Synthesis, Thermal Properties, and Thermo-responsive Behaviors of Cyclic Poly(2-(dimethylamino)ethyl Methacrylate)s

Xiaonan An, Qingquan Tang, Wen Zhu, Ke Zhang,* Youliang Zhao*

This study aims at physicochemical properties of thermo- and pH/CO₂-responsive cyclic homopolymers. Three examples of cyclic poly(2-(dimethylamino)ethyl methacrylate)s (PDMAs) are synthesized by combining the reversible addition–fragmentation chain transfer process and the Diels–Alder ring-closure reaction. After cyclization, the glass transition temperature significantly increases ($\Delta T_g = 51.8–59.7$ °C) due to the different configurational entropy and end groups, and the maximum decomposition temperature to lose the pendent groups is drastically decreased from 309 to 278 °C. Effects of polymerization degree, polymer concentration, additive of NaCl, and pH/CO₂ on lower critical solution temperature behaviors of PDMA aqueous solutions are investigated. The cloud points ($T_c$) of ring PDMAs are usually higher than their linear precursors, and the $\Delta T_c$ values obtained under a fixed condition can reach up to 20.7 °C, revealing the crucial role of the topology effect. This study paves the way for unique properties and applications of smart cyclic polymers and their derivatives.

1. Introduction

The development and enrichment of complex macromolecular architectures have revolutionized polymer science in the past few decades. The significant progress in living/controlled polymerization techniques allows facile construction of a variety of precisely controlled topological polymers. Among them, cyclic polymers prepared via ring-closure and ring-expansion techniques have attracted increasing attention due to the intriguing topological constraint and its impact on comprehensive properties. Because of reduced hydrodynamic volume, ring polymers lacking chain ends have a more compact structure as compared to their linear analogs with the same molecular weight (MW). The influence of “end-to-end”
linkage and the unique conformational properties have prompted studies on bulk and solution properties involving glass transition temperature,\[17–20\] self-assembly,\[21,22\] and thermo-dependent phase transition.\[23–25\] The expansion of functional ring polymers can not only inspire modeling/simulation studies to reveal the topology effect but also realize the unprecedented functions and properties for their eventual applications. Moreover, the introduction of intelligent segments and moieties can further endow cyclic polymers with on-demand functions and applications.\[24–28\]

On the other hand, much emphasis has been paid on stimuli-responsive polymers due to the overwhelming ability to adapt to surrounding environments and great potential in smart materials.\[29–31\] Owing to the vital role as signaling factors in the physiological environment, the intelligent systems bearing thermo and pH dual stimuli have been widely investigated.\[29–34\] In theory, such systems can be constructed via either introduction of different segments/components or utilization of a multifunctional segment, and both are promising for practical applications. At present, an important trend lies in construction of dual- and multiresponsive homopolymers due to the facile synthesis and rapid response to external stimuli.\[32–36\] Among them, poly(2-(dimethylamino)ethyl methacrylate) (PDMA) sensitive to temperature, pH/CO₂, and ionic strength is an ideal choice to reveal the advantages of multiple responsiveness.\[32,35–37\] PDMA is liable to exhibit pH-dependent polyelectrolyte behavior and lower critical solution temperature (LCST) ranging between 32 and 53 °C, leading to widespread therapeutic and biomedical applications.\[32,38–40\] Thus far, the examples of cyclic PDMA and their derivatives are very scarce,\[32\] although abundant PDMA-bearing polymers with distinct architectures have been prepared. Considering that the researches on their functions and properties can underlie the multipurpose applications in functional biomedical and surface materials, it is extremely urgent to systematically explore the architecture–property correlations of cyclic PDMA.

