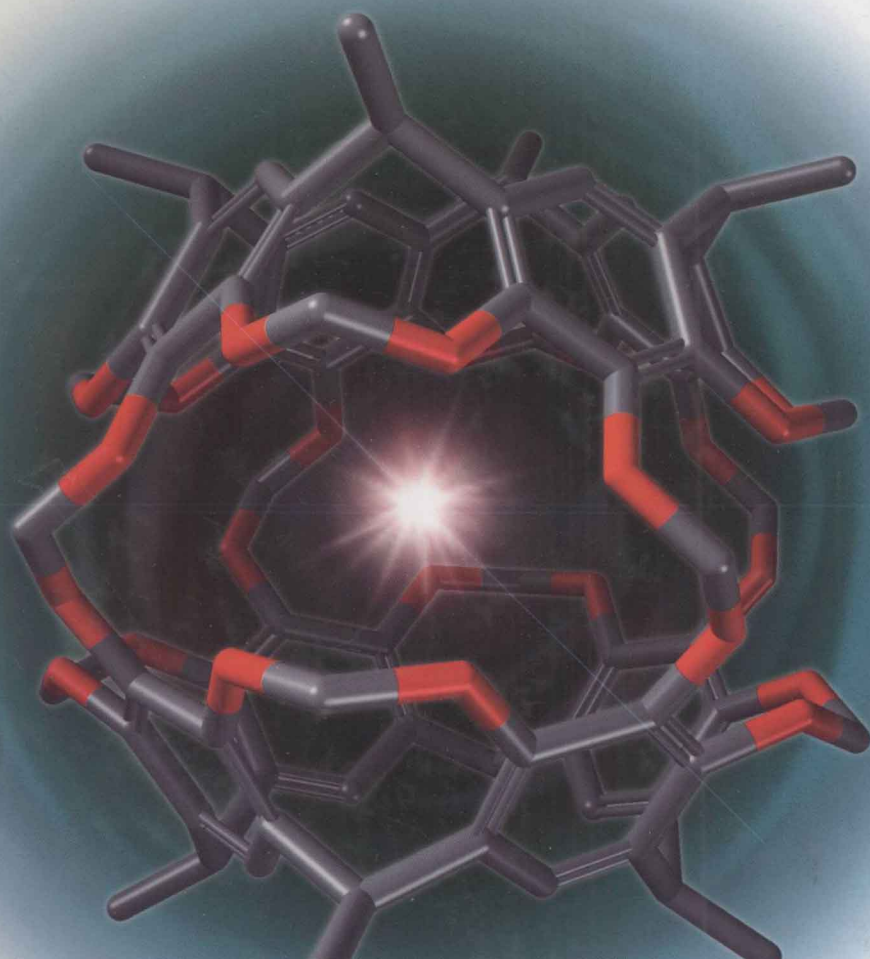


Wanda Sliwa and Cezary Kozlowski

 WILEY-VCH

# Calixarenes and Resorcinarenes

Synthesis, Properties and Applications



*Wanda Sliwa and Cezary Kozlowski*

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## ***Further Reading***

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## 1

## Introduction

Calix[ $n$ ]arenes (usually  $n = 4, 5, 6, 8$ ) are metacyclophanes having a hydrophobic cavity of lower (narrow) and upper (wide) rims, formed by phenol units bridged with methylene links; they are easily accessible via a base-catalyzed, single-step condensation of phenols with formaldehyde. Calixarenes possess soft  $\pi$ -donor cavity consisting of benzene rings and hard oxygen cavity formed by hydroxyl groups. The hydrophilic narrow rim and hydrophobic wide rim encompassing a cavity may be functionalized. The dimensions of cavity depend on the conformation of calixarenes and the appended functional groups. Different conformers of calixarenes have different capabilities for molecular recognition.

Calix[4]arene can adopt four conformations: cone, partial cone (paco), 1,2-alternate (1,2-alt), and 1,3-alternate (1,3-alt). When small substituents (e.g. methyl or ethyl groups) are present at the wide rim, the phenyl units flip through the annulus. Conformational mobility of calix[4]arenes may be constrained by introduction of bridges at narrow or at wide rim, or by attachment of large groups.

Contrary to a big number of functionalized calix[4]arenes, the substitution of higher calixarenes had received far less attention, mostly owing to the high flexibility of their framework. In calix[6]arenes the *through-the-annulus* conformational interconversion occurs owing to their larger dimensions as compared to calix[4]arenes. Two conformations of calix[6]arenes exist: the pinched cone and the 1,2,3-alternate. The attachment of large groups to calix[6]arenes in proximal or distal positions can restrict their flexibility.

