[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NORTHWESTERN UNIVERSITY, EVANSTON, ILL.]

Organoboron Compounds. XVI. Coöperative Functional Group Effects in Reactions of Boronoarylbenzimidazoles[1]

BY ROBERT L. LETSINGER AND DAVID B. MACLEAN[2]

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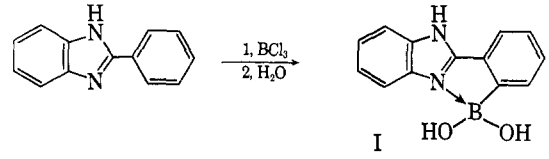
2-(2-Boronophenyl)-benzimidazole (I) and 2-(2-boronobenzyl)-benzimidazole (III) were prepared by passing boron trichloride into melts of 2-phenylbenzimidazole and 2-benzylbenzimidazole and subsequently hydrolyzing the products. They were characterized by derivatives and by ultraviolet and infrared spectral data. These compounds served as catalysts for the formation of ethers from chloroethanol in butanol solutions containing collidine. They were much more effective in this regard than benzeneboronic acid, 2-phenylbenzimidazole or a mixture of these two substances. It is proposed that the borono group in I and III binds the alcoholic substrates and holds them in a position favorable for reaction, while the nitrogen participates by increasing the nucleophilicity of oxygen joined to boron. Collidine functions as a transfer base to take up protons liberated in the reaction.

As part of a general investigation of synergism in reactions involving neighboring functional groups, we undertook the synthesis and study of 2-(2-boronophenyl)-benzimidazole (I). In this substance the basic nitrogen of an imidazole ring would be well positioned for intramolecular coördination with the boron atom. It was of interest to see whether such a compound would exhibit chemical and catalytic properties of the type found with 8-quinolineboronic acid, a substance in which intramolecular coördination between boron and nitrogen is not favored by the molecular geometry.[1,3]

The present paper describes: (a) the preparation and characterization of I; (b) the ultraviolet and infrared spectral properties of I, especially in regard to the question of intramolecular boron–nitrogen coordination; and (c) the reaction of I with chloroethanol. Pertinent information on two related compounds, 1-methyl-2-(2-boronophenyl)-benzimidazole (II) and 2-(2-boronobenzyl)-benzimidazole, which were prepared in connection with this study, is also included.

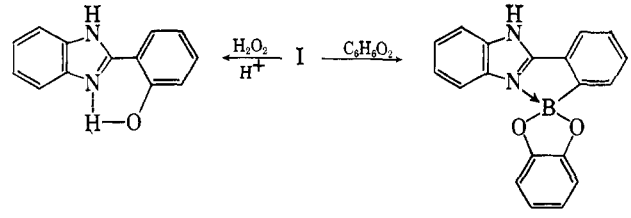
Synthesis and Characterization.—Attempts to prepare compound I by the sequence used for synthesis of 8-quinolineboronic acid were unsuccessful. Thus 2-(2-bromophenyl)-benzimidazole was treated with butyllithium (two equivalents) at low temperature; however, as a consequence of formation of an N-lithium salt of the benzimidazole, the desired lithium–bromine exchange was not realized.[4] It was then found that 2-(2-boronophenyl)-benzimidazole could be obtained conveniently by simply passing a stream of boron chloride into liquid 2-phenylbenzimidazole at 300° and subsequently hydrolyzing the mixture. This aromatic substitution reaction with boron trichloride is novel in that a catalyst is not required.[5] Although no attempt was made to isolate intermediates, it seems likely that



I

the reaction involves formation and cyclization of an N–BCl_2 derivative, as in the conversion of *o*-aminobiphenyl to 9-chloro-9,10-borazarophenanthrene.[6]

2-(2-Boronophenyl)-benzimidazole was relatively stable thermally; it did not melt at temperatures up to 320° and began slowly to decompose only at considerably higher temperatures. In low molecular weight alcohols and in dilute aqueous solutions of strong acids or hydroxides it was quite soluble, but it was relatively insoluble in water and in non-hydroxylic solvents. Both the basic nitrogen and boronic acid functions could be utilized in preparing derivatives; crystalline salts were obtained by adding concentrated hydrochloric acid to dilute acid solutions of I and a solid ester was produced by heating I with *cis*-1,2-cyclopentanediol. The catechol ester was a particularly good derivative since it precipitated in high yield when catechol was added to an alcoholic solution of I. As in simple areneboronic acids the carbon–boron bond could be cleaved with hot aqueous sodium hydroxide or strongly acidic solutions of hydrogen peroxide, the products being 2-phenylbenzimidazole and 2-(2-hydroxyphenyl)-benzimidazole, respectively. The reaction of I with hydrogen peroxide in alcohol was unusual in that a peroxide complex precipitated from the solution.



Compound I resisted most attempts at alkylation; however, a small amount of 1-methyl-2-(2-boronophenyl)-benzimidazole (II), isolated as the catechol derivative, was obtained by treating an alkaline solution of I with excess methyl sulfate. The structure of II was proved by an independent synthesis. 2-(2-Bromophenyl)-benzimidazole was converted to 1,3-dimethyl-2-(2-bromophenyl)-benzimidazolium iodide (67%) by methyl iodide in methanol at 200–220° Upon pyrolysis in small batches at 260–270° this salt afforded 1-methyl-2-(2-bromophenyl)-benz-

(1) This work was supported by the National Science Foundation, Grant-G7414. For the previous paper in this series see R. L. Letsinger and J. D. Morrison, *J. Am. Chem. Soc.*, **85**, 2227 (1963).

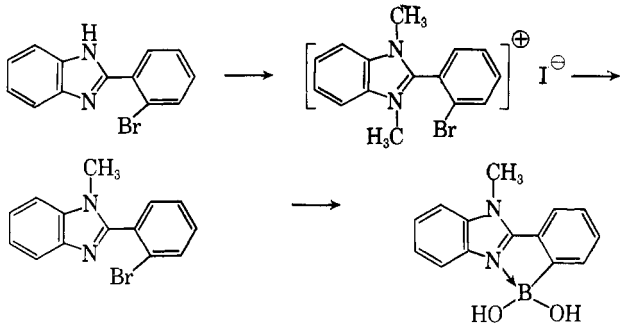
(2) National Science Foundation Fellow, 1958, 1959.

(3) R. L. Letsinger and S. J. Dandegaonker, *J. Am. Chem. Soc.*, **81**, 498 (1959).

(4) The inhibiting effect of the N–Li salt on exchange of the neighboring bromine is indicated by the fact that 1-methyl-2-(2-bromophenyl)-benzimidazole readily underwent lithium–bromine exchange when treated with butyllithium (see later sections of this paper).

