A Reexamination of Substituent Effects in Reactions of Aniline as a Base and as a Nucleophile[1]

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Abstract: Substituent effects of a large group of *meta* and *para* substituents on the base dissociation constant K_B of aniline in methanol and ethanol and on its analog K_iK_d in acetic acid are all equal, but these effects differ qualitatively from those on K_B of aniline in water. In linear free energy correlations of reactivity with basicity in organic solvents, it is better to use the ionization constant, K_i, rather than K_B as the measure of basicity. New pK_A values are reported at 25°. For *m*-methoxyaniline, pK_A = 5.70 in ethanol and 6.04 in methanol; for 3,5-dimethoxyaniline, pK_A = 5.40 in ethanol and 5.66 in methanol.

In connection with recent studies of ionization and ion-pair dissociation of *meta*- and *para*-substituted anilines in acetic acid,[2] we have reexamined substituent effects in various reactions of aniline as a base and as a nucleophile. We now wish to report the three main results of this study.

1. *Substituent effects of a large group of meta and para substituents on* K_B *of aniline in methanol and ethanol and on* K_iK_d *of aniline in acetic acid are all equal.* K_i, K_d, and K_B for a base B in a lyophilic solvent LOH are defined in (1) and are related as in (2).[3] In methanol,

base ionization

$$K_i = [BH^+OL^-]/[B\cdot solv] \qquad (1a)$$

ion-pair dissociation

$$K_d = [BH^+][OL^-]/[BH^+OL^-] \qquad (1b)$$

over-all base dissociation

$$K_B = [BH^+][OL^-]/([B\cdot solv] + [BH^+OL^-]) \qquad (1c)$$

$$K_B = K_iK_d/(1 + K_i) \qquad (2)$$

ethanol, and water, K_i for the anilines considered in this paper is much smaller than unity, so $K_B = K_iK_d$, in good approximation.

The relevant data are listed in Table I. Most of the values for methanol and ethanol are the mean of concordant results obtained in three independent investigations[4-6] and are accurate to 0.05 unit. The values for *m*-OCH$_3$ and 3,5-di-OCH$_3$ were measured by ourselves; see Experimental Section. The values for water are based largely on the work of Biggs;[7,8] those for acetic acid are quoted from the work of Ceska and Grunwald.[2] The table does not include any substituents, such as NO$_2$ or CN, that interact strongly by electron-removing resonance.

Table I. Substituent Effects in the Base Dissociation of Aniline in Various Solvents

Substituent	δ_R log K_i in HAc, 30°	δ_R log (K_iK_d) in HAc, 30°	δ_R log K_B in MeOH, 25°	δ_R log K_B in EtOH, 25°	δ_R log K_B in H$_2$O, 25°
H	0.00	0.00	0.00	0.00	0.00
p-OCH$_3$	0.66	0.72	...	...	0.74
m-OCH$_3$	−0.18	−0.05	0.05	0.00	−0.37
3,5-Di-OCH$_3$	−0.50	−0.43	−0.33	−0.30	−0.78
p-CH$_3$	0.43	...	0.56	0.57	0.48
m-CH$_3$	0.10	0.18	0.20	0.24	0.10
p-Cl	−0.76	−1.17	−1.07	−1.05	−0.62
m-Cl	−1.23	−1.45	−1.53	−1.52	−1.23
p-Br	−0.88	...	−1.20	−1.16	−0.74
p-I	−1.01	...	...	...	−0.82
p-F	−0.31	−0.39	−0.32	−0.35	0.05
m-F	...	...	−1.45	−1.47	−1.01
m-CF$_3$	−1.47	−1.91	...	...	−1.08

The virtual equality of δ_R log K_B in methanol and ethanol is obvious from Table I. Figure 1A compares δ_R log K_B in methanol with δ_R log K_i in acetic acid. The plot shows substantial deviations from equality. The substituents divide themselves roughly into two groups: the halogens are close to one line of unit slope, CH$_3$ and methoxy are close to another. Figure 1B shows that this pattern degenerates into a single straight line of unit slope when δ_R log (K_iK_d) is plotted instead of δ_R log K_i.

