Pre-equilibrium in the Schmidt Reaction of Benzhydrols

by

Hyung Chick Pyun

Atomic Energy Research Institute, Korea

(Received on Jan. 9, 1964)

Introduction

The mechanism for the Schmidt reaction of benzhydrols has been proposed as follows, (1) (2)

\[
\begin{align*}
\phi-N=CH+H_2SO_4 & \quad \xrightarrow{\text{H}_2O} N\overset{\circ}{\phi}-CH-\phi + HSOn H_2O + \overset{\circ}{\phi} \\
\phi-CH-\phi + HSO_4^+ & \quad \xrightarrow{\text{H}_2O} \overset{\circ}{\phi}-CH-\phi + HSOn H_2O + \overset{\circ}{\phi}
\end{align*}
\]

(1)

or

\[
\begin{align*}
\phi-N=CH+H_2SO_4 & \quad \xrightarrow{\text{H}_2O} N\overset{\circ}{\phi}-CH-\phi + HSOn H_2O + \overset{\circ}{\phi} \\
\phi-CH-\phi + HSO_4^+ & \quad \xrightarrow{\text{H}_2O} \overset{\circ}{\phi}-CH-\phi + HSOn H_2O + \overset{\circ}{\phi}
\end{align*}
\]

(1)

We can consider, however, that the process is probably more complicated than the above. Namely, the conjugated acid of benzhydrylazide may exist in an equilibrium state with the benzhydryl ion and azoic acid before rearrangement of molecule as below.

\[
\begin{align*}
\phi-N=CH+H_2SO_4 & \quad \xrightarrow{\text{H}_2O} N\overset{\circ}{\phi}-CH-\phi + HSOn H_2O + \overset{\circ}{\phi} \\
\phi-CH-\phi + HSO_4^+ & \quad \xrightarrow{\text{H}_2O} \overset{\circ}{\phi}-CH-\phi + HSOn H_2O + \overset{\circ}{\phi}
\end{align*}
\]

(1)

or

\[
\begin{align*}
\phi-N=CH+H_2SO_4 & \quad \xrightarrow{\text{H}_2O} N\overset{\circ}{\phi}-CH-\phi + HSOn H_2O + \overset{\circ}{\phi} \\
\phi-CH-\phi + HSO_4^+ & \quad \xrightarrow{\text{H}_2O} \overset{\circ}{\phi}-CH-\phi + HSOn H_2O + \overset{\circ}{\phi}
\end{align*}
\]

(1)
If this assumption was true, it can be regarded that some parts of the azide exist as hydrol in the equilibrium mixture and that there will be radical exchange between them before molecular rearrangement when hydrol is added to azide. In order to examine whether radical exchange between benzhydryl azide and benzhydrol occur or not, the following two types of reactions were carried out.

(a) Schmidt reaction of benzhydryl azides in the existence of benzhydrols labeled with chlorine.

(b) Schmidt reaction of benzhydryl azides labeled with chlorine in the existence of benzhydrols.

From the data obtained, it can be concluded that the assumption made above was reasonable.

Experimental

Preparation of benzhydrols: P-chlorobenzhydrol, m.p. 60, 5°C—61,5°C, was prepared by reduction of p-chlorobenzhydrophenone both by zinc dust and alcoholic sodium hydroxide(3) (70, 5% yield) and aluminium isopropoxide(4) (90, 0% yield); reported m.p.'s are 60-61°(3), 62°(4), 60-61°(5). 4,4'-dichlorobenzhydrol, m.p. 93.5-94°C was prepared by reduction of 4,4'-dichlorobenzhydrophenone by sodium borohydride in methanol(6) (60% yield), reported m.p. is 93,3-93,9°C(8).

Preparation of azoic acid solution(9) (10): The paste was prepared from 97,5gr. (1,5 mole) of sodium azide and 97 ml. of warm water. To the paste 600 ml. of benzene was added and the mixture was cooled to 0°C while the mixture was stirred and 40 ml. (0.75 mole) of concentrated sulfuric acid (SG. 1.84) was added dropwise. The reaction temperature was kept under 10°C. After the addition of acid, the organic layer was decanted and dried by using anhydrous sodium sulfate. The concentration of hydrosulfuric acid in benzene solution was determined by pipetting 1 ml of the solution into 20 ml of water and titrating with 0.1 N NaOH solution. The concentrations of azoic acid obtained in the benzene solutions were as follows:

<table>
<thead>
<tr>
<th>Run No.</th>
<th>Concentration (Mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.43</td>
</tr>
<tr>
<td>2</td>
<td>1.35</td>
</tr>
<tr>
<td>3</td>
<td>1.35</td>
</tr>
<tr>
<td>4</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Table 1. Yields and purities of azides

