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Letter

Synthesis of Rotaxanes with Functional Groups

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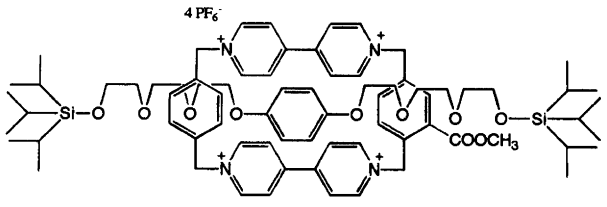
During the past 15 years, several efficient synthetic methods for catenanes and rotaxanes have been developed[1] in which supramolecular interactions are used for pre-organization of the reacting components. By utilizing this synthetic strategy of topologically unique structures, several new methods, including mimicking of a photosynthesis center[2] and construction of molecular shuttles[3,4] or nanotubes,[5] have been reported. Considering the interlocked structure (catenane) and rotaxane-like structure as new types of bonding, one important topic in this field is now the introduction of these units to the main chains of polymers. Schematical structures of polymers that can be synthesized by polycondensation of bifunctional catenanes or rotaxanes are shown in Scheme 1. Since non-chemical bondings exist in these polymer main chains, these kinds of polymers are attracting interest from the view point of their rheological and mechanical properties. Poly[2]-catenanes have already been synthesized by Weidmann *et al.*[6] and ourselves[7] independently.

Scheme 1. Schematical structures of poly[2]-catenanes (top) and poly[2]-rotaxanes (bottom).



2

Scheme 2. Structure of monofunctional rotaxane **2**.

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We now report the synthesis of a rotaxane amino acid, where Fmoc-protected amino and methoxycarbonyl groups are substituted on axle and ring parts of rotaxane, respectively. By using this rotaxane as a monomer for polycondensation, not only a homopolymer but also polypeptides that contain rotaxane-like linkages at any desired position can be synthesized by the application of solid-phase peptide synthesis.[8]

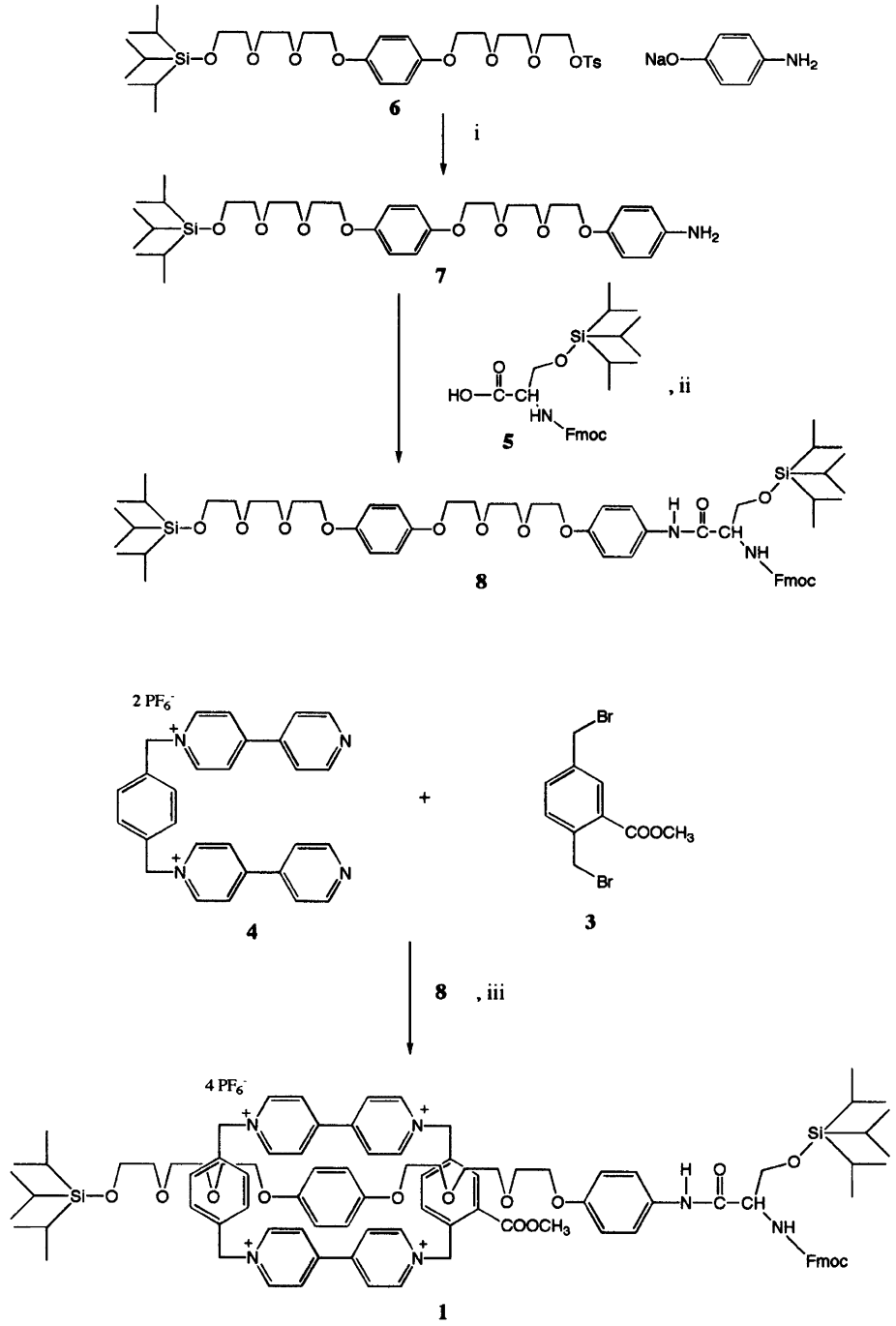
The structure of the target rotaxane **1** was designed on the basis of Stoddart's synthetic strategy for rotaxanes, in which a donor–acceptor interaction between dialkoxybenzene units and 4,4′-bipyridinium units is used for pre-organization of the reacting units.[9]

