Arylboronic Acids. A Medium-Size Ring Containing Boronic Ester Groups[1]

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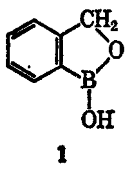
Received July 24, 1968

Dehydration of hydroxyethylboronophthalide (**2**) is shown to occur by a bimolecular route giving a dimeric boronic ester (**4**). This ester is not easily hydrolyzed, and under mild conditions it does not react with such reagents as 2-aminoethanol and *o*-phenylenediamine. Such remarkable stability is attributed to an intramolecular coordination of oxygen atoms to electron-deficient boron atoms. Conditions of aromatic nitration cause aromatic substitution along with solvolysis of the borate bond to form 5-nitroboronophthalidylethyl nitrate. The nitration and esterification of boronophthalidylacetic acid and the esterification of 5-nitroboronophthalidylacetic acid are also studied. Ir and nmr spectra of α-substituted boronophthalides are discussed.

The unusual stability of the boronolactone ring in boronophthalide (**1**) and in many of its functional derivatives[2–6] suggests an examination of the hydroxyethylboronophthalide (**2**), particularly with reference to its behavior under conditions of dehydration. The simplest possible paths of dehydration of **2** are intermolecular esterification of the remaining B–OH function by the primary alcohol group, a process that would lead to a linear polymer, and the corresponding intramolecular esterification, which would lead to the tricyclic monomeric ester (**3**); but there are many possible dehydration paths, including the bimolecular equivalent of the intermolecular esterification, a process which would produce the "dimeric" ester (**4**), opening of the boronophthalide ring to the boronocinnamyl alcohol, which might react further both by esterification and boronic anhydride formation, and others.

To obtain 2-boronophthalidylethanol (**2**) for study, boronophthalidylacetic acid (**5**) was prepared from *o*-formylbenzeneboronic acid by condensation with either malonic acid or isopropylidene malonate,[6] and the acetic acid derivative was reduced with lithium aluminum hydride. The crude oily product from the reduction reacted with phenyl isocyanate to give a crystalline derivative having the composition of the phenylurethan of **2**. But the alcohol proved to be remarkably sensitive to dehydration, and it was not possible to obtain it in the pure state. On storage over a desiccant or even on trituration with cyclohexane, it changed to a colorless high-melting solid. The solid was of low solubility in the common solvents, but it could be purified readily by sublimation at low pressure (2–4 mm). Volatility sufficient to permit sublimation suggests that the substance is one of the cyclic esters (**3** or **4**); microanalysis and molecular weight determinations (by the Rast method and by mass spectrometry) show that it is the "dimeric" ester **4**.



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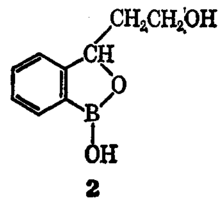

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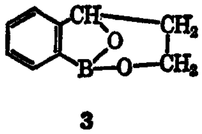

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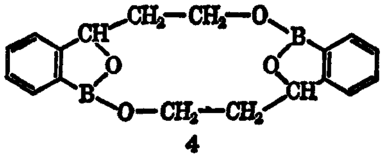

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Although simple boronic esters are very easily solvolyzed, derivatives obtained from 2-aminoethanol[7,8] are remarkably stable as the result of coordination between the nitrogen and boron atoms. Similarly, stablilized derivatives have been obtained from *o*-phenylenediamine.[8] Dimeric ester **4**, however, was recovered from treatment with these reagents. It is apparently slowly hydrolyzed by water alone, for it does dissolve in water on prolonged heating and the solutions so formed do not deposit solid material on cooling. However, extraction of such solutions with benzene and evaporation of the solvent permit the recovery of the dimeric ester **4**, evidently as the result of hydrolysis, extraction of the monomer into the benzene, and re-formation of the dimer during the concentration of the solution. Finally, the dimeric ester gave no indication of the formation of an adduct with pyridine, a reagent which yields isolable solid derivatives with many boronic anhydrides.[9]

The stability of the cyclic dimer suggests that the boron atoms are coordinated with oxygen atoms and that the actual structure may be somewhat similar to that of tribenzotaralene (**6**).[10] The novel feature of the latter structure is the superposition of the trimethylenetriamine ring and the boroxine ring so that each boron atom is near enough a nitrogen atom that coordination occurs and the groups are locked in the multicyclic arrangement (**6**). In the models of the cyclic dimer (**4**), the boron atoms and oxygen atoms of the boronolactone rings are found to be quite near each other. If coordination occurs across the ring system (**7**), the structure can be regarded as equivalent to that having the two six-membered boronic ester rings disposed one above the other and linked by oxygen–boron coordination (**7**). The four-membered ring central to structure **7** is similar to the type proposed to explain the dimerization of methyl difluoroboronite and *n*-butyl difluoroboronite in the liquid state.[11,12]

In a test of the behavior of dimeric ester **4** under

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[1] This work was supported by Grant AT(11-1)-314 from the Atomic Energy Commission, Report No. C00-314-15.

