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Communication

# Temperature-driven braking of $\gamma$ -cyclodextrin-curcubit[6]uril-cowheeled [4]rotaxanes

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#### **Graphical Abstract**



A capping moiety, playing a role of the brake, slowed down the rotation speed of the cyclodextrin of a cyclodextrin-cucurbit[6]uril-cowheeled [3]rotaxane. Lowering the temperature further stopped the rotation at the NMR timescale.

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#### ABSTRACT

Several cyclodextrin-cucurbit[6]uril-cowheeled [4]rotaxanes were synthesized through the cucurbit[6]uril-templated azide-alkyne 1,3-dipolar cycloaddition. The intramolecular interaction between the aromatic axle and the capping groups of cyclodextrin moieties was investigated by UV-vis, fluorescence, circular dichroism and NMR spectroscopic studies. The rotational kinetic of the wheel around the axle can be manipulated by adjusting the temperature. The capping group apparently slowed down the rotation of the wheel, playing a role of the brake, and lowering the temperature can stop the rotation of the wheel on the NMR timescale.

Precisely operating molecular mechanical devices is an intriguing topic of current nanotechnology. The synthesis of molecular motors has attracted considerable attention and a variety of molecular machines on the basis of interlocked molecules, such as rotaxanes, catenanes and molecular knots, have been designed and constructed [1]. Several strategies, including electrochemical and photochemical control, have been applied to drive the motion of molecular motors [2]. Artificial supramolecular chemical structures based on rotaxanes belong to the most extensively studied molecular machines, because of their interesting mechanical interlocking structures, unique physical/chemical properties and a wide range of potential applications. The non-covalent interlocked feature makes the ring freely slidable along the axle, and most studies on the rotaxane-based molecular machines focused on the function arising from the slide motion of the ring along the axle. On the other hand, the study on controlling the rotational kinetic of the ring around the axle was rarely involved [3]. Here, we set up a new strategy to control the rotational kinetic of the wheel by introducing a "brake" on the wheel moiety, and demonstrated that the rotation kinetic of the wheel could be accurately manipulated by temperature variation.

Cyclodextrins (CDs) are one of the most widely studied host molecules, bearing the advantage of good water solubility, inherent chirality, versatile binding ability and ready availability [4]. We have demonstrated that chemical modification could significantly improve the binding and chiral discrimination of CDs [5,6]. Both CDs and curcubit[6]uril (CB[6]) have been applied as the wheels of rotaxanes due to their round shape and unique complexation ability with organic guests in aqueous solution.  $\gamma$ -CD-CB[6]-cowheeled [4]rotaxanes **R1-R6** were synthesized by mixing  $\gamma$ -CD, CB[6], an alkynyl-terminated aromatic axle **2** or **3**, and a bulky azide **1** together in aqueous solution at room temperature. In rotaxanes **R2-R6**, capped  $\gamma$ -CD were used as the wheel part. By introducing capping moiety, the size and shape of CDs as well as their complexation behavior could be significantly varied [7].

CB[6],  $6^A$ , $6^X$ -dideoxy- $6^A$ , $6^X$ -diamino- $\gamma$ -CD and axle molecules were prepared according to the reported procedures [8]. The [4]rotaxanes were formed in good yield at room temperature as a result of CB[6]-catalyzed click-reaction [9]. We have demonstrated that the hydrogen bonding formed between CB[6] and CD played an important role in the efficient formation of [4]rotaxane [7b]. The rotaxanes **R1-R3**, containing an axle of biphenyl have been used as a supramolecular sensitizer for the chiral photoisomerization of cyclooctadiene. The capping part can further confine the orientational freedom of the axle part and therefore improved the reaction selectivity. It occurred to us that the capping moiety may also play a role of brake that can control the rotation kinetic of the axle. The steric hindrance effect between the cap and the axle molecule may slow down the rotation of the axle molecule along the axis of the CD cavity. Therefore, we investigated the NMR spectra of **R1-R3** in water (Fig. 1). All biphenyl protons should stay in a different environment if the rotation of the biphenyl group was stopped due to the unsymmetrical structure caused by the introduction of capping moiety. However, for all these three rotaxanes, only one set of the <sup>1</sup>H NMR spectra were observed, indicating that the biphenyl group in the cavity of  $\gamma$ -CD still can freely rotate on the NMR timescale. We ascribed the failure of braking to the relatively small size of biphenyl and the internal rotation of two benzene rings around the biphenyl linkage, and therefore focused our investigation on the rotaxanes **R4-R6**, in which the relatively bulky naphthalene severs as the axle (Scheme 1).



Scheme 1. Chemical structure of wheels, axles and hetero[4]rotaxanes.

It turned out that the UV-vis spectra of rotaxanes **R4-R6** are primarily the result of the UV-vis spectra of the capping moiety and the axle molecule (Fig. 2). This indicated that the axle part and the capping moiety had not significant electronic interaction at their ground states. **R4** and **R5** showed positive circular dichroism spectra at the <sup>1</sup>B<sub>b</sub> band of naphthalene (Fig. 3). According to the Kajtar's sector rule [10], these positive induced circular dichroism is consistent with the parallel orientation of the naphthalene axle along the longitudinal axis of the CD cavity. However, **R6** exhibited strong exciton coupling type circular dichroism (ECCD), due to the close and chiral orientation of two naphthalenes. The positive ECCD signal (positive peak at 322 nm and a negative peak at 228 nm) indicated a right-handed helical arrangement of the capping moiety and the axle.



Fig. 1. <sup>1</sup>H NMR (400 MHz) of hetero[4]rotaxanes R1 (upper), R2 (middle) and R3 (lower) measured at 25 °C in D<sub>2</sub>O.

