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A facile one-pot access to cone and 1,3-alternate conformers of calix[4]arene-bis(amido)crowns

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Abstract—A facile one-pot access to cone and 1,3-alternate calix[4]arene-bis(amido)crowns by the use of sodium hydride or cesium carbonate as template/base has been reported. The structures of products have been established through detailed chemical, physical, and spectroscopic data and single crystal X-ray analysis of calix[4]arene-bis-(ethyleneamido)crown, **7a**. The preliminary evaluation of the obtained molecular receptors promise opportunities to design molecular capsules/carriers for toxic metal ions (i.e., Hg^{++}) and anionic species (CrO_4^{--}).

1. Introduction

Calix[*n*]arenes are macrocyclic metacyclophanes possessing phenolic units covalently linked through methylene bridges.[1] The observed diversity of calix[4]arene derivatives essentially lies in their conformational isomerism due to rotation of Ar–CH_2–Ar bonds or molecular rotation through the annulus.[2] Though a large volume of data on synthesis of a variety of calixarene derivatives are now known, strategies to achieve the desired conformations of calixarene architecture in good yields are still important challenges.[3] Amongst four possible stable conformations of calix[4]arenes (cone, partial cone, 1,3-, and 1,2-alternate), the cone and the 1,3-alternate conformations possess unique structural features that can be utilized for important applications.[4] For instance, specific neutral molecule and guest recognition systems can be developed from cone conformers by deploying well defined hydrophobic upper and hydrophilic lower rims.[5] Likewise, 1,3-alternate conformers of calix[4]arenes can be expanded to provide multicavity recognition systems for specific end use.[6,7] It has been observed that unlike the cone conformer, the 1,3-alternate conformer provides two modes of binding and can yield molecular receptors either by using phenolic oxygen donor atoms or by two π-donor aromatic moieties (Fig. 1) with helpful cation–π interactions. Elaboration of the basic conformation can be readily realized to give tubular, channel, capsular, or the other possible calixarene architectures[6a–c] with improved selectivity (e.g., for cesium and potassium over sodium,[7] lead over cadmium or mercury, etc. by several orders of magnitude[8e]).[6–8] A variety of complex calix[4]arene conjugates with additional macrocycles (calix-crown ethers, azacrowns, and amidocrowns) have recently been demonstrated to provide extremely useful molecular receptors for specific ionic/molecular recognition.[8b,f,9] Some of these calixarene conjugates (e.g., calixarene amidocrowns) are expected to be better carriers for cations (through nitrogen and/or oxygen ligation), anions (through hydrogen bonds and protonated species), or neutral organic molecules (through hydrophobic cavities and channels).[10]

Calixamidocrowns are obtained by linking calixarenes and amidocrowns. They were first synthesized and evaluated by Reinhoudt et al., in 1991.[8a] Bitter et al.[8g] reported the synthesis of doubly bridged proximal calix[4]arene(amido)-crown compounds through intramolecular ring closure of chloroalkylamide precursors in 1998. Recently, tetrathiacalix[4]arene-bis(amido)crown, calix[4]arene-mono(amido)-

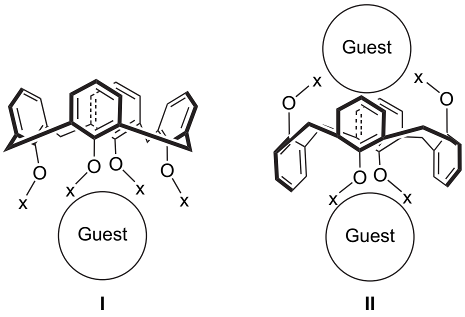

Figure 1. Interaction of cone (**I**) and 1,3-alternate (**II**) conformations of calix[4]arene with ionic or neutral molecular guest.

Keywords: Calix[*n*]arenes; Aminolysis; Amidocrown; Conformation.

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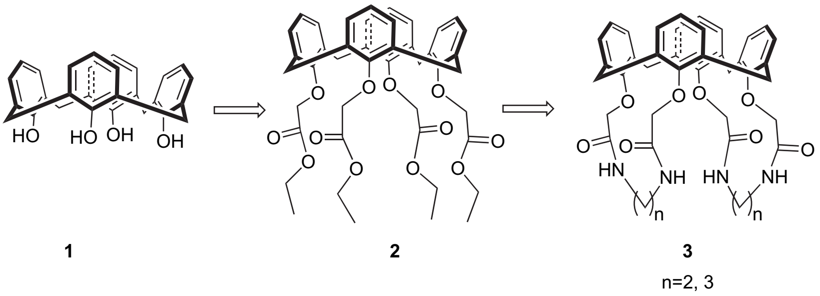
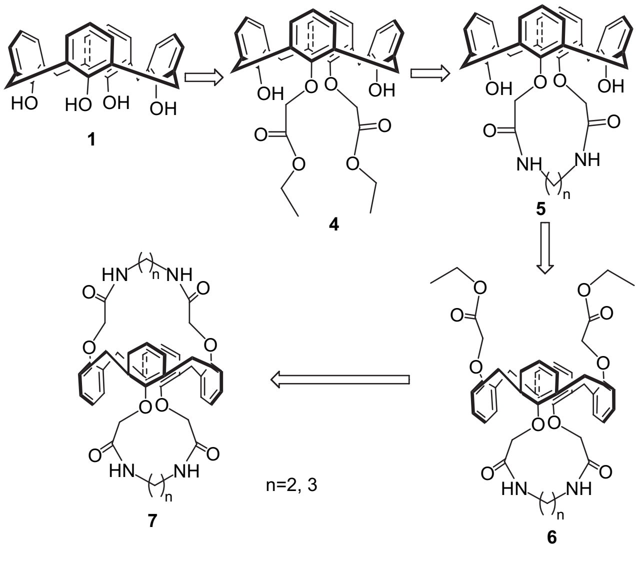


