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An acenaphthopyrrolone-dipicolylamine derivative as a selective and sensitive chemosensor for group IIB cations

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Abstract—The recently reported acenaphthopyrrolone (ACNP) class of fluorophores have remarkably bright emission in the red end of the visible spectrum. We demonstrated that straightforward derivatization with 2-aminoethyl-dipicolylamine yields a selective and sensitive chemosensor for Zn(II), Cd(II) and Hg(II) ions. Further modifications could result in water-soluble derivatives, with practical applications in intracellular imaging of Zn(II) concentrations.
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Selective sensing and signalling of metal ions is an attractive goal considering the biological and environmental implications.[1] Metal ions, such as Cd(II) and Hg(II), are environmental pollutants, and Zn(II) is involved in a number of biological processes like Alzheimer's,[2] and diabetes[3] and in the plant kingdom in a large number of regulatory processes.[4] Regulation of zinc uptake has been linked to human prostate cancer in a recent study.[5] Therefore, sensing and preferential visualization of these ions is of prime importance.[6] As a research group involved in chemosensor design,[7] we are also very interested in the application of novel fluorophores in this field. Thus, a recently reported fluorophore,[8] acenaphthopyrrolone derivative **1** attracted our attention. These acenaphthopyrrolone dyes were shown to emit in the red region of the spectrum (610 nm) with good quantum yields and very good opportunities for straightforward derivatization. The skeletal structure is highly electron deficient, and nucleophilic aromatic substitution is very favorable.

Acenaphthopyrrolone dyes can be obtained in two steps from commercially available precursors with some improvements on the literature procedure.[8] Thus, acenaphthaquinone was reacted with malononitrile in aceto- nitrile at reflux overnight. On cooling to room temperature, the precipitated material was collected by filtration. The intermediate compound was not further purified, but directly transformed into compound **1** by refluxing in acetonitrile in the presence of a catalytic amount of anhydrous K_2CO_3. As the ligand to tether to the core, we chose a very common structural motif **2**, which is used in a large number of zinc chemosensors,[9] derived from dipicolylamine (DPA). The addition of an aminoethyl moiety to DPA is expected to increase the binding, affinity and supply a primary amine for nucleophilic substitution of the core.

The target chemosensor **3** was synthesized by the overnight reaction of 2-aminoethyl-dipicolylamine with compound **1** in acetonitrile at room temperature. The reaction product was purified by silica gel column chromatography ($CHCl_3$–MeOH, 85:15). Satisfactory analytical data was obtained for compound **3**, which was in accord with the expected structure.[10]
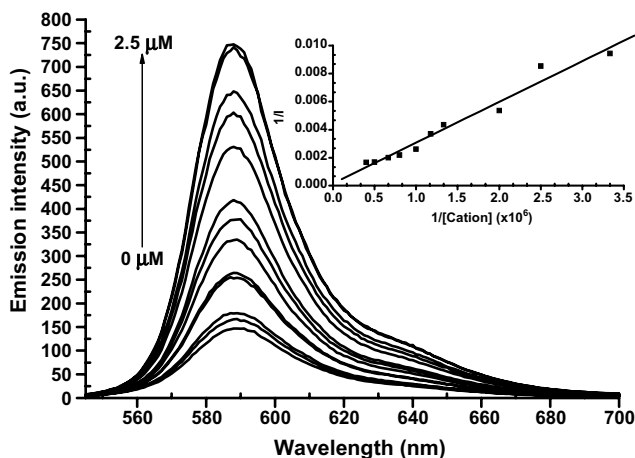
The absorption spectrum of compound **3** in acetonitrile is shown in Figure 1. The spectrum shows one peak in

