PROGRAM & ABSTRACTS

Oral presentations

Local Organizing Committee

Co-chairs Calix 2023
Yoram Cohen
Tel Aviv University

Arkadi Vigalok
Tel Aviv University

Co-chairs ICCB 2023
Ehud Keinan
Technion-Israel Institute of Technology

Ofer Reany
The Open University of Israel

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Sunday, July 16, 2023

16:00 - 18:00 Registration & Reception ***Foyer***

18:00 - 20:00 Session S1 — Israel 2

Chair: Bruce Gibb, Tulane University, USA

18:00 *C. David Gutsche Award Lecture*
Cavitand hosts and their guests in water
Julius Rebek[1], Yang Yu[1]
Department of Chemistry, Shanghai University, Shanghai, China

19:00 *Special Guest Lecture*
Molecular weaving of covalent organic frameworks
Omar Yaghi
Chemistry, UC Berkeley, Berkeley, Ca, USA

Monday, July 17, 2023

08:00 - 18:00 Registration ***Foyer***

09:00 - 09:30 Opening Session — Israel 2

Welcome Addresses

09:30 - 11:00 Session M1 — Israel 2

Chair: Yoram Cohen, Tel Aviv University, Israel

09:30 *Plenary*
Spatiotemporal control of chemical reactions using sound
Kimoon Kim
Department of Chemistry, Pohang University of Science and Technology, Pohang, South Korea

10:00 *Plenary*
Cavitand-based auxetic polymers
Enrico Dalcanale
Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Parma, Italy

10:30 *Invited*
Cucurbiturils and viologens: a good match toward molecular machines in water
David Bardelang
Radical Chemistry Institute, Aix-Marseille University, Marseille, France

11:00 - 11:30 Coffee Break ***Foyer***

Monday, July 17, 2023 (Cont'd)

11:30 - 13:00 Session M2 — Israel 2

Chair: Ehud Keinan, Technion-Israel Institute of Technology, Israel

11:30 *Invited*
Azacalixarene: an ever-growing macrocycle
Olivier Siri
CINaM, UMR 7325 CNRS, Aix-Marseille University, Marseille, France

12:00 *Invited*
Supramolecular synthons in protein – macrocycle assembly
Ronan Flood[1], Niamh Mockler[1], Maura Malińska[2], **Peter Crowley**[1]
[1]*School of Biological & Chemical Science, University of Galway, Galway, Ireland*
[2]*Faculty of Chemistry, University of Warsaw, Warsaw, Poland*

12:30 *Invited*
Calixarenes at the chemistry-biology interface
Peter Cragg[1], Georgia Whitehand[1], Kushal Sharma[1], Khayzuran Iqbal[1], Marcus Allen[1]
School of Applied Sciences, University of Brighton, Brighton, UK

13:00 - 14:30 Lunch — ***Dining Room***

14:30 - 16:00 Session M3 — Israel 2

Chair: Arkadi Vigalok, Tel Aviv University, Israel

14:30 *Invited*
Exploring host-guest interactions with GEST NMR
Invited
Liat Avram[1]
Chemical Research Support, The Weizmann Institute of Science, Rehovot, Israel

15:00 *Invited*
Chemical communication in small supramolecular libraries of cucurbituril complexes
Uwe Pischel
CIQSO – Center for Research in Sustainable Chemistry, University of Huelva, Huelva, Spain

15:30 *Contributed*
Dual-action molecular recognition in a crystalline macrocycle–protein cage
Ngong Beyeh
Chemistry, Oakland University, Rochester, Michigan, USA

15:45 *Contributed*
Programming cucurbituril host-guest systems for imaging life
Sarit Sekhar Agasti
New Chemistry Unit & Chemistry and Physics of Materials Unit, Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore, India

16:00 - 16:30 Coffee Break — ***Foyer***

Monday, July 17, 2023 (Cont'd)

16:30 - 17:50 Session M4 Israel 2

Chair: Liat Avram, Weizmann Institute of Science, Israel

16:30 *Contributed*

Cucurbit[8]uril-assisted transient nanozymes

Debapratim Das[1], Saurav Das[1]
Chemistry, Indian Institute of Information Technology Guwahati, Guwahati, Assam, India

16:45 *Plenary*

The power of yocto-liter inner-spaces to affect reactions

Bruce Gibb
Chemistry, Tulane University, New Orleans, Louisiana, USA

17:15 *Flash talk*

Active role of alkali cations in the kinetics of the base-promoted berberrubine release from cucurbit[7]uril

Zsombor Miskolczy[1], Mónika Megyesi[1], **László Biczók**[1]
Institute of Materials and Environmental Chemistry, Research Centre for Natural Sciences, Budapest, Hungary

17:22 *Flash talk*

Novel fluorinated bambusurils: synthesis, anion binding, and transport properties

Matúš Chvojka[1,2], Hennie Valkenier[2], Vladimír Šindelář[1]
[1]*Department of Chemistry and RECETOX, Masaryk University, Brno, Czech Republic*
[2]*École Polytechnique - Engineering of Molecular Nanosystems, Université libre de Bruxelles, Brussels, Belgium*

17:29 *Flash talk*

Anion-recognition directed supramolecular catalysis

Qi-Qiang Wang
CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing, China

17:36 *Flash talk*

Catalytic enantioselective synthesis of inherently chiral calixarenes

Tong Shuo
Department of Chemistry, Tsinghua University, Beijing, China

17:43 *Flash talk*

Symmetry breaking during self-assembly of racemic mixture of organic cages

Shaodong Zhang
School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, China

Tuesday, July 18, 2023

08:30 - 18:00 Registration — *Foyer*

09:00 - 11:00 Session T1 — Israel 2

Chair: Enrico Dalcanale, University of Parma, Italy

09:00 *Plenary*
Calipyrrole-based materials (and friends)
Jonathan Sessler
Chemistry, The University of Texas at Austin, Austin, Texas, USA

09:30 *Invited*
New macrocyclic arenes for molecular recognition and assembly
Chuan-Feng Chen[1]
CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing, China

10:00 *Invited*
Supramolecular approaches to the detoxification of nerve agents
Stefan Kubik[1]
Department of Chemistry – Organic Chemistry, RPTU Kaiserslautern-Landau, Kaiserslautern, Germany

10:30 *Invited*
Aromaticity - a twisted tale
Ori Gidron[1]
Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem, Israel

11:00 - 11:30 Coffee Break — *Foyer*

11:30 - 13:00 Session T2 — Israel 2

Chair: David Bardelang, Aix-Marseille University, France

11:30 *Invited*
Superselectivity and recruitment as organizing principles in bio-sensing and self-assembly
Jurriaan Huskens
Department of Molecules & Materials, MESA+ Institute, University of Twente, Enschede, Netherlands

12:00 *Invited*
New insights into the chemistry of thiacalixarenes and related systems
Pavel Lhotak
Department of Organic Chemistry, University of Chemistry and Technology Prague, Prague 6, Czech Republic

12:30 *Invited*
Functional cucurbituril-DNA conjugates
Janarthanan Jayawickramarajah[1], Dilanka V. D. Walpita Kankanamalage[1]
Chemistry, Tulane University, New Orleans, Louisiana, USA

13:00 - 14:30 Lunch — *Dining Room*

Tuesday, July 18, 2023 (Cont'd)

14:30 - 16:00 Session T3 — Israel 2

Chair: Stefan Kubik, RPTU Kaiserslautern-Landau, Germany

14:30 *Invited*

Synthesis and applications of bambusuril derivatives

Vladimir Sindelar

Department of Chemistry and RECETOX, Masaryk University, Brno, Czech Republic

15:00 *Invited*

How to capture an atom: Insights from xenon host-guest chemistry

Ivan Dmochowski[1], Zhuangyu Zhao[1], Nathan Rudman[1], Yannan Lin[1]

Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania, USA

15:30 *Contributed*

Strategies to fine control the conformational properties of calix[4]arene derivatives

Laura Baldini

Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Italy

15:45 *Contributed*

Chiroptical properties and multifold arylation of pillar[n]arenes

Kenichi Kato[1], Tomoya Kaneda[1], Yuta Kurakake[1], Shunsuke Ohtani[1], Tomoki Ogoshi[1,2]

[1]*Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Kyoto, Japan*

[2]*WPI Nano Life Science Institute, Kanazawa University, Kanazawa, Japan*

16:00 - 16:30 Coffee Break — Foyer

Tuesday, July 18, 2023 (Cont'd)

16:30 - 17:45 Session T4 — Israel 2

Chair: Ofer Reany, The Open University of Israel, Israel

16:30 *Contributed*

Bromination of calix[4]arenes: breaking (bad) symmetry?

Gareth Arnott

Chemistry and Polymer Science, Stellenbosch University, Stellenbosch, South Africa

16:45 *Plenary*

Pillar[6]MaxQ: synthesis, molecular recognition, and in vivo sequestration

Lyle Isaacs[1]

Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland, USA

17:15 *Flash talk*

Substrate-controlled and template-assisted mechanochemical synthesis of thio-hemicucurbiturils

Raghuram Gujjarappa[1,2], Ehud Keinan[2], Ofer Reany[3]

[1]*Department of Natural Sciences, The Open University of Israel, Ra'anana, Israel*

[2]*The Schulich Faculty of Chemistry, Technion-Israel Institute of Technology, Haifa, Israel*

[3]*Department of Natural Sciences, The Open University of Israel, Ra'anana, Israel*

17:22 *Flash talk*

Water-soluble pseudo-rotaxane with cucurbit[7]uril shuttling along a "dynamic" axle in response pH and light simuli

André Seco[1], Nathan Mcclenaghan[2], A. Jorge Parola[1], Nuno Basílio[1]

[1]*Department of Chemistry, NOVA School of Science and Technology, Lisbon, Portugal*

[2]*Institut des Sciences Moléculaires, CNRS/Univ. Bordeaux, Talence, France*

17:29 *Flash talk*

Colorimetric differentiation of solid-state supramolecular complexes of coumarin and bimane fluorophores

Vincent Joseph[1], Nathaniel Roy[1], Jenisha John[1], Flavio Grynszpan[1], **Mindy Levine**[1]

Department of Chemical Sciences, Ariel University, Ariel, Israel

17:36 *Flash talk*

Electron deficient arms of calix[4] basket for capturing toxic fluoride ion

Anita Nehra[1,2], Sateesh Bandaru[3], Rakesh K Sharma[1]

[1]*Chemistry, Indian Institute of Technology Jodhpur, Jodhpur, Rajasthan, India*

[2]*Chemistry, JECRC University, Jaipur, Rajasthan, India*

[3]*Computational Material Science Division, Hangzhou Dianzi University, Hangzhou, Zhejiang, China*

18:00 - 20:00 POSTER SESSION — Foyer

Wednesday, July 19, 2023

08:00 – 13:00 Registration ***Foyer***

09:00 – 11:00 Session W1 Israel 2

Chair: Janarthanan Jayawickramarajah, Tulane University, USA

09:00 *Plenary*
Supramolecular catalysis with macrocycles
Werner Nau
School of Science, Constructor University, Bremen, Germany

09:30 *Invited*
CB[n]–guest hydrogels with tunable network dynamics
Matthew Webber
Chemical & Biomolecular Engineering, University of Notre Dame, Notre Dame, Indiana, USA

10:00 *Invited*
Heteroditopic calix[6]arene-based intervowen and interlocked molecular devices
Andrea Secchi
Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Italy

10:30 *Invited*
Exploring the potential of hemicucurbiturils: Diverse functionality through simple modifications
Riina Aav
Department of Chemistry and Biotechnology, Tallinn University of Technology, Tallinn, Estonia

11:00 – 11:30 Coffee Break ***Foyer***

11:30 – 12:00 Session W2 Israel 2

Chair: Ivan Dmochowski, University of Pennsylvania, USA

11:30 *Plenary*
Bacteria recognition and inhibition by calixarene derivatives
Alessandro Casnati
Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Italy

12:00 – 13:00 Board Meeting Israel 2

13:00-13:15 Lunch Box ***Conventions Center, ground floor***

13:00 – 19:00 Conference Tour to Jerusalem (Optional)

Assemble for departure in the Hotel Lobby, ground floor.

Thursday, July 20, 2023

08:30 – 18:00 Registration — *Foyer*

09:00 - 11:00 Session TH1 — Israel 2

Chair: Jonathan Sessler, The University of Texas at Austin, USA

09:00 *Plenary*

Mediation of 1,3-dipolar cycloaddition reaction in the cavity of a [4 + 2] octaimine calix[4]pyrrole capsule

Pablo Ballester[1,2]
ICREA, Catalan Institute of Research and Advanced Studies, Barcelona, Spain
Institute of Chemical Research of Catalonia (ICIQ), The Barcelona Institute of Science and Technology (BIST), Tarragona, Spain

09:30 *Invited*

Supramolecular controlled release of proteins

Adam Urbach
Department of Chemistry, Trinity University, San Antonio, TX, USA

10:00 *Invited*

Synthesis, conformational properties, and molecular recognition abilities of prismarenes

Carmine Gaeta
Department of Chemistry and Biology "A. Zambelli", University of Salerno, Salerno, Italy

10:30 *Contributed*

Embedding metals centers in deep cavitands - a step closer to natural metalloenzyme

Yuri Tulchinsky
Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem, Israel

10:45 *Contributed*

Presice self-assembly of calix[4]resorcinarene-based cages via complementary ligand pairing

Yi-Tsu Chan
Chemistry, National Taiwan University, Taipei, Taiwan

11:00 - 11:30 Coffee Break — *Foyer*

Thursday, July 20, 2023 (Cont'd)

11:30 - 13:00 Session TH2 — Israel 2

Chair: Vladimir Sindelar, Masaryk University, Czech Republic

11:30 *Invited*

Cucurbit[8]uril-secured platinum dimers and cation-secured cucurbit[7]uril trimers

Eric Masson[1]

Chemistry and Biochemistry, Ohio University, Athens, Ohio, USA

12:00 *Invited*

Supramolecular catalysis in confined space exploiting self-assembling capsules

Carmen Talotta[1]

Dipartimento di Chimica E Biologia "A. Zambelli", Univesità Di Salerno, Fisciano, Salerno, Italy

12:30 *Contributed*

Second sphere interactions of solvate molecules with lanthanide complexes supported by hybrid calix[4]arene/Schiff-base ligands

Anne Mehnert[1], Lennart Günzel[1], Martin Börner[1], **Berthold Kersting**[1], Ettore Bartalucci[2], Thomas Wiegand[2,3], Alexander A. Malär[3], Beat H. Meier[3], Julius B. Kleine Büning[4], Stefan Grimme[4], Maik Icker[5]

[1]*Institute of Inorganic Chemistry, Leipzig University, Leipzig, Germany*

[2]*RWTH Aachen University, Institute of Technical and Macromolecular Chemistry, Aachen, Germany*

[3]*Physical Chemistry, ETH Zürich, Zürich, Switzerland*

[4]*Clausius Institute of Physical and Theoretical Chemistry, University of Bonn, Bonn, Germany*

[5]*Institute of Analytic Chemistry, Leipzig University, Leipzig, Germany*

12:45 *Contributed*

Noncovalent modulation of chemoselectivity in the gas phase by cucurbit[7]uril

Elina Kalenius

Department of Chemistry, University of Jyväskylä, Jyväskylä, Finland

13:00 - 14:30 Lunch Break — ***Dining Room***

Thursday, July 20, 2023 (Cont'd)

14:30 - 16:00 Session TH3 — Israel 2

Chair: Alessandro Casnati, University of Parma, Italy

14:30 *Plenary*
Supramolecular hosts as enzyme mimics
F. Dean Toste
Department of Chemistry, University of California, Berkeley, California, USA

15:00 *Invited*
Supramolecular polymers formed by molecular recognition of calixarenes
Takeharu Haino[1,2]
Department of Chemistry, Graduate School of Advanced Science and Engineering, Hiroshima University, HIgashi-HIroshima, Hiroshima, Japan
International Institute for Sustainability with Knotted Chiral Meta Matter (SKCM2), Hiroshima University, Higashi-Hiroshima, Hiroshima, Japan

15:30 *Invited*
NMR exchange dynamics studies of metal-caped cyclodextrins uncover unprecedented host-guest interactions in water
Amnon Bar-Shir[1]
Molecular Chemistry and Materials Science, Weizmann Institute of Science, Rehovot, Israel

16:00 - 16:30 Coffee Break — ***Foyer***

16:30 - 17:45 Session TH4 — Israel 2

Chair: Mei-Xiang Wang, Tsinghua University, China

16:30 *Contributed*
The dynamic behavior of hexameric resorcin[4]arene capsules: insights from NMR spectroscopy and molecular simulations
David Poole[1,2], Simon Mathew[1], Joost Reek[1]
[1]*van 't Hoff Institute of Molecular Sciences, Universiteit van Amsterdam, Amsterdam, Netherlands*
[2]*Amsterdam Institute of Molecular and Life Sciences, Vrije Universiteit Amsterdam, Amsterdam, Netherlands*

16:45 *Invited*
The host-guest properties of tiara[n]uril
Anthony Day[1], Satyavisal Pen[1], Islam Marae[1], Asmaa Sakr[1]
School of Science Canberra Campus, University of New South Wales, Canberra, ACT, Australia

17:15 *Plenary*
Redox-active cavities and metal ions: a promising combination inspired by Nature
Olivia Reinaud[1]
Lab. Chimie Et Biochimie - UMR 8601, Univ. Paris Cité, Paris, France

19:30 - 21:30 Conference Dinner at Mishkenot Ruth Daniel, Old Jaffa (Optional)

Address: 47 Jerusalem Boulevard, Tel-Aviv Yafo
Walking distance from the Dan Panorama Hotel (approx. 25 minutes)

Friday, July 21, 2023

08:30 - 13:00 Registration *Foyer*

09:00 - 11:00 Session F1 Israel 2

Chair: Eric Masson, Ohio University, USA

09:00 *Plenary*

From calixarenes and heteracalixaromatics to functionalized zigzag molecular belts and molecular recognition

Mei-Xiang Wang[1]

Chemistry, Tsinghua University, Beijing, China

09:30 *Contributed*

Artificial anion channels

De-Xian Wang[1]

Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing, China

09:45 *Contributed*

Design and synthesis of cyclic nucleobase as a new scaffold for molecular recognition and ion separation

Xiaodong Shi

Department of Chemistry, University of South Florida, Tampa, Florida, USA

10:00 *Invited*

Helix-based transmembrane nanochannels with selective transport activities

Junqiu Liu

College of Material, Chemistry and Chemical Engineering, Hangzhou Normal University, Hangzhou, Zhejiang, China

10:30 *Invited*

Liposome-enhanced suprabiomolecular sensor systems

Andreas Hennig

Center for Cellular Nanoanalytics (CellNanOs) and Department of Biology and Chemistry, Universität Osnabrück, Osnabrück, Germany

11:00 - 11:30 Coffee Break *Foyer*

Friday, July 21, 2023 (Cont'd)

11:30 - 12:30 Session F2 Israel 2

Chair: Peter Crowley, University of Galway, Ireland

11:30 *Invited*

Photoresponsive dithienylethene host-guest complexes with cucurbit[8]uril

Nuno Basílio[1], Miriam Colaço[1], Patrícia Máximo[1], Uwe Pischel[2], A. Jorge Parola[1]

[1]*Laboratório Associado para a Química Verde (LAQV) - Rede de Química e Tecnologia (REQUIMTE) - Departamento de Química, Faculdade de Ciências e Tecnologia - Universidade NOVA de Lisboa, Caparica, Portugal*

[2]*CIQSO – Centre for Research in Sustainable Chemistry and Department of Chemistry, University of Huelva, Huelva, Spain*

12:00 *Plenary*

Advancing supramolecular sensing strategies: cucurbit[n]uril macrocycles for bioactive small molecule detection in biofluids

Frank Biedermann

Institute of Nanotechnology, Karlsruhe Institute of Technology, Karlsruhe, Germany

12:30 - 13:00 Closing Remarks Israel 2

Abstracts

Session S1 (Sunday, July 16, 2023 18:00)

C. David Gutsche Award Lecture
Cavitand hosts and their guests in water

Julius Rebek[1], Yang Yu[1]
Department of Chemistry, Shanghai University, Shanghai, China

Cavitands are deep, open-ended containers built on a macrocyclic platform that largely surround their small molecule targets and confine their motions. Water-soluble cavitands use hydrophobic forces to arrange their guests in unusual conformations that promote otherwise difficult chemical processes. This lecture reports recent applications involving cavitands as chaperones for macrocyclizations and separations of their guest molecules.

Session S1 (Sunday, July 16, 2023 18:00)

Special Guest Lecture
Molecular weaving of covalent organic frameworks

Omar Yaghi[1]
Chemistry, UC Berkeley, Berkeley, Ca, USA

The ability to combine the strong bond approach of reticular chemistry with the mechanical bond results in molecular weaving. This presentation will outline the strategies for carrying out molecular weaving using building blocks of covalent organic framework. I will show how this is a vast chemical space in which robustness and porosity are combined with flexibility to yield materials of exceptional resiliency and mechanical properties. The reaction chemistry and crystallization methodologies for producing woven structures in which threads are interlaced, and rings and polyhedra are interlocked will be discussed. The inclusion chemistry and dynamics in these systems will also be presented.

