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Imidazolium-Salt-Based Fluorescent Chemosensor for Cu(II), Zn(II) and Co(II)

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A ligand of macrocyclic polyamine with an imidazolium salt group (MCP-ISG) and its Cu(II), Zn(II) and Co(II) metallic complexes were synthesized, and MCP-ISG was used as a chelation-enhanced fluorophore. The complexes of Cu(II), Zn(II) and Co(II) have different intensities of fluorescence response in a solution of pyridine/water (1:1). The fluorescence intensity of Cu(II) complex was enhanced in the solution while those of Co(II) and Zn(II) complexes were weakened markedly, with the Zn(II) complex showing the larger reduction. The interaction and fluorescence emission mechanisms of the ligand with the cations are also discussed in this paper.

Key words: macrocyclic polyamine, metallic complex, synthesis, fluorescent sensor, mechanism

1. Introduction

Biosensors are one of the most rapidly developing and challenging novel fields of chemical biology. The biosensor's selective bonding of species can lead to large perturbations in the host environment, particularly when the guest is an ion. Fluoroionophores can provide chemical information on ions; thus, they are important substances in metal ion analysis. Macrocyclic polyamine ligands possess many unique properties, for example, as a catalyst of DNA cleavage,⁽¹⁾ a fluorescent sensor for cations,^(2,3) and as a small molecular sensor.⁽⁴⁾ Fluorescent sensors have been widely applied in the detection of organic compounds and metal ions such as Pb²⁺ and Cu²⁺.^(2,3,5) Due to their high sensitivity, accuracy and efficiency, they are effective for determining trace amounts of pollutants in industrial sewage, textiles and paints, and they are often used in the field of online production analysis.⁽⁶⁻⁹⁾

1,4,7,10-tetraazacyclododecane (Cyclen) is an excellent complex reagent with many transition-metal ions such as Cu(II), Zn(II) and Co(II).⁽²⁾ Many derivatives of Cyclen are good metal-ion-chelating enhanced fluorophores.^(3,5) Because of an additional ethylamine

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group in the pendant group, the macrocyclic ligand 2-(9-anthrylmethylamino)ethyl-appended Cyclen is a more effective and practical zinc(II) fluorophore than 9-anthrylmethylcyclen.^(2,3) Therefore, complexes with a fluorescence response have received much attention from researchers.^(10,11) Unfortunately, most complexes synthesized so far have been heterocyclic aromatics, whose solubility in water and biocompatibility are usually both very poor; thus, they cannot be used universally in practice. It is therefore vital to prepare effective and higher selectivity fluorescence chemosensors.⁽¹²⁾

In this study, we developed a novel fluorescence sensor with better solubility in water and biocompatibility, and a large difference in the fluorescence response to different ions. The macrocyclic polyamine Cyclen containing an imidazolium salt group (MCP-ISG) was synthesized, and the fluorescence response characteristics of its complexes with Cu(II), Zn(II) and Co(II) in a medium of pyridine/water (1:1) were also investigated. Moreover, the interaction and fluorescence emission mechanisms of MCP-ISG with cations were explored.

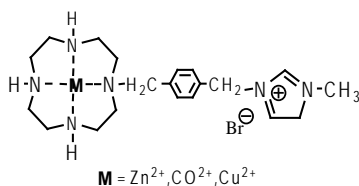
2. Experimental

2.1 General information

All reagents were used without further purification and all aqueous solutions were prepared using deionized or distilled water. Infrared (IR) spectra were recorded on a Shimadzu FTIR-4200 spectrometer using KBr pellets or thin films on KBr plates. Nuclear magnetic resonance (NMR) spectra were measured on a Varian INOVA-400 spectrometer (400 MHz) and the δ scale in parts per million was referenced to residual solvent peaks or internal tetramethylsilane (TMS). Electrospray ionization mass spectrometry (ESI-MS) was performed using a Finnigan LCQDECA and high-resolution mass spectrometry (HR-MS) spectral data were recorded on a Bruker Daltonics BioTOF. Fluorescence titration spectra were measured on an F-4500 fluorescence spectrophotometer. pH acidity titration data were obtained using a pHs-4CT acidity meter.

