

## Progress of calixcrowns chemistry

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**Abstract** The present short paper shows the progress of the calixcrowns chemistry. Calixcrowns which were first investigated for their metal complexation properties are now reaching new fields of research wider than supramolecular chemistry.

**Keywords** Calixcrowns · Nanochemistry · Immobilization of proteins · Single-crystal–single-crystal transformation

The present paper does not intend to be a review on calixcrowns chemistry but rather shows its progress in research fields wider than supramolecular chemistry. Its subject stems its origin from the last sentence of a recent very informative review article of Salorinne and Nissinen [1]: “The chemistry of calixcrowns has not found its limits so far”. In this article the authors reviewed the synthesis and complexing properties of calixcrowns, calixbiscrowns and related compounds such as resorcinarene crowns. These macrocycles exhibit remarkable ionophoric properties toward alkali and alkaline earth metal cations, as well as, to amines and (alkyl) ammoniums [1].

Besides these studies concerning selective complexation of metal cations and their applications in supramolecular techniques, various functionalised calixarenes have been

shown to have “supramolecular” properties, in a wide sense, possibly exploitable in what is the nascent “nanoworld” of the future as for instance metal-tunneling, molecular machines, nanotubes, immobilization of proteins and crystal-to-crystal transformation.

Calix[4]arenes can exist under four discrete forms: cone, partial cone, 1,2-alternate, and 1,3-alternate depending on the topology of the four aromatic rings (Scheme 1).

The calix[4]biscrowns are in the 1,3-alternate conformation which implies the formation of a square aromatic tunnel allowing the communication between the two crown-ether metal-binding sites. It was shown in several cases the oscillation of cations (alkalis and ammonium) through this  $\pi$ -base tunnel (Scheme 2), [2, 3].

This observation has led to the obvious design of 1,3-alternate calix tubes as cation- [4, 5] and anion- [6, 7] conducting channels through membranes such as phospholipids bilayers or liposomes (Scheme 3).

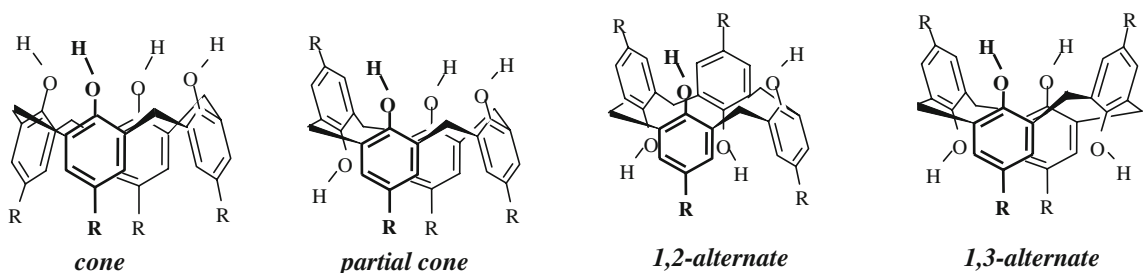
Using the 1,3-alternate calix[4]crown unit as molecular segments it has been built calix[4]arenes nanotubes by modular synthesis with a metal shuttling through several calix crown units (Scheme 4), [8].

Filling single-walled carbon nanotubes (SWNTs) with foreign guest species is an emerging area of research [9]. In this respect, 1,3-alternate calixarene-based nanomaterials have been prepared with application in sensing, storage and fixation of  $\text{NO}_x$  gases [10, 11]. Molecular machines are in vogue and scattered examples are found in literature of thermally, chemically, electrochemically and/or photochemically labile molecular systems or devices, sensors, logic gates etc. [12–14]. The globular shape of calix[4]arenebiscrowns has been exploited to prepare molecular mappemondes (globes) and gyroscopes (Scheme 5).

They are constructed from calix[4]biscrowns-6 held in the arms of a polyether loop via 1 + 1 condensation [15].