Plenary

Spatiotemporal control of chemical reactions using sound

Kimoon Kim[1]
Department of Chemistry, Pohang University of Science and Technology, Pohang, South Korea

Patterns from out-of-equilibrium chemical networks, such as Belousov-Zhabotinsky (BZ) reaction are generally unpredictable and difficult to control in space and time, although they are reproducible over subsequent cycles. Recently, we have shown that it is possible to control spatiotemporal patterns in out-of-equilibrium chemical reactions and self-assembling systems in the presence of audible sound. Audible sound-induced liquid vibrations control the dissolution of atmospheric gases (e.g. O_2, CO_2) into a solution to generate spatiotemporal chemical patterns in the bulk of the fluid, segregating the solution into spatiotemporal domains with different redox properties or pH values. This approach also enables the organization of transiently formed supramolecular aggregates in a predictable spatiotemporal manner. This sound strategy has been extended to regulate multistep enzyme reactions, control the movement small cargos on the surface of a solution with light, and segregate oppositely chiral supramolecular polymers in space and time. Details of this work will be presented.

Plenary

Cavitand-based auxetic polymers

Enrico Dalcanale[1]
Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Parma, Italy

Auxetics are uncommon materials characterized by the counterintuitive property of lateral expansion upon longitudinal stretching, corresponding to a Negative Poisson's Ratio (NPR). The major unresolved issue in auxetics is represented by the design and synthesis of 3D isotropic auxetic materials. They can be obtained only by operating at the molecular level, since foams and related structures are discontinuous at meso and often even at the macroscale. Despite several theoretical studies, experimental evidence of 3D molecular auxeticity in synthetic organic materials is still lacking. The mainstream approaches proposed so far dealt with the mimic at the molecular level of the kinematical properties of metamaterials.

The solution reported in this lecture does not mimic metamaterials at the molecular level like reentrant honeycombs, rotating triangles or egg rack structures. Instead, it relies on a completely novel approach based on the mechanically-driven conformational expansion of a cavitand, which has the unique property to switch between two well-defined conformations: the compact vase and the extended kite. The macroscopic expression of the cavitand conformational expansion is obtained by embedding the auxetic units as crosslinker in a polymer of intrinsic microporosity (PIM). The auxetic behavior of the reported polymer is fully reversible and reproducible, in the presence of a small amount of auxetic unit.[1]

Being the cavitands uniformly distributed in the polymeric network with a random orientation, the auxetic behavior of the single cavitand unit leads to an average 3D isotropic auxetic material. The groundbreaking nature of the present work will enable to obtain intrinsic auxetic materials with tunable NPR, overcoming the current limits in the fabrication of auxetic metamaterials at the nanoscale.

This remarkable result is supported and completed by an accurate micromechanical model capable to match both the observed experimental NPR values and the kinematic behavior of the material. This model has therefore predictive value for future auxetic materials based on this conformational switch.

[1] E. Dalcanale et al. submitted to Adv. Mater.

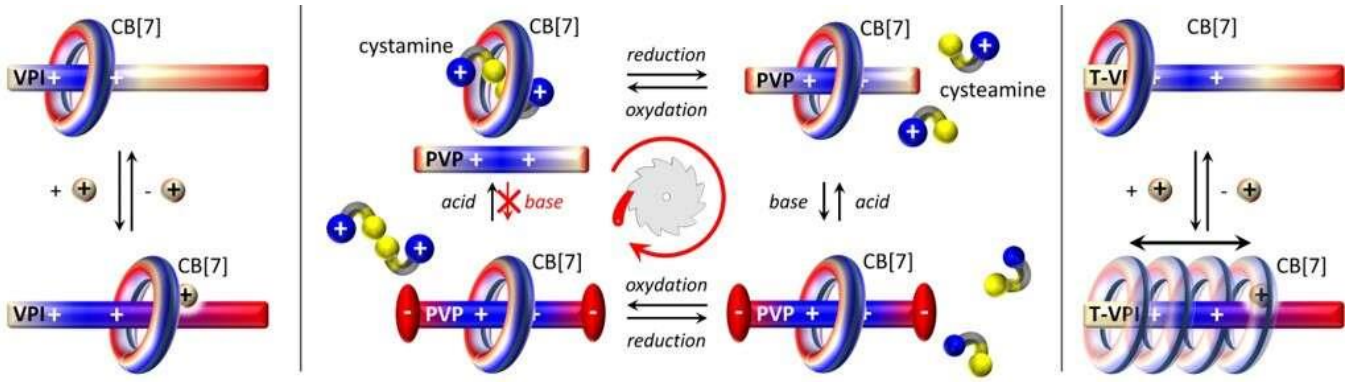
Invited

Cucurbiturils and viologens: A good match toward molecular machines in water

David Bardelang

Radical Chemistry Institute, Aix-Marseille University, Marseille, France

The construction of molecular machines remains difficult in water. For some time, cucurbiturils were found to be good host molecules for molecular switches and shuttles.[1] In 2018, we reported a silver actuated molecular shuttle in which a cucurbit[7]uril (CB[7]) ring could be reversibly translocated from a viologen to a phenylene station of a three-station (VPI) linear guest molecule.[2] By extending the structure of VPI with hydrophobic groups, we recently discovered a silver actuated molecular shuttle.[3] In parallel, considering a viologen diacid derivative, we could perform a unidirectional cycle of guest exchange in CB[7] using two stimuli following the principles of an energy ratchet.[4]



1- V. Sindelar, S. Silvi, A. E. Kaifer, *Chem. Commun.* 2006, 20, 2185-2187.

2- H. Yin, R. Rosas, D. Gigmes, O. Ouari, R. Wang, A. Kermagoret, D. Bardelang, *Org. Lett.* 2018, 20, 3187-3191.

3- A. Kriat, S. Pascal, B. Kauffmann, Y. Ferrand, D. Bergé-Lefranc, D. Gigmes, O. Siri, A. Kermagoret, D. Bardelang, *Chem. Eur. J.* 2023, e202300633.

4- X. Yang, Q. Cheng, V. Monnier, L. Charles, H. Karoui, O. Ouari, D. Gigmes, R. Wang, A. Kermagoret, D. Bardelang, *Angew. Chem. Int. Ed.* 2021, 60, 6617-6623.

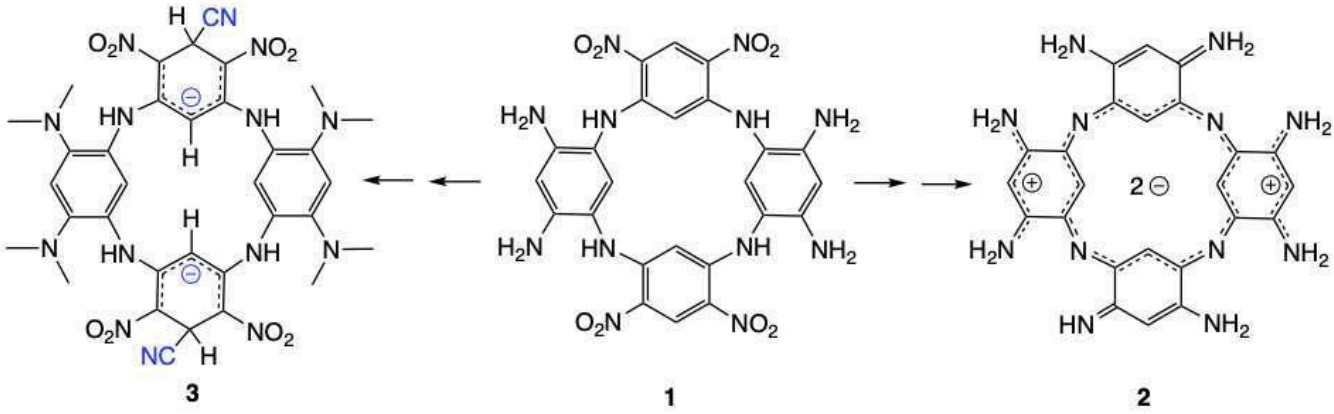
Invited

Azacalixarene: An ever-growing macrocycle

Olivier Siri[1]

CINaM, UMR 7325 CNRS, Aix-Marseille University, Marseille, France

Among the various types of heterocalixarenes, azacalixarenes are of peculiar interest since the introduction of nitrogen-bridging atoms has numerous consequences on the properties, paving the way for a wide range of applications. In this context, macrocycle of type 1 appeared recently highly versatile owing to the presence of four nitro groups and additional amino functions at the periphery and on the bridges.



The presentation will report on our results on the aminoazacalixarene 1 as a key precursor of: 1) a new class of sophisticated receptors for anion bonding,[1] 2) an unprecedented family of porphyrin analogues 2 (azacalixphyrin)[2] absorbing in the NIR-I region, and its corresponding dimer that moves the absorption properties beyond 1000 nm (NIR-II),[3] 3) an azacalix[4]arene-based covalent organic framework for waste treatment,[4] and 4) two emerging classes of charged macrocycles (including 3).[5]

The access to these derivatives and their properties will be described and discussed.

[1] a) G. Canard, O. Siri et al. Chem. Eur. J., 22, 5756 (2016). b) Z. Chen, O. Siri et al. New J. Chem., 41, 5284 (2017).

[2] Z. Chen, O. Siri Angew. Chem. Int. Ed., 52, 6250 (2013). b) L. Lavaud, O. Siri et al. Chem. Commun., 54, 12365 (2018). c) L. Breloy, O. Siri, D.-L. Versace et al. Chem. Commun., 57, 8973 (2021). e) S. Pricl, O. Siri et al. J. Porph. & Phthalo., in press (2023).

[3] L. Lavaud, O. Siri et al. Chem. Commun., 56, 896 (2020).

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Invited

Supramolecular synthons in protein – macrocycle assembly

Ronan Flood[1], Niamh Mockler[1], Maura Malińska[2], **Peter Crowley**[1]
[1]*School of Biological & Chemical Science, University of Galway, Galway, Ireland*
[2]*Faculty of Chemistry, University of Warsaw, Warsaw, Poland*

Sulfonato-calix[8]arene (**sclx$_8$**) is a versatile protein receptor leading to macrocycle-mediated assembly and framework fabrication (Figure 1).[1-3] We have reported four co-crystal forms of **sclx$_8$** and RSL, a 6-bladed β-propeller lectin.[2,4] One of these co-crystals requires acidic conditions and is a cubic assembly mediated by calix[8]arene dimers (Figure 1A). Here, we describe an expanded cubic co-crystal in which the protein nodes are connected by calix[8]arene trimers (Figure 1B). This co-crystal is dependent on an Aspartate to Asparagine mutation as well as on crystal seeding. Crystals of the sodium – **sclx$_8$** complex were obtained from conditions similar to those for the protein – **sclx$_8$** co-crystals. X-ray analysis reveals a coordination polymer of the anionic calix[8]arene and sodium cations in which the calixarene is arranged as staggered stacks, similar to those that occur in the protein co-crystal. Small angle X-ray scattering suggests **sclx$_8$** assembly in solution. Apparently, the calixarene dimer and trimer are variations of a supramolecular synthon that can direct at least two types of protein assembly.

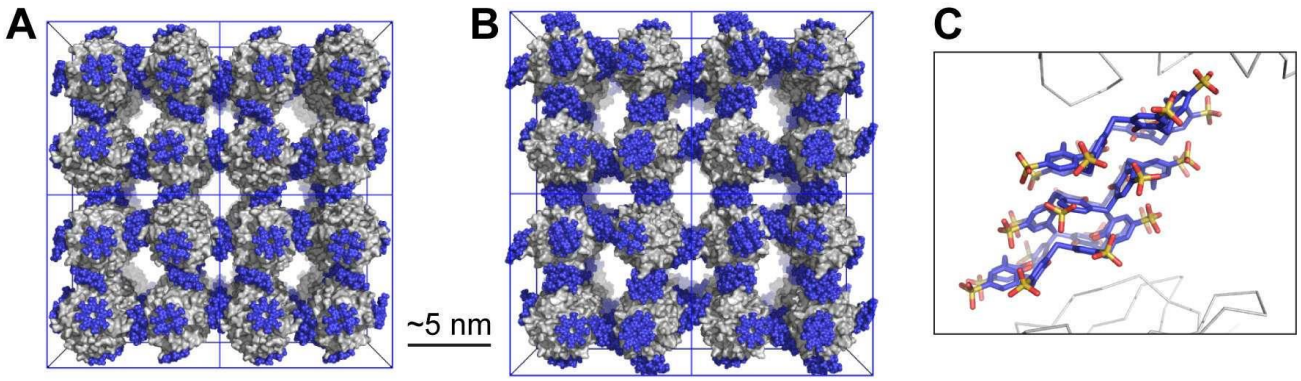

Figure 1. RSL – **sclx$_8$** cubic co-crystals with protein in grey and calixarene in blue. **(A)** The original *I*23 structure with calix[8]arene dimers[2] and **(B)** the expanded structure with calix[8]arene trimers. **(C)** Detail of the **sclx$_8$** trimer mediating protein contacts in the crystal.

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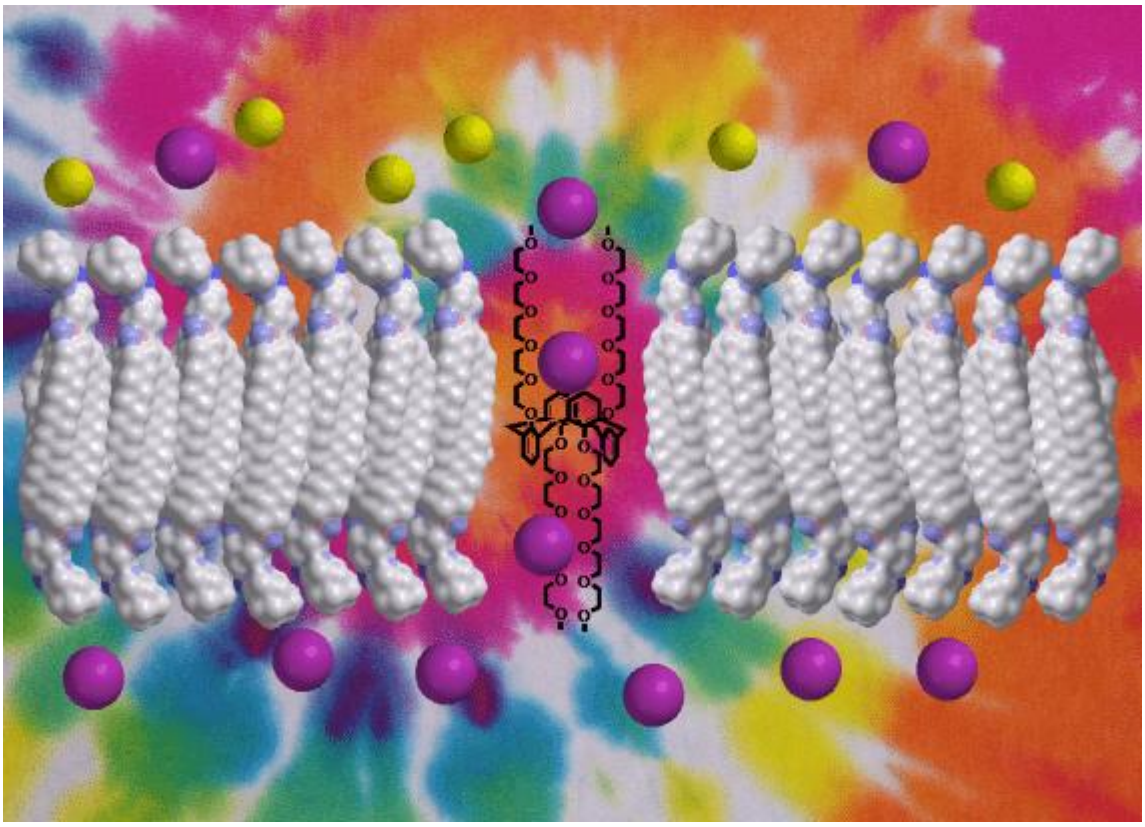
Invited

Calixarenes at the chemistry-biology interface

Peter Cragg[1], Georgia Whitehand[1], Kushal Sharma[1], Khayzuran Iqbal[1], Marcus Allen[1]
School of Applied Sciences, University of Brighton, Brighton, UK



Over the past 25 years we have been exploring the potential for calixarenes to mimic functional biological structures. Starting from the crystal structure of an oxacalix[3]arene complex which, fortuitously, resembled a protein-based cation selectivity filter[1], we developed calixarene derivatives capable of piercing and spanning phospholipid bilayers.[2,3,4] Two processes, slow ion permeation and fast calixarene-facilitated transmembrane transport, were identified and cation selectivity, specifically for Na^+, appears to be achievable. Along with work on pillar[5]arenes, this led us to investigate the potential for these compounds to act as antimicrobials.[5,6] Our current work harnesses the structural motifs of calixarene fragments which have some remarkable antifungal properties.

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Invited

Exploring host-guest interactions with GEST NMR

Liat Avram[1]

Chemical Research Support, The Weizmann Institute of Science, Rehovot, Israel

NMR is a great analytical tool commonly used to study supramolecular systems in solution. However one of its major disadvantage is poor sensitivity. We are using the GEST1 (Guest Exchange Saturation Transfer) NMR technique that allows the detection of micromolar—and even nanomolar —concentrations of a complex with only a few scans. In addition, by fitting the GEST data to computational simulations, the exchange rate of free and bound guest and the fractional occupancy of the host can be evaluated. 19F-GEST experiment was used to extract exchange rates and activation energy for fast exchanging guests in the presence of cucurbit[n]urils.2 The effect of monovalent cations on the extracted activation energy was also tested.2 This method was also used as a platform for multi-color application as was demonstrated by systems such as octa-acid3 and lanthanide-cradleSd cyclodextrin.4 To take the GEST experiment one step further, we collaborated with Or Perlman from TAU and together we built a platform based on machine learning used to detect different Lanthanide in solution. Since the GEST experiment can be easily implemented in any conventional NMR setup, this approach could expand the analytical toolbox available to study dynamic host-guest systems in solution.

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Invited

Chemical communication in small supramolecular libraries of cucurbituril complexes

Uwe Pischel

CIQSO – Center for Research in Sustainable Chemistry, University of Huelva, Huelva, Spain

Chemical communication is a fundamental process in nature. The discovery of artificial systems, that are able to mimic the essential features of chemical communication by exchange of molecular messengers, is a challenging and worthwhile task. In this context supramolecular assemblies are a preferred choice, due to the inherent chemical reversibility of their formation.

As part of our research program we became interested in the possibility to exert light-induced control of host-guest equilibria, involving cucurbituril macrocycles. This was accomplished by implying photoswitches, which show state-dependent differential supramolecular binding qualities.[1] Thus, we employed dithienylethenes which can be reversibly toggled between two isomeric forms. These were found to have significant affinity differences towards cucurbit[8]uril.[2] In combination with a second guest and the smaller cucurbit[7]uril a self-sorted four-component system resulted, whose composition was controlled by light.[3] In other examples, chemically- or light-triggered supramolecular cascades were designed, which allowed us to demonstrate a downstream flow of chemical species.[4,5] The use of guests with biological importance enabled the design of systems which mimic the characteristics of naturally occurring events, such as the phototransduction of signals in the vision process.

In the presentation I will discuss the supramolecular chemistry of the mentioned systems and analyze their application potential in the context of molecular information processing.

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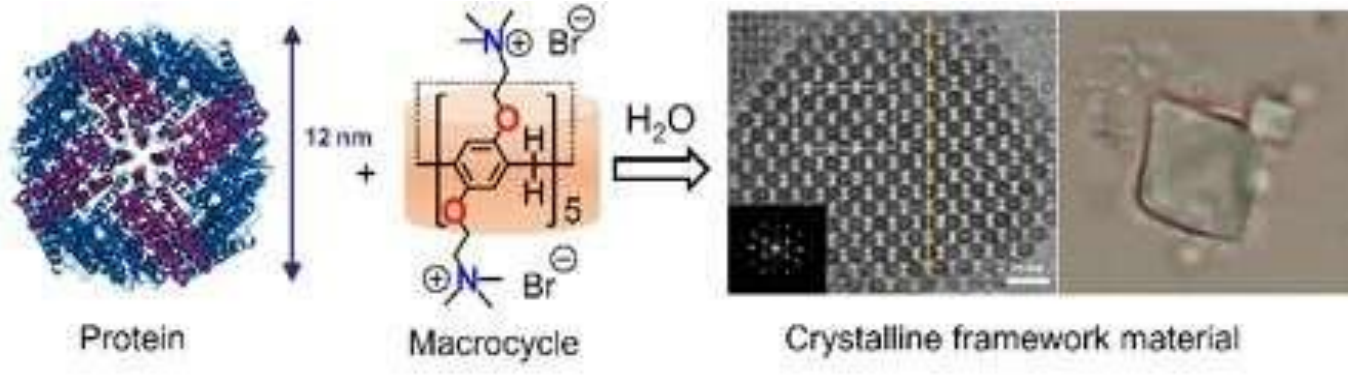
Contributed

Dual-action molecular recognition in a crystalline macrocycle–protein cage

Ngong Beyeh
Chemistry, Oakland University, Rochester, Michigan, USA

Cyclophanes are macrocyclic supramolecular hosts famous for their ability to bind atomic or molecular guests via noncovalent interactions within their well-defined cavities. Supramolecular self-assembly of biomolecules provides a powerful bottom-up strategy to build functional nanostructures and materials. Depending on the complementary features of the macrocycle and the biomolecules, the macrocycles can also function as sensors, glue to connect biopolymers, or components to help enhance and disrupt aggregates. In this talk, I will present recent results of using cavity-containing resorcinarene and pillararene macrocycles as components of amorphous and crystalline protein cages with a dual recognition for common water pollutants such as methyl orange and heavy metal ions.