The rotaxane **R4**, wheeled with native  $\gamma$ -CD, showed fluorescence spectrum similar to **3** with a higher intensity, presumably due to the protection of CD wall. On the contrary, **R6** showed only the fluorescence of the capping moiety, and the fluorescence due to the axle moiety is negligible. We ascribed this to the extremely high efficiency of fluorescence resonant energy transfer from the axle moiety to the capping naphthalene as a result of the close interlocking of the two moieties. No excimer fluorescence could be seen with **R6**, for which the poor orbital overlap between two orthogonal naphthalenes should be responsible. Interestingly, a structureless broad fluorescence peaked at around 430 nm was observed with **R5** in addition to the structural emission of the naphthalene axle (Fig 2, green line). We assigned the emission to the exciplex fluorescence formed between the naphthalene and the terephthalate. This is presumably due to that the terephthalate capping in **R5** has a smaller size than the naphthalene capping in **R6** and is, therefore, more flexible, which makes it easier forming  $\pi$ - $\pi$  stacking with the axle.



Fig. 2. Fluorescence spectra of 1.0 µmol/L of 3 (black), R4 (light blue), R5 (green) and R6 (red) measured in water at 25 °C,  $\lambda_{ex} = 280$  nm.



 $\label{eq:Fig. 3. } {}^{1}\!H\,NMR~(400~MHz)~of~hetero[4] rotaxanes~R4~(upper), R5~(middle)~and~R6~(lower)~measured~at~25~^{\circ}\!C~in~D_{2}O.$ 



Fig. 4. Partial <sup>1</sup>H NMR spectra (600 MHz, D<sub>2</sub>O:CD<sub>3</sub>OD=3:7) of hetero[4]rotaxane **R3** (left) and **R5** (right) recorded at -20 °C, -10 °C, -5 °C, 10 °C and 25 °C.

The <sup>1</sup>H NMR spectra of rotaxanes **R4-R6** were measured in D<sub>2</sub>O at 25 °C. As shown in Fig. 3, all three rotaxanes showed two sets of CB[6]'s proton signals, as a result that two CB[6] positioned at the secondary and primary rims of  $\gamma$ -CD, respectively. The <sup>1</sup>H NMR spectra of **R4** exhibited one set of aromatic proton signals, and the H2, H3, H4, H5 and H6 proton signals of the  $\gamma$ -CD were congested in a narrow region of 3.4-3.8 ppm. This is reasonable as the large cavity of  $\gamma$ -CD should allow the naphthalene axle to freely rotate. For **R5**, the <sup>1</sup>H NMR of CD exhibited a much wider distribution, giving an upfield shift up to 2.5 ppm. This indicated that the aromatic capping and the axle exerted unequal shielding and deshielding effects on each glucose unit of the CD. However, totally only one set of proton signals were seen for **R5**, suggesting that the rotation of the naphthalene axle is still fast on the NMR timescale.

The <sup>1</sup>H NMR spectra of **R6** showed even significant upfield shift, with some CD protons shifted as far as 2.1 ppm (Fig 3). Interestingly, the aromatic and CD proton signals of **R6** were clearly broadened at 25 °C, implying that the rotation of the axle was slow. To confirm

this, the VT NMR of rotaxanes were performed in a mixture of  $D_2O$  and  $CD_3OD$ , which allowed us to measure the NMR spectra at a temperature lower than 0 °C. As illustrated in Fig. 4, both **R3** and **R5** showed only one set of protons even at -20 °C, suggesting a fast rotation of the wheel. Nevertheless, the proton signals became broad when lowering the temperature to -10 °C and -20 °C. This observation raveled that the rotation speed slowed down with decreasing the temperature. In contrast, **R6** showed broad and overlapped <sup>1</sup>H NMR signals at 25 °C (Fig. 5), and raising the temperature to 40 °C led to an even broader and featureless <sup>1</sup>H NMR spectrum. The broad and coalesced proton signals become sharper and differentiable with further increasing the temperature, to show a relatively clear <sup>1</sup>H NMR spectrum at 55 °C and 80 °C. Interestingly, the <sup>1</sup>H NMR signals of **R6** also became clear and sharp when lowering the temperature. The signals divided into two sets of proton signals at -20 °C. The two sets of <sup>1</sup>H NMR signals indicated that the naphthalene axle for **R6**, in which both the capping and the axle moieties constituted with relatively bulky naphthalene group, should cause strong steric interaction and therefore the two conformations of **R6** interconvert slowly at low temperature (Scheme 2).



Scheme 2. Two rotational conformations of R6.



Fig. 5. Partial <sup>1</sup>H NMR (600 MHz, D<sub>2</sub>O:CD<sub>3</sub>OD = 3:7) spectra of **R6** at -20 °C, -10 °C, -5 °C, 10 °C, 25 °C, 40 °C, 55 °C and 80 °C.

In summary, we have synthesized a series of CB[6] and  $\gamma$ -CD co-wheeled [4]rotaxanes through a CB[6]-templated azide-alkyne 1,3dipolar cycloaddition. The aromatic capping moiety on the primary rim of  $\gamma$ -CD can interact with the aromatic axle at the ground and/or excited states. The rotaxanes having a naphthalene axle showed exciton coupling-type circular dichroism when wheeled with a naphthalene-capped  $\gamma$ -CD or exciplex fluorescence when wheeled with a terephthalate-capped  $\gamma$ -CD. Variable temperature <sup>1</sup>H NMR proved that the rotation speed of the axle was affected by both the geometry of capping groups and the temperature. The rotaxane with naphthalene groups on the capping and axle moieties showed rotation kinetics slower than NMR timescale at low temperature, due to the steric interaction. The braking effect caused by capping groups in the present study established a new strategy to control the rotational kinetics of rotaxanes, and thus opens a new window for building intelligent molecular mechanical devices.

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