JOC The Journal of Organic Chemistry

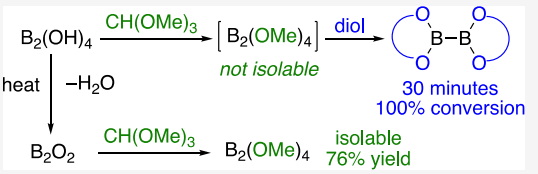
pubs.acs.org/joc Article

Simple and Green Preparation of Tetraalkoxydiborons and Diboron Diolates from Tetrahydroxydiboron

Ryan M. Fornwald,† Anshu Yadav,† Jose R. Montero Bastidas, Milton R. Smith, III,* and Robert E. Maleczka, Jr.*

Cite This: J. Org. Chem. 2024, 89, 6048−6052 Read Online

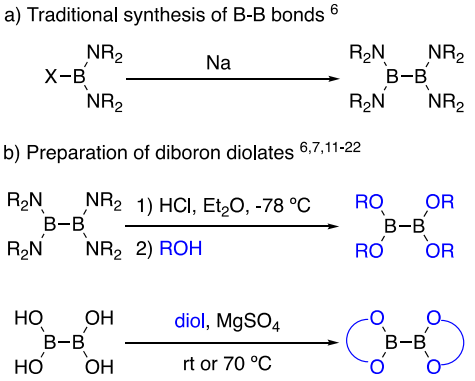
ABSTRACT: Tetraalkoxydiborons can be easily prepared by acid-catalyzed reactions of tetrahydroxydiboron or its anhydride with trialkyl orthoformates. Addition of diols to these reaction mixtures afforded diboron diolates in high yield. In both cases, removal of volatile byproducts is all that is required for the isolation of the diboron. These methods constitute a convenient alternative to previous preparations from tetrakis (dimethylamino) diboron and tetrahydroxydiboron.



1. INTRODUCTION

Diboron diolates have broad applications in synthesis,[1−5] and while they are generally bench-stable compounds, their preparation can be tedious. Boron−boron bonds are commercially prepared via the Wurtz coupling of halobis (dialkylamino) boranes (Scheme 1a).[6,7] While tetrakis (dialkylamino) diborons also have applications in synthesis,[8−10] diboron diolates are far more widely used.[1−5] Their direct preparation from tetrakis (dialkylamino) diborons requires the use of a dry solution of HCl in Et_2O at −78 °C, filtration of dialkylammonium hydrochloride salts, then distillation, sublimation, or crystallization of the diboron diolate.[6,7] However, $B_2(OH)_4$ (**1**) is also readily prepared via hydrolysis of tetrakis (dialkylamino)diboron.[11] Diboron diolates can also be synthesized by stirring a heterogeneous mixture of $B_2(OH)_4$ with a diol and $MgSO_4$ for 24 h (Scheme 1b).[12−22]

Scheme 1. Previous Work



2. RESULTS AND DISCUSSION

Inspired by a previous report for the preparation of thiophene boronic ester from thiophene boronic acid by reaction with trimethyl orthoformate in the presence of an acid catalyst,[23] we have developed an exceptionally fast and convenient method for the preparation of diboron diolates and tetraalkoxydiborons (Scheme 2).

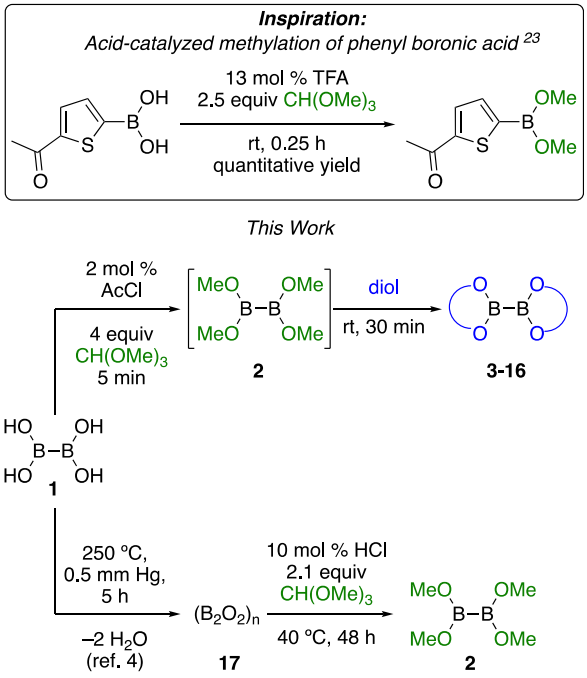
The acetyl chloride-catalyzed reaction of $B_2(OH)_4$ (**1**) with $CH(OMe)_3$ is complete within minutes at room temperature, is not particularly air-sensitive, and offers a visual indicator of completion, producing a homogeneous solution ($B_2(OMe)_4$ (**2**), MeOH, and methyl formate) after consumption of starting material. The diol is then added, the solution stirred briefly, and solvent removed in vacuo to afford the desired diboron in high yield, typically without a need for further purification.

A variety of diboron diolates (**3**−**16**) were prepared on a gram scale (Scheme 3) by using this methodology. Reactions with aliphatic 1,2-diols (**3**−**9**), aliphatic 1,3-diols (**10**−**13**), and phenols such as catechol or 2-hydroxybenzyl alcohol (**14**−**15**) were successful as well as 1,2-diaminobenzene (**16**) formed the desired product. Conversion was low with diisopropyl tartrate, and perfluoropinacol failed to afford any product. Attempts to separate $B_2(OMe)_4$ (**2**) from the MeOH byproduct by distillation were unsuccessful.