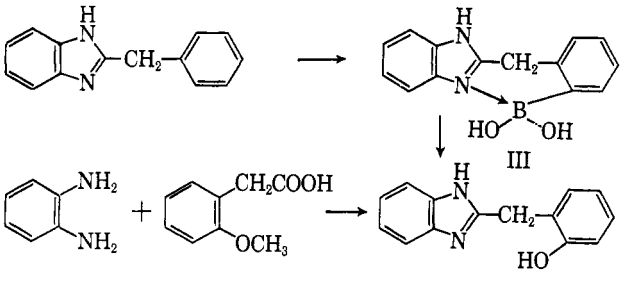
(5) Benzene is converted to phenyldichloroborane by boron chloride at 500° in the presence of a palladium catalyst (E. Pace, *Atti. Accad. Lincei*, **10**, 193 (1929)). A reinvestigation of this process showed the yields to be variable, presumably as a consequence of catalyst poisoning (W. L. Ruigh, *et al.*, WADC Technical Report, 55-26, Parts III–IV (1956), P. B. No. 121,-374 and 121,718, U. S. Department of Commerce, Washington, D. C.). Other catalysts for aromatic boronation reactions include aluminum (E. L. Muetterties, *J. Am. Chem. Soc.*, **81**, 2597 (1959); **82**, 4163 (1960)), aluminum chloride (M. J. S. Dewar, V. P. Kubba and R. Petit, *J. Chem. Soc.*, 3072 (1958) and M. J. S. Dewar and R. Dietz, *ibid.*, 1344 (1960)), and aluminum bromide (Z. J. Brywid, W. Gerrard and M. F. Lappert, *Chem. Ind.* (London), 1091 (1959). With boron bromide, Brywid, Gerrard and Lappert, ref. above, achieved a non-catalyzed substitution in diphenyl ether at 170°. A catalyst was also unnecessary for boronation of the vinyl group in *o*-aminostyrene (M. J. S. Dewar and R. Dietz, *J. Chem. Soc.*, 2728 (1959).

(6) M. J. S. Dewar, V. P. Kubba and R. Petit, *ibid.*, 3073 (1958).



imidazole (83%),[7] which on stepwise treatment with butyllithium and butyl borate yielded (70%), after hydrolysis, a compound identical with that produced by methylation of I. That this substance was 1-methyl-2-(2-boronophenyl)-benzimidazole was confirmed by analytical data and by conversion to the known 1-methyl-2-(2-hydroxyphenyl)-benzimidazole and 1-methyl-2-phenylbenzimidazole by treatment with acidic hydrogen peroxide and ammoniacal silver nitrate solution, respectively. Like 2-(2-boronophenyl)-benzimidazole, compound II yielded a sharp-melting catechol derivative and it formed a relatively insoluble complex when treated with hydrogen peroxide in neutral solution.

In exploring the scope of the direct boronation reaction, we subjected 2-benzylbenzimidazole and 2-(β-phenylethyl)-benzimidazole to the action of boron chloride. Hydrolysis of the product from 2-benzylbenzimidazole gave a boron-containing compound, identified as 2-(2-boronobenzyl)-benzimidazole (III). Only tars were obtained from the reaction with phenylethylbenzimidazole. Compound III resembled compound I in that it decomposed slowly without melting when heated vigorously. The homogeneity of III was demonstrated by conversion to a sharp-melting catechol derivative in essentially quantitative yield. Proof that the borono group was in the *ortho* position of the phenyl ring was obtained by oxidation of III with an acidic solution of hydrogen peroxide. The phenol thus produced was identical with a sample of 2-(2-hydroxyphenyl)-benzimidazole synthesized independently from 2-methoxyphenylacetic acid and *o*-phenylenediamine.



Spectral Data.—Compounds I, II and III have been depicted with boron–nitrogen coördination bonds. Such bonding would be expected on theoretical grounds since a good donor atom (nitrogen) and an acceptor atom (boron) are in position to close a five- or six-membered ring. Moreover, although no analogous cases involving boron and imidazole or benzimidazole bases have been reported, numerous examples of cyclic compounds possessing a coördinate bond between boron and amino nitrogen have been described.[8]

(7) The two step procedure for preparing 1-methyl-2-(2-bromophenyl)-benzimidazole was found to be superior to direct monoalkylation of 2-(2-bromophenyl)-benzimidazole since the latter route afforded mixtures of mono-, di- and non-alkylated benzimidazoles.

(8) For typical cases see H. C. Brown and E. A. Fletcher, *J. Am. Chem. Soc.*, **73**, 2808 (1951); F. Hein and R. Burckhardt, *Z. anorg. Chem.*, **268**, 158 (1962); R. L. Letsinger and I. Skoog, *J. Am. Chem. Soc.*, **77**, 2491 (1955); O. C. Musgrave and T. O. Park, *Chem. Ind.* (London), 1552 (1955); S. Lawesson, *Arkiv Kemi*, **10**, 171 (1956); H. Steinberg and D. L. Hunter, *Ind. Eng. Chem.*, **49**, 174 (1957).

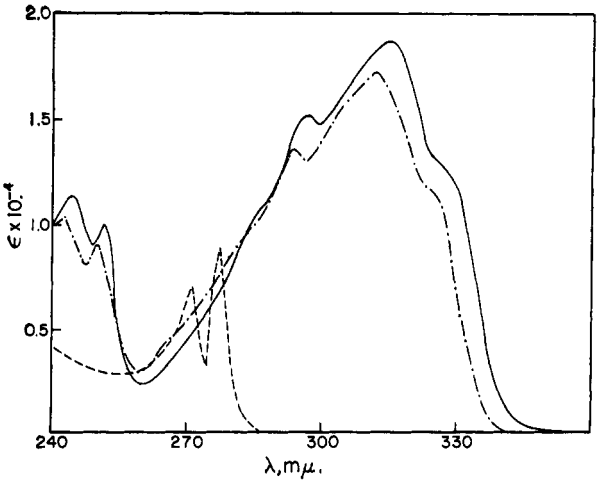


Fig. 1.—Ultraviolet absorption spectra of 2-(2-boronophenyl)-benzimidazole (— · —), 1-methyl-2-(2-boronophenyl)-benzimidazole (———) and 2-(2-boronobenzyl)-benzimidazole (– – – –) in 95% ethanol.

Good evidence that intramolecular boron–nitrogen coördination is indeed an important structural feature in compounds I and II, at least in alcoholic solution, may be derived from ultraviolet spectral data, which provide information relative to the dihedral angle between the 2-aryl group and the benzimidazole ring. Thus, whereas benzimidazole (λ_{max}^{EtOH} 272 mμ, log *E* 3.74; 279 mμ, log *E* 3.80) is transparent above 290 mμ, 2-phenylbenzimidazole absorbs strongly at 303 mμ (log *E* 4.37) and 316 mμ (shoulder, log *E* 4.15).[9,10] The enhanced absorption of 2-phenylbenzimidazole at the longer wave lengths may be attributed to resonance interaction involving the phenyl and benzimidazole rings.[9,11] *o*-Substituents which increase the angle formed by the planes of the phenyl and benzimidazole rings diminish the intensity of absorption and cause a marked hypsochromic shift in the position of the maximum; for example, the spectra of 2-(2-methylphenyl)-benzimidazole[9] and 2-(2-bromophenyl)-benzimidazole (λ_{max}^{EtOH} 277 mμ, log *E* 4.00; 283 mμ, log *E* 4.00) are very similar to that of benzimidazole. Since $-B(OH)_2$ is a relatively large substituent, one would expect the spectra of I and II to resemble the spectra of the *o*-methyl- and bromophenylbenzimidazoles if steric effects alone were operative. In fact, however, I and II absorb strongly in the region near 310 mμ (Fig. 1). This feature is explicable on the basis that, as a consequence of boron–nitrogen coördination, the phenyl and benzimidazole rings in I and II are maintained sufficiently coplanar to permit significant conjugation. It may be noted that the spectrum of III is typical of a simple benzimidazole. In this case, of course, conjugative interaction of the phenyl and benzimidazole rings is prevented by the methylene group.

