

# Polyester-Containing $\alpha$ -Cyclodextrin-Based Polyrotaxane: Synthesis by Living Ring-Opening Polymerization, Polypseudorotaxanation, and End Capping Using Nitrile *N*-Oxide

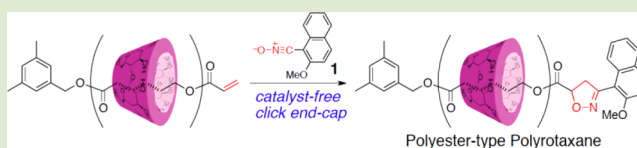
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## S Supporting Information

**ABSTRACT:** The first synthesis of polyrotaxanes consisting of polyester axles and  $\alpha$ -cyclodextrin ( $\alpha$ -CD) wheels was achieved by the catalyst-free click end-capping reaction of polypseudorotaxanes using nitrile *N*-oxide. The polypseudorotaxanes contain acrylate-functionalized polyesters that are obtained by the living ring-opening polymerization of lactones. The yield and coverage ratio of polyrotaxanes are highly dependent on the reaction time, molecular weight of the polyester, polyester structure, and solvent used. From the thermal properties of the resulting polyrotaxanes, it was found that coverage with  $\alpha$ -CDs efficiently suppresses the crystallization of the polyester main chain.

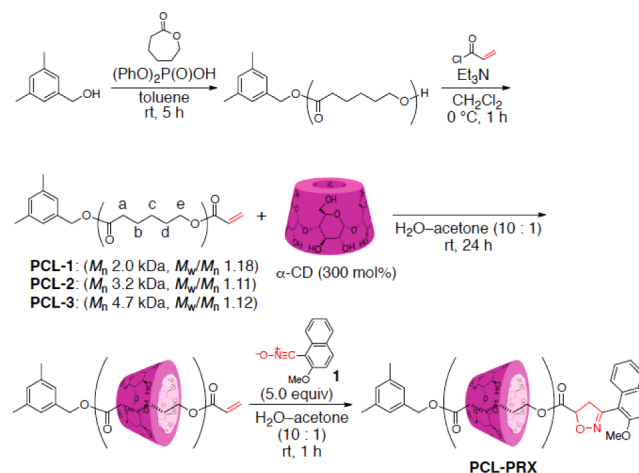


Main chain-type polyrotaxanes (PRXs) consisting of cyclodextrin (CD) as a wheel component have attracted a significant amount of interest in various fields such as supramolecular and polymer chemistry<sup>1</sup> ever since Harada's original reports.<sup>2</sup> To date, many studies have reported that CD can form polypseudorotaxanes (PPRXs) with various linear polymers.<sup>3</sup> However, the end-capping reaction of a PPRX to give a useful PRX is difficult because of the inclination of the axle to dethread from the wheel and the need to develop the end-capping reaction so it can be easily employed with versatile polymer skeletons. To overcome these issues, we recently reported an efficient and reliable synthesis of CD-based PRXs. This is carried out via the 1,3-dipolar cycloaddition of a stable nitrile *N*-oxide, an end-capping agent, to an alkene-terminated PPRX, as one of the one-pot synthetic procedures.<sup>4–6</sup> The developed end-capping method is suitable for not only native- $\alpha$ -CD-based PPRXs but also permethylated- $\alpha$ -CD-based PPRXs with very weak through-space interactions. This is probably because the reaction is carried out under very mild conditions, without any catalyst or byproducts to occasionally weaken the through-space interactions of the PPRX.

In this study, we report the first synthesis and characterization of PRXs consisting of CDs and polyesters with narrow polydispersities by employing the catalyst-free click-end-capping method with a stable nitrile *N*-oxide. Our results indicate that the yield and coverage ratio of polyrotaxanes are highly dependent on the reaction time, molecular weight of the polyester, polyester structure, and reaction solvent. PRXs were characterized by <sup>1</sup>H NMR, IR, gel permeation chromatography (GPC), and wide-angle X-ray diffraction (WAXD). The unique thermal properties of PRXs were also evaluated.

