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New Bio-renewable Polyester with Rich Side Amino-groups from *L*-Lysine via Controlled Ring-opening polymerization

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Abstract

Lysine, a renewable resource from biomass fermentation, was simply converted to its corresponding α-hydroxyl acids and then cyclized to give the pure *O*-carboxyanhydride (OCA) monomer. Ring-opening polymerization of the resulting monomer was carried out using Dimethylaminopyridine (DMAP) as catalyst in CH_2Cl_2 at room temperature, and gave the well-defined lysine-derived polyesters bearing pendant carbobenzyloxy (Cbz) protected amino groups with number average molecular weight up to 45 kg/mol in narrow polydispersity. ^{1}H NMR, GPC, and MALDI-TOF MS measurements of the products clearly indicated a controlled/living character of the polymerization. Moreover, amino-functionalized polyesters were readily prepared by the removal of the Cbz protecting group, and integrity of the polyester backbone was confirmed by ^{1}H NMR. These amino-functionalized polyesters showed tunable glass transition temperature and exhibited excellent cell compatibility, suggesting their potential being used as novel materials in biomedical applications.

1. Introduction

Amino acids are biological monomers and indispensable compounds for the life process in nature.[1] Among the various natural amino acids, *L*-lysine, with pendent amino-group, constitutes a major series of natural amino acids.[2] *L*-lysine is a naturally available renewable resource, and along with dwindling petroleum and eventually depletion of fossil resources, the controlled synthesis of bio-based polymers derived from *L*-lysine has recently become a growing research focus.[3-4] In particular, synthetic polymers based on *L*-lysine have been of great interest in chemistry-biology interface due to their potential application in gene transfection,[5-6] drug delivery,[7] and prevention of viral infections.[8]

Polymerization of *L*-lysine is a long term concern, even though the results are not always satisfactory in the literature. Peptide linkages were routinely formed by the direct self-condendation of *L*-lysine using water removal agents such as EDC; however, this approach can only produce oligomers of *L*-lysine with molecular weight less than 1500 g/mol, and the reaction yield was quite low.[9] Ring-opening polymerization of lysine via *N*-carboxyanhydride (NCA) intermediate was an important approach to make homopolymer of lysine (α-poly-lysine, α-PL).[10-12] However, α-PL has cytotoxic effects, which limits its biomedical applications.[10] ε-poly-lysine (ε-PL) is a naturally occurring polymer comprising 25 to 30 residues of l-lysine with ε-amino group and α-carboxyl group linkages.[9] ε-PL is mostly used as food preservative and cosmetic additive because of its antimicrobial properties and nontoxicity. ε-PL is produced using an aerobic fermentation system, however, this

route was not capable of making higher molecular weight polymers having more than 30 repeating units.[13-14] As we all know, polymers are long chain molecules that comprise covalently connected moieties, and that interact via relatively weak intermolecular forces. These structural features are responsible for many special properties of polymeric materials and make them different from traditional materials such as low molecular weight organic compounds, ceramics and metals. Generally, increasing polymer chain length (molecular weight), many chemical and physical properties improve, notably their mechanical performance.[15] Hence, more effective transformation reaction of lysine into novel functional and higher molecular weight polymers would open up a new direction of research activities toward lysine-based polymers for commercial applications in biodegradable materials.[16]

As a consequence of structural similarity between amino acids and α-hydroxyl acids, the attempt to synthesize *O*-carboxanhydride (OCA) from lysine and polymerize it to make polyesters bearing pendant amino-group has attracted our interest. The ring-opening polymerization (ROP) of OCA by liberating a molecule of CO_2 is able to generate side-chain functionalized polyesters effectively.[17-23] Taking advantage of the OCA ROP strategy, Bourissou and co-workers have demonstrated that the synthesis and ROP of *L*-gluOCA, the *O*-carboxyanhydride derived from glutamic acid.[18] Well-controlled homo- and co-polymers with pendant carboxylic acid groups are shown to be accessible under mild conditions via DMAP-catalyzed ROP. Cheng have reported the design and synthesis of polyesters bearing pendant hydroxyl groups by integrating ROP of *O*-benzyl-*L*-serine carboxyanhydrides followed by the

removal of the benzyl group.[22] However, most of the prior works on ROP of OCA have focused on developing polymers featuring pendant carboxylic acid and hydroxyl groups.[24] Amino-functionalized polyesters are potentially excellent candidates for nonviral gene delivery due to their biocompatibility and biodegradability;[25] however, most of the amino-functionalized polyesters were synthesized by polycondensation leading to polymers with poorly controlled MWs and broad molecular weight distributions (MWDs).[26-30] Synthesis and polymerization of amino-functionalized lactone may also produce polyester with pendent amino group,[31] and amino-functional δ-valerolactone and ε-caprolactone was synthesized and polymerized;[32-33] however, the ROP of these protected amino-functionalized lactones led to polyesters with low molecular weight, attributed to the steric hindrance present from the bulky pendant groups. The combination of ROP and click chemistry methodologies offers another choice, and poly(ε-caprolactone) with pendent quaternized amine groups have been made; however, the ratio of amino groups in the polyester backbone is low.[34-37]

The aim of this study was to develop a strategy to synthesize a new OCA monomer and amino-functionalized renewable polyester from abundant low-cost natural resources: lysine. Highly pure lysine-derived OCA monomer was prepared through diazotization followed by cyclization (Scheme 1). The well-defined lysine-derived polyesters bearing pendant Cbz protected amino groups with low polydispersity and higher molecular weight were obtained using living/controlled ROP. Cleavage of the Cbz protecting groups, ultimately produced

amino-functionalized lysine-based polyesters (Scheme 1). Unlike ROP of amino-functionalized lactone, which can only yield polyester with relatively low molecular weight, our work offers a new route to produce lysine-based polyester with M_n up to 45 kg/mol, which is extremely important for its future applications. Moreover, different from α-poly-lysine from ROP of NCA, lysine-based polyester prepared here showed excellent cell compatibility, which is also quite important for future biomedical applications, especially for *in vivo* applications.

