Synthesis and Secondary Structure of Polyacetylenes Carrying Diketopiperazine Moieties. The First Example of Helical Polymers Stabilized by *s-cis*-Amide-Based Hydrogen Bonding

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ABSTRACT: Novel optically active phenylacetylenes having diketopiperazine were synthesized from L-phenylalanine and polymerized with a rhodium catalyst to obtain the polymers with number-average molecular weights over 10 000 in good yields. The CD and UV−vis spectra of the polymers indicated that they took helical structures with predominantly one-handed screw sense in DMF, while random coil structures in $CHCl_3$. Addition of various carboxylic acids such as trifluoroacetic acid to the polymer solution in $CHCl_3$ promoted the helical formation. Molecular mechanics calculation suggested that the most stable conformer was a right-handed helix accompanying tandem hydrogen-bonding strands between the amide groups.

Introduction

Diketopiperazine (DKP), a cyclic dimer of amino acids, is a typical byproduct in peptide synthesis. DKPs are studied as bioactive and enzyme-inhibitory compounds in a manner similar to linear peptides.[1] DKP has two *s-cis* secondary amide groups, which can hydrogen bond horizontally within the ring plane. Some DKPs form aggregates based on tandem hydrogen bonding between the amide groups in the solid state. The way of aggregation depends on the amino acid components of DKPs. For example, a glycine-based DKP adopts a linear tape orientation, while an alanine-based one forms a layer-type structure.[2] DKP is poorly soluble in organic solvents due to the rigid cyclic structure bearing amide groups. *N*-Alkylation of one amide group effectively enhances the solubility, leading to a change of association state.[3] This type of DKP constructs supramolecular architectures including liquid crystals[4] and microcapsules[5] utilizing noncovalent bonding such as hydrophobic and electrostatic interactions in addition to hydrogen bonding between the amide groups. Phenylalanine-based as well as aspartic- and glutamic acid-based DKPs serve as oil gelators,[6] wherein intermolecular hydrogen bonding plays a key role to form molecular networks. Unsymmetrical DKPs consisting of phenylalanine together with histidine or arginine are used as an organocatalyst for asymmetric hydrocyanation.[7]

Although DKP derivatives have several interesting features as described above, polymers carrying DKPs have been scarcely synthesized, and the molecular weights and the detail of the properties have not been well determined.[8] We have recently reported the polycondensation of aspartic and glutamic acid DKPs with diamines and dibromoxylenes to give polymers with moderate molecular weights.[9] We have also reported the acyclic diene metathesis polycondensation of glutamic acid DKP ω-alkenyl esters with ruthenium catalysts. The formed polymers are associated in the solid and solution states based on hydrogen bonding between the DKP moieties.[10] However, the polymers do not show the evidence of formation of a chiral secondary structure, presumably due to the insufficient control over the stereoregularity (*cis* and *trans*) as well as the presence of nonrigid alkylene spacers in the main chain.

Among various polymers having double bonds in the main chain, substituted polyaceytylenes synthesized by the polymerization with iron−aluminum and rhodium catalysts feature a highly *cis*-stereoregular structure.[11] Introduction of appropriate chiral subsituents to *cis*-polyacetylenes leads to the formation of a helical structure with predominantly one-handed screw sense. A pioneering work on substituted helical polyacetylenes has been done by Ciardelli et al. in the 1970s. They have reported that polyacetylenes having chiral aliphatic side chains synthesized by iron tris(acety1acetonate)aluminum triisobutyl catalyst take a helical conformation in solution.[11a] Since [Rh(norbornadiene)Cl]−triethylamine catalyst was found to polymerize monosubstituted acetylenes to give *cis*-stereoregular polymers satisfactorily,[12] many studies regarding substituted helical polyacetylenes synthesized by rhodium catalysts have been reported so far.[13]

We have reported that *cis*-stereoregular polyacetylene derivatives carrying amide groups such as poly(*N*-propargylamide)s,[14] poly(*N*-propargylsulfamide)s, poly(*N*-propargylphosphonamidate)s,[15] and poly(*N*-butynylamide)s[16] form helical structures with predominantly one-handed screw sense, which are stabilized by regulated intramolecular hydrogen bonding between the amide groups as well as steric repulstion in the biomimetically same way as peptides and proteins. They change the conformation by external stimuli such as heat and the addition of polar solvents, which disturb the formation of intramolecular hydrogen bonding stabilizing the helical structure. It is likely that all the amide moieties take an *s-trans* structure in the aforementioned helical polymers. On the other hand, no example has been reported regarding polyacetylenes carrying quantitatively *s-cis*-amide moieties in the side chains as far as we know. It is expected that such *s-cis*-amide-based polymers exhibit behavior different from that of *s-trans*-amide-based ones. The present article deals with the synthesis and polymerization of novel phenylacetylenes **1a**−**1d** having DKP moieties consisting of *s-cis*-amide (Scheme 1) and examination of the secondary structure of the resultant polymers that possibly form regulated intramolecular hydrogen bonding between the amide groups.

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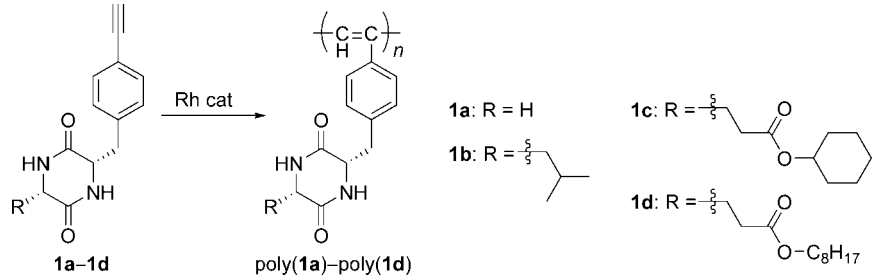
Scheme 1



Experimental Section

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. Number- and weight-average molecular weights (M_n and M_w) of polymers were determined by gel permeation chromatography (GPC) on TSK gel α-M and TSK gel GMH_{XL}, 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.

