mmol) of NBS were suspended in 125 ml of carbon tetrachloride and irradiated with a 225-W high intensity white light for 30 min. The suspension was cooled and filtered. The volume of the filtrate was reduced to 50 ml (steam bath) and the solution was again cooled and filtered. Final evaporation of the filtrate *in vacuo* left a light tan oil which solidified, with darkening, to give 0.67 g (58%) of crude **1,3-diphenyl-1-bromo-1,3-dihydrothieno-[3,4-*b*]quinoxaline 2,2-dioxide.** Recrystallization from chloroform gave the monobromo product as a light yellow, heat-sensitive, crystalline solid: darkened at 130°, mp 230–232° dec; uv max (95% EtOH) 248 mμ (ε 28,000), 279 sh (10,000) and 326 (7200); nmr ($CDCl_3$) δ 8.25–7.20 (m, 14, aromatic) and 6.15 (s, 1, CH).

Bromination of 11.—A solution of 0.25 g (0.81 mmol) of **11** and 0.30 g (1.7 mmol) of NBS in 25 ml of CCl_4 was refluxed for 2 hr. On cooling, the succinimide was filtered, and the filtrate was evaporated to leave a pink oil which solidified to give 0.21 g (63%) of a mixture of *meso*- and *dl*-**2,3-*bis*(α-bromobenzyl)-quinoxaline** (**42**) as pale pink needles: mp 163–165° (from hexane); uv max (95% EtOH) 247 mμ (ε 29,000) and 329 (6500); nmr (CCl_4) δ 8.17–7.08 (m, 14, aromatic) and 6.64 (*meso*) and 6.48 (*dl*) (each singlet, 2, CH).

Anal. Calcd for $C_{22}H_{16}N_2Br_2$: C, 56.54; H, 3.45; N, 7.21. Found: C, 56.54; H, 3.65; N, 7.05.

Registry No.—Sulfur dioxide, 7446-09-5; **5**, 19029-25-5; *cis* **7**, 19029-79-9; *trans* **7**, 19029-80-2; **9**, 19029-26-6; **10**, 19029-27-7; **11**, 19029-28-8; **13**, 19029-29-9; **14**, 19029-30-2; **15**, 19029-31-3; **17**, 19029-32-4; **22**, 19029-33-5; **23**, 19029-34-6; *meso* **24**, 19029-81-3; *dl* **24**, 19029-82-4; **27**, 19029-35-7; **28**, 19029-36-8; **29**, 19029-37-9; **30**, 19029-38-0; **31**, 19029-39-1; **32**, 19029-40-4; **33**, 19029-41-5; **34**, 19029-42-6; *meso* **42**, 19029-83-5; *dl* **42**, 19029-84-6; 1,3-diphenyl-1-bromo-1,3-dihydrothieno[3,4-*b*]-quinoxaline 2,2-dioxide, 19029-43-7.

Acknowledgment.—We wish to thank Dr. A. J. Fritsch and Professors D. J. Hennessy and R. W. Franck for helpful discussions during both the course of this research and the preparation of this manuscript.

Preparation and Reactions of *o*-(Cyanomethyl)benzeneboronic Acid[1]

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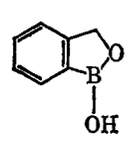
Received July 24, 1968

The synthesis of *o*-(cyanomethyl)benzeneboronic acid **3** is described. Conversion of the nitrile to the amide, acid, alcohol, and amine and cyclodehydration of these substances yield, respectively, the cyclic imide of *o*-boronophenylacetic acid **4**, the cyclic anhydride of *o*-boronophenylacetic acid **5**, the lactone of 2-(*o*-boronophenyl)-ethanol **15** and the lactam of 2-(*o*-boronophenyl)ethylamine **18**. The reaction of cyclic imide **4** and cyclic anhydride **5** with catechol is reported, as is the reaction of **5** with *o*-aminophenol and *o*-phenylenediamine. The ease with which *ortho*-substituted arylboronic acids undergo cyclodehydration and further dehydration to dimeric anhydrides is discussed.

