

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, TEXAS DIVISION, MONSANTO CHEMICAL COMPANY]

The Dissociation of Lactonitrile in Aqueous Solution

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Lactonitrile dissociates in aqueous solution to give HCN and AcH. The equilibrium constant for the dissociation has been determined in the temperature range 25–60° and the heat of dissociation calculated from the data obtained. The calculated heat of dissociation is in good agreement with the heat of reaction of HCN and AcH as determined calorimetrically. The rate of reaction of HCN and AcH has been found to be second order with respect to CN⁻ and AcH concentration. The activation energy calculated from rate studies in the range of 30–60° is 22.9 kcal./mole.

Introduction

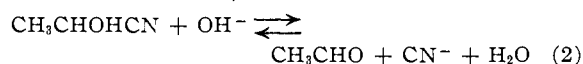
The dissociation of lactonitrile in dilute aqueous solutions into HCN and AcH has been observed to be a reversible process by Jones¹ and Ultée.² The equilibrium constant as defined by the equation

$$K_L = (\text{HCN})(\text{AcH})/(\text{CH}_3\text{CHOHCN}) \quad (1)$$

was found by Jones to be 7×10^{-3} mole/liter at pH 7–8 at 25°. The value calculated from Ultée's data is 2.6×10^{-5} . No explanation can be offered at this time for the large discrepancy in the value of K_L reported by Jones and that reported here, except possibly the effect of pH. Presumably Jones made no attempt to determine the pH of the solutions with which he was working, and it will be shown later that it must be considered as an important variable.

It is of dubious value to cite the work of Ultée as confirmatory for the values reported herein, since his values were obtained using anhydrous reagents.

The probable mechanism for the dissociation (and conversely the reaction of HCN and AcH to form lactonitrile) is as



where k_1 and k_2 are the rate constants for forward and reverse reactions, respectively.

The system as illustrated in Equation (2) can be described kinetically by the following

$$-d(\text{CH}_3\text{CHOHCN})/dt = k_1(\text{CH}_3\text{CHOHCN})(\text{OH}^-) - k_2(\text{AcH})(\text{CN}^-)(\text{H}_2\text{O}) \quad (3)$$

or

$$\frac{-d(\text{CH}_3\text{CHOHCN})}{dt} = \frac{d(\text{HCN})}{dt} = k_1' \frac{(\text{CH}_3\text{CHOHCN})}{(\text{H}^+)} - k_2' \frac{(\text{AcH})(\text{HCN})}{(\text{H}^+)} \quad (4)$$

where

$$k_1' = k_1 K_{\text{H}_2\text{O}} \text{ and } k_2' = k_2 K_{\text{HCN}}$$

Experimental

Materials.—Lactonitrile was obtained from the American Cyanamid Co. Analysis indicated less than 1% free HCN and 99.9% of the theoretical total HCN. Acetaldehyde was obtained from Eastman Kodak Co. HCN was obtained from Rohm and Haas, Inc., with a reported purity of 98.3%. It was distilled from the storage cylinder prior to being used.

Determination of the Equilibrium Constant.—All runs were made in a thermostated water-bath with the temperature maintained constant to $\pm 0.05^\circ$.

In each experiment, 50 ml. of a standard 0.05 *M* solution of lactonitrile was placed in a stoppered flask in the water-bath and allowed to come to constant temperature. The

pH of the solution was adjusted roughly to a value between 8 and 10 by stirring with a glass rod moistened with 10% caustic solution. Chemical equilibrium is reached practically instantaneously in alkaline solution. Accurate measurement of the pH of the system at this point was made with a Beckman Model G instrument, with proper temperature corrections. Immediately following measurement of pH, 10 ml. of standard 0.1 *N* AgNO₃, previously acidified with HNO₃ to a pH of not greater than 1, was added. The addition of acid AgNO₃ causes precipitation of the free HCN and CN⁻ as Ag₂(CN)₂ and at the same time "freezes" the dissociation of lactonitrile. (The fact that lactonitrile will not react with AgNO₃ in acid solution can be readily demonstrated by adding some of the pure compound to acid AgNO₃). Titration of the excess Ag⁺ by the Volhard method³ using standard 0.1 *N* KCNS with ferric alum indicator then made possible the calculation of free HCN + CN⁻ at equilibrium in the solution.

Determination of the Heat of Reaction.—The method of determination of the heat of reaction of 0.05 *M* HCN and 0.05 *M* AcH was essentially the same as that described in the literature for the determination of the heat of neutralization of acids and bases.⁴ Values obtained in three determinations were -11.66, -11.76 and -10.86 kcal./mole.

