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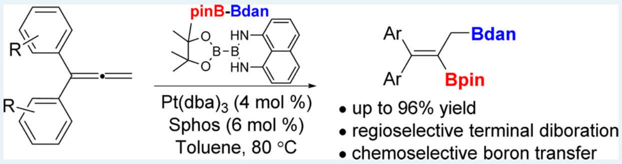
Regio- and Chemoselective Diboration of Allenes with Unsymmetrical Diboron: Formation of Vinyl and Allyl Boronic Acid Derivatives

Xi Guo, Amanda K. Nelson, Carla Slebodnick, and Webster L. Santos*

Department of Chemistry, Virginia Tech, Blacksburg, Virginia 24061, United States

Supporting Information

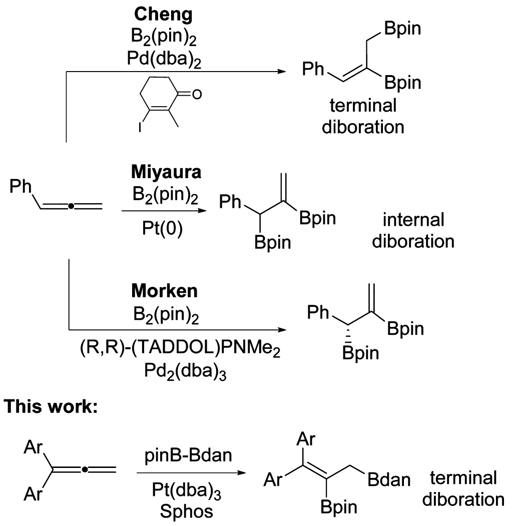
ABSTRACT: A platinum-catalyzed terminal diboration of 1,1-disubstituted allenes using a differentially protected diboron is described. Diboration occurs in a regio- and chemoselective fashion to furnish vinyl and allyl boronates in good to excellent yield and selectivity. Transformation of the bis-boronyl products to other functional groups as well as in chemoselective cross-coupling is demonstrated.



KEYWORDS: *unsymmetrical diboron, diboration, allenes, platinum catalysis, regioselectivity, chemoselectivity*

Transition-metal-catalyzed diboration across unsaturated carbon−carbon bonds such as alkenes,[1] alkynes,[2] and dienes[3] has received increased attention because the intermediates are excellent substrates for cross-coupling reactions and provide a route to valuable functional groups.[4] Among unsaturated substrates, allenes can be uniquely diborated to produce both vinyl and allylic boronates. Consequently, the orthogonal reactivity of the sp^2 and sp^3 C−B bonds allows chemoselective transformations. However, methods for allene diboration are limited. The seminal work by Miyaura and co-workers reported the first Pt(0)-catalyzed reaction of allenes with $B_2(pin)_2$ (pin = pinacolate) with preferential diboration of the internal double bond (Scheme 1).[5] Subsequently, Cheng developed the complementary terminal diboration reaction of monosubstituted allenes employing Pd(0) and alkenyl iodide as cocatalyst.[6] More recently, Morken and co-workers reported a Pd-catalyzed protocol for the diboration of the internal double bond in an enantioselective fashion utilizing a phosphoramidite ligand.[7] In transition-metal-catalyzed boration reactions of allenes and alkenes, symmetrical diboron reagents bearing protecting groups such as pinacol, catechol, and neopentylglycol are frequently employed.[4a] However, there are very few examples of boration processes using unsymmetrical diboron reagents.[8] Notwithstanding the merit of orthogonal reactivity presented by diboration products, the regio- and stereoselectivity issues that arise using the unsymmetrical reagent present a significant challenge. Recent work in our group showed that the internally activated, sp^2−sp^3 hybridized diboron compound, PDIPA diboron (pinacolato diisopropanolaminato diboron) is a particularly effective reagent for a mild, copper-catalyzed β-boration of α,β-unsaturated conjugated compounds and allenoates.[8a−c] Recently, Suginome reported an unsymmetrical diboron reagent, pinBBdan, (dan = 1,8-diaminonaphthalene), for the regioselective diboration of alkynes.[8d] The dan moiety is an effective masking group for the boron atom.[9]