Scheme 1 shows the synthesis of a polyrotaxane consisting of  $\alpha$ -CDs and poly( $\epsilon$ -caprolactone) (PCL). This PCL-type axle

## Scheme 1. Synthesis of PRXs with $\alpha$ -CDs and PCL Using Nitrile *N*-Oxide 1 as an End-Capping Agent



polymer was prepared via the ring-opening polymerization of  $\epsilon$ -caprolactone using 3,5-dimethylbenzyl alcohol as an initiator and diphenyl phosphate as a catalyst, as reported by Kakuchi et al.<sup>7</sup> It was found that polymerization proceeds in a living fashion to manipulate the molecular weights of PCLs with narrow polydispersities.<sup>8</sup> Subsequent treatment of PCL with acryloyl chloride in the presence of Et<sub>3</sub>N produced the corresponding PCL (PCL-1, PCL-2, and PCL-3) with an acrylate group and a bulky end group.

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Having produced these PCL-type axle polymers, we then investigated the synthesis of polyrotaxanes **PCL-PRX** with  $\alpha$ -CDs and PCL. 2-Methoxynaphthalene-1-nitrile *N*-oxide (**1**) was used as the end-capping agent, building on our previous study.<sup>4,9</sup> Initially, a solution of **PCL-2** (3.2 kDa,  $M_w/M_n$  1.11) in acetone was added to an aqueous solution of  $\alpha$ -CD at room temperature, and the mixture was stirred for 12 h. Next, **1** was directly added to the resulting mixture, and the mixture was stirred for 1 h to give a pale yellow precipitate. After washing the solid with H<sub>2</sub>O and THF to remove unreacted CD, **PCL-2**, and **1**, we found that the click-end-capping reaction chemoselectively produced a **PCL-PRX** as a H<sub>2</sub>O- and THF-insoluble product, despite the presence of hydroxyl groups on the CD. The yield was only 0.4% from the axle polymer, and the coverage ratio was 78% (Table 1, entry 1). This relationship

**Table 1.** Effect of Reaction Time and Molecular Weight on Yield of **PCL-PRX**<sup>a</sup>

entry	PCL	$M_n$ /kDa	time/h	yield/% <sup>b</sup>	coverage ratio/% <sup>c</sup>
1	<b>PCL-2</b>	3.2	12	0.4	78
2	<b>PCL-2</b>	3.2	24	5.7	70
3	<b>PCL-2</b>	3.2	48	37	70
4	<b>PCL-2</b>	3.2	96	43	71
5	<b>PCL-1</b>	2.0	24	1.1	72
6	<b>PCL-3</b>	4.7	24	14	78

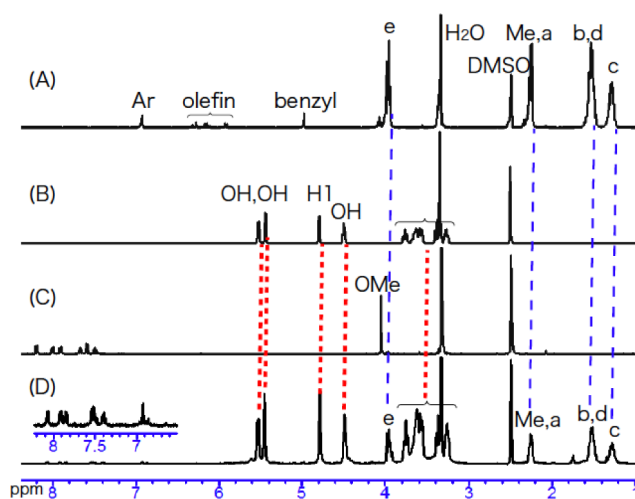
<sup>a</sup>Threading reaction was carried out using  $\alpha$ -CD (300 mol % for the axle monomer unit) and axle polymer (1.17 mmol per repeating unit) in H<sub>2</sub>O–acetone (10:1) at room temperature. Nitrile *N*-oxide **1** (5.0 equiv) was added to the mixture, and the mixture was stirred for 1 h at the same temperature. <sup>b</sup>Yield was calculated on the basis of the amount of the axle component. <sup>c</sup>Coverage (%) was calculated from the ratio of the NMR integrals of the wheel and axle components as a means of the coverage ratio of the polymers by assuming that the 100% complexation ratio is 1.0 repeating units of PCL per  $\alpha$ -CD according to the literature.<sup>3a</sup>

