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Kayo Terada[a]; Fumio Sanda[a]; Toshio Masuda[a]
[a] Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University Katsura Campus, Kyoto, Japan

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Polycondensation of Diketopiperazine-based Dicarboxylic Acids with Diamines and Dibromoxylenes

KAYO TERADA, FUMIO SANDA, and TOSHIO MASUDA

Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University Katsura Campus, Kyoto, Japan

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Aspartic and glutamic acid-based diketopiperazines, *cyclo*(L-asparaginyl-L-asparaginyl) (DKPD) and *cyclo*(L-glutaminyl-L-glutaminyl) (DKPE) were synthesized. Polycondensation of DKPD and DKPE with α,α'-dibromoxylenes was carried out using K_2CO_3 as a base in DMF to obtain polymers with weight-average molecular weights (M_w's) of 1100–3500. Furthermore, polycondensation of DKPE with various diamines was carried out using 4-[4,6-dimethoxy-1,3,5-triazin-2-yl]-4-methylmorpholinium chloride as a condensation agent in DMF to obtain polymers with M_w's of 1200–4100. The polymers were insoluble in common organic solvents except DMF.

Keywords: aspartic acid; diketopiperazine; glutamic acid; hydrogen bonding; polycondensation

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1 Introduction

Amino acids are not only biologically relevant substances but also useful for highly pure chiral sources in organic synthesis. Although their structures are simple, they have plural functional groups including hydroxy and mercapto groups, as well as amino and carboxy groups, which enables them to be transformed into a wide variety of optically active materials. Polypeptides synthesized from amino acids have been examined as models of proteins; their higher-order structure and catalytic activity for various reactions have been investigated. The attempt to synthesize peptide-mimetic polymers has also been made by means of radical, cationic, and anionic polymerizations, coordination polymerization, polycondensation, and polyaddition of amino acid-based monomers (1–3). These peptide-mimetic polymers also attract much attention, because they possibly suppress the environmental burden due to biocompatibility and biodegradability in a similar fashion to naturally derived biopolymers.

Diketopiperazine (DKP), the smallest cyclic peptide, is a typical by-product in peptide synthesis. The s-*cis* secondary amide group is directed in a horizontal position to the DKP ring. It has been reported that DKP molecules construct aggregates based on tandem hydrogen bonding between the amide groups in a solid state. The structure of aggregates depends on the amino acid residues forming DKPs. For instance, a glycine-based DKP adopts a linear tape orientation, while an alanine-based one forms a layer-type structure (4). The solubility of DKP is commonly low due to the lack of flexibility of the ring bearing amide groups. In recent years, it has been reported that *N*-alkylation of one amide group effectively enhances the solubility, resulting in a change of association state (5). These DKPs construct supramolecular architecture utilizing noncovalent bonding such as hydrophobic and electrostatic interaction in addition to hydrogen bonding between the amide groups. The aggregates show liquid crystallinity (6) and form microcapsules (7). Phenylalanine-, aspartic and glutamic acid-based DKPs serve as oil gelators (8), wherein intermolecular hydrogen bonding plays a key importance to form molecular network. As described above, DKPs are useful components in the field of supramolecular chemistry. Consequently, synthesis of polymers consisting of DKP units may lead to development of materials showing interesting features based on the chirality and self-assembling properties of DKP. This article deals with the synthesis of aspartic and glutamic acid-based dicaboxylated DKPs and their polycondensation with α,α'-dibromoxylenes and diamines.

Address correspondence to: Fumio Sanda and Toshio Masuda, Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University Katsura Campus, Kyoto 615-8510, Japan. E-mail: sanda@adv.polym.kyoto-u.ac.jp; masuda@adv.polym.kyoto-u.ac.jp

2 Experimental

2.1 Measurements

^{1}H and ^{13}C-NMR spectra were recorded on a JEOL EX-400 spectrometer. IR spectra were measured on a JASCO FT/

IR-4100 spectrophotometer. Melting points (mp) were measured on a Yanaco micro melting point apparatus. Mass spectra were measured on a JEOL JMS-HX110A mass spectrometer. Specific rotations ($[\alpha]_D$) were measured on a JASCO DIP-100 digital polarimeter with a sodium lamp as a light source. The number- and weight-average molecular weights (M_n and M_w) of polymers were determined by gel permeation chromatography (GPC) on TSK gel α-3000, using a solution of LiBr (10 mM) in *N*,*N*-dimethylformamide (DMF) as an eluent at a flow rate of 1.0 mL/min, calibrated by polystyrene standards at 40°C.

