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Homogeneous isocyanate- and catalyst-free synthesis of polyurethanes in aqueous media†

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We report an efficient and environmentally-friendly method of synthesizing polyurethanes in aqueous solution *via* an isocyanate- and catalyst-free polymerization process. Five different polyurethanes were synthesized by first activating 1,6-hexanediol and poly(ethylene glycol) with bis(pentafluorophenyl)carbonate, and then polycondensing various ratios of the 1,6-hexanediol/poly(ethylene glycol)-derived activated carbonates with JEFFAMINE. The polymerization process was confirmed by FTIR spectroscopy, ^{1}H NMR spectroscopy, and gel permeation chromatography (GPC). The melting temperature was linearly dependent on the 1,6-hexanediol/poly(ethylene glycol) ratio, increasing with greater poly (ethylene glycol) content, as confirmed by differential scanning calorimetry (DSC). Similarly, the degree of crystallinity was also directly proportional to the poly(ethylene glycol) content.

Introduction

Most polyurethanes are phase-separating polymers consisting of "soft" and "hard" segments.[1] This phase separation, brought about by hydrogen bond-based physical cross-linking of the hard segment, imparts unusual morphological and physical properties. These properties can be easily tailored by varying the nature of the reagents used in its synthesis,[2] and as a result, these materials have been employed for a wide range of applications, including thermoplastics, surface coatings, textile coatings, adhesives, elastomers, foams and dispersions.[3–5] For biomedical applications, polyurethanes have been used as tissue engineering scaffolds,[6,7] sutures,[8] and adhesion barriers.[9] Moreover, these materials are promising for drug delivery applications, in particular, for the synthesis of water-soluble linear systems, nanoparticles or nanogels because of their low toxicity, low cost, and biocompatibility.[10] Unfortunately, polyurethane synthesis usually necessitates the use of isocyanate monomers,[11] a tin or a tertiary amine catalyst,[12,13] and organic solvents, all of which have toxicity issues and are environmental pollutants. It is difficult to carry out polymerization in aqueous media due to the inherent incompatibility of water and isocyanates; therefore, most of the water-soluble polyurethanes are prepared through a two-step process where the first step is carried out in a toxic organic solvent[14] or through a complicated process such as mini-emulsion polymerization.[15] Significant effort has been devoted to developing isocyanate- and tin catalyst-free routes to polyurethanes due to the impending regulatory changes.[16–20] One example of a successful isocyanate-free polyurethane synthesis involves the use of dicyclic six- and seven-membered ring carbonate monomers and reacting them with diamine nucleophiles.[21,22] Recently, a series of segmented polyureas were synthesized through an activated carbamate (isocyanate-free) route.[23] The main limitations of this new synthetic approach are the high temperatures required for polymerization, the long reaction times required to generate high molecular weights and the use of toxic organic solvents. Furthermore, cyclic carbonates are often not stable in aqueous solutions; therefore polymerization in aqueous media is limited. An alternative synthetic approach uses activated carbonates. Activated dicarbonates are known to undergo polycondensation with nucleophiles such as diamines, resulting in the formation of various polyurethanes.[24,25] The efficiency of this reaction in aqueous media is extremely dependent on the nature of the leaving group, which is required to demonstrate much higher chemoselectivity towards diamines than towards water.

Poly(ethylene glycol) (PEG) is the gold standard for stealth polymers in polymer-based therapeutic delivery.[26] When PEG is in the bloodstream, water molecules form a protective sheath around the PEG, mitigating opsonization.[27,28] As a

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result, attaching PEG to therapeutic agents significantly decreases toxicity and increases the circulation half-life. Although there are many advantages to using PEG, there are also drawbacks. The most apparent disadvantage of PEG is that it is not biodegradable.[26] The generation of high molecular weight PEG with urethane linkages will introduce a biodegradable linkage within the polymer structure. Furthermore, the incorporation of a "hard" segment such as a short aliphatic chain allows tailoring of thermal and mechanical properties.

