Kinetic Studies on the Addition of Potassium Cyanide to $\alpha,N$-Diphenylnitrone

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The rate constants for the nucleophilic addition of potassium cyanide to $\alpha,N$-diphenylnitrone and its derivatives (p-OCH$_3$, p-CH$_3$, p-Cl, and p-NO$_2$) were determined by ultraviolet spectrophotometry at 25 °C, and the rate equations which can be applied over a wide pH range were obtained. On the basis of pH-rate profile, adduct analysis, general base catalysis and substituent effect, a plausible mechanism of this addition reaction was proposed: At high pH, the cyanide ion to carbon-nitrogen double bond was rate controlling, however, in acidic media, the reaction proceeded by the addition of hydrogen cyanide molecule to carbon-nitrogen double bond after protonation at oxygen of $\alpha,N$-diphenylnitrone. In the range of neutral pH, these two reactions occurred competitively.

Introduction

The nucleophilic addition of activated carbon-carbon double bond and carbon-nitrogen double bond has been subjected to extensive mechanistic and synthetic studies. Nitrone, having carbon-nitrogen double bond and oxygen attached to nitrogen is very reactive and used as an intermediate in organic synthesis. It easily reacts with nucleophiles such as Grignard reagent, thiol, and HCN. In general, nitrones formed a 1,3-adduct with nucleophiles. It has been known that the structures of adducts vary depending upon the reaction conditions. Masui and coworkers have reported the first isolation of $N$-($\alpha$-cyanobenzyl)-$N$-phenylhydroxylamine as a result of $\alpha,N$-diphenylnitrone and $N$-phenylhydroxylamine. Identification of adducts. In acidic media, $\alpha,N$-diphenylnitrone (1.0 mmol) and potassium cyanide (1.0 mmol) were dissolved in 20 mL of HCl solution (pH = 3). The reaction mixture was stirred for 24 h at room temperature under nitrogen atmosphere. The mixture was extracted with CH$_2$Cl$_2$, washed with water, dried over anhydrous MgSO$_4$ and concentrated. The product recrystallized from ethanol to give $N$-($\alpha$-cyanobenzyl)-$N$-phenylhydroxylamine. IR (KBr pellet, cm$^{-1}$): 3100-3500 (OH), 2260 (C≡N); 1H NMR (CDCl$_3$, $\delta$) 7.8-8.9 (m, 10H, phenyl), 5.9 (s, 1H, C$_6$H$_5$(CN)CH$_2$). Synthesis of $\alpha,N$-diphenylnitrone and its derivatives were prepared by condensation of corresponding benzaldehyde derivatives and $N$-phenylhydroxylamine.

Experimental Section

General procedure. All chemicals were reagent grade unless otherwise specified. UV spectra were obtained by a Varian Cary 14 spectrophotometer. IR spectra were taken with a Perkin-Elmer Infrared 710B. NMR spectra were obtained with a Varian Model EM 360 (60 MHz) and melting points were measured with a Haake Buchler apparatus.

Synthesis of $\alpha,N$-diphenylnitrone and its derivatives.
reactions are first order to nitrone and potassium cyanide, respectively. Thus, the second-order rate constants could be calculated from the slope of the plot of $1/A$ against time for the reaction between equal initial concentration ($2.0 \times 10^{-5}$ M) of nitrone and potassium cyanide (Figure 1). The second-order rate constants ($k_t$) determined at various pHs are given Table 1 and Figure 2.

**Table 1.** Rate constants for the addition reaction of potassium cyanide to $\alpha,N$-diphenylnitrones at various pH and 25 °C.

<table>
<thead>
<tr>
<th>pH</th>
<th>Buffer Solution</th>
<th>$k_t$ (M$^{-1}$ sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>obsd</td>
</tr>
<tr>
<td>3.0</td>
<td>HCl</td>
<td>206</td>
</tr>
<tr>
<td>4.0</td>
<td>HOAc + NaOAc</td>
<td>11.4</td>
</tr>
<tr>
<td>5.0</td>
<td></td>
<td>2.00</td>
</tr>
<tr>
<td>6.0</td>
<td>KH$_2$PO$_4$ + K$_2$HPO$_4$</td>
<td>1.76×10$^{-1}$</td>
</tr>
<tr>
<td>7.0</td>
<td>H$_3$BO$_3$ + NaOH</td>
<td>2.00×10$^{-2}$</td>
</tr>
<tr>
<td>8.0</td>
<td></td>
<td>2.10×10$^{-2}$</td>
</tr>
<tr>
<td>9.0</td>
<td></td>
<td>3.80×10$^{-2}$</td>
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<td>18.4</td>
</tr>
<tr>
<td>13.0</td>
<td></td>
<td>182</td>
</tr>
</tbody>
</table>

**Figure 1.** Plot of $1/A$bsorbance of $\alpha,N$-diphenylnitrones vs. time at pH 7.0 and 25 °C.

**Figure 3.** Plot rate constant vs. concentration of acetate ion at pH 4.78 and 25 °C.

**General base catalysis.** To make sure that this reaction is catalyzed by general base, the rate constants were determined at various acetate ion concentrations at pH 4.78. As shown in Figure 3, this reaction is not catalyzed by general base.

**Substituent effect.** As shown in Figure 4, the effect of substituents on the rate of addition was found to conform to the Hammett $\sigma$-constant with $\rho$ is 0.527, 1.46 and 1.52 at pH 3.0, 8.0, and 12.0, respectively. This result indicates that the rate of addition is accelerated by electron withdrawing groups at all pH ranges.

**Rate equation and mechanism.** As shown in Figure 2, the rate of addition of potassium cyanide to $\alpha,N$-diphenylnitrones is given by an expression of the following equation (1).

$$
\text{Rate} = k_0 [S][\text{CN}^-]_T + k_H [H_3O^+][S][\text{CN}^-]_T + k_{OH} [\text{OH}^-] \left[ 1 + \frac{[H_3O^+]}{K_a} \right] [\text{CN}^-][S]$$

(1)

Where, $[\text{CN}^-]_T$ is the total concentration of [CN$^-$] and
Hydronium and hydroxide ion dependent rate constant, addition of cyanide ion was approximately 10^6 times faster than that of hydrolysis of nitrone at basic media. Therefore, the following addition reaction mechanism was proposed:

In alkaline pHs, where the rate limiting step is the direct attacking of cyanide ion at carbon atom, we expected that the rate constant, \( k_{OH} \), should be more sensitive to change \( \sigma \) than \( k_H \) (\( \rho = 0.527 \) at \( pH = 3.0 \), \( \rho = 1.52 \) at \( pH = 12.0 \)). As shown in above, the rate equations which can be applied over a wide pH range were obtained. On the basis of various kinetic results, a reaction mechanism was proposed. However, to better understand the theory for the exact transition state and intermediate, it seems necessary to probe the influence of \( \beta \)-substituent variation from nitroson as well as the change of the nucleophiles.

References