HOKKAIDO UNIVERSITY

Title	Multidimensional Control of Repeating Unit/Sequence/Topology for One-Step Synthesis of Block Polymers from Monomer Mixtures
Author(s)	Xia, Xiaochao; Gao, Tianle; Li, Feng et al.
Citation	Journal of the American Chemical Society, 144(39), 17905-17915 https://doi.org/10.1021/jacs.2c06860
Issue Date	2022-10-05
Doc URL	https://hdl.handle.net/2115/90407
Rights	This document is the Accepted Manuscript version of a Published Work that appeared in final form in Journal of the American Chemical Society, copyright c American Chemical Society after peer review and technical editing by the publisher. To access the final edited and published work see https://pubs.acs.org/articlesonrequest/AOR-PNW7369BK2VW8IN3ITZYI.
Type	journal article
File Information	manuscript (Sato).pdf

Hokkaido University Collection of Scholarly and Academic Papers : HUSCAP

Multi-dimensional control of repeating unit/sequence/topology for one-step synthesis of block polymers from monomer mixtures

Xiaochao Xia,[1,2] Tianle Gao,[3] Feng Li,[2] Ryota Suzuki,[3] Takuya Isono,*[,2] Toshifumi Satoh,*[,2]

[1] College of Materials Science and Engineering, Chongqing University of Technology, Chongqing 400054, China

[2] Division of Applied Chemistry, Faculty of Engineering, Hokkaido University, Sapporo 060-8628, Japan

[3] Graduate School of Chemical Sciences and Engineering, Hokkaido University, Sapporo 060-8628, Japan

KEYWORDS: Ring opening alternating copolymerization, Multi-block polymer, Polyester, Sequence controlled, one step/one pot

ABSTRACT: Synchronously and thoroughly adjusting the chemical structure difference between two blocks of diblock copolymer is very useful for the design of materials, but difficult to achieve via self-switchable alternating copolymerization. Here, we report the self-switchable alternating copolymerization from a mixture of two different cyclic anhydrides, epoxides, and oxetane, where a simple alkali metal carboxylate catalyst switches between ring-opening alternating copolymerization (ROCOP) of cyclic anhydrides/epoxides and ROCOP of cyclic anhydrides/oxetanes, resulting in the formation of a perfect block tetrapolymer. By investigating the reactivity ratio of these comonomers, a reactivity gradient was established, enabling the precise synthesis of block copolymers with synchronous adjustment of each unit chemical structure/sequence/topology. Consequently, a diblock tetrapolymer with two glass transition temperatures (T_g) can be easily produced by adjusting the difference in chemical structures between the two blocks.

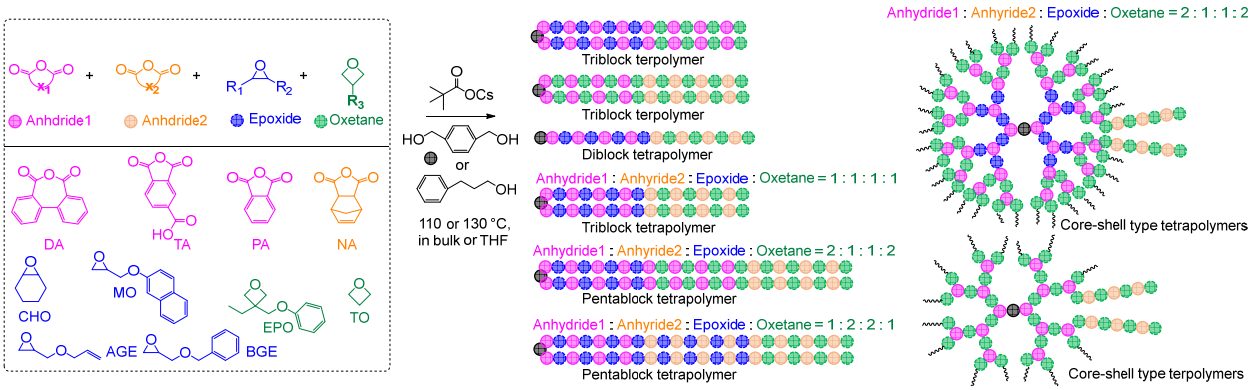
INTRODUCTION

The properties of block polymers can be adjusted by varying their monomer sequence. Consequently, this endows block polymers with the ability to provide a platform for the production of a wide range of advanced materials, with applications in drug delivery,[1,2] data storage,[3] microelectronics,[4,5] and nanolithography.[6] Regarding the synthesis of block polymer, self-switchable polymerization is the most promising method because because it applies mixtures of monomers and uses a single catalyst that spontaneously connects different catalytic cycles to produce block sequence,[7–23] thereby overcoming the disadvantages of conventional procedures, e.g., sequential monomer addition approach and coupling of pre-made blocks.[24,25]

Until now, self-switchable polymerization has been applied to a variety of polymerization cycles, including cyclic ester ring-opening polymerization (ROP),[7,14,22] epoxide ROP,[22,26] epoxide/CO_2 ring-opening alternating copolymerization (ROCOP),[9,12,27] epoxide/cyclic anhydride ROCOP,[28–31] epoxide/isocyanate ROCOP,[32] episulfide/isothiocyanate ROCOP,[33,34] *N*-sulfonyl aziridines/cyclic anhydride ROCOP,[35,36] thioanhydride/epoxide,[37] and anhydrides/epoxides/tetrahydrofurans ROCOP,[38] leading to one-step synthesis of polyesters, poly(ether-*alt*-ester), polyurethanes, polythioether-*b*-poly(episulfide-*alt*-isothiocyanate), poly(ester amide)s, and polyester-*b*-p(ester-*alt*-thioester), respectively. For the self-switchable alternating copolymerization, it is extremely difficult to simultaneously and thoroughly adjust the chemical structure difference between two blocks of the diblock copolymer for the one-step synthesis of block copolymers. Hadjichristidis et al., recently used an organocatalyst to switch between epoxide/cyclic anhydride ROCOP and *N*-sulfonyl aziridines/cyclic anhydride ROCOP, resulting in perfect diblock terpolymers with two completely distinct blocks.[36] Li et al., designed the metal complex catalyst and used it to connect epoxide/cyclic anhydride ROCOP and epoxide/thioanhydride ROCOP.[37] Although these catalytic systems have represented significant progress in increasing the structural diversity of block polymers, the same monomer was incorporated in the two polymerization cycles. The chemical structure difference between two blocks is too small for block phase separation, which limits the resulting thermal mechanical properties.

In addition, the self-switchable polymerization involving ROCOP of anhydride/oxetane are rare, and ROCOP with oxetanes are more challenging because of the low ring strain.[39] Regarding ROCOP of anhydride/oxetane, bulky titanium bisphenolates as an initiator leaded to the formation of ether link.[40] Quaternary onium salts can also be used as an initiator for ROCOP of anhydride/oxetane, avoiding the formation of ether link and showing the perfect selectivity.[41] However, the relative high dispersity of the synthesized polymers is obtained. Although metal complex catalysts can be used as a catalyst for the system, resulting good control, the toxic metal residuals, to some extent, would limit their potential in food packing and biomedical devices.[42]

To address these barriers, a simple alkali metal carboxylate was used for the first time to catalyze ROCOP of anhydride/oxetane, resulting in polyesters with predictive molecular weights and extremely narrow dispersity. We connected this anhydride/oxetane ROCOP with cyclic anhydrides/epoxides ROCOP in order to create a self-switchable alternating copolymerization. The "epoxide >> oxetane" reactivity gradient was determined by comparing the reactivity ratio of the two monomers. Additionally, by combining the established reactivity gradient among different cyclic anhydrides,[23] perfect di-/tri-block tetrapolymers were synthesized from four monomer mixtures (two different cyclic anhydrides, epoxides, and oxetanes) using a one-pot/one-step procedure, allowing multi-dimensional control of each unit chemical structure/sequence/topology (Scheme 1), which provides an opportunity to design block polymers with the targeted thermal mechanical properties and function for high-value emerging applications.



Scheme 1. One-step synthesis of multiblock polymers from a monomer mixture. DA = diphenic anhydride, TA = trimellitic anhydride PA = phthalic anhydride, NA = 5-norbornene-endo-2,3-dicarboxylic anhydride, AGE = allyl glycidyl ether, CHO = 1,2-epoxycyclohexane, BGE = benzyl glycidyl ether, MO = 2-((naphthalen-2-yloxy)methyl)oxirane, PPA = 3-phenyl-1-propanol, ROCOP = ring-opening alternating copolymerization, ROP = ring-opening polymerization.

