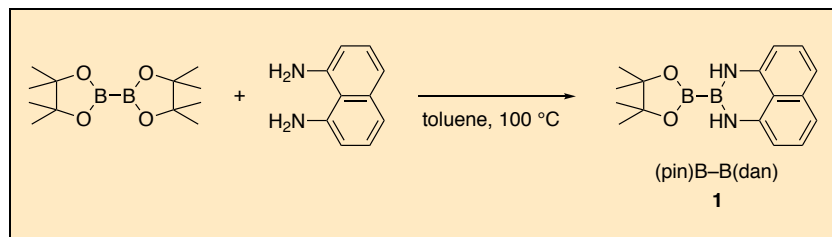


Preparation of (pin)B–B(dan)

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Checked by Feng Peng and Kevin Campos



Procedure (Note 1)

A. (pin)B–B(dan) (1). A flame-dried 50 mL two-necked round-bottomed flask equipped with a 1.5 cm Teflon-coated magnetic oval stir bar, a water condenser capped with rubber septum and a three-way stopcock, which is purged with argon, is charged with bis(pinacolato)diboron (6.35 g, 25.0 mmol) (Note 2) and toluene (15 mL) (Note 3). To the colorless solution (Figure 1), which is degassed by three freeze-pump-thaw cycles, is added 1,8-diaminonaphthalene (3.95 g, 25.0 mmol) (Note 4), and the resulting deep red solution is capped with a glass septum and heated in a silicon oil bath at 100 °C for 48 h under argon atmosphere (Figure 2) (Note 5). The mixture is allowed to cool to ambient temperature and an orange slurry forms. The solvent is removed by rotary evaporation (60 °C, 16 mmHg) to afford a red-brown solid (Figure 3). *n*-Hexane (100 mL) (Note 6) is added to the solid, and the resulting mixture is stirred at ambient temperature for 0.5 h. The suspension is filtered through a vacuum filter holder equipped with a PTFE type membrane filter (Figure 4) (Note 7), and the residue is washed with *n*-hexane (2 x 100 mL). The resulting pale brown solid (Figure 5) is dissolved in ethyl acetate (200 mL) (Note 8), treated with activated charcoal (1.5 g)

(Note 9) at 20 °C for 2 h with stirring (Figure 6), and filtered through a Celite pad (5 g) with a Hirsch funnel (Figures 7 and 8). This activated charcoal treatment of the filtrate is repeated two more times (Figure 9). After removal of the solvent by rotary evaporation (40 °C, 16 mmHg) (Figure 10), the residue is stirred with 1:50 ethanol:*n*-hexane (100 mL) at 20 °C for 0.5 h (Figure 11) (Note 10). The first crop is collected by filtration on a vacuum filter holder equipped with a PTFE type membrane filter (Figure 4), and the filtrate is concentrated by rotary evaporation (40 °C, 16 mmHg). After the same treatment of the residue with 1:50 ethanol:*n*-hexane (100 mL), the second crop is collected by the filtration. Repetitive treatment of the filtrate with 1:50 ethanol:*n*-hexane (100 mL) gives a third crop, and the combined solid is dried overnight at 3.0 mmHg to afford the analytically pure (pin)B–B(dan) (5.20 g, 71%) as an off-white solid (Figure 12) (Notes 11, 12, 13, and 14).