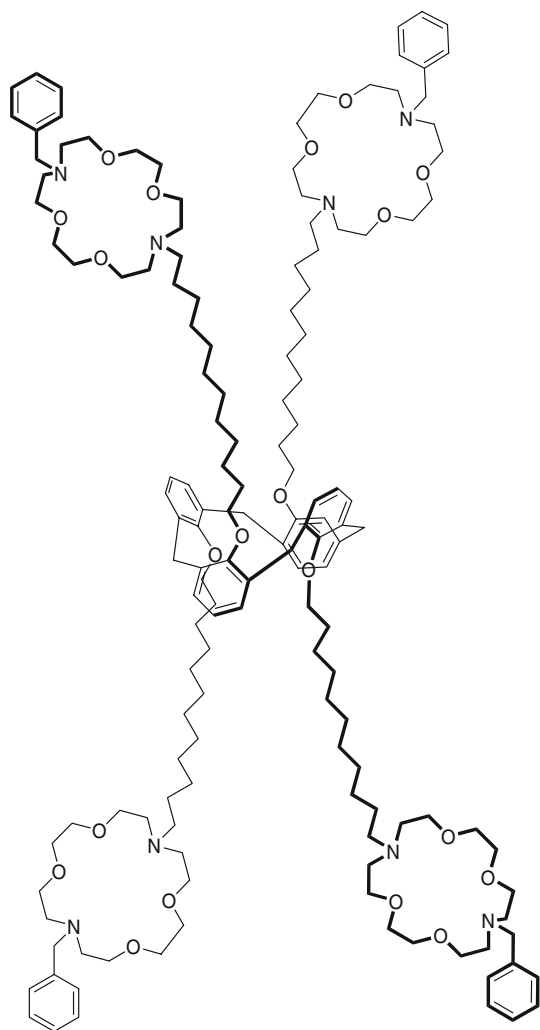
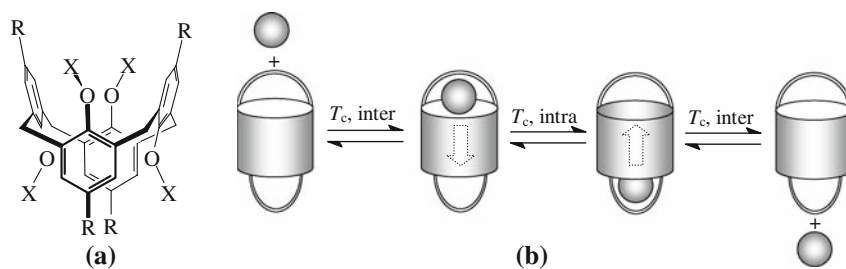
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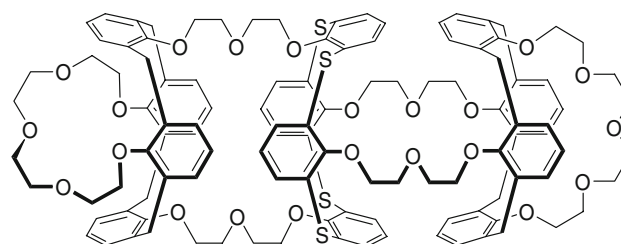


**Scheme 1** The four discrete conformations of calix[4]arenes

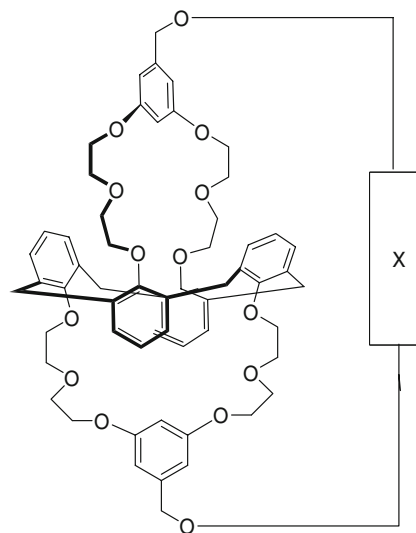
**Scheme 2** Representation of a calix[4]arene in the 1,3-alternate conformation (**a**) and of the metal oscillation through the  $\pi$ -base tunnel (**b**)



**Scheme 3** Representation of a calix[4]arene in the 1,3-alternate conformation used as a conducting channel [4, 5]



**Scheme 4** A calix[4]arene nanotube built with calixarenes in the 1,3-alternate conformation [6]



**Scheme 5** Representation of a calix-mappemonde [10]

Depending on the length of the polyether arm, a 2 + 2 dimer was also isolated, leading to a molecular mill [16]. The spinning of the calix unit can be stopped in the

