[CONTRIBUTION FROM THE DEPARTMENT OF INDUSTRIAL CHEMISTRY, THE FACULTY OF ENGINEERING, KYOTO UNIVERSITY]

Kinetics of the Cyanoethylations of Ethanolamine, Acetylacetone and Methanol

BY YOSHIRO OGATA, MASAYA OKANO, YOSHIAKI FURUYA AND IWAO TABUSHI

RECEIVED MAY 29, 1956

The potassium hydroxide-catalyzed cyanoethylations of ethanolamine and acetylacetone in aqueous media were kinetically investigated by the estimation of remaining acrylonitrile by the *n*-dodecyl mercaptan method. In both cases, the rates were found to be proportional to the product of the concentrations of the corresponding reactants, *i.e.*, $[H_2NCH_2CH_2OH]$-$[CH_2{=}CHCN]$ or $[CH_3COCHCOCH_3^-][CH_2{=}CHCN]$. The rate of the reaction of acrylonitrile with sodium methoxide in methanolic solvent was also measured. The rate was first order with respect to the concentration of acrylonitrile and the initial concentration of methoxide ion, *i.e.*, $[CH_3O^-][CH_2{=}CHCN]$. The rate expressions agree with a mechanism which involves a nucleophilic attack of free amine, carbanion or alkoxide ion on the β-carbon atom of acrylonitrile.

Some synthetic studies have been reported on the cyanoethylation or addition of active hydrogen compounds to the double bond of acrylonitrile,[1] but as yet little systematic kinetic evidence for the reaction mechanism has been presented. Electronic theory easily predicts that the reaction will involve a nucleophilic attack on the positively charged β-carbon atom of acrylonitrile.[2] The present study was undertaken in order to confirm this general mechanism from the kinetic standpoint as well as to identify the attacking species.

Experimental

Materials.—Commercial C.P. grade acrylonitrile, ethanolamine, acetylacetone and methanol were purified by duplicate distillations and their boiling points (acrylonitrile, 76.5°; ethanolamine, 90–91° (30 mm.); acetylacetone, 138°; methanol, 65°) agreed with those in the literature. The *n*-dodecyl mercaptan was prepared satisfactorily from lauryl alcohol *via* the corresponding bromide,[3,4] and purified by vacuum distillation, b.p. 168–170° (38 mm.).

Rate Measurements.—As a typical procedure, an example with ethanolamine is described below. A mixture of 90 cc. of 0.25 *M* aqueous ethanolamine, 120 cc. of *ca.* 1 *M* potassium phosphate–potassium hydroxide or potassium borate–potassium chloride–potassium hydroxide buffer[5] and 15 cc. of distilled water placed in a 500-cc. flask, and thermostated at 30°. After attaining the temperature equilibrium, 75 cc. of 0.15 *M* aqueous acrylonitrile, previously allowed to reach the same temperature, was added. Forty-cc. aliquots were taken at known intervals and the amount of unreacted acrylonitrile was estimated by the *n*-dodecyl mercaptan method.[6] The sample was poured into a solution containing *ca.* 50 cc. of 60% aqueous isopropyl alcohol and 25 cc. of *ca.* 0.1 *M* *n*-dodecyl mercaptan–isopropyl alcohol solution, and then potassium hydroxide solution was added until the *p*H of the solution was *ca.* 12.[7] After the solution was allowed to stand for *ca.* 5 minutes, the solution was acidified with *ca.* 3 cc. of glacial acetic acid, and titrated with a methanolic solution of 0.05 *N* iodine to the point of the appearance of light yellow color.

In the cyanoethylation of acetylacetone, an aqueous solution of potassium hydroxide was used as a catalyst in place of a buffer solution, since it was observed that the buffer action was invalidated owing to the high concentration of acetylacetone. Accordingly, an appreciable variation of *p*H was recognized during the reaction and restricted the rate measurement only to the initial stage of reaction (*ca.* 20–50% conversion).

The cyanoethylation of methanol was carried out in absolute methanol with sodium methoxide as a catalyst to avoid completely the possibility of the competitive attack of hydroxide ion. No variation of the alkali concentration was observed during the reaction. The initial concentration of sodium methoxide was determined by titration with 0.1 *N* oxalic acid.

