Correlation of Base Strengths of Aliphatic and N-Substituted Anilines

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The base strengths of secondary and tertiary aromatic amines of the type $C_6H_5NR_1R_2$ are plotted against the Taft σ^* values. Each class of amine lies on a different line. All of the aliphatic amines reported by Hall[1] and all of the aromatic amines reported herein are approximately correlated to a single line each by the equation $\log K/K_0 = \rho^*\Sigma\sigma^* + H(n)$. The quantity, $\Sigma\sigma^*$, is the sum of the polar substituent constants of the groups attached to the amino nitrogen, n is the number of hydrated $\overset{+}{N}$–H groups in the ammonium ion, and H is an empirical constant measuring the base-strengthening effects of each hydrated $\overset{+}{N}$–H group. The values of the reaction series constant, ρ^*, and the hydration constant, H, are the same for both the aliphatic and aromatic series. The equation attributes the effect of structure on base strength to the sum of independent polar, solvation, and resonance effects and provides an approximate evaluation of hydration effects in amines.

Attempts to explain basic strength of amines in water in terms of structure have met with varying degrees of success. Discrepancies in correlation have been related to various factors including hydration,[1-3] proximity,[4] steric,[1,5] and polarization effects.[6] By far the most successful attempt to correlate basicities was made by Hall[1] who showed that a large number of primary, secondary, and tertiary aliphatic amines could be satisfactorily correlated with the Taft equation, $\log K/K_0 = \rho^*\Sigma\sigma^*$, where $\Sigma\sigma^*$ was the sum of the polar substituent constants of groups attached to the amino nitrogen; each class of amines fell on a different line. Because tertiary amines correlated better by the Taft equation than did the primary and secondary amines, Hall discounted the B-strain theory as an explanation of the base weakening that generally occurs in going from primary to secondary to tertiary amines. He concluded that (1) polar effects were primarily responsible for relative base strengths within a given class of amines, (2) solvation effects were responsible for the separation of amines into four groups (NH_3, 1°, 2°, 3°), and (3) steric hindrance of solvation was responsible for deviations from the correlation lines noted for primary and secondary amines containing bulky groups. To account for the insensitivity of the tertiary ammonium ions to steric effects, Hall postulated that these ions might not be hydrated.

This paper reports the correlation of secondary and tertiary aromatic amines of the type $C_6H_5NR_1R_2$ by the Taft equation and the further correlation of the pK_a values reported by Hall[1] and the pK_a values for aromatic amines by a single equation. While Hall drew correlation lines through amines of minimum steric requirements, the correlations described here include all data in a least-squares fitting process and all slopes and intercepts were determined in this manner.

Results and Discussion

In Table I have been assembled the pK_a and $\Sigma\sigma^*$ values for aromatic amines which have been found in the literature or determined in our laboratories. Plots of the data are given in Fig. 1. Figure 1 reveals that for each class of aromatic amine a linear correlation exists between pK_a and $\Sigma\sigma^*$ with the exception of benzoquinuclidine and the N-*t*-butylanilines which will be discussed later. Table II lists the ρ^* and intercept values of the lines shown in Fig. 1 and for the data given by Hall[1]; although the ρ^* values are nearly identical, the intercepts are distinctly different.

All of the data in Table I (with the exception of compounds 13, 24, and 26) and all of the data given by

