

INVITED REVIEW

Topological polymer chemistry for designing multicyclic macromolecular architectures

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The geometrical conception and current synthetic challenges of topological polymer chemistry have been reviewed. On the basis of the systematic classification and isomeric properties of polymer chain topologies, a variety of novel multicyclic macromolecular constructions have now been rationally designed and subsequently realized by intriguing synthetic protocols. In particular, cyclic and multicyclic polymer products are effectively produced by an electrostatic polymer self-assembly of telechelic precursors that contain cyclic ammonium salt groups accompanying polyfunctional carboxylate counteranions and the subsequent covalent conversion through the ring-opening or through the ring-emitting reaction of the cyclic ammonium salt groups by carboxylate counteranions (Electrostatic Self-assembly and Covalent Fixation (ESA-CF) process). Furthermore, the ESA-CF process, in conjunction with effective linking/cleaving chemistry (including the metathesis condensation (clip) and alkyne-azide addition (click) reactions), has been demonstrated as a new synthetic protocol for unprecedented multicyclic macromolecular topologies.

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INTRODUCTION

In the macroscopic world, we often observe that the form of objects directs their functions and properties.^{1,2} Remarkable developments in nanoscience and nanotechnology now allow the fabrication of extremely small objects with precisely defined structures.^{3–5} In the field of synthetic polymer chemistry, the form of macromolecules has long been restricted to a linear or a randomly branched topology. However, in the last decade, a variety of precisely controlled topologies that include cyclic and multicyclic forms in addition to branched ones have been realized by the introduction of intriguing synthetic techniques based on living polymerization as well as self-assembly protocols.^{6–10}

In this review, recent progress in topological polymer chemistry^{11–14} is discussed (with particular emphasis on cyclic and multicyclic polymers) to provide new perspectives for polymer science and polymer materials engineering.

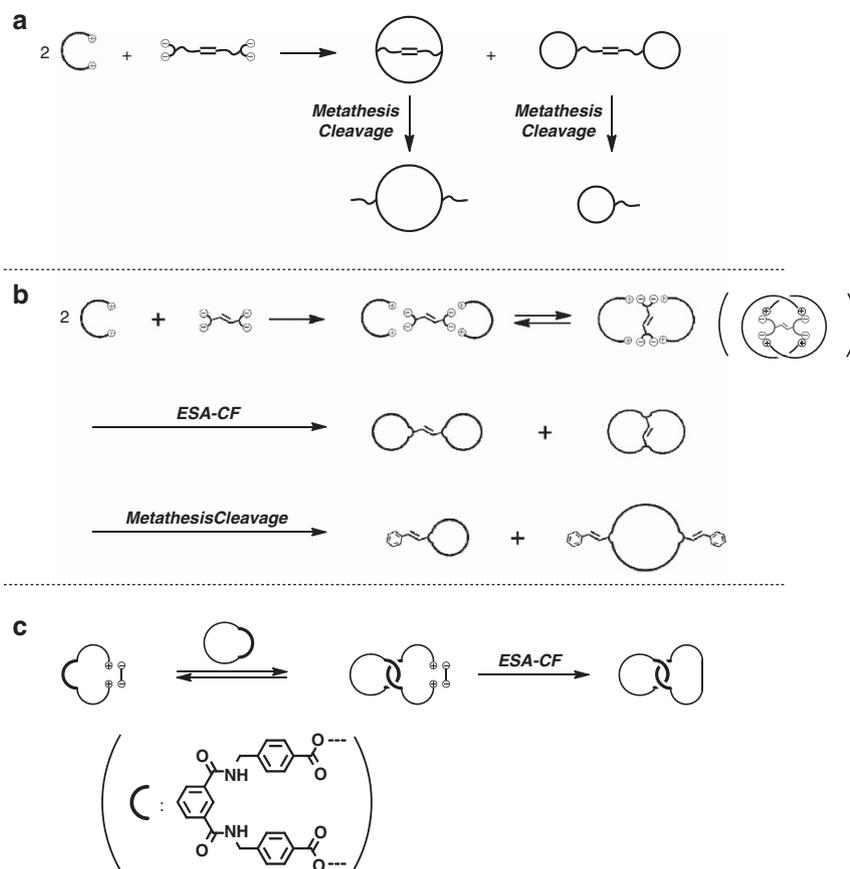
GEOMETRICAL CLASSIFICATION AND ISOMERIC PROPERTIES OF CYCLIC AND MULTICYCLIC POLYMER CONSTRUCTION

A rational classification of distinctive polymer topologies provides a basis for understanding their mutual structural relationships, and this classification should eventually provide their practical synthetic pathways. We have formulated a systematic classification procedure for nonlinear (particularly cyclic and multicyclic) polymer architectures composed of sufficiently long and flexible segment components,¹⁴

which relies on graphical presentation by the constitutional isomerism of alkanes (C_nH_{2n+2}) and mono- and polycycloalkanes (C_nH_{2n} , C_nH_{2n-2} , and so on). In this procedure, the total number of termini (chain ends) and junctions (branch points) as well as the total number of branches at each junction and the connectivity of each junction are taken as invariant (constant) geometric parameters. Euclidian geometric properties such as the distance between two adjacent junctions or the distance between the junction and terminus are taken as variant parameters, conformation with the flexible nature of the randomly coiled polymer segments. Furthermore, topological constructions with five or more branches at one junction are allowed, while relevant hydrocarbon isomers with the corresponding molecular formula are absent.

Thus, a series of branched polymer topologies are hierarchically classified by alkane molecules with a generic molecular formula of C_nH_{2n+2} , namely, a line construction by propane (C_3H_8), a linear and a three- or a four-armed star construction by butane (C_4H_{10}) or by pentane (C_5H_{12}) isomers, respectively, and two new constructions of an H-shaped and a five-armed star architecture by the relevant hexane isomers (C_6H_{14}).

Likewise, a series of 'ring with branches' constructions are classified by the graph representation of the monocycloalkane molecules of the C_nH_{2n} form, namely, a simple ring construction by cyclopropane (C_3H_6), as well as a tadpole, and a simple ring structures defined by the two isomers of C_4H_8 . The two new constructions are produced by



Scheme 3 Chemical processes of polymeric topological isomers. A full color version of this scheme is available at *Polymer Journal* online.

To produce polymer catenanes through the entanglement of the two polymer segments, a modified ESA-CF process was applied, and programmed self-assembly occurred through the cooperative electrostatic and hydrogen-bonding interaction of the polymer precursors (Scheme 3c).²⁵ Thus, a cyclic polymer precursor with a hydrogen-bonded isophthaloylbenzylic amide group and a dicarboxylate counteranion containing the hydrogen-bonding unit was first prepared through the ESA-CF process. Another telechelic polymer precursor that contained an isophthaloylbenzylic amide group at the center position and cyclic ammonium salt groups was subsequently prepared and subjected to polymer cyclization by the ESA-CF protocol in the presence of the preformed cyclic polymer with a hydrogen-bonding unit (Scheme 3c). A polymeric [2]catenane comprising the two different cyclic polymer components was isolated with a yield as high as 7%, and this product was unequivocally characterized by matrix-assisted laser desorption/ionisation-time of flight mass spectroscopy.