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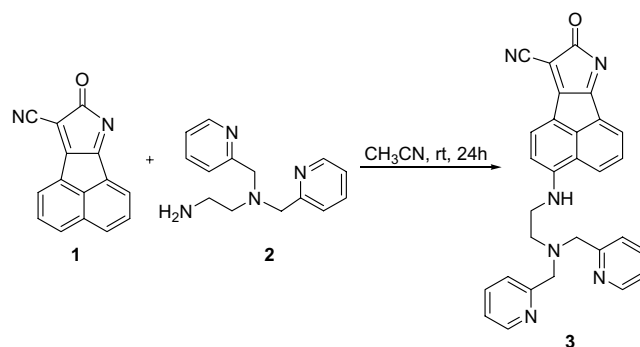
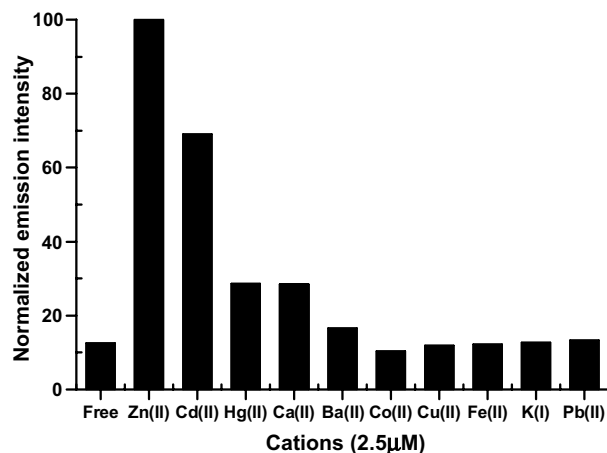* Corresponding author. Tel.: +90 312 210 5126; fax: +90 312 210 1280; e-mail: akkayaeu@metu.edu.tr
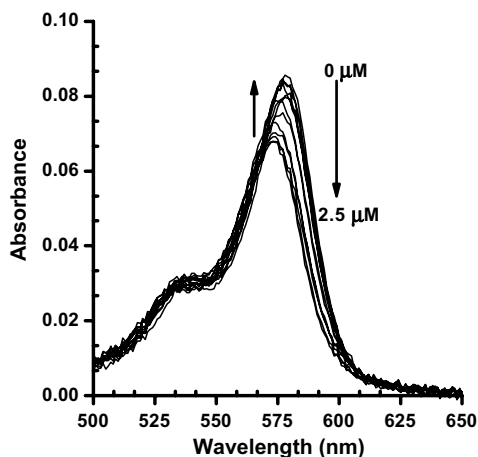
Figure 1. The absorption spectrum of the fluorescent chemosensor **3** $(2 \times 10^{-6}$ M) in acetonitrile in the presence of zinc(II), added as the perchlorate salt.

Figure 2. The emission spectrum of the chemosensor **3** $(2 \times 10^{-6}$ M) in acetonitrile in the presence of increasing concentrations of zinc(II), added as the perchlorate salt. The excitation wavelength was 535 nm with 5 nm slit widths. Inset: The Benesi–Hildebrand plot of the emission data.

Figure 3. The emission intensity of the chemosensor **3** $(2 \times 10^{-6}$ M) in the presence of 2.5 μM metal ions in acetonitrile solutions. The data were normalized to 100 for the most emissive Zn(II)-**3** complex.

the visible region at 578 nm. Addition of zinc(II) into purple solutions of the chemosensor **3** causes a small hypsochromic shift of 15 nm. This is in accordance with the internal charge transfer (ICT) linked sensing action of the chemosensor.[11] The emission spectrum was also studied (Fig. 2). When excited at the shoulder at 535 nm, the emission intensity at the peak emission wavelength of 588 nm increases 7-fold on changing the concentration of Zn(II) from 0 to 2.5 μM.

The selectivity of the interaction was also studied using a series of metal ions in addition to Zn(II): Cd(II), Hg(II), Ca(II), Ba(II), Co(II), Cu(II), Fe(II), K(I) and Pb(II) (Fig. 3). Not surprisingly, fluorescence enhancements were found in the presence of other group of IIB cations, namely, Cd(II) and Hg(II). Benesi–Hildebrand analysis of the binding data revealed strong association constants: 2.3×10^6 for Zn(II), 5.4×10^5 for Cd(II) and 2.9×10^6 for Hg(II), all in M^{-1}. It is also interesting to

note that Ca(II) and Ba(II) cause small enhancements of the emission intensity as well. We believe that these cations most likely target the other side of the molecule and interact with the carbonyl and cyano-functions.[12] Small bathochromic shifts in the presence of these cations also suggest this possibility. The chemosensor is likely to operate by the inhibition of photoelectron transfer quenching upon metal binding, since transfer from the DPA nitrogen is likely to be the dominant means of quenching in the unbound form.

In aqueous solutions however, the fluorescent chemosensor has a tendency to aggregate even at low concentrations. The solubility can be improved by the placement of additional ionic or polar functional groups on the parent structure. Yet, it is clear that the binding affinity is very high, even in highly polar acetonitrile solutions.

Thus, we report the first chemosensor application of a novel and promising acenaphthopyrrolone based fluorophore. Further work on this type of compounds is likely to yield novel chemosensors with practical applications. Work to this end is in progress in our laboratory.

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10. Selected characterization data: ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.73 (br, 1H), 8.97 (d, $J = 7.7$ Hz, 1H), 8.70 (d, $J = 7.8$ Hz, 1H), 8.48–8.45 (m, 2H), 8.02–7.94 (m, 2H), 7.60–7.55 (m, 2H), 7.42 (d, $J = 7.7$ Hz, 2H), 7.20–7.15 (m, 2H), 6.98 (d, $J = 9.2$ Hz, 1H), 3.91 (s, 4H), 3.80–3.75 (t, $J = 6.0$ Hz, 2H), 2.95–2.91 (t, $J = 6.0$ Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.0, 165.0, 164.6, 156.2, 148.7, 147.5, 139.1, 136.2, 126.2, 125.8, 125.4, 124.8, 124.6, 124.1, 123.8, 123.4, 120.9, 115.9, 113.0, 108.9, 60.2, 52.9, 47.7; Elemental analysis: Found: C, 73.84; H, 4.78; N, 17.99%. $C_{29}H_{22}N_6O$ requires C, 74.03; H, 4.71; N, 17.86%.
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