Novel Boron Heterocycles. I. 2,3-Dihydro-1,3,2-benzodiazaborin-4(1H)-ones and 1,2-Dihydro-1,3,2-benzodiazaborines (1,2)

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A series of 2,3-dihydro-1,3,2-benzodiazaborin-4(1H)-ones have been prepared and their ir spectra compared with those of their carbon isosteres. Solvolysis of these boron compounds in ethanol has been followed by uv and reveals a relationship between structure and rates of ethanolysis. Unexpectedly, these boron heterocycles, in contrast to their carbon isosteres, dissolve in aqueous alkali to form stable anions and the significance of this is discussed. The 1:1 adducts of 1 and phosphorus oxychloride has been utilized to prepare two derivatives of the very stable 1,2-dihydro-2-phenyl-1,3,2-benzodiazaborin heterocycle.

o-Aminobenzamide, or its substituted derivatives, and areneboronic acids in nonprotic solvents undergo cyclodehydration at elevated temperatures to give 2,3-dihydro-1,3,2-benzodiazaborin-4(1H)-ones; the same intermediates did not react in these solvents at room temperature in the presence of a reagent like dicyclohexylcarbodiimide. The reaction was most frequently carried out in boiling toluene or xylene, was complete in about two hours and the products were obtained in 60-90% yield. With the above solvents, the water formed in the reaction may be removed mechanically from the distillate by means of a Dean-Stark trap or chemically by allowing the condensed vapors to dry as they percolate downward through a bed of calcium hydride before returning to the reaction flask (3). Alternatively, with a solvent like dioxane, the water formed was continuously removed by a slow distillation of the solvent through a fractionating column. These procedures were unsatisfactory for the preparation of a number of the benzodiazaborinones listed

1

2

(II-17)

(II-25)

in Table II. For example, the reaction of *o*-aminobenzamide (1) and mesityleneboronic acid (2) in toluene gave II-25 (4) as the principal product while the desired II-17 was obtained in about 15% yield. Since 2 could be recrystallized from boiling water, II-25, presumably arose *via* the hydrolytic cleavage of the carbon-boron linkage of II-17 (5). The reaction followed a different course when a blend of the same dry, powdered reactants was heated, for example, in an open flask while diffused with dry nitrogen, or in a drying apparatus at *ca* 1 mm. with phosphorus pentoxide as the desiccant; at 110°, a clear melt formed and water vapor was evolved. The melt remained unchanged at this temperature even after four and one-half hours. When the temperature was raised to 130-135°, the melt promptly solidified. Recrystallization of this solid gave II-17 in 92% yield and only a trace amount of the very insoluble II-25 was formed. Additional examples of the use of the phosphorus pentoxide technique have been found with the 4- and 5-nitro-substituted *o*-aminobenzamides; reaction rate with the areneboronic acid was so slow that even in boiling xylene, chlorobenzene, or cumene, the separation of water did not occur in the condensed distillate and after twenty-four hours of heating under reflux none of the desired products could be detected. Again, when dry blends of the same reactants were heated at *ca* 1 mm. for several hours, at 135°, the nitro derivatives were obtained in 50-90% yield, and no improvement in yields was achieved by carrying out these reactions in xylene or chlorobenzene, at the boiling point, drying the condensed vapors, as described above, by means of calcium hydride. Finally, all of these procedures failed to effect reaction between *N*-cyclohexyl-2-amino-5-nitrobenzamide (3) and benzeneboronic acid or between
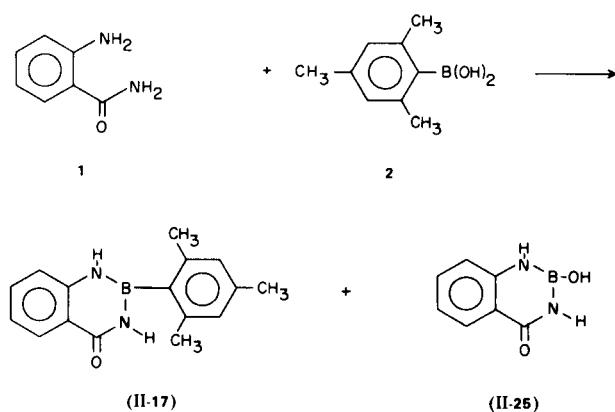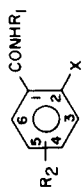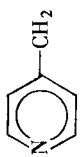
TABLE I

o-Substituted Benzamide Derivatives

No.	R_1	X	R_2	Position	Method	Yield %	M.p., °C	Recrystn. Solvent (a)	Molecular Formula		Analysis C	H	N
1	Et	NH_2	H	—	A	82	100-102	B	$C_9H_{12}N_2O$	Calcd. Found	65.50 65.26	7.33 7.32	16.98 17.02
2	Et	NH_2	Cl	5	A	63	120-122 (b)	B	$C_9H_{11}ClN_2O$	Calcd. Found	— —	— —	14.04 (c) 14.10
3	Et	NH_2	NO_2	5	A	80	162-164	C	$C_9H_{11}N_3O_3$	Calcd. Found	51.67 51.61	5.31 5.04	20.09 20.00
4	$CH_2:CHCH_2$	NH_2	NO_2	5	A	76	164-165	C	$C_{10}H_{11}N_3O_3$	Calcd. Found	54.29 54.53	5.02 4.80	19.00 19.21
5	Cyclohexyl	NH_2	NO_2	—	A	38	220-222	C	$C_{13}H_{17}N_3O_3$	Calcd. Found	59.30 59.36	6.51 6.82	15.96 16.07
6	Me	MeNH	H	—	A	94	89-91	H	$C_9H_{12}N_2O$	Calcd. Found	— —	— —	17.07 16.87
7	$Me_2N(CH_2)_3$	NH_2	H	—	A	78	b.p. 174°/0.5 mm m.p. 76-78	B	$C_{12}H_{19}N_3O$	Calcd. Found	— —	— —	18.99 18.66
8	$PhCH_2$	NH_2	H	—	A	95	121-122	B	$C_{14}H_{14}N_2O$	Calcd. Found	— —	— —	12.38 12.58
9	H	NH_2	Br	5 (d)	A	76	184-186	C	$C_7H_7BrN_2O$	Calcd. Found	— —	— —	12.98 (f) 12.45
10	$o\text{-}MeC_6H_4$	NO_2	H	—	(e)	86	171-173	D	$C_{14}H_{12}N_2O_3$	Calcd. Found	65.62 65.76	4.73 4.85	10.93 11.06
11	$o\text{-}MeC_6H_4$	NH_2	H	—	(e)	33	115-117	B	$C_{14}H_{14}N_2O$	Calcd. Found	74.31 74.29	6.23 6.24	12.38 12.26
12	$p\text{-}MeC_6H_4$	NH_2	H	(g)	A	47	149-151	E	$C_{14}H_{14}N_2O$	Calcd. Found	74.31 74.37	6.23 6.22	12.38 12.29
13	$2,6\text{-}Me_2C_6H_3$	Cl	NO_2	4	(e)	68	240-242	D	$C_{15}H_{13}ClN_2O_3$	Calcd. Found	— —	— —	9.19 (h) 9.12
14	$2,6\text{-}Me_2C_6H_3$	NH_2	NO_2	4	(e)	46	178-180	E	$C_{15}H_{15}N_3O_3$	Calcd. Found	63.20 63.37	5.33 5.52	14.68 14.69
15	$2,6\text{-}Me_2C_6H_3$	Cl	NO_2	5	(e)	66	194-195	D	$C_{15}H_{13}ClN_2O_3$	Calcd. Found	— —	— —	9.19 (i) 9.14
16	$2,6\text{-}Me_2C_6H_3$	NH_2	NO_2	5	(e)	60	216-218	F	$C_{15}H_{15}N_3O_3$	Calcd. Found	63.20 63.14	5.33 5.31	14.68 14.73

No.	Ar	R		Yield %	m.p. °C	Solvent	Formula			C (Calcd./Found)	H	N
17	2,6-Me₂C₆H₃	NO₂	---	63	210-212	(e)	C₁₅H₁₄N₂O₃	D	Calcd. / Found	66.65 / 66.39	5.23 / 4.97	10.37 / 10.12
18	2,6-Me₂C₆H₃	NH₂	H	100	128-130 (j)	(e)	C₁₅H₁₆N₂O	B	Calcd. / Found	74.97 / 74.87	6.71 / 6.71	11.66 / 11.60
19	2,6-Me₂C₆H₃	Cl	Cl	71	158-160	(e)	C₁₅H₁₃Cl₂NO	C	Calcd. / Found	--- / ---	--- / ---	4.76(k) / 4.79
20	(CH₂–pyridyl)	NH₂	H	81	152-154	A	C₁₃H₁₃N₃O	(l)	Calcd. / Found	68.71 / 68.95	5.77 / 5.90	18.49 / 18.27

