

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Electrostatic Influence of Substituents on the Dissociation Constants of Organic Acids. III

BY F. H. WESTHEIMER AND MARTIN W. SHOOKHOFF

Bjerrum originated the hypothesis that the ratio of the ionization constant of an acid with a polar substituent to that of the corresponding unsubstituted acid depends upon a statistical factor and upon the electrostatic influence of the substituent.¹ While his computation of the magnitude of the electrostatic effect can be regarded only as a first approximation, the theory formed the basis of a new mathematical treatment by Kirkwood and one of us.² This development departs from Bjerrum's treatment in the assumption that the molecules are cavities of low dielectric constant in which the charges are imbedded. The equations derived are of the same form as Bjerrum's, but D , the dielectric constant of the solvent, is replaced by D_E , the "effective" dielectric constant, a function of the shape of the molecule, the position of the charges within the molecule, the dielectric constant of the solvent, and the dielectric constant of the cavity. The equation for a symmetrical dibasic acid is

$$\log K_1/\sigma K_2 = \frac{e^2}{2.303kTRD_E}$$

K_1 and K_2 are the first and second dissociation constants of the acid, e the electronic charge, k the Boltzmann constant, T the absolute temperature, and R the interprotonic distance. σ , the statistical factor, in this instance is equal to four. The equation for a dipole substituted acid is

$$\log K_1/\sigma K_2 = \frac{eM \cos \zeta}{2.303kTR^2D_E}$$

K_1 is the ionization constant of the dipole substituted acid, K_2 that of the corresponding unsubstituted acid, M the dipole moment of the substituent, ζ the angle between the dipole and the line joining its center with the ionizable proton, and R is the distance between the center of the dipole and the proton. D_E has been calculated for molecules which approximate in shape either a sphere, or a prolate ellipsoid of revolution in which the proton and the substituent are at the foci.² In the former case, D_E is calculated as a function of the position of the charges in the

molecule, in the latter as a function of the eccentricity of the ellipsoid.

Several illustrating examples showed that the interprotonic distances in dicarboxylic acids calculated on this basis are consistent with distances estimated from independent considerations, even for those cases for which the simple Bjerrum theory is inadequate. Further, in contrast with the simple theory³ reasonable values of the proton dipole distance were obtained for a few dipole substituted acids.

The present paper will give the interprotonic or proton-dipole separation, calculated by the new theory, for a large number of organic acids. For comparison, the distance calculated on the basis of an extended chain model will again be taken as an upper limit, the distance calculated on the basis of free rotation as a reasonable but not a rigid lower limit. It will be shown that this new development of Bjerrum's hypothesis accounts satisfactorily for the ratio of the dissociation constants of aliphatic dibasic acids, for the ratio of the dissociation constants of dipole substituted aliphatic acids to those of unsubstituted acids, for the ratio of the dissociation constants of the salts of the esters of amino acids to those of the corresponding amino acids, for the effect of alkyl groups and of solvent upon the dissociation constant ratio.

In Table I are assembled the data for the symmetrical dibasic saturated aliphatic acids. In column 1 the name of the acid is given with a key to the authority for the dissociation constant data, in column 2, ΔpK , defined by the relationship $\Delta pK = \log K_1/\sigma K_2$ where K_1 and K_2 are the first and second dissociation constants of the dibasic acid, and σ is the statistical factor. In the column marked R , the interprotonic distance in Å. computed from ionization constant data by means of the new formulation, is given to the nearest 0.05 Å. R_{\max} is the maximum interprotonic distance in Å. on the basis of accepted valence angles and bond lengths, placing the protons conventionally 1.45 Å. beyond the terminal carbon atom and on the extension of the last carbon to

(1) Bjerrum, *Z. physik. Chem.*, **106**, 219 (1923).(2) Kirkwood and Westheimer, *J. Chem. Phys.*, **6**, 506 (1938); Westheimer and Kirkwood, *ibid.*, **6**, 513 (1938).(3) Eucken, *Z. angew. Chem.*, **45**, 203 (1932).

