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Regulation of metal ion recognition by allosteric effects in thiacalix[4]-crown based receptors

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ABSTRACT

Three new ditopic receptors **3a–c** based on thiacalix[4]arene of 1,3 *alternate* conformation possessing two different complexation sites have been designed and synthesized for both soft and hard metal ions. The imino nitrogens bind soft metal ion ($Ag^{+}/Pb^{2+}/Cu^{2+}$) and the crown moiety binds K^{+} ion. The preliminary investigations show that **3a–c** behave as ditopic receptors for Ag^{+}/K^{+}, Pb^{2+}/K^{+}, and Cu^{2+}/K^{+} ions, respectively. In all the three receptors it was observed that the formation of **3a**·Ag^{+}/**3b**·Pb^{2+}/**3c**·Cu^{2+} complex triggers the decomplexation of K^{+} ion from crown moiety and acts as a gateway, which regulates the binding of alkali metal to crown moiety. Thus, allosteric binding between metal ions 'switch off' the recognition ability of crown ether ring.

1. Introduction

The present day activity in designing new functional molecules having sensing ability for cations stems from the role these ions play in chemistry, biology and environment.[1] Calixarenes with appropriate appended groups are good candidates for cation recognition[2] because they have been shown to be highly specific ligands and their potential as sensing agents has received increasing interest.[3] Among the different calix[4]arene derivatives, calix[4]crowns are very interesting because it is possible to have different number and nature of donor atoms in the crown ring thus making it possible to accommodate a variety of guests.[4] Thiacalix[4]arene[5] reported as the second generation of the calixarene chemistry is good receptor for soft and transition metal ions.[6] A 1,3 *alternate* thiacalix[4]crown platform provides a crown ether ring for metal ion complexation with a potential for additional binding by cation–π interactions between the two rotated benzene rings.[7] Such systems can also be used for mimicking allosteric regulation that play a major role in biological systems.[8] Allosteric binding can be defined as binding of regulatory molecule or an ion to a specific allosteric site of a protein, structurally distinct from the active site brings about the alteration in the conformation of the protein that indirectly modifies the properties of biologically active site. The guest can either enhance or decrease the binding or catalytic efficiency of the protein. Ultimately, the activity is switched '*ON*' or '*OFF*'.

Our research involves the design, synthesis, and evaluation of calix[4]arene and thiacalix[4]arene based receptors, which are selective for soft metal ions[9] and anions.[10] We recently reported a ratiometric[11] fluorescent sensor for mercury ions based on *partial cone* conformation of calix[4]arene, which behaves as NOR logic gate with YES logic function and a ratiometric[12] fluorescent sensor for copper ions based on a thiacalix[4]arene of 1,3 *alternate* conformation, which behaves as an INHIBIT logic gate with NOT and YES logic functions but no allosteric behavior was observed in above reported receptors. In present manuscript, we have designed and synthesized receptors **3a–c** based on thiacalix[4]crown of 1,3 *alternate* conformation, which show allosteric behavior between two different metal ions. The three receptors **3a–c** contain two binding sites, imine units for binding soft metal ions, and crown ether moiety for binding alkali metal ions. The Ag^{+}, Pb^{2+}, and Cu^{2+} ions bind imino nitrogens and K^{+} ions bind to the crown ether ring in receptors **3a–c**, respectively. The complexation of ligand with soft metal ion '*switch off*' the recognition of crown ether ring and act as a gateway, which regulates the binding of K^{+} ion to crown moiety. Thus, the formation of **3a**·Ag^{+}/**3b**·Pb^{2+}/**3c**·Cu^{2+} complex triggers the decomplexation of K^{+} ion and shows allosteric behavior between Ag^{+}/K^{+}, Pb^{2+}/K^{+}, and Cu^{2+}/K^{+} in receptors **3a–c**, respectively. Earlier Nabeshima et al. and Yamato et al. reported such behaviors in calix[4]arene[13] and thiacalix[4] arene[14] between $Ag^{+}/Na^{+}/K^{+}$ and Ag^{+}/Li^{+}, respectively, but such behaviors between Ag^{+}/K^{+}, Pb^{2+}/K^{+} and Cu^{2+}/K^{+} on thiacalixarene are still unprecedented. Allosteric behavior of K^{+} ions is significant as membrane transport of K^{+} ions in living systems is allosterically controlled and changes in their concentration affect the biological process such as opening of ion channels.

