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

Kinetics of the Condensation of Anilines with Formaldehyde

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The rates of the condensation of aniline and ring-substituted anilines with formaldehyde in aqueous hydrochloric media (*p*H 0.7–1.6) have been measured by means of the sulfite method at 25°. The rate is second-order with respect to the initial concentration of aniline and first-order with respect to the sum of the concentrations of formaldehyde and methyleneanilines present. Decreasing the oxonium-ion concentration, produces an increase in the rate, whereas, in the neighborhood of neutrality, precipitation of the trimer of methyleneaniline retarded the further reaction. A mechanism is postulated, which involves the rapid reversible formation of the conjugate acid of methyleneaniline followed by the rate-determining condensation of it with another aniline molecule. The rate equation derived from this mechanism is consistent with the experimental data. The effect of substituents in aniline on the rate was found to decrease in the following order: *m*-CH_3 > *o*-CH_3 > None > *m*-Cl > *p*-CH_3 > *p*-Cl.

Although many kinetic studies have been reported upon the resin-forming condensation of phenol or urea with formaldehyde, there seems to be few kinetic data on the similar reaction between aniline and formaldehyde. The mechanism of this reaction has been excellently reviewed by Frey[1] from the purely chemical standpoint. The following report summarizes studies upon the rates and probable mechanism of the initial stages in the reaction of aniline or substituted anilines with formaldehyde in aqueous hydrochloric acid.

Experimental

Materials.—Commercial aniline was purified by duplicate vacuum-distillations, b.p. 80.0–80.2° (19 mm.). The formaldehyde (abbreviated as FA in this paper) was of best grade; the trace of formic acid contained in it had no influence on the estimation. The cyclic trimer of methyleneaniline (T), $(C_6H_5NCH_2)_3$, prepared according to Miller and Wagner[2] was crystallized from ligroin, m.p. 139–140°. Commercial substituted anilines were purified by duplicate vacuum-distillations; those which were solid exhibited melting points in agreement with those in the literatures.

General Procedure for the Kinetic Measurements.—The aqueous hydrochloric aniline solution was prepared from appropriate amounts of aniline and aqueous hydrochloric acid, *e.g.*, the concentrations of aniline and hydrochloric acid were 0.40 and 0.60 mole/l., respectively. A mixture of 50 cc. of the solution and 100 cc. of water was placed in one Erlenmeyer flask and 50 cc. of a FA solution of a known concentration (*e.g.*, 0.40 mole/l.) in the other. After reaching the temperature equilibrium of 25.0 ± 0.1° in a thermostat, the two solutions were mixed and 20-cc. aliquots were pipetted out at regular time intervals. It was poured into a flask containing a mixture of 25 cc. of 0.5 *N* aqueous sodium sulfite and such a quantity of sodium hydroxide as to leave an excess of 10 cc. of 0.1 *N* sodium hydroxide after neutralizing the hydrochloric acid present.[3] After adding 5–6 drops of 1% rosolic acid solution as an indicator, the sample was titrated with 0.1 *N* hydrochloric acid and a sum of the amounts of FA, T and methyleneaniline ($C_6H_5N=CH_2$, abbreviated as M) was estimated.[4]

Some Complementary Experiments

A. **Properties of the Products.**—The amounts of resinous products, precipitated after thirty, sixty and one hundred and eighty minutes, after starting the reaction of No. 2 in Table I, weighed 0.8, 1.2 and 1.6 g., respectively. These values were nearly in agreement with those calculated from the consumption of FA, etc. The products obtained were all light-yellow amorphous powders which were soluble in phenol, aniline and strong acid, but insoluble in benzene, ligroin and alcohol, and softened at 90–110°. They probably are condensates of relatively-low molecular weight.

B. **Rate-determining Step.**—In order to ascertain the rate-determining step, T was dissolved in aqueous hydrochloric acid and then its consumption rate was measured by means of the sulfite method. The rate showed no appreciable difference from that of the aniline-formaldehyde reaction under the same conditions. White amorphous precipitates, obtained by neutralizing the solutions at two, five and ten minutes after starting the reaction under the same conditions as in A, were small quantities, and identified as T by mixed melting point determinations; there was no indication of an increase of T during the procession of the reaction. Furthermore, FA was detected in the distillate by Schiff reagent, when a small quantity of T was boiled in dilute aqueous hydrochloric acid. These facts imply mobile reversible equilibriums (3) and (4) in the paragraph Discussion of Results and a small value of the product of two constants, $K_3 \times K_4$.