This study aims at synthesis and properties of cyclic PDMA with low molecular weights via UV-induced Diels–Alder click reaction.\[13–16\] To this end, 3-(2-formyl-3-methylphenoxy)propyl 4-(benzodithioyl)-4-cyanopentanoate (FBCP) mediated reversible addition–fragmentation chain transfer (RAFT) polymerization of DMA was employed to generate α-orthoquinodimethane–ω-dithiobenzoate heterofunctionalized PDMA, and then followed by Diels–Alder reaction between two end groups to form cyclic PDMA (Scheme 1). Owing to its many advantages involving lack of catalyst, low temperature, and tolerance to air, the UV-induced ring-closure method could
afford well-defined ring polymers, as evidenced from $^1$H NMR and gel permeation chromatography (GPC) analyses. On this basis, thermal properties and thermo-dependent phase transition of cyclic PDMA were investigated, and the properties were compared with their linear precursors. To the best of our knowledge, this is the first report on physicochemical properties of multisensitive cyclic homopolymers, which is beneficial to reveal the relationships among degree of polymerization (DP), topology, and functions. The progress in this study further paves the way for synthesis, properties, and applications of PDMA-related cyclic topologies involving cyclic block copolymers, sunflower-like starlike/graft copolymers, and their quaternized derivatives.

2. Results and Discussion

2.1. Synthesis of Cyclic PDMA and Their Linear Precursors

First, linear PDMA (L1–L3) were synthesized by RAFT polymerization of DMA mediated by FBCP in dioxane. Homopolymerization conducted at 60 °C for 8 h afforded linear PDMA in 39.6%–57.5% conversion. In $^1$H NMR spectra (Figure 1a and Figure S1, Supporting Information), typical signals originating from the RAFT agent were noted at 10.67 (ArC$_{6}$H$_{5}$O), 7.87, 7.52, 7.38, 6.83 (PhH and ArH), 2.57 (ArC$_{6}$H$_{5}$), 4.31 (ArC$_{6}$H$_{5}$O), and 4.14 ppm (COOC$_{2}$H$_{5}$), and characteristic signals in PDMA segment appeared at 4.06 (C$_{2}$H$_{2}$O), 2.57 (C$_{2}$H$_{5}$N), and 2.28 ppm (C$_{3}$H$_{3}$). By comparing the integrated signals at 6.83 and 2.28 ppm, the degree of polymerization (DP$_{PDMA}$ = $I_{2.28}/(3I_{6.83})$) was calculated as 11.2 (L1), 30.0 (L2), and 50.6 (L3), respectively. The molecular weight determined by $^1$H NMR analysis ($M_{n,NMR}$) was close to the theoretical values ($M_{n,th}$), and the GPC traces exhibited monomodal distribution (Figure 2), with polydispersity index (PDI) in the range of 1.10–1.16 (Table S1, Supporting Information).

Second, UV-induced ring-closure reaction was used to generate ring PDMA (C1–C3). The dilute solution of linear precursors in acetonitrile ($c$ = 0.05 mg mL$^{-1}$) was subjected to UV irradiation for 12 h at room temperature, and followed by evaporation of solvent to give ring polymers in quantitative yield. Careful inspection of $^1$H NMR spectrum of isolated C3 (Figure 1b) revealed that new signals generated by the cyclization appeared at 6.77 (ArH), 5.26 (ArCHOH), and 3.64 ppm (ArCH$_{3}$), and the characteristic signals corresponding to ArCHO (10.67 ppm), PhH connecting with the RAFT moiety (i.e., 7.87 ppm), and ArCH$_{3}$ (2.57 ppm) were wholly disappeared. In comparison with their linear precursors, the GPC traces of cyclic PDMA completely shifted to lower molecular weight side because of reduced hydrodynamic volume (Figure 2). The apparent molecular weights estimated by GPC ($M_{n,GPC}$) of C1–C3 ranged between 1660 and 6200 g mol$^{-1}$, with PDI values similar to their linear precursors. The $M_{n,GPC}(C_{x})/M_{n,GPC}(L_{x})$ ($x$ = 1–3) values within 0.82–0.84 were roughly comparable to those reported for other cyclic polymers.$^{[13–16]}$

