(1.4 g.) was heated at 180° for 2 hr. The dark brown solid was crystallized twice from methanol, giving colorless prisms melting at 180–182°, yield 0.8 g. (32%). The water-soluble product analyzed for $C_{12}H_{14}N_4O_2$, corresponding to a 1:1 salt of the two starting materials.

Anal. Calcd. for $C_{12}H_{14}N_4O_2$: C, 58.52; H, 5.73; O, 12.99. Found: C, 58.76; H, 5.90; O, 12.55.

2-Styrylimidazo[4,5-*b*]pyridine.—2,3-Diaminopyridine (5.0 g.) was refluxed in acetic anhydride (40 g.) for 2 hr.; the solution was then evaporated to dryness. The residue was dissolved in water (20 ml.), potassium carbonate (4 g.) was added, and the mixture was extracted with chloroform. The extract was dried and evaporated and the residue was crystallized from ethanol to give 2,3-diacetamidopyridine, m.p. 169–171°, yield 3.8 g. (43%).

Anal. Calcd. for $C_9H_{11}N_3O_2$: C, 55.95; H, 5.74; N, 21.75. Found: C, 56.02; H, 5.45; N, 21.76.

A mixture of 2,3-diacetamidopyridine (1.33 g., 0.01 mole) and benzaldehyde (1.06 g., 0.01 mole) was heated at 190° for 2 hr. The residue was crystallized from ether, giving 0.9 g. (41%), m.p. 190–195°. Recrystallization from ethanol raised the melting point to 205–207°.

Organoboron Compounds. XVIII. Bifunctional Binding of Water by the *cis*-1,2-Cyclopentanediol Ester of 8-Quinolineboronic Acid

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It has been shown that 8-quinolineboronic acid is a polyfunctional catalyst for the hydrolysis of 2-chloroethanol and 3-chloropropanol in N,N-dimethylformamide solutions containing water and collidine,[2] and that the reaction of 8-quinolineboronic acid with the isomeric 2-chloroindanols and 2-chloro-1,2-diphenylethanols is highly stereoselective.[3] These properties of 8-quinolineboronic acid and similar compounds[4,5] were attributed to the cooperative action of intramolecular boron and nitrogen atoms.[2-5] The present paper reports spectroscopic evidence for a related manifestation of synergetic activity by boron and nitrogen, the binding of water and phenol by the *cis*-1,2-cyclopentanediol ester of 8-quinolineboronic acid.

The infrared spectrum of a saturated solution of water in carbon tetrachloride is shown in Fig. 1 (spectrum B). The absorption bands at about 3700 and 3610 cm.$^{-1}$ have been assigned to the two fundamental O–H stretching modes of the monomeric water molecules in such solutions.[6] Infrared spectra of dilute solutions (10^{-4} to $10^{-3}M$) of the *cis*-1,2-cyclopentanediol ester of 8-quinolineboronic acid (I) in dry carbon tetrachloride were transparent in the O–H stretching region (*e.g.*, spectrum A in Fig. 1). The spectra of dilute solutions of I in wet carbon tetrachloride, however, exhibited three absorption bands, the two associated with water in carbon tetrachloride plus a new absorption at about 3630 cm.$^{-1}$ (*e.g.*, spectrum C in Fig. 1).

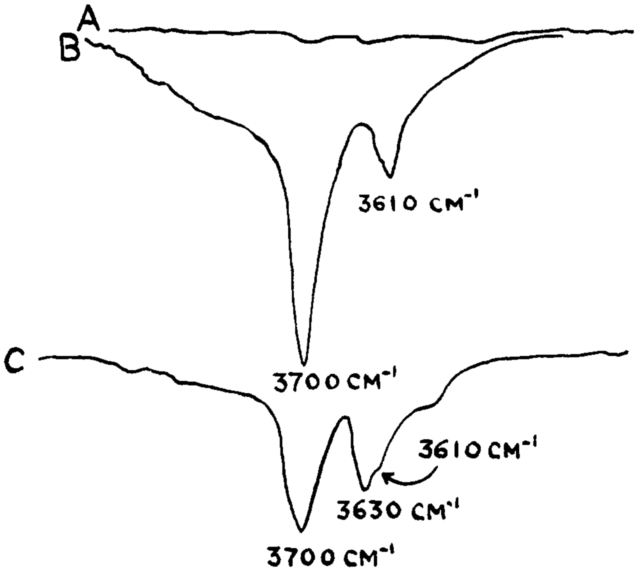

Fig. 1.—The effect of I on the spectrum of water in carbon tetrachloride: A, the spectrum of I (2×10^{-3} *M*) in dry CCl_4; B, the spectrum of water in CCl_4; C, the spectrum of water in CCl_4 containing I (2×10^{-3} *M*). Spectra are recorded as per cent transmittance *vs.* linear frequency (cm.$^{-1}$). Frequencies are ±2 cm.$^{-1}$

