Research Communication

New Preorganized Calix[4]arenes. Part I. A Doubly-crowned Calix and a Double-calixcrown Derived from 4,6,10,12,16,18,22,24,25,26,27,28-Dodecamethyl-5,11,17,23-tetrahydroxycalix[4]arene

ZOUHAIR ASFARI,[1] SEBASTIANO PAPPALARDO*,[2] and J. VICENS*[1]
[1]*E.H.I.C.S., URA 405 du C.N.R.S., 1, rue Blaise Pascal, F-67008, Strasbourg, France.*
[2]*Dipartimento di Scienze Chimiche, Università di Catania, 8, Viale A. Doria I-95125, Catania, Italy.*

Abstract. A doubly-crowned calix and a double-calixcrown derived from 4,6,10,12,16,18,22,24,25,26,27, 28-dodecamethyl-5,11,17, 23-tetrahydroxycalix[4]arene (**1**) have been prepared by reaction of appropriate oligoethylene glycol ditosylates with (**1**) in acetonitrile in the presence of potassium carbonate. A potassium template effect is observed during one of the double cyclizations.

Key words. Preorganized calix[4]arenes, mesitol-derived calix[4]arene.

Calixarenes [1, 2] are a versatile class of macrocyclic compounds that have attracted supramolecular chemists because of their chemical versatility and conformational properties useful for the design of flexible and preorganized molecular receptors such as calixcrowns and calixspherands [3]. The *1,3-alternate conformation* of *p-tert*-butylcalix[4]arene has been shown to be appropriate to afford molecular receptors presenting new and peculiar inherent symmetries as, for example, doubly-crowned calixcrown [4] and a double-calixcrown [5], reported in the literature. These receptors showed special topologies associated with the *1,3-alternate p-tert*-butylcalix[4]arene moieties connected with polyetheral bridging chains [4, 5].

The purpose of the present work was to carry out similar reactions by using a calix[4]arene building block in a preformed fixed *1,3-alternate conformation*. Calix[4]arene (**1**), based on mesitol units [6], was chosen because of its facile synthesis, and because the corresponding OH depleted hydrocarbon macrocycle has been shown to exist in a fixed *1,3-alternate conformation* over a wide temperature range (-60 to $180°C$)[7].
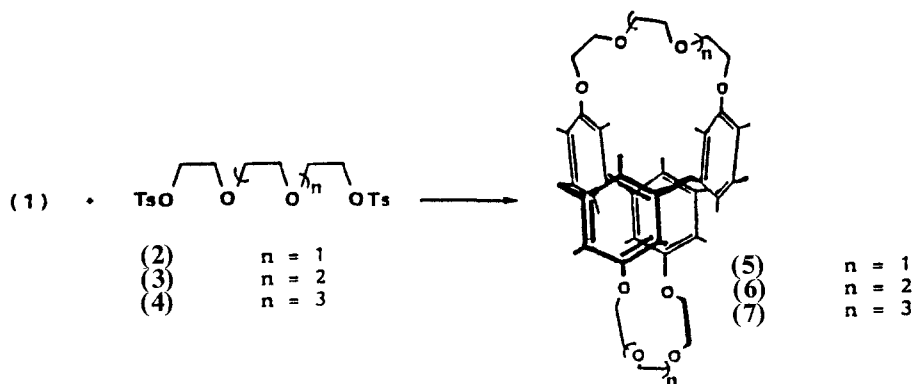
Coupling of equimolecular amounts of bis-(chloromethyl)mesitol and mesitol in nitroethane at $60°C$ in the presence of $SnCl_4$ gave the required calix[4]arene (**1**) in 66% yield [8]. The *1,3-alternate conformation* of (**1**) is substantiated by a singlet at 3.94 ppm for the bridging methylene protons and by an upfield resonance for the intraannular methyl groups (1.11 ppm), which are strongly shielded by the ring current effect of the flanking mesitol units.
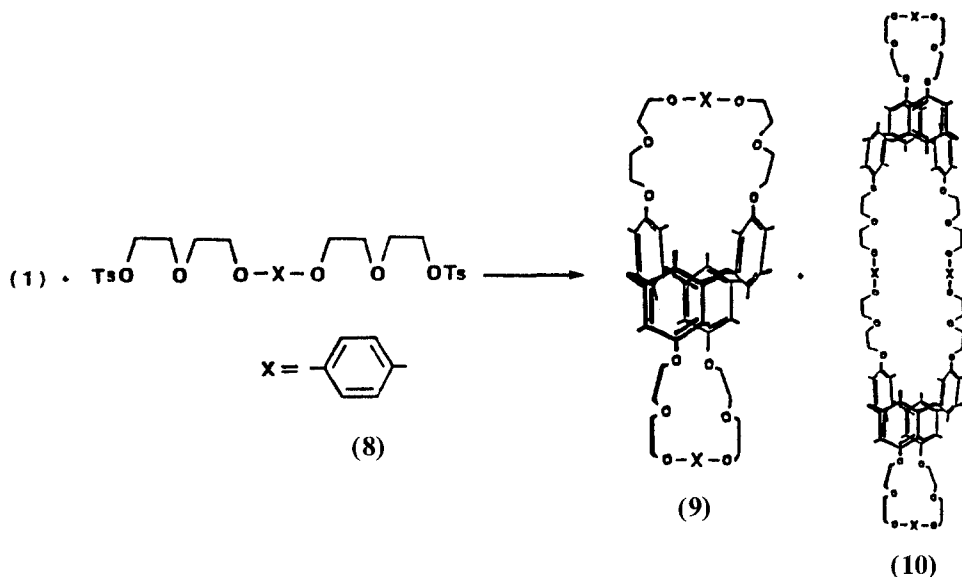
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* Author for correspondence.