2. *Substituent effects of a large group of meta and para substituents on* K_B *of aniline in water are qualitatively different from those on* K_B *in methanol and ethanol or on* K_iK_d *in acetic acid.* Various aspects of this difference are shown graphically in Figures 1, 2, and 3. Figures 1A and 2A show that, although δ_R log K_i in acetic acid is a complex function of δ_R log K_B in both methanol and water, the patterns of the substituent effects in the two cases are quite different. In methanol the line that represents the halogen substituents lies above the line that represents CH$_3$ and OCH$_3$, whereas in water this pattern is reversed. Figure 1B shows that in methanol the correlation of δ_R log K_B by a linear combination of δ_R log K_i and δ_R log K_d (eq 3) is highly successful, with $a = b =$ unity. Figure

$$\delta_R \log K_B = a\delta_R \log K_i \text{ (in HAc)} + b\delta_R \log K_d \text{ (in HAc)} \qquad (3)$$

2B shows the results of an analogous correlation of δ_R log K_B in water. The values of the parameters obtained from the data in Table I by the method of

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[1] This work was supported by the National Science Foundation under Grant GP-3921.

[2] G. Ceska and E. Grunwald, *J. Am. Chem. Soc.*, **89**, 1371 (1967).

[3] I. Kolthoff and S. Bruckenstein, *ibid.*, **78**, 1 (1956).

[4] M. Kilpatrick and C. A. Arenberg, *ibid.*, **75**, 3812 (1953).

[5] N. A. Izmailov and T. V. Mozharova, *Zh. Fiz. Khim.*, **34**, 1709 (1960).

[6] H. Goldschmidt and E. Mathiesen, *Z. Physik. Chem.*, **A119**, 439 (1926).

[7] A. I. Biggs, *J. Chem. Soc.*, 2573 (1961).

[8] See also D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution," Butterworth and Co., Ltd., London, 1965.

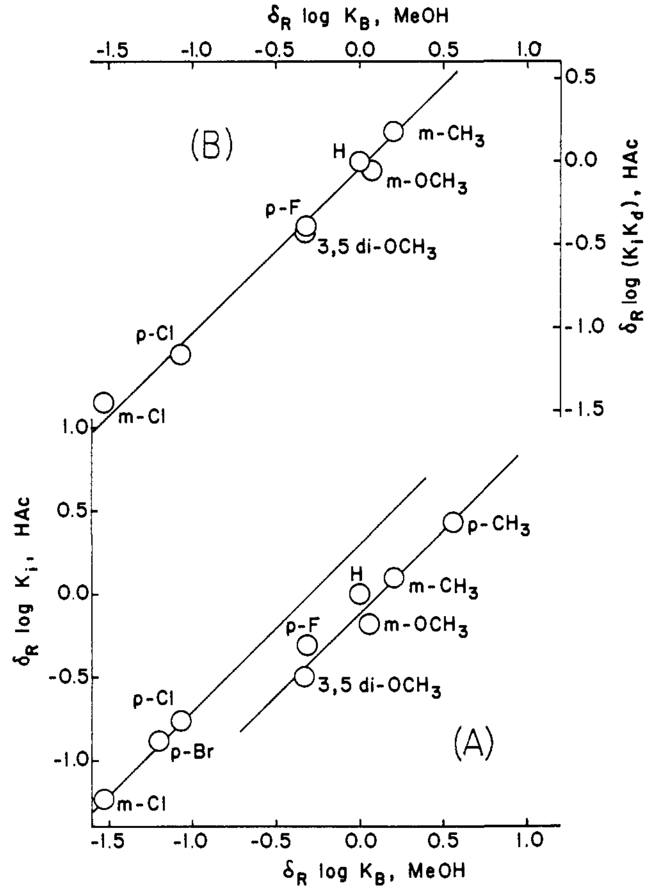

Figure 1. Substituent effects in the base dissociation of aniline in organic solvents: A, δ_R log K_i in acetic acid at 30° *vs.* δ_R log K_B in methanol at 25°; B, δ_R log (K_iK_d) in acetic acid at 30° *vs.* log δ_R log K_B in methanol at 25°. Straight lines are drawn with unit slope.

