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FULL PAPER

Effective Synthesis and Modification of α-Cyclodextrin-Based [3]Rotaxanes Enabling Versatile Molecular Design

Yosuke Akae, Hiromitsu Sogawa, and Toshikazu Takata*

Abstract: One-pot synthesis of various α-cyclodextrin-(α-CD-) based [3]rotaxanes in water and their structural modifications are discussed in detail. Pseudo[3]rotaxane was prepared from α-CD and α,ω-diaminododecane in water (above 100 g, quantitative yield in a 1 L flask). Successive urea-forming end-capping reactions with isocyanate in water selectively afforded [3]rotaxane with head-to-head structured α-CDs. The yields were varied by bulkiness and functionality of end-capping agents. Significant modifications of the axle end and wheel OH group of the [3]rotaxanes were performed by the Suzuki coupling with arylboronic acids and by the perfect acylation with acid anhydrides, respectively.

Introduction

Various synthetic methods of rotaxanes have hitherto been developed to enable the elaborate designs of sophisticated supramolecular architectures.[1,2] Cyclodextrin (CD), a typical wheel component of rotaxane, is widely used to construct unique frameworks, including polyrotaxane, polyrotaxane networks, polymer molecular wires, and biocompatible materials.[3,4] In addition to these polymeric materials, CD-based low molecular weight scaffolds were studied not only for their synthetic interest but also for their application to probes and building blocks for molecular machines.[5] These applications are based on the characteristic structure of CDs, which consists of several glucose units connected in a circular fashion. Meanwhile, synthesis of CD-based rotaxanes is not a simple work, being suffering from the following limitations in molecular design. The most common synthetic method of CD-based rotaxanes is the axle end-cap of pseudorotaxane. In this method, inclusion complex from CD and axle component which was initially formed was treated with bulky end-cap agent to yield the target rotaxane molecule. In this procedure, a highly polar or hydrophilic solvent is required, as CDs incorporate guest molecules in their cavities by the hydrophobic interaction. In the typical synthesis of rotaxanes, polar organic solvents such as DMF, DMSO, and methanol are used instead of water, but the yield is usually low due to the weakened solvophobic interaction. Therefore, the reaction in polar solvent often requires bulky hydrophilic end-cap agents such as 3,5-dicarboxyphenyl, sulfonyl naphthyl, and CD itself.[6]

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However, such requirement significantly restricts the purposive molecular design of CD-based rotaxanes despite its usefulness. Meanwhile, we previously developed a urea-forming end-capping method for high-yielding synthesis of α-CD-based [3]rotaxane, which actually overcame the above synthetic limitation.[7] Namely, the end-cap reaction of α-CD-based pseudorotaxanes having α,ω–diaminoalkane axles efficiently proceeds in water under heterogeneous conditions which allows the use of several aromatic isocyanates without any hydrophilic groups such as 3,5-dimethylphenyl isocyanate. Possible side reactions such as hydrolysis of isocyanate and the reaction of OH group were well controlled to give high yields of the rotaxanes. To enhance the applicability of this protocol for the effective synthesis of CD-based rotaxanes, the systematic study to clarify the structural requirement of the end-cap agents should be needed. Herein we report in detail the scope and limitations of the synthetic protocol using isocyanate end-cap agents in the urea end-capping reactions. In addition, functionalization and modification of the [3]rotaxanes are also discussed in this work to expand the usefulness of the [3]rotaxanes (**Figure 1**).[8]

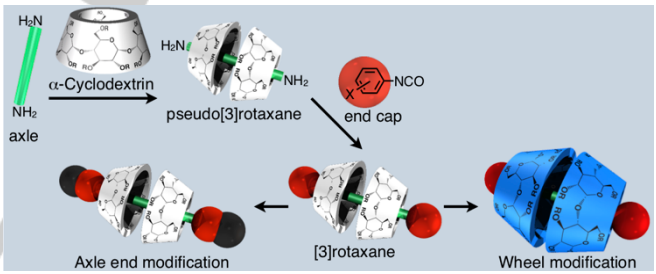


Figure 1. The synthetic concept of this work.

Results and Discussion

Scalable Selective Synthesis of α-CD-Based [3]Rotaxanes via the Urea End-Capping Method

α-CD-based [3]rotaxanes were synthesized as depicted in Scheme 1.[7] A wide range of capping agents were tried here to increase the diversity of axle end structures, focusing particularly on the size effect of bulky end-capping groups. The states of the reagents are given beside the compounds' numbers. Those with no annotation are liquids. Initially, the typical procedure was adjusted to 22 capping agents (**Table 1**, **Figure S4**). Namely, 1,12-diaminododecane and α-CD were mixed in water at reflux temperature for 1 hour to give a homogeneous solution, which was then left to stand overnight at ambient temperature to give pseudo[3]rotaxane **P1** as a block crystal. Note that large-scale synthesis (100 g) could be easily realized using a simple purification protocol involving filtration and washing with water. The obtained pseudo[3]rotaxane **P1** was then dispersed in water, followed by the addition of the capping agents to this

heterogeneous solution. The reaction temperature was basically set at 0 °C to prevent side reactions such as isocyanate addition to the hydroxyl groups on CD. However, the reaction was operated at room temperature for solid cap reagents **6**, **7**, **8** and **9** as these end cap reagents did not afford the corresponding rotaxanes at low temperature. The above mentioned reactions can be performed in one pot; however, in this work, we used a prerequisite amount of **P1** for the end-capping study after preparing this on a large scale. After standard purification, [3]rotaxanes, caps **1**–**10**, were obtained, whereas other capping agents (**11**–**22**) afforded no rotaxanes (**Table 1**, **Figure S4**). We have to note that some of the [3]rotaxanes such as **R1** and **R2** exhibited size-complementary feature. They were stable enough to be isolated at room temperature and have the medium stability between ''rotaxane'' and ''pseudo-rotaxane'' as the size of the axle end group is similar to that of the wheel cavity.[9] Size-complementarity is especially important when we discuss its unique dissociation behavior. Thus, we simply call every rotaxanes isolated by the end-capping reaction as ''rotaxane'' in this manuscript to avoid the complicated description.

Scheme 1. Synthesis of [3]rotaxanes via the urea end-capping method.

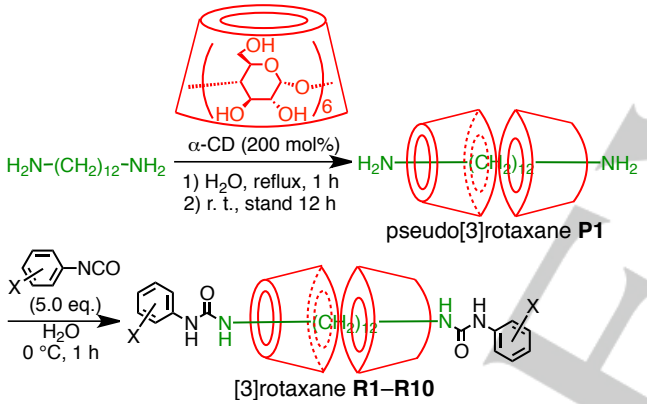
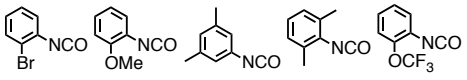
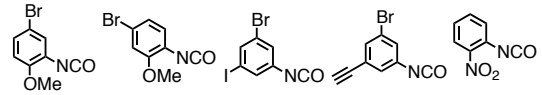


Table 1. Chemical structures of capping agents and yields of [3]rotaxanes.

