

Review

Recent Advances of CuAAC Click Reaction in Building Cyclic Polymer^{*}

Zhi-hao Huang, Yan-yan Zhou, Zi-mu Wang, Ying Li, Wei Zhang, Nian-chen Zhou,
Zheng-biao Zhang^{**} and Xiu-lin Zhu^{**}

State and Local Joint Engineering Laboratory for Novel Functional Polymeric Materials, Jiangsu Key Laboratory of Advanced Functional Polymer Design and Application, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123, China

Abstract Cyclic polymers have attracted more and more attentions in recent years because of their unique topological structures and characteristic properties in both solution and bulk state. There are relatively few reports on cyclic polymers, partly because of the more demanding synthetic procedures. In recent years, “click” reaction, especially Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC), has been widely utilized in the synthesis of cyclic polymer materials because of its high efficiency and low susceptibility to side reactions. In this review, we will focus on three aspects: (1) Constructions of monocyclic polymer using CuAAC “click” chemistry; (2) Formation of complex cyclic polymer topologies through CuAAC reactions; (3) Using CuAAC “click” reaction in the precise synthesis of molecularly defined macrocycles. We believe that the CuAAC click reaction is playing an important role in the design and synthesis of functional cyclic polymers.

Keywords Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC); “Click” chemistry; Cyclic polymer; Reversible deactivation radical polymerization (RDRP); Atom transfer radical polymerization (ATRP); Reversible addition-fragmentation chain transfer polymerization (RAFT)

INTRODUCTION

Cyclic polymers as one of the oldest topological polymers, have regained more and more attention on account of the recent developments in macromolecular architecture approaches and synthetic chemistry^[1–5]. Studies have revealed that, compared with their linear counterparts, cyclic polymers with no terminals demonstrate remarkable and unique performance, including a smaller hydrodynamic volume, less chain entanglement, higher glass transition temperature, increased rate of crystallization^[6, 7] and so on. Some interesting properties, functionalities and utilities of these cyclic polymer-based materials have been investigated including the self-assembly behaviors^[8–12], and potential applications in biomedical area^[13–16]. It was found that, due to the topological effects, functional cyclic polymers usually show specific characteristics with respect to their linear precursors^[17]. For example, cyclic topologies have imparted unique and improved biological properties, such as longer circulation times and improved drug loading and releasing capacity as drug carriers^[15, 18], as well as reduced cytotoxicity and higher transfection efficiency as gene delivery agents^[16, 19]. However, efficient synthetic routes for high-purity cyclic polymers remain an important task within the polymer synthesis

^{*} This work was financially supported by the National Natural Science Foundation of China (No. 21234005), the State and Local Joint Engineering Laboratory for Novel Functional Polymeric Materials, the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD) and the Program of Innovative Research Team of Soochow University.

^{**} Corresponding authors: Zheng-biao Zhang (张正彪), E-mail: zhangzhengbiao@suda.edu.cn

Xiu-lin Zhu (朱秀林), E-mail: xlzhu@suda.edu.cn

Received September 5, 2016; Revised September 27, 2016; Accepted September 28, 2016

doi: 10.1007/s10118-017-1902-0

community.

It is well known that ring-closure and ring-expansion, which are two main synthetic strategies for cyclic polymers, have their respective pros and cons and complement each other in the preparation of cyclic polymers including cyclic polystyrene^[20], polyacrylate^[21], polyester^[22], polynorbornene^[23], and complex cyclic topologies such as theta^[24], eight^[24], tadpole^[25] and block shapes^[26]. Among them, the ring-closure strategy for cyclic polymer is popularly used due to more available monomers, high design ability of linear precursors and good controllability of resultant polymers. The ring-closure strategy is usually conducted in highly dilute condition and requires highly effective intramolecular or intermolecular chain end coupling reactions under mild conditions for more output of resultant cyclic polymer. “Click” reaction is undoubtedly the best choice for fulfilling the criteria.

The term “click” chemistry^[27] was first introduced in 1999 by Sharpless *et al.* at the 217th American Chemical Society annual meeting. A set of stringent criteria is necessary to define a reaction as a click reaction. The reaction must be modular and broad in scope, must afford high to excellent reaction yield, must generate only inoffensive byproducts that could be removed by non-chromatographic method, and must be stereospecific (but not necessarily enantioselective). The required process characteristics include simple reaction conditions, readily available starting materials and reagents, the use of no solvent or a benign solvent easily removed and simple product isolation^[27].

Copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction satisfies all the stringent criteria of the Sharpless click chemistry concept, as this reaction is simple to perform, and is modular and wide in scope, highly efficient, high yielding, and regiospecific. Moreover, it creates no or inoffensive byproducts. Lastly, it requires readily available alkynes/azides as starting materials and reagents such as copper catalysts, along with easily removable or benign solvents. Since its emergence, CuAAC has become an important member of “click” reaction family and has been widely used in polymer synthesis^[27], topology construction^[4] and preparation of biology-related polymer materials^[15].

Our review will focus on the recent applications of CuAAC click reaction in cyclic polymers, focusing on three key aspects as follows:

- (a) Combination of reversible deactivation radical polymerization (RDRP) and CuAAC click reaction to construct monocyclic functional polymers;
- (b) Construction of cyclic polymer-based complex topologies through CuAAC reactions;
- (c) Applications of CuAAC click reaction in the precise synthesis of molecularly defined cyclic oligomers/polymers.

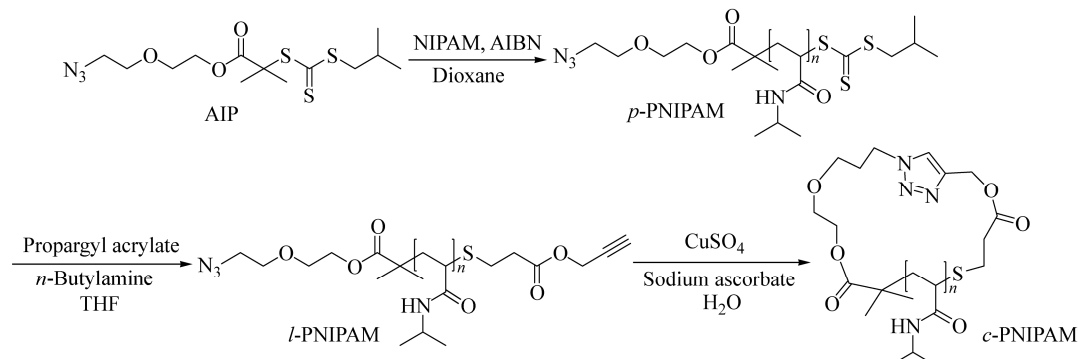
COMBINATION OF RDRP AND CUAAC CLICK REACTION TO CONSTRUCT MONOCYCLIC FUNCTIONAL POLYMERS

The combination of RDRP and click reactions (especially CuAAC click reaction) has allowed a versatile synthetic methodology for building complex polymer architectures. RDRP, mainly including atom transfer radical polymerization (ATRP)^[28], nitroxide-mediated polymerization (NMP), and reversible addition-fragmentation chain transfer polymerization (RAFT)^[29], is a robust technique to produce polymer chains with controlled molecular weight, polydispersity, and chain-end functionality^[28–33]. Modification of these chain ends with appropriate chemical motifs and followed by intra (inter) molecular click coupling reactions in high dilution condition usually produces the cyclic product in high yields^[33–35].

Combination of RAFT and CuAAC Click Reaction

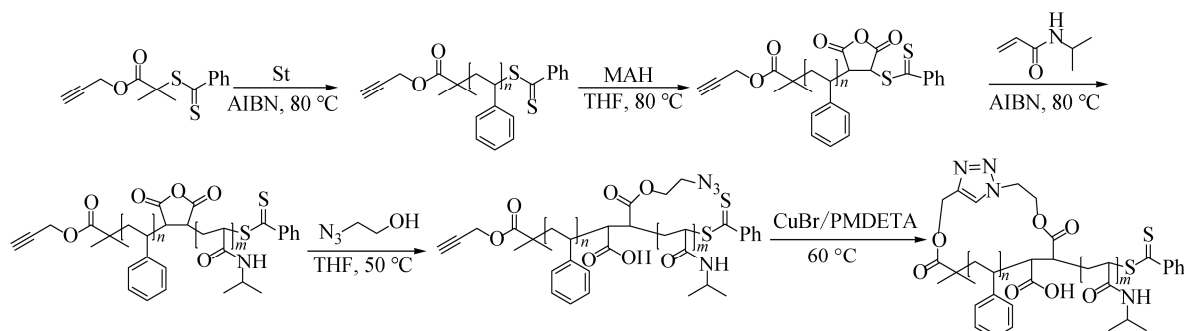
Among RDRP, RAFT polymerization is one of the most robust RDRP techniques. The main advantage of RAFT is that it can be used for a much wider range of functional and nonfunctional monomers, and more importantly, it can be used to polymerize monomers in various solvents even in an aqueous environment at low temperatures. Winnik *et al.* prepared *c*-PNIPAM using RAFT-synthesized α,ω -heterodifunctional telechelic PNIPAAm precursors. The latter was converted to a propargyl group in a one-pot aminolysis/Michael addition sequence,

yielding the desired α -azido- ω -propargyltelechelic linear precursors *l*-PNIPAM. Finally, CuAAC click reaction was used to obtain cyclic polymer *c*-PNIPAM^[36] (Scheme 1).



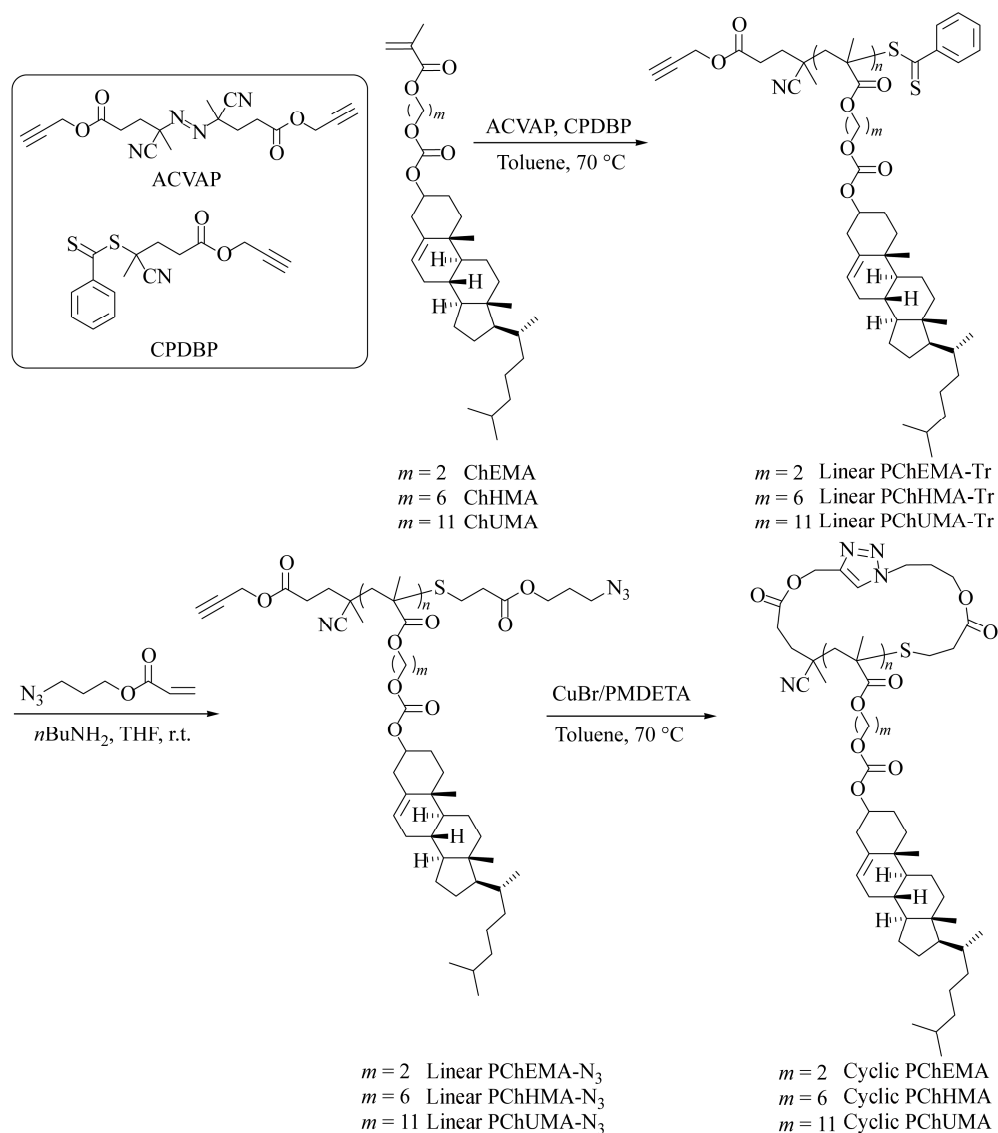
Scheme 1 Synthesis of cyclic PNIPAM (Reprinted with permission from Ref. [36]; Copyright (2007) American Chemical Society)

Pan *et al.* prepared successfully a tadpole-shaped amphiphilic copolymer by combination of RAFT polymerization and CuAAC click chemistry. The synthesis included two steps, preparation of linear acetylene-terminated PS-*b*-PNIPAAM with a side azido group at the junction between PS and PNIPAAM; then cyclization of the linear diblock copolymers under high dilution. A very ingenious design that they made was the addition reaction of PS-SC(S)Ph with MAH and esterification of MAH in the polymer chains with $\text{N}_3\text{CH}_2\text{CH}_2\text{OH}$. In comparison with the linear diblock copolymer, the tadpole-shaped polymers were of lower molecular weight, and the values of $\langle G \rangle$ (the ratio $\langle G \rangle$ of cyclic $[M_n(c)]$ and linear $[M_n(l)]$ polymers' molecular weights measured by GPC method was used to characterize the formation of cyclic polymers) were in the range of 0.86–0.97, which increased with the growth of PNIPAAM chain length. The water contact angle of the linear PNIPAAM-*b*-cyclic PS was higher than that of its parent linear one^[37] (Scheme 2).



Scheme 2 Preparation of tadpole-shaped copolymers (Reprinted with permission from Ref. [37]; Copyright (2008) John Wiley & Sons Inc)

In 2015, our group described a rational design and facile synthesis of biomacrocyclic side-chain liquid crystalline polymers bearing cholesterol mesogens with three different lengths of methylene spacers ($m = 2, 6, 11$) *via* the combination of RAFT polymerization with CuAAC (Scheme 3). Subsequently, the liquid crystalline (LC) phase behaviors of the linear and the cyclic polymers were investigated systematically. Both linear and the cyclic polymers formed the smectic phase and exhibited a similar layer periodicity. However, the cyclic ones exhibited a slightly lower mesophase transition temperature, enthalpy, entropy and smaller textures compared with their linear counterparts. Meanwhile, the smectic C (SmC) phase was preferable in the cyclic polymers with a long methylene spacer ($m = 11$) compared with that in the linear ones^[38].



