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Fast Protolytic Reactions in Aqueous Solutions of Aminobenzoic Acids

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The protolytic reactions in aqueous solutions of benzoic, *o*-, *m*-, *p*-aminobenzoic, N-methylanthranilic and N-dimethyl anthranilic acid have been studied using the high field dispersion and the temperature jump method. The rates of recombination of H^+ with the acid anions are diffusion controlled, although certain structural influences are exhibited. The rates of the conjugate base reactions, *i.e.*, the recombination of the acid molecules with OH^-, are also of the order of magnitude to be expected for a diffusion controlled reaction with the exception of N-dimethylanthranilic acid. In this case, a strong internal hydrogen bond prevents the access of OH^- to the acid proton, slowing down the reaction by several orders of magnitude.

Introduction

The application of high electric field relaxation techniques to the study of rapid reactions has been described in a previous paper.[2] In reaction systems of the type

$$H^+ + R^- \underset{k_D}{\overset{k_R}{\rightleftarrows}} R \qquad (1)$$

(where R represents a weak acid, R^- the corresponding anion), the specific rate constants k_R of a number of such recombination reactions have been shown[3] to approach the theoretical limiting values for a diffusion controlled reaction.[4] Small reproducible differences of rates of recombination have been correlated with predicted steric or electrostatic effects as, for example, in the case of phenols, carboxylic acids, etc.[5] We report here similar investigations of the rates of protolytic reactions in dilute aqueous solutions of several aminobenzoic acids, which, in addition, exhibit some peculiarities due to their ampholytic nature. Cohn and Edsall[6] assembled the ionization constants for several of these acids and expressed the related equilibria in a notation that we will adopt here: (i) the neutral molecule $R \equiv R_2'NRCOOH$ where for the present purpose $R' \equiv H$- or CH_3- and R in the formula is a benzene ring, (ii) the dipolar ion (zwitterion) $R^{\pm} \equiv {}^+HR_2'NCOO^-$, (iii) the ions $R^+ \equiv {}^+HR_2'NCOOH$ and $R^- \equiv R_2'NRCOO^-$. If the over-all concentration c_0 is known, the concentrations of these species and of hydrogen ions are calculable from the experimentally determined equilibrium constants $K_1 = [H^+]([R^{\pm}] + [R])/[R^+]$, $K_2 = [H^+][R^-]/([R^{\pm}] + [R])$, $K_Z = [R^{\pm}]/[R]$, and the conditions of charge neutrality and conservation of matter. Once the relaxation time τ for the recombination reaction 1 has been determined, we can calculate concentrations of H^+ and R^- from the above equations and then the specific rate constants k_R and k_D according to the relations[2,3]

$$\tau = [k_R(c_{H^+} + c_{R^-} + K_{eq})]^{-1} \qquad (2)$$

and

$$K_{eq} = k_D/k_R \qquad (3)$$

Experimental

Method.—As in all relaxation studies of fast reactions,[3] we slightly displaced the system 1 from equilibrium and measured the relaxation time τ for readjustment to the new equilibrium conditions. Our perturbing parameter is the electric field density E and the perturbation is measured as a change in the conductance Λ of the solutions, resulting—at sufficiently high field densities—in a deviation from Ohm's law: the 2nd Wien[7] or Dissociation Field Effect. Onsager[8] has shown this effect to be described quantitatively by the relation

$$(\Delta\Lambda/\Lambda) = [(1 - \alpha)/(2 - \alpha)]b\Delta E \qquad (4)$$

where the degree of dissociation $\alpha = c_i/c_0$, c_i is the concentration of each of the recombining ions, and b is a known function of ion mobilities, ion charge, temperature and the dielectric constant of the solvent. In the present application, the exact expression of b is not required since the dispersion method depends only on the experimentally observed linear dependence of $\Delta\Lambda/\Lambda$ on ΔE over the 30 to 100 kv./cm. range. The high voltage is applied as a pulse in the form of a critically damped, harmonic oscillation, the shortest of which has a duration of 0.2 μsec. This voltage is dropped across a balanced, symmetric, bifilar-concentric bridge. The sample and reference cells have the same dimensions (2.0 mm. electrode distance). The reference cell contains a dilute HCl solution to cancel the 1st Wien Effect[9] in the sample cell. The other two arms of the bridge contain NaCl solutions, but in these the field density does not exceed a few kv./cm. Approximately 30 sec. elapse between pulses so that changes in conductance due to heating are negligible. When the pulse length becomes comparable to the relaxation time τ of equilibration a dispersion of the field effect occurs from which τ can be deduced.[2,3]