B_2eg_2 (**3**) and commonly used B_2pin_2 appear as white solids at room temperature, whereas synthetic B_2pg_2 (**4**) is a colorless liquid. B_2pg_2 was made starting with a racemic mixture of

Received: December 30, 2023
Revised: March 27, 2024
Accepted: April 5, 2024
Published: April 19, 2024

Scheme 2. This Work



propylene glycol that should lead to a mixture of diastereomers and explain its liquid phase (Figure 1). In fact, when the pure enantiomer (*S*)-propylene glycol is used as the starting diol, (*S,S*)-B_2pg_2 is obtained as a crystalline solid. To measure the ratio of the stereoisomers in the mixture of B_2pg_2 diastereomers, we added NMR shift reagents. The methyl groups in the B_2pg_2 mixture appear as one peak, which splits into different ones after the addition of the NMR shift reagent. As expected, the two B_2pg_2 diastereomers are present in a 50:50 mixture corresponding to the meso isomer (*S,R*)-B_2pg_2 and an equimolar mixture of the enantiomers (*S,S*)-B_2pg_2 and (*R,R*)-B_2pg_2.

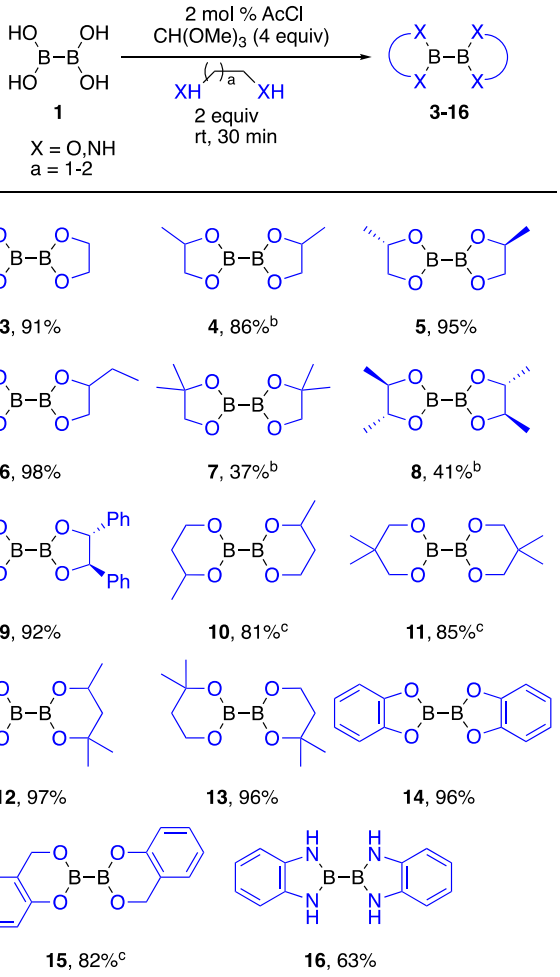
Interestingly, the anhydride of $B_2(OH)_4$ can be prepared quantitatively by heating under vacuum for several hours, generating $(B_2O_2)_n$ (**17**) as a hard white solid (Scheme 2).[11,24] This material failed to react with $CH(OMe)_3$ in the presence of catalytic AcCl, but did so with dry HCl in Et_2O (Scheme 4). These reactions are much slower than those with $B_2(OH)_4$ (**1**) and require gentle heating. Removal of residual $(B_2O_2)_n$ by filtration, and Et_2O and methyl formate by vacuum distillation with a water aspirator afforded $B_2(OMe)_4$ in good yield and 91% purity (containing 4% methyl formate, 2% MeOH, and 3% Et_2O). This is a simple alternative to previous methods for its synthesis from tetrakis(dialkylamino)diborons.[6]

We also attempted to prepare $B_2(OEt)_4$ via this method and obtained a mixture whose primary spectral features were consistent with its structure. However, our assignment is not secure due to the complexity of the spectra. (*Caution: unlike $B_2(OMe)_4$, the reaction of $B_2(OEt)_4$ with air is spontaneous and very exothermic!*)

3. CONCLUSIONS

In conclusion, we have developed a simple, convenient, and high yielding method for the preparation of both diboron diolates and tetraalkoxydiborons using bench-stable $B_2(OH)_4$ as a universal precursor.

Scheme 3. Reaction Scope[a]



[a]Isolated yield. [b]Distilled under vacuum. [c]Isolated by DCM/water extraction.

4. EXPERIMENTAL SECTION

4.1. General Information. All diols were purchased from Sigma except ethane-1,2-diol and 3-methylbutane-1,3-diol, which were purchased from Fischer Chemicals and Oakwood Chemical respectively. Benzene-1,2-diamine was purchased from Eastman Chemicals. All commercial chemicals were used as received unless otherwise indicated. ^{1}H, ^{13}C, and ^{11}B NMR spectra were recorded on a Varian 500 MHz DD2 Spectrometer equipped with a ^{1}H–^{19}F/^{15}N–^{31}P 5 mm Pulsed Field Gradient (PFG) probe. Chemical shifts are reported as parts per million (ppm). Splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublet (dd), and doublet of doublet of doublets (ddd). NMR spectra were processed for display using the MNova software program with only phasing and baseline corrections applied. High-resolution mass spectra (HRMS) were recorded on a Leco GC-ToF spectrometer. All reactions were carried out under a nitrogen atmosphere in oven-dried glassware. Anhydrous dichloromethane was obtained from commercial sources and was used without further purification. Boron monoxide ($(B_2O_2)_n$) was prepared as previously described in the literature.[11,24] The reported yields describe the results of a single experiment.

