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A ratiometric fluorescent sensor for Zn^{2+} based on internal charge transfer (ICT)

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Abstract—A ratiometric fluorescent chemosensor **5** was designed and synthesized based on internal charge transfer (ICT). The indicator absorbs and emits light in the visible wavelength range. In acetonitrile, blue shifts in fluorescent emission upon zinc binding are due to the formation of a 1:2 metal/ligand complex, which induced a fluorescent emission at 616 nm at the expense of the fluorescent emission at 672 nm.

The zinc ion is the second most abundant heavy metal ion[1] and well known to play an important role in cellular events including structural co-factors, regulator of enzymes, DNA binding, catalytic centers, and neuronal signal transmission.[2] However, zinc is a metal pollutant of the environment. Too much zinc may reduce the soil microbial activity causing phytotoxic effects[3] and it is a common contaminant in agricultural and food wastes.[4] Therefore, the detection of trace amounts of Zn^{2+} is a significant issue in environmental and biological analysis. A milestone in the development of chemosensor for Zn^{2+} was 6-methoxy-8-*p*-toluenesulfonamidoquinoline (TQS) which was first applied to detect Zn^{2+} in 1987.[5] However, the excitation wavelength of TQS and its derivatives was not in an optimal UV range.[6] Long-wavelength absorption and emission may be more useful for significantly reducing background absorption, fluorescence, and light scattering.[7]

The internal charge transfer (ICT) mechanism has been successfully utilized in chemosensors. The ratiometric technique has seen a widespread use in biological, polymeric, and sensory materials chemistry. The significant advantages of this technique include reduced artifacts,[8] increased precision,[8] and dynamic range,[9] with a built-in correction for environmental effects.[9] Consequently, the development of ratiometric Zn^{2+} chemosensors[10,8,11] has emerged as an important area of molecular design and synthesis.

Dipyrrin moieties (Fig. 1) have provided the basis for the boron-dipyrrin dyes,[12] which have been widely used as fluorescent labels.[13,14,7,15–17] Free base dipyrrins have also reacted with a wide range of metal salts to form the corresponding bis(dipyrrinato)metal(II) or tris(dipyrrinato)metal(III) complexes.[18] Hans Fischer et al.[19] have found that dipyrrins can form stable complexes with divalent metal ions, opening dipyrrins up to exploitation as metal chemosensors. Variation of the size of substituents (R^3) at the 5,5′ positions on dipyrrin **1** resulted in different configurations on formation of the metal complex, due to varying amounts of steric repulsion.[20,21] Thus, the increasing size of substituents at 5,5′ positions may result in a significant enhancement of selectivity for one cation. For example, **2** with 5, 5′ substituents as thiomethoxy groups was studied and did not afford the corresponding bis(dipyrrinato)zinc complex.[22]

We designed chemosensor **5** which has incorporated dipyrrin as an electron-donating domain and the hydroxyl group of the 8-hydroxyquinoline (8-HQ) moiety as an electron-withdrawing domain. Compound **5** was easily synthesized (Scheme 1) by condensation of 8-HQ-2- carbaldehyde and **4**.[23] Although 8-HQ has been widely used as ionophores for metal recognition,[23–31] **3** does not have a high binding affinity for Zn^{2+}.[23] We anticipated that the dipyrrin moiety of **5** would selectively bind Zn^{2+}. Furthermore, we expected that capture of Zn^{2+} by the dipyrrin would reduce the dipyrrin electron-donating ability and measurably influence

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Keywords: 8-Hydroxyquinoline; Dipyrrin; Ratiometric; ICT; Zn^{2+} ion; Chemosensor.

