Click Construction of Spiro- and Bridged-Quatrefoil Polymer Topologies with Kyklo-Telechelics Having an Azide Group

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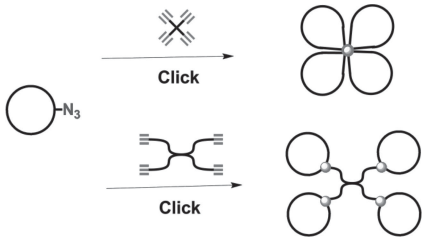
Unprecedented tetracyclic polymer topologies with spiro- and a bridged-type quatrefoil forms are effectively constructed through an alkyne-azide, click-linking reaction by employing a kyklo-telechelic poly(tetrahydrofuran), poly(THF), precursor having an azide group, obtained through an electrostatic self-assembly and covalent fixation (ESA-CF) process, and complementary tetrafunctional alkyne reagents of either a pentaerythritol derivative or a four-armed star telechelic polymer precursor.



1. Introduction

Cyclic and multicyclic polymers have gained growing attention due to their unique topological feature of the elimination of chain termini in contrast to linear and branched counterparts.[1–4] A remarkable progress has now been observed to prepare a wide variety of single cyclic polymers on the basis of intriguing end-to-end pre-polymer-linking processes, as well as on an alternative ring-expansion polymerization.[5–10] By utilizing a variety of cyclic polymers having prescribed chemical structures, unprecedented topology effects by cyclic polymers have now been demonstrated.[1,11]

A class of multicyclic polymer topologies, in contrast, has still been an ongoing synthetic challenge to extend the current frontier of synthetic polymer chemistry.[1,12] We have thus developed an electrostatic self-assembly and covalent fixation (ESA-CF) protocol,[1,13] in which linear and star telechelic precursors having moderately strained cyclic ammonium salt groups carrying plurifunctional carboxylate counteranions were employed to form polymeric self-assemblies as key intermediates. All three dicyclic polymer topologies, i.e., θ (fused), 8 (spiro), and manacle (bridged) forms, have been effectively produced through the covalent conversion of the electrostatic polymer self-assemblies.[13] Moreover, basic types of tricyclic polymer topologies, including spiro-tricyclic, trefoil and tandem forms, as well as a bridged-tricyclic, three-way paddle form, have been constructed through an alkyne–azide addition, i.e., click reaction by employing tailored single-and dicyclic polymer precursors (kyklo-telechelics), obtainable also by the ESA-CF protocol.[13,14] An ATRP (atom transfer radical polymerization)-click and a RAFT (reversible addition–fragmentation chain-transfer polymerization)-click processes have also been applied for the construction of a spiro-tricyclic, trefoil polymer topology.[15,16] Furthermore, the two fused-tricycle polymer topologies (δ-graph and γ-graph forms) have been constructed through the tandem click and olefin metathesis, i.e., clip reactions in conjunction with the ESA-CF process.[17,18] On the other hand, only a few examples of tetracyclic polymer topologies, including spiro-tetracyclic, quatrefoil and tandem forms, and a fused-tetracyclic, unfolded tetrahedron-graph form, have been documented to date.[14,18,19]

We report here our challenge to construct unprecedented tetracyclic polymer topologies, i.e., a spiro- and a bridged-type quatrefoil forms, by employing a cyclic poly(tetrahydrofuran), poly(THF), precursor (kyklo-telechelics) having an azide group, obtained with the ESA-CF protocol.[14] The click process is demonstrated as an effective means to combine the kyklo-telechelics with