2. Materials & Methods

2.1. Materials

Dichloromeane (DCM), tetrahydrofuran (THF) and $CHCl_3$ from Beijing Chemical works was refluxed over CaH_2 then distilled, degassed and stored under a nitrogen atmosphere. Dimethylaminopyridine (DMAP) purchased from Aladdin was purified by recrystallization in toluene and stored under nitrogen. All alcohol initiators were obtained from Aldrich and dried over sodium and distilled before use. *L*-lysine monohydrochloride (99%) was from Chengdu Baishixing Chemical Industrial Co., Ltd. All other chemicals and solvents were obtained from Aldrich and used as received.

2.2. Measurements

^{1}H NMR spectra were recorded on a Varian Unity-400 spectrometer using $CDCl_3$ or D_2O as solvent. Gel-permeation chromatography (GPC) was used to determine the

molecular weights and polydispersities of the synthesized polymers. GPC in Dichloromethane (DCM) was conducted on a system composed of a Waters 2414 Refractive Index Detector quipped with a guard column (Waters Styragel, 50×7.8 mm) and two mixed HT columns (Waters Styragel HT4 and HT5, 300×7.8 mm). Calibrations were performed using polystyrene standards (Shodex M_p = 1270-2700000 g/mol). Matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy (MALDI-TOF/MS) was performed on a Bruker atuoflex III mass spectrometer in linear, positive ion mode. The matrix was 2,5-dihydroxybenzoic acid (DHBA), and solvent was acetonitrile/water (1/2). Differential scanning calorimetry (DSC) measurements were performed on a Perkin-Elmer DSC-7 instrument under a N_2 atmosphere.

2.3. Synthesis of 6-(carbobenzyloxy)-2-hydroxyhexanoic acid (L-lysine(Cbz)-OH)

L-lysine(Cbz)-OH was synthesized by a modified procedure as described earlier.[24,26,38] Briefly, to a suspension of *Nε*-Cbz-*L*-Lysine (0.28 g, 1mmol) in 5mL H_2O/AcOH mixture cooled on an ice bath, 1 mL 2 M $NaNO_2$ was added drop-wise. The reaction mixture was stirred at room temperature until the solution became homogeneous. Add 5 mL of water and extract with ethyl acetate (3×4 mL). The organic layer was washed with brine and dried over sodium sulphate, and then concentrated under vacuum to obtain viscous yellow oil. Perform diacetylation in 3 mL H_2O/MeOH mixture in the presence of K_2CO_3 (pH 8-9). Hydrolysis of the product is completed in 3 hours. Add 2 mL of water and evaporate the methanol.

Extract the aqueous phase with 3 mL of ethyl acetate. Acidify the aqueous phase and extract with ethyl acetate (3×4 mL). Wash with brine and dry on sodium sulphate. Evaporate to get 0.19 g light-yellow powder, which was further purified by recrystallization from ethyl acetate/petroleum ether to get white solid (0.15 g, 52%). ^{1}H NMR($CDCl_3$, 300MHz): δ = 7.42-7.33 (5H, m, -C***H***$_{aromatic}$); 5.15 (1H, s, -C***H***$_2$Ar); 5.09 (1H, s, -C***H***$_2$Ar); 4.86 (1H, s. -N***H***Cbz); 4.26 (1H, s, -C***H***(OH)COOH); 3.23-3.21 (2H, d, C***H***$_2$NHCbz); 1.87-1.79 (2H, m, -C***H***$_2$CH(OH)COOH); 1.60-1.46 (4H, m, -C***H***$_2$C***H***$_2$CH$_2$NHCbz)

2.4. Synthesis of (L-lysine(Cbz)-OCA)

To a solution of *L*-lysine(Cbz)-OH (1 mmol, 1 equiv) and triphosgene (0.67 mmol, 2 equiv) in dry THF (15 mL) was added activated charcoal (15 mg) and triethylamine (20 μL) under nitrogen atmosphere. The resulting mixture was stirred at room temperature for 8 hours. The solution was then filtered off the solid and then concentrated under vacuum. The resulting yellow oil was washed with dry petroleum ether (2×50 mL) and recrystallised from Et_2O/petroleum ether to give clean OCA monomer in crystalline form (0.15 g, 68 % yield). ^{1}H NMR($CDCl_3$, 300MHz): δ = 7.37-7.35 (5H, m, -C***H***$_{aromatic}$); 5.10 (2H, s, -C***H***$_2$Ar); 5.03 (1H, s, -C***H***CH$_2$CH$_2$CH$_2$CH$_2$NHCBZ); 4.83 (1H, s. -N***H***CBZ); 3.24-3.22 (2H, d, C***H***$_2$NHCBZ); 2.08-1.99 (2H, m, -C***H***$_2$CH$_2$CH$_2$CH$_2$NHCBZ); 1.68-1.51 (4H, m, -C***H***$_2$C***H***$_2$CH$_2$NHCBZ)

2.5. General procedure for polymerization of L- lysine(Cbz)-OCA

In a glovebox, a solution of DMAP catalyst (0.01 M, 6.6 mL) and alcohol initiator (0.01 M, 6.6 mL) was added to lysine(Cbz)-OCA (307 mg, 1 mmol) in $CHCl_2$ (2 mL) The solution was left to stir at the room temperature. The conversion of OCA was quantified by ^1H NMR. When the polymerization was complete, the polymer was precipitated with ether, and the precipitate was dried under vacumm (184 mg, 75% isolated yield).

