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# Fluorescence turn-on of salicylaldimine ligands by co-ordination with magnesium and amines†

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**A new fluorescence enhancement mechanism based on Schiff base ligand and magnesium complexation is established. The co-ordination number of the Schiff base ligand–magnesium complex (2 : 1) can be tuned to 1 : 1 in the presence of amines to induce significant fluorescence enhancement. Using this approach, a novel and easily available fluorescent chemosensor was designed, which showed highly selective recognition toward magnesium and amines in ethanol.**

Schiff base ligands are called ''privileged ligands'' because they are easily prepared by the condensation of aldehydes and amines and are well known to be effective in stabilizing many different metals in various oxidation states.[1] The effectiveness of Schiff base–metal complexes enables their use across a diverse range of fields, from medicine[2,3] to catalysis[4,5] and fluorescent probes/chemosensors.[6–9] Fluorescent probes/chemosensors have been widely studied in selectively detecting guest ions and are of particular interest because of their high selectivity, sensitivity, and simplicity. A number of signaling mechanisms have been developed and applied targeting the optical detection of different species. Signaling mechanisms include the following: photo-induced electron/energy transfer (PET),[10] metal–ligand charge transfer (MLCT),[11] intramolecular charge transfer (ICT),[12] excimer/exciplex formation, excited-state intra/intermolecular proton transfer (ESPT),[13] and C=N isomerization.[14] Imines are almost non-fluorescent, partly because of the isomerization of the C=N bond in the excited state and partly because ESPT contains the phenolic protons of the salicylic amide moiety.

Magnesium is one of the most abundant elements in both living organisms and the inorganic environment.[15] There has been an abundance of research studying the effects of magnesium ions in clinical medicine, nutrition and physiology.[16] Hence, considerable efforts have been undertaken to develop fluorescent chemosensors for magnesium.[17–19] However, the majority of fluorescent probe/chemosensor research has focused on signaling magnesium by ligand molecule design. Few cases are related to achieving fluorescence detection of magnesium by complexation of imides and magnesium. It is generally understood that the chelating groups C=N and C=O have a high affinity to transition and post-transition metal cations, but possess a low binding affinity toward alkali metal and alkaline earth metal cations because of their differing electronic structures.[14] Additionally, few studies have reported how to activate the fluorescence of complexes resulting from changes to the coordination number.

Herein, we observe the fluorescence properties from a complex formed *via* ligand–Mg(II) chelating at a 1 : 1 stoichiometric ratio[20] in the absence of imides, while salicylaldimine ligands formed a 2 : 1 complex[21,22] with metal ions in most cases. The Salen ligands were prepared by condensation of diamine and two equivalents of salicylaldehyde, which can directly chelate with Mg(II) at a 1 : 1 stoichiometric ratio.[1] There are Schiff base ligands that can also form a 1 : 1 complex with Mg(II) by co-ordinating with *N*,*N*-dimethylformamide.[9] Ligand L (Scheme 1) is a well-known chelation-enhanced fluorescent chemosensor for Zn(II) and forms a 2 : 1 complex with Mg(II). With this in mind, we speculate that the ESPT and C=N isomerization are inhibited upon co-ordination of L with Mg(II) and amines, thus resulting in a change to the complex stoichiometry.

Based on this hypothesis, we investigated the complexation of Mg(II) with Schiff base ligands in the presence of amines. The synthesis of ligand L is shown in Scheme 1. 3-Aminopropyltriethoxysilane (APTES) and salicylal were conjugated *via* a condensation reaction[23] to obtain ligand L. Mg(II) and tris(hydroxymethyl)aminomethane (Tris) powder were directly added into the reaction system. The structures of L, L + Mg(II),

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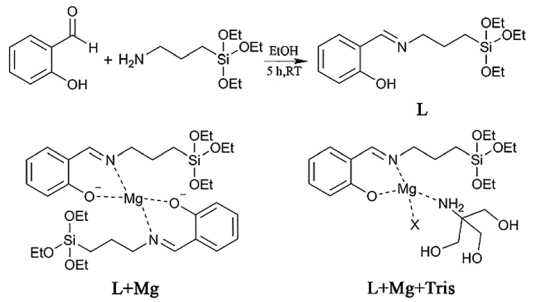


