ganic solvent in the presence of an amide. When phthalimide is used in place of the amide, it is recovered in 92.5% yield, and there is an 11% conversion of the boron compound to phenylboronic anhydride. In order to eliminate the possibility that a factor other than the amide might be responsible for the observed results, diphenyl hydroxyborane was also subjected to the same treatment alone in toluene, leading to the recovery in 44% yield of bis(diphenylboron oxide. No phenylboronic anhydride was found.

These observations suggest that the crucial property required of a deboronating agent may be its Lewis base character rather than any oxidizing power *per se*. This implies that the key step in deboronation is the incipient *reducing* effect produced by the coordination of the Lewis base at the boron atom, and that subsequent steps in the mechanism are more or less incidental, important though they may be on occasion from the preparative standpoint. Such an initial coordination step seems rather well established as a necessary part of the mechanism of deboronation in the aryl dihydroxyboranes[5] by means of relatively powerful nucleophilic agents. The efficiency of weakly nucleophilic reagents such as amides in accomplishing deboronation of a diaryl hydroxyborane indicates that the diaryl compounds are considerably more reactive under such attack than are the monoaryl ones. It also suggests a means for carrying out selective deboronations.

EXPERIMENTAL

Acetamide (0.8 gm.) was added with 450 ml. of toluene to the diphenyl hydroxyborane from hydrolysis of 3.0 gm. of *B,B*-diphenyl boroxazolidine,[6] and the mixture was azeotropically distilled to a residue of 3–5 ml., from which there crystallized overnight 1.3 gm. of phenylboronic anhydride, m.p. 214–216°, after recrystallization from carbon tetrachloride.[7] The product was further characterized by preparing from it the *N*-ethyl-*B*-phenyl diptych boroxazolidine.[8]

Benzamide (1.6 gm.) was added, with 200 ml. of toluene, to the diphenyl hydroxyborane from 3.0 gm. of *B,B*-diphenyl boroxazolidine, and the mixture azeotropically distilled to about 5–7 ml. from which crystallized 1.85 gm. of white product. This product contained a carbon tetrachloride-soluble fraction which crystallized to give phenylboronic anhydride (mixed m.p. which authentic phenylboronic anhydride undepressed), and a water-crystallizable fraction which gave an undepressed mixed m.p. with authentic benzamide.

Phthalimide (1.3 gm.), with 200 ml. of toluene was added to diphenyl hydroxyborane from 2.0 gm. of *B,B*-diphenyl boroxazolidine and azeotropically distilled to 25–30 ml., from which 1.2 g. of phthalimide crystallized in plates on cooling, m. 234–235°. The filtrate was concentrated under vacuum to 3–5 ml. and cooled to give 0.1 gm. of phenylboronic anhydride.

B,B-Diphenyl hydroxyborane (3.0 gm.), in 160 ml. of toluene, was distilled to a residue of 3–5 ml. which, after 4 hours gave 1.0 gm. of white crystalline product which melted at 116–118° after recrystallization from carbon tetrachloride, in good agreement with the melting point of bis(diphenylboron)oxide.[9]

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Preparation of *N,N*-Dialkyl-*N'*-(2-dialkylaminoethyl)benzamidines