Experimental Results and Calculations.—The apparent second-order rate constants, k, in the cyanoethylations of ethanolamine and acetylacetone were calculated by means of the usual equations, and are presented in Table I and II, respectively. On the other hand, the cyanoethylation of methanol showed a pseudo-first-order reaction, the rate constants k' being calculated by means of an equation $k' = k''c$ where k'' is the first-order rate constant and c is the initial concentration of the alkali. These values of k and k' with varying molar ratio were found to remain constant as listed in Tables Ia, IIa and III, thus justifying the rate equations. Tables Ib and IIb show the effect of *p*H on the rate.

Possibility of Acid-catalyzed Cyanoethylation of Ethanolamine.—In view of the fact that glacial acetic acid has often been used as a catalyst in the cyanoethylation of aromatic amines,[1] the following test was carried out. The acidic sample solutions with *p*H 2.5, 3.5 (citric acid–citrate buffer) and 5.0 (acetic acid–acetate buffer), prepared from 0.0375 *M* acrylonitrile and 0.0750 *M* ethanolamine, were heated at 50°, and at definite time intervals the content of acrylonitrile in the solutions was estimated. In each solution, a slight decrease of the content was observed (*e.g.*, *ca.* 5% after 3 hr.), but the decrease was similar to that observed in blank tests. Hence, the acid-catalyzed cyanoethylation of ethanolamine seems impossible at least under these conditions.

TABLE I

RATE CONSTANTS OF THE CYANOETHYLATION OF ETHANOLAMINE AT 30.0 ± 0.1°

(a) The effect of molar ratio

Initial concn. Acrylonitrile (a) *M*	Initial concn. Ethanolamine (b) *M*	*p*H	$k \times 10^3$,[a] l. mole^{-1} sec.$^{-1}$
0.0750	0.0750	9.7[b]	3.13 ± 0.04
.0750	.0375	9.7[b]	3.09 ± .07
.0375	.0750	9.7[b]	3.06 ± .06
.0375	.0375	9.7[b]	3.10 ± .04

(b) The effect of *p*H—initial concn.: acrylonitrile, 0.0375 *M*; ethanolamine, 0.0750 *M*

*p*H	$k \times 10^3$,[a] l. mole^{-1} sec.$^{-1}$	*p*H	$k \times 10^3$,[a] l. mole^{-1} sec.$^{-1}$
7.5[b]	0.057 ± 0.001	9.7[b]	3.12 ± 0.04
7.9[b]	.124 ± .003	9.7[c]	3.06 ± .06
8.3[b]	.315 ± .008	10.2[c]	4.31 ± .07
8.9[c]	.98 ± .03	10.8[c]	5.20 ± .07
9.4[c]	2.29 ± .07		

[a] Figures following ± mean probable errors. [b] Potassium phosphate–potassium hydroxide buffer. [c] Potassium borate–potassium chloride–potassium hydroxide buffer.

(1) *Cf.* H. A. Bruson, *Org. Reactions*, **5**, 49 (1949).

(2) For example, such a mechanism has been proposed for the cyanoethylation of ketones [G. R. Zellars and R. Levine, *J. Org. Chem.*, **13**, 911 (1948)].

(3) O. Kamm and C. S. Marvel, "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 29.

(4) G. G. Urquhart, J. W. Gates, Jr., and R. Conner, *Org. Syntheses*, **21**, 36 (1941).

(5) Since a little decrease of *p*H was recognized during the reaction, the buffer salts were added to the solutions. No effect of ionic strength on the rate was observed on their addition.

(6) D. W. Beesing, W. P. Tyler, D. M. Kurtz and S. T. Harrison, *Anal. Chem.*, **21**, 1073 (1949).

(7) To avoid the chemical change (*e.g.*, hydrolysis or polymerization) and to accelerate the addition of mercaptan, it seems necessary to maintain the alkalinity of the solution near this *p*H range.

