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Syntheses of high molecular weight hydroxy functional copolymers by green and selective polycondensation methods†

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Synthesizing hydroxy-functional linear copolymers with high molecular weights (M_n) and low branching degree (Den%) remains challenging, although there has been much headway in the area of functional copolymers. Here, we studied the effect of polymerization methods (one-step or two-step) and solvents (organic solvent: diphenyl ether or ionic liquids: $[C_n\text{mim}]TF_2N/BF_4/PF_6$, $n = 2, 4, 6, 8$, or 10) on M_n and Den% of copolymers P(OA–GA) (1,8-octanediol adipate (O-A)/glycerol adipate (G-A)). The M_n of P(OA–GA) reached up to 53 937 g mol^{-1} in two-step in diphenyl ether, and the Den% of glycerol can be controlled within 30%. The physical properties of these copolymers were investigated by contact angles, differential scanning calorimetry (DSC), and *in vitro* biodegradation. With increasing glycerol content in the polyesters, both hydrophilic properties and degradation properties increased. This system not only facilitates the synthesis of functional polyesters with high molecular weight and low branching, but also expands the possibility of using bio-based monomers to synthesize functional polymers.

Introduction

Aliphatic polyester is a member of the polyester family, and widely used in packaging, healthcare, pharmacies, and electronics because of its biodegradability, biocompatibility, and good physical and chemical properties *versus* traditional polymers.[1,2] However, the lack of modifiable pendent functional groups on the backbone limits the large-scale application of these polyesters. Thus, much work has been focused on synthesizing polyesters derived from polyols. These are expected to find an efficient method to obtain polyesters with free functional hydroxyl groups which can be further functionalized.[3–5]

Glycerol is the simplest polyol with three hydroxyl groups. It was naturally synthesized from animals, plants, and microorganisms by diversified avenues,[6] and the US Food and Drug Administration (FDA) has confirmed that it is safe for medical applications.[7,8] It can be used directly in polyester synthesis *via* esterification or transesterification, but the synthesis of highly functional, linear polyesters by glycerol remains a major challenge due to its multiple hydroxyl groups. Special reaction conditions and an accurate control method are needed to form selective ester bonds. These steps play critical roles in the maintenance of the integrity and the linearity of the obtained polyester.

Methods using polyol for the synthesis of polymers with functional extension are under intense study. Shibata *et al.*[4] used low temperature polycondensation technology to synthesize polyesters (M_n = *ca.* 1.0 × 10^4 g mol^{-1}) with dangling hydroxyl groups by using Lewis acids catalysed in solvent-free systems. The reactivity of the pendent hydroxyl group was demonstrated through further glycosylation. Gustini *et al.*[9] synthesized a renewable linear polyester derived from sorbitol through solvent-free polycondensation and then studied the efficiency and selectivity of different catalytic systems by incorporating sorbitol. Enzyme catalysis offers several advantages over chemical catalysis, including high enantio- and regioselectivity, mild reaction conditions, and low energy consumption.[10] Despite the many advantages of enzymatic catalysts, solvent-free systems are not an optimal approach to preparing functional polyesters. They require a substantial amount of energy, and polyesters synthesized *via* this method often have a lower molecular weight.

Solution systems may improve the rate of interchain transesterification when N-435 is the catalyst. Taresco V *et al.*[11] used Novozyme-435 (N-435) as a catalyst to synthesize a series of poly(glycerol adipates) (PGA) in tetrahydrofuran (THF) and adjusted the structure (trisubstitution from ~5% up to ~30%) by reaction temperature, M_n was up to 1.3 × 10^4 g mol^{-1}. Mahapatro *et al.*[12] studied the influence of substrates and solvents on polycondensations catalysed by N-435. For polyesterification compared other three solvents (xylene, tetra-

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ethylene glycol dimethyl ether, and 2-methoxyethyl ether), diphenyl ether was a more desirable solvent. The solvent should have a sufficiently high boiling point to remove the by-product from the reaction. Moreover, the catalyst activity in solvent is also a key factor in synthesizing polyesters with high molecular weight. Ionic liquids (ILs), compounds with low vapor pressures and high chemical, thermal stability, and solubility for many organic or inorganic substances[13] and have tunable solubility and are recoverable,[14] have been widely used in polycondensation reactions such as polyamides, polyimides,[15,16] and other good performance polymers[17] to obtain polymers in milder reaction conditions. Heise and others[18–21] synthesized poly(ε-caprolactone) ($M_n \leq$ 10 000 g mol^{-1}) by N-435 catalysed ring opening polymerization, and polyesters ($M_n \leq$ 5400 g mol^{-1}) by N-435 catalysed synthesized from transesterification. Fradet *et al.*[22] synthesized poly (glycolic acid) from glycolic acid or oligomers in imidazolium-based ionic liquids. The number average of oligomers could be up to 45 *via* polymerization in 1-butyl-3-methylimidazolium bis[(trifluoromethyl)-sulfonyl]-imide. Poor miscibility of poly(glycolic acid) with solvent and inferior activity of metal catalysts in ILs results in low molecular weight. Studies by Lv *et al.*[23] indicated that N-435 has higher activity in $[PF_6]^-$- and $[NTf_2]^-$-based ILs than $[BF_4]^-$- and $[N(CN)_2]^-$-based ILs. However, the relationship between the structure of hydroxy-functional polyesters and solvent properties remains largely unexplored.

