

A Publication of Reliable Methods for the Preparation of Organic Compounds

## **Working with Hazardous Chemicals**

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full accessed of charge text can be free at http://www.nap.edu/catalog.php?record\_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.,* its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.



A Publication of Reliable Methods for the Preparation of Organic Compounds

## **Working with Peroxy Compounds**

Caution! Reactions and subsequent operations involving peracids and peroxy compounds should be run behind a safety shield. Peroxy compounds should be added to the organic material, never the reverse. For relatively fast reactions, the rate of addition of the peroxy compound should be slow enough so that it reacts rapidly and no significant unreacted excess is allowed to build up. The reaction mixture should be stirred efficiently while the peroxy compound is being added, and cooling should generally be provided since many reactions of peroxy compounds are exothermic. New or unfamiliar reactions, particularly those run at elevated temperatures, should be run first on a small scale. Reaction products should never be recovered from the final reaction mixture by distillation until all residual active oxygen compounds (including unreacted peroxy compounds) have been destroyed. Decomposition of active oxygen compounds may be accomplished by the procedure described in Korach, M.; Nielsen, D. R.; Rideout, W. H. Org. Synth. 1962, 42, 50 (Org. Synth. 1973, Coll. Vol. 5, 414). [Note added April 2018].



### Synthesis of Arylboronic Pinacol Esters from Corresponding Arylamines

Di Qiu, He Meng, Liang Jin, Shengbo Tang, Shuai Wang, Fangyang Mo, Yan Zhang and Jianbo Wang<sup>\*1</sup>

Beijing National Laboratory of Molecular Sciences (BNLMS) and Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China

Checked by Austin Smith and Margaret Faul Discussion Addendum: Org. Synth. 2019, 96, 232



#### Procedure

A. 4,4,5,5-*Tetramethyl*-2-(4-*nitrophenyl*)-1,3,2-*dioxaborolane* (2). A 3-necked 250-mL round-bottomed flask equipped with a 2.5 cm rod-shaped, Teflon coated magnetic stir bar and fitted with a reflux condenser, glass addition funnel, and thermocouple is charged with 4-nitroaniline **1** (5.52 g, 39.6 mmol, 1.0 equiv), diboronpinacol ester (B<sub>2</sub>pin<sub>2</sub>, 10.66 g, 41.5 mmol, 1.05 equiv), and benzoyl peroxide (193 mg, 0.77 mmol, 0.02 equiv) under ambient atmosphere (Notes 1 and 2). The mixture is dissolved in MeCN (60 mL), and the resulting solution is stirred (700 rpm) at 22 °C with the temperature maintained by a water bath. *tert*-Butyl nitrite (*t*BuONO, 6.17 g, 53.8 mmol, 1.36 equiv) diluted by MeCN (40 mL) is then added via an addition funnel over a 1 h time period (Notes 3 and 4). The solution is allowed to stir at 23 °C for an additional 4 h, with the temperature maintained by a water bath (Note 5). Upon complete consumption of **1** as indicated by TLC analysis, the resulting solution is concentrated with a rotary evaporator to remove MeCN (40 °C, 40 mmHg) (Note 6). The crude

*Org. Synth.* **2014**, *91*, 106-115 DOI: 10.15227/orgsyn.091.0106 106

Published on the Web 1/22/2014 © 2014 Organic Syntheses, Inc.



residue is filtered over a flash silica gel plug (60 g) eluting with petroleum ether-ethyl acetate (20:1, 750 mL) until TLC analysis shows that no product **2** is still eluting from the silica gel (Note 7). The filtrate is then concentrated with a rotary evaporator (25 °C, 40 mmHg), and the residue is further purified by silica gel column chromatography, eluting with approximately 500 mL petroleum ether until product emerges as indicated by TLC, and then eluting with approximately 1000 mL of petroleum ether-ethyl acetate (100:1)(Note 8). The combined eluents are concentrated with a rotary evaporator (25 °C, 40 mmHg) and further evaporated with an oil vacuum pump for 30 min at room temperature to afford the product **2** (7.10–7.32 g, 72–74%) as a pale yellow solid (Note 9), which was >97% pure as determined by GC analysis (Note 10).