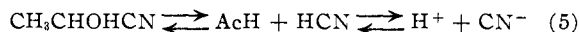
Kinetics of the Reaction of HCN and AcH.—All runs were made in a thermostated bath with temperature controlled to within $\pm 0.05^\circ$.

In separate, stoppered flasks, 200 ml. of standard 1.0 *M* AcH and 0.1 *M* HCN were allowed to come to thermal equilibrium. The tenfold excess of AcH was used in order to drive the reaction toward more complete consumption of HCN. The pH of each flask was adjusted roughly to a value between 2.5–5 with concd. HNO₃. The relatively low pH values are necessary in order to slow the reaction to a rate which can be conveniently followed. At pH values above 5 the reaction is much too rapid to follow conveniently and at values below 2.5 it becomes excessively slow.

When a run was started, the contents of one flask were poured into the other with the simultaneous starting of a stop watch. The pH of the reaction mixture was then accurately determined with the Beckman instrument. Samples containing 50 ml. were pipetted out of the reaction flask at measured time intervals and run into 25 ml. of acidified standard 0.1 *N* AgNO₃. Titration of the excess Ag⁺ with standard KCNS made possible the calculation of free HCN remaining at time *t*.

Data and Calculations

Equilibrium Constant.—The stoichiometric representation of the system at equilibrium is



Since AcH and HCN are formed in equimolar quantities in the solution it follows that

$$(\text{AcH}) = (\text{HCN}) + (\text{CN}^-) \quad (6)$$

Argentometric analysis gave the value of (HCN) + (CN⁻).

(3) F. D. Snell and F. M. Biffen, "Commercial Methods of Analyses," McGraw-Hill Book Co., Inc., New York, N. Y., 1944, p. 154.

(4) F. Daniels, J. H. Matthews, and J. W. Williams, "Experimental Physical Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1934, p. 85.

(1) W. J. Jones, *J. Chem. Soc.*, **105**, 1563 (1914).

(2) A. J. Ultée, *Rec. trav. chim.*, **28**, 248 (1909).

The molar concentration of HCN is given by the expression for its ionization

$$(\text{HCN}) = (\text{H}^+)(\text{CN}^-)/K_{\text{HCN}} \quad (7)$$

Solution of equation (6) for (CN^-) and subsequent substitution in equation (7) gives (HCN) in terms of experimentally determined quantities.

$$(\text{HCN}) = (\text{AcH})(\text{H}^+)/(K_{\text{HCN}} + (\text{H}^+)) \quad (8)$$

The concentration of undissociated lactonitrile at equilibrium is

$$(\text{CH}_3\text{CHOHCN}) = (\text{CH}_3\text{CHOHCN})_{\text{initial}} - (\text{AcH}) \quad (9)$$

Equations (8) and (9) contain all the data necessary for calculation of K_L , as given by equation (1). Experimental data and values of K_L in equation (1) are given in Table I.

TABLE I
(CH_3CHOHCN)_{initial} = 0.05244 M

Run No.	Temp., °C.	(H^+) $\times 10^{10}$	K_{HCN}^a $\times 10^{10}$	(AcH) $\times 10^3$	$K_L \times 10^4$
1	25	1.86	3.98	3.1	6.23
2	25	2.29	3.98	3.2	7.66
3	25	1.86	3.98	3.3	7.20
4	30	2.63	6.92	4.4	11.4
5	30	2.51	6.92	4.1	9.37
6	30	2.40	6.92	4.2	9.52
7	40	4.68	9.55	5.4	20.8
8	40	4.68	9.55	5.5	20.9
9	40	4.68	9.55	5.6	22.2
10	49	12.8	15.8	5.8	31.9
11	49	12.8	15.8	5.6	28.8
12	60	30.2	28.9	6.6	49.1
13	60	30.2	28.9	6.2	42.6
14	60	30.2	28.9	6.6	48.6

^a Calculated from thermodynamic data in "Selected Values of Chemical Thermodynamic Properties," National Bureau of Standards, 1949, Volume I, Table 8, p. 1; Table 23, p. 13.