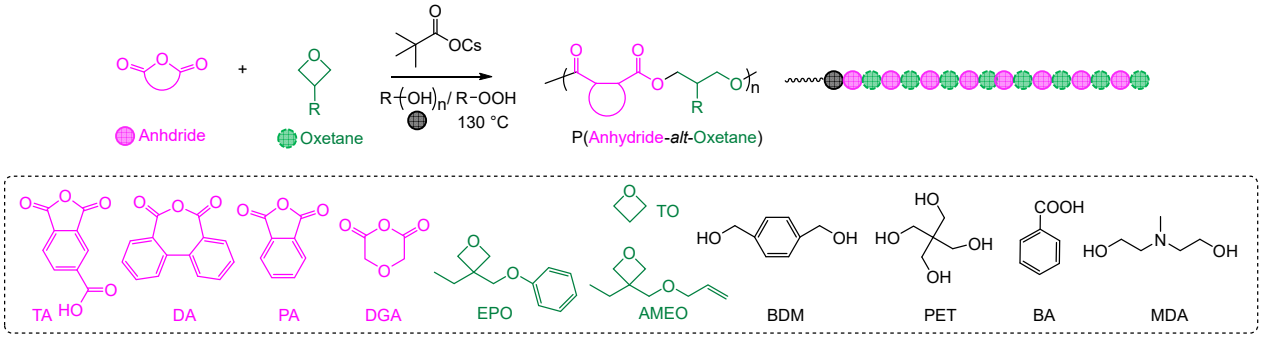
RESULTS AND DISCUSSION

ROCOP of anhydrides and oxetane

Initially, ROCOP of phthalic anhydride (PA) with 3-ethyl-3-(phenoxymethyl)oxetane (EPO) was carried out using cesium pivalate (t-$BuCO_2Cs$) and 1,4-benzenedimethanol (BDM) as the catalyst and bidirectional initiator at 100 °C, with a $[anhydride]_0/[oxetane]_0/[BDM]_0/[t\text{-}BuCO_2Cs]$ ratio of 15/90/1/1. The copolymerization of PA with EPO reached around 2% in 30 h (entry 1 in Table 1), indicating a very low polymerization rate at this temperature. Accordingly, we attempted to increase the reaction temperature from 100 to 130 °C, and the ROCOP reached 86.0% in 19h, resulting in a perfect alternating sequence distribution with a narrow dispersity ($Đ$ = 1.13, entry 2 in Table 1 and Figures S1–S3). After PA was fully consumed in 29 h ($M_{n,SEC}$ = 5.5 kDa), 15 equiv of PA was introduced to verify the living polymerization behavior of the catalytic system. The addition of PA immediately restarted the propagation from the terminus of P(PA-*alt*-EPO), in which $M_{n,\ NMR}$ values increased from 5.5 to 7.3 kDa when PA conversion reached 175% in 56 h and dispersity remained narrow ($Đ$ = 1.13, entry 3 in Table 1 and Figures S4–S5), indicating living behavior. The molecular weight $M_{n,\ NMR}$ values of the obtained copolymer [P(PA-*alt*-EPO)] correlated linearly with PA conversion, and kinetics analysis revealed that the ROCOP of PA with EPO followed zero-order kinetics (entry 4 in Table 1 and Figure 1). Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDITOF MS) MALDITOF MS was utilized to confirm the structure and terminal functional groups of the obtained P(PA-*alt*-EPO). The major series of repeated peaks corresponded to the adduct of poly(PA-*alt*-EPO) with BDM as the initiator and two PA as the two end groups of the chains (Figure 2). Also assignable to BDM-initiated poly(PA-*alt*-EPO) were two minor series of peaks with two EPOs at two chain ends

or PA and EPO at two chain ends, respectively. This indicates that the insertion rate of PA is significantly higher than that of EPO, resulting in the rapid occupation of chain ends by PA. Other minor series of peaks resulted from polymerization initiated by water (PA-*alt*-EPO). The results indicate that the copolymers have perfectly alternating units of PA and EPO, with no transesterification side reaction occurring during polymerization.

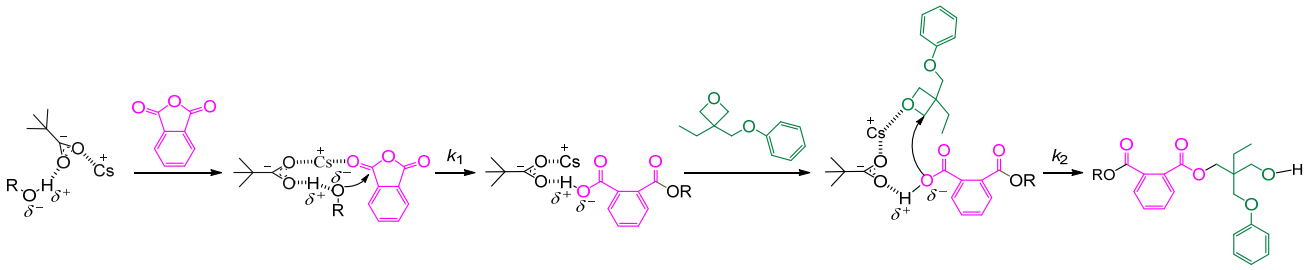
Table 1. The ROCP of anhydrides and oxetanes catalyzed by cesium pivalate.[a]



entry	monomers	Initiator	time [h]	conv. [b] [%] (anhydride)	TOF [b] [h^{-1}]	$M_{n,th}$ [c] [kDa]	$M_{n,NMR}$ [b] [kDa]	$M_{n,SEC}$ [d] [kDa]	Đ [d]
[e]1	PA/EPO	BDM	30	2.0					
2	PA/EPO	BDM	19	86.0	0.68	4.4	4.3	3.1	1.13
[f]3	PA/EPO	BDM	56	175	n.d.	9.1	8.9	7.3	1.13
[g]4	PA/EPO	BDM	25.5	96.2	n.d.	6.7	6.7	6.4	1.08
5	PA/AMEO	BDM	44	78.6	0.27	3.7	3.5	2.3	1.32
[g]6	PA/TO	BDM	4	91.6	3.44	3.9	3.8	3.7	1.13
[h]7	PA/TO	BDM	120	89.8	n.d.	89.7	83.1	27.7	1.07
8	DA/EPO	BDM	18	99.0	0.83	6.3	6.2	3.4	1.21
[i]9	DGA/TO	BDM	72	99.0	n.d.	2.7	3.0	2.2	1.38
10	TA/ EPO	BDM	17	99.0	0.87	8.8	8.9	4.5	1.78
11	PA/EPO	BA	144	55.0	0.05	2.9	n.d.	2.9	1.17
12	PA/EPO	PET	19	98.0	0.77	5.1	5.0	3.4	1.08
13	PA/EPO	MDA	24	89.0	0.56	4.7	4.5	4.5	1.14

[a]Polymerization conditions at a [anhydride]$_0$/[oxetane]$_0$/[BDM]$_0$/[*t*-BuCO2Cs]$_0$ ratio of 15/90/1/1 at 130 °C in the bulk under an Ar atmosphere. [b]Determined by 1H NMR analysis of the obtained polymer in $CDCl_3$ and TOF = turnover frequency. [c]Theoretical *M*n values. [d]Determined by SEC analysis of the obtained polymer in THF with a PSt standard. [e]The polymerization was performed at 100 °C. [f]The initial ratio of [PA]$_0$/[EPO]$_0$/[BDM]$_0$/[*t*-BuCO2Cs]$_0$ is 15/90/1/1, and the additional 15 equiv of PA was introduced after PA was fully consumed in 29 h. [g][PA]$_0$/[TO]$_0$/[BDM]$_0$/[*t*-BuCO2Cs]$_0$ = 20/90/1/1. [h][PA]$_0$/[TO]$_0$/[BDM]$_0$/[*t*-BuCO2Cs]$_0$ = 484/2178/1/1. [i]Polymerization was performed at 110 °C.

On the basis of the above-mentioned studies, a plausible mechanism for the copolymerization of PA and EPO is proposed (Scheme 2). The carboxylate activates the initiator via H-bonding, and a cesium cation activates the carbonyl group of the anhydride. Because the hydroxyl group of the initiator is nucleophilic and PA activated by a cesium cation shows extremely high electrophilicity, the activated PA is prone to nucleophilic attack from the cesium pivalate activated hydroxyl group[22]. The forming carboxylate species is sufficiently reactive to react with the cesium cation-activated EPO via nucleophilic attack (Figure S6), resulting in the formation of a copolymer with a perfect alternating chemical structure.[43,44]



Scheme 2. Proposed mechanism of ROCOP from a mixture of PA and EPO with cesium pivalate as the catalyst and alcohol as the initiator.

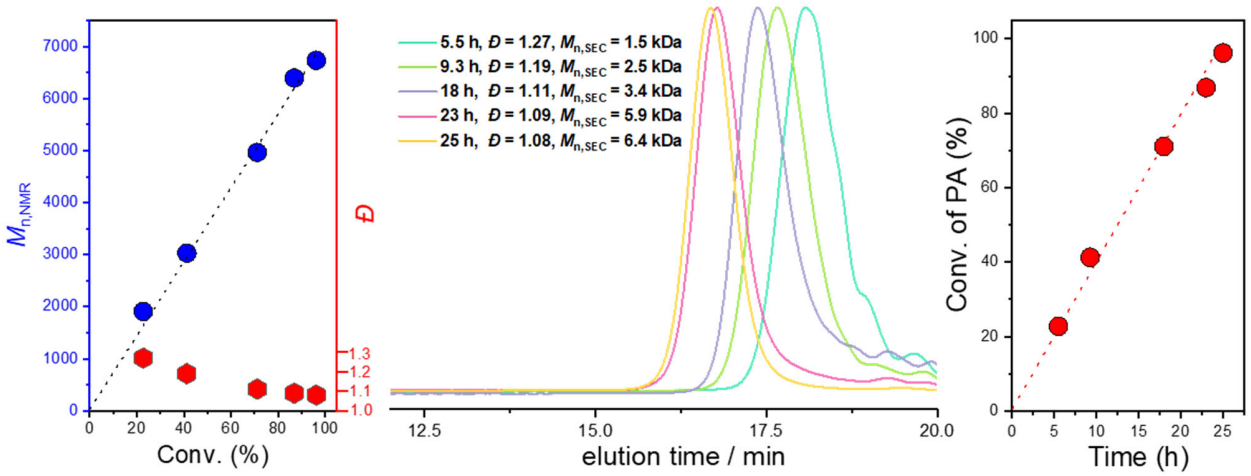


Figure 1. The kinetics analysis of the PA/EPO ROCOP (entry 4 in Table 1): (a) Dependence of $M_{n,NMR}$ and $Đ$ on the monomer conversion. (b) Evolution of SEC traces (THF). (c) Zero-order kinetic plot for the PA/EPO ROCOP.

