KINETICS OF REACTION OF 1,2-DIAMINOBENZENE WITH PHENYLGLYOXAL

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The cyclization reaction kinetics of phenylglyoxal monohydrate with 1,2-diaminobenzene have been studied in formate, acetate, and phosphate buffers. At high pH values and low buffer concentrations the rate-limiting step consists in the protonation of the intermediate formed by addition of the first amino group to aldehydic group of phenylglyoxal. With increasing concentrations of formate and acetate buffers the rate-limiting step shifts to the formation of the intermediate. In phosphate buffers the catalysis by the basic buffer component makes itself felt, too. At higher concentrations of 1,2-diaminobenzene, the dehydration of phenylglyoxal monohydrate gradually becomes the rate-limiting step.

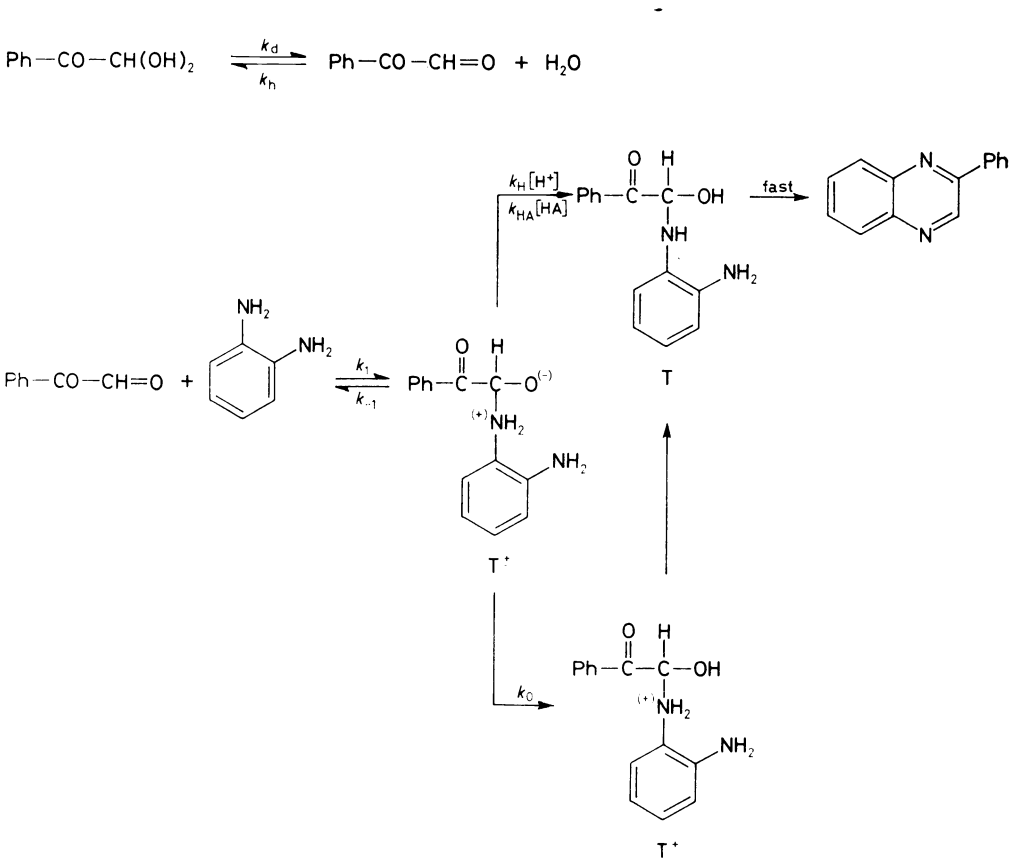
Our previous paper[1] dealt with the cyclization kinetics of 1,2-diaminobenzene with ethyl 2-oxopropanoate and 2,3-butanedione in acetate and phosphate buffers. The reaction with 2,3-butanedione exhibited a linear dependence of k_{obs} upon the buffer concentration within the whole range investigated. The rate-limiting step consisted in protonation of the dipolar tetrahedral intermediate of the carbinolamine formed by addition of NH_2 group of 1,2-diaminobenzene on the carbonyl group of the dione. The reaction with ethyl 2-oxopropanoate showed a non-linear dependence of k_{obs} vs the buffer concentration. Increasing buffer concentration and increasing pH changed the rate-limiting step into the acid catalyzed dehydration of carbinolamine.

