JOC The Journal of Organic Chemistry

Article

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.6b02513 • Publication Date (Web): 20 Dec 2016

Just Accepted

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Design and Function of Supramolecular Recognition Systems Based on Guest Targeting Probe-Modified Cyclodextrin Receptors for ATP

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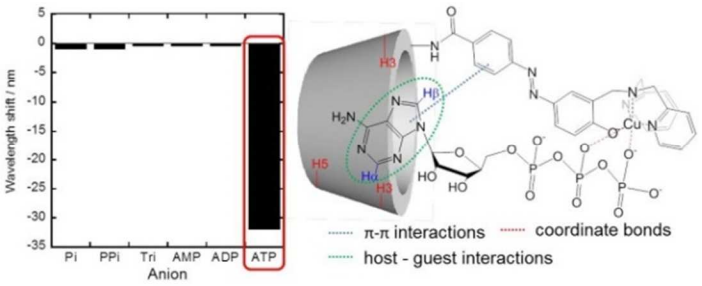
ABSTRACT: In this study, we have developed a rational design strategy to obtain highly selective supramolecular recognition systems of cyclodextrins (CyDs) on the basis of the lock and key principle. We designed and synthesized dipicolylamine (dpa)-modified γ-CyD-Cu^{2+} complexes possessing an azobenzene unit (**Cu·1-γ-CyD**) and examined how they recognized phosphoric acid derivatives in water. The results revealed that **Cu·1-γ-CyD** recognized ATP with high selectivity over other phosphoric acid derivatives. The significant blue shift in the UV-vis spectra and ^{1}H NMR analysis suggested that the selective ATP recognition was based on the multipoint interactions between the adenine moiety of ATP and both the CyD cavity and the azobenzene unit in addition to the recognition of phosphoric moieties by the Cu-dpa complex site. Our unique receptor made it capable of distinguishing ATP from AMP and ADP, revealing the discrimination of even a length of one phosphoric group. This study demonstrates that, compared to conventional recognition systems of CyDs, this multipoint recognition system confers a higher degree of selectivity for certain organic molecules, such as ATP, over their similar derivatives.



INTRODUCTION

The supramolecular chemistry of molecular complexes formed by weak interactions between host molecules and guest molecules has been explored with the intent of developing new functional capabilities for highly selective molecular recognition systems.[1-5] Cyclodextrins (CyDs) are well-known host molecules that include hydrophobic molecules and act to increase the solubilities of the hydrophobic guest molecules in water through the formation of host-guest inclusion complexes.[6,7] Molecular recognition systems of CyDs based on their host-guest interactions have caught a great deal of attention in a variety of chemical fields.[8-10] A various functional CyDs have been studied as versatile receptors for molecular recognitions, building blocks for functional materials, and even drug delivery systems.[11-15] However, these recognition systems have several limitations. For example, it is quite difficult for them to selectively include certain organic molecules over their similar derivatives because most conventional recognition systems of CyDs are based on 1 : 1 type interactions between CyD cavity and guest molecules.[16-18] Until now, certain number of studies for the selective complexation of nucleotides and nucleosides by synthetic CyD hosts have been reported.[19-27] For instance, positively charged CyDs bearing some aminomethyl groups bind adenosine monophosphate (AMP), adenosine diphosphate (ADP) or adenosine triphosphate (ATP) very tightly with interesting structural features, but there were no examples of applications to highly selective chemical sensors.[19,20,26] In the field of supramolecular chemistry, the relationship between CyDs and azobenzene derivatives has been well studied over recent decades.[9,18,28] It is known that azobenzene-modified CyDs provide supramolecular recognition systems possessing the potential for a guest responsive color-change indicator.[9,18,29] However, the potential molecular targets of these CyD probes are limited because the detection mechanisms depend only on the affinity of guest molecules to CyDs cavity. In this research, in order to overcome these limitations, we demonstrate the utility of a novel approach in the design of supramolecular CyD recognition

systems based on the lock and key principle by implementing selective colorimetric receptors for ATP.

Our receptor (**Figure 1**) possesses two recognition sites: the dipicolylamine (dpa)-modified azobenzene unit that appears like a protruding arm (guest targeting probe), and the γ-CyD cavity. The length of the arm was designed to provide multipoint recognition systems by host-guest interactions between the adenine moiety of ATP and the CyD cavity, in addition to the recognition of phosphoric moieties by the metal ion-dpa complex site. The dpa unit is well known ligand for the recognition of phosphoric moieties, and γ-CyD has the adequate cavity size to provide the host-guest interactions with adenine moiety of ATP even after the modification of guest targeting probes. We evaluated the recognition capabilities toward several phosphoric acid derivatives of **1** and **1-γ-CyD** (Scheme 1) metal ion complexes.