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2. Results and discussion

Condensation of thiacalix[4]crown diamine **1**[15] with aromatic monoaldehydes **2a–c** in 20 ml of $CHCl_3$/MeOH (1:1) yielded compounds **3a–c**. The products were virtually insoluble in the mixed solvent to separate out as pure solid. The structures of thiacalix[4]-arene receptors **3a–c** were confirmed from their spectroscopic and analytical data. The IR spectra of receptors **3a–c** showed C=N stretching bands at 1630, 1630, and 1635 cm^{-1}, respectively. There is no absorption band corresponding to free aldehyde and amino groups, which indicates that the condensation has taken place. This was confirmed by the FAB mass spectra, which showed parent ion peaks corresponding to the 1:2 condensation products at *m*/*z* 1143 ($M+H^+$), 1205 ($M+H^+$), and 1173 ($M+H^+$) for receptors **3a–c**, respectively. The ^1H NMR spectra of receptors **3a–c** showed two singlets (18H each) at 1.27–1.28 and 1.36 ppm corresponding to the *tert*-butyl protons, multiplet (8H) at 2.98–3.0 to 3.03–3.13 ppm corresponding to NCH_2 and OCH_2 protons, two broad signals (4H each) corresponding to OCH_2 protons at 3.38–3.39 and 3.59–3.60 ppm, two triplets (4H each) corresponding to OCH_2 protons at 3.94–3.96 and 4.08–4.12 ppm, two singlets (4H each) at 7.36–7.39 and 7.40–7.43 ppm corresponding to aromatic protons of thiacalix[4]arene and a singlet for imino protons (2H) at 8.24, 8.12, and 8.19 ppm, respectively. These spectroscopic data corroborate the structures **3a–c** for these compounds (see Supplementary data S9–S14) (Scheme 1).

The binding abilities of these receptors were studied toward different metal ions by two-phase solvent extraction, UV–vis, and fluorescence methods. To evaluate the binding ability of receptor **3a** toward different metal ions, two-phase solvent extraction of metal picrates (Pb^{2+}, Hg^{2+}, Zn^{2+}, Ni^{2+}, Ag^+, Na^+, K^+, Ca^{2+}, Ba^{2+}) was carried out. A chloroform solution of receptor (0.1 mM) was equilibrated with an aqueous solution of a metal picrate (0.1 mM) under neutral conditions. The ion extractability (*E*) was calculated from the picrate concentration in the organic phase, which was determined by UV–vis spectroscopy. The % age extraction of different metal ions is shown in Figure 1. It is clear from Figure 1 that maximum extraction was observed in case of Ag^+ ions, however, significant extraction of K^+ ions was also observed. Multi-ion recognition of Ag^+ and K^+ ions by **3a** can be attributed to the presence of imino and pyridyl nitrogens, which bind to Ag^+ ions and polyether ring that bind to the K^+ ions. These binding modes were confirmed by ^1H NMR spectroscopy. On addition of 1.0 equiv of Ag^+ ions to **3a**, the signals of imino protons were shifted downfield by 0.25 ppm, which indicates that imino nitrogens were interacting with Ag^+ ions (Fig. 2B). Similarly, on addition of 1.0 equiv of K^+ ions to **3a** there was a shift and coalescence of protons of crown moiety, which indicates that K^+ ions were interacting with oxygens of crown ring of receptor **3a** (Fig. 2C).

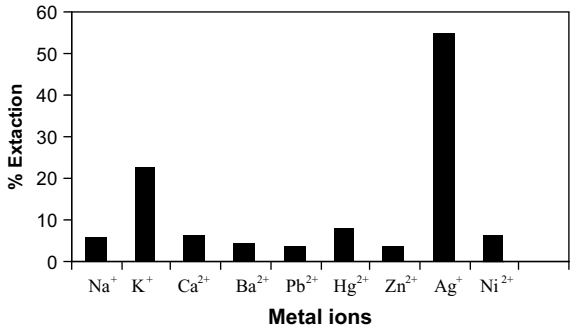


Figure 1. Solvent extraction results for **3a** upon addition of different metal ions. Source phase (aqueous solution of metal picrate, 2 mL), [MPic=0.1 mM]; organic phase ($CHCl_3$, 2 mL), carrier=0.1 mM. Extractability=(concentration of the extracted metal)/(concentration of the organic ligand)×100%. The data are the average value of three independent determinations.

The binding constant log β_1 for Ag^+ and K^+ ions was calculated to be 4.50 and 2.28 from UV–vis spectroscopy.[16] The stoichiometry of the **3a**–Ag^+ complex was determined by a two-phase extraction experiment ($H_2O/CHCl_3$), using the continuous variation method (Job's plot).[17] Thepercent extraction for Ag^+ reach maximum at 0.5 mole

