The Eurasia Proceedings of Science, Technology, Engineering & Mathematics (EPSTEM), 2021

Volume 15, Pages 21-27

ICBAST 2021: International Conference on Basic Science and Technology

Synthesis of Novel Aba-Type Amphiphilic Copolymers Including 2-Hydroxypropyl Propionate and N-Isobutoxymethyl B-Alanine by Peg-Dialkoxide Initiated Hydrogen-Transfer Polymerization

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Abstract: Novel ABA-type amphiphilic copolymers were prepared using end-groups activated poly (ethylene glycol) (PEG) as an initiator of hydrogen-transfer polymerization (HTP). For this purpose, PEG with 1450 Da (PEG-1450) was treated with the equivalent amount of sodium hydride to synthesize PEG with dialkoxide end-groups, namely PEG-dialkoxide. Using the PEG-dialkoxide as a macroinitiator, base-catalysed HTP of 2-hydroxypropyl acrylate (HPA), and N-isobutoxymethyl acrylamide (BMA) were performed to achieve the novel ABA-type block copolymers. The copolymers were obtained with relatively high yields. Characterization of the ABA-type amphiphilic copolymers was carried out using FTIR and MALDI mass spectrometry. FTIR spectra of the copolymers exhibited some characteristic bands assigning to the functional groups arising from the mechanism of HTP. Molar mass distributions of the copolymers from the MALDI mass study pointed out that chain extensions by mass in each copolymer were almost equal. Hence, the MALDI mass spectra of the copolymers revealed that chain extensions of PEGs by HPA, and BMA units were successfully fulfilled.

Keywords: ABA-type amphiphilic copolymer, Hydrogen-transfer polymerization, Macroinitiator, Poly(ethylene glycol).

Introduction

Many novel macromolecules via the extension of polymeric chains (Matyjaszewski, 2003) or coupling reactions (He et.al., 2012; Çatıker et.al., 2020; Çatıker et.al., 2019) have been reported by using the approach. Telechelics are generally synthesized via living radical polymerization (Frey et. al., 2018) and controlled living radical polymerization (Lunn et.al., 2017) because they yield narrow molar mass distribution. Block copolymers can be easily generated by using telechelics (Iijima et.al., 1997; Verso et. al., 2008; Boutevin et.al., 2006; Tasdelen et.al.,2011). Amphiphilic block copolymers are the most common block copolymer systems that self-assemble into different morphologies depending upon the nature of their chemical content (Levit M., et.al., 2020; Lee et. al., 2010) size of the blocks (Burguière et.al., 2002; LaRue et.al., 2008) and physical conditions (temperature, solvent, pH, electrical field, etc.) (Akiba et.al., 2010 November; Karayianni et. al., 2016; Wang et.al., 2017; Yorulmaz-Avşar et.al., 2019). Poly(ethylene glycol) (PEG) is the most common hydrophilic segment (Danafar et.al., 2014; Quadir et.al., 2014) preferred in block copolymers possibly due to its unique physical and biocompatible properties. Polymers based on PEG are attractive materials for biomedical, industrial, and chemical applications, as PEG has these unique characters (Francolini et.al., 2020; Zarrintaj et.al., 2020). PEG units are helpful for hydrophobic polymers to gain hydrophilicity (Zhu et.al., 2012). Hydrogen transfer polymerization (HTP) is a useful route that can insert functional groups into the backbone of a macromolecule. However, it is necessary to use a monomer with a loose proton(s) and vinyl group to obtain the product via HTP (Çatıker et.al., 2018; Iwamura et.al., 2019). The PEG-1450 was treated with the equivalent amount of sodium hydride to sodium PEG-dialkoxide salt as shown ref. (Çatıker et.al., 2020). Using the salt as a macroinitiator, HTP of 2-hydroxypropyl acrylate (HPA), and N-isobutoxymethyl acrylamide (BMA) were carried out to yield PEG based ABA-type amphiphilic copolymers. Structural characterization of the copolymers was achieved using FTIR and MALDI-MS spectrometry.

Experimental

Materials

2-hydroxypropyl acrylate (Sigma), N-isobutoxymethyl acrylamide (Sigma), sodium hydride (Merck, 60 % dispersion in oil), PEG-1450 (Sigma-Aldrich), 2,5-dihydroxybenzoic acid (DHB) (Sigma-Aldrich, 98 %), and formic acid (Sigma-Aldrich, $\geq$ 99 %) were obtained commercially and used without purification. Tetrahydrofuran (Sigma-Aldrich, 99 %) was distilled over sodium mirror.

