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of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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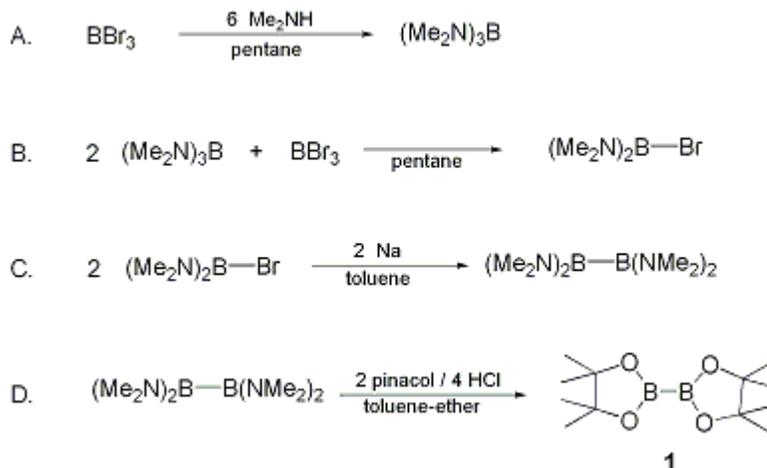
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions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

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BIS(PINACOLATO)DIBORON

[2,2'-Bi-1,3,2-dioxaborolane, 4,4,4',4',5,5,5',5'-octamethyl-]



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Checked by Glenn C. Micalizio and William R. Roush.

1. Procedure

Caution! All the operations should be carried out in a well-ventilated hood, since bromoborane derivatives fume in air and are rapidly hydrolyzed with the evolution of considerable heat.

A. Tris(dimethylamino)borane (Note 1). A 2-L, three-necked flask equipped with a mechanical stirrer, dropping funnel, and a dry ice-cooled reflux condenser connected to a nitrogen source and a bubbler is flushed with nitrogen (Note 2). The flask is charged with 800 mL of pentane (Note 3) and 218 g (4.84 mol) of dimethylamine (Note 4), and cooled to ca. -30°C with a dry ice-methanol bath. A solution of 201 g (0.801 mol) of boron tribromide (Note 5) in 400 mL of pentane is added dropwise through the addition funnel over 3 hr to the vigorously stirred solution while maintaining the bath-temperature at -20°C to -10°C (Note 6). As soon as the addition is begun, a white precipitate of dimethylamine hydrobromide appears. The temperature is allowed to rise to ambient temperature without removing the cooling bath, and the slurry is stirred for 16 hr at room temperature. The precipitate is removed by filtration through a Celite pad on a glass-fritted filter funnel (Note 7). The flask and filter cake are rinsed three times with 60 mL of pentane. The pentane solution is distilled to give 92.7 g (81%) of tris(dimethylamino)borane as a colorless liquid, bp $44-45^\circ\text{C}$ (12 mm), lit.² bp 39°C (10 mm) (Note 8), (Note 9).

B. Bromobis(dimethylamino)borane. A 500-mL, two-necked flask equipped with a magnetic stirring bar, dropping funnel, and a distillation apparatus connected to a nitrogen source and a bubbler is flushed with nitrogen (Note 2). The flask is charged with 100 mL of pentane (Note 3) and 92.7 g (0.648 mol) of tris(dimethylamino)borane, and cooled to -40°C (external bath temperature) with a dry ice-methanol bath. A solution of 81.3 g (0.324 mol) of boron tribromide (Note 5) in 80 mL of pentane is added dropwise to the stirred solution over a period of 1.5 hr maintaining the external bath temperature at -40°C . The cooling bath is removed and the solution is stirred at room temperature for 30 min. Distillation affords 172.8 g (99%) of bromobis(dimethylamino)borane as a colorless liquid, bp $56-58^\circ\text{C}$ (12 mm), lit.³ bp $20-28^\circ\text{C}$ (0.5 mm) (Note 10).

