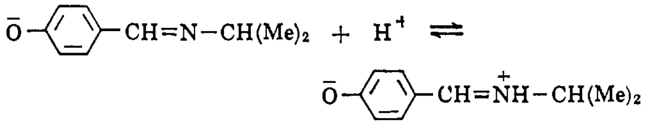
If we accordingly assume a single mechanism for the whole 7–14 pH range, the rate constants are related by the following equation

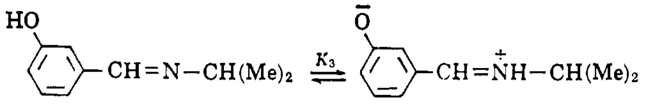
$$k_{\text{obsd}}[\text{S}_0] = k_2[\text{SH}^+][\text{OH}^-] + k_3[\text{S}][\text{OH}^-] \qquad (7a)$$

with $[\text{S}_0] = [\text{S}] + [\text{SH}^+] + [\text{S}^-]$, for the *o*- and *p*-hydroxy compounds, where the protonated form of the anion is identical with the zwitterion, *i.e.*, with the ketoamine tautomer.



This is not the case with the *m*-hydroxy derivative, where the equilibrium constant for the formation of the zwitterion should be introduced.

$$k_{\text{obsd}}[\text{S}_0] = k_2[\text{SH}^+][\text{OH}^-] + k_3K_3[\text{S}][\text{OH}^-] \qquad (7b)$$



As K_3 is unknown, an apparent constant $k_3' = k_3K_3$ will be obtained for the *m*-hydroxy derivative. The values of the rate constants calculated by use of eq 7 are given in Table I.

In conclusion, it appears from our results that hydroxy derivatives of N-benzylidene-2-aminopropane are similar to other derivatives in their kinetic behavior during the hydrolysis reaction, in the full 0–14 pH range. The hypothesis of an internal catalysis by O^- in the *ortho* position[17,18] is not consistent with our results. Indeed, at pH 14, *o*-O^- and *o*-OCH_3 derivatives have rates of the same order of magnitude, as is also the case with the *meta* and *para* derivatives.

As our results show that no accumulation of intermediate occurs at any pH value, we may apply the steady-state approximation to the concentration of the carbinolamine intermediate. This leads to the formula

$$k_{\text{obsd}} = \frac{k_1k_4[\text{H}^+] + k_2k_4 10^{-14} + k_3k_4K_1[\text{OH}^-]}{\{K_1 + [\text{H}^+] + K_1K_2/[\text{H}^+]\}\{k_{-1}[\text{H}^+] + k_{-2} + k_{-3}[\text{OH}^-] + k_4\}} \qquad (8)$$

Moreover, individual values of some real rate constants may be calculated from the horizontal parts of the kinetic curves in Figure 1. This allows us to recalculate the apparent rate constant over the whole pH range—this has been made for the *p*-hydroxy compound in Figure 1—and to note the excellent agreement between the theoretical and the empirical curves.

Acknowledgment. One of us (J. J. C.) is indebted to Industrial Distributors (1946), Johannesburg, for financial support.

(17) R. L. Reeves, *J. Org. Chem.*, 30, 3129 (1965).

(18) T. C. French, D. S. Auld, and T. C. Bruice, *Biochemistry*, **4**, 77 (1965).

Kinetic Studies of Hydrogen Exchange in Dialkylanilines. II

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Abstract: Further kinetic and thermodynamic parameters for hydrogen exchange in substituted dialkylanilines are reported. Qualitative discussion of the reactive species is followed by consideration of the dependence of rate constant on acidity and solvent composition in relation to possible reaction mechanisms. The evidence supports an A-SE2 mechanism, in which exchange occurs on the basic form of the dialkylaniline molecule. A linear relationship between *external* activation enthalpy and entropy is observed.

The kinetic data reported in the previous paper[2] suggested that the exchange reaction is a typical electrophilic substitution occurring only in acid solution. The influence of substituents was shown to follow the Hammett $\rho\sigma$ relationship, giving particularly good linearity when using the electrophilic substituent constants σ^+. In this paper we report the final measurements from this phase of the work and consider possible reaction mechanisms which are consistent with the observations.

Analysis of the kinetic data from variously substituted dialkylanilines has led to the development of a satisfactory relationship between activation entropy and enthalpy, in which a clear distinction has been made between the internal and external components. This relationship not only serves to complement the Hammett $\rho\sigma$ relationship previously established for exchange in this system,[2] but also provides data to support the concept of separability of internal and external entropy and enthalpy effects.[3]

The effect of changing acidity on the reaction rate has been studied, and the application of the Hammett acidity function considered.[4] The role of acidity functions in determination of reaction mechanism in

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[1] Material taken from a thesis by I. Lee submitted in partial fulfillment of the Ph.D. degree.

[2] B. B. P. Tice, I. Lee, and F. H. Kendall, *J. Am. Chem. Soc.*, **85**, 329 (1963).

[3] (a) L. G. Hepler, *ibid.*, **85**, 3089 (1963); (b) K. J. Laidler, *Trans. Faraday Soc.*, **55**, 1725 (1959); (c) C. D. Ritchie and W. F. Sager, *Progr. Phys. Org. Chem.*, **2**, 323 (1964).

[4] L. P. Hammett, *Chem. Rev.*, **16**, 67 (1935).

general[5] and in hydrogen exchange in particular[6] have been widely discussed in recent years.

