

Precise Pentamers with Diverse Monomer Sequences and Their Thermal Properties

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 Electronic Supplementary Information

Abstract Sequenced-defined oligomer has been emerged as one of the hot topics in polymer chemistry due to its capability of precisely controlling both chain length and monomer sequence. Recent efforts have focused on development of synthetic methodologies using state-of-the-art chemistry tools. However, investigating the impact of minor changes in monomer sequence on physical properties of these materials is still underdeveloped. Herein, four sequenced pentamers are synthesized by a reversible addition-fragmentation chain transfer (RAFT) single unit monomer insertion technique, in which a base pentamer possesses a relatively rigid backbone comprising of five cyclic monomer units. One of the cyclic units in this base pentamer is replaced by an acyclic monomer at different locations (the 1st, 3rd and 5th unit) to produce three modified pentamers, which leads to a significant decrease of glass transition temperature (T_g) compared to the base pentamer. Meanwhile, the modified pentamers with identical primary structures but distinct monomer sequences also present different T_g values depending on the position of the acyclic monomer unit. The middle (3rd) position of the acyclic unit causes profound decrease of T_g due to its increased molecular flexibility. These synthetic pentamers have been demonstrated to be excellent oligomeric plasticizers to modulate thermal transitions of bulk polymer materials.

Keywords Pentamer; Sequence control; Single unit monomer insertion; Glass transition temperature; Sequence-defined oligomer

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INTRODUCTION

Monodisperse, sequence-defined oligomer has been one of emerging classes of superior materials for fundamental studies and various applications.^[1–10] These oligomers are comprising of a certain number of repeating units of monomers that can be assembled to produce high molecular weight dispersed polymers, which thus affords the oligomers characteristic properties of macromolecules. However, they generally have small sizes similar to organic molecules. The synthesis procedures also follow small molecular transformations that may involve multiple steps of organic reactions or separation, not one-pot polymerization.^[11–19] They have features of precise structures and monodispersity as most organic compounds have. Therefore, this class of materials exclusively combines traditional molecular precision of organic chemistry with the materials properties of macromolecules. Oligomers have tremendous potential for the development of advanced materials in both scientific and industrial applications.^[7,20] For instance, as small molecule models of long chain polymers, oligomers are crucial to understand fundamental structure-

property relationships. Investigation on a model compound can simplify in-depth understanding of the properties of its parent polymer using commonly used analytical tools and simulation methods.^[21–26]

Taking advantage of precise control over chemical structures, sequence-defined oligomers are widely used to investigate the sequence and stereochemical effect on the kinetics of chemical reactions and physical properties.^[6,7,9,24–39] This includes both conjugated oligomers and linear or dendritic macromolecules with different sequences. However, one of the obstacles in the research of sequence-defined oligomers is their efficient synthesis, although a plethora of synthetic methodologies have been developed in recent decades.^[35] It is still limited in difunctional monomers to be coupled through linear or iterative exponential growth,^[12,34] in most cases using protecting groups. Currently, there are very few cases using vinyl monomers through chain growth mechanism, which thus limits the monomer diversity.^[5] Meanwhile, it thus causes that macroscopic property investigation is underexplored. In our previous work, we developed a unique radical based single unit monomer insertion (SUMI) technique to assemble vinyl monomers into sequence-defined oligomers.^[5,40,41] It brings benefits into the area including the non-protecting chemistry, tolerance towards functional groups and easy reaction setups. It can also prepare diverse

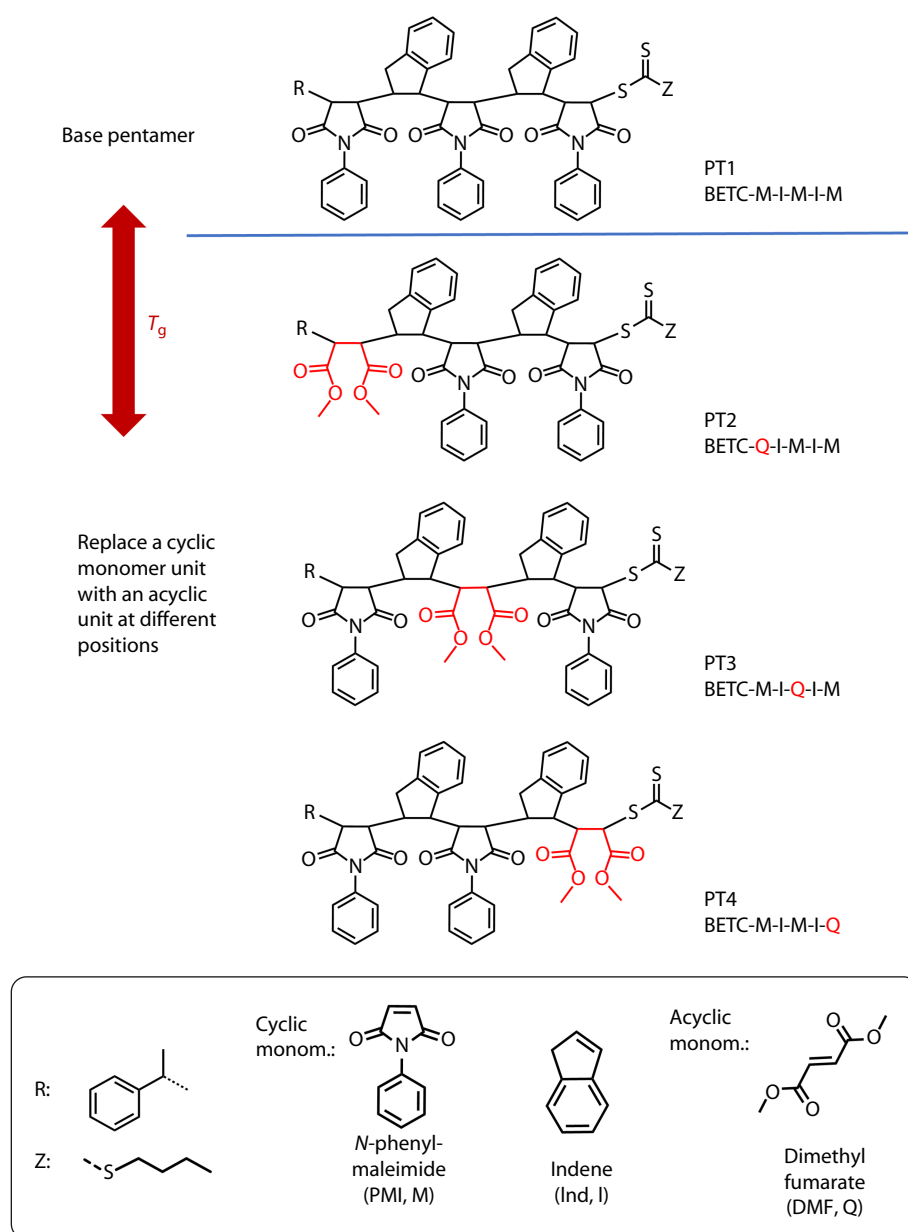
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sequenced oligomers with distinct backbone rigidity for the investigation of physical properties.

