One-Pot Synthesis of Native and Permethylated α-Cyclodextrin-Containing Polyrotaxanes in Water

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ABSTRACT: Efficient one-pot synthesis in water of polyrotaxanes, with native and permethylated α-cyclodextrins (α-CD and PMe α-CD) as the wheel components, is described. The procedure involves initial mixing of α-CDs and an amine-terminated linear polymer, which acts as the axle, by sonication and subsequent addition of an end-capping agent for the axle terminal amino groups. The polyrotaxanes were prepared by mixing the axle and wheel components by sonication for 30 min at room temperature and standing overnight if necessary, followed by treatment with a bulky isocyanate in water at 0 °C for an hour. Both amine-terminated polytetrahydrofuran (ATPT) and poly(ethylene glycol) (ATPEG) afforded the corresponding polyrotaxanes (PRXs) in good yields (27−49%) in the case of a native α-CD wheel. The coverage ratio of the axle component with the wheel component of the PRXs ranged from 85% to 96% when the molecular weight of the axle was M_n 1000−1800, while it was 54% when the axle was long (M_n 7700). The polyrotaxanes (PMePRXs) with PMe α-CD and ATPT were similarly obtained in high yields. In this case, the yield of the PMePRXs was unusually high (66 and 69%) when a higher molecular weight axle (M_n 4100 and 7100, respectively) was used. The formation of a PMePRX from ATPEG axle proceeded with low efficiency. The present work provides the first synthesis of polyrotaxanes with PMe α-CD in solution.

Introduction

Since the discovery of cyclodextrin-containing polyrotaxanes by Harada et al.,[1−3] many attractive concepts and materials originated from their unique structures and functions have been hitherto reported, e.g., stimuli-responsive systems,[4] insulated molecular wires,[5] and polyrotaxane networks.[6] While the polyrotaxanes have long been synthesized by the end-capping of the axle termini of the corresponding polypseudorotaxanes, the end-capping is still a difficult task due to the strong dethreading inclination of the axle from the polypseudorotaxane during the end-capping process, preventing the high yielding synthesis. Therefore, the development of rapid, efficient, and convenient end-capping methods affording the polyrotaxanes has been eagerly desired from viewpoint of a wide variety of applications of them.[7]

Cyclodextrin-containing polyrotaxane can be obtained by the reaction of the corresponding polypseudorotaxane possessing a terminal-functionalized axle polymer with a bulky end-capping agent. There have been reported to date several efficient synthetic methods of cyclodextrin-based polyrotaxanes through the end-capping process: reactions of axle (PEG) terminal amino groups with 2,4-dinitrofluorobenzene (DNFB) in DMF,[8] axle (PTHF) terminal hydroxy groups with 4-tritylphenylisocyanate in solid state,[9] axle (PEG) terminal carboxyl groups with adamantanamine in DMF,[10] and axle (polyethylenimine) terminal amino groups with 9-anthraldehyde in aqueous medium in one pot.[11] These methods require, however, addition of additives such as a catalyst, use of a block copolymer axle, change of pH, and/or prolonged reaction time for the progress of the end-capping reaction. Meanwhile, only a few investigations on the synthesis of polyrotaxanes with permethylated cyclodextrin (PMeCD) have appeared. Synthetic methods of polyrotaxanes with PMeCD reported so far are limited to the methylation of a CD-based polyrotaxane[12] or the end-capping reaction of a polypseudorotaxane with PMeCD in the solid state.[9] It is reported that no polyrotaxane with PMeCD is formed by the reaction in solution.[9a] We have recently developed a highly effective one-pot synthesis of polyrotaxanes via the end-capping of axle terminal amino groups of polypseudorotaxanes with α-CD in water (the urea end-capping method).[13] The present paper describes in detail the one-pot synthesis of not only polyrotaxanes with native α-CD but also those with permethylated α-CD (PMeα-CD). Both amine-terminated PEG and PTHF could function as the axle polymers.

Experimental Section

Materials. α-CD was obtained from Nacalai Tesque Inc. and used after drying at 80 °C under vacuum. PTHF2900 (TERATHANE, M_n 2900), PTHF bis(3-aminopropyl)-terminated (ATPT, M_n 1100), poly(ethylene glycol) bis(3-aminopropyl)-terminated (ATPEG 1500, M_n 1800 estimated by ^{1}H NMR), potassium phthalimide, 4-tritylaniline, and 3,5-dimethylphenyl isocyanate were obtained from Aldrich. *p*-Toluenesulfonyl chloride and hydrazine hydrate were obtained from Tokyo Kasei Kogyo Co. Ltd. Other chemicals were commercially available and used without further purification.

Characterizations. ^{1}H NMR spectra in DMSO-d_6 or $CDCl_3$ were recorded at 400 MHz on a JEOL JNM-LA400/WB spectrometer. Analytical size exclusion chromatography was performed on a JASCO HSS-1500 system equipped with a TOHSO TSK gel G2000 HXL and a TSK guard column HXL-H eluted with chloroform at a flow rate of 0.85 mL/min calibrated using polystyrene standards. Preparative HPLC was carried out using JAI HPLC LC-918 (columns: JASCO Megapack-Gel 201C, Megapack-Gel 201 CP, and JAI JAIGEL-1H; eluent: chloroform; flow rate: 3.5 mL/min). Thermogravimetry was performed on a Shimadzu TGA-50 instrument at a heating rate of 10 °C/min under nitrogen stream.

