Synthesis and Characterization of Poly(ε-caprolactone-*co*-δ-valerolactone) with Pendant Carboxylic Functional Groups

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In this paper, aliphatic polyesters functionalized with pendant carboxylic groups were synthesized via several steps. Firstly, substituted cyclic ketone, 2-(benzyloxycarbonyl methyl)cyclopentanone (BCP) was prepared through the reaction of enamine with benzyl-2-bromoacetate, and subsequently converted into the relevant functionalized *δ*-valerolactone derivative, 5-(benzyloxy carbonylmethyl)-*δ*-valerolactone (BVL) by the Baeyer-Villiger oxidation. Secondly, the ring-opening polymerization of BVL with *ε*-caprolactone was carried out in bulk using stannous octoate as the catalyst to produce poly(*ε*-caprolactone-*co*-*δ*-valerolactone) bearing the benzyl-protected carboxyl functional groups [P(CL-*co*-BVL)]. Finally, the benzyl-protecting groups of P(CL-*co*-BVL) were effectively removed by H_2 using Pd/C as the catalyst to obtain poly(*ε*-caprolactone-*co*-*δ*-valerolactone) bearing pendant carboxylic acids [P(CL-*co*-CVL)]. The structure and the properties of the polymer have been studied by Nuclear Magnetic Resonance (NMR), Fourier Infrared Spectroscopy (FT-IR) and Differential Scan Calorimetry (DSC) *etc*. The NMR and FT-IR results confirmed the polymer structure, and the ^{13}C NMR spectra have clearly interpreted the sequence of *ε*-caprolactone and 5-(benzyloxycarbonylmethyl)-*δ*-valerolactone in the copolymer. When the benzyl-protecting groups were removed, the aliphatic polyesters bearing carboxylic groups were obtained. Moreover, the hydrophilicity of the polymer was improved. Thus, poly(*ε*-caprolactone-*co*-*δ*-valerolactone) might have great potential in biomedical fields.

Keywords *ε*-caprolactone, *δ*-valerolactone, poly(*ε*-caprolactone-*co*-*δ*-valerolactone), pendant groups, ring-opening polymerization

Introduction

Aliphatic polyesters based on *δ*-valerolactone and *ε*-caprolactone are of great interest for medical and pharmaceutical applications because of their biocompatible and biodegradable properties.[1-3] However, the degradation rate of poly(*δ*-valerolactone) (PVL) and poly(*ε*-caprolactone) (PCL) is often slow. Moreover, the simplicity of these polyesters presents limitations in terms of functionality and physical properties, and indeed they are hydrophobic solids. The structural and chemical modifications of the conventional aliphatic polyesters materials have begun to be explored by many researchers, such as the preparation of hyperbranched polyesters,[4,5] end-functionalized polyesters[6-10] and chain-substituted polyesters.[11,12] Thereinto, the functionalized polyesters with the pendant groups are particularly of increasing interest because the lateral functional groups will be beneficial to the further chemical and biological modification, and construction of the new biomaterials.[13-16]

Usually, these functionalized polyesters are often synthesized by copolymerizing *ε*-caprolactone, lactide, or glycolide with a functionalized monomer that often contains the protected functional groups.[17,18] The protected groups must be inert to the polymerization conditions, but they should be removable under mild conditions after polymerization, leaving the polymeric backbone intact. Ring-opening polymerization of the functionalized dilactones was used to obtain the corresponding polyesters which bore the hydrophilic pendant groups after deprotection.

The synthesis of the substituted lactone monomers is the key to produce the functionalized polyesters. Langer *et al.*[13] first reported a new monomer prepared from alanine as early as 1993 that contained a protected amino group and could polymerize by the same mechanism as the monomer used for PLA synthesis. So far, amino acids have been of the important originality to synthesize the functionalized lactone monomers.[13,14,19-24] 4-Substituted *ε*-caprolactones were also

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prepared by the Baeyer-Villiger oxidation of 1,4-cyclohexanedione, 1,4-cyclohexanedione monoethylene acetal, and the 1,4-cyclohexanediol derivatives.[24-31] However, a few synthetic strategies of α-substituted ε-caprolactones have attracted great interest.[32,33]

In the present paper, we explored one synthetic strategy of aliphatic polyesters functionalized with the pendant carboxylic groups through the ring-opening polymerization of the novel functionalized lactone BVL [5-(benzyloxy carbonylmethyl)-δ-valerolactone]. The pendant carboxylic group would improve the hydrophilicity and bio-affinity of the aliphatic polyesters, and facilitate a variety of potential applications of the polyester in controlled drug delivery and tissue engineering.

Experimental

Materials

ε-Caprolactone (ε-CL, Aldrich) was dried over CaH_2 for 3 d and distilled under reduced pressure prior to use. 3-Chloroperoxybenzoic acid (MCPBA, Aldrich), Stannous octate [Sn(II)Oct, Aldrich], benzyl-2-bromoacetate (Chinese Chemical Reagent Co.), and 10% of palladium/carbon (10% of Pd/C, Chinese Chemical Reagent Co.) were used as received. Toluene (Shanghai Chemical Reagent Co.) and tetrahydrofuran (THF, Shanghai Chemical Reagent Co.) were purified by refluxing over a benzophenone-Na complex and distilling under nitrogen prior to use. Cyclopentanone (Shanghai Chemical Reagent Co.) was distilled under reduced pressure before use. All of the other reagents were purchased from Shanghai Chemical Reagent Co. and used without further purification.