TABLE II

RATE CONSTANTS OF THE CYANOETHYLATION OF ACETYLACETONE AT 40.0 ± 0.2°

(a) The effect of molar ratio

Initial concn. Acrylonitrile (a) M	Acetylacetone (b) M	pH[a]	$k \times 10^4$, l. mole^{-1} sec.$^{-1}$
0.084	0.047	9.7	2.67 ± 0.07
.084	.142	9.7	2.54 ± .04
.187	.300	9.6	2.64 ± .02
.117	.150	9.1	2.00 ± .03
.099	.300	9.1	1.95 ± .05

(b) The effect of pH—initial concn.: acrylonitrile, *ca.* 0.090–0.130 M; acetylacetone, 0.150 M

pH[a]	$k \times 10^4$, l. mole^{-1} sec.$^{-1}$	pH[a]	$k \times 10^4$, l. mole^{-1} sec.$^{-1}$
8.3	0.54 ± 0.01	9.1	2.00 ± 0.04
8.5	0.77 ± .03	9.4	2.52 ± .08
8.8	1.20 ± .03	9.9	2.70 ± .11

[a] Mean value during the reaction.

TABLE III

RATE CONSTANTS OF THE CYANOETHYLATION OF METHANOL AT 20.0 ± 0.1°

Initial concn. Acrylonitrile (a) M	Alkali (c) M	$k' \times 10^2$, l. mole^{-1} sec.$^{-1}$
0.0750	0.0750	0.97 ± 0.03
.0750	.0250	.94 ± .01
.0500	.0500	.97 ± .02
.0500	.0250	.96 ± .02
.0250	.0750	.99 ± .02
.0250	.0500	.98 ± .01
.0250	.0250	.94 ± .02

Discussions of Mechanisms

(A) The Cyanoethylation of Ethanolamine.—The results obtained above and the acrylonitrile resonance

$$CH_2{=}CHC{\equiv}N \longleftrightarrow \overset{+}{C}H_2{-}\overset{-}{C}HC{\equiv}N \longleftrightarrow \overset{+}{C}H_2CH{=}C{=}\overset{-}{N} \text{ etc.}$$

which affords an electrophilic activity to the β-carbon atom of the molecule suggest a nucleophilic attack of the free amino nitrogen as shown in the scheme

$$HOCH_2CH_2NH_2 + H^+ \rightleftharpoons HOCH_2CH_2\overset{+}{N}H_3 \quad \text{(mobile)} \quad (1)$$

$$HOCH_2CH_2NH_2 + CH_2{=}CHCN \longrightarrow HOCH_2CH_2\overset{+}{N}H_3CH_2\overset{-}{C}HCN \text{ (slow)} \quad (2)$$

$$HOCH_2CH_2\overset{+}{N}H_2CH_2\overset{-}{C}HCN \longrightarrow HOCH_2CH_2NHCH_2CH_2CN \text{ (fast)} \quad (3)$$

The scheme leads to a rate equation[8]

$$dx/dt = k_2[CH_2CHCN][HOCH_2CH_2NH_2] \quad (4)$$

where k_2 is the rate constant of step 2. In weakly alkaline media, the stoichiometric concentrations of acrylonitrile and ethanolamine may be expressed as

$$a - x = [CH_2CHCN]$$

and

$$b - x = [HOCH_2CH_2NH_2] + [HOCH_2CH_2\overset{+}{N}H_3] \quad (5)$$

$$= [HOCH_2CH_2NH_2](1 + K_1[H^+]) \quad (6)$$

respectively. Here K_1 is the equilibrium constant of equation 1. Thus by equating the calculated and observed rates, relationship 8 between the second-order rate-constant k and the hydrogen ion concentration is obtainable.

$$\frac{dx}{dt} = \frac{k_2(a - x)(b - x)}{1 + K_1[H^+]} \equiv k(a - x)(b - x) \quad (7)$$

$$k_2 = k(1 + K_1[H^+]) = \text{const.} \quad (8)$$

The value of K_1 has been measured to be 2.77×10^9 at 25°.[9] Thence the values of 10^3k_2 were calculated with our data at pH 7.5–10.8 in Table Ib to be 5.1, 4.6, 4.7, 4.5, 4.8, 5.0, 4.9, 5.1 and 5.4, which remain constant and support the mechanism.

Nucleophilic attack of the oxygen anion of the conjugate base of ethanolamine is also conceivable, but was not recognized in terms of product or kinetics in this pH range. This may be accounted for by the strong basicity of the amine. The electron-releasing property of the amino group will render ethanolamine so weakly acidic that the presence of its conjugate base is appreciable only in stronger alkalinities. The failure of the acid-catalyzed cyanoethylation may also be explicable on the basis of the negligible concentration of free base even in weak acidic media.