The present work describes a simple catalyst- and isocyanate-free method for polyurethane synthesis *via* nucleophilic polycondensation of diamines with activated carbonates in aqueous media. To the best of our knowledge, this is the first report of high molecular weight PUs prepared in aqueous media using homogeneous polymerization methodology. Two different diols were employed as starting materials: poly(ethylene glycol) diol (M_n = 1500 g mol^{-1}, "soft" segment) and 1,6-hexanediol ("hard" segment). The respective diol was functionalized with bis(pentafluorophenyl)carbonate (PFC) and subsequently reacted with a linear diamine (JEFFAMINE) to generate PEG-based polyurethane in aqueous media. Five different polyurethanes were synthesized by varying the 1,6-hexanediol/PEG ratio, resulting in biodegradable PEG-like polymers with different thermal and mechanical properties. The polymerization process was confirmed by FTIR spectroscopy, NMR spectroscopy, and gel permeation chromatography (GPC). The thermal properties of the five polyurethanes were evaluated by DSC.

Experimental

Materials and methods

1,6-Hexanediol, 1,8-bis(dimethylamino)naphthalene (Proton-Sponge®) and poly(ethylene glycol) end-capped diol (M_n = 1500 g mol^{-1}) were purchased from Sigma-Aldrich Chemical Corporation. JEFFAMINE® ED-2003 (JEFFAMINE, M_n = 2000 g mol^{-1}) was supplied by Huntsman and PFC was supplied by Central Glass. All materials were used as received without further purification.

^{1}H, proton decoupled ^{13}C and ^{19}F NMR spectra were obtained on a Bruker Avance 400 instrument. GPC was performed in THF at 30 °C using a Waters chromatograph equipped with four 5 mm Waters columns (300 mm × 7.7 mm) connected in series with increasing pore size (100, 1000, 10^5, 10^6 Å). FTIR spectroscopy was used to confirm the polymerization process: using a Nicolet Magna 560 spectrometer at a resolution of 2 cm^{-1}, and a total of 64 interferograms were signal-averaged. Samples were prepared by solution casting the reaction mixture onto the ZnSe window.

Polyurethane films were studied by DSC (Q2000 TA Instruments), using a heating ramp from −80 °C to 150 °C at a rate of 10 °C min^{-1} under an N_2 atmosphere. The DSC thermograms presented in this work correspond to the second scan. The films were stored for a week at 30 °C under vacuum to remove residual water.

Preparation of activated carbonates

Synthesis of C_6F_5O–COO–$(CH_2)_6$–OCO–OC_6F_5 (Monomer A). PFC (2.2 equiv., 1.8 g., 4.4 mmol) and Proton-Sponge® (0.25 equiv., 0.11 g, 0.50 mmol) were dissolved in THF (8.0 mL) and stirred for 30 min. 1,6-Hexanediol (1.0 equiv., 0.24 g, 2.0 mmol) dissolved in 2.0 mL of THF was added dropwise to the reaction mixture and allowed to react at room temperature until completion (4 h). The reaction mixture was evaporated to dryness and the residue was redissolved in cold dichloromethane, in which much of the pentafluorophenol byproduct was precipitated and recovered (0.65 g, 68% recovery, with analytical purity higher than 95%). The product-containing filtrate was rinsed with saturated aqueous $NaHCO_3$ and water, dried over $MgSO_4$, and concentrated. The crude product was recrystallized from hexanes to afford C_6F_5O–COO–$(CH_2)_6$–OCO–OC_6F_5 (Monomer A) as a white crystalline powder (0.77 g, 73% yield). The structure was confirmed by ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.28 (t, OCOOCH_2, 4H), 1.75 (t, OCOOCH$_2$CH_2, 4H), 1.44 (t, CH_2, 4H); ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 151.0 (O*C*OO), 142.0, 140.0, 139.0, 136.0 (C_{Ar}), 70.0 (s, COO*C*H$_2$), 28.0 (COOCH$_2$*C*H$_2$), 25.0 (*C*H$_2$); ^{19}F NMR ($CDCl_3$, 400 MHz): −154 (d, Ar-*F*, 4F), −158 (t, Ar-*F*, 4F), −162 (q, Ar-*F*, 2F).