4.2. General Experimental Procedure. An oven-dried round-bottom flask was charged with $B_2(OH)_4$ (1.0 equiv) and $CH(OMe)_3$ (4.0 equiv) and a stir bar. AcCl was added (0.02 equiv), the vessel was flushed with N_2 and sealed with a silicone septum, and the mixture was stirred rapidly at room temperature until all solid material had dissolved (5 min or less, determined by stir rate and the grain size of

https://doi.org/10.1021/acs.joc.3c02992
J. Org. Chem. 2024, 89, 6048−6052

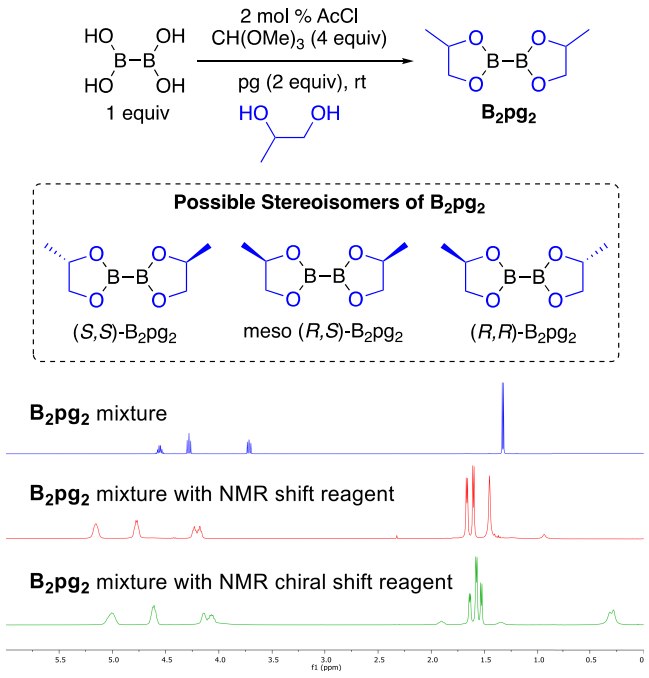
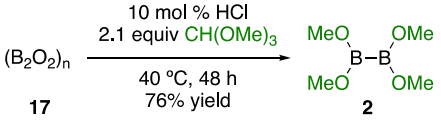


Figure 1. ^{1}H NMR spectra of a mixture of B_2pg_2 with NMR shift reagent $Eu(fod)_3$ and optically active NMR chiral shift reagent $Eu(hfc)_3$.

Scheme 4. Synthesis of Tetramethoxydiboron



the $B_2(OH)_4$). The diol was then added, and the mixture was stirred for 30 min. Solvent was removed in vacuo via rotary evaporation and then under high vacuum to afford the title compound.

*4.2.1. Tetramethoxydiboron ($B_2(OMe)_4$) (**2**).* A 1 dram vial was charged with a stir bar, $(B_2O_2)_n$ (268 mg, 5 mmol), $CH(OMe)_3$ (1.15 mL, 10.5 mmol), and 2.0 M HCl in Et_2O (0.25 mL, 0.5 mmol). The vial was flushed with N_2 and capped and then stirred at 40 °C in an oil bath for 48 h. The cap was replaced with a septum and connected to a water aspirator by a length of PTFE tubing. HCO_2Me and Et_2O were removed via vacuum distillation at room temperature, gradually raising the temperature over 1 h to 40 °C in an oil bath. The remaining liquid was then filtered through glass wool under a N_2 atmosphere. This procedure afforded 608 mg of the title compound in 91% purity (containing 4% methyl formate, 2% methanol, 3% diethyl ether) as a colorless oil for an overall yield of 553 mg (76%). The relative proportions of each component were estimated via spectral deconvolution using the line fitting protocol in Mnova 14.2.0 (Mestrelab Research, S.L.; Santiago de Compostela, Spain) using Gaussian/Lorentzian peak shapes and simulated annealing. Spectral data are for the title compound. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.62 (s, 12H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 52.1; ^{11}B NMR (160 MHz, $CDCl_3$): δ 31.2. (For NMR spectra in C_7D_8 see Braunschweig, H.; Damme, A. Thermodynamic control of oxidative addition and reductive elimination processes in *cis*-bis(dimethoxyboryl)-bis-(tricyclohexylphosphine)platinum(II). *Chem. Commun.* **2013**, *49* (45), 5216−5218).

*4.2.2. 2,2′-Bi(1,3,2-dioxaborolane) (B_2eg_2) (**3**).* The title compound was prepared from $B_2(OH)_4$ (2.24 g, 25 mmol), $CH(OMe)_3$ (10.94 mL, 100 mmol), AcCl (18 μL, 0.25 mmol), and ethylene glycol (2.8 mL, 50 mmol) according to the general procedure. This procedure afforded 3.22 g (91%) of the title compound as a white solid: mp = 163−164 °C (lit mp = 159−160 °C[16]). ^{1}H and ^{13}C, data were inconsistent with literature values as impurities were present in the literature spectrum.[16] ^{1}H NMR (500 MHz, $CDCl_3$):[16] δ 4.18 (s, 8H); ^{13}C NMR (126 MHz, $CDCl_3$):[16] δ 65.7; ^{11}B NMR (160 MHz, $CDCl_3$):[16] δ 30.82. GC-MS (EI) *m*/*z* calcd for $C_4H_8B_2O_4$ $[M]^+$ 142.06, found: 142.1.

