

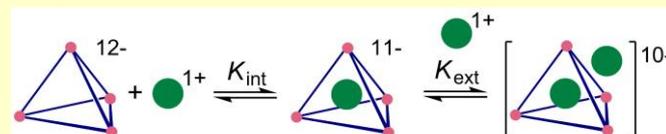
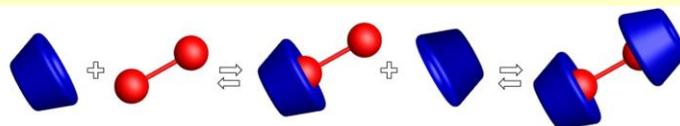
# SOLUTION THERMODYNAMICS OF SUPRAMOLECULAR SYSTEMS

**Giuseppe Arena** (Full professor)

*garena@unict.it*

**Carmelo Sgarlata** (Assistant Professor)

**Giuseppa Ida Grasso** (Post-doctoral fellow)



Molecular recognition is one of the key processes in living systems. Water-soluble synthetic host-guest systems may act as valuable models for a deeper understanding of the basic forces involved in molecular recognition in the solvent where most biological processes occur. Our group aims to accurately determine the driving forces that control molecular recognition events in solution through the complementary use of different analytical techniques. The design and characterization of novel supramolecular architectures (molecular assemblies held together by weak interactions) in water is also a topic of interest. Such systems might be employed as nano-shuttles for drug delivery, nano-reactors and selective receptors in separation processes.

**Keywords:** Molecular recognition, Host-guest systems, Solution equilibria, Driving forces, Calorimetry

## 1. Anion recognition and self-assembled supramolecular capsules in water

A cationic calixarene-based host (a basket-shaped molecular container) has been designed and synthesized for the selective binding of both aliphatic and aromatic anions in aqueous solution. NMR and potentiometric data showed that the host flexibility changes as a function of the pH. The combination of NMR, ESI-MS and nano-isothermal titration calorimetry (nano-ITC) revealed that the guests are included into the tetracationic host thanks to a concerted hydrophobic ( $\pi$ - $\pi$  or CH- $\pi$ ) and electrostatic interaction. The  $\Delta H^\circ$  and  $\Delta S^\circ$  values obtained through the ITC study reveal significant insights that are not conveyed in the affinity values. The inclusion process is enthalpically favored regardless of the nature of the guest and the anionic function but its strength changes with pH due to the different conformational flexibility of the calixarene scaffold in the acidic and in the neutral region.

We further designed suitable dianionic “gemini-like” guests and studied their interactions with the cationic host in water. We were able to show that such “double-headed” guests may trigger the formation of homodimeric capsules in neutral aqueous solution relying on concerted hydrophobic and electrostatic interactions. Combined  $^1\text{H}$  NMR, DOSY, ROESY, nano-ITC and ESI-MS measurements proved that the proper choice of the anchoring groups on the upper rim of the hydrophobic cavity of the calixarene can be a powerful approach to high definition self-assembly in water, provided they match the electrostatic and steric requirements of the guest. Significant amounts of the capsule form even with relatively small host/guest ratios. Studies on the effect of the shape and the length of the dianionic guests on the capsule formation and the determination of the corresponding thermodynamic parameters are currently underway.

## 2. Thermodynamics of the internal and external guest binding of a supramolecular host in water

A combination of NMR, UV-vis and nano-ITC has been used to definitively separate and evaluate multiple guest binding to the interior (encapsulation) and exterior (ion-association) of the highly charged supramolecular host  $[\text{Ga}_4\text{L}_6]^{12-}$  ( $\text{L} = 1,5\text{-bis}(2,3\text{-dihydroxybenzamido})\text{naphthalene}$ ) in water. This host acts as chiral, nanoscale flasks for encapsulated guest catalysts or transient guest substrates and may run enzyme-like chemical transformations. The study has been carried out in collaboration with the group of Professor Kenneth N. Raymond, University of California, Berkeley, USA through a continuous exchange of graduate students and post-doc researchers.

Data obtained by each independent technique measure different components of the host-guest equilibria and only when analyzed together a complete picture of the solution thermodynamics emerges. Striking differences between the internal and external guest binding of alkylammonium cations were found. External binding is an enthalpy driven process mainly due to attractive interactions between the guests and the exterior surface of the assembly whilst encapsulation is entropy driven as a result of desolvation and release of solvent molecules from the host cavity.

This study aims to elucidate and quantify the very different internal and external host-guest interactions of the  $[\text{Ga}_4\text{L}_6]^{12-}$  supramolecular assembly that are a consequence of its high charge and hydrophilic outer space contrasted by its hydrophobic inner space.

### Collaborations and Research Grants

- Prof. Kenneth N. Raymond (University of California, Berkeley, CA, USA)
- Prof. Richard A. Bartsch (Texas Tech University, Lubbock, TX, USA)
- Prof. Roger G. Harrison, Prof. John D. Lamb (Brigham Young University, Provo, UT, USA)
- Istituto di Biostrutture e Bioimmagini, CNR, Sezione di Catania
- PRIN (PRIN 2008F5A3AF\_005)
- Meridionale Impianti (2006, 2008, 2009)

### Selected Publications

C. SGARLATA, J. S. MUGRIDGE, M. D. PLUTH, B. E. F. TIEDEMANN, V. ZITO, G. ARENA, K. N. RAYMOND (2010). External and Internal Guest Binding of a Highly Charged Supramolecular Host in Water: Deconvoluting the Very Different Thermodynamics. *JOURNAL OF THE AMERICAN CHEMICAL SOCIETY*, vol. 132; p. 1005-1009.

C. BONACCORSO, A. CIADAMIDARO, C. SGARLATA, D. SCIOTTO, G. ARENA (2010). Guest-induced capsule formation based on concerted interactions in water at neutral pH. *CHEMICAL COMMUNICATION*, vol. 46; p. 7139-7141.

C. SGARLATA, C. BONACCORSO, F. G. GULINO, V. ZITO, G. ARENA, D. SCIOTTO (2009). Stereochemistry and thermodynamics of the inclusion of aliphatic and aromatic anionic guests in a tetracationic calix[4]arene in acidic and neutral aqueous solutions. *NEW JOURNAL OF CHEMISTRY*, vol. 33; p. 991-997.

C. SGARLATA, C. BONACCORSO, F. G. GULINO, V. ZITO, G. ARENA, D. SCIOTTO (2009). Inclusion of aromatic and aliphatic anions into a cationic water-soluble calix[4]arene at different pH values. *TETRAHEDRON LETTERS*, vol. 50; p. 1610-1613.

C. SGARLATA, G. ARENA, E. LONGO, D. ZHANG, Y. YANG, R. A. BARTSCH (2008). Heavy metal separation with polymer inclusion membranes. *JOURNAL OF MEMBRANE SCIENCE*, vol. 323; p. 444-451.