CURRENT SYNTHETIC CHALLENGES FOR CYCLIC POLYMERS

A variety of novel cyclic and multicyclic macromolecular constructions have now been rationally designed and subsequently synthesized by intriguing protocols either by the end-linking of telechelic precursors^{26,27} or by the ring-expansion polymerization process.^{28–30}

End-linking of telechelic precursors

A direct end-to-end-linking reaction of an α - ω -bifunctional linear polymer precursor with a bifunctional coupling reagent is a straightforward method to prepare ring polymers.⁸ In practice, however, this

bimolecular process has rarely been applied to produce high purity ring polymers in high yields. The rare use of the process has two main causes: first, the asymmetric telechelics formed as the product of the first step is prone to react again with the coupling reagent to form a symmetric telechelic, which cannot undergo cyclization; second, a high dilution condition is required to complete the intramolecular cyclization process and avoid concurrent intermolecular chain extension by using the strictly stoichiometric balance of the large polymer and the small coupling compound. However, this dilution inevitably causes serious suppression of the reaction rate obeyed by the second-order kinetics. Accordingly, to isolate the ring polymer product, a fractionation procedure is required to remove the linear side products that have the same chain length (Scheme 4).³¹

An alternative unimolecular polymer cyclization process has been introduced that uses α - ω -heterobifunctional polymer precursors, which are obtainable through living polymerization techniques. In particular, a highly efficient alkyne-azide addition reaction (a click process) has been demonstrated to be a remarkably improved polymer cyclization process in which a ring poly(styrene) was effectively synthesized with a heterotelechelic polystyrene precursor that contains an alkyne and an azide group at each end (Scheme 4). This precursor is obtainable by the atom transfer radical polymerization protocol.³² This click cyclization has also been used to prepare a ring poly(*N*-isopropyl acrylamide) to examine the effects of topology on its phase transition properties.^{33–35}

We have developed an effective unimolecular polymer cyclization process with symmetric olefinic-telechelics, which are conveniently obtainable through the direct end-capping reaction of a variety

of living polymers.³⁶ The quantitative conversion of the atom transfer radical polymerization-terminal bromoalkyl group into allyl groups was achieved with allyltributylstannane (Keck allylation) for polyacrylates^{37,38} and with allyltrimethylsilane/TiCl₄ for polystyrene.³⁹ These allyl-telechelics were then subjected to a metathesis clip reaction under dilution to effectively produce both cyclic homopolymers and block copolymers, including an amphiphilic poly(butyl acrylate)-*b*-PEO and polystyrene-*b*-PEO.^{37–39} Remarkably, a micelle formed from the obtained cyclic amphiphile exhibited significantly enhanced thermal stability in comparison with that of its linear counterpart.⁴⁰ This finding is regarded as the first example of an amplified topology effect by a synthetic cyclic polymer upon self-assembly (Scheme 4).^{11–13}

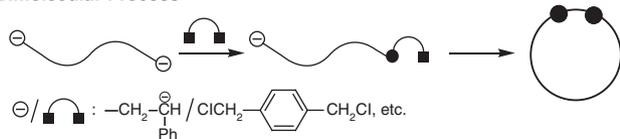
Ring-expansion polymerization

A ring-expansion polymerization proceeds through the repetitive insertion of a monomer into a cyclic initiator. Therefore, the dilution condition is not a prerequisite, in contrast to the end-linking process that uses telechelic precursors. However, the reactive propagating unit is inherently included in the backbone segment, and it is not readily removed by retaining the ring polymer structure.^{41,42}

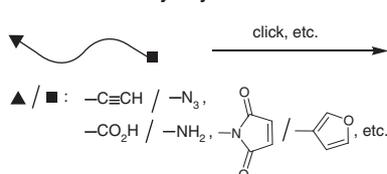
To circumvent this problem, a ring-expansion polymerization has been combined with the end-linking technique.⁴³ Thus, as a typical example, a cyclic stannous dialkoxide has been used as an initiator for the ring-opening polymerization of ϵ -caprolactone. By taking advantage of the living nature of this process, a few units of a photo-cross-linkable acrylate functionalized ϵ -caprolactone derivative have subsequently been introduced, followed by the intramolecular photo-cross-linking of the acrylic groups under dilution. The removal of the stannous dialkoxide initiator fragment by hydrolysis produces a stable ring polymer product, while the precise cross-linking chemical structures are inherently obscure. A ring-shaped nano-object (directly observable by atomic force microscopy) is constructed by this process through the subsequent grafting reaction onto the polymer backbone.⁴⁴

For the one-step synthesis of ring polymers free of initiator residues, a novel ring-opening metathesis polymerization catalyst with a specifically designed cyclic ligand has been developed.⁴⁵ This catalyst polymerizes cycloalkenes like a cyclooctene, and also promotes the end-biting chain transfer reaction to regenerate the

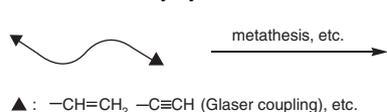
Bimolecular Process



Unimolecular Process by Asymmetric Telechelics



Unimolecular Process by Symmetric Telechelics



Scheme 4 Ring polymer synthesis by the end-linking of telechelic polymers.

catalyst species and reinitiates the polymerization. In this process, the chain transfer occurs randomly during the propagation; consequently the chain length distribution (molecular weight distribution) of the polymer products cannot be controlled. A ring-shaped nano-object is produced by this ring-expansion process by using either a bulky dendronized monomer or post-grafting reactions.^{46,47}

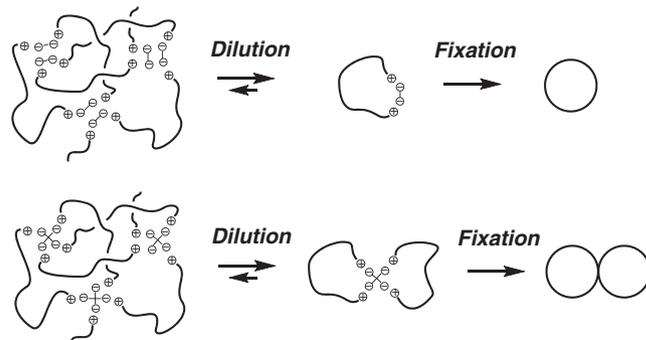
More recently, ring polyesters and polylactams with narrow size distributions have become obtainable with an *N*-heterocyclic carbene initiator.⁴⁸ In this process, the end-biting chain transfer is assumed to eliminate the initiator species after the complete conversion of the monomers by the zwitterionic ring-opening polymerization.

