ARTICLE

Synthesis of Hyperbranched Polyester via Ring-opening Alternating Copolymerisation of Epoxide with Cyclic Anhydride having a Carboxyl Group

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Ryota Suzuki,[a] Xiaochao Xia,[b,c] Tianle Gao,[a] Takuya Yamamoto,[b] Kenji Tajima,[b] Takuya Isono,[*,b] Toshifumi Satoh[*,b]

Hyperbranched polyesters (HBPEs) are well-known interesting materials in many fields. However, the known synthetic approaches to HBPE lack versatility. Herein, we report a novel synthetic approach to HBPE via ring-opening alternating copolymerisation (ROAC) using epoxides and trimellitic anhydride (TA) as the latent difunctional and trifunctional monomers, respectively. Caesium pivalate-catalysed ROACs of TA and excess epoxides were performed in the presence of an alcohol initiator at 80 °C in the bulk. The obtained products, together with their linear counterparts (i.e., poly(phthalic anhydride-*alt*-epoxide)s), were characterised by NMR, viscometry, and light scattering. The results supported successful synthesis of hyperbranched poly(TA-*alt*-epoxide)s. The versatility of the present HBPE synthesis was demonstrated by applying a range of alcohol initiators such as typical diol and functional alcohols (e.g., poly(ethylene glycol) as a mono-alcohol or diol and azido-/alkene-functionalised alcohols as another mono-alcohol), leading to HBPE-based block copolymers and functional HBPEs. Various epoxides such as mono- and disubstituted alkylene oxides, glycidyl ether, and glycidyl amine were found to be applicable to the present polymerisation system, which successfully produced HBPEs with different properties depending on the resulting backbone structures of the polymer.

Introduction

Hyperbranched polymers (HBPs) are highly branched macromolecules comprising a large number of dendritic and terminal units. They exhibit specific properties such as lower viscosity, higher solubility, and more highly dense terminal functionality than those of their linear counterparts.[1] Dendrimers are a type of branched polymers; however, the regular structure of dendrimers makes their synthesis highly complicated. Although HBPs are structurally less regular than dendrimers, the former have usually one-step synthesis methods.[2] In addition, their interesting properties originating from the highly branched architecture and easy synthesis make them greatly valuable in a wide variety of industrial applications such as coatings,[3,4] rheological modifiers,[5] and catalysts.[6] HBPs are particularly useful for fabricating high-strength sheets and films.[7] In addition, the application range of HBPs is expanding in biomedical fields as well such as drug delivery system (DDS) and tissue engineering.[8–10]

Hyperbranched polyesters (HBPEs) are of particular interest for biomedical applications because of their excellent biocompatibility and biodegradability. Wyatt *et al*. reported poly(glycerol succinate)-based HBPEs for application as surgical materials in orthopaedic and ophthalmic operations,[11] while Gao *et al*. reported polyglycerol/poly(lactic acid) copolymer-based HBPEs for application in protein delivery.[12] Although a wide variety of HBPEs have been reported so far, further improvements in their molecular design capacity and synthesis methods are still needed to fabricate novel functional materials that meet the needs of different industries.

In general, the synthesis methods of HBPE can be classified into two categories based on the polymerisation mechanism: (1) step-growth polymerisation and (2) chain-growth polymerisation. Most HBPE syntheses rely on the step-growth polycondensation of a carboxylic acid (A) and an alcohol (B). The first HBPE synthesis was achieved before 1900 by polycondensation of tartaric acid (A_2B_2) and glycerol (B_3), in which ester bonds were formed between two tartaric acid molecules as well as between tartaric acid and glycerol.[13] Subsequently, a large number of monomer combinations of dicarboxylic acids (A_2) and polyols (B_x, $x > 2$) have been reported for constructing HBPEs. Zhang *et al*. reported the polycondensation of adipic acid (A_2) and glycerol (B_3),[14] while Kienle *et al*. reported the polycondensation of phthalic anhydride (A_2) and glycerol (B_3).[15] In addition, polycondensation of AB_x-type monomers (e.g., 3,5-diacetoxybenzoic acid) have been extensively used to synthesise various HBPEs.[16] Yan and Gao extended the

[a.] *Graduate School of Chemical Sciences and Engineering, Hokkaido University, Sapporo 060-8628, Japan.*
[b.] *Division of Applied Chemistry, Faculty of Engineering, Hokkaido University, Sapporo 060-8628, Japan.*
[c.] *School of Materials Science and Engineering, Chongqing University of Technology, Chongqing 400054, China.*
* *E-mail: isono.t@eng.hokudai.ac.jp; satoh@eng.hokudai.ac.jp*
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

monomer variety for polycondensation through the so-called couple-monomer methodology (CMM), in which a condensation reaction between A–A and B–B_2 monomers (e.g., succinic anhydride and trimethylolpropane) was first carried out to produce an AB_2 intermediate, followed by polycondensation to obtain HBP.[17] Although the polycondensation approach is widely used for HBPE synthesis because of the huge variety of available monomers, the step-growth character of this approach makes it difficult to control the molecular weight and dispersity (*Đ*) of the resulting HBPEs. Moreover, the achievable molecular weight is often limited by gelation, by-product formation, and intramolecular cyclisation.

The chain-growth polymerisation approach is advantageous over the polycondensation approach as the former allows control over multibranching polymerisation, thereby providing a precise way to synthesise HBPEs. More importantly, the chain-growth approach easily affords high-molecular-weight HBPEs as it suppresses side reactions and by-product formations. For example, an HBPE was successfully synthesised by multibranching ring-opening polymerisation of a cyclic ester monomer having an alcohol moiety, such as 5-(2-hydroxyethyl)-2-oxepanone.[18] The resulting HBPEs had a high molecular weight (65,000–85,000 in weight-average molecular weight). Similarly, hydroxyl-functionalised cyclic esters such as bis(dihydroxymethyl)-*ε*-caprolactone[19,20] and 5-hydroxymethyl-1,4-dioxan-2-one[21] were also employed for HBPE synthesis via ring-opening multibranching polymerisation. An additional advantage of this approach is the ability to control the initiation end group using a nucleophile as an initiator, which leads to functionalised HBPEs and linear-hyperbranched-block copolymers. Hence, the chain-growth polymerisation approach involving ring-opening polymerisation (ROP) is extremely useful for the synthesis of HBPEs. However, a major drawback of this approach is the narrow range of applicable monomers. Such specially designed monomers often require a multi-step synthesis. Thus, it is highly desirable to establish a simple and versatile synthesis method for well-defined HBPEs via a chain-growth mechanism.

