



Selective recognition of Cu^{2+} by di-O-picoyl derivative of 1,1'-methylene-bis(2-naphthol)

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ABSTRACT

Di-derivatives of 1,1'-methylene-bis(2-naphthol) (L_1) possessing ester (L_2), carboxylic acid (L_3) or picoyl (L_4) as end groups of the pendants have been synthesized and characterized. Titration of these derivatives for their recognition towards M^{2+} (where $M = \text{Mg, Ca, Mn, Fe, Co, Ni, Cu, Zn}$) were performed by following the fluorescence emission intensities in methanol solution. The picoyl derivative (L_4) has been found to be well suited for Cu^{2+} recognition (≤ 630 ppb) via the formation of 1:1 complex that was further proven based on absorption as well as ESI MS studies. On the other hand, L_1 and L_2 were mainly insensitive towards M^{2+} , whereas the carboxylic derivative (L_3) shows fluorescence changes with almost all the metal ions and hence none of the L_1 , L_2 and L_3 are suited for any M^{2+} recognition. The studies clearly suggested that the chemical nature of the functional groups and the coordination preferences of the metal ion seem to play important role in the selective recognition of the metal ion.

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1. Introduction

Derivatized calix[n]arenes possessing metal ion binding cores are attractive molecular platforms for inorganic chemists in order to sense ions [1–15] and to perform biomimetic studies including their metal ion complexation [16–26]. While calix[4]arene systems are being the main subject of the study for quite some time in the literature, calix[4]naphthalenes are much less explored, probably owing to their structural complexity as well as the existence of isomers [27,28]. It is better to study the system that represents at least one-half of these, viz., hemi-calix[4]arene, with appropriate derivatization, owing to the simplicity as well as their resemblance with the parental calix[4]naphthalene derivatives. The work reported in this paper is an attempt to tune the metal ion recognition properties of the di-O-derivatives of 1,1'-methylene-bis(2-naphthol) (L_1), viz., ester (L_2), carboxylic (L_3) and pyridyl (L_4) resulted in simple molecular systems possessing diverse binding cores, such as, phenolic, carboxylic, ester type and pyridyl type. Therefore, the present study includes the synthesis and characterization of these molecular systems, and establishing their selective recognition towards metal ions.

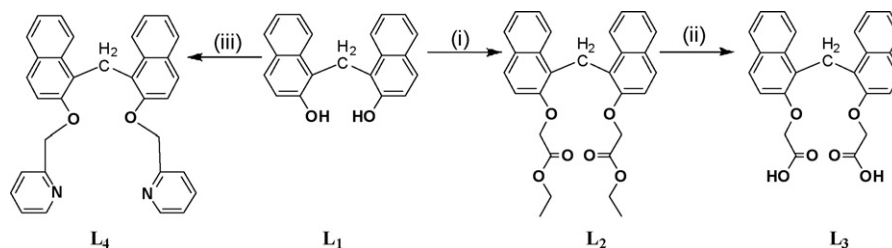
2. Experimental

All the solvents were purified and dried by standard procedures. Fourier transform infrared spectra were recorded on an Impact 400 Nicolet FTIR machine in KBr matrix. C, H and N analysis were performed on a Carlo Erba (Italy) 1106 elemental analyzer. The ^1H and ^{13}C NMR spectra were recorded on a Varian 400S spectrometer in CDCl_3 or DMSO-d_6 . UV–vis spectra were obtained on a Shimadzu UV-260 or UV-2101PC spectrophotometer. The fluorescence emission spectra were recorded on a PerkinElmer LS 55 spectrofluorimeter. ESI MS spectra were measured on Micromass QTOF micro-mass spectrometer.

2.1. Solutions for fluorescence and absorption titrations

A 3.0 mL cuvette solution of ligands containing an effective concentration of 1, 10, 20 and 50 μM were made by taking a fixed volume (150 μL) of solution from their corresponding stock solutions. The stock solution was prepared from a weighed sample of the ligand dissolved in ~ 50 μL of tetrahydrofuran diluted to 5 mL using methanol. Titration of the ligand with different metal ions to give 1–100 mole ratio was achieved at every effective concentration of the ligand by using two working stock solutions, where one of it is the metal ion solution at the same concentration of that of the ligand solution and the other one is where a 10 times concentrated solution of metal ion being used. The final titration solutions were always maintained at 3 mL in the cuvette.

