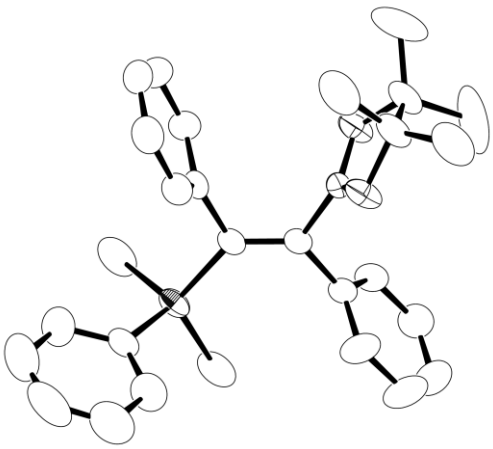
Empirical Formula	$C_{29}H_{20}F_3NO$
Formula Weight	455.48
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.40 X 0.10 X 0.10 mm
Crystal System	triclinic
Lattice Type	Primitive
No. of Reflections Used for Unit	
Cell Determination (2q range)	11130 (6.0 - 54.9^o)
Omega Scan Peak Width	
at Half-height	0.00 ^{o}
Lattice Parameters	a = 10.299(4) Å
	b = 12.070(6) Å
	c = 19.582(6) Å
	a = 89.885(15) ^{o}
	b = 86.412(13) ^{o}
	g = 78.391(17) ^{o}
	V = 2379.6(17) Å^3

Space Group	P-1 (#2)
Z value	4
D_{calc}	1.271 g/cm^3
F_{000}	944.00
m (MoKa)	0.928 cm^{-1}
Diffractometer	AFC7
Radiation	MoKa (l = 0.71075 Å)
	graphite monochromated
Take-off Angle	2.8 ^{o}
Detector Aperture	2.0 - 2.5 mm horizontal
	2.0 mm vertical
Crystal to Detector Distance	21 mm
Scan Type	w-2q
$2q_{max}$	55.0 ^{o}
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.964 - 0.991)
Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares on F
Function Minimized	S w (|Fo| - |Fc|)^2
Least Squares Weights	1
$2q_{max}$ cutoff	55.0 ^{o}
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>2.00s(I))	10725
No. Variables	613
Reflection/Parameter Ratio	17.50
Residuals: R (I>2.00s(I))	0.0759
Residuals: Rw (I>2.00s(I))	0.2460
Goodness of Fit Indicator	0.938

Max Shift/Error in Final Cycle	0.001
Maximum peak in Final Diff. Map	0.58 $e^-/Å^3$
Minimum peak in Final Diff. Map	0.00 $e^-/Å^3$



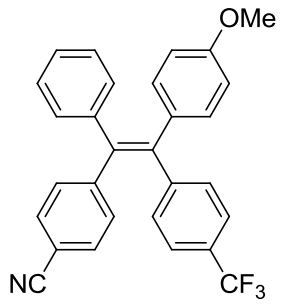
(*E*)-**5a**



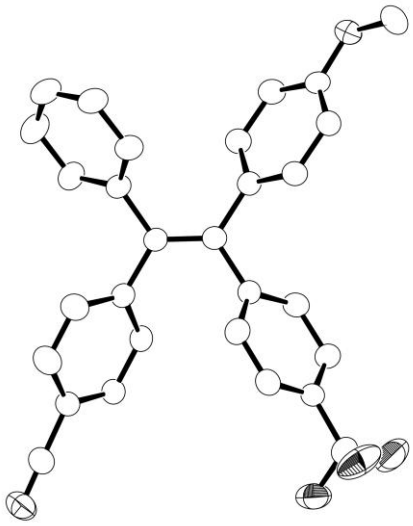
Empirical Formula	$C_{28}H_{33}BO_2Si$
Formula Weight	440.46
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.50 X 0.40 X 0.25 mm
Crystal System	triclinic
Lattice Type	Primitive
No. of Reflections Used for Unit	
Cell Determination (2q range)	11024 (6.8 - 55.1 °)
Lattice Parameters	a = 10.0966(9) Å
	b = 10.7209(9) Å
	c = 13.1753(11) Å
	a = 94.573(2) °
	b = 94.171(2) °
	g = 109.280(2) °
	V = 1334.43(20) $Å^3$
Space Group	P-1 (#2)

Z value	2
D_{calc}	1.096 g/cm^3
F_{000}	472.00
m (MoKa)	1.084 cm^{-1}
Diffractometer	AFC7
Radiation	MoKa (l = 0.71075 Å)
	graphite monochromated
Take-off Angle	2.8 ^{o}
Detector Aperture	2.0 - 2.5 mm horizontal
	2.0 mm vertical
Crystal to Detector Distance	21 mm
Temperature	24.9 ℃
Scan Type	w-2q
$2q_{max}$	55.0 ^{o}
	Unique: 0 (R_{int} = 0.041)
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.948 - 0.973)
Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares on F
Function Minimized	S w (|Fo| - |Fc|)^2
Least Squares Weights	1
$2q_{max}$ cutoff	55.0 ^{o}
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>2.00s(I))	6073
No. Variables	373
Reflection/Parameter Ratio	16.28
Residuals: R (I>2.00s(I))	0.0714
Residuals: Rw (I>2.00s(I))	0.2063
Goodness of Fit Indicator	1.026

Max Shift/Error in Final Cycle	0.001
Maximum peak in Final Diff. Map	0.37 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.24 $e^-/Å^3$



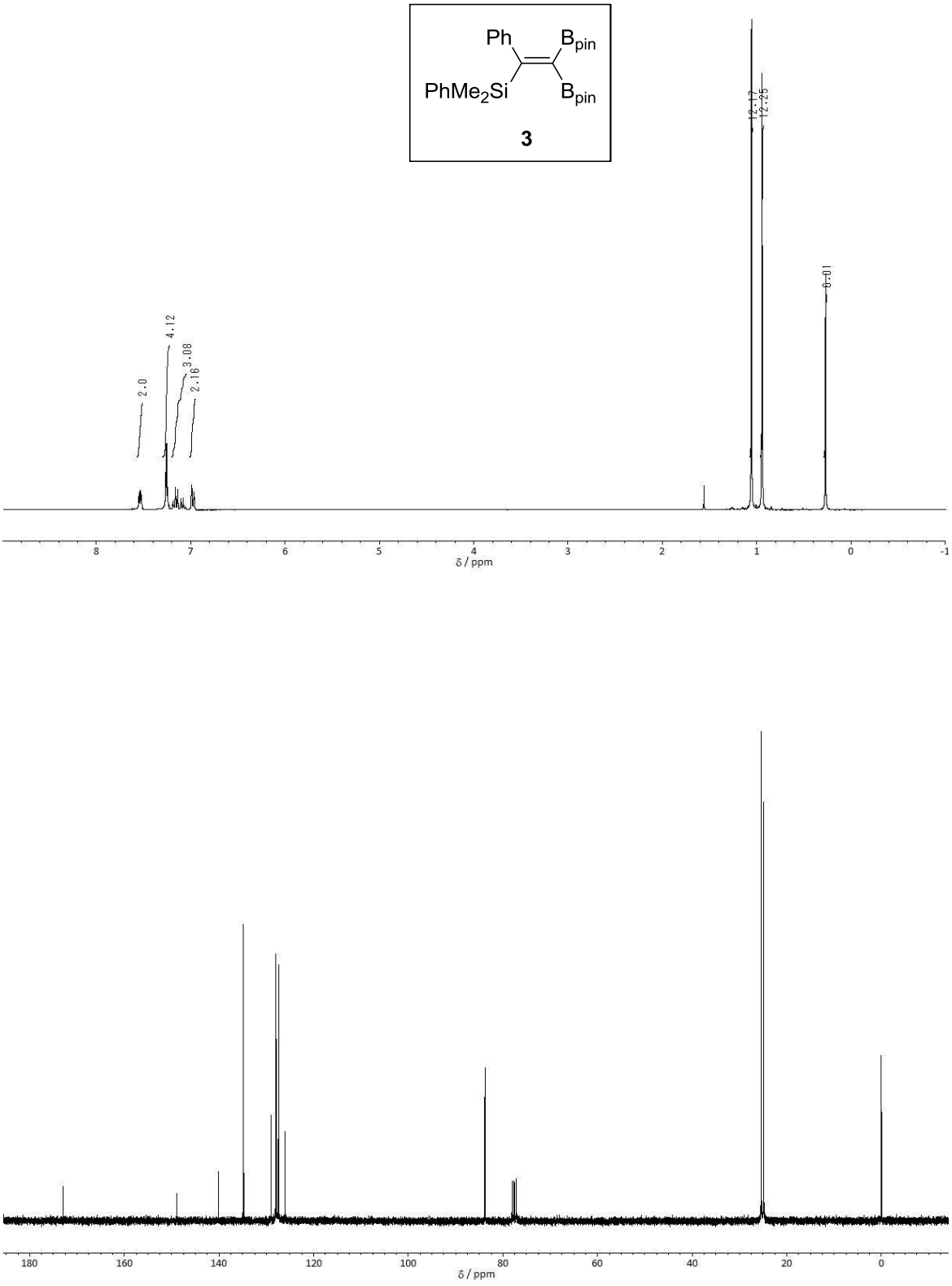
8



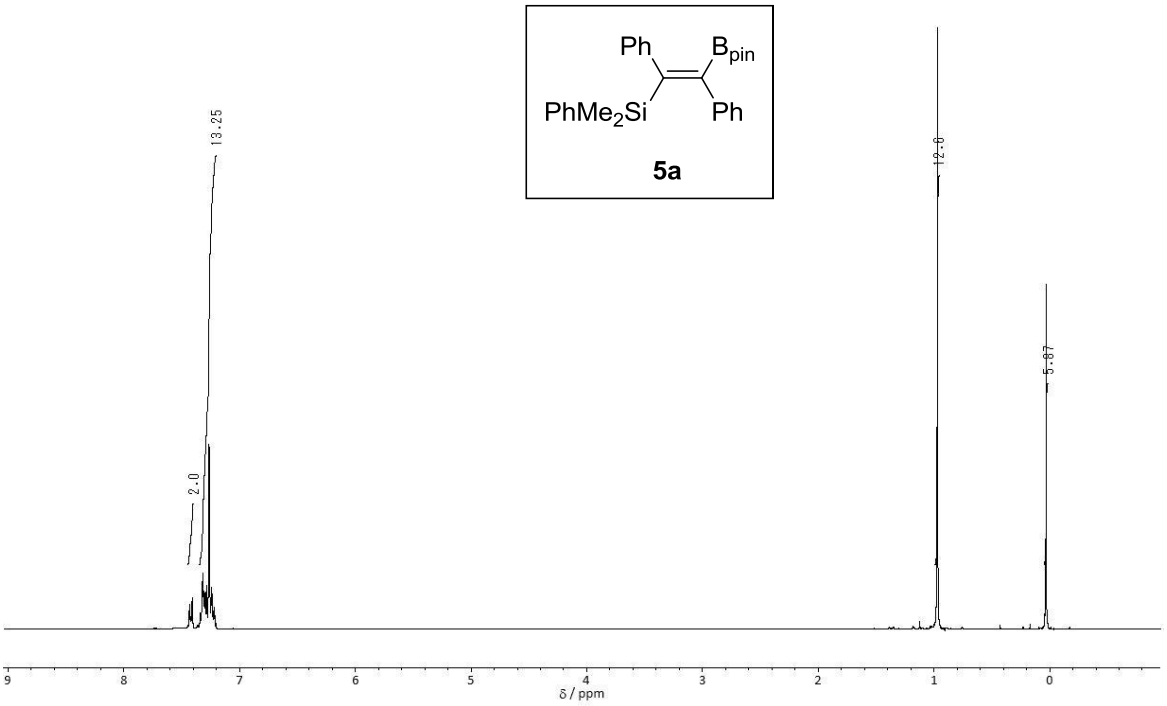
Empirical Formula	$C_{29}H_{20}F_3NO$
Formula Weight	455.48
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.40 X 0.10 X 0.10 mm
Crystal System	triclinic
Lattice Type	Primitive
No. of Reflections Used for Unit	
Cell Determination (2q range)	11130 (6.0 - 54.9 ^{o})
Lattice Parameters	a = 10.299(4) Å
	b = 12.070(6) Å
	c = 19.582(6) Å
	a = 89.885(15) ^{o}
	b = 86.412(13) ^{o}
	g = 78.391(17) ^{o}
	V = 2379.6(17) Å^3
Space Group	P-1 (#2)
Z value	4
D_{calc}	1.271 g/cm^3
F_{000}	944.00

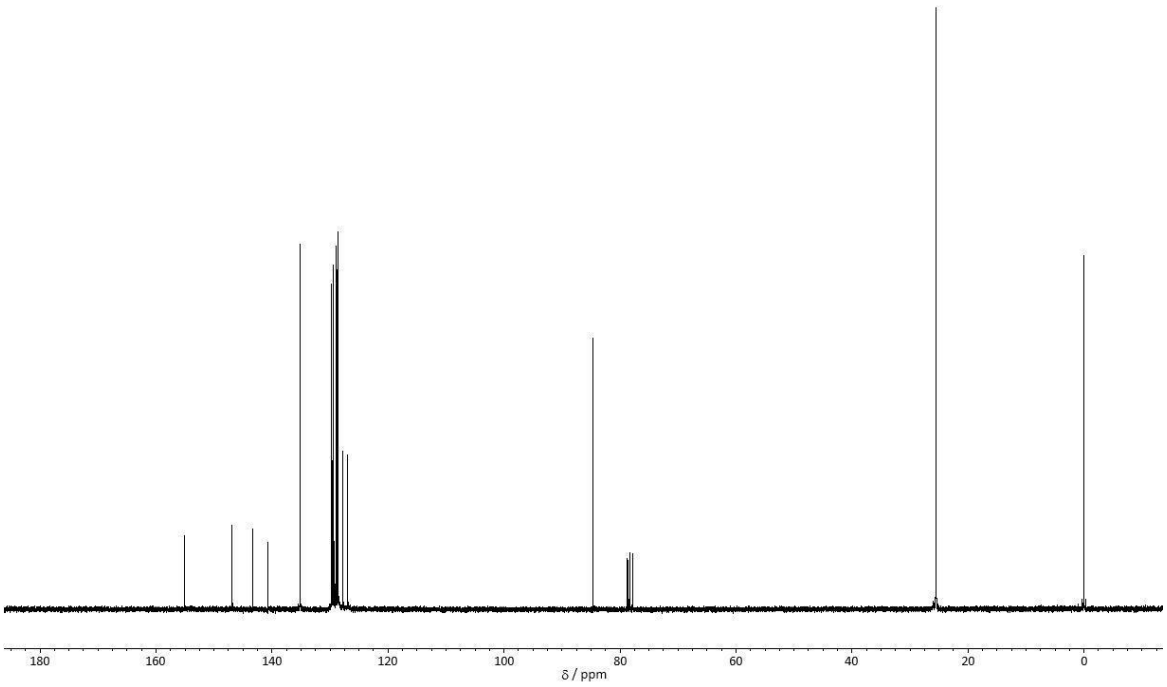
m (MoKa)	0.928 cm^{-1}
Diffractometer	AFC7
Radiation	MoKa (l = 0.71075 Å) graphite monochromated
Take-off Angle	2.8 ^{o}
Detector Aperture	2.0 - 2.5 mm horizontal 2.0 mm vertical
Crystal to Detector Distance	21 mm
Temperature	24.9 ^{o}C
Scan Type	w-2q
$2q_{max}$	55.0 ^{o}
Corrections	Lorentz-polarization Absorption (trans. factors: 0.964 - 0.991)
Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares on F
Function Minimized	S w $(\|Fo\| - \|Fc\|)^2$
Least Squares Weights	1
$2q_{max}$ cutoff	55.0 ^{o}
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>2.00s(I))	10725
No. Variables	613
Reflection/Parameter Ratio	17.50
Residuals: R (I>2.00s(I))	0.0759
Residuals: Rw (I>2.00s(I))	0.2460
Goodness of Fit Indicator	0.938
Max Shift/Error in Final Cycle	0.001
Maximum peak in Final Diff. Map	0.58 $e^{-}/Å^3$
Minimum peak in Final Diff. Map	0.00 $e^{-}/Å^3$

3-4-4 Copies of ^{1}H and $^{13}C\{^{1}H\}$ NMR Charts for the New Compounds

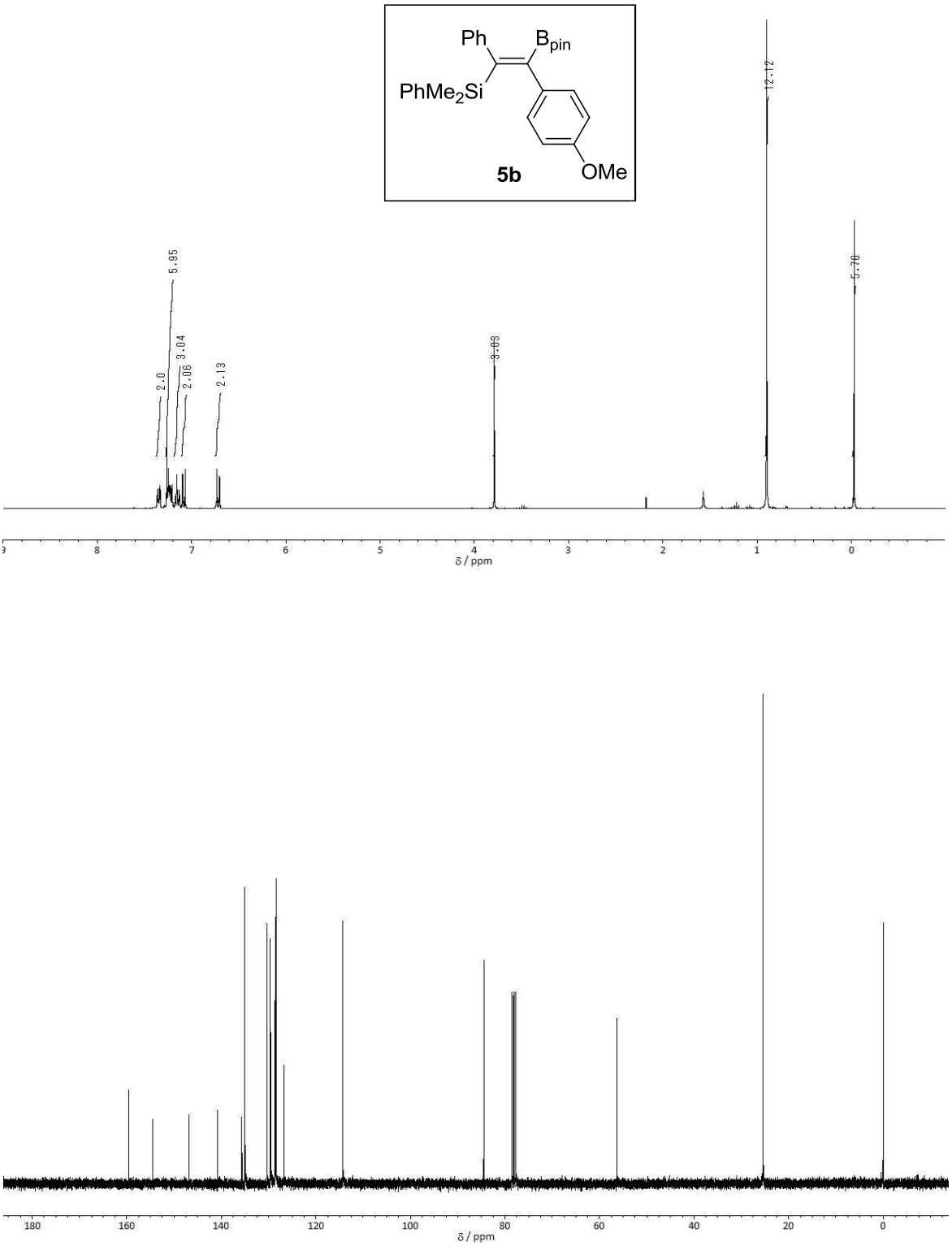


The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3** (in $CDCl_3$)

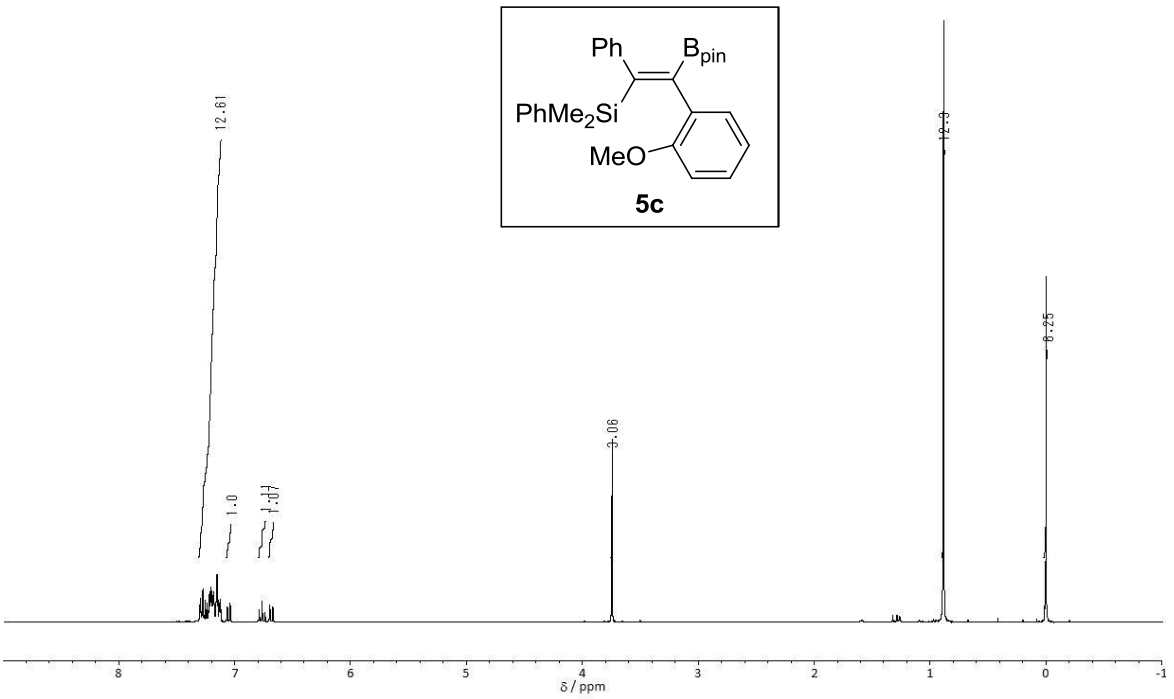


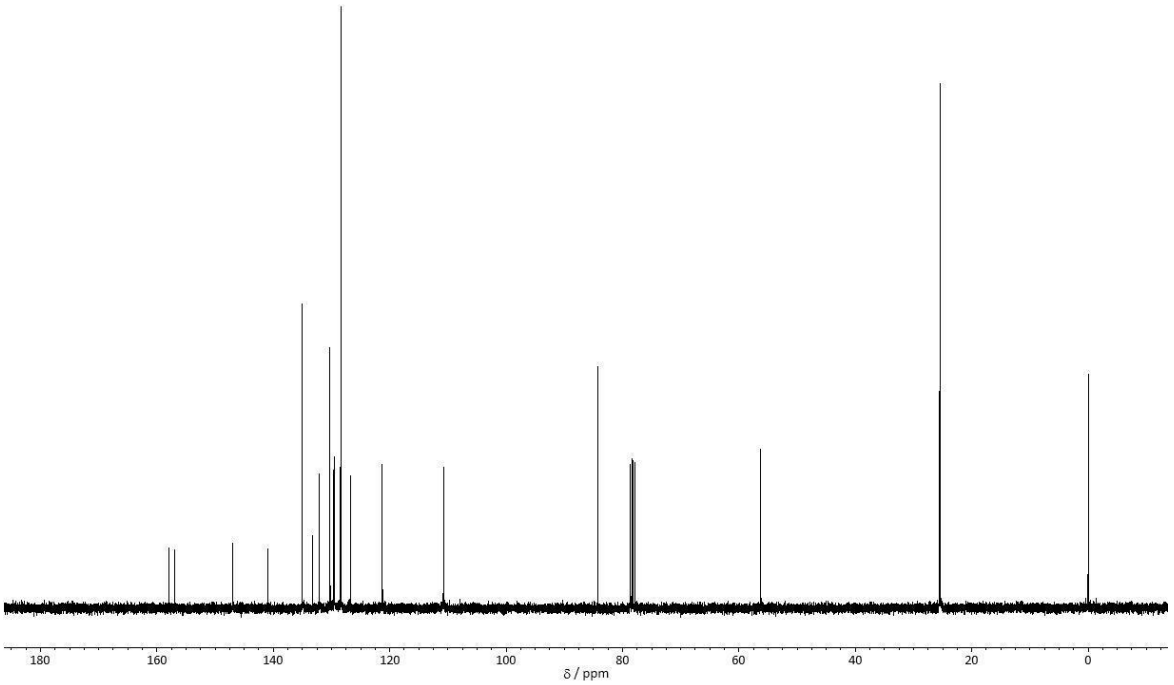


The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound (*Z*)-**5a** (in $CDCl_3$)

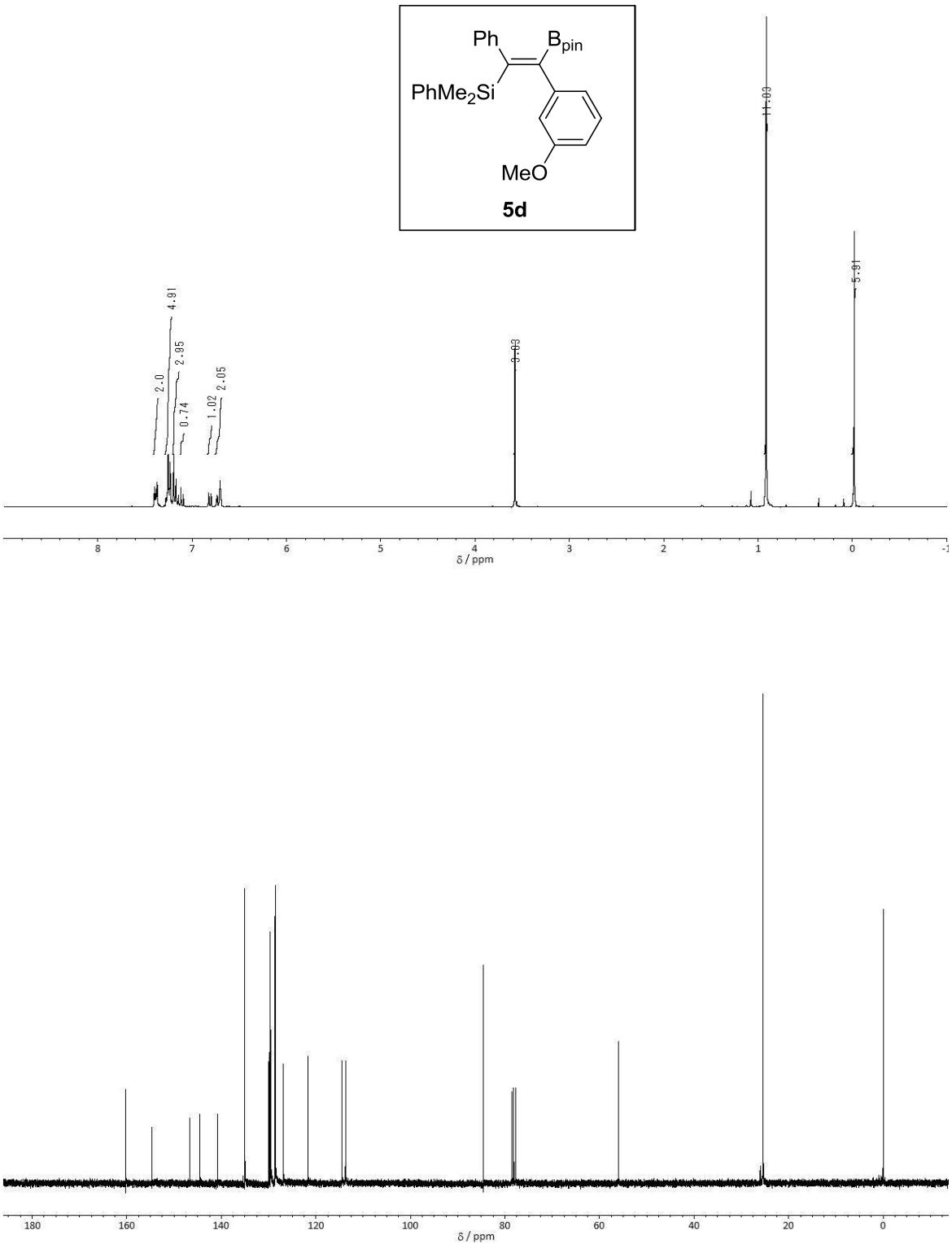


The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound (*Z*)-**5b** (in $CDCl_3$)

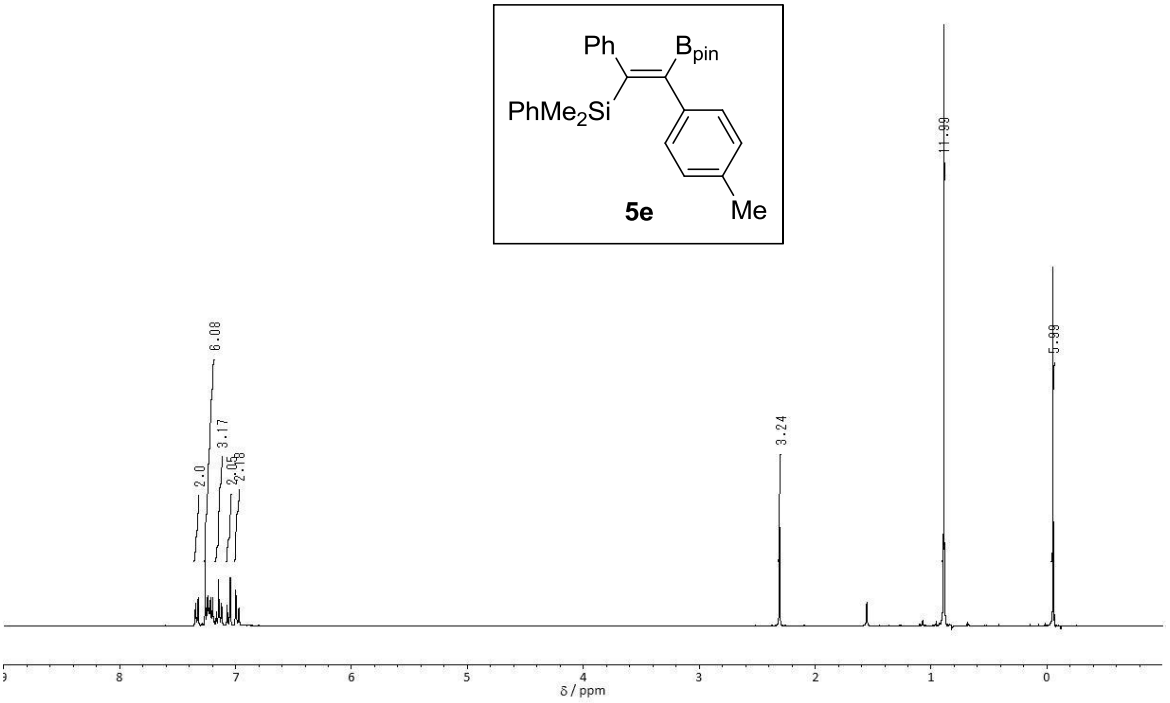


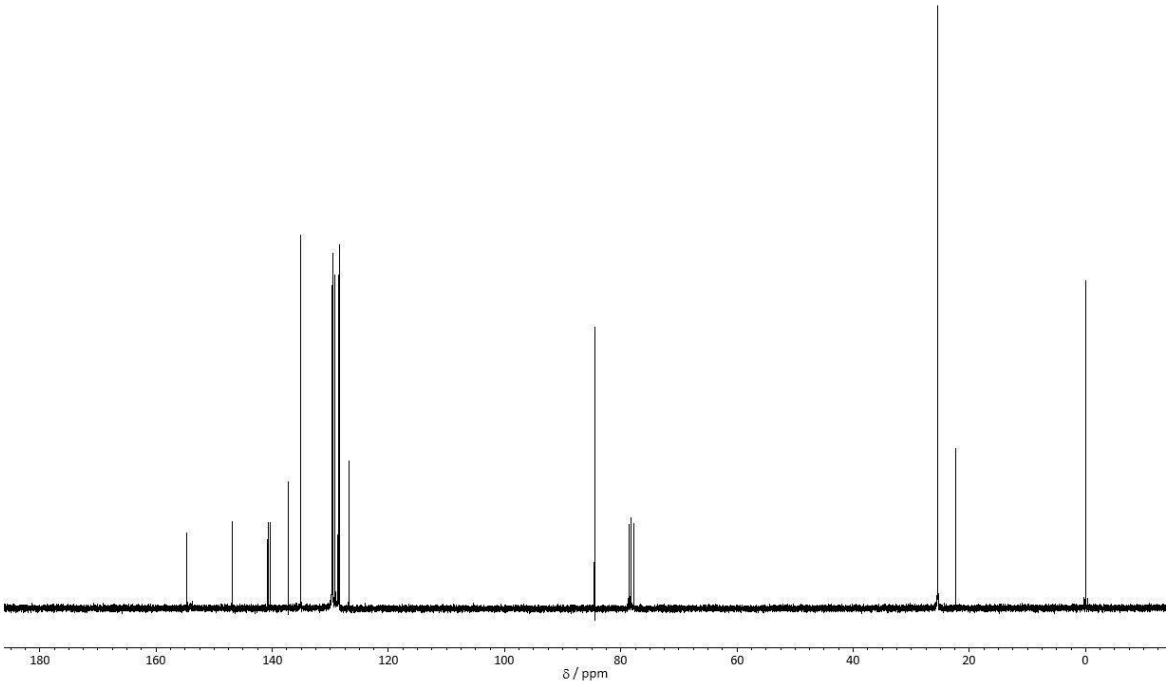


The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound (*Z*)-**5c** (in $CDCl_3$)

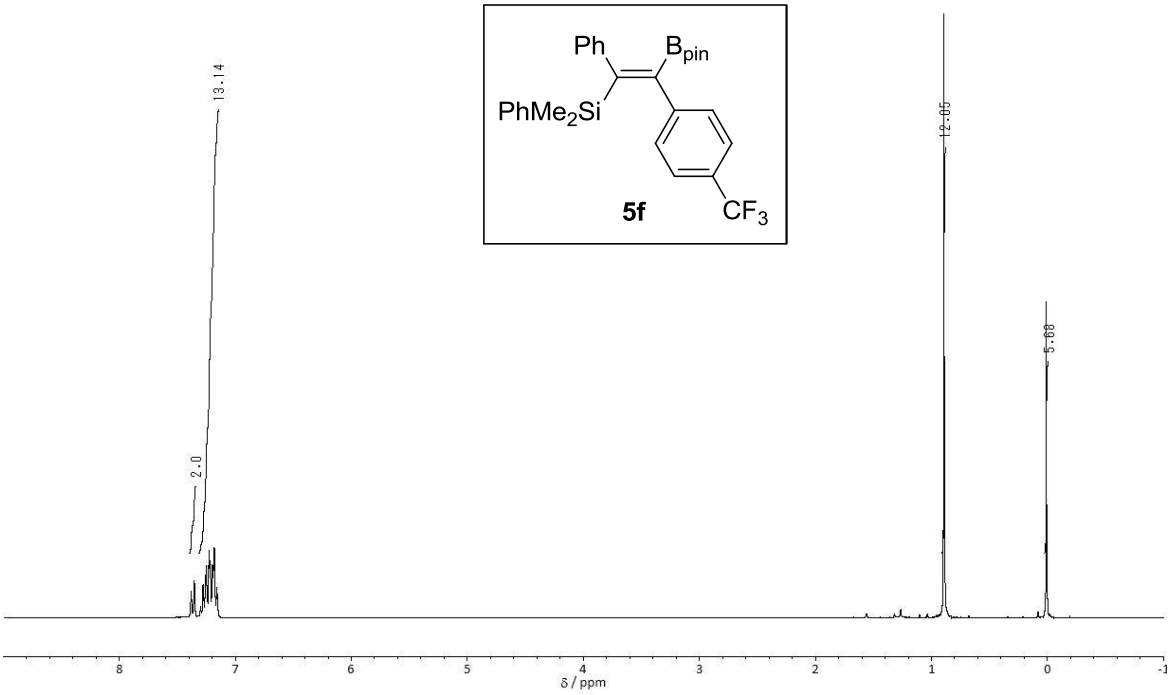


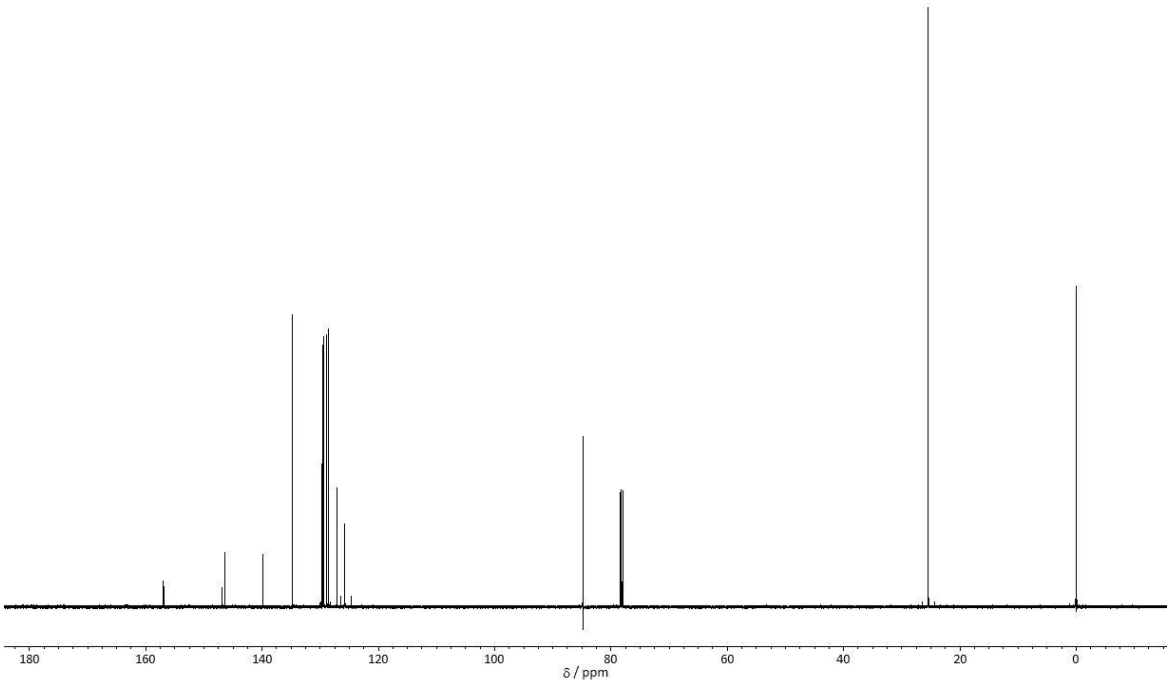
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound (*Z*)-**5d** (in $CDCl_3$)



