

Cucurbit[7]uril (CB7) is known for its ability to bind guest molecules with standard binding free energies as great as $\Delta G^\circ \approx -20 \text{ kcal/mol}$ (1–3), in aqueous solution. These affinities are comparable to some of the tightest-binding protein-ligand systems known. The tightest-binding CB7 guests so far identified have a rigid hydrophobic core, such as ferrocene(2), adamantane(1, 3), or [2.2.2]bicyclooctane(3), which fits snugly into the relatively nonpolar cavity of CB7, along with two cationic moieties, such as ammonium groups, positioned so that one sits at each of the two carbonyl-rich portals. Weaker binding tends to be observed for guests with smaller hydrophobic cores, fewer or no cationic groups, non-optimal shapes, and incorrectly positioned cationic groups(1). For binding of dicationic guests to the smaller but otherwise similar host cucurbit[6]uril (CB6), maximal affinity is achieved when the spacing between the two cations is just right, with affinity falling off for both shorter and longer spacings(4). The ionic strength and the type (e.g. Na⁺, Cs⁺, K⁺) of the metal ions in solution can also significantly affect affinity(4, 5). Thus, metal ions are thought to bind to some extent to the carbonyl groups at the portals of these host molecules, and those to compete with binding of cationic guests. It has been suggested that the unusually high affinities achieved by cucurbiturils with some guest molecules derive from the possibility of achieving a high degree of chemical complementarity for two rather rigid molecules(2, 6) and/or from the expulsion of thermodynamically disfavored water from the cavity upon binding(7, 8).

The experimental methodology used by the Isaacs group to measure the values of K_{rel} for the CB7-guest systems in this round of SAMPL have been detailed previously(1). Note that the buffer pH was 7.4, so all amine groups in the guests are likely to be mainly ionized in solution, and they may well remain ionized in the bound state so long as they can form stabilizing interactions with the host carbonyls.

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