Contributed

Programming cucurbituril host-guest systems for imaging life

Sarit Sekhar Agasti
New Chemistry Unit & Chemistry and Physics of Materials Unit, Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore, India

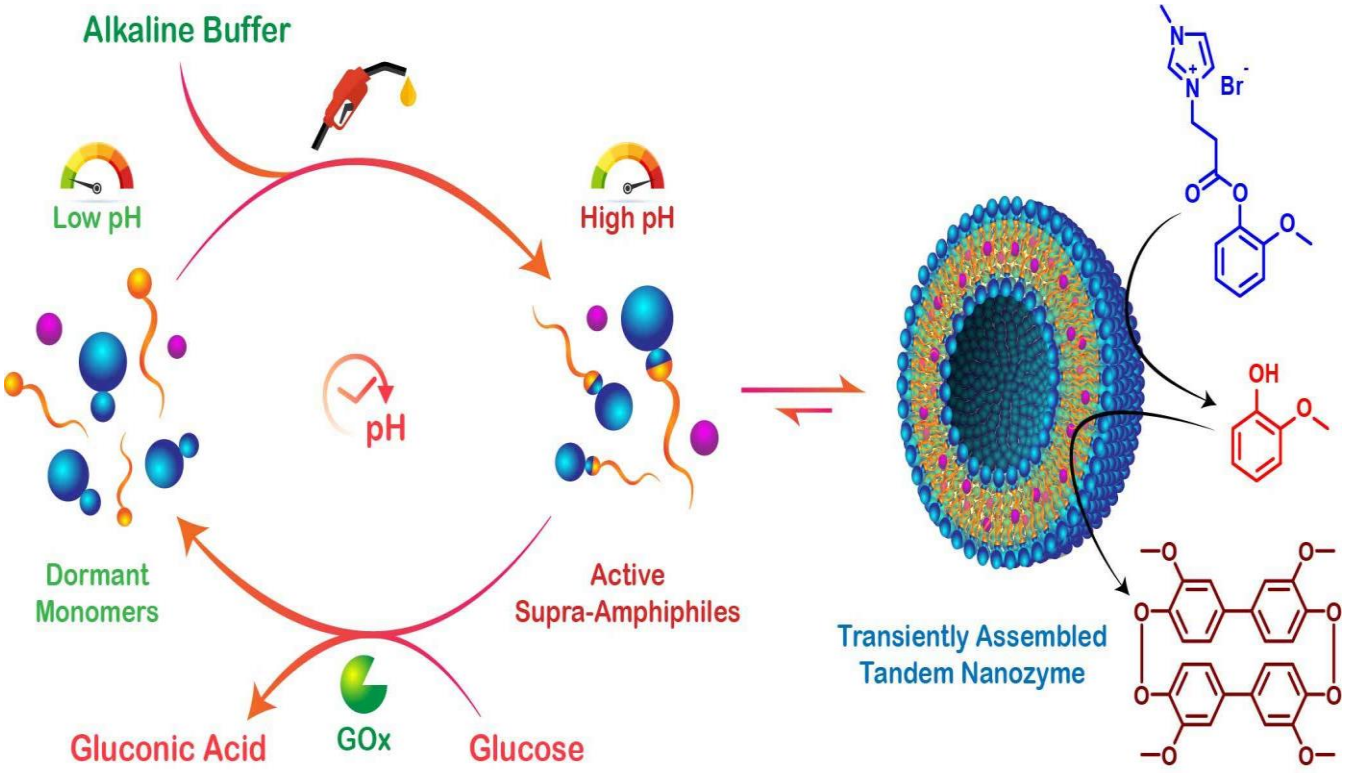
Synthetic assemblies that can be programmed to function within the complexities of cells and tissues are of great interest in biology. It drives advancements in various domains of biological research, one key area being imaging which requires specific molecular tagging or labelling. However, the application of traditional synthetic recognition motifs for programming molecular assemblies in living systems remains a challenging task due to the chemical complexities of the biological system and the lack of selectivity in conventional non-covalent interactions. In my presentation, I will discuss our recent success in programming molecular assemblies in the living system by employing a synthetic host-guest system featuring cucurbit[7]uril (CB[7]). We have shown that host-guest interaction based on CB[7] fulfills the demands of specificity and stability that are required for bioorthogonal labelling and imaging in the living cell and tissue. We further developed a simple, robust, and easy-to-implement super-resolution imaging method using highly selective, strong, yet dynamic supramolecular interaction between synthetic host-guest pairs. Unlike existing techniques that rely on externally controlled ON- and OFF-blinking of fluorophores, our technique strategically exploits transient binding between host-guest pairs to obtain autonomous single-molecule blinking. We showed that this dynamic probe with autonomous blinking property delivers an unprecedented level of imaging resolution (below 20 nm) without using sophisticated instrumentation or employing specialized experimental conditions. We subsequently extended this host-guest-based imaging approach to barcode cells via photochemical programming of their molecular recognition event. In this study, we created a distinct approach to selectively barcode cells by spatially controlling the positioning of fluorescent labels using light. Through this design, we readily achieved multiplexed barcoding of many cells in parallel by cycling the photoactivation and fluorophore anchoring steps at different cellular coordinates. This study paves the way for advanced single-cell studies by learning from their individual spatiotemporal dynamics.

Contributed

Cucurbit[8]uril-assisted transient nanozymes

Debapratim Das[1], Saurav Das[1]
Chemistry, Indian Institute of Information Technology Guwahati, Guwahati, Assam, India

A new strategy to construct Cucurbit[8]uril (CB[8])-assisted transient supramolecular peptide amphiphile (SPA) and its vesicular aggregates is developed.[1] The CB[8]-assisted supramolecular peptide amphiphile (SPA) with an imine linkage is subjected to a pH clock that operates between pH 6 to 9. Under the influence of the pH clock, the SPA and the corresponding vesicles are formed transiently. When the surface is decorated with an enzyme-mimicking peptide, the vesicles temporally work as a nanozyme.2 The concept is used to construct a self-abolishing nanozyme and for cascade catalysis.[3] The newly developed systems will pave the way to construct life-like systems in due course of time.



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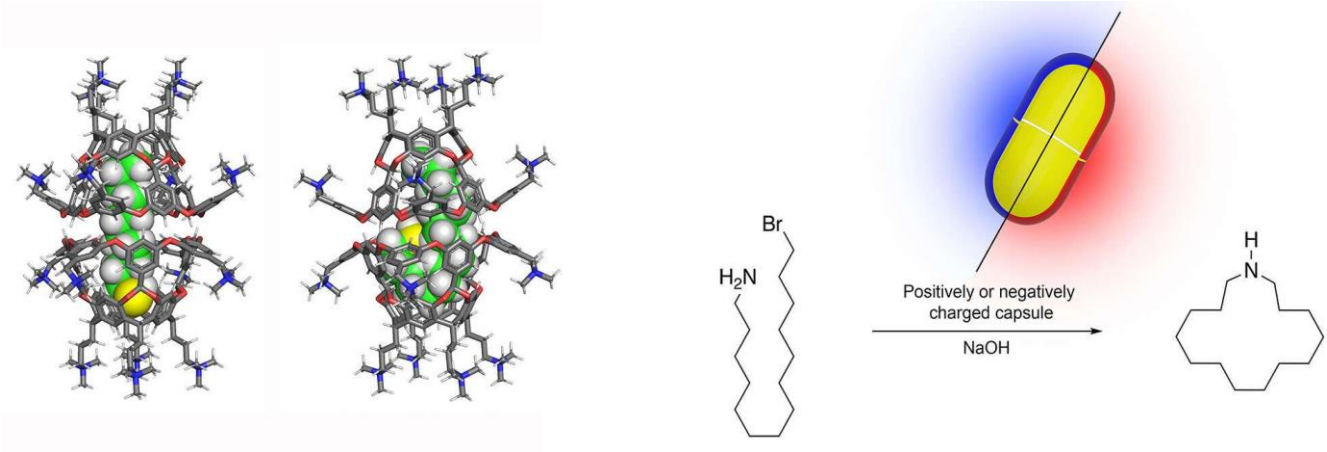
Plenary

The power of yocto-liter inner-spaces to affect reactions

Bruce Gibb
Chemistry, Tulane University, New Orleans, Louisiana, USA

Nature's catalysts such as enzymes utilize yoctoliter (10^{-24} L) spaces to facilitate the conversion of their substrates. Creating such spaces in water, *de novo*, is however no easy task. Approaches can involve the design and folding of foldamers, or they can utilize a brick-by-brick synthetic approach potentially combined with self-assembly. Either way, the state-of-the-art has yet to reach the heady heights of enzyme catalysis.

Our approach to yoctoliter inner-spaces is to take advantage of the self-assembling predisposition of deep-cavity cavitands. Driven by the hydrophobic effect, these form dimeric, supramolecular capsules that engender an inner-space for guest molecule encapsulation. This presentation will discuss the synthesis of the subunits, how they are solvated by water, as well as the types of guests that can be encapsulated in their inner-spaces. Building on this foundational information, the presentation will also detail the ability of these compartments to either selectively prevent reaction and bring about kinetic resolutions, or selectively promote reactions by affecting/controlling the physicochemical properties of encapsulated guests.



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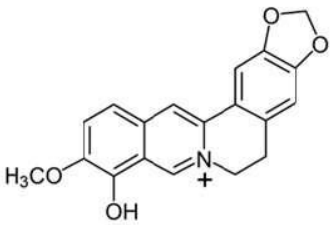
Flash talk

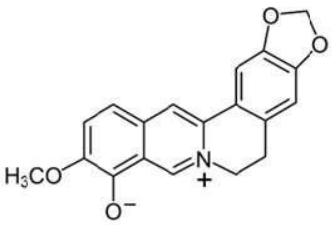
Active role of alkali cations in the kinetics of the base-promoted berberrubine release from cucurbit[7]uril

Zsombor Miskolczy[1], Mónika Megyesi[1], **László Biczók**[1]
Institute of Materials and Environmental Chemistry, Research Centre for Natural Sciences, Budapest, Hungary

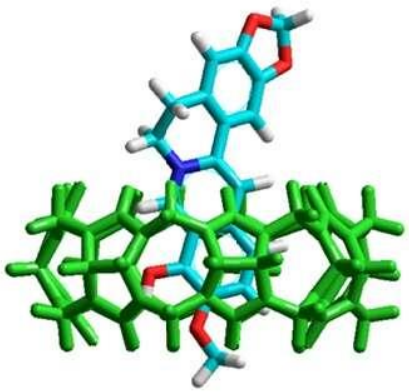
A pH-responsive inclusion complex was created from berberrubine, a pharmacological active natural isoquinoline alkaloid and cucurbit[7]uril (CB7) macrocycle exploiting the more than four orders of magnitude larger binding affinity of the cationic guest (BOH^+) compared to the deprotonated uncharged conjugate base (BO). Since only the CB7-encapsulated BOH^+ emitted strong fluorescence, the transformation of this host-guest complex could be selectively monitored in real time by stopped-flow measurements. Systematic kinetic studies with various alkali hydroxides revealed the mechanism of base-iniciated transformation of BOH^+–CB7 complex and the rate of the reaction steps. Alkali cations expelled BOH^+ from CB7 in a pseudo-first order reaction and formed ternary complex with BOH^+–CB7. The ternary complex was deprotonated by OH^- anions much faster than BOH^+–CB7. The rate of the process could be tuned not only by the OH^- concentration but also by the size and amount of the alkali cation. LiOH induced the proton loss of BOH^+–CB7 much more efficiently than NaOH or KOH. The revealed mechanistic details may be applied to other deprotonable CB7 complexes. The knowledge gained in the present study significantly contribute to the rational design of the tailor-made pH-responsive targeted delivery systems, the fabrication of stimuli-responsive materials, and the development of indicators for the monitoring of the local basicity in their microenvironment.



berberrubine (BOH^+)



deprotonated berberrubine (BO)



berberrubine (BOH^+) inclusion complex with cucurbit[7]uril

Acknowledgement: This research was funded by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund grant number OTKA K142139 and TKP2021-EGA-31.

Flash talk

Novel fluorinated bambusurils: synthesis, anion binding, and transport properties

Matúš Chvojka[1,2], Hennie Valkenier[2], Vladimír Šindelář[1]
[1]*Department of Chemistry and RECETOX, Masaryk University, Brno, Czech Republic*
[2]*École Polytechnique - Engineering of Molecular Nanosystems, Université libre de Bruxelles, Brussels, Belgium*

Bambusurils are macrocyclic substances made of six glycoluril building units connected via methylene linkers.[1] They are appreciated for their strong anion binding in solution, which is mediated by twelve C-H···anion hydrogen bond interactions. Their anion affinity was improved even further by introduction of fluorinated substituents, leading to exceptionally high association constants ranging between 10^7-10^{11} M^{-1} for Cl^-, NO_3^-, and HCO_3^- in acetonitrile.[2] These fluorinated substituents appended to the bambusurils did also increase their lipophilicity and, in combination with their high anion binding strength, very efficient anion transporters were obtained.

Here, fluorinated bambusuril derivatives containing strongly electron-withdrawing substituents will be presented. The low electron density inside the cavity of the bambusuril macrocycles resulted in stronger anion binding, which was comprehensively studied by a ^1H and ^{19}F NMR spectroscopy. The effect of increased anion binding strength on anion transport properties was evaluated using liposomes, using the lucigenin assay for chloride/bicarbonate antiport studies.

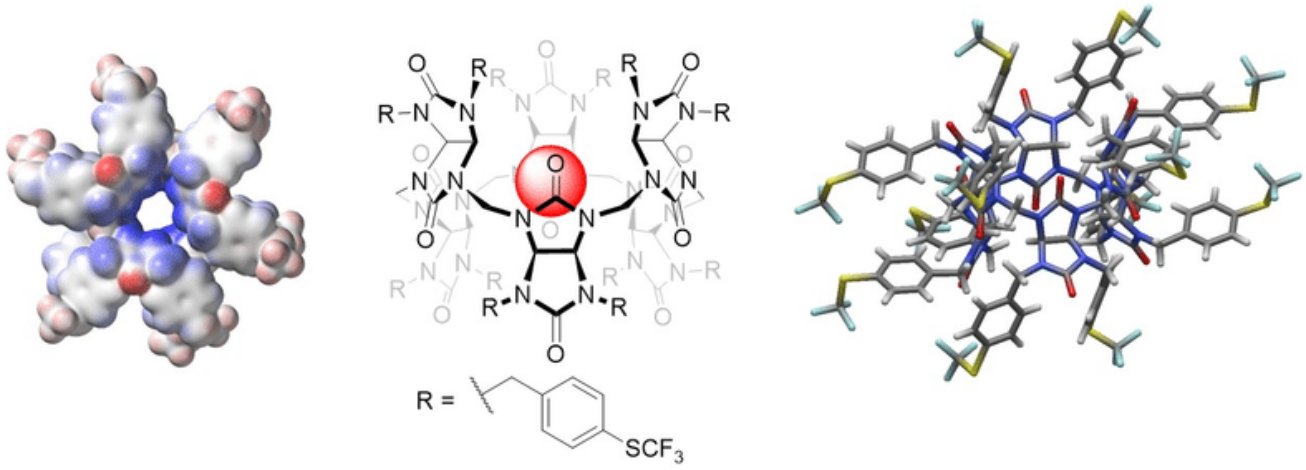


Fig. 1: An example of a fluorinated BU derivative, its electrostatic potential map (left), graphical representation of complex with an anion (middle) and crystal structure (right).

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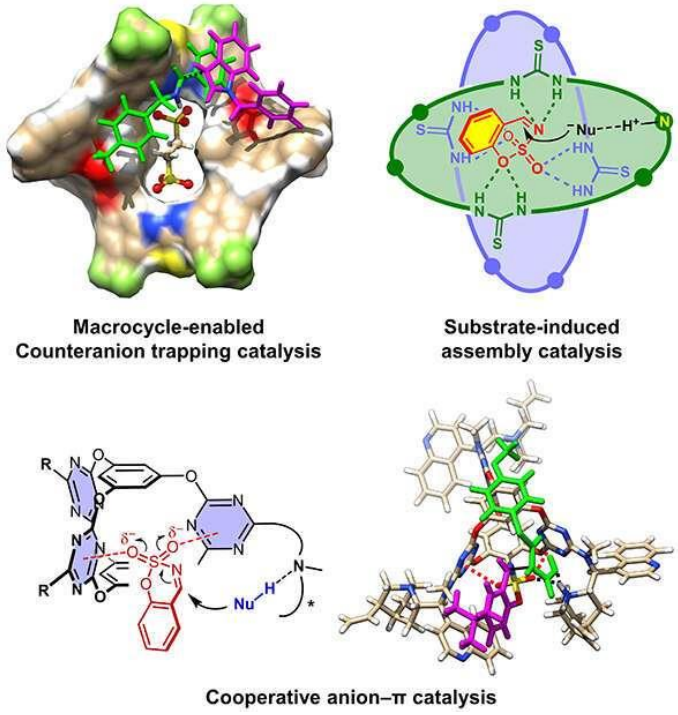
Flash talk

Anion-recognition directed supramolecular catalysis

Qi-Qiang Wang

CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing, China

Our research focuses on the construction of functional macrocycles and cages with enzyme-mimetic pocket and specific recognition ability for boosting highly efficient and selective supramolecular catalysis. Different from the use of conventional, cation-relevant interactions or hydrophobic effects, we came up with anion-recognition direction by taking inspiration from the recent development of anion supramolecular chemistry. The advantages of anions, including rich variety, diverse geometry and multiple interaction sites, are taken for manipulating a sophisticated activation network. Following this concept, we have developed hydrogen-bonding macrocycle-enabled counteranion trapping and substrate-induced assembly catalysis systems with great efficiency and excellent stereocontrol.[1-3] Moreover, exploiting of emerging anion–π interactions for driving highly efficient and selective catalysis was also achieved.[4-6] Cooperative anion–π activation was realized by building molecular cage catalysts with electron-deficient π-cavity. It paves a way to push the novel anion–π activation toward more practical and useful catalyst design and applications.



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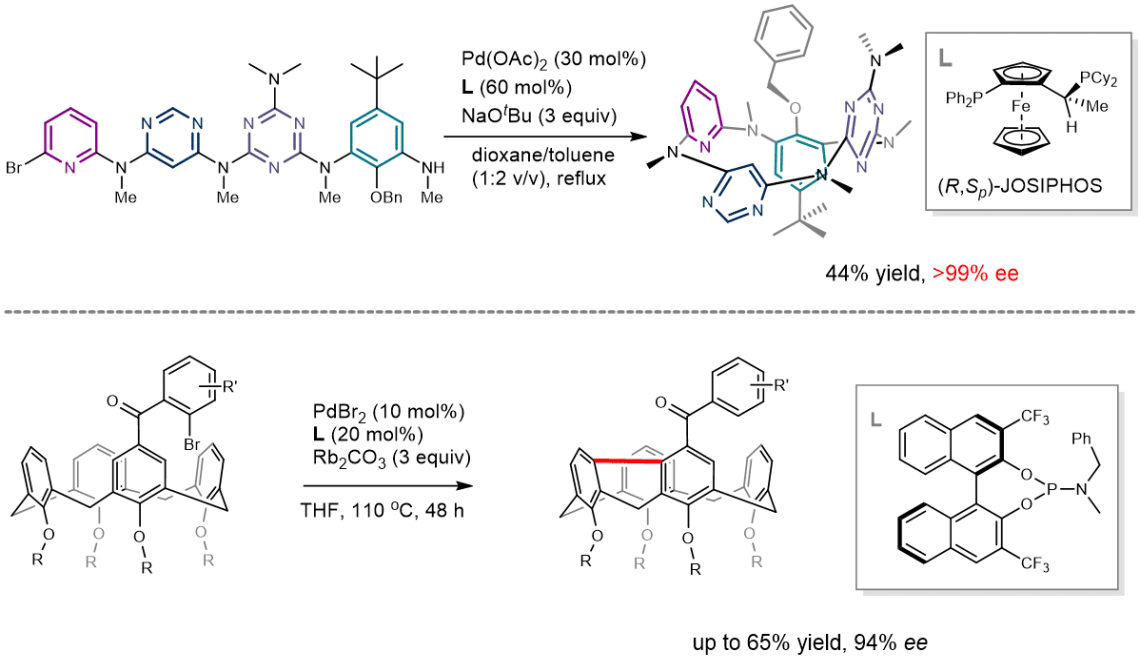
Flash talk

Catalytic enantioselective synthesis of inherently chiral calixarenes

Tong Shuo

Department of Chemistry, Tsinghua University, Beijing, China

Owing to their unique chiral structures and chiral recognition properties, inherently chiral macrocycles have drawn growing attention since the term was coined in 1994. The efficient synthesis of highly enantiopure inherently chiral macrocycles, however, still remains challenging till now. We aim to establish and develop the methodology for the catalytic enantioselective synthesis of inherently chiral calixarenes. To showcase the potential of fragment coupling strategy to create diverse inherently chiral structures, we designed an ABCD-type linear tetramer which contains benzene, pyridine, pyrimidine, and triazine rings. Starting with this linear tetramer, we have developed a catalytic enantioselective intramolecular Buchwald-Hartwig C-N bond forming reaction for the highly enantioselective de novo synthesis of ABCD-type inherently chiral tetraazacalix[4]aromatics. Starting from unchiral macrocycles, we have also developed asymmetric post-macrocyclization transformation for the construction of inherently chiral macrocycles.[1] Under the catalysis of PdBr2 and a chiral phosphoramidite ligand, the upper-rim mono-(2-bromoaroyl)-substituted calix[4]arene derivatives underwent a facile enantioselective desymmetrization reaction to afford 9H-fluorene-embedded inherently chiral calixarenes in good yields with excellent enantioselectivities.[2] The so obtained inherently chiral macrocycles are useful scaffolds for the fabrication of circularly polarized luminescence (CPL) materials.[1-4] The outcomes opened new opportunities for the design and synthesis of novel CPL materials based on the inherently chiral calixarene skeleton.