Alkaline hydrolysis of *o*-(bromomethyl)benzeneboronic acid yields boronophthalide **1**,[2,3] the lactone of *o*-(hydroxymethyl)benzeneboronic acid. This lactone is more stable than would be predicted on the basis of the chemistry of simple boronic esters.[3–5] Similarly, reaction of *o*-formylbenzeneboronic acid with hydroxylamine gives a cyclic product **2**.[3,6,7] It seems likely that additional compounds analogous to **1** and **2** will result from the interaction of an aromatic boronic acid group and a second function suitably located on a side chain in the *ortho* position. *o*-(Cyanomethyl)benzeneboronic acid (**3**) should be a useful precursor for such substances because of the ease with which a nitrile group can be converted into other reactive functions.



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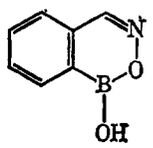


2

Lennarz,[8] in attempts to displace the bromide atom of *o*-(bromomethyl)benzeneboronic anhydride with cyanide, employing strongly basic cyanides and various solvent systems, observed only the formation of boronophthalide **1**. In the present work replacement of the bromine atom is effected when *o*-(bromomethyl)-benzeneboronic anhydride reacts with cyanide ion introduced as the ion associated with a strongly basic ion-exchange resin. The general method is one introduced by Griffin, *et al.*,[9] as a means of avoiding undesirable base-promoted processes brought about by alkali cyanides.

Hydrolysis of *o*-(cyanomethyl)benzeneboronic acid (**3**) with dilute base gives cyclic imide **4** which is further hydrolyzed in acid to cyclic anhydride **5**; neither *o*-(boronophenyl)acetamide nor *o*-(boronophenyl)acetic

(1) This work was supported by Grant AT(11-1)-314 from the Atomic Energy Commission, Report No. C00-314-13.

(2) K. Torssell, *Arkiv Kemi*, **10**, 509 (1957).

(3) H. R. Snyder, A. J. Reedy, and W. J. Lennarz, *J. Amer. Chem. Soc.*, **80**, 835 (1958).

(4) W. J. Lennarz and H. R. Snyder, *ibid.*, **82**, 2172 (1960).

(5) M. F. Lappert, *Chem. Rev.*, **56**, 959 (1956).

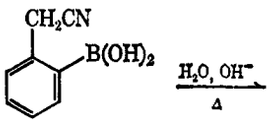
(6) M. J. S. Dewar and R. C. Dougherty, *J. Amer. Chem. Soc.*, **86**, 433 (1964).

(7) For additional examples of cyclic boronic acid derivatives, see P. M. Maitlis, *Chem. Rev.*, **62**, 223 (1962); M. J. S. Dewar, Advances in Chemistry Series, No. 42, American Chemical Society, Washington, D. C., 1964, p 227; M. J. S. Dewar, "Progress in Boron Chemistry," Vol. 1, H. Steinberg and A. L. McCloskey, Ed., The Macmillan Co., New York, N. Y., 1964, p 235.

(8) W. J. Lennarz, Thesis, Doctor of Philosophy, University of Illinois, 1959.

(9) M. Gordon, M. L. DePamphilis, and C. E. Griffin, *J. Org. Chem.*, **28**, 698 (1963).

acid could be isolated as an intermediate. Cyclic imide **4** and cyclic anhydride **5** react with catechol; in both



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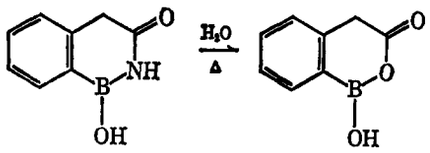
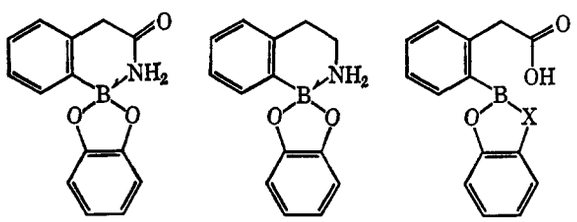