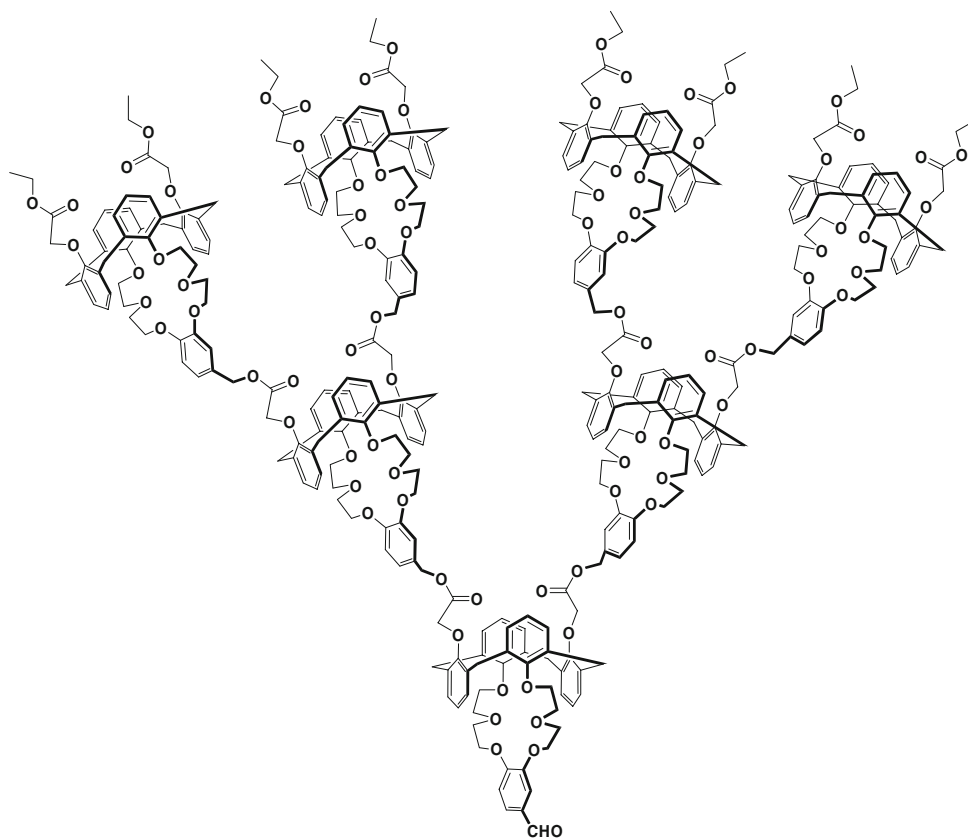
presence of large amounts of ammonium picrate. Dendrimers are an important family of molecules spanning applications in orientated disciplines such as material science and pharmaceutical chemistry and industry [17]. Calixdendrimers [18] some of them being constructed from calixcrowns [19] have been published (Scheme 6).

Protein microarrays (protein chip technology) have recently had an explosion of interest due to the advances in proteomics, robotics, microelectronics, and bioinformatics [20]. Calixcrowns were used to fabricate protein chips for enzyme activity assay, antibody screening and protein–protein interaction, protein–DNA interaction through non-covalent molecular interactions. It has been prepared highly sensitive microarray protein chips, ProteoChips, coated with ProLinker A and ProLinker B

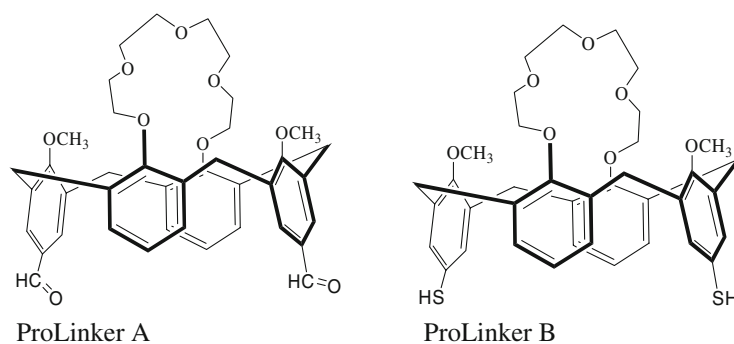
(Scheme 7), two novel calixcrown derivatives with a bifunctional coupling property that permit efficient immobilization of captured proteins on solid matrixes and make high-throughput analysis of protein–protein interactions possible.

