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KINETICS OF THE CONDENSATION OF SOME ALIPHATIC ALDEHYDES WITH AMMONIA

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Abstract—The rate and equilibrium constants of the reaction of some aliphatic aldehydes with ammonia have been measured in aqueous solutions at 20° by means of spectrophotometry. The rate equations are $v = k_f$ [unhydrated aldehyde] [free ammonia] for the forward reaction and $v = k_r$ [α-aminoalcohol] for the reverse. The reaction was subject to acid catalysis. Electron-releasing groups in aldehydes tended to decrease the rate of the forward reaction with Taft's ρ^* of 2·29, while the same groups increased the rate of the reverse reaction with ρ^* of −6·29 (decomposition of α-aminoalcohols). These results agree with the expectation from the suggested reaction mechanism.

IT HAS been known that the simple Hammet's or Taft's rule is not applicable in most cases for the formation and the hydrolysis of various Schiff's bases.[1–12] Some investigators explained these facts by the lack of resonance between carbonyl and aromatic ring at the transition state,[2] but some others by the shift of the rate-determining step from the formation to the dehydration of intermediary α-aminoalcohols.[1,5]

The present paper summarizes our data on the kinetic study of analogous reactions of aliphatic aldehydes with ammonia to form α-aminoalcohols, Eq. 1 in an aqueous solution to obtain information concerning the substituent effect.

$$NH_3 + RCHO \leftrightharpoons RCH(OH)NH_2 \qquad (1)$$

There is no kinetic study of this kind of reaction. The rates of the reactions were determined by the spectrophotometric estimation of remaining aldehydes.

RESULTS AND DISCUSSION

The observed rate and equilibrium constants for the present reactions are summarized in Table 1. As stated previously for acetaldehyde,[13] the corrected equilibrium constant K' remains constant for propionaldehyde and n-butyraldehyde.

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TABLE 1. OBSERVED EQUILIBRIUM AND RATE CONSTANTS OF THE REACTION OF SOME ALIPHATIC ALDEHYDES WITH AMMONIA IN AQUEOUS SOLUTIONS CONTAINING SODIUM CHLORIDE (IONIC STRENGTH 0·5) AT 20°

Acetaldehyde, initial conc. 0·0582 M

Initial conc. NH_3 M	Added CH_3CO_2H N	pH	Corrected equilibrium constant K' M^{-1}	Apparent rate constant forward $k_1 \times 10^2$ $M^{-1}\ sec^{-1}$	reverse $k_{-1} \times 10^3$ sec^{-1}
0·190	0·063	9·735	43·3	2·93	1·20
0·190	0·084	9·535	43·7	2·87	1·52
0·190	0·105	9·35	48·5	2·95	2·03
0·190	0·126	9·145	50·6	2·90	3·07
0·190	0·147	8·93	(73·5)	3·01	4·71
			av. 46·3	av. 2·93	

Propionaldehyde, initial conc. 0·0728 M

NH_3 M	CH_3CO_2H N	pH	K' M^{-1}	$k_1 \times 10^2$ $M^{-1}\ sec^{-1}$	$k_{-1} \times 10^3$ sec^{-1}
0·203	0·021	10·42	11·45	2·07	2·07
0·203	0·042	10·10	10·55	2·16	2·76
0·203	0·063	9·90	10·64	2·13	3·13
0·203	0·084	9·70	10·26	2·28	4·31
0·203	0·105	9·51	10·30	1·94	4·79
0·203	0·126	9·33	10·06	1·78	6·04
			av. 10·54	av. 2·06	

n-Butyraldehyde, initial conc. 0·0530 M

NH_3 M	CH_3CO_2H N	pH	K' M^{-1}	$k_1 \times 10^2$ $M^{-1}\ sec^{-1}$	$k_{-1} \times 10^3$ sec^{-1}
0·203	0·210	10·37	7·13	2·05	3·26
0·203	0·042	10·08	7·68	2·21	3·79
0·298	0·021	10·57	7·79	2·05	2·92
0·298	0·042	10·30	7·93	2·20	3·30
0·298	0·063	10·10	7·45	2·21	3·88
0·305	0·084	10·00	8·16	2·51	4·35
0·305	0·105	9·85	8·27	2·49	4·81
0·305	0·126	9·70	8·58	2·56	5·51
			av. 7·87	av. 2·28	

Isovaleraldehyde,[a] initial conc. 0·0269 M

NH_3 M	CH_3CO_2H N	pH	K' M^{-1}	$k_1 \times 10^2$ $M^{-1}\ sec^{-1}$	$k_{-1} \times 10^3$ sec^{-1}
0·393	0·011	10·72	2·16	0·471	2·24
0·393	0·022	10·54	2·07	0·611	3·12
0·393	0·043	10·30	2·11	0·646	3·46
0·393	0·065	10·14	2·02	0·729	4·36
0·393	0·087	10·06	2·03	0·823	5·68
			av. 2·06		

[a] The reaction was carried out in 40 vol % dioxane–60 vol % water containing NaCl (ionic strength 0·25) at 20°.

