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Differentially Protected Diboron for Regioselective Diboration of Alkynes: Internal-Selective Cross-Coupling of 1-Alkene-1,2-diboronic Acid Derivatives

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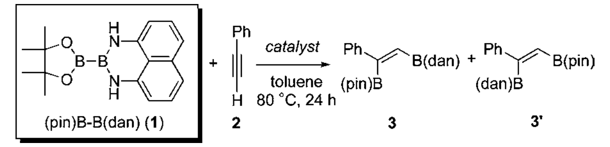
Transition-metal-catalyzed borylations of unsaturated organic compounds now provide the most efficient synthetic access to organoboronic acid derivatives, which serve as useful building blocks in organic synthesis.[1] Among various reagents for catalytic borylations, diborons, which carry B−B bonds, have been utilized in a series of reactions involving diboration,[2] C−H borylation,[3] C−X borylation,[4] and nucleophilic borylation.[5] In these reactions, symmetrical diborons such as $B_2(pin)_2$ (pin = pinacolate) and $B_2(cat)_2$ (cat = catecholate) have been utilized almost exclusively with transition-metal catalysts, in spite of the possibilities for reactivity enhancement as well as the synthetic merits provided by the use of unsymmetrical diborons.[6]

In catalytic diboration reactions using symmetrical diborons, efforts toward selective, stepwise reactions at the two nonequivalent boryl groups have been made.[7] One useful example involves Suzuki−Miyaura coupling of the diboration products of terminal alkynes with $B_2(pin)_2$: the terminal B(pin) group reacts selectively over the internal B(pin) group, allowing the synthesis of monoborylated alkenes that can be used for a second coupling reaction.[8] In the course of our studies of the development of new catalytic borylation reactions,[9] we became interested in use of unsymmetrical diborons, which have different protecting groups on the two boron atoms. Such unsymmetrical diborons can be quite attractive for organic synthesis, provided that catalytic diboration proceeds regioselectively and that the reactivities of the two boronyl groups introduced are sufficiently differentiable. We herein report the reactivity of the unsymmetrical diboron (pin)B−B(dan) (**1**), in which one of the two boron atoms carries the naphthalene-1,8-diaminato (dan) ligand, which we have developed as an effective protecting group for the boronyl group.[7a,10,11] We have established an efficient catalyst system for regioselective diboration of alkynes with this unsymmetrical diboron, leading to the synthesis of 1,2-diborylated alkenes in which the terminal boryl groups are protected.

The unsymmetrical diboron was prepared by reaction of tetrakis(dimethylamino)diboron, $B_2(Me_2N)_4$, with 1,8-diaminonaphthalene and pinacol in a 1:1:1 ratio. Mixing the three components together with a catalytic amount of HCl (1 N in ether, 0.01 equiv) gave **1** in 60% isolated yield as a colorless solid.

The unsymmetrical diboron **1** was reacted with phenylacetylene in the presence of various transition-metal catalysts (Table 1). As established in the original alkyne diboration with $B_2(pin)_2$, Pt catalysts were found to be effective (entries 1−6). Among the phosphine ligands examined, electron-deficient tris[3,5-bis(trifluoromethyl)phenyl]phosphine showed the highest regioselectivity for the product bearing the more reactive B(pin) group at the internal position (entry 6). No scrambling of dan and pin groups took place under the reaction conditions. Pd, Ni,[12] and Rh complexes showed low or no catalytic activity in either the presence or absence of triphenylphosphine. On the other hand, a neutral Ir(I) complex exhibited good catalytic activity, giving **3** with higher regioselectivity than did the Pt complexes. It should be noted that Ir or Ni catalysts have rarely been utilized for catalytic diborations.[13,14]

