

Synthesis and metal-binding properties of [60]fullerene-linked calix[4]arenes: an approach to 'exohedral metallofullerenes'

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'Fullerenocalixarenes' in which [60]fullerene is covalently linked through two ionophoric chains to a cone-calix[4]arene **1** or to a 1,3-alternate calix[4]arene **2** have been synthesized for the first time: although the absorption spectrum of **2** is scarcely changed upon addition of metal cations, that of **1** is affected by added Li^+ , Na^+ and Ag^+ , indicating the formation of exohedral [60]fullerene-metal complexes.

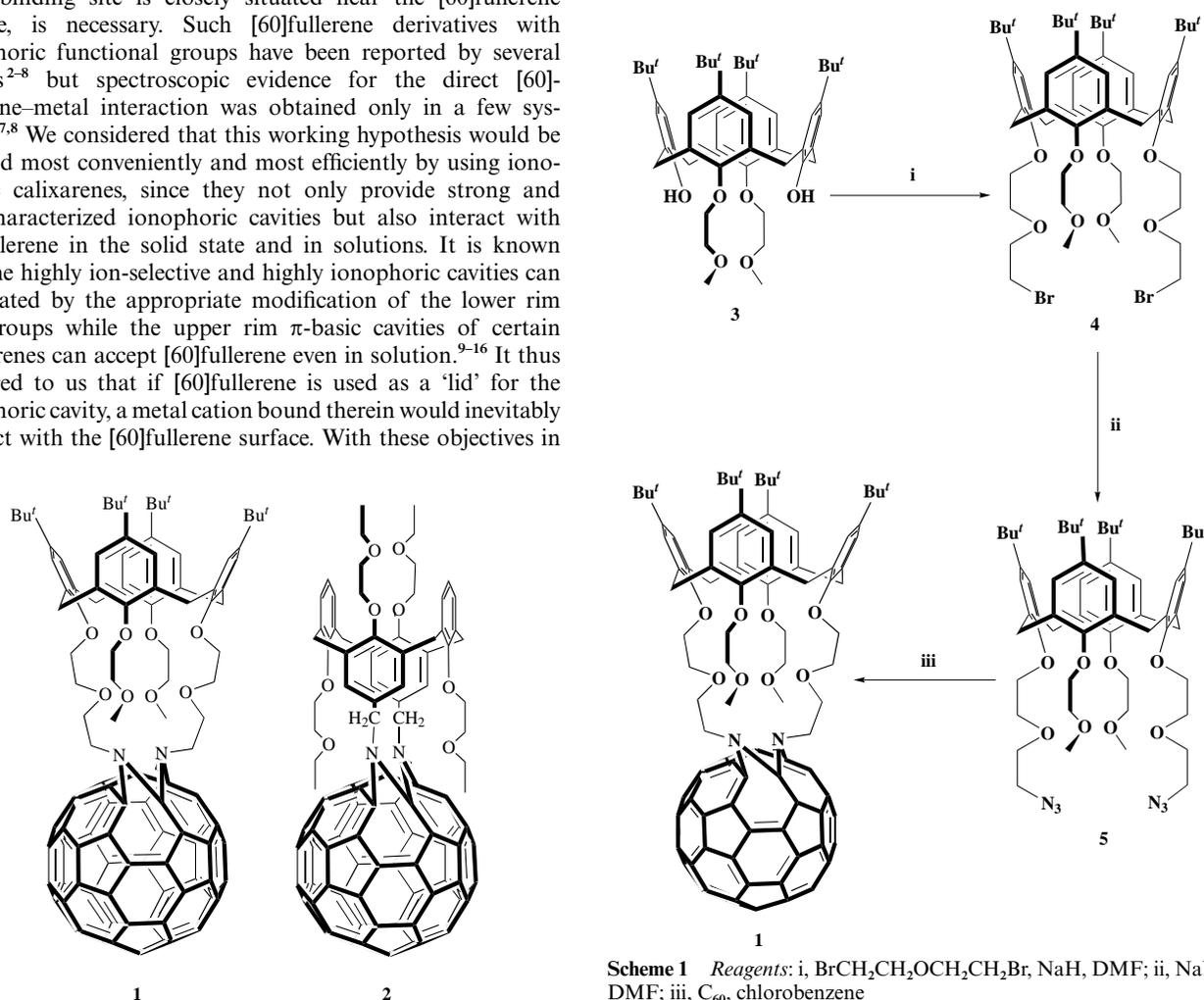
Introduction

The ready availability of [60]fullerene has increasingly invited exploration of its outstanding physical and chemical properties. Of these the superconductivity observed for certain endohedral metallofullerenes has proved a most attractive subject for research.¹ This phenomenon first observed for endohedral metallofullerenes may also be shared by exohedral compounds: that is, the metal cation immobilized onto the [60]fullerene surface should facilitate the electron injection into the [60]fullerene shell and stabilize the $\text{C}_{60}^- \cdot \text{M}^+$ complexes. As the first step to test this intriguing hypothesis, the synthesis of ionophoric [60]fullerene derivatives in which a metal-binding site is closely situated near the [60]fullerene surface, is necessary. Such [60]fullerene derivatives with ionophoric functional groups have been reported by several groups²⁻⁸ but spectroscopic evidence for the direct [60]fullerene-metal interaction was obtained only in a few systems.^{4,7,8} We considered that this working hypothesis would be realized most conveniently and most efficiently by using ionophoric calixarenes, since they not only provide strong and well-characterized ionophoric cavities but also interact with [60]fullerene in the solid state and in solutions. It is known that the highly ion-selective and highly ionophoric cavities can be created by the appropriate modification of the lower rim OH groups while the upper rim π -basic cavities of certain calixarenes can accept [60]fullerene even in solution.⁹⁻¹⁶ It thus occurred to us that if [60]fullerene is used as a 'lid' for the ionophoric cavity, a metal cation bound therein would inevitably interact with the [60]fullerene surface. With these objectives in

mind we designed compounds **1** and **2** in which [60]fullerene is included as a ring member of the ionophoric cavities. We have found that, as expected, several metal cations bound to the ionophoric cavities can change the absorption spectra of the [60]fullerene moiety, supporting the presence of a significant [60]fullerene-metal interaction.