The analysis of quartz crystal microbalance showed that both monoclonal antibody (mAb) and antigen (Ag) bound to the gold film of the sensor surface coated with ProLinker B and that it is useful for studies of mAb–Ag interactions. ProteoChip, aminated glass slide coated with ProLinker A, was also demonstrated to be useful for preparation of high-density array spots by using a microarrayer and for analysis of analyte Ags either by direct or sandwich methods of fluorescence immunoassay. The detection sensitivity of ProteoChip was as low as 1–10 femtogram/mL of analyte

**Scheme 6** A calixdendrimer constructed with calixcrowns units [14]

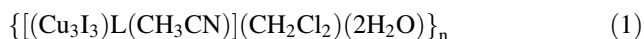


**Scheme 7** Calixcrowns as ProLinker A and ProLinker B

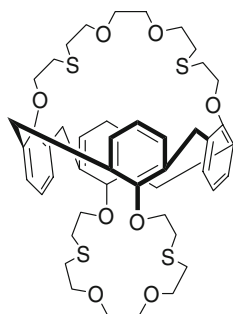


protein, useful for detection of tumor markers. ProteoChip was also useful for studies of direct protein–protein interactions as demonstrated by analysis of integrin–extracellular matrix protein interaction. These experimental results suggest that ProteoChip is a powerful tool for development of chip-based lead screening microarrays to monitor protein–protein interactions (i.e., drug target) as well as for biomarker assays which require high detection sensitivity [21–23]. The major force is the binding of the ionized amine groups (probably an ammonium group) of capture proteins with the crown moiety of the calixcrown used in the coating of the solid phases.

Reactions occurring in crystals are interesting because their outcome is often directed by the steering topology of the reacting atoms and functions constrained by the crystal packing [24]. Single-crystal-to-single-crystal transformations are unobvious since the atomic arrangement of the products is quite different from the one of the starting reactants. However, it seems that the presence of a coordinating metal is of a help in producing such transformations [25, 26]. It has been reported [27] the reaction of a calix[4]bisthiacrown, **L** (see Scheme 8), in dichloromethane with two equiv of CuI in acetonitrile at room temperature giving colorless single crystals exhibiting a 3D polymeric array of formula



The overall geometry of **1** can be described as an interconnected layer where each **L** is linked by a three-rung ladder-type unit  $(\text{Cu}_3(\mu_3 - \text{I})(\mu - \text{I})_2)$ . The two  $\text{Cu}_3\text{I}_3$  units bridge two **L** units via Cu–S bonds to form a 2-D layer. Then the adjacent 2-D layers are bridged via Cu–S bonds to form the 3-D framework. The  $\text{Cu}_2$  atom is tetrahedrally coordinated by three I atoms and one acetonitrile. No photoluminescence is observed. When single crystal **1** is heated at 175 °C, the coordinated acetonitrile molecules are completely removed to yield a desolvated colorless solid of type



**Scheme 8** Calix[4]bisthiacrown, **L**

The single crystallinity is maintained during the process. The overall 3-D structure of **2** is similar to that of **1**. This single-crystal-to-single-crystal transformation gives rise to solvate-luminescence “off-on” behavior due to the removal of coordinated acetonitrile molecules.

Calixcrowns are one of the most widely investigated classes of cation ligands based on calixarenes. This is probably due to the binding properties they deliver toward alkali and alkaline earth metals and ammonium which can be tuned by conformational changes around the binding regions. The numerous chemical transformations they offer allow them to provide the chemists, biochemists and nanochemists with new molecular objects belonging to the field of extended supramolecular chemistry and subsequent fields such as complex matter chemistry [28] and creative advances driven by molecular changes [29, 30].

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