J Incl Phenom Macrocycl Chem (2008) 61:139–145
DOI 10.1007/s10847-007-9406-0

ORIGINAL ARTICLE

Syntheses and extraction properties of novel biscalixarene and thiacalix[4]arene hydrazone derivatives

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Received: 25 July 2007 / Accepted: 14 December 2007 / Published online: 19 January 2008

Abstract By reacting thiacalix[4]arene with *p*-tosyloxyethoxylbenzaldehyde 1, 3-*bis*(benzaldehyde-4-oxyethyloxy)-*p*-*tert*-butylthiacalix[4]arene (**2**) were prepared in yield of 65%. Refluxing compound **2** with aniline, salicylic hydrazide, nicotinic hydrazide and isonicotinic hydrazide, novel ringopening 1,3-*bis*-arylformyl-hydrazone substituted thiacalix[4]arene derivatives (**3a**–**3d**) were obtained in yields of 77–89%. Refluxing compound **2** with *o*-phenylendiamine, oxalyl dihydrazide, malonic dihydrazide and adipic dihydrazide in "1 + 1" intermolecular condensation mode under diluted condition, novel 1,3-*bis*-acyl hydrazone-bridged calix[4]arene derivatives (**4a**–**4d**) were prepared in good yields. Moreover, by condensating compound **2** with 1,3-*bis*(hydrazinocarbonyl-methoxy)-*p*-*tert*-butylcalix[4]arene (**5**), the first example of hydrazone-bridged biscalixarene (**6**) with calix[4]arene and thiacalix[4]arene subunits was facilely synthesized in yield of 90%. The noncompetitive and competitive extracting experiments showed that these novel hosts were good receptors for both metal cations and α-amino acids. Compounds **3a–3d** and **4a–4d** showed similar binding properties with high extraction percentage but low extracting selectivities. Biscalixarene **6** exhibited not only high extracting abilities but also good extracting selectivities.

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Keywords Thiacalix[4]arene · Biscalixarene · Hydrazone · Extraction · Synthesis

Introduction

Calixarenes are one of the most important molecular building platforms in host–guest chemistry [1]. Varieties of sophisticated molecular hosts bearing calixarene skeleton(s) were synthesized and their recognized properties were extensively studied. Among all kind of calixarene derivatives, bridging calixarene and bridging biscalixarene played important roles due to that the bridging chain not only could inhibit the flexibility of calixarene conformation effectively, but also construct new cavities for binding guests [1, 2].

Thiacalixarene is a new member of the calixarene family. Its potential applications based on replacing traditional methyl bridges with sulfur atoms [3]. Up to now, some bridging thiacalixarene, such as thiacalix[4]crowns, and their binding properties were studied by Vicens [4], Bitter [5–9], Reinhoudt [10], Lhoták [11], Miyano [12], Yang [13] etc. As to bisthiacalix[4]arene, several examples were synthesized by condensating thiacalix[4]arene (or its derivatives) directly with bifunctional reagents, such as diethylene glycol [14], bis(tosyloxyethoxy)benzene [15], diimine [16]. However, comparing with "classical" bridging calix[4]arene and biscalix[4]arene, many research fields of bridging thiacalix[4]arene and bisthiacalix[4]arene are still unknown. Lately, thiacalix[4]arene bis-benzaldehyde derivative were used to construct novel bridging thiacalix[4]arene and bisthiacalix[4]arene [17]. In this paper, we wish to report the syntheses and binding properties of series of novel thiacalix[4]arene hydrazone derivatives and biscalixarene by using thiacalix[4]arene bis-benzaldehyde derivative as building block in details.

