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ORIGINAL ARTICLE

Synthesis and extraction abilities of mono-formylated calix[4]-1,3-aza-crown and its hydrazone derivatives

**Fafu Yang · Ziyu Jiao · Zhisheng Huang ·
Jianwei Xie · Hongyu Guo**

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Abstract By formylation of calix[4]-1,3-aza-crown in hexamethylenetetramine/trifluoroacetic acid system, the first formylated calix[4]-aza-crown derivative **6** was synthesized in yield of 61%. Reacting compound **6** with salicyloyl hydrazine, 2,4-dinitrophenyl hydrazine, nicotinyl hydrazine or phenyl thiosemicarbazide afforded four novel calix[4]crown hydrazone derivatives **7a–d** in yields of 70–90%. By condensating compound **6** with series of bifunctional reagents, the novel mono-bridged biscalix[4]-aza-crown hydrazone derivatives **8a–c** were prepared in high yields. The extraction experiments showed that all new compounds were good receptors for metal cations, especially, for soft metal cations. The extraction results suggested that the hydrazone groups produced favorable influences for binding soft cations. The two calix[4]arene units in compounds **8a–c** could bind metal cations concurrently.

Keywords Calix[4]crown · Biscalix[4]arene · Formylation · Hydrazone · Synthesis · Extraction

Introduction

It is well known that calixarenes are excellent building blocks to construct molecular receptors with various structural and functional modifications [1]. Calixarenes are easily modified by all kinds of reaction on their upper rims or lower rims, such as etherification, esterification, formylation, sulphonation, nitration, etc. [2–5]. By introducing the functional groups on upper rim and lower rim synchronously, the “so-called” polytopic systems combining two or more binding sites were conveniently constructed within the same architecture [6, 7]. To attain this aim, some researches focused on the selective formylation on upper rims of calixarene derivatives with functional groups on lower rims. The previous method to prepare this kind of compounds involved three-step sequences including (i) de-*tert*-butylation, (ii) treatment with alkyl halide to yield calix[4]arene ethers on lower rim and (iii) formylation on upper rim to yield formyl calix[4]arenes with $SnCl_4$ or $TiCl_4$ as catalysts [8–12]. Lately, Chawla’s et al. [13, 14] reported a simple method to achieve the direct replacement of *p-tert*-butyl group of calix[4]arenes by formyl group under hexamethylenetetramine/trifluoroacetic acid system. This method gave different formylated calixarene derivatives along with the different groups on lower rims of calixarene, but mono-formylation calixarene was not obtained in most cases. On the other hand, survey of literature indicated that bridging calixarenes were seldom used as the reacting materials for formylation and only two normal calix[4]crowns were formylated on upper rims up to now [15, 16]. In theory, the formylation of calixcrown would give novel bridging calixarene derivatives, which might be more favorable for multiple complexation of guests due to the three-dimensional cavity composed of calixarene and crown ether units. In this paper, we wish to report the first synthesis of formylated derivatives of calix[4]-aza-crown and its related hydrazone derivatives as well as their extraction abilities for metal cations.

F. Yang (✉) · Z. Jiao · Z. Huang · J. Xie · H. Guo
College of Chemistry and Materials, Fujian Normal University,
Fuzhou 350007, People’s Republic of China
e-mail: yangfafu@fjnu.edu.cn

F. Yang
Fujian Key Laboratory of Polymer Materials, Fuzhou 350007,
People’s Republic of China

Experimental

Melting points were uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker-ARX 400 instrument, using TMS as reference. ESI-MS spectra were obtained from DECAX-30000 LCQ Deca XP mass spectrometer. Elemental analyzes were performed at Vario EL III Elemental Analyzer. 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. IR spectra were recorded on a Thermo Nicollet AVATAR 5700 FTIR spectrometer using KBr pellets in spectral range 4,000–400 cm^{-1}. The picrate salts were prepared according to literature [17]. Compound **1–4** and **5** were prepared according to the references [18] and [19], respectively. The organic and inorganic reagents were analytical grade or chemical grade without further purification.