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Flash talk

Symmetry breaking during self-assembly of racemic mixture of organic cages

Shaodong Zhang
School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, Shanghai, China

Symmetry breaking is a process in which the symmetry of a system decreases spontaneously, and the study of symmetry breaking can provide important cognitive tools for the search of new materials, thus attracting widespread interest in physics, chemistry, and materials science. Symmetry breaking is relative and only valid when the temporal and/or spatial scales of the system are explicitly defined, and we herein use the self-assembly process of organic cage and cage catenanes to illustrate this relativity and to elucidate how the symmetry of racemic mixtures is broken at specific temporal, spatial, and logical levels. Symmetry is one of the most universal and important norms in the universe, and deviation from it requires a "driving force to achieve inhomogeneous properties", and we illustrate the driving force of non-covalent interactions in this process through the spontaneous chiral resolution of racemic mixtures of molecular cages during crystallization. Symmetry breaking is an important way to generate phenomena that provide rational design guidance for many functions, which we interpret through the generation of second-order nonlinear optics and ferroelectricity/piezoelectricity in the assembly of organic-cage racemates.

Plenary

Calipyrrole-based materials (and friends)

Jonathan Sessler
Chemistry, The University of Texas at Austin, Austin, Texas, USA

This presentation will provide a summary of recent collaborative efforts to create functional materials based on various pyrrolic macrocycles, including calix[n]pyrrole. Particular attention will be devoted to polymeric networks that incorporate this class of well-characterized anion and ion pair receptors within their extended structural frameworks. These systems are being explored in the context of several potential application areas, including waste remediation, halogen capture, perfluorinated organic acid sensing, and polar compound separations. Early and still-ongoing studies of receptor-containing soft materials that target hard ions, such as lithium cation and the hydroxide anion, will be presented to provide context. The use of ion recognition materials to encode information will be summarized as time permits.

This research has been made possible by the dedicated efforts of numerous students and postdoctoral fellows who will be thanked explicitly during the lecture, as well as collaborations with a number of groups, including those of Profs. Philip A. Gale, Han-Yuan Gong, Qing He, Feihe Huang, Jan Jeppesen, Xiaofan Ji, Xiaodong Chi, Niveen Khashab, Jong Seung Kim, Sung Kuk Kim, Changhee Lee, Bruce A. Moyer, Zachariah A. Page, Jung Su Park, Benzhong Tang, Hongyu Wang, George Schatz, and Yasuhide Inokuma.

This project has been supported at times by the U.S. National Science Foundation, the U.S. DOE Office of Basic Energy Sciences, the R. A. Welch Foundation, and KAUST.

Invited

New macrocyclic arenes for molecular recognition and assembly

Chuan-Feng Chen
CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing, China

On the basis of the previous research work on the macrocyclic arenes derived from triptycene, we have recently designed and synthesized several new kinds of macrocyclic arenes, especially the chiral macrocyclic arenes, including the pagoda[n]arenes with planar chirality, the saucer[4]arenes with inherent chirality, and the octopus[n]arenes with central chirality. Moreover, we have constructed other macrocyclic arenes including fluoren[n]arenes, calix[3]acridan and so on. The photophysical properties and circularly polarized luminescence properties of the novel macrocyclic arenes were studied, and their applications in molecular recognition and assembly were also explored. In this talk, the recent advances in synthesis of new macrocyclic arenes and their applications in molecular recognition and assemblies will be presented.

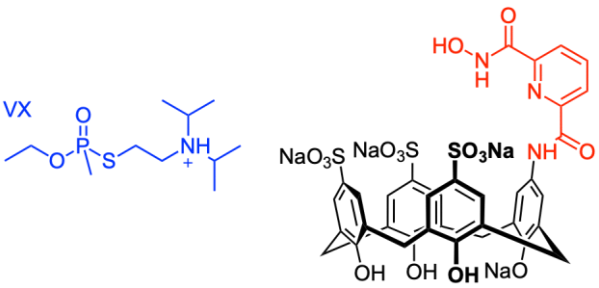
Invited

Supramolecular approaches to the detoxification of nerve agents

Stefan Kubik

Department of Chemistry – Organic Chemistry, RPTU Kaiserslautern-Landau, Kaiserslautern, Germany

Compounds that rapidly detoxify neurotoxic organophosphates (NOPs) under physiological conditions can be used as antidotes to treat intoxications with these nerve agents or to support existing treatment strategies. Such synthetic scavengers typically contain a receptor moiety to which the nerve agent can bind and a nucleophilic group that reacts with the bound NOP, thus mediating its detoxification. The receptor must be adapted to the nature of the toxin that should be detoxified. Highly toxic V-type nerve agents, for example, contain a cationic group at physiological pH that can be targeted with cation-binding receptors such as sulfonated calixarenes or (acyclic) cucurbiturils. Work in my group has indeed demonstrated that substituted sulfonatocalix[4]arenes with hydroxamic acid residues represent potent scavengers for VX and other V-type nerve agents.



While the efficiencies of our first-generation calixarene-based scavengers were too low to be useful, recent efforts afforded much more active compounds. Cucurbiturils, on the other hand, proved to be unsuitable for scavenger development because the incorporation of a nerve agent into the cucurbituril cavity protected it from intermolecular reactions. Interestingly, VX was still reactive inside the cavity and degraded along a normally not very important intramolecular pathway. This talk will give an overview of our work on the development of synthetic nerve agent scavengers, with a focus on the work involving calixarenes and cucurbiturils.

Invited

Aromaticity - a twisted tale

Ori Gidron

Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem, Israel

Planarity plays a crucial role in determining the electronic and optical properties of π-conjugated backbones. Here I will discuss two examples of non-planar and planar systems: twisted acenes and planar furan macrocycles.

In the first part, the recent progress in the study of helically locked twisted acenes will be discussed. These acenes consist of anthracene backbone diagonally tethered by an n-alkyl bridge,[1] which allows us to systematically monitor the effect of twisting on electronic, magnetic and optical properties.[2,3] In the second part, the first series of macrocyclic furans will be discussed.[4] A combination of lower aromaticity and larger exo angle allows the introduction of small planar macrocycles, with 4n+2 and 4n electrons, which display alternating properties such as emission maxima, oxidation potentials and chemical shifts.[5] Finally, a new synthetic approach to highly strained macrocycles will be discussed.[6]

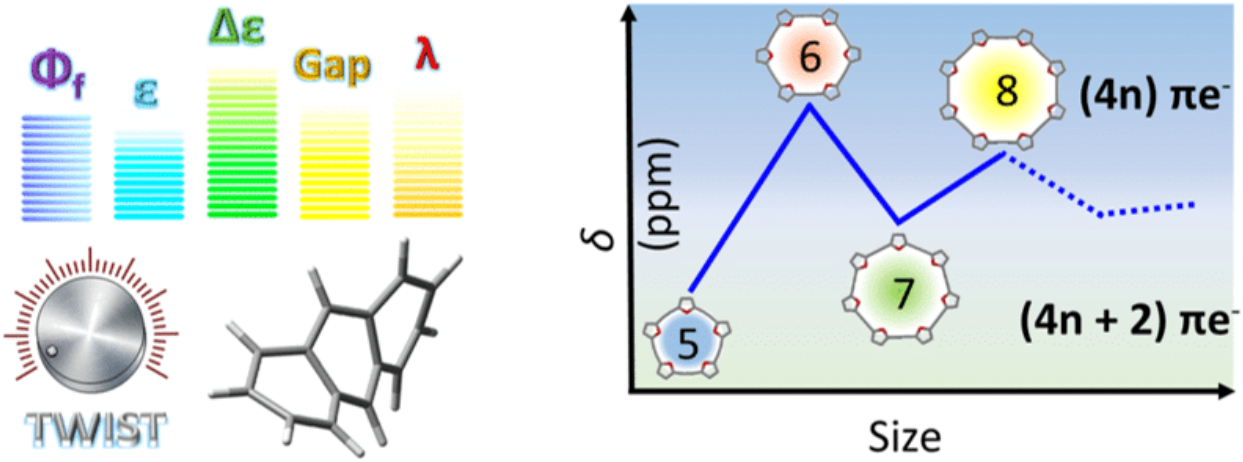


Figure: Twisted acenes (left) and macrocyclic furans (right).

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Invited

Superselectivity and recruitment as organizing principles in bio-sensing and self-assembly

Jurriaan Huskens
Department of Molecules & Materials, MESA+ Institute, University of Twente, Enschede, Netherlands

Multivalent interactions govern biological processes like cell signaling and virus infections [1]. Such interactions are characterized by unique energetic, structural and dynamic properties, and they occur at a well-defined contact area, in which multiple complementary binding sites interact with each other in a reversible and dynamic manner. Emerging properties of such systems are superselectivity and recruitment. Superselectivity describes the nonlinear dependence of binding with receptor/ligand densities, whereas recruitment occurs when mobility allows receptor and/or ligand sites to move in and out of the contact area, typically leading to enhanced binding sites occurring within the contact area and depletion thereof outside. The present report shows how superselectivity and recruitment can be engineered to create new principles for biomarker isolation and for materials self-assembly, respectively.

In the first example, superselectivity is employed to up-concentrate the cancer biomarker hypermethylated DNA (hmDNA) [2]. Surfaces with controlled densities of a methyl-binding domain (MBD) protein show enhanced affinity for DNA with increasing numbers of methylation sites. This allows implementation into a microfluidic device in which hmDNA can be effectively isolated from liquid biopsies to allow highly sensitive detection.

In the second example, recruitment [3] is shown to provide stoichiometrically controlled assemblies of vesicles decorated with complementary receptor and ligand sites implemented in their membranes. The affinity between the vesicles shows signs of superselectivity while receptor/ligand recruitment controls the binding stoichiometry of the vesicles. Fluorescence resonance energy transfer (FRET) of dyes incorporated within the vesicle membranes allows detailed analysis of the contact area between them. Overall, these examples underline the powerful paradigm of multivalent interactions and their functional properties.

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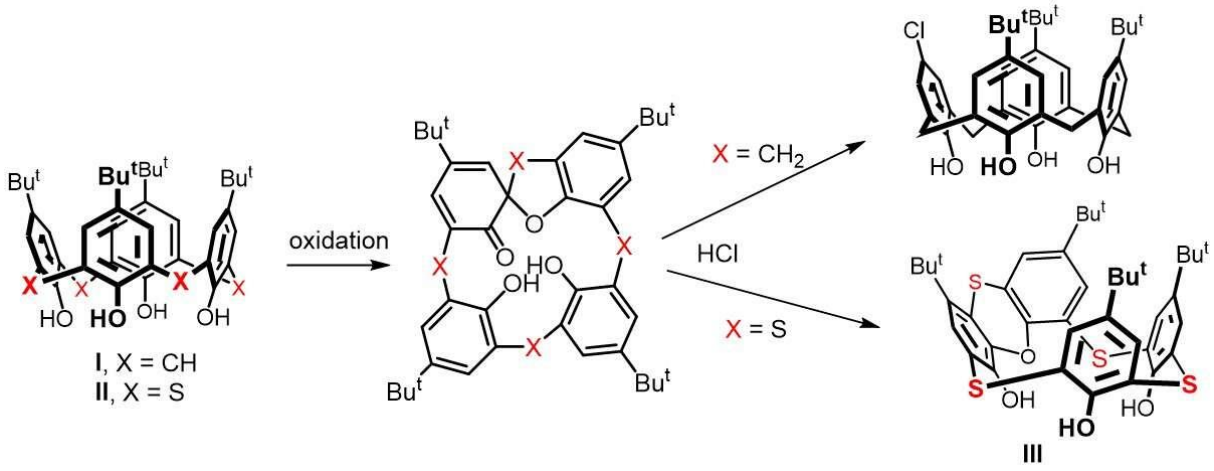
Invited

New insights into the chemistry of thiacalixarenes and related systems

Pavel Lhotak[1]
Department of Organic Chemistry, University of Chemistry and Technology Prague, Prague 6, Czech Republic

The introduction of other moieties instead of methylene bridges has enriched calixarene family with new members like thiacalixarenes. While possessing many shared general features, like shaping the cavity via a simple alkylation of the lower rim of calix[4]arene **I** or thiacalix[4]arene **II**, there are many aspects where the two macrocyclic families do not resemble each other at all. The presence of sulfur enables transformations which are not possible with classical CH_2 analogues. It can be documented by chemistry of the corresponding spirodienone compounds (Figure) leading in thiacalixarene series to completely novel macrocyclic system **III** possessing[1] the phenoxathiin moiety.



The lecture will focus on selected differences in the reactivity of the two basic systems (thia- vs classical calix[4]arenes) and on the chemistry of phenoxathiin-based macrocycles.[2]

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Invited

Functional cucurbituril-DNA conjugates

Janarthanan Jayawickramarajah[1], Dilanka V. D. Walpita Kankanamalage[1]
Chemistry, Tulane University, New Orleans, Louisiana, USA

The construction of controllable molecular- and nano-machines that function in aqueous/biological media is an important endeavor, with potential practical applications in biosensing, theranostics, and computing. In terms of well-controlled systems and assemblies that function in water, DNA nanotechnology has led the way due to the programmability of DNA architectures using simple base-pairing rules. In this talk, we describe how synthetic cucurbituril chemistry can be judiciously combined with DNA nanotechnology to generate novel systems with potential therapeutic and diagnostic applications. We begin by discussing a synthetic transducer that is activated by ATP to release an enzyme inhibitor. We will also describe a novel method of DNA strand displacement that functions via cucurbituril-guest interactions, using a cucurbit[7]uril-DNA conjugate. We will also illustrate how such a synthetic strand displacement process can be (a) finely controlled and (b) integrated into functional devices (that control protein activity and layered reactions that detect specific microRNA). Time permitting, we will provide insight into the new directions that the laboratory is pursuing in terms of cucurbituril-bioconjugates.

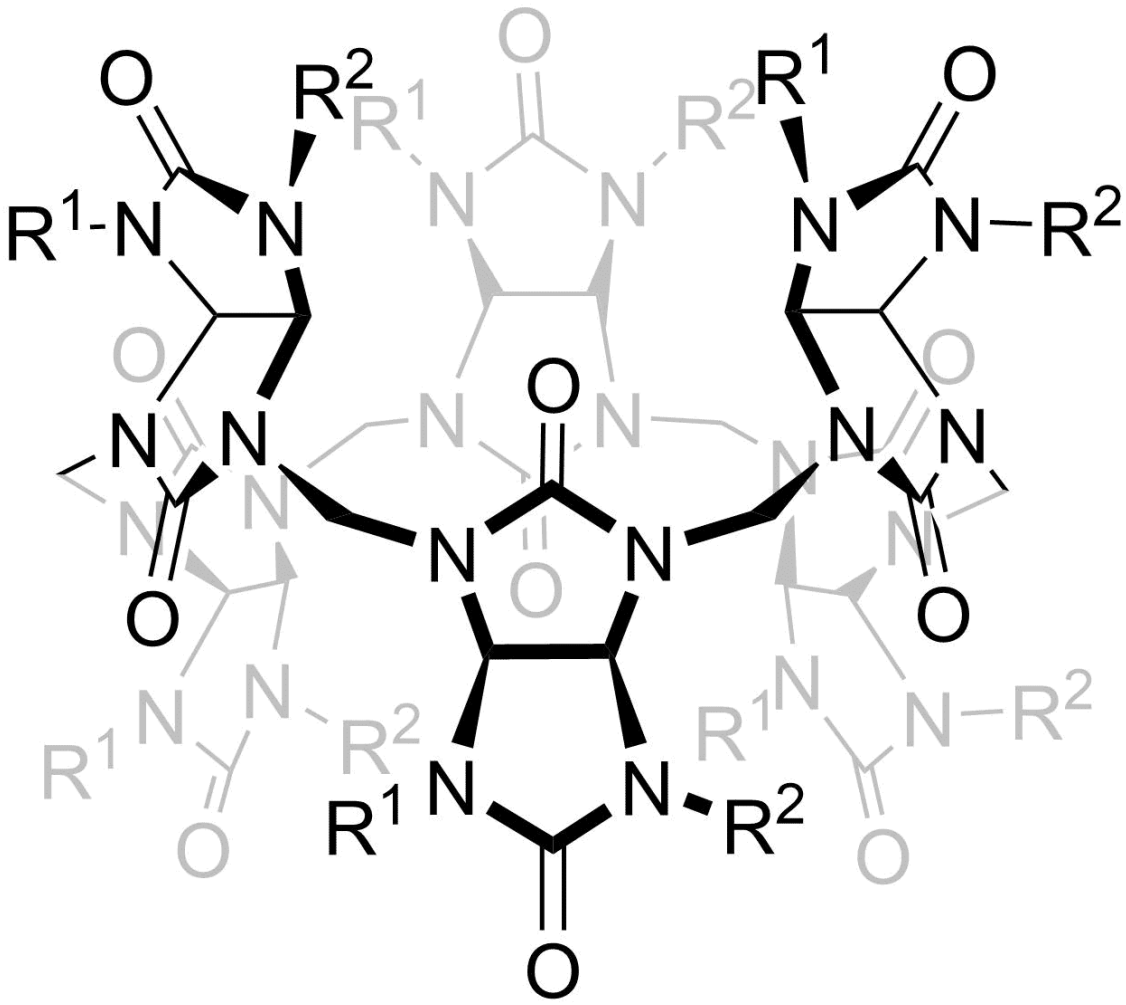
Invited

Synthesis and applications of bambusuril derivatives

Vladimir Sindelar

Department of Chemistry and RECETOX, Masaryk University, Brno, Czech Republic

Bambusurils are macrocycles with high binding affinity to inorganic and organic anions (ref. 1, 2). The first bambusurils consisted of 2,4-disubstituded glycoluril building blocks (Figure 1, where R1 = R2), which were connected by a row of methylene bridges. As a result, the macrocycle contained 12 same substituents on both portals. The types of substituents were varied to influence not only macrocycle solubility but also binding affinity. In my talk, I will discuss our recently developed synthesis of enantiomerically pure bambusurils (R1 ≠ R2). Single glycoluril enantiomers needed for the synthesis were achieved by orthogonal (de)protection of the glycoluril precursors. The synthesis of chiral bambusurils with on-demand substituents via post-macrocyclization reaction will also be presented as well as monofunctionalization of the bambusurils. The application of bambusurils for gold mining, preparation of interlocked molecules, and transmembrane transport will be briefly discussed.



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Invited

How to capture an atom: Insights from xenon host-guest chemistry

Ivan Dmochowski[1], Zhuangyu Zhao[1], Nathan Rudman[1], Yannan Lin[1]
Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania, USA

With FDA approval of Polarean's Xenoview, there is growing interest in performing void-space lung imaging as well as dissolved-phase molecular imaging in humans and animal models using this technology. ^{129}Xe is spin-1/2, and can be hyperpolarized to give a 10^5 signal enhancement over the room-temperature Boltzmann population of nuclear spins. Biology provides endogenous lipid compartments and blood proteins, which bind xenon and provide specific Xe-129 nuclear magnetic resonance (NMR) chemical shifts. To visualize a greater range of molecular targets, including disease biomarkers, there is the opportunity to deliver exogenous contrast agents that bind xenon with good affinity, label molecular targets of interest in vivo, and yield useful Xe-129 NMR signals. For two decades, our laboratory has developed organic capsules as xenon-based sensors, e.g., cryptophanes and cucurbiturils, and explored their functionalization and biocompatibility. In 2020 we discovered that tetrahedral capsules with Co^{2+} at the vertices generate useful Xe-129 NMR signals, as xenon diffuses through portals to access the capsule interior. Replacing paramagnetic Co^{2+} with smaller, diamagnetic Fe^{2+} cations tunes the Xe-129 NMR chemical shift, as well as portal size and Xe exchange rate.