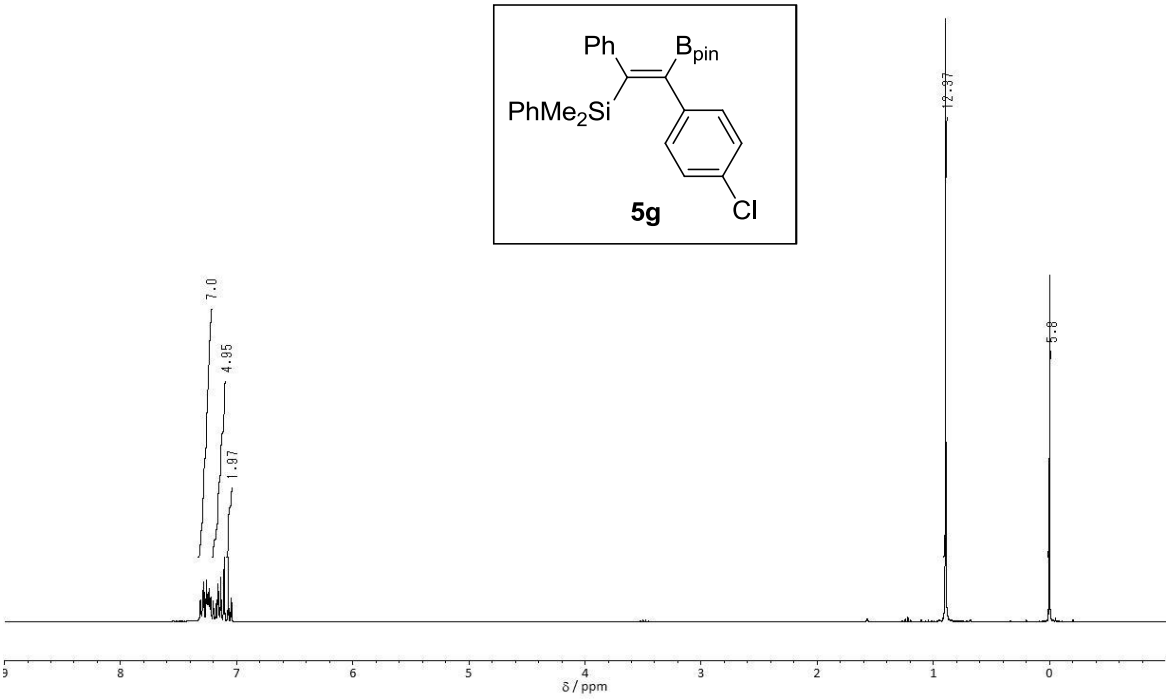


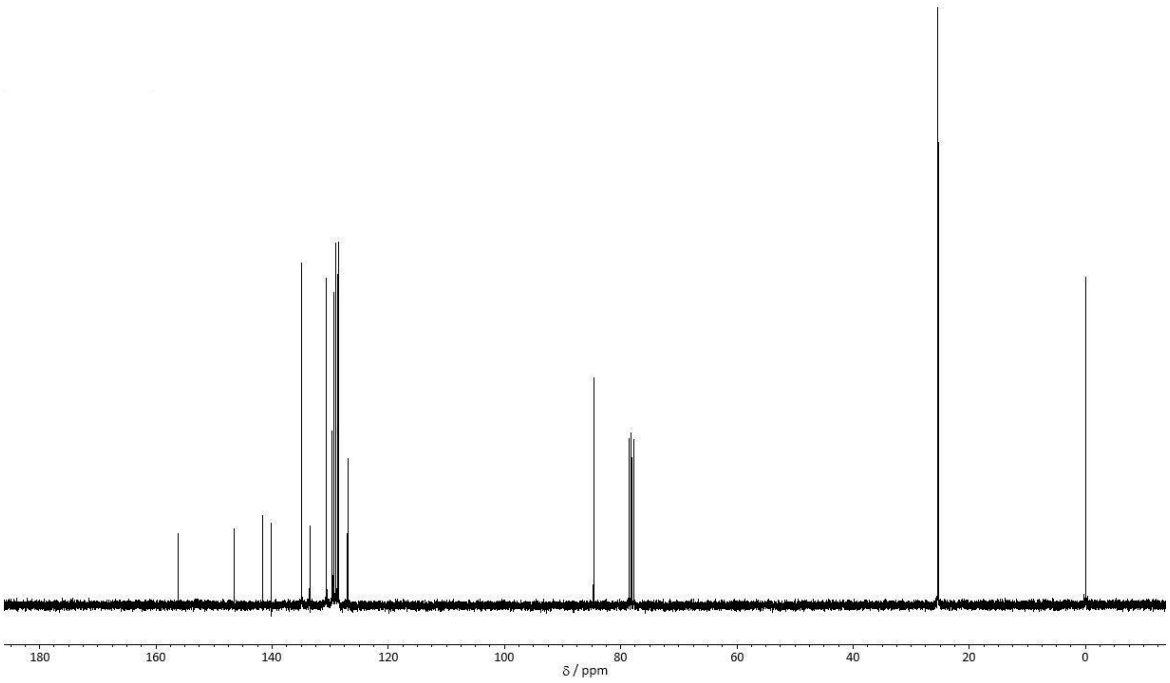
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound (*Z*)-**5e** (in $CDCl_3$)



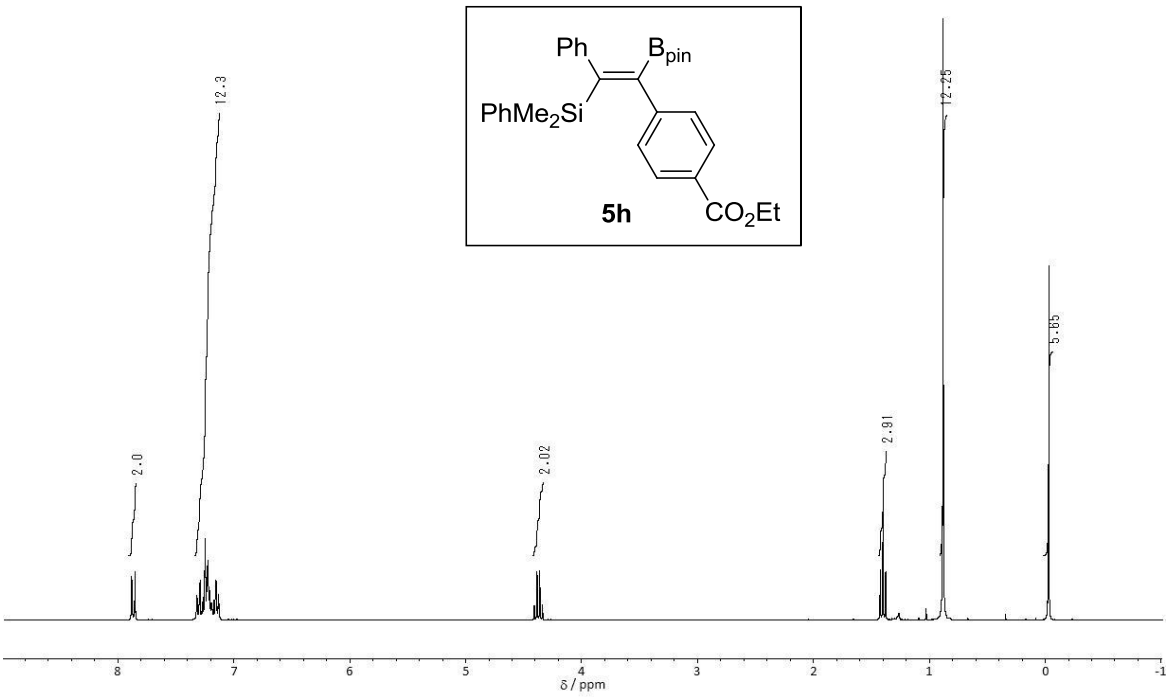


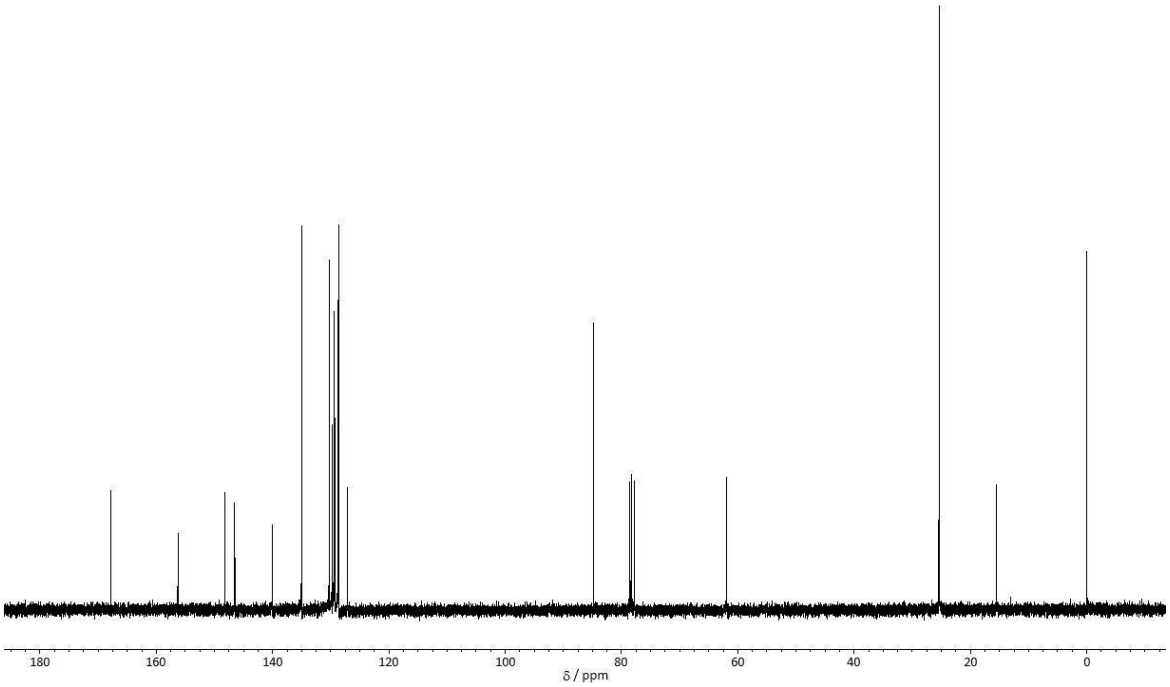
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound (*Z*)-**5f** (in $CDCl_3$)



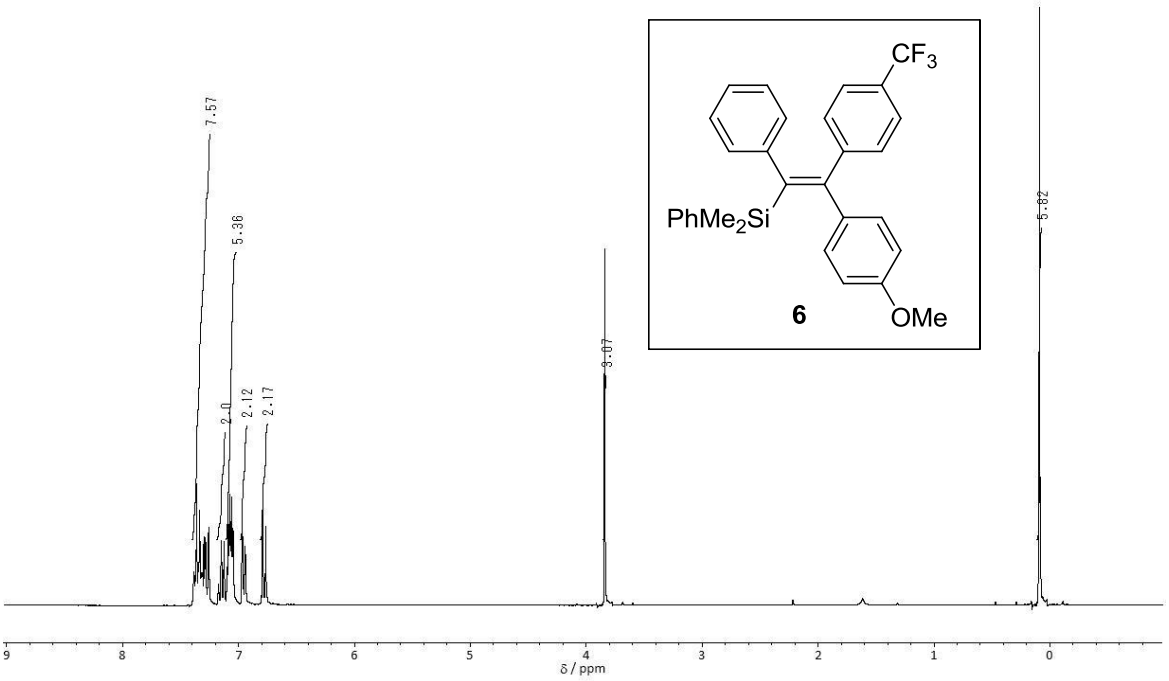


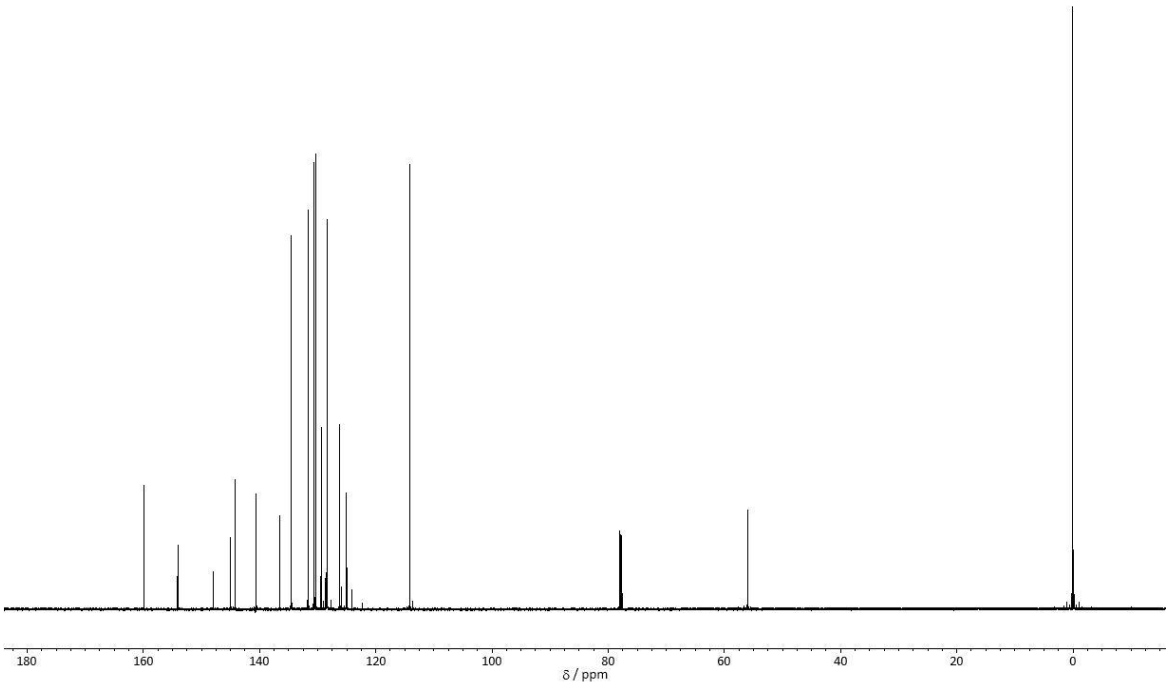
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound (*Z*)-**5g** (in $CDCl_3$)



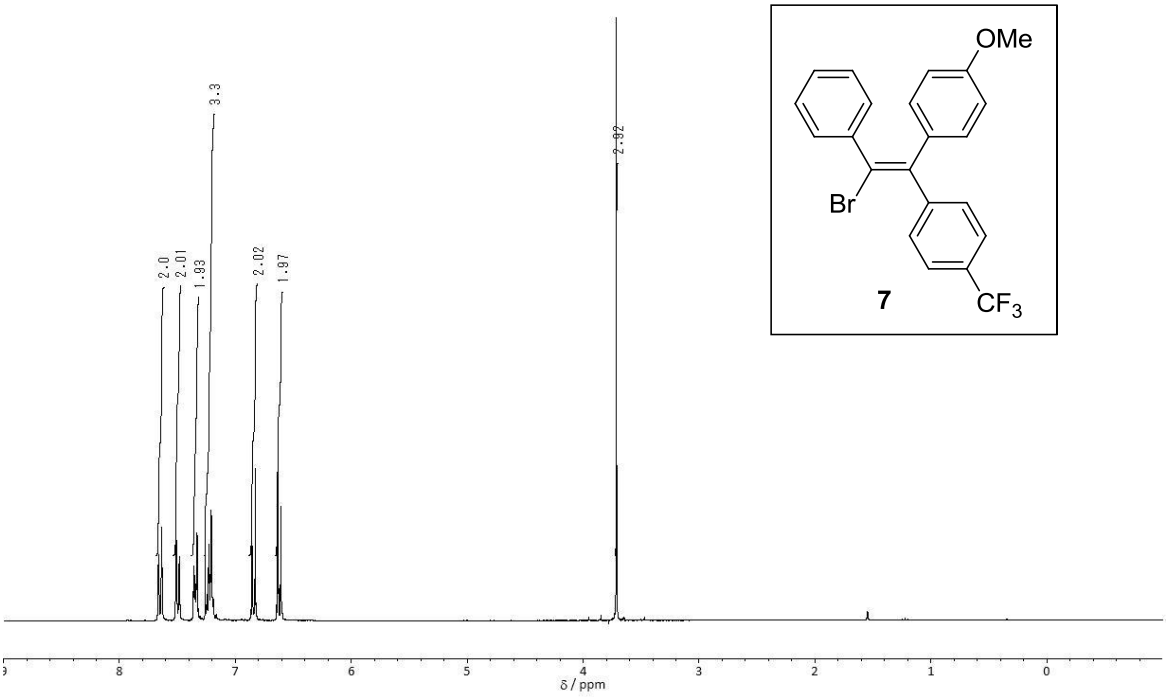


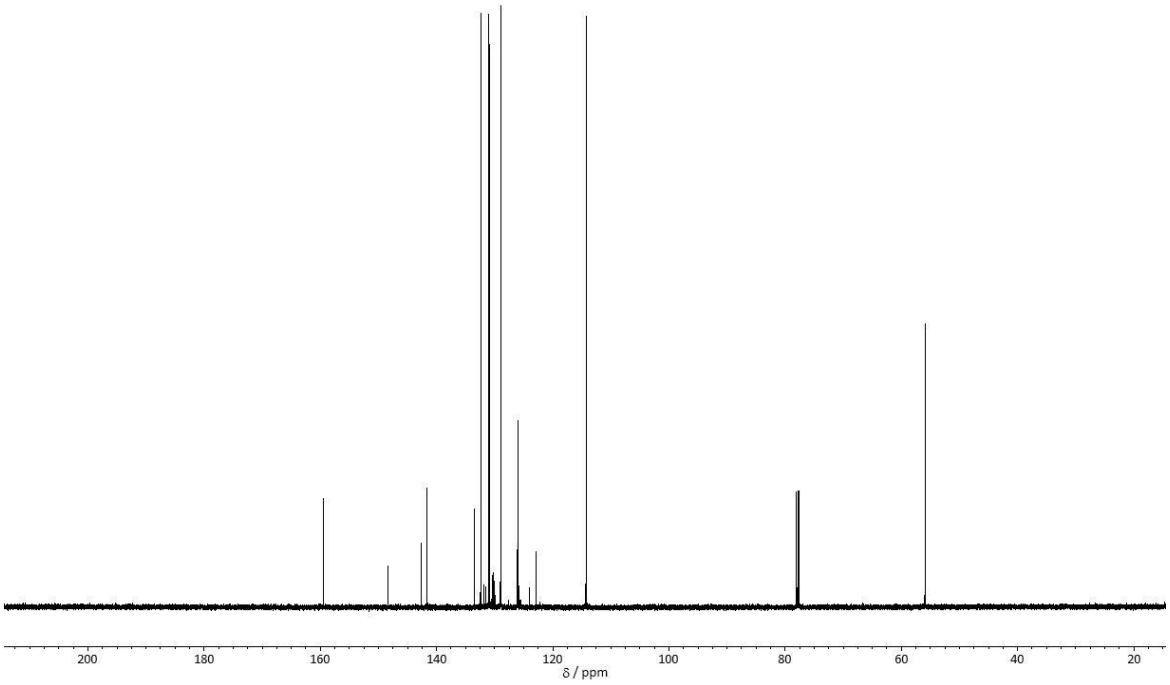
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound (*Z*)-**5h** (in $CDCl_3$)



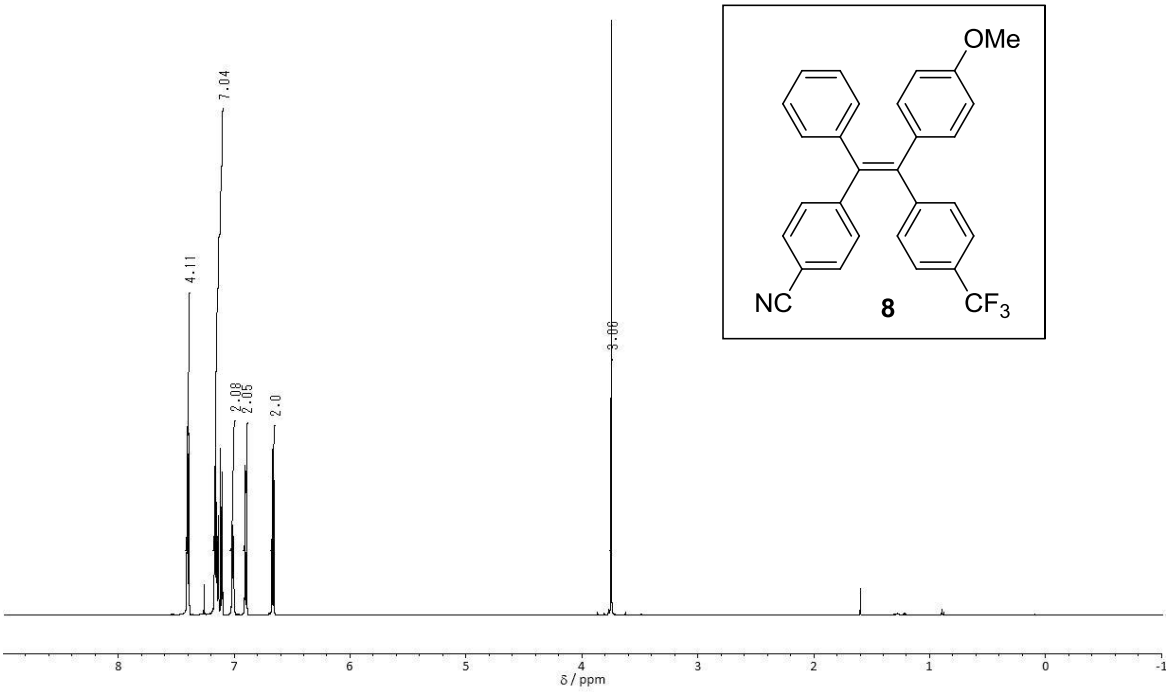


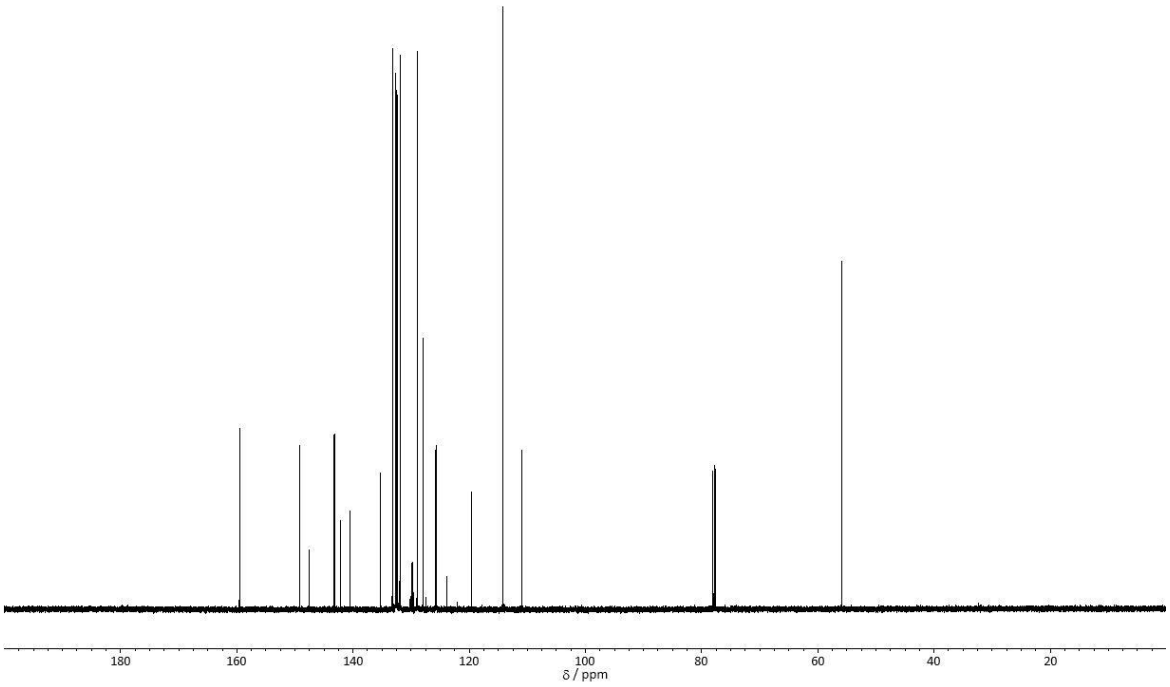
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6** (in $CDCl_3$)





The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **7** (in $CDCl_3$)





The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **8** (in $CDCl_3$)

3-5 References and Notes

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CHAPTER 4

Synthesis of Multisubstituted Olefins through Diborylation of Alkynylsilanes and Highly Chemoselective Suzuki-Miyaura Couplings Sequences

4-1 Introduction

Since multisubstituted olefins (MSOs), owing to their wide range of application in natural product, pharmaceuticals as well as functional materials,[1] have paid much attention, development of facile, efficient, and practical synthetic approaches to the diverse MSOs is important.[2] Nevertheless, regio- and stereodefined synthesis of unsymmetrical MSOs is still one of the most challenging tasks in synthetic organic chemistry. The Author's research group has established general approaches to the synthesis of MSOs from 1-alkynylboronates[3] and 1-alkynylsilanes[4] via regiocontrolled carbozirconation and sequential cross-couplings. Although a stoichiometric amount of a zirconium reagent is necessary in these reactions, this protocol can provide various examples of multisubstituted olefins, utilizing transformative alkyne derivatives. With this strategy, a regio- and stereoselective carbometalation gives rise to a diversity of MSOs efficiently by a stepwise introduction of the substituents selectively.

Based on the previous research in the Author's research group, it was approved that an installation of functional groups onto a C=C core would be a straightforward route to MSOs synthesis. These functional groups are anticipated in further transformations. More importantly, they play an important role to control regio- and stereoselectivities in a construction of key intermediates. These examples have demonstrated that silicon as well as boron functionalities in alkynes are versatile functional groups owing to their tolerance during metalation of unsaturated carbon-carbon bonds.

On the other hand, in recent years, the transition-metal-catalyzed dimetalation of unsaturated compounds[5] has received much attention after the large emergence of inter-element compounds[6] bearing Si–Si,[7] B–B,[5d] Si–B,[8] bonds. The low toxic, economical, and maturely studied boron and silicon-containing compounds[9] intrigued organic chemists to synthesize the borylated or silylated olefins and to obtain more useful bioactive chemicals and functional materials via elaborative bond-forming reactions.

Therefore, a synthetic strategy was envisaged for multifunctionalized olefins having a distinguishable reaction sites for the selective synthesis of MSOs. Very recently, the Author developed the synthesis of tetraarylated olefins featuring a perfectly regio- and stereoselective silylborylation of an alkynylboronate and sequential chemoselective Suzuki-Miyaura couplings.[10] Although chemoselectivity of Suzuki-Miyaura coupling

was not perfectly discriminative among two boron groups in the germinal position of alkenes, it demonstrated two boron groups might show a different reactivity in Suzuki-Miyaura coupling.

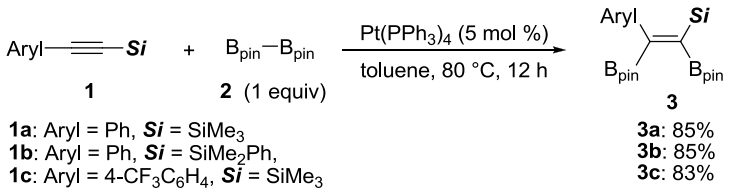
In this Chapter, a continuous research interests of more efficient synthesis of tetrasubstituted olefins, platinum-catalyzed *syn*-diborylation of various alkynylsilanes yielding *syn*-1,2-diborylated alkenylsilanes with perfect stereoselectivity and sequential chemoselective Suzuki-Miyaura coupling giving rise to (*Z*)-1-boryl-silylated stilbenes are reported. This synthetic strategy proves to be more facile and atom economic than previous methods. Moreover, a chemoselectivity in Suzuki-Miyaura coupling was found to be perfect, which is deemed as a more efficient synthetic protocol.

4-2 Results and Discussion

4-2-1 Diborylation of Alkynylsilanes

According to diborylation of terminal and internal alkynes with bis(pinacolato)diboron (B_{2pin2}) in the presence of $Pt(PPh_3)_4$[11] reported by Suzuki and Miyaura, the reaction of a series of alkynylsilanes **1a-1c** with B_{2pin2} **2** were performed in toluene at 80 ℃ for 12 h (Scheme 4-1). A 5 mol % of the platinum catalyst was sufficient to yield the corresponding diborylated products **3a**-**3c** in good yields.

Scheme 4-1. Diborylation of Alkynylsilanes **1** with Bis(pinacolato)diboron **2**.



4-2-2 Chemoselective Suzuki-Miyaura Coupling of Diborylated Compounds

To further test the utility of the synthesized compounds **3** as building blocks of MSOs, Suzuki-Miyaura coupling of **3b** was successively subjected. Compound **3b** was initially employed to clarify the chemoselectivity (Scheme 4-2). The reaction of **3b** with iodobenzene (**4a**) in the presence of $Pd(dba)_2$ and S-Phos gave rise to the coupled product **5ba** as an *E*/*Z* mixture. A configuration of the major isomer was determined to be *Z* by a comparison of spectroscopic data with those of an authentic (*Z*)-**5ba**, obtained from

chemoselective Suzuki-Miyaura coupling of **6**.[10] The authentic (*E*)-**5ba** was also synthesized by the reported synthetic procedure.[12] The *Z*/*E* ratio was determined by the methyl signals of the $SiMe_2Ph$ group in the ^1H NMR spectra.

Scheme 4-2. A Determination of Chemoselectivity.

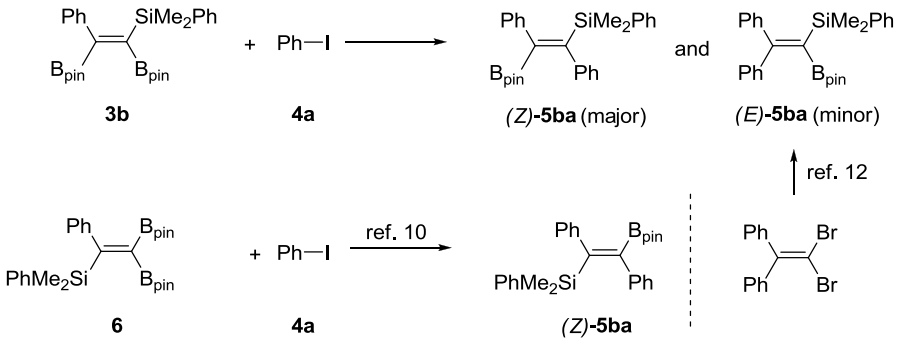
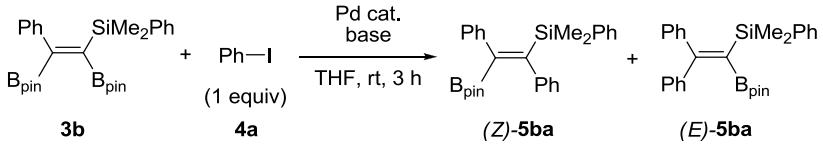


Table 4-1. Screening Conditions of Chemoselective Suzuki-Miyaura Coupling of **3b** with **4a**.[a]



entry [a]	Pd cat./ligand (mol %)	base	yield/% (*Z*:*E*)[b]
1	Pd_2dba_3•$CHCl_3$ (5)/P(*t*-Bu)$_3$ (20)	KOH aq.	68 (86:14)
2	$PdCl_2$(dppf) (5)	KOH aq.	80 (92:8)
3	$PdCl_2$(dppp) (5)	KOH aq.	72 (97:3)
4	$PdCl_2$(dppp) (5)	KOH	43 (94:6)
5	**PEPPSI-IPr (10)**	**KOH aq.**	**76 (>99:1)**
6[c]	$PdCl_2$(dppf) (5)	KOH aq.	75 (97:3)
7[c]	**$PdCl_2$(dppp) (10)**	**KOH aq.**	**78 (>99:1)**
8[c]	PEPPSI-IPr (10)	KOH aq.	36 (>99:1)

[a] Reaction conditions: **3b** (0.1 mmol), **4a** (0.1 mmol), and a base (0.3 mmol) in THF (1 mL).

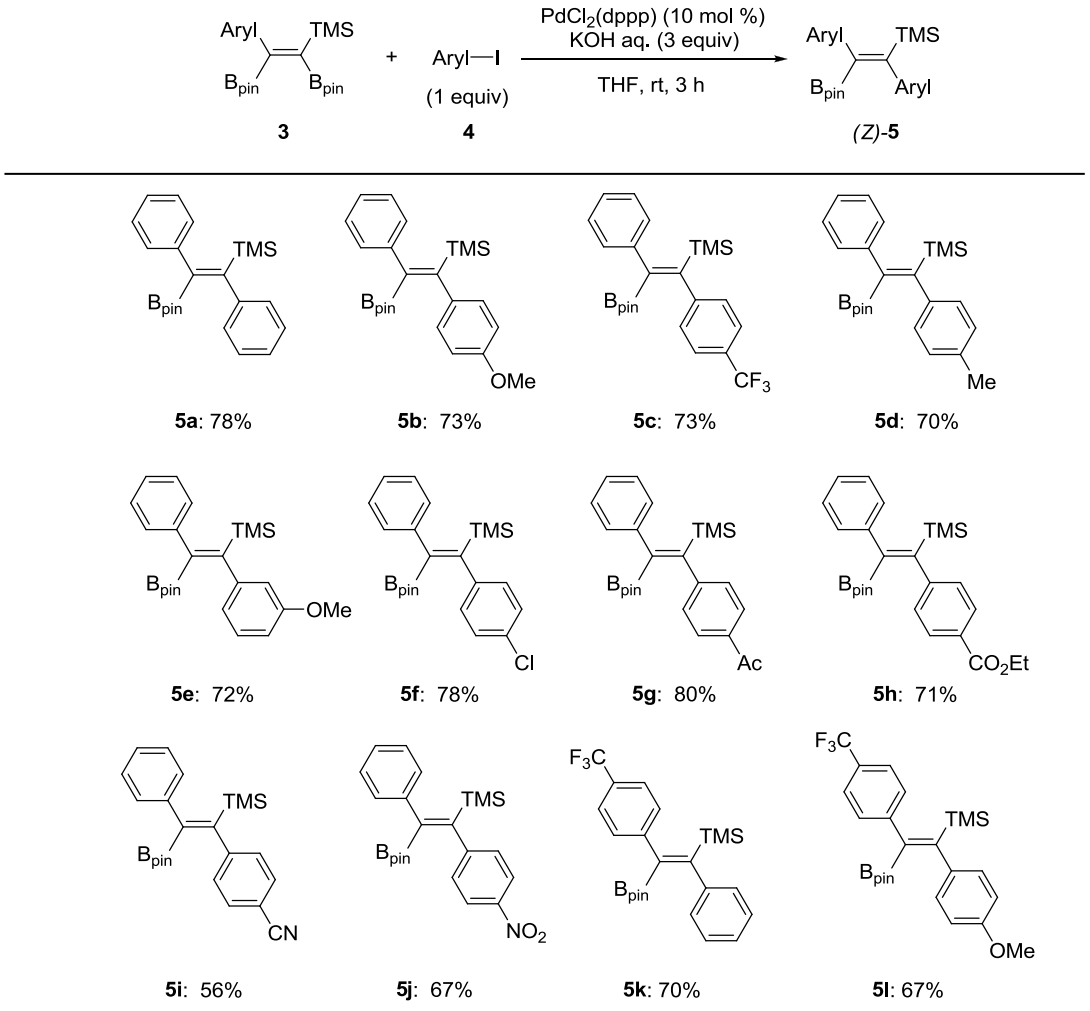
[b] Isolated yields of the isomeric mixture. The *Z*:*E* ratios were determined by the ^1H NMR spectra.

[c] Alkenylsilane **3a** was used instead of **3b**.

The results of an initial screening using **3b** were listed in Table 4-1. Several palladium catalysts and ligands were tested. A 5 mol % of $PdCl_2$(dppf) was sufficient to afford **5ba** in 80% yield with a *Z*:*E* ratio of 92:8 (Table 4-1, entry 2). An excess amount of **4a**

decreased the yield without any loss of chemoselectivity. $PdCl_2$(dppp) also performed well to show higher chemoselectivity, albeit in a slightly decreased yield (Table 4-1, entry 3). Among all examined catalysts for **3b**, PEPPSI-IPr was found to be the best in regard to the *E*/*Z* ratio. When alkenylsilane **3b** was employed instead of **3b**, $PdCl_2$(dppp) is found to be superior to PEPPSI-IPr (Table 4-1, entries 7 vs 8). The nickel catalysts in this reaction was proved to be inferior.

Table 4-2. Chemoselective Suzuki-Miyaura Coupling of **3** with Aryl Iodides **4**.[a]



[a] Reaction conditions: **3** (1.0 mmol), **4** (1.0 mmol), $PdCl_2$(dppp) (10 mol %), and KOH (3 M, 1 mL) in THF (10 mL), isolated yield after column chromatography.