Recently, ring-opening alternating copolymerisation (ROAC) of cyclic anhydrides and epoxides has attracted much attention as a third method to access polyesters following polycondensation and ROP because it affords more advantages than them.[22–31] Polyesters obtained by ROAC have two types of monomers in the repeating unit, which allow easy construction of polymer libraries with a broad structural diversity. In addition, polyesters with functional side chains can be easily synthesised using epoxides having functional side chains. Optically active and isotactic polyesters can also be synthesised simply by employing optically pure epoxide monomers.[32,33] Moreover, owing to its chain-growth nature, precise control over ROAC can be achieved by judiciously selecting the catalytic system, leading to polyesters with predicted molecular weights and narrow dispersities. Recent years have witnessed advancements in ROAC that allow the synthesis of sequence-controlled block copolymers, which, in turn, add various functionalities to polyester materials. Our group recently reported one-pot synthesis of block polyesters through self-switching polymerisation of ROAC, followed by ROP.[34] More specifically, from the three-component monomer mixture (cyclic anhydride, epoxide, and L-lactide (LLA)), the ROAC of cyclic anhydride and epoxide first proceeds until the full anhydride conversion and subsequently the ROP of LLA occur, leading to the synthesis of block copolymer (poly(anhydride-*alt*-epoxide)-*block*-PLA) in a one-step, one-pot manner. Thus, ROAC is now recognised as a greatly useful tool for polyester synthesis because of its high versatility, diversity of monomers, and controlled/living chain-growth mechanisms.

As mentioned above, a versatile synthesis method for HBPE based on chain-growth polymerisation is required to further expand the application range of HBPEs. In this study, we propose a novel synthesis method for HBPEs using the concept of ROAC (Figure 1). ROAC gives rise to only linear polyesters because both the anhydride and epoxide monomers function as latent difunctional monomers. Thus, we selected a cyclic anhydride possessing an extra carboxyl group as the latent A_3-type monomer to produce HBPEs through ROAC. Trimellitic anhydride (TA) is the best candidate of latent A_3-type cyclic anhydride monomers; indeed, a few examples of ROACs using TA have been reported.[34–36] It was first reported by Coates *et al.*, who used TA as a chain-transfer agent to copolymerise propylene oxide and carbic anhydride and obtained an HBP with a high dispersity (*Đ* = 1.79).[28] Our group employed TA as the cyclic anhydride that can undergo self-switching polymerisation.[35,36] We showed that self-switching polymerisation performed using a mixture of TA, ethyl glycidyl ether (EGE), and LLA afforded a core–shell-type block copolymer through the ROAC of TA and EGE, followed by the ROP of LLA.[35] However, the scope of the epoxide monomer and the structural details and physical properties of the HBPEs obtained through ROAC with TA have not been fully investigated. Herein, we report a simple and versatile method for HBPE synthesis via ROAC using TA as a cyclic anhydride monomer (Scheme 1). The characterisation of the resulting polymer revealed a hyperbranched structure, confirming the successful synthesis of the HBPE via ROAC. The versatility of this approach was further demonstrated by the synthesis of HBPEs using various epoxides and alcohol initiators.

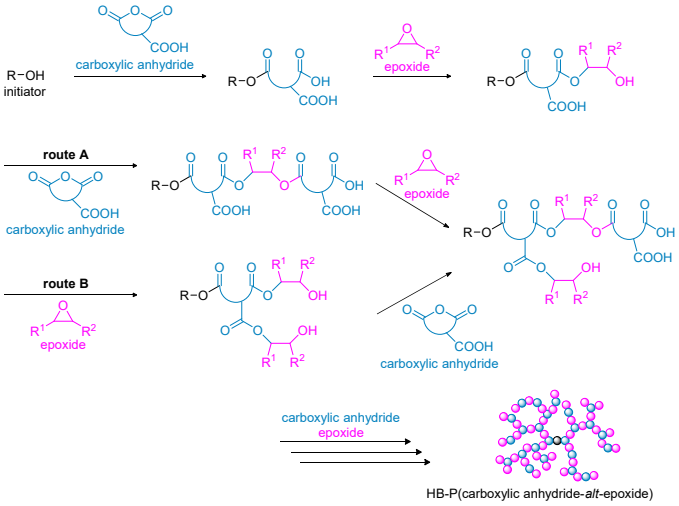
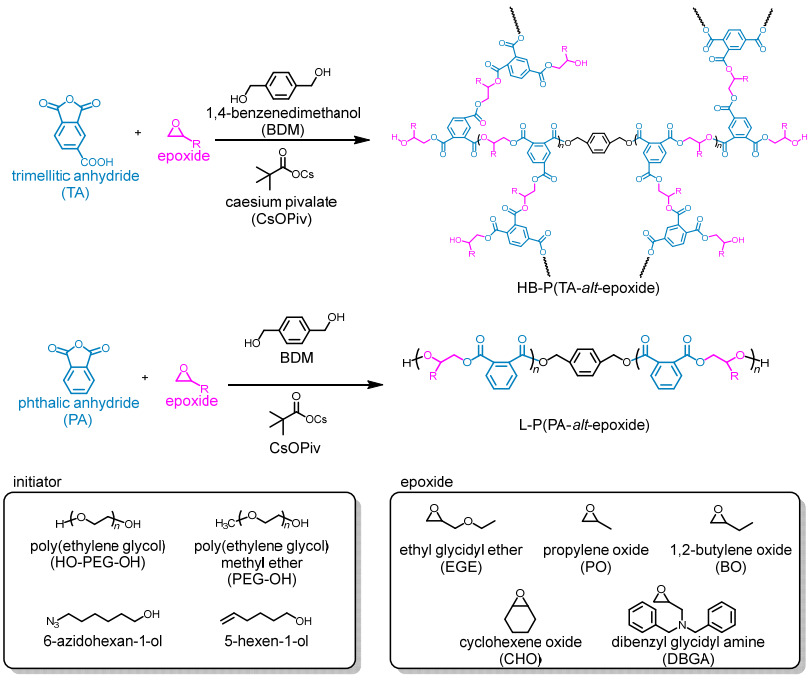


Figure 1. A new pathway to HBPE via ring-opening alternating copolymerisation of carboxylic anhydride and epoxide.

