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New chromogenic bis(isatin hydrazonyl)calix[4]arenes for dual recognition of fluoride and silver ions

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ABSTRACT

New calixarene based dual chromogenic receptors bearing isatin hydrazone units have been synthesized and evaluated for their ion recognition potential. The synthesized molecular receptors can effectively and selectively recognize fluoride and silver ions through visible color changes and pronounced bathochromic shifts in their UV–visible spectra. NMR titration data further support the preliminary conclusions.

The design and synthesis of ditopic receptors for selective binding of both cationic and anionic species have become exciting domains of supramolecular chemistry.[1,2] Macrocyclic compounds such as calixarenes have been employed extensively for this purpose by various workers.[3] These versatile ditopic receptors may possess the cation and anion binding sites on the opposite rims[4] of calixarene structure or together on one[5,6] side of the calixarene scaffold. At the same time, chromogenic receptors that can undergo a vivid color change upon guest interaction are preferred and constitute an emanating territory of interest.[7–9] Indeed, colorimetric sensor molecules based on the formation of hydrogen bonding or anion promoted deprotonation of the binding moiety have been shown to be very efficient and highly sensitive.[10–12]

Amongst the range of commonly occurring anions, fluoride is of special interest due to its proven role in prevention of dental caries[13,14] and treatment of osteoporosis.[15] On the other hand, amongst important metal ions, silver ion has attracted considerable attention[16] during last few years due to its widespread applications in the organic synthesis, electronics, photography, and imaging industry. However, unlike other transition metal ions there are not many reports on silver ion receptors, probably due to the fact that silver ion does not show a pronounced coordination ability. This in turn makes discrimination of silver from other chemically related cations more difficult.

In this Letter we report the synthesis and evaluation of two new ditopic calix[4]arene based molecular receptors (**6**–**7**) bearing isatin hydrazone units in their molecular scaffold for dual colorimetric recognition of Ag^+ and F^-. The synthesis of bis(isatin hydrazonyl)calix[4]arenes involved the formation of a schiff base between calixarene derivative **5** and isatin hydrazones **2a** and **2b**. The choice of isatin hydrazone as chromogenic sensing molecule was driven by the fact that as an indole derivative, isatin could not only serve as an anion sensor based on H-bonding or deprotonation mechanism but it could be linked to the calixarene framework to result in an extended conjugated system to function as a color reporting group. Strong coordination ability of schiff base moiety in the designed receptors further augments the plausibility of their use in metal ion recognition. To the best of our knowledge this is the first report on an isatin functionalized calixarene based molecular receptor for target applications. The designed receptors feature cation binding sites (in the form of hydrazone nitrogens and amide oxygens) and anion binding sites (in the form of amide N**H** and phenolic O**H** groups) which facilitate the dual ionic recognition.

Isatin hydrazones **2a** and **2b** were synthesized by reaction of corresponding isatin with hydrazine hydrate in ethanol. The synthesis of receptors **6** and **7** is outlined in Scheme 1. N-alkylation of isatin was carried out by reaction of isatin with propyl bromide and potassium carbonate in DMF. The structures of compounds **6** and **7** were confirmed from their spectroscopic[17,18] and analytical data. The ^{1}H NMR spectrum of **6** showed two doublets (4H each) for calixarene methylene bridge protons, two singlets (4H each) corresponding to calixarene aryl ring protons, two doublets (2H each) and two triplets (2H each) corresponding to isatin aryl ring

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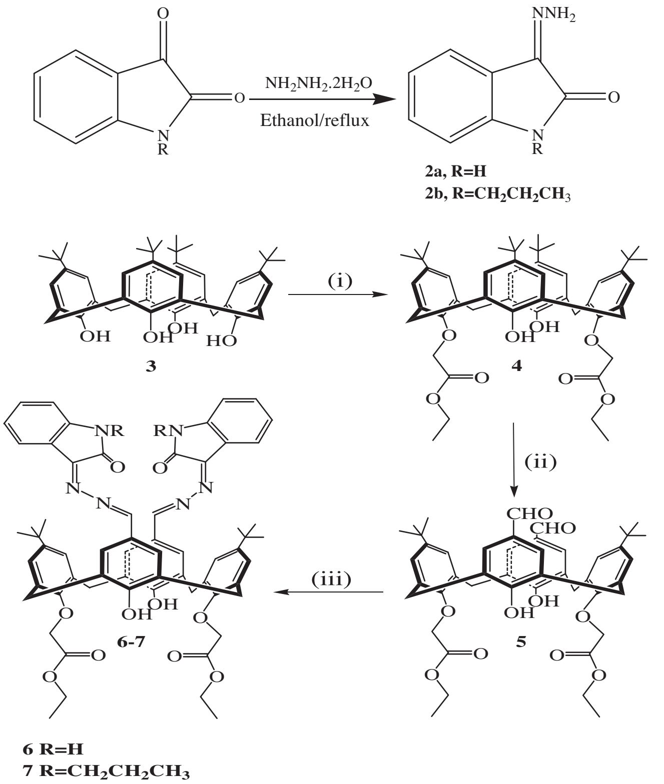

Scheme 1. Synthesis of **6** and **7**. Reagents and conditions: (i) ethyl bromoacetate, K$_2$CO$_3$, CH$_3$CN, reflux; (ii) hexamethylenetetramine, trifluoroacetic acid, reflux; (iii) isatin hydrazone, ethanol, reflux.

protons, and two singlets (2H each) corresponding to isatin NH and calixarene OH, while **7** showed all these peaks except for the peak of isatin NH. This was further confirmed by HRMS analysis which showed peaks at 1073.4369 and 1157.5328 corresponding to **6** and **7**, respectively. Additionally, distinct signals at 30.7 and 31.1 for **6** and **7**, respectively in ^{13}C NMR spectra confirm symmetric cone conformation for **6** and **7**.