Synthesis of mono-formylated calix[4]-aza-crown **6**

A mixture of compound **5** (0.47 g, 0.6 mmol) and hexamethylenetetramine (3.4 g, 24 mmol) was stirred in 15 mL TFA solution for 5 h at room temperature. The detection of TLC showed the disappearance of materials. Then 40 g ice was added in the solution. After unfreeze of ice, the solution was washed by 3 × 10 mL $CHCl_3$ and the $CHCl_3$ solutions were combined together. The combined $CHCl_3$ solution was washed by 10 mL distilled water, dried by $MgSO_4$, concentrated. The residue was purified by chromatographic column (50 cm × 3 cm, SiO_2 100–200 mesh, acetone/CH_2Cl_2 (1:20, *V*/*V*) as eluant, 400 mL), then compound **6** was obtained as white powder in yield of 61%. m.p. 193–195 °C; IR (KBr, cm^{-1}): 1,711 (HC=O), 1,684 (NC=O); ^{1}HNMR (400 MHz, $CDCl_3$) δ: 1.15 (s, 18H, $C(CH_3)_3$), 1.25 [s, 9H, $C(CH_3)_3$], 3.50 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.61 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.68 (bs, 4H, NCH_2), 4.13 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.18 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.54 (s, 4H, OCH_2), 7.06 (bs, 4H, ArH), 7.13 (s, 2H, ArH), 7.66 (s, 2H, ArH), 8.23 (s, 1H, OH), 8.43 (bs, 2H, NH), 9.26 (s, 1H, OH), 9.79 (s, 1H, CHO), *m*/*z* (%): 760.1 (M$^+$, 100), Anal calcd. for $C_{47}H_{56}O_7N_2$, C 74.17, H 7.41, N 3.68; found C 74.10, H 7.49, N 3.59.

Synthesis of calix[4]-aza-crown hydrazone derivatives **7a**, **7b**, **7c**, and **7d**

Under N_2 atmosphere, a mixture of compound **6** (0.23 g, 0.3 mmol), salicyloyl hydrazine (0.053 g, 0.35 mmol) and 0.1 mL glacial acetic acid was stirred and refluxed in 25 mL solution of $CHCl_3$ and MeOH (*V*:*V* = 3:2) for 10 h and some precipitate appeared. TLC analysis revealed that the starting materials were disappeared. After distilling off the solvent by reduced pressure, 10 mL methanol was added and the precipitate was separated. The crude product was then recrystallized in $CHCl_3$/MeOH. Compound **7a** was obtained as hazel powder in yield of 87% m.p. 216–218 °C; IR (KBr, cm^{-1}): 3,436 (N–H and O–H), 1,683 (C=O), 1,650 (C=O), 1,602 (C=N); ^{1}HNMR (400 MHz, $CDCl_3$) δ: 1.14 (s, 18H, $C(CH_3)_3$), 1.23 (s, 9H, $C(CH_3)_3$), 3.52 (d, 2H, $J = 13.6$ Hz, $ArCH_2Ar$), 3.64 (d, 2H, $J = 13.6$ Hz, $ArCH_2Ar$), 3.70 (bs, 4H, NCH_2), 4.13 (d, 2H, $J = 13.6$ Hz, $ArCH_2Ar$), 4.18 (d, 2H, $J = 13.6$ Hz, $ArCH_2Ar$), 4.57 (bs, 4H, OCH_2), 7.04–7.65 (m, 12 H, ArH), 8.15 (bs, 2H, OH), 8.44 (bs, 2H, NH), 8.82 (bs, 1H, OH), 9.21 (s, 1H, CH=N), 11.79 (s, 1H, NH), *m*/*z* (%): 895.4 (M$^+$, 100), Anal calcd. for $C_{54}H_{62}O_8N_4$, C 72.46, H 6.97, N 6.26; found C 72.38, H 6.98, N 6.20.

