

Neopentylglycolborylation of Aryl Mesylates and Tosylates Catalyzed by Ni-Based Mixed-Ligand Systems Activated with Zn

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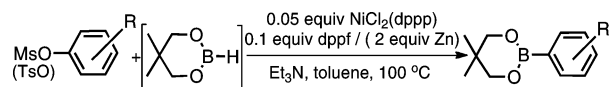
Arylboronic acids and arylboronate esters are critical intermediates in organic synthesis, and their roles as elements of functional materials and as therapeutic agents are emerging.¹ Transition-metal catalysis provides a mild and robust approach to the preparation of diversely functionalized arylboronate esters that overcomes the technical limitations and limited functional group tolerance associated with traditional hard-metalation conditions. Re,² Rh,³ and Ir⁴ catalysts for the direct C–H borylation of arenes using tetraalkoxydiboron and dialkoxyborane have been developed. Although it is a powerful technique, direct C–H borylation cannot always provide the desired regioisomers. Pd-catalyzed borylation is a complementary tool for the regiospecific conversion of aryl triflates, iodides, and bromides to the corresponding arylboronate esters.⁵ Recently, Buchwald-type ligands have expanded Pd-catalyzed borylation to aryl chlorides.⁶ The borylation of aryl mesylates and tosylates has remained a challenge in this field, although it would greatly expand the scope of transition-metal-catalyzed borylation. An efficient solution to this challenge is reported here.

Following an early report that provided two examples of Ni-catalyzed pinacolborylation,⁷ our laboratory reported an efficient, cost-effective Ni-catalyzed borylation using in situ-prepared neopentylglycolborane.⁸ Ni-catalyzed borylation of aryl iodides and bromides was successfully paired with sequential Ni-catalyzed^{8a,b} or complementary one-pot Pd-catalyzed^{8b} cross-coupling for rapid access to biaryls. Earlier, our laboratory determined the improved performance of mixed-ligand systems in Ni-catalyzed cross-coupling.⁹ Development of mixed-ligand catalytic systems, notably NiCl₂(dppp)/dppf, has expanded the scope of Ni-catalyzed neopentylglycolborylation to aryl chlorides^{8c} and ortho-substituted aryl halides.

As NiCl₂(dppp)/dppf demonstrated superior performance to other ligand systems for the borylation of less-reactive aryl chloride and ortho-substituted substrates, we tested its performance in the borylation of aryl mesylates and tosylates (Table 1). Aryl mesylates and tosylates are incompatible with single-ligand Ni catalysts for borylation, and no reports have suggested their applicability in Pd-catalyzed systems. Once again, it was found that the NiCl₂(dppp)/dppf mixed-ligand system excels in comparison to single-ligand systems, providing borylation of all substrates tested. However, high yields were obtained only for phenyl methanesulfonate (entry 1), 2-methanesulfonylnaphthalene (entry 2), and 4-cyanophenyl methanesulfonate (entry 6). The yields obtained for ortho- and para-substituted aryl mesylates were significantly lower, although somewhat better yields were observed for meta-substituted aryl mesylates and tosylates (entries 4, 10, 11, 14, and 15).

Previously, our laboratory utilized Zn as a reductant in Ni-catalyzed homo- and cross-coupling of aryl mesylates and tosylates.¹⁰ Astonishingly, introduction of 2.0 equiv of Zn in the Ni-catalyzed neopentylglycolborylation of aryl mesylates and tosylates

Table 1. Comparison of NiCl₂(dppp)/dppf-Catalyzed Neopentylglycolborylation of Aryl Mesylates and Tosylates with and without Zn



entry	substrate	time (h)	convn ^a / yield ^b (%)	time (h)	convn ^a / yield ^{b,c} (%)
1		25	93 / 93	2	100 / 100 (97)
2		25	90 / 90 (80)	1	100 / 100 (95)
3		21	55 / 55 (30)	1	100 / 100 (88)
4		20	69 / 69 (65)	1	100 / 100 (87)
5		25	25 / 25 (10)	1	100 / 88 (75)
6		24	100 / 96 (80)	2	100 / 100 (83)
7		68	38 / 38 (24)	2	100 / 100 (88)
8		89	33 / 33 (13) ^d	3	100 / 100 (75)
9		68	43 / 43 (28)	2	100 / 100 (95)
10		68	62 / 62 (49)	2	100 / 100 (98)
11		89	65 / 65	2	100 / 100 (91)
12		68	10 / 10	6	100 / 100 (77)
13		48	50 / 50	1	100 / 100 (95)
14		65	65 / 65	2	100 / 100 (86)
15		48	66 / 50 (32)	2	100 / 100 (75)
16		65	40 / 40 (33) ^d	2	100 / 100 (83)

