amount of time (0, 2, 3, 10, or 40 h), after which the solid mass was broken up, 150 mL of pentane was added, and the mixture was mechanically stirred at room temperature for an additional 2 h (for the 0 time experiment the stirring with pentane was carried out for 24 h). The pentane was filtered from the brucine and was washed with an additional 50 mL of pentane, and the pentane extracts were combined. The weight and optical rotation of the solution were measured and the product mixture was analyzed by GLC. The pentane solution was washed with 2 × 50 mL portions of 10% aqueous H_2SO_4 and the pentane was removed by distillation. The weight, volume, and optical rotation of the residue were measured and the product mixture was analyzed by GLC and 200-MHz ^1H NMR spectroscopy.

The absolute rotations listed in Table I were obtained from samples which contained olefin (0.1–2.7%) and <1 mol % of pentane (GLC) and therefore were corrected for their concentrations.

Identification of *trans*-2-Bromo-2-butene. *trans*-2-Bromo-2-butene was identified by comparison of its 200-MHz ^1H NMR spectrum and refractive index with that of the authentic material: ^1H NMR ($CDCl_3$) δ 1.680 (q of d, 3 H), 2.235 (quint., 3 H), 5.628 (q of q, 1 H) [lit.[12] ^1H NMR (CCl_4) δ 1.69 (q of d, 3 H), 2.26 (quint., 3 H), 5.65 (q of q, 1 H)]; n^{25}_D 1.4568 [lit.[10] n^{25}_D 1.4565].

Registry No. *dl*-2,3-Dibromobutane, 598-71-0; brucine, 357-57-3; *trans*-2-bromo-2-butene, 3017-71-8; (–)-2,3-dibromobutane, 49623-63-4.

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Synthesis and Characterization of Novel 1*H*,3*H*-Naphth[1,8-*cd*][1,2,6]oxadiborins

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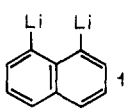
The 1*H*,3*H*-naphth[1,8-*cd*][1,2,6]oxadiborin ring system is a conjugated heterocycle, isoelectronic with the phenalene cation.[1] The only previous mention of this diboryl parent structure was by Letsinger et al.,[2] who synthesized 1,8-naphthalenediboronic anhydride (**2a**) and its ammonia complex. Recently, we observed the 1,3-dimethyl derivative **2d** as an inadvertent oxidation product in the preparation of 1,8-naphthalenediylbis(dimethylborane), "hydride sponge".[3] In this paper, we report the synthesis of compounds **2b–d** via facile substitution reactions starting from **2a**. These compounds are potentially useful as a means of introducing pairs of conformationally defined boron substituents into larger molecular assemblies, besides being novel Lewis acids in their own right.



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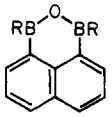

2a, R = OH
2b, R = OMe
2c, R = Cℓ
2d, R = Me

Results and Discussion

Diboronic anhydride **2a** was prepared from 1,8-dilithionaphthalene (1) according to the literature procedure[4] with two modifications: the dilithiate was generated from the more readily obtained 1,8-diiodonaphthalene[5] rather than from 1,8-dibromonaphthalene, and trimethylborate was used instead of tributylborate. The product isolated after recrystallization from Et_2O/petroleum ether was a partial hydrate, according to its elemental analysis.

Compound **2a** was quantitatively converted to dimethyl ester **2b** by reaction with methanol in benzene. The reacting solution was heated at reflux while water was removed from the reflux vapors with molecular sieves and from the pot by azeotropic distillation. Diboronic diester **2b** was transformed into dichloride **2c** by the action of PCl_5 and CCl_4 at reflux; once again, the reaction was quantitative. Compound **2b** was also treated with 5 molar equiv of MeMgBr in $(CH_2)_4O$. The reaction was quenched with 5 molar equiv of $BF_3{\cdot}OEt_2$, leading to the isolation of compound **2d** in 64% yield.

