

## Synthesis and properties of double-calix[4]arenes, doubly-crowned calix[4]arenes, and double-calix-crowns

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**Abstract.** Syntheses of double-calix[4]arenes, doubly-crowned calix[4]arenes, and double-calix-crowns have been achieved by reacting *p*-*tert*-butylcalix[4]arene or a new mesitol based calix[4]arene with various polyethylene glycol ditosylates in the presence of potassium carbonate in refluxing acetonitrile. Depending on the nature of the ditosylate and on the reaction times are differently obtained calixarene ligands. The complexation properties toward alkali cations are presented for the double-calix-crown derived of *p*-*tert*-butylcalix[4]arene.

### INTRODUCTION

Calixarenes (refs 1 & 2) are a new class of macrocyclic compounds that have attracted supramolecular chemists because of their chemical versatility and conformational properties for designing flexible and preorganized molecular receptors such as calixcrowns and calixspherands (ref. 3). The present work enlarges the family of calixcrown based receptors.

### SYNTHESIS AND PROPERTIES

The treatment of *p*-*tert*-butylcalix[4]arene and 1,3-dimethoxy-*p*-*tert*-butylcalix[4]arene with triethylene glycol ditosylate in the presence of potassium carbonate in refluxing acetonitrile for 7 days afforded the corresponding double-calix[4]arenes Ia (R = H) and Ib (R = CH<sub>3</sub>) which were shown to consist of two calix[4]arene moieties linked by two opposite glycolic chains (ref. 4).

It is known that *p*-*tert*-butylcalix[4]arene reacts with ditosylates to give capped *p*-*tert*-butylcalix[4]arenes in which the glycolic chain is intramolecularly connecting the 1- and 3- positions (ref. 5). The preference in the formation of double- or capped calix[4]arenes may be explained by the difference in the experimental conditions. Capping of *p*-*tert*-butylcalix[4]arene was achieved by reaction with the ditosylate (1 equiv.) in refluxing benzene using 2 equiv. of potassium *tert*-butoxide added stepwise in two 1 equiv. portions (ref. 5). Double-calix[4]arenes Ia,b have been prepared by using an excess of potassium carbonate (10 equiv.) in one crop in acetonitrile. It is assumed that in these conditions the 1,3-diphenolate is more easily formed due to the excess of base in a more polar solvent. The 1,3-diphenolate might react simultaneously with two tosylates (2 equiv.) to afford 1,3-dialkylated *p*-*tert*-

butylcalix[4]arene bearing two glycolic chains ended by tosylate leaving groups which can therefore react with a new dianion.

$^1\text{H-NMR}$  showed the two *p-tert*-butylcalix[4]arene units of Ia to exist in the cone conformation as illustrated in Figure 1.

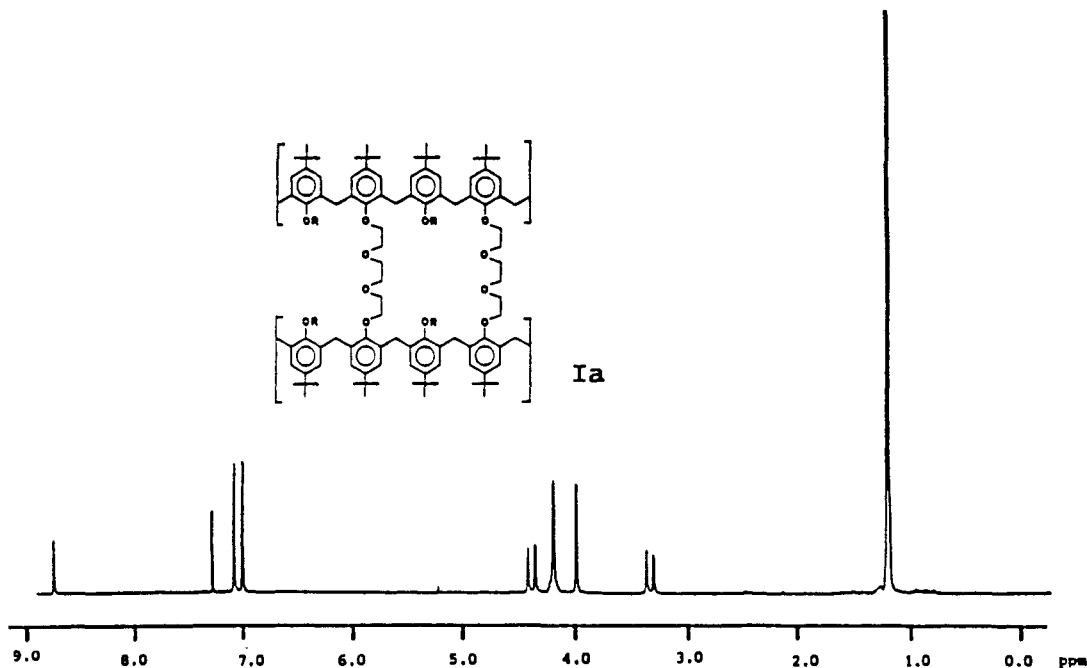


Fig. 1. 200MHz  $^1\text{H-NMR}$  in  $\text{CDCl}_3$  of double-calix[4]arene Ia