Scheme 1. Synthesis of calix[4]arene-bis(amido)crown derivatives in cone conformation.

crown compounds, and their nitro- and azo-substituted derivatives have been evaluated by us as novel photoresponsive molecular receptors for transition metal ions.[3b,8d] Samanta and Banthia have reported *N*-(4-aminophthalimidoethyl)calix[4]-amidocrown as a fluorescent sensor for iron(III) and copper(II).[8h] Recently, calix[4]arene-bis(amido)crowns (**3**, **7**) have been synthesized by a multistep sequence involving alkylation at the lower rim of calix[4]arene esters (**2**) and aminolysis with aliphatic diamines (over 48 h).[8c,e] Though the mechanism of the cyclization step is uncertain, it has been suggested to involve aminolysis to provide calix[4]arene aminoalkylamide intermediates, which then cyclize to yield calix[4]arene-bis(amido)crown with or without the help of a catalyst (Scheme 1).[8c,d]

Recently published studies on the subject have seemingly missed the isolation of more useful 1,3-alternate conformation of calix[4]arene-mono(amido)crowns and bis(amido)crown analogs from the aminolysis reaction. The synthesis of 1,3-alternate conformation of calixarene-bis(amido)crown compounds in low to moderate yields, however, has been achieved through a circuitous route described by Bitter et al.[8e] For example, calix[4]arene-mono(amido)crown (**5**) in the cone conformation on alkylation or esterification gives a 1,3-alternate conformation of mono(amido)crown with two alkyl or ester groups (**6**). Further aminolysis by alkyl diamines (Scheme 2) provides the calix[4]arene-bis(amido)crown in their 1,3-alternate conformation (**7**).[8e]



Scheme 2. Synthesis of calix[4]arene-bis(amido)crown derivatives in 1,3-alternate conformation by multistep methodology.

Since calix[4]arene-bis(amido)crowns represent multicavity molecular receptors with diverse potential applications, we report herein an easy and efficient one-pot entry to both the cone and the 1,3-alternate conformations of calix[4]arene-bis(amido)crown derivatives (**3a**–**c**, **7a**–**c**) in 56–65% yield. The experimental protocol appears to be general and the reaction has been determined to be valid for a number of diamines [$H_2N(CH_2)_nNH_2$; *n*=2, 3, 4]. The synthesized calix[4]arene-bis(amido)crowns have been evaluated for their interaction with alkali, alkaline earth, and transition metal cations and various anions (Cl^-, Br^-, I^-, HSO_4^-, $H_2PO_4^-$, $CH_3CO_2^-$, CrO_4^{2-}, $Cr_2O_7^{2-}$) to reveal specific interaction with Hg^{2+} and chromate ions to suggest a need for further work on anion recognition by calix[4]arene-bis(amido)crowns and their derivatives.

2. Results and discussion

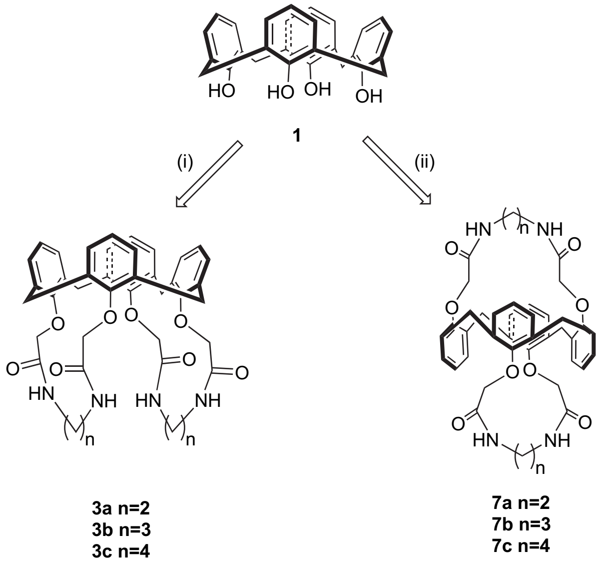
2.1. Synthesis

In the present work, we have observed that when calix[4]arene was subjected to a reaction with ethyl bromoacetate in the presence of excess of sodium hydride in THF, it gave oily residues, which on aminolysis with diaminoalkanes [$H_2N–(CH_2)_n–NH_2$; *n*=2, 3, 4] provided a yellowish solid that could be crystallized from chloroform/methanol to yield calix[4]arene-bis(amido)crowns **3a**–**c** in 60–65% yield (Scheme 3(i)).

