

KINETICS OF REACTION OF ISOBUTYRALDEHYDE WITH ANILINE AND ITS DERIVATIVES

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The isobutylideneanilines formed by reaction of isobutyraldehyde with aniline and *p*-substituted anilines are very unstable even in inert solvents. Kinetic study of their formation in methanolic buffers showed that the formation of the carbinolamine was always faster than its dehydration. The both steps are subject to general acid catalysis. The Brønsted coefficients α and the Hammett reaction constants ρ have been determined for the formation and dehydration of the carbinolamines.

Reactions of isobutyraldehyde with aliphatic amines were given considerable attention recently. Hine and coworkers¹⁻⁵ studied the kinetics and mechanism of their formation and reverse reaction and described physical properties of the Schiff's bases prepared. An entirely different situation is encountered in the case of reactions of isobutyraldehyde with aromatic amines. In literature there are only few data about reaction of isobutyraldehyde with aniline. According to one author⁶ the reaction produces isobutylideneaniline and a crystalline substance of unknown structure. According to other authors⁷ a mixture of monoanil and dianil of isobutyraldehyde is formed, the latter having by 5°C higher boiling point than the former at the same pressure.

Although we tried to prepare isobutylideneaniline under possibly mild reaction conditions, the distillation under reduced pressure gave a mixture containing predominantly aniline and compounds with complicated aliphatic chains which were not identified. In further experiments we abstained from their isolation by distillation, and we focused our attention on the determination of structure of the compounds formed in solution after mixing equal volumes of 1M solutions of aniline and isobutyraldehyde in analytically pure tetrachloromethane. The reaction accompanied by evolution of water is practically finished in few minutes. The NMR spectra measured immediately after finishing the reaction (and removing water by filtration through filter paper and glass wool) showed that practically pure isobutylideneaniline was present in the solution. Similar results were obtained also in reactions of the aldehyde with 4-methoxy- and 4-bromoaniline. The NMR spectra measured after 15 to 20 minutes showed some changes indicating that subsequent reactions occurred. These reactions became considerably faster when the reaction solution was dried over aluminium oxide, molecular sieves or even sodium sulphate, so that,

immediately after drying, the spectra contained considerably broadened peaks. Using of pure instead of analytically pure tetrachloromethane had an even more marked influence. All these observations indicate that isobutyrideneanilines are rather too unstable, and it is very difficult or even impossible to prepare and keep them pure. We decided, therefore, to deal in detail with the reactions leading to their formation and decomposition. In this work we have concerned ourselves with the kinetic study of reactions of isobutyraldehyde with aniline, 4-methoxyaniline and 4-bromoaniline.

EXPERIMENTAL

Commercial isobutyraldehyde was distilled under normal pressure before preparation of its solutions in tetrachloromethane resp. methanol. *p*-Bromoaniline was prepared from acetanilide by known method⁸. The other chemicals used were commercial reagents of p.a. purity grade.

NMR spectra were measured with the use of a Tesla BS-487-A apparatus at 80 MHz at the room temperature. The 0.5M solutions of Schiff's bases in tetrachloromethane were prepared immediately before measurements. Hexamethyldisiloxane was used as internal standard.

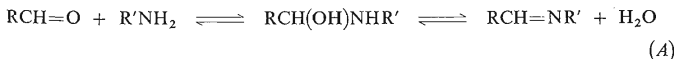
Kinetic measurements were carried out in methanol using acetate, chloroacetate and citrate buffers at 20°C. Ionic strength 0.025 was adjusted by addition of 0.5M-LiCl in methanol. The buffers were prepared by mixing 1M methanolic solution of the respective acid with 0.5M methanolic sodium methoxide prepared by dissolution of required amount of sodium in methanol. Composition of the buffers was checked by measuring pH after dilution with a four-fold amount of 0.5M aqueous potassium chloride. As the pK_a value of citric acid in methanol could not be found in literature, its relative acidity with respect to chloroacetic acid was determined in methanol by using 2,4-dinitrophenol as indicator.

In all the kinetic measurements the concentration of isobutyraldehyde was at least 100× higher than that of the amine. At first, spectra of several reaction solutions were measured at regular time intervals in the range 230 to 350 nm using Unicam SP 800 spectrophotometer. After finishing the reaction character of each spectrum was compared with that of the same product prepared separately in tetrachloromethane and diluted with methanol to the same concentration.

The proper kinetic measurements were carried out with the use of VSU-2P spectrophotometer at the wavelengths 268 and 305 nm (reaction of isobutyraldehyde with aniline and 4-methoxyaniline) and at 283 and 315 nm (reaction with 4-bromoaniline). The wavelengths 268 and 283 nm were used for measuring the rate of formation of the Schiff's bases, whereas 305 and 315 nm for that of the respective carbinolamines.