These facts suggest that there is an analogous equilibrium 1 between the reactants and α-aminoalcohols. The apparent rate constants (k_1) for the forward reaction do not vary with acidity, whereas the constants (k_{-1}) for the reverse reaction increase sharply with increasing acidity of the solution.

As reported previously,[13] the reaction of acetaldehyde with ammonia to form α-aminoethanol is second-order for the forward reaction and first-order for the reverse reaction, and both reactions are acid-catalyzed. Also,[13] the apparent rate constant k_1 for the forward reaction is expressed as:

$$k_1 = k_f \cdot \frac{1}{1 + (K_3[H_2O][H^+]/K_w)} \cdot \frac{1}{1 + K_4[H_2O]} \tag{2}$$

Here, k_f is the true rate constant for step 1, and the K's are the equilibrium constants of the subscripted steps.[14,15]

$$NH_3 + H_2O \leftrightharpoons NH_4^+ + OH^- \tag{3}$$

$$RCHO + H_2O \leftrightharpoons RCH(OH)_2 \tag{4}$$

The calculated values of k_f using Eq. 2 increase with increasing acidity. Hence the rate constant k_f is expressed as:

$$k_f = k_{fw} + k_{fH}[H^+] \tag{5}$$

Similarly, k_{-1} is expressed as:

$$k_{-1} = k_{rw} + k_{rH}[H^+] \tag{6}$$

The catalytic constants calculated by means of the least square method for the forward and reverse reactions are listed in Table 2. For the reaction of isovaleraldehyde with ammonia in 40 vol % dioxane aqueous solution, the apparent rate constant for the forward reaction increases with increasing acidity. The acid–catalytic constants increase by changing the solvent from water to 40 vol % dioxane.

TABLE 2. THE CATALYTIC CONSTANTS FOR THE FORWARD AND REVERSE REACTIONS AT 20°

Aldehyde R in RCHO	Forward $k_{fw} \times 10^2$ M^{-1} sec^{-1}	Forward $k_{fH} \times 10^{-8}$ M^{-2} sec^{-1}	Reverse $k_{rw} \times 10^4$ sec^{-1}	Reverse $k_{rH} \times 10^4$ M^{-1} sec^{-1}
CH_3	4·81	1·54	4·91	3·58
C_2H_5	3·56	1·26	20·3	8·94
n-C_3H_7	2·49	1·31	26·0	15·2
i-C_4H_9[a]	0·38	5·03	14·6	44·7

[a] The values in 40 vol % dioxane–60 vol % water containing sodium chloride of ionic strength 0·25.

Since reactive species are supposed to be unhydrated aldehyde and free base of ammonia as stated previously,[13] it is necessary to see the extent of hydration of aldehydes (Eq. 4) and of acid catalysis for the comparison of their forward reaction

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[15] The equilibrium constant, K_4, was determined by spectrophotometry according to R. Bieber and G. Trüpler, *Helv. Chim. Acta* **30**, 1860 (1946).

rates. The values of the apparent rate constants, k_1, hold approximate constancy with varying acidity of the solution (Table 1). Therefore, the extent of hydration of aldehyde only need be considered. Molar fraction of unhydrated aldehyde, f, is expressed as $K_4[H_2O]/(1 + K_4[H_2O])$ which can be determined by the measurement of K_4. The value of k_1/f may be used to compare the rates of forward reactions.