was calculated from the ratio of the <sup>1</sup>H NMR integrals of the wheel and axle components by assuming that one  $\alpha$ -CD molecule is threaded onto 1.0 repeating unit of PCL.<sup>3a</sup> With the aim of improving the yield, we next investigated the effect of the reaction time for the threading reaction on the yield of **PCL-PRX**, and these results are summarized in Table 1.

**PCL-PRXs** were prepared with different reaction times (entries 1–4). With increasing reaction time, the yield of **PCL-PRX** nonlinearly increased up to 43%, and the coverage ratios of **PCL-PRXs** ranged from 70 to 78%. This implies that the yield and coverage ratio of **PCL-PRXs** are probably dependent on not only the threading rate of PCL into the  $\alpha$ -CD cavity but also the solubility of the intermediary PPRX in the reaction solvent.

Figure 1 shows the <sup>1</sup>H NMR spectra of **PCL-2**,  $\alpha$ -CD, **1**, and **PCL-PRX**. In the spectrum D, the signals originating from the  $\alpha$ -CD, PCL, and the skeleton of **1** along with the disappearance of the olefinic signals of **PCL-2** are in good accordance with the structure of **PCL-PRX**. The IR spectrum of **PCL-PRX** (Figure S7, Supporting Information) indicates the absence of the characteristic peak of a nitrile *N*-oxide around 2200 cm<sup>-1</sup>.<sup>8</sup>

Although the nuclear Overhauser enhancement spectroscopy (NOESY) NMR spectra of the polyrotaxanes measured under different temperature and solvent conditions showed no obvious nuclear Overhauser effect (NOE) correlation between the inner protons of CDs and the polyester axle, the results of the GPC using acetylated **PCL-PRX** having high solubility to



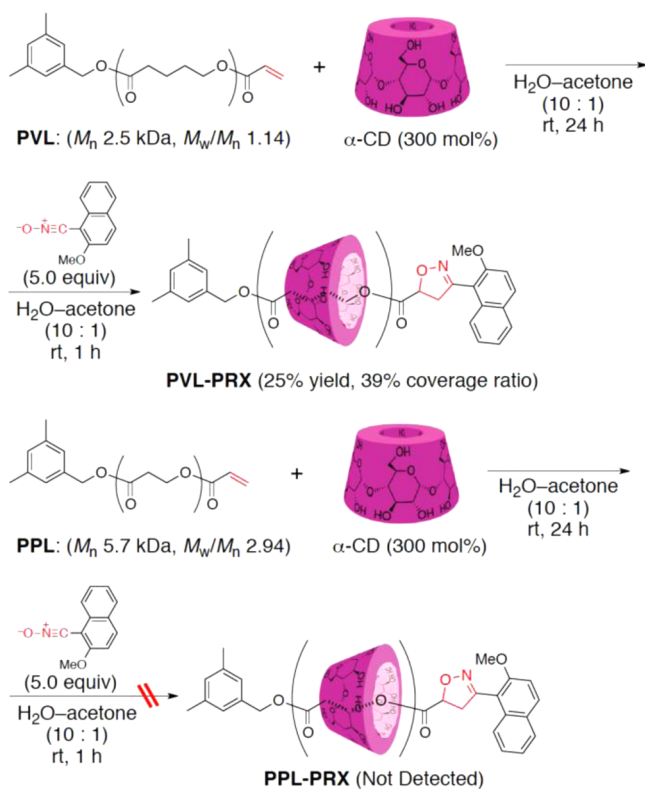
**Figure 1.** <sup>1</sup>H NMR Spectra of (A) **PCL-2**, (B)  $\alpha$ -CD, (C) **1**, and (D) **PCL-PRX** with 41% coverage ratio (400 MHz, DMSO-*d*<sub>6</sub>, 298 K).