However, when calix[4]arene was subjected to a reaction with ethyl bromoacetate in the presence of excess Cs_2CO_3 in acetone, it again gave oily residues, which on aminolysis with diaminoalkanes under similar reaction protocol yielded calix[4]arene-bis(amido)crowns **7a**–**c** in 56–62% yield (Scheme 3(ii)). Efforts expended to crystallize the intermediate oily residues were unsuccessful.

2.2. Characterization of the products

Compounds **3a**–**c** were identified as the cone conformers of calix[4]arene-bis(amido)crowns on the basis of detailed IR, ^{1}H NMR, and ^{13}C NMR spectra. For example, **3a**, which exhibited a pair of doublets for ArOCH_2– protons at δ 4.79 and 4.02 (1:1), two pairs of doublets for methylene protons at



Scheme 3. One-pot methodology for the synthesis of calix[4]arene-bis-(amido)crowns derivatives. Reagents and conditions: (i) 20 equiv NaH, 20 equiv ethyl bromoacetate, THF, rt, stirring, after 24 h THF evaporated and added 40 equiv diamine in toluene/methanol and reaction was continued for 48 h; (ii) 20 equiv Cs_2CO_3, 20 equiv ethyl bromoacetate, acetone, refluxing, after 2 days acetone evaporated and added 40 equiv diamine in toluene/methanol and refluxing continued for 48 h.

δ 4.41, 4.28, 3.35, and 3.22 (1:1:1:1), and two broad triplets for –NHC*H*$_2$ at δ 3.70 and 3.58 (1:1) suggest that **3a** is present in the cone conformation with proximal capping (Fig. 2a). The –CON*H* protons appeared at δ 7.40 (br s) while aromatic protons appeared at δ 6.65 (s). The cone conformation of **3a** was further confirmed with the help of ^{13}C NMR spectrum (DEPT-135) when two signals for methylene carbon could be found at δ 31.5 and 30.1 (Fig. 2b).[11] Similarly, the other calix[4]arene-bis(amido)-crown analogs (**3b**, **c**) in the cone conformation were characterized (Table 1).

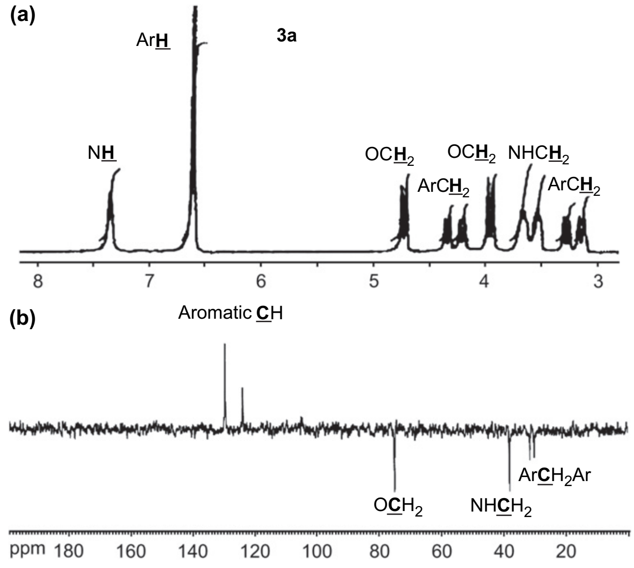


Figure 2. (a) ^{1}H NMR spectrum (300 MHz, 25 °C) of **3a**; (b) ^{13}C NMR spectrum (DEPT-135) (75 MHz, $CDCl_3$, 25 °C) of **3a**.

On critical examination, it was revealed that the reaction when carried out in the presence of Cs_2CO_3 in acetone, it gave a filtrate, which on usual work up revealed the presence of a compound, which exhibited a prominently different ^{1}H NMR spectrum from that of **3a**. The compound was eventually identified as the 1,3-alternate conformer of calix[4]arene-bis(amido)crown **7a** on the basis of detailed spectroscopic evidence. The $ArOCH_2$–, $ArCH_2Ar$, and $–NHCH_2$ protons in **7a** appeared as singlets at δ 4.16, 3.92, and 3.16, respectively, while its aromatic protons appeared at δ 6.97 (triplet) and δ 7.15 (doublet) (Fig. 3a). A singlet for the $ArOCH_2$– protons suggested a symmetric structure while a singlet for the $ArCH_2Ar$ protons indicated that **7a** is present in a 1,3-alternate conformation. The symmetric 1,3-alternate conformation for **7a** was further confirmed with the help of ^{13}C NMR spectrum (DEPT-135) when a signal for the methylene carbon could be found at δ 37.2 (Fig. 3b).[11] The conformation was confirmed by single crystal X-ray analysis. Similarly, the other calix[4]arene-bis(amido)crown analogs synthesized in the 1,3-alternate conformation were characterized (Table 1).

