

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

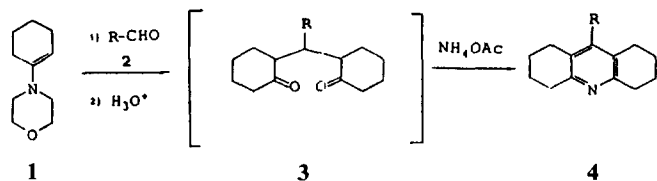
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Received September 9, 1991

Carbocycle-fused pyridines and related systems are attractive because of their potential to construct new host compounds.¹ The most popular synthetic approach to 2,3:5,6-bisannulated pyridines employs the treatment of 1,5-diketones with ammonium acetate in refluxing acetic acid, typically yielding the pyridines in 50-70% yields.² The synthetic pathways to prerequisite symmetric 1,5-diketones, however, are somewhat limited to involve the reaction of enamines with paraformaldehyde³ and the base treatment of cyclic ketones and aldehydes.⁴ Although the enamine approach has been extended to the preparation of carbocycle-fused 2,2':6',2''-terpyridine with various aryl substituents at 4'-position, the introduction of aliphatic substituents at the 4'-position has not been as yet achieved.⁵ 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.⁶ When enamine **1** treated with paraformaldehyde in the presence of aluminum trichloride followed by hydrolysis, the 1,5-diketone **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.*⁴ The reactions of enamine **1** with aromatic aldehydes also proceed smoothly, but diastomeric 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.⁷ 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 17% yields, respectively, reported earlier.² 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.

Other Lewis acids, such as FeCl_3 , ZnCl_2 , SnCl_4 , Et_2AlCl , have also been studied for the condensation reactions and

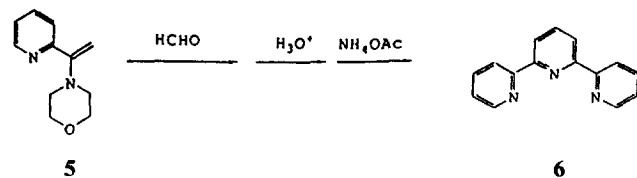
Table 1. Preparation of 1,5-Diketones and/or 4'-Substituted Bis-Annulated Pyridines from Aldehydes

Aldehyde	1,5-Diketone [yield ^a]	Pyridine [yield ^b]	Mp. °C
2a HCHO	3a (93%)	4a (95%)	71 (lit. ⁸ mp. 69°C)
b CH_3CHO	b (24%)	b (93%)	53
c Pentanal	c (35%)	c (93%)	37-38 (lit. ⁹ mp. 37-38°C)
d Benzaldehyde	d (93%)	d (95%)	221-222
e <i>p</i> -Tolualdehyde	f (90%)	e (92%)	236-238
f <i>p</i> -Chlorobenzaldehyde	g (92%)	f (92%)	>300
g <i>p</i> -Nitrobenzaldehyde	h (94%)	g (94%)	>300

^aYield of the crude product, except **3a**, checked by glc. ^bIsolated yield of the product.

the yields of their reactions were found to be not as good as the reaction with aluminum chloride, although their yields are still better than that of the reactions without Lewis acid.¹⁰

The present result could be culminated in the preparation of 2,2':6',2''-terpyridine. Morpholine enamine **5**¹¹ of 2-acetylpyridine was reacted with paraformaldehyde in the presence of aluminum trichloride to give 2,2':6',2''-terpyridine **6** in the overall yield of 60%. Without a Lewis acid, this reaction is too sluggish to employ for the preparation of 2,2':6',2''-terpyridine.^{1d}



In conclusion, the present method offers advantages over the previously reported methods.^{1,2,12} The reaction requires readily available reagents, is applicable to the synthesis of symmetric pyridines as well as polypyridines 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 resulting mixture was stirred at room temperature for *ca.* 30 min, a solution of enamine **1** (3.34 g, 0.02 mol) in 30 ml of dioxane was added *via* 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 acetate⁹ 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).

Acknowledgement. Financial support by the Ministry of Education (non-directed fund of 1990) is gratefully acknowledged.

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- New compounds are characterized by spectroscopic and elemental analysis to show satisfactory results as follows: **4b** ¹H-NMR (CDCl₃, 80 MHz) δ 2.95-2.83 (overlapped t, 8H), 2.33 (s, 3H, CH₃), 1.92-1.74 (m, 8H); IR (thin film) ν 3020, 2930, 2860, 1605, 1570, 1442, 1415, 1305, 1230, 1215 and 730 cm⁻¹; mass spectrum, m/e (rel. intensity) 202 (M+1, 2.2), 201 (M, 10.7), 144 (20.3), 136 (15.4), 91 (100), 76 (45), 56 (35); Anal. Calcd. for N₁₄H₁₉N: C, 83.52; H, 9.52; N, 6.96. Found: C, 83.44; H, 9.56; N, 7.00; **4d** ¹H-NMR (CDCl₃, 80 MHz) δ 7.68-7.32 (m, 5H), 2.93 (t, 4H, J=6.7 Hz), 2.81 (t, 4H, J=6.7 Hz), 1.88-1.75 (m, 8H); IR (KBr) ν 3020, 2930, 2860, 1605, 1560, 1445, 1410, 1315, 1230, 1215, 750 and 730 cm⁻¹; Anal. Calcd. for N₁₉H₂₁N: C, 86.65; H, 8.04; N, 5.32. Found: C, 86.76; H, 7.96; N, 5.28; **4e** ¹H-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) ν 3020, 2950, 2870, 1600, 1570, 1452, 1410, 1305, 1250, 1220, 830 and 730 cm⁻¹; **4f** ¹H-NMR (CDCl₃, 80 MHz) δ 8.00-7.60 (m, 2H), 7.58-7.43 (m, 2H), 2.95-2.86 (m, 8H), 1.74 (m, 8H); IR (KBr) ν 3020, 2930, 2860, 1605, 1570, 1442, 1415, 1305, 1240, 1215, 830 and 750 cm⁻¹; **4g** ¹H-NMR (CDCl₃, 80 MHz) δ 8.12 (d, 2H, J=8.2 Hz), 7.45 (d, 2H), 2.89-2.78 (m, 8H), 1.76 (m, 8H); IR (KBr) ν 3020, 2930, 2860, 1605, 1570, 1450, 1425, 1320, 1230, 1210, 820 and 750 cm⁻¹.
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The Adsorption Behaviors of Heavy Metal Ions on the Sawdusts

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Received October 12, 1991

Ion-exchange resins have been used to separate and pre-concentrate metal ions¹⁻⁴ and organic compounds⁵⁻⁶. Activated charcoal has been used to remove metal ions and organic compounds in the water supply facilities⁷. 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 (K_d 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 5984 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 K_d values of