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CYCLOSEXIPYRIDINES

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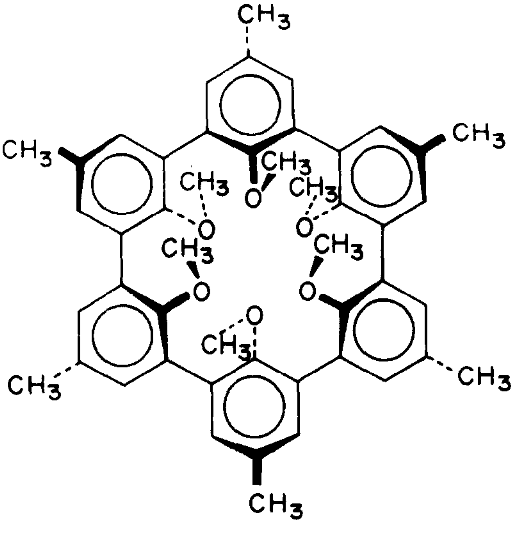
Summary: The synthesis and some complexation behavior are described for two cyclosexipyridines, a new class of highly structured complexing agents.

The recent chemistry of synthetic complexing agents has been highlighted by the properties of a new class of highly structured hosts, the spherands.[1] Host 1, the parent spherand, is a powerful complexing agent with -ΔG° values for Li^+ and Na^+ of >23 and 19 kcal/mol, respectively.[1a,d] In addition, host 1 is totally selective for Li^+ and Na^+, excluding larger or divalent cations completely. The dramatic increase in binding gained by the preorganization of anisole, itself a poor ligand,[2] suggests the synthesis of other highly structured hosts with subunits that are good ligands, such as pyridine.



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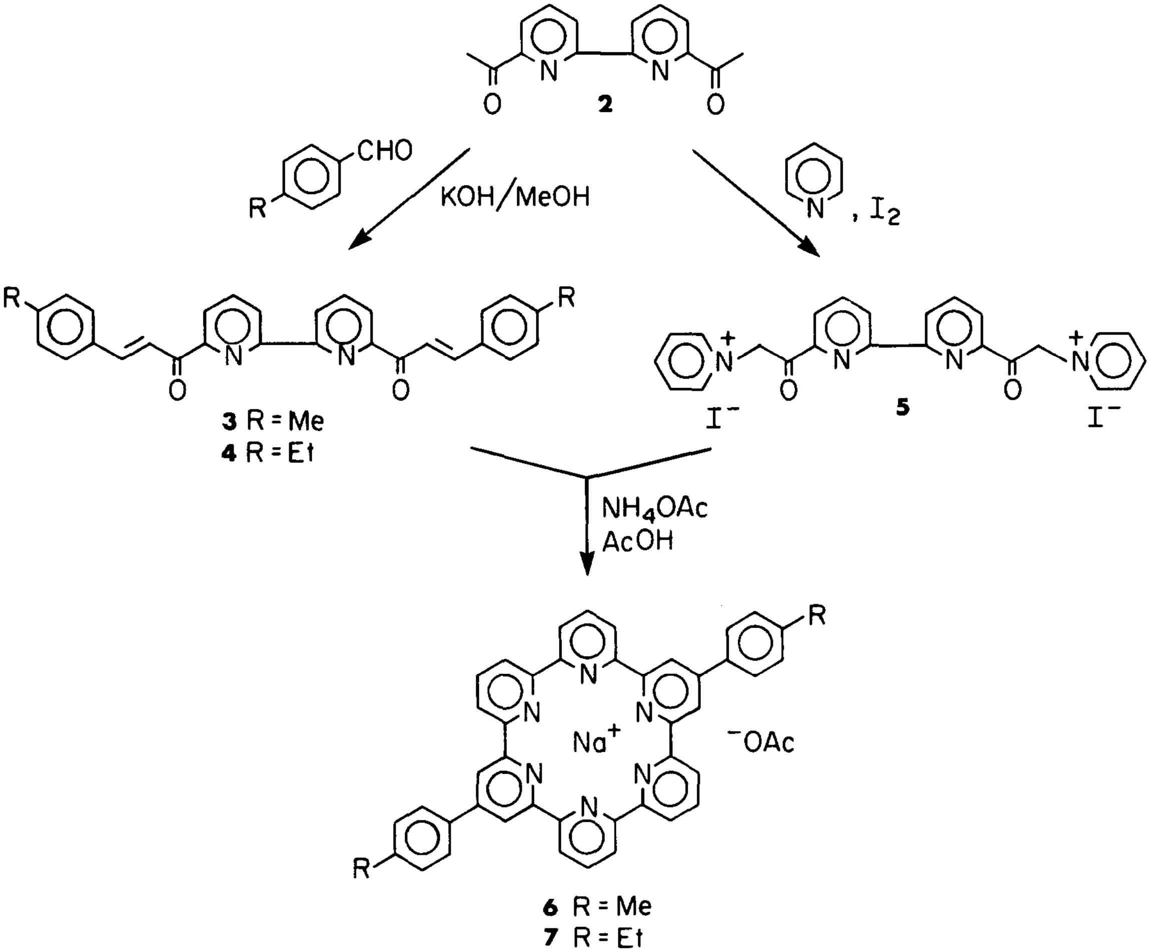
I report here the synthesis and some properties of two examples of a new group of highly structured hosts, the cyclosexipyridines. Scheme I depicts the synthetic route used. The key intermediate, 6,6'-diacetyl-2,2'-bipyridine 2, was synthesized in two steps by a known procedure from 2,6-dibromopyridine.[3] Treatment of diacetylbipyridine 2 with either p-tolualdehyde or p-ethylbenzaldehyde in refluxing KOH/MeOH gave the derivatives 3 and 4, which crystallized from the reaction mixtures (85 and 74% yields, respectively). Compound 2 was also refluxed in pyridine with 2 equiv of I_2 to give the bispyridinium iodide **5**, which crystallized from the reaction mixture (82%).[4]