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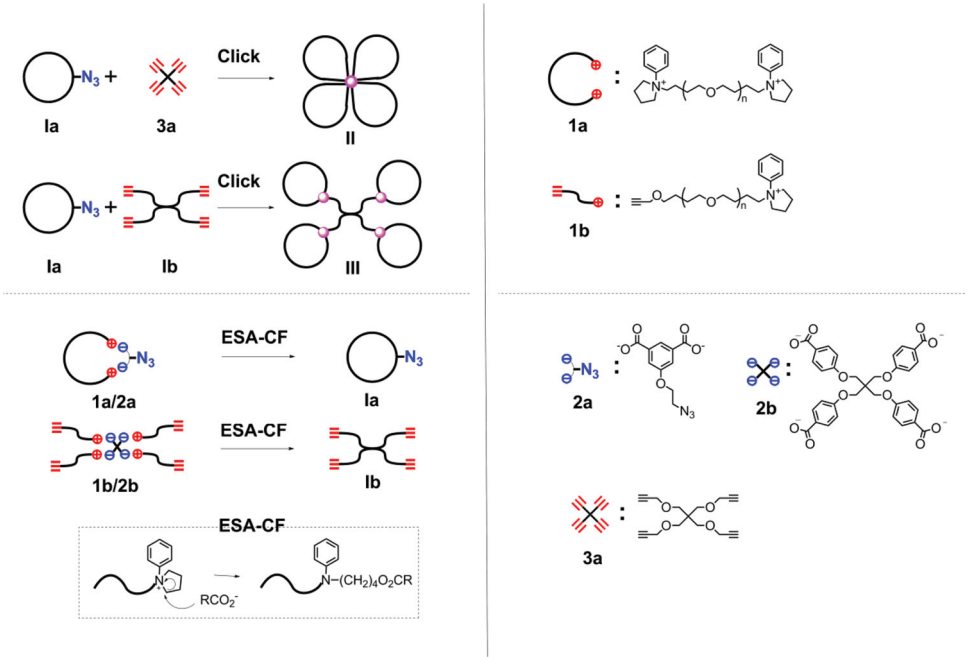

Scheme 1. Click construction of spir and bridged-quatrefoil polymer topologies with a *kyklo*-telechelic precursor obtained by the ESA-CF process.

linear/branched small or a star-shaped polymeric counterparts, respectively (Scheme 1).

2. Results and Discussion

A single cyclic poly(THF) precursor having an azide group (**Ia**) was prepared through an electrostatic self-assembly with a telechelic poly(THF) having *N*-phenylpyrrolidinium salt groups accompanying a dicarboxylate counteranion carrying an azide group (**1a/2a**) (Scheme 1).[14] The subsequent click reaction was conducted either with a tetra-alkyne derivative from pentaerythritol (**3a**), or with a four-armed star polymer precursor having alkyne end groups (**Ib**), obtainable also by the ESA-CF technique using the relevant monofunctional polymer precursor accompanying a tetracarboxylate counteranion (**1b/2b**) (Scheme 1).[20] A slightly excess amount of **Ia** was charged relative to the tetra-alkyne counterpart, **3a** or **Ib** (5:4 in azide/alkyne ratio) to complete the click reaction to produce a spiro- and a bridged-quatrefoil polymer products, **II** and **III**, respectively.

The SEC analysis showed the formation of **II** and **III** by noticeable peak-shifts toward the higher molecular weight region in comparison with the precursors **Ia** or **Ib**, together with peak due to the remaining **Ia** charged in excess (Figure 1, broken lines in the bottom charts). Thus, more quantitatively, the peak molecular weight (M_p) for **II** (M_p = 7.2 kDa) was nearly equal to the total of the corresponding precursors, i.e., four units of **Ia** and one unit of **3a** (4 × 1.8 + 0.2 kDa = 7.4 kDa). In a similar manner, the M_p of **III** (12 kDa) was close to the total of the corresponding precursors, i.e., four units of **Ia** and one unit of **Ib** (4 × 1.8 + 6.0 kDa = 13 kDa). The yields of **II** and **III** were estimated to be 52% and 67% respectively, based on the weights and SEC peak area ratios of the crude products (Figure 1, broken lines in the bottom charts).