2.2 Materials

All the reagents in monomer synthesis were used as purchased without purification. *cyclo*(L-glutaminyl-L-glutaminyl) (DKPE) was prepared from pyroglutamic acid as described in the literature ($[\alpha]_D = -34°$ (DMSO, $c =$ 0.10 g/dL)) (9). DMF was distilled over calcium hydride.

2.3 Monomer Synthesis

2.3.1 *O-cyclohexyl-L-aspartic acid benzyl ester tosylate (1)*

A solution of *N-tert*-butoxycarbonyl-*O*-cyclohexyl-L-aspartic acid (11.0 g, 35.0 mmol) and $TsOH \cdot H_2O$ (7.99 g, 42.0 mmol) in benzyl alcohol (20 mL) and benzene (35 mL) was heated under reflux with a Dean-Stark trap for 3.5 h until water formation stopped. The resulting mixture was added to a solution of ether (60 mL) and hexane (60 mL) to precipitate a solid. It was purified by recrystallization with ether/ethanol = 2/1 (v/v) to obtain **1** as a colorless solid in 83% yield.

2.3.2 *N-tert-butoxycarbonyl-O-cyclohexyl-L-asparaginyl-O-cyclohexyl-L-aspartic acid benzyl ester (2)*

Compound **1** (14.0 g, 29.2 mmol) was dissolved in ethyl acetate (150 mL), and triethylamine (10 mL, 71.9 mmol) was added to the solution at 0°C.

4-[4,6-Dimethoxy-1,3,5-triazin-2-yl]-4-methylmorpholinium chloride (Triazimoch, Tokuyama Co., 9.79 g, 30.0 mmol) and *N-tert*-butoxycarbonyl-*O*-cyclohexyl-L-aspartic acid (9.21 g, 29.2 mmol) were added to the mixture, and the resulting mixture was stirred at room temperature overnight. It was washed with 0.5 M HCl, saturated $NaHCO_3$ aq., and saturated NaCl aq., and then dried over anhydrous $MgSO_4$. Ethyl acetate was distilled off using a rotary evaporator. The residual mass was purified by silica gel column chromatography eluted with hexane/ethyl acetate = 4/1 (v/v) to obtain **2** as a colorless viscous liquid in 88% yield. ^{1}H-NMR (400 Hz, $CDCl_3$): δ 1.32–1.81 [m, 29H, -OC(CH_3)$_3$, -(CH_2)$_5$-], 2.64–3.02 [m, 4H, -CH_2-], 4.54 [s, 1H, -NHC*H*CONH-], 4.67–4.81 [m, 2H, OCH<], 4.81–4.93 [m, 1H, -NHC*H*COO-], 5.08–5.21 [m, 2H, -OC*H*$_2$-], 5.61 [d, $J = 8.4$ Hz, 1H, -NHCO-], 7.28–7.35 [m, 5H, Ar], 7.44 [d, $J = 8.0$ Hz, 1H, -NHCOO-].

2.3.3 *N-tert-butoxycarbonyl-O-cyclohexyl-L-asparaginyl-O-cyclohexyl-L-aspartic acid (3)*

Pd-C (10%, 260 mg) was added to a solution of **2** (15.5 g, 25.7 mmol) in methanol (320 mL). The suspension was degassed and flushed with hydrogen gas three times, and then the mixture was stirred at room temperature overnight. Then, the catalyst was filtered off, and the filtrate was concentrated on a rotary evaporator. The residue was dissolved in $CHCl_3$ and washed with saturated NaCl aq. twice. The organic layer was dried over anhydrous $MgSO_4$, and concentrated to obtain **3** as a white solid in 89% yield.

^{1}H-NMR (400 Hz, $CDCl_3$): δ 1.26–1.83 [m, 29H, -OC(CH_3)$_3$, -(CH_2)$_5$-], 2.70–3.02 [m, 4H, -CH_2-], 4.59 [s, 1H, -NHC*H*CONH-], 4.68–4.98 [m, 2H, OCH<], 4.84 [s, 1H, -NHC*H*COO-], 5.73 [d, $J = 4.0$ Hz, 1H, -NHCO-], 7.56 [d, $J = 7.2$ Hz, 1H, -NHCOO-], 8.33 [s, 1H, COOH].