The treatment of *p-tert*-butylcalix[4]arene with *diethylene* glycol ditosylate in similar conditions afforded double-calix[4]arene Ic triply bonded via the oxygen atoms by glycolic chains (ref. 6). Ic was identified by FABMS (fast atom bombardment mass spectrometry) as shown in Figure 2 (ref. 6).

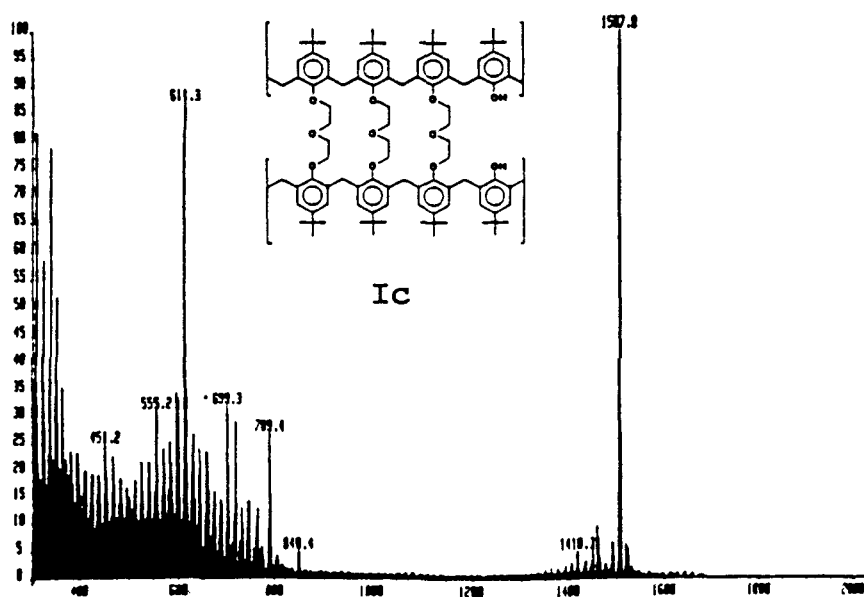
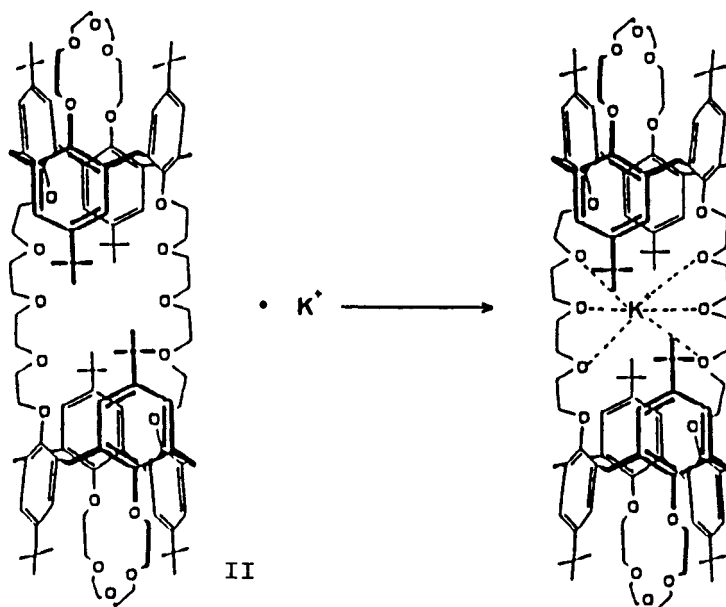


Fig. 2. FABMS of double-calix[4]arene Ic.

$^1\text{H}$ - and  $^{13}\text{C}$ -NMR showed complex spectrometric data probably due to the presence of several conformations of the *p*-*tert*-butylcalix[4]arene subunits and/or *anti* or *syn* linkages (ref. 6). In this case the formation of a double-calix[4]arene is preferred over a capped-calix[4]arene because of the shortness of the diethylene glycolic chain (ref. 6).

