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Guest-induced supramolecular chirality in a ditopic azoprobe–cyclodextrin complex in water†

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We report a novel supramolecular chirality induced by the twisted structural change of two ditopic azoprobes (15C5-Azo-dpa) inside the chiral cavity of γ-cyclodextrin (γ-CyD) due to multi-point recognition of guest ions by 15C5-Azo-dpa molecules in water.

Chirality control by supramolecular assemblies and helical polymers based on chiral templates has received much attention in recent years.[1] Those systems have been widely used in chiroptical devices,[2] memory devices,[3] and chiral catalysis.[4] Pioneering work on supramolecular chirality was conducted by Yashima's group, who designed chiral recognition systems by using helical polymers.[5] Recently, Kumar *et al.* reported that naphthalene diimide amphiphiles functionalized with the dipicolylethylenediamine motif self-assembled with tunable chirality upon molecular recognition of various adenosine phosphates.[6] They showed that competitive guest binding induced the dynamic reversal of the helix assemblies. Such guest-induced chirality control is expected to have potential application in the development of versatile chiral switching and sensing devices.[7]

Here we report a simple system of guest-induced chirality control in the 2 : 1 inclusion complex of ditopic azoprobes with γ-cyclodextrin (γ-CyD) in water. The ditopic azoprobe is a receptor possessing two different recognition sites that are expected to show excellent recognition function when two guest molecules exist in the system. As shown in Fig. 1, we have designed a ditopic azoprobe (**15C5-Azo-dpa**) that bears benzo-15-crown-5 (B15C5) and dipicolylamine (dpa) as the recognition sites (Fig. 1).

The azochromophore moiety can be used as a photosignal transducer.[8] Although **15C5-Azo-dpa** is almost insoluble in water, γ-CyD can improve its solubility in water by forming a stable inclusion complex with it. The **15C5-Azo-dpa**–γ-CyD complex was found to show a unique response based on the guest-induced supramolecular chirality in water. An induced circular dichroism (ICD) response was noted upon the addition of carbonate ($CO_3{}^{2-}$) or acetate ($CH_3CO_2{}^-$) ions in the presence of both K^+ and Zn^{2+} ions. Such supramolecular responses were successfully used to sense guest anions in water.

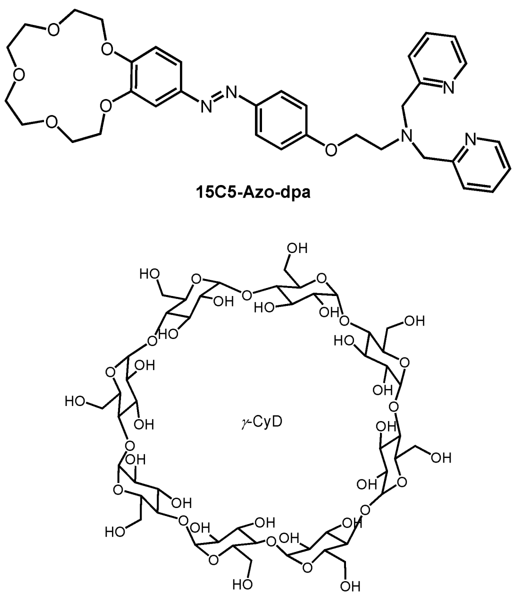

Fig. 1 Structures of **15C5-azo-dpa** and γ-CyD.

The synthesis of **15C5-Azo-dpa** proceeded with the azocoupling of 4′-aminobenzo-15-crown-5 with phenol, followed by the introduction of a bromoethylene spacer using the Williamson ether synthesis.[9] Then, a dpa moiety was introduced under basic conditions with K_2CO_3, and the obtained product was purified by silica column chromatography. The structure of **15C5-Azo-dpa** was confirmed by ^1H NMR and combustion analyses (Fig. S1–S3, ESI†). Details of the synthesis are available in the ESI (Scheme S1, ESI†).

