Synthesis, Chiroptical Properties, and pH Responsibility of Aspartic Acid- and Glutamic Acid-Based Helical Polyacetylenes

Fumio Sanda,* Kayo Terada, and Toshio Masuda*

Department of Polymer Chemistry, Graduate School of Engineering, Kyoto university, Kyoto Daigaku Katsura, Nishikyo-ku, Kyoto 615-8510, Japan

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ABSTRACT: L-Aspartic and L-glutamic acid-based novel *N*-propargylamides, (*S*)-HC≡CCH_2NHCOCH-(CH_2COOcyclohexyl)NHCOO*t*-Bu (**1**) and (*S*)-HC≡CCH_2NHCOCH(CH_2CH_2COOcyclohexyl)NHCOO*t*-Bu, were synthesized and polymerized using a rhodium catalyst. The corresponding polymers [poly(**1**) and poly(**2**)] with moderate molecular weights were obtained in good yields. CD and UV−vis spectroscopic analyses revealed that poly(**1**) and poly(**2**) took helical structures, whose tightness was different. The presence of intramolecular hydrogen bonding was confirmed by liquid-state IR spectroscopy. Poly(**1a**) and poly(**2a**) carrying free carboxyl groups were obtained by alkaline hydrolysis of poly(**1**) and poly(**2**). Poly(**1a**) did not form a helix, while poly(**2a**) formed a helix undergoing inversion of helical sense and change of tightness upon addition of KOH.

Introduction

Stimuli-responsive polymers attract attention in a wide variety of fields including pharmacy, life sciences, agriculture, and chemical engineering. Heat, light, and change of medium conditions including polarity and pH are commonly employed as stimuli, since these stimuli are easily controllable and applicable to practical usage. For instance, polymers carrying carboxyl groups such as poly(acrylic acid) and poly(methacrylic acid) have been extensively investigated as pH-responsive materials.[1] The pendent carboxyl groups accept protons at low pH and release them at high pH. They change the conformation and molecule size drastically according to pH due to the change of electrostatic repulsion between the side chains. Helical peptides containing aspartic and/or glutamic acids undergo helix−coil transition depending on pH.[2] The conformation of these peptides is decided by both the stabilization effect based on hydrogen bonding between the amide groups and the state of electrostatic repulsion between the carboxyl groups.

We have recently reported the synthesis of several amino acid-carrying polyacetylenes with well-defined higher order structures. For example, an alanine-derived poly(*N*-propargylamide) takes a helical conformation in chloroform.[3] Hydrogen bonding involving N−H linkage plays an important role in stabilizing the helical conformation. Serine- and threonine-derived poly(*N*-propargylamides) also form a helix, which is tight compared to alanine-derived one.[4] This is due to the presence of hydroxyl groups that participate in the hydrogen-bonding strands between the amide groups, resulting in change of torsional angles of the polyacetylene main chain.

If we employ aspartic or glutamic acid as a component of poly(*N*-propargylamides), it is expected to obtain a polymer undergoing helix−coil transition caused by competition between hydrogen bonding and electrostatic repulsion in a manner similar to some peptides. The present study deals with synthesis of aspartic and glutamic acid-derived novel poly(*N*-propargylamides) (Scheme 1), chiroptical properties of the polymers, hydrolysis of the ester parts, and change of the chiroptical properties of the hydrolyzed polymers with pH.

* Corresponding authors: F. Sanda (e-mail sanda@adv.polym.kyoto-u.ac.jp) or T. Masuda (e-mail masuda@adv.polym.kyoto-u.ac.jp).

Experimental Section

Measurements. ^{1}H NMR spectra were recorded on a JEOL EX-400 spectrometer. IR spectra were measured using a Shimadzu FTIR-8100 spectrophotometer. Melting points (mp) were measured on a Yanaco micro-melting point apparatus. Elemental analysis was done at the Kyoto University Elemental Analysis Center. 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 a JASCO Gulliver system (PU-980, CO-965, RI-930, and UV-1570) equipped with polystyrene gel columns (Shodex columns K804, K805, and J806), using THF as an eluent at a flow rate of 1.0 mL/min, calibrated by polystyrene standards at 40 °C. CD and UV−vis spectra were measured in a quartz cell (thickness: 1 cm) at room temperature using a JASCO J-820 spectropolarimeter.