Scheme 1. Transition-Metal-Catalyzed Diboration of Allenes



In this paper, we disclose an efficient method for the diboration of allenes utilizing an unsymmetrical diboron reagent, pinBBdan, in a regio- and chemoselective fashion. 1,1-Diarylsubstituted allenes were diborated on the terminal double bond to transfer the B(pin) moiety to the sp carbon and B(dan) group on the sp^2 carbon, affording vinylic and allylic boronyl groups, respectively (Scheme 1).

Preliminary studies were initiated using phenylallene. Diboration of phenyl allene with an unsymmetrical diboron reagent poses regio- and stereoselectivity issues; in principle, up

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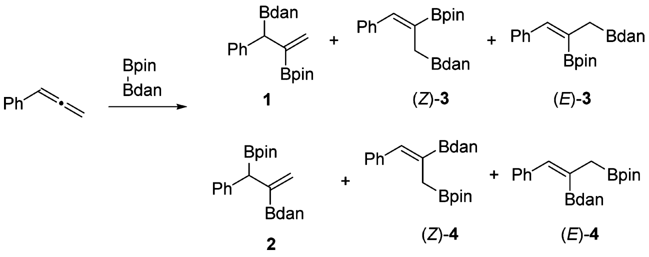
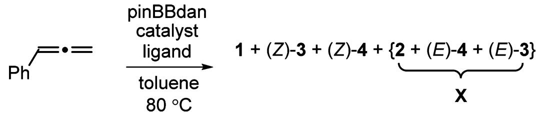
to six bis-borylated products could be produced (Scheme 2). These issues can be exacerbated if scrambling[6] of the boryl groups occurs, affording four additional products bearing two Bpin and two Bdan groups. To address this challenge, we investigated a variety of reaction conditions (transition metals, ligands, etc.), as shown in Table 1. Treatment of phenylallene with Pt(dba)$_3$ and diboron in toluene at 80 °C resulted in the diboration of the internal double bond with a predominant installation of the Bdan moiety on the sp^3 carbon in moderate yield (entry 1). Increasing or decreasing catalyst loading did not affect the regioselectivity of the reaction; however, lower catalyst loading decreased reaction yield (entries 2–3). Screening of ligands such as triphenylphosphine resulted in a mixture of six products (**1**–**4**) while tricyclohexylphosphine decreased product yield (entries 4–5). Although effective in the diboration of alkynes as Pt ligand, P[3,5-(CF$_3$)$_2$C$_6$H$_3$]$_3$ demonstrated good yield of diborated products although with diminished selectivity (entry 6).[8d] Use of Sphos facilitated the chemoselective transfer of Bdan to the internal double bond, affording an (sp^3)C-Bdan albeit at a lower yield. Ruphos, Dppe, and DPEphos showed no reaction (entries 8–10). In contrast, Xantphos provided regioisomers (*Z*)-**3** and (*Z*)-**4** as the major products (entry 11). The more bulky triphenylphosphite was ineffective while triethylphosphite gave a mixture of isomers (entries 12–13). Switching the transition metal catalyst from Pt to Ir resulted in exclusive formation of (*Z*)-**3** in low yield and possibly formation of polymeric byproducts. Numerous attempts to improve this yield were unsuccessful (entries 14–15). Other metals such as Rh or Pd were also ineffective as catalysts (entries 16–17). It is noteworthy that scrambling of the boryl moieties was not observed during the analysis of the products.

