Polymer Journal (2012) 44, 30–37

www.nature.com/pj

REVIEW

Polymer architectures assisted by dynamic covalent bonds: synthesis and properties of boronate-functionalized polyrotaxane and graft polyrotaxane

Yasuhito Koyama[1], Yudai Suzuki[1], Tomonori Asakawa[1], Nobuhiro Kihara[2], Kazuko Nakazono[1] and Toshikazu Takata[1]

Poly[2]rotaxane and graft polyrotaxane were synthesized from a mixture of poly(crown ether) (polyester-10 and polyisoxazole-13) as a trunk polymer, boronic-acid-terminated secondary ammonium salt 5 as an axle component, and diol as an end-capping group by pseudorotaxane formation and subsequent catalyst-free dehydrative bondage between the boronic acid and the diol moieties. Trunk polymers 10 and 13 were prepared by copolymerization of diol- or diyne-substituted dibenzo-24-crown-8-ether 9 or 11 and ditopic comonomers such as bifunctional acid dichloride and nitrile *N*-oxide. The use of the sufficiently bulky and stable homoditopic nitrile *N*-oxide 12 gave the high-molecular-weight isoxazole-containing poly(crown ether) 13 efficiently and without accidental penetration of the propagation end into the crown cavity, which would have caused gelation. The treatment of these poly(crown ether)s with boronic acid 5 in CH_2Cl_2 gave the corresponding polypseudorotaxanes, and subsequent graft-onto reaction with pinacol and a polymeric terminal diol gave poly[2]rotaxane and graft polyrotaxane. The chemical stability of these supramolecular architectures primarily depends on the bulkiness of the diol group as the end-capping moiety and the inherence originating from the dynamic covalent bond of boronate, as determined by detailed ^1H nuclear magnetic resonance study of model [2]rotaxanes 6–8 and the dissociation behavior of the polymers.
Polymer Journal (2012) **44,** 30–37; doi:10.1038/pj.2011.64; published online 27 July 2011

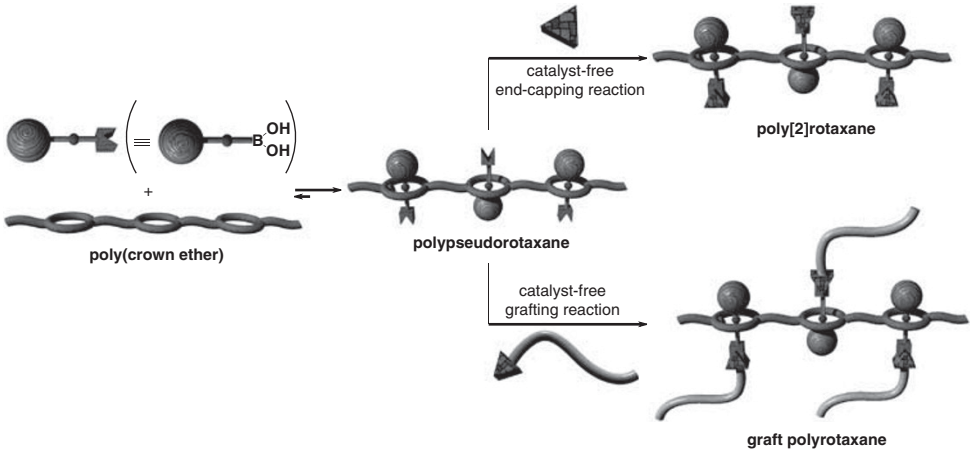
Keywords: polyrotaxane; dynamic covalent chemistry; boronic ester; stable homoditopic nitrile *N*-oxide; graft polyrotaxane

INTRODUCTION

Polyrotaxane, a new class of polymer, characterized by the mechanical linkage of its components exhibits unique physical, chemical, mechanical and rheological properties.[1–18] Most polyrotaxanes contain a cyclodextrine or crown ether as the wheel components. Crown-ether-based polyrotaxanes are easily identifiable by nuclear magnetic resonance (NMR) measurements and have a distinctive structure that provides a simple motif for the evaluation of characteristic properties of the mechanical linkage. However, construction of the interlocked framework generally requires specific conditions to avoid decomposition of the intermediary pseudorotaxane or half rotaxane. Among crown-ether-based main-chain-type polyrotaxanes,[19–23] those containing poly(crown ether) as the trunk polymer are particularly fascinating because of their unique structure. Notably, they are capable of conversion to 'graft polyrotaxanes' with interlocked graft chains, which are of interest because of their structure, dynamic behavior and physical properties.[24–27] Therefore, development of an efficient synthetic route to rotaxanes as the key framework is an important issue. The significance of dynamic covalent chemistry in rotaxane synthesis is clearly recognized.[28–31] We have reported the efficient synthesis of [2]- and [3]rotaxanes by reversible cleavage of aliphatic or aromatic disulfide linkages,[32,33] and have used this system to construct more complex materials such as poly[3]rotaxane[34] and polyrotaxane networks.[35,36] Although reversible cleavage of the disulfide bond is a powerful synthetic method for constructing rotaxane skeletons, its use is inherently limited to C_s-symmetric molecules. To overcome this limitation, we envisioned that reversible boronic ester formation between a boronate and a diol as an end-capping reaction of pseudorotaxanes should enable flexible conversion to highly sophisticated C_s-asymmetric rotaxanes, considering Tokunaga's rotaxane–boroxine chemistry.[37] In addition, since the end-capping reaction of pseudorotaxane absolutely requires mild conditions to avoid decomposition of the labile-complex structure, catalyst-free boronate formation as the end-capping reaction should be a reliable synthetic method for obtaining rotaxane architectures.

Herein, we describe the effective construction of polyrotaxane architectures by exploiting the dynamic covalent bond of boronate,

[1]Department of Organic and Polymeric Materials, Tokyo Institute of Technology, Tokyo, Japan and [2]Department of Chemistry, Faculty of Science, Kanagawa University, Hiratsuka, Japan
Correspondence: Professor T Takata, Department of Organic and Polymeric Materials, Tokyo Institute of Technology, 2-12-1 (H-126), Tokyo 152-8552, Japan.
E-mail: ttakata@polymer.titech.ac.jp
Received 24 March 2011; revised 13 May 2011; accepted 16 May 2011; published online 27 July 2011



Scheme 1 Strategy for synthesis of polyrotaxane architectures by exploiting the dynamic covalent bond of boronate.

with emphasis on the practical use of main-chain-type polyrotaxanes possessing rotaxane structures as the repeating unit (Scheme 1).

EXPERIMENTAL PROCEDURE

Materials

Axle component **1**,[38] boronic acid **3**,[39] bis(hydroxymethyl)dibenzo-24-crown-8-ether **9**,[40] poly(crown ether) **polyester-10**[19] and stable homoditopic nitrile *N*-oxide **12**[23] were prepared according to the literature. Other materials are available commercially and were used without further purification.

Measurements

^{1}H- and ^{13}C-NMR spectra were recorded on a JEOL AL-400 spectrometer (JEOL, Tokyo, Japan) using $CDCl_3$ as the solvent and tetramethylsilane as an internal standard. Molecular weights and distributions were estimated by size-exclusion chromatography (SEC) on a JASCO Gulliver system (JASCO, Tokyo, Japan) equipped with two consecutive linear polystyrene gel columns (Tosoh TSK-gel GMHXL and G5000HXL, Tosoh, Tokyo, Japan) at 30 °C (column flow rate 0.85 ml min^{-1}) according to polystyrene standards using $CHCl_3$ as the eluent. Glass transition temperatures (T_g) were measured with a Shimadzu DSC-60 instrument (Shimadzu, Kyoto, Japan) under nitrogen (heating rate 10 °C min^{-1}, nitrogen flow rate 50 ml min^{-1}). Thermogravimetric analyses were performed with a Shimadzu TGA-50 instrument (Shimadzu) under nitrogen (heating rate 10 °C min^{-1}, nitrogen flow rate 50 ml min^{-1}). Fourier-transform infrared spectra were recorded on a JASCO FT/IR-460 Plus spectrophotometer (JASCO). Melting points were measured with a Stuart Scientific SMP3. Matrix-assisted laser desorption/ionization–time-of-flight mass spectroscopy (MALDI–TOF MS) spectra were measured with a Shimazdu AXIMA-CFR mass spectrometer (Shimazdu) using a dithranol matrix. Fast atom bombardment high resolution mass (FAB-HRMS) spectra were recorded on a JEOL JMS-700 spectrometer (JEOL).