Table 1. Optimization of the Diboration of Phenylacetylene Using Unsymmetrical Diboron **1**[a]



entry	complex (mol %)	ligand (mol %)	% yield[b]	3/3′[c]
1	$Pt(dba)_2$ (2)	−	79	81:19
2	$Pt(dba)_2$ (2)	Ph_3P (2.2)	59	73:27
3	$Pt(dba)_2$ (2)	$(4\text{-}MeOC_6H_4)_3P$ (2.2)	73	62:38
4	$Pt(dba)_2$ (2)	$(2\text{-}MeC_6H_4)_3P$ (2.2)	62	69:31
5	$Pt(dba)_2$ (2)	$(4\text{-}CF_3C_6H_4)_3P$ (2.2)	83	84:16
6	$Pt(dba)_2$ (2)	$[3,5\text{-}(CF_3)_2C_6H_3]_3P$ (2.2)	74[d]	96:4
7	$Pd(dba)_2$ (3)	−	0	−
8	$Pd(dba)_2$ (3)	Ph_3P (3.3)	21	53:47
9	$Ni(cod)_2$ (3)	−	0	−
10	$Ni(cod)_2$ (3)	Ph_3P (3.3)	6	88:12
11	$[RhCl(cod)]_2$ (1.5)	−	5	58:42
12	$[RhCl(cod)]_2$ (1.5)	Ph_3P (3.3)	3	87:13
13	$[IrCl(cod)]_2$ (1)	−	51	98:2
14	$[IrCl(cod)]_2$ (1.5)	Ph_3P (3.3)	0	−

[a] **1** (0.1 mmol), **2** (0.15 mmol), metal complex (2−3 μmol of metal), and ligand were stirred in toluene (0.75 mL) at 80 °C for 24 h, unless otherwise noted. [b] GC yields. [c] Determined by GC analysis of the crude reaction mixture. [d] Reaction time 48 h.

Under the optimized reaction conditions using either $Pt(dba)_2$/$[3,5\text{-}(CF_3)_2C_6H_3]_3P$ or $[IrCl(cod)]_2$ as the catalyst, diboration of other alkynes was examined (Table 2). The Pt system in general gave good yields with high regioselectivities. Arylalkynes bearing electron-donating or -withdrawing groups at the ortho, meta, or para positions gave the corresponding 1,2-diboration products with high regioselectivities. Ethynylthiophene and even aliphatic terminal alkenes furnished the corresponding products in a regioselective manner. Ester, ketone, and bromine groups were tolerant of the reaction conditions. The corresponding reaction with the Ir catalyst was also found to be efficient. The Ir-catalyzed reactions generally showed comparable or even higher regioselectivities, except for the electron-rich arylalkyne (entry 4). Notably, an internal unsymmetrical alkyne underwent the diboration with high regioselectivity in the presence of the Pt catalyst (entry 11).

The obtained diboration products were subjected to Suzuki−Miyaura coupling with aryl halides (Table 3). The present diboration products bearing a protected terminal boronyl group underwent coupling at the *internal* B(pin) group with excellent chemoselectivity. This is in sharp contrast to the $B_2(pin)_2$-based diboration system, in which the diboration products undergo the coupling reaction selectively at the *terminal* B(pin) group.[8]

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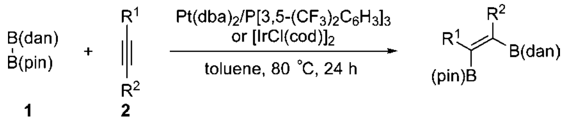
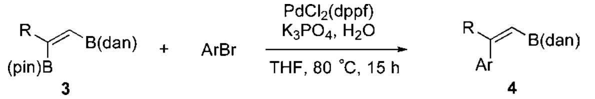
Table 2. Pt- or Ir-Catalyzed Diboration of Alkynes Using Unsymmetrical Diboron **1**



				Pt catalysis[a]		Ir catalysis[b]	
entry	R^1	R^2	product	% yield[c]	**3/3′**[d]	% yield[c]	**3/3′**[d]
1	Ph	H	**3a**	69[e]	96:4	85[f]	99:1
2	4-MeC$_6$H$_4$	H	**3b**	67	93:7	67	93:7
3	2-MeC$_6$H$_4$	H	**3c**	96	95:5	79	95:5
4	4-MeOC$_6$H$_4$	H	**3d**	90[e]	93:7	57[f]	85:15
5	4-EtO$_2$CC$_6$H$_4$	H	**3e**	92[e]	97:3	74[f]	98:2
6	4-AcC$_6$H$_4$	H	**3f**	77	95:5	84[f]	98:2
7	4-BrC$_6$H$_4$	H	**3g**	81	96:4	83	98:2
8	3-BrC$_6$H$_4$	H	**3h**	65	94:6	81	99:1
9	2-thiophenyl	H	**3i**	61	89:11	64[e,g]	99:1
10	*n*-Hex	H	**3j**	73	93:7	74	93:7
11	Ph	Me	**3k**	92	97:3	49	83:17