Materials. All the reagents in monomer synthesis were used as purchased without purification. (nbd)$Rh^+[\eta^6$-$C_6H_5B^-$-(C_6H_5)$_3$] (nbd = 2,5-norbornadiene) was prepared by the reaction of [(nbd)RhCl]$_2$ with $NaB(C_6H_5)_4$ as described in the literature.[5] THF used for polymerization was distilled by the standard procedure.

Monomer Synthesis. *N*-*tert*-Butoxycarbonyl-*O*-cyclohexyl-L-aspartic Acid *N*′-Propargylamide (1). *N*-Methylmorpholine (8.05 g, 79.3 mmol) and isobutyl chloroformate (10.8 g, 79.1 mmol) were added to a solution of *N*-*tert*-butoxycarbonyl-*O*-cyclohexyl-L-aspartic acid (25.0 g, 79.3 mmol) in THF (450 mL) at room temperature.[6] Then, propargylamine (4.36 g, 79.3 mmol) was added to the mixture at 0 °C, and the resulting mixture was stirred at room temperature overnight. Precipitate formed was filtered off, and the filtrate was concentrated by rotary evaporation. The residual mass was dissolved in ethyl acetate (400 mL), and the solution was washed with water (400 mL) three times. The organic layer was separated and dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by recrystallization with hexane/ethyl acetate = 2/1 (v/v) to obtain **1** as white powder.

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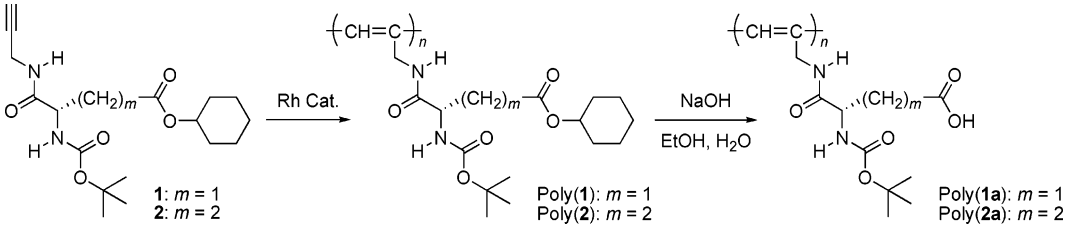
Scheme 1



Yield 23.8 g (82%); mp 104−105 °C; $[\alpha]_D$ −16.9°(c = 0.131 g/dL in THF at room temperature). ^{1}H NMR (400 Hz, $CDCl_3$): δ 1.44 [s, 15H, (CH_3)$_3$, (CH_2)$_3$], 1.70 [m, 2H, OCH(CH_2)], 1.83 [m, 2H, OCH(CH_2)], 2.22 [s, 1H, HC≡], 2.66 [m, 1H, CHCH_2], 2.96 [m, 1H, CHCH_2], 4.04 [s, 2H, CH_2], 4.49 [s, 1H, CHNH], 4.77 [m, 1H, OCH_2], 5.66 [s, 1H, NHCOO], 6.74 [s, 1H, NHCO]. ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.35 [OCHCH$_2$CH_2], 25.95 [OCHCH$_2$CH$_2$CH_2], 28.97 [(CH_3)$_3$],29.97 [OCHCH$_2$], 32.15 [CH$_2$], 37.01[CHCH$_2$], 51.27 [NHCH], 72.32 [HC≡], 74.37 [C(CH$_3$)$_3$], 79.80 [OCH], 81.23 [CH$_2$$C$≡], 156.20 [C(CH$_3$)$_3OC$O], 171.13 [$C$OO], 171.83 [NH$C$O]. IR (cm^{-1}, KBr): 3248 (H−C≡), 2126 (H−C≡), 1734 (C=O), 1687 (NHCOO), 1664 (NHCO), 1538, 1509, 1252, 1184, 1055, 1011, 710, 660. HRMS Calcd for $C_{18}H_{28}N_2O_5$ (m/z): 353.2076. Found: 353.2082.