To further reveal the formation of ring topology, typical samples L2 and C2 were chosen to perform MALDI-TOF MS measurements (Figure S3, Supporting Information). As shown in the full spectra (left), the absolute molecular weights were similar for both cases expanding from 3000 to 8000. Comparing to the apparent $M_{n,GPC}$ ratio of
0.82 between C2 and L2, the similar absolute molecular weight indicated a more compact molecular structure for C2, strongly indicating the successful formation of cyclic topology. From the expanded spectra (right), two main peak distributions of L2 could be accurately assigned to topology. From the expanded spectra (right), two main peak distributions of C2 were possibly ascribed to C2 ionized with H+ (a) and Na+ (b), and two main peak distributions of C2 were possibly ascribed to C2 ionized with H+ (c) and its corresponding derivative to lose HCN ionized with K+ (d). A regular m/z interval of cal. 157.1 was observed between neighboring peaks in the main distribution for both cases, corresponding to the molar mass of the DMA monomer unit. No intermolecular coupling was noted in this study, and the possible reasons lay in some factors such as relatively low concentration, medium steric hindrance during orthoquinodimethane—dithiobenzoate coupling, and suitable chain length and flexibility of PDMA segment.

2.2. Thermal Properties

The glass transition temperatures ($T_g$s) of cyclic PST$^{[17,18]}$ and PMMA$^{[19,20]}$ usually go up with increasing MW. Differential scanning calorimetry (DSC) measurements were initially performed to describe the effects of MW and topology on chain relaxation of PDMA segments. Both linear and cyclic PDMAs exhibited significant MW dependence of $T_g$ (Figure 3). With rising molecular weight, $T_g$(Lx) slightly varied from 15.0 to 20.7 °C, while $T_g$(Cx) substantially jumped from 66.8 to 80.4 °C. The PMDAs obtained after cyclization exhibited much higher $T_g$s, possibly originating from the end-to-end linkage, relatively low configurational entropy,$^{[17,18]}$ and the presence of hydroxyl moiety in the rigid linker. The ring closure introduced a bulky linkage bearing a 3,4-dihydro-3,8-trisubstituted-1H-isothiochromen-1-ol moiety, which comprised a bicyclic moiety and a hydroxyl group. The constrained architecture of cyclic polymers restricted long-range segmental motions, the formation of more rigid coupling structure bearing bicyclic moiety led to less flexibility as compared to C−C linkages, and the hydroxyl moiety may enhance intermolecular interactions via hydrogen bonds. To reveal the influence of the new functionality formed by DA reaction, the linear PDMA with terminal DA linkage (L3-OH) was synthesized via successive radical-induced reaction to remove the RAFT end of L3 and a subsequent DA reaction with 2-(2-cyanopropyl)dithiobenzoate to generate the hydroxyl-bearing DA moiety (Scheme S1, Supporting Information). DSC analysis revealed $T_g$(L3-OH) was higher than its precursor ($\Delta T_g = 6.8 °C; Figure S4, Supporting Information). Since L3-OH was similar to the linear analog of C3, the introduction of new functionality could partly lead to the significantly enhanced $T_g$s via cyclization besides the architectural role. As DP(PDMA) varied from 11.2 to 50.6, the $T_g$ differences between ring and linear polymers ($\Delta T_g = T_g$(Cx) − $T_g$(Lx), $x = 1−3$) increased from 51.8 to 59.7 °C.

Meanwhile, thermogravimetric analysis (TGA) measurements of typical samples L3 and C3 were performed to understand the different thermal stabilities between linear and cyclic PMDAs (Figure S5, Supporting Information). The decomposition of L3 could be roughly classified into three stages corresponding to the loss of end groups, side groups, and the polymer backbone, and the maximum decomposition temperatures ($T_{\text{max}}$) at each stage were deduced to be 188, 309, and 434 °C by differential curves. Due to the lack of end group, only two obvious decomposition stages were noted in TGA curve of C3, and the $T_{\text{max}}$ values appeared at 278 and 427 °C. Careful
inspection of TGA curves revealed that the decomposition temperature to lose \(N,N\)-dimethylethanolamine in ring PDMA was remarkably reduced when compared with its linear precursor (\(\Delta T_{\text{max}} = -31^\circ\text{C}\)), possibly resulting from more expanding conformations of pendent groups in cyclic architecture.

2.3. Thermoresponse of DPMAs in Aqueous Solution

Some factors such as topology, DP, polymer concentration \(c_p\), additive, and pH can affect phase transition of polymer solutions, and cyclic polymers usually exhibit enhanced cloud point \(T_c\) than their linear counterparts.\(^\text{[23–25]}\) To reveal the role of cyclic topology, the thermoresponsive behaviors of \(L_x\) and \(C_x\) \((x = 1–3)\) under different conditions were compared.