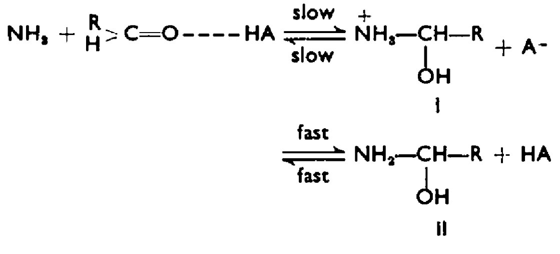
As the susceptibility to oxonium ion catalysis is not uniform as has been suggested,[8] the value of k_{rw} may be used to compare the rates of reverse reactions. Further, if the equilibrium constant, K_0, is defined as $(k_1/f)/k_{rw}$, the constant may be considered to represent the stability of α-aminoalcohols independent of the acidity and of the hydration of aldehydes as shown in Table 3.

TABLE 3. THE RELATIVE RATE AND EQUILIBRIUM CONSTANTS FOR THE REACTION OF ALIPHATIC ALDEHYDE WITH AMMONIA AT 20°

Aldehyde R in RCHO	f	Relative rate constant Forward $(k_1/f) \times 10^2$ M^{-1} sec^{-1}	Reverse $k_{rw} \times 10^4$ sec^{-1}	Equilibrium K_0 M^{-1}
CH_3	0·541	5·42	4·91	110
C_2H_5	0·562	3·67	20·3	18·1
n-C_3H_7	0·774	2·95	26·0	11·4
i-C_4H_8	—	—	24·3[a]	—

[a] The value in pure water calc. by neglecting the solvent effect.

The rate with isobutyraldehyde could not be determined, because the reaction rate was too fast and the conversion to the α-aminoalcohol was too low as expected from the data in Table 3. The plot of the Taft's equation gave a positive ρ^* value for the forward rate (2·29) and a negative ρ^* value for the reverse rate (−6·29). These results suggest a mechanism:[13]



$$NH_3 + \overset{R}{\underset{H}{>}}C{=}O\text{----}HA \underset{\text{slow}}{\overset{\text{slow}}{\rightleftharpoons}} \underset{\text{I}}{\overset{+}{N}H_3\text{—}\underset{\displaystyle OH}{\underset{|}{C}H}\text{—}R} + A^- \underset{\text{fast}}{\overset{\text{fast}}{\rightleftharpoons}} \underset{\text{II}}{NH_2\text{—}\underset{\displaystyle OH}{\underset{|}{C}H}\text{—}R} + HA \qquad (7)$$

The positive ρ^* value for the forward reaction shows that an electron-releasing group R in the aldehyde deactivates the electrophilicity of the carbonyl group, resulting in a decrease of the rate of the nucleophilic attack of ammonia on the carbonyl group. The negative high ρ^* value for the reverse reaction is probably caused by overlapping of favorable effects of alkyl group on the protonation of α-aminoalcohol II (equilibrium) and on the cleavage of C—N$^+$ bond of the conjugate acid I (rate), which means that an electron-releasing group may increase the basicity of α-aminoalcohol II, resulting in an increase of the concentration of protonated α-aminoalcohol I, and that the same group may stabilize the carbonyl group or carbonium ion produced by the C—N$^+$ fission. Such negative high ρ^* values have been observed for the hydrolysis of formals in water (−8·345),[16] ketals and acetals in 50% aqueous dioxane (−3·600)[17] via the analogous mechanism (cleavage of C—O$^+$ bond) and for the dissociation of trimethyl boron addition compounds with primary amines[18] (−7·26). On the contrary, if the rate-determining step were the dehydration of α-aminoalcohol

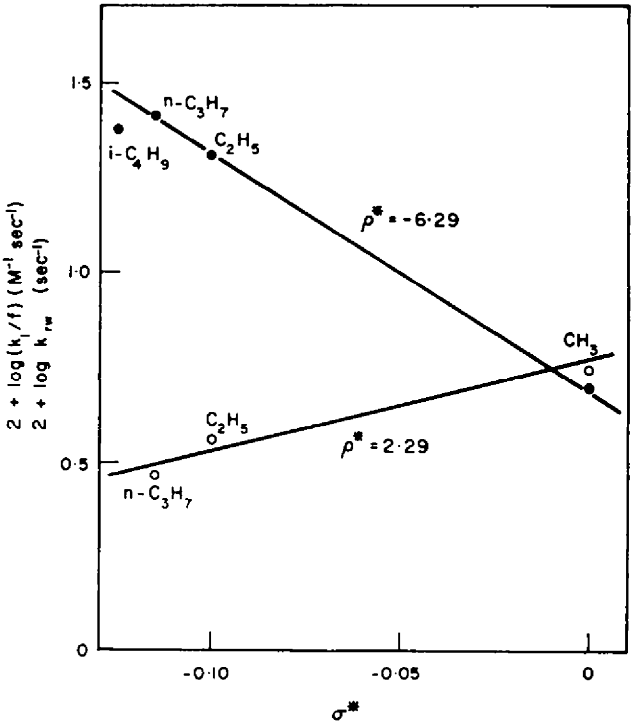


FIG. 1. Plots of log (k_1/f), ○, and log k_{rw}, ◐, for the reaction of aliphatic aldehydes with ammonia vs. Taft's sigma constants.