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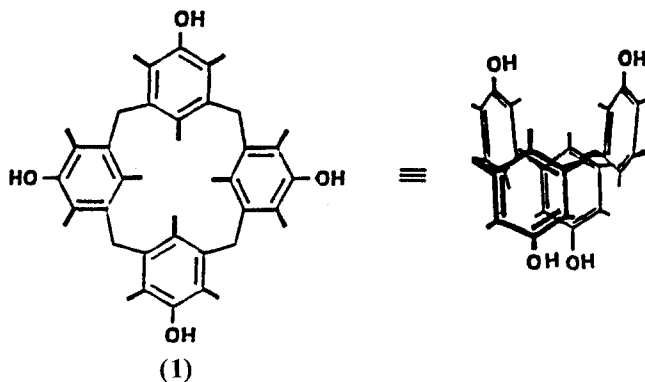
According to a procedure described by us [5] mesitol-derived calix[4]arene (1) was reacted with triethylene glycol ditosylate (2) (2 equiv., 10 days), tetraethylene glycol ditosylate (3) (2 equiv., 10 days) and pentaethylene glycol ditosylate (4) (2 equiv., 24 h) in refluxing acetonitrile in the presence of potassium carbonate (6 equiv.). After the usual work up, the corresponding doubly-crowned mesitol calix[4]arenes (5)–(7) were isolated as EtOH adducts in 85%, 85%, and 58% yield respectively [9]. The shortest conversion time observed for the reaction of (1) with pentaethylene glycol ditosylate (4) is probably due to a potassium template effect during the double cyclization process. Doubly-crowned mesitol calix[4]arenes (5)– (7) retain the *1,3-alternate conformation* of the calix[4]arene moiety, as deduced from ^{1}H-NMR spectra showing only one singlet at 3.56, 3.66, and 3.66 ppm respectively for the bridging methylene protons.

Similarly, compound (1) was reacted with the dihydroxybenzene diethylene glycol ditosylate derivative (8) (2 equiv., 12 days). After removal of the solvent, neutralization with 5% HCl, and extraction with chloroform, the crude mixture was chromatographed on a silica column (Merck 9385) using a mixture of 95:5 chloroform–acetone as an eluent to afford the doubly-crowned calix[4]arene (9) and the double calix[4]crown (10) in 16% and 8% yields respectively [9]. The structure of the double calix[4]crown (10) is based on FAB mass spectrometry and

(1)   +   TsO   O   O$_n$ OTs   ⟶

(2)	n = 1
(3)	n = 2
(4)	n = 3

(5)	n = 1
(6)	n = 2
(7)	n = 3

(1) ⋅ TsO   O   O—X—O   O   OTs   ⟶

X = ⟨⎯◯⎯⟩

(8)

(9)

(10)

on its ^{1}H-NMR spectrum showing the presence of two singlets in the ratio 1:1 at 2.10 ppm and 2.27 ppm for the extraannular methyl protons which are exposed to different chemical environments (*i.e.* the two different branchings of the glycolic chains). Conversely, the doubly-crowned calix[4]arenes (5)–(7), and (9) exhibit a single resonance for the extraannular methyl at 2.32 ppm. The doubly-crowned calix[4]arene (9) and the double calixcrown (10) were shown to be also in the *1,3-alternate conformation* with two singlets at 3.93 and 3.81 ppm respectively [9].

