



# Free Radical Polymerization of Dimethyl Amino Ethyl Methacrylate Initiated by Poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) Macroazo Initiator: Thermal and Physicochemical Characterization

Baki Hazer<sup>1,2</sup> · Tina Modjinou<sup>3</sup> · Valérie Langlois<sup>3</sup> · Melahat Göktaş<sup>4</sup> · Fulya Taşçı<sup>5</sup> · Richard D. Ashby<sup>6</sup> · Baozhong Zhang<sup>7</sup>

Accepted: 27 March 2023 / Published online: 7 April 2023

© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2023

## Abstract

A novel macro intermediate based on poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) (PHBHHx) was synthesized for use in the copolymerization with dimethyl amino ethyl methacrylate (DMAEMA). Methyl amino ethanol was reacted with PHBHHx to prepare a dihydroxy terminated polyester. The hydroxyl ends of the obtained PHBHHx derivatives were capped with 4,4'-azobis cyanopentanoic acid to obtain the PHBHHx macroazo initiator (PHBHHx-AI) for free radical copolymerization of DMAEMA at 70°C. A steady increase in DMAEMA units in the synthesized block copolymer as a function of time was observed. The overall rate constants for the free radical polymerization of DMAEMA initiated by PHBHHx-AI was  $k = 2.33 \times 10^{-4} \text{ Lmol}^{-1}\text{s}^{-1}$ . Block copolymers were characterized using the <sup>1</sup>H NMR, FTIR, DSC and TGA techniques.

**Keywords** Poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) · Macroazo initiator · Dimethyl amino ethyl methacrylate · Polymerization kinetics

Disclaimer: Mention of trade names or commercial products in this article is solely for the purpose of providing specific information and does not imply recommendation or endorsement by the U.S. Department of Agriculture (USDA). USDA is an equal opportunity provider and employer.

✉ Baki Hazer  
bhazer2@yahoo.com

✉ Melahat Göktaş  
melahat\_36@hotmail.com

<sup>1</sup> Department of Aircraft Airframe Engine Maintenance, Kapadokya University, 50420 Ürgüp, Nevşehir, Turkey

<sup>2</sup> Department of Chemistry, Zonguldak Bülent Ecevit University, 67100 Zonguldak, Turkey

<sup>3</sup> CNRS, Inst Chim & Mat Paris Est, UMR 7182, 2-8 Rue Henri Dunant, University of Paris Est, F-94320 Thiais, France

<sup>4</sup> Department of Science Education, Van Yüzüncü Yıl University, Van 65100, Turkey

<sup>5</sup> Fac Vet Med, Dept Food Hyg & Technol, Burdur Mehmet Akif Ersoy Univ, Istiklal Campus, 15030 Burdur, Turkey

<sup>6</sup> United States Department of Agriculture, Agricultural Research Service, Eastern Regional Research Center, 600 East Mermaid Lane, Wyndmoor, PA 19038, USA

<sup>7</sup> Center for Analysis and Synthesis, Dept Chem, Lund University, S-22100 Lund, Sweden

## Introduction

Owing to the evolving plastic disposal problem, modern technology is in constant need of new, environmentally friendly polymeric materials with varying properties over those demonstrated by many homopolymers. Block copolymers combine two or more polymer segments into a main chain that reflect the thermal, mechanical and physicochemical properties of each related segment [1, 2]. In many polymerization methods, macro initiators are used to synthesize block (or block/graft) copolymers [3–10]. Free radical macroinitiators are frequently prepared from macromolecules containing azo and/or peroxide groups. Typically, 2,2'-azobis cyanopentanoyl chloride is reacted with the hydroxyl termini of the polymers (e.g., polyethylene glycol (PEG), polytetrahydrofuran diol, poly(dimethyl siloxane) diol and polycaprolactone diol) to produce macroazo initiators that can be used in the synthetic process [11–18]. Another type of macroazo initiator involves the reaction of PEG with 2,2'-azobis isobutyronitrile under dry hydrogen chloride to produce a PEG-azo ester [19, 20].

Anionic polymerization has garnered a significant role in the synthesis of well-defined polymers. This technique allows excellent molecular weight control by regulating the ratios of monomer and initiator throughout the polymerization process [21–24]. Recent progress in controlled/living radical polymerization (CLRP) has provided a powerful tool for the controlled synthesis of well-defined polymers. CLRP covers a myriad of polymerization techniques including nitroxide-mediated radical polymerization (NMP) [25–27], atom transfer radical polymerization (ATRP) [28–31], and reversible addition fragmentation chain transfer (RAFT) polymerization [32–40], among others.

Biopolymers are gaining importance for biomedical and industrial applications in view of their biorenewability, biodegradability and other environmental benefits. Among the known biopolymers, microbial polyesters can be obtained from bacteria when grown on renewable resources such as sugar, and/or aliphatic carboxylic acids under favorable growth conditions. Poly(3-hydroxyalkanoate)s, (PHA)s, are accumulated in bacterial cells as a result of a metabolic stress causing unbalanced growth due to a limited supply of an essential nutrient and an excess of utilizable carbon. These polymers are promising materials for many different applications due to their biocompatibility and biodegradability [41–49]. Improvements in the mechanical, thermal, and hydrophilic properties of PHA biopolymers have been previously reported [50–63]. One interesting class of PHA with enhanced mechanical properties is the copolymer composed of 3-hydroxybutyric acid (3HB) and 3-hydroxyhexanoic acid (3HHx). 3HHx-containing PHA copolymers are typically prepared by bacterial fermentation using bacteria

such as wild-type *Aeromonas hydrophila*, and *Pseudomonas* species resulting in copolymers with 3HHx units comprising as much as 12% of the total polymer composition [64–66]. By varying the amount of 3HHx subunits within the mature copolymer, the melting transition ( $T_m$ ) and glass transition ( $T_g$ ) temperatures can be controlled. For example, Doi et al. synthesized PHBHHx with a  $T_m$  of 112.7 °C and a  $T_g$  of 1.6 °C while those of PHB are around 170 °C and 3 °C, respectively [67]. DMAEMA was chosen as the monomer for the copolymerization initiated by the chemically synthesized PHBHHx macroazo initiator. PDMAEMA is an interesting polymer because it is a thermosensitive polymer in aqueous solution at neutral pH and temperatures up to about 50 °C [68–70].

Great efforts have been undertaken to synthesize polymeric derivatives of microbial polyesters for use in medical applications such as drug delivery systems and tissue engineering. Previous reports have documented the synthesis of amphiphilic and thermoresponsive copolymers of PHB for this purpose [56, 71, 72] however, to our knowledge, there are no reports detailing the synthesis of PHBHHx amphiphilic and thermoresponsive block copolymers using PHBHHx macroazo initiator with DMAEMA.

In this work, we report a new macroazo initiator based on PHBHHx and 2,2' azobis cyanopentanoic acid (PHBHHx-AI). While PHBHHx derivatives are known, they are only minimally described in the literature and until now, specific PHBHHx free radical macroinitiators have not been published. To our knowledge, this is the first report of this type of free radical macro intermediate. Specifically, free radical polymerization of DMAEMA was initiated by this macroazo initiator to obtain a PHBHHx-b-PDMAEMA block copolymer. Polymerization kinetics were evaluated and the synthesized block copolymers were characterized by physicochemical methods.

## Experimental

### Materials

PHBHHx samples containing 9 mol% of 3-hydroxyhexanoic acid (PHBHHx-9) was supplied by Procter & Gamble Company (Cincinnati, OH, USA).  $Al_2O_3$  ( $\geq 99.9\%$ ), DMAEMA (98%), dimethyl formamide (99.8%), chloroform ( $\geq 99.9\%$ ), 4,4'-azobis cyanopentanoic acid (AI-COOH), and dichloromethane ( $\geq 99.9\%$ ) were supplied from Sigma-Aldrich (St. Louis, MO, USA) and passed through  $Al_2O_3$  before use. Carbon disulfide ( $\geq 98\%$ ), methyl amino ethanol (mae) ( $\geq 98\%$ ), 4, 4'-azobis cyanopentanoic acid (98%), N, N'-dicyclohexylcarbodiimid (DCC; 99%), dimethyl amino pyridine (DMAP; 99%), stannous 2-ethyl

hexanoate (Sn-oct;  $\geq 92.5\%$ ), and all other chemicals were purchased from Sigma-Aldrich.

