Novel Boron Heterocycles. II. 2,3-Dihydro-1,3,5,2-oxadiazaboroles, 1,2-Dihydro-1,3,2-benzodiazaborine 3-Oxide, and 3,4-Dihydro-2*H*-1,2,4,3-benzothiadiazaborine 1,1-Dioxide.

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Received October 12, 1970

A number of arylamidoximes, an *o*-aminobenzaloxime, and an *o*-aminobenzenesulfonamide have been reacted with boronic acids to give three novel boron containing heterocycles. Evidence, based on mass spectroscopy, that the product from *o*-aminobenzaloxime is a 1,2-dihydro-1,3,2-benzodiazaborine 3-oxide, is presented.

The first paper of this series (1) described the synthesis of 1,2-dihydro-1,3,2-benzodiazaborin-4(3*H*)-ones by the cyclodehydration reaction between an areneboronic acid and an *o*-aminobenzamide. The present paper describes the formation of several novel boron heterocycles by the cyclodehydration reaction between an arene- or an arylethaneboronic acid and (a) an amidoxime, **1**, (b) an *o*-aminobenzaloxime, **2**, and (c) an *o*-aminobenzenesulfonamide, **3**. With all of these intermediates, the heterocycles formed readily in toluene or xylene solution at reflux temperature, using a Dean-Stark trap or a reagent like calcium hydride to remove water as formed; compounds represented by **4** have also been formed when a dry blend of the reactants was heated at 110° in an evacuated drying chamber with a desiccant, *e.g.*, phosphorus pentoxide.

The several boron heterocycles represented by **4**, **5**, and **6** were significantly less stable toward ethanolysis than the 1,2-dihydro-1,3,2-benzodiazaborin-4(3*H*)-ones described in the first paper. Thus, **4**, where R is mesityl (one of the three most stable derivatives in the borin-4(3*H*)-one series) was completely solvolyzed within one hour in absolute ethanol; **5** and **6** were even less stable in ethanol, in fact so unstable that they could not be recrystallized from non-protic solvents without decomposition. Compounds with structures **5** and **6** were rapidly degraded by aqueous alkali, and this was true also with compounds of structure **4**, except those carrying a *p*-nitrophenyl group in position four. Four derivatives of this type were prepared (see Table I, compounds I-**12** to I-**15**. When dissolved in acetone and titrated with 0.01 *N* aqueous sodium hydroxide, using phenolphthalein as

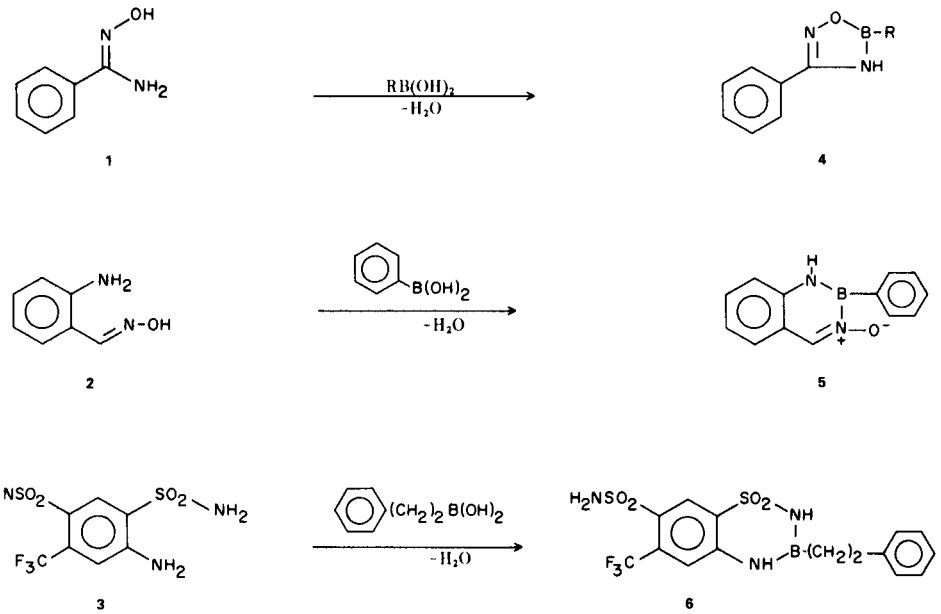
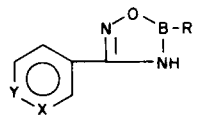