In our recent report,^[42] we investigated the thermal glass transitions of three pairs of sequence-defined unconjugated trimers comprising of different combinations of four monomers, indene (Ind, I), *N*-phenylmaleimide (PMI, M), fumaronitrile and dimethyl fumarate (DMF, Q). In each pair, although the trimers possess identical compositions, different monomer sequences cause a significant change of their glass transition temperatures (T_g s) up to 11.6 °C. The monomer connections of cyclic indene (Ind, I, Scheme 1) monomer and cyclic *N*-phenylmaleimide (PMI, M) monomer (head-tail versus tail-head, *i.e.*, M-I versus I-M) led to distinct intramolecular ro-

tational barriers along the oligomer backbone, with a higher steric hindrance between two monomer units in M-I than that in I-M. This result demonstrated the connection types and sequences of two monomers, particularly rigid cyclic monomers, play important roles in the macroscopic properties.^[42] Due to short chain length (only three units) of the investigated oligomers, this segment difference (M-I versus I-M) is reasonable. However, it is not applicable to a long polymer chain, such as an alternating copolymer of two M and I monomers. Specifically, as shown in Scheme 1, there are both connection diads of M-I and I-M in all pentamers. The intramolecular rotational barrier may be unable to explain the sequence impact on their properties. Instead, the molecular



Scheme 1 Placement of DMF (Q) unit at different (1st, 3rd and 5th) positions of a base pentamer BET-M-I-M-I-M (PT1) producing three sequenced pentamers, BET-Q-I-M-I-M (PT2), BET-M-I-Q-I-M (PT3) and BET-M-I-M-I-Q (PT4). BETC: *n*-butyl-1-phenylethyl trithiocarbonate; M: *N*-phenyl maleimide (PMI); I: indene (Ind); Q: dimethyl fumarate (DMF).

rigidity of the whole molecules plays a more important role.

To specifically investigate the impact of molecular rigidity on the T_g values of oligomers, we herein synthesize a series of sequence-defined pentamers that are comprising of diverse sequences of cyclic (M and I) and acyclic (Q) monomers (Scheme 1). Starting from a base pentamer with alternating cyclic I and M monomers, we replace one of the M units in the backbone with an acyclic Q monomer at different positions synthesized through a reversible addition-fragmentation chain transfer (RAFT) SUMI method, which produces three sequenced pentamers with identical primary structures but different monomer sequences. Compared to their base pentamer, these pentamers have relatively less rigid chain backbone and cause the decrease of T_g values. Meanwhile, the T_g s are investigated on these three pentamers with distinct monomer sequences. Additionally, we employ the pentamers as efficient oligomeric plasticizers to tune T_g of a high molecular weight polymer.

EXPERIMENTAL

Materials

Dimethyl fumarate (DMF, Q, 97%), *N*-phenylmaleimide (PMI, M, 97%), indene (Ind, I, 98%), styrene (St, 99%), 2-cyano-2-propyl dodecyl trithiocarbonate (CPDTC) and 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine zinc (ZnTPP, 98%) were all purchased from Sigma-Aldrich and used as received. *n*-Butyl-1-phenylethyl trithiocarbonate (BETC) were synthesized according to the reported literature.^[41,43] Azodiisobutyronitrile (AIBN) purchased from Sigma-Aldrich was recrystallized in hot toluene before use. Dimethyl sulfoxide (DMSO), dichloromethane, *n*-hexane, ethyl acetate and silica gel (40–63 micron) were purchased from Ajax Chemical and used as received. Cartridges for automated flash chromatography were purchased from Biotage® and used as received.

Instrumentation

Nuclear magnetic resonance (NMR) spectroscopy was carried out on a Bruker Advance III with SampleXpress operating at 300 MHz Bruker Advance III for ^1H , ^{13}C , ^1H - ^{13}C HMBC, ^1H - using DMSO- d_6 as the solvents. Data obtained was reported as chemical shift (δ) measured in ppm.

Gel permeation chromatography (GPC) was performed using tetrahydrofuran (THF) as the eluent. The GPC system was a Shimadzu modular system comprising of an auto injector, a Phenomenex 5.0 μm bead size guard column (50 $\times$ 7.5 mm) followed by two MIX C columns provided by Polymer Lab, and a differential refractive-index detector. The system was calibrated with narrow molecular weight distribution polystyrene standards with molecular weights of 200 g·mol $^{-1}$ to 10 ^{6} g·mol $^{-1}$.

Differential scanning calorimetry (DSC) was performed on TA Q20 with a heating rate of 5 $^\circ\text{C}/\text{min}$ or 10 $^\circ\text{C}/\text{min}$ depending on different oligomers or polymers under a nitrogen atmosphere. Glass transition temperature (T_g) was reported based on the second heating cycle in the temperature range of 10–110 $^\circ\text{C}$ (3 heating cycles) for all oligomers, and 10–250 $^\circ\text{C}$ (3 heating cycles) for plasticizing measurements (more specifics refer to the electronic supplementary information, ESI). Each sample around 2–5 mg (vacuum-dried overnight at

50 $^\circ\text{C}$) was sealed in aluminum pans.

Electrospray ionization mass spectroscopy (ESI-MS) was performed using a Finnigan LCQ Deca mass spectrometer (Thermo Finnigan, San Jose, CA) equipped with an atmospheric pressure ionization source operating in the nebulizer-assisted electrospray voltage of 5 kV, with nitrogen as sheath gas. Xcalibur ver. 1.3 (Finnigan) was used for spectral processing.

SUMI experiments were carried out in a glass bath rearranged by LED RGB strip light, where the reaction mixtures are irradiated in the centre of round bath reactor with a diameter of 9 cm and 0.46 mW·cm $^{-2}$ under red light irradiation (reactor setup refers to Fig. S1 in ESI).

Biotage® (Isolera One) automated flash chromatography was used to purify SUMI products. The purification procedure is very similar for all SUMI products except the composition of gradient eluent (*n*-hexane/ethyl acetate, from 1/1 to 1/19, V/V). After the solvent removal from the reaction mixture, the crude product was then subjected to automated flash chromatography using SNAP Ultra 50 g cartridge (HP-Sphere™ 25 μm silica) as column and *n*-hexane/ethyl acetate as the gradient eluent. The collected fractions were dried under reduced pressure.

Synthesis and Characterization of SUMI Products

Taking the SUMI reaction of the pentamer BETC-Q-I-M-I as an example. A solution containing RAFT agent trimer (BETC-Q-I-M, 530 mg, 0.75 mmol), monomer (Ind, 435.6 mg, 3.75 mmol), photocatalyst (ZnTPP, 2.6 mg, 0.0038 mmol) and DMSO (7.5 mL) was charged in a 21 mL glass vial, using the molar ratio [Ind]/[BETC-Q-I-M]/[ZnTPP]=5/1/0.005. The glass vial was sealed with a rubber septum and the reaction solution was degassed with nitrogen for 20 min. The reaction mixture was then irradiated under red LED light (λ_{max} =635 nm, 0.46 mW·cm $^{-2}$) at room temperature. After 18 h light irradiation, DMSO was removed by extraction of water. The crude product was then subject to flash chromatography using Biotage®. The final product (827 mg, isolated yield 80%) was subjected to ^1H -NMR, GPC and ESI-MS analysis.