### Synthesis of Hydroxylated PHBHHx Using Methyl Amino Ethanol (mae), (PHBHHx-mae-9)

Hydroxylated PHBHHx was obtained by the reaction of PHBHHx with mae according to the slightly modified procedure reported in the cited reference [73]. Briefly, a mixture of 15.6 g of PHBHHx-9, 4.13 g of mae (or dea depending on the desired product) and 0.29 g of Sn-oct in 250 mL of  $\text{CHCl}_3$  was stirred at room temperature for 24 h. Then, the mixture was refluxed for 1 h. The solvent was distilled under atmospheric conditions at between 90 °C and 105 °C. The product was washed with excess methanol and filtered. The crude product was dried under vacuum at 40 °C. For further purification, the obtained polymer was dissolved in 100 mL of  $\text{CHCl}_3$  and filtered from any undissolved residue. The polymer solution was poured into excess methanol. The obtained polymer was filtered and dried under vacuum at 40 °C for 24 h. Yield was 9.3 g. Characteristic FTIR signals were at  $1567\text{ cm}^{-1}$  corresponding to the amide carbonyl,  $3301\text{ cm}^{-1}$  attributed to the primary hydroxyl groups of dea,  $1721\text{ cm}^{-1}$  which belongs to the ester carbonyl of PHB. The characteristic chemical shifts of the PHBHHx-mae sample in  $^1\text{H}$  NMR spectrum were observed at 1.3 ppm for  $-\text{CH}_3$ , 2.4–2.6 ppm for  $-\text{CH}_2\text{-COO-}$ , 2.8 ppm for  $-\text{N-CH}_2-$ , 3.3 ppm for  $-\text{N-CH}_3$ , 3.5–3.8 ppm for  $-\text{CH}_2\text{-OH}$ , 4.1 ppm for  $-\text{CH-OH}$  and 5.1–5.3 ppm for  $-\text{CH-O-}$ .

### Synthesis of PHBHHx Macroazo Initiator (PHBHHx-mae-AI-9)

The synthesis of the PHBHHx macroazo initiator was carried out by the reaction between PHBHHx-mae-OH (8.15 g) and 2,2'-azobis cyanopentanoic acid (0.70 g) in the presence of DCC (0.28 g) and DMAP (0.20 g) in  $\text{CH}_2\text{Cl}_2$  (20 mL). After the mixture was stirred at room temperature for 48 h the precipitated side product formed in the excess methanol was filtered through the solution. The solvent was evaporated and the obtained PHBHHx macroazo initiator was dried under vacuum at room temperature giving a yield of 7.0 g.

### Free Radical Polymerization of DMAEMA Initiated by (PHBHHx-AI-9) at 70 °C in DMF

A solution of PHBHHx-AI-9 (0.40 g), DMAEMA (2.50 g) and DMF (2.50 mL) was reacted at 70 °C for from 10 to 65 min under argon. The obtained polymer solution was poured into excess petroleum benzene to isolate the

PHBHHx-b-PDMAEMA block copolymer which was dried under vacuum at 40 °C for 24 h.

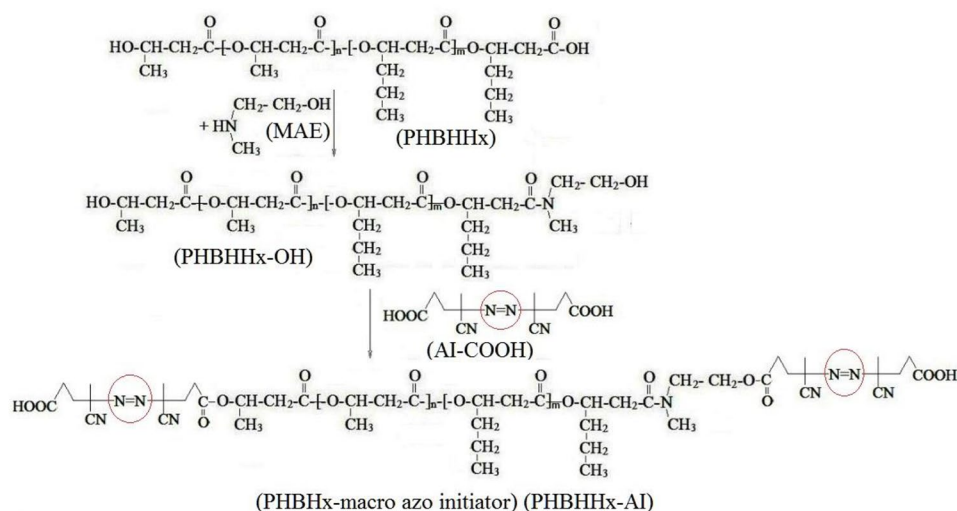
### Characterization

$^1\text{H}$  NMR spectra of the synthesized products were taken at 25 °C with an Agilent NMR 600 MHz NMR (Agilent, Santa Clara, CA, USA) spectrometer equipped with a 3 mm broadband probe. Acquisition parameters included a 45° hard pulse angle, a sweep width of 14 ppm, 1.7 s acquisition time, 0.1 s pulse delay and continuous WALTZ – 16 broadband  $^1\text{H}$  decoupling. Up to 2000 scans were collected per sample, corresponding to ~1 h of collection time. FT-IR spectra of the polymer samples were recorded using a Perkin-Elmer FT-IR Spectrometer 100. Size exclusion chromatography (SEC) was used to determine the molecular weights of the reacted polymers. A calibration curve was generated with five polystyrene (PS) standards of molecular weight 2960, 8450, 50,400, 200,000 and 696,500 Da with low polydispersity. A gel permeation chromatography instrument was used which included a Viscotek GPC max auto sampler system, consisting of a pump, three ViscoGEL GPC columns (G2000H HR, G3000H HR and G4000H HR), and a Viscotek differential refractive index (RI) detector.  $\text{CHCl}_3$  (or THF) was used as the mobile phase with a flow rate of 1.0 mL/min at 30 °C. The RI detector was calibrated with polystyrene standards having narrow molecular weight distributions. Data were analyzed using Viscotek OmniSEC Omni – 01 software.

Differential scanning calorimetry (DSC) was used in the thermal analysis of the obtained polymers. The DSC analysis was carried out under nitrogen using a TA Q2000 DSC instrument that was calibrated using indium ( $T_m = 156.6\text{ °C}$ ) and a Q600 Simultaneous DSC-TGA (SDT) series thermal analysis system. DSC measures the temperatures and heat flows associated with thermal transitions in the polymer samples obtained. The dried polymer samples were heated from –60 to 120 °C under a nitrogen atmosphere. All melting endotherms ( $T_m$ ) were reported as peak temperatures while all glass transition temperatures ( $T_g$ ) were reported as midpoint temperatures. Thermogravimetric analysis (TGA) is used to determine the decomposition temperature ( $T_d$ ) characteristics of the polymers by measuring weight loss under a nitrogen atmosphere over time. In these analyses the obtained polymers were heated from 20 to 600 °C at a rate of 10 °C/min and the results were determined based on the 1st derivative of each curve.

Dynamic light scattering (DLS) was used to determine micelle formation within the synthesized polymers. In order to prepare micelles, 10 mg of the PHBHHx-PDMAEMA was dissolved in 1 mL of DMF under stirring for 2 h. Then, 10 mL of Milli-Q ultra-purified water was added dropwise to

**Fig. 1** Chemical reactions for the synthesis of PHBHHx-macroazo initiator



**Table 1** Free radical polymerization of DMAEMA initiated by the AIBN-COOH terminated PHBHHx (PHBHHx-AI-9) at 70°C, in DMF under argon

Code <sup>a</sup>	Time (min.)	Yield (g)	PHBHHx in copolymer (%)	$\ln[M_0]/[M]$
PHDM-AI-0	10	0.605	24	0.086
PHDM-AI-1	20	0.841	40	0.194
PHDM-AI-2	35	1.085	54	0.569
PHDM-AI-3	50	1.355	66	0.781
PHDM-AI-4	65	1.432	67	0.851

<sup>a</sup>The PHBHHx-AI-9 and the DMAEMA amounts used in all reactions were 0.40 and 2.50 g, respectively.

the solution under stirring. After 3 h of stirring at room temperature, the DMF was removed by dialysis against water for 3 days. DLS measurements were performed at 633 nm on a Malvern Instrument Zetasizer Nano ZS provided with a He-Ne laser source. Measurements were conducted at an angle of 173° at 25 °C. The cumulative method was used to analyze the autocorrelation functions to determine diameters and distributions.

## Results and Discussion

PHBHHx-9 was chosen as the precursor for the macroazo initiator. The PHBHHx chain originally contains one OH group and one -COOH terminal group. The carboxylic acid terminus was converted into a hydroxyl group by the reaction with methyl amino ethanol to obtain dihydroxyl terminated PHBHHx. The hydroxyl ends were reacted with the carboxylic acid terminated reagent, 4,4'-azobis cyanopentanoic acid, to obtain the PHBHHx-macroazo initiator (PHBHHx-AI-9). The reaction scheme can be seen in Fig. 1. An excess amount of azobis cyanopentanoic acid was

used in this reaction to prepare the azo terminated PHBHHx derivative.