Results and discussion

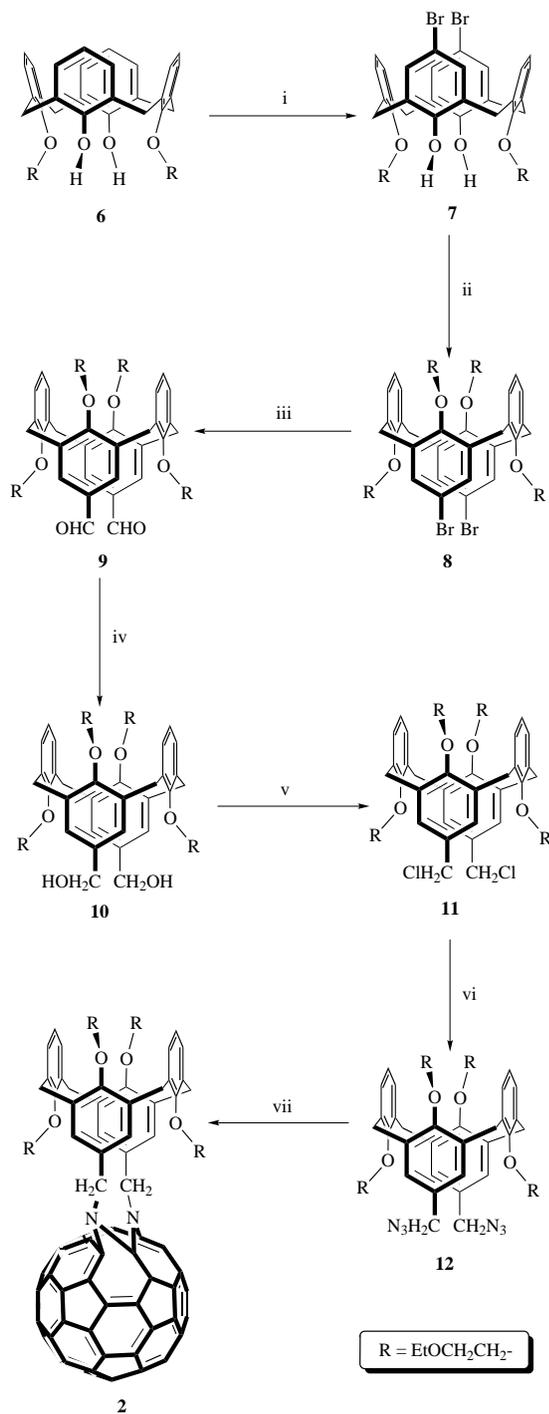
Compound **1** was synthesized from 25,27-dihydroxy-26,28-bis(methoxyethoxy)-5,11,17,23-tetra-*tert*-butylcalix[4]arene **3**¹⁷ in three steps (Scheme 1). Compound **3** was treated with an



Scheme 1 Reagents: i, $\text{BrCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{Br}$, NaH, DMF; ii, NaN_3 , DMF; iii, C_{60} , chlorobenzene

excess of bis(2-bromoethyl) ether in order to avoid the possible intramolecular cyclization with the 25- and 27-OH groups. NaH was chosen as base to keep the conformation in a cone. The terminal Br groups in **4** were treated with NaN_3 after which the resultant azide **5** was allowed to react with [60]fullerene in chlorobenzene under conditions of high dilution. The yield of **1** (from compound **4**) was 21%.

Compound **2** was synthesized from 25,27-dihydroxy-26,28-bis(ethoxyethoxy)calix[4]arene¹⁸ in seven steps (Scheme 2). The



Scheme 2 Reagents: i, Br_2 , CHCl_3 ; ii, $\text{EtOCH}_2\text{CH}_2\text{Br}$, Cs_2CO_3 , acetone; iii, BuLi , DMF, THF; iv, LiBH_4 , THF; v, SOCl_2 , pyridine, CH_2Cl_2 ; vi, NaN_3 , DMF; vii, C_{60} , chlorobenzene

first essential step is **7**→**8** where the conformation is immobilized in a 1,3-alternate fashion by using Cs_2CO_3 as base. The yield is very high (95%). The second essential step is **12**→**2** where [60]fullerene is appended to 1,3-alternate-calix[4]arene as a ring member. Although the reaction was carried out

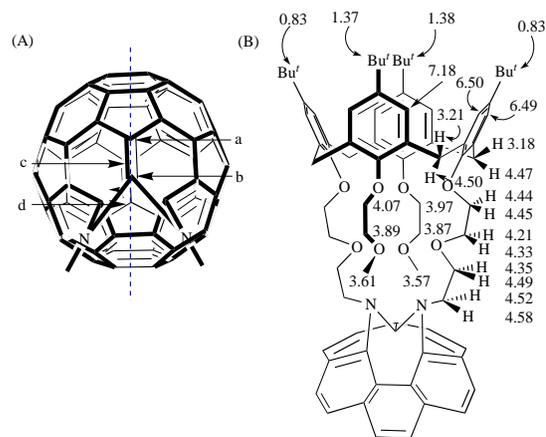


Fig. 1 (A) Binding mode of the C_{60} moiety in **1**. (B) ^1H NMR chemical shifts (in ppm) in **1**.