The intensity of the absorption at 3630 cm.$^{-1}$ increased as the concentration of I in wet carbon tetrachloride was increased from 3.2×10^{-4} to 3×10^{-3} *M*. Below a concentration of 3.2×10^{-4} *M* absorption at 3630 cm.$^{-1}$ was not significant, and the spectrum was that of water in carbon tetrachloride. Increasing the concentration of I from 3.2×10^{-4} to 1.2×10^{-3} *M* caused a decrease in the intensity of the 3700-cm.$^{-1}$ band and the appearance of the 3630-cm.$^{-1}$ band. At an ester concentration of about 3×10^{-3} *M* the 3700- and 3630-cm.$^{-1}$ bands were of approximately equal intensity. Increasing the concentration of I from 3×10^{-3} to 5×10^{-3} *M* produced no detectable change in the solution spectrum in the O–H stretching region.[7]

The spectrum of a dilute solution of I in D_2O-saturated carbon tetrachloride exhibited a band at about 2665 cm.$^{-1}$. This band was not present in the spectrum of a dilute solution of I in dry carbon tetrachloride nor was it present in the spectrum of CCl_4 saturated with D_2O.[8]

In contrast to these results it was found that the spectrum of water in carbon tetrachloride was not altered when the solution contained, as added reagents, pyridine (3×10^{-3} *M*), the *cis*-1,2-cyclopentanediol ester of benzeneboronic acid (3×10^{-3} *M*), a mixture

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(1) Department of Chemistry, Wake Forest College, Winston-Salem, N. C. 27106.

(2) R. L. Letsinger, S. Dandegaonker, W. J. Vullo, and J. D. Morrison, *J. Am. Chem. Soc.*, **85**, 2223 (1963).

(3) R. L. Letsinger and James D. Morrison, *ibid.*, **85**, 2227 (1963).

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(5) R. L. Letsinger and A. J. Wysocki, *J. Org. Chem.*, **28**, 3199 (1963).

(6) E. Greinacher, W. Luttke, and R. Mecke, *Z. Elektrochem.*, **59**, 23 (1955); P. Saumagne and M. L. Josien, *Bull. soc. chim. France*, **25**, 813 (1958); J. R. Holmes, D. Kivelson, and W. C. Drinkard, *J. Am. Chem. Soc.*, **84**, 4677 (1962).

(7) The intensity of C–H stretching bands in the 3050–2850-cm.$^{-1}$ region of the spectrum provided a qualitative means of observing the increasing ester concentration. These bands were evident at concentrations less than 3.2×10^{-4} *M* and became more intense as the ester concentration was increased.

(8) The spectrum of CCl_4 saturated with D_2O had absorption bands centered at 2745 (strong) and 2630 cm.$^{-1}$ (weak). These represent the fundamental O–D stretching modes of unassociated D_2O. A very weak band observed at about 2685 cm.$^{-1}$ is probably due to O–D stretching absorption in HOD, while another very weak absorption at about 3650 cm.$^{-1}$ is most likely that due to O–H stretch in HOD.