(a) Recrystallization Solvents: B = Skellysolve E; C = Toluene; D = 2-Propanol; E = Benzene; F = 2-Propanol-Water; G = 95% Ethanol; H = Hexane. (b) Warming with N aqueous hydrochloric acid until solution occurred, followed by cooling gave the hydrochloride, m.p. 230-231° dec. Anal. Calcd.: Total Cl, 30.17. Found: Total Cl, 30.36. (c) Anal. Calcd.: Cl, 17.85. Found: Cl, 17.67. (d) Prepared from 6-bromoisatoic anhydride as described by R. Adams and H. R. Snyder, J. Am. Chem. Soc., 60, 1411 (1938). They report a m.p. of 286-288° for a crude material that was not analyzed. Our material, recrystallized from acetic acid, melted at 306-308°. (Anal. Calcd. for C₈H₄BrNO₃: Br, 33.02; N, 5.79. Found: Br, 33.22; N, 5.83.) (e) See Experimental. (f) Anal. Calcd.: Br, 37.07. Found: Br, 37.50. (g) A solid, insoluble in the boiling benzene used for recrystallization, was recovered by filtration. The m.p. of 178-182° dec. was raised, by two recrystallizations from acetonitrile, to 199-200° dec. (Anal. Calcd. for C₁₅H₁₄N₂O₃: C, 65.92; H, 5.21; N, 10.34; N.E. 270. Found: C, 65.72; H, 5.55; N, 10.25; N.E. (potassium methoxide in DMF) 268. Authentic N-[(p-tolyl)carbamoyl]anthranilic acid, prepared by the reaction of anthranilic acid with p-tolylisocyanate in Skellysolve E at 125°, also melted at 199-200° dec. [Anal. (C₁₅H₁₄N₂O₃) Found: N, 10.37; N.E. (potassium methoxide in DMF) 268] and a mixture m.p. with the by-product from the p-toluidine reaction was 199-200° dec.; in addition, their ir spectra were identical; ν 3330(s), 3285(s), 2630(w), 2560(w), 1690(s), 1670(s) cm⁻¹. (h) Anal. Calcd.: Cl, 11.84. (i) Anal. Calcd.: Cl, 11.67. Found: Cl, 11.64. (j) The hydrochloride was obtained as in (a), m.p. 238-240°. Anal. Calcd.: Cl, 12.81. Found: Cl, 12.68. (k) Anal. Calcd.: Cl, 24.10. Found: Cl, 24.13. (l) Not recrystallized.

2-amino-5-nitrobenzamide and mesityleneboronic acid; since 3 reacted with benzaldehyde to form 2,3-dihydro-6-nitro-2-cyclohexyl-4(1H)-quinazolinone, the electron deficient boron atom obviously plays a role as significant as the bulkiness of both the cyclohexyl and mesityl groups in prohibiting these cyclodehydrations (6).

The prototype heterocycle, 2,3-dihydro-1,3,2-benzodiazaborin-4(1H)-one (II-1) reacted with phosphorus oxychloride to give a deep yellow crystalline adduct (4) in 85% yield (7). A covalent structure has been assigned to 4 due (a) to its failure to titrate as a base with perchloric acid in acetic acid-mercuric acetate and (b) to its chemical behavior (see Fig. 1). Treatment of 4 with concentrated aqueous ammonia at room temperature gave o-amino-benzonitrile and benzeneboronic acid; a suggested mechanism for this reaction is also shown in Fig. 1. When 4, a difficultly soluble compound, was recrystallized from a large volume of chloroform that contained 0.75% ethanol as a stabilizer, displacement of the 4-chloro atom by ethoxy occurred and a new product (5) was formed in 76% yield; 5 was an ionized species since it titrated as a base with perchloric acid in acetic acid-mercuric acetate. With aqueous sodium bicarbonate, 5 gave the base 6, but with concentrated aqueous ammonia, the 4-ethoxy group underwent displacement by the more nucleophilic amino group, to give 7 in 50% yield.
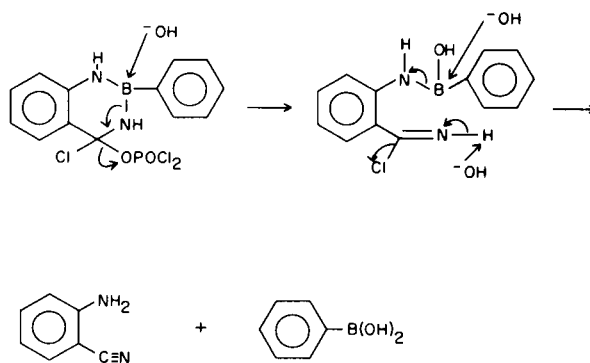
Among the boron compounds described in this paper, 7 was uniquely stable in being the single compound that could be recrystallized unchanged from boiling water. Since most of the compounds in Table II were insoluble in water, a measure of their relative stability toward solvolysis in ethanol could be determined by observing in their uv spectra, the emergence of the absorption at ~340 mμ characteristic of the parent o-aminobenzamide. Fig. 2 shows a plot obtained with the data for several typical compounds. It was apparent that the most stable compounds were II-17, 6 and 7, whereas the least stable compound was II-2 with a methyl group at position-1. In
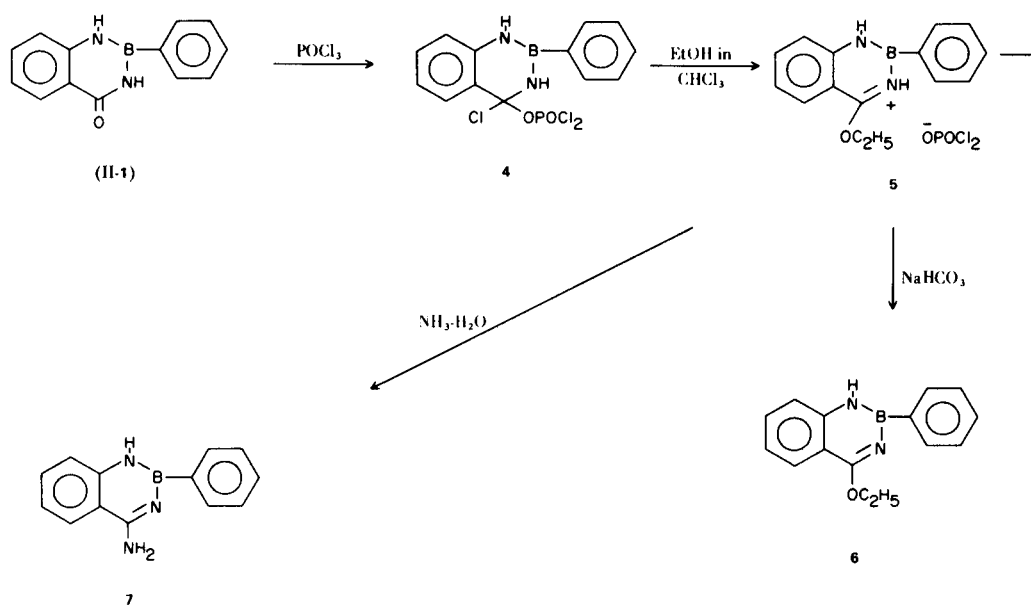
Fig. 1. Reactions of 4-Chloro-1,2,3,4-tetrahydro-2-phenyl-1,3,2-benzodiazaborin-4-ol phosphorodichloridate (4).
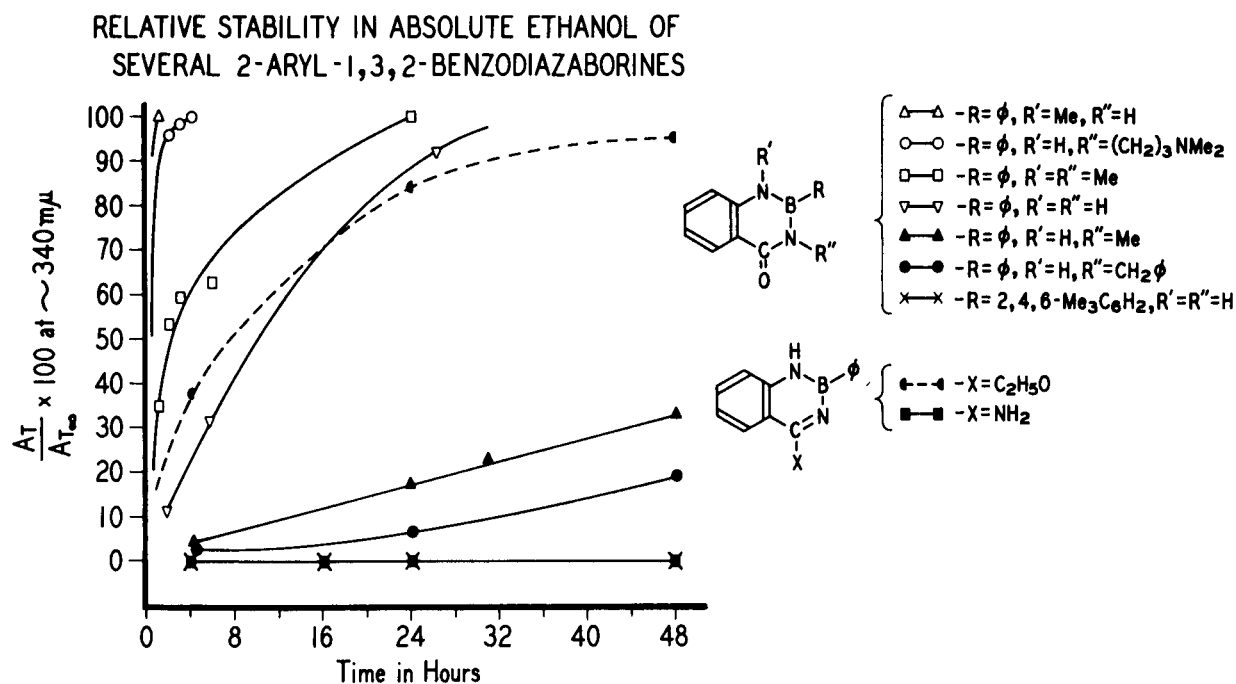
Fig. 2
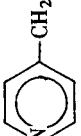
contrast to the effect of alkylation at position-1, methylation or benzylation at position-3 gave a stability greater than that observed with II-1 where both positions were substituted by hydrogen. So significant was the destabilizing effect of alkylation at position-1 that even the additional methylation at position-3 in II-2 did not stabilize II-5 toward solvolysis. Finally, basic groups like 3-(dimethylamino)propyl or 4-pyridylmethyl at position-3 in II-6 and II-24, respectively, enhanced the rate of solvolysis.