***N*-*tert*-Butoxycarbonyl-*O*-cyclohexyl-L-glutamic Acid *N*′-Propargylamide (2).** The title compound was synthesized from *N*-*tert*-butoxycarbonyl-*O*-cyclohexyl-L-glutamic acid and propargylamine in a manner similar to **1**. Yield 19%; mp 107−108 °C; $[\alpha]_D$ −14.6°(c = 0.098 g/dL in THF at room temperature). ^{1}H NMR (400 Hz, $CDCl_3$): δ 1.44 [s, 9H, (CH_3)$_3$], 1.61 [m, 6H, (CH_2)$_3$], 1.73 [m, 2H, OCH(CH_2)], 1.84 [m, 2H, OCH-(CH_2)], 1.94 [t, J = 8.00 Hz, 1H, CH_2CO], 2.11 [t, J = 8.00 Hz, 1H, CH_2CO], 2.23 [s, 1H, HC≡], 2.35 [m, 1H, CHCH_2CH$_2$], 2.48 [m, 1H, CHCH_2CH$_2$], 4.04 [s, 2H, CH_2], 4.14 [s, 1H, CHNH], 4.77 [s, 1H, OCH_2], 5.25 [s, 1H, NHCOO], 6.57 [s, 1H, NHCO]. ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.04 [OCHCH$_2$CH_2], 25.62 [OCH$_2$CH$_2$CH_2], 27.97 [CHCH$_2$CH$_2$], 28.58 [CHCH$_2$CH_2], 29.47 [(CH_3)$_3$], 31.23 [OCH(CH_2)], 31.90 [CH_2], 71.98 [HC≡], 73.52 [OCH], 79.43 [CH$_2$$C$≡], 173.09 [C(CH$_3$)$_3OC$O], 183.53 [$C$OO], 186.55 [NH$C$O]. IR (cm^{-1}, KBr): 3262 (H−C≡), 1728 (C=O), 1694 (NHCOO), 1659 (NHCO), 1454, 1308, 1198, 1102, 1009, 722, 685. Anal. Calcd for $C_{19}H_{30}N_2O_5$: C, 62.27; H, 8.25; N, 7.64. Found: C, 62.16; H, 8.26; N, 7.53.

Polymerization. The polymerization was carried out in a glass tube equipped with a three-way stopcock under nitrogen. (nbd)Rh$^+$[η^6-C$_6$H$_5$B$^-$(C$_6$H$_5$)$_3$] (10.3 mg, 0.02 mmol) was added to a solution of a monomer (1.0 mmol) in THF (5.0 mL), and the resulting mixture was vigorously stirred. It was kept in a water bath at 30 °C for 1 h. The resulting mixture was poured into *n*-hexane (250 mL) to precipitate a polymer. It was separated by filtration using a membrane filter (ADVANTEC H100A047A) and dried under reduced pressure.

Alkaline Hydrolysis of the Polymers. To a solution of poly(**1**) (619 mg, 1.76 mmol) in THF (10 mL), 1 M NaOH aqueous solution (2.3 mL, 2.3 mmol) was added at 0 °C, and the resulting mixture was stirred at 50 °C for 2.5 h. The reaction mixture was acidified with 0.5 M solution of citric acid in methanol (45 mL) and concentrated by rotary evaporation. The resulting mixture was poured into water (300 mL) to precipitate poly(**1a**). It was separated by filtration using a membrane filter (ADVANTEC H100A047A) and dried under reduced pressure.

Spectroscopic Data of the Polymers. Poly(1): ^{1}H NMR (400 Hz, $CDCl_3$): δ 1.41 [br, 15H, (CH_3)$_3$, (CH_2)$_3$], 1.75 [br, 4H, OCH(CH_2)$_2$], 2.83 [br, 2H, CH_2CO], 4.11 [s, 1H, HC=], 4.73 [br, 3H, CH, CH_2], 6.10 [br, 1H, NHCOO], 7.94 [br, 1H, NHCO]. IR (cm^{-1}, KBr): 3351 (NHCO), 2940 (CH), 1728 (C=O), 1655 (NHCO), 1173, 1049, 1017. **Poly(2)**: ^{1}H NMR (400 Hz, $CDCl_3$): δ 1.42 [br, 15H, (CH_3)$_3$, (CH_2)$_3$], 1.72 [br, 2H, OCH(CH_2)], 1.83 [br, 2H, OCH(CH_2)], 2.36 [br, 2H, CH_2CO], 3.49 [s, 1H, HC=], 4.05 [br, 1H, CH], 4.73 [br, 2H, CH_2]. IR (cm^{-1}, KBr): 3292 (NHCO), 2940 (CH), 1717 (C=O), 1647 (NHCO), 1173, 1046, 1019. **Poly(1a)**: ^{1}H NMR (400 Hz, CD_3OD): δ 1.44 [br, 9H, (CH_3)$_3$], 2.86 [br, 2H, CH_2CO], 3.96 [br, 2H, CH_2C≡C], 4.55 [br, 1H, CHNH], 6.16 [br, 1H, NH]. IR (cm^{-1}, KBr): 3336 (NHCO), 2980 (CH), 1717 (C=O), 1655 (NHCO). **Poly(2a)**: ^{1}H NMR (400 Hz, CD_3OD): δ 1.44 [br, 9H, (CH_3)$_3$], 4.12 [br, 2H, CH_2C≡C], 4.23 [br, 1H, CHNH], 6.18 [br, 1H, NH].