[2] K. Torssell, *Arkiv Kemi*, **10**, 507 (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] R. R. Haynes and H. R. Snyder, *J. Org. Chem.*, **29**, 3229 (1964).

[6] P. Tschampel and H. R. Snyder, *ibid.*, **29**, 2168 (1964).

[7] R. K. Kurz, Ph.D. Thesis, University of Illinois, 1961.

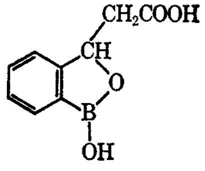
[8] R. L. Letsinger and S. B. Hamilton, *J. Amer. Chem. Soc.*, **80**, 5411 (1958).

[9] H. R. Snyder, M. S. Konecky, and W. J. Lennarz, *ibid.*, **80**, 3611 (1958).

[10] The authors are indebted to Professor Dewar for permission to reproduce the tribenzotaralene structure shown by M. J. S. Dewar, R. C. Dougherty, and E. B. Fleischer, *ibid.*, **84**, 4882 (1962).

[11] J. Goubeau and K. E. Lücke, *Ann.*, **575**, 37 (1952).

[12] M. F. Lappert, *J. Chem. Soc.*, 784 (1955).



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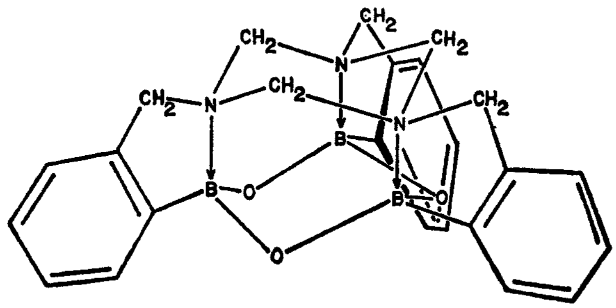

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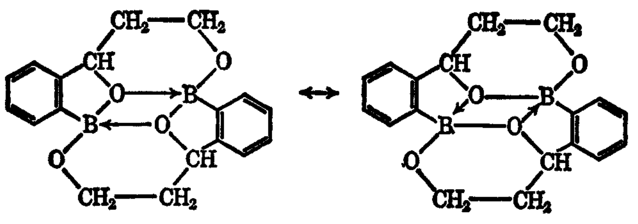

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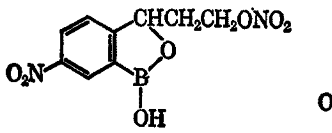

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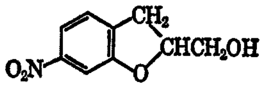

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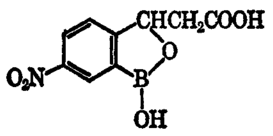

10

conditions of aromatic substitution, the substance was treated with fuming nitric acid at −40°. Both nitration and cleavage occurred, the product being nitro nitrate **8**. The nitrate ester function in **8** was unaffected by aqueous or methanolic sodium hydroxide under conditions that cause the solvolysis of ethyl nitrate. Alkaline hydrogen peroxide effected both oxidative removal of the boron and solvolysis of the nitrate function, the product obtained after acidification being 2-(hydroxymethyl)-6-nitro-2,3-dihydrobenzofuran (**9**). This structure, rather than that of the isomeric hydroxycinnamyl alcohol, for the deboronation product was suggested by the failure of the substance to give a color with ferric chloride and is in agreement with the nmr spectral measurements (see Experimental Section).

Because of the unexpected course of the dehydration of alcohol **2**, it would be of interest to examine the behavior of the next lower homolog, α-hydroxymethylboronophthalide. α-Carboxyboronophthalide is readily available,[6] and it was assumed that its reduction with lithium aluminum hydride would parallel that of the higher homolog. Surprisingly, the reduction took an entirely different course; the only product obtained upon working up the reaction mixture in the usual way, without exclusion of air, was *o*-tolueneboronic acid, isolated as its anhydride. It is tempting to consider that at some stage in the process the boronophthalide ring was opened reductively and the B–H link so formed underwent oxidation during handling in the air; the question has not been studied, nor is the fate of the carbon atom lost in the reduction known.

