completed by adding water, and the solid was filtered off and dried over phosphorus pentoxide to yield 8.6 g. (94%) of material, m.p. 126.8–127.8°, m.p. 126.9–127.5° after recrystallization. Keller[6a] observed m.p. 128.3–128.8° for *n*-butylmercuric chloride.

Dineophylmercury.—Dineophylmercury (5.5 g., 0.0118 mole) was dissolved in 65 ml. of glacial acetic acid and this solution was sealed in a 100-ml. ampule. After 40 hr. at 100° (20 half-lives), the ampule was opened and the solution was decanted from 0.160 g. (0.0008 mole) of metallic mercury. Aqueous lithium chloride was added to the solution to precipitate neophylmercuric chloride which was filtered off, washed with water and air-dried. The crude yield was 3.9 g. (89%), m.p. 70–79°, m.p. 79.5–80.5° after one recrystallization from ethyl acetate–Skellysolve B. Keller[6a] observed 79.2–79.5° and Kent[23] 80.6–81.2° for the m.p. of neophylmercuric chloride.

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[23] L. Kent, unpublished work.

LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

The Base Strengths and Ultraviolet Absorption Spectra of the 2- and 3-Monohalopyridines[1,2]

BY HERBERT C. BROWN AND DARL H. MCDANIEL[3]

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Ultraviolet absorption spectra have been determined for the 2- and 3-monohalopyridines in basic and acidic aqueous solution. The spectra exhibit a regularity which is absent in the corresponding monohalonitrobenzenes. The data have been utilized to determine the dissociation constants for these pyridine bases. The following thermodynamic pK_a values at 25° have been observed: 2-fluoro-, −0.44; 2-chloro-, 0.72; 2-bromo-, 0.90; 2-iodo-, 1.82; 3-fluoro-, 2.97; 3-chloro-, 2.84; 3-bromo-, 2.84; 3-iodo-, 3.25. Thus the introduction of a fluorine atom in the 2-position of the pyridine ring results in an enormous decrease of 5.6 pK_a units. The remaining halogens are somewhat less effective in decreasing the base strength and the magnitude of the effect decreases with increasing atomic weight of the halogen. In the 3-position the effect is less marked. There is a decrease of approximately 2 pK_a units with no simple regularity in the pK_a values.

In a previous paper the dissociation constants of pyridine, 2,6-lutidine and thirteen monoalkylpyridines were reported.[4] It was considered desirable to extend the series of measured dissociation constants to include pyridine bases with more highly polar substituents. Therefore, the dissociation constants were measured for the 2- and 3-moonhalopyridines. The 4-halopyridines were not included in this investigation because of the reported instability of some of these compounds.[5]

The pK_a values of the pyridine bases were determined by utilizing ultraviolet absorption spectra to measure the concentration of the free and protonated pyridine bases in solutions of measured pH.[4,6] The method required the determination of the ultraviolet absorption spectra of both the free and protonated form of each of the monohalopyridines. These spectra reveal interesting similarities and differences with the corresponding spectra of the monohalonitrobenzenes.[7] Accordingly, consideration of the spectra appears of interest.

Results and Discussion

Dissociation Constants.—The pK_a values obtained for the 2- and 3-monohalopyridines are summarized in Table I. The error given represents the precision of the results, not the accuracy. It is probable that the error in terms of accuracy is greater than the error in precision by at least 0.02 pK_a unit.

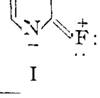
In the case of 2-fluoropyridine it was necessary to make certain assumptions in correcting the spectral data, assumptions that might result in a considerable error. Moreover, the common practice was followed of not correcting for the activity coefficient of the neutral species in rather strong acid solutions. The recent work of Long and McIntyre[8] indicates that such activity coefficients may vary appreciably from unity. Thus the error in the case of 2-fluoropyridine may be considerably larger than in the other case, possibly as large as ±0.3 pK_a unit.