Preparation of Amine-Terminated PTHF (ATPT). Amine-terminated PTHF was prepared from PTHF2900 according to the method described by Pillai et al.[14] *p*-Toluenesulfonyl chloride (9.7 g, 51 mmol) and pyridine (6 mL) were added to a solution of PTHF2900 (5.0 g, 1.7 mmol) in chloroform (30 mL), and the

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Table 1. One-Pot Synthesis of PRX with Native α-CD in Water[a]

entry	axle component[b]	M_n of axle[c] (kg/mol)	capping agent[d]	product	yield (%)[e]	coverage ratio (%)[f]	av no. of included CDs[c]
1	ATPT1	1.1	TPI	PRX1	29	99	10
2	ATPT1	1.1	DPI	PRX2	49	96	10
3	ATPT2	7.7	DPI	PRX3	27	54	39
4	ATPEG1	1.8	DPI	PRX4	30	85	17
5[g]	ATPT1	1.1	DNFB	PRX5	28	93	10

[a] The initial threading reaction was carried out using ATPT (or ATPEG) and α-CD (2 equiv vs monomer unit) at room temperature for 30 min (sonication) and standing overnight. The subsequent end-capping with a capping agent (10 equiv) was performed at 0 °C for 60 min. [b] ATPT: amine-terminated poly(tetrahydrofuran); ATPEG: amine-terminated poly(ethylene glycol). [c] Calculated by ^{1}H NMR. [d] TPI: 4-tritylphenyl isocyanate; DPI: 3,5-dimethylphenyl isocyanate; DNFB: 2,4-dinitrofluorobenzene. [e] Yield was calculated based on the amount of the axle component used. [f] Coverage ratio: percent ratio of covered length of axle polymer chain based on the α-CD-complexation ratio of 1.5 (= 1.5 PTHF repeating units per CD) or 2 (= 2 PEG repeating units per CD). [g] Experimental results obtained according to the reported method (ref 8).

Table 2. Solubilities of Polyrotaxanes in Various Solvents[a]

polyrotaxane	DMSO	DMF	THF	methanol	acetone	$CHCl_3$	CH_2Cl_2	toluene	H_2O
unmodified (PRX2)	s	i	i	i	i	i	i	i	i
methylated (PMePRX1)	i	i	i	i	i	s	s	i	i

[a] s = soluble, i = insoluble.

Table 3. One-Pot Synthesis of PRX with PMeα-CD in Water[a]

				molecular weight M_n (kg/mol)				
entry	axle component[b]	Mn of axle[c] (kg/mol)	product	by SEC[d]	by NMR[c]	polydispersity[d] (M_w/M_n)	yield (%)[e]	coverage ratio (%)[f]
1	ATPT1	1.1	PMePRX1	9	10	1.5	20	93
2	ATPT3	4.1	PMePRX2	26	26	1.4	66	63
3	ATPT2	7.7	PMePRX3	29	43	1.5	69	54
4	ATPEG1	1.8	PMePRX4	10	10	1.7	5	45

[a] The initial threading reaction was carried out using ATPT or ATPEG and PMeα-CD (1 equiv vs monomer unit) at room temperature for 30 min (sonication) and standing overnight. The subsequent end-capping with a capping agent (12.5 equiv) was performed at room temperature for 60 min. [b] ATPT: amine-terminated poly(tetrahydrofuran); ATPEG: amine-terminated poly(ethylene glycol). [c] Calculated by ^{1}H NMR. [d] Calculated by SEC with CH_3Cl as an eluent. [e] Yield is calculated based on the amount of the axle component used. [f] Coverage ratio: percent ratio of covered length of axle polymer chain based on the complexation ratio of 2 (= 2 PTHF repeating units per PMeα-CD) and 2.7 (= 2.7 PEG repeating units per PMeα-CD).

mixture was stirred overnight under an argon atmosphere. The polymer precipitated by the addition of diethyl ether at −75 °C to the mixture was collected by filtration and dried under vacuum to yield ditosylated-PTHF. The product was directly used in the following reaction without purification.

A mixture of ditosylated-PTHF (3.5 g, 1.1 mmol) and potassium phthalimide (6.7 g, 37 mmol) in DMF (40 mL) was refluxed under an argon atmosphere for 5 h. The precipitate formed was then filtered. Diethyl ether was added to the transparent filtrate at −75 °C. The precipitate was filtered and dried under vacuum to yield phthalimide−PTHF (M_n 7200, M_w/M_n 1.4 by SEC). The product was directly used in the following reaction without purification.

