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(Self) assembled news: *recent highlights from the supramolecular chemistry literature (Quarter 2, 2023)*

Hiral A. Kotak[a], Nicholas G. White[b] and Cally J. E. Haynes[a]

[a]Department of Chemistry, University College London, London, UK; [b]Research School of Chemistry, Australian National University, Canberra, ACT, Australia

Allosteric regulation with water as an effector in a protein-mimicking cage

Allostery – the control of macromolecule conformation and function by the remote binding to an effector molecule – allows numerous biological machines to carry out their roles in the body. Writing in *Chem*, Cheng-Yong Su and colleagues have described a metallo-amine cage (MOC-68, Figure 1) that exhibits intricate, proton-driven allostery underpinned by water binding and release [1], with implications in controlled guest binding, transport and release.

MOC-68 (Figure 1) comprises flexible, amine corners and face-capping metalloligands containing imidazole linkers; thus, numerous acid/base sites are accessible. When protonated, these sites bind water molecules which rigidify the cage; when deprotonated, water is released and the conformational flexibility of the cage increases.

The initial state can only bind guests on the exterior of the cage (exo-binding); however, pH-driven allosteric switching provides a larger cavity, allowing endo-binding. Interestingly, the corners of the cage can be capped with CB[10], yielding a rare 'ring-on-cage' system. This locks the conformation of the cage, can trigger the release of endo-bound guests, and prevents allosteric switching and endo-guest binding.

Another consequence of the changes in protonation state is that the charge of the cage can be drastically altered by changing the pH. This affects the polarity of the system and means that the cage can reversibly phase transfer from polar to non-polar solvent mixtures.

Synthetic hosts make materials smarter

Smart materials that respond to stimuli are a hot topic of research with potential applications in the chemical and medical industries. A minireview from Niveen Khashab and co-workers describes recent advances in integrating the principles of host-guest chemistry into the design of smart materials [2]. They describe how molecular recognition can be used to (i) drive the assembly of materials such as hydrogels and polymer membranes; (ii) achieve controlled guest uptake and release for applications such as adsorption and separation; and (iii) induce macroscopic property changes upon guest complexation, such as luminescence changes, photo-triggered self-healing/adhesion and actuation. Ultimately, these technologies mean that we can translate molecular-scale events to macroscopic functions.

The focus on the role of the host-guest recognition within materials fabrication and function means that this minireview can be great inspiration for anyone looking to apply fundamental supramolecular concepts in new, applied contexts. A detailed discussion of the challenges that need to be met in order to realise industrial translation is also a valuable inclusion, highlighting key topics and productive avenues for future research.

Tackling Alzheimer's with supramolecular vesicles

Alzheimer's disease (AD) is the most common type of dementia, affecting over 55 million people worldwide. Currently, there is no treatment or cure for this disease. In recent work, Liu and co-workers are aiming to tackle AD by using host-guest chemistry to form a supramolecular vesicle with two therapeutically useful functions.

The vesicles are composed of carboxylated pillar[5]arenes that can a) bind the long-chain lipophile dodecyl pyridinium chloride, making the complexes themselves amphiphilic; and b) sequester free Zn(II) ions that accumulate within the extracellular space in the brain. Free Zn(II) ions promote the aggregation of fibrils and production of reactive oxygen species – both of which induce neuroinflammation in the brain and worsening of AD.

Liu and co-workers found they were able to load the vesicle with a drug called resveratrol, which switches on

CONTACT Nicholas G. White nicholas.white@anu.edu.au Research School of Chemistry, Australian National University, Canberra, ACT, Australia; Cally J. E. Haynes cally.haynes@ucl.ac.uk Department of Chemistry, University College London, London, UK