Figure 1. Reaction setup



Figure 2. After heating

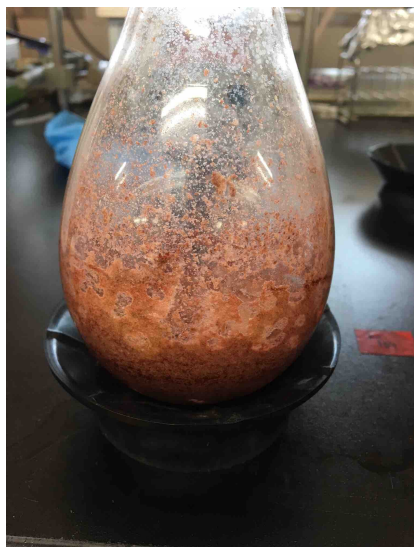


Figure 3. After evaporation

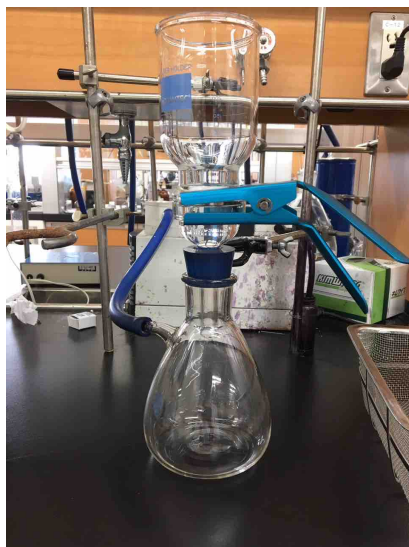


Figure 4. Filtration apparatus



Figure 5. After washing



Figure 6. Activated charcoal treatment



Figure 7. Filtration apparatus



Figure 8. After first treatment

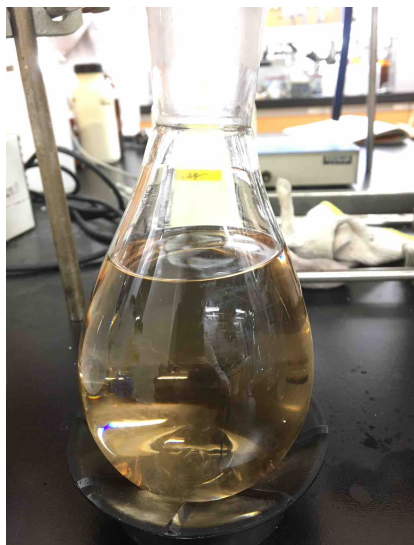


Figure 9. After third treatment

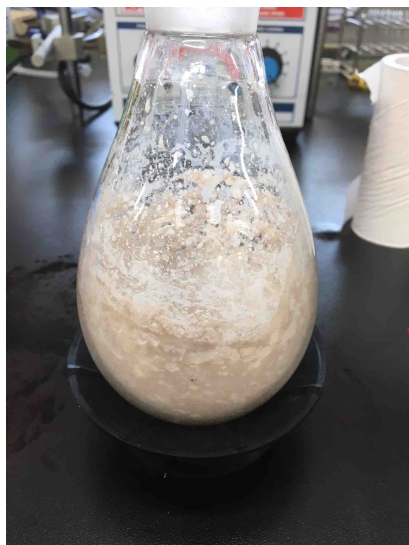


Figure 10. After evaporation

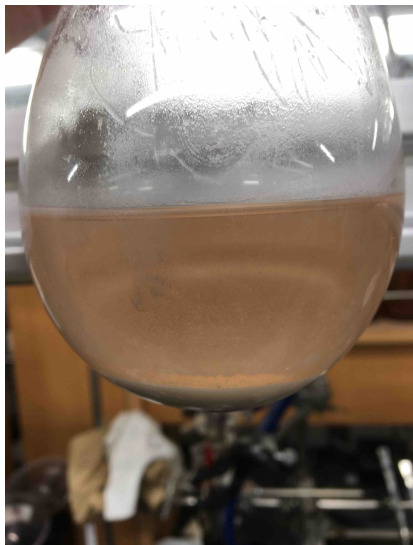


Figure 11. After ethanol-hexane treatment



Figure 12. Product 1

Notes

1. Prior to performing each reaction, a thorough hazard analysis and risk assessment should be carried out with regard to each chemical substance and experimental operation on the scale planned and in the context of the laboratory where the procedures will be carried out. Guidelines for carrying out risk assessments and for analyzing the hazards associated with chemicals can be found in references such as Chapter 4 of "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at <https://www.nap.edu/catalog/12654/prudent-practices-in-the-laboratory-handling-and-management-of-chemical>. See also "Identifying and Evaluating Hazards in Research Laboratories" (American Chemical Society, 2015) which is available via the associated website "Hazard Assessment in Research Laboratories" at <https://www.acs.org/content/acs/en/about/governance/committees/chemicalsafety/hazard-assessment.html>. In the case of this procedure, the risk assessment should include (but not necessarily be limited to) an evaluation of the potential hazards associated with