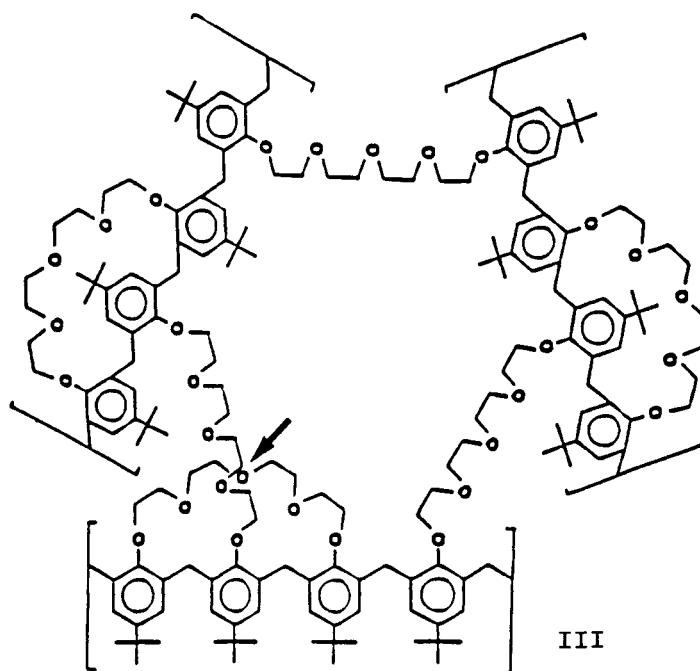
Subsequently to these results, we discovered a striking example of the formation of double-calix[4]-crown ether II by *covalent self-assembly process*. During this process 8 bonds are formed in one time. *p*-*tert*-Butylcalix[4]arene was treated with tetraethylene glycol ditosylate under the above reaction conditions to afford III, in which the two calix[4]arene moieties are in the 1,3-alternate conformation, as shown by  $^1\text{H}$ -NMR and capped by a tetraethylene glycolic chain (ref. 7).



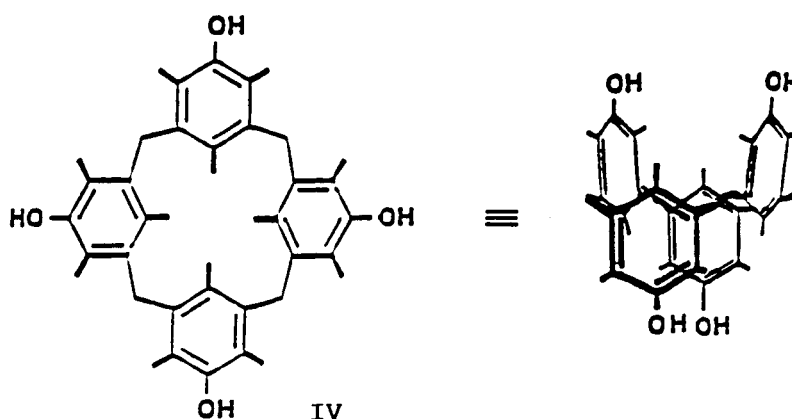
By  $^1\text{H}$ -NMR experiments, ligand II was shown to form 1:1 complexes with potassium and rubidium picrates in the solid state and in solution in deuteriated chloroform. The formation of 1:1 complexes in acetonitrile was established with all the alkali cations by uv absorption spectrophotometry (ref. 7). Potassium cation is less strongly complexed by the double-calix[4]-crown ether ( $\log K = 4.90$ ) than by 18C6 ( $\log K = 5.70$ ) and DB18C6 ( $\log K = 6.60$ ) in acetonitrile (ref. 7). Potassium complex is as stable as its homolog with DB30C10 ( $\log K = 4.70$  in the same medium) which has the same number of oxygen atoms (ref. 7). All the results were accounted for by locating the metal cation in the central cavity of the potential tritopic receptor (ref. 7).

Along with the double-calix[4]-crown ether, the reaction produced also triple-calix[4]-crown ether III whose structure was ascertained by elemental analysis, FABMS, and  $^1\text{H}$ -NMR. The conformation of the calix[4]-crown units were deduced from  $^1\text{H}$ -NMR which showed that one calix[4]-crown is in cone conformation the two other being in the 1,3-alternate conformation.

In this special arrangement it is to be noticed that one part of the molecule (the tetraethylene glycolic chain of the calix[4]-crown in cone conformation) is passing through the central annulus of the molecule as indicated by the arrow.



