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Dimethylcyclam based fluoroionophore having Hg^{2+}- and Cd^{2+}-selective signaling behaviors

Na Jin Youn and Suk-Kyu Chang*

Department of Chemistry, Chung-Ang University, Seoul 156-756, Republic of Korea

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Abstract—Diametrically disubstituted bis(anthrylmethyl) derivative of 1,8-dimethylcyclam exhibited pronounced Hg^{2+}- and Cd^{2+}-selective fluorogenic behaviors in aqueous acetonitrile solution. A distinctive OFF–ON type signaling was observed for Hg^{2+} and Cd^{2+} ions in aqueous acetonitrile (CH_3CN–H_2O = 90:10, v/v) solution, while a selective ON–OFF type switching behavior toward Hg^{2+} ions was observed in solution having higher water content (CH_3CN–H_2O = 50:50, v/v). The detection limit for the analysis of Hg^{2+} ions in 50% aqueous acetonitrile was found to be 3.8×10^{-6} M. The selective OR logic gate behavior of the prepared compound toward two toxic heavy metal ions of Hg^{2+} and Cd^{2+} ions in CH_3CN–H_2O (90:10, v/v) suggests the possibility as a new chemosensing device for the two important target metal ions.

Developments of chemosensors for the sensing of important ionic species are one of the most attractive research areas in supramolecular chemistry.[1] The underlying principle of the molecular design for the construction of selective chemosensors is generally the conjugation of the target-selective binding site with suitable signaling handles.[2] Crown ethers having anthrylmethyl groups[3] are classical examples of this principle and are well known for their characteristic PET (photoinduced electron transfer) type OFF–ON signaling toward many of the important ionic guests.[4] We are interested in the design of fluorogenic ionophores based upon cyclam (cyclam = 1,4,8,11-tetraazacyclotetradecane, **3**), a widely used molecular platform of nitrogen analogue of crown ethers, aiming for the selective and efficient sensing of transition metal ions.[5] In fact a variety of compounds derived from cyclams by appending suitable subunits having signaling functions have been devised to probe the important ionic guests and physical properties of the system.[6] For this purpose, chromogenic or fluorogenic signaling is much more attractive due to their sensitivity and easiness of signal detection.[7] Among the fluorophores, anthracene[8] and pyrene[9] functions are most widely employed due to their relatively well exploited photophysical behaviors. Particularly, 1,8-dianthryl derivative of the cyclam **4** has been prepared through the alkylation of tetraazatricyclohexadecane intermediate and the photophysical properties of Cr^{3+} complex[10] and intramolecular reductive nitrosylation by **4**-Cu^{2+} complex[11] were investigated. However, in spite of the potentially interesting structural characteristics of **4** as a fluorescence sensor, detailed sensing behavior toward transition metal ions has not been investigated. We report in this letter that the closely related 1,8-dimethylcyclam based dianthryl derivative **2** revealed a pronouncedly selective fluorescence enhancement or quenching behavior toward Hg^{2+} or Cd^{2+} ions in aqueous media. In fact, the developments of the detection[12] and treatment technique[13] for the heavy metal ions are very important in view of their extremely toxic impact on our environment.[14] The prepared compound can be used as a selective fluorescent molecular probe for the presence of the two toxic metal ions of Hg^{2+} or Cd^{2+} ions in environmental or biological samples.

Dianthryl derivative **2** was prepared by the alkylation of 1,8-dimethylcyclam **1** with 9-chloromethylanthracene (K_2CO_3, KI, CH_3CN) in good yield (89%) (Scheme 1).[15] The preparation of cyclam analogue **4** by direct alkylation of **3** was believed to be synthetically demanding due to the difficulties in the control of the degree of alkylation and regioselectivity. In fact, DeRosa et al.[10] have synthesized compound **4** by a three step reaction from **3** following the general procedure for the preparation

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* Corresponding author. Tel.: +82 2 820 5199; fax: +82 2 825 4736; e-mail: skchang@cau.ac.kr

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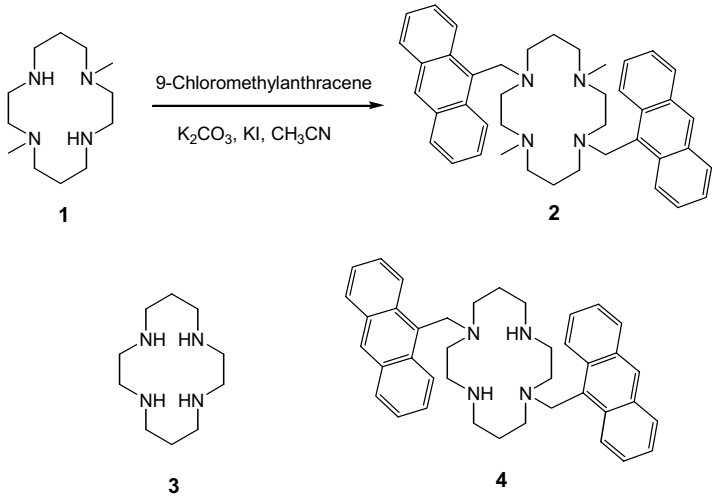