C. Tetrakis(dimethylamino)diboron. A 500-mL, three-necked flask equipped with an airtight mechanical stirrer, a dropping funnel, and a reflux condenser connected to a nitrogen source and a

bubbler is flushed with **nitrogen** (Note 2). The flask is charged with 78 mL of **toluene** (Note 11) and 22.3 g (0.97 g-atom) of **sodium**. The mixture is brought to reflux with an oil bath and the **sodium** is finely pulverized by vigorous stirring. A solution of 135.6 g (0.758 mol) of **bromobis(dimethylamino)borane** in 55 mL of **toluene** is added dropwise at a rate sufficient to maintain a gentle reflux over 45 min. Shortly after the addition is begun, a deep-blue precipitate appears (Note 12). The suspension is heated at reflux for an additional 2.5 hr. The slurry is cooled to room temperature, and filtered through a Celite pad on a sintered-glass funnel (Note 7). The flask and filter cake are rinsed three times with 50 mL of **toluene** (Note 13). The yellow filtrate is concentrated under reduced pressure, and the residual oil is distilled under reduced pressure to give 54 g (72%) of **tetrakis(dimethylamino)diboron** as a colorless liquid, bp 92°C (12 mm), lit.³ bp 55-57°C (2.5 mm) (Note 14).

D. Bis(pinacolato)diboron (1). A 2-L, three-necked flask fitted with a mechanical stirrer, dropping funnel, and a reflux condenser connected to a **nitrogen** source and a bubbler is flushed with **nitrogen** (Note 2). To the flask are added 53.7 g (0.271 mol) of **tetrakis(dimethylamino)diboron** and 510 mL of **toluene** (Note 11), and then a solution of 64.4 g (0.545 mol) of **pinacol** (Note 15) in 340 mL of **toluene**. The flask is immersed in an ice-water bath and a 5.4 M ethereal solution of **hydrogen chloride** (Note 16) (203 mL, 1.10 mol) is added dropwise during 2 hr. As soon as the addition is started, a white precipitate of **dimethylamine hydrochloride** appears. The slurry is stirred at room temperature for an additional 4 hr. The precipitate is removed by filtration in a Büchner funnel with suction, and the filtrate is concentrated on a rotary evaporator to give a white solid. The solid is dissolved in ca. 700 mL of **pentane** and the remaining solid is again removed by filtration. The filtrate is washed three times with 500 mL of water and dried over anhydrous **magnesium sulfate**. The drying agent is removed by filtration and the filtrate is concentrated to ca. 150 mL. The flask is heated to dissolve the resulting precipitate, allowed to cool to room temperature, and then thoroughly chilled in a freezer (−30°C). The first crop is collected by filtration and washed twice with 30 mL of cold **pentane**. The mother liquor is again concentrated to give another crop of crystals. The procedure is repeated two additional times. The combined crystals are dried under reduced pressure (0.1 mm) for 16 hr at room temperature to give 54.3 g (79%) of **1** as colorless plates, mp 138°C, lit.⁴ mp 138°C (Note 17), (Note 18).

2. Notes

1. **Tris(dimethylamino)borane** is available from Aldrich Chemical Company, Inc. It may also be synthesized from **boron trichloride**.²
2. All glassware is predried in an oven at 120°C for 1 hr, assembled while hot, and allowed to cool under a stream of **nitrogen**.
3. **Pentane** is distilled from **lithium aluminum hydride** before use.
4. **Dimethylamine** (bp 6°C) is condensed at −78°C into a 500-mL flask fitted with an inlet tube and a **nitrogen** bubbler. The quantity of **dimethylamine** in the flask is determined by periodic weighing. **Dimethylamine** is either taken from a cylinder (Aldrich Chemical Company, Inc.) or from a mixture of an aqueous 50% solution of **dimethylamine** and **potassium hydroxide**.⁵ Checkers condensed **dimethylamine** directly into the 2-L reaction vessel with periodic weighing.
5. **Boron tribromide** was purchased from Wako Pure Chemical Industries, Ltd. or Aldrich Chemical Company, Inc., and used without further purification.
6. *Caution! Addition at lower than −20°C leads to a violent reaction during warming up to −10-0°C.*
7. A large filter area is recommended. A 1-cm layer of Celite is pressed on a sintered-glass funnel (6 cm × 17 cm). The Celite is dried in an oven at 120°C for 12 hr. A 6-mm Teflon tube is used to connect the flask and the filter funnel through the septa, and the stirred slurry is then transferred to the funnel with the aid of **nitrogen** pressure. Inner pressure of the receiver flask and the funnel is leaked through oil bubblers. The checkers had difficulty with the filter clogging, so they used a Schlenk filter apparatus instead.
8. **Tris(dimethylamino)borane** is moisture sensitive. ¹H NMR (CDCl₃) δ: 2.52 (s, 18 H).
9. The checkers obtained a 63% yield of **tris(dimethylamino)borane**. The checkers obtained bp 57°C (11 mm).
10. **Bromobis(dimethylamino)borane** is moisture sensitive and fumes in air: ¹H NMR (CDCl₃) δ: 2.75 (s, 12 H). The checkers obtained a 96% yield of material with bp 71°C (13 mm).
11. **Toluene** is distilled from molten **sodium** before use.
12. The checkers observed an induction period of approximately 20 min followed by a vigorous

exotherm. It was only after this exotherm occurred that any blue precipitate was observed in the reaction vessel.