2.3.4 *N-tert-butoxycarbonyl-O-cyclohexyl-L-asparaginyl-O-cyclohexyl-L-aspartic acid N′-hydroxysuccinimide ester (4)*

1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC · HCl, 4.80 g, 25.0 mmol), 4-(dimethylamino) pyridine (DMAP, 302 mg, 2.47 mmol), and *N*-hydroxysuccinimide (2.87 g, 25.0 mmol) was added to a solution of **3** (11.7 g, 22.9 mmol) in CH_2Cl_2 (100 mL) at 0°C, and then the resulting mixture was stirred at room temperature overnight. CH_2Cl_2 was then distilled off using a rotary evaporator, and the residue was dissolved in ethyl acetate. The solution was washed with 0.5 M HCl, saturated $NaHCO_3$ aq., and saturated NaCl aq., and then dried over anhydrous $MgSO_4$. Ethyl acetate was evaporated to obtain **4** as a white solid in 62% yield. ^{1}H-NMR (400 Hz, $CDCl_3$): δ 1.26–1.84 [m, 29H, -OC(CH_3)$_3$, -(CH_2)$_5$-], 2.73–3.12 [m, 4H, -CH_2-], 2.83 [s, 4H, -COC*H*$_2$C*H*$_2$CO-], 4.56 [s, 1H, -NHC*H*CONH-], 4.76 [m, 2H, OCH<], 5.22–5.37 [m, 1H, -NHC*H*COO-], 5.68–5.75 [m, 1H, -NHCO-], 7.63 [d, $J = 8.8$ Hz, 1H, -NHCOO-]. ^{13}C-NMR (100 Hz, $CDCl_3$): δ 23.81 [-OCHCH$_2$*C*H$_2$CH$_2$-], 25.26 [-CO*C*H$_2$*C*H$_2$CO-], 28.00 [-OCHCH$_2$CH$_2$*C*H$_2$-], 28.23 [-OC(*C*H$_3$)$_3$], 31.43 [-OCH*C*H$_2$-], 36.39 and 36.45 [>CH*C*H$_2$-], 47.06 [-NH*C*HCOO-], 50.74 [-NH*C*HCO-], 73.59 and 74.35 [-OCH<], 80.44 [-O*C*(CH$_3$)$_3$], 155.45 [C(CH_3)$_3$O*C*O-], 166.24 [-*C*ON*C*O-], 168.27 and 168.31 [>CHO*C*OCH$_2$-], 169.08 [-NO*C*OCH<], 170.61 [>CH*C*ON<].

2.3.5 *Cyclo(O-cyclohexyl-L-asparaginyl-O-cyclohexyl-L-asparaginyl) (5)*

Trifluoroacetic acid (TFA, 5 mL) was added to a solution of **4** (8.66 g, 14.2 mmol) in CH_2Cl_2 (100 mL) using a dropping funnel at 0°C, and the resulting mixture was stirred at room temperature overnight. After confirming the complete consumption of **4** by TLC, CH_2Cl_2 and TFA were distilled off *in vacuo*. The residual viscous liquid was dissolved in $CHCl_3$ (600 mL), and Na_2CO_3 (5.0 g) was added to the solution. The mixture was heated under reflux for 12 h, and

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then concentrated to ca. 200 mL. The mixture was washed with water and dried over anhydrous $MgSO_4$. It was concentrated on a rotary evaporator. The residue was purified by recrystallization with $CHCl_3$/hexane to obtain **5** as a white solid in 27% yield. Mp 225–228°C. $[\alpha]_D = -64^\circ$ ($CHCl_3$, $c = 0.10$ g/dL). ^{1}H-NMR (400 Hz, $CDCl_3$): δ 1.25–1.84 [m, 20H, -$(CH_2)_5$-], 2.74–2.87, 3.05–3.12 [m, 4H, -CH_2-], 4.37–4.39 [m, 2H, -NHC*H*CO-], 4.81 [s, 2H, OCH<], 6.70 and 6.73 [s, 2H, NH]. ^{13}C-NMR (100 Hz, $CDCl_3$): δ 23.44 [-OCHCH$_2$*C*H$_2$CH$_2$-], 25.01 [-OCHCH$_2$CH$_2$*C*H$_2$-], 31.29 [-OCH*C*H$_2$-], 38.21 [>CH*C*H$_2$-], 51.40 and 73.85 [-OCH<], 165.64 [>CHO*C*OCH$_2$-], 170.03 [>CH*C*ONH-]. IR (cm^{-1}, KBr): 3198 (NH), 3065 (NH), 2944 (CH), 2862 (CH), 1733 (C═O), 1672 (NHCO), 1451, 1269, 1184, 1015. HRMS (m/z) Calcd for $C_{20}H_{31}N_2O_6$ 395.2182. Found: 395.2188 $[M+H]^+$.