General Procedures for RAFT Copolymerization of St and PMI

A solution containing RAFT agent (CPDTC, 10 mg, 0.03 mmol), PMI (250.6 mg, 1.44 mmol), styrene (150.6 mg, 1.44 mmol), thermal initiator (AIBN, 0.95 mg, 0.006 mmol) and solvent (toluene, 1.5 mL) was prepared in a 4 mL glass vial by using the molar ratio [CPDTC]/[PMI]/[styrene]/[AIBN]=1/50/50/0.2. The glass vial was sealed with a rubber septum, and the reaction solution was degassed with nitrogen for 20 min. The reaction mixture was then placed in an oil bath at 70 $^\circ\text{C}$ with stirring. After 1 h reaction, the reaction solution was precipitated in methanol, followed by filtration. The solid powder was collected and dried (380 mg), which was then submitted for GPC analysis (M_n =17720 g/mol, M_w/M_n =1.21) calibrated by polystyrene standard.

RESULTS AND DISCUSSION

Synthesis and Characterization of Sequenced Pentamers

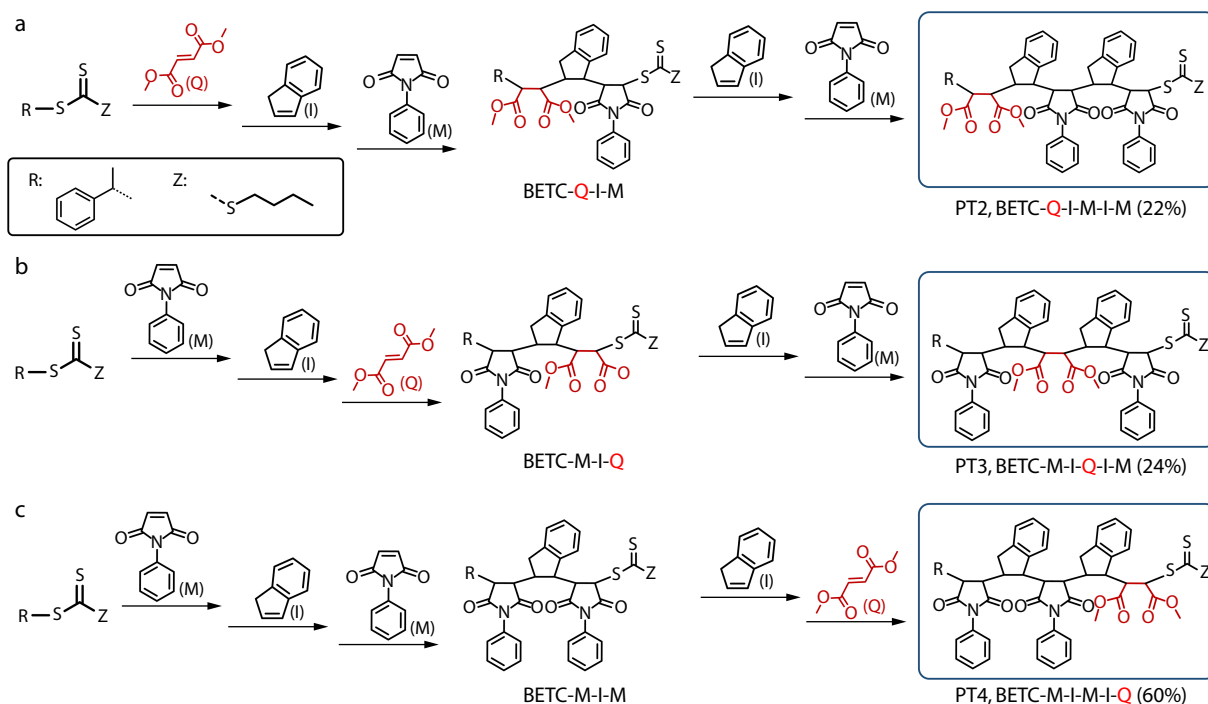
The base pentamer BETC-M-I-M-I-M (PT1), as synthesized in our

previous report,^[32,41] is comprising of alternating sequence of M and I monomers. M and I monomers are both cyclic vinyl monomers with planar five-membered rings, which provide a relatively hindered and rigid backbone for the resulting pentamer. The synthesis of this pentamer involves iterative additions of these two monomers one at a time through radical based RAFT SUMI mechanism, using visible light catalysis under mild reaction conditions (room temperature, low intensity of red LED light and low catalyst loading). M is an electron-accepting monomer and I is an electron-donating monomer, which allows for highly efficient alternating radical additions during SUMI processes attributed to the possible formation of electron-donor-acceptor complex.^[44] Most significantly, this pentamer can be synthesized in a large scale (grams level) and high isolated yield (59% for five iterations).^[41] The selection of acyclic vinyl monomer to replace cyclic M unit in the base pentamer is Q monomer, which has been demonstrated to be a good electron-accepting monomer in oligomer synthesis through a SUMI process.^[32] In this study, the Q monomer unit is placed in the 1st, 3rd or 5th positions, respectively, to prepare three pentamers, BETC-Q-I-M-I-M (PT2), BETC-M-I-Q-I-M (PT3), and BETC-M-I-M-I-Q (PT4) as shown in Scheme 1. These three pentamers have identical compositions but different monomer sequences, which are thus ideal models to investigate sequence effect on the material properties.

The synthesis involves the sequential insertion of the required monomer into a RAFT agent. In our previous report, the trimers with three successive monomer units, BETC-Q-I-M, BETC-M-I-Q, BETC-M-I-M, have been synthesized in moderate to high yields depending on the monomer sequences.^[32] For instance, BETC-Q-I-M is prepared by sequentially inserting Q, I and M into a trithiocarbonate (BETC, Scheme 2) using ZnTPP

as the photocatalyst, DMSO as the solvent under red light irradiation. In these SUMI steps, the insertions of Q and M monomers presented very high isolated yield (>95%), whereas the insertion of I monomer into the corresponding RAFT agent, BETC-Q, has been demonstrated to be a low conversion of BETC-Q and low isolated yield (~26%) of the production of BETC-Q-I. This is attributed to the much lower activation rate of BETC-Q than that of its SUMI product BETC-Q-I, that is, BETC-Q has a poorer R leaving group than BETC-Q-I. The SUMI product BETC-Q-I in the reaction mixture is more competitive than BETC-Q to be activated by the catalyst. The chain transfer from the SUMI product radical to BETC-Q is also ineffective. As a result, the generation of these two competing species reaches an equilibrium, that is, the initial BETC-Q is unable to be fully converted. Fortunately, the unreacted BETC-Q can be effectively removed by column chromatography after purification.^[32]

Having these three trimers on hand and the established synthetic method, we are able to prepare the designed pentamers (PT2, PT3 and PT4, in Scheme 2) using very similar reaction conditions and synthetic procedures due to repeating synthetic processes. The photocatalyst (ZnTPP), solvent (DMSO), reaction temperature (25 °C), molar ratio of monomer to RAFT agent are the same. For instance, the SUMI of I monomer into BETC-Q-I-M ([I]/[BETC-Q-I-M]/[ZnTPP]=5/1/0.005) produced tetramer BETC-Q-I-M-I, followed by further insertion of M to generate the final pentamer PT2 (Scheme 2a). Both steps gave high isolated yields, 80% and 98%, respectively (Table 1, #1 and #4). The product of each step of insertion was purified by automated flash chromatography. The total isolated yield after five iterations is around 22%, in which the determining step on the



Scheme 2 Synthetic routes to three sequenced pentamers. (a) BETC-Q-I-M-I-M (PT2); (b) BETC-M-I-Q-I-M (PT3); (c) BETC-M-I-M-I-Q (PT4); The total isolated yields of the pentamers after five SUMI iterations are shown in parentheses.

