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Cd(II) Sensing in Water Using Novel Aromatic Iminodiacetate Based Fluorescent Chemosensors

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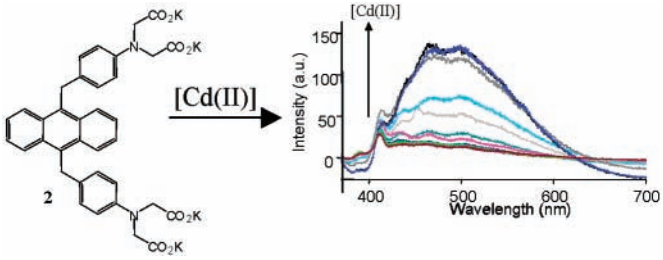
ABSTRACT



Compounds 1 and 2 were designed as fluorescent chemosensors for Cd(II). For both, a selective determination of Cd(II) over Zn(II) was achieved. The fluorescence emission of both was pH-independent and *switched off* between pH 3–11 in 100% water. Whereas the recognition of Cd(II) at pH 7.4 gave rise to the formation of charge-transfer complexes (exciplexes) for both (λ_{max} ca. 500 and 506 nm, respectively), the recognition of Zn(II) only *switched on* the (monomeric) anthracene emission of 2, while for 1 it was red-shifted (λ_{max} = 468 nm).

The developments of luminescent chemical devices is an active field of research in supramolecular chemistry.[1,2] An important area within this field is the development of luminescent chemosensors.[2] Such sensors have the advantage of possessing high sensitivity and selectivity, as well as providing on-line and real-time analysis that has revolutionized the field of chemical analysis, particularly in critical care analysis of blood and serum samples.[3,4] Of the many literature cases reported, only a few examples of fluorescent chemosensors for Cd(II) have been described.[5] Cadmium is currently used in many processes such as the production of nickel−cadmium rechargeable batteries for cellular phones[6] and is also found in phosphate fertilizers. Because of the

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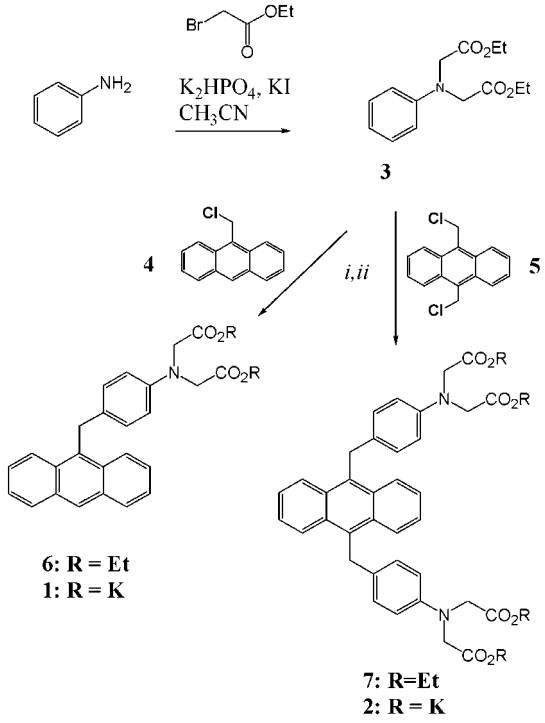
toxicity of the metal, the use of cadmium has several environmental impacts,[7] and as lithium-based batteries become common, this gives rise to an increased level of disused cadmium batteries, with an increased environmental effect.[6] Consequently the uptake of Cd(II) has increased in humans in recent times,[8] where it can have several physiological effects as it can accumulate in organs such as the kidney, thyroid gland, and spleen.[8] It is thus important to be able to monitor such uptake in humans as well as in the environment by employing simple responsive chemosensors.

We are interested in the development of luminescent devices such as switches,[9] chemosensors,[10] and logic-gates.[11] Herein we describe the design, synthesis, and photophysical properties of two new fluorescent chemosensors for Cd(II), **1** and **2**. Several researchers have recently developed potential chemosensors for Cd(II).[5] However, the drawback to all of these was the use of receptors consisting of aliphatic amines that are easily protonated under physiological conditions. Moreover, the Cd(II) selectivity in water was not fully demonstrated for many of these examples. Our sensors **1** and **2** are based upon the *fluorophore-spacer-receptor* and *receptor-spacer-fluorophore-spacer-receptor* models developed by de Silva for PET (photoinduced electron transfer) sensors.[12] Here we have selected anthracene[12] as a fluorophore, and a simple aromatic iminodiacetate (shown in its ester form in **3**) as the receptor.[13] As the receptor is aniline-based, we foresaw that it could be used either under physiological conditions or for detection of soil samples, as the protonation of the receptor nitrogen moiety would only occur under high acidic conditions.[14] Moreover, the use of this simple design would overcome interferences from other physiologically important cations such as Mg(II) and Ca(II),[13] and the use of potassium salts of the carboxylates impart high water solubility to **1** and **2**.