TABLE I

pK^a OF AROMATIC AMINES, $C_6H_5NR_1R_2$, IN WATER AT 25°

No.	R_1	R_2	$\Sigma\sigma^*$	pK_a	Ref
1	H	$CH{\equiv}CCH_2$	1.85	3.07	*a, b*
2	H	$C_6H_5CH_2$	1.31	4.04	*c*
3	H	$HOCH_2CH_2$	1.29	4.06	*c, d*
4	H	$CH_2{=}CHCH_2$	1.23	4.18	*b, e*
5	H	CH_3	1.09	4.89	*f*
6	H	CH_3CH_2	0.99	5.10	*f*
7	H	$CH_3CH{=}CHCH_2$	1.22	5.12	*b*
8	H	*sec*-C_4H_9	0.87	5.24	*b*
9	H	*n*-C_3H_8	0.88	5.24	*b*
10	H	*i*-C_3H_8	0.89	5.30	*c*
11	H	*n*-C_4H_9	0.96	5.44	*c*
12	H	*t*-C_5H_{11}	0.77	6.35	*b, g*
13	H	*t*-C_4H_9	0.77	7.10	*h*
14	N-Morpholine		1.27	3.20	*a, c*
15	$C_6H_5CH_2$	$C_6H_5CH_2$	1.05	4.00	*i*
16	$HOCH_2CH_2$	$HOCH_2CH_2$	1.00	4.07	*c*
17	CH_3	CH_3	0.60	5.07	*c, f*
18	N-Piperidine		0.46	5.20	*a*
19	*n*-C_3H_8	*n*-C_3H_8	0.37	5.63	*f*
20	CH_3	*n*-C_3H_8	0.49	5.68	*f*
21	CH_3	CH_3CH_2	0.50	5.99	*j*
22	CH_3CH_2	*n*-C_3H_8	0.39	6.40	*c, f*
23	CH_3CH_2	CH_3CH_2	0.40	6.52	*c, j*
24	Benzoquinuclidine		0.64	7.79	*k, l*
25	H	H	1.58	4.65	*j*
26	CH_3	*t*-C_4H_9	0.3	7.25	*h*

[a] The σ^* values were those given by Hall.[1] [b] V. Wolf and D. Ramin, *Ann.*, **626**, 47 (1959). [c] These values were determined by us using the Hammett spectrophotometric method. [d] R. Miguel, A. Lattes, and P. Maraval, *Bull. soc. chim. France*, 303 (1962). [e] The σ^* values of the crotyl group were used. [f] N. F. Hall and M. R. Sprinkle, *J. Am. Chem. Soc.*, **54**, 3469 (1932). [g] The σ^* values of the *t*-butyl group was used. [h] N-*t*-Butylaniline value is for 19° while the value for N-methyl-N-*t*-butylaniline is at 31° [G. Verlearschi and P. Rumpf, *Compt. rend.*, **229**, 1152 (1949)]. [i] These values were determined by us by potentiometric titrations in nitromethane after the method of C. A. Streuli, *Anal. Chem.*, **31**, 1652 (1959). [j] N. F. Hall, *J. Am. Chem. Soc.*, **52**, 5124 (1930). [k] For this compound we considered $\Sigma\sigma^* = \sigma_{C_6H_5}{}^* + 2\sigma_{C_6H_5(CH_2)_2}{}^*$. [l] B. M. Wepster, *Rec. trav. chim.*, **71**, 1171 (1952).

(1) H. K. Hall, Jr., *J. Am. Chem. Soc.*, **79**, 5441 (1957).
(2) A. F. Trotman-Dickenson, *J. Chem. Soc.*, 1299 (1949).
(3) T. S. Moore and T. F. Winmill, *ibid.*, 1635 (1912).
(4) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 225.
(5)(a) H. C. Brown, *Science*, **103**, 385 (1946); (b) G. Vexlearschi and P. Rumpf, *Compt. rend.*, **229**, 1152 (1949); **228**, 1655 (1949).
(6) S. R. Palit, *J. Phys. Colloid Chem.*, **51**, 1028 (1947).

TABLE II

ρ^* AND INTERCEPT VALUES FOR TAFT PLOTS OF AMINE BASICITIES

Amine type	ρ^*	Intercept (pK_a)	r	Std. dev.
C_6H_5NRH	2.96	8.19	0.897	0.52
$C_6H_5NR_2$	3.15[a]	7.25[a]	0.939[a]	0.40[a]
Av. for aromatic amines	3.06 ± 0.09			
RNH_2	3.07 ± 0.09[b]	13.06[b]	0.990	0.23
R_2NH	2.94 ± 0.10[b]	11.66[b]	0.985	0.33
R_3N	3.23 ± 0.05[b]	9.55[b]	0.997	0.15
Av. for aliphatic amines	3.08 ± 0.10			

[a] Value does not include data for benzoquinuclidine. [b] From data given by Hall (see ref. 1) using a least-square fitting process.