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Scheme 1. (i) 2 equivalents of $\text{BrCH}_2\text{CO}_2\text{C}_2\text{H}_5$, K_2CO_3 , CH_3CN ; (ii) 15% aqueous NaOH , $\text{C}_2\text{H}_5\text{OH}$; (iii) 2 equivalents of 2-(chloromethyl) pyridine, K_2CO_3 , CH_3CN .

All the organic derivatives, viz., L_1 – L_4 were synthesized as given in Scheme 1 and the products were characterized as given in this section.

2.2. 1,1'-Methylene-bis(2-naphthol) (L_1)

This was synthesized as per the reported procedure with some modifications [27,28]. In 250 mL acetic acid, β -naphthol (75 g, 0.52 mol) was dissolved, and 37% formaldehyde (350 mL) was added and the reaction mixture was heated. In about 45 min, the reaction mixture turned to pale pink solid, which was further heated for another 45 min. This was then cooled to room temperature, filtered, washed with water till the un-reacted formaldehyde was removed. The pale pink solid was air dried and recrystallized from $\text{CH}_3\text{CN}/\text{C}_6\text{H}_6$ to give off white crystalline product. Yield: 109.38 g (70%). M.P. 195–200 °C (decomp.). Anal. Calc. for $\text{C}_{21}\text{H}_{16}\text{O}_2$ (300.35): C 83.98, H 5.37; found C 83.95, H 5.87%. FTIR (KBr, cm^{-1}): 3331 (ν_{OH}). ^1H NMR (CDCl_3 , δ ppm): 8.213 (d, 2H, naph-H, $J=8.55$ Hz), 7.769 (d, 2H, naph-H, $J=8.25$ Hz), 7.668 (d, 2H, naph-H, $J=8.86$ Hz), 7.456 (t, 2H, naph-H, $J=8.25$ Hz), 7.336 (t, 2H, naph-H, $J=7.94$ Hz), 7.045 (d, 2H, naph-H, $J=8.86$ Hz), 6.667 (s, 2H, OH), 4.808 (s, 2H, Ar- CH_2 -Ar). ^{13}C NMR (CDCl_3 , δ ppm): 21.91 (Ar- CH_2 -Ar), 118.1, 118.5, 120.6, 123.1, 123.3, 126.9, 128.91, 129.8, 133.5, 151.9 (Nap-C). ESI MS: m/z (%), 281 (100, $\text{M}^+ - 19$), 300 (56, M^+).

2.3. 1,1'-Methylene-bis(2-naphthoxy acetic ester) (L_2)

To 120 mL of CH_3CN taken in a two necked flask fitted with a nitrogen inlet and a reflux condenser, L_1 (2.40 g, 8 mmol), K_2CO_3 (1.216 g, 8.8 mmol) and $\text{BrCH}_2\text{CO}_2\text{Et}$ (1.84 mL, 16.8 mmol) were added and stirred under N_2 . The reaction mixture was refluxed for 16 h, and then cooled to room temperature, filtered and the filtrate was evaporated under vacuum (50–60 °C) to give pale yellow thick mass, which was then dissolved in $\text{CH}_2\text{Cl}_2/\text{C}_2\text{H}_5\text{OH}$ (1:1, v/v) and kept for 1–2 days to obtain white crystalline solid. Yield: 1.74 g (46%). M.P. 90–95 °C. Anal. Calc. for $\text{C}_{29}\text{H}_{28}\text{O}_6$ (472.19): C 73.73, H 5.93; found C 73.95, H 5.87%. FTIR (KBr, cm^{-1}): 1751 ($\nu_{\text{C=O}}$). ^1H NMR (CDCl_3 , δ ppm): 8.249 (d, 2H, Nap-H, $J=8.55$ Hz), 7.699 (t, 4H, Nap-H, $J=9.17$ Hz), 7.368–7.246 (m, 4H, Nap-H), 7.147 (d, 2H, Nap-H, $J=8.86$ Hz), 5.059 (s, 2H, Nap- CH_2 -Nap), 4.596 (s, 4H, - CH_2 -CO-), 4.239 (q, 4H, -CO- CH_2 - CH_3 , $J=7.23$ Hz), 1.266 (t, 6H, -CO- CH_2 - CH_3 , $J=7.18$ Hz). ^{13}C NMR (CDCl_3 , δ ppm): 14.1 (- CH_3), 22.2 (Ar- CH_2 -Ar), 61.2 (-CO CH_2 - CH_3), 67.2 (-O- CH_2 -CO-), 114.8, 123.7, 124.7, 124.8, 126.1, 128.0, 128.2, 130.0, 133.7, 153.1 (Nap-C), 169.3 (C=O). ESI MS: m/z (%), 248 (100, $\text{M}^+ - 224$), 472 (48, M^+).

