Dual-mode recognition of transition metal ions by bis-triazoles chained pyrenes

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The development of selective chemosensors for the signaling of chemically and biologically important metal ions continues to draw much attention in the field of supramolecular chemistry.1 An effective fluorescent chemosensor must convert the event of cation recognition by the ionophore into an easily monitored and highly sensitive light signal from the fluorophore. Pyrene is one of the most useful fluorogenic units because it emits not only from the monomer but also from the excimer, moreover, the ratio of its monomer to excimer emission is a sensitive probe for conformational change.5 For example, it was reported that two pyrenyl moieties, connected by a series of polyoxy-ethylenes2b or dioxaoc-tanediamides,2c showed moderate to excellent selectivities toward Ca2+ and Hg2+ ions, respectively. It has also been shown that a pentapyrene system, bearing two end pyrenyl moieties connected by polyoxyethylenes, exhibited a novel blue shift along with an intensity enhancement of the pyrene excimer emission in the presence of Cu2+.2d These reports prompted us to explore the possibility of combining two terminal pyrenes with bistriazoles for metal ion screening studies because the latter heterocycles are lately recognized as potential metal ion coordination ligands.3,4c

We have previously reported4 the synthesis of a new fluorescent on–off switchable calix[4]crown using the ‘click chemistry’5 of an azide and an alkyn using the ‘click chemistry’5 of an azide and an alkyn to form a triazole metal ion binding site. Herein, we report the synthesis of 1, n-bispyrenyl-methoxymethyl-triazole-alkanes 7–10 and the study of their reversible conformational transformation in the presence of metal ions using the pyrene monomer/excimer emission as a probe.

The reaction of 1-(propargyloxymethyl)pyrene 2 with corresponding 1,n-bisazides (3–6) and benzylzide under click conditions afforded the target molecules 7–11 in 53–79% yields, where triazoles are designed to function as the metal ion binding sites and pyrenes are used as the reporting fluorophores2,6–9

(Scheme 1). The formation of triazoles 7–11 was readily monitored by 1H NMR by the appearance of a new singlet of triazole proton around δ 7.4 while the triplet acetylenic proton of compound 2 around δ 2.4 (J = 2.1 Hz) disappeared.

The fluorescence spectra of 7–10 were then taken in MeCN which showed a strong intramolecular excimer emission around 482 nm and a weak monomer emission around 376 and 396 nm. The former emission band was attributed to the overlap of two
pyrene units in an intramolecular π−π stacking under UV irradiation. The changes of fluorescence intensities of 7–10 (10 μM) in the presence of 15 metal perchlorates (10 equiv) were studied and the results are summarized in Table S1. The fluorescence of compound 7 was found to be selectively quenched by the addition of Cu²⁺, Hg²⁺, and Cr³⁺ ions. Such a selective quenching by the same group of metal ions (Cu²⁺, Hg²⁺, and Cr³⁺) was also observed on the mono-triazole model compound 11. The results suggest that metal ions may be complexed by both the triazole group(s) and the oxygen atom(s) of 7 and 11, which then quenched the fluorescence intensity of the pyrenes. The quenching of monomer emission in 7 and 11 can be explained as a reverse PET as well as a heavy atom effect, that is, the pyrene units behaved as a PET group(s) and the oxygen atom(s) of Cu²⁺, Hg²⁺, and Cr³⁺ was also observed for compounds 8–10, respectively. Similar fluorescence quenching by Cu²⁺, Hg²⁺, and Cr³⁺ in MeCN, using Stern-Volmer equation at low guest concentration (0–1.0 equiv), were calculated to be 1.2 × 10⁵, 1.6 × 10⁹, and 2.1 × 10¹⁰ M⁻¹, respectively. Similar fluorescence quenching by Cu²⁺, Hg²⁺, and Cr³⁺ was also observed for compounds 8–10, however, the emission of 9 was further quenched by Pb²⁺ and the emission of 10 was further quenched by Pb²⁺ and Ni²⁺ ions (see Table S1). The fluorescence of compound 10 toward the 15 metal ions screened revealed two types of binding modes: (1) for Cu²⁺, Hg²⁺, Cr³⁺, Pb²⁺, and Ni²⁺ ions, the monomer and excimer emissions were both quenched, and (2) for Cd²⁺ and Zn²⁺ ions, the monomer emission was enhanced but the excimer emission was quenched (see Figs. 1a and b). The association constants of 10 with Pb²⁺, Ni²⁺, Cd²⁺, and Zn²⁺ ions in MeCN using Stern-Volmer plots were determined to be 1.2 × 10⁵, 5.1 × 10³, 3.2 × 10², and 2.9 × 10⁶ M⁻¹, respectively.

In order to gain insights into the complexation modes of these receptors with metal ions, we compared the ¹H NMR spectra of 10 (5 mM) in the absence and presence of various metal cations in CDCl₃/CD₃CN = 3/1 at 25 °C (see Figs. 2a–d). The ¹H NMR spectra of 10 with Cu²⁺, Cr³⁺, and Ni²⁺ were broadened due to the high spin states of these metal ions, therefore, they were not analyzed. In the titration of 10 with Hg²⁺, precipitate was observed which decreased the ¹H NMR signals substantially. Nevertheless, the methine protons H₅ of triazoles disappeared in the presence of Hg²⁺ and the methylene protons (H₆a, H₆c, H₆d, H₆e, and H₆f) exhibited substantial up-field shifts (Δδ = −0.20, −0.43, −0.57, −0.33, and −0.47 ppm) upon complexation with 1 equiv of Hg²⁺. The complexation of 10 with Hg²⁺ is expected to reduce the electron density of the coordination sites and induce a down-field shift of the nearby proton signals; however, up-field shift was observed for all the methylene protons. Thus, we believe that there must be a change of conformation which causes the methylene protons to be shielded by the pyrene rings. A similar change in proton chemical shifts of 10 was observed when it was titrated with Pb²⁺ ion. In the complexation of 10 with Cd²⁺, the signals of H₆a and H₆c were slightly up-field shifted by 0.02 and 0.11 ppm, however, the signals of H₆b, H₆e, and H₆f were more up-field shifted by 0.17, 0.14, and 0.36 ppm, respectively. The fact that the chemical shift of H₆b of compound 10 was more affected by Pb²⁺ than by Cd²⁺ implies that 10 complexed with these two metal ions in a different mode (vide infra). On the one hand, compounds 7–9 did not show any fluorescence change upon adding Cd²⁺ or Zn²⁺ probably because their bis-triazoles could not find a proper conformation to accommodate either one of them. On the other hand, compound 10 did form complexes with Cd²⁺ and Zn²⁺ because the cavity formed by the methylene chains and the two triazoles was just big enough to accommodate them.