Table 1. Polymerization of 1 and 2[a]

monomer	yield[b] (%)	M_n[c]	M_w/M_n[c]	$[\alpha]_D$[d] (deg)
1	91	9600	1.71	−35
2	95	24 900	2.05	−813

[a] Catalyst: (nbd)Rh$^+$[η^6-C$_6$H$_5$B$^-$(C$_6$H$_5$)$_3$], in THF, 30 °C, 1 h, [M]$_0$ = 0.20 M, [M]$_0$/[Cat] = 50. [b] Hexane-insoluble part. [c] Determined by GPC calibrated by polystyrene standards. Eluent: THF. [d] Measured by polarimetry at room temperature, c = 0.097−0.102 g/dL, in THF. $[\alpha]_D$ of monomers, **1**: −17°, **2**: −15°.

Results and Discussion

Synthesis and Chiroptical Properties of Poly-(1) and Poly(2). Table 1 summarizes the conditions and results of the polymerization of aspartic and glutamic acid-based acetylene monomers **1** and **2** catalyzed with (nbd)Rh$^+$[η^6-C$_6$H$_5$B$^-$(C$_6$H$_5$)$_3$] in THF (Scheme 1). The corresponding polymers, poly(**1**) and poly(**2**), with M_n's of 9600 and 24 900 were obtained in nearly quantitative yields. The specific rotations of the polymers were −35° and −813°, respectively.

The structures of poly(**1**) and poly(**2**) were examined by ^{1}H NMR spectroscopy. It has been reported that the Rh zwitterion complex efficiently catalyzes the polymerization of monosubstituted acetylenes by the insertion mechanism to give *cis*-transoidal polyacetylenes.[7] In the present study, the *cis* content could not be decided from the integration ratio of the *cis*-olefinic proton signal around 5 ppm because it appeared very broadly. Since several poly(*N*-propargylamides) obtained by the polymerization using the Rh catalyst are confirmed to have *cis* structure,[8] it is assumed that the steric structure of poly(**1**) and poly(**2**) is also the case.

Figure 1 depicts the CD and UV−vis spectra of poly-(**1**) and poly(**2**) along with those of poly(**1a**) and poly-(**2a**) that will be described later. Poly(**1**) exhibited a clear CD signal around 260 nm based on the conjugated polyacetylene main chain. The wavelength was as much as 120−140 nm short compared to common poly(*N*-propargylamides) reported so far.[9] It is likely that poly-(**1**) forms a helix with a small pitch/diameter ratio compared to that of poly(*N*-propargylamides).[10] On the other hand, poly(**2**) exhibited a CD signal at 400 nm, where common helical poly(*N*-propargylamides) show the signals.

It is assumed that the drastic difference of CD spectroscopic patterns between the aspartic acid- and glutamic acid-based poly(**1**) and poly(**2**) is brought about by the difference of orientation of the ester groups in the side chains. Because of even and odd methylene chains between the chiral centers and ester moieties, the ester carbonyl groups of poly(**1**) and poly(**2**) should

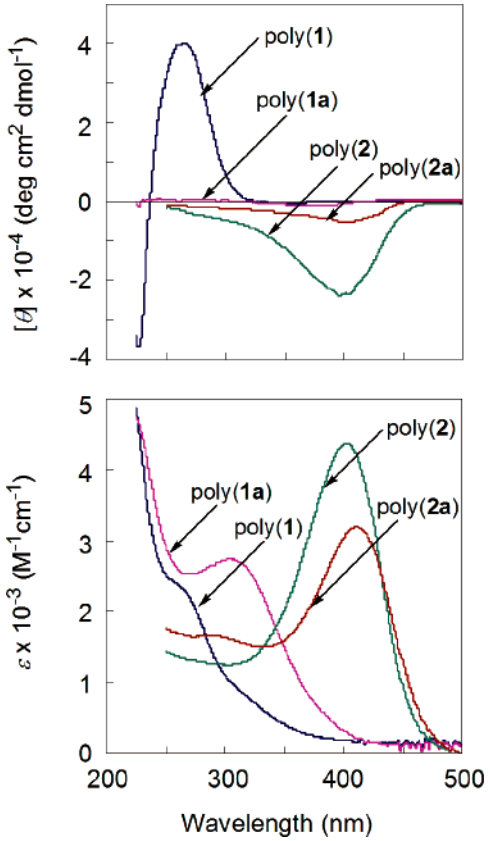


Figure 1. CD and UV−vis spectra of poly(**1**), poly(**2**), poly(**1a**), and poly(**2a**) measured in THF (c = 0.5 mM) at 0 °C.