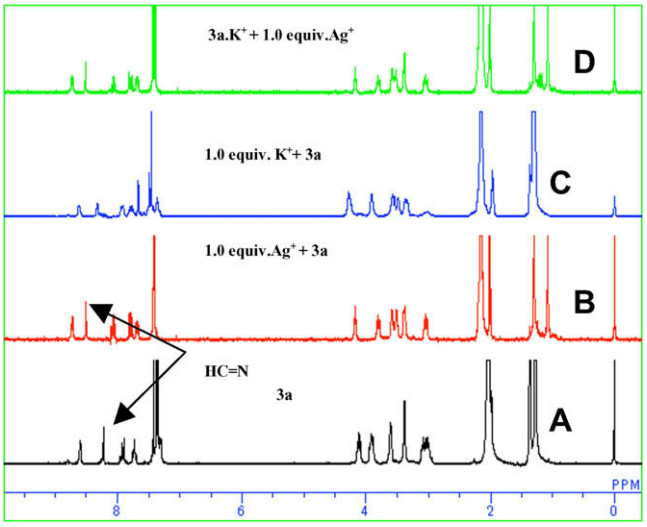
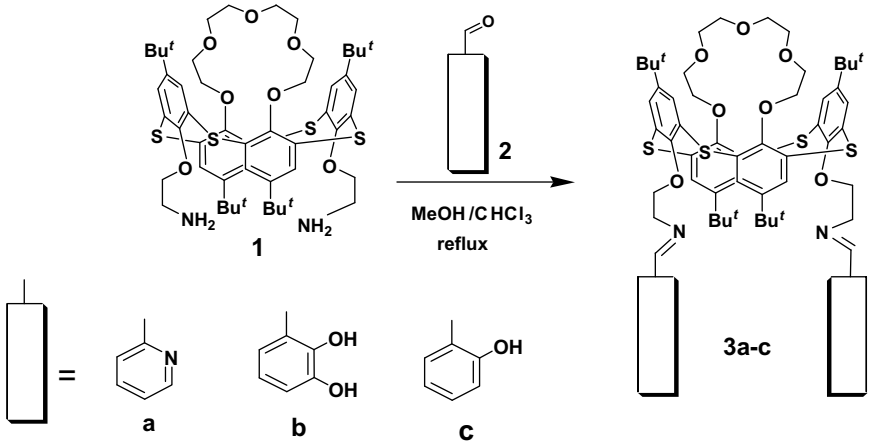


Figure 2. ^1H NMR spectra of **3a** in $CDCl_3/CD_3CN$ (8:2). (A) Free ligand; (B) in presence of 1.0 equiv of silver perchlorate; (C) in presence of 1.0 equiv of potassium perchlorate; (D) addition of 1.0 equiv of silver perchlorate to ligand/potassium complex. NMR frequency is 300 MHz.



Scheme 1.

fraction, indicating the formation of 1:1 complex (see Supplementary data S2). The possible *'switch on-switch off'* of the recognition behavior of **3a** was studied by a set of ^{1}H NMR experiments. On adding 1.0 equiv of Ag^+ ions to **3a**–K^+ complex, ^{1}H NMR spectrum of compound completely changed to that of to **3**–Ag^+ complex (Fig. 2D) When K^+ ions were added to **3**–Ag^+ complex no spectral changes were observed, which indicate that the complexation of **3a** with Ag^+ ion suppresses the recognition of K^+ ion in crown moiety. Thus, the formations of Ag^+ complex *'switch off'* the recognition ability of crown ether ring.

In receptor **3b**, the pyridine unit of **3a** was replaced by catechol moiety. UV–vis spectroscopy was used to evaluate the binding behavior of **3b** toward different metal ions. Receptor **3b** shows an absorption band at λ=267 nm in THF/H_2O (9.5:0.5). On addition of Pb^{2+} ions (1.0– 15.0 equiv), two new bands were formed at 320 nm and 450 nm with an isosbestic point at 345 nm (Fig. 3). The modulation in the electron-donating capabilities of the nitrogen atom of imine nitrogen in the presence and in the absence of Pb^{2+} ions directly influences the intramolecular charge transfer (ICT) from imine nitrogen to catechol moiety. Pb^{2+} ions bind with the imino nitrogens and phenolic oxygen with simultaneous deprotonation of phenolic OH, which reduces extent of ICT from nitrogen to catechol moiety. Kim et al. had reported similar binding of Pb^{2+} ions with nitrogen and oxygen of phenol with simultaneous deprotonation of phenolic OH.[18] Under the same conditions as used for the Pb^{2+} ions, we also tested the UV–vis response of receptor **3b** toward various metal ions (Cu^{2+}, Hg^{2+}, Zn^{2+}, Cd^{2+}, Ni^{2+}, Ag^+, K^+, Na^+, and Li^+), no significant variation was observed with any other metal ion (see Supplementary data S3). Thus, **3b** is selective for Pb^{2+} ions.

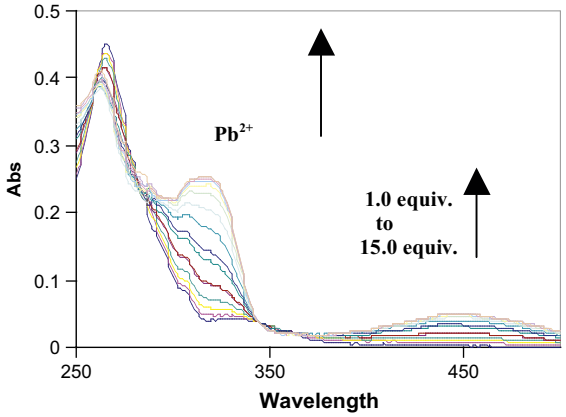


Figure 3. UV–vis spectrum of **3b** (1×10^{-5} M) in the presence of Pb^{2+} ions (1.0–15.0 equiv) in THF/H_2O (9.5:0.5, v/v) buffered with HEPES, pH=7.0.

