

Photoresponsive Formation of Pseudo[2]rotaxane with Cyclodextrin Derivatives

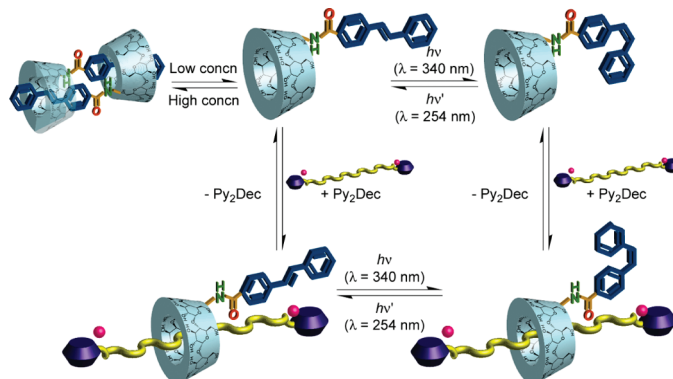
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ABSTRACT



The two isomers of 6-stilbene-amide- α -CD (6-StiNH- α -CD) exhibit different inclusion behaviors upon complexation with an alkyl chain bearing pyridinium end caps. Photoisomerization of the stilbene moiety of the CD derivative affects threading due to complexation between the axle and *trans*- or *cis*-6-StiNH- α -CD.

Biological molecular motors can be roughly divided into linear molecular motors (e.g., myosin, kinesin, dynein, etc.^{1–4}) and rotary motors (e.g., F₀F₁-ATP synthase, F₁-ATPase, etc.^{5,6}). Rotaxanes consisting of mechanically

interlocked macrocycles and dumbbell-shaped components have been studied as an example of controlled molecular movements for both artificial linear and rotary molecular motors. Recently, controlled synthetic linear^{7,8} and rotary molecular motors using rotaxane building

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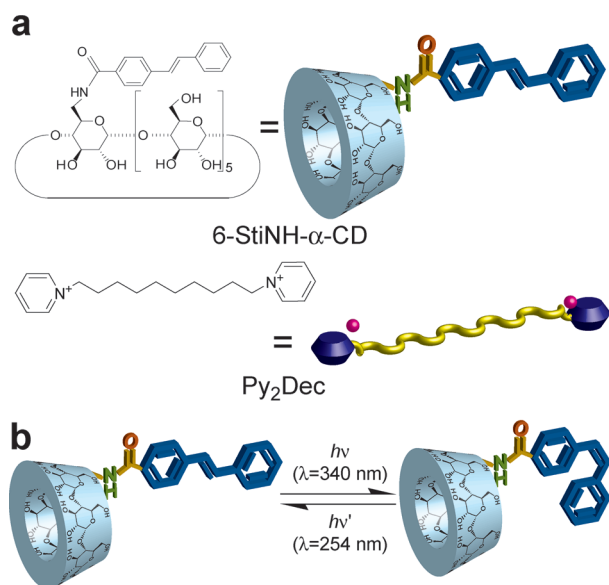


Figure 1. (a) Chemical structures of 6-StiNH- α -CD and Py₂Dec as an axis molecule. (b) Photoisomerization of 6-StiNH- α -CD.

blocks have been achieved by controlling the rotary movement.^{9–12} We have previously reported that the direction of the faces of α -CD by the terminal group of the axle molecule controls the linear movement of α -cyclodextrin (α -CD) on *pseudo*[2]rotaxane with dicationic axle molecules.^{13a,b} Upon complexation of modified α -CDs as host molecules for guest molecules consisting of an alkyl chain with pyridinium end caps, we have controlled complex formation and dissociation by pH responses of the functional groups on modified α -CDs.^{13c} Although numerous types of CD-based *pseudo*-rotaxanes and rotaxanes have been prepared in the past two decades,¹⁴ there are few reports on the threading–dethreading of CD-based *pseudo*-rotaxanes.¹⁵ Moreover, *pseudo*-rotaxanes

formed by CD derivatives with substituents sensitive to light or heat have yet to be reported. Herein we report *pseudo*-rotaxanes formed by 6-stilbene-amide- α -CD (6-StiNH- α -CD) and an alkyl chain with pyridinium end caps (Figure 1) where threading of the axle into the cavity of 6-StiNH- α -CD is controlled by light.