We have shown that for the dialkylaniline system, proportionality between the rate constant and the acidity function h_0 can be consistent with the remaining evidence which points to an A-SE2 mechanism,[7] although on its own, application of the acidity function may lead to ambiguous conclusions. It has not been practicable to apply all the diagnostic tests summarized by Schulze,[6c] but all the results obtained are consistent with the suggestion that, in general, aromatic hydrogen exchange proceeds by a common A-SE2-type mechanism.[6b,c]

Experimental Section

(1) **Materials.** A commercial grade (British Drug Houses) of *p*-nitroaniline was purified by double recrystallization from ethanol, mp 149°; lit.[8] mp 149°.

Nitrobenzene, a commercial grade (BDH), was purified by distillation under reduced pressure through a 10-in. Dufton column, bp 76° 10 mm), lit.[8] bp 93° (18 mm). The other materials used were prepared as previously described.[2]

(2) **Indicator Measurements.** Indicator solutions were prepared by separately dissolving accurately weighed, purified *p*-nitroaniline and nitrobenzene in 50% aqueous ethanol by weight, to give concentrations of 4×10^{-3} and 5.78×10^{-3} mole/l., respectively. For a series of ethanol–water compositions, sulfuric acid was added to give acid concentrations of 1.09 and 1.82 *M*. Portions of indicator solutions (1 ml) were diluted with each of these solvent mixtures and bulked to 100 ml in standard flasks.

Optical densities were measured at wavelength λ 382.5 mμ for each solution with a Beckman DK2 spectrophotometer, and molar extinction coefficients were calculated. The conjugate acid to base ratio, *I*, was determined from the relationship

$$I = \frac{C_{\mathrm{BH^+}}}{C_{\mathrm{B}}} = \frac{\epsilon^{\lambda}{}_{\mathrm{B}} - \epsilon^{\lambda}}{\epsilon^{\lambda} - \epsilon^{\lambda}{}_{\mathrm{BH^+}}}$$

where $\epsilon^{\lambda}{}_{\mathrm{B}}$ and $\epsilon^{\lambda}{}_{\mathrm{BH^+}}$ are the molar extinction coefficients at wavelength λ of the basic and the conjugate acid forms, and ϵ^{λ} is the coefficient for a solution containing both forms.[8,9]

For the measurement of $\epsilon^{\lambda}{}_{\mathrm{B}}$ and ϵ^{λ}, *p*-nitroaniline was used since it has a large difference between $\epsilon^{\lambda}{}_{\mathrm{B}}$ and $\epsilon^{\lambda}{}_{\mathrm{BH^+}}$, and a basicity which gives a suitable value of $[\mathrm{BH^+}]/[\mathrm{B}]$ in the acidities used. The ultraviolet and the visible light absorption of *p*-nitroaniline becomes almost identical with that of nitrobenzene in sufficiently strong acid, and therefore nitrobenzene was used for the determination of $\epsilon^{\lambda}{}_{\mathrm{BH^+}}$. The data obtained are given in Table I.

(3) **Kinetic Results.** The general procedure used for the kinetic measurements was the same as that described previously.[2] The effect of solvent composition on reaction rate was determined by measuring the rate of exchange between N,N-dimethylaniline and tritium in aqueous reaction media of varying acidity and ethanol content. In each series, the temperature and N,N-dimethylaniline concentration were kept constant. The results are summarized in Tables II and III.

Rate constants for exchange in 95% ethanol were also determined at two or more temperatures for varying acid/amine ratios, from which activation energies were calculated (Table IV).

Table I. The Indicator Measurements[a]

Solvent, wt % ethanol	H_2SO_4, *M*	Optical density	Extinction coef[b]	*I*
20	0.00	0.590	14,750	
	1.09	0.042	1,050	13.048
	1.82	0.015	375	38.333
35	0.00	0.629	15,725	
	1.09	0.114	2,850	4.518
	1.82	0.036	900	16.472
50	0.00	0.631	15,775	
	1.09	0.198	4,950	2.187
	1.82	0.060	1,500	9.517
65	0.00	0.587	14,675	
	1.09	0.226	5,650	1.597
	1.82	0.082	2,050	6.159
80	0.00	0.650	16,250	
	1.09	0.256	6,400	1.539
	1.82	0.104	260	5.231
95	0.00	0.638	15,950	
	1.09	0.129	3,225	3.946
	1.82	0.037	925	16.243

[a] The indicator was 4.00×10^{-5} *M p*-nitroaniline; temperature 20 ± 0.1°. For nitrobenzene indicator solutions, optical densities were zero and therefore $\epsilon^{\lambda}{}_{\mathrm{BH^+}} = 0$. [b] Molar extinction coefficient measured at λ 382.5 mμ.

Table II. Rates of Tritium Exchange, Varying Acidity

H_2SO_4, *M*	Ethanol, wt %	Rate × 10^3, mole $l.^{-1}$ hr^{-1}
0.5	0	6.41[a]
1.0	0	7.15
1.5	0	7.02
2.0	0	6.32
2.5	0	5.98
3.0	0	5.58
0.06	95	5.07[b]
0.125	95	16.9
0.25	95	45.8
0.50	95	52.9
1.0	95	61.7

[a] N,N-Dimethylaniline, 0.46 *M*; 75 ± 0.1°. [b] N,N-Dimethylaniline, 0.5 *M*; 83.9 ± 0.1°.

Table III. Rates of Tritium Exchange, Varying Ethanol Content

H_2SO_4, *M*	Ethanol, wt %	Rate × 10^3, mole $l.^{-1}$ hr^{-1}
1.09	20	8.87[a]
1.09	35	9.97
1.09	50	11.9
1.09	65	13.6
1.09	80	15.5
1.09	95	19.4
1.82	20	7.47
1.82	35	8.72
1.82	50	9.49
1.82	65	10.4
1.82	80	11.6
1.82	95	14.0

[a] N,N-Dimethylaniline, 0.46 *M*; 75 ± 0.1°.

