diameter) of 300 g. of acid-washed alumina, Merck. A volume of 2 l. of benzene in 250-ml. fractions was used first and only traces of fat isolated. The elution was then continued with benzene–chloroform mixtures (5:1, 8:3 and 1:1 in fractions of 250 ml.) yielding a total of 1.91 g. of crude alkaloid A. After repeated crystallization from acetone–water 650 mg. of shiny, slightly yellowish plates was obtained, m.p. 243–244° dec., $[\alpha]^{26}D$ −131° (*c* 1.18 in $CHCl_3$). For analysis the sample was dried at 110° (0.05 mm.) for 8 hours.

Anal. Calcd. for $C_{22}H_{26}N_2O_4$: C, 69.09; H, 6.85; N, 7.33; OCH_3 (2), 16.23; mol. wt., 382.44. Found: C, 69.25; H, 6.80; N, 7.32; OCH_3 (2), 16.15; pK'_a 6.25 (electrometric titration); ϵ_{228} max 45,700, log ϵ 4.66; ϵ_{298} max 6,990, log ϵ 3.845; ϵ_{282} min 4,820, log ϵ 3.68; ultraviolet spectrum Fig. 2; infrared spectrum Fig. 1, D.

Alkaloid A Hydrochloride.—The hydrochloride was prepared by the usual procedure and recrystallized twice from methanol–ether, m.p. 237–238° dec. For analysis the sample was dried at 120° (0.5 mm.) for 4 hours.

Anal. Calcd. for $C_{22}H_{26}N_2O_4{\cdot}HCl$: C, 63.07; H, 6.50; N, 6.69; Cl, 8.46. Found: C, 62.77; H, 6.60; N, 6.60; Cl, 8.01.

Isolation and Characterization of Alkaloid F.—After changing the solvent ratio successively from 1:1 benzene–chloroform to 1:2 and 1:3 and then finally to chloroform alone a total of 650 mg. of crude alkaloid was isolated. It was recrystallized twice from absolute methanol and afforded colorless, shiny prisms, m.p. 253–254° dec., $[\alpha]^{26}D$ −44.6, −44.2° (*c*, 0.408 in MeOH–$CHCl_3$ 2:3), $[\alpha]^{26}D$ −47.7° (*c*, 0.712 in pyridine). For analysis the sample was dried at 100° (0.3 mm.) for 6 hours.

Anal. Calcd. for $C_{21}H_{24}N_2O_3$: C, 71.57; H, 6.86; N, 7.95; mol. wt., 352.4. Found: C, 71.43, 71.61; H, 6.93, 6.81; N, 8.13; mol. wt., 348 ± 10 (electrometric titration pK'_a 6.46); ϵ_{226} max 46,000, log ϵ 4.662; ϵ_{283} max 8,540, log ϵ 3.93; ϵ_{291} max 7,230, log ϵ 3.86. Ultraviolet spectrum Fig. 2; infrared spectrum Fig. 1, A.

Alkaloid F Hydrochloride.—The hydrochloride of this alkaloid was prepared by the procedure of Schwarz and Bader[4] and melted at 264–265° dec. The sample for analysis was dried at 120° for 5 hours (0.5 mm.).

Anal. Calcd. for $C_{21}H_{24}N_2O_3{\cdot}HCl$: C, 64.85; H, 6.48; Cl, 9.12. Found: C, 64.65; H, 6.57; Cl, 9.41.

Tetrahydroalstonine.—A slightly colored sample of the alkaloid was repeatedly recrystallized from absolute methanol and afforded colorless, shiny plates, m.p. 230–231° dec.; pK'_a 5.98 (electrometric titration), $[\alpha]^{26}D$ −100.7°, −102.3° (*c*, 0.418 in $CHCl_3$). Ultraviolet spectrum Fig. 2; infrared spectrum Fig. 1, B; ϵ_{226} max 45,200, log ϵ 4.655; ϵ_{283} max 8,540, log ϵ 3.93; ϵ_{291} max 7,230, log ϵ 3.86.