Finally, our laboratory has identified several monomeric proteins that yield unique Xe-129 NMR chemical shifts, either alone in solution (i.e., Xe-beta-lactamase) or upon binding a small molecule analyte, e.g., maltose-binding protein (MBP) and ribose-binding protein (RBP). These proteins give significant saturation contrast at 100 nM using the hyper-CEST NMR technique. Recently, we determined via molecular dynamics simulations and site-directed mutagenesis that maltose binding to MBP stabilizes a salt bridge at the mouth of a 2-nm channel where xenon resides, which slows the exchange rate and yields MR signal. Replacing the salt bridge with a zinc-binding motif produces zinc-selective Xe-129 NMR signal.

Contributed

Strategies to fine control the conformational properties of calix[4]arene derivatives

Laura Baldini

Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Italy

Besides providing a suitable platform to anchor binding sites for a variety of guests, the calix[4]arene macrocycle plays a key role in supramolecular chemistry thanks to its rich conformational plasticity that unfolds at two different levels:

(i) the overall geometry of the calix[4]arene scaffold, that can be fixed in one of four well-defined structures (*cone*, *partial cone*, *1,3-* and *1,2-alternate*);

(ii) the residual flexibility given by the swinging motion of the aromatic rings about the methylene hinges.

Particularly interesting is the second kind of conformational flexibility experienced by the calix[4]arene derivatives in *cone* geometry, which undergo a conformational equilibration between two flattened or pinched cone conformations (Fig. 1).[1]

This contribution will show how the ability to control this interconversion can be exploited to modulate many properties of calix[4]arene derivatives, ranging from the chemical reactivity to the binding properties to the photophysical features.

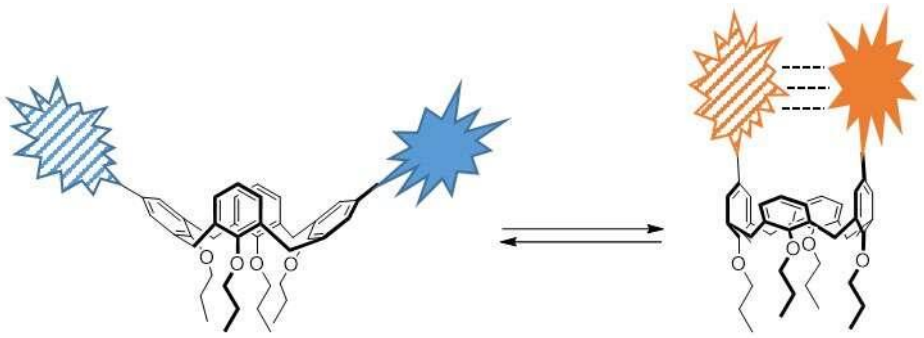

Figure 1. Interconversion between two pinched cone conformations of calix[4]arene

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Contributed

Chiroptical properties and multifold arylation of pillar[*n*]arenes

Kenichi Kato[1], Tomoya Kaneda[1], Yuta Kurakake[1], Shunsuke Ohtani[1], Tomoki Ogoshi[1,2]
[1]*Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Kyoto, Japan*
[2]*WPI Nano Life Science Institute, Kanazawa University, Kanazawa, Japan*

Pillar[*n*]arenes 1nOR (n = 5,6) are calix[*n*]arene-related macrocyclic compounds and usually have 1,4-methylene linkage and alkoxy groups at 2,5-positions. These structural features endow pillar[*n*]arenes with highly symmetric C_5- or C_6-axes and planar chirality, being different from other macrocyclic molecules. In this presentation, we report direct fivefold arylation at one rim of a bulky cyclohexylmethoxy-substituted pillar[5]arene.[1] The series of products possessed fixed chiral and two-sided natures as a rare example and displayed circularly polarized luminescence (CPL). Due to the retained C_5-symmetry, 2OMe showed higher dissymmetry in CPL than previous C_1- and C_2-symmetric derivatives, whereas clearly two-sided 2CO_2Et showed improved luminescence properties with a longer wavelength and higher quantum yield at the expense of lower dissymmetry. In the latter part, we also show recent progress in direct rim functionalization. By using furan- and benzofuran-2-boronic acid, per-arylation of pillar[5,6]arenes has been achieved for the first time.[2] The structural, optical, and host–guest properties of the per-arylated pillar[5,6]arenes were investigated in comparison with common per-alkoxyl-substituted ones, which revealed large deviations from conventional pillar[*n*]arenes.

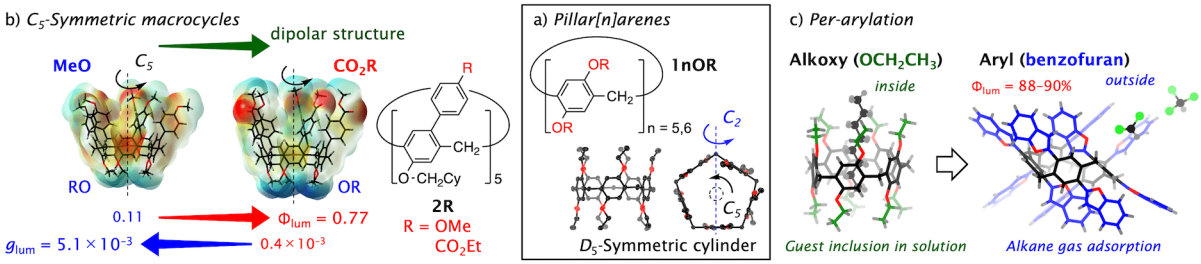

Figure. a) Chemical and single-crystal structures of pillar[*n*]arenes with solution-state symmetry elements. b) Chemical structures and ground-state electrostatic potential maps of chiral two-sided macrocycles. c) Comparison of per-alkoxy-substituted and per-arylated pillar[5]arenes.

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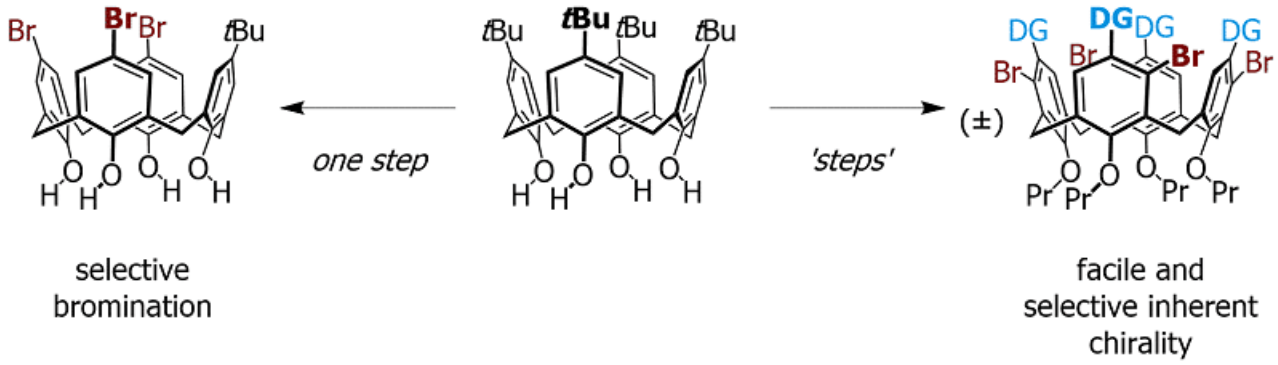
Contributed

Bromination of calix[4]arenes: breaking (bad) symmetry?

Gareth Arnott

Chemistry and Polymer Science, Stellenbosch University, Stellenbosch, South Africa

My research group is dedicated to the synthesis of inherently chiral calix[4]arenes and the development of scalable methods for their production. Although we initially demonstrated highly diastereoselective methods for obtaining these structures, the reactions were found to be capricious and unsuitable for large-scale synthesis. To address this challenge, we recently reported a new method for producing inherently chiral calixarenes with C_4 symmetry, which holds promise for enabling their large-scale, non-racemic production. In addition to discussing these findings, the talk will also cover other methods we have explored for generating desymmetrised calixarenes with interesting properties.



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Plenary

Pillar[6]MaxQ: synthesis, molecular recognition, and in vivo sequestration

Isaacs Lyle
Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland, USA

In this presentation, I describe the thought process that lead us from ultratight CB[n]•guest complexes to the design and synthesis of a new class of ultrahigh affinity pillararene hosts dubbed Pillar[n]MaxQ (K_a up to 10^{12} M^{-1} in phosphate buffered water).[1] Pillar[n]MaxQ (Figure 1) bind substantially more tightly toward their guests than the analogous pillararenes featuring OCH_2CO_2H groups.[1-3] Pillar[n]MaxQ selectively bind hydrophobic Quaternary ammonium ions in preference to hydrophobic primary ammonium ions. Pillar[6]MaxQ binds to biologically and medicinally important guest compounds like neuromuscular blockers (rocuronium, vecuronium) and drugs of abuse with high affinity.[1,3] In vitro cytoxicity assays for Pillar[6]MaxQ performed with kidney and liver cells indicate good compatibility up to 100 uM whereas an in vivo (Swiss Webster mice) maximum tolerated dose study showed that Pillar[6]MaxQ is well tolerated up to 40 mg/kg. Pillar[6]MaxQ does not inhibit the hERG ion channel and is not mutagenic according to the Ames fluctuation test. Finally, we perform open-field tests to quantify locomotor activity of animals treated with methamphetamine or fentanyl followed by Pillar[6]MaxQ as supramolecular antidote.[3]

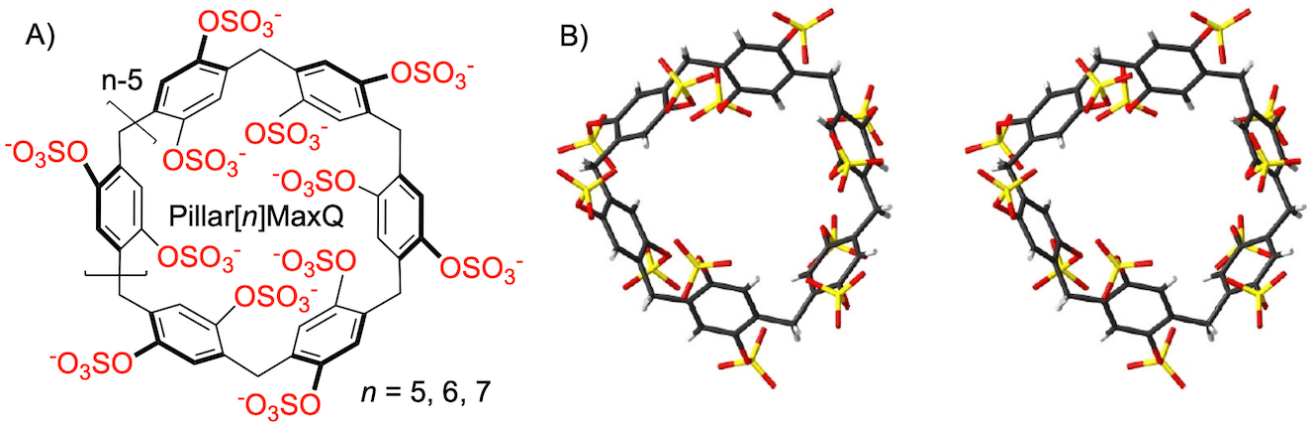

Figure 1. A) Chemical structure and B) Cross-eyed stereoview of Pillar[6]MaxQ in the crystal.

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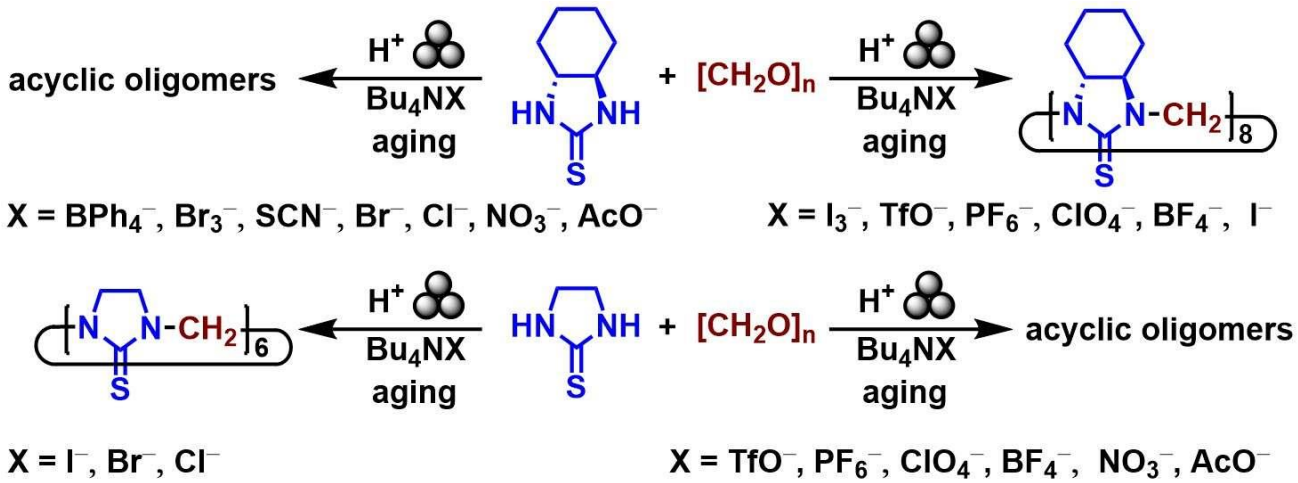
Flash talk

Substrate-controlled and template-assisted mechanochemical synthesis of *thio*-hemicucurbiturils

Raghuram Gujjarappa[1,2], Ehud Keinan[2], Ofer Reany[3]
[1]*Department of Natural Sciences, The Open University of Israel, Ra'anana, Israel*
[2]*The Schulich Faculty of Chemistry, Technion-Israel Institute of Technology, Haifa, Israel*
[3]*Department of Natural Sciences, The Open University of Israel, Ra'anana, Israel*

Hemicucurbiturils (hemiCB[n]s) consist single hoop of methylene linkers interconnecting 2-imidazolidone (ethylene urea) subunits. In contrast to the rigid pumpkin shape of cucurbiturils and their affinity toward cationic species, the structure of hemiCB[n] adopts an alternating conformation and encapsulates anions. To date, selected 2-imidazolidone derivatives were successfully cyclooligomerized, and the size of the resulting macrocycles was controlled by the anion-template nature.

Here we present the synthesis of *thio*-hemiCB[n] (n = 6, 8) employing the heteroatom replacement approach.[1] However, the commonly used synthetic methodology for cyclooligomerization of imidazolidone-2-thione and its derivatives is not applicable because the substrates are acid-sensitive. Instead, we applied a mechanochemical approach that involves solid-phase reactants in a nearly solvent-free environment. Optimization reactions included the effect of the templating agent, the nature of the acid catalyst, aging duration and temperature. Under the optimized reaction conditions, we successfully prepared 6- and 8-membered *thio*-hemiCB[n]s in high selectivity. Ring-size selectivity was attributed to the nature of the building block. Acyclic oligomers vs. macrocycles were determined by choice of anion template. X-ray studies and isothermal titration calorimetry (ITC) confirmed the selective anion-binding affinities of each *thio*-hemiCB[n] homolog.



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Flash talk

Water-soluble pseudo-rotaxane with cucurbit[7]uril shuttling along a "dynamic" axle in response pH and light simuli

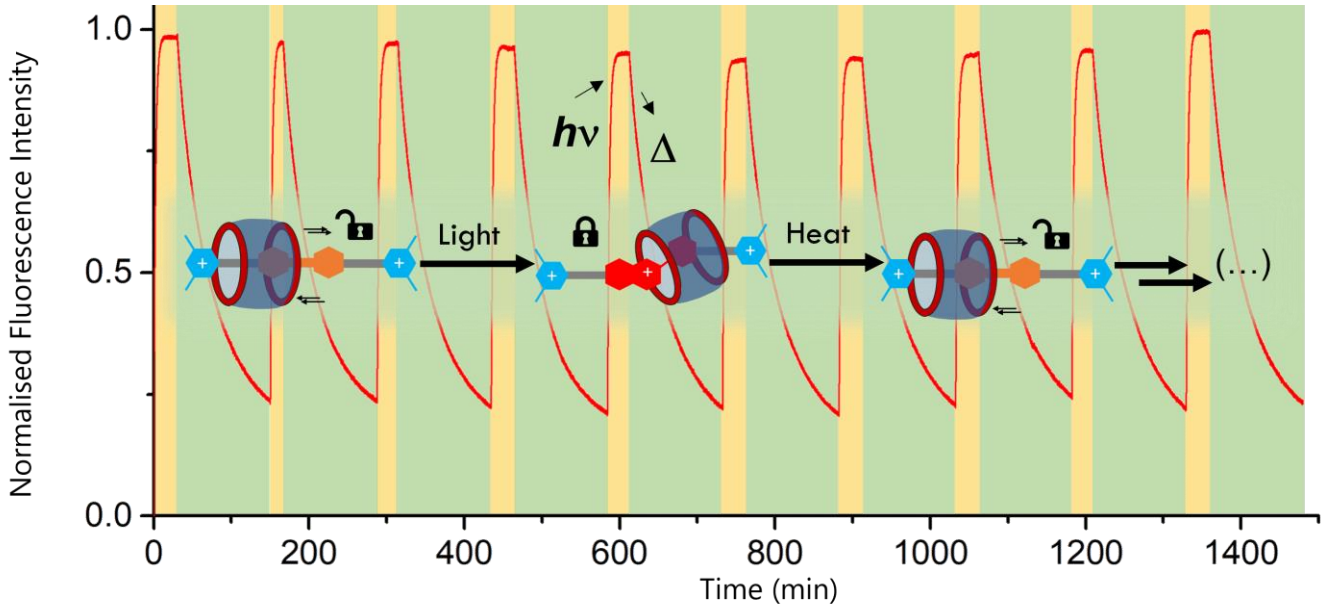
André Seco[1], Nathan Mcclenaghan[2], A. Jorge Parola[1], Nuno Basílio[1]
[1]*Department of Chemistry, NOVA School of Science and Technology, Lisbon, Portugal*
[2]*Institut des Sciences Moléculaires, CNRS/Univ. Bordeaux, Talence, France*

Rotaxanes and pseudo-rotaxanes are among the most well studied types of supramolecular devices and cucurbiturils have proven over the last two decades that they are an ideal macrocycle to build this kind of devices in aqueous media, something that still presents a challenge in the field. In this work we will present a pseudo-rotaxane assembled from a cucurbit[7]uril, CB7, wheel and a 2-hydroxychalcone based axle.

This 2-hydroxychalcone based axle was designed to take advantage of the pH dependence and light sensitivity that are characteristics of these compounds, related to the anthocyanin's family multistate [1]. Indeed, while the chalcone is stable at neutral pH and has a measured affinity constant towards CB7 of K_{11}=1.2x10^5 M^{-1}, at very acidic pH (

$_{11}$=1.5x10^8 M^{-1}). This flavylium form is also highly fluorescent on its own (QY_{free} = 0.29) and upon 1:1 complexation the quantum yield increases drastically to an almost unitarian quantum yield (QY_{11} = 0.97) [2].

Considering these stark differences in affinity, we can work at an intermediate pH where we start with the chalcone form and use light to promote the formation of the flavylium in a metastable equilibrium that eventually reverts to the chalcone form. That causes the CB7 wheel to switch from a loose binding on the chalcone, to a locked conformation on the flavylium and back to a loose binding on the chalcone again, and so on, as shown by the cycling experiment in the picture bellow.