The axle molecule (Py₂Dec) and *trans*-6-StiNH- α -CD were prepared according to the previously reported methods.^{13a,16} Stilbene derivatives show photoinduced isomerization; irradiating with UV and visible light induces isomerization from *trans* to *cis* and from *cis* to *trans*, respectively.¹⁷ After photoirradiation with visible light ($\lambda = 340$ nm), 92% of *trans*-6-StiNH- α -CD was isomerized to *cis*-6-StiNH- α -CD (*trans*/*cis* = 8:92). However, the *trans* form was recovered by irradiating at $\lambda = 254$ nm.

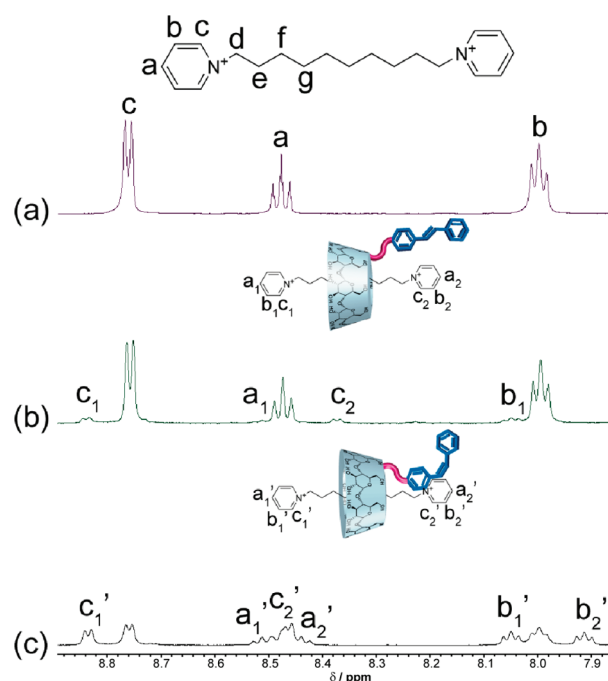


Figure 2. Partial ¹H NMR of Py₂Dec (4.0 mM) (a) in the absence of 6-StiNH- α -CD, (b) in the presence of *trans*-6-StiNH- α -CD (4.0 mM), and (c) in the presence of *cis*-6-StiNH- α -CD in D₂O (4.0 mM) at 30 °C.

Based on the isomerization of 6-StiNH- α -CD described above, Py₂Dec was mixed with *trans*-6-StiNH- α -CD or *cis*-6-StiNH- α -CD at room temperature. ¹H NMR spectroscopy in D₂O monitored the formation of *pseudo*-rotaxanes. These 6-StiNH- α -CDs were isolated by preparative reversed phase HPLC. Figure 2 shows the partial ¹H NMR spectra of Py₂Dec, Py₂Dec/*trans*-6-StiNH- α -CD, and Py₂Dec/*cis*-6-StiNH- α -CD. After 10 min, equilibrium of the complexation was reached. Mixing