2.2 Synthesis of MCP-ISG and complexes

The ligand N-methyl-N'-(1,4,7,10-tetraazacyclododecan-4-yl-methyl)-1-benzyl-imidazolium bromide (L) and its complexes (L-M) with Cu(II), Zn(II) and Co(II) (Scheme 1) were prepared as described in ref. 13. Table 1 shows the IR, ¹H-NMR and HR-MS data of the ligand and its complex L-Zn²⁺. Moreover, their IR spectra are shown in Fig. 1. The stretching vibration of C-H of benzene clearly increased in the complex L-Zn²⁺, and that of N-Zn²⁺ was very strong at 1092 cm⁻¹.



Scheme 1. Structures of L and L-M.

Table 1.
Data of ligand L and complex L-Zn²⁺

	Ligand L (yellow liquid, yield: 83.4%)	Complex L-Zn ²⁺ (yield: 85.4%)
IR (KBr, cm ⁻¹) ^a	3444 (m), 3128 (w), 2978 (s), 2904 (m), 1754 (w), 1662 (vs), 1567 (m), 1430 (s), 1416 (s), 1368 (s), 1256 (s), 1181 (vs), 1045 (w), 866 (w), 799 (m) and 706 (m)	3448 (m), 3159 (m), 2938 (w), 1884 (w), 1625 (w), 1557 (w), 1458 (m), 1092 (vs), 856 (w), 787(w) and 624 (s)
¹ H-NMR (400 MHz, TMS) ^b	^c 2.54 (t, 8 H, <i>J</i> = 8 Hz, NCH ₂), 2.65 (m, 7 H, NCH ₂ , NCH ₃), 2.78 (t, 4 H, <i>J</i> = 4 Hz, NCH ₂), 3.39 (s, 3 H, NH), 3.60 (s, 2 H, ArNCH ₂), 5.07 (s, 2 H, ArCH ₂ -Ar), 7.06 (d, 2 H, <i>J</i> = 8 Hz, imidazole-H), 7.27–7.38 (m, 4 H, ArH) and 7.53 (s, 1 H, imidazole-H).	^d 2.89 (t, 4 H, NCH ₂), 3.00 (s, 4 H, NCH ₂), 3.17 (t, 6 H, NCH ₂), 3.24 (s, 4 H, NCH ₂), 3.92 (s, 3 H, NCH ₃), 4.85 (s, 2 H, ArCH ₂ Ar), 7.40 (d, 2 H, <i>J</i> = 4 Hz, imidazole-H), 7.4–7.70 (m, 4 H, ArH) and 8.61 (s, 1 H, imidazole-H)
HR-MS (ESI)	C ₂₀ H ₃₃ N ₆ : experimental 357.2748, calculated 357.2761	C ₂₀ H ₃₃ N ₆ Zn: experimental 426.4093, calculated 426.9608

^a IR intensity, vs: very strong, s: strong, m: medium, w: weak. ^b ¹H-NMR peak shape, s: single, d: double, t: triple, m: multiple. ^c CHCl₃ solution, ^d H₂O solution.

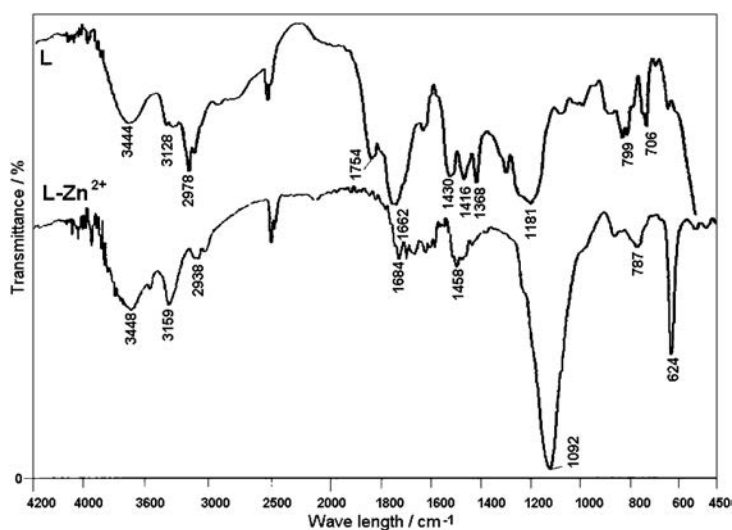


Fig. 1. IR spectra of L and L-Zn²⁺.