Instrumentation

FTIR spectra of the copolymers were achieved with Shimadzu IRaffinity 1 spectrometer in the range of 600-4000 cm^{-1}. MALDI-MS analyses were performed using a Bruker Rapiflex MALDI-TOF/TOF mass spectrometer (Bruker Daltonics, Bremen, Germany) equipped with a smartbeam™ 3D laser. The data were acquired in positive ion mode for each sample. DHB solution (20 mg/mL in 1:1, ACN:THF containing 1.0% (v/v) formic acid) was used as the matrix.

Preparation of Sodium PEG-dialkoxide

Sodium PEG-1450 dialkoxide was obtained by a reaction between PEG-1450 and equimolar NaH at about 45 ^{o}C as the ref. (Çatıker et.al., 2020). Briefly, a certain amount of PEG-1450 and NaH (two times of PEG-1450 as moles) were placed in a round bottom glass balloon under argon flux. The mixture was stirred at 45 ^{o}C (slightly above the melting temperature of PEG-1450) under argon flux until hydrogen gas evolution has stopped. The dark brown waxy paste was obtained and then directly used as a macroinitiator for HTP.

Synthesis of the ABA-type Amphiphilic Copolymers by HTP

Poly (2-hydroxypropyl propionate-b-ethylene glycol-b-2-hydroxypropyl propionate) [P(HPP-EG-HPP] and poly (N-isobutoxymethyl β-alanine-b-ethylene glycol-b-N-isobutoxymethyl β-alanine) [P(BMBA-EG-BMBA] were synthesized by HTP of 2-hydroxypropyl acrylate (HPA) and N-isobutoxymethyl acrylamide (BMA) using the sodium PEG-1450 dialkoxide as a macroinitiator. Reaction parameters were outlined in Table 1. The specified amounts of the monomers given in Table 1 were added into the separate balloons containing the sodium PEG-dialkoxide as an initiator of HTP. After nitrogen purging, the reaction mixture was stirred until the mixture becomes too viscous, or solid. Then, cold excess THF was poured into the reaction mixture to extract the purities. The product was filtered and washed with cold THF to remove possible unreacted PEG and monomer (HPA or BMA). The percentage yields of the ABA-type block copolymer were determined gravimetrically and calculated as 71.3 wt. % and 93.1 wt. %.

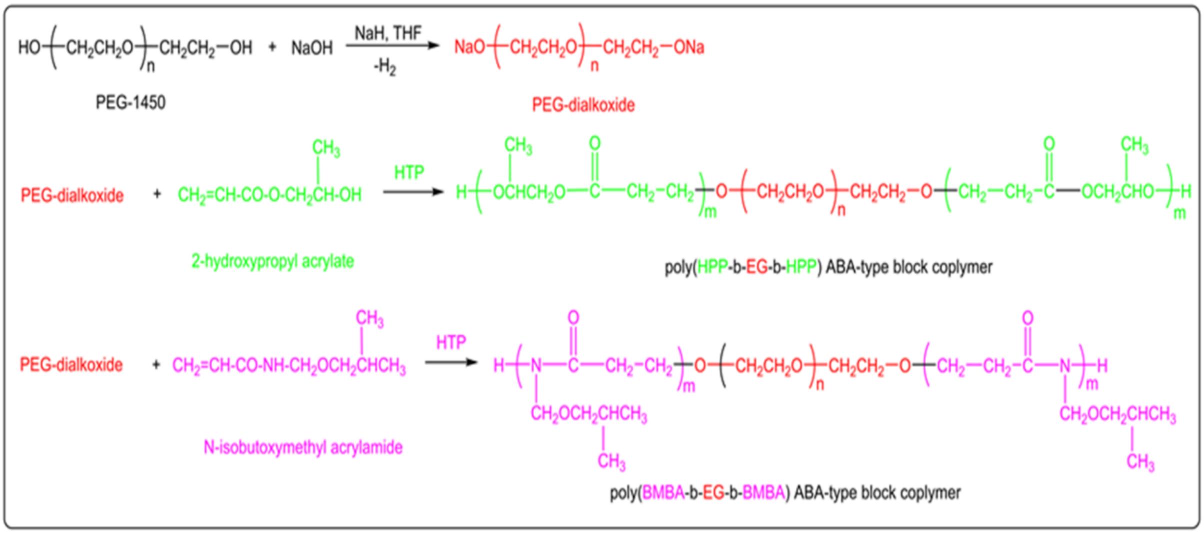
Table 1. Synthesis condition of the ABA-type triblock copolymers through HTP.