The aim of this work is to explore a benign, eco-friendly method of polymerization for hydroxy-functional polyesters with high molecular weight. The first goal was to construct a model reaction of P(OA–GA) *via* solution polymerization. Adipic acid and 1,8-octanediol (OD) act as co-monomers for glycerol. These monomers are available from renewable sources.[24,25] Diphenyl ether and [C$_6$mim] Tf$_2$N were selected as reaction solvents due to their sufficiently high boiling point and activities for N-435. Polymers were first synthesized *via* a one-step or two-step method. Relevant factors in this comparative study included pre-condensation and condensation conditions. Specifically, they include the influence of the feed ratio, the amount of catalyst used, the reaction time, and the reaction temperature on properties of the products. Further study evaluated different ionic liquids including [C$_n$mim]Tf$_2$N/BF$_4$/PF$_6$ (n = 2, 4, 6, 8, or 10) to discover the influence of ILs characteristic on structure and molecular weight of hydroxy-functional polyesters. This is a new approach to synthesizing co-polyesters with high molecular weights and low degrees of branching.

The details of the copolyesters were studied in detail *via* ^{1}H NMR, ^{13}C NMR, and GPC. The hydrophilic, thermal properties and degradation properties of the hydroxyl-functional polyesters were tested *via* contact angles, DSC and vitro biodegradation, respectively.

Experimental section

Materials

Glycerol (99% pure) was purchased from Aldrich; 1,8-octanediol (98%, 1,8-OD) and adipic acid (98%) were purchased from Macklin. Diphenyl ether was purchased from Adamas. All ionic liquids were purchased from Shanghai Chengjie Chemical Co., Ltd. Tetrahydrofuran (THF) and methanol were purchased from Tianjin Fuyu Fine Chemical Co., Ltd. All reagents were used without further purification. Novozyme-435 (specified activity 7000 PLU g^{-1}) was provided by Novozymes.

Syntheses of oligo-esters

Prepolymer P(OA–GA) (1,8-octanediol adipate (O-A)/glycerol adipate (G-A)) was synthesized by solvent-free polymerization. In this process, 2.92 g (0.02 mol) adipic acid, 2.34 g (0.016 mol) 1,8-OD, and 0.37 g (0.004 mol) glycerol were added in a 25 ml two-necked round bottom flask. The flask was placed into an oil bath with a magnetic stirrer at 500 rpm and heated at 130 °C, 140 °C, and 150 °C for 1 h and 160 °C for 2 h. Nitrogen is used to remove the byproduct water. The prepolymer was collected after cooling and directly applied to the polycondensation.

Lipase-catalysed post-polycondensations in different solvents

The prepolymer and catalyst (N-435) (10 wt% of monomer) were placed in a 10 ml round-bottom flask and then reacted in diphenyl ether (2 : 1 v/w of prepolymer) or [C$_n$mim]Tf$_2$N/BF$_4$/PF$_6$ (n = 2, 4, 6, 8, 10) (35 wt% prepolymer, 65 wt% ionic liquid). The flask with the reactants was vacuumed and filled with dry nitrogen three times. The flask was then heated at 60 °C in an oil bath at 500 rpm for 24 h under vacuum (1.5–3 mmHg). The product was cooled and dissolved in tetrahydrofuran (THF); the N-435 was removed by filtration. Excess THF of the polymer solution was removed by rotary evaporation and precipitated in methanol. The precipitate was dried in a vacuum oven for 24 h.

Nuclear magnetic resonance

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 MHz spectrometer using chloroform-d$_6$ as solvent. Chemical shifts (ppm) are expressed relative to the internal reference tetramethylsilane (TMS, 0.00 ppm).

Molecular weight

The number-average molecular weight and polydispersity of copolymers were determined by gel permeation chromatography (GPC) equipped with a Waters HPLC system. The Waters HPLC system consists of a 510 pump, a 717 autosampler, and a 410 refractive index detector. Separations were achieved using a Waters Stryragel HT3, HT4, and HT5 columns in series. Tetrahydrofuran (THF) was the solvent, and the flow rate was 0.8 ml min^{-1}. The system was calibrated with polystyrene molecular weight standards from 2830 K to 2640 K (from Polymer Laboratory). The sample concentration was 3–4 mg ml^{-1}, the injection volume was 10 μL, and then the data were analysed by Trisec GPC software version 3.

Contact angles

Contact angles of the copolymers were measured using a KSV Cam200 (KSV Instruments Ltd., Helsinki, Finland) at 25 °C. The resulting copolymers were adhered to the slides and compressed into flakes. The shape and the contact angle were analysed by dedicated software (CAM200). Each sample was measured at five different sites and then averaged.

Differential scanning calorimetry (DSC)

Differential scanning was documented by an analyser (Q2000, TA Instruments, Leatherhead, UK). Two heating/cooling cycles from −70 °C to 120 °C were used to analyse the sample at a heating rate of 10 °C min^{-1}. Nitrogen gas at 50 ml min^{-1} purged the DSC cell. Data were reported and analysed with software (Version 4.5.05A).

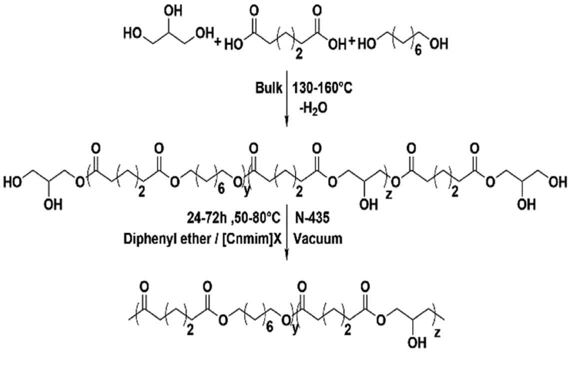
Vitro biodegradation

The *in vitro* biodegradation rates of the P(OA–GA) sample were measured by changes in dry weight. The sample (20 mg) was weighed and melted at 60 °C in a 1.5 ml small vial for 6 h in a vacuumed drying oven. The sample was cooled to room temperature and treated with phosphate-buffered saline (1.5 ml) and then incubated on a shaking table. The temperature of the shaking table is 37 °C. It was rotated at 160 rpm. After 24 h, the sample was removed and washed with deionized water and then vacuum dried at 30 °C until the mass of the sample remained constant. The weight loss was calculated with eqn (1) (W_i: initial weight, and W_d: dried weight). Three replicates were averaged:

$$\text{Weight loss } (\%) = \left[\frac{W_\text{i} - W_\text{d}}{W_\text{i}}\right] \times 100. \qquad (1)$$