2.6. Removal of the protecting group

The polymer was dissolved in 33% w/w HBr in AcOH under anhydrous conditions. The mixture was stirred at 0 ^OC under a nitrogen atmosphere for 1h. The deprotected polymer was precipitated by the addition of Et_2O and dried in vacuo. The obtained polymer was then dissolved in distilled water and dialyzed against water to yield final polymer as white powder (79% yield).

2.7. Cell viability assays

HeLa cells were seeded in a 96-well plate at 1×10^4 cells/well and incubated for 24 h at 37 ^oC. Lysine-based polyester and α-poly-lysine was diluted with fresh medium (Dulbecco's Modified Eagle Medium supplemented with 10% (v/v) fetal bovine serum) to desired concentrations and added to the corresponding well, respectively. After incubation for 48 h at 37 ^oC, cell viability was assessed using the standard MTT assay.

3 Results

3.1. Monomer synthesis and characterization

We have focused on developing a new class of renewable polymers using *L*-lysine due to its abundance, low cost, and its potential ability to be derivatized into polymerizable monomers. As shown in Scheme 1, our synthetic strategy is based on the simple conversion of *L*-lysine to its corresponding *α*-hydroxyl acids. These are then coupled with triphosgene and cyclized to provide the OCA monomer. We chose commercial *L*-lysine monohydrochloride as our starting materials. First, the *ε*-amino group of *L*-lysine monohydrochloride was protected with the carbobenzyloxy group (abbreviated as Cbz group) according to literature's method.[10] The monomer lysine(Cbz)-OCA was then prepared via diazotization of *Nε*-Cbz-*L*-Lysine with sodium nitrite in acetic acid aqueous solution followed by cyclization of the resulting lysine-based *α*-hydroxy acid with triphosgene, as outlined in Scheme 1. The obtained product was viscous liquid at room temperature. Impurities were removed by recrystallization from petroleum ether and diethyl ether. After recrystallization, lysine(Cbz)-OCA turned to a white crystalline with isolated yield of about 68%. The structures of the monomer were confirmed by ^{1}H NMR and ^{13}C NMR. ^{1}H NMR spectra (Figure 1A) analysis of the monomer showed the characteristic peak of methine at 5.03 ppm, indicated the formation of OCA ring. ^{13}C NMR spectroscopy (Figure 1B) also confirmed the monomer structure, with the characteristic peaks of the OCA ring at 148.3 and 167.2 ppm, respectively.

3.2. Living/Controlled Ring-opening Polymerization of Lysine(CBZ)-OCA

After obtaining pure lysine(Cbz)-OCA, we initially attempted to polymerize using *iso*-butanol (IB) as initiator and DMAP as a catalyst at 25 ^{o}C in CH_2Cl_2 solution, comparable to the conditions successfully used for the ROP of *L*-lacOCA and *L*-gluOCA. As shown in Figure 2, the M_n values of the resulting polymer at monomer-to-initiator (M/I) ratios of 15 and 100 were 4.0×10^3 g/mol and 2.5×10^4 g/mol, respectively, both of which were in excellent agreement with the calculated M_n values (4.0×10^3 g/mol and 2.6×10^4 g/mol, respectively), suggesting that DMAP/IB showed significant control for the ROP of lysine(Cbz)-OCA and gave the polymer with the expected molecular weights. It was very encouraging to note that the M_n value of the polyester at M/I ratios of 200 was up to 45 kg/mol (Table 1), which was approximately 5～10 times as much as that of polyesters from ROP of these protected amino-functionalized lactones.[31] Gel permeation chromatography (GPC) traces showed a symmetric single peak with low polydispersity index (PDI, around 1.15-1.26) at different M/I ratios. Figure 3 showed that the number-average molecular weight of the polymer increased with the monomer conversion, suggesting that the ROP of lysine(Cbz)-OCA with DMAP as catalyst might have proceeded in a living/controlled fashion.

Analysis of a plot of $\ln([M]_0/[M])$ versus polymerization time (Figure 4) revealed that the reaction was first order with respect to the OCA monomer concentration, indicating a constant concentration of active centers during the polymerization.

The polymerizations catalyzed by DMAP/IB in THF and toluene also produced polyesters with the expected molecular weight, although the molecular weight distribution of the polymer obtained in THF were slightly lower than those in toluene (entries 4-7, Table 1). We also investigated the DMAP-catalyzed ROP of lysine(Cbz)-OCA with other initiators. Both of DMAP/*n*-pentanol and DMAP/*neo*-pentanol in CH_2Cl_2 solution gave similarly well-controlled polymerization (entries 8-11, Table 1).

The end-group structures of the polymers obtained with *neo*-pentanol as initiator were analyzed by ^{1}H NMR spectroscopy (Figure 5). Besides the large absorptions ascribed to the repeat units of the monomer, several characteristic signals originating from *neo*-pentanol were also observed. The methyl and methylene of the initiator moiety at the α-end were clearly seen at 0.9 and 3.7 ppm, respectively. The number-average degree of the polymerization or molecular weight of the polymers can be estimated from the peak intensity ratio of monomer to the end-group. The M_n(NMR) estimated from the peak intensity ratio was 4200, which was close to the calculated value [M_n(calcd) = 4032], assuming that one molecule of the *neo*-pentanol generates one polymer chain and was slightly higher than that by SEC [M_n(SEC) = 3600] based on the PS calibration. These results suggest that DMAP and *neo*-pentanol controls the ROP of lysine(Cbz)-OCA to control the molecular weight of the polymers.