Synthesis of C_6F_5O–COO–PEG–OCO–OC_6F_5 (Monomer B). PFC (2.2 equiv., 2.9 g, 7.3 mmol) and Proton-Sponge® (0.50 equiv., 0.36 g, 1.7 mmol) were dissolved in THF (40 mL) and stirred for 30 min. PEG diol (M_n = 1500 Da) (1.0 equiv., 5.0 g, 3.3 mmol) dissolved in 10.0 mL of THF was added dropwise to the reaction mixture, and stirred at room temperature for 8 h. The reaction mixture was precipitated into cold diethyl ether to afford C_6F_5O–COO–PEG–OCO–OC_6F_5 (Monomer B) as a white crystalline powder (6.0 g, 86% yield, by GPC M_{nPEG} = 2000 g mol^{-1}/polydispersity index (PDI) = 1.04; $M_{nMonomer\ B}$ = 2400 g mol^{-1}/PDI = 1.05). The structure was confirmed by ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.47 (t, OCOOCH_2, 2H), 3.81 (t, OCOOCH$_2$CH_2, 2H), 3.64 (m, OCH_2, 64H); ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 151.0 (O*C*OO), 142.0, 140.0, 139.0, 136.0 (C_{Ar}), 70.5 (O*C*H$_2$), 69.5 (OCOO*C*H$_2$), 68.5 (OCOO*C*H$_2$); ^{19}F NMR ($CDCl_3$ 400 MHz): −153 (d, Ar-*F*, 2F), −158 (t, Ar-*F*, 2F), −162 (q, Ar-*F*, 1F). The ether-based filtrate was passed through a short pad of silica gel to separate impurities from the recoverable pentafluorophenol byproduct (1.3 g, 81% of recovery, with analytical purity higher than 98%).

Polyurethane synthesis

Five different polyurethanes were synthesized by varying the monomer ratios. In a typical polymerization, the modified diols (1.0 equiv., 0.33 mmol) were dissolved in 2.5 mL of deionized water. Separately JEFFAMINE (M_n = 2000 g mol^{-1}) (1.0 equiv., 0.66 g, 0.33 mmol) and triethylamine (2 equiv., 0.07 g, 0.7 mmol) were dissolved in 2.5 mL of distilled water and added dropwise to the modified diols. The reaction was

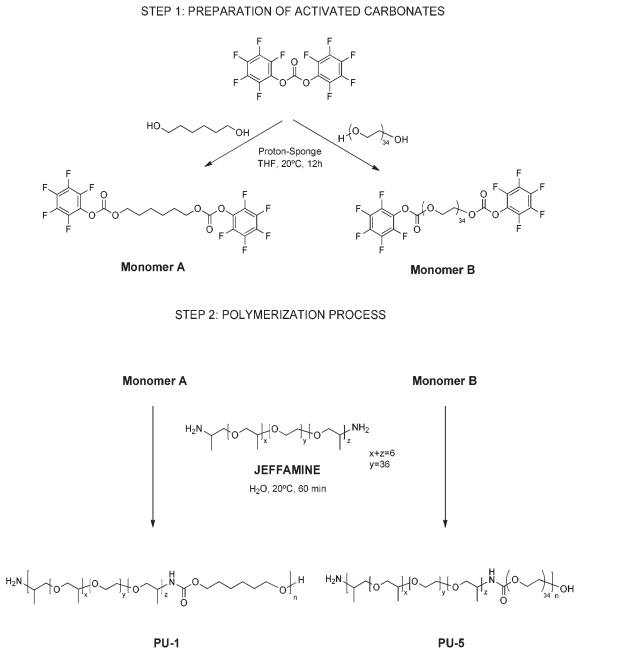
Table 1 Reagent ratios employed for the synthesis of the five different polyurethanes and the observed molecular weight distributions

Sample	Monomer_A (equiv./mmol)	Monomer_B (equiv./mmol)	PEG (equiv./mmol)	M_n (kDa)/PDI
PU-1	1.0/0.33	0/0	1.0/0.33	15.5/1.96
PU-2	0.75/0.25	0.25/0.080	1.0/0.33	16.4/1.92
PU-3	0.50/0.17	0.5/0.17	1.0/0.33	15.2/1.93
PU-4	0.25/0.080	0.75/0.25	1.0/0.33	15.9/1.98
PU-5	0/0	1.00/0.33	1.0/0.33	15.0/1.94

