



Pentakis-thiacalix[4]arenes with nitrile fragments: receptor properties toward cations of *s*- and *d*-metals and self-assembly of nanoscale aggregates

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Pentakis-thiacalix[4]arenes containing thiacalix[4]arene fragments in *cone*, *partial cone* and *1,3-alternate* conformations as their central core have been obtained. Their interaction with cations of *s*- and *d*-metals gives supramolecular assemblies whose composition depends on the conformation of pentakis-thiacalix[4]arenes and the nature of the ‘guests’.

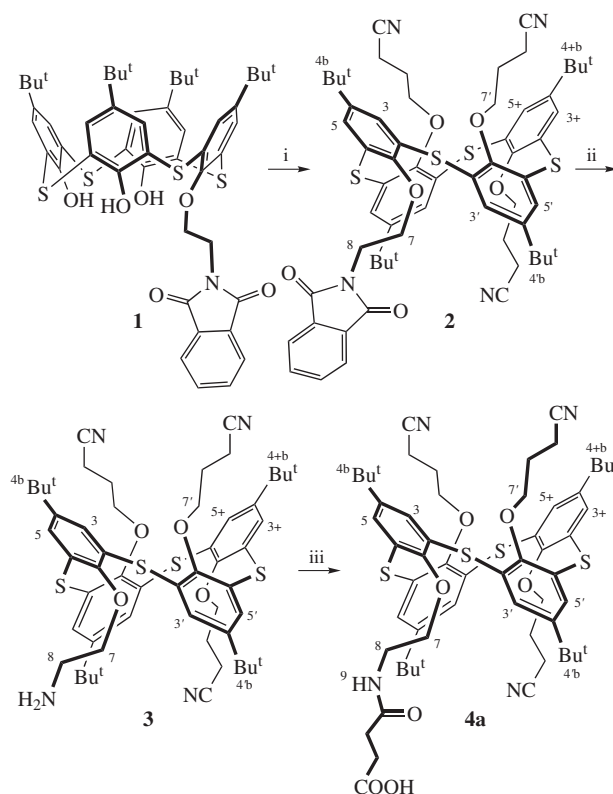
Organic nanoscale structures are widely used to create materials able to molecular recognition of targeted substrates.^{1,2} Calixarenes have proved to be promising synthetic building blocks for the design of selective ‘host’ molecules.^{3–8} Combining multiple calixarene fragments in one structure yields multifunctional nanoscale receptors able to recognize ion pairs,^{9,10} surface of biomacromolecules and also, to transfer them through cell membranes.¹¹ Nitrile group is one of topical due to its synthetic potential and complexation properties.^{12,13} Polymers containing nitrile groups are used in lithium-ion batteries as electrodes.^{14,15} For thiacalix[4]arenes tetrasubstituted at the lower rim, three conformational isomers of the macrocycle (*cone*, *partial cone*, *1,3-alternate*) are easily synthesized.^{16,17}

In this regard we studied the block synthesis of nitrile-containing pentakis-thiacalix[4]arenes in which the central core is formed by thiacalix[4]arene fragments in *cone*, *partial cone* and *1,3-alternate* conformations.

Previously we have shown^{18,19} that variation of the length of a spacer linking the phthalimide fragment and leaving group in bromoalkylphthalimides makes it possible to vary the number of phthalimide groups at the lower rim of thiacalix[4]arene. Mono-substituted derivative **1** containing the phthalimide fragment¹⁸ was selected as starting compound for the synthesis of the terminal fragment precursor of pentakis-thiacalix[4]arenes. The target compound **4a** was obtained by alkylation of the monosubstituted macrocycle **1** with 4-chlorobutyronitrile followed by removing the phthaloyl protection with hydrazine hydrate and amine acylation with succinic anhydride (Scheme 1).[†]

Conformations of thiacalix[4]arenes **2–4** were established by two-dimensional ¹H–¹H NMR NOESY spectroscopy. The presence of cross-peaks between spatially close protons of *tert*-butyl groups and the substituents at the lower rim of the macrocycle clearly indicates that they possess *1,3-alternate* conformation.

Recently, it was found that thiacalix[4]arene derivatives containing aminoethylidene fragments exist in solution as a mixture of conformers¹⁹ due to twisting of the fragment through the macrocyclic ring. Using ¹H NMR spectroscopy, it was shown that macrocycle **3** exists as a single conformer at room temperature. Acylation of the amine group of **3** with succinic anhydride at room temperature does not lead to the formation of products



Scheme 1 Reagents and conditions: i, 4-chlorobutyronitrile, K₂CO₃, acetone; ii, N₂H₄·H₂O, THF–EtOH; (iii) succinic anhydride, CH₂Cl₂, 0 °C.

related to other conformations. However, raising temperature (35 °C or higher) results in a mixture of conformational isomers of *1,3-alternate* and *partial cone* in the ratio 82 : 18 (Scheme 2). In the ¹H NMR spectrum of such reaction mixture, the proton signals of the *partial cone* conformer **4b** are clearly observed (see Figure S1, Online Supplementary Materials).

We selected thiacalix[4]arene based tetraethanolamide stereoisomers **5–7** (Scheme 3) as the central core of pentakis-thiacalix[4]arenes because they can be easily synthesized from corresponding tetraesters.²⁰ In addition, they contain primary hydroxy groups available for further functionalization. The condensation between thiacalix[4]arenes **4a** and **5–7** was performed using dicyclohexylcarbodiimide (DCC) and dimethylaminopyridine (DMAP).²¹

[†] For synthetic procedures and characteristics of compounds **2**, **3**, **4a**, **8–10**, see Online Supplementary Materials.