

Synthesis and evaluation of novel 1,3-bridged calix[4]arene-crown ethers for selective interaction with Na⁺/K⁺ cations

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Abstract Calix[4]arenes possessing electron-donating groups (OH and OR) at the lower rim when reacted with tosylated polyethers under basic conditions give the corresponding 1,3-disubstituted calix[4]arene-crown ethers **2a–2h**, in good yields. The binding properties of the synthesized 1,3-bridged calix[4]arene-crown ethers for alkali metal cations have been investigated by atomic emission spectrometric analysis. It has been observed that recognition of sodium and potassium varies with the size of the polyether chain as well as the substituents on the free phenolics of the calix[4]arene-crown ether. The potassium/sodium selectivity seems to be governed primarily by the size of the crown ring, relative hydrophobicity and cation- π interaction capability to give efficiency order as **2a**, **2d** > **2h** > **2c**, **2e** > **2b**, **2f** > **2g**.

Keywords Calix[4]arenes · Calix[4]arene-crown ethers · Synthesis · Cationic recognition · Flame atomic emission spectrometric assay

Introduction

Calix[*n*]arenes are stable high melting macrocyclic phenolic metacyclophanes with a marked potential for applications in molecular separation, recognition and construction of molecular devices. They are readily obtained by acid and

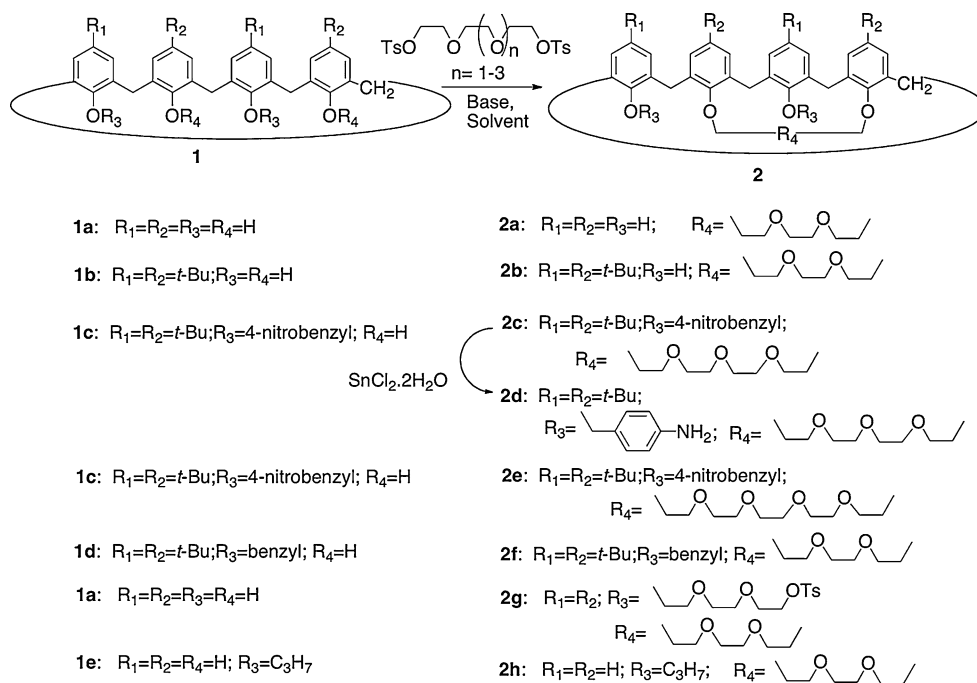
base catalyzed condensation of *p*-alkylated phenols with a formaldehyde source [1–3]. Likewise crown ethers also represent an extremely useful macrocyclic polyethers with wide range of ion selective applications [4]. A number of supramolecular receptors have been described in the literature during the past decade which combine the unique properties of calixarenes and crown ethers to achieve solid state matrices for chemical separations [5]. Since parent calixarenes are poor metal ion extractants, several calix[4]arene-crown ether conjugates (also called calix[4]arene-crowns or simply calix[4]crowns) have been investigated for ionic recognition in the recent past. For example Asfari et al. [6–8] have reported the synthesis of macropolycyclic crown ethers by bridging the opposite OH groups in *p*-*tert*-butylcalix[4]arene through a pentaethylene glycol chain. However, this reaction was determined to lead to several by-products that include calix[4]-bis-crowns. Reinhoudt et al. [9] have also attempted a more general route to calix[4]arene-crown ethers through selective 1,3-dialkylation of calix[4]arenes followed by base catalyzed bridging of the remaining phenolic groups with the appropriate polyethylene glycol ditosylates [9]. They have determined that the bridging pattern, regio- and stereo-control of this reaction is strongly dependent on the cyclizing agent as well as the template effect of the cation of bases used for the condensation reaction. It has also been observed that the alkali metal carbonate mediated ring closure leads to 1,3-bridged calix[4]arene-crown ethers in cone or 1,3-alternate conformations on heating for a period of about 2 weeks in CH₃CN. On the other hand, use of stronger bases (NaH, in THF/toluene) under milder conditions and shorter times provide workable yield of mono calix[4]arene-crown ethers [10, 11] (Scheme 1).