#### Notes

- 1. 4-Nitroaniline (99%) was purchased from Aldrich Chemical Company, Inc. and used as received. The submitters used 4-nitroaniline that was supplied by Sinopharm.
- 2. Diboronpinacol ester (B<sub>2</sub>pin<sub>2</sub>, 99%) and benzoyl peroxide (BPO, 97%) were purchased from Aldrich Chemical Company, Inc. and used as received. The submitters used diboronpinacol ester (B<sub>2</sub>pin<sub>2</sub>) from Ouhe Corporation in Beijing, China.
- 3. MeCN (>99%) was purchased from Aldrich Chemical Company and used as received. The submitters used MeCN (AR) from Beijing Chemical Corporation. There action is not sensitive to the presence of water. *tert*-Butyl nitrite (*t*BuONO, 90%) was purchased from Aldrich Chemical Company, Inc. and used as received.
- 4. The temperature of the solution rose from 22 °C to 23.5 °C during the 1h addition of *t*BuONO. No gas evolution or solvent reflux was observed.
- 5. A water bath was used throughout the course of the 4 h reaction, with the temperature stabilizing at 23 °C. No gas evolution or solvent reflux was observed.
- 6. TLC analysis was performed with silica gel plates (2.5 cm x 7.5 cm, glass backed, purchased from EMD Chemicals in Darmstadt, Germany), using petroleum ether-ethyl acetate (3:2) as eluent. The aniline **1** is yellow by visible light and dark gray under 254 nm UV lamp.  $R_f$ = 0.31 (petroleum ether-ethyl acetate, 3:2).

Org. Synth. 2014, 91, 106-115

107



- 7. For silica gel column chromatography, 230-400 mesh, 0.040-0.063 mm particle size silica gel (EMD Chemicals, Darmstadt, Germany) was employed. TLC analysis was performed with silica gel plates (2.5 cm x 7.5 cm, glass backed, purchased from EMD Chemicals in Darmstadt, Germany), using petroleum ether-ethyl acetate (20:1) as eluent. The product **2** is purple under 254 nm UV lamp.  $R_f$ = 0.23 (petroleum ether-ethyl acetate, 20:1).
- 8. The crude residue was dissolved in 20:1 petroleum ether-ethyl acetate (15 mL), and the solution was charged onto a column (diameter = 5 cm) of silica gel (220 g). The column was eluted with approximately 500 mL petroleum ether. When TLC analysis showed that product 2 appeared from the column, the eluent was changed to petroleum ether-ethyl acetate (100:1, approximately 1000 mL). Fractions 16-35 were indicated by TLC to contain 2 and thus combined and evaporated (25 °C, 40 mmHg).
- Characterization data of 2: 4,4,5,5-Tetramethyl-2-(4-nitrophenyl)-1,3,2-dioxaborolane (2). Pale yellow solid; R<sub>f</sub>= 0.23(petroleum ether-ethyl acetate, 20:1); mp = 108.5–109.5 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 1.37 (s, 12H), 7.96 (d, *J* = 8.0 Hz, 2H), 8.18 (d, *J* = 8.0 Hz, 2 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 24.8, 84.6, 122.3, 135.6, 149.8, IR (thin film): 2961, 1600, 1519, 1365, 1343, 1141, 1086, 857, 701 cm<sup>-1</sup>. EI-MS (*m*/*z*, relative intensity): 249 (M<sup>+</sup>, 18), 234 (100), 163 (51), 150 (23), 149 (6), 104 (9), 85 (7), 59 (7), 43 (11), 42 (7). HRMS (ESI) calcd for C<sub>12</sub>H<sub>17</sub>BNO<sub>4</sub> [M+H]<sup>+</sup> 250.1251; found 250.1245. Anal. calcd for C<sub>12</sub>H<sub>16</sub>BNO<sub>4</sub>: C, 57.87; H, 6.47; N, 5.62. Found: C, 58.12; H, 6.88; N, 5.41.
- 10. GC conditions: Agilent 6890N; column 19091J-413 (30 m x 0.32 mm), HP-5; temperature profile: initial temp = 61 °C, final temp = 280 °C, temperature gradient = 20 °C /min. Retention time of **2**: 11.29 min.

#### Handling and Disposal of Hazardous Chemicals

The procedures in this article are intended for use only by persons with prior training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011 www.nap.edu). All chemical waste should be disposed of in accordance with local regulations.

Org. Synth. 2014, 91, 106-115

108



For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

These procedures must be conducted at one's own risk. *Organic Syntheses, Inc.,* its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

#### Discussion

The pinacol arylboronates can be accessed by Pd-catalyzed borylation of arylhalides (Miyaura borylation), or by Ir- or Rh-catalyzed direct borylation via aromatic C-H bond activation. These borylation methods have been widely applied in organic synthesis. The direct conversion of aromatic amine to arylboronates represents an entirely different method. It is metalfree, using cheap and abundant arylamines as starting materials. The reaction is carried out under mild conditions and tolerates various functional groups.