The present paper studies the reaction kinetics of 1,2-diaminobenzene with phenylglyoxal hydrate in formate, acetate, and phosphate buffers. The reaction mechanism should resemble that of the reaction with 2,3-butanedione but, with regard to much higher stability of the intermediate formed by addition of NH_2 group to the aldehydic group, the formation of intermediate should become more significant with increasing buffer concentrations.

EXPERIMENTAL

Phenylglyoxal was prepared by oxidation of acetophenone with selenium dioxide[2]. Phenylglyoxal hydrate was crystallized from water and then from a mixture of 80% dichloromethane and 20% acetone by addition of hexane[3]. The other chemicals used were commercial samples of p.a. purity grade. For each kinetic measurement the following fresh solutions were prepared: 0·01M

1,2-diaminobenzene in 0·02M hydrochloric acid, and $5 \cdot 10^{-3}$M phenylglyoxal monohydrate in redistilled water. Solutions of formate, acetate and phosphate buffers were prepared from the p.a. chemicals and redistilled water. The kinetics of the cyclization to quinoxaline (Scheme 1) was monitored spectrophotometrically using a Specord UV-VIS apparatus (Zeiss) at the ionic strength 0·5 mol l^{-1} adjusted by addition of KCl at the temperature of 25°C. The solution of 1,2-diaminobenzene (10 µl) was injected into 2 ml buffer solution containing KCl and phenylglyoxal (usually $1 \cdot 10^{-3}$ mol l^{-1}) in a 1 cm cell and the absorbance increase was monitored at 340 nm. The rate constants were calculated from the relation $k_{obs}t = -\ln(A_\infty - A_t) +$ const. The ratio f of the free base of 1,2-diaminobenzene to the total concentration of 1,2-diaminobenzene in the buffer solutions was determined spectrophotometrically at 294 nm at 25°C from the ratio $(A - A_{BH})/(A_B - A_{BH})$, where A means the absorbance in the buffer and A_{BH} and A_B stand for the absorbances in 0·1M-HCl and in 4 : 1 basic phosphate buffer, respectively. The concentration of 1,2-diaminobenzene was $1{\cdot}6 \cdot 10^{-4}$ mol l^{-1} and the ionic strength was 0·5 mol l^{-1}. The f values found for the 1 : 1 formate buffer and the 4 : 1, 1 : 1, and 1 : 4 acetate buffers were 0·065, 0·15, 0·41, and 0·70, respectively.



SCHEME 1

RESULTS AND DISCUSSION

First of all we measured the UV spectra of $6 . 10^{-5}$M solutions of 1,2-diaminobenzene or phenylglyoxal hydrate containing ten- and twenty-fold concentration of the other component in 0·2M acetate buffer (1 : 1) within the wavelength range from 320 to 380 nm after the cyclization was finished. The shape of spectra was the same in all the experiments, however, the maximum absorbance of product was by 2% lower in the case of excess 1,2-diaminobenzene. Since the content of 1,2-diaminobenzene in the p.a. sample adopted was practically 100%, we presumed that the phenylglyoxal hydrate contained c. 2% humidity, and in preparation of its solutions for kinetic measurements we used its amount higher by 2%.

In a preliminary experimental series we determined the dependence of k_{obs} on the concentration of the excess component in an (1 : 1) acetate buffer with 0·25 mol . $. l^{-1}$ acetic acid concentration. In the experiments with excess phenylglyoxal $[FG]_h$, the k_{obs} value exhibited a linear increase with increasing phenylglyoxal concentration and was equal to zero when extrapolated to zero phenylglyoxal concentration. In the presence of excess 1,2-diaminobenzene $[DAB]_f$ (the phenylglyoxal concentration equal to $5 . 10^{-5}$ mol l^{-1}) the increase of k_{obs} was not linear (Fig. 1) and was approaching the constant value.

It is possible to suggest – for the reaction of phenylglyoxal with 1,2-diaminobenzene – a reaction mechanism similar to that of the reaction with 2,3-butanedione[1] (see Scheme 1) and the respective rate equation (*1*).

$$v = k_d k_1 \frac{k_0 + k_H[H^+] + k_{HA}[HA]}{k_{-1} + k_0 + k_H[H^+] + k_{HA}[HA]} [FG]_h [DAB]_f \cdot$$
$$\cdot \left[k_h + k_1 \frac{k_0 + k_H[H^+] + k_{HA}[HA]}{k_{-1} + k_0 + k_H[H^+] + k_{HA}[HA]} [DAB]_f \right]^{-1} \qquad (1)$$