Conditions and Results.—Our experimental results are shown in Figs. 1–5. These are plots of the dispersion of the dissociation field effect resulting from the application of high voltage pulses of 2.0, 1.0 and 0.2 μsec. duration. The aqueous solutions were prepared under a nitrogen atmosphere from water having a conductance of about $10^{-7}\ \Omega^{-1}\ cm.^{-1}$. Concentrations were determined volumetrically and agreed well with the values from conductance and pH measurements (error limits of $\tau \pm 20\%$) with the exception of the N-dimethyl-*o*-aminobenzoic acid. In this case the measured and calculated pH were identical, but an excess in conductance ($12 \times 10^{-6}\ \Omega^{-1}\ cm.^{-1}$, instead of 8×10^{-6}) indicated some ionic impurities, which, however, do not appreciably influence the τ values (error limit ± 50 %). All measurements were made at 25 ± 2°.

An appreciable 2nd Wien Effect is observed throughout for recombinations involving a neutralization of charge. Therefore, the equilibrium designated by $K_c = [H^+][R^-]/[R^{\pm}]$ might be expected to show a somewhat smaller effect than the equilibrium $K_D = [H^+][R^-]/[R]$ since $R^{\pm}$ possesses a small residual separation of charge. We see then that the relaxation time τ that we have measured represents a composite of two relaxation processes of the two different reactions proceeding concurrently. Two considerations lead us

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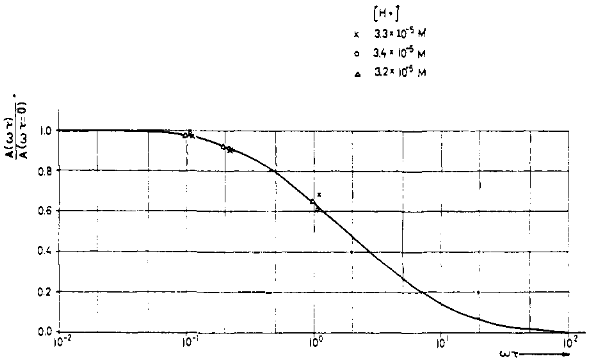

Fig. 1.—Experimental dispersion of the field effect in aqueous benzoic acid solutions. Each set of three points corresponds to the three different pulse lengths (frequencies $\omega_1 = 5 \times 10^5$ sec.$^{-1}$, $\omega_2 = 10^6$ sec.$^{-1}$, and $\omega_3 = 5 \times 10^6$ sec.$^{-1}$ reading from left to right).

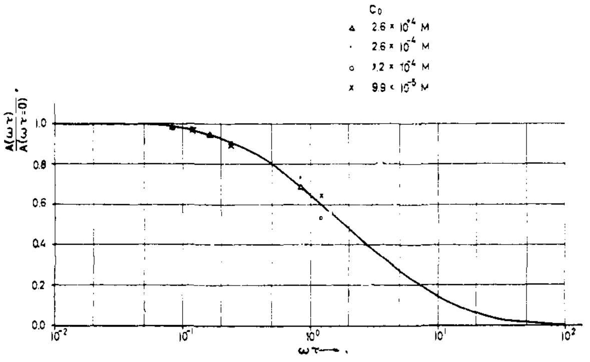

Fig. 2.—Experimental dispersion of the field effect in aqueous *o*-aminobenzoic acid solutions.

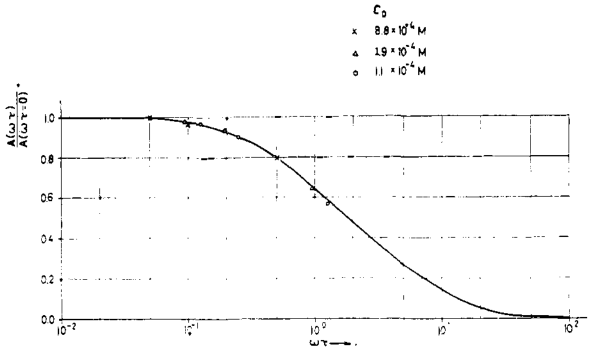

Fig. 3.—Experimental dispersion of the field effect in aqueous *m*-aminobenzoic acid solutions.