<table>
<thead>
<tr>
<th>Run No.</th>
<th>Yield (gr.)</th>
<th>Purity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>crude</td>
<td>final</td>
</tr>
<tr>
<td>Benzhydrol azide</td>
<td>24.9</td>
<td>6.9 (33.7%)</td>
</tr>
<tr>
<td>1</td>
<td>25.7</td>
<td>11.4 (54.5%)</td>
</tr>
<tr>
<td>2</td>
<td>25.0</td>
<td>11.4 (54.5%)</td>
</tr>
<tr>
<td>p-Chlorobenzhydrol azide</td>
<td>25.0</td>
<td>11.4 (54.5%)</td>
</tr>
<tr>
<td>3</td>
<td>25.0</td>
<td>11.4 (54.5%)</td>
</tr>
<tr>
<td>4,4'-Dichlorobenzhydrol azide</td>
<td>25.0</td>
<td>11.4 (54.5%)</td>
</tr>
<tr>
<td>5</td>
<td>27.0</td>
<td>15.7 (62.2%)</td>
</tr>
</tbody>
</table>

* used 0.5 mole of hydrosulfuric acid for 0.1 mole of 4,4'-Dichlorobenzhydrol.

Schmidt reaction: The procedure which was proposed by McEwen and Godumnsen(1) was used in this research. A 50-ml flask which contained 0.002 mole of benzhydrols and 10 ml of 5M sulfuric acid in...
glacial acetic acid was immered in a water-bath maintained at 25 ± 0.05°C, and 0.002 mole of azide was dropped into the flask with sample vial which was already supported over the solution. Shaking was commenced immediately after the introduction of the azide. The evolution of nitrogen was measured by mercury gas buret to determine the end points and the purities of the azides.

**Preparation of sample for the determination of product**

The reaction mixture was diluted to three times its volume with water and exhaustively extracted with 75 ml of n-pentane (three times with 25 ml each). The aqueous phase was then made basic with 45% sodium hydroxide solution and again extracted by the same method. The pentane extracts then dried over anhydrous magnesium sulfate, filtered, and most of pentane was evaporated under vacuum. The residues were made up to 5 ml of n-pentane solution using 5 ml volumetric flask.

**The determination of product ratio:** Two types of gas chromatograph machine were used for the analysis of products.

For Run No. 3 and 4
Perkin-Elmer Model 154B, Column 154-0012C.
Column temperature 175°C, Column pressure 20 lb/in.

Volts between filaments 7.95 v, Recorder range 1, sample injected 0.1 ml.
Recorder Speedomax Type G Model S.

For Run No. 6–13
Column Temperature 242~255 °C,
Column Pressure 60 lb/in,
Current of filament 200 ma;
Sample injected 0.005 ml.

The retention times of the products at above condition were

For Model 154B
Benzaldehyde 4.4 min,
p-chlorobenzaldehyde 8.1 min,
Aniline 4.5 min, p-chloroaniline 10.8 min.

For Model A-90-P
Benzaldehyde 2.76 min,
p-chlorobenzaldehyde 4.1 min,
Aniline 2.76 min, p-chloroaniline 4.9 min.

Although there was no difference between benzaldehyde and aniline in retention time, the p-chloro compounds gave complete separation into benzaldehydes and anilines.

The determination of quantities of products was performed by using peak height (except #3 & #4, these were determined by using peak areas). More

<table>
<thead>
<tr>
<th>React No.</th>
<th>% of Azide</th>
<th>Benzaldehyde</th>
<th>p-chlorobenzaldehyde</th>
<th>Aniline</th>
<th>p-chloroaniline</th>
<th>Total Products (mole)</th>
<th>Total Recovery (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzhydrol azide + p-chlorobenzaldehyde</td>
<td>3</td>
<td>99.2</td>
<td>0.52</td>
<td>0.13</td>
<td>0.32</td>
<td>0.03</td>
<td>0.001987</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>99.8</td>
<td>0.53</td>
<td>0.15</td>
<td>0.25</td>
<td>0.05</td>
<td>0.001924</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>93.0</td>
<td>0.48</td>
<td>0.15</td>
<td>0.26</td>
<td>0.05</td>
<td>0.001777</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>97.3</td>
<td>0.51</td>
<td>0.15</td>
<td>0.29</td>
<td>0.05</td>
<td>0.002290</td>
</tr>
<tr>
<td>p-chlorobenzaldehyde + Benzhydrol</td>
<td>4</td>
<td>91.8</td>
<td>0.50</td>
<td>0.13</td>
<td>0.29</td>
<td>0.04</td>
<td>0.002904</td>
</tr>
<tr>
<td></td>
<td>8*</td>
<td>91.5</td>
<td>0.53</td>
<td>0.13</td>
<td>0.30</td>
<td>0.04</td>
<td>0.001905</td>
</tr>
<tr>
<td>44'-Dichlorobenzaldehyde azide + Benzhydrol</td>
<td>11</td>
<td>91.3</td>
<td>0.50</td>
<td>0.12</td>
<td>0.32</td>
<td>0.001952</td>
<td>52.8</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>88.8</td>
<td>0.67</td>
<td>0.11</td>
<td>0.19</td>
<td>0.03</td>
<td>0.001477</td>
</tr>
<tr>
<td>Benzhydrol azide + 44'-p-Dichlorobenzaldehyde</td>
<td>13</td>
<td>95.3</td>
<td>0.50</td>
<td>0.15</td>
<td>0.26</td>
<td>0.09</td>
<td>0.002308</td>
</tr>
</tbody>
</table>