Scheme 1 Synthesis of the Schiff base ligand (L).

and L + Mg(II) + Tris were confirmed by $^{1}$H nuclear magnetic resonance (NMR), $^{13}$CNMR, FT-IR and electrospray ionization-mass spectrometry (ESI-MS) data. Further synthetic details are given in the ESI.†

All absorption and emission spectral studies were performed after reactants were mixed for 3 h in pure ethanol at room temperature. Variations in the absorption and fluorescence spectra of L upon addition of magnesium with and without Tris are shown in Fig. 1. The free ligand L and L + Mg were almost nonfluorescent due to the isomerization of the C=N double bond in the excited state. However, L, Mg and amines formed a new chelating structure, which inhibited the C=N isomerization, and fluorescence was clicked on. Metal-free L shows maximum absorption at 315 nm and weak fluorescence. The fluorescence quantum yield ($\Phi_f$) of L is ~0.296% of the standard rhodamine B in ethanol.[17] A significant enhancement in absorbance and fluorescence (17-fold) at 459 nm was observed in the presence of one equivalent of Mg(II) in ethanol. Furthermore, in the presence of Tris (5 mM), an additional absorbance peak at a higher wavelength (365 nm) appeared, indicating that a new complex was formed. Conversely, the fluorescence of the solution increased dramatically and the maximum emission wavelength shifted from 459 to 438 nm. $\Phi_f$ increased to 31% in the presence of Tris. The complexation of L, Mg(II) and Tris resulted in a significant enhancement (100-fold) of $\Phi_f$ and a visible bluish emission of the solution was observed.

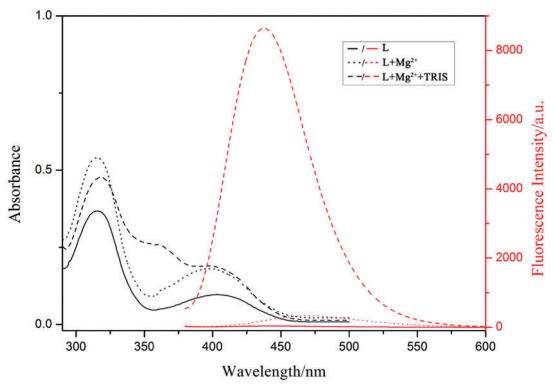


Fig. 1 Absorption and emission spectra (excitation wavelength: 365 nm) of L (1 mM), a L–Mg(II) complex (1 : 1, 1 mM) and a L–Mg(II) complex (1 : 1, 1 mM) in the presence of five equivalents of tris(hydroxymethyl)-aminomethane (Tris) in ethanol.

Binding analysis using the method of continuous variations (Job plot)[24] provided evidence of a 2 : 1 stoichiometric ratio of L : Mg(II) for the L–Mg(II) complex in ethanol and a 1 : 1 stoichiometric ratio of a L : Mg(II) for the L–Mg(II) complex in the presence of Tris (Scheme 1). Fig. 2 shows an increase in the fluorescence intensity of both L in ethanol and in a Tris solution as a function of Mg(II) concentration. However, changes to the fluorescence of L were more remarkable in the presence of Tris. The limit of detection (LOD) of Mg(II) was 0.221 μM at a signal-to-noise ratio of 3, which was calculated using the IUPAC recommended methodology.[25,26] The stability constant between L and Mg(II) in a 5 mM Tris solution was calculated to be 1.196 (±0.08) × $10^{4}$ $M^{-1}$ by the linear Benesi–Hildebrand expression[27] according to the fluorescence titration data in Fig. 2B having a high correlation factor ($R$ = 0.992), which further supported that the complex was formed at a 1 : 1 stoichiometric ratio. Therefore, the coordination number of L and Mg(II) changed (2 : 1 to 1 : 1) by the complexation of Mg(II) and Tris, which subsequently enhanced the fluorescence of L. Furthermore, changes to the coordination states of L and Mg(II) in the presence of Tris can also be observed by FT-IR, $^{1}$H NMR and $^{13}$CNMR (Fig. S3 and S4, ESI†). L, Mg(II) and Tris complexes could not be observed by ESI-MS (Fig. S5, ESI†) because of a low binding affinity ($K_a$ = 1.196 (±0.08) × $10^{4}$ $M^{-1}$); however, ESI-MS, FT-IR and $^{1}$H NMR data suggest that no reaction occurred between L and Tris. The effect of pH on the emission intensity of the L–Mg(II) complex (Fig. S6, ESI†) shows that the fluorescence was highest at pH 7. The fluorescence intensity of L + Mg(II) + Tris remained almost unchanged under continuous irradiation at intervals of 10 min for 120 min (Fig. S7, ESI†). This implies that L + Mg(II) + Tris possessed excellent long term stability. Furthermore, three additional salicylaldimine ligand–Mg(II) complexes (Fig. S8, ESI†) were synthesized, with two complexes showing fluorescence enhancement (Table S1, ESI†) upon addition of Tris, while the third formed a 1 : 1 complex with Mg(II).