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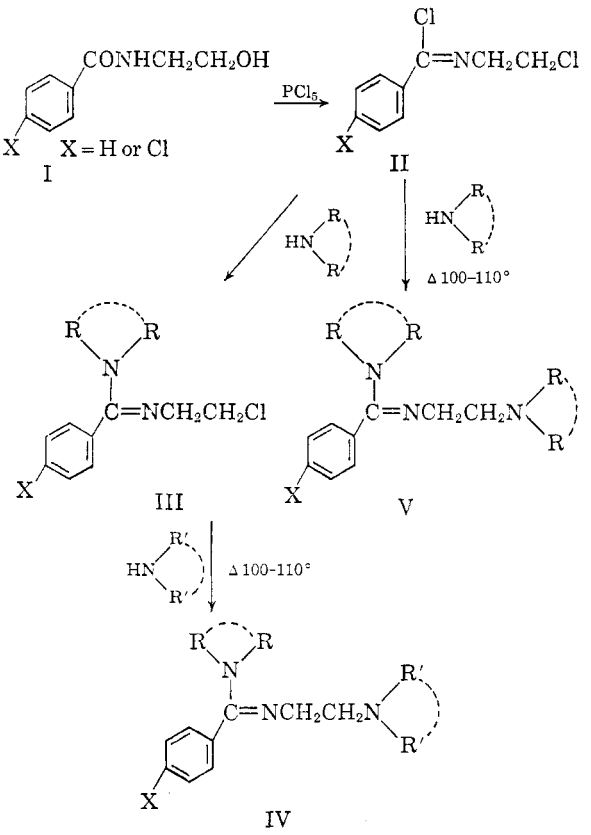
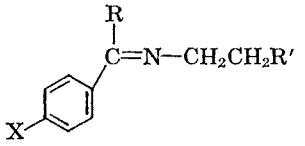
In the course of work carried out in these laboratories to synthesize compounds of interest as pharmaceuticals, we have prepared some benzamidines which exhibit diuretic activity of an order approximately equal to that of theophylline.[2]



(1) Present address: National Drug Co., Philadelphia, Pa.

(2) Of the compounds listed in Table I, Nos. 4, 14, and 16 gave the greatest diuretic response in dogs. The authors wish to thank William B. McKeon, Jr., of our pharmacology division for the diuretic screening.

TABLE I



No.	R	R′	X	M.P. or B.P.[a]	Mm.	Formula	Yield, %	n_D^{25}	Recryst. Solvent	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Halide, % Calcd.	Halide, % Found
1	Cl	Cl	H	78–82	0.1	$C_9H_9Cl_2N$	76	1.5670		53.49	53.3	4.49	4.5			35.09	35.0
2	$N(C_2H_5)_2$	Cl	H	105–110	0.8	$C_{13}H_{19}ClN_2$	61	1.5344		65.39	65.1	8.02	8.5	11.74	11.8		
3	$N(C_2H_5)_2$	1-Piperidyl	H	116–133	0.03	$C_{18}H_{29}N_3$	43	1.5291		75.21	75.1	10.17	10.1	14.62	14.6		
4	$N(C_2H_5)_2$	1-Piperidyl[b]	H	210–221		$C_{18}H_{31}Cl_2N_3$			Acetone					11.66	11.4	19.68	19.5
5	$N(C_2H_5)_2$	1-Piperidyl[c]	H	132–135		$C_{19}H_{32}IN_3$	84		Acetone	53.14	53.4	7.51	7.7			29.56	29.6
6	$N(C_2H_5)_2$	4-Morpholinyl	H	130–137	0.1	$C_{17}H_{27}N_2O$	81	1.5298		70.55	70.9	9.41	9.4	14.52	14.3		
7	$N(C_2H_5)_2$	4-Morpholinyl[b]	H	197–198		$C_{17}H_{29}Cl_2N_3O$			C_2H_5OH-Ether	56.35	56.4	8.07	7.4	11.60	11.4		
8	$N(C_2H_5)_2$	$N(CH_3)_2$	H	91–94	0.03	$C_{15}H_{25}N_3$	48	1.5180		72.82	72.8	10.19	10.1	16.99	16.8		
9	$N(C_2H_5)_2$	$N(CH_3)_2$[b,d]	H	185–187		$C_{16}H_{27}Cl_2N_3$			Acetone-CH_3OH					13.12	13.3	22.14	22.1
10	$N(C_2H_5)_2$	$N(CH_3)_2$[c]	H	150–151		$C_{16}H_{28}IN_3$	48		Acetone-ether	49.36	49.4	7.25	7.3			32.60	32.0
11	$N(C_2H_5)_2$	$N(C_2H_5)_2$	H	108–114	0.04	$C_{17}H_{29}N_3$	38	1.5114		74.13	74.5	10.61	10.4	15.26	15.2		
12	$N(C_2H_5)_2$	$N(C_2H_5)_2$[c]	H	114–115		$C_{18}H_{32}IN_3$	78		Acetone-ether	51.79	51.8	7.73	7.5			30.41	30.4
13	1-Piperidyl	1-Piperidyl	H	136–138	0.05	$C_{19}H_{29}N_3$	67	1.5493		76.21	76.0	9.76	9.7	14.03	14.1		
14	1-Piperidyl	1-Piperidyl[b]	H	184–186		$C_{19}H_{31}Cl_2N_3$			Acetone-CH_3OH					11.28	11.0	19.05	18.8
15	Cl	Cl	Cl	115–123	0.05	$C_9H_8Cl_3N$	85	1.5819		45.7	45.8	3.4	3.3			30.00	30.0
16	$N(C_2H_5)_2$	Cl	Cl	172–173		$C_{13}H_{19}Cl_3N_2$	51		Acetone							22.90	22.6
																11.45	11.41
17	$N(C_2H_5)_2$	1-Piperidyl	Cl	141–148	0.1	$C_{18}H_{28}ClN_3$	83	1.5392		67.16	67.4	8.77	9.0	13.05	13.0		
18	$N(C_2H_5)_2$	1-Piperidyl[b]	Cl	195–198		$C_{18}H_{30}Cl_3N_3$			Acetone-CH_3OH					10.64	10.6	17.96	17.9
19	$N(C_2H_5)_2$	1-Piperidyl[e]	Cl	170–178		$C_{20}H_{34}ClI_2N_3$			2-Propanol					6.92	6.9	41.90	41.8
20	$N(C_2H_5)_2$	4-Morpholinyl	Cl	163–166	0.1	$C_{17}H_{26}ClN_3O$	92	1.5407		63.04	65.1	8.09	9.2	8.65	8.5		
21	$N(C_2H_5)_2$	4-Morpholinyl[b]	Cl	166–169		$C_{17}H_{28}Cl_3N_3O$			Acetone-CH_3OH					10.59	10.5	17.87	17.5
22	$N(C_2H_5)_2$	4-Morpholinyl[c]	Cl	149–151		$C_{18}H_{29}ClIN_3O$			Acetone	46.41	46.7	6.28	5.9			27.25	27.1