Synthesis of BCP

Synthesis of enamine (**1**): Cyclopentanone (84.0 g, 1 mol), morpholine (130.0 g, 1.5 mol) and toluene-*p*-sulfonic acid (0.20 g, 1.16 mmol) were refluxed in toluene (200 mL) at 140 ℃ for 48 h. The enamine was collected by distillation under reduced pressure. The conversion of cyclopentanone was about 70%.

Enamine (**1**) (45.9 g, 0.3 mol), methanol (50 mL) and benzyl-2-bromoacetate (57.3 g, 0.3 mol) were in turn added into a 250 mL two-necked flask and were refluxed at 75 ℃ for 2 h. After evaporating the methanol under reduced pressure, 60 mL of deionized water was added into the reaction mixture and continuously stirred at 70 ℃ for another 1.5 h, and then extracted with diethyl ether (60 mL) for three times and dried with anhydrous sodium sulfate over night. After distilling the solvent, the product was purified by column chromatography on silica gel using ethyl acetate/petroleum ether (1/4, *V*/*V*) as the eluent to give the colorless oil. The yield was 53%.

Synthesis of BVL

MCPBA (6.7 g, 0.039 mol), sodium bicarbonate (3.2 g, 0.039 mol) and chloroform (150 mL) were added into a flask and stirred until the solid was completely dissolved. Subsequently, BCP (6.96 g, 0.03 mol) were added dropwise over a period of 1 h at 0 ℃ by external cooling, and the reaction mixture was stirred at room temperature for another 48 h. The solution was then washed with a saturated solution of sodium thiosulfate for three times, a saturated solution of sodium bicarbonate for three times and a saturated sodium chloride solution for one time, respectively. After drying over anhydrous magnesium sulfate, the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using ethyl acetate/petroleum ether (1/4, *V*/*V*) as the eluent to obtain the colorless unctuous BVL. The yield was 60%.

Synthesis of P(CL-*co*-BVL)

The ring-opening polymerization of BCP and ε-caprolactone (CL) was carried out in the polymerization tube using stannous octoate as the catalyst (weight ratio: 0.5‰). Exhausted-refilled with dry argon repeatedly for several times, the polymerization tube was sealed in vacuum and placed in an oil bath at 150 ℃ for 60 h. After cooled to room temperature, the resulted product was dissolved in $CHCl_3$. The solution was added dropwise into the excess petroleum ether to precipitate. The obtained P(CL-*co*-BVL) was washed with methanol for three times to remove the residual monomers and dried over phosphoric pentoxide in vacuum at room temperature until constant weight.

Deprotection of P(CL-*co*-BVL) to produce P(CL-*co*-CVL)

P(CL-*co*-BVL) (0.90 g) were completely dissolved in anhydrous tetrahydrofuran (40 mL) and then 10% Pd/C catalyst (0.50 g) were added. After being purged with argon for three times, the reaction mixture was bubbled with hydrogen gas and stirred vigorously at room temperature for 30 h. After the removal of the Pd/C powder, the solution was dropped into excess petroleum ether to obtain the final copolymer P(CL-*co*-CVL). The degree of benzyl group removal was 100%.

Characterization

The NMR spectra were recorded on Bruker AVANCE 500 spectrometer in $CDCl_3$. ^1H NMR and ^{13}C NMR measurements were made at frequencies of 500 and 125 MHZ, respectively, and calibrated with respect to the solvent signal with tetramethylsilane as standard. FT-IR spectra were recorded on films or KBr pellets by Nicolet FT-IR spectrometer (Magna-IR 550). SEC measurements were carried out with tetrahydrofuran (THF) as the eluent (1.0 mL/min) with a Water 2414 HPLC pump, three Ultrastyragel columns (2×10^5, 10^5, and 5×10^4 Å) in series, and refractive index detector. The sample concentration was 5—10 mg/mL of THF. The columns were calibrated with polystyrene standards with a narrow molecular weight distribution. The thermal behavior of the polymers was studied by means of differential scanning calorimetry (DSC) with a DSC2910 Modulated DSC system. The specimens were heated in sealed aluminum pans and scanned from −100 to 200 ℃. First cooled to −100 ℃, and finally heated to 200 ℃ using heating and cooling rates of 10 ℃/min. All experiments were done under a flow of dry N_2. The wettability of the polymer film was assessed by the JC200A contact angle measuring instrument. Droplets of distilled water (10 μL) were deposited with a microsyringe onto the polymer surface, and the static contact angle was measured. All the reported data were the average of five measurements collected from different areas of the coated surface.

Results and discussion

The synthesis of P(CL-*co*-CVL) was performed through the reaction steps as shown in Scheme 1, including the preparation of the substituted cyclic ketone 2-(benzyloxycarbonylmethyl)cyclopentanone (BCP), the synthesis of the functionalized lactone 5-(benzyloxycarbonylmethyl)-δ-valerolactone (BVL), the polymerization of BVL with ε-caprolactone to produce the random copolymer P(CL-co-BVL) and the benzyl deprotection of P(CL-*co*-BVL) to obtain the desired P(CL-*co*-CVL).

