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Acid/base-controllable Fluorescent Molecular Switches Based on Cryptands and Basic N-Heteroaromatics

Received 00th January 20xx, Accepted 00th January 20xx

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DOI: 10.1039/x0xx00000x

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Two kinds of fluorescent BMP32C10-based cryptands 1 and 2 have been developed. Cryptand 1 contains a binaphthol group, while cryptand 2 bears a coumarin group in their third arms respectively. Based on this design, novel self-assemblies constructed between cryptands 1 or 2 and basic N-heteroaromatics guests 3-6 were successfully obtained. Moreover, the threading/dethreading processes of the host-guest complexes could be well-switched by the alternate addition of acid/base, and accompanied by concurrent changes in fluorescence.

Stimuli-responsive systems¹ have attracted more and more attention in recent decades due to their potential applications in constructing complicated artificial molecular machines, such as molecular sensors, shuttles, switches, and probes. As one of fundamental building motifs, pseudo[2]rotaxane plays the critical role in the construction of stimuli-responsive systems. The external stimuli includes chemical acid/base,² photochemical, $^{1f, 3}$ ion binding, 4 and so on. 5 The external stimuli could act on either hosts or guests to dexterously regulate the threading/dethreading process of the pseudo[2]rotaxane. Meanwhile, the threading/dethreading process was always accompanied by the recognizable changes in physical properties, such as dichroism,⁶ conductivity,⁷ and fluorescence.^{1a, 1e, 1f} Among them, the fluorescence change can be detected easily and remotely, and thus it was widely used diagnose the threading/dethreading states to of pseudo[2]rotaxane. For example, in 1998, Prodi et al. reported a pseudo[2]rotaxane formed by dibenzo-24-crown-8 (DB24C8) and (9-anthrylmethyl)methylammonium hexafluorophosphate salt, the fluorescence of anthracene unit could be observed in the form of pseudo[2]rotaxane. But with the addition of NBu₄Cl, the fluorescence of anthracene disappeared due to the dethreading of pseudo[2]rotaxane.⁸ In 2011, Liu et al.

reported a pseudo[2]rotaxane constructed by DB24C8 derivative bearing terpyridine moiety with lanthanide ion and fullerene-containing ammonium salt, the formation of pseudo[2]rotaxane induced an efficient quenching of the lanthanide ion due to the PET effect between the fullerene unit and terpyridine moiety.9

Although many crown ether-based fluorescent responsive pseudo[2]rotaxanes were reported so far, the cryptand-based fluorescent responsive pseudo[2]rotaxane was really limited. Compared with crown ethers, cryptands have threedimensional spatial structures, higher association constants, and additional binding sites.¹⁰ Moreover, among cryptandbased systems, the responsive stimuli were mostly acted on cryptands rather than guests. Thus, it is desirable to develop cryptand-based stimuli-responsive systems, especially those with the responsive stimuli acted on the guest molecules.

As well known, paraguat and its derivatives were the most common guests for bis(m-phenylene)-32-crown-10 (BMP32C10-based) cryptand.^{1c, 1g, 10-11} However, a main limitation for employing paraquat derivatives as guests lies in the lack of enough way to regulate such a host-guest system, which greatly restricted the development and application of BMP32C10-based cryptand system.^{1c, 5c, 12} For example, more recently, we have designed and synthesized a fluorescent coumarin-bridged BMP32C10-based cryptand 2, and the fluorescence of cryptand 2 was guenched when it complexed with a paraguat guest.^{12d} However, such a host-guest complex was stable, and the threading/dethreading process was difficult to be regulated. Therefore, it is important to develop novel guest molecules for cryptand host with external stimuliresponsive ability.

Along this line, N-heteroaromatics guest molecules (3, 4, 5, and 6) fell into our sights based on the following considerations: (i) all of the four guests keep lone electron pairs on N-atoms, and possess a certain degree of basicity; (ii)

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Electronic Supplementary Information (ESI) available: [synthetic procedures, characterizations, crystal data, NMR]. See DOI: 10.1039/x0xx00000x



Scheme 1 Chemical structures and cartoon represents of two cryptands 1, 2 and

guest molecules 3-6 could be protonated/deprotonated by

Herein, two kinds of fluorescent BMP32C10-based cryptands 1 and 2 are employed as hosts, in which cryptand 1 contains a binaphthol group, and cryptand 2^{12d} has a coumarin group in its individual third arm. Then novel self-assemblies have been successfully constructed from cryptands 1 or 2 and protonated guests 3'-6' (Scheme 2). Moreover, by alternatively adding acid/base, the threading/dethreading processes of the obtained host-guest assemblies could be well-controlled, and accompanied by the concurrent changes in fluorescence due to the possible PET effect. To the best of our knowledge, this is the first example of regulating the fluorescence of BMP32C10-based cryptands by external stimuli acting on guest molecules so far. It will open up new dimension in constructing stimuli-responsive self-assemblies based on cryptands