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Salt Effects on the Indicator Acidity Function, H_0[1]

BY MARTIN A. PAUL

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The effects of neutral salts on the indicator acidity function, H_0, have been measured by spectrophotometric means in 0.01, 0.1 and 1 *M* aqueous HCl solutions with the simple basic indicators, 2,4-dichloroaniline, *p*-nitroaniline, diphenylamine and *o*-nitroaniline. In 0.01 and 0.1 *M* HCl, the salt concentration effect is linear up to salt concentrations of at least 4 *M*, and is specific for the particular salt. The apparent acidity is increased by salts in the order, LiCl > NaCl > KCl, while it is decreased by tetramethylammonium bromide and tetraethylammonium bromide. Diphenylamine shows a larger salt effect than *p*-nitroaniline, attributable to its larger molecular size. The data support the conclusion that salt effects on the activity coefficients of the uncharged basic indicator molecules (which were measured independently by the solubility method) play a predominant role, with the implication that general salt effects may help to account also for the marked increase of $-H_0$ over log (H^+) with increasing concentration of strong acid itself, in the absence of added electrolyte.

Previous investigations[2a,b] in isolated instances have shown that neutral salts apparently have a marked effect on acidity as measured according to the method of Hammett and Deyrup[3] by means of uncharged basic indicators. Since there is evidence that certain acid-catalyzed reactions whose rates have been shown to follow the indicator acidity are likewise subject to large salt effects,[4-7] it seemed worthwhile to undertake a systematic investigation. Aside from its possible bearing on reaction kinetics, such an investigation promised to afford further insight into the nature of the indicator acidity function, H_0, itself, particularly in regard to its rapid increase with increasing electrolyte concentration in aqueous solutions of strong acids.

The effects of several neutral salts on H_0 were therefore measured in 0.01, 0.1 and 1 *M* aqueous HCl solutions, with the indicators 2,4-dichloroaniline, *p*-nitroaniline, diphenylamine and *o*-nitroaniline. These free bases show maximum light absorption at the respective wave lengths, 240, 380, 279 and 412 mμ, the cationic acid form in each case being transparent. In addition, the effects of salts on the activity coefficients of the free bases were determined for three of the indicators by the solubility method.

Experimental

The indicator acidity function, H_0, is defined by the equation[3]

$$H_0 = -\log (BH^+)/(B) + pK_a \qquad (1)$$

where K_a represents the acid ionization constant of BH^+, the cationic acid conjugate to the uncharged basic indicator, B. The concentration ratio, $(BH^+)/(B)$, was determined by means of light absorption of the basic form, B, as measured with a Beckman model DU spectrophotometer at a standard total concentration of the indicator in both forms. The indicator concentrations were approximately 5 × 10^{-5} *M* for diphenylamine, 8 × 10^{-5} *M* for 2,4-dichloroaniline and for *p*-nitroaniline, and 2 × 10^{-4} *M* for *o*-nitroaniline. Beer's law was satisfied within experimental precision at these concentrations. Corrections were made where necessary for light absorption by the salt.

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(1) Paper presented at the Chicago Meeting of the American Chemical Society, September, 1953.

(2) (a) L. P. Hammett and M. A. Paul, THIS JOURNAL, **56**, 827 (1934); (b) G. Harbottle, *ibid.*, **73**, 4024 (1951).

(3) L. P. Hammett and A. J. Deyrup, *ibid.*, **54**, 2721 (1932).

(4) Sucrose inversion, L. P. Hammett and M. A. Paul, *ibid.*, **56**, 830 (1934).

(5) Hydrolysis of β-propiolactone. F. A. Long and M. Purchase, *ibid.*, **72**, 3267 (1950).

(6) Trioxane decomposition, M. A. Paul, *ibid.*, **74**, 141 (1952).

(7) Methylal hydrolysis. F. A. Long and D. McIntyre, *ibid.*, **76**, 3240, 3243 (1954).

The indicators were all Eastman Kodak Co. products; *p*-nitroaniline was recrystallized from 95% ethyl alcohol, while the other indicators were recrystallized below their melting points from mixtures of ethyl alcohol with water. The HCl solutions were prepared by dilution from constant-boiling acid distilled through a three-foot Vigreux column; the concentration of a stock solution prepared by dilution of this acid was verified by titration against potassium acid phthalate as primary standard. Tetramethylammonium bromide and tetraethylammonium bromide were obtained from Eastman Kodak Co.; the other salts were standard analytical reagents. All were dried at 120° before weighing, but were not otherwise further treated. Lithium chloride stock solutions were analyzed gravimetrically; solutions of the other salts were prepared by weighing out directly the required quantity of the dried salt.