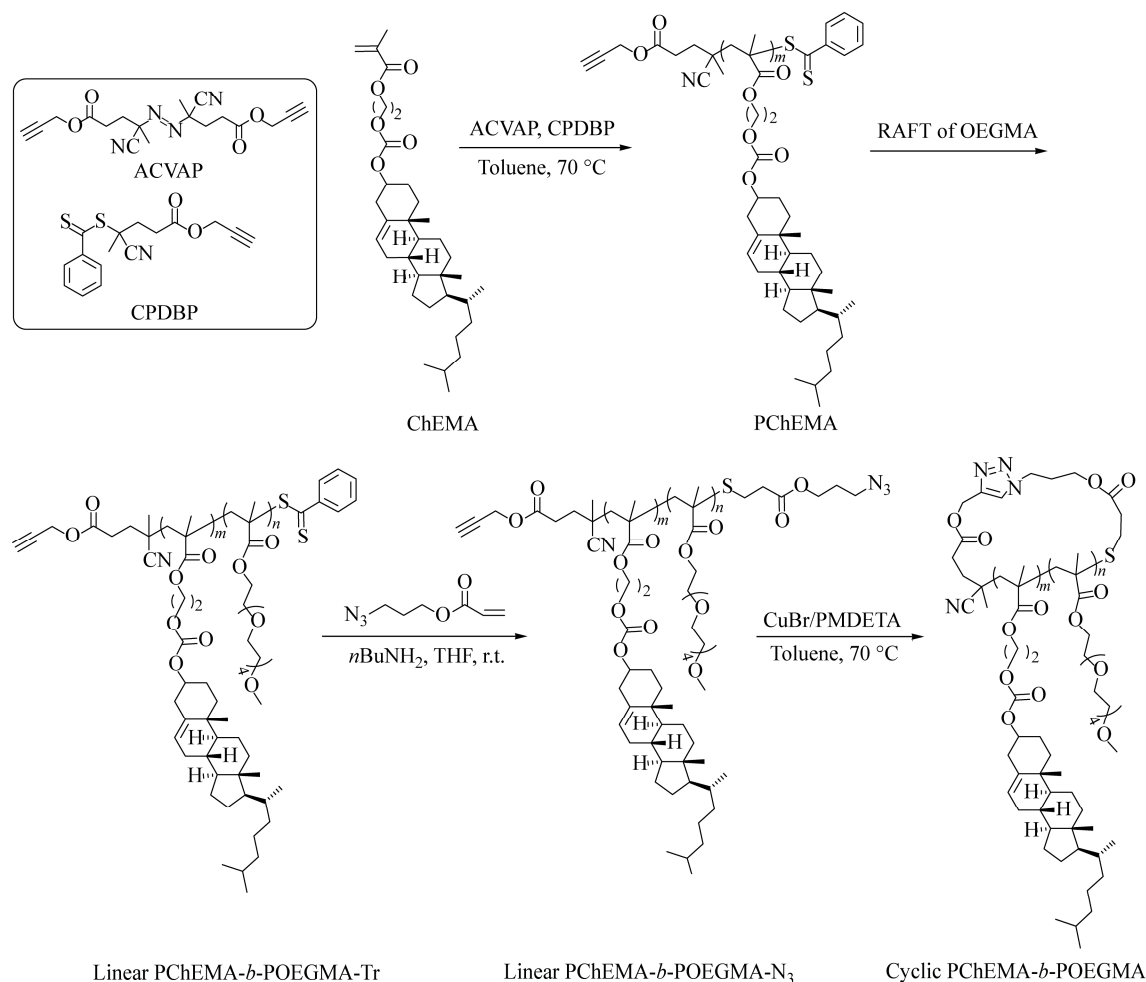
Scheme 3 The synthetic routes towards SCLCP-containing linear and cyclic cholesteryl (Reproduced from Ref. [38] with permission from The Royal Society of Chemistry)

In a further research, our group reported the synthesis of amphiphilic macrocycles containing polymeric liquid crystal grafts. The combination of RAFT copolymerization with CuAAC click ring-closure reaction successfully produced the amphiphilic LC macrocycles (Scheme 4). It was found that macrocyclic LC block copolymer amphiphiles and their linear analogues exhibited distinct self-assembly behavior owing to their inherent topological differences. In particular, the macrocyclic architecture would weaken the order of cholesteryl mesogens, thereby not being able to drive the whole macromolecule to self-organize into the classic smectic cylindrical micelles, which were usually formed by most linear LC amphiphiles^[39].

Combination of ATRP and CuAAC Click Reaction

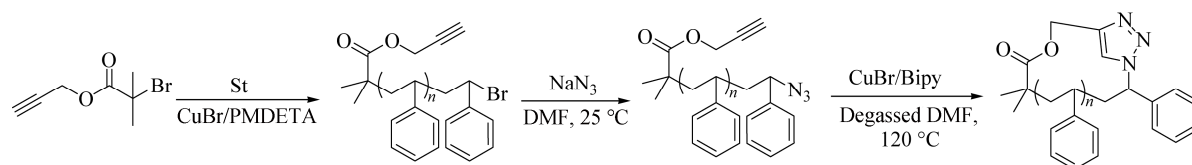
The combination of ATRP and CuAAC seems to be a classic and convenient ring-closure method to achieve cyclic polymers^[6, 40]. ATRP can introduce necessary functional groups, such as alkynyl group, into polymers by designing multifunctional initiators in advance, and the halogen atom at the chain end of the linear-polymer can be easily substituted by azide group, which is essential to CuAAC. The following CuAAC carried out under high

dilution can provide cyclic polymers in nearly quantitative. A series of monomers, including styrene, methacrylates, acrylates, acrylamides and other functional monomers, have been successfully adopted to construct cyclic polymers by the combination of ATRP and CuAAC^[41–43].



Scheme 4 Synthesis of cholesterol-functionalized amphiphilic liquid crystalline macrocycles (Reproduced from Ref. [39] with permission from The Royal Society of Chemistry)

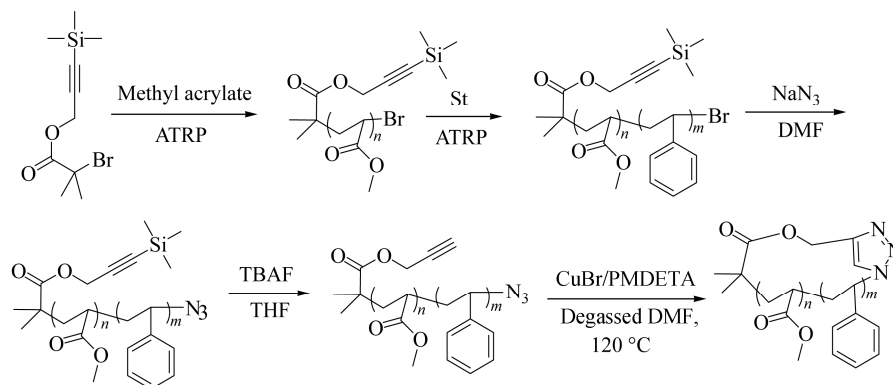
Grayson *et al.* creatively applied CuAAC click chemistry to cyclic polymers in 2006. They prepared polystyrene macrocycles from ATRP precursors containing a terminal alkyne, followed by conversion of the terminal bromide to an azide. The cyclic polystyrene was obtained by the end to end CuAAC click reaction in a highly dilute condition (Scheme 5). The product was rigorously verified by SEC, MALDI-TOF MS, NMR and FTIR^[20].



Scheme 5 The terminal azidation and “click” cyclization of polystyrene prepared *via* ATRP (Reprinted with permission from Ref. [20]; Copyright (2006) American Chemical Society)

Similarly, Monteiro *et al.* figured out in 2010 that the strategy based on the CuAAC methodology was not guided by theory and relied on the very slow feeding of polymer into a highly diluted reaction mixture of solvent and Cu catalyst. They cleverly applied the Jacobson-Stockmayer theory to the CuAAC click reaction. The same way as the reaction done by Grayson *et al.* described above, they investigated the effect of *l*-PSTY concentration, temperature, feeding rate, Cu(I)Br concentration and *l*-PSTY molecular weight in order to find out the optimal conditions for the synthesis of the monocyclic polymers. It was found that monocyclic polymers could be formed with high yield as long as the feeding rate was greater than or equal to the reaction rate. According to this strategy, *c*-PSTY (with 51 monomer units) was produced with high purity (> 95%) at a concentration of 1.85×10^{-3} mol/L in less than 9 min at 25 °C. This was the highest concentration, the shortest time, and the lowest temperature that anyone has used to obtain macrocycles in high purity by the CuAAC methodology^[41].

In 2008, Grayson *et al.* synthesized a well-defined cyclic diblock copolymers by ATRP with click coupling to cyclize α,ω -difunctional linear block copolymers (Scheme 6). And they predicted that the cyclic diblock copolymers were also able to self-assemble in solution to yield unique aggregates with their own function, such as encapsulating guests and becoming more robust nanoscale carriers. Exciting results of the later experiments by other researchers proved that such prediction was correct^[44].

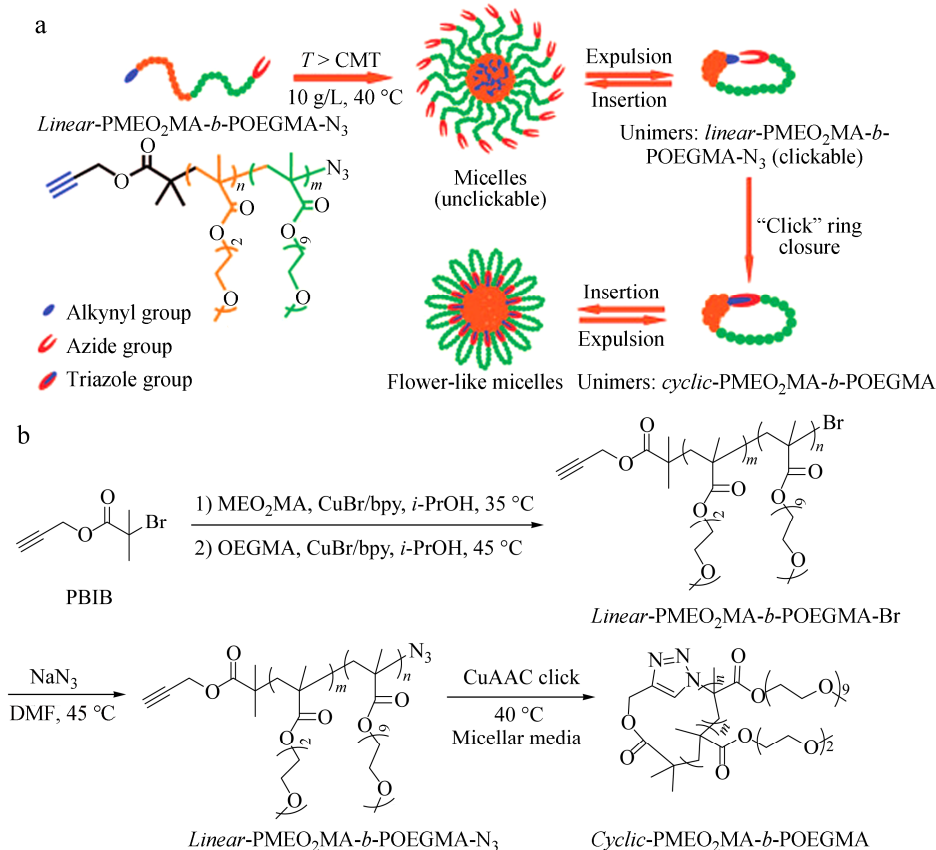


Scheme 6 Polymerization and cyclization of poly(methyl acrylate)-*b*-poly(styrene) (Reprinted with permission from Ref. [44]; Copyright (2008) American Chemical Society)

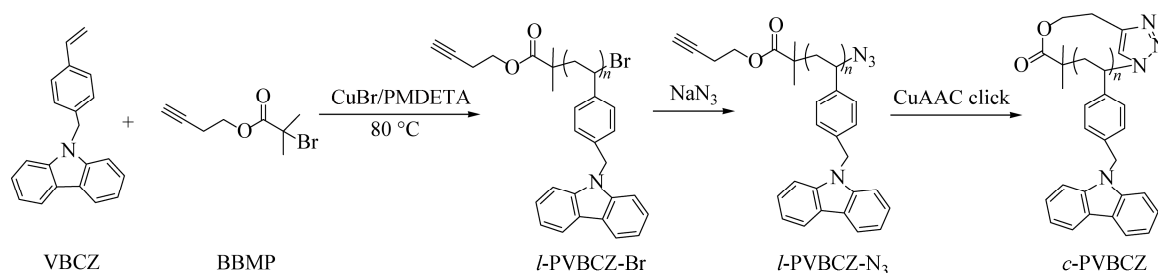
In 2009, Liu *et al.* reported a smart and alternative strategy for high-efficiency preparation of the cyclic diblock copolymers *via* the combination of supramolecular self-assembly and “selective” CuAAC click reaction (Scheme 7), taking advantage of the unimer-micelle exchange equilibrium. Within self-assembled aggregates, reactive alkynyl and azide groups were spatially separated, and intramolecular click reactions occurred exclusively for unimers, the concentration of which was well-known to be the critical micellization concentration (CMC). This led to a facile preparation of cyclic diblock copolymers from linear precursors at relatively high concentration^[42].

Cyclic polymers with functional moieties have exhibited improved or unique properties compared with their linear precursors. Therefore, it is quite meaningful to design and fabricate cyclic topologic polymers with multifunctional moieties and to investigate their topological effects on characteristic properties by comparing with their linear counterparts.

In 2011, our group presented the first example of cyclic poly((4-vinylbenzyl) carbazole) (PVBCZ) synthesized by combination of ATRP and CuAAC click reaction (Scheme 8). And its thermal properties, fluorescence, and redox behaviors were investigated. Cyclic PVBCZ exhibited unique properties in comparison with its linear form: a higher T_g , enhanced fluorescence with a longer fluorescence lifetime, and higher ΔI_p . Owing to its unique properties, cyclic PVBCZ might be a potential candidate for a charge injection/transport layer for organic electronic devices^[43].



Scheme 7 (a) Schematic illustration for the high-efficiency preparation of macrocyclic diblock copolymers *via* the combination of supramolecular self-assembly and "selective" intramolecular "click" ring closure; (b) Synthetic routes for high-efficiency preparation of *cyclic*-PMEO₂MA-*b*-POEGMA from *linear*-PMEO₂MA-*b*-POEGMA-N₃ *via* selective CuAAC click reaction under micellar conditions in aqueous solution (Reprinted with permission from Ref. [42]; Copyright (2009) American Chemical Society) (The online version is colorful.)