Experimental

Melting points were uncorrected. ^{1}H-NMR spectra were recorded in $CDCl_3$ on a Bruker-ARX 500 instrument, using TMS as reference. ESI-MS spectra were obtained from DECAX-30000 LCQ Deca XP mass spectrometer. Elemental analyses were performed at Vario EL III Elemental Analyzer. IR spectra were recorded on AVATAR360 spectrometer. The UV-Vis measurements were performed on Varian UV-Vis spectrometer. Cation concentrations in *competitive extracting experiments* were measured with Thermo Intrepid XSP Radial ICP-OES. *p*-Tosyloxyethoxylbenzaldehyde and 1,3-*bis*(hydrazine-carbonylmethoxy)-*p*-*tert*-butylcalix[4]arene **5** were prepared according to published procedures [18]. The organic and inorganic reagents, except special instruction, were analytical grade or chemical grade without further purification.

The syntheses of 1, 3-*bis*(benzaldehyde-4-oxyethyloxy)-*p*-*tert*-butylthiacalix[4]arene (**2**)

A mixture of *p*-*tert*-butylthiacalix[4]arene (2 mmol, 1.44 g), *p*-tosyloxyethoxylbenzaldehyde (4 mmol, 1.28 g) and Na_2CO_3 (8 mmol, 1.10 g) was stirred in refluxing dry toluene (100 mL) for 48 h under N_2 atmosphere. After distilling off the solvent under reduced pressure, the residue was treated with 30 mL HCl (10%) and extracted with 40 mL $CHCl_3$. The organic layer was separated, dried over anhydrous $MgSO_4$, then filtered and concentrated. After column chromatography (100–200 mesh silica gel, 60–90 °C petroleum ether-CH_2Cl_2 (1:5, V/V) as an eluent), thiacalix[4]arene bis-benzaldehyde derivative **1** was obtained as white powder in yield of 65%.

Compound **2**: m.p. 212–214 °C; ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 0.79 [s, 18H, $C(CH_3)_3$], 1.35 [s, 18H, $C(CH_3)_3$], 4.21 (bs, 4H, OCH_2), 4.86 (bs, 4H, OCH_2), 6.95 (s, 4 H, ArH), 7.01 (d, J = 8.0 Hz, 4H, ArH); 7.70 (s, 4 H, ArH), 7.79 (d, J = 8.0 Hz, 4H, ArH), 8.10 (s, 2H, OH), 9.74 (s, 2H, ArCHO); IR (KBr) v:1694 cm^{-1}(C=O); MS m/z (%): 1016.5 (M^+, 100). Anal. calcd. for $C_{58}H_{64}O_8S_4$: C 68.49, H 6.34; found C 68.43, H 6.41.

The syntheses of ringopening 1,3-bis-arylformyl-hydrazone substituted thiacalix[4]arene derivatives (**3a–3d**)

The mixture of compound **2** (0.30 g, 0.3 mmol) and 0.80 mmol aniline or corresponding hydrazide (salicylic hydrazide, nicotinic hydrazide and isonicotinic hydrazide) was stirred and refluxed in 20 mL chloroform/methanol (1:1, V/V), using 0.3 mL acetic acid as catalyst. The materials were disappeared by TLC detection (approximate 12 h) and some precipitation separated out. After the solvent was removed under reduced pressure, the residue was treated with MeOH (15 mL) to give compounds **3a–3d** as white powder in yield of 83, 80, 77, and 89%, respectively.

3a: m.p. 189–192 °C; ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 0.80 [s, 18H, $C(CH_3)_3$], 1.34 [s, 18H, $C(CH_3)_3$], 4.18–4.89 (m, 8H, OCH_2), 6.69–8.18 (m, 26 H, ArH), 9.53 (bs, 2H, OH), 9.73(s, 2H, ArCH); IR (KBr) v:1617 cm^{-1}(C=N); MS m/z (%): 1167.7 (M^+, 100). Anal. calcd. for $C_{70}H_{74}O_6S_4N_2$: C 72.02, H 6.39; found C 71.93, H 6.45.