According to the similar procedures as described above, reacting compound **6** with corresponding reactants (2,4-dinitrophenyl hydrazine, nicotinyl hydrazine, or phenyl thiosemicarbazide) gave compounds **7b**, **7c**, and **7d** in yields of 86, 76, and 71%, respectively. Compound **7b**: red powder, m.p. 216–218 °C; IR (KBr, cm^{-1}): 3,385 (N–H and O–H), 1,692 (NC=O), 1,616 (C=N); ^{1}HNMR (400 MHz, $CDCl_3$) δ: 1.17 (s, 18H, $C(CH_3)_3$), 1.25 (s, 9H, $C(CH_3)_3$), 3.50 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.58 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.70 (bs, 4H, NCH_2), 4.14 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.19 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.55 (s, 4H, OCH_2), 7.07 (s, 4H, ArH), 7.14 (s, 2H, ArH), 7.50 (s, 2H, ArH), 8.0 (s, 1H, ArH), 8.06 (d, 1H, $J = 9.6$ Hz, ArH), 8.24 (s, 1H, OH), 8.35 (d, 1H, $J = 9.6$ Hz, ArH), 8.47 (bs, 2H, NH), 8.97 (bs, 1H, OH), 9.14 (s, 1H, CH=N), 11.25 (s, 1H, NH), *m*/*z* (%): 940.1 (M$^+$, 100), Anal calcd. for $C_{53}H_{60}O_{10}N_6$, C 67.63, H 6.42, N 8.93; found C 67.69, H 6.43, N 8.88.

Compound **7c**: straw yellow powder, m.p. 264–266 °C; IR (KBr, cm^{-1}): 3,375 (N–H and O–H), 1,677 (C=O), 1,596 (C=N); ^{1}HNMR (400 MHz, $CDCl_3$) δ: 1.13 (s, 18H, $C(CH_3)_3$), 1.24 (s, 9H, $C(CH_3)_3$), 3.49 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.56 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.68 (s, 4H, NCH_2), 4.11 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.15 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.53 (s, 4H, OCH_2), 7.06 (s, 4H, ArH), 7.10 (s, 2H, ArH), 7.55 (s, 2H, ArH), 7.78 (s, 1H, OH), 8.21 (bs, 2H, ArH), 8.48 (bs, 2H, ArH), 8.72 (s, 1H, OH), 8.90 (s, 2H, NH), 9.25 (s, 1H, CH=N), 9.84 (s, 1H, NH), *m*/*z* (%): 902.9 (MNa$^+$, 100), Anal calcd. for $C_{53}H_{61}O_7N_5$, C 72.33, H 6.99, N 7.96; found C 72.24, H 6.94, N 7.89.

Compound **7d**: straw yellow powder, m.p. 256–257 °C; IR (KBr, cm^{-1}): 3,380 (N–H and O–H), 1,678 (C=O), 1,599 (C=N); ^{1}HNMR (400 MHz, $CDCl_3$) δ: 1.15 (s, 18H, $C(CH_3)_3$), 1.25 (s, 9H, $C(CH_3)_3$), 3.49 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.54 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.68 (s, 4H, NCH_2), 4.13 (d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.17

(d, 2H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.54 (s, 4H, OCH_2), 7.04–7.71 (m, 13H, ArH), 8.19 (s, 1H, OH), 8.27 (s, 1H, OH), 8.43 (s, 1H, NH), 8.78 (s, 1H, NH), 8.88 (s, 1H, CH=N), 9.13 (s, 2H, NH), *m/z* (%): 909.3 (M^+, 100), Anal calcd. for $C_{54}H_{63}O_6N_5S$, C 71.25, H 6.97, N 7.69; found C 71.17, H 6.91, N 7.58.