TABLE I

THERMODYNAMIC pK_a VALUES FOR THE 2- AND 3-MONOHALOPYRIDINES IN AQUEOUS SOLUTION AT 25°

Compound	pK_a
Pyridine[4]	5.17 ± 0.02
2-Fluoropyridine	−0.44 ± .08
2-Chloropyridine	+ .72 ± .03
2-Bromopyridine	.90 ± .05
2-Iodopyridine	1.82 ± .02
3-Fluoropyridine	2.97 ± .05
3-Chloropyridine	2.84 ± .03
3-Bromopyridine	2.84 ± .03
3-Iodopyridine	3.25 ± .05

The introduction of a fluorine atom in the 2-position of the pyridine base results in the surprisingly large decrease in pK_a value of 5.6 units. This large decrease is unexpected since fluorine is believed to participate in resonance interactions I which should tend to decrease the inductive effect of the substituent II. It must be concluded that in this



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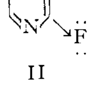

II

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[1] Steric Effects in Displacement Reactions. VII.

[2] Based upon a thesis submitted by Darl H. McDaniel in August, 1954, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[3] Research assistant at Purdue University, 1952–1953, on a National Science Foundation grant; Allied Chemical and Dye Corporation Fellow at Purdue University, 1953–1954.

[4] H. C. Brown and X. R. Mihm, THIS JOURNAL, **77**, 1723 (1955).

[5] J. P. Wibaut and F. W. Broekman, *Rec. trav. chim.*, **58**, 885 (1939); E. Koenigs and H. Greiner, *Ber.*, **64**, 1049 (1931).

[6] E. B. Hughes, H. H. G. Jellinek and B. A. Ambrose, *J. Phys. Colloid Chem.*, **53**, 410 (1949).

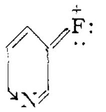
[7] H. E. Ungnade, THIS JOURNAL, **76**, 1601 (1954).

[8] F. A. Long and D. McIntyre, *ibid.*, **76**, 3243 (1954).

system the inductive effect of the substituent is much greater than the opposing resonance effect.

The decreasing base-weakening effect of chlorine, bromine and iodine substituents in the 2-position can be interpreted similarly in terms of the decreasing inductive effect of the halogen substituents with increasing atomic number. In these cases also we must assume that the inductive effect of the substituent, as in II, is of predominant importance, with the resonance interactions, as in I, playing only an insignificant role in modifying the relative strengths of the bases.

With the substituent in the more remote 3-position, the inductive effect becomes considerably smaller. Thus in this position the halogen substituents cause a decrease of but 1.9–2.3 pK_a units. With a smaller inductive effect, resonance interactions apparently become more important. At least it appears necessary to call upon some type of resonance interaction, as in III, to account for the relative magnitude of pK_a values for the 3-fluoro- and 3-chloropyridines (Table I).



III

Similar peculiarities are observed for halogen substituents in the *meta* positions of benzoic acid and phenol.[9] It must be evident from this discussion that our understanding of the more subtle effects of halogen substituents in the 3-positions of aromatic rings is not yet in a satisfactory state.

Absorption Spectra.—The ultraviolet absorption spectra of 2- and 3-fluoropyridine in aqueous ethanol containing 0.01 *N* hydrochloric acid have been reported previously.[10] Also, the ultraviolet spectra of 2- and 3-chloro-, bromo- and iodopyridine in heptane are available.[11] The present study makes available the spectra of both the free and the protonated bases for all of the 2- and 3-monohalopyridines under identical conditions.

The spectra are shown in Figs. 1–4. It is of interest that in the 3-halopyridines, the absorbancy index of the maxima in the region between 250 and 300 mμ is in the order F– > Cl– > Br– > I– both for the free and the protonated bases (Figs. 3 and 4).[12] On the other hand, the corresponding maxima in the spectra for the free and protonated 2-halopyridines give the opposite order I– > Br– > Cl– > F– (Figs. 1 and 2).

These spectra show interesting similarities and differences with the corresponding spectra for the monohalonitrobenzenes.[7] In the 3-isomers of the latter compounds the maxima in the 250–300 mμ region is in the order F– > Cl– > Br– > I–, corresponding to the order observed for the 3-halopyridines.