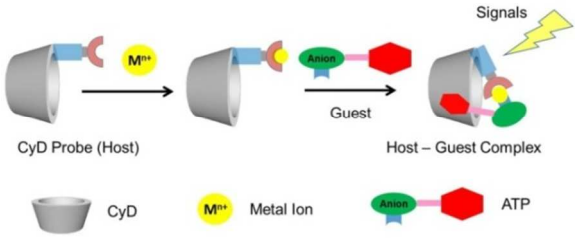
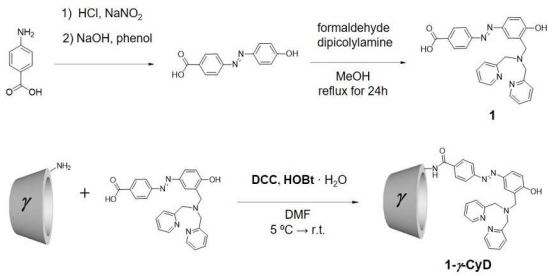


Figure 1. Images of CyD probe for ATP based on host–guest interactions.

Scheme 1. Synthesis of dipicolylamine-modified CyD



In order to increase selectivity and versatility of the receptor, we not only focused on the affinity of the CyD cavity to the guest but also the length of the arm, thereby allowing for a potential range of guest lengths. To confirm the validity of our unique recognition strategy based on guest targeting probe-modified CyDs, we chose ATP as a target molecule, because it is difficult for conventional host-guest interactions of CyDs to selectively include such complicated molecules over their similar derivatives.

RESULTS AND DISCUSSION

The probe **1** was synthesized by azo coupling[30] and the Mannich reaction. Then, the probe **1** and 3-amino-γ-CyD were coupled by a condensation reaction.[31] The crude product was purified by acetone reprecipitation and gel filtration chromatography.[18,29] The probe **1-γ-CyD** was obtained and identified by ^{1}H NMR, ^{13}C NMR, ^{1}H-^{1}H COSY experiments, and ESI-HRMS (See Experimental Section).

At first, the UV-vis spectra around the π-π* transition of **Cu·1** possessing no CyD cavity in the presence of monophosphate (Pi), pyrophosphate (PPi), triphosphate (Tri), AMP, ADP, and ATP were measured. No remarkable selectivity for certain phosphoric acid derivatives was observed in both the absorbance changes and the wavelength shifts (**Figure 2**). However, a small blue shift was observed in the presence of ATP.

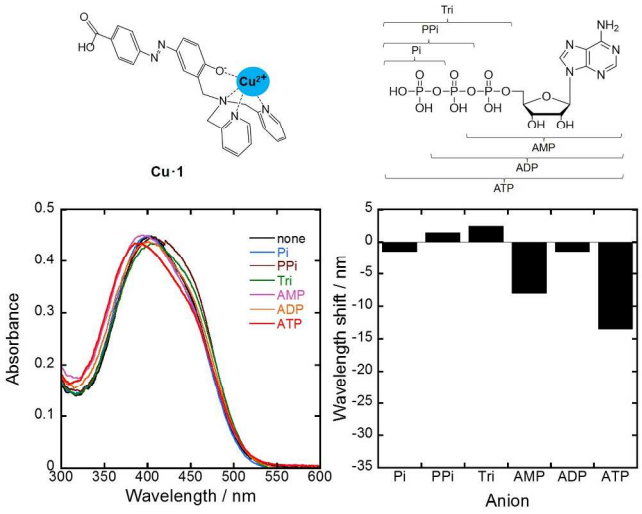


Figure 2. Selectivity of **Cu·1** in the presence of phosphoric acid derivatives in 1% DMSO-99% water (*v*/*v*), pH 7.4 adjusted with HEPES/NaOH buffer, at 25 °C. [**1**] = 0.020 mM, [$Cu(NO_3)_2$] = 0.020 mM, [phosphoric acid derivative] = 2.0 mM, [γ-CyD] = 0.020 mM.

