Trans. Mat. Res. Soc. Japan 38[3] 473-476 (2013)

Syntheses and Physical Properties of Polyester and Poly(ester-urethane) Containing Phosphorylcholine Moiety

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The syntheses of novel polyesters and poly(ester-urethane)s containing phosphorylcholine (PC) group was carried out. The obtained polymers were soluble in aprotic polar solvents such as DMSO and NMP. By the way, the copolyesters containing polycarbonate segment showed the better solubility than the homopolyester, which were soluble in the low boiling point solvents such as THF and chloroform. Furthermore, the obtained polymers showed the high thermal stability up to 250°C, at which the thermal degradation of PC moiety occurred. In particular, the self-standing polymer films could be prepared from poly(ester-urethane). The poly(ester-urethane) films exhibited the elastic properties with high tensile strength, therefore, these polymers could be expected as elastic biocompatible materials for the use of biomedical devices.
Key words: biomaterial / diol monomer / phosphorylcholine / polyester / mechanical property

1. INTRODUCTION

In recent years, the developments of medical technology and devices have become more important because of the growing of an aging population. The safety of medical materials is considered as the most important factor for the use in a living body such as an implantable artificial organ. For example, segmented polyurethane, polydimethylsiloxane and poly(ester-urethane) have been investigated as biomaterials, due to its favorable physical properties, chemical inertness and biocompatibility [1-3]. On the other hand, 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer has been developed by Ishihara *et al.* as an excellent biocompatible material, which efficiently reduces the adhesion of cells and proteins on the polymer surface [4-7]. Then, MPC polymer has been widely applied in the cosmetic and medical fields.

In our previous study [8-10], we have investigated the syntheses of novel diamine and diol monomers containing phosphorylcholine (PC) group to prepare the thermally stable and mechanically strong polymers rather than MPC polymer. From these monomers, the preparations of polyamides and polyurethanes containing PC group have been carried out by polycondensation or polyaddition, and it has been found that these polymers exhibited the good biocompatibility and physical properties [11]. In fact, the amounts of platelet and proteins adhered on these polymer films efficiently decreased as the increase of the content of PC unit in these polymers. However, it was also found that the solubility of polymers became poor as the PC content of these polymers increased. It would be due to the high molecular interaction between the PC group in the side chain and the polar group in the main chain, such as amide or urethane bond.

The purpose of this study is to improve the solubility of PC-containing polymers by changing the main chain structure. For this purpose, we have attempted to prepare polyester and poly(ester-urethane) containing PC group by using 2-(3,5-bis(2-hydroloxyethoxy)benzoyloxy)-ethyl phosphorylcholine (BHPC) as a diol monomer. In this paper, the synthetic procedure of polyester containing PC group was described, and the control of the molecular weight of polyester was attempted by adding diisocyanate monomer in the polycondensation mixture to obtain poly(ester-urethane). Furthermore, the solubility, the thermal stability and the mechanical property of the obtained polymers were evaluated to reveal the possibility of practical materials.

2. EXPERIMENTAL

2.1 Materials

PC-containing diol monomer, 2-(3,5-bis(2-hydroloxyethoxy)benzoyloxy)ethyl phosphorylcholine (BHPC), was synthesized according to the procedure described in our previous report [10]. 4,4'-Diphenylmethane diisocyanate (MDI) and poly(carbonate diol) (PCD, *M*n = 1000, m = 6) were kindly supplied from Nippon Polyurethane Industry Co., Ltd. and Asahi Kasei Corporation, respectively. Other chemical reagents were used without further purification.

2.2 Syntheses of polyesters (HPE-1 and HPE-2)

Under an argon atmosphere, BHPC (0.80 g, 1.78 mmol) and terephthaloyl chloride (TPC, 0.36 g, 1.78 mmol) were mixed in 8.0 mL of NMP at -78°C. The mixture was stirred for 67 h with increasing the temperature to r. t. Then, the mixture was poured into excess THF to precipitate the polymer, and it was filtered and purified by reprecipitation from its NMP solution to excess THF. Finally, the product was dried *in vacuo* to obtain HPE-1 as a brown solid. Yield: 1.01 g (87.0%).

