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Calix[4]arene based dendrimers†

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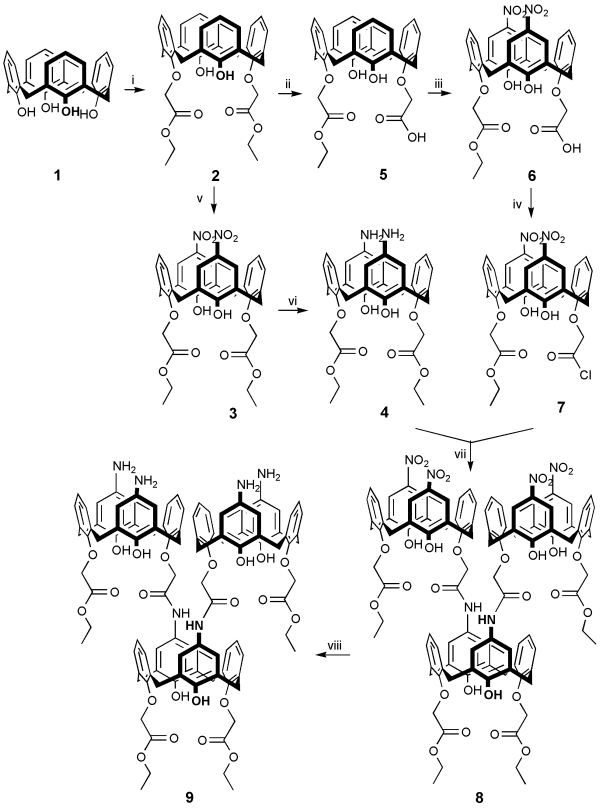
The synthesis of calix[4]arene based dendrimers containing up to seven calix[4]arene moieties is described, including the X-ray crystal structure of a tris-calix[4]arene branching derivative.

The discovery of specific functions and novel properties that are a direct consequence of the tree-like dendritic architecture has stimulated spectacular growth in this macromolecular field of chemistry.[1] Dendrimers contain three topologically different regions (core, branches and surface), each of which can be designed to exhibit functional properties including the recognition of guest substrates, catalysis and energy transfer.[1,2] Calixarenes are macrocyclic molecules that can be modified to bind a variety of charged and neutral guest species,[3] however, their integration into *dendritic* structural frameworks remains largely unexplored.[4] Interestingly, the physical and chemical properties of such polycalixarene dendritic materials will be dependent upon the nature of calixarene complexed species. We report here the preparation of novel calix[4]arene based dendrimers containing up to seven calix[4]arene moieties.

The calix[4]arene moiety by virtue of its unique three-dimensional ′cone′ topology is an attractive building motif to use as a potential dendrimer branching unit *via* appropriate upper and lower rim functionality. The synthetic strategy for the preparation of the target dendritic hepta-calix[4]arene (**11**) involved the initial preparation of the tetra-amine-tricalix[4]arene branching synthon (**9**). (Scheme 1). The dinitro diethyl ester calix[4]arene derivative (**3**)[5] was prepared in 50% overall yield from calix[4]arene (**1**). Hydrogenation of (**3**) gave the diamine (**4**) quantitatively. Selective hydrolysis of (**2**) using one equiv. of KOH afforded the potassium salt of (**5**) in 80% yield. Nitration of (**5**) gave (**6**) which on reaction with oxalyl chloride produced the acid chloride (**7**) in near quantitative yield. Reaction of (**4**) with two equivalents of (**7**) in the presence of excess pyridine produced the tetra-nitro-tris-calix[4]arene branching synthon (**8**) in 60% yield.‡ The structure of (**8**) was also characterised by X-ray crystallography.§ The structure consists of discrete molecules as shown in Fig. 1 together with solvent molecules. The molecule contains three calix[4]arenes all in the ′cone′ conformation with the well-known C_2 distortion. Two of the calixarenes are side-by-side (Fig. 1) with ′cone′ axes directed in approximately parallel directions (angle of intersection 20.8°). At the lower rim of each of these two calix[4]arenes, an amide link leads to the upper rim of a third calixarene. These links are connected to the two phenyl rings unsubstituted at the lower rim. Hydrogenation of (**8**) gave the tetra-amine (**9**) which on reaction with four equiv. of acid chloride (**10**) produced the dendritic poly-calix[4]arene compound (**11**) as a white powder in 27% yield after silica column chromatography and recrystallisation from acetonitrile‡ (Scheme 2). The MALDI-TOF spectrum of (**11**) displayed peaks at 4975 and 4991, corresponding to $[M + 2Na + MeCN]^+$ and $[M + Na + K + MeCN]^+$ respectively. We have shown that simple lower rim 1,3-acid-dialkylamide substituted calix[4]arenes form neutral 1 : 1 complexes with lanthanides[6] and it was of