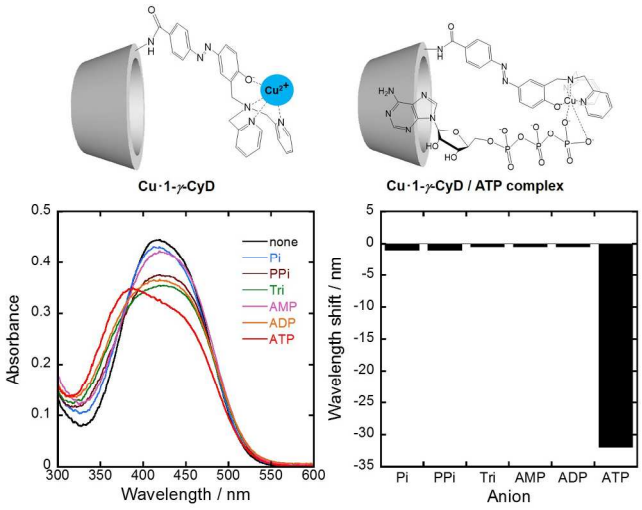


Figure 3. Selectivity of **Cu·1-γ-CyD** in the presence of phosphoric acid derivatives in 1% DMSO-99% water (*v*/*v*), pH 7.4 adjusted with HEPES/NaOH buffer, at 25 °C. [**1-γ-CyD**] = 0.020 mM, [$Cu(NO_3)_2$] = 0.020 mM, [phosphoric acid derivative] = 2.0 mM.

In order to evaluate the recognition capability of the CyD cavity, the UV-vis spectra of **Cu·1-γ-CyD** in the presence of phosphoric acid derivatives were also examined. **Cu·1-γ-CyD** showed a significant blue shift only in the presence of ATP (**Figure 3**). The Cu^{2+} complex exhibited the most remarkable response to ATP, compared to that of other metal ions such as Zn^{2+}.

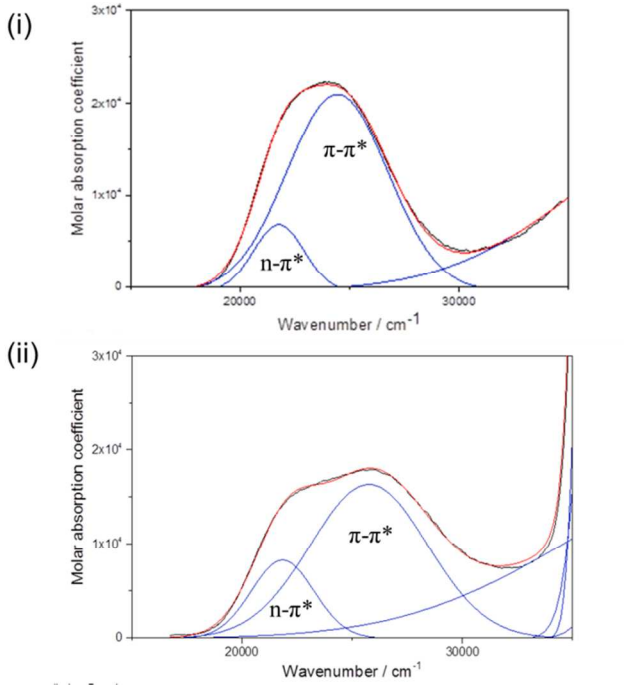


Figure 4. The curve of molar absorption coefficients of **Cu·1-γ-CyD** in the absence and presence of ATP in 99% water-1% DMSO (*v*/*v*), pH 7.4 adjusted by HEPES/NaOH buffer, at 25°C. [**1-γ-CyD**] = 0.020 mM, (i) in the absence of ATP, (ii) [ATP] = 2.0 mM.

To analyze this ATP-selective blue shift, each spectrum was fitted by a Gaussian function (**Figure 4**). The fitting results revealed that the UV-vis spectra were composed of two optical transitions: an optically allowed π-π* transition and an optically forbidden n-π* transition. In particular, the oscillator strength of the n-π* transition was increased in the presence of ATP (**Tables S5 and S6**). The UV-vis spectra of the π-π* transition also broadened and shifted to the high-energy region. The results demonstrated that the π-π interactions between the adenine moiety and the azobenzene unit were affected by the spectral shift. In general, the energy gap between HOMO (corresponding to π orbitals) and LUMO (corresponding to π* orbitals) is enlarged by the formation of a more stable complex, and the absorption maximum wavelength shifts to the high-energy region (It is known that adenosine moiety easily interacts with other aromatic compounds).[12,32] Therefore, it was suggested that π-π interactions induced a change in the electronic states around the dye moiety and slightly broke the optically forbidden n-π* transition. As conventional spectral shifts of azobenzene derivatives are due to photoisomerization or protonation/deprotonation of the functional groups, this is a unique response mechanism based on π-π interactions for azobenzene derivatives.[9,15]