ESA-CF FOR CYCLIC POLYMER TOPOLOGIES

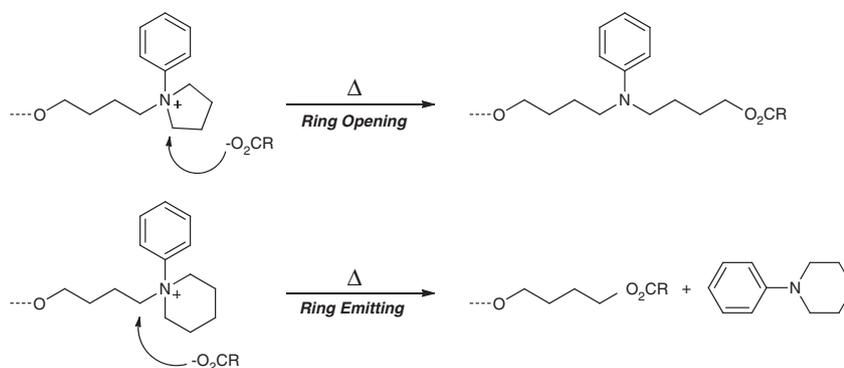
As the previous sections have briefly shown, we have developed an ESA-CF technique for the design of nonlinear polymer architectures (Scheme 5).^{11–13,18} In the ESA-CF process, a variety of linear and star telechelic precursors of poly(tetrahydrofuran (THF)), poly(ethylene oxide), poly(styrene) and poly(dimethylsiloxane) have been used as key polymer precursors. These precursors have moderately strained cyclic ammonium salt groups that are typically five membered, accompanying appropriately nucleophilic counteranions such as carboxylates. Small (low-molecular weight and water soluble) and large (polymeric and water insoluble) carboxylates can be used in this ESA-CF process, as shown previously in Scheme 3.⁴⁹ The corresponding electrostatic polymer complexes are formed in high yields by the simple precipitation of a telechelic precursor with cationic end-groups into an aqueous solution containing small carboxylate salts. They can also be formed by the coprecipitation of an equimolar mixture of cationic and anionic polymer precursors. The cations and anions always balance the charges, even under dilution, and the selective nucleophilic ring-opening reaction occurs at an elevated temperature, to convert the ionic interaction into a permanent covalent linkage (Scheme 5).

This ESA-CF protocol has been applied successfully for the efficient synthesis of various ring polymers, which have optional specific functional groups at the designated positions of the ring polymer structures (kykko-telechelics and cyclic macromonomers) for the construction of further complex polymer topologies, including a variety of ‘ring with branches’ polymers (that is, a simple tadpole, as well as twin-tail and two-tail tadpole forms).^{11–13}

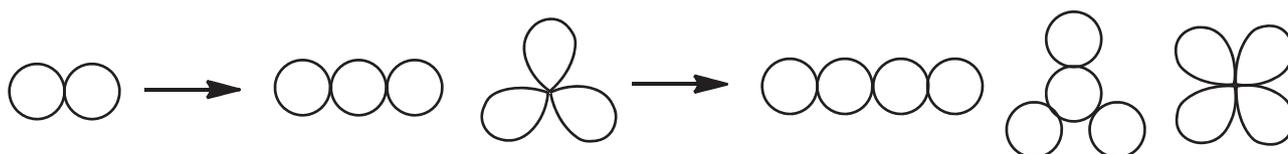
An alternative covalent conversion process has also been developed by using a telechelic precursor with unstrained cyclic ammonium salt end groups (Scheme 6).^{50,51} Thus, telechelics with six membered, *N*-phenylpiperidinium salt groups carrying either monofunctional benzoate or bifunctional biphenyldicarboxylate counteranions can be prepared. Upon subsequent heating, the carboxylate counteranion



Scheme 5 Electrostatic polymer self-assembly and covalent fixation.



Scheme 6 Ring-opening and ring-emitting processes for covalent conversion.



Scheme 7 Spiro-multicyclic constructions.

undergoes selective nucleophilic attack at the exo-position of the cyclic ammonium salt group to cause the elimination of the *N*-phenylpiperidine units from the polymer chain ends. Consequently, by the ESA-CF procedure, ring polymers containing simple ester linking groups are effectively obtainable through the ring-emitting covalent conversion under dilution (Scheme 6). This result contrasts with the impractical bimolecular process for ring polymer synthesis by a conventional esterification reaction under dilution involving a polymeric diol and a dicarboxylic acid.⁵²

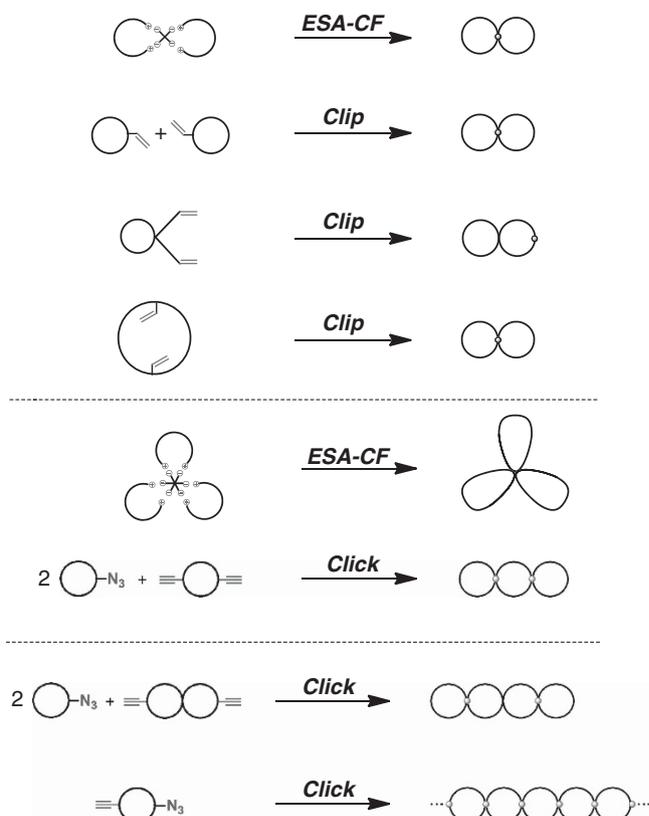
MULTICYCLIC POLYMER CONSTRUCTIONS BY THE ESA-CF PROCESS IN CONJUNCTION WITH EFFECTIVE COVALENT LINKING CHEMISTRIES

The multicyclic polymer constructions shown in Scheme 1 include three subgroups (that is, spiro, bridged and fused forms). The dicyclic constructions correspond to 8-shaped, manacle-shaped (or two-way paddle shaped) and θ -shaped forms.^{11–14} The ESA-CF process, which can be conducted in conjunction with an effective linking chemistry by the intramolecular metathesis condensation of olefinic groups (clip) and by the alkyne-azide addition (click) reactions, has now been demonstrated to be a powerful synthetic protocol for the construction of multicyclic polymer topologies.^{11–13}

Spiro-multicyclic constructions

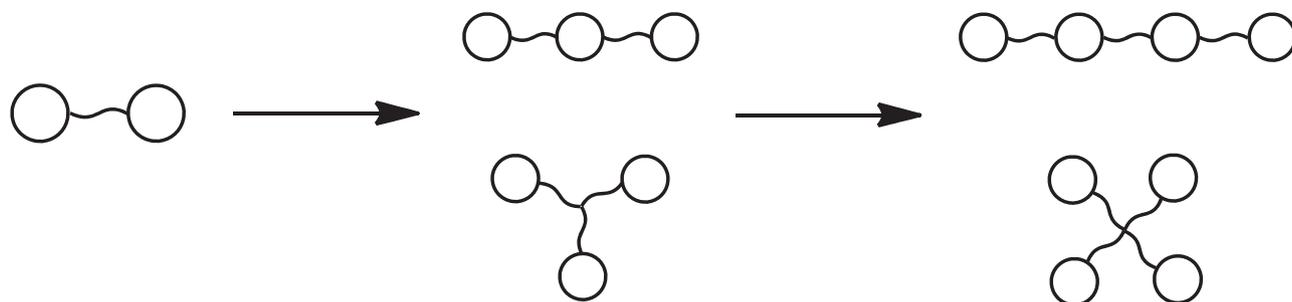
Among a series of spiro-multicyclic constructions, (Scheme 7) a dicyclic 8-shaped polymer was directly obtainable with the ESA-CF process, but it could also be produced by conjunction with the metathesis (clip) process (Scheme 8). First, an 8-shaped polymer was produced with a self-assembly containing two linear telechelic precursor units carrying one tetracarboxylate counteranion unit.¹⁸ The alternative metathesis condensation (clip process) could be applied by using either a ring prepolymer with an allyloxy group, a twin-tailed tadpole polymer precursor with two allyloxy groups at the tail-end positions or a ring polymer precursor with two allyloxy groups at opposite positions (Scheme 8).⁵³