2.3.6 Cyclo(L-asparaginyl-L-asparaginyl) (DKPD)

2 M NaOH aq. (1.2 mL) was added to a suspension of **5** (396 mg, 1.00 mmol) in methanol (10 mL) and $CHCl_3$ (10 mL) at 0°C, and stirred at room temperature for 4 h. An excess amount of citric acid was added to the resultant mixture, and it was concentrated on a rotary evaporator. The residual solid was washed with water and $CHCl_3$ to obtain DKPD as white solid in 42% yield. Mp could not be determined due to decomposition. $[\alpha]_D = -10^\circ$ (DMSO, $c = 0.10$ g/dL). ^{1}H NMR (400 Hz, DMSO-d_6): δ 2.58–2.76 [m, 4H, -CH_2-], 4.08, 4.23 [s, 2H, -NHC*H*CO-], 8.04 [s, 2H, NH], 12.22 [s, 2H, -COOH]. ^{13}C-NMR (100 Hz, DMSO-d_6): δ 36.95 [>CH*C*H$_2$-], 51.21 [-NH*C*HCO-], 167.22 [-COOH], 171.59 [>CH*C*ONH-]. IR (cm^{-1}, KBr): 3263 (NH), 3082 (NH), 2946, 1713 (C═O), 1643 (NHCO), 1468, 1427, 1327, 1230, 1202. HRMS (m/z) Calcd for $C_8H_{11}N_2O_6$ 231.0617. Found: 231.0617 $[M+H]^+$.

2.4 Polycondensation: Typical Procedures

2.4.1 Poly(DKPD-6)

A solution of DKPD (116 mg, 0.504 mmol), **6** (133 mg, 0.504 mmol), and potassium carbonate (170 mg, 1.24 mmol) in DMF (2.5 mL) was stirred at room temperature for 24 h. The resulting mixture was concentrated and washed with 1.0 M HCl. The residue was isolated by filtration with a membrane filter (pore size 1 μm), and dried *in vacuo* overnight.

2.4.2 Poly(DKPE-9)

A solution of DKPE (130 mg, 0.503 mmol), **9** (54 mg, 0.50 mmol), and TRIAZIMOCH (324 mg, 1.21 mmol) in DMF (2.5 mL) was stirred at room temperature for 24 h. The resulting mixture was concentrated and washed with 1.0 M HCl. The residue was isolated by filtration with a membrane filter (pore size 1 μm), and dried *in vacuo* overnight.