A variety of cyclic anhydrides and oxetanes were evaluated in order to confirm the potential of the copolymerization for a large library of structurally and functionally diverse monomers. Using PA as a model anhydride, the current catalysis system was applied to two additional oxetanes. A less active 3-((allyloxy)methyl)-3-ethyloxetane (AMEO) was copolymerized with PA, producing a functional copolymer for post-modification (entry 5 in Table 1 and Figures S7–S9). Trimethylene oxide (TO) has the highest activity of these monomers because of without any substituent.[39] After 4h, the PA conversion reached 91.6%, resulting in copolymers with a narrow dispersity (entry 6 in Table 1 and Figures S10–S12). The MALDITOF MS results indicated that the major series of peaks corresponded to the sodium adduct of poly(PA-*alt*-TO) containing BDM as

the initiator and two PA or two TO at the two chain ends, and that no transesterification side reaction was observed (Figure S13). The highest molecular weight of P(PA-*alt*-TO) can reach 27.7 kDa (entry 7 in table 1 and Figure S12b). Then, utilizing EPO as the oxetane, numerous anhydrides were investigated. Compared to PA, faster conversion of diphenyl anhydride (DA) was observed during copolymerization of DA/EPO (entry 8 in Table 1 and Figures S14–S16), which was consistent with the increased reactivity brought about by the ring strain of the seven-membered anhydride.[42] Comparing to TO, EPO is very difficult to be removed from polymers during the purification process, which resulted in that peaks of EPO were observed in ^{1}H NMR spectrum. Additionally, DGA was used to react with TO, resulting in the P(DGA-*alt*-TO) (entry 9 in Table 1 and Figures S17 and S18). Since trimellitic anhydride (TA) has an additional carboxylic acid group that can serve as a propagating site for ROCOP, the copolymerization of TA/EPO resulted in hyperbranched copolymers (entry 10 in Table 1 and Figures S19–S21). The broad SEC trace is likely owing to non-uniform branching.[22,23]

The impact of the initiator structure was studied. In comparison to benzoic acid (entry 11 in Table 1 and Figures S22 and S23), alcohol exhibited greater initiation efficiency, enabling the synthesis of copolymers with narrow dispersity ($Đ$ ≤ 1.17). Using the ROCOP initiated by pentaerythritol (PET), a four-armed star-block copolymer was synthesized (entry 12 in Table 1 and Figures S24 and S25). Using *N*-methyldiethanolamine (MDA) as an amine-functionalized initiator, a well-defined cationizable polyester was also prepared, and such a cationizable polymer is widely used for genetic materials delivery (entry 13 in Table 1 and Figures S26 and S27).[45]

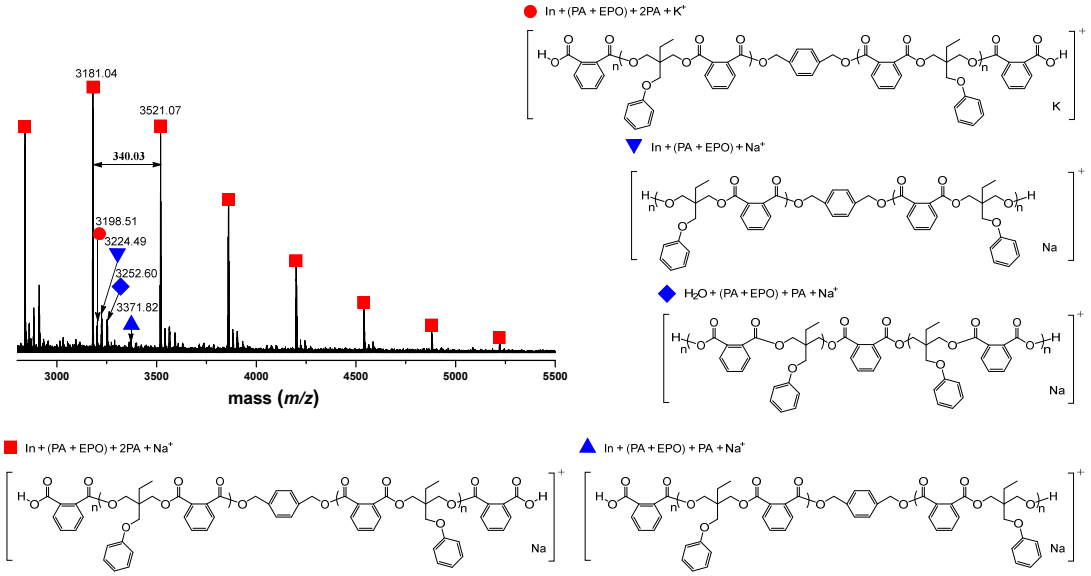


Figure 2. MALDI TOF-MS spectrum of the P(PA-*alt*-EPO) from entry 2 in Table 1.

Terpolymerization of anhydride, epoxide, and oxetane

In previous research, the cesium pivalate catalyst exhibited a high monomer selectivity and kinetic control for ROCOP of anhydrides/epoxide.[22] This motivates us to create a new self-switchable polymerization system by using this catalyst to spontaneously connect ROCOP of anhydrides/epoxide with ROCOP of anhydrides/oxetane. The mixture of PA, EPO, and cyclohexene oxide (CHO) was copolymerized for the first time using cesium pivalate and BDM as the catalyst and bidirectional initiator, respectively. The ^{1}H NMR analysis revealed that the initial PA/CHO copolymerization was followed by ROCOP of PA/EPO to form perfect triblock copolymers devoid of a tapered region and with extremely narrow dispersity (entry 1 in Table 2 and Figures S28–S30). The CHO and EPO reactivity ratio (Figure S31) revealed that the resultant polymers were most consistent with a nearly perfect triblock copolymer.[46–48] To further evaluate the catalytic pathway, copolymerization was conducted with the following ratios: $[PA]_0/[CHO]_0/[EPO]_0/[BDM]_0/[t\text{-}BuCO_2Cs]$: 45/15/90/1/1. After CHO was completely consumed and EPO conversion reached 7.2%, we added another 7.5 equiv of CHO to the reaction mixture, causing PA/EPO ROCOP to temporarily cease and PA/CHO ROCOP to commence. Perfect chemoselectivity was observed by ^{1}H NMR analysis of aliquots taken at regular intervals throughout the process (entry 2 in Table 2 and Figure 3). Extended reaction time initially caused the resonance signals of PA (proton 2' at 8.0 and 7.9 ppm) and CHO (proton 3' at 3.1 ppm) to decrease gradually. During this time period, there was no signal at 4.0–3.8 ppm (proton 6), indicating that (PA-*alt*-EPO) did not form.

ROCOP of PA/EPO begins only after CHO is completely consumed in 2h (degree of polymerization (DP) of PA is 15.1, DP_{CHO} is 15.0, Figures 3a and c), as demonstrated by the decrease in signal at 4.1 ppm (proton 6') and the appearance of signal at 4.0–3.8 ppm (proton 6). 7.5 equiv of CHO was introduced to temporarily stop the ROCOP of PA/EPO when conversion of EPO reached 7.2% in 19h (DP_{PA} is 21.5, DP_{CHO} is 15, DP_{EPO} is 6.5, Figures 3a and c), and the ROCOP of PA/CHO restarted the propagation from the terminus of P(PA-*alt*-EPO)-*b*-P(PA-*alt*-CHO)-*b*-P(PA-*alt*-EPO). Only after CHO is completely consumed again in 21h (DP_{PA} is 28.9, DP_{CHO} is 22.5, DP_{EPO} is 6.5, Figures 3a and c), does the ROCOP of PA/EPO activate, resulting in the formation of a heptablock copolymer (Figures 3 and S32–S34). SEC detects the narrow and unimodal *Đ*s, and the molecular weight increases continuously with monomer consumption (Figures 3b), indicating that the propagation from the mixtures of PA, CHO, and EPO was well-controlled. The formation of triblock copolymers rather than blends was confirmed by a diffusion-ordered NMR spectroscopy (DOSY) result displaying a single diffusion coefficient (Figures 3d).[49] To confirm that no EPO was incorporated into the P(PA-*alt*-CHO) block during polymerization, a copolymerization was performed from a mixture of PA/CHO/EPO with a molar ratio of 15/15/90, and the process was terminated when PA was completely consumed. Utilizing MALDITOF MS, the chemical structure of the obtained polymer was analyzed. MALDITOF MS of P(PA-*alt*-CHO) copolymers revealed six peaks, with the major series of peaks corresponding to poly(PA-*alt*-CHO) with BDM as initiator and CHO at two chain ends, and the minor series of peaks resulting from the sodium adduct of poly(PA-*alt*-CHO) with BDM or H_2O as initiator and two PAs or both PA and CHO at two chain ends, respectively (Figure S35). The alcohol end group continued to react with residual CHO instead of EPO, resulting in the formation of an ether link at the chain's terminus. This demonstrated that no EPO was inserted into the P(PA-*alt*-CHO) and no transesterification side reaction occurred during terpolymerization.