*4.2.3. 4,4′-Dimethyl-2,2′-bi(1,3,2-dioxaborolane) (B_2pg_2) (**4**).* The title compound was prepared from $B_2(OH)_4$ (2.24 g, 25 mmol), $CH(OMe)_3$ (10.94 mL, 100 mmol), AcCl (18 μL, 0.25 mmol), and propylene glycol (3.65 mL, 50 mmol) according to the general procedure. The mixture was concentrated and then distilled at 0.07 torr to afford 3.64 g (86%) of the title compound as a colorless oil. The title compound has been reported before, but no spectroscopic data were provided. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.57−4.50 (m, 2H), 4.26 (dd, J = 8.0, 0.9 Hz, 2H), 3.70 (ddd, J = 8.3, 7.4, 1.0 Hz, 2H), 1.31 (dd, J = 6.2, 0.5 Hz, 6H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 73.6, 73.6, 72.1, 21.8; ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.7. HRMS (GC/ToF) *m*/*z* calc for $C_6H_{12}B_2O_4$ $[M]^+$ 170.0922, found: 170.0911.

*4.2.4. (4S,4′S) 4,4′-Dimethyl-2,2′-bi(1,3,2-dioxaborolane) ((S,S)-B_2pg_2) (**5**).* The title compound was prepared from $B_2(OH)_4$ (2.24 g, 25 mmol), $CH(OMe)_3$ (10.94 mL, 100 mmol), AcCl (18 μL, 0.25 mmol), and (S)-propylene glycol (3.65 mL, 50 mmol) according to the general procedure. This procedure afforded 4.04 g (95%) of the title compound as a white solid: mp = 152−154 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.63−4.46 (m, 2H), 4.24 (dd, J = 8.2, 1.0 Hz, 2H), 3.68 (dd, J = 7.4, 1.5 Hz, 2H), 1.29 (d, J = 6.3 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 73.5, 72.1, 21.8. ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.66. HRMS (GC/ToF) *m*/*z* calc for $C_6H_{12}B_2O_4$ $[M]^+$ 170.0922, found: 170.0664.

*4.2.5. 4,4′-Diethyl-2,2′-bi(1,3,2-dioxaborolane) (B_2bg_2) (**6**).* The title compound was prepared from $B_2(OH)_4$ (2.24 g, 25 mmol), $CH(OMe)_3$ (10.94 mL, 100 mmol), AcCl (18 μL, 0.25 mmol), and 1,2-butanediol (4.5 mL, 50 mmol) according to the general procedure. This procedure afforded 4.85 g (98%) of the title compound as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.39−4.33 (m, 2H), 4.24 (dd, J = 8.3, 0.5 Hz, 2H), 3.78 (ddd, J = 8.9, 7.4, 1.7 Hz, 2H), 1.70−1.53 (m, 4H), 0.95 (t, J = 7.4 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 78.6, 70.4, 29.0, 29.0, 9.3. ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.65. HRMS (GC/ToF) *m*/*z* calc for $C_8H_{16}B_2O_4$ $[M]^+$ 198.1235, found: 198.1224.

*4.2.6. 4,4,4′,4′-Tetramethyl-2,2′-bi(1,3,2-dioxaborolane) (**7**).* $B_2(OH)_4$ (896 mg, 10 mmol) and $CH(OMe)_3$ (4.24 g, 40 mmol) were stirred in a Schlenk flask and the suspension was degassed with N_2 for 15 min. One drop of acetyl chloride, AcCl, was added, and the mixture became a homogeneous solution. 2-methyl-1,2-propandiol (mpg, 1.80 g, 20 mmol) was added, and the reaction was stirred at room temperature overnight. The mixture was concentrated and then distilled under reduced pressure to yield 730 mg of the title compound as a colorless oil (37% yield). The ^{1}H NMR spectrum is inconsistent with literature due to different field strengths. However, our ^{1}H, ^{13}C, and ^{11}B are self-consistent.[25] ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.89 (s, 4H), 1.36 (s, 12H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 80.5, 77.4, 28.6. ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.80. GC-MS (EI) *m*/*z* calcd for $C_8H_{16}B_2O_4$ $[M]^+$ 198.1, found: 198.1.

*4.2.7. (4R,4′R,5R,5′R)-4,4′,5,5′-Tetramethyl-2,2′-bi(1,3,2-dioxaborolane) (**8**).* $B_2(OH)_4$ (896 mg, 10 mmol) and $CH(OMe)_3$ (4.24 g, 40 mmol) were stirred in a Schlenk flask, and the suspension was degassed with N_2 for 15 min. One drop of acetyl chloride, AcCl, was added, and the mixture became a homogeneous solution. (2R,3R)-butanediol (1.80 g, 20 mmol) was added, and the reaction was stirred at room temperature overnight. The mixture was concentrated and then distilled under reduced pressure to yield 820 mg of the title compound as a colorless oil (41% yield) that matched previously reported spectra.[25] ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.99−3.93 (m, 4H), 1.28−1.23 (m, 12H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 80.3, 20.9. ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.5. GC-MS (EI) *m*/*z* calcd for $C_8H_{16}B_2O_4$ $[M]^+$ 198.1, found: 198.1.