A mixture of phthalimide−PTHF (3.4 g, 1.1 mmol) and hydrazine hydrate (6.0 mL, 0.16 mol) in ethanol (50 mL) was refluxed for 20 h. The mixture was poured into diethyl ether, and the insoluble material was filtered. The precipitates formed by cooling to −75 °C were collected by filtration and dried under vacuum to yield amine-terminated PTHF (ATPT) (2.7 g, 54% yield, M_n 7700 estimated by ^{1}H NMR). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 3.41 (m, 4H, CH_2O), 2.71 (t, 4H, CH_2N), 1.62 (m, 4H, methylene).

One-Pot Synthesis of Polyrotaxanes with Native α-Cyclodextrin (Urea End-Capping Method).[13] The synthesis of native α-cyclodextrin-based polyrotaxane from PTHF or PEG was accomplished under the conditions listed in Table 1. 4-Tritylphenylisocyanate (TPI) was prepared according to the reported procedure.[15] A typical procedure using 3,5-dimethylphenylisocyanate (DPI) is as follows.

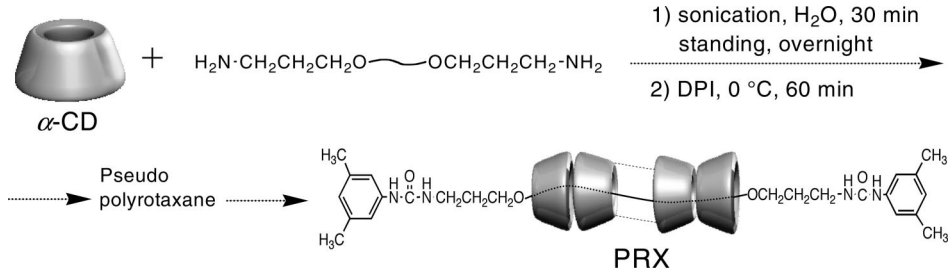
ATPT (54 mg, 0.75 mmol vs monomer unit) was added to a solution of α-CD (1.5 g, 1.5 mmol) in distilled water (10 mL), and the mixture was sonicated for 30 min at room temperature. The turbid mixture was allowed to stand overnight. Addition of DPI (72 mg, 0.5 mmol) to the resulting mixture was followed by stirring at 0 °C for 1 h. The reaction mixture was poured into THF (200 mL). The precipitates were collected by filtration, washed with water, and dried in vacuo to yield polyrotaxane (PRX, 260 mg, 49%, Table 1, entry 2). ^{1}H NMR (DMSO-d_6, 400 MHz, 295 K): δ 8.22 (s, 2H, CONH of PRX), 6.98 (s, 4H, ortho ArH), 6.51 (s, 2H, para ArH), 6.05 (t, 2H, J = 5.6 Hz, NHCONH of PRX), 5.53 (s, 6H, O(2)H of α-CD), 5.44 (s, 6H, O(3)H of α-CD), 4.78 (d, 6H, J = 3.1 Hz, C(1)H of α-CD), 4.50 (s, 6H, O(6)H of α-CD), 3.55−3.78 (m, 6H, C(3)H, 12H, C(6)H, 6H, C(5)H of α-CD), 3.40 (m, 4H, OCH_2 of ATPT), 3.27−3.34 (m, 6H, C(2)H, 6H, C(4)H of α-CD), 2.17 (s, 12H, $CH_3$of DPI), 1.49 (m, 4H, methylene H of ATPT); T_{d5} 329 °C.

Synthesis of Polyrotaxanes with Native α-Cyclodextrin (Conventional Harada's Method[8]). A mixture of α-CD (0.73 g, 0.75 mmol) and ATPT (M_n 1100, 54 mg, 0.75 mmol vs THF unit) in water (10 mL) was subjected to sonication for 30 min and then allowed to stand overnight at room temperature. The resulting precipitates were collected by centrifugation and dried in vacuo to yield a white powder (polypseudorotaxane). A mixture of the product and 2,4-dinitrofluorobenzene (DNFB) (0.8 g, 4.6 mmol) in dry DMF (30 mL) was stirred overnight in an argon atmosphere at room temperature. The yellow solid precipitated by the addition of diethyl ether (200 mL) was collected and washed with water to yield polyrotaxane (146 mg, 28%, Table 1, entry 5). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ 8.87 (s, 2H, meta ArH), 8.30 (s, 2H, meta ArH), 7.26 (s, 2H, ortho ArH), 5.46 (s, 6H, O(2)H of α-CD), 5.39 (s,6H, O(3)H of α-CD), 4.73 (s, 6H, C(1)H of α-CD), 4.44 (s, 6H, O(6)H of α-CD), 3.51−3.72 (m, 6H, C(3)H, 12H, C(6)H, 6H, C(5)H of α CD), 3.39 (m, 4H, CH_2O of ATPT), 3.21−3.32 (m, 6H, C(2)H, 6H, C(4)H of α-CD), 1.44 (m, 4H, C-methylene H of ATPT); T_{d5} 324 °C.