Synthesis of Boc-protected axle 2

To a solution of amine **1**[38] (1.5 g, 5.9 mmol) and Boc_2O (1.3 g, 15 mmol) in $CHCl_3$ (10 ml) was added a catalytic amount of 4-dimethylaminopyridine at room temperature. The mixture was stirred for 1 day and evaporated *in vacuo*. The residue was diluted with EtOAc, washed with 1 M aqueous HCl and brine, dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The obtained crude material was purified by column chromatography on silica gel (eluent: EtOAc:hexane=1:1) to give the corresponding Boc-protected axle **2** (1.5 g, 73%) as a yellow oil.

^{1}H NMR (400 Hz, $CDCl_3$, 298 K): 7.31 (d, *J*=7.8 Hz, 2H), 7.20 (d, *J*=7.8 Hz, 2H), 6.85 (s, 1H), 6.79 (s, 2H), 4.67 (s, 2H), 4.37 (s, 2H), 4.30 (s, 2H), 2.24 (s, 6H), 1.49 (s, 9H) p.p.m.; ^{13}C NMR (100 Hz, $CDCl_3$, 298 K): 156.2, 140.0 138.1, 134.9, 128.9, 128.2, 127.3, 125.9, 125.3, 80.2, 65.1, 49.0, 48.7, 28.5, 21.4 p.p.m.; infrared (IR, neat): υ 3426, 2974, 2920, 2868, 1693, 1412, 1365, 1243, 1164, 1119, 1038, 1017, 876, 843, 768 cm^{-1}; FAB-HRMS (matrix: NBA) $C_{22}H_{30}NO_3$ [M+H $^+$] calcd for 356.2226, found 356.2228.

Synthesis of boronic acid 4

To a mixture of axle **2** (0.36 g, 1.0 mmol) and *p*-carboxyphenylboronic acid **3**[39] (0.17 g, 1.0 mmol) in dimethylformamide (5.0 ml) was added 4-dimethylaminopyridine (60 mg, 0.50 mmol) at room temperature. 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (1.48 g, 8.0 mmol) was added gradually to the mixture over a period of 12 h. The reaction was stopped by addition of H_2O and the obtained products were extracted with CH_2Cl_2. The combined organic layer was washed with H_2O and brine, dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The obtained crude material was purified by column chromatography on silica gel (eluent: EtOAc:hexane=1:1) to give the corresponding boronic acid **4** (0.41 g, 81%) as a colorless oil.

^{1}H NMR (400 Hz, $CDCl_3$, 298 K): 8.28 (d, *J*=7.6 Hz, 2H), 8.20 (d, *J*=7.6 Hz, 2H), 7.44 (d, *J*=7.8 Hz, 2H), 7.40 (d, *J*=7.8 Hz, 2H), 6.89 (s, 1H), 6.80 (s, 2H), 5.40 (s, 2H), 4.40 (s, 2H), 4.32 (s, 2H), 2.20 (s, 6H), 1.51 (s, 9H) p.p.m.; ^{13}C NMR (100 Hz, $CDCl_3$, 298 K): 166.7, 156.2, 140.2, 138.1, 133.9, 128.8, 128.6, 128.5, 128.1, 127.5, 127.2, 125.8, 125.2, 80.2, 65.1, 49.0, 48.7, 28.5, 21.4 p.p.m.; IR (neat): υ 3431, 2978, 2923, 2249, 1677, 1459, 1412, 1366, 1245, 1167, 1119, 909, 733, 648 cm^{-1}; FAB-MS (matrix: NBA) $C_{29}H_{35}BNO_6$ [M+H$^+$] calcd for 504.26, found 504.23.

Synthesis of ammonium salt 5

To a solution of boronic acid **4** (80 mg, 0.16 mmol) in $CHCl_3$ (3.0 ml) CF_3COOH (0.37 ml, 4.8 mmol) was added at room temperature. The resulting mixture was stirred for 6 h and concentrated *in vacuo*. The obtained crude material was dissolved into MeOH; then, NH_4PF_6 (0.39 g, 2.4 mmol) was added at room temperature and the mixture was concentrated *in vacuo*. The obtained precipitate was collected by filtration to give the corresponding axle component **5** (78 mg, 90%) as a white solid.

^{1}H NMR (400 Hz, CD_3OD, 298 K): 8.01 (s, 1H), 7.99 (s, 1H), 7.57 (d, *J*=8.3 Hz, 2H), 7.50 (d, *J*=8.3 Hz, 2H), 7.08 (s, 4H), 5.40 (s, 2H), 4.22 (s, 2H), 4.14 (s, 2H), 2.33 (s, 6H) p.p.m.; ^{13}C NMR (100 Hz, CD_3OD, 298 K): 167.8, 140.2, 139.3, 137.3, 134.8, 132.3, 132.1, 131.3, 130.9, 129.8, 129.4, 128.6, 126.9, 67.9, 67.0, 52.1, 51.6, 21.2 p.p.m.; IR (neat): υ 3449, 3247, 2925, 2853, 1702, 1610, 1561, 1509, 1276, 1186, 1119, 1018, 845, 711, 559 cm^{-1}; MALDI–TOF MS (matrix: CHCα): $C_{24}H_{27}BNO_4$ [M–PF_6] calcd for 404.20, found 404.74.

Synthesis of pseudorotaxane 6

A suspension of axle **5** (99 mg, 0.18 mmol) and dibenzo-24-crown-8-ether (DB24C8, 81 mg, 0.18 mmol) in CH_2Cl_2 (0.90 ml) was sonicated at 0 °C for 60 min. The obtained clear solution was precipitated into an Et_2O–hexane mixture to give the corresponding pseudorotaxane **6** (0.16 g, 90%) as a white

solid. Compound **6** was used for the rotaxanation reaction without further purification.

^{1}H NMR (400 Hz, $CDCl_3$, 298 K): 8.01 (s, *J*=8.1 Hz, 2H), 7.88 (d, *J*=8.1 Hz, 2H), 7.55 (brd, 2H), 7.34 (d, *J*=8.0 Hz, 2H), 7.25 (d, *J*=8.0 Hz, 2H), 6.87–6.84 (m, 7H), 6.80–6.76 (m, 4H), 5.26 (s, 2H), 4.66–4.63 (m, 2H), 4.50–4.46 (m, 2H), 4.09–4.08 (m, 8H), 3.78–3.71 (m, 12H), 3.50–3.46 (m, 4H), 2.14 (s, 6H) p.p.m.

Synthesis of boron 2,2-dimethyl-1,3-propanediolester-terminated rotaxane 7

A suspension of axle **5** (99 mg, 0.18 mmol) and DB24C8 (81 mg, 0.18 mmol) in CH_2Cl_2 (0.90 ml) was sonicated at 0 °C for 60 min. To the obtained clear solution 2,2-dimethylpropane-1,3-diol (0.90 ml, 0.18 mmol) was added at the same temperature. The mixture was warmed to room temperature, stirred for 3 h and concentrated *in vacuo*. The obtained white solid was diluted with CH_2Cl_2 and reprecipitated into Et_2O to give the corresponding rotaxane **7** (0.19 g, 90%) as a white solid.

