

POLYAZA CAVITY SHAPED MOLECULES 13. A VERSATILE NEW TERPYRIDINE SYNTHESIS

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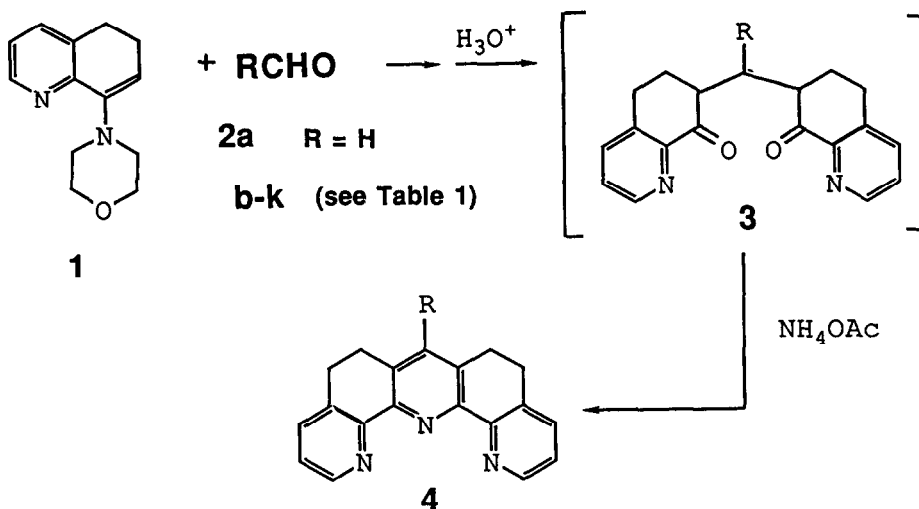
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Abstract: The reaction of morpholine enamines derived from α -pyridyl ketones with aromatic aldehydes leads to the formation of a 1,5-diketone intermediate which in turn provides a 4'-substituted derivative of 2,2';6',2"-terpyridine.

The 2,2';6',2"-terpyridine molecule is a very effective tridentate chelating system. Although considerable coordination chemistry has been accomplished with this molecule, relatively little has been done with substituted derivatives primarily due to synthetic limitations in their preparation. The two principal approaches to terpyridines involve either low yield coupling reactions of pyridine subunits¹ or condensations on 2,6-diacetylpyridines.^{2,3} Newkome⁴ and Bell⁵ have also utilized the pyrolysis of a trimethylhydrazonium salt to build up the central ring of a terpyridine system. Herein we wish to elaborate on an enamine approach to the terpyridine molecule which we reported earlier.⁶

The enamine **1** and its higher homologs can be obtained (70-90%) in the normal fashion from the corresponding ketones. When treated with paraformaldehyde followed by hydrolysis, the diketone **3a** (R=H) was formed. Due to the potential for diastereomeric mixtures, **3a** was not isolated, but instead was reacted directly with ammonium acetate to provide the annelated terpyridine **4a** (31% overall). Although modest, this yield is substantially improved over the 2-5% yields which we reported earlier for the Friedlander preparation of these compounds.⁶

It is apparent that the utilization of appropriate aldehydes, RCHO, in place of formaldehyde might result in the preparation of 4'-substituted terpyridines. Aliphatic aldehydes appear to be quite sluggish in this synthesis and attempts with acetaldehyde and hexanal did not lead to the desired 4'-alkyl terpyridines. Aromatic aldehydes, on the other hand, react comparatively smoothly. Table 1



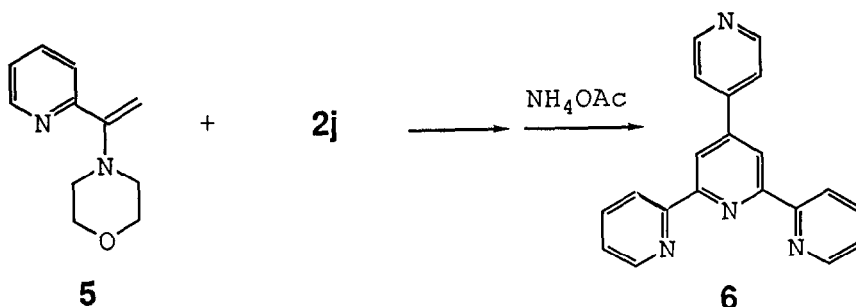
summarizes the results for ten different systems and indicates that the generality extends to aromatic substrates such as pyridine and ferrocene. The attempted reaction of 9-anthracene carboxaldehyde did not succeed presumably due to steric hindrance imposed by the 1,8-peri-hydrogens.