Before the synthesis of the bifunctional rotaxane, we first synthesized [2]-rotaxane (**2**) with one methoxycarbonyl group on the ring part, to obtain knowledge concerning the effect of the methoxycarbonyl group on the yield of rotaxane and the stability of the rotaxane structure under the conditions of hydrolysis of the carboxylate to free carboxylic acid.*

Cyclization of methyl 2,5-bis(bromomethyl)benzoate (**3**), synthesized by bromination of methyl 2,5-dimethylbenzoate with *N*-bromosuccinimide in CCl_4, and 1,1′-[1,4-phenylene bis(methylene)]-bis-4,4′-bipyridinium bis(hexafluorophosphate) (**4**) in the presence of 1,4-bis[2-[2-[2-[[tris(1-methylethyl) silyl]oxy]ethoxy]ethoxy]-benzene as an axle was carried out using the Stoddart's template method, and gave the corresponding rotaxane **2** with 5.4% yield.[9]

We attribute the relatively low yield of this cyclization reaction to steric hindrance of the methoxycarbonyl group of **3**. This rotaxane with methoxycarbonyl group

* Introduction of carboxylic acid or carboxylate groups into the ring part of rotaxanes of Stoddart's type has already been attemted by Benniston and Harriman.[10] They succeeded in the synthesis of ring parts with functional groups and observed the formation of pseudo-rotaxane with 1,4-dimethoxybenzene by absorption spectra.



Scheme 3. Reagents and conditions: (i) DMF, room temperature, 12 h, 76%; (ii) DCC, DMAP, CH_2Cl_2, 12 h, 41%; (iii) $AgPF_6$, CH_3CN, 7 d, 8.9%.

was deblocked without any destruction of the rotaxane structure to release free carboxylic acid by hydrolysis with LiOH in a mixture of nitromethane:methanol:water = 2:2:1.

Encouraged by the result that a rotaxane was produced by Stoddart's method even with a methoxycarbonyl group, the same method was applied but with a different axle for the synthesis of bifunctional rotaxane. The axle part of bifunctional rotaxane was synthesized in three steps. The hydroxyl group of *N*-Fmoc-l-serine was selectively protected with the triisopropylsilyl group by the reaction with triisopropylsilyl chloride in dry DMF containing imidazole. Aniline derivative **7** was synthesized by the reaction of tosylate **6** and sodium 4-aminophenoxide in DMF. *O*-Triisopropyl-*N*-Fmoc-serine (**5**) and **7** were condensed in dichloromethane containing DCC and DMAP to produce the axle part **8**.