Scheme 1 *Reagents and conditions:* i, $BrCH_2C(O)OEt$ (2.1 eq.), K_2CO_3 (1 eq.), Me_2CO, reflux 22 h; ii, KOH (1 eq.), Me_2CO, rt 24 h; iii, 10% soln of HNO_3 and HCl in H_2O, CH_2Cl_2, 0.5 h; iv, $(COCl)_2$, CH_2Cl_2, reflux, 5 h; v, 65% HNO_3–AcOH, CH_2Cl_2, vi, H_2, 10% Pd/C, THF–EtOH, 0.1 bar, 55 °C, 5 h; vii, CH_2Cl_2, Pyr., rt,1 h, viii = vi, 7 h.

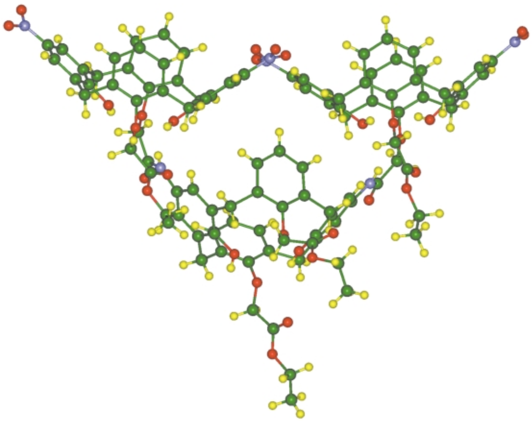


Fig. 1 The structure of (**8**). Oxygen red, nitrogen blue, carbon green, hydrogen yellow.

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† Electronic supplementary information (ESI) available: ¹H NMR and UV-Vis spectra and data analysis. See http://www.rsc.org/suppdata/cc/b2/b202315f/

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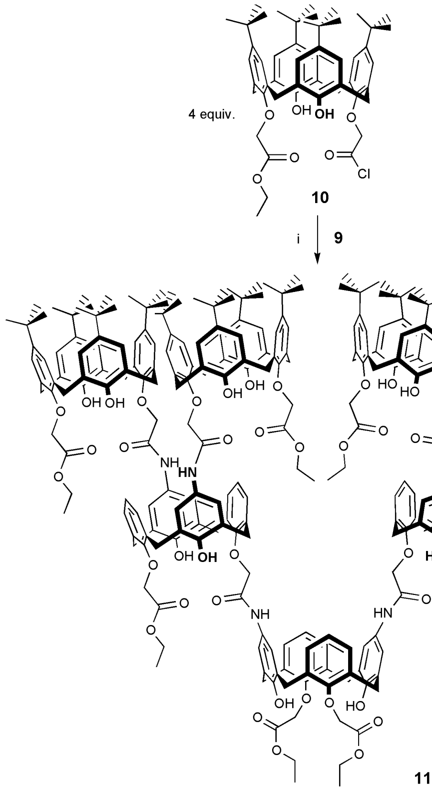

Scheme 2 *Reagents and conditions:* i, CH_2Cl_2, Pyr., rt, 1 h.

interest therefore to convert the ester groups of (**11**) to carboxylic acids. Attempted saponification of the ester groups of (**11**) by treating with excess NaOH in ethanol however, disappointingly produced a complex mixture of inseparable products.

An alternative synthetic strategy was used to prepare the calixarene based dendritic synthon (**20**) containing lower rim acid-amide functionality for lanthanide complexation (Scheme 3).

Treatment of (**1**) with two equiv. of *tert*-butyl bromoacetate in the presence of K_2CO_3 afforded the bis-ester (**12**) in 87% yield. Monohydrolysis, reaction with oxalyl chloride and condensation with diethyl amine produced the ester amide (**14**) in 75% overall yield. In order to prevent the removal of the *tert*-butyl ester groups under the strongly acidic conditions typically used in nitration reactions a new heterogeneous preparative method was employed. Silica gel treated with concentrated HNO_3 was vigorously stirred with a CH_2Cl_2 solution of calixarenes (**13**) or (**14**) and dinitro derivatives (**15**) and (**17**) were isolated in 70 and 60% respective yields. Catalytic hydrogenation of (**15**) gave the diamine (**16**) which on reaction with two equiv. of acid chloride (**18**) afforded (**19**) in 53% yield. Acid removal of the *tert*-butyl ester groups produced the tris-calix[4]arene acid amide dendritic compound (**20**) in 55% yield.‡

Preliminary lanthanide cation coordination investigations using UV-Vis titration experiments revealed (**20**) to form strong trimetallic complexes with La^{3+}, Gd^{3+} and Lu^{3+} in polar organic solvents such as methanol, acetonitrile and DMSO.