carried out at room temperature until completion (60 min). Table 1 shows the amount of reagents employed for the preparation of different polyurethanes. In order to render this process sustainable, recovery of pentafluorophenol was carried out. Details can be found in the ESI.† The polymerization was confirmed by ^{1}H NMR FTIR and GPC. **PU-1**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.10 (s, NHCOOCH_2, 4H), 3.80–3.30 (m, OCH_2, 170H), (m, OCONHC*H*, 2H), (m, OCOC*H*, 5H), 1.70 (s, NHCOOCH$_2$CH_2, 4H), 1.44 (s, CH_2, 4H), 1.10 (m, NHCHCH_3, 21H). **PU-2**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.20 (s, NHCOOCH_2, 1H), δ = 4.10 (s, NHCOOCH_2, 3H), 3.80–3.30 (m, OCH_2, 32H), (m, OCH_2, 170H), (m, OCONHC*H*, 2H), (m, OCOC*H*, 5H), 1.70 (s, NHCOOCH$_2$CH_2, 3H), 1.44 (s, CH_2, 3H), 1.10 (m, NHCHCH_3, 21H). **PU-3**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.20 (s, NHCOOCH_2, 2H), δ = 4.10 (s, NHCOOCH_2, 2H), 3.64 (m, OCH$_2$, 64H), (m, OCH$_2$, 170), (m, OCONHC*H*, 2H), (m, OCOC*H*, 5H), 1.70 (s, NHCOOCH$_2$CH_2, 2H), 1.44 (s, CH_2, 2H), 1.10 (m, NHCHCH_3, 21H). **PU-4**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.20 (s, NHCOOCH_2, 3H), δ = 4.10 (s, NHCOOCH_2, 1H), 3.64 (m, OCH_2, 96H), (m, OCH_2, 170), (m, OCONHC*H*, 2H), (m, OCOC*H*, 5H), 1.70 (s, NHCOOCH$_2$CH_2, 1H), 1.44 (s, CH_2, 1H), 1.10 (m, NHCHCH_3, 21H). **PU-5**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.20 (s, NHCOOCH_2, 4H), 3.80–3.30 (s, NHCOOCH$_2$CH_2, 4H), (m, OCH_2, 128H), (m, OCH_2, 170), (m, OCONHC*H*, 2H), (m, OCOC*H*, 5H), 1.10 (m, NHCHCH_3, 21H).

Results and discussion

Polyurethanes were prepared using a two-step approach: (1) preparation of the monomers and (2) formation of the polymer (Scheme 1). In the first step, aliphatic diols were reacted with the bis(pentafluorophenyl)carbonate to form activated carbonates. The reaction was monitored by ^{1}H NMR (Fig. 1). Quantitative conversion of the terminal alcohol groups to pentafluorophenyl esters was achieved with both monomers. As observed in Fig. 1-A, in the case of 1,6-hexanediol, the characteristic signal of the methylene protons adjacent to the hydroxyl group at δ = 3.65 ppm completely disappeared, while new signals corresponding to methylene protons proximal to the activated carbonates appeared at δ = 4.45 ppm (Monomer A). The relative integral values were indicative of complete functionalization. In the case of PEG diol (Fig. 1-B), the characteristic signals of the terminal methylene protons next to the hydroxyl group (δ = 3.85 ppm) completely



Scheme 1 Isocyanate- and catalyst-free synthesis of polyurethanes in aqueous media.

disappeared, accompanied by the appearance of new signals (δ = 4.45 ppm) corresponding to methylene protons proximal to the activated carbonate units, thus confirming the completion of the reaction (Monomer B).

In the second step, polyurethanes were formed in aqueous media by reacting the activated carbonate with JEFFAMINE (Scheme 1). A discussion of the stability of the activated carbonated in water can be found in the ESI.† Five different polyurethanes were synthesized with various Monomer A (hard)/Monomer B (soft) segment ratios, as shown in Table 1. The polymerization was monitored by ^{1}H NMR, FTIR, and GPC. In all cases, >98% conversion by ^{1}H NMR was observed within 60 minutes, demonstrating high monomer reactivity.