TABLE I

2,3-Dihydro-1,3,5,2-oxadiazaboroles

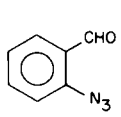


No.	X	Y	R	Molecular Formula	M.p., °C	Recrystn. Solvent (a)	Yield, %	B Analysis Calcd.	B Analysis Found	N Analysis Calcd.	N Analysis Found
1	CH	CH	C_6H_5	$C_{13}H_{11}BN_2O$	160-161	A	82	4.87	4.65	12.60	12.40
2	CH	CCl	C_6H_5	$C_{13}H_{10}BClN_2O$	214-215	B	89	4.21	4.20 (b)	---	---
3	CH	CCl	4-$CH_3C_6H_4$	$C_{14}H_{12}BClN_2O$	240-241	B	89	3.99	3.93 (c)	---	---
4	CH	CH	1-$C_{10}H_7$	$C_{17}H_{13}BN_2O$	146-147	A	60	3.98	3.86	10.30	10.29
5	CH	CCl	2,4,6-$(CH_3)_3C_6H_2$	$C_{16}H_{16}BClN_2O$	185-187	C	92	3.63	3.65	9.38	9.58
6	CH	CCl	1-$C_{10}H_7$	$C_{17}H_{12}BClN_2O$	148-150	A	66	3.52	3.68	9.15	9.13
7	N	CH	1-$C_{10}H_7$	$C_{16}H_{12}BN_3O$	198-200	B	82	3.96	3.76	15.89	15.47
8	CH	N	C_6H_5	$C_{12}H_{10}BN_3O$	211-213	B	67	4.85	4.74	18.84	18.62
9	CH	N	2,4,6-$(CH_3)_3C_6H_2$	$C_{15}H_{16}BN_3O$	159-160	A	83	4.08	4.06	15.86	15.54
10	CH	N	1-$C_{10}H_7$	$C_{16}H_{12}BN_3O$	200-202	B	86	3.96	4.16	15.39	15.14
11	CH	CCl	OH	$C_7H_6BClN_2O_2$	>300	(e)	30	---	---	14.26	14.27 (d)
12	CH	CNO_2	C_6H_5	$C_{13}H_{10}BN_3O_3$	227-229	C	78	4.05	3.80	15.74	15.71 (f)
13	CH	CNO_2	*o*-$CH_3C_6H_4$	$C_{14}H_{12}BN_3O_3$	214-216	B	90	3.85	3.87	14.95	14.71 (g)
14	CH	CNO_2	*p*-$CH_3C_6H_4$	$C_{14}H_{12}BN_3O_3$	237-238	C	55	3.85	3.88	14.95	14.95 (h)
15	CH	CNO_2	α-$C_{10}H_7$	$C_{17}H_{12}BN_3O_3$	230-232	C	95	3.41	3.66	13.26	13.51 (i)

(a) Recrystn. Solvents: A = Skellysolve E; B = Toluene; C = Xylene. (b) *Anal.* Calcd.: Cl, 13.78. Found: Cl, 13.99. (c) *Anal.* Calcd.: Cl, 13.07. Found: Cl, 13.24. (d) *Anal.* Calcd.: Cl, 18.05. Found: Cl, 18.26. (e) Not recrystallized. (f) *Anal.* Calcd.: C, 58.48; H, 3.78; N.E. 267. Found: C, 58.26; H, 3.91; N.E. (aqueous sodium hydroxide, mannitol, phenolphthalein in acetone), 260. (g) *Anal.* Calcd.: N.E., 281. Found: N.E. (aqueous sodium hydroxide, mannitol, phenolphthalein, in acetone), 279. (h) *Anal.* Calcd.: N.E., 281. Found: N.E. (aqueous sodium hydroxide, mannitol, phenolphthalein, in acetone), 279. (i) *Anal.* Calcd.: N.E., 318. Found: N.E. (aqueous sodium hydroxide, mannitol, phenolphthalein, in acetone), 312.

indicator, an indicator color change occurred when about one-half that of theory had been added. The addition of mannitol prior to the titration, however, made possible very precise titrations and gave good neutralization equivalents. Two relevant points, in passing, were that in concentrated solution, in acetone, these *p*-nitrophenyl derivatives, as well as the intermediate *p*-nitrobenzamidoxime, and aqueous alkali gave intense red colored solutions; however, *p*-nitrobenzamidoxime in acetone solution was neutral toward aqueous alkali under these titration conditions. Thus, the nitro derivatives in this series of boron heterocycles were somewhat weaker acids than those described in the first paper.

