Highly sensitive chemosensor for detection of PPI with improved detection limit

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ABSTRACT

We have developed a new chemosensor 1,2Zn for the detection of PPI in an aqueous solution by photo-induced electron transfer. Two coumarin units were introduced to enhance the fluorescent signals. Consequently, this chemosensor showed an improved detection limit as compared to the previously reported chemosensor 2,2Zn.

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The development of chemosensors for the detection of biologically significant anions is a growing research topic.1 Chemosensor-based detection of pyrophosphate (P2O74−, PPI) is particularly important as PPI is involved in a range of bioenergetic and metabolic processes, such as gene duplication, gene transcription, and signal transduction.2 Additionally, PPI is closely related to diseases: Accumulations of calcium pyrophosphate dihydrate crystals are frequently found in patients with osteoarthropathy or psuedogout.3 Generally, anion sensors consist of two basic elements.4 The first one is the binding moiety, which overcomes strong hydration and can be achieved by coordinating the metal ion with an amine (reductive quencher) is commonly observed in fluorescence chemosensor studies (Fig. 1). We expected that the addition of PPI would weaken the metal coordination with the reductive quencher and lead to a significant change in the fluorescence intensity of 1,2Zn and 1,2Cd by restoring the PET pathway (Fig. 1).

The synthesis of compound 1 is outlined in Scheme 2. The conversion of 1,3-phenylenedicarboxylic acid into its acyl chloride facilitated the formation of the diacid chloride 3 through the reaction between compound 4 and di-(2-picolyl)amine in the presence of potassium carbonate and sodium hydride. Hydrolysis of compound 3 followed by amide bond formation between the resulting diacid and 2 equiv of 3-aminooctanoic acid furnished compound 1.
As expected, we found that the fluorescence of the complex (1/C12Zn) between 1 and zinc cations was significantly reduced on the addition of PPi (Fig. 2). The effect of other anions on the emission spectra of 1/C12Zn was examined by adding various anions to 1/C12Zn in an aqueous 2-[4-(2-hydroxyethyl)-1-piperazinyl]ethanesulfonic acid (HEPES) buffer solution (0.01 M, pH 7.4) at 25 °C. However, other anions, including those of phosphate, showed no detectable changes in the fluorescence of 1/C12Zn (Fig. 2). These results suggest that 1/C12Zn has a high selectivity for PPi over other anions.

To measure the change in the fluorescence of 1/C12Zn upon the addition of PPi, fluorescence titration was carried out in an aqueous HEPES buffer solution (10 mM, pH 7.4). On the addition of PPi, fluorescence decreased by a factor of 9.8 and was saturated at 3.3 equiv (Fig. 3). 1:1 Complexation between 1/C12Zn and PPi was confirmed by Job’s plot (Fig. 3 inset, refer to Supplementary data for the Job’s plot for adenosine triphosphate).

The emission spectra of 1/C12Zn containing coumarin dye were expected to vary significantly upon the addition of PPi, resulting in an improved detection limit. As depicted in Figure 4, the change in fluorescence intensity of 1/C12Zn was 4.7 times greater than that of 2/C12Zn upon the addition of PPi under the same conditions. The detection limit was calculated to be three times that of the standard deviation of the background noise. As expected, the detection limit of 1/C12Zn for PPi (49 nM; refer to Supplementary data) was better than that of 2/C12Zn (83 nM). Considering the reduced binding affinity of 1/C12Zn compared to that of 2/C12Zn, the improved detection limit of 1/C12Zn indicates that high quantum yield fluorophores may have a dominant effect on the determination of the detection limit.

In summary, we developed a new fluorescent chemosensor (1/C12Zn) for the detection of PPi in an aqueous solution. The sensor system shows an improved detection limit for PPi compared to that of the naphthyl-based PPi sensor by the introduction of coumarin dye. In addition, it shows good selectivity for PPi over other anions.

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Supplementary data (spectral data for the new compounds, effect of metal cations and anions on the emission spectra, detection of the limit of detection, and Job's plot for ATP) associated with this article can be found in the online version, at doi:10.1016/j.tetlet.2011.07.067.

References and notes

11. Adenosine triphosphate (ATP) also caused notable fluorescence quenching of 1,2Zn as most PPI chemosensors suffer from poor selectivity between PPI and ATP. However, on addition of an equal amount of ATP (10 μM) to 1,2Zn (10 μM), ATP showed only 51% fluorescence quenching ability compared to that of PPI (refer to Supplementary data).