Experimental Results and Calculations.—The effects of *p*H (No. 1–6), molar ratio of reactants (No. 7–13), and the concentration (No. 14–17) upon the rate are tabulated in Table I. Pseudo-first-order rate constants were calculated by means of the usual equation

$$k = \frac{1}{t} \ln \left(\frac{f}{f - x}\right)$$

TABLE I

PSEUDO-FIRST-ORDER CONSTANTS IN THE CONDENSATION OF ANILINE WITH FORMALDEHYDE AT 25 ± 0.1°

	Initial concn.				
No.	*M* Aniline (*a*)	*M* CH_2O (*f*)	*M* HCl	$k \times 10^4$ (sec.$^{-1}$)[a]	*p*H
1	0.100	0.100	0.125	2.31 ± 0.03	1.6
2	.100	.100	.150	2.09 ± .02	1.3
3	.100	.100	.175	1.80 ± .02	1.1
4	.100	.100	.200	1.57 ± .03	1.0
5	.100	.100	.250	1.23 ± .02	0.8
6	.100	.100	.300	1.11 ± .01	0.7
7	.100	.050	.150	2.08 ± .03	1.3
8	.100	.075	.150	2.12 ± .03	1.3
2	.100	.100	.150	2.09 ± .02	1.3
9	.100	.150	.150	2.05 ± .03[b]	1.3
10	.100	.200	.150	2.02 ± .04[b]	1.3
11	.050	.100	.150	0.42 ± .01	1.0
12	.075	.100	.150	1.07 ± .01	1.1
2	.100	.100	.150	2.09 ± .02	1.3
13	.125	.100	.150	3.74 ± .05	1.6
14	.050	.050	.075	0.62 ± .01	1.6
15	.075	.075	.1125	1.27 ± .02	1.4
2	.100	.100	.150	2.09 ± .02	1.3
16	.150	.150	.225	4.13 ± .04	1.1
17	.200	.200	.300	7.0 ± .2	1.0

[a] Figures following ± mean probable errors. [b] With the molar ratio *f*:*a* over 1, the first-order kinetics applies only below about 40% consumption of FA, etc.

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(1) Frey, *Helv. Chim. Acta*, **18**, 491 (1935).

(2) Miller and Wagner, THIS JOURNAL, **54**, 3698 (1932).

(3) If estimated in acidic or neutral medium as in our previous report [Ogata and Okano, *ibid.*, **72**, 1459 (1950)], the further aniline-formaldehyde condensation proceeded to an appreciable extent during the estimation; it is necessary, therefore, to treat with aqueous sulfite in an alkaline solution.

(4) From the estimation with pure T under these conditions, three moles of sulfite added to one mole of T, *cf.* B. A. S. F., German Patent 132,621; *Frdl.*, **6**, 534 (1904). Several attempts to estimate FA separately from M or T were unsuccessful. The sum of the amounts of FA, T and M is expressed as FA, etc., in this paper.

Here, f (moles/l.) is the stoichiometric initial concentration of FA, and x (moles/l.) is the sum of the decreased concentrations of FA, M, and T after t seconds estimated by the sulfite method. Deviations of k values were relatively small in the range of about 15–70% consumption of FA, etc., but the constants tended to be smaller as the reaction proceeded. The stoichiometric initial concentration of aniline is indicated as a (moles/l.) in the following pages. The pH's in the reaction mixtures were measured with a glass electrode at 25°.

The Effect of Substituents in the Benzene Ring upon the Rate.—Similar experiments as described above were done with o-, m- and p-substituted anilines; with chloroanilines, the estimation was not easy, since the solution soon emulsified and a resinous precipitate separated. However, the rate of consumption of FA, etc., estimated by means of the sulfite method, decreased in the following order of substituents

$$m\text{-CH}_3 > o\text{-CH}_3 > \text{None} > m\text{-Cl} > p\text{-CH}_3 > p\text{-Cl}$$

With p-CH_3 and p-Cl derivatives, the products contained substituted hydroquinazolines[5] as well as the resinous matter. In the reaction with toluidines, the solutions were always homogeneous and, therefore, the following pseudo-first-order rate constants could be obtained under the same conditions as expt. 4 with aniline, though their deviations from constancy were larger than with aniline: $k \times 10^4$ (sec.$^{-1}$): m-CH_3, 9.8 ± 0.4; o-CH_3, 1.73 ± 0.06: p-CH_3, 0.010 ± 0.001. Since the electrophilic attack of carbonium ion on the ring carbon seems to be rate-determining (see equation 5), the fact that the m-CH_3 substituent increases the rate while m-Cl decreases it is explained.