RESULTS AND DISCUSSION

Aldehydes react with aliphatic and aromatic amines to give carbinolamines which split off a water molecule and form a compound containing azomethine group (Eq. (A)).



NMR spectra of the reaction solutions obtained by mixing equimolecular amounts of isobutyraldehyde and the respective amine were measured shortly after finishing the reaction (indicated by separation of water), and only the peaks corresponding to the respective isobutylideneaniline were found. Only in the case of 4-bromoaniline the reaction mixture contained a small amount of the starting substances. The structure of the reaction products was confirmed by both the overall character of NMR spectra and values of the proton chemical shifts. The main difference as compared with the starting substances was in the chemical shift of the proton of azomethine group (about 2.5τ as compared with 0.45τ in isobutyraldehyde) and disappearing of the proton signal of NH_2 group. The fact that only signals of isobutylideneanilines (except for *p*-bromo derivative, see above) were found in the spectra indicates that the concentration of the eventually present carbinolamines was at least $20\times$ lower than that of the isobutylideneanilines.

The reaction kinetics was followed by UV spectroscopy. The products of reactions of isobutyraldehyde with aniline and 4-methoxy- and 4-bromoaniline absorb in methanolic solutions in the range of wavelengths 250 to 340 nm more than the respective starting substances, so that the absorbance of the reaction solution increases in the course of the reaction.

In the first experiments kinetics of the reaction of isobutyraldehyde with 4-methoxyaniline was followed in acetate buffer at 268 nm where the difference in absorbances of 4-methoxyaniline and the respective Schiff's base is maximum. Although a great excess of isobutyraldehyde was always used, the time dependence of $\log E$ was not linear in the whole range. In fact, it was divided into two different parts, which indicates that the reaction (A) proceeds in two steps having considerably different velocities. From the second part of the dependence, *i.e.* the region of linearity, the rate constant of the slower reaction was determined. The rate constant value does not depend on concentration of the aldehyde in this case. This indicates that dehydration of carbinolamine giving the Schiff's base is the reaction being measured, and that practically all amine is transformed into carbinolamine in this reaction phase. The rapid reaction corresponds to the formation of carbinolamine; it was studied at 305 nm, because at this wavelength there is a sufficient difference between absorbances of 4-methoxyaniline and carbinolamine, whereas the difference between absorbances of carbinolamine and final product is negligible.

Experimental rate constant of carbinolamine formation is directly proportional to concentration of the aldehyde (Eq. (1)). The reaction constant k_2 was obtained by dividing k_{exp} by the overall concentration of the aldehyde (NMR spectrum of isobutyraldehyde in methanol showed that about 90% of the aldehyde is present in the form of hemiacetal, so that the k_2 value related to free aldehyde would be about 10 times greater).

$$\text{r.r.} = k_{\text{exp}}[\text{amine}] = k_2[\text{amine}][\text{aldehyde}] \quad (1)$$

$$k_{\text{exp}} = k_0 + k_{\text{H}^+}[\text{H}^+] + k_{\text{HA}}[\text{HA}] \quad (2)$$

The k_{exp} values of the both reactions (*i.e.* formation and dehydration of carbinolamine) increase linearly with increasing buffer concentration, and, at the same time,

the rate constant values extrapolated to zero buffer concentration increase with increasing ratio of acidic to basic buffer components. The experimental rate constants are defined by Eq. (2). It means that the both reactions are subject to general acid catalysis.

The rate constants k_{HA} of the reactions catalyzed by acetic acid were determined from the dependence of k_{exp} on the acetic acid concentration. The magnitude of intercept at y axis, determined by extrapolation of k_{exp} to the zero buffer concentration, is given by Eq. (3).

$$y = k_0 + k_{H^+} [H^+] . \quad (3)$$

The rate constants k_0 and k_{H^+} of non-catalyzed (or solvent-catalyzed) and proton-catalyzed reactions, respectively, were obtained by plotting the intercept y against the corresponding proton concentrations in the reaction mixture. The proton concentrations were calculated from the ratios of acidic and basic buffer components and pK_a value 9.52 of acetic acid in methanol⁹.