(B) The Cyanoethylation of Acetylacetone.—Since the reaction occurs in the presence of an alkaline catalyst, the rate-determining step must be attack of the carbanion of acetylacetone, and a probable mechanism is

$$(CH_3CO)_2CH_2 + OH^- \rightleftharpoons (CH_3CO)_2\overset{-}{C}H + H_2O \text{ (mobile)} \quad (9)$$

$$(CH_3CO)_2\overset{-}{C}H + CH_2{=}CHCN \longrightarrow (CH_3CO)_2CHCH_2\overset{-}{C}HCN \text{ (slow)} \quad (10)$$

$$(CH_3CO)_2CHCH_2\overset{-}{C}HCN + H_2O \longrightarrow (CH_3CO)_2CHCH_2CH_2CN + OH^- \text{ (fast)} \quad (11)$$

This mechanism readily leads to a rate equation

$$dx/dt = k_{10}[CH_2CHCN][(CH_3CO)_2\overset{-}{C}H] = \frac{k_{10}(a - x)(b - x)}{1 + ([H_2O]/K_9[OH^-])} \equiv k(a - x)(b - x) \quad (12)$$

Hence a relation

$$k_{10} = k\left(1 + \frac{[H_2O]}{K_9[OH^-]}\right) = \text{const.} \quad (13)$$

will be expected. The value of K_9 at 25° has been reported[10] to be 6.4×10^6. By employing equation 13, 10^4k_{10} was calculated to be 2.9, 2.8, 2.9, 3.3, 3.4 and 3.0 from our data at pH 8.3–9.9 in Table IIb, *i.e.*, the expectation was perfectly fulfilled.

(8) If the step 3 was rate-determining with step 2 in mobile equilibrium, the same rate equation would be obtainable. But it seems less probable, since the intermolecular addition of neutral molecule must be slower than the intramolecular proton shift.

(9) N. F. Hall and M. R. Sprinkle, THIS JOURNAL, **54**, 3469 (1932); calculated from $K_B = 2.77 \times 10^{-5}$.

(10) G. Schwarzenbach and K. Lutz, *Helv. Chim. Acta*, **23**, 1147 (1940); M. L. Eidinoff, THIS JOURNAL, **67**, 2072 (1945); calculated from $K_A = 1.16 \times 10^{-9}$

(C) The Cyanoethylation of Methanol.—Similarly, the experimental data suggest the mechanism

$$CH_3O^- + CH_2{=}CHCN \longrightarrow CH_3OCH_2\bar{C}HCN \text{ (slow)} \quad (14)$$

$$CH_3OCH_2\bar{C}HCN + CH_3OH \longrightarrow CH_3OCH_2CH_2CN + CH_3O^- \text{ (fast)} \quad (15)$$

Therefore

$$dx/dt = k_{14}[CH_2CHCN][CH_3O^-] \equiv k'(a - x)c \quad (16)$$

It is not possible to estimate the concentration of methoxide ion in equation 16. However, it was found that the observed rate constants k' at various alkaline concentrations hold constancy, hence the dissociation of sodium methoxide seems to be almost complete in such a dilute solution.

Acknowledgments.—The authors thank Prof. R. Oda for his advice and Teikoku Jinken Co. for their material assistance.

KYOTO, JAPAN

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, AEROJET-GENERAL CORP.]

Derivatives of 4-Nitrazapentanonitrile

BY MILTON B. FRANKEL AND KARL KLAGER

RECEIVED MAY 25, 1956

4-Nitrazapentanonitrile has been prepared and converted to 4-nitrazapentanoyl chloride, 3-nitrazabutyl isocyanate and 3-nitrazabutylamine. Derivatives of these compounds are reported.

The preparation of aliphatic *gem*-dinitro dinitriles, such as 4,4-dinitroheptanedinitrile,[1] and monoesters, such as methyl 4,4-dinitropentanoate,[2] has been reported recently. Aliphatic secondary nitraza dinitriles such as nitrimino-bis-acetonitrile[3] and nitrimino-bis-propionitrile[4] have also been synthesized, but the secondary nitraza aliphatic mononitriles have not been reported. Because of the desire for comparing the physical properties and chemical reactions of the aliphatic *gem*-dinitro compounds and the nitramino analogs, it was of interest to study the chemistry of a simple aliphatic secondary nitramine containing a mononitrile group.