The arguments for boron–nitrogen dative bonding are buttressed by the observation that λ_{max} for II shifts to 277 and 284 mμ, respectively, in acidic and in alkaline solution (Fig. 2), in accord with the view that either protonation of nitrogen or addition of hydroxide to the boronic acid group would break the boron–nitrogen

(9) G. Leandri, A. Mangini, F. Montanari and R. Passerini, *Gazz. chim. ital.*, **85**, 769 (1955).

(10) A. Mangini and F. Montanari, *Boll. Sci., Bologna*, **14**, 36 (1956).

(11) The case is analogous to biphenyl, which exhibits absorption bands arising from conjugation of the two aromatic rings; see E. A. Braude, *Experientia*, **11**, 457 (1955); E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 177.

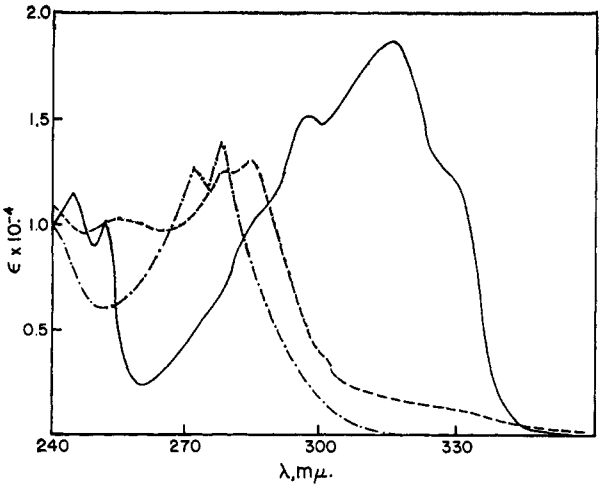


Fig. 2.—Ultraviolet absorption spectra of 1-methyl-2-(2-boronophenyl)-benzimidazole in 95% ethanol: no added acid or base (———), 3 × 10^{-3} *M* in HCl (— · —), 3 × 10^{-3} *M* in NaOH (- - - -).

bond and permit, or as a result of steric interference of non-bonded neighboring groups cause, the phenyl ring to swing far out of the plane of the benzimidazole ring. By contrast, λ_{max} for 2-phenylbenzimidazole is not very sensitive to the pH of the solution; the band at 303 mμ is shifted to 300 mμ in 2 *M* HCl and to 310 mμ in 0.1 *M* NaOH.[9] It is also pertinent that the spectra of I and II are very similar to the spectrum of 2-(2-hydroxyphenyl)-benzimidazole (λ_{max}^{EtOH} 292, 317, 330 mμ; log *E* 4.430, 4.361, 4.328, respectively), a compound which absorbs at much longer wave lengths than 2-(2-hydroxybenzyl)-benzimidazole (λ_{max}^{EtOH} 242, 275, 281 mμ; log *E* 3.80, 4.014, 4.053). An enhanced absorption of 2-(2-hydroxyphenyl)-benzimidazole relative to 2-(3-hydroxyphenyl)-benzimidazole and 2-(4-hydroxyphenyl)-benzimidazole was previously noted Wiegand and Merket,[12] who cited it as evidence for coplanarity of the phenyl and benzimidazole rings induced by hydrogen bonding between O–H and N.

Infrared spectral data also indicate interaction between boron and nitrogen in the boronoarylbenzimidazoles. Three spectral regions— 3.4–4.0 μ, 7.2–7.8 μ and 8.2–8.8 μ—are especially significant.

Benzimidazole and a variety of 2-substituted derivatives[13] show an intense, broad absorption band extending through the 3.4–4.0 μ region with a maximum at about 3.5–3.7 μ. This band, which is associated with intermolecular N–H hydrogen bonding, is absent in the spectra of N-methyl- and N-acetylbenzimidazole and is greatly reduced in intensity (with a shift of the maximum to 3.7–4.0 μ) in the spectra of 2-(2-hydroxyphenyl)-benzimidazole and 2-(2-hydroxybenzyl)-benzimidazole, compounds for which intramolecular bonding between the phenolic and imidazole groups has been postulated. Absorption in the 3.4–4.0 μ region is much weaker for the benzimidazoles possessing boron in the vicinity of the basic nitrogen (compounds I and III and their ester derivatives) than for the usual benzimidazoles. This fact suggests that intermolecular hydrogen bonding is minimal in I and III. The decrease in intermolecular hydrogen bonding may be attributed to the competition of boron for the electron pair on nitrogen.

(12) C. Wiegand and E. Merket, *Ann.*, **557**, 242 (1947); see also A. Mangini and F. Montanari, ref. 10.

(13) These include 2-phenyl-, 2-(2-bromophenyl)-, 2-benzyl-, 2-methyl-2-β-phenylethyl-, 2-α-naphthyl-; 4-bromo-2-methyl- and 5-nitro-2-methylbenzimidazole.

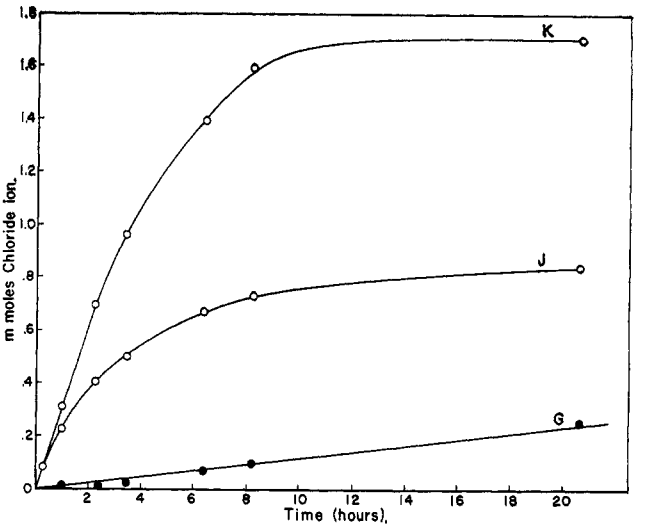


Fig. 3.—Chloride ion formation from chloroethanol in butanol at 89°. The solutions contained: (G) 1.00 mmole of 2-phenylbenzimidazole, (J) 1.00 mmole of 2-(2-boronophenyl)-benzimidazole, and (K) 1.00 mmole of 2-phenylbenzimidazole plus 1.00 mmole of 2-(2-boronophenyl)-benzimidazole.

The absence of strong absorption in the 7.2–7.8 μ region of the infrared spectrum of a boronic acid derivative is evidence that the boron is tetracoördinated.[14,15] Since compound III and the catechol ester derivatives of I, II and III absorb weakly in this region, it may be concluded that boron is tetracoördinated in these compounds. Several bands of moderate intensity are found between 7.2 and 7.8 μ in the spectra of I and II; however, since these might be due to groupings other than B–O (in trivalent boron), their significance cannot at present be ascertained.

An absorption band characteristic for amine coordination compounds of boronic acids is generally found between 8.2 and 8.8 μ.[15,16] In agreement with the concept of boron–nitrogen bonding, I, II and their ester derivatives absorb strongly in the 8.4–8.6 μ region, whereas 2-phenylbenzimidazole and the hydrochloride of I do not. This spectral region is less decisive for III and its catechol derivative; however, a relatively weak band at 8.3 μ exhibited by these compounds may be due to a boron–nitrogen bond.