2.3. Metal template effect on the formation of cone and 1,3-alternate conformers of calix[4]arene-bis(amido)crowns

The formation of the 1,3-alternate conformer of calix[4]-arene-bis(amido)crowns in the described experiments is unique. The reaction possibly involves a metal template effect can be inferred from the fact that when fewer equivalents of Cs_2CO_3 were used in the reaction or when Cs_2CO_3 was replaced by K_2CO_3 in the above reaction, **3a**–**c** were the major products. Thus when the quantity of cesium carbonate was reduced from 20 equiv to 6 equiv, the yield of the 1,3-alternate conformer dropped from 56–62% to 10–15% (Table 2). Likewise, when the solvent was changed from acetone to acetonitrile, the yield of the conformers was markedly affected. On the other hand, when a strong base like NaH was used, proximal cone selectivity was observed in the reaction (Table 2). These observations are in accordance with literature precedents on metal template effect.[12]

Table 1. Assignment of characteristic signals of calix[4]arene-bis(amido)crowns

Compd no.	IR ν (NH, C═O)	^{1}H NMR signals for the –NH–protons (δ)	NMR signals for the methylene bridge region (δ)	
			^{1}H NMR	^{13}C NMR
3a	3362, 3296, 1657	7.39 (br s)	4.41 (d, *J*=13.5), 4.28 (d, *J*=14.1), 3.35 (d, *J*=14.1), 3.25 (d, *J*=13.5)	31.5, 30.1
3b	3419, 3268, 1672	7.48 (br s)	4.54 (d, *J*=13.2), 4.27 (d, *J*=14.4), 3.37 (d, *J*=14.4), 3.25 (d, *J*=13.2)	30.9, 29.8
3c	3412, 3262, 1678	7.42 (br s)	4.51 (d, *J*=13.5), 4.18 (d, *J*=14.1), 3.37 (d, *J*=13.5), 3.25 (d, *J*=12.9)	—
7a	3396, 1681	5.22 (br s)	3.92 (s)	37.8
7b	3392, 1680	5.25 (br s)	3.87 (s)	—
7c	3385, 1680	5.32 (br s)	3.79 (s)	37.6

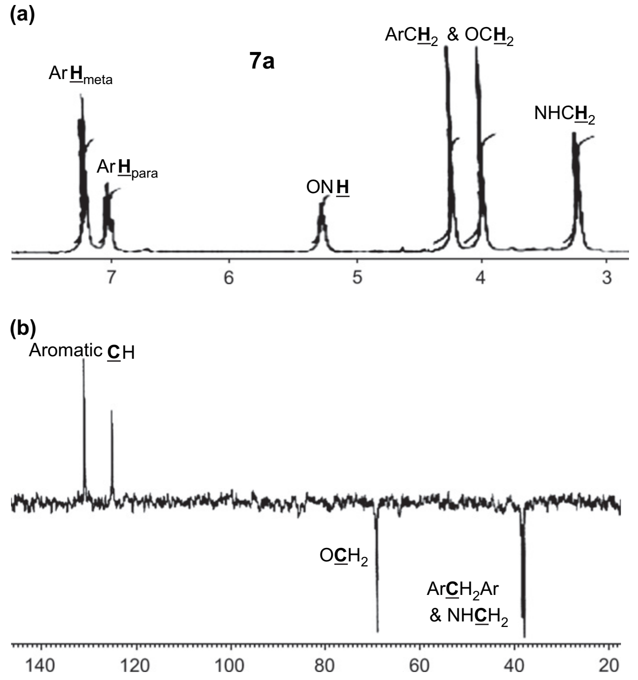


Figure 3. (a) ^{1}H NMR spectrum (300 MHz, 25 °C) of **7a**; (b) ^{13}C NMR spectrum (DEPT-135) (75 MHz, $CDCl_3$, 25 °C) of **7a**.

2.4. X-ray crystallographic analysis of 7a

Definitive proof for geometry of **7a** (Fig. 4a) was obtained by X-ray analysis of a single crystal obtained by slow evaporation of its chloroform/ethyl acetate solution. The space group of **7a** is *Cc* with two crystallographically different molecules. The torsion angles at the methylene bridge revealed a sequence of ++, −−, ++, −− as per the symbolic representation devised for the 1,3-alternate conformation of calix[4]arenes.[13] The molecule is approximately capsule shaped with estimated dimensions of 7.6×7.6×11.4 Å^3. The distance of the two distal rings ranged from 4.2 Å (lower rim) to 6.9 Å (upper rim) with an inclination angle of around 37°. This arrangement of aromatic rings creates a symmetrical square type cavity of around 6×6 Å (measured from centroids of aromatic rings), which is considerably different from the rectangular shaped cavity (7.4×6.1 Å) of calix[4]arene-mono(ethylene amido)crown **5** (Scheme 2, *n*=2), which existed in the cone conformation.[8d] The other significant difference between **5** and **7a** is in the nature of hydrogen bonding among the amidic protons. They are not involved in any intra or intermolecular hydrogen bonding in the case of **7a**, while they form a moderate hydrogen bond (~2.5 Å) with neighboring phenolic oxygens in the case of **5**.