In our previous work, we showed that B15C5 azoprobes selectively formed a 2 : 1 inclusion complex with γ-CyD in the presence of K^+ ions in water.[10] Meanwhile, Hamachi's group and other research groups reported that the Zn^{2+} complexes of dpa units interacted with various phosphate anion derivatives

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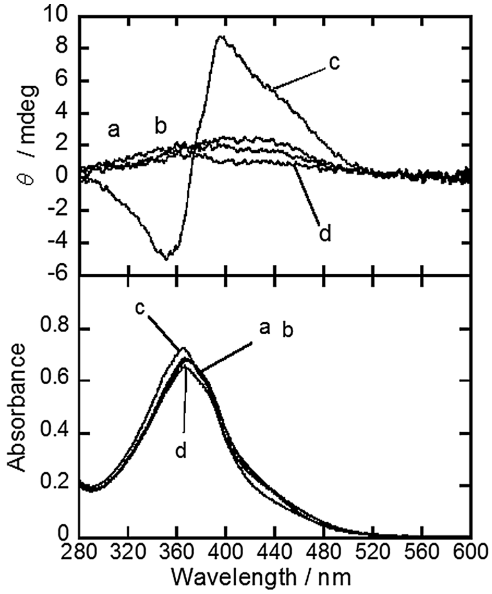

Fig. 2 ICD and UV-Vis spectra of **15C5-Azo-dpa**–γ-CyD sensors. [**15C5-Azo-dpa**] = 40 μM, [γ-CyD] = 5 mM, and (a) K^+, (b) Zn^{2+}, (c) K^+ + Zn^{2+}, (d) K^+ + Zn^{2+} + Tri, in 4% DMSO aq., pH = 11.0 at 25 °C; K^+ (50 mM K_2CO_3), Zn^{2+} (40 μM $Zn(NO_3)_2$), Tri (3.0 mM $Na_5P_3O_{10}$); (M = mol dm^{-3}).

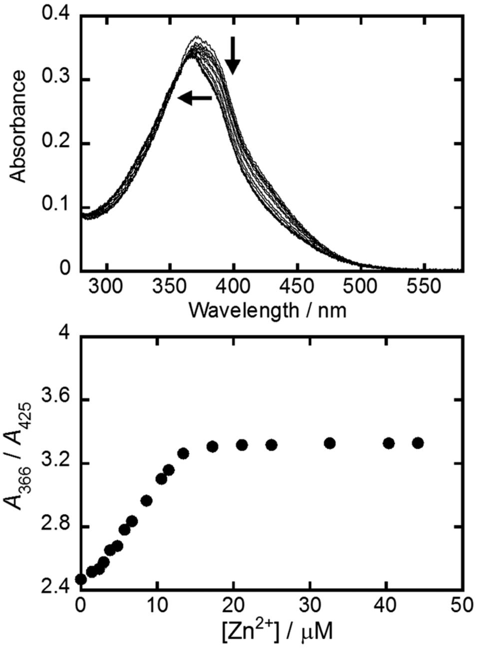

Fig. 3 The changes in UV-Vis spectra and the absorbance ratio of **15C5-Azo-dpa**–γ-CyD sensor as a function of zinc ion concentration. [**15C5-Azo-dpa**] = 20 μM, $[Zn^{2+}]$ = 0 – 45 μM, $[K_2CO_3]$ = 50 mM, [γ-CyD] = 5 mM, in 4% aq. DMSO, pH = 11.0, at 25 °C (M = mol dm^{-3}).