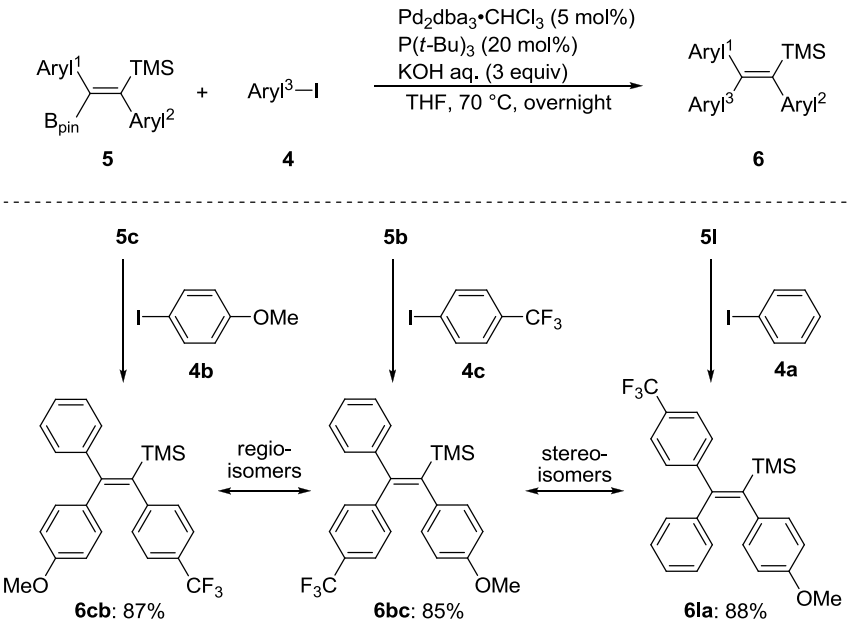
In view of a generality of this protocol, compound **5a** bearing a TMS group is considered to be relatively broader than $SiMe_2Ph$ for further tranaformations. With the optimized reaction conditions in hand, the Author next screened a substrate scope of

cross-couplings of **3a** with a series of aryl iodides **4**, as shown in Table 4-2. Various aryl iodides **4** having electron-donating and -withdrawing groups were used for the chemoselective couplings. For example, compounds **5b** and **5c** were formed in comparable yields. A chlorine group in **5f** remained intact during the reaction without any formation of by-products. Reactive functional groups such as acetyl, ester, cyano, and nitro groups were tolerant in the reaction to generate a variety of (*Z*)-**5** in moderate to good yields. The stereodefined alkenylsilane **3c** instead of **3a** also coupled smoothly to give **5k** and **5l** in good yields.

4-2-3 Synthesis of Triarylated Olefins

With the diverse reagent **5** in hand, the second aryl group was successively introduced to the remaining boron moiety by Suzuki-Miyaura coupling. As a result, triarylated alkenylsilanes **6** were successfully synthesized in the presence of Pd_2dba_3•$CHCl_3$/P(*t*-Bu)$_3$ as the catalyst (Scheme 4-3). It is noteworthy that with the different starting substrates **5**, sequential introduction of various aryl groups on an opposite order of the first and second Suzuki-Miyaura coupling partners afforded the corresponding regio- and stereoisomers.

Scheme 4-3. Synthesis of Structural Isomers of Triarylated Alkenylsilanes **6** via Suzuki-Miyaura Couplings.



4-3 Summary

In summary, the Author has developed a facile and efficient protocol for the synthesis of multisubstituted olefins by diborylation of alkynylsilanes and sequential two Suzuki-Miyaura couplings chemoselectively. This protocol can be applicable to the aryl groups bearing a variety of functional groups and provides general and practical synthetic approaches to a series of useful multisubstituted olefins.

4-4 Experimental Section

4-4-1 General Instrumentation and Chemicals.

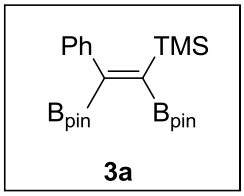
All the reactions were carried out under an Ar atmosphere using standard Schlenk techniques. Glassware was dried in an oven (130 ℃) and heated under reduced pressure prior to use. Bis(pinacolato)diboron was purchased from Aldrich, all the chlorosilanes were purchased from TCI. Dehydrated THF, dichloromethane, and toluene were purchased from Kanto Chemicals Co., Ltd. For thin layer chromatography (TLC) analyses throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. Silica gel column chromatography was carried out using Silica gel 60 N (spherical, 40-100 μm) from Kanto Chemicals Co., Ltd. The ^{1}H, $^{13}C\{^{1}H\}$, $^{19}F\{^{1}H\}$ and $^{11}B\{^{1}H\}$ NMR spectra were recorded on Varian INOVA-600 (600 MHz) spectrometers. The chemical shifts of $^{19}F\{^{1}H\}$ NMR and $^{11}B\{^{1}H\}$ NMR were referenced to an external standard $CFCl_3$ (in $CDCl_3$) and BF_3•Et_2O (in $CDCl_3$), respectively. Infrared spectra were recorded on a Shimadzu IRPrestige-21 spectrophotometer. GC analyses were performed on a Shimadzu GC-14A equipped with a flame ionization detector using Shimadzu Capillary Column (CBP1-M25-025) and Shimadzu C-R6A-Chromatopac integrator. GC/MS analyses were carried out on a SHIMADZU GC-17A equipped with a SHIMADZU QP-5050 GC-MS system. Elemental analyses were carried out with a Perkin-Elmer 2400 CHN elemental analyzer at Okayama University.

4-4-2 Experimental Procedures

Synthesis of 1-(Phenylethynyl)trimethylsilane (1a). According to the literature methods,[4] to a solution of phenylacetylene (2.2 mL, 20 mmol) in THF (12 mL) in a 100 mL of a Schlenk tube at 0 ℃ under an Ar atmosphere was added dropwise EtMgBr (30 mL, 1.0 M THF solution, 30 mmol). The reaction mixture was stirred for 30 min at 0 ℃. To the resulting reaction mixture was then added chlorotrimethylsilane (2.5 mL, 20 mmol). After being stirred at 0 ℃ for 5 min, the reaction mixture was warmed to room temperature with additional 1 h stirring. The mixture was quenched with 1 M hydrochloric acid (30 mL), extracted with diethyl ether (25 mL x 2). The combined ethereal layers were washed with brine and dried over $MgSO_4$. Filtration and evaporation afforded a yellow oil. Bulb to bulb distillation (93-98 ℃/9.2 Torr) gave **1a** (3.4 g, 19.4 mmol, 97% yield) as a colorless oil. Accordingly, 1-alkynylsilane **1b** was

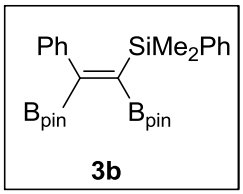
synthesized using $PhMe_2SiCl$, and 1-alkynylsilane **1c** was synthesized from $F_3CC_6H_4CCH$ in the same procedure.

A Typical Procedure for Synthesis of (*Z*)-1,2-Diboryl-1-silylated Styrenes 3 by Highly Selective Diborylation of 1. A 100-mL flask equipped with a magnetic stirring bar and reflux condenser was charged with $Pt(PPh_3)_4$ (311 mg ,0.25 mmol, 5 mol %) and bis(pinacolato)diboron (1.27 g, 5 mmol, 1.0 equiv) under Ar atmosphere. Addition of toluene (50 mL) and alkynylsilane **1** (5 mmol) afforded a yellow solution. After the reaction was completed overnight at 80 ℃, and the reaction mixture was cooled to room temperature. Toluene was removed with a rotary evaporator to yield a yellow residue, which was subjected to a short column chromatography on neutral silica gel with a mixture of hexanes and EtOAc (20:1) as the eluent to afford off-white solid. Further recrystallization with CH_2Cl_2/hexane gave analytically pure white crystals of **3**.



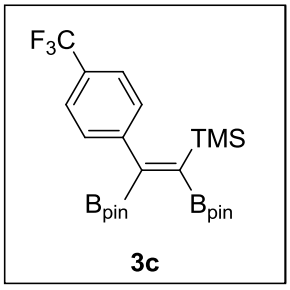
3a

(*Z*)-1-(Trimethylsilyl)-2-phenyl-1,2-di-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) ethene (3a). White crystals (1.82 g, 4.25 mmol, 85%). Mp = 169-170 ℃. FT-IR (neat, cm^{-1}): 2980 (m), 1371 (w), 1317 (s), 1296 (s), 1269 (m), 1146 (s), 845 (s), 704 (w). ^1H NMR (600 MHz, $CDCl_3$, rt): δ –0.19 (s, 9H), 1.22 (s, 12H), 1.37 (s, 12H), 7.10-7.12 (m, 2H), 7.19-7.20 (m, 1H), 7.22-7.25 (m, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.8, 24.7, 25.5, 83.6, 83.9, 126.2, 127.4, 127.8, 145.8. Two carbon signals attached to B were not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.2, 30.9. MS (EI, m/z (relative intensity)): 429 (M^+, 0.01), 413 (7), 287(13), 286 (6), 231 (5), 129 (4), 84 (100), 69 (30). Anal. Calcd for $C_{23}H_{38}B_2O_4Si$: C, 64.51; H, 8.94%. Found: C, 64.49; H, 8.97%.



3b

(*Z*)-1-(Dimethylphenylsilyl)-2-phenyl-1,2-di-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (3b). White crystals (2.08 g, 4.25 mmol, 85%). Mp = 127-128 ℃. FT-IR (neat, cm^{-1}): 2974 (m), 1369 (m), 1339 (m), 1321 (s), 1300 (s), 1202 (m), 1146 (s), 1111 (w), 843 (m), 772 (w), 704 (m). ^{1}H NMR (600 MHz, $CDCl_3$, rt): δ 0.09 (s, 6H), 1.34 (s, 12H), 1.35 (s, 12H), 7.10-7.12 (m, 2H), 7.25-7.26 (m, 3H), 7.38-7.39 (m, 3H) 7.58-7.59 (m, 2H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$, rt): δ –0.7, 24.7, 25.3, 83.6, 83.9, 126.3, 127.3, 127.4, 127.8, 128.2, 134.2, 140.9, 145.4. Two carbon signals attached to B were not observed due to low intensity; $^{11}B\{^{1}H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.2 (brs, overlapped). MS (EI, m/z (relative intensity)): 490 (M^+, 2), 475 (3), 363 (6), 307(14), 271 (7), 221 (7), 135(13), 119 (21), 84 (100), 83 (27), 69 (24). Anal. Calcd for $C_{28}H_{40}B_2O_4Si$: C, 68.59; H, 8.22%. Found: C, 68.61; H, 8.06%.



3c

(*Z*)-1-(Trimethylsilyl)-2-(4-trifluoromethylphenyl)-1,2-di-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (3c). White needle-like crystals (2.06 g, 4.15 mmol, 83%). Mp = 170 ℃. FT-IR (neat, cm^{-1}): 2984 (w), 1310 (s), 1204 (w), 1119 (m), 1064 (m), 1018 (w), 851 (s), 604 (w). ^{1}H NMR (600 MHz, $CDCl_3$, rt): δ –0.19 (s, 9H), 1.23 (s, 12H), 1.38 (s, 12H), 7.21 (d, J = 9 Hz, 2H), 7.50 (d, J = 9 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.8, 24.7, 25.6, 83.8, 84.2, 124.4 (q, $J_{C\text{-}F}$ = 270.5 Hz), 124.4 (q, $J_{C\text{-}F}$ = 3.5 Hz), 128.1, 128.3 (q, $J_{C\text{-}F}$ = 32.0 Hz), 149.6. Two carbon signals attached to B were not observed due to low intensity; $^{11}B\{^{1}H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 28.8 (brs, overlapped); $^{19}F\{^{1}H\}$ NMR (564 MHz, $CDCl_3$, rt): δ –62.5. MS (EI, m/z (relative intensity)): 496 (M^+, 0), 481 (3), 438 (4), 355 (16), 84 (100), 83 (29), 69 (25). Anal.

Calcd for $C_{24}H_{37}B_2F_3O_4Si$: C, 58.09; H, 7.51%. Found: C, 58.23; H, 7.11%.

A Typical Procedure for the Chemoselective Suzuki-Miyaura Cross-Coupling of 3 with Aryl Iodides 4a. Determination of a Ratio of *Z*/*E* Isomers. To a THF solution of the palladium catalyst and the ligand in a 20 mL of Schlenk tube under an Ar atmosphere was added **3b** (49 mg, 0.1 mmol). To the reaction mixture were then added iodobenzene (**4a**) (11.2 μL, 20.4 mg, 0.1 mmol) and the base (3.0 equiv). After being stirred at room temperature for 3 h, the reaction mixture was quenched by sat. NH_4Cl solution, then extracted with diethyl ether (10 mL x 2). The combined ethereal layers were washed with brine and dried over $MgSO_4$. Filtration, evaporation, and preparative TLC gave a mixture of regioisomers of **5ba**. The reaction of **3a** with **4a** proceeded in a same manner. A ratio of two isomers was determined by the ^{1}H NMR spectra; proton signals assigned to the methyl groups of $SiMe_2Ph$ were compared as the references. The representative ^{1}H NMR spectrum is shown in Figure 4-1.

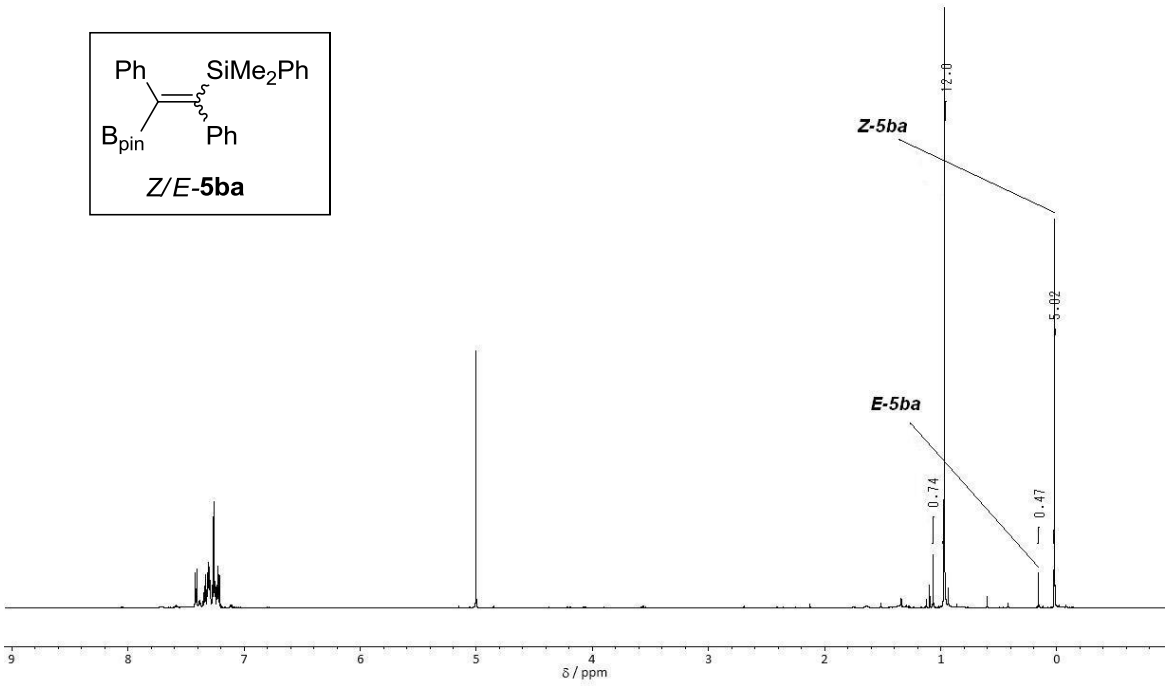
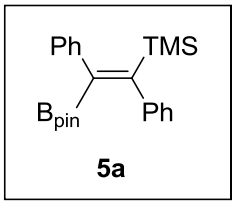


Figure 4-1. The determination of *Z*/*E* ratio of **5ba** by the ^{1}H NMR spectrum.

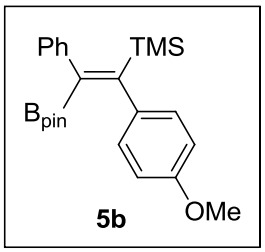
(*Z*)-1-(Trimethylsilyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,2-diaryleth ene ((*Z*)-5). To a solution of $PdCl_2$(dppp) (29 mg, 0.025 mmol 10 mol %) in THF (5 mL) as off-white suspension in a 20 mL of Schlenk tube at room temperature under an Ar

atmosphere were added **3** (0.5 mmol) and aryl halides **4** (0.5 mmol, 1.0 equiv). When aqueous 3 M KOH solution (1.5 mmol, 0.5 mL) was added to the reaction mixture, the reaction mixture immediately turned to deep brown solution. The reaction mixture was stirred for 3 h at room temperature. After the reaction completed, the reaction mixture was quenched by sat. NH_4Cl solution, then extracted with diethyl ether (20 mL x 2). The combined ethereal layers were washed with brine and dried over $MgSO_4$. Filtration, evaporation and column chromatography on silica gel gave the analytically pure (*Z*)-**5**.



5a

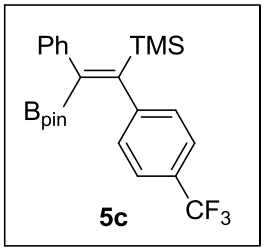
(*Z*)-1-(Trimethylsilyl)-1,2-diphenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5a): White solid (147 mg, 0.39 mmol, 78%). Mp = 72-73 ℃. R_f = 0.38 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2978 (m), 1344 (s), 1310 (s), 1246 (m), 1144 (s), 852 (s), 837 (s), 700 (s). ^1H NMR (600 MHz, $CDCl_3$, rt): δ –0.25 (s, 9H), 0.90 (s, 12H), 7.15-7.18 (m, 3H), 7.23-7.27 (m, 3H), 7.30-7.31 (m, 4H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.2, 24.3, 83.4, 125.6, 126.5, 127.6, 127.9, 128.0, 128.1, 142.6, 146.0, 156.0. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.3. MS (EI, m/z (relative intensity)): 378 (M^+, 71), 363 (58), 263 (52), 221 (41), 178 (85), 135 (28), 101 (22), 84 (100), 73 (64), 69 (22). Anal. Calcd for $C_{23}H_{31}BO_2Si$: C, 73.01; H, 8.26%. Found: C, 73.05; H, 8.25%.



5b

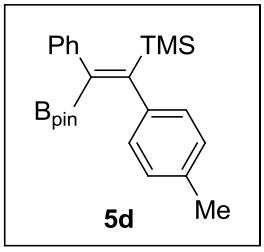
(*Z*)-1-(Trimethylsilyl)-1-(4-methoxyphenyl)-2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5b). White solid (148 mg, 0.36 mmol, 73%). Mp = 106-107 ℃. R_f = 0.21 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2980 (m), 1506 (m),

1342 (m), 1302 (m), 1246 (s), 1142 (m), 849 (s), 708 (m). ^{1}H NMR (600 MHz, $CDCl_3$, rt): δ –0.25 (s, 9H), 0.93 (s, 12H), 3.80 (s, 3H), 6.83 (d, J = 9 Hz, 2H), 7.08 (d, J = 9 Hz, 2H), 7.23-7.24 (m, 1H), 7.28-7.30 (m, 4H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt): δ 0.2 , 24.3, 55.3, 83.3, 113.0, 126.4, 127.8, 128.1, 129.1, 138.4, 142.6, 155.5, 157.9. The carbon signal attached to B was not observed due to low intensity; ^{11}B{^{1}H} NMR (192 MHz, $CDCl_3$, rt): δ 29.5. MS (EI, m/z (relative intensity)): 408 (M^+, 100), 393 (65), 293 (30), 251 (47), 208 (81), 165 (29), 135 (16), 84 (26), 83 (41), 73 (45). Anal. Calcd for $C_{24}H_{33}BO_3Si$: C, 70.58; H, 8.14%. Found: C, 70.43; H, 8.14%.



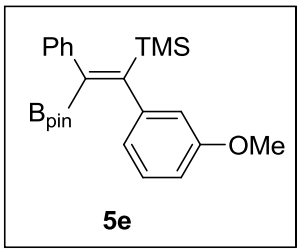
5c

(*Z*)-1-(Trimethylsilyl)-1-(4-trifluoromethylphenyl)-2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5c). White solid (163 mg, 0.37 mmol, 73%). Mp = 107-108 ℃. R_f = 0.37 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2990 (w), 2978 (w), 1341 (s), 1329 (s), 1315 (m), 1248 (w), 1155 (m), 1121 (m), 1069 (m), 851 (s). ^{1}H NMR (600 MHz, $CDCl_3$, rt): δ –0.24 (s, 9H), 0.89 (s, 12H), 7.27-7.29 (m, 5H), 7.31-7.34 (m, 2H), 7.54 (d, J = 8 Hz, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt): δ 0.1, 24.2, 83.6, 124.47 (q, $J_{C\text{-}F}$ = 270.2 Hz), 124.50 (q, $J_{C\text{-}F}$ = 3.5 Hz), 126.8, 127.98, 127.99 (q, $J_{C\text{-}F}$ = 21.6 Hz), 128.0, 128.4, 142.2, 150.1, 155.3. The carbon signal attached to B was not observed due to low intensity; ^{11}B{^{1}H} NMR (192 MHz, $CDCl_3$, rt): δ 29.4; ^{19}F{^{1}H} NMR (564 MHz, $CDCl_3$, rt): δ –62.6. MS (EI, m/z (relative intensity)): 446 (M^+, 37), 431 (46), 354 (19), 289 (13), 227 (16), 135 (11), 101 (53), 84 (100), 73 (53). Anal. Calcd for $C_{24}H_{30}BO_2SiF_3$: C, 64.58; H, 6.77%. Found: C, 64.60; H, 6.42%.



5d

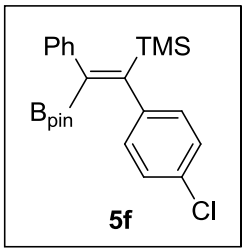
(*Z*)-1-(Trimethylsilyl)-1-(4-methylphenyl)-2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5d). White solid (137 mg, 0.35 mmol, 70%). Mp = 102-103 ℃. R_f = 0.37 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2980 (m), 2953 (w), 1506 (w), 1340 (s), 1304 (s), 1246 (m), 1142 (s), 984 (m), 845 (s), 706 (m). ^1H NMR (600 MHz, $CDCl_3$, rt): δ –0.25 (s, 9H), 0.91 (s, 12H), 2.32 (s, 3H), 7.04 (d, J = 8 Hz, 2H), 7.08 (d, J = 8 Hz, 2H), 7.23-7.25 (m, 1H), 7.28-7.32 (m, 4H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.2, 21.0, 24.3, 83.3, 126.4, 127.8, 127.9, 128.1, 128.2, 135.0, 142.7, 142.9, 156.0. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.3. MS (EI, m/z (relative intensity)): 392 (M^+, 82), 377 (52), 295 (15), 277 (48), 235 (41), 193 (20), 192 (100), 84 (53), 83 (37), 73 (47). Anal. Calcd for $C_{24}H_{33}BO_2Si$: C, 73.46; H, 8.48%. Found: C, 73.26; H, 8.47%.



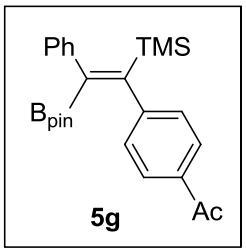
5e

(*Z*)-1-(Trimethylsilyl)-1-(3-methoxyphenyl)-2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5e). White solid (147 mg, 0.36 mmol, 72%). Mp = 90 ℃. R_f = 0.25 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2978 (m), 1585 (m), 1508 (s), 1489 (m), 1341 (s), 1304 (s), 1167 (m), 839 (s), 708 (m), 852(s). ^1H NMR (600 MHz, $CDCl_3$, rt): δ –0.23 (s, 9H), 0.93 (s, 12H), 3.82 (s, 3H), 6.72-6.77 (m, 3H), 7.17 (t, J = 8 Hz, 1H), 7.22-7.26 (m, 1H), 7.29-7.32 (m, 4H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.3, 24.3, 55.2, 83.4, 111.7, 113.1, 120.6, 126.5, 127.9, 128.1, 128.6, 142.5, 147.4, 155.8, 159.0. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.4. MS (EI, m/z (relative intensity)): 408 (M^+, 85), 393

(82), 294 (25), 293 (100), 292 (32), 251 (43), 208 (90), 135 (20), 84 (50), 83 (50, 73 (65). Anal. Calcd for $C_{24}H_{33}BO_3Si$: C, 70.58; H, 8.14%. Found: C, 70.78; H, 8.34%.

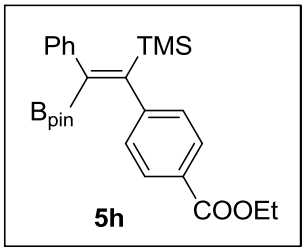


(*Z*)-1-(Trimethylsilyl)-1-(4-chlorophenyl)-2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5f). White solid (161 mg, 0.39 mmol, 78%). Mp = 141-142 ℃. R_f = 0.20 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2976 (w), 1489 (m), 1371 (m), 1337 (s), 1302 (s), 1140 (s), 1011 (w), 849 (s), 702 (m). ^1H NMR (600 MHz, $CDCl_3$, rt): δ –0.26 (s, 9H), 0.93 (s, 12H), 7.09 (d, J = 8 Hz, 2H), 7.24-7.32 (m, 7H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.1, 24.3, 83.5, 126.7, 127.6, 127.9, 128.0, 129.4, 131.5, 142.3, 144.5, 155.0. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.4. MS (EI, m/z (relative intensity)): 412 (M^+, 47), 397 (37), 255 (17), 212 (43), 101 (45), 84 (100), 83 (40), 73 (68), 69 (19). Anal. Calcd for $C_{23}H_{30}BClO_2Si$: C, 66.92; H, 7.32%. Found: C, 66.52; H, 7.03%.

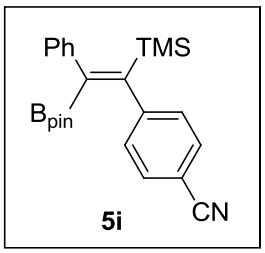


(*Z*)-1-(Trimethylsilyl)-1-(4-acetylphenyl)-2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5g). White solid (168 mg, 0.40 mmol, 80%). Mp = 132-133 ℃. R_f = 0.18 (hexane/ethyl acetate = 10:1). FT-IR (KBr, cm^{-1}): 2980 (w), 2959 (w), 1678 (s), 1601 (m), 1341 (m), 1317 (m), 1267 (m), 1142 (m), 851 (s). ^1H NMR (600 MHz, $CDCl_3$, rt): δ –0.28 (s, 9H), 0.85 (s, 12H), 2.57 (s, 3H), 7.22-7.30 (m, 7H), 7.86 (d, J = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.2, 24.2, 26.6, 83.5, 126.7, 127.8, 127.9, 128.0, 128.2, 134.7, 142.2, 151.7, 155.6, 198.0. The carbon signal attached to B was not

observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.1. MS (EI, m/z (relative intensity)): 420 (M^+, 68), 405 (22), 305 (24), 205 (29), 204 (100), 84 (51), 73 (65). Anal. Calcd for $C_{25}H_{33}BO_3Si$: C, 71.42; H, 7.91%. Found: C, 71.53; H, 7.59%.

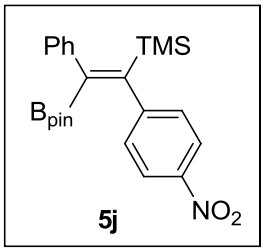


4-[(1*Z*)-1-(Trimethylsilyl)-2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) ethenyl]benzoic acid ethyl ester (5h). White solid (159 mg, 0.35 mmol, 71%). Mp = 97-98 ℃. R_f = 0.11 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2980 (m), 1717 (s), 1605 (m), 1341 (m), 1271 (s), 1142 (m), 851 (m), 700 (w). ^1H NMR (600 MHz, $CDCl_3$, rt): δ –0.26 (s, 9H), 0.90 (s, 12H), 1.41 (t, J = 7 Hz, 3H), 4.38 (q, J = 7 Hz, 2H), 7.23 (d, J = 8 Hz, 2H), 7.25-7.26 (m, 1H), 7.29-7.32 (m, 4H), 7.97 (d, J = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.2, 14.3, 24.2, 60.8, 83.5, 126.7, 127.7, 127.9, 127.99, 128.01, 129.0, 142.2, 151.3, 155.6, 166.8. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.2. MS (EI, m/z (relative intensity)): 450 (M^+, 48), 435 (17), 289 (19), 205 (100), 84 (29), 73 (32). Anal. Calcd for $C_{26}H_{35}BO_4Si$: C, 69.33; H, 7.83%. Found: C, 68.93; H, 7.76%.

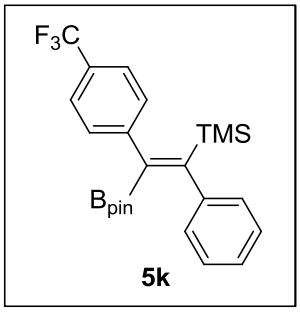


(*Z*)-1-(Trimethylsilyl)-1-(4-cyanophenyl)-2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-diox aborolan-2-yl)ethene (5i). Off-white solid (113 mg, 0.28 mmol, 56%). Mp = 214 ℃. R_f = 0.11 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2978 (m), 2956 (m), 2224 (m), 1601 (w), 1327 (s), 1302 (s), 1140 (s), 982 (w), 849 (s), 708 (m). ^1H NMR (600 MHz, $CDCl_3$, rt): δ –0.25 (s, 9H), 0.91 (s, 12H), 7.26-7.28 (m, 5H), 7.31-7.34 (m, 2H),

7.59 (d, J = 8 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.1, 24.2, 83.6, 109.3, 119.3, 126.9, 127.9 128.0, 128.8, 131.4, 141.9, 151.6, 155.1. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^{1}H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.2. MS (EI, m/z (relative intensity)): 403 (M^+, 589), 402 (28), 388 (40), 263 (52), 175 (20), 101 (49), 84 (96), 83 (27), 73 (100). Anal. Calcd for $C_{24}H_{30}BNO_2Si$: C, 71.46; H, 7.50; N, 3.47%. Found: C, 71.49; H, 7.43; N, 3.43%.

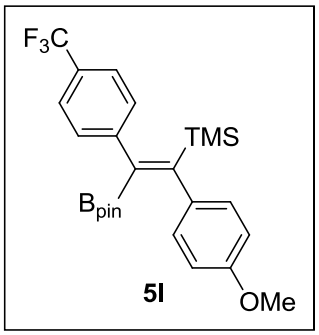


(*Z*)-1-(Trimethylsilyl)-1-(4-nitrophenyl)-2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5j). White solid (142 mg, 0.34 mmol, 67%). Mp = 204 ℃. R_f = 0.13 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2976 (w), 1589 (w), 1512 (m), 1344 (s), 1140 (m), 986 (w), 849 (m), 712 (w). ^{1}H NMR (600 MHz, $CDCl_3$, rt): δ –0.24 (s, 9H), 0.91 (s, 12H), 7.27-7.29 (m, 3H), 7.32-7.34 (m, 4H), 8.17 (d, J = 9 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.1, 24.2, 83.7, 122.9, 127.0, 127.9, 128.0, 128.8, 141.9, 146.1, 153.9, 155.0. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^{1}H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.4. MS (EI, m/z (relative intensity)): 423 (M^+, 37), 408 (45), 280 (68), 101 (52), 84 (100), 83 (38), 73 (86). Anal. Calcd for $C_{23}H_{30}BNO_4Si$: C, 65.25; H, 7.14; N, 3.31%. Found: C, 65.10; H, 6.75; N, 3.23%.



(*Z*)-1-(Trimethylsilyl)-1-phenyl-2-(4-trifluoromethylphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5k). White solid (156 mg, 0.35 mmol, 70%). Mp =

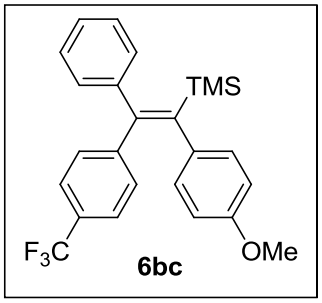
103-104 ℃. R_f = 0.32 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2978 (m), 1612 (w), 1312 (s), 1269 (w), 1151 (s), 1124 (s), 1066 (m), 986 (w), 845 (s), 708 (m). ^1H NMR (600 MHz, $CDCl_3$, rt): δ –0.26 (s, 9H), 0.89 (s, 12H), 7.13 (d, J = 7 Hz, 2H), 7.17-7.19 (m, 1H), 7.24-7.27 (m, 2H), 7.41 (d J = 7 Hz, 2H), 7.57 (d, J = 7 Hz, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.2, 24.2, 83.6, 124.4 (q, $J_{C\text{-}F}$ = 270.4 Hz), 124.8 (q, $J_{C\text{-}F}$ = 3.7 Hz), 125.8, 127.7, 127.8, 128.4, 128.9 (q, $J_{C\text{-}F}$ = 31.8 Hz), 145.5, 146.5, 157.7. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.3; $^{19}F\{^1H\}$ NMR (564 MHz, $CDCl_3$, rt): δ –62.6. MS (EI, m/z (relative intensity)): 446 (M^+, 27), 431 (34), 354 (15), 289 (14), 227 (14), 101 (21), 84 (100), 73 (47), 69 (16). Anal. Calcd for $C_{24}H_{30}BF_3O_2Si$: C, 64.58; H, 6.77%. Found: C, 64.49; H, 6.42%.



5l

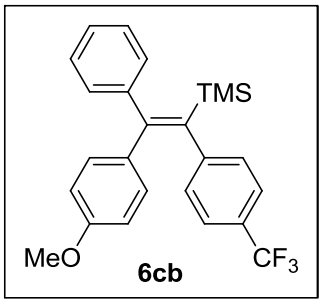
(*Z*)-1-(Trimethylsilyl)-1-(4-methoxyphenyl)-2-(4-trifluoromethylphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethene (5l). White solid (160 mg, 0.34 mmol, 67%). Mp = 148 ℃. R_f = 0.19 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2981 (w), 1612 (w), 1506 (m), 1373 (w), 1325 (s), 1284 (w), 1244 (m), 1064 (m), 848 (s). ^1H NMR (600 MHz, $CDCl_3$, rt): δ –0.25 (s, 9H), 0.93 (s, 12H), 3.80 (s, 3H), 6.83 (d, J = 8 Hz, 2H), 7.06 (d, J = 8 Hz, 2H), 7.40 (d, J = 8 Hz, 2H), 7.57 (d, J = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 0.2, 24.3, 55.3, 83.6, 113.1, 124.4 (q, $J_{C\text{-}F}$ = 270.5 Hz), 124.8 (q, $J_{C\text{-}F}$ = 3.7 Hz), 128.4, 128.7 (q, $J_{C\text{-}F}$ = 32.1 Hz), 128.9, 138.0, 146.5, 157.3, 158.1. The carbon signal attached to B was not observed due to low intensity; $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$, rt): δ 29.4; $^{19}F\{^1H\}$ NMR (564 MHz, $CDCl_3$, rt): δ –62.6. MS (EI, m/z (relative intensity)): 476 (M^+, 81), 475 (18), 462 (30), 461 (100), 460 (22), 361 (20), 319 (43), 276 (68), 165 (22), 84 (59), 83 (65), 73 (63). Anal. Calcd for $C_{25}H_{32}BF_3O_3Si$: C, 63.03; H, 6.77%. Found: C, 63.00; H, 6.40%.

Suzuki-Miyaura Cross-Coupling of 5 with 4: Synthesis of (*Z*)-1-(Trimethylsilyl)-1,1,2-triarylethenes (6). To a deep purple solution of $Pd_2(dba)_3$•$CHCl_3$ (26 mg, 0.025 mmol, 5 mol%) and P(*t*-Bu)$_3$ (20 mg, 0.1 mmol, 20 mol%) in THF (5 mL) in 20 mL of a Schlenk tube were added **5** (0.5 mmol) and aryl halides **4** (0.75 mmol, 1.5 equiv) at room temperature under an Ar atmosphere. After aqueous 3 M KOH solution (1.5 mmol, 0.5 mL) was added, the reaction mixture was heated to a reflux temperature and stirred for 12 h. After the reaction completed, the reaction mixture was quenched by sat. NH_4Cl solution, then extracted with diethyl ether (20 mL x 2). The combined ethereal layers were washed with brine and dried over $MgSO_4$. Filtration, evaporation, and column chromatography on silica gel (hexane:ethyl acetate = 20:1) gave compound **6**.



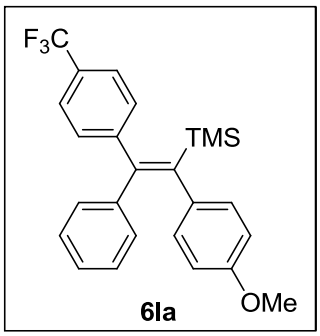
6bc

(*Z*)-1-(Trimethylsilyl)-1-(4-methoxyphenyl)-2-phenyl-2-(4-trifluoromethylphenyl)ethene (**6bc**). White solid (182 mg, 0.43 mmol, 85%). Mp = 88-89 ℃. R_f = 0.44 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2958 (w), 1506 (m), 1321 (s), 1286 (w), 1242 (s), 1122 (s), 1109 (m), 837 (s), 700 (m). ^{1}H NMR (600 MHz, $CDCl_3$, rt): δ – 0.19 (s, 9H), 3.74 (s, 3H), 6.70 (d, J = 8 Hz, 2H), 6.86 (d, J = 8 Hz, 2H), 7.06 (d, J = 8 Hz, 2H), 7.26 (d, J = 8 Hz, 2H), 7.29-7.32 (m, 3H), 7.34-7.36 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt): δ 0.3, 55.0, 113.1, 124.2 (q, $J_{C\text{-}F}$ = 270.5 Hz), 124.3 (q, $J_{C\text{-}F}$ = 3.7 Hz), 127.4, 127.7 (q, $J_{C\text{-}F}$ = 32.1 Hz), 128.1, 129.5, 129.6, 130.1, 135.5, 143.6, 145.7, 147.0, 152.4, 157.3; ^{19}F{^{1}H} NMR (564 MHz, $CDCl_3$, rt): δ –62.7. MS (EI, m/z (relative intensity)): 426 (M^+, 100), 412 (25), 411 (78), 257 (26), 227 (22), 203 (16), 165 (29), 135 (28), 73 (93). HRMS (FAB) Calcd for $C_{25}H_{25}F_3OSi$: 426.1627. Found: 426.1628.