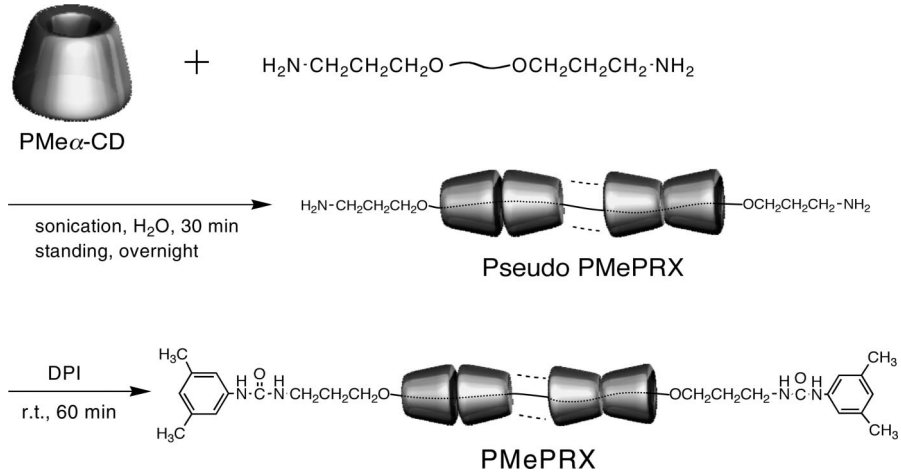
One-Pot Synthesis of Polyrotaxanes with Permethylated α-Cyclodextrin (Urea End-Capping Method). The synthesis of permethylated cyclodextrin-based polyrotaxane from PTHF or PEG was accomplished under the conditions listed in Table 3. Permethylated α-CD (PMeα-CD) was prepared according to the reported procedure.[16] A typical procedure using ATPT (M_n 1100) and DPI is as follows.

ATPT (M_n 1100) (44 mg, 0.61 mmol vs monomer unit) was added to a solution of PMeα-CD (0.80 g, 0.65 mmol) in distilled water (2 mL), and the mixture was sonicated for 30 min at room temperature. The turbid mixture was allowed to stand overnight. Addition of DPI (72 mg, 0.50 mmol) to the resulting mixture was

Scheme 1



Scheme 2



followed by stirring at room temperature for 1 h. The precipitate was collected by centrifugation, washed with diethyl ether, dried in vacuo, and purified by preparative HPLC (eluent: chloroform) to yield permethylated polyrotaxane (PMePRX) (85 mg, 20%, Table 3, entry 1). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ 7.09 (s, 4H, ortho ArH), 6.60 (s, 2H, para ArH), 5.00 (s, 6H, C(1)H of PMeα-CD), 3.98−3.05 (m, 6H, C(2−6) H, O (2, 3, 6) CH_3 of PMeα-CD and OCH_2 of ATPT), 2.21 (s, 12H, CH_3 of DPI), 1.62 (s, 4H, methylene H of ATPT); T_{d5} 290 °C.

Results and Discussion

One-Pot Synthesis of Polyrotaxanes with Native α-Cyclodextrin. Polyrotaxane (PRX) was prepared from α-CD, an amine-terminated linear polymer, and a bulky aromatic isocyanate as the end-capping agent through initial threading to polypseudorotaxane (pseudoPRX) followed by the end-capping of the axle terminal (Scheme 1). The reason why aromatic isocyanate was chosen as an end-capping agent is because primary amine can readily react with aromatic isocyanate without any catalyst, much faster than the alcohol-like OH group of α-CD. The synthetic procedure is very simple: a mixture of α-CD and ATPT was mixed by sonication for 30 min in water at room temperature. After allowing to stand overnight, DPI was added and stirred for 1 h at 0 °C. The work-up is also quite simple: the mixture was poured into THF, and the precipitated product was collected and washed with water to yield pure polyrotaxane (PRX2, ATPT1, M_n 1100, Table 1, entry 2). The product yield (49%) was determined on the basis of the amount of ATPT used.

The coverage ratio, the percentage of axle polymer chain covered with native α-CD, is calculated from the ^{1}H NMR integration ratio of the wheel and axle components by assuming that 1 α-CD molecule is threaded onto 1.5 repeating units of PTHF and 2.0 repeating units of PEG. The PTHF chain was nearly completely covered with α-CD (96%) in the case of PRX2. The present one-pot method was compared with the conventional method using 2,4-dinitrofluorobenzene (DNFB) instead of DPI as the end-capping agent, i.e., a two-step reaction involving threading in water and end-capping in DMF.

As shown in entry 5, the yield of PRX5 (28%) was lower than that by the one-pot method (PRX2, 49%), although the coverage ratio was similarly high (93%, 96%). This result clearly suggests the usefulness of the one-pot method compared to the conventional method. Namely, pseudoPRX possessing a sufficient amount of α-CD formed during the initial mixing is completely converted to PRX by the reaction with DPI because isolation of pseudoPRX was not required before end-capping due to the one-pot reaction in water. In the conventional method, the isolation process of pseudoPRX probably results in a lower yield of PRX. An additional reason is possibly attributed to the higher reactivity and efficiency of DPI toward the primary amine of the axle terminal than that of DNFB requiring the aromatic nucleophilic substitution of the terminal amino group. The fact that the end-capping reaction proceeds efficiently despite the heterogeneous conditions seems to support the above reason.

