

The synthesis and anions complexation property of novel biscalixarene: dumbbell shaped biscalix[4]-1,3-aza-crown

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Abstract By reacting calix[4]-1,3-aza-crown **2** with 1,6-diisocyanatohexane in “1+2” condensation mode, the first example dumbbell shaped biscalix[4]-1,3-aza-crown **3** was conveniently prepared in yield of 94%. The complexation properties of compound **3** were investigated by UV-vis spectra and ^1H NMR experiments. The results showed that compound **3** has good complexation abilities for anions. Compound **3** binded monoacidic anions with 1:2 binding-stoichiometry and binded binary acidic anions with 1:1 binding-stoichiometry.

Keywords Biscalix[4]crown · Dumbbell shaped · Synthesis · Complexation · Anion

Introduction

It is well-known that calixarenes are the macrocyclic compounds with three-dimensional cavities. They frequently serve as molecular scaffolds to construct elaborate supramolecular systems with interesting recognition abilities towards guests. In order to study the cooperative complexation abilities of two calixarene units, all kinds of biscalixarenes had been investigated extensively in the recent past. Biscalixarenes possessed two recognition sites obviously and conformation of the bites could be mutually changed through appropriate linker between two calixarene moieties [1–4]. Up to now, the biscalixarenes were usually constructed by bridging at their upper rims (“head-to-head” type), lower rims (tail-to-tail type) or upper-lower rims (“head-to-tail” type)

through one or more spacers, including aliphatic chains, ether, esters, amides, imines, sulfides, etc, and some of them exhibited excellent complexation properties for guests [1–15].

In this paper, we wish to report the synthesis and complexation property of a novel dumbbell shaped biscalix[4]arene **3**, in which the two calixarene units were linked on the crown ether moieties of calix[4]-1,3-aza-crown instead of upper rims or lower rims of calixarene skeleton. The novel biscalix[4]arene not only was facilely prepared in high yield but also exhibited good complexation ability towards monoacidic and binary acidic anions.

Experimental

Melting point was uncorrected. ^1H NMR spectra and ^1H NMR titration were recorded in CDCl_3 on a Bruker-ARX 500 instrument at room temperature. ^1H - ^1H COSY spectrum was recorded in CDCl_3 on a Bruker-ARX 400 instrument, using TMS as an internal standard. ESI-MS spectra were recorded on DECAX-30000 LCQ Deca XP mass spectrometer. Elemental analyses were performed at Vario EL III Elemental Analyzer. UV spectra were measured by Varian spectrophotometer. Compound **1** was synthesized according to the published procedures [16]. The organic and inorganic reagents, except special instruction, were analytical grade or chemical grade without further purification.

The synthesis of *p*-tert-butylcalix[4]-1,3-aza-crown (**2**)

The mixture of compound **1** (1.0 mmol) and diethylenetriamine (0.005 mol), in 100 mL of toluene/methanol (V:V = 1:1) was stirred and refluxed. TLC detection indicated the disappearance of compound **1** in 12 h. The solvent was evaporated and the residue was purified by SiO_2 chromatographic column

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(100–200 mesh, acetone as eluent). Compound **2** was obtained as white powder in 53% yield. m.p. 188–189 °C (literature[17]: 183–185 °C), $^1\text{H NMR}$ (500 MHz, CDCl_3) δ : 1.00 (s, 18H, $\text{C}(\text{CH}_3)_3$), 1.25 (s, 18H, $\text{C}(\text{CH}_3)_3$), 3.42 (4H, $J = 13.5$ Hz, ArCH_2Ar), 3.73 (bs, 4H, OCH_2), 4.02 (4H, $J = 13.5$ Hz, ArCH_2Ar), 4.19 (bs, 4H, OCH_2), 4.46 (bs, 4H, OCH_2), 6.88–7.65 (m, 11H, ArH and NH), 8.58 (bs, 2H, OH). MS m/z (%): 831.8 (M^+ , 100). Anal. calcd for $\text{C}_{52}\text{H}_{69}\text{O}_6\text{N}_3$: C 75.06, H 8.36; found C 75.01, H 8.43.