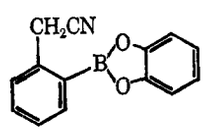
4 **5**

cases ring opening occurs yielding, respectively, the catechol derivative of *o*-(boronophenyl)acetamide **6** and the catechol derivative of *o*-(boronophenyl)acetic acid **8a**. Opening of the imide ring of **4** with subsequent



6 **7** **8a**, X = O; **b**, X = NH

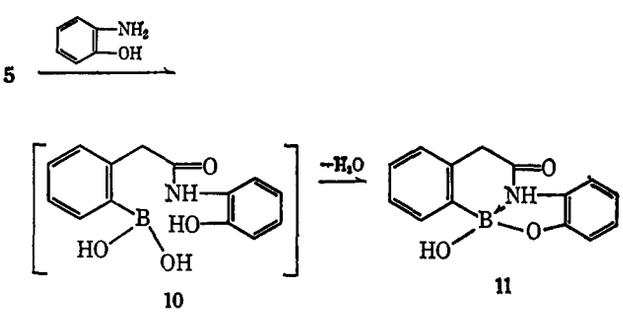
formation of a cyclic catechol derivative is evident from a comparison of the infrared spectra of the catechol derivative of *o*-boronophenylacetamide **6**, the cyclic imide (**4**), and the catechol derivative of *o*-(2-aminoethyl)benzeneboronic acid **7**.[10] The bands from 1350 to 1400 cm^{-1} in the infrared spectrum of **4** are indicative of a tricovalent boronic acid derivative.[11] In the infrared spectrum of **6** these bands are absent and there is a strong infrared absorption at 1240 cm^{-1} which can be attributed to the boron-nitrogen dative bond stretch (>NB<).[11] That **6** and **7** have analogous structures is best indicated by the fact that their infrared spectra are nearly identical; in both cases the boron–nitrogen stretch is observed at 1240 cm^{-1}. The similarity of the infrared spectrum of the catechol derivative of *o*-(cyanomethyl)benzeneboronic acid **9**



9

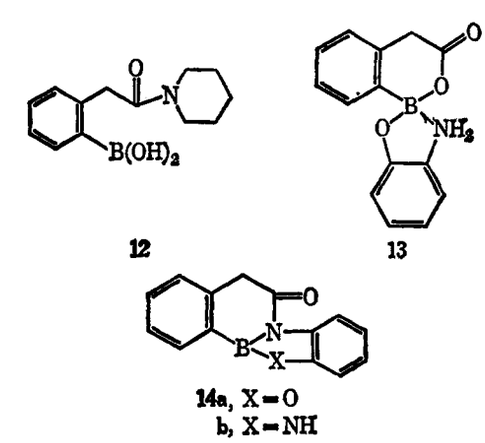
to the infrared spectrum of the catechol derivative of the cyclic anhydride, *i.e.*, **8a**, suggests that **9** and **8a** have similar structures; they are both cyclic catechol derivatives of arylboronic acids. The infrared spectra indicate that the boron atom is tricovalent; the boron–oxygen absorption in **8a** is found at 1330 cm^{-1} and that in **9** at 1325 cm^{-1}.[11] This indicates the lack of coordination between the hydroxyl oxygen of the carboxyl and the boron atom in **8a**.

Cyclic anhydride **5** also reacts with *o*-aminophenol, ring cleavage occurring as in the case of its reaction with catechol; however, in this case the boronic acid function is incorporated into a nine-membered ring (**11**) rather than a five-membered ring. In the macrocyclic ring there is a cross-annular interaction between the boron and the nitrogen, *i.e.*, a boron–nitrogen dative bond. The boron–nitrogen dative bond is indicated by the major infrared absorption band at 1250 cm^{-1}.[11] Formation of **11** is believed to proceed *via* amide **10**, which undergoes spontaneous dehydration to yield **11**. The facile dehydration is due to the phenolic hydroxyl being held in proximity to the boronic acid function.