The synthesis of **1** and **2** is shown in Scheme 1.[15] Both sensors utilize the same receptor and fluorophore moieties, and **1** and **2** were obtained easily in two-step syntheses from

Scheme 1. Syntheses of the Two Chemosensors **1** and **2**[a]



[a] Reagents: (i) $AlCl_3$, $CHCl_3$; (ii) Koh, H_2O, MeOH.

3 in good yield. The phenyl iminodiester **3** was made in a single step by reacting aniline with ethyl bromoacetate using potassium dihydrogen phosphate as a base in acetonitrile in 89% yield. This was followed by Friedel−Craft alkylation of **3** with 9-chloro-methylanthracene,[14b] **4**, giving the diethyl ester **6** in 60% yield. Similarly, **2** was made by reacting **3** with 9,10-bischloromethylanthracne,[16] **5**, under identical conditions, yielding the desired product **7** in 58% yield after flash column chromatography. The final products were obtained by alkaline ester hydrolysis of **6** and **7** using aqueous KOH in refluxing MeOH solution, yielding **1** and **2** in 92% and 90% yields, respectively, after precipitation from the cold solution.

The ground and the excited-state properties of **1** and **2** were investigated in water and at pH 7.4 in buffered HEPES solution in the presence of 0.135 M of NaCl to maintain constant ionic strength. First, the response of **1** and **2** toward pH was investigated. The changes in the fluorescence emission spectra of **2** as a function of pH are shown in the Supporting Information ($\lambda_{ex} = 370$ nm). Here the emission was completely switched off upon treating an acidic solution of **2** (pH ~1) with diluted NaOH solution. This switching was fully reversible. The concomitant changes in the absorption spectra of **2** were, however, only minor. This is a typical PET effect,[12] where the excited state of the

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(15) Calculated for **1** ($C_{25}H_{19}K_2NO_4 \cdot 2H_2O$): C, 58.69; H, 4.53, N, 2.74. Found: 57.80; H, 4.33; N, 2.56. Calculated for **2** ($C_{36}H_{28}K_4N_2O_8 \cdot 3H_2O$): C, 52.28; H, 4.14; N, 3.39. Found: C, 52.46; H, 4.02; N, 3.23. See Supporting Information for more details.

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anthracene is quenched by electron transfer from the receptor unit causing the *switching off*.[12] Similar results were observed for **1**. For **2** a pK_a of ca. 2.4 ± 0.1 was determined from these changes, whereas for **1**, a pK_a of 2.0 ± 0.1 was determined.[17] From these results it is clear that the emission is pH-independent in a physiological pH range.

The ability of **1** and **2** to recognize group II and various transition metal ions was investigated at pH 7.4. Using Mg(II) and Ca(II), no changes were observed in the fluorescence emission spectra, indicating that the simple receptor was not coordinating to the ions to prevent PET quenching.[13,17] When using transition metal ions such as Co(II), Ni(II), Cu(II), Zn(II), Cd(II), and Hg(II) (as their Cl^-, NO_3^-, or ClO_4^- salts), only Zn(II) and Cd(II) gave rise to any significant changes in the fluorescence emission spectra. Consequently the ability of **1** and **2** to recognize these ions was further investigated. Upon titrating **2** at pH 7.4 (I = 0.135 M NaCl) using Zn(II), the fluorescence was *switched on*, Figure 1, with large

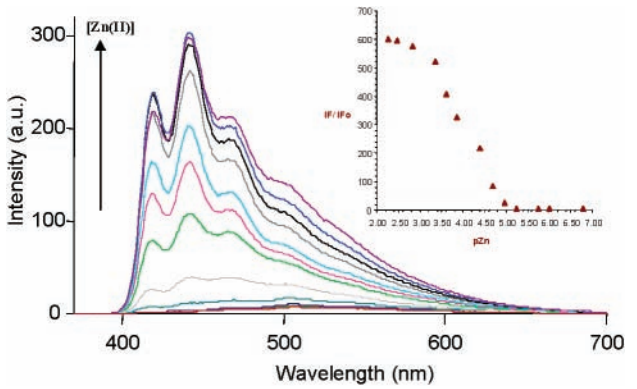

Figure 1. Changes in the fluorescence emission spectra of **2** at pH 7.4, as a function of added Zn(II) concentration, upon excitation at 370 nm. Insert: relative fluorescence changes at 415 nm as a function of pZn (pZn = −log[Zn(II)]).