### Free Radical Polymerization of DMAEMA Initiated by PHBHHx-AI

A series of PHBHHx-b-PDMAEMA block copolymers were obtained by varying the polymerization times from between 10 and 65 min at 70°C in DMF solution. The individual copolymers were coded as PHDM-AI-0, -1, -2, -3, and -4. The results and the reaction conditions can be seen in Table 1.

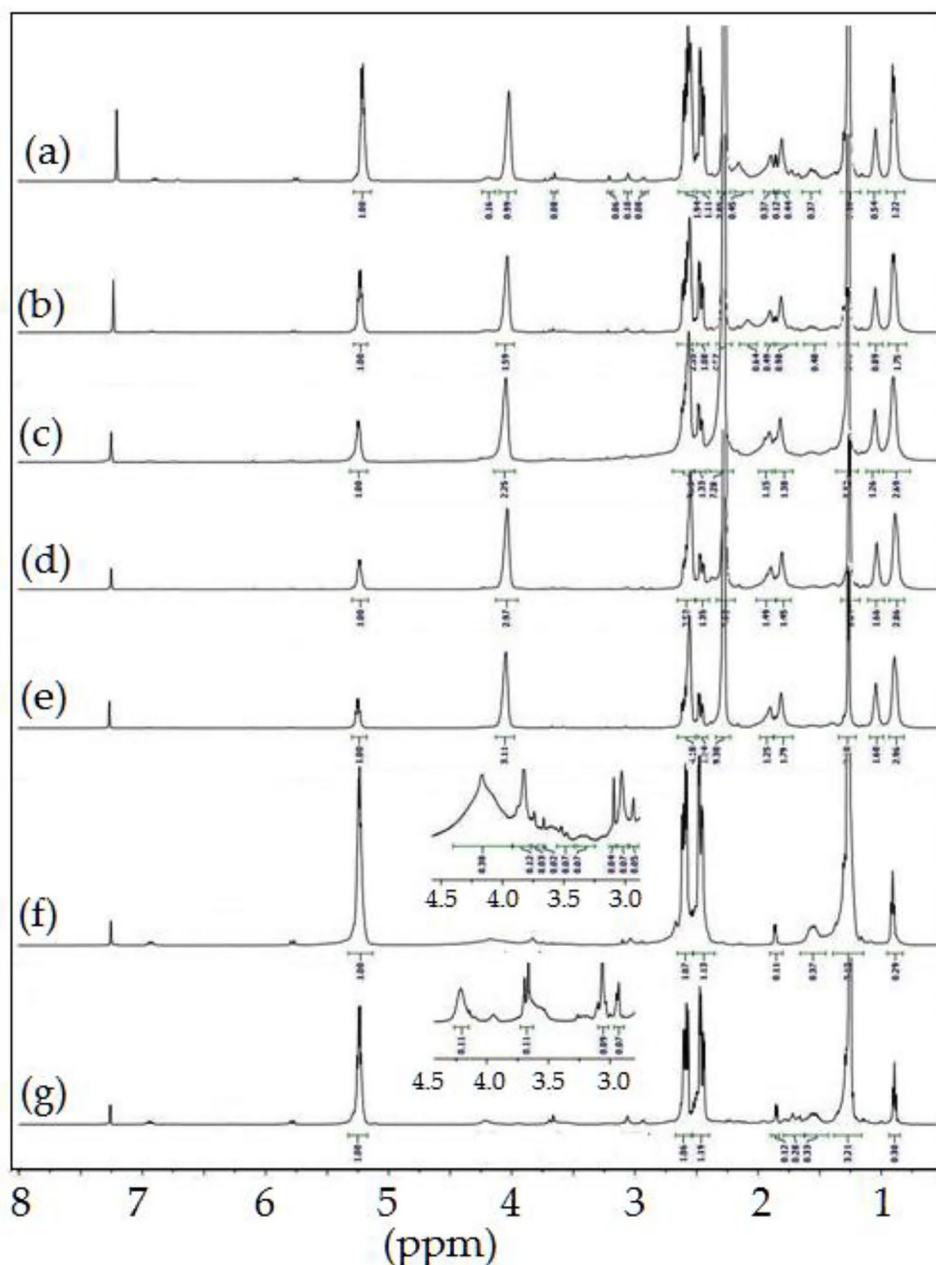
The polymer yield improved by approximately 0.02 g/min as the polymerization reaction time increased from 10 to 50 min. Beyond that, yields stabilized culminating at 1.43 g in 65 min. The obtained block copolymers were characterized by <sup>1</sup>H NMR (Fig. 2). The PHBHHx contents of the block copolymers were calculated by using the integral ratio of the signal at 5.2 ppm (O-CH- of PHBHHx) and the integral ratio of the signal at 4.0 ppm (-COO-CH<sub>2</sub>- of DMAEMA units) (Table 1).

The FTIR spectra of the PHBHHx-PDMAEMA series also confirmed their chemical structures. Figure 3 shows the FTIR results from the synthesized copolymers with the characteristic signals at 3430 (-OH and quarternary ammonium), 2936 (-C-H), 1721 (-C=O) and 748 cm<sup>-1</sup> (tertiary nitrogen) [70, 74].

### Free Radical Polymerization Kinetics of DMAEMA Initiated by the PHBHHx-macroazoinitiator

Conventional radical polymerization is usually a first order (or pseudo first order) reaction [36, 75, 76]. In this case, the rate of the polymerization reaction of DMAEMA using the PHBHHx-AI macroazo initiator at 70°C obeyed the first

**Fig. 2**  $^1\text{H}$  NMR spectra of the PHDM block copolymers: (a) PHDM-AI-0, (b) PHDM-AI-1, (c) PHDM-AI-2, (d) PHDM-AI-3, (e) PHDM-AI-4, (f) PHBHHx-OH-9, (g) PHBHHx-AI.



order kinetics and the reaction rate constant ( $k$ ) was calculated according to Eq. (1).

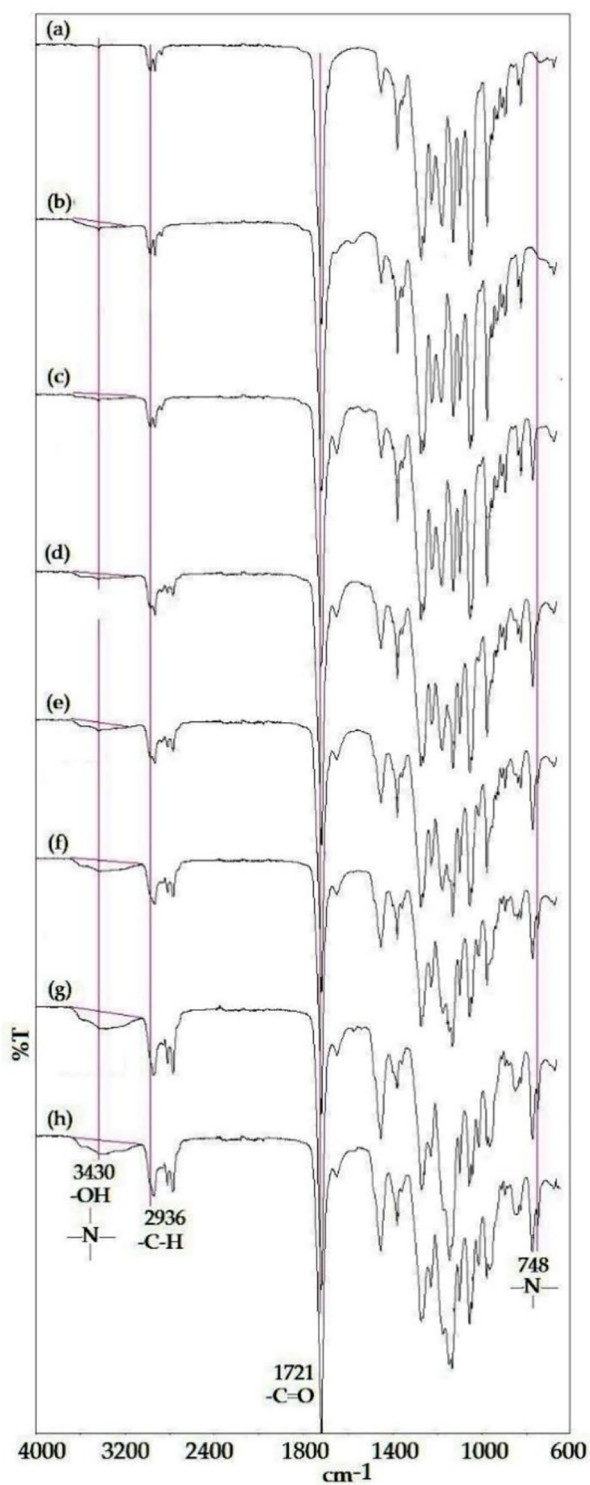
$$\ln [M_0] / [M] = k_{app} \times t \quad (1)$$

Where  $[M_0]$  and  $[M]$  are the total concentrations of the monomer in the beginning and after a polymerization time ( $t$ ), respectively. Figure 4 shows the plot of  $\ln[M_0]/[M]$  against the polymerization time  $t$  (s). The calculated overall rate constant was found to be  $k = 2.33 \times 10^{-4} \text{ L mol}^{-1} \text{ s}^{-1}$ .