^a Conversion calculated from GC. ^b Yield determined by GC. Isolated yield in parentheses. ^c Using 2 equiv of Zn powder. ^d Isolated as the solid trifluoroborate since the corresponding arylboronate is a liquid.

provided excellent yields. In addition to the enhanced yield, the reaction time to achieve maximum conversion was dramatically

reduced from 1–4 days in the absence of Zn to 1–3 h in its presence (Table 1 and Table ST1 in the Supporting Information).

Table 2. Catalyst Screening in the Ni-Catalyzed Neopentylglycolborylation of Aryl Mesylates Using Zn

entry	catalyst (%)	ligand (%)	convn ^a /yield ^b (%)		
			1 h	2 h	4 h
1	NiCl ₂ (dppp) (5)	dppf (10)	100/100	—	—
2	NiCl ₂ (dppp) (5)	PPh ₃ (10)	79/79	93/93	100/100
3	NiCl ₂ (dppp) (5)	PTol ₃ (10)	61/61	83/83	97/97

^a Conversion calculated from GC. ^b Yield determined by GC.

Other mixed-ligand systems can also mediate effective neopentylglycolborylation of aryl mesylates and tosylates (Table 2), though longer reaction times are needed to obtain maximum yield. With 5 mol % NiCl₂(dppp) and 10 mol % dppf, quantitative borylation of methyl 4-methanesulfonyloxybenzoate in 1 h was achieved (entry 1). Using 10 mol % PPh₃ (entry 2) or PTol₃ (entry 3) as the coligand provided 100 and 97% yield, respectively, after 4 h.

Table 3. Optimization of Catalyst and Zn Additive Loading in the NiCl₂(dppp)/dppf-Catalyzed Neopentylglycolborylation of Aryl Mesylates

entry	catalyst (%)	ligand (%)	equiv of Zn	convn ^a /yield ^b (%)			
				1 h	2 h	4 h	7 h
1	NiCl ₂ (dppp)(5)	dppf (10)	2	100/100	—	—	—
2	NiCl ₂ (dppp)(3)	dppf (6)	2	—	95/95	100/100	—
3	NiCl ₂ (dppp)(2)	dppf (4)	2	46/46	63/63	86/86	100/100
4	NiCl ₂ (dppp)(5)	dppf (10)	1.5	—	100/98	—	—
5	NiCl ₂ (dppp)(5)	dppf (10)	1	—	—	100/95	—
6	NiCl ₂ (dppp)(5)	dppf (10)	0.5	—	—	100/91	—
7	—	—	2	0/0	0/0	0/0	0/0
8	NiCl ₂ (dppp)(5)	—	2	—	—	—	30/30

^a Conversion calculated from GC. ^b Yield determined by GC.

A control experiment was performed in which only Zn, neopentylglycolborane, Et₃N, and methyl 4-methanesulfonyloxybenzoate were heated in toluene (Table 3, entry 7). Without the Ni catalyst, no borylation was observed, indicating the role of Zn as an additive, presumably as a reductant. As expected, subsequent addition of the Ni catalyst to this system allowed the borylation to commence (entry 8). Ideally, low catalyst and reductant loadings are desired. With 5 mol % NiCl₂(dppp), 10 mol % dppf, and 2 equiv of Zn, quantitative borylation of methyl 4-methanesulfonyloxybenzoate was achieved in 1 h (entry 1). Reducing the catalyst loading level to 3 mol % NiCl₂ (dppp) and 6 mol % dppf resulted in a slower reaction that achieved complete conversion after 4 h

(entry 2). Further reduction in the catalyst loading level to 2 mol % NiCl₂(dppp) and 4 mol % dppf provided quantitative yield only after 7 h (entry 3). Effective borylation could also be achieved with reduced Zn levels as low as 0.5 equiv (entries 4–6). However, decreasing the Zn level gave a corresponding decrease in yield.

The borylation of substrates containing aldehydes, ketones, and pyridines in the presence of Zn is accompanied by side reactions and will be reported in a scope and limitations manuscript together with mechanistic studies.

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Supporting Information Available: Experimental details and compound characterization. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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