2.4. 1,1'-Methylene-bis(2-naphthoxy acetic acid) (L_3)

To ethanol (40 mL), L_2 (0.772 g, 1.63 mmol) and NaOH (0.196 g, 4.89 mmol, dissolved in 5 mL water) were added and stirred while refluxing for 24 h. The reaction mixture was then cooled to room temperature and was evaporated under vacuum (60–70 °C) to dryness. To this, ice cold water (30 mL) was added and neutralized with 3N HCl. The solid product formed was filtered and dried

under vacuum. Yield: 0.578 g (85%). M.P. 222 °C (decomp.). Anal. Calc. for $\text{C}_{25}\text{H}_{20}\text{O}_6 \cdot \text{H}_2\text{O}$ (434.17): C 69.12, H 5.10; found: C 69.41, H 4.89%. FTIR (KBr, cm^{-1}): 1716 ($\nu_{\text{C=O}}$), 3432 (ν_{OH}). ^1H NMR ($\text{DMSO}-d_6$, δ ppm): 13.123 (br, 2H, -COOH), 8.178 (t, 2H, Nap-H, $J=4.75$ Hz), 7.778 (d, 2H, Nap-H, $J=9.14$ Hz), 7.745 (m, 2H, Nap-H), 7.378 (d, 2H, Nap-H, $J=9.14$ Hz), 7.203 (m, 4H, Nap-H), 5.045 (s, 4H, -O- CH_2 -COOH), 4.953 (s, 2H, Nap- CH_2 -Nap). ^{13}C NMR ($\text{DMSO}-d_6$, δ ppm): 21.1 (Nap- CH_2 -Nap), 65.9 (- CH_2 -CO $_2\text{H}$), 114.2, 122.7, 123.2, 124.4, 125.9, 127.8, 127.9, 129.1, 133.0, 152.4 (Nap-C), 170.5 (C=O). ESI MS: m/z (%), 416 (56, M^+).

2.5. 1,1'-Methylene-bis(2-naphthoxy-methyl-2'-pyridine) (L_4)