End cap agent					
	1	**2**	**3**	**4**	**5**
[3]rotaxane (Yield%)	**R1**(73)[a]	**R2**(64)[a]	**R3**(60)[a]	**R4**(13)[a]	**R5**(50)
End cap agent					
	6 (solid)	**7** (solid)	**8** (solid)	**9** (solid)	**10** (solid)
[3]rotaxane (Yield%)	**R6**(9.6)[b]	**R7**(12)[b]	**R8**(4.3)[b]	**R9**(16)[b, c]	**R10**(21)

[a]These data have been reported in reference 7c. [b]The reaction was performed at room temperature. [c]Overnight reaction

Every obtained [3]rotaxane had a head-to-head structure owing to hydrogen bonding between two CD units as verified by ^{1}H NMR and X-ray crystal structure analysis (**Figures. S2** and **S5**).[7c] In the ^{1}H NMR spectrum of **R2**, a lower field shift of O(2)H for CD and a higher field shift of O(3)H around 5-6 ppm were observed as characteristic shifts of the head-to-head [3]rotaxane structure (for other [3]rotaxanes, see ESI). These shifts were probably due to initial intramolecular hydrogen bonding within single α-CD molecules changing to intermolecular bonds between two CD units in [3]rotaxanes. Larger shifts were observed in [3]rotaxanes obtained from shorter axles, such as 1,10-diaminododecane. The same tendency was observed when we applied *ortho*-substituted (**1**, **2**, **4**, **5**, **6**, **7** and **10**) rather than *meta*-substituted phenyl isocyanates (**3**, **8** and **9**). These results indicate that a shorter distance between two CD units induces large chemical shifts. Additionally, compared with the dumbbell and [3]rotaxane, only the g proton of urea shifted upfield from 6.8 to 6.3 ppm, whereas other benzene signals of axle ends remained with slight shifts. This upfield shift was probably derived from the difference in hydrogen bonding interaction between [3]rotaxane and single dumbbell compound. Single dumbbell could has a hydrogen bonding between urea N–H bond and solvent DMSO. However, in [3]rotaxane, this urea N–H would form the hydrogen bonding with hydroxyl group of CD moiety, caused the different chemical shift. Meanwhile, the X-ray structure analysis gave the distance between two CD units as 2.7–2.9 Å, clearly indicating the existence of hydrogen bonds. Besides, out of six primary hydroxyl groups of one CD unit on the narrower rim side, five pointed outside and one pointed inside, which sounded interact urea bonds of the dumbbell. Their interaction distances were around 3 Å, and the configuration indicated the presence of N–H...O bonds between urea N–H and the hydroxyl groups. In this crystal structure, benzene rings and bromo substituents exhibited no interactions with other moieties, even in the intermolecular region. Specifically, both ^{1}H NMR and X-ray structure analysis were consistent with respect to the hydrogen bonds between two CD units, as well as those between the urea and the hydroxyl groups of CD. Furthermore, it is noteworthy that no shifts of O(3)H, O(2)H of CD, or the g proton of urea were observed for [2]rotaxanes **R11** and **R12**, which was prepared via a deslipping reaction from [3]rotaxane **R1** and **R2**, respectively (for the structures of **R11** and **R12**, see ESI). This observation also verified that these shifts originated from the head-to-head structure of [3]rotaxane.

When we considered ineffective capping reagents for this reaction (**1**–**10** in **Table 1** versus **11**–**22** in **Figure S4**), several important insights were elucidated. The details were described in ESI, section 3. Besides, when we focus on rotaxane-affording capping agents, it can be concluded that they have well-balanced substituents, which are bulky enough to function as stoppers, but not too large to decrease the reactivity of the isocyanate. Even among these capping agents, the yield from 2,6-dimethylphenyl isocyanate **4** was lower than that from 3,5-dimethyl **3** because of the steric hindrance to the isocyanate moiety. Meanwhile, liquids **1**–**5** tended to show higher yields than solids **6**–**10**. This was because the liquid capping agents dispersed more effectively than the solid ones in this heterogeneous system. This proposal was also supported by the results that solid agents **21** and **22**, gave no rotaxanes (**Figure S4**). In addition, the yields tended to increase by improving the dispersity of solids caps **8**, **9** and **10** (For details, see section 4 in ESI). Briefly, **10** afforded [3]rotaxane in as high a yield as with liquids **1**, **2**, and **3** (69% versus 60–70%)

at optimized condition. These results suggested not only simple bulkiness but also the dispersity in water of capping agents is important for our developed system. Finally, different capping candidates, other than isocyanate, including 3,5-dimethylphenyl aldehyde **23**, fluoro-group-substituted **24**, and **25**, were also examined, but unfortunately, they were ineffective in this system (see ESI).

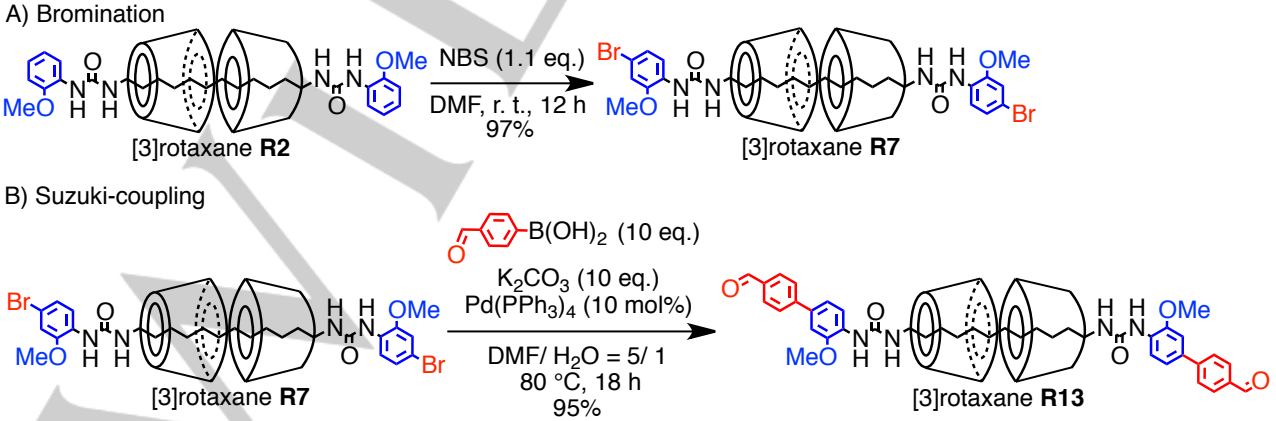
Axle End Modification via Bromination Followed by Suzuki Coupling

To expand the further versatility of molecular design, modification of the currently obtained rotaxanes via urea end capping is also a reasonable functionalization method. Firstly, a methodology for modifying axle ends was then studied. In order to determine the synthetic strategy, the following five points should be considered. (1) The decomposition of components, such as urea bonds and glucose, must be prevented. Heating above 120 °C could induce gradual decomposition of urea in this rotaxane and should be avoided. (2) The deslipping reactions of size-complementary rotaxanes induced by heating had to be considered. The tolerant temperature depended on the rotaxane structures.[7b,c] (3) For the native CD-based rotaxane studied here, the solvent candidates were limited and included DMF, DMSO, and pyridine, because of its poor solubility in other solvents. (4) The obtained [3]rotaxane was also soluble in a narrow range of solvents; the products then required purification via the limited methods available with these solvents, such as washing and reprecipitation. Another reason for this purification limit was that heating during drying under a reduced pressure to eliminate the solvent was often accompanied by a deslipping reaction as mentioned above. (5) The [3]rotaxanes contained 36 hydroxyl groups and two functionalized dumbbell. When these multiple functional groups partially react, their separation can become extremely difficult. Thus, the modification reaction needed to be complete. Considering the above synthetic limitations, neutral or relatively mild reactive conditions might be preferred rather than nucleophilic attack by generating strong anions. Meanwhile, it should be noted that when the rotaxanes became soluble in common organic solvents via wheel modification, purification methods such as silica gel column chromatography and preparative GPC could be applied. Finally, we selected the following route: bromo substituents were introduced into the phenyl moieties of the axle ends of rotaxane via *N*-bromosuccinimide (NBS), followed by transition-metal-catalyzed cross-coupling reactions, including Suzuki coupling.