As the final step, **3** and **4** were reacted in the presence

of **8** to produce the bifunctional rotaxane **1** as a dark red solid with 8.9% yield.* The higher yield of this protected bifunctional rotaxane than that of **2** is attributable to the participation of the second phenyl ring on the axle part as a donor to the charge transfer complex between the ring and axle parts.[3]

In summary, we have succeeded in the synthesis of monofunctional and bifunctional rotaxanes with moderate yields. Experiments introducing this newly synthesized bifunctional rotaxane unit into polymers are in progress.

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* All new compounds gave satisfactory analytical and spectral data. Selected data for **1**: M.p. 110 °C (decom.). ^{1}H NMR (CD_3COCD_3): δ 0.94–1.10 (42 H, m), 3.67–4.15 (28 H, m), 4.24–4.40 (3 H, m), 4.40–4.50 (2 H, m), 5.40 (1 H, br s), 6.05 (4 H, s), 6.17 (2 H, s), 6.57 (2 H, s), 7.33 (2 H, q), 7.44 (2 H, t), 7.40 (2 H, d), 7.89 (2 H, d), 8.07 (4 H, s), 8.25–8.31 (8 H, m), 8.61 (2 H, br s), 8.74 (1 H, br s), 9.09 (2 H, br s), 9.38–9.47 (8 H, m). FABMS: (*m/z*) 2100 ($M-PF_6^-$), 1954 ($M-2PF_6^-$), 1810 ($M-3PF_6^-$). For **2**: M.p. 288–289 °C. ^{1}H NMR (CD_3CN): δ 1.00–1.03 (42 H, m), 3.50 (4 H, br s), 3.59 (4 H, br s), 3.70–3.75 (4 H, m), 3.85–3.89 (8 H, m), 3.95 (4 H, br s), 4.10 (3 H, s), 5.71 (4 H, s), 5.78 (2 H, s), 6.13 (2 H, s), 7.77–7.85 (11 H, m), 7.96–8.06 (8 H, m), 8.42 (1 H, s), 8.91–9.43 (8 H, m). FABMS: (*m/z*) 1699 ($M-PF_6^-$), 1555 ($M-2PF_6^-$). For **3**: M.p. 78.0–79.5 °C. ^{1}H NMR ($CDCl_3$): δ 3.96 (3 H, s), 4.48 (2 H, s), 4.94 (2 H, s), 7.45 (1 H, d), 7.53 (1 H, q), 8.00 (1 H, d). For **5**: oil. ^{1}H NMR ($CDCl_3$): δ 1.06–1.08 (21 H, m), 2.15 (1 H, br), 3.94 (1 H, m), 4.26 (2 H, d), 4.39 (2 H, d), 4.45 (1 H, m), 5.69 (1 H, d), 7.32 (2 H, d), 7.40 (2 H, t), 7.60 (2 H, t), 7.77 (2 H, d). For **7**: oil. ^{1}H NMR ($CDCl_3$): δ 1.05–1.08 (21 H, m), 3.30 (2 H, br), 3.60 (2 H, t), 3.71 (4 H, s), 3.74 (4 H, s), 3.80–3.87 (8 H, m), 3.03–4.09 (6 H, m), 7.62 (2 H, d), 7.75 (2 H, d), 6.83 (4 H, s). For **8**: oil. ^{1}H NMR ($CDCl_3$): δ 1.01–1.10 (42 H, m), 3.60 (2 H, t), 3.71 (4 H, s), 3.76 (4 H, s), 3.79–3.88 (9 H, m), 4.05–4.14 (6 H, m), 4.20–4.23 (2 H, m), 4.28–4.43 (1 H, m), 4.43 (2 H, d), 5.85 (1 H, br), 6.84 (4 H, s), 6.89 (2 H, d), 7.30 (2 H, t), 7.39 (2 H, d), 7.40 (2 H, t), 7.61 (2 H, d), 7.77 (2 H, d), 8.38 (1 H, br).