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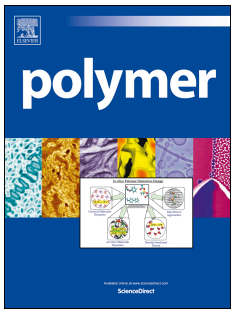

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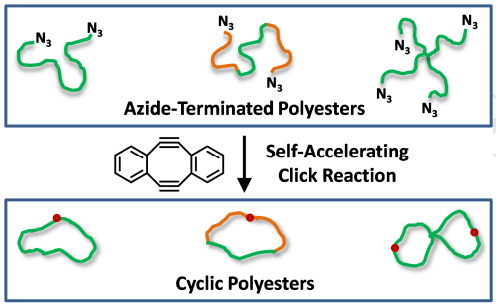
Graphical Abstract:



Synthesis of Well-Defined Cyclic Polyesters via Self-Accelerating Click Reaction

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Abstract

A metal-free and efficient homodifunctional bimolecular ring-closure method was developed specifically for the formation of well-defined cyclic polyesters based on the combination of ring opening polymerization (ROP) and self-accelerating double strain-promoted azide-alkyne cycloaddition (DSPAAC) reaction. In this method, ROP and the following end group modification were used to prepare the azide-terminated liner polyester precursors. The self-accelerating DSPAAC click reaction was then used to prepare the corresponding cyclic polyesters by ring-closing the linear polyester precursors with the small linkers of *sym*-dibenzo-1,5-cyclooctadiene-3,7-diyne (DBA). The distinct advantage of this novel homodifunctional bimolecular ring-closure method lied in the

fact that the pure cyclic polyesters could be efficiently prepared by using excess molar amounts of DBA small linkers to ring-close the linear polyester precursors. This was resulted from the self-accelerating property of the DSPAAC ring-closing reaction.

Keywords: Bimolecular ring-closure; Cyclic polyesters; Double strain-promoted azide-alkyne cycloaddition; Ring opening polymerization; Self-accelerating click reaction

Introduction

Aliphatic polyesters play an important role in biomedical applications such as prosthetics, degradable sutures, and drug delivery scaffolds due to their biocompatibility and biodegradability [1-3]. To manipulate the physical properties for fulfilling the wide applications, many kinds of aliphatic polyesters have been developed with different chemical structures, such as poly(lactide) (PLA), poly(ε-caprolactone) (PCL), poly(δ-valerolactone) (PVL), and their copolymers [4-7]. In addition to this, aliphatic polyesters with different polymer chain topology have been prepared to further manipulate their physical properties, including the linear, branched, and cyclic polyesters [8-10]. Due to the endless molecular topology, cyclic polymers hold distinctly different physical properties compared to their linear counterparts, such as smaller hydrodynamic radius, reduced intrinsic viscosity, and higher thermostability [11-14]. As an example of cyclic polyesters, the cyclic PCL has been demonstrated to have the retarded hydrolytic degradation [15], faster crystallization [16], and higher melting temperature [17], compared to those of linear PCL analogues.

The known synthetic methods for cyclic polyesters with high purity can be divided into two categories. The first one is based on the ring-expansion strategy, which mainly includes two specific methods: the ring-opening polymerization (ROP) with cyclic tin initiators [18] and the zwitterionic polymerization with N-heterocyclic carbene organocatalysts [19]. Although the ring-expansion

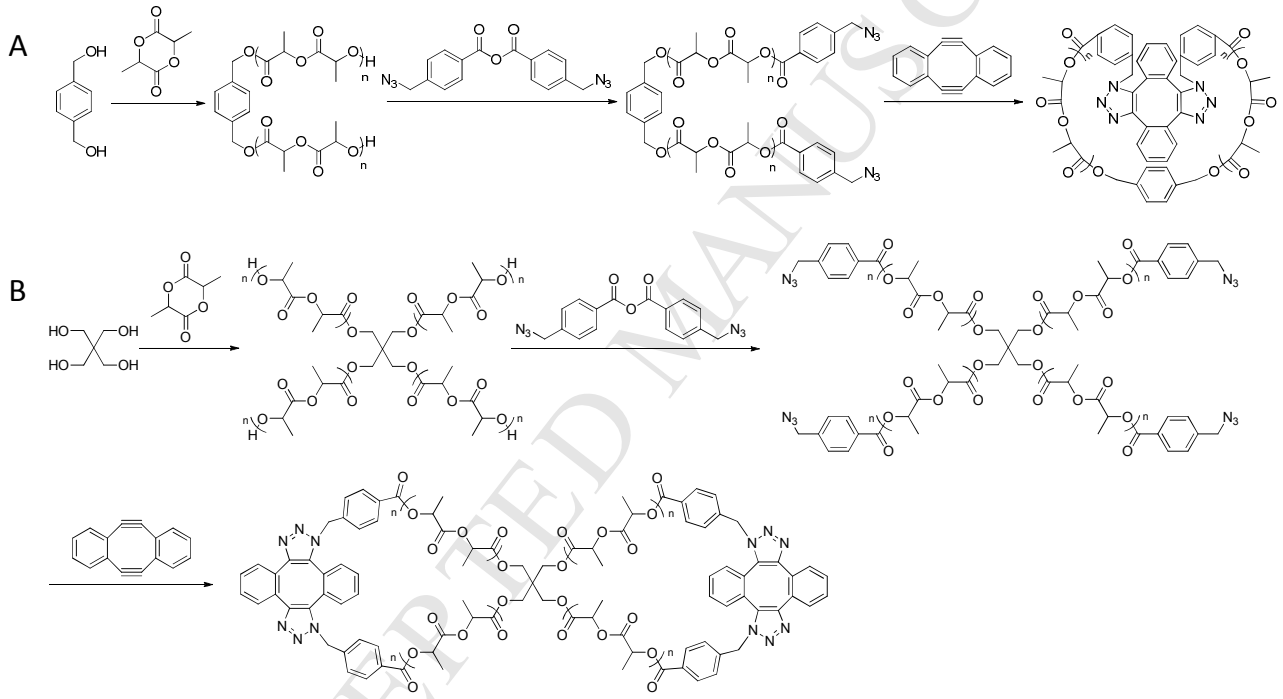
methods can produce pure cyclic polyesters in a large scale, they suffer from a limited control over the molecular weight and distribution of the resultant cyclic polyesters. The second one is based on the ring-closure strategy, in which the well-defined cyclic polyesters are prepared by ring-closing the telechelic polyesters under highly dilute solution [15]. Although the ring-closure methods produce cyclic polyesters with lower production efficiency and low to medium molecular weight [20,21], they are preferred since the molecular weight and distribution of the resultant cyclic polyesters can be finely tuned through the control of the corresponding linear precursors. In addition, the ring-closure methods have obvious advantages to produce polyesters with advanced cyclic topologies, such as theta, eight, and tadpole shapes [22,23].

