Indian Journal of Chemistry
Vol. 46A, July 2007, pp. 1095-1100

Fluorescence and absorption studies on the selective recognition of iodide by lower rim 1,3-bis(aminoethoxy)-*p*-*t*-butyl-calix[4]arene derivative

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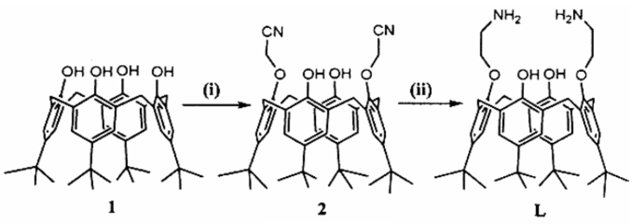
Received 25 January 2007; revised 4 June 2007

Lower rim 1,3-bis(aminoethoxy)-*p*-*t*-butyl-calix[4]arene derivative (**L**) has been subjected to fluorescence and absorption studies to evaluate its utility to recognize halides. This derivative has been found to be selective towards iodide, immaterial of its counter cation as well as the presence of other halide ions. Combining this data with that of the negative ion mass spectrometry and ^{1}H NMR spectra, an arene cavity bound iodide species is proposed.

Molecular systems pertinent to the anion recognition are of great importance presently because of their sensitivity and specificity to identify and/or bind anionic species. The anion sensors are different from the cation ones owing to their variations in size, shape and geometry when compared to the usual spherical shape of cations. Further, the anions interact with the host mostly through hydrogen bonds and/or through electrostatic interactions while the cations interact through coordination and/or ion-dipole type. Since the size of the anions are usually larger than that of the cations, host molecules of appropriate cavity diameter are necessary for anion recognition. There are several reports in literature that discuss anion sensing by pyrrole based[1], guanidinuium based[2], ammonium based[3], amide based[4], coumarine based[5] and metal ion/complex based[6] systems, while some of these are calixarene based ones. A large number of calix[4]arene derivatives were shown to be good receptors towards variety of cations. However, reports on their anion recognition were rather limited in the literature. The anion sensors also find applications in biology, medicine, catalysis and environment[7]. Therefore, molecular recognition systems for halide species are of great concern and among these the iodide sensing is important owing to its involvement in the thyroid related problems.

We report here the ability of a simple calix[4]arene based molecule, viz. lower rim 1,3-bis(aminoethoxy)-*p*-*t*-butyl-calix[4]arene derivative (**L**) towards recognizing iodide among the four halides. In order to study the interaction between **L** and halides, emission and absorption spectral methods were employed. It was the intrinsic fluorescence of the arene moieties of the derivative that was monitored during the emission studies. **L** was synthesized in two well known steps[8] starting from *p*-*t*-butyl-calix[4]arene as shown in Scheme 1 and the compound **L** gave satisfactory analytical and spectral results.



Scheme 1

Synthesis of **L** involves: (I) **1** (10.0 g, 15.4 mmol), K_2CO_3 (8.52 g, 61.64 mmol), Nal (9.24 g, 61.64 mmol), chloroacetonitrile (4.77 g, 63.18 mmol), 500 mL acetone, reflux under N_2 for 7 h; (ii) **2** (4.70 g, 6.50 mmol), $LiA1H_4$ (2.0 g, 56.93 mmol), 250 mL diethylether, reflux for 5h. involving: (i) **1** (10.0 g, 15.4 mmol), K_2CO_3 (8.52 g, 61.64 mmol), NaI (9.24 g, 61.64 mmol), chloroacetonitrile (4.77 g, 63.18 mmol), 500 mL acetone, reflux under N_2 for 7 h; (ii) **2** (4.70 g, 6.50 mmol), $LiAlH_4$ (2.0 g, 56.93 mmol), 250 mL diethylether, reflux for 5 h.