Materials. All reagents for monomer synthesis were used as purchased without purification. 4-Iodo-L-phenylalanine was prepared from phenylalanine as described in the literature.[17] DMF used for polymerization was distilled over calcium hydride. (nbd)$Rh^+[\eta^6$-$C_6H_5B^-(C_6H_5)_3]$ was prepared by the reaction of $[(nbd)RhCl]_2$ with $NaB(C_6H_5)_4$ as described in the literature.[18]

Monomer Synthesis. *N-tert-Butoxycarbonyl-4-iodo-L-phenylalanine (**2**).* Triethylamine (7.00 mL, 50.3 mmol) was added to a solution of 4-iodo-L-phenylalanine (5.96 g, 20.5 mmol) in H_2O/dioxane (30 mL/30 mL) at 0 °C. Then, di-*tert*-butyl dicarbonate (5.74 g, 26.3 mmol) was added to the solution, and the resulting solution was stirred at room temperature overnight. H_2O (30 mL) was added, and the mixture was washed with ethyl acetate. The aqueous layer was acidified to pH 2 with 2 M HCl, and then **2** was extracted from the mixture with ethyl acetate twice. The organic layer was washed with saturated NaCl(aq) and dried over anhydrous $MgSO_4$. It was concentrated on a rotary evaporator to obtain **2** as a pale brown viscous liquid in 37% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.41 [s, 9H, $(CH_3)_3C-$], 2.94−3.21 [m, 2H, $-CH_2Ar$], 4.97−5.08 [m, 1H, $\rangle CHCH_2-$], 6.93 [d, J = 7.6 Hz, 2H, Ar], 7.62 [d, J = 8.0 Hz, 2H, Ar], 8.23 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.23 [$(CH_3)_3C-$], 37.36 [$-CH_2Ar$], 60.48 [$\rangle CHCH_2-$], 80.36 [$(CH_3)_3C-$], 92.53 [$\rangle CHI$], 131.40 [Ar], 135.58 [Ar], 137.56 [Ar], 155.24 [−NHCOO−], 176.93 [−COOH].

*N-tert-Butoxycarbonyl-4-iodo-L-phenylalanylglycine Methyl Ester (**3a**).* Triethylamine (4 mL, 28.8 mmol) was added to a dispersion of glycine methyl ester hydrochloride (3.18 g, 25.3 mmol) in ethyl acetate (150 mL) at 0 °C. Compound **2** (3.74 g, 9.55 mmol) and 4-[4,6-dimethoxy-1,3,5-triazin-2-yl]-4-methylmorpholinium chloride (TRIAZIMOCH, Tokuyama Co., 9.00 g, 27.6 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 $NaHCO_3$, aqueous $NaHCO_3$, and saturated NaCl(aq). The organic layer was dried over anhydrous $MgSO_4$ and concentrated on a rotary evaporator. The residual mass was purified by recrystallization from ethyl acetate/hexane to obtain **3a** as a colorless solid in 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45 [s, 9H, $(CH_3)_3C-$], 3.01−3.13 [m, 2H, $-CH_2Ar$], 3.72 [s, 3H, $-COOCH_3$], 3.74−4.15 [m, 2H, $-NHCH_2COO-$], 4.83−4.88 [m, 1H, $-CONHCH_2-$], 5.13 [s, 1H, $\rangle CHCH_2-$], 6.64 [s, 1H, −COONH−], 6.85 [d, J = 8.0 Hz, 2H, Ar], 7.60 [d, J = 8.0 Hz, 2H, Ar]. ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.23 [$(CH_3)_3C-$], 37.33 [$-CH_2Ar$], 44.28 [$-NHCH_2COO-$], 52.44 [$-COOCH_3$], 60.36 [$\rangle CHCH_2-$], 80.36 [$(CH_3)_3C-$], 92.67 [$\rangle CHI$], 131.23 [Ar], 135.29 [Ar], 137.64 [Ar], 155.96 [−NHCOO−], 169.14 [$-CHCONH-$], 171.40 [$-CH_2COO-$].

*N-tert-Butoxycarbonyl-4-iodo-L-phenylalanyl-L-leucine Methyl Ester (**3b**).* The title compound was synthesized from L-leucine methyl ester hydrochloride and **2** in a manner similar to **3a**. Yield 37%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 [d, 6H, 4.0 Hz, $-CH(CH_3)_2$], 1.41 [s, 9H, $(CH_3)_3C-$], 1.46−1.61 [m, 3H, $-CH(CH_3)_2$ and $-CH_2CH(CH_3)_2$], 2.92−3.06 [m, 2H, $-CH_2Ar$], 3.71 [s, 3H, $-COOCH_3$], 4.34 [s, 1H, $-CONHCH_2-$], 4.50−4.61 [m, 1H, $\rangle CHCH_2CH(CH_3)_2$], 5.05−5.13 [m, 1H, $\rangle CHCH_2Ar$], 6.41 [d, 1H, J = 7.8 Hz, −COONH−], 6.96 [d, J = 8.0 Hz, 2H, Ar], 7.61 [d, J = 8.0 Hz, 2H, Ar]. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.79 and 22.69 [$-CH(CH_3)_2$], 24.60 [$-CH(CH_3)_2$], 28.17 [$(CH_3)_3C-$], 37.55 [$-CH_2Ar$], 41.42 [$-CH_2CH(CH_3)_2$], 50.67 [$\rangle CHCH_2CH(CH_3)_2$], 52.30 [$-COOCH_3$], 55.84 [$\rangle CHCH_2Ar$], 80.25 [$(CH_3)_3C-$], 92.27 [$\rangle CHI$], 131.38 [Ar], 136.22 [Ar], 137.53 [Ar], 155.27 [−NHCOO−], 170.63 [$-CHCONH-$], 172.76 [$-CH_2COO-$].

*N-tert-Butoxycarbonyl-4-iodo-L-phenylalanyl-O-cyclohexyl-L-glutamic Acid Methyl Ester (**3c**).* The title compound was synthesized from *O*-cyclohexyl-L-glutamic acid methyl ester trifluoroacetate and **2** in a manner similar to **3a**. Yield 44%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40 [s, 9H, $(CH_3)_3C-$], 1.33−1.82 [m, 10H, $-OCHH(CH_2)_5$], 1.91−2.18 [m, 2H, $\rangle CHCH_2CH_2COO-$], 2.25−2.40 [m, 2H, $\rangle CHCH_2CH_2COO-$], 2.91−3.08 [m, 2H, $-CH_2Ar$], 3.72 [s, 3H, $-COOCH_3$], 4.37 [s, 1H, $\rangle CHCH_2CH_2COO-$], 4.54−4.65 [m, 1H, −NH−], 4.70−4.80 [m, 1H, $-OCHH(CH_2)_5$], 5.19 [s, 1H, $\rangle CHCH_2Ar$], 6.96 [d, J = 8.3 Hz, 2H, Ar], 7.59 [d, J = 8.3 Hz, 2H, Ar]. ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.57, 25.16, 27.13, 30.27, and 31.41 [$-OCHH(CH_2)_5$ and $\rangle CHCH_2CH_2COO-$], 28.10 [$(CH_3)_3C-$], 37.52 [$-CH_2Ar$], 52.35 [$-COOCH_3$], 55.17 [$\rangle CHCH_2Ar$], 60.22 [$\rangle CHCH_2CH_2COO-$], 72.92 [$-OCH(CH_2)_5$], 80.05 [$(CH_3)_3C-$], 92.20 [$\rangle CHI$], 131.30 [Ar], 136.10 [Ar], 137.41 [Ar], 155.15 [−NHCOO−], 170.90 [$-CHCONH-$], 171.61 [$-COOCH(CH_2)_5$], 171.89 [$-COOCH_3$].