Melting point: 97–100 °C; ^{1}H NMR (400 Hz, $CDCl_3$, 298 K): 8.02 (d, *J*=8.1 Hz, 2H), 7.87 (d, *J*=8.1 Hz, 2H), 7.55 (brd, 2H), 7.34 (d, *J*=8.0 Hz, 2H), 7.25 (d, *J*=8.0 Hz, 2H), 6.87–6.84 (m, 7H), 6.80–6.76 (m, 4H), 5.26 (s, 2H), 4.66–4.63 (m, 2H), 4.50–4.46 (m, 2H), 4.09–4.08 (m, 8H), 3.78–3.71 (m, 12H), 3.50–3.46 (m, 4H), 2.14 (s, 6H), 1.02 (s, 6H) p.p.m.; ^{13}C NMR (100 Hz, $CDCl_3$, 298 K): 166.6, 147.5, 138.5, 137.5, 134.0, 132.2, 131.7, 131.5, 130.8, 129.8, 128.7, 128.2, 126.7, 121.8, 112.8, 72.5, 70.8, 70.3, 68.3, 65.9, 52.8, 52.4, 32.0, 22.0, 21.3 p.p.m.; IR (neat): υ 2923, 1719, 1594, 1505, 1454, 1424, 1378, 1342, 1316, 1253, 1215, 1128, 1108, 1057, 1020, 954, 841, 747, 711 cm^{-1}; FAB-HR-MS (matrix: NBA) $C_{53}H_{67}BNO_{12}$ [M–PF_6] calcd for 920.4756, found 920.4757.

Synthesis of boron pinacolate-terminated rotaxane 8

A suspension of axle **5** (25 mg, 0.050 mmol) and DB24C8 (20 mg, 0.050 mmol) in CH_2Cl_2 (0.23 ml) was sonicated at 0 °C for 60 min. To the obtained clear solution pinacol (5.3 ml, 0.050 mmol) was added at the same temperature. The mixture was warmed to room temperature, stirred for 3 h and concentrated *in vacuo*. The obtained white solid was diluted with CH_2Cl_2 and reprecipitated into Et_2O to give the corresponding rotaxane **8** (51 mg, 94%) as a white solid.

Melting point: 164.0–166.0 °C; ^{1}H NMR (400 Hz, $CDCl_3$, 298 K): 8.03 (d, *J*=8.1 Hz, 2H), 7.88 (d, *J*=8.1 Hz, 2H), 7.55 (brd, 2H), 7.34 (d, *J*=8.0 Hz, 2H), 7.25 (d, *J*=8.0 Hz, 2H), 6.87–6.76 (m, 11H), 5.27 (s, 2H), 4.64–4.63 (m, 2H), 4.48–4.46 (m, 2H), 4.09–4.08 (m, 8H), 3.77–3.76 (m, 8H), 3.49–3.45 (m, 8H), 2.14 (s, 6H), 1.35 (s, 12H) p.p.m.; ^{13}C NMR (100 Hz, $CDCl_3$, 298 K): 166.3, 147.5, 138.5, 137.3, 134.8, 132.2, 131.7, 131.5, 130.8, 129.7, 128.7, 128.1, 126.7, 121.7, 112.7, 70.7, 70.2, 69.4, 68.2, 66.0, 52.7, 52.3, 25.0, 21.3 p.p.m.; IR (KBr): υ 3151, 3066, 2977, 2928, 2878, 1719, 1595, 1506, 1455, 1400, 1361, 1327, 1254, 1213, 1107, 1057, 1020, 955, 843, 743, 711, 652, 557 cm^{-1}; FAB-MS (matrix: NBA) $C_{54}H_{69}BNO_{12}$ [M–PF_6] calcd for 934.95, found 934.49.

Synthesis of diyne-functionalized crown ether 11

NaH (60 wt% in a mineral oil, 0.96 g, 20 mmol) was washed with hexane repeatedly to remove the oil before use. To the resulting NaH was added a solution of bis(hydroxymethyl)DB24C8 **9**[40] (1.0 g, 2.0 mmol) in dimethylformamide (20 ml) at 0 °C. The suspension was warmed to room temperature and stirred for 30 min. Propargyl bromide (0.29 g, 2.4 mmol) was added dropwise to the mixture and the resulting mixture was stirred overnight at room temperature. The reaction was stopped by addition of H_2O (ca 50 ml) and the products were extracted with $CHCl_3$. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The obtained crude product was purified by column chromatography on silica gel (eluent: EtOAc) to give the corresponding diyne-functionalized DB24C8 **11** (0.60 g, 55%) as a white solid.

^{1}H NMR (400 Hz, $CDCl_3$, 298 K): 6.87–6.79 (m, 6H), 4.49 (s, 2H), 4.21–4.10 (m, 12H), 3.80–3.70 (m, 16H), 2.45–2.44 (m, 2H) p.p.m.; IR (KBr): υ 3291, 3268, 3186, 2879, 2113, 1594, 1506, 1457, 1399, 1362, 1244, 1088, 985, 960, 908, 843, 742, 658, 557 cm^{-1}; MALDI–TOF MS (matrix: CHCα) $C_{32}H_{40}NaO_{10}$ [M+Na^+] calcd for 607.2519, found 607.2508.

Synthesis of isoxazole-containing poly(crown ether) 13

A mixture of diyne-functionalized DB24C8 **11** (0.17 g, 0.30 mmol) and stable homoditopic nitrile *N*-oxide **12**[23] (0.18 g, 0.30 mmol) in $CHCl_3$ (0.16 ml) was refluxed for 12 h and then poured into MeOH to precipitate the corresponding isoxazole-containing poly(crown ether) **13** (0.34 g, 95%) as a white solid.

M_w=33 700; M_w/M_n=1.7; T_g=97 °C; T_{d5}=320 °C; ^{1}H NMR (400 Hz, $CDCl_3$, 298 K): 7.19–7.15 (t, *J*=8.4 Hz, 1H), 7.00–6.80 (m, 8H), 6.73 (d, *J*=8.1 Hz, 2H), 6.57 (s, 2H), 6.07 (d, *J*=8.1 Hz, 2H), 4.63 (s, 4H), 4.55 (s, 4H), 4.16–4.14 (m, 8H), 3.71–3.65 (m, 22H), 2.06 (s, 12H), 1.64 (s, 6H) p.p.m.; IR (KBr): υ 2925, 2249, 1608, 1510, 1469, 1360, 1241, 1177, 1081, 948, 780, 733, 609 cm^{-1}.

Typical procedure for synthesis of poly[2]rotaxane: synthesis of poly[2]rotaxane 17

A suspension of poly(crown ether) **13** (19 mg, 0.016 mmol) and axle **5** (18 mg, 0.032 mmol) in CH_2Cl_2 (0.32 ml) was sonicated at room temperature for 30 min to give a clear solution of the corresponding polypseudorotaxane **15**. To the mixture pinacol (7.6 mg 0.064 mmol) was added at the same temperature. The resulting mixture was stirred for 5 min and precipitated into MeOH. The obtained white solid was collected by filtration and washed with MeOH and Et_2O to give the corresponding poly[2]rotaxane **17** (17 mg, 84%) with a 99% grafting ratio as a white solid.

No T_g appeared; T_{d5}=220 °C; ^{1}H NMR (400 Hz, $CDCl_3$, 298 K): 8.00 (d, *J*=7.1 Hz, 2H), 7.85 (d, *J*=7.1 Hz, 2H), 7.52–6.70 (m, 21H), 6.62 (d, *J*=7.8 Hz, 2H), 6.51 (s, 2H), 6.08 (d, *J*=7.8 Hz, 2H), 5.28–5.26 (m, 2H), 4.61–4.45 (m, 12H), 4.10–4.05 (m, 8H), 3.87–3.74 (m, 14H), 3.49–3.45 (m, 8H), 2.11–2.00 (m, 18H), 1.62 (s, 6H), 1.33 (s, 12H) p.p.m.; IR (KBr): υ 3430, 3145, 2925, 2882, 1720, 1687, 1609, 1515, 1469, 1399, 1361, 1268, 1178, 1110, 1020, 950, 842, 737, 712, 651, 558 cm^{-1}.