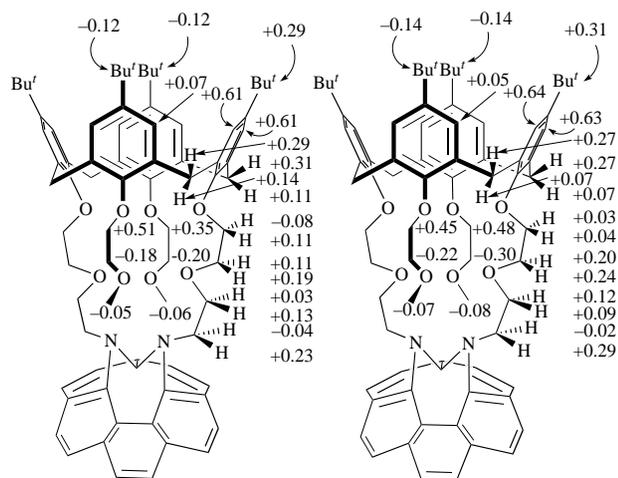
under conditions of high dilution, the yield was very low (3% from **11**).[†]

It is known that when [60]fullerene reacts with an azide reagent,¹⁹ there are two theoretically possible modes of bond formation, which can lead to 5,6-open and 6,6-closed isomers. The ^{13}C NMR spectra of **1** (100 MHz, CDCl_3 , 25°C) gave 59 peaks. Of these, 32 peaks were assignable to the fullerene carbons, which consist of 28 pairs of two equivalent carbons and four inequivalent carbons created by the adduct formation. This splitting pattern is commensurate with the 5,6-open bisaza-substituted homofullerene structure.^{8,19} This view is further supported by the following findings: (i) no peak appeared in the sp^3 -carbon region, (ii) a carbon which is covalently-linked to two nitrogens (carbon b in Fig. 1A) appears at very low magnetic field (164 ppm), which is a characteristic of the 5,6-open structure,^{8,19} and (iii) there exist three peaks which are assignable to the Bu' group (30.98, 31.13 and 31.77 ppm); this implies that two Bu' groups in the methoxyethoxyphenyl units are inequivalent because of asymmetry between the right hemisphere and the left hemisphere (in Fig. 1A) of the 5,6-open structure.

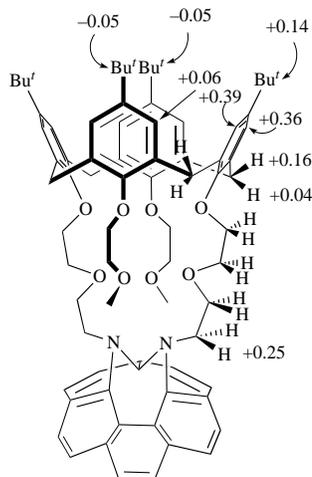
In the ^1H NMR spectrum of **1** (400 MHz, CDCl_3 : $\text{CD}_3\text{OD} = 5:1$, v/v, 25°C), the assignment was accomplished with the aid of ^1H - ^1H COSY and ^1H - ^1H NOESY measurements. The results are shown in Fig. 1B. Because of asymmetry in the 5,6-open structure, all methylene protons in two bridge chains appeared as a pair of doublets. On the other hand, two Bu' groups in the methoxyethoxyphenyl units, which were inequivalent in ^{13}C NMR spectroscopy, appeared very closely (1.37 and 1.38 ppm). Interestingly, the chemical shifts of Bu' and ArH protons in the methoxyethoxyphenyl units largely shift to lower magnetic field (1.37–1.38 ppm and 7.18 ppm, respectively) compared with those in the [60]fullerene-bridged phenyl units (0.83 and 6.49–6.50 ppm, respectively). The difference suggests that the two [60]fullerene-bridged phenyl units are erect because of steric regulation arising from the [60]fullerene-containing ring system whereas the two methoxyethoxyphenyl units are more flattened, resulting in a C_{2v} -symmetrical calix[4]arene skeleton. The foregoing ^1H and ^{13}C NMR spectroscopic data support the structure of **1** in which [60]fullerene is linked to a C_{2v} -symmetrical calix[4]arene via two ethylene oxide chains.[‡]

[†] As a solvent for the reaction of benzyl azide derivatives, ethanol is more favourable than DMF. In the present system, however, compound **11** was almost insoluble in ethanol. Hence, we were obliged to use DMF, which may be the main reason for the low yield.

[‡] The structure of **2** was also determined according to a similar procedure (see Experimental section). However, detailed discussions of the structure determination are omitted because of the limited change in the absorption spectrum (*vide post*).



Addition of Ag^+ ion (10 equiv.) Addition of Na^+ ion (10 equiv.)



Addition of Li^+ ion (100 equiv.)

Fig. 2 ^1H NMR chemical shift changes in metal (Li^+ , Na^+ and Ag^+) complexes of **1**: $[\mathbf{1}] = 5.00 \text{ mmol dm}^{-3}$, $[\text{LiClO}_4] = 500 \text{ mmol dm}^{-3}$, $[\text{NaClO}_4] = [\text{AgCF}_3\text{SO}_3] = 50.0 \text{ mmol dm}^{-3}$, $\text{CDCl}_3\text{-CD}_3\text{OD} = 5:1$ (v/v), 400 MHz, 25 °C. The + sign denotes a downfield shift while the - sign denotes an upfield shift (in ppm).