be positioned in the opposite direction. Consequently, the ester parts of the polymers play a role very differently to decide the polymer conformation. In fact, poly(β-benzyl L-aspartate) and poly(γ-benzyl L-glutamate) show very different conformations. The former can change the structure from right-handed α-helix, left-handed α-helix, left-handed ω-helix, and then β-sheet upon heating.[11] On the other hand, the latter can only take right-handed α-helix as a stable conformation.[12]

Liquid-state IR spectroscopic study was carried out to obtain information on hydrogen bonding. Figure 2 depicts the partial IR spectra of **1**, **2**, poly(**1**), and poly(**2**) measured in THF. The peaks of C=O stretching of the amide and carbamate moieties of poly(**1**) were observed at 37 and 38 cm^{-1} lower wavenumbers than those of **1**. In a similar fashion, those of poly(**2**) were 41 and 9 cm^{-1} lower than those of **2**. These results indicate that the amide and carbamate moieties form hydrogen bonding, and it is *intramolecular* one judging from the low reagent concentration (50 mM).

From the results of the liquid-state IR spectroscopic study, it is necessary to consider a molecular geometry accompanying intramolecular hydrogen bonding. Two ways of intramolecular hydrogen bonding are possible as shown in Chart 1. One is the hydrogen bonding formed between the amide−amide and carbamate−carbamate moieties at nth and (n + 2)th units (pattern [A]), and another one is formed at nth and (n + 3)th units (pattern [B]). The dihedral angle ϕ at the single bond in the main chain possibly ranges from 100° to 160° and from 50° to 110° in the former and latter cases, respectively. The conformers out of these ranges cannot form sequential hydrogen-bonding strands because the amide−amide and carbamate−carbamate distances become too long. Molecular mechanics calculation suggested that the most stable conformer of poly(**1**) is the one with ϕ = 70°, which accompanies hydrogen-bonding strands formed between nth and (n + 3)th units. On the other hand, it was suggested that the conformer with ϕ = 140° is the most stable in the case of poly(**2**), which forms hydrogen bonding between nth and (n + 2)th units.[13]

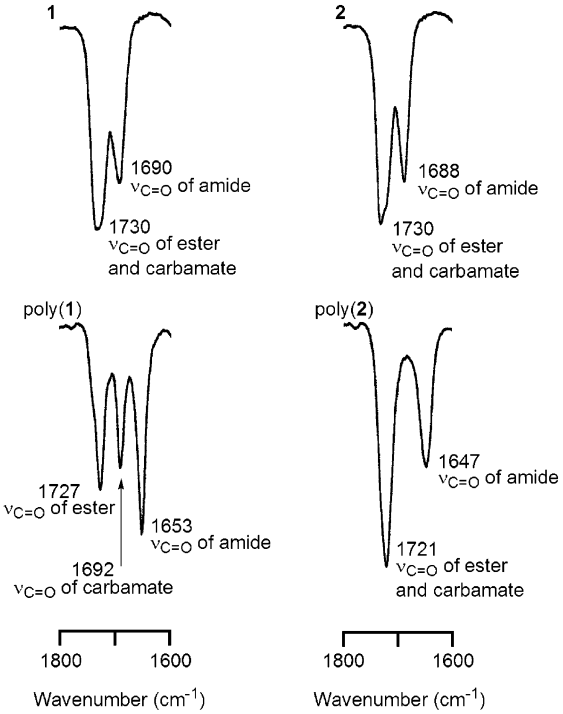
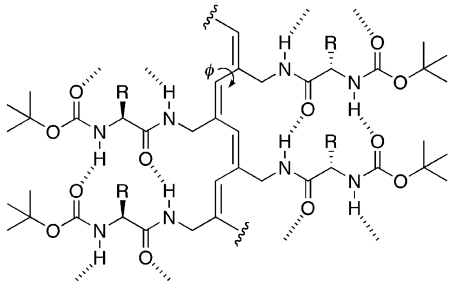


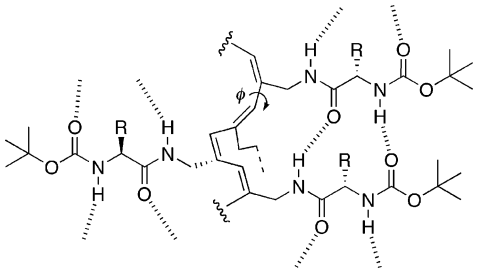
Figure 2. IR spectra of **1**, **2**, poly(**1**), and poly(**2**) measured in THF at a concentration of 50 mM.

