MS33-2-4 Shape and Volume – Molecular Recognition Rules of Big Calixarene Rings
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Abstract
Calixarenes are vase-shaped host molecules that can form complexes with one or more guest molecules. To establish molecular recognition rules, the hosts p-tert-butylcalix[6]arene (TBC6) and p-tert-butylcalix[8]arene (TBC8) were crystallized with different guest molecules (cyclohexane, anisole, heptane, toluene, benzene, methyl acetate, ethyl acetate, dichloromethane, chloroform, tetrahydrofuran, acetonitrile, dimethyl sulfoxide, dimethylformamide, and pyridine) and the obtained structures were characterized by X-ray diffraction (1,2). With most solvents, 1:1 and/or 1:3 TBC6–guest complexes were formed, although other stoichiometries were also observed with small guest molecules, and crystallization from ethyl acetate produced the unsolvated form. A common structural feature of most TBC(4/6/8)-guest structures is off-set bilayer packing, which is built by the strongest dimers (for TBC6 dimers energies are lower than −110 kJ mol^{-1}). This structural feature was also present in pure TBC6 crystal structure. The incorporation of solvent molecules with volumes <100 $Å^3$ in TBC6 crystal structures leads to the separation of the off-set bilayers, whereas larger solvent molecules prevent the formation of this layer. Even though the formation of a structural motif with the tert-butyl group in the TBC6 cavity is energetically favoured, its slow rate of formation possibly limits the formation of pure TBC6 crystals. Hence, the crystal structure of a high macrocycle-to-solvent ratio system can transform into a more thermodynamically stable crystal structure with a lower ratio through solvent evaporation or recrystallization(3). The calculated fill percentage of the TBC6 cavity was ~55% for apolar guests and significantly lower for polar solvents, indicating that polar molecules can bind to apolar cavities with significantly lower packing coefficients. All guest molecules that occupy the TBC6 cavity interact with the host with an energy close to −50 kJ mol^{-1}; therefore, this property does not determine molecular recognition. The ratio between the apolar surface area and the volume was used to predict the formation of inclusion versus exclusion complexes, with inclusion complexes observed at ratios <40. These findings allow the binding of potential guest molecules to be predicted and a suitable crystal packing for the designed properties to be obtained.

References
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