Fig. 1-C shows the ^{1}H NMR of PU-1 after the polymerization reaction was completed (60 min). Characteristic signals (δ = 4.45 ppm) of the methylene protons located next to activated carbonates decreased in intensity and a new signal due to methylene protons linked to the urethane groups appeared at δ = 4.2 ppm confirming the formation of urethane linkages. Fig. 1D shows the ^{1}H NMR of the polyurethane generated when PEG is the sole reactant (PU-5) after the polymerization reaction was complete. As with PU-1, characteristic signals of activated carbonates again disappear and a new signal from methylene protons linked to the urethane functionality appear. These results were similar for all Monomer A/Monomer B ratios.

The polymerization process was also monitored by FTIR and GPC. The infrared spectra shown in Fig. 2 correspond to Monomer B and PU-5. As the reaction proceeds, there is an intensity decrease and a complete disappearance of the carbonate (C═O) stretch at 1760 cm^{-1}. Two new bands appear

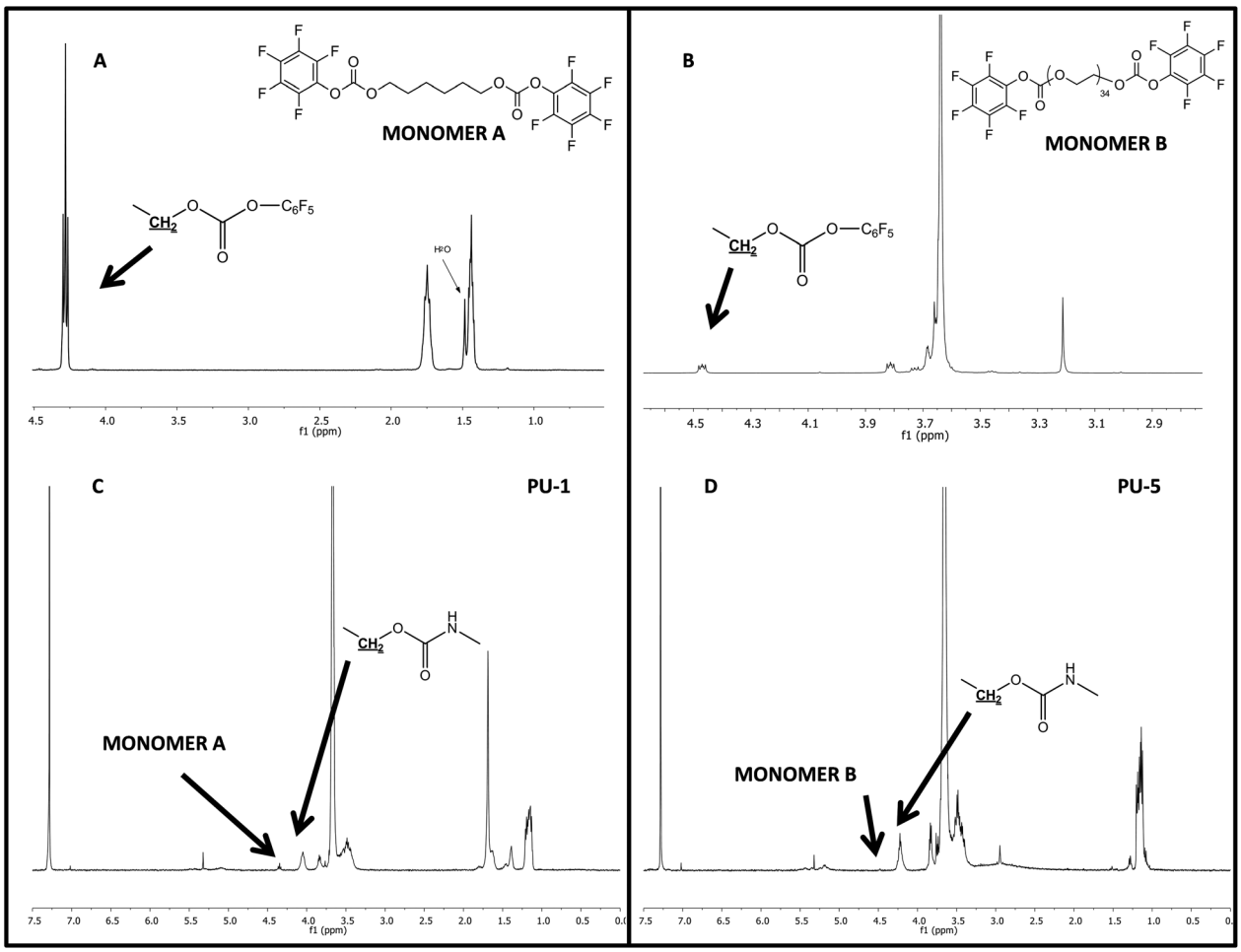


Fig. 1 Scale expanded ^{1}H NMR spectra of Monomer A (1-A), PU-1 (C), Monomer B (B) and PU-5 (D).