Two spiro-tricyclic polymer forms with either a trefoil or a tandem tricyclic topology were also produced by the ESA-CF process. The first

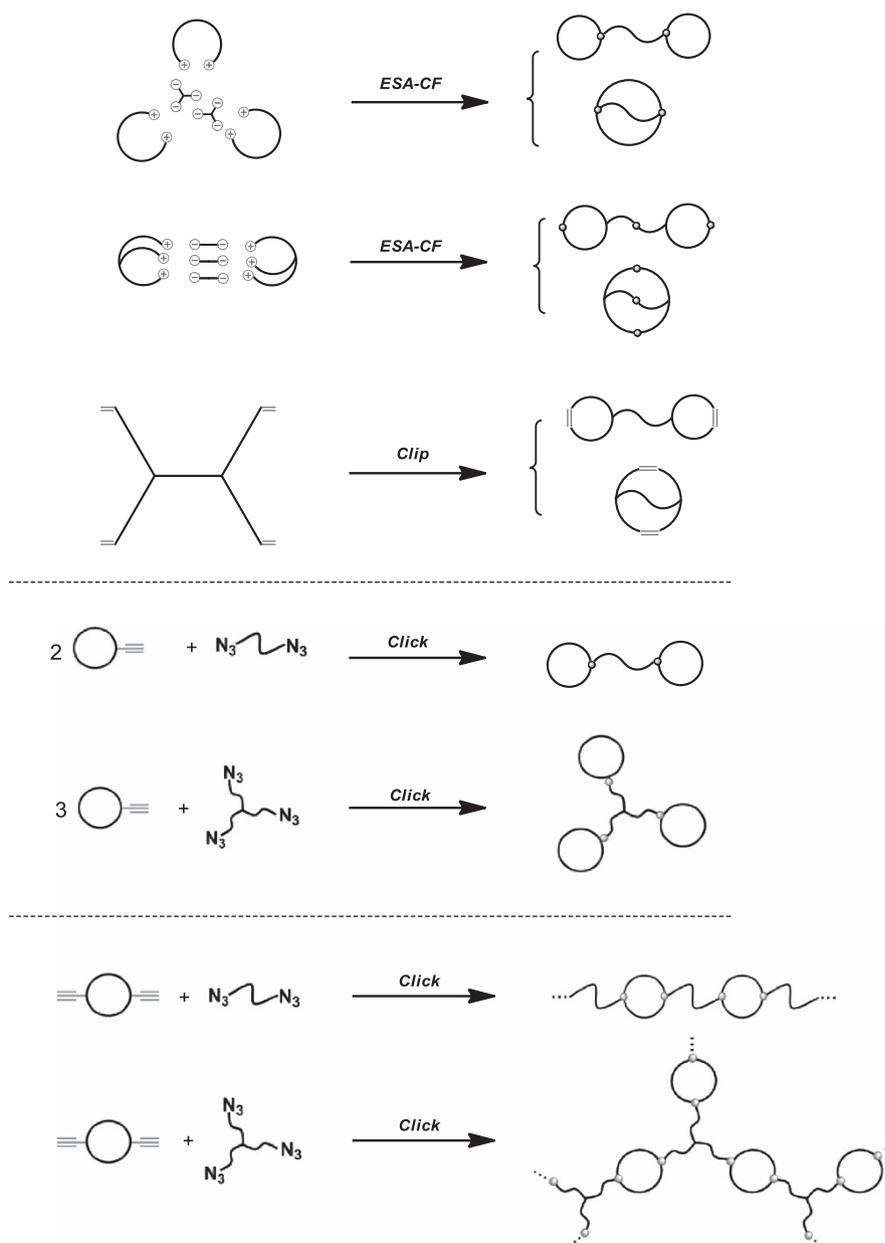


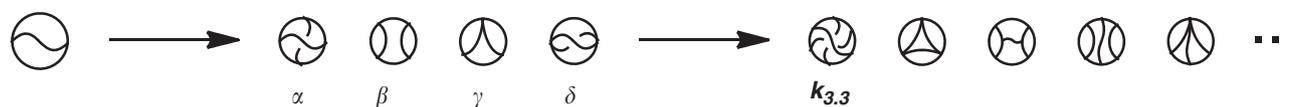
Scheme 8 Synthesis of spiro-multicyclic polymers. A full color version of this scheme is available at *Polymer Journal* online.

form was produced by a self-assembly consisting of three linear telechelic precursor units carrying a hexafunctional carboxylate counteranion,¹⁸ and the second form was produced by the click linking of two cyclic prepolymers with two alkyne groups at the opposite positions of the ring unit and another with an azide group, both of which are obtainable by the ESA-CF technique (Scheme 8).⁵⁴



Scheme 9 Bridged-multicyclic constructions.

Scheme 10 Synthesis of bridged-multicyclic polymers. A full color version of this scheme is available at *Polymer Journal* online.

**Scheme 11** Fused-multicyclic constructions.

Likewise, a tandem spiro-tetracyclic polymer construction was produced by the click coupling between an 8-shaped dicyclic prepolymer with two alkyne groups at the opposite positions of the two ring unit and another single cyclic precursor with an azide group (Scheme 8).⁵⁴ Tandem spiro-multicyclic polymers with multiple ring units were also produced by the click self-polycondensation of a cyclic precursor with alkyne and azide groups at opposite positions of the ring unit, which is obtainable by the ESA-CF technique (Scheme 8).⁵⁴

Bridged-multicyclic constructions

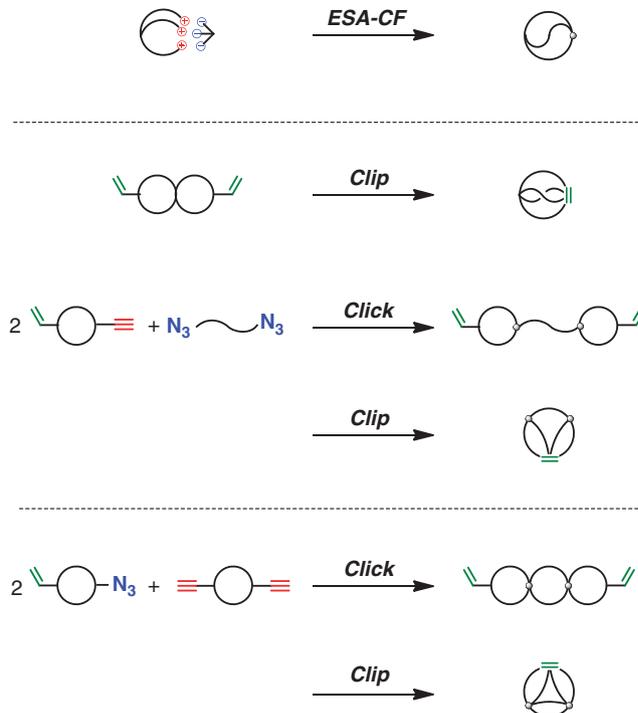
Among a series of bridged-multicyclic constructions (Scheme 9), a dicyclic manacle-shaped polymer was obtainable in conjunction with a θ -shaped polymeric isomer through the ESA-CF with an assembly composed of three linear bifunctional precursor units carrying two trifunctional carboxylate counteranion units (Scheme 10), as described in the previous section.^{18,19} The ESA-CF procedure was also applicable to an assembly composed of two star-shaped trifunctional precursor units carrying three bifunctional carboxylate counteranion units (Scheme 10).²⁰ Alternatively, a pair of dicyclic polymeric topological isomers with θ and manacle constructions were formed through the metathesis clip process using an H-shaped precursor with allyloxy end groups at each chain end (Scheme 10).²¹