*4.2.8. (4R,4′R,5R,5′R)-4,4′,5,5′-Tetraphenyl-2,2′-bi(1,3,2-dioxaborolane) (**9**).* The title compound was prepared from $B_2(OH)_4$ (0.56 g, 6.25 mmol), $CH(OMe)_3$ (2.73 mL, 25 mmol), 2 mol % AcCl

https://doi.org/10.1021/acs.joc.3c02992
J. Org. Chem. 2024, 89, 6048−6052

(4.5 μL, 0.0625 mmol), and (1R,2R)-1,2-diphenylethylene glycol (2.67 g, 12.5 mmol) according to the general procedure. This procedure afforded 2.57 g (92%) of the title compound as a pale pink-white solid: mp = 191−194 °C. ^{1}H and ^{13}C NMR data were consistent with literature values.[26] ^{1}H NMR (500 MHz, $CDCl_3$):[26] δ 7.45−7.35 (m, 20H), 5.30 (s, 4H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$):[26] δ 139.9, 128.9, 128.5, 126.1, 86.8; ^{11}B NMR (160 MHz, $CDCl_3$):[26] δ 31.46.

*4.2.9. 4,4′-Dimethyl-2,2′-bi(1,3,2-dioxaborinane) (**10**).* The title compound was prepared from $B_2(OH)_4$ (1.12 g, 12.5 mmol), $CH(OMe)_3$ (5.47 mL, 50 mmol), AcCl (9 μL, 0.125 mmol), and 1,3-butanediol (2.27 mL, 25 mmol) according to the general procedure. DCM/water extraction was performed to obtain a pure compound. This procedure afforded 2.0 g (81%) of the title compound as a viscous oil. ^{1}H NMR spectrum is inconsistent with the literature due to different field strengths but our ^{1}H, ^{13}C, and ^{11}B are self-consistent.[25] ^{1}H NMR (500 MHz, $CDCl_3$):[25] δ 4.13−4.06 (m, 2H), 4.02−3.98 (m, 2H), 3.95−3.90 (m, 2H), 1.94−1.88 (m, 2H), 1.73−1.66 (m, 2H), 1.28 (d, *J* = 6.3 Hz, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$):[25] δ 66.8, 60.6, 60.5, 34.3, 34.3, 22.9, 22.9; ^{11}B NMR (160 MHz, $CDCl_3$):[25] δ 28.04. GC-MS (EI) *m*/*z* calcd for $C_8H_{16}B_2O_4$ $[M]^+$ 198.1, found: 198.1.

*4.2.10. 5,5,5′,5′-Tetramethyl-2,2′-bi(1,3,2-dioxaborinane) (**11**).* The title compound was prepared from $B_2(OH)_4$ (1.12 g, 12.5 mmol), $CH(OMe)_3$ (5.47 mL, 50 mmol), AcCl (9 μL, 0.125 mmol), and neopentyl glycol (2.6 g, 25 mmol) according to the general procedure. DCM/water extraction was performed to obtain a pure compound. This procedure afforded 2.4 g (85%) of the title compound as a white solid that matched previously reported spectra.[27] mp = 184−186 °C (lit mp = 182.5−184.5)[28] ^{1}H NMR (500 MHz, $CDCl_3$):[27] δ 3.59 (s, 8H), 0.94 (s, 12H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$):[27] δ 71.6, 31.8, 22.2; ^{11}B NMR (160 MHz, $CDCl_3$):[27] δ 27.76. GC-MS (EI) *m*/*z* calcd for $C_{10}H_{20}B_2O_4$ $[M]^+$ 226.15, found: 226.1.

*4.2.11. 4,4,4′,4′,6,6′-Hexamethyl-2,2′-bi(1,3,2-dioxaborinane) (**12**).* The title compound was prepared from $B_2(OH)_4$ (1.12 g, 12.5 mmol), $CH(OMe)_3$ (5.47 mL, 50 mmol), AcCl (9 μL, 0.125 mmol), and hexylene glycol (3.21 mL, 25 mmol) according to the general procedure. This procedure afforded 3.0 g (97%) of the title compound as a white solid that matched previously reported spectra.[27] mp = 102−104 °C (lit mp = 99−101 °C)[28] ^{1}H NMR (500 MHz, $CDCl_3$):[27] δ 4.21−4.10 (m, 2H), 1.75−1.71 (dt, *J* = 13.8, 2.8 Hz, 2H), 1.50 (dd, *J* = 11.6, 2.0 Hz, 2H), 1.28 (d, *J* = 4.2 Hz, 12H), 1.24 (dd, *J* = 6.2, 1.2 Hz, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$):[27] δ 70.2, 70.1, 64.1, 64.1, 46.3, 46.3, 31.3, 31.2, 28.5, 28.4, 23.3, 23.2; ^{11}B NMR (160 MHz, $CDCl_3$):[27] δ 28.01. GC-MS (EI) *m*/*z* calcd for $C_{12}H_{24}B_2O_4$ $[M]^+$ 254.19, found: 254.15.