N,N -Dimethylformamide (dmf) (160 mL) was taken in a two necked flask fitted with a nitrogen inlet and a reflux condenser. To this L_1 (4.2 g, 14 mmol); K_2CO_3 (9.66 g, 70 mmol) and 2-picolylchloride hydrochloride (6.9 g, 56 mmol) were added and the reaction mixture was heated at 60–70 °C under nitrogen atmosphere for 12 h. The reaction mixture was then cooled to room temperature, and was poured into water and extracted with CHCl_3 . The chloroform layer was washed twice with water, and dried over anhydrous NaHSO_4 . The filtrate was evaporated under vacuum (45–50 °C) to dryness and the residue was washed with petroleum ether. Orange solid product formed was crystallized from $\text{CHCl}_3/\text{CH}_3\text{OH}$ to give pale orange crystals. Yield: 5.4 g (80%). M.P. 134–137 °C. Anal. Calc. for $\text{C}_{33}\text{H}_{26}\text{O}_2\text{N}_2$: C 82.16, H 5.39, N 5.81, Found C 81.91, H 5.59, N 5.59. ^1H NMR (CDCl_3 , ppm): 8.578 (d, 2H, Py-H, $J=4.89$ Hz); 8.285 (d, 2H, Nap-H, $J=8.55$ Hz); 7.722 (t, 4H, Nap-H, $J=9.01$ Hz); 7.494 (dt, 2H, Py-H); 7.285 (m, 6H, Nap-H); 7.134 (m, 4H, Py-H); 5.265 (s, 4H, Py- CH_2 -); 5.148 (s, 2H, Nap- CH_2 -Nap). ^{13}C NMR (CDCl_3 , δ ppm): 21.9 (Nap- CH_2 -Nap), 71.9 (-O- CH_2 -Py), naphthyl and pyridyl carbon resonances are 114.6, 118.1, 119.1, 120.8, 121.2, 121.8, 122.4, 122.9, 123.1, 123.3, 123.8, 124.3, 125.59, 126.0, 127.6, 127.9, 128.0, 128.3, 129.6, 133.2, 133.6, 136.3, 136.5, 148.5, 151.9, 152.6, 156.8. ESI MS: m/z (%), 483 (100, M^+).

3. Results and discussion

In order to understand the selective binding preference of M^{2+} towards these molecules, appropriate fluorescence and absorption titration experiments were performed and the corresponding results were discussed. The complex species formed were established by ESI MS studies.

3.1. Fluorescence titration

All the four derivatives were studied for their binding towards divalent metal ions (M^{2+}), viz., Mg^{2+} , Ca^{2+} , Mn^{2+} , Fe^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} and Zn^{2+} by fluorescence spectroscopy by exciting the reaction mixture at 280 nm and measuring the emission in 290–450 nm region. Spectra obtained during the titration of 1 μM concentrations of L_1 , L_2 , L_3 or L_4 with Cu^{2+} are shown in Fig. 1a–d and the corresponding plots of relative fluorescence intensity ratios (I/I_0)

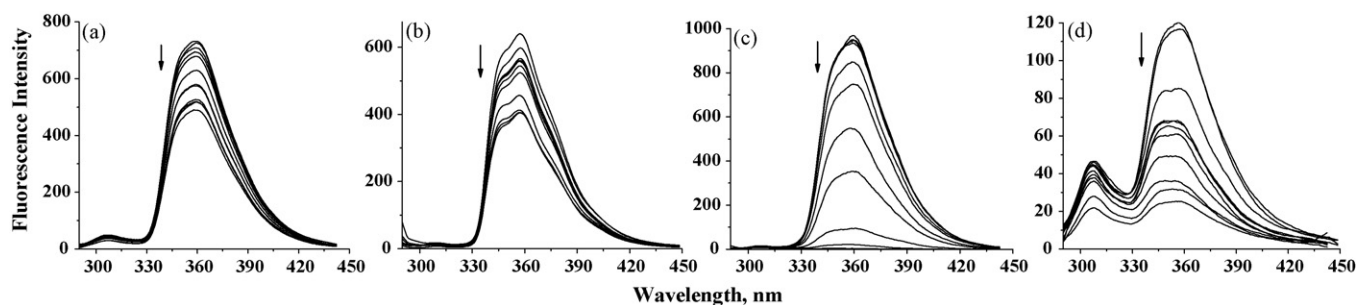


Fig. 1. Fluorescence spectral traces obtained during the titration of the derivatives at 1 μM with varying mole ratios of Cu^{2+} in CH_3OH : (a) L_1 ; (b) L_2 ; (c) L_3 and (d) L_4 .