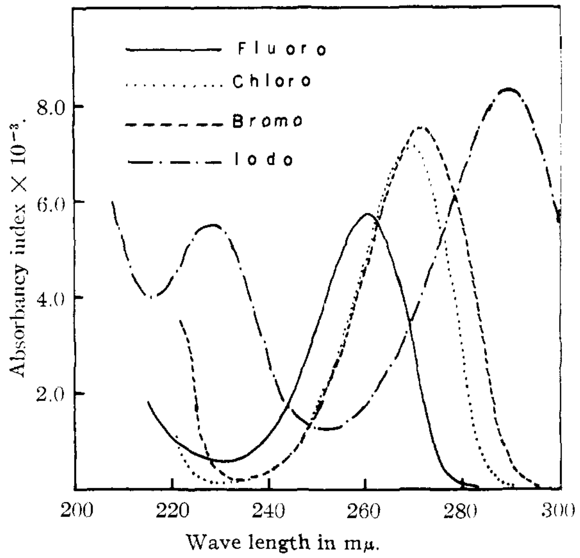


Fig. 1.—Ultraviolet absorption spectra of the 2-halopyridines in 1.2 *N* hydrochloric acid.

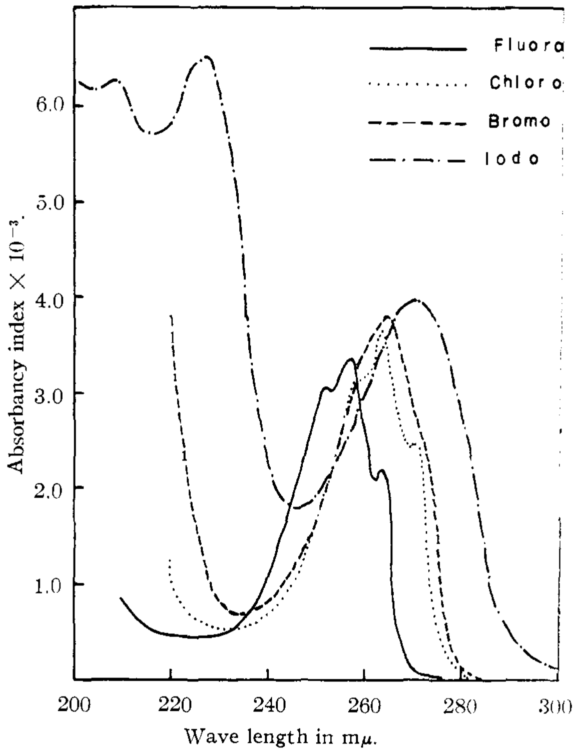


Fig. 2.—Ultraviolet absorption spectra of the 2-halopyridines in 0.013 *N* sodium hydroxide.

In the 4-halonitrobenzenes the opposite is observed, I– > Br– > Cl– > F–. The same order would have been expected for the 2-halonitrobenzenes, but the observed order is the opposite: F– > Cl– > Br – > I–. The difference between the spectra of the 2- and 4-halonitrobenzenes was interpreted by Ungnade[7] as being due to steric inhibition of resonance of the nitro group by the 2-halogen substituent.

This interpretation is supported by the present results. Steric inhibition of resonance is not possible in the pyridine compounds and the observed

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[9] For data and pertinent references see the accompanying paper: D. H. McDaniel and H. C. Brown, THIS JOURNAL, **77**, 3756 (1955).

[10] W. K. Miller, S. B. Knight and A. Roe, *ibid.*, **72**, 1629 (1950).

[11] C. W. F. Spiers and J. P. Wibaut, *Rec. trav. chim.*, **56**, 573 (1937).

[12] The slight irregularity exhibited by free 3-iodopyridine is due to the strong iodine absorption, as in the related compound, 3-iodonitrobenzene (ref. 7).

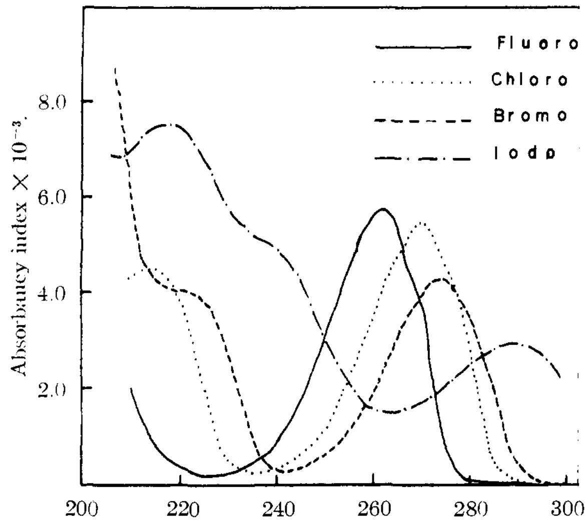

Fig. 3.—Ultraviolet absorption spectra of the 3-halopyridines in 1.2 N hydrochloric acid.