Structure **5** of boronophthalidylacetic acid was originally assigned on the basis of its infrared spectrum.[6] Study of the nmr spectrum (see below) confirms the structure and, together with molecular weight measurements in solution, indicates coordination between the boron atom and a carboxylate oxygen atom. Although mixed anhydrides do not readily form from boronic and carboxylic acids, the proximity of the two functions in **5** might promote such anhydride formation. The other possible consequence of the proximity of the two functions, however, is facilitation of acid-catalyzed deboronation. The latter influence is the dominating one. When the acid was heated under diminished pressure near its melting point, cinnamic acid was the only organic product isolated. The action of thionyl chloride under mild conditions also caused extensive deboronation of **5**. The acid could be converted into its methyl ester by the action of methanol. In the mass spectrometer the methyl ester gave peaks corresponding to the expected molecular weight (mass 206) and to that of the anhydride (mass 394) formed by combination of two molecules by elimination of water between >B–OH functions.

Boronophthalidylacetic acid also could be nitrated by fuming nitric acid at −40°, the nitro group entering the 5 position (**10**). The infrared spectrum of the nitration product does not alone suffice for the assignment of the boronophthalide structure (rather than the isomeric cinnamic acid), but the nmr evidence favors this formulation and confirms the position of the nitro group. The nitro acid also gives a methyl ester which in the mass spectrometer gave only the peak corresponding to its anhydride (mass 484).

Spectral Data.—The structures suggested for the various compounds above rest in part on ir and nmr spectral data. The infrared spectra (Table I) contain three features which have been reported earlier in the spectra of various boronophthalides.[6,13] (1) Except in c, the oxygen–hydrogen stretching frequency of these systems is in the range 3350–3450 cm^{-1}. (2) Two bands appear in the 1340–1380-cm^{-1} region. These have been attributed to the symmetric and asymmetric B–O stretching frequencies, respectively. However, for d and f, the band near 1350 cm^{-1} is assigned to the asymmetric NO_2 stretching frequency because of the known intensity of this band which would obscure the band due to the asymmetric B–O stretching frequency. (3) All spectra contain a band in the 1070–1100-cm^{-1} region. This band has been assigned previously to the C–O stretch in five-membered cyclic ethers.[14] All boronophthalide spectra studied previously[5,6,13] had a band in the region 970–1005 cm^{-1}, which had been attributed to a C–O stretching frequency. All but c and e show this band. Why c and e do not show this absorption is not clear, but other properties of the compounds support their formulation as boronophthalides. The carbonyl frequencies of a and c, taken

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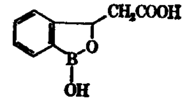
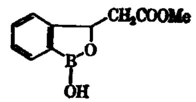
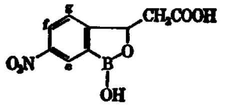
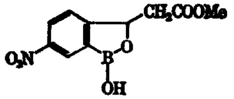
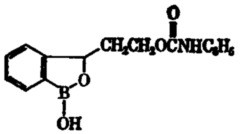
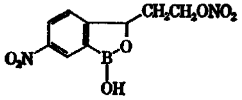
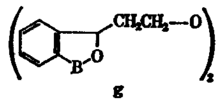
[13] W. J. Dale and J. E. Rush, *J. Org. Chem.*, **27**, 2598 (1962).

[14] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, Methuen and Co., London, 1956, p 119.

TABLE I

SPECTRAL DATA OF α-SUBSTITUTED BORONOPHTHALIDES

Compound	Infrared[a]						Nmr						
	OH	B–O	Cyclic ether	C–O			Solvent	H_X	$H_{B(endo)}$	$H_{A(exo)}$	H^b	Aromatic	Coupling constants, cps
 a	3350	1340, 1365	1090	1002 (s)	C=O	1740 1740 (Nujol)	TFA[c] DMSO-d_6	4.13 (dd) 4.48 (dd)	6.72 (dd) 6.95 (dd)	7.25 (dd) 7.50 (dd)			J_{AB} = 16.0 J_{AX} = 9.0 J_{BX} = 4.0
 b	3400	1340, 1370	1100	990 (m)	C=O	1725	Acetone-d_6	4.42 (dd)	7.05 (dd)	7.51 (dd)	6.30 (s)		J_{AB} = 15.0 J_{AX} = 8.5 J_{BX} = 4.5
 c	3100	1365	1090		C=O NO₂ (asym) (sym)	1690 1690 (Nujol) 1510 1340	DMSO-d_6	4.36 (dd)	6.88 (dd)	7.50 (dd)		H_e 1.85 (s) H_f 2.05 (d) H_g 2.65 (d)	J_{AB} = 15.5, J_{ortho} = 9.0 J_{AX} = 9.5, J_{meta} = 2.0 J_{BX} = 5.0
 d	3400	1370	1070	980 (m)	C=O NO₂ (asym) (sym)	1720 1520 1350	Acetone-d_6	4.30 (dd)	6.95 (dd)	7.34 (dd)	6.30 (s)		J_{AB} = 16.0 J_{AX} = 8.0 J_{BX} = 5.0
 e	3400	1340, 1365	1070		C=O	1660 (amide I) 1620 (amide II)	CDCl₃	4.65 (dd)	8.0 (m)	8.0 (m)	5.65 (t)		J_{AX} = 8.0 J_{BX} = 5.0
 f	3450	1355	1080	965 (m)	ONO₂ (asym) NO₂ (asym) NO₂ (sym) ONO₂ (sym)	1635 1510 1340 1285	CDCl₃	4.55 (dd)	8.0 (m)	8.0 (m)	5.30 (t)		J_{AX} = 9.0 J_{BX} = 5.0
 g		1345, 1365	1100	975 (s)									