Heterocycle **2d** is the first example of 1*H*,3*H*-naphth[1,8-*cd*]oxadiborin whose substituents are not π-electron donors. It is slightly sensitive to air and decomposes in aqueous acid. The compound displayed irreversible redox potentials at –1.1 V (reduction) and +1.4 V (oxidation) vs. SCE in CH_2Cl_2 containing 0.1 M n-$Bu_4N^+PF_6^-$.

The B–O–B linkage proved to be robust, as attempts to dislodge the oxygen atom with MeOH/AcOH, NaOMe/CH_3I, PCl_5, P_4S_{10}, Lawesson's reagent,[6] MeMgBr, and $C_5H_{11}NH_2$/$PhCH_3$ all failed. Dichloride **2c** was resistant to attack by excess PCl_5 and by $TiCl_4$ in C_6D_5Cl at 130 °C.

When **2d** was treated with C_5H_5N, $C_5H_{11}NH_2$, or quinuclidine, 1:1 addition compounds were formed, as indicated by NMR and IR spectroscopy. The quinuclidine complex was observed in a temperature-dependent 90-MHz ^1H NMR experiment and appeared to be symmetrical or rapidly equilibrating at $T \gtrsim -80$ °C. This is in contrast to the result reported[7] for triethylboroxin, on which quinuclidine was localized at a single boron atom at –20 °C on the 400-MHz time scale. Perhaps the inclusion of the boron atoms in a conjugated system alters the orbital overlap or lowers the electron deficiency of **2d** relative to the boroxin, so that an amine would form a less stable complex with a single boron atom of **2d** relative to the boroxin.

The precursors to compound **2d** are all stable, isolable substances whose orbitals are geometrically defined at the boron atoms, and whose substituents may be easily replaced. As such, they might serve as useful intermediates in the syntheses of oligomeric or polymeric boron Lewis acids.

Experimental Section

1,3-Dimethoxy-1*H*,3*H*-naphth[1,8-*cd*][1,2,6]oxadiborin (2b). Compound **2a** (0.50 g) was dissolved in 25 mL of MeOH and 125 mL of C_6H_6 and the solution was heated for 20 h at reflux under Ar, while removing water from the solvent vapors with molecular sieves. Distillation of the solvents left crude product, which was freed from trace contaminants by crystallization from dry hexane to yield 0.34 g of **2b** as light yellow rectangular prisms, mp 80–82 °C; IR (KBr) 1330 (B–O–B), ^1H NMR (C_6D_6 vs. Me_4Si) δ 3.64 (s, 6, CH_3), 7.35 (d of d, 2, β-H), 7.71 (d of d, 2, $J_{\alpha\gamma}$ = 1.4 Hz, $J_{\beta\gamma}$ = 7.8 Hz, γ-H), 8.38 (d of d, 2, $J_{\alpha\gamma}$ = 1.4 Hz, $J_{\alpha\beta}$ = 6.7 Hz, α-H); ^{13}C NMR (CD_2Cl_2 vs. Me_4Si) 51.13, 125.90, 126.32, 132.01, 132.50, 134.28, 141.87; ^{11}B NMR (CD_2Cl_2 vs. BF_3OEt_2) +29.6; mass spectrum, m/z 226 (M^+). Anal. Calcd for $C_{12}H_{12}B_2O_3$: C, 63.82; H, 5.36; B, 9.57. Found: C, 63.99; H, 5.34; B, 9.71.

1,3-Dichloro-1*H*,3*H*-naphth[1,8-*cd*][1,2,6]oxadiborin (2c). Diester **2b** (0.30 g) and PCl_5 (1.1 g) were added to 6 mL of CCl_4

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and heated for 3 h at reflux under Ar. Analysis of the solution by ^1H NMR indicated quantitative reaction. Upon cooling to ambient temperature, the product separated as white needles (0.23 g, 74%): mp >180 °C dec; IR (KBr) 1330 (B–O–B); ^1H NMR (CD_2Cl_2 vs. Me_4Si) δ 7.70 (d of d, 2, β-H); 8.21 (d, 2, J = 8 Hz, γ-H); 8.44 (d, 2, J = 7 Hz, α-H); ^{11}B NMR (CD_2Cl_2 vs. BF_3OEt_2) +41.5; mass spectrum, m/z 234 (M^+). Anal. Calcd for $C_{10}H_8B_2Cl_2O$: C, 51.18; H, 2.58; B, 9.21. Found: C, 51.40; H, 2.76; B, 9.48.