Table 1 PET-RAFT SUMI reaction conditions and isolated yields.^a

#	[Mon.]/[RAFT]	RAFT	Monomer	SUMI product	Time (h)	Yield ^b (single iteration)	Yield ^b (five iterations)
1	5/1	BETC-Q-I-M	Ind (I)	BETC-Q-I-M-I	18	80%	—
2	5/1	BETC-M-I-Q	Ind (I)	BETC-M-I-Q-I	18	31%	—
3	5/1	BETC-M-I-M	Ind (I)	BETC-M-I-M-I	18	80%	—
4	1/1	BETC-Q-I-M-I	PMI (M)	BETC-Q-I-M-I-M (PT2)	24	98%	22%
5	1/1	BETC-M-I-Q-I	PMI (M)	BETC-M-I-Q-I-M (PT3)	24	98%	24%
6	5/1	BETC-M-I-M-I	DMF (Q)	BETC-M-I-M-I-Q (PT4)	24	97%	60%

^a Reaction condition: DMSO as the solvent, ZnTPP as the photocatalyst, red LED light ($\lambda_{\text{max}}=635$ nm, 0.46 mW/cm²), [Monomer]/[RAFT]/[ZnTPP] = $x/1/0.005$;

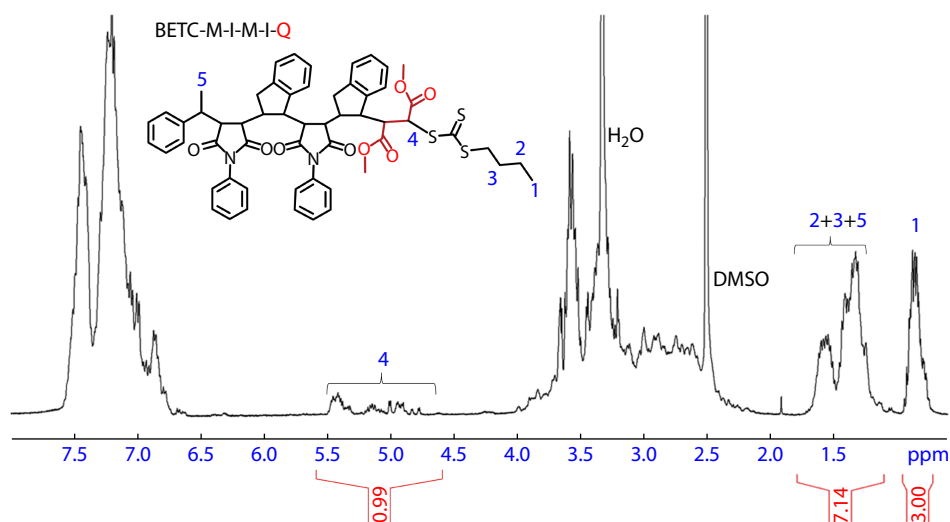
^b Isolated yields were measured by weighing the purified products and comparing to the theoretical masses.

yield is the second step of BETC-Q to BETC-Q-I. The flaw of low yield still exists in the synthesis of PT3, as it also involves the same step of insertion of I into the RAFT agent with the terminal Q unit (BETC-M-I-Q), which gave 31% isolated yield (Table 1, #2). Therefore, the total isolated yield for the five steps of insertions is similar as that for PT2 (~24%, #5 in Table 1). In contrast, the synthesis of PT4 has a much higher total isolated yield (~60%, #6 in Table 1) due to the fact that Q is the last monomer unit in the pentamer.

After purification by automated flash chromatography (Figs. S5–S7 in ESI), the full characterization of these three sequenced pentamers is performed on ¹H-NMR, gel permeation chromatography (GPC) and electrospray ionization mass spectroscopy (ESI-MS) analysis. The ¹H-NMR spectra of the tetramers (Figs. S2–S4 in ESI) and pentamers (Fig. 1 and Figs. S8 and S9 in ESI) show quite complex spectra with massive peaks overlapped due to the presence of diastereoisomers for each oligomer. Specifically, it is observed that there are many small peaks in the range of $\delta=6.5$ –4.5 ppm, which are assigned to the terminal proton in the last monomer unit adjacent to thiocarbonylthio group in each oligomer. In our study, each synthetic pentamer has eleven chiral carbons which theoretically lead to 1024 (2^{n-1} , n is the number of chiral carbon) diastereoisomers. Given that the cyclic monomers with five-membered rings in the backbone have only *trans* configurations,^[40] the actual number of the diastereoisomers for each pentamer (PT2, PT3 and PT3) is 128 (2^7). For all diastereoisomers of one pentamer, they possess

distinctive stereochemistry and molecular configurations. The protons in the diastereoisomers consequently have more or less different chemical environments. As a consequence, these diastereoisomers present a large number of overlapped peak signals in ¹H-NMR spectrum (Fig. 1). Fortunately, the multiple signals of the terminal proton adjacent to thiocarbonylthio are separate in the range of $\delta=5.5$ –4.7 ppm far away from other signals, which can thus be used to quantify the RAFT end integrity of the final pentamers. By calculating the integrals of this terminal proton and methyl in butyl tail ($\delta=0.8$ ppm), it shows that the molar ratio is almost 1/3, demonstrating excellent integrity of RAFT end group during the SUMI reaction. However, ¹H-NMR is unable to prove the purity and chemical structure of final products. We did not perform ¹³C-NMR characterization due to the same reason. Therefore, we further employed GPC and ESI-MS for the analysis. Most importantly, ESI-MS will not be influenced by multiple diastereoisomers.

GPC analysis (Fig. 2) of all the three pentamers clearly shows narrow, symmetric and monomodal peaks without obvious shoulders and tailing for each pentamer, suggesting nearly monodispersed characteristics of the products. Meanwhile, all of the three traces for three pentamers are almost the same, indicative of similar hydrodynamic volumes and molecular weights. From ESI-MS analysis, all the three pentamers with identical compositions present the same mass (993.32 for the product ionized by H⁺) for the major species in the products and excellent match with theoretical val-

**Fig. 1** ¹H-NMR (DMSO-*d*₆, 300 MHz) spectrum of the purified BETC-M-I-M-I-Q (PT4).

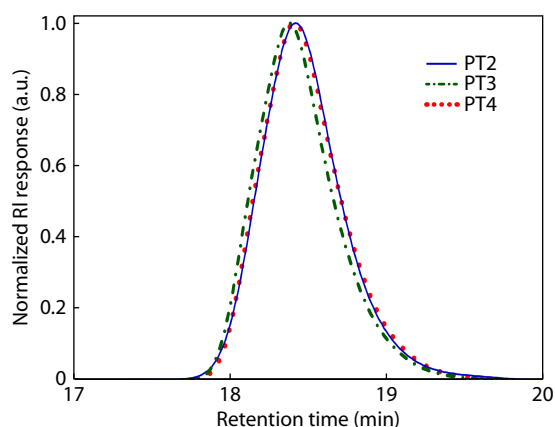


Fig. 2 GPC traces for three sequenced pentamers, BETC-Q-I-M-I-M (PT2), BETC-M-I-Q-I-M (PT3) and BETC-M-I-M-I-Q (PT4).

ues (Fig. 3a). The experimental isotopic distributions of the main peaks at 993.32 for all the three products present no difference with the simulated isotope pattern (Fig. 3b), further

indicating of the targeted products. Although a small amount of impurities including P-Ind dimer and degraded product also presents in the purified polymers, it is very minor.