The fluorescence responses of L to the different metal ions including Ba(II), Pb(II), Hg(II), Fe(III), Cu(II), Co(II), Cd(II), Zn(II), Mn(II), Mg(II) and Ca(II) with and without Tris were studied. As shown in Fig. 3, in the absence of Tris, only the L–Zn(II) complex showed an obvious fluorescence enhancement. In the presence of Tris (5 mM), a remarkable fluorescence

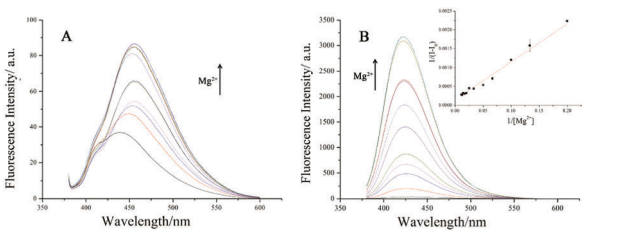


Fig. 2 Fluorescence spectra (excitation wavelength: 365 nm) of L (10 μM) as a function of increasing Mg(II) concentration (0, 2.5, 5, 7.5, 10, 15, 20, 30, 40, 50, 60 μM) in (A) ethanol and (B) ethanol in the presence of 5 mM Tris. Inset: Linear regression plot of the fluorescence titration of L with Mg(II) in a 5 mM Tris solution.

 

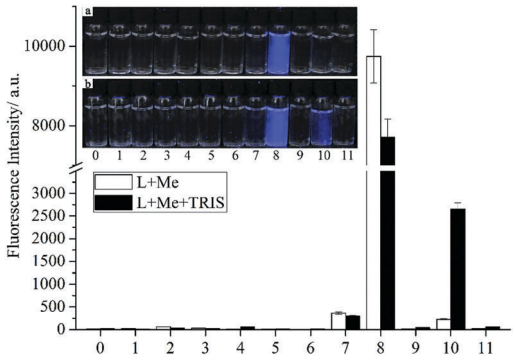


Fig. 3 Fluorescence response of L (20 μM) to different metal ions (0, only L; 1, Ba(II); 2, Pb(II); 3, Hg(II); 4, Fe(III); 5, Cu(II); 6, Co(II); 7, Cd(II); 8, Zn(II); 9, Mn(II); 10, Mg(II); 11, Ca(II); 20 μM) in ethanol (white) and in a 5 mM Tris solution (black). Inset: Visual fluorescence emissions of L (20 μM) after the addition of metal ions (as above) in (a) EtOH and (b) a 5 mM Tris solution during excitation at 365 nm using a UV lamp at room temperature.

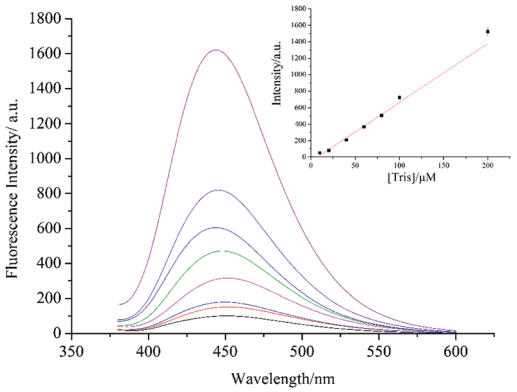


Fig. 5 Fluorescence spectra (excitation wavelength: 365 nm) of a L–Mg(II) (1 : 1, 100 μM) complex as a function of Tris concentration (0, 10, 20, 40, 60, 80, 100, 200 μM). Inset: Linear regression plot of the fluorescence titration of Tris with L–Mg(II) (1 : 1, 100 μM) in ethanol.