To date, most of the successful ring-closure methods for cyclic polyesters can be categorized as the unimolecular heterodifunctional/homodifunctional approach [9]. In this approach, the well-defined telechelic polyesters with complementarily reactive terminals are prepared by ROP and post-modification of end hydroxyl groups. Under highly dilute solution, the linear precursors are ring-closed to produce the corresponding cyclic polyesters using the highly efficient ring-closing reactions such as copper-catalyzed azide-alkyne cycloaddition (CuAAC) [15,24,25], ring-closing metathesis reaction [26,27], and Diels-Alder reaction [28-30]. As the most straightforward ring-closure approach, however, the bimolecular homodifunctional technique is seldom used to prepare cyclic polyesters. In this approach, the cyclic polyesters are prepared by using the difunctional small molecule linkers to ring-close the homodifunctional linear polyester precursors. This approach is indeed attractive since the homodifunctional linear polyester precursors can be prepared with much more convenience. As far as we know, only one example was reported to prepare cyclic PLA based on the bimolecular homodifunctional technique, in which the same thiol-ene click reaction was used to perform the intermolecular and subsequently intramolecular coupling reactions [31]. Theoretically, the traditional bimolecular homodifunctional methods with

the same intermolecular and intramolecular coupling reactions are hard to produce the pure cyclic polymers. Using the same reaction to perform these two-step couplings, the traditional bimolecular ring-closure methods require accurate 1 : 1 stoichiometry between homodifunctional linear polymers and small molecule linkers to guarantee the purity of the resultant cyclic polymers. This is hardly achieved in practice because polymer has molecular weight distribution. Additionally, even with 1 : 1 stoichiometry, the traditional bimolecular ring-closure methods still hardly prepare pure cyclic polymers since the intermolecular and intramolecular coupling reactions require incompatible reaction concentrations. The efficient intermolecular coupling prefers high reaction concentration but the selective intramolecular cyclization requires low polymer concentration.

Recently, we developed a novel bimolecular homodifunctional method for the formation of pure cyclic polymers based on the combination of self-accelerating double strain-promoted azide-alkyne click reaction (DSPAAC) and atom transfer radical polymerization (ATRP) [32]. In this approach, the *sym*-dibenzo-1,5-cyclooctadiene-3,7-diyne (DBA) small linkers were used to ring-close the homodifunctional linear polymers with azide terminals. The intermolecular coupling reaction between the first alkynyl group of DBA and one azide terminal of a polymer chain in-situ activated the second alkynyl moiety of the DBA. It gained a much larger rate constant to react with the other azide terminal of the same polymer chain under dilute solution, facilitating the intramolecular cyclization and the formation of cyclic polymers. Due to the self-accelerating DSPAAC coupling reaction, this novel bimolecular method ingeniously eliminated the requirement of 1 : 1 stoichiometry and successfully produced pure cyclic polymers in the presence of an excess molar amounts of DBA small linkers. More importantly, the employment of excess DBA small linkers could increase the intermolecular coupling reaction rate, further resulting in a significantly enhanced preparation efficiency of cyclic polymers. In addition, because of the convenient reaction conditions of DSPAAC, this method could efficiently produce cyclic polymers in a very mild reaction

condition, such as in air, at room temperature, and without requiring any catalysts or chemical stimuli. Base on this, we developed a metal-free bimolecular homodifunctional ring-closure method for preparation of varied cyclic polyesters by combining ROP and DSPAAC click reaction herein. As shown in **Scheme 1**, the azide end-functionalized linear poly(L-lactide) (PLLA) precursors were prepared by ROP and post-modification of hydroxyl end groups. They were then ring-closed by self-accelerating DSPAAC reaction to prepare the corresponding cyclic PLLA using DBA as small linkers.



Scheme 1. Preparation of monocyclic (A) and bicyclic (B) PLLA based on the combination of ROP and DSPAAC, where one isomer was used to demonstrate the molecular structures of the monocyclic and bicyclic PLLA respectively.

Experimental

All experimental sections are detailed in the Supporting Information.

Preparation of monocyclic polyesters

As shown in Scheme 1A, the formation of cyclic PLLA was used as an example to demnostrate the scussess of the novel bimolecular homodifunctional ring-closure method for preparing varied monocyclic polyesters. Using 1,4-benzenedimethanol as a difunctional initiator, the homodifunctional PLLA with hydroxyl terminals (HO-PLLA-OH) could be produced from ROP of L-lactide (LLA) monomer, in which the diazabicycloundecene (DBU) was chosen as an organic catalyst to develop a completely metal-free method. By virtue of a $[LLA]_0$ of 3.3 M and a feed ratio of 1/30/0.3 among $[1,4\text{-benzenedimethanol}]_0/[LLA]_0/[DBU]_0$, the ROP of LLA was performed in DMF at 25 °C for 1 min to produce the well-defined HO-PLLA-OH with a monomer conversion of 87%. Fig. 1A shows the corresponding ^{1}H-NMR spectrum, where the average degree of polymerization (DP) was calculated as 26 from (Area(Hc_1)+ Area(Hc_2))/2. In addition, the peak area ratio of 2/1 between Ha_1 and Hb_1 indicated the quantitative location of the hydroxyl groups at the both ends of HO-PLLA-OH. Fig. S1A (black curve) shows the GPC characterization of HO-PLLA-OH, in which a monomodal and symmetrical peak shape was observed corresponding to M_n = 6470 and PDI (polydispersity index) = 1.05.