Catalysis.—A reaction of chloroethanol was used to test for synergetic activity of boron and nitrogen in 2-(2-boronophenyl)-benzimidazole. For this purpose the boronic acid and the supplementary base, if any, were dissolved in 5 ml. of 1-butanol at 89° and at zero time sufficient prewarmed chloroethanol was added to bring the volume to 10 ml. The rate of formation of chloride ion in the solution was determined by removal of 1-ml. aliquots at suitable intervals and titration by the Volhard procedure.[17,18]

Relative to 2-phenylbenzimidazole, 2-(2-boronophenyl)-benzimidazole reacted very rapidly with chloroethanol (Fig. 3). When an equimolar mixture of 2-

(14) L. J. Bellamy, W. Gerrard, M. F. Lappert and R. L. Williams, *J. Chem. Soc.*, 2412 (1958).

(15) R. L. Letsinger and S. B. Hamilton, *J. Am. Chem. Soc.*, **80**, 5411 (1958); R. L. Letsinger and J. D. Morrison, unpublished results.

(16) N. N. Greenwood and K. Wade, *J. Chem. Soc.*, 113 (1960).

(17) For these solutions, which contained large amounts of chloroethanol, small "blank" titration values, corresponding to approximately 0.3 mmole of chloride ion, were observed at zero reaction time. These blanks were subtracted from subsequent measurements prior to plotting the data in Fig. 3 and 4.

(18) A butanol–chloroethanol solvent was selected rather than dimethylformamide, which had been used in previous studies with 8-quinolineboronic acid (footnote 3), since compounds I and III were only very slightly soluble in dimethylformamide.

phenylbenzimidazole and 2-(2-boronophenyl)-benzimidazole was used in the reaction, the rate was characteristic of the boronophenylbenzimidazole until most of the total base had been converted to hydrochloride. Phenylbenzimidazole probably functions here as a transfer base, removing protons from the boronophenylbenzimidazolium ions produced in the reaction, thereby regenerating the active agent.

Data for a series of reactions involving 2,4,6-trimethylpyridine (collidine) (5 mmoles) and excess chloroethanol in butanol are represented in Fig. 4. A small amount (1 mmole) of 2-(2-boronophenyl)-benzimidazole, 2-(2-boronobenzyl)-benzimidazole or 8-quinolineboronic acid exerted a striking effect upon the reaction; the rate of liberation of chloride ion was markedly increased by these substances and the accelerated reactions proceeded at constant rates until essentially all of the collidine had been converted to hydrochloride. Therefore, it is clear that the boron–nitrogen compounds functioned catalytically in these reactions. Catalyst turnover was efficient and was not inhibited by the reaction products.

Rate constants for these and related reactions are assembled in Table I and the relative rates of reaction with collidine, benzimidazole and the boron–nitrogen compounds are indicated in Table II. From reactions B, C and I (Table I) it is apparent that the boron and nitrogen functional groups in 2-(2-boronophenyl)-benzimidazole and 2-(2-boronobenzyl)-benzimidazole exhibit a synergetic effect, *i.e.*, an enhanced activity relative to the same functional groups disposed in separate molecules. Reactions C, D and E show that within the range investigated (0.05–0.10 *M* boronophenylbenzimidazole) the rate is proportional to the catalyst concentration. Finally, it may be noted that the catalytic reactions involving the bases collidine and 2-phenylbenzimidazole proceeded at about the same rate (reactions C and K), although the ratio of the rates for the corresponding non-catalyzed reactions was 0.37 (Table II). This result is consistent with the view that the rate-determining step in the catalyzed reactions does not involve the transfer base.

TABLE I

REACTION OF CHLOROETHANOL WITH B–N COMPOUNDS AND NITROGEN BASES IN BUTANOL AT 89°

Reaction	Boron compd.	mmoles[c]	Added base	mmoles	k_{obs},[a] moles/l./hr.	$k_{obs} - k_{tb}$[b] $[B_{cpd}]$
A	QBA[d]	1.03	$C_5H_{11}N$[e]	5.0	0.0407	0.374
B	III	0.82	$C_5H_{11}N$	5.0	.0358	.410
C	I	1.00	$C_5H_{11}N$	5.0	.0305	.283
D	I	0.75	$C_5H_{11}N$	5.0	.0234	.283
E	I	0.50	$C_5H_{11}N$	5.0	.0164	.284
F	...	..	$C_5H_{11}N$	5.0	.0022	...
G	...	..	$C_{13}H_{10}N_2$[f]	1.0	.0012	...
H	...	..	$C_5H_{11}N$	5.0	.0030	...
			$C_{13}H_{10}N_2$	1.0		
I	$C_6H_5B(OH)_2$	1.00	$C_5H_{11}N$	5.0	.0036	...
			$C_{13}H_{10}N_2$	1.0		
J	I	1.00	.....	...	.03	0.3
K	I	1.00	$C_{13}H_{10}N_2$	1.0	.0304	0.29
L	...	..	.....	...	0	

[a] Initial rate of Cl^- formation. [b] k_{tb} = the rate due to direct reaction of the transfer base with chloroethanol. [c] The volume of the solution was 10 ml.; therefore 1.00 mmole of solute corresponds to a 0.100 *M* solution. [d] 8-Quinolineboronic acid. [e] Collidine. [f] 2-Phenylbenzimidazole.

Products were examined for the reaction catalyzed by 2-(2-boronophenyl)-benzimidazole. In addition to the catalyst, which could be recovered in high yield, there was obtained collidine hydrochloride, 2-butoxyethanol (61% indicated by v.p.c., 21% isolated by extraction and distillation), dioxane (2% by v.p.c.), and a liquid residue which probably consisted of low molecular weight hydroxypolyethers. Titrations of aliquots of the reaction mixtures with periodic acid[19] revealed that ethylene glycol was only a very minor product. Even when water (10 moles per mole of boronic acid) was added to the reaction mixture the yield of glycol was very low (Table III). It is interesting that 8-quinolineboronic acid was much more selective than the boronophenylbenzimidazole with respect to water as a substrate; in a reaction catalyzed by 8-quinolineboronic acid in which the mole ratio of water to alcohol was less than 0.1 the yield of ethylene glycol, based on hydrogen chloride produced in the reaction, was 69% (Table III).

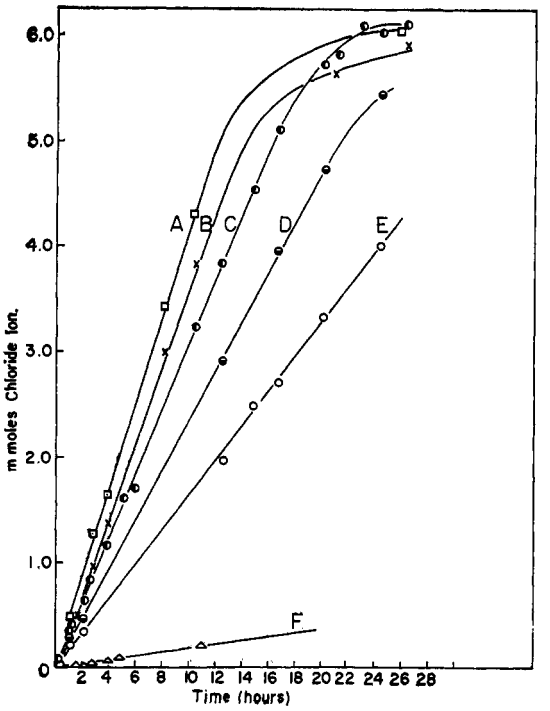


Fig. 4.—Chloride ion formation at 89° from chloroethanol in butanol. The solutions contained 5.00 mmoles of collidine and: (A) 1.03 mmoles of 8-qinolineboronic acid; (B) 0.82 mmole of 2-(2-boronobenzyl)-benzimidazole; (C), (D) and (E) 1.00, 0.75 and 0.50 mmole, respectively, of 2-(2-boronophenyl)-benzimidazole; (F) no added boron compound.