TABLE II

2,3-Dihydro-1,3,2-Benzodiazaborin-4(1H)-ones
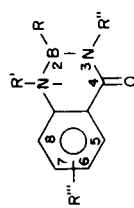
| No.	R'''	R'	R	R''	M.p., °C	Recrystn. Solvent	Yield %	Molecular Formula	N Calcd.	N Found	B Calcd.	B Found
1	H	H	Ph	H	214-215	A	85	$C_{13}H_{11}BN_2O$	12.62	12.88	4.87(a)	4.66
2	H	Me	Ph	H	170-172	B	53	$C_{14}H_{13}BN_2O$	11.87	11.60	4.60	4.33
3	H	H	Ph	Et	180-181	C	75	$C_{15}H_{15}BN_2O$	11.21	11.07	4.33	4.26
4	H	H	Ph	Me	182-184	B	60	$C_{14}H_{13}BN_2O$	11.87	11.97	4.60	4.38
5	H	Me	Ph	Me	92-94	D	42	$C_{15}H_{15}BN_2O$	11.21	11.02	4.33	4.08
6	H	H	Ph	$Me_2N(CH_2)_3$	170-172	(b)	91	$C_{18}H_{22}BN_3O$	13.72	13.68	3.54	3.66
7	H	H	Ph	$PhCH_2$	190-192	B	70	$C_{20}H_{17}BN_2O$	8.97	9.26	3.47	3.63
8	6-Br	H	Ph	H	282-284	A	84	$C_{13}H_{10}BBrN_2O$	—	—	3.59(c)	3.76
9	6-NO2	H	Ph	Et	279-281	A	74	$C_{15}H_{14}BN_3O_3$	14.25	14.21	3.67	3.92
10	H	H	Ph	$2,6\text{-}Me_2C_6H_3$	265-267	A	67	$C_{21}H_{19}BN_2O$	8.59	8.87	3.32(d)	3.14
11	6-NO2	H	Ph	$2,6\text{-}Me_2C_6H_3$	263-265	E	53	$C_{21}H_{18}BN_3O_3$	11.32	11.11	2.92	2.99
12	7-NO2	H	Ph	$2,6\text{-}Me_2C_6H_3$	256-258	F	92	$C_{21}H_{18}BN_3O_3$	11.32	11.50	2.92	3.12
13	H	H	Ph	$o\text{-}MeC_6H_4$	255-257	A	67	$C_{20}H_{17}BN_2O$	—	—	3.47(e)	3.72
14	H	H	Ph	$p\text{-}MeC_6H_4$	287-289	A	62	$C_{20}H_{17}BN_2O$	8.95	8.73	3.47	3.72
15	H	H	$p\text{-}MeC_6H_4$	H	265-267	F	89	$C_{14}H_{13}BN_2O$	11.87	11.71	4.58	4.52
16	6-Br	H	$p\text{-}MeC_6H_4$	H	307-308 dec.	E	87	$C_{14}H_{12}BBrN_2O$	8.89	8.93	3.43	3.41
17	H	H	$2,4,6\text{-}Me_3C_6H_2$	H	203-205	B	92	$C_{16}H_{17}BN_2O$	10.60	10.60	4.10	3.95
18	6-Br	H	$2,4,6\text{-}Me_3C_6H_2$	H	230-232	B	79	$C_{16}H_{16}BBrN_2O$	—	—	3.15(f)	3.02
19	6-Cl	H	$2,4,6\text{-}Me_3C_6H_2$	H	201-203	B	50	$C_{16}H_{16}BClN_2O$	11.88	12.09	3.62	3.58
20	H	H	$1\text{-}C_{10}H_7$	H	164-165	B	37	$C_{17}H_{13}BN_2O$	10.30	10.11	3.98	3.95
21	H	H	$1\text{-}C_{10}H_7$	Me	250-252	B	40	$C_{18}H_{15}BN_2O$	9.80	9.86	3.78	3.72
22	H	H	$1\text{-}C_{10}H_7$	$PhCH_2$	218-220	A	48	$C_{24}H_{19}BN_2O$	7.74	7.55	2.99	2.98
23	6-NO2	H	$1\text{-}C_{10}H_7$	Et	310-313	A	52	$C_{19}H_{16}BN_3O_3$	12.18	12.31	3.14	3.09
24	H	H	Ph	(pyridyl-CH_2)	83-85	(b)	72	$C_{19}H_{16}BN_3O$	13.47	13.32	3.47	3.64
25	H	H	OH	H	>315	(a)	70	$C_7H_7BN_2O_2$	17.29	17.73	6.70	7.09
26	H	H	OH	$PhCH_2$	>315	A	21	$C_{14}H_{13}BN_2O_2$	11.11	11.29	4.29	4.40
27	H	Me	OH	Me	>315	B	21	$C_9H_{11}BN_2O_2$	14.75	14.56	5.69	5.82
28	H	Me	OH	$PhCH_2$	>315	E	21	$C_{15}H_{15}BN_2O_2$	11.12	11.29	4.29	4.40
29	6-NO2	H	OH	Et	>315	E	15	$C_9H_{10}BN_3O_4$	—	—	4.60(g)	4.73
30	6-Br	H	OH	H	>315	(a)	18	$C_7H_6BBrN_2O_2$	11.62	11.83	4.49	4.27

Recrystallization Solvents: A = Toluene; B = Skellysolve E; C = Diisopropyl Ether; D = Hexane; E = Xylene; F = Chlorobenzene. (a) Anal. Calcd.: C, 70.27; H, 4.95. Found: C, 70.36; H, 5.07. (b) Not recrystallized. (c) Anal. Calcd.: C, 77.33; H, 5.87. Found: C, 77.38; H, 5.82. (d) Anal. Calcd.: Br, 26.55. Found: Br, 26.38. (e) Anal. Calcd.: C, 76.94; H, 5.49. (f) Anal. Calcd.: C, 77.02; H, 5.67. Found: Br, 23.30. (g) Anal. Calcd.: Br, 23.29. Found: Br, 23.29. (g) Anal. Calcd.: C, 46.00; H, 4.29. Found: C, 45.81; H, 4.40.

The stability of **6** and **7** could be attributed to their enhanced aromatic character (8), whereas the stability of II-17 was due to both steric and inductive effects; the inductive effects were significant, since the electron-releasing methyl group in the 2-(*p*-tolyl) derivative made II-15 significantly more stable than the 2-phenyl derivative (II-1). The striking sensitivity of the 1-methyl derivative (II-2) could arise by way of the back coordination (9) of nitrogen to boron that produced a labile boron-nitrogen bond resembling that of boron-oxygen, **8**. In contrast, alkylation at position-3 was presumed to release electrons toward oxygen, thus setting up the more stable conjugate anion **9**. The decrease in stability seen with II-6 and II-24

8   **9**
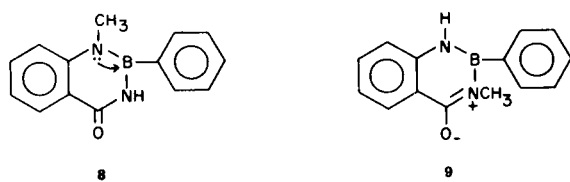
was difficult to explain although there may be a precedent in the report that the carbon-boron bond in *p*-(dimethylamino)benzeneboronic acid was more readily cleaved by mild acid or alkaline hydrolysis than was the same bond in *p*-bromobenzeneboronic acid or *p*-tolueneboronic acid (10).