Chart 1

[A] Hydrogen Bonding between nth and (n+2)th Units



[B] Hydrogen Bonding between nth and (n+3)th Units



R = CH_2CO_2cyclohexyl, $CH_2CH_2CO_2$cyclohexyl

Hydrolysis of the Ester Groups of Poly(1) and Poly(2). Alkaline hydrolysis of the ester groups of poly(**1**) and poly(**2**) was carried out to obtain the corresponding polymers with carboxyl groups, poly(**1a**) and poly(**2a**). At first, we attempted to obtain these polymers directly by the polymerization of the monomers with

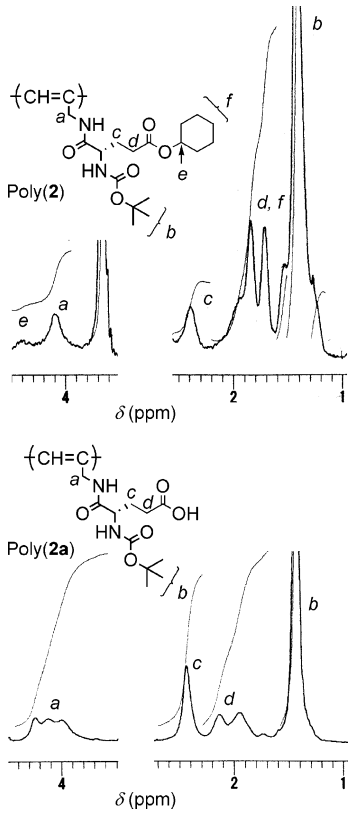


Figure 3. Partial ^{1}H NMR spectra of poly(**2**) measured in $CDCl_3$ and poly(**2a**) measured in CD_3OD.

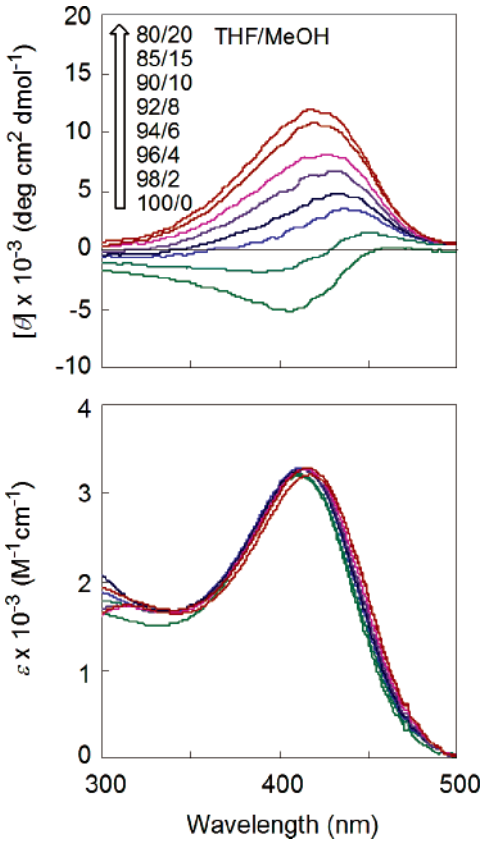


Figure 4. CD and UV−vis spectra of poly(**2a**) measured in THF/MeOH (c = 0.5 mM) with various compositions at 0 °C.

carboxyl groups, **1a** and **2a**, which were synthesized by hydrolysis of **1** and **2**. Unfortunately, however, no polymerization took place despite the addition of NaOH or triethylamine, unlike the case of the polymerization of 4-ethynylbenzoic acid.[14] Therefore, we abandoned the method and employed polymer reaction to obtain the polymers with carboxyl groups. Figure 3 depicts the partial ^{1}H NMR spectra of poly(**2**) and poly(**2a**).[15] The hydrolysis of the cyclohexyl ester was confirmed by the disappearance of signals *e* and *f*, which was evident from the integration ratio between the residual methylene proton signals *a*, *c*, and *d*. In a similar manner, the hydrolysis of the ester part of poly(**1**) was also confirmed. The alkaline hydrolysis of poly(**1**) and poly(**2**) successfully proceeded to give poly(**1a**) and poly(**2a**).