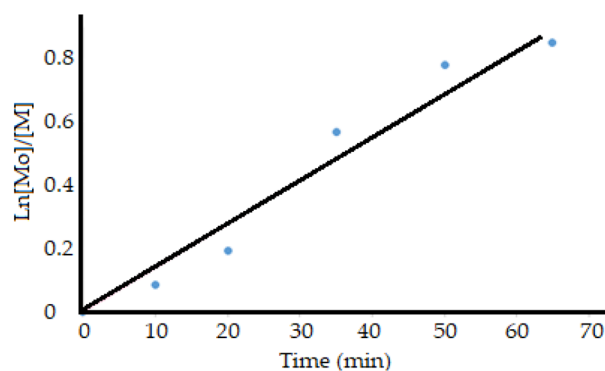
### Molecular Weights of the PHBHHx-PDMA Block Copolymers and PHBHHx Precursors

The molecular weights of the obtained block copolymers and PHBHHx precursors were determined by size exclusion chromatography in  $\text{CHCl}_3$  (Table 2).

Figure 5 shows the unimodal SEC chromatograms which were used to determine the molecular weights of the copolymers. Because of degradability issues associated with the PHAs upon hydroxylation with methyl amino ethanol, there was a dramatic decrease on the molecular weights of the resultant copolymers. The  $M_n$  of the pristine PHBHHx-9



**Fig. 3** FTIR spectra of the PHBHHx-PDMAEMA (PHDM) block copolymers: (a) PHBHHx-H9, (b) PHBHHx-OH-9, (c) PHDM-AI-9, (d) PHDM-AI-0, (e) PHDM-AI-1, (f) PHDM-AI-2, (g) PHDM-AI-3, (h) PHDM-AI-4.



**Fig. 4** The plot of  $\text{Ln}[\text{Mo}]/[\text{M}]$  against the polymerization time  $t$  (s) in free radical polymerization kinetics of DMAEMA initiated by the PHBHHx-macro azoinitiator

**Table 2** The molecular weights of the block copolymers, the precursors, and the micelle diameters of the amphiphilic block copolymers

Code	$M_n^a$ (g/mol)	Poly-dispersity Index <sup>a</sup>	Micelle Diameter <sup>b</sup> (nm)	Poly-dispersity Index <sup>b</sup>
PHBHHx-H-9	70,300	2.2	-	-
PHBHHx-OH-9	2500	1.6	-	-
PHBHHx-AI-9	3900	1.5	-	-
PHDM-AI-0	4300	1.4	602	0.391
PHDM-AI-1	4500	1.4	1136	0.421
PHDM-AI-2	4900	1.4	971	0.425
PHDM-AI-3	4900	1.5	1097	0.317
PHDM-AI-4	5100	1.4	1351	0.437

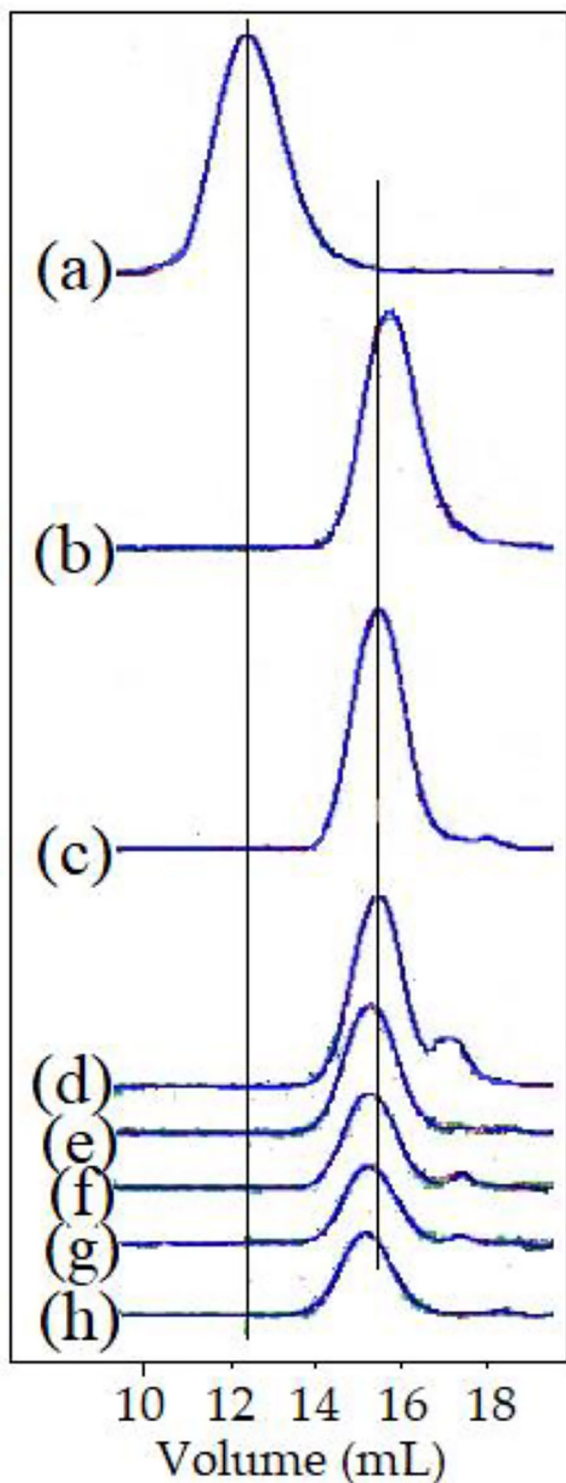
<sup>a</sup>Determined by SEC in  $\text{CHCl}_3$ , <sup>b</sup>Determined by DLS.

was 70300 g/mol but, after capping with 4, 4'-azobis cyano-pentanoic acid there was a marked decrease in the  $M_n$  value for the obtained macroazo initiator, PHBHHx-AI-9 however, once this initiator was reacted with the DMAEMA to form the block copolymer series (PHDM-AI-0 through PHDM-AI-4), the molecular weights of the block copolymers increased by 19% as polymerization time increased from 10 to 65 min.

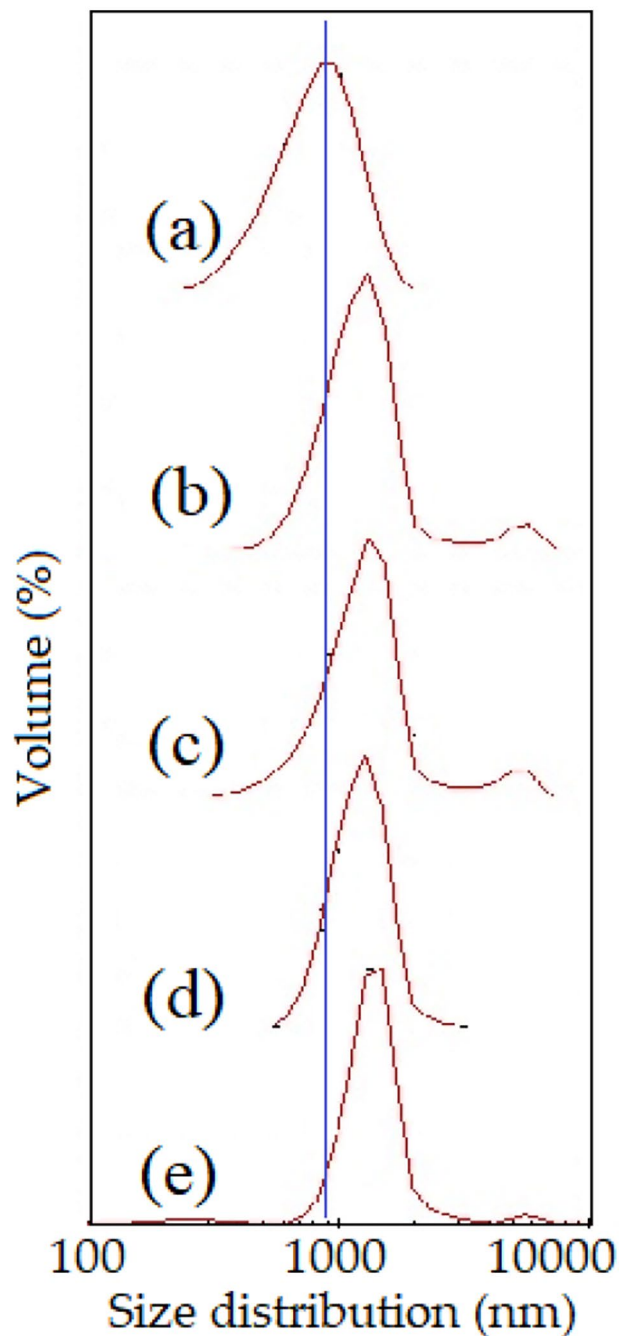
Because of the high hydrophilic effect of PDMAEMA, micelle formation of the obtained block copolymers was measured in aqueous medium. The micelle sizes of the block copolymers varied from 602 to 1351 nm with polydispersity indices varying from 0.317 to 0.437. From this, we can infer that micelle size increases with the increase in DMAEMA content in the block copolymer. Size distribution can be seen in Fig. 6.