TABLE II

RELATIVE RATES OF REACTION OF AMINES WITH CHLOROETHANOL AT 89°

Base	Relative rate
Collidine	0.37
2-Phenylbenzimidazole	1
2-Phenylbenzimidazole + benzeneboronic acid	1.2
2-(2-Boronophenyl)-benzimidazole	23.6
2-(2-Boronobenzyl)-benzimidazole	34.2
8-Quinolineboronic acid	31.2

A plausible pathway for the reaction of chloroethanol with 2-(2-boronophenyl)-benzimidazole involves (see formula IV): (a) reversible esterification of the boronic acid group by 1-butanol and chloroethanol; (b) displacement of chlorine by esterified butoxy, which has enhanced nucleophilic character as a result of coördination of nitrogen with boron; (c) re-esterification of boron and ester interchange to liberate butoxyethanol; and (d) transfer of a proton from the boronoamine to collidine.

(19) The procedure was the same as employed previously; ref. 1. In a control test with known amounts of glycol it was shown that 2-(2-boronophenyl)-benzimidazole, collidine, butanol and choroethanol did not interfer with the determination.

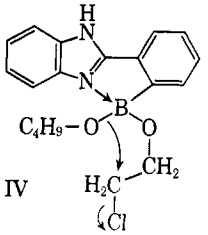
TABLE III

ETHYLENE GLYCOL FROM CHLOROETHANOL REACTIONS[a]

Reactants			Products		
Catalyst	H_2O added, mmoles	Collidine, mmoles	Chloride ion, mmoles	Glycol, mmoles	Glycol [Cl^-] × 100
I	0	5	6.04[b]	0.07[c]	1
I	10	5	5.97[b]	.55[c]	9
III	0	5	5.90[d]	.10[e]	2
QBA	0	10	10.7[b]	1.2[f]	11
QBA	10	10	8.4[f]	5.8[f]	69

[a] Reaction conditions: 1 mmole of catalyst and collidine and water (amounts as indicated) were dissolved in 1-butanol, 5 ml. of chloroethanol was added and the volume of the solution was brought to 10 ml. by addition of 1-butanol at 89°. [b] Determined after 30-hr. reaction. [c] After 26.4 hr. [d] After 27 hr. [e] After 21 hr. [f] After 28 hr.

The rate-determining step probably involves cleavage of the carbon–chlorine bond.



IV

Experimental

The ultraviolet spectra were obtained with a Cary recording spectrophotometer, model II; the infrared spectra were obtained with a Baird instrument, model AB2, with the sample in a potassium bromide disk. Carbon, hydrogen and nitrogen analyses were performed by Miss H. Beck.[20]

2-(2-Boronophenyl)-benzimidazole (I).—A stream of boron chloride gas was passed directly into 2-phenylbenzimidazole (6.2 g.) in a small test tube maintained at 300–325° by a metal bath. As the gas was absorbed the liquid darkened and after 6 min. it rapidly solidified to a hard, gray-brown glass. After a total of 12 min. the mixture was cooled and the solid removed. The product (15.7 g.) from two such runs was ground up and repeatedly extracted with dilute hydrochloric acid. The acid-insoluble residue amounted to 2.6 g. On neutralization of the acid extract a precipitate formed; it was collected by filtration and treated with 25% aqueous sodium hydroxide. 2-Phenylbenzimidazole (1.66 g., m.p. 295–296° after recrystallization from ethanol–water) was recovered as an alkaline-insoluble fraction. When the alkaline solution was brought to pH 7 by addition of acid, 6.4 g. (47%, calculated on the basis of phenylbenzimidazole consumed) of 2-(2-boronophenyl)-benzimidazole precipitated. For purification, the material was redissolved in aqueous sodium hydroxide and reprecipitated by neutralization of the solution with dilute hydrochloric acid. It was then dried by heating at 112° at 1 mm. for 24 hr. The compound did not melt below 330° and it burned with a green flame.

Anal. Calcd. for $C_{13}H_{11}O_2N_2B$: C, 65.6; H, 4.62; N, 11.70; neut. equiv., 238. Found: C, 56.1[20]; H, 4.46; N, 11.53; neut. equiv. (alkaline titration in presence of mannitol), 241.

Derivatives of 2-(2-Boronophenyl)-benzimidazole. (a) Hydrohalides.—The hydrochloride salt of I was obtained by adding 5 ml. of concd. hydrochloric acid to 10 ml. of a warm, dilute hydrochloric acid solution of 2-(2-boronophenyl)-benzimidazole (0.5 g.). Within 10 min. a crystalline precipitate appeared; wt. 0.45 g., m.p. 248–258°. The analysis corresponded to a hydrate of the hydrochloride.

Anal. Calcd. for $C_{13}H_{14}O_3N_2BCl$: C, 53.36; H, 4.82; N, 9.53; Cl, 12.12. Found: C, 53.45; H, 5.12; N, 9.89; Cl, 12.32.

By the same procedure with hydrobromic acid in place of hydrochloric acid there was obtained from 0.45 g. of I, 0.36 g. of the hydrobromide salt as granular crystals, m.p. 320–325°.

Anal. Calcd. for $C_{13}H_{12}O_2N_2BBr$: C, 48.72; H, 3.79; N, 8.78. Found: C, 48.99; H, 4.00; N, 8.85.

(b) **Catechol Derivative.**—To a solution of 0.1408 g. of I in 10 ml. of ethanol was added 0.5 g. of catechol. On standing, needle-like crystals of the catechol derivative appeared. After drying at 95° for 5 hr., the sample weighed 0.1835 g. (99%) and melted at 259–261° (in order to obtain a sharp m.p. and to avoid slow decomposition the sample was placed on the hot-plate at a temperature within a few degrees of the melting point; the temperature was then raised at the rate of 1 deg. per 20 sec.).

Anal. Calcd. for $C_{21}H_{19}O_3N_2B$: C, 73.0; H, 4.16; N, 8.96. Found: C, 70.1[20]; H, 4.70; N, 8.23.

(c) **2-(2-Hydroxyphenyl)-benzimidazole.**—A solution containing 0.32 g. of I and 1.6 ml. of 30% hydrogen peroxide in 15 ml. of 15% aqueous sulfuric acid was warmed for 2 hr. on a steam-bath, cooled, and neutralized. The precipitate of 2-(2-hydroxyphenyl)-benzimidazole which separated (wt. 0.18 g., 64%, m.p. 224–233°) melted after several recrystallizations at 237.5–239°, lit.[10] m.p. 237–238°. The ultraviolet spectrum checked that reported by Mangini and Montanari[10] for 2-(2-hydroxyphenyl)-benzimidazole.

On addition of 1 ml. of 30% hydrogen peroxide to 0.5 g. of I in 20 ml. of ethanol a white, powdery precipitate (0.32 g.) formed. Under the same conditions with water in place of hydrogen peroxide no precipitate developed. This substance decomposed with a flash when heated over a flame.

(d) **2-Phenylbenzimidazole.**—A white precipitate of 2-phenylbenzimidazole appeared when a solution containing 0.50 g. of I in 10 ml. of 10% aqueous sodium hydroxide was refluxed for 2 hours. After filtration and drying it melted at 292–295° and weighed 0.32 g. (78%). On neutralization of the filtrate 0.07 g. (14%) of compound I was recovered.