Discussion

Reactive Species. The results reported here and previously[2] were obtained from kinetic measurements on dialkylanilines dissolved in excess strong acid in which the dialkylaniline was present mainly as the conjugate-acid ion $[\mathrm{R_2N^+HArH}]$. However, theoretical considerations and present experimental evidence suggest that hydrogen exchange does not occur directly on this ionic species.

The quaternary ammonium group in the conjugate acid ion would be strongly deactivating and *meta*

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[5] F. A. Long and M. A. Paul, *Chem. Rev.*, **57**, 935 (1957).

[6] (a) V. Gold, R. W. Lambert, and D. P. N. Satchell, *J. Chem. Soc.*, 2461 (1960), and earlier references therein; (b) A. J. Kresge and Y. Chiang, *J. Am. Chem. Soc.*, **84**, 3976 (1962); (c) J. Schulze and F. A. Long, *ibid.*, **86**, 331 (1964).

[7] (a) The terminology used is that of C. K. Ingold, "The Structure and Mechanism of Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953. (b) A. J. Kresge and Y. Chiang, (*J. Am. Chem. Soc.*, 83, 2887 (1961)) have discussed this terminology in relation to hydrogen exchange.

[8] E. A. Braude, *J. Chem. Soc.*, 1971 (1948).

[9] H. Kwart and A. L. Goodman, *J. Am. Chem. Soc.*, **82**, 1947 (1960).

Table IV. Activation Energies at Varying Acid/Amine Ratios

Acid/amine	Temp, ±0.1 °K	Log k + 3[a]	E_A, kcal
0.25	343.4	0.514	
	357.0	1.100	23.8
2.00	337.1	0.544	
	344.3	0.912	
	350.4	1.229	
	353.1	1.334	
	357.0	1.548	27.8
4.00	348.1	0.874	
	353.3	1.101	
	357.0	1.313	
	363.1	1.581	27.7

[a] $k = \{-2.303/([A] + [B])\}$ [log $(1 - F)/t$], l. mole^{-1} hr^{-1}, as previously.[2]

Table V. Some Thermodynamic Parameters

	Aniline	ΔH^*_B, kcal	$-\Delta S^*_B$, eu	σ^+ [a]	$(\delta\Delta H^*_B + 2.3RT\rho\sigma^+)$, kcal	$\delta\Delta S^*_B$, eu
1	N,N-Dimethyl-	19.3	18.3	0	0	0
2	*p*-Methyl-N,N-dimethyl-	19.9	15.7	−0.066	+0.9	+2.6
3	*p*-Methoxy-N,N-dimethyl-	20.4	16.0	+0.047	+0.9	+2.3
4	*p*-Fluoro-N,N-dimethyl-	19.8	22.8	+0.352	−1.2	−4.5
5	*p*-Chloro-N,N-dimethyl-	16.1	32.5	+0.399	−5.1	−14.2
6	*p*-Bromo-N,N-dimethyl-	15.8	35.8	+0.405	−5.5	−17.5
7	*m*-Methyl-N,N-dimethyl-	17.0	20.1	−0.311	−0.8	−1.8
8	3,5-Dimethyl-N,N-dimethyl-	18.9	11.8	−0.622	+2.6	+6.5
9	*m*-Ethoxy-N,N-diethyl-[b]	18.1	10.4	−0.778	+2.2	+2.6
10	*m*-Nitro-N,N-dimethyl-	19.9	29.9	+0.790	−3.7	−11.6
11	*o*-Fluoro-N,N-dimethyl-	22.7	21.0	+0.352	+1.5	−2.7
12	*o*-Chloro-N,N-dimethyl-[c]	32.9	+2.4	+0.399	+11.4	+20.7

[a] The modified electrophilic substituent constant of H. C. Brown and M. Okamoto, *J. Am. Chem. Soc.*, **80**, 4979 (1958). σ^+_m or σ^+_p were chosen with regard to effect of substituent on reactive sites which are assumed to be *ortho* and/or *para* to N,N-dimethyl group. [b] Values of $\delta\Delta H^*_B$ and $\delta\Delta S^*_B$ for this compound were derived from ΔH^*_B and ΔS^*_B for N,N-diethylaniline reported previously.[2] [c] For this compound the kinetic data in paper I were incomplete. A value has now been obtained for k at 90° of 1.04×10^{-4} l. mole^{-1} hr^{-1}. This value and the previous one at 106° give an activation energy, E_A, of 40.4 kcal.

directing to electrophilic attack, whereas the experimental results indicate *ortho–para* exchange, which can be further activated by electron-releasing substituents on the aromatic ring. Thus the exchange numbers reported previously[2] can only be reasonably interpreted by assuming *ortho–para* exchange. Further convincing support comes from 3,5-dimethyl-N,N-dimethylaniline in which both *meta* positions are blocked; the measured rate constant is higher than that for N,N-dimethylaniline itself or for any other of the compounds studied. Similar conclusions were reached by Best and Wilson[10] in respect of aniline and phenol undergoing deuterium exchange.

It seems certain therefore that hydrogen exchange must occur on the small concentration of the basic dialkylaniline molecular species always present in the acid–base equilibrium. The experimental results can then be satisfactorily interpreted if it is assumed that the apparent activation enthalpy $\Delta H^*_{BH^+}$ and entropy $\Delta S^*_{BH^+}$, as calculated from measured kinetic data, refer to two consecutive reactions, *i.e.*, initial dissociation of the conjugate-acid ion followed by hydrogen exchange

$$[R_2{}^+NHArH] \longrightarrow [R_2NArH] + H^+(H_2O)_n$$

with dissociation parameters $\Delta H°$ and $\Delta S°$ followed by

$$[R_2NArH] + T^+(H_2O)_n \longrightarrow [R_2NArT] + H^+(H_2O)_n$$

with true activation parameters ΔH^*_B and ΔS^*_B.

