

Acyclic Congener of Cucurbituril: Synthesis and Recognition Properties

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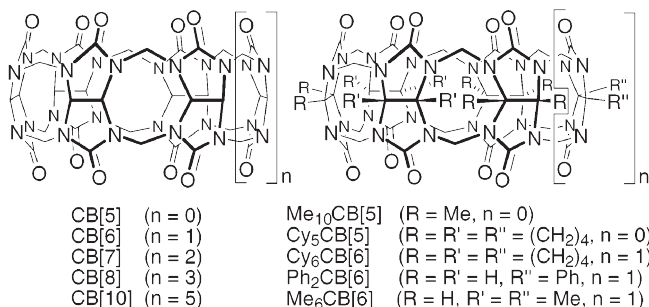
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The cucurbit[*n*]uril (CB[*n*]) family of macrocycles occupies a prominent role in molecular recognition and self-assembly studies despite the current inability to access specific cucurbit[*n*]uril homologues, derivatives, and analogues by straightforward tailor-made synthetic procedures. In this paper, we explore an approach that circumvents the challenges posed by the tailor-made synthesis of macrocyclic CB[*n*] by preparing **1**, which functions as an acyclic CB[6] congener. The *o*-xylylene connections to the glycoluril rings preorganize **1** into the (a,a,a,a)-**1** conformation required for binding and reduce its tendency to undergo self-association. We surveyed the binding properties of **1** toward 16 amines ($K_a \leq 1.52 \times 10^4 \text{ M}^{-1}$) and diol, diacid, guanidinium, and pyridinium species in pD 7.4 phosphate-buffered D₂O. We find that the recognition properties of **1** parallel those of CB[6], binding tightly to alkaneammonium species in water and exhibiting length-dependent selectivity and competitive binding with alkali metals present in solution. Compound **1** binds hexanediammonium ion only 180-fold less tightly than CB[6]. The modular synthesis of **1** suggests synthetic methods toward the preparation of acyclic CB[*n*] congeners with complex functional groups on the edges of their aromatic rings and cavity volumes similar to CB[7] and CB[8]. In combination, these results suggest that acyclic CB[*n*] congeners hold promise in molecular recognition and self-assembly studies that complements that of macrocyclic CB[*n*].

I. Introduction

Cucurbituril (CB[6]) is a macrocyclic hexamer composed of six glycoluril rings and twelve methylene bridges.^{1,2} The molecular structure of CB[6] defines a hydrophobic cavity with a diameter of 5.8 Å and a volume of 164 Å³.³ Access to this cavity is provided by two ureidyl-

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carbonyl-lined portals 3.9 Å in diameter. In accord with these structural parameters, CB[6] binds to alkanedi-

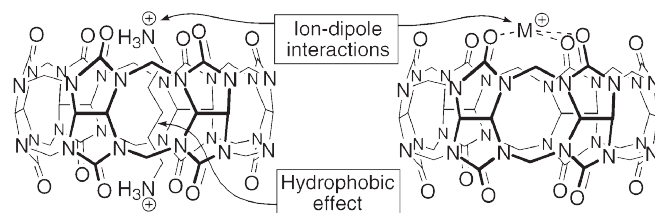


FIGURE 1. Illustration of the binding of alkanediammonium species and metal ions to CB[6].

ammonium ions in aqueous solution with high affinity ($K_d \approx 1 \mu\text{M}$) driven by the hydrophobic effect and ion-dipole interactions (Figure 1).⁴ The carbonyl-lined portal also functions as a ligand for a variety of metal cations. In addition to good affinity, CB[6] exhibits high selectivity in its binding processes as a result of the rigidity of its macrocyclic structure. As a result of these outstanding recognition properties, CB[6] has been used in a variety of applications, including the catalysis of dipolar cycloadditions,^{5–7} as a molecular bead in molecular necklaces and polyrotaxanes,^{8,9} molecular bowls,¹⁰ DNA complexation,^{11,12} and for the removal of contaminants from aqueous waste streams.¹³

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