Poly[2]rotaxane 16

A white solid: No T_g appeared; T_{d5}=220 °C; ^{1}H NMR (400 Hz, $CDCl_3$, 298 K): 8.00 (d, *J*=7.3 Hz, 2H), 7.86 (d, *J*=7.3 Hz, 2H), 7.30 (d, *J*=7.6 Hz, 2H), 6.80–6.71 (m, 11H), 5.26 (s, 2H), 5.00 (s, 4H), 4.65 (s, 2H), 4.50 (s, 2H), 4.11–4.05 (m, 8H), 3.89–3.77 (m, 8H), 3.48–3.40 (m, 8H), 2.34 (s, 4H), 2.10 (s, 6H), 1.66 (s, 4H), 1.34 (s, 12H) p.p.m.; IR (KBr): υ 3447, 3147, 3067, 2932, 2872, 1733, 1610, 1594, 1517, 1459, 1430, 1402, 1361, 1322, 1268, 1173, 1108, 1057, 1020, 955, 841, 773, 731, 711, 650, 557 cm^{-1}.

Synthesis of diol-terminated poly(α-methylstyrene) 18

To a solution of α-methylstyrene (5.0 g, 0.042 mol) in THF (50 ml) BuLi (2.64 M in hexane, 1.60 ml, 4.23 mmol) was added at room temperature. The reaction mixture was cooled to −78 °C and stirred for 2 h. Allylbromide (366.1 µl, 4.23 mmol) was added to the mixture and the resulting mixture was stirred for 1 h, warmed to room temperature and precipitated into MeOH. The obtained white solid was collected by filtration to give the corresponding allyl-terminated poly(α-methylstyrene) (4.74 g, 95%, M_n=5600; M_w/M_n=1.2, estimated by SEC based on polystyrene standards) as a white solid. The polymer was used for the next reaction without further purification.

To a mixture of allyl-terminated poly(α-methylstyrene) (3.00 g, 0.536 mmol) and *N*-methylmorpholine *N*-oxide (314 mg, 2.68 mmol) in dioxane–H_2O (1:1) was added a solution of OsO_4 in *t*-BuOH (2.5 wt%, 703 µl, 0.1 mol%) at room temperature. The mixture was stirred for 18 h, quenched by addition of saturated aqueous $Na_2S_2O_3$ and diluted with $CHCl_3$. The layers were separated and the organic layer was washed with 3 M aqueous HCl, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was reprecipitated into MeOH to give the corresponding diol-terminated poly(α-methylstyrene) **18** (2.6 g, 85%) with a 99% conversion ratio.

M_n=2200; M_w/M_n=1.4, estimated by SEC based on polystyrene standards; T_g=127 °C; T_{d5}=300 °C; ^{1}H NMR (400 Hz, $CDCl_3$, 298 K): 7.25–6.66 (m, ArH), 3.50–3.01 (m, protons of diol terminus), 2.05–0.01 (m, aliphatic protons) p.p.m.; IR (KBr): υ 3570, 3450, 3087, 3055, 3020, 2929, 1600, 1580, 1496, 1444, 1382, 1283, 1236, 1193, 1157, 1093, 1030, 949, 840, 758, 700, 549 cm^{-1}.

Typical procedure for synthesis of graft polyrotaxane 19

A suspension of poly(crown ether) **10** (20 mg, 0.032 mmol) and axle **5** (3.6 mg, 0.006 mmol) in CH_2Cl_2 (1 ml) was sonicated at room temperature for 15 min. To the obtained clear solution diol-terminated poly(α-methylstyrene) **18** (200 mg 0.032 mmol) was added at the same temperature. The resulting mixture was stirred for 15 min and precipitated into Et_2O. The obtained white solid was collected by filtration and washed with Et_2O to give the corresponding poly[2]rotaxane **19** (43 mg, 73%) as a white solid with a 99% grafting ratio.

No T_g appeared; T_{d5}=230 °C; ^{1}H NMR (400 Hz, $CDCl_3$, 298 K): 7.98–6.69 (m, ArH), 5.28 (brd), 4.97 (brd), 4.61–4.59 (m, *N*-benzyl protons), 4.13–4.07 (m, crown ether), 3.82–3.75 (m, crown ether), 3.49–3.35 (m, crown ether), 2.36–0.00 (m, aliphatic protons) p.p.m.; IR (KBr): υ 3450, 3161, 3087, 3056, 3023, 2929, 1732, 1686, 1599, 1516, 1496, 1445, 1381, 1269, 1178, 1126, 1057, 955, 843, 762, 699, 558 cm^{-1}.

RESULTS AND DISCUSSION

Synthesis and evaluation of chemical stability of model [2]rotaxanes

Scheme 2 shows the preparation of the axle component **5** carrying a boronic acid moiety. *sec*-Amine **1** with 3,5-dimethylphenyl group as a bulky end group was prepared as a starting material as described in the literature.[38] Temporary protection of **1** with Boc_2O and subsequent esterification with 4-carboxyphenylboronic acid **3** gave boronic acid **4**. Successive deprotection of the Boc group with trifluoroacetic acid and counter-anion exchange with NH_4PF_6 afforded boronic-acid-moiety-containing axle component **5** in a high overall yield.

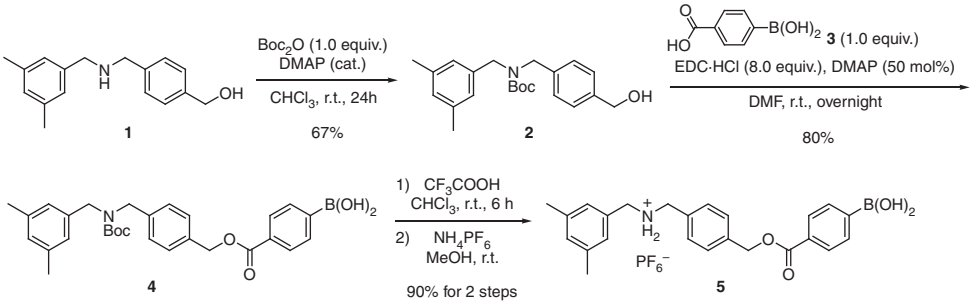
Before synthesizing the polyrotaxane architectures, we examined the synthetic protocol for [2]rotaxane that exploits the dynamic covalent bond of boronic ester to evaluate the chemical stability of the resulting compounds. In our previous investigation of several reaction conditions for pseudorotaxane formation,[38] we discovered that problems caused by low solubility of the axle component **5** led to unfruitful results. After considerable effort, we found that sonication of a suspension of dibenzo-24-crown-8-ether (DB24C8) and **5** in CH_2Cl_2 for 30 min at room temperature efficiently afforded a clear solution, leading to the formation of pseudorotaxane **6** (Scheme 3), as confirmed by ^{1}H NMR. The subsequent treatment of **6** with diols without any catalyst rapidly gave the corresponding rotaxanes **7** and **8** in high yields by the formation of a boronate that is sufficiently bulky to prevent the dissociation of the DB24C8 wheel.