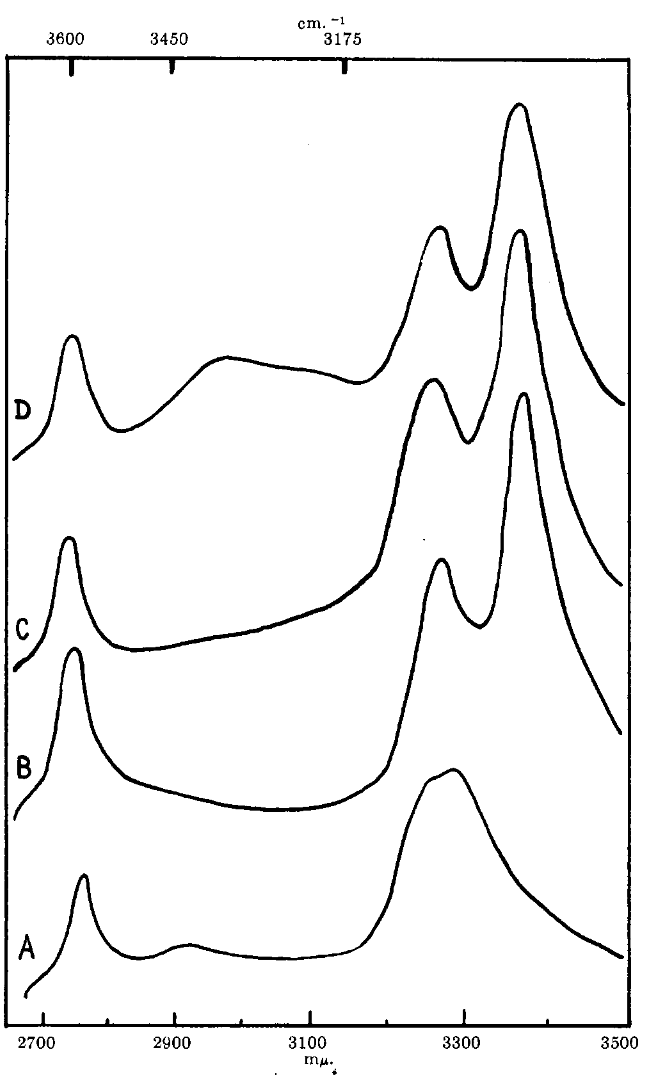
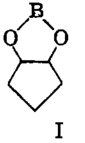
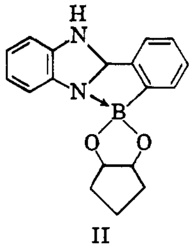


Fig. 2.—The effect of I on the spectrum of phenol in carbon tetrachloride: A, the spectrum of phenol (3.6 × 10^{-3} *M*), and pyridine (3.7 × 10^{-3} *M*); B, phenol (5 × 10^{-3} *M*) and the *cis*-1,2-cyclopentanediol ester of benzeneboronic acid (5 × 10^{-3} *M*); C, phenol (3.3 × 10^{-3} *M*), pyridine (3.3 × 10^{-3} *M*), and the *cis*-1,2-cyclopentanediol ester of benzeneboronic acid (3.3 × 10^{-3} *M*); D, phenol (4 × 10^{-3} *M*) and the *cis*-1,2-cyclopentanediol ester of 8-quinolineboronic acid (3.3 × 10^{-3} *M*). These spectra were recorded as absorbance *vs.* wave length (mμ).

of these two reagents (each 3 × 10^{-3} *M*), or the *cis*-1,2-cyclopentanediol ester of 2-(2-boronophenyl)benzimidazole (II).

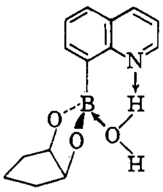


I

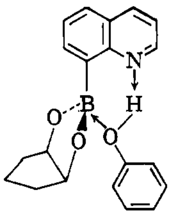


II

These data may be rationalized on the basis that water forms a complex (III) selectively with the ester of 8-quinolineboronic acid, in which the electrophilic center (boron) and the basic site (nitrogen) are favorably positioned for concerted action on the hydroxyl group. Lack of reaction in the other cases may be ascribed, in part at least, to the greater entropy of the pyridine–benzeneboronate ester system and to the fact that the activity of the boron and nitrogen in II is reduced as a consequence of direct boron–nitrogen coordination.[4]