*4.2.12. 4,4,4′,4′-Tetramethyl-2,2′-bi(1,3,2-dioxaborinane) (**13**).* The title compound was prepared from $B_2(OH)_4$ (2.24 g, 25.0 mmol), $CH(OMe)_3$ (10.94 mL, 100 mmol), AcCl (18 μL, 0.25 mmol), and 3-methylbutane-1,3-diol (9.15 mL, 50 mmol) according to the general procedure. This procedure afforded 5.04 g (96%) of the title compound as a white solid that matched previously reported spectra.[25] mp = 62−64 °C ^{1}H NMR (500 MHz, $CDCl_3$):[25] δ 3.99 (m, 4H), 1.78 (m, 4H), 1.31 (s, 12H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$):[25] δ 69.6, 58.7, 38.5, 29.5; ^{11}B NMR (160 MHz, $CDCl_3$):[25] δ 28.01. GC-MS (EI) *m*/*z* calcd for $C_{10}H_{20}B_2O_4$ $[M]^+$ 226.15, found: 226.15.

*4.2.13. 2,2′-Bibenzo[d][1,3,2]dioxaborole (**14**).* The title compound was prepared from $B_2(OH)_4$ (1, 1.12 g, 12.5 mmol), $CH(OMe)_3$ (5.47 mL, 50 mmol), AcCl (9 μL, 0.125 mmol), and catechol (2.75 g, 25 mmol) according to the general procedure. This procedure afforded 2.85g (96%) of the title compound as an off-white solid that matched previously reported spectra.[29] mp = 192−195 °C (lit mp = 195−198 °C)[30] ^{1}H NMR (500 MHz, $CDCl_3$):[29] δ 7.41−7.37 (m, 4H), 7.21−7.17 (m, 4H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$):[29] δ 147.8, 123.6, 113.2; ^{11}B NMR (160 MHz, $CDCl_3$):[29] δ 30.76. GC-MS (EI) *m*/*z* calcd for $C_{12}H_8B_2O_4$ $[M]^+$ 238.06, found: 238.06.

*4.2.14. 4H,4′H-2,2′-Bibenzo[d][1,3,2]dioxaborinine (**15**).* The title compound was prepared from $B_2(OH)_4$ (1, 1.12 g, 12.5 mmol), $CH(OMe)_3$ (5.47 mL, 50 mmol), AcCl (9 μL, 0.125 mmol), and 2-hydroxybenzyl alcohol (3.1 g, 25 mmol) according to the general procedure. DCM/water extraction was performed to obtain a pure compound. This procedure afforded 2.72 g (82%) of the title compound as an orange solid (mp = 160−164 °C) that matched previously reported data.[25] ^{1}H NMR (500 MHz, $CDCl_3$):[25] δ 7.23−7.19 (m, 2H), 7.07 (dd, *J* = 8.0, 0.9 Hz, 2H), 7.03 (td, *J* = 7.4, 1.2 Hz, 2H), 6.93 (dd, *J* = 7.5, 1.0 Hz, 2H), 5.12 (s, 4H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$):[25] δ 147.9, 128.9, 125.0, 123.6, 122.8, 118.2, 62.1; ^{11}B NMR (160 MHz, $CDCl_3$):[25] δ 28.35. GC-MS (EI) *m*/*z* calcd for $C_{14}H_{12}B_2O_4$ $[M]^+$ 266.09, found: 266.05.

*4.2.15. 1,1′,3,3′-Tetrahydro-2,2′-bibenzo[d][1,3,2]diazaborole (**16**).* The title compound was prepared from $B_2(OH)_4$ (0.56 g, 6.25 mmol), $CH(OMe)_3$ (2.73 mL, 25 mmol), AcCl (4.5 μL, 0.0625 mmol), and 1,2-diaminobenzene (1.35 g, 12.5 mmol) according to the general procedure. The crude product was dissolved into hot dry tetrahydrofuran (THF), filtered through a frit funnel, and transferred into a Schlenk tube, and the solvent was removed by vacuum. Redissolution in the THF followed by solvent diffusion of hexane from an overlayer at room temperature afforded 0.92 g (63%) of the title compound as an off-white solid that matched previously reported spectra.[31] (mp = 316-319 °C) ^{1}H NMR (500 MHz, $(CD_3)SO$):[31] δ 8.77 (s, 4H), 7.12−7.09 (m, 4H), 6.83−6.79 (m, 4H); ^{13}C{^{1}H} NMR (126 MHz, $(CD_3)SO$):[31] δ 137.3, 118.1, 110.8; ^{11}B NMR (160 MHz, dmf-d_7):[31] δ 27.75. GC-MS (EI) *m*/*z* calcd for $C_{12}H_{12}B_2N_4$ $[M]^+$ 234.1, found: 234.1.

4.2.16. Procedure for Mixture of B_2pg_2 with NMR Shift Reagents. (a) In an oven-dried NMR tube, a mixture of NMR shift reagent $Eu(fod)_3$ (11.2 mg, 0.01 mmol) and B_2pg_2 (11.9 mg, 0.07 mmol) was made in 1 mL of $CDCl_3$. (b) In an oven-dried NMR tube, a mixture of optical active NMR chiral shift reagent $Eu(hfc)_3$ (11.9 mg, 0.01 mmol) and B_2pg_2 (11.9 mg, 0.07 mmol) was made in 0.7 mL of $CDCl_3$. The associated spectra were then acquired on a Varian 500 MHz DD2 NMR Spectrometer.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.3c02992.