Synthesis of the new lactone monomer

Firstly, the novel α-substituted cyclopentanone BCP was synthesized by the reaction of enamine with benzyl-2-bromoacetate. As shown in Figures 1(a) and 2(a), ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.75 and 2.30 (2H, c, $CH_2C\mathbf{H}_2CH$), 1.60 and 2.10 (2H, b, $C\mathbf{H}_2CH_2CH$), 2.00 and 2.30 (2H, a, $COC\mathbf{H}_2CH_2$), 2.45 and 2.75 (2H, e, $CHC\mathbf{H}_2CO$), 2.45 (H, d, $C\mathbf{H}$), 5.15 (2H, f, $C\mathbf{H}_2C_6H_5$), 7.35 (5H, g, $C_6\mathbf{H}_5$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 21.05 (b, $CH_2\mathbf{C}H_2CH_2$), 29.73 (c, $CH_2\mathbf{C}H_2CH$), 34.45 (e, $CH\mathbf{C}H_2CO$), 37.82 (a, $CO\mathbf{C}H_2CH_2$), 46.04 (d, $\mathbf{C}H$), 66.89 (f, $CO\mathbf{C}H_2CH_2$), 128.66, 128.71, 129.02, 136.30 (g, $\mathbf{C}_6H_5$), 172.34 (h, $CH_2\mathbf{C}OOCH_2$), 219.30 (i, $CH_2\mathbf{C}OCH$).

BCP was subsequently converted into BVL by the Baeyer-Villiger oxidation reaction using 3-chloroperoxybenzoic acid (MCPBA) as the oxidant. The ^{1}H and ^{13}C peaks of BVL [Figures 1(b) and 2(b)] can be assigned easily by comparison with the ^{1}H and ^{13}C NMR spectra of BCP. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.60 and 2.05 (2H, c,c', $CH_2C\mathbf{H}_2CH$), 1.90 (2H, b, $CH_2C\mathbf{H}_2CH_2$), 2.45 and 2.85 (2H, e,e', $CHC\mathbf{H}_2CO$), 2.65 (2H, a, $COC\mathbf{H}_2CH_2$), 4.50 (H, d, $C\mathbf{H}$) , 5.2 (2H, f, $C\mathbf{H}_2C_6H_5$), 7.35 (5H, g, $C_6\mathbf{H}_5$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 18.80 (b, $CH_2\mathbf{C}H_2CH_2$), 27.91 (a, $CO\mathbf{C}H_2CH_2$), 29.72 (c, $CH_2\mathbf{C}H_2CH$), 41.07 (e, $CH\mathbf{C}H_2CO$), 67.21 (f, $CO\mathbf{C}H_2CH_2$), 76.83 (d, $\mathbf{C}H$), 128.80, 128.89, 129.12, 136.04 (g, $\mathbf{C}_6H_5$), 170.07 (h, $CH_2\mathbf{C}OOCH_2$), 171.41 (i, $CH_2\mathbf{C}OOCH$). NMR spectra indicated that the oxidation of BCP by MCPBA was performed in the perfect regioselectivity that only resulted in BVL (Scheme 1). 2-(Benzyloxycarbonylmethyl)-δ-valerolactone was not

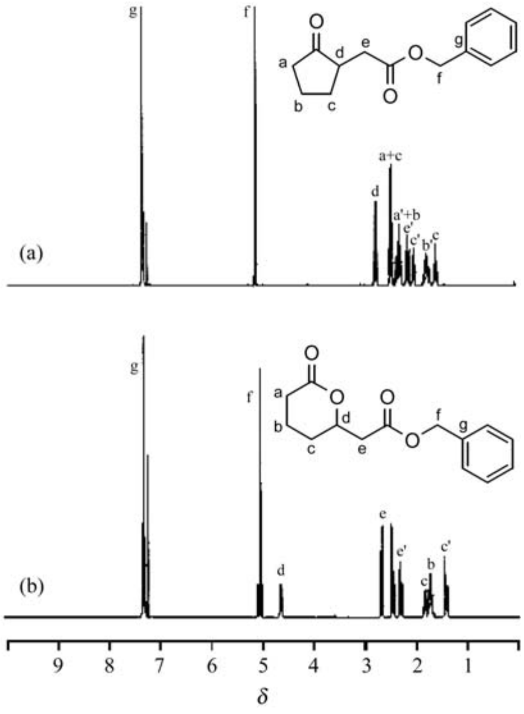
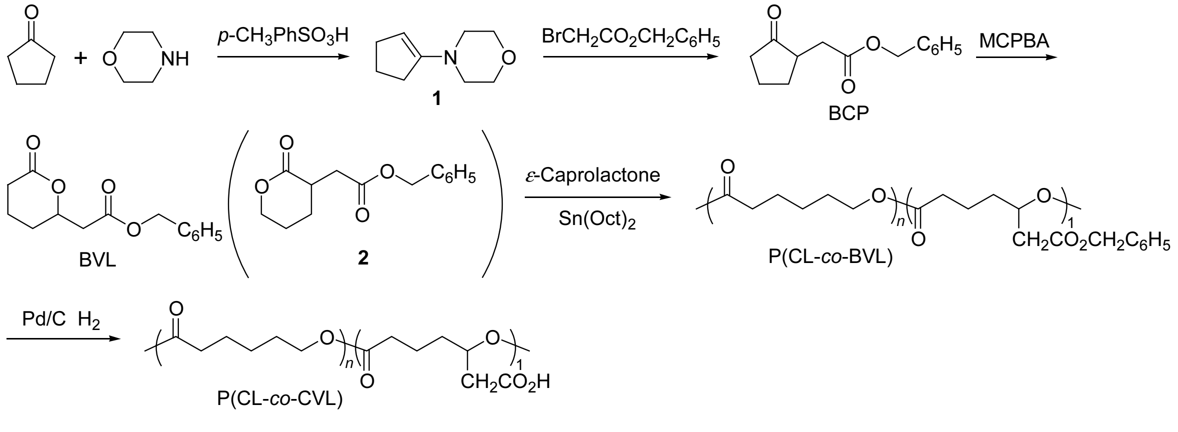