Only a few references to the reactions of *o*-aminobenzaloxime (**2**) were to be found in the literature. Two of these were of particular interest. In 1901, Bamberger and Demuth (3) reported that the diazotization of **2** gave a deep yellow-colored solid and to this product, based on its chemical behavior, they assigned the *o*-azidobenzaldehyde (**7**) structure. In 1927, Meisenheimer, Senn, and Zimmermann (4) while studying the diazotization of *o*-aminobenzophenones, concluded that their products, also deep yellow solids, were 4-substituted-1,2,3-benzotriazine 3-oxides (**8**) and suggested that the product obtained by Bamberger and Demuth was not **7**, but the isomeric 1,2,3-benzotriazine 3-oxide (**9**). The cyclization of **2** with benzeneboronic acid also gave a deep yellow colored solid, whose structure could be the boron derivative, **10** or **11**; the correct structure assignment here



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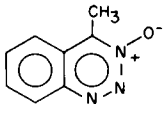

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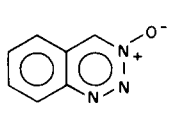

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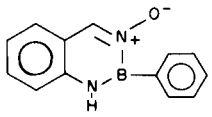

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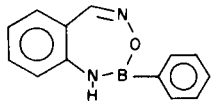

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would strengthen Meisenheimer's suggestion regarding **7** and **9**. Additional relevant evidence came from the recent report that 2-amino-5-chlorobenzophenone and 2-chloroacetamidic acid, ethyl ester yielded 2-(chloromethyl)-4-methylquinazoline 3-oxide (5). Thus, there appears to be a strong tendency to form the 6-membered *N*-oxide heterocycle.

The high resolution mass spectrum of the boron derivative showed that oxygen was readily lost to yield ions with 16, 17 and 18 mass units less than that of the molecular ion. There is considerable precedent for this characteristic fragmentation pattern for aromatic *N*-oxides (6). It was also significant that loss of similar mass units did not occur with the isomeric 1,3,5,2-oxadiazaboroles. Thus, the evidence, collectively, strongly supports the assignment of structure **9** to the product obtained by Bamberger.

EXPERIMENTAL

The ir spectra were determined on Potassium bromide pellets on a Perkin Elmer 621 and the mass spectra on an AEI MS 902 double focusing high resolution mass spectrometer. The author is indebted to Miss Barbara Keeler and Dr. A. I. Cohen for these spectra. The microanalyses were performed by Mr. J. F. Alicino and his associates in this Institute.

2,3-Dihydro-2,4-diphenyl-1,3,5,2-oxadiazaborole (I-**1**).

(a) A solution of benzeneboronic acid (1.22 g., 0.01 mole) and benzamidoxime (1.36 g., 0.01 mole) in 100 ml. of anhydrous xylene was heated under reflux for two hours under a Dean-Stark trap. When the xylene solution was cooled, the product, 2.15 g., m.p. 158-160°, crystallized. Recrystallization from Skellysolve E gave 1.80 g. of I-**1**; ν 3400 (s), 1600 (s) cm^{-1}.

(b) A thoroughly ground and blended mixture of benzamidoxime (0.68 g., 0.005 mole) and benzeneboronic acid (0.61 g., 0.005 mole) was heated in a drying pistol by means of boiling toluene, employing phosphorus pentoxide as the desiccant. The solid melted partially and then after ten minutes, solidified. Heating was continued for one hour and the material recrystallized from Skellysolve E to give 0.88 g. (66% yield) of I-**1**, m.p. and mixture m.p., 160-161°.

2,3-Dihydro-4-(*p*-nitrophenyl)-2-phenyl-1,3,5,2-oxadiazaborole (I-**12**).

A solution of *p*-nitrobenzamidoxime (1.81 g., 0.01 mole), benzeneboronic acid (1.22 g., 0.01 mole), and 225 ml. of anhydrous toluene was heated so that the distillate percolated downward through a bed of calcium hydride before returning to the reaction flask (7). The evolution of water was rapid and complete in about one hour. The reaction mixture was allowed to cool, the solid filtered, and air-dried to give 2.60 g. of material, m.p. 227-229°. Recrystallization from anhydrous xylene gave 2.08 g. of I-**12**; ν 3420 (s), 1600 (s), 1555 cm^{-1}.

The physical constants and analyses for the 2,3-dihydro-1,3,5,2-oxadiazaboroles are listed in Table I.

Nicotinamidoxime.