Scheme 2. Diboration of Phenylallene with pinBBdan



We next focused our studies on Pt ligands P[3,5-(CF$_3$)$_2$C$_6$H$_3$]$_3$ and Sphos because of the enhanced reaction yield and selectivity observed, respectively (Table 1). In particular, we investigated the effect of 1,1-disubstitution on the allene to determine its effect on yield and selectivity (Table 2). 1-Methyl-1-phenylallene or 1,1-diphenylallene reacted with pinBBdan in good to excellent yield using either Pt ligands to afford, surprisingly, terminal diboration products **5a**–**b**/**6a**–**b** (entries 1–4). While the configuration of **5a**–**b** were readily assigned from NOE studies (see the SI), the identity of diboration products **6a**–**b** were unambiguously assigned from chromatographic separation of each isomer and determining the X-ray structure of the resulting crystals.[10] As shown in Figure 1, methylene C3 forms a direct bond with boron B1 protected with pinacol in **6a** while B1 in **6b** has the dan moiety. We suspect that the increase in sterics on the 1 position of the allene may have a significant effect on the regioselectivity of the reaction. Whereas P[3,5-(CF$_3$)$_2$C$_6$H$_3$]$_3$ was inconsistent in delivering Bdan or Bpin on either terminal carbon atoms (entries 3–4), Sphos as Pt ligand facilitated the chemoselective

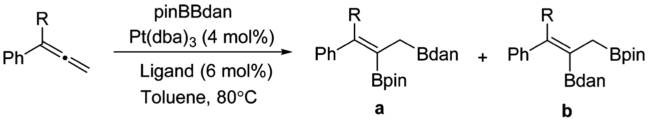
Table 1. Optimization of Reaction Conditions[a]



entry	catalyst (mol %)	ligand (mol %)	yield[b]	ratio **1**:(*Z*)-**3**:(*Z*)-**4**:**X**[c]
1	Pt(dba)$_3$ (4)	--	56	78:22:0:0
2	Pt(dba)$_3$ (2)	--	16	73:27:0:0
3	Pt(dba)$_3$ (8)	--	45	76:24:0:0
4	Pt(dba)$_3$ (4)	PPh$_3$ (6)	63	67:16:5:12
5	Pt(dba)$_3$ (4)	PCy$_3$ (6)	34	80:20:0:0
6	Pt(dba)$_3$ (4)	P[3,5-(CF$_3$)$_2$ C$_6$H$_3$]$_3$ (6)	72	45:5:28:22[d]
7	Pt(dba)$_3$ (4)	Sphos (6)	36	90:10:0:0[e]
8	Pt(dba)$_3$ (4)	Ruphos (6)	--	--
9	Pt(dba)$_3$ (4)	Dppe (6)	--	--
10	Pt(dba)$_3$ (4)	DPEphos (6)	--	--
11	Pt(dba)$_3$ (4)	Xantphos (6)	66	3:62:35:0
12	Pt(dba)$_3$ (4)	P(OPh)$_3$ (6)	trace	--
13	Pt(dba)$_3$ (4)	P(OEt)$_3$ (6)	68	68:19:9:4
14	[IrCl(cod)]$_2$ (2.5)	--	12	0:100:0:0
15	[IrCl(cod)]$_2$(2.5)	PPh$_3$ (6)	--	--
16	[RhCl(cod)]$_2$ (2.5)	--	--	--
17	Pd$_2$(dba)$_3$ (2.5)	--	--	--

[a] Reaction conditions: pinBBdan (0.136 mmol), phenylallene (0.163 mmol), toluene (1 mL) at 80 °C for 24 h. [b] Isolated yields. [c] Determined by GC analysis of the crude reaction mixture. [d] Reaction did not proceed in dioxane or DMF. [e] The same isomeric ratio and yield were obtained at 100 °C. Abbreviations: Sphos = 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl; Ruphos = 2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl; Xantphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene; dppe = ethylenebis(diphenylphosphine); DPEphos = (Oxydi-2,1-phenylene)bis-(diphenylphosphine).