Sequence Effect of Pentamers on Glass Transition Temperatures

As we discussed above, these three sequenced pentamers offer ideal models to investigate sequence effect on thermal property, particularly T_g . Therefore, DSC was employed to analyze the T_g s of the three sequenced pentamers (Fig. 4 and Figs. S10–S12 in ESI) and their base pentamer. All the three pentamers display only one single transition in the temperature range of 10–110 °C in their respective curves, which are corresponding to their T_g values (86.2 °C for PT2, 75.9 °C for PT3, and 88.7 °C for PT4). The base pentamer PT1 exhibited a T_g of 103.2 °C, which is much higher (more than 15 °C) than the other three pentamers. This result suggests the oligomers with five-membered cyclic monomer units in the backbone present higher thermal transition temperatures than those with acyclic monomer units due to relatively lower molecular flexibility, even if their molecular weights are comparable (1022 g/mol for PT1

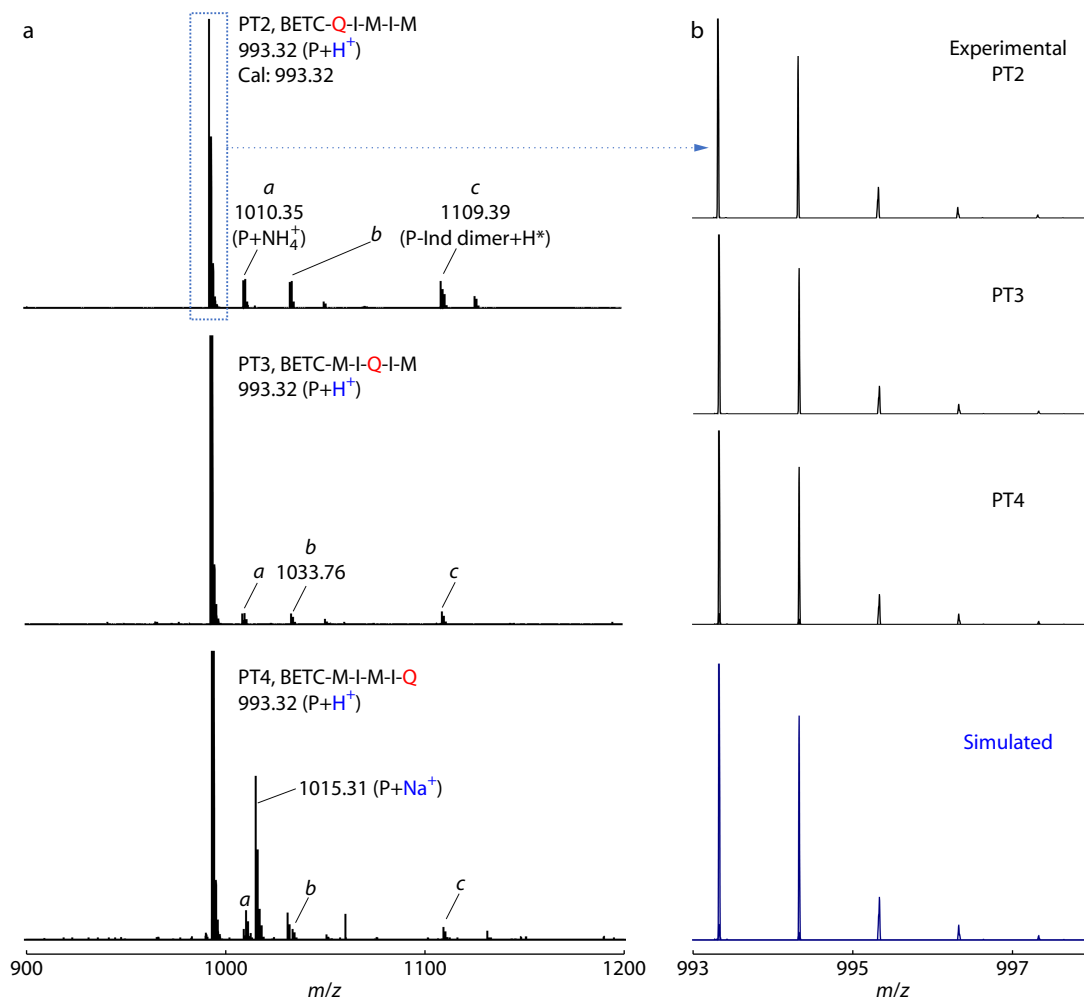


Fig. 3 ESI-MS characterization of three sequenced pentamers. (a) ESI-MS spectra for BETC-Q-I-M-I-M (PT2, top), BETC-M-I-Q-I-M (PT3, middle) and BETC-M-I-M-I-Q (PT4, bottom); (b) The isotopic distributions of the pentamer by comparing the experimental and simulated results. Note: A small amount of impurities include *b* (most likely degraded P-PMI + H⁺) and *c* (P-Ind + H⁺). The possible chemical structures refer to Scheme S1 in ESI. Other small peaks from fragmentation products and artifacts have not been assigned.

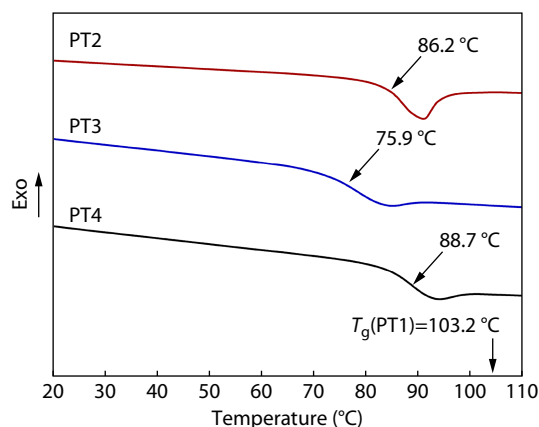


Fig. 4 DSC curves (5 °C/min) and glass transition temperatures (T_g) of three sequenced pentamers (PT2, PT3 and PT4) in comparison to their base pentamer PT1. The DSC result of PT1 oligomer has been reported in our previous study.^[42]

and 993 g/mol for PT2). This result is consistent with those in our previous study.^[42] Meanwhile, by comparing three pentamers (PT2, PT3 and PT4) with the same compositions but different monomer sequences, it reveals that the T_g value of PT3 with Q unit at the 3rd position (75.9 °C) is lower (~10 °C) than those of the other two with Q units at the 1st (PT2, 86.2 °C) and 5th (PT4, 88.7 °C) positions. The T_g value of PT2 is close to that of PT4. By contrast to monomer structure, monomer sequence has less effect on the values of T_g . However, given the fact of low molecular weights of these pentamers (less than 1000 g/mol), this difference is still significant.