To nicotinonitrile (20.8 g., 0.2 mole), hydroxylamine hydrochloride (14.0 g., 0.2 mole), 70 ml. of water, and 100 ml. of 95% ethanol was added, portionwise, with stirring, anhydrous sodium carbonate (10.8 g., 0.1 mole). The mixture was stirred at room temperature for eighteen hours, concentrated *in vacuo*, and the residue cooled. The solid that separated was recrystallized from chlorobenzene to give 6.2 g. (23% yield) of product, m.p. 122-124°.

Anal. Calcd. for $C_6H_6N_3O$: N, 30.88. Found: N, 30.54.

p-Nitrobenzamidoxime.

p-Nitrobenzonitrile was reacted in similar fashion to give *p*-nitrobenzamidoxime, m.p. 182-184° dec.; ν (mineral oil) 3480 (s), 3370 (s), 3260-3160 (s, broad), 1660 (s), 1600 (s) cm^{-1}. The yield was 75%.

Anal. Calcd. for $C_7H_7N_3O_3$: C, 46.41; H, 3.90; N, 23.20. Found: C, 46.19; H, 3.99; N, 23.27.

4-(*p*-Chlorophenyl)-2,3-dihydro-2-hydroxy-1,3,5,2-oxadiazaborole (I-**11**).

A solution of *p*-chlorobenzamidoxime (3.4 g., 0.02 mole), trimethylborate (2.3 g., 0.022 mole), and 125 ml. of anhydrous toluene was distilled slowly through a short fractionating column so that during four hours, 56 ml. of distillate was collected. During this procedure no attempt was made to exclude atmospheric moisture, and during the four hours increasing quantities of a crystalline product separated from the hot solution. The hot solution was filtered and the product washed with ordinary ether to give 1.16 g. of I-**11**; ν 3460 (s), 3340-3160 (broad, s), 1610 cm^{-1}.

1,2-Dihydro-2-phenyl-1,3,2-benzodiazaborine 3-Oxide.

To a solution of hydroxylamine hydrochloride (3.60 g., 0.054 mole) in 100 ml. of 1.05 *N* aqueous sodium hydroxide was added *o*-nitrobenzaldehyde (7.55 g., 0.05 mole), the whole warmed for five minutes, filtered, and the filtrate treated with an excess of 10% aqueous hydrochloric acid to give the *crude oxime.* The crude oxime and 25 ml. of 20% aqueous ammonium sulfide solution were heated in an open flask on the steam bath to dryness, 25 ml. of water added, the mixture heated to boiling and filtered to give 4.3 g. of crude *o*-aminobenzaloxime, m.p. 129-131°; the yield was 2.72 g. (40%). The oxime (1.36 g., 0.01 mole), benzeneboronic acid (1.22 g., 0.01 mole), and 100 ml. of anhydrous xylene were heated under reflux for three hours under a Dean-Stark trap; during this time, the product separated as a dense yellow solid. The whole was cooled, the solid filtered, and dried to give 1.50 g. of crude product, m.p. 246-248°. No satisfactory recrystallization solvent could be found. Consequently, the product was washed repeatedly with anhydrous ether to give 1.20 g. (53% yield) of 1,2-dihydro-2-phenyl-1,3,2-phenyl-1,3,2-benzodiazaborine 3-oxide, m.p. 249-251°; ν 3400 (s), 1640 (s), 1295 (s) cm^{-1}.

3,4-Dihydro-3-phenethyl-6-(trifluoromethyl)-2*H*-1,2,4,3-benzothiadiazaborine-7-sulfonamide 1,1-Dioxide.

A mixture of 50 ml. each of anhydrous diglyme and xylene was distilled azeotropically into a Dean-Stark trap previously filled with anhydrous xylene to remove any traces of water, then cooled to about 80° and 5-amino-α,α,α-trifluorotoluene-2,4-disulfonamide (6.80 g., 0.021 mole) and 2-phenylethaneboronic acid (3.0 g., 0.02 mole) added, and the whole heated under reflux under the Dean-Stark trap for three hours to separate the water formed in the reaction. No product separated on cooling, and the solution, consequently, was concentrated *in vacuo* to a semisolid mass; this was dried to a tan solid by heating in a drying apparatus at 110°. No satisfactory recrystallization solvent could be found. The yield of product was 8.0 g. (92%); ν 3470 (s), 3380 (s), 3290 (s), 3230 (s), 1340-1315 (broad, s), 1650 (s) cm^{-1}.

Anal. Calcd. for $C_{15}H_{15}BF_3N_3O_4S_2$: B, 2.50; N, 9.70. Found: B, 2.87; N, 9.47.

REFERENCES

(1) For Paper I in this series, see H. L. Yale, *J. Heterocyclic Chem.*, 8, 193 (1971).

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