Figure 1 Typical ^{1}H NMR spectra of (a) BCP and (b) BVL.

Scheme 1 Synthetic route of poly(ε-caprolactone-*co*-δ-valerolactone) bearing pendant carboxylic groups



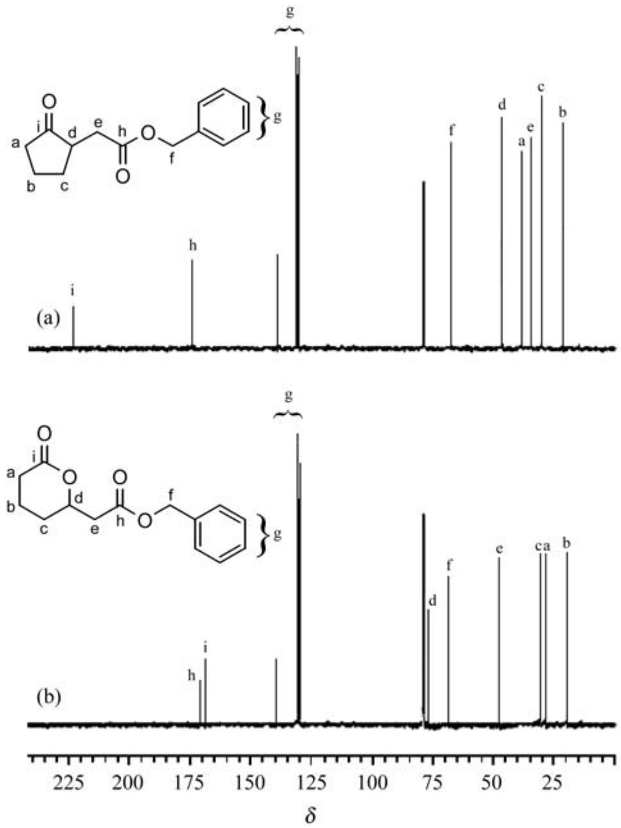


Figure 2 Typical ^{13}C NMR spectra of (a) BCP and (b) BVL.

found, which was much different from the reported oxidation of α-chlorocyclohexanone by MCPBA that results in a mixture of two isomeric lactones (α-Cl-ε-CL/ε-Cl-ε-CL) in a 95/5 molar ratio.[34]

Synthesis of poly(CL-*co*-CVL)

The structure and properties of poly(CL-*co*-BVL) The ability of the ring-opening polymerization depended critically on the ring size of the monomer.[35-37] In the case of polyesters prepared from lactones, the particular lactone used affected not only the polymerization rate but the thermal and degradation properties of the polymer.[38] On the basis of the ring stability, γ-butyrolactone (BL) was very difficult to homopolymerize under most of the conditions, whereas ε-caprolactone (CL) can be easily homopolymerized, and δ-valerolactone (VL) represents a "middle ground" between BL and CL. When the hydrogen of 5-position of VL was substituted by benzyloxycarbonylmethyl, the ring-opening polymerization became much more difficult. Only few of BVL was converted into its homopolymer with low molecular weight although lots of different polymerization conditions were tried. However, the copolymerization of BVL with CL was carried out successfully to produce the copolymers P(CL-*co*-BVL) under the same polymerization condition. As shown in Table 1, the actual molar fraction of BVL unit in the copolymer was lower than that in the comonomer feed. With increasing the amount of BVL monomers in the feed, both the molecular weight and the yield of copolymer decreased. This may be due to the lower reactivity of BVL as compared with CL and the steric hindrance of 5-benzyloxycarbonylmethyl functional groups.