The obtention of receptor molecules presenting the 1,3-alternate conformation giving to the ligands new geometries and peculiar inherent symmetries led us to continue our synthesis by using calix[4]arene IV based on mesitylene units which exists in the stable 1,3-alternate conformation in a wide range of temperature (-60 to 180° C) (ref. 8).

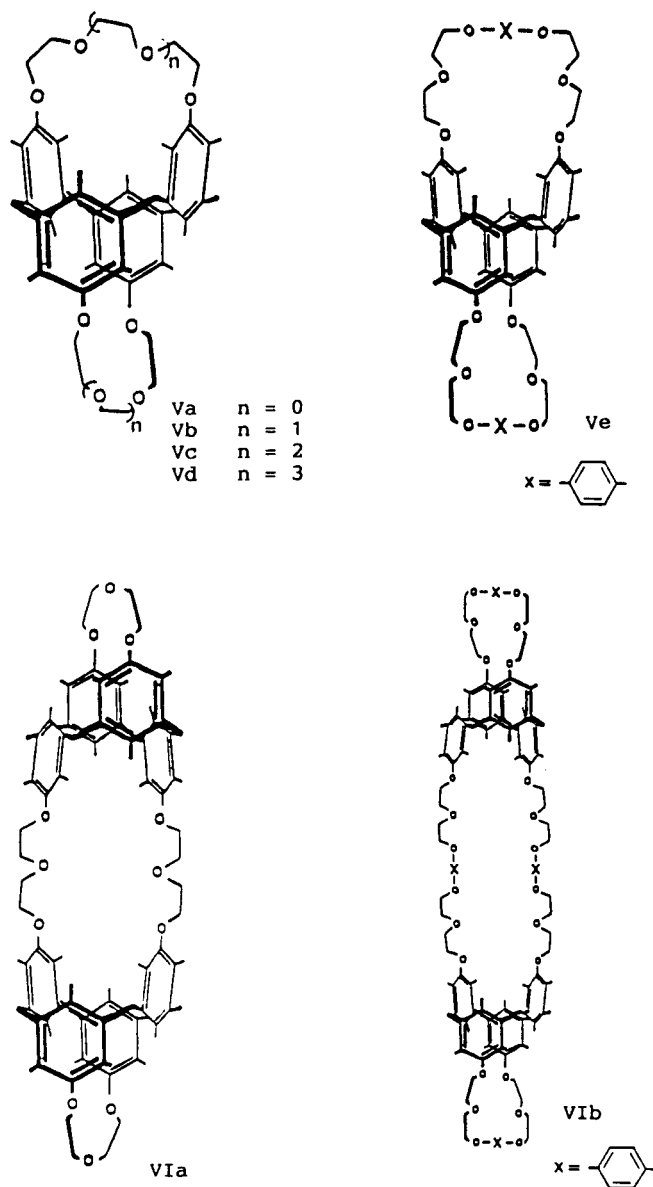


Thus the reaction of 4,6,10,12,16,18,22,24,25,26,27,28-dodecamethyl-5,11,17,23-tetrahydroxycalix[4]arene or mesitol-based calix[4]arene IV with *di*-, *tri*-, *tetra*-, and *pentaethylene* glycol ditosylates in the presence of potassium carbonate in refluxing acetonitrile afforded the respective doubly-crowned-calix[4]arenes Va-d ( $n = 0, 1, 2,$  and  $3$ ) in yields ranging from 35 to 70% (ref. 9). The reaction times were 10 days except for the formation of Vd which occurred in 25 h. This shortest conversion time was likely attributed to a potassium template effect during the double cyclization process. In addition to Va was also produced the expected double-calix-crown ether VIa related to II. Similarly, compound IV was reacted (12

days) with *dihydroxy benzene diethylene glycol ditosylate* to yield the corresponding doubly-crowned-calix[4]arene **Ve** and double-calix-crown ether **VIb** in 16% and 8% yield respectively (ref. 9).

$^1\text{H-NMR}$  of **Ve** showed the presence of *one singlet* at 2.32 ppm for the extraannular methyl protons while *two singlets* in a ratio 1:1 at 2.10 ppm and 2.27 ppm were observed for same protons in the spectrum of **VIb**. The presence of the two singlets were indicative of two different branchings of the glycolic chains. All the molecular structures are presented in Chart 1.

Chart 1



The work presented here shows that sophisticated molecular structures can be obtained in one pot reactions by the formation of 4 or 8 bonds in one time by *covalent self-assembly process* (ref.10). This observation is in good agreement with the sentence of Ashton et al. : "It is easier to construct the molecular assemblies than it is to create one of their components by itself." (ref. 11).

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