5 **10** **11**

Amide **12**, analogous to **10**, has been prepared by reaction of cyclic anhydride **5** with piperidine. In this case there was no opportunity for cyclodehydration to



12 **13**

14a, X = O; **b**, X = NH

occur. If the first step in the formation of **11** had been reaction of the phenolic function with the boronic acid, an ester would have been formed in which the amine would be coordinated to the boron[12] (**13**) and would presumably have reacted with the boron to form a catechol-like derivative (**8b**). Vacuum sublimation at 200° of the nine-membered ring component, **11**, causes it to be dehydrated with concurrent formation of a boron–nitrogen bond. This cross-annular reaction yields tetracyclic product **14a**.

A tetracyclic product, analogous to **14a**, **14b** is formed by the reaction of *o*-phenylenediamine with cyclic anhydride **5**; in this case, no intermediate similar to **11** was observed. Boronophthalide (**1**) does not react with *o*-phenylenediamine under similar conditions;[8] the failure of **1** to react indicates that the five-membered

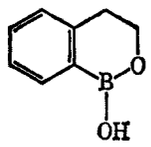
(10) J. C. Catlin, Thesis, Doctor of Philosophy, University of Illinois, 1966.

(11) R. L. Letsinger, Advances in Chemistry Series, No. 42, American Chemical Society, Washington, D. C., 1964, p 3.

(12) R. L. Letsinger and J. R. Nazy, *J. Org. Chem.*, **23**, 914 (1958).

lactone, *i.e.*, boronophthalide (**1**), is more stable than the six-membered anhydride, **5**.

Reduction of cyclic anhydride **5** with lithium aluminum hydride yields, after an aqueous work-up, the lactone of 2-(*o*-boronophenyl)ethanol (**15**), a homolog of boronophthalide (**1**). In contrast, under similar conditions cyclic amide **4** gives 1,2-boraztetralin (**16**);



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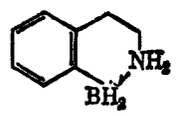
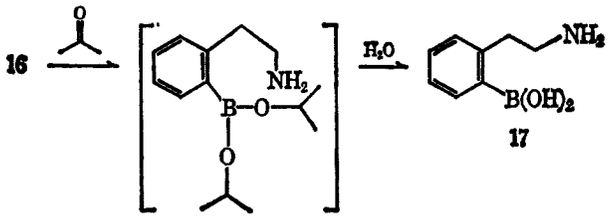


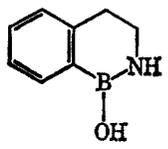
16

16 was hydrolyzed in refluxing aqueous acetone to 2-(*o*-boronophenyl)ethylamine (**17**). 1,2-Boraztetralin (**16**) reacts with acetone, presumably to form a boronic ester[13] which in the aqueous acetone medium is hydrolyzed to acid **17**, as predicted[14] (see Scheme I).

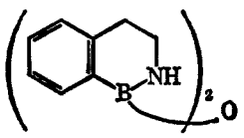
SCHEME I



In the mass spectrometer 2-(*o*-boronophenyl)ethylamine (**17**) is thermally dehydrated to a mixture of lactam **18** and anhydride **19** (molecular ion peaks at *m/e* 147 and *m/e* 276).