Table 2. The self-switchable polymerizations catalyzed by cesium pivalate.[a]

entry	monomers	[anhydride1]o/[anhydride2]o/[epoxide]o/[oxetane]o/[BDM]o/[cat.]o	Temp. [°C]	Time (h)	conv. [b] [%] (anhydride, epoxide, and oxetane)	$M_{n,th.}$ [c][kDa]	$M_{n,NMR.}$ [b][kDa]	$M_{n,SEC}$ [d][kDa]	Đ [d]
1	PA/CHO/EPO	30/15/90/1/1	130	19	PA = 89.5, CHO > 99, EPO = 13.2	7.9	7.1	4.9	1.14
2	PA/CHO/EPO	45/22.5/90/1/1	130	36	PA = 82.9, CHO > 99, EPO = 16.1	10.7	9.7	6.1	1.09
3	PA/AGE/EPO	30/15/90/1/1	130	24	PA = 96.3, AGE > 99, EPO = 15.6	8.8	7.6	6.2	1.14
4	DA/NA/EPO	15/15/90/1/1	130	42	DA > 99, NA = 58	9.5	n.d.	4.3	1.26
5	TA/NA/EPO	15/15/90/1/1	130	42	TA > 99, NA = 84.4	13.3	n.d.	6.1	1.71
6	DA/CHO/NA/EPO	15/15/15/160/1/1	130	30	DA > 99, CHO > 99, NA = 64.8, EPO = 6.0	8.5	e11.7	4.9	1.28
7	DA/CHO/NA/EPO	30/15/15/160/1/1	130	56	DA > 99, CHO > 99, NA = 54, EPO = 14.4	14.1	e40.0	6.2	1.23
8	DA/CHO/NA/EPO	15/30/30/160/1/1	130	41	DA > 99, CHO > 99, NA = 87.4, EPO = 6.7	13.5	e27.8	6.0	1.23
[f]9	PA/BGE/NA/TO	15/15/15/22.5/1/1	110	114	PA > 99, BGE > 99, NA = 74.2, EPO = 49.3	7.3	7.0	7.4	1.21
[f,g]10	PA/MO/NA/TO	20/20/31/62/1/1	110	256	TA > 99, MO > 99, NA = 99, EPO = 49.5	11.5	n.d.	8.1	1.22
11	TA/AGE/NA/EPO	30/15/15/160/1/1	130	28	TA > 99, AGE > 99, NA = 69.7, EPO = 15.2	19.0	e30.5	6.6	1.79

[a] Polymerization conditions: Ar atmosphere. [b] Determined by ^{1}H NMR analysis of the obtained polymer in $CDCl_3$. [c] Theoretical M_n values. [d] Determined by the SEC analysis of the obtained polymer in THF with a PSt standard. [e] Determined by SEC with multi-angle light scattering detector (SEC-MALS). [f] THF acted as solvent: $[PA]_0 = 1.5$. [g] PPA is used as initiator.

The self-switchable polymerization was then applied to allyl glycidyl ether (AGE). The perfect BAB triblock copolymers, where the A and B blocks were prepared by ROCOP of PA/AGE and ROCOP of PA/EPO, respectively, were obtained by copolymerizing the mixture of PA/AGE/EPO, demonstrating a high degree of control (entry 3 in Table 2, Figures S36–S41), as evidenced by a narrow dispersity and an increase in molecular weight with monomer consumption (Figure S37). The copolymerization of a PA/AGE/EPO mixture with a molar ratio of 15/15/90 was stopped when the reaction time reached 2h. The MALDITOF MS result of the obtained polymer confirmed the absence of EPO incorporation and any transesterification side reaction during ROCOP of PA/AGE. Because the major series of peaks corresponded to poly(PA-*alt*-AGE) containing BDM as an initiator and AGE and PA at two chain ends, and the minor series of peaks resulted from the sodium adduct of poly(PA-*alt*-AGE) containing BDM and two AGEs at two chain ends (Figure S40). Following the reactivity order of anhydrides, the analysis of reactivity ratios revealed that these epoxides are significantly more active than EPO, following the current reactivity order: anhydrides >> epoxide >> oxetane.

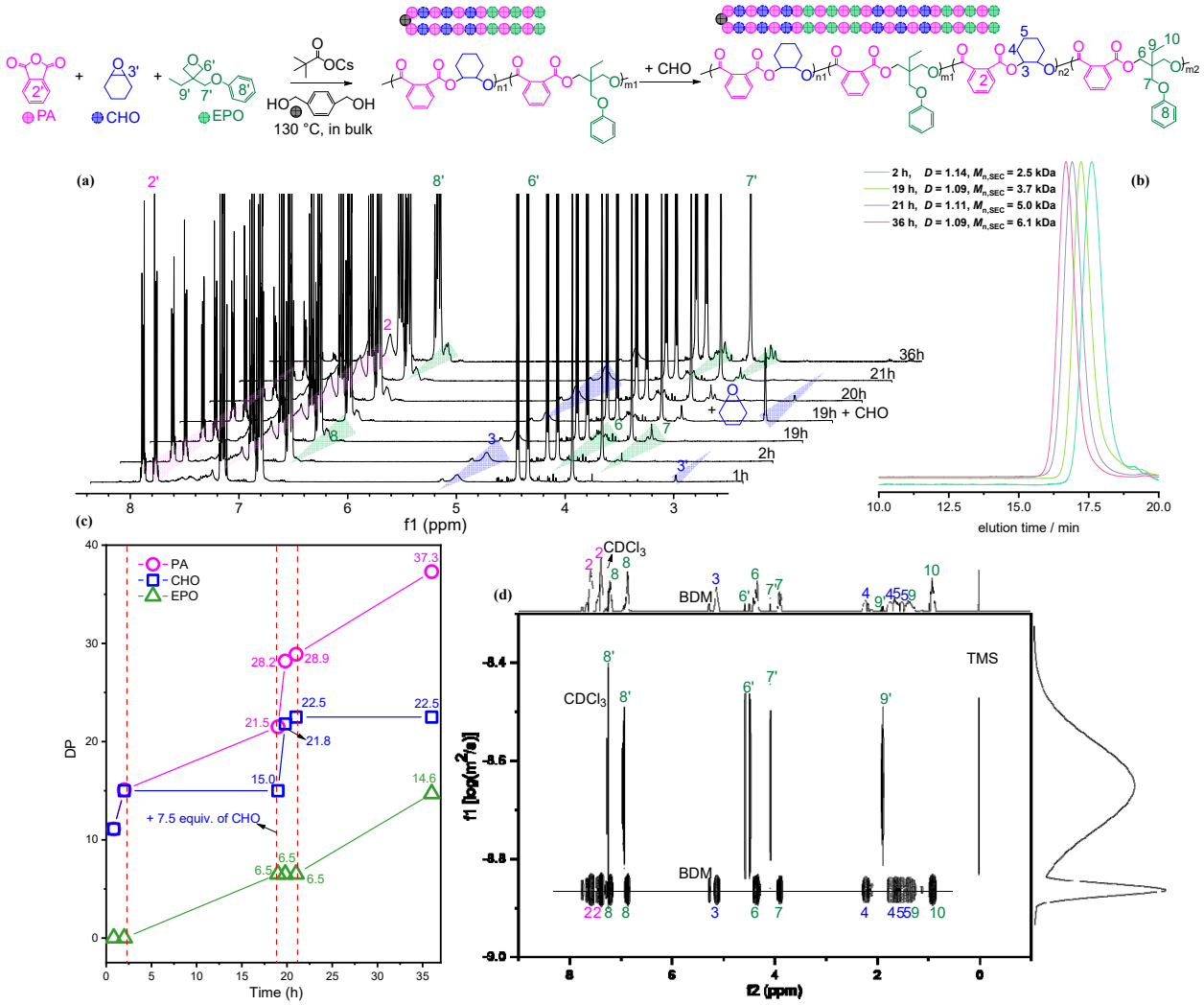


Figure 3. The polymerization from a mixture of PA/CHO/EPO monitored by NMR spectrum and SEC (entry 2 in Table 2): (a) The ^{1}H NMR ($CDCl_3$) spectrum of crude aliquots withdrawn from the reaction system for monitoring the conversion of PA, CHO, EPO, and the formation of resultant polymers. (b) Evolution of SEC traces (THF). (c) Plots of the degree of polymerization (DP) versus time. (d) DOSY ($CDCl_3$) spectrum of resultant polymers.

