Acid–Base Reactions in Concentrated Aqueous Quaternary Ammonium Salt Solutions. I. Strong Acids and Bases, Carboxylic Acids, Amines, and Phenol

Joseph Steigman and Donald Sussman[1]

Contribution from the Department of Chemistry, Polytechnic Institute of Brooklyn, Brooklyn, New York, and the Institute of Organic Chemistry, University of Padua, Padua, Italy. *Received March 15, 1967*

Abstract: Titrations of HCl with KOH were carried out at 25° in aqueous 7.75 *m* tetra-*n*-butylammonium bromide solution and in concentrated solutions of other tetraalkylammonium salts. The acidity scale of water was found to be lengthened in these media. It was hypothesized that this effect was due mainly to an increase in the basicity of the hydroxyl ion. Very concentrated choline salt solutions (up to 25 *m*) extended the water acidity scale to some extent, but not on the basic side. In 7.75 *m* tetra-*n*-butylammonium bromide solutions primary amines (to *n*-dodecylamine) showed almost no change in basicity from their values in water (relative to ammonia as a reference). Secondary amines beyond diethylamine showed a marked decrease in basicity. Tertiary amines showed a steadily decreasing basicity with increasing chain length. Monoethanolamine was a stronger base (relatively) than in water; polyhydroxylamines were virtually unchanged. Arylamines became weaker bases, an effect which was due to the π electrons interacting with the solvent. Aliphatic carboxylic acids from propionic to *n*-dodecanoic showed almost no change in acidity from water (relative to *n*-valeric acid as a reference). The same was true of benzoic acid and phenol. It was hypothesized that all of these acids had become weaker acids than in water, and that their conjugate bases were stronger. *dl*-α-Alanine, which cannot be titrated in water, was titrated to a satisfactory end point in 7.75 *m* tetra-*n*-butylammonium bromide solution or in 20 *m* tetramethylammonium chloride solution with KOH, and was satisfactorily titrated with HCl in a number of concentrated choline salt solutions and in 20 *m* tetramethylammonium chloride.

Concentrated aqueous solutions of inorganic salts have been found useful for the titration of weak neutral bases by HCl, apparently because of a marked increase in the acidity of the hydronium ion.[2] Measurements of pH and H_0 of dilute HCl have been reported in such salt solutions,[3] and the reactions of the acid with a variety of bases have been investigated.[4,5] Comparable studies have not been made of the behavior of acids and bases in concentrated solutions of organic electrolytes like alkali metal tosylates and quaternary ammonium salts. It has been reported that in dilute solution the lower tetraalkylammonium salts caused a shift in the equilibrium of bromcresol green in acetate buffer which was opposite to that caused by inorganic electrolytes.[6] In addition, it is known that in somewhat more concentrated solution (up to 2 *M*) of sodium tosylate and of several quaternary ammonium salts there was substantial salting in of substituted aniline indicators.[7] This accompanied a change in the H_0 of HCl in the quaternary ammonium salt solution which could be partly attributed to the decrease in the activity coefficient of the indicator, suggesting that these salt solutions decrease the basicity of amines. (There was no change in H_0 in the tosylate solution, but it is probable that water structure-enforced ion-pair formation took place between the tosylate anion and the indicator cation,[8] lowering the latter's activity coefficient.)

In certain ways the organic electrolytes in water behave quite differently from inorganic salts. Their solutions have positive molar heat capacities[9] rather than the negative capacities of the inorganic compounds,[10] positive viscosity *B* coefficients,[11] and increased dielectric relaxation times.[12] In addition, as a general rule, the inorganic salts tend to salt out organic solutes, whereas the organic electrolytes salt them in.[13] These differences in behavior are probably associated with the ability of the organic salts to increase the extent of hydrogen bonding in liquid water and thus promote the organization of the solvent,[9] and with the tendency of most inorganic salts to disrupt the water structure.[14] The present research describes a number of acid–base reactions in concentrated aqueous quaternary ammonium salt solutions. Concentrated salt solutions were used for several reasons. The marked salting in of organic compounds by these solutions made possible the titration of compounds like lauric acid which are quite insoluble in water itself. At the same time, since the water in these solutions is strongly hydrogen bonded, as is water in the vicinity of proteins and polyelectrolytes in solution, it was thought that a qualitative picture could be obtained of acid–base behavior in aqueous solutions of macromolecules.

Experimental Section

1. Materials. A. Solvents. Methanol, Spectroquality (Matheson Coleman and Bell) was dried according to the method of

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[1] From a thesis submitted by D. Sussman to the Graduate School of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] F. E. Critchfield and J. B. Johnson, *Anal Chem.*, 30, 1247 (1958).

[3] D. Rosenthal and J. S. Dwyer, *ibid.*, **35**, 161 (1963).

[4] J. S. Dwyer and D. Rosenthal, *J. Phys. Chem.*, **67**, 779 (1963).

[5] D. Rosenthal, I. T. Oiwa, A. D. Saxton, and L. R. Lieto, *ibid.*, **69**, 1588 (1965).

[6] A. Indelli and G. Saglietto, *Trans. Faraday Soc.*, 24, 133 (1957).

[7] M. A. Paul, *J. Am. Chem. Soc.*, **76**, 3236 (1954).

[8] R. M. Diamond, *J. Phys. Chem.*, **67**, 2513 (1963).

[9] H. S. Frank and W. Y. Wen, *Discussions Faraday Soc.*, 24, 133 (1957).

[10] F. D. Rossini, *J. Res. Natl. Bur. Std.*, 7, 47 (1931).

[11] E R. Nightingale, Jr., *J. Phys. Chem.*, **66**, 894 (1962).

[12] G. H. Haggis, J. B. Hasted, and T. J. Buchanan, *J. Chem. Phys.*, 20, 1452 (1952).

