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A Coumarin-Derived Fluorescence Probe Selective for Magnesium

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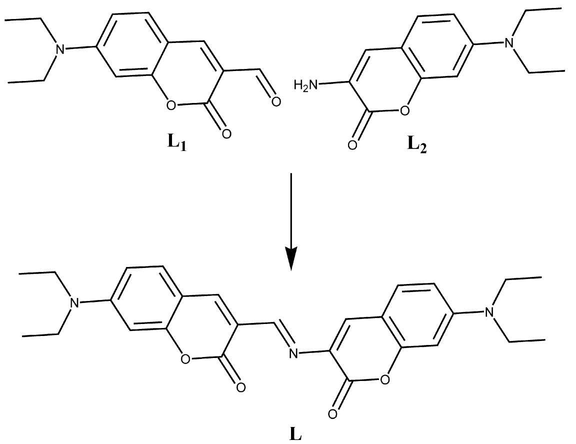
Two different coumarin derivatives have been connected via an imine linkage to obtain a new fluorescence signaling system. This compound itself does not show any emission due to rapid isomerization around the C═N bond. However, in the presence of a Mg(II) ion, this isomerization is stopped because of bonding to the metal ion resulting in high-intensity (∼550-fold) emission. Other metal ions like Li(I), Ca(II), and Zn(II) show very little emission, while biologically relevant transition-metal ions do not show any emission. In this way, the Mg(II) ion can be detected in the presence of these ions.

The design of fluorescent chemosensors is an active field of research for biological as well as analytical and environmental problems.[1] Selective detection of biologically important cations such as Na(I), K(I), Mg(II), and Ca(II) is extremely important to ascertain their spatial concentration inside biosystems for understanding cell physiology.[2] In this respect, detection of Mg(II) in the presence of Ca(II), Na(I), and K(I) as well as biologically relevant transition-metal ions is of particular significance. Mg(II) is one of the most abundant divalent ions in the cell and plays a crucial role in cell proliferation and cell death. It also participates in the modulation of signal transduction, various transporters, and ion channels.[3–9] To understand its roll in regulating cellular processes, it is important to monitor the Mg(II) ion concentration in the intracellular compartments as well as its distribution throughout the body. Herein, we describe a fluorophore built from two different coumarin groups connected via an imine linkage to have a metal binding site (NO_2 donor set) in the middle (Scheme 1). Our choice of coumarin as the flurophore stems from the fact that it possesses desirable photophysical properties such as a large Stock shift and visible excitation and emission wavelengths.[10]

Scheme 1. Schematic Representation of **L**



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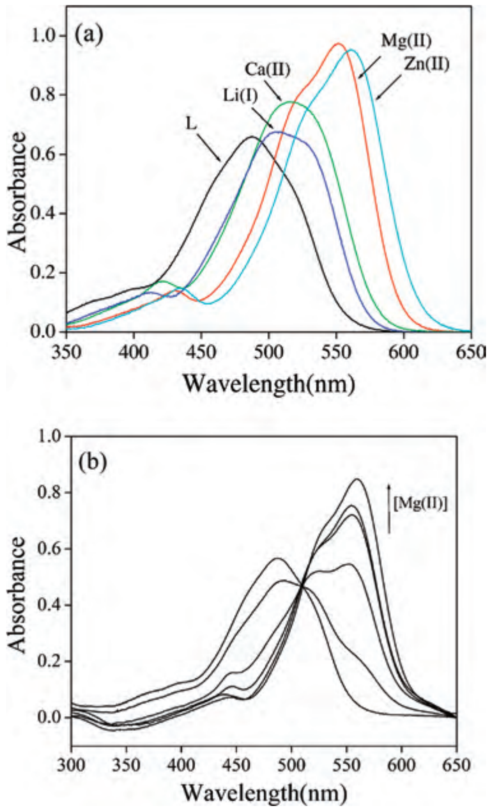


Figure 1. (a) UV/vis spectrum of ligand **L** (0.01 mM) in the presence of various metal ions (0.1 mM as their perchlorate salts) in MeCN. (b) Absorption spectra of **L** (0.01 mM) in MeCN at room temperature upon the addition of increasing concentrations of Mg(II) ions (0−0.01 mM).

A few Mg(II) signaling systems are available in the literature.[3,11−13]

The ligand **L** is synthesized by Schiff base condensation of two coumarin derivatives; the coumarin derivatives, $\mathbf{L_1}$ and $\mathbf{L_2}$, are synthesized in several steps.[14] All synthesized compounds are characterized by NMR, electrospray ionization mass spectrometry (ESI-MS), and elemental analysis. The magnesium complex, $Mg(\mathbf{L})(ClO_4)_2$, has also been synthesized and characterized by ESI-MS.[14]

All absorption and emission spectral studies are carried out in freshly purified MeCN at room temperature, while metal perchlorates are used as the source of metal ions. Metal-free **L** shows an absorption maximum at 488 nm with a shoulder at higher wavelength that is appreciably red-shifted with increased intensity in the presence of Mg(II) and Zn(II) and to a lesser extent in the presence of Li(I) and Ca(II) (Figure 1a). An isosbestic point is observed at 510 nm (Figure 1b) on recording the spectra with varying concentrations of Mg(II) ion, indicating 1:1 complex formation.