Table 2. Ligand Screening of 1,1-Disubstituted Allenes[a]



entry	R	ligand	yield[b]	ratio **a**:**b**[c]
1	Me (**5**)	Sphos	75	94:6[d]
2	Ph (**6**)	Sphos	85	94:6
3	Me (**5**)	$P[3,5\text{-}(CF_3)_2C_6H_3]_3$	76	76:24[d]
4	Ph (**6**)	$P[3,5\text{-}(CF_3)_2C_6H_3]_3$	91	33:67

[a] Reaction conditions: pinBBdan (0.136 mmol), disubstitued allene (0.163 mmol), $Pt(dba)_3$ (5.35 μmol), ligand (8.16 μmol), and toluene (1 mL) at 80 °C for 24 h. [b] Isolated yields. [c] Determined by GC analysis of the crude reaction mixture. [d] The 6% or 24% are composed of the remaining isomers.

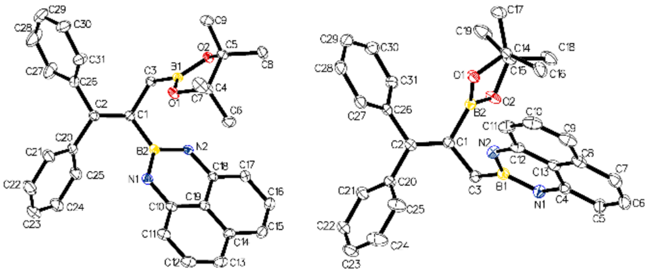
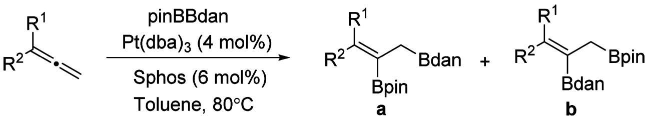
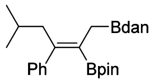
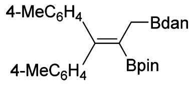
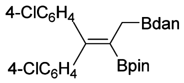
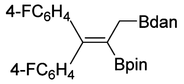
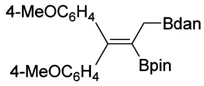
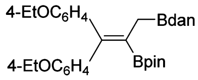
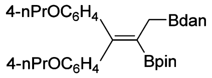
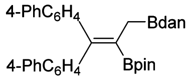
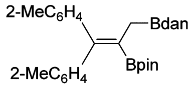
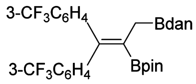


Figure 1. Anisotropic displacement ellipsoid drawings (50%) of **6a** (left) and **6b** (right). Hydrogen atoms have been omitted for clarity.

Table 3. Diboration of Disubstituted Allenes with pinBBdan[a]



entry	major product		yield[b]	ratio **a**:**b**[c]
1		(**7a**)	95	68:32[d]
2		(**8a**)	82	92:8
3		(**9a**)	86	94:6
4		(**10a**)	90	95:5
5		(**11a**)	94	90:10
6		(**12a**)	93	90:10
7		(**13a**)	74	84:16[e]
8		(**14a**)	76	81:19[e]
9		(**15a**)	96	70:30
10		(**16a**)	98	97:3

[a] Reaction conditions: pinBBdan (0.136 mmol), disubstituted allene (0.163 mmol), $Pt(dba)_3$ (5.35 μmol), ligand (8.16 μmol), and toluene (1 mL) at 80 °C for 24 h. [b] Isolated yields. [c] Determined by GC analysis of the crude reaction mixture, unless otherwise noted. [d] The 32% is composed of the remaining isomers. [e] Determined by ^1H NMR analysis of the crude reaction mixture.

transfer of Bpin to the sp carbon with excellent selectivity (entries 1−2).