Results and discussion

First, we investigated the ROAC of TA with EGE under bulk conditions (Table 1, run 1). We employed caesium pivalate (CsOPiv) as a catalyst, as it shows sufficient catalytic ability for ROAC.[35,36] The ROAC was conducted at 80 °C in the presence of 1,4-benzenedimethanol (BDM) as an initiator at a $[CsOPiv]/[BDM]_0/[TA]_0/[EGE]_0$ molar ratio of 0.5/1/25/75. After the reaction started, the conversion of TA ($conv._{TA}$) increased and finally reached 95%, as confirmed by ^{1}H NMR analysis of the crude aliquot. This result confirmed the progress of polymerisation, even in the presence of the free carboxyl group. As the free carboxyl group on TA is also involved in the ROAC to generate a branching point, the consumption of EGE ($cons._{EGE}$) should be higher than that of $cons._{TA}$. More specifically, $cons._{EGE}$ should be twofold of $cons._{TA}$ when all the free carboxyl groups participate in ROAC. To test this hypothesis, we monitored the consumption of two monomers during polymerisation. Interestingly, $cons._{EGE}$ was always higher than that of TA, and it was eventually found to be approximately twice the amount of consumed TA (Figure 2). This result suggests that the obtained polymer had a hyperbranched structure, as expected, and most of the free carboxyl groups reacted with EGE to generate the branching point (degree of branching ≈ 1). The absolute molecular weight ($M_{n,MALS}$) and dispersity ($Đ$) of the obtained hyperbranched poly(TA-*alt*-EGE) (HB-P(TA-*alt*-EGE)) were determined to be 16,900 g mol^{-1} and 1.11, respectively, using a triple-detection SEC equipped with refractive index, light scattering, and viscosity detectors (SEC-MALS-VISCO). Since the obtained products possess highly branched, the standard SEC analysis against linear polystyrene standards did not provide any meaningful information about the molecular weight. Note that the observed $M_{n,MALS}$ is much greater than the theoretical molecular weight ($M_{n,theo.}$) calculated based on the initial monomer-to-initiator ratio and $conv._{TA}$. This result implies that the intermolecular coupling should occur along with the propagation reaction.



Scheme 1. Synthesis of HBPE and linear polyester via ROAC of cyclic anhydrides and various epoxides.

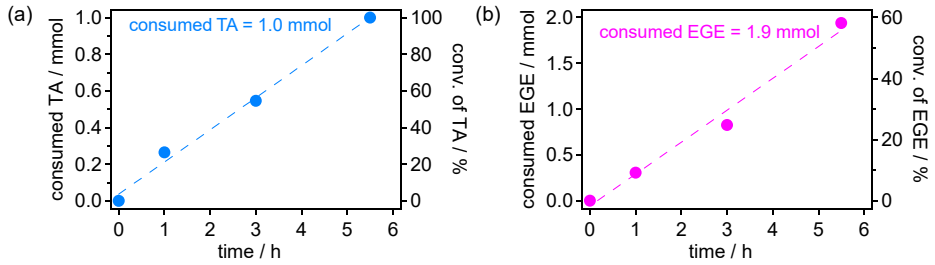


Figure 2. Plots of monomer consumption vs time for (a) TA and (b) EGE as monitored by ^{1}H NMR spectroscopy.

Table 1. Synthesis of hyperbranched polyesters via ROAC of TA with various epoxides [a]

run	initiator	epoxide	time / h	conv.$_{TA}$ / % [b]	$M_{n,theo.}$ [c]	$M_{n,MALS}$ [d]	$M_{w,MALS}$ [d]	$Đ$ [d]	[η] / mL min^{-1} [d]	T_g / °C [e]
1	BDM	EGE	5.5	95	9,600	16,900	18,700	1.11	3.07	−20.1
2	HO-PEG-OH	EGE	1.5	>99	9,300	36,010	37,600	1.05	2.99	- [f]
3	MeO-PEG-OH	EGE	2.0	77	9,200	46,500	49,200	1.06	1.17	- [f]
4	6-azidohexan-1-ol	EGE	2.0	72	6,300	24,000	28,900	1.20	2.61	- [f]
5	5-hexen-1-ol	EGE	9.0	>99	11,000	10,900	14,000	1.28	1.91	- [f]
6	BDM	PO	4.0	87	6,800	24,300	31,600	1.30	4.42	30.3
7	BDM	BO	4.0	>99	8,500	28,500	34,500	1.21	3.54	−1.8
8	BDM	CHO	2.0	- [f]	- [f]	98,600	156,000	1.58	2.00	0.1
9	BDM	DBGA	5.3	>99	14,000	134,000	224,000	1.68	2.11	70.0

[a] Polymerisation conditions: [CsOPiv]/[BDM]$_0$/[TA]$_0$/[epoxide]$_0$ = 0.5/1/25/75; atmosphere, Ar; temperature, 80 °C. [b] Determined by ^{1}H NMR spectroscopy in $CDCl_3$. [c] Calculated from (M.W. of BDM) + [TA]$_0$/[BDM]$_0$ × (M.W. of TA) × (conv. of TA) + [epoxide]$_0$/[BDM]$_0$ × (M.W. of epoxide) × (conv. of epoxide). [d] Determined by SEC-MALS-VISCO measurements in $CHCl_3$. [e] Measured by DSC. [f] Not determined.

To characterise the polymer structure in detail, we prepared the corresponding linear polyesters and homopolymers of EGE as reference for NMR analysis. According to a previous report,[35] the ROAC of phthalic anhydride (PA) and EGE using a BDM initiator and CsOPiv catalyst successfully produced the corresponding linear polyester, that is, linear-poly(PA-*alt*-EGE) (L-P(PA-*alt*-EGE); $M_{n,MALS}$ = 8,000, $Đ$ = 1.06; run 1, Table S1). CsOPiv-catalysed ROP of EGE was carried out at 100 °C to prepare the related homopolymer, poly(EGE) (PEGE; $M_{n,NMR}$ = 6,000). Overlay of ^{1}H and ^{13}C NMR spectra of these three polymers is shown in Figure 3.