^{1}H-NMR, δ (400 MHz, DMSO-d_6, ppm):
3.09 (-$N^+(C\underline{H}_3)_3$, m), 3.57 (-$POCH_2C\underline{H}_2N$-, m), 4.11 (-$OC\underline{H}_2CH_2OPh$-, m), 4.22 (-$COOCH_2C\underline{H}_2OP$-, m), 4.37 (-$POC\underline{H}_2CH_2N$-,m), 4.59 (-$OCH_2C\underline{H}_2OPh$-, -$COO-C\underline{H}_2CH_2OP$-, m), 6.94 (-Ph-, m), 7.11 (-Ph-, m), 8.03 (-Ph-, m).
IR, ν (KBr, cm^{-1}): 2955, 2880, 1720 (C=O), 1597, 1493, 1450, 1408, 1373, 1269 (P=O), 1165, 1126, 1099, 729.

In the above polymerization reaction, 3,5-bis(2-hydroxyethyl)benzene (BHE) was used instead of BHPC, and the similar reaction and reprecipitation were carried out to afford HPE-2 as a white solid. Yield: 2.10 g (75.0%).
IR, ν (KBr, cm^{-1}): 2951, 2878, 1720 (C=O), 1605, 1493, 1454, 1408, 1130, 1099, 1068, 725.

2.3 Syntheses of copolyesters (CPE-1 and CPE-2)

Under an argon atmosphere, BHPC (0.55 g, 1.22 mmol), PCD (1.22 g, 1.22 mmol) and TPC (0.49 g, 2.44 mmol) were mixed in 6.5 mL of NMP at -78°C. The mixture was stirred for 42 h with increasing the temperature to r. t. Then, the mixture was poured into excess methanol to precipitate the polymer, and it was filtered and purified by reprecipitation from its NMP solution to excss methanol. Finally, the product was dried *in vacuo* to afford PE-2 as a yellow solid. Yield: 1.19 g (61.6%).

^{1}H-NMR, δ (400 MHz, DMSO-d_6, ppm):

1.29 (-OCH$_2$CH$_2$C$\underline{H_2}$C$\underline{H_2}$CH$_2$CH$_2$OCO-, m), 1.56 (-OCH$_2$C$\underline{H_2}$CH$_2$CH$_2$C$\underline{H_2}$CH$_2$OCO-, m), 3.11 (-N$^+$(C$\underline{H_3}$)$_3$, m), 3.45 (-POCH$_2$C$\underline{H_2}$N-, m), 4.03 (-OC$\underline{H_2}$CH$_2$OPh-, -OC$\underline{H_2}$CH$_2$CH$_2$CH$_2$CH$_2$C$\underline{H_2}$OCO-, m), 4.16 (-COOCH$_2$C$\underline{H_2}$OP-, m), 4.28 (-POC$\underline{H_2}$CH$_2$N-, m), 4.34 (-OCH$_2$C$\underline{H_2}$OPh-, -COOC$\underline{H_2}$CH$_2$OP-, m), 6.84 (-Ph-, m), 7.12 (-Ph-, m), 8.05 (-Ph-, m).

IR, ν (Film, cm^{-1}): 2937, 2868, 2366, 2343, 1736 (C=O), 1595, 1524, 1466, 1408, 1346, 1329 (P=O), 1242, 1173, 1069, 951, 791.

In the above polymerization reaction, BHE was used instead of BHPC, and the similar reactions and reprecipitation were carried out to afford CPE-2 as a white solid. Yield: 5.78 g (73.5%).

^{1}H-NMR, δ (400 MHz, DMSO-d_6, ppm):

1.27 (-OCH$_2$CH$_2$C$\underline{H_2}$C$\underline{H_2}$CH$_2$CH$_2$OCO-, m), 1.54 (-OCH$_2$C$\underline{H_2}$CH$_2$CH$_2$C$\underline{H_2}$CH$_2$OCO-, m), 4.01 (-OC$\underline{H_2}$-CH$_2$CH$_2$CH$_2$CH$_2$C$\underline{H_2}$OCO-, m), 4.39 (-OCH$_2$C$\underline{H_2}$OPh-, m), 6.55 (-Ph-, m), 7.15 (-Ph-, m), 8.04 (-Ph-, m).