### Thermal Properties

The thermal properties of the PHBHHx-PDMAEMA block copolymers were determined using DSC and TGA techniques. The thermal analysis results are shown in Table 3



**Fig. 5** SEC chromatograms of the block copolymers and the precursors: (a) PHBHHx-9, (b) PHBHHx-OH-9, (c) PHBHHx-AI-9, (d) PHDM-AI-0, (e) PHDM-AI-1, (f) PHDM-AI-2, (g) PHDM-AI-3, (h) PHDM-AI-4.

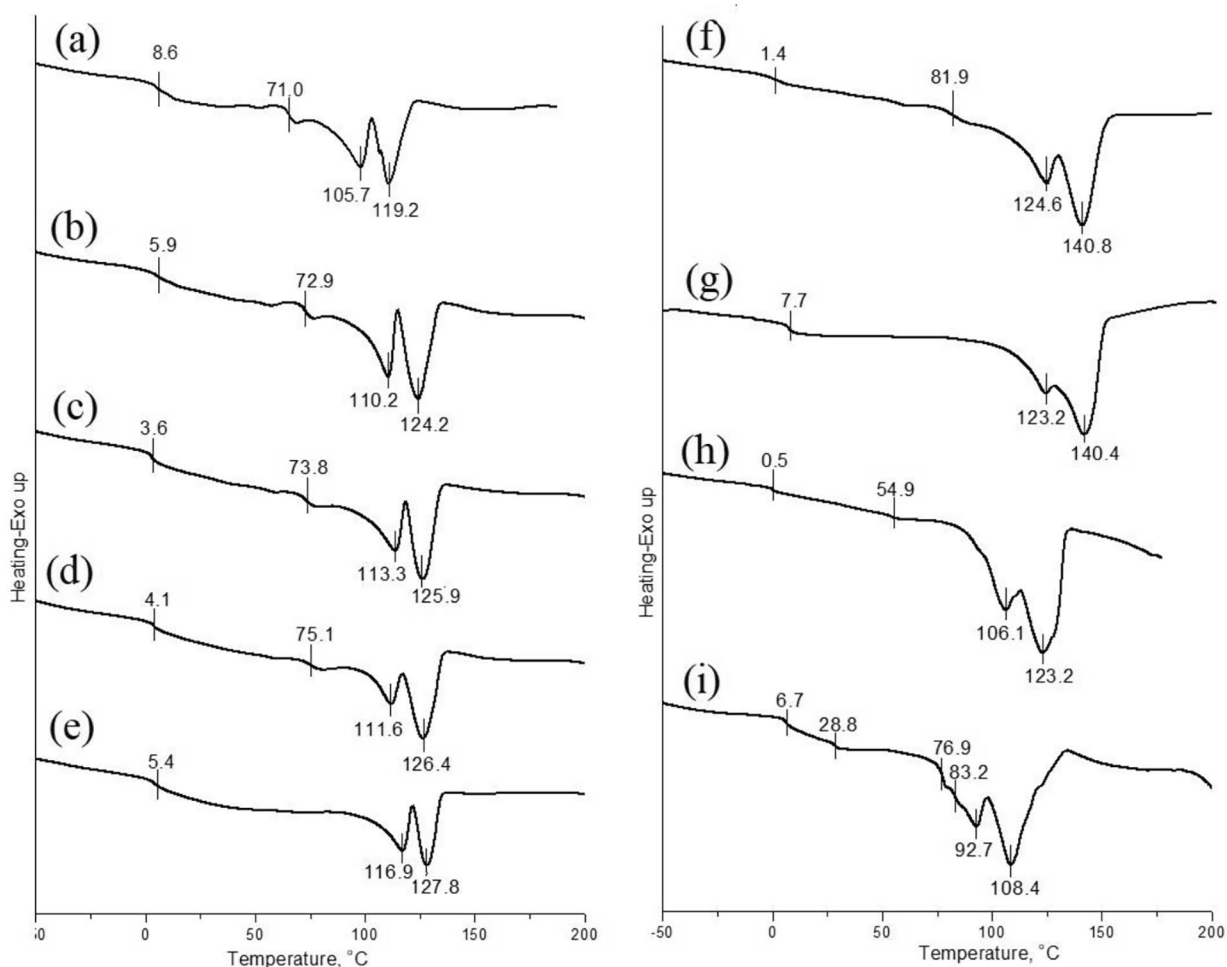


**Fig. 6** Micelle size distribution of the PHBHHx-PDMAEMA amphiphilic block copolymers: (a) PHDM-0, (b) PHDM-1, (c) PHDM-2, (d) PHDM-3, (e) PHDM-4.

While the actual curves are shown in Fig. 7. Glass transition ( $T_g$ ) and melting transition temperatures ( $T_m$ ) were determined by DSC. The typical  $T_m$  values of the PHBHHx block copolymers were observed at around  $125 \pm 3^\circ\text{C}$ . Additionally, multiple  $T_g$ s and  $T_m$ s were observed in some of the copolymers. Presumably, during the polymerization, small amounts of degraded polymer segments can cause these

**Table 3** Results of thermal analysis of the PHBHHx-PDMAEMA block copolymers. <sup>a</sup>Determined by DSC analysis. <sup>b</sup>Determined by TGA analysis

Code	$T_g^a$ (°C)	$T_m^a$ (°C)	$T_d^b$ (°C)			
			1	2	3	4
PHDM-AI-0	8.6, 71	106, 119	239		413	513
PHDM-AI-1	5.9, 73	110, 124	228	278	396	487
PHDM-AI-2	3.6, 74	113, 126	238	294	404	513
PHDM-AI-3	4.1, 75	112, 126	244	296	413	526
PHDM-AI-4	5.4, 75	117, 128	242	300	417	525
PHBHHx-9	1.4, 82	125, 141	254			
PHBHHx-OH-9	7.7	123, 140	258			
PHBHHx-mae-OH	0.5, 55	106, 123	238			
PHBHHx-AI-9	6.7, 29, 77, 83	93, 108	252			
PDMAEMA				325	423	

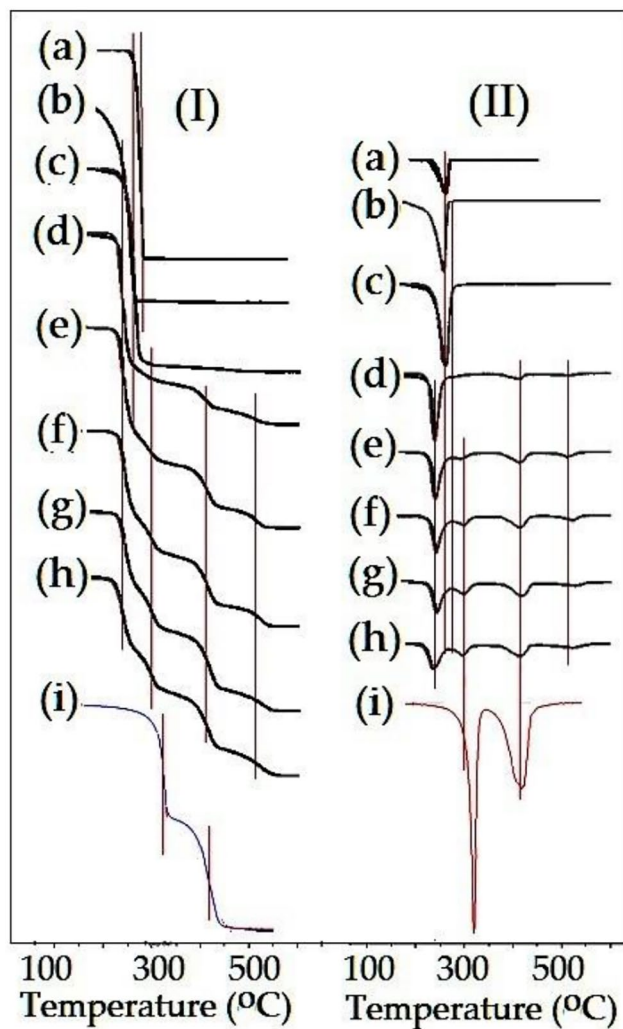
**Fig. 7** DSC analysis of the PHBHHx-b-PDMAEMA block copolymers: (a) PHDM-AI-0, (b) PHDM-AI-1, (c) PHDM-AI-2, (d) PHDM-AI-3, (e) PHDM-AI-4, (f) PHBHHx-9 (pristine), (g) PHBHHx-dea-OH, (h) PHBHHx-mae-OH, (i) PHBHHx-AI-9.

multiple  $T_g$ s and  $T_m$ s. Homo PDMAEMA is an amorphous polymer with a  $T_g$  of around 10 °C [77].