The ^{1}H NMR spectrum of L-P(PA-*alt*-EGE) shows characteristic peaks owing to the benzene ring (7.42–7.85 ppm), polyester main chain (-CH_2CH- (*b′*), 5.37–5.73 ppm; -CH_2CH- (*a′*), 4.44–4.92 ppm), and EGE side chain (-$CH_2OCH_2CH_3$ (*c′, d′*), 3.39–3.86 ppm; -$CH_2OCH_2CH_3$ (*e′*), 1.09–1.33 ppm), which agreed with the previously reported data.[35] According to previous reports, alternating polyesters synthesised by ROAC in the presence of excess epoxide over cyclic anhydride are known to possess hydroxyl terminal groups. Indeed, the methine proton adjacent to the terminal hydroxyl group was confirmed as a weak signal at 4.0 ppm (b_T′). Comparing this spectrum with that of HB-P(TA-*alt*-EGE), the signals at 5.15–5.75 and 4.23–4.89 ppm observed in the latter could be reasonably assigned to the polyester main chain protons *b* and *a*, respectively. The aromatic signals in the HB-P(TA-*alt*-EGE) spectra appeared as three peaks on the downfield side (7.29–8.75 ppm) compared to that in the L-P(TA-*alt*-EGE) spectrum (7.42–7.85 ppm). The additional carbonyl group led to a downfield shift of the phenyl protons. In addition, it led to desymmetrisation of the benzene ring, which explains the splitting of its peak into three different peaks. Similarly, the signals at approximately 3.30–4.02 and 0.99–1.26 ppm can be assigned to the side-chain protons (*c*–*e*). These results suggest that HB-P(TA-*alt*-EGE) and L-P(TA-*alt*-EGE) share the same repeating unit.

Notably, the NMR signals of HB-P(TA-*alt*-EGE) are much broader than those of L-P(TA-*alt*-EGE), owing to the lower structural regularity originating from the asymmetric nature of the TA unit.[1] Here, we conducted a model reaction of TA with alcohol to investigate the regioselectivity in the cyclic anhydride ring-opening. 2-Propanol was selected as the substrate to simulate the secondary alcohol nature of the growing chain end derived from the epoxide. The model reaction was carried out in the presence of CsOPiv at 80 °C ([CsOPiv]/[TA]$_0$/[2-propanol]$_0$ = 1/5/15). After 2 h, TA was quantitatively consumed, and the ^{1}H NMR spectrum of the resulting mixture revealed the formation of two regioisomeric monoesters with 60:40 ratio. This result demonstrated the absence of any significant regioselectivity in the ring-opening of the TA monomer (Figure S2). Additionally, the reactivity of the anhydride and carboxy moieties in TA was investigated. Thus, we conducted the following two model reactions: (a) 2-propanol +PA and (b) 2-propanol + benzoic acid (BA) in the presence of CsOPiv with the feed ratio of [CsOPiv]/[PA or BA]$_0$/[2-propanol]$_0$ being 0.5/5/15. After 90 min, 30.4% of PA was reacted with 2-propanol in model reaction (a) to produce the corresponding monoester, whereas no reaction was observed in reaction (b) (Figure S3). This observation

demonstrates that the alcohol initiator/growing hydroxy chain end first reacts with the anhydride moiety of TA and subsequently the carboxy groups react with the epoxide monomer. More importantly, a broad signal was confirmed at approximately 4 ppm (b_T), which was observed in the same range as the b_T' of L-P(PA-*alt*-EGE). Although it was difficult to quantify the signal intensity because of the overlap with the neighbouring signals, the signal intensity of b_T was much higher than that expected for the product without branching.