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[14] H. S. Frank and M. W. Evans, *J. Chem. Phys.*, **13**, 507 (1945).

Fieser.[15] Ethanol (absolute) was a product of U. S. Industrial Chemicals and was used without treatment. Ethyl acetate (Brothers reagent grade) was washed with 10% aqueous K_2CO_3 solution, dried over K_2CO_3, filtered, and distilled. Immediately before use it was treated with P_2O_5 and redistilled. Acetone (Fisher Certified reagent grade) was used without purification, as was diethyl ether (Mallinckrodt analytical grade anhydrous). Dioxane (Brothers solvent) was refluxed over sodium metal and distilled, then subjected to the same treatment just before use. Benzene (Spectroquality, Matheson Coleman and Bell) was refluxed over calcium hydride and distilled just before use. Dichloroethane was a reagent grade solvent (Fisher Scientific Co.) and was redistilled. Carbon tetrachloride, a Spectroquality reagent (Matheson Coleman and Bell) was used without further treatment.

B. Quaternary Ammonium Salts. Tetra-*n*-butylammonium bromide (*n*-Bu_4NBr), polarographic grade, Southwestern Analytical Chemicals, was dissolved in ethyl acetate, precipitated with ether, and dried *in vacuo*. The maximum content of any acidic or basic impurity was 0.02 mole %. Tetra-*n*-propylammonium bromide (*n*-Pr_4NBr), highest purity reagent, Eastman, was recrystallized three times in ethyl acetate and dried *in vacuo*. The maximum content of acidic and basic impurities was 0.10%. Tetraethylammonium bromide (Et_4NBr) was an Eastman product and was recrystallized four times in an ethanol–ethyl acetate mixture and dried *in vacuo*. The maximum concentration of acidic and basic impurities was 0.15%. Tetramethylammonium chloride (Me_4NCl) was an Eastman product which was recrystallized three times from ethanol and dried *in vacuo*. The content of acidic and basic impurities was 0.10 mole %. Choline chloride was an Eastman product, recrystallized five times from ethanol and dried *in vacuo*. The mole % of acidic and basic impurities was 0.09. Choline bromide (British Drug Houses Ltd.) was recrystallized three times from ethanol and dried *in vacuo*. The mole % of titrable impurities was 0.06. Other choline salts were prepared from the purified chloride by conversion to the hydroxide through an anion-exchange column (Dowex-21K) followed by potentiometric titration with concentrated pure acid solutions, evaporation *in vacuo* to yield the salts, and recrystallization three to four times from methanol or ethanol.

C. Other Chemicals. The various liquid amines were either of reagent grade or were industrial products of high purity. They were stored over KOH pellets and distilled from fresh pellets. For each amine a small constant-boiling middle cut was taken which was used immediately. The hydrochlorides were prepared by mixing equivalent quantities of the amine and HCl in water, removing the solvent by rotary evaporation *in vacuo*, and recrystallizing the solid residue twice from a methanol–ether mixture. The alkanolamines were distilled at 20 mm. *p,p'*-Dimethylaminoazobenzene was recrystallized from ethanol–water. *n*-Dodecylamine was dissolved in ethanol and precipitated with water.

The liquid carboxylic acids were of the highest commercial purity and were distilled immediately before use. Triethylacetic acid was of reagent grade (Aldrich) and was recrystallized three times in water. *dl*-α-Alanine ("A" grade, Calbiochem, Gold Label) was recrystallized in ethanol–water. Benzoic acid (Mallinckrodt, primary standard grade) was recrystallized in water. Phenol (Baker and Adamson reagent grade) was used without purification. *p*-Nitrophenol (Certified reagent, Fisher Scientific) was recrystallized three times in water. Other chemicals were of reagent grade and were used without purification.

2. Spectrophotometry. Ultraviolet and visible spectra were obtained on a Cary Model 14 double-beam spectrophotometer equipped with a jacketed cell compartment through which water was circulated from a bath maintained at 25.0 ± 0.1°. The absorption cells were filled at 25.0°, placed in the thermostated compartment, and allowed to remain for at least 10 min before recording. The quartz cells (Pyrocell Manufacturing Co.) were calibrated by Haupt's method.[16]

3. Potentiometric Titrations. Titrations were performed with a Radiometer Model 4 pH meter or a Beckman Model G pH meter with a glass electrode (Beckman 39177) and a saturated calomel reference electrode (Beckman 39178). A jacketed beaker was used with circulating water maintained at 25.00 ± 0.05°. Prepurified nitrogen gas was passed through the beaker during titrations. Solutions for titration were prepared by weighing the quaternary ammonium salt solution in the jacketed beaker and adding enough of the compound to be titrated so that its molarity was approximately 0.02. Approximately 1 *M* KOH and 1 *M* HCl in water were used as titrants and were delivered from Gilmont micropipet burets. There were usually eight to nine points distributed over the entire titration curve from which the p*K'* values of the weak electrolytes were calculated. After each addition of reagent a series of readings was taken at 5-min intervals. When two successive readings agreed within 0.01 pH, the succeeding addition of reagent was made. These readings are referred to as pH_{GE}.

The hydrogen electrode measurements were made with a Leeds and Northrup Model K-2 potentiometer and a Leeds and Northrup galvanometer. Prepurified hydrogen gas (Matheson) was passed through a Deoxo gas purifier (Model D-10-2500, Engelhard Industries) into distilled water, and then into the test solution. The area of the platinum indicator electrode was 1 cm^2. It was platinized before each titration. The reference electrode was the same saturated calomel electrode which was used with the glass electrode. The potentiometer was standardized against a Weston cell (1.0192 ± 0.0002 v), and the instrument was calibrated with two standard buffer solutions (pH 4.01 and 6.86) before each titration.