Synthesis of mono-bridged biscalix[4]-aza-crown hydrazone derivatives **8a**, **8b** and **8c**

Under N_2 atmosphere, a mixture of compound **5** (0.23 g, 0.3 mmol), 0.1 mL glacial acetic acid and corresponding difunctional reagent (compounds **2**, **3** or **4**) was stirred and refluxed in 25 mL solution of $CHCl_3$ and MeOH (V:$V = 3$:2) for 12 h, and some precipitate appeared. TLC analysis revealed that the starting materials were disappeared. After distilling off the solvent by reduced pressure, 10 mL methanol was added and the precipitate was separated. The crude product was then recrystallized in $CHCl_3$/MeOH. Compounds **8a**, **8b** and **8c** were obtained as powders in yields of 87, 74, and 76%, respectively. Compound **8a**: gray powder, m.p. 264–265 °C; IR (KBr, cm^{-1}): 3,370 (N–H and O–H), 1,682 (C=O), 1,605 (C=N); ^{1}HNMR (400 MHz, $CDCl_3$) δ: 1.15 [s, 36H, $C(CH_3)_3$], 1.25 (s, 18H, $C(CH_3)_3$), 1.85 (bs, 4H, CH_2CH_2CO), 2.83 (bs, 4H, CH_2CH_2CO), 3.48 (d, 4H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.55 (d, 4H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.67 (s, 8H, NCH_2), 4.10 (d, 4H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.14 (d, 4H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.52 (s, 8H, OCH_2), 7.06 (s, 8H, ArH), 7.11 (s, 4H, ArH), 7.37 (s, 4H, ArH), 7.50 (s, 2H, OH), 7.60 (s, 2H, OH), 8.46 (s, 2H, NH), 8.77 (s, 4H, NH), 9.01(s, 2H, CH=N), *m/z*(%): 1,683.5 (MNa^+, 100), Anal calcd. for $C_{100}H_{122}O_{14}N_8$: C 72.35, H 7.41, N 6.75; found C 72.27, H 7.47, N 6.67.

Compound **8b**: brown powder, m.p. 269–271 °C; IR (KBr, cm^{-1}): 3,440 (N–H and O–H), 1,650 (C=O), 1,601 (C=N); ^{1}HNMR (400 MHz, $CDCl_3$) δ: 1.15 (s, 36H, $C(CH_3)_3$), 1.26 (s, 18H, $C(CH_3)_3$), 1.42 (bs, 4H, $CH_2CH_2CH_2N$), 2.00 (bs, 4H, $CH_2CH_2CH_2N$), 3.34 (bs, 4H, $CH_2CH_2CH_2N$), 3.47 (d, 4H, $J = 14.0$ Hz, $ArCH_2Ar$), 3.52 (d, 4H, $J = 14.0$ Hz, $ArCH_2Ar$), 3.67 (s, 8H, NCH_2), 4.10 (d, 4H, $J = 14.0$ Hz, $ArCH_2Ar$), 4.16 (d, 4H, $J = 14.0$ Hz, $ArCH_2Ar$), 4.53 (s, 8H, OCH_2), 7.07 (s, 8H, ArH), 7.10 (s, 4H, ArH), 7.33 (s, 4H, ArH), 7.60 (s, 2H, OH), 7.65 (s, 2H, OH), 8.17 (s, 2H, NH), 8.46 (s, 4H, NH), 8.67 (s, 2H, NH), 9.03 (s, 2H, CH=N), *m/z* (%): 1717.3 (M^+, 100), Anal calcd. for $C_{102}H_{128}O_{14}N_{10}$: C 71.30, H 7.51, N 8.15; found C 71.34, H 7.45, N 8.10.

Compound **8c**: yellow powder, m.p. 262–264 °C; IR (KBr, cm^{-1}): 3,371 (N–H and O–H), 1,692 (C=O), 1,622 (C=N); ^{1}HNMR (400 MHz, $CDCl_3$) δ: 1.16 (s, 36H, $C(CH_3)_3$), 1.26 (s, 18H, $C(CH_3)_3$), 3.49 (d, 4H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.59 (d, 4H, $J = 13.2$ Hz, $ArCH_2Ar$), 3.69 (s, 8H, NCH_2), 4.14 (d, 4H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.18 (d, 4H, $J = 13.2$ Hz, $ArCH_2Ar$), 4.54 (s, 8H, OCH_2), 7.07 (s, 8H, ArH), 7.10 (s, 4H, ArH), 7.13 (s, 4H, ArH), 7.65 (s, 4H, ArH), 7.90 (s, 2H, OH), 7.93 (s, 2H, OH), 8.22 (s, 2H, CH=N), 8.47 (s, 4H, NH), 8.71 (s, 2H, CH=N), *m/z* (%): 1646.4 (M^+, 100), Anal calcd. for $C_{102}H_{118}O_{12}N_{18}$: C 74.33, H 7.22, N 6.80; found C 74.39, H 7.26, N 6.69.

