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A selective fluorescent sensor for Zn²⁺ based on aggregationinduced emission (AIE) activity and metal chelating ability of bis(2-pyridyl)diphenylethylene[†]

Moustafa T. Gabr and F. Christopher Pigge*

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Polypyridyl ethylenes have been prepared as heterocyclic analogues of tetraphenylethylene. In addition to conventional AIE effects, a derivative possessing a 1,1-bis(2-pyridyl)ethylene fragment displays Zn^{2+} -selective enhanced fluorescence in aqeuous solution, in contrast to the behavior of isomeric bis(3and 4-pyridyl)ethylenes. The Zn^{2+} -sensing capability of this material is attributed to formation of chelated Zn^{2+} -bis(pyridyl) complexes and is supported by the X-ray crystal structure of a bis(2-pyridyl)ethylene-Zn(OAc)₂ complex.

The development of fluorescent sensors and/or detectors capable of signalling the presence of specific analytes or chemical events remains an important objective in both materials and biological chemistry.¹ Luminophores that exhibit "turn-on" fluorescence are particularly desirable, and in this context organic fluorophores that display aggregation-induced emission (AIE) or aggregation-induced enhanced emission (AIEE) are emerging as valuable building blocks for sensor design across a range of disciplines.²

AlE active compounds are typically non-fluorescent in dilute solution but become emissive upon aggregation in the presence of poor solvents.³ Emissive properties of AlE active compounds are often observed in the solid state as well. This behaviour contrasts with that of many conventional organic dyes that exhibit fluorescence quenching at high concentration or when forced to aggregate in solution. The origin of enhanced emission in many AlE-active compounds is believed to stem from restriction of intramolecular motions (e.g., sp²-sp² bond rotations) when individual molecules are present as nano-aggregates or in condensed phases.⁴

Tetraphenylethylene (TPE) is an iconic example of an AIEactive compound whose fluorescence can be switched on as a function of molecular environment. A number of TPE derivatives have been investigated for use as fluorescent indicators, particularly in bioanalytical settings in which the AIE response has been used to signal the presence of targeted analytes, such as specific organic or biomolecules and metal ions.⁵ The TPEs employed in these studies generally feature substituents that mediate aggregation events grafted onto the periphery of an intact tetraphenylethylene core. In contrast, AIE-based compounds that possess functionality in the form of one or more heterocyclic rings in place of the core phenyl rings are much less investigated.⁶

We are developing concise synthetic routes to heteroaromatic tetraarylethylenes and examining the AIE properties of these new small-molecule organic luminophores. For example, we recently reported the synthesis and characterization of bis(pyridyl)-tetraarylethylenes 1 and 2 (Scheme 1).⁷ While both compounds displayed typical AIE fluorescence profiles (weak emission in CH₃CN that increased significantly upon addition of H₂O), neither compound showed a fluorescence response when combined with various metal ions, despite the presence of potential pyridine ligands. Consequently, we have redesigned these bis(pyridyl) TPE analogues to incorporate heteroarenes capable of acting as chelating ligands toward a metal center with the aim of eliciting a metal-selective AIE response. We report here the synthesis and characterization of three new 2,2'-bis(pyridyl) tetraarylethylenes (4-6) and the ability of these compounds to function as fluorescent metal ion sensors selective for detection of Zn²⁺ ions in aqueous solution.



Scheme 1 Synthesis of 2,2'-bis(pyridyl) tetraarylethylenes 4-6

The synthesis of 2,2'-bis(pyridyl) tetraarylethylenes **4-6** is illustrated in Scheme 1 and is similar to the straightforward procedures we reported previously for the preparation of **1** and **2**.^{7,8} Briefly, 2,2'-bis(pyridyl) ketone was converted to **3** upon treatment with CBr_4/PPh_3 . Double Suzuki coupling between **3** and an aryl boronic acid then afforded **4-6** in good

Department of Chemistry, University of Iowa, Iowa City, Iowa 52242, USA. E-mail: chris-piqge@uiowa.edu

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yields. The aryl boronic acids employed in this study were selected to highlight the ease with which both simple and electronically distinct arenes (phenyl and substituted phenyl) as well as more elaborate arenes (e.g., dibenzothiophene) can be incorporated into the final products.

The fluorescence properties of 4-6 were next examined in CH₃CN (a solvent in which all three compounds dissolve easily) and CH₃CN/H₂O mixtures (4-6 are insoluble in H₂O). The fluorescence spectra of 4 in various combinations of CH₃CN/H₂O are shown in Figure 1A. In 100% CH₃CN 4 exhibits a fluorescence emission at 447 nm that decreases upon addition of H₂O. Concomitantly, a new blue-shifted emission peak appears at 378 nm that increases in intensity as a function of added H₂O (Figure 1B). The shift to higher energy emission upon aggregation likely reflects a change in molecular shape from a more planar conformation when highly solvated to a more propeller-like arrangement of the aryl rings in multimolecular aggregates.⁹ In contrast, **5** exhibits weak emission in CH₃CN at 451 nm that becomes red shifted upon addition of H₂O. The AIE effect in 5, however, is much less pronounced compared to 4 (see ESI, Figure S6). Finally, 6 exhibits more or less conventional AIE behaviour with a significant increase in fluorescence emission observed in 9:1 H₂O:CH₃CN (Figure S7).