- bis(pinacolato)diboron, 1,8-diaminonaphthalene, toluene, *n*-hexane, ethyl acetate and ethanol.
2. Bis(pinacolato)diboron (>99%, ChemICHIBA) was used as received.
 3. Toluene (99.5%, Wako Pure Chemical Industries, Ltd.) was dried over activated 4Å molecular sieves (1/16, Wako Pure Chemical Industries, Ltd.) before use. The submitters activated 4Å molecular sieves by using microwaves (500W, 3 x 90 s) and subsequent cycles of vacuum/argon purge.
 4. 1,8-Diaminonaphthalene (>98%, Tokyo Chemical Industry Co., Ltd.) was used as received.
 5. The reaction progress was monitored by GC. A reaction mixture aliquot was withdrawn and diluted with ethyl acetate. GC conditions: Column: TC-1 (GL Science), 30 m x 0.25 mm, film 0.25 µm; Flow rate: 1.89 mL/min; Injector temperature: 250 °C; Oven temperature: 100 °C to 250 °C at 20 °C/min, hold at 250 °C for 10 min; FID temperature: 250 °C; Retention times: (pin)B–B(pin) = 4.4 min, 1,8-diaminonaphthalene = 6.9 min, (pin)B–B(dan) = 12.5 min.
 6. *n*-Hexane (95%, Kanto Chemical Co., Inc.) was used as received.
 7. A vacuum filter holder (KGS-47) and a PTFE type membrane filter (T100A047A) were purchased from ADVANTEC. Pore size = 1 µm.
 8. Ethyl acetate (99%, Japan Alcohol Trading Co., Ltd.) was used as received.
 9. Activated charcoal (Merck, 102186) was used as received.
 10. Ethanol (99.5%, Wako Pure Chemical Industries, Ltd.) was used as received.
 11. The product (**1**) exhibits the following analytical data: mp 191–193 °C; ¹H NMR (500 MHz, CDCl₃) δ: 1.31 (s, 12H), 6.21 (br s, 2H), 6.27 (d, *J* = 7.3 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 2H), 7.08 (dd, *J* = 7.7 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ: 25.1, 83.3, 105.4, 117.6, 121.1, 127.5, 136.4, 140.5; [M + H] calcd for C₁₂H₂₀B₂N₂O₂: 293.1862 Found: 293.1866.
 12. The purity was determined to be 99.8% wt. by quantitative ¹H NMR spectroscopy in CDCl₃ using 47.3 mg of the compound **1** and 76.5 mg of 1,3,5-trimethoxybenzene as an internal standard (D1 = 20 s).
 13. A second reaction on identical scale provided 5.15 g (70%) of the identical product
 14. Alternative isolation procedure: The end-of-reaction mixture is allowed to cool to ambient temperature (an orange slurry formed), 10 mL of toluene is distilled out via rotavap. The resulting orange slurry is filtered to afford a tan cake. Cake is then washed with hexane

(3 x 15 mL) and dried under vacuum (100 mmHg) via N₂ sweep for 3 h (tan solid, 6.1 g) (Figure 13). The resulting tan solid is dissolved in ethyl acetate (200 mL) treated with activated charcoal (1.5 g) at ambient temperature for 2 h with stirring, and filtered through a celite pad (5 g) with a Hirsch funnel. After removal of the solvent by rotary evaporation (40 °C, 16 mmHg), the residue dissolves in 50 mL of isopropyl acetate (IPAC) at 78 °C with a 1.5 cm Teflon-coated magnetic oval stir bar. The resulting solution is then cooled down to rt with stirring in 2 h and a slurry forms. The solvent (40 mL) is then distilled out via rotary evaporation and hexane (60 mL) is charged into the slurry in 1 h under stirring. This slurry is filtered and the cake is washed with hexane (2 x 10 mL). The cake is dried under vacuum with N₂ sweep for 3 h. Analytically pure (pin)B–B(dan) (5.1 g, 99.6 NMR wt%, 70%) as a white solid.