In contrast to 2,3-butanedione, only a small part of phenylglyoxal remains non-hydrated in aqueous solutions. Hine[3] used the equation $\log K_d = 2·70 - 2·65 \sum\sigma^* - 1·35 \sum FG$ for calculation of the K_d constant of dissociation of hydrates of carbonyl groups and he arrived at a conclusion that in aqueous solution less than 0·1% of aldehydic groups of phenylglyoxal exist in non-hydrated form. For the experimental series with various amounts of diaminobenzene in excess and with one of the buffers mentioned we can write Eq. (*2*) wherefrom Eq. (*3*) immediately follows:

$$k_1 \frac{k_0 + k_H[H^+] + k_{HA}[HA]}{k_{-1} + k_0 + k_H[H^+] + k_{HA}[HA]} = \text{const} = k_c \qquad (2)$$

$$k_{obs} = \frac{k_d k_c [DAB]_f}{k_H + k_c [DAB]_f} = \frac{k_d k_c k_h^{-1} [DAB]_f}{1 + k_c k^{-1} [DAB]_f} \qquad (3)$$

From the k_{obs} values found we calculated (by non-linear regression and application of Eq. (3)) the values $k_d = (2{\cdot}0 \pm 0{\cdot}1) \cdot 10^{-2}\ s^{-1}$ and $k_c k_h^{-1} = (9{\cdot}80 \pm 0{\cdot}30) \cdot 10^3\ l \cdot mol^{-1}$. Since with application of excess 1,2-diaminobenzene the evaluation of kinetic experiments would be complicated by the rate of dehydration of phenylglyoxal monohydrate, which is a general acid and base catalyzed reaction[4], all the subsequent experiments were carried out with excess phenylglyoxal (usually a twenty-fold excess). The observed rate constants were transferred to k_c' ($= K_d k_c$) by dividing them by the phenylglyoxal concentration and the ratio f of the base to the total concentration of diaminobenzene in the given buffer. The dependence of k_c' on concentration of formate and acetate buffers is presented in Fig. 2 and that on the total concentration of the phosphate buffers in Fig. 3.

The rate constant k_c' is defined by Eq. (4):

$$k_c' = k_d k_c k_h^{-1} \,. \tag{4}$$

The k_c' value read from Fig. 2 for 1 : 1 acetate buffer and 0·25M acetic acid concentration is equal to $2{\cdot}15 \cdot 10^2\ l\ mol^{-1}\ s^{-1}$, and the value of the fraction at the right-hand side of Eq. (4) found from the kinetic experiments using variable excess of diaminobenzene is equal to $1{\cdot}9 \cdot 10^2\ l\ mol^{-1}\ s^{-1}$. This very good agreement supports the mechanism suggested.

On the basis of the reaction mechanism in Scheme 1 and of the presumption that the dehydration of phenylglyoxal hydrate represents a rapid pre-equilibrium we can derive Eq. (5) for the k_c' values in formate and acetate buffers.

$$k_c' = K_d \frac{k_1(k_0 + k_H[H^+] + k_{HA}[HA])}{k_{-1} + k_0 + k_H[H^+] + k_{HA}[HA]} = \frac{k_1'(k_0 k_{-1}^{-1} + k_H k_{-1}^{-1}[H^+] + k_{HA} k_{-1}^{-1}[HA])}{1 + (k_0 k_{-1}^{-1} + k_H k_{-1}^{-1}[H^+] + k_{HA} k_{-1}^{-1}[HA])}, \tag{5}$$

where $k_1' = K_d k_1$.

In phosphate buffers several changes take place. The dependence of k_c' on the buffer concentrations is linear within the whole range investigated, i.e. no change occurs in the rate-limiting step. The reaction is catalyzed by both the acidic and the basic buffer components (in contrast to the reaction with 2,3-butanedione). The k_c' values extrapolated to the zero buffer concentration are the same for all the three buffer ratios, i.e. at high pH values the reaction of the dipolar intermediate with the proton is kinetically insignificant (similar situation is encountered in the reaction

with 2,3-butanedione). The dependence of k'_c on the buffer concentration is given by Eq. (6) in this particular case.

$$k'_c = k'_1 k_{-1}^{-1}(k_0 + k_{HA}[HA] + k_A[A]) \qquad (6)$$

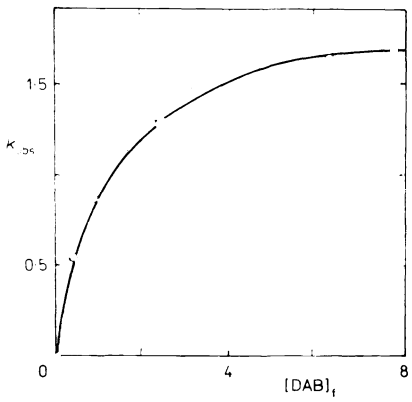


FIG. 1

The dependence of k_{obs}, s^{-1} on the concentration of 1,2-diaminobenzene $[DAB]_f$. Acetate buffer 1 : 1, acetic acid concentration 0·25 mol l^{-1}. Solid line (theoretical curve) was calculated from Eq. (3), values k_d and k_c/k_h given in the text