TABLE I
 DIBASIC ALIPHATIC ACIDS

Acid	ΔpK	$\cos \vartheta$	R	Length in Å.		R_B
				R_{Max}	R_F^f	
Oxalic acid ^a	2.36	-1.00	3.85	4.44	3.50	0.91
Malonic acid ^a	2.26	-1.00	4.10	4.87	4.12	1.36
Methylmalonic acid ^a	1.89	-0.33	4.05	4.87	4.12	1.62
Ethylmalonic acid ^a	2.05	- .33	4.10	4.87	4.12	1.50
Dimethylmalonic acid ^a	2.29	- .33	4.15	4.87	4.12	1.34
Diethylmalonic acid ^a	4.48		3.75	4.87	4.12	0.69
Methylethylmalonic acid ^a	2.95	- .33	4.10	4.87	4.12	1.04
Succinic acid ^b	0.84		5.75	6.66	4.66	3.65
α, α' -Dimethylsuccinic acid (209°) ^a	1.56		5.35	6.66	4.66	1.97
α, α' -Dimethylsuccinic acid (129°) ^a	1.66		5.30	6.66	4.66	1.85
α, α' -Diethylsuccinic acid (192°) ^a	2.23	-1.00	5.10	6.66	4.66	1.37
α, α' -Diethylsuccinic acid (129°) ^a	2.49	-1.00	5.00	6.66	4.66	1.23
Tetramethylsuccinic acid ^a	4.19	-1.00	4.80	6.66	4.66	0.74
<i>dl</i> -Tartaric acid ^a	0.75		6.00	6.66	4.66	4.09
<i>meso</i> -Tartaric acid ^a	.99		5.50	6.66	4.66	3.10
Glutaric acid ^b	.47		7.00	7.59	5.15	6.53
β -Methylglutaric acid ^b	.56		6.85	7.59	5.15	5.48
β -Ethylglutaric acid ^c	.44		7.60	7.59	5.15	7.05
β -Propylglutaric acid ^c	.47		7.75	7.59	5.15	6.89
β, β -Dimethylglutaric acid ^b	1.97		5.25	7.59	5.15	1.56
β, β -Diethylglutaric acid ^d	3.66	-1.00	4.70	7.59	5.15	0.84
β, β -Dipropylglutaric acid ^a	3.02	-1.00	5.15	7.59	5.15	1.03
β, β -Methylethylglutaric acid ^a	2.48		5.10	7.59	5.15	1.24
Adipic acid ^b	0.38		7.75	9.02	5.59	8.11
Pimelic acid ^d	.34		8.30	9.91	6.00	9.12
Suberic acid ^a	.28		9.30	11.46	6.38	10.9
Azelaic acid ^a	.26		9.85	12.42	6.74	11.9
<i>cis</i> -Caronic acid ^{b, e}	5.36	+0.15	3.30	4.26	4.08	0.58
<i>trans</i> -Caronic acid ^{b, e}	0.90	- .73	5.45	6.65	5.52	3.44
Cyclopropane- <i>cis</i> -dicarboxylic acid ^{a, e}	2.54	+ .16	3.40	4.26	4.08	1.22
Cyclopropane- <i>trans</i> -dicarboxylic acid ^{a, e}	0.87	- .72	5.00	6.65	5.52	3.56

^a Landolt-Börnstein, "Physikalisch-chemische Tabellen," Erg. III c. ^b Jones and Soper, *J. Chem. Soc.*, 133 (1936).
^c Ingold and Mohrhenh, *ibid.*, 951 (1935), correction. ^d Landolt-Börnstein, "Physikalisch-chemische Tabellen," Erg. II b. ^e The protonic separation on the basis of free rotation for the caronic and cyclopropane-dicarboxylic acids was computed according to an equation kindly supplied to the authors by Professor J. G. Kirkwood. The ring was assumed rigid, and the extracyclic valence angle set equal to the angle between each gem substituent and the adjacent ring bond. In these cases $\cos \vartheta$ and R were determined by the method of successive approximations; elsewhere $\cos \vartheta$ refers to the extended model. ^f The length of the carbon-oxygen bond in the carboxyl group was chosen as 1.29 Å.; otherwise the accepted bond lengths were used. The tetrahedral angle was used throughout except that the angle between the terminal carbon to carbon bond and the carbon to oxygen bond of the carboxyl group was taken as 120°, and the angle between the carbon to oxygen and the oxygen to hydrogen bonds was taken as 90°.