Initially, bridged by a binaphthol group, a BMP32C10-based fluorescent cryptand **1** was obtained in moderate yield by using commercially available starting materials according to the reported methods (see ESI, Scheme S1).^{12b, 13} The structure

Fig. 1 X-ray crystal structures of complex 1>paraquat in two different view

angles. Solvent molecules were omitted for clarity. Hydrogen bond parameters are as follows: H⁻⁻O distances (Å), C⁻⁻O distances (Å), C-H⁻⁻O angles (deg): (a) 2.59, 3.23, 126.63; (b) 2.73, 3.60, 157.93; (c) 2.88, 3.48, 123.21; (d) 2.76, 3.43, 130.03. Face-to-face π-stacking parameters in the stacked structure: centroid-centroid distance (Å): (e) 3.96; (f) 3.63.

of cryptand **1** was fully characterized by ¹H NMR, ¹³C NMR, and HR-ESI-MS (see ESI, Section 2), and further confirmed by the single crystal X-ray diffraction of complex **1** \supset paraquat. As shown in Fig.1, the complex **1** \supset paraquat was mainly stabilized by (i) hydrogen bonds marked in green dashed lines; four hydrogen bonds (a-d) were found between cryptand **1** and paraquat (Fig. 1a); (ii) face-to-face π -stacking interactions marked with yellow dashed lines as shown in Fig. 1.

Host-guest interactions between cryptands **1** or **2** and guests **3'-6'** were investigated in detail by ¹H NMR spectroscopy (see ESI, Section 3). It was found that both cryptand **1** and guest **3'** in CH₃CN solutions were colorless, but the equimolar mixture of cryptand **1** and **3'** became yellow immediately due to the charge-transfer interactions between the electron-rich aromatic rings of guest **3'**. This colour changes were also observed in the equimolar mixtures of cryptand **2** and guest **5'**, respectively.

Meanwhile, when cryptand **1** was mixed with guest **3'** in 1:1 ratio in CD₃CN, significant upfield chemical shift changes assigned to H_{3a}, H_{3b} of guest **3'** and H_{1a}, H_{1b} of cryptand **1** were observed (Δ H_{3a} = -0.26, Δ H_{3b} = -0.10 for guest **3'**, Δ H_{1a} = -0.44, Δ H_{1b} = -0.36 for cryptand **1**) (Fig. 2a, 2b, and 2c). Similarly, obvious upfield chemical shift changes assigned to H_{5a}, H_{5b}, H_{5c} were observed in the 1:1 mixture of cryptand **1** and guest **5'** (Δ H_{5a} = -0.26, Δ H_{5b} = -0.43, Δ H_{5c} = -0.27 for guest **5'**, Δ H_{1a} = -0.63, Δ H_{1b} = -0.52 for cryptand **1**) (Fig. 2c, 2d, and 2e). Notable chemical shift changes could also be observed when cryptand **1** was mixed with guests **4'** and **6'**, respectively (See ESI, Fig. S11, S13).

Subsequently, 2D NOESY experiment was performed, which supported further the formation of host-guest complex between cryptands **1** or **2** and guests **3-6** (see ESI, Section 4). For example, when cryptand **1** and guest **3'** was mixed in 1:1 ratio in CD₃CN solution, obvious NOE correlation signals between H_{1a}, H_{1b}, H_{1c} of cryptand **1** and H_{3a}, H_{3b} of guest **3'** were clearly observed (Fig. S36).

BMP32C10-based cryptand **2**, which was synthesized by us recently,^{12d} was bridged by a fluorescent coumarin unit in the third arm. Thus, we wondered if cryptand **2** could be used as a fluorescent-responsive cryptand candidate. Similar to cryptand

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four guests 3, 4, 5, 6.

DOI: 10.1039/C7CC07469G

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Fig. 2 Partial ¹H NMR spectra (500 MHz, CD₃CN, 298 K): (a) guest **3'**; (b) host-guest complexation $1\supset 3'$; (c) host **1**; (d) host-guest complexation $1\supset 5'$; (e) guest **5'**.

1, Job plots based on ¹H NMR data showed that all complexes between cryptand **2** and guests **3'**, **4'**, **5'** or **6'** had 1:1 stoichiometries (see ESI, Fig. S18 and S19). The corresponding association constants K_a measured in CD₃CN were listed in Scheme 2.^{14a} Interestingly, the K_a values between cryptand **2** and four guests were almost an order of magnitude higher than that of cryptand **1**. Presumably, cryptand **2** has a smaller and more appropriate cavity which could combine with guests more tightly.^{14b} Another reason might be ascribed to that the two phenolic hydroxyl groups on cryptand **1** are more acidic, leading to the charge repulsion between cryptand **1** and the guests **3'-6'**. So both cryptand **1** and **2** were freshly synthesized for further investigating their fluorescent-responsive property.