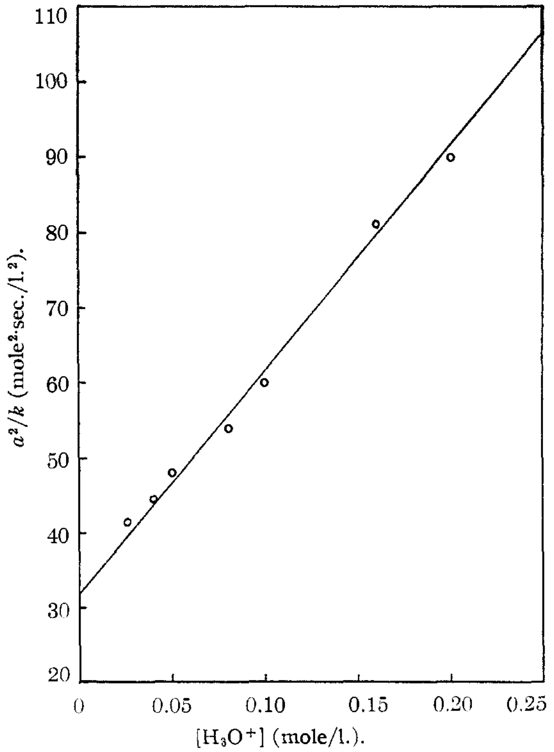

Fig. 1.—Relationship between a^2/k and $[H_3O]^+$.

Discussion of Results

The results obtained above suggest a reaction mechanism for the initial stages of the condensation[6]

$$C_6H_5NH_2 + H_3O^+ \rightleftarrows C_6H_5NH_3^+ + H_2O \quad (1)$$

$$CH_2O + H_3O^+ \rightleftarrows {}^+CH_2OH + H_2O \quad (2)$$

$$C_6H_5\text{–}NH_2 + {}^+CH_2OH \rightleftarrows C_6H_5\text{-}NH\text{–}{}^+CH_2 + H_2O \text{ (mobile)} \quad (3)$$

$$3C_6H_5NHCH_2^+ + 3H_2O \rightleftarrows (C_6H_5NCH_2)_3 + 3H_3O^+ \text{ (mobile)} \quad (4)$$

$$C_6H_5NHCH_2^+ + C_6H_5NH_2 \longrightarrow p\text{- or } o\text{-}C_6H_5NHCH_2C_6H_4NH_2 + H^+ \text{ (slow)} \quad (5)$$

More generally, equations (3) and (5) should be indicated in the form, respectively

$$ArNH_2 + {}^+CH_2OH \rightleftarrows ArNHCH_2^+ + H_2O \quad (6)$$

$$ArNHCH_2^+ + Ar'NH_2 \xrightarrow{k'} ArNHCH_2Ar'NH_2 + H^+ \quad (7)$$

Here, Ar and Ar′ mean aromatic residues which involve C_6H_5–, $C_6H_5NHCH_2C_6H_4$– and C_6H_5-$(NHCH_2C_6H_4)_nNHCH_2C_6H_4$–, and Ar′ on the right side of equation (7) means their dehydrogenated forms, *e. g.*, –C_6H_4–. When Ar and Ar′ are of relatively-low molecular weight, the over-all rate will be given by equation (8), if step (7) with an average rate constant k' is rate-determining

$$\begin{aligned} dx/\mathrm{d}t &= k'(\Sigma[ArNHCH_2^+])(\Sigma[Ar'NH_2]) \\ &= k'[YNHCH_2^+][ZNH_2] \end{aligned} \quad (8)$$

where $[YNHCH_2^+]$ is the sum of $[ArNHCH_2^+]$ and $[ZNH_2]$ is that of $[Ar'NH_2]$. In the relation

