[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

Comparison of Basicity of Aliphatic Amines in Different Solvents

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Introduction

Dissociation constants of organic bases in nonaqueous solution have been measured by the hydrogen electrode,[1] and by conductimetric[2] or colorimetric[3] methods. These methods have been used only for alcohols as solvents. This paper utilizes a method adaptable to the determination of the relative basicities of two or more amines in a wide variety of solvents. Should the base strength of any one amine be known, that of the rest may be calculated. The method is based upon the increased dissociation of a cyanohydrin in the presence of an amine and therefore corresponds to the measurement of the distribution of hydrocyanic acid between a ketone on the one hand and the respective amine on the other. The reaction may be written

$$R_2C(OH)(CN) + B \rightleftarrows R_2CO + {}^+BH + CN^- \qquad (1)$$

as the sum of the competitive reactions

$$R_2C(OH)(CN) \rightleftarrows R_2CO + HCN \qquad (2)$$

$$B + HCN \rightleftarrows BH^+ + CN^- \qquad (3)$$

where B is any amine. It shall be assumed that the degrees of ionization of the amine salts are the same for the different amines in a given solvent and for the sake of simplicity complete ionization is assumed.

Cyanohydrin formation and dissociation are catalyzed in rate by alkali[4] and in most solvents the catalyzed reactions are rapid; equilibrium is readily reached and the analysis is simple.

The acidity of hydrocyanic acid and the basicity of an amine in any solvent will be defined by the equilibria

$$HCN \rightleftarrows H^+ + CN^- \qquad (4)$$

$$B + H \rightleftarrows BH^+ \qquad (5)$$

The equilibrium constant for equation (1) then is

$$K_1 = \frac{(R_2CO)(BH^+)(CN^-)}{[R_2C(OH)(CN)](B)} = K_2K_4K_5 \qquad (6)$$

where K_2, K_4, and K_5[5] are the equilibrium constants corresponding to equations (2), (4), and (5), respectively. Therefore for two bases, B and B′

$$K_1/K'_1 = K_5/K'_5 \qquad (7)$$

since in any given solvent the dissociations of the cyanohydrin and of hydrocyanic acid are constant.

The simplest evaluation of K_1 in any given case involves the assumption that all cyanide that is titratable is cyanide ion and not hydrocyanic acid, in other words, that equation (2) can be neglected in comparison to equation (1) in its contribution to titratable cyanide. In the case of water as solvent this is not true, but K_1 may be calculated as follows.

Let α be the fraction of cyanide in titratable form, and c the initial concentration of cyanohydrin and of amine, then

$$(HCN) = K_2(1 - \alpha)/\alpha \qquad (8)$$

$$(R_2CO) = c\alpha \qquad (9)$$

$$(BH^+) = (CN^-) = c\alpha - (HCN) \qquad (10)$$

$$R_2C(OH)(CN) = c(1 - \alpha) \qquad (11)$$

$$B = c - (BH^+) \qquad (12)$$

Substituting these values into equation (6) we obtain

$$K_1 = \frac{c\alpha^3}{(1 - \alpha)^2} - \frac{K_2}{c\alpha + K_2}\left[\left(\frac{\alpha}{1 - \alpha}\right)^2 c(2 - \alpha) - K_2\right] \qquad (13)$$

Where K_2 is small, which is the case for all solvents used except water and methanol (Table I), this reduces to

$$K_1 = c\alpha^3/(1 - \alpha)^2 \qquad (14)$$

that is, to the first term only of equation (13).

Using water as solvent the values of K_1 calculated from equations (13) and (14) are, respectively, for diethylamine 5.57 and 10.89, and for triethylamine 2.66 and 5.58. The ratios of the constants are correspondingly 2.09 and 1.95, hence using equation (14) involves an error in the ratio of the basic dissociation constants in water of about 7%. For the solvents ethanol, dioxane, propanol, *t*-butyl alcohol and carbon tetrachloride, equation (14) introduces an error of less than 1% in the ratios.

Experimental Results

The dissociation constants, K_2, of acetonecyanohydrin in pure solvents without any alkali

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[1] L. D. Goodhue and R. M. Hixon, THIS JOURNAL, **56**, 1329 (1934); **57**, 1688 (1935).

[2] (a) H. Goldschmidt and E. Matheisen, *Z. physik. Chem.*, **120**, 439 (1926); (b) A. G. Ogston, *J. Chem. Soc.*, 1023 (1936).

[3] T. D. Stewart and V. Cook, THIS JOURNAL, **50**, 1973 (1928).