carbon bond. R_F is the root mean square separation of the protons calculated on the basis of free rotation according to Eyring.⁴ Finally, R_B refers to the distance obtained from Bjerrum's formula. In those cases treated on the basis of an ellipsoidal model, the protons were placed at the foci. However, when a spherical model was employed, it was necessary to choose a center for the molecule. In some instances, as with dimethylmalonic acid, the location of the center is quite obvious. In others, however, such as malonic acid itself, or its diethyl derivative, it is

more difficult to choose a center without ambiguity. In these latter cases, it was customary to make the computation with two or more different values of ϑ , the angle made by the lines joining the two protons with the center. While the value of $\cos \vartheta$ is given appropriate to the interprotonic distance quoted, in some cases variation of ϑ between reasonable limits caused an uncertainty in R as great as 0.3 Å. Likewise, in those cases in which the shape of the molecule is intermediate between a sphere and a prolate ellipsoid, a computation on the basis of both possibilities revealed uncertainties in the value of R of the same order of magnitude. Where no value of $\cos \vartheta$ is given

(4) Eyring, *Phys. Rev.*, **39**, 746 (1932). It is worth pointing out that, for Eyring's formula to be valid, free rotation is not actually necessary. See ref. 2, p. 510, footnote 8.

in Table I, the computation was made on the basis of an ellipsoidal model.

On inspection, Table I reveals that in all cases the new formulation gives a reasonable value for the interprotonic distance. Bjerrum's equation, while equally effective for glutaric acid and its normal higher homologs, gives distances which are almost certainly too short for its lower homologs and for polymethylated acids.

Of especial interest is the comparison of the lengths of the methylated with those of the unsubstituted acids. In the case of the malonic acids, for example, the interprotonic distance computed by the Bjerrum equation varies from 0.69 Å. for diethylmalonic acid to 1.62 Å. for the methyl substituted compound. Not only is the magnitude of separation small, but the large variation in distance with a slight structural change is unlikely. On the basis of the new formulation, the separation varies from 3.75 to 4.15 Å., lengths all of which are quite close to the interprotonic distance computed for free rotation. In view of the approximate constancy of the interprotonic distance, it may prove necessary to reexamine the part of the evidence for Ingold's theory of the deflection of the valence angles in alkylated acids which received its support from a consideration of dissociation constant data.⁵ Since the present formulation shows quite clearly that the variation of interprotonic distance with substitution is a phenomenon of the second order in magnitude, it is interesting to account qualitatively for the approximate constancy of R despite the large variation of ΔpK . The new equations predict, to be sure, a smaller change of R with variation in ΔpK than does Bjerrum's. But a second effect is also noticeable. The more alkyl substituents in the acid, the larger is the cavity in the solvent. This lowers the effective dielectric constant and hence magnifies the electrostatic effect of the negative charge of the acid-ion on the ionization of the second proton. In this connection it is possible to discuss the first and second dissociation constants separately. In a later section of this paper it is shown that, at least as a first approximation, the fact that the first dissociation constant of malonic acid is greater than the dissociation constant of propionic acid can be explained on the basis of a statistical factor of two and the electrostatic effect of one carboxyl dipole

(5) Ingold, *et al.*, *J. Chem. Soc.*, 1318, 1594, 2267 (1928); 1691 (1929); 2153 (1931); 949 (1935).

on the dissociation of a proton from the other carboxyl group. It is noteworthy that the first ionization constant of diethylmalonic acid is greater than the first ionization constant of malonic acid, while the second ionization constant of the substituted acid is decidedly less than that of the unsubstituted acid. The reason is at once clear why the ethyl groups increase one ionization constant but decrease the other. In each case the alkyl groups have little direct influence, but, by lowering the effective dielectric constant, they increase the electrostatic potential of the charges already present. It is noteworthy that variation in the angle between the lines joining the protons with the center of the sphere also changes the effective dielectric constant.