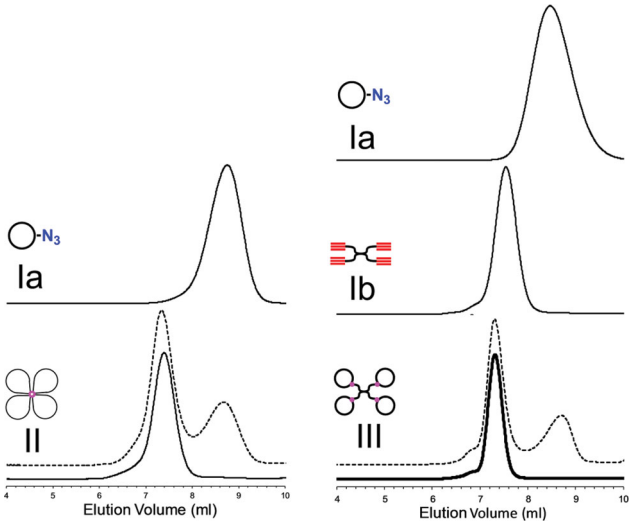

Figure 1. SEC traces of (**left**) a cyclic prepolymer, **Ia** (top), and the click-linking product, **II** (bottom) formed with **3a**, and (**right**) a cyclic prepolymer, **Ia** (top), a four-armed star prepolymer, **Ib** (middle), and the click-linking product, **III** (bottom). Broken lines and sold lines show those obtained before and after fractionation, respectively. (THF was used as eluent at the flow rate of 1.0 mL min^{-1}.)