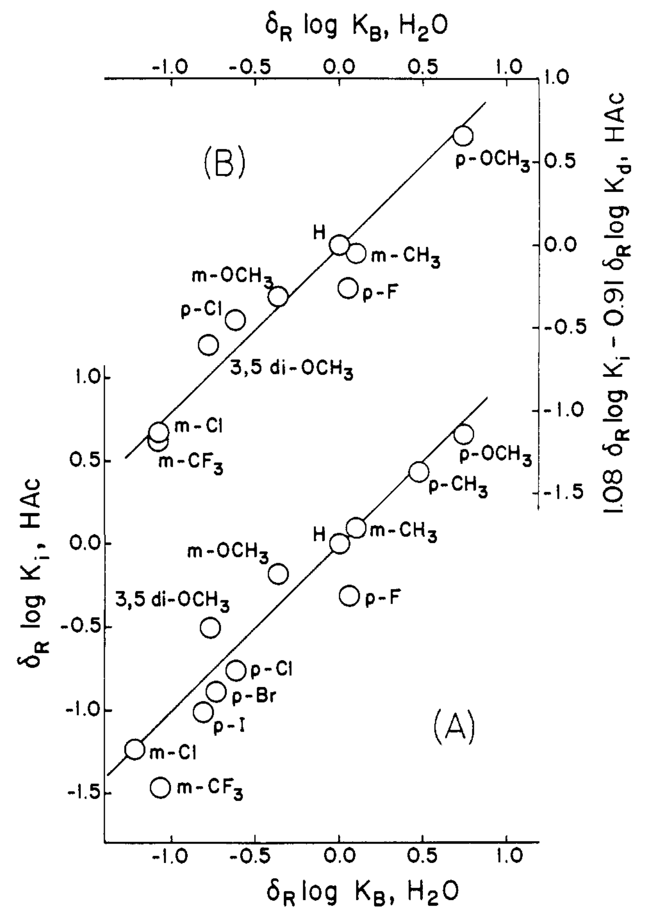

Figure 2. Substituent effects δ_R log K_B in the base dissociation of aniline in water at 25°: A, plot *vs.* δ_R log K_i in acetic acid at 30°; B, plot *vs.* 1.08 δ_R log K_i (in HAc) − 0.91 δ_R log K_d (in HAc). Straight lines are drawn with unit slope.

least squares are $a = 1.08$ and $b = -0.91$. (Note the minus sign!) The correlation is not very successful. The deviations from the line in Figure 2B are only slightly smaller than those from the line of unit slope drawn in Figure 2A, in spite of two adjustable parameters. However, the grouping of the substituents into two classes, (a) the halogens and (b) CH$_3$ or OCH$_3$, that was evident in Figure 2A has disappeared in Figure 2B.

The difference between substituent effects in water and in the nonaqueous solvents is shown perhaps most clearly in Figure 3A. All halogens lie close to a single straight line of slope unity and intercept about −0.4. H, CH$_3$, and OCH$_3$ show a more complicated pattern, but one can argue that H, CH$_3$, and *p*-OCH$_3$ define another straight line of unit slope and zero intercept. In any event, it is perfectly clear that any function that gives a linear correlation with δ_R log K_B in water cannot give a linear correlation with δ_R log K_B in the nonaqueous solvents.

If we examine this matter from the point of view of the Hammett $\rho\sigma$ relationship,[9] then it follows that the correlation with σ, which is good in water,[10] cannot be good in the nonaqueous solvents. This fact has been noted before, particularly by Kilpatrick and Arenberg.[4] One way to repair the discrepancies and force agreement with the Hammett relationship is to introduce a new set of σ^- values, defined so as to reproduce the data specifically in nonaqueous solvents. This approach was used by Taft on a previous occasion[11] and is justified if the new σ^- values have a wide and clearly definable applicability. We fear, however, that this requirement cannot be met in the present case, because it is possible to generate patterns of substituent effects resembling those on K_B of aniline in nonaqueous solvents, without having to employ a nonaqueous solvent! There has long been a feeling among physical organic chemists that a change of solvent is somewhat analogous to a structural modification of the substrate, especially when the solvent molecules interact strongly and at short range with the substrate molecules. Thus Figure 3B compares values of δ_R log K_B for aniline *in water* with those[12] for N-dimethylaniline *in water*. There is an obvious resemblance between the pattern shown here and that produced by δ_R log K_B of aniline *as the solvent is changed* from water to methanol. (Compare Figures 3A and 3B.) In both cases, the halogens define a separate line of unit slope which lies below a line passing through H, *p*-CH$_3$, and *p*-OCH$_3$.