*N-tert-Butoxycarbonyl-4-iodo-L-phenylalanyl-O-n-octyl-L-glutamic Acid Methyl Ester (**3d**).* The title compound was synthesized from *O*-*n*-octyl-L-glutamic acid methyl ester trifluoroacetate and **2** in a manner similar to **3a**. Yield 45%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 [t, 3H, J = 6.8 Hz, $-COO(CH_2)_7CH_3$], 1.24−1.36 [m, 10H, $-COOCH_2CH_2(CH_2)_5CH_3$], 1.41 [s, 9H, $(CH_3)_3C-$], 1.54−1.69 [m, 2H, $-COOCH_2CH_2(CH_2)_5CH_3$], 1.89−2.22 [m, 2H, $\rangle CHCH_2CH_2COO-$], 2.22−2.45 [m, 2H, $\rangle CHCH_2CH_2COO-$], 2.92−3.12 [m, 2H, $-CH_2Ar$], 3.73 [s, 3H, $-COOCH_3$], 4.05 [t, 2H, J = 6.6 Hz, $-COOCH_2CH_2(CH_2)_5CH_3$], 4.35 [s, 1H, $\rangle CHCH_2CH_2COO-$], 4.53−4.64 [m, 1H, −NH−], 5.01−5.14 [m, 1H, $\rangle CHCH_2Ar$], 6.68−6.78 [m, 1H, −NH−], 6.96 [d, J = 8.1 Hz, 2H, Ar], 7.60 [d, J = 8.3 Hz, 2H, Ar]. ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.00 [$-COOCH_2CH_2(CH_2)_5CH_3$], 22.54, 25.81, 27.19, 28.50, 29.13, and 31.69 [$-COOCH_2CH_2(CH_2)_5CH_3$ and $\rangle CHCH_2CH_2COO-$], 28.15 [$(CH_3)_3C-$], 37.59 [$-CH_2Ar$], 52.52 [$-COOCH_3$], 55.34 [$\rangle CHCH_2Ar$], 60.31 [$\rangle CHCH_2CH_2COO-$], 64.91 [$-COOCH_2CH_2(CH_2)_5CH_3$], 80.24 [$(CH_3)_3C-$], 92.31 [$\rangle CHI$], 131.35 [Ar], 136.11 [Ar], 137.55 [Ar], 155.18 [−NHCOO−], 170.82 [$-CHCONH-$], 171.60 [$-COOCH(CH_2)_5$], 172.68 [$-COOCH_3$].

*Cyclo(4-iodo-L-phenylalanylglycinyl) (**4a**).* Trifluoroacetic acid (TFA, 2.5 mL, 33.7 mmol) was added to a solution of **3a** (3.90 g, 8.43 mmol) in CH_2Cl_2 (50 mL) at 0 °C overnight. The resulting solution was concentrated in vacuo to obtain 4-iodo-L-phenylalanyl

glycine methyl ester trifluoroacetate. It was dissolved in mesitylene (200 mL), and then triethylamine (20 mL) was added to the solution. The reaction mixture was refluxed for 6 h, and a mass precipitated was separated by filtration. It was washed with H_2O to obtain **4a** as a white solid in 27% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.77−3.12 [m, 2H, −CH_2Ar], 3.38−3.58 [m, 2H, −NHCH_2CO−], 3.96−4.15 [m, 1H, ⟩CHCH$_2$−], 6.99 [d, J = 7.6 Hz, 2H, Ar], 7.62 [d, J = 7.6 Hz, 2H, Ar], 7.80 [s, 1H, −NH−], 8.02 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ 37.96 [−CH$_2$Ar], 43.76 [−NHCH$_2$CO−], 55.10 [⟩CHCH$_2$Ar], 92.35 [⟩CHI], 132.19 [Ar], 135.90 [Ar], 136.73 [Ar], 165.50 [C═O], 166.83 [C═O].

*Cyclo(4-iodo-L-phenylalanyl-L-leucinyl) (**4b**).* The title compound was synthesized from **3b** in a manner similar to **4a**. Yield 28%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.68 [d, 6H, J = 6.6 Hz, −CH(CH_3)$_2$], 0.28−0.38 and 0.80−0.92 [m, 2H, −CH_2CH(CH$_3$)$_2$], 1.38−1.51 [m, 1H, −CH(CH$_3$)$_2$], 2.78−3.10 [m, 2H, −CH_2Ar], 3.51 [s, 1H, ⟩CHCH$_2$CH(CH$_3$)$_2$], 4.15 [s, 1H, ⟩CHCH$_2$Ar], 6.95 [d, J = 8.0 Hz, 2H, Ar], 7.62 [d, J = 8.1 Hz, 2H, Ar], 7.95 [s, 1H, −NH−], 7.97 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.50 [−CH(CH$_3$)$_2$], 22.92 [−CH(CH$_3$)$_2$], 37.75 [−CH$_2$Ar], 43.50 [−CH_2CH(CH$_3$)$_2$], 52.27 [⟩CHCH$_2$CH(CH$_3$)$_2$], 57.40 [⟩CHCH$_2$Ar], 92.54 [⟩CHI], 132.50 [Ar], 135.73 [Ar], 136.66 [Ar], 165.75 [C═O], 167.23 [C═O].

*Cyclo(4-iodo-L-phenylalanyl-O-cyclohexyl-L-glutaminyl) (**4c**).* The title compound was synthesized from **3c** in a manner similar to **4a**. Yield 70%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.24−1.88 [m, 14H, −COOCH(CH_2)$_5$, ⟩CHCH_2CH_2COO−], 2.78−3.13 [m, 2H, −CH_2Ar], 3.70−3.84 [m, 1H, ⟩CHCH$_2$CH$_2$COO−], 4.11−4.22 [m, 1H, ⟩CHCH$_2$Ar], 4.56−4.70 [m, 1H, −COOCH(CH$_2$)$_5$], 6.97 [d, J = 7.8 Hz, 2H, Ar], 7.60 [d, J = 8.0 Hz, 2H, Ar], 7.99 [s, 1H, −NH−], 8.08 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ 23.01, 24.71, 25.50, 28.83, and 30.94 [−COOCH(CH$_2$)$_5$ and ⟩CHCH$_2$$CH_2$COO−], 37.30 [−$CH_2$Ar], 52.80 [⟩$CHCH_2CH_2$-COO−], 54.87 [⟩$CHCH_2$Ar], 71.73 [−COO$C$H($CH_2$)$_5$], 92.23 [⟩CHI], 132.39 [Ar], 135.80 [Ar], 136.63 [Ar], 166.06 [C═O], 166.42 [C═O], 171.26 [−COO−].