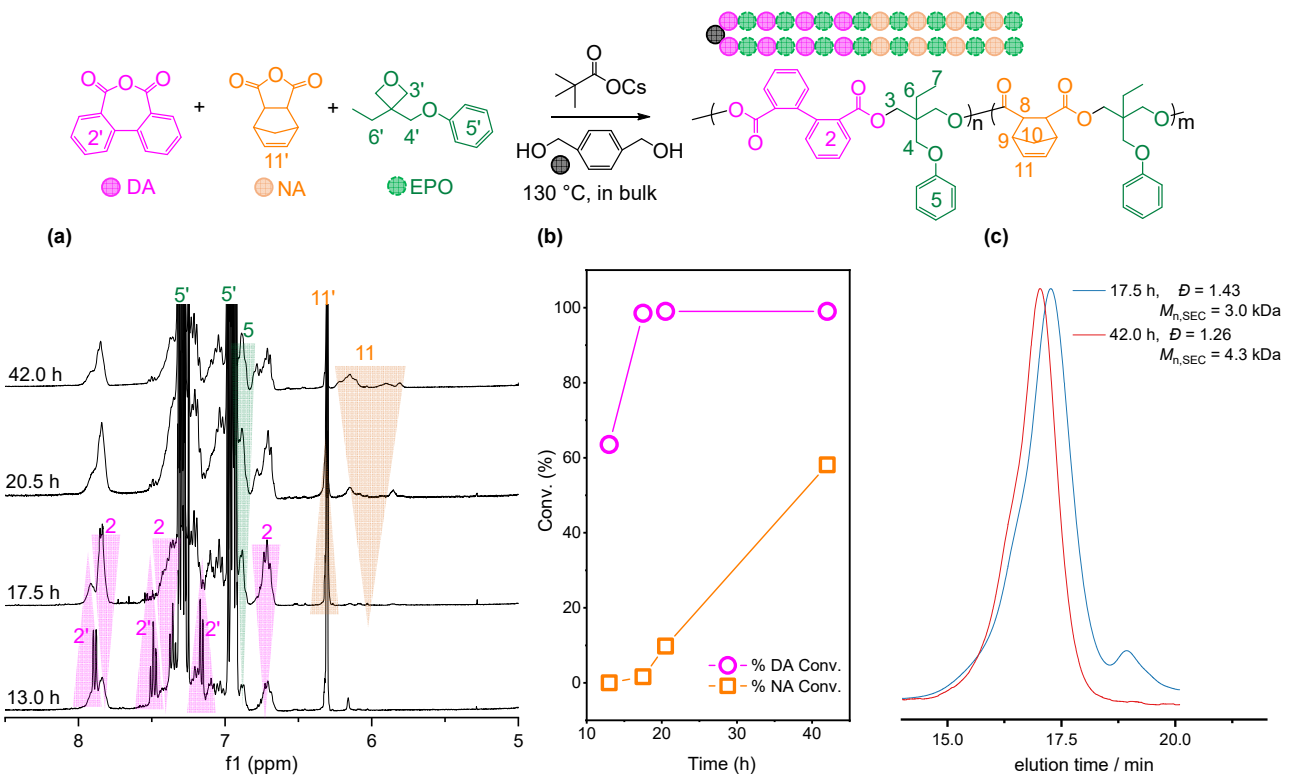


Figure 4. The polymerization from a mixture of DA/NA/EPO monitored by NMR spectrum and SEC (entry 4 in Table 2): (a) The ^{1}H NMR ($CDCl_3$) spectrum of crude aliquots withdrawn from the reaction system for monitoring the conversion of DA, NA, EPO, and the formation of resultant polymers. (b) Plots of monomers conversion versus time. (c) Evolution of SEC traces (THF).

Terpolymerization of two different anhydrides and oxetane

We successfully established a reactivity gradient among different anhydrides in the previous study.[23] In light of this, the possibility of sequential incorporation based on the difference in reactivity between these anhydrides was investigated. First, ROCOP was produced by combining DA, 5-norbornene-*endo*-2,3-dicarboxylic anhydride (NA), and EPO. This experiment produced a triblock copolymer with a sharp junction between P(DA-*alt*-EPO) and P(NA-*alt*-EPO) rather than a random copolymer, as predicted. The ROCOP of DA/EPO occurred first, as indicated by the decrease in ^{1}H NMR signals (proton 2', Figure 4a) due to DA and the appearance of ^{1}H NMR signals associated with P(DA-*alt*-EGE) (proton 2, Figure 4a). Once the DA conversion reached 98.5% (Figure 4b), the ROCOP of NA/EPO turned on and eventually formed triblock copolymers with a very small tapered section consisting of P(NA-*alt*-EPO)-*b*-P(DA-*alt*-EPO)-*b*-P(NA-*alt*-EPO). The SEC analysis of the obtained copolymers revealed a unimodal distribution ($Đ$ =1.26, entry 4 in Table 2), and the elution peak maximum shifted continuously toward shorter elution times (higher molecular weights) as copolymerization progressed (Figure 4c). The reactivity ratio between DA and NA indicates that DA is significantly more reactive than NA, forming a nearly perfect triblock polymer (Figures S42–S44). Observing only one diffusion coefficient (Figure S45) in DOSY further demonstrated the formation of copolymers as opposed to blends of P(DA-*alt*-EPO) and P(NA-*alt*-EPO). By competitively copolymerizing a mixture of trimellitic anhydride (TA), NA, and EPO, the perfect chemoselectivity was also observed, enabling the synthesis of a core-shell-type block copolymer with a hyperbranched P(TA-*alt*-EPO) core and a P(NA-*alt*-EPO) outer shell, with a broad SEC trace and high dispersity ($Đ$ = 1.90, entry 5 in Table 2, Figures S46–S51), which is likely owing to non-uniform branching.[50]

Quarterpolymerization of two different anhydrides, epoxide, and oxetane

Synchronous control of each unit structure in both blocks for self-switchable alternating copolymerization is a formidable obstacle; thus, no relevant reports have been published to date. Following the above studies, using reactivity gradient among different anhydrides to combine with extremely large reactivity difference between epoxide and oxetane can provide an opportunity for multi-dimensional control of block copolymer. As a proof of concept, the cesium pivalate catalyst was used to attempt to link DA/CHO ROCOP and NA/EPO ROCOP, thereby

establishing multidimensional controlled self-switchable alternating copolymerization. The ^{1}H NMR spectra indicated that the ROCOP of DA/CHO began immediately (Figure 5a), as evidenced by the simultaneous decrease of peaks due to DA (proton 2') and CHO (3') and the increase of P(DA-*alt*-CHO) signals (proton 2). Within 2h, the conversion of DA and CHO reached 99% (DP = 15) and 99% (DP = 15), respectively, and the conversion of NA and EPO reached 1.5 % (DP = 0.23) and 1.7 % (DP = 0.26) (Figures 5b and 5c), indicating that only a very small tapered section was formed. As the reaction progresses, the signal from the second-stage alternating units, i.e., P(NA-*alt*-EPO), increases, resulting in the formation of the triblock tetrapolymer (entry 6 in Table 2, Figures S52–S54). SEC were shifted to the higher molecular weight region while maintaining unimodal/narrow distributions (Đ < 1.30, Figure 5d), indicating that ROCOP is well controlled without transesterification. By simply adjusting the molar ratio of DA/CHO/NA/EPO from 15:15:15:160 to 30:15:15:160, pentablock tetrapolymers were obtained from the polymerization of DA/CHO/NA/EPO with BDM as an initiator. In particular, due to reactivity order of DA >> NA >> CHO >> EPO for the alkoxide end group and reactivity order of CHO >> EPO for carboxylic end group, ROCOP of DA/CHO occurred first. Upon complete consumption of CHO in 2h, excess DA began to copolymerize with EPO, forming P(DA-*alt*-EPO) block. Once the conversion of DA reached 100%, the ROCOP of NA/EPO turned on and finally formed P(NA-*alt*-EPO)-*b*-P(DA-*alt*-EPO)-*b*-P(DA-*alt*-CHO)-*b*-P(DA-*alt*-EPO)-*b*-P(NA-*alt*-EPO). As evidenced by SEC and 1H, 13C analyses, pentablock tetrapolymers with a tapered section of less than 3% (entry 7 in Table 2, Figures S55–S58). By changing the molar ratio of DA/CHO/NA/EPO from 30:15:15:160 to 15:30:30:160, DA/CHO ROCOP first formed a P(DA-*alt*-CHO) (Figure S59), followed by the serial incorporation of P(NA-*alt*-CHO) and P(NA-*alt*-EPO) blocks generated by NA/CHO ROCOP and NA/EPO ROCOP, respectively. Finally, P(DA-*alt*-EPO)-*b*-P(NA-*alt*-CHO)-*b*-P(DA-*alt*-CHO)-*b*-P(NA-*alt*-CHO)-*b*-P(DA-*alt*-EPO) pentablock tetrapolymers were produced in an one-step procedure (entry 8 in Table 2, Figures S59–S62) and showed different sequence structure from the above resulting copolymers, suggesting that various sequence-controlled block tetrapolymers can be synthesized by simply adjusting the molar ratio of the monomer mixture. Other anhydrides, epoxides, and oxetanes were used in the quarterpolymerization to synthesize diverse block tetrapolymers by one-step procedure. The quarterpolymerization from PA/benzyl glycidyl ether (BGE)/NA/TO with the molar ratio of 15:15:15:22.5 was performed in 110 °C, leading to the triblock tetrapolymer with narrow dispersity (entry 9 in Table 2, Figures S63–S67). The diblock tetrapolymers synthesized by using 3-phenyl-1-propanol (PPA) as an initiator for the quarterpolymerization of PA/2-((naphthalen-2-yloxy)methyl)oxirane (MO)/NA/TO, and Poly(PA-*alt*-MO)-*b*-Poly(NA-*alt*-TO) show two glass transition temperature (T_g) values at comparable temperature to the corresponding homopolymers ($T_{g,\,P(PA\text{-}alt\text{-}MO)} \cong 64$ °C, Figure S72, $T_{g,\,P(NA\text{-}alt\text{-}TO)} \cong -23$ °C, Figure S74), implying presence of microphase separation (entry 10 in Table 2, Figures S68–S75). Our previous work has reported that the reactivity between TA and NA follows the trend of TA >> NA, providing an opportunity to synthesize core-shell type multi-block copolymers by a one-step procedure, in which alternating copolymer as core and block copolymer as the outer shell.[23] Here, the core and shell structure can be flexibly adjusted by controlling the ratio of monomers, for example, when the molar ratio of TA/AGE/NA/EPO is 30:15:15:160, the copolymerization from this mixture leads to a special core-shell type block copolymer with hyperbranched P(TA-*alt*-AGE)-*b*-P(TA-*alt*-EPO) and P(NA-*alt*-EPO) as the core and outer shells (entry 11 in Table 2, Figures S76–S81), respectively. The formation of the polymers was confirmed by both ^{1}H and ^{13}C NMR (Figures S76 and S77) and this topology is different from the previous report. Thus, this catalytic system provides an efficient, simple, one-step procedure, in comparison to conventional stepwise synthetic procedures for preparing various core-shell type multiblock copolymers.