The efficacy of calix[*n*]arene-crown ethers (*n* = 4, 6) for selective extraction from aqueous phase has often been

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Scheme 1 Reaction conditions:
 (i) NaH:THF:Toluene (10:1), reflux (for **2a**, **2b**, **2f**, **2h**) (ii) K_2CO_3 (anh), CH_3CN (dry), reflux [**2c**, **2d** (with $SnCl_2 \cdot 2H_2O$) and ethanol], **2e**, **2g**]



measured by the picrate protocol perfected by Cram and coworkers [12]. This protocol involves extraction of the metal picrates from aqueous to the organic (usually chloroform or methylene chloride) phase. It has been felt that the selectivities observed in the picrate extraction methodology would be inadequate unless the analysis was also done for both the aqueous and the organic phases of the extraction protocols adopted. For example, the results on sodium/potassium selectivity by picrate extraction method might be blurred because both these ions in the Na^+/K^+ mixture would contribute to total picrate extraction percentage and would not distinguish them individually unless the studies were accompanied by complete analysis of the aqueous phase for these metal ions. In the present paper we report the synthesis and evaluation of ionophores (**2a–2h**) for recognition of sodium and potassium through flame atomic emission spectrometry. Since the technique measures the emission of energy from atomic species directly, the study represents the real time measure of recognition potential of the calix[4]arene-crown ethers studied.

Results and discussion

Synthesis and characterization

2a–2h were prepared from the respective calix[4]arenes by the reaction with oligoethylene glycol ditosylates with

appropriate calixarene derivatives (Scheme 1). For example, the reaction of calix[4]arene (**1**) with oligoethylene glycol ditosylate gave the expected 1,2-ethylene bridged 1,3-calix[4]arene-crown ethers (**2**). Higher analogues of oligoethylene glycols, provided the 1,3-bridged derivatives (**2d**, **2e**) with an expanded crown ether arm. These observations were somewhat different from earlier reports that led to the formation of double calixarenes with large excess of Na_2CO_3/K_2CO_3 . The reaction of **1** with K_2CO_3 gave 1,2-calix[4]arene-crown ethers (**2c**, **2e**, **2g**) in 52–53% yields, respectively. When a more rigid and hard base (NaH) was used, different products (**2a–2b**, **2f**, **2h**) were obtained in 55% yield.

Calix[4]arene-crown ethers obtained in the present work were purified by column chromatography followed by crystallization from chloroform–methanol (4:1) (Table 1). Calix[4]arene-crown ethers obtained above were found to exhibit prominent signals for Ar–CH₂–Ar methylene carbons in its range 31.0 ± 1.3 ppm to reveal that the calix(4)arene unit in calix[4]arene-crown ethers was present in the cone conformation. A pair of doublets in the region between 3.35 and 4.3 ppm observed in the ¹H NMR and signals at 31.3 and 33.7 ppm in the ¹³C NMR spectra confirmed this conclusion. Though, good crystals of most of the synthesized calix[4]arene-crown ethers could not be obtained, preliminary X-ray studies on **3** established that the synthesized calix[4]arene-crown ethers do stabilize in their cone conformation even when the tertiary butyl groups were removed from the calixarene skeleton (unpublished work) corroborating the generality of cone

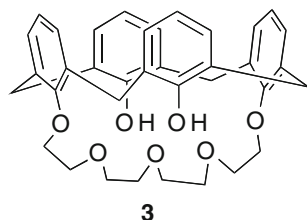
Table 1 Reaction conditions for the synthesis of calix[4]arene-crown ethers