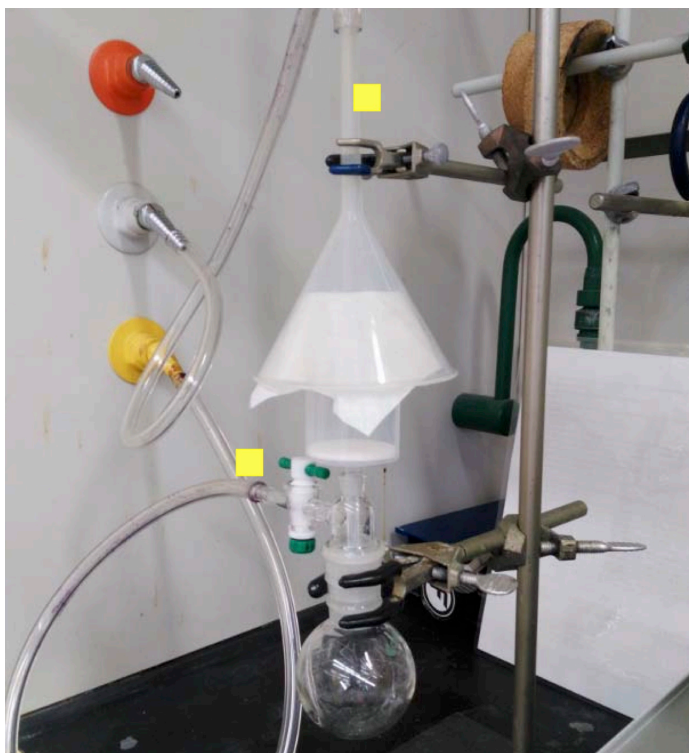


Figure 13. Drying under vacuum with nitrogen sweep

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 text can be accessed free of charge 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.

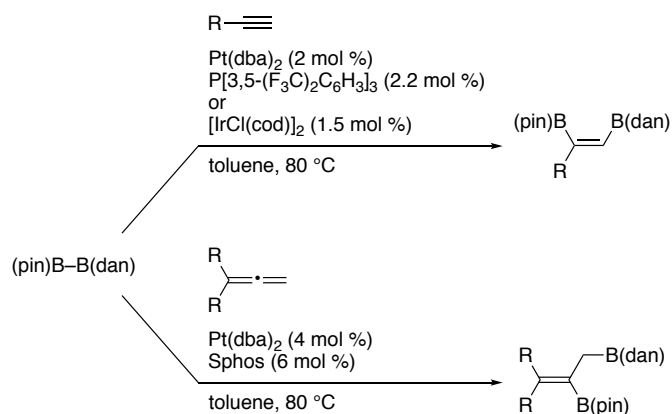
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.

Discussion

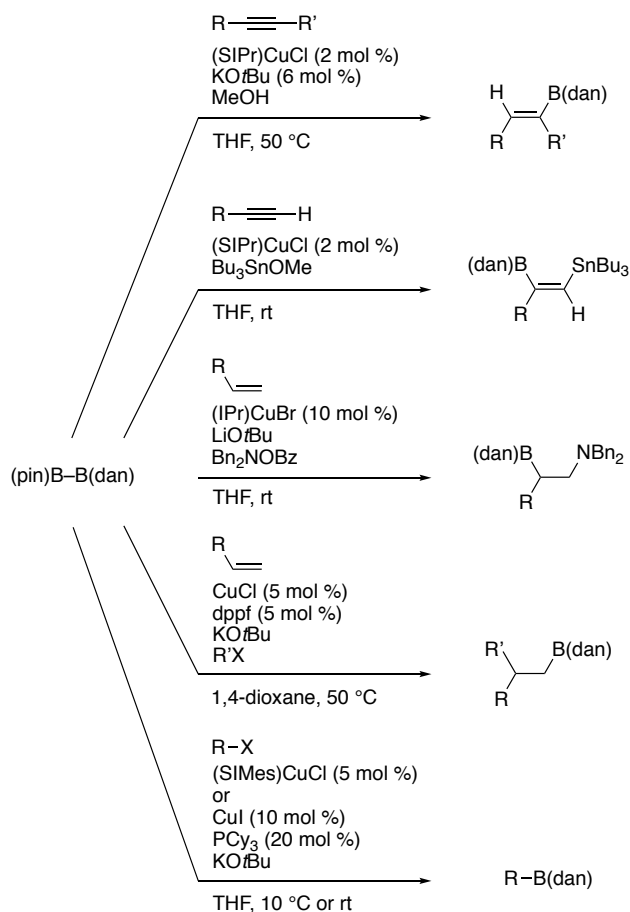
The unsymmetrical diboron (**1**) has proven to be a powerful borylating reagent in organic synthesis, since the first synthesis of **1** and its synthetic application to the Pt- or Ir-catalyzed regioselective diboration of alkynes were reported in 2010 (Scheme 1).² The Pt-catalyzed diboration was also applicable to allenes,³ in which a B(dan) moiety was regioselectively