In the fluorescence spectrum, receptor **3b** exhibits an emission band at 330 nm in THF/H_2O (9.5:0.5, v/v). Upon addition of Pb^{2+} ions (500 μM) quenching in the emission band was observed (Fig. 4), whereas in the presence of K^+ ions an enhancement of the emission band was observed (see Supplementary data S5). The quenching with Pb^{2+} ions can be attributed to the reverse photo induced electron transfer process (PET)[19] and the enhancement with K^+ ions can be ascribed to the fact that the K^+ ions binds to the polyether chain and as a result of which the photo induced electron transfer to the photo excited catechol moiety is suppressed. Earlier, we[12] and Kim et al. have reported similar fluorescence enhancement in the presence of K^+ ions where the K^+ ions bound to crown ether ring of calixarene of 1,3 alternate conformation bearing pyrene moieties.[19] The binding of Pb^{2+} and K^+ ions was also confirmed by NMR spectroscopy. Imino protons of **3b** show downfield shift of 0.15 ppm on addition of 1.0 equiv of Pb^{2+} ions, which indicates the formation of **3b**·Pb^{2+} complex (Fig. 5B). Protons of crown ring show

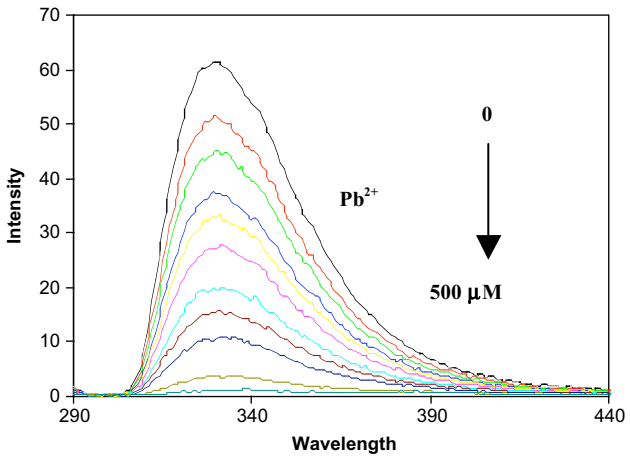


Figure 4. Fluorescence response of **3b** (10 μM) on addition of Pb^{2+} ions (500 μM) in THF/H_2O (9.5:0.5,v/v) buffered with HEPES, pH=7.0; λ_{ex}=267 nm.

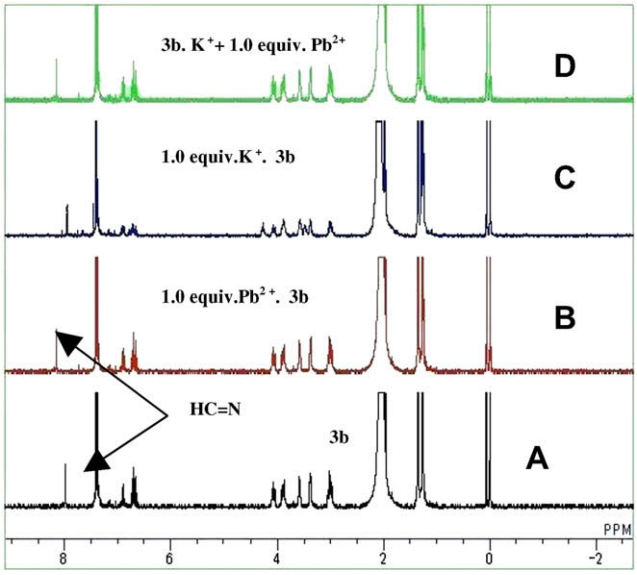


Figure 5. ^{1}H NMR spectra of **3b** in $CDCl_3/CD_3CN$ (8:2). (A) Free ligand; (B) in presence of 1.0 equiv of lead perchlorate; (C) in presence of 1.0 equiv of potassium perchlorate; (D) addition of 1.0 equiv of lead perchlorate to ligand/potassium complex. NMR frequency is 300 MHz.

similar change in the chemical shift as was observed in case of **3a** in presence of K^+ ions (Fig. 5C). Fitting the changes in the fluorescence spectrum of compound **3b** with Pb^{2+} and K^+ ions using the non-linear regression analysis program SPECFIT[20] gave a good fit and demonstrated that 1:1 stoichiometry (host/guest) was the most stable species in the solution with a binding constant log β_1=3.52 and log β_1=2.22 for Pb^{2+} and K^+ ions, respectively (for SPECFIT data of **3b**·Pb^{2+} complex see Supplementary data S15). The method of continuous variation (Job's plot)[17] was also used to prove the 1:1 stoichiometry (host/guest) (see Supplementary data S4). To test the practical applicability of compound **3b** as a Pb^{2+} selective sensor, competitive experiments were carried out using UV–vis spectroscopy in the presence of Pb^{2+} ions at 15.0 equiv mixed with Cu^{2+}, Hg^{2+}, Zn^{2+}, Ni^{2+}, Cd^{2+}, Ag^+, K^+, Na^+, and Li^+ at 15.0 equiv, no significant variation in the absorption was found by comparison with and without the other metal ions. The allosteric behavior was observed between Pb^{2+} and K^+ ions with ^{1}H NMR and fluorescence spectroscopy. On adding 1.0 equiv of Pb^{2+} ions to **3b**–K^+ complex, the ^{1}H NMR spectrum of compound completely changed to that of **3b**–Pb^{2+} complex (Fig. 5D). In contrast, when **3b**–Pb^{2+} complex

was titrated to K^+ ions, no spectral changes were observed. These findings suggest that the complexation of **3b** with Pb^{2+} ion act as a gateway, which regulates the binding of K^+ ion in crown moiety. The allosteric behavior between Pb^{2+} and K^+ ions was also investigated by fluorescence spectroscopy. Thus, addition of Pb^{2+} ions (850 μM vs **3b**) to **3b**·K^+ (1.66 μM) complex results in quenching of fluorescence (Fig. 6). However, no change in fluorescence was observed when K^+ ions were added to **3b**–Pb^{2+} complex Thus, the formations of Pb^{2+} complex '*switch off*' the recognition ability of crown ether ring.