The metal-binding properties were estimated using UV-VIS absorption spectroscopy and ^1H NMR spectroscopy. Addition of metal cations (Li^+ , Na^+ , K^+ and Ag^+) to **2** in solution ($\text{CHCl}_3\text{-CH}_3\text{OH} = 5:1$, v/v) scarcely changed its absorption spectrum. It is known that 1,3-alternate-calix[4]arenes have two metal-binding sites composed of two phenolic oxygens and two benzene π -systems where the cation- π interaction significantly participates in the metal-binding event.^{18,20,21} The distribution ratio between these two metal-binding sites is dependent upon the relative strength of their ionophoricity.^{18,20,21} The ^1H NMR studies ($\text{CDCl}_3\text{-CD}_3\text{OD} = 5:1$, v/v) showed that K^+ and Ag^+ are bound to **2** but localized in the upper (in the illustration of **2**) binding site but not in the [60]fullerene-connected lower (in the illustration of **2**) binding site. Presumably, the [60]fullerene-containing ring deforms the regular architecture of the lower metal-binding site.

The ^1H NMR spectra of **1** were measured in the presence of each and every alkali-metal cation and Ag^+ . Of these ions, only Li^+ , Na^+ and Ag^+ affected the chemical shifts, although no peak splitting assignable to free **1** and $\mathbf{1}\cdot\text{M}^+$ complex was observed at 25 °C (Fig. 2). In the presence of Ag^+ , most OCH_2 methylene protons shift to lower magnetic field. Although there are a few precedents in which Ag^+ is bound to the upper rim π -basic cavity,²² the chemical-shift change indicates that the present calix[4]arene accepts Ag^+ into the lower rim oxygenic cavity. The large downfield shift and the small upfield shift observed for the NCH_2 methylene protons suggest that two nitrogens also contribute to the Ag^+ -binding. The chemical shift change

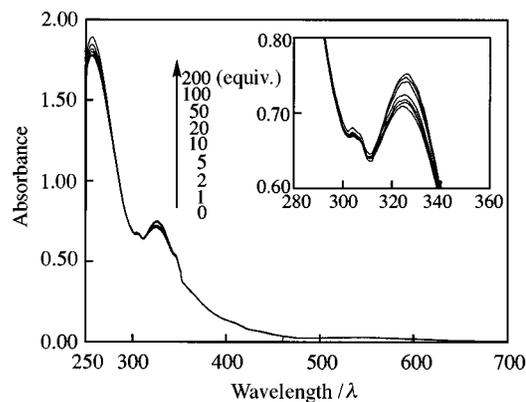


Fig. 3 Absorption spectral change of **1** in the absence and the presence of AgCF_3SO_3 : $[\mathbf{1}] = 2.00 \times 10^{-5} \text{ mol dm}^{-3}$, $[\text{AgCF}_3\text{SO}_3] = 0\text{-}4.00 \text{ mmol dm}^{-3}$, 25 °C, $\text{CHCl}_3\text{-CH}_3\text{OH} = 5:1$ (v/v)

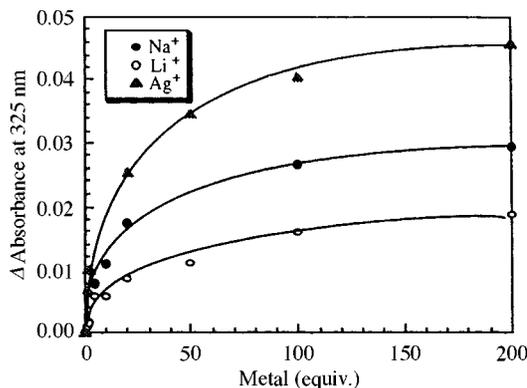


Fig. 4 Plots of A_{325} versus metal concentrations

in this system is affected by two independent factors, *i.e.* the downfield shift effect induced by Ag^+ complexation and the upfield shift effect induced by the deshielding of [60]fullerene anisotropy. The NCH_2 protons give two different chemical shifts. We explain this as follows: upon binding of the Ag^+ , one proton, the chemical shift of which moves to lower magnetic field, becomes close to the [60]fullerene surface whereas another proton, the chemical shift of which moves to higher magnetic field, leaves it. Of further interest is the chemical-shift change observed for the Bu' groups: the Bu' groups in the erect [60]fullerene-bridged phenyl units shift to lower magnetic field, whereas those in the flattened methoxyethoxyphenyl units shift to higher magnetic field. This result suggests that the erect [60]fullerene-bridged phenyl units are flattened whereas the flattened methoxyethoxy phenyl units become erect to give a nearly C_{4v} -symmetrical structure with an ionophoric cavity suitable to bind the Ag^+ .

The chemical-shift change induced by addition of Na^+ was basically similar to that induced by the addition of Ag^+ (Fig. 2). We thus consider that Na^+ is also bound to a lower rim oxygenic cavity constructed on a C_{4v} symmetrical calix[4]arene. In contrast, the chemical-shift change induced upon addition of Li^+ was relatively small and the signals were partially broadened. Hence, the chemical-shift assignment was possible only for several characteristic protons (Fig. 2). The chemical-shift change in the Bu' groups indicates that the C_{2v} symmetrical calix[4]arene ring is converted into the C_{4v} symmetrical one upon binding with Li^+ . Hence, Li^+ is bound to **1** in a similar manner to that of Ag^+ .