*Cyclo(4-iodo-L-phenylalanyl-O-n-octyl-L-glutaminyl) (**4d**).* The title compound was synthesized from **3d** in a manner similar to **4a**. Yield 65%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.86 [t, 3H, J = 6.8 Hz, −COO(CH$_2$)$_7$CH_3], 1.21−1.50 [m, 12H, −COOCH$_2$-CH_2(CH_2)$_5$CH$_3$], 1.50−1.69 [m, 2H, ⟩CHCH_2CH$_2$COO−], 1.69−2.01 [m, 2H, ⟩CHCH$_2$CH_2COO−], 2.76−3.13 [m, 2H, −CH_2Ar], 3.71−3.83 [m, 1H, ⟩CHCH$_2$CH$_2$COO−], 3.91−4.08 [m, 2H, −COOCH_2CH$_2$(CH$_2$)$_5$CH$_3$], 4.13−4.34 [m, 1H, ⟩CHCH$_2$Ar], 6.97 [d, J = 8.0 Hz, 2H, Ar], 7.60 [d, J = 8.0 Hz, 2H, Ar], 7.99 [s, 1H, −NH−], 8.08 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.62 [−COOCH$_2$CH$_2$(CH$_2$)$_5$$CH_3$], 21.79, 25.15, 27.96, 28.31, and 30.94 [−COOCH$_2$$CH_2$($CH_2$)$_5CH_3$ and ⟩CHCH$_2$$CH_2$COO−], 37.50 [−$CH_2$Ar], 52.84 [⟩$CHCH_2CH_2$COO−], 54.85 [⟩$CHCH_2$Ar], 63.67 [−COO$CH_2CH_2$(CH$_2$)$_5CH_3$], 92.31 [⟩CHI], 132.36 [Ar], 135.77 [Ar], 136.59 [Ar], 166.01 [C═O], 166.33 [C═O], 171.85 [−COO−].

*Cyclo(4-trimethylsilylethynyl-L-phenylalanylglycinyl) (**5a**).* Compound **4a** (762 mg, 2.31 mmol), $PdCl_2(PPh_3)_2$ (12.5 mg, 17.8 μmol), PPh_3 (19.9 mg, 75.9 μmol), and CuI (23.0 mg, 121 μmol) were added into a two-neck flask, and it was flushed with hydrogen. DMF (12 mL) and triethylamine (2 mL) were added to the flask, then (trimethylsilyl)acetylene (1.5 mL) was added dropwise to the solution, and the yellow mixture was stirred at room temperature overnight. The resulting mixture was concentrated in vacuo, and the residual mass was washed with 0.5 M HCl and hexane to obtain **5a** in 65% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.22 [s, 9H, (CH$_3$)$_3$Si−], 2.49−2.94 [m, 2H, −CH_2Ar], 3.40−3.45 [m, 2H, −NHCH_2CO−], 4.07 [s, 1H, −NHCHCO−], 7.18 [d, 2H, J = 8.3 Hz, Ar], 7.35 [d, 2H, J = 8.1 Hz, Ar], 7.79 [s, 1H, −NH−], 8.02 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ −0.36 [(CH$_3$)$_3$Si−], 38.40 [−CH$_2$Ar], 43.65 [−NHCH$_2$CO−], 55.10 [−NHCHCO−], 93.92 [−C≡CSi(CH$_3$)$_3$], 105.01 [−C≡CSi(CH$_3$)$_3$], 120.46 [Ar], 130.07 [Ar], 131.13 [Ar], 137.17 [Ar], 165.34 [C═O], 166.73 [C═O].

*Cyclo(4-trimethylsilylethynyl-L-phenylalanyl-L-leucinyl) (**5b**).* The title compound was synthesized from **4b** in a manner similar to **5a**. Yield 63%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.19 [s, 9H, (CH$_3$)$_3$Si−], 0.66 [s, 6H, J = 7.2 Hz, −CH(CH_3)$_2$], 1.19 [t, 2H, J = 7.3 Hz, −CH_2CH(CH$_3$)$_2$], 1.36−1.53 [m, 1H, −CH(CH$_3$)$_2$], 3.04−3.17 [m, 2H, −CH_2Ar], 3.50 [s, 1H, ⟩CHCH$_2$CH(CH$_3$)$_2$], 4.16 [s, 1H, ⟩CHCH$_2$Ar], 7.13 [d, J = 7.8 Hz, 2H, Ar], 7.34 [d, J = 7.8 Hz, 2H, Ar], 7.94 [s, 1H, −NH−], 7.96 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ −0.20 [(CH$_3$)$_3$Si−], 21.31 [−CH(CH$_3$)$_2$], 22.95 [−CH(CH$_3$)$_2$], 38.23 [−CH$_2$Ar], 43.55 [−CH_2CH(CH$_3$)$_2$], 52.28 [⟩CHCH$_2$CH(CH$_3$)$_2$], 55.39 [⟩CHCH$_2$Ar], 93.82 [−C≡CSi(CH$_3$)$_3$], 105.09 [−C≡CSi(CH$_3$)$_3$], 120.74 [Ar], 130.45 [Ar], 131.16 [Ar], 137.11 [Ar], 165.88 [C═O], 167.33 [C═O].

*Cyclo(4-trimethylsilylethynyl-L-phenylalanyl-O-cyclohexyl-L-glutaminyl) (**5c**).* The title compound was synthesized from **4c** in a manner similar to **5a**. Yield 56%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.20 [s, 9H, (CH$_3$)$_3$Si−], 1.19−1.86 [m, 14H, −CO-OCH(CH_2)$_5$, ⟩CHCH_2CH_2COO−], 2.79−3.17 [m, 2H, −CH_2Ar], 3.70−3.81 [m, 1H, ⟩CHCH$_2$CH$_2$COO−], 4.16−4.27 [m, 1H, ⟩CHCH$_2$Ar], 4.54−4.66 [m, 1H, −COOCH(CH$_2$)$_5$], 7.16 [d, J = 7.8 Hz, 2H, Ar], 7.32 [d, J = 8.1 Hz, 2H, Ar], 7.99 [s, 1H, −NH−], 8.09 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ −0.26 [(CH$_3$)$_3$Si−], 23.01, 24.72, 28.45, 28.73, and 30.88 [−COOCH(CH$_2$)$_5$ and ⟩CHCH$_2$$CH_2$COO−], 37.64 [−$CH_2$Ar], 52.94 [⟩$CHCH_2CH_2$COO−], 54.93 [⟩$CHCH_2$Ar], 71.52 [−COO-$C$H($CH_2$)$_5$], 93.70 [−C≡$C$Si(CH$_3$)$_3$], 105.09 [−$C$≡CSi(CH$_3$)$_3$], 120.62 [Ar], 130.35 [Ar], 131.08 [Ar], 137.15 [Ar], 166.08 [C═O], 166.43 [C═O], 171.25 [−COO−].