It is not necessary to employ an annelated pyridyl ketone precursor. The morpholine enamine of 2-acetylpyridine (5) is a relatively labile species and substantial compound is lost during its preparation. Reaction of 5 with 2j results in a 20% yield of 4'-(4-pyridyl)-2,2';6',2"-terpyridine (6). Our ultimate interest in such molecules is the preparation of metal complexes possessing remote

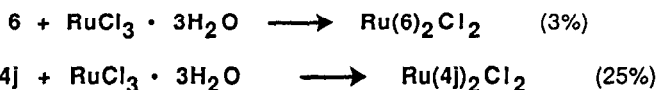
Table 1. Preparation of 4'-Substituted Bis-Annelated Terpyridines from Aromatic Aldehydes.

Aldehyde	Terpyridine ^a (yield)	m.p.
2b Benzaldehyde	4b (20%)	255-57°C
2c p-Tolualdehyde	4c (39%)	242-44°
2d p-Chlorobenzaldehyde	4d (35%)	>300°
2e p-Nitrobenzaldehyde	4e (19%)	280-82°
2f 4-Benzyloxybenzaldehyde	4f (31%)	270-72°
2g 4-(N,N-dimethylamino)benzaldehyde	4g (35%)	275-77°
2h 2,5-Dimethoxybenzaldehyde	4h (21%)	>300°
2i 3-Pyridinecarboxaldehyde	4i (53%)	254-56°
2j 4-Pyridinecarboxaldehyde	4j (36%)	>300°
2k Ferrocenecarboxaldehyde	4k (26%)	220-22°

(a) All compounds gave satisfactory spectral analysis.

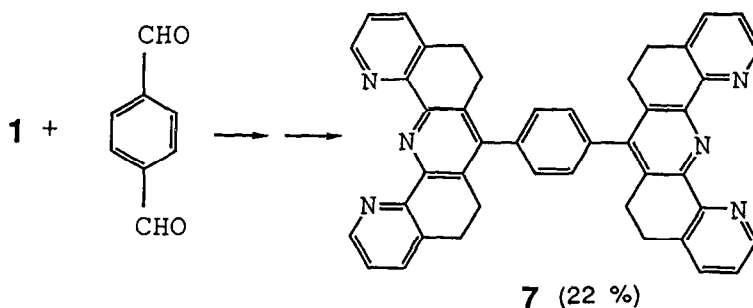


functionalization. To this end we find that **6** will form a bis-complex with ruthenium in only 3% yield while the bis-dimethylene annelated analog **4j** forms a similar complex in 25% yield. The dimethylene bridges in **4j** hold the tridentate chelating moiety in a cavity shaped conformation which



is favorable for the desired complexation. Cyclometallation pathways which might compete through other conformations are likewise inhibited.

A double-barrelled reaction can be realized when terephthalaldehyde is utilized in this sequence and the phenyl bridged bis-terpyridine system **7** can be obtained in 22% overall yield. The corresponding *m*-phthalaldehyde reacts in a similar fashion, but the yield of meta-bis-terpyridyl benzene is quite low and pure product is difficult to obtain. We are examining other oriented dialdehyde precursors to construct unique bis-chelating systems.



A typical experimental procedure is as follows: A solution of 2.16 g (0.01 mol) of 8-N-morpholino-5,6-dihydroquinoline (**1**) and 0.50 g (0.005 mol) of benzaldehyde in 25 mL of dioxane was refluxed under N_2 for 18 h. The reaction mixture was acidified with 1N propanoic acid⁷ and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layer was dried over anhyd MgSO_4 and,

after removal of the solvent, the crude diketone was treated with 1.0 g of NH_4OAc in 10 mL of 1N propanoic acid and refluxed for 2 h. After cooling, the solution was made basic with 50% NaOH and extracted with CH_2Cl_2 (3 x 50 mL). The organic extracts were washed with H_2O and dried over anhyd MgSO_4 . Evaporation of the solvent gave a residue which was chromatographed on alumina (40 g) eluting with CH_2Cl_2 , followed by $\text{CH}_2\text{Cl}_2:\text{CHCl}_3$ (1:4) to afford 0.36 g (20%) of **4b** which was recrystallized from CHCl_3 , mp 255-57°C.

Acknowledgement

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References and Notes

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7. The use of 1N propanoic acid is preferred over stronger acid (HCl) since protonation of the quinolone rings does not occur leaving **3** in the organic phase. Furthermore the residual propanoic acid from the hydrolysis step serves as the solvent for the NH_4OAc condensation.

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