Materials and Methods

Synthesis and characterization of L

To a vigorously stirred solution of **2** (4.70 g, 6.50 mmol) in 250 mL diethylether, $LiAlH_4$ (2.00 g, 56.93

mmol) was added and the reaction mixture was refluxed for 5 h. After that, the reaction flask was immersed into an ice-water bath and excess $LiAlH_4$ was destroyed by the addition of wet benzene into the reaction mixture. The clear organic layer was decanted and the inorganic salts were rinsed with benzene. The combined organic layers were evaporated to dryness to yield diamine, as a light yellow solid. Yield 85%. ^{1}H NMR: ($CDCl_3$, δ ppm, 400 MHz): 7.03 (s, 4H, Ar-*H*), 6.99 (s, 4H, Ar-*H*), 4.33 (d, *J* = 12.82 Hz, 4H, Ar-C*H*$_2$-Ar), 4.07 (t, *J* = 4.76 Hz, 4H, OC*H*$_2$), 3.36 (d, *J* = 12.82 Hz, 4H, Ar-C*H*$_2$-Ar), 3.28 (t, *J* = 4.75, 4H, NC*H*$_2$), 1.25 [s, 18H, C(C*H*$_3$)$_3$], 1.10 [s, 18H, C(C*H*$_3$)$_3$]; *m/z* (ES-MS) 735.26 ($[M+H]^+$, 100%); Anal. (% found) C 78.29, H 8.37, N 3.97, $C_{48}H_{66}N_2O_4$ (% requires) C 78.43, H 9.05, N 3.81; FTIR (KBr, cm^{-1}) 3362 ($\nu_{OH/NH}$). ^{13}C NMR (400 MHz, $CDCl_3$): 31.28, 37.78 [(**C**(CH_3)], 33.98, 34.30 [**C**(CH_3)], 32.32 (Ar-CH_2-Ar), 42.74 (-CH_2-N-), 78.7 (-O-CH_2-), 125.58, 126.01, 127.75, 133.31, 142.21, 147.66, 149.27, 150.42 (aromatic carbons).

Materials used and solutions prepared

Different metal salts, viz. NaX (where X = F, Cl, Br and I), KX (where X = Cl, Br and I), $(C_4H_9)_4NX$ (where X = F, Br and I), $(C_2H_5)_4NX$ (where X = Br and I), $(CH_3)_4NCl$ were purchased from local sources. Analytical grade $CHCl_3$ and CH_3OH were also obtained from local sources and were purified and dried by routine procedures immediately before use. The bulk concentration of **L** in $CHCl_3$ was 1.5 m*M* and the halide salts were initially dissolved in 0.5 mL of water and diluted to 10 mL using CH_3OH to give a concentration of 15 m*M* for the bulk solutions.

Fluorescence spectral measurements

Fluorescence emission spectra were measured on Perkin-Elmer LS55 by exciting the solutions at 240 nm and by recording the emission spectra in 250-400 nm range. All the measurements were made in 1 cm quartz cell maintaining a final **L** concentration at 50 μ*M*. During the titration, the concentration of halide salts was varied accordingly in order to result in requisite mole ratios of halide to **L** and the total volume of the solution was maintained constant at 3 mL in each case by adding appropriate volume of CH_3OH. Normalized emission (relative fluorescence) intensities (I/I_0) were plotted against the mole ratio of metal ion to the **L**. The binding constants of the complexes formed in the solution were quantitatively estimated by plotting $\log[(I-I_0)/(I^* - I)]$ versus log [S] (where, I_0, intensity with no metal ion; I^*, maximum Intensity; I, intensity at different metal ion to **L** mole ratios; and S, concentration of the metal salt added). The slope of the straight line gives the ratio of metal cation versus **L** in the fully saturated case and pK_{ass} for the complex equals to the value of log[S] at $\log[(I-I_0)/(I^* - I)] = 0$.

Absorption spectral measurements

All the solutions used in the fluorescence titration were also subjected to absorption spectral measurements in 200-400 nm range. Appropriate controls were used for subtraction of the absorbance of the salt component used at every measurement in the titration. In the control studies, L is not used but the same concentration of salt is being used. All the absorption spectra were measured on Shimadzu UV 2101 PC in 1 cm quartz cells.