2.4.3 Spectroscopic data of the polymers

Poly(DKPD-**6**); ^{1}H-NMR (400 Hz, DMSO-d_6): δ 2.72–2.90 [m, 4H, -CH_2-], 4.11 [s, 2H, -CH-], 5.15 [s, 4H, -C*H*$_2$Ar-], 7.24–7.60 [m, 4H, Ar], 8.04–8.22 [m, 2H, NH]. Poly(DKPD-**7**); ^{1}H-NMR (400 Hz, DMSO-d_6): δ 2.68–3.00 [m, 4H, -CH_2-], 4.15 [s, 2H, -CH-], 5.09 and 5.16 [s, 4H, -C*H*$_2$Ar-], 7.22–7.53 [m, 4H, Ar], 8.21 [s, 2H, NH]. Poly(DKPD-**8**); ^{1}H-NMR (400 Hz, DMSO-d_6): δ 2.68–3.00 [m, 4H, -CH_2-], 4.14 [s, 2H, -CH-], 5.09 and 5.17 [s, 4H, -C*H*$_2$Ar-], 7.30 and 7.34 [s, 4H, Ar], 8.19 [s, 2H, NH]. Poly(DKPE-**6**); ^{1}H-NMR (400 Hz, DMSO-d_6): δ 1.81–2.13 [m, 4H, -CHC*H*$_2$-], 2.27–2.64 [m, 4H, -CH_2CO-], 3.90 [s, 2H, -CH-], 5.15, 5.24 and 5.28 [s, 4H, -C*H*$_2$Ar-], 7.25–7.61 [m, 4H, Ar], 8.24 [s, 2H, NH]. Poly(DKPE-**7**); ^{1}H-NMR (400 Hz, DMSO-d_6): δ 1.82–2.11 [m, 4H, -CHC*H*$_2$-], 2.36–2.64 [m, 4H, -CH_2CO-], 3.90 [s, 2H, -CH-], 5.08 and 5.14 [s, 4H, -C*H*$_2$Ar-], 7.22–7.57 [m, 4H, Ar], 8.24 [s, 2H, NH]. Poly(DKPE-**8**); ^{1}H-NMR (400 Hz, DMSO-d_6): δ 1.85–2.14 [m, 4H, -CHC*H*$_2$-], 2.37–2.66 [m, 4H, -CH_2C O-], 3.90 [s, 2H, -CH-], 5.07 and 5.16 [s, 4H, -C*H*$_2$Ar-], 7.33 [d, $J = 19.6$ Hz, 4H, Ar], 8.23 [s, 2H, NH]. Poly(DKPE-**9**); ^{1}H-NMR (400 Hz, DMSO-d_6): δ 1.85–2.16 [m, 4H, -CHC*H*$_2$-], 2.28–2.46 [m, 4H, -CH_2CO-], 3.79–4.07 [m, 2H, -CH-], 7.12 and 7.55 [s, 4H, Ar], 8.28 [s, 2H, -CHN*H*CO-], 9.36 [s, 2H, CONHAr]. Poly(DKPE-**10**); ^{1}HNMR (400 Hz, DMSO-d_6): δ 1.76–2.13 [m, 4H, -CHC*H*$_2$-], 2.28–2.45 [m, 4H, -CH_2CO-], 3.66–3.81 [m, 2H, -CH-], 7.08–7.59 [m, 4H, Ar], 8.15–8.41 [m, 2H, -CHN*H*CO-], 8.88–8.98 [m, 2H, CONHAr]. Poly(DKPE-**11**); ^{1}HNMR (400 Hz, DMSO-d_6): δ 1.91–2.12 [m, 4H, -CHC*H*$_2$-], 2.26–2.49 [m, 4H, -C H$_2$CO-], 3.90 [s, 2H, -CH-], 7.45–7.65 [m, 4H, Ar], 8.23 [s, 2H, -CHN*H*CO-], 9.88–10.05 [m, 2H, CONHAr]. Poly(DKPE-**12**); ^{1}H-NMR (400 Hz, DMSO-d_6): δ 1.80–2.09 [m, 4H, -CHC*H*$_2$-], 2.17–2.41 [m, 4H, -CH_2CO-], 3.88 [s, 2H, -CH-], 4.00, 4.23 [s, 4H, CH_2Ar], 7.10–7.54 [m, 4H, Ar], 8.20 [s, 2H, -CHN*H*CO-], 8.37 [s, 2H, CONHAr]. Poly(DKPE-**13**); ^{1}H-NMR (400 Hz, DMSO-d_6): δ 1.78–2.06 [m, 4H, -CHC*H*$_2$-], 2.08–2.39 [m, 4H, -CH_2CO-], 3.86 [s, 2H, -CH-], 4.04, 4.22 [s, 4H, CH_2Ar], 7.18 and 7.51 [s, 4H, Ar], 8.181 [s, 2H, -CHN *H*CO-], 8.34 [s, 2H, CONHAr]. Poly(DKPE-**14**); ^{1}H-NMR (400 Hz, DMSO-d_6): δ 1.75–2.02 [m, 4H, -CHC*H*$_2$-], 2.02–2.25 [m, 4H, -CH_2CO-], 3.08–3.52 [m, 4H, -NH(C*H*$_2$)$_2$NH-] 3.86 [s, 2H, -C H-], 7.90 [s, 2H, CONHAr], 8.17 [s, 2H, -CHN*H*CO-].

3 Results and Discussion

3.1 Synthesis of DKPs

DKPE, a glutamic acid-based DKP was prepared by dimerization of pyroglutamic acid (2-carboxy-γ-butyrolactam), followed by hydrolysis (9). On the other hand, aspartic acid-based DKPD cannot be synthesized in a similar manner, because pyroaspartic acid (2-carboxy-β-propiolactam) is unstable and unavailable due to a large ring strain.