As above-mentioned, all of the four guests **3-6** keep the lone electron pairs on N-atoms, and hence, guests **3-6** would be protonated/deprotonated by adding acid/base alternatively. Therefore, we firstly tried to control the threading-dethreading processes of complexes formed between cryptands **1** or **2** and guests **3'-6'** by adding acid/base. As shown in Fig. 3, after adding 4.0 *equiv*. of trifluoroacetic acid (TFA) into the mixture of cryptand **1** and guest **3** (Fig. 3b), the chemical shift assigned to H_{1a} and H_{1b} of cryptand **1** showed obvious upfield shift. Subsequently, with the addition of 6.0 *equiv*. of trimethylamine (TEA) to remove protons from nitrogen atoms of pyridinium (Fig. 3c), H_{3a} and H_{3b} of guest **3** returned back to the original position of free guest **3**. The chemical shift



Scheme 2 K_a Values between cryptands 1 or 2 and guests 3', 4', 5', and 6' with 1:1 complexation. ¹H NMR titrations were performed with a constant concentration of host (2.00 mM) and varying concentrations of guest in the range of 1.00 - 40.00 mM in CD₃CN at 298 K. The standard concentration of the reference state is fixed to 1.0 mol/dm³



DOI: 10.1039/C7CC07469G

Fig. 3 Partial ¹H NMR spectra (500 MHz, CD_3CN , 298 K): (a) 5.00 mM cryptand **1** + 5.00 mM guest **3**; (b) the mixture obtained after addition of 4.0 equiv. **TFA** to (a); (c) the mixture obtained after addition of 6.0 equiv. **TEA** to (b); (d) 5.00 mM guest **3**; (e) 5.00 mM cryptand **1**.

assigned to H_{1a}, H_{1b} of cryptand **1** also returned back to its original position, indicating the dethreading of complex **1** \supset **3**'. It is the first example that the threading/dethreading processes between BMP32C10-based cryptands and guests are successfully controlled by regulating on guest molecules.

The key point for fabricating fluorescent switches is how to achieve the well-controlled fluorescence changes during the threading/dethreading process.^{8-9, 15} It was interesting when guest 3 was added to the solution of cryptand 1, obvious changes in fluorescent emission was observed (Fig. 4b). Differently, when guest 3 was added into the solution of cryptand 2, almost no change in fluorescent intensity was observed. We speculated that possible proton transfer between hydroxyl of cryptand 1 and nitrogen atom of guest 3 might lead to the result. Moreover, after adding TFA to the mixture solution of cryptand 2 and guest 3, the fluorescent emission intensity of cryptand 2 decreased remarkably (Fig. 4c), resulting from the formation of threaded complex of $2 \supset 3'$. An efficient PET process occurred between guest 3' and the coumarin unit of cryptand 2.^{12d} After adding TEA to remove protons from guest 3', the fluorescent emission intensity recovered again, indicating the dissociation of complex $2 \supset 3'$.



Fig. 4 (a) Cartoons represent of the changes in fluorescence intensity. Changes of the fluorescence emission spectra in CHCl₃/CH₃CN (1:1 v/v), (b) cryptand **1** (1 × 10⁻⁶ M). λ_{ex} = 250 nm; (c) cryptand **2** (1 × 10⁻⁶ M). λ_{ex} = 320 nm

DOI: 10.1039/C7CC07469G

As a result, the threading/dethreading process of $2\supset 3'$ could be well-controlled by adding acid/base alternatively, and accompanied by the concurrent changes in fluorescent intensity.

In summary, two kinds of BMP32C10-based fluorescent cryptands 1 and 2 have been used as host molecules. Cryptand 1 is bridged by a binaphthol group, while cryptand 2 is bridged by a coumarin group in its individual third arm. On the basis of host-guest interactions, novel self-assemblies constructed between cryptands 1 or 2 and *N*-heteroaromatics guests 3-6 have been developed successfully. By adding acid/base, the threading/dethreading processes of the obtained assemblies could be well-controlled, and accompanied by the concurrent changes in fluorescent intensity. It is the first example of regulating the fluorescence of BMP32C10-based cryptands by external stimuli acting on guest molecules.

The present study provides a new choice to construct external stimuli responsive assemblies based on cryptands by regulating the behaviour of guest molecules rather than hosts. It also brings more opportunities in designing more complicated molecular sensors and other devices, benefiting from relative easily syntheses and functionalization of guest molecules.

Acknowledgements

We gratefully thank the financial support of the National Natural Science Foundation of China (Nos. 21472088, 21472089).

Conflicts of interest

There are no conflicts of interest to declare.

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