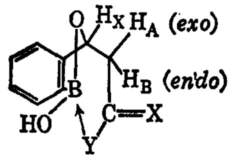
[a] All spectra were taken in potassium bromide disks unless otherwise noted. [b] Other aliphatic hydrogens. [c] TFA (trifluoroacetic acid). H_X = the hydrogen on the borono hetero ring. H_A and H_B = the methylene hydrogens in the position α to the hetero ring.

from spectra in potassium bromide disks and Nujol mulls, are separated by 50 cm^{-1}. A frequency of 1740 cm^{-1} might be expected for the carbonyl of a if there is internal coordination by the hydroxyl group of the carboxyl group with the boron atom forming a pseudo[3.2.1] system similar to a cyclic acyl derivative of a boronic acid. The low value for the carbonyl absorption of c (1690 cm^{-1}) cannot be explained in this fashion. This low carbonyl frequency could result from the coordination of the carbonyl oxygen with the boron atom, creating an effect similar to that of hydrogen bonding.[15] The carbonyl frequencies of the methyl esters of a and c are almost the same but still 15–20 cm^{-1} lower than the carbonyl absorptions for normal methyl esters.[16] Again, this can be explained by a perturbation of the carbonyl oxygen by the boron atom.

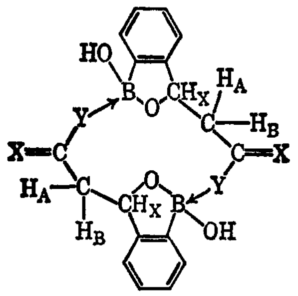
The nuclear magnetic resonance spectra of these α-substituted boronophthalides (Table I) are more complex than would be expected *a priori*. All (a–f) contain a one-proton double doublet between τ 3.95 and 4.75. This absorption has been previously assigned to the proton of the boronophthalide ring system (in boronophthalide[17] itself, τ 4.98). The two-proton absorptions in the τ 6.72–8.00 region are assigned to the methylene protons adjacent to the boronophthalide ring. These methylene proton absorptions in a–d are characterized by two well-defined double doublets while in e and f only a complex multiplet is observed. In addition to these absorptions, e and f each have a well-defined, two-proton triplet in the τ 5.30–5.65 region.

This pattern of double doublets in a–d is characteristic of an ABX system in which two nonequivalent protons attached to the same carbon are splitting each other in the presence of a third proton on an adjacent carbon. In e and f, the AB part of the spectrum is further split by two additional adjacent protons, producing a very complex multiplet.

There are three ways to explain this ABX splitting pattern: (1) there is internal coordination by the electrons of a heteroatom to an empty orbital of boron, forming a pseudobicyclic[3.2.1] system; (2) there is a head–tail association of two molecules, again with available electrons filling the vacant orbital of boron, thereby restricting the rotation of the methylene group by locking it into a cyclic conformation;[18] (3) the AB nonequivalence results from the asymmetry of the methylene hydrogens caused by the adjacent asymmetric center.[19]



A, X = methylene or heteroatom
Y = grouping containing heteroatom



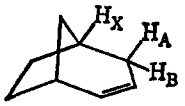
B

Molecular weight studies in acetone or chloroform indicate that these compounds are monomeric in these solvents. Spectra obtained in these solvents and in more polar solvents [DMSO and TFA (trifluoroacetic acid)] should be of a monomeric species.

Infrared studies indicate that there is some type of internal coordination to the boron atom. This is particularly evident in a whose acid carbonyl is at 1740 cm^{-1} [14] and in the methyl esters of b and d whose carbonyl frequencies are 15–20 cm^{-1} lower than would normally be expected in methyl esters.[16] These data suggest some type of perturbation by the boron atom. Molecular models of these compounds show that there is very little bond distortion in forming a pseudo[3.2.1] bicyclic ring system from the most stable conformer.

Generally, then, the spectra of a–f can best be explained on the basis of a structure such as A with the appropriate heteroatom forming the weak bond to the boron atom.