6cb

(*Z*)-1-(Trimethylsilyl)-1-(4-trifluoromethylphenyl)-2-phenyl-2-(4-methoxyphenyl)-ethene (**6cb**)**.** White solid (185 mg, 0.43 mmol, 87%). Mp = 74-75 ℃. R_f = 0.42 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2955 (w), 1609 (m), 1506 (m), 1321 (s), 1113 (s), 1065 (m), 868 (m), 829 (m), 704 (m). ^{1}H NMR (600 MHz, $CDCl_3$, rt): δ –0.19 (s, 9H), 3.66 (s, 3H), 6.56 (d, J = 8 Hz, 2H), 6.85 (d, J = 8 Hz, 2H), 7.13 (d, J = 8 Hz, 2H), 7.31-7.33 (m, 3H), 7.34-7.38 (m, 2H), 7.44 (d, J = 8 Hz, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt): δ 0.4, 54.9, 112.8, 124.5 (q, $J_{C\text{-}F}$ = 270.5 Hz), 124.5 (q, $J_{C\text{-}F}$ = 3.5 Hz), 127.1 (q, $J_{C\text{-}F}$ = 32.0 Hz), 127.3, 128.0, 129.4, 129.6, 130.7, 135.1, 142.3, 144.2, 148.5, 154.0, 157.9; ^{19}F{^{1}H} NMR (564 MHz, $CDCl_3$, rt): δ –62.4. MS (EI, m/z (relative intensity)): 426 (M^+, 100), 411 (28), 257 (54), 227 (62), 165 (52), 135 (51), 73 (81). HRMS (FAB) Calcd for $C_{25}H_{25}F_3OSi$: 426.1627. Found: 426.1611.

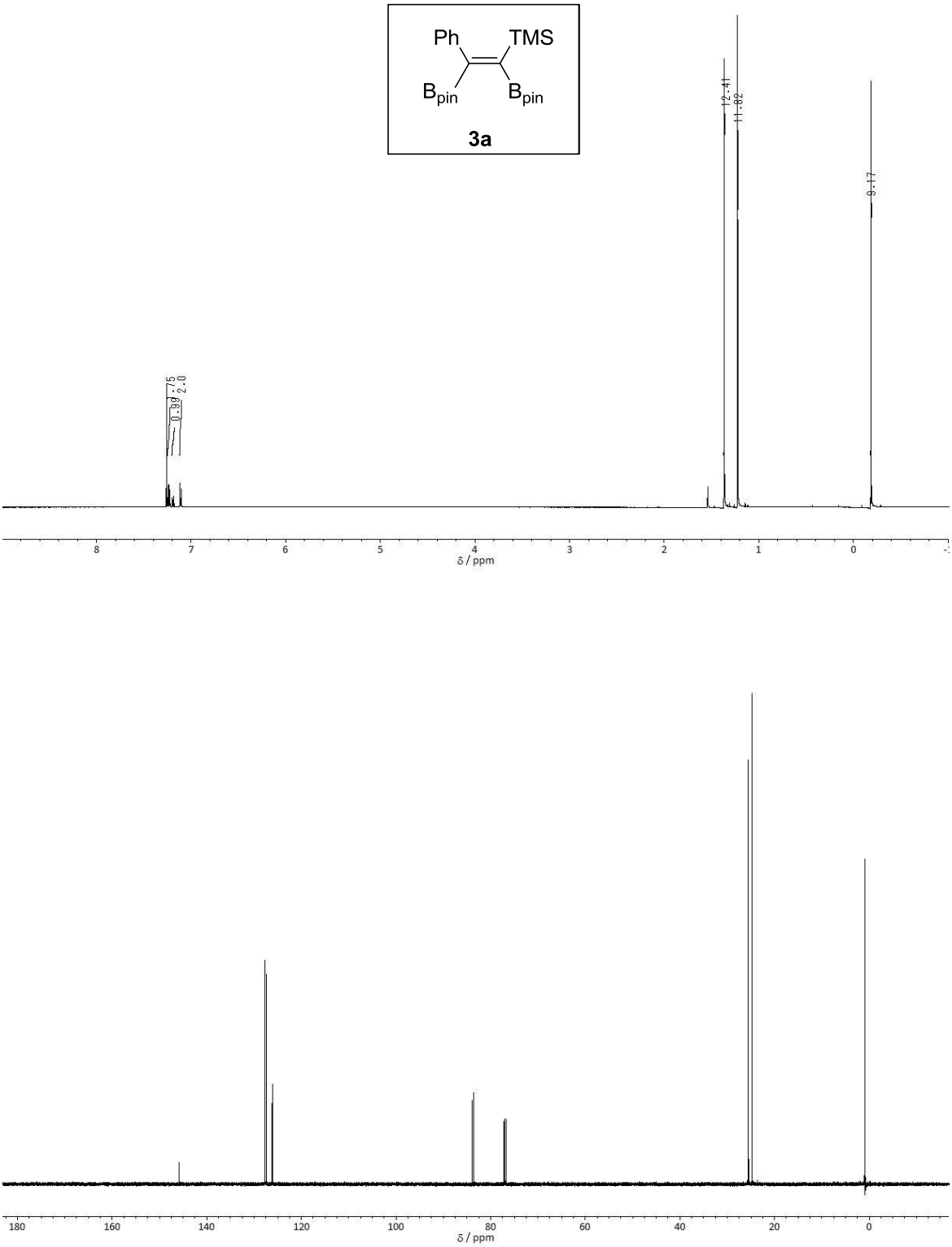


6la

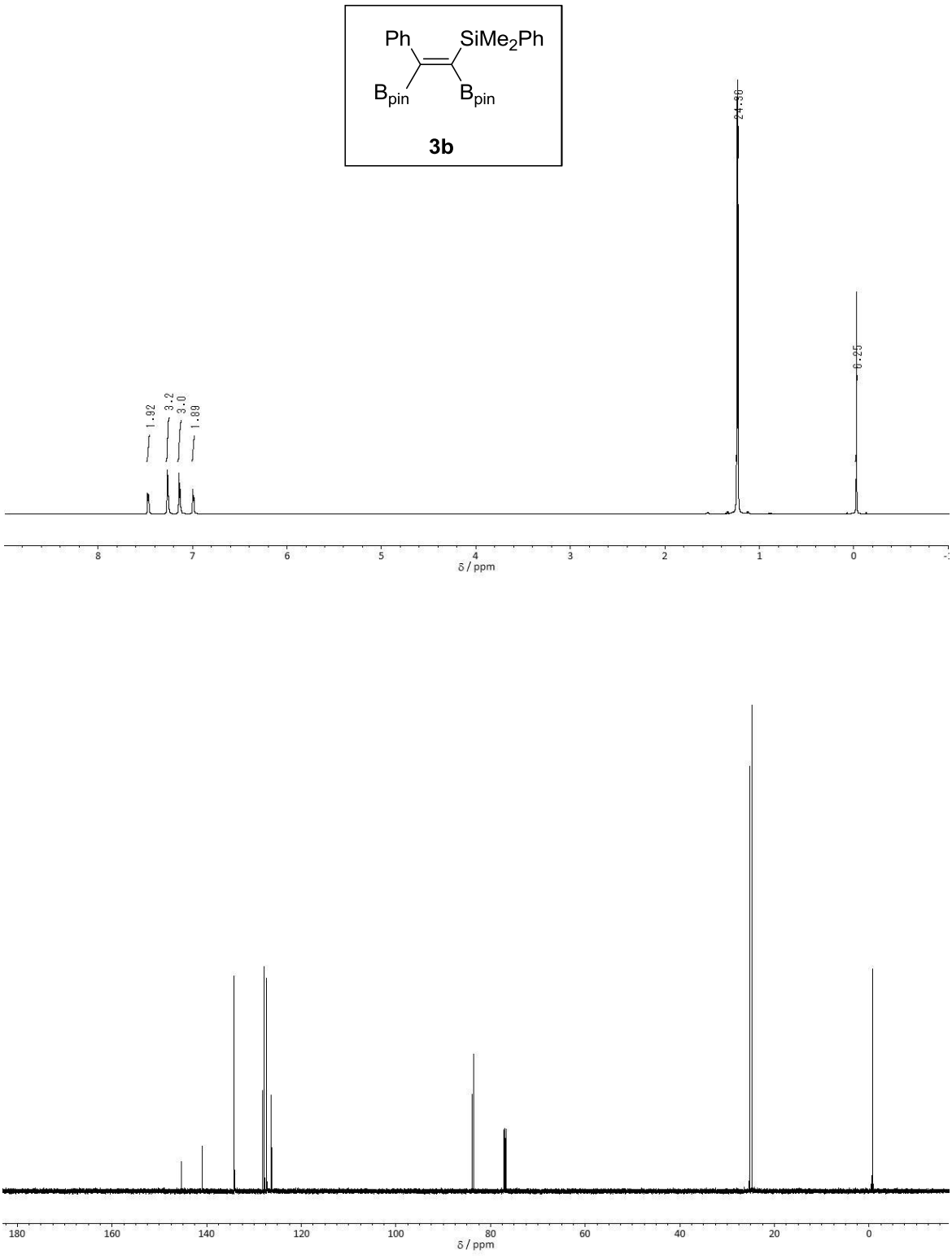
(*E*)-1-(Trimethylsilyl)-1-(4-methoxyphenyl)-2-phenyl-2-(4-trifluoromethylphenyl)ethene (**6cb**). White solid (188 mg, 0.44 mmol, 88%). Mp = 117-118 ℃. R_f = 0.42 (hexane/ethyl acetate = 20:1). FT-IR (KBr, cm^{-1}): 2955 (w), 1504 (m), 1325 (s), 1244 (m), 1122 (m), 1064 (m), 867 (m), 840 (m). ^{1}H NMR (600 MHz, $CDCl_3$, rt): δ –0.20 (s, 9H), 3.73 (s, 3H), 6.69 (d, J = 8 Hz, 2H), 6.86 (d, J = 8 Hz, 2H), 6.91-6.92 (m, 2H), 6.97-6.98 (m, 1H), 7.02 (t, J = 8 Hz, 2H), 7.44 (d, J = 8 Hz, 2H), 7.60 (d, J = 8 Hz, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt): δ 0.4, 54.9, 113.0, 124.2 (q, $J_{C\text{-}F}$ = 270.4 Hz), 124.9

(q, $J_{C\text{-}F}$ = 3.5 Hz), 126.2, 127.5, 129.29 (q, $J_{C\text{-}F}$ = 32.1 Hz), 129.3, 129.8, 130.1, 135.6, 142.6, 145.1, 148.1, 152.4, 157.2; $^{19}F\{^{1}H\}$ NMR (564 MHz, $CDCl_3$, rt): δ –62.6. MS (EI, m/z (relative intensity)): 426 (M^+, 100), 412 (25), 411 (77), 257 (24), 227 (20), 203 (18), 165 (27), 135 (24), 73 (51). HRMS (FAB) Calcd for $C_{25}H_{25}F_3OSi$: 426.1627. Found: 426.1607.

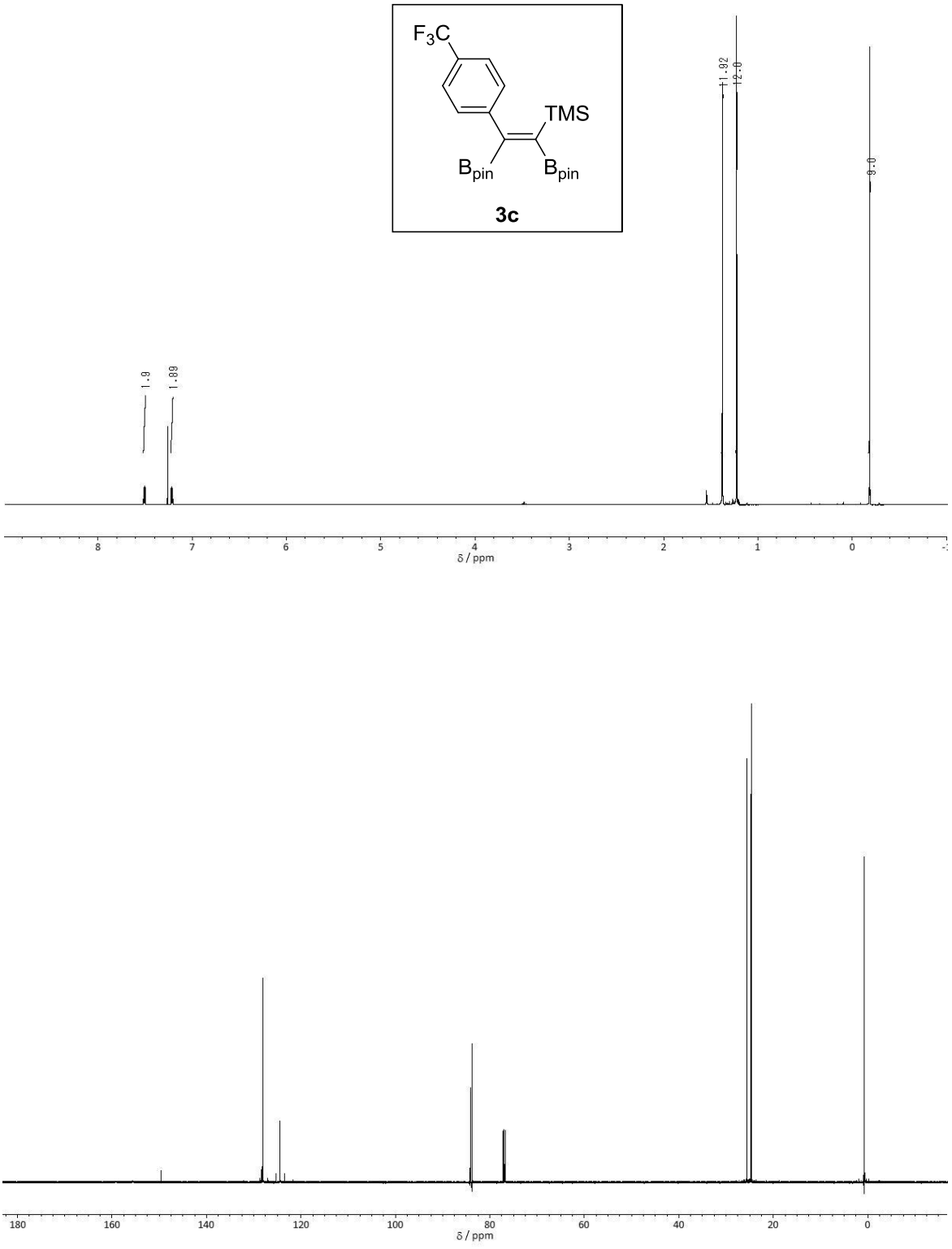
4-4-3 Copies of ^{1}H and $^{13}C\{^{1}H\}$ NMR Charts for the New Compounds.



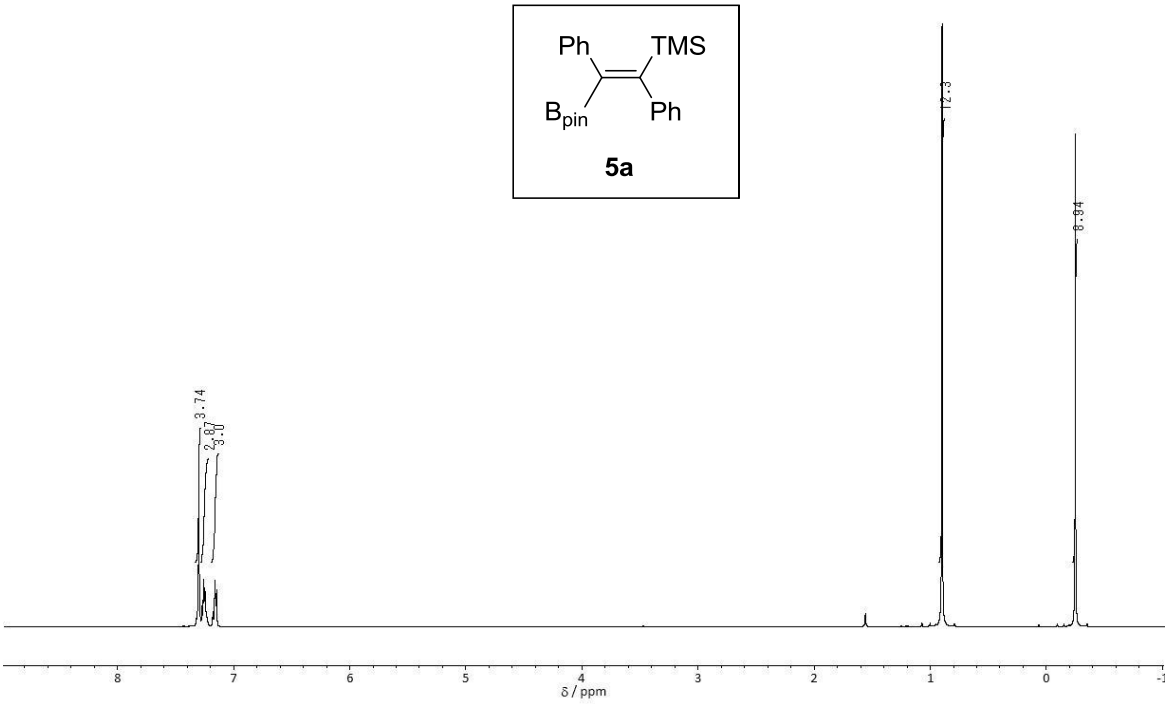
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3a** (in $CDCl_3$).

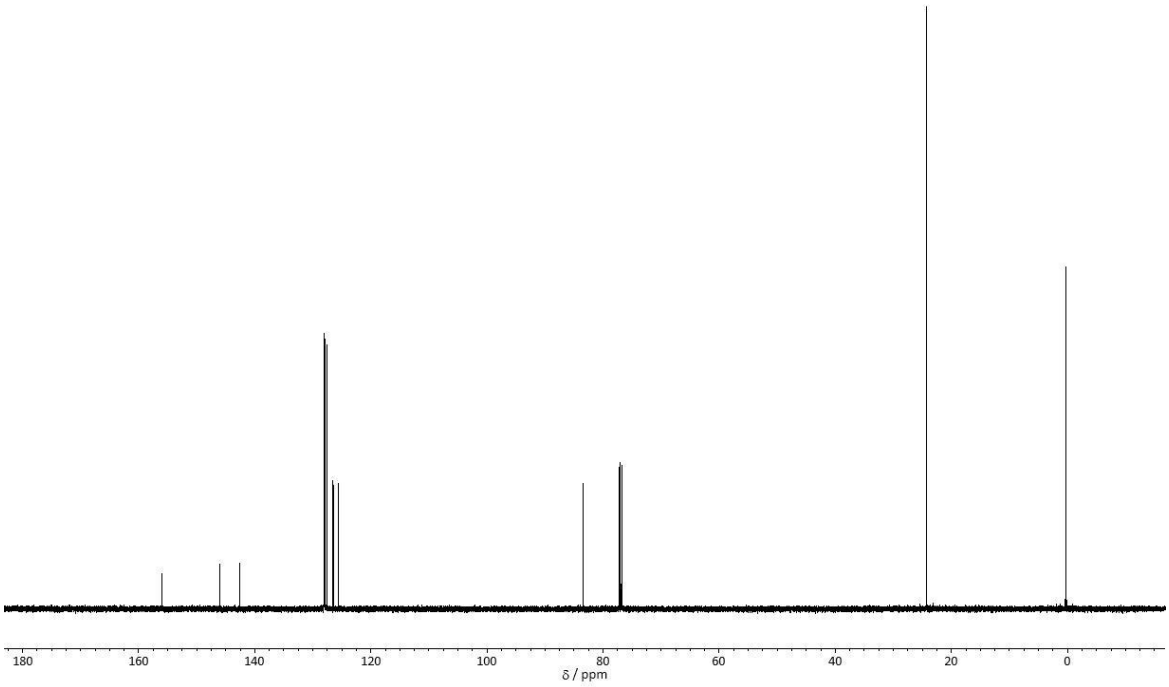


The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3b** (in $CDCl_3$).

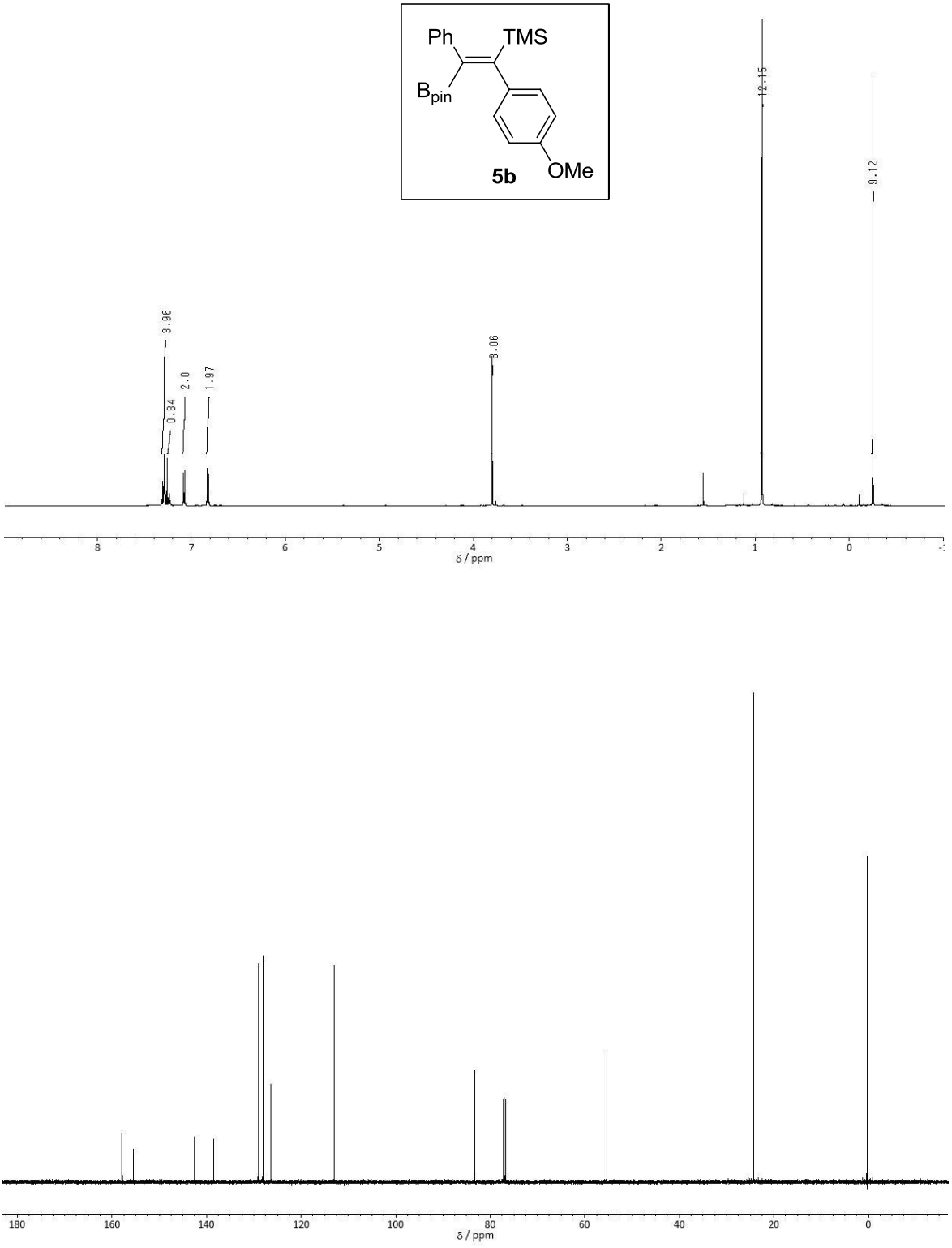


The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3c** (in $CDCl_3$).

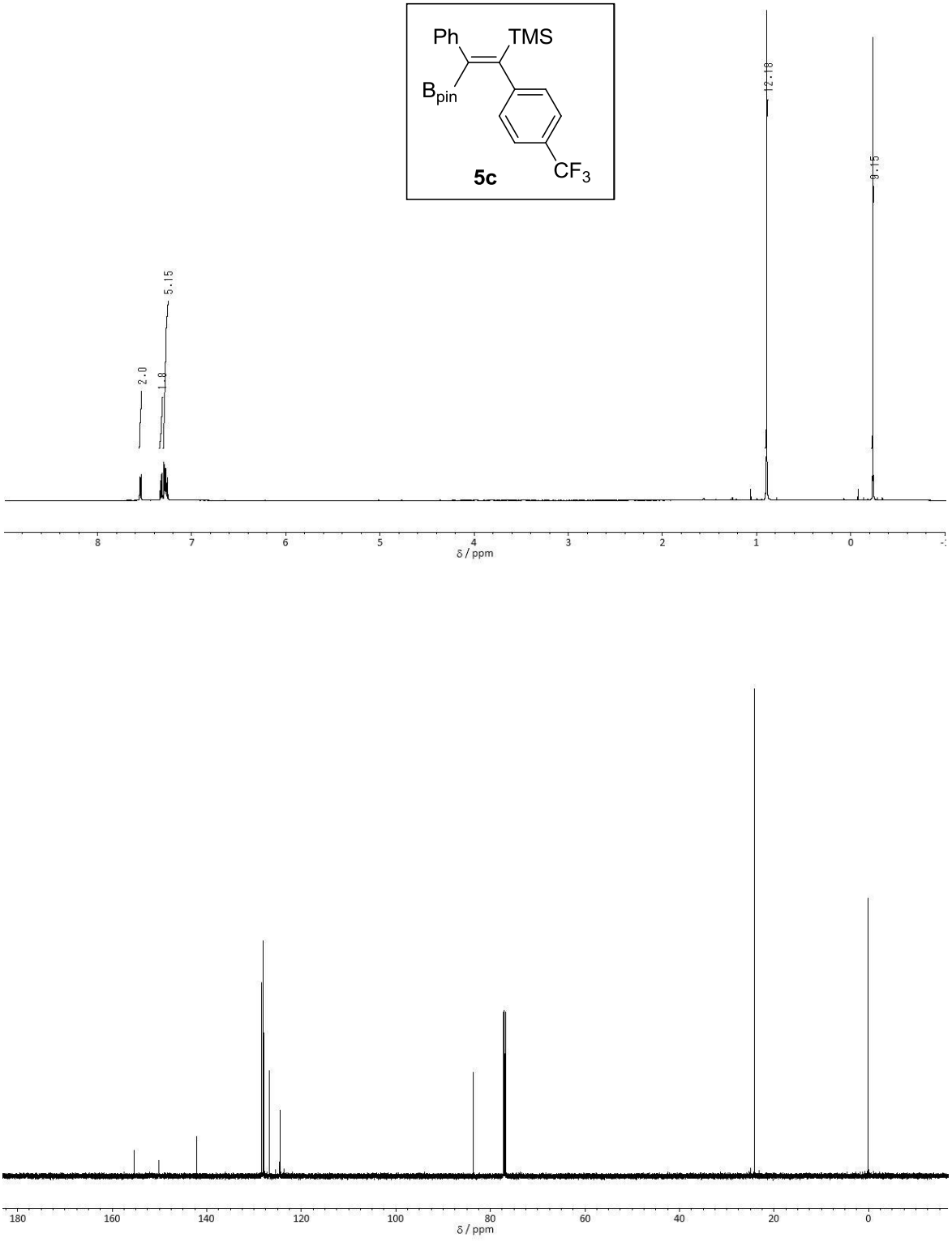




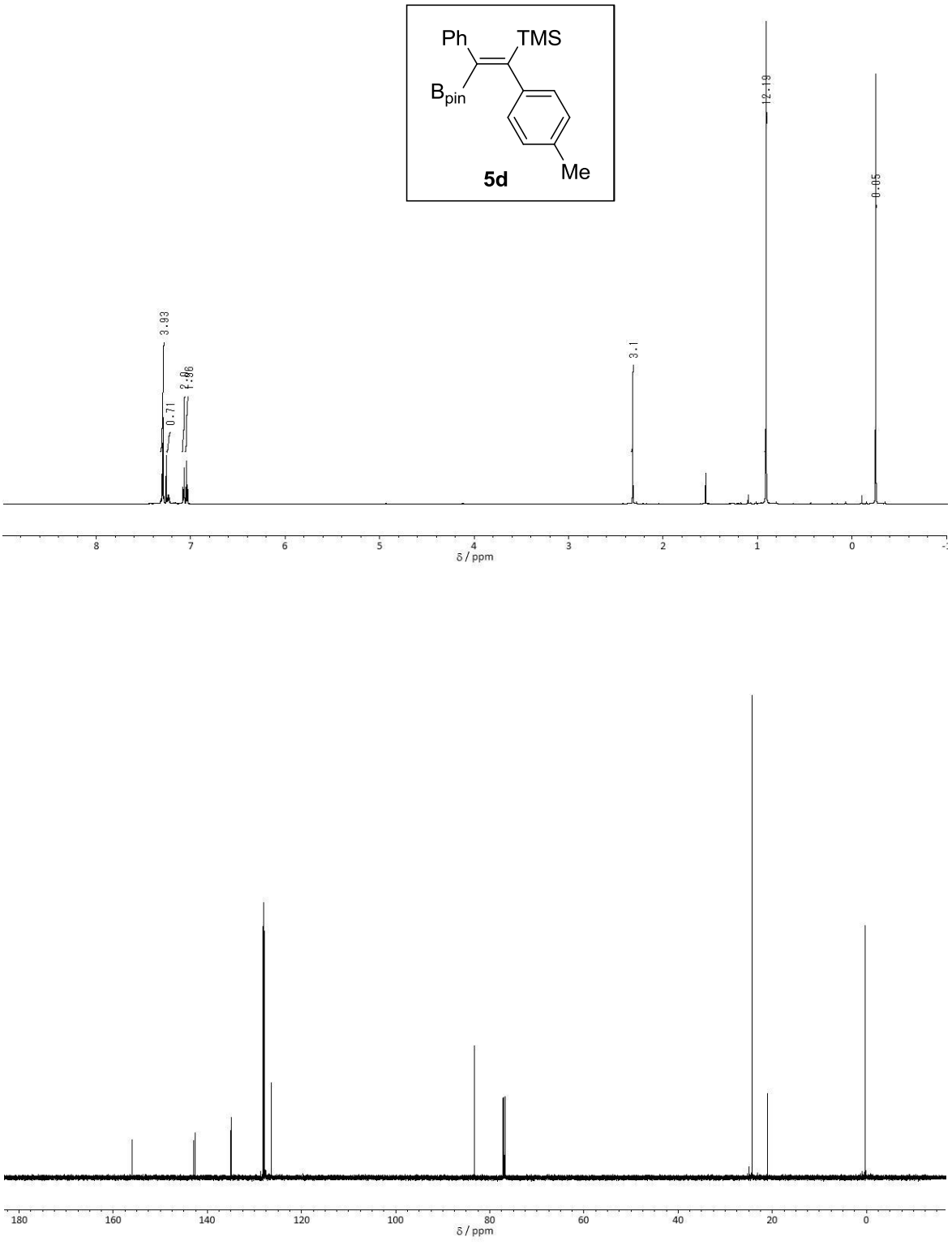
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5a** (in $CDCl_3$).



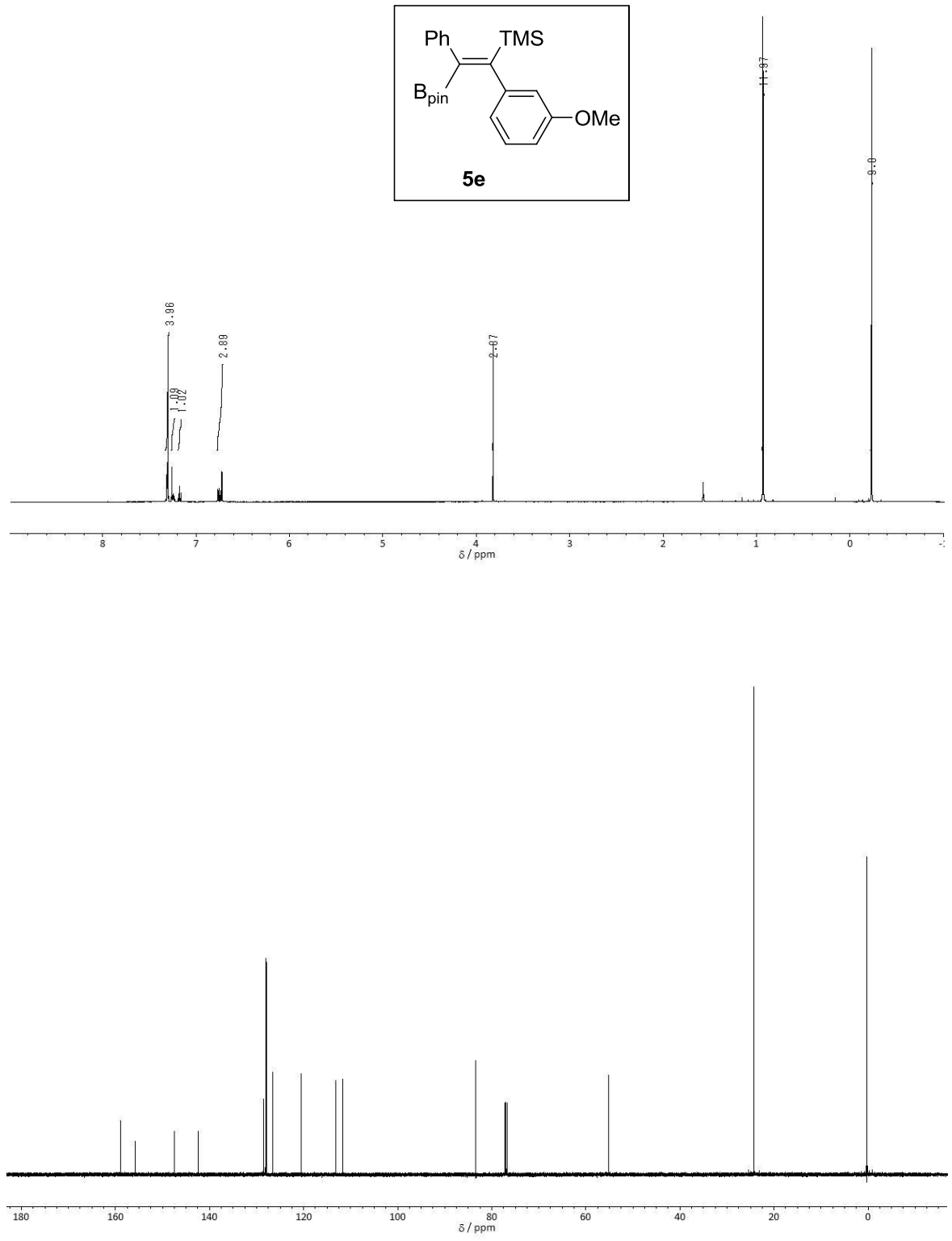
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5b** (in $CDCl_3$).



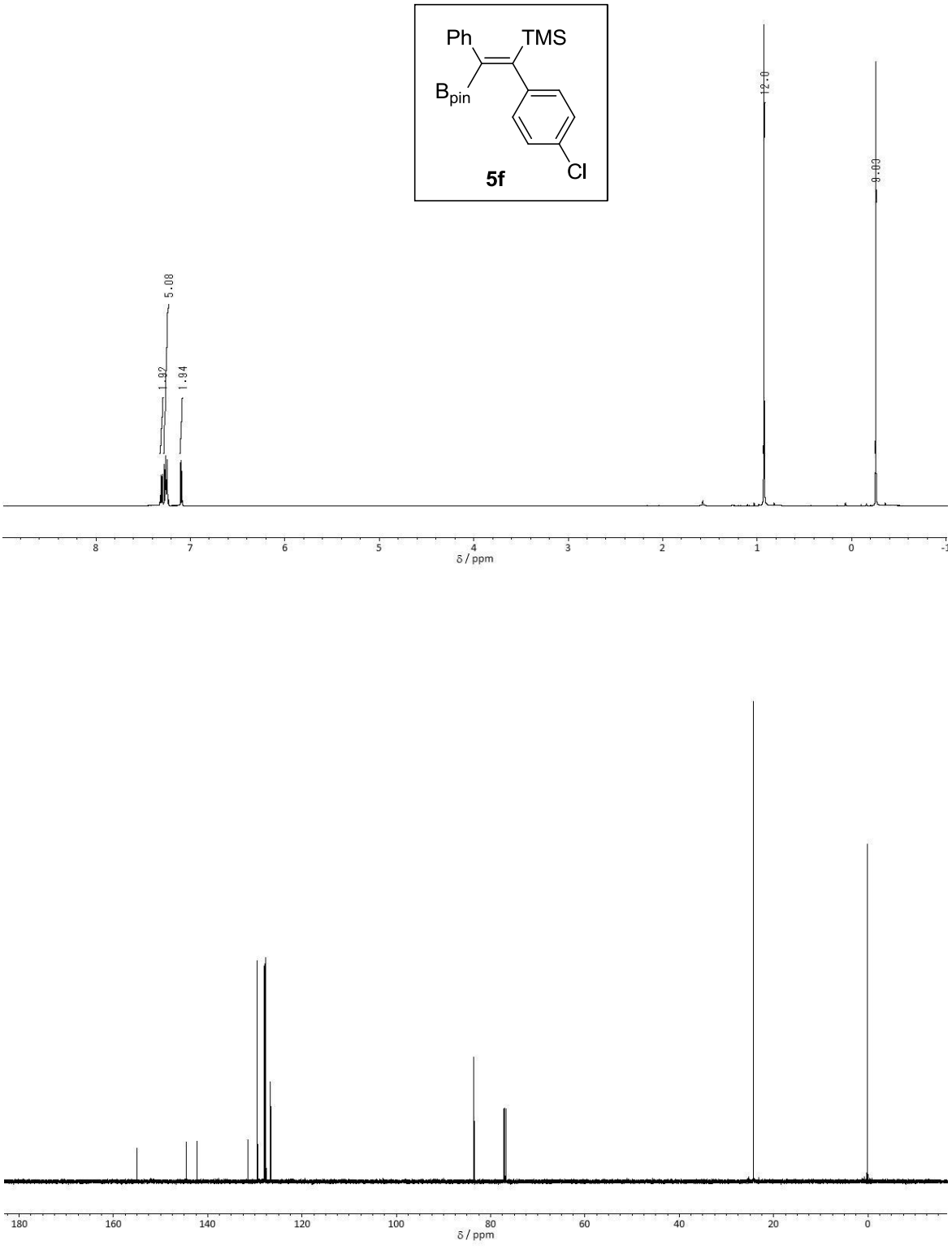
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5c** (in $CDCl_3$).