The formation of (10) in this case is attributed to a more rigidified polyethereal chain, due to the presence of the hydroquinone unit.

Preliminary reactions of ligand (7) with solid alkali picrates (Li^+Pic^-, Na^+Pic^-, and K^+Pic^-) in $CHCl_3$ [5] showed the 1:1 complex K^+Pic^--ligand (7) to be the more easily isolable. This observation was also accounted for by rationalizing the *potassium template effect* in the double cyclization of (7). Current work is devoted to the determination of the stability constants and stoichiometry of alkaline and alkaline-earth complexes with ligands (5)–(7) in comparison with their metal extraction capabilities. With respect to lego chemistry, the double calix crown (10) is a good candidate for self-assembly reactions to give elaborate catenate and rotaxane molecules [10].

Acknowledgement

References and Notes

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6. The name of the *mesitol derived calix[4]arene* (**1**) according to Ref. 1: 4,6,10,12,16,18,22,24, 25,26,27,28-dodecamethyl-5,11,17, 23-tetrahydroxycalix[4]arene.

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9. A typical procedure is described for the preparation of (**7**): a slurry of *mesitol derived calix[4]arene* (**1**) (1.18 g, 2 mmol), pentaethylene glycol ditosylate (2.20 g, 4 mmol), and potassium carbonate (3.75 g, 6 mmol), and acetonitrile (300 mL) was refluxed under nitrogen for 24 h. The solvent was evaporated to dryness under reduced pressure. The residue was taken up in chloroform and washed with 5% HCl. The organic layer was dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was precipitated with ethanol to afford pure doubly-crowned calix[4]arene (**7**) (1.15 g, 58%).

  Characterisation data for (**5**) ^{1}H-NMR (CDCl$_3$, with CHCl$_3$ at 7.26 ppm): 3.94–3.49 (*m*, 32 H, OCH$_2$CH$_2$O and aromatic–CH$_2$–aromatic), 2.32 (*s*, 24H, ext. CH$_3$), and 1.14 (*s*, 12 H, int. CH$_3$); FAB position $m/z = 820.4$. *Elemental analysis calc.* for C$_{52}$H$_{68}$O$_8$·C$_2$H$_5$OH: C% 74.79 H% 8.60. *Found* C% 74.61 H% 8.25. For (**6**) ^{1}H-NMR: 3.88–3.66 (*m*, 40 H, OCH$_2$CH$_2$O and aromatic–CH$_2$– aromatic), 2.32 (*s*, 24 H, ext. CH$_3$), and 1.09 (*s*, 12 H, int. CH$_3$); FAB positive $m/z = 908.5$. *Elemental analysis calc.* for C$_{56}$H$_{76}$O$_{10}$·C$_2$H$_5$OH: C% 72.58 H% 8.76. *Found* C% 72.12 H% 8.37. For (**7**) ^{1}H-NMR: 3.89–3.48 (*m*, 48 H, OCH$_2$CH$_2$O and aromatic–CH$_2$–aromatic), 2.32 (*s*, 24 H, ext·CH), and 1.09 (*s*, 12 H, int. CH); FAB positive $m/z = 996.4$. *Elemental analysis calc.* for C$_{60}$H$_{84}$O$_{12}$·C$_2$H$_5$OH: C% 71.37 H% 8.69. *Found* C% 71.52 H% 8.56.

  For (**9**) ^{1}H-NMR: 6.87 (*s*, 8 H, aromatics in the glycol chain), 4.25–3.77 (*m*, 40 H, OCH$_2$CH$_O$ and aromatic–CH$_2$–aromatic), 2.32 (*s*, 24 H, ext. CH$_3$), and 1.12 (*s*, 12 H, int. CH$_3$); FAB positive $m/z = 1092.5$. *Elemental analysis calc.* for C$_{68}$H$_{84}$O$_{12}$: C% 74.69 H% 7.74. *Found* C% 74.39 H% 7.58.

  For (**10**) ^{1}H-NMR: 6.73 (*s*, 16 H, aromatics in the glycol chain), 4.04–3.38 (*m*, 80 H, OCH$_2$CH$_2$O and aromatic–CH$_2$–aromatic), 2.27 (*s*, 24 H, ext. CH$_3$), 2.10 (*s*, 24 H, int. CH$_3$), and 0.912 (*s*, 24 H, int. CH$_3$); FAB positive $m/z = 2184.0$. *Elemental analysis calc.* for C$_{136}$H$_{168}$O$_{24}$: C% 74.69 H% 7.74. *Found* C% 74.57 H% 7.71.

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