Results and discussion

This work concentrated on the synthesis of functional polyester P(OA–GA) (Scheme 1) with a high molecular weight by N-435 catalysed in solvent polycondensations. Of particular interest is the construction of the P(OA–GA) model. Diphenyl ether and $[\text{C}_6\text{mim}]\text{Tf}_2\text{N}$ were used as solvents to compare the effects of polycondensation method, pre-polycondensation, and polycondensation conditions on the structure and molecular weight of P(OA–GA). These included the feed ratio, species of solvent, catalyst amount, reaction time, and temperature. Further studies were conducted in different ionic liquids to understand the characteristics of ionic liquids as a polymerization solvent.



Scheme 1 Procedure for two step polycondensation.

Model reaction of P(OA–GA)

Glycerol has multiple hydroxyl groups, and esterification of carboxylic acid and their derivatives can be performed at both primary and secondary hydroxyls of glycerol. These systems can lead to the branching of the chain and even chain–chain crosslinking. The main challenge faced by many experiments is the preparation of highly functional linear polyesters.[26] The P(OA–GA) copolymer can be dissolved in tetrahydrofuran, and no chain–chain crosslinking was seen.

The P(OA–GA) structure was determined by ^{1}H NMR (Fig. S1†). The main chain of the methylene protons of adipic acid and 1,8-octanediol in P(OA–GA) is clearly observed at 1.3–2.4 ppm and 4.05 ppm followed by the –OH proton peak at 3.7 ppm. All protons of glyceride with repeating units were found between 3.5 and 5.3 ppm. Peaks among 5.1–5.3 ppm were believed to be the secondary ester signal, which indicated that a part of secondary hydroxyl of glycerol participated in the reaction. The peak at 5.10 and 5.26 ppm (h' and h'' in Fig. S1 and Fig. S1† inset) corresponds to the methyl proton of a disubstituted glycerol unit ($L_{1,2}$) by esterification of adipic acid with primary-secondary and a methine proton of trisubstituted glycerol unit (Den), respectively. Interestingly, the peak was not noticeable when $[\text{C}_6\text{mim}]\text{Tf}_2\text{N}$ was the solvent (Fig. S1,† inset), which indicated that glycerol with lower branching degree in $[\text{C}_6\text{mim}]\text{Tf}_2\text{N}$ than diphenyl ether. A sharp singlet was observed at 7.26 ppm due to CDCl_3. The multiple peak groups next to the solvent peak were attributed to the diphenyl ether. The diphenyl ether has a high boiling point (259 °C) and melting point (27 °C); thus, it is difficult to separate from the product.

The macromolecular architecture of P(OA–GA) was further accurately defined by ^{13}C NMR (Fig. 1). The ^{13}C NMR qualitatively analysed the type of methine carbon (which determined the existence of different glyceride groups). It also quantitatively determined the proportion of each glyceride group. Peak distribution is consistent with Kulshrestha *et al.*[27] Four methine (–CH–) signals of glycerol units from different substitution patterns were found in the 67–73 ppm (Fig. 1). The observation of a single peak at 70.3 ppm is due to the terminal glycerol units (Ter) that were formed *via* esterification of the adipic acid with a glycerol primary hydroxyl. The peak at 68.9 ppm is due to trisubstituted or dendritic glycerol units (Den). The signal of disubstituted glycerol units was seen at 72.1 and 68.2 ppm including $L_{1,2}$ and $L_{1,3}$ formed by esterification of adipic acid with primary–secondary or primary–primary hydroxyls of glycerol, respectively. The relative percentages of Ter, $L_{1,2}$, $L_{1,3}$, and Den were calculated by eqn (2)–(5) and are summarized in Table 1.

The effects of the polymerization method on the relative percentages were explored in diphenyl ether (entries M1 and M2, Table 1) and in $[\text{C}_6\text{mim}]\text{Tf}_2\text{N}$ (entries M6 and M7, Table 1). The degree branching (Den) of products using the two-step method was higher than that using the one-step due to the higher pre-polymerization temperature. Entries M2–M4 (Table

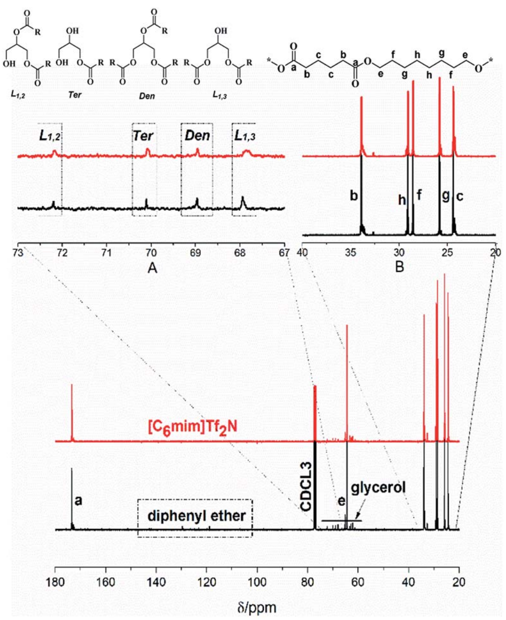


Fig. 1 ^{13}C-NMR spectrum of P(OA–GA), showing the signals corresponding to different methine groups of the synthesized P(OA–GA) polymers.