through the unoccupied coordination sites in the Zn^{2+}–dpa complexes.[11] Thus, it is interesting to examine how such guest species affect the response function of the **15C5-Azo-dpa**–γ-CyD complex in water. Fig. 2 shows the ICD spectra and the UV-Vis absorption spectra of **15C5-Azo-dpa** (40 μM) in 5.0 mM γ-CyD aqueous solution with K^+ ions (a), with Zn^{2+} ions (b), with K^+ and Zn^{2+} ions (c), and with K^+, Zn^{2+}, and triphosphate (Tri) ions (d). Interestingly, the split-type Cotton effect was observed only in the presence of both K^+ and Zn^{2+} ions (spectrum c in the top panel of Fig. 2). In addition, the UV-Vis absorbance ratio of 366 nm to 425 nm (A_{366}/A_{425}) exhibited the largest blue shift in the presence of both K^+ and Zn^{2+} ions. The azobenzene chromophores are known to exhibit strong ICD by forming an inclusion complex with CyDs based on the chiral nature of the CyD cavities.[12] We have shown that this ICD response was affected by the dimer formation of the azoprobes inside γ-CyD to induce a split-type Cotton effect.[8] In addition, an exciton interaction of the azodimer was found to induce clear changes in the UV-Vis absorption spectra. Thus, the observed split ICD in spectrum c in the top panel of Fig. 2 and the largest blue shift in the UV-Vis spectra indicated the formation of a clockwise twisted dimer of **15C5-Azo-dpa** probes inside γ-CyD in the presence of both K^+ and Zn^{2+} ions. The addition of triphosphate was found to inhibit the twisted structure formation of the **15C5-Azo-dpa**–γ-CyD complex in water, probably due to the coordination of the triphosphate anion with the Zn^{2+}–dpa complex in **15C5-Azo-dpa**.

Fig. 3 shows an absorbance *vs.* wavelength plot and the effects of Zn^{2+} concentration on the UV-Vis absorbance ratio (A_{366}/A_{425}) of the **15C5-Azo-dpa**–γ-CyD complex in the presence of 50 mM K_2CO_3 in water. It is evident that the absorbance ratio gradually increased with the addition of Zn^{2+} and reached a plateau near the equivalence point with **15C5-Azo-dpa** (20 μM). The finding that an equivalent amount of Zn^{2+} in excess of 20 μM caused no spectral changes attests the 1 : 1 complex formation of Zn^{2+} with the dpa binding site in **15C5-Azo-dpa**. The sigmoid response observed in Fig. 3 indicates the occurrence of a successive binding reaction of Zn^{2+} with the two **15C5-Azo-dpa** molecules inside γ-CyD. The formation of the 2 : 1 complex of **15C5-Azo-dpa** probes with γ-CyD was confirmed by the analysis of Job's plots (Fig. S4, ESI†).

To elucidate the mechanism of the split ICD noted for the **15C5-Azo-dpa**–γ-CyD complex, we examined the salt effect by substituting 100 mM KNO_3 and 100 mM KOH for 50 mM K_2CO_3 in the presence of 40 μM Zn^{2+}. Interestingly, no split ICD was observed for the KNO_3 and KOH systems, indicating the possibility of CO_3^{2-} bridging between the two Zn^{2+}–dpa binding sites (data not shown). The effect of CO_3^{2-} concentration on the ICD spectra of the **15C5-Azo-dpa**–γ-CyD complex is depicted in Fig. 4. It is evident that the addition of CO_3^{2-} ions enhanced the split ICD for the **15C5-Azo-dpa**–γ-CyD complex at pH 11.0. The ICD intensity change as a function of CO_3^{2-} concentration at a constant K^+ concentration of 0.10 M was well fitted by a 1 : 1 binding isotherm, and the apparent 1 : 1 binding constant of CO_3^{2-} ions was calculated to be 83.5 ± 6.0 M^{-1} (Fig. S5, ESI†). The triphosphate binding may break this CO_3^{2-} bridging of the two **15C5-Azo-dpa** molecules inside γ-CyD to reduce the split ICD. In addition, direct evidence of the relative orientation of the azoprobes and the macrocyclic ring was obtained by NOESY experiments. Cross peaks between H3 protons inside the CyD cavity and protons of the azoprobes were clearly observed (Fig. S8, ESI†).