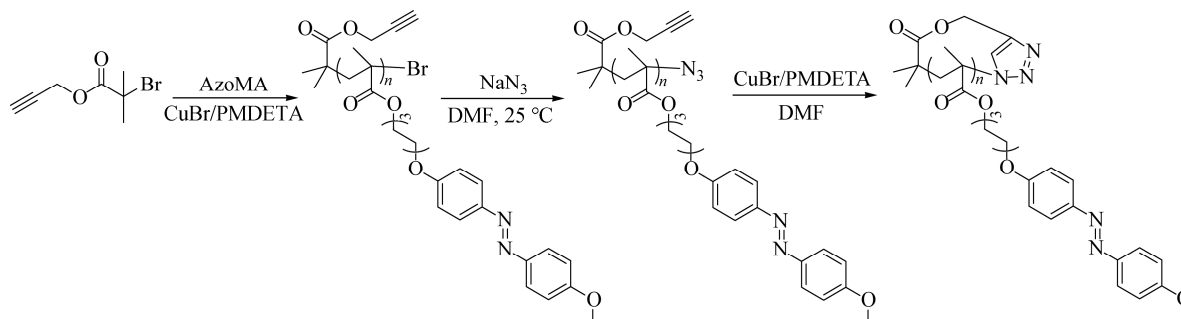


Scheme 8 Routes to the synthesis of cyclic poly((4-vinylbenzyl) carbazole) (PVBCZ) (Reprinted with permission from Ref. [43]; Copyright (2011) John Wiley & Sons Inc)

Polymers that contain an azobenzene chromophore have been extensively studied for their unique reversible photo-isomerization properties^[45–48]. Such azobenzene polymers can be potentially useful in fascinating photo-responsive applications, such as optical data storage^[49], liquid crystal displays^[50], optical switching^[51], holographic surface relief gratings (SRGs)^[52] and so on. However, there were very few reports about the cyclic polymers with the azobenzene chromophore either in the main chain or in the side chain.

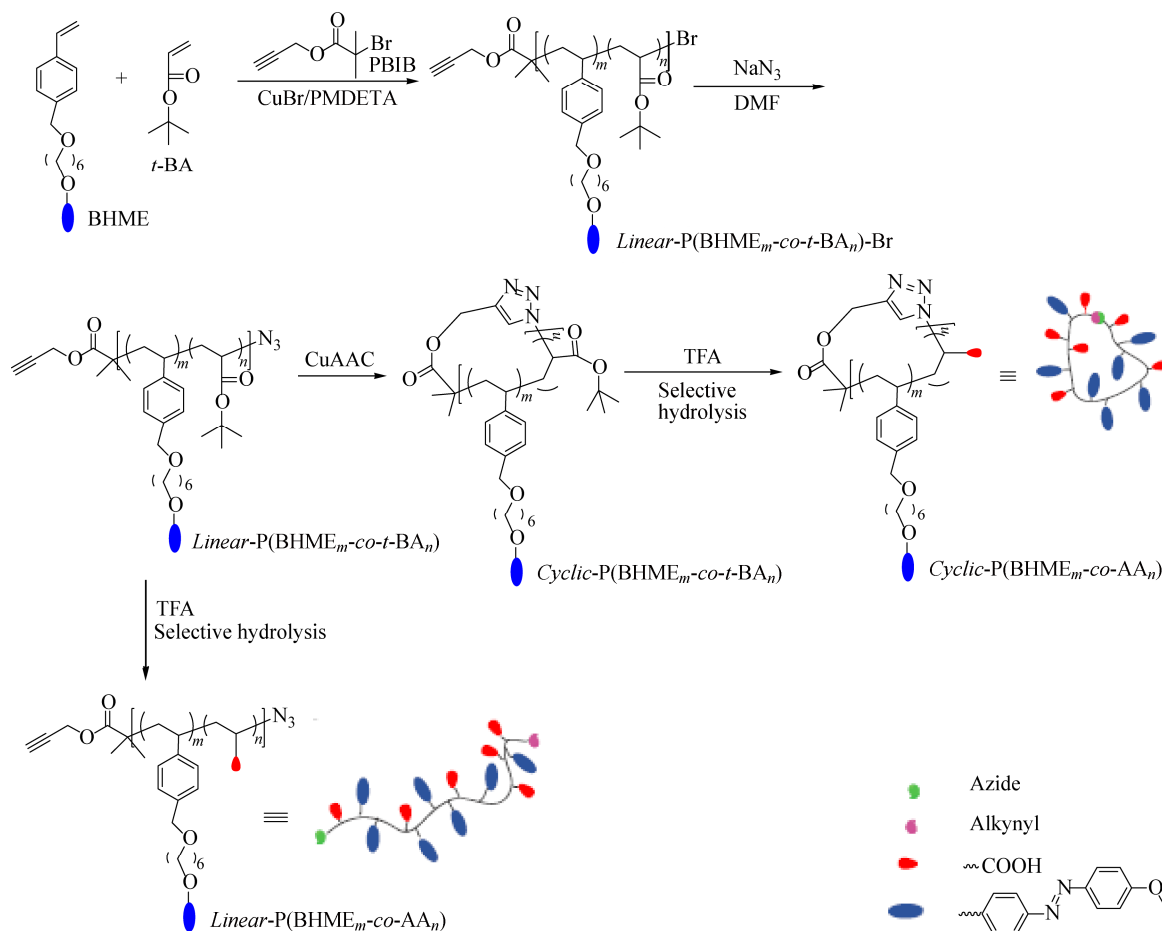
In 2010, Zhao *et al.* reported the first cyclic side-chain liquid crystalline polymer (*c*-SCLCP) with pendant azobenzene mesogenic groups. The synthesis of *c*-SCLCP was achieved by using the combination of ATRP and CuAAC click reaction (Scheme 9). The topological constraint of cyclic structure could greatly affect the

arrangement and organization of mesogenic side groups. Hence, cyclic polymers exhibited a lower mesophase transition temperature, lower enthalpy and entropy compared with the linear analogues. Moreover, they also investigated the photo-induced anisotropy in the polymer films^[53].



Scheme 9 Synthetic route to cyclic azobenzene-containing side-chain liquid crystalline polymers (Reprinted with permission from Ref. [53]; Copyright (2010) American Chemical Society)

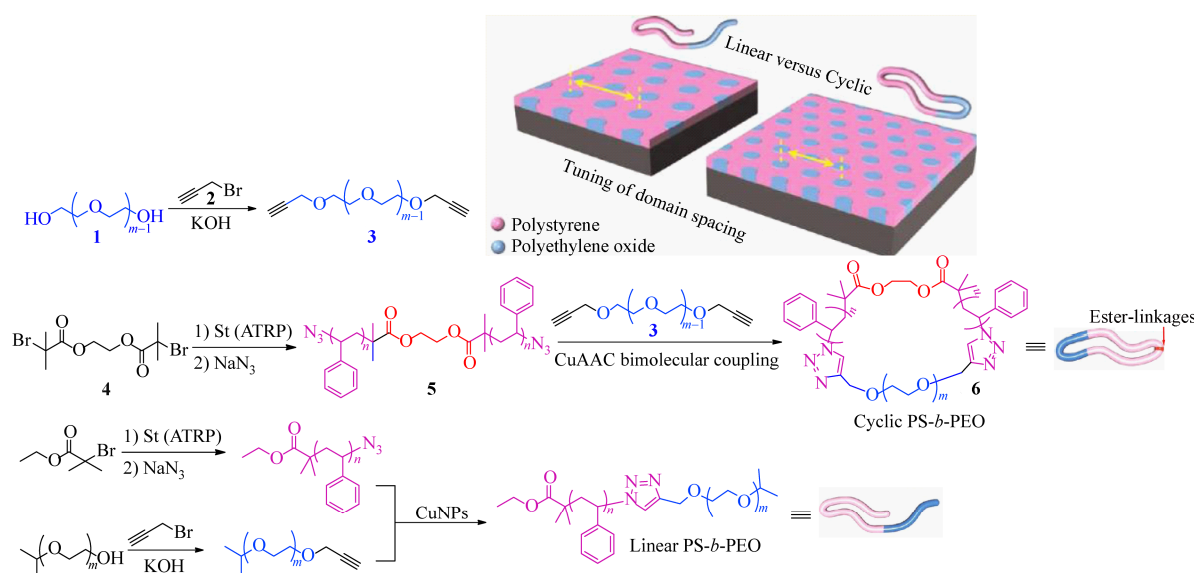
In 2014, our group reported that some well-defined cyclic amphiphilic random copolymers, bearing azobenzene side chains and pendent carboxyl moieties-cyclic $P(\text{BHME}_m\text{-co-AA}_n)$ s, were synthesized by combining ATRP with CuAAC “click” reaction and selective hydrolysis of *tert*-butyl ester (Scheme 10). The



Scheme 10 The synthetic route of the linear and cyclic $P(\text{BHME}_m\text{-co-AA}_n)$ (Reprinted with permission from Ref. [54]; Copyright (2014) John Wiley & Sons Inc) (The online version is colorful.)

cyclic-P(BHME_m-co-AA_n) exhibited higher T_g and faster *trans-cis-trans* photo-isomerization in THF than the linear ones. Due to the cyclic topology, the self-assembled aggregates of the cyclic-P(BHME_m-co-AA_n) in ethanol/THF presented smaller spherical size and slower photo-response in comparison with those of the linear precursor. The interesting photo-induced reversible formation-disruption-recovery behavior of the self-assemblies should have potential applications in drug delivery or controlled release area^[54].

In 2012, Hawker *et al.* reported a general and modular approach to the synthesis of cyclic block copolymers (cyclic PS-*b*-PEO) by Cu-catalyzed azide/alkyne bimolecular coupling of α,ω -azide-functionalized PS **5** and α,ω -alkyne PEO homopolymers **3**. The α,ω -azide-functionalized PS was synthesized from the difunctional initiator **4** via ATRP (Scheme 11). Compared with their linear (linear PS-*b*-PEO) analogues, the cyclic BCPs yielded phase-separated thin films with feature sizes less than 20 nm, which corresponded to a decrease of ~33%. These results demonstrated that macromolecular architecture should be considered as an important design feature for controlling feature size in block copolymer lithography, especially in the important sub-20 nm scale^[55].



Scheme 11 The synthetic route of the linear and cyclic PS-*b*-PEO (Reprinted with permission from Ref. [55]; Copyright (2012) American Chemical Society) (The online version is colorful.)

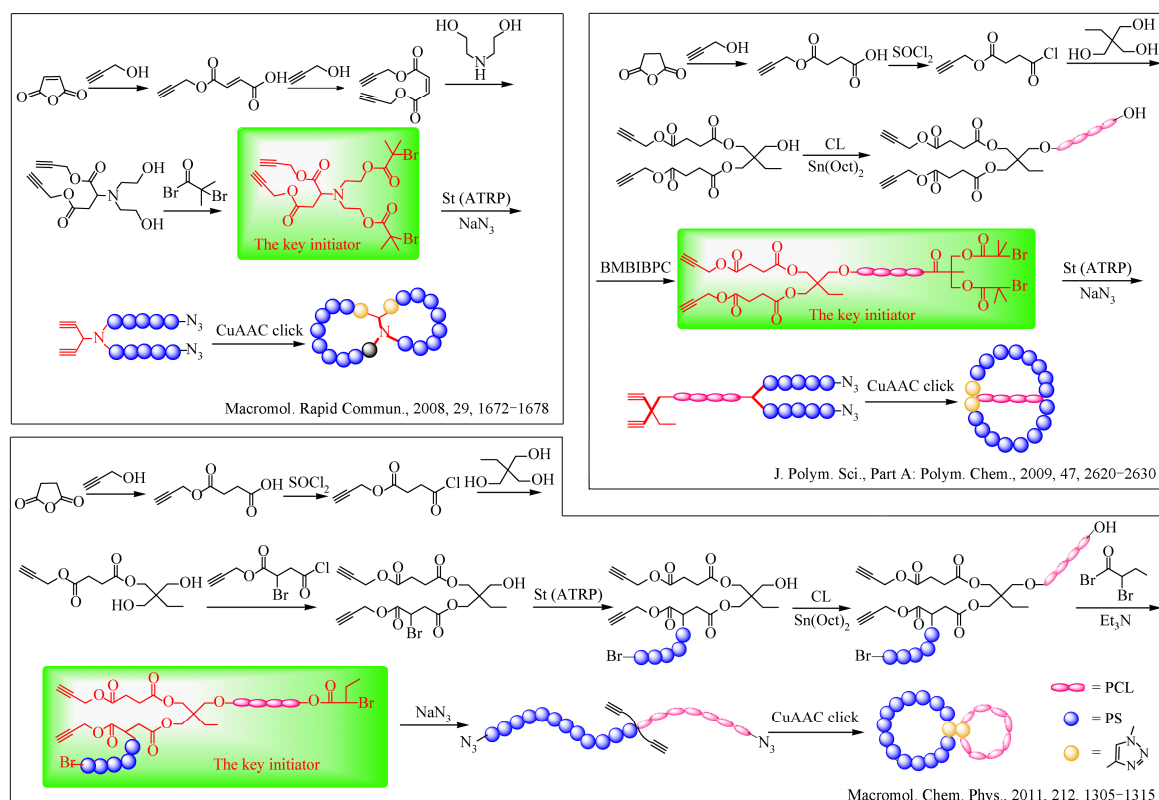
CONSTRUCTION OF CYCLIC POLYMER-BASED COMPLEX TOPOLOGIES THROUGH CUAAC REACTIONS

“Click” chemistry, like the CuAAC reaction^[27, 56], offers a toolbox for synthesis of many multi-component cyclic polymers with complicated architectures, such as β -graph, γ -graph, δ -graph^[57] and θ -shape (fused-) polymers^[24, 58]. Spiro- and bridged-polymers^[59, 60] have been constructed *via* the combination of CuAAC with electrostatic self-assembly and covalent fixation (ESA-CF). Tadpole-shaped^[25, 61, 62], sun-shaped^[63], bicyclic polymers^[64], tricyclic polymers and more^[4, 65] were also fabricated from tandem ATRP and CuAAC. For the development of cyclic-based topological polymers, CuAAC “click” reaction was usually utilized for both the ring closure reaction to afford monocyclic polymers and chemical connections between monocyclic polymer chains and other motifs. The following section will elaborate on three aspects:

- (1) Building complicated topologies *via* intramolecular CuAAC cyclization;
- (2) “Click” fragments together: build complex cyclic polymers by connecting either monocyclic building blocks or functional building blocks together using different strategies, such as CuAAC, clip and so on;
- (3) Using some novel methods, such as “insert-folding method” to form complex cyclic topologies.

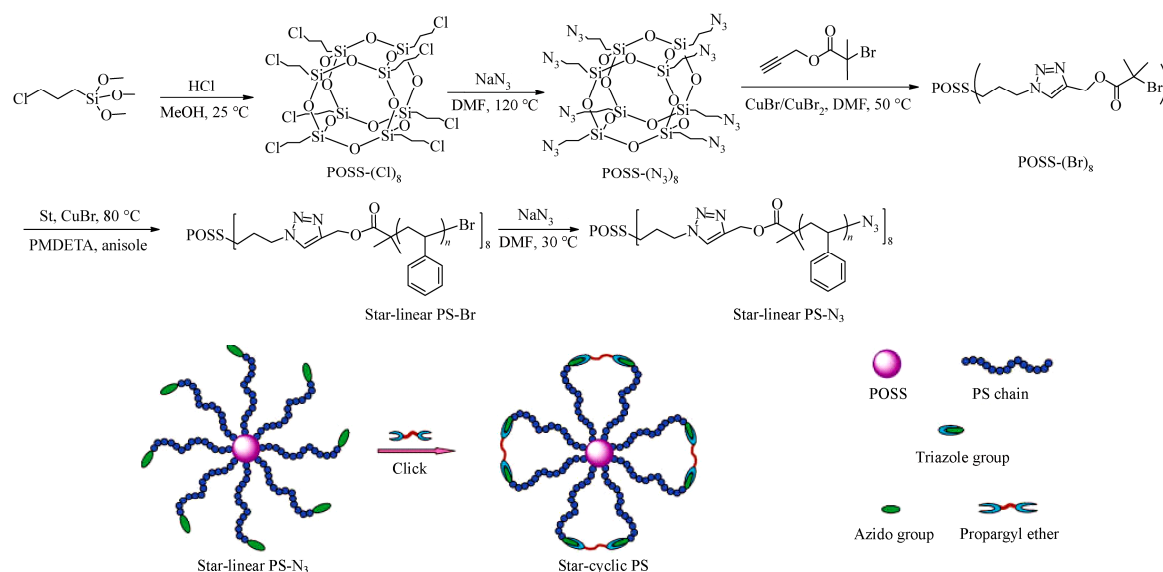
Building Complicated Topologies via Intramolecular CuAAC Cyclization (Which Is Based on the Artful Design of the Linear Precursor)

In 2008, 2009 and 2011, Pan's group described a series of complicated topology construction, including figure-of-eight-shaped, miktozyme eight-shaped and θ -shaped polymers. All of them were prepared by combination of ATRP, ring-opening polymerization (ROP) and CuAAC click chemistry. Generally, these strategies were made up of two parts: (i) Ingenious design and construction of a linear tetrafunctional key initiator; (ii) Intramolecular cyclization of the tetrafunctional linear precursor *via* CuAAC click reaction to produce the cyclic polymer with corresponding topology^[40, 66, 67] (Scheme 12).