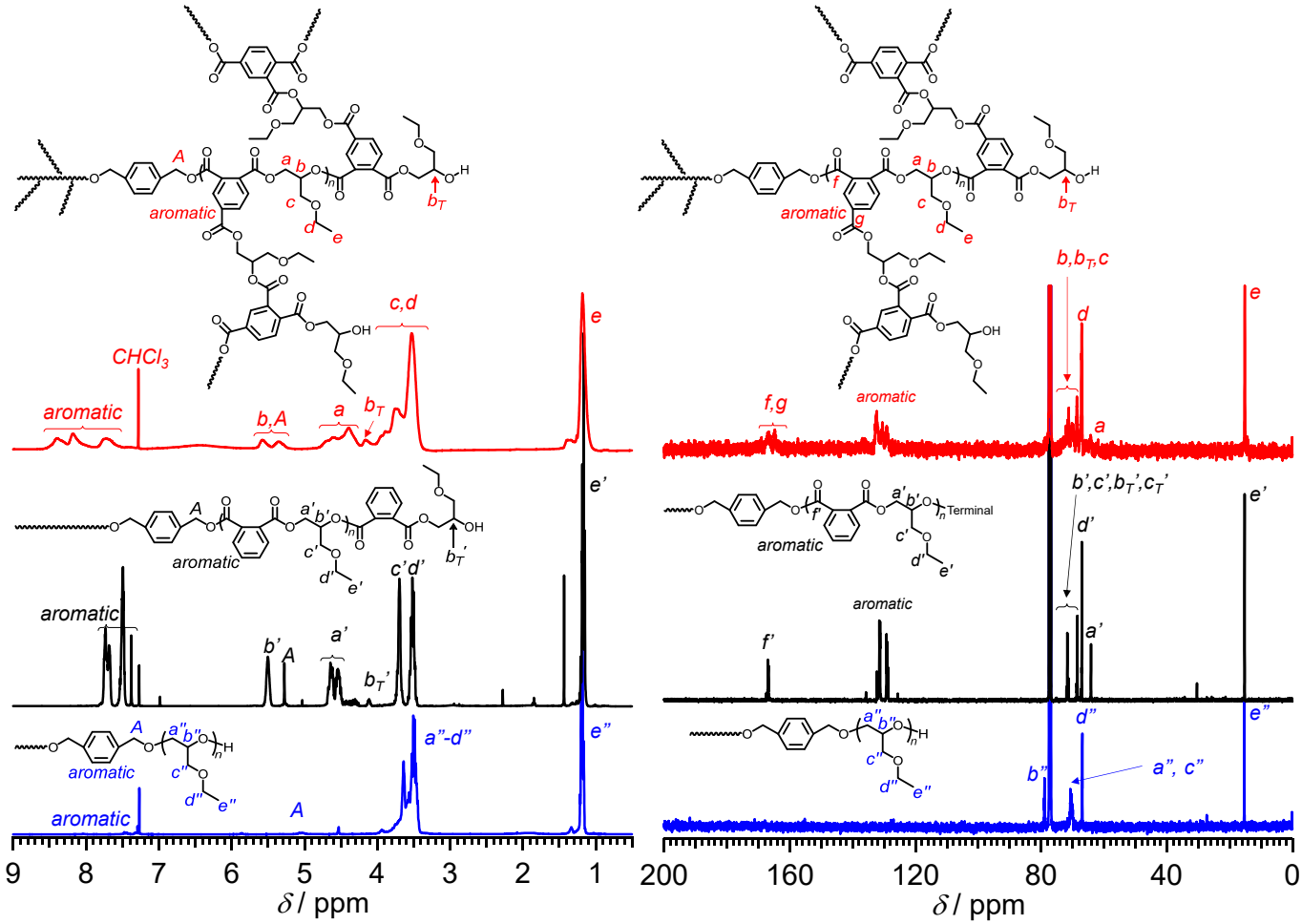


Figure 3. ^{1}H (400 MHz; left panel) and ^{13}C NMR (100 MHz; right panel) spectra of PEGE (blue), L-P(PA-*alt*-EGE) (black), and HB-P(TA-*alt*-EGE) (red) in $CDCl_3$.

This observation proves the presence of multiple polymer chain ends resulting from the multibranching structure.

Similar to the ^{1}H NMR spectra, the ^{13}C NMR spectra of HB-P(PA-*alt*-EGE) was analogous to that of L-P(PA-*alt*-EGE), such as carbonyl signals (164–168 ppm, *f, g*), main chain (benzene ring, 128–133 ppm; -CH_2CH- (*b, b_T*), 68.0–71.0 ppm; -CH_2CH- (a), 64.3 ppm), and side chain (-CH_2O- (*c*), 71.0–72.3 ppm; -OCH_2CH$_3$ (*d*), 67.5 ppm; -OCH$_2$CH_3 (*e*), 15.1 ppm). It is worthwhile to compare the ^{13}C NMR spectra of HB-P(PA-*alt*-EGE) and PEGE to exclude the possibility of epoxide homopolymerisation during ROAC. Therefore, one could expect that ROP may also proceed in addition to the ROAC of anhydride and epoxide in the current polymerisation system. The ^{13}C NMR spectrum of PEGE shows a characteristic signal at 79.0 ppm because of the main-chain methine (*b''*), which can be used as a proof to determine whether ROP occurred concomitantly during ROAC. A closer look at approximately 80 ppm showed the absence of any signal for HB-P(PA-*alt*-EGE). This result unambiguously demonstrated that the ROP of EGE did not occur, and all the consumed EGE monomers were incorporated in the form of polyesters.

In the present polymerisation system, three routes are expected as the initiation pathway: the initiation from the alcohol initiator, initiation from pivalate, and initiation from the carboxyl group of TA. In our previous paper, we have confirmed that the carboxylate does not initiate the ROAC of cyclic anhydride and epoxide in the presence of an alcohol initiator. In contrast, Luo found that alkali metal carboxylates can work as a non-alcohol initiator for the ROAC.[37] If pivalate could also be used as an initiator in the present system, it may complicate the structure of the HBPEs. To intentionally synthesise HB-P(TA-*alt*-EGE) containing a pivalate end group, we conducted the ROAC of TA and EGE without an alcohol initiator and with the increased CsOPiv ratio. As expected, the ^{13}C NMR spectrum of the product showed a characteristic signal owing to the presence of the pivalate group (26.8 ppm, a; 32.2 ppm b; Figure S5). However, no such signal appeared in the spectrum of the

HB-P(TA-*alt*-EGE) obtained from run 1 in Table 1. Therefore, the HBPEs synthesised by our optimised condition are virtually free from the pivalate moiety. Next, we conducted the model reaction to check whether TA can also work as an initiator. The model reaction of BA with three equivalents of EGE in the presence of CsOPiv indeed proceeded (10.5% conversion of BA in 90 min at 80 °C), which supported the initiation from TA, producing TA-epoxide adduct (**2**) in Figure S6.

Based on the above discussions, we propose the reaction mechanism to form HBPEs (Figure S6). The initiation reaction involves two routes. The first route involves the addition reaction of the alcohol initiator to TA and subsequent ring-opening reaction of epoxide, producing the initiator-TA-epoxide adduct (**1**). The second route is the ring-opening reaction of epoxide from the carboxyl group of TA to form TA-epoxide adduct (**2**). In the propagation reaction, the alkoxide species, such as **1** and **2**, react with TA and subsequently EGE, resulting in the formation of HBPEs (**3** and **4**). The unreacted anhydride moiety in **3** will be consumed when reacting with the alkoxide species, which finally produces the HBPEs with an initiator residue.

HBP is well known to exhibit lower viscosity, higher solubility, and a smaller hydrodynamic radius than those of their linear counterparts. To identify the specific properties originating from the hyperbranched structure, we measured and compared the intrinsic viscosity ([η]) and hydrodynamic radius (R_h) of HB-P(TA-*alt*-EGE) and L-P(PA-*alt*-EGE) (Figure 4). The Mark–Houwink–Sakurada plots revealed that the [η] of HB-P(TA-*alt*-EGE) was apparently lower than that of L-P(PA-*alt*-EGE) within the same molecular weight range. The R_h conformation plots also revealed the smaller R_h of HB-P(TA-*alt*-EGE) than that of L-P(PA-*alt*-EGE). These results confirmed that HB-P(TA-*alt*-EGE) exhibits a smaller molecular dimension than that of L-P(PA-*alt*-EGE) with a comparable molecular weight. Based on NMR and solution property analyses, we concluded that HB-P(TA-*alt*-EGE) possesses a truly hyperbranched structure. Thus, the ROAC of TA and epoxide is an efficient and convenient means of synthesising HBPEs.