S.No	Reactant	Product	Reaction conditions (reflux, h)		Yield (%)	Solvent of crystallization.
1	1a	2a	NaH/THF	14–16	53	CH ₂ Cl ₂ –CH ₃ OH
2	1b	2b	NaH/THF	14–16	52	CH ₂ Cl ₂ –CH ₃ OH
3	1c	2c	K ₂ CO ₃ /CH ₃ CN	6–8	53	CH ₂ Cl ₂ –CH ₃ OH
4	2c	2d	SnCl ₂ ·2H ₂ O/EtOH	6–8	54	CH ₂ Cl ₂ –CH ₃ OH
5	1c	2e	K ₂ CO ₃ /CH ₃ CN	6–8	55	CH ₂ Cl ₂ –CH ₃ OH
6	1d	2f	NaH/THF	14–16	55	CH ₂ Cl ₂ –CH ₃ OH
7	1a	2g	K ₂ CO ₃ /CH ₃ CN	6–8	54	CH ₂ Cl ₂ –CH ₃ OH
8	1e	2h	NaH/THF	14–16	56	CH ₂ Cl ₂ –CH ₃ OH

Table 2 Extraction of potassium/sodium ions from a solution of their mixture

S. no.	Ligand	No. of moles of metal cations complexed per mole of ligand		Ratio of K ⁺ /Na ⁺
		Na ⁺	K ⁺	
1	2a	0.34	1.52	4.44
2	2b	3.51	2.66	0.76
3	2c	0.85	3.31	3.89
4	2d	0.72	3.27	4.55
5	2e	0.59	2.04	3.42
6	2f	0.84	2.20	2.62
7	2g	1.86	2.89	1.54
8	2h	0.43	1.75	4.07

conformation for calix[4]arene-crown ethers as deduced from ¹H and ¹³C- NMR evidences.



Recognition potential of synthesized calix[4]arene-crown ether compounds for sodium and potassium

The evaluation of recognition potential of synthesized calix[4]arene-crown ethers was carried out by two phase complexation of alkali metal ions by the calix[4]arene-crown ethers followed by flame atomic emission spectrometry. Since flame emission spectrometry is heavily dependent upon reaction conditions and the flame temperature and other parameters, strict identity of experimental conditions for the analytes and the standards were maintained. In the present experiments, standard solutions of alkali metals (Na₂CO₃, K₂CO₃) were used for distribution in the chloroform-water phases at room temperature. Freshly distilled CHCl₃ solution of calix[4]arene-crown ethers (**2a–2h**) were taken in a clean stoppered bottle and

was vigorously stirred with a standard solution of alkali metal salts in deionized double distilled water with the help of magnetic stirrer for 3 h at 25 °C. The mixture was left undisturbed for an additional 30 min and the concentration of metal cation in the aqueous phase was determined by using output signal of the flame atomic emission spectrometer. The blank experiments were also performed with the respective metal cation solutions prepared separately and the instrument was calibrated each time with standardized solutions and the output was compared with different calix[4]arene-crown ether metal ion solutions. The results obtained are summarized in Table 2. Since sodium/potassium ratio is the most important parameter for biological analytes, the emission data obtained for sodium and potassium have also been recorded as the sodium/potassium ratio. Figure 1 represents the number of moles of sodium and potassium ions extracted from their aqueous solutions by different calix[4]arene-crown ethers. The output parameters of flame photometer for blank ionic solution of alkali metal cations and metal solution-crown ethers were also noted down. The analytical calculations give the number of moles of metal cation complexed per mole of calix[4]arene crown ether (Table 2). Table 3 compiles the data of number of moles of complexed and un-complexed metal cations for calix[4]arene-crown ethers (**2a–h**)

Fig. 1 Number of moles of metal (Na^+ and K^+) cation complexed per mole of ligand from an aqueous phase into dichloromethane at 25 °C

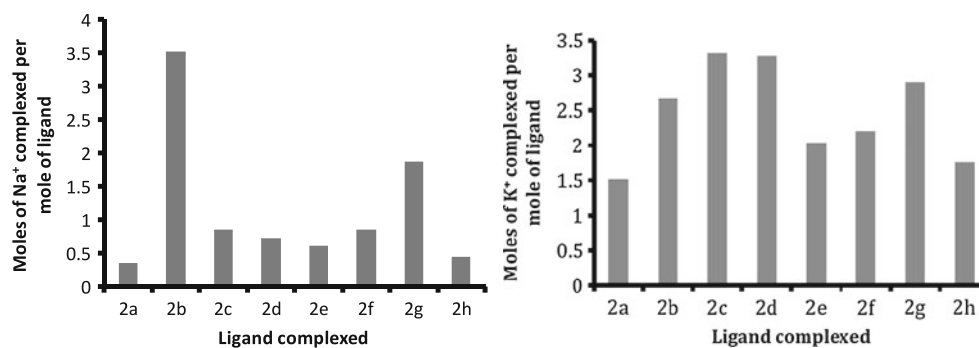


Table 3 Number of moles of complexed and un-complexed metal cations with calix[4]arene-crown ethers (**2a–h**)