[4] (a) A. J. Ultee, *Rec. trav. chim.*, **28**, 248 (1909); (b) W. J. Jones, *J. Chem. Soc.*, **105**, 1560 (1914); (c) A. Lapworth, R. H. F. Manske and E. B. Robinson, *ibid.*, 2052 (1927).

[5] K_5 is the reciprocal of K_H, the constant of hydrolysis of an amine salt as normally used. Then for water as solvent the basic dissociation constant, K_b, equals K_5K_W.

present have been measured and summarized in Table I.

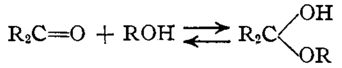
TABLE I

THE DISSOCIATION CONSTANTS OF $(CH_3)_2C(OH)(CN)$ AT 25°

Solvents	K_2
Water	6.49×10^{-2}
Methanol	4.29×10^{-3}
Ethanol	6.64×10^{-4}
Dioxane	1.29×10^{-5}

Jones[4b] found the value in water to be 7.96×10^{-2} which may be in error because of a small amount of base which was introduced as catalyst, but which also shifted the equilibrium.

In *t*-butyl alcohol and carbon tetrachloride the dissociations are too small and too slow in the absence of base to be measured readily; in propanol the dissociation is estimated to lie between those in ethanol and dioxane. The order of decreasing dissociation follows the decreasing order of the dielectric constants for these solvents, but it is probable that this relationship is fortuitous and that the real reason for the difference lies in the solvating power of the respective solvents. Stabilization of acetone or hydrocyanic acid (equation 2) through solvation would increase dissociation, while solvation of the cyanohydrin would decrease it. Of these factors, it is believed that varying solvation of the acetone largely accounts for the differences in dissociation observed. The solvated complex can be represented as an addition product



$$R_2C{=}O + ROH \rightleftarrows R_2C\begin{smallmatrix}OH\\OR\end{smallmatrix}$$

or a union through a hydrogen bond

$$R_2C{=}O + HOR \rightleftarrows R_2C{=}O\text{---}H\text{---}OR$$

Both modes of solvation are forbidden to dioxane and carbon tetrachloride. It is also significant that the rates of dissociation are faster in those cases in which solvation of the acetone is indicated, suggesting an actual displacement of the hydrocyanic acid by the solvent rather than a spontaneous dissociation followed by solvation.

Table II gives the equilibrium constant, K_1, of diethylamine and triethylamine, respectively, with acetonecyanohydrin in different solvents and the last column of the table is the ratio of the basic dissociation constant of diethylamine to that of triethylamine. The values of K_1 in the cases of water and methanol were obtained using equation (13); for the other solvents equation (14) was used. The rate of attainment of equilibrium was rapid except for the solvents dioxane, *t*-butyl alcohol and carbon tetrachloride, which required more than one day. An attempt was made to use hexane as a solvent but it failed because of the low solubility of acetonecyanohydrin in the hexane.

TABLE II

THE EQUILIBRIUM CONSTANTS OF ACETONECYANOHYDRIN WITH AMINES IN DIFFERENT SOLVENTS AT 25°

Solvent	*D*[6]	Et_3N	Et_2NH	Ratio, K_1/K'
Water	80.0	2.66	5.57	2.09
Methanol	33.7	0.0483	0.0572	1.18
Dioxane	2.27	.0276	.0346	1.25
Ethanol	25.7	.0301	.0283	0.94
t-Butanol	11.4	.0268	.0244	.91
Propanol-1	21.8	.0139	.0170	1.23
Carbon tetrachloride	2.24	.0125	.00936	0.75

Discussion of Results

The dissociation constants of diethylamine and triethylamine in water are known, and for comparison values of their constants have been calculated using equation (6), our values for K_2 and K_1 reported in Tables I and II, and the value 7.2×10^{-10} for K_4 (dissociation constant of hydrocyanic acid). Our results, given in Table III, agree well with values given by Hall and Sprinkle obtained by a conductimetric method. Using the value for the dissociation constant of *n*-butylamine in alcohol, measured by Goodhue and Hixon,[1] and combining it with our values of K_1 for the corresponding amines in the same solvents, we obtain dissociation constants for diethylamine and triethylamine in both methanol and ethanol, also given in Table III.

TABLE III

THE BASIC DISSOCIATION CONSTANTS OF *n*-$BuNH_2$, Et_2NH AND Et_3N IN WATER, METHANOL AND ETHANOL AT 25°

	Solvent			
Amine	Water, $\times 10^4$		Methanol, $\times 10^5$	Ethanol, $\times 10^6$
n-$BuNH_2$	4.07[a]		1.20[b]	3.98[b]
Et_2NH	12.6[a]	11.9[c]	5.01[c]	5.31[c]
Et_3N	6.4[a]	5.69[c]	4.23[c]	5.65[c]

[a] N. F. Hall and M. R. Sprinkle, THIS JOURNAL, **54**, 3469 (1932). [b] Reported by Goodhue and Hixon, ref. 1. [c] Determined by the present method. Values of K_1 for *n*-$BuNH_2$ in ethanol and methanol were determined to be 0.0212 and 0.0137, respectively, using equation (14) for ethanol and equation (13) for methanol.