The ^1H NMR and ^{13}C NMR spectra of P(CL-*co*-BVL) are shown in Figures 3(a) and 4(a). By comparison with ^1H and ^{13}C NMR spectra of P(CL-*b*-VL), each group of peaks in ^1H and ^{13}C spectra of P(CL-*co*-BVL) were assigned in the corresponding figures.[39] ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.25 and 2.62 (2H, e,e', $CHCH_2CO$), 2.30 (4H, a+h, $COCH_2CH_2$), 5.10 (1H, d, CH), 5.25 (2H, f, $CH_2C_6H_5$), 7.35 (5H, d, C_6H_5); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 18.79 and 20.95 (b,b', $CH_2CH_2CH_2$), 25.16 (p, $CH_2CH_2CH_2$), 25.98 (j, $CH_2CH_2CH_2$), 28.80 (k, $CH_2CH_2CH_2$), 29.67, 34.12 (a,a', $COCH_2$), 33.78 and 27.92 (c,c', CH_2CH_2CH), 34.56 (m, $COCH_2CH_2$), 39.57 and 41.02 (e',e, $COCH_2CH$), 65.21 (l, $COCH_2CH_2$), 66.58 and 66.93 (f',f, $CH_2C_6H_5$), 70.25 (d, CH), 128.66—136.49 (g, C_6H_5), 170.50 (h, CH_2COOCH), 173.20 (i, CO), 173.98 (n, CO). Figure 5(a) shows the typical spectra of P(CL-*co*-BVL): 1730 ($\upsilon_{C=O}$), 1180 ($\upsilon_{C-O-Cas}$), 1046 (υ_{C-O-Cs}), 733, 704 ($\delta_{=CH}$) cm^{-1}.

Sequence analysis The properties are closely related to the sequence distribution of the two components in the copolymers. Both ^1H NMR and ^{13}C NMR spectra are considered in the sequence analysis of P(CL-*co*-BVL). ^{13}C NMR spectrum has been proved to be an

Table 1 Molecular characteristics and properties of poly(CL-*co*-BVL)

Entry	f_V[a]	X_V[a]	Conversion/%		Yield/%	M_n[c]/10^4	M_w[c]/10^4	Poly dispersity (M_w/M_n)	T_m[d]/℃	ΔH_a[d]/($J•g^{-1}$)	T_g[d]/℃
			BVL[b]	CL[b]							
P(CL-*co*-BVL)-1	0.111	0.048	34.0	84.1	78.6	1.58	2.84	1.80	53.7	86.1	−56.5
P(CL-*co*-BVL)-2	0.143	0.048	24.5	82.6	74.2	1.35	2.50	1.85	52.0	71.3	−51.6
P(CL-*co*-BVL)-3	0.200	0.064	21.7	79.2	67.7	1.31	2.18	1.67	51.6	70.7	−49.1
P(CL-*co*-BVL)-4	0.333	0.091	13.2	65.7	48.2	1.13	1.84	1.62	48.7	69.9	−48.0
P(CL-*co*-BVL)-5	0.500	0.132	8.2	53.6	30.9	1.13	1.7.	1.54	45.0	61.8	−44.9

[a] f_V is the molar fraction of BVL in the comonomer feed; X_V is the molar fraction of BVL in the copolymer, and calculated by ^1H NMR integration according to the benzyl signal at δ of about 7.4—7.5. [b] Measured by ^1H NMR spectrum ($CDCl_3$). [c] Determined by SEC in THF using polystyrene as calibration standard. [d] The melting points T_m, heat of fusion ΔH_m and glass transition temperature T_g were measured by the first scan at a heating rate of 10 ℃/min.

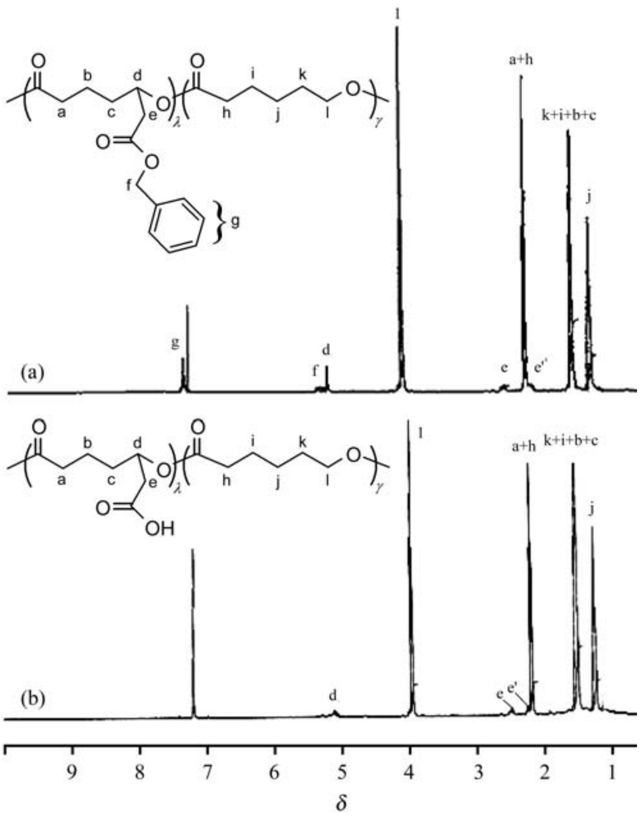


Figure 3 Typical ^{1}H NMR spectra of (a) P(CL-*co*-BVL)-3 and (b) P(CL-*co*-CVL)-3.