Results and Discussion

The ligand, **L** was studied for its interaction with halides, viz. F^-, Cl^-, Br^- and I^- in MeOH, where the

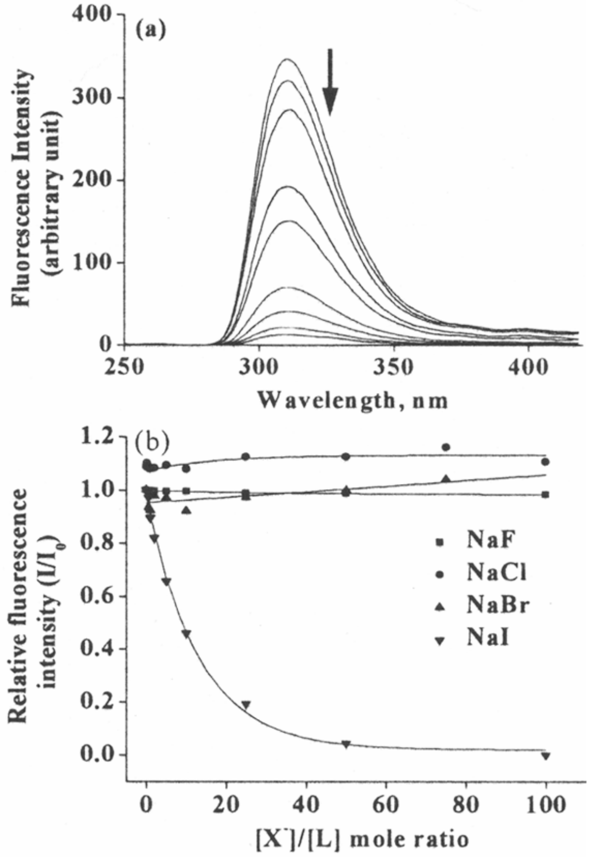


Fig. 1— (a) Spectral traces in the fluorescence titration of **L** with varying mole ratios of NaI; (b) Plot of relative fluorescence intensity (I/I_0) *vs.* $[X^-]/[\mathbf{L}]$ mole ratio for all the four sodium halides, *viz.* NaF, NaCl, NaBr and NaI.

halides were drawn from different salts, and the studies were performed using fluorescence and absorption spectroscopy. A single emission band at 312 nm arising from the π*→π transition of the phenyl core of the calix[4]arene derivative was observed for **L**. The fluorescence intensity of this band was not significantly affected with the addition of sodium salts of fluoride, chloride and bromide even till >100 mole equivalents of the anion. However, the same is quenched by the gradual addition of sodium iodide and approaches saturation around 40 mole equivalents as can be seen from the spectral traces given in Fig. 1a. Relative fluorescence intensity (I/I_0) as a function of [X^-]/[**L**] mole ratio were plotted in Fig. 1b for the titrations of sodium halides. This behaviour is a clear indication of the equilibrium shift reaction between the iodide and **L**. The effect of these ions on the fluorescence of **L** was further confirmed by repeating the titration four times. Fluorescence quench of 2-naphthol by iodide is already shown in literature[9].

In order to check the effect of counter cation on the recognition of iodide by **L**, several other iodide salts, viz., KI, Bu_4NI and Et_4NI were used for the fluorescence titration. The I/I_0 plots from all these titrations exhibited a great overlap immaterial of the counter cation used (Fig. 2). The results clearly suggest that there is no significant influence of the counter cation on the interaction of I^- with **L** and hence **L** is very specific for I^- among halides.