In Figures 1–3 we have included lines of unit slope to represent solvent effects to the same first order of approximation that leads to linear free energy correla-

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[9] (a) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter 7; (b) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

[10] The correlation coefficient is 0.995; see ref 9b.

[11] R. W. Taft, Jr., *J. Phys. Chem.*, **64**, 1805 (1960).

[12] A. V. Willi, *Helv. Chim. Acta*, 40, 2019, 2032 (1957).

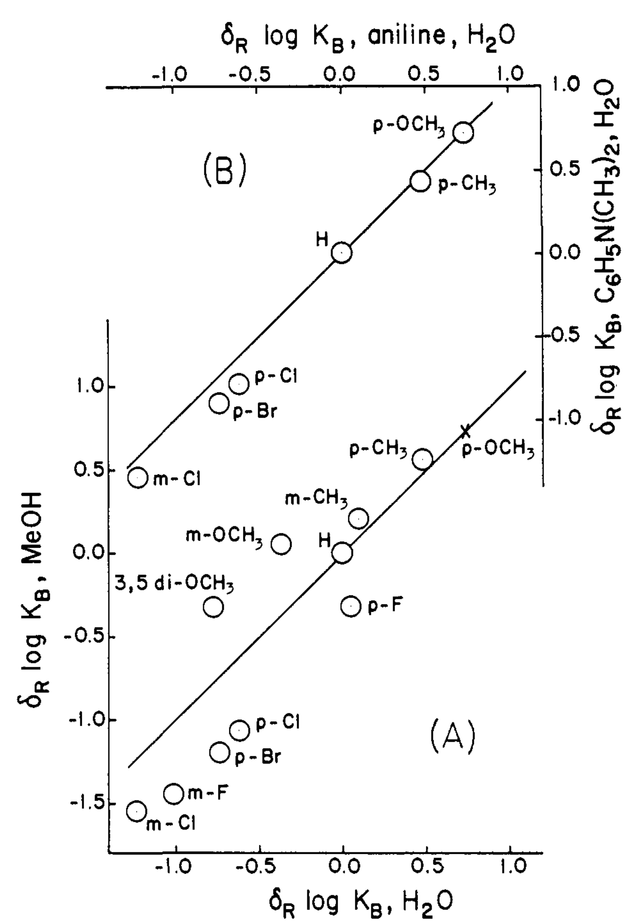

Figure 3. Analogy of a change of solvent to a structural modification of the substrate: A, $\delta_R \log K_B$ for aniline in water *vs.* $\delta_R \log K_B$ for aniline in methanol; B, $\delta_R \log K_B$ for aniline in water *vs.* $\delta_R \log K_B$ for N-dimethylaniline in water. All data at 25°. Straight lines are drawn with unit slope.

tions of substituent effects.[13] To this order of approximation the interaction of substituent and solvent effects is neglected.

3. *In linear free energy correlations of reactivity with basicity in nonaqueous solvents, one should probably use K_i as a measure of basicity rather than K_B.* In general base catalysis or in nucleophilic displacement reactions, the transition state is more like an ion pair than like a pair of dissociated ions. Hence ionization rather than base dissociation is the better model of basicity. The distinction is meaningful because substituent effects in ionization and in ion-pair dissociation involve different interaction mechanisms.[2] For example, Figure 4 shows a plot of substituent effects on the second-order rate constant, k, of a reaction in which aniline acts as a nucleophile[14] against two different measures of basicity. Although the solvent used in the rate determinations is ethanol, the plot of $\delta_R \log k$ *vs.* $\delta_R \log K_B$ of aniline in ethanol is a poor approximation to a single straight line, whereas the plot *vs.* $\delta_R \log K_i$ of aniline in acetic acid conforms to a straight line within the experimental error.