2.3 pH acidity titration

The protonation constants K_{a_i} of L were determined by the potentiometric pH titration of 1 mM L•3HCl (prepared from the ligand (0.1 mol) dissolved completely in a suitable amount of a medium of water/pyridine (1:1), with 3 equivalent volumes of HCl added, then diluted to 50 ml) against 0.1 M NaOH with $I = 0.1$ M (NaNO_3) at 298 K.

The electrode system was adjusted using 0.05 M potassium hydrogen phthalic acid buffer solution ($\text{pH} = 4.003$) and 0.025 M phosphate mixture buffer solution ($\text{pH} = 8.643$) with ion strength (I) 0.10 (KNO_3) and temperature (T) 298 ± 0.1 K. Under the same conditions, all the samples were titrated three times independently.

2.4 Fluorescence titration

Fluorescence titration was performed using 2 mM MCP-ISG in a medium of water/pyridine (1:1). In the titration, three different aqueous solutions containing three different cations, Cu^{2+} , Zn^{2+} and Co^{2+} (0.1 mM), were added to the ligand solution drop by drop using a mini-injector. The fluorescence quantum efficiency was adjusted using standard p-terphenyl in cyclohexane, with an excitation wavelength of 265 nm (quantum efficiency $\phi = 0.87$). All fluorescence emission spectra were measured at a fixed excitation wavelength of 330 nm. The existence of metal ions was judged by the increase or decrease in the intensity of the fluorescent emission.

3. Results and Discussion

3.1 pH during metal complex formation

The pH is an important factor that affects the formation of ligands with metal ions; thus, it is necessary to confirm that the pH is suitable for the ligand to be combined with metal ions effectively. In the experiment, 0.1 mM NaOH solution was added to solution (a) without any metal ions, solution (b) with 1 equiv of $\text{Zn}(\text{NO}_3)_2$; solution (c) with 1 equiv of $\text{Cu}(\text{NO}_3)_2$ and solution (d) with 1 equiv of $\text{Co}(\text{NO}_3)_2$ at 298 K. Their pH-eq (OH^-) curves are shown in Fig. 2.

In titration curve a (in Fig. 2), there are three abrupt changes in the pH, which indicates that a protonation reaction of MCP-ISG probably occurred at around these three pH values. Details of the protonation process are shown in Scheme 2, and ligand L can exist in a solution containing H^+ ions as four forms: single L, H^+L , H_2^+L and H_3^+L . Using the formula $\log K_{a_i} (i = 1-3) = [\text{L} \cdot i\text{H}^+]/[\text{L} (i-1)\text{H}^+]\text{aH}^+ ((i-1)\text{H}^+ + \text{H}^+ \text{L} \cdot i\text{H}^+)$, the proton dissociation constants are 3.98, 6.23 and 8.93. When the pH was lower than 3.98, ligand L existed mainly as H_3^+L , and when the pH was greater than 8.93, it existed almost exclusively as single L. Once the cavity of ligand L is occupied by a H^+ ion, it is very difficult for other ions to form a complex with L. Consequently, a higher pH is beneficial for producing a stable L-M complex ($M = \text{metal ion, Cu}^{2+}, \text{Zn}^{2+}$ or Co^{2+}), which ensures that ligand L can detect metal ions effectively and rapidly in the fluorescence analysis method.