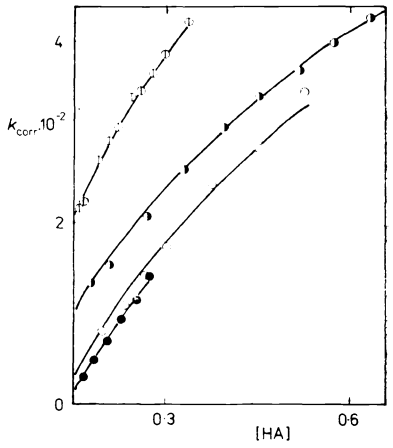


FIG. 2

The dependence of k_{corr}, 1 mol^{-1} s^{-1}, on the concentration of acid ([HA], mol l^{-1}) in 1 : 1 (⊙) formate buffer and in 4 : 1 (◑), 1 : 1 (○), and 1 : 4 (●) acetate buffers. The theoretical curve was calculated from Eq. (5) and the values of constants given in Table I

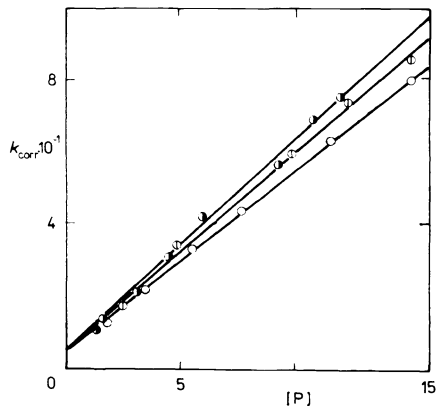


FIG. 3

The dependence of k_{corr}, 1 mol^{-1} s^{-1}, on the concentration of phosphate buffers ([P], mol l^{-1}).$[H_2PO_4^-]$: $[HPO_4^{2-}]$ = 4 : 1 (◑), 1 : 1 (⊙), and 1 : 2 (○)

From the slope of dependence of k_c' on the buffer concentration and from the fraction of dihydrogenphosphate in the phosphate buffer we calculated the values $k_1'k_{HA}k_{-1}^{-1} = 4{\cdot}95 \cdot 10^2\ l^2\ mol^{-2}\ s^{-1}$ and $k_1'k_Ak_{-1}^{-1} = 3{\cdot}3 \cdot 10^2\ mol^{-2}\ s^{-1}$, and from the intercept at the y axis we calculated the value $k_1'k_0k_{-1}^{-1} = 5{\cdot}0\ l\ mol^{-1}\ s^{-1}$. The parameters $k_1'k_Hk_{-1}^{-1}$ and $k_1'k_Ak_{-1}^{-1}$ were calculated from the k_c' values (found for the formate and 4 : 1 acidic acetate buffers) by non-linear regression using Eq. (*5*) but neglecting the fraction $k_0k_{-1}^{-1}$. Introducing the k_1' value calculated into the relation for $k_1'k_0k_{-1}^{-1}$ we found the value $k_0k_{-1}^{-1} = 6 \cdot 10^{-3}$, and using this value we again calculated the values of all three parameters for the formate and all the acetate buffers according to the complete equation (*5*).

As the protonation of negatively charged oxygen atom in the dipolar intermediate by hydroxonium ion is a reaction of considerable thermodynamic advantageousness, it can be presumed that the rate of this reaction is diffusion-controlled, and the k_H value is $(4 \pm 1) \cdot 10^{10}\ l\ mol^{-1}\ s^{-1}$ (ref.[5]). Using this value we calculated the values of constants k_1', k_{-1}, k_0, k_{HA}, and k_A (Table I). For comparison the table also gives the values of the corresponding constants of the reaction of 1,2-diaminobenzene with 2,3-butanedione[1]. The k_{HA} value for the acetic-acid-catalyzed reaction is 2 orders higher than that for the reaction of 1,2-diaminobenzene with 2,3-butanedione. Using extrathermodynamic relations[6] for the reaction with 2,3-butanedione, the pK_a value 6 to 6·5 was calculated[1] for the equilibrium $T^+ = T^{\pm} + H^+$, i.e. the reaction of acetic acid with negatively charged oxygen atom should be considerably favourable thermodynamically, and the k_{HA} value should approach the value of 5 .