We investigated the stability of pseudorotaxane and rotaxanes **6–8** in DMSO-d_6, a polar solvent capable of disturbing hydrogen bonds. The results are listed in Table 1. Compound **6** decomposes promptly (entry 1), **7** dissociated slowly (entry 2) and **8** dissociates at a rate too slow to measure (entry 3). The boronate moiety of **7** behaves as an end-capping group whose size is complementary to the DB24C8 cavity,[41–44] whereas the boronate moiety of **8** is sufficiently enough

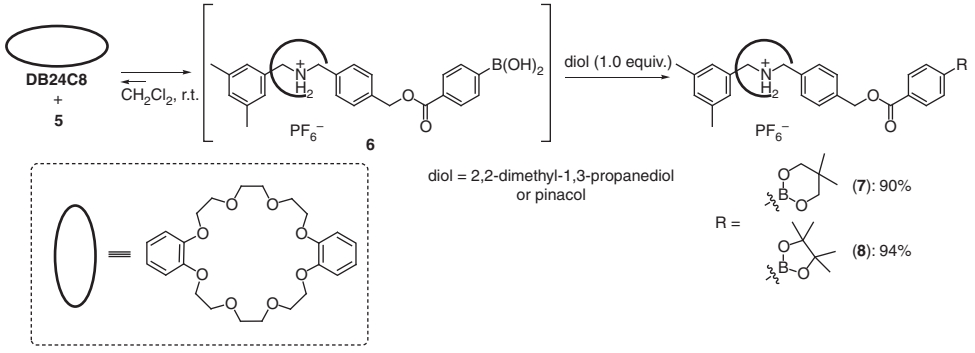
Table 1 Dissociation ratio of rotaxanes under solvation and neutralization conditions[a]

				Deslipping ratio (%)[b]	
Entry	*Rotaxane*	*Solvent*	*Additive*	*r.t.*[c]	*110 °C*
1	**6**	DMSO-d_6	–	100	ND[d]
2	**7**	DMSO-d_6	–	10 (100[e])	100
3	**8**	DMSO-d_6	–	0	0
4	**7**	DMSO-d_6	Et_3N[f]	100	ND[d]
5	**8**	DMSO-d_6	Et_3N[f]	9 (100[e])	ND[d]

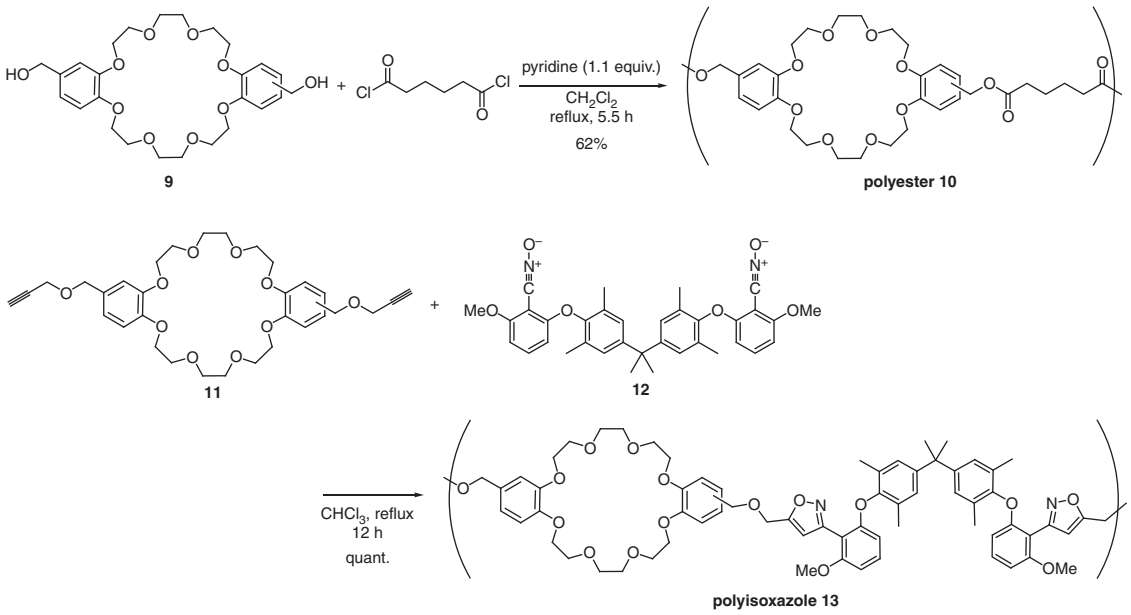
Abbreviations: DMSO, dimethyl sulfoxide; ND, not determined; r.t., room temperature.
[a]Reaction was carried out using rotaxane (0.05 mmol) in DMSO-d_6 (0.6 ml).
[b]As determined by ^{1}H nuclear magnetic resonance analysis.
[c]Measured 5 min after the dissolution of rotaxane in DMSO-d_6.
[d]Dissociation was too rapid to observe the intermediate.
[e]After 1 day.
[f]3.0 equiv.



Scheme 2 Synthesis of axle component **5**.



Scheme 3 Synthesis of model [2]rotaxane.



Scheme 4 Synthesis of poly(crown ether)s.

to prevent dissociation. On the other hand, the addition of triethylamine (Et_3N) prompted the dissociation of **7** and **8** in comparison with the Et_3N-free conditions (entries 4 and 5), probably due to not only a neutralization of the *sec*-ammonium moiety that disturbs the interaction between DB24C8 and axle component but also a dissociation of the dynamic covalent bond of boronate by humidity in the system.

Synthesis of poly(crown ether)s

On the basis of these results, we approached the synthesis of poly[2]-rotaxane by typical end-capping protocol using a main-chain-type poly(crown ether), axle **5**, and pinacol. Scheme 4 shows two synthetic routes where poly(crown ether) is the trunk polymer. We previously reported the synthesis of several poly(crown ether)s, where high temperatures and prolonged reaction times during polymerization gave only the crosslinked polymers because of accidental penetration of the propagation end into the crown ether cavity (see Delaviz and Gibson[45] for a selected report). Therefore, poly(crown ether) (**polyester-10**) was carefully prepared from bis(hydroxymethylbenzo)-24-crown-8-ether **9** and adipoyl chloride under mild conditions to give polyester **10** with a moderate molecular weight (M_w=12 000, M_w/M_n=1.2).

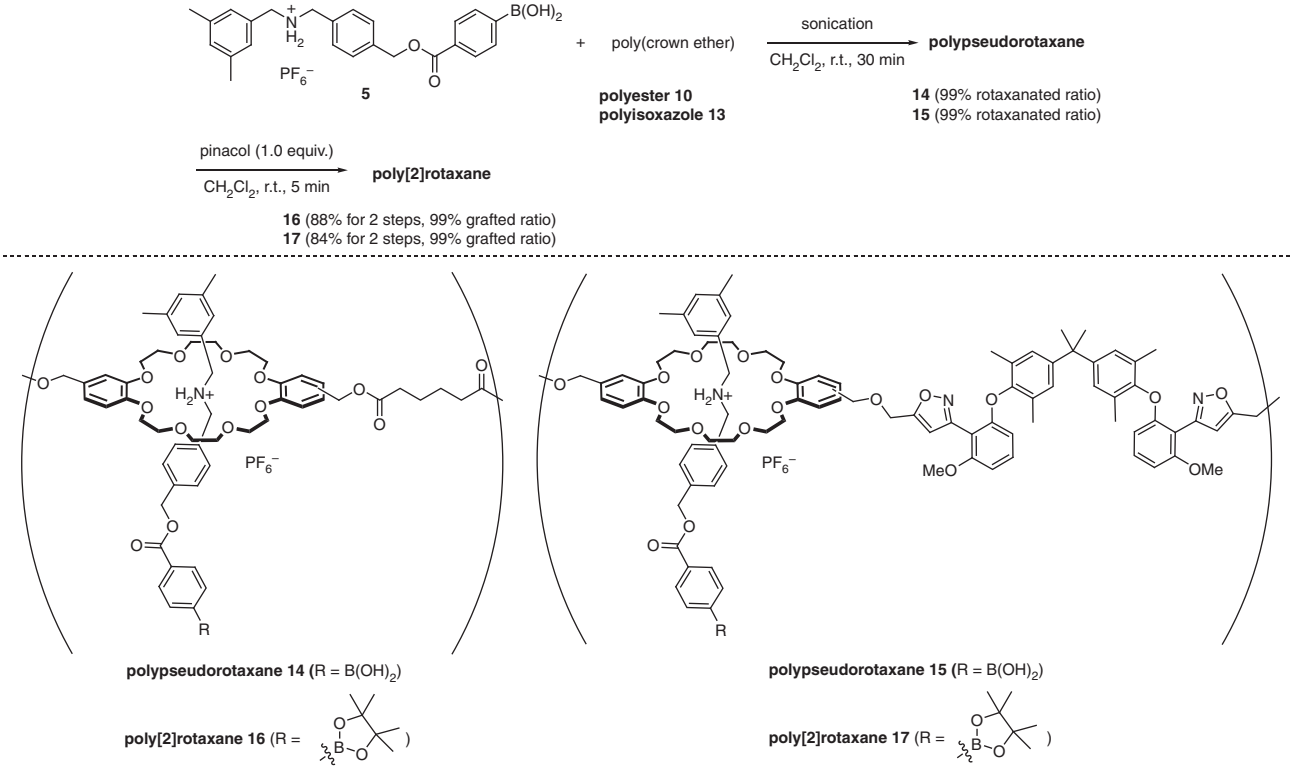
We then tried another approach to synthesize poly(crown ether), this time using sufficiently bulky and stable ditopic nitrile *N*-oxide **12** as a crucial comonomer to functionalized DB24C8, which we recently developed as a powerful chemical ligation tool.[46] The reaction of diethynyl-functionalized DB24C8 **11** with **12** in refluxing $CHCl_3$ without any catalyst afforded the isoxazole-containing poly(crown ether) (**polyisoxazole-13**) in quantitative yield by poly[2+3]cycloaddition. The molecular weight and its distribution, estimated by SEC based on polystyrene standards, were M_w=33 700 and M_w/M_n=1.7. The ^{1}H NMR spectrum, identical to that for **13**, has sharp signals, suggesting the formation of **13** without structural disorder caused by penetration.