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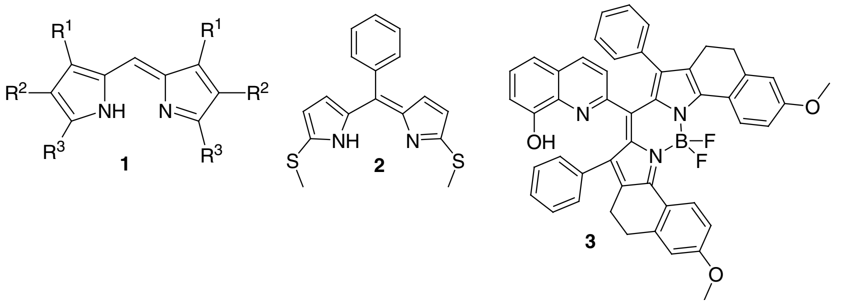
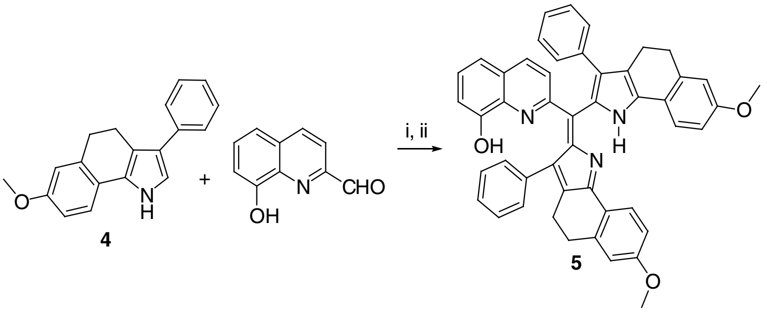


Figure 1. Dipyrrin based compounds.



Scheme 1. Synthesis of chemosensor **5**. TFA, DCM, 25 °C, N_2 (g); ii. *p*-chloranil, DCM, 25 °C, N_2 (g) overall yield 42%.

the emission properties. Chemosensor **5** has an absorption wavelength at 580 nm and an emission wavelength at 672 nm. Both absorption and emission wavelengths are in the visible region. Indeed, **5** in the presence of Zn^{2+} showed a 56 nm blue shift of fluorescence emission.

Fluorescence emission was monitored to determine the sensitivity of the **5** toward Zn^{2+} (Fig. 2). An acetonitrile solution of **5** (5 µM) was titrated with Zn^{2+}. Free **5** displays a band with maximum at 672 nm. With increasing concentration of Zn^{2+}, a decrease in fluorescence emission at 672 nm was observed, whilst the emission intensity at 616 nm increased. An isoemission point was also observed at 635 nm. These data are consistent with a 1:2 Zn^{2+}:**5** complex.

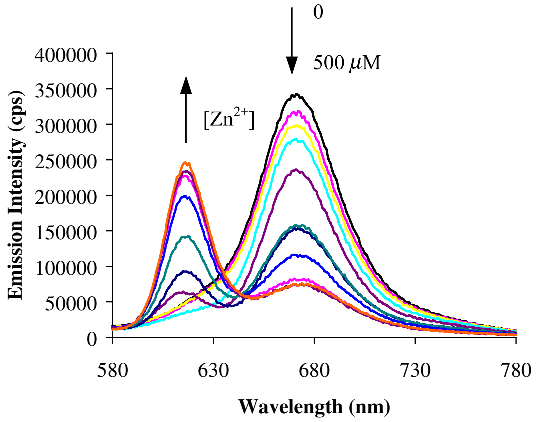


Figure 2. Fluorescence emission spectra of **5** in an acetonitrile solution in the presence of different concentrations of Zn^{2+} (0, 2.5, 5, 10, 20, 50, 100, 200, 300, 400, and 500 µM). Excitation wavelength was 550 nm. Emission wavelengths were 616 (which increased in intensity with concentration) and 672 nm (which decreased in intensity with concentration). The concentration of **5** was 5 µM.

Figure 3 shows the dependence of emission intensity ratios between 616 nm and 672 nm on the concentration of Zn^{2+}. Relatively low concentrations of Zn^{2+} (2.5, 5, and 10 µM) only slightly quenched the emission intensity and I_{616}/I_{672} remained unchanged at 0.14. With a 20 µM concentration of Zn^{2+} a clear new peak centered at 616 nm was observed and I_{616}/I_{672} increased to 0.27.

The selectivity of **5** was examined in an acetonitrile solution by titration of **5** with various metal ions (Fig. 4). The titration of Na^+, K^+, and Ca^{2+} did not affect the emission intensity, and Ni^{2+}, Mg^{2+}, Cd^{2+}, and Co^{2+} generated a 34%, 37%, 40%, and 43% quench of emission intensity, respectively. Since **3** showed no sensitivity to

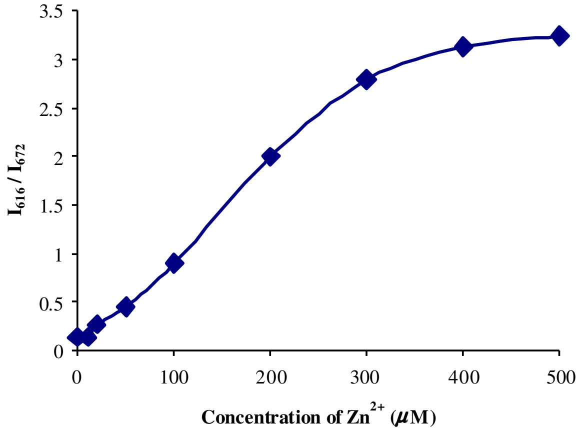


Figure 3. The plot of the fluorescence intensity ratio between 616 and 672 nm (I_{616}/I_{672}).