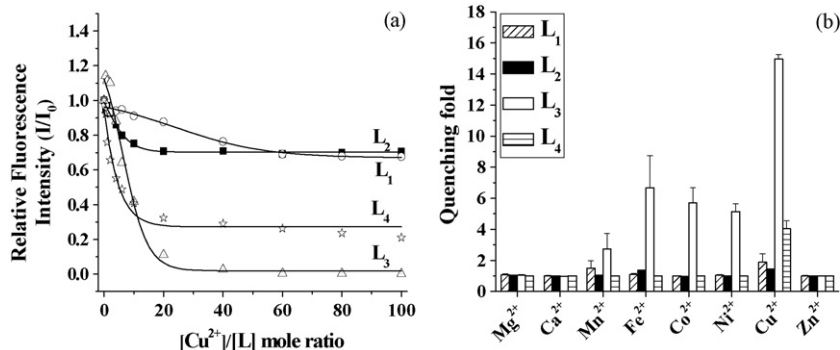


Fig. 2. (a) Plot of relative fluorescence intensity (I/I_0) vs. $[\text{Cu}^{2+}]/[\text{L}]$ mole ratio in the titration of the derivatives with Cu^{2+} . (b) Histogram indicating the fold of quenching of fluorescence intensity in the titration of M^{2+} with L_1 , L_2 , L_3 and L_4 at their saturation. Error bars were determined based on four different experiments.

are shown in Fig. 2a. Titration of L_1 with M^{2+} in CH_3OH resulted in little or no substantial quenching in the fluorescence intensity till the $[\text{M}^{2+}]/[\text{L}_1]$ mole ratio of 100, indicating that L_1 does not show much binding affinity towards M^{2+} ions studied (SI 01). Similar results were obtained even in case of the titration of L_2 , the di-O-ester derivative with M^{2+} (SI 02).

However, the titration of M^{2+} with L_3 showed substantial decrease in the fluorescence intensity by different ions, viz., Mn^{2+} , Fe^{2+} , Co^{2+} , Ni^{2+} and Cu^{2+} , owing to the presence of $-\text{COOH}$ groups and hence exhibit no selectivity towards any of the M^{2+} (SI 03). On the other hand, the titration of L_4 with M^{2+} showed substantial quenching in the fluorescence intensity only in case of Cu^{2+} and exhibits saturation beyond 20 equivalents of $[\text{Cu}^{2+}]/[\text{L}_4]$ with 4.0 ± 0.5 fold quenching (SI 04). Maximum fluorescence quenching fold for all these derivatives in presence of different M^{2+} has been given in Fig. 2b. Further in order to check the binding nature of L_4 towards alkali (Na^+ , K^+) as well as heavy metal ions (Hg^{2+} , Cd^{2+} , Pb^{2+}), in addition to ions mentioned earlier, corresponding titrations were carried out. Titrations carried out with these ions exhibited no significant change in the fluorescence intensity except in case of Hg^{2+} , which shows marginal quenching up to 20 equivalents and substantial quenching beyond 40 equivalents (SI 04). Thus L_4 has shown considerable selectivity and sensitivity towards Cu^{2+} compared to the other three molecules as well as other metal ions reported here.

In order to check the equilibrium nature of the binding, the Cu^{2+} , titrations were also carried out at 10, 20 and 50 μM concentrations of L_4 , respectively. The relative fluorescence intensity plots (Fig. 3) in all these three cases were found to be similar with attaining saturation at around 10 ± 3 mole equivalents of $[\text{Cu}^{2+}]/[\text{L}_4]$ with 6.5 ± 1.2 , 7.3 ± 0.7 and 10.5 ± 1.2 fold quenching, respectively at the L_4 concentrations of 10, 20 and 50 μM , respectively. The double logarithmic plots [14,29–33] of the fluorescence titration data yielded a 1:1 species with K_{ass} being $(1.13 \pm 0.11) \times 10^5$, $(1.97 \pm 0.04) \times 10^5$, $(2.73 \pm 0.10) \times 10^5$, and $(4.61 \pm 0.30) \times 10^5 \text{ M}^{-1}$, respectively at 1, 10, 20 and 50 μM titrations and these values follow almost a linear

trend. While 1 μM titration is of equilibrium type, those titrations of 10 μM or higher exhibit stoichiometric behaviour. The composition of the species has been further confirmed to be 1:1 based on absorption and ESI MS spectra as reported in this paper.