3b: m.p. 199–202 °C; ^{1}H-NMR (500 MHz, $CDCl_3$, δ): 0.79 [s, 18H, $C(CH_3)_3$], 1.33 [s, 18H, $C(CH_3)_3$], 4.08–4.87 (m, 8H, OCH_2), 6.69–8.18 (m, 28 H, ArH and OH), 8.93(bs, 2H, CH=N), 9.73 (bs, 2H, NHCO); IR (KBr) v:1671 cm^{-1}(C=O); MS m/z (%): 1284.3 (M^+, 100). Anal. calcd. for $C_{72}H_{76}O_{10}S_4N_4$: C 67.32, H 5.96; found C 67.23, H 6.07.

3c: m.p. 206–209 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.76 [s, 18H, $C(CH_3)_3$], 1.33 [s, 18H, $C(CH_3)_3$], 4.07–4.97 (m, 8H, OCH_2), 6.48–8.73 (m, 26 H, ArH and OH), 10.40 (bs, 2H, CH=N), 11.49 (s, 2H, NHCO); IR (KBr) v:1667 cm^{-1}(C=O); MS m/z (%): 1254.4 (M^+, 100). Anal. calcd for $C_{70}H_{74}O_8N_6S_4$: C 66.97, H 5.94; found C 66.88, H 6.01.

3d: m.p. 184–187 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.77 [s, 18H, $C(CH_3)_3$], 1.33 [s, 18H, $C(CH_3)_3$], 4.08–4.96 (m, 8H, OCH_2), 6.49–8.74(m, 26 H, ArH and OH), 10.41 (bs, 2H, CH=N), 11.46 (s, 2H, NHCO); IR (KBr) v:1669cm^{-1}(C=O); MS m/z (%): 1254.5 (M^+, 100). Anal. calcd for $C_{70}H_{74}O_8N_6S_4$: C 66.97, H 5.94; found C 66.85, H 6.03.

The syntheses of 1,3-bis-acyl hydrazone-bridged calix[4]arene derivatives (**4a–4d**)

A mixture of compound **2** (0.30 g, 0.3 mmol) and *o*-phenylendiamine or series of dihydrazide (oxalyl dihydrazide, malonic dihydrazide and adipic dihydrazide) (0.35 mmol) was refluxed in 80 mL MeOH–$CHCl_3$ (1:1, V/V), using 0.5 mL acetic acid as catalyst. The materials were disappeared by the detection of TLC (approximate 24 h) and some precipitation separated out. The solvent was removed under reduced pressure and the residue was treated with MeOH (15 mL) to give compounds **4a–4d** as white powder in yield of 53, 51, 59, and 66%, respectively.

4a: m.p. 220–223 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.86 [s, 18H, $C(CH_3)_3$], 1.35 (s, 18H, $C(CH_3)_3$), 4.01–4.96 (m, 8H, OCH_2), 6.58–8.17 (m, 22 H, ArH and OH), 9.80 (bs, 2 H, CH=N); IR (KBr) v:1629 cm^{-1}(C=N); MS m/z (%): 1089.3 (M^+, 100). Anal. calcd. for $C_{64}H_{68}O_6S_4N_2$: C 70.57, H 6.29; found C 70.50, H 6.37.

4b: m.p. 179–182 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.79 [s, 18H, $C(CH_3)_3$], 1.34 [s, 18H, $C(CH_3)_3$], 4.13–4.87 (m, 8 H, OCH_2), 6.77–7.76 (m, 16 H, ArH), 8.21 (s, 2 H, OH), 8.24 (s, 2 H, CH=N), 8.94 (bs, 2 H, NHCO); IR (KBr) v:1664 cm^{-1}(C=O); MS m/z (%): 1099.1 (M^+, 100). Anal. calcd for $C_{60}H_{66}O_8S_4N_4$: C 65.56, H 6.05; found C 65.41, H 6.17.

4c: m.p. 182–185 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.80 [s, 18H, $C(CH_3)_3$], 1.35 [s, 18H, $C(CH_3)_3$], 4.10–4.88 (m, 10 H, OCH_2 and $COCH_2CO$), 6.74–8.13 (m, 20 H, ArH, CH=N and OH), 9.01 (bs, 2H, NHCO); IR (KBr) v:1669 cm^{-1}(C=O); MS m/z (%): 1113.1 (M^+, 100). Anal. calcd for $C_{61}H_{68}O_8S_4N_4$: C 65.81, H 6.16; found C 65.76, H 6.20.