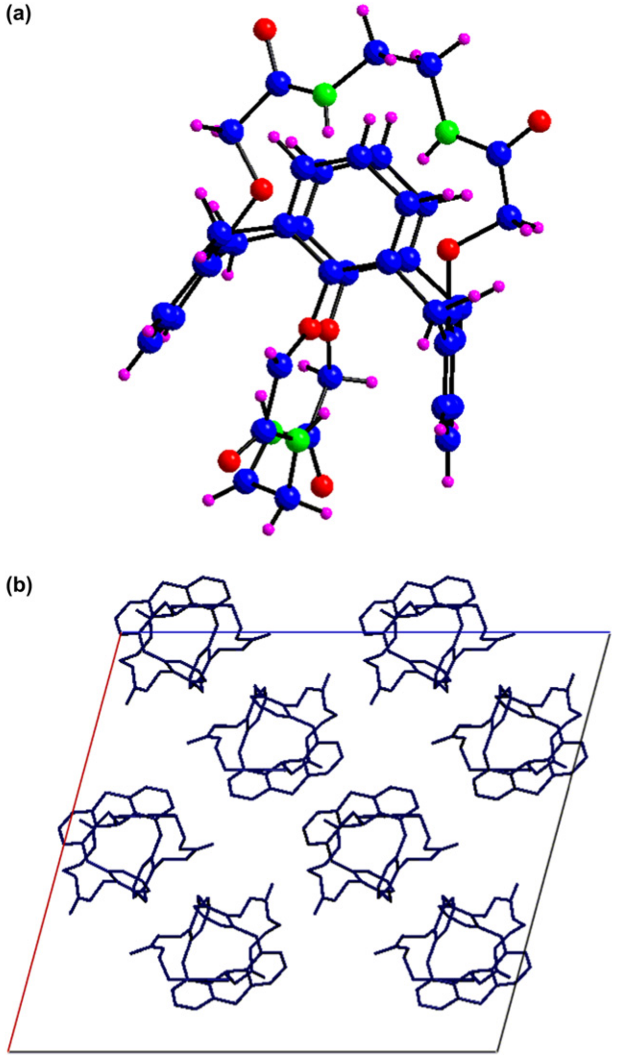


Figure 4. (a) Molecular structure of **7a**; (b) unit cell of **7a** along axis b. (Hydrogens and solvent molecules are omitted for clarity.)

However, a prominent intermolecular CH···π interaction with H···π distance of 2.97–3.03 Å exists between the amidic protons and the neighboring phenyl ring in the case of **7a**. All the PhO–C–C–O and O–C–N–H are trans, thereby making the carbonyl groups *exo* and the hydrogen of the amide group *endo* with respect to the calix cavity. This *endo* nature of the amidic protons is very specific for molecular recognition because this orientation calix[4]arene-bis(amido)-crowns are very attractive molecular carriers for anion or soft metal ion transport. Figure 4b represents the unit cell for **7a**.

Table 2. Effect of reaction parameter on the product formation

S. No.	Base (equiv)	Ethyl bromoacetate (equiv)	Solvent	Reaction time for step 1	Reaction time for aminolysis (h)	Cone (**3a**–**c**) yield	1,3-Alternate (**7a**–**c**) (yield)
1	NaH (15)	8	THF	24 h	48	60–65	—
2	K_2CO_3 (20)	10	Acetone	24 h	48	35	20
3	Cs_2CO_3 (6)	6	Acetone	24 h	48	30–35	10–15
4	Cs_2CO_3 (10)	10	Acetonitrile	24 h	48	25	10–15
5	Cs_2CO_3 (10)	10	Acetone	7 days	48	20–25	56–62
6	Cs_2CO_3 (20)	20	Acetone	48 h	48	5–7	56–62

3. Preliminary investigation of synthesized calix[4]arene-bis(amido)crowns for ionic recognition

In order to obtain insight into the affinity of the synthesized calix[4]arene-bis(amido)crowns for ions, the changes in their λ_{max} upon interaction with a variety of metal cations and anions were investigated. The affinity of calix[4]arene-bis(amido)crowns (**3a**, **7a**) for group I (Li^+, Na^+, K^+, Cs^+, and Rb^+), group II (Ca^{2+}, Mg^{2+}, and Ba^{2+}), and transition metal cations (Cr^{3+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Ag^+, Cd^{++}, Pb^{++}, Hg^{2+}, Pd^{2+}, and Pt^{2+}) was examined in solution by using methanol as the solvent. The changes in λ_{max} of these compounds upon addition of various cations were noted. Calix[4]arene-bis(amido)crown (**3a**) exhibits a selective interaction with Hg^{++} metal ion as it gave significant increase in absorbance on addition of Hg^{++} ion. Insignificant change in the UV–vis spectra of **3a** and **7a** could be observed on their interaction with other metal ions.

When the synthesized receptors were examined for interaction with anions (Cl^-, Br^-, I^-, HSO_4^-, $H_2PO_4^-$, $CH_3CO_2^-$), the UV–vis and NMR spectra of calix[4]arene-bis(amido)crowns (**3a**, **7a**) remain unchanged. Calix[4]arene-bis(amido)crowns were also evaluated for their extraction capability toward oxo-anions (CrO_4^{2-}, $Cr_2O_7^{2-}$) by taking alkali metal chromates and dichromates (Na_2CrO_4, K_2CrO_4, $Na_2Cr_2O_7$, $K_2Cr_2O_7$). Extraction of oxo-anions into the organic phase containing calix[4]arene-bis(amido)crown in $CHCl_3$ could be easily observed with corresponding decrease in the UV–vis absorbance of the anion in the aqueous phase. It was observed that calix[4]arene-bis(amido)crown **7a** shows ~18% extraction of chromate anion while no extraction was observed for dichromate anions.