For such sequence effect on T_g , we postulate that it is caused by the changes of relative rigidity of the oligomer backbone that leads to different efficiencies of polymer chain packing. It has been commonly recognized that relative rigidity of chain backbone is one of the key factors determining polymer glass transitions.^[45,46] In PT1, all five cyclic monomer units connect to form a relatively hindered and rigid backbone with high rotational barriers between any two neighboring monomer units. While one cyclic M monomer unit is replaced by an acyclic Q unit at different positions, the rigi-

dity of the backbone is thus reduced by the relatively flexible C—C bond of the Q unit. Particularly, for the pentamer PT3 with Q at the 3rd (or middle) position, this effect is more significant, which may cause twisted or bended molecular structures and consequently lower efficiency of chain packing and lower T_g . In contrast, for the pentamers PT2 and PT4 with Q at the 1st and 5th positions (at the end of pentamer backbone), the influence on the molecular rigidity is relatively lower than PT3. There are still four cyclic monomer units (two I and two M monomer units) being connected with each other, which also explains why PT2 and PT4 have not much difference in their T_g s.

Pentamer as Oligomeric Plasticizer

One of the potential applications of well-defined oligomers is as small molecule plasticizers to tune thermal property of high T_g polymers and to increase processability and ductility.^[47] In this study, we demonstrate the synthetic pentamers are useful for plasticizing bulk polymer materials with high T_g s. We employed a copolymer, poly(St-co-PMI), synthesized from thermal RAFT copolymerization of styrene and PMI (Fig. S13 in ESI). After purified by precipitation in methanol, the obtained solid powder has a moderate number-average molecular weight (M_n =17720 g/mol) and low polydispersity (M_w/M_n =1.21). Its T_g was measured to be 204.6 °C (Fig. S14 in ESI) that matches well with the reported value,^[48] and much higher than that of the pentamer PT3 (75.9 °C). We mixed this copolymer with different weight ratios of PT3 plasticizer. To prepare well-blended polymer solids, we dissolved these two materials in a common solvent (dichloromethane) and evaporated the solvent completely. The dried solid powders were subsequently subject to DSC analysis. The DSC curves for the blended polymers at three different ratios of PT2 plasticizer showed only one single transition in each curve in the temperature range of 20–230 °C, which are corresponding to the T_g values of the blended materials (Fig. 5a and Fig. S15 in ESI). The pentamer PT3 effectively lowered the T_g of poly(St-co-PMI) from 204.6 °C to 182.4 °C with 5% PT3, 173.4 °C with 10% PT3 and 155.7 °C with 20% PT3, respectively. This demonstrated that PT3 and the copolymer have good compatibility to blend due to their similar chemical structures. PT3 is also an efficient plasticizer to adjust

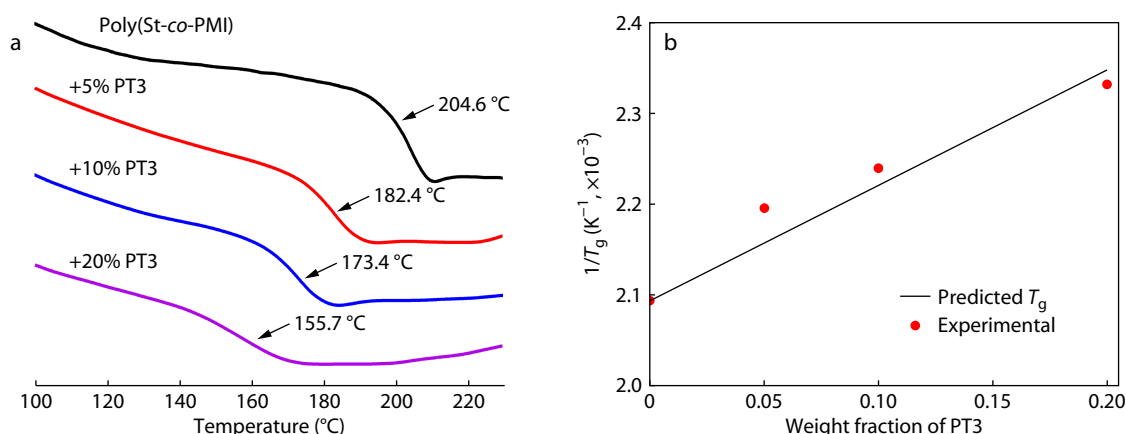


Fig. 5 Glass transition temperatures (T_g) of the copolymer poly(St-co-PMI) blended with different weight percentages of PT3. (a) DSC curves (exo up, 10 °C/min, 100–230 °C) and T_g measurement; (b) The plot of $1/T_g$ versus weight percentage of PT3 with experimental results (red dots) and predicted results by Fox equation (black line).

the T_g values of the copolymer.

Fox equation is widely used to predict the T_g values of blended mixtures of two or more amorphous polymers.^[49,50] It is a simple empirical formula with the following equation:

$$1/T_{g,mix} = \omega_A/T_{g,A} + \omega_B/T_{g,B} \quad (1)$$

where $T_{g,mix}$ is the T_g of blended mixture at various ratios of two components of A and B, $T_{g,A}$ and $T_{g,B}$ are the T_g of the components of A and B, respectively, ω_A and ω_B are the weight percentage of A and B. This equation applies to polymers with comparable chemical structures and/or solubility parameters. That is, the mixtures of components have very weak intermolecular interactions (van der Waal or electrostatic interactions, etc.) without specific strong bonding (e.g., π - π interaction or hydrogen bonding). In our study, we plotted the relationships of $1/T_g$ and weight percentage of PT3 with experimental results in Fig. 5(b). By comparison to the predicted values derived from Fox equation, the experimental result shows a good agreement with the theoretical values, although the first data point with 5% PT3 presents a slight deviation from the theoretical linear plot possibly attributed to the weighing error caused by a small amount of solid powder during blending. This result demonstrates the intermolecular interactions between the copolymer and oligomeric plasticizer (PT3) are limited in the weak van der Waal or electrostatic forces rather than other strong interactions.

CONCLUSIONS

To summarize, three sequence-defined pentamers with identical primary structures but different monomer sequences (PT2, PT3, and PT4) were synthesized by replacing an acyclic monomer in a base pentamer (PT1) with five cyclic monomer units at difference positions (1st, 3rd and 5th). The structures of the pentamers are fully characterized by ¹H-NMR, GPC and ESI-MS. Compared to their base pentamer, the structure variants of one monomer unit induced a considerable decrease (more than 15 °C) of glass transition temperature (T_g) possibly attributed to reduced molecular rigidity. The significant sequence effect on T_g is also evidenced from these three sequenced pentamer with identical compositions but different sequences. The middle (3rd) position of acyclic monomer unit in the pentamer (PT3) featured a 10 °C lower of T_g than the other two pentamers (PT2 and PT4). These pentamers can be used as oligomeric plasticizers for tuning the T_g values of bulk polymer materials. This study shows an illustrative example for fundamental understanding of how monomer sequence influences polymer physical properties. It also provides a synthetic strategy to access sequence-defined polymers that should be useful for designing advanced synthetic materials.