$$f - x = [CH_2O] + [{}^+CH_2OH] + [YNHCH_2^+] + 3[T] \quad (9)$$

the experiment confirmed that the terms $[YNHCH_2^+]$ and [T] are very small compared with $[CH_2O]$, since the deposition as well as the solubility of T in the reaction mixture was small. Also $[{}^+CH_2OH]$ is negligible. Therefore

$$f - x = [CH_2O] \quad (10)$$

Thus, by assuming K_6, an average equilibrium constant of the equation (6), the concentration of the conjugate acids of methyleneanilines is expressed as

$$[YNHCH_2^+] = K_2K_6[H_3O^+][ZNH_2](f - x)/[H_2O]^2 \quad (11)$$

Consequently, equation (8) is given by

$$\mathrm{d}x/\mathrm{d}t = k'K_2K_6[H_3O^+][ZNH_2]^2(f - x)/[H_2O]^2 \quad (12)$$

Since $Ar'NH_2$ has many points of attack by $ArNHCH_2^+$, the rate of decrease of these points is not so fast in comparison with that of FA; therefore, at least in initial stages of the reaction and with molar ratio $f : a$ below 1, the initial concentration of aniline a, or $[ZNH_2]$ and each following term in the equation

$$a = [ZNH_2] + [ZNH_3^+] + [YNHCH_2^+] + 3[T] \quad (13)$$

may possibly be kept nearly constant. However, the second term on the right side seems under these conditions to be larger than the others expressed as $C[ZNH_2]$ for convenience,[7] *i.e.*

$$a = [ZNH_3^+] + C[ZNH_2] \quad (14)$$

or

$$[ZNH_2] = a/\{(K_A/K_W)[H_3O^+] + C\} \quad (15)$$

where K_W is the solubility product of water at 25° (10^{-14}), and K_A is the average ionization constant of aniline and its condensate $ArNH_2$, or $[ZNH_3^+]$-

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(5) Wagner, *et al.*, THIS JOURNAL, **56**, 1938 (1934), **59**, 879 (1937).

(6) For methyleneanilines as general intermediates in the similar reactions see Wagner, *ibid.*, **55**, 724 (1933); Sprung. *Chem. Rev.*, **26**, 297 (1940).

(7) The term $C[ZNH_2]$ seems to be necessary, since the ionization of the condensate is probably not as complete as that of aniline itself.

$[OH^-]/[ZNH_2]$. Introduction of the value of $[ZNH_2]$ into equation (12) leads to

$$\frac{dx}{dt} = \frac{k'K_2K_6[H_3O^+]a^2(f - x)}{[H_2O]^2\{[K_A/K_W)^2[H_3O^+]^2 + 2(K_A/K_W)[H_3O^+]C + C^2\}} \qquad (16)$$

Since (K_A/K_W) $[H_3O^+]$ seems to be larger than C, the equation is simplified to

$$\frac{dx}{dt} = \frac{k'K_2K_6K_W\, a^2(f - x)}{[H_2O]^2K_A\{(K_A/K_W)[H_3O^+] + 2C\}} = k(f - x) \qquad (17)$$

Hence, the reaction follows first-order kinetics with regard to $(f - x)$ in agreement with the experiment. The equation (17) may be expressed in the form

$$\left(\frac{k'K_2K_6K_W}{[H_2O]^2K_A}\right)\frac{a^2}{k} = (K_A/K_W)[H_3O^+] + 2C \qquad (18)$$

where the value of C and the variation of it with pH are relatively small. In agreement with equation (18), average values of a^2/k at each pH vary linearly with the concentration of the oxonium ion as Fig. 1 shows.

When the acidity of the reaction mixture was decreased (pH *ca.* 2–7), large amount of T precipitated according to the equation (4); hence, the formation of the resinous product was greatly retarded and the estimation of the accurate rate was difficult. Since the amount of free base of aniline in this range of pH is not negligible, the rate equation (12) will hold rather than equation (17). This expectation was confirmed by the observation that a maximum rate was found at about pH 5–6 at the very early stages of the reaction.