The MALDI-TOF spectrum consists of a series of peaks separated by a 263 Da interval, which corresponds to the molecular weight of monomer unit (Figure 6). The

molecular weight of each individual peak was close to the calculated value; i.e., a polymer processing one initiator moiety at the α-end and the sodium ion from the salt for MALDI-TOF-MS analysis. These results again suggest that DMAP catalyzed ROP of lysine(Cbz)-OCA was initiated by *neo*-pentanol and presented a controlled/living character. Despite the evidence suggesting that the DMAP-catalyzed ROP of lysine(Cbz)-OCA proceeds in a highly controlled manner, some minor peaks were observed at the MALDI-TOF MS spectra of the polymer obtained (* of Figure 6). We supposed that the side reaction products were caused by the misinsertion of the propagating chain end into the disfavored 2-position of the OCA ring, leading to a carbonate linkage and a carboxylic acid ω-chain end group (Scheme 2). The absolute molecular weights agreed with the molecular weight of carboxylic acid group at ω end, which suggested our presume: 3314.8 = 88.1 (M_W of *neo*-pentanol) + 12×263.29 (M_W of OCA - M_W of CO_2) + 23.0 (M_W of Na^+)+ 44.2 (M_W of CO_2). The generation of carboxylic acid ω-chain end group was also observed by Dove in the living/controlled ROP of *L*-malic acid (benzyl)-OCA.[19] Moreover, the nucleophilic ability of carboxylic acid is weaker than alcohol, so perhaps the carboxylic acid end group has no ability to re-initiate and is incapable of further propagation, which may be responsible for small bump in the GPC trace for M/I at 100 (Figure 2B).

3.3. Block copolymer synthesis

The success of the living/controlled ROP prompted us to examine the block polymerization of lysine(Cbz)-OCA. Initiation of ROP of lysine(Cbz)-OCA from commercially available PEO macro-initiators resulted in >99% monomer conversion.

The GPC curve of the resultant block copolymer shifted to higher molecular weights while almost keeping MWDs (Table 2 and Figure S3). ^{1}H NMR spectroscopy confirmed the presence of PEO and lysine units at 3.6 and 5.3 ppm, respectively (Figure S4 of the Supporting Information).

3.4. Removal of carbobenzyloxy groups

The carbobenzyloxy protecting groups were deprotected following a classical procedure under acidic conditions to yield the corresponding polyester with pendant amino groups. ^{1}H NMR analysis of the deprotected polymer showed the disappearance of all of the aromatic signals at 7.2 ppm (Figure 7), indicating the clean and complete removal of the protecting groups. Further confirmation was obtained from the change in solubility of the resulting polymer. Before deprotection, the polyester is soluble in $CHCl_3$ but is insoluble in MeOH or water. However, the deprotected polyester exhibits opposite solubility in those solvents; it is soluble in MeOH and water but insoluble in $CHCl_3$. As de-protection was carried out in a strong acidic medium, a major concern was the integrity of the polyester backbone. Reaction temperature was kept at 0 ^{o}C and reaction time was kept short, typically about 1 h, to avoid degradation while insuring the quantitative de-protection of the amino groups.[11,14,31-32] Deprotection process did not result in the degradation of the polyester backbone, as shown by the lack of signals between 4.2 and 4.4 ppm associated with the α-hydroxy proton that would be apparent upon the cleavage of the backbone (Figure 7).[25,31] Unfortunately, the amino-functionalized polyester precluded their

characterization by GPC owing to solubility problems of the de-protected polymers in CH_2Cl_2 and the different hydrodynamic volumes of the de-protected polymers.[31]

3.5. Properties of the bio-renewable lysine-based polyester

Figure 8 showed the powders and granules of resultant lysine-based amino-functionalized polyester. Figure 9 showed the DSC curves of various amino-functionalized polyester, T_g was 39.8 ^oC for polyester with M_n of 4.0 kg/mol, and it increased to 45.2 ^oC for polyester with M_n of 12.3 kg/mol, and it was further raised to 52.3 ^oC for polyester with M_n of 21.9 kg/mol. Therefore, we have confirmed here that the T_g of the lysine-based amino-functionalized polyester was increased with the increasing of M_n.

The cytotoxicity of lysine-based polyester was evaluated in HeLa cells using the MTT assay. Lysine-based polyester showed no obvious cytotoxicity at concentrations up to 250 μg/mL at 48h incubation (Figure 10), whereas, α-poly-lysine provided significant toxicity to HeLa cells after 2 days of cultivation. The excellent cell compatibility along with its functionality makes bio-renewable lysine-based polyester a useful material for the construction of a gene and drug delivery system.

Conclusions

In conclusion, the synthesis of lysine(Cbz)-OCA monomer from renewable lysine has been demonstrated. Homopolymerization of lysine(Cbz)-OCA catalyzed by

DMAP enabled the synthesis of functional polyesters bearing pendant Cbz protected amino groups with controlled molecular weight and low polydispersity. Well-defined water-soluble polyesters with amino groups were recovered by cleavage of the Cbz protecting group without polymer backbone scission. These new amino-functionalized polyester yielded bio-renewable materials with a multitude of potential applications in biodegradable plastics and biomedical field.