Several PRXs were similarly prepared as listed in Table 1. When a bulky isocyanate (tritylphenyl isocyanate, TPI) was employed, the corresponding polyrotaxane PRX1 was similarly obtained, although the yield of PRX1 was slightly low (29%, entry 1), probably because the use of solid TPI did not permit a sufficiently high concentration to react efficiently in water with the terminal amino group of pseudoPRX, in addition to the bulkiness of the electrophile in the amine addition. The use of higher molecular weight PTHF (ATPT3, M_n 7700) also resulted in the formation of polyrotaxane PRX3, but both yield (27%) and coverage ratio (54%) were not high (entry 3). This result is consistent with the reported result, i.e., lower yield and coverage ratio with higher molecular weight polymer axle.[17] In this case, the average number of α-CDs per one PRX3 molecule was 39, which is larger than that for PRX1 (10), suggesting that a higher molecular weight polymer axle can thread larger number of α-CDs, while the coverage ratio is less than that for a lower molecular weight axle. PEG could also

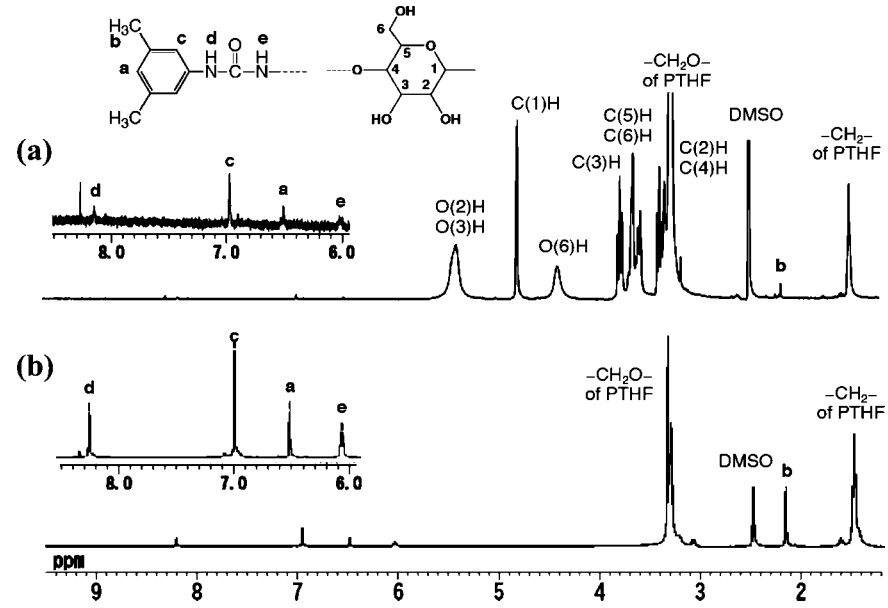


Figure 1. [1]H NMR spectra (400 MHz, DMSO-d_6, 298 K) of (a) PRX2 (Table 1, entry 2) and (b) UEPT prepared from ATPT1 and DPI.