Scheme 1.

of 1,8-R_2cyclam by Guilard and co-workers[16] with 9-chloromethylanthracene. The synthesis of **2** instead of **4** seems to be reasonable and straightforward because the two distal tertiary amino groups are in a sense protected against the required alkylation reaction. Therefore, we prepared compound **2** having similar structural characteristics compared with **4** except for the two methyl groups on 1,8-positions and investigated the chemosensor behavior toward transition metal ions in aqueous media.

The fluorescence behavior of the prepared compound was strongly dependent on the pH of the medium due to the presence of basic amino groups adjacent to the PET type signaling anthrylmethyl fluorophores as expected.[3,4] Therefore, we first measured the fluorescence intensity changes of **2** at 417 nm as a function of the solution pH in CH_3CN–H_2O (50:50, v/v) (Fig. 1). In this case, the indicated pH values are pertinent to the apparent ones because the mixed aqueous acetonitrile solution was employed. In basic region of pH 11 the fluorescence of **2** was weak and starts to increase considerably around pH 6.5. Then the changes in intensity became plateau down to pH 5 with almost 10-fold increase in fluorescence intensity compared with that of pH 8. From pH 5 the intensity increased further 4.5-fold again down to pH 4 then no significant changes were observed until very acidic region of pH 2. This fluorescence enhancement behavior in the acidic solution is due to the inhibition of the PET processes between amine and anthracene fluorophore by the protonation of the amine groups of cyclam, which is responsible for the quenching of the fluorescence of **2**. Based on this preliminary observation, we carried out all the fluorescence experiments in acetate buffered solution at pH 5.0 where relatively optimized selectivity toward targeted metal ions was observed.

An interesting observation is that the fluorescence profiles for the compound **2** were somewhat different in the presence and absence of two most responding metal ions of Hg^{2+} and Cd^{2+} in varying water compositions of aqueous organic solvents. Figure 2 shows the effects of

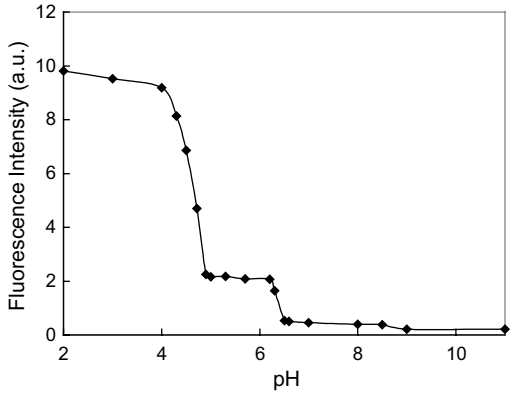

Figure 1. The fluorescence intensity of **2** at 417 nm as a function of apparent pH values in CH_3CN–H_2O (50:50, v/v). [**2**] = 5.0×10^{-6} M, λ_{ex} = 340 nm.

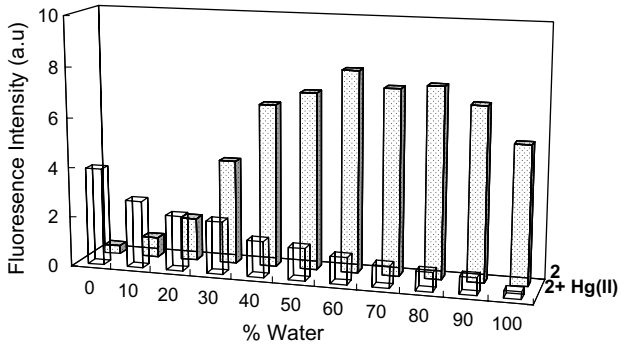

Figure 2. Fluorescence intensity of **2** at 417 nm in aqueous acetonitrile. [**2**] = 5.0×10^{-6} M, [Hg^{2+}] = 5.0×10^{-4} M, [acetate buffer] = 1.0×10^{-2} M at pH 5, λ_{ex} = 340 nm.

water composition on the fluorescence behavior of **2**-Hg^{2+} system in aqueous acetonitrile solution ([**2**] = 5.0×10^{-6} M and [Hg^{2+}] = 5.0×10^{-4} M). As the water composition increased, the fluorescence intensity at 417 nm for the ionophore itself gradually increased in lower water content region then decreased steadily, while that of **2** in the presence of 100 equiv of Hg^{2+} ions decreased monotonously. This profile suggests that the 90:10