III



IV

The 3630-cm.$^{-1}$ absorption band in the spectrum of solutions containing both water and I may be assigned to one of the O–H stretching vibrations of the water molecule in complex III. Likewise, the 2665-cm.$^{-1}$ band in the solutions containing D_2O may be attributed to an O–D stretching absorption in chelated D_2O. More specifically, it appears that these new bands arise from the free O–H or O–D in the complex. This tentative conclusion is based on a comparison of these spectra with those for related systems possessing both free and hydrogen bonded O–H groups. Thus the spectra of N-benzoylephedrine and N-methyl-ψ-ephedrine exhibit a sharp band near 3615 cm.$^{-1}$ and a broad absorption band in the region near 3420 cm.$^{-1}$.[9] The former band has been assigned to nonassociated hydroxyl and the latter to hydroxyl which is bonded to nitrogen.[9] Assuming that these compounds provide a valid model for III, we attribute the absorption at 3700 and the shoulder at 3610 cm.$^{-1}$ in spectrum C, Fig. 1, to water which has not been bound by the ester and the band at 3630 cm.$^{-1}$ to free O–H in the complex. Absorption due to O–H bonded to nitrogen should be observed near 3400 cm.$^{-1}$.[10] We did not find a definite band in this region; however, absorption between 3200 and 3500 cm.$^{-1}$ was relatively more intense for the solution containing both water and I than for carbon tetrachloride solutions containing I or water alone. This is suggestive of a very broad absorption in this region. Much better evidence for O—H · · · N bonding in a complex of an 8-quinolineboronate was obtained by investigating the interaction of phenol with I. The pertinent spectral region for carbon tetrachloride solutions containing either mixtures of phenol, pyridine and the *cis*-1,2-cyclopentanediol ester of 8-quinolineboronic acid or phenol and the *cis*-1,2-cyclopentanediol ester of 8-quinolineboronic acid is shown in Fig. 2. The band at about 3600 cm.$^{-1}$, due to nonassociated O–H, decreased slightly in intensity when I was added to phenol, and a new, broad band developed between 3450 and 3175 cm.$^{-1}$. The benzeneboronate ester had no effect on the phenol spectrum in the O–H stretching region.

These results indicate that in carbon tetrachloride phenol forms a hydrogen-bonded complex (IV) with I but not with a mixture of the *cis*-1,2-cyclopentanediol ester of benzeneboronic acid and pyridine. The positions and shapes of the bands are in accord with expectations based on the ephedrine model for nonassociated and hydrogen-bonded hydroxyl groups,[9] and the experi-

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[9] T. Kanzawa, *Bull. Chem. Soc. Japan*, **29**, 398, 604 (1956).

[10] The probability of finding a band in this region was pointed out by a referee.

mental results of other studies concerned with hydrogen bonds between hydroxyl and nitrogen.[11]

Experimental

***cis*-1,2-Cyclopentanediol Ester of 8-Quinolineboronic Acid.**—8-Quinolineboronic acid[12] (0.519 g.) and *cis*-1,2-cyclopentanediol[13] (0.306 g.) were refluxed with benzene (50 ml.) for 2 hr. in a Dean–Stark apparatus. The benzene was then distilled until the volume of solution was 10 ml. Pentane (40 ml.) was added to the residue and the resulting solution was cooled at 0–5° for 24 hr. The white crystalline product which formed was filtered rapidly and dried in a vacuum desiccator over P_2O_5, yielding 0.545 g. (76%), m.p. 120–121°.

Anal. Calcd. for $C_{14}H_{14}BNO_2$: C, 70.4; H, 5.90; N, 5.86. Found: C, 69.10[14]; H, 5.93; N, 6.03.

***cis*-1,2-Cyclopentanediol Ester of Benzeneboronic Acid.**—The procedure of Sugihara and Bowman[15] was followed: b.p. 83–84° (1 mm.), m.p. about 17°.

***cis*-1,2-Cyclopentanediol Ester of 2-(2-Boronophenyl)benzimidazole.**—2-(2-Boronophenyl)benzimidazole[4] (0.5 g.) was dissolved in 3 ml. of *cis*-1,2-cyclopentanediol. Benzene (30 ml.) was added to the solution, which was then refluxed with continuous removal of water for 4 hr. Pentane (50 ml.) was then added and the solution was cooled for 1 week at 0–5°. The white powder (0.24 g.) which formed was filtered, washed with pentane, and dried. After recrystallization from carbon tetrachloride it was obtained as felted needles, m.p. 130–134°.

Anal. Calcd. for $C_{18}H_{17}BN_2O$: C, 71.1; H, 5.61; N, 9.22. Found: C, 68.35[14]; H, 5.75; N, 9.47.

Infrared Spectra.—Spectra reproduced in Fig. 1 were obtained on a Perkin-Elmer Model 421 grating spectrophotometer using 1-cm. Pyrocell near-infrared cells. Spectra shown in Fig. 2 were obtained on a Beckman DK-2A recording spectrophotometer using silica cells. Carbon tetrachloride was dried over P_2O_5 and distilled. Wet carbon tetrachloride was prepared by shaking purified carbon tetrachloride with either H_2O or D_2O.

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(11) H. H. Freedman, *J. Am. Chem. Soc.*, **83**, 2900 (1961).

(12) R. L. Letsinger and S. H. Dandegaonker, *ibid.*, **81**, 498 (1959).