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Flash talk

Colorimetric differentiation of solid-state supramolecular complexes of coumarin and bimane fluorophores

Vincent Joseph[1], Nathaniel Roy[1], Jenisha John[1], Flavio Grynszpan[1], **Mindy Levine**[1]
Department of Chemical Sciences, Ariel University, Ariel, Israel

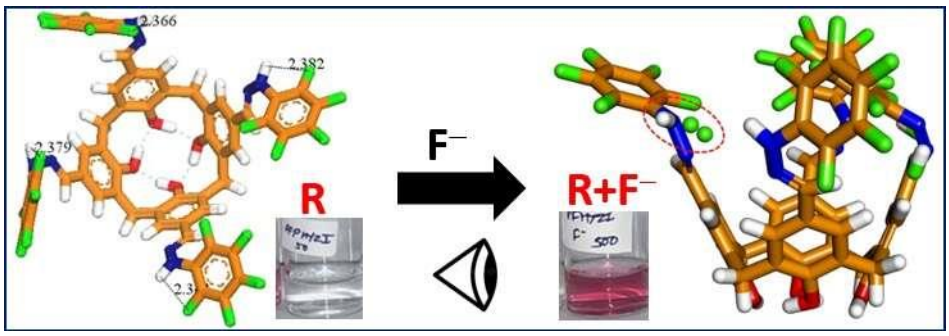
Supramolecular complexation of small-molecule fluorophores in macrocyclic hosts has the potential to dramatically alter the photophysical properties of such fluorophores, their stability, and a variety of other physicochemical properties. Our research groups have pioneered the development of novel bimane and coumarin fluorophores, the supramolecular complexation of such fluorophores in cyclodextrin hosts, and the use of these fluorophores as highly effective fluorescent and colorimetric sensors. The majority of our research to date has focused on investigating solution-state complexation, which has the advantage of facilitating a multitude of spectroscopic analytical techniques, while the majority of our effective sensors operate in the solid-state. Our work reported herein aims at bridging the gap between solution-state complexation and solid-state chemical sensing, through the rational formation, analysis, and optimization of solid-state supramolecular complexes. These complexes, formed from a variety of calixarene and cyclodextrin hosts combined with bimane and coumarin fluorophores, display unique solid-state properties, particularly for methyl-beta-cyclodextrin combined with an aldehyde-substituted coumarin. A detailed analysis of these results provides both improved understanding of solid-state complexation, including critical differences between cyclodextrin and calixarene scaffolds, as well as critical information for the development and optimization of next-generation supramolecular sensors.

Flash talk

Electron deficient arms of calix[4] basket for capturing toxic fluoride ion

Anita Nehra[1,2], Sateesh Bandaru[3], Rakesh K Sharma[1]
[1]*Chemistry, Indian Institute of Technology Jodhpur, Jodhpur, Rajasthan, India*
[2]*Chemistry, JECRC University, Jaipur, Rajasthan, India*
[3]*Computational Material Science Division, Hangzhou Dianzi University, Hangzhou, Zhejiang, China*

Owing to a stable cone conformation of calix[4]arene, it is one of the most widely used macrocycles for highly selective recognition of ions.[1] Moreover, a broad range of anion sensors have been developed using the calix[4] platform.[2] Intake of excess fluoride is highly toxic and detrimental to human body. Therefore, its detection is crucial. Here we present a neutral electron-deficient receptor of calix[4]arene, R is synthesized and characterized. The R showed naked eye detection of fluoride by giving instant deep pink color among other 19 anions studied in acetonitrile. No interference of other anions is observed. Two isosbestic absorption points in the UV-vis studies implied transition from free R to fluoride complexed species. The fluoride interacted with electron-deficient centres identified by 1H & 19F NMR studies. Variable temperature NMR studies revealed the formation of HF2– when ten equivalent of fluoride is added to the R. The fluoride ion bound species along with counter ion are detected by ESI-MS. DFT calculations demonstrate the strong interaction of F– ions with the R and an optical absorption shift towards longer wavelengths in R+F– complexes as revealed by TD-DFT studies as shown in the Scheme 1.[3]



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Plenary

Supramolecular catalysis with macrocycles

Werner Nau

School of Science, Constructor University, Bremen, Germany

Supramolecular catalysis with macrocycles [1-10] has proven to be conceptually insightful in regard to the fundamental roles of effective molarity, substrate preorganization, transition-state stabilization, competitive binding, and product inhibition. One reason that macrocycles such as cyclodextrins, calixarenes, cyclophanes, cavitands, capsules, molecular metallacages, and cucurbiturils have been elevated in focus is their potential to mimic active sites, which could eventually rival the enzymatic function. Besides the in-situ click reaction with cucurbituril pioneered by Mock [1], Diels−Alder reactions have emerged as the gold standard to benchmark the catalytic activity of macrocycles [2-7], but the rational use of macrocycles in acid-catalyzed reactions [8] or photoreactions [9,10] has been similarly instructive.

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Invited
CB[n]–guest hydrogels with tunable network dynamics

Matthew Webber
Chemical & Biomolecular Engineering, University of Notre Dame, Notre Dame, Indiana, USA

The recognition afforded by CB[n] macrocycle hosts in binding a suite of different guests enables routes to rationally design soft materials from the molecular scale and afford specific and tunable functionality. CB[n]–guest chemistries achieve among the highest affinity interactions ever observed for supramolecular complexes, offering a non-covalent approach to enable recognition and bond formation in a variety of environments. One particular member of this family, cucurbit[7]uril (CB[7]), affords binding affinities (Keq) to an array of guests extending over ~8-10 orders of magnitude. Using CB[7], we have probed the parameter of host–guest affinity in the design of assorted supramolecular hydrogels. The affinity of crosslinking interactions in this platform enables a molecular-scale approach to control the crosslink exchange dynamics of the material, translates to tunable release of macromolecular payloads, and dictates the rate of cell infiltration and material clearance in vivo. In building on these responsive soft materials, photo-responsive guest chemistries are also explored for external and reversible control of the affinity and dynamics of supramolecular recognition. Using a larger macrocycle, CB[8], ternary complex formation then enables dynamic crosslinking of macromers using the soluble macrocycle bound to two guests simultaneously. The CB[8] macrocycle furthermore catalyzes reversible light-mediated cycloaddition of certain guests, offering an external stimulus for reversible in situ conversion between soft materials dynamic supramolecular and covalent elastic crosslinking. Finally, hydrogel states are also possible through transiently upgrading guest binding affinity, enabling temporal control over material formation and crosslinking dynamics.

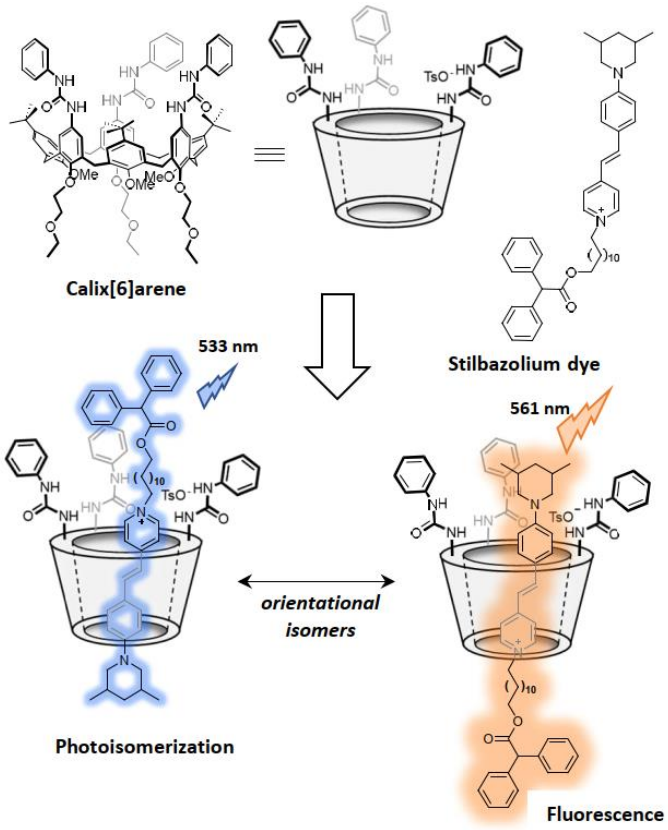
Invited

Heteroditopic calix[6]arene-based intervowen and interlocked molecular devices

Andrea Secchi

Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Italy

Since the downing of supramolecular chemistry, calixarenes have been employed as platforms onto which functional groups and binding sites can be loaded in a regio- and stereocontrolled manner for the recognition of charged and neutral species. However, despite their wider annulus, potentially suitable to bind large guests, the larger members of the calixarene series have been relatively less employed, mainly because of the synthetic difficulties in controlling their conformational flexibility and regioselective functionalization.



In this communication, the achievement gained during the last decade on using the calix[6]arene as a platform to build up structures in which the macrocycle acts as a wheel for the synthesis of oriented (pseudo)rotaxanes will be presented. It will be also shown how these non-symmetric heteroditopic calix[6]arenes (see Figure) may affect the reactivity[1] or spectroscopic properties of their bound guests.[2]

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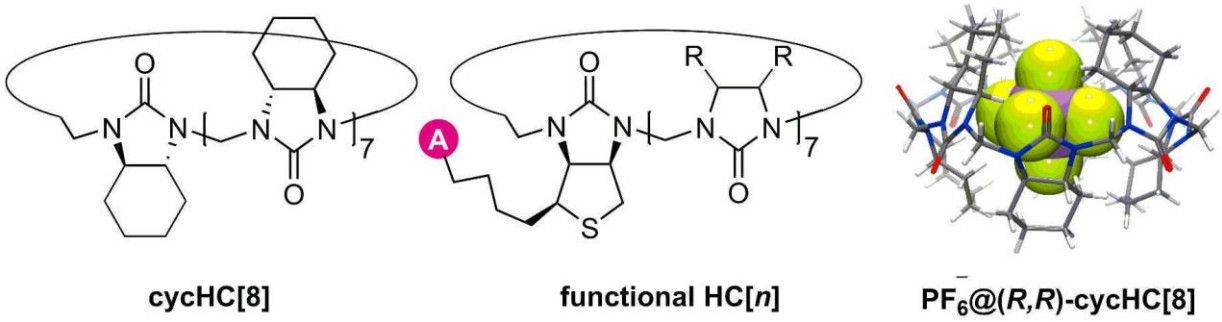
Invited

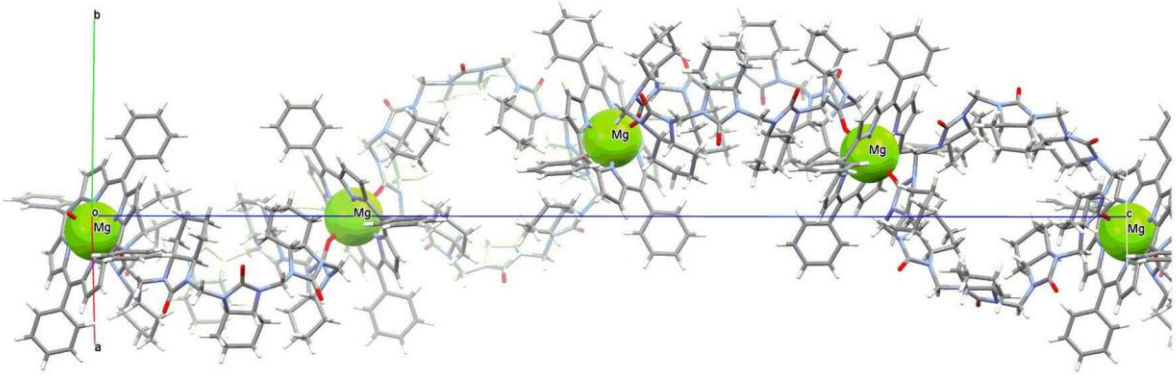
Exploring the potential of hemicucurbiturils: diverse functionality through simple modifications

Riina Aav

Department of Chemistry and Biotechnology, Tallinn Univeristy of Technology, Tallinn, Estonia

Hemicucurbiturils (HCs) are members of the single-bridged cucurbituril family that are formed through templated synthesis in a single step. We have previously shown[1-5] that cyclohexanohemicucurbit[*n*]urils (*n* = 6, 8, 12) can be isolated with the largest diversity in the number of homologues among other HCs. To further increase the structural diversity of hemicucurbiturils, monomers with carboxylic groups, such as biotin, can be utilized to insert new functionality.[6,7] Another way to diversify the functionality of HCs is through their host-guest complexes.[8-10] Properties of new chiral HCs will be discussed.





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Plenary

Bacteria recognition and inhibition by calixarene derivatives

Alessandro Casnati

Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Italy

Bacterial infections have led to a variety of complex issues having a great impact on human wellbeing. These issues include matters involving food safety, water pollution, biodefense, and the identification and treatment of bacterial illnesses. The development of selective, rapid, robust, and inexpensive sensors able to discriminate between different bacterial strains can therefore provide a very useful tool in the management of bacterial infections and to mitigate antimicrobial resistance.[1] Beside the use of biosensors, supramolecular receptors might result a solid alternative in the recognition of bacteria through the binding to their metabolites or to specific elements of their cell wall. Since calixarenes showed remarkable ability to selectively recognized different types of biomacromolecules,[2,3] we used them to distinguish between the three main bacteria families of Gram-positive, Gram-negative and Mycobacteria also using on-cell Saturation Transfer Difference NMR techniques.[4] Our recent results in this research line will be reported.

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Plenary

Mediation of 1,3-dipolar cycloaddition reaction in the cavity of a [4 + 2] octa-imine calix[4]pyrrole capsule

Pablo Ballester[1,2]
ICREA, Catalan Institute of Research and Advanced Studies, Barcelona, Spain
Institute of Chemical Research of Catalonia (ICIQ), The Barcelona Institute of Science and Technology (BIST), Tarragona, Spain

The azide-alkyne Huisgen 1,3-dipolar cycloaddition was accelerated in the cavity of a cucurbit[6]uril[1] and a self-assembled dimeric capsule derived from a resorcin[4]arene cavitand[2]. In both cases, the regioselectivity of the reaction was also altered providing exclusively the 1,4-cycloaddition isomer. In this presentation, I will describe the self-assembly of a [4+2] octa-imine capsule based on calix[4]pyrrole scaffolds and its application as a supramolecular reaction vessel.[3],[4] I will show that the dynamic covalent capsule promotes the cycloaddition reaction between two pyridine-N-oxide derivatives properly functionalized with azide and ethynyl groups at their para-positions. The reactants are bound in the polar capsule's cavity by establishing mainly hydrogen bonding interactions between the oxygen atom of the pyridine N-oxides and the pyrrole NHs of the calix[4]pyrrole hemispheres. The formed hetero-ternary complex results in a constrained convergence of the p-pyridyl substituents favoring their reaction and the exclusive formation of the 1,4-isomer. I will also report on: a) the measured changes in reaction rates using different conditions and b) the calculation of the rate constant of the reaction taking place inside the capsule and c) its comparison with those in the bulk solution and in other molecular vessels.

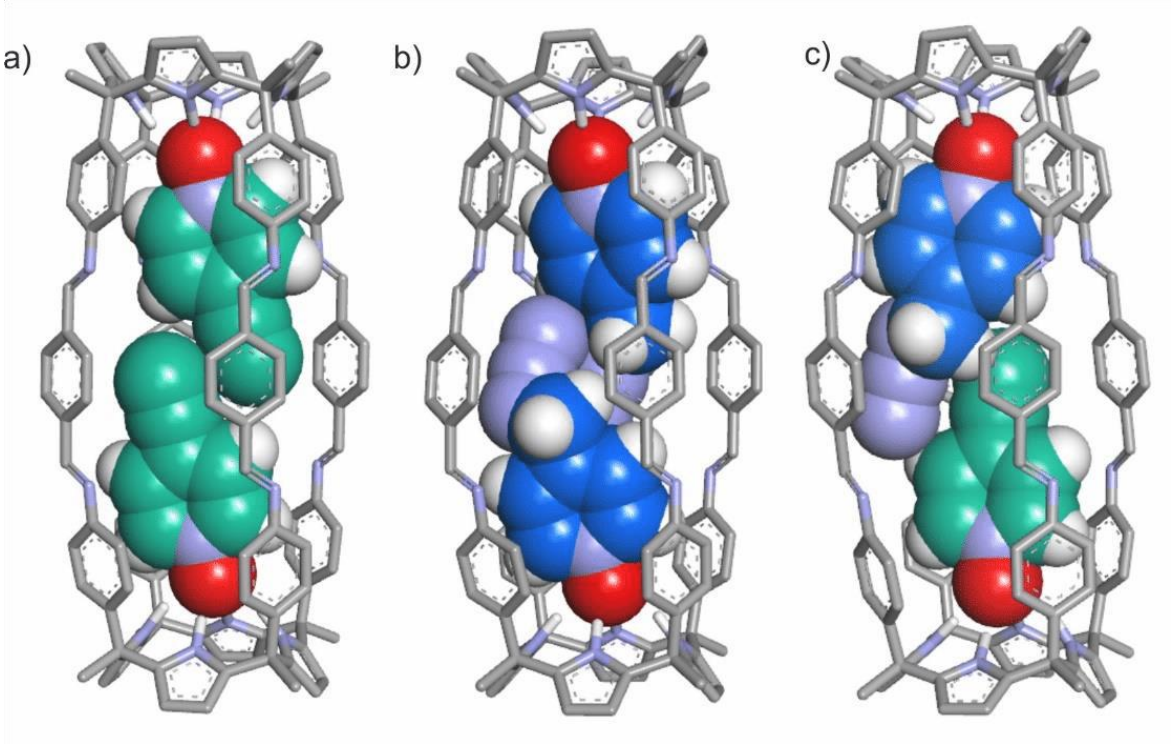

Figure 1. Energy minimized structures (MM3) of the ternary homo-complexes of the pyridine-derivatives and the octa-imine: a) azide, b) ethynyl and c) the hetero-encapsulation complex

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Invited
Supramolecular controlled release of proteins

Adam Urbach
Department of Chemistry, Trinity University, San Antonio, TX, USA

Therapeutic proteins can treat a wide variety of medical issues, but their methods of administration are currently limited, and frequent dosing is often required. Toward the development of controlled release formulations for proteins, we are pursuing an affinity-based strategy using cucurbit[n]uril receptors within a hydrogel matrix. Release kinetics are controlled by the Kd of the ligand, and we have exploited this property to control the kinetics of release of antibodies by conjugating ligands with desired Kd values. This presentation will cover the design, construction, and characterization of this system, showing protein controlled release based on affinity, concentration, and valency.

Invited

Synthesis, conformational properties, and molecular recognition abilities of prismarenes

Carmine Gaeta

Department of Chemistry and Biology "A. Zambelli", University of Salerno, Salerno, Italy

In the last years, many efforts have been focused on studying macrocycles bearing deep-aromatic cavity. Recently[1] we have reported a novel class of chiral macrocyclic hosts, based on methylene-bridged 1,5-naphthalene units, named prismarenes.[1-6] Prismarene macrocycles have an π-electron-rich aromatic cavity and prism-like structures that inspired the prismarene name.[7] Prism[n]arenes exhibit planar chirality, and the hexamers and pentamers show six and five planes of chirality, respectively, which are coplanar with the 2,6-dialkoxynaphthalene rings and the bridged-methylene groups. In this communication, we will discuss aspects related to the synthesis, conformational properties, and (chiral) recognition abilities of this new class of macrocyclic hosts.

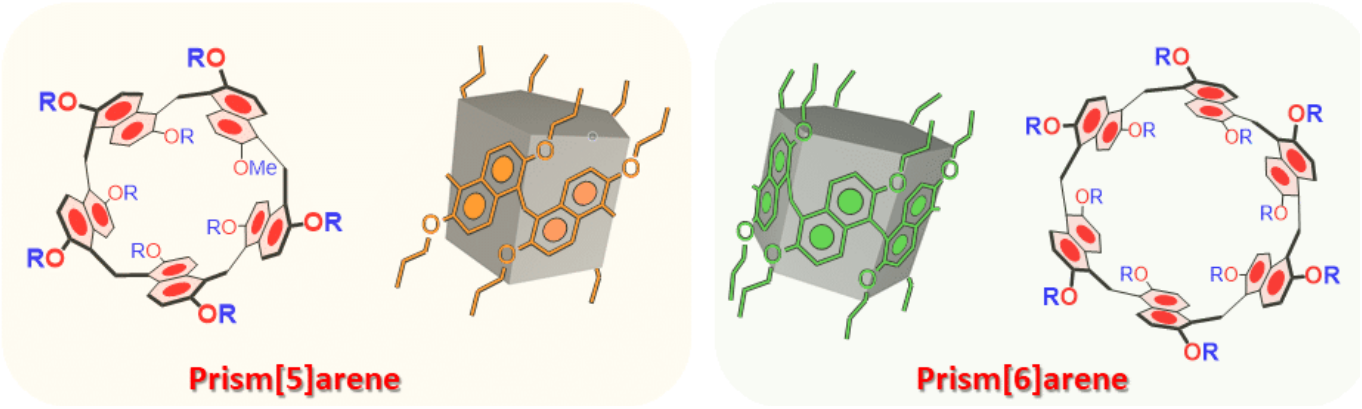

Figure. Chemical drawing of prismarene macrocycles.

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Contributed

Embedding metals centers in deep cavitands - a step closer to natural metalloenzyme

Yuri Tulchinsky
Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem, Israel

Deep cavitands are unique molecules consisting of a resorcin[4]arene macrocycle extended by four aromatic walls. In solution these walls are in equilibrium between an open and a folded state, akin to petals of a flower. When folded, they create a pocket where small guest molecules may be trapped. Combining such a well-defined molecular pocket which exhibits a controllable conformational dynamics together with reactive transition metal centers can lead to novel catalytic systems of an exceptional efficiency and selectivity, comparable to those of natural metalloenzymes. Yet, so far, the biomimetic potential of such systems was not fully realized, since in those attempts, the active metal centers were not located deep enough within the cavity to prevent undesired interactions with the surrounding medium. This was due to the lack of synthetically-modular groups at the bottom part of cavitand molecules.