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We therefore synthesized DKPD from Boc-Asp(OcHex)-OH according to the route illustrated in Scheme 1. Intramolecular cyclization commonly competes with intermolecular coupling reaction. In the present study, the cyclization through intramolecular ester-amide exchange reaction of a linear dipeptide having *N*-hydroxysuccinimide ester as carboxy terminus successfully proceeded by heating under diluted conditions to give DKP **5**. DKPD was obtained by alkaline hydrolysis of the cyclohexyl ester part of **5**, followed by acidification with citric acid. DKPD was soluble in DMF and DMSO, but insoluble in MeOH, CH_2Cl_2, $CHCl_3$, benzene, and toluene.

Prior to synthesizing DKP-based polymers, the intermolecular interaction of DKP **5** was examined by ^{1}H-NMR spectroscopy, as commonly done to characterize molecular associations (10), including the self-association of cyclic secondary *cis*-amide (11–13). The ^{1}H-NMR spectra of **5** were measured in $CDCl_3$ with various concentrations (1–60 mM) at the temperature ranging from −50 to 50°C at every 10°C increment to examine the association of **5**. The chemical shift of the amide NH proton depended both on concentration and temperature as depicted in Figures 1 and 2, where the NH proton signal split due to coupling with chiral methine proton on the DKP ring. An increase in concentration and decrease in temperature resulted in a downfield shift of the signal, both of which indicate the formation of intermolecular hydrogen bonding between the amide groups. The ^{1}H-NMR measurement in less polar solvents such as benzene was preferable to that in $CDCl_3$ to determine the association, but **5** was insoluble in benzene.

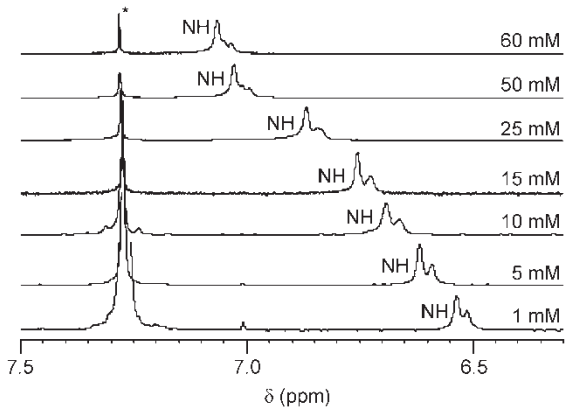
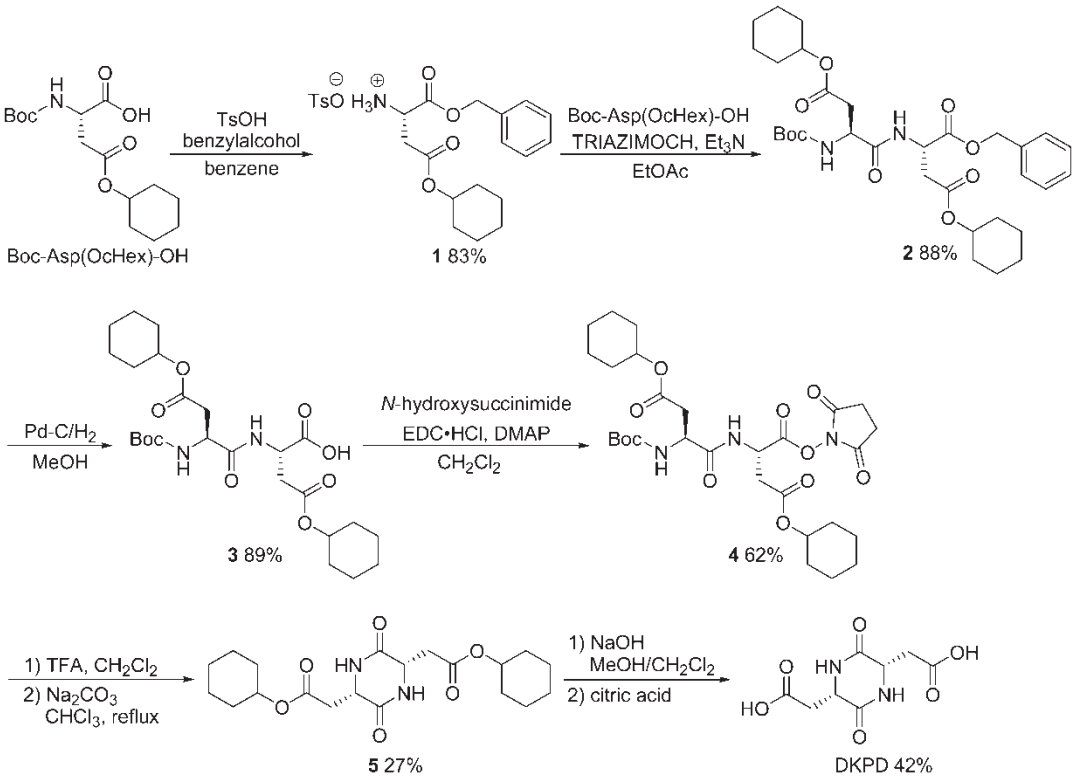