The true activation parameters ΔH^*_B and ΔS^*_B can then be calculated from the kinetically measured parameters $\Delta^*_{BH^+}$, $\Delta S^*_{BH^+}$ and $\Delta H°$, $\Delta S°$ derived from measured pK values for the dialkylanilines. These calculations have been completed for all the compounds studied, and values of ΔH^*_B and ΔS^*_B are given in Table V. Free energy values, ΔF^*_B, were used to construct a Hammett $\rho\sigma$ plot for which a correlation coefficient of 0.992 was obtained. Attempts to prepare such plots using $\Delta F^*_{BH^+}$, assuming *meta* exchange on the conjugate acid ion, failed completely, with no evidence of linearity.

In addition to this indirect evidence of exchange occurring on the basic dialkylaniline molecule, it seemed likely that under conditions of stoichiometric acid deficiency (acid/amine ratios < 0.5), it would be possible to detect a reduction in measured activation energy corresponding to the increased proportion of direct exchange on the basic molecular species. Under these conditions both single-step and two-step consecutive reactions will occur and the *measured* activation energy would be the weighted mean of the activation energy for the single-step exchange occurring directly on the basic form and of the activation energy for the two consecutive reactions. Table IV records results from experiments of this kind; E_A of 23.8 kcal for acid/amine ratio of 0.25 does indeed lie between expected limits of 27.8 and 20 kcal, the latter value being calculated from $\Delta H^*_B = \Delta H^*_{BH^+} - \Delta H°$, where $\Delta H°$ is the dissociation enthalpy for the conjugate-acid ion.

Influence of Acidity on Exchange Rate. Preliminary experiments reported previously indicated that the exchange rate became almost constant for acid/amine ratios greater than 1. Quantitative measurements of the effect of acidity on the exchange rate have been extended, and the results summarized in Table II confirm the earlier indications. These results for aqueous and ethanolic reaction media are illustrated by the full lines in Figure 1.

A quantitative expression showing the effect of acidity on the specific rate constant of exchange may be derived. When the stoichiometric acid/amino ratio is greater than 1, the free acid concentration greatly exceeds that of the free base, and a pseudo-first-order rate constant

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(10) A. P. Best and C. L. Wilson, *J. Chem. Soc.*, 28 (1938).

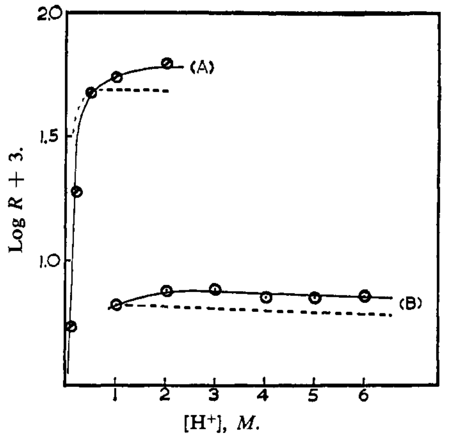


Figure 1. Effect of acidity on reaction rate: (A) 0.5 *M* dimethylaniline in 95% ethanol at 83.9°; (B) 0.5 *M* dimethylaniline in water at 75°.

k' can be defined as

$$k' = R/[B] \tag{1}$$

where R is the measured exchange rate and [B] is the concentration of the free-base species [R_2NArH]. The free base will exist in equilibrium with its conjugate-acid ion as shown in eq I. Applying the definition of

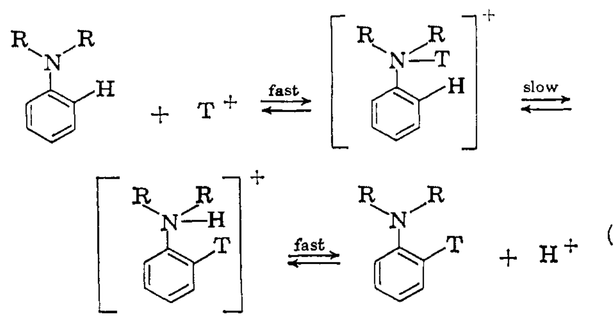
$$R_2NArH + H_3O^+ \longrightarrow R_2N^+HArH + (H_2O) \quad \text{(I)}$$

the Hammett acidity function, H_0, the concentration of free base, [B], at equilibrium can be calculated from

$$\log [B] = H_0 - pK_a + \log [BH^+]$$

where pK_a is the dissociation constant of the conjugate acid. Because the acid is in excess, the concentration of [BH^+] can be assumed constant and sensibly equal to the stoichiometric amount of base added.

Values of the rate constant k' for various acidities were obtained from eq 1 by substitution of calculated values of free base [B] and the measured exchange rates, R. In Figure 2, values of log k' are plotted against $-H_0$ and [H_3O^+] (lines A and B). The slope of the linear log $k'/-H_0$ function is 0.94. Following Hammett[4] and Gold and Satchell,[11] the proportionality between the rate constant and h_0 may be interpreted in terms of an A-1 type mechanism for exchange. Such a mechanism would require a rate-determining unimolecular rearrangement within a conjugate-acid ion, and one possibility may be initial protonation on the basic nitrogen followed by internal rearrangement (II). However, with this type of mechanism it is difficult to account for the observation that exchange occurs in positions *ortho* and *para* to the dialkylnitrogen group and for the observed effect of substituents in the aromatic ring.