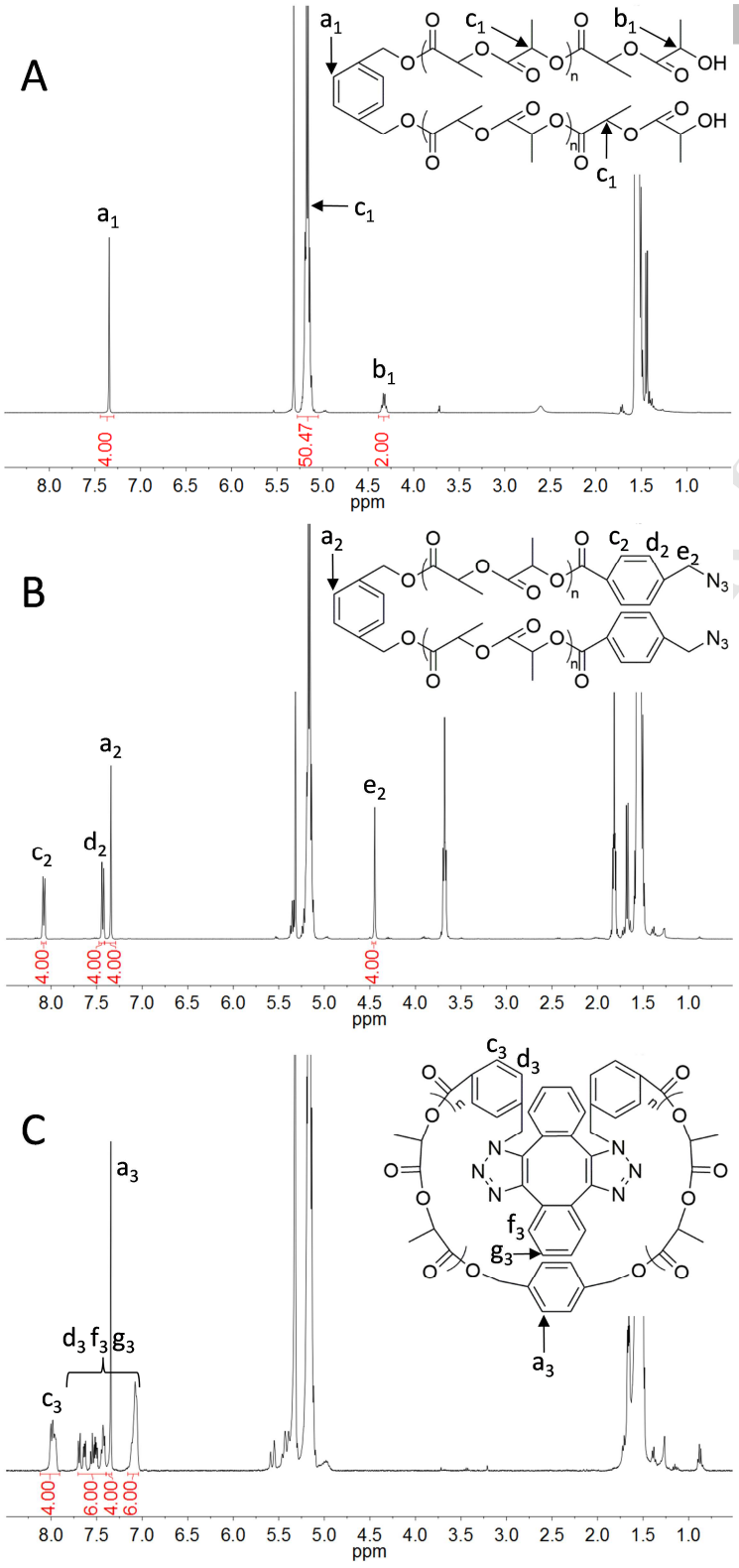


Fig. 1. ^{1}H-NMR spectra of HO-PLLA-OH (A), N_3-PLLA-N_3 (B) and the corresponding monocyclic PLLA (C) in CD_2Cl_2, where one isomer was used to demonstrate the molecular structure of monocyclic PLLA.

The homodifunctional PLLA with azide terminals (N_3-PLLA-N_3) was then prepared by esterifying the terminal hydroxyl groups of HO-PLLA-OH with 4-(azidomethyl)benzoic anhydride, which was detailed in Experimental section of Supporting Information. Fig. 2A (black curve) shows the GPC characterization of N_3-PLLA-N_3, in which the monomodal and symmetric peak shape was inherited from that of HO-PLLA-OH (Fig. S1A, black curve). The corresponding M_n and PDI were calculated as 6800 and 1.05, respectively. Fig. S2A (red curve) shows the FT-IR spectrum of N_3-PLLA-N_3, where the characteristic azide adsorption peak was clearly observed at 2100 cm^{-1} compared to that of (black curve) HO-PLLA-OH. Fig. 1B shows the ^{1}H-NMR spectrum of N_3-PLLA-N_3, in which the peak area ratio of 1/1 between Ha_2 and He_2 indicated the quantitative modification efficiency of hydroxyl end groups and the successful formation of N_3-PLLA-N_3.

According to our previous publication [32], the rate constant ratio ($K = k_2/k_1$) between the second (k_2) and first (k_1, 5.84×10^{-2} $M^{-1}s^{-1}$) azide-alkyne cycloaddition reactions was calculate as 185 for the self-accelerating DSPAAC reaction. This allowed the novel bimolecular approach to produce pure cyclic polymers even with a molar ratio above 100 between the DBA small linkers and the homodifunctional linear polymers with azide terminals. After optimization, a molar ratio of 400 between DBA and N_3-PLLA-N_3 and a PLLA concentration of 2.5×10^{-6} M in THF was employed to efficiently produce the well-defined monocyclic PLLA. The cyclization reaction was conveniently performed at room temperature in air for 24 h. Fig. 2A (red) shows the GPC curve of the resultant monocyclic PLLA. Compared to that (black curve) of linear N_3-PLLA-N_3, the well-defined monomodal and symmetric peak shape preserved but the peak position completely shifted to the lower molecular weight direction. A similar PDI of 1.03 and a 0.75 times smaller M_n were obtained between monocyclic (M_n = 5130) and linear (M_n = 6800) PLLA. This resulted from the characteristic smaller hydrodynamic volume of cyclic polymers than that of linear counterparts, strongly indicating the successful formation of monocyclic PLLA. Fig. S2A (blue curve) shows the