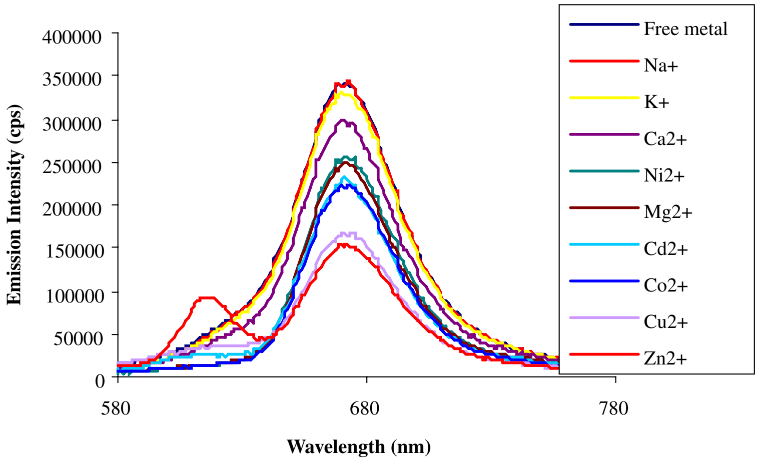


Figure 4. Fluorescence emission spectra of **5** (5.0 µM) in an acetonitrile solution in the presence of different metal ions (50 µM). Excitation wavelength was 550 nm. Emission wavelengths were 672 and 616 nm.

Ni^{2+}, Mg^{2+}, Cd^{2+} and Co^{2+},[23] the emission intensities were diminished due to their low affinity for the dipyrrin moiety of **5** which has large size of substituents at the α,α′ positions on dipyrrin moiety. In contrast to other metals, Cu^{2+} (50 µM) reduced emission (55%) to a similar degree as Zn^{2+} at the same concentration at 672 nm. However, no blue shift was observed in the Cu^{2+} binding experiment. This may be due to binding with the 8-HQ moiety[23] and leads to an increase in the electron-withdrawing ability of the hydroxyl group (balancing the effect of dipyrrin binding).

Prodi and co-workers[32] have found that a proton can transfer to amino group due to the decrease of pK_a values of the hydroxyl proton by chelation of metal ions. This transfer also can affect the fluorescence emission. The titration of 10 equiv TFA only slightly diminished the fluorescence emission, and this may be due to the difficulty of proton binding with the nitrogen of imine groups in dipyrrin moiety (Fig. 5).

In summary, we have presented a ratiometric fluorescent sensor for Zn^{2+} based on an internal charge transfer (ICT) mechanism. The obvious blue-shift emission upon addition of Zn^{2+} to **5** can be observed by optical responses, and it is attributed to the capture of Zn^{2+} by a dipyrrin moiety leading to a diminished electron-donating ability. Improvement in the solubility of **5** in water and the study of detail mechanism of complexation are underway.

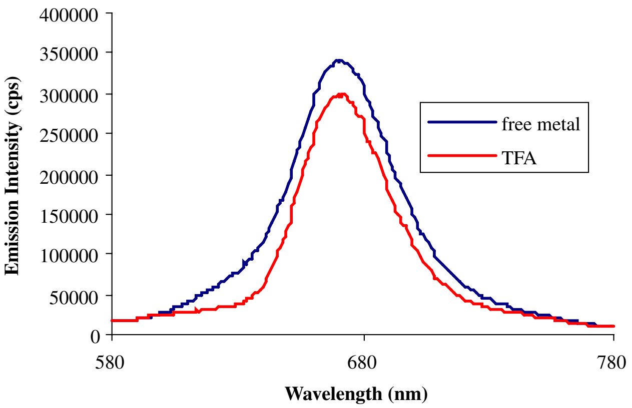


Figure 5. Fluorescence emission spectra of **5** (5.0 µM) in an acetonitrile solution in the presence of TFA (50 µM). Excitation wavelength was 550 nm. Emission wavelengths were 672 nm.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bmcl.2006.03.058.

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