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Diborylation of Alkynyl MIDA Boronates and Sequential Chemoselective Suzuki–Miyaura Couplings: A Formal Carboborylation of Alkynes

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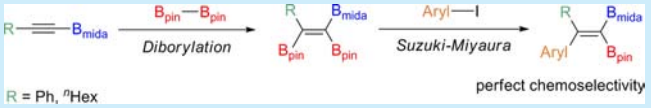
Supporting Information

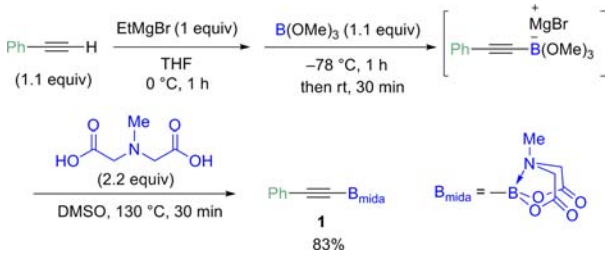
ABSTRACT: Platinum-catalyzed diborylation of phenylethynyl MIDA boronate with B_{pin}–B_{pin} proceeds to yield 1,1,2-triboryl-2-phenylethene with two different classes of the boron functionalities. Sequentially, the obtained 1,1,2-triboryl-2-phenylethene are subjected to Suzuki–Miyaura coupling to introduce a series of aryl groups chemoselectively to afford 1,1-boryl-2,2-diarylethenes.



Transition-metal-mediated[1] and -catalyzed[2] diborylation of unsaturated organic molecules has received much attention in the past decades after an emergence of compounds bearing the B–B bond because of low toxic, economical and maturely synthetic studies on these compounds.[3] To synthesize *vic*-bis(boryl)alkenes that are valuable starting materials for the preparation of, for instance, bioactive chemicals or functional materials through iterative transfomations, particularly, Suzuki–Miyaura coupling,[4] the transition-metal-catalyzed diborylation of alkynes has been exploited extensively.[5−8] The kinetic and mechanistic studies on the platinum-catalyzed diborylation of internal alkynes has been extensively exploited; platinum diboryl complexes derived from oxidative addition of the B–B bond have been isolated.[9] The synthesized diborylated alkenes can be transformed to the various organic compounds with an aid of Suzuki–Miyaura coupling and other methods.[10] But, when unsymmetrical *vic*-diborylalkenes are employed, an accomplishment of chemoselective monofuctinalization was found to be troublesome.[11] We thus chose the masked alkynylboron compounds alternative to the internal alkynes because the diborylated product have different reactivity among three C–B bonds. Among the reported several protective groups,[12,13] we chose the MIDA (*N*-methyliminodiacetic acid) boronates.[14,15] Herein, we report the platinum-catalyzed diborylation of phenylethynyl MIDA boronates with bis(pinacolato)diboron ($(B_{pin})_2$), yielding 1,1,2-triboryalkenes with a perfect stereoselectivity, followed by chemoselective Suzuki–Miyaura coupling to give rise to an exclusive formation of (*Z*)-1,1-diboryl-2-diarylethenes.[16]

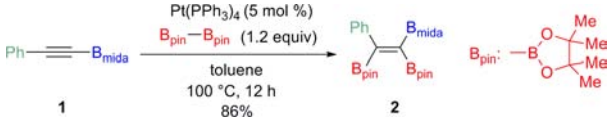
We first prepared phenylethynyl MIDA boronate **1** according to the synthetic procedure for ethynyl MIDA boronate, utilizing ethynylmagnesium bromide.[15f] Treatment of phenylethyne with an equimolar of EtMgBr, followed by reaction with $B(OMe)_3$ at −78 °C for 1 h and an excess of MIDA at 130 °C, gave rise to the desired 1-phenyethynyl MIDA boronate **1** in 83% yield as a white powder (Scheme 1).

Scheme 1. Synthesis of Phenylethynyl MIDA Boronate 1



Next, we investigated the platinum-catalyzed diborylation[5b] of **1** with bis(pinacolato)diboron in toluene at 100 °C to afford triborylated ethene **2** in 86% yield, as shown in Scheme 2. The $^{11}B\{^1H\}$ NMR spectrum of **2** in DMSO-d_6 showed three independent signals at δ 6.94, 11.1, 31.4.