3.2. Absorption studies

Titration of L_4 with Cu^{2+} clearly indicate changes in the absorbance of bands arising from pyridyl as well as naphthyl moieties in the range 250–350 nm with an isosbestic point centered at 318 nm (Fig. 4a) indicating a transition in the species between the simple ligand and its Cu^{2+} bound ones. The spectral changes as well as the plots of $[\text{Cu}^{2+}]/[\text{L}_4]$ mole ratio vs. absorbance shown in Fig. 4b clearly indicate the binding of Cu^{2+} to L_4 . The $d \rightarrow d$ and charge transfer bands observed during titration of L_4 with Cu^{2+} , suggests the formation of the corresponding copper complex (SI 05). On the other hand, the Job's plot shown in Fig. 4c suggests the formation of 1:1 complex species for L_4 with Cu^{2+} .

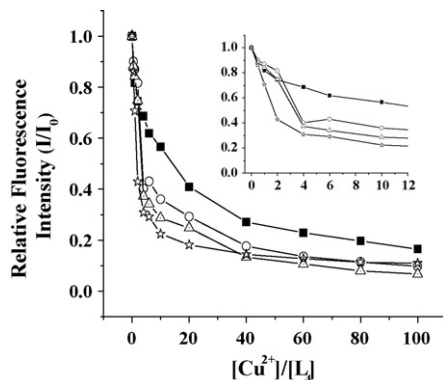


Fig. 3. Relative fluorescence intensity vs. $[\text{Cu}^{2+}]/[\text{L}_4]$ at different concentrations of L_4 (μM): 1 (\blacksquare); 10 (\circ); 20 (\triangle) and 50 (\star). Inset: expanded in the region of 0–12 mole ratio.

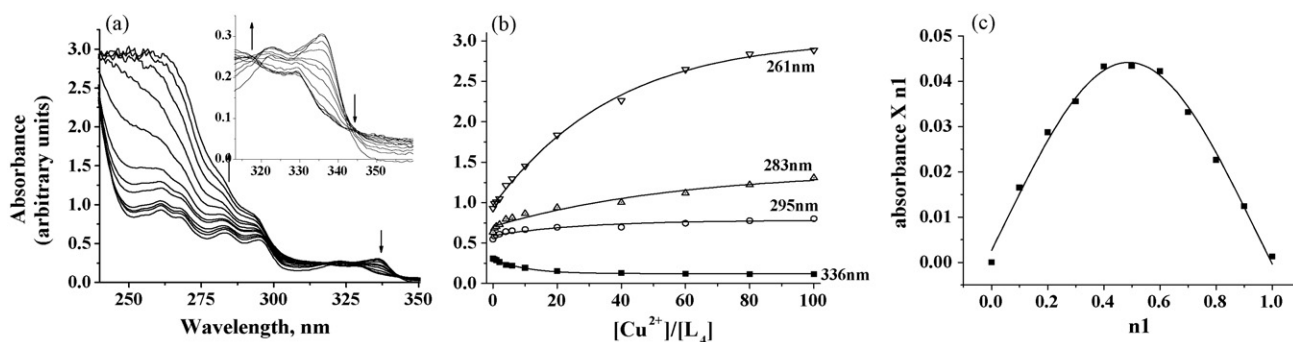


Fig. 4. Absorption titration of L_4 ($50 \mu\text{M}$) with varying mole ratios of Cu^{2+} in methanol: (a) spectral traces during the titration (inset: expanded in the region 310–360 nm); (b) plot of absorbance vs. $[\text{Cu}^{2+}]/[L_4]$ mole ratio for different absorption bands and (c) Job's plot indicating the mole fraction of L_4 (n_1) vs. product of absorbance and mole fraction.

3.3. Mass spectral titration

ESI mass spectrum of L_4 shows abundant molecular ion peak at m/z 483. During the titration of L_4 with Cu^{2+} , the mass spectra (Fig. 5) exhibited an ion at m/z 545 corresponding to 1:1 Cu^{2+} to L_4 complex species.