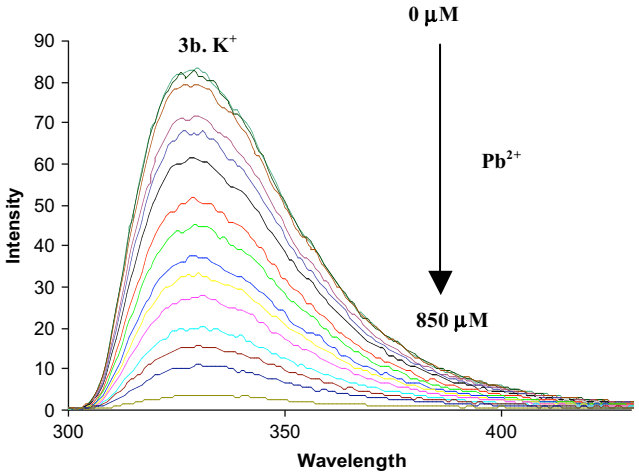


Figure 6. Fluorescence response of **3b**·K^+ (1.66 μM) in presence of Pb^{2+}(850 μM) ions in THF/H_2O (9.5:0.5, v/v) buffered with HEPES, pH=7.0; λ_{ex}=267 nm.

Receptor **3c**, which has a phenolic moiety was found to have preference for Cu^{2+} ions. In the UV spectrum receptor **3c** shows an absorption band at λ=264 nm in THF/H_2O (9.5:0.5, v/v). On addition of Cu^{2+} ions (1.0–10.0 equiv), new band was formed at 367 nm with an isosbestic point at 333 nm (Fig. 7), which can be attributed to the deprotonation of hydroxyl group with simultaneous complexation of Cu^{2+} ions.[21] Under the same conditions as used above for the Cu^{2+} ions, we also tested the UV–vis response of receptor **3c** toward various metal ions (Pb^{2+} Hg^{2+}, Zn^{2+}, Cd^{2+}, Ni^{2+}, Ag^+, K^+, Na^+, and Li^+), no significant variation was observed with any other metal ion (see Supplementary data S6). To test the practical applicability of compound **3c** as a Cu^{2+} selective sensor, competitive experiments were carried out using UV–vis spectroscopy in the presence of Cu^{2+} ions at 10.0 equiv mixed with Pb^{2+}, Hg^{2+}, Zn^{2+}, Ni^+, Cd^{2+}, Ag^+, K^+, Na^+, and Li^+ at 10.0 equiv, no significant variation in the absorption was found by comparison with and without the other metal ions.

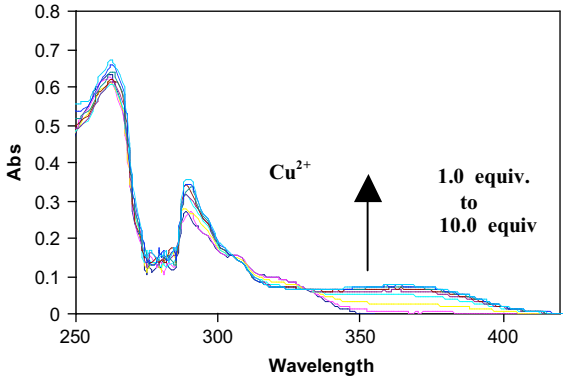


Figure 7. UV–vis spectrum of **3c** (1×10^{-5} M) in the presence of Cu^{2+} ions (1.0–10.0 equiv) in THF/H_2O (9.5:0. 5, v/v) buffered with HEPES, pH=7.0.

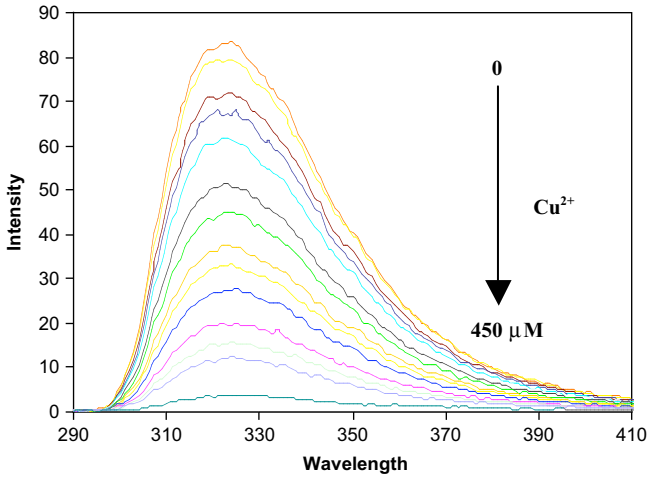


Figure 8. Fluorescence response of **3c** (10 μM) in response to addition of Cu^{2+} ions (450 μM) in THF/H_2O (9.5:0.5,v/v) buffered with HEPES, pH=7.0; λ_{ex}=264 nm.

