

Studies on Aryl Boronic Acids I: Synthesis of Naphthalene-1,4-diboronic Acid

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Abstract □ A new aryl boronic acid, naphthalene-1,4-diboronic acid, was synthesized *via* a Grignard reaction and conveniently characterized by its neopentyl glycol and diethanolamine derivatives. A preliminary infrared correlation chart for three aryl boronic acids is also presented.

Keyphases □ Naphthalene-1,4-diboronic acid, derivatives—synthesis □ IR spectrophotometry—structure □ Spectral data correlation, IR—aryl boronic acids.

As a preliminary step in preparation of more complex organo-boron compounds of possible chemotherapeutic value, a new aryl diboronic acid, naphthalene-1,4-diboronic acid (I), was synthesized utilizing essentially the method of Nielsen and McEwen (1).

EXPERIMENTAL¹

Naphthalene-1,4-diboronic Acid—A solution of 1,4-dibromonaphthalene, 22.9 g. (80 mmoles), in 240 ml. of freshly distilled anhydrous tetrahydrofuran (THF) was added dropwise to 4.86 g. (0.2 mole) of Mg turnings in a dry nitrogen atmosphere in a 2-l., four-neck flask equipped with condenser and stirrer. It was necessary to initiate the reaction by adding a few crystals of iodine and warming 40 ml. of the solution to 45°. After initiation the reaction continued smoothly and the remaining 200 ml. of solution was added over a period of 30 min. The reaction was allowed to continue for another 30 min. then slowly was warmed to 65° and allowed to reflux for 12 hr. The dark, olive-green slurry was cooled to room temperature, then to -65° in a dry ice-acetone bath. Trimethyl borate, 30 ml. (0.25 mole), and 75 ml. of dry THF were transferred in a dry N₂ atmosphere to a 125-ml. dropping funnel. The trimethyl borate solution was added slowly over a period of 90 min. to the cold, well stirred, light-green mixture. This solution was allowed to warm to room temperature overnight then subsequently was cooled to 0° in an ice bath and hydrolyzed with 200 ml. of 1 N HCl. After decomposition of the excess Mg turnings, the solution was extracted twice with 100-ml. portions of ether, then once again with 50 ml. of ether. Each ether extract was washed with 50 ml. of water, and the combined ether extracts dried overnight over anhydrous MgSO₄. A dark resinous fluid was recovered after filtration of the extracts and removal of the ether by distillation. This resin was dissolved in 20 ml. of hot methanol, diluted with 2 l. of hot 1 N HCl, and filtered twice through charcoal. The filtrate was concentrated to one-half its volume, then set aside in the refrigerator to allow for crystallization. The dry, light-gray crystals weighed 6.48 g. (37.6% yield) and had no detectable melting point below 350°. This product was conveniently decolorized by adding 400 mg. to 2 ml. each of benzene and glacial acetic acid, warming the solution, filtering rapidly by suction, then washing the crystals with cold hexane. After drying overnight and *in vacuo* at 70° for 2 hours, the colorless product was recovered in a 70% yield. This substance, which still gave no detectable m.p. below 350°, was found by its IR spectrum (see Table I) and elemental analysis to be naphthalene-1,4-diboronic acid (I).

Anal.—Calcd. for C₁₀H₁₀B₂O₄: C, 55.66; H, 4.67; B, 10.02. Found: C, 55.41; H, 4.77; B, 9.80.

¹All melting points listed are uncorrected as taken on a Kofler Micro Hot Stage. The analyses were done by Galbraith Laboratories, Inc., Knoxville, Tenn.

Bis (2,2-dimethyl-1,3-propanediol) naphthalene-1,4-diboronate—A mixture of 107.9 mg. (0.5 mmole) of I and 108.2 mg. (1.25 mmole) of 2,2-dimethyl-1,3-propanediol (neopentyl glycol) in 15 ml. of benzene was stirred and heated for 15 min. to produce a solution. After the removal of water by azeotropic distillation the solution was concentrated to 5 ml. and set aside overnight to allow for crystallization. It was necessary to concentrate the solution further, nearly to dryness, before the ester would crystallize in the cold. This gave 132 mg. (75% yield) of colorless crystals. After recrystallization from methanol the crystals melted at 145.5–147.5°.

Anal.—Calcd. for C₂₀H₂₈B₂O₄: C, 68.23; H, 7.44. Found: C, 68.49; H, 7.48.

Bis (2,2'-iminodiethanol) naphthalene-1,4-diboronate—This diboroxazolidine derivative of I was prepared by a modification of the method of Letsinger and Skoog (2). I, 108.6 mg. (0.5 mmole), and diethanolamine, 131.4 mg. (1.25 mmoles), were dissolved in a mixture of 10 ml. absolute ethanol and 1 ml. water. The solution was concentrated to 1 ml. by heating then set aside in the cold to allow for crystallization. The product was recrystallized from ethanol then dried *in vacuo* with P₂O₅ for 2 days to give 115.1 mg. (65% yield) of very hygroscopic colorless crystals. This diboroxazolidine slowly melted at 231° dec. (1°/3 min. near the m.p.).

Anal.—Calcd. for C₁₈H₂₄B₂N₂O₄: C, 61.07; H, 6.84; N, 7.92. Found: C, 60.86; H, 7.04; N, 7.87.