In summary we have demonstrated the use of the calix[4]arene moiety as a dendrimer branching unit in the construction of novel calix[4]arene based dendrimers containing up to seven calixarene moieties. The inclusion and metal cation coordination properties of such materials are currently under investigation.

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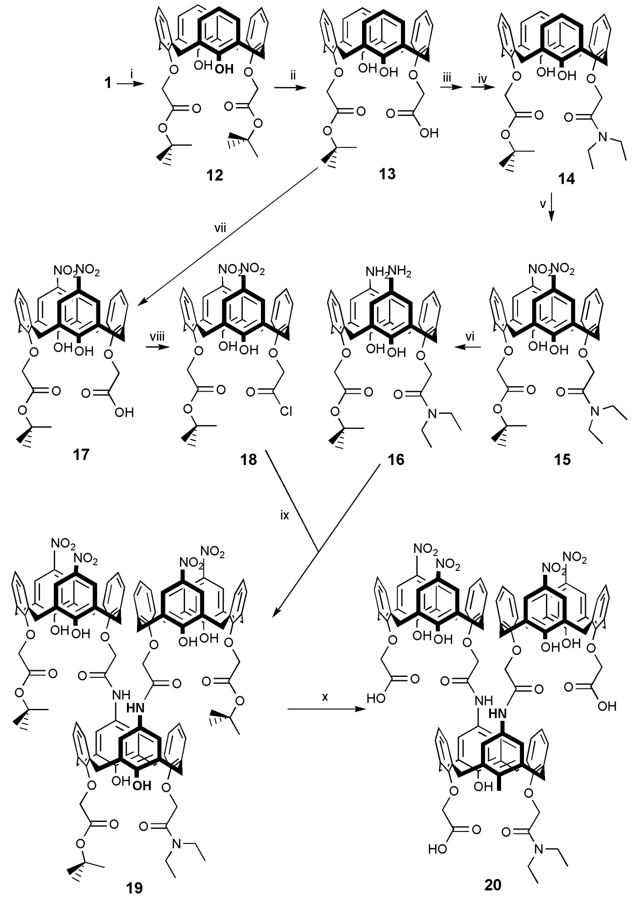

Scheme 3 *Reagents and conditions:* i, $BrCH_2C(O)O^tBu$ (2.1 eq.), K_2CO_3 (1 eq.), Me_2CO, reflux, 22 h; ii, KOH (1 eq.), Me_2CO, rt, 24 h; iii, $(COCl)_2$, CH_2Cl_2, reflux, 4 h; iv, $HNEt_2$ (5 eq.), CH_2Cl_2; v, HNO_3–SiO_2, CH_2Cl_2; vi, H_2, 10% Pd/C, THF–EtOH, 0.1 bar, 55 °C, 5 h; vii = v; viii $(COCl)_2$, CH_2Cl_2, reflux, 4 h; ix, MeCN, Pyr., rt,1 h; x, TFA–CH_2Cl_2, reflux.

Notes and references

‡ All new compounds were characterised by ^1H, ^{13}C NMR and mass spectrometry.

§ Crystal data for (**8**). $2(CH_3)_2CO$, EtOH, H_2O, $C_{112}H_{113}N_6O_{34}$, M = 2087.08, triclinic, spacegroup $P1$, a = 15.32(2), b = 15.59(2), c = 25.11(3) Å, α = 82.42(1), β = 80.29(1), γ = 68.87(1)°, U = 5496 Å^3, Z = 2, D_c = 1.261 Mg m^{-3}. Intensity data were collected with Mo-Kα radiation using the MARresearch Image Plate System. The crystal was positioned at 70 mm from the image plate. 100 frames were measured at 2° intervals with a counting time of 4 min to give 19156 independent reflections.The final R values were $R1$ 0.114 and $wR2$ 0.2951 for 10247 data with $I > 2\sigma(I)$. CCDC 181269. See http://www.rsc.org/suppdata/cc/b2/b202315f/ for crystallographic files in cif or other electronic format.

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