By using these trunk polymers, we investigated the synthesis of poly[2]rotaxanes by the grafting-onto protocol according to model reactions for **7** and **8**. Surprisingly, the sonication of a mixture of poly(crown ether) (**10** or **13**) and two equivalents of axle component **5** in CH_2Cl_2 at room temperature for 30 min gave the corresponding polypseudorotaxane (**14** or **15**) with a 99% rotaxanated ratio (Scheme 5). The ^{1}H NMR spectrum clearly shows that the rotaxanated ratio does not depend on the spacer structure of the poly(crown ether)s. To a solution of **14** or **15** was added pinacol as the end-capping agent. The end-capping reaction proceeded rapidly to completion within 5 min with quantitative conversion. The resulting solution was precipitated into MeOH to remove the residual axle component and pinacol, giving poly[2]rotaxanes **16** and **17** with a 99% rotaxanated ratio in high yields. The structures of **16** and **17** were determined by ^{1}H NMR (Figure 1).

Figure 1 shows NMR spectra of DB24C8, axle **5**, model [2]rotaxane **8** and poly[2]rotaxane **16**. All aliphatic signals can be assigned rationally. For **8** (Figure 1c), a signal originating from *N*-benzyl protons around the ammonium moiety appears as a broad peak because of geminal coupling, strongly supporting the formation of rotaxane in accordance with the literatures.[47,48] In addition, the observed methyl signal supports the formation of boron pinacolate of **8**. The other signals are consistent with the structure of **8**. Similar patterns in the spectrum d of poly[2]rotaxane **16** (Figure 1d) clearly suggests the formation of poly[2]rotaxane **16** with a quantitatively rotaxanated ratio.

Polyrotaxanes **16** and **17** are stable enough in various organic solvents, including $CHCl_3$, MeOH and DMSO, not to incur decomposition of the rotaxane moieties. In addition, the high 5%-weight-loss temperatures of these polymers, $\sim$220 °C, indicate good thermal stability. Thus, these poly[2]rotaxanes are at least as stable as covalent-bond polymers, despite their flexible mechanical linkages and reversible dynamic covalent bonds based on boronate.

The dissociation reaction of the poly[2]rotaxanes is interesting because of the dynamic covalent nature of boronate. The exposure of a solution of **16** in DMSO to 60% HPF_6 aqueous at room temperature resulted in efficient hydrolysis of the boronate moiety, with subsequent dissociation reaction of the axle moieties (Scheme 6).



Scheme 5 Synthesis of poly[2]rotaxanes.

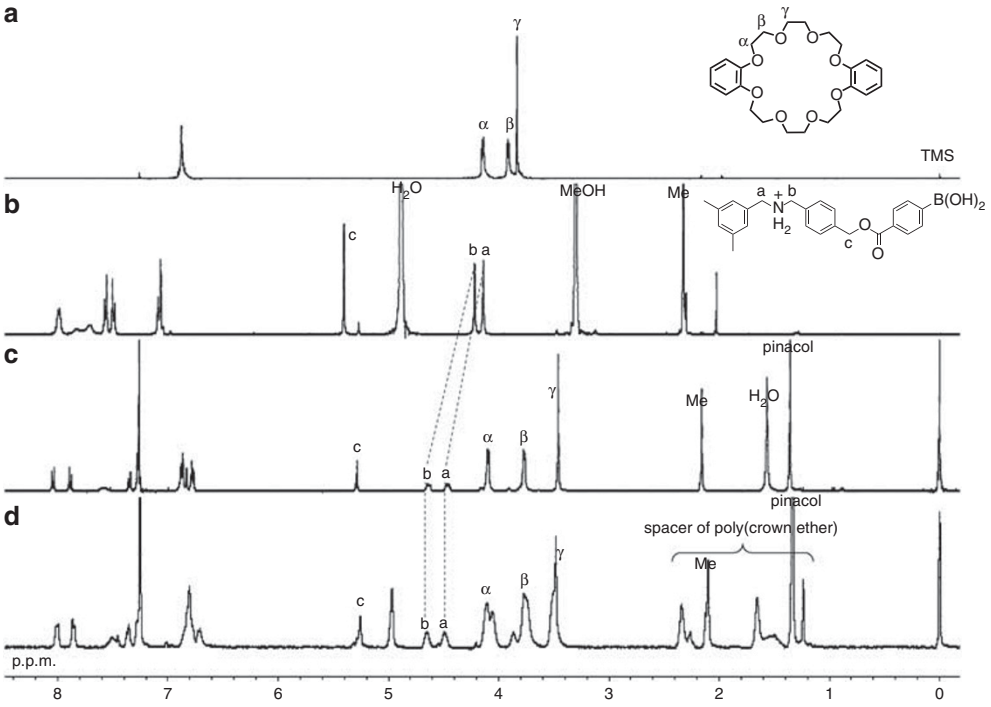
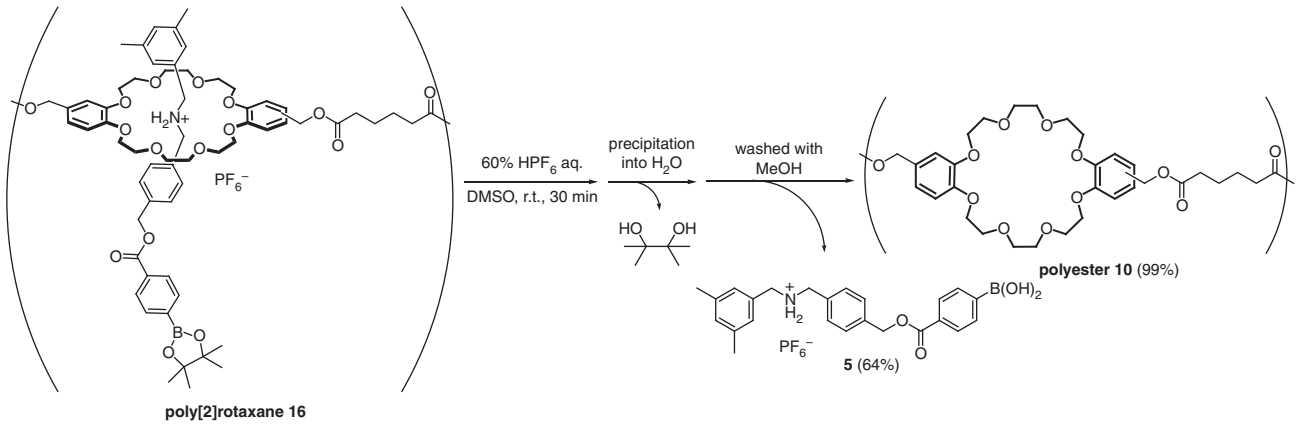
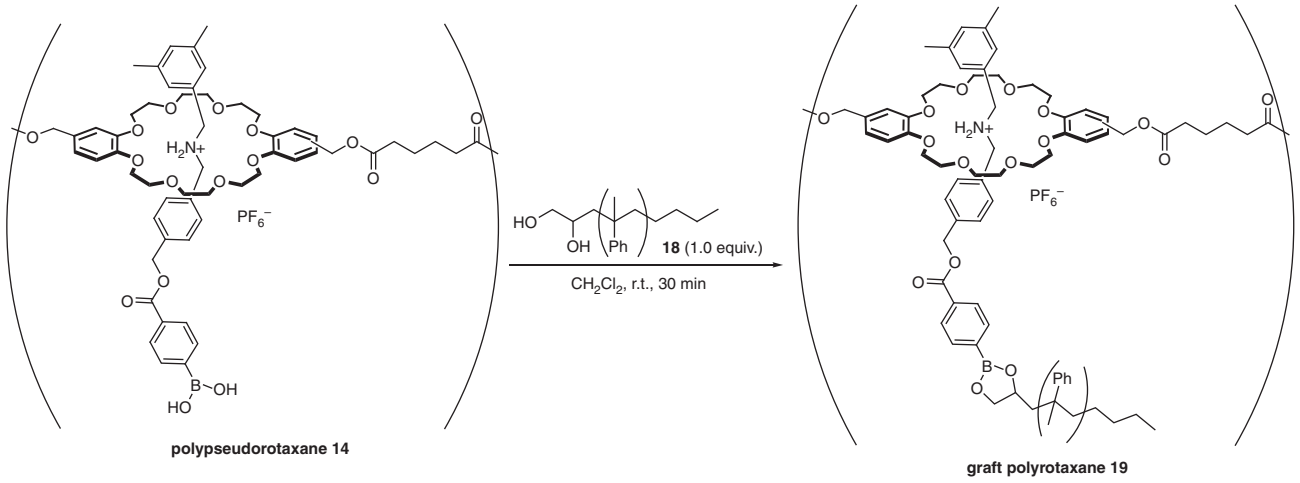