4d: m.p. 176–179 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.80 [s, 18 H, $C(CH_3)_3$], 1.34 [s, 18 H, $C(CH_3)_3$], 1.93–2.95 (m, 8 H, CH_2 and CH_2CO), 4.14–4.88 (m, 8 H, OCH_2), 6.78–7.74 (m, 16 H, ArH), 8.22 (bs, 4 H, CH=N and OH), 8.96 (s, 2 H, NHCO); IR (KBr) v:1667 cm^{-1} (C=O); MS m/z (%): 1154.3 (M^+, 100). Anal. calcd for $C_{64}H_{74}O_8S_4N_4$: C 66.53, H 6.45; found C 66.49, H 6.55.

The syntheses of hydrazone-bridged biscalixarene with calix[4]arene and thiacalix[4]arene subunits (**6**)

The mixture of compound **2** (0.25 g, 0.25 mmol) and 1,3-*bis*(hydrazinecarbonyl-methoxy)-*p*-*tert*-butylcalix[4]arene (**5**) (0.20 g, 0.25 mmol) was stirred and refluxed in 100 mL chloroform/methanol (1:1, V/V). The materials were disappeared by TLC detection (approximate 18 h) and some precipitation separated out. Then solvent was removed under reduced pressure. The residue was treated with 20 mL methanol to give compound **6** as white powder in yield of 90%.

Compound **6**: m.p. 231–234 °C; ^{1}H-NMR (500 MHz, $CDCl_3$, δ ppm): 0.95 [s, 18 H, $C(CH_3)_3$], 1.18 [s, 18 H, $C(CH_2)_3$], 1.25 [s, 18 H, $C(CH_3)_3$], 1.35 [s, 18 H, $C(CH_2)_3$], 3.38 (d, 4 H, J = 15.0 Hz, $ArCH_2Ar$), 4.13 (bs, 4 H, OCH_2), 4.33 (d, 4 H, J = 15.0 Hz, $ArCH_2Ar$), 4.46 (bs, 4 H, OCH_2), 4.68 (bs, 4 H, OCH_2CO), 6.65–7.76(m, 24 H, ArH), 7.75 (s, 2 H, ArCHO), 7.89 (bs, 2 H, NH), 8.45 (s, 2 H, OH), 8.80 (s, 2 H, OH); MS m/z (%): 1773.8 (M^+, 100). Anal. Calcd. for $C_{106}H_{124}O_{12}N_4S_4$: C 71.76, H 7.05; found C 71.67, H 7.10.

Noncompetitive extracting experiment of metallic picrate and α-amino acids

According to the reported method [19], 3 mL of chloroform solution containing calixarene derivatives (1.0×10^{-4}M) and 3 mL of aqueous solution containing a metallic picrate (1.0×10^{-4}M) were placed in a flask. The mixture was shaken for 5 min and stored for 2 h at room temperature. The extraction ability was not affected by further shaking, indicating that the equilibrium had been attained within 2 h. The aqueous phase was separated and subjected to the analysis by UV absorption spectrometry in near 357 nm. The extracting percentage (E%) was determined by the decrease of the picrate concentration in the aqueous phase: $E\% = \{([Pic]_{blank} - [Pic]_{water})/[Pic]_{blank}\} \times 100$, where $[Pic]_{blank}$ denoted the picrate concentrations in the aqueous phase after extraction with pure chloroform, and $[Pic]_{water}$ denoted the picrate concentrations in the aqueous phase after extraction with chloroform solution containing calixarene derivatives as extractants. Average of twice-independent experiments was carried out.

The α-amino acids extracting experiments were performed by the same method as mentioned above. The concentrations of amino acids after extraction were assessed by classical ninhydrin tests [20]. Control experiments showed that the extracting percentages for amino acids were less than 0.3% in the absence of the calixarene derivatives.