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(6) Dielectric constant of the solvent at 20° obtained from "I. C. T." Olson and Voge, THIS JOURNAL, **56**, 1690 (1934), have stressed the lack of connection between the dielectric constants of solvents and rates of reaction. Here also there is no correlation.

Recently, Ogston[2b] has studied the possible reaction of amine with ethanol by the conductimetric method and obtained the base strength of diethylamine to be 7.2×10^{-8}, which is in qualitative accord with our value based on Goodhue and Hixon's result.

It is surprising to observe that the secondary amines are always stronger bases than the corresponding tertiary amines in water (see Table IV). Generally an alkyl group is considered more electropositive[7] than a hydrogen atom. Its replacement of the hydrogen atom of ammonia would be expected to increase progressively the basicity of ammonia. Bredig[8] pointed out years ago that diethylamine is exceptionally strong as compared to its near homologs but he gave no explanation.[9,10] The difficulty has since been ascribed to an effect of the solvent on the polarity of groups. For instance, Wynne-Jones[11] suggests the use of the "intrinsic strength," obtained by extrapolating the results for different solvents to a hypothetical solvent of infinite dielectric constant, for investigating the relationship between constitution and acid or base strength. His treatment may be inapplicable, for the influence of solvent on amines is not purely electrostatic, and yet he is able to show that the "intrinsic strengths" of primary, secondary, and tertiary amines are in the named order.

TABLE IV

DISSOCIATION CONSTANTS, $K_b \times 10^4$ OF AMINES IN WATER AT 25°

Radical	RNH_2	R_2NH	R_3N
CH_3-	5.0	7.4	0.74
CH_3CH_2-	5.6	12.6	6.40
$CH_3CH_2CH_2$-	4.7	10.2	5.50
$CH_3CH_2CH_2CH_2$-	4.07	20.5	0.86
$(CH_3)_2CHCH_2$-	3.1	4.8	2.60

For the equilibrium

$$B + H_2O \rightleftharpoons BH^+ + OH^-$$

solvation[12] may be more important in the cation than in hydroxide ion or in B. This would be particularly true in the comparison of basicities if the percentage change in solvation with change in solvent were much greater for the cation than for the free amine and different for variously substituted cations. Solvation of the cation operates to increase base strength. For these ions, solvation occurs through hydrogen bond formation, by sharing a lone pair of electrons in an atom of the solvent molecule. For the free amine, solvation may occur through the hydrogen, if present, of the amine, or through the hydrogen, if present, of the solvent.

Our present results offer a clue as to which of the processes is the more important. Referring to Table II, it is noted that the effect of dioxane upon the ratio of basicities is more similar to that of the hydrogen containing solvents, methanol and w ·, than to the effect of carbon tetrachloride. In fact, it lies above other hydroxylated solvents of higher dielectric constant. It is obvious that this similarity cannot be achieved by solvation of the free base and shows the inadequacy of an explanation based upon dielectric constants of the medium; it can more readily be ascribed to a similarity in degree of solvation of the respective cations, by utilizing the hydrogens of the cations and the oxygen of the solvents for hydrogen bond formation.[13] In the three cases it appears that the secondary ammonium ion is stabilized preferentially by this solvation.

In carbon tetrachloride we have a solvent of low "onium" properties and with no hydrogen to solvate the free amines. This offers the best comparison for a study of the relative tendencies of the amines to acquire protons, if we assume that the activity functions of the salts are comparable; they cannot be identical if we assume variable capacity for solvation of the cations. In this solvent the tertiary amine is stronger than the secondary, as expected on the assumption of greater positivity over hydrogen of the alkyl group.

The alcohols studied present considerable variation with respect to each other. It is clear that they differ perceptibly in their solvations of the system studied. The few cases reported do not warrant extended discussion, but it may be observed that ethanol and *t*-butyl alcohol are anomalous with respect to methanol and propanol in their effects. The results can be interpreted on the basis of arbitrary assumptions regarding the nature and relative stabilities of the complexes formed; it remains to be seen whether this tool

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[7] (a) C. G. Derick, THIS JOURNAL, **33**, 1152 (1911); (b) R. M. Hixon and I. B. Johns, *ibid.*, **49**, 1786 (1927).