*Cyclo(4-trimethylsilylethynyl-L-phenylalanyl-O-n-octyl-L-glutaminyl) (**5d**).* The title compound was synthesized from **4d** in a manner similar to **5a**. Yield 62%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.20 [s, 9H, (CH$_3$)$_3$Si−], 0.86 [t, 3H, J = 6.7 Hz, −COO(CH$_2$)$_7$CH_3], 1.20−1.36 [m, 10H, −COOCH$_2$CH$_2$(CH_2)$_5$CH$_3$], 1.36−1.48 [m, 2H, −COOCH$_2$CH_2(CH$_2$)$_5$CH$_3$], 1.48−1.64 [m, 2H, ⟩CH-CH_2CH$_2$COO−], 1.64−1.84 [m, 2H, ⟩CHCH$_2$CH_2COO−], 2.76−3.17 [m, 2H, −CH_2Ar], 3.70−3.76 [m, 1H, ⟩CHCH$_2$CH$_2$COO−], 3.96 [t, J = 6.6 Hz, 2H, −COOCH_2CH$_2$(CH$_2$)$_5$CH$_3$], 4.16−4.23 [m, 1H, ⟩CHCH$_2$Ar], 7.16 [d, J = 7.8 Hz, 2H, Ar], 7.32 [d, J = 8.0 Hz, 2H, Ar], 7.99 [s, 1H, −NH−], 8.09 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ 0.00 [(CH$_3$)$_3$Si−], 13.92 [−COOCH$_2$CH$_2$(CH$_2$)$_5$$CH_3$], 21.08, 25.48, 28.26, 28.68, and 31.24 [−COOCH$_2$$CH_2$($CH_2$)$_5CH_3$ and ⟩CHCH$_2$$CH_2$COO−], 37.94 [−$CH_2$Ar], 53.18 [⟩$CHCH_2CH_2$COO−], 55.22 [⟩$CHCH_2$Ar], 63.83 [−COO$CH_2CH_2$(CH$_2$)$_5CH_3$], 91.70 [−C≡$C$Si(CH$_3$)$_3$], 105.38 [−$C$≡CSi(CH$_3$)$_3$], 120.91 [Ar], 130.59 [Ar], 131.33 [Ar], 137.42 [Ar], 166.30 [C═O], 166.65 [C═O], 172.13 [−COO−].

*Cyclo(4-ethynyl-L-phenylalanylglycinyl) (**1a**).* 1 M tetrabutylammonium fluoride solution in THF (1.0 mL) was added dropwise to a solution of **5a** (449 mg, 1.49 mmol) in DMF (12 mL), and the solution was stirred for 20 min. The resulting solution was concentrated in vacuo, and the residual mass was washed with 0.5 M HCl and ethyl acetate to obtain **1a** in 43% yield. No mp was observed below 270 °C. $[\alpha]_D$ −2° (c = 0.10 g/dL in DMF at room temperature). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.91−3.12 [m, 2H, −CH_2Ar], 3.42−3.47 [m, 2H, −NHCH_2CO−], 4.05 [s, 1H, −C≡CH], 4.07 [m, 1H, −NHCHCO−], 7.19 [d, 2H, J = 8.0 Hz, Ar], 7.38 [d, 2H, J = 8.0 Hz, Ar], 7.80 [s, 1H, −NH−], 8.03 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ 38.33 [−CH$_2$Ar], 43.65 [−NHCH$_2$CO−], 55.29 [−NHCHCO−], 77.75 [−C≡CH], 83.27 [−C≡CH], 129.94 [Ar], 129.99 [Ar], 131.22 [Ar], 137.17 [Ar], 165.37 [C═O], 166.75 [C═O]. IR (cm^{-1}, KBr): 3579, 3464, 3251 (NH), 3197 (NH), 3049, 2977 (CH), 2926 (CH), 2878 (CH), 2106 (C≡C), 1924 (Ar), 1678 (NHCO), 1505, 1467, 1333, 822. HRMS. Calcd for $C_{13}H_{12}N_2O_2$ (m/z) 228.0899. Found: 228.0900.

*Cyclo(4-ethynyl-L-phenylalanyl-L-leucinyl) (**1b**).* The title compound was synthesized from **5b** in a manner similar to **1a**. Yield 40%; mp 229−232 °C. $[\alpha]_D$ −34° (c = 0.10 g/dL in DMF at room temperature). ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.66 [t, 6H, J = 6.1 Hz, −CH(CH_3)$_2$], 1.17 [t, 2H, J = 7.1 Hz, −CH_2CH(CH$_3$)$_2$],