The majority of the titrations reported in this paper were carried out (at 25.00 ± 0.05°) in a 7.75 *m* aqueous solution of tetra-*n*-butylammonium bromide with a glass electrode. The acidity constants of weak acids which are reported here are mixed constants[17] in which the ratio of concentrations of the acid and conjugate base are multiplied by the hydrion activity (or its reciprocal). The negative logarithms of the resulting constants are called p*K'* and are not thermodynamic constants. The activities of species other than the hydronium ion are not known, and there is in addition an unknown junction potential. In order to make better comparisons of the relative acidities of various solutes in these salt solutions, the initial solute concentrations were approximately equal (about 0.02 *M*). The titrants were 1 *M* HCl or 1 *M* KOH, so that dilution of the quaternary ammonium salt solutions by the water of the titrants was small and was roughly the same for most of the titrations. The average dilution was about 2% by volume. It had the effect of decreasing the pH_{GE} of benzoic acid buffers by about 0.05 unit. The effect of this dilution was ignored in calculating the mixed acidity constants.

A check was made of the internal consistency of the acidity measurements in 7.75 *m* *n*-Bu_4NBr at 25.00° by determining the mixed acidity constant (p*K'*) of *p*-nitrophenol by direct potentiometric titration with KOH and by spectrophotometry in five buffer solutions of tris(hydroxymethyl)aminomethane and its hydrochloride ranging in pH_{GE} from 8 to 9.5. The direct titration of 0.02 *M* *p*-nitrophenol yielded a value for p*K'* of 7.95 ± 0.03. The spectrophotometric value (based on p*K'* = 8.30 for the Tris) was 7.92 ± 0.02.

The readings of the glass electrode were compared with hydrogen electrode potentials of the same solutions (0.02 *M* HCl in 7.75 *m* *n*-Bu_4NBr and in 7.75 *m* Et_4NBr titrated with 1 *M* KOH). The high viscosities of these solutions impeded the passage of hydrogen gas. In some cases steady-state potential readings were obtained only after 8 hr. In the *n*-Bu_4NBr solution the maximum divergence between the two curves was 0.29 pH unit (near the equivalence point) but only about 0.07 unit on the alkaline side. The maximum divergence in Et_4NBr solution was 0.07 unit on the acid side. Agreement was much better on the alkaline side. It was concluded that the general character of the titration curve obtained with the glass electrode was confirmed (see below).

Halving the concentration of *n*-octylamine and of tri-*n*-propylamine produced virtually no change in the value of the mixed acidity constant for either amine on titration with 1.0 *M* HCl. The same was true for *n*-octanoic acid when its concentration was varied and it was titrated with 1 *M* KOH.

Results and Discussion

I. The Water Acidity Scale in Concentrated Aqueous Quaternary Ammonium Salt Solutions. Figure 1 shows the titration curves of 0.02 *M* HCl with 1 *M* KOH at 25.00° in water and in four concentrated tetraalkylammonium salt solutions. Me_4NCl was used (in 20 *M* solution) in place of Me_4NBr because of the latter's limited solubility. On the acid side the glass electrode

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[15] L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1957, p 289.

[16] G. W. Haupt, *J. Res. Natl. Bur. Std.*, **48**, 414 (1952).

[17] A. Albert and E. Serjeant, "Ionization Constants of Acids and Bases," Methuen and Co., Ltd., London, 1962, p 30.

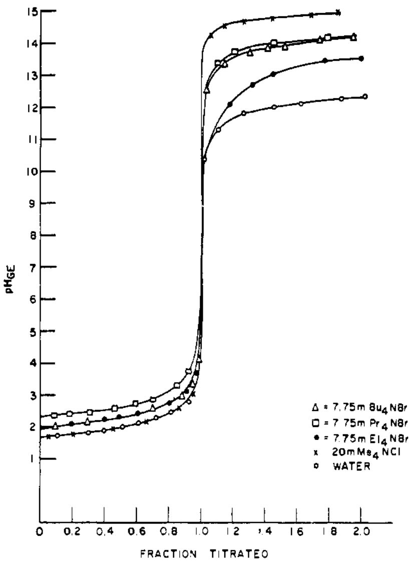

Figure 1. Titrations of 0.02 *M* HCl with 1.0 *M* KOH in concentrated aqueous tetraalkylammonium salt solutions and in water.

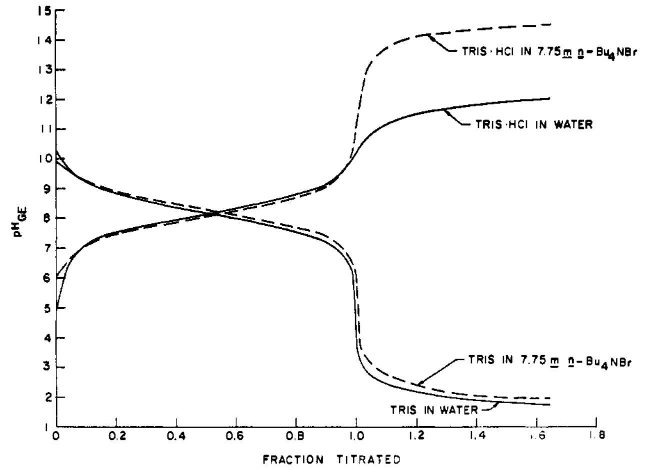

Figure 2. Titrations of 0.02 *M* tris(hydroxymethyl)aminomethane with 1.0 *M* HCl in water and in 7.75 *m* tetra-*n*-butylammonium bromide, and titrations of 0.02 *M* tris(hydroxymethyl)aminomethane hydrochloride with 1.0 *M* KOH in water and in 7.75 *m* tetra-*n*-butylammonium bromide at 25.0°.

readings (called pH$_{GE}$) are not too different from those in water. On the alkaline side they are very much higher than in water: by 2 pH$_{GE}$ units in the *n*-Pr_4BBr and *n*-Bu_4NBr solutions, and by almost 3 units in 20 *m* Me_4NCl. The effect is smallest in Et_4NBr.