[a] All melting points are corrected. All boiling points are uncorrected. [b] Dihydrochloride. [c] Methiodide (position of quaternization uncertain). [d] Contained 1.73% water by Karl Fischer determination. Analyses calcd. to dry basis. [e] Dimethiodide.

When *N*-(2-hydroxyethyl)benzamides (I) were treated with phosphorus pentachloride, stable *N*-(2-chloroethyl)benzimidyl chlorides (II) were produced which reacted readily with various secondary amines to give good yields of *N'*-(2-chloroethyl)-*N,N*-dialkylbenzamidines (III). At elevated temperatures in a high-boiling solvent or an autoclave, either the remaining alkyl halogen of III was replaced to give the desired *N,N*-dialkyl-*N'*-(2-dialkylaminoethyl)benzamidines (IV), or both halogens of II were replaced simultaneously to give other *N,N*-dialkyl-*N'*-(2-dialkylaminoethyl)benzamidines (V). We were thus able to control the placement of NRR groups in the tertiary benzamidines which are listed in Table I.

EXPERIMENTAL[3]

The following examples illustrate the general procedures used for preparation of the compounds listed in Table I.

N-(2-Chloroethyl)benzimidyl chloride. To a vigorously stirred solution of 33.0 g. (0.2 mole) of *N*-(2-hydroxyethyl)-benzamide[4] in 500 ml. of boiling benzene was added 83.3 g. (0.4 mole) of phosphorus pentachloride in small portions. With each addition a vigorous reaction ensued, and hydrogen chloride was evolved. As the reaction progressed, a heavy white crystalline precipitate separated. During a period of 3 hr. of stirring and refluxing the solid dissolved. Benzene and phosphorus oxychloride were removed by warming *in vacuo*, and the residual pale green oil was distilled through a 6-in. Vigreux column. Occasionally, a portion of phosphorus pentachloride preceded the distillate which made it necessary to disassemble the apparatus and wash out the solid collected on the walls of the condenser. Distillation was then continued to give 30.6 g. of *N*-(2-chloroethyl)benzimidyl chloride (compound No. 1, Table I) as a colorless oil.