DISCUSSION

The IR frequency correlation chart (see Table I) depicts pertinent IR spectral assignments for the arylboronic acids and their ester derivatives. The strong broad band at 1,340 ± 20 cm.⁻¹ for these arylboronic acids is consistent with assignments made by Werner and O'Brien (3) for the B—O asymmetric stretching frequency. They suggested that the intensity and stability of this band reflect some double bond character due to π—π bonding *via* back coordination from oxygen to boron. If an amine is complexed to an oxyborane, the amine's lone pair of electrons can complete the boron octet and reduce back coordination between oxygen and boron to a minimum (4). IR absorption for the asymmetric B—O stretch in these oxyborane-amine complexes is weak or absent reflecting the reduced B—O bond strength (4).

Greenwood and Wade (5) have assigned the IR frequency range 1099–1250 cm.⁻¹ to a stretching mode of the coordinated boron-nitrogen bond (dative bond). Letsinger and Hamilton (4), however, have indicated a narrower range (1136–1250 cm.⁻¹) for the complexes. Zimmerman *et al.* (6) have assigned to the stretching and bending modes for the N → B dative bond in a series of boroxazolidines the IR frequencies 1,200 and 920 cm.⁻¹, respectively. However, Zimmerman claimed that subsequent studies failed to confirm his assignments, at least in a simple way, and no confidence to date (1963) could be placed in IR spectral data as direct proof of N → B dative bonding (7). Prominent and stable IR bands were found near 1,225 and 921 cm.⁻¹ for the three aryl diptych boroxazolidines prepared in this laboratory. These bands did not appear for components of the diptych boroxazolidines.

Many conflicting IR spectral assignments have been made for the B-aryl bond. Bellamy *et al.* (8) assigned a strong sharp absorption band to the B-aryl bond between 1,430–1,440 cm.⁻¹. Gerrard (9) assigned the strong absorption between 1,250–1,280 cm.⁻¹ to the B-aryl bond, and Santucci and Gilman (10) assigned a strong band between 1,086–1,095 cm.⁻¹ to this bond. However, the 1,430–1,440-cm.⁻¹ and 1,250–1,280-cm.⁻¹ bands, which also appear for aryl bromides, probably represent aromatic C=C stretching and C—H in-plane bending modes, respectively (11, 12). The band at 1,086–1,095 cm.⁻¹, which invariably appears in boronic acid esters, probably represents a —C—O—B—O—C— or aromatic in-plane deformation mode (11, 12). The authors' IR spectral analysis of

Table I—Infrared^a Frequency Correlation Chart for Aryl Boronic Acids and Their Derivatives^b

Compd.	Frequency Assignments, cm. ^{-1c}						
	O—H	N—H	B—C Stretching	Asymmetric B—O	N→B	C—O	N→B bend
Benzene-1,4-diboronic Acid	3300 s,bd		1410 s,sh 1418 s,sh	1360 s,sh 1342 m,bd		1095 w,bd	
Bis (neopentyl glycol) ester		3110 m,sh	weak	1360 w,sh	1222 s,sh	1070 s,bd	926 s,sh
Bis (diethanolamine) ester	3250 m,bd		1400 m,bd 1405 s,sh	1340 s,sh 1320 m,sh			
Naphthalene-1-Boronic Acid						1088 m,sh	
Neopentyl glycol ester		3150 m,bd	weak	1340 w,sh	1222 s,sh	1072 s,bd	915 m,bd
Diethanolamine ester	3300 s,bd		1399 s,sh 1410 s,sh	1340 s,sh 1320 m,sh		1075 w,sh	
Naphthalene-1,4-diboronic Acid						1072 s,bd	921 s,sh
Bis (neopentyl glycol) ester		3110 m,sh	weak	1340 w,sh	1230 s,sh	1072 s,bd	
Bis (diethanolamine) ester							

^a Taken in KBr pellets with a Beckman IR-5A or Perkin Elmer 337 infrared spectrophotometer. ^b See Table II. ^c s = strong, m = moderate, w = weak, sh = sharp, bd = broad.

Table II—Other Aryl Boronic Acids Synthesized for Compiling Table I

Compd.	Yield, %	M.p., °C.
Benzene-1,4-diboronic acid	42[lit.(1)35]	> 300
Bis (neopentyl glycol) ester	72	233[lit.(13)233-233.5]
Bis (diethanolamine) ester	95[lit.(14)99]	300[lit.(14)295(dec)]
Naphthalene-1-boronic acid	40[lit.(15)37.5]	213[lit.(16)202.259]
Neopentyl glycol ester	96 ^a	68-68.5
Diethanolamine ester	77.5[lit.(2)88]	244[lit.(2)242-3]

^a Calcd. for C₁₅H₁₇BO₂: C, 75.03; H, 7.14. Found: C, 74.92; H, 7.16.

three aryl boronic acids and their neopentyl glycol ester derivatives revealed a strong sharp band at 1408 ± 10 cm.⁻¹ which did not appear for *p*-dibromobenzene, 1-bromonaphthalene, or 1,4-dibromonaphthalene. Furthermore, upon boron-amine coordination in diptych boroxazolidines, this band was observed to decrease in intensity in the same manner as the B-O asymmetric stretching band. Should there exist some partial double bond character in the B-aryl bond due to delocalization of the aromatic π-electrons from carbon to boron, then upon boron-amine coordination one might well expect the B-C (B-aryl) bond to be weakened; likewise the IR absorption would decrease.

The authors agree with Zimmerman (7) that correlation of IR spectral data is not a simple task, especially for the boroxazolidines, and more detailed IR investigations are most certainly needed.

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