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Table1. Polymerization of lysine(Cbz)-OCA [a]

Entry	monomer	initiator [b]	M/I	solvent	M_n (M_n*) ($\times 10^{-3}$g/mol) [c]	M_w/M_n [c]
1	lysine(Cbz)-OCA	IB	15	DCM	4.6 (3.9)	1.24
2	lysine(Cbz)-OCA	IB	100	DCM	24.8 (26.3)	1.26
3	lysine(Cbz)-OCA	IB	200	DCM	45.1 (52.6)	1.15
4	lysine(Cbz)-OCA	IB	15	THF	4.6 (3.9)	1.06

5	lysine(Cbz)-OCA	IB	50	THF	11.3 (13.2)	1.12
6	lysine(Cbz)-OCA	IB	15	toluene	4.5 (3.9)	1.24
7	lysine(Cbz)-OCA	IB	50	toluene	12.0 (13.2)	1.25
8	lysine(Cbz)-OCA	*neo*-P	15	DCM	3.6 (3.9)	1.19
9	lysine(Cbz)-OCA	*neo*-P	50	DCM	16.2 (13.2)	1.08
10	lysine(Cbz)-OCA	*n*-P	15	DCM	4.4 (3.9)	1.28
11	lysine(Cbz)-OCA	*n*-P	50	DCM	17.1 (13.2)	1.06

[a] polymerization at room temperature with an alcohol as the initiator and DMAP as the catalyst (1 equiv) . In all experiments, the monomer conversions (determined by ^{1}H NMR) exceeded 96%. [b] IB = isobutanol, *neo*-P = *neo*-pentanol *n*-P = *n*-pentanol. [c] M_n was determined by GPC analysis, the expected M_n* was calculated from the equation: 263.29 × M/I × Conversion % + the molar mass of the initiators.

Table 2. Synthesis of block copolymers using lysine(Cbz)-OCA [a]

Entry	Polymer	M_n (g/mol) [b]	M_w/M_n [b]	DP [c]
1	MeO-PEO_{112}-OH	9200	1.05	--
2	PEO_{112}-*b*-$Polyester_9$	11500	1.12	9
3	PEO_{112}-*b*-$Polyester_{25}$	14670	1.10	25

[a] [PEO_{112}] = 0.01 M; 1 equiv DMAP as catalyst, 25 °C. [b] Determined by GPC analysis. [c] Degree of Polymerization, determined by ^{1}H NMR Spectroscopy.

Figure legends:

Scheme 1. Synthesis and Polymerization of lysine (Cbz) - OCA.

Scheme 2. Ring-opening of lysine(Cbz) - OCA at (a) 5-position of the OCA ring and (b) 2-position of the OCA ring.

Figure 1. ^{1}H NMR spectrum (A) and ^{13}C NMR spectrum (B) of lysine-derived OCA monomer in $CDCl_3$.

Figure 2. M_n (○), M_w/M_n (△), and GPC curves of the polymers versus M/I for polymerization with DMAP as the catalyst and *iso*-butanol (IB) as the initiator in CH_2Cl_2 at room temperature; $[IB]_O=[DMAP]_O$ = 0.001 M.

Figure 3. M_n, M_w/M_n, and GPC curves of the polymers obtained with the living/controlled ROP with DMAP as the catalyst and IB as the initiator in CH_2Cl_2 at room temperature; $[M]_O$ /$[IB]_O$/$[DMAP]_O$ = 0.1/0.1/0.001 M.

Figure 4. 1st-order kinetic plots for the living/controlled ROP with DMAP as the catalyst and IB as the initiator in CH_2Cl_2 at room temperature; $[M]_O$ /$[IB]_O$/$[DMAP]_O$ = 0.1/0.1/0.001 M.

Figure 5. ^{1}H NMR spectrum (400 MHZ, $CDCl_3$) of the polymer prepared with DMAP/ *neo*-pentanol in CH_2Cl_2 at room temperature.

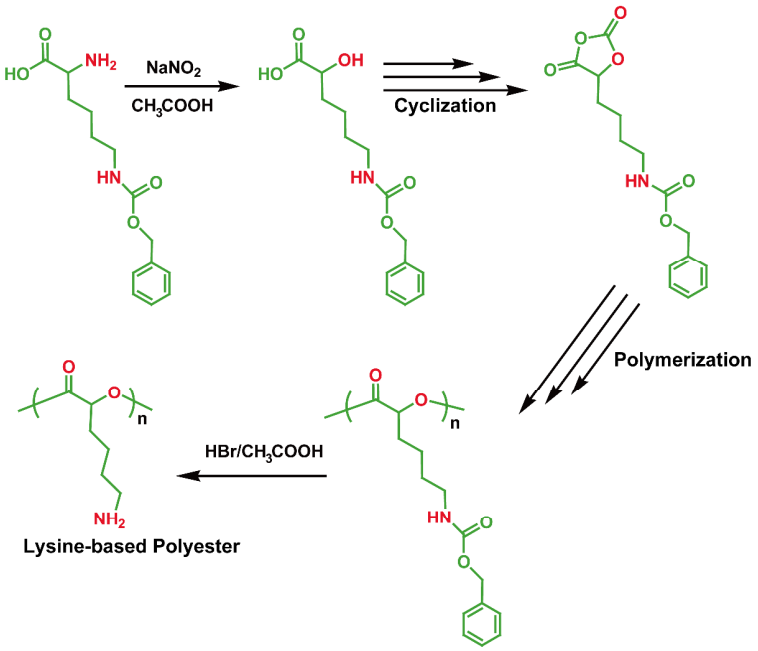
Figure 6. MALDI-TOF-MS spectra of the polymer prepared with DMAP/ *neo*-pentanol in CH_2Cl_2 at room temperature and the presence of impurities (*).

Figure 7. ^{1}H NMR spectrum (400 MHZ, D_2O) of the deprotected lysine-based polyester.