In addition, the results demonstrated that the anion selectivity of **Cu·1-γ-CyD** was altered by the length of phosphoric anion moieties and the existence of adenine moieties. This selectivity was considered to be based on host-guest interactions between the adenine moiety of ATP and the γ-CyD cavity. It was assumed that the hydrophobic CyD cavity induced stronger π-π interactions by immobilizing the adenine moiety in close proximity to the azobenzene unit, compared to the **Cu·1** recognition system. The adenine moieties of both AMP and ADP did not interact with the azobenzene unit because the lengths of their phosphate anion moieties were inadequate for interacting with the CyD cavity and the azobenzene unit. It is evident that the distance between the dpa unit and the CyD cavity plays an important role in the selective ATP recognition in this system.

To evaluate the real selectivity of **Cu·1-γ-CyD** for ATP, the competitive binding experiments are conducted in the presence of other interfering anions (Pi, PPi, Tri, AMP, and ADP), with the subsequent addition of ATP (**Figure 5**).[32] The **Cu·1-γ-CyD** also showed blue shifts derived from ATP recognition in the presence of interfering anions, indicating that **Cu·1-γ-CyD** recognized ATP selectively in responses even if other similar derivatives existed (The UV-vis spectra and the absorbance changes are depicted in **Figure S25**).

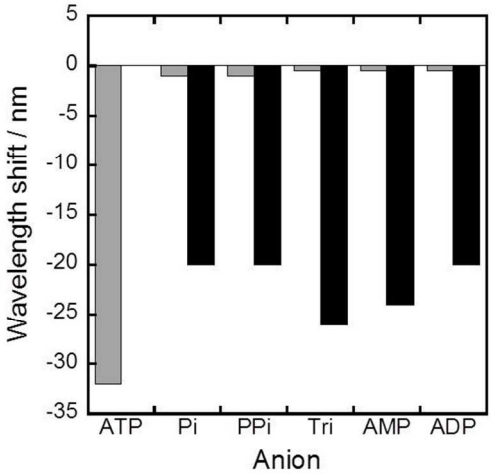


Figure 5. Real selectivity of **Cu·1-γ-CyD** for ATP in wavelength shifts toward anions in 99% water-1% DMSO (*v*/*v*), pH 7.4 adjusted by HEPES/NaOH buffer, at 25°C. [**1-γ-CyD**] = 0.020 mM, [$Cu(NO_3)_2$] = 0.020 mM, [ATP] = [Anion] = 2.0 mM. The gray bar represents the wavelength shifts in the presence of each anion (100 equiv.). The black bar represents wavelength shifts in the presence of ATP (100 equiv.) and each anion (100 equiv.).

In order to calculate the binding constant to ATP, the absorption spectra of **1** and **1-γ-CyD** metal ion complexes at pH 7.4 in the presence of various concentrations of ATP were examined (**Figures S21-S24**). The binding constant of **Cu·1** to ATP was 2630 ± 310 M^{-1} by curve fitting. On the other hand, that of **Cu·1-γ-CyD** was 6640 ± 890 M^{-1}, which was 2.5 times higher than that of **Cu·1** having no CyD. Also, the binding constant of **Zn·1** to ATP was 857 ± 119 M^{-1}. On the other hand, that of **Zn·1-γ-CyD** was 2898 ± 146 M^{-1}, which was 3.4 times higher than that of **Zn·1** having no CyD. These results confirmed that the CyD cavity enhances the binding constant to ATP in this recognition system.

We also analyzed the supramolecular conformation of the **Cu·1-γ-CyD**/ATP complex by conducting the ^{1}H NMR titration and NOESY measurements of the **Zn·1-γ-CyD** /ATP complex (Cu^{2+} is not appropriate for NMR measurements because of its paramagnetism). The peaks of NMR spectra were identified by ^{1}H-^{1}H COSY experiments (See SI). In the NMR titration, proton peaks assigned to j and k in the ^{1}H NMR spectra were shifted to the high magnetic field region in the presence of ATP (**Figure 6**), which confirmed that π-π interactions with the adenine moiety increased the electron density around the azobenzene unit.