Based on the titration results of ¹H NMR and fluorescence spectrometry on 10, we proposed that 10 shows a dual-mode recognition toward transition metal ions (see Scheme 2): (a) Ni²⁺ and Pb²⁺ were bound between the oxygen atoms of the ether groups and the triazoles 3'-N which distorted the original conformation and...
quenched the monomer and excimer emission; (b) Cd\(^{2+}\) and Zn\(^{2+}\) were bound with 10 by the two triazoles which not only enhanced the monomer emission but also quenched the excimer emission due to the separation of the two pyrene rings.

With regard to cation exchange of 10 with Cd\(^{2+}\) and Pb\(^{2+}\) ions, we observed an interesting on–off switching process. When Pb\(^{2+}\) was titrated into a solution of preformed complex of 10: Cd\(^{2+}\) (10: Cd\(^{2+}\) = 1:200), both the excimer and monomer emission bands gradually quenched and became saturated after adding about same equiv of Pb\(^{2+}\) (vs Cd\(^{2+}\)) (see Fig. 3a). In the reverse of this metal ion exchange process, Cd\(^{2+}\) was titrated into a preformed complex of 10: Pb\(^{2+}\) (10: Pb\(^{2+}\) = 1:30), producing the fluorescence changes, shown in Figure 3b. In the former case, only 1 equiv of Pb\(^{2+}\) (vs Cd\(^{2+}\)) was needed to fully substitute the Cd\(^{2+}\), whereas in the latter case, about 130 equiv of Cd\(^{2+}\) (vs Pb\(^{2+}\)) was needed to liberate Pb\(^{2+}\) ion from the 10 Pb\(^{2+}\) complex. The results confirm that 10 forms a stronger complex with Pb\(^{2+}\) than Cd\(^{2+}\); furthermore, it also shows that metal ion exchange is possible through the electrostatic repulsion between the two metal ions in two different binding sites. Thus, when a metal ion is bound by 10, which contains two different recognition sites, it chooses the more favorable binding site.

If the proposed binding modes of 10 toward Cd\(^{2+}\) and Zn\(^{2+}\) are correct, we predicted that a new receptor 13, where an oxygen atom replacing the middle carbon of the methylene spacer of 9, should enhance its binding affinity toward the two metal ions (Scheme 3). Note that receptor 9 did not show any change in its monomer and excimer emission upon adding excess Cd\(^{2+}\) or Zn\(^{2+}\); however, receptor 13 showed an increase of monomer emission and a decrease of excimer emission upon adding Cd\(^{2+}\) or Zn\(^{2+}\). Similar to receptor 10, receptor 13 also showed significant fluorescence quenching toward Cu\(^{2+}\), Hg\(^{2+}\), Cr\(^{3+}\), and Pb\(^{2+}\) (Fig. 4). The results support that the binding mode of receptor 13 toward Cd\(^{2+}\) and Zn\(^{2+}\) is similar to that of receptor 10 (Scheme 2) and is therefore enhanced by the addition of an ether linkage in the middle of the methylene chain of receptor 9.

In conclusion, we have synthesized a series of new fluorophores 7–10 with pyrenylmethyl-oxy-methyl-bis-triazoles as the cationic binding sites. The series of receptors, like their control compound 11, all showed strong fluorescence quenching toward Cu\(^{2+}\), Hg\(^{2+}\), and Cr\(^{3+}\), implying that they do not need two triazoles for the complexation of these ions. As the methylene chain length increases, the receptors 9 and 10 further responded to Ni\(^{2+}\), Pb\(^{2+}\),

**Figure 3.** Fluorescence emission changes for (a) 10 Cd\(^{2+}\) complex (10: Cd\(^{2+}\) = 1:200) in MeCN upon adding various amounts of Pb\(^{2+}\) and (b) 10 Pb\(^{2+}\) complex (10: Pb\(^{2+}\) = 1:30) in MeCN upon adding various amounts of Cd\(^{2+}\) (The excitation wavelength was 312 nm).
Cd\textsuperscript{2+}, and Zn\textsuperscript{2+}. Two types of binding models were proposed for fluoroionophore \textit{10} based on \textit{1H} NMR titration and fluorescence quenching studies (see Scheme 2). Thus, through the systematic variation of the chain length of these readily synthesized bistriazole-oxy-methylpyrenes, we found that fluoroionophores \textit{7-10} and \textit{13} are excellent chemosensors for heavy metal ions and they provide us valuable information about the conformational changes and ligation behavior toward various metal ions.

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Supplementary data

Experimental procedures, \textit{1H} and \textit{13C} NMR spectral data of compounds \textit{7–11} and \textit{13}, and fluorescence and \textit{1H} NMR titration spectra of \textit{10} with various metal perchlorates are available. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.10.147.

References and notes