fluorescence enhancements in a similar manner as seen for the above pH titration. Minor bathochromic changes were observed in the absorption spectra. Hence, only the emission intensity changed as a function of Zn(II), indicating that the Zn(II) ion was able to coordinate to the carboxylates as well as the aniline nitrogen and increase the oxidation potential of the receptors in **2**, in a usual PET fashion.[12,13,17,18] From the relative fluorescence changes at 415 nm as a function of pZn (pZn = −log[Zn(II)]), a sigmoidal curve was observed, which switched on over two logarithmic units between pZn ≈ 5−3 (Figure 1 insert). From these changes a binding constant log β of 3.8 ± 0.1 was determined. When these titrations were repeated using **1**, the emission spectra were, however, very different from that observed for **2**, as is evident from Figure 2. Here, the (monomeric) anthracene emission

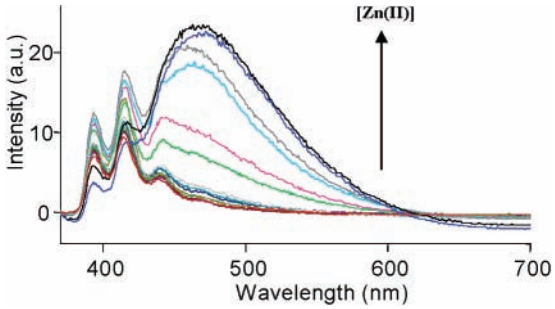

Figure 2. Uncorrected changes in the florescence emission spectra of **1** as a function of [Zn(II)] at pH 7.4, λ_{ex} = 360 nm.

was only slightly enhanced upon ion recognition, with the formation of a new structureless band centered at 468 nm. We suggest that these changes are due to the formation of a bound receptor charge transfer complex, or an exciplex, between the Zn(II) moiety and the anthracene that is highly luminescence at long wavelengths.[19] From the changes at 468 nm, as a function of pZn, we obtained a sigmoidal curve, which changed over 2 pZn units. From these changes we determined log β of 3.8 ± 0.15, for the binding of Zn(II) to **1**. Unlike that seen for **2**, the concomitant changes in the absorption spectra (though only minor) showed that the anthracene vibrational bands were bathochromically shifted with isosbestic points at 370, 385, and 410 nm for **2**.

However, the most interesting results were observed when **1** and **2** were titrated with Cd(II), as the emission spectra of both were reminiscent of that seen for **1** when titrated with Zn(II), as is evident from Figure 3, for **2**. For **2**, only minor

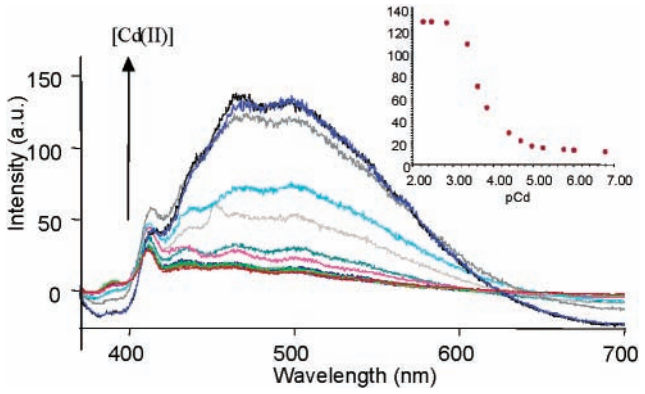

Figure 3. Changes in the fluorescence emission spectra of **2** upon titration with Cd(II) at pH 7.4. λ_{ex} = 370 nm. Insert: changes in the relative intensity at 500 nm as a function of pCd.

changes were seen in the monomeric emission, which was reduced, with large concomitant changes at long wavelengths, where again a rather structureless band was observed

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centered at ca. 500 nm. Similar results were seen for **1**, with a narrower band centered on 506 nm, Figure 4. Furthermore,