[8] Bredig, *Z. physik. Chem.*, **13**, 191 (1894).

[9] M. L. Huggins, *J. Org. Chem.*, **1**, 443 (1936), discusses the point.

[10] N. F. Hall, *Chem. Rev.*, **19**, 98 (1936).

[11] W. F. K. Wynne-Jones, *Proc. Roy. Soc.* (London), **A140**, 440 (1933).

[12] N. V. Sidgwick, "The Electronic Theory of Valency," Oxford Press, New York, 1929, p. 189.

[13] D. P. Earp and S. Glasstone, *J. Chem. Soc.*, 1723 (1935), have observed hydrogen bond formation between chloroform and dioxane.

can be used to measure the relative hydrogen-donor and hydrogen-acceptor properties of alcohols. Further work is in progress on other solvents.

Estimates of Accuracy of K_1.—The titratable cyanide varied in concentration from 0.04 to 0.09 M and the reproducibility of the titration was within 0.05 cc. The factor α is known to between 0.1 and 0.25%. From equation (14) this gives a probable error in K_1 of between 1 and 2.2% with greater accuracy in the non-polar solvents.

Experimental Part

Materials. (a) **Acetonecyanohydrin.**—Acetonecyanohydrin was prepared by adding sulfuric acid slowly to a solution of sodium cyanide and acetone.[14] Before the vacuum distillation, one or two drops of concentrated sulfuric acid must be added to stabilize the cyanohydrin. The equivalent weight may be determined accurately by dissolving a weighed sample in a known excess of 0.02 M silver nitrate solution; the solution is then made ammoniacal and finally acidified. The silver cyanide is removed and the excess silver is titrated with a standard thiocyanate using ferric alum as indicator. The product should be colorless and odorless and stored in a desiccator; upon standing no cyanide ion should develop, b. p. 73–74° (10 mm.); $n^{25}\text{D}$ 1.39898.

(b) **Amines.**—Liquids were kept over caustic potash for at least one week and then fractionated. They were characterized by their boiling points.

(c) **Alcohols.**—Commercial absolute ethanol was refluxed over lime for a few days and distilled. This was again distilled from fresh lime through a 1-meter fractionating column. Methanol and propanol were purified in the same way.

t-Butyl alcohol was purified in the manner recommended by Smyth and McNeight.[15] It was first washed with a saturated solution of sodium bisulfite and then refluxed for several hours with 10% sodium hydroxide solution. The alcohol was distilled and dried with anhydrous sodium sulfate and then refluxed over lime for several hours before distilling. The distillate stood over calcium turnings for two days and was finally fractionated.

(d) **Dioxane.**—This was kept over sodium wire for a few months and then carefully fractionated.

(e) **Carbon Tetrachloride.**—Pure commercial carbon tetrachloride was dried over calcium chloride and distilled.

Method to Determine the Equilibrium.—All pipets and burets were calibrated carefully. Two solutions of known strength of amine and of cyanohydrin were put then into the thermostat at 25 ± 02°; when temperature equilibrium was reached they were mixed with fresh solvent similarly treated to give an initial concentration of each reactant of 0.1 M. The solution was then analyzed by a method based on that of Ultee[4a] which depends on the fact that the cyanohydrin is stable and does not give any silver cyanide precipitate in acidified silver nitrate solution. An aliquot portion of the solution was removed and added to 40 cc. of 0.01 M silver nitrate solution containing 0.25 M nitric acid. The silver cyanide precipitate was filtered off, thoroughly washed with water, and the excess of silver determined. The end-point must be carefully watched in the light given by a daylight electric bulb in order to obtain readings concordant within 0.02 cc. Each experiment was repeated two or three times and the results should be concordant within 0.05 cc. With carbon tetrachloride as solvent, no difficulty was found with the analysis, since the ionizable cyanide was extracted readily by continuous shaking for fifteen minutes.

Summary

1. A new method has been developed to determine the relative strengths of organic bases in different solvents.

2. The relative base strengths of diethylamine and triethylamine have been measured in ethanol, methanol, propanol, *t*-butyl alcohol, dioxane, and carbon tetrachloride. It is found that triethylamine becomes a stronger base in carbon tetrachloride and some alcohols as compared to diethylamine; in water, dioxane, methanol, and propanol the latter is the stronger.

3. The dissociation constants of diethylamine and triethylamine in methanol and ethanol are obtained by the present method.

4. The reason for the inversion of the relative base strengths in different solvents is discussed.

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[14] "Organic Syntheses," John Wiley and Sons, Inc., New York, 1935, Vol. XV, p. 1.

[15] C. P. Smyth and S. A. McNeight, THIS JOURNAL, **58**, 1597 (1936).