Initially, bromination of the axle ends of [3]rotaxane was studied (**Scheme 2**). [3]Rotaxane **R2** was mixed with a slight excess of NBS in DMF. This was purified by reprecipitation into water, followed by washing with water and acetone. In this reaction, we first assumed the bromination at the para position of methoxy group, which is strong electron-donating group, would take place. But, the reaction proceeded at the para position of the urea group, selectively. The substitution position was elucidated by comparing the NMR spectra of **R6** and **R7**. Note that the substitution position did not change when the single dumbbell molecule without any CD was treated under the same conditions, indicating that this result is not specific case for rotaxane. DFT calculation of model compound was performed to gain the information about the substitution position. However, calculated electron density of the para position for the urea group and methoxy group was almost same. indicating that the bromination could be happened at either positions without any selectivity (More detail for DFT calculation, see ESI and **Figure S3**).[10] **R7** was also obtained by direct urea end capping with capping agent **7**, but bromination of **R2** afforded a higher yield (12% versus 62%) with no unexpected byproducts. The stepwise modification route was more effective than the direct end capping reaction. This is probably because liquid cap **2** was more suited for our developed end-capping method compared to solid cap **7** in terms of higher water dispersity. Meanwhile, dibromo substitution at one phenyl ring failed to proceed. Furthermore, this *para* bromination via NBS was applied in a similar manner to [3]rotaxane **R1** having bromophenyl axle ends and to [3]rotaxane **R10** having nitrophenyl ones under harsher reaction conditions.

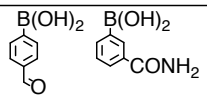
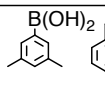
The obtained [3]rotaxane **R7** was then used for Suzuki coupling (**Scheme 2**). The reaction proceeded to completion as expected to give [3]rotaxane **R13**. This showed a deslipping behavior when heated to 100°C in DMSO, indicating its potential as a building block for a stimuli-responsive supramolecular framework.[11]

Scheme 2. Modification of axle ends of [3]rotaxane.



The synthetically most crucial point was using excess phenylboronic acid (10 eq.). When this was reduced to 5 eq., a mixture of **R7** and a partially reacted byproduct, which was difficult to purify, was obtained after reacting for one day. Several phenylboronic acids were applicable to this reaction, such as 3-carbamoyl-, 3,5-dimethyl-, 3-hydroxyl-, 3-formyl-, and 3-nitro-substituted phenylboronic acid and 1-pyreneboronic acid to give the corresponding rotaxanes **R14**, **R15**, **R17**, **R18**, **R19**, and **R16**, respectively (**Table 2**). However, boronic pinacol esters were ineffective, probably because of their low reactivity and hydrophobicity. Successive bromination followed by Suzuki coupling was also achieved for [3]rotaxanes **R1** and **R10**. With some reagents, the reaction proceeded even at room temperature or in a $PdCl_2$ catalyzed system,[12] but the conditions shown in **Scheme 2** were generally effective.

Table 2. Chemical structures of phenylboronic acid reagents and yields of [3]rotaxanes.

Reagent					
[3]rotaxane Yield(%)	**R13**(95)	**R14**(77)	**R15**(67)	**R16**(88)	**R17**(88)

Reagent		
[3]rotaxane Yield(%)	**R18**(79)	**R19**(76)

Figure 2 shows ^{1}H NMR spectra of **R13**. Only the k peak of the urea shifted from the corresponding dumbbell **27** to [3]rotaxane **R13**, whereas no significant shifts were observed for other protons. Thus, wheels were estimated to locate around urea bonds, far away from the aldehyde groups on the axle ends. These results indicate that the obtained [3]rotaxanes could be further modified, and even polymerization could be initiated from this point as experimentally confirmed.[11] This modification methodology can expand the uses of CD-based rotaxane; however, one drawback is its poor solubility in organic solvents. Solubility was improved by wheel modification, which is described in the following section.

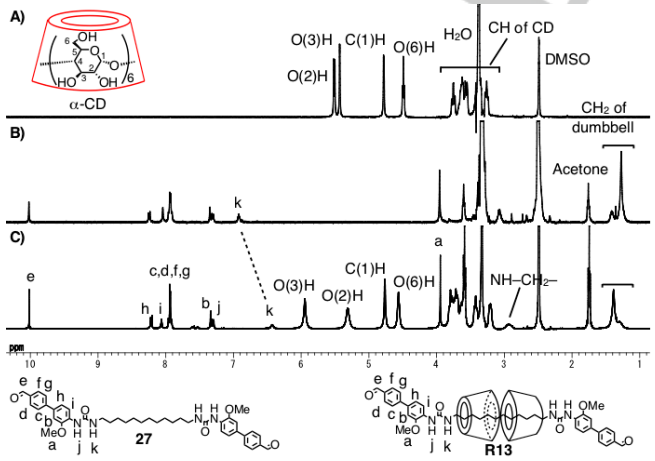


Figure. 2 ^{1}H NMR spectra of (A) α-CD, (B) dumbbell **27**, and (C) [3]rotaxane **R13** (400 MHz, DMSO-d_6, 298 K).

Wheel Modification via Acylation Using Anhydride

Next, the acylation of [3]rotaxane wheels was studied (**Scheme 3**, **Table 3**).[13] This acylation was selected because reaction with excess amount of highly reactive anhydride can be performed homogeneously in a pyridine solvent and is expected to easily lead to complete modification of 36 hydroxyl groups on one [3]rotaxane.

Consequently, acylation proceeded successfully to give the corresponding products **R20**–**R22**, and the following five points should be noted. (1) Every acylation of α-CD proceeded at around 60 °C to give the peracylated α-CD in an almost quantitative yield (Entries 1–4). (2) With [3]rotaxanes **R1** and **R2**, mixtures of decomposed products were obtained with peracetylated α-CD (Entries 5 and 6). Acetylation could accelerate deslipping because strong intermolecular hydrogen bonds between the two CD wheels in [3]rotaxane were lost.[11] (3) Heating was a significant factor here. With [3]rotaxane **R7**, whose deslipping reaction was restricted, acetylation at 60 °C afforded partially acetylated products, although free α-CD was completely acetylated under the same conditions (Entry 7).

Scheme 3 Acylation of [3]rotaxanes and α-CD.

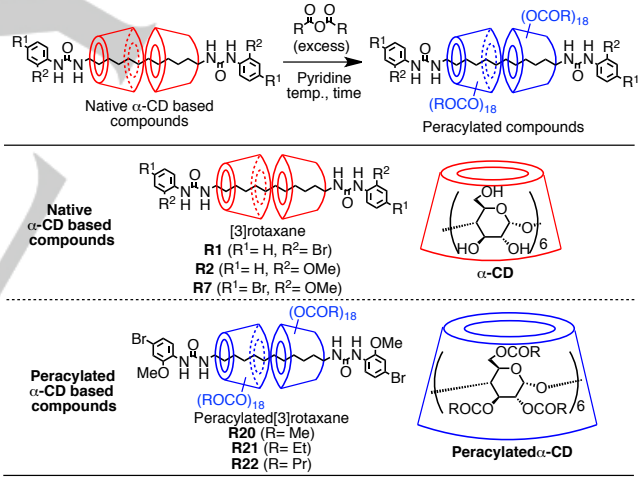


Table 3. Reaction conditions of acylation.