IR, ν (Film, cm^{-1}): 2938, 2860, 1738 (C=O), 1597, 1530, 1464, 1404, 1381, 1242, 1220, 1065, 1016, 914, 814, 770.

2.4 Syntheses of copoly(ester-urethane)s (CPEU-1 and CPEU-2)

Under an argon atmosphere, BHPC (0.97 g, 2.16 mmol), PCD (2.16 g, 2.16 mmol) and TPC (0.44 g, 2.16 mmol) were mixed in 6.0 mL of NMP at -78°C. The mixture was stirred for 24 h with increasing the temperature to r. t. Then, the solution containing MDI (0.54 g, 2.16 mmol) in 2.5 ml of NMP was gradually added to the mixture at r. t. After the mixture was stirred at 50°C for 38 h. The mixture was poured into excess methanol to precipitate the polymer, and it was filtered and purified by reprecipitation from its NMP solution to excess methanol. Finally, the product was dried *in vacuo* to afford CPEU-1 as a brown solid. Yield: 2.43 g (59.7%).

^{1}H-NMR, δ (400 MHz, DMSO-d_6, ppm):

1.28 (-OCH$_2$CH$_2$C$\underline{H_2}$C$\underline{H_2}$CH$_2$CH$_2$OCO-, m), 1.55 (-OCH$_2$C$\underline{H_2}$CH$_2$CH$_2$C$\underline{H_2}$CH$_2$OCO-, m), 3.08 (-N$^+$(C$\underline{H_3}$)$_3$, m), 3.42 (-POCH$_2$C$\underline{H_2}$N-, m), 3.75 (-Ph-C$\underline{H_2}$-Ph-, bs), 4.01 (-OC$\underline{H_2}$CH$_2$OPh-, -OC$\underline{H_2}$CH$_2$CH$_2$CH$_2$CH$_2$C$\underline{H_2}$-OCO-, m), 4.15 (-COOCH$_2$C$\underline{H_2}$OP-, m), 4.24 (-PO-C$\underline{H_2}$CH$_2$N-, m), 4.36 (-OCH$_2$C$\underline{H_2}$OPh-, -COOC$\underline{H_2}$CH$_2$-OP-, m), 6.83 (-Ph-, m), 7.08 (-Ph-, m), 7.33 (-Ph-, m), 8.04 (-Ph-, m), 9.48 (-N$\underline{H}$COO-, bs), 9.70 (-N$\underline{H}$COO-, bs).

IR, ν (Film, cm^{-1}): 3500 (N-H), 2938, 2868, 2310, 1734 (C=O), 1716, 1597, 1541, 1375, 1346 (P=O), 1242, 1115, 1067, 876, 729.

In the above polymerization reaction, BHE was used instead of BHPC, and the similar reactions and reprecipitation were carried out to afford CPEU-2 as a white powder. Yield: 6.54 g (80.8%).

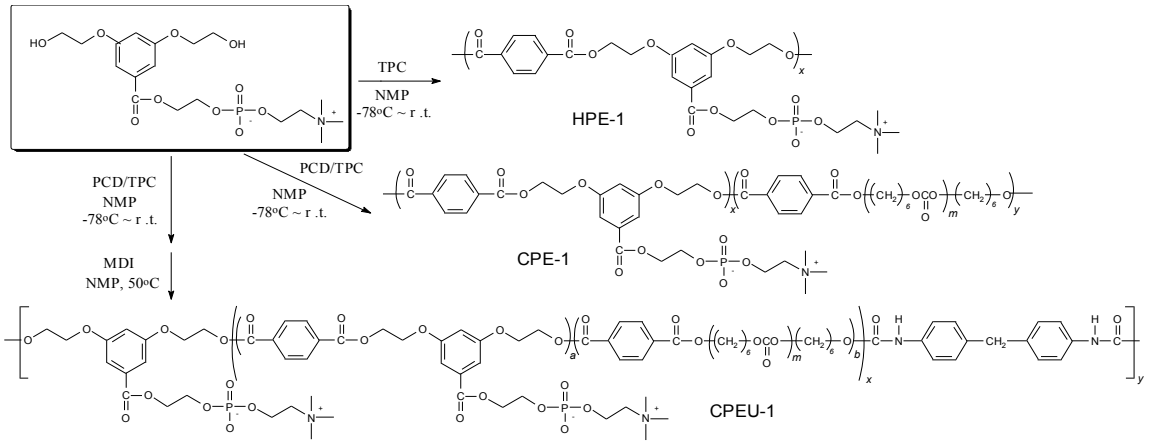
^{1}H-NMR, δ (400 MHz, DMSO-d_6, ppm):