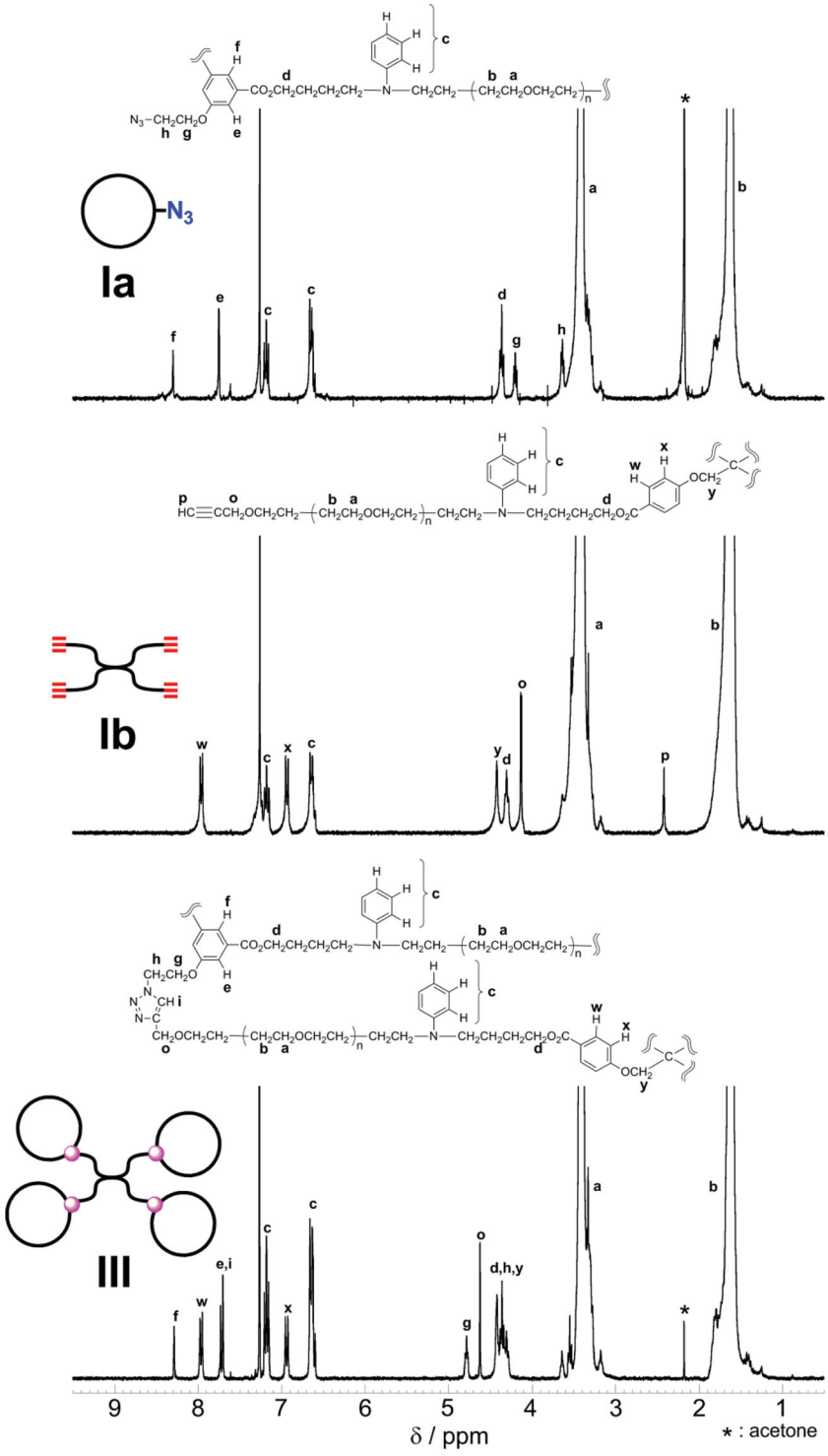

Figure 2. 300 MHz ^{1}H NMR spectra of a cyclic prepolymer, **Ia** (top), a four-armed star prepolymer, **Ib** (middle), and the click-linking product, **III** (bottom); ($CDCl_3$, 40 °C).

The subsequent isolation of **II** and **III** was performed by means of a preparative SEC fractionation technique (Figure 1, solid lines in the bottom charts).

The ^{1}H NMR analysis of the isolated product **II** together with the precursors **Ia** and **3a** (Figure S1, Supporting Information), as well as of the product **III** together with **Ia** and **Ib** (Figure 2) confirmed the selective coupling reaction between the alkyne and azide groups of the complementary prepolymer pairs. Thus, the signals for both the azidomethylene protons (3.62 ppm) in **Ia** and the ethynyl protons (2.46 and 2.42 ppm, respectively) in **3a** and **Ib** were replaced by the triazole proton signals emerged at 7.82 and 7.73 ppm in **II** and in **III**, respectively. Moreover, the signal for the propargyl methylene protons (4.11 ppm in **3a** and 4.13 ppm in **Ib**, respectively) was replaced by that for the methylene protons adjacent to the 4-position of the triazole unit (4.58 ppm in **II** and 4.62 ppm in **III**, respectively). The IR absorbance of the azide groups at 2104 cm^{-1} observed in the precursor **Ia** was scarcely visible in the products **II** and **III**, indicating that the reaction proceeded effectively (Figure S2, Supporting Information).

The MALDI-TOF mass spectrum of **II** showed a uniform series of peaks with an interval of 72 mass units corresponding to the repeating THF unit, and each peak exactly matched the total molar mass of the chemical structure produced from the complementary precursors (Figure 3). Thus, the peak at m/z = 9921.9, assumed to be the adduct with Na^+, corresponds to **II** with a $\overline{DP}_n$ of 100; $(C_4H_8O) \times 100 + C_{153}H_{184}N_{20}O_{24}$ plus Na^+ equals 9920.990. Furthermore, the sum of four-times the molar mass of **Ia** with a $\overline{DP}_n$ of 25 ($4 \times (2425.4 - [Na^+]) = 9609.7$) and the molar mass of **3a** is 9897.8, in agreement with the molar mass of **II** with a $\overline{DP}_n$ of 100 ($9921.0 - [Na^+] = 9897.0$) given above. For the product **III**, on the other hand, the MALDI-TOF analysis was not successful because the molecular weight of **III** was beyond the detection limit.