Hall can be satisfactorily correlated to single lines by use of eq. 1. This equation attributes the effect of structure on the relative basicity of amines to the sum of independent polar and hydration effects and assumes constant resonance effects within the aromatic series.[7]

$$\log K/K_0 = \rho^*\Sigma\sigma^* + H(n) \qquad (1)$$

In eq. 1, n is the number of hydrated $\overset{+}{N}$–H groups in the ammonium ion. The empirical constant, H (-1.12 ± 0.14), is attributed to the base-strengthening effect of hydrating a single $\overset{+}{N}$–H group. The reaction series constant ρ^* (3.23 ± 0.05) used is the ρ^* value for the tertiary aliphatic amines. The best fit of the data is obtained when the following values of n are used: NH_4^+, $n = 4$; RNH_3^+ and $C_6H_5NH_3^+$, $n = 3$; $R_2NH_2^+$ and $C_6H_5NRH_2^+$, $n = 2$; $C_6H_5NR_2H^+$, $n = 1$; R_3NH^+, $n = 0$.

The correlations by eq. 1 shown in Fig. 2 include the 77 amines listed by Hall[1] and the 26 aromatic amines listed in Table I; the aliphatic series covers eight powers of 10 and the aromatic series covers nearly six powers of 10. The correlation coefficients for the aliphatic and aromatic series are 0.988 and 0.939, respectively.

The success of eq. 1 in correlating the pK_a values of both aliphatic and aromatic amines by using the parameters indicated supports the following hypotheses: (a) relative polar effects in both the aliphatic and aromatic amines are proportional to the substituent constants σ^* and are additive; (b) the relative polar effects are equal in each class of amines; (c) polar, resonance, and solvation effects are separate and independent variables; (d) solvation effects are directly proportional to the number of $\overset{+}{N}$–H groups in the ammonium ions with the exception of the tertiary ammonium ions, which have no water of hydration associated with the $\overset{+}{N}$–H group; (e) the difference in the intercepts of the two lines in Fig. 2 represents the base-weakening effect of a single aromatic ring conjugated with the amine nitrogen; and (f) in comparison to polar, resonance, and solvation effects, steric effects are of secondary importance (however, see below).

Condition b, that relative polar effects are equal in each class of amines, is supported by the similarities of re-

(7) A more general equation of the form $\log K/K_0 = \rho^*\Sigma\sigma^* + H(n) + R$ when R accounts for the resonance effect of a single phenyl group on the base strength of amines would allow correlation of all the aliphatic and aromatic amines to a single line. For the data given the value of the resonance effect R would be 3.61 pK units. (Referee's comment: "The independent estimate of R from the pK_a of benzoquinuclidine is in good agreement with this value.")