Comp. no.	Total no. of moles of $\text{Na}^+(\text{N}_{\text{Na}^+})$	Un-complxd. Na^+ (n_{Na^+})	Complxd. Na^+ ($(\text{N}-n)_{\text{Na}^+}$)	Total no. of moles of $\text{K}^+(\text{N}_{\text{K}^+})$	Un-complxd K^+ (n_{K^+})	Complxd. K^+ ($(\text{N}-n)_{\text{K}^+}$)
2a	4.608×10^{-4}	3.972×10^{-4}	6.36×10^{-5}	3.54×10^{-4}	7.12×10^{-5}	2.83×10^{-4}
2b	4.608×10^{-4}	–	4.60×10^{-4}	3.54×10^{-4}	4.60×10^{-6}	3.49×10^{-4}
2c	4.608×10^{-4}	3.816×10^{-4}	7.92×10^{-5}	3.54×10^{-4}	4.53×10^{-5}	3.09×10^{-4}
2d	4.608×10^{-4}	3.898×10^{-4}	7.09×10^{-5}	3.54×10^{-4}	3.05×10^{-5}	3.23×10^{-4}
2e	4.608×10^{-4}	3.659×10^{-4}	9.49×10^{-5}	3.54×10^{-4}	2.94×10^{-5}	3.24×10^{-4}
2f	4.608×10^{-4}	3.438×10^{-4}	1.17×10^{-4}	3.54×10^{-4}	4.70×10^{-5}	3.49×10^{-4}
2g	4.608×10^{-4}	2.35×10^{-4}	2.25×10^{-4}	3.54×10^{-4}	4.61×10^{-6}	3.49×10^{-4}
2h	4.608×10^{-4}	3.912×10^{-4}	6.95×10^{-5}	3.54×10^{-4}	7.05×10^{-5}	2.83×10^{-4}

It was determined that **2a**, **2c–2h**, transfer potassium cation to organic phase in preference to sodium while **2b** showed significant selectivity for sodium.

The preference for sodium ions by calix[4]-crown derivatives of former category is probably due to appropriate size of calix[4]-crown. The calix[4]arene-crown ethers, **2a**, **2d** and **2h** showed selective extraction capability for K^+ . The sequence of extraction capabilities of various calix[4]arene-crowns mentioned above for potassium has been found to be **2a**, **2d** > **2h** > **2c**, **2e** > **2f** > **2g** > **2b**. This order is in accordance with earlier findings on crown ether complexation with alkali metal ions [6, 11, 13].

Although, the selectivity has been only 4:1, one can work further for comparing potassium/sodium selectivity by modifying the calix[4]arene skeleton. For example the potassium ion selectivity is decreased on introduction of the tertiary butyl groups at the upper rim of calixarene skeleton. The retention of tertiary butyl groups in the calixarene skeleton of calix[4]arene-crown ethers promoted the selectivity for sodium. The extension of the crown ether chain did not markedly affect the potassium/sodium selectivity. Another marked influence determined concerned with the marked increase in potassium selectivity on etherification of calix[4]arene hydroxyls with alkyl groups up to three carbon atoms. For example potassium/sodium ratio dropped from 4.4 to 4.07 in the case of **2a** and **2h** when calixarene hydroxyls were subjected to propylation.

From the present studies we can safely conclude that from amongst all the calix[4]arene-crown ethers synthesized, **2d** is best for extraction of potassium. The potassium/sodium selectivity ratio is dependent upon the calixarene skeleton rather than the crown ether structure.