Fig. 1. Concentration dependence of the ^{1}H-NMR (400 MHz) chemical shift of the NH proton of **5** measured in $CDCl_3$ at 0°C. The asterisk represents the signal of $CHCl_3$.

3.2 Polycondensation of DKPE and DKPD with α,α′-dibromoxylenes

It is likely that DKP-based polymers carrying benzyl ester moieties are similarly assembled to DKP **5** carrying cyclohexyl ester moieties. We examined the polycondensations of DKPE and DKPD with α,α′-dibromoxylenes **6**–**8** to



Sch. 1. Synthesis of DKPD.

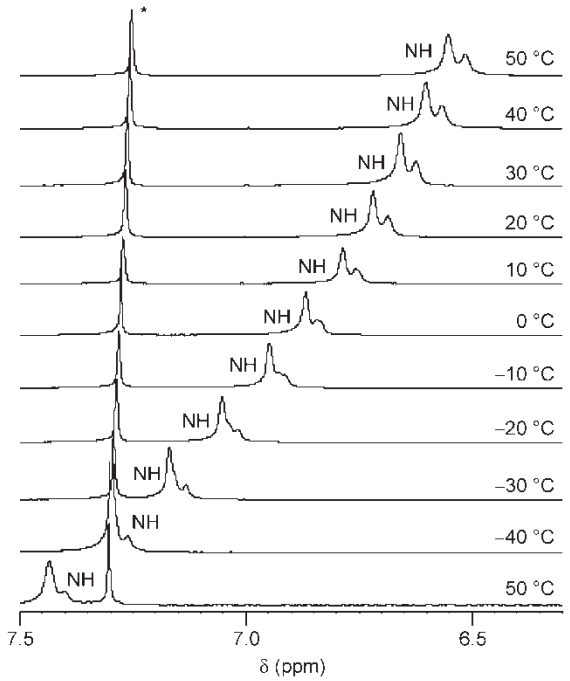
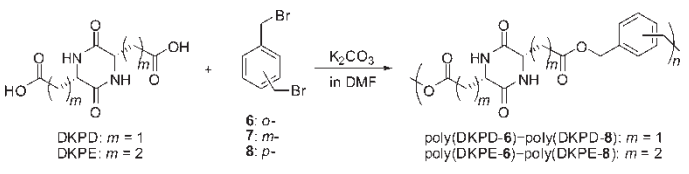


Fig. 2. Temperature dependence of the ^{1}H-NMR (400 MHz) chemical shift of the NH proton of **5** measured in $CDCl_3$ at a concentration of 25 mM. The asterisk represents the signal of $CHCl_3$.

obtain the polymers having DKP benzyl ester structures. The polycondensation was carried out in DMF using potassium carbonate as base at room temperature for 24 h (Scheme 2). Due to the low solubility of DKPD and DKPE in DMF, the monomer concentration was set at 0.2 M, which was relatively low compared to common solution polycondensation (14). A trace amount of polymeric mass precipitated along with KBr salt in the reaction mixture during polycondensation. We removed the white precipitate by filtration, and then subjected the filtrate to GPC measurement eluted with DMF without isolating the polymers. At first, we tried to isolate the polymers by pouring the reaction mixture into 1.0 M HCl, but no polymer precipitated. Along with a GPC peak at a monomer region, a shoulder peak was observed at a molecular weight region around several thousands, which should come from a polymer formed. The M_w's of the polymers were estimated to be 1100–3500 as summarized in Table 1. We also concentrated the polymerization mixture on a vacuum pump, and washed the residue with 1.0 M HCl to obtain a small amount of solid. It also showed GPC peaks both at polymer and



Sch. 2. Polycondensation of DKPD and DKPE with α,α'-dibromoxylenes **6**–**8**.