To expand the synthetic utility of this method, ROACs of TA and EGE were carried out in the presence of various functional alcohol initiators such as bifunctional poly(ethylene glycol) (HO-PEG-OH), mono-functional PEG (PEG-OH), 6-azidohexan-1-ol, and 5-hexen-1-ol under established conditions ([CsOPiv]/[initiator]$_0$/[TA]$_0$/[EGE]$_0$ = 0.5/1/25/75 at 80 °C). When HO-PEG-OH and MeO-PEG-OH were used as the initiator, the obtained products clearly showed the signals owing to the methylene protons of the PEG backbone in their ^{1}H NMR spectra (runs 2 and 3, Table 1; Figures S7 and S8). These initiators are useful for one-step reactions that synthesise block copolymers such as dendritic-*b*-linear-*b*-dendritic and linear-*b*-dendritic block copolymers consisting of HB-P(TA-*alt*-EGE) and PEG blocks. These block copolymers may find interesting biomedical applications owing to their amphiphilic nature.[38] Subsequently, alcohol initiators with azido and olefin groups were employed for the ROAC of TA and EGE (runs 4 and 5, Table 1). The ^{1}H NMR spectrum of the product obtained from run 4 showed the signals owing to the methylene protons of the initiator (1.60–2.00, 2.60, and 4.00 ppm; Figure S9). Moreover, the FT-IR spectrum showed a characteristic absorption peak at approximately 2100 cm^{-1}, confirming the presence of the azido group (Figure S10). In the ^{1}H NMR spectrum of the product obtained from run 5, the characteristic signals owing to the olefinic protons were observed at 1.40, 1,61, 1.77, 1.97, 2.63, and 3.95 ppm, supporting the successful installation of the reactive functional groups (Figure S11). These functional groups are useful for further functionalisation via azido-alkyne and thiol-ene click chemistry. These results demonstrated successful synthesis of functional HBPEs and HBPE-based block copolymers consisting of HBPE and PEG segments via ROAC with TA.

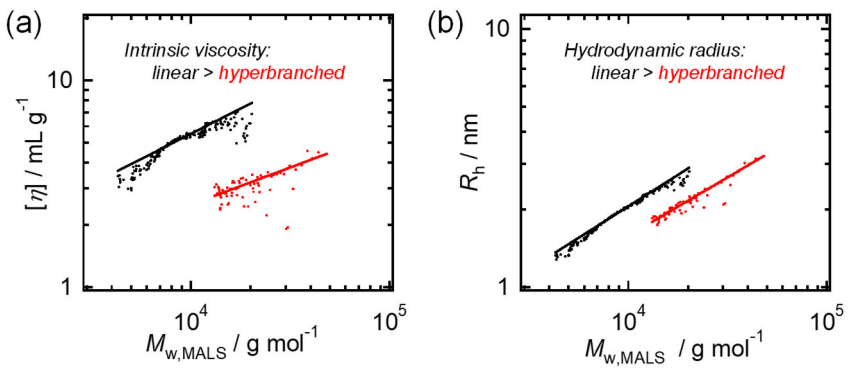


Figure 4. (a) Mark–Houwink–Sakurada plots and (b) conformation plots for HB-P(TA-*alt*-EGE) ($M_{n,MALS}$ = 16,900 g mol^{-1}, red) and L-P(PA-*alt*-EGE) ($M_{n,MALS}$ = 8,000 g mol^{-1}, black).

Next, we investigated the scope of applicable epoxide monomers. The monosubstituted epoxides propylene oxide (PO) and 1,2-butylene oxide (BO) were used under the optimised polymerisation conditions, yielding HB-P(TA-*alt*-PO) and HB-P(TA-*alt*-BO), respectively (runs 6 and 7, Table 1; Figures S12–S13). The obtained HBPEs were characterised by ^{1}H NMR. These spectra showed the signals resulting from alkyl side chains (run 6, 0.68–1.53 (-C*H*$_3$); run 7, 1.36–1.96 (-C*H*$_2$CH$_3$) and 0.77–1.11 (-

CH_2CH_3)). These polymers showed sufficient molecular weights ($M_{n,MALS}$ = 24,300 and 28,500) with relatively narrow *Đ* (*Đ* = 1.30 and 1.21). We also employed cyclohexene oxide (CHO) as a representative example of disubstituted epoxides (run 8, Table 1). The ^{1}H NMR spectrum showed the characteristic signals resulting from the cyclohexyl moiety at 0.80–2.50 ppm (*b* and *c* in Figure S14) and methine group adjacent to the terminal hydroxy group (a_T), which confirmed that the ROAC of TA and CHO also proceeded in a multibranching polymerisation manner to produce HB-P(TA-*alt*-CHO). Finally, we tested *N,N*-dibenzyl glycidyl amine (DBGA) as a representative example of glycidyl amines. The ROAC of TA and DBGA gives rise to HBP with tertiary amino groups along the polymer backbone. These polymers are quite interesting for application as non-viral vectors for gene transfection.[39] After copolymerisation of DBGA and TA for 5.3 h, the ^{1}H NMR spectrum showed aromatic (6.71–7.39 ppm) and methylene signals (-CH_2Ph, 2.37–4.72 ppm; -CH_2NBn_2, 0.73–1.55 ppm) owing to the DBGA unit, which confirmed that ROAC proceeded and formed HB-P(TA-*alt*-DBGA) with a high molecular weight ($M_{n,MALS}$ = 134,000 g mol^{-1}; run 9, Table 1; Figure S15). To verify the hyperbranched structures for HB-P(PA-*alt*-PO), HB-P(PA-*alt*-BO), HB-P(PA-*alt*-CHO), and HB-P(PA-*alt*-DBGA), we prepared the corresponding linear polyesters (i.e., L-P(PA-*alt*-PO), L-P(PA-*alt*-BO), L-P(PA-*alt*-CHO), and L-P(PA-*alt*-DBGA)) by the ROAC using PA instead of TA (runs 2–5, Table S1; Figures S16–S19) and compared their SEC-MALS-VISCO data against those of the corresponding HBPEs (Figures S20–S23). The HBPEs showed smaller [η] and R_h values than those of their linear counterparts. These results demonstrate that a wide range of epoxide monomers can be used for ROAC with TA, supporting the versatility of this approach.