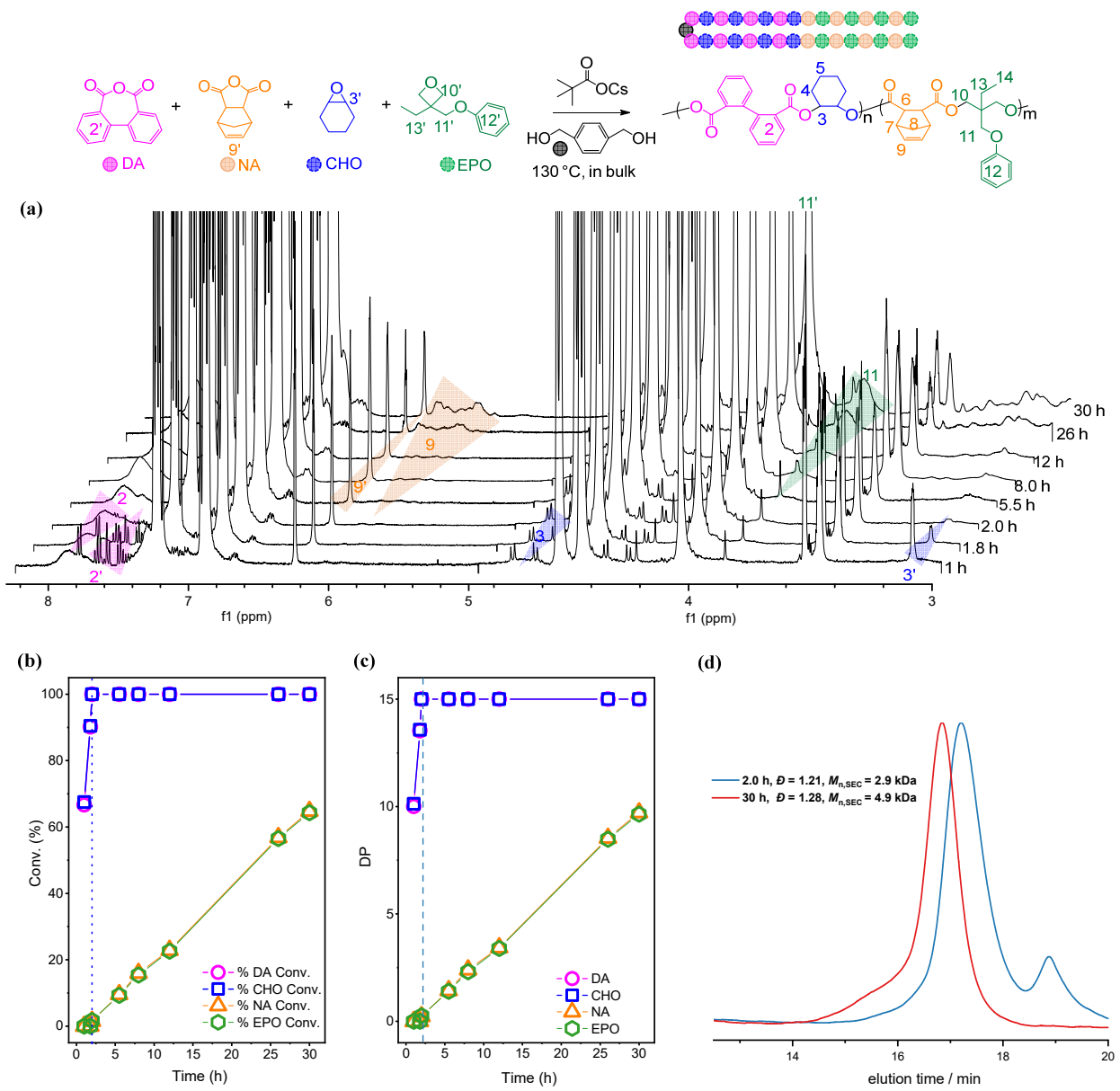
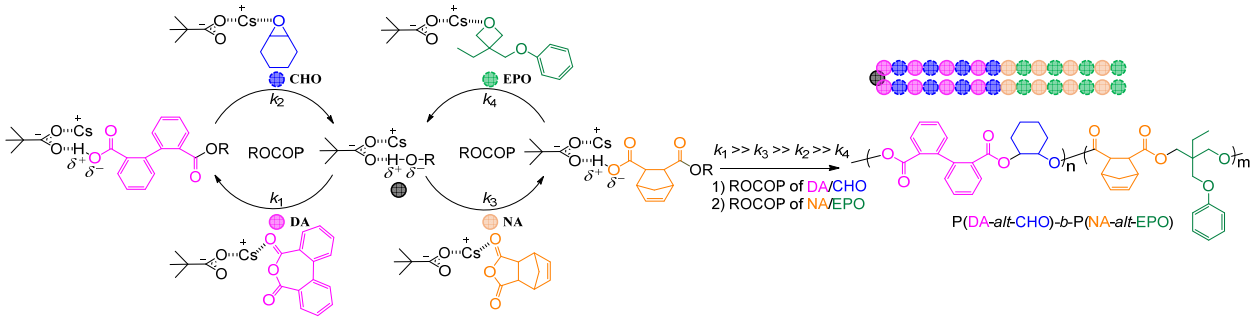


Figure 5. The polymerization from a mixture of DA/CHO/NA/EPO monitored by NMR spectrum and SEC (entry 6 in Table 2): (a) The ^{1}H NMR ($CDCl_3$) spectrum of crude aliquots withdrawn from the reaction system for monitoring the conversion of DA, CHO, NA, EPO, and the formation of resultant polymers. (b) Plots of monomers conversion versus time and conversion of EPO are normalized. (c) Plots of the degree of polymerization versus time. (d) Evolution of SEC traces (THF).

Mechanistic Studies



Scheme 3. Proposed mechanism of the self-switchable alternating polymerization from a mixture of DA, NA, CHO, and EPO with cesium pivalate as the catalyst and alcohol as the initiator.

Scheme 3 illustrates a chemoselective mechanistic pathway for quarterpolymerization from the mixture of DA/CHO/NA/EPO based on the multiactivation mechanism reported in our previous work.[22,23] Due to the reactivity order of DA >> NA >> CHO >> EPO, the initial DA/CHO copolymerization reaction was followed by ROCOP of NA/EPO to form triblock tetrapolymers. In the first cycle, the reactivity of DA is significantly greater than that of NA, so the hydroxyl group activated by cesium pivalate is likely to nucleophilically attack cesium cation-activated DA. Because CHO is significantly more active than EPO, the resulting carboxylate species reacts with CHO rather than EPO, resulting in the formation of a first block with a perfect alternating chemical structure. After both DA and CHO has been completely consumed, the cesium pivalate-activated termini of the P(DA-*alt*-CHO) blocks switch to initiate the second copolymerization cycle of NA/EPO in the same manner, resulting in the production of perfect triblock copolymers. There are two possible mechanisms for catalytic polymerization: the monometallic pathway and the bimetallic pathway.[51] For both alternating copolymerization cycles, the insertion of anhydrides is significantly faster than that of epoxide and oxetane, and the rate-determining step is the slow insertion of epoxides and oxetanes.

CONCLUSION

The one-step synthesis of block tetrapolymers containing two types of alternating sequences, poly(cyclic anhydride-*alt*-epoxide) and poly(cyclic anhydride-*alt*-oxetane), was successful. Cesium pivalate was used for the first time as a catalyst for ROCOP of cyclic anhydrides/oxetane, synthesizing end-functionalized poly(cyclic anhydride-*alt*-oxetane) as well as multihydroxyl-containing copolymers with a four-armed star structure. A significant advantage of the cesium pivalate catalyst is that it automatically switches between the two distinct alternating copolymerization cycles, demonstrating high monomer selectivity and kinetic control. In this study, various block copolymers, including hyperbranched copolymers, core-shell type terpolymers, core-shell type tetrapolymers, BAB triblock terpolymers, BAB-type triblock tetrapolymers, and pentablock tetrapolymers, were successfully synthesized via one-step procedures by combining the reactivity gradient among different anhydrides with the established reactivity order of epoxides >> oxetane. This self-switchable alternating copolymerization is therefore promising and significant for both laboratory- and industrial-scale productions of industrial block polymers with complex macromolecular architectures.

ASSOCIATED CONTENT

Supporting Information. Supplementary Information accompanies this paper.