4. Uniqueness of 1,3-alternate conformers of calix[4]arene-bis(amido)crown compounds

It is important to note that the calix[4]arene-bis(amido)crowns in the cone and 1,3-alternate conformations significantly differ in their ionic and molecular interactions. Distinct shift of the –CONH protons of **7a** (δ 5.22) as compared to **3a** (δ 7.40) indicated a shift in the hydrophobicity/hydrophilicity balance in these two conformers, which can be utilized for development of new model receptors for anion recognition. Further work on the utilization of inter- and intramolecular –CONH– interactions is in progress.

5. Conclusion

In conclusion, we have developed an experimental protocol to obtain calix[4]arene-bis(amido)crowns in their cone and 1,3-alternate conformations have been developed by aminolysis of calixarene tetraesters through a metal template effect. It has been determined that use of sodium hydride as template/base provides the cone conformer, while cesium carbonate template/base gives the 1,3-alternate conformer of calix[4]arene-bis(amido)crowns during aminolysis. The synthesized molecular receptors exhibit interaction with Hg^{2+} ions and are capable of selective extraction of chromate ions.

6. Experimental section

6.1. General

All the reagents used in the study were purchased from Sigma–Aldrich or Merck and were chemically pure. ^{1}H NMR, ^{13}C NMR, and DEPT-135 spectra were recorded on a 300 MHz Bruker DPX 300 instrument at room temperature using tetramethylsilane (TMS) at 0.00 as an internal standard. IR spectra were recorded on a Nicolet Protégé 460 spectrometer in KBr disks while X-ray data were recorded on a Bruker SMART CCD single crystal diffractometer. UV–vis spectra were obtained on a Perkin–Elmer (Lambda-3B) recording spectrophotometer while FAB mass spectra were obtained on a JEOL SX 102/DA-6000 Mass spectrometer/Data System using argon/xenon (6 kV, 10 mA) as the FAB gas. Melting points were determined on an electrothermal Toshniwal melting point apparatus and were uncorrected.

6.2. General procedure for the synthesis of calix[4]arene-bis(amido)crowns

6.2.1. General procedure for the synthesis of calix[4]arene-bis(amido)crowns in cone conformation (for 3a–c). Calix[4]arene (**1**) was stirred with sodium hydride (20 equiv) and ethyl bromoacetate (20 equiv) in THF under dry conditions for 1 day. The solvent was removed under reduced pressure to yield yellowish oily liquid and methanol was added dropwise while keeping the temperature below 10 °C. After 10 min toluene was added to this mixture to make an equimolar ratio of toluene/methanol (1:1 ratio) and the respective diamine (40 equiv) was added. The reaction was continued for 2 days under reflux and the solvent was removed under reduced pressure to yield a solid, which was dissolved in chloroform or ethyl acetate and quickly washed with 1 M H_2SO_4 followed by extensive washing with water. The organic extract was collected and evaporated to dryness under reduced pressure to yield calix[4]arene-bis(amido)crown derivatives in the cone conformation as white solids, which were further purified by recrystallization.

6.2.1.1. Compound 3a. Obtained as white solid, yield: 65%, mp >300 °C (decomp.). IR (KBr, ν_{max}/cm^{-1}): 3362, 3296, 1657. ^{1}H NMR (300 MHz, $CDCl_3$, δ in ppm): 7.39 (br s, 4H, CONH), 6.65 (s, 12H, ArH), 4.79 (d, 4H, J=13.2 Hz, OCH_2), 4.41 (d, 2H, J=13.5 Hz, $ArCH_2Ar$), 4.28 (d, 2H, J=14.1 Hz, $ArCH_2Ar$), 4.02 (d, 4H, J=13.2 Hz, OCH_2), 3.70 (br t, 4H, $CONHCH_2$), 3.58 (br t, 4H, $CONHCH_2$), 3.35 (d, 2H, J=14.1 Hz, $ArCH_2Ar$), 3.22 (d, 2H, J=13.5 Hz, $ArCH_2Ar$). DEPT-135 NMR (75 MHz, $CDCl_3$, δ in ppm): 129.1, 123.4 (aromatic CH), 74.8 (OCH_2), 38.1 ($CONHCH_2$), 31.5, 30.1 ($ArCH_2Ar$). FABMS m/z: 705 (M^++1). Anal. Calcd for $C_{40}H_{42}N_4O_8$: C, 67.97; H, 5.99; N, 7.93. Found: C, 67.86; H, 6.02; N, 7.97.

