Sandmeyer-Type Reaction to Pinacol Arylboronates in Water Phase: A Green Borylation Process

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Abstract: Copper(I)-catalyzed cross-coupling reactions of aryl diazonium salts with bis(pinacolato)diboron can proceed smoothly in the water phase at room temperature to give the corresponding arylboronate esters in good to high yields. The Sandmeyer-type borylation not only provides direct access to arylboronate bearing halo and acidic substituents, but also achieves a green borylation process.

Key words: aryldiazonium salts, pinacol arylboronate, borylation, Sandmeyer reaction, 4-carboxylphenylboronate ester

Arylboronate esters and arylboronic acids may be one of the most important intermediates that are used in a broad range of transition-metal-catalyzed C–C,¹ C–N,² C–O,³ and C–P⁴ bond-forming reactions. Fundamental preparations of the boronate esters have been studied to a lesser extent. The most commonly utilized methods to access arylboronate esters require harsh conditions or expensive reagents,^{5–8} such as the direct Pd-catalyzed attachment of boron to aromatics to afford arylboronates using aryl halides or triflates with a diboron pinacol.⁶

In recent ten years, investigations on the development of synthetic methodologies for arylboronates have continuously attracted the attention of organic chemists, and some new representative synthetic alternatives to arylboronic acids and arylboronic esters are summarized as follows: (1) Strongin et al. afforded various arylboronic esters via a palladium-catalyzed coupling of bis(pinacolato)diboron(B₂pin₂) with arydiazonium tetrafluoro borate salts under mild reaction conditions;⁹ (2) Andrus et al. used a carbene-palladium catalyst to accomplish the borylation of aryldiazonium ions without added base;¹⁰ and (3) Wang et al. explored diazonium ions formed in situ using tert-butyl nitrite to give pinacol arylboronates in the presence of benzoyl peroxide.11 It is worth noting that these methods employ the cheap and abundant arylamines as starting materials, so aryldiazonium salts easily obtained from arylamines are highly attractive synthetic alternatives to the corresponding halides and triflates. The above procedures are highly reliable and tolerate a wide range of functional groups and allow easy access to a diverse set of arylboronate esters, but these reactions also require expensive palladium catalyst and ligand, proceed

SYNLETT 2012, 23, 1394–1396 Advanced online publication: 08.05.2012 DOI: 10.1055/s-0031-1290960; Art ID: ST-2012-W0153-L © Georg Thieme Verlag Stuttgart · New York in organic solvent, and yet are inherently inefficient to acidic substituents, such as carboxyl, aminosulfonyl, etc.

In this communication, we describe a facile and green method for the preparation of arylboronates bearing acidic substituents by the classic Sandmeyer-type reaction of aryldiazonium tetrafluoroborate salts with bis(pinacolato)diboron. The reaction can be carried out in water under air at room temperature. To the best of our knowledge, this procedure has not been reported to date.

In light of a few reports of transformations to pinacol boronates that occur via aryldiazonium salts in the presence of a Pd catalyst, we surmised that it might be possible to achieve the transformation under traditional Sandmeyer reaction conditions. Inspired by the report from Wang and co-workers that Cu(I) and Cu(II) salts could afford pinacol phenylboronate in 8% yield from phenyldiazonium ion and B₂pin₂,¹¹ we decided to explore the potential of the reaction by extending the Sandmeyer-type reactions.

After some initial attempts, one can conclude that aryldiazonium tetrafluoroborate salts were very suitable intermediates for this transformation, which are easily available from arylamines and prone to be isolated.¹² During the course of our studies on the reaction, we prepared pinacol phenylboronate catalyzed by CuBr with the use of commercial acetone in 20% yield from phenyldiazonium tetrafluoroborate and B₂pin₂. Considering that commercial acetone contains a little water, we considered that compared with CuBr in pure organic solvent - Cu(I) ionized in a small amount of water might give better yield. In the studies of Wang and co-workers, Cu(I) and Cu(II) salt catalysts could not be resolved in organic solvent, so the vield was low. In several experiments, we adjusted the ratio between water and acetone such that the clear solution mixed with all materials including catalyst. We were pleased to find that the reaction gave pinacolato phenylboronate in 70% yield within five hours at room temperature.