The effect of conformation of calixarene on recognition of sodium potassium was attempted by crystallizing calix[4]arene **3** from methylene chloride and determining its crystal structure. Unfortunately the single crystal obtained was not of sufficient purity and crystallinity though preliminary data suggested it to be in the cone conformer. Since selectivity seemed to be controlled by the calixarene moiety, one can anticipate an increase in the selectivity of sodium/potassium by calix[4]arene-crown ethers through change of conformation of calixarene skeleton as confirmed by recent results published by other groups [8, 14]. The present study also confirmed the experimental deductions from experiments conducted by using the picrate extraction methods deployed earlier [8, 14].

Experimental

Instrumental

Melting points were determined on Toshniwal apparatus in a sealed capillary. The ^1H NMR spectra were recorded on a Bruker 300 MHz spectrometer in $\text{CDCl}_3/\text{DMSO}$ using

TMS as the internal standard. IR spectra were recorded on a Perkin-Elmer 1605 FTIR spectrometer in KBr pallets. Flame atomic emission spectrometric determinations were carried out on a Knauer flame photometer at concentration of cations between 100 and 40 ppm in freshly distilled CH_2Cl_2 . Analytical TLC was performed on pre-coated silica gel plates (SiO_2 , Merck), while silica gel 60 (Merck, particle size 0.040–0.063 mm, 230–240 mesh) was used for preparative column chromatography. NaH was used as 80% dispersion in oil and washed twice with *n*-hexane before use. Solvents were generally dried by storing them over molecular sieves (4A, 8–12 mesh) or by the use of anhydrous sodium sulphate. All chemicals were purchased from Merck. All aqueous solutions were prepared with deionized water which was further pumped through a Millipore milli-Q Plus water purification system before using it for making solutions for the alkali metal cations.

Synthesis of *p*-*tert*-butylcalix[4]arene

The *p*-*tert*-butylcalix[4]arene [1], debutylated calix[4]arene [1], **1d** [15] and **1e** [16] were synthesized by using the procedure described in the literature.

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,27-bis-(4-nitrobenzyloxy)-26,28-dihydroxycalix[4]arene **1c**

A mixture of *p*-*tert*-butylcalix[4]arene (10.0 g, 15.43 mmol) and K_2CO_3 (2.13 g, 15.43 mmol) in acetonitrile (400 mL) was heated for 30 min. *p*-Nitrobenzyl bromide (6.7 g, 30.82 mmol) was added and the reaction mixture refluxed for additional 8 h with continuous stirring. While the reaction mixture was standing over night, fine crystals of **1c** were observed in the flask. The crystals were filtered and then half of the solvent was removed under vacuum and left for further crystallization. All the crystals were combined, washed with MeOH and finally recrystallized from acetonitrile. Yield 6.8 g (48%); m.p. 148 °C; IR (KBr) 3440 cm^{-1} , 1526 cm^{-1} ; ^1H NMR (CDCl_3): δ 0.93 (s, 18H, Bu^t), 1.32 (s, 18H, Bu^t), 3.36 (d, 4H, ArCH_2Ar), 5.19 (s, 4H, OCH_2Ar), 6.85 (s, 4H, ArH), 7.10 (s, 4H, ArH), 7.14 (s, 2H, ArOH), 7.28 (d, 4H, ArH, 4-nitrophenyl- $\text{H}_{3,5}$), 8.19 (d 4H, ArH, 4-nitrophenyl- $\text{H}_{2,6}$); Anal calcd. for $\text{C}_{58}\text{H}_{66}\text{N}_2\text{O}_8$: C, 75.79; H, 7.24; N, 3.05; found: C, 75.80; H 7.22; N, 3.08. FAB-MS (*m/z*): 919.1 (M^+), found: 918.7.

General procedure for the reaction of calix[4]arene with oligoethylene glycol-*p*-ditosylates (**2c**)

In a 250 mL round bottom flask, 5,11,17,23-tetra-*tert*-butyl-25,27-dihydroxy-26,28-*p*-nitrobenzylcalix[4]arene [13] (**1c**), (1.00 g, 1.08 mmol) and K_2CO_3 (1.20 g,

