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Directed one-pot syntheses of crown ether wheel-containing main chain-type polyrotaxanes with controlled rotaxanation ratios†

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The directed synthesis of main chain-type polyrotaxanes possessing crown ether wheels was successfully achieved through two methods, A and B. Method A involved the direct wheel threading of poly(sec-ammonium salt) followed by end-capping with a bulky group, while method B utilized polyaddition of a pseudo[2]rotaxane monomer to facilitate the control of the structure, *i.e.* the rotaxanation ratio.

The first synthesis of a polypseudorotaxane (PPRX) from cyclodextrin (CD) and a linear polymer by Ogata¹ and its end-capping to give a polyrotaxane (CD-PRX) by Harada² heralded significant progress in the science of main chain-type CD-PRX, opening the door to various applications³ such as cross-linked gels.⁴ Efficient syntheses of CD-PRX have now led to its actual use.⁵ However, little is known about PRXs having other wheel components,^{6,7} in particular crown ether (CE) wheels, despite Gibson's pioneering work on PRXs.⁸ Therefore, the synthesis of PRX (not poly[2]rotaxane⁹) with a sufficiently high or controlled CE content and effective end-cap groups is an important challenge in this area.^{8a,10} CE-ammonium-salt-type rotaxane chemistry has enabled the synthesis of end-capped [5]^{sd} and [20]rotaxanes;^{6a,b} however, both rotaxanes exhibit low solubility because of their oligoionic structures. Since CE-ammonium interaction-driven self-assembly often achieves accurate supramolecular systems, the greater ease with which functional groups can be introduced into CE as compared to CD, as has been proven in rotaxane chemistry,¹¹ strongly indicates the potential utility of CE-based main chain-type PRX (CE-PRX), and hence, its synthesis becomes of paramount importance. We have long studied the development of an effective synthetic method for CE-PRX with a controlled structure, and have found effective synthetic methods.¹² A recent Grubbs' simple approach to CE-PRX *via* the polymerization of a CE-based pseudo[2]rotaxane monomer,¹³ has prompted us to report our results on the successful

synthesis of CE-PRX with controlled structures. We report herein the directed one-pot synthesis of CE-PRXs by two reliable synthetic protocols to yield structure-definite PRXs with controlled number of wheel components and effective end-cap groups (Fig. 1), building on our recent results on the synthesis of dibenzo-24-crown-8-ether (DB24C8)-containing PRXs.¹⁴ We also describe the simple modification to nonionic PRX that enables size-exclusion-chromatographic (SEC) measurements.

Fig. 1 shows the two strategies for the synthesis of CE-PRXs. Method A consists of the initial wheel threading of poly(sec-ammonium salt) and subsequent end-cap with a bulky agent. In the method B, copolymerization of pseudo[2]rotaxane monomer and appropriate comonomer to CE-PRX by the successive end-cap to facilitate the control of the structure, *i.e.* the rotaxanation ratio.

Method A: direct wheel threading of poly(sec-ammonium salt) followed by end-capping. We started with this synthetic protocol because rotaxane synthesis by this route is usually known to proceed efficiently in one-pot,¹⁵ and it seems to be suitable for giving high-molecular-weight PRX. Although poly(sec-ammonium salt)

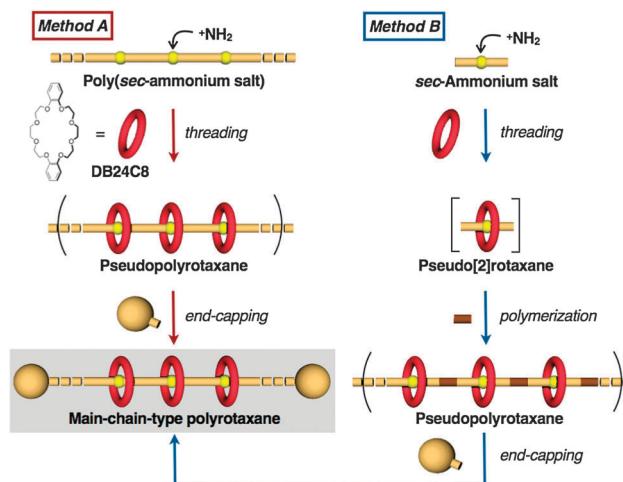


Fig. 1 Two independent strategies for preparing CE-based main chain-type PRXs *via* one-pot reaction.

