

Structure and Function of Metallocalix[4]arenes: Past, Present and Future

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Calixarenes are cyclic phenol-formaldehyde oligomers (see Figure). The number of monomeric units is designated by a number in square brackets in the name. Thus a calix[4]arene is made of four phenol derivatives linked by methylene groups. Calixarenes are often substituted at the para position of the phenol. These substitution can be polar or non-polar, typically chosen to control solubilities. The most common polar substitution is a sulfonate¹ group, but the synthesis generally begins with the *p-tert*-butyl calixarene.² Calixarenes were first synthesized in the 1870's,³ their cyclic structure was proposed in the 1940's and their crystal structure was solved in 1979.⁴ New chemistry of calixarenes and their metal complexes⁵ (metallocalixarenes) is still being discovered today. Calixarenes have applications in removal of ions from radioactive waste⁶ and from sea water,⁷ metallocalixarenes act as ion selective optical sensors⁸ and bio-mimetic catalysts⁹. In addition, metallocalixarenes form three dimensional supramolecular structures.

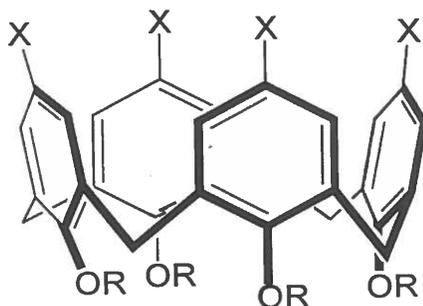


Figure 1

One of the recently discovered applications of calix[4]arenes is catalysis of phosphate diester transesterification.¹⁰ Mono- and dinuclear zinc complexes are known to catalyze this reaction.¹¹ When one, two or three zinc ions are complexed with a 2,6-bis aminomethyl pyridyl groups attached to the top of the calix[4]arene, the rates of diester transesterification are dramatically increased. Specifically, the zinc calix[4]arenes increase the rate of cleavage of an RNA model compound by a factor of 32,000.¹⁰ While these complexes could probably not be used in vivo, there are in vitro applications of RNA cleavage as well, and a better understanding of RNA cleavage could lead to gene therapy and anti-viral drugs.

When water-soluble calixarenes pack in the solid state, their interactions are dominated by hydrophobic interactions.¹² The calixarenes pack "up, down, up, down" forming a bilayer structure where the sulfonate groups layer with the solvent and counter-ions. Metal ions can interact with these layers in several ways. They can intercalate between the layers as hydrated ions, they can bind to one calixarene per metal ion or they can bind to more than one calixarene per metal ion. All three types are observed.¹³

Several novel structural features of calixarenes have recently been discovered. When certain organic molecules are combined with metal ions and calixarenes, crystalline material containing three dimensional structures such as spheres, tubules and capsules is obtained. For example, when pyridine n-oxide is combined with p-sulfonatocalix[4]arene along with a lanthanide nitrate, spherical and tubular structures are obtained, depending on the amount of pyridine n-oxide(see Figure 2).¹⁶ In essence, the organic molecule and metal ion allow the calixarenes to pack "up, up, up," making curved rather than planar layers. In addition to the spherical and tubular morphologies, remarkable ionic capsules can be produced by the addition of a crown ether and chromium ions to calix[4]arenes.¹⁵ These capsules act as superanions enabling the crystallization of aqua complexes of chromium ions.

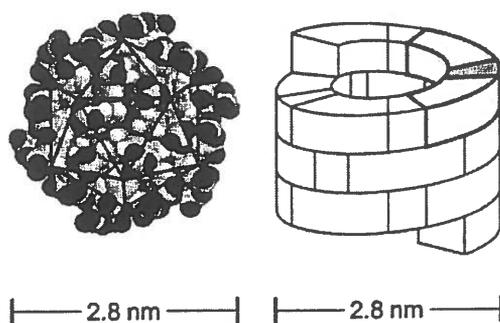


Figure 2

Many possible applications of metallocalixarenes are suggested by these novel structures. The tubular and spherical structures are large enough to contain molecules, probably with a high degree of specificity. Other applications could include further catalysis, or even more likely medical or engineering applications.¹⁶

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