Initiator (g)	Monomer (mL)	Yield % (wt.)	Average Molar Mass (Da)
~ 0.45 (PEG-dialkoxide)	0.40 mL (HPA)	71.3	~ 3000
~ 0.45 (PEG-dialkoxide)	0.40 mL (BMA)	93.1	~ 2500

Results and Discussion

Synthesis of the ABA-type Block Copolymers

PEG-1450 was treated with sodium hydride to obtain PEG-dialkoxide salts. Line 1 in Scheme 1 shows the reaction pathway for the PEG-dialkoxide macroinitiator. Line 2 and 3 in Scheme 1 show the reaction outlines for P(HPP-EG-HPP) and P(BMBA-EG-BMBA) ABA-type block copolymers. The copolymers obtained from HTP were extracted with THF to remove unreacted PEG units and by-products. Then, the insoluble fractions were dried under vacuum at 40 ^{o}C.



Scheme 1**.** Reaction pathways in the synthesis of PEG-dialkoxide, and novel ABA-type block copolymers.

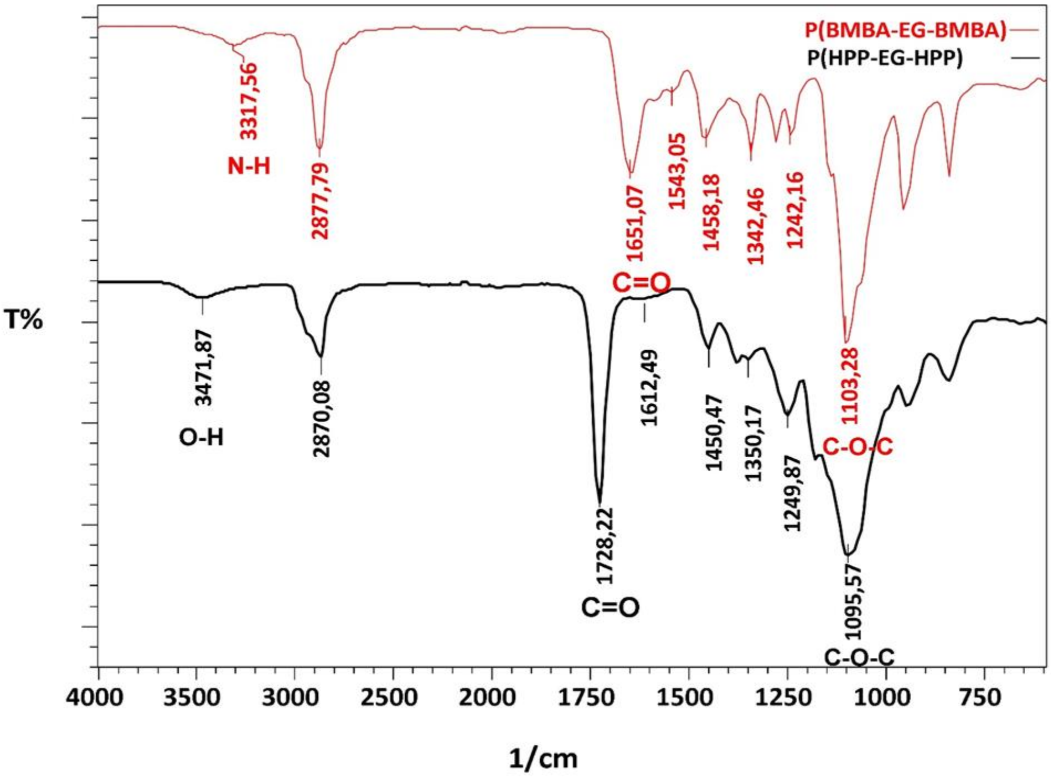


Figure 1. FTIR spectra of the ABA-type amphiphilic copolymers.

Characterization of the ABA-type Amphiphilic Copolymers

FTIR spectra of the ABA-type amphiphilic copolymers were comparatively given in Figure 1. FTIR spectrum of P(HPP-EG-HPP) has characteristic PEG bands as well as ester (1728 cm^{-1}) band in the HPP units. For the FTIR spectrum of P(BMBA-EG-BMBA), the characteristic secondary amide (I) (Çatıker et.al., 2018) at about 1650 cm^{-1} (C=O stretching vibration) and ether about 1095 cm^{-1} (asymmetric C-O stretching vibration) show the existence of both repeating units in the products. The FTIR spectra of both THF-insoluble copolymer samples include the characteristic bands of PEG, normally known as very soluble in THF. This may be attributed to the formation of covalent bonding between the PEG units, and the chain extensions by HTP. The weak bands at 3472 and 3318 cm^{-1} belong to the OH and NH stretching vibrations in P(HPP-EG-HPP) and P(BMBA-EG-BMBA), respectively. The weakness of the bands shows the chain extensions are limited.

