Lewis Acid Catalyzed Synthesis of 1,5-Diketones, Precursor of Carbocycle-fused pyridine, form Enamine and Aldehyde

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Carbocycle-fused pyridines and related systems are attractive because of their potential to construct new host compounds. The most popular synthetic approach to 2,3:5,6-bisannelated pyridines employs the treatment of 1,5-diketones with ammonium acetate in refluxing acetic acid, typically yielding the pyridines in 50-70% yields. The synthetic pathways to prerequisite symmetric 1,5-diketones, however, are somewhat limited to involve the reaction of enamines with paraformaldehyde and the base treatment of cyclic ketones and aldehydes. Although the enamine approach has been extended to the preparation of carbocycle-fused 2,2':6',2'-terpyridines with various aromatic substituents at 4'-position, the introduction of aliphatic substituents at the 4'-position has not been as yet achieved. In this note we report that a Lewis acid may be used as a catalyst to boost the yield as well as to extend the scope of this reaction.

The enamine 1 and its homologs can be prepared in the normal fashion from the corresponding ketones in 70-90% yield. When enamine 1 treated with paraformaldehyde in the presence of aluminum trichloride followed by hydrolysis, the 1,5-diketon 3a was formed in an excellent yield. The yield of this reaction is improved more than two folds compared to the method reported by Colonge et al. The reactions of enamine 1 with aromatic aldehydes also proceed smoothly, but diastereomeric mixtures obtained. They are not fully characterized, and they were treated with ammonium acetate directly without isolation of the isomers to afford the corresponding carbocycle-fused pyridines with a substituent at 4'-position. The reactions with aliphatic aldehydes, however, appear to be little sluggish and the reactions with acetaldehyde and pentanal afforded the desired 4'-alkyl pyridines in 22% and 33% yields only, respectively. Although little low or modest, the yields are increased over the 22 and 37% yields, respectively, reported earlier. Table 1 summarizes the results obtained from 7 different systems and shows that aluminum trichloride can be employed as a catalyst to improve the yields in the reactions of enamine with aldehyde to give 1,5-diketones by reacting enamine with aldehydes.

Table 1. Preparation of 1,5-Diketones and/or 4'-Substituted Bisannelated Pyridines from Aldehydes

<table>
<thead>
<tr>
<th>Aldehyde</th>
<th>1,5-Diketone Pyridine</th>
<th>Yield</th>
<th>Mp. °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a HCHO</td>
<td>3a (93%) 4a (95%)</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>2a (24%) b (93%)</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>4a</td>
<td>c (35%) d (93%)</td>
<td>37-38</td>
<td></td>
</tr>
<tr>
<td>5a</td>
<td>e (90%) f (92%)</td>
<td>&gt;300</td>
<td></td>
</tr>
<tr>
<td>6a</td>
<td>g (92%) h (94%)</td>
<td>&gt;300</td>
<td></td>
</tr>
</tbody>
</table>

*Yield of the crude product, except 3a, checked by glc. *Isolated yield of the product.

In conclusion, the present method offers advantages over the previously reported methods. The reaction requires readily available reagents, is applicable to the synthesis of symmetric pyridines as well as pyridazines with high yields, as well as is able to carry out under relatively mild conditions.

A Typical Experimental Procedure is as Follows.

A suspension of paraformaldehyde (0.30 g, 0.01 mol) in 20 ml of dioxane was slowly added to a suspension of aluminum trichloride (1.22 g, 0.009 mol, 0.90 equiv.) in 30 ml of dioxane at room temperature under nitrogen. After the reaction mixture was stirred at room temperature for 30 min, a solution of enamine 1 (3.34 g, 0.02 mol) in 30 ml of dioxane was added to a cannula. The resulting solution was stirred at room temperature for 2 h or until complete consumption of the aldehyde which was checked by TLC. The reaction mixture was acidified with 1 N aq. propanoic acid and extracted with methylene chloride (3×30 ml). The combined organic layer was dried over anhydrous magnesium sulfate, followed by the evaporation of solvent, the crude 1,5-diketone was either characterized or treated directly with 3.0 molar equivalents of ammonium acetate in 10 ml of 1 N aq. propanoic acid and 2.5 molar equivalents of cupric acetate under reflux for 0.75-1.0 h. Work-up as usual...
gave 1.65 g (88%) of 1,2,3,4,5,6,7,8-octahydroacridine; mp. 71°C (lit. 8 mp. 71°C).

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References
7. New compounds are characterized by spectroscopic and elemental analysis to show satisfactory results as follows: 4b H-NMR (CDCl3, 80 MHz) δ 2.95-2.93 (overlapped t, 8H); 2.33 (s, 3H, CH3). L92-1.74 (m, 8H); IR (thin film) v 3020, 2930, 2860, 1605, 1570, 1442, 1415, 1305, 1230, 1215 and 730 cm⁻¹; mass spectrum, m/e (rel. intensity) 232 (M+1, 22), 201 (M, 10), 144 (20), 136 (15), 91 (100), 76 (45), 56 (35); Anal. Calcd. for N₄H₂N: C, 83.52; H, 9.52; N, 6.96. Found: C, 83.44; H, 9.56; N, 7.00.
8. 4d H-NMR (CDCl3, 80 MHz) δ 7.58-7.32 (m, 9H); 2.93 (t, 4H, J = 6.7 Hz); 2.81 (t, 4H, J = 6.7 Hz; 1.86-1.75 (m, 8H); IR (KBr) v 3020, 2930, 2860, 1605, 1565, 1445, 1410, 1315, 1230, 1215, 750 and 730 cm⁻¹; Anal. Calcd. for N₄H₂N:N: C, 86.68; H, 8.04; N, 5.32. Found: C, 86.76; H, 7.96; N, 5.28.
9. 4f H-NMR (CDCl3, 80 MHz) δ 7.95 (d, 2H, J = 8.1 Hz), 7.55 (dm, 2H), 2.91-2.80 (m, 8H), 2.35 (s, 3H), 1.75 (m, 8H); IR (KBr) v 3020, 2950, 2870, 1600, 1570, 1452, 1410, 1305, 1250, 830 and 730 cm⁻¹.

The Adsorption Behaviors of Heavy Metal Ions on the Sawdusts

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Ion-exchange resins have been used to separate and preconcentrate metal ions1-4 and organic compounds5-6. Activated charcoal has been used to remove metal ions and organic compounds in the water supply facilities.7 However, ion-exchange resins and activated charcoal couldn’t be used to remove heavy metal ions from waste water because of their cost.

The aim of this work was to furnish the basic data to remove heavy metal ions in the industrial and laboratory waste water with the low-priced adsorbent. We thought that sawdusts would be a proper one for that purpose if they adsorb heavy metal ions favorably. Therefore, we examined in this experiment the pH effect on the distribution coefficients (Kd values) of the heavy metal ions on the sawdusts to inspect the optimum adsorption condition and whether the break through points at the frontal chromatography of the heavy metal ions in the solution of the condition by a column packed with a sawdust would be large enough or not.

Experimental

Instrumental. The pH of the sample solution was measured with Chemcadet Model 5986 pH meter and the metal ion concentrations were determined with Hitachi Model Z-8,000 atomic absorption spectrophotometer. The horizontal shaking of the sample vials to determine the Kd values of