1) showed the effect of pre-polymerization temperature on the polymer structure. The amount of Den, $L_{1,2}$, and $L_{1,3}$ increased with temperature; the content of Ter decreased slightly, which indicates that more glycerol is incorporated into the polymer backbone. The results of entries M4 and M5 and M7–M9 in Table 1 showed that the diol/diacid ratio was over unity is necessary to formulate low-branched polymers. In addition, more low-branched polymers were discovered in [C$_6$mim]Tf$_2$N (entry M8, Table 1) than in diphenyl ether (entry M5, Table 1). It's worth noting that the gel content in the reaction increased based on visual observation when using a one-step method in diphenyl ether after 24 h. The solvent test found that the product was even difficult to dissolve in a strong polar solvent such as dimethyl sulfoxide (DMSO). Gel formation is attributed to cross-linking reactions. No gelation was observed when the reaction time was shortened to 12 h. The copolymer can be completely dissolved in THF.

$$\mathrm{Ter}\% = \frac{[\mathrm{Ter}]_\mathrm{I}}{[L_{1,2}]_\mathrm{I} + [L_{1,3}]_\mathrm{I} + [\mathrm{Ter}]_\mathrm{I} + [\mathrm{Den}]_\mathrm{I}} \times 100 \tag{2}$$

$$L_{1,2}\% = \frac{[L_{1,2}]_\mathrm{I}}{[L_{1,2}]_\mathrm{I} + [L_{1,3}]_\mathrm{I} + [\mathrm{Ter}]_\mathrm{I} + [\mathrm{Den}]_\mathrm{I}} \times 100 \tag{3}$$

$$L_{1,3}\% = \frac{[L_{1,3}]_\mathrm{I}}{[L_{1,2}]_\mathrm{I} + [L_{1,3}]_\mathrm{I} + [\mathrm{Ter}]_\mathrm{I} + [\mathrm{Den}]_\mathrm{I}} \times 100 \tag{4}$$

$$\mathrm{Den}\% = \frac{[\mathrm{Den}]_\mathrm{I}}{[L_{1,2}]_\mathrm{I} + [L_{1,3}]_\mathrm{I} + [\mathrm{Ter}]_\mathrm{I} + [\mathrm{Den}]_\mathrm{I}} \times 100 \tag{5}$$

The results of number-average molecular weight (M_n) and polydispersity (PDI) were determined by GPC and summarized in Table 2. The highest M_n of the co-polyester was up to 53 937 g mol^{-1} (diphenyl ether): This is far higher than that obtained in bulk (M_n < 2.0 × 10^4 g mol^{-1}). The comparisons have been provided in Table S2.†[4,8,11,28] This proves that when N-435 is the catalyst, the solvent system is an ideal reaction system for obtaining high molecular weight copolyesters. The detailed trend of the M_n of the products are shown in Fig. 2.

Fig. 2A summarizes the influence of a condensation method on M_n of P(OA–GA). The two-step method has obvious advantages for the synthesis of high molecular weight copolyesters. The two-step method can reduce the acidity of the polycondensation system, thereby reducing the damage to the activity of the N-435. Furthermore, oligomers replaced the diacid and diol that can remove the water produced in the incipient phase of the formation of oligomers. Water affects the stability of fluorinated inorganic anions especially at elevated temperatures.[29] Fig. 2B displays the influence of pre-condensation temperature and acid/alcohol ratio for the products' M_n. The M_n of products increased with pre-temperature and higher molecular weight products could be obtained when the diol/diacid ratio was slightly over unity. This because

Table 1 The proportion of glycerol repeat unit substitution of copolymer P(OA–GA)[a]

Entry	Molar ratio A : O : G[b]	Pre-polymerization temperature[c] (°C)	Solvent	Time (h)	Ter[d] (%)	$L_{1,2}$[e] (%)	$L_{1,3}$[f] (%)	Den[g] (%)
M1	1 : 0.8 : 0.2	—	Diphenyl ether	12	11.76	14.12	58.82	15.29
M2	1 : 0.8 : 0.2	100–130	Diphenyl ether	24	18.66	10.07	39.93	31.34
M3	1 : 0.8 : 0.2	110–140	Diphenyl ether	24	14.98	10.58	39.96	34.49
M4	1 : 0.8 : 0.2	130–160	Diphenyl ether	24	12.80	12.40	40.00	34.80
M5	1 : 0.84 : 0.21	130–160	Diphenyl ether	24	12.89	15.11	44.44	27.56
M6	1 : 0.8 : 0.2	—	[C$_6$mim]Tf$_2$N	24	13.74	17.53	47.39	21.33
M7	1 : 0.8 : 0.2	130–160	[C$_6$mim]Tf$_2$N	24	13.78	15.11	44.44	26.67
M8	1 : 0.84 : 0.21	130–160	[C$_6$mim]Tf$_2$N	24	20.42	19.58	40.83	19.20
M9	1 : 0.88 : 0.22	130–160	[C$_6$mim]Tf$_2$N	24	n.d.	n.d.	n.d.	n.d.

[a] The products were synthesized through two-step method (entries M2–M5, M7–M9) or directly synthesized from monomers (M1 and M6); all post-polymerization were conducted at 60 °C, N-435 (10 wt% of monomers), in vacuum 1.5–3 mmHg. [b] A = adipic acid; O = 1,8-octanediol; G = glycerol. [c] Pre-polymerization were conducted under N$_2$ atmosphere. Data were analysed by ^{13}C NMR and calculated based on. [d] Eqn (2). [e] Eqn (3). [f] Eqn (4). [g] Eqn (5).