If this CO_3^{2-} bridging were the key mechanism for the induction of the split ICD, a similar split ICD induced by the $CH_3CO_2^-$ bridging would be expected under neutral pH conditions. In fact, we observed the typical split ICD in the presence of 50 mM CH_3CO_2K at pH 7.0 (Fig. 5). However, it should be noted that the split ICD had peak

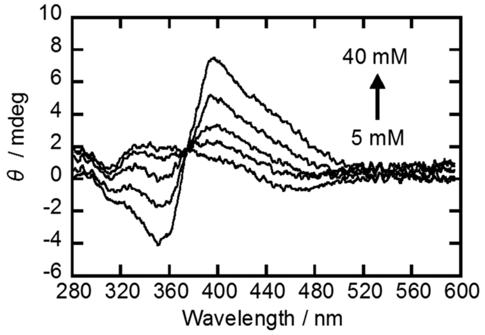

Fig. 4 ICD spectra of **15C5-Azo-dpa**–γ-CyD sensors, [**15C5-Azo-dpa**] = 40 μM, [Zn^{2+}] = 40 μM, [K_2CO_3] = 5–40 mM, [γ-CyD] = 5 mM, in 4% DMSO aq., pH = 11.0 at 25 °C; (M = mol dm^{-3}).

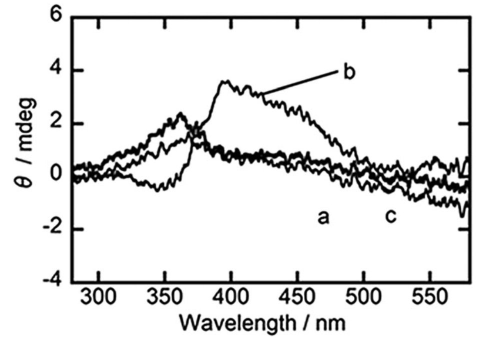

Fig. 5 ICD spectra of **15C5-Azo-dpa**–γ-CyD sensors, [**15C5-Azo-dpa**] = 40 μM, [Zn^{2+}] = 40 μM, [γ-CyD] = 5 mM, (a) [CH_3CO_2Na] = 50 mM, (b) [CH_3CO_2K] = 50 mM, (c) [CH_3CO_2Cs] = 50 mM, in 4% DMSO aq., pH = 7.0 at 25 °C; (M = mol dm^{-3}).

shapes that differed from those of the CO_3^{2-} bridging system, indicating that a somewhat different mode of the twisted structure was formed inside γ-CyD. In contrast, no split ICD was noted in the presence of 50 mM CH_3CO_2Na or 50 mM CH_3CO_2Cs. This indicated that the clockwise twisted structure of the two **15C5-Azo-dpa** molecules inside γ-CyD was induced only in the presence of K^+, Zn^{2+}, and the bridging anions of the two dpa–Zn^{2+} binding sites, such as CO_3^{2-} or $CH_3CO_2^-$ ions. By titration analysis of $CH_3CO_2^-$ at a constant K^+ concentration of 0.10 M, the apparent 1 : 1 binding constant of $CH_3CO_2^-$ for the **15C5-Azo-dpa**–γ-CyD complex in the presence of an equivalent amount of Zn^{2+} was determined to be 180 ± 27 M^{-1} at pH 7.0 (Fig. S6, ESI†).

In conclusion, we have shown a novel supramolecular chirality induced by the twisted structural change of two **15C5-Azo-dpa** molecules inside the γ-CyD chiral cavity due to multi-point recognition of guest ions by the ditopic azoprobes in water. In this system, all components of the guest species induce the split ICD response, making the specific detection of each component feasible by maintaining the other two components in the **15C5-Azo-dpa**–γ-CyD complex solution. To the best of our knowledge, this is the first example of a simple ditopic receptor exhibiting multi-recognition function based on supramolecular chirality in water.

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