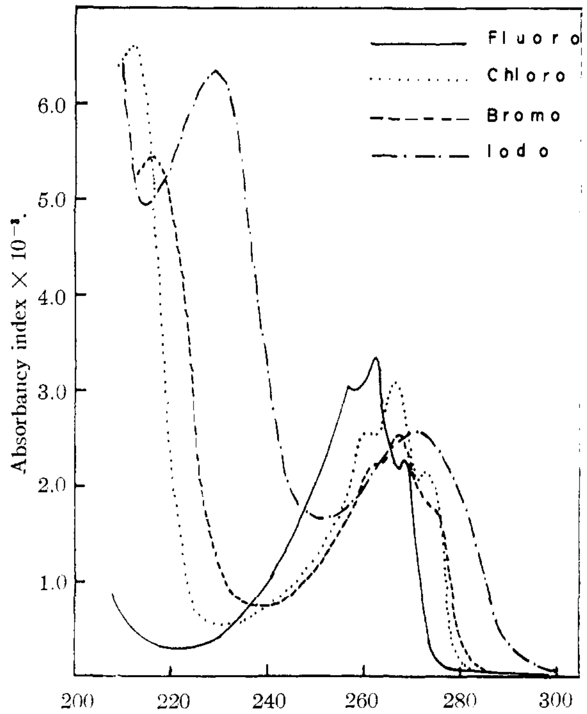

Fig. 4.—Ultraviolet absorption spectra of the 3-halopyridines in 0.013 N sodium hydroxide.

order for the 2-halopyridines, I– > Br– > Cl– > F–, agrees with the experimental order for the 4-halonitrobenzenes as well as for the order predicted for the 2-halonitrobenzenes in the absence of steric inhibition of resonance.

Experimental Part

Materials.—The halopyridines used were prepared and purified by Solomon[13] and D. Williams by standard procedures available in the literature. They were purified by fractionation, with the exception of 3-iodopyridine, which was crystallized to constant melting point. The physical properties of the materials used are summarized in Table II.

TABLE II

PHYSICAL PROPERTIES OF THE MONOHALOPYRIDINES

Compound	B.p. °C.	Mm.	$n^{20}D$
2-Fluoropyridine	124.8–125.4	755	1.4679
3-Fluoropyridine	106.0–106.6	734	1.4734
2-Chloropyridine	167.3–167.5	744	1.5322
3-Chloropyridine	145.2–146.2	722	1.5330
2-Bromopyridine	86.8–87.5	21.5	1.5713
3-Bromopyridine	73.5–73.8	23.4	1.5692
2-Iodopyridine	93–96	12.2	1.6363
3-Iodopyridine	M.p. 52.3–53.0		

Dissociation Constants.—The pH measurements were made by means of a Beckman model G pH meter which was standardized immediately before use by means of Leeds and Northrup standard buffer of pH 4.01. At least four different solvents of suitable pH range were used for each pK_a measurement.

The procedure of Hughes, Jellinek and Ambrose[6] was modified for the determination of the pK_a values of the halopyridines. Their procedure was to obtain the absorption spectra from 220 to 300 mμ of pyridine in 0.1 N sodium hydroxide, of the pyridinium ion in 0.1 N sulfuric acid, and of an approximately 1:1 mixture of the two forms in suitable acetate buffer solutions. From these data together with the measured pH of the buffer solution the pK_a value was calculated from the absorbancy values at a given wave length by means of the relationship

$$pK_a = pH + \log \frac{A_B - A_{OH^-}}{A_{H^+} - A_B} + \log \gamma_+ \qquad (1)$$

where A_B, A_{OH^-} and A_{H^+} is the absorbancy in the buffer, in 0.1 N sodium hydroxide and 0.1 N sulfuric acid, respectively, and γ_+ is the activity coefficient of the pyridinium ion in the buffer solution.