The fluorescence spectrum of **3c** (10 μM) gave an emission band at 322 nm in THF/H_2O (9.5:0.5, v/v). The addition of Cu^{2+} ions (450 μM) to the solution of **3c** quenches the fluorescence emission (Fig. 8), while on adding K^+ ions, enhancement in the emission spectrum was observed (see Supplementary data S7). Binding constant (log β_1) of **3c** with Cu^{2+} and K^+ ions was found to be 4.18 and 2.44, respectively, using nonlinear regression analysis program SPECFIT,[20] which gave a good fit for 1:1 species. Job's plot also proved 1:1 stoichiometry (host/guest) (see Supplementary data S8). Fluorescence spectroscopy was used to observe switching behavior of receptor **3c**. When Cu^{2+} ions (640 μM vs **3c**) were gradually added to the solution of **3c**·K^+ (2.75 μM) complex fluorescence was quenched by the Cu^{2+} ions (Fig. 9) showing that the Cu^{2+} moves in and the K^+ moves out from **3c**. In the reverse of this metal ion exchange process, when K^+ ions were added to solution of **3c**·Cu^{2+} complex, no change in emission spectrum was observed. Thus, the formation of **3c**·Cu^{2+} complex, triggers the decomplexation of K^+ ion and '*switch off*' the recognition ability of crown ether ring. Thus, in all the three receptors **3a–c** formation of soft metal ion (Ag^+/Pb^{2+}/Cu^{2+}) complex inhibits the binding of receptor with K^+ ions. The binding constant data reveals that in all the three cases binding of receptors through imine units with soft metal ion (Ag^+/Pb^{2+}/Cu^{2+}) is stronger than binding with K^+ ion in crown ether ring. When soft metal ion (Ag^+/Pb^{2+}/Cu^{2+}) is added to the **3a**·K^+/**3b**·K^+/**3c**·K^+ complex, respectively, imine units having

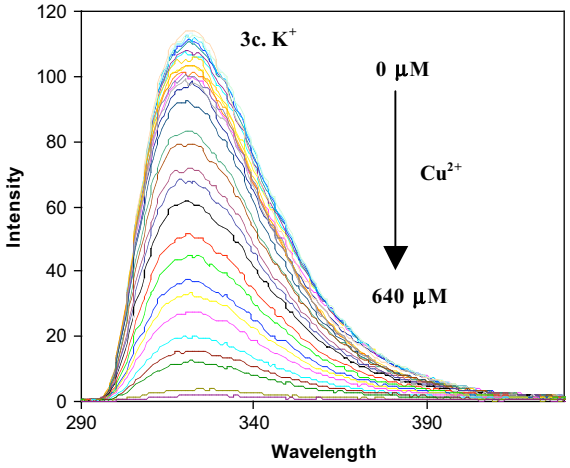


Figure 9. Fluorescence response of **3c**·K+ (2.75 μM) in presence of Cu^{2+} ions (640 μM) in THF/H_2O (9.5:0.5, v/v) buffered with HEPES, pH=7.0; λ_{ex}=264 nm.

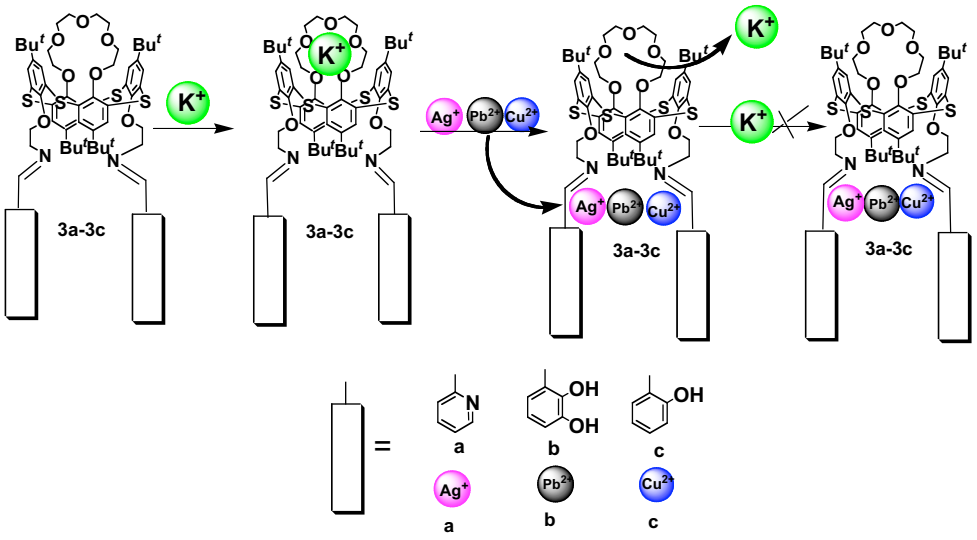


Figure 10. Schematic scheme representing allosteric behavior between metal ions.

stronger affinity for soft metal ion forms complex with simultaneous decomplexation of K^+ ion due to the conformational changes induced during formation of **3a**·Ag^+/**3b**·Pb^{2+}/**3c**·Cu^{2+} complex. When K^+ ions were added to **3a**·Ag^+/**3b**·Pb^{2+}/**3c**·Cu^{2+} complex, no change was observed, due to weak binding of K^+ ion with receptor it is unable to decomplex soft metal ion (Ag^+/ Pb^{2+} / Cu^{2+}). The behavior can be summarized in schematic representation (Fig. 10).