In Table II the data for the amino acids are presented. A direct computation of the protonic separation in a glycinium salt, for example, would result from a comparison of the ionization constants of the ammonium groups regarded as acids in the Brönsted sense, in $^+\text{NH}_3\text{CH}_2\text{COO}^-$ and in $^+\text{NH}_3\text{CH}_2\text{COOH}$. According to the zwitterion hypothesis, the ionization constant of the ammonium group of the latter cannot be measured, but it is probable that it will not differ greatly from the dissociation constant of the ester-salt, $^+\text{NH}_3\text{CH}_2\text{COOCH}_3$.⁶ On the basis of this approximation, Neuberger⁷ applied the simple Bjerrum theory to the amino acids. The data presented here show again that the simple Bjerrum theory is only approximate for the smaller molecules, while the present theory adequately accounts for the ratio of the ionization constant of the ester salt to that of the amino acid.

In the column of Table II marked R_C are given the distances between the positive and negative charges in the neutral amino acids, as estimated by Cohn and his co-workers⁸ from dielectric constant measurements. While these lengths should be somewhat less than the interprotonic distances, they are of especial interest because they are experimental values. A comparison of R with them is independent of the uncertainties relative to the extent of hindered rotation which affect the comparison of R with the separation computed on the basis of free rotation or an extended chain model.

(6) See Wegscheider, *Monatsh.*, **16**, 153 (1895), for a comparison of the effect of carbethoxy and carboxyl groups upon the dissociation constants of acids.

(7) Neuberger, *Proc. Roy. Soc. (London)*, **A158**, 68 (1937).

(8) Cohn, *Ann. Rev. Biochem.*, **4**, 93 (1935).

TABLE II
AMINO ACIDS

Amino acid	ΔpK^b	Cos ϑ	R	R_{MAX}	Length in Å.		
					R_F^c	R_C	R_B
Glycine ^a	2.02	-1.00	4.05	3.97	3.56	3.17	1.53
Alanine ^a	2.07	-0.33	3.85	3.97	3.56	3.17	1.50
β -Alanine ^a	1.06		5.15	5.49	4.19	3.97	2.92
γ -Aminobutyric acid ^a	0.72		6.10	6.46	4.72	4.75	4.31
δ -Aminovaleric acid ^a	.62		6.55	7.90	5.19	5.23	5.00
ϵ -Aminocaproic acid ^a	.38		7.85	8.97	5.63	5.76	8.16
Glycylglycine ^a	.56		6.50	7.65	5.17	5.51	5.54

^a Neuberger, *Proc. Roy. Soc. (London)*, **A158**, 68 (1937). ^b ΔpK is defined as $\log_{10} K_E/K_Z$, where K_E is the ionization constant of the ester salt, K_Z of the free amino acid, each regarded as an acid according to the Brönsted definition. ^c The average position of the hydrogen atoms attached to nitrogen was chosen as 0.33 Å. beyond the nitrogen atom in the direction of the carbon to nitrogen bond. In glycylglycine, the angle between the amide linkage and the adjacent carbon to carbon bond was chosen as 120°.