As shown in Figure 1, poly(**1a**) obtained by hydrolysis of poly(**1**) exhibited no CD signal around 260 nm where poly(**1**) exhibited the Cotton effect. Meanwhile, poly(**1a**) exhibited a UV−vis absorption peak at 320 nm, which is assignable to randomly coiled polyacetylene backbone.[16] This result indicates that the hydrolysis of the ester moiety of poly(**1**) resulted in transformation of helical structure into random coil. It is considered that electrostatic repulsion between the carboxyl groups is unfavorable to stabilize the helix. On the contrary, poly(**2a**) obtained by hydrolysis of poly(**2**) exhibited a CD signal and UV−vis absorption around 400 nm. Comparing the intensities of the CD and UV−vis peaks before and after hydrolysis (before: −23 683 deg cm^2 dmol^{-1} and 4378 M^{-1} cm^{-1}; after: −5138 deg cm^2 dmol^{-1} and 3196 M^{-1} cm^{-1}; both decreased to 78% and 27% of the original ones by hydrolysis), it seems that the polymer still remained in a helical form after hydrolysis but decreased the degree of predominance of one-handedness of screw sense. Random coiled structure should be contaminated in poly(**2a**) to some extent because a small absorption peak was present around 320 nm in the UV−vis spectrum.[16]

Figure 4 shows the CD and UV−vis spectra of poly(**2a**) measured in THF/MeOH with various compositions. The minus CD signal gradually turned into a plus one upon raising MeOH content. No CD spectroscopic change occurred after more than 20% MeOH was added. Thus, we can say that poly(**2a**) inverted the helical sense by the addition of MeOH because the CD signal is based on the conjugated polyacetylene backbone.[17] Since the UV−vis absorption was observed around 400 nm in all cases,[9,16] it is concluded that the helix inversion of poly(**2a**) did not take place via random coil but directly from helix to helix.

Figure 5 depicts the change of CD and UV−vis spectra upon addition of KOH to a solution of poly(**2a**) in THF/MeOH = 1/1 (v/v). The CD signal around 400 nm gradually decreased in conjunction with the UV−vis absorption by raising the amount of KOH. Further addition of KOH brought about the appearance of a new CD signal at 340 nm. These results suggest that poly(**2a**) transformed the conformation into another helix with different tightness and opposite sense to the initial one. This transformation seems to be caused by the difference of electrostatic repulsion between carboxyl and carboxylate anion groups. After the addition of 1.5 equiv of KOH to the solution of poly(**2a**), HCl was added to the resulting solution. The CD spectroscopic pattern completely returned to the one before KOH addition. Thus, we could confirm the reversible conformational change of poly(**2a**) according to pH. The specific rotations of poly(**2a**) measured in THF, THF/MeOH = 1/1 (v/v), and THF/MeOH in the presence of 1.5 equiv of KOH were −369°, +315°, and −158°, respectively. The much large values compared to **2a** (−3°, −6°, and −9°

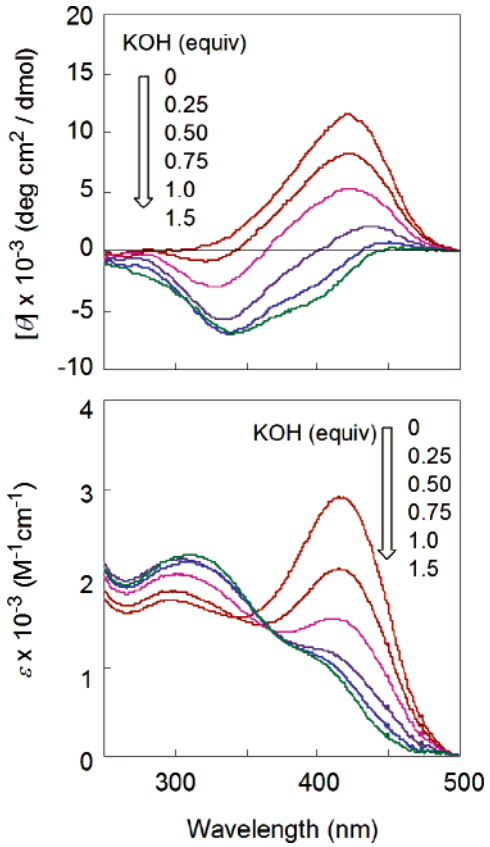


Figure 5. Change of CD and UV−vis spectra of poly(**2a**) upon addition of KOH measured in THF/MeOH = 1/1 (v/v, c = 0.5 mM) at 0 °C.