The extent of the contraction in the 3D sizes of **II** and of **III** was then estimated by the ratio of the peak molecular weight by SEC to the number-average molecular weight by ^{1}H NMR after the fractionation [M_p(SEC)/$\overline{M}_n$(NMR)]. The obtained values, 0.59 and 0.61 for **II** and for **III**, respectively, were marginally smaller than those of previously reported

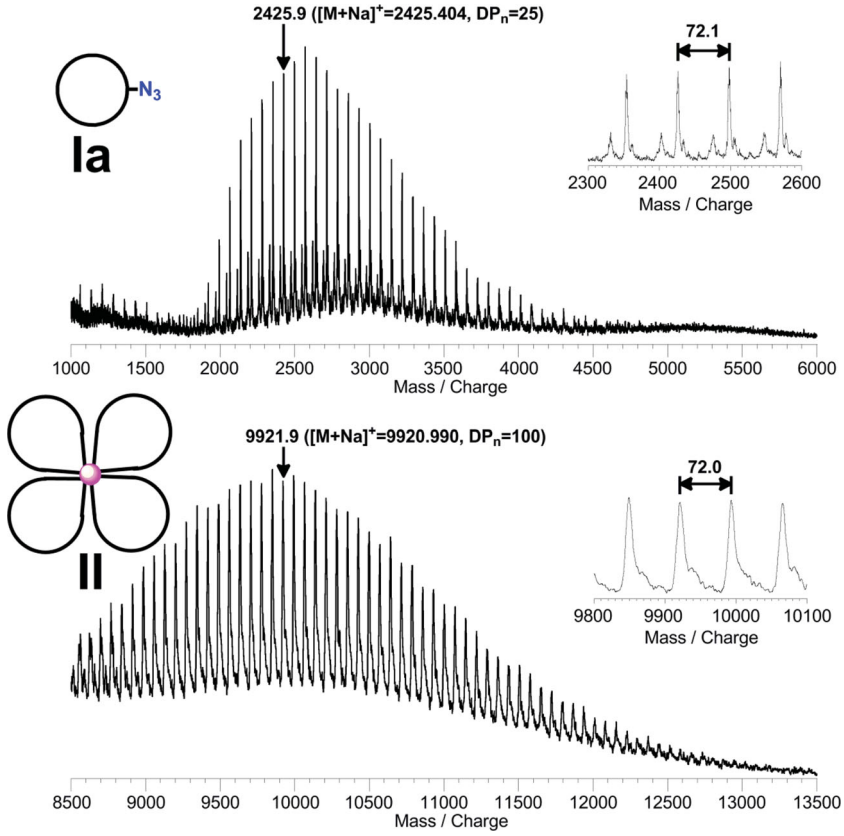

Figure 3. MALDI-TOF mass spectra of a cyclic prepolymer, **Ia** (top), and the click-linking product, **II** (bottom) formed with **3a** (bottom). (Linear mode, matrix: dithranol with sodium trifluoroacetate. $\overline{DP}_n$ denotes the number of monomer units in the products.)

various spiro-multicyclic topologies such as a dicyclic 8-shaped (0.69–0.80)[13,21] and a tricyclic trefoil-shaped (0.65)[13] constructions.

To conclude, we have shown the click-linking of *kyklo*-telechelics obtainable by the ESA-CF process as a powerful means to construct complex multicyclic polymer topologies. The quatrefoil polymer **II** is an unequivocally characterized, one of the three forms of spiro-tetracyclic topologies, achieved next to the tandem tetracyclic counterpart. Moreover, the polymer **III** is a first example produced among the three bridg*ed*-tetracyclic topologies.

3. Experimental Section

3.1. Synthesis of a Spiro-Form Quatrefoil Poly(THF) (II)

A cyclic poly(THF) having an azide group Ia ($\overline{M}_n$(NMR) = 3000, M_p(SEC) = 1800, and PDI = 1.19, 21 mg, 7.0 μmol) and tetrapropargylpentaerythritol 3a (0.5 mg, 1.7 μmol) together with copper sulfate pentahydrate (6.5 mg, 26 μmol) and sodium ascorbate (10 mg, 52 μmol) were added to a THF/water mixture (0.17/0.043 mL/mL). The resulting suspension was stirred at ambient temperature for 20 h. The product was then extracted by CH_2Cl_2 and washed by a saturated aqueous NH_4Cl solution four times and by water once. The collected organic phase was concentrated under reduced pressure, and the residue passed through a plug of silica gel with acetone. The recovered product (17 mg) was subjected to a preparative SEC fractionation technique (Japan Analytical Industry Co. Ltd., LC-908 equipped with two columns, JAIGEL-3H and JAIGEL-2H, and $CHCl_3$ as eluent at 3.5 mL min^{-1}), followed by the column chromatography with silica gel and ethyl acetate as eluent first to remove impurities and switching it to acetone midway to isolate the product II, in the yield of 7.5 mg. ($\overline{M}_n$(NMR) = 12 200, M_p(SEC) = 7200, PDI = 1.08).

