Note

General acid catalysis of boric acid and water on dehydration step in formation of phenylhydrazone from salicylaldehyde

R Mostaghim, A. Habibi Yangjeh & M R Gholami*
Department of Chemistry, Sharif University of Technology, Tehran, Iran
Received 12 December 1998; accepted (revised) 14 June 1999

Hydrazone formation from salicylaldehyde and phenylhydrazine has been studied in water-ethanol (60:40 volume) solution at 35°C and ionic strength of 0.25 (with KCl). The reaction exhibits specific acid (in pH <4) and general acid catalysis (in 4<pH<6.5). In pH<4 attack of phenylhydrazine to salicylaldehyde, and in pH>4 dehydration of intermediate is rate determining step. Apparent catalytic rate constants of water and boric acid in the reaction are in good agreement with predicted values from Bronsted relationship. The kinetic results, UV, IR and NMR spectroscopic analyses exhibit general acid catalysis by boric acid and water.

It is generally believed that most enzyme-catalyzed reactions involve the occurrence of inter and intramolecular general acid-base catalysis. The kinetics, mechanism and catalysis of reaction between amines and carbonyl compounds have been studied, but dehydration mechanism of intermediate has not been widely studied. Boric acid retards hydrolysis of N-salicylidene-2-methoxy ethylamine below pH 5.5 but accelerates the hydrolysis above pH 5.5. Oxime formation from salicylaldehyde is accelerated by boric acid (in pH range of 7-10). The kinetics and spectroscopic results demonstrated that boric acid forms complex with intermediate (formed by a rapid equilibrium between salicylaldehyde and hydroxylamine) of the reaction (1). The catalytic rate constant of water in nitroine formation from furfural is higher than that predicted from the Brønsted relationship. In this paper, hydrazone formation from salicylaldehyde and phenylhydrazine has been studied to develop the experimental basis in these kind of reactions.

Experimental Section

Materials. Phenylhydrazine, salicylaldehyde and other reagents were obtained commercially (from Aldrich and Fluka) and used without additional purifications. Glass double distilled water was used throughout the work.

Kinetic measurements. The reaction was followed spectrophotometrically at 35°C by monitoring formation of the hydrazone at 360 nm in solution of salicylaldehyde (5x10⁻³ M) and phenylhydrazine (5x10⁻³ M) which showed a pseudo first-order kinetics. Reaction was occurred in water-ethanol (60:40) solution with an ionic strength of 0.25 (with KCl). Spectrophotometer equipped with a cell with water from a thermostated bath continuously circulated around it. FT-IR and FT-NMR spectrometers were Mattson 1000, Unicam and Bruker, Ac-(80 MHz) respectively.

Results and Discussion

The rate constants, kobs (pseudo first-order rate constant working with excess of phenylhydrazine) as a function of pH for the reaction between salicylaldehyde and phenylhydrazine is shown in Figure 1 (with and without boric acid). The reaction takes place in two steps: first nucleophile attaches to the aldehyde and then dehydration of intermediate occurs. At conditions pH<4, attack of phenylhydrazine to salicylaldehyde is rate determining step; because in these conditions phenylhydrazine converts to phenylhydrazine chloride (pKₐ=3.8). In this pH range, second-order rate constants are not sensitive to the type and concentration of buffers. As a result, the reaction exhibits a specific acid catalysis; therefore second-order rate constant of the reaction is:

\[ k₂ = k_\text{obs} / [\text{phenNHNH}_2] = k_o + k_H[H^+] \]  \hspace{1cm} (1)

in which k₀ and kₜ are catalytic rate constants of water and H⁺ respectively. By plotting the values of k₂ vs. [H⁺] values of k₀, kₜ are obtained from intercept and slope of the diagram, respectively (k₀=30.7 M⁻¹min⁻¹, kₜ=3.9x10⁴ M⁻²min⁻¹).
The $k_{obs}$-pH curve (Figure 1) indicates that hydronium ion catalyzes dehydration step at pH 4-6.5. The pH-independent region ($pH > 6.5$) indicates that the reaction cannot be catalyzed by bases. At pH 4-6.5 dehydration is rate determining step, because in these conditions phenylhydrazinium ion converts to phenylhydrazine, and its attack to aldehyde is fast. The second-order apparent catalytic rate constants ($k_{2app}$) are sensitive to the type and concentration of buffers and the reaction rate increases linearly with acid concentration, therefore dehydration step is catalyzed by general acid (Eqns 2, 3 and 4):

\[
\text{Rate} = (k_0 + k_{H}[H^+] + k_{HA}[HA])[\text{adduct}] = (k_0 + k_{H}[H^+] + k_{HA}[HA])K_{add}[\text{aldehyde}] \\
\times [\text{phNHNH}_2] \\
\]

\[
k_{2app} = k_{obs}/[\text{phNHNH}_2] = k_{H}K_{add} + k_{HA}K_{add}[H^+] + k_{HA}K_{add}[HA] \\
\]

where $k_{H}K_{add}$ and $k_{HA}K_{add}$ (or $k_{2app}$) are apparent catalytic rate constants of water, $H^+$ and HA respectively. The $k_{2app}$ for each acid is obtained by plotting of $k_{2app}$ vs. [HA] (concentration of the free acid at constant pH) using different concentrations of buffer corresponding to each acid.

The Brønsted plot of the reaction for general acid catalysis by acetic acid, propanoic acid and phosphate monoanion ($\alpha = 0.37, r = 0.99$) is shown in Figure 2. The apparent catalytic rate constant of boric acid (in this reaction $[B]_1 < 0.04$ is chosen to avoid the association of boric acid molecules that may diminish its activity$^6$) matches with the value predicted by Bronsted relationship (Figure 2).

![Figure 2](image2.png)

**Figure 2**—Bronsted plot for general acid catalysis of the reaction in dehydration step at 35°C

<table>
<thead>
<tr>
<th>Activation parameter</th>
<th>$E_a$ (kJ mol$^{-1}$)</th>
<th>$\Delta H^\circ$ (kJ mol$^{-1}$)</th>
<th>$\Delta S^\circ$ (J mol$^{-1}$ K$^{-1}$)</th>
<th>$\Delta G^\circ$ (kJ mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without boric acid</td>
<td>31.4</td>
<td>28.9</td>
<td>167</td>
<td>80.3</td>
</tr>
<tr>
<td>With boric acid</td>
<td>32.6</td>
<td>30.1</td>
<td>155</td>
<td>77.8</td>
</tr>
</tbody>
</table>

The reaction occurs in toluene ($k_{obs} = 0.0014$ min$^{-1}$) in spite of its poor anion solvating ability$^7$. The theoretical study of the reaction intermediate using
MOPAC shows that there is a hydrogen bonding between OH of leaving group and the OH attached to the ring (3). Therefore the reaction is proceeding by reasonable rate in spite of poor solvating strength of toluene. It appears that water cannot catalyze dehydration step by bifunctional mechanism. As a result, catalytic rate constant of water shows good agreement with the predicted value of Brönsted plot.

References