Based on the Benesi-Hildebrand equation, the association constant (K_{ass}) for the binding of I^- with **L** was estimated for different iodide salts. The plots yielded K_{ass} of 2923 M^{-1} (KI); 2700 M^{-1} (n-Bu_4NI); 3162 M^{-1} (Et_4NI); 3700 M^{-1} (NaI), and the slope corresponds to a 1:1 species in all the cases. The presence of 1:1 species was further supported by Job's plot as reported in this paper. However, K_{ass} could not be derived for F^-, Cl^- or Br^- titrations, as there were no significant changes observed in their spectra. Fluorescence titration studies carried out using other halide salts, viz. Bu_4NF, Me_4NCl, KBr, Et_4NBr and Bu_4NBr, did not show any change in the fluorescence intensity.

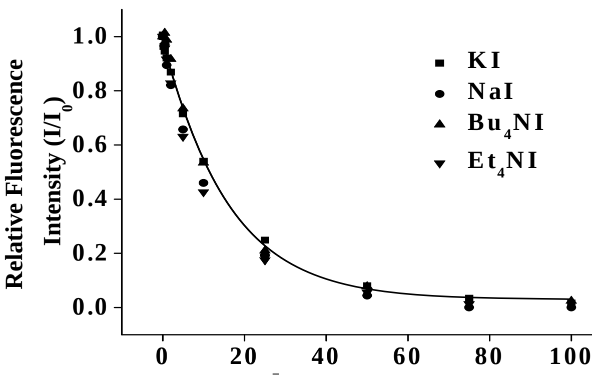


Fig. 2—Plot of relative fluorescence intensity (I/I_0) *vs.* [I^-]/[**L**] mole ratio for iodide salts with different counter cations (The solid line is a fit for the data of the KI, but the same fit suits well for the other cases too).

The absorption spectrum of **L** shows two bands in the UV region, one centered at 280 nm and the other at 222 nm. Since the iodide is expected to absorb in the UV region around 220 nm, special care was taken to subtract the absorbance of the iodide salt present in the solution. During the titration with KI, the absorbance of 222 nm band diminishes as a function of iodide concentration as can be seen from the spectra shown in Fig. 3a. The plot of absorbance versus mole ratio (Fig. 3b) resembles exactly that of the relative fluorescence intensity plot (Fig. 2). The log plot of this band yielded K_{ass} = 3550 ± 100 M^{-1}, a value that is comparable with that obtained from the fluorescence data. The Job's plot (data not shown) indicated the formation of a 1:1 species between **L** and I^-. Absorption titration of **L** with Et_4NI also yielded results similar to that of the KI titration.

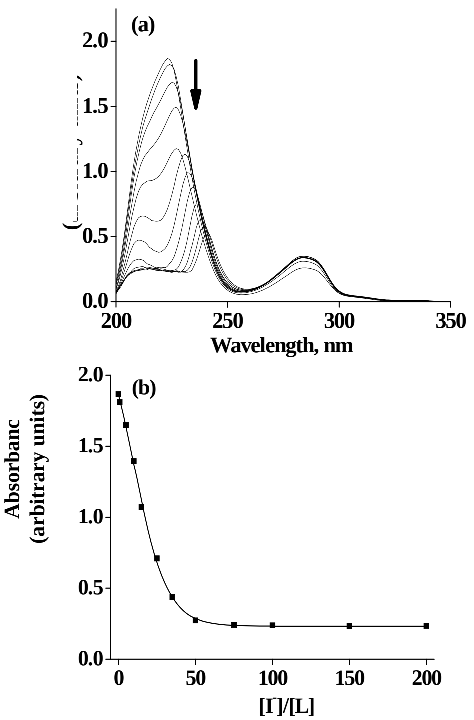


Fig. 3—(a) Absorption titration of L with KI; (b) Plot of absorbance at 222 nm *vs.* [I^-]/[**L**] mole ratio for the titration shown in (a).

However, similar absorption experiments conducted with the salts of F^-, Cl^-, or Br^- showed no change in any of these bands. The absorption spectral results concur with that of the fluorescence results. Thus, based on the fluorescence and absorption studies it is possible to deduce that **L** selectively recognizes iodide among the four halides.

Competition among the halides towards **L** was studied by fluorescence spectra. The pattern observed in the fluorescence titration of **L** with I^- (Figs 1 to 3) continues to be present even when **L** was titrated with I^- in the presence of one or more of other halide salts to an extent of 20 or 50 mole equivalents (Fig. 4).