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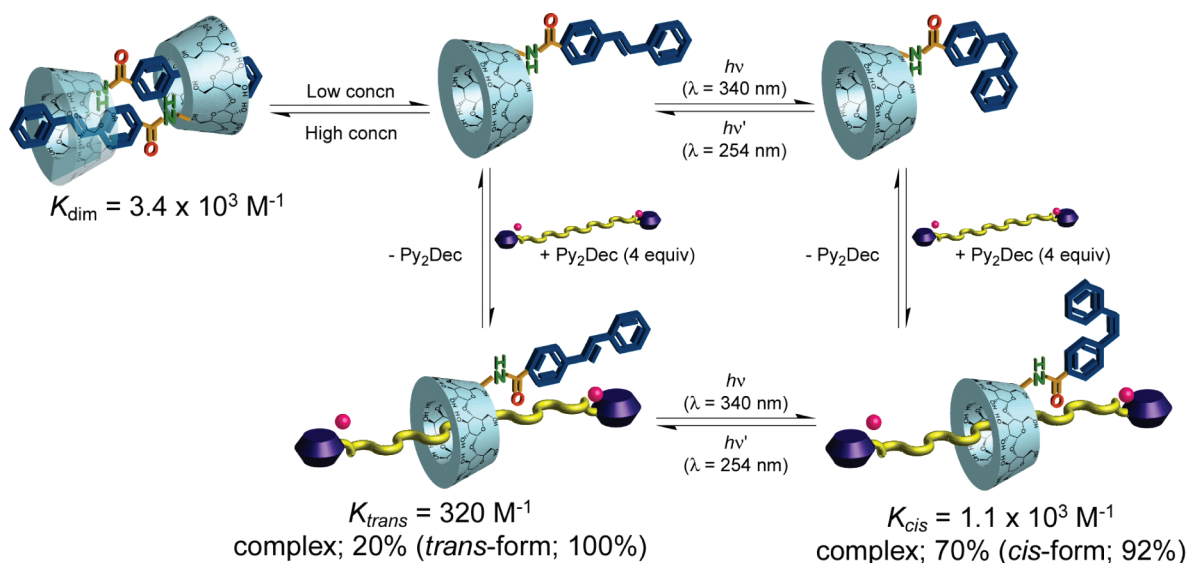
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Table 1. Thermodynamic Parameters of Complexation between 6-StiNH- α -CD and Py₂Dec at 298 K

<i>pseudo</i> [2]rotaxane	$\Delta H^\circ /$ kJ·mol ⁻¹	$\Delta S^\circ /$ J·mol ⁻¹ ·K ⁻¹	$\Delta G^\circ /$ kJ·mol ⁻¹	$K /$ M
Py ₂ Dec/ <i>trans</i> -6-StiNH- α -CD	-31.5 ± 2.2	-57.7 ± 6.9	-14.3	320
Py ₂ Dec/ <i>cis</i> -6-StiNH- α -CD	-33.9 ± 1.1	-55.6 ± 3.4	-17.4	1.1 × 10 ³

**Figure 3.** Schematic illustration of the formation of *pseudo*[2]rotaxane and the double threaded dimer with 6-StiNH- α -CDs. 6-StiNH- α -CD photoisomerizes between the *trans*- and *cis*-forms by irradiating with UV lights ($\lambda = 340$ and 254 nm).

trans-6-StiNH- α -CD with Py₂Dec caused the protons in the axis molecule to split in an aqueous solution (Figure 2b). This splitting was related to the formation of *pseudo*[2]rotaxane. 2D-ROESY NMR spectroscopy indicated that the inner protons of 6-*trans*-StiNH- α -CD and alkyl protons of Py₂Dec were correlated, suggesting the formation of *pseudo*[2]rotaxane (Figure S18).

The degree of complexation of Py₂Dec/*trans*-6-StiNH- α -CD, which was determined by the integrated intensity of the protons (such as proton c) for the complexed and uncomplexed axle Py₂Dec, reached 13%, which was lower than we initially envisioned. When the axle was mixed with *cis*-6-StiNH- α -CD in D₂O (equal molar), the protons of Py₂Dec split (Figure 2c). The degree of complexation reached 55%, which was calculated by the splitting of proton b. *Pseudo*[2]rotaxane with *cis*-6-StiNH- α -CD and Py₂Dec more easily formed than that with *trans*-6-StiNH- α -CD.