(II)

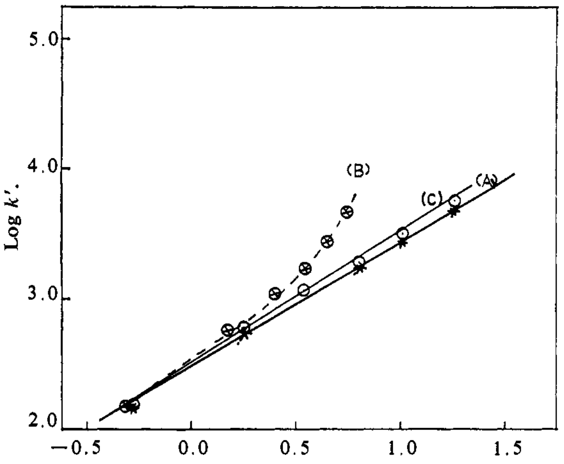
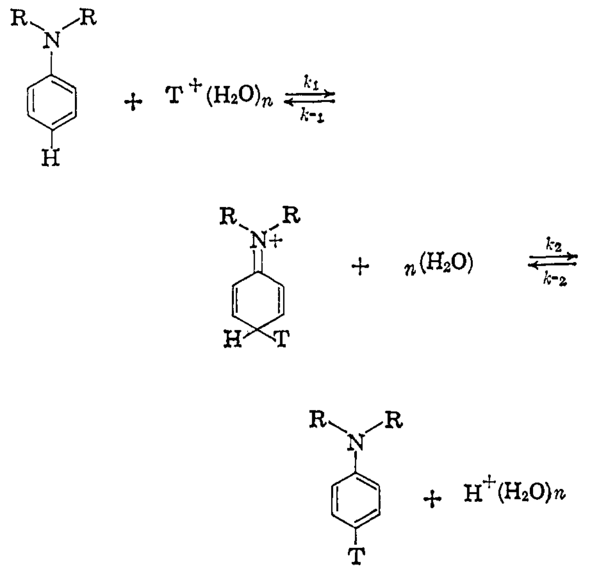


Figure 2. Dependence of rate constant on acidity function at 75° ± 0.1° in aqueous solution: (A) log $k' = -H_0$ + constant; (B) log k' = log [H_3O^+] + constant; (C) log $k' = -H_0$ + log a_{H_2O} + constant.

Other authors have recently emphasized that a linear relationship between exchange rates and the acidity function h_0 may not be restricted to A-1 mechanisms.[5,6b,c] In fact the trend in recent literature appears to be toward acceptance of an A-SE2 or slow proton-tranfer mechanism for aromatic hydrogen exchange.[6c,7b]

For the dialkylaniline system too, it is possible to derive an expression which accounts for the observations if it is assumed that A-SE2-type exchange occurs through a *carbon* conjugate-acid ion formed by protonation of the basic form of the molecule. The reaction sequence may be written as in (III). In this reaction scheme the intermediate state is represented as a general carbonium ion. The nature of the transition state in various hydrogen exchanges has been discussed by other workers,[6a,b,12] and generally they favor the participation of an intermediate complex rather than just a true



(III)

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(11) V. Gold and D. P. N. Satchell, *J. Chem. Soc.*, 3609 (1955).

(12) C. Eaborne and R. Taylor, *ibid.*, 3301 (1960).

transition state. For the dialkylaniline system also, a σ-bonded *carbon* conjugate-acid ion is a plausible intermediate in view of the stabilizing influence of electron delocalization from the nitrogen atom. In this context, it is relevant to recall that when electron delocalization is strongly hindered, as in 2,6-dimethyl-N,N-dimethylaniline, 2-methoxy-N,N-dimethylaniline, etc., hydrogen exchange is negligible under all conditions tested.[2] An intermediate complex is also consistent with preliminary results of isotope effect measurements on dialkylanilines currently in progress.[13]

The transition state corresponding to the formation and decomposition of the intermediate may, to a first approximation, be regarded as symmetrical. Then assuming that the intermediate ion is in steady-state concentration and that in the early stages the back reaction can be ignored, application of the transition-state kinetic theory leads to eq 2 for the rate of exchange, R, in the forward direction.

$$R = k''[\mathrm{B}][\mathrm{A}]\frac{f_\mathrm{B}f_\mathrm{A}}{f^*} \qquad (2)$$

where k'' is the observed specific rate constant for exchange, and it is related to reaction scheme III by

$$k'' = \frac{k_1}{1 + \dfrac{k_{-1}}{k_2}}$$

f_B and f_A are the activity coefficients of the base [R_2NArH], and the acid [$T^+(H_2O)_n$]; f^* is the activity coefficient of the transition state corresponding to decomposition of the intermediate complex.

The activity of the hydrated tritium ion $a_\mathrm{A} = [\mathrm{A}]f_\mathrm{A}$ in eq 2 is proportional to the hydrogen ion activity given by eq 3 for the preequilibrium shown in (I).

$$a_{\mathrm{H_3{}^+O}} = K_\mathrm{a}\frac{a_{\mathrm{BH^+}}a_{\mathrm{H_2O}}}{a_\mathrm{B}} \qquad (3)$$

Substituting from eq 3 for $[\mathrm{A}]f_\mathrm{A}$ in eq 2 and taking logarithms

$$\log R = \log [\mathrm{BH^+}] + \log a_{\mathrm{H_2O}}\frac{f_{\mathrm{BH^+}}}{f^*} + \text{constant} \qquad (4)$$

where the constant includes k'', K_a, and the proportionality factor between $a_{\mathrm{T^+}}$ and $a_{\mathrm{H^+}}$, all of which may be regarded as sensibly constant for any given substrate in dilute solution.