3. Conclusion

To conclude, three new ditopic receptors based on thiacalix[4]arene of 1,3 *alternate* conformation have been designed and synthesized possessing two complexation sites. The complexations of the receptors with soft metal ion '*switch off*' the recognition ability of hard metal ion binding site. Thus, the binding of soft metal ion acts as a gate, which regulates the binding of hard metal ion. Such type of gate systems utilizing the co-ordination of metal ions provides an insight to regulate molecular systems by external effector. The regulatory process in living systems is complicated since conformational changes induced by an allosteric effector binding to one subunit can be transmitted to the other subunits. Allosteric modulation of activity is fundamental for cellular function and is a common feature of biological receptors and enzymes, in particular those involved in metabolic pathways. Moreover, this type of work has been inspired in part by role played by metal ions in the transduction of nerve signals. Thus, designing more synthetic receptors to mimic biological systems will help in understanding biological processes in more simplified way.

4. Experimental

4.1. General

All reagents were purchased from Aldrich and were used without further purification before use. UV Spectra were recorded on SHIMADZU UV-2450 spectrophotometer, with a quartz cuvette (path length: 1 cm). All the fluorescence spectra were recorded on SHIMADZU RF 5301 PC spectrofluorometer. Binding studies were performed in THF AR grade and deionized distilled water was used to prepare THF/H_2O mixture. ^1H and ^{13}C NMR spectra were recorded on JEOL-FT NMR-AL 300 MHz spectrophotometer using $CDCl_3$ and CD_3CN as solvent and TMS as internal standards. Data are reported as follows: chemical shifts in parts per million (δ), multiplicity (s=singlet, d=doublet, br s=broad singlet, m=multiplet), coupling constants (Hz), integration, and interpretation. Silica Gel 60 (60–120 mesh) was used for column chromatography.

4.2. General procedure for synthesis of 3a–3c

To a solution of thiacalix[4]crown diamine **1** (0.10 g, 0.10 mmol) in 1:1 mixture of chloroform and methanol (20 ml) was added a solution of aldehyde **2a–c** (0.21 mmol) in methanol (5 ml). The mixtures were refluxed for 24 h to separate a solid, which was filtered, washed, and recrystallized from $CHCl_3$/MeOH (1:9) to obtain compounds **3a–3c**.

*4.2.1. Compound **3a***

Yield 85% (0.10 g); mp 252 °C; ν_{max} (KBr pellet) 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ=1.28 [s, 18H, $C(CH_3)_3$], 1.36 [s, 18H, $C(CH_3)_3$], 3.0–3.13 [m, 8H, (OCH_2, NCH_2)], 3.39 [br s, 4H, OCH_2], 3.60 [br s, 4H, OCH_2], 3.96 [t, J=7.95, 4H, OCH_2], 4.12 [t, J=8.25, 4H, OCH_2], 7.27–7.31 [m, 2H, ArH], 7.36 [s, 4H, ArH], 7.43 [s, 4H, ArH], 7.71 [t, J=7.35, 2H, ArH], 7.91 [d, J=7.8, 2H, ArH], 8.60 [d, J=4.2, 2H, ArH], 8.24 [s, 2H, HC=N]; ^{13}C NMR ($CDCl_3$, 75 MHz): δ=31.42 [CH_3], 31.47 [CH_3], 34.35 [C], 34.40 [C], 58.39 [NCH_2], 65.61 [OCH_2], 66.68 [OCH_2], 70.26 [OCH_2], 73.48 [OCH_2], 103.16 [ArC], 121.15 [ArC], 124.60 [ArC], 126.14 [ArC], 127.40 [ArC], 127.67 [ArC], 127.99 [ArC], 136.38 [ArC], 146.34 [ArC], 146.41 [ArC], 149.26 [ArC], 154.54 [ArC], 155.55 [ArC], 156.50 [ArC=N], 162.63[ArC]; FABMS *m/z* 1143 ($M+H^+$). Anal. Calcd for $C_{64}H_{78}N_4O_7S_4$: C, 67.25%; H, 6.83%; N, 4.90%. Found: C, 67.20%; H, 6.35%; N, 4.87%.