The selective construction of a dicyclic, manacle-shaped polymer topology was achieved through the click coupling of a bifunctional linear telechelic precursor containing azide groups with a cyclic polymer precursor bearing an alkyne group obtainable through the ESA-CF protocol (Scheme 10).⁵⁴

Likewise, a bridged-tricyclic three-way paddle-shaped polymer was obtained by the relevant click coupling reaction between a star-shaped trifunctional precursor containing azide groups with a cyclic polymer precursor bearing an alkyne group (Scheme 10).⁵⁴ Bridged-multicyclic polymers consisting of cyclic and linear or branched polymer units were also produced by the click polycondensation of a cyclic precursor containing two alkyne groups at the opposite positions of the ring unit from the respective linear/branched telechelic precursors with azide groups (Scheme 10).⁵⁴ These topologically unique polymers are considered to be topological block copolymers that include alternate cyclic and linear (or branched) segments.

Fused-multicyclic constructions

In contrast to their spiro and bridged counterparts, the class of fused multicyclic polymer topologies (Scheme 11) is considered to be particularly intriguing in the context of programmed polymer folding. This folding is recognized to be crucial in diverse events in biopolymer systems, such as DNA packaging and the three-dimensional structure formation of proteins, as well as the remarkable stability and activity revealed by some cyclic proteins (cyclotides).⁵⁵ Moreover, the topologically significant polymer constructions that include a doubly fused tricyclic α -graph, a triply fused tetracyclic $K_{3,3}$ graph and a triply fused tetracyclic prisman graph remain an ongoing synthetic challenge to extend the current frontier of polymer chemistry (Scheme 1).^{11–14}

**Scheme 12** Synthesis of fused-multicyclic polymers.

A fused-dicyclic θ -shaped polymer was obtained selectively through the ESA-CF process with a self-assembly containing a three-armed, star telechelic precursor carrying a tricarboxylate counteranion (Scheme 12).⁵⁶ Alternatively, as described in the preceding section, the θ -shaped polymer could be formed along with a manacle-shaped polymeric isomer, either through ESA-CF or the metathesis clip process using the relevant polymer precursors (Scheme 10).

A doubly fused tricyclic polymer with a δ -graph construction was produced from an 8-shaped *kyklo*-telechelic precursor with two allyl groups at opposite positions, which was prepared by the ESA-CF protocol.⁵⁷ In this process, a prescribed self-assembly consisting of two units of a linear precursor with cyclic ammonium salt groups and an allyl group at the center position was used, accompanying a tetracarboxylate counteranion. The subsequent metathesis clip process could fold the two polymer ring units together (Scheme 12).⁵⁷

The ESA-CF process, in conjunction with a tandem alkyne-azide click and an olefin metathesis clip reaction, has now been developed as an effective means for the production of programmed folding forms by synthetic polymers, such as a doubly fused tricyclic γ -graph and a triply fused tetracyclic unfolded tetrahedron graph construction (Scheme 12).⁵⁸

A summary of the synthetic procedure and characterization of the γ -graph polymer is described as a typical example.⁵⁸ Thus, a cyclic poly(THF) precursor with an allyloxy and alkyne group was first synthesized by the ESA-CF protocol. A linear poly(THF) with azide end groups was prepared by simply terminating a living polymerization of THF with tetrabutylammonium azide. The

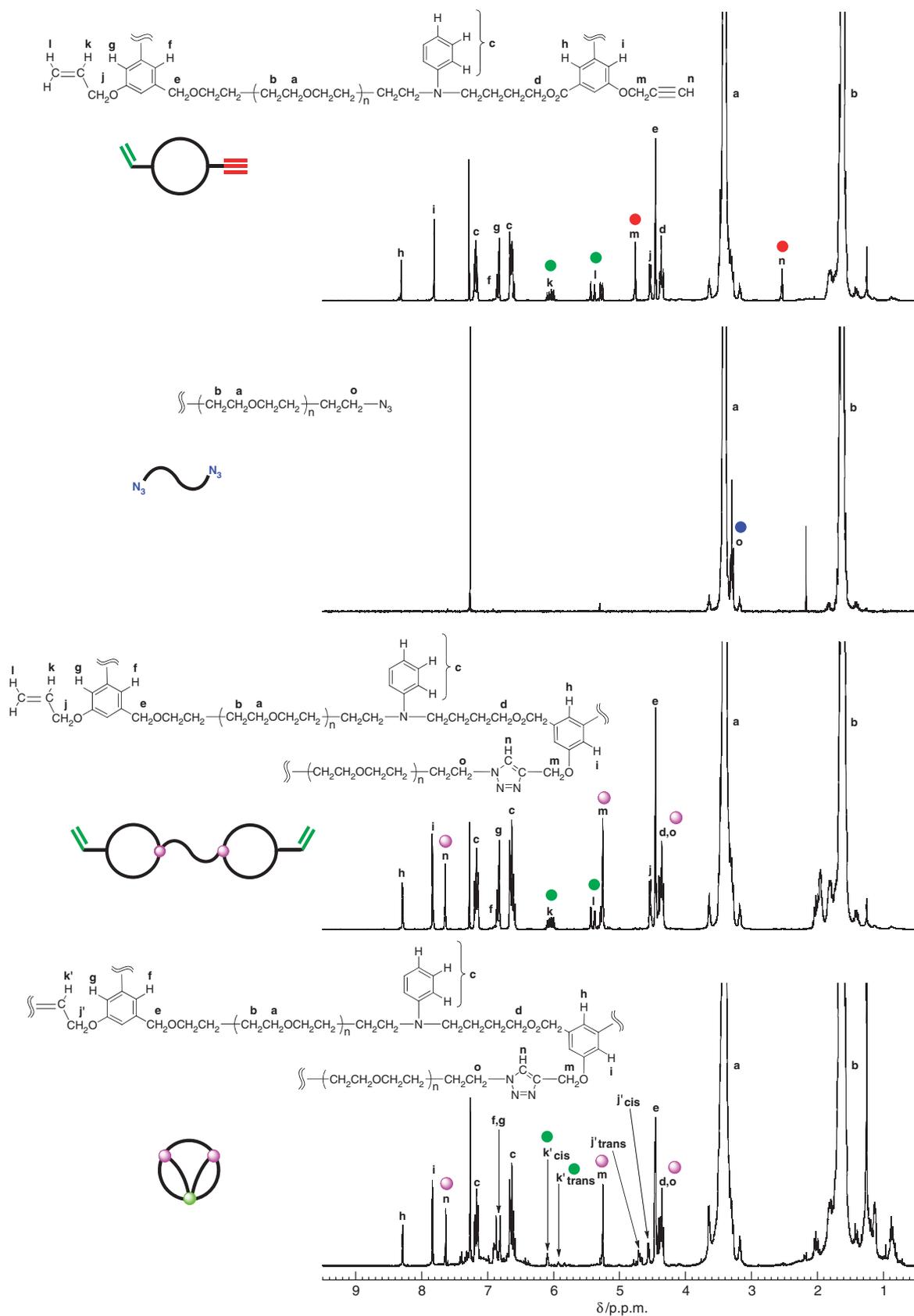


Figure 1 ^1H -nuclear magnetic resonance spectra of a γ -graph polymer and its precursors. Reprinted with permission from Sugai *et al.*⁵⁸ Copyright (2011) American Chemical Society.