First, the influence of DP on thermoresponse was studied, and the polymer concentration was fixed at 5.0 mg mL\(^{-1}\) due to relatively high cloud point of ring polymers. Figure 4a shows the temperature-dependent transmittance, in which the LCST-type soluble-to-insoluble phase transition was observed in each case, and both linear and cyclic PDMAs tended to augment their \(T_c\) values with an increase in MW (Figure S6, Supporting Information). As DP varied from 11.2 to 50.6, \(T_c(L_x)\) was enhanced from 32.8 to 48.1 °C, and \(T_c(C_x)\) increased from 50.6 to 68.8 °C. These results revealed the molecular weight played an important role in thermoresponsive properties, in which the enhanced \(T_c\) with extended chain length was primarily resulted from the promoted intra- and interchain hydrophilic interactions. Owing to the presence of repulsive forces between rings and the influence of topological constraint on heat-induced dehydration and coil-to-globule collapse,\(^\text{[41,42]}\) cyclic PDMA exhibited a much higher \(T_c\) value than its linear precursor, and the \(\Delta T_c\) values were fluctuated between 17.8 and 20.7 °C. Apart from the turbidity analysis, dynamic light scattering (DLS) is another powerful tool to reveal the phase transition behaviors. The DLS curves of \(C_1\) and \(C_2\) solutions at different temperatures are plotted in Figure S7 (Supporting Information). With increasing temperature, the hydrodynamic diameter (\(D_h\)) of polymer solution was slightly changed at a low temperature range, rapidly increased to a maximum value, and then slightly decreased. The temperature range for phase transition process was roughly comparable to that determined by the turbidity measurement.

Second, \(L_2\) and \(C_2\) were chosen as typical samples to illustrate the effects of polymer concentration on phase
transition. As well documented, the $T_c$'s tend to increase with reduced concentration due to the dilution effect.$^{[32–37]}$ As $c_p$ varied from 0.5 to 5.0 mg mL$^{-1}$, the curves of transmittance versus temperature are plotted in Figure 4b. With lowered concentration, $T_c$(L2) gradually shifted from 39.0 to 70.2 °C, however, the tendency for $T_c$(C2) was a bit different. It first increased from 57.4 ($c_p$ = 5.0 mg mL$^{-1}$) to 75.8 °C ($c_p$ = 1.0 mg mL$^{-1}$) and then stabilized at about 76 °C as $c_p$ was further reduced (Figure S8, Supporting Information), which may be ascribed to the topology effect. At suitable concentrations, the cyclic topology allowed more expanding condensation of pendant groups, and the repulsive forces between rings induced formation of loose packing of polymer chains, leading to similar temperature-dependent phase transition. Another finding lies in their close cloud point at lower concentration, in which the $\Delta T_c$ value noticeably decreased from 18.4 to 6.0 °C as $c_p$ dropped from 5.0 to 0.5 mg mL$^{-1}$. These results suggest the dilution effect can compete with the topology effect as the polymer concentration is relatively low.

Third, the LCST curves of L2 and C2 aqueous solutions ($c_p$ = 5.0 mg mL$^{-1}$) were measured in the presence of NaCl to reveal the salt effect. By adding inorganic salts into the aqueous solution of thermoresponsive polymers, the cloud points are normally reduced due to the salting-out effect originating from the disruption of hydrogen bonding interactions between polymer chains and water.$^{[32–37]}$ $T_c$(L2) moderately fell from 39.0 °C (without salt) to 37.2 °C ($c_{\text{NaCl}}$ = 1.0 mol L$^{-1}$) and then further dropped to 30.5 °C ($c_{\text{NaCl}}$ = 5.0 mol L$^{-1}$), while $T_c$(C2) initially stabilized at about 57 °C ($c_{\text{NaCl}}$ = 0–0.5 mol L$^{-1}$) and then drastically reduced to 37.0 °C ($c_{\text{NaCl}}$ = 5.0 mol L$^{-1}$). The $T_c$ values of ring PDMA were similar as salt concentration decreased owing to the cyclic topology. The improved stability of cyclic PDMA solution upon addition of salt was in good accordance with the reported results, in which cyclic polymers usually exhibited enhanced thermal and salt stability as compared with their linear counterparts.$^{[43]}$ For linear PDMA, the increasing dehydration with addition of salt initially led to the intermicellar bridging, and followed by the formation of large agglomerate as the temperature was further enhanced. However, the chain motions in ring PDMA micelles were topologically prohibited to circumvent bridging, and thus the stability against salt (dehydration) and heating (the thermal motion of chain ends and side groups) was significantly improved. As $c_{\text{NaCl}}$ increased from 0.2 to 5.0 mol L$^{-1}$, the $\Delta T_c$ value dropped from 18.7 to 6.5 °C (Figure S9, Supporting Information), suggesting that the disruption of hydrogen bonds at high salt concentration can efficiently reduce the influence of cyclic topology on heat-induced phase transition.