The carboxyl ends of PHBHHx were converted into hydroxyl groups using methyl amino ethanol amine. Thermal properties of the hydroxylated PHBHHx were also compared with their melting transitions in Fig. 7(g and h).

The hydroxylated PHBHHx obtained using dea showed a bimodal  $T_m$  whose peak values were both approximately 15% higher than those corresponding to the mae derived copolymers. The effect of the PDMAEMA blocks lowered the  $T_m$  of pure PHBHHx (ca. 145°C).





**Fig. 8** TGA (I) and DTG (II) curves: (a) PHBHHx-9, (b) PHBHHx-mae-OH, (c) PHBHHx-AI-9, (d) PHDM-AI-0, (e) PHDM-AI-1, (f) PHDM-AI-2, (g) PHDM-AI-3, (h) PHDM-AI-4, (i) PDMAEMA.

Figure 8 shows the TGA (I) and DTG (II) curves. PHBHHx intermediates showed a single decomposition at around 250°C (Fig. 8a-c) while the synthesized block copolymers showed multiple decomposition temperatures (Fig. 8d-h) whose initial  $T_d$  ( $T_{d1}$ ) values were approximately 4% on average lower than those from the PHBHHx intermediates. The very low peak of  $T_{d4}$  decomposition temperature presumably occurs during the side reactions of the PHBHHx and PDMAEMA carbonaceous residues.

## Conclusion

Microbial polyesters require modification to improve the hydrophilicity, hydrophobicity, thermal resistance, and the mechanical properties. To modify the PHAs, block copolymers were prepared using functional intermediates.

PHBHHx macroazo initiators were prepared and used in the synthesis of DMAEMA amphiphilic block copolymers with a reasonable polydispersity. This type of macroazo initiator can be used to prepare block copolymers with a wide range of vinyl monomers to obtain very versatile PHA derivatives. Because of the mild polymerization conditions, PHBHHx macroazo initiators can also be promising macrointermediates to prepare bioconjugates for medical applications.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s10924-023-02857-3>.

**Acknowledgements** This work was supported by the Kapadokya University Research Funds (#KÜN.2020-BAGP-001).

**Credit authorship contribution statement** Baki Hazer: Supervision, Conceptualization. Fulya Taşçı: Conceptualization. Valerie Langlois: Conceptualization, Supervision. Tina Modjinou: Conceptualization. Richard Ashby: Conceptualization, Supervision. Melahat Göktaş: Conceptualization. Baozhong Zhang: Conceptualization.

## Declarations

**Conflict of interest** Compliance with ethics requirements Authors have no financial relationship with the organization that sponsored the research.

**Ethical approval** This article does not contain any studies with human or animal subjects.

## References

- Bates CM, Bates FS (2017) 50th anniversary perspective: Block Polymers—Pure potential. *Macromolecules* 50(1):3–22. <https://doi.org/10.1021/acs.macromol.6b02355>
- Dau H, Jones GR, Tsogtgerel E, Nguyen D, Keyes A, Liu YS, Rauf H, Ordonez E, Puchelle V, Alhan HB, Zhao C, Harth E (2022) Linear Block Copolymer Synthesis. *Chem Rev* 122(18):14471–14553. <https://doi.org/10.1021/acs.chemrev.2c00189>
- Gao H, Matyjaszewski K (2008) Synthesis of low-polydispersity miktoarm star copolymers via a simple “arm-first” method: macromonomers as arm precursors. *Macromolecules* 41(12):4250–4257. <https://doi.org/10.1021/ma800618d>
- Degirmenci M, Hizal G, Yagci Y (2002) Synthesis and characterization of macrophotoinitiators of poly( $\epsilon$ -caprolactone) and their use in block copolymerization. *Macromolecules* 35(22):8265–8270. <https://doi.org/10.1021/ma020668t>
- Edmondson S, Armes SP (2009) Synthesis of surface-initiated polymer brushes using macro-initiators. *Polym Intern* 58(3):307–316. <https://doi.org/10.1002/pi.2529>
- Hazer B (1992) New macromonomeric initiators (macroinimers), 2 gelation in bulk polymerization of styrene with macroinimers. *Makromol Chem* 193(5):1081–1086. <https://doi.org/10.1002/macp.1992.02193050>
- Voit BI, Lederer A (2009) Hyperbranched and highly branched polymer architectures – synthetic strategies and major characterization aspects. *Chem Rev* 109(11):5924–5973. <https://doi.org/10.1021/cr900068q>