Scheme 2. Platinum-Catalyzed Diborylation of 1



With the synthesized triborylated compound **2** in hand, we screened the reaction conditions of the palladium-catalyzed arylation reaction with 4-anisyl iodide. The results are listed in Table 1. Among the palladium catalysts tested without any ligands, $Pd(dba)_2$ was found to be the best catalyst to give the arylated product **3a** in 67% yield (entries 1–4). In the ^1H NMR spectrum of the formed product **3a** only one set of the B_{pin} moiety was observed, indicating that one of two B_{pin} was

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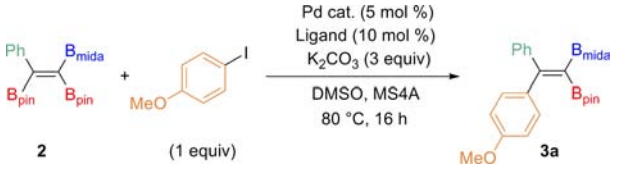
Table 1. Screening the Palladium Catalyst and the Ligand for Suzuki–Miyaura Coupling of 2 with 4-Anisyl Iodide[a]



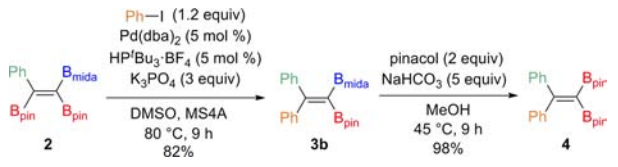
entry	Pd cat.	ligand (mol %)	yield[b] (%)
1	$Pd(PPh_3)_4$		39
2	$Pd(dba)_2$		67
3	$PdCl_2(NCPh)_2$		53
4	PdCl(dppf)		50
5	$Pd(dba)_2$	PEt_3	57
6[c]	$Pd(dba)_2$	P^tBu_3	72
7	$Pd(dba)_2$	PPh_3	61
8	$Pd(dba)_2$	P(mesityl)$_3$	72
9	$Pd(dba)_2$	XPhos	62
10	$Pd(dba)_2$	SPhos	49
11[d]	**$Pd(dba)_2$**	**$HP^tBu_3BF_4$**	**91**

[a]Reaction conditions: **2** (0.1 mmol), 4-anisyl iodide (0.1 mmol), Pd catalyst (5 mol %), ligand (10 mol %), K_2CO_3 (0.3 mmol) in DMSO (2 mL) at 80 °C for 16 h, unless otherwise stated. [b]NMR yields. [c]Ligand (5 mol %). [d]Pd catalyst (5 mol %), ligand (5 mol %), K_3PO_4 (0.3 mmol), 4-anisyl iodide (0.12 mmol), reaction time 9 h.

replaced with a 4-anisyl group in preference to the B_{mida} moiety. Next, we elucidated the effect of the ligand. With a comparison of the phosphine ligands, the bulkier ligands gave the higher yield of the desired product (entry 5 vs 6 and entry 7 vs 8). Buchwald's biphenyl-based ligands such as Xphos (2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl)[17] and Sphos (2-dicyclohexylphosphine-2′,6′-dimethoxybiphenyl)[18] gave inferior results (entries 9 and 10). Finally, we found that the optimized condition; $Pd(dba)_2$ (5 mol %), $HP^tBu_3BF_4$ (5 mol %) in the presence of K_3PO_4 as the base, gave 91% of **3a** (entry 11). Although a variety of aryl iodides reacted smoothly, under the optimized reaction conditions, the corresponding aryl bromide (28%) and aryl chloride (0%) are found to be unsuitable for the present reaction.

In order to determine the configuration of the arylated product **3**, Suzuki–Miyaura coupling of **2** with iodobenzene affording **3b** and sequential transformation of the B_{mida} group into the B_{pin} group was carried out (Scheme 3). With a

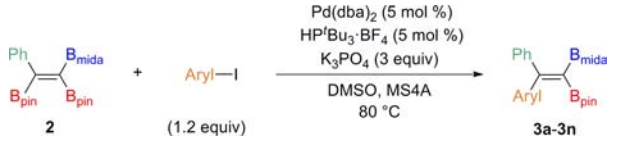
Scheme 3. Determination of Stereochemistry of the Arylated Product 3



procedure reported by Burke,[15i] the intermediate **3b** was treated with pinacol in the presence of $NaHCO_3$ to generate **4** whose spectroscopic data were identical to those of an authentic sample.[19] The *gem*-diborylated olefins have been known as useful building blocks for functional materials, natural products, as well as bioactive pharmaceuticals.[20]

Next, a series of aryl iodides were subjected to survey the reaction scope. As shown in Table 2, the reactions of aryl

Table 2. Chemoselective Suzuki–Miyaura Coupling of 2 with Aryl Iodides[a]



entry	aryl	time (h)	product	yield[b] (%)
1	4-$Me_2NC_6H_4$	9	**3c**	74
2	4-$MeCOC_6H_4$	12	**3d**	77
3	4-$EtCO_2C_6H_4$	9	**3e**	88
4	4-NCC_6H_4	9	**3f**	84
5	4-$CF_3C_6H_4$	6	**3g**	87
6	3-$MeOC_6H_4$	16	**3h**	75
7	3-MeC_6H_4	12	**3i**	80
8	2-MeC_6H_4	9	**3j**	83
9	1-naphthyl	24	**3k**	60
10	4-FC_6H_4	9	**3l**	85
11	3-FC_6H_4	12	**3m**	83
12	2-FC_6H_4	16	**3n**	46

