

# Poster Presentations

## [MS38-P03] Structural Insight into Two-Step Complexation of Adrenaline Guest with Cucurbituril Host.

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Cucurbiturils are highly-symmetric pumpkin-shaped macrocyclic receptors with an exceptional host-guest complexation behaviour towards organic and inorganic cations. Cucurbiturils possess two distinctive binding sites: the hydrophobic cavity that promotes the inclusion of organic residues through hydrophobic effect and carbonyl-rimmed portals that favour binding of cationic sites of organic guests or inorganic cations through ion-dipole interactions. In the course of our investigation of the potential of cucurbiturils to act as co-crystal formers towards active pharmaceutical ingredients, we discovered that it is possible to crystallize the host-guest intermediate that precludes the formation of inclusion complex between cucurbit[6]uril and protonated adrenaline. [1] In the intermediate association complex the protonated adrenaline interacts with cucurbit[6]uril through one portal only without entering of its methyl group into the host cavity which is occupied by three water molecules. The protonated amino group of adrenaline is in close proximity to carbonyl oxygen atoms of the host portal suitable for ion-dipole and hydrogen bonding interactions. The methyl group of the guest perches above the portal and is unfavorably exposed to portal carbonyl oxygen atoms and water molecules in the crystal lattice. Evidently, the ion-dipole and hydrogen bonding anchoring of the protonated amino group provides enough

stabilization to overcome the penalty of one methyl group exposure to the aqueous phase. Surprisingly, the crystallization of the kinetic intermediate does not act as 'dead-end' in the host-guest complexation process. The needle-like crystals of the intermediate exclusion complex left in mother solution slowly dissolve and recrystallize to form prismatic crystals of the thermodynamically stable inclusion complex. The main driving force for the inclusion of adrenaline methyl group is the hydrophobic effect due to removal of three high-energy water molecules from the host cavity. The isolation and structural characterization of both complexes enabled to reproduce the each step of the inclusion process, thus, to ultimately confirm the predicted two-step complexation model for cucurbit[6]uril host-guest systems with organic cations. [2]

[1] Danylyuk, O., Fedin, V. P., Sashuk, V. (2013). *Chem. Commun.* **49**, 1859-1861.

[2] Marquez, C., Nau, W. M. (2001). *Angew. Chem. Int. Ed.* **40**, 3155-3160.

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