

## DOUBLE AND TRIPLE CALIX[4]ARENES CONNECTED VIA THE OXYGEN FUNCTIONS

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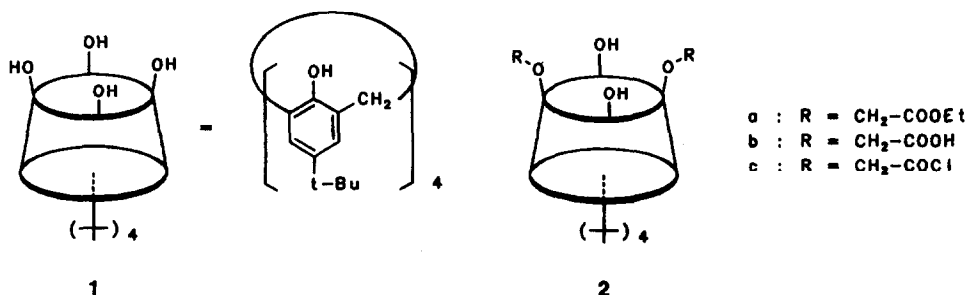
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**Abstract:** New macrocyclic molecules are described containing two or three *p*-tert-butylcalix[4]arene subunits connected via their oxygen atoms. These macrocycles are available by two general methods which are capable of producing assemblies with bridges of varying rigidity and length.

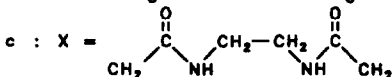
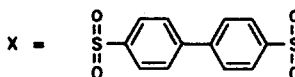
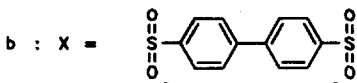
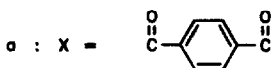
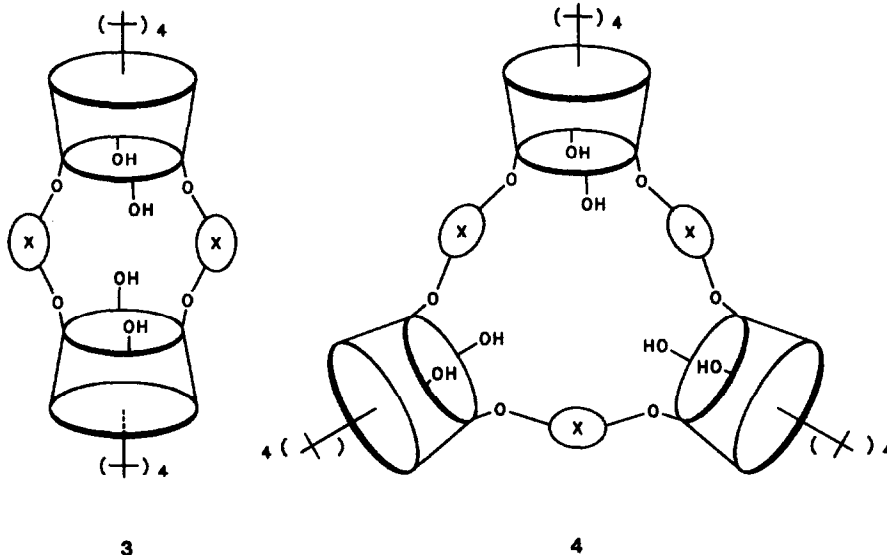
Recent work by several groups has established that calix[4]arenes are useful molecular substructures on which to assemble collections of covalently bound functional groups capable of acting as ligating podands in ion or molecule receptors<sup>1</sup>. The majority of such chemically modified calix[4]arenes exist in the cone conformation which confers on the receptor a considerable degree of preorganisation. *p*-tert-Butylcalix[4]arene **1** is now so readily accessible<sup>2</sup> that this member of the series is being increasingly used as a building block for larger, more elaborate molecular assemblies. Our interest in larger systems includes the synthesis of double and triple calixarenes possessing well defined molecular cavities and clefts capable of selective receptor activity.

One approach to such systems requires the regioselective modification or further functionalization of the phenolic groups in **1**.



Diametrically (1,3-) functionalized calix[4]arenes, i.e. 1,3-derivatives of type 2, have been synthesized by several groups in good to excellent yields<sup>3</sup>. Suitable (sufficiently flexible) difunctional reagents may then lead to bridging of the molecule<sup>4</sup>.