With the optimized reaction condition in hand, ($Pt(dba)_3$ (4 mol %), Sphos (6 mol %), toluene, 80 °C), we investigated the substrate scope of the reaction using a variety of disubstituted allenes. As shown in Table 3, 1,1-diaryl allenes reacted with pinBBdan efficiently to afford products in high yields with good to excellent regio- and chemoselectivity. When 1-phenyl,1-isobutylallene was utilized as a substrate, product **7a** was isolated in excellent yield and good selectivity (entry 1). A panel of symmetrical 1,1-diarylsubstituted allenes were also good substrates. Aryl rings bearing methyl or electron-withdrawing halogens such as chlorine or fluorine generated products **8a**−**10a** in excellent yields and selectivity (entries 2−4). Further, electron-donating groups on the aryl ring such as methyl, ethyl, and propyl ether were also efficient substrates (entries 5−7). Reaction with a larger phenyl ring on the 4-position produced **14a** in good yield, although a slight decrease in selectivity was observed (entry 8). Substituents on the aryl ring such as the ortho or meta position resulted in excellent yield and good to excellent selectivity (entries 9−10). Interestingly, the structure of the products cannot be assigned using NOE studies; X-ray crystallographic studies were used to unambiguously identify where the boron protected with pinacol or diaminonaphthalene were installed (Figure 2, see the SI). Our investigations indicated that the ^1H NMR chemical shift of the methylene unit attached to Bdan was shifted downfield relative to Bpin.

A proposed mechanism is illustrated in Scheme 3. Oxidative addition of pinBBdan into Pt(0) generates bis(boryl)platinum intermediate **17**[11] that coordinates to the less substituted terminal double bond. Insertion of Bpin to the sp carbon and Pt on the sp^2 carbon furnishes **19**, which undergoes reductive elimination when R = Ph to yield the terminal diboration product **6a**. In contrast, when R = H, platinum complex **19** isomerizes to the internal double bond in an analogous manner to palladium-catalyzed diboration of allenes.[7a] Reductive elimination generates diborated product **1**.

To ascertain whether the described protocol is scalable, 1,1-diphenylallene (1.6 mmol) was subjected to the reaction conditions, which afforded product **6a** in 78% yield with excellent 98:2 selectivity. As both vinylic and allylic boron moieties as well as orthogonal protection are present in **6a**, chemoselective functionalization of the diboration product is envisioned (Scheme 4). Indeed, treatment of compound **6a** with standard Suzuki−Miyaura cross-coupling reagents and 4-

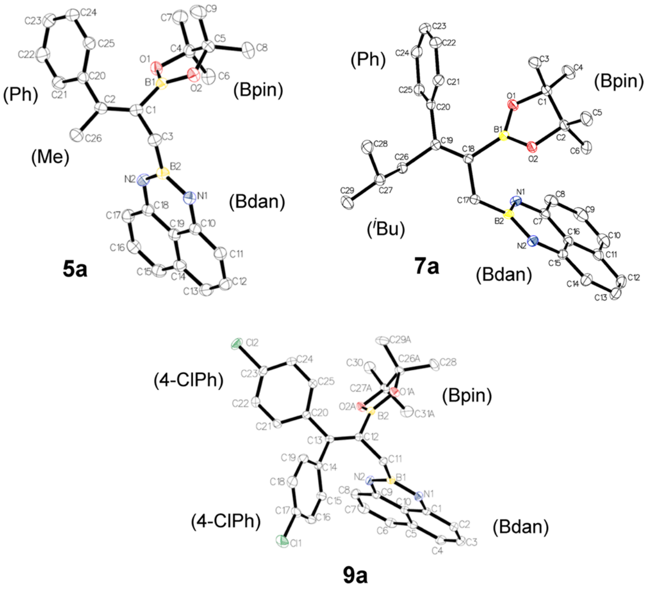
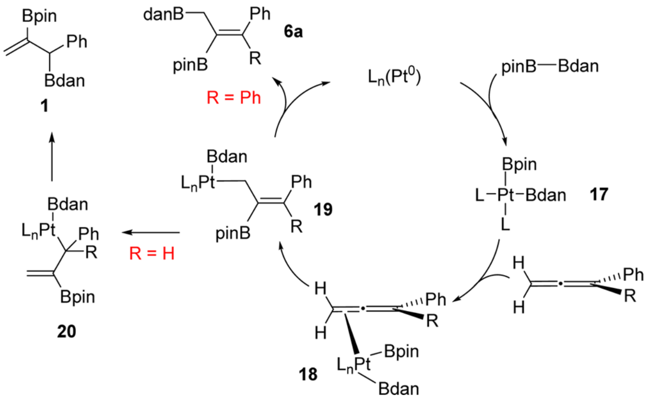
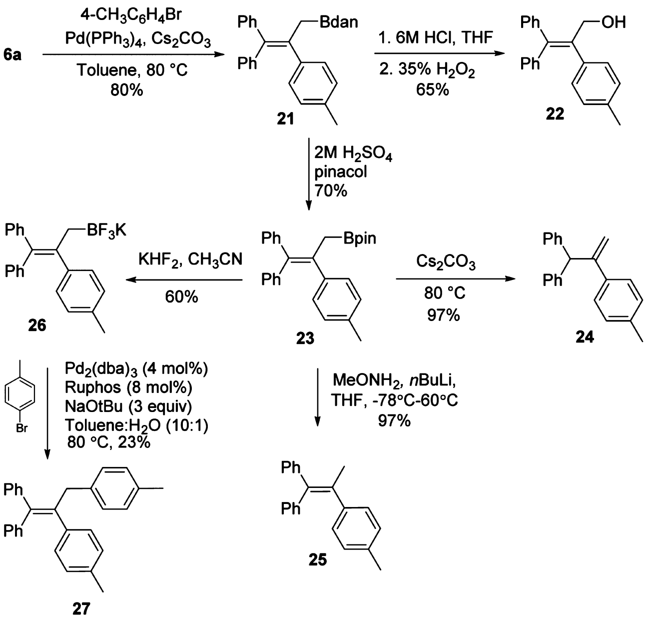