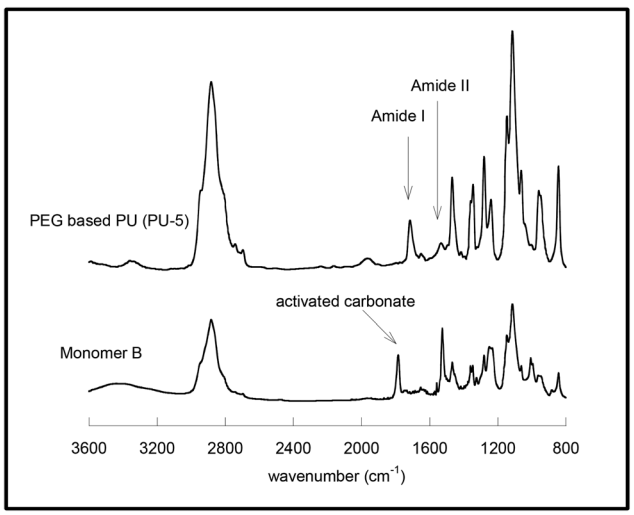


Fig. 2 Infrared spectra of Monomer B and at 98% conversion for the ≈100% PEG based PU (PU-5).

(amide I at 1720 cm^{-1}, and amide II at 1550 cm^{-1}), confirming successful urethane linkages formation. To further verify high molecular weight polymers formation, GPC analysis was done for all the Monomer A/Monomer B ratios tested (Table 1). The data in Fig. 3 show a comparison between the GPC traces of PU-5, JEFFAMINE, and Monomer B. High molecular weight polyurethanes were synthesized *via* the activated carbonate route when either a small molecule monomer (Monomer A) or a macromolecular monomer (Monomer B) was exclusively copolymerized with JEFFAMINE. The molecular weights achieved are significantly higher than those attained through different aqueous-phase methods. Landfester *et al.* reported an $M_n \approx 7000$ g mol^{-1} product using mini-emulsion polymerization,[15] and Endo *et al.* reported $M_n \approx 4500$ g mol^{-1} using a method involving the aqueous-phase polyaddition reaction between bifunctional cyclic carbonates and diamines.[29] Furthermore, molecular weight stagnation often observed with step growth polymerizations was not observed. When preparing polyurethanes *via* isocyanate-based step growth polymerization, the molecular weight is generally dependent on stoichiometry and molar balance, especially at high conversions.[30] These factors usually prevent high molecular weights from being achieved.

To avoid stagnation, polyurethanes obtained by isocyanate chemistry are usually prepared in a two-step process using an external catalyst. In a preliminary step, polymer materials of

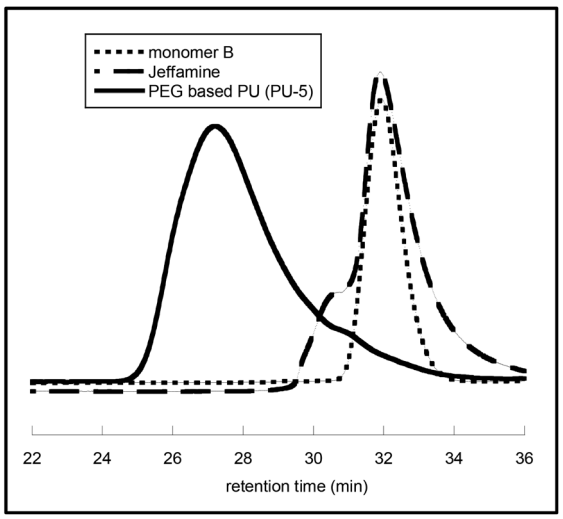


Fig. 3 GPC traces of starting materials, PEG, JEFFAMINE, and the resulting polyurethane (PU-5) at near-complete conversion.