* 0.00176 mole of azide was used.
than three standard solutions which closed to sample concentration were used for each element of products.

As the peak heights were variable (0-4%) from day to day even if the same experimental conditions such as column temperature, column pressure and filament voltage were maintained, the determination of a sample and standard solution was carried out in the same day. When the temperature of column was changed during the determination, the values of concentration were calibrated (in #9, 2%/°C).

As shown in Fig 1, a graph of peak height versus concentration, the peak height increases linearly with increasing concentration from 0.5%. Therefore, based on this, the author concludes that for the solutions of 0.5% or more, only two standards are sufficient for inter- or extrapolation of unknowns.

Discussion and Conclusion

In the Schmidt reaction, benzaldehyde decomposes into benzaldehyde and aniline by strong sulfuric acid. Therefore, if no other reagents were present in the system, we would expect normally the products consisting of aldehyde and aniline. However, as it was assumed in the introduction, if a pre-equilibrium of the type (4) exist within the reaction system, we could ascertain this fact by introducing a reagent which is non-reactive but involves in the pre-equilibrium into the reaction system.

In reactions #3, #6, #9 and #10 in Table 2, p-chlorobenzaldehyde was introduced in the Schmidt reaction of benzaldehyde with no substituent. In this type of reaction, if one assumes no equilibrium, products, i.e. aniline and aldehyde, will consist of those with no substituents.

On the other hand, we would obtain p-chloro species in the products if the pre-equilibrium actually existed, since in the equilibrium radical exchange would certainly involve.

The results in Table 2 indicate that p-chlorobenzaldehyde are approximately 1/4 of the total benzaldehyde as expected from purely statistical ground. The small variations from this, however, may be due to errors in the experiments. According to McEwen (3), the transition state of the Schmidt reaction is a form with the partial bond formed between nitrogen and one of the benzene ring.

In this state, phenyl or substituted phenyl group attaches partially itself with nitrogen atom, and the ratio of aldehydes formed indicated that this migration was assisted by the electron-releasing groups.

Therefore, when chlorine is substituted at p-position (electron withdrawing), we would expect that more p-chlorobenzaldehyde be formed compared with unsubstituted aldehyde in the Schmidt reaction of unassymmetrical benzaldehyde azide.

As already mentioned, however, the results of the products ratio for the reaction with only one substitution on either benzaldehyde or benzalcohol (first two types, i.e. reaction #3, #6, #9, #10 and #4, #8), conform to this expectation only approximately.

However, it is striking that the ratio in these two cases turned out to be the same within experimental error. This could only be the result of a complete pre-equilibrium,

\[
\text{H} - \text{N} = \text{N} \equiv \text{N} \\
\phi - \text{CH} - \phi + \text{H} - \text{N} = \text{N} \equiv \text{N} \\
\text{OH} \\
\phi - \text{CH} - \phi + \text{H}^+ 
\]

This was further confirmed by using dichloro compounds as shown in Table 2 (Reaction #11, #12 and #13).
Here again we find the same products ratio regardless of the substrate (benzhydryl azide or benzhydrol) which was substituted with chlorine on p-positions of both benzene rings. The slight decrease of p-chloro-products compared with the reaction with mono-substituted substrate, may be explained as the decreased reactivity of p-substituted phenyl group in the rearrangement step. In other words, the rate is determined by the partial bond formation between phenyl group and nitrogen atom, according to McEwen, and is less reactive when electron-withdrawing group is present.

Agreement shown by these two types of reaction, i.e., mono-substituted and di-substituted, strongly supports the pre-equilibrium theory proposed in this work. The fact that the recoveries were only about 50% of the expected, can be interpreted as the result of other products formed (especially for anilines) which were the compounds not soluble in n-pentane e.g. aniline sulfate etc. or the compounds which has longer retention times than those of the normal products. This was shown by the fact that the increase in the amount of solvent and the repetition of extraction procedure had almost no effect in the amounts of the normal products obtained (less than 1%).

Acknowledgement

The author thanks professor W. E. McEwen (University of Kansas) for his advice and the provision of grants.

References

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