6.2.1.2. Compound 3b. Obtained as white solid, yield: 61%, mp >300 °C (decomp.). IR (KBr, ν_{max}/cm^{-1}): 3419, 3268, 1672. ^{1}H NMR (300 MHz, $CDCl_3$, δ in ppm): 7.48 (br s, 4H, CONH), 6.63–6.58 (m, 12H, ArH), 4.73 (d, 4H, J=14.1 Hz, OCH_2), 4.54 (d, 2H, J=13.2 Hz, $ArCH_2Ar$), 4.27 (d, 2H, J=14.4 Hz, $ArCH_2Ar$), 4.18 (d, 4H,

J=14.1 Hz, OCH_2), 3.61 (br s, 8H, $CONHCH_2$), 3.37 (d, 2H, J=14.4 Hz, $ArCH_2Ar$), 3.25 (d, 2H, J=13.2 Hz, $ArCH_2Ar$), 1.84 (br m, 4H, $CONHCH_2CH_2$). DEPT-135 NMR (75 MHz, $CDCl_3$, δ in ppm): 129.4, 128.9, 123.3 (aromatic CH), 74.6 (OCH_2), 39.9 ($CONHCH_2$), 30.9, 29.8, 28.1 ($ArCH_2Ar$, $CONHCH_2CH_2$). FABMS *m/z*: 733 (M^++1). Anal. Calcd for $C_{42}H_{46}N_4O_8$: C, 68.65; H, 6.31; N, 7.62. Found: C, 68.59; H, 6.28; N, 7.60.

6.2.1.3. Compound 3c. Obtained as white solid, yield: 57%, mp >300 °C (decomp.). ^1H NMR (300 MHz, $CDCl_3$, δ in ppm): 7.42 (br s, 4H, CONH), 6.65–6.56 (m, 12H, ArH), 4.72 (d, 4H, J=14.1 Hz, OCH_2), 4.51 (d, 2H, J=12.9 Hz, $ArCH_2Ar$), 4.28 (d, 2H, J=13.5 Hz, $ArCH_2Ar$), 4.18 (d, 4H, J=14.1 Hz, OCH_2), 3.56 (br s, 8H, $CONHCH_2$), 3.37 (d, 2H, J=13.5 Hz, $ArCH_2Ar$), 3.25 (d, 2H, J=12.9 Hz, $ArCH_2Ar$), 1.84 (br m, 8H, $CONHCH_2CH_2$). FABMS *m/z*: 761 (M^++1). Anal. Calcd for $C_{44}H_{50}N_4O_8$: C, 69.27; H, 6.61; N, 7.34. Found: C, 69.09; H, 6.62; N, 7.30.

6.2.2. General procedure for the synthesis of calix[4]arene-bis(amido)crowns in 1,3-alternate conformation (for 7a–c). Calix[4]arene (**1**) was refluxed with cesium carbonate (20 equiv) and ethyl bromoacetate (20 equiv) in acetone under dry conditions for 7 days. The solvent was removed under reduced pressure to yield a yellowish oily liquid, which was dissolved in toluene/methanol (1:1 ratio) and the respective diamine (40 equiv) was added. The reaction was continued for 2 days under reflux and work up was done in the usual manner as described above to give calix[4]arene-bis(amido)crowns derivatives in 1,3-alternate conformation.

6.2.2.1. Compound 7a. Recrystallized from $CHCl_3$/CH_3OH as white solid, yield: 62%, mp >300 °C (decomp.). IR (KBr, ν_{max}/cm^{-1}): 3396, 1681. ^1H NMR (300 MHz, $CDCl_3$, δ in ppm): 7.15 (d, 8H, J=7.5 Hz, ArH_{meta}), 6.97 (t, 4H, J=7.5 Hz, ArH_{para}), 5.22 (br s, 4H, CONH), 4.16 (s, 8H, OCH_2), 3.92 (s, 8H, $ArCH_2Ar$), 3.16 (br s, 8H, $CONHCH_2$). DEPT-135 NMR (75 MHz, $CDCl_3$, δ in ppm): 130.2, 124.4 (aromatic CH), 68.4 (OCH_2), 37.3, 37.8 ($CONHCH_2$, $ArCH_2Ar$). FABMS *m/z*: 705 (M^++1). Anal. Calcd for $C_{40}H_{42}N_4O_8$: C, 67.97; H, 5.99; N, 7.93. Found: C, 67.86; H, 6.02; N, 7.97.

6.2.2.2. Compound 7b. Recrystallized from $CHCl_3$/CH_3OH as white solid, yield: 60%, mp >300 °C (decomp.). IR (KBr, ν_{max}/cm^{-1}): 3392, 1680. ^1H NMR (300 MHz, $CDCl_3$, δ in ppm): 7.12 (d, 8H, J=7.5 Hz, ArH_{meta}), 6.95 (t, 4H, J=7.5 Hz, ArH_{para}), 5.25 (br s, 4H, CONH), 4.17 (s, 8H, OCH_2), 3.87 (s, 8H, $ArCH_2Ar$), 3.26 (br s, 8H, $CONHCH_2$), 1.79 (br s, 4H, $CONHCH_2CH_2$). DEPT-135 NMR (75 MHz, $CDCl_3$, δ in ppm): 129.7, 124.0 (aromatic CH), 68.3 (OCH_2), 37.9, 37.2 ($CONHCH_2$, $ArCH_2Ar$), 27.7 ($CONHCH_2CH_2$). FABMS *m/z*: 733 (M^++1). Anal. Calcd for $C_{42}H_{46}N_4O_8$: C, 68.65; H, 6.31; N, 7.62. Found: C, 68.56; H, 6.28; N, 7.58.