A reverse experiment comprising the titration of {**L**+50 eq. of I^-} with other halides, viz. F^-, Cl^- and Br^-, was carried out using fluorescence spectroscopy. In fact, the original fluorescence intensity of **L**, viz. 350±25 was quenched dramatically when 50 equivalents of iodide was added to result in a final intensity of 25±5, and no further changes were observed in the fluorescence intensity when this mixture was titrated with NaF, NaCl or NaBr (Fig. 5). Thus, based on both these two kinds of experiments, it is possible to implicate that F^-, Cl^- and Br^- ions do not compete for **L** in the presence of I^- and hence **L** is very specific towards I^- over other halides.

The negative ion electro spray mass spectrum of the reaction mixture of 10 mole equivalents of KI and **L**, shown in Fig. 6, clearly exhibited peaks at *m/z* values of 690.5, 647.5 and 857.8 corresponding to {**L** - $CH_2CH_2NH_2$}, {**L** – 2 × $CH_2CH_2NH_2$} and {**L** - $CH_2CH_2NH_2$ + I^- + K^+} and hence supports the iodide bound species.

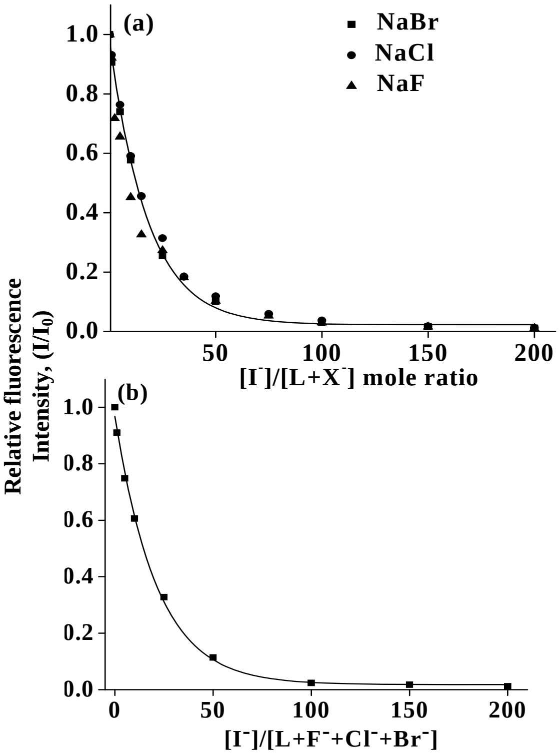


Fig. 4—Fluorescence titration of {**L**+NaX} with NaI: (a) Plot of relative fluorescence intensity (I/I_0) *vs.* $[I^-]/[$**L**+50 eq. of NaX] mole ratio, where X^- = F^-, Cl^- or Br^-. (b) Plot of (I/I_0) *vs.* $[I^-]/[$**L**+15 eq. of each of NaF, NaCl, NaBr] mole ratio.

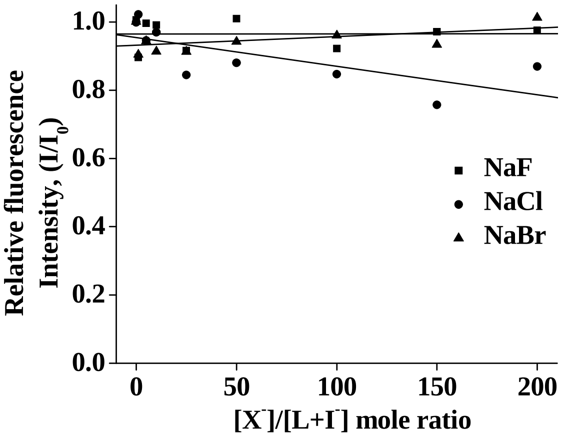


Fig. 5—Plot of relative fluorescence intensity (I/I_0) *vs.* [NaX]/[L+50 eq. of NaI] mole ratio, where X = F, Cl and Br.