Scheme 1



In an extension of the Kröhnke pyridine synthesis,[5] compounds **3** and **5** (1.54 mmol each) were combined and refluxed in 500 mL of freshly distilled AcOH until a homogeneous solution was obtained. To the yellow solution, 5 g of NH_4OAc (freshly made from NH_3 gas and distilled AcOH) was added. The solution immediately turned dark green. During 16 h of reflux, a cream-colored precipitate formed. Isolation of the precipitate followed by trituration with boiling DMF (distilled), then washing with anhydrous ether gave 0.47 g of off-white powder, the 1:1 NaOAc complex **6** of the desired cyclosexipyridine, in 42% yield.

The compound is insoluble in most solvents but readily dissolves in CF_3CO_2H. Host **6** was examined by field-desorption mass spectrometry (FDMS) in DMSO from m/e 281 to 1001. Two clusters of ions were detected, with the major peak at m/e

642 (M^+) with associated M^{+1} and M^{+2} peaks. A smaller cluster of peaks began at m/e 665 (M^+ + Na^+) with associated M^{+1} and M^{+2} peaks. After drying at 110°C *in vacuo*, host **6** gave C, H, and N elemental analyses consistent for the 1:1 NaOAc complex plus 1.5 waters of hydration. The IR had peaks at 1600 and 1390 cm^{-1} characteristic of carboxylate anions. No evidence was present in the IR for NH_4^+ complexation. The ^1H NMR spectrum (CF_3CO_2H) was line broadened, with a broad peak centered at δ 2.4 ppm ($ArCH_3$) and three broad peaks in the aromatic region centered at δ 7.4, 7.8, and 8.6 ppm. The compound did not melt but decomposed upon attempted sublimation using an argon entrainer gas (3 torr) at 586°C. These data coupled with the designed synthesis indicate **6** has the structure shown.

The diethylcyclosexipyridine was synthesized from **4** and **5** by the procedure used for host **6**. The NaOAc complex **7** was isolated (56%), as indicated by FDMS which showed the major peak at m/e 693 (M^+ + Na^+) and a peak at m/e 670 (M^+). The host gave C, H, and N analyses consistent for the NaOAc complex with one water of hydration.

The excellent yields for the formation of the cyclosexipyridine complexes might be due to the NH_4^+ templation of the intermediate quinquepyridine to facilitate intramolecular rather than intermolecular reaction of the two ends (Fig. 1). However, the isolated complexes are of NaOAc rather than NH_4OAc. Care was taken to minimize the presence of adventitious metals in the materials and solvents used. Therefore, the intriguing possibility exists that the cyclosexipyridines are capable of stripping Na^+ from glass.

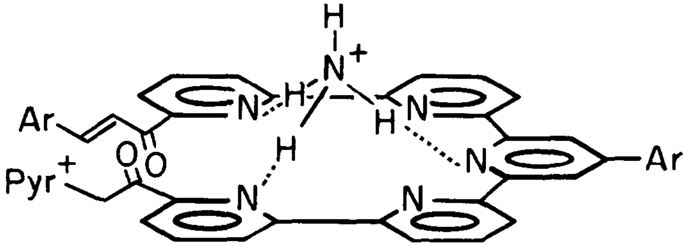


Figure 1. Proposed templation by NH_4^+ of the quinquepyridine intermediate in the synthesis of cyclosexipyridines.

Examination of the Corey-Pauling-Koltun molecular models of cyclosexipyridines suggests that the pyridine rings are much more conformationally mobile than the aryl rings of spherand **1**. Consequently, the cyclosexipyridine cavity can probably reorganize to accommodate cations of various sizes. The average cavity size appears ideal for K^+ and Rb^+ rather than the smaller cations. Detailed complexation studies must await the synthesis of a solubilized cyclosexipyridine.

Acknowledgment

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