Table I shows the effect of increasing *n*-Bu_4NBr concentration on the pH$_{GE}$ of a number of KOH solutions. The pH$_{GE}$ at first decreases with added salt and then increases rather markedly, especially in the two most concentrated electrolyte solutions.

Table I. pH$_{GE}$ of KOH Solutions in *n*-Bu_4NBr Solutions at 25.0°

KOH, *M*	H_2O	Bu$_4$NBr 0.1 *m*	1.0 *m*	2.0 *m*	7.75 *m*	10 *m*
3.00×10^{-3}	11.59	11.41	11.56	11.92	13.27	14.37
7.70×10^{-3}	11.95	11.83	11.98	12.41	13.67	14.57
1.00×10^{-2}	12.04	11.91	12.14	12.58	13.81	14.64
1.54×10^{-2}	12.23	12.09	12.35	12.76	14.09	14.75

From Figure 1 it can be concluded that the acidity scale of water is expanded in the quaternary ammonium salt solutions. A rough quantitative measure of this scale can be found in the mixed dissociation constant of water. From Table I the value of this constant (called pK_w') is about 15.8. The same number was calculated from measurements with the hydrogen electrode in alkaline solutions (see Experimental Section). In the titration of phenol with 1 *M* KOH in 7.75 *m* *n*-Bu_4NBr, a series of successive approximations yielded 12.08 for pK' and 15.72 for pK_w'.

A lengthened acidity scale means that the dissociation of water is decreased in these media. In solutions of a given stoichiometric hydroxyl ion concentration there should then be a lower concentration of hydronium ions in quaternary ammonium salt solutions than in water. This in turn should result in a larger sodium error for the glass electrode than in water. At 25° in 1.54×10^{-2} *M* NaOH in water, pH$_{GE}$ is 0.16 unit lower than in the corresponding KOH solution. In 7.75 *m* *n*-Bu_4NBr, the pH$_{GE}$ in 1.54×10^{-2} *M* NaOH is 0.90 unit lower than in KOH.

The expansion of the acidity scale could arise from a greater acidity of the hydronium ion, a greater basicity of the hydroxyl ion, or from a combination of both effects. We propose that the major part of the scale expansion is due to the increased basicity of the hydroxyl ion. This hypothesis is based on three considerations: the pH$_{GE}$ readings themselves, the titration of amines and amine salts with HCl and with KOH, and coacervate formation. In concentrated inorganic salt solutions, for example, 8 *M* NaI, Critchfield and Johnson[2] found that the pH$_{GE}$ of 0.0192 *M* HCl was less than zero, a value which was confirmed with the hydrogen electrode.[3] The salt is a water-structure breaker and may also reverse the leveling and the hydration of the hydronium ion, making it a stronger acid than in water. In 8 *M* NaI the end point of the titration of a weak neutral baselike aniline with HCl is very much improved, and from the curves it is evident that the main reason for this improvement is the markedly increased acidity of HCl. In 7.75 *m* *n*-Bu_4NBr, on the other hand, the water is very strongly organized into hydrogen-bonded clusters. The pH$_{GE}$ readings of HCl are roughly the same as in water, and the end point of the titration of aniline with HCl is poorer than in water, largely because aniline becomes a weaker base in this medium (see below). The amine Tris [tris(hydroxymethyl)aminomethane] shows approximately the same relative strength in *n*-Bu_4NBr solution as in water. Figure 2 shows titrations of Tris with 1 *M* HCl in water and in the quaternary ammonium bromide solution. The two curves are almost identical. On the other hand, when Tris hydrochloride is titrated with KOH, there is a marked increase in the end-point slope in *n*-Bu_4NBr solution compared to that in water. This shows the effect of the expanded water acidity scale and suggests that it arises from an increased basicity of the hydroxyl ion in this medium.

If 7.75 *m* *n*-Bu_4NBr is treated with concentrated KBr, when the latter is approximately 6 *m*, there is a separation into two aqueous phases, a coacervation, in which one layer has almost all the KBr, and the other contains almost all the quaternary ammonium salt. Other inorganic electrolytes like KCl and KNO_3 produce similar coacervates at high concentrations. However, when KOH is added to 7.75 *m* *n*-Bu_4NBr, the coacervate forms with 0.1 *M* KOH. This observation supports the hypothesis that the hydroxyl ion has a higher activity coefficient and hence a higher escaping tendency in the organic salt solution than in water and is thus more strongly basic than in water.

These results suggest that the hydronium and the hydroxyl ions are not incorporated with equal facility into strongly hydrogen-bonded water structures. The difference may arise from the two additional protons on the hydronium ion, which enable it to fit more easily than the linear hydroxyl ion into water clusters.

Not all quaternary ammonium salts behave like the tetraalkylammonium compounds. Choline salts (β-hydroxyethyltrimethylammonium salts) have a hydroxyl group as well as hydrophobic alkyl groups. Fleming[18] found that choline chloride in water behaved very much like tetramethylammonium chloride in viscosity, density, and limiting equivalent conductance. On the other hand, Franks[19] concluded from a study of partial molal volumes that aliphatic alcohols tend to break the water structures. There is thus a water-structure-breaking group accompanying structure-forming radicals in the choline salts. Table II shows the pH_{GE} values of a number of points in the titration of 0.02 *M* HCl with 1 *M* KOH or 1 *M* NaOH in concentrated solutions of four choline salt solutions. The corresponding values in water are included for comparison. The column marked *f* refers to the fraction of the stoichiometric quantity of KOH delivered at the particular point.