Figure 1 is a plot of $\log K_L$ vs. $1/T$. The value of the heat of reaction, ΔH , for the dissociation of lactonitrile calculated from the slope is +11.5 kcal./mole. This value is in agreement with the

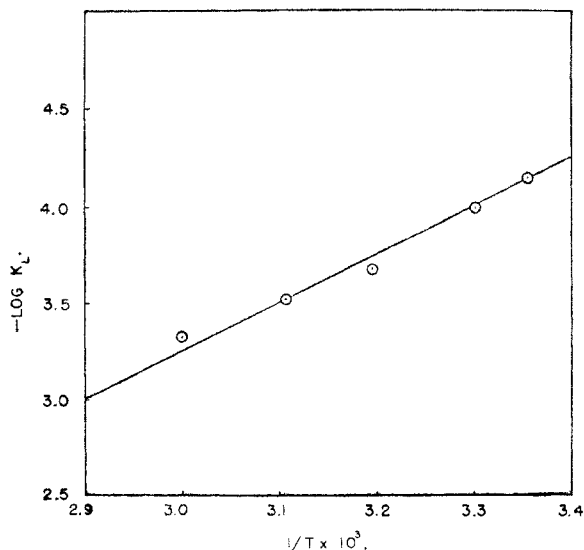


Fig. 1.—Effect of temperature on equilibrium constant for the dissociation of lactonitrile.

measured heat of reaction of AcH and HCN (−11.4 kcal./mole).

Kinetics of the Reaction.—Inspection of the equilibrium constant shows that the reaction of HCN and AcH goes to virtual completion, within the limitations of the analytical methods employed. The term $k_1'(\text{CH}_3\text{CHOHCN})/(\text{H}^+)$ can then be dropped from equation (4), giving it the form

$$\frac{-d(\text{HCN})}{dt} = k_2' \frac{(\text{AcH})(\text{HCN})}{(\text{H}^+)} \quad (10)$$

The solution to this equation is

$$\frac{2.303(\text{H}^+)}{(\text{AcH})_i - (\text{HCN})_i} \log \frac{(\text{HCN})}{(\text{HCN}) + (\text{AcH})_i - (\text{HCN})_i} = k_2' t + \text{constant} \quad (11)$$

where $(\text{AcH})_i$ and $(\text{HCN})_i$ are initial molar concentrations.

Figure 2 plots $\log \frac{(\text{HCN})}{(\text{HCN}) + (\text{AcH})_i - (\text{HCN})_i}$ in equation (11) vs. time, t , for two typical experi-

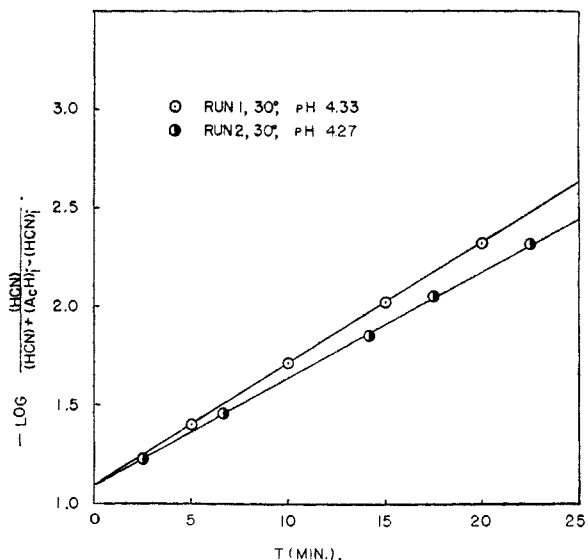


Fig. 2.—Plot of kinetic data for two typical runs.

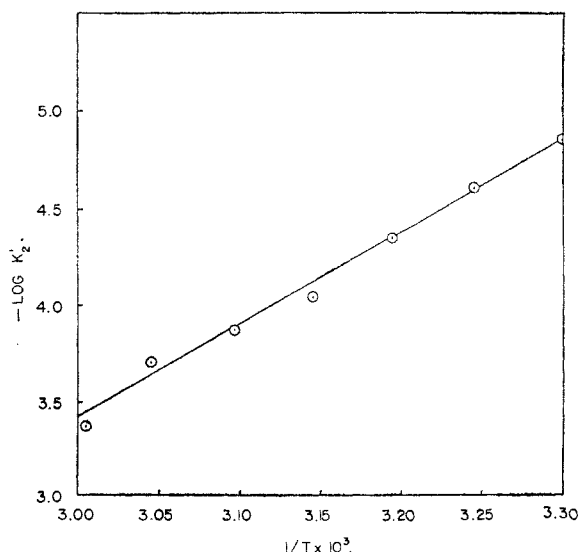


Fig. 3.—Effect of temperature on rate of reaction of HCN and AcH.

ments: Run 1 at 30°, pH 4.33 and Run 2 at 30°, pH 4.27.

TABLE II

Run No.	Temp., °C.	$k_2' \times 10^5$ min. ⁻¹	Run No.	Temp., °C.	$k_2' \times 10^5$ min. ⁻¹
1	30	1.38	8	45	9.76
2	30	1.38	9	50	14.1
3	35	2.50	10	50	12.6
4	35	2.46	11	55	19.5
5	40	4.75	12	55	19.9
6	40	4.25	13	60	43.1
7	45	8.84	14	60	41.0

The values of k_2' can be readily calculated from the slopes of the straight lines obtained. Table II is a complete summary of calculated values of

k_2' determined at various temperatures in this investigation.