6.2.2.3. Compound 7c. Recrystallized from $CHCl_3$/CH_3OH as white solid, yield: 60%, mp >300 °C (decomp.). IR (KBr, ν_{max}/cm^{-1}): 3385, 1680. ^1H NMR (300 MHz, $CDCl_3$, δ in ppm): 7.12 (d, 8H, J=7.5 Hz, ArH_{meta}), 6.94 (t, 4H, J=7.5 Hz, ArH_{para}), 5.32 (br s, 4H, CONH), 4.17 (s, 8H, OCH_2), 3.79 (s, 8H, $ArCH_2Ar$), 3.36 (br s, 8H, $CONHCH_2$), 1.49 (br s, 8H, $CONHCH_2CH_2$). DEPT-135 NMR (75 MHz, $CDCl_3$, δ in ppm): 130.7, 124.3 (aromatic CH), 69.8 (OCH_2), 37.9, 37.6 ($CONHCH_2$, $ArCH_2Ar$), 24.8 ($CONHCH_2CH_2$). FABMS *m/z*: 761 (M^++1). Anal. Calcd for $C_{44}H_{50}N_4O_8$: C, 69.27; H, 6.61; N, 7.34. Found: C, 69.11; H, 6.59; N, 7.29.

6.3. X-ray structure determination of 7a

X-ray crystal data for **7a**—$C_{83}H_{79}Cl_9N_8O_{22}$, M=1859.59, monoclinic, a=27.126(3) Å, b=10.843(1) Å, c=30.455(3) Å, α=90°, β=105.053(2)°, γ=90°, V=8650.8(15) Å^3, Z=4, D_c=1.428 g cm^{-3}, μ (Mo Kα)=0.369 mm^{-1}, GOF=1.256, space group=Cc. Intensity data were collected up to θ=50° by using 2θ scanning mode with graphite filtered Mo Kα radiation (λ=0.71073) on a 0.221×0.106×0.097 mm^3 crystal at 273 K. A total of 28,609 reflections were measured, 11,317 were independent of which 7615 [$I>2\sigma(I)$] were observed. Final R indices [$I>2\sigma(I)$]$R1$=0.0995, $wR2$=0.2680, and R indices (all data) $R1$=0.1143, $wR2$=0.2940 was found for 9276 observed reflections, 2 restraints, and 1112 parameters. Because of poor crystal quality, intensity statistics accomplished at lower 2θ deprived and inconsistent reflections were omitted from the refinement to achieve better R factor. The structure was solved by direct methods and refined by full matrix least-square techniques on F^2 using SHELXTL. Some of the observed intensities were anomalously large due to contributions from overlapping reflections from other minor component. TWIN 100010001 matrix was applied and significant convergence was observed during subsequent refinement cycles. All the non-hydrogen atoms were refined anisotropically. A water molecule in the asymmetric unit was found disordered and after occupancy refinement this was fixed at two crystallographically independent positions with 50% occupancy factor. C–H hydrogen atoms were placed in geometrically calculated positions by using a riding model. No hydrogen could be located from the difference map. Torsion angles and H-bonding were calculated by using PARST. Crystal data have been deposited with the Cambridge Crystallographic Data Center, under reference CCDC No. 294508.

6.4. General procedures for UV–vis experiments

6.4.1. Interaction study. All the UV–vis experiments were carried out in methanol. Any shift in the UV–vis spectra of the synthesized compounds was recorded on addition of salt solutions (100 equiv). Carbonates–(Li^+, Na^+, K^+, Rb^+, Cs^+, and Ag^+), chlorides–(Mg^{2+}, Ca^{2+}, Ba^{2+}, Cr^{3+}, Fe^{2+}, Cd^{2+}, Pb^{2+}, Hg^{2+}, Pd^{2+}, and Pt^{2+}), acetate (Co^{2+}, Ni^{2+}, and Cu^{2+}), and *tert*-butyl ammonium salts (Cl^-, Br^-, I^-, HSO_4^-, $H_2PO_4^-$, and $CH_3CO_2^-$) were used for the UV–vis experiments.

6.4.2. Liquid–liquid extraction experiments. Solutions of the synthesized compounds used for the extraction of anions from aqueous phase were prepared in ethanol free chloroform. Stock solutions of 2.5×10^{-4} M of calix[4]arene-bis(amido)crown (**7a**), sodium chromate, potassium chromate, sodium dichromate, and potassium dichromate were prepared. A solution (5 mL) of 2.5×10^{-4} M of calix[4]arene-bis(amido)crown (**7a**) was stirred for 3 h with an aqueous solution (5 mL) of 2.5×10^{-4} M of chromate or dichromate salt; followed by measuring the anion concentration in the aqueous phase by UV–vis spectroscopy. The temperature was kept constant during all the experiments at 25 °C (±2). All the experiments were carried out in a set of three to avoid experimental errors. The blank experiments between the organic layer in the absence of calix[4]arene-bis(amido)crowns were also conducted. The percentage extraction was calculated according to the following relationship—extraction $(\%)=[(A_{\text{blank}}-A_{\text{extracted}})/A_{\text{blank}}]\times100$.[14]

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