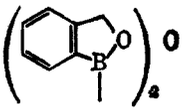


18



19

The ease with which *ortho*-substituted boronic acid derivatives undergo cyclic dehydration appears to depend upon the basicity of the *ortho* substituent. Compounds with weakly basic *ortho* substituents, with the exception of N-substituted *o*-boronophenylacetamides (for example **11**), have not been isolated because of their facile cyclic dehydration. The boronic acid derivatives which undergo this facile dehydration resist further dehydration except under the most stringent conditions. There is no indication that cyclic imide **4**, cyclic anhydride **5** and the lactone of 2-(*o*-boronophenyl)ethanol (**15**) undergo dehydration to their dimeric anhydrides in the mass spectrometer. The dimeric anhydride of boronophthalide **20** is prepared by vacuum distillation of boronophthalide **1** [bp 136° (0.4 mm)].[15] In contrast 2-(*o*-boronophenyl)ethylamine (**17**), a compound with a relatively basic *ortho* substituent, has been isolated, but in the mass spectrometer **17** is dehydrated to its lactam (**18**) and the lactam anhydride (**19**).



20

Experimental Section[16]

Preparation of *o*-(Cyanomethyl)benzeneboronic Acid (3).—Following the procedure of Griffin, *et al.*,[9] 100 ml of Amberlite IRA 400 was washed three times with three times its volume of 20% aqueous sodium cyanide solution. Each time after stirring for 5 min the slurry was diluted with 150 ml of distilled water, and after the resin had settled the cyanide solution was decanted. The resin was washed with distilled water until the wash water gave a negative silver nitrate test for cyanide. The resin was then washed three times with 100-ml portions of tetrahydrofuran (THF). At this point the resin can be stored in THF until needed.

The ion-exchange resin in the cyanide form, 200 ml of THF, and 20 g of *o*-(bromomethyl)benzeneboronic anhydride were stirred under reflux for 4 hr. The resin then was placed in a Soxhlet extractor and extracted overnight with the THF from the reaction mixture. The THF solution was filtered and evaporated *in vacuo*. The oil obtained was placed in 25 ml of water and chilled until it crystallized, yielding 13.0 g (81%) of crude product. An analytically pure sample (6.9 g, 43%) was prepared by recrystallizing the crude material twice from water with Darco treatment (mp 150–152°, dehydration 85°).

Anal. Calcd for $C_8H_8BO_2N$: C, 59.68; H, 5.01; N, 8.70. Found: C, 59.79; H, 4.91; N, 8.93.

Preparation of the Cyclic Imide of *o*-Boronophenylacetic Acid (4).—A mixture of 6.4 g of *o*-(cyanomethyl)benzeneboronic acid and 80 ml of 5% aqueous potassium hydroxide was heated on the steam bath for 2 hr and then chilled. The cold solution was treated with Darco; following acidification with concentrated hydrochloric acid, the cyclic imide (4.1 g, 63%) was collected by filtration. An analytical sample, melting at 202–204°, was prepared by washing with hot acetone.

Anal. Calcd for $C_8H_8BO_2N$: C, 59.68; H, 5.01; N, 8.70; mol wt, 161. Found: C, 59.35; H, 4.97; N, 8.31; mol wt (by mass spectrum), 161.

Preparation of the Cyclic Anhydride of *o*-Boronophenylacetic Acid (5).—A mixture of 6.4 g of *o*-(cyanomethyl)benzeneboronic acid and 80 ml of 5% aqueous potassium hydroxide was heated on the steam bath for 2 hr, acidified by addition of concentrated hydrochloric acid and heated again until a solution was obtained. This solution was heated for 1 hr and chilled overnight. The cyclic anhydride was collected by filtration (5.9 g, 90%). An analytical sample, melting at 136–136.5°, was prepared by recrystallization from water.

Anal. Calcd for $C_8H_7BO_3$: C, 59.31; H, 4.36; mol wt, 162. Found: C, 59.59; H, 4.27; mol wt (by mass spectrum), 162.

Reaction of the Cyclic Imide of *o*-Boronophenylacetic Acid with Catechol.—A stirred slurry of 1.61 g of the cyclic imide of *o*-boronophenylacetic acid, 1.10 g of catechol and 100 ml of xylene was heated at reflux until it appeared that water was no longer being removed. The solution was chilled and the product was washed with ether. The catechol derivative of *o*-boronophenylacetamide (**6**) was obtained in 30% (0.75 g) yield. Recrystallization from benzene–hexane gave an analytical sample melting at 135–137°.