The percent of the 1:1 species increases from 5 to 40 on going from the titration of 0.2:1 to 2:1 of Cu^{2+} to L_4 . Spectra obtained in the titrations of 1:1 or above exhibit an additional peak at m/z of 644 corresponding to $[\text{Cu}L_4(\text{ClO}_4)]^+$. The peak corresponding to the ligand completely diminishes when the ratio approaches 10:1. Thus the mass spectral data clearly supports the formation of 1:1 complex. The molecular ion peak observed at m/z 545 was further confirmed for the presence of Cu^{2+} based on its characteristic isotopic pattern. On the other hand the isotopic pattern observed with the peak at m/z 644 can be interpreted by taking the isotopes of both the copper and chlorine into consideration.

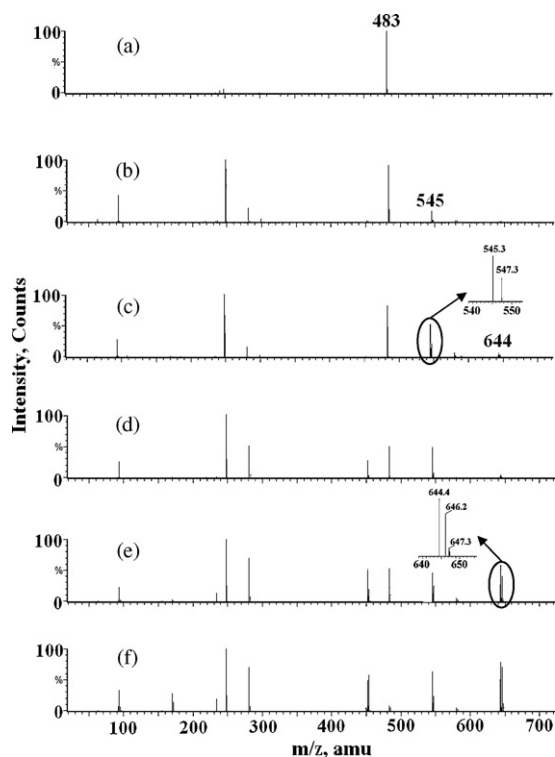


Fig. 5. ES MS spectra during the titration of L_4 with Cu^{2+} at various mole ratios of $[\text{Cu}^{2+}]/[L_4]$: (a) 0, (b) 0.2, (c) 0.5, (d) 1.0, (e) 2.0 and (f) 10.0. Expansions are shown in case of (c) and (e) for the circled portion.

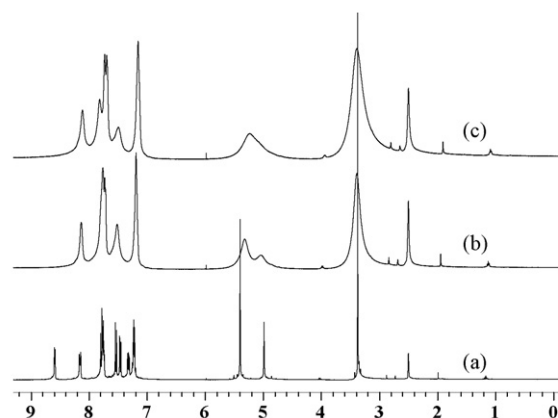


Fig. 6. ^1H NMR spectra measured during the titration of L with Cu^{2+} (in DMSO-d_6). (a) L , (b) $L + 0.5 \text{ eq } \text{Cu}^{2+}$, (c) $L + \text{eq } 1 \text{ Cu}^{2+}$.

3.4. NMR titration

Titration of L_4 with copper perchlorate resulted in broadening as well as merging of the signals (Fig. 6) associated with the arm methylene and the pyridyl moieties suggesting the binding of ether-O- and pyridyl nitrogens. The broadening occurs because of the paramagnetic nature of Cu^{2+} .