Equation 4 satisfactorily accounts for the observed dependence of exchange rate on acidity. This is demonstrated by the broken lines in Figure 1 which are derived from eq 4 and closely follow the observed change in rate with increasing conjugate-acid ion concentration. The term $\log a_{\mathrm{H_2O}}(f_{\mathrm{BH^+}}/f^*)$ only becomes important in more concentrated solutions.

Reaction scheme III can also account for the observed linearity between $\log k'$ and H_0 (Figure 2). Thus by combining eq 1 and 2 to eliminate R

$$k' = k''a_\mathrm{A}\frac{f_\mathrm{B}}{f^*}$$

Substitution for a_A in terms of the Hammett acidity function H_0 and taking logarithms then leads to

$$\log k' = -H_0 + \log a_{\mathrm{H_2O}}\frac{f_\mathrm{B}f_{\mathrm{CH^+}}}{f^*f_\mathrm{C}} + \text{constant} \qquad (5)$$

where f_C = activity coefficient of basic form of indicator and $f_{\mathrm{CH^+}}$ = activity coefficient of protonated form. The constant includes k'' and the proportionality factor between $a_{\mathrm{T^+}}$ and $a_{\mathrm{H^+}}$.

A similar equation but without the $\log a_{\mathrm{H_2O}}$ term can be derived if the water molecule is excluded from reaction Scheme III. In these measurements the $\log a_{\mathrm{H_2O}}$ term was never more than 2% of $\log k'$ so that it has very little effect on the slope of the $\log k'/H_0$ plot. However, it is of interest to note that a replot (Figure 2, line C), taking into account the $\log a_{\mathrm{H_2O}}$ term, changes the slope from 0.94 to almost exactly 1.0.

Effect of Solvent Composition. It has already been established that in the dialkylaniline system, exchange between free base and solvent does not occur in the absence of acid. A strong proton donor is required and for these reaction mixtures the most likely species are hydroxonium and ethoxonium ions. Since the amount of each species and their proton-transfer ability depend on the relative proportion of water and ethanol, a series of measurements were made of changes in exchange rate with increasing ethanol content. The results are summarized in Table III, from which the pseudo-first-order constant k' was calculated. Values of k' are plotted against ethanol content as full lines A_1, A_2 in Figure 3.

The observed decrease in rate constant with increasing ethanol content also may be accounted for in terms of the A-SE2 exchange mechanism. The ability of a solvent system to transfer protons to a substrate can be measured by the indicator ratio $I = [\mathrm{BH^+}]/[\mathrm{B}]$. As discussed by Braude,[14] the extent of proton transfer to a substrate from the water–ethanol solvent is dependent on the dissociation of acid in the solvent and on the properties of the solvated hydrogen ion so formed. Dissociation of mineral acids becomes less complete with increasing alcohol content (that is with decreasing dielectric constant) of the medium, leading to corresponding decrease in the number of protons available for transfer. In Figure 3 the broken lines demonstrate the relationship between indicator ratio values and dielectric constant, and the corresponding change in rate constant shown by the full lines in the region of 20–70% ethanol supports the proposal that proton transfer is concerned in the rate-determining steps. At higher ethanol concentrations, the change in slope of the indicator ratio and rate constant curves may be due, in part, to the ethoxonium ion transferring a proton more readily than the hydroxonium ion. On this account, proton-transfer ability would increase with ethanol content. The equilibrium constant of the reaction $C_2H_5OH_2^+ + H_2O \rightleftarrows C_2H_5OH + H_3O^+$ has been variously reported with values ranging from 5 to 200.[14,15]

Enthalpy–Entropy Relationship. In view of the satisfactory Hammett substituent plot based on ΔF^*_B values, it was of interest to examine the relationship between activation enthalpy and entropy, likewise

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(13) A. Campbell-Ling and F. H. Kendall, unpublished work.

(14) E. A. Braude, *J. Chem. Soc.*, 443 (1944).

(15) (a) C. E. Newall and A. M. Eastham, *Can. J. Chem.*, 39, 1752 (1961); (b) J. M. Kolthoff and S. Bruckenstein, *J. Am. Chem. Soc.*, 78, 1, 10 (1956).

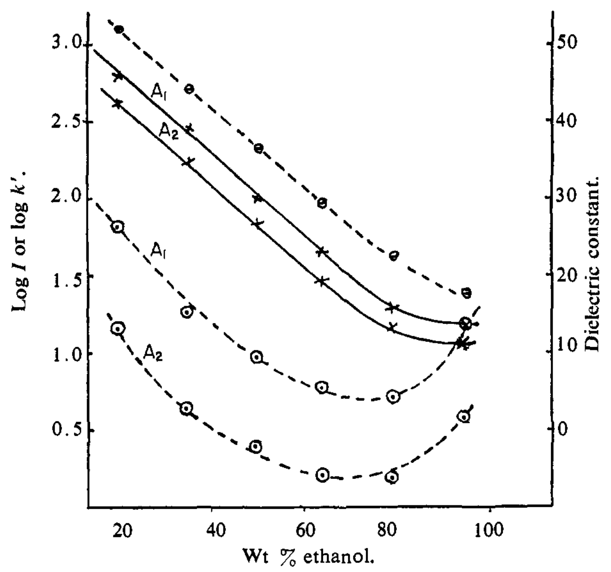

Figure 3. Effect of solvent composition: ⊖, dielectric constant at 75°; ×, log rate constant at 75°; ⊙, log indicator ratio. A₁ = 1.82 *M* H_2SO_4 solution. A₂ = 1.09 *M* H_2SO_4 solution.

assuming exchange on the basic form. The possibility of a correlation between ΔS^*_B and ΔH^*_B was investigated by a conventional isokinetic type plot. For the same 12 compounds, a correlation coefficient of 0.727 was obtained. This is considered to be inadequate to demonstrate a satisfactory and significant "isokinetic relationship." In fact, this reaction appears to fit into the general class of reactions exhibiting satisfactory Hammett $\rho\sigma$ plots, but for which entropies and enthalpies cannot be correlated by Leffler's isokinetic relationship.[16]

However, closer examination of the $\Delta H^*_B/\Delta^*_B$ plot suggested that the rather wide scatter was not indiscriminate and that there was a tendency for the points to form families characteristic of the nature and position of the substituent groups in the aromatic ring.