*4.2.2. Compound **3b***

Yield 80% (0.10 g); mp 245 °C; ν_{max} (KBr pellet) 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ=1.27 [s, 18H, $C(CH_3)_3$], 1.36 [s, 18H, $C(CH_3)_3$], 2.98–3.04 [m, 8H, (OCH_2, NCH_2)], 3.39 [br s, 4H, OCH_2], 3.60 [br s, 4H, OCH_2], 3.94 [t, J=8.1, 4H, OCH_2], 4.08 [t, J=7.95, 4H, OCH_2], 6.69–6.71 [m, 4H, ArH], 6.95 [t, J=4.65, 2H, ArH], 7.37 [s, 4H, ArH], 7.40 [s, 4H, ArH], 8.12 [s, 2H, HC=N]; ^{13}C NMR ($CDCl_3$, 75 MHz): 31.12 [CH_3], 31.47 [CH_3], 34.25 [C], 34.33 [C], 56.98 [NCH_2], 65.57 [OCH_2], 70.39 [OCH_2], 71.50 [OCH_2], 73.52 [OCH_2], 115.25 [ArC], 117.15 [ArC], 118.50 [ArC], 127.75 [ArC], 128.13 [ArC], 128.33 [ArC], 145.89 [ArC], 146.24 [ArC], 155.74 [ArC], 157.41 [ArC=N], 164.70 [ArC], 167.65 [ArC]; FABMS *m/z* 1205 ($M+H^+$). Anal. Calcd for $C_{66}H_{80}N_2O_{11}S_4$: C, 65.78%; H, 6.64%; N, 2.33%. Found: C, 65.73%; H, 6.35%; N, 2.09%.

4.2.3. Compound ***3c***

Yield 82% (0.10 g); mp 247 °C; ν_{max} (KBr pellet) 1635 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ=1.28 [s, 18H, $C(CH_3)_3$], 1.36 [s, 18H, $C(CH_3)_3$], 2.99–3.03 [m, 8H, (OCH_2, NCH_2)], 3.38 [br s, 4H, OCH_2], 3.59 [br s, 4H, OCH_2], 3.95 [t, J=8.25, 4H, OCH_2], 4.08 [t, J=8.1, 4H, OCH_2], 6.82–6.95 [m, 4H, ArH], 7.12–7.15 [m, 2H, ArH], 7.29–7.32 [m, 2H, ArH], 7.36 [s, 4H, ArH], 7.40 [s, 4H, ArH], 8.19 [s, 2H, HC=N]; ^{13}C NMR ($CDCl_3$, 75 MHz): δ=31.43[CH_3], 31.47 [CH_3], 34.37 [C], 55.97 [NCH_2], 66.36 [OCH_2], 70.13 [OCH_2], 71.41 [OCH_2], 73.54 [OCH_2], 116.73 [ArC], 117.17 [ArC], 118.10 [ArC], 121.88 [ArC], 126.36 [ArC], 126.88 [ArC], 127.69 [ArC], 127.94 [ArC], 145.39 [ArC], 146.91 [ArC], 151.12 [ArC=N], 165.65 [ArC]; FABMS m/z 1173 ($M+H^+$). Anal. Calcd for $C_{66}H_{80}N_2O_9S_4$: C, 67.58%; H, 6.83%; N, 2.39%. Found: C, 67.33%; H, 6.55%; N, 2.29%.

4.3. UV–vis and fluorescence titrations

UV–vis and fluorescence titrations were performed on 1×10^{-5} M solution of ligands in THF/H_2O (9.5:0.5, v/v) buffered with *N*-2-hydroxyethylpiperazine-*N*′-2-ethane sulphonic acid (HEPES) buffer. Typically, aliquots of freshly prepared $M(ClO_4)_2$ (M=Cu^{2+}, Hg^{2+}, Pb^{2+}, Zn^{2+}, Ni^{2+}, Cd^{2+}, Ag^+, K^+, Na^+, Li^+) standard solutions (10^{-1} to 10^{-3} M in THF/H_2O (9.5:0.5, v/v)) buffered with *N*-2-hydroxyethylpiperazine-*N*′-2-ethane sulphonic acid (HEPES) buffer were added and UV and fluorescence spectra of the samples were recorded.

4.4. ^1H NMR experiments

Stock solutions (10 mM) of receptors **2a** and **2b** were prepared in $CDCl_3/CD_3CN$ (8:2). Similarly, stock solutions (20 mM) of cations (K^+, Ag^+, Pb^{2+}) perchlorate salts were prepared in $CDCl_3/CD_3CN$ (8:2) for ^1H NMR experiments.

4.5. Extraction measurements

For the extraction experiments, metal picrate solutions (0.1 mM) were prepared in deionized distilled water. The solutions of receptor **2a** (0.1 mM) were prepared in chloroform (AR grade). An aqueous solution (2 mL) of metal picrate (0.1 mM) and a chloroform solution (2 mL) of the **2a** (0.1 mM) were shaken in a glass tube closed with a stopper for 10 min and kept at 27 °C±1 °C for 5 h. An aliquot of the chloroform layer (1 mL) was withdrawn with a syringe and diluted with acetonitrile to 10 mL. The UV absorptions were measured against $CHCl_3/CH_3CN$ (1:9) solution at 374 nm. Extraction of the metal picrate was calculated as the percentage of the metal picrate extracted in the chloroform layer and the values reported here are the mean of the three independent measurements, which were within ±2% error.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.07.014.

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