MALDI mass spectrum of the P(HPP-EG-HPP) in Figure 2 was acquired and examined to show molar mass distribution. The unimodal mass distribution centered at about m/z 3000 Da may be accepted as another proof of the successful chain extension.

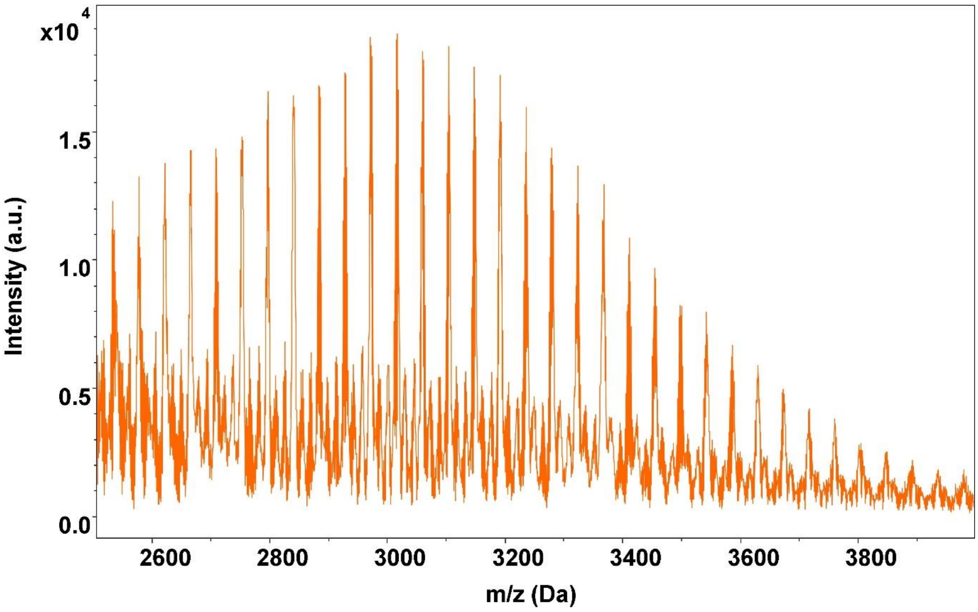


Figure 2. Wide-range MALDI mass spectra of P(HPP-EG-HPP)

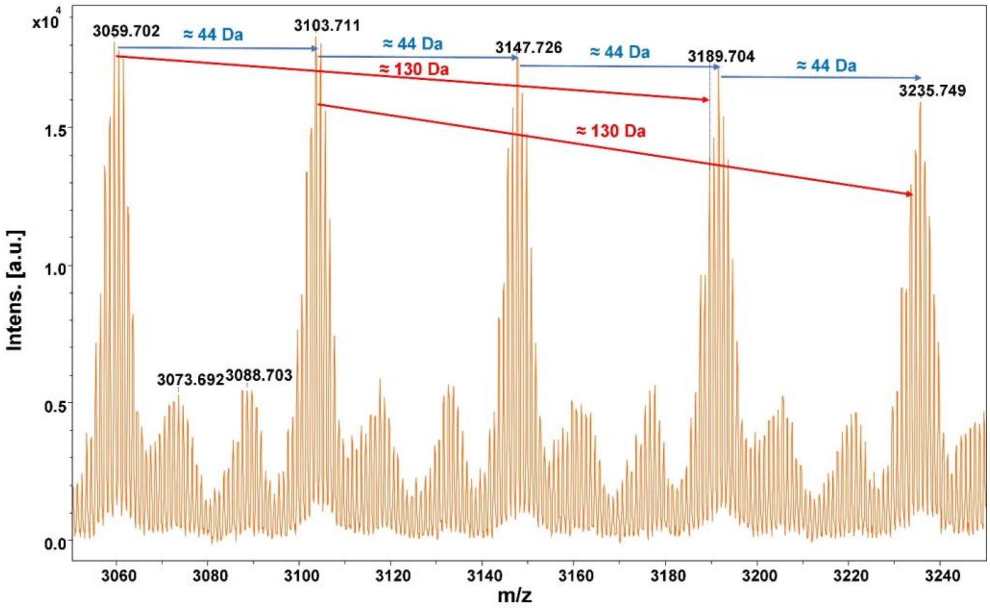


Figure 3. An expanded view of m/z the 3050-3250 region of MALDI-MS spectrum of P(HPP-EG-HPP).