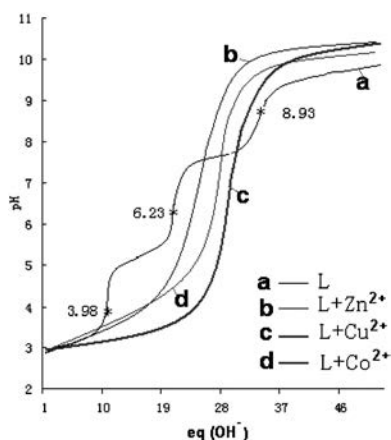
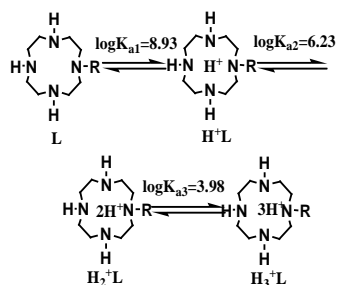


Fig. 2. pH titration curves of 1mM L•3HCl (a), 1 mM L•3HCl + 1 equiv Zn(NO₃)₂ (b), 1 mM L•3HCl + 1 equiv Cu(NO₃)₂ (c) and 1 mM L•3HCl + 1 equiv Co(NO₃)₂ (d) at 298 K with $I = 0.1$ (KNO₃). Here eq (OH⁻) is the number of equivalents of NaOH added.



Scheme 2. Protonation process of MCP-ISG. The protonation constants are $\log K_{a_i} (i = 1-3) = [L \cdot iH^+]/[L (i-1)H^+][H^+]$ ($(i-1)H^+ + H^+ + L \cdot iH^+$).

There is only one abrupt change in titration curves b, c and d in contrast with curve a in Fig. 2. Below pH 3–4, as Cu²⁺, Zn²⁺ or Co²⁺ was added to the solution of L, few L-M complexes formed, but a large number of L-M complexes appeared when the pH was greater than 9.

3.2 Fluorescence property of metal complexes

A fluorescence sensor may be regarded as useful and effective if it has a different fluorescence performance when it combines with different substances (i.e., metal ions). Thus, the fluorescence properties of ligand L synthesized with Cu²⁺, Zn²⁺ and Co²⁺ were evaluated and recorded. In all the tests conducted here, the concentrations of ligand L and L-M complexes are 2 mM.

Figure 3 shows the fluorescence spectra of metal ions (Cu^{2+} , Zn^{2+} and Co^{2+}) with and without ligand L in water/pyridine solution. It is clear that MCP-ISG has different effects on different metal ions in terms of the fluorescence response, which can be summarized as follows: the fluorescence intensities of L-Zn-Py and L-Cu-Py are both greater than those of Zn-Py and Cu-Py, while for Co^{2+} the fluorescence intensity is decreased when L is added to the solution. In particular, the fluorescence intensity of L-Cu-Py is more than 4000 arb. unit, which is much larger than that of Cu-Py (about 500) at an excitation wavelength of 330 nm. This indicates that MCP-ISG has high selectivity to Cu^{2+} , Zn^{2+} and Co^{2+} and is useful for detecting copper ions.

The efficiency and selectivity of MCP-ISG in its response to Cu^{2+} , Zn^{2+} and Co^{2+} probably derive from the special space structure of the L-M-Py complex and the nature of fluorescence emission. The proposed complex structure and the mechanism of fluorescence emission are displayed in Scheme 3. In this structure, the center ion, a metal ion and six nitrogen atoms form an octahedral structure; four of the nitrogen atoms are from MCP-ISG and the other two are from pyridine. π - π stacking interaction occurs between the benzene ring of MCP-ISG and the pyridine ring, which increases the stability of the complex. Simultaneously, the positive charge of the metal ion repulses that of the imidazolium cation, which makes the π - π stacking interaction more stable.⁽¹⁴⁾