While the compounds listed in Table II were insoluble in water, those that carry a proton at either position-1 or -3 were readily soluble in dilute aqueous sodium or potassium hydroxide. In aqueous solution, the heterocyclic anion had an unexpected stability (11). For example, when II-1 was dissolved in one equivalent of N sodium hydroxide and the solution was kept at room temperature for 0.25 hour, the uv spectrum underwent slight alteration from the original and, from the solution, 90% of the II-1 was recovered. A comparison of the uv spectra of II-1 and II-9 in 0.04 N aqueous sodium hydroxide showed that II-1 was completely hydrolyzed in 1 hour while the spectrum of II-9 remained unchanged after 5 hours, and the recovery of II-9 upon neutralization was quantitative. It was of interest that all of the nitro derivatives in Table II, although colorless or pale yellow crystalline solids, dissolved in aqueous alkali to form deep orange colored solutions. Another significant finding was that the several nitro derivatives in Table II were significantly stronger acids than the other alkali-soluble derivatives in that Table, since in acetone solution, when phenolphthalein was used as the indicator, only the nitro derivatives could be titrated to a sharp endpoint with exactly one equivalent of 0.01 N aqueous sodium hydroxide. Mannitol was not required for these titrations, and its presence during the titrations did not aid in the titrations of the other deriva-

tives not containing the *ar*-nitro group. These are the only known organic compounds of boron that possess this property. It was noteworthy that the nitroborazarophenanthrenes reported by Dewar, Jones, and Logan (12) also developed intense colors on treatment with alkali and these authors have presented evidence to prove that the phenomenon involved salt formation by addition of base to boron, rather than loss of a proton from oxygen or nitrogen. The anion was, therefore, represented by **10**, and proof for this structure was found in the ir spectra of the nitro compound under neutral and basic conditions in a potassium bromide pellet; both spectra showed strong NH absorption at 3030-2940 cm^{-1}. The ir spectra of II-9 were determined in similar fashion under both neutral and basic conditions and both spectra showed strong NH absorption. These data suggest that the anion of II-9 is represented by **11**.

10   **11**
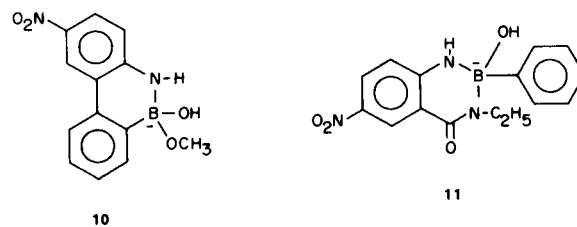
The *ar*-nitroderivatives, in contrast to the others in this paper, form stable pyridine salts (13) and the latter also give precise neutralization equivalents with one equivalent of 0.01 N aqueous sodium hydroxide.

It should be emphasized that these 2,3-dihydro-1,3,2-benzodiazaborin-4(1H)-ones are isosteres of the 2,3-dihydro-4(1H)-quinazolinones. None of the latter, even those with *ar*-nitro groups (3) was soluble in aqueous alkali, and none titrated with aqueous base.

Although II-26 was obtained in 70% yield as a by-product of the reaction between *o*-aminobenzamide and mesityleneboronic acid in boiling toluene, these 2-hydroxy derivatives were more conveniently prepared by the slow distillation of a solution of the *o*-aminobenzamide in trimethylborate followed by workup that exposed the intermediate 2-methoxy derivative to normal laboratory humidity. The yields were about 20% but the availability of trimethylborate as an industrial chemical made this synthetic route more attractive than that involving mesityleneboronic acid.

Infrared Spectra.

A study of the ir spectra of a number of boron heterocycles has suggested (14) that the absorptions at ~ 1465, ~ 1362, and ~ 1175-1115 cm^{-1} were due to nitrogen-boron bonds having double bond character. Our exper-

ience would suggest that the assignments in the 1465-1115 cm^{-1} region are not definitive. Thus, in Fig. 3 are listed, for comparison, selected ir absorption bands for four pairs of related 2,3-dihydro-1,3,2-benzodiazaborin-4(1H)-ones and 2,3-dihydro-4(1H)-quinazolinones. These ir absorptions in potassium bromide pellets were typical of those seen with fifteen pairs of isosteres. It was apparent that absorptions assigned to boron-nitrogen bonds with double bond character were also seen with the carbon isosteres that had no double bond character. Such assignments, therefore, must be considered as questionable.

Fig. 3. Infrared Spectra of 2,3-Dihydro-1,3,2-benzodiazaborin-4(1H)-ones and 2,3-Dihydro-4(1H)-quinazolinones in Potassium Bromide Pellet.

A: R = C₂H₅; R' = O₂N	3310 (s) 1610-1630 1460 (s) 1365 (s) 1145 (s) (s, broad) 1470 (s)
B: R = C₃H₅; R' = O₂N	3280 (s) 1610-1630 1450 (s) 1370 (m) 1155 (s) (s, broad) 1470 (s)

A: R = R' = H	3340 (s) 1600-1640 1480 (s) 1360 (m) 1140 (s) (s, broad)
B: R = R' = H	3300 (s) 1635-1655 1477 (s) 1357 (m) 1142 (s) (s, broad)
A: R = H; R' = Br	3300 (s) 1640-1660 1470 (s) 1350 (m) 1150 (s) (s, broad)
B: R = H; R' = Br	3300 (s) 1640-1660 1470 (s) 1355 (m) 1160 (s) (s, broad)
A: R = H; R' = PhCH₂	3310 (s) 1625 (s) 1477 (s) 1347 (m) 1150 (s)
B: R = H; R' = PhCH₂	3400 (s) 1610-1630 1480 (s) 1350 (m) 1145 (s) (s, broad)

Ultraviolet Spectra.

The 2,3-dihydro-1,3,2-benzodiazaborin-4(1H)-one system showed three maxima in the uv at ~ 220, ~ 260, and ~ 320 mμ. The introduction of bromine at position-6 did not alter the spectrum, but the introduction of a nitro group, as anticipated, produced a bathochromic shift of the ~ 320 mμ band to 340-360 mμ. The carbon isosteres show maxima at 219-225 mμ.

Proton Magnetic Resonance Spectra.

These compounds are too insoluble for their pmr spectra to be determined in deuteriochloroform. The spectrum of II-1 in DMSO-d₆ showed all eleven protons in a complex group of signals at τ 1.7-3.0, and no assignments were possible. When deuterium oxide-triethylamine were added, the spectrum became far more complex, and no information was derived from this experiment.

Mass Spectroscopy.

The mass spectroscopy of organic compounds of boron

has been reviewed (15a) and reveals that very little is known concerning the fragmentation of nitrogen containing boron heterocycles. The high resolution mass spectral data on II-1 has been examined with the aid of a computer program. The molecular ions are found at mass 222.0946 (theory 222.0964) (C₁₃H₁₁N₂OB¹¹). Loss of water to give the aromatized species, 12, 204.0820 (theory 204.0859) (C₁₃H₉N₂B¹¹), loss of CO to give 13, 193.0885 (theory 193.0947) (C₁₂H₁₀N₂B¹¹), or loss of HCN to give the anticipated C₁₂H₁₀N₁B¹⁰, 194.0938 (theory 194.0892) can be confirmed. The remainder of the spectrum is represented by ions of mass 181.0665 and lesser
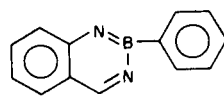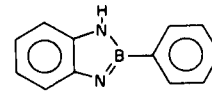
mass, and the molecular formulas assigned to these fragments do not correspond to any possible structures (15b).

o-Aminobenzamide Intermediates.

A number of the o-aminobenzamides required as intermediates have been prepared in good yields by Method A, Experimental, the reaction of isatoic anhydride or a substituted isatoic anhydride (14) with ammonia or a primary aliphatic amine in an alcohol solvent. This approach was not generally useful with primary aromatic amines (16), particularly those with ortho-substituents, where the major reactions became the formation of a urea, 15, or an ester, 16, derived from the alcohol solvent. The N-aryl-o-aminobenzamides were best prepared by the

R = H, Br, Cl, NO₂
R¹ = o- and p-CH₃C₆H₄, 2,6-(CH₃)₂C₆H₃
R² = CH₃, C₂H₅
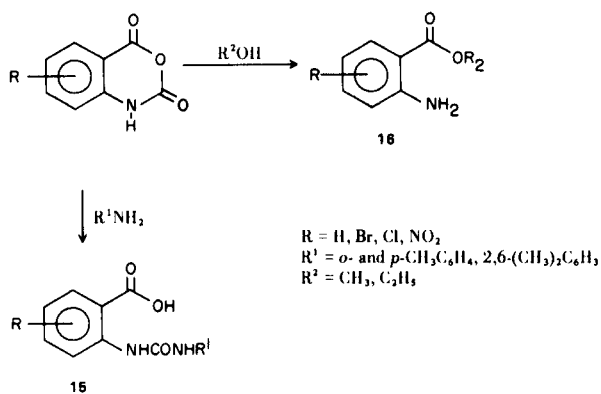
sequences outlined in Fig. 4. Even with these procedures, 2,4-dichloro-N-(2,6-xylyl)benzamide could not be converted to the 2-amino derivative.