The [60]fullerene-metal interaction in **1** was investigated with UV-VIS absorption spectroscopy in a $\text{CHCl}_3\text{-CH}_3\text{OH}$ (5:1, v/v) solution at 25 °C. In accordance with the ^1H NMR spectroscopic data, Li^+ , Na^+ and Ag^+ changed the absorption spectra. Since the spectral pattern was similar for each, a typical spectral change for Ag^+ is shown in Fig. 3 and plots of A_{325} versus metal concentrations are illustrated in Fig. 4. It is seen from Fig. 4 that

Ag⁺ shows the largest spectral change which is visually detectable as a solution colour change from brownish orange to red-dish orange. The large influence of Ag⁺ on the [60]fullerene absorption spectrum is rationalized by the following two major factors: (i) in contrast to 'hard' alkali-metal cations which feature high affinity with 'hard' oxygenic bases, 'soft' Ag⁺ tends to be bound to the 'soft' nitrogen site (*i.e.* near the [60]fullerene surface)^{7,8} and (ii) participation of cation- π interactions is expected between Ag⁺ and the π -basic [60]fullerene surface.^{23,25}

In order to determine the association constants (K_{ass}) from Fig. 4 one has to estimate the stoichiometry of these complexes. Although it seems reasonable to consider that only a 1:1 complex results from a closed ionophoric cavity like **1**, the concomitant formation of a 1:2 calixarene-metal complex is reported for a few systems.^{26,27} Although we tried Job's plots for A_{325} versus [metal]/([1] + [metal]), the absorbance change was too small to determine the maximum points. Hence, we obtained evidence for the 1:1 stoichiometry by indirect methods. Firstly, mass spectrometry (positive SIMS) of **1** was measured in the absence and the presence of 1.5 equiv. of metal salt (LiClO₄, NaClO₄ or AgCF₃SO₃) using *o*-nitrophenyl octyl ether as a matrix. In the absence of metal salt the parent peak appeared at m/z 1656 ([M + H]⁺). In the presence of metal salts the parent peak appeared at m/z 1662 for [M + Li]⁺, 1678 for [M + Na]⁺ and 1763 for [M + Ag]⁺, whereas the peak [M + 2 metal + anion]⁺ which is assignable to a 1:2 calixarene-metal complex^{26,27} was not detected. Secondly, the plots in Fig. 4 were analysed according to Hill's equation;²⁸ y (degree of saturation) = $K_{\text{ass}}[\text{metal}]^n/(1 + K_{\text{ass}}[\text{metal}]^n)$. The Hill coefficients (n) were 0.99 for Li⁺, 0.84 for Na⁺ and 0.89 for Ag⁺. These results consistently support the view that **1** forms only 1:1 complexes with these metal cations. Thus, the K_{ass} values were determined according to Benesi-Hildebrand's equation²⁹ assuming the formation of 1:1 complexes: $K_{\text{ass}} = 2.2 \times 10^3 \text{ dm}^3 \text{ mol}^{-1}$ for Li⁺, $2.0 \times 10^3 \text{ dm}^3 \text{ mol}^{-1}$ for Na⁺ and $3.0 \times 10^3 \text{ dm}^3 \text{ mol}^{-1}$ for Ag⁺. Although the spectral change in the presence of Ag⁺ is much greater than those in the presence of Li⁺ or Na⁺, the K_{ass} for Ag⁺ is only slightly larger than those for Li⁺ or Na⁺. This again supports the idea that Ag⁺ is bound mainly to nitrogen atoms and favourably interacts with the π -basic [60]fullerene surface.

In conclusion, the present paper reports the first synthesis of 'fullerenocalixarenes' in which calix[4]arene and [60]fullerene are included in the same ionophoric ring system. As expected, several metal cations added from the outside of [60]fullerene can influence the electronic spectra of the [60]fullerene moiety. It is not yet clear whether this influence is due to the direct metal-[60]fullerene surface interaction or due to the indirect inductive effect through the metal-N interaction, but this effect is undoubtedly a new method to change the electronic state of [60]fullerene by added metal cations. The preparation of endohedral metallofullerenes is complicated and a large-quantity synthesis has yet to be accomplished. We believe that exohedral metallofullerenes in which an ionophoric site to trap metal cations is located near the [60]fullerene surface can be a potential alternate approach to the control of fullerene functions. Further studies (including electrochemical investigations) are now being continued in this laboratory.

Experimental

¹H NMR measurements (250 MHz) were carried out with a Bruker AC-250P instrument. For the structural characterization a JEOL GX-400 spectrometer was used (400 MHz for ¹H and 100 MHz for ¹³C). Mass spectra were recorded on a Hitachi M-2500 spectrometer.

25,27-Bis(methoxyethoxy)-26,28-bis(5-bromo-3-oxapentoxy)-5,11,17,23-tetra-*tert*-butylcalix[4]arene **4**

25,27-Dihydroxy-26,28-bis(methoxyethoxy)-5,11,17,23-tetra-

tert-butylcalix[4]arene **3** (1.00 g, 1.30 mmol) dissolved in DMF (30 ml) was treated with oil-dispersed NaH (0.50 g, net NaH 13.1 mol) under a nitrogen atmosphere for 30 min. After this, bis(2-bromoethyl) ether (1.30 ml, 11.2 mmol) was added to the mixture which was then stirred at room temperature for 48 h. The reaction was stopped by adding aqueous 1 mol dm⁻³ HCl to the mixture which was then extracted with chloroform. The organic layer was washed twice with water, dried (MgSO₄) and evaporated to dryness. The oily residue was then subjected to preparative TLC separation (silica gel, eluent: hexane-ethyl acetate = 2:1, v/v) to give **4** (0.21 g, 15%) as an oil; δ_{H} (250 MHz; CDCl₃) 1.01 and 1.38 [each 9 H, each s, C(CH₃)₃], 3.12 (2 H, d, J 12.6, ArCH₂Ar), 3.46 (3 H, s, OCH₃), 3.50 (2 H, t, J 6.4, CH₂CH₂Br), 3.83–3.85 (4 H, m, ArOCH₂CH₂), 4.07 (4 H, t, J 6.6, ArOCH₂CH₂), 4.16 (2 H, t, J 5.7, OCH₂CH₂Br), 4.41 (2 H, d, J 12.6, ArCH₂Ar) and 6.70 and 6.86 (each 2 H, each s, ArH) (Found: C, 65.86; H, 8.02. C₅₈H₈₂O₈Br₂·0.4C₆H₁₂ requires C, 66.05; H, 7.84%).