Table II. pH_{GE} Values at Different Points in the Titration of 0.02 *M* HCl with 1.0 *M* KOH in Choline Salt Solutions at 25.0° (1 *M* NaOH for the Perchlorate)

f	Water	15 *m* choline ClO_4	15 *m* choline I	25 *m* choline Br	25 *m* choline Cl
0.0	1.67	<0.00	0.88	0.79	1.14
0.1	1.72	0.01	0.99	0.82	1.21
0.2	1.78	0.05	1.04	0.87	1.23
0.4	1.90	0.12	1.18	1.00	1.34
0.6	2.07	0.21	1.37	1.19	1.52
0.8	2.40	0.57	1.68	1.54	1.87
1.2	11.64	10.78	11.74	11.77	11.77
1.4	11.96	10.91	12.07	12.11	12.05
1.6	12.12	11.02	12.23	12.28	12.21

It can be seen that the water acidity scale is lengthened in each of the four choline salt solutions. If the differing salt concentrations are taken into account (they are not equal because of solubility limitations), the order of acidity scale expansion is $ClO_4^- > I^- > Br^- > Cl^-$. In all cases the main direction of the expansion is on the acid side. For the chloride, bromide, and iodide, the readings on the alkaline side are virtually the same as in water. In the case of the perchlorate, the entire scale is shifted toward the acid side. From the point of view of acid-base titrations, the data suggest that there would be no advantage in using concentrated choline salt solutions for the titration of weak acids, but that there might be some advantage to using them for weak bases because of the (implied) increase in hydronium-ion acidity. There would be two advantages over concentrated inorganic salt solutions: the latter salt out solutes, whereas the choline salts would probably salt them in, and the alkaline side of the pH scale cannot be measured with the glass electrode in the inorganic salt solutions but can be determined in the choline salt solutions.

It was concluded that the choline salts in concentrated solutions, unlike the tetraalkylammonium salts, are without effect on the basicity of the hydroxyl ion, but increase the acidity of the hydronium ion.

II. The Titration of Amines in 7.75 *m* *n*-Bu_4NBr Solutions. Table III shows the acidity constants of a number of amines in water (denoted as pK_A) and the corresponding mixed constants (pK') in 7.75 *m* *n*-Bu_4NBr at 25°. Ammonia is the reference base in each medium. The next-to-the-last columns, headed ΔpK_A, shows the difference between the pK_A of the base and that of ammonia in water, and the last column, with the heading $\Delta pK'$, shows the difference between the corresponding mixed acidity constants in *n*-Bu_4NBr solution.

Table III. Acidity Constants of Amines in Water, Their Mixed Acidity Constants in 7.75 *m* *n*-Bu_4NBr, and the Differences between These Constants and Those of Ammonia at 25°

Compound	pK_A[a]	pK'	ΔpK_A	$\Delta pK'$
Primary Aliphatic Amines				
Ammonia	9.25	9.19 ± 0.02	...	...
Methylamine	10.62	10.57 ± 0.03	1.37	1.38
Ethylamine	10.63	10.70 ± 0.02	1.38	1.51
n-Propylamine	10.53	10.60 ± 0.01	1.33	1.41
Isopropylamine	10.63	10.55 ± 0.03	1.38	1.36
Allylamine	9.69	9.71 ± 0.01	0.44	0.52
n-Butylamine	10.60	10.45 ± 0.02	1.35	1.26
Isobutylamine	10.42	10.23 ± 0.03	1.17	1.04
t-Butylamine	10.45	10.39 ± 0.02	1.20	1.20
n-Octylamine	10.65	10.53 ± 0.03	1.40	1.34
n-Dodecylamine	10.63	10.42 ± 0.06	1.38	1.23
Cyclohexylamine	10.64	10.49 ± 0.01	1.39	1.30
Secondary Aliphatic Amines				
Dimethylamine	10.77	10.66 ± 0.02	1.52	1.42
Diethylamine	10.93	10.83 ± 0.03	1.68	1.67
Di-*n*-propylamine	10.91	10.58 ± 0.03	1.66	1.39
Diisopropylamine	11.05	10.86 ± 0.03	1.80	1.67
Diallylamine	9.29	9.02 ± 0.01	0.04	−0.17
Di-*n*-butylamine	11.31	10.34 ± 0.02	2.06	1.25
Diisobutylamine	10.82	9.87 ± 0.01	1.57	0.68
Di-*n*-amylamine	11.18	10.24 ± 0.02	1.93	1.05
Di-*n*-hexylamine	11.01	10.56 ± 0.01	1.76	0.68
Tertiary Aliphatic Amines				
Trimethylamine	9.80	9.48 ± 0.02	0.55	0.29
Triethylamine	10.87	9.90 ± 0.03	1.62	0.71
Tri-*n*-propylamine	10.65	9.49 ± 0.01	1.40	0.30
Alkanolamines				
Ethanolamine	9.50	10.23 ± 0.02	0.25	1.04
Diethanolamine	8.90	9.19 ± 0.02	−0.33	0.00
Triethanolamine	7.82	7.92 ± 0.02	−1.43	−1.27
Tris(hydroxymethyl)-aminomethane	8.18	8.30 ± 0.02	−1.07	−0.89
Aromatic Amines				
Aniline	4.58	4.03 ± 0.03	−4.67	−5.16
N,N′-Dimethylaniline	5.06	3.85 ± 0.03	−4.19	−5.34
N,N′-Diethylaniline	6.56	5.24 ± 0.03	−2.69	−3.95
p,*p*-Dimethylaminoazo-benzene	3.40	2.38 ± 0.02	−5.85	−6.81

[a] See ref 17 and N. F. Hall and M. R. Sprinkle, *J. Am. Chem. Soc.*, **54**, 3469 (1932).

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(18) R. Fleming, *J. Chem. Soc.*, 4914 (1960).
(19) F. Franks, *Ann. N. Y. Acad. Sci.*, **125**, 277 (1965).