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and the corresponding CE-PRX seemed insoluble in ordinary organic solvents because of their polyionic structures, we expected to observe CE-PRX formation because the oligorotaxane is more soluble than its axle polymer precursor oligo(*sec*-ammonium salt).^{6a,b} We chose poly(hexamethyleneammonium PF₆) (PHMAP) as the axle polymer because the hexamethylene spacer distance between the ammonium groups is appropriate for a high-yield synthesis of [3]rotaxane.^{6e} PHMAP was obtained by the reduction of 6,6-nylon with BH₃-THF complex¹⁶ followed by treatment with NH₄PF₆. PHMAP was relatively insoluble in organic solvents and the corresponding PPRX was obtained in only a minimal yield with DB24C8 in a CHCl₃-CH₃CN mixed solvent system. To address this problem, benzyl ammonium salt moieties were introduced at both PHMAP termini to enhance complexation capability.^{15,17} 4-Hydroxymethyl-benzyl-terminated PHMAP **1** was prepared by condensation of amine-terminated 6,6-nylon and methyl 4-formylbenzoate followed by reduction and subsequent treatment with NH₄PF₆. The molecular weight of **1** was calculated by ¹H NMR to be $M_n = 3200$. One-pot synthesis of **PRX 3** *via* intermediate **PPRX 2** was carried out as follows (Scheme 1): a heterogeneous mixture of **1** and DB24C8 was allowed to stand and then 3,5-dimethylphenylisocyanate and a catalytic amount of dibutyltindilaurate (DBTDL) in solvent at room temperature was added to it¹⁵ (Table 1). The structure of **PRX 3** was confirmed by spectroscopic analyses.

The reactions proceeded under heterogeneous conditions even with polar solvents such as CH₃CN and CH₃NO₂ (Table 1). For **PRX 3**, the yield increased to 76% with increasing solvent polarity and hence the solubility of **PPRX 2** during the end-capping process. For **1**, the rotaxanation ratio (RR) of the NH₂ group was sufficiently high (>92%) without solvent dependency. These results suggest the following important reaction features: (i) the formation of **PPRX 2** is accelerated by introducing a more strongly interactive unit (benzyl group) with CE at the axle termini;¹⁸ (ii) complexation between **1** and CE proceeds under heterogeneous conditions; and (iii) the CE wheel can

Table 1 Synthesis of **PRX 3** by method A

Entry	Solvent	Yield of PRX 3 ^a (%)	RR ^b (%)
1	CHCl ₃	33	90
2	ClCH ₂ CH ₂ Cl	58	98
3	CH ₃ CN	68	92
4	CH ₃ NO ₂	76	98

^a Calculated on the basis of **1**. ^b Rotaxanation ratio determined by ¹H NMR (range of error $\pm 2\%$).

enter into the center of the axle polymer chain. For **PRX 3**, neutralization by N-acetylation,¹⁹ which is required for estimating M_n , was incomplete, presumably because CE is densely packed because of its short CE-CE distance.^{6c} To address this issue, we turned to method B.

Method B: step polymerization of a reactive pseudo[2]rotaxane monomer followed by end-capping. We designed this synthetic protocol because of the reported efficiency of end-capping pseudo[2]rotaxane to give [2]rotaxane¹⁵ in addition to the high solubility of the monomer.^{6e,20}

We chose a dibenzylammonium-type axle **4**¹⁷ because of the enhanced stability of the corresponding pseudorotaxane monomer. One-pot synthesis of **PRX 6** was carried out as follows (Scheme 2): a mixture of pseudo[2]rotaxane (derived *in situ* from **4** and DB24C8) and diphenylmethane diisocyanate was treated with DBTDL in CH₂Cl₂. The resulting **PPRX 5** was treated successively with 3,5-dimethylphenylisocyanate and 3,5-dimethylphenol to give **PRX 6** selectively in high yield. The RR value and M_n were determined by ¹H NMR (Table 2).