Entry	Native α-CD based compound	Acid anhydride	Temp. [°C]	Time [h]	Products
1	α-CD	Acetic	60	12	Peracetylated α-CD (quant.)
2	α-CD	Propionic	80	12	Perpropionylated α-CD (98%)
3	α-CD	Butyric	80	12	Perbutyrylated α-CD (98%)
4	α-CD	Isobutyric	80	12	Perisobutyrylated α-CD (98%)
5	[3]rotaxane **R1**	Acetic	60	12	decomp.
6	[3]rotaxane **R2**	Acetic	60	12	decomp.
7	[3]rotaxane **R7**	Acetic	60	12	Partially reacted crude
8	[3]rotaxane **R7**	Acetic	60	168	Partially reacted crude
9	[3]rotaxane **R7**	Acetic	80	12	**R20** (72%)
10	[3]rotaxane **R7**	Acetic	80	2.5	**R20** (85%)
11	[3]rotaxane **R7**	Propionic	80	12	**R21** (72%)
12	[3]rotaxane **R7**	Butyric	80	12	**R22** (46%)
13	[3]rotaxane **R7**	Isobutyric	80	12	Partially reacted crude

The reaction remained incomplete even after a prolonged reaction time (one week) (Entry 8). However, reaction at 80 °C for 12 h resulted in complete acetylation to give [3]rotaxane **R20** (Entry 9). With [3]rotaxane, the reaction points were more crowded owing to the existence of a dumbbell and another wheel; thus, harsher conditions were required compared to those with α-CD at the single molecular level. (4) Propionylation and butylation of [3]rotaxane **R7** also proceeded similarly to acetylation, but only partial isobutylation occurred, although single α-CD could be perisobutylated (Entries 11–13; see ESI). This was caused by steric hindrance around the wheels in [3]rotaxane. (5) The yields of acylated rotaxanes were less than those of single α-CD. This was probably because the deslipping reaction of [3]rotaxane occurred during acylation. Besides, bulky butylated rotaxane showed a faster deslipping reaction than smaller acylated rotaxanes.[11] In order to prevent this decrease in the acylation yield, a shorter reaction time was considered, and 2.5 h was found to be suitable (Entry 10). The obtained peracylated rotaxanes were soluble in various organic solvents, including CH_2Cl_2, $CHCl_3$, PhCl, and tetrahydrofuran (THF). Notably, the C–H signals of C(1)H to C(6)H of the glucose units of CD in ^{1}H NMR were clearly observed for peracetylated rotaxane **R20**, showing its usefulness in dynamic property analysis (**Figure. 3**). Besides, axle end modified rotaxanes such as **R13** could also be peracetylated. Briefly, increasing the solubility of CD-based [3]rotaxane in organic solvents was achieved here in a facile manner. Although further experimental results would be needed to claim its generality and the utility of this approach, these features are surely important to fabricate novel rotaxane-based nanomaterials.

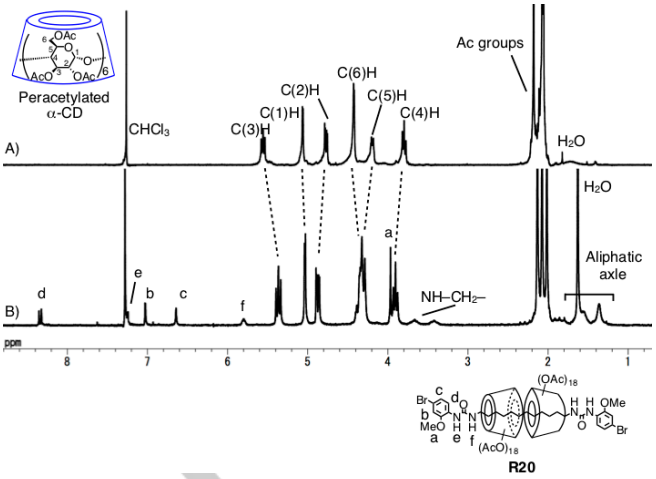


Figure. 3 ^{1}H NMR spectra of (A) peracetylated α-CD and (B) [3]rotaxane **R20** (400 MHz, $CDCl_3$, 298 K).

Conclusions

In conclusion, we determined the scope and limitations of the urea end-capping method for synthesizing α-CD-based [3]rotaxanes with head-to-head structure. Although it was still difficult to claim wide generality of this method, the appropriate steric hinderance, reactivity and the water dispersity of capping agents is definitely important for our developed system. Besides, the successive modification and functionalization of the axle ends and wheels of the obtained [3]rotaxanes were also developed. Wheel acylation made the rotaxanes highly soluble in various organic solvents, although the further trails would be added to claim its wide generality. The obtained rotaxanes had relatively simple structures, consisting of two CD wheels and an alkylene axle with bulky phenyl substituents on its edge, making them potentially suitable as building blocks for further functional systems. These findings expanded the synthetic flexibility of CD-based rotaxanes, enabling further development of novel supramolecular architectures.

Experimental section

1. General Method

^{1}H- (400 MHz) and ^{13}C- (100 MHz) NMR spectra were recorded on a JEOL AL-400 spectrometer and ^{1}H- (300 MHz) NMR spectra were recorded on a Bruker DPX spectrometer 300 using $CDCl_3$ and DMSO-d_6 as the solvents, calibrated using residual undeuterated solvent or tetramethylsilane as the internal standard. IR spectra were recorded on a JASCO FT/IR-230 spectrometer. Melting points were measured on a MELTING POINT APPARATUS SMP3 (Stuart Scientific) instrument. Preparative GPC was carried out using a HPLC LC-918 instrument by Japan Analytical Industry with a Megapack-Gel 201C and a JAIGEL-H. ESI HR-MS spectra were taken on a Bruker Daltonics micrOTOF II at the Center for Advanced Material Analysis, Tokyo Institute of Technology on request. Wako Gel® C-400HG (Wako Pure

Chemical Industries) was used for silica gel column chromatography. Cerite® (Wako Pure Chemical Industries) was used for removal of metal compounds. α-Cyclodextrin (α-CD) was dried at 70 °C overnight under reduced pressure before use. Dry DMF was purchased from Sigma-Aldrich Company. CH_2Cl_2 was purchased from Tokyo Chemical Industry Company and distilled before using. Other commercially available reagents and solvents were used without further purification unless otherwise noted.

2. Chemical Synthesis

Synthesis of pseudo[3]rotaxane P1 consisting of native α-CDs and 1,12-Diaminododecane

Diaminododecane (8.8 g, 44 mmol) was added to a solution of α-CD (86 g, 89 mmol) in H_2O (600 mL), then, the mixture was refluxed for 1 h, and stood overnight at room temperature. The resulting mixture was filtered to collect the precipitate. It was washed with water and dried *in vacuo* to give pseudo[3]rotaxane **P1** (95 g, quant.) as a white crystal. The obtained inclusion complex was immediately decomposed when dissolved in solvent. Therefore, the structure was assigned after further end-capping reaction as follow.

Typical procedure for the synthesis of [3]rotaxanes: synthesis of [3]rotaxane R1 consisting of native α-CDs and *o*-bromophenylurea termini

Pseudo[3]rotaxane **P1** (0.81 g, 0.37 mmol) was dispersed in H_2O (5.0 mL), to the resulting mixture cooled to 0 °C was added *o*-bromophenylisocyanate (0.73 g, 3.7 mmol), and the mixture was stirred for 1 h at 0 °C. The heterogeneous mixture was poured into THF and filtered to collect the precipitated solid. The residue was washed with water and dried *in vacuo* to give the [3]rotaxane **R1** (0.69 g, 73%) as a white solid; m.p. 280.0–281.0 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.03 (d, 2H, *J* = 7.8 Hz, d), 7.78 (s, 2H, e), 7.54 (d, 2H, *J* = 7.8 Hz, a), 7.28 (t, 2H, *J* = 7.8 Hz, b), 6.90 (t, 2H, *J* = 7.8 Hz, c), 6.50 (br, 2H, f), 5.94 (s, 12H, O(3)H), 5.32 (d, 12H, *J* = 7.1 Hz, O(2)H), 4.77 (s, 12H, C(1)H), 4.58 (t, 12H, *J* = 5.0 Hz, O(6)H), 3.81–3.17 (m, 72H, H of CD), 3.00–2.86 (m, 4H, g), 1.43–1.25 (m, 20H, h, i, j, k and l) ppm; ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ154.7, 137.7, 132.3, 128.0, 123.4, 121.8, 112.5, 102.4, 81.5, 73.4, 72.4, 72.2, 59.6, 40.0, 31.4, 31.1 (4C), 30.9, 28.3 ppm; IR (KBr) υ 3339, 2928, 2858, 1675, 1558, 1436, 1293, 1154, 1077, 1031, 572, 448, 433, 422 cm^{-1}; MALDI-TOF MS (m/z): calc'd for $C_{98}H_{156}Br_2N_4NaO_{62}^+$ [M + Na$^+$] 2563.74; found 2563.58. Crystals of **R1** suitable for X-ray analysis were obtained by recrystallization from a solution of DMSO and H_2O. Single crystal data of **R1**: $C_{98}H_{156}Br_2N_4O_{62}$ · C_2H_6SO · $(H_2O)_{15.5}$ M_w = 2899.47, colorless prism, size: 0.420 × 0.160 × 0.030 mm, monoclinic, space group *C*2 (#5), *Z* = 4, *a* = 28.654(5) Å, *b* = 26.847(5) Å, *c* = 21.393(4) Å, b = 112.238(4)°, *V* = 15233 (5) Å^3, D_{calc} = 1.264 g/cm^{-3}, μ = 0.643 mm^{-1}, *T* = 113 K, *F*(000) = 6140.0; 63313 reflections measured, of which 34390 were unique (R_{int} = 0.0447). 383 refined parameters, final R_1 = 0.1524 for reflections with $I > 2\sigma$, *wR* = 0.1883 (all data), GOF = 1.742. Final largest diffraction peak and hole: 6.71 and –2.69 e Å^3. CCDC deposit number: 915456.