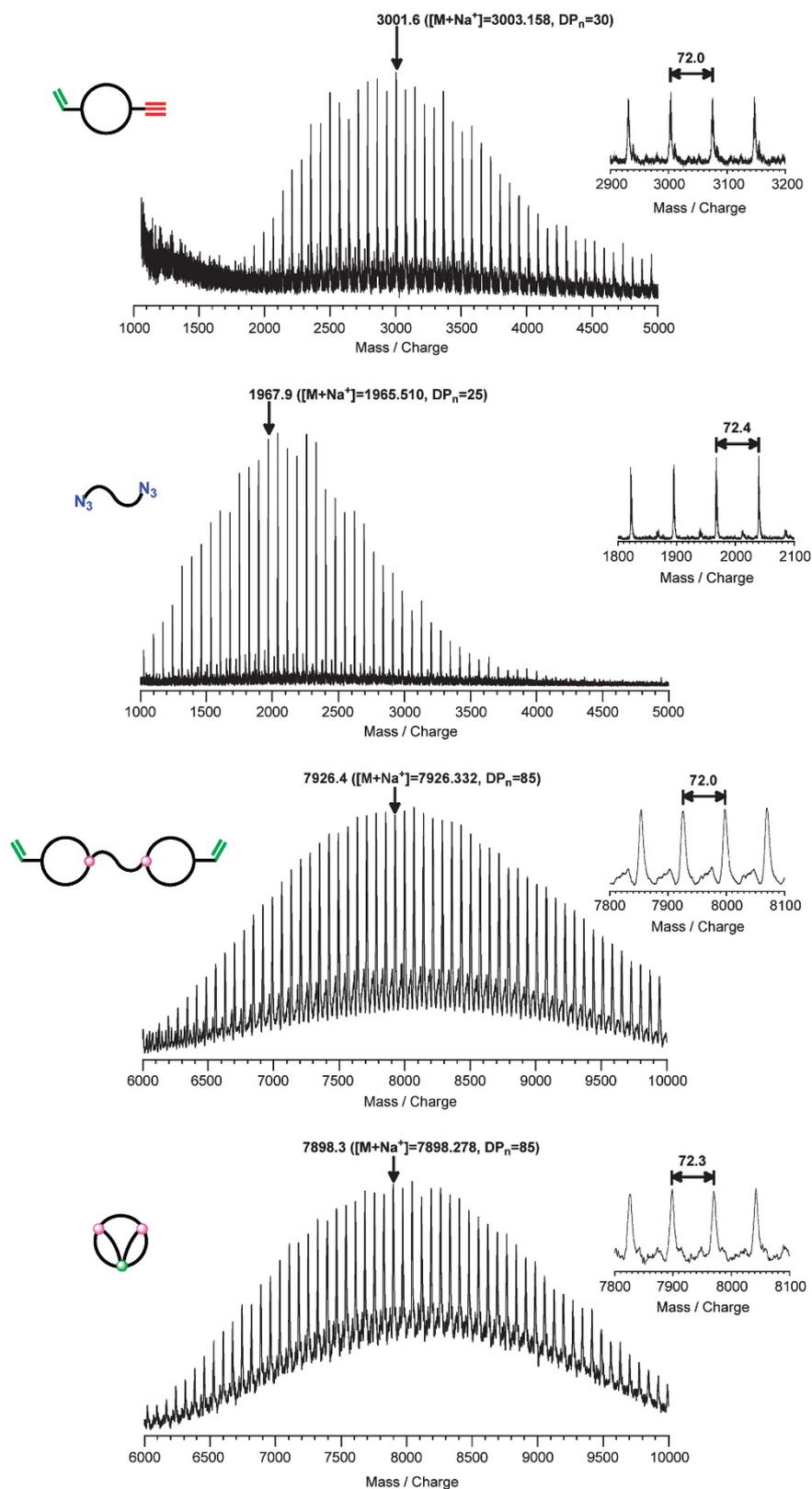


Figure 2 Matrix-assisted laser desorption/ionisation-time of flight mass spectra of a γ -graph polymer and its precursors. Reprinted with permission from Sugai *et al.*⁵⁸ Copyright (2011) American Chemical Society.

subsequent click reaction was performed in the presence of copper sulfate and sodium ascorbate by using these complementary polymer precursors to produce a bridged-dicyclic (manacle) polymer precursor with two allyloxy groups at the opposite positions of the ring units. Finally, an intramolecular olefin metathesis reaction (clip) of the bridged-dicyclic polymer precursor was conducted under dilution (0.2 g l^{-1}) by the repeated addition of a Grubbs' catalyst first generation into the reaction solution.

^1H -nuclear magnetic resonance was used to monitor the chemical transformation to produce the γ -graph polymer from the polymer precursors. As shown in Figure 1, the signal of the ethynyl protons at 2.53 p.p.m. in the cyclic polymer precursor and the signal of the azidomethylene protons at 3.30 p.p.m. in the linear polymer precursor were replaced by a triazole proton signal at 7.65 p.p.m., confirming the effective click reaction producing a manacle-shaped precursor. The signals for the allyloxy units at 5.26–5.44 and 5.99–6.12 p.p.m. can be seen to remain intact during the click process. After the metathesis (clip) reaction, the signals of the allyloxy units are completely replaced by those of the inner olefinic units at 6.07–6.12 (*cis*) and 5.90–5.95 (*trans*) p.p.m., which is indicative of effective γ -graph polymer production even under applied dilution.

Moreover, matrix-assisted laser desorption/ionisation-time of flight mass spectral analysis unequivocally substantiated the production of the γ -graph polymer. In the series of precursor and the product spectra shown in Figure 2, a uniform series of peaks with an interval of 72 mass units was observed for all samples, corresponding to the repeating THF units; moreover, each peak exactly matched the molar mass calculated from the chemical structures of the products. Thus, for the manacle-shaped polymer precursor, the peak at $m/z = 7926.4$, which is assumed to be the adduct with Na^+ , corresponds to the expected chemical structure with the expected degree of polymerization, DP_n of 85; $(\text{C}_4\text{H}_8\text{O}) \times 85 + \text{C}_{104}\text{H}_{128}\text{N}_{10}\text{O}_{16}$, plus Na^+ equals 7926.332. For the γ -graph polymer, the peak at $m/z = 7898.3$, which is assumed to be the adduct with Na^+ , corresponds to the expected chemical structure with a DP_n of 85; $(\text{C}_4\text{H}_8\text{O}) \times 85 + \text{C}_{102}\text{H}_{124}\text{N}_{10}\text{O}_{16}$, plus Na^+ equals 7898.278. As the γ -graph polymer is produced from a manacle-shaped precursor by the elimination of an ethylene molecule, their molecular weights differ by 28 mass units. This result was confirmed by the comparison of the two mass spectra shown in Figure 2.