Scheme 12 The synthesis of figure-of-eight-shaped, miktozyme eight-shaped and θ -shaped polymers (Reprinted with permission from Ref. [40]; Copyright (2008) John Wiley & Sons Inc) (Reprinted with permission from Ref. [66]; Copyright (2009) John Wiley & Sons Inc) (Reprinted with permission from Ref. [67]; Copyright (2011) John Wiley & Sons Inc) (The online version is colorful.)

In 2009, Liu *et al.* reported a proof-of-concept example of the synthesis of quatrefoil-shaped star-cyclic polystyrene (star-cyclic PS) containing polyhedral oligomeric silsesquioxane (POSS) core *via* combination of ATRP and click reactions (Scheme 13). Star-linear PS (star-linear PS- N_3) with 8-arms bearing eight terminal azide was prepared by ATRP of styrene using a POSS-based octafunctional initiator, followed by a subsequent azidation reaction. Under bimolecular CuAAC click conditions, difunctional linker propargyl ether was slowly added into the extremely diluted solution of star-linear PS- N_3 , leading to highly efficient construction of quatrefoil-shaped star-cyclic PS bearing an inorganic POSS core. DSC results revealed that the star-cyclic PS possessed higher T_g than the star-linear PS. Due to the presence of the POSS core, the star-cyclic PS could also be considered as organic/inorganic hybrid nanocomposites^[68].

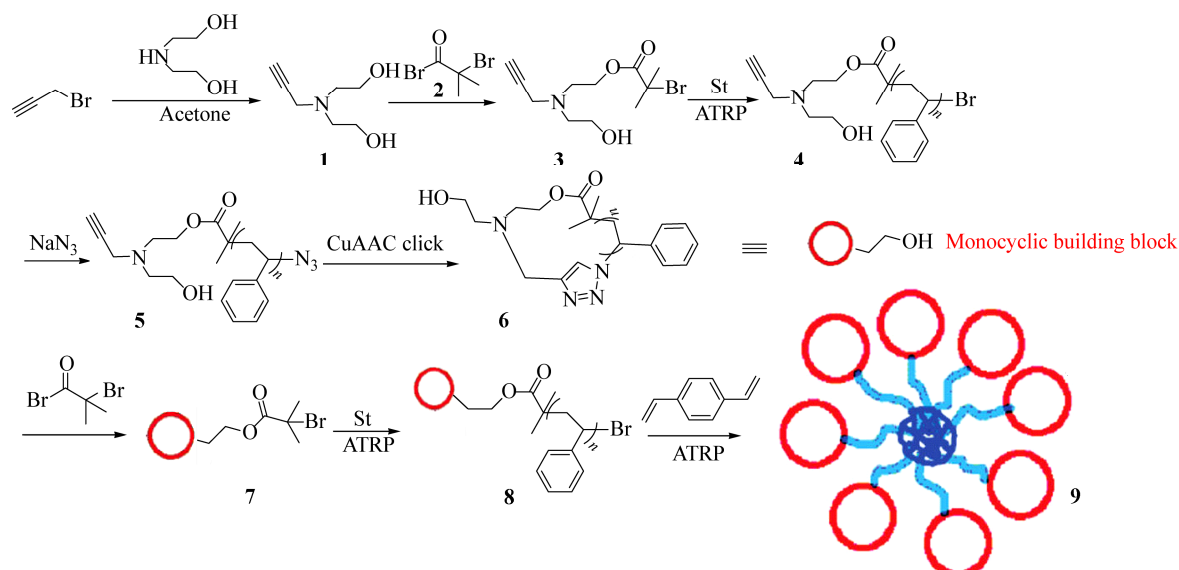


Scheme 13 Synthesis of POSS-based quaterefoil-shaped star-cyclic PS (Reprinted with permission from Ref. [68]; Copyright (2009) American Chemical Society) (The online version is colorful.)

“Click” Fragments Together: Building Complex Cyclic Polymer by Connecting Either Monocyclic Building Blocks or Functional Parts Together Using Different Strategy

Protocols of combining several monocyclic building blocks together

In 2009, Liu *et al.* synthesized macrocyclic polystyrene-terminated PS star polymers *via* a core-cross-linking approach. A tadpole-shaped macrocyclic PS-linear-PS copolymer was synthesized at first *via* click chemistry and ATRP. ATRP initiated chain-ends of the tadpole-shaped copolymers were linked together *via* ATRP polymerization with divinylbenzene to form a core-cross-linked macrocyclic star polymer (Scheme 14). The number of arms attached to the macrocyclic star polymer was measured with NMR, and the absolute molecular weight was determined by gel permeation chromatography (GPC) with multi angle laser light scattering detector.



Scheme 14 Synthesis of macrocyclic star polymer (Reprinted with permission from Ref. [69]; Copyright (2009) American Chemical Society) (The online version is colorful.)

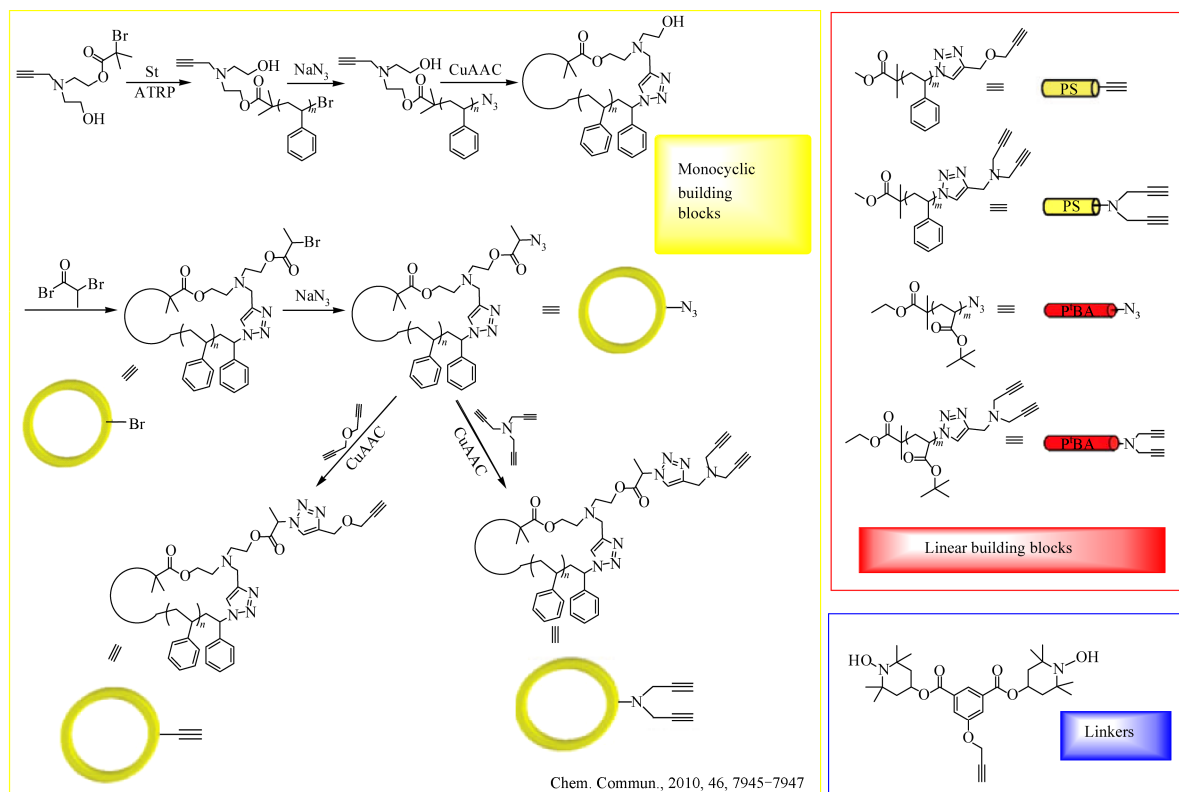
These macrocyclic star polymers were featured by a highly cross-linked core and many radiating arms. The shorter tadpole-shaped precursors caused core-cross-linked star polymers with higher molecular weight and several arm numbers. The macrocycle-terminated core-cross-linked star polymers showed two glass transition temperatures, one arising from the linear branches and the other from the macrocycles^[69].

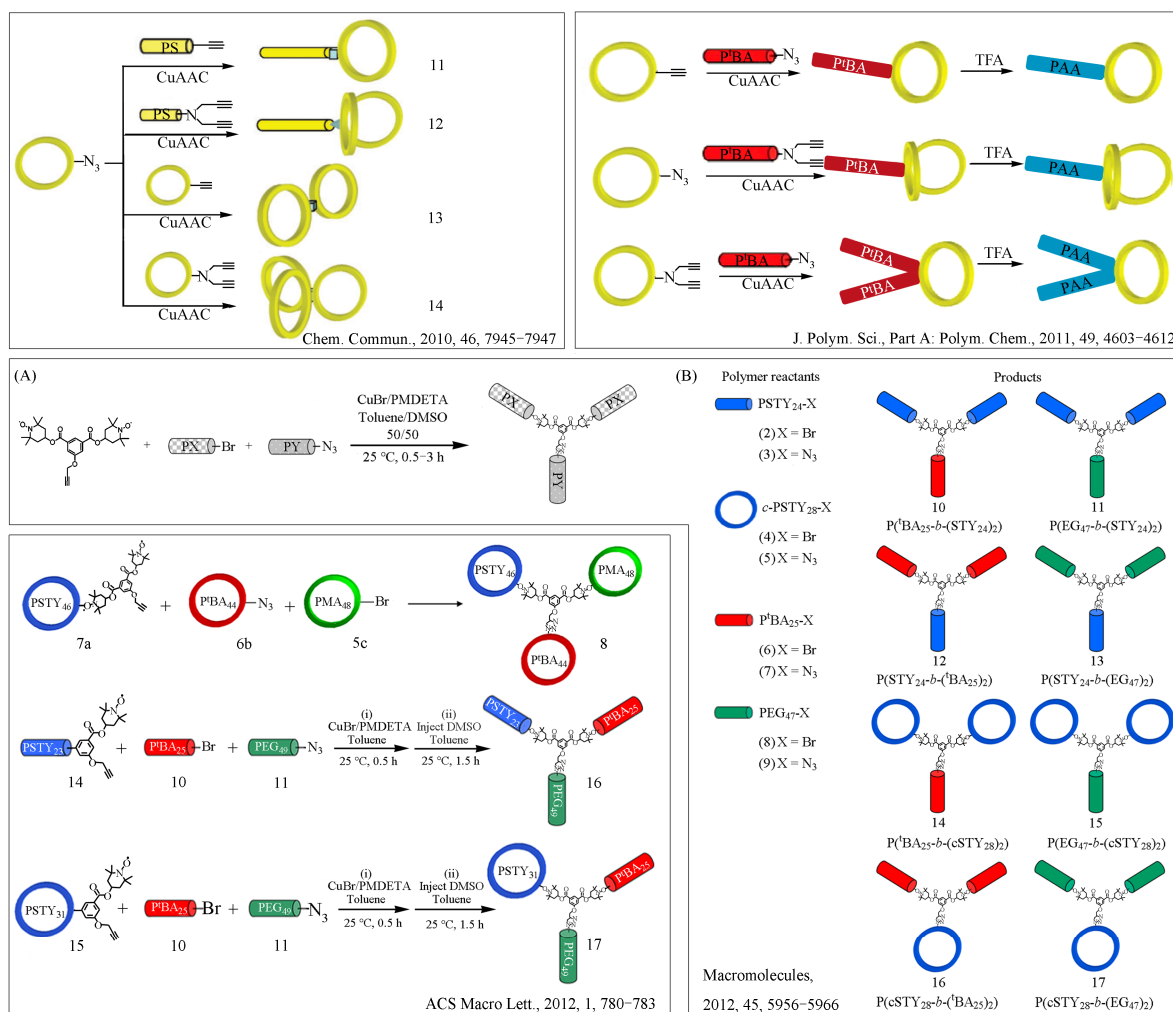
From 2010 to 2012, Monteiro's group has published several papers with elucidation of the conception of "small to big, easy to complex". All the building blocks and the linker used in those papers are summarized in Scheme 15, and specifically introduced here.

In 2010, they first reported the use of the enhanced rate of CuAAC cross-coupling reactions in the presence of CuBr/PMDETA catalyst and toluene to create complex architectures from functional polymeric cyclic building blocks. They were able to make various topologies, such as paddle-like, 3-miktoarm stars, figure-8, and 3-arm stars, in very high purity (> 80%) and with high coupling efficiency (> 90%) at 25 °C and in a time as short as 1.5 h. This work opened a methodology to synthesize a wide range of cyclic structures in high yield with a wide range of chemical functionality^[25] (Scheme 15).

Second, in 2011, they demonstrated the synthesis of a variety of miktoarms stars from a cyclic polymer *c*-PSTY and *l*-PBA. These structures were produced using the combination of ATRP and CuAAC with high coupling efficiency. All the *l*-PBA arms on the structures were de-protected to the hydrophilic PAA using TFA, producing amphiphilic macrocyclic structures. They also found that the self-assembly of these structures resulted in the formation of micelles close to their equilibrium structures^[62] (Scheme 15).

Third, in 2012, they demonstrated the rapid and highly efficient one-pot synthesis of mikto 3-arm AB₂ star at 25 °C, using two copper catalyzed "click"-type reactions (CuAAC and nitroxide radical coupling NRC). By modulating activity of the copper catalyst, the rates of NRC and CuAAC could be significantly changed. Under these conditions, both the NRC and CuAAC reactions were similar. Well-defined linear and cyclic building blocks, consisting of linear polystyrene, cyclic polystyrene, poly(*tert*-butyl acrylate) and PEG, were combined to form a wide variety of chemically different AB₂ stars^[65] (Scheme 15).