FT-IR spectrum of monocyclic PLLA, in which the characteristic azide adsorption peak disappeared completely at 2100 cm^{-1} compared to that of N_3-PLLA-N_3 linear precursor. This indicated a complete consumption of aizde terminals of N_3-PLLA-N_3 during the ring-closing reaction. Fig. 1C shows the ^{1}H-NMR spectrum of the resultant monocyclic PLLA. Where the peak ratio of 1/1/3 among Ha_3/Hc_3/Hd_3,f_3,g_3 clearly demonstrated the quantitative formation of monocyclic PLLA. Fig. 3 shows the MALDI-TOF mass spectra of linear (A) and monocyclic (B) PLLA. As shown in the full spectra (left), the absolute molecular weight was similar for both cases expanding from 3250 to 4750. The similar absolute molecular weight from MALDI-TOF mass spectrum and the significantly reduced apparent M_n from GPC indicated a more compact molecular structure of monocyclic PLLA, again confirming the formation of cyclic topology. From the expanded spectra (right), the peak distributions of linear and monocyclic PLLA could be accurately assigned to N_3-PLLA-N_3 with Na^+ and cyclic PLLA with Na^+, respectively. A regular m/z of 144 was observed between the neighboring peaks for both cases, which corresponded to the molar mass of the LLA monomer unit. These results strongly confirmed the successful preparation of the monocyclic PLLA.

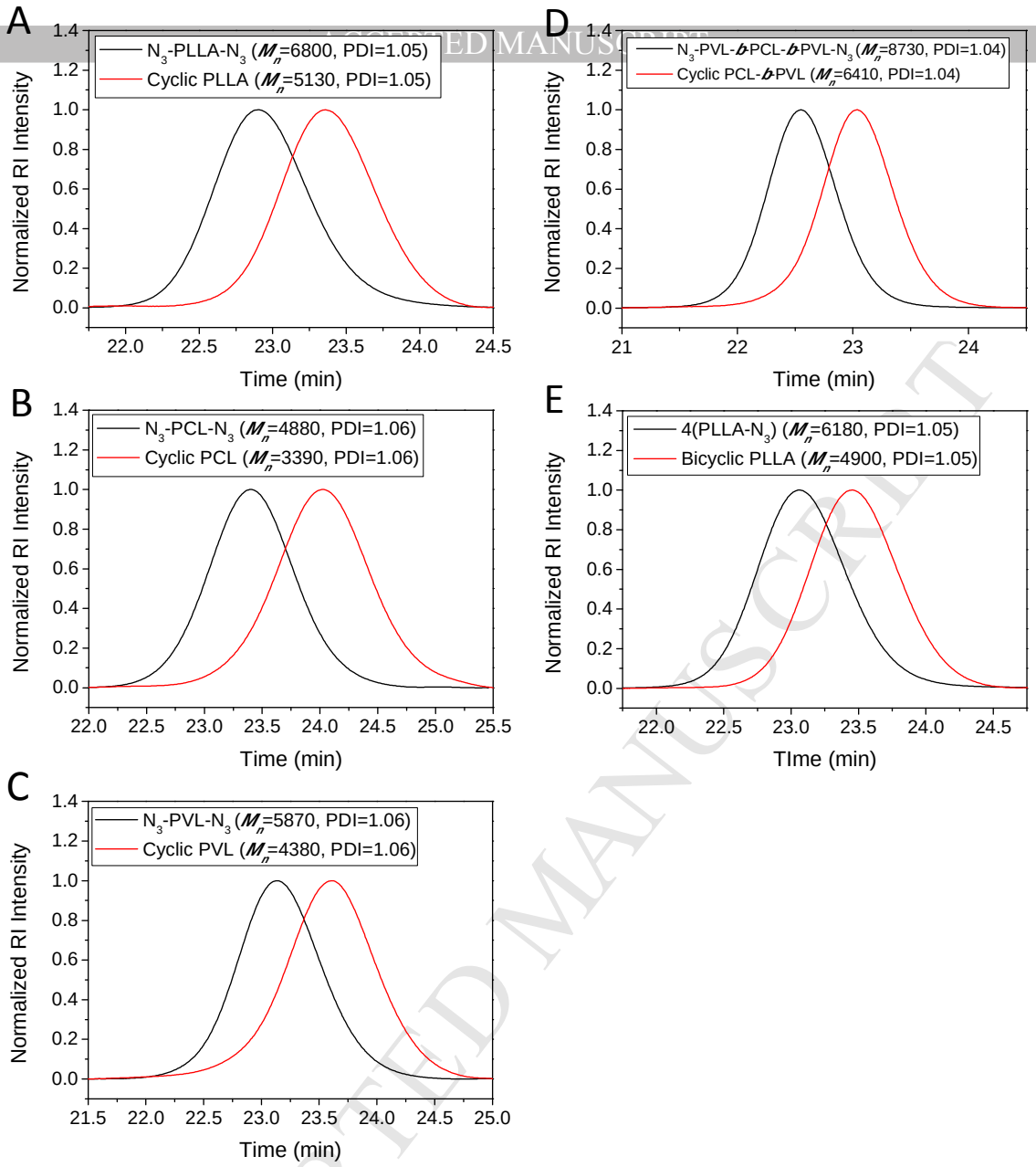


Fig. 2. GPC curves of the linear polyester precursors and the resultant cyclic polyesters: (A) N_3-PLLA-N_3 (black) and monocyclic PLLA (red); (B) N_3-PCL-N_3 (black) and monocyclic PCL (red); (C) N_3-PVL-N_3 (black) and monocyclic PVL (red); (D) N_3-PVL-*b*-PCL-*b*-PVL-N_3 (black) and monocyclic PCL-*b*-PVL (red); (E) 4(PLLA-N_3) (black) and bicyclic PLLA (red). THF was used as the eluent and PS standards were used for calibration.