AUTHOR INFORMATION

Corresponding Authors

Takuya Isono-Division of Applied Chemistry, Faculty of Engineering, Hokkaido University, Sapporo 060-8628, Japan
Email: isono.t@eng.hokudai.ac.jp

Toshifumi Satoh- Division of Applied Chemistry, Faculty of Engineering, Hokkaido University, Sapporo 060-8628, Japan
Email: satoh@eng.hokudai.ac.jp

Author Contributions

Xiaochao Xia: Writing original draft, Methodology, Visualization. Tianle Gao and Ryota Suzuki: Data curation, Visualization. Xiaochao Xia, Feng Li, Takuya Isono, and Toshifumi Satoh: Supervision, Conceptualization, Methodology, Writing – review & editing

Funding Sources

The Japan Society for the Promotion of Science Grant-in-Aid for Scientific Research (B) (Grant Number 19H02769); the Ministry of Education, Culture, Sports, Science, and Technology of Japan Grant-in-Aid for Scientific Research on

Innovative Areas (Hybrid Catalysis for Enabling Molecular Synthesis on Demand; Grant Numbers 18H04639 and 20H04798); the Frontier Chemistry Center (Hokkaido University); the Photo-excitonic Project (Hokkaido University); the Creative Research Institution (CRIS, Hokkaido University); the Project of Junior Scientist Promotion in Hokkaido University; Cultivation Plan of National Natural Science Foundation of China and Social Science Foundation Project (Grant Number: 2021PYZ03); the Science and Technology Research Program of Chongqing Municipal Education Commission (Grant Numbers: KJQN201901109).

ACKNOWLEDGMENT

This work was financially supported by the Japan Society for the Promotion of Science Grant-in-Aid for Scientific Research (B) (Grant Number 19H02769); the Ministry of Education, Culture, Sports, Science, and Technology of Japan Grant-in-Aid for Scientific Research on Innovative Areas (Hybrid Catalysis for Enabling Molecular Synthesis on Demand; Grant Numbers 18H04639 and 20H04798); the Frontier Chemistry Center (Hokkaido University); the Photo-excitonic Project (Hokkaido University); the Creative Research Institution (CRIS, Hokkaido University); the Project of Junior Scientist Promotion in Hokkaido University; Cultivation Plan of National Natural Science Foundation of China and Social Science Foundation Project (Grant Number: 2021PYZ03); the Science and Technology Research Program of Chongqing Municipal Education Commission (Grant Numbers: KJQN201901109).

Competing interests

The authors declare no conflict of interest.

REFERENCES

1. Jazani, A. M.; Shetty, C.; Movasat, H.; Bawa, K. K.; Oh, J. K. Imidazole-mediated dual location disassembly of acid-degradable intracellular drug delivery block copolymer nanoassemblies. Macromol. Rapid Commun., **2021**, *42* (16), e2100262. DOI: 10.1002/marc.202100262

2. Kumar, N.; Ravikumar, M. N. V.; Domb, A. J. Biodegradable block copolymers. Adv. Drug Deliv. Rev., **2001**, *53* (1), 23–44. DOI: 10.1016/s0169-409x(01)00219-8

3. Lutz, J. F.; Ouchi, M.; Liu, D. R.; Sawamoto, M. Sequence-controlled polymers. Science, **2013**, *341* (6146), 1238149. DOI: 10.1126/science.1238149

4. Austin, M. J.; Rosales, A. M. Tunable biomaterials from synthetic, sequence-controlled polymers. Biomater. Sci., **2019**, *7* (2), 490–505. DOI: 10.1039/c8bm01215f

5. Bressers, H. J. L.; van Driel, W. D.; Jansen, K. M. B.; Ernst, L. J.; Zhang, G. Q. Correlation between chemistry of polymer building blocks and microelectronics reliability. Microelectron. Reliab., **2007**, *47* (2-3), 290–294. DOI: 10.1016/j.microrel.2006.09.035

6. Yang, C.; Wu, K. B.; Deng, Y.; Yuan, J.; Niu, J. Geared Toward Applications: A Perspective on Functional Sequence-Controlled Polymers. ACS Macro Lett., **2021**, *10* (2), 243–257. DOI: 10.1021/acsmacrolett.0c00855

7. Romain, C.; Williams, C. K. Chemoselective polymerization control: from mixed - monomer feedstock to copolymers. Angew. Chem. Int. Ed. Engl. **2014**, *53* (6), 1607–1610. DOI: 10.1002/anie.201309575

8. Romain, C.; Zhu, Y.; Dingwall, P.; Paul, S.; Rzepa, H. S.; Buchard, A.; Williams, C. K. Chemoselective polymerizations from mixtures of epoxide, lactone, anhydride, and carbon dioxide. J. Am. Chem. Soc., **2016**, *138* (12), 4120–4131. DOI: 10.1021/jacs.5b13070

9. Jeske, R. Q.; Rowley, J. M.; Coates, G. W. Pre-rate-determining selectivity in the terpolymerization of epoxides, cyclic anhydrides, and CO_2: a one-step route to diblock copolymers. Angew. Chem. Int. Ed. Engl., **2008**, *47* (32), 6041–6044. DOI: 10.1002/anie.200801415

10. Zhu, Y.; Romain, C.; Williams, C. K. Selective polymerization catalysis: controlling the metal chain end group to prepare block copolyesters. J. Am. Chem. Soc., **2015**, *137* (38), 12179–12182. DOI: 10.1021/jacs.5b04541

11. Paul, S.; Romain, C.; Shaw, J.; Williams, C. K., Sequence selective polymerization catalysis: a new route to ABA block copoly (ester-b-carbonate-b-ester). Macromolecules, **2015**, *48* (17), 6047–6056. DOI: 0.1021/acs.macromol.5b01293

12. Kernbichl, S.; Reiter, M.; Adams, F.; Vagin, S.; Rieger, B. CO_2-controlled one-pot synthesis of ab, aba block, and statistical terpolymers from β-butyrolactone, epoxides, and CO_2. J. Am. Chem. Soc., **2017**, *139* (20), 6787–6790. DOI: 10.1021/jacs.7b01295

13. Chen, T. T.; Zhu, Y.; Williams, C. K.; Pentablock copolymer from tetracomponent monomer mixture using a switchable dizinc catalyst. Macromolecules, **2018**, *51* (14), 5346–5351. DOI: 0.1021/acs.macromol.8b01224

14. Ji, H. Y.; Wang, B.; Pan, L.; Li, Y. S. One-step access to sequence-controlled block copolymers by self-switchable organocatalytic multicomponent polymerization. Angew. Chem. Int. Ed. Engl., **2018**, *57* (51), 16888–16892. DOI: 10.1002/anie.201810083

15. Stößer, T.; Williams, C. K. Selective Polymerization Catalysis from Monomer Mixtures: Using a Commercial Cr-Salen Catalyst to Access ABA Block Polyesters. Angew. Chem. Int. Ed. Engl., **2018**, *57* (21), 6337–6341. DOI: 10.1002/anie.201801400

16. Stößer, T.; Chen, T. T. D.; Zhu, Y.; Williams, C. K., 'Switch' catalysis: from monomer mixtures to sequence-controlled block copolymers. Philos. Trans. A Math. Phys. Eng. Sci., **2018**, *376* (2110), 20170066. DOI: 10.1098/rsta.2017.0066

17. Stößer, T.; Mulryan, D.; Williams, C. K. Switch catalysis to deliver multi-block polyesters from mixtures of propene oxide, lactide, and phthalic anhydride. Angew. Chem. Int. Ed. Engl., **2018**, *57* (51), 16893–16897. DOI: 10.1002/anie.201810245

18. Stößer, T.; Sulley, G. S.; Gregory, G. L.; Williams, C. K. Easy access to oxygenated block polymers via switchable catalysis. Nat. Commun., **2019**, *10* (1), 2668. DOI: 10.1038/s41467-019-10481-w

19. Hu, C.; Duan, R.; Yang, S.; Pang, X.; Chen, X. CO_2 Controlled catalysis: switchable homopolymerization and copolymerization. Macromolecules, **2018**, *51* (12), 4699–4704. DOI: 10.1021/acs.macromol.8b00696

20. Li, H.; Luo, H.; Zhao, J.; Zhang, G. Sequence-selective terpolymerization from monomer mixtures using a simple organocatalyst. ACS Macro Lett., **2018**, *7* (12), 1420–1425. DOI: 10.1021/acsmacrolett.8b00865

21. Diment, W. T.; Stößer, T.; Kerr, R. W.; Phanopoulos, A.; Durr, C. B.; Williams, C. K. Ortho-vanillin derived Al (III) and Co (III) catalyst systems for switchable catalysis using ε-decalactone, phthalic anhydride and cyclohexene oxide. Catal. Sci. Tech., **2021**, *11*, 1737–1745. DOI: 10.1039/D0CY02164D

22. Xia, X. C.; Ryota, S.; Takojima, K.; Jiang, D. H.; Isono, T.; Satoh, T.; Smart access to sequentially and architecturally controlled block polymers via a simple catalytic polymerization

system. ACS Catal., **2021**, *11* (10), 5999–6009. DOI: 10.1021/acscatal.1c00382

23. Xia, X.C.; Suzuki, R.; Gao, T.; Isono, T.; Satoh, T. One-step synthesis of sequence-controlled multiblock polymers with up to 11 segments from monomer mixture. Nat. Commun., **2022**, *13* (1), 1–11. DOI: 10.1038/s41467-021-27830-3

24. Hsu, L. C.; Isono, T.; Lin, Y. C.; Kobayashi, S.; Chiang, Y. C.; Jiang, D. H.; Hung, C. C.; Ercan, E.; Yang, W. C.; Hsieh, H. C.; Tajima, K.; Satoch, T.; Chen, W. C. Stretchable OFET memories: tuning the morphology and the charge-trapping ability of conjugated block copolymers through soft segment branching. ACS Appl. Mater. Interfaces, **2021**, *13* (2), 2932–2943. DOI: 10.1021/acsami.0c18820

25. Liu, S.; Bai, T.; Ni, K.; Chen, Y.; Zhao, J.; Ling, J.; Ye, X.; Zhang, G. Biased lewis pairs: a general catalytic approach to ether-ester block copolymers with unlimited ordering of sequences. Angew. Chem. Int. Ed. Engl. **2019**, *58* (43), 15478–15487. DOI: 10.1002/anie.201908904