Fig. 4. Preparation of N-Aryl-o-aminobenzamides.

EXPERIMENTAL

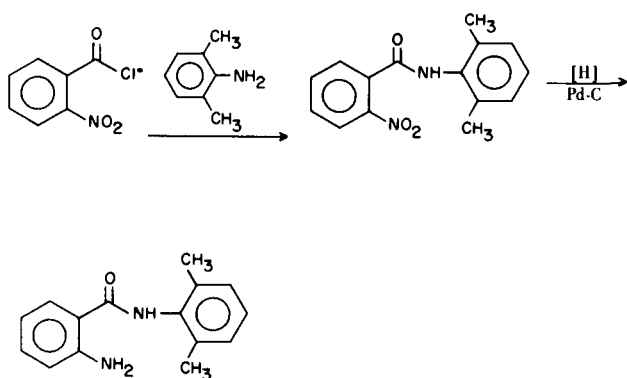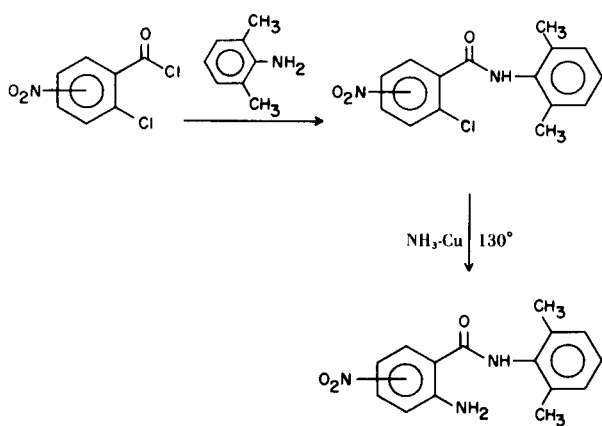The ir spectra were determined on mineral oil mulls by means of a Perkin Elmer 621 spectrophotometer, the uv spectra were determined with the Cary 14, the pmr spectra were carried out with a Varian A-60, and the mass spectrum on an AEI MS902 double focusing high resolution mass spectrometer, analyzing the data with the Squibb computer program. The author is indebted to Miss Barbara Keeler and Dr. A. I. Cohen for these spectra. The microanalyses were carried out by Mr. J. Alicino and his associates of this Institute.

N-Methyl-o-methylaminobenzamide (I-6) (Method A, Table I).

To 1-methylisatoic anhydride (17) (13.0 g., 0.07 mole) suspended in 150 ml. of 95% ethanol was added dropwise, at room temperature, 40% aqueous methylamine (5.8 g., 0.07 mole). A solution formed during the addition; subsequently, the solution was concentrated in vacuo on the steam bath. The residual oil crystallized spontaneously, m.p. 82-84°. Recrystallization from hexane gave 10.8 g. of I-6, m.p. 89-91°; ν 3360 (s), 3300 (s), 1630 (s) cm⁻¹.

o-Amino-N-[3-(dimethylamino)propyl]benzamide (I-7) (Method A, Table I).

To isatoic anhydride (10.0 g., 0.067 mole) suspended in 125 ml. of 95% ethanol was added, dropwise, redistilled 3-(dimethylamino)propylamine. The product was isolated as in the procedure above but the residue in this instance did not crystallize. Distillation gave an oil, b.p. 174°/0.5 mm., that crystallized spontane-

ously. Recrystallization from Skellysolve E gave 11.6 g. of I-7, m.p. 76-78°; ν 3435 (s), 3280 (s), 3160 (m), 1615 (s) cm⁻¹.

2-Amino-N-(2,6-sylyl)-4-nitrobenzamide (I-14).

To 2-chloro-4-nitrobenzoic acid (50.5 g., 0.25 mole) in 200 ml. of anhydrous chloroform was added thionyl chloride (40.0 ml., 0.55 mole), dropwise. The solution was heated under reflux for 2 hours, and then concentrated to dryness in vacuo. The residue was dissolved in 200 ml. of dry chloroform and the concentration repeated. To the residue, in 200 ml. of anhydrous chloroform, was added, dropwise, a solution of 2,6-xylidine (36.3 g., 0.3 mole) and dry pyridine (20.0 g., 0.25 mole) in 200 ml. of anhydrous chloroform. Subsequent to the addition, the semisolid mixture was stirred and heated under reflux for 18 hours, cooled, and the solid filtered. Recrystallization from 2-propanol gave 35.0 g. of I-13, m.p. 240-242°; ν 3210 (m), 3180 (m), 1700 (s) cm⁻¹. The chloroform filtrate from the above product was concentrated to dryness in vacuo, the residual solid was washed with water, dried, and recrystallized from 2-propanol to give 17.0 g. of additional product. The combined yield was 52.0 g.

The I-13 (15.2 g., 0.05 mole), copper bronze (1.5 g.), sodium iodide (1.5 g.), and 360 ml. of 1.8 N absolute ethanolic ammonia were heated for 20 hours at 120° in a sealed glass vessel. The reaction mixture was concentrated to dryness in vacuo, the residue was suspended in 100 ml. of water containing 1.0 g. of sodium bisulfite, and the whole extracted with four 50 ml. portions of ether. The ether extracts were dried, and concentrated. The residual solid, 15.0 g., m.p. 180-185°, was dissolved in 150 ml. of benzene and the solution chromatographed on 150 g. of activated alumina (Harshaw Chromatographic Grade). The colorless benzene eluates yielded no product. Continued elution with benzene gave deep yellow eluates; these were concentrated in vacuo, the residues combined, and recrystallized from benzene to give 6.4 g. of I-14, m.p. 178-180°; ν 3460 (s), 3350 (s), 3260 (s), 1610 (s) cm⁻¹.

5-Nitro-N-(2,6-xylyl)-2-aminobenzamide (I-16).

To 2-chloro-5-nitrobenzoic acid (101.0 g., 0.5 mole) in 500 ml. of anhydrous chloroform, with stirring, was added, dropwise, thionyl chloride (80.0 ml., 1.1 mole); following the addition, the mixture was stirred and heated under reflux for 22 hours, concentrated to one-half volume, 250 ml. of anhydrous chloroform added, and the solution concentrated to dryness in vacuo. The residue was dissolved in 200 ml. of dry chloroform and to this, with stirring, was added, dropwise, a solution of 2,6-xylidine (72.5 g., 0.6 mole) and pyridine (40.0 g., 0.5 mole) in 400 ml. of anhydrous chloroform. The mixture was subsequently stirred and heated under reflux for eight hours, cooled, and the solid filtered. Recrystallization from 2-propanol gave I-15, m.p. 194-195°; ν 3200, 1700 cm⁻¹. The yield was 101.0 g. The chloroform solution from the crude I-6 on concentration gave 8.0 g. of 2-chloro-5-nitrobenzoic acid. Into each of four glass tubes was placed I-15 (2.5 g., 0.0082 mole), ethanolic ammonia (100 ml., 5.5 N), sodium iodide, and copper bronze (0.25 g. each), the tubes sealed, and heated for 18 hours at 130°, cooled, opened, and filtered. The combined filtrates were concentrated to dryness to give 10.0 g. of solid, giving a positive test for halogen, m.p. 208-215°. This was distributed between ether and aqueous sodium bisulfite and agitated vigorously. The ether solution was washed with water, dried, and the solution concentrated to give a halogen-free solid, m.p. 207-211°. Repeated recrystallizations from 70% 2-propanol-30% water gave 5.7 g. of I-16, m.p. 212-215°; ν 3470 (s), 3370 (s), 3260 (s), 1670 cm⁻¹.

2-Amino-*N*-(2,6-xylyl)benzamide (I-18).

To 2,6-xylidine (36.3 g., 0.3 mole) in 300 ml. of anhydrous chloroform was added dropwise 50 ml. of a chloroform solution containing *o*-nitrobenzoyl chloride [0.15 mole, from *o*-nitrobenzoic acid (25.0 g., 0.15 mole)]. A solid separated during the addition and persisted during the one-hour reflux. The cooled mixture was filtered to give 37.5 g. of crude product, m.p. 210-212°. Recrystallization from 2-propanol gave 25.5 g. of I-17, m.p. unchanged at 210-212°; ν 3210 (s), 1700 (s) cm^{-1}. The I-17 (9.0 g., 0.033 mole), 5% palladium on carbon (1.0 g.), and 250 ml. of absolute ethanol were hydrogenated at 45° and 50 psi of hydrogen. Reduction was rapid to give 8.0 g. (100% yield) of I-18, m.p. 128-130°; ν 3400 (s), 3240, 1610 cm^{-1}. When the I-18 was dissolved in boiling 10% aqueous hydrochloric acid and the solution cooled, there was obtained the *hydrochloride*, m.p. 238-240°; ν 3240 (s), 2600 (s), 1620 (s) cm^{-1}.

2-Amino-*N*-(*o*-tolyl)benzamide (I-11).