Anal. Calcd for $C_{14}H_{12}BO_3N$: C, 66.46; H, 4.78; N, 5.54; mol wt, 253. Found: C, 66.86, 66.33; H, 4.80, 5.08; N, 5.14,

(13) F. G. A. Stone, *Quart. Rev.*, (London) **9**, 174 (1955).
(14) K. Torssell, *Acta Chem. Scand.*, **8**, 1779 (1954).
(15) R. R. Haynes and H. R. Snyder, *J. Org. Chem.*, **29**, 3229 (1964).

(16) Microanalyses were performed by Josef Nemeth and his associates. Infrared spectra were determined by the staff of the Spectroscopy Laboratory of the Department of Chemistry and Chemical Engineering of the University of Illinois, using a Perkin-Elmer Model 21 infrared spectrophotometer (equipped with sodium chloride optics). All melting points are uncorrected and were obtained on a Kofler microstage apparatus. Evaporations done *in vacuo* were carried out on a rotary evaporator unless specified otherwise. The mass spectra were obtained by Mr. Joseph Wrona on an Atlas CH4 spectrometer.

5.24. In the mass spectrum the $(m + 1)/e$ peak at 254 is more intense than the m/e peak at 253.

Reaction of the Cyclic Anhydride of o-Boronophenylacetic Acid with Catechol.—A solution of 0.81 g of the cyclic anhydride of o-boronophenylacetic acid and 0.55 g of catechol in 25 ml of benzene was heated at reflux for 1 hr. The solution was chilled and 0.78 g (39%) of the catechol derivative of o-boronophenylacetic acid **8a** was collected by filtration. Recrystallization from benzene yielded an analytical sample which changed form at about 119° and melted at 131–132°.

Anal. Calcd for $C_{14}H_{11}BO_4$: C, 66.14; H, 4.33; mol wt, 254. Found: C, 66.20; H, 4.37; mol wt (by mass spectrum), 254.

Preparation of the Catechol Derivative of o-(Cyanomethyl)benzeneboronic Acid (9).—Water was azeotropically removed from a benzene solution of 1.6 g of o-(cyanomethyl)benzeneboronic acid and 1.1 g of catechol. The hot solution was filtered and concentrated under a stream of air to yield 1.4 g (59%) of the catechol derivative of o-(cyanomethyl)benzeneboronic acid. An analytical sample melting at 123–125° was prepared by recrystallization from hexane.

Anal. Calcd for $C_{14}H_{10}BO_2N$: C, 71.55; H, 4.29; N, 5.96. Found: C, 71.79; H, 4.37; N, 5.95.

Reaction of the Cyclic Anhydride of o-Boronophenylacetic Acid with o-Aminophenol.—A solution of 1.62 g of the cyclic anhydride of o-boronophenylacetic acid and 1.09 g of o-aminophenol in 100 ml of xylene was heated at reflux until water was no longer removed. The reaction mixture was poured into hexane and chilled, and the product (1.4 g, 55%) was collected by filtration. Recrystallization from chloroform followed by sublimation at a pot temperature of 150–180° at reduced pressure gave an analytical sample of **11** melting at 179–180°.

Anal. Calcd for $C_{14}H_{12}BO_3N$: C, 66.46; H, 4.78; N, 5.54; mol wt, 253. Found: C, 66.53; H, 4.74; N, 5.57; mol wt (by mass spectrum), 253.

Dehydration of the Product from the Reaction of the Cyclic Anhydride of o-Boronophenylacetic Acid with o-Aminophenol.—A sample of crude material from the above reaction was washed with ether and sublimed *in vacuo* at a pot temperature of 200–210°. The dehydration product which was obtained in 64% yield after 3 hr was recrystallized from acetone. The analytical sample of **14a** melted at 204–206°.