13. The residual solid containing unreacted sodium is carefully treated with ethanol.

14. Tetrakis(dimethylamino)diboron is moisture sensitive. ^1H NMR (CDCl_3) δ : 2.67 (s, 24 H) . The checkers observed an unidentified impurity in the ^1H NMR spectrum (δ 2.51, s). The checkers also obtained a slightly better yield (72%) than reported by the submitters (67%) when a freshly opened bottle of sodium was used in this experiment.

15. Pinacol was purchased from Tokyo Kasei Kogyo Co., Ltd. or Aldrich Chemical Company, Inc. , and used without further purification.

16. An ethereal solution of hydrogen chloride is titrated with 0.1 M sodium hydroxide before use.

17. The submitters obtained a 91% yield of bis(pinacolato)diboron.

18. Crystalline bis(pinacolato)diboron can be handled in air and stored in a capped bottle. The physical properties are as follows: ^1H NMR (300 MHz, CDCl_3) δ : 1.25 (s, 24 H) ; ^{11}B NMR (128.3 MHz, toluene) δ 30.61 ($\text{BF}_3 \cdot \text{Et}_2\text{O}$ as external reference, δ 0.00) ; ^{13}C NMR (100 MHz, CDCl_3) δ : 83.4, 24.9 ; IR (KBr) cm^{-1} : 2978, 2930, 1372, 1289, 1189, 1177, 1127, 960, 850, 744, 660, 547 ; high resolution mass spectrum, calcd for $\text{C}_{12}\text{H}_{24}\text{B}_2\text{O}_4$ [M^+], 254.1861, found 254.1867 . Anal. Calcd. for $\text{C}_{12}\text{H}_{24}\text{B}_2\text{O}_4$: C, 56.76; H, 9.53. Found: C, 56.66; H, 9.50.

Bis(pinacolato)diboron is now commercially available from Lancaster Synthesis Ltd., Callery Chemical Co., Aldrich Chemical Company, Inc., and Frontier Scientific Inc.

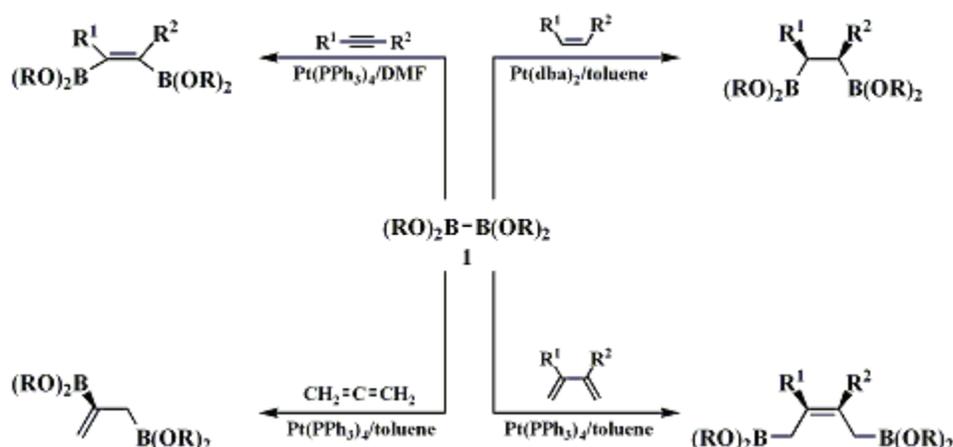
Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