The primary amines, from methylamine to *n*-dodecylamine, show almost no relative change in basicity from their water values. Since the solubility of *n*-dodecylamine in water at 25° is 2.0×10^{-5} *M*[20] and its concentration in the quaternary salt solution was 0.02 *M*, it was very strongly salted in, and its activity coefficient must be quite low as a consequence. Such salting in occurs with the other amines, but undoubtedly to different extents. Thus one would not expect the activity coefficients of these neutral bases to be identical with each other. In spite of this, there is almost no (relative) change in basicity for the entire series. This indicates that changes in the activity coefficient of a primary amine and its ammonium conjugate acid are about the same when they are transferred from water to the quaternary ammonium salt solution. Frank and Wen suggested that a primary amino group can easily replace a water molecule in an organized structure, and this is probably equally true of the primary ammonium ion.[9] Franks expressed the opinion that even a long paraffin chain may accommodate itself in water solution by occupying voids, and there are undoubtedly many voids in a highly organized water structure.[19]

The aliphatic secondary amines behave differently from the primary amines. There is very little relative change in basicity from the water values for dimethylamine and diethylamine. As the chain length is further increased, the secondary amines become weaker bases in the organic electrolyte solution. There is a decrease in p*K'* of one unit for di-*n*-butylamine, diisobutylamine and di-*n*-amylamine. Hydrogen bonding to water molecules is more difficult for a secondary amine than for a primary amine. There may be voids in the vicinity of the quaternary ammonium ions which can accommodate the two smallest secondary amines, but which are too small for the larger members of the series.

The aliphatic tertiary amines, which are least capable of hydrogen bonding to water, show a steadily decreasing basicity with increasing chain length.

The alkanolamines, which are weaker bases in water than their simple aliphatic amine analogs, can exert effects on the water structure through their hydroxyl groups, through the paraffin chains, and through the amino groups. It is assumed that the effects of the latter two groups are the same as those of the corresponding alkylamines. The effect of an alcohol group on the water structure is difficult to assess. Franks[19] concluded from a study of the partial molal volumes of alcohols in water that a single alcohol group can break the water structure perhaps by preferential hydrogen bonding between the alcohol group and a water molecule. He observed further that two or more alcohol groups in the same molecule reverse this effect in some fashion, so that the molecule does not noticeably disrupt the water structure. Effects of these structural differences are evident in Table III. Ethanolamine is a much stronger base in the quaternary ammonium salt solution than in water. Diethanolamine and triethanolamine show much smaller changes, the increase in basic strength being smallest for triethanolamine. A similar very small shift is noted for the primary amine, tris(hydroxyethyl)aminomethane, which also has three hydroxyl groups.

The titration of a number of aromatic amines shows that they are all weaker bases in *n*-Bu_4NBr solution than in water. The acidity constant of aniline is decreased by 0.5 p*K* unit. Since the p*K'* of cyclohexylamine shows almost no change from water, it can be concluded that it is the π electrons of the ring which are responsible for the effect. N,N'-Dimethylaniline and N,N'-diethylaniline show the combined effects of the tertiary amine structures and π electrons.

From Table III, it can be concluded that the relation reported between the shift in H_0 and the change in indicator activity coefficient in quaternary ammonium salt solutions[7] is not due solely to the salting in of the indicators (which are substituted anilines) but probably represents an interaction between the organized water structure and the benzene ring of the neutral molecule, ultimately decreasing the base strength of the indicator but not affecting the conjugate acid to any great extent. The aliphatic primary amines, which are also salted into this medium, do not become weaker bases in this fashion.

The indicator *p,p'*-dimethylaminoazobenzene has an acidity constant which is ten times larger in the organic salt medium than in water. This molecule was chemically bonded to various proteins by Klotz, who then spectrophotometrically titrated the azo dye.[21] He found that it became a weaker base in each case, the acidity constant increasing by a factor of about 10 with β-lactoglobulin, and by as much as 200 with ovalbumin. Klotz concluded that the effect was due to the formation of a highly organized ice-like water layer around the protein.

III. **Carboxylic Acids and Phenol.** Table IV shows the pK_A values of a number of carboxylic acids and of phenol in water and their p*K'* values in 7.75 *m* *n*-Bu_4NBr at 25°. *n*-Valeric acid (pentanoic acid) was selected as the reference acid in each medium, and ΔpK_A and $\Delta pK'$ values are shown in the last two columns of the table.

Table IV. pK_A Values of Carboxylic Acids and Phenol in H_2O at 25°, p*K'* Values in 7.75 *m* *n*-Bu_4NBr, and ΔpK_A and $\Delta pK'$ Values[a]

Acid	pK_A[b]	p*K'*	ΔpK_A	$\Delta pK'$
Formic	3.75	5.74 ± 0.02	−1.10	−1.34
Acetic	4.76	6.85 ± 0.01	−0.09	−0.23
n-Propionic	4.87	7.04 ± 0.03	0.02	0.04
n-Butyric	4.82	7.18 ± 0.02	−0.03	0.10
n-Valeric	4.85	7.08 ± 0.03	...	...
n-Hexanoic	4.88	7.20 ± 0.04	0.03	0.12
n-Octanoic	4.89	7.18 ± 0.01	0.04	0.10
n-Dodecanoic (lauric)	4.92	7.17 ± 0.03	0.07	0.09
Triethylacetic	5.45	7.75 ± 0.03	0.60	0.67
Benzoic	4.20	6.30 ± 0.01	−0.67	−0.78
Phenol	9.99	12.08 ± 0.01	5.14	5.00

[a] Referred to valeric acid. [b] See ref 17 and H. C. Brown, D. H. McDaniel, and O. Haflinger, in "Determination of Organic Structures by Physical Methods," E. A. Braude and F. C. Nachod, Ed., Academic Press Inc., New York, N. Y., 1955.

Apart from formic and acetic acids, the members of the homologous series of aliphatic carboxylic acids from *n*-propionic acid to *n*-dodecanoic acid show relative p*K'* values which are practically the same as the

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(20) D. Brown, *J. Colloid Sci.*, 13, 286 (1958).