Non-competitive extraction experiments of single metal cation

According to the reported method, 3 mL of chloroform solution containing calixarene derivatives (2.0×10^{-5} M) and 3 mL of aqueous solution containing a metal picrate (2.0×10^{-5} M) were placed in a flask [20]. The mixture was shaken for 5 min and stored for 2 h at 25 °C. 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 extraction 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 two independent experiments was carried out. Control experiments showed that no picrate extraction occurred in the absence of the calixarene derivatives. The relative standard deviations from the mean were less than 5%. The test showed that the pH value in each aqueous phase were neutral (6.9–7.1) and the values made no change before and after extraction, which indicated the metal picrates were extracted successfully.

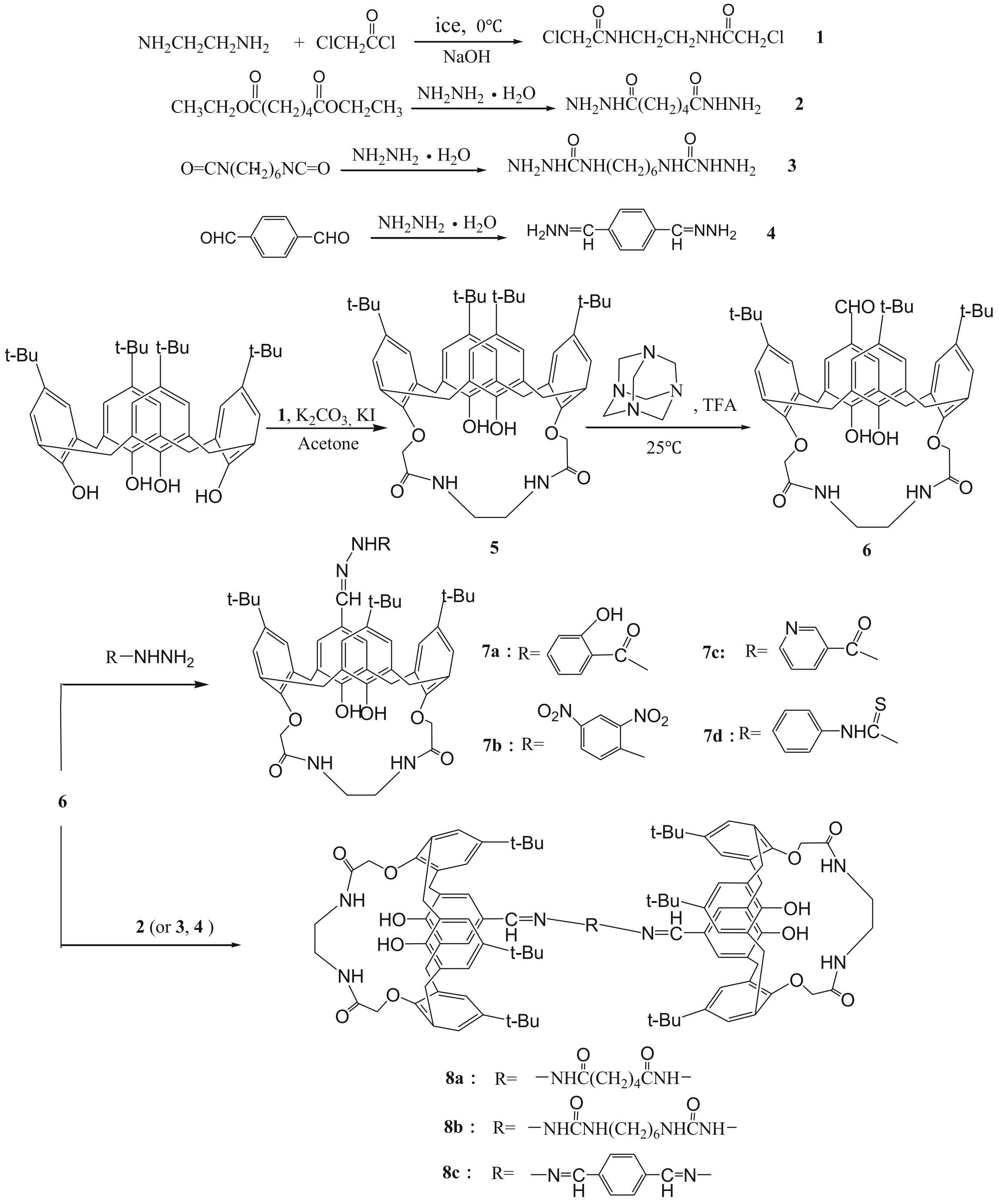
Competitive extraction experiments of metal cations