The carbon–boron bond in compound I was relatively resistant to cleavage by hydrochloric acid. Only a trace of 2-phenylbenzimidazole was obtained when 15 ml. of a 6 *M* hydrochloric acid solution of I (0.50 g.) was refluxed for 1.3 hr. and subsequently made basic.

(e) **1-Methyl Derivative.**—Excess methyl sulfate was added portionwise over a period of 1.5 hours to 1.0 g. of I dissolved in 10 ml. of boiling 10% sodium hydroxide. After cooling, the alkaline solution was extracted with chloroform and neutralized, and the precipitate which formed was filtered off and extracted with benzene. A benzene solution of catechol (0.04 g.) was added to the benzene extract; within 5 min. a white precipitate of the catechol derivative of 1-methyl-2-(2-boronophenyl)-benzimidazole appeared; weight 0.06 g. after recrystallization from a chloroform–benzene mixture; m.p. 336–340° (taken in a sealed capillary tube which was inserted into the heating block at an initial temperature of 310°). The infrared spectrum was identical with that for the catechol derivative prepared from a sample of III synthesized independently from 1-methyl-2-(2-bromophenyl)-benzimidazole.

1-Methyl-2-(2-bromophenyl)-benzimidazole.—2-(2-Bromophenyl)-benzimidazole was prepared by condensation of 2-bromobenzoic acid with *o*-phenylenediamine in polyphosphoric acid.[2] Attempts to methylate it directly afforded only low yields of the desired product; therefore, the following two-step synthesis was developed. A mixture of 17.1 g. of 2-(2-bromophenyl)-benzimidazole, 23.1 ml. of methyl iodide and 23 ml. of methanol was heated in a sealed tube in an Ipatieff rotating autoclave at 200–220° for 8 hours. On dissolving the product in ethanol, reprecipitating it by addition of ether, and recrystallizing it from ethanol, 18 g. (67%) of 1,3-dimethyl-2-(2-bromophenyl)-benzimidazolium iodide, m.p. 247.5–251°, was obtained.

Anal. Calcd. for $C_{15}H_{14}N_2BrI$: N, 6.59; I, 29.5. Found: N, 6.53; I, 28.7.

Pyrolysis of 15.2 g. of this salt in 0.5-g. lots at about 260° at 1 mm. afforded 1-methyl-2-(2-bromophenyl)-benzimidazole as a sublimate. After recrystallization from chloroform–hexane the sample melted at 115–117° (8.3 g., 83% yield).

Anal. Calcd. for $C_{14}H_{11}N_2Br$: C, 58.55; H, 3.86; N, 9.76. Found: C, 58.06; H, 3.66; N, 10.02.

1-Methyl-2-(2-boronophenyl)-benzimidazole (II).—A solution of 4.5 g. (16 mmoles) of 1-methyl-2-(2-bromophenyl)-benzimidazole in 200 ml. of ether was added over an hour period to a stirred solution of 31 mmoles of butyllithium in 100 ml. of ether at −70° under a nitrogen atmosphere. After an additional 2 hr. of stirring, 15.5 ml. of *n*-butyl borate in 180 ml. of ether was added slowly (45 min.) and the mixture was stirred at −70° for 2 hr. It was then allowed to warm to room temperature, 200 ml. of 5% aqueous sodium hydroxide was added, and the layers were separated. The aqueous layer was acidified to pH 1–2, extracted with ether, brought to pH 7 by addition of sodium hydroxide,

(20) The carbon analyses for the benzimidazole–boron derivatives were in general low and erratic as a result of incomplete carbon combustion, even when potassium persulfate was mixed with the sample. The furnace temperature was in the range of 900°. Hydrogen and nitrogen analyses were reproducible within the usual experimental accuracy. The carbon analyses are reported, however, in accordance with custom, even though they are not quantitatively significant.

(21) The method was that employed by O. W. Hein, R. J. Alheim and J. J. Leavitt, *J. Am. Chem. Soc.*, **79**, 427 (1957), for the preparation of closely related arylbenzimidazoles.

saturated with salt, and extracted with chloroform. Evaporation of the chloroform and addition of hexane yielded the boronic acid as a white solid, 3.0 g. (74%), m.p. 222–230° (after preliminary softening at 155–178° and resolidification as the temperature was increased).

Anal. Calcd. for $C_{14}H_{11}N_2OB$: C, 71.7, H, 4.70; N, 11.97. neut. equiv., 270. Found: C, 63.22[20]; H, 4.54; N, 11.63; neut. equiv. (sodium hydroxide titration in presence of mannitol), 267.

Derivatives of 1-Methyl-2-(2-boronophenyl)-benzimidazole. (a) **Catechol Derivative.**—Concentration of a toluene solution containing 0.50 g. of II and 0.22 g. of catechol afforded a crystalline precipitate of a catechol ester, which after recrystallization from chloroform amounted to 0.33 g. (50%) and melted (sealed capillary tube) at 332–333° with some decomposition.

Anal. Calcd. for $C_{20}H_{15}O_2N_2B$: C, 73.6; H, 4.64; N, 8.59; B, 3.32. Found: C, 69.93[20]; H, 4.56; N, 8.56; B, 3.75.[22]

(b) **1-Methyl-2-(2-hydroxyphenyl)-benzimidazole.**—The boronic acid (0.40 g.) was dissolved in 15% aqueous sulfuric acid and oxidized by addition of 1 ml. of 20% hydrogen peroxide at 25–30°. The solution was then neutralized and the resulting precipitate extracted with chloroform. On concentration of the chloroform solution and addition of hexane, 0.15 g. (44%) of 1-methyl-2-(2-hydroxyphenyl)-benzimidazole was obtained, m.p. 163–165.5°; λ_{max}^{EtOH} 243 (log E 4.104), 292 (4.120), 320 (4.26). The literature values for this compound are m.p. 166–167°; λ_{max}^{EtOH} 243 (log E 4.10), 292 (log E 4.12) and 320 (log E 4.26).

Anal. Calcd. for $C_{14}H_{12}N_2O$: N, 12.50. Found: N, 12.64.

When 1 ml. of 30% hydrogen peroxide was added to a solution of 0.5 g. of II in 6 ml. of ethanol, a white powdery precipitate formed immediately; wt. 0.51 g., m.p. 186–206°. This substance had properties of a complex of I and hydrogen peroxide since it decomposed with a flash when heated over a flame (II did not) and it oxidized iodide in acidic solution to iodine. A quantitative titration with iodide ion indicated 1.26 moles of hydrogen peroxide per mole of II.

Anal. Calcd. for $C_{14}H_{13}N_2O_3B$: N, 10.45. Found: N, 10.37.

(c) **1-Methyl-2-phenylbenzimidazole.**—Aqueous ammonium hydroxide (10 ml.) and 10 ml. of aqueous 5% silver nitrate were added to 0.7 g. of II in 50 ml. of 50% ethanol–water. The mixture was warmed on a steam-bath briefly and then extracted with chloroform. From the chloroform solution was obtained 0.4 g. (69%) of 1-methyl-2-phenylbenzimidazole, m.p. 95–96°; lit.[23] m.p. 98°.