8.70 mmol) was dissolved in 100 mL of acetonitrile. The contents were refluxed for half an hour followed by dropwise addition of a warm solution of tetraethylene glycol-*p*-tosylate (1.09 g, 2.17 mmol) in CH_3CN (75 mL). The mixture was refluxed for 6 days. The content of the flask was rotary evaporated, the residue was washed twice with 10% HCl (150 mL) and then with water followed by drying over Na_2SO_4 . The impure product was purified by column chromatography using ethyl acetate/hexane (3.5:1.5) as the eluant to provide the pure product, Yield: (52.7%), m.p > 210 °C, IR (KBr) 1447 cm^{-1} , ^1H NMR (CDCl_3): δ 3.8 (d, ArCH_2Ar), 3.9–4.4 (m, 36H, ArCH_2Ar , OCH_2 , OCH_3), 7.2–6.6 (m, 24H, ArH). ^{13}C NMR (CDCl_3): 144.5, 134.1, 133.5, 128.5, 125.7, 125.0 (ArC); 74.8, 73.2, 71.1, 70.4, 68.2, 67.2 (ArOCH_2C , $\text{ArOCH}_2\text{CH}_2\text{C}$); 31.3, 33.7, 30.2 (ArCH_2ArC , ^tBu). Anal Calcd. for $\text{C}_{66}\text{H}_{76}\text{N}_2\text{O}_{11}$: C, 73.60; H, 7.06; N, 2.6 Found: C, 73.49, H, &.12, N, 2.76. FAB-MS (*m/z*): 1074.0 (M^+), found: 1074.0

General procedure for synthesis of calix[4]arene-crowns (**2a–2h**)

The synthesis of crown ethers, **2a–2h**, was accomplished by using the above mentioned general method:

Compound **2a**

The calix[4]arene, **1a** (0.80 g, 1.88 mmol) was dissolved in THF/Toluene (10:1, 22 mL) and NaH (0.09 g, 3.76 mmol) was added. The mixture was refluxed for half an hour and a solution of tetraethylene glycol-*p*-ditosylate (2.16 g, 4.71 mmol) in THF (5 mL) was added drop wise. The reaction mixture was refluxed for 15 h and then cooled to room temperature. The solvent was evaporated and the contents were extracted with dichloromethane (150 mL), washed two to three times with 10% HCl (200 mL) and finally with water (250 mL) followed by drying over Na_2SO_4 . The combined organic layers were rotary evaporated to remove residual solvent. The crude product obtained was dissolved in distilled chloroform and subjected to chromatography over silica gel column by using hexane: ethyl acetate, (4.5:5) as the eluent. Yield : (53%), m.p. 210 °C, IR(KBr) 3433 cm^{-1} , ^1H NMR (CDCl_3): δ 3.31 (d, 4H, ArCH_2Ar), 3.73–4.70 (m, 16H, ArCH_2Ar , $\text{OCH}_2\text{CH}_2\text{O}$, OCH_2), 6.40 (m, 2H, ArH), 6.69 (m, 2H, ArH), 7.39 (d, 4H, ArH), 7.68 (d, 4H, ArH). Anal calcd. for $\text{C}_{34}\text{H}_{34}\text{O}_6$: C, 75.76; H, 6.31. Found: C, 74.93; H, 6.09. FAB-MS (*m/z*): 538.0 (M^+).

Compound **2b**

The calix[4]arene, **1b** (0.50 g, 0.77 mmol) was dissolved in THF/Toluene (10:1, 22 mL) and NaH (0.04 g, 1.54 mmol)

was added. The mixture was refluxed for half an hour and triethylene glycol-*p*-ditosylate (0.88 g, 1.93 mmol) in THF (5 mL) was added drop wise. The reaction mixture was refluxed for 12 h and then cooled and worked up as mentioned above to purify as **2a**. Yield : (51.8%), m.p > 210 °C, IR (KBr): 1463 cm⁻¹, ¹H-NMR (CDCl₃): δ 0.9 (s, 18H, C[(CH₃)₃]), 1.15 [s, 18H, C[(CH₃)₃]], 3.33 (d, 4H, ArCH₂Ar), 3.36–4.38 (m, 16H, ArCH₂Ar, OCH₂-CH₂O, OCH₂CH₂), 6.9 (d, 4H, ArH), 7.72(d, 4H, ArH), 0.1 (s, 2H, OH), Anal Calcd. for C₅₀H₆₆O₆: C, 78.40; H, 8.66. Found: C, 77.89; H, 8.50. FAB-MS (m/z): 763.0 (M⁺), found 763.0.