In this talk I present a conceptually novel design of metallocavitands which provides an ingenious solution to this challenge. Such an architecture features a chelating cage located deep inside the cavitand, allowing access towards a coordinatively unsaturated metal center from within the cavity only, thus imposing size and shape discrimination on potential substrates. We showed that the resulting cavitand-based ligand scaffolds exhibit high affinity towards biologically relevant metals, such as Fe, Mn, and Co, in 2+ and 3+ oxidation states. Moreover, our synthetic methodology allows to modify the metal-chelating groups at both the axial and equatorial positions independently of each other. Such modularity of the primary coordination sphere might be crucial for achieving a desired catalytic activity of the metal center. Importantly, the most distinctive characteristic of deep cavitands, i.e. their unique fluxional conformational behavior, is not compromised by the presence of metal center, since both open and folded metallocavitands were characterized by XRD. Altogether, these novel supramolecular edifices could prove highly efficient for site-selective C-H activation and other challenging reactions.

Contributed

Presice self-assembly of calix[4]resorcinarene-based cages via complementary ligand pairing

Yi-Tsu Chan
Chemistry, National Taiwan University, Taipei, Taiwan

Calix[4]resorcinarene with fourfold symmetry is a commonly used scaffold for generation of coordination-driven self-assembled architectures, but the structural diversity is mostly restricted to dimeric and hexameric species. Herein, the predesigned dynamic heteroleptic complexation based on a complementary pair of terpyridine (tpy) ligands is employed to enhance the topological complexity of resorcinanrene-based assemblies. The quantitative multicomponent self-assembly of a series of resorcinarene-containing metallo-supramolecules, such as dimeric capsules of varying sizes, a Sierpiński triangular prism, and a cubic star, was achieved through the complexation of metal ions with the calix[4]resorcinarene-based tpy ligand and multitopic connectors. The efficient self-assembly methodology presented here leads to facile preparation of resorcinarene-based nanocapsules with tunable size and geometry, which are potential candidates for applications in molecular self-recognition and catalysis.

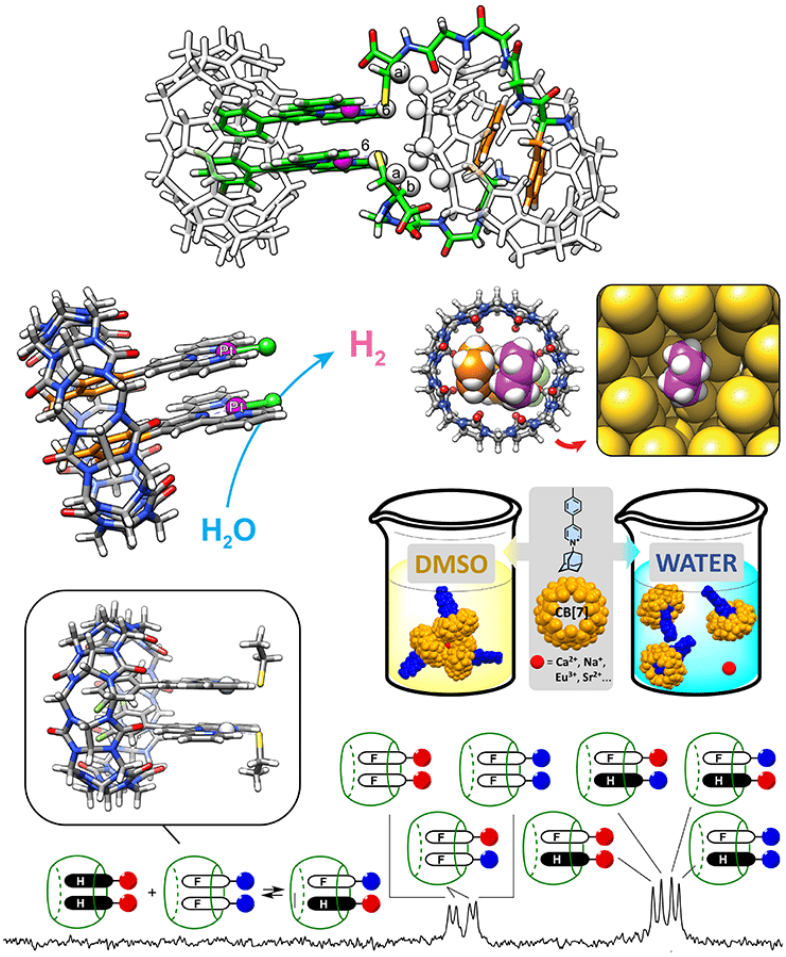
Invited

Cucurbit[8]uril-secured platinum dimers and cation-secured cucurbit[7]uril trimers

Eric Masson

Chemistry and Biochemistry, Ohio University, Athens, Ohio, USA

We will first discuss the formation of CB[8]-secured head-to-head, “stacked” platinum terpyridyl (tpy) acetylide and thiolate dimers. Both positive Pt centers sit on top of each other at one CB[8] portal, leaving the other void of any guest interaction. Favorable dispersive interactions between the stacked tpy ligands and possible metal-metal bonding through dz2-dz2 orbital overlap are proposed as driving forces for the recognition pattern. We will present some self-sorting properties of these assemblies and use them as catalysts for the photoreduction of water. We will then show that a selection of alkali-, alkali-earth and lanthanide cations mediates the aggregation of CB[7] complexes into well-defined trimers in solution, as long as (1) the solvent is dimethyl sulfoxide (and not water or deuterium oxide), and (2) the cavity of CB[7] is filled with a guest that leaves one carbonylated portal available for cation binding. In other terms, we will show that the CB[7]/guest trimer, with its carbonyl groups pointing towards its inner core, acts as a cryptand with exceptional affinity to a selection of metallic cations in dimethyl sulfoxide. Finally, we will conclude with a rather provocative study showing that the binding selectivity of CB[n]s (n = 5 – 8), at least when guests are hydrocarbons or noble gases, can be predicted by mimicking the macrocycles with hard-sphere fluids with low polarities and low polarizabilities and “pre-formed” cavities.



Invited

Supramolecular catalysis in confined space exploiting self-assembling capsules

Carmen Talotta
Dipartimento di Chimica E Biologia "A. Zambelli", Univesità Di Salerno, Fisciano, Salerno, Italy

In recent years, our research group has been investigating several aspects of supramolecular catalysis inside the confined space of self-assembling resorcinarene or pyrogallolarene capsules [1].

In this lecture, we will report our recent results on this topic, emphasizing the catalytic role of the resorcinarene capsule CR6 [2], in promoting metal-free Friedel-Crafts acylation reactions. In particular, it will be discussed the catalytic role of the bridging water molecules of CR6, able to act as H-bonding donor groups for the polarization of the C–Cl bond.

Concerning the pyrogallol[4]arene capsule CP6, it will be highlighted its ability to promote organic reactions by confinement of substrates under appropriate reaction conditions [3].

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Contributed

Second sphere interactions of solvate molecules with lanthanide complexes supported by hybrid calix[4]arene/Schiff-base ligands

Anne Mehnert[1], Lennart Günzel[1], Martin Börner[1], **Berthold Kersting**[1], Ettore Bartalucci[2], Thomas Wiegand[2,3], Alexander A. Malär[3], Beat H. Meier[3], Julius B. Kleine Büning[4], Stefan Grimme[4], Maik Icker[5]

[1]*Institute of Inorganic Chemistry, Leipzig University, Leipzig, Germany*

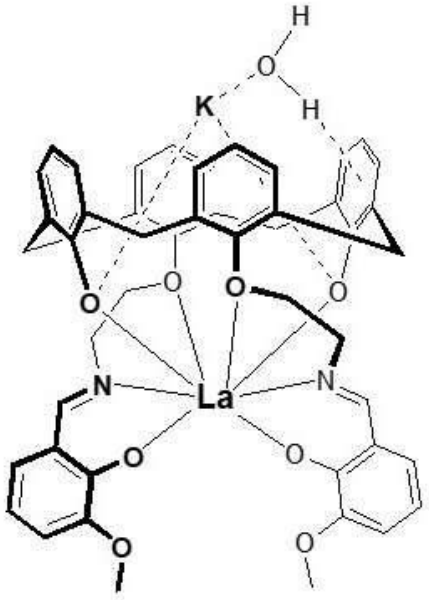
[2]*RWTH Aachen University, Institute of Technical and Macromolecular Chemistry, Aachen, Germany*

[3]*Physical Chemistry, ETH Zürich, Zürich, Switzerland*

[4]*Clausius Institute of Physical and Theoretical Chemistry, University of Bonn, Bonn, Germany*

[5]*Institute of Analytic Chemistry, Leipzig University, Leipzig, Germany*

The synthesis, structures, and properties of some lanthanide complexes supported by calix[4]arene ligands with two appended salicylaldimine units are reported. Particular attention is paid to structural elucidation of second sphere interactions of co-crystallized ROH molecules (R = H, alkyl) with the aryl rings of neutral [M@LnL] complexes (M = Cs^+, Rb^+, K^+, Ln = La^{3+}, Eu^{3+}). X-ray crystallographic and NMR spectroscopic studies reveal an isostructural set of complexes with eight-coordinate lanthanide ions surrounded by calixarene O and Schiff base N,O donors. The alkali metal cations sit in the calixarene cavities held in place by cation-π and electrostatic (phenolate···M^+) interactions. The aryl rings of the calix[4]arenes were found to have a strong propensity to interact with the co-crystallized solvate molecules by OH···π interactions.



Acknowledgements

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Contributed

Noncovalent modulation of chemoselectivity in the gas phase by cucurbit[7]uril

Elina Kalenius

Department of Chemistry, University of Jyväskylä, Jyväskylä, Finland

In the gas phase, thermal activation of host-guest complexes leads commonly to dissociation of the complex into its individual components. Chemical reactions of the encapsulated guest molecules are only found in exceptional cases. We previously showed, in mass spectrometric study for bicyclic azoalkenes, that cucurbiturils are able serve as molecular containers and enhance the inner-phase reactivity of the guest molecules.[1] More recently, we have discovered that cucurbit[7]uril (CB7) can even modulate reactivity and reaction mechanisms of 1-amino-methyl-2,3-diazabicyclo[2.2.2]oct-2-ene (DBOA) depending on protonation state of the formed inner-phase host-guest complex.[2] The chemical reaction pathways observed with protonated host-guest complexes stand in contrast to the gas-phase chemistry of uncomplexed monoprotonated DBOA. In fact, the full spectrum of organic-chemical reaction types can be covered, ranging from heterolytic bond cleavage to homolytic bond cleavage and to concerted cyclo-reversion reaction. These results show how a noncovalent approach can be employed to gain control over chemoselectivity and how to steer multiple pathways of thermally activated reactions of small molecules in gas phase.

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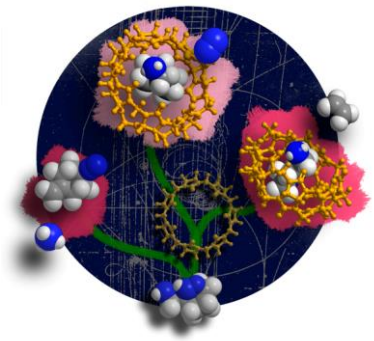

Plenary

Supramolecular hosts as enzyme mimics

F. Dean Toste
Department of Chemistry, University of California, Berkeley, California, USA

Modern organic synthesis relies heavily on selective reactions to enable sustainable access to fine chemicals and pharmaceuticals. In enzymatic catalysis, nature employs various mechanisms to achieve the desired selectivity and activity. Similarly, we have explored organic and organometallic reactions catalyzed by self-assembled water-soluble supramolecular clusters. These supramolecular hosts offer a confined environment that can enhance selectivity and accelerate reaction rates, as well as enable new product formation not achievable by uncatalyzed processes. The lecture will focus on the research in the field of supramolecular catalysis, discussing the reactions promoted by encapsulation, the underlying interactions enabling catalysis, and the mechanisms involved.

Invited

Supramolecular polymers formed by molecular recognition of calixarenes

Takeharu Haino[1,2]
Department of Chemistry, Graduate School of Advanced Science and Engineering, Hiroshima University, HIgashi-HIroshima, Hiroshima, Japan
International Institute for Sustainability with Knotted Chiral Meta Matter (SKCM2), Hiroshima University, Higashi-Hiroshima, Hiroshima, Japan

Our group has been developing calixarene-based synthetic host molecules that have been used for constructing supramolecular polymers with unique structures and topologies. We will describe two main topics, encompassing supramolecular helical fullerene polymers and supramolecular graft polymers. A biscalix[5]arene encapsulates [60]fullerene within the cavity, which was utilized for supramolecular fullerene polymers. We newly designed chiral ditopic tetrakiscalix[5]arene hosts and a dumbbell-shaped fullerene. The calix[5]arene-fullerene host-guest complexation drove the supramolecular polymerization of a dumbbell-shaped fullerene.[1] The helical fullerene array was visualized by atomic force microscopy. The right-handed and left-handed supramolecular helical polymers were self-sorted when a racemic mixture of ditopic hosts was employed.[2]
A resorcinarene cavitand with four bipyridine units is self-assembled via metal coordination. The cavity of the self-assembled capsule encapsulates 4,4`-diacetoxybiphenyl as a guest. Polymer-attached capsule bound 4,4`-diacetoxybiphenyl units located to polyesters, which resulted in supramolecular graft polymers.[3,4] The capsule encapsulation extended the chain of the polyester chains via steric interaction between the capsules on the same polymer chain. The graft polymer gels in tetrachloroethane showed self-healing properties.

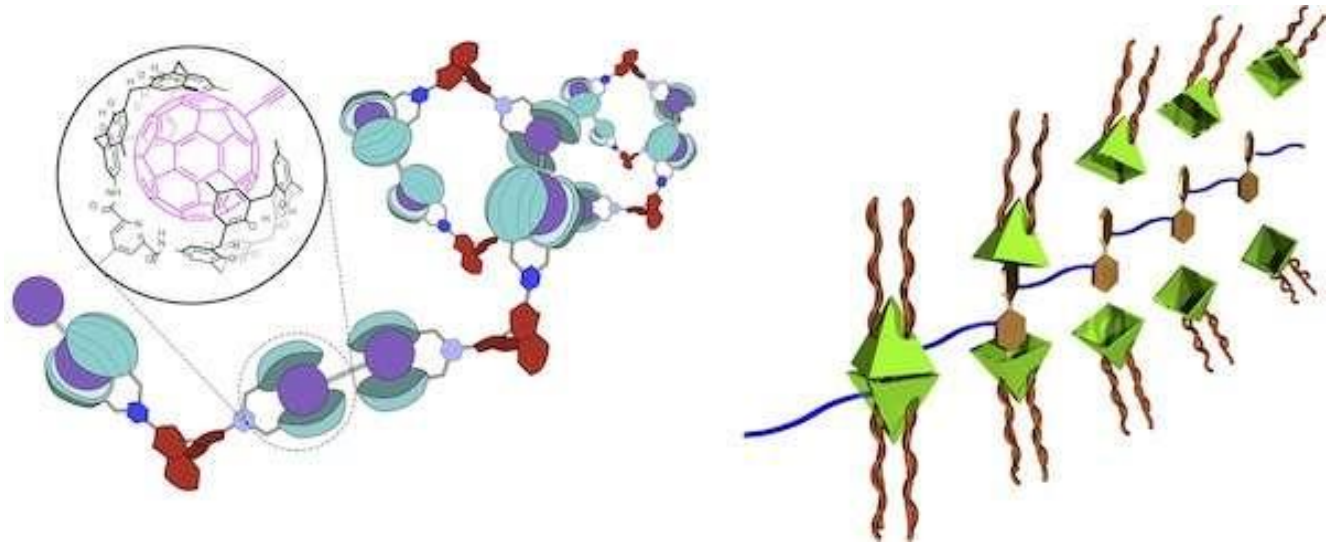

Figure 1. (left) Supramolecular helical fullerene polymer. (right) Supramolecular graft polymer.[1,3]

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Invited

NMR exchange dynamics studies of metal-caped cyclodextrins uncover unprecedented host-guest interactions in water

Amnon Bar-Shir
Molecular Chemistry and Materials Science, Weizmann Institute of Science, Rehovot, Israel

Metal-capped molecular hosts are widely developed in supramolecular chemistry, benefitting from the inner cavity's hydrophobic nature and the metal center`s electrochemical properties. Implementing these supramolecular hosts in a desired field is driven by reversible host-guest interactions. However, studies of such dynamic processes are limited for specific (and slow) dynamic regimes, primarily due to the inaccessibility of proper analytical tools. Therefore, robust approaches are greatly needed, which can be quickly and extensively used for the quantitative evaluations of kinetic characteristics of such molecular systems. We show that the pseudo-contact shifts (PCS) properties of the paramagnetic metal center in lanthanide-capped cyclodextrins (Ln-α-CD and Ln-β-CD) allow us to study very fast guest exchange rates with the GEST NMR method developed by us. Namely, paraGEST, we show the ability to use a library of Ln-α-CDs to generate artificial colors for MRI studies. In addition, we show that using Ln3+ metal having strong PCS induction capabilities such as Yb3+ (compared to Eu3+ and Ho3+) in Ln-β-CD provides paraGEST with an enhanced spectral resolution uncovering that a specific molecular guest can adopt two different orientations within the Ln-β-CD. In contrast, within the smaller and symmetric (c2) Ln-α-CD, the exact molecular guest adopts a single orientation, emphasizing the very different binding features of molecular guests to metal-caped α- and β- CDs. Our results show that paraGEST NMR is beneficial for studying various binding features in metal-caped molecular hosts.

Contributed

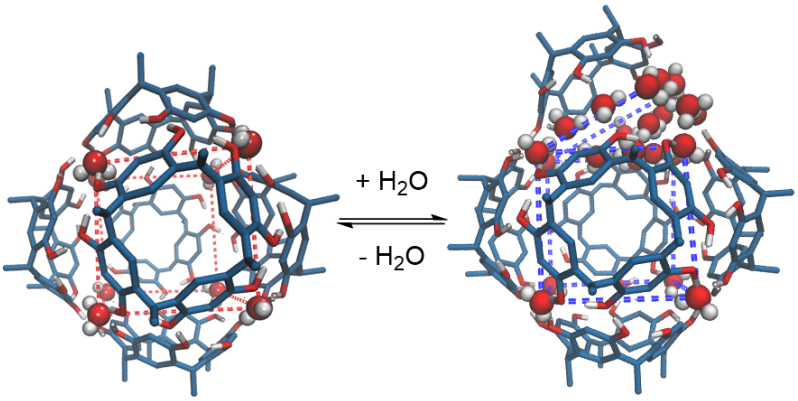
The dynamic behavior of hexameric resorcin[4]arene capsules: insights from NMR spectroscopy and molecular simulations

David Poole[1,2], Simon Mathew[1], Joost Reek[1]
[1]*van 't Hoff Institute of Molecular Sciences, Universiteit van Amsterdam, Amsterdam, Netherlands*
[2]*Amsterdam Institute of Molecular and Life Sciences, Vrije Universiteit Amsterdam, Amsterdam, Netherlands*

The hexameric resorcin[4]arene capsule is a supramolecular assembly that catalyzes a range of reactions owing to its Brønsted acidity and internal hydrogen-bond network.[1] Interestingly, water plays critical roles in the formation of these capsules by incorporation of 8 water molecules to complete the hydrogen-bond network as well as the acidity of these capsules by facilitating proton exchange.[2,3]

From subtle changes in the ^{1}H-NMR spectra concomitant to the solvent water content, we identified two distinct capsule morphologies differing by their degree of hydration.[4] This hydrated morphology bears 15 water molecules rather than the minimal 8 needed for capsule formation. We modelled this morphology using molecular dynamics simulations, revealing the integration of additional water molecules into an expanded hydrogen-bond network, with 15 water molecules being thermodynamically favored. Using ^{31}P-NMR with a phosphine oxide probe, we determined that the hydrated morphology was significantly more acidic with an Guttman–Becket Acceptor Number of 68, similar to $TiCl_4$. Lastly, we demonstrated the effect of capsule morphology using a model Diels–Adler reaction finding the hydrated capsule is responsible for a majority of catalysis.

While changes in hydration were observed with NMR, molecular dynamics simulations of supramolecular assemblies were critical to elucidate structural features arising in solution guiding our further studies. Additionally, we will discuss further refinement of these approaches to study capsule stability and dynamics.