Figure 2. Anisotropic displacement ellipsoid drawings (50%) of **5a**, **7a**, and **9a**. Hydrogen atoms have been omitted for clarity.

Scheme 3. Proposed Mechanism



Scheme 4. Application of the Diboration Product



methylbromobenzene furnished tetrasubstituted alkene **21**. In this particular case, the vinylboronic ester preferentially cross-coupled in the presence of the allylboronyl group. Hydrolysis of Bdan was accomplished under acidic conditions to reveal the boronic acid, which can be oxidized with hydrogen peroxide to afford allylic alcohol **22** or trapped as the pinacol ester **23**. Treatment of **23** with a mild base such as cesium carbonate at 80 °C furnished terminal alkene **24** in near quantitative yield, whereas strong base typically employed for amination reactions provided the protodeboration product **25**. As allylboronic ester **23** was unstable, it was converted to the corresponding trifluoroborate salt **26**, which was utilized for sp^2−sp^3 cross-coupling reaction to generate product **27**.

In summary, we have developed a platinum-catalyzed diboration of 1,1-disubstituted allenes using Sphos as ligand and demonstrated the regioselective addition of two differentially protected boron moieties to the terminal position. These studies further demonstrate the chemoselective transfer of Bpin to the internal sp-hybridized carbon atom, whereas the transfer of Bdan to the terminal end affords a major isomer. Furthermore, we demonstrated the utility of bis-boronyl products in their transformation to other functional groups and chemoselective cross-coupling reactions. Detailed mechanistic studies as well as other catalytic studies are currently underway.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The following files are available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.5b00387.

Detailed experimental procedures and characterizations (PDF)
Crystallographic information (CIF File 1)
Crystallographic information (CIF File 2)
Crystallographic information (CIF File 3)
Crystallographic information (CIF File 4)
Crystallographic information (CIF File 5)
Crystallographic information (CIF File 6)
Crystallographic information (CIF File 7)
Crystallographic information (CIF File 8)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: santosw@vt.edu.

Author Contributions

All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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(11) Unsymmetrical diboryl platinum complexes have been characterized: Borner, C.; Kleeberg, C. *Eur. J. Inorg. Chem.* **2014**, *2014*, 2486−2489.