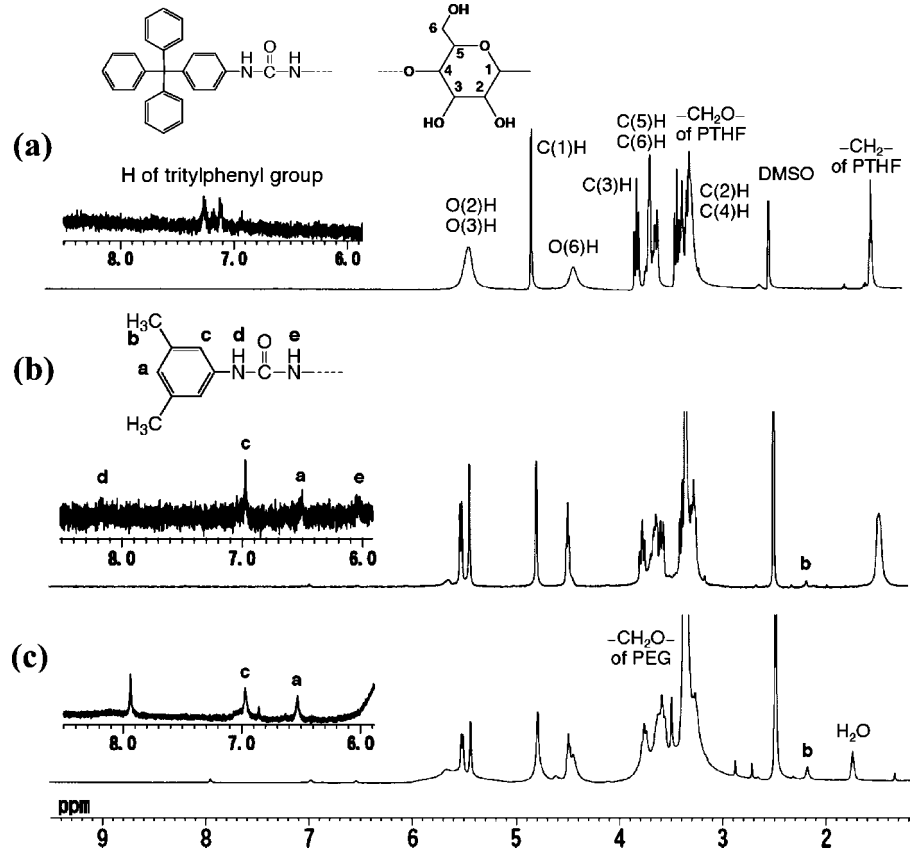


Figure 2. [1]H NMR spectra (400 MHz, DMSO-d_6, 298 K) of (a) PRX1 (Table 1, entry 1), (b) PRX3 (Table 1, entry 3), and (c) PRX4 (Table 1, entry 4).

become an axle polymer of PRX in the present synthetic method (PRX4, entry 4), although both the yield (30%) and coverage ratio (85%) were lower than those of PTHF (entry 2).

The structures of the PRXs were determined by spectroscopic analyses, and their solubilities were also determined (Table 2). The PRXs had low solubility in THF, which enabled their easy isolation: the reaction mixture including solvent water was directly poured into THF for isolation. Figure 1 shows the [1]H NMR spectrum of PRX2 along with the dumbbell-shaped molecule (UEPT) independently prepared by the reaction of ATPT with DPI. The spectra clearly indicate the formation of polyrotaxane (PRX2) from the presence of the aromatic proton signals (a and b) and the urea NH signals (d and e) of the end groups other than those of α-CD and PTHF at 3−6 ppm. [1]H NMR spectra of other PRXs (PRX1, PRX3, and PRX4) are depicted in Figure 2.

The aromatic proton signals are confirmed in PRX1 and PRX3 as small peaks, whose intensity changed depending on the length of the axle polymer chain. In the case of PRX4 with the PEG axle chain, the aromatic signals (a and c) of the 3,5-

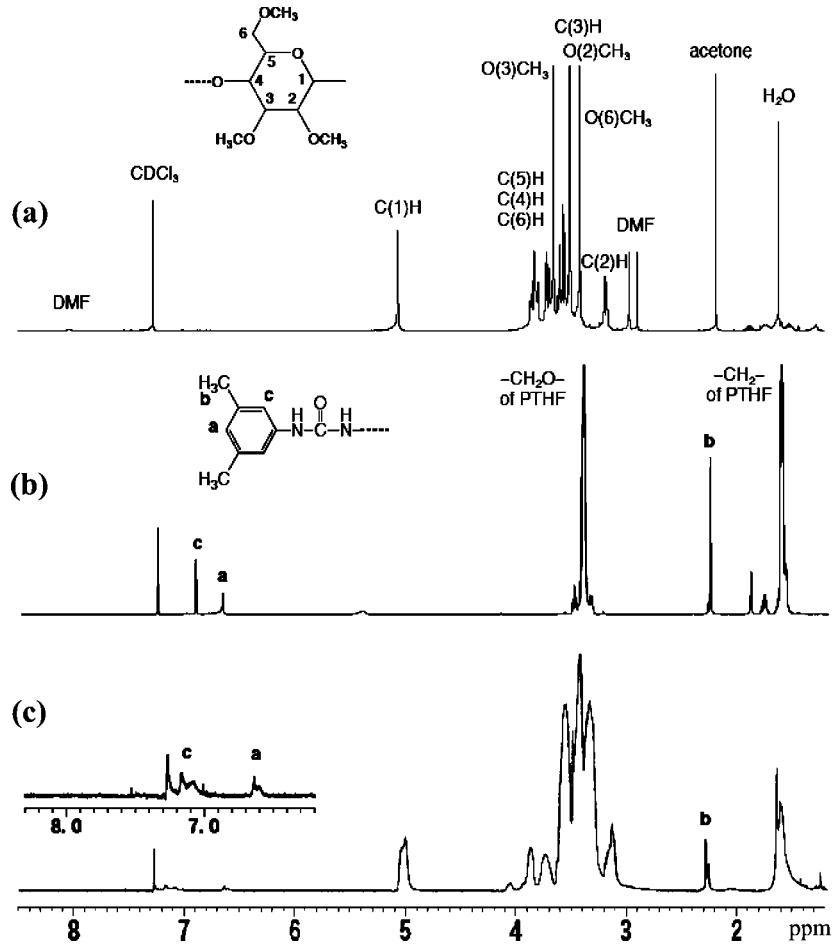


Figure 3. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of (a) PMeα-CD, (b) UEPT prepared from ATPT1 and DPI, and (c) PMePRX (Table 3, entry 1).

dimethylphenyl end-cap group appear around 6.5−7.0 ppm in addition to other aliphatic signals of the CD wheel and PEG axle. As our previous study has shown that the possible side reaction of hydroxyl groups of α-CD with isocyanate groups of capping agents is completely suppressed by reacting at low temperature around 0 °C, no signals based on the reaction of the α-CD OH group were observed in any case.[13]