1,3-Dimethyl-1*H*,3*H*-naphth[1,8-*cd*][1,2,6]oxadiborin (2d). Crude diester **2b** (1.5 g) was dissolved in 100 mL of $(CH_2)_4O$. An aliquot of MeMgBr (32.6 mmol, 5 equiv) in Et_2O was added and the mixture was stirred for 3 h under Ar. The anions were quenched with $BF_3{\cdot}OEt_2$ (4.0 mL, 32.5 mmol), the solvents were evaporated, and the residue was extracted with 2 × 60 mL of petroleum ether. The extracts were filtered, concentrated, and crystallized from minimal petroleum ether. The yield was 0.83 g (64%) of beige needles: mp 97–99 °C; UV max (CH_2Cl_2) 323 nm (ϵ 9300), 311 (10 500), 232 (25 000); IR (KBr) 1307 (B–O–B); ^1H NMR (CD_2Cl_2 vs. Me_4Si) δ 1.06 (s, 6, CH_3), 7.64 (d of d, 2, β-H), 8.09 (d of d, 2, $J_{\alpha\gamma}$ = 1.2 Hz, $J_{\beta\gamma}$ = 8.2 Hz, γ-H); 8.31 (d of d, 2, $J_{\alpha\gamma}$ = 1.2 Hz, $J_{\alpha\beta}$ = 6.6 Hz, α-H); ^{13}C NMR (CD_2Cl_2 vs. Me_4Si) 3.5, 126.2, 131.6, 133.5, 138.1, 138.8; ^{11}B NMR (CD_2Cl_2 vs. $BF_3{\cdot}OEt_2$) 50.7; mass spectrum, m/z 194 (M^+). Anal. Calcd for $C_{12}H_{12}B_2O$: C, 74.35; H, 6.24; B, 11.15. Found: C, 74.19; H, 6.46; B, 10.93.

Acknowledgment. We are grateful to A. M. Mujsce for obtaining the mass spectra.

Registry No. **2a**, 1730-05-8; **2b**, 96482-87-0; **2c**, 96502-45-3; **2d**, 96482-88-1.

Organic Reactions at High Pressure. The Preparative Scale Synthesis of Cantharidin[1]

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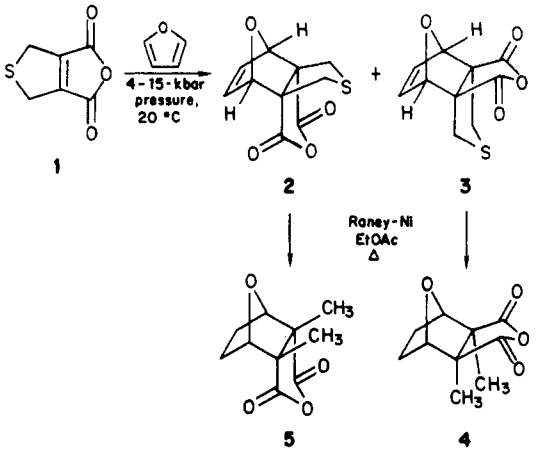
The benefits of applying high pressure (1–20 kbar; 0.1–2.0 GPa) to organic reactions which have a $-\Delta V^*$ are readily seen by considering the variety of synthetic organic reactions recently found to be accelerated under elevated pressures.[2] One example which is of possible commercial interest is the synthesis of the potent vesicant cantharidin which is used in the removal of benign epithelial growths (warts). This synthesis proceeds via the Diels–Alder reaction of the dihydrothiophene anhydride 1[3] with furan, a reaction which proceeds at pressures in the 4–15 kbar range and yields the adducts **2** and **3**.[4] Subsequent hydrogenation and desulfurization of the mixture of isomeric adducts and selective recrystallization affords the desired cantharidin (**4**). The efficiency of this high pressure procedure has prompted the study of a preparative scale synthesis of **4**.