The course similar to that in acetate buffers was found also in chloroacetate buffers

TABLE I

Rate Constants of Non-Catalyzed (k_0 , $l \text{ mol}^{-1} \text{ min}^{-1}$) and Acid-Catalyzed ($l^2 \text{ mol}^{-2} \text{ min}^{-1}$) Carbinolamine Formation in Methanolic Acetate (k_1), Chloroacetate (k_2) and Citrate (k_3) Buffers (20°C) and Rate Constants of Non-Catalyzed ($k_0 \text{ min}^{-1}$) and Acid-Catalyzed ($l \text{ mol}^{-1} \text{ min}^{-1}$) Carbinolamine Dehydration in Methanolic Buffers of Mentioned Acids (20°C)

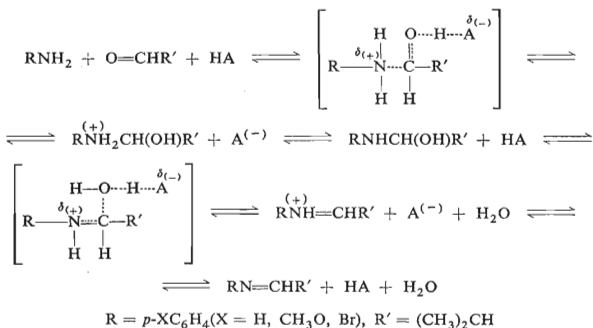
X	$k_1 \cdot 10^{-1}$	$k_2 \cdot 10^{-1}$	$k_3 \cdot 10^{-1}$	$k_{H^+} \cdot 10^{-8}$	k_0
<i>Formation of carbinolamines</i>					
4-CH ₃ O	39 ± 2	130 ± 10	—	125 ± 25 ^a (42 ± 6) ^b	6 ± 1
H	15 ± 2	45 ± 4	100 ± 20	55 ± 9 ^a (14 ± 3) ^b	2.5 ± 0.6
4-Br	6 ± 1	17 ± 2	27 ± 4	20 ± 5 ^a (6.5 ± 2) ^b	0.8 ± 0.3
<i>Dehydration of carbinolamines</i>					
4-CH ₃ O	0.34 ± 0.01	7.8 ± 0.5	—	1.3 ± 0.15	5 ± 1.5
H	0.027 ± 0.003	0.96 ± 0.15	1.5 ± 0.2	0.12 ± 0.03	0.35 ± 0.15
4-Br	—	0.18 ± 0.02	0.34 ± 0.04	0.01 ± 0.005	—

^a Values found in acetate buffers; ^b values found in chloroacetate and citrate buffers.

(i.e. formation of carbinolamine and its slower dehydration) with the only difference that the both reactions are substantially faster.

In the case of aniline, and to a still greater extent with 4-bromoaniline, the reaction rate was considerably lower, and the difference between the rates of formation and dehydration of carbinolamine gradually increased. The reaction of both these amines was followed also in citrate buffers; here the reaction was faster in accordance with our finding that citric acid is (2.4 ± 0.3) times more acidic than chloroacetic acid in methanol.

The calculated rate constants of formation and dehydration of carbinolamines are given in Table I. The following reaction scheme can be written for generally acid-catalyzed formation of carbinolamine and its subsequent splitting into Schiff's base which is also generally acid-catalyzed:



From the rate constants of the acid-catalyzed reactions and from the $\text{p}K_a$ values of the acids used the coefficients α of the Brønsted relation¹⁰ were computed. For dehydration of the carbinolamines $\alpha = 0.8 \pm 0.1$, which means that in the activated complexes the proton is considerably transferred to the carbinolamine oxygen atom. Values α close to unity were found for dehydrations of the carbinols formed by reactions of slightly basic amines with carbonyl compounds¹¹.

The situation is rather obscure with the rate constants of formation of the carbinolamines. The α value calculated from rate constants of the reactions catalyzed by acetic and chloroacetic acids is about 0.3; this value quite agrees with $\alpha = 0.25$ found for the acid-catalyzed formation of *p*-chlorobenzylideneaniline in water¹². On the contrary, the α value calculated from the reaction catalyzed by the proton, chloroacetic acid and citric acid is 0.6 to 0.7. Different results are obtained also for the rate constants of the proton-catalyzed reactions: the k_{H^+} values found in citrate and chloroacetate buffers are about $3 \times$ smaller than those found in acetate buffers (Table I). This difference can be due to deactivating influence of stronger acids on reactivity of amines; definitely this is not a consequence of protonation of the amines, because even the most basic of them, 4-methoxyaniline, was protonated maximum to 30% in the buffers used.

From the calculated rate constants given for the individual derivatives in Table I and from the Hammett σ constants the values of ρ constants were calculated by applying the Hammett equation: for formation of the carbinolamine (catalyzed by organic acids) and for its dehydration to the Schiff's base the respective ρ values are 1.6 ± 0.2 and 3.4 ± 0.4 . These relatively high values (especially the latter one) indicate that in the activated complexes the N—C resp. N=C bonds are formed to a great extent. The ρ value of the splitting of carbinolamines into Schiff's bases is greater than that of dissociation of substituted anilinium ions in water, which is caused by the influence of the substituents on formation or splitting of N—C bond being greater than that on formation or splitting of N—H bond¹³.

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