In order to get an insight into the spectroscopic behavior of designed receptors toward cations and anions, UV–visible and ^{1}H NMR titrations were performed.

In the absence of external analytes, UV–vis spectrum of **6** and **7** in THF could be characterized by absorption peaks at 373 and 369 nm, respectively, which could be attributed to intramolecular charge transfer band. The cation binding and sensing ability of receptor **6** was investigated in detail by following its absorption spectral changes upon addition of various metal perchlorates. Figure S3 (Supplementary data) represents the UV–vis absorption changes upon addition of different transition metal ions (Mn^{2+}, Co^{2+}, Cu^{2+}, Fe^{2+}, Ni^{2+}, Hg^{2+}, Ag^{+}, Cd^{2+}, and Zn^{2+}) to the THF solution of receptor **6** (30 μM). It was found that the UV–vis spectrum of **6** exhibited a considerable red shift ($\Delta\lambda_{max}$ 37 nm) only in the presence of silver ions while other tested cations did not produce any substantial change in the absorption spectrum. Figure S4 (Supplementary data) shows a comparative view when different metal ions were added in 1.5 equiv amount to the THF solution of **6**.

Upon successive addition of silver ion to the solution of receptor **6**, the absorption band at 373 nm decreased while a new peak gradually moving toward longer wavelength and finally reaching a maximum value at 410 nm appeared. Figure 1 exhibits the UV–vis spectral changes for receptor **6** (30 μM) on gradual addition of silver from 0 to 1.5 mol equiv. This change in absorption spectra was accompanied by a visible color change from pale yellow to dark yellow while no other cation gave colorimetric response. Moreover, the absorbance at 410 nm got saturated in the presence of 1 equiv of silver ions, suggesting the formation of a 1:1 complex between **6** and silver ion, which is in good agreement with 1:1 stoichiometry for the silver complex, as confirmed by the Job's plot analysis (Supplementary data, Fig. S9). The corresponding binding constant on the basis of Benesi–Hildebrand plot[19] was calculated to be 8.4×10^3 M^{-1} (Supplementary data, Fig. S5).

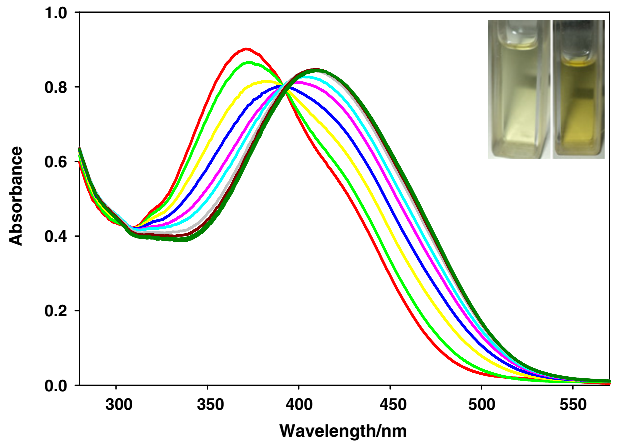

Figure 1. Variation in absorption spectrum of **6** (30 μM) upon titration with Ag$^+$ (0–1.5 equiv). Inset: the color change of **6** upon silver addition.

In order to understand the binding mode of **6** with Ag$^+$ ion, ^{1}H NMR titrations were performed in DMSO-d_6. Upon addition of 1 equiv of silver to the receptor solution (0.01 M), the chemical shift of amide protons exhibited a downfield shift by $\Delta\delta$ 0.23 ppm from δ 10.795 ppm (Fig. 3). Similarly azo-methine protons (**H**C=N) showed a downfield shift by $\Delta\delta$ 0.18 ppm. These spectral changes suggest that silver ion could be bound by hydrazonyl nitrogens and amide oxygens of **6**.

To ascertain the practical applicability of **6** as a silver selective sensor, competitive experiments were carried out in THF, where in absorption spectra of transition metal ion/silver ion coexisted systems were examined. No significant change in the absorption value was seen even when other metal ions (1 equiv) were present along with silver ion in the receptor solution (Fig. 2). Based on the UV titrations and colorimetric response shown by sensor **6** with Ag$^+$, it could be inferred that **6** shows a pronounced selectivity for Ag$^+$ ion over other transition metal cations being tested.

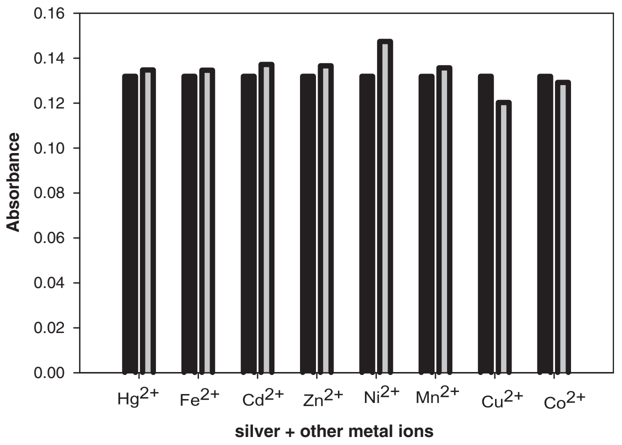

Figure 2. Competitive selectivity and sensitivity of **6** for Ag$^+$ in preference to other related metal ions. Black bar represents the absorbance of **6** in the presence of Ag$^+$ alone. Gray bar denotes absorbance of Ag$^+$/M^{n+} coexisting systems.