TABLE I

The rate and equilibrium constants of reaction of 1,2-diaminobenzene with phenylglyoxal monohydrate (A) and with 2,3-butanedione (B), ref.[1]

Constant	Unit	A	B
K_1'	$l\ mol^{-1}$	$2 \cdot 10^{-6}$	$4 \cdot 10^{-5}$
k_1'	$l\ mol^{-1}\ s^{-1}$	$8{\cdot}5 \cdot 10^2$	—
k_0	s^{-1}	$3 \cdot 10^6$	$5 \cdot 10^4$
k_H	$l\ mol^{-1}\ s^{-1}$	$4 \cdot 10^{10}$	$4 \cdot 10^{10}$
$k_{HA}{}^a$	$l\ mol^{-1}\ s^{-1}$	$1{\cdot}2 \cdot 10^9$	—
$k_{HA}{}^b$	$l\ mol^{-1}\ s^{-1}$	$5 \cdot 10^8$	$7{\cdot}5 \cdot 10^6$
$k_{HA}{}^c$	$l\ mol^{-1}\ s^{-1}$	$2{\cdot}3 \cdot 10^8$	$6 \cdot 10^6$
$k_A{}^c$	$l\ mol^{-1}\ s^{-1}$	$1{\cdot}6 \cdot 10^8$	~ 0
k_{-1}	s^{-1}	$4 \cdot 10^8$	—

[a] HA = HCOOH; [b] HA = CH_3COOH; [c] HA = $H_2PO_4^-$.

. 10^9 l mol^{-1} s^{-1} for the diffusion-controlled reaction. The real pK_a value is 3 orders lower, i.e. the pK_a value of the T^+ intermediate is much smaller. In protonated amines the positive charge of nitrogen atom is considerably delocalized by action of the solvating water molecules[7]. In the intermediates $T^\pm$ and T^+ the NH_2^+ group is "hidden" in the molecule and formation of hydrogen bonds is sterically hindered. As a consequence, the resulting greater positive charge of nitrogen atom strongly attracts the electrons of neighbouring groups and hence increases the acidity of OH groups. In the intermediates formed by the reaction with phenylglyoxal the neighbouring methyl group is replaced by hydrogen. Thereby the steric hindrance to solvation is considerably lowered and the pK_a value is increased, hence the protonation of the negatively charged oxygen is thermodynamically more favourable and proceeds faster. The smaller steric hindrance to formation of hydrogen bonds with NH_2^+ groups also explains the almost 2 orders greater value of the rate constant k_0 for the water-molecule-mediated proton transfer from NH_2^+ to O^- group.

The reaction with phenylglyoxal in phosphate buffers is catalyzed by both acids and bases, whereas that with 2,3-butanedione showed no signs of base catalysis. This difference can be due to (i) an easier access of a base to NH_2^+ group, (ii) its higher acidity caused by replacement of two methyl groups by hydrogen and phenyl. The K_1' value for phenylglyoxal is one order smaller than that for 2,3-butanedione, but this fact is caused by these values involving also K_d of the hydration pre-equilibrium of the hydrate. Whereas the K_d value is 0·475 for 2,3-butanedione[8], it is c. $1 . 10^{-3}$ for phenylglyoxal[3], hence the real K_1 value for phenylglyoxal is 2–3 orders of magnitude greater than that of 2,3-butanedione in accordance with the fact that the tetrahedral intermediates formed by addition of nucleophiles to the aldehydic group are much more stable.

REFERENCES

1. Klicnar J., Mindl J., Obořilová I., Petříček J., Štěrba V.: Collect. Czech. Chem. Commun. *53*, 3154 (1988).
2. Riley H. A., Gray A. R.: Org. Synth., Coll. Vol. *II*, 509 (1943).
3. Hine J., Koser G. F.: J. Org. Chem. *36*, 3591 (1971).
4. Bell R. P.: Adv. Phys. Org. Chem. *4*, 1 (1966).
5. Eigen M.: Angew. Chem., Int. Ed. *3*, 1 (1964).
6. Fox J. P., Jencks W. P.: J. Am. Chem. Soc. *96*, 1436 (1974).
7. Meot-Ner (Mautner) M.: J. Phys. Chem. *91*, 417 (1987).
8. Buschmann H. J., Dutkewicz E., Knoche W.: Ber. Bunsenges. Phys. Chem. *86*, 129 (1982).

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