attached to a terminal carbon of allenes. One of the most characteristic



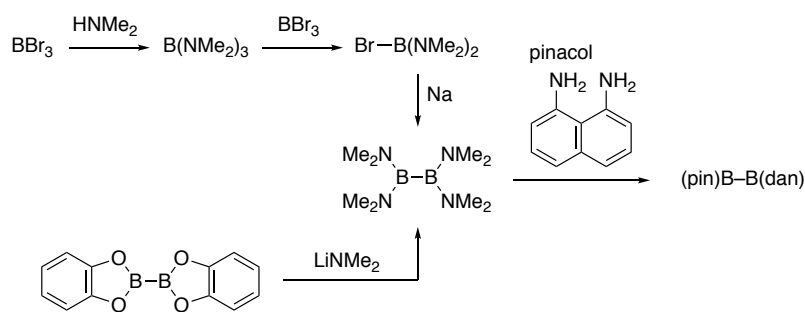
Scheme 1. Catalytic diboration using (pin)B–B(dan)

features of the diboration with **1** is that we can install a cross-coupling-active [B(pin)] and -inactive (“masked”) [B(dan)] moieties into organic frameworks synchronously, leading to the chemoselective cross-coupling of the resulting diborylated compounds at the B(pin) moiety.^{2,3} Furthermore, the high synthetic significance of **1** has also been demonstrated by its conversion into a masked borylcopper species [Cu–B(dan)] through selective σ -bond metathesis. The generated masked borylcopper species acted as a key intermediate in three-component B(dan)-installing reactions of unsaturated C–C bonds, including hydroboration,⁴ borylstannylation,⁵ aminoboration⁶ and carboboration (Scheme 2).⁷ In addition, various organic halides were directly convertible into R–B(dan) by copper-catalyzed substitution reaction.^{8,9}



Scheme 2. Copper-catalyzed borylation using (pin)B-B(dan)

There have been two alternatives for synthesizing **1**, where equimolar amounts of pinacol, 1,8-diaminonaphthalene and tetrakis(dimethylamino)diboron are employed in the presence or absence of 1N ethereal solution of hydrogen chloride (Scheme 3). The required tetrakis(dimethylamino)diboron is prepared from tribromoborane² or bis(catecholato)diboron.^{9c,d} These methods use relatively moisture-sensitive substrates, which have to be handled with care. In contrast, the present method enables **1** to be readily accessed by simply mixing bench-stable substrates of high availability in one step.



Scheme 3. Reported methods for synthesizing (pin)B-B(dan)

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Appendix

Chemical Abstracts Nomenclature (Registry Number)

(pin)B–B(dan): 1*H*-Naphtho[1,8-*de*]-1,3,2-diazaborine, 2,3-dihydro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-; (1214264-88-6)

Bis(pinacolato)diboron: 2,2'-Bi-1,3,2-dioxaborolane, 4,4,4',4',5,5,5',5'-octamethyl-; (73183-34-3)

1,8-Diaminonaphthalene: 1,8-Naphthalenediamine; (479-27-6)



Hiroto Yoshida was born in Fukuoka, Japan, in 1973. He graduated from Kyoto University in 1996 and received his Ph.D. from Kyoto University under the supervision of Professors Tamejiro Hiyama and Eiji Shirakawa in 2001. He then became an Assistant Professor at Hiroshima University in 2001 and was promoted to an Associate Professor in 2006. He received many awards including The Chemical Society of Japan Award for Young Chemists (2007) and The Young Scientists' Prize, The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology (2009). His research interests include (1) catalytic reactions for synthesis of main group organometallics containing boron, tin or silicon, and (2) aryne-based organic synthesis.



Yuya Murashige was born in Yamaguchi, Japan, in 1993. He graduated from Hiroshima University in 2017, and has been a master's course student in the same department, focusing on development of copper-catalyzed borylation reactions.