The geminal coupling constants for a–d are 15.0–16.0 cps. These are quite similar to the geminal coupling constants found for bicyclo[3.2.1]oct-2-ene.[20]



J_{AB} = 17.0 cps
J_{AX} = 4.7 cps
J_{BX} = 2.0 cps

The vicinal coupling constants, however, are quite different. Both in the bicyclo[3.2.1]oct-2-ene series[20] and in the dibenzobicyclo[3.2.1]octadiene,[21] J_{BX}(*endo*) was found to be *ca.* 1.5–2.5 cps and J_{AX}(*exo*) = 4.7–5.5 cps. Since the *exo* proton is shown to couple more strongly than the *endo* in these bicyclic systems, the larger coupling (8.0–9.0 cps) can be assigned to the pseudo-*exo* proton in the pseudobicyclo[3.2.1] system. The highest chemical shift can then be assigned to the pseudo-*exo* proton.

Compounds with more than one heteroatom in proximity (e and f) to the boron atom could coordinate to give systems other than pseudobicyclo[3.2.1] systems. However, the invariance of the vicinal coupling constants J_{AX} and J_{BX} of the ABX system suggests that the steric relationship between these protons remains the same throughout the series. A preference for bicyclo[3.2.1] coordination is thus seen.

Nuclear magnetic resonance studies of the dimeric ester were accomplished with more difficulty. In most common nmr solvents, the solubility of this dimer was so low that good spectra could not be obtained. Even

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(15) L. A. Duncanson, W. Gerrard, M. F. Lappert, H. Pyszora, and R. Shafferman, *J. Chem. Soc.*, 3652 (1958).

(16) R. G. Sinclair, A. F. McKay, and R. N. Jones, *J. Amer. Chem. Soc.*, **74**, 2570 (1952).

(17) R. T. Hawkins, W. J. Lennarz, and H. R. Snyder, *ibid.*, **82**, 3053 (1960).

(18) R. F. Watson and J. F. Eastman, *ibid.*, **87**, 665 (1965).

(19) G. M. Whitesides, F. Kaplan, K. Nagarajan, and J. D. Roberts, *Proc. Natl. Acad. Sci. U. S.*, **48**, 1113 (1962).

(20) C. W. Jefford, B. Waegell, and K. Ramey, *J. Amer. Chem. Soc.*, **87**, 2191 (1965).

(21) S. J. Cristol, J. R. Mohrig, and D. E. Plorde, *J. Org. Chem.*, **30**, 1956 (1965).

in DMSO-d_6 only a 4% solution could be obtained. However, this ester did dissolve in TFA and gave a spectrum similar to those of e and f.

A low-field triplet at τ 5.45 indicates that the dimeric ester has been solvolyzed and most likely a trifluoroacetate of the monomer has formed. If solvolysis had not occurred, a chemical-shift value for this triplet would be expected to occur near τ 6.3 (*n*-butyl borate, 6.25). This shift of almost 1 ppm can most easily be explained by this solvolysis of the dimeric ester. A similar shift for alcohols in TFA has been noticed before. Peterson[22] reports a value of τ 6.02 for the α-methylene hydrogens of ethyl trifluoroacetate, a shift of 0.63 ppm from value of τ 6.65 for ethanol itself.

The nuclear magnetic resonance spectrum of urethan e has two one-proton, singlet absorptions at very low field (τ 0.4 and 0.8). The position of the former (the other being the amido proton absorption) is consistent with the BO–H proton absorptions found for boronophthalidylacetic acid (τ 0.5) and 2-(5-nitroboronophthalidyl)ethyl nitrate and with that found for α-(nitromethyl)boronophthalide (τ 0.3).[6] This low-field, singlet BO–H proton absorption thus appears to be a characteristic feature in the nuclear magnetic resonance spectra of α-substituted boronophthalides containing a heteroatom in the side chain capable of coordination with the electron-deficient boron atom of the boronophthalide ring system. Its appearance in the spectrum of urethan e is evidence that the phenyl isocyanate has indeed added to the alcoholic hydroxyl group, and not to the boronic hydroxyl group.

Mass Spectrometric Measurements.—The course of decomposition of thermally unstable compounds can sometimes be determined by mass spectrometry. Compounds a, c, and e decompose in the mass spectrometer when the samples are heated. The mass spectrograms of cinnamic and *p*-nitrocinnamic acids were obtained when a and c were so heated. When urethan e was heated *in vacuo* decomposition to its precursors (*o*-boronophthalidylethanol and phenyl isocyanate) occurred. This mode of breakdown in the mass spectrometer is characteristic of urethans containing a phenyl group as a N substituent.[23] Water was also immediately lost, forming dimeric ester g. The newly formed water reacted with phenyl isocyanate to give the expected products (aniline and symmetrical diphenylurea). All these molecular ions are observed in the low-voltage mass spectrogram.

This thermal behavior is also noted outside the mass spectrometer. Subjecting a, c, and e to heat and reduced pressure in a sublimation apparatus gives cinnamic acid, *p*-nitrocinnamic acid, and dimeric ester g, respectively.