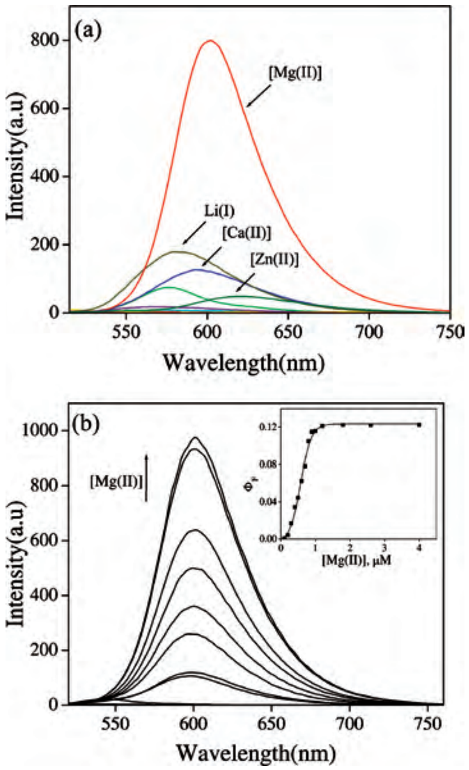


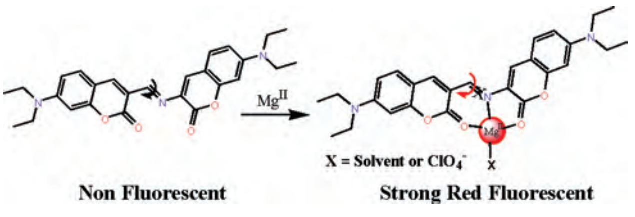
Figure 2. (a) Fluorescence intensity change of **L** (0.8 μM) upon the addition of various metal cations: 10 μM for Mg(II) and 10 mM for other metal ions. (b) Fluorescence spectra (λ_{ex} = 505 nm) of **L** (1.2 μM) at room temperature upon the addition of increasing amounts of Mg(II) ions (0–1.2 μM). Inset: Change of the quantum yield upon the addition of increasing [Mg(II)].

Table 1. Spectroscopic Data for **L** in the Presence of Different Cationic Input[a]

compound	λ_{max}, nm	λ_{em}, nm	ϕ^b	K_a, M^{-1}
L	488		0.0003	
L + Li(I)	505	583	0.010	2.0×10^4
L + Mg(II)	555	602	0.176	$1.1\ 24 > 10^6$
L + Ca(II)	510	596	0.010	6.0×10^4
L + Zn(II)	562	625	0.009	nd

[a] Excitation wavelengths were 505 nm for [**L**·Mg(II)] and 488 nm for the rest. Fluorescence maxima were obtained by taking [**L**] = 0.8 μM, [M^{n+}] = 10 μM for Mg(II), and 100 mM for Li(I) and Ca(II). [b] The quantum yield (ϕ) is calculated by taking standard fluorescein in 0.1 N NaOH (ϕ = 0.85).[16]

Scheme 2. Schematic Representation of Mg^{II}-Induced Fluorescence



In the absence of a metal ion, **L** does not show any noticeable emission when excited at 488 nm because the C=N isomerization is the predominant decay process[15] of the excited state. First-row transition-metal ions, Na(I), K(I), or heavy-metal ions such as Hg(II) and Pb(II), do not show any emission enhancement. On the other hand, the addition of Zn(II), Ca(II), or Li(I) shows very little emission response

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(Figure 2a). In contrast, the addition of Mg(II) affords a very high-intensity emission centering around 600 nm. The quantum yield values are collected in Table 1. The remarkable increase of the fluorescence quantum yield is due to inhibition of the C═N isomerization process[15] upon Mg(II) binding at the NO_2 site (Scheme 2). The solvent or perchlorate anion or a water molecule (perchlorate salts are hydrated) provides the fourth or higher coordination site.

It is presumed that, at the concentration of measurements, other metal ions either bind weakly or do not bind at all. Similar results are obtained upon changing the solvent to ethanol or THF. However, the emission response significantly decreases upon the addition of water and completely vanishes in 10% water (v/v). The solvent dependency of the emission response suggests that the water molecule is successively competing with the carbonyl oxygen of coumarin for coordination to the metal center, resulting in degradation of the emission response.

The fluorescence quantum yield steadily increases upon the addition of Mg(II), as shown in Figure 2b. The maximum is reached upon the addition of 1 equiv of the metal ion.

The association constants of the complexes between ligand **L** and metal cations are determined[17] from absorption and fluorometric titration data as a function of the metal ion concentration. The data (Table 1) show that **L** forms a more stable complex with Mg(II) compared to Ca(II).

In conclusion, we have designed a fluorescent probe **L** based on imine bond isomerization that gives very strong fluorescence upon the addition of Mg(II). The binding of Mg(II) is highly selective, allowing its detection in the presence of Ca(II), alkali metal, and a host of first-row transition-metal ions. We are presently working on other acyclic receptors with selectivity for particular metal ions.

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Supporting Information Available: Synthesis, spectroscopic characterization, fluorescence measurement, and Job's plot. This material is available free of charge via the Internet at http://pubs.acs.org.

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