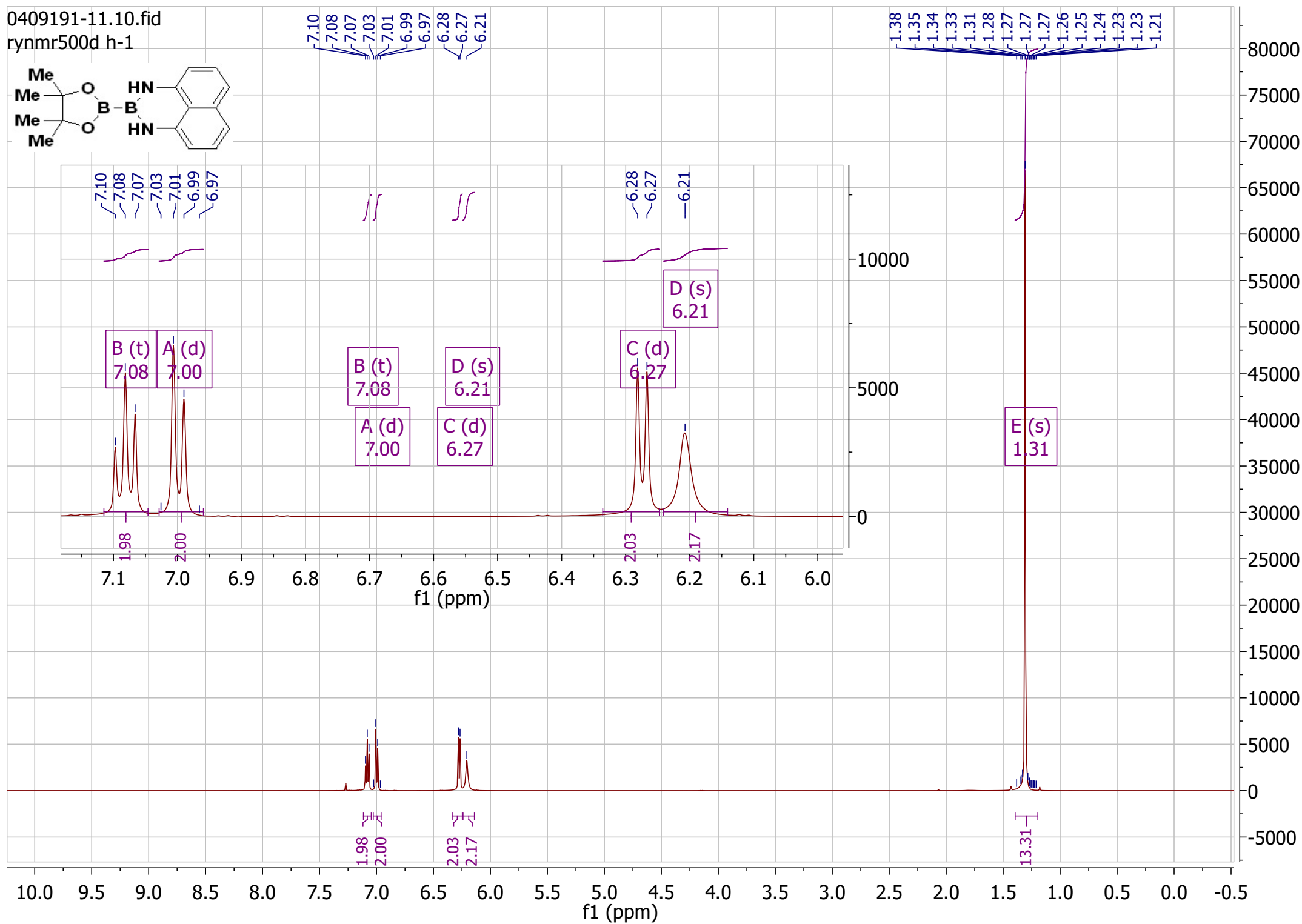
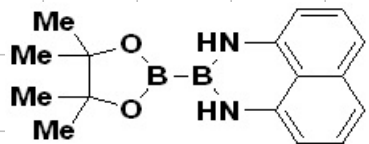


Itaru Osaka received his Ph.D. from University of Tsukuba in 2002 under the supervision of Professor Kazuo Akagi and Professor Hideki Shirakawa. After a 4-year research stint at Fujifilm, he joined Professor R. D. McCullough's group at Carnegie Mellon University as a postdoctoral fellow in 2006. He started his professional carrier at Hiroshima University as an assistant professor in 2009, and moved to RIKEN as a senior research scientist in 2013. He was then appointed as a professor at Hiroshima University in 2016. His research focuses the design and synthesis of π -conjugated polymers for organic electronics.