Inspection of Table 2 reveals that method B is versatile and gives the desired CE-based PRXs in high yield. The RR values were controllable by the DB24C8 feed ratio; for example, 0.5–2.0 equiv. of DB24C8 yielded **PRX 6** with RR values in the range 55–95%. The end-capped structure of **PRX 6** was confirmed by a decomposition study of **PRX 6** in DMSO-*d*₆, which indicated that no DB24C8 was liberated from **PRX 6** at ambient temperature.²¹ The structure of **PRX 6** was determined using NMR, IR, and SEC. The ¹H NMR spectra clearly indicate the

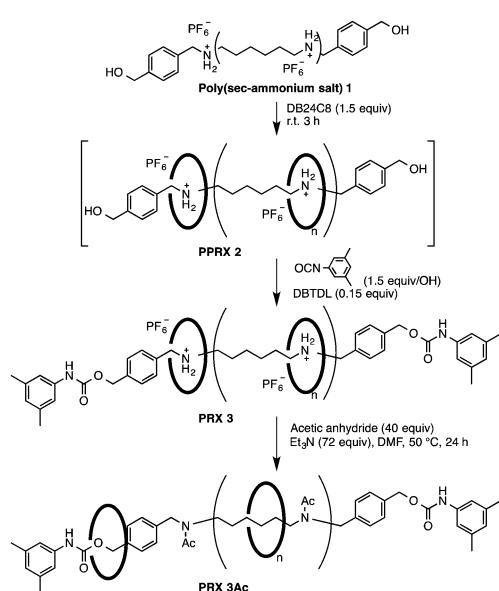
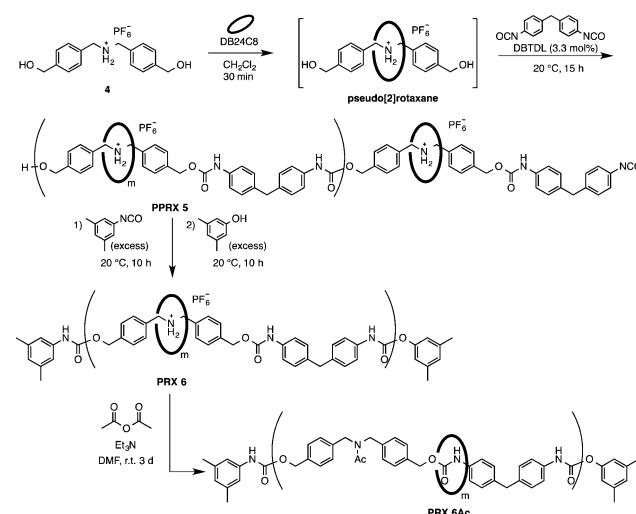
Scheme 1 Synthesis of **PRX 3** and **PRX 3Ac** ($0 \leq n \leq 1$).Scheme 2 Synthesis of **PRX 6** and **PRX 6Ac** ($0 \leq m \leq 1$).

Table 2 Controlled synthesis of **PRX 6** by method B^a

Entry	DB24C8/NH ₂ (equiv.)	Yield ^b (%)	RR ^c (%)	PRX 6 (NMR)		PRX 6Ac^d (SEC)		
				<i>M_n</i> / 10 ⁴ /Da	<i>M_n</i> / 10 ⁴ /Da	<i>M_w</i> / 10 ⁴ /Da	PDI	
1	2.0	93	95	2.6	2.8	6.0	3.6	
2	1.0	84	90	2.5	4.2	9.3	2.2	
3	0.5	84	55	1.4	3.3	7.4	2.2	

^a **4** = 0.5 M. ^b Calculated on the basis of **4**. ^c Determined by ¹H NMR (range of error $\pm 2\%$). ^d Estimated by SEC (DMF, PST) after N-acetylation.

involvement of the rotaxane structure, with DB24C8 localized at the ammonium moieties (Fig. 2). All signals are reasonably assignable; the two signals around 4.6 (A) and 4.8 (a) ppm indicate uncomplexed and complexed *N*-benzyl protons, respectively, whose ratio corresponds to the RR value.