Table I. Optimization of the Preparative Scale Diels–Alder Reaction of 1 with Furan at High Pressure[a]

entry	1, mmol (g)	mmol of furan/ mmol of 1	time, h	conversn,[c] %
1	65 (10.07)	26	24	95
2	45 (7.0)	34	29	100
3	97 (15.09)	15	26	67
4	98 (15.26)	16	48	97
5	90 (14.02)	16	74	100
6	0.7 (0.103)	62	144[b]	95

[a] All reactions were carried out at 20 °C and except where noted under 7-kbar pressure. [b] 1-kbar pressure. [c] Conversion of anhydride 1 was determined by ^1H NMR (90-MHz) spectroscopy. All of the reactions afforded approximately a 20:80 ratio of isomers **2**/**3**.



Performing large-scale (>100 mL) reactions at pressures greater than 7 kbar is limited by the engineering problems associated with the scaling-up of the pressure apparatus.[5] Reaction vessels of the piston-and-cylinder design which operate at pressures greater than 7 kbar require a costly conical inner liner so that the vessel can withstand very high pressures.[5] The construction of such a reaction vessel with a piston having a diameter greater than 1 in. so as to allow larger scale preparative reactions is impractical due to the mass of the vessel required. The construction of a reaction vessel having a wide bore (>2 in.) which can be used at pressures less than 7 kbar can be achieved by a reaction cylinder devoid of the extra inner linear.[6,7] This pressure restriction as related to large scale preparative reactions requires a study of reaction conditions to see if lower pressures can be utilized in the desired reaction. The ease by which preparative scale reactions (0.065 mol) can be carried out at the lower pressure (7 kbar) is reported in this study of the optimization of the [4 + 2] cycloaddition synthesis of cantharidin.

In our earlier study,[4] it was found that the cycloaddition reaction proceeded at a pressure of 7 kbar in solvents such as methylene chloride, acetone, or acetonitrile. The time required for 80% conversion at 8-kbar pressure (42 h) was increased 2–4-fold as compared to that needed at 15-kbar

(1) This work was supported by National Science Foundation Grant No. CHE-8401434.

(2) For recent high-pressure applications. (a) Quaternization of triphenylphosphine: Dauben, W. G.; Gerdes, J. M.; Bunce, R. A. *J. Org. Chem.* **1984**, *49*, 4293. (b) Asymmetric reduction: Midland, M. M.; McLoughlin, J. I. *J. Org. Chem.* **1984**, *49*, 1317. (c) 1,4-Addition reactions: Yamamoto, Y.; Maruyama, K.; Matsumoto, K. *Tetrahedron Lett.* **1984**, *25*, 1075. (d) Alcohol protection: Dauben, W. G.; Bunce, R. A.; Gerdes, J. M.; Henegar, K. E.; Cunningham, A. C.; Ottoboni, T. B. *Tetrahedron Lett.* **1983**, *24*, 5709. (e) Wittig reactions: Nonnemacker, A.; Mayer, R.; Plieniger, H. *Liebigs Ann. Chem.* **1983**, 2135. (f) Diels-Alder reactions: Jurczak, J.; Bauer, T.; Filipek, S.; Tkacz, M.; Zygo, K. *J. Chem. Soc., Chem. Commun.* **1983**, 540.

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(5) For a discussion of high-pressure equipment see: Isaacs, J. S. "Liquid Phase High Pressure Chemistry"; Wiley Interscience: New York, 1981; Chapter 1.

(6) Semipreparative and preparative high-pressure apparatus are available from Harwood Engineering Co., Inc., South Street, Walpole, MA 02081, and Tem-Pres Division, Leco Corp., Bellefonte, PA 16823.

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