low average molecular weights (prepolymers) are synthesized through the reaction of polyol and excess of diisocyanate. In the second step, a more reactive short-chain diol is added to efficiently complete the polymerization.[31] In the few examples where very high MW polyurethanes were obtained, very harsh and specific conditions had to be employed: (a) high temperatures, (b) bulk polymerization conditions, and (c) the use of a strong catalyst (*e.g.* bicyclic penta-alkylated guanidines or an organotin reagent).[19] The high reactivity of the monomers utilized with our protocol permits the formation of high molecular weight polyurethanes in a single step without an external catalyst or high temperatures.

Polyurethanes are considered ideal materials for adhesives due to their affinity for a wide variety of substrates, and the ability to tailor the melting temperature is crucial in designing hot-melt bioadhesives. The thermal properties of the synthesized polyurethanes were evaluated by DSC. The glass transition temperature (T_g), melting temperature (T_m), and transition enthalpy (ΔH) values of all the synthesized polyurethanes, JEFFAMINE and Monomer B are reported in Table 2. Pure PEG (M_n = 1500 Da) is a semi-crystalline polymer with a T_m of 50 °C while JEFFAMINE is an aliphatic diamine derived from a propylene oxide capped poly(ethylene glycol) with a T_m of 10 °C.

All the synthesized polymers showed endothermic transitions between 27 °C and 33 °C, attributed to crystalline PEG segment melting. In all cases, one endothermic peak is observed, confirming the presence of the polymeric structure. As expected, the polyurethane degree of crystallinity and T_m decrease as the proportion of crystalline monomer (Monomer B) was reduced. Nevertheless, it is important to highlight that, in the case of PU-1, the T_m is significantly higher than pure JEFFAMINE, increasing from 10 °C to 27 °C. The increase in T_m is a result of the polymerization event between the JEFFAMINE and Monomer A and shows that with a simple change in reagents, T_m can be readily tailored for various applications. The T_g of the polyurethanes have similar values, −55 ± 2 °C. As expected, this T_g value is between those of PEG and JEFFAMINE.

Table 2 T_g, T_m and ΔH values of all the synthesized polyurethanes

Sample	T_g (°C)	T_m (°C)	ΔH (J g^{-1})
JEFFAMINE	−50	10	70
PEG	−68	51	129
PU-1	−55	27	65
PU-2	−55	28	68
PU-3	−53	31	74
PU-4	−56	32	80
PU-5	−55	33	82

Conclusions

In conclusion, a series of polyurethanes were synthesized in aqueous solution *via* an isocyanate- and catalyst-free polymerization method. Five different polyurethanes were synthesized by first converting 1,6-hexanediol or poly(ethylene glycol) to activated dicarbonates and then copolymerizing various ratios of these two dicarbonates with JEFFAMINE (M_n = 2000 g mol^{-1}). The polymerization process was confirmed by FTIR, ^{1}H NMR, and GPC analysis. High molecular weight polyurethanes were easily obtained in one step due to the high reactivity of activated carbonates. Molecular weights were not significantly affected by the chain length of activated carbonate. The melting temperature (T_m) was linearly dependent on the 1,6-hexanediol/poly(ethylene glycol) ratio, with higher T_m values and increased crystallinity observed with greater poly (ethylene glycol) content, as confirmed by DSC analysis.

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Notes and references

1 K. Mequanint, A. Patel and D. Bezuidenhout, *Biomacromolecules*, 2006, **7**, 883–891.
2 P. Vermette, H. J. Griesser, G. Laroche and R. Guidoin, *Biomedical Applications of Polyurethanes*, Landes Bioscience, Georgetown, TX, USA, 2001.
3 D. K. Chattopadhyay and K. V. S. N. Raju, *Prog. Polym. Sci.*, 2007, **32**, 352–418.
4 D. K. Chattopadhyay and D. C. Webster, *Prog. Polym. Sci.*, 2009, **34**, 1068–1133.
5 C. Hepburn, *Polyurethane elastomers*, Elsevier Applied Science, New York, New York, 1992.