enhancement was observed in the L–Mg(II) complex, yielding a visible blue emission. The fluorescence spectra of the other L–metal complexes barely changed. The L–Zn(II) complex showed a decrease in fluorescence intensity at 449 nm; we speculate this to be a result of pH increase (5 mM Tris/ethanol solution ~ pH 9.53). Therefore, the specific complexation among L, metal ions, and Tris demonstrated that L has a high affinity toward Mg(II) in the presence of Tris.

Fig. 4 indicates that only amine-containing nitrogenous compounds can significantly enhance the fluorescence intensity of the L–Mg(II) complex. Amides and nitro compounds cannot promote L and Mg(II) to generate a 1 : 1 complex. Fluorescence enhancement is proportional to the quantity of the free amino group; however, this trend is not observed for diethylenetriamine because of the influence of stereohindrance. The fluorescence intensity of the L–Mg(II) complex was studied as a function of Tris concentration (Fig. 5). The fluorescence intensity of the L–Mg(II) complex increased with increasing Tris concentration, and showed linear growth at low Tris concentration (Fig. 5, inset). Furthermore, $\Phi_f$ of L increased too. Meanwhile, the LOD of Tris was obtained as 0.667 μM at a signal-to-noise ratio of 3. Consequently, the L–Mg(II) complex has a high affinity toward amines, and can be used for the quantitative detection of amino groups across a specific concentration range.

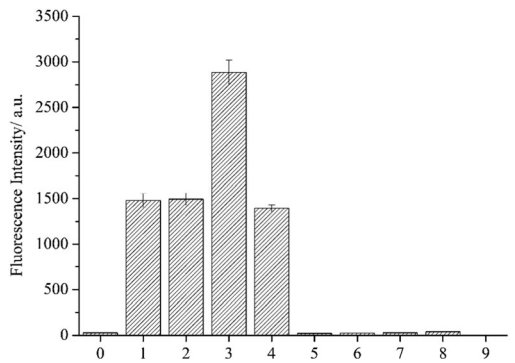


Fig. 4 Fluorescence intensity change of the L–Mg(II) (1 : 1, 20 μM) complex upon the addition of various nitrogenous compounds (5 mM) in ethanol: 0, CK; 1, Tris; 2, 2-aminoethanol; 3, ethylenediamine; 4, diethylenetriamine; 5, acrylamide; 6, methanamide; 7, *n*,*n*-dimethylacetamide; 8, nitromethane; 9, *p*-nitrophenol.

Table 1 Determination results of Mg(II) in human serum samples (unit: mmol $L^{-1}$)

| Method | Mg assay kit | AAS | Sensor reported in this work |
|---|---|---|---|
| Human serum-pooled | 0.876 ± 0.025 | 0.968 ± 0.025 | 0.868 ± 0.011 |
| Human serum 1 | 0.904 ± 0.010 | 0.972 ± 0.021 | 0.953 ± 0.014 |
| Human serum 2 | 0.934 ± 0.036 | 1.013 ± 0.042 | 0.993 ± 0.038 |

To assess the reliability of the developed approach in serum samples, the L was used for Mg(II) activity assays of human serum samples. The results detected by our standard addition approach are displayed in Table S2 (ESI†). The recoveries varied from 87% to 107%, and the relative standard deviation (RSD) was from 3.89% to 22.71%. The result of the actual magnesium content in the serum is determined as shown in Table 1. Fluorescence quantitative results are similar to those measured using a commercialized Mg assay kit and atomic absorption spectrophotometer (AAS).

In summary, we have reported a novel, easily available fluorescent chemosensor based on the co-ordination of salicylaldimine with magnesium and amines. It was proved that fluorescence enhancement was induced by changing the co-ordination number of the salicylaldimine and magnesium complex. The fluorescent chemosensor has high sensitivity and affinity toward magnesium and amines because of the specific complexation among L, Mg(II) and Tris. We believe that this study can provide a reference for the design of fluorescent chemosensors in molecular detection and triggered release, *etc.*

## Conflicts of interest

There are no conflicts to declare.

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