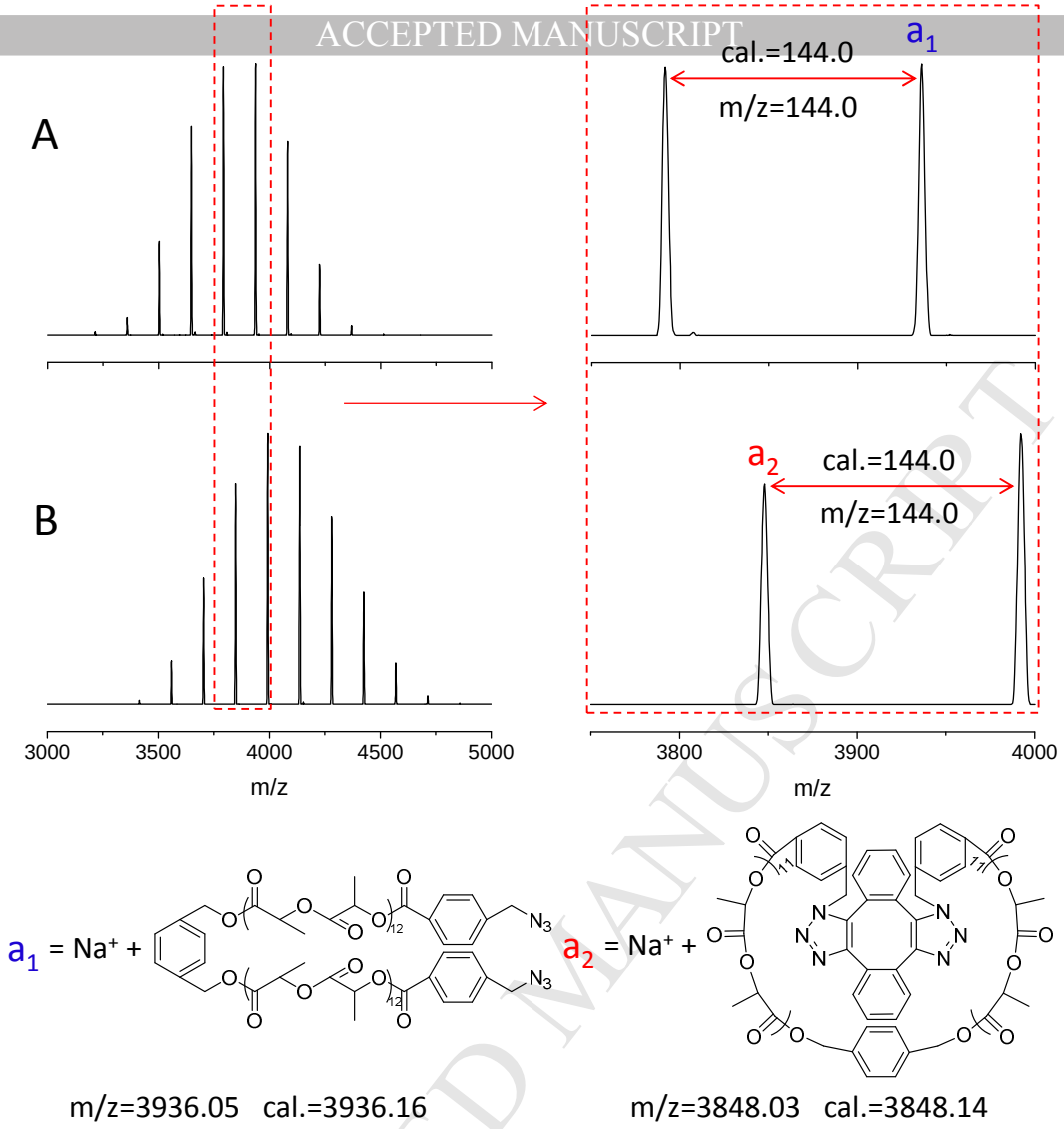


Fig. 3. MALDI-TOF mass spectra of N_3-PLLA-N_3 linear precursor (A) and the resultant monocyclic PLLA (B), where one isomer was used to demonstrate the molecular structure of monocyclic PLLA.

Encouraged by the successful preparation of monocyclic PLLA, the universality of this novel bimolecular homodifunctional method for cyclic polyesters was further demnostrated for the formation of monocyclic PCL, PVL, and their block copolymers. The corresponding preparation process and characterization were detailed in the Supporting Information.

Using the similar ROP condition for HO-PLLA-OH, hydroxyl-terminated homodifunctional PCL (HO-PCL-OH) and PVL (HO-PVL-OH) were prepared with the DP of 19 and 27, respectively. The successful formation of well-defined HO-PCL-OH and HO-PVL-OH was demonstrated by the GPC

(Fig. S1 B and C) and ^{1}H-NMR (Fig. S3A and S4A) characterization. Same to the synthesis of N_3-PLLA-N_3, the azide-terminated PCL (N_3-PCL-N_3) and PVL (N_3-PVL-N_3) were then prepared by esterifying the hydroxyl terminals of HO-PCL-OH and HO-PVL-OH with 4-(azidomethyl)benzoic anhydride. The quantitative formation of well-defined N_3-PVL-*b*-PCL-*b*-PVL-N_3 was proved by the FT-IR (Fig. S2 B and C, red curves), ^{1}H-NMR (Fig. S3B and S4B), and GPC (Fig. 2 B and C, black curves) characerization. Subsequently, the same ring-closing reaction condition was employed to prepare the well-defined monocyclic PCL and PVL. As shown in GPC curves of monocyclic PCL (Fig.2B, red curve) and PVL (Fig. 2C, red curve), the well-defined monomodal and symmetric peak shapes preserved but the peak position completely shifted to the lower molecular weight direction for both cases, compared to those (Fig. 2 B and C, black curves) characerization. Subsequently, the same ring-closing reaction condition was employed to prepare the well-defined monocyclic PCL and PVL. As shown in GPC curves of monocyclic PCL (Fig. 2B, red curve) and PVL (Fig. 2C, red curve), the well-defined monomodal and symmetric peak shapes preserved but the peak position completely shifted to the lower molecular weight direction for both cases, compared to those (Fig. S1 B and C, black curves) of linear precursors. The integration of GPC curves showed the same PDI and less than 0.75 times smaller M_n between monocyclic polyester and the corresponding linear precursors, indicating successful formation of cyclic topology. From the FT-IR spectra of monocyclic PCL (Fig. S2B, blue curve) and PVL (Fig. S2C, blue curve), the azide adsorption peak disappeared completely at 2100 cm^{-1} compared to those of N_3-PCL-N_3 and N_3-PVL-N_3 linear precursors. From the ^{1}H-NMR spectra of the monocyclic PCL (Fig. S3C) and PVL (Fig. S4C), the peak ratio of 1 between Hd_3 and Hg_3 clearly demonstrated the quantitative formation of monocyclic PCL and PVL. The MALDI-TOF mass spectra of linear (A) and cyclic (B) PCL and PVL were shown in Fig. S5 and S6**.** From the full spectra (left), the absolute molecular weights were similar between the linear precursors and the resultant cyclic polyesters for both cases. From the expanded

spectra (right), the peak distributions of linear and monocyclic PCL and PVL could be accurately assigned to the corresponding linear and cyclic polyester species with Na^+. These results strongly confirmed the successful preparation of the monocyclic PCL and PVL.