The synthesis of dumbbell shaped biscalix[4]-1,3-aza-crown (**3**)

The mixture of compound **2** (1 mmol) and 1,6-diisocyanatohexane (0.5 mmol) in 25 mL of CHCl_3 was stirred and refluxed for 2 h. Evaporation of the solvent obtained crude product. The recrystallization from methanol gave a white powder **3** in 94% yield. Compound **3**: m.p. 224–226 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm: 0.98 [s, 36H, $\text{C}(\text{CH}_3)_3$], 1.27 [s, 36H, $\text{C}(\text{CH}_3)_3$], 1.36 (bs, 4H, CH_2), 1.51 (bs, 4H, CH_2), 3.18 (q, 4H, NCH_2), 3.40 (d, 8H, $J = 13.5$ Hz, ArCH_2Ar), 3.56 (bs, 8H, NCH_2), 3.61 (bs, 8H, NCH_2), 4.08 (d, 8H, $J = 13.5$ Hz, ArCH_2Ar), 4.52 (s, 8H, OCH_2CO), 5.48 (s, 2H, NHCO), 6.83 (s, 8H, ArH), 7.09 (s, 8H, ArH), 7.34 (s, 4H, OH), 8.58 (bs, 4H, NHCO); MS m/z (%): 1855.2 (MNa^+ , 100). Anal. calcd for $\text{C}_{112}\text{H}_{150}\text{O}_{14}\text{N}_8$: C 73.41, H 8.25, N 6.11; found C 73.34, H 8.31, N 5.98.

UV–vis spectra binding experiments of anions

All UV–vis experiments were performed in DMSO solutions at 293 K upon addition of Cl^- , H_2PO_4^- , HSO_4^- , CH_3COO^- , $^- \text{OOC}(\text{CH}_2)_2\text{COO}^-$ and $^- \text{OOC}(\text{CH}_2)_4\text{COO}^-$ as their tetrabutylammonium salts. The stoichiometry of the complexes was determined by the Job method of continuous variations.

$^1\text{H NMR}$ complexation experiments of anions

Solution of receptor **3** was prepared at a concentration of 5×10^{-3} M in CDCl_3 . The initial $^1\text{H NMR}$ spectrum was recorded and aliquots of H_2PO_4^- (or $^- \text{OOC}(\text{CH}_2)_4\text{COO}^-$) in the same solvent, were added by a microsyringe from a solution made such that from 0.5 molar equiv to 2.5 molar equiv. were added in 20 μL , and the $^1\text{H NMR}$ spectrum was recorded.

Results and discussion

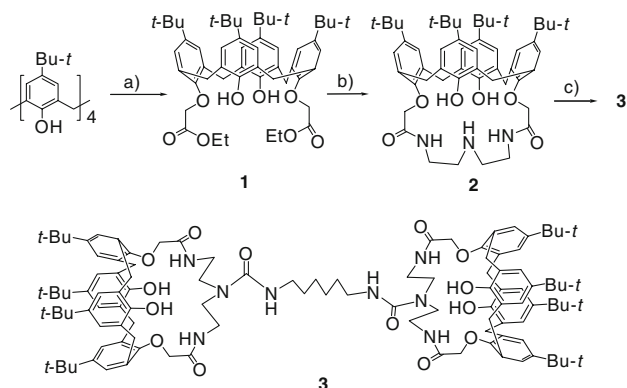
Synthesis and characterization

The synthetic route was depicted in Scheme 1. Compound **1** was obtained in yield of 85% by reacting *p*-tert-butylcalix[4]arene