In order to obtain relatively complete protonation of the halopyridines, it was necessary to use a higher acid concentration. Accordingly, a solution of 1.2 N hydrochloric acid was used as the acid medium for all of the halopyridines with the exception of 2-fluoropyridine. In this case it was necessary to go to 10.8 N hydrochloric acid to obtain reasonably complete protonation. Similarly, the acetate buffers were replaced by appropriate concentrations of hydrochloric acid in order to attain appropriate pH ranges in which the halopyridines would be approximately half-ionized. The concentration of hydrochloric acid was of the order of 10^{-3} N for the 3-halopyridines, 0.1 N for the 2-halopyridines with the exception of 2-fluoropyridine, and 1.2 N for the latter.

The Debye–Hückel equation was used to calculate log γ_+ when the hydrochloric acid concentration was below 0.1 N. For higher concentrations the log γ_+ values were taken from data on e.m.f. cells.[14]

Calculations of the pK_a values were made both on the basis of equation 1 using the measured pH and on the basis of equation 2, using the known concentration of the hydrochloric acid solutions.

$$pK_a = -\log [H^+] + \log \frac{A_B - A_{OH^-}}{A_{OH^+} - A_B} \qquad (2)$$

In using this equation the term $-\log \gamma_{H^+}$ is assumed to cancel the log γ_+ term of equation 1. In other words the activity coefficients of hydrogen ion and of pyridinium ion in these solutions are assumed to be the same.

Calculations based upon both equation 1 and equation 2 were made for all of the halopyridines studied with the exception of 2-fluoropyridine. The results obtained by the use of the two different equations generally agreed within 0.04 pK_a unit. The limits of precision reported in Table I include the combined errors. Thus the two results for 2-iodopyridine are 1.835 ± 0.01 and 1.815 ± 0.01; the result is reported in Table I as 1.82 ± 0.02.

Because of the high acid concentration necessary to neutralize 2-fluoropyridine, it was not possible to determine the

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[13] M. Solomon, Ph.D. Thesis, Purdue University, 1951.

[14] H. Hunt, "Physical Chemistry," Thomas Crowell Co., New York, N. Y., 1947, p. 258.

TABLE III

TYPICAL DATA FOR THE DETERMINATION OF pK_a FOR 2-BROMOPYRIDINE BY THE USE OF SUCCESSIVE APPROXIMATIONS

Wave length, mμ	Absorbances A_{H^+}[a]	A_B[b]	A_{OH^-}[c]	$\log \frac{A_B - A_{OH^-}}{A_{H^+} - A_B}$	C_1[d]	$\log \frac{A_B - A_{OH^-}}{(A_{H^+} + C_1) - A_B}$	C_2[e]	$\log \frac{A_B - A_{OH^-}}{(A_H + C_2) - A_B}$
268	0.671	0.484	0.304	−0.018	0.024	−0.071	0.026	−0.074
269	.700	.489	.284	− .014	.026	− .066	.029	− .070
270	.730	.492	.270	− .032	.029	− .082	.033	− .088
271	.752	.499	.262	− .030	.031	− .080	.035	− .086
272	.771	.499	.248	− .036	.033	− .086	.037	− .092
273	.780	.488	.220	− .040	.035	− .087	.040	− .094
274	.780	.460	.177	− .054	.038	− .103	.043	− .109
Average				− .032		− .082		− .088
pK_a[f]				.95		.90		.89

[a] In 1.2 N hydrochloric acid. [b] In 0.097 N hydrochloric acid (pH 1.10). [c] In 0.013 N sodium hydroxide. [d] $C_1 = A_{H^+} - A_{OH^-}/15.8$. The value $[BH^+]/[B] = 15.8$ is obtained by substituting the quantities pK_a 0.95, pH 0.00, $\log \gamma_+ = 0.25$ (in 1.2 N HCl) into the expression $pK_a = pH + \log [BH^+]/[B] + \log \gamma_+$. [e] $C_2 = A_{H^+} - A_{OH^-}/14.1$. The value $[BH^+]/[B] = 14.1$ is obtained as in the previous case by the use of the value $pK_a = 0.90$, the other quantities remaining the same. [f] $pK_a = pH + \log \frac{A_B - A_{OH^-}}{(A_{H^+} + C) - A_B} + \log \gamma_+$ where for 0.097 N hydrochloric acid $\log \gamma_+ = -0.509\sqrt{0.097}/(1 + \sqrt{0.097}) = -0.123$.

pH values of these solutions. Accordingly, in this case the calculation of the pK_a value was based only on equation 2.