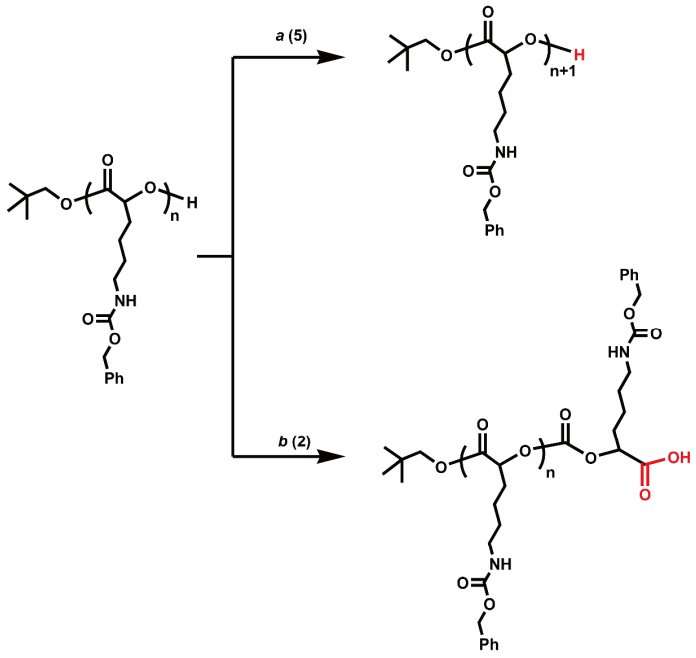
Figure 8. Picture of powders and granules of amino-functionalized polyester.

Figure 9. DSC curves of various amino-functionalized polyesters. The molecular weight values of amino-functionalized polyester are estimated from values of its corresponding protected one after subtraction of the Cbz groups.

Figure 10. (A) Viability of HeLa cells as determined by the MTT assay following treatment with lysine-based polyester and α-poly-lysine for 48h, respectively. (B) Microscopy images of HeLa cells treated with 1 mg mL^{-1} polymer.



Scheme 1.



Scheme 2.

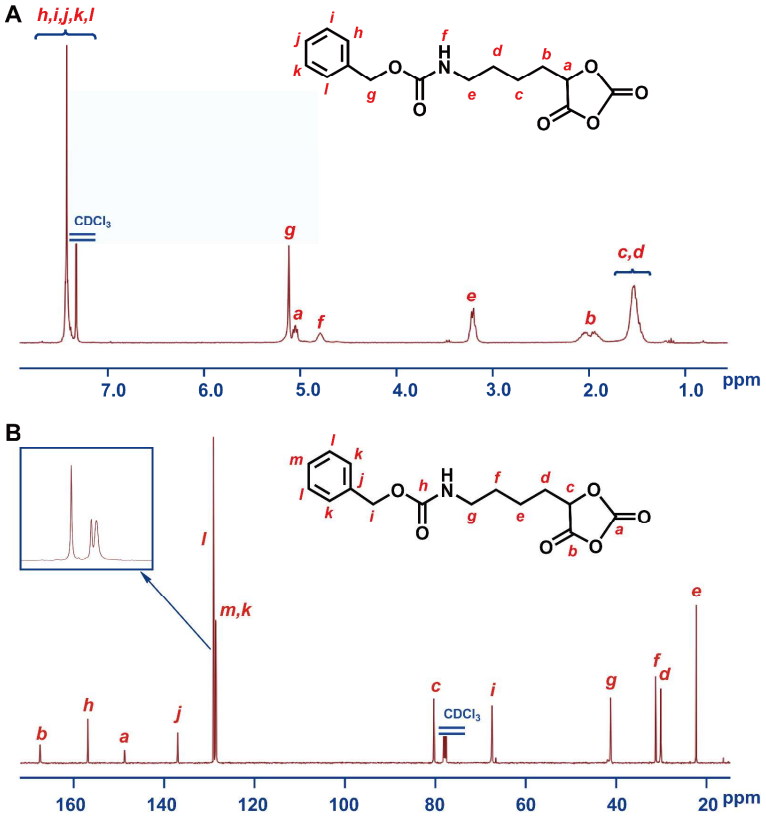


Figure 1.

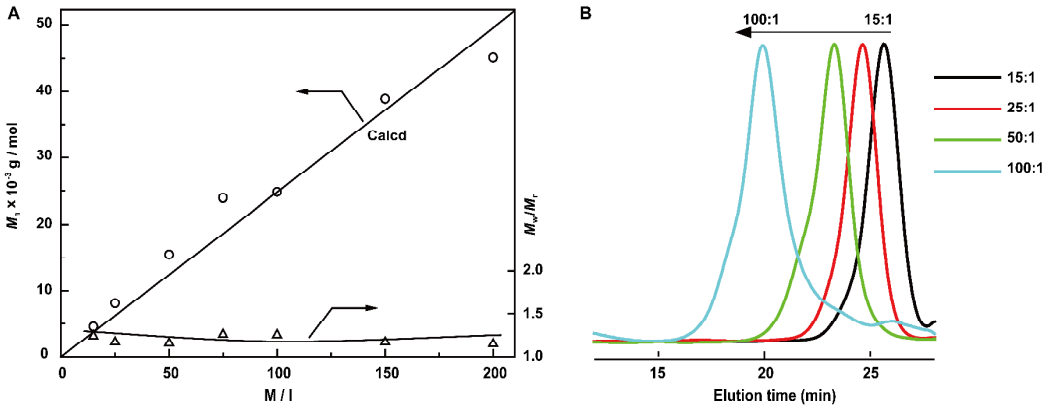


Figure 2.