TABLE III
SUBSTITUTED MONOBASIC ACIDS

Acid	pK	Eq.	Cos ζ	R	R_{MAX}	R_F	R_{MIN}	R_B
Fluoroacetic acid ^{a,b}	2.09	S	0.55	2.80	3.29	2.91	1.85	0.49
Chloroacetic acid ^{a,c}	1.89	S	.58	3.00	3.39	2.99	1.84	.55
Bromoacetic acid ^{a,c}	1.87	S	.60	3.05	3.43	3.05	1.82	.54
Iodoacetic acid ^{a,c}	1.59	S	.62	3.10	3.49	3.09	1.81	.55
Glycolic acid ^{a,e}	0.93	E	.36	3.10	3.72	3.33	1.86	.61
Cyanoacetic acid ^a	2.30	E	.78	3.80	4.21	3.81	2.11	.86
β -Chloropropionic acid ^{a,c}	0.85	E	.94	4.25	4.61	3.69	1.27	1.06
β -Bromopropionic acid ^{a,e}	.88	E	.94	4.30	4.69	3.73	1.22	1.02
β -Iodopropionic acid ^{a,c}	.79	E	.94	5.20	4.78	3.78	1.18	1.01
γ -Chlorobutyric acid ^{a,d}	.30	E	.71	5.40	5.80	4.29		1.52
γ -Bromobutyric acid ^{a,d}	.23	E	.70	4.40	5.86	4.33		1.70

^a Landolt-Börnstein, "Physikalisch-chemische Tabellen," Erg. III c. ^b Swarts, *Bull. sci. acad. roy. Belg.*, [5] **8**, 343 (1922). ^c Larsson, *Z. physik. Chem.*, **165A**, 53 (1933). ^d Landolt-Börnstein, "Physikalisch-chemische Tabellen," Hauptwerke. ^e The average value of cos ζ is given.

The fact that reasonable values of R can be obtained completes that argument in favor of the zwitterion hypothesis which is founded upon the comparison of ionization constants.

In Table III the available data for the dipole substituted aliphatic acids are summarized. Here the dissociation constant of each substituted acid is compared with that of the corresponding unsubstituted acid; the statistical factor is, of course, unity. Rather than the dipole moments of the substituent groups, used in the previous publications, the difference between a carbon-hydrogen moment and the moment of the substituent group is desired. Since the resultant moment of the three carbon-hydrogen bonds in a monosubstituted methane is approximately equal to that of one carbon-hydrogen bond directly opposed to the substituent, the dipole moments, determined in the gas phase, of the substituted methanes were used in the computations quoted in Table III.⁹ The letter S in column three refers to the fact that the computations were

(9) Smyth, *J. Phys. Chem.*, **41**, 209 (1937).

made with a spherical model, placing the center of the dipole and the ionizable proton on a diameter; the letter E refers to the fact that an ellipsoidal model was used, and that the center of the dipole and the ionizable proton were placed at the foci. ζ is the angle the dipole makes with the line joining its center to the proton. When the dipole group is not linear (as in the case of the hydroxyl group), the average value of cos ζ was employed, assuming free rotation of the dipolar group. In each case, the proton was conventionally placed on the extension of the last carbon to carbon bond and beyond the terminal carbon atom, and cos ζ determined by the method of successive approximations. The values of cos ζ found in this manner always closely approximated that in the fully extended acid.

For the computation of R_B , the separation of proton and dipole according to the Bjerrum-Eucken hypothesis, cos ζ was assumed equal to that in the fully extended model. Even when cos ζ is assigned the maximum possible value of unity, the simple theory often leads to values of

R_B less than the minimum separation (R_{Min} . in Table III) possible without distortion of valence bonds or angles. Under these circumstances, the method of successive approximations is no longer sensible.

While the simple Bjerrum-Eucken equation is inadequate, the reasonable values of the proton-dipole separation obtained from the new formulation provide a broad justification for Bjerrum's hypothesis.

Among the dipolar substituents which increase the strength of an acid is the carboxyl group. The first dissociation constant of succinic acid, for example, is considerably greater than the dissociation constant of butyric acid, even when the statistical factor of two for the dibasic acid is taken into account. The application of the present theory is made difficult, however, by the following considerations: while Zahn¹⁰ has determined the dipole moment of the carboxyl group in monomeric aliphatic acids, the angle between the dipole and the terminal carbon to carbon bond is unknown. It can be estimated, using Williams' formula¹¹ and the dipole moments of the methyl esters of terephthalic acid and of diphenyl *p,p'*-dicarboxylic acid,¹² that the ester group exerts a moment which is approximately at an angle of 60° with the last carbon to carbon bond. The recent work of Marsden and Sutton¹³ is roughly in accord with this estimate. While the angle of the carboxyl moment is not known, it is a reasonable assumption, in the absence of further information, that the carboxyl group is at least no less symmetrical than the carbomethoxy group.