Last, the pH/CO$_2$ response was also investigated to depict the role of external stimuli. When L2 and C2 were directly dissolved in neutral water ($c_p$ = 5.0 mg mL$^{-1}$), their aqueous solutions exhibited pH 7.8 (L2) and 7.9 (C2), respectively. As the solution pH was initially adjusted to be less than 7.0 by addition of suitable amount of dilute HCl, no LCST-type phase transition was noted at the temperature window of 20–80 °C (figure not shown). The LCST curves were further measured under basic conditions by utilization of NaOH aqueous solution, and the transmittance–temperature correlations are plotted in Figure 4d. $T_c$(L2) slightly dropped from 39.0 to 34.9 °C as pH increased from 7.8 to 11.9, while $T_c$(C2) continuously decreased from 57.4 to 49.0 °C as pH rose from 7.9 to 12.1 (Figure S10, Supporting Information). The dropped $T_c$ with enhanced pH under basic conditions could be mainly ascribed to the deprotonation of the appending protonated dimethylamino groups and/or the salting-out effect in the presence of NaOH. As pH jumped from 7.8 to about 12, the maximum reduced $T_c$ was value was around 4.1 °C (for L2) and 8.4 °C (for C2), while the $\Delta T_c$ value only slightly decreased from 18.4 to 14.1 °C. These results indicated the topology effect still played a predominant role in phase transition under basic conditions. Similar to other CO$_2$-switchable polymers due to protonation of the amine groups,$^{[32–34]}$ the LCST behaviors of both linear and cyclic PDMA as could be switchable with CO$_2$ and N$_2$ (Figures S11 and S12, Supporting Information). The solution pH after purge of CO$_2$ for 5 min was about 6.2 (for L2) and 6.3 (for C2), revealing lack of phase transition under acidic conditions. The presence and absence of thermo-dependent phase transitions could be efficiently recycled for many times via bubbling with the acidic or inert gas for 2–5 min, and no obvious change in $T_c$ was noted.

3. Conclusions

Well-defined cyclic PDMA were efficiently synthesized by combination of RAFT polymerization and UV-induced Diels–Alder click reaction. The ring-closure reaction was successfully conducted, evident from $^1$H NMR, GPC, and MALDI-TOF MS analyses. As compared with their linear precursors, the cyclic PDMA were liable to exhibit quite different thermal properties, in which the glass transition temperature was significantly enhanced (Δ$T_g$ = 51.8–59.7 °C) due to the differences in configurational entropy and end groups, while the maximum decomposition temperature corresponding to the loss of pendent 2-(dimethylamino)ethoxy groups was remarkably decreased owing to the cyclic topology. The thermoresponsive behaviors of PDMA in water were affected by some factors such as polymerization degree, polymer concentration, additive of NaCl, and pH/CO$_2$. The cloud points of
ring PDMSs were usually higher than their linear precursors, and the ΔTc values obtained under a fixed condition could reach up to 20.7 °C due to the combined influences of topology effect and other factors. Considering the great potential of RAFT process in construction of complex architectures such as random, block, and alternating copolymers, the ring-closure method can be used to generate a wide range of cyclic polymers and their derivatives with rich compositions and versatile functions. This study can not only afford insight into structure–property relationships of smart ring homopolymers but also pave the way for exploring the unique properties and applications of multifunctional cyclic polymers and their derivatives.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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