8. Hazer B (1995) Grafting on polybutadiene with macro or macromonomer initiators containing poly(ethylene glycol) units. *Macromol Chem Phys* 196(6):1945–1952. <https://doi.org/10.1002/macp.1995.021960614>
9. Wang YZ, Liu L, Dong SB, Zhou XL, Wang CL, Shi Z (2021) The “Living” feature of the ATRP macroinitiators in different Catalytic Systems. *Electron Mater Lett* 17(2):136–141. <https://doi.org/10.1007/s13391-021-00268-x>
10. Ueda A, Nagai S (1986) Block copolymers derived from azobiscyanopentanoic acid. VI. Synthesis of a polyethyleneglycol – polystyrene block copolymer. *J Polym Sci Part A Polym Chem* 24(3):405–418. <https://doi.org/10.1002/pola.1986.080240302>
11. Yıldız U, Hazer B, Tauer K (2012) Tailoring polymer architectures with macromonomer azoinitiators. *Polym Chem* 5:1107–1118. <https://doi.org/10.1039/C2PY00513A>
12. Çakmak I, Hazer B, Yağcı Y (1991) Polymerization of acrylamide by the redox system cerium(IV) with poly(ethylene glycol) with azo groups. *Eur Polym J* 27(1):101–103. [https://doi.org/10.1016/0014-3057\(91\)90134-A](https://doi.org/10.1016/0014-3057(91)90134-A)
13. Yıldız U, Hazer B, Capek I (1995) Dispersion polymerization of styrene and methyl methacrylate initiated by poly(oxyethylene) macromonomeric azoinitiators. *Angew Macromol Chem* 231(1):135–144. <https://doi.org/10.1002/apmc.1995.052310112>
14. Yıldız U, Hazer B (2000) Dispersion redox copolymerization of methyl methacrylate with macromonomeric azoinitiator as a macrocrosslinker. *Polymer* 41(2):539–544. [https://doi.org/10.1016/S0032-3861\(99\)00217-7](https://doi.org/10.1016/S0032-3861(99)00217-7)
15. Erdem A, Mammadli N, Yildiz U (2021) Preparation of hydrophobic macroinimer – based novel hybrid sorbents for efficient removal of organic liquids from wastewater. *Environ Sci Pollut Res* 28:22064–22076. <https://doi.org/10.1007/s11356-020-11841-6>
16. Hazer B (1987) Polymerization of vinyl monomers by a new oligoperoxide: Oligo(adipoyl-5-peroxy-2,5-dimethyl *n*-hexyl peroxide). *J Polym Sci: Polym Chem Edition* 25(12):3349–3354. <https://doi.org/10.1002/pola.1987.080251214>
17. Hazer B, Savaşkan S (1998) Cross-linked multicomponent copolymers with macromonomer peroxyinitiators (MMPI). *Eur Polym J* 34(5–6):863–870. [https://doi.org/10.1016/S0014-3057\(97\)00193-6](https://doi.org/10.1016/S0014-3057(97)00193-6)
18. Hazer B, Baysal BM (1986) Preparation of block copolymers using a new polymeric peroxy carbamate. *Polymer* 27(6):961–986. [https://doi.org/10.1016/0032-3861\(86\)90312-5](https://doi.org/10.1016/0032-3861(86)90312-5)
19. Hazer B, Ayas A, Beşirli N, Saltek N, Baysal BM (1989) Preparation of ABCBA-type block copolymers by use of macro-initiators containing peroxy and azo groups. *Makromol Chem* 190(8):1987–1996. <https://doi.org/10.1002/macp.1989.021900822>
20. Oppenheimer C, Heitz W (1981) The synthesis of blockcopolymers by radical polymerization. *Die Angew Makromole Chemie* 98(1):167–184. <https://doi.org/10.1002/APMC.1981.050980108>
21. Frey H, Ishizone T (2017) Living Anionic polymerization celebrates 60 years: unique features and polymer architectures. *Macromol Chem Phys* 218:1700217. <https://doi.org/10.1002/macp.201700217>
22. Boopathi SK, Hadjichristidis N, Gnanou Y, Feng X (2019) Direct access to poly(glycidyl azide) and its copolymers through anionic (co-polymerization of glycidyl azide. *Nat Commun* 10:293–301. <https://doi.org/10.1038/s41467-018-08251-1>
23. Hirao A, Goseki R, Ishizone T (2014) Advances in living anionic polymerization: from functional monomers, polymerization systems, to macromolecular architectures. *Macromolecules* 47(6):1883–1905. <https://doi.org/10.1021/ma401175m>
24. Adamus G, Domiński A, Kowalczyk M, Kurcok P, Radecka I (2021) From Anionic Ring-Opening polymerization of  $\beta$ -Butyrolactone to biodegradable poly(hydroxyalkanoate)s: our contributions in this field. *Polymers* 13(24):4365. <https://doi.org/10.3390/polym13244365>
25. Maric M (2021) History of nitroxide mediated polymerization in Canada. *Can J Chem Eng* 99:832–852. <https://doi.org/10.1002/cjce.23989>
26. Matyjaszewski K, Tsarevsky NV (2017) Nanostructured functional materials prepared by atom transfer radical polymerization. *Nat Chem* 1(4):276–288. <https://doi.org/10.1038/nchem.257>
27. Allı A, Allı S, Becer CR, Hazer B (2016) Nitroxide-mediated copolymerization of styrene and pentafluorostyrene initiated by polymeric linoleic acid. *Eur J Lipid Sci Technol* 118(2):279–287. <https://doi.org/10.1002/ejlt.201500129>
28. Kapil K, Szczepaniak G, Martinez MR, Murata H, Jazani AM, Jeong J, Das SR, Matyjaszewski K (2023) Visible-light-mediated controlled radical branching polymerization in Water. *Angew Chem Int Ed* 62:e20221765. <https://doi.org/10.1002/anie.202217658>
29. Dworakowska S, Lorandi F, Gorczynski A, Matyjaszewski K (2022) Toward green atom transfer Radical polymerization: current Status and Future Challenges. *Adv Sci* 9:2106076. <https://doi.org/10.1002/advs.202106076>
30. Corbin DA, Miyake GM (2022) Photoinduced Organocatalyzed atom transfer Radical polymerization (O-ATRP): Precision Polymer Synthesis using Organic Photoredox Catalysis. *Chem Rev* 122:1830–1874. <https://doi.org/10.1021/acs.chemrev.1c00603>
31. Öztürk T, Yavuz M, Göktaş M, Hazer B (2016) One-step synthesis of triarm block copolymers by simultaneous atom transfer radical and ring-opening polymerization. *Polym Bull* 73:1497–1513. <https://doi.org/10.1021/ja00125a035>
32. Becer CR, Growth AM, Hoogenboom R, Paulus RM, Schubert US (2008) Protocol for automated kinetic investigation/optimization of the RAFT polymerization of various monomers. *QSAR & Comb Sci* 27(8):977–983. <https://doi.org/10.1002/qsar.200720159>
33. Aksakal S, Beyer VP, Aksakal R, Becer CR (2019) Copper mediated RDRP of thioacrylates and their combination with acrylates and acrylamides. *Polym Chem* 10(48):6622–6629. <https://doi.org/10.1039/C9PY01518C>
34. Şanal T, Oruç O, Öztürk T, Hazer B (2015) Synthesis of pH- and thermo-responsive poly( $\epsilon$ -caprolactone-*b*-4-vinyl benzyl-*g*-dimethyl amino ethyl methacrylate) brush type graft copolymers via RAFT polymerization. *J Polym Res* 22:article3. <https://doi.org/10.1007/s10965-014-0640-z>
35. Whitfield R, Anastasaki A, Nikolaou V, Jones GR, Engelis NG, Discekici EH, Fleischmann C, Willenbacher J, Hawker CJ, Haddleton DM (2017) Universal conditions for the controlled polymerization of acrylates, methacrylates, and styrene via Cu(0)-RDRP. *J Am Chem Soc* 139(2):1003–1010. <https://doi.org/10.1021/jacs.6b11783>
36. Hazer B, Subramaniyan S, Zhang B (2021) RAFT polymerization of the novel methacrylated methyl salicylate. Block copolymerization with poly (3-hydroxy butyrate). *ChemistrySelect* 6:12255–12265. <https://doi.org/10.1002/slct.202102977>
37. Hazer B, Arslan H, Senemoğlu Y, Şen S (2019) Synthesis of block/graft copolymers based on vinyl benzyl chloride via reversible addition fragmentation chain transfer (RAFT) polymerization using the carboxylic acid functionalized trithiocarbonate. *J Polym Res* 26:article101. <https://doi.org/10.1007/s10965-019-1763-z>
38. Chiefari J, Chong YK, Ercole F, Krstina J, Jeffery J, Le TPT, Mayadunne RTA, Meijs GF, Moad CL, Moad G, Rizzardo E, Thang SH (1998) Living free-radical polymerization by reversible addition – fragmentation chain transfer: the RAFT process. *Macromolecules* 31(16):5559–5562. <https://doi.org/10.1021/ma9804951>
39. Allı A, Allı S, Hazer B, Zinn M (2022) Synthesis and characterization of Star-Shaped Block Copolymers composed of poly