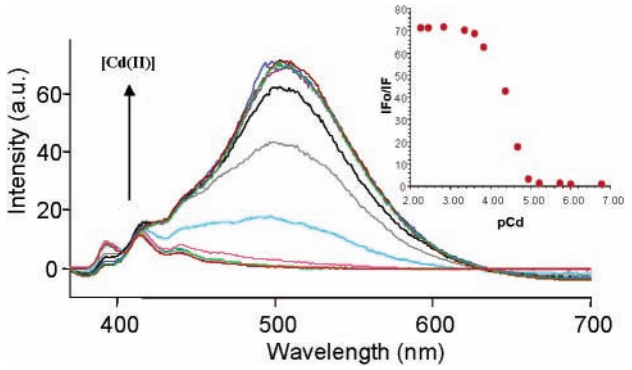

Figure 4. Changes in the fluorescence emission spectra of **1** upon titration with Cd(II) at pH 7.4, $\lambda_{ex} = 360$ nm. Insert: changes in the relative intensity at 506 nm as a function of pCd.

whereas the absorption spectra of **2** was slightly bathochromically shifted, the absorption spectra of **1** was reduced in intensity by ca. 10% upon addition of 6 μM $\rightarrow$ 2 mM of $CdCl_2$. When these measurements were repeated using the esters **6** or **7**, no fluorescent enhancements were observed, signifying that neither were binding to either Zn(II) or Cd(II).

Plotting the relative changes in the 500 nm band for **2**, as a function of pCd (pCd $= -\log$[Cd(II)]), gave a sigmoadal curve that changed over 2 pCd units. From these changes a binding constant log β of 3.9 $\pm$ 0.1 was determined. For **1**, similar results were observed, with log β of 4.2 $\pm$ 0.1. Once more, we suggest that these changes are due to the formation of charge-transfer complexes between the anthracene moiety and the bound receptors. Both Yoon et al. and Czarnik et al. have reported that they observed red shifts in the fluorescence emission spectra of anthracene-based sensors upon interactions of aliphatic receptors with Cd(II).[5c,h] They concluded that indeed this was due to the formation of a π-complex, which subsequently gives rise to the formation of a σ-complex. In both cases the emission was centered around 446 nm, which is a substantially smaller shift than seen for both **1** and **2** upon Cd(II) recognition. Even though we do not envisage that such direct σ-complex interaction is occurring for our sensors, purely as a result of steric effects, the formation of the long emitting emission bands for both **1** and **2** suggests strong π-complex interactions.

As can be seen from the above results, both sensors display moderate selectivity for Cd(II) over Zn(II). To investigate the ability of these sensors to recognize Cd(II) in the presence of Zn(II), we carried out Cd(II) titrations on **1** and **2** in the presence of high concentrations of Zn(II). On both occasion a selective detection of Cd(II) was possible. This was particularly noticeable for **2**, which only showed a monomeric emission in the presence of Zn(II). However, upon Cd(II) addition the fluorescence emission spectra was found to be shifted to longer wavelengths, Figure 5.

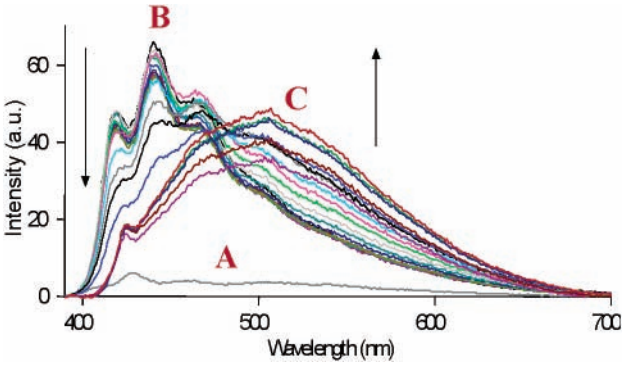

Figure 5. Changes in the florescence emission spectra of **2** at pH 7.4, in the presence of Zn(II) upon titration with Cd(II), [Cd(II)] = 0 M $\rightarrow$ 2 mM: (A) free sensor **2**; (B) after addition of Zn(II) [Zn(II)] = 3 mM; (C) in the presence of of Cd(II).

In summary, we have developed two new fluorescent chemosensors **1** and **2**, which have good water solubility, are pH-independent in the physiological pH range, and show sufficient selectivity and photophysical changes upon ion recognition to allow for the selective sensing of Cd(II) over Zn(II) at pH 7.4.

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Supporting Information Available: Synthesis and ^{1}H and ^{13}C NMR of **1** and **2**, pH fluorescence, and Zn(II) and Cd(II) absorption titrations of **1** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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