Besides the uncertainty in the angle of the carboxyl dipole, an additional complication arises from the fact that the moment is a composite one. The charge distribution is such that the carboxyl group will be more effective in increasing the strength of an acid than could be predicted from the resultant moment.

The data of Table IV were calculated using the following assumptions. The moment of the carboxyl group was chosen as 1.7 Debye units, and was placed in the center of the carboxyl group, at an angle of 60° with the terminal carbon to carbon bond. In addition to R_{Max} . and R_F , the protonic separation R_D , determined from the first and second dissociation constants of the

dibasic acid and recorded in Table I, is included as a standard of reference. Since the carboxyl dipole is located somewhere near the center of the carboxyl group, R_D should exceed R by about 0.7 Å. The fact that the actual difference between R_D and R is greater than 0.7 Å. is in qualitative agreement with the deviations anticipated because of the composite nature of the carboxyl moment and the uncertainty relative to its angle.

TABLE IV
DIBASIC ALIPHATIC ACIDS REGARDED AS CARBOXYL SUBSTITUTED MONOBASIC ACIDS

Acid	ΔpK	Eq.	Average Cos \angle	R	R_{Max} .	R_F	R_D	R_B
Oxalic acid ^a	3.22	S	0.50	2.3	3.71	3.24	3.85	0.4
Malonic acid ^a	1.75	S	.38	2.6	4.30	3.91	4.10	.4
Succinic acid ^{a,b}	0.36	E	.49	4.6	5.94	4.48	5.75	1.2
Glutaric acid ^{a,b}	.18	E	.39	5.1	6.81	4.98	7.00	1.5

^a Landolt-Börnstein, "Physikalisch-chemische Tabellen," Erg. III c. ^b Jones and Soper, *J. Chem. Soc.*, 133 (1936).

Finally, the effect of change of solvent upon ΔpK is of interest. There are very few data available relating to the dissociation constants of saturated aliphatic carboxylic acids in pure solvents other than water. This much, however, can be noted. In the Bjerrum expression for ΔpK , the dielectric constant of the medium enters in the denominator to the first power. It would then be anticipated that the logarithm of the ratio of the dissociation constant of chloroacetic acid to that of acetic acid would be from two and a half to three times as great in methyl or ethyl alcohol as in water. The data are available for the chloroacetic acid-acetic acid pair and for the glycolic acid-acetic acid pair in various alcohol-water mixtures.¹⁴ Since ΔpK remains essentially constant throughout, it is probably safe to extrapolate, and estimate that the ratio of the dissociation constants will be the same in pure alcohol as in water. As a matter of fact, the H function of Hammett and Deyrup¹⁵ is based on the assumption, experimentally justifiable for carboxylic acids, that the ratio of the dissociation constants of two acids of the same charge type is little affected by change of solvent. This statement, directly opposed to the predictions of the simple Bjerrum-Eucken equations, is in conformity with the present theory. The effective dielectric constant in the case of chloroacetic and

(10) Zahn, *Phys. Rev.*, **37**, 1516 (1931).

(11) Williams, *Z. physik. Chem.*, **138A**, 75 (1928).

(12) See Sidgwick, *Trans. Faraday Soc.*, **30**, 904 (1934).

(13) Marsden and Sutton, *J. Chem. Soc.*, 1383 (1936).

(14) Michaelis and Mizutani, *Z. physik. Chem.*, **116**, 135 (1925); Mizutani, *ibid.*, **118**, 318 (1925).