Competitive extracting experiments of metallic cations

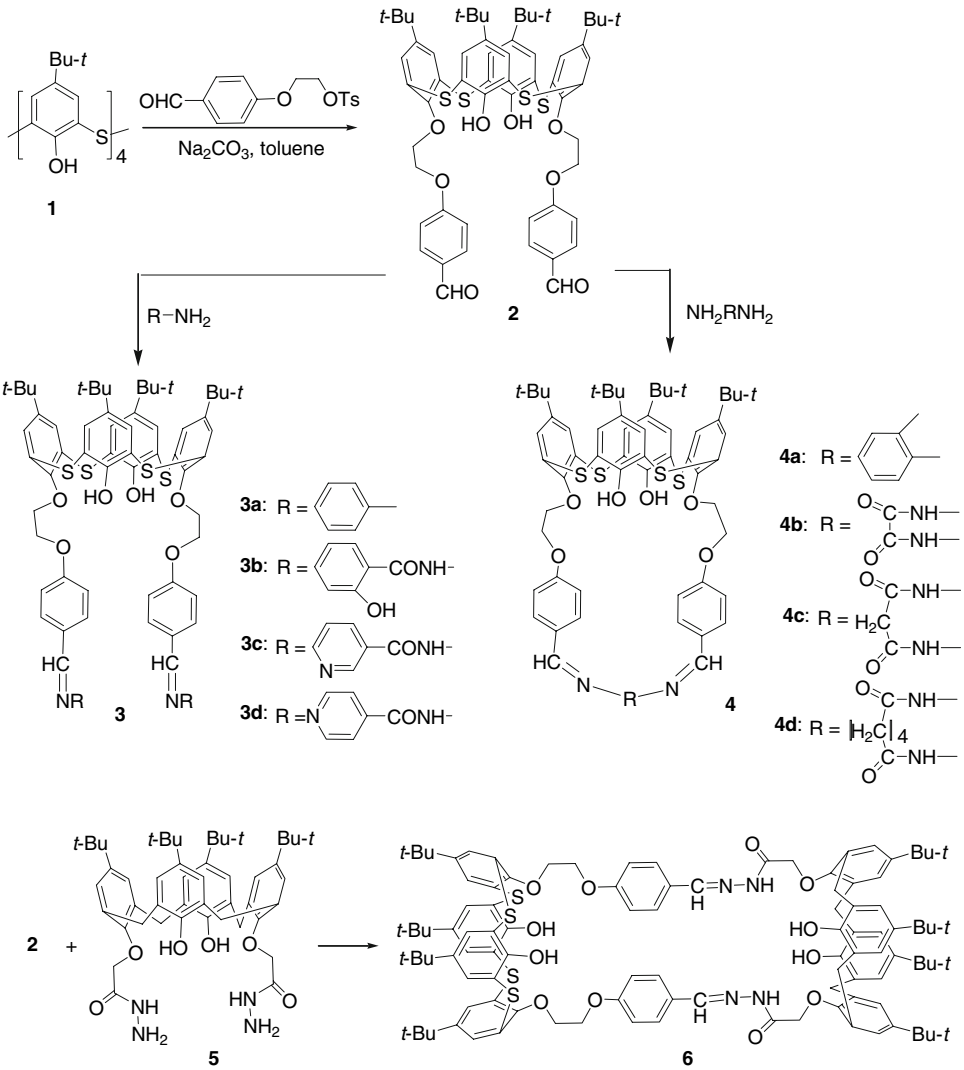
Competitive extraction experiments were performed with equal volumes (10 mL) of an aqueous solution of an equimolar mixture of picrate salts (Na^+, K^+, Cs^+, Co^{2+}, Ni^{2+}, Hg^{2+}, and Ag^+, 2 mM each) and a $CHCl_3$ solution (10 mL) of the hosts (2mM) were mixed in a stoppered flask and vigorously shaken for 15 min. The solution was stored for 2 h. This was repeated 3 times, then the solutions were left standing for 24 h until phase separation was complete. The relative concentrations of the cations in the aqueous phase were determined by ICP-OES. Quantification was made by using a standard solution containing a mixture of picrate salts (Na^+, K^+, Cs^+, Co^{2+}, Ni^{2+}, Hg^{2+}, and Ag^+). A blank experiment without added hosts was carried out under similar experimental conditions.

