

The octa-acid host (**1**) for this study is known for its ability to bind guests in aqueous solution. This host is a curved amphiphile with a ca. 1 nm deep hydrophobic pocket (Figure 1) and an outer surface decorated with eight, water-solubilizing, carboxylate groups (studies are typically carried out at pH 9.2 to ensure deprotonation of the carboxylic acid groups). If a guest is relatively hydrophobic, then two copies of the host molecule will dimerize around the guest (or guests) to form a capsular complex in which the guest is (reversibly) trapped within a dry nano-environment defined by the assembly.¹⁻⁷ The driving force of these complexations is the hydrophobic effect. In other words, desolvation of the guest, as well as the hydrophobic pocket of the host and the hydrophobic rim around the cavity portal, are important in guest binding and assembly. If on the other hand the guest is amphiphilic, then a 1:1 complex with the host is formed. In these complexes the guest binds in an orientation-specific manner such that the polar head group is located at the portal of the hydrophobic pocket. As this decreases the net hydrophobicity of the rim region of the host, dimerization is not usually observed. In such cases, the binding constant for host-guest complexes can be determined by techniques such as isothermal titration calorimetry (ITC) and NMR.^{8,9}

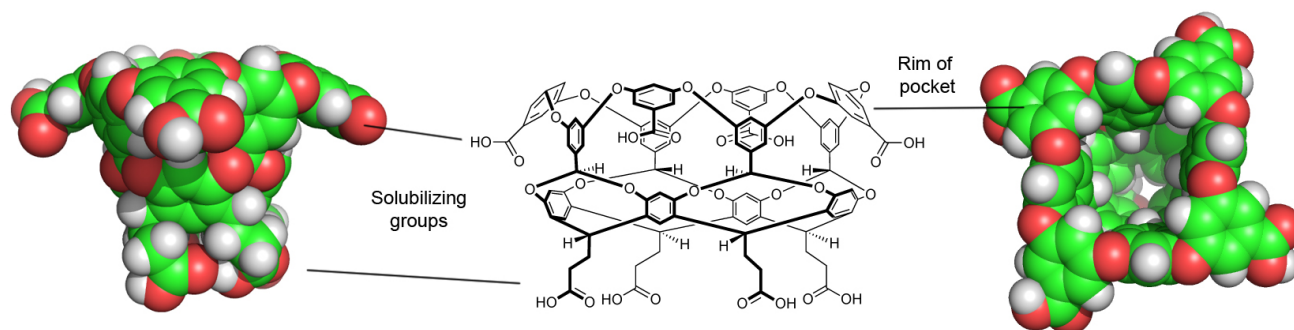


Figure 1: Octa-acid host **1**: (Left) Side view of space-filling representation of host; (Center) Chemical structure representation from the same perspective as the space-filling model on left; (Right) Plan view of the host looking down into the hydrophobic pocket. Both the rim of the host, and the outer solubilizing groups are indicated.

We have observed three key factors in the affinities of these host-guest complexes. First is the net hydrophobicity of the guest; the more hydrophilic the guest the weaker the binding.⁹ Second, the more complementary the guest is to the hydrophobic pocket the stronger it will bind.⁸ Finally, certain hydrogen-bond accepting groups such as halogen substituents have an affinity for the four hydrogens that point into the pocket near its base.¹⁰ The presence of these increases affinity relative to examples where this lowest (tapering) region of the pocket is simply occupied by, for example, a methyl group of the guest.

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