The spectrophotometer was equipped with thermospacers through which water was circulated from a thermostat; by this means the temperature within the compartment holding the standard 1-cm. cells was maintained at 25.0 ± 0.1° during all measurements.

For the solubility measurements, approximately 0.1 g. of the base was introduced into a 50-ml. glass-stoppered flask containing about 30 ml. of solution, and the flask was then agitated continuously for a period of at least 48 hours in a thermostat operating at 25.0 ± 0.1°. A sample of the solution was then withdrawn through a cotton plug into a transfer pipet and accurately diluted for analysis by means of its optical density as measured with the spectrophotometer.

Results and Discussion

TABLE I

IONIZATION OF INDICATORS IN HCl SOLUTIONS AT 25°

HCl, mole/liter	2,4-Dichloroaniline	*p*-Nitroaniline	Diphenylamine	*o*-Nitroaniline
		log $(BH^+)/(B)$		
0.005	−0.284			
.01	+ .008	−1.003		
.025	.400	−0.601	−0.812	
.05	.701	− .301	− .509	
.1	1.020	+ .012	− .208	
.2		.329	+ .117	−0.901
.5		.788	.580	− .464
1.0	2.0	1.178	1.012	− .077
2.0		1.62		+ .414
3.0				.818
		log $(BH^+)/(B)$ − log (H^+)		
0	(2.00)	(1.00)	(0.79)	(−0.25)
0.005	2.017			
.01	1.992	0.997		
.025	2.001	1.001	0.790	
.05	2.002	1.000	.792	
.1	2.020	1.012	.792	
.2		1.028	.816	−0.202
.5		1.089	.881	− .163
1.0	2.0	1.178	1.012	− .077
2.0		1.32		+ .113
3.0				.341

Table I shows the extent of ionization of each indicator in HCl solutions, without added salt. The reproducibility of log $(BH^+)/(B)$ at the middle of the indicator's range is within about ±0.005. It is noteworthy that up to 0.05 *M* acid concentration, as shown in the lower half of the table, log $(BH^+)/(B)$ for a given indicator differs from log (H^+) by a quite constant amount, which may be taken to define pK_a on the supposition that activity coefficient ratios cancel out. At higher concentrations, while log $(BH^+)/(B)$ no longer stays parallel with log (H^+), the difference between the values for a given pair of indicators displays the approximate constancy expected for indicators of the given charge type, as shown by Hammett and Deyrup.[3] Provisional pK_a values, though they are not actually required in the present investigation, are

Base	pK_a
2,4-Dichloroaniline	2.00
p-Nitroaniline	1.00
Diphenylamine	0.79
o-Nitroaniline	−0.25

The values for *p*-nitroaniline and *o*-nitroaniline are about 0.10 unit more negative than those previously assigned by Hammett and Paul,[1] the difference being attributable in part to the fact that H_0 was previously equated to $-\log a_\pm$ in dilute HCl solutions instead of simply to $-\log (H^+)$, as now seems reasonable. The earlier data, obtained with an optical colorimeter, were not sufficiently sensitive to discriminate between constancy of log $(BH^+)/(B)$ − log (H^+) and constancy of log $(BH^+)/(B) - \log a_\pm$.

The effects of neutral salts on H_0 are summarized in Table II. The quantity presented is the slope of the approximately linear relationship which the data indicate at the lower HCl concentrations between $-\Delta H_0$ and the salt concentration, C_s, for salt concentrations ranging as high as 4 moles per liter. One should note that a positive value of $-\Delta H_0 = \Delta \log (BH^+)/(B)$ signifies an increase in apparent acidity. Figure 1 shows graphically the nature of the results for *p*-nitroaniline in 0.1 *M* HCl. This figure includes also the results obtained by Long and McIntyre with $NaClO_4$ and sodium *p*-toluenesulfonate.[7] The results for NaBr were not included, as they practically overlap those for NaCl; the results for NH_4Cl depart somewhat from linearity, but would lie slightly below those for KCl.

TABLE II

SALT EFFECTS ON INDICATOR ACIDITY

	$\Delta H_0/C_s$			
Salt	2,4-Dichloroaniline in 0.01 *M* HCl	*p*-Nitroaniline in 0.1 *M* HCl	Diphenylamine in 0.1 *M* HCl	*o*-Nitroaniline in 1 *M* HCl
LiCl	0.248	0.245	0.292	0.25
NaCl	.203	.205	.251[a]	.20
NaBr		.203		
KCl	.177	.145	.179	.14
NH_4Cl		.14		
$(CH_3)_4NBr$	− .112	− .119	− .326	
$(C_2H_5)_4NBr$		− .410		

[a] 0.246 in 0.05 *M* HCl.