organic solvents gave direct evidence for the structure of **PCL-PRX**. The GPC of the acetylated **PCL-PRX** had a much higher molecular weight peak than those of PCL or acetylated  $\alpha$ -CD (Figure S23, Supporting Information). The structure of a **PCL-PRX** was also confirmed by X-ray powder diffraction (WAXD).<sup>8</sup> The WAXD patterns (Figures S24 and S25, Supporting Information) showed a main crystalline peak around  $2\theta = 20^\circ$ . Since this peak corresponds to the (210) reflection for the hexagonal  $\alpha$ -CD/polymer inclusion complexes with channel-type crystal structure,<sup>10</sup> the result strongly suggested a threading structure of a **PCL-PRX** into the CD cavities. These results clearly support the fact that the 1,3-dipolar cycloaddition reaction of **1** to the terminal olefin of PPRX underwent the complexation to form a **PCL-PRX** via the end-capping reaction.

The effect of the molecular weight of the axle polymer on the yield and coverage ratio was summarized in Table 1 (entries 2, 5, and 6). These data show that **PCL-3** with the highest molecular weight produced a higher yield of a **PCL-PRX** than both **PCL-1** and **PCL-2**. However, the coverage ratios were almost the same. The reasons for this are suggested as follows: (i) when the coverage of PPRX reached around 70%, the PPRX would precipitate as a stable solid from the deslippage and (ii) the threading reaction of PCL with a higher molecular weight would afford a considerable increase in the molecular weight of the resulting **PCL-PRX** because of the existence of excess CDs, which would exhibit a higher aggregation behavior, even if the PPRX has the same coverage ratio as that with PCL with a lower molecular weight.

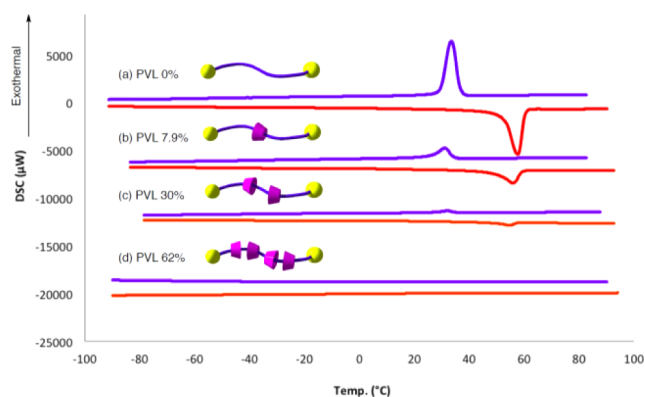
Variation of the polyester structure in the synthesis of PRXs was investigated using poly( $\delta$ -valerolactone) (**PVL-1**,  $M_n$  2.5 kDa,  $M_w/M_n$  1.14) and poly( $\beta$ -propiolactone) (**PPL-1**,  $M_n$  5.7 kDa,  $M_w/M_n$  2.94) using the same reaction conditions (Scheme 2). The threading reaction of **PVL-1** with  $\alpha$ -CD and end-capping reaction with **1** gave the corresponding **PVL-PRX** in 25% yield and 39% coverage ratio as 1.0 repeating unit of PVL per  $\alpha$ -CD estimated by Corey, Pauling, and later improved by Kultun (CPK) model studies. On the other hand, surprisingly, the use of PPL as the axle polymer does not produce **PPL-PRX**. Although the precise reason for this is not currently obvious, the explanation can be probably attributed to the steric and/or electronic factor of the carbonyl groups on the axle component

Scheme 2. Effect of Polymer Structure on Synthesis of PRX



in destabilizing the inclusion structure of the intermediary PPRX.