2-(2-Boronobenzyl)-benzimidazole (III).—As in the preparation of I, boron chloride was passed into a melt of 6.6 g. of 2-benzylbenzimidazole at 230–260° for 12 min. The resulting solid was mixed with the product from a similar run (obtained from 7.0 g. of 2-benzylbenzimidazole), ground to a powder, and extracted with several portions of 5% aqueous sodium hydroxide. Unreacted 2-benzylbenzimidazole (1.8 g.) was recovered by extracting the alkali-insoluble precipitate with ethanol. On neutralization of the alkaline extract with acid, 2-(2-boronobenzyl)-benzimidazole was obtained; weight 7.6 g.; yield, based on benzylbenzimidazole which reacted, 53%. For purification, this substance was recrystallized from ethanol. Well formed, rectangular crystals were obtained. They began to char and sinter in the range of 260° but did not melt below 320°. The analysis and infrared spectrum of this substance, designated as IIIe, were consistent with formulation as the diethyl ester of the boronic acid.

Anal. Calcd. for $C_{18}H_{21}O_2N_2B$: C, 70.5; H, 6.90; N, 9.14. Found: C, 62.1[20]; H, 6.52; N, 9.37.

To obtain the boronic acid, the ester was dissolved in hot alcohol and the solution was diluted with aqueous ammonium hydroxide. On neutralization with hydrochloric acid, a powdery, white precipitate of 2-(2-boronobenzyl)-benzimidazole appeared. It was separated and dried at 112° at 6 mm. for 12 hr. The infrared spectrum differed in several respects from that of the ethyl ester, showing strong absorption at 2.9 μ and weak absorption in the 3.4–3.5 μ region characteristic of aliphatic C–H. The melting behavior was similar to that of the ethyl ester.

Anal. Calcd. for $C_{14}H_{13}O_2N_2B$: C, 66.7; H, 5.16; N, 11.10. Found: C, 64.2[20]; H, 5.24; N, 10.72.

Derivatives of 2-(2-Boronobenzyl)-benzimidazole. (a) **Catechol Derivative.**—Catechol (0.5 g.) was added to a solution of 0.1630 g. of III (as the ethyl ester) in 20 ml. of ethanol. After 5–10 min., needle-like crystals of the derivative began to separate. The solution was cooled to 0° and filtered, yielding 0.1882 g. of the catechol ester derivative, m.p. 285–286°. In the range of 150–200° the crystals changed in appearance from translucent to an opaque white. The analytical data were also consistent with a transition in this region. The analysis for a sample dried at 110° agreed with the formula for an ethanol adduct of the catechol ester.

Anal. Calcd. for $C_{20}H_{15}O_2N_2B \cdot C_2H_6O$: C, 71.0; H, 5.83; N, 7.54. Found: C, 70.0[20]; H, 5.35; N, 7.61.

After 0.1882 g. of the derivative was heated at 205° at 5 mm. for 1.2 hr., it weighed 0.1725 g. (quantitative over-all yield based on the ethyl ester of III) and melted at 285–285.5°. The analysis corresponded to the simple catechol ester.

Anal. Calcd. for $C_{20}H_{15}O_2N_2B$: C, 73.6; H, 4.63; N, 8.58. Found: C, 71.6; H, 4.69; N, 8.46.

(b) **2-(2-Hydroxybenzyl)-benzimidazole.**—A solution containing 3 ml. of 30% hydrogen peroxide and 0.5 g. of IIIe in 60 ml. of 7% aqueous sulfuric acid was warmed at 70° for 30° min.; then it was neutralized and filtered to collect the precipitate that formed on neutralization. The precipitate was extracted with aqueous sodium hydroxide and the extract was filtered and acidified to liberate the phenol, which weighed 0.16 g. (44%) and melted at 222.5–225.5°. Subsequent recrystallizations from alcohol–benzene afforded purified 2-(2-hydroxybenzyl)-benzimidazole, m.p. 229.5–231° (for identification see independent preparation of this substance).

Anal. Calcd. for $C_{14}H_{12}N_2O$: C, 74.2; H, 5.14; N, 12.49. Found: C, 75.0; H, 5.36; N, 12.50.

(c) **2-Benzylbenzimidazole.**—A solution of 0.5 g. of IIIe in 20 ml. of 6 M hydrochloric acid was refluxed for 1.3 hr. On basification, 2-benzylbenzimidazole separated from the solution. After recrystallization from benzene it weighed 0.24 g. (71%), m.p. 186.5–187.5°. The melting point was undepressed when the sample was mixed with authentic 2-benzylbenzimidazole.

Attempts to prepare hydrohalide salts by the method employed with I were unsuccessful since the carbon–boron bond in III was sensitive to cleavage by strong mineral acid.

2-(2-Hydroxybenzyl)-benzimidazole.—2-(2-Methoxybenzyl)-benzimidazole (0.5 g., m.p. 191–192.5°, prepared from 2-methoxyphenylacetic acid and *o*-phenylenediamine by the method of Mittal and Seshadri[24]) was heated 5.5 hr. with excess refluxing 48% hydrobromic acid. The solid which separated on neutralization was recrystallized twice from aqueous ethanol to give 0.34 g. (72%) of 2-(2-hydroxybenzyl)-benzimidazole, m.p. 228.5–230°. This substance did not depress the melting point of the product obtained by oxidation of IIIe with hydrogen peroxide, and the infrared spectra of the two samples were identical.

Reagents.—The solvents and liquid reagents for the kinetic studies were fractionally distilled prior to use, the boiling ranges being 116–116.2° for 1-butanol, 126.4–127.8° for chloroethanol and 168.4–169.1° for collidine.

Vapor Phase Chromatography.—The samples were chromatographed on a Podbielniak Chromacon, series 9400 vapor phase chromatographic analytic apparatus, using a 6 ft. column packed with 15% Carbowax 1500 on 30–60 mesh Chromosorb P at temperatures ranging from 80–106°. The products were identified and quantitatively determined by comparison of retention times and peak areas with data from chromatography of a series of known mixtures containing varying amounts of butoxyethanol, chloroethoxyethanol, dioxane, butanol and chloroethanol.

Products from Reaction of Chloroethanol with I. (**A**).—A solution containing 0.43 g. (1.8 mmoles) of 2-(2-boronophenyl)-benzimidazole, 0.72 g. (5.9 mmoles) of collidine, 4.4 g. of 2-chloroethanol and 4.0 g. of 1-butanol was heated at 89.0° for 19 hr., at which time a Volhard titration indicated that 6.62 mmoles (86%) of chlorine added as chloroethanol had been converted to chloride ion. No gaseous products were evolved. Most of the liquid was then distilled off at reduced pressure through a Vigreux column (the distillate is designated as fraction 1). Then chloroethanol (1.5 g.) was added to the pot residue and the distillation continued to remove all butanol (fraction 2). Finally 2-phenylethanol was added as a chaser for butoxyethanol and the distillation continued until phenylethanol began to distil (90° at 4.5 mm.) (fraction 3). It was found in a control test that not more than a trace of butoxyethanol was formed under the conditions of the distillation. Analysis by v.p.c. show that the products of the reaction were dioxane (0.15 mmole, 2% yield, found in fraction 1) and 2-butoxyethanol (0.05 mmole found in fraction 2 and 4.0 mmoles found in fraction 3; 61% yield total).

(**B**).—2-(2-Chloroethoxy)-ethanol was not found among the products of reaction A; however, it was obtained from the reaction of I and chloroethanol carried out under non-catalytic conditions. In this case, 1.03 g. (4.3 mmoles) of I was heated in 10 ml. of chloroethanol at 89° for 12 hr. The formation of 3.9 mmoles of HCl was indicated by Volhard titration. Distillation

(22) Boron analysis by the Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

(23) R. Weidenhagen and G. Train. *Ber.*, **75**, 1936 (1942).