Table 2 Molecular weight and polydispersity of P(OA–GA) from model reaction[a]

Entry	Molar ratio A : O : G[b]	Pre-polymerization temperature[c] (°C)	Solvent	Time (h)	M_n[d] (g mol^{-1})	PDI[d] (M_w/M_n)
M1	1 : 0.8 : 0.2	—	Diphenyl ether	12	33 921	1.49
M2	1 : 0.8 : 0.2	100–130	Diphenyl ether	24	17 623	3.34
M3	1 : 0.8 : 0.2	110–140	Diphenyl ether	24	38 516	1.28
M4	1 : 0.8 : 0.2	130–160	Diphenyl ether	24	39 687	1.36
M5	1 : 0.84 : 0.21	130–160	Diphenyl ether	24	53 937	1.79
M6	1 : 0.8 : 0.2	—	[C$_6$mim]Tf$_2$N	24	4905	1.28
M7	1 : 0.8 : 0.2	130–160	[C$_6$mim]Tf$_2$N	24	11 322	1.71
M8	1 : 0.84 : 0.21	130–160	[C$_6$mim]Tf$_2$N	24	13 913	1.73
M9	1 : 0.88 : 0.22	130–160	[C$_6$mim]Tf$_2$N	24	8039	1.55

[a] The products were synthesized through two-step method (entries M2–M5, M7–M9) or directly synthesized from monomers (M1 and M6); all post-polymerization were conducted at 60 °C, N-435 (10 wt% of monomers), in vacuum 1.5–3 mmHg. [b] A = adipic acid; O = 1,8-octanediol; G = glycerol. [c] Pre-polymerization were conducted at 130, 140, 150 °C for 1 h and 160 °C for 2 h under N$_2$ atmosphere. [d] Determined by GPC measurement in THF.

diol in excess is easier to get an oligomer with a hydroxyl end-group. This is conducive to the progress of postcondensation. The unreacted alcohol monomer can function as a chain extender in the post-polycondensation to obtain higher molecular weight products. Although it is a different reaction system, Fu *et al.*[30] proved that the diol/diacid ratio of the oligomers is a key factor affecting the molecular weight of polyesters. The synthesis of P(OA–GA) by two-step method in diphenyl ether and [C$_6$mim]Tf$_2$N was repeated several times in order to evaluate the reproducibility of that procedure. It was found that the amount of trisubstituted units ranged between 15 and 30% while molecular weights in diphenyl ether up to 50 000 g mol^{-1} and in [C$_6$mim]Tf$_2$N it stays around 13 000 g mol^{-1} (Table S3†).

Post-condensation conditions of P(OA–GA) in [C$_6$mim]Tf$_2$N

Copolyester synthesized in [C$_6$mim]Tf$_2$N has lower-branched and lower molecular weight, so the polycondensation of P(OA–GA) catalysed by N-435 was further explored at different postcondensation conditions (amount of catalyst, reaction temperature, and reaction time) to further increase the molecular weight of the copolyester. The results are listed in Table 3 and Fig. 3.

The amount of catalyst affects the structure of P(OA–GA) (entries C1–C4). $L_{1,2}$ and Den increased, $L_{1,3}$ and Ter decreased slightly with increasing catalyst, which suggesting that more glycerol units are incorporated into the polymer backbone with increasing catalyst dose. There was no significant glycerol signal in ^{1}H NMR or ^{13}C NMR without catalyst. In addition, the presence of glycerol repeat unit substitution patterns changed only slightly when the temperature increased from 50 °C to 60 °C; however, the percent of Den increased from 16.17% to 20.51% when the temperature increased to 80 °C. Concurrently, the percent of Ter decreased from 20.82% to 15.81%, and the percent of $L_{1,2}$ and $L_{1,3}$ showed only minor variation (<1%). This demonstrated that the degree of branching of the product increased with polycondensation temperature. This trend is consistent with the findings of Taresco *et al.*[11] High temperatures lead to lower enzyme regioselectivity and high polymer

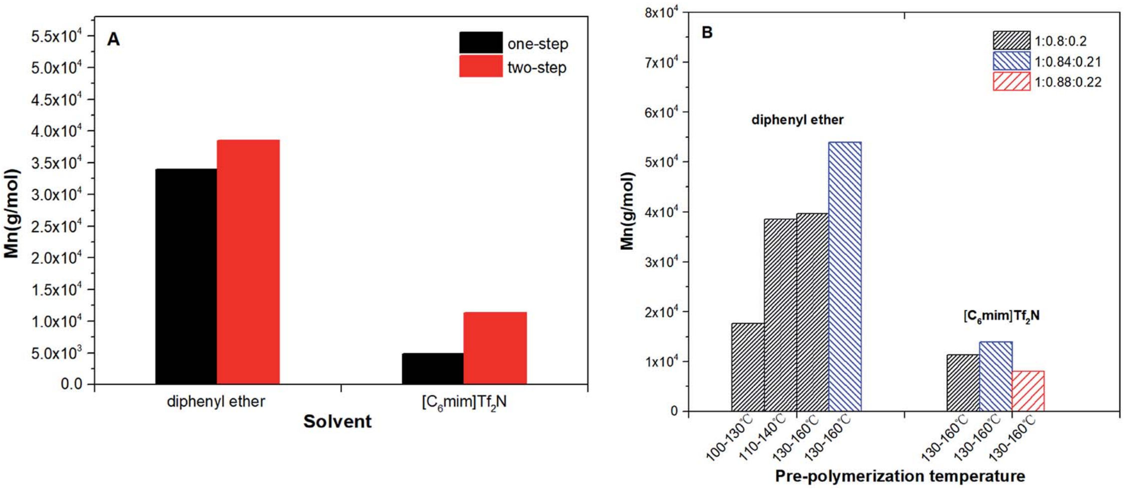


Fig. 2 P(OA–GA), synthesized by N-435 catalysis: (A) effect of solvent and polycondensation method on M_n and PDI (M_w/M_n); (B) effect of solvent and pre-condensation temperature and molar ratio on M_n and PDI (M_w/M_n).