26. Li, H.; He, G.; Chen, Y.; Zhao, J.; Zhang, G. One-step approach to polyester–polyether block copolymers using highly tunable bicomponent catalyst. ACS Macro Lett., **2019**, *8* (8), 973–978. DOI: 10.1021/acsmacrolett.9b00439

27. Yang, Z.; Hu, C.; Cui, F.; Pang, X.; Huang, Y.; Zhou, Y.; Chen, X. One-pot precision synthesis of AB, ABA and ABC block copolymers via switchable catalysis. Angew. Chem. Int. Ed. Engl., **2022**, *61* (12), e202117533. DOI: 10.1002/anie.202117533

28. Jeske, R. C.; DiCiccio, A. M.; Coates, G. W. Alternating copolymerization of epoxides and cyclic anhydrides: an improved route to aliphatic polyesters. J. Am. Chem. Soc., **2007**, *129* (37), 11330–11331. DOI: 10.1021/ja0737568

29. Van Zee, N. J.; Coates, G. W. Alternating copolymerization of propylene oxide with biorenewable terpene-based cyclic anhydrides: a sustainable route to aliphatic polyesters with high glass transition temperatures. Angew. Chem. Int. Ed. Engl, **2015**, *54* (9), 2665-2668. DOI: 10.1002/anie.201410641

30. Ji, H. Y.; Song, D. P.; Wang, B.; Pan, L.; Li, Y. S. Organic lewis pairs for selective copolymerization of epoxides with anhydrides to access sequence-controlled block copolymers. Green Chem., **2019**, *21*, 6123–6132. DOI: 10.1039/C9GC02429H

31. Zhu, S.; Zhao, Y.; Ni, M.; Xu, J.; Zhou, X.; Liao, Y.; Wang, Y.; Xie, X. One-step and metal-free synthesis of triblock quaterpolymers by concurrent and switchable polymerization. ACS Macro Lett., **2020**, *9* (2), 204–209. DOI: 10.1021/acsmacrolett.9b00895

32. Jurrat, M.; Pointer-Gleadhill, B. J.; Ball, L. T.; Chapman, A.; Adriaenssens, L. Polyurethanes and polyallophanates via sequence-selective copolymerization of epoxides and isocyanates. J. Am. Chem. Soc., **2020**. *142* (18), 8136–8141. DOI: 10.1021/jacs.0c03520

33. Zhu, X. F.; Yang, G. W.; Xie, R.; Wu, G. P. One-pot construction of sulfur-rich thermoplastic elastomers enabled by metal-free self-switchable catalysis and air-assisted coupling. Angew. Chem. Int. Ed. Engl., **2021**, *61* (7), e202115189. DOI: 10.1002/anie.202115189

34. Lai, T.; Zhang, P.; Zhao, J.; Zhang, G. Simple and precision approach to polythioimidocarbonates and hybrid block copolymer derivatives. Macromolecules, **2021**, *54* (23), 11113–11125. DOI: 10.1021/acs.macromol.1c01889

35. Xu, J., Hadjichristidis, N. Well-Defined poly (Ester Amide)-based homo- and block copolymers by one-pot organocatalytic anionic ring-opening copolymerization of N-sulfonyl aziridines and cyclic anhydrides. Angew. Chem. Int. Ed. Engl., **2021**, *60* (13), 6949–6954. DOI: 10.1002/anie.202015339

36. Xu, J., Wang, X., Hadjichristidis, N. Diblock dialternating terpolymers by one-step/one-pot highly selective organocatalytic multimonomer polymerization. Nat. Commun., **2021**, *12* (1), 1–10. DOI: 10.1038/s41467-021-27377-3

37. Chen, X. L.; Wang, B.; Song, D. P.; Pan, L.; Li, Y. S. One-step synthesis of sequence-controlled polyester-*block*-poly (ester-alt-thioester) by chemoselective multicomponent polymerization. Macromolecules, **2022**, 55 (4), 1153–1164. DOI: 10.1021/acs.macromol.1c02303

38. Kerr, R. W.; Williams, C. K. Zr (IV) Catalyst for the ring-opening copolymerization of anhydrides (A) with epoxides (B), oxetane (B), and tetrahydrofurans (C) to make ABB-and/or ABC-poly (ester-*alt*-ethers). J. Am. Chem. Soc., **2022**, *144* (15), 6882–6893. DOI: 10.1021/jacs.2c01225

39. Bull, J. A.; Croft, R. A.; Davis, O. A.; Doran, R.; Morgan, K. F. Oxetanes: recent advances in synthesis, reactivity, and medicinal chemistry. Chem. Rev. 2016, 116, 12150–12233. DOI: 10.1021/acs.chemrev.6b00274

40. Takeuchi, D.; Aida, T.; Endo, T. The first example of the copolymerization of cyclic acid anhydrides with oxetane by bulky titanium bisphenolates. Macromol. Rapid Commun., **1999**, *20* (12), 646–649. DOI: 10.1002/(SICI)1521-3927(19991201)20:12<646::AID-MARC646>3.0.CO;2-N

41. Kameyama, A.; Ueda, K.; Kudo, H.; Nishikubo, T. The First Synthesis of alternating copolymers of oxetanes with cyclic carboxylic anhydrides using quaternary onium salts. Macromolecules, **2002**, 35 (10), 3792–3794. DOI: 10.1021/ma020106+

42. McGuire, T. M.; Clark, E. F.; Buchard, A. Polymers from sugars and cyclic anhydrides: ring-opening copolymerization of a $_{d}$-xylose anhydrosugar oxetane. Macromolecules, **2021**, *54* (11), 5094–5105. DOI: 10.1021/acs.macromol.1c00365

43. Bhat, G. A.; Luo, M.; Darensbourg, D. J. Catalysis of carbon dioxide and oxetanes to produce aliphatic polycarbonates. Green Chem., **2020**, *22* (22): 7707–7724. DOI: 10.1039/D0GC03219K

44. Huang, J., De Winter, J., Dove, A. P., Coulembier, O. Metal-free synthesis of poly (trimethylene carbonate) by efficient valorization of carbon dioxide. Green Chem., **2019**, *21* (3): 472–477. DOI: 10.1039/C8GC03607A

45. Abd Elwakil, M. M.; Gao, T.; Isono, T.; Sato, Y.; Elewa, Y. H.; Satoh, T.; Harashima, H. Engineered ε-decalactone lipomers bypass the liver to selectively in vivo deliver mRNA to the lungs without targeting ligands. Mater. Horiz., **2021**, *8* (8), 2251–2259. DOI: 10.1039/d1mh00185j

46. Gleede, T.; Markwart, J. C.; Huber, N., Rieger, E.; Wurm, F. R. Competitive copolymerization: access to aziridine copolymers with adjustable gradient strengths. Macromolecules, **2019**, *52* (24): 9703–9714. DOI: 10.1021/acs.macromol.9b01623

47. Beckingham, B. S., Sanoja, G. E., Lynd, N. A. Simple and accurate determination of reactivity ratios using a nonterminal model of chain copolymerization. Macromolecules, **2015**, *48* (19): 6922–6930. DOI: 10.1021/acs.macromol.5b01631

48. Chwatko, M., Lynd, N. A. Statistical copolymerization of epoxides and lactones to high molecular weight. Macromolecules, **2017**, *50* (7): 2714–2723. DOI: 10.1021/acs.macromol.7b00410

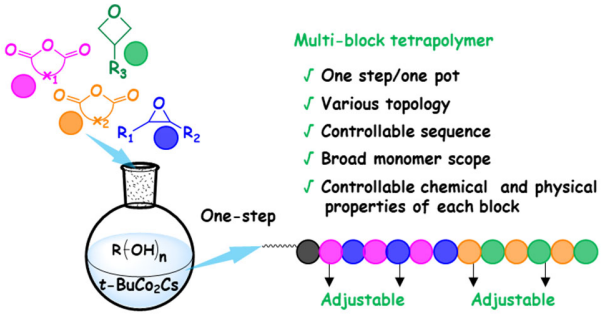
49. Chen, X. L.; Wang, B.; Song, D. P.; Pan, L.; Li, Y. S. Constructing ABA-and ABCBA-type multiblock copolyesters with structural diversity by organocatalytic self-switchable copolymerization. Macromolecules, **2021**, *54* (13), 6171–6181. DOI: 10.1021/acs.macromol.1c00767

50. Lidston, C. A.; Abel, B. A.; Coates, G. W. Bifunctional catalysis prevents inhibition in reversible-deactivation ring-opening copolymerizations of epoxides and cyclic anhydrides. J.

Am. Chem. Soc., **2020**, *142* (47), 20161–20169. DOI: 10.1021/jacs.0c10014

51. Ohkawara, T.; Suzuki, K.; Nakano, K.; Mori, S.; Nozaki, K. Facile estimation of catalytic activity and selectivities in copolymerization of propylene oxide with carbon dioxide mediated by metal complexes with planar tetradentate ligand. J. Am. Chem. Soc., **2014**, *136* (30), 10728–10735. DOI: 10.1021/ja5046814

SYNOPSIS TOC.



Synchronously and thoroughly adjusting the chemical structure difference between two blocks of diblock copolymer is very useful for the design of materials, but difficult to achieve via self-switchable alternating copolymerization. Our study used the cesium pivalate catalyst to automatically switches between the two distinct alternating copolymerization cycles, allowing one step synthesis of block tetrapolymers from the four-component system.