(24) O. P. Mittal and T. R. Seshadri, *J. Chem. Soc.*, 3053 (1955).

of the products at reduced pressure afforded a volatile fraction which contained 0.40 mmole (10% yield) of dioxane. On addition of ether and 2 ml. of concentrated hydrochloric acid to the residue, a white precipitate of 2-(2-boronophenyl)-benzimidazole hydrochloride, 1.10 g. (87%, calcd. as a monohydrate), m.p. 250–260°, was obtained. Analysis of the ether solution, after concentration, by v.p.c. indicated 1.75 mmoles (45% yield based on chloride ion) of 2-(2-chloroethoxy)-ethanol.

(C).—A mixture containing 1.35 g. of I, 12.6 g. of collidine, 10 ml. of 2-chloroethanol and 20 ml. of 1-butanol was heated at 89° for 181 hr. During this time collidine hydrochloride separated as a crystalline precipitate. The mixture was added to ether and filtered, yielding 14 g. (84%) of collidine hydrochloride, which was identified by its infrared spectrum. The filtrate was concentrated and extracted with dilute hydrochloric acid, and the acid extracts were washed several times with ether. Distillation of the organic and combined ether layers afforded 2.80 g. (21%) of 2-butoxyethanol, b.p. 53–54° (2.7 mm.), $n^{24}D$ 1.4180 (lit. $n^{26}D$ 1.4177), identified by its infrared spectrum, and 1.12 of higher boiling residue.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STATE UNIVERSITY OF NEW YORK AT BUFFALO, BUFFALO 14, N. Y.]

Lithium Tetrakis-(N-dihydropyridyl)-aluminate: Structure and Reducing Properties[1]

BY PETER T. LANSBURY AND JAMES O. PETERSON

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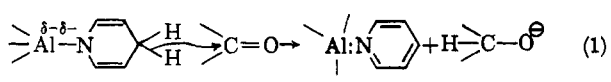
The reaction of lithium aluminum hydride with excess pyridine, in the absence of more readily attacked substrates, including aldehydes, ketones, carboxylic acids and their derivatives, results in the formation of lithium tetrakis-(N-dihydropyridyl)-aluminate (I). Solutions of I, as well as the crystalline salt, have been examined by n.m.r. and infrared spectroscopy and found to lack Al–H bonds and to contain both 1,2- and 1,4-dihydropyridine groups bound to aluminum. Compound I reacts with highly electrophilic carbonyl groups by hydrogen transfer from the dihydropyridine moieties. Diaryl ketones react quite rapidly, other ketones sluggishly, and carboxylic acids and esters are essentially unaffected. Several novel selective reductions of bifunctional compounds by I are described.

Introduction

Several years ago we undertook a study of lithium aluminum hydride (LAH) reactions in pyridine solution.[2] It was anticipated that carbonyl compounds would undergo reduction faster than pyridine solvent,[3] if the former were initially present when the hydride was added. As expected, aldehydes, ketones and carboxylic acids and esters are cleanly and rapidly reduced when LAH is added to their pyridine solutions. It was of interest to study the reactions of lithium aluminum salts of dihydropyridines and related compounds, which result from attack of LAH on the heteroaromatic ring, with reducible substrates, since free dihydro-N-heteroaromatic compounds are known to undergo hydrogen transfer to certain organic compounds.[4] Accordingly, solutions of LAH in pyridine were allowed to interact until no free LAH remained (see below) and carbonyl compounds were then added to the resulting solution which supposedly contained species such as $LiAl(NR_2)_4$ (where NR_2 is 1,2- and/or 1,4-dihydropyridyl), by analogy with the reaction of secondary amines with LAH.[5] It was anticipated that the anionic[6] dihydropyridine groups in such salts would be more potent hydride donors than the more covalent 1,4-dihydropyridines studied by Westheimer[4a,b] and Braude.[4c] We have observed that the anionic complex prepared as described above does



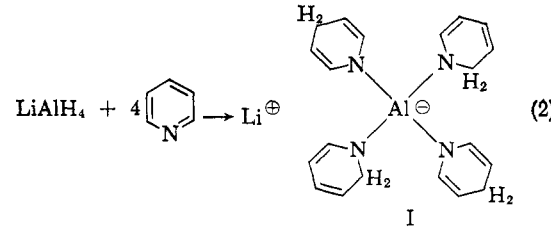
(1)

indeed readily reduce certain aldehydes and ketones, but not carboxylic acids and esters,[1] in contrast to the parent LAH. Furthermore, novel selectivity is exhibited toward various types of ketones in that diaryl ketones are reduced with greater ease than other types,[1] which is in the opposite order of reactivities observed in other carbonyl addition reactions.

It is the purpose of this report to present information concerning the preparation and structural features of this novel reducing agent and to describe procedures for its use. In addition, the results of several reductions of bifunctional compounds, where the selectivity of the reagent is used to advantage, are described, and a rationalization of its capabilities is attempted.

Discussion

Lithium tetrakis-(N-dihydropyridyl)-aluminate (I), the responsible reducing agent generated from LAH and pyridine, is generated on a small scale by aging the orange-colored solution (*ca.* 0.25 *M*) for at least 24 hr. in a rubber-capped serum flask (initially at 0°, then at room temperature), from which aliquots can be removed by a hypodermic syringe. Crystalline I is obtained from more concentrated solutions (0.5 *M*) by filtration in a dry box and subsequent vacuum drying. Reproducible C, H, and N analyses could not be obtained, possibly because aluminum and lithium carbides and/or nitrides are formed during combustion, thus resulting in the observed low C and N analyses. Furthermore, reliable analytical results were hampered by the inability to remove all pyridine from I without decomposition. However, compelling evidence for the major structural features in I has been obtained from chemical and physical evidence, as discussed below.



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I

Initial indications that hydrogen transfer to substrate originated from dihydropyridine groups in I came from studies using lithium aluminum deuteride and pyridine.[1] When relatively fresh solutions of these reactants were added to benzophenone and the resultant

(1) For preliminary accounts of portions of this work, see P. T. Lansbury and J. O. Peterson, *J. Am. Chem. Soc.*, **83**, 3537 (1961); **84**, 1756 (1962).

(2) P. T. Lansbury, *ibid.*, **83**, 429 (1961); P. T. Lansbury, J. R. Rogozinski and F. L. Coblentz, *J. Org. Chem.*, **26**, 2277 (1961); P. T. Lansbury and R. Thedford, *ibid.*, **27**, 2383 (1962).

(3) F. Bohlmann, *Chem. Ber.*, **85**, 390 (1952).

(4) (a) R. H. Abeles, R. F. Hutton and F. H. Westheimer, *J. Am. Chem. Soc.*, **79**, 712 (1957); (b) R. H. Abeles and F. H. Westheimer, *ibid.*, **80**, 5459 (1958); (c) E. A. Braude, J. Hannah and R. Linstead, *J. Chem. Soc.*, 3249, 3257, 3268 (1960).

(5) J. K. Ruff, *J. Am. Chem. Soc.*, **83**, 2835 (1961). Reaction of excess dimethylamine with LAH in ether gave $LiAl(N(CH_3)_2)_4$.

(6) On the basis of electronegativities, the Al–N bond has *ca.* six times as much ionic character as the C–N bond.