The Arrhenius equation represents the rate behavior of chemical reactions as a function of temperature

$$k_2' = se^{-\Delta H_a/RT} \quad (12)$$

Figure 3 plots $\log k_2'$ vs. $1/T$ for calculation of the heat of activation, ΔH_a , for the reaction of (HCN) and (AcH). The value of ΔH_a from Fig. 3 is found to be +22.9 kcal./mole. The frequency factor, s , in the Arrhenius equation is found to be 4.36×10^{11} min.⁻¹ by substitution of known values of k_2' , T , and the calculated value of ΔH_a .

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[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

Diffusion Measurements, at 1°, of Aqueous Solutions of Amino Acids, Peptides and Sugars

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Using the method of free diffusion from an initially sharp boundary between solution and solvent, the spreading of the boundary with time being followed with the aid of Rayleigh interference fringes, the diffusion coefficients, D , of 13 amino acids, 4 peptides and 5 sugars have been determined in dilute aqueous solution at 1°. Since the molecular weight, M , and volume, V , of these materials are known it has been possible to obtain empirical relations between D and M or V . These relations should be of value in providing preliminary estimates of molecular weight from diffusion measurements on structurally similar materials, such as polypeptides, where conventional methods are not applicable.

As is well known Stoke's law, $D = kT/6\pi\eta r$, relating the diffusion coefficient, D , to the radius, r , of the solute particle and the viscosity, η , of the solvent, is valid only for large molecules in dilute solutions and even for these the radius computed from the diffusion coefficient generally exceeds, as a result of hydration and asymmetry, that obtained from the molal volume, V , i.e., $r = (3V/4\pi N)^{1/3}$. Here N is Avogadro's number whereas the k and T in Stoke's relation are the Boltzmann constant and the absolute temperature, respectively. Except in the case of extreme asymmetry the product $DV^{1/3}$ is, however, roughly constant for large molecules, whereas for small ones Polson¹ has noted a decrease in the product $DM^{1/3}$ with increasing molecular weight, M . Consequently he has proposed² the empirical equation

$$D = \frac{A'}{M^{1/3}} + \frac{B'}{M^{2/3}} + \frac{C'}{M} \quad (1)$$

with three adjustable constants. Actually the simpler relation

$$D = A/(M^{1/3} - B) \quad (2)$$

fits his data about as well as (1) and has the advantage that a plot of $DM^{1/3}$ vs. D is linear. In terms of molal volumes the expression is

$$D = a/(V^{1/3} - b) \quad (3)$$

As a further test of the validity of these empirical relations the diffusion coefficients of a variety of substances of known molecular weight and volume

have been determined and are reported later in this paper. Since these relations are potentially useful in providing preliminary estimates of molecular weight from diffusion measurements in the case of such materials as the polypeptides,³ the present study has been restricted to structurally similar substances. Moreover, since the method that has been employed has proved to be a practical one for precise diffusion measurements, and permits the use of much existing electrophoresis equipment with only minor changes, the experimental procedures are also described in some detail.

Experimental

Method.—The method used in the present research is that of free diffusion from an initially sharp boundary between solution and solvent, the spreading of the boundary with time being followed with the aid of Rayleigh interference fringes.^{4,5} The modified Tiselius cell shown diagrammatically in Fig. 1 has been used as a diffusion cell in conjunction with the capillary siphoning procedure of Polson⁶ for sharpening the boundary initially. The modification of the cell consists in the addition of duplicates of the channel windows at W. Together with the thermostat water these windows provide a comparison path of essentially the same optical properties as the boundary channel. Before the boundary is first formed in the left-hand side of the channel at the junction of the bottom and center sections of the cell, a thin-walled glass capillary is inserted, as shown in Fig. 1, with its tip near the center of the channel. As soon as the boundary is formed it is caused to rise in the channel by withdrawal of liquid through the capillary.

(3) K. O. Pedersen and R. L. M. Synge, *Acta Chem. Scand.*, **2**, 408 (1948).

(4) J. St. L. Philpot and G. H. Cook, *Research*, **1**, 234 (1948).

(5) Harry Svensson, *Acta Chem. Scand.*, **5**, 72 (1951).

(6) D. S. Kahn and Alfred Polson, *J. Phys. Colloid Chem.*, **51**, 816 (1947).

(1) A. Polson, *J. Phys. Colloid Chem.*, **54**, 649 (1950).

(2) A. Polson and D. van der Reyden, *Biochim. Biophys. Acta*, **5**, 358 (1950).