NOTES

The authors declare no competing financial interest.

Electronic Supplementary Information

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REFERENCES

- Lutz, J. F.; Ouchi, M.; Liu, D. R.; Sawamoto, M. Sequence-controlled polymers. *Science* **2013**, *341*, 1238149.
- Lutz, J. F. Defining the field of sequence-controlled polymers. *Macromol. Rapid Commun.* **2017**, *38*, 1700582.
- van Genabeek, B.; Lamers, B. A. G.; Hawker, C. J.; Meijer, E. W.; Gutekunst, W. R.; Schmidt, B. V. K. J. Properties and applications of precision oligomer materials; where organic and polymer chemistry join forces. *J. Polym. Sci.* **2021**, *59*, 373–403.
- De Neve, J.; Haven, J. J.; Maes, L.; Junkers, T. Sequence-definition from controlled polymerization: the next generation of materials. *Polym. Chem.* **2018**, *9*, 4692–4705.
- Xu, J. Single unit monomer insertion: a versatile platform for molecular engineering through radical addition reactions and polymerization. *Macromolecules* **2019**, *52*, 9068–9093.
- Solleder, S. C.; Schneider, R. V.; Wetzel, K. S.; Boukis, A. C.; Meier, M. A. R. Recent progress in the design of monodisperse, sequence-defined macromolecules. *Macromol. Rapid Commun.* **2017**, *38*, 1600711.
- Meier, M. A. R.; Barner-Kowollik, C. A new class of materials: sequence-defined macromolecules and their emerging applications. *Adv. Mater.* **2019**, *31*, 1806027.
- Huang, Z.; Shi, Q.; Guo, J.; Meng, F.; Zhang, Y.; Lu, Y.; Qian, Z.; Li, X.; Zhou, N.; Zhang, Z.; Zhu, X. Binary tree-inspired digital dendrimer. *Nat. Commun.* **2019**, *10*, 1918.
- Solleder, S. C.; Zengel, D.; Wetzel, K. S.; Meier, M. A. R. A scalable and high-yield strategy for the synthesis of sequence-defined macromolecules. *Angew. Chem. Int. Ed.* **2016**, *55*, 1204–1207.
- Wu, Y.-H.; Zhang, J.; Du, F. S.; Li, Z. C. Dual sequence control of uniform macromolecules through consecutive single addition by selective passerini reaction. *ACS Macro Lett.* **2017**, *6*, 1398–1403.
- Takizawa, K.; Tang, C.; Hawker, C. J. Molecularly defined caprolactone oligomers and polymers: synthesis and characterization. *J. Am. Chem. Soc.* **2008**, *130*, 1718–1726.
- Takizawa, K.; Nulwala, H.; Hu, J.; Yoshinaga, K.; Hawker, C. J. Molecularly defined (L)-lactic acid oligomers and polymers: synthesis and characterization. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 5977–5990.
- Ren, J. M.; Lawrence, J.; Knight, A. S.; Abdilla, A.; Zerdan, R. B.; Levi, A. E.; Oschmann, B.; Gutekunst, W. R.; Lee, S. H.; Li, Y.; McGrath, A. J.; Bates, C. M.; Qiao, G. G.; Hawker, C. J. Controlled formation and binding selectivity of discrete oligo(methyl methacrylate) stereocomplexes. *J. Am. Chem. Soc.* **2018**, *140*, 1945–1951.
- Ji, Y.; Zhang, L.; Gu, X.; Zhang, W.; Zhou, N.; Zhang, Z.; Zhu, X. Sequence-controlled polymers with furan-protected maleimide as a latent monomer. *Angew. Chem. Int. Ed.* **2017**, *56*, 2328–2333.
- Huang, Z.; Zhao, J.; Wang, Z.; Meng, F.; Ding, K.; Pan, X.; Zhou, N.; Li, X.; Zhang, Z.; Zhu, X. Combining orthogonal chain-end deprotections and thiol-maleimide Michael coupling: engineering discrete oligomers by an iterative growth strategy. *Angew. Chem. Int. Ed.* **2017**, *56*, 13612–13617.
- Wang, S.; Tao, Y.; Wang, J.; Tao, Y.; Wang, X. A versatile strategy for the synthesis of sequence-defined peptoids with side-chain and backbone diversity via amino acid building blocks. *Chem. Sci.* **2019**, *10*, 1531–1538.
- Tao, Y.; Wang, S.; Zhang, X.; Wang, Z.; Tao, Y.; Wang, X. Synthesis and properties of alternating polypeptoids and polyampholytes as protein-resistant polymers. *Biomacromolecules* **2018**, *19*,