CONCLUDING REMARKS AND FUTURE PERSPECTIVES

Numerous future opportunities are anticipated with ongoing progress in topological polymer chemistry. The new concept of topological isomerism has now been introduced for the hierarchical classification of nonlinear and multicyclic polymer constructions. A pair of topological isomers that occur uniquely in flexible nonlinear polymer architectures has indeed been synthesized by the ESA-CF process with newly designed telechelic polymer precursors that contain cyclic ammonium salt groups. Further synthetic challenges should include topologically significant polymers, such as tricyclic α - and β -graph constructions, as well as a tetracyclic $\text{K}_{3,3}$ construction by using specifically designed telechelic precursors with appropriate Cayley-tree constructions. These syntheses will extend the current frontier of synthetic polymer chemistry.¹⁴ In addition, topological polymer chemistry now offers unique opportunities for the exploration of any topological effects in polymer materials because a variety of topologically defined polymers have now become systematically available.¹⁴ With theoretical and simulation progress, we expect to achieve unique topological control over static and dynamic properties that rely on conjectures of topological geometry, particularly but not

limited to those intuitively envisaged from common Euclidian geometry.

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- 1 Tezuka, Y. *Topology Designing (in Japanese)* (NTS, Tokyo, 2009) (ISBN978-4-86043-162-4).
- 2 Tezuka, Y. Topological polymer chemistry: an insight with Poincaré into nonlinear macromolecular constructions (in Japanese). *Kobunshi* **57**, 81–85 (2008).
- 3 Service, R. F. DNA nanotechnology grows up. *Science* **332**, 1140–1143 (2011).
- 4 Turberfield, A. J. Geometrical self-assembly. *Nature Chem.* **3**, 580–581 (2011).
- 5 Lin, C., Liu, Y. & Yan, H. Designer DNA nanoarchitectures. *Biochemistry* **48**, 1663–1674 (2009).
- 6 Hadjichristidis, N., Hiraio, A., Tezuka, Y. & Du Prez, F. eds *Complex Macromolecular Architectures, Synthesis, Characterization and Self-Assembly* (Wiley, Singapore, 2011).
- 7 Ouchi, M., Badi, N., Lutz, J.-F. & Sawamoto, M. Single-chain technology using discrete synthetic macromolecules. *Nature Chem.* **3**, 917–924 (2011).
- 8 Semlyen, J. A. ed. *Cyclic Polymers*. 2nd edn (Kluwer, Dordrecht, 2000).
- 9 Semlyen, J. A. *Large Ring Molecules* (John-Wiley & Sons, Chichester (1996)).
- 10 Yamamoto, T. & Tezuka, Y. *Synthesis of Polymers* (eds Schlueter, A. D., Hawker, C. & Sakamoto, J.) Ch. 18 (Wiley-VCH, Weinheim, 2012).
- 11 Yamamoto, T. & Tezuka, Y. Topological polymer chemistry: a cyclic approach toward novel polymer properties and functions. *Polym. Chem.* **2**, 1930–1941 (2011).
- 12 Yamamoto, T. & Tezuka, Y. Topological polymer chemistry by programmed self-assembly and effective linking chemistry. *Eur. Polym. J.* **47**, 535–541 (2011).
- 13 Yamamoto, T. & Tezuka, Y. Topological polymer chemistry: new synthesis of cyclic and multicyclic polymers and topology effects thereby (in Japanese). *Kobunshi Ronbunshu* **68**, 782–794 (2011).
- 14 Tezuka, Y. & Oike, H. Topological polymer chemistry: systematic classification of nonlinear polymer topologies. *J. Am. Chem. Soc.* **123**, 11570–11576 (2001).
- 15 Rouvray, D. H. Isomer enumeration methods. *Chem. Soc. Rev.* **3**, 355–372 (1974) references cited therein.
- 16 Berzelius, J. J. Ueber die Zusammensetzung der Weinsäure und Traubensäure (John's Säure aus den Vogesen), über das Atomgewicht des Bleioxyds, nebst allgemeinen Bemerkungen über solcher Körper, die gleiche Zusammensetzung, aber ungleiche Eigenschaften besitzen. *Pogg. Ann.* **19**, 305–335 (1830).
- 17 Kekulé, F. A. Ueber die Constitution und die Metamorphosen der chemischen Verbindungen und über die chemische Natur des Kohlenstoffs. *Ann. Chem.* **106**, 129–159 (1858).
- 18 Oike, H., Imaizumi, H., Mouri, T., Yoshioka, Y., Uchibori, A. & Tezuka, Y. Designing unusual polymer topologies by electrostatic self-assembly and covalent fixation. *J. Am. Chem. Soc.* **122**, 9592–9599 (2000).
- 19 Tezuka, Y., Tsuchitani, A. & Oike, H. Synthesis of polymeric topological isomers through electrostatic self-assembly and covalent fixation with telechelic poly(THF) having cyclic ammonium salt groups. *Polym. Int.* **52**, 1579–1583 (2003).
- 20 Tezuka, Y., Tsuchitani, A. & Oike, H. Synthesis of polymeric topological isomers through electrostatic self-assembly and covalent fixation with star telechelic precursors. *Macromol. Rapid Commun.* **25**, 1531–1535 (2004).
- 21 Tezuka, Y. & Ohashi, F. Synthesis of polymeric topological isomers through double metathesis condensation with H-shaped telechelic precursors. *Macromol. Rapid Commun.* **26**, 608–612 (2005).
- 22 Vakhrushev, A., Gorbunov, A., Tezuka, Y., Tsuchitani, A. & Oike, H. Liquid chromatography of theta-shaped and three-armed star poly(THF)s: theory and experimental evidence of topological separation. *Anal. Chem.* **80**, 8153–8162 (2008).
- 23 Tezuka, Y., Takahashi, N., Sato, T. & Adachi, K. Synthesis of polymeric topological isomers having theta- and manacle-constructions with olefinic groups at designated positions. *Macromolecules* **40**, 7910–7918 (2007).
- 24 Ishikawa, K., Yamamoto, T., Harada, H. & Tezuka, Y. Synthesis and topological conversion of an 8-shaped poly(THF) having a metathesis-cleavable unit at the focal position. *Macromolecules* **43**, 7062–7067 (2010).
- 25 Ishikawa, K., Yamamoto, T., Asakawa, M. & Tezuka, Y. Effective synthesis of polymer catenanes by cooperative electrostatic/hydrogen-bonding self-assembly and covalent fixation. *Macromolecules* **43**, 168–176 (2010).
- 26 Endo, K. Synthesis and properties of cyclic polymers. *Adv. Polym. Sci.* **217**, 121–183 (2008).
- 27 Laurent, B. A. & Grayson, S. M. Synthetic approaches for the preparation of cyclic polymers. *Chem. Soc. Rev.* **38**, 2202–2213 (2009).
- 28 Kricheldorf, H. R. Cyclic polymers: synthetic strategies and physical properties. *J. Polym. Sci., Part A: Polym. Chem.* **48**, 251–284 (2010).
- 29 Adachi, K. & Tezuka, Y. Topological polymer chemistry in pursuit of elusive polymer ring constructions. *J. Synth. Org. Chem., Jpn.* **67**, 1136–1143 (2009).