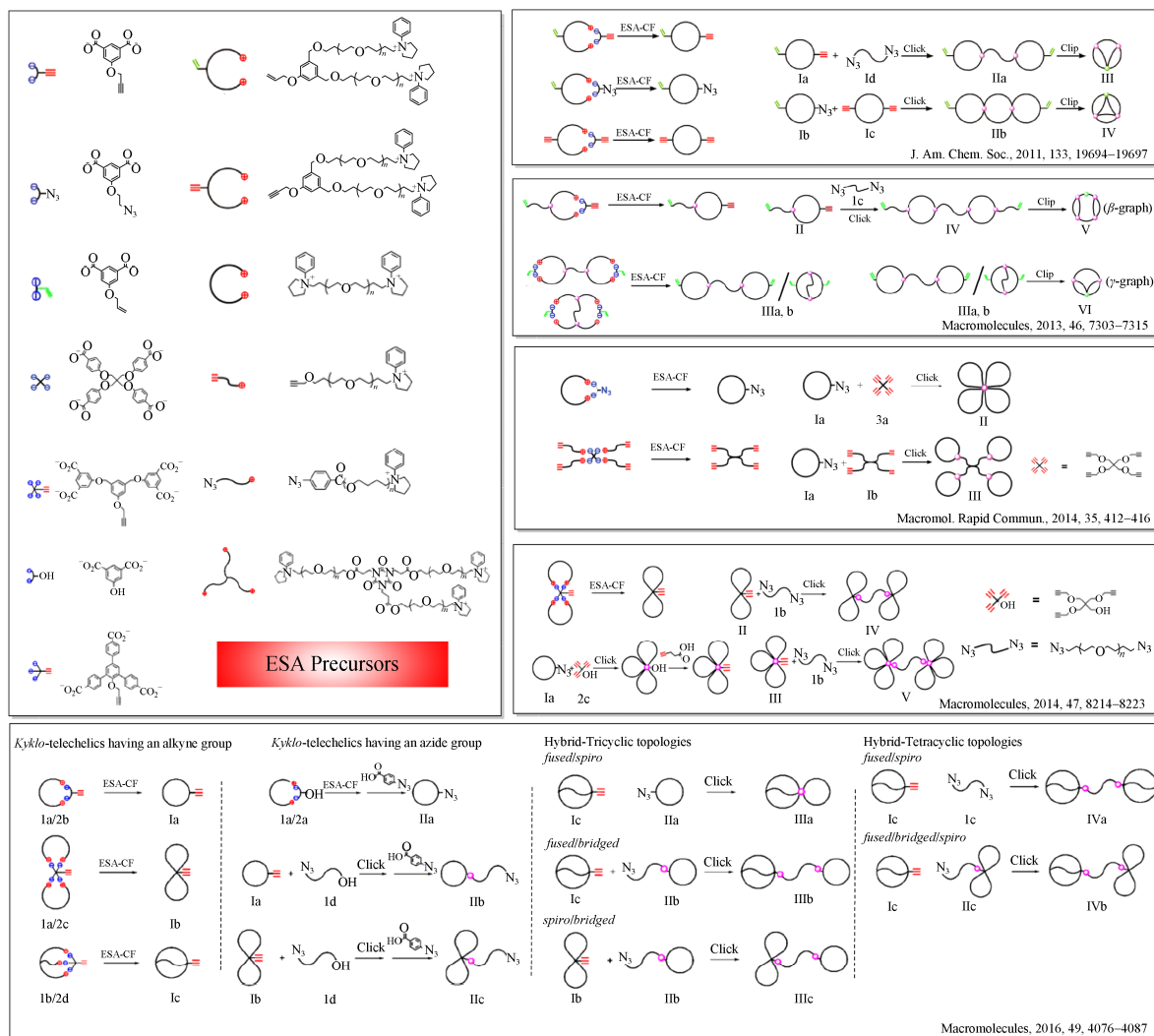
Scheme 15 Summary of the building blocks, linkers and the complex topologies reported by Monteiro's group from 2010 to 2012 (Reproduced from Ref. [25] with permission from The Royal Society of Chemistry) (Reprinted with permission from Ref. [62]; Copyright (2011) John Wiley & Sons Inc) (Reprinted with permission from Ref. [70]; Copyright (2012) American Chemical Society) (Reprinted with permission from Ref. [65]; Copyright (2012) American Chemical Society) (The online version is colorful.)

Finally, in 2012, they constructed monodisperse ABC miktoarm stars with a similar strategy to the one described in their third paper mentioned above. Therefore, this synthetic methodology allowed such architectures to be used in a variety of applications (e.g., temperature, salt, and acid stable micelles for drug and vaccine delivery), some of which are not reported yet^[70] (Scheme 15).

Tezuka *et al.* developed an efficient process called “electrostatic self-assembly and covalent fixation” (ESA-CF) and applied it to achieve an efficient one-step formation of well-defined polymers comprising mono- or multi-cyclic polymer in 2000^[24]. Just as its name implied, it consisted of two steps: (1) telechelic poly(THF)s with cyclic ammonium salt group and pluricarboxylate counter anions turned into the smallest assembly in dilute solvent in the charge of cations and anions balance; (2) covalent fixation by ring opening of the cyclic ammonium salt group by the carboxylate counter anion produced a variety of unconventional polymer architectures comprising mono- and multi-cyclic polymer units. In the past 15 years, his group constructed a variety of unusual macromolecular containing cyclic polymer units. Here, some of them, related to tandem CuAAC click reaction conjunct with ESA-CF process, are discussed.

In 2011, they reported the constructions of programmed folding of polymers such as doubly fused tricyclic

and triply fused tetracyclic polymer topologies by tandem CuAAC click reaction and an olefin metathesis condensation in conjunction with ESA-CF process. The topologies have been fully characterized by NMR, SEC, and MALDI-TOF techniques^[71] (Scheme16).



Scheme 16 Summary of the complex topologies reported by Tezuka's group from 2011 to 2016 (Reprinted with permission from Ref. [60]; Copyright (2013) John Wiley & Sons Inc) (Reprinted with permission from Ref. [71]; Copyright (2011) American Chemical Society) (Reprinted with permission from Ref. [57]; Copyright (2013) American Chemical Society) (Reprinted with permission from Ref. [3]; Copyright (2014) American Chemical Society) (Reprinted with permission from Ref. [72]; Copyright (2016) American Chemical Society) (The online version is colorful.)

In 2013, they illustrated the constructions of doubly fused tricyclic, β - and γ -graph polymer topologies^[57]. The key polymer precursors, an asymmetric three-armed star and an H-shaped telechelic polymer precursor with cyclic ammonium salt groups at the chain ends, were obtained through CuAAC using a polymer precursor with cyclic ammonium salt end groups and an additional alkyne group at the center. The CuAAC click reaction with complementary precursors with azide end groups was conducted to give the star-shaped and the H-shaped telechelic polymer precursor keeping cyclic ammonium salt groups intact during the reaction. The subsequent ESA-CF process with designated dicarboxylate counter anions containing additional alkene or alkyne group could afford the *kyklo*-telechelic precursors, having either a tadpole form with an alkene and an alkyne group at

the top-head or the tail-end positions, and a manacle/theta isomeric mixture with two alkene groups at the opposite position, respectively. A further CuAAC click coupling of the former with a linear telechelic precursor having azide group, followed by clip folding process produced a doubly fused tricyclic polymers with β -graph topology. Moreover, the convergent clip folding of the latter isomeric mixture precursors could produce a sole form of a doubly fused tricyclic polymer with γ -graph topology^[57] (Scheme 16).

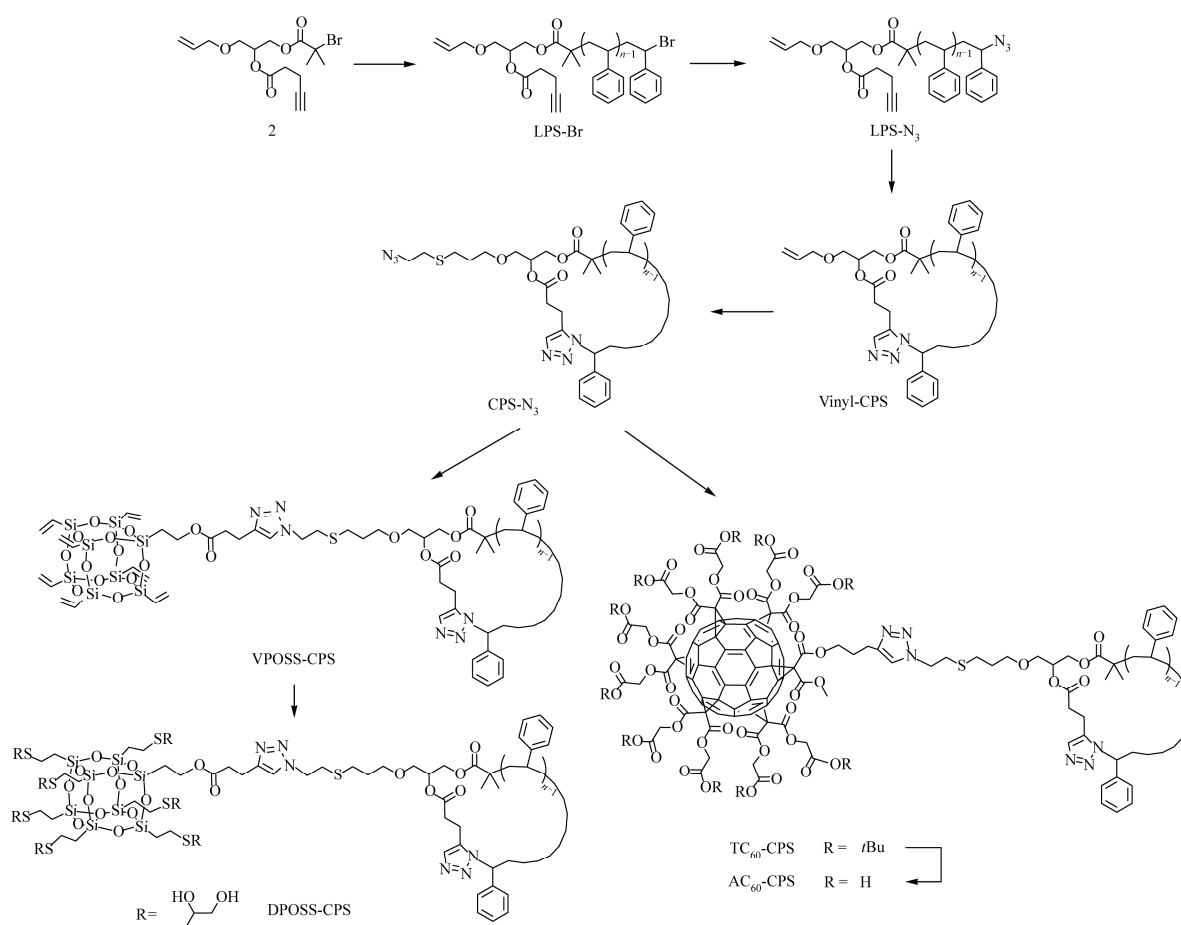
In 2014, a dicyclic, eight-shaped and a tricyclic, trefoil-shaped poly(THF), both having an alkyne group at the core position, were introduced as versatile core-clickable *kyklo*-telechelic precursors. The eight-shaped prepolymer was prepared by an ESA-CF process using an assembly, composed of two units of linear poly(THF) with *N*-phenylpyrrolidinium salt groups carrying one unit of a tetrafunctional carboxylate with an alkyne group as a counter anion. Alternatively, the trefoil-shaped prepolymer was prepared through a CuAAC click process using a cyclic poly(THF) precursor with an azide group which was also obtained by the ESA-CF technique, with a tripropargylated pentaerythritol derivative followed by esterification with 4-pentynoic acid to introduce again an alkyne group. The subsequent CuAAC click coupling reaction of II and III with a linear telechelic poly(THF) with azide groups afforded novel tetra- and hexacyclic bridged-spiro hybrid polymer topologies, *i.e.*, double-eight and double-trefoil constructions^[3] (Scheme 16).

Recently, they constructed a variety of tricyclic polymer topologies with a mixture of a dicyclic (theta- or eight-shaped) and a simple ring unit and moreover, unprecedented tetracyclic topologies including double-theta and another composed of three elemental dicyclic units of theta-, eight- and manacle-forms, through effective CuAAC click-linking of complementarily reactive *kyklo*-telechelic precursors. These products were then fully characterized using ¹H-NMR, MALDI-TOF mass, FTIR, and SEC techniques^[72] (Scheme 16).

Protocols of building complex cyclic topologies using monocycles and functional parts

From 2014 to 2015, Cheng *et al.* demonstrated fabrications of cyclic polymers with functional group of POSS or fullerene. Two series of novel “nano-diamond-ring-like” giant surfactants, based on hydrophilic POSS and C₆₀ tethered with a cyclic polystyrene (CPS) tail, were synthesized using successive ATRP, CuAAC and the thiol-ene “click” reactions. Starting from a specifically designed initiator, trifunctional linear polystyrene (LPS) precursor bearing vinyl, bromo, and alkyne groups, was prepared by ATRP. Upon subsequent azidation of LPS, CuAAC click reaction was employed to afford vinyl-functionalized CPS ring in high yield and purity (Vinyl-CPS). The vinyl group was then subjected to thiol-ene reaction to introduce an azide group onto the CPS, providing an azide functionalized CPS (CPS-N₃) as a “clickable” cyclic building block to construct giant molecules. And the “diamonds”, such as hydrophilic POSS or C₆₀, were installed on the “ring” (cyclic building block) *via* CuAAC click reaction^[73] (Scheme 17). The sequential “click” strategy was used to further expand the scope of synthetically available giant molecules by precisely constructing new giant surfactants based on POSS tethered cyclic polymers. Every “click” reaction played a unique “role”. For example, strain-promoted azide-alkyne cycloaddition (SPAAC) was used for bimolecular homobifunctional ring closure to afford VPOSS-cPS and VPOSS-cPS-alkyne; CuAAC was used for POSS-polymer conjugation to obtain VPOSS-cPS-ACPOSS, and thiol-Michael/thiol-ene reactions was used for POSS surface functionalization to get APOSS-cPS, VPOSS-cPS-FPOSS and APOSS-cPS-FPOSS (Scheme 18). This work not only offered a new method in macrocycle-based topological polymer chemistry but also allowed the rational design and precise synthesis of a wide range of POSS-based giant surfactants with complex shapes and architectures, which provided a systematic study of their structure-property relationships^[74].