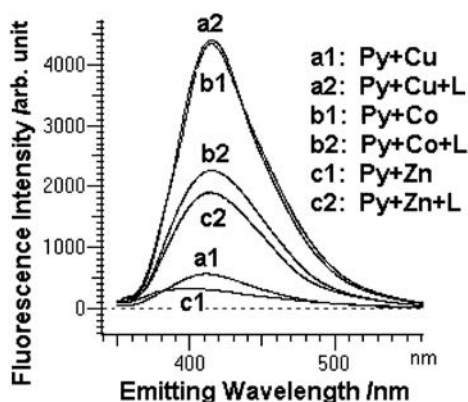
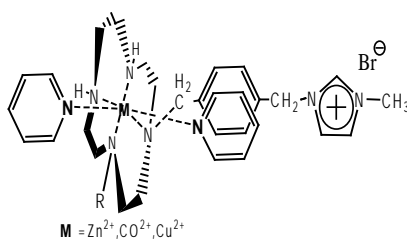


Fig. 3. Fluorescence spectra ($\lambda_{\text{max}} = 414 \text{ nm}$) of L-M complex and metal ions in medium of water/pyridine (1:1) (excitation wavelength of 330 nm).

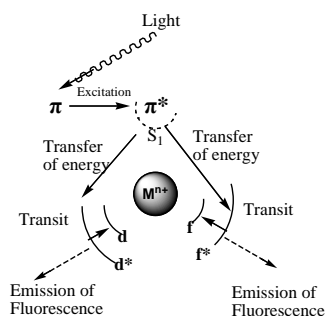


Scheme 3. Structure of metallic complexes.

The metallic complex can emit very strong fluorescence because of the enhanced rigidity and the coplanar molecular structure of L-M-Py.

Generally, the fluorescence emission mechanism of a metallic complex is as follows: first, the π -electrons in the conjugation system in the ligand molecule absorb visible light. The energy of the π -electrons increases accordingly, then they are excited and transit to a π^* orbit. Because the energy of the d^* and f^* orbits is less than the minimum energy of the single excited state (S_1), the energy of S_1 is transferred to the π^* , d^* or f^* orbit. Finally when the d^* or f^* electrons (in the excited state) return to their ground state, their superfluous energy is transformed into strong fluorescence⁽¹⁵⁾ (Scheme 4). The differences in the L-M complex fluorescence properties are attributed to different electron arrangements for different metal atoms; thus, the energies of the d and f orbitals are different.

In this study, we noticed that pyridine played a vital role in the emission of fluorescence in this system. Pyridine was used as not only a solvent but also a coordination reagent of the metal ions, which can be seen from Fig. 4. By comparing



Scheme 4. Schematic diagram of the mechanism for the origin of fluorescence of metallic complex.

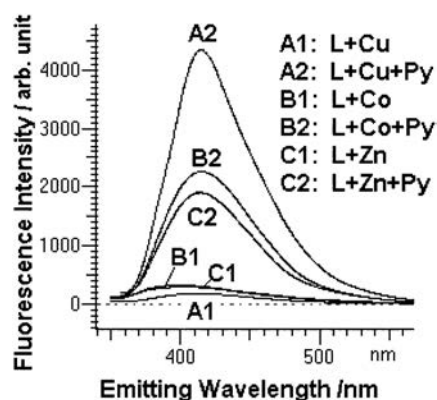


Fig. 4. Fluorescence spectra ($\lambda_{\text{max}} = 414$ nm) of L-M with and without pyridine (excitation wavelength of 330 nm).

the fluorescence intensities of A1, B1 and C1 with those of A2, B2 and C2 in Fig. 4, respectively, it is deduced that the fluorescence intensity will be reduced sharply if there is no pyridine in the solution. As discussed above, the pyridine contributes to the absorbance of visible light, which provides energy for the excitation of electrons from π orbitals to π^* ones, thus, resulting in the reinforcement of fluorescence.

4. Conclusion

A biocompatible fluorescent sensor with better solubility in water was synthesized, which was composed of macrocyclic polyamine Cyclen and an imidazolium salt group. Its fluorescence response to various metal ions was investigated. The results indicated that it can distinguish between Cu^{2+} , Zn^{2+} and Co^{2+} ions, and is particularly useful for the detection of Cu^{2+} . The higher selectivity and efficiency may be explained by the special octahedral structure of the complex, which was first proposed in this paper.

Acknowledgments

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