Scheme 2

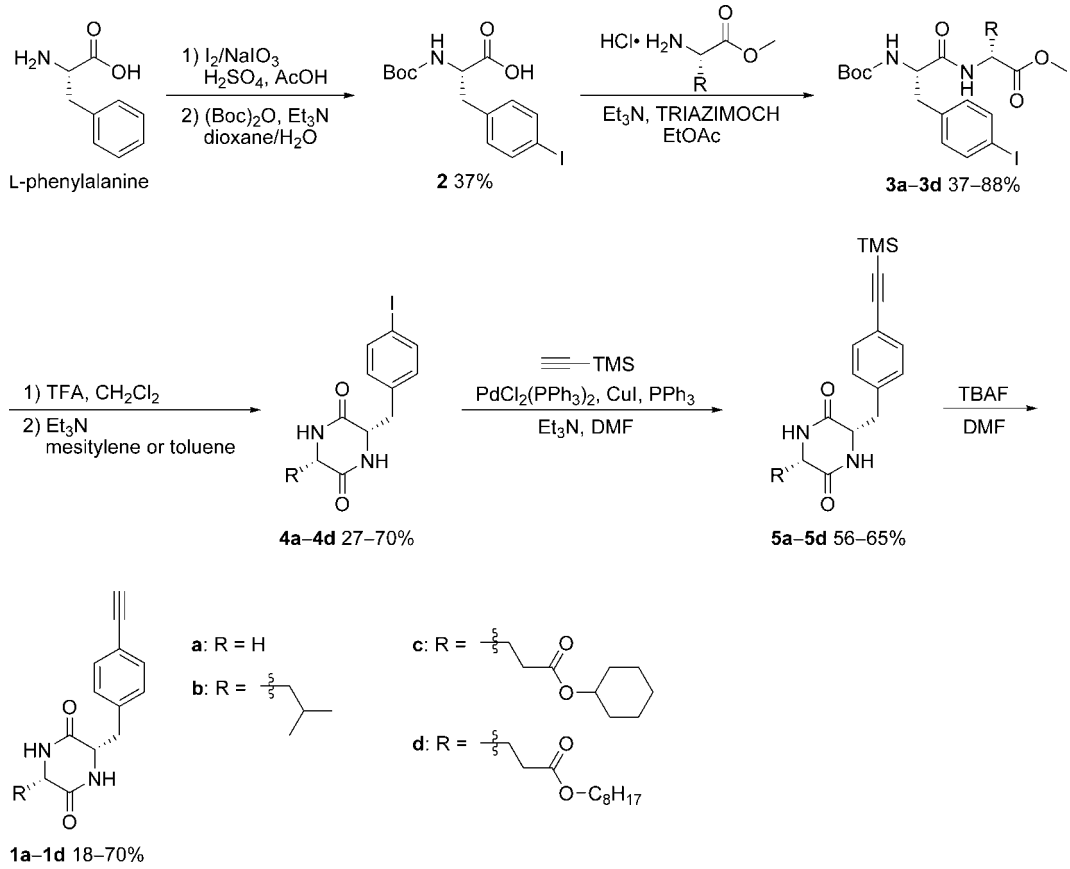


Table 1. Polymerization of 1a−1d[a]

monomer		polymer			
	$[\alpha]_D$[b] (deg)	yield[c] (%)	M_n[d]	M_w/M_n[d]	$[\alpha]_D$[b] (deg)
1a	−2	100	−[e]	−[e]	−[e]
1b	−34	79	−[e]	−[e]	−[e]
1c	−34	100	15 500	3.38	−119
1d	−3	96	54 600	3.07	−190

[a] Catalyst: (nbd)$Rh^+[\eta^6$-$C_6H_5B^-(C_6H_5)_3]$. Conditions: $[M]_0 = 0.20$ M, $[M]_0/[Cat.] = 50$ in DMF at 30 °C for 24 h. [b] Measured by polarimetry at room temperature, $c = 0.10$ g/dL in DMF. [c] MeOH-insoluble part. [d] Estimated by GPC based on polystyrene standards, eluent; LiBr solution in DMF (10 mM). [e] Could not be determined due to the insolubility in solvents.

1.38−1.52 [m, 1H, −C*H*$(CH_3)_2$], 2.85−3.15 [m, 2H, −C*H*$_2$Ar], 3.51 [s, 1H, ⟩C*H*$CH_2CH(CH_3)_2$], 4.00 [s, 1H, −C≡CH], 4.17 [s, 1H, ⟩C*H*CH_2Ar], 7.15 [d, $J = 8.0$ Hz, 2H, Ar], 7.37 [d, $J = 7.8$ Hz, 2H, Ar], 7.95 [s, 1H, −NH−], 7.97 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.51 [−CH(*C*$H_3)_2$], 22.86 [−*C*$H(CH_3)_2$], 38.87 [−*C*H_2Ar], 43.44 [−*C*$H_2CH(CH_3)_2$], 52.10 [⟩*C*HCH_2-$CH(CH_3)_2$], 59.47 [⟩*C*HCH_2Ar], 80.27 [−C≡*C*H], 83.09 [−*C*≡CH], 120.15 [Ar], 130.41 [Ar], 131.21 [Ar], 137.07 [Ar], 165.85 [C═O], 167.26 [C═O]. IR (cm^{-1}, KBr): 3302 (NH), 3198 (NH), 3049 (Ar), 2959 (CH), 2927 (CH), 2897 (CH), 2109 (C≡C), 1924 (Ar), 1663 (NHCO), 1505, 1460, 1330, 1117, 826. HRMS. Calcd for $C_{17}H_{20}N_2O_2$ (*m*/*z*) 284.1525. Found: 284.1526.

*Cyclo(4-ethynyl-L-phenylalanyl-O-cyclohexyl-L-glutaminyl) (**1c**).* The title compound was synthesized from **5c** in a manner similar to **1a**. Yield 18%; mp 196−200 °C. $[\alpha]_D$ −34° ($c = 0.10$ g/dL in DMF at room temperature). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.22−1.90[m,14H,−COOCH(C$H_2)_5$,⟩CHCH_2CH_2COO-],2.83−3.19 [m, 2H, −CH_2Ar], 3.55−3.70 [m, 1H, ⟩C*H*CH_2CH_2COO−], 3.99 [s, 1H, −C≡CH], 4.12−4.28 [m, 1H, ⟩C*H*CH_2Ar], 4.53−4.67 [m, 1H, −COOC*H*$(CH_2)_5$], 7.19 [d, $J = 7.8$ Hz, 2H, Ar], 7.35 [d, $J = 8.1$ Hz, 2H, Ar], 7.99 [s, 1H, −NH−], 8.09 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ 23.02, 24.70, 28.48, 28.81, 29.11, and 30.85 [−COOCH(*C*$H_2)_5$ and ⟩CH*C*H_2*C*H_2COO−], 37.65 [−*C*H_2Ar], 53.10 [⟩*C*HCH_2CH_2COO−], 54.86 [⟩*C*HCH_2Ar], 71.70 [−COO*C*$H(CH_2)_5$], 79.78 [−C≡*C*H], 83.23 [−*C*≡CH], 120.11 [Ar], 130.33 [Ar], 131.13 [Ar], 137.06 [Ar], 166.05 [C═O], 166.98 [C═O], 171.24 [−COO−]. IR (cm^{-1}, KBr): 3270 (NH), 3234 (NH), 3192 (NH), 3051 (Ar), 2936 (CH), 2858 (CH), 2109 (C≡C), 1926 (Ar), 1732 (C═O), 1671 (NHCO), 1458, 1335, 1252, 1169, 825. HRMS. Calcd for $C_{22}H_{26}N_2O_4$ (*m*/*z*) 382.1891. Found: 382.1893.