[3]Rotaxane **R2** (0.57 g, 64%); m.p. 274.0–275.0 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.03 (dd, 2H, J_1 = 1.5 Hz, J_2 = 7.3 Hz), 7.86 (s, 2H), 6.94 (dd, 2H, J_1 = 1.7 Hz, J_2 = 7.9 Hz), 6.84 (m, 4H), 6.31 (br, 2H), 5.93 (s, 12H, O(3)H), 5.33 (d, 12H, *J* = 6.2 Hz, O(2)H), 4.77 (s, 12H, C(1)H), 4.55 (t, 12H, *J* = 5.1 Hz, O(6)H), 3.84–3.17 (m, 78H), 3.00–2.86 (m, 4H), 1.46–1.23 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ 155.1, 147.4, 129.4, 121.0, 120.4, 118.1, 110.5, 102.4, 81.5, 73.4, 72.4, 72.1, 59.5, 55.8, 40.0, 31.5, 31.1 (4C), 30.8, 28.3 ppm; IR (KBr) υ 3311, 2929, 2854, 1666, 1552, 1459, 1435, 1407, 1362, 1330, 1288, 1251, 1152, 1080, 1031, 949, 851, 754, 704, 571, 433, 411 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{100}H_{161}N_4O_{64}^-$ [M$^-$] 2442.9514; found 2442.9505.

[3]Rotaxane **R3** (0.54 g, 60%); m.p. 260.0–261.0 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.08 (s, 2H), 6.98 (s, 4H), 6.52 (s, 2H), 5.73 (s, 12H, O(3)H), 5.56 (d, 12H, *J* = 5.8 Hz, O(2)H), 5.27 (br, 2H), 4.78 (s, 12H, C(1)H), 4.61 (t, 12H, *J* = 4.9 Hz, O(6)H), 3.87–3.18 (m, 72H, H of CD), 3.10–2.89 (m, 4H), 2.19 (s, 12H), 1.56–1.20 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ 154.9, 140.1, 137.4, 122.8, 115.6, 102.2, 81.8, 73.5, 72.2, 72.1, 59.7, 40.3, 31.0, 30.8, 30.7, 30.6, 28.0, 21.2 ppm; IR (KBr) υ 3345, 2927, 2857, 1667, 1615, 1550, 1458, 1417, 1366, 1329, 1284, 1239, 1152, 1081, 1031, 948, 844, 749, 703, 608, 575 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{102}H_{165}N_4O_{62}^-$ [M$^-$] 2437.9887; found 2437.9860.

[3]Rotaxane **R4** (0.12 g, 13%); m.p. 273.0–274.0 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 7.42 (s, 2H), 7.06–6.96 (m, 6H), 5.78 (s, 12H, O(3)H), 5.53 (s, 12H, O(2)H), 5.11 (br, 2H), 4.78 (s, 12H, C(1)H), 4.56 (s, 12H, O(6)H), 3.85–3.15 (m, 72H, H of CD), 3.05–2.95 (m, 4H), 2.12 (s, 12H), 1.57–1.18 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ 155.0, 144.1, 127.3, 125.3, 120.5, 118.7, 110.5, 102.0, 81.6, 73.2, 72.1, 71.9, 59.5, 38.9, 32.3, 30.4, 29.7, 27.8, 25.5, 17.8 ppm; IR (KBr) υ 3325, 2924, 2853, 1635, 1567, 1468, 1440, 1408, 1371, 1325, 1293, 1260, 1153, 1079, 1034, 948, 855, 762, 705, 575, 430 cm^{-1}; ESI-TOF MS (m/z): $C_{102}H_{165}N_4O_{62}^-$ [M–H]$^-$ 2437.9887; found 2437.9900.

[3]Rotaxane **R5** (0.47 g, 50%); m.p. 329.6–331.2 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.26–8.16 (m, 4H), 7.34–7.23 (m, 4H), 7.01 (t, 2H, *J* = 7.9 Hz), 6.38 (br, 2H), 5.94 (s, 12H, O(3)H), 5.33 (d, 12H, *J* = 6.2 Hz, O(2)H), 4.77 (s, 12H, C(1)H), 4.59 (t, 12H, *J* = 5.1 Hz, O(6)H), 3.86–3.17 (m, 72H, H of CD), 3.00–2.86 (m, 4H), 1.49–1.20 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ 154.7, 136.9, 133.0, 127.6, 121.7, 121.0, 120.8 119.0, 110.5, 102.3, 81.5, 73.4, 72.4, 72.1, 59.5, 31.3, 31.2, 31.1, 30.8, 28.3, 28.1 ppm; IR (KBr) υ 3350, 2928, 2859, 1675, 1609, 1554, 1486, 1454, 1408, 1363, 1315, 1296, 1252, 1218, 1153, 1080, 1033, 1006, 949, 938, 861, 758, 704, 608, 574 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{100}H_{156}F_6N_4O_{64}Na^+$ [M + Na]$^+$ 2574.8905; found 2574.8855.

[3]Rotaxane **R6** (0.092 g, 9.6%); m.p. 309.2–311.8 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.29 (d, 2H, *J* = 2.2 Hz), 8.03 (s, 2H), 7.02 (dd, 2H, J_1 = 2.2 Hz , J_2 = 8.8 Hz), 6.90 (d, 2H, *J* = 8.8 Hz), 6.35 (br, 2H), 5.92 (s, 12H, O(3)H), 5.33 (d, 12H, *J* =

6.2 Hz, O(2)H), 4.78 (s, 12H, C(1)H), 4.57 (t, 12H, *J* = 5.1 Hz, O(6)H), 3.86–3.16 (m, 78H, OMe, H of CD), 3.10–2.80 (m, 4H), 1.49–1.20 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ 154.7, 146.5, 131.1, 123.0, 119.9, 112.3, 112.2, 102.3, 81.5, 73.4, 72.4, 72.1, 59.5, 56.1, 40.0, 31.2, 31.0 (4C), 30.8, 28.2 ppm; IR (KBr) υ 3357, 2927, 2856, 1671, 1595, 1546, 1482, 1459, 1412, 1363, 1328, 1295, 1244, 1152, 1080, 1032, 1006, 949, 862, 749, 704, 609, 574 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{100}H_{160}Br_2N_4O_{64}Na^+$ [M + Na]$^+$ 2623.7631; found 2623.7589.