Figure 1 ^{1}H nuclear magnetic resonance spectra of (**a**) DB24C8 in $CDCl_3$, (**b**) axle **5** in CD_3OD, (**c**) [2]rotaxane **8** in $CDCl_3$ and (**d**) poly[2]rotaxane **16** in $CDCl_3$ (400 MHz, 298 K). Abbreviation: TMS, tetramethylsilane.



Scheme 6 Dissociation reaction of poly[2]rotaxane **16** by exploiting the dynamic covalent bond of boronate.



Scheme 7 Synthesis of graft polyrotaxane.

The precipitation of the resulting mixture into H_2O to remove water-soluble pinacol gave a mixture of poly(crown ether) **10** and axle **5** as solids. The solids were washed repeatedly with MeOH. The remaining solid product was pure **10**, whereas the filtrate contained only **5**. The ^1H NMR spectra of recovered **10** and **5** were in good agreement with those of the starting materials (see Supplementary Information). In addition, the SEC profile of **10** shows no degradation of the main-chain skeleton of the original polymer **10**: that is, the molecular weight of **10** coincides perfectly with that of the starting material (see Supplementary Information). Thus, the poly[2]rotaxanes **16** and **17** contain both mechanical linkage and dynamic covalent bond.

Finally, we applied the present protocol to the synthesis of graft polyrotaxane, a new type of graft copolymer, because boronate end-capping proved to be highly efficient, as mentioned above. A polymer with a 1,2-diol terminus as a graft chain was prepared by the two-step procedure of allylation reaction of a living anion end of poly(α-methylstyrene) followed by the oxidation of the terminal olefin with OsO_4. In a manner similar to the synthesis of the poly[2]rotaxanes, diol-terminated poly(α-methylstyrene) **18** was added to a solution of polypseudorotaxane **14** at room temperature (Scheme 7). The reaction mixture was stirred for 30 min, and then quenched by a reprecipitation into Et_2O to give the corresponding graft polyrotaxane **19** in a 99% grafted ratio.

These results emphasize the reliability and versatility of the present protocol, which combines mechanical linkage and dynamic covalent bond for the construction of a sophisticated polymer system.

CONCLUSION

We achieved efficient synthesis of polyrotaxane architectures by exploiting the dynamic nature of the boronic ester linkage and the mechanically linked rotaxane skeleton. Boronic ester formation from the boronic-acid-functionalized axle component and various diols is sufficiently favorable to shift the equilibrium to the product side, enabling efficient synthesis of not only poly[2]rotaxane but also graft polyrotaxane with bulky side chains in high conversion ratios. We will continue to investigate the significance and usefulness of the dynamic covalent bond of boronic ester for construction of additional supramolecular architectures.

ACKNOWLEDGEMENTS

This study was supported financially by Grant-in-Aid for Scientific Research on Priority Areas (No. 18064008, Synergy of Elements) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

