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

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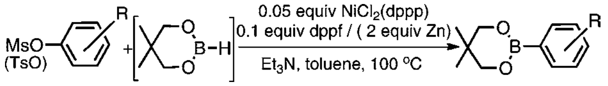
Arylboronic acids and arylboronate esters are critical intermediates in organic synthesis, and their roles as elements of functional materials and as therapeutic agents are emerging.[1] Transition-metal catalysis provides a mild and robust approach to the preparation of diversely functionalized arylboronate esters that overcomes the technical limitations and limited functional group tolerance associated with traditional hard-metalation conditions. Re,[2] Rh,[3] and Ir[4] 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.

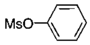
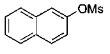
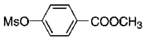
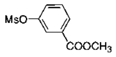
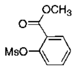
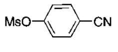
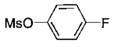
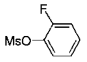
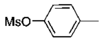
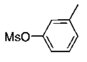
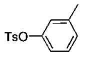
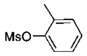
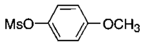
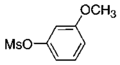
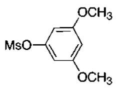
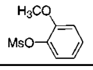
Following an early report that provided two examples of Ni-catalyzed pinacolborylation,[7] our laboratory reported an efficient, cost-effective Ni-catalyzed borylation using in situ-prepared neopentylglycolborane.[8] Ni-catalyzed borylation of aryl iodides and bromides was successfully paired with sequential 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 $NiCl_2$(dppp)/dppf, has expanded the scope of Ni-catalyzed neopentylglycolborylation to aryl chlorides[8c] and ortho-substituted aryl halides.

As $NiCl_2$(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 $NiCl_2$(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 provided excellent yields. In addition to the enhanced yield, the reaction time to achieve maximum conversion was dramatically

Table 1. Comparison of $NiCl_2$(dppp)/dppf-Catalyzed Neopentylglycolborylation of Aryl Mesylates and Tosylates with and without Zn



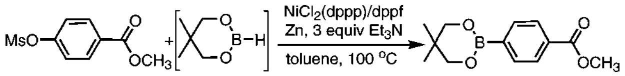
entry	substrate	time (h)	convn[a] / yield[b] (%)	time (h)	convn[a] / yield[b,c] (%)
1		25	93 / 93	2	100 / 100 (97)
2		25	90 / 90 (80)	1	100 / 100 (95)
3		21	55 / 55 (30)	1	100 / 100 (88)
4		20	69 / 69 (65)	1	100 / 100 (87)
5		25	25 / 25 (10)	1	100 / 88 (75)
6		24	100 / 96 (80)	2	100 / 100 (83)
7		68	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.

10.1021/ja910808x

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

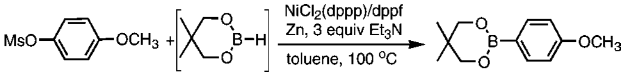


entry	catalyst (%)	ligand (%)	convn[a]/yield[b] (%) 1 h	2 h	4 h
1	$NiCl_2$(dppp) (5)	dppf (10)	100/100	−	−
2	$NiCl_2$(dppp) (5)	PPh_3 (10)	79/79	93/93	100/100
3	$NiCl_2$(dppp) (5)	$PTol_3$ (10)	61/61	83/83	97/97

[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 % $NiCl_2$(dppp) and 10 mol % dppf, quantitative borylation of methyl 4-methanesulfonyloxybenzoate in 1 h was achieved (entry 1). Using 10 mol % PPh_3 (entry 2) or $PTol_3$ (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 $NiCl_2$(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, Et_3N, 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 % $NiCl_2$(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 % $NiCl_2$ (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 % $NiCl_2$(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.

Acknowledgment. Financial support by the National Science Foundation (DMR-0548559 and DMR-0520020) and the P. Roy Vagelos Chair at the University of Pennsylvania is gratefully acknowledged. We also thank Professor G. A. Molander of the University of Pennsylvania for reading the final version of the manuscript and for suggestions.

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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JA910808X