Competitive extraction experiments were performed with equal volumes (10 mL) of an aqueous solution of an equimolar mixture of picrate salts (Li^+, Na^+, K^+, Cs^+, Cu^{2+}, Ni^{2+}, Co^{2+}, Ag^+ and Hg^{2+}, 2.0×10^{-5} M each) and a $CHCl_3$ solution (10 mL) of the hosts (2.0×10^{-5} M) were mixed in a stopper flask and vigorously shaken for 15 min. The solution was stored for 2 h. This was repeated three times. Then, the solutions were left standing for 24 h at 25 °C until phase separation was completed. 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 (Li^+, Na^+, K^+, Cs^+, Cu^{2+}, Ni^{2+}, Co^{2+}, Ag^+ and Hg^{2+}). Blank experiments without adding hosts were carried out under same experimental conditions.

Results and discussion

Synthesis and characterization

The synthetic route was shown in Scheme 1. Compounds **1**–**5** were obtained according to the methods in references [18, 19]. Then reacting calix[4]-1,3-aza-crown **5** with hexamethylenetetramine in trifluoroacetic acid, mono-formylated calix[4]-aza-crown **6** was prepared in 61% after chromatographic column. Moreover, it was interesting that mono-formylated calix[4]-aza-crown **6** was the main product and no bis-formylated product was separated no matter how to change the reaction condition, such as prolonging the reaction time and raising the reaction temperature. This result was utterly different from the formylated results of other calix[4]-1,3-substituted esters or ethers,



Scheme 1

which gave bis-formylation as main products reported by Chawla's et al. and our previous experiments [6, 13]. The different formylated results might be attributed to the influences of bridging structures of calix[4]-aza-crown. By condensating compound **6** with salicyloyl hydrazine, 2,4-dinitrophenyl hydrazine, nicotinyl hydrazine or phenyl thiosemicarbazide, respectively, a series of novel calix[4]-aza-crown hydrazone derivatives **7a**, **7b**, **7c**, and **7d** were prepared conveniently in yields of 70–90% after recrystallization. On the other hand, by reacting compound **6** with bifunctional reagents **2**, **3** or **4**, novel mono-bridged bis-calix[4]-aza-crown hydrazone derivatives **8a**, **8b** and **8c** were obtained after recrystallization in high yields. It was worthy of noting that compounds **7a**–**c** and **8a**–**c** were the first examples of formylated calix[4]-aza-crown derivatives and biscalix[4]crown derivatives.

The structures of new compounds **7a–d** and **8a**–**c** were confirmed by IR spectra, ESI-MS spectra, elemental analyzes, ^{1}H NMR spectra. In the IR spectra, the adsorption peaks (1,711 cm^{-1}) of formyl groups of compound **6** was disappeared utterly and new adsorption peaks of C=N groups were appeared. The ESI-MS spectra of all new compounds clearly showed corresponding molecular base peaks (M$^+$ or MNa$^+$) respectively, which indicated the intermolecular Schiff-base condensations were accomplished completely. The ^{1}H NMR spectra of all new compounds exhibited two singlets (2:1) for *tert*-butyl groups, two pairs of doublets (1:1:1:1) for the methylene bridges of the calix[4]arene skeleton, which indicated that the calix[4]arene units adopt the cone conformation as showed in Scheme 1. As to the *cis*/*trans* conformers about C(O)–N bond and *E*/*Z* geometrical isomers respect to the C=N double bonds in these new compounds, it could be deduced that the mixed conformers and isomers were existed by comparing with the similar structures [21]. But it was difficult to determine the percentage of different isomers due to the overlapped signal of NH and OH in IR spectra and the absence of CH$_2$ groups beside the C(O)–N bond and C=N double bond, which were crucial factor to study the percentages of different isomers [21].