In the case of the 2-halopyridines it was observed that protonation was not complete even in the relatively high concentration of 1.2 N hydrochloric acid used. An attempt to overcome the difficulty by setting up a set of simultaneous equations yielded erratic results. The difficulty was overcome finally by utilizing a method of successive approximations to correct for the incomplete protonation of these bases in the acid solution.

In these cases the absorbancy values were corrected by adding to the measured absorbancy value, A_{H^+}, a term C, calculated with the aid of equation 3

$$C = \frac{A_{H^+} - A_{OH^-}}{[BH^+]/[B]} \qquad (3)$$

where $[BH^+]/[B]$ represents the ratio of the amount of the protonated form of the base to that of the free base. The ratio $[BH^+]/[B]$ was calculated from equation 4

$$[BH^+]/[B] = N(10pK_a) \qquad (4)$$

where N represents the normality of the acid medium. Alternatively, we can write

$$[BH^+]/[B] = 10(pK_a - pH - \log \gamma_+) \qquad (5)$$

where the terms pH and $\log \gamma_+$ refer to the acid medium. A trial pK_a for this calculation was obtained by use of equations 1 and 2 using the uncorrected data. From the absorbancy values thus obtained, a new value of pK_a was calculated. This procedure was repeated until the change in the pK_a value became negligible on further approximation. The procedure may be rendered clearer by an examination of the data in Table III.

In the case of 2-fluoropyridine it was necessary to use 10.8 N hydrochloric acid to approach relatively complete protonation. Because of this change from a predominantly aqueous system to a concentrated acid system exaltation and a displacement in wave length were anticipated. In order to observe the magnitude of this solvent effect, the spectrum of 3-fluoropyridine also was measured in 10.8 N acid. The maximum of the spectrum in this medium was shifted 2 mμ toward the red and the absorbancy value of the maximum had increased by 9.9%. Therefore, before calculating the pK_a value of 2-fluoropyridine, the spectrum was adjusted to compensate for an assumed similar shift in the spectrum of the 2-fluoropyridine in the concentrated acid. Since this assumption may not be entirely valid, the error of the pK_a value calculated on this basis may be considerably greater than the precision of the measurements would indicate.

Absorption Spectra.—All of the spectra reported in this paper were obtained by means of a Cary recording spectrophotometer. In addition, many of the absorbances used in the calculations were also obtained by means of a Beckman model DU spectrophotometer (slit width equivalent to 1 or 2 mμ). Thermospacers were used to keep the temperature of the sample at 25 ± 0.2° with the Beckman spectrophotometer. (The sample also was brought to 25° before measuring the pH.) No temperature control was maintained with the Cary instrument and room temperature for the different measurements varied from 25 to 29°.

Spiers and Wibaut[11] state that 3-chloropyridine does not obey Beer's law in heptane solution. We found that Beer's law is obeyed by both the free base and the pyridinium ion of 3-chloropyridine in the concentration range of 5×10^{-5} to 15×10^{-5} M in aqueous solution.

The characteristic features of the absorption curves for the free and protonated bases are shown in Figs. 1–4.

It already has been mentioned that the 2-halopyridines are not completely protonated even in 1.2 N hydrochloric acid, the fraction of unprotonated molecules being $1/[H^+]\cdot(10^{pK_a})$ or $1/1.2(10^{pK_a})$. For 2-chloro-, 2-bromo- and 2-iodopyridine in 1.2 N acid, the $[B]/[BH^+]$ ratios are 1/6.3, 1/9.3 and 1/79.5, respectively. For 2-fluoropyridine in 10.8 N acid, the $[B]/[BH^+]$ ratio is 1/3.9.

LAFAYETTE, INDIANA