Table 3 Polycondensations of P(OA–GA) in different conditions[a]

Entry	Tem. (°C)	Time (h)	Catalyst (wt%)	Ter[b] (%)	$L_{1,2}$[c] (%)	$L_{1,3}$[d] (%)	Den[e] (%)	M_n[f] (g mol^{-1})	PDI[f] (M_w/M_n)	Yield (%)
C1	60	24	0	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
C2	60	24	1	28.36	16.83	48.08	6.07	7087	1.34	54
C3	60	24	5	25.46	17.13	46.76	10.65	9015	1.48	77
C4	60	24	10	18.30	21.90	42.86	16.94	13 913	1.73	56
C5	50	24	10	20.82	19.18	43.83	16.17	10 298	2.03	57
C6	80	24	10	15.81	20.94	42.74	20.51	13 303	2.32	43
C7	60	48	10	19.97	17.49	42.84	19.70	16 240	1.85	66
C8	60	72	10	20.59	17.23	42.01	20.17	16 282	2.30	73

[a] All products were synthesized by two-step method. Pre-condensation conditions: adipic acid : 1,8-octanediol : glycerol = 1 : 0.84 : 0.21; 130, 140, 150 °C for 1 h and 160 °C for 2 h. Post-polycondensations of all entries were in vacuum 1.5–3 mmHg, N-435 catalysed. Data were analysed by ^{13}C NMR and calculated based on. [b] Eqn (2). [c] Eqn (3). [d] Eqn (4). [e] Eqn (5). [f] Determined by GPC measurement in THF n.d. = not determined.

branching. This is due to higher miscibility between the oligomer and the ionic liquid as the temperature increased. The degree of branching of the product also increased with reaction time (entries C4, C7, and C8). These results indicated that the quantity of catalyst is the determinants of the P(OA–GA) structure. Furthermore, a distinct correlation could be discovered on the M_n and PDI of P(OA–GA) with the amount of catalyst (Fig. 3A). There M_n increased from 7087 to 9015 and 13 913 g mol^{-1} as the catalyst increased from 1 wt% to 5 wt% and 10 wt% suggesting that N-435 is also critical in the synthesis of high molecular weight P(OA–GA). The PDI of products remained under 2.0. Fig. 3B shows the variation of M_n and PDI of P(OA–GA) with increasing reaction temperature. Reactions at 50 °C, 60 °C, and 80 °C gave products with M_n values of 10 298, 13 913, and 13 303 g mol^{-1}, respectively. The PDI reached a maximum of 2.32 at 80 °C. Fig. 3C shows that M_n and PDI continued to increase as the reaction time became longer.

Development of the ionic liquid species

The type of ILs will affect the activity of the catalyst and the solubility of the oligomer/ILs and thus the structure and molecular weight of the copolyester. N-435 has higher activity and stability in ILs with $[Tf_2N]^-$, $[PF_6]^-$, and $[BF_4]^-$ anions than ILs with anion containing stronger hydrogen bond ability such as Cl^- or $[OctSO_4]^-$.[31] Therefore, the design of this section is mainly to explore the effect of the types of ILs on M_n and Den of polyesters. The results are shown in Table 4. Higher M_n (M_n > 13 725 g mol^{-1}) was obtained in $[Tf_2N]^-$-based ILs (entries L1–L4) than $[PF_6]^-$ (entries L5–L7) or $[BF_4]^-$-based (entries L8–L10) ILs. This is because ILs containing anions $[PF_6]^-$ or $[BF_4]^-$ have more nucleophilic properties than those containing $[Tf_2N]^-$, which reduces the activity of N-435.[32]

The M_n of copolymer increased at first and then decreased with viscosity of the ILs, which suggests that an increase in the viscosity of the ILs will limit further diffusion of the polymer chain. However, the viscosity of the ILs has little effect on the molecular structure of the copolymer. The proportion of Ter, $L_{1,2}$, $L_{1,3}$ and Den changes within 3%. Oligomers were stratified with BF_4^--based ILs in post-polycondensation (entries L8–L10). The reaction is a heterogeneous reaction. Poor miscibility resulted in a lower glycerol incorporation rate, and no significant glycerol peak was observed in the ^{13}C NMR.

The addition of glycerol was increased (entries L11–L16) to further understand the influence of the ILs on the synthesis efficiency and structure of P(OA–GA). The results indicated that oligomer can be miscible with $[BF_4]^-$-based ILs (entries L14–L16), and a distinct glycerol signal could be observed in ^{13}C NMR. This is attributed to increases in the glycerin content causing an increase of the oligomer polarity. This facilitates good miscibility between oligomer and ILs with higher polarity such as BF_4^-. Nevertheless, the percent Ter in the polymer obtained in the BF_4^--based (entries L15 and L16) ILs is still higher

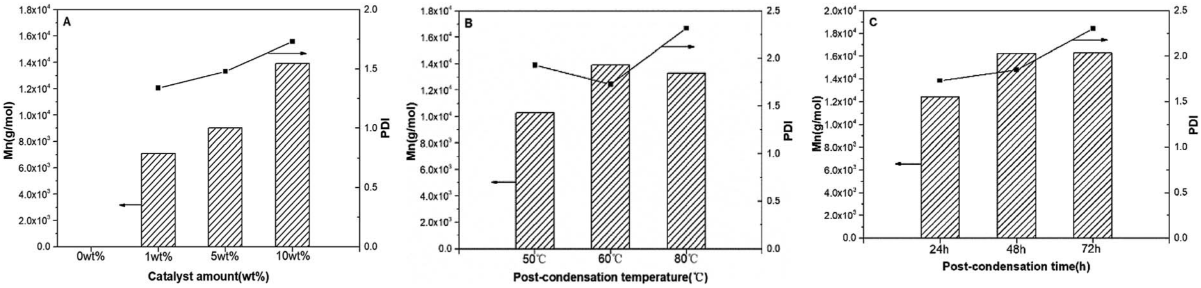


Fig. 3 P(OA–GA), synthesized by N-435 catalysis: plots of M_n and PDI (M_w/M_n) as a function of catalyst amount (A); post-condensation temperature (B); post-condensation time (C).