The formation of monocyclic PCL-*b*-PVL diblock copolymer was used to demonstrate the power of this novel bimolecular homodifunctional method for preparing cyclic copolyesters. The hydroxyl-terminated triblock copolymer PVL-*b*-PCL-*b*-PVL (HO-PVL-*b*-PCL-*b*-PVL-OH) was prepared by a sequential ROP procedure and detailed in Experimental section of Supporting Information. In short, the HO-PCL-OH was synthesized first and then used as a macroinitiator to perform ROP of VL monomer and produce HO-PVL-*b*-PCL-*b*-PVL-OH. The successful formation of well-defined HO-PVL-*b*-PCL-*b*-PVL-OH was demonstrated by the GPC (Fig. S1D) and ^{1}H-NMR (Fig. S7 A and B) characterization. Fig. S1D (red curve) shows the corresponding GPC characterization, in which the monomodal and symmetric peak shapes were observed with M_n = 8200 and PDI = 1.04. Fig. S7B shows the ^{1}H-NMR spectrum, where the area ratio of 1/1 between peak Hb_2 and Hd_2 indicated the quantitative location of hydroxyl groups at both ends of HO-PVL-*b*-PCL-*b*-PVL-OH. The azide-terminated triblock copolymer PVL-*b*-PCL-*b*-PVL (N_3-PVL-*b*-PCL-*b*-PVL-N_3) was then synthesized by esterifying the hydroxyl end groups of HO-PVL-*b*-PCL-*b*-PVL-OH with 4-(azidomethyl)benzoic anhydride. Fig. S2D (red curve) shows the corresponding FT-IR spectrum, where the azide adsorption peaks were clearly observed at 2100 cm^{-1} compared to that of HO-PVL-*b*-PCL-*b*-PVL-OH. Fig. S7C shows the ^{1}H-NMR spectrum of N_3-PVL-*b*-PCL-*b*-PVL-N_3, in which the peak area ratio of 1/1/1 among Hb_3/Hd_3/Hg_3 indicated the quantitative modification efficiency of hydroxyl end groups and the successful formation of N_3-PVL-*b*-PCL-*b*-PVL-N_3. Fig. 2D (black curve) shows the GPC characterization of N_3-PVL-*b*-PCL-*b*-PVL-N_3, in which the monomodal and symmetric peak shapes preserved, corresponding to M_n = 8730 and PDI = 1.04. Subsequently, the same ring-closing reaction condition

was employed to prepare the well-defined monocyclic PCL-*b*-PVL diblock copolymer. From the FT-IR spectrum of monocyclic PCL-*b*-PVL (Fig. S2D, blue curve), the azide adsorption peak disappeared at 2100 cm^{-1} after the ring-closing reaction. As shown in the ^{1}H-NMR spectrum of monocyclic PCL-*b*-PVL (Fig. S7D), the peak area ratio of between Hb_4 and Hh_4 indicated the quantitative formation of monocyclic PCL-*b*-PVL. As shown in the GPC characterization of monocyclic PCL-*b*-PVL (Fig. 2D, red curve), a monomodal and symmetric peak shape preserved, but the peak position completely shifted to lower molecular weight direction, compared to that (black curve) of the linear precursor. The GPC calculation showed a similar PDI of 1.04 and a 0.73 times smaller M_n between monocyclic PCL-*b*-PVL (M_n = 6410) and linear N_3-PVL-*b*-PCL-*b*-PVL-N_3 (M_n = 8730), indicating the successful formation of cyclic topology. Fig. S8 shows the MALDI-TOF mass spectra of N_3-PVL-*b*-PCL-*b*-PVL-N_3 (A) and the resultant monocyclic PCL-*b*-PVL (B). Similar to the previous publication, the MALDI-TOF mass spectra of block copolymers were complex and couldn't be accurately assigned due to the overlapping nature of the various chain compositions and chain lengths in the samples [33,34]. However, the absolute molecular weight was similar for both cases expanding from 3500 to 6000. Compared to the significantly reduced apparent molecular weight from GPC, the similar absolute molecular weight between N_3-PVL-*b*-PCL-*b*-PVL-N_3 and monocyclic PCL-*b*-PVL strongly indicated the successful formation of cyclic topology.

Preparation of bicyclic polyesters

An obvious advantage of the ring-closure strategy lies in the fact that it can produce varied cyclic polymers with more advanced cyclic topology. After the successful fabrication of monocyclic polyesters, this novel bimolecular homodifunctional method was further explored to prepare multicyclic polyesters. As shown in Scheme 1B, the formation of bicyclic PLLA was demonstrated

as an example. As the first step, 4 arms hydroxyl-terminated star PLLA (4(PLLA-OH)) was prepared using pentaerythritol as the ROP initiators. Using a feed ratio of 1/40/0.6 among $[pentaerythritol]_0/[LLA]_0/[DBU]_0$ and a $[LLA]_0$ of 1.6 M in DMF, the well-defined 4(PLLA-OH) was obtained with the monomer conversion of 63%. Fig. 4A shows the corresponding ^{1}H-NMR spectrum, in which DP was calculated as 7 for each arm from (Area(Ha_1)+ Area(Hc_1))/8. In addition, a peak area ratio of 2/1 between Hb_1 and Ha_1 indicated the high loyalty of the hydroxyl terminals for the resultant 4(PLLA-OH). From the GPC characterization (Fig. S1F, black curve), a monomodal and symmetrical peak was observed with M_n = 5500 and PDI = 1.05. The following substitution of hydroxyl terminals by azide produced the corresponding star PLLA precursors with 4 azide-terminated linear arms (4(PLLA-N_3)). Fig. 2E (black curve) shows the GPC characterization, in which a monomodal and symmetrical peak preserved with M_n = 6180 and PDI = 1.05. From the FT-IR spectrum of 4(PLLA-N_3) (Fig. S2E), the azide adsorption peak was clearly observed at 2100 cm^{-1}. From the ^{1}H-NMR spectrum of 4(PLLA-N_3) (Fig. 4B), a peak area ratio of 1 between Hb_2 and Hc_2 indicated the quantitative modification efficiency and formation of 4(PLLA-N_3).