6 S. Grad, L. Kupcsik, K. Gorna, S. Gogolewski and M. Alini, *Biomaterials*, 2003, **24**, 5163–5171.
7 A. Karchin, F. I. Simonovsky, B. D. Ratner and J. E. Sanders, *Acta Biomater.*, 2011, **7**, 3277–3284.
8 X. Gu and P. T. Mather, *Polymer*, 2012, **53**, 5924–5934.
9 P. K. Maji, N. K. Das and A. K. Bhowmick, *Polymer*, 2010, **51**, 1100–1110.
10 R. J. Zdrahala and I. J. Zdrahala, *J. Biomater. Appl.*, 1999, **14**, 67–90.
11 J. Zimmermann, T. Loontjens, B. J. R. Scholtens and R. Mülhaupt, *Biomaterials*, 2004, **25**, 2713–2719.
12 H. Sardon, L. Irusta and M. J. Fernández-Berridi, *Prog. Org. Coat.*, 2009, **66**, 291–295.
13 M. C. Tanzi, P. Verderio, M. G. Lampugnani, M. Resnati, E. Dejana and E. Sturani, *J. Mater. Sci.: Mater. Med.*, 1994, **5**, 393–396.
14 H. Sardon, L. Irusta, M. J. Fernández-Berridi, M. Lansalot and E. Bourgeat-Lami, *Polymer*, 2010, **51**, 5051–5057.
15 M. Barrère and K. Landfester, *Polymer*, 2003, **44**, 2833–2841.
16 M. Helou, J.-F. Carpentier and S. M. Guillaume, *Green Chem.*, 2011, **13**, 266–271.
17 M. Sobczak, C. Dębek, E. Olędzka, G. Nałęcz-Jawecki, W. L. Kołodziejski and M. Rajkiewicz, *J. Polym. Sci., Part A: Polym. Chem.*, 2012, **50**, 3904–3913.
18 M. Firdaus and M. A. R. Meier, *Green Chem.*, 2013, **15**, 370–380.
19 D. Tang, B. A. J. Noordover, R. J. Sablong and C. E. Koning, *J. Polym. Sci., Part A: Polym. Chem.*, 2011, **49**, 2959–2968.
20 J. Alsarraf, Y. A. Ammar, F. Robert, E. Cloutet, H. Cramail and Y. Landais, *Macromolecules*, 2012, **45**, 2249–2256.
21 S. Guillaurme, M. Helou, J.-F. Carpentier and M. Slawinski, *World Pat.*, WO/2012/007254, 2012.
22 S. H. Pyo, P. Persson, M. A. Mollaahmad, K. Sorensen, S. Lundmark and R. Hatti-Kaul, *Pure Appl. Chem.*, 2012, **84**, 637–661.
23 D. Tang, D.-J. Mulder, B. A. J. Noordover and C. E. Koning, *Macromol. Rapid Commun.*, 2011, **32**, 1379–1385.
24 J. M. J. Fréchet, M. S. Standley, R. Jain and C. C. Lee, *United States Pat.*, WO/2007/131193, 2007.
25 F. B. Stilmar, *United States Pat.*, US2757191, 1955.
26 K. Knop, R. Hoogenboom, D. Fischer and U. S. Schubert, *Angew. Chem., Int. Ed.*, 2010, **49**, 6288–6308.
27 C. Kojima, K. Kono, K. Maruyama and T. Takagishi, *Bioconjugate Chem.*, 2000, **11**, 910–917.
28 Y. P. Li, Y. Y. Pei, X. Y. Zhang, Z. H. Gu, Z. H. Zhou, W. F. Yuan, J. J. Zhou, J. H. Zhu and X. J. Gao, *J. Controlled Release*, 2001, **71**, 203–211.
29 B. Ochiai, Y. Satoh and T. Endo, *Green Chem.*, 2005, **7**, 765–767.
30 B. Pukánszky Jr., K. Bagdi, Z. Tóvölgyi, J. Varga, L. Botz, S. Hudak, T. Dóczi and B. Pukánszky, *Eur. Polym. J.*, 2008, **44**, 2431–2438.
31 N. M. K. Lamba, K. A. Woodhouse and S. L. Cooper, *Polyurethanes in Biomedical Applications*, CRC Press LLC, Boca Raton, Florida, 1998.