Next, the thermal properties of the HBPEs were evaluated using differential scanning calorimetry (DSC). The HBPEs showed no transition because of crystallisation and melting; only a glass transition temperature (T_g) was observed (Table 1; Figures 5(a), S24–27). The T_g value varied from −20.1 to 70.0 °C, depending on the structure of the epoxide monomer. Notably, HB-P(TA-*alt*-DBGA) showed the highest T_g among the HBPEs because of the presence of two benzene side chains on the polyester side chain. Generally, the T_g of hyperbranched polymers is known to be lower than that of their corresponding linear counterparts owing to the increased number of highly mobile chain ends in the former.[40] Indeed, a comparison of the T_g values of HBPEs and their corresponding linear counterparts showed that HB-P(PA-*alt*-EGE), HB-P(PA-*alt*-BO), and HB-P(PA-*alt*-CHO) followed this rule. However, HB-P(TA-*alt*-PO) and HB-P(TA-*alt*-DBGA) exhibited higher T_g than those of the corresponding linear polyesters. To explain the higher T_g of these HBPEs, other factors such as molecular weight, end group, and intrinsic chemical composition need to be taken into account. Indeed, previous literatures found that these factors also affect the T_g of HBPs. The increased T_g of HB-P(TA-*alt*-PO) compared to that of its linear counterpart can be explained by the contribution from the end group; polar end group is known to increase the T_g of HBPs.[41] It is known that the end group of the polyester obtained via ROAC mainly consists of carboxyl group when the anhydride is not fully consumed.[42] When synthesising HB-P(TA-*alt*-PO), the conv.$_{TA}$ was 87%. Therefore, the end group is supposed to be mainly consisted of the carboxyl group, which is the main reason for the increased T_g. This result can also explain the large difference in the T_g values of HB-P(TA-*alt*-PO) and HB-P(TA-*alt*-BO). In contrast, the increased T_g of HB-P(TA-*alt*-DBGA) could be explained by its higher molecular weight compared to that of the liner counterpart. In addition, the densely attached benzene ring around the branching unit presumably restricts the chain motion, which might also contribute to increased T_g.

Hence, based on these results, it can be suggested that the proposed method is an excellent strategy for synthesising HBPEs with various thermal properties by simply changing the epoxide monomer.

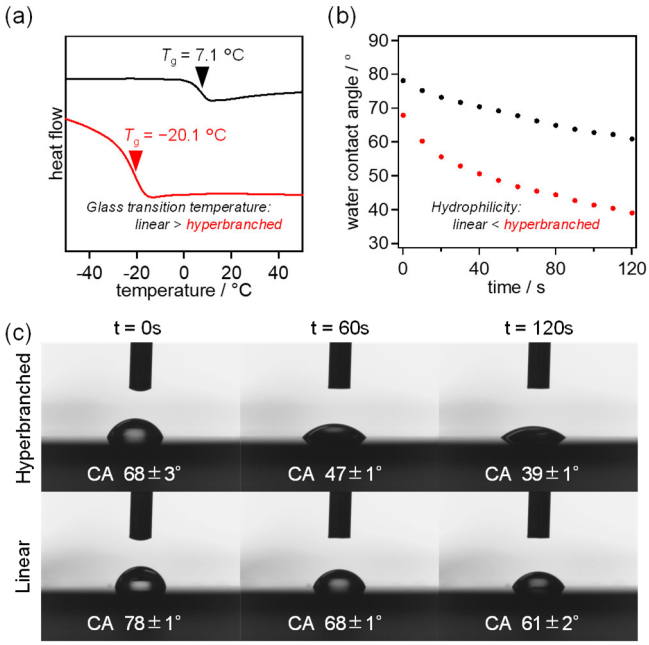


Figure 5. (a) DSC curve of HB-P(TA-*alt*-EGE) (red) and L-P(PA-*alt*-EGE) (black). (b) Contact angle versus time measurements of HB-P(TA-*alt*-EGE) (red) and L-P(PA-*alt*-EGE) (black). (c) Images used in the contact-angle analysis of HB-P(TA-*alt*-EGE) (upper) and L-P(PA-*alt*-EGE) (lower).

Finally, water contact angle (WCA) measurements were performed on the thin films of HBPE and its linear counterpart to further explore the characteristic properties stemming from the hyperbranched structure. Thin films were prepared by spin-coating the polymer solution in $CHCl_3$ onto a silicone substrate. The film thickness was in the range of 26–110 nm, as determined by reflectometry. As shown in Figures 5(b,c) and S28–S31, the WCA of the HBPEs was always smaller than that of their linear counterparts, indicating that the hydrophilicity of the HBPEs was higher than that of their linear counterparts because of the presence of a large number of hydroxyl terminal groups. Additionally, these HBPEs are intrinsically much more hydrophilic than their linear counterparts because of the repeating units of the former contain tricarboxylate moieties. Such higher hydrophilicity of the HBPEs is of interesting for their application as a coating material.

Conclusions

We successfully demonstrated the caesium pivalate-catalysed ROAC of TA with various epoxides in the presence of an alcohol initiator, leading to the formation of HBPEs. This is the first systematic study of the synthesis of HBPE based on ROAC. The HBPEs obtained via ROAC showed lower viscosity, smaller hydrodynamic radius, and higher hydrophobicity than those of their linear counterparts. By judiciously choosing anhydride and epoxide monomers and the alcohol initiator, the present approach can afford a variety of HBPEs with different backbone structures and architects, which will eventually allow design HBPEs with the desired properties and functions. Considering its versatility and simplicity, this approach may find broader use in the development of HBPE materials for additive, coating, and biomedical applications.

Author Contributions

Ryota Suzuki: Investigation, Methodology, Writing - original draft, Visualisation. **Xiaochao Xia:** Investigation, Methodology. **Tianle Gao:** Investigation, Methodology. **Takuya Yamamoto:** Investigation, Supervision. **Kenji Tajima:** Investigation, Supervision. **Takuya Isono:** Investigation, Supervision, Writing - review & editing, Funding acquisition. **Toshifumi Satoh:** Conceptualization, Writing - review & editing, Supervision, Project administration, Funding acquisition.

Conflicts of interest

There are no conflicts to declare

Acknowledgements

This work was financially supported by a Japan Society for the Promotion of Science Grant-in-Aid for Scientific Research (B) (Grant Number 19H02769); Ministry of Education, Culture, Sports, Science, and Technology of Japan Grants-in-Aid for Scientific Research on Innovative Areas (Hybrid Catalysis for Enabling Molecular Synthesis on Demand; Grant Numbers 18H04639 and 20H04798); the Inamori Foundation; the Frontier Chemistry Center (Hokkaido University); the Photo-excitonic Project (Hokkaido University); the Creative Research Institution (CRIS, Hokkaido University); and the Project of Junior Scientist Promotion in Hokkaido University.