Several striking facts emerge, as follows: (1) The neutral salt effect on H_0 at the lower HCl concentrations, at least, is impressively linear with respect to the salt concentration. (2) It is specific for the particular salt. (3) The salts show an order reminiscent of their relative effects on the activity coefficients of non-electrolytes, particularly of the weakly basic type.[8] The marked inversion of the effect in the case of the large cations, tetramethylammonium and tetraethylammonium, is

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[8] F. A. Long and W. F. McDevit, *Chem. Revs.*, **51**, 119 (1952).

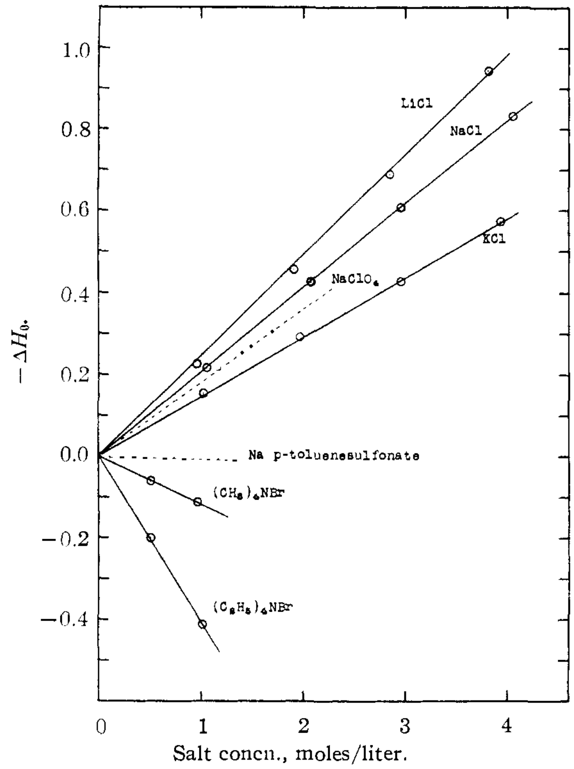

Fig. 1.—Effect of salts on ionization of *p*-nitroaniline in 0.1 *M* HCl.

particularly noteworthy in this respect. (4) The idea expressed in 3 is supported by the larger effect obtained with the larger indicator molecule, diphenylamine, as compared with *p*-nitroaniline at the same acid and salt concentrations, and by the almost identical effects obtained on the other hand with indicator molecules of the same size (*p*-nitroaniline and 2,4-dichloroaniline) even at different acid concentrations; these facts are seen clearly in the data for NaCl plotted in Fig. 2.

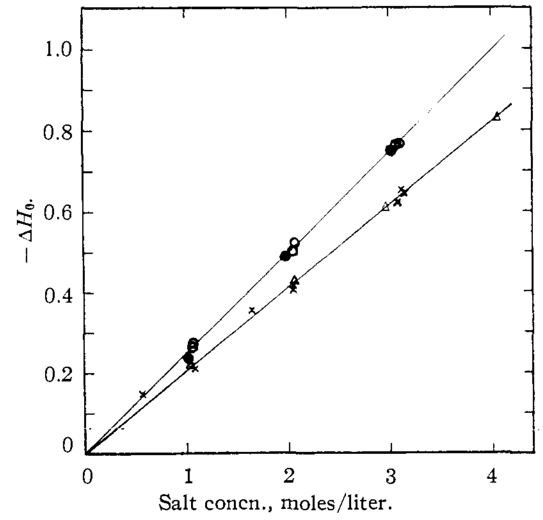

Fig. 2.—Effect of NaCl on ionization of indicators: ●, diphenylamine in 0.05 *M* HCl; ○, diphenylamine in 0.1 *M* HCl; Δ, *p*-nitroaniline in 0.1 *M* HCl; ×, 2,4-dichloroaniline in 0.01 *M* HCl.