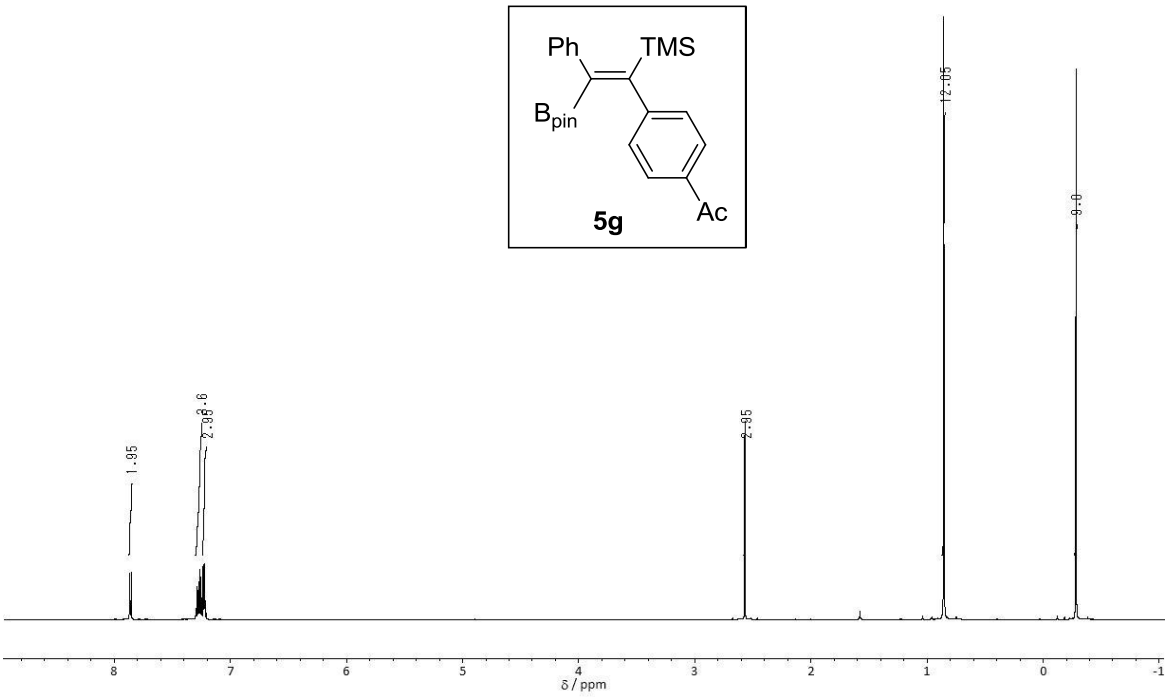
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5d** (in $CDCl_3$).

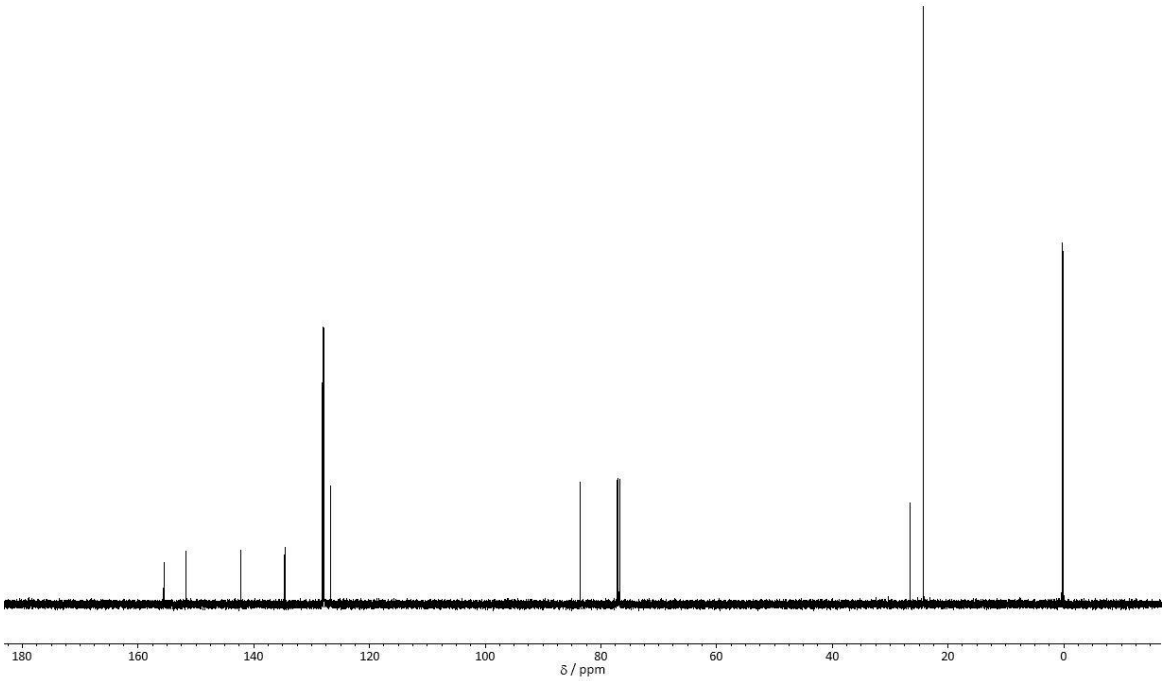


The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5e** (in $CDCl_3$).

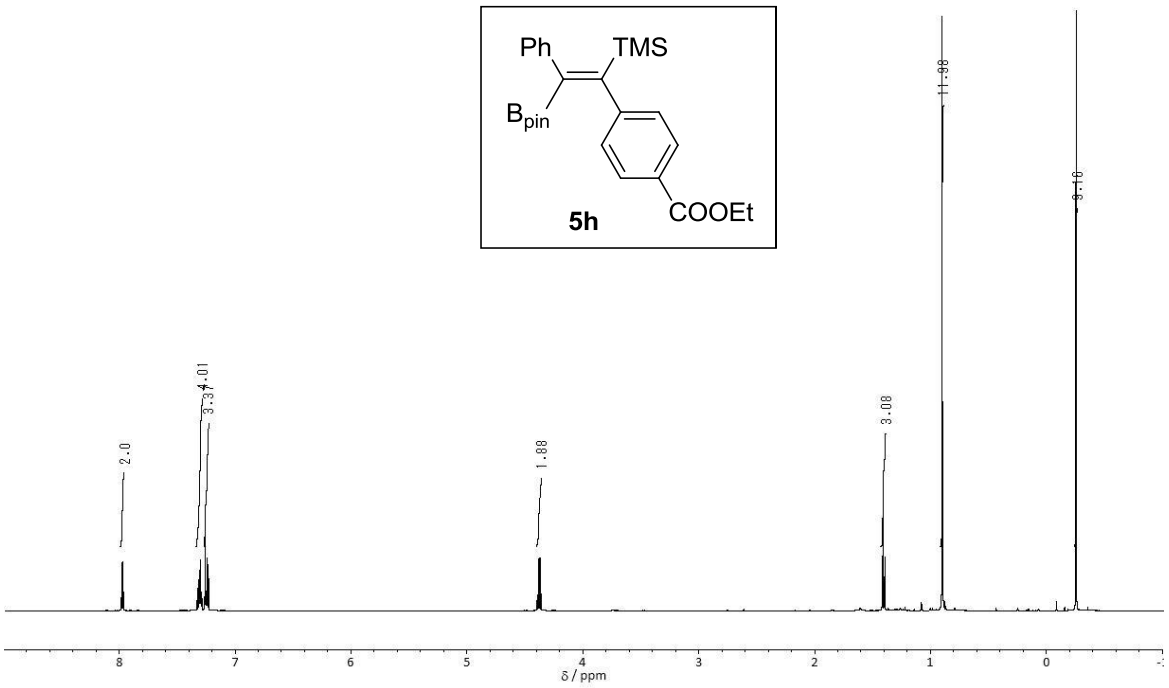


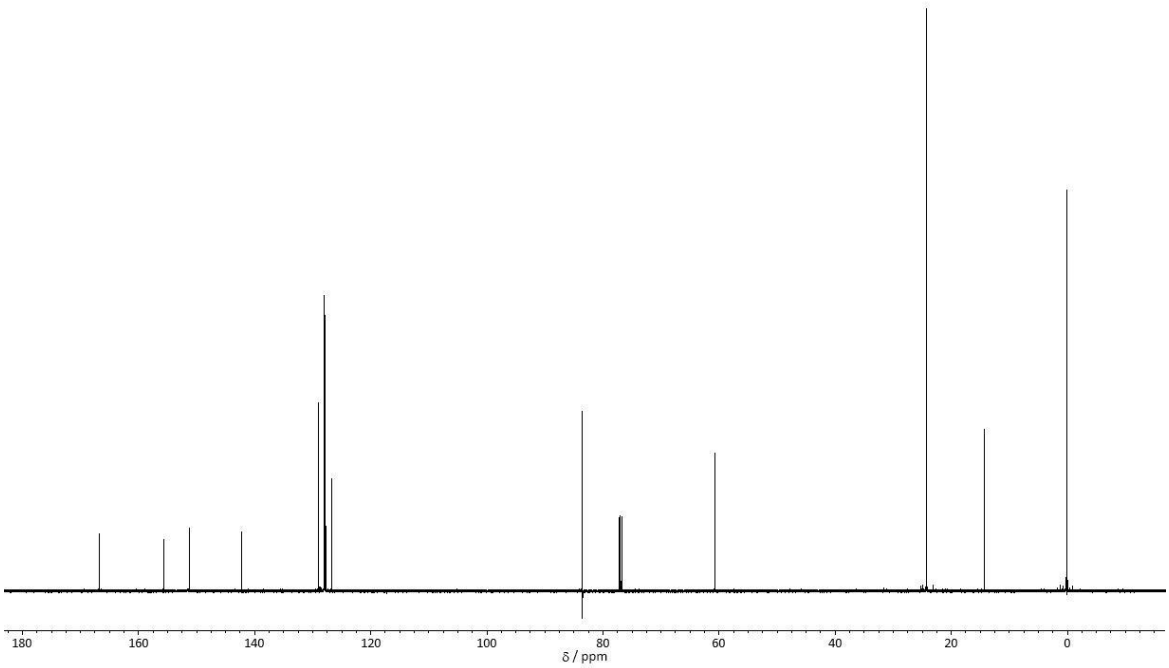
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5f** (in $CDCl_3$).



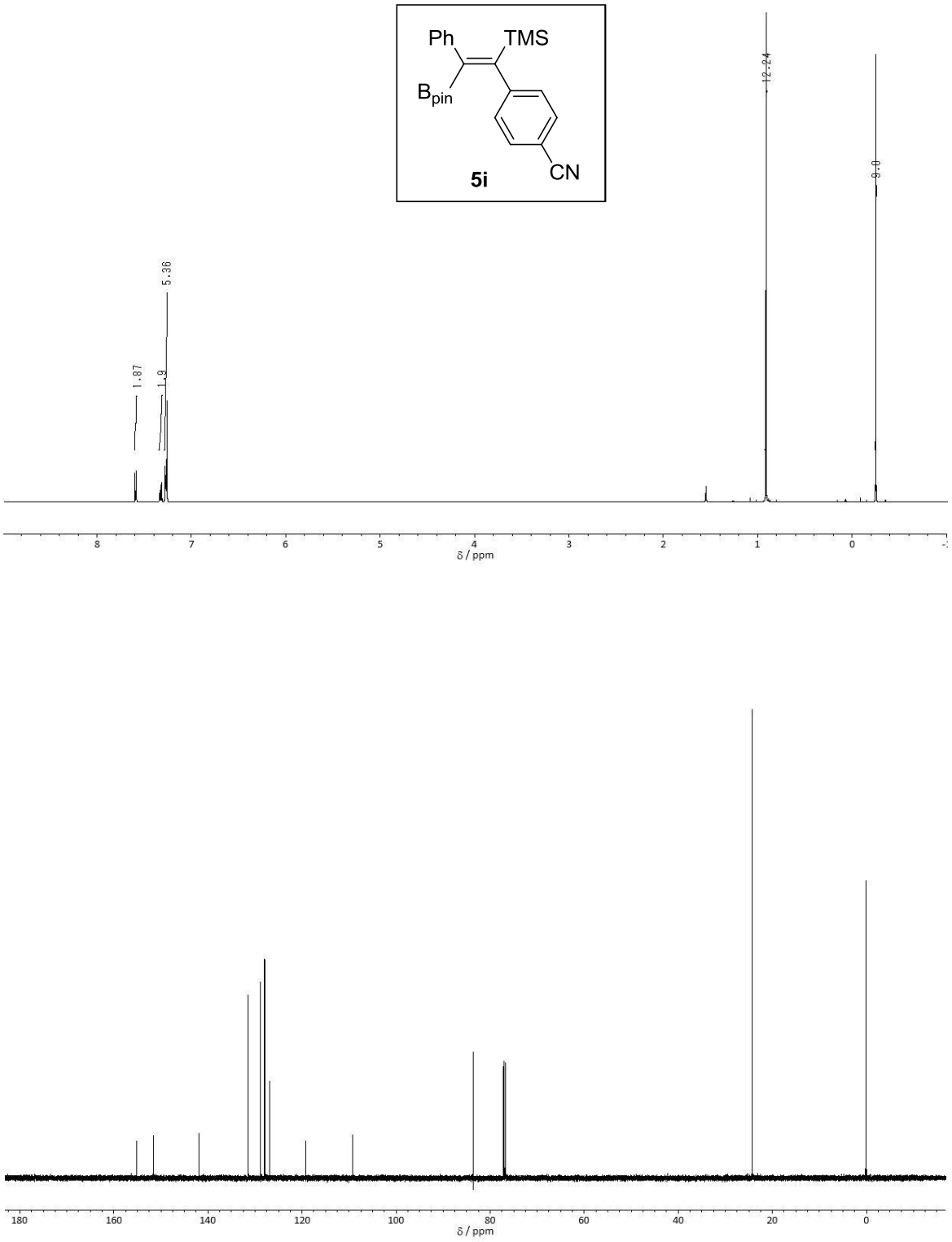


The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5g** (in $CDCl_3$).

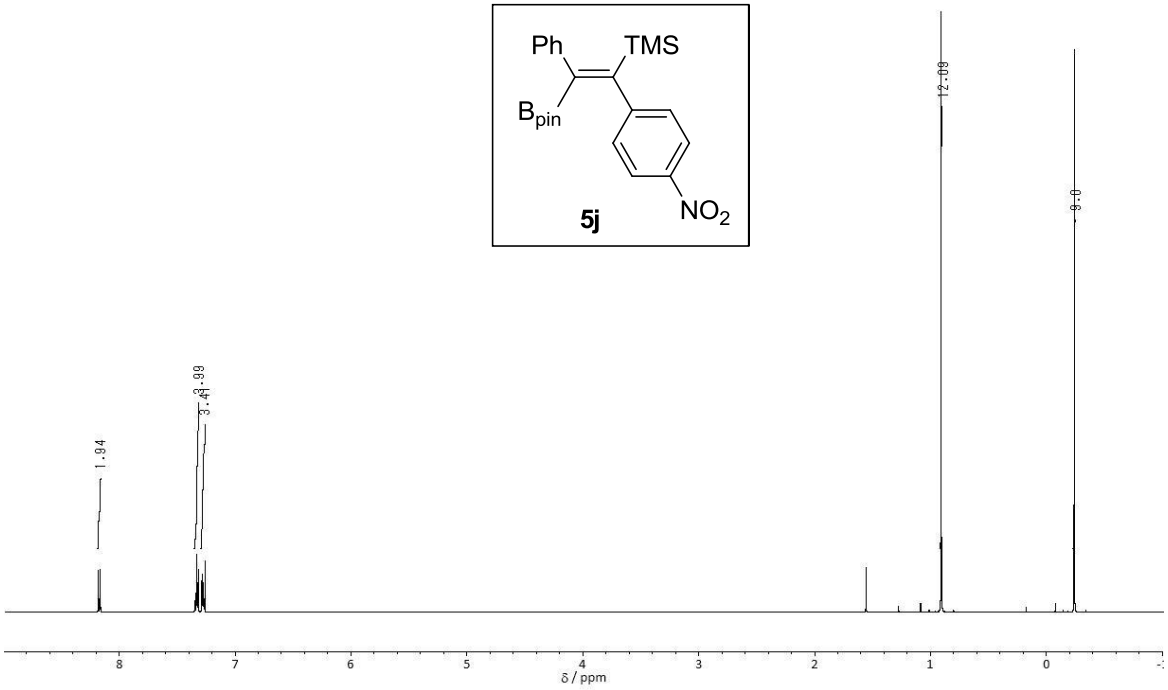


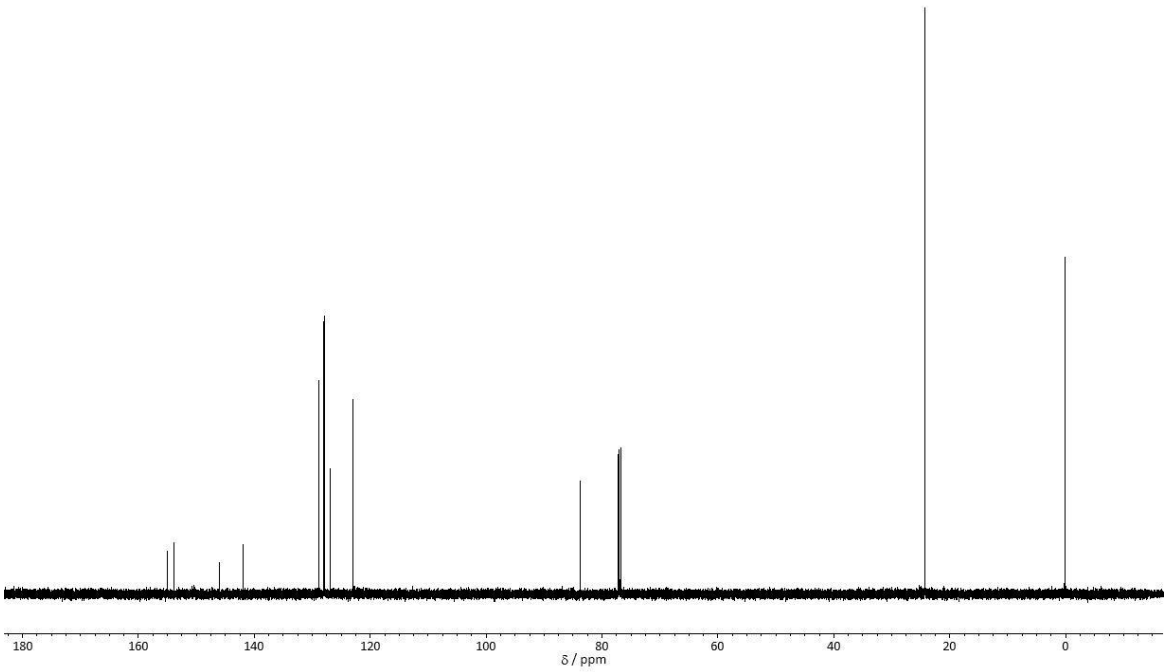


The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5h** (in $CDCl_3$).

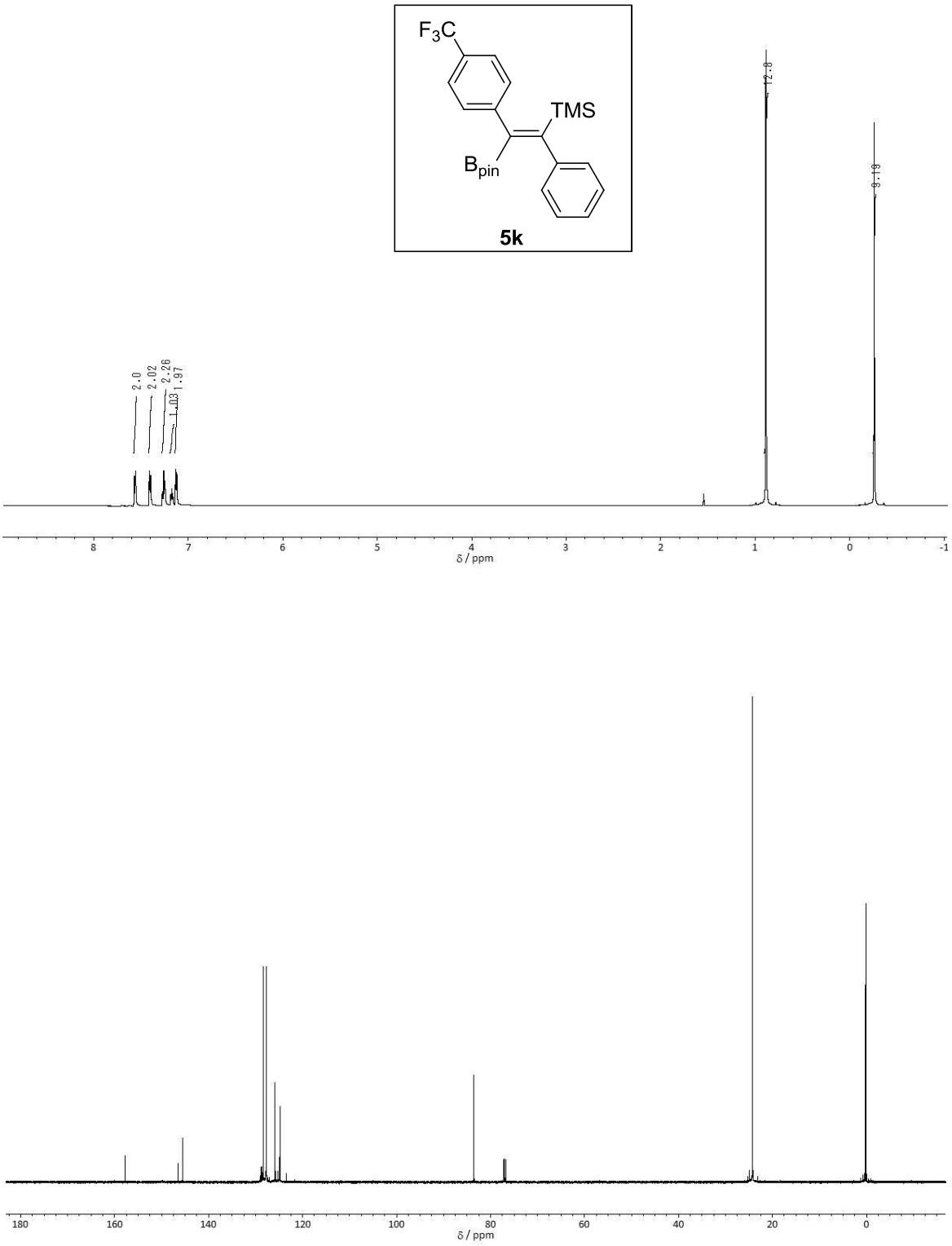


The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5i** (in $CDCl_3$).

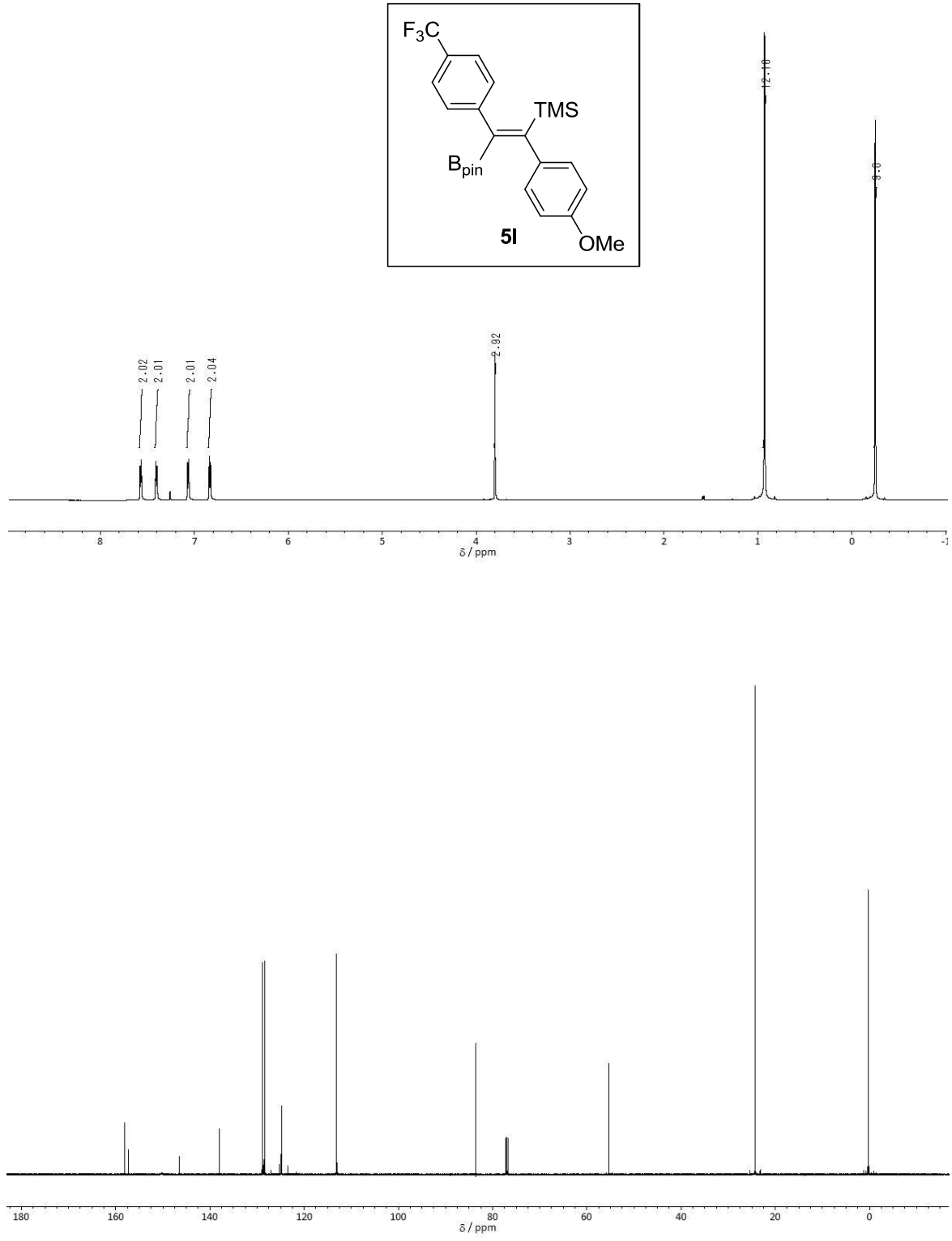




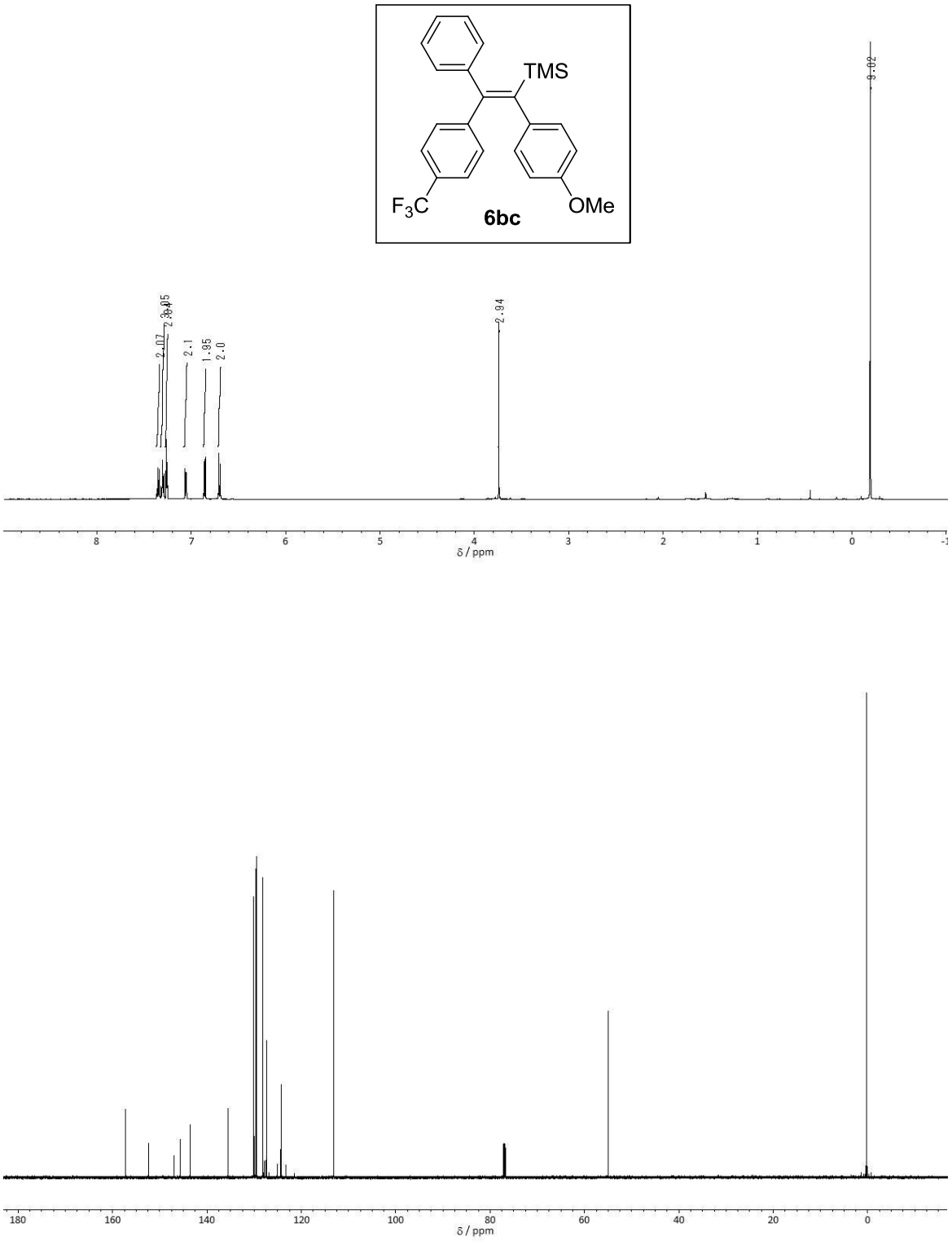
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5j** (in $CDCl_3$).



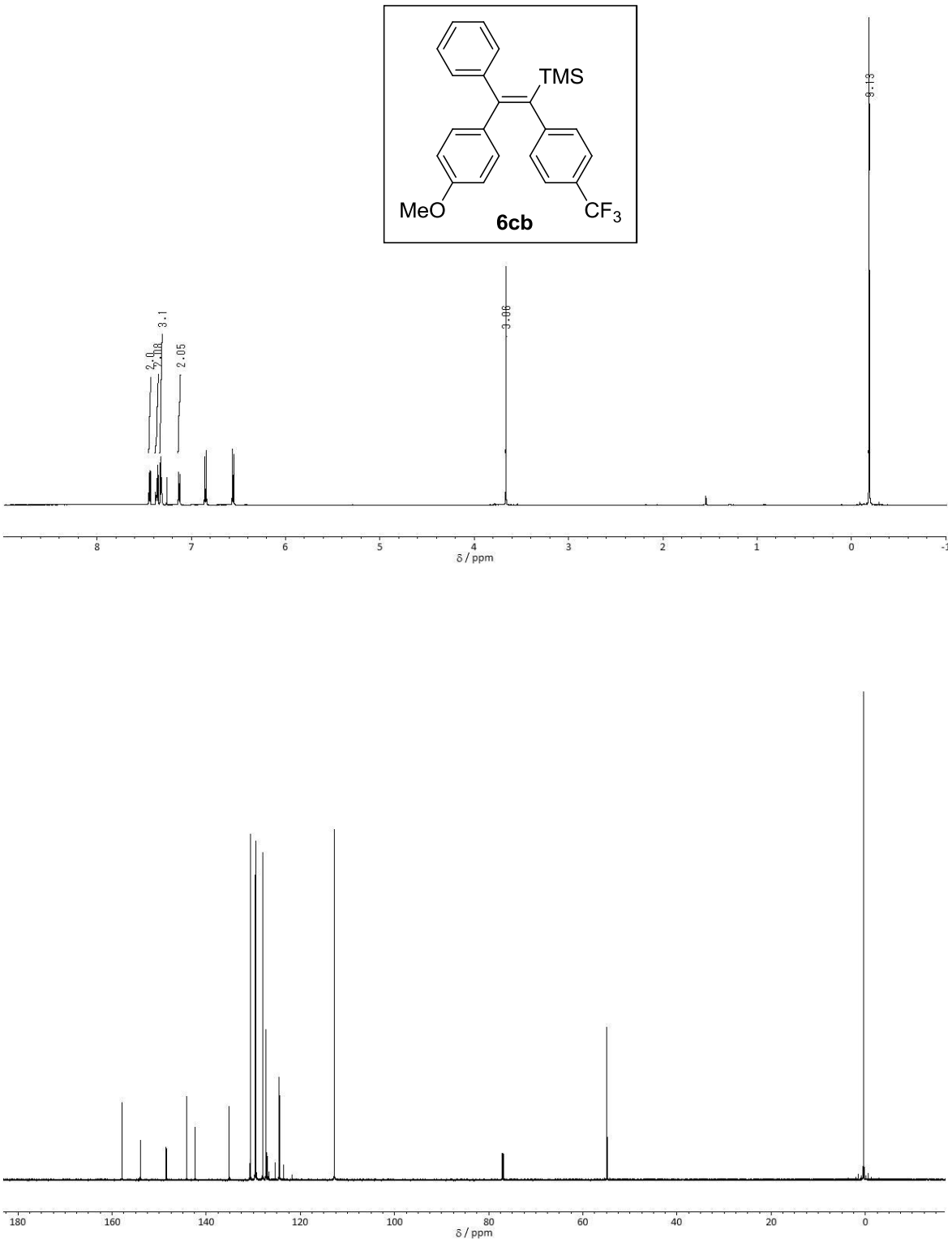
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5k** (in $CDCl_3$).



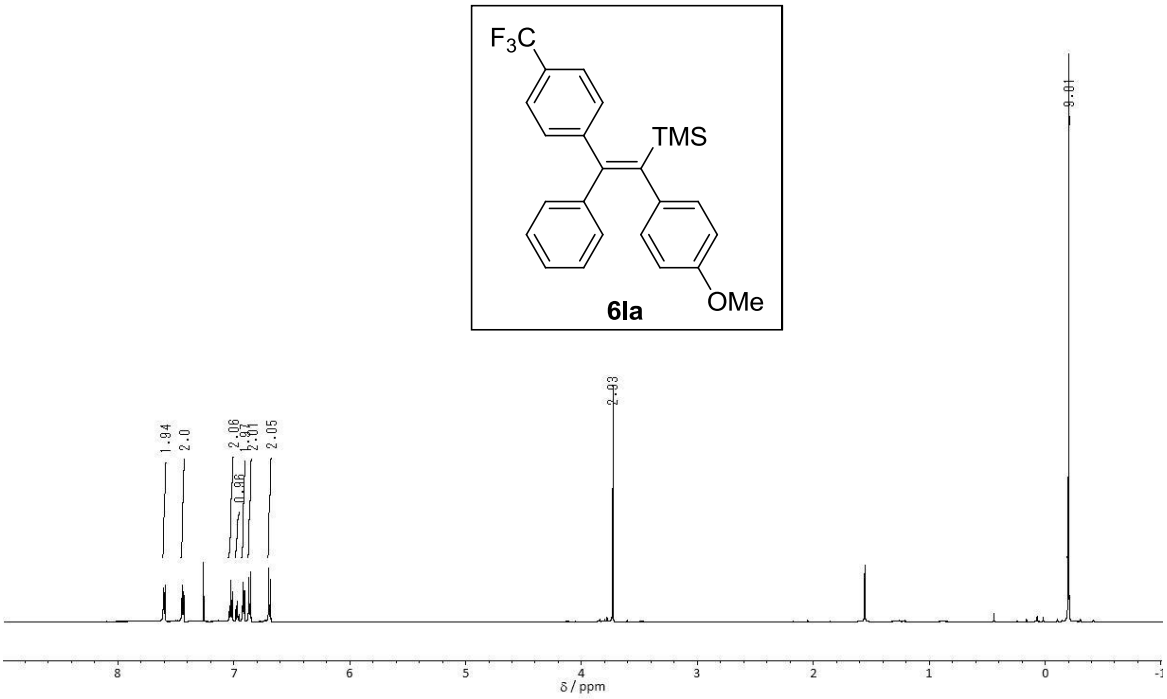
The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **5l** (in $CDCl_3$).

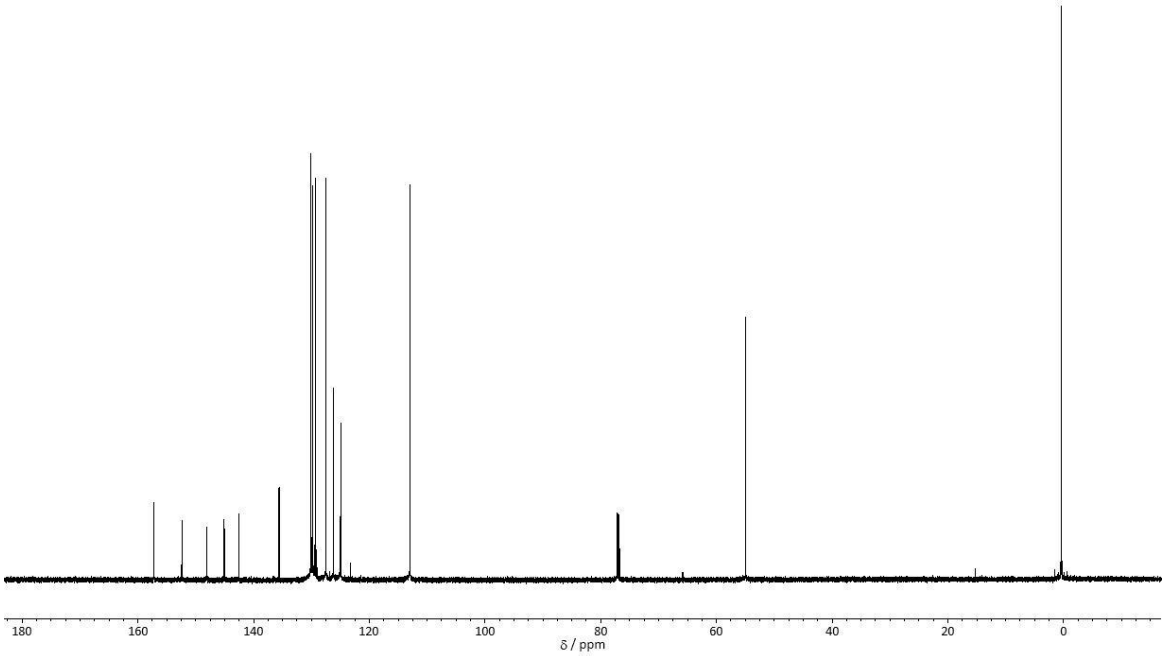


The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6bc** (in $CDCl_3$).



The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6cb** (in $CDCl_3$).





The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6la**(in $CDCl_3$).