Compound 2d

The compound **2c** (0.27 g, 0.25 mmol) was added to SnCl₂·2H₂O (0.41 g, 1.99 mmol) in dry ethanol (15 mL) and refluxed for 6 h. The content was poured into alkaline water and the pH was adjusted till neutral. Extract the product with CH₂Cl₂, evaporated the solvent and precipitated the product with methanol. The product was purified by column chromatography (SiO₂, ethyl acetate: hexane: 1:1) Yield : (54%), m.p > 210 °C, IR (KBr) 1467 cm⁻¹, ¹H-NMR (CDCl₃): δ 0.97 (s, 18 H, ¹Bu), 1.19 (s, 18 H, Bu^t), 3.35 (d, 4H, ArCH₂Ar), 3.6–5.1 (m, 28H, ArCH₂Ar, OCH₂Ar, OCH₂), 6.81 (s, 4H, ArH), 7.12 (s, 4H, ArH), 7.8 (d, 4H, ArH, 4-aminophenyl-H_{3,5}), 8.1 (d, 4H, ArH, 4-aminophenyl-H_{2,6}). Anal calcd. for C₆₆H₈₀N₂O₇: C, 77.95; H, 7.87; N, 2.75. Found: C, 77.84; H, 7.62; N, 2.58. FAB-MS (m/z): 1013.3 (M⁺), found 1013.0.

Compound 2e

The calix[4]arene, **1c** (0.45 g, 1.06 mmol) and K₂CO₃ (1.17 g, 8.48 mmol) was dissolved in CH₃CN (20 mL) and refluxed for 25–30 min and a warm solution of pentaethylene glycol-*p*-ditosylate (1.16 g, 2.12 mmol) was added dropwise and mixture was further refluxed for 8 days and worked up and purified as described for the compound **2a**. Yield : (54.9%), m.p > 210 °C, IR (KBr pallets): 3397 cm⁻¹; ¹H-NMR (CDCl₃): δ 0.95 (s, 18H, C[(CH₃)₃]), 1.29 [s, 18H, C[(CH₃)₃]], 3.31 (d, 4H, ArCH₂Ar), 3.53–4.38 (m, 16H, ArCH₂Ar, OCH₂CH₂O, OCH₂CH₂), 6.82 (d, 4H, ArH), 7.12(d, 4H, ArH), 7.93 (d, 4H, ArH_{NO₂}), 8.17(d, 4H, ArH_{NO₂}). Anal calcd. for C₃₈H₄₂O₈: C, 69.48; H, 7.71; N, 2.38. Found: C, 69.07; H, &.69; N, 2.21. FAB-MS (m/z): 628.5 (M⁺), found: 629.0.

Compound 2f

The calix[4]arene, **1d** (0.60 g, 0.95 mmol) was dissolved in THF/toluene (10:1, 25 mL) and NaH (0.05 g, 1.91 mmol) was added. The mixture was refluxed for half an hour and a

solution of triethylene glycol-*p*-ditosylate (1.09 g, 2.39 mmol) in THF (5 mL) was added drop wise. The reaction was refluxed for 15 h and then cooled down and worked up as above and purified by column chromatography as in **2a**. Yield: (55.2%), m.p > 210 °C, ¹H-NMR CDCl₃: δ 3.33 (d, ArCH₂Ar), 3.53–5.16 (m, 24H, ArCH₂Ar, OCH₂Ar, OCH₂), 6.82 (s, 4H, ArH), 7.17 (d, 4H, ArH), 7.35 (d, 4H, ArH), 7.78 (d, 4H, ArH). Anal calcd. for C₄₈H₄₆O₆: C, 80.16; H, 6.4. Found: C, 81.02; H, 6.61. FAB-MS (m/z): 718.8 (M⁺), found: 719.0.

Compound 2g

A mixture of calix[4]arene, **1a** (0.40 g, 0.94 mmol) and K₂CO₃ (1.04 g, 7.54 mmol) was refluxed in CH₃CN (15 mL) for 25–30 min and a warm solution of triethylene glycol-*p*-ditosylate, (0.86 g, 1.88 mmol) in CH₃CN (10 mL) was added drop wise and mixture was further refluxed for 6 days, worked up and purified as described for the compound **2c**. Yield : (53.7%), m.p > 210 °C IR (KBr pallets): 3401 cm⁻¹, ¹H-NMR CDCl₃: δ 3.08 (d, 4H, ArCH₂Ar), 3.44–4.75 (m, 20H, ArCH₂Ar, OCH₂CH₂O, OCH₂), 6.07 (m 2H, ArH), 6.34 (m, 2H, ArH), 6.60 (d, 4H, ArH), 6.76 (d, 4H, ArH), 7.29 (d, 4H, ArH_{phenyl}), 7.48 (d, 4H, ArH_{phenyl}). Anal calcd. for C₄₇H₅₃O₁₁S: C, 68.19; H, 6.41. Found: 67.82; H, 6.02. FAB-MS C₄₇H₅₃O₁₁S (m/z): 828.0, found: 827.0.