Now, eq. 1 may be expressed in the equivalent form

$$-H_0 = \log(\mathrm{BH}^+)/(\mathrm{B}) - pK_a = \log(\mathrm{H}^+) + \log f_\mathrm{B} + \log f_{\mathrm{H}^+}/f_{\mathrm{BH}^+} \quad (2)$$

so that in the present investigation, we are essentially measuring the quantity

$$\Delta\log(\mathrm{BH}^+)/(\mathrm{B}) = -\Delta H_0 = \Delta\log f_\mathrm{B} + \Delta\log f_{\mathrm{H}^+}/f_{\mathrm{BH}^+} \quad (3)$$

the reference state being the dilute HCl solution of given concentration, without added salt. It appears therefore that a considerable part of the observed effect, though not necessarily all of it, may come simply from the first term on the right of eq. 3.

To test this hypothesis, activity coefficient data for the free indicator bases were obtained by measuring the effects of neutral salts on their solubilities, with results summarized in Table III. The solubilities are sufficiently low so that self-interaction terms are negligible,[8] and one can equate the constant, K, in the Setchénow equation

$$\log s_0/s = KC_s \quad (4)$$

with the salting-out constant, $k_s = (\log f_\mathrm{B})/C_s$, for the electrolyte. The experimental data turn out to be in satisfactory agreement with eq. 4, and Table III presents the corresponding values of k_s. The salting-out order observed with 2,4-dichloroaniline and with diphenylamine is one typical of weak bases,[8] while the actual magnitudes of the salting-out constants, whose relative magnitudes reflect the size influence of the non-electrolyte molecule, are about the same, respectively, as for benzene and biphenyl.[9] The order with *p*-nitroaniline is atypical, and appears to be associated generally with the presence of the nitro group.[8]

TABLE III

SALT EFFECTS ON SOLUBILITY AT 25°[a]

$$k_s = \frac{1}{C_s}\log(s_0/s)$$

Salt	2,4-Dichloroaniline	*p*-Nitroaniline	Diphenylamine
NaCl	0.195	0.080	0.271
KCl	.168	.024	.220
LiCl	.145	.....	.199
$(CH_3)_4NBr$	− .291	− .271	− .496

[a] The solubilities in water, derived by comparison with unsaturated standard solutions of known concentrations, are, respectively, 0.52 g./liter for 2,4-dichloroaniline, 0.58 g./liter for *p*-nitroaniline, and 0.046 g./liter for diphenylamine. For *p*-nitroaniline, H. R. Kruyt and C. Robinson report 0.5735 g./liter at 25°, while A. R. Collett and J. Johnston report 0.568 g. per 1000 g. of H_2O; Kruyt and Robinson also give solubilities of *p*-nitroaniline in 0.2 *M* salt solutions, from which the derived values of k_s are, respectively, 0.098, 0.049 and 0.119 for NaCl, KCl and LiCl. For diphenylamine, the water solubility of 0.3 g. per 1000 g. of H_2O reported by W. M. Dehn and currently quoted in the chemical handbooks is certainly too high; L. Desvergnes reports 0.03 g. per 1000 g. of H_2O at 0° and 0.07 g. at 28°. These data and the corresponding references are given by A. Seidell, "Solubilities of Organic Compounds," 3rd ed., D. Van Nostrand Co., Inc., New York, N. Y., 1941.

Table IV is a summary comparing the magnitude of $-\Delta H_0$ at unit salt concentration (not including the HCl concentration) with the magnitude of

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(9) W. F. McDevit and F. A. Long, THIS JOURNAL, **74**, 1773 (1952); M. A. Paul, *ibid.*, **74**, 5274 (1952).

Δ log f_B. One sees that with 2,4-dichloroaniline and with diphenylamine, the effects of NaCl and of KCl on H_0 are practically entirely included within the term Δ log f_B; for LiCl, the term Δ log f_{H^+}/f_{BH^+} evidently contributes about +0.1 unit, but it is noteworthy that this term must also be linear in the salt concentration, since both $-\Delta H_0$ and Δ log f_B are. With *p*-nitroaniline, all three alkali halides evidently contribute at unit concentration about +0.12 to the term Δ log f_{H^+}/f_{BH^+}, while with all three indicators, tetramethylammonium bromide has an effect of about +0.15–0.18 on this term.

The salt concentration effects on H_0 as measured in 1 *M* HCl with *o*-nitroaniline are not quite linear, as one can see from the plots of log $(BH^+)/(B)$ against electrolyte concentration shown in Fig. 3, but the HCl concentration itself here constitutes an appreciable fraction of the total electrolyte concentration. The magnitude of the effect for a given salt is still, however, about the same as with *p*-nitroaniline in 0.1 *M* HCl.