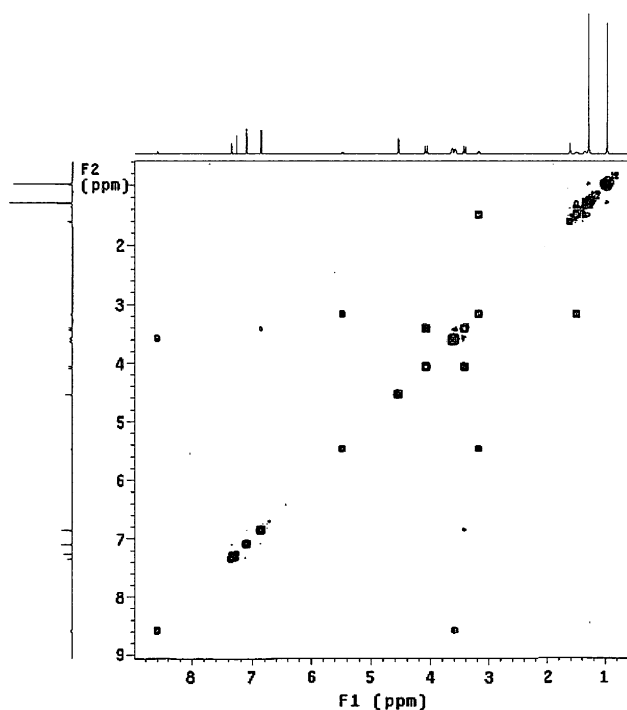
with ethyl bromoacetate in K_2CO_3 /dry acetone system according to the published procedures [16]. However, we failed to prepare compound **2** by ammonolysis reaction of compound **1** with diethylenetriamine in mol ratio of 1:3 according to the reported procedures [17]. Most materials were not reacted even the reaction time was prolonged to 48 h. We found that compound **2** could be synthesized when mol ratio was raised to 1:5. Although some intermolecular bridging products were also produced under this ratio, compound **2** was easily separated by chromatographic column in moderate yield of 53%. By refluxing compound **2** with 1,6-diisocyanatohexane in CHCl_3 , a novel dumbbell shaped biscalix[4]arene **3** was obtained in “1+2” condensation mode, and the yield was as high as 94%. The novel biscalix[4]arene **3** was easily purified by simple procedure of recrystallization. The yield was far higher than that of other previous reported biscalix[4]arenes [4–15]. Moreover, the linking chain of biscalixarene **3** was not on the upper or lower rim of calixarene skeleton, but on the crown ether moieties of calix[4]-1,3-aza-crown. To the best of our knowledge, compound **3** was the first example of dumbbell shaped biscalix[4]arene with two original calix[4]crown cavities.

The structure and conformation of compound **3** were confirmed by $^1\text{H NMR}$, FAB-MS, ^1H - ^1H COSY spectrum and elemental analysis. Molecular base peak at 1855.2 (MNa^+) in ESI-MS spectrum indicated that “1+2” condensation was accomplished thoroughly. $^1\text{H NMR}$ spectrum of compound **3** showed two singlets (1:1) for the *tert*-butyl groups, two singlets (1:1) for ArH and a pair of doublets (1:1) with an AB pattern for the methylene protons of the calix[4]arene skeleton, which revealed that the calixarene units adopt cone conformation and biscalix[4]arene **3** adopt high symmetric structure.

In order to confirm the structure and conformation of compound **3** further, the ^1H - ^1H COSY spectrum was done to study the coupling relationship of H atom. The result was showed in Scheme 2. The coupling signals of $^1\text{H}(\delta_{\text{H}}1.25)$ - $^1\text{H}(\delta_{\text{H}}3.18)$ and $^1\text{H}(\delta_{\text{H}}3.18)$ - $^1\text{H}(\delta_{\text{H}}5.48)$ were



Scheme 1 (a) Bromoacetate, K_2CO_3 /acetone; (b) diethylenetriamine; (c) 1,6-diisocyanatohexane