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[CONTRIBUTION FROM THE PENNSYLVANIA STATE COLLEGE AND PURDUE UNIVERSITY]

Polarographic Behavior of Organic Compounds. IX. Iodoacetic Acid and the Bromoacetic Acids

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In the pH range of 1 to 12 iodoacetic acid gives one polarographic wave while tribromoacetic acid gives three waves, the most negative of which is identical in characteristics with the one wave of monobromoacetic acid and the more negative of the two waves of dibromoacetic acid. The intermediate tribromoacetate wave is identical in behavior with the more positive dibromoacetate wave. Each wave is irreversible with the possible exception of the most positive tribromoacetate wave. Each wave represents a two-electron current-producing process, which is due to the fission of a carbon–halogen bond.[3] The mechanism of reduction is the step-wise removal of halogen, *e.g.*, tribromoacetic going to dibromoacetic and then to bromoacetic. There is an S-shaped relation between $E_{0.5}$ and pH; the pH value equal to the pK_a of the acid is located on the rising portion of the curve. The $E_{0.5}$ becomes more negative with increasing pH and may be pH-independent in portions of the acidic and basic regions.

The step-wise removal of halogen atoms from polyhalogenated compounds has been recently described in the case of the chlorinated methanes[2] and the chlorinated acetic acids.[3a] Reduction of the carbon–halogen bond has also been reported for α-bromopropionic acid.[3b] These compounds were studied in buffered solutions. Other organic compounds containing carbon–halogen bonds either have been studied in unbuffered solutions or have not been examined from the viewpoint of the variation of $E_{0.5}$ with pH[4]; the data in these papers is not readily susceptible to theoretical discussion.

It seems possible that by studying the ease of reduction of halogenated compounds polarographically, data would be obtained on the relative reactivities of carbon–halogen bonds in given environments. Since the polarographic reduction of the compounds involves the fission of such bonds, it would be of interest to attempt correlation of the relative reactivity scale so prepared with the chemical reactivity of the carbon–halogen bonds in various types of reactions. Accordingly, a systematic study has been begun of halogenated organic compounds, in which an effort is being made to study the behavior of these compounds over a considerable range of pH. In the present paper no attempt is made to explain theoretically the various phenomena encountered or to attempt correlation with general reactivity, but the polarographic behavior of iodoacetic and of the three bromoacetic acids is described. It is felt that after the completion of work in progress on several types of related compounds, a valid basis for an explanation of the data will exist. However, the data for the four compounds studied will be correlated and the theoretical problems to be faced will be indicated.

Each wave obtained represents the cleavage of a carbon–halogen bond with a successive stepwise removal of the halogen atoms in the case of the polyhalogenated compounds. Of the three waves given by tribromoacetic acid, the two more negative ones coincide with the two waves of dibromo-

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(1) A portion of the material presented is based on the thesis submitted by Marilyn Koll Kramer for the M.S. degree at Purdue University in August, 1949.

(2) I. M. Kolthoff, T. S. Lee, D. Stocesova and E. P. Parry, *Anal. Chem.*, **22**, 521 (1950).

(3) (a) P. J. Elving and C. S. Tang, THIS JOURNAL, **72**, 3244 (1950); (b) E. Saito, *Bull. soc. chim. France*, 404 (1948).

(4) (a) R. Brdicka, *J. Gen. Physiol.*, **19**, 843 (1936); (b) G. Dragt, *Anal. Chem.*, **20**, 737 (1948); (c) H. Keller, M. Hochweber and H. V. Halban, *Helv. Chim. Acta*, **29**, 761 (1946); (d) J. J. Lingane, C. G. Swain and M. Fields, THIS JOURNAL, **65**, 1348 (1943); (e) M. B. Neiman, A. V. Ryabov and E. M. Sheyanova, *Doklady Akad. Nauk S. S. S. R.*, **68**, 1065 (1949); (f) R. Pasternak and H. V. Halban, *Helv. Chim. Acta*, **29**, 190 (1946); (g) K. Schwabe, *Z. Naturforsch*, **3**, 217 (1948); (h) G. K. Simpson, A. G. Johnsten and D. Trail, *Biochem. J.*, **41**, 181 (1947); (i) M. V. Stackelberg and W. Stracke, *Z. Elektrochem.*, **53**, 118 (1949); (j) M. V. Stackelberg, "Polarographische Arbeitsmethoden," Walter de Gruyter, Berlin, 1950, pages 212–214; (k) A. Winkel and G. Proske, *Ber.*, **69**, 693 (1936).