Therefore we drew a conclusion that the borylation procedure might tolerate the presence of free protons. In other words, we might directly prepare pinacol arylboronates substituted by groups containing active hydrogen, such as aminosulfonyl, carboxyl, etc. We selected 4-carboxylic phenyldiazonium tetrafluoroborate (1a) as the model compound to examine its behavior in the presence of different metal salts, which may accelerate the decomposition of the aryldiazonium ions (Table 1). Furthermore, the





Entry	Solvent ratio 2:1 (v/v)Additive (mol%)		Time (h)	Yield (%) ^b
1	acetone-H ₂ O	$Cu(Ac)_{2}(50)$	6	35
2	acetone-H2O	FeCl ₃ (10)	6	21
3	acetone-H2O	$Co(Ac)_2$ (10)	6	15
4	acetone-H2O	$\operatorname{CeCl}_{2}(10)$	6	12
5	acetone-H2O	CuBr (5)	5	70°
6	MeCN-H ₂ O	CuBr (5)	3	80°
7	MeCN-H ₂ O	CuBr (20)	3	65
8	DME-H ₂ O	CuBr (5)	3	71
9	dioxane-H ₂ O	CuBr (5)	3	68
10	$\rm H_2O^d$	CuBr (5)	12	10
11	acetone ^d	CuBr (5)	6	25

^a Reaction conditions: **1a** (1mmol), B₂pin₂ (1 mmol), solvent (4.5 mL), r.t.

^b HPLC yield with commercial 2a as external standard.

^c Yields after isolation by column chromatography.

^d Single solvent.

optimization of the reaction conditions, including solvent and reaction time, were then investigated.

As the catalyst, CuBr was superior to other inorganic salts (Table 1, entries 1–5). We also tested other Cu(I) salts, like CuI and CuCl. Although CuI gave a comparable yield, the reaction solution showed a deeper color and purification of the product was problematic. Additionally, CuCl yielded only 50% of the desired compound. Increasing the amount of CuBr led to a sharp decrease, with 0.2 equivalents of additive giving the desired compound in only 65% yield (Table 1, entry 7). As it is suggested that the Sandmeyer reaction proceeds via a radical mechanism,¹³ a lot of halogen anions can take a competing reaction with B_2pin_2 as radical receptor. It was indeed observed that only a trace of the desired compound could be obtained with 4-carboxylic phenyldiazonium bromide as starting material under the same conditions. Finally, we found that the reaction was marginally affected by solvents (Table 1, entries 5–11). It was observed that pure acetone or pure water as solvents afforded 1b in only 25% and 10% yields, respectively (Table 1, entries 10 and 11). The optimized reaction conditions used only 5 mol% of CuBr to afford an isolated yield of 80% in a 2:1 MeCN– water ratio (Table 1, entry 6).

 Table 2
 Synthesis of Pinacol Arylboronate

N; I	₂ BF ₄		Bpin I			
$R \xrightarrow[l]{} + B_2 pin_2 \xrightarrow{CuBr (5 mol\%), r.t.} R \xrightarrow[l]{} B_2 pin_2 \xrightarrow{MeCN-H_2O (2:1)} R \xrightarrow{II}$						
Entry	Products ^a		Time (h)	Yield (%) ^b		
1		2b	5	70		
2	$H_2N - S = O + O + O + O + O + O + O + O + O + O$	2c	3	75		
3	HOOC	2d	3	78		
4	MeOOC	2e	4	72		
5		2f	4	73		
6	O ₂ N-C	2g	4	85		
7	O_2N	2h	5	54		
8		2i	6	24		
9		2j	4	70		
10	BrB-O	2k	5	40		
11		21	3	77		
12	F ₃ C-C-BO-C	2m	3	68		
13		2n	6	42		

^a All products were confirmed by comparison of ¹H NMR and mass spectra.

^b Isolated yields.

With these results in hand, we examined the scope of the reaction and obtained a variety of the expected pinacolsubstituted phenylboronates in moderate to good yields under the optimized reaction conditions (Table 2).¹⁴

All of the reactions were completed within six hours and afforded the desired pinacol arylboronates. Moreover present reaction rules of the steric and electronic effects were in agreement with results reported which using aryldiazonium salts as borylation material.9-11 The meta- and para-substituted aryldiazonium salts favored the reaction while ortho-substituted aryldiazonium salts gave only lower yields (Table 2, entry 8). Substrates with electronwithdrawing groups showed better reactivity than electron-donating groups did. But the electronic effect might play a dominant role in the case of pinacol 3-nitro-5-methylphenyl boronate (Table 2, entry 9). Finally, it was worth noting that substrates bearing bromo and aminosulfonyl substituents could also be employed in this reaction affording moderate yields (Table 2, entries 2 and 10).

In conclusion, we have developed a new procedure, which is compatible with green chemistry principles, for the synthesis of arylboronates. Putative advantages over the known methodology include: 1) providing direct access to arylboronates bearing halo and acidic substituents; 2) mild conditions and using water as solvent; and 3) a catalytic amount of Cu(I) salt additive reduces the metal contamination. Though the negative effect from steric hindrance can reduce the scope of the method, we believe that this protocol is a useful addition to known procedures for arylboronate synthesis.