The above procedure, using *o*-toluidine, gave an 86% yield of I-10, m.p. 171-173°, and, the I-10, hydrogenated at 50 psi over 5% palladium on carbon in absolute ethanol, gave an 89% yield of I-11, m.p. 115-117°; ν 3450 (m), 3340 (m), 3280 (m), 1630 (s) cm^{-1}.

Attempted Preparation of 2-Amino-4-chloro-*N*-(2,6-xylyl)benzamide.

The procedure described above employing 2,4-dichlorobenzoic acid (201.0 g., 1.0 mole) gave 215.0 g. of I-19, m.p. 158-160°; ν 3240 (s), 1700 (s) cm^{-1} after recrystallization from toluene. Heating I-19 as described above in absolute ethanolic ammonia, with copper bronze and potassium iodide, yielded only unchanged starting material as shown by m.p., mixture m.p., and a comparison of ir spectra.

Reaction of 5-Chloroisatoic Anhydride with 2,6-Xylidine; Formation of 5-Chloro-*N*-[(2,6-xylyl)carbamoyl]anthranilic Acid.

5-Chloroisatoic anhydride (19.8 g., 0.1 mole), 2,6-xylidine (24.2 g., 0.2 mole), and 750 ml. of *t*-butyl alcohol were stirred and heated under reflux for 114 hours, the whole cooled, the solid filtered, and dried to give 5.5 g. of material, m.p. 237-239°. The *t*-butyl alcohol filtrate was concentrated to dryness to give 17.0 g. of solid, m.p. 230-232°. The combined solids were stirred at room temperature with a solution of 8.0 g. of sodium hydroxide in 200 ml. of water, and filtered. The filtrate was cooled, and treated with an excess of 10% aqueous hydrochloric acid to give 13.0 g. of solid, m.p. 225-227°. Recrystallization from 95% ethanol gave 7.5 g. (24% yield) of 5-chloro-*N*-[(2,6-xylyl)carbamoyl]anthranilic acid, m.p. 226-227°; ν 3300 (s), 2700 (w), 2600 (w), 2530 (w), 1700 (s), 1660 (s), 1540 (s), 1250 (s) cm^{-1}.

Anal. Calcd. for C$_{16}$H$_{15}$ClN$_2$O$_3$: C, 60.29; H, 4.74; N, 8.78. Found: C, 60.48; H, 4.82; N, 8.88.

Authentic 5-chloro-*N*-[(2,6-xylyl)carbamoyl]anthranilic acid, m.p. 226-227° was prepared by the reaction of 5-chloroanthranilic acid and 2,6-xylylisocyanate; a mixture m.p. with the above product was 226-227°.

The solid insoluble in the aqueous sodium hydroxide was unchanged 5-chloroisatoic anhydride.

Reactions of 5-Nitroisatoic Anhydride with 2,6-Dimethylaniline in Various Solvents.

(a) 5-Nitroisatoic anhydride (20.8 g., 0.1 mole), 2,6-xylidine (24.2 g., 0.2 mole), and 100 ml. of absolute ethanol gave after one hour of heating under reflux 16.5 g. (79% yield) of ethyl 2-amino-

5-nitrobenzoate, m.p. 149-151° (18) after recrystallization from Skellysolve E; ν 3410 (s), 3300 (s), 1695 (s), 1625 (s) cm^{-1}.

Anal. Calcd. for C$_9$H$_{10}$N$_2$O$_4$: C, 51.42; H, 4.80; N, 13.33. Found: C, 51.52; H, 5.01; N, 13.50.

(b) The use of methanol as the solvent in (a) gave a 28% yield of methyl 2-amino-5-nitrobenzoate, m.p. 167-168° (19), after recrystallization from Skellysolve E; ν 3450 (s), 3340 (s), 1720 (s), 1635 (s) cm^{-1}.

Anal. Calcd. for C$_8$H$_8$N$_2$O$_4$: C, 48.97; H, 4.11; N, 14.28. Found: C, 49.03; H, 4.11; N, 14.23.

The recovery of 2,6-xylidine was 16.0 g. (66%), b.p. 126-128° (50 mm.), n$_D^{21}$ 1.5612; its ir spectrum was identical with that of authentic material.

(c) The substitution of *t*-butyl alcohol for the ethanol in (a) gave 5-nitro-*N*-[(2,6-xylyl)carbamoyl]anthranilic acid, m.p. 233-235°, after recrystallization from acetonitrile; ν 3280 (s), 2620 (w), 2560 (w), 1695 (s), 1665 (s) cm^{-1}.

Anal. Calcd. for C$_{16}$H$_{15}$N$_3$O$_5$: C, 58.35; H, 4.66; N, 12.76. Found: C, 58.55; H, 4.37; N, 12.95.

Attempted Ammonolysis of Methyl 2-Amino-5-nitrobenzoate.

When the *methyl ester* (2.45 g., 0.0125 moles), 2,6-dimethylaniline (3.0 g., 0.025 mole), and 40.0 ml. of *o*-dichlorobenzene was heated under reflux and under nitrogen for eight hours, 2.42 g. of the methyl ester was recovered.

Cyclization Procedures to Prepare 2,3-Dihydro-1,3,2-benzodiazaborin-4(1*H*)-ones.

(a) 6-Bromo-2,3-dihydro-2-phenyl-1,3,2-benzodiazaborin-4(1*H*)-one (II-8).

A solution of 5-bromo-2-aminobenzamide (2.15 g., 0.01 mole) and benzeneboronic acid (1.22 g., 0.01 mole) in 200 ml. of dry toluene was heated under reflux for two hours, collecting the water formed in a Dean-Stark trap. The cooled solution was filtered to give 2.7 g. of crude product, m.p. 279-281°. Recrystallization from dry xylene gave 2.53 g. of II-8; ν 3280 (s), 1640 (s) cm^{-1}.

(b) 2,3-Dihydro-1-methyl-2-phenyl-1,3,2-benzodiazoborin-4(1*H*)-one (II-2).

o-(Methylamino)benzamide (20) (3.0 g., 0.02 mole), benzeneboronic acid (2.44 g., 0.02 mole) and 100 ml. of dry xylene were distilled so that the condensed distillate percolated down through a bed of calcium hydride (3.0 g., 8-14 mesh) before returning to the reaction flask. A vigorous evolution of hydrogen continued for about one hour, but the distillation was continued for one more hour, the whole cooled, and the solid filtered to give 3.3 g. of crude II-2, m.p. 166-168°. Recrystallization from Skellysolve E gave 2.5 g. of II-2; ν 3200 (s), 3070 (m), 1670 cm^{-1}.

(c) 2,3-Dihydro-2-mesityl-1,3,2-benzodiazaborin-4(1*H*)-one (II-17) and 2,3-Dihydro-2-hydroxy-1,3,2-benzodiazaborin-4(1*H*)-one (II-25).

(1) A solution of anthranilamide (0.71 g., 0.052 mole) and mesityleneboronic acid (0.86 g., 0.052 mole) in 50 ml. of dry benzene was heated as in (a); no water was evolved and only the reactants were recovered. The same reactants in 50 ml. of dry toluene were heated as in (1); water was evolved, a clear solution remained for 25 minutes, but at that time a flocculent solid began to separate. When one hour of heating was completed, the mixture was cooled and filtered to give 0.56 g. of II-25, mp. >315°; ν 3400 (s), 3340-3160 (broad, s), 1655 cm^{-1}; II-25 was too insoluble in all of the solvents available to recrystallize. The

filtrate from the II-25 was concentrated to dryness *in vacuo* to give 0.56 g. of an oil that crystallized spontaneously, m.p. 110-140°. Recrystallization from dry Skellysolve E gave a product, m.p. 202-204°; and this m.p. was not altered by a second recrystallization from the same solvent. The yield of II-17 was 0.20 g. (15%).

(2) A thoroughly blended mixture of anthranilamide (1.49 g., 0.01 mole) and mesityleneboronic acid (1.80 g., 0.01 mole) in an open 25 ml. round bottom flask was swept continuously with nitrogen while heating in an oil bath maintained at 110-113°. A clear melt formed within 10 minutes and water vapor was evolved. The clear melt persisted during 4.5 hours but solidified on cooling to give a solid, m.p. 70-110°, effervescing at 130°, resolidifying at 135°, and melting clear at 198-200°. When this solid was returned to an oil bath at 135°, it remelted, and within two minutes, resolidified. The heating at 135° was maintained for 2.5 hours to give 2.59 g. of product, m.p. 203-205°. Recrystallization from dry Skellysolve E gave 2.42 g. (92% yield) of II-17; ν 3400 (s), 3280 (s), 1655 cm^{-1}.

(d) 2,3-Dihydro-2-phenyl-1,3,2-benzodiazaborin-4(1*H*)-one (II-1).

A solution of anthranilamide (8.1 g., 0.06 mole) and benzeneboronic acid (7.32 g., 0.06 mole) in 250 ml. of reagent grade dioxane was heated so that the vapors distilled through a helice-packed column, 15 mm. in diameter and 6 in. long. During two hours, 50 ml. of distillate was collected. The solution was filtered hot and allowed to cool. The crystalline product that separated was filtered to give 8.52 g. of II-1, m.p. and mixture m.p. 214-215°; ν 3350 (s), 3250 (m), 1640 (s) cm^{-1}. The filtrate was concentrated to one-half volume *in vacuo* and cooled to give an additional 2.80 g. of II-1. The combined yield was 11.32 g. (85%).