N'-(2-Chloroethyl)-N,N-diethylbenzamidine. A solution of 20.2 g. (0.1 mole) of *N*-(2-chloroethyl)benzimidyl chloride in 150 ml. of benzene was mixed with 14.6 g. (0.2 mole) of diethylamine, and refluxed for 2 hr. The mixture was cooled, and the diethylamine hydrochloride collected by filtration. It weighed 10 g. (92% yield). The filtrate was washed with two 300-ml. portions of water and was then concentrated by warming *in vacuo* to a red oily residue. The oil was distilled to give 14.6 g. of *N'*-(2-chloroethyl)-*N,N*-diethylbenzamidine (compound No. 2, Table I).

N,N-Diethyl-N'-[2-(1-piperidyl)ethyl]benzamidine. A mixture of 16.7 g. (0.07 mole) of *N'*-(2-chloroethyl-*N,N*-diethylbenzamidine, 29.9 g. (0.35 mole) of piperidine, and 100 ml. of toluene was refluxed for 24 hr. The precipitated piperidine hydrochloride was collected by filtration (7 g., 83% yield). Toluene was removed from the filtrate by warming *in vacuo*, and the residual yellow oil was distilled to furnish 8.7 g. of *N,N*-diethyl-*N'*-[2-(1-piperidyl)ethyl]-benzamidine as a colorless oil (compound No. 3, Table I).

N,N-Pentamethylene-N'-[2-(1-piperidyl)ethyl]benzamidine. *N*-(2-Chloroethyl)benzimidyl chloride (32.4 g., 0.16 mole) dissolved in 500 ml. of toluene was stirred and mixed with 68.1 g. (0.8 mole) of piperidine. The solution became warm and piperidine hydrochloride separated. The mixture was then heated at reflux for 16 hr. From the chilled mixture 35 g. (90% yield) of piperidine hydrochloride was collected by filtration. The filtrate was extracted with two 300-ml. portions of water, dried over Drierite, and the toluene removed by heating *in vacuo*. Upon distillation of the red oily residue there was obtained 32 g. of *N,N*-pentamethylene-*N'*-[2-(1-piperidyl)ethyl]benzamidine (compound No. 13, Table I) as a yellow oil.

The *dihydrochloride salts* were obtained by treating the benzamidine bases in absolute ether with an excess of ethereal hydrogen chloride. *Quaternization* was carried out by treating the bases in acetone at room temperature with a 2:1 ratio of methyl iodide to benzamidine base. Under these conditions, with the exception of *N,N*-diethyl-*N'*-[2-[1-piperidyl)ethyl]benzamidine dimethiodide (compound No. 19, Table I), only the monomethiodides were produced.

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(3) Analyses were carried out in the Institute's microanalytical laboratory by Mr. K. D. Fleischer and staff.

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Further Studies in the Synthesis of Long-Chain Hydroxy Acids[1]

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In a previous paper,[3] the authors reported the preparation of four long-chain hydroxy acids by Raney nickel-catalyzed reduction and desulfurization of selected acidic derivatives of thiophene.

References concerning the development of the desulfurization reaction and its application to the synthesis of various classes of long-chain compounds may be found in the original article.[3] In addition to these previously cited references, the work of Gol'dfarb and co-workers[4–7] should be mentioned.

The work reported in our original article has now been extended to the preparation of four more long-chain hydroxy acids. All acids prepared in this extension were 10-hydroxy acids.

The initial work was undertaken to investigate the application of the desulfurization reaction to the preparation of hydroxy acids, as the older methods of synthesis, based on reduction of keto

(1) Presented in part before the 139th meeting of the American Chemical Society in St. Louis, Mo., March 1961.

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