Figure 1 (A) AIE profile of 4 in CH₃CN/H₂O mixtures. (B) Change in fluorescence intensity at 378 nm as a function of added H₂O. λ_{ex} = 317 nm, [4] = 10 μ M

The effect of added metal ions on the fluorescence of 4-6 was then examined. Figure 2A shows a series of fluorescence spectra of 4 obtained in 9:1 H₂O:CH₃CN in the presence of 2 equivalents added metal ions (as ClO₄ salts). The addition of Zn²⁺ elicited a markedly enhanced emission at 378 nm that far surpassed the effect of any other metal ion examined (Mg^{2+}) , Ca²⁺, Ba²⁺, Co²⁺, Cd²⁺, Pb²⁺, Cu²⁺, Ni²⁺, Hg²⁺, Fe³⁺, Fe²⁺, Mn²⁺, $Na^{^{+}}\!\!\!\!\!\!$, and $K^{^{+}}\!\!\!\!\!$). This is significant as $Zn^{2^{+}}$ is one of the most abundant metal ions in the environment and is an essential element in living organisms. As a result, new and selective capable of detecting and/or sensors monitoring Zn²⁺ concentration in aqueous solution are highly desired.¹⁰ A

plot showing the change in fluorescence intensity of 4 as a function of added Zn²⁺ is provided in Figure 2B. The emission rapidly increases with increasing amounts of Zn²⁺ until a plateau is reached at ~ 4 equivalents added $Zn(ClO_4)_2$. This effect is also reflected in a threefold change in quantum yield $(\Phi_{378}$ = 9.1% in 9:1 H₂O:CH₃CN increasing to 31.9% in the presence of 2 equivalents Zn^{2+}).¹¹ The selectivity of **4** toward Zn^{2+} ions is evident from the graph in Figure 2C. The fluorescence at 378 nm is normalized to $\mathbf{4} + Zn^{2+}$, and only the presence of Cd²⁺ was observed to produce any other notable emission enhancement. Furthermore, most other metal ions were found not to interfere with emission enhancement of 4 in the presence of Zn^{2+} with the exception of Cu^{2+} and, to a lesser extent, Fe³⁺. Compound **4** also displays high sensitivity toward Zn²⁺ under these conditions with the limit of detection determined to be ~94 nM (ESI Figure S8).



Figure 2 (A) Fluorescence spectra of **4** in the presence of various metal ions (2 equivalents). Inset: Picture taken under UV light of **4** in 9:1 H₂O:CH₃CN with no Zn²⁺ added (left) and 2 equivalents of Zn²⁺ (right). (B) Change in fluorescence intensity (I/I₀) at 378 nm of **4** as a function of added Zn²⁺. (C) Emission of **4** in the presence of various metal ions and Zn²⁺-metal ion combinations (normalized to emission in the presence of Zn²⁺). $\lambda_{ex} = 317$ nm, **[4]** = 10 μ M

The effect of Zn^{2+} counterion on fluorescence was also probed. As shown in Figure 3A, emission enhancement of **4** in the presence of $Zn(ClO_4)_2$, $Zn(OAc)_2$, and $ZnCl_2$ were similar,

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with $Zn(NO_3)_2$ exhibiting a diminished effect. To gauge whether these differences might be due to protonation of **4** under these conditions, the fluorescence spectrum was obtained in 1M aqueous HCI (ESI Figure S9).¹² The emission of **4** was observed to red-shift (λ_{em} ~430 nm) relative to fluorescence in 9:1 H₂O:CH₃CN, thus pyridine protonation does not appear to be contributing to the fluorescence response in the presence of metal salts. The effect of pH on Zn²⁺ binding by **4** was also probed and maximum emission enhancement was observed between pH ~4 – 9 (Figure 3B). Thus **4** is capable of Zn²⁺ sensing at physiologically relevant pH.



Figure 3 (A) Fluorescence spectra of 4 in the presence of Zn^{2+} with different counterions. (B) Fluorescence intensity (378 nm) of 4 in the absence and presence of Zn^{2+} (2 equiv) as a function of pH. λ_{ex} = 317 nm, [4] = 10 μ M

To obtain insight into structural features that might contribute to fluorescence enhancement in this system, a single crystal X-ray structure of 4·Zn(OAc)₂ was obtained. The molecular structure of the coordination complex is illustrated in Figure 4. The Zn²⁺ ion exhibits a distorted tetrahedral coordination geometry with two N donors from the pyridine rings and two acetate O donors. One acetate ligand exhibits a weak bidentate coordination mode with one Zn - O distance significantly shorter than the other (2.032 Å and 2.313 Å). The Zn – O distance to the monodendate acetate and the Zn – N distances are typical for Zn²⁺ complexes of this type (see ESI). Indeed, the structure resembles the asymmetric unit found in the crystal structure of Zn(OAc)₂ with tetra(2-pyridyl)ethane and tetra(2-pyridyl)ethylene ligands.¹³ As envisioned, the tetraarylethylene 4 functions as a chelating bidendate ligand toward the metal center with the Zn²⁺ ion coordinated below the plane of the ethylene unit (torsion angles between the pyridine rings and the alkene are 53.80° and 57.25°). Formation of similar solution-phase chelated complexes in aggregates of 4 would further restrict intramolecular pyridine