The procedure described here is based on our initial communication.<sup>2</sup> We have noted that the substituents on the aromatic ring of arylamine substrates significantly affect the yields of borylation products. Recently, we have reported modified reaction conditions, under which the borylation is carried out in MeCN at 80 °C without the use of BPO.<sup>3</sup> In most cases, the modified reaction conditions give slightly improved yields. For *p*-nitroaniline **1** and *p*-toluidine **5**, the borylation has also been carried out under modified reaction conditions (MeCN, 80 °C, without BPO). The borylation products were obtained in 59% and 58% yields, respectively. In Figure 1 and Figure 2, the substrate scope of the metal-free borylation has been summarized.

Org. Synth. 2014, 91, 106-115

109



# Figure 1. Substrate Scope of Borylation in the Presence of BPO at Room Temperature<sup>2</sup>



<sup>*a*</sup> Isolated yields by column chromatography. <sup>*b*</sup> The reaction gave complex mixture with trace amount of product. <sup>*c*</sup> Benzidine was used as substrate. B<sub>2</sub>pin<sub>2</sub> (2.2 equiv) and *t*BuONO (3 equiv) were used. <sup>*d*</sup> Reaction was carried out at 60 °C with 10% BPO and 1.2 equiv of B<sub>2</sub>pin<sub>2</sub>.

Org. Synth. 2014, 91, 106-115

110



Figure 2. Substrate Scope of Borylation without the use of BPO at 80 °C<sup>3</sup>

<sup>a</sup> Isolated yields by column chromatography. <sup>b</sup> Arylamine (0.5 mmol), B<sub>2</sub>pin<sub>2</sub> (1.1 equiv), *t*BuONO (1.5 equiv), MeCN (1.5 mL), 2 h. <sup>c</sup> Isolated by recrystallization. <sup>d</sup> Yields in brackets refer to GC yield measured with GC-MS instrument (mesitylene as internal standard).

#### References

1. Beijing National Laboratory of Molecular Sciences (BNLMS) and Key Laboratory of Bioorganic Chemistry and Molecular Engineering of

Org. Synth. 2014, 91, 106-115

111

rganic ntheses

Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China; Email: <u>wangjb@pku.edu.cn</u>. The project is supported by National Basic Research Program (973 Program, No. 2012CB821600), Natural Science Foundation of China (No. 21272010).

- 2. Mo, F.; Jiang, Y.; Qiu, D.; Zhang, Y.; Wang, J. Angew. Chem. Int. Ed. 2010, 49, 1846–1849.
- Qiu, D.; Jin, L.; Zheng, Z.; Meng, H.; Mo, F.; Wang, X.; Zhang, Y.; Wang, J. J. Org. Chem. 2013, 78, 1923–1933.

#### Appendix Chemical Abstracts Nomenclature (Registry Number)

4,4,4',4',5,5,5',5'-Octamethyl-2,2'-bi(1,3,2-dioxaborolane): diboronpinacol ester; (73183-34-3) *tert*-Butyl nitrite; (540-80-7) Benzoyl peroxide; (94-36-0) 4-Nitroaniline; (100-01-6) 4,4,5,5-Tetramethyl-2-(4-nitrophenyl)-1,3,2-dioxaborolane; (171364-83-3)



Di Qiu was born in Tianjin of China. He received his B.S. degree from Peking University in 2010. He is now a graduate student in Prof. Jianbo Wang's laboratory. His current research projects are focused on gold-catalyzed C-H bond functionalization and the transformations based on aryldiazonium salts.

Org. Synth. 2014, 91, 106-115

112





He Meng was born in September 1991 in Shijiazhuang of Hebei province. He is expecting B.S.degree in chemistry of Peking University. Now he is a senior student in Prof. Jianbo Wang's group.



Liang Jin was born in April 1991 in Shanghai of China. He has received his B.S. degree (in Prof. Jianbo Wang's group) from Peking University in 2013. Now he is a graduate student in Prof. Huwei Liu's group in chemistry department of Peking University.



Shengbo Tang was born in September 1992 in Jilin province of China. He is expecting B.S. degree in chemistry of Peking University. Now he is a junior student in Prof. Jianbo Wang's group. His hobbies are playing basketball and playing guitar.

Org. Synth. 2014, 91, 106-115

113





Shuai Wang was born in April 1993 in Tianjin of China. He is expecting B.S. degree in chemistry of Peking University. Now he is a junior student in Prof. Jianbo Wang's group. His favorite hobby is fitness.