Experimental details and compound characterization data (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

Robert E. Maleczka, Jr. − *Department of Chemistry, Michigan State University, East Lansing, Michigan 48824, United States;* orcid.org/0000-0002-1119-5160; Email: smithmil@msu.edu

Milton R. Smith, III − *Department of Chemistry, Michigan State University, East Lansing, Michigan 48824, United States;* orcid.org/0000-0002-8036-4503; Email: maleczka@chemistry.msu.edu

Authors

Ryan M. Fornwald − *Department of Chemistry, Michigan State University, East Lansing, Michigan 48824, United States*

Anshu Yadav − *Department of Chemistry, Michigan State University, East Lansing, Michigan 48824, United States;* orcid.org/0000-0001-7233-2280

https://doi.org/10.1021/acs.joc.3c02992
J. Org. Chem. 2024, 89, 6048−6052

Jose R. Montero Bastidas − *Department of Chemistry, Michigan State University, East Lansing, Michigan 48824, United States;* orcid.org/0000-0002-6325-8565

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.3c02992

Author Contributions

†R.M.F. and A.Y. contributed equally to this work.

Notes

The authors declare the following competing financial interest(s): M.R.S. and R.E.M. own a percentage of BoroPharm, Inc.

■ ACKNOWLEDGMENTS

We thank Drs. Daniel Holmes and Li Xie of the MSU Max. T. Rogers NMR Facility, and Cassandra Johnny of the MSU Mass Spectrometry and Metabolomics Core facility. We thank NIH (GM63188) for generous financial support and BoroPharm, Inc. for supplying $B_2(OH)_4$.

■ REFERENCES

(1) Neeve, E. C.; Geier, S. J.; Mkhalid, I. A. I.; Westcott, S. A.; Marder, T. B. Diboron(4) Compounds: From Structural Curiosity to Synthetic Workhorse. *Chem. Rev.* **2016**, *116* (16), 9091−9161.

(2) Ishiyama, T.; Murata, M.; Miyaura, N. Palladium(0)-Catalyzed Cross-Coupling Reaction of Alkoxydiboron with Haloarenes: A Direct Procedure for Arylboronic Esters. *J. Org. Chem.* **1995**, *60* (23), 7508−7510.

(3) Dudnik, A. S.; Fu, G. C. Nickel-Catalyzed Coupling Reactions of Alkyl Electrophiles, Including Unactivated Tertiary Halides, To Generate Carbon−Boron Bonds. *J. Am. Chem. Soc.* **2012**, *134* (25), 10693−10697.

(4) Cheng, Y.; Mück-Lichtenfeld, C.; Studer, A. Metal-free Radical Borylation of Alkyl and Aryl Iodides. *Angew. Chem. Weinheim Bergstr. Ger.* **2018**, *130* (51), 17074−17078.

(5) Tian, Y.-M.; Guo, X.-N.; Braunschweig, H.; Radius, U.; Marder, T. B. Photoinduced Borylation for the Synthesis of Organoboron Compounds. *Chem. Rev.* **2021**, *121* (7), 3561−3597.

(6) Brotherton, R. J.; Mccloskey, A. L. Tetra-(amino)-diborons1,2. *J. Am. Chem. Soc.* **1960**, *82* (24), 6242−6245.

(7) Ishiyama, T.; Murata, M.; Ahiko, T.-A.; Miyaura, N. Bis (pinacolato) Diboron. *Org. Synth.* **2000**, *77*, 176−185.

(8) Bello, C. S.; Schmidt-Leithoff, J. Borylation of Organo Halides and Triflates Using Tetrakis(dimethylamino)diboron. *Tetrahedron Lett.* **2012**, *53* (46), 6230−6235.

(9) Molander, G. A.; Trice, S. L. J.; Kennedy, S. M. Palladium-Catalyzed Borylation of Aryl and Heteroaryl Halides Utilizing Tetrakis(dimethylamino)diboron: One Step Greener. *Org. Lett.* **2012**, *14* (18), 4814−4817.

(10) Molander, G. A.; Wisniewski, S. R.; Hosseini-Sarvari, M. Synthesis and Suzuki-Miyaura Cross-Coupling of Enantioenriched Secondary Potassium β-Trifluoroboratoamides: Catalytic, Asymmetric Conjugate Addition of Bisboronic Acid and Tetrakis-(dimethylamino)diboron to α,β-Unsaturated Carbonyl Compounds. *Adv. Synth. Catal.* **2013**, *355* (14−15), 3037−3057.

(11) McCloskey, A. L.; Brotherton, R. J.; Boone, J. L. The Preparation of Boron Monoxide and Its Conversion to Diboron Tetrachloride1. *J. Am. Chem. Soc.* **1961**, *83* (23), 4750−4754.

(12) Liu, Q.S.; Wang, F.; Gao, X. Method for Preparing Diboric Acid Ester. CN102718787, October 10, 2012.

(13) Henschke, J. P.; Lin, C. W.; Wu, P. Y.; Hsiao, C. N.; Liao, J. H.; Hsiao, T. Y. Process for the Preparation of β-C-Aryl Glucosides US20140128595, May 8, 2014.

(14) Tang, W.; Xu, G.; Zhou, M.Bis(Pinacolato)DiBoron, Preparation Method Thereof, Intermediate Thereof and Application Thereof. CN111440205, July 24, 2020.

(15) Unsworth, P. J.; Leonori, D.; Aggarwal, V. K. Stereocontrolled Synthesis of 1,5-Stereogenic Centers through Three-Carbon Homologation of Boronic Esters. *Angew. Chem., Int. Ed. Engl.* **2014**, *53* (37), 9846−9850.