This observation, together with ideas put forward by Hepler and others,[3] suggested that if the enthalpy and entropy changes were resolved into internal and external components, a relationship may exist between the external parameters. In this treatment, external contributions to enthalpy and entropy are associated with solvent interactions, and the internal contributions arise from differences in enthalpy and entropy within the reactant molecules and the transition state. If the reasonable assumption is made that internal motions of the substituents do not contribute to the activation free energy, *i.e.*, internal activation entropy changes are zero, eq 6 may be used as a test of the external entropy–enthalpy relationship[17]

$$(\delta\Delta H^*_B + 2.3RT\rho\sigma) = b\delta\Delta S^*_B \qquad (6)$$

where the δ and Δ operator symbols represent the effect of substituents and of chemical reaction on the activation enthalpy and entropy; σ is the electrophilic substituent constant of Brown and Okamoto; ρ is the Hammett reaction constant, which for the dialkylaniline system is -3.54 at 65°;[2] b is a constant characteristic of the reaction and can be obtained from the slope of a plot of $(\delta\Delta H^*_B + 2.3RT\rho\sigma)$ against $\delta\Delta S^*_B$. The right-hand side of eq 6 represents the *external* entropy change. Since $\delta\Delta S^*_B = \delta\Delta S^*_{\text{int}} + \delta\Delta S^*_{\text{ext}}$, then for $\delta\Delta S^*_{\text{int}} = 0$, $\delta\Delta S^*_B = \Delta S^*_{\text{ext}}$. Similarly, since $\delta\Delta H^*_B = \delta\Delta H^*_{\text{int}} + \delta\Delta H^*_{\text{ext}}$, it follows that the left-hand side of eq 6 represents the *external* enthalpy changes due to substituents, providing that the term $2.3RT\rho\sigma$ may be identified with $-\delta\Delta H^*_{\text{int}}$. This assumption is consistent with Hammett's original concept in which the σ-substituent constants represent changes in the potential energy of the system. The same result also follows from the Hammett equation $\delta\Delta G^* = -2.3RT\rho\sigma$ for the condition that $\delta\Delta S^*_{\text{int}} = 0$ and b is not too different from T.[18]

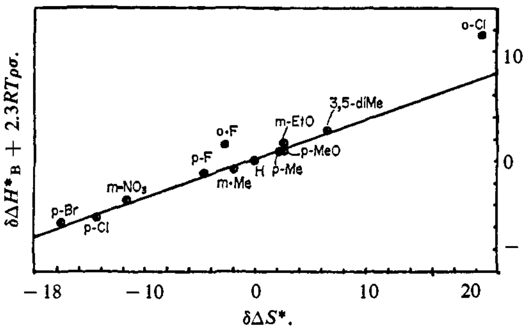

Figure 4. Enthalpy-entropy plot.

Equation 6 was tested by the plot shown in Figure 4 which is based on the data in Table V. The correlation coefficient is 0.971 taking all compounds, but improves to 0.996 when the *ortho* compounds are excluded.

An interpretation of these results may be found in terms of solvation changes accompanying the activation process. Referring to reaction scheme III it may be assumed that formation of the transition-state complex will be a disentropic process giving rise to the over-all negative activation entropies represented by $-\Delta S^*_B$. However, the numerical value of $-\Delta S^*_B$ for each compound will depend strongly on the change in the solvation pattern during activation. Formation of the transition complex from a small, highly solvated tritium ion and the basic aniline molecule would almost certainly lead to net desolvation, the extent depending on the distribution and density of charge on the transition-state positive ion.

The effect of substituents on the degree of desolvation during the activation process will be revealed by the $\delta\Delta S^*_B$ values. Substituents on the aromatic ring which can readily delocalize the positive charge on the transition state will reduce the surface charge density and therefore cause greater desolvation than occurs during activation of the unsubstituted compound. Desolvation corresponds to an increase of entropy, so that we expect these substituents to give positive values of $\delta\Delta S^*_B$ relative to the unsubstituted compound. The

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[16] Reference 3c, p 356.

[17] I. Lee, *J. Korean Chem. Soc.*, 7, 211, 238 (1963); *Chem. Abstr.*, **61**, 5015*e*, 7770*e* (1964).

[18] Using Hepler's approach,[3a] by substituting in $\delta\Delta G^* = \delta\Delta H^*_B - T\delta\Delta S^*_B$ for the condition that $\delta\Delta H^*_{\text{ext}} = b\delta\Delta S^*_{\text{ext}}$ (*i.e.*, compensation occurs) and $\delta\Delta S^*_{\text{int}} = 0$, it follows that

$$\frac{\delta\Delta G^*}{\delta\Delta H^*_{\text{int}}} = 1 + \frac{\delta\Delta S^*_B}{\delta\Delta H^*_{\text{int}}}(b - T)$$

For the dialkylanilines, $\delta\Delta S^*_B/\delta\Delta H^*_{\text{int}}$ ranges from 0.0018 to 0.0038 deg⁻¹ and $(b - T) = 30°$ so that the second term is small and therefore $\delta\Delta G^* \cong \delta\Delta H^*_{\text{int}}$. Substituting in the Hammett equation, $\delta\Delta G^* = -2.3 RT\rho\sigma$ leads to $\delta\Delta H^*_{\text{int}} \cong -2.3RT\rho\sigma$.

increased entropy of desolvation corresponds to greater freedom for solvent molecules, which in turn means decreased interaction energy or increased enthalpy, thus qualitatively accounting for the compensation observed between the external parameters and demonstrated by Figure 4. Those substituents which tend to localize or accentuate the positive charge should give negative values of $\delta\Delta S^*_B$ and $\delta\Delta H^*_{ext}$. With the exception of *m*-methyl-N,N-dimethylaniline and the *ortho*-substituted compounds, all the results follow these predictions.