Synthesis of Polyrotaxanes with Permethylated α-Cyclodextrin. There has been no report on the synthesis of polyrotaxane with PMeα-CD as far as we know. Therefore, we examined the preparation of PRX from PMeα-CD and PTHF or PEG axle because the present one-pot synthesis with native α-CD allowed highly efficient polyrotaxane formation. In fact, similar synthetic procedures using PMeα-CD instead of native α-CD afforded PRXs, as summarized in Table 3. Since PMeα-CD has no OH group, the end-capping reaction with DPI could be carried out at room temperature. ATPT1 and PMeα-CD yielded PMePRX1 (20%, Table 3, entry 1). As mentioned above, this is the first synthesis of polyrotaxane with PMeα-CD in the solution state; we had already reported the synthesis of polyrotaxane with PMeα-CD in the solid state.[9]

The fact that PMePRX1 was actually isolated in the above polyrotaxane synthesis clearly suggests the formation of pseudoPMePRX1 by mixing PMeα-CD and ATPT1 in water. However, pseudoPMePRX1 did not precipitate after sonication of the mixture in this case, in accordance with the report by Harada et al.,[18] and this is inconsistent with the case of pseudoPRX1 described above. Namely, the results reveal that pseudoPMePRX1 is soluble in water. The direct addition of DPI to the reaction mixture, including pseudoPMePRX1 in a solution form, actually allowed the efficient end-capping to yield PMePRX1 with a sufficiently high coverage ratio (93%). These results clearly indicate the intermediary formation of pseudoPMePRX1 containing highly dense wheels. This feature of the present method should therefore be emphasized as the most characteristic advantage of the one-pot method, since it cannot be accomplished by the conventional two-step method involving the isolation of the intermediate polypseudorotaxane. Furthermore, the present one-pot method is also suitable for the synthesis of polyrotaxanes having α-CDs without an OH group other than PMeα-CD.

Figure 3 shows ^{1}H NMR spectra of PMeα-CD, a dumbbell molecule UEPT, and PMePRX1 (Table 3, entry 1). The spectrum of PMePRX1 contains broadened signals, probably attributed to the decrease in conformational flexibility caused by polyrotaxanation. Furthermore, the comparison of ^{1}H NMR spectra in Figure 3a−c strongly suggests that the terminal amine groups of ATPT were converted to the urea groups by the reaction with DPI.

Figure 4 shows the SEC profiles of PMePRX1 (Table 3, entry 1) along with those of PMeα-CD and UEPT for comparison. Molecular weight of PMePRX1 was evaluated higher than that of UEPT in SEC (Figure 4, in which the SEC curve of UEPT was much more broad than that of PMePRX1 probably due to the presence of the naked urea moieties capable of interacting with the SEC column). This result coupled with the NMR result indicates that PMePRX comprises PMeα-CDs and the dumbbell PTHF capped with DPI.

The solubility of PMePRX1 with PMeCDs was quite different from that of PRX2 with native CDs, as shown in Table 2.

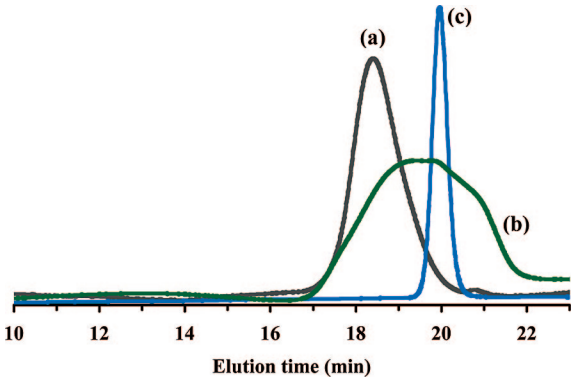


Figure 4. SEC profiles of (a) PMePRX1 (Table 3, entry 1), (b) UEPT prepared from ATPT1 (M_n 1100) and DPI, and (c) PMeα-CD.

Whereas PRX2 was soluble only in DMSO among the solvents tested due to the strong inter- and intramolecular hydrogen bonding between native CDs, PMePRX1 was soluble in a few organic solvents such as chloroform and dichloromethane but not in DMSO, probably owing to the absence of hydrogen bonding between PMeCDs.

As shown in Table 3, the molecular weights of PMePRXs, estimated by SEC (^{1}H NMR), were 9000 (10 000), 26 000 (26 000), 29 000 (43 000), and 10 000 (10 000) for $ATPT_{1100}$, $ATPT_{4100}$, $ATPT_{7700}$, and $ATPEG_{1800}$, respectively. The molecular weight of PMePRX3 with $ATPT_{7700}$ measured by SEC was lower than that by NMR, probably because the difference of molecular sizes between actual PMePRX's conformation and ideal random coils model is larger in PMePRX using long axle polymer.