- 30 Grayson, S. M. Polymer kept in the loop. *Nature Chem.* **1**, 178–179 (2009).
- 31 Takano, A., Kushida, Y., Aoki, K., Masuoka, K., Hayashida, L., Cho, D., Kawaguchi, D. & Matsushita, Y. HPLC characterization of cyclization reaction product obtained by end-to-end ring closure reaction of a telechelic polystyrene. *Macromolecules* **40**, 679–681 (2007).
- 32 Laurent, B. A. & Grayson, S. M. An efficient route to well-defined macrocyclic polymers via 'click' cyclization. *J. Am. Chem. Soc.* **128**, 4238–4239 (2006).
- 33 Ye, J., Xu, J., Hu, J., Wang, X., Zhang, G., Liu, S. & Wu, C. Comparative study of temperature-induced association of cyclic and linear poly(*N*-isopropylacrylamide) chains in dilute solutions by laser light scattering and stopped-flow temperature jump. *Macromolecules* **41**, 4416–4422 (2008).
- 34 Qiu, X. P., Tanaka, F. & Winnik, F. M. Temperature-induced phase transition of well-defined cyclic poly(*N*-isopropylacrylamide)s in aqueous solution. *Macromolecules* **40**, 7069–7071 (2007).
- 35 Xu, J., Ye, J. & Liu, S. Y. Synthesis of well-defined cyclic poly(*N*-isopropylacrylamide) via click chemistry and its unique thermal phase transition behavior. *Macromolecules* **40**, 9103–9110 (2007).
- 36 Tezuka, Y. & Komiya, R. Metathesis polymer cyclization with telechelic poly(THF) having allyl groups. *Macromolecules* **35**, 8667–8669 (2002).
- 37 Hayashi, S., Adachi, K. & Tezuka, Y. An Efficient Route to cyclic polymers by ATRP-RCM process. *Chem. Lett.* **36**, 982–983 (2007).
- 38 Adachi, K., Honda, S., Hayashi, S. & Tezuka, Y. ATRP-RCM synthesis of cyclic diblock copolymers. *Macromolecules* **41**, 7898–7903 (2008).
- 39 Baba, E., Honda, S., Yamamoto, T. & Tezuka, Y. ATRP-RCM polymer cyclization: Synthesis of amphiphilic cyclic polystyrene-*b*-poly(ethylene oxide) copolymers. *Polym. Chem.* (doi:10.1039/c1py00475a).
- 40 Honda, S., Yamamoto, T. & Tezuka, Y. Topology-directed control of thermal stability: Micelles formed from linear and cyclized amphiphilic block copolymers. *J. Am. Chem. Soc.* **132**, 10251–10253 (2010).
- 41 Kricheldorf, H. R. & Eggerstedt, S. Macrocycles, 5. Ring expansion of macrocyclic tin alkoxides with cyclic anhydrides. *Macromol. Chem. Phys.* **200**, 587–593 (1999).
- 42 Shea, K. J., Lee, S. Y. & Busch, B. B. A new strategy for the synthesis of macrocycles. The polyhomologation of boracyclanes. *J. Org. Chem.* **63**, 5746–5747 (1998).
- 43 Li, H., Debuigne, A., Jérôme, R. & Lecomte, P. Synthesis of Macrocylic poly(ϵ -caprolactone) by intramolecular cross-linking of unsaturated end groups of chains precyclic by the initiation. *Angew. Chem., Int. Ed.* **45**, 2264–2267 (2006).
- 44 Schappacher, M. & Deffieux, A. Synthesis of macrocyclic copolymer brushes and their self-assembly into supramolecular tubes. *Science* **319**, 1512–1515 (2008).
- 45 Bielawski, C. W., Benitez, D. & Grubbs, R. H. An 'endless' route to cyclic polymers. *Science* **297**, 2041–2044 (2002).
- 46 Boydston, A. J., Holcombe, T. W., Unruh, D. A., Fréchet, J. M. J. & Grubbs, R. H. A direct route to cyclic organic nanostructures via ring-expansion metathesis polymerization of a dendronized macromonomer. *J. Am. Chem. Soc.* **131**, 5388–5389 (2009).
- 47 Zhang, K., Lackey, M. A., Wu, Y. & Tew, G. N. Universal cyclic polymer templates. *J. Am. Chem. Soc.* **133**, 6906–6909, 10253 (2011).
- 48 Culkin, D. A., Jeong, W., Csihony, S., Gomez, E. D., Balsara, N. P., Hedrick, J. L. & Waymouth, R. M. Zwitterionic polymerization of lactide to cyclic poly(lactide) by using *N*-heterocyclic carbene organocatalysts. *Angew. Chem., Int. Ed.* **46**, 2627–2630 (2007).
- 49 Adachi, K., Irie, H., Sato, T., Uchibori, A., Shiozawa, M. & Tezuka, Y. Electrostatic self-assembly and covalent fixation with cationic and anionic telechelic precursors for new loop and branch polymer topologies. *Macromolecules* **38**, 10210–10219 (2005).
- 50 Adachi, K., Takasugi, H. & Tezuka, Y. Telechelics having unstrained cyclic ammonium salt groups for electrostatic polymer self-assembly and ring-emitting covalent fixation. *Macromolecules* **39**, 5585–5588 (2006).
- 51 Habuchi, S., Satoh, N., Yamamoto, T., Tezuka, Y. & Vacha, M. Multimode diffusion of ring polymer molecules revealed by a single-molecule study. *Angew. Chem., Int. Ed.* **49**, 1418–1421 (2010).
- 52 Otera, J. & Nishikido, J. (eds) *Esterification Methods, Reactions and Applications* (Wiley-VCH, Weinheim, 2010).
- 53 Tezuka, Y., Komiya, R. & Washizuka, M. Designing 8-shaped polymer topology by metathesis condensation with cyclic poly(THF) precursors having allyl groups. *Macromolecules* **36**, 12–17 (2003).
- 54 Sugai, N., Heguri, H., Ohta, K., Meng, Q., Yamamoto, T. & Tezuka, Y. Effective click construction of bridged- and spiro-multicyclic polymer topologies with tailored cyclic prepolymers (*kyklo*-telechelics). *J. Am. Chem. Soc.* **132**, 14790–14802 (2010).
- 55 Craik, D. J. Seamless Proteins tie up their loose ends. *Science* **311**, 1563–1564 (2006).
- 56 Tezuka, Y., Tsuchitani, A., Yoshioka, Y. & Oike, H. Synthesis of theta-shaped poly(THF) by electrostatic self-assembly and covalent fixation with three-armed star telechelics having cyclic ammonium salt groups. *Macromolecules* **36**, 65–70 (2003).
- 57 Tezuka, Y. & Fujiyama, K. Construction of polymeric delta-graph: a doubly-fused tricyclic topology. *J. Am. Chem. Soc.* **127**, 6266–6270 (2005).
- 58 Sugai, N., Heguri, H., Yamamoto, T. & Tezuka, Y. A programmed polymer folding: Click and clip construction of doubly fused tricyclic and triply fused tetracyclic polymer topologies. *J. Am. Chem. Soc.* **133**, 19694–19697 (2011).



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