Experimental Section[24]

Boronophthalidylacetic Acid (a).—The following modification of Tschampel's preparation from *o*-formylbenzeneboronic acid and malonic acid[6] is about three times more productive and hence also superior to the preparation from isopropylidene malonate.[6] Into 30 ml of reagent grade dioxane was put 3.0 g (20 mmol) of *o*-formylbenzeneboronic acid along with 3.0 g (34 mmol) of malonic acid. After the addition of 5 drops of pyridine, the reaction solution was heated on a steam bath for 24 hr during which time the evolution of carbon dioxide was noticed. The reaction mixture was cooled to ambient temperature and saturated with ammonia. A light yellow solid precipitated which was collected and dried *in vacuo* to give 4.5 g of product. It was dissolved in 20 ml of water and extracted three times with 20-ml portions of ether. These extracts were discarded. The aqueous portion was acidified to pH 3 with concentrated hydrochloric acid and extracted three times with 20-ml portions of ether. These ethereal portions were combined and the ether then allowed to evaporate into the air, leaving a colorless oil which crystallized within 24 hr. After the wet, light yellow crystals had dried on a porous clay plate, 2.0 g of *o*-boronophthalidylacetic acid (53%), mp 120–130°, was collected.

Again these crystals were dissolved in 10 ml of water; this solution was saturated with ammonia and then extracted three times with 20-ml portions of ether which were discarded. After acidification, the aqueous solution was extracted three times with 20-ml portions of ether. The ethereal portions were combined and the ether was allowed to evaporate into the air. Again, crystallization occurred within 24 hr, giving an off-white product, mp 128–130° (lit.[6] mp 129–130°). Lack of any absorption in the 1670-cm^{-1} region of the infrared spectrum of this product showed that there was no starting aldehyde present. The molecular weight, determined in acetone, was 177 (calcd 192). In subsequent preparations, rapid crystallization (within 8 hr) could be induced by seeding the colorless oil with a crystal of *o*-boronophthalidylacetic acid.

This acid (50 mg) was heated at 120° at 2.0-mm pressure in a microsublimation apparatus. From the cold finger, 35 mg (95%) of cinnamic acid, mp 132–133° (lit.[25] mp 132.5–133°), was recovered.

5-Nitroboronophthalidylacetic Acid (c).—To 2 ml of fuming nitric acid held at −40 to −50° was added 0.32 g (1.7 mmol) of boronophthalidylacetic acid. The addition was done in small portions and completed within 15 min. The mixture was then stirred and maintained at −30 to −40° until all the solid had gone into solution. This solution was poured into ice water and allowed to remain at 0° for 2 hr. White crystals (0.25 g, 62%) were collected by filtration. An analytical sample, mp 217–218°, was prepared by recrystallizing twice from water, followed by drying at 55° over phosphorus pentoxide at 0.1 mm overnight.

Anal. Calcd for $C_9H_8BNO_6$: C, 45.61; H, 3.40; N, 5.91, mol wt, 237. Found: C, 45.55; H, 3.53; N, 5.73, mol wt, 240 (in acetone).

This acid (50 mg) was heated at 240° at 2.0-mm pressure in a microsublimation unit. From the cold finger was collected 30 mg (75%) of 4-nitrocinnamic acid, mp 284–286° (lit.[26] mp 285–286°).

Methyl Boronophthalidylacetate (b).—Into 10 ml of methanol was added 400 mg (2.1 mmol) of boronophthalidylacetic acid along with 3 drops of concentrated hydrochloric acid. This mixture was heated at reflux for 20 hr. After cooling to room temperature, the solvent was removed *in vacuo* to give 360 mg (84%) of product, mp 88–90°. An analytical sample was prepared by recrystallization from a chloroform–petroleum ether (bp 30–60°) mixture.

Anal. Calcd for $C_{10}H_{11}BO_4$: C, 58.16; H, 5.51. Found: C, 58.30; H, 5.38.

Methyl 5-nitroboronophthalidylacetate (d), mp 118–120°, was prepared in a manner similar to preparation of methyl boronophthalidylacetate. An analytical sample was prepared by one recrystallization from water.

Anal. Calcd for $C_{10}H_{10}BNO_6$: C, 47.85; H, 4.02; N, 5.58. Found: C, 47.92; H, 4.17; N, 5.48.

Dimeric Ester of 2-Boronophthalidylethanol (g).—To 1.0 g (26 mmol) of lithium aluminum hydride suspended in 20 ml

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[22] P. E. Peterson, *ibid.*, **31**, 439 (1966).

[23] H. Budzibiewicz, C. Djerassi, and D. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, p 501.