Compound **1**

A solution of compound **4** (0.20 g, 0.18 mmol) in DMF (30 ml) under a nitrogen atmosphere was treated with NaN₃ (26.8 mg, 0.40 mmol) and the resultant solution was heated at 100 °C for 6.5 h. The solution was then diluted with water and the product **5** was extracted with diethyl ether. The ether layer was washed twice with water, dried (MgSO₄) and after filtration was mixed with chlorobenzene (100 ml). After diethyl ether had been removed by evaporation from the mixed solvent, the remaining chlorobenzene solution was treated with C₆₀ (0.13 g, 0.18 mmol). The mixture was then refluxed for 12 h after which it was evaporated. The products were subjected to flash column chromatography (silica gel, toluene) to remove unchanged C₆₀. The residual products were isolated by preparative TLC (silica gel, eluent: dichloromethane-ethyl acetate = 15:1, v/v) to give **1** (67 mg, 21%) as a brown solid, mp (decomp.) >300 °C; δ_{H} (250 MHz; CDCl₃) 0.83 and 1.37 [each 18 H, each s, C(CH₃)₃], 3.18–3.20 (4 H, m, ArCH₂Ar), 3.56 and 3.59 (each 3 H, each s, OCH₃), 3.82–3.88 (4 H, m, ArOCH₂CH₂OCH₃), 3.94–4.07 (4 H, m, ArOCH₂CH₂OCH₃), 4.19 (2 H, t, J 5.4, ArOCH₂CH₂OCH₂CH₂N), 4.33–4.53 (18 H, m, ArCH₂Ar, OCH₂CH₂N, OCH₂CH₂N, ArOCH₂CH₂OCH₂CH₂N), 6.49 (each 2 H, each s, ArH) and 7.17 (4 H, s, ArH) (Found: C, 84.02; H, 5.20; N, 1.62. C₁₁₈H₈₂O₈N₂·CH₃CO₂C₂H₅ requires C, 83.74; H, 5.40; N, 1.57%); m/z 1656 (M + H⁺).

5,17-Dibromo-25,27-dihydroxy-26,28-bis(ethoxyethoxy)-calix[4]arene **7**

A solution of compound **6** (2.81 g, 4.94 mmol) in chloroform was treated with a chloroform solution (60 ml) containing bromine (1.90 g, 11.9 mmol), added from a dropping funnel over 1 h. The mixture was stirred at room temperature for 3 h after which it was concentrated to dryness. The residue was washed with methanol to give **7** (3.57 g, 98%) as a solid, mp 249.3–250.6 °C; δ_{H} (250 MHz; CDCl₃) 1.27 (6 H, t, J 7.0, CH₃), 3.30 and 4.39 (each 4 H, each d, each J 13.1, ArCH₂Ar), 3.69 (4 H, q, J 7.0, CH₂CH₃), 3.91 (4 H, t, J 4.7, ArOCH₂CH₂), 4.15 (4 H, t, J 4.7, ArOCH₂CH₂), 6.78, 6.90 and 7.91 (2 H, 4 H and 2 H, respectively, t, d and s, respectively, each J 7.5, ArH) and 7.26 (2 H, s, OH) (Found: C, 58.62; H, 5.16. C₃₆H₃₈O₆Br₂·0.11CHCl₃ requires C, 58.64; H, 5.19%).

5,17-Dibromo-25,26,27,28-tetrakis(ethoxyethoxy)calix[4]arene **8**

A suspension of compound **7** (3.00 g, 4.13 mmol) in acetone (300 ml) was treated with Cs₂CO₃ (29.1 g, 82.6 mmol). Bis(2-bromoethyl) ether (6.32 g, 41.3 mmol) was then added to the reaction mixture after which it was heated at reflux temperature for 24 h. After cooling, the mixture was diluted with ice-water and extracted with chloroform. The extract was washed twice with water, dried (MgSO₄), filtered and concentrated to dryness.

The residue was recrystallized from chloroform–methanol to give **8** (3.40 g, 95%) as a solid, mp 168.0–170.2 °C; δ_{H} (250 MHz; CDCl₃) 1.30 and 1.48 (each 3 H, each t, each *J* 7.0, CH₂CH₃), 3.45–3.96 (16 H, m, CH₂CH₃, ArOCH₂CH₂, ArOCH₂CH₂, ArCH₂Ar) and 6.63, 7.06 and 7.33 (1 H, 2 H and 2 H, respectively, t, d and s, respectively, each *J* 7.5, ArH) (Found: C, 60.13; H, 6.15. C₄₄H₅₄O₈Br₂·0.08CHCl₃ requires C, 60.15; H, 6.19%).