^{1}H NMR of II ($CDCl_3$) δ: 1.48–1.90 (m, CH_2CH$_2$O), 3.23–3.61 (m, CH$_2$CH_2O, CH_2OCH$_2$-triazole), 4.28–4.40 (m, 16H, ArCO$_2$CH_2), 4.40–4.52 (m, 8H, CH$_2$CH_2-triazole), 4.58 (s, 8H, CH$_2$OCH_2-triazole), 4.82 (s, 8H, CH_2CH$_2$-triazole), 6.57–6.72 (m, 24H, Ar–*H* ortho and para to N), 7.12–7.24 (m, 16H, Ar–*H*, meta to N), 7.71 (s, 8H, Ar–*H* ortho to OCH$_2$-triazole), 7.82 (s, 4H, triazole-*H*), 8.25 (s, 4H, Ar–*H* para to OCH$_2$-triazole).

3.2. Synthesis of a Bridged-Form Quatrefoil Poly(THF) (III)

A cyclic poly(THF) having an azide group Ia ($\overline{M}_n$(NMR) = 3000, M_p(SEC) = 1800, and PDI = 1.19, 25 mg, 8.3 μmol) and four-armed star poly(THF) having ethynyl end groups Ib ($\overline{M}_n$(NMR) = 8100, M_p(SEC) = 6000, PDI = 1.05, 10 mg, 1.7 μmol) together with copper sulfate pentahydrate (6.2 mg, 25 μmol) and sodium ascorbate (9.9 mg, 50 μmol) were added to a THF/water mixture (0.4/0.1 mL/mL). The resulting suspension was stirred at ambient temperature for 24 h. The product was then extracted by CH_2Cl_2 and washed by a saturated aqueous NH_4Cl solution three times and by water once. The collected organic phase was concentrated under reduced pressure and the residue passed through a plug of silica gel with acetone. The recovered product (30 mg) was subjected to a preparative SEC fractionation technique (Japan Analytical Industry Co. Ltd., LC-908 equipped with two columns, JAIGEL-3H and JAIGEL-2H, and $CHCl_3$ as eluent at 3.5 mL min^{-1}), followed by the column chromatography with silica gel and ethyl acetate as eluent first to remove impurities and switching it to acetone midway to isolate the product III in the yield of 15 mg). ($\overline{M}_n$(NMR) = 19 100, M_p(SEC) = 11 700, PDI = 1.09).

^{1}H NMR of III ($CDCl_3$) δ: 1.51–3.26 (m, CH_2CH$_2$O), 3.26–3.50 (m, CH$_2$CH_2O), 4.27–4.48 (m, 40H, ArOCH_2, CH$_2$CH_2-triazole, ArCO$_2$CH_2), 4.62 (s, 16H, CH$_2$OCH_2-triazole), 4.78 (t, 16H, J = 4.6 Hz, CH_2CH$_2$-triazole), 6.58–6.68 (m, 24H, Ar–*H* ortho and para to N), 6.94 (d, 8H, J = 8.7 Hz, Ar–*H* meta to OCH$_2$C), 7.18 (t, 16H, J = 7.9 Hz, Ar–*H*, meta to N), 7.70 (s, 8H, Ar–*H* ortho to OCH$_2$-triazole), 7.73 (s, 4H, triazole-*H*), 7.95 (d, 8H, J = 8.6 Hz, Ar–*H* ortho to OCH$_2$C), 8.28 (s, 4H, Ar–*H* para to OCH$_2$-triazole).

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author. Experimental procedures for the preparation of **3a**, **1b/**$CF_3SO_3^-$, and **Ib** and ^1H NMR spectra of **3a** and **II**, and IR spectra of **Ia**, **II**, and **III** are given in the Supporting Information.

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