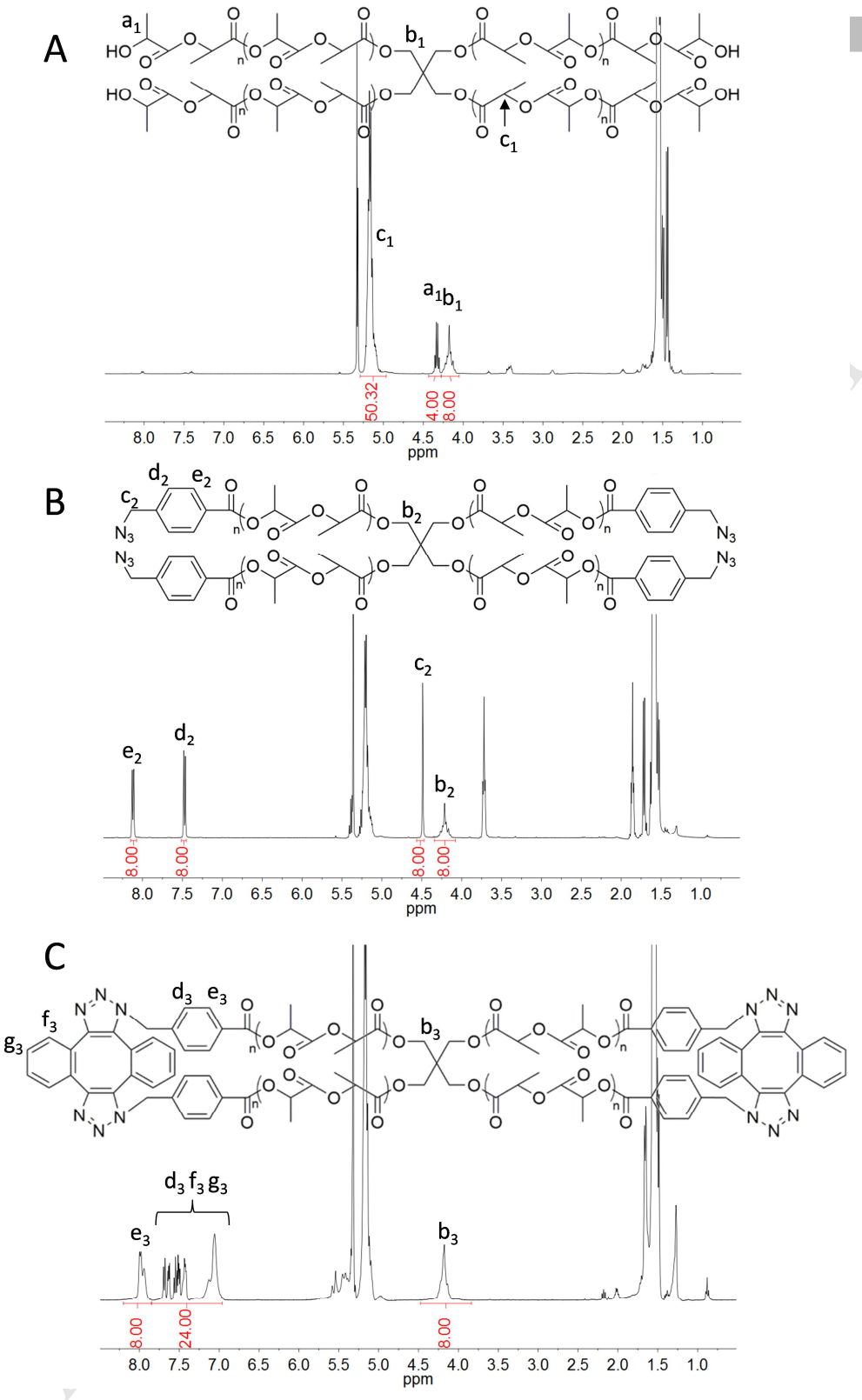


Fig. 4. ^{1}H-NMR spectra of 4(PLLA-OH) (A), 4(PLLA-N_3) (B), and the resultant bicyclic PLLA (C) in CD_2Cl_2, where one isomer was used to demonstrate the molecular structure of bicyclic PLLA.

The subsequent cyclization was performed at room temperature in air for 24 h using THF as

solvent, in which the concentration of 4(PLLA-N_3) and the feed ratio of DBA/4(PLLA-N_3) were 2.5 $\times 10^{-6}$ M and 400, respectively. Fig. 2E (red curve) shows the GPC characterization of the resultant bicyclic PLLA. Compared to that (Fig. 2E, black curve) of 4(PLLA-N_3) precursor, the monomodal and symmetric peak shape preserved but the peak position completely shifted to the lower molecular weight direction. A similar PDI of 1.05 and 0.79 times smaller M_n between bicyclic PLLA (M_n = 4900) and 4(PLLA-N_3) (M_n = 6180) from GPC calculation clearly indicated the successful formation of bicyclic topology. Fig. S2E shows the FT-IR spectrum of bicyclic PLLA, in which a complete disappearance of azide peak at 2100 cm^{-1} indicated a complete consumption of the azido groups during the ring-closing reaction. From the ^{1}H-NMR spectrum of the bicyclic PLLA (Fig. 4C), the peak area ratio of 1/1/3 among Hb_3/He_3/Hd_3,f_3,g_3 clearly indicated the quantitative formation of bicyclic PLLA. Fig. 5 shows the MALDI-TOF mass spectra of 4(PLLA-N_3) precursor (A) and bicyclic PLLA (B). From the full spectra (left), the absolute molecular weight of the bicyclic PLLA expanded from 4000 to 6000, which was higher than that of 4(PLLA-N_3) expanding from 3500 to 5500. This molecular weight increase was caused by the introduction of two DBA molecules to ring-close one 4(PLLA-N_3) precursor and form one bicyclic PLLA. From the expanded spectra (right), the peak distribution of 4(PLLA-N_3) precursor was accurately assigned to 4(PLLA-N_3) with Na^+, while the peak distribution of bicyclic PLLA was precisely ascribed to bicyclic PLLA with Na^+. The regular m/z interval of 144 between the neighboring peaks was corresponded to the molar mass of LLA monomer unit. These results strongly indicated the successful preparation of bicyclic polyester based on the combination of ROP and self-accelerating DSPAAC.