to aldimine, as in the semicarbazone formation of aromatic aldehydes,[5] a very small or negative ρ^* value for the rate of the forward reaction and a very small or positive ρ^* value for the rate of the reverse reaction should be obtained. For an electron-releasing group should increase the dehydration rate of aminoalcohol III by electron donation to leaving oxygen atom ($\rho = -1{\cdot}74$ for the semicarbazone formation),[5,19] but it should decrease the equilibrium concentration of α-aminoalcohol III ($\rho = 1{\cdot}81$ for the equilibria of the formation of α-aminoalcohols),[5] which results in an increase or a small decrease in the overall forward rate. Conversely, for the reverse reaction, the same group should retard the hydration rate of aldimine ($\rho^+ = 1{\cdot}26$ for OH$^-$ attack, 1·71 for H_2O attack on the conjugate acid of aldimine IV),[9] but should increase the

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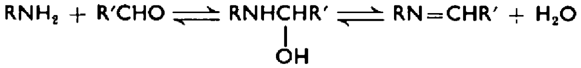
[19] R. Wolfenden and W. P. Jencks, *J. Amer. Chem. Soc.* **83**, 2763 (1961).

equilibrium concentration of the conjugate acid of the aldimine IV, resulting in a decrease or a small increase in the overall reverse rate.



$$RNH_2 + R'CHO \rightleftharpoons RNHCHR'(OH) \rightleftharpoons RN{=}CHR' + H_2O$$

III IV

These expectations were not observed in the present reactions, hence it is rational that the dehydration of α-aminoalcohol is not rate-determining.

EXPERIMENTAL

Materials. Ammonia used was of G. R. grade. Commercial acetaldehyde, propionaldehyde and n-butyraldehyde of C. P. grade were purified by repeated distillations. Acetaldehyde, b.p. 22–23°; propionaldehyde, b.p. 48·0–48·5°; n-butyraldehyde, b.p. 74–75°. Isovaleraldehyde was prepared by the chromic acid oxidation[20] of isoamylalcohol, b.p. 91–93°.

The reaction product criterion. The product of the reaction of acetaldehyde with ammonia was acetaldehyde ammonia, m.p. 92–93°.[13] Similarly, the condensation of other aliphatic aldehydes with ammonia give unstable aldehyde ammonia. For example, a crystalline product, n-butyraldehyde ammonia, m.p. 25·5–26,[21] was obtained in 63% yield by the condensation of conc. NH_4OH with n-butyraldehyde at 0°. This material was very soluble in water and unstable at room temp. It decomposed or polymerized to yellow viscous liquid.

Kinetic procedure. The rate of the reaction in aqueous solution was determined spectrophotometrically at 20° according to our previous report,[13] i.e., the decrease of the carbonyl peak at 278 mμ (acetaldehyde), 280 mμ (propionaldehyde), 283 mμ (n-butyraldehyde), or 288 mμ (isovaleraldehyde) was followed by a Shimadzu SV50A spectrophotometer. Sodium chloride was added to the reaction mixture to keep the ionic strength constant ($\mu = 0{\cdot}5$). For the reaction of isovaleraldehyde, a mixture of 40% dioxane and 60% water was used as a solvent because of the poor solubility of isovaleraldehyde in water. The rate constant was calculated by means of the following equations.

$$k_1 = \frac{1}{t} \cdot \frac{2{\cdot}303x_e}{ab - x_e^2} \log \frac{(ab - xx_e)x_e}{(x_e - x)ab}$$

$$k_{-1} = \frac{1}{K} k_1 = \frac{(a - x_e)(b - x_e)}{x_e} k_1$$

Here, k_1 and k_{-1} are the apparent rate constants for the forward and reverse reactions, respectively, a the initial concentration of ammonia and b that of aldehyde, x the concentration of consumed aldehyde at time t and x_e that at the equilibrium, and K is the equilibrium constant of step 1.

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