more effective method in the sequence analysis of polyesters, while ^{1}H NMR spectrum was seldom used.[24,27,40]

The expanded ^{13}C NMR spectrum of the P(CL-*co*-BVL) is shown in Figure 6. CL and BVL units in copolymer were abbreviated with C and V, respectively. The methylene carbon signals of j—j''', p—p''', m—m''' of the central C units in the sequences C-C-C, V-C-C, C-C-V, V-C-V were assigned as follows. Peaks j, p, and m can be easily assigned to the C-C-C sequence by comparison with the corresponding methylene carbon signals in PCL.[39] It was found that the smaller the mole fraction of the BVL was in the copolymer, the weaker the signals of j''', p''' and m''' were. So the signals of j''', p''' and m''' can be assigned to the V-C-V sequence. It will cause a larger upshift of these methylene carbons that replacing a C unit by a V unit at the side of the carbonyl group than at the other side of the central ε-oxycaproyl unit (C).[39] According to this, peaks j', p', m' and peaks j'', p'', m'' were assigned to the sequences of V-C-C and C-C-V, respectively. Figure 6 also indicates that C_n, C_l and C_k only show diad sensitivity. Compared with the data from ^{13}C NMR spectrum of PCL, peaks n, k and l were assigned to the C-C-C sequence. Furthermore, peak n' was signed to C-V dyad, l' and k' were assigned to the V-C dyad, because their signal intensities increased when X_V was raised.

When V was considered as the central unit, all the carbon signals of it show diad sensitivity (Figure 6).

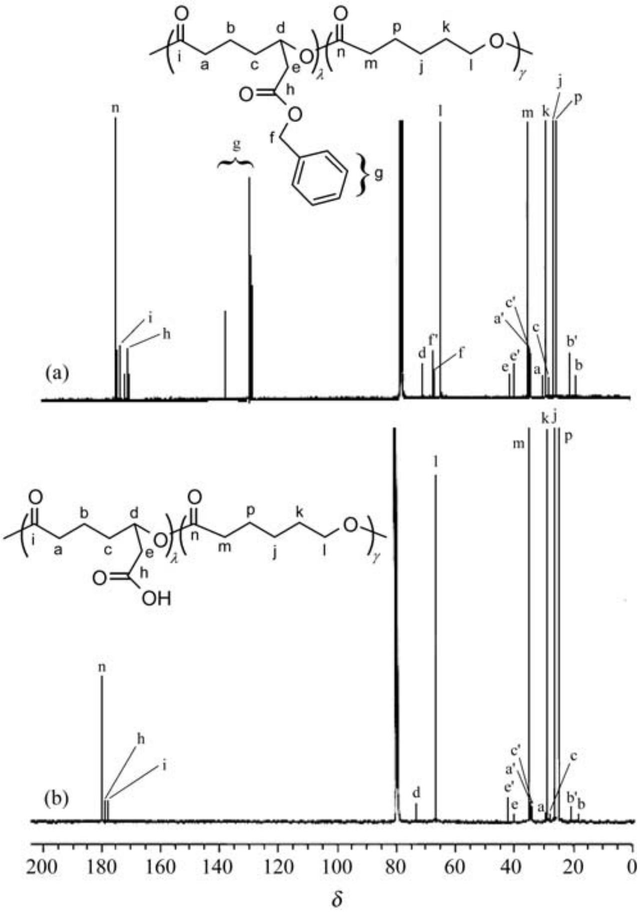


Figure 4 Typical ^{13}C NMR spectra of (a) P(CL-*co*-BVL)-3 and (b) P(CL-*co*-CVL)-3.

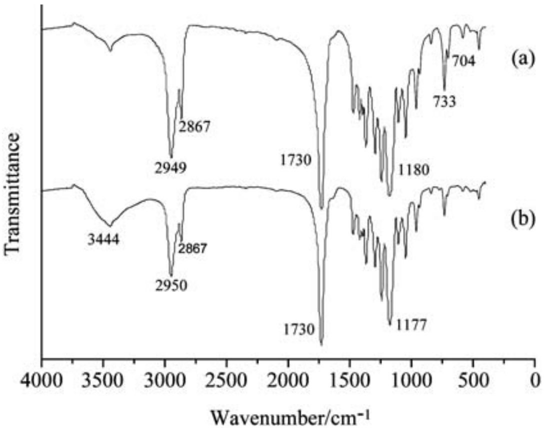


Figure 5 FT-IR spectra of (a) P(CL-*co*-BVL)-3 and (b) P(CL-*co*-CVL)-3.

Compared with the data from ^{13}C NMR spectrum of PVL[41] and PCL-*b*-PVL,[39] and considering the low molar fraction of BVL in copolymer, the low intensity peak groups of a, b, c, d, e, h, f and i are assigned to the V-V sequence, a', b' and i' are assigned to V-C sequence, c', d', e', h', and f' are assigned to C-V sequence.