Table 2. IR Absorption (Amide I) of 1a, 2a, Poly(1a), and Poly(2a)[a]

	wavenumber (cm^{-1})		
compound	in THF	in THF/MeOH	in THF/MeOH with 1.5 equiv of KOH
1a	1686	1665	—[b]
poly(**1a**)	1650	1655	—[b]
2a	1686	1672	—[c]
poly(**2a**)	1647	1653	1653

[a] Reagent concentration 50 mM. [b] Not measured. [c] Could not be measured because the sample was insoluble.

in these solvents) and the signs strongly support the assumption on the helical senses of poly(**2a**) in these solvents.

Table 2 summarizes the liquid-state IR spectroscopic data of C=O stretching of the amide groups of **1a**, **2a**, poly(**1a**), and poly(**2a**) measured in THF and THF/MeOH = 1/1 (v/v) in the absence and presence of 1.5 equiv of KOH. Poly(**2a**) exhibited the amide I absorption peak at 1647 cm^{-1} in THF, which was 39 cm^{-1} lower than that of **2a**. Judging from the low reagent concentration (50 mM), it is concluded that poly(**2a**) forms intramolecular hydrogen bonding between the amide groups. A similar result was observed in THF/MeOH. In this case, the efficiency of intramolecular hydrogen bonding should be lower than that in THF because the difference between **2a** and poly(**2a**) was diminished to 19 cm^{-1}. This is likely to result from intermolecular hydrogen bonding between the amide groups and MeOH molecules. When 1.5 equiv of KOH was added to the solution of **2a** in THF/MeOH, the potassium salt of **2a** precipitated as white powder and the IR could not be measured. Meanwhile, no precipitate formed from the solution of poly(**2a**) by the addition of KOH. It seems that the degree of neutralization of poly(**2a**) was lower than that of **2a**, which resulted in this difference. Since poly(**2a**) exhibited the amide I absorption peak at the same wavenumber in the absence and presence of KOH, it is considered that poly(**2a**) forms intramolecular hydrogen bonding similarly in both cases. Poly(**1a**) also exhibited the amide I absorption peaks at the lower wavenumber than those of **1a**. Intramolecular hydrogen bonding should exit, but it seems to be a random one. In fact, the degrees of shift of wavenumber are smaller than those in **2a** and poly(**2a**).

Conclusions

In this article, we have demonstrated the polymerization of L-aspartic and L-glutamic acid-based novel *N*-propargylamides **1** and **2** with a rhodium catalyst. The polymerization satisfactorily proceeded to give the corresponding polymers [poly(**1**) and poly(**2**)], which showed strong Cotton effects. Liquid state IR spectroscopic measurement revealed that they take helical conformations stabilized by intramolecular hydrogen bonding at the amide−amide and carbamate−carbamate moieties. They were satisfactorily converted into the corresponding polymers [poly(**1a**) and poly(**2a**)] with free carboxyl groups by alkaline hydrolysis. Poly(**1a**) did not form a helix, while poly(**2a**) took helical structure, which was responsive to the composition of THF and MeOH as a mixed solvent. Poly(**2a**) changed the helical sense and tightness in THF/MeOH = 1/1 (v/v) by the addition of KOH, presumably based on the difference of electronic repulsion between the carboxylate groups. By the addition of HCl, the polymer changed the helical sense and tightness again to recover the conformation before KOH addition. We could thus successfully construct a pH-responsive system reversibly undergoing transformation of helical structure.

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Supporting Information Available: Figure S1 showing relationships between the dihedral angle ϕ at the single bond in the main chain of 18-mers of **1** and **2** and the energy calculated by MMFF94; Figure S2 showing top and side views of the stable conformers of poly(**1**) and poly(**2**) (48-mer). This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Poly(**2**) was soluble in $CDCl_3$ and insoluble in CD_3OD, while poly(**2a**) was soluble in CD_3OD and insoluble in $CDCl_3$. We also tried DMSO-d_6, but neither of the polymers was soluble in the solvent.

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(17) It has recently been reported that side-chain reorientations of helical polyguanidines can be driven by temperature, solvent polarity, or preferential solvation. They show a change in sign of the Cotton effect by just a reorientation of the anthracene side chains with no change in helical sense (Tang, H.-Z.; Boyle, P. D.; Novak, B. M. *J. Am. Chem. Soc.* **2005**, *127*, 2136), wherein the CD signal does not come from the main chain but does from the side chain, different from the present study.

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