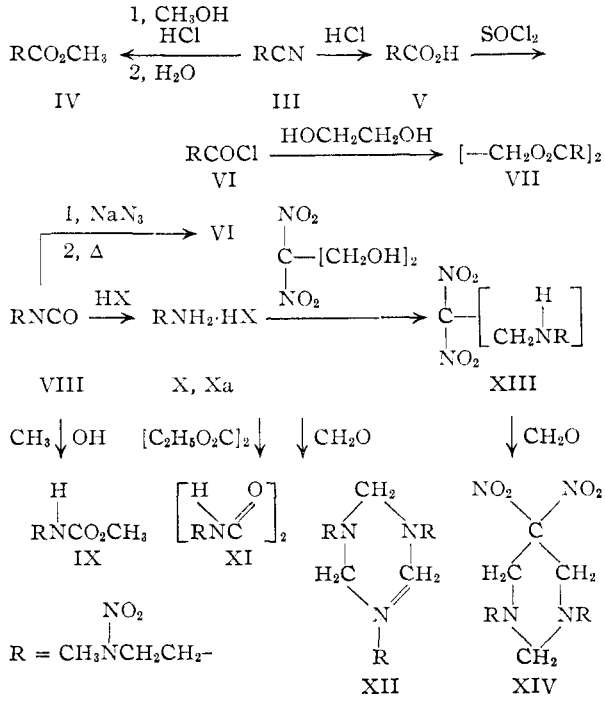
For this purpose 4-nitrazapentanonitrile (III) was chosen since 4-azapentanonitrile (I) was readily available from the Michael reaction of methylamine and acrylonitrile.[5] Using the Wright procedure[4] for the nitration of secondary amines, Compound I was converted *via* the nitric acid salt II into III.

$$CH_3NH_2 + CH_2{=}CHCN \longrightarrow \underset{\text{I}}{CH_3\overset{H}{\overset{|}{N}}CH_2CH_2CN} \xrightarrow{HNO_3} \underset{\text{II}}{CH_3\overset{H\cdot HNO_3}{\overset{|}{N}}CH_2CH_2CN} \xrightarrow[HCl]{Ac_2O} \underset{\text{III}}{CH_3\overset{NO_2}{\overset{|}{N}}CH_2CH_2CN}$$

The chemical reactions of 4-nitrazapentanonitrile (III) are summarized in Chart I.

4-Nitrazapentanonitrile (III) was converted *via* the imino ester hydrochloride to methyl 4-nitrazapentanoate (IV). The ethyl ester was prepared in the same manner. Hydrolysis of III or IV with concentrated hydrochloric acid gave 4-nitrazapentanoic acid (V), which was refluxed with thionyl chloride to yield 4-nitrazapentanoyl chloride (VI). Ethylene bis-4-nitrazapentanoate (VII) was prepared from VI and ethylene glycol. Compound VI was converted to the corresponding azide which was decomposed *in situ* to give 3-nitrazabutyl isocyanate (VIII). The methyl carbamate (IX) of VIII was prepared. Treatment of VIII with 35% nitric acid and concentrated hydrochloric acid gave 3-nitrazabutylammonium nitrate (X) and 3-nitrazabutylammonium chloride (Xa), respectively. The condensation of 3-nitrazabutylamine with ethyl oxalate gave N,N'-bis-(3-nitrazabutyl)-oxamide (XI), and with formaldehyde yielded 1,3,5-tris-(3'-nitrazabutyl)-hexahydro-1,3,5-triazine (XII). The Mannich reaction of X and 2,2-

CHART I



(1) L. Herzog, M. H. Gold and R. D. Geckler, THIS JOURNAL, **73**, 749 (1951).

(2) H. Shechter and L. Zeldin, *ibid.*, **73**, 1276 (1951).

(3) A. P. N. Franchimont and J. V. Dubsky, *Rec. trav. chim.*, **36**, 80 (1916).

(4) G. F. Wright, *et al.*, *Can. J. Research*, [B] **26**, 114 (1948).

(5) A. H. Cook and K. J. Reed, *J. Chem. Soc.*, 399 (1945).