AN EFFICIENT METHOD FOR SYNTHESIS OF 1,1-DIARYLHYDRAZINES
AS AN INTERMEDIATE FOR INDOLE SYNTHESIS

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Abstract—The Hofmann reaction of 1,1-diarylureas (2) to afford the corresponding hydrazines (3) is described. Diarylamines (1) were converted to 1,1-diarylureas (2) with sodium cyanate and trifluoroacetic acid, or chlorosulfonyl isocyanate. The Hofmann reaction of 2 with alkaline sodium hypochlorite in ethanol successfully gave the corresponding hydrazines (3) in good yields. This method is especially effective for the preparation of easily reducible 1,1-diarylhydrazine derivatives.

In the course of the studies on the mechanism of abnormal Fischer indolization 1), we needed to carry out the Fischer indolization of 1,1-diarylhydrazones. However, all efforts 2) to synthesize some key intermediate 1,1-diarylhydrazines by various methods were failed. This situation forced us to develop another novel route for preparing 1,1-diarylhydrazines.

Recently, O'Connor reported 3) a synthetic method of 1,1-diphenylhydrazine by a Curtius rearrangement of N,N-diphenylcarbamoyl azide. However, in order to find an easier method, we examined the Hofmann reaction 4) of 1,1-diarylureas and obtained a satisfactory result. The Hofmann reaction of some mono-substituted ureas has been reported, 5) but no systematic report about 1,1-diarylureas.

Thus ureas (2) were prepared by the reaction of the corresponding amines (1)
Table I

<table>
<thead>
<tr>
<th>starting materials</th>
<th>Urea derivatives(2)(yield, %) method a&lt;sup&gt;1&lt;/sup&gt;</th>
<th>method b&lt;sup&gt;2&lt;/sup&gt;</th>
<th>mp</th>
<th>Hydrazines(3) (yield, % from 2)</th>
<th>mp</th>
</tr>
</thead>
<tbody>
<tr>
<td>la</td>
<td>78.9</td>
<td>—</td>
<td>188.5-190°</td>
<td>85.0 %&lt;sup&gt;c&lt;/sup&gt;</td>
<td>89-91°</td>
</tr>
<tr>
<td>lb</td>
<td>66.9</td>
<td>—</td>
<td>196-197°&lt;sup&gt;7)&lt;/sup&gt;</td>
<td>62.0&lt;sup&gt;d&lt;/sup&gt;</td>
<td>196-198°&lt;sup&gt;3)&lt;/sup&gt;</td>
</tr>
<tr>
<td>lc</td>
<td>6.2</td>
<td>66.4</td>
<td>186-188°</td>
<td>73.0&lt;sup&gt;d, e&lt;/sup&gt;</td>
<td>180-181°</td>
</tr>
<tr>
<td>ld</td>
<td>50.3</td>
<td>—</td>
<td>185-186.5°&lt;sup&gt;7)&lt;/sup&gt;</td>
<td>62.8&lt;sup&gt;d&lt;/sup&gt;</td>
<td>173-174.5°</td>
</tr>
</tbody>
</table>

a):NaOCN/CF<sub>3</sub>CO<sub>2</sub>H, b):ClSO<sub>2</sub>NCO, c):hydrazone with ethyl pyruvate, d):salt with TsOH, e):Higher temperature(70-80°) was used for the reaction.

in benzene with sodium cyanate and trifluoroacetic acid.<sup>7)</sup> However, since this method did not give satisfactory result in the case of lc, a reaction with chlorosulfonyl isocyanate<sup>8)</sup> was examined to give 2c in a moderate yield. These results were summarized in Table I.

The Hofmann reaction was carried out with alkaline aq.NaOCl in ethanol at room temperature for 1 to 2 hr. The yields and the identification of the hydrazines(3) in Table 1 were based on their hydrazone derivative or salts with TsOH.

General procedure for the Hofmann reaction of urea is as follows.

To an ice-cooling solution of an urea(2, 1.0 mmol) in ethanol(5 ml) was slowly added a mixture of 14 % aq.NaOH(1.5 ml) and aq.NaOCl(0.86 ml) containing 10.2 % active chlorine, and the resulted suspension (or solution) was stirred for 1 to 2 hr. at room temperature. After the reaction had been completed, the mixture was diluted with water, and then extracted with appropriate solvent to remove the amine(1) which formed as by-product. The aqueous layer was acidified with aq.HCl, then basified with aq.K<sub>2</sub>CO<sub>3</sub>, extracted with appropriate solvent, and dried over anhyd. K<sub>2</sub>CO<sub>3</sub>. The removal of solvent gave crude hydrazine(3), which was treated with ethyl pyruvate in ethanol to afford ethyl pyruvate [di(o-methoxyphenyl)-hydrazone] or with TsOH in a mixture of ether and benzene to afford TsOH salt.
The yields were good in all cases, and our method is especially effective for preparing easily reducible 1,1-diarylhydrazine. It should be noted that this procedure can be a general method of amination of 1,1-diarylamines to the corresponding hydrazines, which were difficult to be obtained even by the aminating reagents.\(^{2b}\) Although there is only one report\(^9\) on the Hofmann reaction of 1,1-disubstituted urea derivatives for preparing some triazanes, we would like to emphasize that this is the first synthetic study of the Hofmann reaction of 1,1-diarylureas, which is interesting from a point of view of the C-N bond migration. Application of our reaction for 1-alkyl-1-aryl- or 1,1-dialkylureas is now in progress in our laboratory.

ACKNOWLEDGEMENT

we wish to thank Dr. Hisashi Ishii, Chiba University, for helpful discussion.

REFERENCES AND NOTES


2. a) Even the most general method for preparing 1,1-diarylhydrazine, which involves the reduction of corresponding nitrosamine, and the method for using the aminating reagents\(^{2b}\) gave miserable results.\(^{2c}\) b) Y. Tamura, J. Minamikawa and M. Ikeda, Synthesis, 1977, 1; c) H. Ishii, Y. Murakami, and T. Hagiwara, unpublished data.


6. All compounds prepared for this study gave satisfactory elemental
analysis and spectral data.


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