All the peak assignments of the copolymer P(CL-*co*-BVL)-3 in the ^{13}C NMR spectrum were summarized in Table 2. The average length of homogenous C block

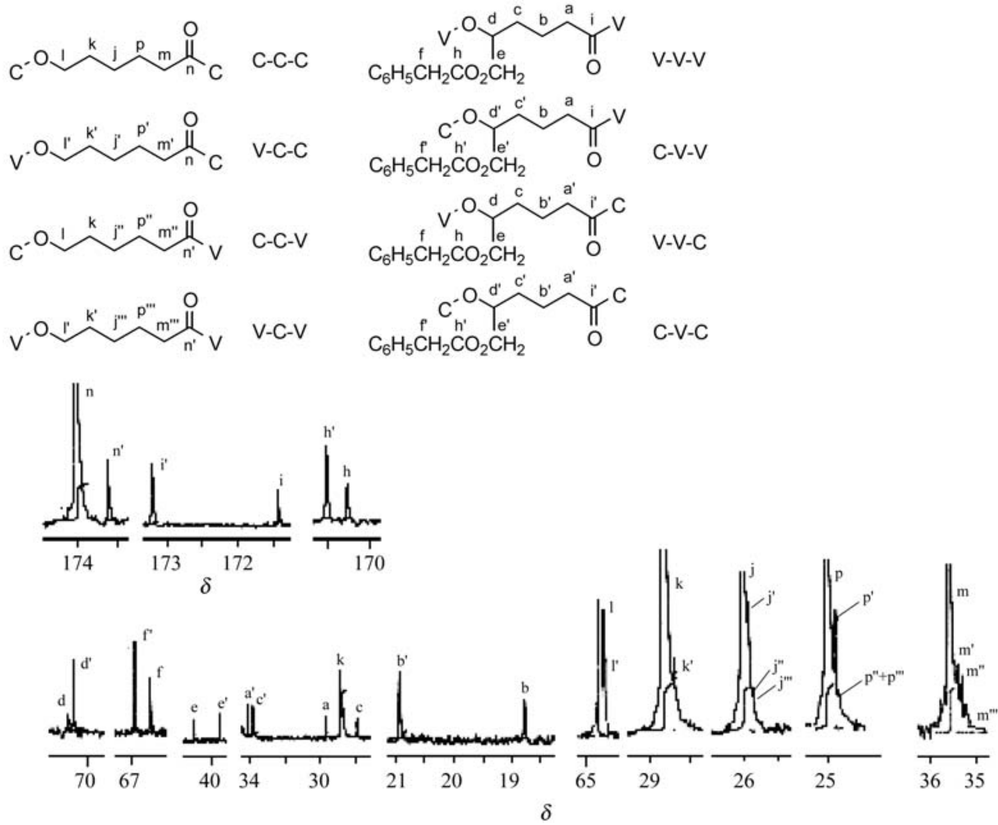


Figure 6 Expanded ^{13}C NMR spectrum ($CDCl_3$) of P(CL-*co*-BVL)-3. C and V represent CL unit and BVL unit, respectively.

Table 2 Average length of C blocks (L_C) and V blocks (L_V)

Carbon atoms in C block	L_C	Carbon atoms in V block	L_V
C_l	19.06	C_i	1.40
C_n	20.18	C_a	1.44
C_m	20.84	C_b	1.50
C_p	21.06	C_c	1.38
C_j	21.63	C_d	1.37
C_k	19.70	C_e	1.47
		C_h	1.45
		C_f	1.60
Avg of L_C	20.41	Avg of L_V	1.45

(L_C) and V block (L_V) were calculated by the following equations:[24,27,40,42]

$$L_C=\frac{I_j+I_{j'}}{I_{j''}+I_{j'''}}+1=\frac{I_p+I_{p'}}{I_{p''}+I_{p'''}}+1=\frac{I_m+I_{m'}}{I_{m''}+I_{m'''}}+1=\frac{I_l}{I_{l'}}+1=\frac{I_k}{I_{k'}}+1=\frac{I_n}{I_{n'}}+1 \quad (1)$$

$$L_V=\frac{I_l}{I_{l'}}+1=\frac{I_a}{I_{a'}}+1=\frac{I_b}{I_{b'}}+1=\frac{I_c}{I_{c'}}+1=\frac{I_d}{I_{d'}}+1=\frac{I_e}{I_{e'}}+1=\frac{I_h}{I_{h'}}+1=\frac{I_f}{I_{f'}}+1 \quad (2)$$

I represented the peak intensity. The results of the average lengths were shown in Table 3. It was found that the data of L_C and L_V of P(CL-*co*-BVL)-3 calculated from different carbon peaks have small error. The average L_C was 20.41 and L_V was 1.45.

On the basis of the average block length, the mole fraction of BVL (X_V) in P(CL-*co*-BVL) can be calculated from the following equation:[20]

$$X_V=\frac{L_V}{L_V+L_C} \quad (3)$$

X_V of P(CL-*co*-BVL)-3 calculated from L_V according to above equation was 0.066, which was in reasonable agreement with 0.064 calculated from ^{1}H NMR spectrum (Table 1). This result further confirmed the interpretation of the ^{13}C NMR spectra of poly(CL-*co*-BVL).

The DSC results were summarized in Table 1. Both the T_g and the heat of fusion values of the P(CL-*co*-BVL)s tended to remarkably decrease with increase of the BVL unit contents as a result of the disruption of polymer crystallinity. However, the glass transition temperatures of the product P(CL-*co*-BVL)s tended to increase with the increase of their BVL unit contents. These results indicated that the higher the BVL unit content was, the lower the chain/segmental mobility would be detected for copolyester P(CL-*co*-BVL).