Results and discussion

Syntheses and characterization

The synthetic route was showed in Scheme 1. The normal methods of nitration and deoxidization in preparing calix[4]arene aza derivatives were not suitable for thiacalix[4]arene, because its bridging S atoms were easily oxidized into sulfone. In this paper, using thiacalix[4]arene bis-benzaldehyde derivative **2** as the new synthetic platform, the novel thiacalix[4]arene acyl-hydrazone derivatives

Scheme 1 The synthetic routes of new hosts



3a–3d and **4a–4d**, were facilely prepared by condensating compound **2** with corresponding hydrazides or dihydrazides. The yields were high and the separate procedures were simple with precipitation. In the step of synthesizing compound **2**, the reaction could hardly occur if toluene was replaced by other solvents such as acetonitrile, acetone or tetrahydrofuran, even the reaction time was prolonged and the amount of Na_2CO_3 was double. When K_2CO_3 or Cs_2CO_3 was used instead of Na_2CO_3, the reaction was accelerated and the starting material was utterly disappeared in 24 h, but the products were too complicated to separation. This phenomenon might be explained by the template effect of Na^+, which made thiacalix[4]arene prefer to 1, 3-substituted and adopt cone conformation [21, 22].

Moreover, refluxing compound **2** and compound **5** in MeOH—$CHCl_3$ (V:V = 1:1) solution for 18 h under diluted condition, the "1 + 1" condensation mode were occurred and novel biscalixarene **6** was obtained as white precipitate in 90% yield. To the best of our knowledge, compound **6** was the first example of biscalixarene with calix[4]arene and thiacalix[4]arene subunits. Also, the yield was highest among all kinds of syntheses of biscalixarene. In general, biscalix[4]arenes were usually synthesized by reacting calix[4]arene or its derivatives with *bis*-functional reagents directly. As a result, two calix[4]-arene derivative subunits had same structures and cavities. However, novel biscalixarene **6** with two different calix[4]arene derivatives units, possessed asymmetric two cavities which was favorable for binding two different guests independently or one complex guest cooperatively.

The structures and conformations of all new compounds were confirmed by ^{1}H-NMR, ESI-MS and elemental analyses. Their ESI-MS spectra showed corresponding molecular ion base peaks, which supported the corresponding condensation mode in Scheme 1. In the ^{1}H-NMR spectrum of compound **2**, the thiacalix[4]arene skeleton showed two singlets (1:1) for the *tert*-butyl groups, two singlets (1:1) for the aromatic protons, which indicated it

was 1, 3-substituted pattern and in cone conformation or 1, 3-alternate conformation. The cone and 1, 3-alternate conformations were difficult to distinguish due to the absence of bridging CH_2 on thiacalix[4]arene skeleton. However, based on similar ^{1}H-NMR spectrum and analogy with other similar thiacalix[4]arene derivatives using Na_2CO_3 as catalyst which preferred to form cone conformation [21, 22], We can deduce that the thiacalix[4]arene skeleton also adopted cone conformation. Compound **3** and **4** were also deduced to adopt cone conformation not only because they were the derivatives of compound **2** but also their spectra were similar to that of 1, 3-conic monocrown thiacalix[4]arene [6, 8, 15]. The calixarene derivative subunits of compound **6** also adopted cone conformation based on the ^{1}H-NMR spectrum and analogy with other similar bisthiacalix[4]arene derivatives [23]. Cultivation of the single crystal for X-diffraction analysis was unsuccessful presently.

