One-pot Synthesis of Main Chain-type Polyrotaxane Containing Cyclodextrin Wheels

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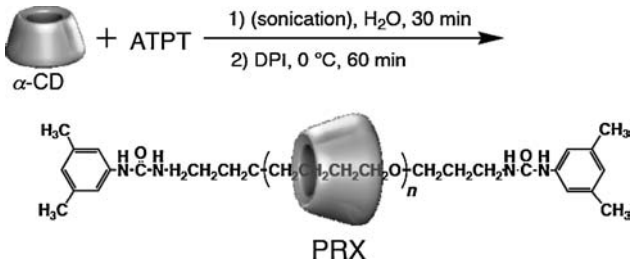
Polyrotaxane possessing cyclodextrin wheels was prepared in one pot through the initial threading complexation of polytetrahydrofuran axle and α-cyclodextrin wheel followed by the end-capping reaction of the terminal amino groups of the axle with a bulky isocyanate in water.

Pseudopolyrotaxanes and polyrotaxanes consisting of cyclodextrin (CD) and linear polymers such as poly(ethylene glycol) (PEG) and poly(tetrahydrofuran) (PTHF) have been widely investigated by a number of research groups since their first discovery by Harada and co-workers.[1–3] Many attractive concepts and materials based on the unique structure of the polyrotaxane formed by the end-capping of the pseudopolyrotaxane have been hitherto reported: stimuli-responding systems,[4] insulated molecular wires,[5] and polyrotaxane network.[6] End-capping, which is necessary to fix pseudopolyrotaxane to polyrotaxane prior to such studies, however, is a difficult task owing to the strong dethreading inclination of the axle from the pseudorotaxane. For the wider practical application of polyrotaxanes, development of rapid, efficient and convenient end-capping method for the preparation is required.[7]

Several synthetic methods of cyclodextrin-based polyrotaxanes have been reported to date by the end-capping of axle terminal of pseudopolyrotaxane with a bulky stopper: end-capping of terminal amino groups of PEG-pseudorotaxane with 2,4-dinitrofluorobenzene (DNFB) in DMF,[8] terminal hydroxy groups of PTHF–pseudopolyrotaxane with 4-tritylphenyl isocyanate in solid state,[9] terminal carboxyl groups of PEG–pseudopolyrotaxane with adamantanamine in DMF,[10] and terminal amino groups of polyethylenimine–pseudopolyrotaxane with 9-anthraldehyde in aqueous medium in one-pot.[11] These methods require, however, addition of additives such as catalyst, use of a block copolymer axle, change of reaction medium pH, and/or prolonged reaction time for progress of the reaction. We have recently developed an effective one-pot synthesis of polyrotaxanes via the end-capping of axle terminal amino groups of pseudopolyrotaxane in situ prepared from PTHF and α-cyclodextrin in water, which is described in this paper.

A mixture of α-CDs and amine-terminated PTHF (ATPT, M_n 1100) in water was subjected to the sonication for 30 min at room temperature. To the resulting mixture containing white precipitate was directly added 3,5-dimethylphenylisocyanate (DPI, 5.0 equiv.) at 0 °C, and the mixture was stirred for 1 h at that temperature (Scheme 1). The white solid precipitated by the addition of THF was collected and washed with water to give pure polyrotaxane (PRX, 29% yield, Run 1). The structure of PRX was determined by the spectroscopic analyses. Figure 1 shows ^{1}H NMR spectra of PRX (a)[14] and model axle UEPT (b) prepared independently by the reaction of ATPT with DPI



Scheme 1. One-pot synthesis of polyrotaxane.

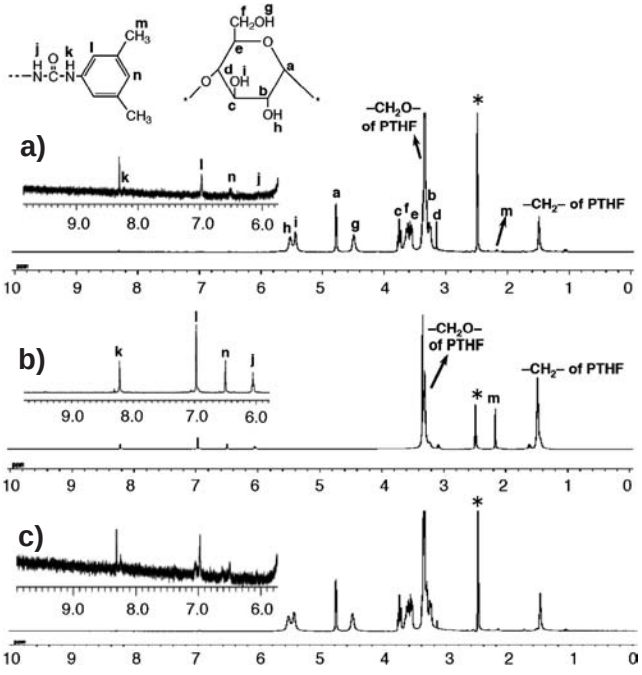


Figure 1. ^{1}H NMR spectra (400 MHz, DMSO-d_6, 298 K) of a) PRX in one-pot (Table 1. Run 2), b) UEPT, c) APRX (Table 1, Run 4). The mark ∗ denotes the signals of DMSO.