The significant divergence of the *o*-fluoro and -chloro compounds from the line in Figure 4 may be accounted for in terms of partial steric inhibition of resonance, so that in these circumstances the assumption that $\delta\Delta S^*_{int} = 0$ would be untrue, and the measured $\delta\Delta S^*_B$ represents the sum of activation structural changes, both internal and external to the molecule.

Amination of Haloaromatics with Trichloramine–Aluminum Chloride. σ Substitution and Nucleophilic σ Substitution[1,2]

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Abstract: Amination of halobenzenes (fluoro, chloro, and bromo) and halotoluenes (*o*-, *m*-, and *p*-fluoro, *o*-, *m*-, and *p*-chloro, and *m*-bromo) with trichloramine under Friedel–Crafts conditions was found to proceed by two main competing processes in yields of 20–41%. For example, the system, trichloramine–aluminum chloride–fluorobenzene, gave predominantly *m*-fluoroaniline and *p*-chloroaniline. We propose that the former is produced by a σ-substitution route while the latter is formed by a pathway involving nucleophilic displacement of halide in an intermediate chlorarenonium ion by a nitrogen-containing species (nucleophilic σ substitution). Analogous products were obtained from the other haloaromatics. The ratio of nucleophilic σ substitution/σ substitution was found to vary depending upon the nature of the aromatic substrate, with fluorobenzene and *m*-fluorotoluene providing the highest values. The pathway involving halide displacement represents a new method of aromatic substitution. In certain cases minor amounts of basic materials were isolated, arising from side reactions such as rearrangement and disproportionation. Several other reaction variables were also investigated: time, temperature, and additives. By means of a competitive technique the relative rate of amination, $k_{C_6H_5Cl}/k_{C_6H_6}$, was found to be 0.26–0.44.

Recent reports from this laboratory revealed that direct amination of alkylbenzenes with N-halamines in the presence of a Lewis acid catalyst represents a new method of aromatic substitution (σ substitution) resulting in unusual orientation.[4-6] For example, the predominant basic product from toluene–trichloramine–aluminum chloride consisted of *m*-toluidine. Biphenyl and naphthalene were also investigated in this system.[6] Relative rate studies provided evidence for the crucial involvement of an intermediate arenonium ion.[7] The purpose of the present study was to investigate the behavior of halogen-containing aromatic compounds, specifically the halobenzenes and halotoluenes, toward trichloramine–aluminum chloride.

Results and Discussion

Amination of the haloaromatics was generally carried out by addition of a solution of trichloramine to a heterogeneous mixture of catalyst and aromatic component. In earlier studies with toluene, optimum yields of *m*-toluidine were observed at low temperatures and short reaction times.[4,5,7] However, our investigations with bromobenzene revealed a marked variation in yield with time (Table I), *i.e.*, use of longer reaction periods resulted in greatly improved yields. Temperature was found to have a similar, profound influence (Table II). An increase from 5 to 25° tripled the amount of basic product formed from chlorobenzene (Table II). A further beneficial effect was noted when the reaction was carried out at 50°. At 25°, extending the reaction time beyond 2 hr evoked no change. A temperature of 25° and a reaction period of 2 hr were chosen for the standardized procedure. Higher temperatures were generally avoided due to the volatility, toxicity, and explosive nature of the halamine, and in

Table I. Yield *vs.* Time in Amination of Bromobenzene[a,b]

Time, hr	Basic product, % yield: Aniline	Chloroanilines	Bromoanilines[c]	Total
1.5	0.3	0.8	5.8	6.9
2	0.2	2.4[d]	12.3	14.9[e]
3	0.4	1.8	18.2	20.4

[a] *o*-Dichlorobenzene solvent, 5 ± 5°. [b] Analyzed on column A, 180°. [c] Typical isomer distribution, *o*/*m*/*p*/ ≃ 5/90/5. [d] *o*/*m*/*p*/ ≃ 30/0/70. [e] About 6% of the product was a higher boiling amine whose infrared spectrum indicated a 1,2,4-trisubstitution pattern.

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[1] Paper VI: Chemistry of N-Halamines.

[2] For preliminary reports, see P. Kovacic, J. J. Hiller, Jr., J. F. Gormish, and J. A. Levisky, *Chem. Commun.*, No. 22, 580 (1965); P. Kovacic, R. M. Lange, J. L. Foote, C. T. Goralski, J. J. Hiller, Jr., and J. A. Levisky, *J. Am. Chem. Soc.*, **86**, 1650 (1964).

[3] National Defense Education Act Fellow, 1964–1966.

[4] P. Kovacic, C. T. Goralski, J. J. Hiller, Jr., J. A. Levisky, and R. M. Lange, *J. Am. Chem. Soc.*, **87**, 1262 (1965).

[5] P. Kovacic, J. A. Levisky, and C. T. Goralski, *ibid.*, **88**, 100 (1966).

[6] P. Kovacic and A. K. Harrison, unpublished work.

[7] P. Kovacic and J. A. Levisky, *J. Am. Chem. Soc.*, **88**, 1000 (1966).