We wished to build up macrocyclic assemblies in which two calix[4]arene subunits are connected via two bridges between their respective oxygen atoms at the 1- and 3-positions. One way of achieving this goal was to use a difunctional reagent, e.g. a diacid dichloride, which is too rigid to make an intramolecular bridging of the calix[4]arene possible.



When terephthaloyl chloride (1 mmol in 50 ml of THF) was added at 40°C over a period of 15 h to a solution of 1 (1 mmol in 200 ml of benzene/acetonitrile = 1/1) in the presence of K<sub>2</sub>CO<sub>3</sub> after purification by flash chromatography double calixarene 3a, mp. >300°C was isolated in 33% yield.

In contrast, use of isophthalic acid dichloride with 1 under various conditions gave no identifiable products.

The distance between the calixarene moieties in 3a can be varied by varying the length of the bridging difunctional reagents. Thus, the biphenyl-containing double calixarene 3b, mp. >300°C, could be obtained in 32% yield from 1 (1 mmol in 200 ml of THF) and KOtBu (2 mmol) after adding the appropriate diacid dichloride (1 mmol in 50 ml of THF) over 18 h under reflux<sup>5</sup>.

Interestingly, reduction of the addition time to 9 h in the synthesis of 3b caused the yield to decrease to 15%, but led to the triply inter-bridged triscalixarene or "triple calixarene" 4, mp. 280°C (decomp.), in 18% yield. To the best of our knowledge 4 is the first example of a molecule in which three calix[4]arene moieties are connected by three bridges.

An alternative strategy to obtain doubly bridged double calixarenes<sup>6</sup> consists of fixing activated functional groups at the 1- and 3-positions of calixarene 1. Thus the known diester 2a, obtained from 1 and ethyl bromoacetate, could be hydrolysed to diacid 2b and transformed into diacid dichloride 2c by the action of thionyl chloride. 3c was prepared by adding 2c and ethylenediamine (each 2.3 mmol in 100 ml of dry benzene) at room temperature simultaneously in a dropwise fashion to a stirred solution of triethylamine (7.2 mmol) in 100 ml of dry benzene. After 24 h the reaction mixture afforded after purification by chromatography and recrystallization from methanol/CH<sub>2</sub>Cl<sub>2</sub> 16% of 3c, mp. 320-322°C (decomp.). Other diamines may be used as bridging reagents in a similar way. These new double and triple calixarenes were characterised by microanalysis and FAB mass spectrometry. Their structures are supported by <sup>1</sup>H- and <sup>13</sup>C-NMR data.

Table 1 summarizes the <sup>1</sup>H-NMR data of compounds 3 and 4. The differences in chemical shift found for the t-butyl and aromatic protons reflect the different types of bridging.

Table 1. <sup>1</sup>H-NMR data (δ-values in ppm, 200 MHz, CDCl<sub>3</sub>)

Compound	Calix		t-Bu	Bridge
	ArH	OH		
3a	6.93	4.68	3.50 (14.4)	8.41
	6.99		3.90 (14.4)	
3b	6.80	4.85	3.48 (14.1)	7.72 (8.4)
	7.12		4.26 (14.1)	1.30
3c <sup>a</sup>	7.04	8.28	3.45 (13.2)	Bridge-data <sup>b</sup>
			4.12 (13.2)	
4 <sup>a, c</sup>	7.03	5.61	3.30 (13.7)	7.99 (8.6)
	7.04		4.11 (13.7)	1.23

<sup>a</sup>) 400 MHz; <sup>b</sup>) NH: 8.56, OCH<sub>2</sub>: 3.65 broad, (CH<sub>2</sub>)<sub>2</sub>: 4.51; <sup>c</sup>) CD<sub>2</sub>Cl<sub>2</sub>

These new bridged calix[4]arenes may form the basis for highly organised molecular receptors with well defined cavity dimensions. Furthermore the remaining hydroxyl groups in 3 or 4 should be amenable to further chemical modification with ligating functional groups. Alternatively they could be used to insert additional bridges, thereby producing a new series of polyfunctional and highly organised calixcryptands and calixsperands.

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- [5] Double calixarenes of type 3 were also obtained as by-products in the bridging of 1 with the 3,3'-disulfonylchloride of benzophenone and of diphenylsulfoxide<sup>4</sup>.
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