Table 4 Polycondensations of P(OA–GA) in different ionic liquids[a]

Entry	Molar ratio A : O : G[b]	Ionic liquid	Vis.[c]	Ter[d] (%)	$L_{1,2}$[e] (%)	$L_{1,3}$[f] (%)	Den[g] (%)	M_n[h] (g mol^{-1})	PDI[h]
L1	1 : 0.84 : 0.21	[C_2mim]TF_2N	33	21.28	19.15	42.55	17.02	13 885	2.35
L2	1 : 0.84 : 0.21	[C_4mim]TF_2N	52	20.23	19.84	41.25	18.68	17 509	1.56
L3	1 : 0.84 : 0.21	[C_6mim]TF_2N	87.3	18.30	21.90	42.86	16.94	13 913	1.73
L4	1 : 0.84 : 0.21	[C_{10}mim]TF_2N	142	21.04	20.25	42.67	16.04	13 725	2.02
L5	1 : 0.84 : 0.21	[C_4mim]PF_6	204	21.25	18.33	41.67	18.75	3280	1.04
L6	1 : 0.84 : 0.21	[C_6mim]PF_6	585	19.05	19.44	42.86	18.65	11 461	2.30
L7	1 : 0.84 : 0.21	[C_8mim]PF_6	682	26.85	18.52	46.30	8.33	5640	1.32
L8	1 : 0.84 : 0.21	[C_2mim]BF_4	38	n.d.	n.d.	n.d.	n.d.	10 945	2.06
L9	1 : 0.84 : 0.21	[C_6mim]BF_4	220	n.d.	n.d.	n.d.	n.d.	12 310	1.69
L10	1 : 0.84 : 0.21	[C_{10}mim]BF_4	930	n.d.	n.d.	n.d.	n.d.	11 223	2.15
L11	1 : 0.53 : 0.53	[C_6mim]TF_2N	87.3	17.21	17.49	39.86	25.44	10 795	1.32
L12	1 : 0.53 : 0.53	[C_4mim]PF_6	204	16.87	19.28	40.16	23.69	10 605	1.24
L13	1 : 0.53 : 0.53	[C_6mim]PF_6	585	14.8	18.4	40.00	26.80	15 158	1.37
L14	1 : 0.53 : 0.53	[C_2mim]BF_4	38	15.98	18.26	45.66	20.09	12 599	1.73
L15	1 : 0.53 : 0.53	[C_6mim]BF_4	220	31.02	16.67	46.30	6.02	5371	1.27
L16	1 : 0.53 : 0.53	[C_{10}mim]BF_4	930	33.93	16.07	44.64	5.36	4349	1.15

[a] All products were synthesized through two-step method. Pre-condensation conditions: 130, 140, 150 °C for 1 h and 160 °C for 2 h. Post-polycondensations conditions: 60 °C, N-435 (10 wt% of monomers), 24 h, in vacuum 1.5–3 mmHg. [b] A = adipic acid; O = 1,8-octanediol; G = glycerol. [c] Viscosity (mPa s, 25 °C) were provide by Shanghai Chengjie Chemical Co., Ltd. Data were analyzed by ^{13}C NMR and calculated based on. [d] Eqn (2). [e] Eqn (3). [f] Eqn (4). [g] Eqn (5). [h] Determined by GPC measurement in THF n.d. = not determined.

than that of PF_6^--based (entries L12 and L13) and Tf_2N^--based (entry L11) except [C_2mim]BF_4 (entry L14). Meanwhile, the degree of branching was reduced and terminated with glycerol, this led to lower molecular weights. [C_2mim]BF_4 (entry L14) differs from this situation with high M_n because of the low-viscosity, which indicated that an ideal viscosity of the reaction system will lead to a higher molecular weight.

Characterization

Hydrophilic test

The wettability properties were measured on polymer-coated glass by contact angle (θ) to understand the hydrophilicity/hydrophobicity characteristics of copolymer (Fig. 4). Contact angle tests indicated that the value decreased from 120° to 70° as the amount of glycerol added. P(OA–GA) prepared at feed ratio (adipic acid : 1,8-octanediol : glycerol = 1 : 0.8 : 0.2) had contact angles between 123.70° ± 1.86°. This value kept falling with the increase of the glycerol addition. The contact angles of the copolymers were $\theta = 101.54 \pm 5.29$ (adipic acid : 1,8-octanediol : glycerol = 1 : 0.84 : 0.21) and 71.05 ± 3.85 (adipic acid : 1,8-octanediol : glycerol = 1 : 0.53 : 0.53). These observations were due to the increased glycerol content and pendant hydroxyl groups of P(OA–GA). By increasing the glycerin content, more pendant hydroxyl groups are available. More hydroxyl groups pendent on the copolymer chain enhances the hydrophilicity of the material. The hydroxyl content of the products was quantitatively calculated by ^{31}P NMR (Fig. S2†) as previously reported by Gustini *et al.*[33] The data are summarized in Table S1.† Here, the 2-chloro-4,4,5,5-tetramethyl-dioxaphospholane compound reacts with the primary and secondary hydroxyl groups present on the polymer backbone. Cyclohexanol is an internal standard that quantifies the number of hydroxyl groups. Data afforded by these experiments are expressed in $mg_{KOH}\ g_{sample}^{-1}$ (Table S1†). This confirmed that the hydrophilicity increased with hydroxyl content.