Non-competitive extraction experiments of single metal cation

The metal cation complexation properties of all new compounds were preliminarily studied by non-competitive extraction experiments. There were two methods to study the extraction abilities. One was that metal picrate was extracted directly in neutral solution and another was in buffered solution [20, 22]. Due to the binding abilities of NH and OH were greatly influenced by pH, the method of using metal picrates as extract directly in neutral solution was employed in our extraction experiments to avoid the fall of complexation abilities in buffered solution. In our extraction experiment, the pH value in each aqueous phase were neutral (6.9–7.1) and the values made no change before and after extraction, which indicated the metal picrate were extracted successfully. The extraction results were showed in Figs. 1, 2. It could be seen that new compounds **6**, **7a**–**7d** and **8a**–**8c** showed good extraction abilities for both hard and soft metal cations. Comparing with the extraction results of calixarene derivatives with similar structures in references [6, 14, 21], the good extraction abilities of new compounds **7a**–**7d** and **8a**–**8c** for hard and soft metal cations should be attributed to the favorable influences of oxo-functional groups (including phenolic hydroxyl group, ether group and carbonyl group) for binding hard cations and aza(or sulf)-functional groups

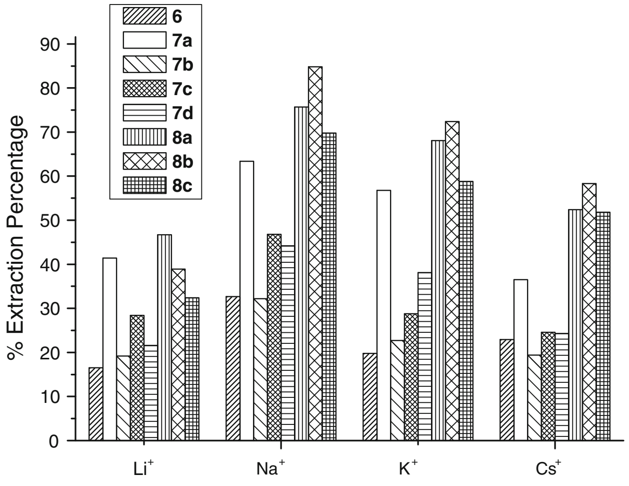


Fig. 1 The extraction percentages of receptors **6**, **7a**–**d** and **8a**–**c** for hard metal cations

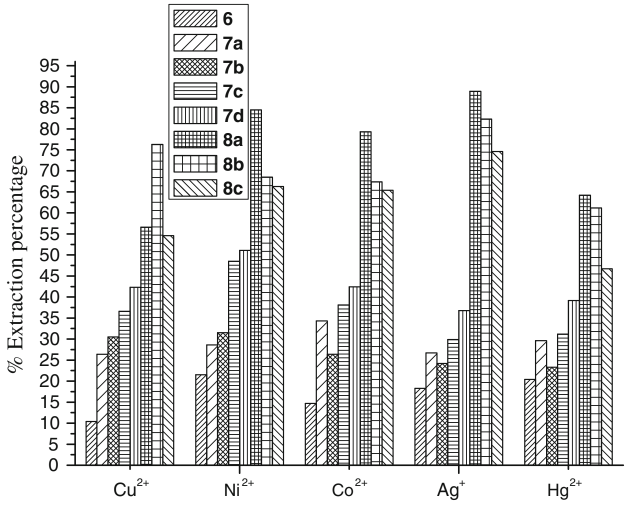


Fig. 2 The extraction percentages of receptors **6**, **7a**–**d** and **8a**–**c** for soft metal cations