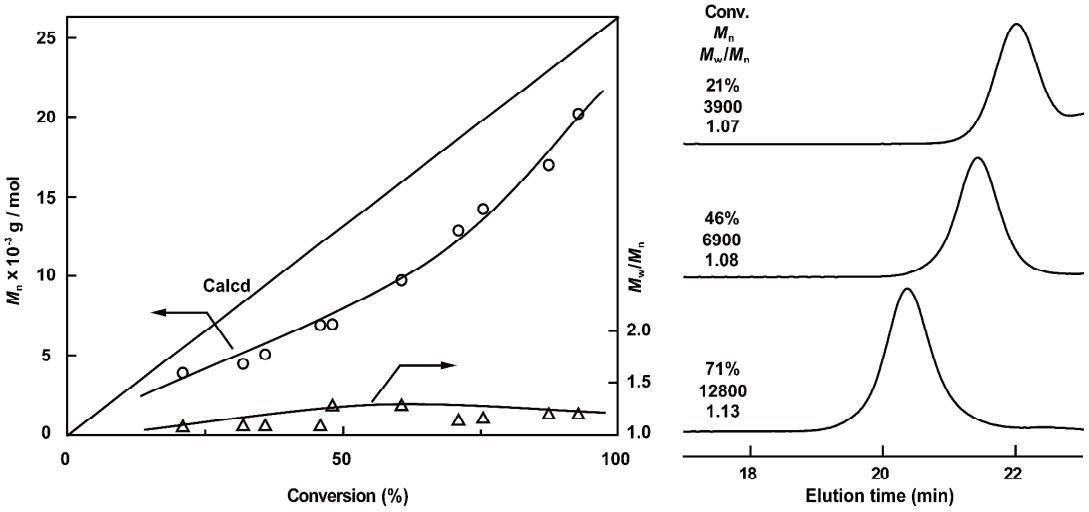


Figure 3.

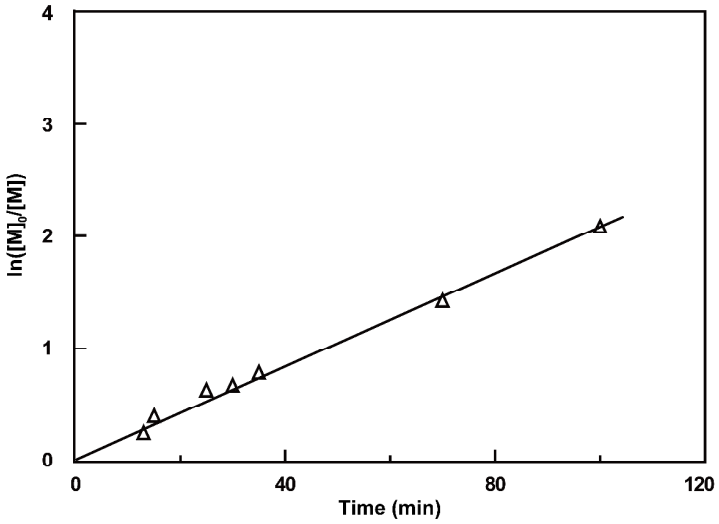


Figure 4.

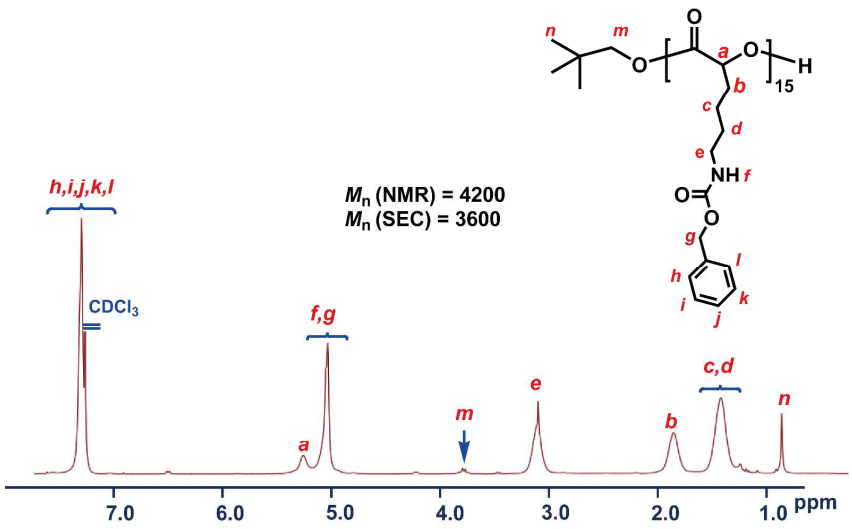


Figure 5.

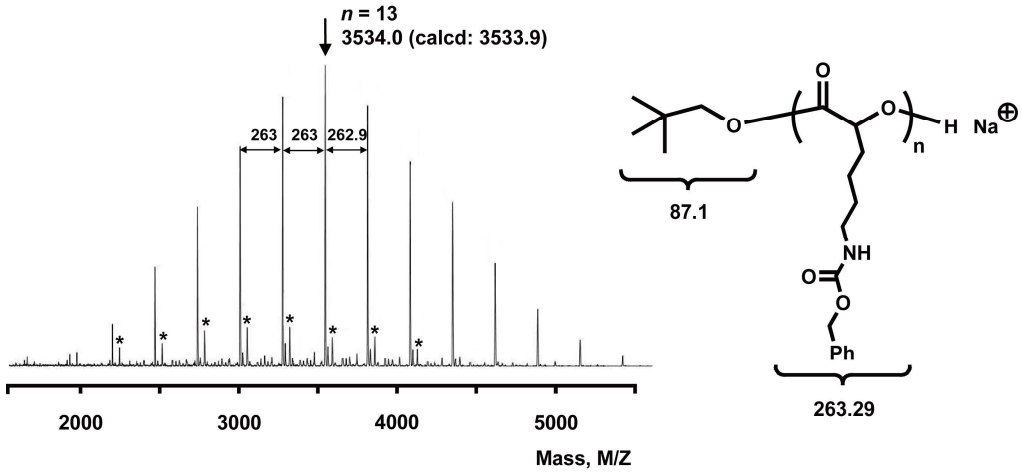


Figure 6.