The thermal properties of some PRXs were evaluated by differential scanning calorimetry (DSC) to mainly determine the influence of the coverage ratio shown in Figure 2. PVL-



**Figure 2.** DSC profiles of PVL-PRXs with various coverage ratios: (a) 0%, (b) 7.9%, (c) 30%, and (d) 62% (scan rate 10 °C/min).

PRXs with different coverage ratios (7.9%, 30%, and 62%) were successfully prepared<sup>8</sup> using PVL-2 ( $M_n$  23 kDa,  $M_w/M_n$  1.15) in a H<sub>2</sub>O-acetone-DMF mixed solvent by procedures described by Yui et al.<sup>11</sup> As the coverage ratio of PVL-PRX increased from 0% to 30% (Table 2, entries 1–3), the melting point ( $T_m$ ) originating from the PVL skeleton decreased most probably because of the CD-based molar depression of  $T_m$ . PVL-PRX with a 62% coverage ratio exhibited no  $T_m$  (entry 4). Notably, it is found that the enthalpy of fusion ( $\Delta H$ ) dramatically decreased with the increase in the coverage ratio. To further strengthen the DSC results, the thermal property of

**Table 2.** Effect of Coverage Ratio of PVL-PRX on Thermal Properties<sup>a</sup>

entry	coverage ratio/% <sup>b</sup>	$T_m$ /°C <sup>c</sup>	$\Delta H_m$ /mJ·mg <sup>-1c</sup>
1	0	57.5–57.7	30.3 ± 0.80
2	7.9	55.8–56.0	9.09 ± 0.13
3	30	54.6–54.7	2.71 ± 0.05
4	62	– <sup>d</sup>	– <sup>d</sup>

<sup>a</sup>Preparation of PVL-PRXs was performed using PVL-2 ( $M_n$  23 kDa,  $M_w/M_n$  1.15),  $\alpha$ -CD (300 mol % per repeating unit of PVL), and nitrile *N*-oxide **1** (5.0 equiv) in H<sub>2</sub>O-acetone-DMF. <sup>b</sup>Coverage ratio (%) was calculated from the ratio of the NMR integrals of the wheel and axle components as a means of the coverage ratio of the polymers by assuming that the 100% complexation ratio is 1.0 PVL per  $\alpha$ -CD. <sup>c</sup>Measured by DSC (heating rate of 10 °C min<sup>-1</sup> under nitrogen atmosphere). <sup>d</sup>Not observed.

a mixture of PVL and  $\alpha$ -CD was evaluated by DSC (Scheme S26, Supporting Information). As a result,  $\Delta H$  of the mixture was the same as that of PVL but different from those of the polyrotaxanes or molecularly mixed systems. Such results indicate that the dynamic coverage of the polyester with  $\alpha$ -CDs efficiently suppresses the crystallization of the polyester main chain, providing a new method to effectively change the thermal properties of a polyester based on the introduction of a through-space linkage.

In conclusion, we demonstrate the use of a stable nitrile *N*-oxide **1** as a catalyst-free click-end-capping agent in the effective synthesis of polyester-based PRXs,<sup>12</sup> which features both catalyst- and byproduct-free reaction in contrast to Cu-catalyzed click chemistry.<sup>13</sup> The effect of polyester structure on PRX synthesis and the unique thermal properties of the PRX, dependent on the coverage ratio, were elucidated. Further studies directed toward the synthesis of new types of PRXs that consist of other axle polymers such as vinyl or condensation polymers are currently underway.

## ■ ASSOCIATED CONTENT

### Supporting Information

Experimental section, <sup>1</sup>H NMR and IR spectra, DSC, TGA, and SEC profiles for all compounds tested. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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### Notes

The authors declare no competing financial interest.

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