Table 1 Competitive extracting percentages (E%) of compounds **7a–d** and **8a–c** for picrate salts

Cations	Li^+	Na^+	K^+	Cs^+	Cu^{2+}	Ni^{2+}	Co^{2+}	Ag^+	Hg^{2+}
7a	3.2	8.9	4.6	5.3	10.8	12.5	10.6	9.4	17.3
7b	3.4	6.8	5.5	4.9	8.3	16.7	9.4	10.2	13.9
7c	2.6	4.8	3.5	5.2	6.9	18.8	10.3	12.8	19.5
7d	4.6	8.6	7.8	8.4	9.2	18.2	10.9	13.5	16.3
8a	7.6	14.5	8.9	9.7	10.3	16.9	17.4	24.8	19.3
8b	6.2	13.7	8.4	10.6	23.6	20.8	17.3	27.6	16.8
8c	5.6	10.7	6.8	9.9	11.5	27.7	19.4	25.3	9.8

for binding soft cations according to principle of "hard and soft acids and bases". On the other hand, the extraction percentages of compounds **7a–7d**, especially for soft metal cations, were higher than that of precursor **6**, which indicated that the hydrazone groups produced advantageous influences for binding soft metal cations. Moreover, biscalixarene derivatives **8a–8c** exhibited far higher extraction percentage than precursor **6** and compounds **7**, which might suggest the two calix[4]arene units of compounds **8** could bind metal cations synchronously. The extraction percentages of compound **8a** for Ni^{2+} and Ag^+ were as high as 85 and 89%, respectively. These non-competitive extraction experiments suggested that some of novel hosts were good receptors for test metal cations.

Competitive extraction experiments of metal cations

Based on the non-competitive extraction experiments, the competitive extraction experiments were carried out to investigate the complexation selectivity for metal cations. The competitive extraction percentages were summarized in Table 1. It can be seen that compounds **7a–d** and **8a–c** showed good extraction abilities towards both hard and soft metal cations, the extraction percentages for soft metal cations were higher than that for hard metal cations. Also, the extraction percentages of biscalix[4]arenes **8a–c** were higher than that of compounds **7a–d**. These results were in accordance with non-competitive extraction experiments. Moreover, it was worthy of noting that the total extraction percentages (the addition of each extraction percentage) of compounds **8a–c** for metal cations exceeded 100%. The biggest total extraction percentage of compound **8b** was as high as 145%. These results could be explained that the two calix[4]arene units of compounds **8a–c** could bind metal cations concurrently. On the other hand, comparing with the extraction selectivity in non-competitive extraction experiments, the extraction selectivity was improved in competitive extraction experiments. For examples, the extraction ratios Ni^{2+}/Li^+ and Ag^+/Hg^{2+} of compound **8c** were up to 4.9 and 2.6 in competitive extraction experiments, whereas it were only 2.1 and 1.6 in non-competitive extraction experiments, respectively. All these extraction results suggested that new compounds **7a–d** and **8a–c** were good receptors for metal cations. Especially, compounds **8a–c** with two calixarene units might possess cooperative complexation capabilities for other complicated guests, such as ion pairs and amino acids, which will be studied in further work.

Conclusions

The first formylated calix[4]-aza-crown **6** was synthesized by reacting calix[4]-1,3-aza-crown with hexamethylenetetramine in TFA in high yield. Reacting compound **6** with salicyloyl hydrazine, 2,4-dinitrophenyl hydrazine, nicotinyl hydrazine or phenyl thiosemicarbazide afforded four novel calix[4]arene hydrazone-based receptors **7a–d** in yields of 70–90%. On the other hand, by reacting compound **6** with series of bifunctional reagents, novel mono-bridged biscalix[4]-aza-crown hydrazone derivatives **8a–c** were prepared in high yields. The non-competitive and competitive extraction experiments showed that all new compounds were good receptors for hard and soft metal cations. The extraction results suggested that the hydrazone groups are favorable for binding soft metal cations and the two calix[4]arene units in compounds **8a–c** could bind metal cations concurrently.

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