Anal. Calcd for $C_{14}H_{10}BO_2N$; C, 71.55; H, 4.29; N, 5.96; mol wt, 235. Found: C, 71.46; H, 4.34; N, 5.73; mol wt (by mass spectrum), 235.

Reaction of the Cyclic Anhydride of o-Boronophenylacetic Acid with Piperidine.—A benzene solution (100 ml) of 0.81 g of the cyclic anhydride of o-boronophenylacetic acid and 1 ml of piperidine was heated at reflux for 1 hr. The solution was poured into twice its volume of hexane and the product was collected by filtration (yield 0.77 g, 63%). An analytical sample of **12** melting at 125–126° was prepared by crystallization from benzene to which had been added a few drops of piperidine.

Anal. Calcd for $C_{18}H_{18}BO_3N$: C, 63.21; H, 7.35; N, 5.67. Found: C, 63.51; H, 7.62; N, 5.23.

Reaction of the Cyclic Anhydride of o-Boronophenylacetic Acid with o-Phenylenediamine.—A stirred solution of 0.81 g of the cyclic anhydride of o-boronophenylacetic acid and 0.54 g of o-phenylenediamine in xylene was heated under reflux until water was no longer removed. The remaining solvent was evaporated *in vacuo* yielding 0.87 g, 74%. An analytical sample of **14b** was prepared by washing with acetone and recrystallizing from benzene, mp ~200° dec.

Anal. Calcd for $C_{14}H_{11}BON_2$: C, 71.85; H, 4.74; N, 11.97; mol wt, 234. Found: C, 71.60; H, 4.93; N, 11.89; mol wt (by mass spectrum), 234.

Preparation of the Lactone of 2-(o-Boronophenyl)ethanol (15).—A solution of 0.81 g of the cyclic anhydride in 25 ml of THF was added slowly to a stirred slurry of 0.23 g of lithium aluminum hydride in 30 ml of THF. Upon the completion of the addition the reaction mixture was heated at reflux for 1 hr. The excess hydride was decomposed (1% HCl), and the solution was extracted with THF. Upon evaporation of the THF solution a 30% yield of lactone was obtained. After recrystallization from water, the melting point was found to be 60–61°.

Anal. Calcd for $C_8H_9BO_2$: C, 64.92; H, 6.13; mol wt, 148. Found: C, 64.86; H, 5.86; mol wt (by mass spectrum), 148.

Reduction of the Cyclic Imide of o-Boronophenylacetic Acid.—A stirred mixture of 1.61 g of the cyclic imide and 0.76 g of $LiAlH_4$ in THF was heated under reflux 2.5 hr and then stirred overnight. The excess hydride was decomposed (water) and the mixture was filtered. The filtrate was concentrated and extracted with ether. Evaporation of the ethereal solution gave 0.83 g (62%) of 1,2-boraztetralin **16** (mp 135–138° dec) which was identified by comparison of its infrared spectrum with the spectrum of an authentic sample.[10]

Preparation of 2-(o-Boronophenyl)ethylamine (17).—A solution of 0.5 g of 1,2-boraztetralin in 30 ml of 5:1 acetone–water was heated at reflux for 1 hr. The solution was concentrated under a stream of air, and the product was collected in 60% yield by filtration. A sample melting at 116–118° was prepared by recrystallization from benzene.

Anal. Calcd for $C_8H_{12}BO_2N$: C, 58.23; H, 7.33; N, 8.49. Calcd for $C_8H_{10}BON$: mol wt, 147. Calcd for $C_{16}H_{18}B_2ON_2$: mol wt, 276. Found: C, 58.74; H, 7.42; N, 7.70; mol wt (by mass spectrum), 147 and 276.

Registry No.—**3,** 16538-46-8; **4,** 19206-44-1; **5,** 19206-45-2; **6,** 19214-80-3; **8a,** 19206-46-3; **9,** 19206-47-4; **11,** 19227-69-1; **12,** 19206-48-5; **14a,** 19206-49-6; **14b,** 19206-50-9; **15,** 19206-51-0.