TABLE IV

SUMMARY OF SALT EFFECTS ON INDICATORS AT UNIT SALT CONCENTRATION

Salt	2,4-Dichloroaniline Δ log f_B	2,4-Dichloroaniline $-\Delta H_0$ (0.01 *M* HCl)	Diphenylamine Δ log f_B	Diphenylamine $-\Delta H_0$ (0.1 *M* HCl)	*p*-Nitroaniline Δ log f_B	*p*-Nitroaniline $-\Delta H_0$ (0.1 *M* HCl)
LiCl	0.145	0.248	0.199	0.292	0.105[a]	0.245
NaCl	.195	.203	.271	.251	.080	.205
KCl	.168	.177	.220	.179	.024	.145
$(CH_3)_4NBr$	− .291	− .112	− .496	− .326	− .271	− .119

[a] Long and McIntyre, ref. 7.

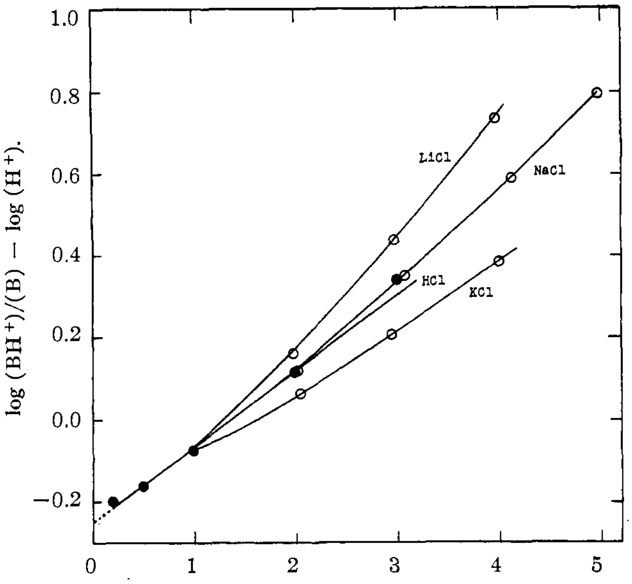

Fig. 3.—Salt effects on ionization of *o*-nitroaniline: ●, straight HCl; ○, 1 *M* HCl + salt.

It is interesting to speculate on the salt effect produced by the electrolyte HCl itself. Equation 2 may be rearranged in the form

$$\log (BH^+)/(B) - \log (H^+) = pK_a + \log f_B + \log f_{H^+}/f_{BH^+} \quad (5)$$

from which one sees that the differences between the quantity log $(BH^+)/(B)$ − log (H^+) and pK_a are equal to the respective increments in the quantity log f_B + log f_{H^+}/f_{BH^+}, from a standard state of infinite dilution in water. We have shown empirically that this latter quantity, through eq. 3, increases linearly with electrolyte concentration for ordinary neutral salts. Inspection of the data for *o*-nitroaniline in the lower part of Table I suggests that the effect of HCl itself is consistent with an approximately linear relationship between log f_B + log f_{H^+}/f_{BH^+} and C_{HCl} having slope of about +0.18 that is, having approximately the same magnitude as for the electrolyte NaCl. This relationship is indicated by the straight line drawn in Fig. 3 for HCl. The result for diphenylamine in 1 *M* HCl, which though well beyond the middle of the indicator's range has been verified repeatedly, is significantly high in comparison with the figures for *p*-nitroaniline and *o*-nitroaniline, but is consistent with the larger salt effects actually observed for this larger indicator molecule in the case of the other neutral electrolytes. The possibility is therefore suggested that the rapid increase of $-H_0$ over log (H^+) with increasing acid concentration is a general salt effect part of which is contributed by a term Δ log f_B and part by a term Δ log f_{H^+}/f_{BH^+}; each of these terms appears empirically to be an approximately linear function of the electrolyte concentration up to concentrations of order, 4 *M* at least. While it is not feasible to measure independently the effect of the strong acid on the term log f_B, for indicator bases as strong as those used in the present investigation, one could no doubt obtain such information in the case of much weaker bases such as 2,4-dinitroaniline and others in the series developed by Hammett and Deyrup.

The author takes pleasure in acknowledging his indebtedness to Dr. F. A. Long for helpful comments during the course of this investigation.

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