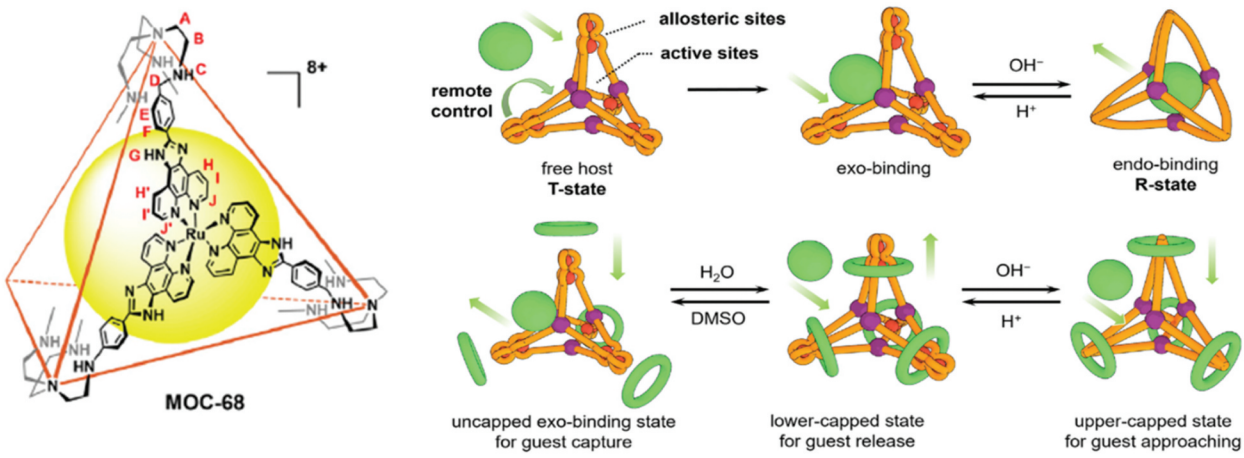

Figure 1. MOC-68, reported by Su and colleagues to display proton-driven allosteric control of cage conformation and guest binding. Reprinted from Chem, Y.-L. Lu, X.-D. Zhang, Y.-H. Qin, J.-Q. Song, Y.-H. Huang, C.-H. Liu, J.-J. Chen, H.-S. Xu, M. Pan, C.-Y. Su., a robust protein-mimicking metallo-amine cage showing proton-driven allostery with water as the effector, 2023, DOI: 10.1016/j.Chempr.2023.03.019, with permission from Elsevier.

an anti-inflammatory pathway in the brain. After loading and dosing the vesicle within mouse models, they found that fibril aggregation had decreased and that the neuroinflammation pathway in the brain had not been turned on. Most importantly, they were able to rescue memory deficits in mouse models [3].

In brief

Original catenane (re)synthesized

In 1960, Wasserman reported the first synthesis of a catenane [4]. This catenane was prepared using a statistical synthesis in very low yield, and subsequent papers have disputed whether this catenane was ever formed at all [5]. Now, Leigh and co-workers report a painstaking and meticulous reinvestigation of this catenane synthesis using modern organic chemistry and modern characterisation techniques [6]. They were able to reproduce Wasserman's synthesis and purification protocols and conclusively identify catenated product. Derivation with a dansyl sulphonate group allowed the isolation and characterisation of 0.7 mg of a mixture of catenanes from a gram-scale reaction!

Metal organic cage stabilises sarin

A team led by Ward, Dennison and Tuck reports the unusual stabilisation of the chemical warfare agent sarin (and the related simulant *O,O'*-diisopropyl fluorophosphate) by highly charged *octa*-nuclear $M_8L_{12}^{16+}$ cube-shaped cages [7]. Previous work within the Ward group has shown that this family of cages typically (but not always) accelerates the rate of hydrolysis of guests because the high cationic charge of the cage leads to build-up of hydroxide close to the guest. In this detailed study, the cage actually protects the warfare agent. While not the intended result, the authors suggest that this may prove useful in the preservation of forensic samples.

Chloride nanochannels kill cancer

Talukdar and co-workers report readily prepared benzohydrazide derivatives that self-assemble into nanotubes through intermolecular hydrogen bonding and stacking interactions [8]. The resulting nanotubes have hydrophobic exteriors and hydrophilic cavities. They can assemble in vesicles and cell membranes and act as efficient chloride channels. The authors show that chloride transport mediated by the nanotube induced apoptosis in a human breast cancer cell-line but was relatively non-toxic in non-cancerous cells.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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