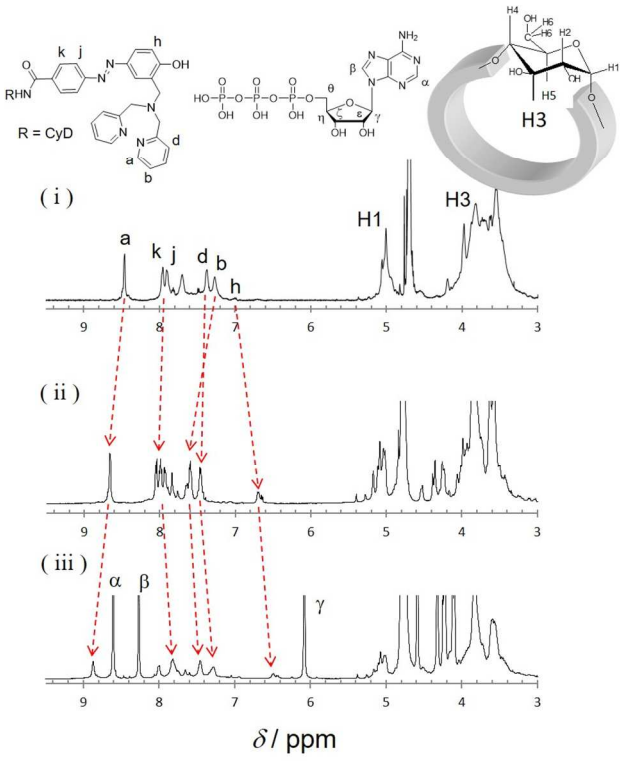


Figure 6. ^{1}H NMR spectra of **1-γ-CyD, Zn·1-γ-CyD** and **Zn · 1-γ-CyD**/ATP complex (500 MHz, solvent: 33% DMSO-d_6-67% D_2O). [**1-γ-CyD**] = 0.50 mM, (i) in the absence of Zn^{2+} and ATP, (ii) [$Zn(NO_3)_2$] = 0.50 mM, (iii) [$Zn(NO_3)_2$] = 0.50 mM, [ATP] = 50 mM.

In addition, the shifts of the proton peaks assigned to a, b, and d, which were derived from the dpa unit, implicated the recognition of phosphoric moieties by the Zn-dpa complex site.[35-37] The shift of the proton peak assigned to h, which was derived from the proton of the hydroxyl group at the *ortho* position, was also noted, indicating that the hydroxyl group is related to the coordination to Zn^{2+} as a phenolate ion.

In NOESY measurements, protons that are in close proximity to each other give rise to correlation peaks.[33,34] According to **Figure 7 (i)**, there are correlations between ^{1}H derived from the dpa-azobenzene unit and H3 derived from the inside cavity of CyD in the presence of one equivalent of ATP (enclosed in blue circles). The result suggested that conformations including and excluding CyD-dpa-azobenzene unit exist in equilibrium in solution.[18] However, in the presence of five equivalents of ATP, correlations between α and β protons derived from the adenine moiety and H3 derived from the inside cavity of CyD (enclosed in red circles) were observed, and the former correlation disappeared, as shown in **Figure 7 (ii)**. However, there were no correlations between α and β protons and H5 derived from the inside cavity of CyD. Therefore, it is evident that the adenine moiety interacts with the inside cavity of CyD shallowly.[27,34]

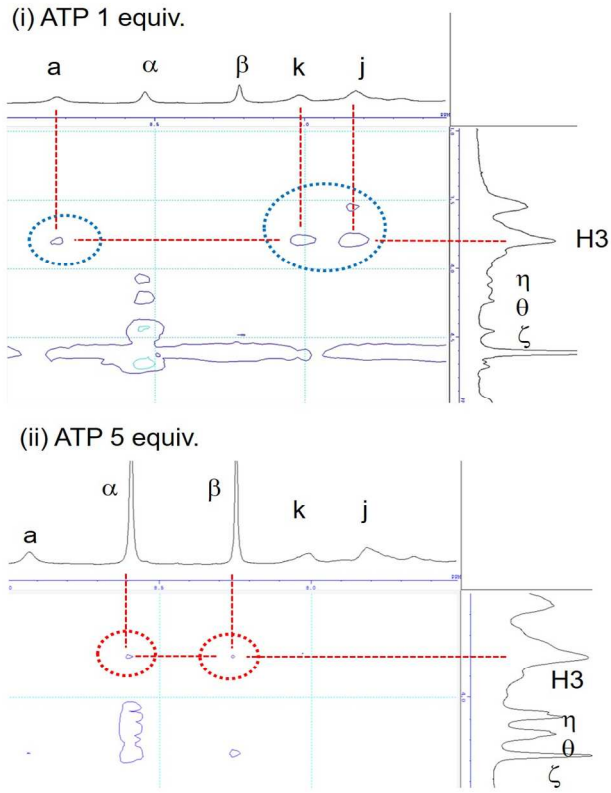


Figure 7. NOESY spectra of **Zn·1-γ-CyD**/ATP complex (500 MHz, solvent: 50% DMSO-d_6-50% D_2O (*v*/*v*)). [**1-γ-CyD**] = [$Zn(NO_3)_2$] = 5.0 mM, (i) [ATP] = 5.0 mM, (ii) [ATP] = 25 mM.