- (3-hydroxy octanoate) and Styrene via RAFT polymerization. *J Macromol Sci Part A: Pure and Appl Chem* 59:526–536. <https://doi.org/10.1080/10601325.2022.2092408>
40. Ozturk T, Atalar MN, Goktas M, Hazer B (2013) One-step synthesis of block-graft copolymers via simultaneous reversible-addition fragmentation chain transfer and ring-opening polymerization using a novel macroinitiator. *J Polym Sci: Part A: Polym Chem* 51(12):2651–2659. <https://doi.org/10.1002/pola.26654>
  41. Guzik M, Witko T, Steinbuechel A, Wojnarowska M, Soltysik M, Wawak S (2020) What has been trending in the research of polyhydroxyalkanoates? A systematic review. *Front Bioengin Biotechnol* 8:article959. <https://doi.org/10.3389/fbioe.2020.00959>
  42. Bedade DK, Edson CB, Gross RA (2021) Emergent approaches to efficient and sustainable polyhydroxyalkanoate production. *Molecules* 26(11):article3463. <https://doi.org/10.3390/molecules26113463>
  43. Ashby RD, Foglia TA (1998) Poly(hydroxyalkanoate) biosynthesis from triglyceride substrates. *Appl Microbiol Biotechnol* 49:431–437. <https://doi.org/10.1007/s002530051194>
  44. Koray O, Koksall MS, Hazer B (2010) Simple production experiment of poly (3-hydroxy butyrate) for science laboratories and its importance for science process skills of prospective teachers. *Energy Educ Sci Technol Part B-Soc Educ Stud* 2(1–2):39–54
  45. Kocer H, Borcakli M, Demirel S, Hazer B (2003) Production of bacterial polyesters from some various new substrates by *Alcaligenes eutrophus* and *Pseudomonas oleovorans*. *Turk J Chem* 27(3):365–374
  46. Chen GQ (2009) A microbial polyhydroxyalkanoates (PHA) based bio- and materials industry. *Chem Soc Rev* 38(8):2434–2446. <https://doi.org/10.1039/b812677c>
  47. Hazer B, Steinbüchel A (2007) Increased diversification of polyhydroxyalkanoates by modification reactions for industrial and medical applications. *Appl Microbiol Biotechnol* 74(1):1–12. <https://doi.org/10.1007/s00253-006-0732-8>
  48. Hazer DB, Kilicay E, Hazer B (2012) Poly(3-hydroxyalkanoate) s: diversification and biomedical applications: a state of the art review. *Mater Sci Eng C* 32(4):637–647. <https://doi.org/10.1016/j.msec.2012.01.021>
  49. Ashby RD, Solaiman DK, Strahan GD (2019) The Use of *Azohydromonas lata* DSM 1122 to produce 4-hydroxyvalerate-containing polyhydroxyalkanoate terpolymers, and unique polymer blends from mixed-cultures with *Burkholderia sacchari* DSM 17165. *J Polym Environ* 27:198–209. <https://doi.org/10.1007/s10924-018-1332-2>
  50. Guennec A, Brelle L, Balnois E, Linossier I, Renard E, Langlois V, Fay F, Chen GQ, Simon-Colin C, Vallée-Réhel K (2021) Anti-fouling properties of amphiphilic poly(3-hydroxyalkanoate): an environmentally-friendly coating. *Biofouling* 37(8):894–910. <https://doi.org/10.1080/08927014.2021.1981298>
  51. Le Fer G, Babinot J, Versace D-L, Langlois V, Renard E (2012) An efficient thiol-ene chemistry for the preparation of amphiphilic PHA-based graft copolymers. *Macromol Rapid Commun* 33(23):2041–2045. <https://doi.org/10.1002/marc.201200485>
  52. Domenek S, Langlois V, Renard E (2007) Bacterial polyesters grafted with poly(ethylene glycol): Behaviour in aqueous media. *Polym Degrad Stab* 92(7):1384–1392. <https://doi.org/10.1016/j.polyimdeggradstab.2007.03.001>
  53. Hazer B, Akyol E, Şanal T, Guillaume S, Çakmakli B, Steinbuechel A (2019) Synthesis of novel biodegradable elastomers based on poly[3-hydroxy butyrate] and poly[3-hydroxy octanoate] via transamidation reaction. *Polym Bull* 76:919–932. <https://doi.org/10.1007/s00289-018-2410-2>
  54. Arkin AH, Hazer B (2002) Chemical modification of chlorinated microbial polyesters *Biomacromolecules* 3(6):1327–1335. DOI: <https://doi.org/10.1021/bm020079v>
  55. Arslan H, Hazer B, Kowalczyk M (2002) Synthesis and characterization of poly[(*R,S*)-3-hydroxybutyrate] telechelics and their use in the synthesis of poly(methyl methacrylate)-*b*-poly(3-hydroxybutyrate) block copolymers. *J Appl Polym Sci* 85(5):965–973. <https://doi.org/10.1002/app.10435>
  56. Loh XJ, Zhang Z-X, Wu Y-L, Lee TS, Li J (2009) Synthesis of novel biodegradable thermoresponsive triblock copolymers based on poly[(*R*)-3-hydroxybutyrate] and poly(*N*-isopropylacrylamide) and their formation of thermoresponsive micelles. *Macromolecules* 42(1):194–202. <https://doi.org/10.1021/ma8019865>
  57. Arslan H, Menteş A, Hazer B (2004) Synthesis and characterization of diblock, triblock, and multiblock copolymers containing poly(3-hydroxy butyrate) units. *J Appl Polym Sci* 94(4):1789–1796. <https://doi.org/10.1002/app.21112>
  58. Raza ZA, Riaz S, Banat IM (2018) Polyhydroxyalkanoates: Properties and chemical modification approaches for their functionalization. *Biotechnol Prog* 34(1):29–41. <https://doi.org/10.1002/btpr.2565>
  59. Chaber P, Kwiecien M, Zieba M, Sobota M, Adamus G (2017) The heterogeneous selective reduction of PHB as a useful method for preparation of oligodiols and surface modification. *RSC Adv* 7(56):35096–35104. <https://doi.org/10.1039/C7RA06111K>
  60. Hazer B (2015) Simple synthesis of amphiphilic poly(3-hydroxy alkanooate)s with pendant hydroxyl and carboxylic groups via thiol-ene photo click reactions. *Polym Degrad Stab* 119:159–166. <https://doi.org/10.1016/j.polyimdeggradstab.2015.04.024>
  61. Hazer B (2010) Amphiphilic poly(3-hydroxy alkanooate)s: potential candidates for medical applications. *Int J Polym Sci* 2010:article 423460. <https://doi.org/10.1155/2010/423460>
  62. Hazer B (2020) Amphiphiles from poly(3-hydroxyalkanoates). In: Koller M (ed) *The handbook of polyhydroxyalkanoates*. CRC Press, Taylor & Francis, London, New York., pp 43–64
  63. Erol A, Rosberg DBH, Hazer B, Göncü BS (2020) Biodegradable and biocompatible radiopaque iodinated poly-3-hydroxy butyrate: synthesis, characterization and in vitro/in vivo X-ray visibility. *Polym Bull* 77:275–289. <https://doi.org/10.1007/s00289-019-02747-6>
  64. Sato H, Nakamura M, Padermshoke A, Yamaguchi H, Terauchi H, Ekgasit S, Noda I, Ozaki Y (2004) Thermal behavior and molecular interaction of poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) studied by wide-angle X-ray diffraction. *Macromolecules* 37(10):3763–3769. <https://doi.org/10.1021/ma049863t>
  65. Noda I, Satkowski MM, Dowrey AE, Marcott C (2004) Polymer alloys of Nodax copolymers and poly(lactic acid). *Macromol Biosci* 4(3):269–275. <https://doi.org/10.1002/mabi.200300093>
  66. Bayram C, Denkbas EB, Kiliçay E, Hazer B, Çakmak HB, Noda I (2008) Preparation and characterization of triamcinolone acetonide-loaded poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) (PHBHx) microspheres. *J Bioact Compat Polym* 23(4):334–347. <https://doi.org/10.1177/0883911508092790>
  67. Doi Y, Kitamura S, Abe H (1995) Microbial synthesis and characterization of poly(3-hydroxybutyrate-co-3-hydroxyhexanoate). *Macromolecules* 28(14):4822–4828. <https://doi.org/10.1021/ma00118a007>
  68. Stawski D, Nowak A (2019) Thermal properties of poly(*N,N*-dimethylaminoethyl methacrylate). *PLoS ONE* 14(6):e0217441. <https://doi.org/10.1371/journal.pone.0217441>
  69. Plamper FA, Ruppel M, Schmalz A, Borisov O, Ballauff M, Müller AHE (2007) Tuning the thermoresponsive properties of weak polyelectrolytes: aqueous solutions of star-shaped and linear poly(*N,N*-dimethylaminoethyl methacrylate). *Macromolecules* 40(23):8361–8366. <https://doi.org/10.1021/ma071203b>
  70. Karjalainen E, Aseyev V, Tenhu H (2014) Influence of hydrophobic anion on solution properties of PDMAEMA. *Macromolecules* 47(6):2103–2111. <https://doi.org/10.1021/ma5000706>

71. Hossain MdA, Mushill L, Rahaman MS, Mains SM, Vickers T, Tulaphol T, Dong J, Sathitsuksanoh N (2022) Upcycling agricultural waste to biodegradable polyhydroxyalkanoates by combined ambient alkaline pretreatment and bacterial fermentation. *Industrial Crops & Products* 185:114867. <https://doi.org/10.1016/j.indcrop.2022.114867>
72. Allı A, Hazer B, Adamus G, Kowalczyk M (2017) Telechelic Polyhydroxyalkanoates /Polyhydroxybutyrates (PHAs/PHBs) in Handbook of Telechelic Polyesters, Polycarbonates, and Polyethers (editor: S. M. Guillaume). Pan Stanford Publishing, Singapore. Chapter 3. 65–113
73. Hazer B, Eren M, Senemoğlu Y, Modjinou T, Renard E, Langlois V (2020) Novel poly(3-hydroxy butyrate) macro RAFT agent. Synthesis and characterization of thermoresponsive block copolymers. *J Polym Res* 27:article147. <https://doi.org/10.1007/s10965-020-02133-1>
74. Yin J-J, Wahid F, Zhang Q, Tao Y-C, Zhong C, Chu L-Q (2017) Facile incorporation of silver nanoparticles into quaternized poly(2-(dimethylamino)ethyl methacrylate) brushes as bifunctional antibacterial coatings. *Macromol Mater Eng* 302(6):article 1700069. DOI: <https://doi.org/10.1002/mame.201700069>
75. Perrier S (2017) 50th anniversary perspective: RAFT polymerization – a user guide. *Macromolecules* 50(19):7433–7447. <https://doi.org/10.1021/acs.macromol.7b00767>
76. Buback M, Kurz CH, Schmaltz C (1998) Pressure dependence of propagation rate coefficients in free-radical homopolymerizations of methyl acrylate and dodecyl acrylate. *Macromol Chem Phys* 199(8):1721–1727. [https://doi.org/10.1002/\(SICI\)1521-3935\(19980801\)199:8<1721::AID-MACP1721>3.0.CO;2-5](https://doi.org/10.1002/(SICI)1521-3935(19980801)199:8<1721::AID-MACP1721>3.0.CO;2-5)
77. Bruce C, Javakhishvili I, Fogelström L, Carlmark A, Hvilsted S, Malmström E (2014) Well-defined ABA- and BAB-type block copolymers of PDMAEMA and PCL. *RSC Adv* 4:25809–25818. <https://doi.org/10.1039/C4RA04325A>

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.