(15) Hammett and Deyrup, *THIS JOURNAL*, **54**, 2721 (1932); cf. Wynne-Jones, *Proc. Roy. Soc. (London)*, **A140**, 440 (1933).

glycolic acids is already low, and near the value of D_i , the internal dielectric constant. Computations of D_E for methanol and ethanol show that, for the case of the dipoles in chloroacetic and glycolic acids, using alcohol instead of water as solvent will not appreciably increase the electrostatic effect.

While it is not advisable to extrapolate the data for the aliphatic dicarboxylic acids¹⁴ obtained in water-alcohol mixtures to pure alcohol as solvent, it is obvious that the ratio of the first and second dissociation constants for malonic and succinic acids, while greater in methyl and ethyl alcohols than in water, is certainly not increased by as much as the simple theory predicts, but by a smaller amount, a fact at least qualitatively in agreement with the prediction of the present theory for these cases. Quantitative agreement, in the case of non-aqueous solutions, must await further experimentation.

The errors inherent in the present method of estimating the electrostatic effect, other than those given here, have been discussed in the previous publications. The reasons for omitting

consideration of Ingold's attempt to take electrostriction and electrical saturation into account¹⁶ have been presented elsewhere.² The molecular volumes necessary for the calculations have been estimated from Traube's rule.¹⁷

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Summary

The new mathematical formulation, by Kirkwood and Westheimer, of the electrostatic effect of a substituent, has been shown to account satisfactorily for the ratio of the ionization constant of a dibasic acid, for the ratio of the ionization constant of a dipole substituted acid to that of the unsubstituted acid, for the ratio of the ionization constant of an amino acid with that of a salt of its ester. The theory also accounts for the effect of alkyl groups and, at least in the few cases which can now be examined, for the effect of solvent, upon the ionization constant ratio.

(16) Ingold, *J. Chem. Soc.*, 2179 (1931).

(17) Traube, *Saml. chem.-tech. Vortr.*, 4, 255 (1899).

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The Hydrolysis of Nitriles with Acids

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In previous communications from this Laboratory attempts have been made to correlate reaction rates in hydrolytic reactions catalyzed by concentrated solutions of strong mineral acids with physical properties of these acid solutions.¹ One of the most interesting of these reactions was the hydrolysis of hydrogen cyanide with hydrochloric acid, in which case the velocity constants varied as the square of the mean ion activity. It also was shown that in this particular reaction hydrobromic acid and especially sulfuric acid are much inferior to hydrochloric acid as catalysts for concentrations greater than 3 molal. The investigation has been continued covering the hydrolysis of substituted hydrogen cyanide or organic nitriles using the same mineral acids as catalysts.

Preparation of Material and Method of Procedure

Acetonitrile.—The Eastman Kodak Company preparation was fractionated through a Widmer distilling column.

(1) (a) *THIS JOURNAL*, 51, 3368 (1929); (b) 55, 2326 (1933); (c) 57, 15 (1935); (d) 57, 19 (1935); (e) 60, 2976 (1938).

The fraction used distilled over completely in the temperature range 82.0–82.5°.

Propionitrile.—The Eastman product was treated in the same way, using a fraction boiling over between 96.6–96.8°.

β -Hydroxypropionitrile.—The Eastman preparation was fractionated at 21.5 mm. pressure. The fraction used came over at 122–123°.

Cyanoacetic Acid.—The preparation used was manufactured by C. A. F. Kahlbaum. It was purified by heating it in chloroform and then shaking the solution until cold. In this way large white crystals separated. In a sealed tube they melted 69–70°.

α -Hydroxypropionitrile.—We were unable to get a pure sample of this nitrile. An attempt was made to distil a Kahlbaum preparation under reduced pressure but it decomposed. The best sample we could get was obtained by taking the middle fraction in a vacuum distillation with the aid of solid carbon dioxide-ether bath. This fraction was free of inorganic compounds which would act as catalysts in the hydrolytic studies. The nitrile, however, still had organic impurities as complete hydrolysis only gave 91.2% of the theoretical ammonia.

Acids.—The c. p. grades of acid supplied by Baker and Adamson were used. The hydrobromic acid was distilled