[3]Rotaxane **R7** (0.12 g, 12%); m.p. 315.0–318.0 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.02 (d, 2H, *J* = 7.0 Hz), 7.95 (s, 2H), 7.11 (d, 2H, *J* = 2.0 Hz), 7.01 (dd, 2H, J_1 = 2.0 Hz , J_2 = 7.0 Hz), 6.37 (br, 2H), 5.94 (s, 12H, O(3)H), 5.29 (d, 12H, *J* = 6.2 Hz, O(2)H), 4.76 (s, 12H, C(1)H), 4.55 (t, 12H, *J* = 5.1 Hz, O(6)H), 3.86–3.16 (m, 78H, OMe, H of CD), 3.07–2.80 (m, 4H), 1.49–1.19 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ 155.7, 149.1, 129.8, 123.9, 120.0, 114.5, 113.0, 103.2, 82.3, 74.3, 73.2, 73.0, 60.3, 57.1, 40.0, 32.2, 31.9 (4C), 31.7, 29.0 ppm; IR (KBr) υ 3360, 2927, 2858, 1671, 1599, 1550, 1488, 1458, 1401, 1363, 1330, 1295, 1249, 1218, 1152, 1079, 1032, 1006, 949, 862, 748, 703, 656, 608, 577 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{100}H_{160}N_4O_{64}^-$ [M$^-$] 2597.7682; found 2597.7639.

[3]Rotaxane **R8** (0.044 g, 4.3%); m.p. 314.1–315.9 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.53 (s, 2H), 7.72 (s, 2H), 7.70 (s, 2H), 7.42 (s, 2H), 5.74 (s, 12H, O(3)H), 5.58 (d, 12H, *J* = 6.2 Hz, O(2)H), 5.48 (br, 2H), 4.79 (s, 12H, C(1)H), 4.67 (t, 12H, *J* = 5.1 Hz, O(6)H), 3.86–3.16 (m, 72H, H of CD), 3.10–2.80 (m, 4H), 1.58–1.24 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ 154.2, 143.1, 131.1, 124.6, 122.4, 119.2, 102.2, 95.3, 81.8, 73.5, 72.3, 72.1, 59.7, 40.0, 30.8 (8C), 28.0 ppm; IR (KBr) υ 3375, 2926, 2858, 1677, 1576, 1534, 1438, 1401, 1363, 1329, 1299, 1265, 1229, 1152, 1079, 1032, 1005, 949, 843, 748, 704, 667, 607, 576 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{98}H_{154}Br_2I_2N_4O_{62}Na^+$ [M + Na$^+$] 2814.5402; found 2814.5352.

[3]Rotaxane **R9** (0.15 g, 16%); m.p. 305.0–308.0 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.56 (s, 2H), 7.76 (s, 2H), 7.40 (s, 2H), 7.17 (s, 2H), 5.74 (s, 12H, O(3)H), 5.56 (d, 12H, *J* = 6.2 Hz, O(2)H), 5.47 (br, 2H), 4.78 (s, 12H, C(1)H), 4.67 (t, 12H, *J* = 5.1 Hz, O(6)H), 4.29 (s, 2H), 3.86–3.16 (m, 72H, H of CD), 3.10–2.80 (m, 4H), 1.58–1.20 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ 154.8, 142.6, 126.7, 124.3, 122.1, 121.0, 119.7, 102.6, 82.6, 82.3, 82.2, 73.9, 72.7, 72.5, 60.1, 31.3 (8C), 31.2, 28.4 ppm; IR (KBr) υ 3360, 2927, 2857, 1671, 1599, 1575, 1542, 1438, 1410, 1363, 1328, 1294, 1229, 1152, 1080, 1033, 949, 853, 747, 703, 666, 610, 573 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{102}H_{156}Br_2N_4O_{62}Na^+$ [M + Na$^+$] 2610.7470; found 2610.7380.

[3]Rotaxane **R10** (0.19 g, 21%); m.p. 311.5–313.6 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 9.34 (s, 2H), 8.39 (d, 2H, *J* = 8.6 Hz), 8.09 (dd, 2H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.65 (t, 2H, *J* = 8.2 Hz), 7.18–7.05 (m, 4H), 5.98 (s, 12H, O(3)H), 5.26 (d, 12H, *J* = 6.2 Hz, O(2)H), 4.77 (s, 12H, C(1)H), 4.53 (t, 12H, *J* = 5.1 Hz, O(6)H), 3.87–3.16 (m, 72H, H of CD), 3.03–2.85 (m, 4H), 1.51–1.21 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ 154.0, 136.3, 136.1, 135.2, 125.4, 121.7, 121.3, 102.4, 81.4, 73.4, 72.4, 72.1, 59.5, 31.2, 31.1 (4C), 30.9, 28.3 (4C) ppm; IR (KBr) υ 3358, 2927, 2859, 2064, 1683, 1583, 1558, 1501, 1456, 1433, 1362, 1341, 1262, 1152, 1079, 1032, 1006, 949, 863, 785, 747, 703, 651, 608, 575 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{98}H_{156}N_6O_{66}$ Na^+ [M + Na$^+$] 2495.8870; found 2495.8927.

Preparation of phenylisocyanate derivatives as end-capping agents

Simple phenylisocyanates were widely commercially available. In case of multiple substituted phenylisocyanates, preparations had to be carried out as shown in **Scheme S1**. Isocyanates were formed by using triphosgene with aniline derivatives and Curtius rearrangement with benzoic acid derivatives.

Bromination of [3]rotaxane R2 via *N*-bromosuccinimide

N-Bromosuccinimide (0.82 g, 4.6 mmol) was added to a solution of **R2** (5.3 g, 2.1 mmol) in DMF (20 mL), the mixture was stirred at ambient condition for 12 hours. The mixture was poured into H_2O and filtered to collect the precipitate. It was washed with acetone dried *in vacuo* to give **R7** (5.3 g, 97%) as a pale brown solid.

Typical method for suzuki coupling reaction with [3]rotaxane R7

K_2CO_3 aq. (0.22 g, 1.6 mmol, H_2O 0.4 mL) was added to a solution of 4-formylphenylboronic acid (0.24 g, 1.6 mmol) and [3]rotaxane **R7** (0.26 g, 0.10 mmol) in DMF (2.0 mL), then the system was freeze degassed. $Pd(PPh_3)_4$ (12 mg, 0.010 mmol) was added to a solution quickly, and the mixture was stirred for 17 hours at 80 °C. The heterogeneous mixture was poured into H_2O and filtered to collect the precipitate. It was washed with water and acetone dried *in vacuo* to give the [3]rotaxane **R13** (0.25 g, 95%) as a gray solid; m.p. 315.5–317.6 °C (decomp.); ^{1}H NMR (300 MHz, 298 K, DMSO-d_6) δ 10.03 (s, 2H), 8.22 (d, 2H, *J* = 8.7 Hz), 8.07 (br, 2H), 7.99–7.90 (m, 8H), 7.37–7.29 (m, 4H), 6.44 (br, 2H), 5.95 (s, 12H, O(3)H), 5.31 (s, 12H, O(2)H), 4.78 (s, 12H, C(1)H), 4.57 (s, 12H, O(6)H), 3.96 (s, 6H, OMe), 3.86–3.16 (m, 72H, H of CD), 3.07–2.80 (m, 4H), 1.49–1.19 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, $DMSO_6$) δ 192.7, 154.9, 147.8, 146.0, 134.5, 131.1, 130.3, 130.1 (4C), 126.7 (4C), 119.6, 118.0, 109.1, 102.3, 81.5, 73.4, 72.4, 72.1, 67.0, 59.5, 56.0, 41.1, 31.4, 31.0 (4C), 30.8, 28.2 ppm; IR (KBr) υ 3360, 2928, 2859, 1680, 1597, 1566, 1536, 1508, 1487, 1462, 1405, 1364, 1333, 1296, 1237, 1215, 1153, 1080, 1033, 1006, 948, 820, 750, 704, 651, 609, 573 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{114}H_{170}N_4O_{66}^-$ [M$^-$] 2649.9996; found 2649.9937.