5,17-Diformyl-25,26,27,28-tetrakis(ethoxyethoxy)calix[4]arene **9**

A suspension of compound **8** (2.00 g, 2.30 mmol) in THF (50 ml) was stirred at –78 °C whilst a hexane solution of butyllithium (1.45 mol dm⁻³; 7.92 ml) was added to it from a dropping funnel over 1 h. After 1 h, DMF (3.53 ml, 45.9 mmol) was added to the reaction mixture which was then stirred at room temperature for 24 h. The reaction was stopped by addition of aqueous 1 mol dm⁻³ HCl to the mixture which was then extracted with THF. The extract was concentrated to dryness and the residue was dissolved in chloroform. The solution was washed twice with water, dried (MgSO₄), filtered and concentrated to dryness. The residue was recrystallized from chloroform–methanol to give **9** (0.32 g, 18%) as a solid, mp 69.1–72.5 °C; ν_{max} (Nujol)/cm⁻¹ 1690 (C=O stretch); δ_{H} (250 MHz; CDCl₃) 1.32 and 1.35 (each 3 H, each t, each *J* 7.1, CH₂CH₃), 3.44–4.12 (16 H, m, CH₂CH₃, ArOCH₂CH₂, ArOCH₂CH₂, ArCH₂Ar), 6.63, 7.07 and 7.69 (1 H, 2 H and 2 H, respectively, t, d and s, respectively, each *J* 7.6, ArH) and 9.68 (1 H, s, CHO) (Found: C, 71.23; H, 7.43. C₄₆H₅₆O₁₀·0.06CHCl₃ requires C, 71.28; H, 7.28%).

5,17-Bis(hydroxymethyl)-25,26,27,28-tetrakis(ethoxyethoxy)calix[4]arene **10**

A solution of compound 1,3-alternate-**9** (0.50 g, 0.65 mmol) in THF (10 ml) was treated with LiBH₄ (32.8 mg, 1.51 mmol) at room temperature. After 3 h, the reaction was stopped by addition of ice–water and aqueous 1 mol dm⁻³ HCl to the mixture which was then extracted with chloroform. The extract was washed twice with water, dried (MgSO₄), filtered and concentrated to dryness. The residue was recrystallized from chloroform–hexane to give **10** (0.25 g, 50%), mp 88.4–89.2 °C; ν_{max} (Nujol)/cm⁻¹ 3300 (OH stretch); δ_{H} (250 MHz; CDCl₃) 1.30 and 1.33 (each 3 H, each t, each *J* 7.0, CH₂CH₃), 3.45–3.96 (17 H, m, CH₂CH₃, ArOCH₂CH₂, ArOCH₂CH₂, ArCH₂Ar, OH), 4.44 (2 H, s, CH₂OH), 6.70, 7.12 and 7.15 (1 H, 2 H and 2 H, respectively, t, d and s, respectively, each *J* 7.5, ArH) (Found: C, 71.27; H, 7.82. C₄₆H₆₀O₁₀ requires C, 71.48; H, 7.82%).

5,17-Bis(chloromethyl)-25,26,27,28-tetrakis(ethoxyethoxy)calix[4]arene **11**

A solution of compound **10** (0.15 g, 0.19 mmol) in dichloromethane (20 ml) containing pyridine (0.07 g, 0.85 mmol) was stirred at room temperature whilst a dichloromethane solution (5 ml) containing thionyl chloride solution (0.11 g, 0.85 mmol) was added to it from a dropping funnel over 1 h. After 6 h, the reaction was stopped by addition of water to the mixture which was then extracted with chloroform. The extract was washed twice with water, dried (MgSO₄), filtered and concentrated to dryness to give **11** (0.13 g, 83%), mp 53.3–56.1 °C; δ_{H} (250 MHz; CDCl₃) 1.31 and 1.36 (each 3 H, each t, CH₂CH₃), 3.42–3.93 (16 H, m, CH₂CH₃, ArOCH₂CH₂, ArOCH₂CH₂, ArCH₂Ar), 4.46 (2 H, s, CH₂Cl) and 6.62, 7.08 and 7.14 (1 H, 2 H and 2 H, respectively, t, d and s, respectively, each *J* 7.5, ArH) (Found: C, 67.90; H, 7.30. C₄₆H₅₈O₈Cl₂·0.04CHCl₃ requires C, 67.88; H, 7.18%).

Compound **2**

A solution of compound **11** (90 mg, 0.12 mmol) in DMF (30 ml) under a nitrogen atmosphere was treated with NaN₃ (20 mg, 0.26 mmol). The resultant mixture was heated at 100 °C for 6.5 h after which it was diluted with water and extracted

with diethyl ether. The ether layer was washed twice with water, dried (MgSO₄) and filtered. The filtrate was mixed with chlorobenzene (100 ml) after which diethyl ether was evaporated from the mixed solvent. To the residual chlorobenzene solution was added C₆₀ (80 mg, 0.11 mmol) and the mixture was refluxed for 36 h. After evaporation of the mixture, the products were subjected to flash column chromatography (silica gel, toluene) to remove unchanged C₆₀. The residual products were isolated by preparative TLC (silica gel, dichloromethane) to give **2** (4 mg, 3%) as a brown solid, mp (decomp.) >300 °C; δ_{H} (250 MHz; CDCl₃) 1.09 (6 H, t, *J* 6.9, OCH₂CH₃), 1.43 (6 H, t, *J* 7.1, OCH₂CH₃), 3.35–4.16 (32 H, m, ArCH₂Ar, OCH₂), 4.94 (2 H, t, *J* 14.7, NCH₂), 5.44 (2 H, t, *J* 14.8, NCH₂), 6.59–6.70 [2 H, m, ArH(*para*)], 7.11 [2 H, d, *J* 7.5, ArH(*meta*)], 7.17 [2 H, d, *J* 7.5, ArH'(*meta*)], 7.38 [2 H, s, ArH(*para*)] and 7.47 [2 H, s, ArH'(*para*)].