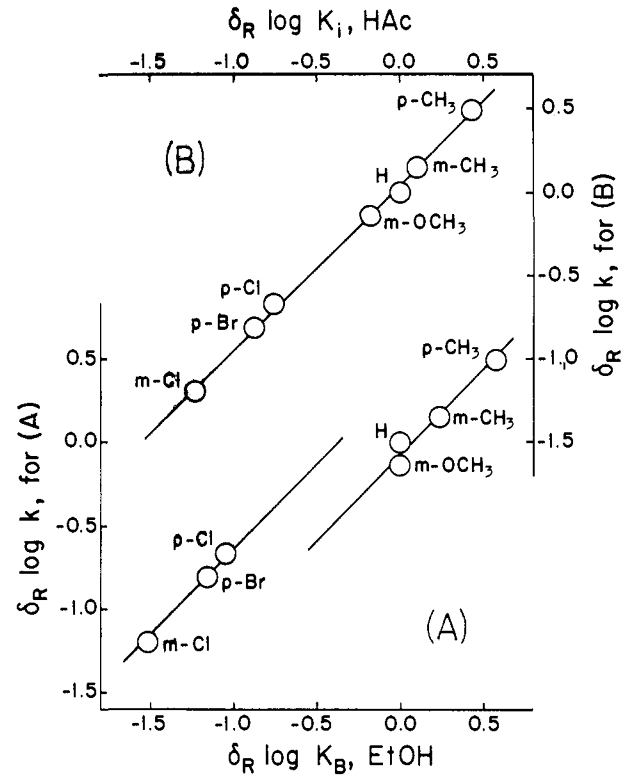

Figure 4. Linear free energy correlation of reactivity with different measures of basicity. $\delta_R \log k$ for the reaction of *meta*- and *para*-substituted anilines with 2,4-dinitrophenyl chloride in ethanol at 35° plotted *vs.* A, $\delta_R \log K_B$ of aniline in ethanol at 25°; B, $\delta_R \log K_i$ of aniline in acetic acid at 30°. k is the second-order rate constant.

Experimental Section

Materials. Reagent grade methanol and ethanol were distilled from calcium hydride. For other materials, see the preceding paper.[2]

Measurements of Relative Basicity. Equilibrium constants, K_4, for reaction 4 were measured spectrophotometrically at 30° in methanol and ethanol; B is *m*-methoxyaniline or 3,5-dimethoxyaniline.

$$p\text{-FC}_6\text{H}_4\text{NH}_3^+ + \text{B} \rightleftharpoons p\text{-FC}_6\text{H}_4\text{NH}_2 + \text{BH}^+ \qquad (4)$$

aniline. Log K_4 is equal to the difference in log K_B for B and *p*-fluoroaniline. $\delta_R \log K_B$ (relative to aniline) is known for *p*-fluoroaniline at 25° (Table I), and if we neglect the small temperature dependence of log K_4, $\delta_R \log K_B$ is thus evaluated for B. To obtain absolute values for pK_A we used as standards: (a) pK_A = 6.55 for *p*-toluidinium ion in methanol at 25°,[15] and (b) pK_A = 5.70 for anilinium ion in ethanol at 25°.[6]

Details of spectral measurements are the same as reported previously.[2] The following procedure was used. Dilute solutions of *p*-fluoroaniline and HCl in the given solvent were mixed such that the equivalents of *p*-fluoroaniline were slightly in excess of those of HCl, and the precise ratio of [p-FC$_6$H$_4$NH$_3^+$] to [p-FC$_6$H$_4$NH$_2$] was determined spectrophotometrically at 315 mμ where dilute *p*-fluoroanilinium ion does not absorb measurably. A suitable, small quantity of B was then introduced and the extent of reaction 4 at equilibrium measured at 265 mμ (where BH$^+$ is the major absorbing species). Required extinction coefficients in the given solvents were determined (a) for the anilines, from optical data on solutions of the anilines without added HCl; (b) for the anilinium ions, from optical data on solutions of the anilines in 0.1 *M* HCl.

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[13] J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, pp 139–155.

[14] (a) A. Singh and D. H. Peacock, *J. Phys. Chem.*, **40**, 669 (1936); (b) N. B. Chapman, D. K. Chaudhuri, and J. Shorter, *J. Chem. Soc.*, 1975 (1962).

[15] M. Cocivera, E. Grunwald, and C. F. Jumper, *J. Phys. Chem.*, **68**, 3234 (1964).