- 936–942.
- 18 Tao, Y.; Tao, Y. Ugi reaction of amino acids: from facile synthesis of polypeptoids to sequence-defined macromolecules. *Macromol. Rapid Commun.* **2021**, *42*, 2000515.
 - 19 Zhu, Y.; Tao, Y. Sequence-controlled and sequence-defined polypeptoids via the Ugi reaction: synthesis and sequence-driven properties. *Polym. Chem.* **2021**, *12*, 4895–4902.
 - 20 Zydziak, N.; Konrad, W.; Feist, F.; Afonin, S.; Weidner, S.; Barner-Kowollik, C. Coding and decoding libraries of sequence-defined functional copolymers synthesized via photoligation. *Nat. Commun.* **2016**, *7*, 13672.
 - 21 Kametani, Y.; Ouchi, M. One-pot preparation of methacrylate/styrene alternating copolymers via radical copolymerization and alcoholysis modification: sequence impacts on glass transition temperature. *ACS Polym. Au* **2021**, *1*, 10–15.
 - 22 Kametani, Y.; Tournilhac, F.; Sawamoto, M.; Ouchi, M. Unprecedented sequence control and sequence-driven properties in a series of AB-alternating copolymers consisting solely of acrylamide units. *Angew. Chem. Int. Ed.* **2020**, *59*, 5193–5201.
 - 23 Nishimori, K.; Ouchi, M. AB-alternating copolymers via chain-growth polymerization: synthesis, characterization, self-assembly, and functions. *Chem. Commun.* **2020**, *56*, 3473–3483.
 - 24 Zhang, S.; Bauer, N. E.; Kanal, I. Y.; You, W.; Hutchison, G. R.; Meyer, T. Y. Sequence effects in donor-acceptor oligomeric semiconductors comprising benzothiadiazole and phenylenevinylene monomers. *Macromolecules* **2017**, *50*, 151–161.
 - 25 Zhang, S.; Hutchison, G. R.; Meyer, T. Y. Sequence effects in conjugated donor-acceptor trimers and polymers. *Macromol. Rapid Commun.* **2016**, *37*, 882–887.
 - 26 Li, J.; Stayshich, R. M.; Meyer, T. Y. Exploiting sequence to control the hydrolysis behavior of biodegradable PLGA copolymers. *J. Am. Chem. Soc.* **2011**, *133*, 6910–6913.
 - 27 Maron, E.; Swisher, J. H.; Haven, J. J.; Meyer, T. Y.; Junkers, T.; Börner, H. G. Learning from peptides to access functional precision polymer sequences. *Angew. Chem. Int. Ed.* **2019**, *58*, 10747–10751.
 - 28 Li, J.; Rothstein, S. N.; Little, S. R.; Edenborn, H. M.; Meyer, T. Y. The effect of monomer order on the hydrolysis of biodegradable poly(lactic-co-glycolic acid) repeating sequence copolymers. *J. Am. Chem. Soc.* **2012**, *134*, 16352–16359.
 - 29 Norris, B. N.; Zhang, S.; Campbell, C. M.; Auletta, J. T.; Calvo-Marzal, P.; Hutchison, G. R.; Meyer, T. Y. Sequence matters: modulating electronic and optical properties of conjugated oligomers via tailored sequence. *Macromolecules* **2013**, *46*, 1384–1392.
 - 30 Washington, M. A.; Swiner, D. J.; Bell, K. R.; Fedorchak, M. V.; Little, S. R.; Meyer, T. Y. The impact of monomer sequence and stereochemistry on the swelling and erosion of biodegradable poly(lactic-co-glycolic acid) matrices. *Biomaterials* **2017**, *117*, 66–76.
 - 31 Schneider, R. V.; Waibel, K. A.; Arndt, A. P.; Lang, M.; Seim, R.; Busko, D.; Bräse, S.; Lemmer, U.; Meier, M. A. R. Sequence-definition in stiff conjugated oligomers. *Sci. Rep.* **2018**, *8*, 17483.
 - 32 Liu, R.; Zhang, L.; Huang, Z.; Xu, J. Sequential and alternating RAFT single unit monomer insertion: model trimers as the guide for discrete oligomer synthesis. *Polym. Chem.* **2020**, *11*, 4557–4567.
 - 33 Lin, S.; Zhang, L.; Huang, Z.; Kumar, P. V.; Xu, J. Discriminatory photoactivation of diastereomeric RAFT agents. *Macromolecules* **2019**, *52*, 7157–7166.
 - 34 Barnes, J. C.; Ehrlich, D. J. C.; Gao, A. X.; Leibfarth, F. A.; Jiang, Y.; Zhou, E.; Jamison, T. F.; Johnson, J. A. Iterative exponential growth of stereo- and sequence-controlled polymers. *Nat. Chem.* **2015**, *7*, 810–815.
 - 35 Leibfarth, F. A.; Johnson, J. A.; Jamison, T. F. Scalable synthesis of sequence-defined, unimolecular macromolecules by flow-IEG. *Proc. Natl. Acad. Sci. U.S.A.* **2015**, *112*, 10617–10622.
 - 36 Golder, M. R.; Jiang, Y.; Teichen, P. E.; Nguyen, H. V. T.; Wang, W.; Milos, N.; Freedman, S. A.; Willard, A. P.; Johnson, J. A. Stereochemical sequence dictates unimolecular diblock copolymer assembly. *J. Am. Chem. Soc.* **2018**, *140*, 1596–1599.
 - 37 Nguyen, H. V. T.; Jiang, Y.; Mohapatra, S.; Wang, W.; Barnes, J. C.; Oldenhuis, N. J.; Chen, K. K.; Axelrod, S.; Huang, Z.; Chen, Q.; Golder, M. R.; Young, K.; Suvlu, D.; Shen, Y.; Willard, A. P.; Hore, M. J. A.; Gómez-Bombarelli, R.; Johnson, J. A. Bottlebrush polymers with flexible enantiomeric side chains display differential biological properties. *Nat. Chem.* **2021**, doi:10.1038/s41557-021-00826-8.
 - 38 Hartweg, M.; Jiang, Y.; Yilmaz, G.; Jarvis, C. M.; Nguyen, H. V. T.; Primo, G. A.; Monaco, A.; Beyer, V. P.; Chen, K. K.; Mohapatra, S.; Axelrod, S.; Gómez-Bombarelli, R.; Kiessling, L. L.; Becer, C. R.; Johnson, J. A. Synthetic glycomacromolecules of defined valency, absolute configuration, and topology distinguish between human lectins. *JACS Au* **2021**, *1*, 1621–1630.
 - 39 Martens, S.; Van den Begin, J.; Maddar, A.; Du Prez, F. E.; Espeel, P. Automated synthesis of monodisperse oligomers, featuring sequence control and tailored functionalization. *J. Am. Chem. Soc.* **2016**, *138*, 14182–14185.
 - 40 Huang, Z.; Noble, B. B.; Corrigan, N.; Chu, Y.; Satoh, K.; Thomas, D. S.; Hawker, C. J.; Moad, G.; Kamigaito, M.; Coote, M. L.; Boyer, C.; Xu, J. Discrete and stereospecific oligomers prepared by sequential and alternating single unit monomer insertion. *J. Am. Chem. Soc.* **2018**, *140*, 13392–13406.
 - 41 Huang, Z.; Corrigan, N.; Lin, S.; Boyer, C.; Xu, J. Upscaling single unit monomer insertion to synthesize discrete oligomers. *J. Polym. Sci., Part A: Polym. Chem.* **2019**, *57*, 1947–1955.
 - 42 Liu, R.; Yang, C.; Huang, Z.; French, R.; Gu, Z.; Cheng, J.; Guo, K.; Xu, J. Unravelling sequence effect on glass transition temperatures of discrete unconjugated oligomers. *Macromol. Rapid Commun.* **2021**, *42*, 2100666.
 - 43 Zhang, L.; Liu, R.; Huang, Z.; Xu, J. How does the single unit monomer insertion technique promote kinetic analysis of activation and initiation in photo-RAFT processes. *Polym. Chem.* **2021**, *12*, 581–593.
 - 44 Mokhtar, S. M.; Mikhael, M. G.; Aly, R. O.; Elsabee, M. Z. Copolymerization of indene with *N*-phenylmaleimide. *Polym. J.* **1988**, *20*, 979–985.
 - 45 Xu, X.; Douglas, J. F.; Xu, W. S. Influence of side-chain length and relative rigidities of backbone and side chains on glass formation of branched polymers. *Macromolecules* **2021**, *54*, 6327–6341.
 - 46 Dudowicz, J.; Freed, K. F.; Douglas, J. F. The glass transition temperature of polymer melts. *J. Phys. Chem. B* **2005**, *109*, 21285–21292.
 - 47 Rahman, M.; Brazel, C. S. The plasticizer market: an assessment of traditional plasticizers and research trends to meet new challenges. *Prog. Polym. Sci.* **2004**, *29*, 1223–1248.
 - 48 Yao, F.; Liu, Q.; Zhang, Z.; Zhu, X. RAFT polymerization of styrene and maleimide in the presence of fluoroalcohol: hydrogen bonding effects with classical alternating copolymerization as reference. *Polymers* **2017**, *9*, 89.
 - 49 Fox, T. G. Influence of diluent and of copolymer composition on the glass temperature of a polymer system. *Bull. Am. Phys. Soc.* **1956**, *1*, 123.
 - 50 Hiemenz, P. C.; Lodge, T. P. *Polymer chemistry*. Chapter 12. CRC Press, **2007**.