The relatively flat molecule of *t*-butylcalix[8]arene adopts the pleated loop conformation in solid state and in solution. The strong circular hydrogen bond between hydroxyl groups occurs and the ArCH<sub>2</sub>Ar units are situated above and below the mean plane, in alternate positions.

Calixarenes may be functionalized by the introduction of various groups at the narrow and the wide rim. The narrow rim functionalization can be achieved by etherification or esterification of the phenolic hydroxyl groups. The wide rim functionalized calixarenes can be obtained either directly by electrophilic substitution reactions or in two-step procedures from suitable precursors; halogenated calix[4]arenes are very useful for this purpose. The regioselective functionalization of calix[8]arenes is difficult owing to the equivalence of the reactive sites, and

therefore the chemistry of calix[8]arene is not so developed as that of its lower analogs.

Calixarenes are the topic of a great number of works, including books [1, 2], reviews dealing with calixarenes [3–9], resorcinarenes [10–12] and capsules [13–16], as well as original articles on calixarenes [17–30], and resorcinarenes [31–34].

Calixcrowns are a special class of compounds related to calixarenes; they contain crown ether moieties that are able to coordinate metal ions. This property is of great importance in their application in the separation of metal ions [35, 36], and is promising with respect to environment protection.

Resorcinarenes are compounds related to calixarenes. They possess two hydroxyl groups on benzene units. Synthesis of resorcinarenes involves condensation of resorcinol, instead of phenol as in the case of calixarenes, with aldehydes. Resorcinarenes form cavitands as well as dimeric and hexameric capsules.

Calixarenes belong to receptors used in supramolecular chemistry; they are building blocks of supramolecular assemblies. Besides calixarenes, examples of other supramolecular receptors are crown ethers [37, 38], cyclodextrins [39, 40], and cucurbiturils [41, 42]; these compounds mimic natural recognition processes, creating new supramolecular structures via self-assembly.

It should be mentioned that calixpyrroles [43–45] are special classes of calixarenes belonging to heterocalixarenes, that is, calixarenes in which phenol units are replaced by heterocyclic moieties as well as calixquinones [46] bearing quinone moieties instead of phenol units; moreover the formal replacement of methylene links in calixarenes by sulfur, oxygen, or nitrogen atoms leads to thiacalixarenes [47–49], oxa (homooxa)calixarenes [50–52], and aza (or homoaza)calixarenes [53–55], respectively. The above compounds are not dealt with in this work.

The presented text is a recent development of our former papers concerning calixarenes – their complexes with transition-metal ions [56, 57], cavitands [58], as well as dimeric [59] and hexameric [60] capsules.

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## **Part I**

### **General Characteristics of Calixarenes**



## 1

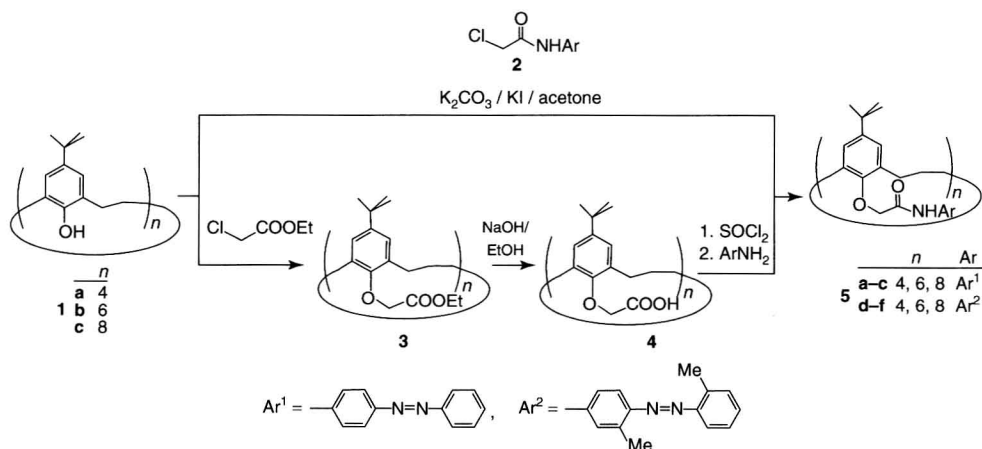
## Reactivity of Calixarenes

Numerous reactions of calixarenes have been reported [1–14]; some examples of these are described here. To improve the properties of calixarenes, functionalization of the narrow [15–17] as well as of the wide rim is carried out [18–20]. In the first part, functionalization of the narrow rim of calixarenes is described, followed by functionalization of the wide rim. Then some examples of calixarene bridging are presented.