Fanyang Mo was born in Liaoning Province of China. He received his B.Sc. and M.Sc. degrees from Beijing Institute of Technology (P. R. of China) in 2004 and 2006 under the supervision of Professor Zhiming Zhou. He then obtained his Ph.D. from Peking University, under the supervision of Prof. Jianbo Wang in 2010. He is currently a postdoctoral fellow in Prof. Guangbin Dong's group at University of Texas at Austin.



Yan Zhang was born in Shandong province of China. She received her B.S. and Ph. D. degrees from Lanzhou University. She continued her research as a postdoctoral fellow in Hong Kong University of Science and Technology (2002 -2004), University of Innsbruck & Leibniz Institute of Surface Modification (IOM) e. V. (2004-2005), University of Missouri-St. Louis (2005-2006), and Auburn University (2006-2008). She has joined Peking University since 2008 as an associate professor. Her research focuses on the application of transition metal complexes of *N*-heterocyclic carbenes and synthesis of small biological compounds.

Org. Synth. 2014, 91, 106-115

114





Jianbo Wang was born in Zhejiang province of China. He received his B.S. degree from Nanjing University of Science and Technology in 1983, and his Ph.D. from Hokkaido University in 1990. He was a postdoctoral associate at the University of Geneva from 1990 to 1993, and University of Wisconsin-Madison from 1993 to 1995. He began his independent academic career at Peking University in 1995. His research interests include the catalytic metal carbene transformations.



Austin G. Smith was born in Hartford, CT in 1984. He graduated in 2006 with a B.A. in chemistry from the College of the Holy Cross in Worcester, MA. He obtained his Ph.D from the University of North Carolina at Chapel Hill in 2011, where he studied stereoselective ring-opening reactions with donor-acceptor cyclopropanes under the direction of Professor Jeffrey Johnson. From 2011-2012 he was a postdoctoral research associate under the direction of Professor Huw M. L. Davies at Emory University. Austin joined the Chemical Process Research & Development group at Amgen in Thousand Oaks, CA in 2012.

Org. Synth. 2014, 91, 106-115

115

#### 11/8/2013 8:18:22 AM

Acquisition Time (sec)	5.1118	Comment	ausmith	Date	07 Nov 2013 14:06:56				
Date Stamp	07 Nov 2013 14	4:06:56		File Name	\\scone\NMR-Archive\data\ausmith\nmr\120985-46-4\10\PDATA\1\1r				
Frequency (MHz)	400.23	Nucleus	1H	Number of Transients	32	Origin spect			
Original Points Count	32768	Owner	shr-ato-nmr1	Points Count	32768	Pulse Sequence zg30			
Receiver Gain	36.00	SW(cyclical) (Hz)	6410.26	Solvent	CHLOROFORM-d				
Spectrum Offset (Hz)	2406.7605	Spectrum Type	STANDARD	Sweep Width (Hz)	6410.06 Temperature (degree C) 27.000				



#### 11/8/2013 1:56:12 PM

Acquisition Time (se	<b>c)</b> 1.1534	Comment	ausmith	Date	07 Nov 2013 2 <sup>-</sup>	1:39:12				
Date Stamp	07 Nov 2013 21	1:39:12		File Name	\\scone\NMR-A	rchive\data\ausmith\nmr\^	20985-46-5	10\PDATA\1\	1r	
Frequency (MHz)	100.64	Nucleus	13C	Number of Transients	4096	Origin	spect			
Original Points Coun	t 32768	Owner	shr-ato-nmr1	Points Count	32768	Pulse Sequence	zgpg30			
Receiver Gain	645.00	SW(cyclical) (Hz)	28409.09	Solvent	CHLOROFORM	И-d				
Spectrum Offset (Hz)	12076.5537	Spectrum Type	STANDARD	Sweep Width (Hz)	28408.22	Temperature (degree	<b>C)</b> 27.000			
120985-46-5.	010.001.1r.♥₽tica	alScaleFactor = 0.4 B + B + C + C 2 2 2 2 2 2 2 2 2 2 2 2 2				64,60 76,7.37 76,7.3 76,7.3		24.83		
				Chemical Shift (p	ppm)					
1 24.83 24	12) Height									
2 7673 77	22.2 0.0505									
3 77.05 77	54.2 0.0529									
4 77 37 77	36.3 0.0526									
5 84.60 85	13.7 0.1272									
6 122 34 123	11.9 0.1723									
7 135.63 136	49.7 0.2287									
2 76.73 77.   3 77.05 77.   4 77.37 77.   5 84.60 85   6 122.34 123   7 135.63 136	22.2 0.0505   54.2 0.0529   36.3 0.0526   13.7 0.1272   11.9 0.1723   49.7 0.2287									