[24] All melting points were taken on a Kofler hot-stage microscope and are uncorrected. Microanalysis and molecular weight determinations (with a Mechrolab Model 310A vapor-pressure osmometer) were performed by Mr. Josef Nemeth and his associates. Infrared spectra in potassium bromide pellets were determined with a Perkin-Elmer Model 21 infrared spectrophotometer and nuclear magnetic resonance spectra were obtained with a Varian Associates Model A-60 nuclear magnetic resonance spectrophotometer. These were done by the staff of the Spectroscopy Laboratory of the Department of Chemistry and Chemical Engineering of the University of Illinois. Other infrared spectra were obtained in Nujol mulls on a Perkin-Elmer Model 137. Mass spectra were obtained by Mr. Joseph Wrona on an Atlas CH4 spectrometer.

[25] J. H. Mathews, *J. Amer. Chem. Soc.*, **39**, 1132 (1917).

[26] E. Knoevenagel, *Ber.*, **31**, 2612 (1898).

of ether was added 1.0 g (6 mmol) of boronophthalidylacetic acid in 40 ml of ether at such a rate that the reaction solution refluxed gently. After the addition, the mixture was allowed to reflux for 1 hr and then allowed to cool to room temperature. It was chilled by means of an ice bath, and the excess lithium aluminum hydride decomposed by the dropwise addition of 10 ml of water. Next, 40 ml of 10% hydrochloric acid was added and the layers were separated. The aqueous layer was extracted three times with 30-ml portions of ether; the combined ethereal portions were washed with 5% hydrochloric acid and then dried over magnesium sulfate. The ether was removed *in vacuo*, giving a colorless oil which, after 1 day over phosphorus pentoxide at 3-mm pressure, changed to a white solid. This was washed with acetone or cyclohexane, giving 600 mg (65%) of the dimeric ester of 2-boronophthalidylethanol, mp 226–229°. An analytical sample was prepared by subliming a sample at 225° at 3-mm pressure.

Anal. Calcd for $C_9H_9BO_2$: C, 67.56; H, 5.67; B, 6.76; mol wt, 160 (monomer), 320 (dimer). Found: C, 67.35, H, 5.68; B, 6.44; mol wt, 320 (mass spectrum).

2-Boronophthalidylethyl N-Phenyl Carbamate (e).—As described previously, 1.9 g (10 mmol) of *o*-boronophthalidylacetic acid was reduced with lithium aluminum hydride to give a clear, colorless oil. This oil was treated with 1.1 ml of phenyl isocyanate with warming on a steam bath. After drying for 2 days over phosphorus pentoxide, the oily, yellow solid obtained changed to 2.8 g of a pale yellow solid. This solid was heated in 20 ml of carbon tetrachloride. The solid residue (0.8 g) was collected by filtration and was identified as *sym*-diphenylurea, mp 236–238° (lit.[27] mp 235°). From the filtrate, upon evaporation, was obtained 2.0 g (67%) of 2-boronophthalidylethyl N-phenyl carbamate. This was recrystallized twice from petroleum ether, methylene chloride, and carbon tetrachloride (1:1:1), giving white needles, mp 103–105°.

An analytical sample was prepared by two additional recrystallizations from cyclohexane–benzene, followed by drying at 55° under reduced pressure.

Anal. Calcd for $C_{16}H_{16}BNO_4$: C, 64.67; H, 5.43; N, 4.72; mol wt, 297. Found: C, 64.68; H, 5.41; N, 4.45; mol wt (in chloroform), 266.

Attempted Hydrolysis of Dimeric Ester of Boronophthalidylethanol. In Water.—To 10 ml of water was added 160 mg (0.5 mmol) of the dimeric ester, and the reaction mixture was heated until no precipitate formed upon cooling. This aqueous solution was extracted three times with 15-ml portions of anhydrous benzene. The benzene extracts were combined and dried over molecular sieves. To this solution were added 12 drops of phenyl isocyanate. As the solution was being concentrated, a white solid began to precipitate. The solution was then concentrated to 10 ml and the white solid collected to give 100 mg of starting material (62% recovery), mp 230–232°.

In Dimethyl Sulfoxide.—Into 7 ml of dimethyl sulfoxide was placed 50 mg (0.18 mmmol) of the dimeric ester, along with three drops of water. This solution was heated gently on a steam bath for 2 days and cooled to room temperature; a 25-ml portion of a cold, saturated sodium chloride solution was added. Then this aqueous solution was extracted three times with 25-ml portions of ether. The ethereal extracts were combined and dried over anhydrous magnesium sulfate. After the ethereal solution had been concentrated to 10 ml, 3 drops of phenyl isocyanate were added to it. No visible reaction occurred. After 0.5 hr, the ether was removed *in vacuo*, giving a sticky, yellowish solid. This solid was placed in a porous clay plate to dry. Both the infrared spectrum of this compound and its melting point, 228–238°, indicated that it was a mixture of *sym*-diphenylurea and the dimeric ester.