1.28 (-OCH$_2$CH$_2$C$\underline{H_2}$C$\underline{H_2}$CH$_2$CH$_2$OCO, m), 1.54 (OCH$_2$C$\underline{H_2}$CH$_2$CH$_2$C$\underline{H_2}$CH$_2$OCO-, m), 3.75 (-PhC$\underline{H_2}$-Ph-, bs), 4.01 (-OC$\underline{H_2}$CH$_2$OPh-, -OC$\underline{H_2}$CH$_2$CH$_2$-CH$_2$CH$_2$C$\underline{H_2}$OCO-, m), 4.36 (-OCH$_2$C$\underline{H_2}$OPh-, -COO-C$\underline{H_2}$CH$_2$OP-, m), 6.54 (-Ph-, m), 7.06 (-Ph-, m), 7.35 (-Ph-, m), 8.04 (-Ph-, m), 9.45 (-N$\underline{H}$COO-, bs), 9.67 (-N$\underline{H}$COO-, bs).

IR, ν (Film, cm^{-1}): 3342 (N-H), 2937, 2862, 1736 (C=O), 1718, 1597, 1531, 1458, 1240, 1184, 1066, 1018, 961, 790.

2.5 Characterizations

^{1}H-NMR spectra were conducted with a JEOL NM-TH5SK 400MHz FT-NMR spectrometer. Infrared (IR) spectra were recorded with Shimadzu FTIR-8400 or IRAffnity-1 spectrometer. The molecular weights of polymers were estimated by Tosoh gel permeation chromatography system (HLC-8320GPC) equipped with three columns of TSK gels, Super Multipore HZ-H, using THF as an eluent. The average molecular weights were calibrated based on polystyrene standards. Differential scanning calorimetry (DSC) and thermal gravimetric analysis (TGA) were carried out on Seiko Instruments DSC-6200 and TG/DTA-6200, respectively,



Scheme 1 Preparations of polymers.

at a heating rate of 10°C/min under a nitrogen atmosphere. X-ray diffraction (XRD) of polymers was measured by Philip's Analytical X'Pert.

2.6 Measurements of stress-strain behavior

The polymers were dissolved in chloroform or THF and the solutions were poured on Teflon sheet. Then, the solvent was vaporized at 40°C under the vapor atmosphere. The obtained films were then dried *in vacuo* at 80°C for overnight, and the self-standing films were obtained. The polymer films were cut into rectangular strips with a length of 40 mm, a width of 10 mm and a thickness of 0.10 mm. Stress-strain curves were obtained on a JT Torsi LSC-01/30, where the gauge length was 20 mm and the crosshead speed was 0.2 mm sec^{-1}.

3. RESULTS AND DISCUSSION

3.1 Preparations of polyesters and poly(ester-urethane)s containing PC group

Scheme 1 shows the polymerization procedures of each polymers containing PC unit. At first, the preparations of two kinds of polyesters were carried out by the low-temperature polycondensation, one of which was a homopolyester, HPE-1, polymerized from BHPC with TPC, and the other was a copolyester, CPE-1, copolymerized from BHPC and PCD with TPC. Then, poly(ester-urethane) (CPEU-1) was prepared by polycondensation of BHPC and PCD followed by adding a diisocyanate monomer, MDI, to couple the oligoester. On the other hand, a homopolyester (HPE-2), copolyester (CPE-2) and poly(ester-urethane) (CPEU-2) without PC group were prepared from BHE instead of BHPC to compare the physical properties with the polymers containing PC group, HPE-1, CPE-1 and CPEU-1.