(21) I. M. Klotz, *Science*, 128, 815 (1958).

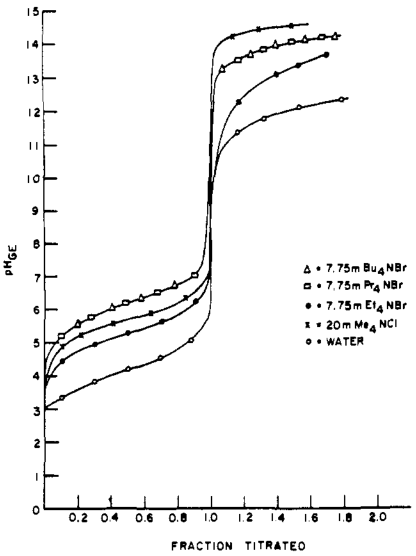

Figure 3. Titrations of 0.02 *M* benzoic acid with 1.0 *M* KOH in concentrated aqueous tetraalkylammonium salt solutions and in water at 25.0°.

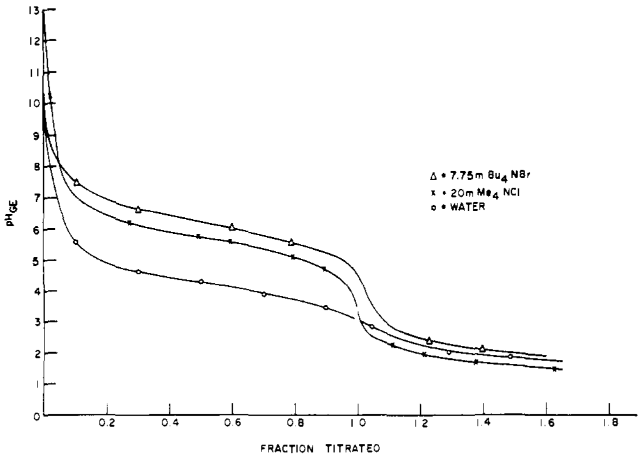

Figure 4. Titration of 0.02 *M* potassium benzoate with 1.0 *M* HCl in 7.75 *m* tetra-*n*-butylammonium bromide, in 20 *m* tetramethylammonium chloride, and in water at 25.0°.

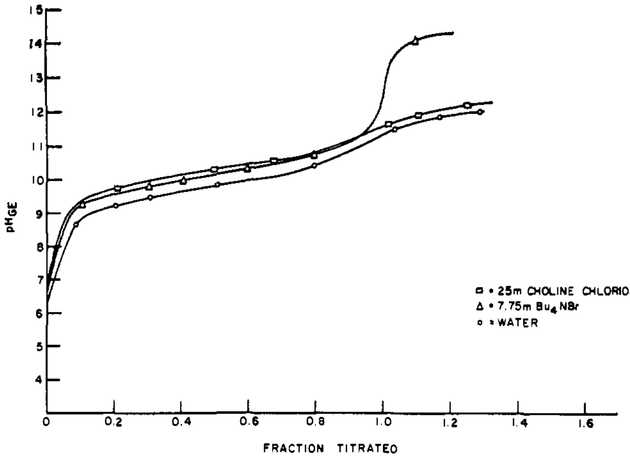

Figure 5. Titrations of 0.02 *M* *dl*-α-alanine with 1.0 *M* KOH in 7.75 *m* *n*-Bu$_4$NBr, 25 *m* choline chloride, and water.

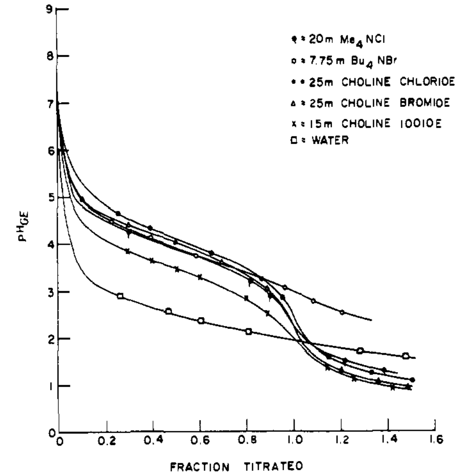

Figure 6. Titration of 0.02 *M* *dl*-α-alanine with 1.0 *M* HCl in 20 *m* Me$_4$NCl, 7.75 *m* *n*-Bu$_4$NBr, 25 *m* choline chloride, 25 *m* choline bromide, 15 *m* choline iodide, and water.

relative pK_A values in water. This is also the case for benzoic acid and for phenol. It should be noted that the branched-chain acid triethylacetic acid behaves like the straight-chain acids.

On the average, the mixed acidity constants of the carboxylic acids are about 2 pK' units larger than the pK_A values in water. A direct quantitative comparison between the values in the two media for any one acid cannot be made. However, additional potentiometric data suggest that these acids have become weaker acids in the quaternary ammonium salt solution. Figure 3 shows the titration of 0.02 *M* benzoic acid with 1 *M* KOH in the concentrated aqueous quaternary ammonium salt solutions which are used for the titrations shown in Figure 1. The 7.75 *m* *n*-Pr$_4$NBr and *n*-Bu$_4$NBr solutions show identical behavior. The curve for the titration in the solution is almost superimposable on the water curve, but is displaced approximately two units upward for a large part of the titration. In the early part of the curve, however, the slope is clearly greater in the quaternary salt solution than in water. If the hydroxyl ion is a stronger base in the salt solution than in water, the benzoic acid must have become a much weaker acid to account for this initial slope. As a consequence, benzoate ion should be a stronger base in the quaternary salt solution than in water. Figure 4 shows the titration at 25° of 0.02 *M* potassium benzoate with 1 *M* HCl in 7.75 *m* *n*-Bu$_4$NBr, in 20 *m* Me$_4$NCl, and in water. It is evident that the slope in the vicinity of the equivalence point is much greater in the quaternary ammonium salt solutions than in water. We assume that the strength of the hydronium ion is not very different in these media than in water. The increase in slope at the end points in the quaternary ammonium salt solutions is therefore attributed to the increased basicity of the benzoate ion.