To remove the polyionic nature from **PRX 6**, we subjected **PRX 6** to N-acetylation with acetic anhydride and triethylamine.¹⁹ The acetylation reaction proceeded very efficiently to yield **PRX 6Ac** (93% yield, Table 2, entry 1). Table 2 shows the SEC results of **PRX 6Ac**s with different rotaxanation ratios (RR). All **PRX 6Ac**s gave unimodal SEC profiles to support the occurrence of complete N-acetylation of the ammonium moieties of **PRX 6s**, agreeing with other spectral data.²² The ¹H NMR spectrum of **PRX 6Ac**s suggested two sets of signals assignable to the protons around the urethane moiety, although the axle component is symmetric. Thus, the conversion of the ammonium moiety caused the positional change of the crown ether wheel from the ammonium moiety to the urethane moiety probably due to the hydrogen bonding interaction as same as the model [2]rotaxane **S9**.²² This is the first synthesis of a nonionic DB24C8-based main chain-type polyrotaxane. The solubility of the **PRXs** in typical organic solvents was investigated. **PRX 3** was soluble in some polar solvents such as DMF and CH₃CN, whereas **PRX 6** and **PRX 6Ac** showed the higher solubility to various solvents including acetone, as we expected.²²

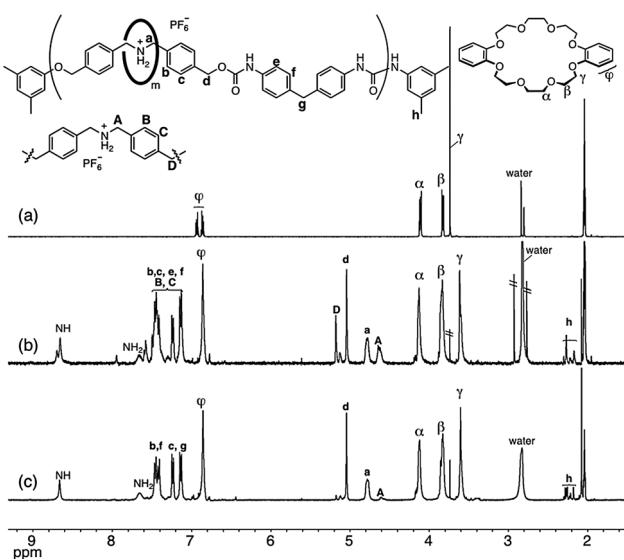


Fig. 2 Partial ¹H NMR spectra of (a) DB24C8, (b) **PRX 6** (RR = 55%), and (c) **PRX 6** (RR = 95%) (400 MHz, (CD₃)₂CO).

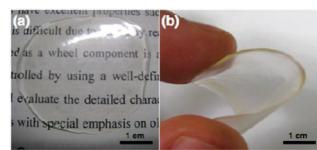


Fig. 3 Photographs of a transparent thin film of **PRX 6** (RR = 95%) prepared by casting from the acetone solution.

In addition, the high molecular weight of **PRX 6** was confirmed by its good film-forming property, which resulted in the formation of flexible transparent films by casting from the acetone solutions (Fig. 3).²²

In conclusion, we have successfully accomplished the directed one-pot synthesis of a challenging target polymer in the PRX family: CE-based main chain-type PRXs. We showed that CE-PRXs are unusually soluble in typical organic solvents such as DMF, despite their polyionic structures. Method B, involving step polymerization of pseudo[2]rotaxane monomers, enables the controlled synthesis of PRXs possessing the desired rotaxanation ratios (RR values). Complete neutralization by the N-acetylation of the ammonium moieties that promotes the CE translation on the axle²³ proceeded remarkably well. A variety of modifications of CEs established so far enable versatile functionalization of PRXs. Thus, the present study heralds continuing rapid progress in the synthesis and application of CE-PRXs.

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