Notes and references

1 C. Gao and D. Yan, *Prog. Polym. Sci.*, 2004, **29**, 183–275.

2 M. Jikei and M. Kakimoto, *Prog. Polym. Sci.*, 2001, **26**,1233–1285.

3 P. Zhao, F. Mecozzi, S. Wessel, B. Fieten, M. Driesse, W. Woudstra, H. J. Busscher, H. C. van der Mei and T. J. A. Loontjens, *Langmuir*, 2019, **35**, 5779–5786.

4 E. Murillo and B. López, *Polimeros*, 2016, **26**, 343–351.

5 R. Hobzová, J. Peter and P. Sysel, *J. Macromol. Sci. C,* 2006, **102**, 906–913.

6 L. Xu and Z. Ye, *Chem. Commun. (Camb)*, 2013, **49**, 8800–8802.

7 L. J. Ma, H. Q. Wang, L. F. He and X. Y. Li, *Chin. J. Polym. Sci.,* 2011, **29**, 300–307.

8 J. Pan, L. Mei, H. Zhou, C. Zhang, Q. Xie and C. Ma, *Prog. Org. Coat.*, 2022, **163**, 106674.

9 S. E. Stiriba, H. Frey and R. Haag, *Angew. Chem. Int. Ed.*, 2002, **41**, 1329–1334.

10 S. Son, E. Shin and B.-S. Kim, *Macromolecules*, 2015, **48**, 600–609.

11 V. T. Wyatt, A. Nuñez, T. A. Foglia and W. N. Marmer, *J. Am. Oil Chem. Soc.*, 2006, **83**, 1033–1039.

12 X. Gao, X. Zhang, Z. Wu, X. Zhang, Z. Wang and C. Li, *J. Control. Release*, 2009, **140**, 141–147.

13 R. H. Kienle and A. G. Hovey, *J. Am. Chem. Soc.*, 1929, **51**, 509–519.

14 X. Zhang, *Journal of Macromolecular Science Part A*, 2010, **48**, 128–134.

15 R. H. Kienle, P.A. van der. Meulen and F. E. Petke, *J. Am. Chem. Soc.*, 1939, **61**, 2258–2268.

16 S. R. Turner, B. I. Voit and T. H. Mourey, *Macromolecules*, 1993, **26**, 4617–4623.

17 D. Yan and C. Gao, *Macromolecules*, 2000, **33**, 7693–7699.

18 M. Liu, N. Vladimirov and J. M. J. Fréchet, *Macromolecules*, 1999, **32**, 6881–6884.

19 M. Trollsås, P. Löwenhielm, V. Y. Lee, M. Möller, R. D. Miller and J. L. Hedrick, *Macromolecules*, 1999, **32**, 9062–9066.

20 X. H. Yu, J. Feng and R. X. Zhuo, *Macromolecules*, 2005, **38**, 6244–6247.

21 P. G. Parzuchowski, M. Grabowska, M. Tryznowski and G. Rokicki, *Macromolecules*, 2006, **39**, 7181–7186.

22 J. M. Longo, M. J. Sanford and G. W. Coates, *Chem. Rev.*, 2016, **116**, 15167–15197.

23 S. Paul, Y. Zhu, C. Romain, R. Brooks, P. K. Saini and C. K. Williams, *Chem. Commun. (Camb)*, 2015, **51**, 6459–6479.

24 B. Han, L. Zhang, B. Liu, X. Dong, I. Kim, Z. Duan and P. Theato, *Macromolecules*, 2015, **48**, 3431–3437.

25 R. C. Jeske, A. M. DiCiccio, and G. W. Coates, *J. Am. Chem. Soc.*, 2007, **129**, 11330–11331.

26 H.-Y. Ji, X.-L. Chen, B. Wang, L. Pan, and Y. S. Li, *Green Chem.*, 2018, **20**, 3963–3973.

27 J. Xu, X. Wang and N. Hadjichristidis, *Nat. Commun.*, 2021, **12**, 7124.

28 L. Hu, X. Zhang, X. Cao, D. Chen, Y. Sun, C. Zhang, and X. Zhang, *Macromolecules*, 2021, **54**, 6182–6190.

29 W. T. Diment, G. L. Gregory, R. W. F. Kerr, A. Phanopoulos, A. Buchard, and C. K. Williams, *ACS Catal.*, 2021, **11**, 12532–12542.

30 X. Liang, F. Tan, and Y. Zhu, *Front. Chem.*, 2021, **9**, 647245.

31 G.-H. He, B.-H. Ren, S.-Y. Chen, Y. Liu, X.-B. Lu, *Angew. Chem. Int. Ed.*, 2021, **60**, 5994–6002.

32 J. Li, Y. Liu, W.-M. Ren, and X.-B. Lu, *J. Am. Chem. Soc.*, 2016, **138**, 11493–11496.

33 J. M. Longo, A. M. DiCiccio and G. W. Coates, *J. Am. Chem. Soc.*, 2014, **136**, 15897–15900

34 C. A. L. Lidston, B. A. Abel and G. W. Coates, *J. Am. Chem. Soc.*, 2020, **142**, 20161–20169.

35 X. Xia, R. Suzuki, K. Takojima, D. H. Jiang, T. Isono and T. Satoh, *ACS Catal.*, 2021, **11**, 5999–6009.

36 X. Xia, R. Suzuki, T. Gao, T. Isono and T. Satoh, *Nat. Commun.*, 2022, **13**, 163.

37 C.-M. Chen, X. Xu, H.-Y. Ji, B. Wang, L. Pan, Y. Luo, and Y.-S. Li, *Macromolecules*, **54**, 713–724.

38 J. K. Oh, *Soft Matter*, 2011, **7**, 5096–5108.

39 T. Isono, S. Asai, Y. Satoh, T. Takaoka, K. Tajima, T. Kakuchi and T. Satoh, *Macromolecules*, 2015, **48**, 3217–3229.

40 G. C. Behera, A. Saha and S. Ramakrishnan, *Macromolecules*, 2005, **38**, 7695–7701.

41 A. Hult, M. Johansson and E. Malmström, *Branched Polym.*, 1999, **II**, 1–34.

42 H. Li, J. Zhao, and G. Zhang, *ACS Macro Lett.*, 2017, **6**, 1094–1098.