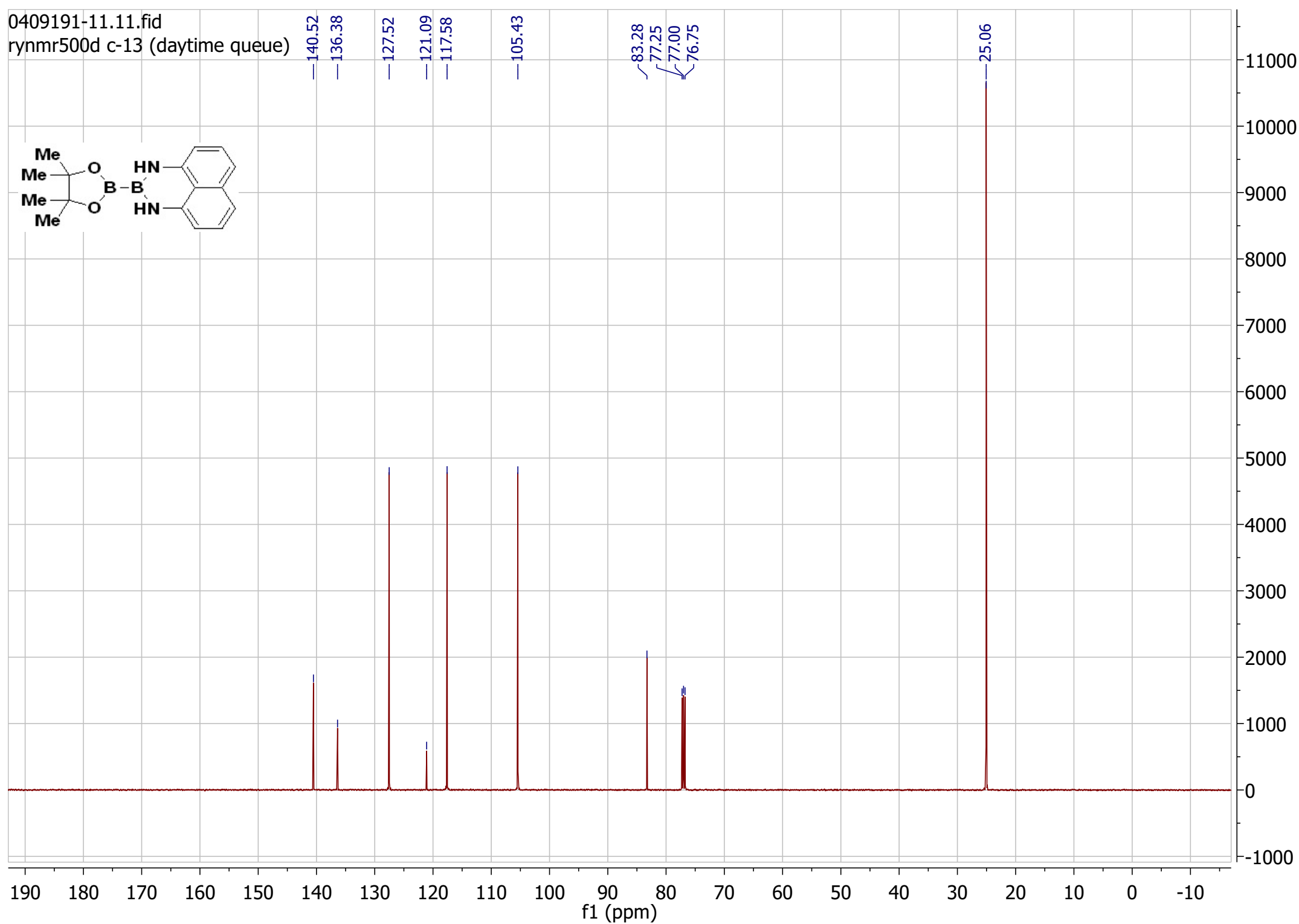
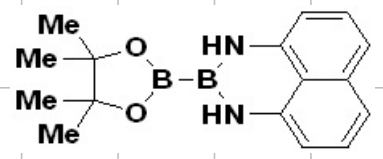
Feng Peng joined the Process Research Department of Merck & Co., Inc. in 2012. His research focuses on using state-of-art organic chemistry to address critical problems in drug development. He received his B. S. degree from Beijing Normal University. He obtained his M.S. under the supervision of Professor Dennis Hall at University of Alberta with a research focus on Boron Chemistry. Feng then moved to New York City, where he obtained Ph.D. in the area of total synthesis (maoecrystal V) with Professor Samuel Danishefsky at Columbia University.

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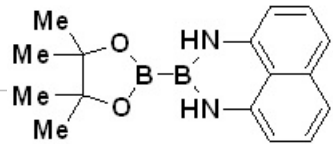


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