IV. *dl*-α-Alanine. Because of their zwitterion structure, α-amino acids cannot be titrated satisfactorily in water with either a strong base or a strong acid. At 25° the pK_A of the ammonium acid of *dl*-α-alanine is 9.87, so that it is as weakly acidic as phenol. The pK_A of the carboxyl group is 2.35, so that the carboxylate anion is a very weak base.

Critchfield and Johnson reported that the increased acidity of HCl in concentrated NaI solutions did not materially improve the titrations of α-amino acids.[2] On the other hand, concentrated solutions of some quaternary ammonium salts do improve these titrations. Figure 5 shows the titration of 0.02 *M* *dl*-α-alanine with 1 *M* KOH in water, in 7.75 *m* *n*-Bu$_4$NBr, and in 25 *m* choline chloride. The titration curves in water and in the choline salt solution are similar and show quite poor end points (see Table II). However, in the *n*-Bu_4NBr solution, because of the expanded acidity scale and the increased basicity of the hydroxyl ion, the end point is easily detectable (a similar result is found in 20 *m* Me_4NCl).

Figure 6 shows the titration of 0.02 *M dl*-α-alanine with 1 *M* HCl in water, in 7.75 *m n*-Bu_4NBr, in 20 *m* Me_4NCl, in 15 *m* choline iodide, in 25 *m* choline chloride, and 25 *m* choline bromide. The titration end points are poor in water and in the tetra-*n*-butylammonium bromide solution, but for reasons which are not yet understood they are satisfactory in the Me_4NCl solution and in the choline salt solutions. However, it must be said that these titrations are not necessarily useful, since α-amino acids, unlike many other organic compounds, do not appear to be salted into quaternary ammonium salt solutions.

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Acid–Base Reactions in Concentrated Aqueous Quaternary Ammonium Salt Solutions. II. Steric Effects

Joseph Steigman and Donald Sussman[1]

Contribution from the Department of Chemistry, Polytechnic Institute of Brooklyn, Brooklyn, New York, and the Institute of Organic Chemistry, University of Padua, Padua, Italy. *Received March 15, 1967*

Abstract: A series of monosubstituted benzoic acids were titrated at 25.0° with KOH in 7.75 *m* aqueous tetra-*n*-butylammonium bromide. Unlike their behavior in water, the *ortho*-substituted acids (fluoro-, chloro-, bromo-, iodo-, nitro-, methyl-, methoxy-, and phenylbenzoic acids) had mixed acidity constants which were almost the same as those of their *para* isomers. The *ortho* effect in the ionization of these acids had disappeared. The *ortho* effect is attributed to the disruption of hydrogen-bonded water clusters above and below the plane of the ring by π electrons and the encounter between the carbonyl and alcohol groups of the acid and water molecules from these disrupted clusters. Its disappearance is attributed to the very strong solvent organization through hydrogen bonding caused by the quaternary ammonium salt. This hypothesis is generalized further. Ionol (2,6-di-*t*-butyl-*p*-cresol) is a sterically hindered phenol which ordinarily is very weakly acidic. In 10 *m* tetra-*n*-butylammonium bromide it dissolved and was titrated at 25.0° with KOH. Its mixed acidity constant was $^1/_{25}$th that of phenol in the same medium. The difference in acidity constants is attributed to inductive effects on the phenolic group by the alkyl groups. The disappearance of the steric hindrance is thought to be caused by the incorporation of the ionol into a strongly hydrogen-bonded medium in which the water molecules have restricted molecular rotation and are properly aligned for proton jumps.

This paper describes the disappearance of the *ortho* effect in the ionization of monosubstituted benzoic acids and of steric hindrance in the ionization of a hindered phenol when the solvent is a concentrated aqueous solution of a quaternary ammonium salt.

Experimental Section

1. Materials. a. Substituted Benzoic Acids. The various substituted benzoic acids were the highest purity acids of Eastman Kodak, Matheson Coleman and Bell, Fluka, Aldrich, Fisher, or K & K. Each was recrystallized several times from water and dried *in vacuo*. The melting points were close to the literature values. An indirect check on the purity of each acid was made from the stoichiometry of each titration.

b. Substituted Phenols. The various nitrophenols were reagent grade chemicals obtained from Eastman, Matheson Coleman and Bell, Fisher, or K & K. Each was recrystallized several times from water, and dried *in vacuo*. The melting points were in good agreement with those reported in the literature. Ionol (2,6-di-*t*-butyl-*p*-cresol) was obtained through the courtesy of The Shell Chemical Co. Three recrystallizations were made from carbon tetrachloride, followed by drying *in vacuo*. D_2O was 99.7% pure (Columbia Organic Chemicals).

c. Other Reagents. All other reagents have been previously described.[2]

2. Potentiometric and Spectrophotometric Measurements. Some of these techniques have been previously described.[2] Infrared measurements were made on a Perkin-Elmer Model 521 recording infrared spectrophotometer. The spectra of solutions in water and in D_2O were determined in C.I.C. demountable cells with CaF_2 windows and 0.1- or 0.2-mm Teflon spacers. Both cells were filled with the electrolyte solutions and base lines were run with adjustment of the thickness of the sample cell until the transmission in the region of interest was equal in the two cells. The benzoic acid solution was run immediately afterwards in one of the cells.

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[1] From a thesis submitted by D. Sussman to the Graduate School of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] J. Steigman and D. Sussman, *J. Am. Chem. Soc.*, **89**, 6400 (1967).