It can be seen that the structures and cavities of novel compounds **3**, **4** and **6** were similar to calix[4](aza)crowns reported by Vicens and Tuntulani [24, 25]. The complexation cavities included two binding sites: one binding site was composed of calixarene unit and full-oxygen crown ether chain, which could bind cations, especially, metallic cations and ammonium cations effectively. Another binding site was similar to *aza*-crown ether or calix[4]-*aza*-crown composed of amido groups and Schiff-base groups etc., which could bind soft metal cations or recognize anions by hydrogen bond, such as carboxylate. Thus, the complexation abilities of compounds **3a–3d**, **4a–4d** and **6** towards metallic cations and series of zwitterionic α-amino acids were studied by extracting experiments.

Noncompetitive and competitive extraction studies for cations

The extraction percentages of series of metallic picrates with compounds **3a–3d**, **4a–4d** and **6** from water into $CHCl_3$ at room temperature were summarized in Table 1. Compounds **3a–3d** and **4a–4d** showed higher extraction percentages towards soft metal cations than that of hard metal cations. Comparing with the binding capabilities of similar calix[4]arene derivatives [18], the extraction percentage of them towards soft metal cations were improved greatly, which could be attributed to influence of S atoms and polyaza groups according to the "soft and hard acids and bases" concept. The similar binding selectivities of compounds **3a–3d** and **4a–4d** might indicate that the functional groups played the crucial role in complexation. On the other hand, the extracting properties of biscalix[4]arene 6 were different from that of compounds **3a–3d** and **4a–4d**. Compound **6** showed good extracting abilities towards both hard cations and soft cations, which could be attributed to the influence of two different calix[4]arene derivative subunits. Moreover, compound **6** exhibited some good extraction selectivity, for example, the extraction percentage of $Ag^+/Hg^{2+} = 6.0$, which might be attributed to more rigid and stable cone conformation of biscalix[4]arene 6.

Table 1 Extracting percentages (%E) of picrate salts from water into $CHCl_3$

Cation	3a	3b	3c	3d	4a	4b	4c	4d	6
Na^+	6.0	10.2	8.6	6.8	8.3	5.5	6.1	7.1	3.9
K^+	9.8	12.5	7.1	5.2	6.6	8.2	4.2	6.7	15.9
Cs^+	11.2	13.6	10.4	8.9	9.2	10.1	9.5	11.4	22.1
Ni^{2+}	17.2	34.8	22.5	19.9	13.8	39.1	14.2	68.4	4.2
Co^{2+}	19.6	40.4	19.3	30.7	22.1	52.3	72.1	25.6	15.3
Hg^{2+}	20.3	35.3	38.4	36.3	18.9	46.6	56.5	19.2	4.8
Ag^+	13.2	27.4	32.4	28.5	19.2	22.4	47.2	71.3	28.9

On the other hand, to assess the competitive extraction selectivity of new hosts, competitive solvent extractions experiments of new hosts, with alkali and transition metallic cations from aqueous solutions into chloroform were performed. The extraction percentages (%E) were summarized in Table 2. It can be seen that, in the competition experiments, the extractabilities towards the competing metallic ions showed similar capability order of noncompetitive extraction experiment: soft metallic cations ≫ hard metallic cations. Although the extraction percentages were lower a little than that noncompetitive extraction experiment, however, the extraction selectivtities in competition experiments were far higher than that of noncompetitive experiment. For example, the Ag^+/Hg^{2+} extraction percentage of host **6** was as high as 25.

Extraction studies for α-amino acids

The extraction percentages of series of zwitterionic α-amino acids from water into $CHCl_3$ were summarized in

Table 2 Competitive extracting percentages (%E) of picrate salts from water into $CHCl_3$

Cation	3a	3b	3c	3d	4a	4b	4c	4d	6
Na^+	2.0	1.4	0.7	1.8	2.0	0.6	1.3	1.8	0.3
K^+	1.7	1.0	1.9	2.2	1.2	2.1	2.0	1.3	0.8
Cs^+	0.9	1.2	0.8	0.9	1.1	1.2	0.9	2.0	9.6
Ni^{2+}	2.1	8.6	6.3	7.1	3.5	3.5	2.1	51.2	1.1
Co^{2+}	6.9	13.4	2.7	10.4	16.7	20.8	48.9	7.9	1.6
Hg^{2+}	17.2	6.5	14.5	14.2	4.2	11.3	11.2	6.3	0.9
Ag^+	3.1	8.4	8.3	11.3	5.1	4.9	9.9	12.2	22.6