– ethylene bond rotation and produce enhanced fluorescence. A Job plot constructed from NMR titration of **4** and $Zn(ClO_4)_2$ in 1:1 $D_2O:CD_3CN$ indicated a 1:1 binding stoichiometry (ESI Figures S10-S11), consistent with the solid state structure. The absence of enhanced emission in the presence of metals other than Zn^{2+} may reflect an inability to form similar chelated adducts with these ions.



Figure 4 Molecular structure of 4.Zn(OAc)₂.

The behaviour of **5** in the presence of Zn^{2+} qualitatively mirrors that of **4**. The fluorescence spectra of **5** obtained in the presence of various metal ions is shown in Figure S12 (ESI). A selective fluorescence enhancement was observed in the presence of Zn^{2+} (and Cd^{2+}), but other metals produced little to no change in emission. Added Zn^{2+} continued to increase fluorescence emission up to ~4 equivalents, after which additional Zn^{2+} had little effect (Figure S13). Most other metals (with the exception of paramagnetic Cu^{2+}) were also found not to interfere with fluorescence of $5/Zn^{2+}$ (Figure S14). In contrast, addition of metal ions to **6** in 9:1 H₂O:CH₃CN did not produce any fluorescence enhancement (Figures S15-S16). We attribute this to steric effects from the dibenzothiophene groups that impede pyridine-metal interaction.

Differences in metal ion-mediated enhanced fluorescence in 4 compared to the 4-pyridyl and 3-pyridyl isomers 1 and 2 highlights the ability to alter AIE sensing properties of heteroaromatic tetraarylethylenes through synthetic modification. Among these three compounds, the potential to form chelated metal ion interactions in 4 appears to be important in governing fluorescence response compared to 1 and 2, which are both incapable of metal chelation. The addition of Zn²⁺ to these heteroarylethylenes was performed under conditions in which the organic substrates were already aggregated (9:1 H₂O:CH₃CN solution). Thus, formation of a chelated adduct in 4 would serve to further rigidify the molecular framework by placing additional restraints on intramolecular bond rotation, thereby resulting in enhanced fluorescence. In the case of 1 and 2, intercalation of metal ions such as Zn²⁺ into aggregated assemblies may afford intermolecular coordination complexes without concomitant increases in molecular rigidity, resulting in an attenuated fluorescence response.

To explore this issue further and to expand the range of heteroaromatic tetraarylethylenes, we prepared the symmetrical tetrapyridylethylenes **9** and **10** via Suzuki coupling of pyridine boronic acids and geminal dibromoethylenes **7** and **8** (Scheme 2). We envisioned that the additional pyridine rings

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in 9 and 10 would contribute to formation of more highly "cross-linked" coordination aggregates in the presence of metal ions, resulting in altered (increased) fluorescence. Hetero-TPE analogues 9 and 10 exhibited conventional AIE luminescence in CH₃CN/H₂O mixtures, similar to the behaviour of 1 and 2. Addition of metal ions to aqueous solution phase aggregates of 9, however, elicited only a small fluorescence enhancement in the case of Zn²⁺. Similar experiments performed with 10 showed little to no fluorescence enhancement (Figures S19-S22). Thus, the results with 9 and 10 seem to further implicate the importance of chelated coordination complexes for enhanced emission under aqueous conditions. Despite the absence of effective metal ion sensing, the potential tetracoordinate ligand framework embodied in AIE-active 9 and 10 renders these compounds attractive building blocks for other applications in supramolecular chemistry.



Scheme 2 Synthesis of tetrapyridylethylenes 9 and 10.

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In conclusion, a convenient synthetic approach to AIE active poly(pyridyl) tetraarylethylenes is reported. A subset of these compounds possessing a 1,1-bis(2-pyridyl) ethylene fragment (i.e., 4 and 5) exhibit Zn^{2+} -selective aggregation-induced enhanced emission in 9:1 H₂O:CH₃CN solution that is not exhibited in isomeric 3- and 4-pyridyl tetraarylethylenes. The ability of 4 and 5 to form chelated coordination complexes with Zn²⁺ ions, as confirmed through X-ray crystallography, is believed to be important in governing the fluorescence response. "Turn-on" luminescent metal ion sensors capable of operating in aqueous environments have many potential applications in environmental and biological chemistry, and examples of Zn²⁺-selective AIE-active sensors are rare.¹⁴ Tetraarylethylene 4 shows excellent selectivity and submicromolar sensitivity in its fluorescence response toward Zn²⁺ ions in predominantly aqueous solution. The molecular framework of 4 can be easily modified, and we are currently investigating structural analogues of 4 designed to display enhanced metal ion sensing abilities that further exploit the inherent AIE properties of these materials.

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