(16) Chattopadhyay, B.; Dannatt, J. E.; Andujar-De Sanctis, I. L.; Gore, K. A.; Maleczka, R. E., Jr; Singleton, D. A.; Smith, M. R., III Ir-Catalyzed Ortho-Borylation of Phenols Directed by Substrate−ligand Electrostatic Interactions: A Combined Experimental/in Silico Strategy for Optimizing Weak Interactions. *J. Am. Chem. Soc.* **2017**, *139* (23), 7864−7871.

(17) Chen, D.; Xu, G.; Zhou, Q.; Chung, L. W.; Tang, W. Practical and Asymmetric Reductive Coupling of Isoquinolines Templated by Chiral Diborons. *J. Am. Chem. Soc.* **2017**, *139* (29), 9767−9770.

(18) Bisht, R.; Chaturvedi, J.; Pandey, G.; Chattopadhyay, B. Double-Fold Ortho and Remote C−H Bond Activation/Borylation of BINOL: A Unified Strategy for Arylation of BINOL. *Org. Lett.* **2019**, *21* (16), 6476−6480.

(19) Yuan, J.; Jain, P.; Antilla, J. C. Bi(cyclopentyl)diol-Derived Boronates in Highly Enantioselective Chiral Phosphoric Acid-Catalyzed Allylation, Propargylation, and Crotylation of Aldehydes. *J. Org. Chem.* **2020**, *85* (20), 12988−13003.

(20) Zhou, M.; Li, K.; Chen, D.; Xu, R.; Xu, G.; Tang, W. Enantioselective Reductive Coupling of Imines Templated by Chiral Diboron. *J. Am. Chem. Soc.* **2020**, *142* (23), 10337−10342.

(21) Yang, H.; Zhang, L.; Zhou, F.-Y.; Jiao, L. An Umpolung Approach to the Hydroboration of Pyridines: A Novel and Efficient Synthesis of N-H 1,4-Dihydropyridines. *Chem. Sci.* **2020**, *11* (3), 742−747.

(22) Qiao, B.; Mohapatra, S.; Lopez, J.; Leverick, G. M.; Tatara, R.; Shibuya, Y.; Jiang, Y.; France-Lanord, A.; Grossman, J. C.; Gómez-Bombarelli, R.; Johnson, J. A.; Shao-Horn, Y. Quantitative Mapping of Molecular Substituents to Macroscopic Properties Enables Predictive Design of Oligoethylene Glycol-Based Lithium Electrolytes. *ACS Cent. Sci.* **2020**, *6* (7), 1115−1128.

(23) Elkin, P. K.; Levin, V. V.; Dilman, A. D.; Struchkova, M. I.; Belyakov, P. A.; Arkhipov, D. E.; Korlyukov, A. A.; Tartakovsky, V. A. Reactions of CF_3-Substituted Boranes with α-Diazocarbonyl Compounds. *Tetrahedron Lett.* **2011**, *52* (41), 5259−5263.

(24) Wartik, T.; Apple, E. F. A NEW MODIFICATION OF BORON MONOXIDE. *J. Am. Chem. Soc.* **1955**, *77* (23), 6400−6401.

(25) Marcuccio, S. M.; Rodopoulos, M.; Weigold, H. Boronic Compounds. US6346639B1, February, 12, 2002.

(26) Clegg, W.; Johann, T. R. F.; Marder, T. B.; Norman, N. C.; Orpen, A. G.; Peakman, T. M.; Quayle, M. J.; Rice, C. R.; Scott, A. J. Platinum-Catalysed 1,4-Diboration of 1,3-Dienes. *J. Chem. Soc., Dalton Trans.* **1998**, *9*, 1431−1438.

(27) Herrera-Luna, J. C.; Díaz Díaz, D.; Abramov, A.; Encinas, S.; Jiménez, M. C.; Pérez-Ruiz, R. Aerobic Visible-Light-Driven Borylation of Heteroarenes in a Gel Nanoreactor. *Org. Lett.* **2021**, *23* (6), 2320−2325.

(28) Marcuccio, S. M.; Moorhoff, C. M. Preparation of diboronic esters. WO2004/076467A1.

(29) Lawlor, F. J.; Norman, N. C.; Pickett, N. L.; Robins, E. G.; Nguyen, P.; Lesley, G.; Marder, T. B.; Ashmore, J. A.; Green, J. C. Bis-Catecholate, Bis-Dithiocatecholate, and Tetraalkoxy diborane(4) Compounds: Aspects of Synthesis and Electronic Structure. *Inorg. Chem.* **1998**, *37* (20), 5282−5288.

(30) Welch, C. N.; Shore, S. G. Boron heterocycles. V. Preparation and Characterization of Selected Heteronuclear Diboron Ring Systems. *Inorg. Chem.* **1968**, *7* (2), 225−230.

(31) Alibadi, M. A. M.; Batsanov, A. S.; Bramham, G.; Charmant, J. P. H.; Haddow, M. F.; MacKay, L.; Mansell, S. M.; McGrady, J. E.; Norman, N. C.; Roffey, A.; Russell, C. A. 1, 1-and 1, 2-Isomers of the Diborane (4) Compound $B_2\{1, 2\text{-}(NH)_2C_6H_4\}_2$ and a TCNQ Co-Crystal of the 1, 1-Isomer. *Dalton Trans.* **2009**, *27*, 5348−5354.