Figure 3 shows an expanded view of m/z the 3050-3250 region of MALDI-MS spectrum of P(HPP-EG-HPP). The indisputable proof of the copolymer formation can be seen when the differences between consecutive signals are about m/z 130 and m/z 44 corresponding to the masses of HPP ($C_6H_{10}O_3$) and EG (C_2H_4O) repeating units of the copolymer, respectively. MALDI-TOF-MS analyzes of the copolymer sample show that the ABA-type poly(HPP-EG-HPP) copolymer has been synthesized successfully by confirming the targeted chemical structure with high mass accuracy.

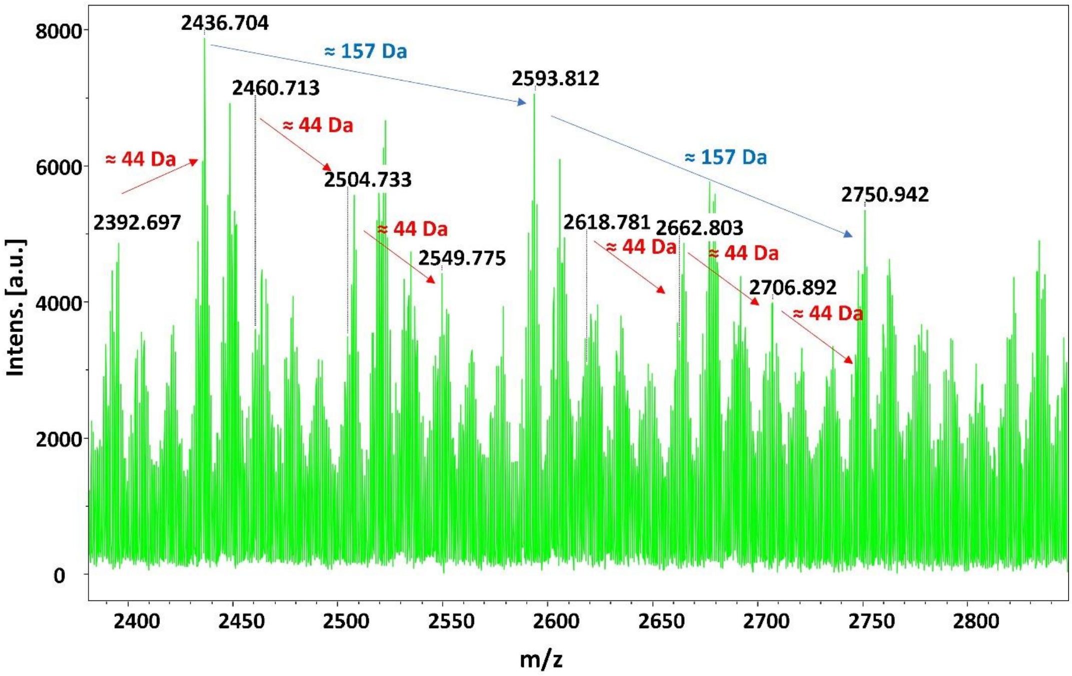


Figure 4. An expanded view of m/z the 2380-2900 region of MALDI mass spectrum of P(BMBA-EG-BMBA) block copolymer.

An expanded view of the m/z 2380-2900 region of the MALDI spectrum of P(BMBA-EG-BMBA) block copolymer was also illustrated in Figure 4. The differences between consecutive signals are about m/z 157 and m/z 44 corresponding to the masses of BMBA ($C_8H_{15}NO_2$) and EG (C_2H_4O) units in the copolymer, respectively. MALDI-TOF-MS analyzes of the ABA-type poly(BMBA-EG-BMBA) copolymer shows that chain extension of the PEG-1450 dialkoxide was fulfilled via HTP of isobutoxymethyl acrylamide.

Conclusion

The synthesis strategy given in the study to yield ABA-type triblock copolymers is simple and efficient. Results of the FTIR and MALDI mass methods prove indisputably the formation of novel ABA-type amphiphilic block copolymers. By a selection of appropriate lengths of PEG and the monomers capable of being involved in HTP, it may be possible to obtain well-defined ABA-type triblock copolymers for specific applications.

Scientific Ethics Declaration

The authors declare that the scientific ethical and legal responsibility of this article published in EPSTEM journal belongs to the authors.

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To cite this article:

Catiker, E., Ozturk, T., Savas, B., Atakay, M. & Salih, B. (2021). Synthesis of novel aba-type amphiphilic copolymers including 2-hydroxypropyl propionate and n-isobutoxymethyl β-alanine by peg-dialkoxide initiated hydrogen-transfer polymerization. *The Eurasia Proceedings of Science, Technology, Engineering & Mathematics (EPSTEM), 15*, 21-27.