*Cyclo(4-ethynyl-L-phenylalanyl-O-n-octyl-L-glutaminyl) (**1d**).* The title compound was synthesized from **5d** in a manner similar to **1a**. Yield 70%; mp 176−177 °C. $[\alpha]_D$ −3° ($c = 0.10$ g/dL in DMF at room temperature). ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.87 [t, 3H, $J = 6.6$ Hz, −COO$(CH_2)_7$CH_3], 1.21−1.37 [m, 10H, −COOCH_2C$H_2(CH_2)_5CH_3$], 1.37−1.50 [m, 2H, −COOCH_2-C$H_2(CH_2)_5CH_3$], 1.50−1.62 [m, 2H, ⟩CHCH_2CH_2COO−], 1.71−1.88 [m, 2H, ⟩CHCH_2CH_2COO−], 2.83−3.17 [m, 2H, −CH_2Ar], 3.71−3.77 [m, 1H, ⟩C*H*CH_2CH_2COO−], 3.96 [t, $J = 6.6$ Hz, 2H, −COOCH_2C$H_2(CH_2)_5CH_3$], 3.98 [s, 1H, −C≡CH], 4.16−4.23 [m, 1H, ⟩C*H*CH_2Ar], 7.18 [d, $J = 8.1$ Hz, 2H, Ar], 7.35 [d, $J = 8.0$ Hz, 2H, Ar], 7.99 [s, 1H, −NH−], 8.09 [s, 1H, −NH−]. ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.69 [−COOCH_2C$H_2(CH_2)_5$CH_3], 21.86, 25.21, 27.98, 28.39, 28.43, and 31.01 [−COOCH_2C$H_2(CH_2)_5CH_3$ and ⟩CHCH_2CH_2COO−], 37.76 [-CH_2Ar], 52.93 [⟩*C*HCH_2-CH_2COO−], 55.01 [⟩*C*HCH_2Ar], 63.70 [−COO*C*H_2CH_2-$(CH_2)_5CH_3$], 79.86 [−C≡*C*H], 83.26 [−*C*≡CH], 120.21 [Ar], 130.35 [Ar], 131.19 [Ar], 137.09 [Ar], 166.13 [C═O], 166.16 [C═O], 171.94 [−COO−]. IR (cm^{-1}, KBr): 3306 (NH), 3263 (NH), 3192 (NH), 3050 (Ar), 2957 (CH), 2925 (CH), 2856 (CH), 2111 (C≡C), 1925 (Ar), 1734 (C═O), 1686 (NHCO), 1672 (NHCO), 1460, 1337, 1250, 1170, 1110, 825. HRMS. Calcd for $C_{24}H_{32}N_2O_4$ (*m*/*z*) 412.2362. Found: 412.2363.

Polymerization. The polymerization was carried out in a glass tube equipped with a three-way stopcock under nitrogen. (nbd)$Rh^+[\eta^6$-$C_6H_5B^-(C_6H_5)_3]$ (2.1 mg, 5 μmol) was added to a solution of a monomer (0.20 mmol) in DMF (1.0 mL), and the resulting mixture was vigorously stirred. It was kept in a water bath at 30 °C for 24 h. The resulting mixture was poured into MeOH (50

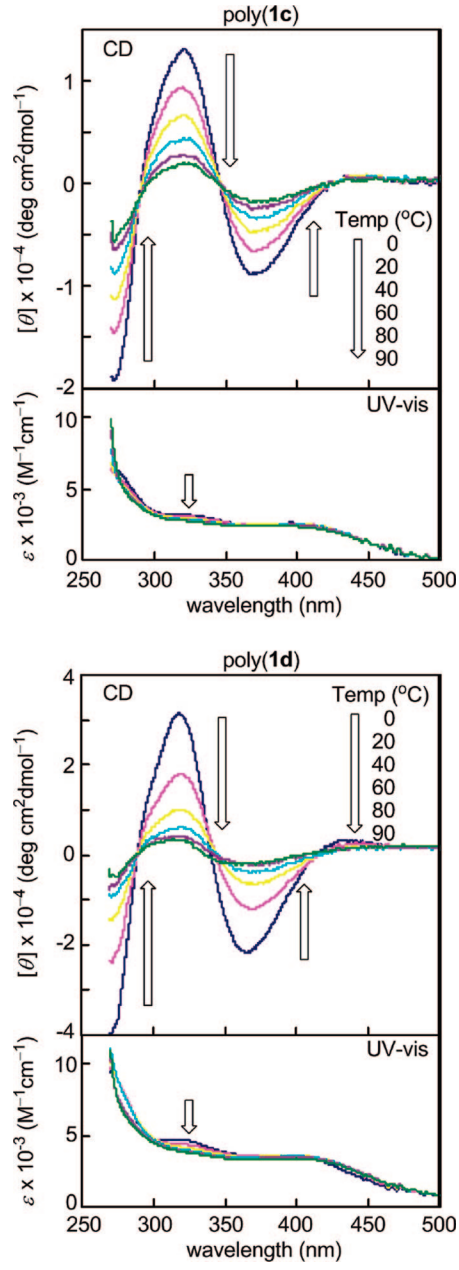


Figure 1. CD and UV−vis spectra of poly(**1c**) and poly(**1d**) measured in DMF (c = 0.20 mM) at 0−90 °C.

mL) to precipitate a polymer. It was separated by filtration using a membrane filter (ADVANTEC H100A047A) and dried under reduced pressure.

Spectroscopic Data of the Polymers. Poly(**1a**). IR (cm^{-1}, KBr): 3368, 3230 (NH), 2962 (CH), 2919 (CH), 2854 (CH), 1925 (Ar), 1670 (NHCO), 1458, 1325. Poly(**1b**). IR (cm^{-1}, KBr): 3213 (NH), 3084 (NH), 2956 (CH), 2870 (CH), 1911(Ar), 1671 (NHCO), 1459, 1318. Poly(**1c**). ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.88−1.94 [br, 12H, −COOCH(CH_2)$_5$, ⟩CHCH_2CH$_2$COO−], 2.06−2.39 [br, 2H, ⟩CHCH$_2$CH_2COO−], 3.68−3.95 [br, 1H, ⟩CHCH$_2$CH$_2$COO−], 3.95−4.38 [br, 2H, ⟩CHCH$_2$Ar], 4.47−4.76 [br, 1H, −COOCH(CH$_2$)$_5$], 5.46−6.00 [br, 1H, −CH═C⟨], 6.18−7.35 [br, 4H, Ar], 7.57−7.88 [br, 1H, −NH−], 7.88−8.33 [br, 1H, −NH−]. IR (cm^{-1}, KBr): 3230 (NH), 2932 (CH), 2858 (CH), 1919 (Ar), 1725 (C═O), 1675 (NHCO), 1450, 1329, 1254, 1174. Poly(**1d**). ^{1}H NMR (400 MHz, DMF-d_7): δ 0.86 [s, 3H, −COO(CH$_2$)$_7$CH_3], 1.26 [s, 10H, −COOCH$_2$CH$_2$(CH_2)$_5$CH$_3$], 1.56 [s, 2H, ⟩CHCH_2CH$_2$COO−], 2.15−2.62 [br, 2H, ⟩CHCH$_2$CH_2COO−], 3.76−4.58 [br, 3H, −COOCH_2CH$_2$(CH$_2$)$_5$CH$_3$ and ⟩CHCH$_2$Ar], 5.56−6.20 [br, 1H, −CH═C⟨], 6.20−7.68 [br, 4H, Ar], 7.68−8.70 [br, 2H, −NH−].