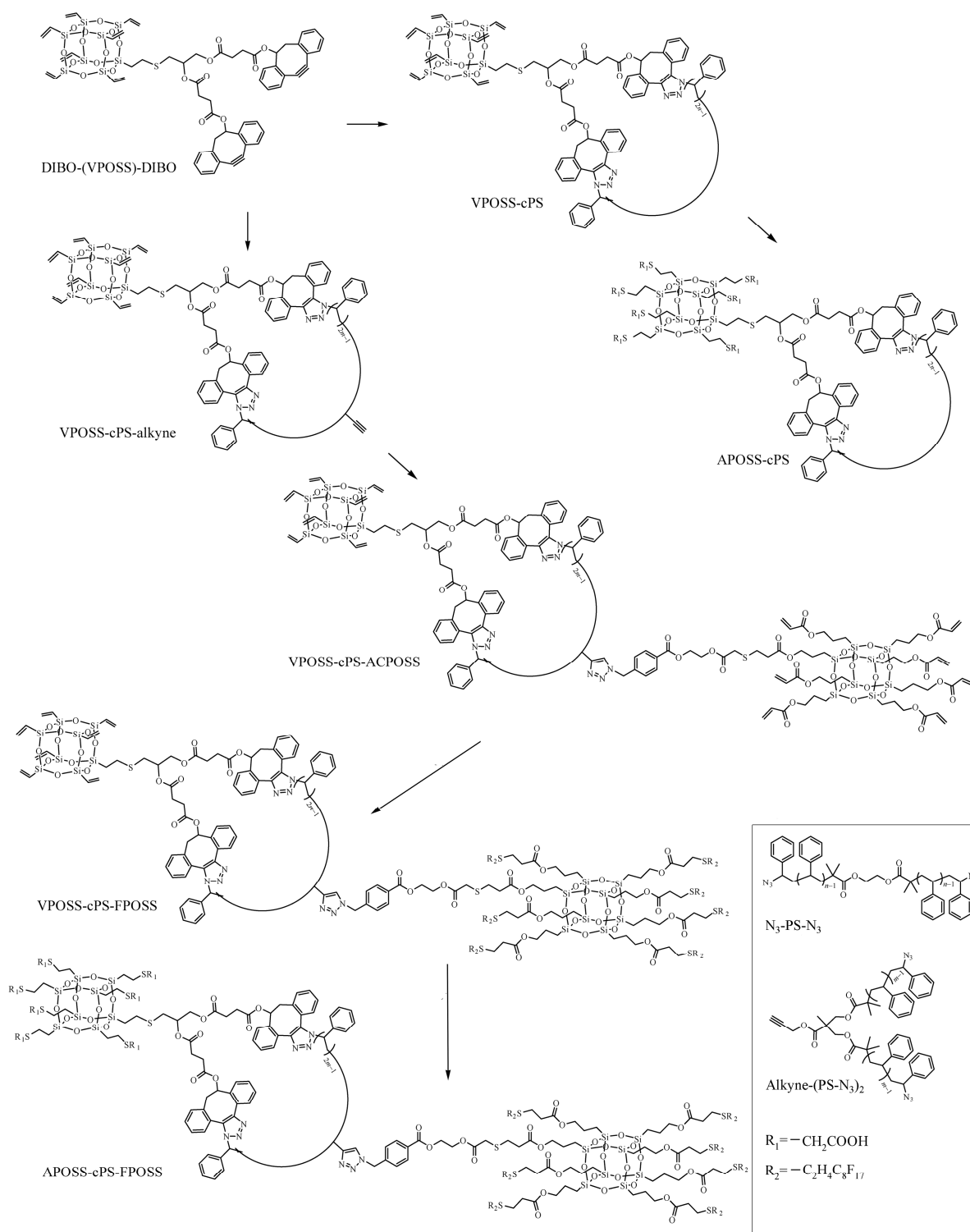
In 2015, our group successfully synthesized thiol-functionalized monocyclic and fused-bicyclic polymers *via* a combination of ATRP and CuAAC cyclization reaction. Using these cyclic polymers as building blocks, several tadpole- and spiro-shaped topological polymers were facilely constructed *via* a modular approach (Scheme 19). Taking advantage of the versatile thiol chemistry, this work offered a modular methodology for the facile and precise construction of cyclic-based topological polymers with thiol-functionalized cyclic polymers as building blocks^[75].



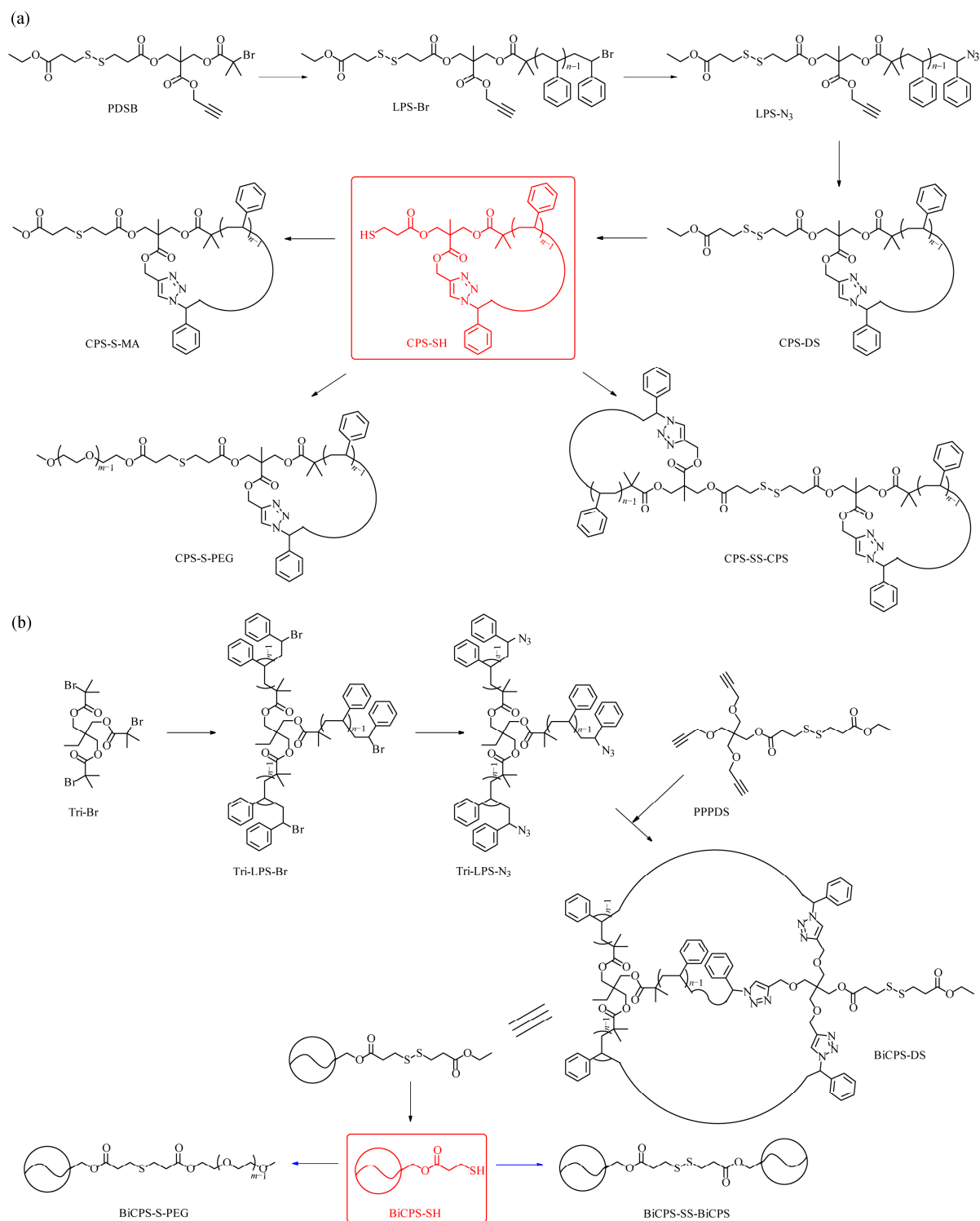
Scheme 17 Synthesis of DPOSS-CPS and AC₆₀-CPS (Reprinted with permission from Ref. [73]; Copyright (2014) American Chemical Society)

Cyclic-brush polymer is a new cyclic polymeric topology which combines cyclic with brush architectures. In 2015, our group reported a modular construction of cyclic-brush polymer using Suzuki coupling reaction for a post-polymerization modification. A cyclic polymer precursor, cyclic PBrS (*c*-PBrS), was synthesized by combining ATRP and CuAAC click ring closure. The post-polymerization modifications of *c*-PBrS to cyclic poly[(4-methoxyphenyl)styrene] (*c*-PMOPS) and cyclic-brush polymer (*c*-PS-*g*-PS) were successfully achieved with high efficiency, as illustrated in Scheme 20^[76]. This study provided a promising protocol for efficient preparation of cyclic-brush polymers or other complex topological cyclic-based polymers.

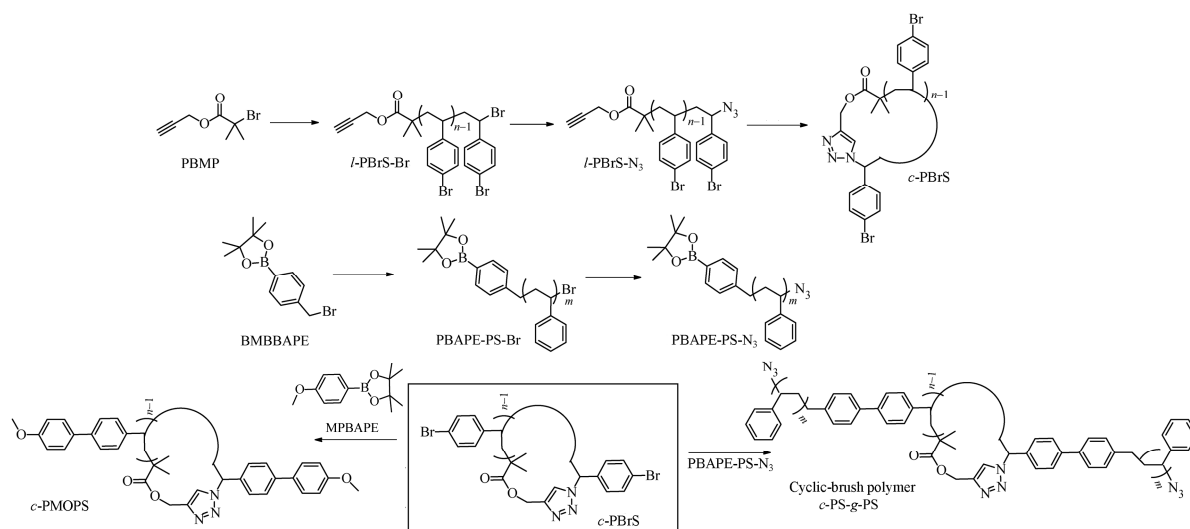
As a further investigation, our group reported a novel synthetic strategy for preparation of cyclic-brush polymers with controlled grafting density. The cyclic polystyrene (*c*-PS) precursor was synthesized using the general methods of activators generated by electron transfer for atom transfer radical polymerization (AGET-ATRP) and CuAAC. The benzylic hydrogen atoms of *c*-PS were substituted with bromine to afford a tertiary bromide ATRP macroinitiator (*c*-PSBr). Macro-RAFT agents with azole (*c*-PSN) or ethoxyl (*c*-PSO) as the Z group were synthesized from *c*-PSBr. Using the as-prepared ATRP macroinitiator or macro-RAFT agents, a series of cyclic-brush polymers, including *c*-PS-*g*-PS, *c*-PS-*g*-PNIPAM, *c*-PS-*g*-PMMA, *c*-PS-*g*-PMA and *c*-PS-*g*-PVAc, were successfully prepared^[77] (Scheme 21). This work provided a novel strategy for preparation of cyclic-brush polymers by controlled radical polymerization, including ATRP, RAFT and so on, which could eventually enrich the topological architecture and benefit the study on cyclic polymers.



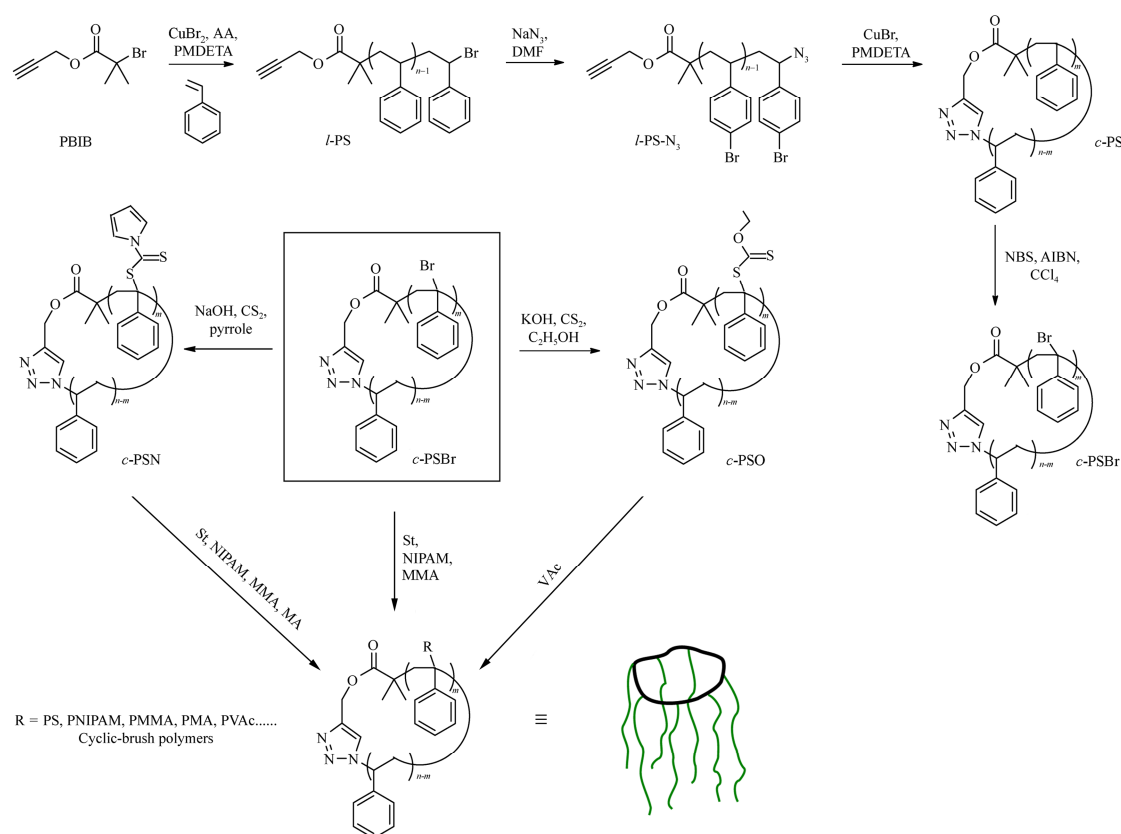
Scheme 18 Synthetic route using sequential “click” chemistry (Reproduced from Ref. [74] with permission from The Royal Society of Chemistry)



Scheme 19 (a) Synthetic route to the thiol-functionalized macrocycle building blocks *via* ATRP; (b) CuAAC and synthetic route to the macrocycle-based topological polymers from the building blocks *via* thiol chemistry (Reproduced from Ref. [75] with permission from The Royal Society of Chemistry)