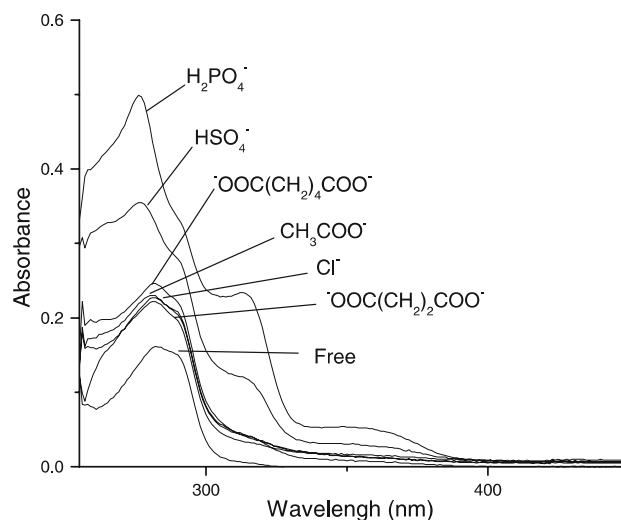


Scheme 2 The ^1H - ^1H COSY spectrum of compound **3**

ascribed to protons of $\text{NHCH}_2\text{CH}_2\text{-NHCH}_2\text{CH}_2$ and $\text{NHCH}_2\text{CH}_2\text{-NHCH}_2\text{CH}_2$ on linking chain. The coupling signals of $^1\text{H}(\delta_{\text{H}}3.40)\text{-}^1\text{H}(\delta_{\text{H}}4.08)$ was ascribed to protons of ArCH_2Ar on calixarene skeleton. The coupling signals $^1\text{H}(\delta_{\text{H}}3.61)\text{-}^1\text{H}(\delta_{\text{H}}8.58)$ was ascribed to protons of $\text{NHCH}_2\text{-NHCH}_2$ on crown ether annulus. All these coupling signals of ^1H - ^1H COSY spectrum certainly further supported the cone conformation and high symmetric structure of biscalix[4]arene **3**.

Complexation studies for anions

It had been widely reported that calix[4]-aza-crowns possessed good complexation abilities for all kinds of anions. The UV-vis spectra experiments of compound **3** were done to investigate the complexation abilities for monoacidic anions and binary acidic anions. Scheme 3 showed the changes of absorption spectrum of compound **3** (2.0×10^{-5} M in DMSO solution) upon addition of Cl^- , H_2PO_4^- , HSO_4^- , CH_3COO^- , $^-\text{OOC}(\text{CH}_2)_2\text{COO}^-$ and $^-\text{OOC}(\text{CH}_2)_4\text{COO}^-$ (6.0×10^{-5} M as their tetrabutylammonium salts). It could be seen that the absorption curve of compound **3** with all test anions changed obviously. Although the maximum wavenumbers in UV spectra were little shifts, the maximum absorbances at 283 nm increased greatly by the complexation action. These incremental absorbances at 283 nm indicated unambiguously that the strong complexation actions were occurred between compound **3** and tested anions.



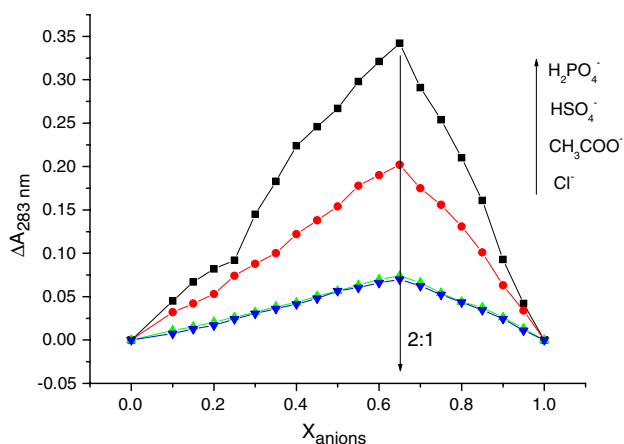
Scheme 3 UV-vis spectra of compound **3** (2.0×10^{-5} M) upon addition of tetrabutylammonium salts of Cl^- , H_2PO_4^- , HSO_4^- , CH_3COO^- , $^-\text{OOC}(\text{CH}_2)_2\text{COO}^-$ and $^-\text{OOC}(\text{CH}_2)_4\text{COO}^-$ (6.0×10^{-5} M)

In order to investigate the stoichiometry of compound **3**—anion complex, the method of continuous variations was used. The Job plot experiment showed that the maxima of compound **3** with monoacidic anions (Cl^- , H_2PO_4^- , HSO_4^- , CH_3COO^-) at the mole fraction of 0.65 indicated the formation of approximate 1:2 receptor–anion complexes (Scheme 4). However, the maxima of compound **3** with binary acidic anions ($^-\text{OOC}(\text{CH}_2)_2\text{COO}^-$ and $^-\text{OOC}(\text{CH}_2)_4\text{COO}^-$) at the mole fraction of 0.5 (Scheme 5) indicated the formation of 1:1 receptor–anion complexes.