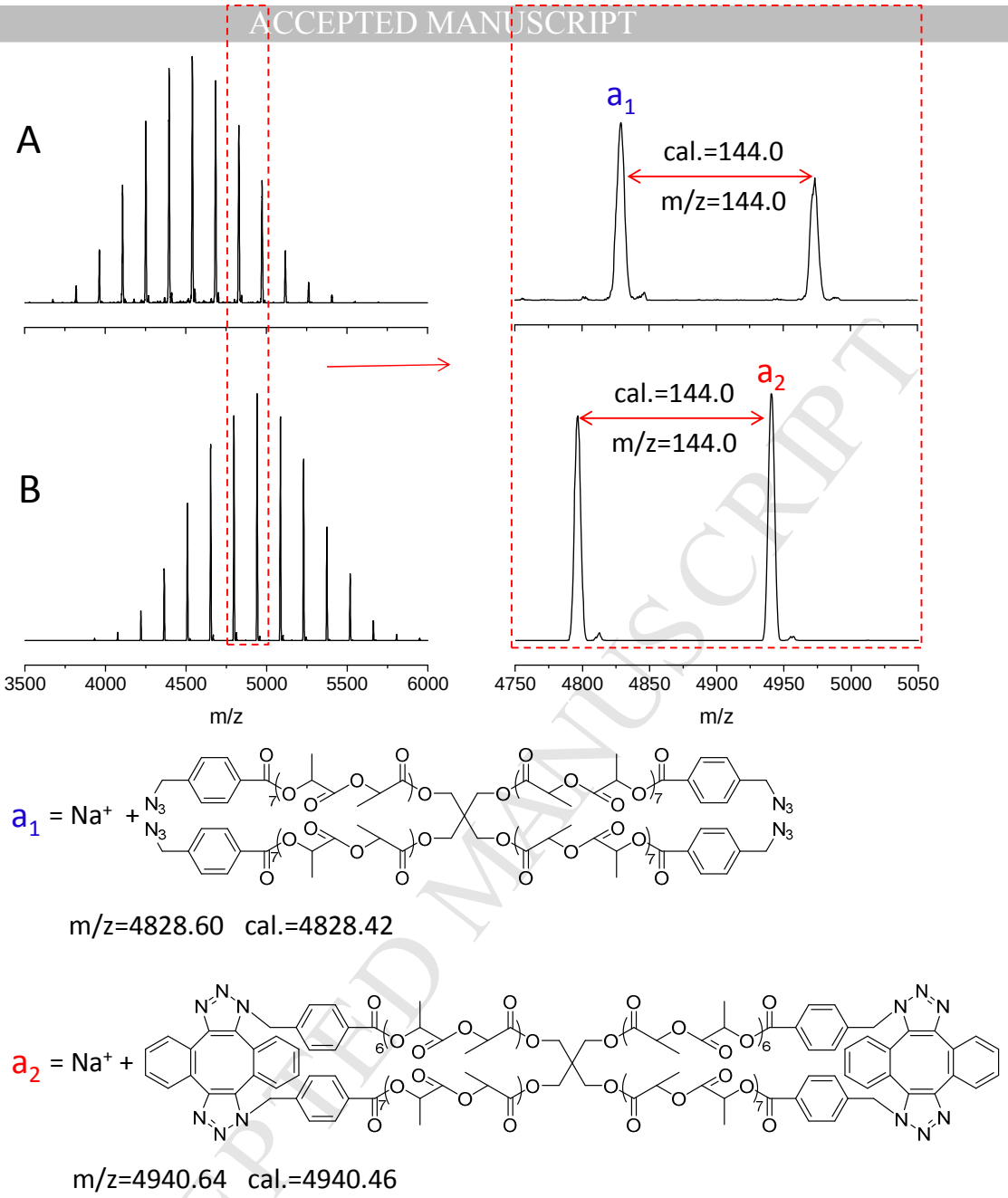


Fig. 5. MALDI-TOF mass spectra of 4(PLLA-N_3) precursor (A) and the resultant bicyclic PLLA (B), where one isomer was used to demonstrate the molecular structure of bicyclic PLLA.

Conclusions

A powerful homodifunctional bimolecular ring-closure method was developed to successfully prepare varied cyclic polyesters by combining ROP and self-accelerating DSPAAC click reaction. The well-defined telechelic polyesters with hydroxyl terminals were synthesized by ROP of cyclic

ester monomers with dihydroxyl initiators. The azide-terminated homodifunctional polyester linear precursors were then prepared by esterifying the hydroxyl end groups of the hydroxyl-terminated polyesters. The self-accelerating DSPAAC click reaction was then applied to ring-close the linear polyester precursors with DBA as small linkers and produce the corresponding cyclic polyesters. Due to the self-accelerating property of DSPAAC ring-closing reaction, this novel method eliminated the requirement of 1 : 1 stoichiometry between homodifunctional linear polymers and small linkers in the traditional bimolecular ring-closure method was further explored to successfully prepare the bicyclic polyesters as a representative of muticyclic polyesters. Considering the advantages of high efficiency, metal-free process, and very convenient ring-closing reaction operation, this novel bimolecular ring-closure method is expected to become a basic tool for the formation of varied cyclic polyesters.

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Appendix A. Supplementary data

Supplementary data related to this article, including the Experimental section and Fig. S1-S8, can be found at http://dx.doi.org/10.1016/j.polymer...

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Highlights:

- Well-defined cyclic polyesters are prepared via the metal-free homodifunctional bimolecular ring-closure method.
- The self-accelerating double strain-promoted azide-alkyne cycloaddition reaction is applied for the ring-closure, eliminating the traditional requirement of 1:1 stoichiometry between the linear polyester precursor and the small molecule linker.
- Pure cyclic polyesters, including monocyclic homo/block polyesters and bicyclic polyesters, are efficiently prepared by using excess molar amounts of small linkers to ring-close the linear polyester precursors.