Table 3 Extracting percentages (%E) of zwitterionic α-amino acids from water into $CHCl_3$

Amino acids	**3a**	**3b**	**3c**	**3d**	**4a**	**4b**	**4c**	**4d**	**6**
Gly	4.6	21.2	19.4	16.5	4.8	13.7	14.1	19.1	40.0
Trp	16.8	22.6	17.3	24.3	8.4	15.3	24.9	12.3	6.8
His	11.4	10.5	11.9	21.8	8.5	20.0	18.6	14.6	14.7
Lys	16.4	31.2	26.6	22.5	19.3	22.3	19.4	17.8	6.8
Ile	19.9	23.5	38.1	33.1	12.4	20.9	26.2	26.8	36.0
Arg	13.3	15.6	22.3	26.2	9.1	17.9	30.9	29.1	28.1
Pro	13.2	40.1	38.4	38.0	12.4	32.1	21.9	32.2	17.9
Thr	12.1	39.2	52.2	44.6	11.2	40.1	16.8	27.9	51.4

Table 3. All new compounds exhibited good extraction abilities towards tested α-amino acids. The little extraction selectivities of compound **3a–3d** and **4a–4d** might also indicate that the functional groups played the crucial role in complexation. However, compound **6** showed good extraction selectivity, for example, the extraction percentage of threonine/tryptophan = 8.0, which might also be attributed to the more rigid and stable cone conformation of biscalix[4]arene **6**. It was worthy of noting that these zwitterionic α-amino acids extracting capabilities were outstanding among all kinds of calixarene derivatives, although some hydrophilic calixarene derivatives containing carboxylic acid or sulphonate were reported to bind amino acids or their esters [26, 27].

Conclusion

1, 3-substituted thiacalix[4]arene bis-benzaldehyde derivative **2** were prepared in yield of 65% by reacting thiacalix[4]arene with *p*-tosyloxyethoxylbenzaldehyde. Refluxing compound **2** with aniline, salicylic hydrazide, nicotinic hydrazide and isonicotinic hydrazide, novel ringopening 1,3-*bis*-arylformyl-hydrazone substituted thiacalix[4]arene derivatives **3a–3d** were obtained in high yields. Refluxing compound **2** with *o*-phenylendiamine, oxalyl dihydrazide, malonic dihydrazide and adipic dihydrazide in "1 + 1" intermolecular condensation under diluted condition, novel 1,3-*bis*-acyl hydrazone-bridged calix[4]arene derivatives **4a–4d** were prepared in good yields. Moreover, condensating compound **2** with 1,3-*bis*(hydrazinocarbonyl-methoxy)-*p*-*tert*-butylcalix[4]arene **5**, the first example of hydrazone-bridged biscalixarene **6** with of calix[4]arene and thiacalix[4]arene subunits was facilely synthesized in 90%. The Noncompetitive and competitive extracting experiments showed that they were good receptors for both metal cations and zwitterionic α-amino acids. The similar binding properties of compounds **3** and **4** indicated that the functional groups played the crucial role in complexation. Biscalixarene **6** exhibited better extracting selectivity than that of compounds **3a–3d** and **4a–4d**, which indicated the more rigid and stable cone conformation of biscalixarene were favorable for binding selectivity. The extraction results indicated that these novel thiacalixarene polyaza derivatives and biscalixarene were effective receptors not only for metalic cations, but also for bioorganic molecules, such as amino acids.

Acknowledgments Financial supports from the National Natural Science Foundation of China (No. 20402002), Fujian Natural Science Foundation of China (No. E0220002 and 2006J0155) and Program for New Century Excellent Talents in University of Fujian Province were greatly acknowledged.

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