3.5. Sensitivity of L_4 towards Cu^{2+}

Fluorescence titration performed at varying concentrations of L_4 , yet maintaining a mole ratio of L_4 to Cu^{2+} as 1:1 clearly suggests that a concentration of $10 \mu\text{M}$ yields recognizable quenching of about 10% (Fig. 7) and hence 630 ppb of Cu^{2+} can be detected by L_4 . Thus L_4 acts as specific as well as selective molecule towards Cu^{2+} sensing among the derivatives reported here, viz., L_1 – L_4 . The selectivity could perhaps be attributed to the preferential coordination behaviour of pyridyl moieties present in L_4 towards Cu^{2+} .

4. Conclusions and correlations

Di-derivatization of 1,1'-methylene-bis(2-naphthol) (L_1) using ester (L_2), carboxylic acid (L_3) or picolyl (L_4) end groups at the pendant arms resulted in hemi-calix[4]naphthalene derivatives. Owing to the anti-like structure of L_1 -based ligands, it is reasonable to predict that the derivatives must undergo conformational changes in order to bring both the arms in binding range to the M^{2+} . This feature, indeed, seem to have played a role in the selective recognition of M^{2+} towards these derivatives. Thus, while L_4 is sensitive and

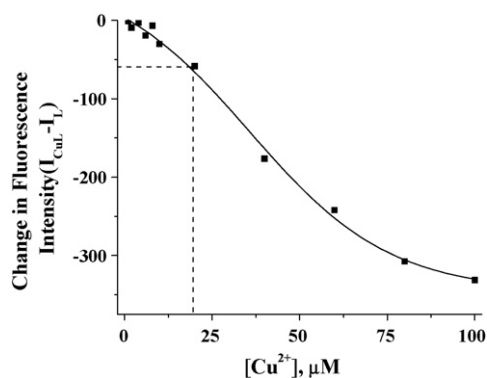


Fig. 7. Plot of the difference in the fluorescence intensity of the ($L_4 + Cu^{2+}$) and that of L_4 . During the titration, the Cu^{2+} to L_4 ratio was maintained at 1:1.

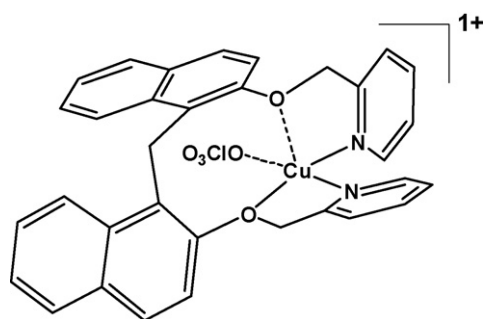


Fig. 8. Schematic representation of the proposed species of recognition of Cu^{2+} by L_4 .

selective towards Cu^{2+} , none of the other derivatives was suited for the selective recognition of any M^{2+} . Thus L_4 having pyridyl moieties on its two arms is best suited for selective recognition of Cu^{2+} , while the presence of $-OH$ (L_1), ester (L_2) or carboxylic (L_3) moieties on the same molecule does not yield selectivity towards any M^{2+} though these molecules show fluorescence response towards several M^{2+} . While insensitivity of L_2 can be explained owing to its ester moieties, the non-selectivity of L_3 can be explained to the high complexation behaviour of the carboxylic units towards a number of M^{2+} . The affinity of the pyridyl nitrogens towards M^{2+} provides optimal interaction in case of Cu^{2+} and hence is selective towards divalent copper when compared to the other derivatives reported here, though the other derivatives exhibit changes in the fluorescence response. Based on all the studies reported in this paper, the structure shown in Fig. 8 has been proposed as species of recognition of Cu^{2+} by L_4 and the presence of perchlorate moiety has origin from ESI MS spectra. In effect, the selectivity of L_4 can be attributed to the chemical affinity of the groups present in the arm towards the divalent metal ions as well as to the coordination preferences of the latter. As a result L_4 possessing N_2O_2 binding core exhibit high selectivity towards Cu^{2+} owing to the presence of the pyridyl nitrogens. The absorption spectral features as well as the broadened proton NMR signals of the arm in L_4 supports the proposed binding.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jphotochem.2008.11.021.

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