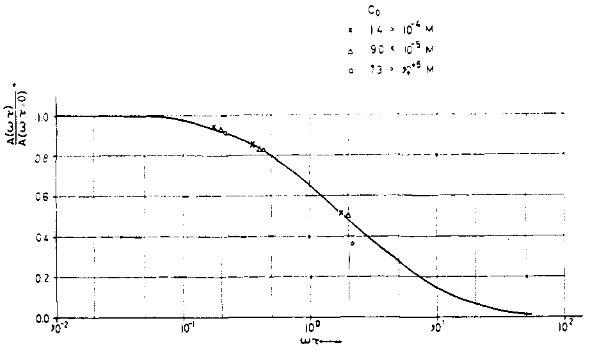

Fig. 4.—Experimental dispersion of the field effect in aqueous *p*-aminobenzoic acid solutions.

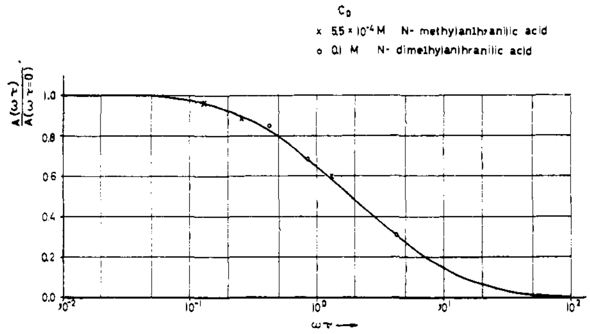

Fig. 5.—Experimental dispersion of the field effect in aqueous solutions of N-dimethyl-*o*-aminobenzoic acid and of N-methyl-*o*-aminobenzoic acid.

to believe, however, that a resolution of the two τ's is not essential. The factor $(1 - \alpha)/(2 - \alpha)$ (*cf.* above), determined from the absolute value of the field effect indicates that *m*-aminobenzoic acid, although predominantly present in the zwitterion form, contributes almost as much to the field effect as the *o*- and *p*-compounds ($\Delta\Lambda/\Lambda = 2.9\%$ for *m*-, 3.5% for both *o*- and *p*-aminobenzoic acids measured at comparable concentrations, pulse length and $\Delta E = (100 - 40)$ kv./cm.).[10]

The specific rate of the intramolecular proton transfer in these acids has been measured by sound absorption techniques and has been found to be between 10^7 and 10^8 sec.$^{-1}$.[11] This means that complete equilibration between the neutral and zwitterion forms occurs even within the time of the shortest high field pulse. We may therefore treat the recombination and dissociation process, measured by the dispersion of the field effect, as a whole regardless of whether the primary process involves R or R$^{\pm}$.

Small differences in the values of K_1, K_2, and K_Z reported by different investigators should not significantly alter k_R values calculated from our data (Table I). For instance, from Johnston's data[12] on *p*-aminobenzoic acid (pK_1 = 2.32, pK_2 = 4.92, pK_Z = 0.87) and our data ($\tau = 0.40$ μ sec. for $c_0 = 9.0 \times 10^{-5}$ M), we calculate $k_R = 3.75 \times 10^{10}$ M^{-1} sec.$^{-1}$ whereas from the data of Robinson and Biggs[13] (pK_1 = 2.45, pK_2 = 4.85, pK_Z = 0.67), we obtain $k_R = 3.46 \times 10^{10}$ M^{-1} sec.$^{-1}$. This difference is well within our estimated experimental error of ± 20%.

We also have determined the specific rate constants of the equilibrium

$$\mathrm{R} + \mathrm{OH}^- \underset{k_D}{\overset{k_R}{\rightleftarrows}} \mathrm{R}^- + \mathrm{H_2O} \qquad (5)$$

in aqueous N-dimethyl-*o*-aminobenzoic acid solution. For these measurements we used the "temperature jump" method which is described elsewhere.[8,14] The relaxation process, *i.e.*, the readjustment of concentrations in system 5, is determined spectrophotometrically using phenolphthalein as an indicator. Our calculated results appear in Table II. Since this experimental method again makes no distinction between R and R$^{\pm}$, we have used the experimental second acid ionization constant at 0.1 M ionic strength[15] to calculate

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[10] These values, as well as those for the other substances studied, are in good agreement with expectations from Onsager's theory (*cf.* also measurements by A. Patterson and co-workers, *J. Am. Chem. Soc.*, **74**, 4756 (1952)). Values reported by O. Blüh and F. Terentiuk (*J. Chem. Phys.*, **18**, 1664 (1950)), are much higher. As shown previously (ref. 2), polarization effects may be responsible for such values deviating strongly from theory.