(e) 2,3-Dihydro-3-ethyl-6-nitro-1,3,2-benzodiazaborin-4(1*H*)-one (II-9).

2-Amino-*N*-ethyl-5-nitrobenzamide (I-3) (2.09 g., 0.01 mole) and benzeneboronic acid (1.22 g., 0.01 mole) were thoroughly blended, placed in a porcelain boat and heated in a drying pistol (phosphorus pentoxide) by means of boiling xylene for 6 hours. The yellow solid remaining in the boat, m.p. 270-280°, was dissolved in 50 ml. of 2% aqueous potassium hydroxide solution, the deep orange colored solution was filtered, and the filtrate adjusted to pH 7.0. The colorless solid that separated was filtered, dried, and recrystallized from toluene to give 1.3 g. of colorless II-9; λ max (tetrahydrofuran) 319, 330 (sh) mμ (ϵ, 17,900, 16,900); ν 3310 (s), 1640 (s) cm^{-1}.

2,3-Dihydro-3-ethyl-6-nitro-1,3,2-benzodiazaborin-4(1*H*)-one, Pyridine Salt, Monohydrate.

To reagent grade pyridine (1.0 ml.) at room temperature was added II-9 (0.30 g., 0.001 mole). The deep orange solution was evaporated at room temperature in a stream of nitrogen to give 0.04 g. of a yellow, crystalline, non-hygroscopic solid, m.p. 135° with immediate solidification followed by remelting at 265°; λ max (tetrahydrofuran) 333 mμ (ϵ, 16,000). The analytical sample was prepared by drying *in vacuo* at room temperature.

Anal. Calcd. for C$_{15}$H$_{14}$BN$_3$O$_3$·C$_5$H$_5$N·H$_2$O: B, 2.76; N, 14.29; N.E. 392. Found: B, 2.99; N, 14.36; N.E. (aqueous sodium hydroxide) 375.

(f) 3-Benzyl-2,3-dihydro-2-hydroxy-1,3,2-benzodiazaborin-4(1*H*)-one (II-25).

A solution of 2-amino-*N*-benzylbenzamide (1.85 g., 0.082 mole), redistilled trimethylborate (0.85 g., 0.082 mole), and 125 ml. of dry xylene were distilled slowly while exposed to atmo-

spheric humidity during two hours. The still head temperature rose slowly from 40° to 130° during this time, and a solid separated. The reaction mixture was cooled, the solid filtered, and dried; it weighed 1.28 g. and was a mixture of white and yellow solid. The white solid was separated and recrystallized from industrial grade xylene to give 0.44 g. (21% yield) of II-26, no m.p. to 315°; ν 3470 (s), 3390 (s), 3360 (s), 3300 (s), 1620 (s), 1610 (s) cm^{-1}.

The derivatives of 2,3-dihydro-1,3,2-benzodiazaborin-4(1*H*)-one are found in Table II.

4-Chloro-1,2,3,4-tetrahydro-2-phenyl-1,3,2-benzodiazaborin-4-ol Phosphorodichloridate (4).

To redistilled phosphorus oxychloride (800 ml.) was added in small portions with stirring, at room temperature, II-1 (20.0 g., 0.09 mole), the whole stirred until solution occurred, then heated under reflux for 0.75 hours, filtered, and the filtrate concentrated to 100 ml. On cooling, a deep yellow colored crystalline solid separated; this was filtered, washed with anhydrous ether, and dried to give 28.6 g. (85% yield) of 4, m.p. 181-182° dec.; λ max (tetrahydrofuran) 323 mμ (ϵ, 4,805); ν 3080 (s), 1905 (s), 1625 (s), 1603 (s), 1577 (s) cm^{-1}.

Anal. Calcd. for C$_{13}$H$_{11}$BN$_2$O·POCl$_3$: B, 2.88; Cl, 28.40. N, 7.47; P, 8.26. Found: B, 2.61; Cl, 28.21; N, 7.53; P, 7.98.

This compound, in glacial acetic acid-mercuric acetate, was neutral toward perchloric acid.

4-Ethoxy-1,2-dihydro-2-phenyl-1,3,2-benzodiazaborine Phosphorodichloridate (5).

The *adduct*, 4, (9.1 g., 0.024 mole) and 5 liters of reagent grade chloroform (stabilized with 0.75% ethanol) were heated under reflux for 0.33 hour under anhydrous conditions, filtered, and the filtrate concentrated *in vacuo* to 500 ml. The solid that crystallized from the cooled solution was filtered to give 7.0 g. (76% yield) of 5, m.p. 138-140° dec; λ max (tetrahydrofuran) 359 mμ (ϵ, 4,200); ν 3175 (s), 1635 (s), 1610 (s), 1595 (s) cm^{-1}.

Anal. Calcd. for C$_{15}$H$_{16}$BCl$_2$N$_2$O$_3$P: B, 2.81; Cl, 18.42; N, 7.28; P, 8.04; OEt, 11.70; N.E., 385. Found: B, 2.53; Cl, 18.64; N, 7.33; P, 7.48; OEt, 11.93; N.E. [HClO$_4$ in AcOH, Hg(OAC)$_2$], 388.

4-Ethoxy-1,2-dihydro-2-phenyl-1,3,2-benzodiazaborine Monohydrate (6).

To a suspension of 5 (2.0 g., 0.05 mole) in 50 ml. of methylene chloride was added, in portions, sodium bicarbonate solution (1.26 g., 0.15 moles in 20 ml. of water), the whole shaken, the methylene chloride solution separated, dried, and concentrated *in vacuo*. The residual solid, m.p. 118-119° was recrystallized from methylene chloride to give 0.5 g. (30% yield) of 6, m.p. 120-121°; λ max (ethanol) 233, 390 mμ (ϵ, 29,400, 4,790); ν 3520 (s), 3340 (s), 1640 (s), 1615 (s), 1590 (s), 1560 (s) cm^{-1}.

Anal. Calcd. for C$_{15}$H$_{15}$BN$_2$O·H$_2$O: C, 67.19; H, 6.38; N, 10.44; EtO, 16.80; Total Volatiles, 6.7. Found: C, 67.12; H, 6.43; N, 10.90; EtO, 16.74; Total Volatiles (78°), 2.2, (100°) 9.28.

The methylene chloride filtrate from the recrystallization when kept in a stoppered flask slowly deposited a crystalline solid, m.p. 213-215°, shown to be identical with II-1 by m.p. and mixture m.p.

4-Amino-1,2-dihydro-2-phenyl-1,3,2-benzodiazaborine (7).

Compound 6 (8.0 g., 0.021 mole) and 100 ml. of concentrated aqueous ammonia (d. 0.7) were kept at room temperature for 24 hours. The crystalline product was filtered to give 3.8 g. of

material, m.p. 249-252° dec. Recrystallization from *boiling water* gave 1.0 g. (14% yield) of the product as a trihydrate; this was stable at room temperature but drying at 110° *in vacuo* gave anhydrous **7**, m.p. 260-263° dec.; λ max (ethanol) 378 mμ (ε, 4,350); ν 3330 (s), 1640 (s), 1600 (s) cm⁻¹.

Anal. Calcd. for $C_{13}H_{12}BN_3$: C, 70.65; H, 5.48; N, 19.02; B. 4.89. Found: C, 70.45; H, 5.84; N, 18.61; B, 4.73.

Evaporation of the ammonia filtrate from the above crude product yielded 0.25 g. of benzeneboronic acid, m.p. and mixture m.p. 218-220°.

Reaction of **4** with Aqueous Ammonia.

To 100 ml. of concentrated aqueous ammonia (d. 0.7) was added, with stirring, **4** (4.8 g., 0.013 mole), at room temperature. The solid, except for a trace of gummy material, dissolved to form a colorless solution. The solution was filtered and the filtrates evacuated at room temperature to remove excess ammonia. During this process, a solid separated and this was filtered to give 0.50 g. (37% yield) of o-aminobenzonitrile, m.p. 44-46°. Recrystallization from hexane raised the m.p. to 49-51°, identical with that of authentic o-aminobenzonitrile, alone, or mixed, and their ir spectra were superimposable.

Anal. Calcd. for C_7H_6N: C, 71.16; H, 5.12; N, 23.70. Found: C, 70.78; H, 5.04; N, 23.49.

The aqueous filtrate from the above product was lyophilized to give 3.5 g. of residual solid, m.p. about 200°. This was extracted with hexane to give 0.7 g. (45% yield) of benzeneboronic acid, m.p. and mixture m.p. 218-220°.

2-Cyclohexyl-2,3-dihydro-6-nitro-4(1H)-quinazolinone.