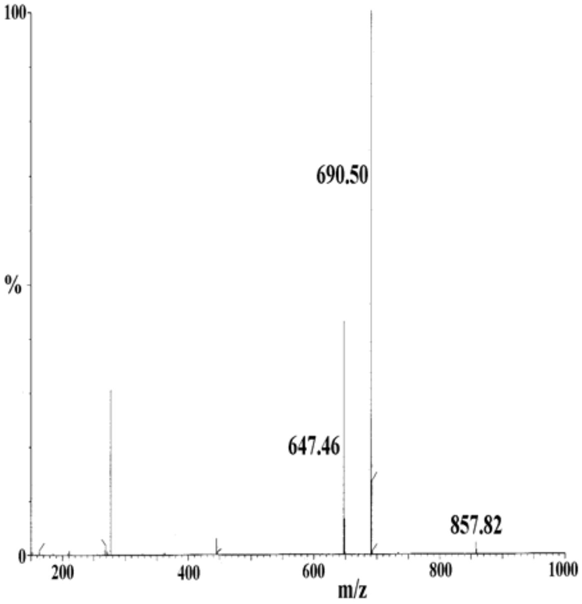


Fig. 6—Negative ion electro spray mass spectrum of the mixture of L and 10 equivalents of KI.

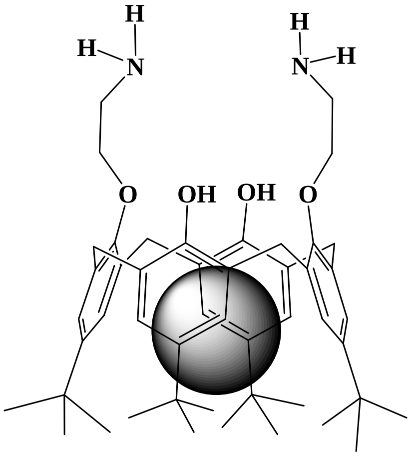


Fig. 7—Proposed species for the interaction of I$^-$ with the arene cavity of L. Grey sphere indicates the iodide ion.

^{1}H NMR spectra were measured in the titration of **L** with KI and NaI at different equivalents. The methylene protons of –O-CH_2-CH_2-NH$_2$ strands result in two triplets, one corresponding to the O-bound and the other corresponding to the N-bound. These chemical shifts show no significant change even in the presence of iodide salt, suggesting that the iodide is not interacting at the lower rim of the calixarene. The aromatic *meta*-protons showed two lines throughout the titration with iodide salt while the peaks were shifted up-field marginally, suggesting a possible interaction of I$^-$ with the arene cavity. The bridged methylene groups of the calixarene moiety exhibited two diastereotopic doublets at all the equivalents of iodide salt indicating that the **L** exhibits cone conformation during the interaction.

The results of fluorescence and absorption studies support each other and **L** recognizes only iodide preferentially among the four halides. The iodide can interact with the ligand **L** at least in two possible ways, viz. one through the hydrophobic arene cavity and the other through the amine moiety present on the lower rim pendants. The reason for the selectivity of **L** towards I$^-$ is attributable to the large hydrophobic cavity present in the derivative and also the flexibility of the pendants attached to the calixarene moiety at the lower rim. Owing to the large size of I$^-$ (ionic radius being ~2.06 Å), it is not possible for the I$^-$ to approach the lower rim in the cone conformation of the ligand, **L**. The low K_{ass} constants clearly indicate that the interactions are rather weak and support strongly the proposed species (Fig. 7) for the binding of iodide. Inclusion of Cl$^-$, I$^-$, BF$_4^-$ or HSO$_4^-$ in arene cavity of calix[4]arene derivatives or their π-metal ion complexes is known[10].

Acknowledgement

C.P.R. acknowledges the financial support from the DST, CSIR and BRNS. R.J. and A.A. acknowledge UGC and CSIR, respectively for their fellowships.

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