[a]Reaction conditions: **2** (0.1 mmol), aryl iodide (0.12 mmol), $Pd(dba)_2$ (5 mol %), $HP^tBu_3BF_4$ (5 mol %), K_3PO_4 (0.3 mmol) in DMSO (2 mL) at 80 °C. [b]Isolated yields after column chromatography.

iodides bearing electron-donating (entry 1) and electron-withdrawing (entries 2–5) groups in the 4-position with **2** proceeded in high yields. The substituted aryl iodides in the 3-position also afforded the corresponding cross-coupling products **3h** and **3i** in 75% and 80% yields, respectively (entries 6 and 7). However, a sterically hindered 1-naphthyl iodide required a longer reaction time and gave the desired product **3k** in 60% yield (entry 9).

In order to compare an effect of the substituents in the present cross-coupling reaction, the reactions of **2** with various aryl fluorides were subjected. Under the optimized conditions, chemoselective cross-coupling of *p*- and *m*-fluoroiodobenzenes occurred to generate the corresponding arylated products **3l** and **3m** as a sole product in 85% and 83% yields, respectively (entries 10 and 11). In a sharp contrast, *o*-fluoroiodobenzene gave the formation of **3n** in only 46% yield, indicating that reductive elimination of the cross-coupled product **3n** was certainly suppressed owing to the fluorine atom (entry 12).[21]

This is the first example to obtain *gem*-diborylated olefins with two different boryl groups via a chemoselective arylation, which is synthetically equivalent to carboborylation of the alkynyl MIDA boronate. Although the conformational energies (*A* values)[22] of the B_{mida} groups has not been reported, the chemoselectivity can be explained simply by a steric effect because even an addition of 2 molar amounts of aryl iodides did not form the diarylated products.[23] Although other electrophiles such as allyl chloride, ethyl iodide, (*E*)-octenyl iodide were subjected to Suzuki–Miyaura coupling reactions of **2**, no desired coupled products were formed. When **2** reacted with benzyl chloride (Scheme 4), only one isomer **5** was obtained in 38% yield as observed in the case of reactions with aryl iodides.[24]

Furthermore, the present reaction of aromatic 1-alkynyl MIDA boronate was extended to the reaction of an aliphatic 1-alkynyl MIDA boronate. Accordingly, an 1-octynyl MIDA boronate **6** was successfully synthesized from octynylmagnesium bromide in 53% yield. Compound **6** was subjected to the

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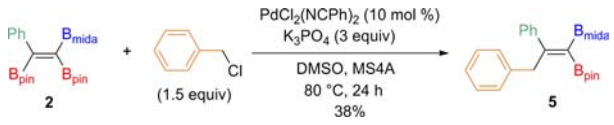
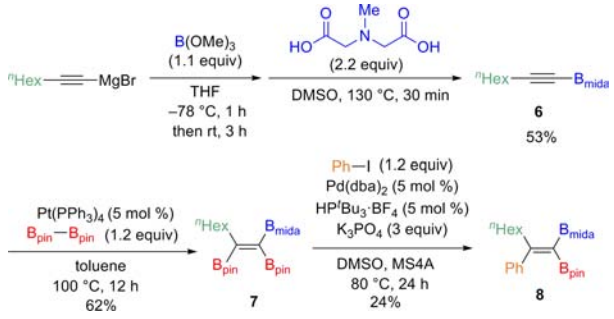
Scheme 4. Suzuki–Miyaura Coupling of 2 with Benzyl Chloride



Pt-catalyzed diborylation with bis(pinacolato)diboron, affording **7** in 62% yield. Finally, the obtained hexylated triborylated ethene **7** reacted with iodobenzene to produce the desired products **8** (Scheme 5).

Scheme 5. Application to an Aliphatic 1-Alkynyl MIDA Boronate



In summary, we have successfully performed the synthesis of *gem*-diborylated olefins having two types of boryl groups via a formal carboborylation of an alkyne; diborylation and chemoselective arylation sequences. Utilizing a different reactivity between the B_{mida} and B_{pin} moieties, our attempts to realize selective transformations such as Suzuki–Miyaura coupling reactions,[15i] palladium-catalyzed fluorination,[25] and copper-mediated fluorination[26] have thus far been unsuccessful. Efforts to clarify the factors for the selectivity and to explore the chemoselective transformation toward the synthesis of multisubstituted olefins are in progress in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and full characterizations are available for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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