(Figure 2). The comparison of the ^{1}H NMR spectra strongly suggests that the terminal amine groups of ATPT were converted to the urea groups by the reaction with DPI.

Table 1 lists the results of the one-pot reactions (Runs 1–4) and some reference reactions for comparison such as two-step reaction. When the sonicated mixture was allowed to stand overnight before the reaction with DPI, the yield of PRX increased up to 49% (Run 2).[12,13] When the end-capping reaction was prolonged to 2 h at 0 °C, no yield increase was confirmed while no side reaction took place (Run 3). Therefore, the reaction at 0 °C for 1 h was suggested as that under the optimum condition (Run 2).

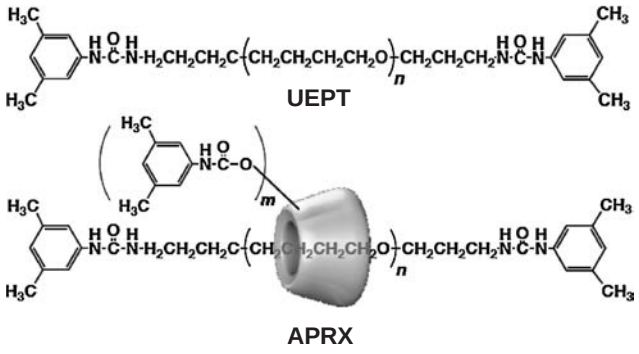


Figure 2. Structures of UEPT and APRX.

Table 1. Synthesis of polyrotaxane by the urea end-capping

Run No.	Solvent	Reaction type	Temp. /°C	Time[a] /h	Yield[b] /%	Coverage ratio θ /%
1	H_2O	One-pot	0	1	29	95
2[c]	H_2O	One-pot	0	1	49	96
3[c]	H_2O	One-pot	0	2	48	95
4[c]	H_2O	One-pot	r.t.	1	46[d]	99
5	DMF	Two-step[e]	0	1	35	90
6	DMF	Two-step[e]	r.t.	1	41[d]	96
7	THF	Two-step[e]	0	1	45	90
8	THF	Two-step[e]	r.t.	1	40	96
9[f]	DMF	Two-step[e]	r.t.	24	28	93

[a]Reaction time of end-capping. [b]Yield based on PTHF used. [c]The sonicated mixture was allowed to stand overnight at room temperature. [d]Crude yield (include APRX). [e]Involving isolation of pseudopolyrotaxane. [f]Reported method (Ref. 8).

Two-step reactions in DMF and THF usually used as the solvent (Runs 5–8) showed approximately 40% yield of PRX which can be compared with one-pot reactions. The yield by the present urea end-capping method using DPI was higher than that of the reported method using DNFB (Run 9).[8] Meanwhile, the present one-pot reaction is faster than any other end-capping reactions reported so far.[8–11] The coverage ratio[15] of PRX formed was more than 90% in any case.

The occurrence of the reaction of OH groups of α-CD with DPI during the end-capping reaction was ruled out by comparing with the ^{1}H NMR spectrum of PRX obtained by the reaction at room temperature (Figure 1c). Figure 1c shows the spectrum of APRX bearing a small number of urethane moieties formed by the reaction of hydroxy groups of α-CD with PDI. The formation of the urethane groups was confirmed by the signals at 7.05 and 6.60 ppm which were attributed to those of the aromatic protons of the end-caps. The results clearly indicate that such side reaction of the hydroxy groups with PDI can be suppressed simply by controlling the reaction temperature.

In conclusion, the present urea end-capping method via one-pot process provides a quite useful synthetic entry to polyrotaxane consisting of α-CD. The method can be characterized by the easy procedure without isolation of pseudopolyrotaxane, without any extra additive, in short reaction, at low temperature, and with pure product.

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11 H. S. Choi, T. Ooya, N. Yui, *Macromol. Biosci.* **2006**, *6*, 420.
12 One-pot synthesis of PRX: To a solution of α-CD (1.5 g) in distilled water (10 mL) was added ATPT 54 mg (0.75 mmol vs. monomer unit), 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 excess THF. The precipitate was isolated by filtration, washed with water, and dry in vacuo to yield 260 mg (49%) of PRX.
13 The structure of PRX was confirmed by X-ray powder diffraction (XRD). The XRD pattern which showed a main crystalline peak at $2\theta = 20°$, indicating that PRX has a channel structure of α-CDs. The thermal property of PRX was studied by thermogravimetric analysis (TGA, N_2 flow rate:50 mL/min, heating rate:10 °C/min). The initial decomposition temperature of PRX (Td_5. 329 °C) was almost the same as that of conventional polyrotaxane prepared with DNFB.
14 ^{1}H NMR (DMSO-d_6, 400 MHz, 295 K), 8.22 (s, 2H, CONH of PRX), 6.98 (s, 4H, ortho ArH), 6.51 (s, 2H, para ArH), 6.05 (t, 2H, 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, 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).
15 The coverage ratio (θ) of the PTHF chain with α-CD in PRX was calculated from ^{1}H NMR integration of the signals at 4.79 ppm (C (1)H of α-CD) and 1.49 ppm (CH_2 of PTHF), assuming one α-CD molecule is threaded onto 1.5 repeating units of PTHF.

Published on the web (Advance View) February 10, 2007; doi:10.1246/cl.2007.418