These correlations were even observed in 50% DMSO-d_6-50% D_2O (v/v) condition, which we can expect much stronger interactions in 1% DMSO-99% water (v/v) condition. Also, if we could measure NMR spectra of **Cu·1-γ-CyD**, much stronger correlations would be observed because Cu^{2+} complex showed the higher binding ability to ATP (See **Table S7**). This important piece of evidence supported that host-guest interactions occurred between the adenine moiety of ATP and the CyD cavity.

These results suggested the supramolecular conformation shown in **Figure 8**. Thus, the host-guest interactions between the adenine moiety of ATP and the CyD cavity are responsible for the highly selective ATP recognition in this supramolecular system. Our results confirm the successful binding of ATP to the **Cu·1-γ-CyD**, suggesting that, compared to conventional recognition systems of CyD—which were based on 1 : 1 type interactions between the CyD cavity and guest molecules and not sufficient for selective ATP recognition—the present multipoint recognition system confers a higher degree of selectivity for certain organic molecules, such as ATP, over their similar derivatives. These results also suggested that, in order to increase selectivity and versatility of the receptor, it is important not only to focus on the affinity of the CyD cavity to the guest but also the distance between the CyD cavity and the other recognition site, thereby allowing for a potential range of guest lengths. By introducing this strategy into the design of selective host-guest interactions of CyDs, unprecedented selectivity and specificity not observed with conventional CyD systems can be expected. The present recognition system is very simple but provides a real model for the design of artificial receptors based on the lock and key principle.

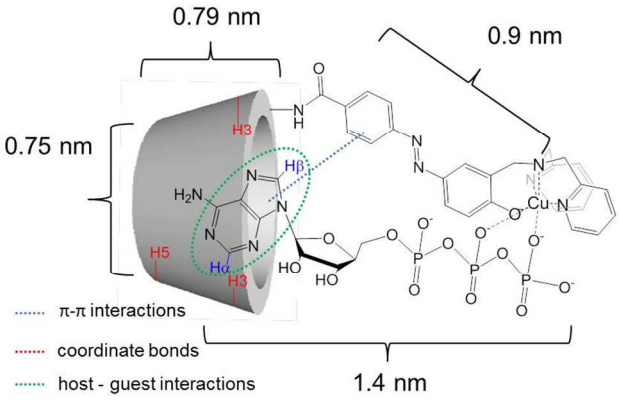


Figure 8. Suggested supramolecular conformation of **Cu·1-γ-CyD**/ATP complex.[38,39]

CONCLUSION

We have designed, synthesized, and evaluated the guest targeting probe-modified CyD (**Cu·1-γ-CyD**) as the novel design strategy of supramolecular recognition systems of CyDs. The results revealed that **Cu·1-γ-CyD** recognized ATP with high selectivity over other phosphoric acid derivatives possessing similar phosphate anion moieties or the same nucleobase. The significant blue shift in the UV-vis spectra and NMR analysis suggested that this selectivity was based on the multipoint interactions between the adenine moiety of ATP and both the CyD cavity and the azobenzene unit in addition to the recognition of phosphoric moieties by the Cu-dpa complex site. These results, which confirmed the successful binding of ATP to **Cu·1-γ-CyD**, provided evidence that the distance between the dpa unit and the CyD cavity plays an important role in the selective ATP recognition. Thus our unique recognition system made it capable of distinguishing ATP from AMP and ADP, revealing the discrimination of even a length of one phosphoric group. This supramolecular recognition system based on the lock and key principle would enable us to design novel highly selective chemical receptors of CyDs for various kinds of organic molecules in water.

EXPERIMENTAL SECTION

Reagents. All organic solvents and reagents were commercially available with guaranteed grades and used without further purification. Water was doubly distilled and deionized by a Milli-Q water system before use.

Apparatus. UV-vis absorption spectra were measured with a UV-vis spectrophotometer equipped with a Peltier thermocontroller with a 10 mm quartz cell.

