Synthetic receptors for transition metal cations – tetrahydrazides on the basis of *p-tert*-butylthiacalix[4]arene

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Stereoisomers of tetrahydrazide on the basis of *p-tert*-butylthiacalix[4]arene have been synthesised and characterised by IR spectroscopy, ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry; the receptor properties of novel compounds towards metal cations, including most dangerous environmental pollutants, have been characterised by picrate extraction.

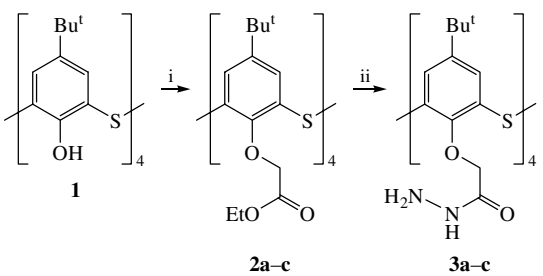
Recently, much attention has been paid to chemical separation techniques, which involve the design and synthesis of new extractants for transition metal ions.[1]

Calixarenes and thiacalixarenes are cyclic oligomers, prepared by condensation of *para*-substituted phenols and formaldehyde or sulfur under alkaline conditions.[2–4] These macrocycles are an excellent molecular platform for the design of sophisticated structures capable of molecular recognition of cations, anions and neutral molecules.[5,6] The calixarene structure provides a unique combination of a conformationally flexible macrocyclic ring, conformationally rigid aromatic units and easy-to-modify hydroxyls to construct multi-armed podand receptors with different geometries of binding sites.

p-tert-Butylthiacalix[4]arene **1** is known to bind transition metal cations by coordination with bridging sulfide fragments.[7] Nevertheless, there are only few publications concerning the extraction of transition metal cations by derivatives of **1**, substituted at the lower rim.[8] Miyano with coworkers reported on the facile synthesis[9] of three tetraester stereoisomers: cone **2a**, partial cone **2b**, 1,3-alternate **2c**, providing a direct synthetic route to stereoisomers of tetrasubstituted thiacalix[4]arenes. A usual synthetic approach to further modification consists of three stages: hydrolysis leading to an acid, its conversion into chloroanhydride and further modification with appropriate reagent.[10]

In this work, we report a one-step synthesis of three macrocyclic receptors: *cone* **3a**, *partial cone* **3b**, and 1,3-*alternate* **3c** stereoisomers of tetrahydrazide on the basis of thiacalix[4]arene by hydrazinolysis† of corresponding tetraesters **2a–c** (Scheme 1) with good to excellent yields (80, 95 and 90%, respectively). Note that the interconversion of stereoisomers does not occur under the conditions of hydrazinolysis.

Structures of the compounds obtained (Scheme 2) were characterised by a number of physical methods.† The conformation of tetrasubstituted thiacalix[4]arenes can be determined by signal patterns and chemical shifts of methylene and *tert*-butyl groups in ^{1}H NMR spectra.[8] Partial cone (**3b**) is the only stereoisomer possessing three nonequivalent groups of *tert*-butyl residues, which will give a 2:1:1 resonance pattern in NMR spectra (1.17, 1.30 and 1.37 ppm). Symmetrical structures of cone and 1,3-alternate stereoisomers should give the same pattern in NMR spectra; however, it is possible to distinguish between these stereoisomers considering chemical shifts of $–OCH_2C(O)–$ units. In a 1,3-alternate conformation, these protons are located in a shielding zone of two adjacent benzene rings, and signals



Scheme 1 *Reagents and conditions*: i, see ref. 8; ii, see footnote.†

of these protons are located in a higher field than the signal of corresponding protons of cone stereoisomer (4.57 and 4.86 ppm, respectively). *tert*-Butyl protons of the 1,3-alternate stereoisomer are located in a deshielding zone of not only attaching phenyl unit but also two adjacent benzene rings. By that reason *tert*-butyl protons signal of 1,3-alternate should appear in a lower field, compared to *tert*-butyl protons signal of the cone stereoisomer (1.26 and 1.10 ppm, respectively). Thus, structures of compounds **3a** and **3c** could be unambiguously assigned for cone and 1,3-alternate stereoisomers, respectively.