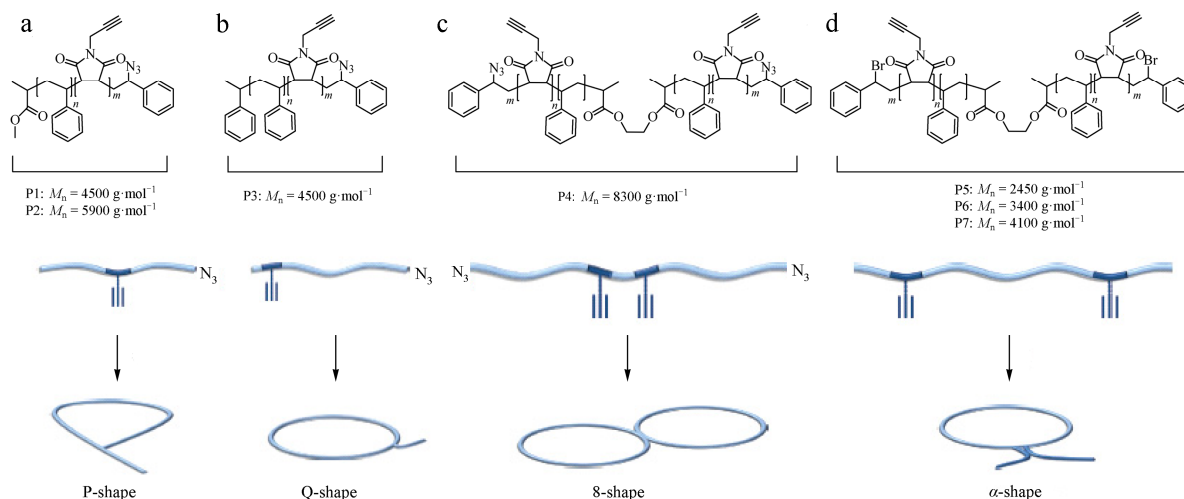
Scheme 20 Synthetic routes for the cyclic functional polymer poly[(4-methoxyphenyl)styrene] and cyclic polymer brush (Reproduced from Ref. [76] with permission from The Royal Society of Chemistry)



Scheme 21 Illustration of synthetic routes of the cyclic-brush polymers with cyclic PS as main-chain template (Reproduced from Ref. [77] with permission from The Royal Society of Chemistry)

Using Some Novel Methods, Such as Precise “Insert-folding” Protocols to Form Complex Cyclic Topologies

In 2001, Lutz *et al.* introduced a versatile strategy of precise “insert-folding” to form complex cyclic topologies. First, well-defined polymers were synthesized by ATRP of styrene. The controlled addition of discrete amounts of protect-modified maleimide at precise time during the synthesis enabled the formation of polystyrene chains with positionable reactive alkyne functions. Then intramolecular reaction between these functional groups subsequently led to the formation of different types of covalently folded polymer chains by CuAAC or Glaser coupling. For example, tadpole (P-shaped), pseudo cyclic (Q-shaped), bicyclic (8-shaped) and knotted (α -shaped) macromolecular were prepared in a relatively straight forward manner^[78] (Scheme 22).



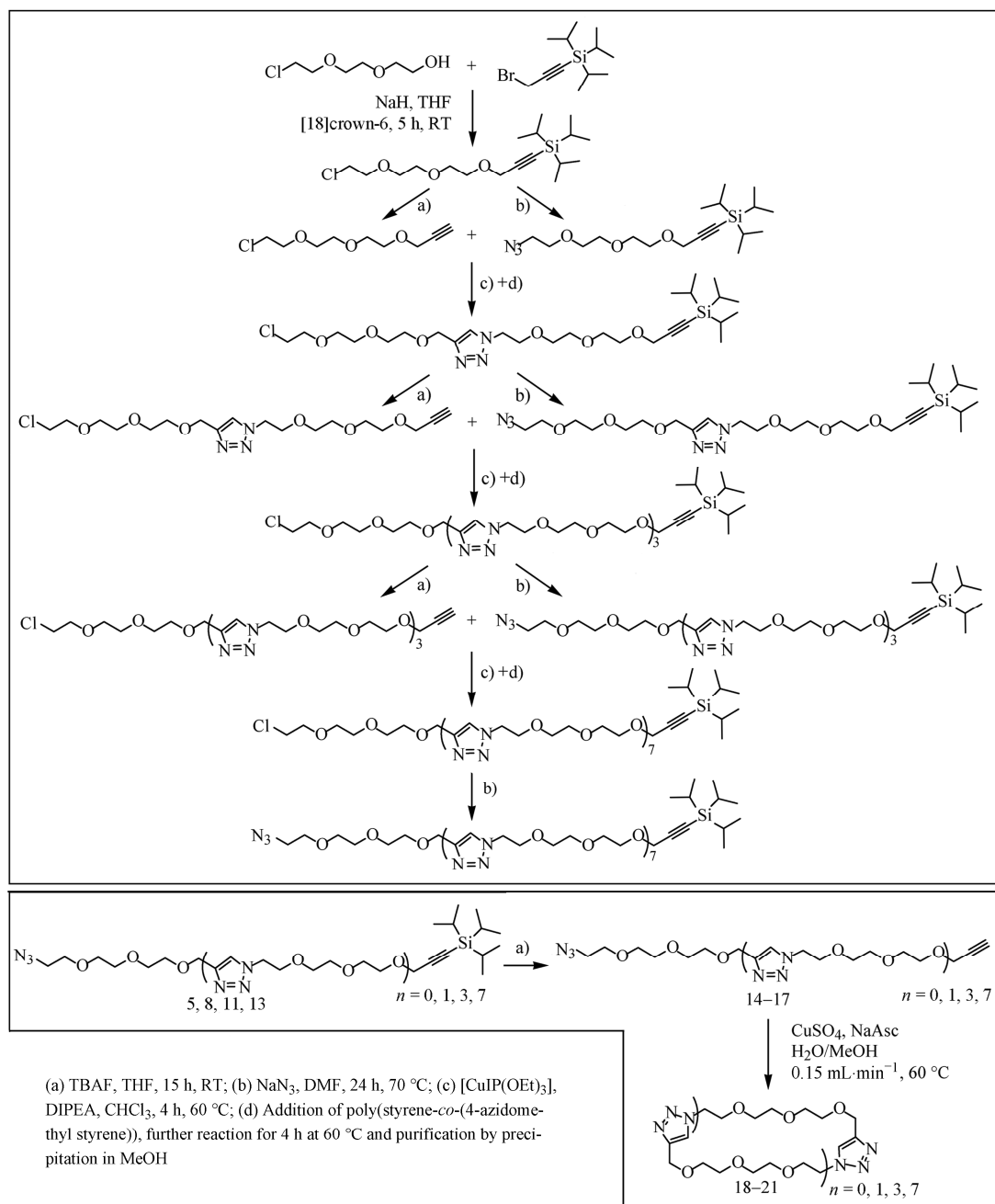
Scheme 22 Covalent folding of linear synthetic polymer chains (Reprinted by permission from Macmillan Publishers Ltd: Ref. [78], Copyright (2011))

APPLICATIONS OF CUAAC CLICK REACTION TO PRECISE SYNTHESIS OF MOLECULARLY DEFINED CYCLIC OLIGOMERS/POLYMERS

It is known that the property and the function of the polymers depend on their molecular weight, topology and sequence distribution. Therefore, the precision synthesis of a polymer with molecularly-defined chain length (*i.e.*, monodisperse molecular weight), monomer unit sequence and topologies is a prerequisite. Nature provides perfect examples for producing such precisely-defined polymers, such as DNA, proteins, and peptides, which are well known to have definite chain length, functional sequence, and topology. Although the synthesis of molecularly-defined polymer is a high challenge, great efforts have been made. Generally speaking, there are two approaches to achieve the objective. The first one is the stepwise chain-growth approach from solid^[79–81] or liquid^[82] phase substrate, or without substrate but using highly effective coupling reaction and equivalent feeding^[83–87]. This approach is proposed and developed for effective synthesis of polypeptides^[79, 80, 83]. The other one is “geometrical approach or iterative exponential growth (IEG)”^[88–110], which starts with the monomer with the two ends orthogonally protected. Selective de-protection of one end from the monomer produces two mono-protected intermediates, which react mutually to give the dimer of the monomer, and the oligomer or polymer with definite chain length. Through this approach, the chain growth proceeds with a geometric progression, *i.e.*, yields the sequence of length 2^n for n repeat cycles. IEG strategy has shown its enormous potential in the scalable synthesis of molecularly-defined macromolecules. Here, we introduce some applications of this “geometrical approach or iterative exponential growth (IEG)” with CuAAC click reaction in cyclic polymeric construction.

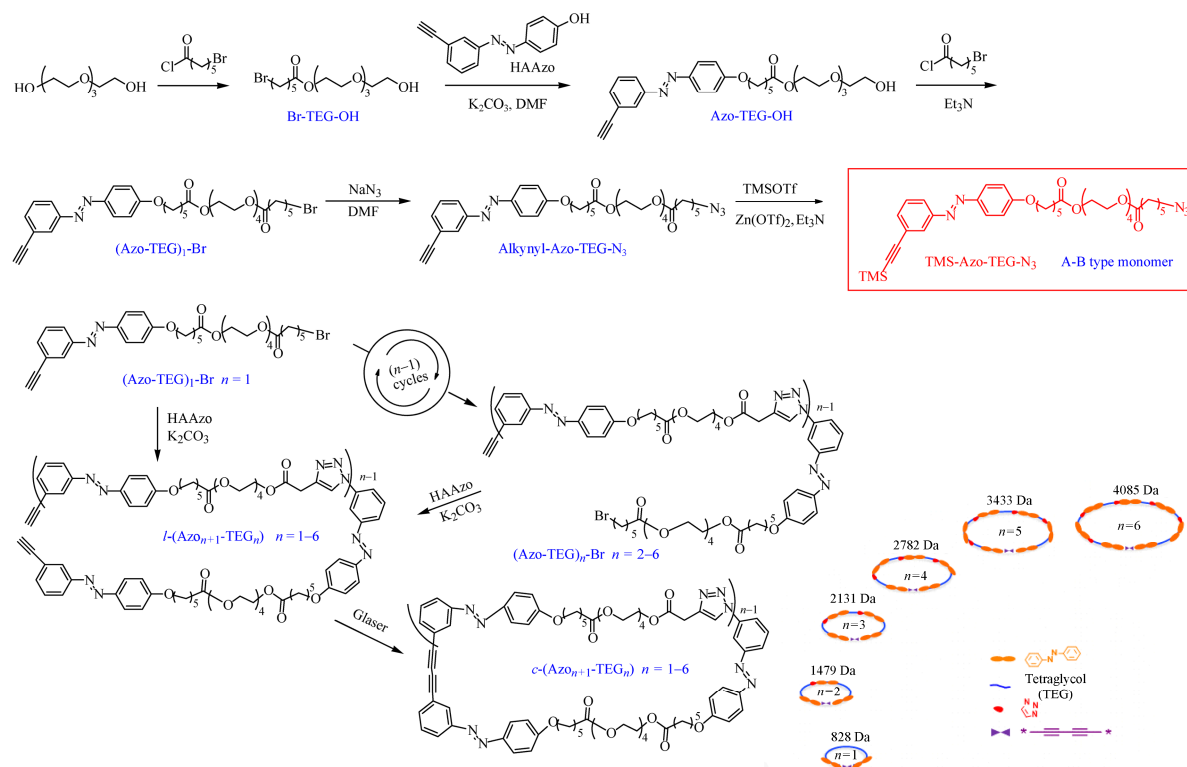
In 2009, Hawker *et al.* reported an efficient strategy for the synthesis and characterization of a series of molecularly defined ethylene glycol based oligomers and their associated macrocycles that significantly

enhanced structural diversity for these materials. By combining protection-deprotection and CuAAC exponential chain-growth strategies, α -azide- ω -alkyne-functionalized oligo(ethylene glycol) derivatives were prepared (degree of polymerization $DP = 2^n$, with $n = 0-3$), and CuAAC intramolecular cyclization was used to give a series of novel, molecularly defined macrocycles with 1–8 triazole units in the cyclic backbone^[105] (Scheme 23).



Scheme 23 Iterative strategy for the synthesis of molecularly defined mono- and di-protected tri(ethylene glycol)-based oligomers ($n = 2, 4$, and 8) and synthesis of molecularly defined α -azide- ω -alkyne reactive oligomers 14–17 and corresponding macrocycles 18–21 (Reprinted with permission from Ref. [105]; Copyright (2009) John Wiley & Sons Inc)

In 2016, our group reported that a series of molecularly-defined macrocycles with main-chain azobenzene-containing oligomers (sixth generation) were prepared, based on click chemistry and a stepwise chain-growth strategy (Scheme 24). The cyclic topology and chain-length effects on the properties/functions of the cyclic oligomers were investigated in detail by comparison with the linear analogues. This work undoubtedly illustrated an example for demonstrating the dependence of properties/functions on both cyclic topology and chain-length, allowing in-depth insight into the structure-property relationship. Therefore, the modular strategy was extended to various molecularly-defined macrocycles with a wide variety of functions^[111].



Scheme 24 Synthetic routes of monomer TMS-Azo-TEG-N₃ by stepwise chain-growth approach using molecularly-defined linear and cyclic oligomers (Reproduced from Ref. [111] with permission from The Royal Society of Chemistry) (The online version is colorful.)

SUMMARY AND PERSPECTIVES

CuAAC click reaction has been developed and become a robust and versatile synthesis technique for preparation of cyclic polymers. And it is also considered as one of the most versatile organic reactions useful to “click” fragments together as molecular LEGO’s to form complex molecular architectures. Especially for the research on cyclic polymer, CuAAC is an unbreakable bridge between structures and properties.