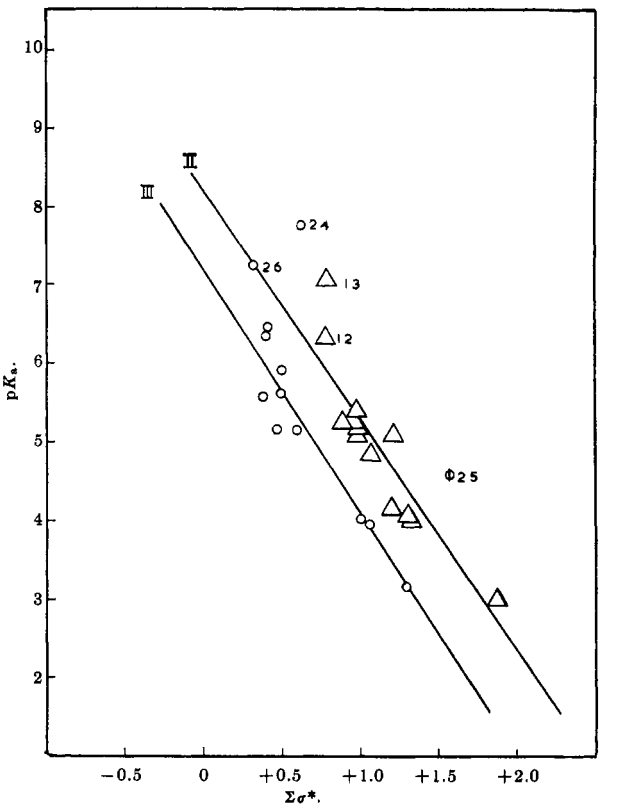

Fig. 1.—Variation of pK_a with $\Sigma\sigma^*$ for aromatic amines: ○, $C_6H_5NR_1R_2$; △, C_6H_5NHR; ϕ, $C_6H_5NH_2$.

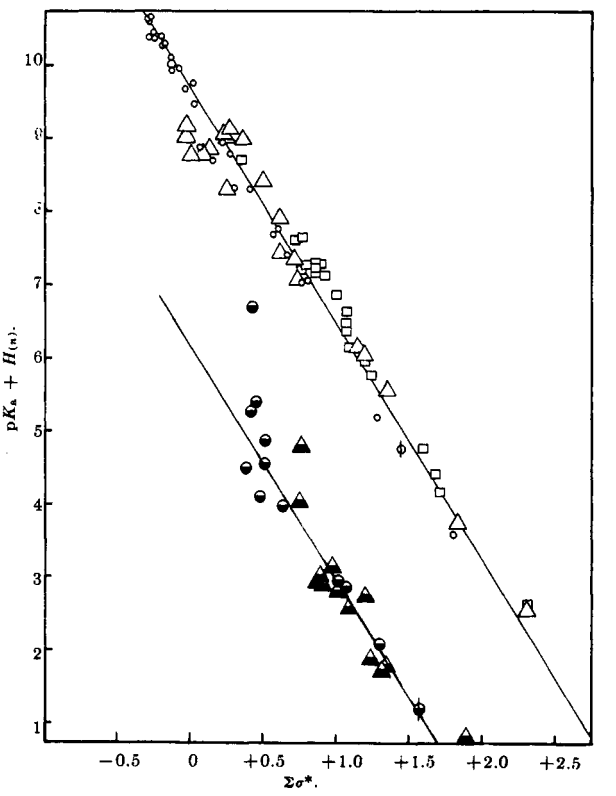

Fig. 2.—Variation of $pK_a - H(n)$ with $\Sigma\sigma^*$ for aliphatic and aromatic amines: ○, $R_1R_2R_3N$; △, R_1R_2NH; □, R_1NH_2; ϕ, NH_3; ◒, $C_6H_5NR_1R_2$; ▲, $C_6H_5NR_1H$; ◒, $C_6H_5NH_2$.

action series constants ρ^* listed in Table II. Others[1-3,8] have postulated that hydration is proportional to the number of hydrated $\overset{+}{N}$–H groups in the ammonium ion. That hydration is directly proportional to the number of $\overset{+}{N}$–H groups (condition d) is supported by the fact that a single hydration constant, H, is applicable to all classes of amines; the use of a single constant H for both the aliphatic and aromatic amines also implies that the hydration of a single $\overset{+}{N}$–H group is little affected by the electron density on the amino nitrogen.

The effect of steric hindrance on base strength of aliphatic amines has been discussed by Hall.[1,9] For aromatic amines, steric hindrance to solvation (base weakening) may occur as in the aliphatic series; in addition, steric inhibition of resonance (base strengthening) may take place. Benzoquinuclidine appears to be a clear example of this latter effect.[10] In fact, if this compound is considered an "aliphatic" tertiary amine ($n = 0$), the correlation with eq. 1 is good (pK_a 7.79; pK_a 7.60, calcd. from eq. 1).

(8) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **82**, 2965 (1960).
(9) H. K. Hall, Jr., *ibid.*, **79**, 5444 (1957).
(10) B. M. Wepster, *Rec. trav. chim.*, **71**, 1171 (1952).