Phosphoric acid derivatives recognition by Cu·1. To evaluate the phosphoric acid recognition ability of **Cu·1**, spectral measurements were performed. Solutions containing **1** (0.020 mM), $Cu(NO_3)_2$ (0.020 mM), phosphoric acid derivatives (2.0 mM, pH 7.4, adjusted using NaOH), γ-CyD (0.020 mM), and HEPES/NaOH buffer (5.0 mM, pH 7.4, adjusted using NaOH) were prepared and spectra were recorded at 25°C.

Phosphoric acid derivatives recognition by Cu·1-γ-CyD. To evaluate the phosphoric acid recognition ability of **Cu·1-γ-CyD**, UV-vis spectral measurements were performed. Solutions containing **1-γ-CyD** (0.020 mM), $Cu(NO_3)_2$ (0.020 mM), phosphoric acid derivatives (2.0 mM, pH 7.4, adjusted using NaOH), and HEPES/NaOH buffer (5.0 mM, pH 7.4, adjusted using NaOH) were prepared and spectra were recorded at 25°C.

Spectral fitting analysis. UV-vis spectra obtained from phosphoric acid derivatives recognition were fitted by Gaussian functions.

The competitive binding experiments of Cu·1-γ-CyD. To evaluate the real selectivity of **Cu·1-γ-CyD**, spectral measurements were performed. Solutions containing **1-γ-CyD** (0.020 mM), $Cu(NO_3)_2$ (0.020 mM), ATP (2.0 mM, pH 7.4, adjusted using NaOH), interfering anions (2.0 mM, pH 7.4, adjusted using NaOH), and HEPES/NaOH buffer (5.0 mM, pH 7.4, adjusted using NaOH) were prepared and spectra were recorded at 25°C.

Calculation of binding constants of 1 and 1-γ-CyD metal ion complexes to ATP. To calculate the binding constant of **1** and **1-γ-CyD metal ion complexes** to ATP, UV-vis spectral measurements were performed. Solutions containing **1-γ-CyD** (0.010 mM), $Cu(NO_3)_2$ or $Zn(NO_3)_2$ (0.010 mM), and HEPES/NaOH buffer (5.0 mM, pH 7.4, adjusted using NaOH) were prepared and spectra were recorded at 25ºC while ATP concentrations were varied from 0.0 to 4.0 mM. The binding constants were calculated by curve fitting (See SI).

NOESY measurements of Zn·1-γ-CyD/ATP complex. To evaluate the supramolecular conformation of the **Cu·1-γ-CyD**/ATP complex, NOESY spectral measurements of **Zn·1-γ-CyD**/ATP complex were performed. Solutions containing **1-γ-CyD** (5.0 mM), $Zn(NO_3)_2$ (5.0 mM), and ATP (5.0 mM or 25 mM, pH 7.4, adjusted using NaOD) were prepared and NOESY spectra were recorded.

General Procedure for the Synthesis of 4'-Hydroxyazobenzene-4-carboxylic acid.[40] The compound *p*-aminobenzoic acid (2.034 g, 14.80 mmol) was dissolved in 3 M HClaq. (50 cm^3), the solution was stirred for 10 min in an ice bath (pH = 1). Sodium nitrite (1.056 g, 14.49 mmol) dissolved in 6.0 cm^3 cooled DI water was added, the solution was stirred for 15 min. Phenol (1.406 g, 14.87 mmol) and 4.0 cm^3 5 M NaOHaq. dissolved in 4.0 cm^3 cooled DI water was slowly added, stirred for 15 min in an ice bath at 0 ºC. The solution was adjusted to pH = 7 with 5 M NaOHaq. Sodium chloride (2.072 g) was added and heated at 65 ºC in a hot bath for 10 min, cooled at room temperature and salted it out. Yellow precipitation was filtered by suction filtration. The crude product was recrystallized from MeOH and water to obtain the desired product 4'-Hydroxyazobenzene-4-carboxylic acid (2.248 g) as orange-red crystals in 64% yield. The sample was identified by ^{1}H NMR, ^{13}C NMR and ESI-HRMS. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.17 (s, 1H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.56 (dd, *J* = 8.8 Hz, 9.9 Hz, 4H), 5.66 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (400 MHz, DMSO-d_6): δ 167.8, 161.9, 153.7, 145.1, 135.9, 130.3, 125.1, 121.6, 116.1. ESI-HRMS (-) m/z calcd. for $[M-H]^-$, 241.0619; found, 241.0627.