4-5 References and Notes

1. (a) Negishi, E.; Abramovitch, A. *Tetrahedron Lett.* **1977**, *18*, 411–414. (b) Jordan, V. C. *Nat. Rev. Drug. Discovery* **2003**, *2*, 205–213. (c) Flynn, A. B.; Ogilvie, W. W. *Chem. Rev*. **2007**, *107*, 4698–4745. (d) Negishi, E.; Huang, Z.; Wang, G.; Mohan, S.; Wang, C.; Hattori, H. *Acc. Chem. Res.* **2008**, *41*, 1474–1485.
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4. Nishihara, Y.; Saito, D.; Tanemura, K.; Noyori, S.; Takagi, K. *Org. Lett.* **2009**, *11*, 3546–3549.
5. (a) Han, L. B.; Tanaka, M. *Chem. Commun*. **1999**, 395–402. (b) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev*. **2000**, *100*, 3067–3126. (c) Suginome, M.; Ito, Y. *Chem. Rev*. **2000**, *100*, 3221–3256. (d) Ishiyama, T.; Miyaura, N. *Chem. Rec*. **2004**, *3*, 271–280. (e) Moberg, C.; Beletskaya, I. *Chem. Rev.* **2006,** *106*, 2320–2354.
6. The term "inter-element" is used for chemical bonds such as mutual linkages within main group elements and linkages between main group elements and transition metals. See, Special Volume entitled "The Chemistry of Interelement Linkage" *J. Organomet. Chem.* **2000**, *611*, 1.
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Conclusion

Conclusion

In this PhD Thesis, the Author discribed synthetic protocols for multisubstituted olefins, in particular, unsymmetrical tetraarylethenes with four different substituents. Highly regioselective *syn*-silylborylation of alkynylboronates and *syn*-diborylation of alkynylsilanes were investigated, respectively, to synthesize versatile, stable trimetalated olefins. The inter-element compounds having Si–B and B–B bonds were found to be good candidates owing to their low-toxicity, easy handling, and ready availability. The obtained products containing two boron groups were subsequently subjected to Suzuki-Miyaura cross-couplings. After the reaction conditions were extensively screened, chemoselectivity was realized by discriminating the different boron groups. This PhD Thesis provides a good combination of well-documented fundamental reactions, which allow the synthesis of multisubstituted olefins.

Chapter 2. Synthesis of Alkynylboron Compounds toward Organic Synthesis

In Chapter 2, a series of alkynylboron compounds were successfully synthesized. Alkynylboronates bearing various alkyl and aryl groups were readily obtained from terminal alkynes. Alkynyllithium species are generated smoothly with *n*-BuLi at low temperature, transmetalation using organoboron reagent followed by HCl/Et_2O afforded various alkynylboronates. With these synthesized alkynylboronates, a versatile direct synthesis was developed for multialkylated olefins bearing various alkyl groups by a regioselective formation of zirconacyclopentenes using alkynylboronates followed by the successive Pd-catalyzed Negishi and Suzuki-Miyaura cross-couplings. The utilization of alkyl-substituted alkynylboronates for the synthesis of tetraalkylated olefins indicates that alkynylboron compound as versatile and synthetically valuable substrates in novel organic reactions, which contributes to promising perspectives for the synthesis of functional materials and pharmaceuticals.

Chapter 3. Synthesis of Multisubstituted Olefins through Regio- and Stereoselective Silylborylation of an Alkynylboronate/Chemoselective Cross-Coupling Sequences

In this Chapter, the Author described the synthesis of unsymmetrical tetraarylethenes. Highly regio- and stereoselective silylborylation of an alkynylboronate was disclosed.

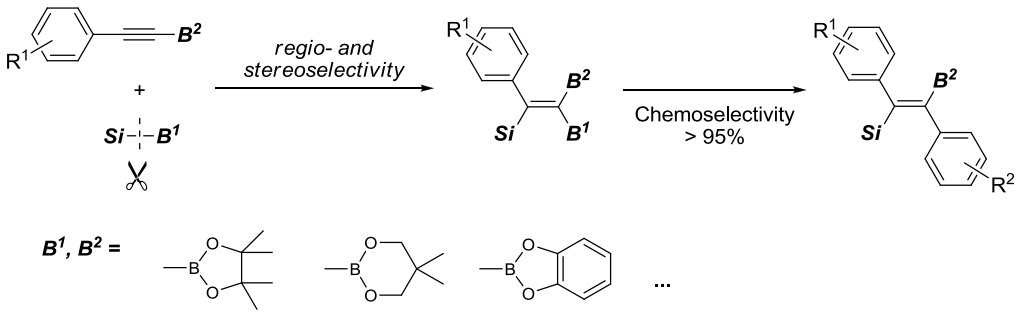
$PhMe_2Si$–Bpin underwent the $Pd(OAc)_2$/*t*-OctNC-catalyzed *syn*-addition to an alkynylboronate to yield 1-phenyl-1-silyl-2,2-diborylethene with high regioselectivity. Successively, chemoselective Suzuki-Miyaura cross-couplings of the *gem*-diborylated alkenylsilanes were conducted to regulate monoarylation. The X-ray analyses showed that the B_{pin} group in the *cis*-position of $SiMe_2Ph$ was more reactive to afford (*Z*)-1-silyl-2-borylstilbene derivatives. A 5 mol% of $PdCl_2$(dppf) was effective to yield the coupling products with high chemoselectivity. Not only aryl iodides but also aryl bromides were involved as coupling partners. The second Suzuki-Miyaura cross-couplings readily introduced the additional aryl groups. The silyl group was also transformed to the aryl group by desilybromination in the presence of Br_2/NaOMe, followed by Suzuki-Miyaura cross-couplings. This protocol was proved to be a good synthetic approach to unsymetrical tetraarylated olefins.

Chapter 4. Synthesis of Multisubstituted Olefins through Regio- and Stereoselective Silylborylation of an Alkynylboronate/Chemoselective Cross-Coupling Sequences

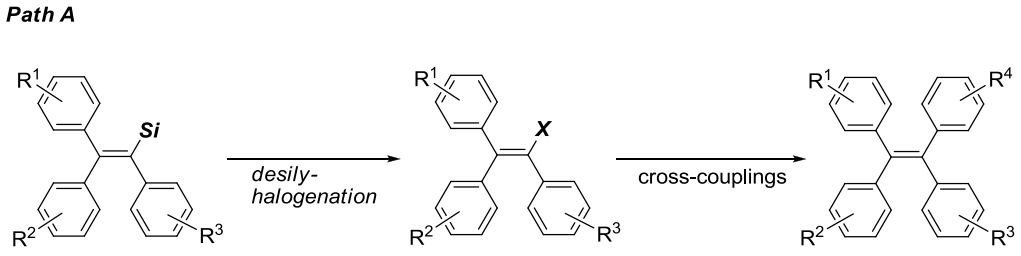
In Chapter 4, another pathway of regio- and stereoselective synthesis of multisubstituted olefins is reported. Bis(pinacolato)diboron (B_{2pin2}) underwent the $Pt(PPh_3)_4$-catalyzed *syn*-addition to alkynylsilanes, to yield 1-aryl-1-silyl-2,2-diborylethenes in good yields with a perfect stereoselectivity. In the sequential chemoselective Suzuki–Miyaura cross-coupling, among all screened catalysts, $PdCl_2$(dppp) performed the best to give rise to (*Z*)-1-boryl-trimethylsilyl stilbene derivatives with a perfect chemoselectivity up to >99:1. A wide range of aryl halides regardless electron-donating, -withdrawing, or active functional groups such as –OMe, –CF_3, –Cl, –CO_2Et, –Ac, –CN, –NO_2, *etc*. were examined. The subsequent Suzuki-Miyaura cross-coupling readily introduced another aryl group in good yields. Moreover, different regio- and stereoisomers of multisubstituted olefins were successfully synthesized, which cannot be achieved through the known methodologies reported in Chapter 1. Although more efficient transformations of the silyl group to the aryl group are now in progress, this protocol provides an alternative to more efficient and practical synthesis of tetraarylethenes.

Future Perspective

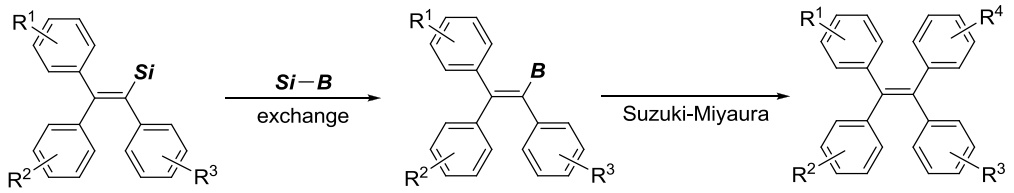
In Chapter 3, *gem*-diborylated alkenylsilane **3** produced from alkynylboronic acid pinacol ester **2** was extensively studied in the chemoselective Suzuki-Miyaura cross-coupling. However, the two B_{pin} groups in a germinal position were not perfectly discriminated. Less reactive B_{pin} in the trans position of the silyl group also reacted to yield a minor product with (*E*)-configuration, which diminished the chemoselectivity. In the future, this strategy can be broadened to silylborylation of other Si–B reagents with alkynylboron compounds; those products bearing different boron groups will demonstrate different reactivity in Suzuki-Miyaura cross-couplings, which are expected to attain higher chemoselectivity.



In Chapter 4, a more regio- and stereodefined synthesis of triarylated olefins was achieved with almost perfect selectivity through *syn*-diborylation of alkynylsilanes and high chemoselective Suzuki-Miyaura cross-couplings. A more efficient transformation of the remaining silyl group is highly demanded to optimize this synthetic strategy.



Path B



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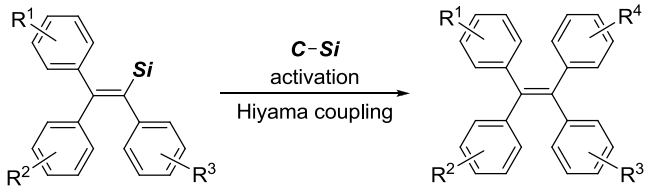

A further investigation of desilylhalogenation will be conducted to obtain iodination or bromination products in higher yields. Also, silicon-boron exchange will afford a good candidate for Suzuki-Miyaura cross-couplings.

List of Publications

Publications Related to the Ph.D Thesis

Chapter 2

1) Highly Regio- and Stereoselective Synthesis of Multialkylated Olefins through Carbozirconation of Alkynylboronates and Sequential Negishi and Suzuki-Miyaura Coupling Reactions.
   Yasushi Nishihara, Yoshiaki Okada, Jiao Jiao, Masato Suetsugu, Ming-Tzu Lan, Megumi Kinoshita, Masayuki Iwasaki, and Kentaro Takagi
   Angew. Chem. Int. Ed. **2011**, *50*, 8660–8664.

2) Alkynylboron Compounds in Organic Synthesis
   Jiao Jiao and Yasushi Nishihara
   J. Organomet. Chem. **2012**, *721–722*, 3–16.

Chapter 3

3) Synthesis of Multisubstituted Olefins through Regio- and Stereoselective Silylborylation of an Alkynylboronate/Chemoselective Cross-Coupling Sequences
   Jiao Jiao, Kiyohiko Nakajima, and Yasushi Nishihara
   Org. Lett. **2013**, *15*, 3294–3297.

Chapter 4

4) Synthesis of Multisubstituted Olefins through Diborylation of Alkynylsilanes and Highly Chemoselective Suzuki–Miyaura Couplings Sequences
   Jiao Jiao, Keita Hyodo, Hao Hu, and Yasushi Nishihara
   Manuscript in preparation

Other Publications

Paper

5) Palladium-Free Synthesis of Unsymmetrical Diarylethynes by Cross-Coupling Reaction of Alkynylboronates with Aryl Iodides Catalyzed by CuCl
Daisuke Ogawa, Jing Li, Masato Suetsugu, Jiao Jiao, Masayuki Iwasaki, and Yasushi Nishihara
Tetrahedron Lett. **2013**, *54*, 518–521.

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Highly Regio- and Stereoselective Synthesis of Multialkylated Olefins through Carbozirconation of Alkynylboronates and Sequential Negishi and Suzuki–Miyaura Coupling Reactions**

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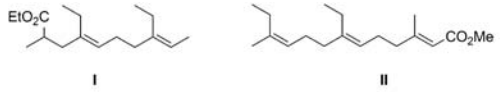
Dedicated to Professor Tamejiro Hiyama on the occasion of his 65th birthday

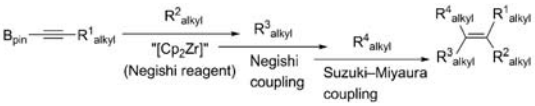
The regio- and stereoselective synthesis of multisubstituted olefins is one of the most challenging tasks in synthetic organic chemistry.[1] Established synthetic methods to directly construct carbon–carbon double bonds, such as Wittig, Horner–Wadsworth–Emmons, or olefin metathesis have limitations and often afford inseparable mixtures of stereoisomers. Recent advances in carbometalation or bimetalation/cross-coupling strategies have provided a facile entry to multisubstituted olefins, albeit often with problematic regio- and stereoselectivities.[2] Although efficient multicomponent coupling reactions have been used to achieve the synthesis of multisubstituted olefins bearing aromatic substituents,[3] a general approach to multialkylated olefins has yet to be defined.[4]

Aliphatic multialkylated olefins are common motif in natural products and occur, for example, in various insect sex pheromones and hormones.[5] In addition to their importance in nature, multialkylated olefins are often used as key intermediates in the synthesis of other compounds. For example, the diene **I** is a precursor of the antibiotic lasalocid A,[6] and triene **II** is the final intermediate in a synthesis of Cecropia juvenile hormone.[7]



I II

Although the simple textbook approach to multialkylated olefins would be an elimination reaction (e.g. E2 reaction), neither Hofmann (less-substituted olefins)[8] nor Saytzeff (more-substituted olefins)[9] elimination can perfectly control reaction selectivity with mixtures of structural isomers being obtained. Recently, our research group has demonstrated the usefulness of 1-alkynylboronates[10] and 1-alkynylsilanes[11] as applied to zirconium chemistry to afford a highly regio- and stereoselective syntheses of multisubstituted olefins. Herein, we describe a practical and versatile procedure for the formation of tri- and tetrasubstituted olefins bearing different β-hydrogen-containing alkyl groups by carbozirconation of 1-alkynylboronates and successive Negishi[12] and/or Suzuki–Miyaura[13] cross-coupling reactions with high regio- and stereoselectivities (Scheme 1).



Scheme 1. Synthetic concept. B_{pin} = pinacolatoboryl, Cp = cyclopentadienyl.

Addition of 1-alkynylboronates **1a–1e**[14] to Negishi reagent ($[Cp_2ZrCl_2]/2\,n$BuLi)[15] generated in situ under an atmosphere of ethylene smoothly produced zirconacyclopentenes[16] which, upon hydrolysis, afforded the corresponding alkenylboronates **2a–2e** in moderate to high yields with excellent regioselectivity [Eq. (1)].[17] The regiochemistry of **2a–2e** was confirmed by comparison of their spectroscopic data with those reported for authentic compounds[18] prepared by the reactions of 1-alkynylboronates with Takahashi reagent ($[Cp_2ZrCl_2]/2\,$EtMgBr),[19] as well as ^{1}H NMR spectra that show the presence of a highly shifted triplet with a small coupling constants ($J = 1.5$ Hz) in the double bond region (5.02–5.13 ppm), and is indicative of a hydrogen atom located geminal to the boron functionality. Alternately, the $^{11}B\{^1H\}$ NMR chemical shift of **2a** (29.9 ppm) is characteristic of vinylboronates.

With the regiocontrolled alkenylboronates **2a** in hand, we pursued the Suzuki–Miyaura coupling of alkenylboronates with alkyl bromides. In general, organoboronates are relatively inert compounds compared to the corresponding

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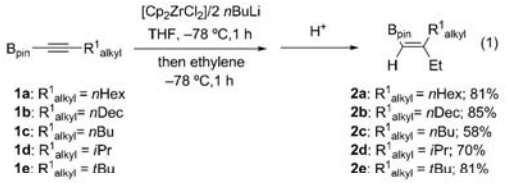
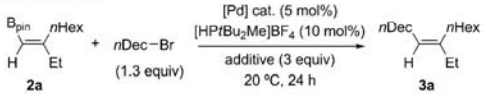


organoboronic acids.[20] Although it has been reported that the Suzuki–Miyaura coupling of alkenylboronates with alkyl bromides possessing β-hydrogen atoms proceed at 60 °C,[21] the higher temperature caused undesired β-hydrogen elimination in our previously reported nickel-catalyzed cross-coupling of alkenylboronates with alkyl iodides.[10] Thus, we screened various milder reaction conditions (Pd catalyst, additive, and solvent) and discovered that, under the basic conditions developed by Fu and co-workers,[22] wherein $[HPtBu_2Me]BF_4$ is used as a precursor of the phosphine ligand, the reaction proceeded smoothly at room temperature.

As a test reaction, we chose to examine the cross-coupling of a β-hydrogen-containing alkyl bromide (1-bromodecane) with an alkenylboronate **2a** to yield **3a**. In this case, the conditions that Fu had found to be optimal for Suzuki–Miyaura coupling of alkyl bromides with arylboronic acids[22] were not optimal for the present reaction (Table 1, entry 1). We thus surveyed a broad range of conditions, and an illustrative subset of our findings is provided in Table 1. For example, we explored the use of Lewis base additives, and determined KOH to be the best (Table 1, entries 1–5). The choice of solvent had a significant impact on the efficiency of the reaction; use of THF rather than *tert*-amyl alcohol led to a marked enhancement in yield of **3a** (Table 1, entry 6). Use of

Table 1: Suzuki–Miyaura cross-coupling of 1-bromodecane with alkenylboronate **2a**.[a]



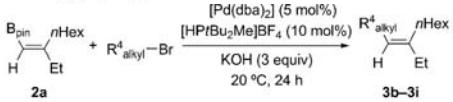
Entry	[Pd] cat.	Additive	Solvent	Yield [%][b]
1[c]	$Pd(OAc)_2$	KO*t*Bu	*tert*-amyl alcohol	47
2[d]	$Pd(OAc)_2$	KO*t*Bu	*tert*-amyl alcohol	32
3	$Pd(OAc)_2$	KOH	*tert*-amyl alcohol	63
4	$Pd(OAc)_2$	$Ba(OH)_2$	*tert*-amyl alcohol	<1
5	$Pd(OAc)_2$	CsF	*tert*-amyl alcohol	<1
6	$Pd(OAc)_2$	KOH	THF	81
7	$[Pd(dba)_2]$	KOH	THF	96
8	[PdCp(π-allyl)]	KOH	THF	91
9[e]	$[Pd(dba)_2]$	KOH	THF	99 (93)

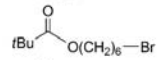
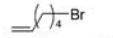
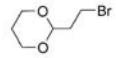
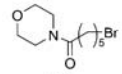
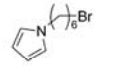
[a] The reactions were carried out using **2a** (0.2 mmol), 1-bromodecane (0.26 mmol), and additive (0.6 mmol) in solvent (1 mL). [b] Determined by GC analysis of the crude reaction mixture. Yield of isolated product is shown in parenthesis. [c] Reaction carried out according to the procedure in Ref. [22]. [d] 6 equivalents of additive was used. [e] 0.5 mL of solvent was used. dba = dibenzylideneacetone, THF = tetrahydrofuran.

$[Pd(dba)_2]$, rather than $Pd(OAc)_2$ was beneficial and resulted in a slightly more effective coupling (Table 1, entry 7). Although [PdCp(π-allyl)] was found to be as effective as $[Pd(dba)_2]$ (Table 1, entry 8), we chose to focus our study on $[Pd(dba)_2]$/KOH because of cost considerations. Increasing the reaction concentration delivered a quantitative yield of the product (Table 1, entry 9).

Using our optimized reaction conditions, we performed Suzuki–Miyaura cross-coupling of an array of β-hydrogen-containing alkyl bromides (Table 2). The process produced

Table 2: Synthesis of trialkylated ethenes **3b–3i** by stereocontorolled Suzuki–Miyaura cross-coupling of alkenylboronate **2a** with alkyl bromides bearing β-hydrogen atoms.[a]

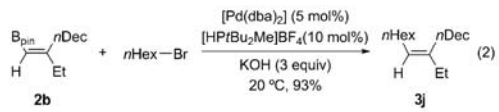


Entry	R^4_{alkyl}−Br	Product	Yield [%][b]
1	$Ph(CH_2)_3$−Br	**3b**	79
2	$Cl(CH_2)_6$−Br	**3c**	98
3	$NC(CH_2)_4$−Br	**3d**	64
4		**3e**	78
5		**3f**	78
6		**3g**	83
7		**3h**	81
8		**3i**	80

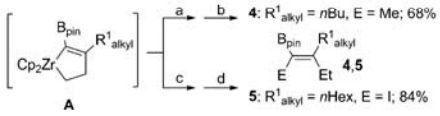
[a] The reactions were carried out using **2a** (1 mmol) and alkyl bromide (1.3 mmol) in THF (2.5 mL). [b] Yield of isolated product.

the desired cross-coupled products **3b–3i** in good to excellent yields and was compatible with variety of functional groups, including aryl, chloride, nitrile, ester, alkene, acetal, amide, and pyrrole (Table 2, entries 1–8). As a result of the mild reaction condition, no alkenes produced by β-hydrogen elimination were detected.

Notably, the regiochemistry of the cross-coupled product can be readily reversed by swapping the functionality on the alkyl group in alkynylboronates **1** and the alkyl bromide. For example, 1-alkynylboronate **2b** was successfully treated with 1-bromohexane to produce the cross-coupled product **3j**, which is a regioisomer of **3a** [Eq. (2)].



Prior to hydrolysis, the intermediate zirconacyclopentenes **A**[23] formed in situ can serve as versatile precursors of tetrasubstituted olefins bearing a boron functionality. For example, as shown in Scheme 2, the selective protonolysis of a

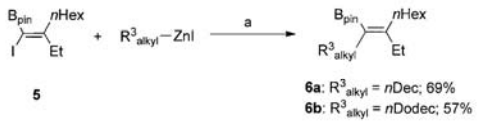


Scheme 2. Reagents and conditions: Synthesis of **4**: a) *i*PrOH (0.8 equiv), RT, 1 h; b) then CuCl (1.2 equiv), DMPU (1.8 equiv), [Pd(PPh$_3$)$_4$] (10 mol%), iodomethane (2.0 equiv), THF, 50 °C, 1 h. Synthesis of **5**: c) *i*PrOH (0.8 equiv), RT, 1 h; d) then I_2 (1.0 equiv), RT, 12 h. DMPU = 1,3-dimethylhexahydro-2-pyrimidinone, THF = tetrahydrofuran.

Zr–C(sp^3) bond with isopropyl alcohol, and subsequent one-pot palladium-catalyzed coupling reactions with iodomethane in the presence of CuCl,[24] and iodolysis[23] afforded 1,2,2-trifunctionalized alkenylboronates **4** and **5** in a stereocontrolled manner (68 and 84% yield, respectively).

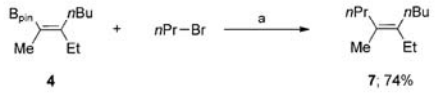
An additional motivation for this study is our interest in developing an efficient route to various tetraalkylated olefins bearing longer alkyl chains that are not readily available. However, the introduction of longer carbon chains containing β-hydrogen atoms proved challenging. For example, our attempt to perform one-pot cross-coupling of the intermediate alkenylzirconocene complex with 1-bromodecane under Fu's conditions (2.5% of Pd(OAc)$_2$, 2.0 equiv of LiBr, NMP/THF (1:1), 55 °C, 24 h)[25] afforded no product. Presumably, the steric bulk of the tetrasubstituted alkenyl(alkoxy)zirconocene complex suppresses the desired reaction. We thus developed an alternate strategy to introduce the longer alkyl chains bearing β-hydrogen atoms that involved a Negishi coupling of the isolated 1-iodoalkenylboronate **5** and alkylzinc reagents.[26]

We investigated the Negishi coupling reactions of **5** with alkylzinc iodides under several reaction conditions. PEPPSI,[27] recently introduced by Organ and co-workers, displayed the necessary catalytic activity in THF and afforded 1,2,2-trialkylated alkenylboronate **6a** in 42% yield (based on GC analysis), albeit along with a considerable amount (>15%) of the undesired protodeiodinated product **2a**. We found that [PdCl$_2$(dppf)][28] was the best catalyst and afforded **6a** in 60% yield (based on GC analysis).[29] Solvent and additive effects greatly influenced the yield of the reaction; DMI as a solvent with NEt$_3$ as an additive (7:1) furnished **6a** in 75% yield (based on GC analysis, 69% yield of isolated product; Scheme 3).[30] The *n*-dodecyl analogue **6b** was synthesized under identical conditions and was isolated in 57% yield (Scheme 3). Notably, the reaction is highly stereoselective (> 99:1 as determined by ^{1}H NMR spectroscopy) because isomerization during Negishi cross-coupling was suppressed and resulted in retention of configuration. During the reactions, the boron moieties remained intact.[31]



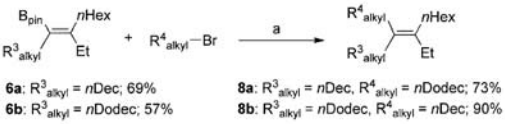
Scheme 3. Reagents and conditions: a) **5** (1 mmol), alkylzinc reagents (1.5 mmol), [PdCl$_2$(dppf)] (4.5 mol%), DMI/NEt$_3$ (7:1), 60 °C, 12 h. DMI = 1,3-dimethyl-2-imidazolidinone, dppf = 1,1′-bis(diphenylphosphanyl)ferrocene.

Our route to the tetraalkylated olefin **7** bearing four different substituents involved the aforementioned Suzuki–Miyaura cross-coupling reaction of **4** and 1-bromopropane (Scheme 4). Compound **7** is the first example of a regio- and stereocontrolled tetrasubstituted olefin that contains four different linear unfunctionalized alkyl groups.[32]



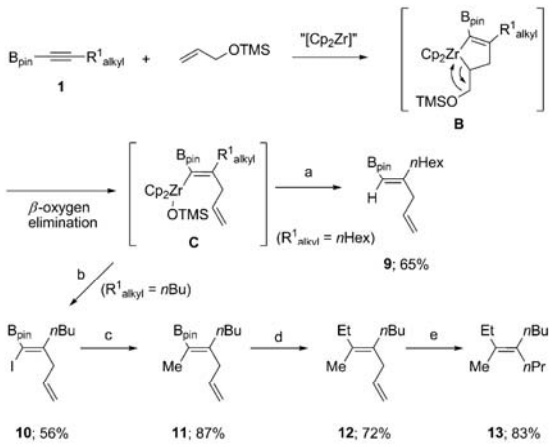
Scheme 4. Reagents and conditions: a) **4** (1 mmol), 1-bromopropane (1.3 mmol), KOH (3 mmol), [Pd(dba)$_2$] (5 mol%), [HP*t*Bu$_2$Me]BF$_4$ (15 mol%), THF, 20 °C, 24 h.

In the same manner the 1,2,2-trialkylated alkenylboronates **6a** and **6b** were subjected to Suzuki–Miyaura coupling with 1-bromoalkanes and afforded tetraalkylated olefins **8a** and **8b** as the pure stereoisomer in 73% and 90% yields, respectively, (Scheme 5).[33] The two reactions, thus, complement each other and provide access to various tetrasubstituted olefins, in which all alkyl groups contain β-hydrogen atoms.



Scheme 5. Reagents and conditions: a) **6** (0.5 mmol), 1-bromoalkanes (0.78 mmol), KOH (1.8 mmol), [Pd(dba)$_2$] (5 mol%), [HP*t*Bu$_2$Me]BF$_4$ (15 mol%), THF, 20 °C, 24 h.

To achieve the introduction of hydrocarbon functionalities other than ethyl, we chose a zircono/allylation approach,[34] as summarized in Scheme 6. Srebnik and co-workers have reported that the phosphine-stabilized boryl-zirconacyclopropene species were formed by the reactions of 1-alkynylboronates **1** with the Negishi reagent in the presence of tributylphosphine.[35] The added allyloxytrimethylsilane rapidly reacted with the intermediate zirconacyclopropenes to form the zirconacyclopentene **B** in a regioselective manner with the boron moiety at the α position. The spontaneous β-oxygen elimination resulted in the formation of a transient alkenylzirconocene intermediate **C**. Hydrolysis of the remain-



Scheme 6. Regio- and stereoselective synthesis of the tri- and tetrasubstituted alkenylboronates **9**–**11** and the cross-coupled tetra-substituted olefins **12** and **13**. Reagents and conditions: a) $[Cp_2ZrCl_2]$ (1.2 equiv), *n*BuLi (2.4 equiv), tributylphosphine (1.2 equiv), −78 °C to RT, 1 h; then **1a** (1.0 equiv), allyloxytrimethylsilane (1.5 equiv), 50 °C, 1 h; then hydrolysis; b) $[Cp_2ZrCl_2]$ (1.2 equiv), Mg (3.0 equiv), **1c** (1.2 equiv), allyloxytrimethylsilane (1.0 equiv), 50 °C, 1 h; then I_2 (2.0 equiv), RT, 12 h; c) $ZnBr_2$ (1.65 equiv), MeMgBr (1.35 equiv), THF, 0 °C, 30 min; then **10** (1.0 equiv), $[Pd(PPh_3)_4]$ (2 mol%), RT, 18 h; d) **11** (1.0 equiv), bromoethane (1.3 mmol), KOH (3 mmol), $[Pd(dba)_2]$ (5 mol%), $[HPtBu_2Me]BF_4$ (15 mol%), THF, 20 °C, 12 h; e) $[RhCl(PPh_3)_3]$ (10 mol%), H_2, benzene, RT, 18 h. TMS = trimethylsilyl.

ing Zr–C bond delivered the trisubstituted alkenylboronate **9** in 65% yield. Again, the regioselectivity of **9** was determined by ^{1}H NMR spectroscopy. As can be seen in the ^{1}H NMR spectra the presence of a triplet in the double bond region (around 5.14 ppm) is indicative of the vinyl hydrogen atom that is located at the α position with respect to the boryl groups.

1-Iodo-1-alkenylboronate **10** was then synthesized from **1** using allyloxytrimethylsilane by initial zirconacycle formation with $[Cp_2ZrCl_2]$/Mg,[36] and subsequent iodonolysis in 56% yield. The palladium-catalyzed alkylation[37] with MeZnBr in the presence of 2 mol% of $[Pd(PPh_3)_4]$ in THF afforded the methylated alkenylboronate **11** in 87% yield with >99% isomeric purity.[38] Compound **11** was subjected to the palladium-catalyzed Suzuki–Miyaura coupling with bromoethane and afforded **12** in 72% yield.[39] Finally a chemoselective catalytic hydrogenation of **12** with 10 mol% of Wilkinson's catalyst was performed to deliver **13**, a structural isomer of **7**, in >99% isomeric purity and 83% yield.

In summary, we have developed a versatile, direct synthesis of multialkylated olefins bearing various alkyl groups by a regioselective formation of zirconacyclopentene species using alkynylboronates followed by successive palladium-catalyzed Negishi and Suzuki–Miyaura cross-coupling reactions. This method is practical and simple, and more importantly, provides the products as single isomers (selectivity >99%). Furthermore, the addition of β-hydrogen-containing alkyl electrophiles to alkenylboronates and the reaction of 1-iodo-1-borylethenes with alkylzinc reagents expands the cross-coupling repertoire. Further studies to develop a cross-coupling with secondary alkyl functionalities and the application of this approach to the synthesis of natural products will be the subject of forthcoming papers.

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Keywords: cross-coupling · Negishi coupling · palladium · Suzuki–Miyaura coupling · zirconacycles

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Review

Alkynylboron compounds in organic synthesis

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ABSTRACT

Alkynylboron compounds, consisting of alkynyl and boron moieties, can be categorized according to the substituents on the boron atom, such as alkynylboranes, -boronates, and -borates. In this review, the synthesis and reactions of alkynylboron compounds are systematically introduced. Alkynylpinacolatoboranes and alkynyltrifluoroborates are the most widely utilized classes in organic reactions, owing to their stability and ease of handling. Other alkynylboron compounds have also been developed as convenient substrates for various organic reactions. Thanks to the dedication of many chemists in this field, great advances of facile synthesis and wide utilization of alkynylboron compounds have been made with these versatile building blocks for diverse structures in organic synthesis.

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1. Introduction

The organic chemistry of organoboron compounds has been widely developed because these compounds are readily available, water-stable, and non-toxic; and the inorganic by-products are easily separable after the reactions. Although the research of organoboron compounds bearing sp^2 and sp^3 carbon–boron bonds has been extensively studied [1], the organoboron compounds bearing the sp carbon–boron bonds have received less attention. The utility of alkynylboron compounds in organic synthesis began to be investigated in the 1970s when they were found to be useful, diversified synthetic intermediates. Brown et al. in 1987, succeeded in establishing the most reliable synthetic method of 1-alkynylboronates simply by lithiation of terminal alkynes and subsequent treatment with triisopropylborate [2,3]. Because of the feature of facile conversion of the boron moiety into other

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functional groups [4], alkynylboron compounds proved to be versatile candidates in a series of classical reactions, e.g., coupling, addition, and cycloaddition reactions. Moreover, since alkynylboron compounds bear both alkynyl and boron moieties, when alkynylboron compounds are subjected to organic reactions, they show additional, unique reactivities that neither typical alkynes nor other organoboron compounds possess. In the past two decades, studies on alkynylboron compounds in various organic reactions have been diligently elucidated. This paper reviews studies on the synthesis of various alkynylboron compounds and their applications to a number of organic reactions.

2. Synthesis of alkynylboron compounds

2.1. Alkynyldialkylboranes

The synthesis of alkynyldialkylboranes, one of the earliest classes of alkynylboron compounds used in organic reactions, was systematically described by Brown. *B*-1-alkynyl-9-BBN·THF complexes **1** were synthesized from the reaction of lithium acetylides with *B*-MeO-9-BBN and the subsequent treatment with boron trifluoride diethyl etherate at −78 °C (Scheme 1) [5].

These reactions yielded stable crystalline solids which have been stored at room temperature for up to one year. Later, Yamaguchi [6] utilized **1** for the synthesis of alkynyl ketones, and Singleton [7] used compound **1** for [4 + 2] cycloaddition reactions. Soderquist et al. synthesized the stable complexes **1** [8], which have been used in Suzuki–Miyaura couplings as well as cycloaddition reactions [9].

2.2. Alkynyldihaloboranes

Compared with the aforementioned alkynyldialkylboranes, halogenated alkynylboranes would be expected to be more highly reactive dienophiles in cycloaddition reactions. Therefore, Singleton employed alkynyltributylstannanes as versatile precursors to synthesize alkynyldihaloboranes **2** via boron-tin exchange with BCl_3 and BBr_3 (Scheme 2) [10].

In addition, to avoid the toxic tin reagents, the analogous alkynyldihaloboranes were also obtained by transmetalation of alkynylsilanes through boron-silicon exchange [11]. Furthermore, Kabalka et al. succeeded in the preparation of alkynyldichloroboranes by the in situ treatment of terminal alkynes with ^{n}BuLi, followed by addition of boron trichloride at 0 °C [12]. Compared with previous work, this facile synthesis was a novel method for the efficient generation of alkynyldihaloboranes.

Frohn also described the preparation of a series of alkynyldifluoroboranes, $RC{\equiv}CBF_2$ bearing a variety of alkyl and perfluoroorganic groups [13]. Fluoride was abstracted from K $[RC{\equiv}CBF_3]$ salts using BF_3 in suitable solvents (dichloromethane, 1,1,1,3,3-pentafluoropropane, or -butane) to afford the corresponding alkynyldifluoroborane. The yields were determined by the ^{19}F NMR spectra due to their moisture sensitivity, strong Lewis acidity, and instability at ambient temperature.

2.3. Alkynylboramides

An earlier synthetic method for alkynylboramides was reported by Nöth [14]. Bis[(dialkylamino)(phenylethynyl)boryl]methanes were obtained in good yields by the reaction of lithium phenylacetylide with bis[(dialkylamino)chloroboryl]methane. Similarly, Mortier et al. later prepared bis(diisopropylamino)boracetylene as an intermediate for the synthesis of a series of terminal alkynes [15]. They used chlorobis(diisopropylamino)borane and lithium acetylide to synthesize the desired alkynyldiaminoborane, which was further subjected to lithiation and a successive trap with electrophiles to furnish the corresponding air-sensitive alkynyldiaminoboranes.

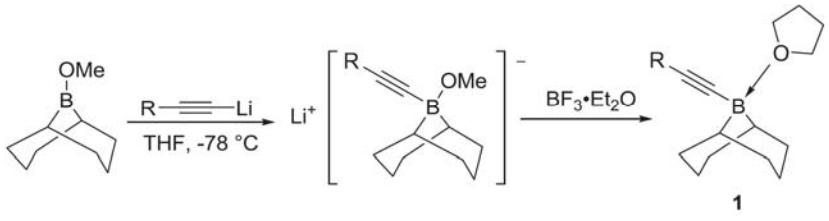
A recent example of the synthesis of alkynylboramides was reported by Gandon [16]. Compound **3** was prepared from alkynylboronate by pinacol/naphthalene-1,8-diamine exchange in toluene under reflux (Scheme 3). This approach provided the desired alkynylboramide quantitatively after conventional flash chromatography on silica gel without special precautions.

2.4. Alkynylboronates

Alkynylboronates, owing to their stability, moderate reactivity, and ease of handling, have been the most widely used among all the alkynylboron compounds. Based on their previous studies in the synthesis of alkyldiisopropylborates **4** [17], Brown et al. have successfully expanded the high-yield synthesis of 1-alkynylboronates with a wide range of substituents in the acetylenic moiety [2,3]. This simple and general synthetic method, starting from alkynyllithium, triisopropylborate, and hydrogen chloride in diethyl ether, is regarded as one of the most facile pathways for alkynylboronates **4** (Scheme 4).

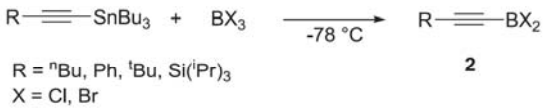
Similarly, a procedure for the synthesis of a difunctionalized alkynylboronate **5** was discovered by Brown and Srebnik (Scheme 5) [3], in which dilithioacetylide was generated from trichloroethylene and 3 equivalents of ^{n}BuLi. Reaction of the in situ formed dilithioacetylide with 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, followed by treatment with anhydrous HCl, cleanly afforded **5** in 77% yield, which exhibited high solubility in basic water and virtually all organic solvents.

The synthesis of ethynyl *N*-methyliminodiacetic acid (MIDA) boronate as a newly developed building block was reported by Burke in 2010 [18]. This compound has a wide range of favorable



R = Et, ^{n}Bu, ^{t}Bu, ^{n}Hex, Ph, 3-chloro-^{n}Pr

Scheme 1.



Scheme 2.

chemical and physical properties; it is especially air-stable, monomeric, highly soluble, and compatible with chromatography on silica gel.

2.5. Alkynylborates

Like alkynylboronates, alkynylborates are also useful synthetic intermediates for carbon–carbon bond formation [7,8,19]. In 2000, Deng reported the easy preparation of lithium 1-alkynyl(trialkoxy) borates, which were directly used for allylation reactions without any purification [20].

Potassium alkynyltrifluoroborates are another class of alkynylborates; they are more nucleophilic than the corresponding neutral alkynylboron compounds, and they are air- and moisture-stable in their crystalline solid states. The first report of potassium alkynyltrifluoroborates **6** was provided by Genêt et al. as shown in Scheme 6 [21–23]. The treatment of the in situ formed alkynylborates **7** with KHF_2 provided an efficient and versatile procedure for the synthesis of **6**. Moreover, analogous alkynyltrifluoroborates bearing tetraethyl ammonium as a counter ion were readily prepared via cation exchange from potassium alkynyltrifluoroborates [24].