R14 (0.21 g, 77%); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.18 (d, *J* = 8.3 Hz, 2H), 8.14–8.09 (m, 2H), 8.00 (br, 2H), 7.84–7.77 (m, 4H), 7.51 (dd, J_1 = J_2 = 7.5 Hz, 2H), 7.44 (s, 2H), 7.28 (s, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 6.39 (br, 2H), 5.94 (s, 12H, O(3)H), 5.34 (d, *J* = 5.0 Hz, 12H, O(2)H), 4.78 (s, 12H, C(1)H), 4.58 (s, 12H, O(6)H), 3.95 (s, 6H, OMe), 3.86–3.15 (m, 72H, H of CD), 3.02–2.87 (m, 4H), 1.49–1.19 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, $DMSO_6$) δ 168.4, 155.4, 148.2, 140.7, 135.3, 132.7, 129.8, 129.5, 129.3, 126.5, 125.5, 119.4, 118.6, 109.4, 102.8, 82.0, 73.8, 72.8, 72.6, 60.0, 56.5, 31.9, 31.6 (6C), 31.3, 28.8 ppm; ESI-TOF

MS (m/z): calc'd for $C_{114}H_{172}N_6O_{66}^{2+}$ [M^{2+}] 1364.0052; found 1364.0068.

R15 (0.18 g, 67%); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.09 (d, J = 8.3 Hz, 2H), 7.93 (br, 2H), 7.25 (s, 4H), 7.16 (s, 2H), 7.11 (d, J = 8.3 Hz, 2H), 6.92 (s, 2H), 6.34 (br, 2H), 5.93 (s, 12H, O(3)H), 5.33 (d, J = 5.0 Hz, 12H, O(2)H), 4.76 (s, 12H, C(1)H), 4.56 (s, 12H, O(6)H), 3.91 (s, 6H, OMe), 3.85–3.11 (m, 72H, H of CD), 3.01–2.83 (m, 4H), 2.31 (s, 12H), 1.47–1.19 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, $DMSO_6$) δ 155.5, 148.1, 140.6, 138.1, 133.6, 132.0, 129.3, 129.2, 128.6, 124.6, 119.1, 118.6, 109.2, 102.8, 82.0, 73.8, 72.8, 72.6, 60.0, 56.4, 31.9, 31.5 (6C), 31.3, 28.7, 21.5 (12C) ppm; ESI-TOF MS (m/z): calc'd for $C_{116}H_{178}N_4O_{64}Na^+$ [M + Na^+] 2674.0689; found 2674.0665.

R16 (0.25 g, 88%); m.p. 295.4–297.0 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.37–8.03 (m, 22H), 7.20 (s, 2H), 7.12 (d, J = 8.7 Hz, 2H), 6.45 (br, 2H), 5.97 (s, 12H, O(3)H), 5.32 (d, J = 5.0 Hz, 12H, O(2)H), 4.79 (s, 12H, C(1)H), 4.60 (s, 12H, O(6)H), 3.92 (s, 6H, OMe), 3.87–3.16 (m, 72H, H of CD), 3.05–2.88 (m, 4H), 1.49–1.18 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, $DMSO_6$) δ155.6, 147.9, 138.0, 137.2, 131.5, 130.9, 130.3, 129.3, 128.6, 128.3, 128.2, 128.0, 127.9, 126.8, 125.8, 125.5 (4C), 125.3, 124.7, 124.6, 123.0, 114.1, 113.0, 102.8, 82.0, 73.8, 72.8, 72.6, 60.0, 56.4, 32.0, 31.6 (8C), 31.3 ppm; IR (KBr) υ 3364, 2928, 2858, 1654, 1595, 1543, 1507, 1488, 1458, 1435, 1406, 1363, 1328, 1295, 1243, 1152, 1079, 1035, 1006, 948, 902, 851, 751, 723, 702, 655, 609, 575 cm^{-1} ESI-TOF MS (m/z): calc'd for $C_{132}H_{178}N_4O_{64}^{2+}$ [M^{2+}] 1445.0307; found 1445.0338.

R17 (0.23 g, 88%); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 9.41 (br, 2H), 8.11 (d, J = 7.6 Hz, 2H), 7.93 (br, 2H), 7.20 (dd, J_1 = J_2 = 7.6 Hz, 2H), 7.13 (d, J = 1.7 Hz, 2H), 7.11–7.04 (m, 4H), 7.00 (dd, J_1 = J_2 = 1.7 Hz, 2H), 6.70 (dd, J_1 = 7.6 Hz, J_2 = 1.7 Hz, 2H), 6.35 (br, 2H), 5.92 (s, 12H, O(3)H), 5.29 (d, J = 6.3 Hz, 12H, O(2)H), 4.76 (s, 12H, C(1)H), 4.54 (t, J = 5.6 Hz, 12H, O(6)H), 3.90 (s, 6H, OMe), 3.85–3.14 (m, 72H, H of CD), 3.00–2.86 (m, 4H), 1.49–1.19 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, $DMSO_6$) δ158.2, 155.4, 148.1, 142.2, 133.6, 130.2 (4C), 119.0, 118.5, 117.6, 114.2, 113.5, 109.2, 102.8, 82.0, 73.8, 72.8, 72.5, 59.9, 56.3, 31.9, 31.5 (6C), 31.3, 28.7 ppm; ESI-TOF MS (m/z): calc'd for $C_{112}H_{170}N_4O_{66}^{2+}$ [M^{2+}] 1336.9944; found 1336.9970.

R18 (0.21 g, 79%); m.p. 278.3–280.2 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 10.10 (s, 2H), 8.23–8.18 (m, 4H), 8.06–8.00 (m, 4H), 7.84 (d, J = 8.0 Hz, 2H), 7.66 (dd, J_1 = J_2 = 7.5 Hz, 2H), 7.32 (d, J = 1.7 Hz, 2H), 7.26 (dd, J_1 = 8.0 Hz, J_2 = 1.7 Hz, 2H), 6.41 (br, 2H), 5.95 (s, 12H, O(3)H), 5.32 (d, J = 6.2 Hz, 12H, O(2)H), 4.78 (s, 12H, C(1)H), 4.57 (s, J = 5.4 Hz, 12H, O(6)H), 3.96 (s, 6H, OMe), 3.87–3.11 (m, 72H, H of CD), 3.02–2.87 (m, 4H), 1.49–1.19 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, $DMSO_6$) δ 193.8, 155.4, 148.2, 141.5, 137.3, 132.7, 131.9, 130.2, 130.1, 128.2, 127.6, 119.4, 118.6, 109.4, 102.8, 82.0, 73.8, 72.8, 72.6, 59.9, 56.5, 31.9, 31.6 (6C), 31.3, 28.7 ppm; ESI-TOF MS (m/z): calc'd for $C_{114}H_{170}N_4O_{66}^+$ [M^+] 2673.9961; found 2673.9882.

R19 (0.21 g, 76%); m.p. 309.7–311.5 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 8.44 (dd, J_1 = J_2 = 1.9 Hz, 2H), 8.22 (d, J = 8.2 Hz, 2H), 8.16 (dd, J_1 = 8.2 Hz, J_2 = 1.9 Hz, 2H), 8.07 (br, 2H), 7.72 (dd, J_1 = J_2 = 8.2 Hz, 2H), 7.35 (d, J = 1.7 Hz, 2H), 7.29 (dd, J_1 = 8.2 Hz, J_2 = 1.7 Hz, 2H), 6.41 (br, 2H), 5.98 (s, 12H, O(3)H), 5.28 (d, J = 7.2 Hz, 12H, O(2)H), 4.78 (s, 12H, C(1)H), 4.61 (s, J = 5.2 Hz, 12H, O(6)H), 3.96 (s, 6H, OMe), 3.88–3.14 (m, 72H, H of CD), 3.02–2.83 (m, 4H), 1.49–1.19 (m, 20H) ppm; ^{13}C NMR (100 MHz, 298 K, $DMSO_6$) δ155.3, 148.9, 148.3, 142.4, 133.3, 130.8, 130.6 (4C), 121.8, 121.0, 119.7, 118.5, 109.6, 102.8, 82.0, 73.8, 72.8, 72.5, 59.9, 56.5, 31.9, 31.6 (6C), 31.3, 28.7 ppm; IR (KBr) υ 3367, 2927, 2859, 2144, 1673, 1599, 1524, 1459, 1406, 1351, 1266, 1237, 1213, 1152, 1079, 1032, 1005, 949, 937, 902, 857, 806, 744, 704, 649, 608, 574 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{112}H_{168}N_6O_{68}^{2+}$ [M^{2+}] 1365.9845; found 1365.9864.