Debenzylation of P(CL-*co*-BVL) to produce P(CL-*co*-CVL) The debenzylation of the pendant benzyloxycarbonylmethyl groups of P(CL-*co*-BVL) was performed by catalytic hydrogenolysis with H_2 over

Pd/C (10%) as a catalyst in the solvent of anhydrous tetrahydrofuran at room temperature over 30 h to produce the corresponding copolymer P(CL-*co*-CVL) with pendant carboxyl groups. The ^{1}H NMR, ^{13}C NMR and FT-IR of P(CL-*co*-CVL) were shown in Figures 3(b), 4(b) and 5(b). Compared with the ^{1}H NMR spectrum of the protected copolymer P(CL-*co*-BVL), the peaks around δ 5.2 and 7.3 which were assigned to the hydrogen atoms of the benzylprotected groups (CH_2 and Ar-H, respectively) disappeared in the spectrum of the deprotected copolymer P(CL-*co*-CVL) after 30 h of hydrogenation [Figure 3(b)]. No benzyl signals were detected in the ^{13}C NMR spectrum either [Figure 4(b)]. All of these clearly demonstrated that the benzyl groups were removed completely. The other effective evidence of this deprotection method was the disappearance of the δ_{CH} vibrations of benzyl group at 733 and 703 cm^{-1} in the FT-IR spectrum [Figure 5(b)]. In addition, the —OH stretching band centered at 3444 cm^{-1} was strengthened tremendously after hydrogenolysis due to the formation of pendant —COOH groups. All of these clearly demonstrate that the benzyl groups were removed completely.

The debenzylation of the pendant groups sharply affected the copolymer thermal properties. For example, T_m of the benzyl-deprotected P(CL-*co*-CVL)-3 was much higher than that of the benzyl-protected P(CL-*co*-BVL)-3 (Table 3), and P(CL-*co*-CVL)-3 exhibited a little higher glass transition temperature than that of the corresponding P(CL-*co*-BVL)-3. However, ΔH_m of the benzyl-deprotected P(CL-*co*-CVL)-3 was much lower than that of the benzyl-protected P(CL-*co*-BVL)-3. It might be attributed to the two possible reasons: (i) a carboxylic side group with less steric hindrance would be more energetically favorable for accommodating a secondary CVL unit than the BVL unit; (ii) an intermolecular interaction caused by the possible intermolecular hydroxyl bond between two neighboring hydroxyl and hydroxyl or carbonyl groups can stabilize the aggregated solid crystalline structure for P(CL-*co*-BVL).[43]

Table 3 Thermal properties of debenzylated P(CL-*co*-CVL)-3

$M_n^a/10^4$	X_V^a	T_m^b/℃	ΔH_m^b/(J•g^{-1})	T_g^b/℃	Contact angle/(°)
1.29	—	80.8	53.3	−46.7	81

[a] Determined with SEC in THF using polystyrene as calibration standard. [b] The melting points T_m, heat of fusion ΔH_m and glass transition temperature T_g were measured by the first scan at a heating rate of 10 ℃/min.

The water contact angle could be used to characterize the hydrophilicity of the resulting deprotected copolymer. Compared with P(CL-*co*-BVL)-3 films, after deprotection, the average contact angle of water on P(CL-*co*-CVL)-3 films decreased by 4° (From 85°→81°), accordingly, the hydrophilicity increased.

Conclusion

The novel functionalized lactone monomer 5-(benzyloxycarbonylmethyl)-δ-valerolactone BVL has been successfully synthesized, and copolymerized with ε-caprolactone in bulk at wide range of mole fractions in the feed initiated by $Sn(Oct)_2$ to produce poly(ε-caprolactone-*co*-δ-valerolactone) containing the lateral benzyl-protected carboxyl functional group. The average molecular weight of P(CL-*co*-BVL) deceased with the increase of the molar feed ratio of BVL/CL, while the melting point (T_m) and the heat of fusion (ΔH_m) decreased and the glass transition temperature (T_g) increased. The ^{13}C NMR interpretation and the sequence analysis of the copolymer with the feed ratio of 0.25 showed a random sequence distribution for the composition of the copolymer.

The deprotection method using Pd/C as catalyst was proved to be effective to transform benzyl-protected P(CL-*co*-BVL) into benzyl-deprotected P(CL-*co*-CVL) bearing the lateral carboxyl group with little main-chain cleavage. The melting point (T_m), the glass transition temperature (T_g) and the hydrophilicity of the benzyl-deprotected P(CL-*co*-CVL) bearing the lateral carboxylmethyl functional group were higher than those of the benzyl-protected P(CL-*co*-BVL), however, the crystallinity was reversed.

The presence of carboxylic acid pendant-groups in the P(CL-*co*-CVL) is expected to improve the biodegradability and hydrophilicity of the copolymer. Meanwhile, the achieved copolymer architecture gives versatility to further derivatization, such as the introduction of some moiety such as RGD, biotin *etc*. through the carboxylic acid pendant groups.

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