The yield of PMePRX increases with increase in ATPT molecular weight (Table 3, entries 1 and 2), in contrast to that of PRXs with ATPT. This result seems to suggest that higher molecular weight ATPT undergoes a slower dethreading reaction during complexation with PMeα-CD than the lower molecular weight ATPT. The yield of PMePRX3 (69%) is quite high, suggesting the efficient formation of pseudoPMePRX3, although no precipitation was observed before end-capping with DPI. Meanwhile, the coverage ratio was 54%, in good agreement with the reported results for native α-CD.[17] The coverage ratio of the ATPT or ATPEG chain with PMeα-CD in PMePRX was calculated from ^{1}H NMR integration, assuming that one PMeα-CD molecule is threaded onto two repeating units of PTHF or 2.7 repeating units of PEG. The CPK model study as well as the stable conformation of PMeα-CD calculated by MM2 force field suggested a height of ca. 12 Å, which is consistent with the height (12−15 Å) estimated by the stoichiometry of the PMeβ-CD/PTHF complex.[18] This height is 1.5 times higher than that of native α-CD (7.9 Å).[19] In other words, when the number of CDs per one polyrotaxane molecule is the same, the coverage ratio of PMePRX is 1.5 times higher than that of PRX.

Formation of PMePRX4 from ATPEG was confirmed by ^{1}H NMR and SEC, as shown in Figures 5 and 6. The ^{1}H NMR spectrum indicates the formation of the polyrotaxane from the presence of the aromatic proton signals (a and c) and methyl proton signal (b) of DPI other than those of PMeα-CD and PEG at 3−6 ppm. The SEC profiles show that PMePRX4 was eluted in a higher molecular weight region than PMeα-CD and the dumbbell molecule (UEPEG) prepared independently. (Figure 6, in which the SEC curve of PMePRX4 had a shoulder at lower molecular weight region, probably because the SEC retention time of polyrotaxanes with lower coverage ratios is more likely to be affected by the uncovered urea moieties of the axle). The results reveal that PMePRX4 is composed of PMeα-CD and UEPEG. It is well-known that hydrophilic polymers such as

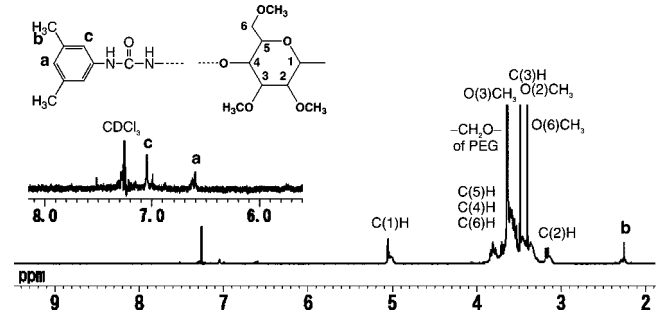


Figure 5. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of PMePRX4 (Table 3, entry 4).

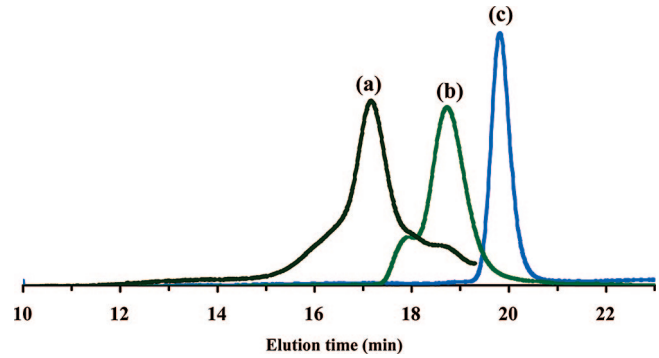


Figure 6. SEC profiles of (a) PMePRX4 (Table 3, entry 4), (b) UEPEG prepared from ATPEG1 (M_n 1800) and DPI, and (c) PMeα-CD.

PEG cannot effectively form inclusion complexes with PMeα-CD in aqueous solution. This is attributed to the fact that PEG is so hydrophilic that the hydrophobic interaction with PMeα-CD is not sufficiently strong to accelerate the complex formation. Although numerous studies have been reported the synthesis of methylated CD-polyrotaxanes, to the best of our knowledge, this is the first synthesis of PEG-based polyrotaxane from methylated CD. Therefore, the usefulness of the present one-pot method is again emphasized.

Conclusion

A series of polyrotaxanes having native α-CD and PMeα-CD wheels were prepared in good yields by a one-pot reaction in water, via initial mixing of CD and an amine-terminated linear polymer, and subsequent addition of a bulky isocyanate to the mixture. The side reaction of hydroxyl groups of α-CD with the isocyanate could be completely suppressed by carrying out the end-capping reaction at 0 °C to selectively yield polyrotaxanes PRXs with α-CD. Meanwhile, PMePRXs with PMeα-CD were similarly obtained in reasonably high yields by a simple one-pot method. The best feature of the present one-pot method is its remarkable applicability to the system in which the formation of intermediate polypseudorotaxane is not confirmed. By the present method, the synthesis of polyrotaxane from PEG and PMeα-CD was achieved for the first time. Thus, the present one-pot method with urea end-capping provides a remarkably useful synthetic method to obtain polyrotaxanes consisting of CD and MeCD. The method is characterized by an easy procedure without the isolation of a polypseudorotaxane intermediate, without any extra additives, a short reaction time, and pure product isolation.

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