A solution of N-cyclohexyl-4-nitro-o-aminobenzamide (1.32 g., 0.005 mole), benzaldehyde (1.05 g., 0.01 mole), 150 ml. of anhydrous chlorobenzene, and p-toluenesulfonic acid (0.25 g.) was distilled so that the condensed distillate was dried by passage through a bed of calcium hydride (3.0 g., 8-14 mesh) before returning to the reaction flask. The heating was continued for two hours, the hot solution filtered, and the filtrate cooled to give 1.0 g. of crystalline material, m.p. 217-222°. Recrystallization from 2-propanol gave 0.86 g. (49% yield) of the product, m.p. 231-232°.

Anal. Calcd. for $C_{20}H_{21}N_3O_3$: C, 68.35; H, 6.02; N, 11.97. Found: C, 68.35; H, 6.04; N, 12.11.

REFERENCES

(1) A Communication from this Institute on several of the compounds described in this paper has appeared; see, *J. Am. Chem. Soc.*, 84, 688 (1962).

(2) The literature on "Organic Compounds of Boron" has been reviewed by M. F. Lappert, *Chem. Revs.*, 56, 959 (1956) while P. M. Maitlis, *ibid.*, 62, 223 (1962) has performed a similar task for the literature on "Heterocyclic Organic Boron Compounds".

(3) H. L. Yale and M. Kalkstein [*J. Med. Chem.*, 10, 334 (1967)] employed this technique to prepare 2,3-dihydro-6-nitro-2-phenyl-4(1H)-quinazolinone.

(4) This designation refers to compound **25** in Table II; this reference system is employed throughout the paper.

(5) The stability of the carbon-boron linkage in aromatic compounds varies and is dependent upon substitution in the aromatic ring [*cf.* A. H. Soloway and P. Szabady, *J. Org. Chem.*, 25, 1683 (1960) and R. T. Hawkins, W. J. Lennarz, and H. R. Snyder, *J. Am. Chem. Soc.*, 82, 3053 (1960)].

(6) R. L. Letsinger and S. B. Hamilton [*ibid.*, 80, 5411 (1958)] have suggested that the failure of benzeneboronic acid to react with either aniline or ethylenediamine in boiling toluene while it reacts under the same conditions with o-phenylenediamine to form dihydrobenzoboradiazole must be attributed to the particular geometry of the o-phenylenediamine molecule rather than to the fact that it is an aromatic diamine. To this concept must now be added the role of the electron deficient boron atom in these cyclizations; no one apparently has compared the ease of formation of boron and carbon isosteres.

(7) S. S. Chissick, M. J. S. Dewar, and P. M. Maitlis [*J. Am. Chem. Soc.*, 83, 2708 (1961)] reported that in their hands the same reactants gave only o-aminobenzamide hydrochloride. It should be noted that there are numerous references in the literature to 1:1 addition compounds of carboxylic acid amides and phosphorus oxychloride; see, for example, R. C. Shah, R. K. Deshpande, and J. S. Chaubal, *J. Chem. Soc.*, 642 (1942). More recently, H. Bredereck and his coworkers [*Chem. Ber.*, 92, 837, 1456 (1959); *ibid.*, 94, 1883, 2278 (1961)] have found that a large variety of amides and lactams form 1:1 addition compounds. 1:1-Addition products of 9-acridanones and phosphorus oxychloride have been described by K. Gleu, S. Nitsche and A. Schubert, *Ber.*, 72, 1093 (1939); K. Gleu and A. Schubert, *ibid.*, 73, 805 (1940), and N. S. Drozdov, *Trudy Kafedry Biochim. Moskov Zootekh. Inst. Konevodsta,* 42, 1944 (1945); *Chem. Abstr.*, 41, 763b (1947); *J. Gen. Chem. USSR*, 16, 455 (1946); *Chem. Abstr.*, 41, 966d (1947).

(8) M. J. S. Dewar and P. M. Maitlis, *Tetrahedron*, 15, 35 (1961).

(9) W. Gerrard, "The Organic Chemistry of Boron," Academic Press, N. Y., p. 12 *et seq.* See, also, Y. F. Shealy and R. F. Struck, *J. Med. Chem.*, 12, 907 (1969).

(10) H. R. Snyder and F. W. Wyman, *J. Am. Chem. Soc.*, 70, 232 (1949).

(11) S. S. Chissick, M. J. S. Dewar, and P. M. Maitlis (Ref. 6) prepared only II-1 and, in studying its solvolysis in ethanol, reported that in the presence of alkali, "the solvolysis seemed to be slower". They observed that the addition of alkali produced a large bathochromic shift of the main uv absorption from 312 to 358 mμ; they attributed this shift to the formation of a conjugate anion. They did not study II-1 in aqueous alkali where it shows a single maxima at 225 mμ. In aqueous alkali, II-9 shows three maxima at 227, 235 (sh), and 438 mμ. J. E. Milks, G. W. Kennerly, and J. H. Polevy [*J. Am. Chem. Soc.*, 84, 2529 (1962)] have reported that base also stabilizes the 1,2,3-trihydro-3,5,1,2-diazazoniaboronide heterocycle toward ethanolysis.

(12) One of the referees has requested explanations for (a) the role of mannitol in these titrations and (b) for the enhanced acidity and the deep colors of these nitro derivatives in the presence of aqueous base. (a) Neither boric acid nor an areneboronic acid can be titrated with aqueous sodium hydroxide (or potassium hydroxide), using phenolphthalein as indicator, unless mannitol, glycerol, or a similar 1,2-dihydroxy (not phenolic) compound is present. The titration is highly specific [*cf.* C. L. Wilson and D. W. Wilson, "Comprehensive Analytical Chemistry," Elsevier Publishing Co., Amsterdam, 1960, p. 591-2; I. M. Kolthoff and P. J. Elving, "Treatise in Analytical Chemistry," Interscience Publishers, New York, N. Y., 1965, Part II, Vol. 9, p. 152-153]. Since boric acid in the presence of mannitol is a monobasic acid, an accepted explanation is that two of the three hydroxyl groups in boric acid are complexed as a 1,3,2-dioxaborolane and that this event confers enhanced acidity to the remaining OH group. This representation

is an oversimplification, and does not take into account the inherent instability of a dioxaboralane in aqueous systems, nor does it take into account that areneboronic acids, again, in the presence of mannitol, are monobasic and yet a dioxaborolane cannot form. In any event, no color changes are observed in these titrations other than those associated with the indicator. (b) The boron heterocycles described in this paper that do not contain a nitro group, although soluble in aqueous base, do not titrate with aqueous base to a precise end-point with phenolphthalein as indicator, in the presence or absence of mannitol; they are such weak acids that they do not titrate even with potassium methoxide in non-aqueous systems. Since the precise role of mannitol in these titrations is not known, it is necessary to do the titration with and without that reagent with compounds other than boric or boronic acids. Dr. M. J. S. Dewar, in a personal communication to the author, has suggested that his explanation for the enhanced acidity seen with his compound, 10 [M. J. S. Dewar, R. Jones, and R. H. Logan, Jr., J. Org. Chem., 33, 1353 (1968)] might well explain the similar phenomenon seen with the nitro derivatives described in this paper. Thus, there is presumed to be a strong π bonding between boron and nitrogen in the benzodiazaborinones as shown in 17 and 18. The participation of these resonance structures must be significant, e.g., the boron heterocycles dissolve in dilute aqueous alkali whereas their carbon isosteres do not. The introduction of a nitro group leads to cross conjugation, a decrease in π electron density on the boron atom, and the mesomeric

stabilization of the heterocycle, and these effects lead to an increase in the Lewis acidity of the boron. Again, addition of the base to boron removes it from conjugation with the adjacent 1-NH group, thus greatly increasing the interaction of the latter with the p-nitro group and creating the highly colored cation, 19.

(13) Complexes of pyridine and areneboronic acids and areneboronic acid anhydrides are well known; cf. H. R. Snyder, M. S. Konecky, and W. J. Lennarz, J. Am. Chem. Soc., 80, 3611 (1958). These complexes are colorless solids.

(14) The most recent study is by R. T. Hawkins and H. R. Snyder, [ibid., 82, 3864 (1960)], who also cite earlier literature.

(15a) J. H. Beynon, R. A Saunders, and A. E. Williams, "The Mass Spectra of Boron Compounds," in "The Mass Spectra of Organic Molecules," Elsevier Publishing Co., New York, N. Y., 1968, pp. 398-411.   (b) The pathway that R. C. Dougherty [Tetrahedron, 24, 6755 (1968)] has suggested for the fragmentation of 4-methyl-4,3-borazaroisoquinoline reveals the complexity of the decompositions of boron heterocycles.

(16) See, for example, R. Staiger and E. Miller, J. Org. Chem., 24, 1214 (1959).

(17) J. Houben, Ber., 42, 3188 (1909).

(18) A. Grohmann [ibid., 24, 3810 (1891)] reported a m.p. of 148°.

(19) M. T. Bogert and G. Schatchard [J. Am. Chem. Soc., 41, 2066 (1919)] reported a m.p. of 168°.

(20) A. Weddige, J. Prakt. Chem., [2], 36, 150 (1887).

17   18   19