(13) L. N. Owen and P. N. Smith, *J. Chem. Soc.*, 4026 (1952).

(14) Carbon analyses for many B–N compounds are low.[5]

(15) J. M. Sugihara and C. A. Bowman, *J. Am. Chem. Soc.*, **80**, 2443 (1958).

A Synthesis of 1,2,3,4,6,7,12,12b-Octahydro-2-oxoindolo[2,3-*a*]quinolizine[1]

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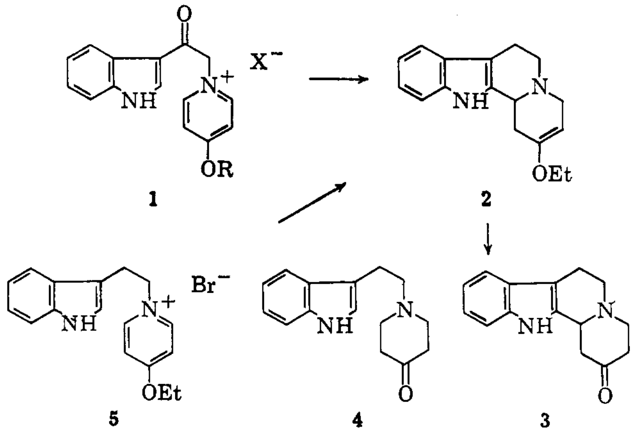
As part of a study of the synthesis of various types of indole alkaloids, one of the approaches envisaged utilized the tetracyclic intermediate (**3**). This ketone has been described previously,[2] as have various 3-substituted[3] and 4,4-disubstituted[4] derivatives, but for the proposed syntheses a simple, direct route was required. Using the reductive cyclization route to quinolizine derivatives described in earlier papers of this series, we have established a very convenient synthesis of **3** and, because of the potential usefulness of this reaction sequence in related areas, these results are reported in this communication.

Lithium aluminum hydride reduction of 1-[2-(3-indolyl)-2-oxoethyl]pyridinium salts[5] or 1-[2-(3-indolyl)-ethyl]pyridinium salts[6] has recently been shown to be a means of obtaining indolo[2,3-*a*]quinolizine derivatives in satisfactory yield. Application of this procedure to the synthesis of the desired ketone (**3**) was found to be possible by the choice of an appropriate pyridinium derivative. The use of a 4-alkoxy-1-[2-(3-indolyl)-2-oxoethyl]pyridinium salt in the reduction gave the quinolizine (**2**) which, being an enol ether, under the acid reaction work-up conditions readily yielded the ketone. In this way, 4-ethoxy-1-[2-(3-indolyl)-2-oxoethyl]pyridinium bromide (**1**) gave 1,2,3,4,6,7,12,12b-octahydro-2-oxoindolo[2,3-*a*]quinolizine (**3**) in 48% yield.

The pyridinium salts were readily prepared either from 4-ethoxy- or 4-methoxypyridine and 3-indolyl bromomethyl ketone or 3-indolyl methyl ketone and iodine, the former method resulting in better yields. Exchange of the anion for the perchlorate or picrate ion gave highly crystalline salts, all of which showed strong hydrogen bonding characteristics in their infrared spectra, and salts prepared by both methods yielded an identical perchlorate, thus confirming the structural assignments. Their ultraviolet absorption spectra were similar to those of other 3-acyl indole systems and these data are reported in the Experimental. Reaction of 4-ethoxypyridine with 2-(3-indolyl)ethyl bromide[7] gave the salt **5** which, though crystalline, does not have



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(1) (a) Part V in the series, Synthetic Experiments Related to the Indole Alkaloids; (b) Part IV: K. T. Potts and D. R. Liljegren, *J. Org. Chem.*, **28**, 3202 (1963); (c) support of this work by Grant HE-06475, National Heart Institute, Public Health Service, is gratefully acknowledged.

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(4) R. N. Schut, U. S. Patent 3,087,930 (1963); *Chem. Abstr.*, **59**, 11,497*b* (1963).

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(6) E. Wenkert, R. A. Massy-Westropp, and R. G. Lewis, *J. Am. Chem. Soc.*, **84**, 3732 (1962).

(7) The recent synthesis of 2-(3-indolyl)ethanol from ethyl 3-indolylglyoxylate and lithium aluminum hydride [T. Nogrady and T. W. Doyle, *Can. J. Chem.*, **42**, 485 (1964)] now makes this bromo compound readily available.