Compound 2h

The calix[4]arene, **1e** (0.50 g, 0.98 mmol) was dissolved in THF/toluene (10:1, 25 mL) and NaH (0.05 g, 1.97 mmol) was added. The mixture was refluxed for half an hour and a solution of triethylene glycol-*p*-ditosylate (1.13 g, 2.46 mmol) in THF (5 mL) was added drop wise. The reaction was refluxed for 14 h and then cooled down and worked up as above and purified by column chromatography as in **2a**. Yield : (56%), m.p > 210 °C, IR (KBr) 3345 cm⁻¹, ¹H-NMR CDCl₃: δ 2.55 (s, 3H, CH₃), 4.38 (d, 4H, ArCH₂Ar), 3.40–4.09 (m, 28H, ArCH₂Ar, OCH₂-CH₂O, OCH₂), 6.41 (m, 2H, ArH), 6.61 (m, 2H, ArH), 6.82 (d, 4H, ArH), 6.92 (d, 4H, ArH), 7.04 (d, 2H, ArHOTs), 7.17 (d, 2H, ArHOTs), 8.1(s, H, OH). Anal calcd. for C₄₀H₄₄O₆: C, 77.36; H, 7.03. Found: 76.81; H, 6.98. FAB-MS (m/z): 620.7 (M⁺), found 622.0.

General procedure for the preparation of alkali metal solutions

The metal carbonates (Na₂CO₃, K₂CO₃) were accurately weighed and 100 ppm solutions (25 mL) of both the carbonates were prepared in distilled water. The prepared

solutions were then administered individually to the flame photometer and the process was repeated several times until we get the maximum display on the digital output, which implies that the instrument has been standardized and is ready to be used for testing the calix[4]arene-crown ligands.

General procedure for the preparation of ligand solutions

For the preparation of 60 ppm solution of different calix[4]arene-crown ethers, the ligands were accurately weighed and dissolved in (25 mL) chloroform and carefully stoppered. The volume of the solution was made up to the mark by addition of chloroform. The prepared ligand solutions were then administered to the previously standardized flame photometer (for the particular cation) and the digital output was recorded as described below.

General procedure employed for atomic emission spectrometric studies on calix[4]arene-crown ethers as metal ion receptors

The chloroform solutions (60 ppm) of calix[4]arene-crown ethers (**2a–h**) and an aqueous solution of Na_2CO_3 and K_2CO_3 (100 and 40 ppm) were prepared at 298 K. A fixed volume (15 mL) of chloroform solution of each ligand and aqueous solution (15 mL) of Na_2CO_3 and K_2CO_3 were allowed to stir for about an hour. The aqueous and organic phases of all the solutions (using Na_2CO_3 and K_2CO_3) were then separated and aqueous phases were administered to the flame photometer. The flame photometer was kept on at least 1 h before starting the experiment. A blank sample was run in flame photometer using Na_2CO_3 solution (100 ppm/15 mL) and the process was repeated (2–3 times) until we get the stable output (which is equal to 100) on photo detector. After the instrument has been standardized with Na_2CO_3 , the aqueous solutions of ligands were administered and the digital output was recorded. Since the metal carbonates are insoluble in chloroform, there is a transfer of cations (Na^+ , K^+) from aqueous phase to calix[4]arene-crown ether phase resulting in a decrease in the total number of moles of cations which were originally present in the aqueous solution of Na_2CO_3 or K_2CO_3 .

Table 4 Flame photometer measurements recorded with ligands (**2a–h**) using Na^+ and K^+ cations as ion sources

With Na^+ ions	86.2	0.6	84.9	82.8	79.4	84.5	51.1	74.6
Ligand	2a	2b	2c	2d	2e	2f	2g	2h
With K^+ ions	20.1	1.3	12.8	8.6	8.3	1.3	1.3	19.9

Table 4 represents the output from flame photometer when irradiated with aqueous solution of sodium or potassium ions.

Table 4 reveals that significant changes in concentrations of sodium and potassium takes place after their stirring with chloroform solution of different calix[4]arene-crown ethers. The observed data was used to calculate the moles of sodium or potassium ions as complexed with the ligand.

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