The deviation of the *t*-butylanilines (compounds 13 and 26) can be abscribed to steric inhibition of resonance, however, neither pK_a value was determined at 25°. In view of the deviation of N-*t*-amylaniline (compound 12) it would seem that steric factors alone cannot explain the deviation of the N-*t*-butylanilines.

In order to obtain the correlation of the data by eq. 1 using a single adjustable parameter, H, the value of ρ^* (3.23 ± 0.05) for the 3° aliphatic amines was used. It was then assumed that the correlation line for the aliphatic amines would pass through the trimethylamine point. This method permits the evaluation of H by eq. 2 and gives the value of −1.12 ± 0.14.

$$H = \frac{\Sigma[\log K/K_0 - 3.23(\Sigma\sigma^*)]}{\Sigma(n)} \qquad (2)$$

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A New Synthesis of Amino Phosphonic Acids[1]

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A new synthesis of amino phosphonic acids has been developed, involving the Curtius degradation of substituted diethyl phosphonoacetylhydrazides. This appears to be a general synthesis for 1-aminoalkylphosphonic acids since aminomethylphosphonic (glycine analog), 1-aminoethylphosphonic (alanine analog), and 1-amino-2-phenylethylphosphonic (phenylalanine analog) acids were synthesized in this manner successfully. Two additional phosphonic acid analogs of the naturally occurring amino carboxylic acids also were synthesized by special methods. These were 2-amino-4-phosphonobutyric acid (a glutamic acid analog) and 2-amino-3-phosphonopropionic acid (an aspartic acid analog). An improved isolation procedure for amino phosphonic acids is described and the over-all yields of the three amino acids produced by the Curtius degradation were 56–80%, based on the parent phosphonoacetic esters.

Kabachnik and Medved[3] have described what appears to be a general method for producing 1-aminoalkylphosphonic acids. They condensed both aldehydes and ketones with ammonia and a dialkyl phosphonate to give dialkyl esters of 1-aminoalkylphosphonic acids. Hydrolysis of the esters produced the free amino acids. Kabachnik and Medved did not prepare any phosphonic acid analog of a naturally occurring amino acid and their method gave over-all yields of 40% or less. Chalmers and Kosolapoff[4] used the same method for preparing 1-amino-2-phenylethylphosphonic acid (phenylalanine analog) and 1-aminoethylphosphonic acid (α-alanine analog) as well as a number of additional similar products. Their over-all yields were never greater than 41.5%. Aminomethylphosphonic acid (glycine analog) has been prepared by the ammonolysis of halomethylphosphonic acid esters[5] and by condensing N-(bromomethyl)phthalimide with dibutyl sodiophosphonate, followed by the hydrolysis of the resulting product.[4,6]

Since so few phosphonic acid analogs of the naturally occurring amino carboxylic acids have been prepared, it seemed desirable to consider the synthesis of additional ones. However, Kabachnik and Medved's method suffers from serious deficiencies—many of the aldehydes necessary for the synthesis of additional 1-aminoalkylphosphonic acids are not available readily and the yields of the phosphonic acids prepared by this method have been relatively poor. We report the first use of the Curtuis reaction[7] for the preparation of 1-amino-

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(2) Submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the A. and M. College of Texas, Aug., 1958; Department of Chemistry, Walla Walla College, College Place, Wash.
(3)(a) M. I. Kabachnik and T. Ya. Medved, *Dokl. Akad. Nauk SSSR*, **83**, 689 (1952); (b) M. I. Kabachnik and T. Ya. Medved, *Izv. Akad. Nauk SSSR Otd. Khim. Nauk*, 868 (1953); (c) T. Ya. Medved and M. I. Kabachnik, *ibid.*, 314 (1954).
(4) M. E. Chalmers and G. M. Kosolapoff, *J. Am. Chem. Soc.*, **75**, 5278 (1953).
(5) (a) M. I. Kabachnik and T. Ya. Medved, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 635 (1950); (b) M. I. Kabachnik and T. Ya. Medved, *ibid.*, 95 (1951).
(6) V. Chavane, *Bull. soc. chim. France*, 774 (1948).
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