1 Gibson, H. W., Bheda, M. C. & Engen, P. T. ROTAXANES, CATENANES, POLYROTAXANES, POLYCATENANES AND RELATED MATERIALS. *Prog. Polym. Sci.* **19,** 843–945 (1994).
2 Vögtle, F., Duennwald, T. & Schmidt, T. Catenanes and rotaxanes of the amide type. *Acc. Chem. Res.* **29,** 451–460 (1996).
3 Gibson, H. W. in *Large Ring Molecules* (ed. Semlyen, J. A.) Ch. 6, 191–262 (John Wiley and Sons, New York, 1996).
4 Fyfe, M. C. T. & Stoddart, J. F. Synthetic supramolecular chemistry. *Acc. Chem. Res.* **30,** 393–401 (1997).
5 Harada, A. Design and construction of supramolecular architectures consisting of cyclodextrins and polymers. *Adv. Polym. Sci.* **133,** 141–191 (1997).
6 Nepogodiev, S. A. & Stoddart, J. F. Cyclodextrin-based catenanes and rotaxanes. *Chem. Rev.* **98,** 1959–1976 (1998).
7 Sauvage, J.- P. in *Molecular Catenanes, Rotaxanes, and Knots* (ed. Dietrich-Buchecker, C.) (Wiley-VCH, Weinheim, 1999).
8 Raymo, F. M. & Stoddart, J. F. Interlocked macromolecules. *Chem. Rev.* **99,** 1643–1663 (1999).
9 Takata, T. & Kihara, N. Rotaxanes synthesized from crown ethers and sec-ammonium salts. *Rev. Heteroat. Chem.* **22,** 197–218 (2000).
10 Mahan, E. & Gibson, H. W. in *Cyclic Polymers,* 2nd edn (ed. Semlyen, J. A.) 415–560 (Kluwer Publishers, Dordrecht, 2000).
11 Hubin, T. J. & Busch, D. H. Template routes to interlocked molecular structures and orderly molecular entanglements. *Coord. Chem. Rev.* **200,** 5–52 (2000).
12 Harada, A. Cyclodextrin-based molecular machines. *Acc. Chem. Res.* **34,** 456–464 (2001).
13 Mayumi, K. & Ito, K. Structure and dynamics of polyrotaxane and slide-ring materials. *Polymer* **51,** 959–967 (2010).
14 Yamaguchi, I., Osakada, K. & Yamamoto, T. A novel crown ether stopping group for side chain polyrotaxane. Preparation of side chain polybenzimidazole rotaxane containing alkyl side chain ended by crown ether-ONa group. *Macromolecules* **33,** 2315–2319 (2000).
15 Takata, T., Kihara, N. & Furusho, Y. Polyrotaxanes and polycatenanes: recent advances in syntheses and applications of polymers comprising of interlocked structures. *Adv. Polym. Sci.* **171,** 1–75 (2005).
16 Huang, F. & Gibson, H. W. Polypseudorotaxanes and polyrotaxanes. *Prog. Polym. Sci.* **30,** 982–1018 (2005).
17 Cantrill, S. J., Chichak, K. S., Peters, A. J. & Stoddart, J. F. Nanoscale borromean rings. *Acc. Chem. Res.* **38,** 1–9 (2005).
18 Wenz, G., Han, B.- H. & Müller, A. Cyclodextrin rotaxanes and polyrotaxanes. *Chem. Rev.* **106,** 782–812 (2006).
19 Takata, T., Kohsaka, Y. & Konishi, G. Main chain-type polyrotaxane with controlled ratio of rotaxanated units. *Chem. Lett.* **36,** 292–293 (2007).
20 Bilig, T., Koyama, Y. & Takata, T. A novel synthetic route to poly(crown ether) through rotaxanation-protection protocol. *Chem. Lett.* **37,** 468–469 (2008).
21 Sato, T. & Takata, T. Synthesis of main-chain-type polyrotaxane by polymerization of homoditopic [2]rotaxane through Mizoroki–Heck coupling. *Macromolecules* **41,** 2739–2742 (2008).
22 Sato, T. & Takata, T. Synthesis and characterization of poly[3]rotaxane through the Mizoroki–Heck coupling polymerization of divinyl-functinalized [3]rotaxane. *Polym. J.* **41,** 470–476 (2009).
23 Lee, Y.- G., Koyama, Y., Yonekawa, M. & Takata, T. Synthesis of main-chain-type polyrotaxanes by new click polymerization using homoditopic nitrile N-oxides via rotaxanation–polymerization protocol. *Macromolecules* **43,** 4070–4080 (2010).
24 Araki, J., Kataoka, T. & Ito, K. Preparation of a 'sliding graft copolymer', an organic solvent-soluble polyrotaxane containing mobile side chains, and its application for a crosslinked elastomeric supramolecular film. *Soft Matter.* **4,** 245–249 (2008).
25 Takashima, T., Hinoue, K., Kihara, N., Hayashi, M., Koyama, Y. & Takata, T. Graftpolyrotaxane: graft polymer possessing movable graft chains on cyclodextrins as the polyrotaxane wheels. *J. Phys. Conf. Ser.* **184,** 012024 (2009).
26 Wu, J. & Gao, C. Sliding supramolecular polymer brushes with tunable amphiphilicity: one-step parallel click synthesis and self-assembly. *Macromolecules* **43,** 7139–7146 (2010).
27 Kohsaka, Y., Koyama, Y., Konishi, G. & Takata, T. Graft polyrotaxane: a new class of graft copolymer with length-variable graft chains (submitted for publication).
28 Rowan, S. J., Cantrill, S. J., Cousins, G. R. L., Sanders, J. K. M. & Stoddart, J. F. Dynamic covalent chemistry. *Angew. Chem. Int. Ed.* **41,** 898–952 (2002).
29 Furusho, Y. & Takata, T. Supramol. Synthesis by imine exchange through hard and soft variable covalent bondings. *Kagaku (Chemistry, Japan)* **57,** 72–73 (2002).
30 Takata, T. & Otsuka, H. Novel synthetic protocol for supramolecules and polymers by molecular construction and integration based on dynamic covalent chemistry. *Yukigosei Kagaku Kyoukai-shi (Japanese)* **64,** 194–207 (2006).
31 Haussmann, P. C. & Stoddart, J. F. Synthesizing interlocked molecules dynamically. *Chem. Rec.* **9,** 136–154 (2009).
32 Furusho, Y., Hasegawa, T., Tsuboi, A., Kihara, N. & Takata, T. 'Unlock-lock' approach to [2] and [3]rotaxanes: entering of a ring through disulfide linkage that is unlocked by thiol 'key'. *Chem. Lett.* **29,** 18–19 (2000).
33 Yoshii, T., Kohsaka, Y., Moriyama, T., Suzuki, T., Koyama, Y. & Takata, T. An efficient synthetic entry to rotaxanes utilizing reversible cleavage of aromatic disulfide bonds. *Supramolecular Chem.* **22,** 1029-0478 (2010).
34 Oku, T., Furusho, Y. & Takata, T. First poly[3]rotaxane synthesized through the nonvocalent step-growth polymerization of a homoditopic dumbbell compound and a macrocycle with a reversible thiol–disulfide interchange reaction. *J. Polym. Sci. Part A Polym. Chem.* **41,** 119–123 (2003).
35 Oku, T., Furusho, Y. & Takata, T. A concept for recyclable cross-linked polymers: topologically networked polyrotaxane capable o undergoing reversible assembly and disassembly. *Angew. Chem. Int. Ed.* **43,** 966–968 (2004).
36 Bilig, T., Oku, T., Furusho, Y., Koyama, Y., Asai, S. & Takata, T. Polyrotaxane networks formed via rotaxanation utilizing dynamic covalent chemistry of disulfide. *Macromolecules* **41,** 8496–8503 (2008).
37 Tokunaga, Y., Ito, T., Sugawara, H. & Nakata, R. Dynamic covalent chemistry of a boronylammonium ion and a crown ether: formation of a C_3-symmetric [4]rotaxane. *Tetrahedron Lett.* **49,** 3449–3452 (2008).
38 Tachibana, Y., Kawasaki, H., Kihara, N. & Takata, T. Sequential *O*- and *N*-acylation protocol for high-yield preparation and modification of rotaxanes: synthesis, fuctionalization, structure, and intercomponent interaction of rotaxanes. *J. Org. Chem.* **71,** 5093–5104 (2006).
39 Li, W., Nelson, D. P., Jensen, M. S., Hoerrner, R. S., Cai, D., Larsen, R. D. & Reider, P. J. An improved protocol for the preparation of 3-pyridyl- and some arylboronic acids. *J. Org. Chem.* **67,** 5394–5397 (2002).
40 Sato, T. & Takata, T. Rotaxane axle as an effective scaffold: synthesis of fuctionalized [3]rotaxane and connection of the wheel components arranged on the axle. *Tetrahedron Lett.* **48,** 2797–2801 (2007).
41 Ashton, P. R., Baxter, I., Fyfe, M. C. T., Raymo, F. M., Spencer, N., Stoddart., J. F., White, A. J. P. & Williams, D. J. Rotaxane or pseudorotaxane? That is the question!. *J. Am. Chem. Soc.* **120,** 2297–2307 (1998).
42 Tachibana, Y., Kihara, N., Furusho, Y. & Takata, T. Is the tert-butyl group bulky enough to end-cap a pseudorotaxane with a 24-crown-8-ether wheel? *Org. Lett.* **6,** 4507–4509 (2004).
43 Makita, Y., Kihara, N. & Takata, T. Quantitative active transport in [2]rotaxane using a one-shot acylation reaction toward the linear molecular motor. *J. Org. Chem.* **73,** 9245–9250 (2008).
44 Kohsaka, Y., Nakazono, K., Koyama, Y. & Takata, T. Size-complementary rotaxane cross-link: effect on stabilization and degradation of supramolecular network. *Angew. Chem. Int. Ed.* **50,** 4872–4875 (2011).
45 Delaviz, Y. & Gibson, H. W. Macrocyclic polymers 2. Synthesis of poly(amide crown ethers) based on bis(5-carboxy-1,3-phenylene)-32-crown-10. Network formation through threading. *Macromolecules* **25,** 4859–4862 (1992).
46 Lee, Y.- G., Yonekawa, M., Koyama, Y. & Takata, T. Synthesis of a kinetically stabilized homoditopic nitrile N-oxide directed toward catalyst-free click polymerization. *Chem. Lett.* **39,** 420–421 (2010).
47 Kawasaki, H., Kihara, N. & Takata, T. High yielding and practical synthesis of rotaxanes by acylative end-capping catalyzed by tributylphosphine. *Chem. Lett.* **28,** 1015–1016 (1999).
48 Matsumura, T., Ishiwari, F., Koyama, Y. & Takata, T. C–C bond forming click synthesis of rotaxanes exploiting nitrile *N*-oxide. *Org. Lett.* **12,** 3828–3831 (2010).

Supplementary Information accompanies the paper on Polymer Journal website (http://www.nature.com/pj)