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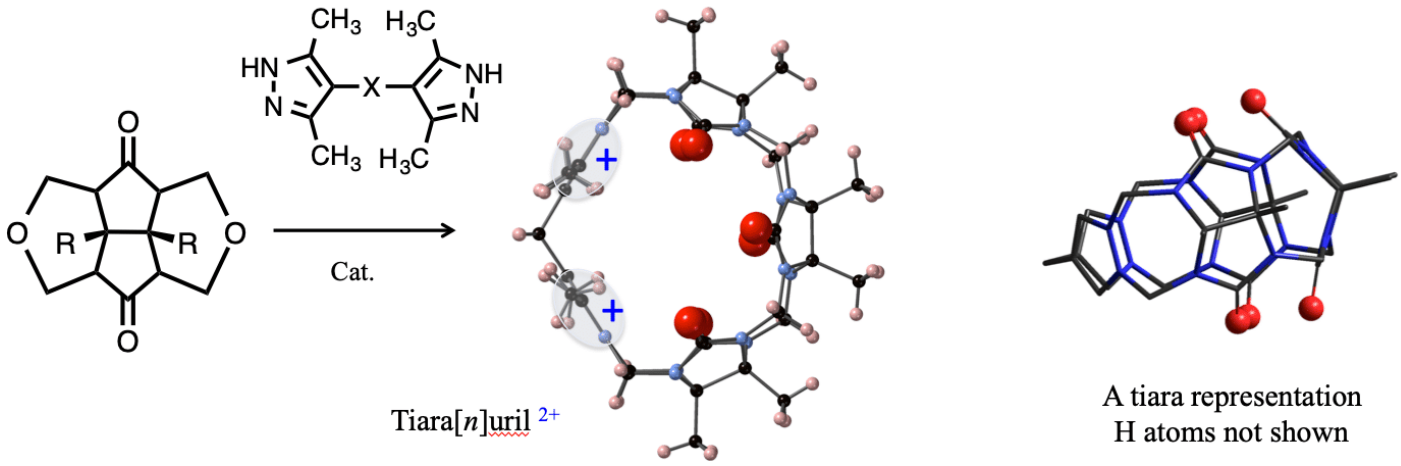
Invited

The host-guest properties of tiara[*n*]uril

Anthony Day[1], Satyavisal Pen[1], Islam Marae[1], Asmaa Sakr[1]
School of Science Canberra Campus, University of New South Wales, Canberra, ACT, Australia

Recently, we reported the synthesis of a new dicationic macrocycle that is derived from the condensation of dipyrazoles and several substituted glycoluril diethers to complete the cyclisation.[1,2] The molecular skeleton of the simplest of these macrocycles has a structure in a form similar to that of a tiara, where the C=O groups represent the jewels at the front and the dipyrazolium the band at the back (Scheme 1). In view of the resemblance, we named this family of molecules tiara[*n*]uril.

We are now exploring the host-guest properties of these highly water soluble macrocycles, with a view to understanding their potential as host molecules. The arc of C=O's at the top and bottom of each portal and the known characteristic feature of the concave face of the glycoluril moieties within a cavity but opposite a diffuse cationic wall suggested a potential for lipophilic, H-bonding and electronegative molecules as guests. We have been testing this assumption and some of our findings in this context will be presented.



Scheme 1. General reaction on the left and a resemblance to a tiara on the right.

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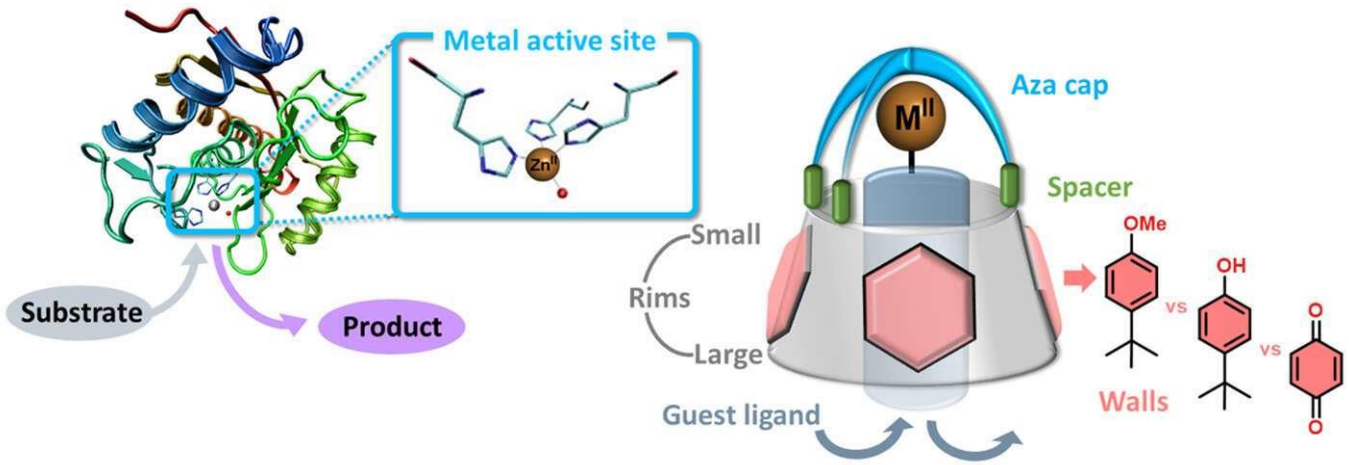
Plenary

Redox-active cavities and metal ions: a promising combination inspired by Nature

Olivia Reinaud[1]
Lab. Chimie Et Biochimie - UMR 8601, Univ. Paris Cité, Paris, France

In the biomimetic context, many studies have evidenced the importance of the 1st and 2nd coordination spheres of a metal ion for controlling its properties. Here, we propose to evaluate a yet poorly explored aspect, which is the nature of the cavity that surrounds the metal labile site. Three calix[6]arene-based aza-ligands[1] are compared, that differ only by the nature of cavity walls, anisole, phenol or quinone (L^{OMe}, L^{OH} and L^{Q}) surrounding the metal labile site. Exploring the coordination properties of their Zn^{II} complexes revealed important differences in terms of metal ion binding, guest ligand affinities, and ligand exchange kinetics.[2] These functional groups (phenol, quinone) can play the role of cofactor in catalysis. Indeed, they can act as acid/base co-catalyst participating to proton transfers, but also as electron reservoir (hydroquinone) during redox processes. Preliminary results will be presented relative to the corresponding cobalt complexes and their redox activity illustrated by electrochemical studies related to CO_2 electro-reduction.[3]



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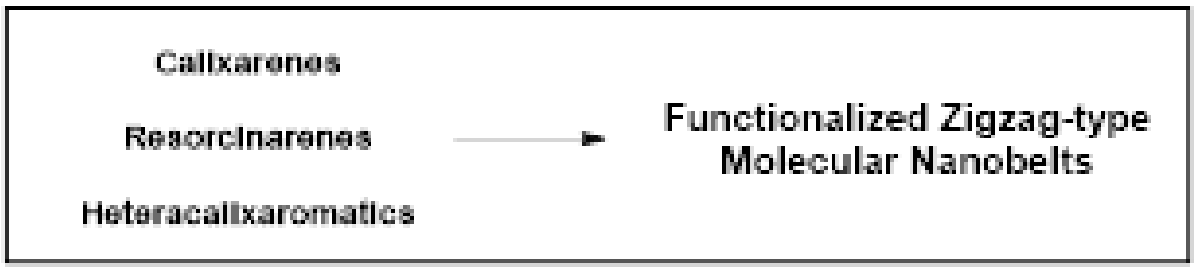
Plenary

From calixarenes and heteracalixaromatics to functionalized zigzag molecular belts and molecular recognition

Mei-Xiang Wang
Chemistry, Tsinghua University, Beijing, China

In this talk, I will present the latest development of our study on the chemistry of zigzag-type molecular belts.1,2 The synthesis of functionalized hydrocarbon belts and their heteroatom-embedded analogs from conventional calixarenes, resorcinarenes and heteracalixaromatics will be discussed. Structures of acquired belt molecules and their applications in molecular recognition will be demonstrated.3



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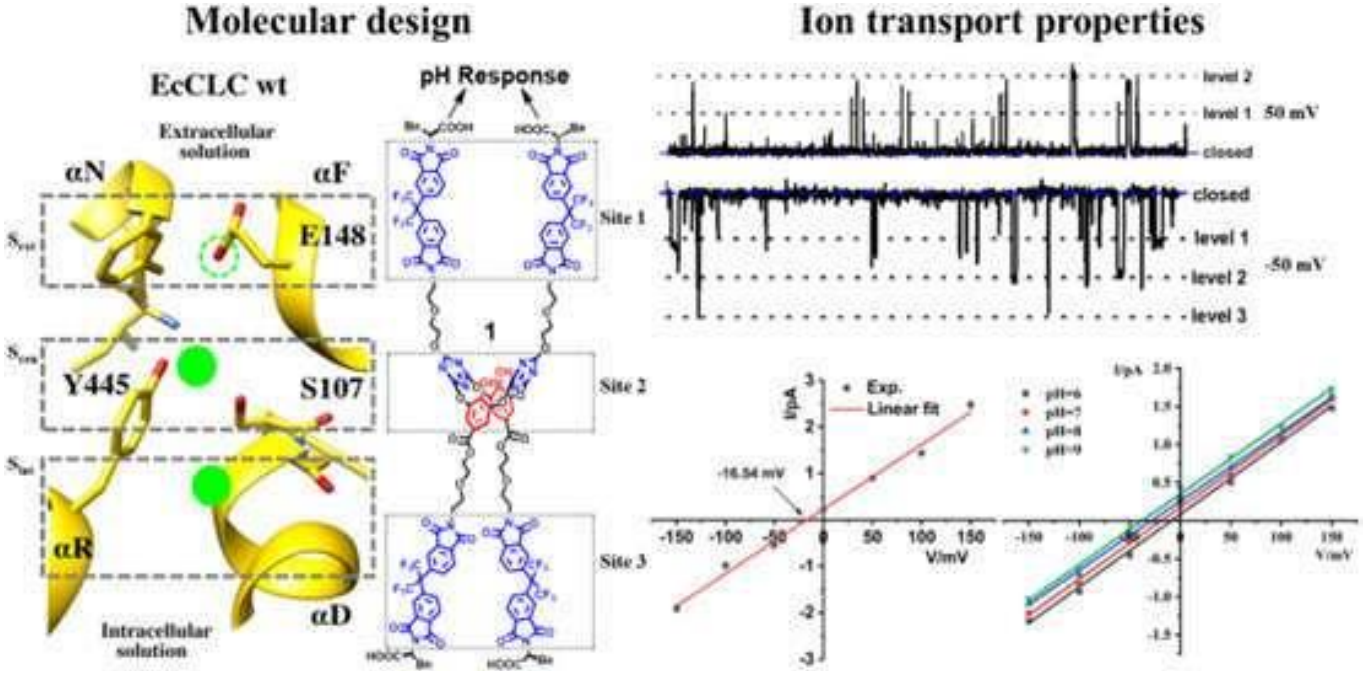
Contributed

Artificial anion channels

De-Xian Wang

Laboratory of Molecular Recognition and Function, Institute of Chemsitry, Chinese Academy of Sciences, Beijing, China

Chloride is the most abundant anion in nature. The transport of chloride across membranes is the basis of important physiological processes such as regulating electrical excitability, transepithelial transport, and cell volume.[1] Chloride transfer across the cell membrane is primarily mediated by chloride channel protein such as ClC and CFTR.[2] Genetic defects in chloride channels could cause many severe diseases, including Bartter syndrome, Dent's disease and cystic fibrosis.[1,2] It is anticipated that the preparation of a simple artificial molecule, which can mimic both the shape and function of the selective pore, would be one of the most interesting attempts. Presented here are artificial channel molecules that mimics the shape and function of the natural chloride channel selective pore. To facilitate the transport of chloride along a unimolecular pathway, anion-p interactions were introduced as the noncovalent driving force. The hourglass- or funnel-like molecules were constructed with 1,3-alternate tetraoxacalix[2]arene[2]triazine as the narrowest (central) unit, diglycolamine-linked imide arms were tethered as the extending part, and phenylalanine moieties were fixed as the terminal anchoring groups. [3,4] Chloride transport activity and Cl-/K+ selectivity and chloride transport coupled sub-conductance were demonstrated.



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Contributed

Design and synthesis of cyclic nucleobase as a new scaffold for molecular recognition and ion separation

Xiaodong Shi

Department of Chemistry, University of South Florida, Tampa, Florida, USA

Guanosine with 2-amino and 6-carbonyl groups as a hydrogen bond donor and receptor can assemble into a unique G_4-quartet building block through ion-dipole interactions between the central oxygens and cations. With the modification on guanine (8-aryl) and ribose (sterically hindered 2', 3'position), a well-defined metal templated G_8-octamer was formed. K^+ complexes showed an excellent binding affinity over Ba^{2+}, even over the potassium 18-crown-6, indicating the potential potassium receptor. Furthermore, the covalently tethered 8-aryl G_8-octamer remains intact in protic solvent, which demonstrates the significantly enhanced stability of G-quadruplexes. This is one of the few stable G-quadruplex systems from small molecule self-assembly to survive in a H-bond competitive environment. Isoguanosine is a structural isomer of guanosine. The self-assembled pentaplexes are excellent Cs^+ ionophores. To avoid the dynamic equilibrium of isoG subunits in solution, the post-assembly modification of a templated isoG complex through the olefin metathesis is applied to cross-link subunits within isoG pentaplexes constructing cyclic pentamer. The covalently tethered isoG oligomer can be used more effective than the corresponding free monomer to extract Cs^+ from an aqueous source into an organic receiving phase. The results clearly demonstrate the power of covalent tethered molecular self-assembly for the construction of highly selective and stable ionophores. The successful synthesis and study of these covalent tethered cyclic complexes based on the supramolecular template are very promising building blocks in chemical, material, and medicinal research.

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Invited

Helix-based transmembrane nanochannels with selective transport activities

Junqiu Liu

College of Material, Chemistry and Chemical Engineering, Hangzhou Normal University, Hangzhou, Zhejiang, China

Natural protein channels have evolved with exquisite structures to transport ions selectively and rapidly. Learning from nature to construct biomimetic artificial channels is always challenging. Here we show a series of synthetic helix which exhibited highly selective and ultrafast ion transport behaviors. Such artificial channels exhibited high selectivity ratios during transmembrane ion conduction. The disassembly and reassembly of hollow helical tubes gave rise to the reversible switching of channel activity in situ inside the bilayers. The synthetic helical system provides the first model of reversible ligand-gated ion channel by means of dynamic transition between single and double helices, which will be available for developing intelligent artificial nanochannels for potential biological and medicinal applications[1-5].

Acknowledgement: This work was supported by the National Natural Science Foundation of China (Nos. 22161142015 and No.22275046).

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Invited

Liposome-enhanced suprabiomolecular sensor systems

Andreas Hennig

Center for Cellular Nanoanalytics (CellNanOs) and Department of Biology and Chemistry, Universität Osnabrück, Osnabrück, Germany

Water-soluble, macrocyclic host molecules such as calixarenes and cucurbiturils have afforded new avenues in the design of useful sensors and assays for monitoring biomolecular processes. This includes new enzyme assays[1] as well as methods to monitor transport of ions, low molecular weight drugs, and peptides across lipid membranes.[2]

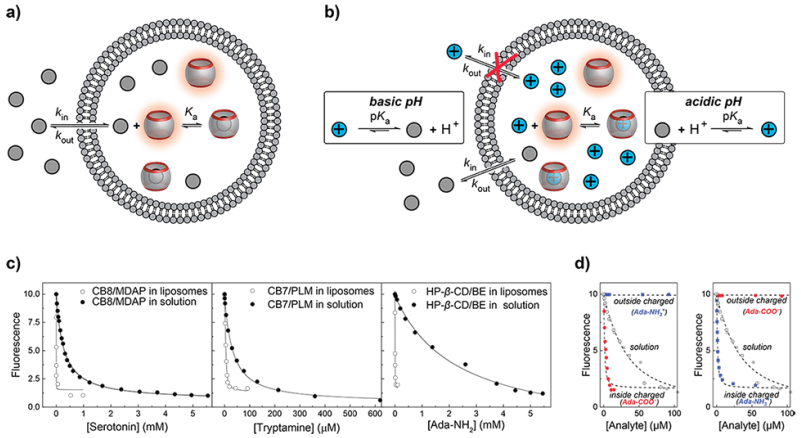

Figure 1. Liposome-enhanced sensing.

Most recently, we have shown that liposome encapsulation of supramolecular chemosensors can greatly enhance the sensitivity and selectivity of the encapsulated sensor (Figure 1).[3] By application of pH gradients, protonatable biologically relevant analytes can be enriched in the vesicle lumen, such that the liposome-enhanced sensor systems afford an increased sensitivity. For example, the sensitivity of the cucurbit[8]uril/2,7-dimethyldiazapyrenium (CB8/MDAP) chemosensor for the neurotransmitter serotonin could be increased by a factor of ca. 135 in solution and ca. 50 in blood serum. Similarly, enhancement factors in the range of 10-200 were found for other host-dye reporter pairs. We have further shown, that hydroxypropyl-β-cyclodextrin (HP-β-CD), which cannot discriminate between adamantane carboxylic acid and adamantylamine in solution becomes strikingly selective using our pH gradient-based enhancement strategy. The approach can be further advanced towards miniaturized, liposome-enhanced suprabiomolecular sensor systems using gated membrane transport mechanisms, enzyme-mediated recognition, multi-color sensing, and pattern recognition.[4]

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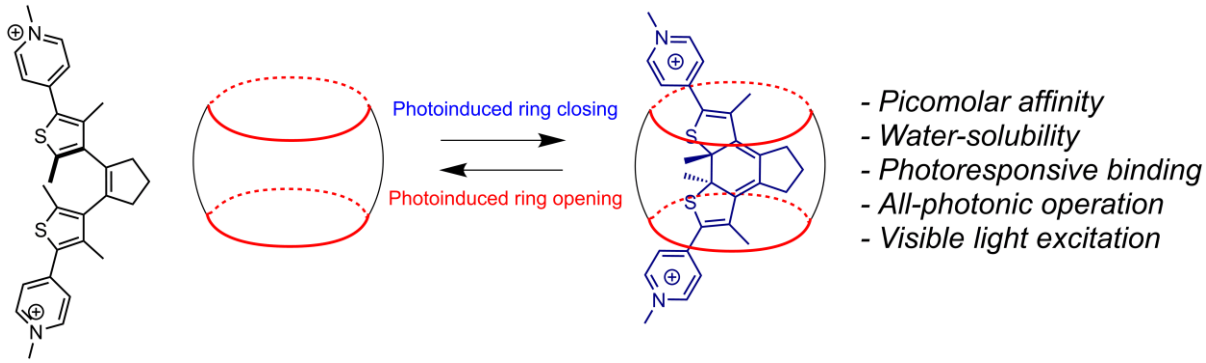
Invited

Photoresponsive dithienylethene host-guest complexes with cucurbit[8]uril

Nuno Basílio[1], Miriam Colaço[1], Patrícia Máximo[1], Uwe Pischel[2], A. Jorge Parola[1]
[1]*Laboratório Associado para a Química Verde (LAQV) - Rede de Química e Tecnologia (REQUIMTE) - Departamento de Química, Faculdade de Ciências e Tecnologia - Universidade NOVA de Lisboa, Caparica, Portugal*
[2]*CIQSO – Centre for Research in Sustainable Chemistry and Department of Chemistry, University of Huelva, Huelva, Spain*

Host-guest pairs have emerged as promising building blocks for the development of advanced supramolecular systems, molecular machines, and self-assembled materials. Despite the growing number of new host-guest systems, the design of complementary binding pairs with high affinity and selectivity in aqueous environments remains a significant challenge. Our group has recently reported new host-guest affinity pairs based on cucurbit[8]uril (CB8) and photochromic dithienylethene (DTE) guests, demonstrating binding affinities of log K 11 in water.[1-3] These remarkable affinities can be modulated with light stimulation due to the exceptional selectivity (Kclosed/Kopen up to 10000-fold) displayed by CB8 towards the closed DTE isomers. In this communication, I will present our recent work on CB8:DTE host-guest systems and discuss potential thermodynamic and structural factors responsible for the observed selectivity.



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Plenary

Advancing supramolecular sensing strategies: cucurbit[n]uril macrocycles for bioactive small molecule detection in biofluids

Frank Biedermann

Institute of Nanotechnology, Karlsruhe Institute of Technology, Karlsruhe, Germany

The development of high-fidelity detection mechanisms for bioactive small molecules in biofluids presents a significant challenge. This presentation discusses innovative approaches that utilize cucurbit[*n*]uril macrocycles as high-affinity binders for improved selectivity and sensitivity.

In one strategy, we use novel cucurbit[7]uril-dye conjugate that adapts to salt-induced changes. This enables the successful differentiation of 14 bioorganic analytes via a data-driven method involving stepwise salt addition, with mechanistic insights gained through ion mobility experiments and density functional theory calculations.[1]

We also showcase a cucurbit[8]uril-based rotaxane chemosensor capable of detecting the health-relevant biomarker tryptophan at physiologically relevant concentrations in complex biofluids. This innovative chemosensor facilitates high-throughput screening, label-free enzymatic reaction monitoring, and chirality sensing while overcoming existing limitations of other supramolecular host-guest chemosensors for tryptophan.[2]

Finally, we discuss our findings on a chemiluminescence-based supramolecular assay, designed for enhancement of the signal-to-noise ratio. The host-guest complex of a chemiluminescent phenoxy 1,2-dioxetane and cucurbit[8]uril permits low-micromolar detection of drugs in human biofluids. in Our work demonstrates the potential of cucurbit[n]uril macrocycles in developing supramolecular sensors for molecular diagnostics, paving the way for future applications in medical and environmental monitoring.[3]

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