The compositions and the molecular weights of the obtained polymers were summarized in Table 1. The chemical structures of these polymers were confirmed by ^{1}H-NMR and IR spectra. The contents of PC unit in these copolymers were determined from the ratio of the peak intensities of the ammonium proton (3.08 - 3.11 ppm) of PC unit and the methylene proton (1.27 - 1.29, 1.54 - 1.56 ppm) of polycarbonate segment. The observed PC content in mol % was slightly lower than the molar ratio of BHPC and PCD in the copolymerization. The molecular weights of the PC-containing copolymers were in the range of 8.0 x10^3 - 1.3 x10^4.

The CPE and CPEU series containing polycarbonate segment exhibited a good solubility in aprotic polar solvents such as DMF, NMP, DMSO and the low boiling point solvents such as THF and chloroform at r. t., whereas there were insoluble in water, methanol and ethanol. By the way, the homopolyester containing PC group, HPE-1, was soluble in NMP and DMSO after heating at 70°C, even though HPE-2 was insoluble in these solvents. Therefore, it was found that the homopolyester containing PC group showed the better solubility than the homopolyester without PC group. It is speculated that the PC group would reduce the strong aggregation between the main chains of polyester such as HPE-2. Furthermore, the copolyesters and poly(ester-urethane)s containing polycarbonate segment showed the better solubility than the homopolyester, which were soluble even in THF and chloroform. It would be due to the reduction of the interaction between the polymer chains by polycarbonate soft segment.

Table 1 Compositions and molecular weights of polymers.

Code	Molar ratio of diol monomers BHPC/BHE/PCD	PC content [a] (mol%)	PC content [a] (wt.%)	$M_n \times 10^{-3}$ [b]	M_w/M
HPE-1	100/ 0/ 0	100	100	-	-
HPE-2	0/100/0	0	0	-	-
CPE-1	50/ 0/50	44.3	29.0	8.26	1.31
CPE-2	0/50/50	0	0	12.3	1.73
CPEU-1	50/ 0/50	49.6	26.7	12.9	1.35
CPEU-2	0/50/50	0	0	28.1	2.03

a) Calculated from the ratio of peak intensities of ^{1}H NMR spectra.
b) M_n and M_w were estimated by GPC using THF as eluent.

Table 2 Solubility of polymers.

Code	Solubility [a]						
	Water	Ethanol	Chloroform	THF	DMF	NMP	DMSO
HPE-1	×	×	×	×	×	○	○
HPE-2	×	×	×	×	×	×	×
CPE-1	×	×	○	○	○	○	○
CPE-2	×	×	○	○	○	○	○
CPEU-1	×	×	○	○	○	○	○
CPEU-2	×	×	×	○	○	○	○

a) The concentration of the solubility test was 0.5 wt. % in each solvent.
Symbols: ○ : Soluble × : Insoluble

3.2 Thermal property of polymers

The thermal property of the copolymers was investigated by DSC and TGA. In the DSC thermo grams, the glass transition temperature (*T*g) was observed for all of the polymers in the range between -26°C to -19°C. In the case of CPE-1 and CPE-2, the melting temperature (*T*m) was observed in the range between 33°C to 38°C. It is considered that the observed *T*g and *T*m of CPE-1 and CPE-2 would be derived from the glass transition and melting of polycarbonate segment. Actually, *T*g and *T*m of PCD was confirmed by DSC at -20°C and 42°C, respectively, and CPE-1 and CPE-2 films were softened and became elastic and transparent at *ca.* 40°C.

Then, XRD measurements of these polymers were conducted as shown in Fig. 1. It was obvious from these XRD patterns that CPE-1 and 2 showed the crystalline patterns of XRD, and CPEU-1 and 2 showed the glassy patterns. Therefore, it was suggested that the urethane component would reduce the crystallinity of polycarbonate segment in the polymer.

From the results of TGA measurements, the weight loss of all of the polymers started at *ca*. 250°C as shown in Fig. 2. The starting point of the weight loss would be

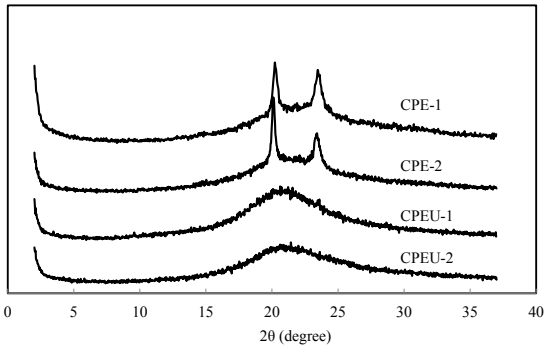


Fig. 1 XRD patterns of polymer films at r. t.