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TABLE I

Acid	K_2 (10^{-5} M)	$\bar{k}_R$ (10^{10} M^{-1} sec.$^{-1}$)	k_D (10^5 sec.$^{-1}$)
Acetic[a] ($c_0 = 8.3 \times 10^{-5}$ M, $\tau =$ 0.24 μsec.)	1.7[h]	5.1	8.7
Benzoic[b]	6.3[i]	3.7	23
o-Aminobenzoic (anthranilic)[c]	1.1[j]	5.8	6.4
m-Aminobenzoic[d]	1.6[k]	4.6	7.4
p-Aminobenzoic[e]	1.2[l]	3.7	4.4
N-Dimethyl-*o*-aminobenzoic[f]	0.00038[m]	~2.5	~0.00095
N-Methyl-*o*-aminobenzoic[g]	~1.2[n]	~5	~6

[a] Riedel-DeHaen, Hannover, Fixanal solution. [b] E. Merck, Darmstadt, analytical grade, m.p. 121.5°. [c] T. Schuchardt, Munich, analytical grade, m.p. 145°. [d] T. Schuchardt, analytical grade, recrystallized from water, m.p. 172°. [e] Fluka, Basel, purum., recrystallized from water, m.p. 185°. [f] Dr. B. Franck, Goettingen, m.p. 68–69°. [g] Eastman, Rochester, recrystallized from ethanol, m.p. 178.5°. [h] H. S. Harned and R. W. Ehlers, *J. Am. Chem. Soc.*, **54**, 1350 (1932). [i] Ref. 13. [j] A. C. Cumming, *Proc. Roy. Soc.* (London), **A78**, 138 (1906). [k] *Loc. cit.*; see also A. K. Willi and W. Meier, *Helv. Chim. Acta*, **39**, 318 (1956). [l] Ref. 12 and 13. [m] J. T. Edsall and J. Wyman, *J. Am. Chem. Soc.*, **57**, 1964 (1935). [n] *cf.* ref. 16.

TABLE II

	c_0 (M)	τ (μsec.)	K_{eq}[a] (M)	k_R (M^{-1} sec.$^{-1}$)	k_D (sec.$^{-1}$)
N-Dimethyl-*o*-aminobenzoic acid (pH = 9.0)	5.57×10^{-3}	31	$\sim 3 \times 10^{-6}$	1.1×10^7	$\sim 3 \times 10^1$
	2.79×10^{-3}	52		1.3×10^7	$\sim 4 \times 10^1$
o-Aminobenzoic acid (pH = 8.9)	1.01×10^{-1}	<3	$\sim 1.35 \times 10^{-9}$	$>1.4 \times 10^{10}$	>19

[a] $K_{eq} = k_D/k_R$ according to eq. 5.

$K_{eq} = K_w/K_2$. In a similar experiment with *o*-aminobenzoic acid the relaxation time was found to be too short to be measured as indicated in Table II.

Discussion

Referring to Table I, we note first that k_R for acetic acid is slightly larger than the previously reported value of 4.5×10^{10} M^{-1} sec.$^{-1}$ obtained by the same method.[2] The difference is within our limits of experimental error and emphasizes the need for caution in making comparisons of k_R values where the differences are small. The values of k_R differ from the predicted maximum value[4] of 8.3×10^{10} M^{-1} sec.$^{-1}$ for the reaction $X^- + H^+ \rightarrow$ by a structural or steric factor of about 0.5 to 0.7. This result is similar to that obtained with *m*- and *p*-nitrophenol.[5]

We also see that there is a progression in k_R values for the *ortho*, *meta* and *para* isomers. The recombination of protons with the amino group is slower than with the carboxyl group where the excess charge causes some acceleration. Therefore, no large differences are to be expected for benzoic and *p*-aminobenzoic acids. The differences with respect to the *o*- and *m*-compounds may be caused by solvent structure around the proton acceptors. For N-dimethyl-*o*-aminobenzoic acid steric hindrance by the methyl groups should be responsible for the lower k_R value for this compound in Table I.

The most interesting results are those of Table II. Since there is a consequent relief of steric strain, hydrogen bonding is presumed to stabilize the dipolar ion of the N-dimethyl-*o*-derivative and thus to increase the acid pK_2 by more than three orders of magnitude over that of the parent acid.[16] As we see from eq. 3, this would explain a smaller k_D for proton dissociation. It also explains the decrease in k_R for the recombination of the protonated species with OH^- by three orders of magnitude from the expected diffusion controlled value of $\sim 10^{10} M^{-1}$sec^{-1}. Before the hydroxyl ion can recombine with the proton the chelate like hydrogen bond must open. Such delayed recombinations in hydrogen bonded ring structures have been observed also with other species, such as salicylic acid and certain azo-compounds.[17]

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