General Procedure for the Synthesis of 1. A mixture of dipicolylamine (0.825 g, 4.13 mmol) and 37% formaldehyde solution (0.338 g, 4.13 mmol) in 15 cm^3 MeOH was reflexed for 1.5 h at 70 ºC. The compound 4'-Hydroxyazobenzene-4-carboxylic acid (1.008 g, 4.13 mmol) dissolved in 30 cm^3 MeOH was added, the reaction was maintained at reflux temperature of 70 ºC for 24 h. The solution was concentrated under reduced pressure to obtain orange-red viscous fluid. The fluid was washed with small amount of MeOH and filtered by suction filtration to afford the desired product. The compound **1** (0.751 g) was obtained as a blight yellow solid in 40% yield. The sample was identified by ^{1}H NMR, ^{13}C NMR, DEPT, and ESI-HRMS. mp 207 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.54 (dd, *J* = 1.1 Hz, 5.0 Hz, 2H), 8.11 (d, *J* = 8.8 Hz, 2H), 7.92 (d, *J* = 5.1 Hz, 1H), 7.89 (d, *J* = 10.2 Hz, 2H), 7.77-7.80 (m, 3H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.29 (td, *J* = 5.5 Hz, 7.2 Hz, 7.2 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 1H), 3.86 (s, 4H), 3.83 (s, 2H). ^{13}C NMR (500 MHz, DMSO-d_6): δ 166.8, 161.2, 158.2, 154.6, 148.7, 145.0, 136.9, 131.9, 130.5, 125.3, 124.7, 124.5, 122.7, 122.4, 122.1, 116.6, 58.5, 54.1. ESI-HRMS (-) m/z calcd. for $[M-H]^-$, 452.1728; found, 452.1750.

General Procedure for the Synthesis of 1-γ-CyD. A mixture of **1** (0.0530 g, 0.116 mmol), **DCC** (0.0238 g, 0.115 mmol), **HOBt** · H_2O (0.0177 g, 0.115 mmol) in 3.0 cm^3 dry DMF was stirred in an ice bath for 15 min. The compound 3-amino-γ-CyD (0.100 g, 0.0770 mmol) dissolved in a small amount of dry DMF was slowly added, the solution was stirred in an ice bath for 30 min again. After removing an ice bath, the reaction mixture was stirred at room temperature for 24 h. The solution was concentrated under reduced pressure until a half of DMF was removed. The sample was put in refrigerator and left a day. The resulting solution was poured into acetone (1000 cm^3) to obtain yellow precipitations, followed by washing with acetone several times. The crude product was charged on a column of Sephadex G10 and eluted with 0.2 M aqueous solution of ammonium carbonate (pH = 8.9). The first yellow spot was collected as the desired product. The purity was checked with TLC. The fraction was lyophilized under reduced pressure to form a yellow powder. The compound **1-γ-CyD** (110 mg) was obtained in 82% yield. The sample was identified by ^{1}H NMR, ^{1}H-^{1}H COSY experiments (See SI), and ESI-HRMS. mp 305-306 ºC; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.55 (d, *J* = 5.2 Hz, 2H), 8.05 (d, *J* = 8.6 Hz, 2H), 7.91 (d, *J* = 8.6 Hz, 1H), 7.82 (d, *J* = 6.9 Hz, 2H), 7.72-7.82 (m, 3H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.29 (td, *J* = 6.0 Hz, 7.2 Hz, 7.2 Hz, 2H), 7.01 (d, *J* = 8.6 Hz, 1H), 6.56 (s, 1H), 5.57-6.01 (m, 19 H), 4.39-5.07 (m, 22 H), 3.90-3.10 (m, overlaps with HOD), 3.81 (s, 4H), 3.78 (s, 2H). ESI-HRMS (-) m/z calcd. for $[M-H]^-$, 1729.6019; found, 1729.6019.

ASSOCIATED CONTENT

Supporting Information

The supporting information is available free of charge on the ACS publication web site.

Compound characterization data, phosphoric acid recognition by UV-vis measurements of **1** and **1-γ-CyD** metal ion complexes, calculation of binding constants by curve fitting, competitive experiments and copies of ^{1}H-^{1}H COSY and NOESY spectra of **Zn·1-γ-CyD**/ATP complex.

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Author Contributions

All the authors have contributed equally to this work and approved the final version of the manuscript.

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

This work was financially supported by a Grant-in-Aid for Scientific Research (C) (Grant No. 15Ko5548) from Japan Society for the Promotion of Science (JSPS) and a Grant-in Aid for Scientific Research (A) (Grant No. 26248038) from the Ministry of Education, Culture, Sports, Science and Technology (MEXT) of Japan.

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