To investigate the stabilities of *pseudo*[2]rotaxanes, the thermodynamic parameters of the complexation were evaluated by a van't Hoff plot. Table 1 shows the results. Complexation between *cis*-6-StiNH- α -CD and Py₂Dec had more negative enthalpy changes (ΔH°) than that between *trans*-6-StiNH- α -CD and Py₂Dec. The larger ΔH° is attributed to stronger van der Waals interactions.

The association constants of *trans*-6-StiNH- α -CD with Py₂Dec exhibited $K_{\text{trans}} = 320 \text{ M}^{-1}$, whereas that of *cis*-6-StiNH- α -CD with Py₂Dec exhibited $K_{\text{cis}} = 1.1 \times 10^3 \text{ M}^{-1}$. These results indicate the *pseudo*[2]rotaxane formed by Py₂Dec/*cis*-6-StiNH- α -CD is more stable than that by Py₂Dec/*trans*-6-StiNH- α -CD due to the steric repulsion between the *trans*-stilbene group and Py₂Dec.

Next, we examined the influence of photoirradiation on the complex formation ratio of Py₂Dec/6-StiNH- α -CD. When a mixture of Py₂Dec and *trans*-6-StiNH- α -CD (4 molar excess) in D₂O was sequentially irradiated by UV light ($\lambda = 350$ nm) at room temperature, 92% of *trans*-6-StiNH- α -CD was converted into *cis*-6-StiNH- α -CD. The degree of complexation of *pseudo*[2]rotaxane increased from 20% to 70%. After irradiating the aforementioned solution at 254 nm, 62% of the *cis*-6-StiNH- α -CD returned to *trans*-6-StiNH- α -CD (*trans/cis* = 62:38).¹⁸ The degree of complexation decreased from 70% to 46%.

Additionally, we investigated the formation of supra-molecular complexes with 6-StiNH- α -CD and its influence on the formation of *pseudo*[2]rotaxane because our previous

(18) The decline in the photoisomerization efficiency from *cis* to *trans* is attributed to the pyridinium group, which serves as an energy acceptor, and the steric hindrance between Py₂Dec and the stilbene group.

report indicated that *trans*-3-StiNH- α -CD in aqueous solutions forms a double-threaded dimer.¹⁹ Circular dichroism spectra, 2D NMR spectra, and vapor pressure osmometry measurements of *trans*-6-StiNH- α -CD suggested the formation of a double-threaded dimer in aqueous solutions, but *cis*-6-StiNH- α -CD did not form supramolecular complexes (see Supporting Information). The association constant (K_{dim}) of *trans*-6-StiNH- α -CD for dimerization was $3.4 \times 10^3 \text{ M}^{-1}$, which was higher than that (K_{trans}) for complexation between *trans*-6-StiNH- α -CD and Py₂Dec. These results indicate that mixing *trans*-6-StiNH- α -CD with Py₂Dec preferentially forms the double-threaded dimer over *pseudo*[2]rotaxane (Py₂Dec/*trans*-6-StiNH- α -CD).

In conclusion, we studied the threading/dethreading of Py₂Dec into/out of the cavity of 6-StiNH- α -CD by photoinduced isomerization of the stilbene moiety of the CD derivative (Figure 3). Although we hypothesized that *trans*-6-StiNH- α -CD would effectively form *pseudo*[2]rotaxane, and *cis*-6-StiNH- α -CD would decompose

pseudo[2]rotaxane after photoirradiation, our results are contrary to our expectations. The thermodynamic studies exhibited that *trans*-6-StiNH- α -CD shows a relatively low complex formation ratio compared to *cis*-6-StiNH- α -CD due to the low stability. *Cis*-6-StiNH- α -CD formed *pseudo*[2]rotaxane with Py₂Dec. Regardless, complex formation of *pseudo*[2]rotaxane was observed upon irradiating with the appropriate wavelength. This threading–dethreading process might be applicable to light-powered molecular machines or logic gates based on CD derivatives.

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Supporting Information Available. Select NMR data (1D NMR and ROESY spectrum), determination of the diffusion coefficient, UV spectra, cd spectra, and turbo-ion spray mass spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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