[a] **1** (0.1 mmol), **2** (0.15 mmol), Pt(dba)$_2$ (2 μmol), and the ligand (2.2 μmol) were stirred in toluene (0.75 mL) at 80 °C for 24 h, unless otherwise noted. [b] **1** (0.1 mmol), **2** (0.15 mmol), and [IrCl(cod)$_2$]$_2$ (1.5 μmol) were stirred in toluene (0.75 mL) at 80 °C for 24 h, unless otherwise noted. [c] Isolated yield. [d] Determined by GC or ^{1}H NMR analysis of the crude reaction mixture. [e] Reaction time 48 h. [f] At 110 °C. [g] Using 3.0 mol % [IrCl(cod)]$_2$.

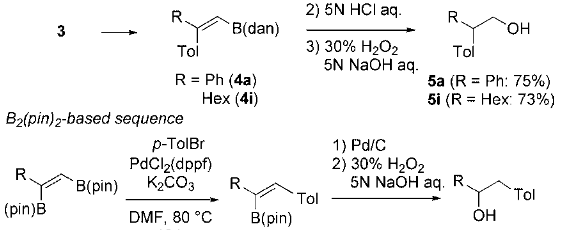
Table 3. Internal-Selective Suzuki−Miyaura Coupling of **3**[a]



entry	**3** (R)	Ar	product (% yield)[b]	ratio (stereo)[c]
1	**3a** (Ph)	*p*-Tol	**4a** (91)	99:1
2	**3a** (Ph)	4-MeOC$_6$H$_4$	**4b** (96)	95:5
3	**3a** (Ph)	4-EtO$_2$CC$_6$H$_4$	**4c** (79)	99:1
4	**3a** (Ph)	*o*-Tol	**4d** (99)	95:5
5	**3a** (Ph)	2-thiophenyl	**4e** (75)	83:17
6	**3d** (4-MeOC$_6$H$_4$)	*p*-Tol	**4f** (88)	98:2
7	**3f** (4-AcC$_6$H$_4$)	*p*-Tol	**4g** (99)	98:2
8	**3i** (2-thiophenyl)	*p*-Tol	**4h** (93)	98:2
9	**3j** (*n*-Hex)	*p*-Tol	**4i** (88)	98:2

[a] **3** (0.070 mmol), aryl bromide (0.077 mmol), PdCl$_2$(dppf) (1.4 μmol), base (0.21 mmol), and H$_2$O (0.7 mmol) were stirred in THF (0.75 mL) at 80 °C for 15 h. [b] Isolated yield. [c] Ratio of **4** and its stereoisomer **4′** (GC analysis and/or ^{1}H NMR).

Scheme 1. Regiocomplementary Synthesis of β-Arylethanols



The cross-coupling products **4** derived from the present diboration system can be further utilized for the synthesis of 2,2-diarylethanol derivatives **5** via Pd/C-catalyzed hydrogenation followed by deprotection of dan and H$_2$O$_2$ oxidation (Scheme 1). These results contrast highly with B$_2$(pin)$_2$-based diboration product **6**, which provides regioisomeric alcohol **8** selectively through formation of **7**.

In this paper, we have demonstrated that unsymmetrical diboron **1** undergoes regioselective addition toward unsymmetrical alkynes in the presence of Ir or Pt catalysts, leading to the synthesis of 1-alkene-1,2-diboronic acid derivatives in which the internal boronyl groups are more reactive. In addition, remarkably higher reactivity of the unsymmetrical diboron than B$_2$(pin)$_2$ in the presence of Ir catalysts has also been established. The mechanism of the regioselectivity and applications of the unsymmetrical diboron to other catalytic reactions are now being studied in this laboratory.

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Supporting Information Available: Experimental procedures and spectral data for the new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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