In similar experiments, the dimer was recovered from solutions of ethanol and pyridine. When the dimeric ester was treated with 2-aminoethanol, *o*-phenylenediamine, and *n*-propylamine, no boron-containing organic compounds could be isolated.

2-(5-Nitroboronophthalidyl)ethyl nitrate (f) was prepared in 85% yield by the same procedure used to prepare 5-nitroboronophthalidylacetic acid. The cream-colored product melted at 100–102°.

A sample was prepared for analysis by twofold recrystallization from benzene and subsequent twofold recrystallization from benzene–cyclohexane. This analytical sample melted at 105–106°.

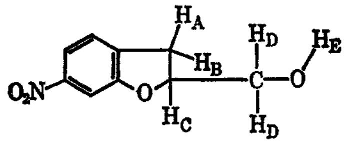
Anal. Calcd for $C_9H_9BN_2O_7$: C, 40.33; H, 3.39; N, 10.45; mol wt, 268. Found: C, 40.24; H, 3.58; N, 10.31; mol wt, 278 (in chloroform).

Treatment of 2-(5-Nitrophthalidyl)ethyl Nitrate with Basic Hydrogen Peroxide Solution.—To 4.0 ml of 3% hydrogen peroxide in 15 ml of ethanol was added 100 mg (0.4 mmol) of 2-(5-nitrophthalidyl)ethyl nitrate, along with 100 mg (2.5 mmol) of sodium hydroxide. This solution was stirred at room temperature for 24 hr. Then, it was acidified to pH 4 with concentrated hydrochloric acid. This clear, colorless solution was concentrated to 5 ml. After chilling in an ice bath, 50 mg (66%) of 2-hydroxymethyl-6-nitro-2,3-dihydrobenzofuran, mp 124–125°, was collected.

An analytical sample was prepared by recrystallization from ethanol-water followed by drying over phosphorus pentoxide at 3 mm for 24 hr.

Anal. Calcd for $C_9H_9NO_4$: C, 55.38; H, 4.65; N, 7.17; mol wt, 195. Found: C, 55.45; H, 4.86; N, 7.28; mol wt, 195 (mass spectrum).

The structure assigned to this compound depends mostly on nmr spectral data taken in DMSO-d_6.



H_A or H_B, τ 7.91 or 8.12, J_{AB} = 10.0 cps
H_C (m), τ 6.30
H_D (t), τ 5.71
H_E (t), τ 5.28, $J_{CD} \cong J_{DE} \cong$ 5.0 cps

α-**Cyanoboronophthalide.**—*α*-Cyanoboronophthalide, mp 113–115° (lit.[6] mp 118–119°), was prepared according to the method of Tschampel[6] in 80–90% yields.

α-**Carboxyboronophthalide.**—*α*-Cyanoboronophthalide (1 g, 6 mmol) was dissolved in 15 ml of concentrated hydrochloric acid and stirred at room temperature for 24 hr. The clear solution was extracted three times with 20-ml portions of ether. The ethereal extracts were combined and dried over magnesium sulfate. The solvent was then allowed to evaporate into the air giving a colorless oil. This oil crystallized within 24 hr to give 600 mg (54%) of *α*-carboxyboronophthalide, mp 140–145° (lit.[6] mp 140–142°).

Treatment of *α*-Carboxyboronophthalide with Lithium Aluminum Hydride.—To a slurry of 600 mg (16 mmol) of lithium aluminum hydride in 20 ml of anhydrous ether was added 480 mg (2.6 mmol) of *α*-carboxyboronophthalide in 20 ml of ether at such a rate to maintain a gentle reflux. After the addition, the reaction mixture was refluxed for 3 hr. Water was added dropwise to the reaction mixture now chilled by an ice bath to decompose the excess lithium aluminum hydride. Then concentrated hydrochloric acid was added until pH 1 was attained. The layers were separated and the aqueous layer extracted three times with 20-ml portions of ether. The ethereal portions were combined, washed once with 20 ml of water, and dried over anhydrous magnesium sulfate. The solvent was evaporated *in vacuo* to give 250 mg of white product, mp 145–155°. One recrystallization from carbon tetrachloride raised the melting point to 155–158°. An infrared spectrum of this impure substance was almost identical with that of authentic *o*-tolueneboronic anhydride. A mass spectrogram gave *m/e* 354 (*o*-tolueneboronic anhydride *m/e* 354).

Registry No.—a, 19203-45-3; b, 19203-46-4; c, 19203-47-5; d, 19203-48-6; e, 19203-49-7; f, 19203-50-0; g, 19214-71-2; 2-hydroxymethyl-6-nitro-2,3-dihydrobenzofuran, 19203-51-1.

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[27] A. Sonn, *Ber.*, **47**, 2440 (1914).