REFERENCES

- 1 Kricheldorf, H.R., J. Polym. Sci., Part A: Polym. Chem., 2010, 48(2): 251
- 2 Laurent, B.A. and Grayson, S.M., Chem. Soc. Rev., 2009, 38(8): 2202
- 3 Tomikawa, Y., Fukata, H., Ko, Y.S., Yamamoto, T. and Tezuka, Y., Macromolecules, 2014, 47(23): 8214
- 4 Hossain, M.D., Jia, Z. and Monteiro, M.J., Macromolecules, 2014, 47(15): 4955
- 5 Tezuka, Y., Polym. J., 2012, 44(12): 1159

- 6 Jia, Z. and Monteiro, M.J., *J. Polym. Sci., Part A: Polym. Chem.*, 2012, 50(11): 2085
- 7 Yamamoto, T. and Tezuka, Y., *Polym. Chem.*, 2011, 2(9): 1930
- 8 Schappacher, M. and Deffieux, A., *Science*, 2008, 319(5869): 1512
- 9 Coulembier, O., Moins, S.B., de Winter, J., Gerbaux, P., Leclère, P., Lazzaroni, R. and Dubois, P., *Macromolecules*, 2010, 43(1): 575
- 10 Chen, R., Ling, J. and Hogen-Esch, T.E., *Macromolecules*, 2009, 42(16): 6015
- 11 Quirk, R.P., Wang, S.F., Foster, M.D., Wesdemiotis, C. and Yol, A.M., *Macromolecules*, 2011, 44(19): 7538
- 12 Shin, E.J., Brown, H.A., Gonzalez, S., Jeong, W., Hedrick, J.L. and Waymouth, R.M., *Angew. Chem. Int. Ed. Eng.*, 2011, 50(28): 6388
- 13 Zhang, K., Lackey, M.A., Cui, J. and Tew, G.N., *J. Am. Chem. Soc.*, 2011, 133(11): 4140
- 14 Qin, L., He, X.W., Yuan, X., Li, W.Y. and Zhang, Y.K., *Anal. Bioanal. Chem.*, 2011, 399(10): 3375
- 15 Wan, X., Liu, T. and Liu, S., *Biomacromolecules*, 2011, 12(4): 1146
- 16 Wei, H., Chu, D.S., Zhao, J., Pahang, J.A. and Pun, S.H., *ACS Macro Lett.*, 2013, 2(12):
- 17 Zhang, B., Zhang, H., Li, Y., Hoskins, J.N. and Grayson, S.M., *ACS Macro Lett.*, 2013, 2(10): 845
- 18 Chen, B., Jerger, K., Frechet, J.M. and Szoka, F.C., *J. Control. Release*, 2009, 140(3): 203
- 19 Cortez, M.A., Godbey, W.T., Fang, Y., Payne, M.E., Cafferty, B.J., Kosakowska, K.A. and Grayson, S.M., *J. Am. Chem. Soc.*, 2015, 137(20): 6541
- 20 Laurent, B. and Grayson, S., *J. Am. Chem. Soc.*, 2006, 128(13): 4238
- 21 Nicolaÿ, R. and Matyjaszewski, K., *Macromolecules*, 2011, 44(2): 240
- 22 Jeong, W., Hedrick, J.L. and Waymouth, R.M., *J. Am. Chem. Soc.*, 2007, 129(27): 8414
- 23 Boydston, A.J., Holcombe, T.W., Unruh, D.A., Fréchet, J.M. and Grubbs, R.H., *J. Am. Chem. Soc.*, 2009, 131(15): 5388
- 24 Oike, H., Imaizumi, H., Mouri, T., Yoshioka, Y., Uchibori, A. and Tezuka, Y., *J. Am. Chem. Soc.*, 2000, 122(40): 9592
- 25 Lonsdale, D.E. and Monteiro, M.J., *Chem. Commun.*, 2010, 46(42): 7945
- 26 Honda, S., Yamamoto, T. and Tezuka, Y., *J. Am. Chem. Soc.*, 2010, 132(30): 10251
- 27 Kolb, H.C., Finn, M. and Sharpless, K.B., *Angew. Chem. Int. Ed.*, 2001, 40(11): 2004
- 28 Matyjaszewski, K. and Xia, J., *Chem. Rev.*, 2001, 101(9): 2921
- 29 Chiefari, J., Chong, Y., Ercole, F., Krstina, J., Jeffery, J., Le, T.P., Mayadunne, R.T., Meijs, G.F., Moad, C.L. and Moad, G., *Macromolecules*, 1998, 31(16): 5559
- 30 Hawker, C.J., Bosman, A.W. and Harth, E., *Chem. Rev.*, 2001, 101(12): 3661
- 31 Rosen, B.M. and Percec, V., *Chem. Rev.*, 2009, 109(11): 5069
- 32 Percec, V., Guliashvili, T., Ladislav, J.S., Wistrand, A., Stjerndahl, A., Sienkowska, M.J., Monteiro, M.J. and Sahoo, S., *J. Am. Chem. Soc.*, 2006, 128(43): 14156
- 33 Matyjaszewski, K. and Tsarevsky, N.V., *Nat. Chem.*, 2009, 1(4): 276
- 34 Sumerlin, B.S. and Vogt, A.P., *Macromolecules*, 2010, 43(1): 1
- 35 Hadjichristidis, N., Iatrou, H., Pitsikalis, M. and Mays, J., *Prog. Polym. Sci.*, 2006, 31(12): 1068
- 36 Qiu, X.P., Tanaka, F. and Winnik, F.M., *Macromolecules*, 2007, 40(20): 7069
- 37 Shi, G.Y., Tang, X.Z. and Pan, C.Y., *J. Polym. Sci., Part A: Polym. Chem.*, 2008, 46(7): 2390
- 38 Zhou, F., Li, Y., Jiang, G., Zhang, Z., Tu, Y., Chen, X., Zhou, N. and Zhu, X., *Polym. Chem.*, 2015, 6(38): 6885
- 39 Zhou, F., Zhang, Z., Jiang, G., Lu, J., Chen, X., Li, Y., Zhou, N. and Zhu, X., *Polym. Chem.*, 2016, 7(16): 2785
- 40 Shi, G.Y. and Pan, C.Y., *Macromol. Rapid Commun.*, 2008, 29(20): 1672
- 41 Lonsdale, D.E., Bell, C.A. and Monteiro, M.J., *Macromolecules*, 2010, 43(7): 3331
- 42 Ge, Z., Zhou, Y., Xu, J., Liu, H., Chen, D. and Liu, S., *J. Am. Chem. Soc.*, 2009, 131(5): 1628
- 43 Zhu, X., Zhou, N., Zhang, Z., Sun, B., Yang, Y., Zhu, J. and Zhu, X., *Angew. Chem.*, 2011, 50(29): 6615
- 44 Eugene, D.M. and Grayson, S.M., *Macromolecules*, 2008, 41(14): 5082
- 45 Gibbons, W.M., Shannon, P.J., Sun, S.T. and Swetlin, B.J., *Nature*, 1991, 351(6321):49
- 46 Delaire, J.A. and Nakatani, K., *Chem. Rev.*, 2000, 100(5): 1817
- 47 Barrett, C.J., Mamiya, J.I., Yager, K.G. and Ikeda, T., *Soft Matter*, 2007, 3(10): 1249
- 48 Wang, D., Ye, G., Zhu, Y. and Wang, X., *Macromolecules*, 2009, 42(7): 2651

- 49 Pedersen, T.G., Johansen, P.M. and Pedersen, H.C., *J. Opt. A-Pure. Appl. Op.*, 2000, 2(4): 272
- 50 He, X., Zhang, H., Yan, D. and Wang, X., *J. Polym. Sci., Part A: Polym. Chem.*, 2003, 41(18): 2854
- 51 Rasmussen, P.H., Ramanujam, P., Hvilsted, S. and Berg, R.H., *J. Am. Chem. Soc.*, 1999, 121(20): 4738
- 52 Rochon, P., Batalla, E. and Natansohn, A., *Appl. Phys. Lett.*, 1995, 66(2): 136
- 53 Han, D., Tong, X., Zhao, Y., Galstian, T. and Zhao, Y., *Macromolecules*, 2010, 43(8): 3664
- 54 Cai, Y., Lu, J., Zhou, F., Zhou, X., Zhou, N., Zhang, Z. and Zhu, X., *Macromol. Rapid Commun.*, 2014, 35(9): 901
- 55 Poelma, J.E., Ono, K., Miyajima, D., Aida, T., Satoh, K. and Hawker, C.J., *ACS Nano*, 2012, 6(12): 10845
- 56 Zhang, B., Zhang, H., Elupula, R., Alb, A.M. and Grayson, S.M., *Macromol. Rapid Commun.*, 2014, 35(2): 146
- 57 Igari, M., Heguri, H., Yamamoto, T. and Tezuka, Y., *Macromolecules*, 2013, 46(18): 7303
- 58 Tezuka, Y., Tsuchitani, A., Yoshioka, Y. and Oike, H., *Macromolecules*, 2003, 36(1): 65
- 59 Sugai, N., Heguri, H., Ohta, K., Meng, Q., Yamamoto, T. and Tezuka, Y., *J. Am. Chem. Soc.*, 2010, 132(42): 14790
- 60 Ko, Y.S., Yamamoto, T. and Tezuka, Y., *Macromol. Rapid Commun.*, 2014, 35(4): 412
- 61 Dong, Y.Q., Tong, Y.Y., Dong, B.T., Du, F.S. and Li, Z.C., *Macromolecules*, 2009, 42(8): 2940
- 62 Lonsdale, D.E. and Monteiro, M.J., *J. Polym. Sci., Part A: Polym. Chem.*, 2011, 49(21): 4603
- 63 Fan, X., Wang, G. and Huang, J., *J. Polym. Sci., Part A: Polym. Chem.*, 2011, 49(6): 1361
- 64 Jeong, J., Kim, K., Lee, R., Lee, S., Kim, H., Jung, H., Kadir, M.A., Jang, Y., Jeon, H.B., Matyjaszewski, K., Chang, T. and Paik, H.J., *Macromolecules*, 2014, 47(12): 3791
- 65 Jia, Z., Lonsdale, D.E., Kulis, J. and Monteiro, M.J., *ACS Macro Lett.*, 2012, 1(6): 780
- 66 Shi, G.Y. and Pan, C.Y., *J. Polym. Sci., Part A: Polym. Chem.*, 2009, 47(10): 2620
- 67 Shi, G.Y., Sun, J.T. and Pan, C.Y., *Macromol. Chem. Phys.*, 2011, 212(12): 1305
- 68 Ge, Z., Wang, D., Zhou, Y., Liu, H. and Liu, S., *Macromolecules*, 2009, 42(8): 2903
- 69 Peng, Y., Liu, H., Zhang, X., Liu, S. and Li, Y., *Macromolecules*, 2009, 42(17): 6457
- 70 Kulis, J., Jia, Z. and Monteiro, M.J., *Macromolecules*, 2012, 45(15): 5956
- 71 Sugai, N., Heguri, H., Yamamoto, T. and Tezuka, Y., *J. Am. Chem. Soc.*, 2011, 133(49): 19694
- 72 Tomikawa, Y., Yamamoto, T. and Tezuka, Y., *Macromolecules*, 2016, 49(11): 4076
- 73 Lin, Z., Lu, P., Yu, X., Zhang, W.B., Huang, M., Wu, K., Guo, K., Wesdemiotis, C., Zhu, X., Zhang, Z., Yue, K. and Cheng, S.Z.D., *Macromolecules*, 2014, 47(13): 4160
- 74 Li, Y., Su, H., Feng, X., Yue, K., Wang, Z., Lin, Z., Zhu, X., Fu, Q., Zhang, Z., Cheng, S.Z.D. and Zhang, W.B., *Polym. Chem.*, 2015, 6(5): 827
- 75 Zhao, J., Zhou, Y., Li, Y., Pan, X., Zhang, W., Zhou, N., Zhang, K., Zhang, Z. and Zhu, X., *Polym. Chem.*, 2015, 6(15): 2879
- 76 Wang, Y., Zhang, S., Wang, L., Zhang, W., Zhou, N., Zhang, Z. and Zhu, X., *Polym. Chem.*, 2015, 6(25): 4669
- 77 Zhang, S., Yin, L., Zhang, W., Zhang, Z. and Zhu, X., *Polym. Chem.*, 2016, 7(11): 2112
- 78 Schmidt, B.V.K.J., Fechner, N., Falkenhagen, J. and Lutz, J.F., *Nat. Chem.*, 2011, 3(3): 234
- 79 Merrifield, R.B., *J. Am. Chem. Soc.*, 1963, 85(14): 2149
- 80 Merrifield, R.B., *Angew. Chem. Int. Ed.*, 1985, 24(10): 799
- 81 Gothard, C.M., Rao, N.A. and Nowick, J.S., *J. Am. Chem. Soc.*, 2007, 129(23): 7272
- 82 Pfeifer, S., Zarafshani, Z., Badi, N. and Lutz, J.F., *J. Am. Chem. Soc.*, 2009, 131(26): 9195
- 83 Duvigneaud, V., Ressler, C., Swan, J.M., Roberts, C.W., Katsoyannis, P.G. and Gordon, S., *J. Am. Chem. Soc.*, 1953, 75(19): 4879
- 84 Muthana, S., Yu, H., Cao, H.Z., Cheng, J.S. and Chen, X., *J. Org. Chem.*, 2009, 74(8): 2928
- 85 Lu, G.L., Lam, S. and Burgess, K., *Chem. Commun.*, 2006, (15): 1652
- 86 Montagnat, O.D., Lessene, G. and Hughes, A.B., *Tetrahedron Lett.*, 2006, 47(39): 6971
- 87 Angelo, N.G. and Arora, P.S., *J. Am. Chem. Soc.*, 2005, 127(49): 17134
- 88 Paynter, O.I., Simmonds, D.J. and Whiting, M.C., *J. Chem. Soc., Chem. Commun.*, 1982, (20): 1165
- 89 Bidd, I. and Whiting, M.C., *J. Chem. Soc., Chem. Commun.*, 1985, (9): 543
- 90 Tomalia, D.A., Naylor, A.M. and Goddard, W.A., *Angew. Chem. Int. Ed.*, 1990, 29(2): 138
- 91 Zhang, J., Moore, J.S., Xu, Z. and Aguirre, R.A., *J. Am. Chem. Soc.*, 1992, 114(6): 2273

- 92 Schumm, J.S., Pearson, D.L. and Tour, J.M., *Angew. Chem. Int. Ed.*, 1994, 33(13): 1360
- 93 Hawker, C.J., Malmstrom, E.E., Frank, C.W. and Kampf, J.P., *J. Am. Chem. Soc.*, 1997, 119(41): 9903
- 94 Percec, V. and Asandei, A.D., *Macromolecules*, 1997, 30(25): 7701
- 95 Sadighi, J.P., Singer, R.A. and Buchwald, S.L., *J. Am. Chem. Soc.*, 1998, 120(20): 4960
- 96 Louie, J. and Hartwig, J.F., *Macromolecules*, 1998, 31(19): 6737
- 97 Martin, R.E. and Diederich, F., *Angew. Chem. Int. Ed.*, 1999, 38(10): 1350
- 98 Brooke, G.M., MacBride, J.A.H., Mohammed, S. and Whiting, M.C., *Polymer*, 2000, 41(17): 6457
- 99 Brooke, G.M., Farren, C., Harden, A. and Whiting, M.C., *Polymer*, 2001, 42(7): 2777
- 100 Brooke, G.M., Cameron, N.R., MacBride, J.A.H. and Whiting, M.C., *Polymer*, 2002, 43(4): 1139
- 101 Zhou, C.Z., Liu, T.X., Xu, J.M. and Chen, Z.K., *Macromolecules*, 2003, 36(5): 1457
- 102 Williams, J.B., Chapman, T.M. and Hercules, D.M., *Macromolecules*, 2003, 36(11): 3898
- 103 Takizawa, K., Nulwala, H., Hu, J., Yoshinaga, K. and Hawker, C.J., *J. Polym. Sci., Part A: Polym. Chem.*, 2008, 46(18): 5977
- 104 Takizawa, K., Tang, C. and Hawker, C.J., *J. Am. Chem. Soc.*, 2008, 130(5): 1718
- 105 Binauld, S., Hawker, C.J., Fleury, E. and Drockenmuller, E., *Angew. Chem. Int. Ed.*, 2009, 48(36): 6654
- 106 Wang, Q., Qu, Y., Tian, H., Geng, Y. and Wang, F., *Macromolecules*, 2011, 44(6): 1256
- 107 Binauld, S., Damiron, D., Connal, L.A., Hawker, C.J. and Drockenmuller, E., *Macromol. Rapid Commun.*, 2011, 32(2): 147
- 108 Koch, F.P.V., Smith, P. and Heeney, M., *J. Am. Chem. Soc.*, 2013, 135(37): 13695
- 109 Leibfarth, F.A., Johnson, J.A. and Jamison, T.F., *Proc. Natl. Acad. Sci.*, 2015, 112(34): 10617
- 110 Barnes, J.C., Ehrlich, D.J.C., Gao, A.X., Leibfarth, F.A., Jiang, Y., Zhou, E., Jamison, T.F. and Johnson, J.A., *Nat. Chem.*, 2015, 7(10): 810
- 111 Jiang, X., Lu, J., Zhou, F., Zhang, Z., Pan, X., Zhang, W., Wang, Y., Zhou, N. and Zhu, X., *Polym. Chem.*, 2016, 7(15): 2645