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References

- 1 D. S. Bethune, R. D. Johnson, J. R. Salem, M. S. de Vries and C. S. Yonori, *Nature*, 1993, **123**, 366.
- 2 A. Gügel, A. Kraus, J. Spickermann, P. Belik and K. Müllen, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 559; A. Kraus, A. Gügel, P. Belik, M. Walter and K. Müllen, *Tetrahedron*, 1995, **51**, 9927.
- 3 S. N. Davey, D. A. Leigh, A. E. Moody, L. W. Tetler and F. A. Wade, *J. Chem. Soc., Chem. Commun.*, 1994, 397.
- 4 J. Osterodt, M. Nieger, P.-M. Windscheif and F. Vögtle, *Chem. Ber.*, 1993, **126**, 2331; J. Osterodt, A. Zett and F. Vögtle, *Tetrahedron*, 1996, **52**, 4949.
- 5 F. Diederich, U. Jonas, V. Gramlich, A. Herrmann, H. Ringsdorf and C. Thilgen, *Helv. Chim. Acta*, 1993, **76**, 2445; U. Jonas, F. Cardullo, P. Belik, F. Diederich, A. Gügel, E. Harth, A. Herrmann, L. Isaacs, K. Müllen, H. Ringsdorf, C. Thilgen, P. Uhlmann, A. Vasella, C. A. A. Waldruff and M. Walter, *Chem. Eur. J.*, 1995, **1**, 243.
- 6 A. Ikeda and S. Shinkai, *Chem. Lett.*, 1996, 803.
- 7 A. Ikeda, C. Fukuhara and S. Shinkai, *Tetrahedron Lett.*, 1996, **37**, 7091.
- 8 A. Ikeda, C. Fukuhara and S. Shinkai, *Chem. Lett.*, 1997, 407.
- 9 J. L. Atwood, G. A. Koutsantonis and C. L. Raston, *Nature*, 1994, **368**, 229.
- 10 C. L. Raston, J. L. Atwood, P. J. Nichols and I. B. N. Sudria, *Chem. Commun.*, 1996, 2615.
- 11 T. Suzuki, K. Nakashima and S. Shinkai, *Chem. Lett.*, 1994, 699.
- 12 T. Suzuki, K. Nakashima and S. Shinkai, *Tetrahedron Lett.*, 1995, **36**, 249.
- 13 T. Haino, M. Yanase and Y. Fukazawa, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 360.
- 14 K. Araki, K. Akao, A. Ikeda, T. Suzuki and S. Shinkai, *Tetrahedron Lett.*, 1996, **37**, 73.
- 15 A. Ikeda, M. Yoshimura and S. Shinkai, *Tetrahedron Lett.*, 1997, **38**, 2107.
- 16 For comprehensive reviews see C. D. Gutsche, *Calixarenes*, Royal Society of Chemistry, Cambridge, 1989; *Calixarenes*, eds. J. Vicens and V. Böhmer, Kluwer Academic Express, Dordrecht, 1991; V. Böhmer, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 713; S. Shinkai, *Tetrahedron*, 1993, **49**, 8933; H. Otsuka and S. Shinkai, *Supramol. Sci.*, 1996, **3**, 189.
- 17 F. Ohseto and S. Shinkai, *Chem. Lett.*, 1993, 2045.
- 18 A. Ikeda, T. Tsudera and S. Shinkai, *J. Org. Chem.*, 1997, **62**, 3568.
- 19 T. Grösser, M. Prato, V. Lucchini, A. Hirsch and F. Wudl, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1343.
- 20 A. Ikeda and S. Shinkai, *Tetrahedron Lett.*, 1992, **33**, 7385.
- 21 A. Ikeda and S. Shinkai, *J. Am. Chem. Soc.*, 1994, **116**, 3102 and references cited therein.
- 22 A. Ikeda, H. Tsuzuki and S. Shinkai, *J. Chem. Soc., Perkin Trans. 2*, 1994, 2073.
- 23 F. Vögtle, J. Gross, C. Seel and M. Nieger, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 1069 and references cited therein.
- 24 For the π -donor participation see: M. Iyoda, Y. Kuwatani, T. Yamauchi and J. Oda, *J. Chem. Soc., Chem. Commun.*, 1988, 65; R. Leokes and F. Vögtle, *Chem. Ber.*, 1983, **116**, 215; J.-L. Pierre,

- P. Baret, P. Chautemps and M. Armand, *J. Am. Chem. Soc.*, 1981, **103**, 2986; H. C. Kang, A. W. Hanson, B. Eaton and V. Boekelheide, *J. Am. Chem. Soc.*, 1985, **107**, 1079; F. R. Heirtzler, H. Hopf, P. G. Jones, P. Bubenitschek and V. Lehne, *J. Org. Chem.*, 1993, **58**, 2781; J. E. Gano, G. Subramaniam and R. Birnbaum, *J. Org. Chem.*, 1990, **55**, 4760.
- 25 For a theoretical consideration of the cation- π interaction see D. A. Dougherty, *Science*, 1996, **271**, 163.
- 26 A. Casnati, P. Minari, A. Pochini, R. Ungaro, W. F. Nigenhuis, F. de Jong and D. N. Reinhoudt, *Isr. J. Chem.*, 1992, **32**, 79.
- 27 F. Inokuchi, Y. Shiomi, H. Kawabata, T. Sakaki and S. Shinkai, *Chem. Lett.*, 1993, 1595.
- 28 A. V. Hill, *J. Physiol.*, 1910, **40**, iv-vii.
- 29 H. A. Benesi and J. H. Hildebrand, *J. Am. Chem. Soc.*, 1949, **71**, 2073.

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