Table 1. Polycondensation of DKPD and DKPE with α,α'-dibromoxylene[a]

Run	DKP	α,α'-dibromoxylene	M_w^b	M_w/M_n^b
1	DKPD	**6**	3400	1.13
2	DKPD	**7**	1100	1.35
3	DKPD	**8**	1300	1.28
4	DKPE	**6**	3500	1.14
5	DKPE	**7**	3400	1.11
6	DKPE	**8**	3100	1.12

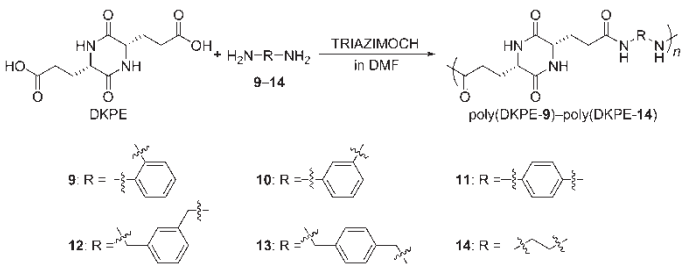
[a]Conditions: $[DKP]_0 = [\alpha,\alpha'\text{-dibromoxylene}]_0 = 0.20$ M, in DMF, room temperature, 24 h.
[b]Estimated by GPC based on polystyrene standards, eluent: LiBr solution in DMF (10 mM).

monomer regions, in which the ratio of the polymer was larger than the case without isolation.

As described above, the molecular weights of the polymers were not high. This is attributable to the relatively low concentration of DKPD and DKPE in DMF in polycondensation due to the low solubility. It seems that the precipitation of a DMF-insoluble polymer also prevented it from increasing the molecular weight. We also examined the polycondensation in DMSO, but the results were unsatisfactory. The polymer yields were not determined in Table 1, because the polymers could not be isolated.

3.3 Polycondensation of DKPE with Diamines

The polycondensation of DKPE with diamines **9**–**14** was carried out using TRIAZIMOCH as a condensation agent at room temperature for 12 h (Scheme 3). In a manner similar to the polyester synthesis described above, the polycondensation was also performed at a low monomer concentration (0.2 M), because of the low solubility of DKPE in DMF. In runs 3–6 in Table 2, a solid gradually precipitated during the polymerization. After a set time, the DMF-insoluble part was filtered off and the GPC measurement of the filtrate was conducted without isolation, because no polymeric mass was obtained when the reaction mixture was poured into 1.0 M HCl. Except run 3, a polymeric GPC peak was observed as a shoulder at a molecular weight region of several thousands. The M_w's of the polymers were 1200–4100. It is likely that the low molecular weights are also caused by the low



Sch. 3. Polycondensation of DKPE with diamines **9**–**14**.

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Table 2. Polycondensation of DKPE with diamines[a]

Run	Diamine	M_w^b	M_w/M_n^b
1	**9**	3200	1.07
2	**10**	2200	1.07
3	**11**	460	1.24
4	**12**	4100	3.70
5	**13**	1200	1.48
6	**14**	2800	1.06

[a]Conditions: $[DKPE]_0 = [diamine]_0 = 0.20$ M, [4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride] = 0.44 M in DMF, room temperature, 24 h.
[b]Estimated by GPC based on polystyrene standards, eluent: LiBr solution in DMF (10 mM).

reagent concentration and low solubility of the polymers. We also examined the polycondensation in DMSO, but the results were unsatisfactory. The polymerization mixtures were insoluble in common organic solvents except DMF and DMSO. The polymer solutions in DMF exhibited negligibly small specific rotations and CD signal, and they showed no birefringence on a polarized optical microscope.

4 Conclusions

In this article, we have demonstrated the polycondensation of dicarboxylated DKPs with α,α'-dibromoxylenes and diamines to obtain the oligomeric polyesters and polyamides. The polymers exhibited no evidence to take a higher order structure. We suppose that improvement of solubility of the polymers by introducing long alkyl chains leads to the formation of higher order structure and assembly of DKP-based polymers, because the presence of intermolecular hydrogen bonding of DKP **5** was confirmed by ^{1}H-NMR spectroscopy. Further studies on introducing other functional groups into the polymers are now under progress.

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