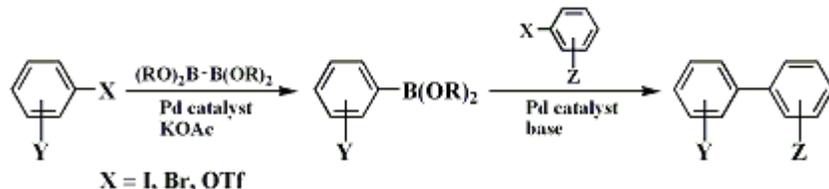
This method is an adaption of the U. S. Borax Research group's procedure³ that illustrates a practical and efficient method for the synthesis of tetra(alkoxo)diborons. Several (alkoxo)diborons, such as tetra(methoxo)-,³ bis(catecholato)-,⁶ and bis(pinacolato)diboron⁴ (**1**), are synthesized from tetrakis(dimethylamino)diboron. The diborons are excellent reagents for the synthesis of various organoboronic esters via the transition metal-catalyzed addition and cross-coupling reactions.^{7,8,9,10,11,12,13,14,15}

The platinum(0) complexes catalyze the addition of **1** to unsaturated hydrocarbons (Scheme 1). The addition to alkynes,⁷ alkenes,⁸ 1,3-dienes,⁹ or allenes¹⁰ stereoselectively provides cis-addition products.

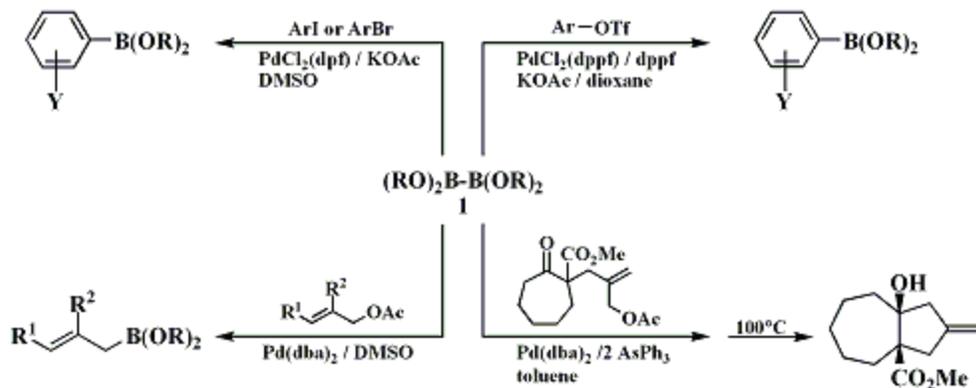


The cross-coupling reaction of **1** with palladium catalyst provides a convenient method for the synthesis of organoboronic esters from organic electrophiles (Scheme 2). Aromatic halides¹¹ and triflates¹² couple with **1** in the presence of $\text{PdCl}_2(\text{dppf})$ and potassium acetate (KOAc) to give arylboronates in high yields. The procedure has a wider application over the conventional synthesis based on the addition of aryllithium or Grignard reagents to trialkyl borates, because the reaction tolerates various functional groups, e.g., $-\text{CO}_2\text{Me}$, $-\text{COMe}$, $-\text{CN}$, and $-\text{NO}_2$. Arylboronic acids and esters

have been used for the synthesis of biaryls via the palladium-catalyzed cross-coupling reaction with aryl electrophiles. The use of diboron allows sequential, double cross-couplings in the same flask to provide biaryls (eq. 1).^{12,13}



Coupling with allyl acetates gives allyl boronates,¹⁴ which exhibit a high diastereoselectivity in the intramolecular allyl boration of carbonyl compounds¹⁵ (Scheme 2).



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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

Bis(pinacolato)diboron:
2,2'-Bi-1,3,2-dioxaborolane, 4,4,4',4',5,5,5',5'-octamethyl- (10); (73183-34-3)

Dimethylamine (8);
Methanamine, N-methyl- (9); (124-40-3)

Tris(dimethylamino)borane:
Borane, tris(dimethylamino)- (8);
Boranetriamine, hexamethyl- (9); (4375-83-1)

Boron tribromide:
Boron bromide (8);
Borane, tribromo- (9); (10294-33-4)

Bromobis(dimethylamino)borane:
Borane, bromobis(dimethylamino)- (8);
Boranediamine, 1-bromo-N,N,N',N'-tetramethyl- (9); (6990-27-8)

Tetrakis(dimethylamino)diboron:
Diborane(4), tetrakis(dimethylamino)- (8);
Diborane(4)tetramine, octamethyl- (9); (1630-79-1)

Sodium (8,9); (7440-23-5)

Pinacol:
2,3-Butanediol, 2,3-dimethyl- (8,9); (76-09-5)