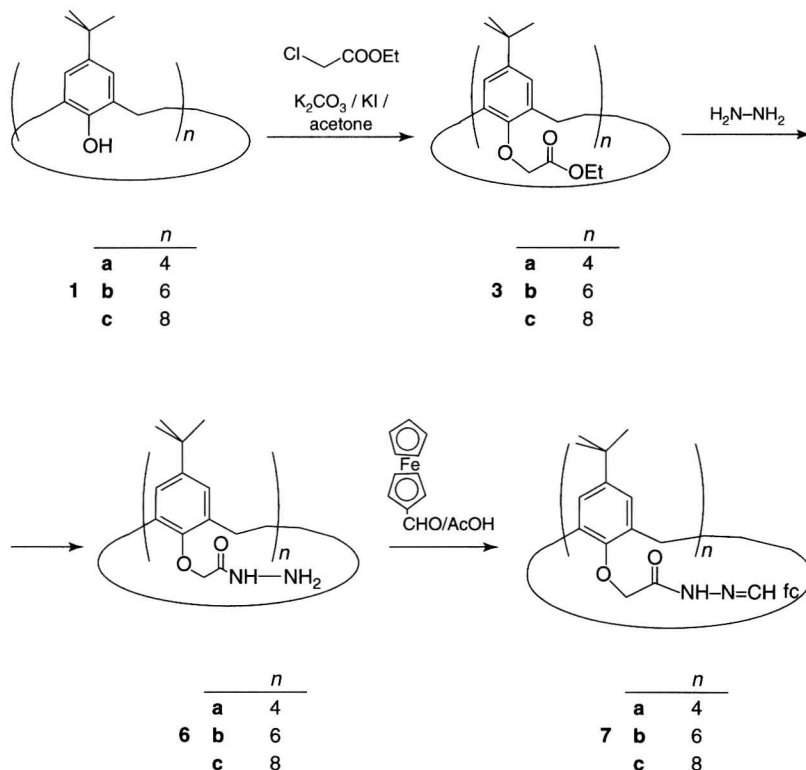
## 1.1

### Functionalization of the Narrow Rim

A series of calixarenes bearing azo chromophores on the narrow rim were synthesized using two routes. The first one was a direct reaction of calixarenes **1a–c** with 4-chloroacetoaminoazobenzene **2** in the presence of  $K_2CO_3$  and KI. In the second, indirect approach calixarenes reacted with ethyl chloroacetate affording esters **3** hydrolyzed to give acids **4**, which were treated with thionyl chloride, followed by *p*-aminoazobenzenes  $ArNH_2$ . Both procedures led to the formation of calixarenes **5** containing azo chromophores [21].



In order to introduce the ferrocenyl unit into calixarenes, the reaction of **1a–c** with ethyl chloroacetate affording esters **3** was performed. These compounds reacted with hydrazine to give hydrazides **6**, which upon treatment with ferrocenecarboxaldehyde yielded derivatives **7** [22].

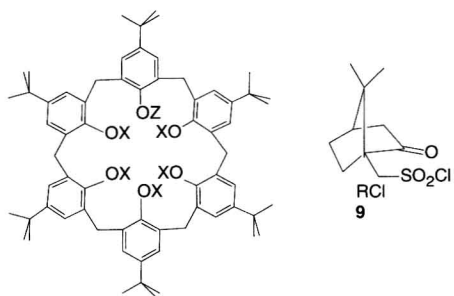


The reaction of calix[6]arene **8a** with (+)-camphor-10-sulfonyl chloride **9** affords either the mono-*O*-sulfonylated product **8b** or the hexa-*O*-sulfonylated product **8c**, depending on the stoichiometry [23]. This rather unexpected result, i.e. the absence of di- to pentasubstituted products, is due to the structure of **8b** in which the camphor-sulfonyl unit covers the narrow rim of calixarene, thus forming a steric hindrance for substitution of the second hydroxyl group.

However, if the second hydroxyl group is sulfonylated, the two substituents repulse one another; therefore, other hydroxyl groups are exposed to reaction with excess sulfonyl chloride to give **8c**.

It was established that 1,3,5-trimethoxy-*t*-butylcalix[6]arene **10** reacts with phenylpyridines **11** and **12** and with fluorenylpyridine **13** to give calix[6]arenes **14**, **15**, and **16** respectively, functionalized at alternate rings on the narrow rim [24]. The  $^1\text{H}$  NMR measurements show that **14–16** exist predominantly in the  $C_{3v}$  cone conformation and have unusually deep cavities.





	X	Z
a	H	H
b	H	R
c	R	R