Murakami has reported the preparation of alkynyltrialkylborates by the reaction of *B*-Ph-9-BBN with 1-butynyllithium and subsequent cation exchange with tetramethyl ammonium chloride in methanol. This process provided white precipitates, which were stable to air and moisture, and therefore storable without any decomposition for several months [25].

3. Reactions of alkynylboron compounds

3.1. Cycloaddition reactions

Diels–Alder reactions of alkynylboron compounds utilized were reported in 1992 by Singleton et al. [7]. Initially, it was described that the effective dienophile (trimethylsilyl)ethynyl-9-BBN (**8**) reacted with acyclic dienes at 100 °C to afford the corresponding 1,4-cyclohexadienes **9** with high regioselectivity (Scheme 7).

Subsequently, Singleton reported Diels–Alder reactions of 1,3-dienes and alkynyldihaloboranes, which were readily generated in situ from boron-tin or boron-silane exchange reaction of BCl_3 or BBr_3 with alkynylstannanes or -silanes, respectively, [10,11]. Although the preferable explanation involves that these [4 + 2] cycloaddition reactions of alkynyldihaloboranes as dienophiles proceed through a concerted process in hexane, a stepwise ionic process, attributed to the novel reactivity and regioselectivity associated with the formal 1,4-alkynylboration of dienes, was believed to be plausible in CH_2Cl_2.

Later, Goodman investigated the cycloaddition mechanism of a series of alkynylboranes with butadiene using density functional theory (DFT) calculations (Scheme 8) [26]. A transition structure for both the concerted [4 + 2] process (**TS-A**) and the process to form enynes **10** via 1,4-alkynylboration (**TS-C**) have been observed in cycloaddition. Calculations suggested the presence of a stepwise process in another reaction pathway for the cycloaddition through zwitterionic **11** with strong [4 + 3] character (**TS-B**).

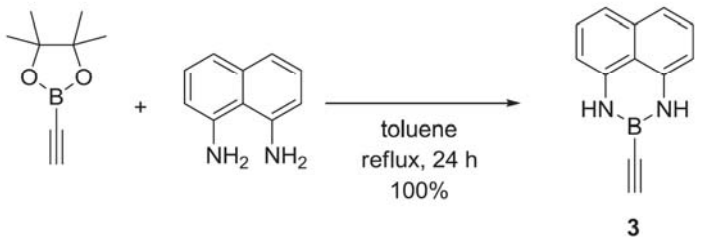
Furthermore, metal-free routes to cyclic compounds using alkynylboronates were ultimately exploited for the synthesis of functionalized aromatic boron compounds to obviate the requirement of transition metals [27,28]. Cycloaddition reactions of tetrazine with alkynylboronates were examined, as shown in Scheme 9 [29,30], and the mechanism via kinetic experiments as well as DFT studies revealed that this reaction proceeds via a concerted pathway [31].

Regioselective cycloaddition reactions of alkynylboronates with nitrile oxides [32], 1,4-oxazin-2-ones and 2-pyrazinones [33], 2-pyrone [28,34], and syndnones [35] for the preparation of various heteroaryl- and arylboronates are illustrated in Scheme 10. Additionally, these organoboron compounds were found to undergo Pd-catalyzed cross-coupling reactions with various aryl and allyl halides.

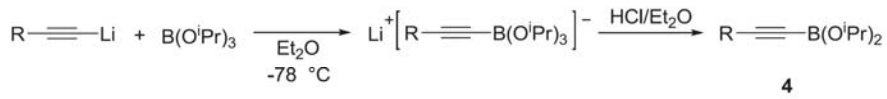
3.2. Transition-metal-mediated or -catalyzed cyclization reactions

Alkynylboron compounds have been employed as practical and versatile precursors for a variety of π-conjugated organic compounds. Unlike conventional methods to synthesize (hetero) arylboronic acids and their esters via carbon–boron bond formation, these new synthetic protocols for (hetero)arylboron compounds from cycloaddition of alkynylboron compounds have been embarked upon as an attractive program, because the regioselective [4 + 2] cycloaddition reactions of alkynylboron compounds were initially studied. In 2001, Harrity et al. described the synthesis of a novel class of quinone boronic esters **12** prepared by a highly regioselective Dötz annulation of Fischer carbene complexes **13** [36,37] with alkynylboronates (Scheme 11) [38].

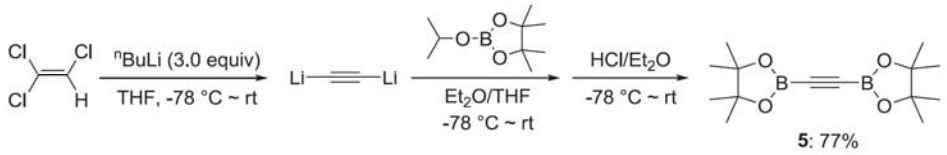
In sharp contrast to alkynylboranes, alkynylboronates rarely undergo thermal cycloaddition reactions due to their low reactivity. In 2003, however, Hilt reported the first cobalt-catalyzed [4 + 2] cycloaddition reaction. It was reported that the reaction of alkynylboronates with isoprene gave rise to cycloadducts regioselectively (>95:<5) using [$CoBr_2$(dppe)] as an efficient catalyst with the assistance of Zn or ZnI_2, generating the corresponding 1-boryl-



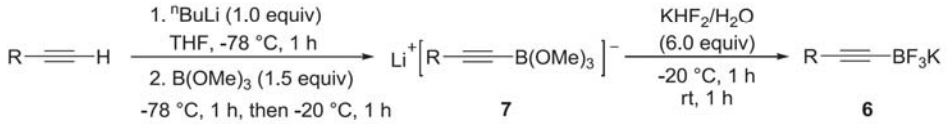
Scheme 3.



Scheme 4.



Scheme 5.

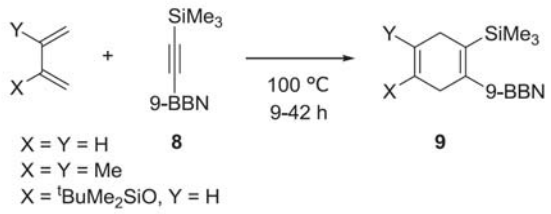


Scheme 6.

1,4-cyclohexadienes **14** under mild conditions (Scheme 12) [39]. Subsequent Suzuki–Miyaura cross-coupling reactions afforded the formation of new carbon–carbon bonds.

Other examples exhibited cobalt-catalyzed [4 + 2] cycloaddition and the ensuing palladium-catalyzed Suzuki–Miyaura couplings furnished tricyclic heterocycles [40] and regioselective synthesis of substituted phenanthrene and phenanthridine derivatives [41]. Since the dihydroaromatic compounds can be useful synthetic platforms for the generation of aromatics by oxidation, this method can be used as a fast, efficient, and diversity-directed synthesis of the functionalized benzene derivatives.

In addition, Yamamoto et al. described the ruthenium-catalyzed cyclotrimerization of alkynylboronates, propargyl alcohol, and terminal alkynes, giving rise to the regioselective formation of arylboronates **15**, which were subjected to one-pot Suzuki–Miyaura coupling to afford highly substituted biaryls as single regioisomers (Scheme 13) [42,43]. The synthetic methodology of arylboronates was extended to the ruthenium-catalyzed cycloaddition of alkynylboronates in the presence of a Ru(I) catalyst (5–10 mol%); 1,6- and 1,7-diynes were allowed to react with an ethynylboronate at ambient temperature to give rise to bicyclic arylboronates in moderate to excellent isolated yields [44].



Scheme 7.

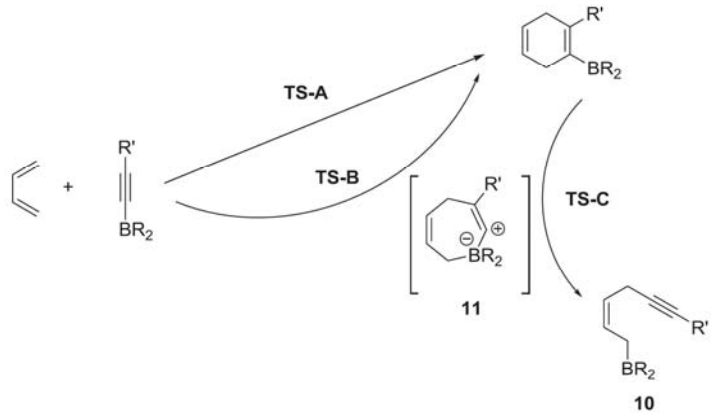
Recently, Gandon reported the rhodium-catalyzed [2 + 2 + 2] cycloaddition of alkynylboronates and alkynyldiaminoboranes, followed by chemoselective Suzuki–Miyaura cross-coupling reactions with aryl halides toward the boronate moiety to produce biaryls (Scheme 14). After an acidic work-up, a second Suzuki–Miyaura coupling to introduce another aryl group was investigated, affording the corresponding terphenyls [16].

3.3. Zirconocene-mediated reactions

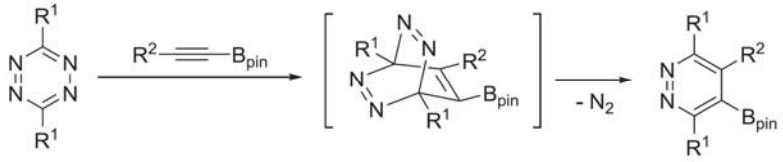
The use of alkynylboron compounds in zirconium chemistry was initially conducted by Srebnik's group for the synthesis of (*Z*)-1-alkenylboronates, which cannot be obtained directly by hydroboration of terminal alkynes due to the *syn* addition of hydroboranes to the carbon–carbon triple bond [45]. The hydrozirconation of alkynylboronates with $Cp_2Zr(H)Cl$ (Schwartz's reagent) gave the regioselective formation of 1,1-dimetallic compounds **16**; these were subsequently treated with CuBr to form the homo-coupled products **17** in good yields (62–67%) even for the hindered alkyne (R = ^{t}Bu) (Scheme 15). $Cp_2Zr(^n Bu)_2$ (Negishi reagent)-mediated oxidative cyclization of 2 mol of alkynylboronates led to the formation of zirconacyclopentadiene, which upon hydrolysis, gave rise to regioisomers of 1,3-butadiene derivatives [46].

Later, Srebnik reported the synthesis of alkenylboronates by the reaction of Cp_2ZrEt_2 (Takahashi reagent) with alkynylboronates (Scheme 16) [47], in which the five-membered zirconacyclopentenes **18** were formed, as indicated by deuterium labeling. The formed zirconacyclopentenes reacted with aldehydes to form the seven-membered oxazirconacycloheptenes **19**. Hydrolysis of the latter provided 5-hydroxy-1-pentenylboronates in good isolated yields.

Moreover, substituted alkenylboronates were also synthesized using the stabilized borylated zirconacyclopropenes from alkynylboronates with $Cp_2Zr(^n Bu)_2$ (Negishi reagent) in the presence of the Bu_3P ligand (Scheme 17) [48]. Aldehydes and ketones successfully reacted with the stabilized zirconacyclopropenes **20** to



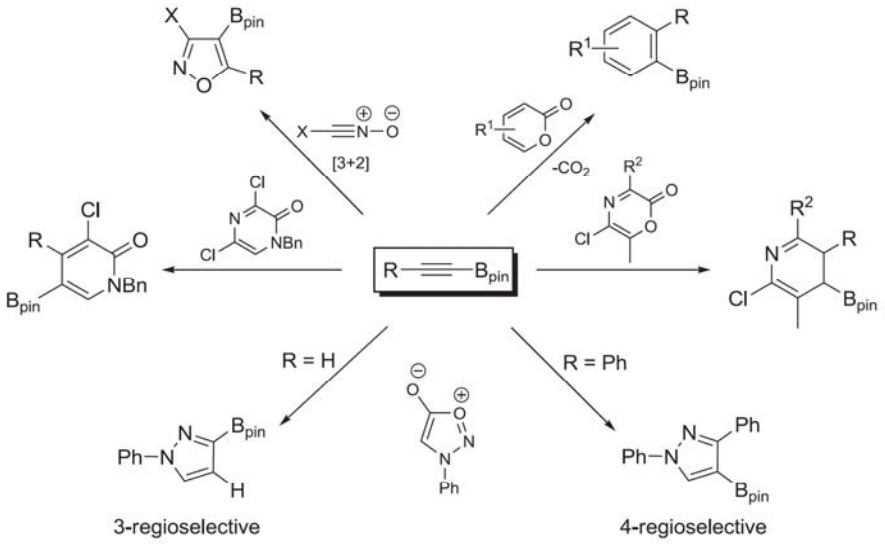
Scheme 8.



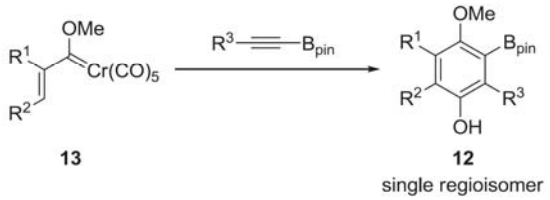
Scheme 9.

generate oxazirconacyclopentenes, which were quenched by HCl/Et_2O to provide 3-hydroxy-1-alkenylboronates **21**. Various alkynes also reacted with zirconacyclopropenes to give 2-boryl-1,3-butadienes **22** in 40–81% isolated yields, accompanied by 1-boryl-1,3-butadienes **23** when terminal alkynes were employed (R^5 = H) [49].

Building upon pioneering work by Srebnik to utilize zirconacycles in synthesizing alkenylboronates from alkynylboronates, the regio- and stereoselective synthesis of multi-substituted olefins through zirconacycle formation of alkynylboronates were also demonstrated. In 2007, a versatile and direct synthesis of tetrasubstituted olefins was developed by a regioselective formation



Scheme 10.



Scheme 11.

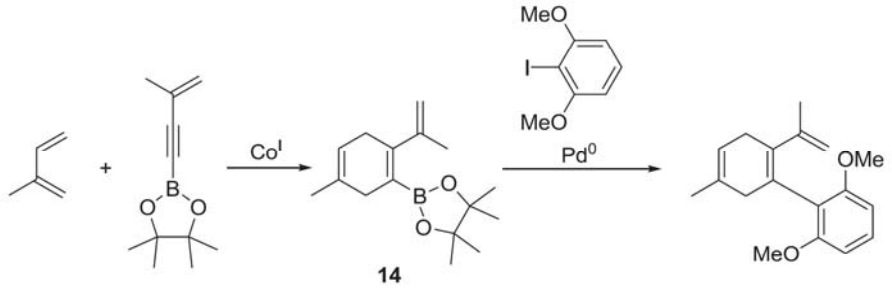
of zirconacyclopentenes **24** from alkynylboronates, followed by a series of functionalizations, and Cu/Pd-cocatalyzed arylation with various aryl iodides (Scheme 18) [50].

Very recently, an unprecedented synthetic method was developed to synthesize tetra-alkylated olefins **25** via regioselective formation of zirconacyclopentenes starting from alkynylboronates, followed by sequential palladium-catalyzed Negishi and Suzuki-Miyaura cross-coupling reactions (Scheme 19) [51]. Gratifyingly, the β-hydrogen-containing alkyl electrophiles were tolerated in the couplings, in which β-hydrogen elimination could be suppressed after optimization of the reaction conditions using the bulky, electron-rich phosphine ligand on the Pd catalyst.

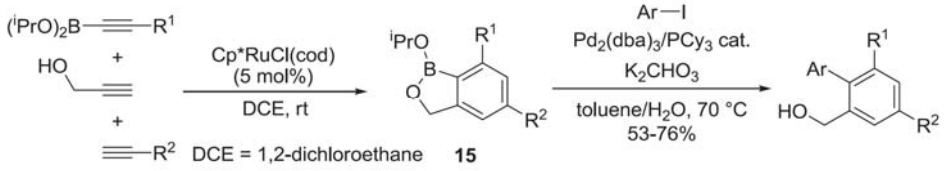
3.4. Coupling reactions

Coupling reactions of alkynylboron compounds can also be an efficient synthetic method for transformation of the boron moiety into various functional groups. In 1983, Yamaguchi et al. reported a novel method for the synthesis of 1,3-ynones **26** from alkynylboranes and amides under mild reaction conditions (Scheme 20) [6].

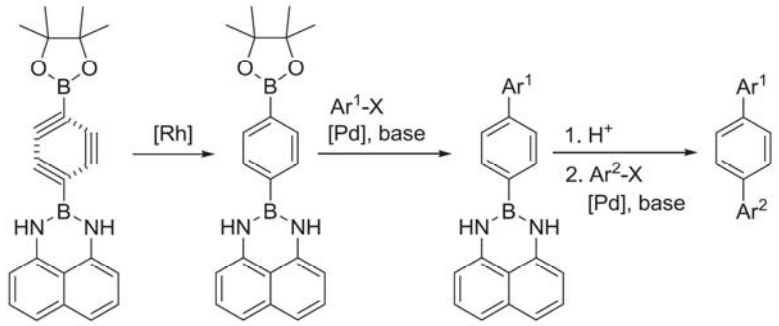
Oh et al. also found an efficient synthetic pathway of conjugate ynones from lithium alkynyltriisopropylborates with acid chlorides cocatalyzed by palladium and copper under mild and neutral conditions [52]. Recently reported, was a very economic synthesis of 1,3-ynones by the cross-coupling reactions of acid chlorides with alkynylboronates in the presence of CuCl, which took place in aprotic polar solvents such as DMI under Pd-free and neutral conditions [53]. In 2005, copper-mediated homo-coupling reactions of alkynylboronates were found to generate the corresponding 1,3-diynes [54]. Similarly, synthesis of 1,3-diynes was



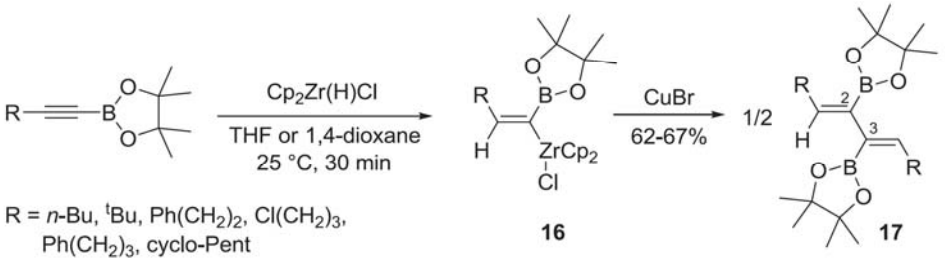
Scheme 12.



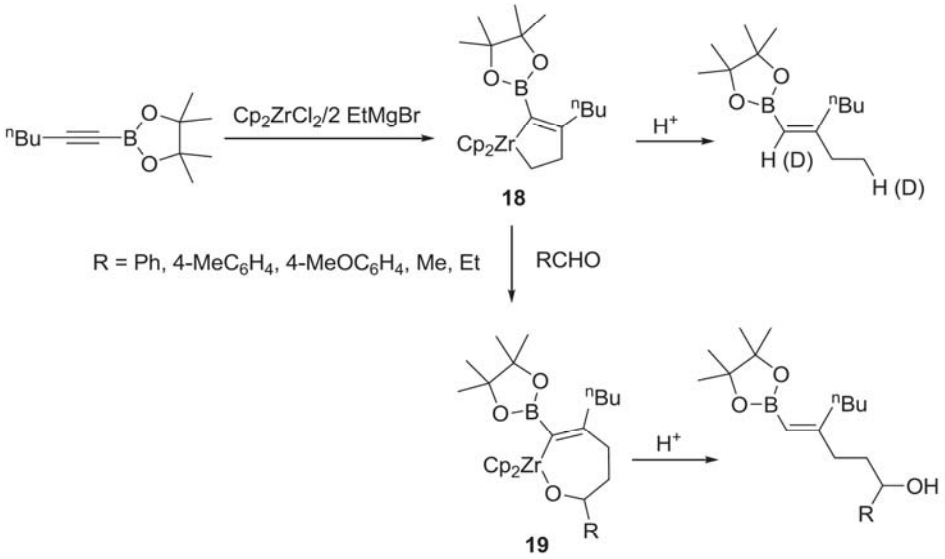
Scheme 13.



Scheme 14.



Scheme 15.



Scheme 16.

completed through the copper-catalyzed homo-coupling of alkynyltrifluoroborates in DMSO in good yields [55].

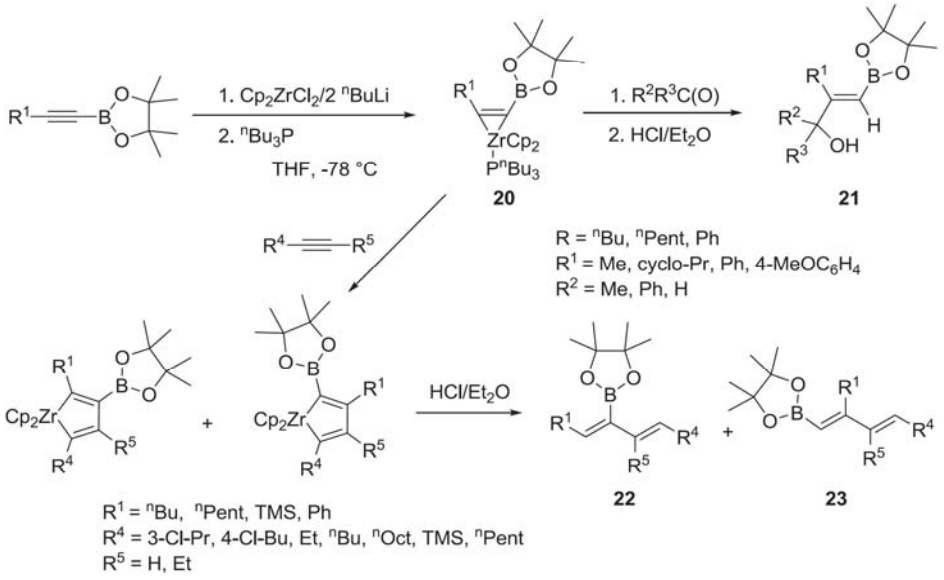
The first cross-coupling reactions of alkynylborates with 1,3-disubstituted allyl carbonates were studied by Deng et al. It was found that the nickel complex readily catalyzed the substrate-controlled reaction with high regioselectivity, giving the coupled products **27** in good to excellent yields (Scheme 21) [20]. The asymmetric variants of alkynylborates and allyl carbonate enantioselectively produced the desired product with only 13% ee.

Soderquist observed that Suzuki–Miyaura couplings of alkynylborates with aryl and vinyl bromides efficiently produced arylethynes [8], and the stereodefined conjugate enynes [9], respectively. Colobert reported efficient Suzuki–Miyaura coupling reactions – lithium alkynyltrimethylborates generated in situ from terminal alkynes were reacted with various aryl chlorides in the presence of $Pd_2(dba)_3$ combined with the sterically hindered *N*-heterocyclic carbene ligand [56]. In these reactions, aryl chlorides gave the corresponding arylethynes in good to excellent yields. Kabalka has focused on alkynyldihaloborane chemistry for many years [57–60], since these compounds were readily synthesized by the boron-tin exchange reported by Singleton [10]. Alkynyldichloroboranes are easily generated by the sequential treatment of terminal alkynes with ^{n}BuLi, followed by boron trichloride at 0 °C. The reactions of alkynyldichloroboranes with benzylic, allylic, and propargylic alcohols provide an efficient route to secondary alkylethynes [12].

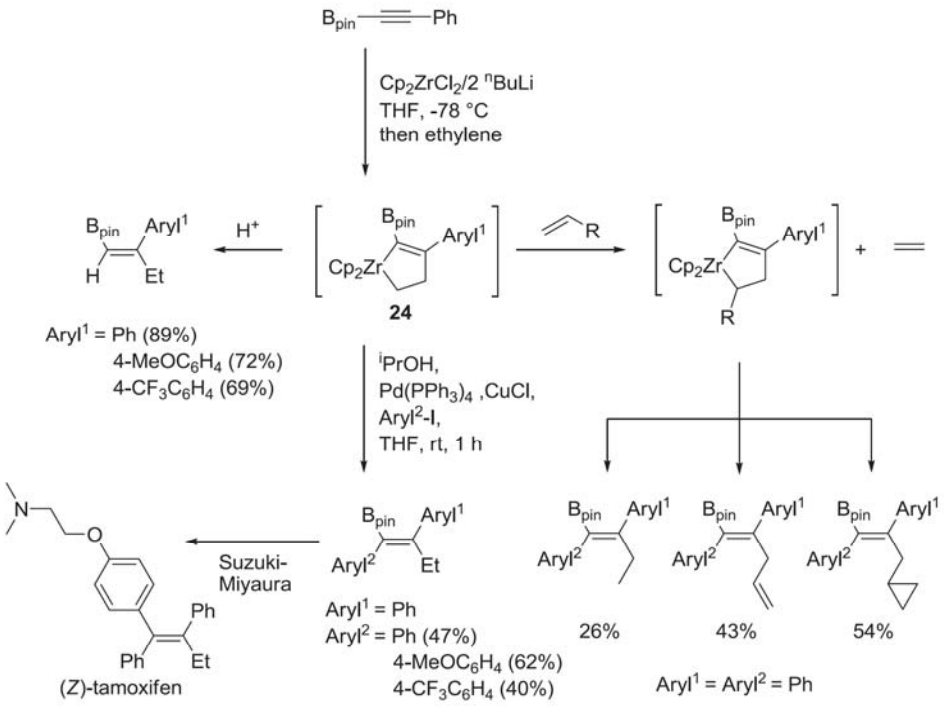
Alkynyl *N*-methyiminodiacetic acid (MIDA) boronates are newly developed alkynylboron compounds synthesized by Burke and are readily accessible and highly versatile acetylenic building blocks [18]. They showed inert reactivity toward cross-couplings under anhydrous conditions, but could be converted into the more reactive alkynylboronic acids by treatment with mild aqueous base. Ethynyl MIDA boronates were utilized for Sonogashira–Hagihara coupling and sequential Suzuki–Miyaura coupling, providing an efficient strategy to synthesize unsymmetrical diaryethynes **28** (Scheme 22).

3.5. Halodeboration

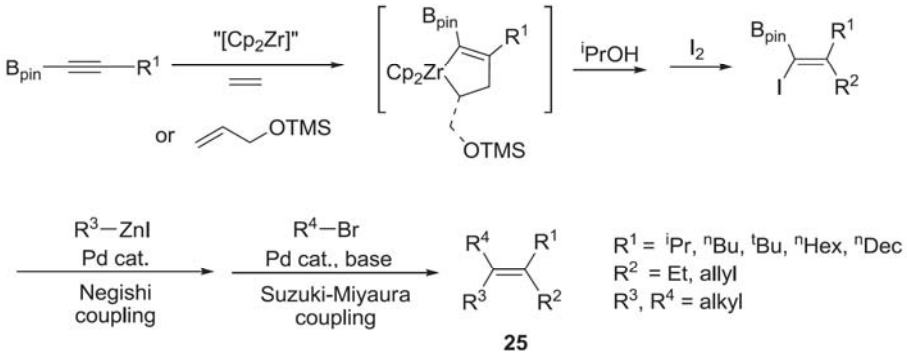
Kabalka also studied the halodeboration of alkynylborates, which were rapidly converted into the corresponding alkynyl bromides [61,62], iodides [63], as well as radio-labeled halides [64] such as ^{123}I and ^{76}Br under mild conditions (Scheme 23).



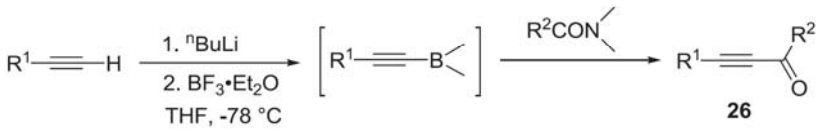
Scheme 17.



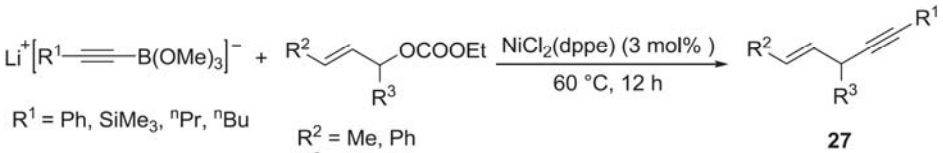
Scheme 18.



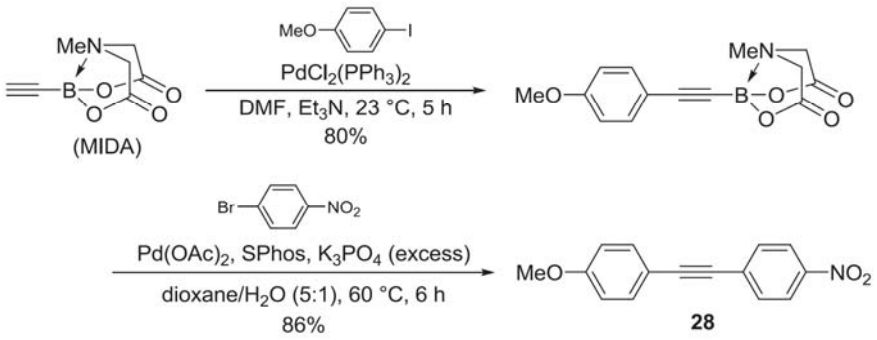
Scheme 19.



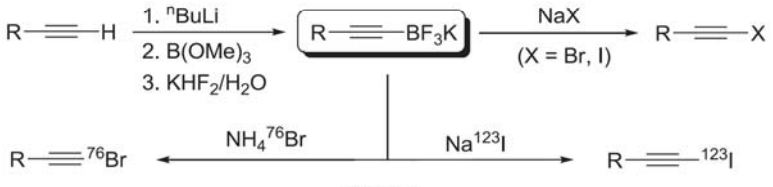
Scheme 20.



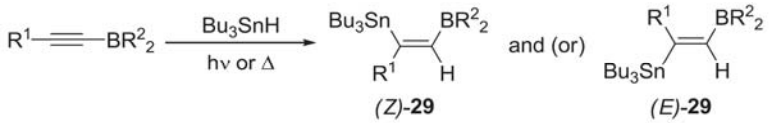
Scheme 21.



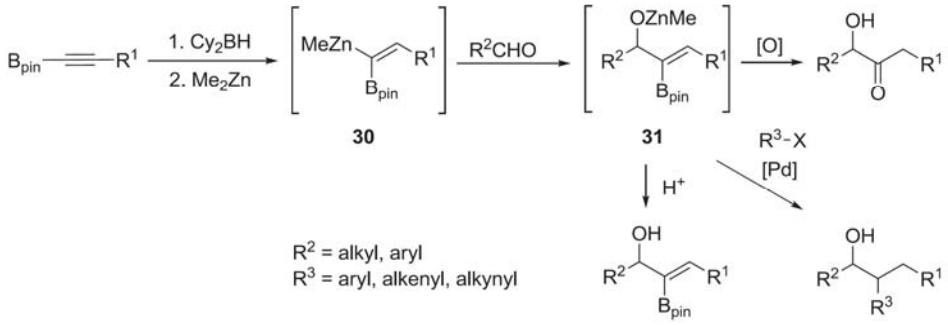
Scheme 22.



Scheme 23.



Scheme 24.



Scheme 25.

3.6. Addition reactions

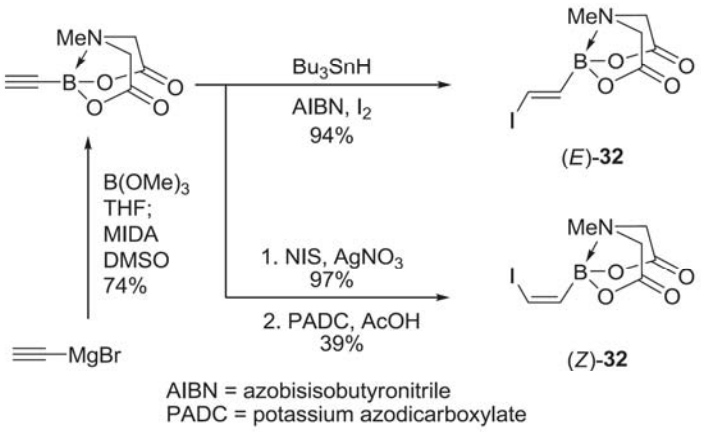
3.6.1. Synthesis of alkenylboron compounds through metalation

Addition reactions of alkynylboron compounds, as well as cycloaddition reactions, are another group of well-developed reactions. Using metalation across alkynylboron compounds, tri- and tetra-substituted olefins have been synthesized. Carboni reported efficient routes to tri-substituted olefins bearing both stannyl and boryl groups, in which a regio- and stereodefined addition of tributyltin hydride to alkynylboron compounds was observed (Scheme 24) [65]. Pure *Z* or *E* isomers **29** were prepared by carefully choosing the substituents on boron and the reaction conditions.

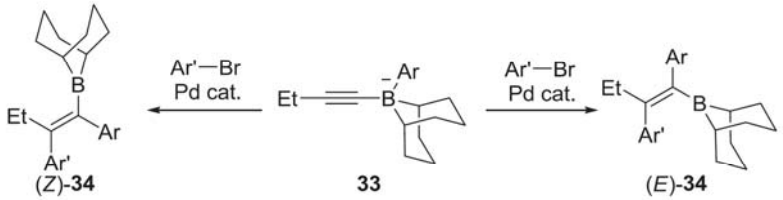
In 2002, Srebnik et al. described addition reactions for the synthesis of 1,1,2-triboronated alkenes in high yields through platinum(0)-catalyzed diboration of alkynylboronates with bis(pinacolato)diborane [66].

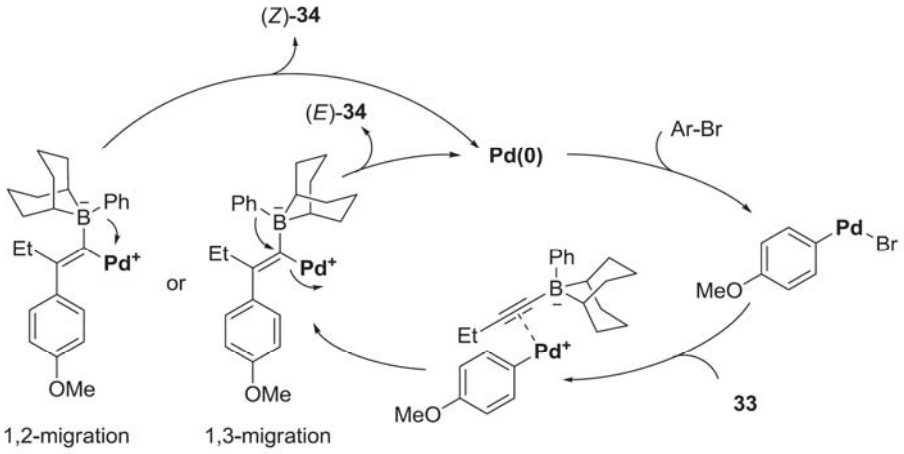
A practical and straightforward method for the generation of the versatile 1,1-heterobimetallic alkenes and their application to the construction of functionalized building blocks such as boronate-substituted allylic alcohols, α-hydroxy ketones, dienols, and α,β-unsaturated aldehydes has been outlined by Walsh et al. [67,68]. For instance, with the readily available alkynylboronates in hand, the regio- and stereoselective hydroboration of alkynylboronates with dicyclohexylborane generated 1,1-diborylated alkenes **30** as shown in Scheme 25 [69–71]. Subsequently, the Cy_2B group underwent the boron/zinc transmetalation with dimethylzinc to give **30**, which further added to aldehydes to generate the B_{pin} substituted *E*-allylic alkoxides **31**.

Molander also reported that hydroboration of alkynylboronates with Cy_2BH provided a facile protocol to synthesize (*Z*)-alkenylboronates [72], analogous to the synthetic method reported by Srebnik using hydrozirconation in 1994 [45]. Alkynylboronates were reported to be stereoselectively transformed to (*Z*)-alkenylboronates via hydroboration with dicyclohexylborane, followed by chemoselective protodeboronation with acetic acid. Treatment of the boronic acid pinacolate moiety with potassium hydrogen difluoride smoothly gave rise to the

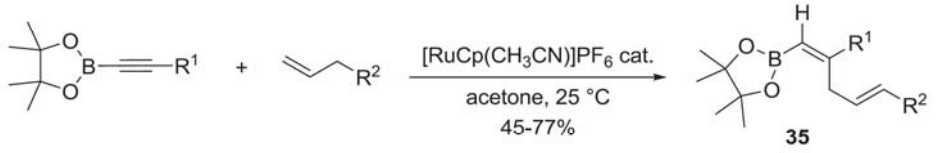


Scheme 26.

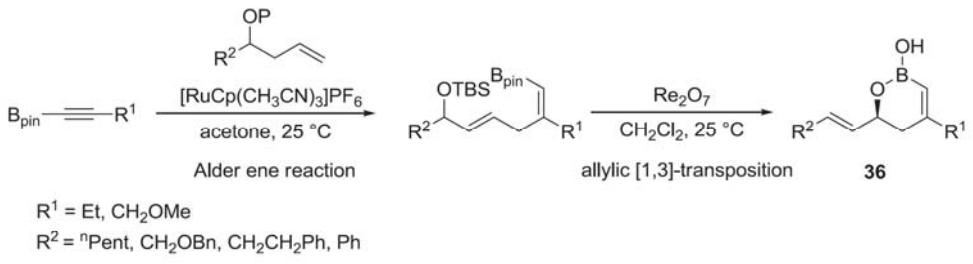




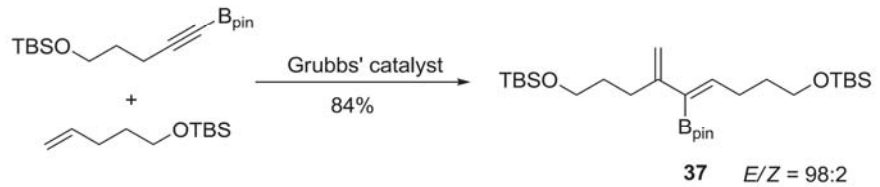
Scheme 27.



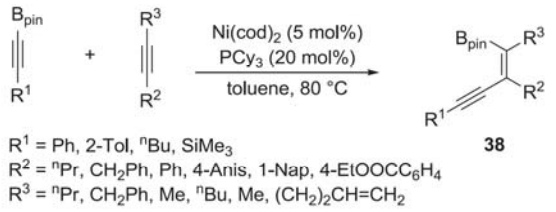
Scheme 28.



Scheme 29.



Scheme 30.



Scheme 31.

corresponding (*Z*)-alkenyltrifluoroborates, which are good candidates for stereospecific Suzuki–Miyaura coupling in nature product synthesis.