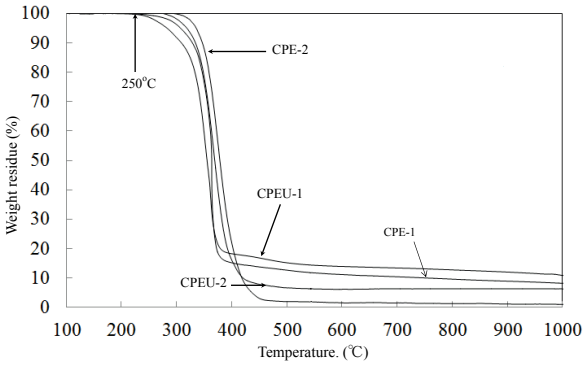


Fig. 2 TGA curves of polymers at a heating rate of 10°C/min in N_2 flow.

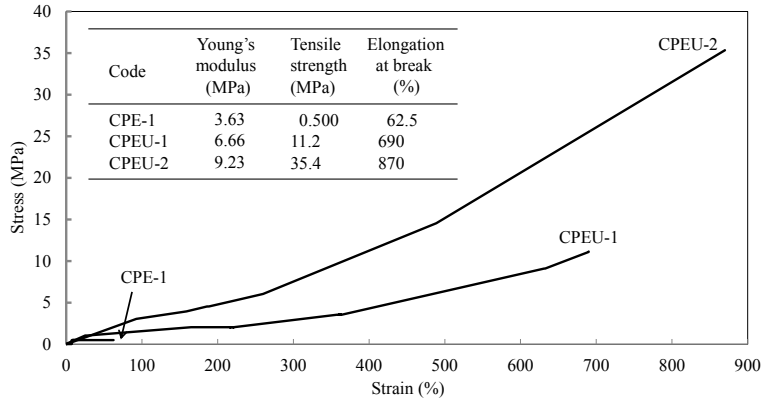
due to the thermal degradation of the PC component. This tendency was similar to the case of other PC containing polymers [8-11]. The heat resistance of PC-containing polymers over 200°C would be enough to apply it for the use as medical devices, for example, for the thermal sterilization process over 150°C.

3.3 Mechanical property of polymers

The mechanical properties of CPE-1, CPEU-1 and CPEU-2 films were evaluated to reveal the effect of introduction of PC unit on the mechanical property. From HPE-1, HPE-2 and CPE-2, the self-standing films could not be obtained. Fig. 3 shows the stress-strain behaviors of the polymer films, where the Young's modulus, the tensile strength and the elongation to break are also summarized. As seen in Fig. 3, a large elongation over 690 % was observed for CPEU-1 and 2 films, which seemed a rubberlike elastically. However, the tensile strength of CPE-1 film was extremely lower than that of CPEU-1 and 2 films. It was considered that the crystalline part of CPE-1 would make the film brittle. Therefore, the increase of the mechanical strength would be due to the existence of urethane bond in CPEU-1 and 2, which would enhance the molecular interaction in the hard segments rather than ester bond.

4. CONCLUSION

Polyesters and poly(ester-urethane) containing PC group were successfully prepared from PC-containing diol monomer, BHPC. The polymers containing the soft segment, polycarbonate unit, showed the good solubility in DMF, NMP, DMSO, THF and chloroform. In particular, the self-standing tough films could be prepared by casting from poly(ester-urethane), which showed the elastic property. In conclusion, these polymers could be expected as elastic biocompatible materials for the use of biomedical devices, although the biocompatibility of these polymers should be evaluated in the future.



Code	Young's modulus (MPa)	Tensile strength (MPa)	Elongation at break (%)
CPE-1	3.63	0.500	62.5
CPEU-1	6.66	11.2	690
CPEU-2	9.23	35.4	870

Fig. 3 Stress-Strain curves and physical data of polymers.

(Received February 26, 2013; Accepted May 27, 2013)

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