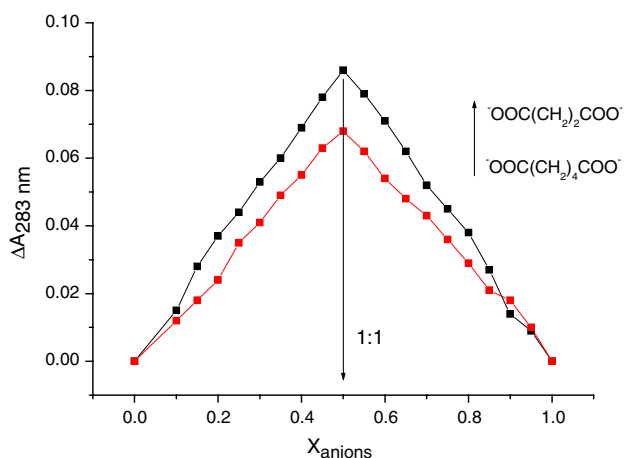
The complexation behaviors of compound **3** with H_2PO_4^- and $^-\text{OOC}(\text{CH}_2)_4\text{COO}^-$ were also investigated by ^1H NMR spectra titrations. The chemical shifts of the amide protons were the most affected ones and moved to low magnetic field obviously in the ^1H NMR spectra. It was found that the negligible chemical shifts were observed when excess 2 equiv. H_2PO_4^- or excess 1 equiv. $^-\text{OOC}(\text{CH}_2)_4\text{COO}^-$ were added. These results indicated 1:2 complex of compound **3** with H_2PO_4^- and 1:1 complex of compound **3** with $^-\text{OOC}(\text{CH}_2)_4\text{COO}^-$, which were in accordance with the UV-vis spectra experiments. Scheme 6 showed the changes of part spectra of compound **3**, compound **3** with 2 equiv. H_2PO_4^- , and compound **3** with 1 equiv. $^-\text{OOC}(\text{CH}_2)_4\text{COO}^-$, in which the chemical shifts of the amide protons moved from 5.48 ppm to 5.81 ppm and 5.88 ppm, respectively.

Conclusion

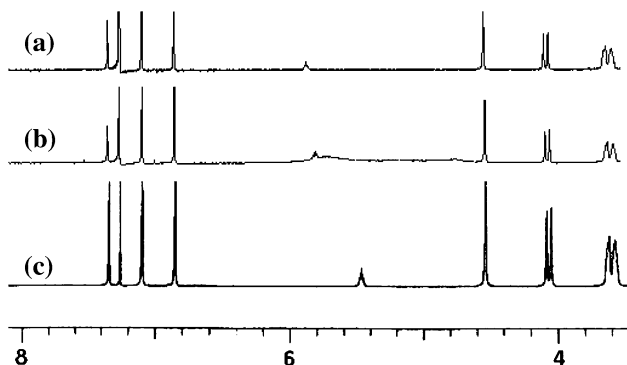
In conclusion, the first example of dumbbell shaped biscalix[4]arene **3** was designed and synthesized by “1+2” condensation of calix[4]-1,3-aza-crown **2** with



Scheme 4 The Job plot documenting the stoichiometry of 2:1 for complexation of monoacidic anion (Cl^- , H_2PO_4^- , HSO_4^- , CH_3COO^-) by **3** in DMSO. The plot was constructed from absorbance changes at 283 nm using the sum of concentrations 2.0×10^{-5} M



Scheme 5 The Job plot documenting the stoichiometry of 1:1 for complexation of binary acidic anion ($^-\text{OOC}(\text{CH}_2)_2\text{COO}^-$ and $^-\text{OOC}(\text{CH}_2)_4\text{COO}^-$) by **3** in DMSO. The plot was constructed from absorbance changes at 283 nm using the sum of concentrations 2.0×10^{-5} M



Scheme 6 Partial ^1H NMR spectra. (a) Compound **3** with 1 equiv. $^-\text{OOC}(\text{CH}_2)_4\text{COO}^-$, (b) compound **3** with 2 equiv. H_2PO_4^- , (c) compound **3**

1,6-diisocyanatohexane. The separated procedure was simple and the yield was as high as 94%. The novel bicalixarene **3** adopted the high symmetric structure and cone conformation. The complexation behaviors of receptor **3** with anions were investigated by UV-vis and ^1H NMR titrations experiments. Compound **3** possessed good binding abilities for tested anions. The 1:2 complexes of receptor **3**-monocarboxylic anions, and 1:1 complexes of receptor **3**-dicarboxylic anions were formed.

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