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]10 and [20]rotaxanes;6a,9 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)
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(4-aminophenyethyl ammonium salt). We chose poly(hexamethyleneammonium PF$_6$)$_2$ (PHMAP) as the axle polymer because the hexamethylene spacer distance between the ammonium groups is appropriate for a high-yield synthesis of [3]rotaxane. PHMAP was obtained by the reduction of 6,6-nylon with BH$_3$–THF complex followed by treatment with NH$_4$PF$_6$. PHMAP was relatively insoluble in organic solvents and the corresponding PPRX was obtained in only a minimal yield with DB24C$_8$ in a CHCl$_3$–CH$_3$CN mixed solvent system. To address this problem, benzyl ammonium salt moieties were introduced at both PHMAP termini to enhance complexation capability. 4-Hydroxymethyl-benzyl-terminated PHMAP was prepared by condensation of amine-terminated 6,6-nylon and methyl 4-formylbenzoate followed by reduction and subsequent treatment with NH$_4$PF$_6$. The molecular weight of 1 was calculated by $^1$HNMR 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 DB24C$_8$ was allowed to stand and then 3,5-dimethylphenylisocyanate and 3,5-dimethylphenol to give the corresponding CE-PRXs in high yield. The RR value and $M_n$ were determined by $^1$HNMR (range of error ±2%).

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]rotaxane in addition to the high solubility of the monomer. We chose a dibenzylammonium-type axle 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 DB24C$_8$) and diphenylmethane diisocyanate was treated with DBTDL in CH$_2$Cl$_2$. 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 $^1$HNMR.

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 DB24C$_8$ feed ratio; for example, 0.5–2.0 equiv. of DB24C$_8$ 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 DB24C$_8$ was liberated from PRX 6 at ambient temperature. The structure of PRX 6 was determined using NMR, IR, and SEC. The $^1$HNMR spectra clearly indicate the

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

| Entry | Solvent | Yield of PRX 3 (%) | RR (%) |
|-------|---------|-------------------|--------|
| 1     | CHCl$_3$| 33                | 90     |
| 2     | CICH$_2$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. Rotaxanation ratio determined by $^1$HNMR (range of error ±2%).

**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

| Entry | DB24C8/NH₂ (equiv.) | Yield | RR (%) | Mₐ / 10³/Da | Mₕ / 10⁴/Da | Mₙ / 10⁴/Da | PDI |
|-------|----------------------|-------|---------|-------------|-------------|-------------|-----|
| 1     | 2.0                  | 93    | 95      | 2.6         | 2.8         | 6.0         | 3.6 |
| 2     | 1.0                  | 94    | 90      | 2.5         | 4.2         | 9.3         | 2.2 |
| 3     | 0.5                  | 85    | 55      | 1.4         | 3.3         | 7.4         | 2.2 |

* 4 = 0.5 M. * Calculated on the basis of 4. * Determined by 1H NMR (range of error ±2%). * Estimated by SEC (DMF, PSt) after N-acetylation.

The 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. The acetylation reaction proceeded very efficiently to yield PRX 6Ac (93% yield, Table 2, entry 1). Table 2 shows the SEC results of PRX 6AcS with different rotaxanation ratios (RR). All PRX 6AcS gave unimodal SEC profiles to support the occurrence of complete N-acetylation of the ammonium moieties of PRX 6s, agreeing with other spectral data. The 1H NMR spectrum of PRX 6AcS 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. 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 CH₂CN, whereas PRX 6 and PRX 6Ac showed the higher solubility to various solvents including acetone, as we expected.²²

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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