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References

- (1) For reviews, see: (a) Suzuki, A. Acc. Chem. Res. 1982, 15, 178. (b) Miyaura, N.; Suzuki, A. Chem. Rev. 1995, 2457. (c) Miyaura, N. Top. Curr. Chem. 2002, 219, 11. (d) Miyaura, N. Bull. Chem. Soc. Jpn. 2008, 81, 1535.
 - (e) Miyaura, N. Synlett 2009, 2039.
- (2) (a) Beveridge, R. E.; Fernando, D.; Gerstenberger, B. S. Tetrahedron Lett. 2010, 5, 5005. (b) Collman, J. P.; Zhong, M. Org. Lett. 2000, 2, 1233.
- (3) Xu, J. M.; Wang, X. Y.; Shao, C. W.; Su, D. Y.; Cheng, G. L.; Hu, Y. F. Org. Lett. 2010, 12, 1964.
- (4) Andaloussi, M.; Lindh, J.; Savmarker, J.; Sjöberg, P. J. R.; Larhed, M. Chem.-Eur. J. 2009, 15, 13069.

- (5) For reviews, see: (a) Ishiyama, T.; Miyaura, N. J. Synth. Org. Chem. Jpn. 1999, 57, 503. (b) Ishiyama, T.; Miyaura, N. J. Organomet. Chem. 2000, 611, 392. (c) Miyaura, N. In Catalytic Heterofunctionalization; Togni, A.; Grützmacher, H., Eds.; Wiley-VCH: Chichester, 2001, Chap. 3.
- (6) (a) Murata, M.; Watanabe, S.; Masuda, Y. J. Org. Chem. 1997, 62, 6458. (b) Murata, M.; Oyama, T.; Watanbe, S.; Masuda, Y. J. Org. Chem. 2000, 65, 164. (c) Baudoin, O.; Guénard, D.; Guéritte, F. J. Org. Chem. 2000, 65, 9268. (d) Broutin, P. E.; Cerna, I.; Campaniello, M.; Leroux, F.; Colobert, F. Org. Lett. 2004, 6, 4419. (e) Murata, M.; Sambommatsu, T.; Watanabe, S.; Masuda, Y. Synlett 2006, 1867.
- (7) (a) Brown, H. C.; Srebnik, M.; Cole, T. E. Organometallics 1986, 5, 2300. (b) Brown, H. C.; Cole, T. E. Organometallics 1983, 2, 1316.
- (8) (a) Fürstner, A.; Seidel, G. Org. Lett. 2002, 4, 541. (b) Zhu, L.; Duquette, J.; Zhang, M. J. Org. Chem. 2003, 68, 3729. (c) Giroux, A. Tetrahedron Lett. 2003, 44, 233. (d) Billingsley, K.; Barder, T. E.; Buchwald, S. L. Angew. Chem. Int. Ed. 2007, 46, 5359.
- (9) Willis, M. D.; Strongin, M. R. Tetrahedron Lett. 2000, 41, 8683
- (10) Ma, Y. D.; Song, C.; Jiang, W.; Xue, G. P.; Cannon, F. J.; Wang, X. M.; Andrus, B. M. Org. Lett. 2003, 5, 4635.
- (11) Mo, F. Y.; Jiang, Y. B.; Qiu, D.; Zhang, Y.; Wang, J. B. Angew. Chem. Int. Ed. 2010, 49, 1846.
- (12) General Procedure for the Synthesis of 1a-n A solution of aromatic amines (20 mmol) in HCl (6 mL) in a flask was cooled to 0 °C and diazotized with 1.42 g (22 mmol) of NaNO2. The temperature must be kept below 5 °C. After 15 min, the ice-cold solution of NaBF₄ was rapidly poured into the flask, which had been cooled below 0 °C. The temperature should remain below 5 °C. Powerful stirring was required to agitate the thick magma at this stage. After 30 min stirring, the solid was filtered with Büchner funnels. The crystal of aryldiazonium salts was washed with iced H₂O, with MeOH, and with commercial Et₂O.
- (13) Kochi, J. K. J. Am. Chem. Soc. 1957, 79, 2942.
- (14) General Procedure for the Synthesis of 2a-n Aryldiazonium tetrafluoroborate salts (2 mmol) and B₂pin₂ (2 mmol) were resolved in MeCN (6 mL) and H₂O (3 mL). After the solution was clear, CuBr (0.1 mmol) was added. The resulting reaction mixture was allowed to stir for 5-6 h at r.t. The solution was then concentrated under reduced pressure. The residue was diluted with brine. The H₂O layer was extracted with EtOAc several times. The combined organic layer was dried over anhyd Na2SO4 and concentrated under reduced pressure. The crude product was purified on silica gel by flash column chromatography with EtOAc and hexane.

Compound **2a**: ¹H NMR (400 MHz, CDCl₂): $\delta = 1.39$ (s, 12 H, CH₃), 7.93 (d, J = 8.1 Hz, 2 H, HAr), 8.12 (d, J = 8.1 Hz, 2 H, HAr). MS (EI): *m/z* (%) = 248 (2.8) [M⁺], 233 (57.3), 162 (57.9), 149 (100), 148 (24.9), 85 (10.9), 43 (10.1).