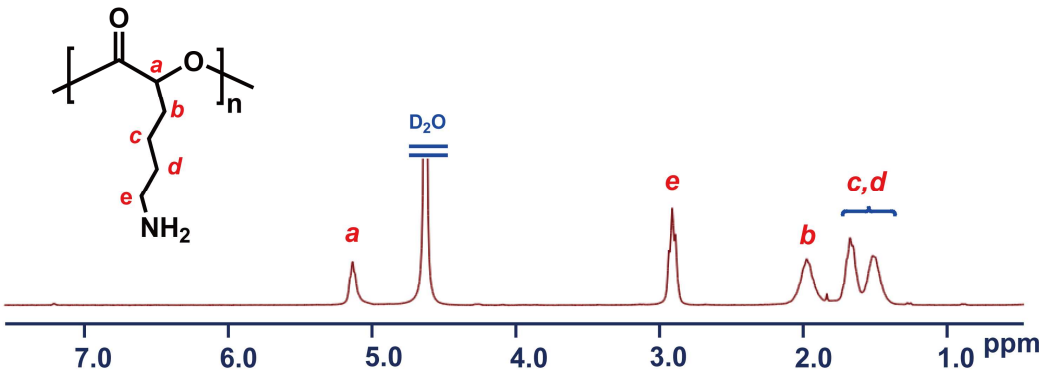


Figure 7.

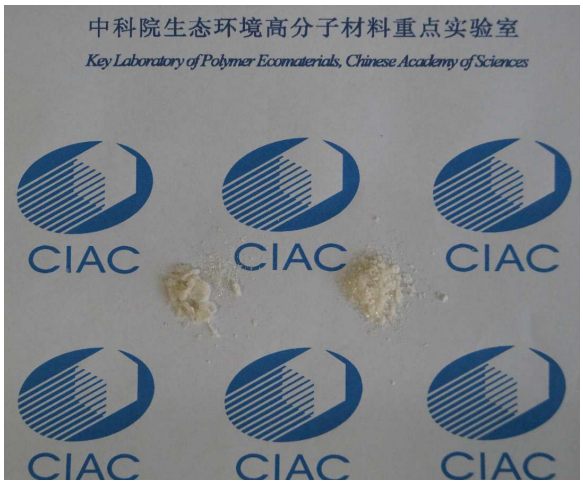


Figure 8.

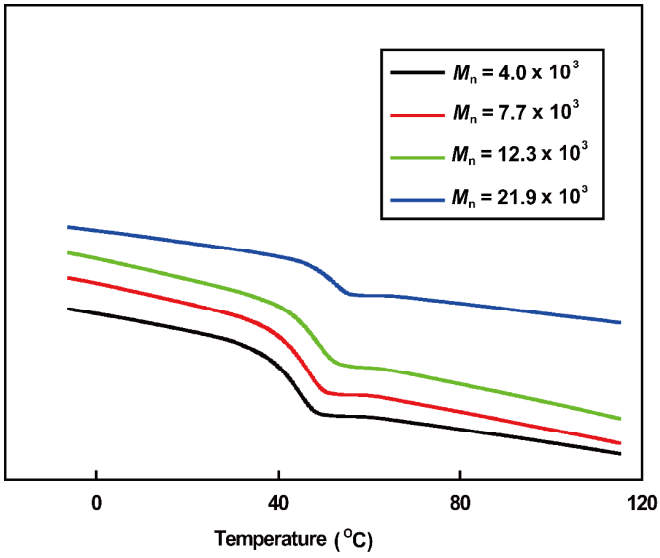


Figure 9.

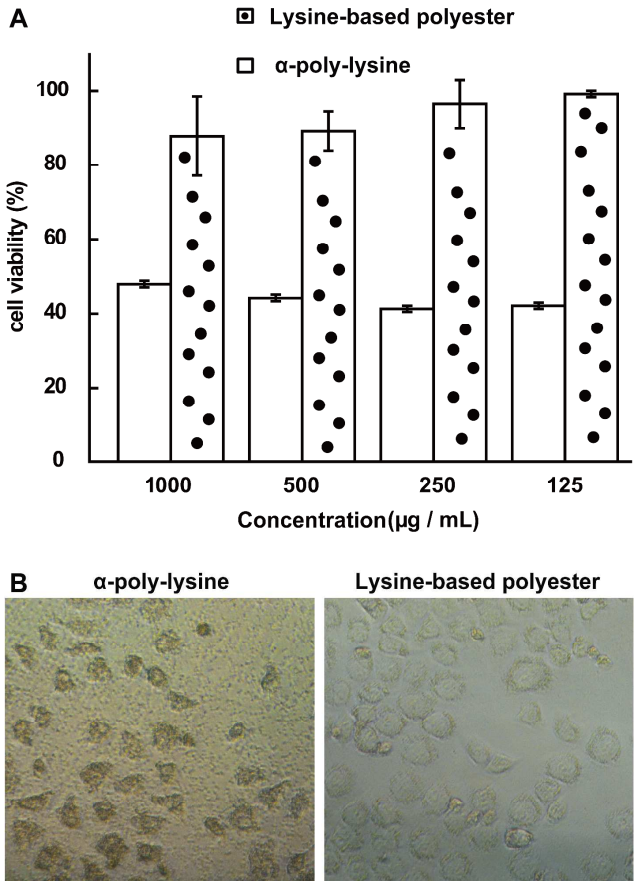


Figure 10.