Synthesis of [3]rotaxane R20

Ac_2O (0.50 mL, 0.50 g, 5.0 mmol) was added to a solution of [3]rotaxane **R7** (0.10 g, 0.040 mmol) in pyridine (0.50 mL),then the mixture was stirred at 80 °C for 2.5 hours. The mixture was poured into H_2O and filtered to collect the precipitate. It was washed with water, dried *in vacuo* to give the [3]rotaxane **R20** (0.14 g, 85%) as a pale yellow solid; ^{1}H NMR (300 MHz, 298 K, $CDCl_3$) δ 8.33 (d, J = 8.8 Hz, 2H), 7.25 (dd, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 2H), 7.02 (d, J = 2.0 Hz, 2H), 6.63 (br, 2H), 5.79 (br, 2H), 5.36 (t, J = 8.5 Hz, 12H, C(3)H), 5.03 (d, J = 3.4 Hz, 12H, C(1)H), 4.87 (dd, J_1 = 8.5 Hz, J_2 = 3.4 Hz, 12H, C(2)H), 4.45–4.21 (m, 36H, $C(6)H_a$, $C(6)H_b$, C(5)H), 3.96 (s, 6H, OMe), 3.90 (t, J = 8.5 Hz, 12H, C(4)H), 3.76–3.31 (m, 4H, NH–**CH_2**–), 2.13 (s, 36H, Ac), 2.07 (s, 36H, Ac), 2.01 (s, 36H, Ac), 1.70-1.18 (m, 20H, methylene) ppm; ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ 170.6, 170.3, 169.0, 154.4, 147.0, 127.3, 124.7, 119.1, 114.5, 113.6, 98.6, 78.4, 71.3, 70.7, 70.5, 62.1, 56.0, 41.1, 32.1, 31.5, 31.0, 29.8, 27.3, 21.0, 20.8, 20.7 ppm; ESI-TOF MS (m/z): calc'd for $C_{172}H_{232}N_4O_{100}Br_2^{2+}$ [M^{2+}] 2080.5693; found 2080.5725.

Synthesis of [3]rotaxane R21

Propionyl anhydride (1.0 mL, 1.0 g, 7.7 mmol) was added to a solution of [3]rotaxane **R7** (0.10 g, 0.040 mmol) in pyridine (1.0 mL), then the mixture was stirred at 80 °C for 12 hours. The mixture was poured into H_2O and filtered to collect the precipitate. It was washed with water, purified by preparative GPC (eluent; $CHCl_3$) to give the [3]rotaxane **R21** (0.13 g, 72%) as a pale yellow solid; m.p. 155.8–156.9 °C; ^{1}H NMR (300 MHz, 298 K, $CDCl_3$) δ 8.36 (d, J = 8.8 Hz, 2H), 7.31–7.21 (m, 2H), 7.03 (d, J = 2.0 Hz, 2H), 6.69 (br, 2H), 5.89 (br, 2H), 5.38 (t, J = 8.5 Hz, 12H, C(3)H), 5.01 (d, J = 3.4 Hz, 12H, C(1)H), 4.84 (dd, J_1 = 8.5 Hz, J_2 = 3.4 Hz, 12H, C(2)H), 4.41–4.24 (m, 36H, $C(6)H_a$, $C(6)H_b$, C(5)H), 3.97 (s, 6H, OMe), 3.86 (t, J = 8.5 Hz, 12H, C(4)H), 3.74–3.29 (m, 4H, NH–**CH_2**–), 2.50–2.14 (m, 72H, OCO–**CH_2**–), 1.70-1.19 (m, 20H, methylene), 1.18–1.00 (m, 108H, $OCOCH_2$–**CH_3**) ppm; IR (KBr) υ 3413, 2981, 2944, 2884, 1747, 1689, 1595, 1525, 1464, 1421, 1382, 1352, 1275, 1177, 1087, 1045, 1021, 952, 884, 860, 807, 765, 584 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{208}H_{304}N_4O_{100}Br_2^{3+}$ [M^{3+}] 1562.5629; found 1562.5622.

Synthesis of [3]rotaxane R22

Butyric anhydride (1.0 mL, 0.97 g, 6.1 mmol) was added to a solution of [3]rotaxane **R7** (0.10 g, 0.040 mmol) in pyridine (1.0 mL), then the mixture was stirred at 80 °C for 12 hours. The mixture was poured into H_2O and filtered to collect the precipitate. The residue was washed with water, purified by preparative GPC (eluent; $CHCl_3$) to give the [3]rotaxane **R22** (95 mg, 46%) as a pale yellow solid; m.p. 105.0–106.0 °C; ^{1}H NMR (300 MHz, 298 K, $CDCl_3$) δ 8.28 (d, J = 8.8 Hz, 2H), 7.31–7.21 (m, 2H), 7.04 (d, J = 2.0 Hz, 2H), 6.79 (br, 2H), 5.81 (br, 2H), 5.36 (t, J = 8.5 Hz, 12H, C(3)H), 4.99 (d, J = 3.4 Hz, 12H, C(1)H), 4.84 (dd, J_1 = 3.4 Hz, J_2 = 8.5 Hz, 12H, C(2)H), 4.46–4.14 (m, 36H, C(6)H_a, C(6)H_b, C(5)H), 3.98 (s, 6H, OMe), 3.87 (t, J = 8.5 Hz, 12H, C(4)H), 3.79–3.32 (m, 4H, NH–**CH_2**–), 2.49–2.09 (m, 72H, OCO–**CH_2**–), 1.78–0.83 (m, 200H, $OCOCH_2$–**CH_2**–, $OCOCH_2CH_2$–**CH_3**, methylene of axle) ppm; IR (KBr) υ 3553, 3415, 2966, 2936, 2877, 1747, 1689, 1594, 1523, 1466, 1416, 1384, 1366, 1306, 1250, 1175, 1104, 1042, 1010, 963, 924, 861, 814, 751, 584 cm^{-1}; ESI-TOF MS (m/z): calc'd for $C_{244}H_{376}N_4O_{100}Br_2^{3+}$ [M^{3+}] 1731.0854; found 1731.0849.

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Keywords: Cyclodextrins • Rotaxanes • Alkylchain • Heterogeneous reaction • Urea end-capping

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[8] A part of this work has already been reported in the reference 7c and 9.

[9] As the size-complementary rotaxane can be decomposed at certain condition, it can also be classified as "kinetically stabilized pseudorotaxane"

[10] Some other factors must operate in directing the bromine in the para position of the urea group, which is opposite to our first assumption. Although this high regioselectivity is interesting in terms of basic chemistry, we did not further evaluate it in this manuscript.

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FULL PAPER

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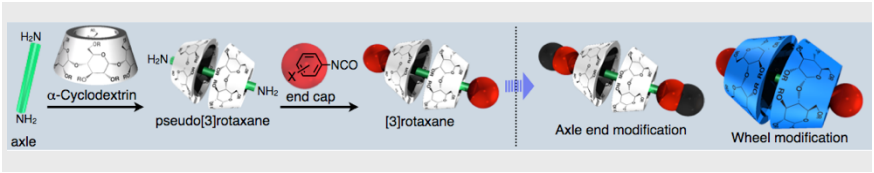
Layout 2:

FULL PAPER: **Rotaxane Synthesis**



Facile synthesis of α-cyclodextrin-(α-CD-) based [3]rotaxanes and their structural modifications are discussed in detail. Pseudo[3]rotaxane was prepared from α-CD and α,ω-diaminododecane in water, successive urea-forming end-capping reactions with isocyanate afforded [3]rotaxane. Significant modifications of the axle end and wheel OH group of the [3]rotaxanes were performed by the Suzuki coupling with arylboronic acids and by the perfect acylation with acid anhydrides, respectively.

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Effective Synthesis and Modification of α-Cyclodextrin-Based [3]Rotaxanes Enabling Versatile Molecular Design