Recently, Burke described a series of metalation reactions of alkynyl MIDA boronates for the stereodefined synthesis of 2-iodoalkenyl MIDA boronates. Hydrostannation of an alkynylboronate, followed by iododestannylation in one-pot resulted in (*E*)-**32** (Scheme 26) [73]. Stereoselectively (*Z*)-**32** was obtained through a silver-promoted iodination, followed by PADC-mediated semireduction.

3.6.2. Addition with migration of the substituents on boron

Some addition reactions of anionic alkynylborates occur with substituted group migration. In 1988, Pelter noted an earlier example of a methyl group migration in the reactions of alkynyltrialkylborates; the alkynylborates reacted with various electrophiles at the β-position, leading to 1,2-migration of an alkyl group from boron to carbon to yield alkenylboranes [74].

Recently, Murakami et al. reported the stereodefined synthesis of (*Z*)- [75,76] and (*E*)-1,2-diarylated alkenylboranes [25,77] catalyzed by palladium through addition of the aryl group to alkynylborates **33** (Scheme 27). The preferable 1,3-migration of the aryl group took place to afford (Z)-**34**, when a less stereo-demanding ligand was used. Whereas, using a bulky bidentate ligand such as 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos), made 1,2-migration more favorably occur, to give (*E*)-**34**.

3.6.3. Ru-catalyzed reactions

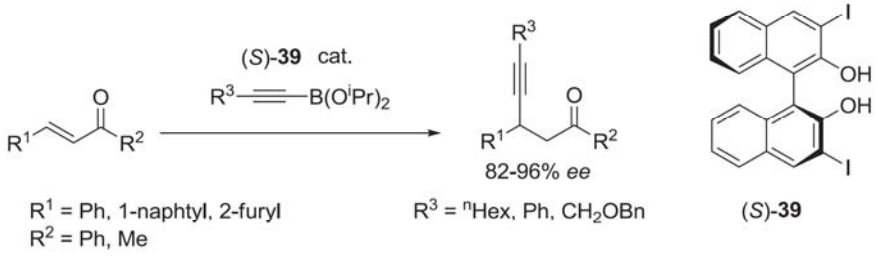
The stereocontrolled synthesis of alkenylboronates from addition reactions has been frequently studied in recent years, owing to prominent roles of alkynylboronates as versatile substrates in organic synthesis. A synthesis of β,β-disubstituted alkenylboronates **35** via the ruthenium-catalyzed Alder ene reaction [78–80] of alkynylboronates was developed by Lee (Scheme 28) [81]. The reaction displayed a strong directing effect of the boronate substituent to result in *trans* addition. This reaction has generality for a series of alkynylboronates and terminal alkenes to generate a variety of alkenylboronates. It is noteworthy that only branched isomers were obtained in all cases.

Lee also developed a highly efficient protocol to synthesize the functionalized alkenylboronates catalyzed by the cationic ruthenium complex, $[RuCp(CH_3CN)_3]PF_6$. After allylic [1,3]-transposition of the generated alkenylboronates, cyclic alkenylboronic acids **36** were formed with regiochemical control (Scheme 29) [82].

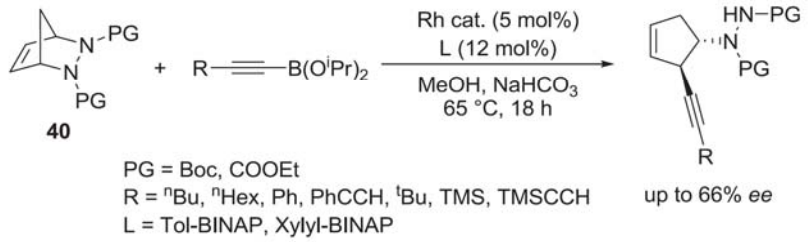
Also, synthesis of the functionalized alkenylboronates by regio- and stereoselective cross enyne metathesis [83–85] was demonstrated between alkynylboronates and terminal alkenes, based on the utilization of cross metathesis (CM) developed by Grubbs et al. [86–88]. Lee et al. demonstrated enyne CM to synthesize alkenylboronates **37** and found that high chemical yield and regioselectivity were achieved irrespective of substituents on the alkyne and alkene counterparts; whereas stereoselectivity was found to be largely dependent on the substituents in both alkynes and alkenes (Scheme 30) [71].

3.6.4. Alkynylation of unsaturated organic molecules

In 2006, Suginome et al. achieved the nickel-catalyzed regio- and stereoselective alkynylboration of internal alkynes via direct carbon–boron bond activation (Scheme 31) [89]. The boryl-substituted enynes **38** were reacted with aryl- and alkenyl halides



Scheme 32.



Scheme 33.

under Suzuki–Miyaura coupling conditions to give highly conjugated enynes in good yields.

Chong demonstrated asymmetric 1,4-addition of alkynylboronates across conjugate enones using catalytic amount of chiral binaphthol **39**, which proves that the use of catalytic amounts of chiral ligands on boron can promote asymmetric transformations (Scheme 32) [90].

Based on this, Goodman achieved the DFT study to explain that the high reactivity of alkynylboronates derived from binaphthol seemed to arise from electronic effects since its acidic boron atom binds tightly to the enone carbonyl and lowers the activation energy of the alkynylboration step [91].

A synthetically useful rhodium-catalyzed asymmetric alkynylation of bicyclic hydrazines **40**, a symmetrical strained alkene, was reported (Scheme 33) [92]. This protocol offered a straightforward regio- and stereoselective entry to valuable alkynyl cyclopentenic hydrazines. The definitive experimental evidence indicated transmetalation from alkynylboronates (or terminal alkynes) formed the intermediate alkynylrhodium(I) species.

4. Concluding remarks

In summary, alkynylboron compounds are versatile and synthetically valuable substrates in organic synthesis. This review has explored various organic reactions which use alkynylboron compounds to give rise to useful products or intermediates. The role of alkynylboron compounds in academic study can contribute to promising perspectives for industry toward the synthesis of functional materials and pharmaceuticals.

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Synthesis of Multisubstituted Olefins through Regio- and Stereoselective Silylborylation of an Alkynylboronate/ Chemoselective Cross-Coupling Sequences

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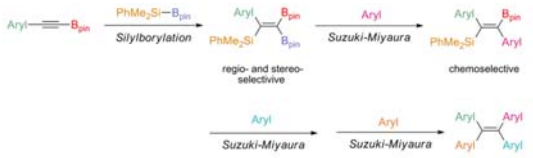
ABSTRACT



A highly regio- and stereoselective silylborylation of an alkynylboronate is disclosed. PhMe$_2$Si−B$_{pin}$ undergoes a Pd(OAc)$_2$/^{t}OctNC-catalyzed *syn*-addition to the alkynylboronate to yield 1-phenyl-1-silyl-2,2-diborylethene with high regioselectivity. The product 1-phenyl-1-silyl-2,2-diborylethene is then chemoselectively arylated by Suzuki−Miyaura coupling to afford (*Z*)-1-silyl-2-borylstilbene derivatives. This approach is extended to the synthesis of a tetraarylated olefin with four different substituents.

The regio- and stereodefined synthesis of multisubstituted olefins is one of the most challenging goals in synthetic organic chemistry. Owing to their interesting photophysical and redox properties, tetraarylethenes are interesting functional materials and their ring-substituted analogues are valuable synthetic targets in materials science.[1] Moreover, since the reported procedures are mainly limited to the preparation of symmetrical tetraarylethenes via homocoupling reactions of diaryldiazomethanes,[2] diaryldichloromethanes,[3] diaryl thioketones,[4] and diaryl ketones,[5] the development of a general method for the synthesis of unsymmetrically substituted tetraarylated olefins, preferably with four different aryl groups, has been a valuable target for organic chemists.[6]

We envisaged that a combination of transition-metal-catalyzed silylborylation[7−9] of unsymmetrical internal alkynes with cross-coupling reactions could provide a straightforward synthetic entry for various tetraarylethenes. However, silylborylation of unsymmetrical internal alkynes, e.g. 1-phenyl-1-propyne, was reported to decrease the regioselectivity obviously while the use of unsymmetrical diarylethynes[10] as the substrates is readily

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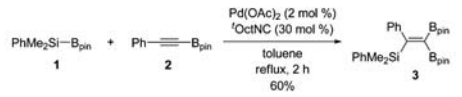
anticipated to form a mixture of the regioisomers, which limits a diversity of regio- and stereospecific silylborylated olefins.[7d]

In this communication, we report a novel synthetic protocol for the preparation of tetrasubstituted olefins, especially for tetraarylated analogues with four different aryl groups, using the palladium-catalyzed silylborylation of alkynylboronates,[11] to yield 1-phenyl-1-silyl-2,2-diborylated olefins with perfect regio- and stereoselectivities, followed by chemoselective Suzuki–Miyaura coupling[12] to deliver (*Z*)-1-silyl-2-borylstilbene motifs. Because the reagents are readily available and the operations are simple, this synthetic strategy proves more selective and tolerant than those previously reported.

According to a report in 1999,[7d] in the presence of the *in situ* generated palladium(0)–isonitrile complex, the reaction of the silylborane **1** with the alkynylboronate **2** took place in refluxing toluene (Scheme 1; B_{pin} is pinacolatoboryl). A catalytic amount of $Pd(OAc)_2$ (2 mol %) and 1,1,3,3-tetramethylbutyl isonitrile (^{t}OctNC) (30 mol %) efficiently gave rise to the silylborylation product **3** in 60% yield as a single isomer. However, the reaction did not proceed smoothly at lower temperatures with decreased yields being obtained (17% yield at 50 °C). $Pd(OAc)_2$ in conjunction with cyclohexyl isonitrile (CyNC) likewise gave a poor yield (19%). In addition, phosphine and phosphite ligands could not generate an efficient Pd catalyst for the reaction.

Scheme 1. Regio- and Stereoselective Silylborylation of **2**



The stereochemistry of the adduct **3** was confirmed by X-ray crystallographic analysis.[13,14] Thus, silylborylation was found to take place regio- and stereoselectively with the silyl moiety geminal to the phenyl group. Although the similar 1,1-diboryl-1-alkenes have been prepared by *gem*-diborylation of 1,1-dibromo-1-alkenes with ^{n}BuLi/bis(pinacolato)diboron[15] or ketone addition of tris(pinacolato)borylmethyllithium,[16] to the best of our knowledge, there are no known examples of the silylated 1,1-diboryl-1-alkenes, and they would be difficult to synthesize under basic conditions due to desilylation.

A possible catalytic cycle forming **3** is proposed to explain the observed regioselectivity. This proposed cycle is presented in Scheme 2. We propose that silylborane **1** oxidatively adds to the Pd(0) catalyst to generate the Pd(II) species **A**. Intermediate **A** then undergoes migratory insertion, wherein alkynylboronate **2** inserts into the Pd–B bond (borylpalladation) to form **B**. Although the borylpalladation mechanism has been proposed as the result of theoretical studies,[8c,17] another possibility, silylpalladation, cannot be neglected. This selectivity is opposite to that observed for the analogous process with organozirconium species.[18] Finally, the adduct **3** is produced by reductive elimination, regenerating the Pd catalyst.

Since functional materials, natural products, and bioactive pharmaceuticals have all been synthesized with 1,1-diborylated olefins,[19,20] to further test the utility of this building block, compound **3** was successively subjected to Suzuki–Miyaura coupling with an equimolar amount of

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(14) CCDC-643360 (**3**), -643361 (**5a**), and -643362 (**8**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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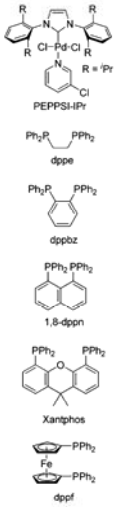
Table 1. Screening the Optimal Conditions of Chemoselective Suzuki–Miyaura Coupling[a]

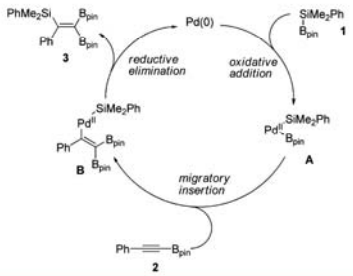
3 4a (Z)-5a (E)-5a

entry	Pd cat. (mol %)	ligand (mol %)	base	solvent	temp/°C	time/h	isolated yield/% (Z:E)[b]
1	$Pd(dba)_2$ (5)	$[HP^tBuMe_2]BF_4$ (20)	KOH	THF	rt	12	0
2	$Pd(PPh_3)_4$ (10)	--	KOH aq.	dioxane	70	12	24 (96:4)
3	$Pd(PPh_3)_4$ (20)	--	KOH aq.	THF	rt	12	38 (92:8)
4	PEPPSI-IPr (5)	--	KOH aq.	toluene	50	12	55 (92:8)
5	PEPPSI-IPr (10)	--	KOH aq.	THF	rt	3	59 (75:25)
6	Pd_2dba_3•$CHCl_3$ (5)	P^tBu_3 (20)	KOH aq.	THF	rt	3	76 (75:25)
7	Pd_2dba_3•$CHCl_3$ (5)	P^tBu_3 (20)	Cs_2CO_3 aq.	THF	rt	12	64 (92:8)
8	$PdCl_2(NCPh)$ (10)	dppe (20)	KOH aq.	THF	rt	12	60 (86:14)
9	$PdCl_2(NCPh)$ (10)	dppbz (20)	KOH aq.	THF	rt	12	27 (>99:1)
10	$PdCl_2(NCPh)$ (10)	1,8-dppn (20)	KOH aq.	THF	rt	12	64 (85:15)
11	$PdCl_2(NCPh)$ (10)	Xantphos (20)	KOH aq.	THF	rt	12	41 (86:14)
12	**$PdCl_2$(dppf) (5)**	**--**	**KOH aq.**	**THF**	**rt**	**3**	**85 (88:12)**

[a] Reaction conditions: **3** (0.1 mmol), **4a** (0.1 mmol), Pd cat./ligand, base (0.3 mmol), solvent (1 mL). [b] Isolated yield of the isomeric mixture, the *Z*:*E* ratios were determined by the ^1H NMR spectra.



Scheme 2. A Plausible Mechanism of Silylborylation of an Alkynylboronate **2**



iodobenzene (**4a**) to ascertain whether the first coupling would be chemoselective. Various palladium catalysts and ligands were tested, and the results obtained are listed in Table 1. A combination of $Pd(dba)_2$ with the $[HP^tBuMe_2]BF_4$ salt, which had proven to be the best catalyst for the Suzuki–Miyaura coupling reaction of alkenylboronates with alkyl bromides,[12b] was found to be suboptimal for the present reaction due to desilylation of **3**. $Pd(PPh_3)_4$ also exhibited lower reactivity (entries 2 and 3). PEPPSI-IPr[21] and $Pd_2dba_3 \cdot CHCl_3/P^tBu_3$ proved more reactive and afforded a relatively higher yield, albeit with reduced chemoselectivity (entries 4 and 5). An initial survey demonstrated that aqueous KOH accelerated the reaction. Palladium catalysts with monodentate ligands were not particularly efficient.

Therefore, several representative bidentate ligands were examined (entries 8–12). We were delighted to find that $PdCl_2$(dppf)[22] performed significantly better (entry 12). Although all the examined catalysts gave rise to the coupling product **5a** as a mixture of stereoisomers, the isomeric mixture was separated by silica gel column chromatography. The *Z*-geometry of the major isomer of product **5a** was confirmed by X-ray crystallographic analysis.[13,14] An authentic product (*E*)-**5a** was synthesized by silylborylation of diphenylethyne to provide comparator NMR data,[13] and this was indeed distinct from that of (*Z*)-**5a**. This observed chemoselectivity is consistent with that reported by Shimizu and Hiyama,[15a] wherein the C–C bond formation at the cis position of the alkyl groups was observed in the reaction of 1,1-diboryl-1-alkene with aryl iodides. The C–C bond at the cis position of the $SiMe_2Ph$ group was formed with moderate discrimination of two geminal boryl groups in **3**. Considering the conformational energies (*A*-values) of the Ph (2.8) and $SiMe_2Ph$ (2.5–2.8) groups,[23] the chemoselectivity cannot be explained simply by a steric effect. From the viewpoint of electronic demands, the ^{11}B NMR spectrum of **3** showed an overlapped signal at 29.9 ppm, indicating that the two boryl groups are electronically similar. Thus, at present, the reason why the two boryl groups in **3** are discriminated remains unclear.

After optimizing the reaction conditions for the chemoselective Suzuki–Miyaura coupling of **3**, a series of aryl

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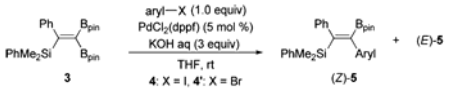
Table 2. Chemoselective Suzuki–Miyaura Coupling of **3** with Aryl Iodides **4** or Aryl Bromides **4′**[a]



entry	aryl–X	5	yield (Z/E)[b]
1	Ph-I (**4a**)	**5a**	85 (88:12)
2[c]	Ph-Br (**4a′**)	**5a**	78 (87:13)
3	4-$MeOC_6H_4$-I (**4b**)	**5b**	87 (89:11)
4	2-$MeOC_6H_4$-I (**4c**)	**5c**	57 (92:8)
5	3-$MeOC_6H_4$-I (**4d**)	**5d**	83 (89:11)
6	4-MeC_6H_4-I (**4e**)	**5e**	92 (88:12)
7	4-$CF_3C_6H_4$-I (**4f**)	**5f**	57 (87:13)
8[c]	4-$CF_3C_6H_4$-Br (**4f′**)	**5f**	59 (85:15)
9	4- ClC_6H_4-I (**4g**)	**5g**	92 (88:12)
10	4- $EtO_2CC_6H_4$-I (**4h**)	**5h**	70 (86:14)

[a] Reaction conditions: **3** (245 mg, 0.5 mmol), **4** or **4′** (0.5 mmol), $PdCl_2$(dppf) (18 mg, 5 mol %), 3 M KOH solution (1.5 mmol, 0.5 mL) in THF (5 mL). [b] Isolated yields after silica gel column chromatography; Z/E ratios were determined by the ^{1}H NMR spectra. [c] The reaction time was 18 h.

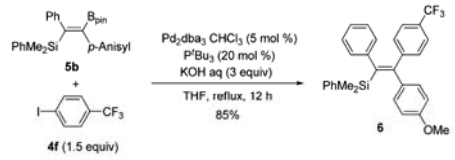
iodides **4** were subjected to survey the reaction scope. 2-Iodoanisole (**4c**) afforded the desired product **5c** in moderate yield that we ascribe to a steric effect (entry 4). As shown in Table 2, it is noteworthy that some aryl bromides **4′** also gave moderate to good yields when the reaction time was extended to 18 h (entries 2 and 8). It is also notable that a chloro group in the substrate **4g** remained intact during the reaction with no trace of side product observed. Synthesis of compounds **5** would be impracticable via *anti*-silylborylation[7k] of unsymmetrical diarylethynes because the regioselectivity of the addition would not be controllable.

With a diverse range of reagents **5** in hand, we sequentially introduced an additional aryl group by Suzuki–Miyaura coupling of the remaining boron moiety. The triarylated alkenylsilane **6** was synthesized successfully by the reaction of (*Z*)-**5b** with **4f** in the presence of $Pd_2dba_3 \cdot CHCl_3/P^tBu_3$ as the catalyst (Scheme 3).

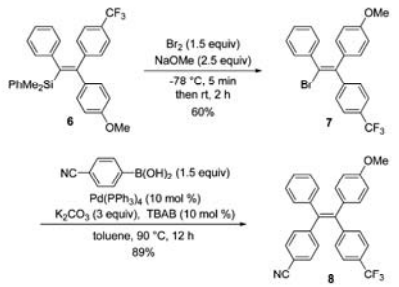
Finally, we addressed the synthesis of a tetraarylated olefin **8** with four different aryl groups through sequential cross-couplings by utilizing the remaining silyl moiety. With Br_2 and NaOMe in MeOH,[24] the silyl group in **6** was successfully transformed to the corresponding bromide **7** along an inversion of stereochemistry. A sequential Suzuki–Miyaura coupling of **7** with 4-cyanophenylboronic acid then afforded the tetraarylated olefin **8** in 88% yield as a sole product whose structure was unambiguously confirmed by X-ray diffraction (Scheme 4).[13,14]

In summary, we have successfully developed a synthesis of tetraarylated olefins featuring a perfectly regio- and

Scheme 3. Sequential Suzuki–Miyaura Coupling for Synthesis of Triarylated Alkenylsilane **6**



Scheme 4. Synthesis of Tetraarylated Olefin **8**



stereoselective silylborylation of the alkynylboronate and sequential chemoselective Suzuki–Miyaura couplings. This protocol can be applicable to a variety of functional groups on the aryl moieties, including those not compatible with the organolithium reagents required in previous approaches. Further studies to clarify the factors for the selectivity and to expand this synthetic method to a more general approach to the complicated π-conjugated molecules are in progress.

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Supporting Information Available. Copies of ^{1}H NMR and $^{13}C\{^1H\}$ NMR spectra for all the new compounds, as well as details on experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Palladium-free synthesis of unsymmetrical diarylethynes by cross-coupling reaction of alkynylboronates with aryl iodides catalyzed by CuCl

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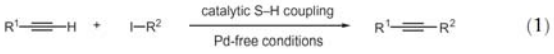
ABSTRACT

A series of unsymmetrical diarylethynes have been synthesized by the copper-catalyzed cross-coupling reaction of alkynylboronates with aryl iodides in high to excellent yields under palladium-free conditions. A wide range of substrates bearing an electron-donating or an electron-withdrawing substituent on the aromatic ring are compatible with this reaction.

Unsymmetrical diarylethynes, which are among the most significant scaffolds in synthetic organic chemistry, have been developed in pharmaceutical chemistry[1] and organic functional materials.[2] These compounds have been generally synthesized by the cross-coupling reaction of terminal alkynes with aryl halides or pseudohalides by palladium/copper co-catalysts under basic conditions (Sonogashira–Hagihara (S–H) coupling reaction).[3] Recently, palladium-free S–H coupling (Eq. (1)) of terminal alkynes with aryl iodides has gained increasing attention because of the expense of palladium.[4]

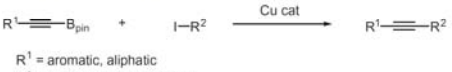


(1)

We have continuously explored the synthesis of unsymmetrical diarylethynes by cross-coupling reactions of alkynylsilanes with aryl halides,[5–7] triflates,[8,9] or tosylates or mesylates[10] (sila-S–H coupling reaction) via the direct activation of a carbon–silicon bond. In addition, we have recently reported the copper-catalyzed cross-coupling reaction of alkynylsilanes with aryl iodides under palladium-free conditions.[11,12]

On the other hand, the boron analogues of alkynylsilanes, alkynylboronates[13] are also known to be useful synthetic intermediates in organic synthesis, and these reagents have been widely used in transition metal-mediated or -catalyzed reactions.[14–18] For instance, we have previously reported the copper-mediated homocoupling reaction of alkynylboronates[19] and cross-coupling reaction of alkynylboronates with acid chlorides for the conjugated enone synthesis[20] under palladium- and base-free conditions.

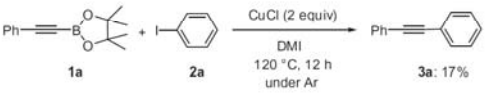
Palladium-catalyzed Suzuki–Miyaura cross-coupling reactions of alkynylboronic acids with aryl halides are scarce,[21] presumably due to the instability of these compounds. However, there are several reports of success using the more stable alkynylboronates,[22] alkynyltrifluoroborates,[23–25] and alkynyl *N*-methyliminodiacetic acid (MIDA) boronates[26] under basic conditions. Since all the aforementioned reactions require the addition of the palladium catalyst, to the best of our knowledge. herein we report the first syntheses of unsymmetrical diarylethynes by copper-catalyzed cross-coupling reaction of alkynyl pinacol boronates (B_{pin}) with various aryl iodides (Eq. (2)).



R^1 = aromatic, aliphatic
R^2 = aromatic, heteroaromatic

(2)

We first elucidated a reaction of phenylethynylboronic acid pinacol ester (**1a**) with iodobenzene (**2a**) in the presence of a stoichiometric amount of CuCl, as shown in Eq. (3). Unfortunately, the desired cross-coupled product **3a** was obtained in only 17% GC yield.



(3)

We have previously disclosed that an alkynyl group of alkynylboronates **1a** can transmetalate from boron to copper with the assistance of CuCl without any nucleophilic activator—namely, a

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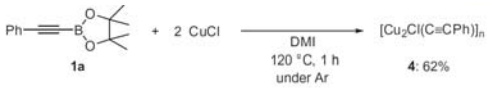
stoichiometric reaction of **1a** with CuCl in 1:2 molar ratio in DMI at 120 °C under an Ar atmosphere to furnish $[Cu_2Cl(C{\equiv}CPh)]_n$ (**4**)[27] in 62% yield as a bright yellow solid (Eq. (4)).[20] In this regard, we suspected that the formation of B_{pin}–Cl (**5**), generated by transmetalation between alkynylboronate **1a** and CuCl, was an important factor to be considered, although we could not confirm the fate of the boron moiety. We postulated the retardation process as follows: the Lewis acidic **5** would interact with the electron-rich alkynylcopper species **4** and inhibit the approach of aryl iodide **2a**, leading to the suppression of the generation of the cross-coupled product **3a** in the stoichiometric reaction shown in Eq. (3).

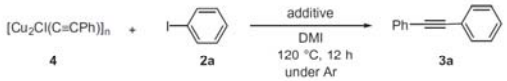


(4)

We thus investigated the stoichiometric reaction of iodobenzene (**2a**) with once isolated, alkynylcopper **4** because Stephens and Castro reported couplings between aryl iodides and stoichiometric copper acetylides, without the palladium catalysis, in refluxing pyridine, the so-called Stephens–Castro reaction.[28] The results are summarized in Table 1. Although the reaction of **2a** with **4** gave the desired cross-coupled product **3a** in 6% yield (Table 1, entry 1), the addition of the PPh_3 ligand dramatically improved the yield (Table 1, entry 3). To our delight, we found that the reaction with an assistance of both PPh_3 and potassium carbonate as an additive cleanly formed the corresponding diarylethyne **3a** in 98% yield (Table 1, entry 4). These effects of additives encouraged us to conduct the catalytic variants of this reaction.

We next screened the effects of additives for the catalytic reaction of alkynylboronate **1a** with unreactive 4-iodoanisole (**2b**) using 10 mol % of CuCl as the catalyst in DMI (0.4 M) at 120 °C for 12 h. The results are summarized in Table 2. As expected, potassium carbonate greatly enhanced the catalytic reaction to afford the desired product **3b** in 97% yield (Table 2, entry 1).[29] The cross-coupled product **3b** was also formed in 57% yield with $PhCO_2K$ as an additive, which was found to be the best reagent in the copper-catalyzed cross-coupling reaction of alkynylsilanes with aryl iodides.[12] After screening other carboxylate additives, it was discovered that $PhCO_2K$ afforded the best yield of **3b** (Table 2, entry 3 vs entries 4 and 5). Acetate salts gave rise to moderate yields of the product (Table 2, entries 6 and 7). An organic base such as Et_3N was found to be inferior (Table 2, entry 8). Again, without the added PPh_3, the yield of **2b** was dramatically decreased to 14% (Table 2, entry 9). Although other phosphine ligands were examined, none of them was superior to PPh_3: P^nBu_3, 9%; $P(OPh)_3$, 12%, respectively. The reaction was found to be minimally sensitive to the amount of the PPh_3 ligand added; the PPh_3/Cu ratio can be varied between 1 and 3. No reaction occurred in the absence of a copper catalyst (Table 2, entry 10). Furthermore, analysis of the reaction mixture by ^1H NMR and GC–MS revealed no formation of the homo-coupled product, 1,4-diphenyl-1,3-butadiyne (**6**). This result suggests that the present copper-catalyzed protocols have significant advantages. Because the formed alkynylcopper species **4** can undergo oxidative homocoupling (the so-called Glaser coupling)[30] leading to lower yields of the desired cross-coupled product **3b** and, in turn, complicating their purification, a gradually generated alkynylcopper species in the reaction mixture can be selectively transformed to the cross-coupled products **3b**.

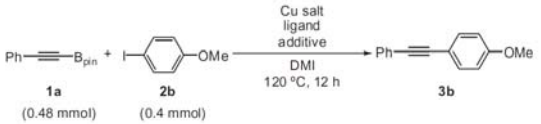
Table 1
A stoichiometric reaction of iodobenzene (**2a**) with alkynylcopper species **4**[a]



Entry	Ligand	Additive	Yield[b] (%)
1	None	None	6
2	None	K_2CO_3	<1
3	PPh_3	None	65
4	**PPh_3**	**K_2CO_3**	**98(90)**

[a] The reaction was carried out with **4** (0.2 mmol), **2a** (0.2 mmol), PPh_3 (0.2 mmol), additive (0.2 mmol) in 1 mL (0.2 M) of DMI at 120 °C.
[b] GC yields. An isolated yield is shown in parenthesis.

Table 2
Copper-catalyzed cross-coupling reaction of phenylethynylboronate (**1a**) with 4-iodoanisole (**2b**)[a]

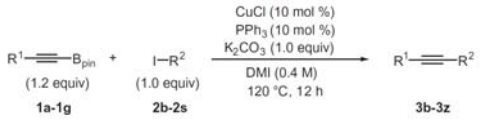


Entry	Cu salt	Ligand	Additive	Yield[b] (%)
1	CuCl (10 mol %)	PPh_3 (10 mol %)	K_2CO_3	97(90)
2			K_3PO_4	76
3			$PhCO_2K$	57
4			$PhCO_2Na$	48
5			$PhCO_2Li$	53
6			AcOK	45
7			AcONa	41
8			Et_3N	8
9		None	K_2CO_3	14
10	None	PPh_3 (10 mol %)		0

[a] The reaction was carried out with **1a** (0.48 mmol), **2c** (0.4 mmol), CuCl (10 mol %), PPh_3 (10 mol %), additive (0.4 mmol) in 1 mL (0.4 M) of DMI at 120 °C, unless otherwise stated.
[b] GC yields based on an aryl iodide **2c**. An isolated yield is shown in parenthesis.

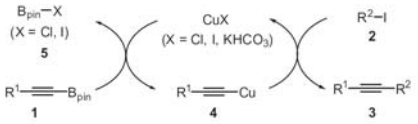
Finally, we were able to apply this new method to a broad range of targets, including aryl- and alkyl-substituted alkynylboronates **1a**–**1g** and various aryl iodides **2b**–**2s** substituted by electron-withdrawing and electron-donating groups, using 10 mol % of CuCl/PPh_3. The results obtained are presented in Table 3. This protocol is rather general in scope for the reaction of 4-substituted aryl iodides **2b**–**2h** with alkynylboronate **1a**; good to excellent yields of the cross-coupled products **3b**–**3h** (Table 3, entries 1–7) were obtained for systems featuring either electron-donating or electron-withdrawing groups at a 4-position. In sharp contrast, aryl bromides and chlorides did not react at all under these reaction conditions. Therefore, 4-chloro and 4-bromoiodobenzenes reacted with **1a** to afford **3i** and **3j**, respectively, in which the chloride and bromide remain intact (Table 3, entries 8 and 9). Bulkier aryl iodides such as 2-iodoanisole, 2-iodotoluene, and 2-iodoacetophenone afforded the corresponding cross-coupled products **3k**–**3m** in moderate to good yields (Table 3, entries 10–12). When 2-iodoaniline (**2n**) was reacted with **1a**, 2-phenylethynylaniline (**3n**) was obtained quantitatively rather than the cyclized product, 2-phenylindole (<1%) (Table 3, entry 13). The bulky substrates such as 2,4,6-trimethyliodobenzene and 1-iodonaphthalene also smoothly reacted with **1a** to give the desired products **3p** and **3q** in 63% and 95% yields, respectively (Table 3, entries 15 and 16). The heteroaromatic iodides **2r** and **2s** gave rise to the formation of **3r** and **3s**, respectively. As demonstrated in other entries 19–25, the present catalytic systems proved to accelerate the cross-coupling reactions of the aromatic-substituted alkynylboronates **1b**–**1f** to generate the desired products **3b** and **3t**–**3y** in moderate to excellent yields. Although longer reaction times and the increased loading of alkynylboronate required, the reactions of aliphatic alkynylboronate **1g** proceeded slowly to give the desired product **3z** albeit in 58% yield (Table 3, entry 26).

Table 3
CuCl-catalyzed cross-coupling reaction of alkynylboronates **1** with aryl iodides **2**[a]



Entry	Alkynylboronate **1**, R^1=	Aryl Halide **2**, R^2=	Product **3**	Yield[b] (%)
1	C_6H_5-(**1a**)	4-MeO-C_6H_4 (**2b**)	**3b**	90
2	**1a**	4-NC-C_6H_4 (**2c**)	**3c**	93
3	**1a**	4-Me-C_6H_4 (**2d**)	**3d**	78
4	**1a**	4-MeCO-C_6H_4 (**2e**)	**3e**	99
5	**1a**	4-EtO_2C-C_6H_4 (**2f**)	**3f**	98
6	**1a**	4-O_2N-C_6H_4 (**2g**)	**3g**	99
7	**1a**	4-H_2N-C_6H_4 (**2h**)	**3h**	88
8	**1a**	4-Cl-C_6H_4 (**2i**)	**3i**	98
9	**1a**	4-Br-C_6H_4 (**2j**)	**3j**	82
10	**1a**	2-MeO-C_6H_4 (**2k**)	**3k**	82
11	**1a**	2-Me-C_6H_4 (**2l**)	**3l**	68
12	**1a**	2-MeCO-C_6H_4 (**2m**)	**3m**	78
13	**1a**	2-H_2N-C_6H_4 (**2n**)	**3n**	99
14	**1a**	2-Br-C_6H_4 (**2o**)	**3o**	56
15	**1a**	2,4,6-Me_3-C_6H_2 (**2p**)	**3p**	63
16	**1a**	1-Naphthyl (**2q**)	**3q**	95
17	**1a**	2-Pyridyl (**2r**)	**3r**	80
18	**1a**	2-Thienyl (**2s**)	**3s**	93
19	4-MeO-C_6H_4- (**1b**)	C_6H_5 (**2a**)	**3b**	99
20		**2d**	**3t**	97
21		**2e**	**3u**	95
22	4-NC-C_6H_4 (**1c**)	**2c**	**3v**	49
23	4-CF_3-C_6H_4 (**1d**)	**2c**	**3w**	97
24	4-Cl-C_6H_4 (**1e**)	**2k**	**3x**	88
25	1-Naphthyl (**1f**)	**2c**	**3y**	90
26[c]	*n*-C_6H_{13} (**1g**)	**2b**	**3z**	58

[a] Conditions: **1** (0.48 mmol), **2** (0.4 mmol), CuCl (10 mol %), PPh_3 (10 mol %), K_2CO_3 (0.4 mmol), DMI (1.0 mL) unless otherwise stated.
[b] Isolated yields based on aryl iodides **2**.
[c] Compound **1** (0.6 mmol), 24 h.



Scheme 1.

Concerning the mechanism, we proposed catalytic cycles of the cross-coupling reaction using alkynylboronates **1** and aryl iodides **2**, as depicted in Scheme 1. On the basis of our previous studies,[19] it seems reasonable to propose CuCl or the regenerated CuI as a catalytic species, with a triphenylphosphine ligand coordinating to copper to form a more soluble and/or active species. In the first step, transmetalation of alkynylboronates **1** could generate an alkynylcopper species **4**, which would react, by oxidative addition, with aryl iodides **2** to form a four-coordinated copper(III) complex, from which reductive elimination expels the cross-coupled product **3**, followed by the regeneration of the CuI catalyst. We have already found that copper iodide is more effective for transmetalation of alkynylboronates **1** than CuCl.[19] The additive, potassium carbonate, might play dual roles: activating relatively inactive alkynylboronates into more active alkynylborates (although transmetalation of alkynylboronates was found to smoothly occur to form alkynylcopper species in DMI) while also trapping B_{pin}–X **5** which would otherwise retard the reaction of organocopper species **4** with aryl iodides **2** to generate the requisite cross-coupled products **3**. Since the regenerated copper iodide is highly effective for the transmetalation of the alkynyl group from boron to copper, an initial addition of 10 mol % of CuCl is enough for completion of the catalytic cycles in the case of reactions with aryl iodides.

In summary, we have discovered copper-catalyzed cross-coupling reaction of alkynylboronates with aryl iodides. This is a novel system for the synthesis of unsymmetrical diarylethynes using alkynylboronates, without the use of palladium catalysis.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.11.069. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

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29. Typical procedure is as follows. To a solution of CuCl (3.9 mg, 0.04 mmol, 10 mol %), PPh_3 (10.5 mg, 0.04 mmol, 10 mol %), and K_2CO_3 (55.3 mg, 0.4 mmol) in DMI (1.0 mL) were added phenylethynylboronate **1a** (109.5 mg, 0.48 mmol), and 4-iodoanisole **2b** (93.6 mg, 0.4 mmol) at room temperature. The reaction mixture was stirred for 12 h at 120°C, quenched with 3 M HCl, and extracted with diethyl ether (10 mL ×2). The combined ethereal layer was washed with brine and dried over $MgSO_4$. Filtration and evaporation provided a brown oil (GC yield 97%). Purification by column chromatography (SiO_2, hexane:ethyl acetate = 20:1, R_f = 0.48) gave product **3b** (75 mg, 90% yield) as a white solid.
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Presentation

1) Highly Selective Synthesis of Multialkylated Olefins through Carbozirconation of Alkynylboronates and Sequential Negishi and Suzuki-Miyaura Couplings
   Jiao Jiao, Yoshiaki Okada, Masato Suetsugu, Ming-Tzu Lan, Megumi Kinoshita, Masayuki Iwasaki, Kentaro Takagi, and Yasushi Nishihara
   The 58th Symposium on Organometallic Chemistry 2011 (2011.9.7-9/Nagoya University, Higashiyama Campus, Nagoya, Japan)

2) Highly Selective Synthesis of Multisubstituted Olefins through Silaboration of Alkynylboronates and Sequential Cross-Couplings
   Jiao Jiao, Masayuki Iwasaki, and Yasushi Nishihara
   The 92nd CSJ Annual Meeting 2012 (2012.3.25-28/Keio University, Hiyoshi Campus, Yokohama, Japan)

3) Highly Selective Synthesis of Multisubstituted Olefins through Silaboration of Alkynylboronates and Chemoselective Suzuki-Miyaura Couplings
   Jiao Jiao, Masayuki Iwasaki, Kiyohiko Nakajima, and Yasushi Nishihara
   The 93rd CSJ Annual Meeting 2013 (2013.3.22-25/Ritsumeikan University, Biwako-Kusatsu Campus, Shiga, Japan)

4) Highly Selective Synthesis of Multi-substituted Olefins through Diborylation of Alkynylsilanes and Cross-Coupling Reaction Sequences
   Jiao Jiao, Keita Hyodo, Hao Hu, and Yasushi Nishihara
   The 60th Symposium on Organometallic Chemistry 2013 (2013.9.12-14/Gakushuin University, Mejiro Campus, Tokyo, Japan)

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