The signal of amide protons of compound **3a** in the ^{1}H NMR spectrum appears in a very weak field (9.90 ppm) indicating strong H-bonding between four amide moieties located on the same side of the macrocyclic plane. This is confirmed by the presence of only H-bonded amide group absorption band (3330 cm^{-1}) in IR spectra of **3a** in solid state and solution. The chemical shift (7.37 ppm) and sharp form of an amide proton peak in ^{1}H NMR spectrum of **3c** and IR spectra in solid state and solution, where both bonded (3330 cm^{-1}) and free (3416 cm^{-1}) amide absorption bands are present, indicate the existence of

† For **3a**. Solution of compound **2a** (1.00 g, 0.95 mmol) and $N_2H_4·H_2O$ (0.96 ml, 19 mmol) in a mixture of Et_2O (20 ml) and ethanol (5 ml) was stirred at reflux for 20 h, concentrated at reduced pressure and dried *in vacuo*. The pure product was obtained by recrystallization from Pr^{i}OH. Yield 0.76 g (80%); mp 258 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.10 (s, 36H, Bu^t), 3.95 (br. s, 8H, NH_2), 4.86 (s, 8H, COCH), 7.34 (s, 8H, ArH), 9.90 (br. s, 4H, CONH). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 30.9, 34.1, 75.0, 128.2, 134.8, 147.9, 158.0, 168.8. IR (KBr pellet, ν/cm^{-1}): 3324 (NH-bonded), 1675 (CO), 1266 (COC). IR (0.05 M $CHCl_3$ solution, ν/cm^{-1}): 3330 (NH-bonded), 1670 (CO), 1265 (COC). MS ESI, *m/z*: 1031 (M + Na$^+$), 1047 (M + K$^+$).

For **3b**. Suspension of compound **2b** (1.00 g, 0.95 mmol) and $N_2H_4·H_2O$ (0.96 ml, 19 mmol) in ethanol (10 ml) was stirred at reflux for 40 h, concentrated at reduced pressure and dried *in vacuo*. The pure product was obtained by recrystallization from CH_2Cl_2–EtOH. Yield, 0.90 g (95%); mp 226 C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.17 (s, 18H, Bu^t), 1.30 (s, 9H, Bu^t), 1.37 (s, 9H, Bu^t), 2.26 (d, 2H, NH_2, $^3J_{HH}$ 4.3 Hz), 3.86 (br. s, 2H, NH_2), 3.94 (br. s, 4H, NH_2), 4.27 (s, 2H, O–CH_2), 4.45 (br. t, 1H, NH, $^3J_{HH}$ 4.3 Hz), 4.75, 4.64 (AB-q, 4H, O-CH_2, $^2J_{HH}$ 14.2 Hz), 4.80 (s, 2H, O–CH_2), 7.38 (d, 2H, ArH, $^4J_{HH}$ 2.6 Hz), 7.44 (s, 2H, ArH), 7.59 (d, 2H, ArH, $^4J_{HH}$ 2.6 Hz), 7.85 (s, 2H, ArH), 8.50 (br. s, 2H, NH), 8.96 (br. s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 31.2, 34.3, 34.5, 31.0, 34.7, 64.6, 72.6, 74.1, 126.0, 126.9, 127.8, 128.3, 128.4, 131.1, 135.5, 137.1, 148.8, 149.6, 152.4, 156.5, 158.4, 165.5, 168.3, 168.4. IR (KBr pellet, ν/cm^{-1}): 3434, 3416 (NH-free), 3323, 3278 (NH-bonded), 1680 (CO), 1268 (COC). IR (0.05 M $CHCl_3$ solution, ν/cm^{-1}): 3416 (NH-free), 3330 (NH-bonded), 1677 (CO), 1264 (COC). MS ESI, *m/z*: 1031 (M + Na$^+$), 1047 (M + K$^+$).

For **3c**. Suspension of compound **2c** (1.00 g, 0.95 mmol) and $N_2H_4·H_2O$ (0.96 ml, 19 mmol) in a mixture of THF (15 ml) and ethanol (15 ml) was stirred at reflux for 50 h, concentrated at reduced pressure and dried *in vacuo*. The pure product was obtained by recrystallization from CH_2Cl_2–EtOH. Yield, 0.85 g (90%); mp 274 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.26 (s, 36H, Bu^t), 3.58 (br. s, 8H, NH_2), 4.57 (s, 8H, COCH), 7.37 (s, 4H, CONH), 7.41 (s, 8H, Ar*H*). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 31.3, 34.5, 68.3, 127.2, 128.5, 148.8, 154.7, 168.1. IR (KBr pellet, ν/cm^{-1}): 3416 (NH-free), 3320 (NH-bonded), 1676 (CO), 1270 (COC). IR (0.05 M $CHCl_3$ solution, ν/cm^{-1}): 3415 (NH-free), 3321 (NH-bonded), 1676 (CO), 1263 (COC). MS MALDI-TOF, *m/z*: 1009 (M + H$^+$), 1031 (M + Na$^+$).