Thermal performance test

Fig. 5 displays the first scan of DSC curves of these products P(OA–GA). From Fig. 5, the melting endotherms peaks were observed at 30–53 °C. Obviously, the melting temperature decreases with increasing glycerol content. This is because the crystallinity of P(OA–GA) was disrupted by glycerol units along the polyester chain. In addition, thermodynamic measurements showed that we can adjust the melting temperature of the copolymer by fine-tuning the glycerol content.

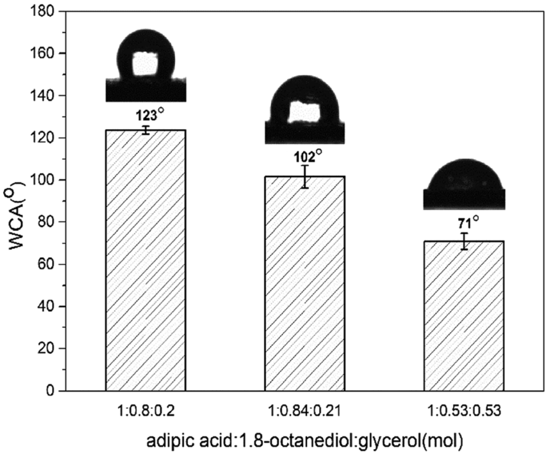


Fig. 4 Contact angle of P(OA-GA) synthesized in different feed ratio.

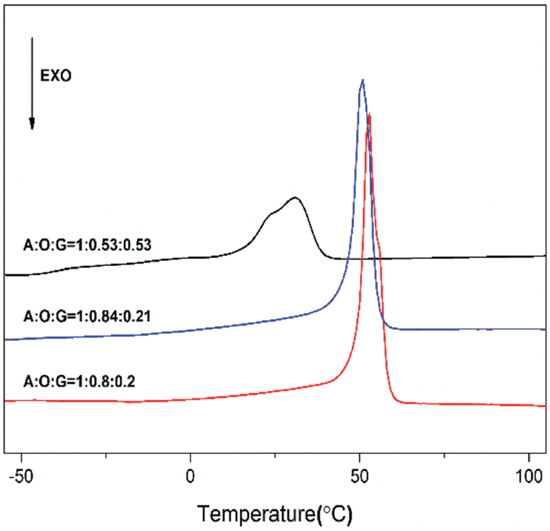


Fig. 5 DSC curves (first scan) of P(OA–GA) (content in material ratio on curves).

In vitro degradability test

P(OA–GA) was immersed in phosphate buffer (37 °C) for a predetermined time, and the degradation was studied *via* weight loss. Fig. 6 shows that no samples had significant weight loss on the first day. Two days later, P(OA–GA) (adipate : 1,8-octanoic acid : glycerol = 1 : 0.53 : 0.53) had a higher degradation than the other glycerin-doped samples. After 7 days, P(OA–GA) (adipic acid : 1,8-octanediol : glycerol = 1 : 0.8 : 0.2) lost the least amount of weight 20.4 ± 2.7%. The weight loss of P(OA–GA) (adipic acid : 1,8-octanediol : glycerol = 1 : 0.84 : 0.21) is 29 ± 0.6%. As expected, P(OA–GA) (adipic acid : 1,8-octanediol : - glycerol = 1 : 0.53 : 0.53) have the highest degradation rate, and the weight loss is 55.4 ± 2%. Which proved that the composition and hydrophobicity of the polymer can affect its degradation rate under the same environmental conditions[34,35] and the amount of added glycerol can largely adjust the degradation rate of P(OA–GA).

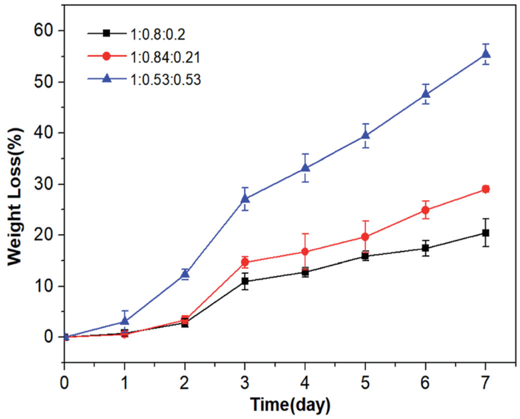


Fig. 6 P(OA–GA) co-polyester weight loss as a function of soaking time.

Conclusions

In this work, we described the polycondensation of adipic acid, 1,8-OD, and glycerol catalysed by N-435 to produce a hydroxyl functionalized polyester with high molecular weight and lower degree of branching *via* a benign and eco-friendly technique. Diphenyl ether was found to be the preferred solvent to prepare P(OA–GA) co-polyester with a high M_n ($M_n = 53\ 937$ g mol^{-1} in 24 h). Although ILs gave functional polyesters with relatively low molecular weight, this is a more environmentally-friendly route. The molecular weight of the polyesters depends on the activity of the catalyst in the ILs and the miscibility of aliphatic polyester/ionic liquid. The N-435 remained active in Tf_2N^- and PF_6^--based ionic liquids. This was substantially suppressed in BF_4^- systems. The miscibility of aliphatic polyester/ionic was determined by their viscosity and polarity. The contact angle, DSC, and *in vitro* biodegradation data confirmed that the character of products can be adjusted *via* the extent of glycerin addition. This will further expand the range of applications for hydroxyl functional polyesters. Examples include biomedical applications such as drug delivery applications and gene therapy as well as improved inks, paints, and adhesive materials. Moreover, ILs can extend the possibility of using polyol monomers to synthesize a higher molecular weight functional polymer. Our lab is extending this approach to other complex polyols, carbohydrate derivatives and polymer classes. We expect to generate polyesters of structurally unprecedented types.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

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