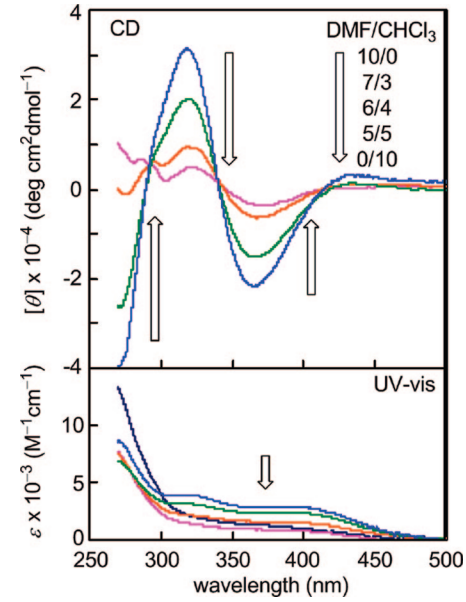


Figure 2. CD and UV−vis spectra of poly(**1d**) measured in DMF/CHCl$_3$ (c = 0.20 mM) at 0 °C.

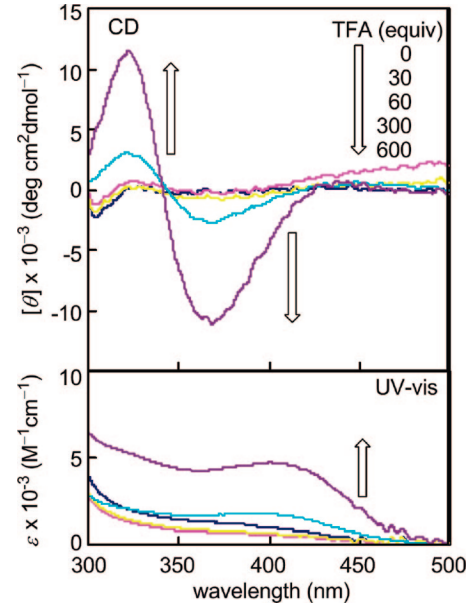


Figure 3. CD and UV−vis spectra of poly(**1d**) upon addition of TFA measured in CHCl$_3$ (c = 0.20 mM) at 0 °C.

IR (cm^{-1}, KBr): 3231 (NH), 2954 (CH), 2927 (CH), 2855 (CH), 1911(Ar), 1735 (C═O), 1678 (NHCO), 1450, 1330, 1173.

Results and Discussion

Monomer Synthesis. Monomers **1a**−**1d** were synthesized via the corresponding linear dipeptides according to the route illustrated in Scheme 2. Namely, the amino group of 4-iodinated-L-phenylalanine was protected with a Boc group, followed by condensation with the corresponding amino acid methyl ester hydrochlorides to obtain dipeptides **3a**−**3d**. After the deprotection of *N*-terminal site with TFA, the residue was dissolved in a hydrocarbon solvent (mesitylene or toluene) at a low reagent concentration (ca. 40 mM), followed by heating for 6 h to promote the cyclization through intramolecular ester−amide exchange reaction of the linear dipeptides to obtain DKPs **4a**−**4d**. Gelation occurred in toluene in the case of **4d**, which was presumably due to the aggregation through hydrogen

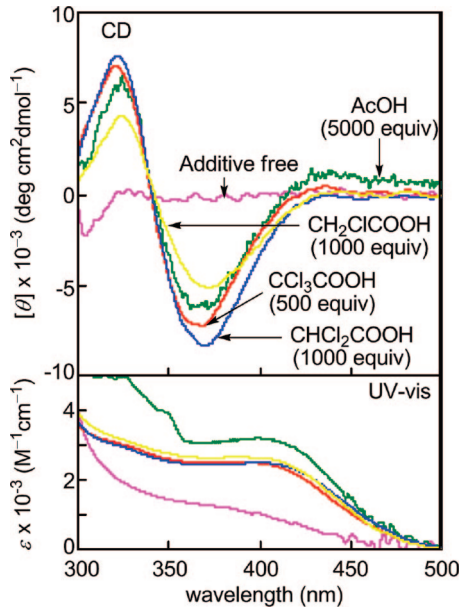


Figure 4. CD and UV−vis spectra of poly(**1d**) upon addition of various carboxylic acids measured in $CHCl_3$ (c = 0.20 mM) at 0 °C.

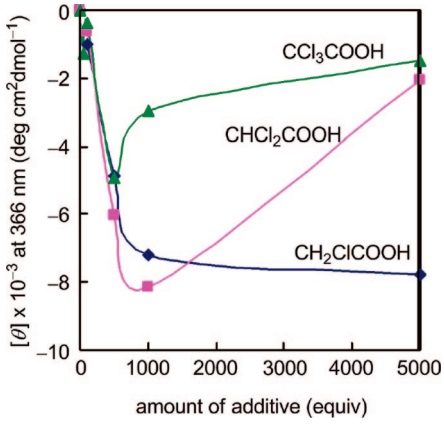


Figure 5. Plots of amount of additive vs [θ] at 366 nm in the CD spectra of poly(**1d**) measured in $CHCl_3$ (c = 0.20 mM) at 0 °C.

bonding between the amide groups and van der Waals interaction between the long alkyl chains as reported by Hanabusa et al.[6] It is expected that a similar interaction might be observed between the side chains of the polymers. Subsequently, the Sonogashira coupling reaction of the 4-iodinated-L-phenylalanine-derived DKPs with TMS acetylene, and desilylation of the protected ethynyl group were carried out to obtain monomers **1a**−**1d**. Monomers **1a** and **1b** were soluble in MeOH, DMF, and DMSO while insoluble in $CHCl_3$. Monomers **1c** and **1d** were soluble in all these solvents.

Synthesis and Secondary Structures of the Polymers. Table 1 summarizes the conditions and results of the polymerization of DKP-containing phenylacetylenes **1a**−**1d** catalyzed with (nbd)$Rh^+[\eta^6$-$C_6H_5B^-(C_6H_5)_3]$ in DMF (Scheme 1). The corresponding polymers were isolated as methanol-insoluble parts in good yields. In the polymerization of **1a** and **1b**, the polymers began precipitating in a little while after initiating the polymerization. Poly(**1a**) and poly(**1b**) isolated were insoluble in common organic solvents such as DMF. Meanwhile, poly(**1c**) and poly(**1d**) with M_n's of 15 500 and 54 600 were soluble in DMF and $CHCl_3$. The specific rotations were −119° and −190°, respectively, both of which were much larger than those of the monomers (−34° and −3°).

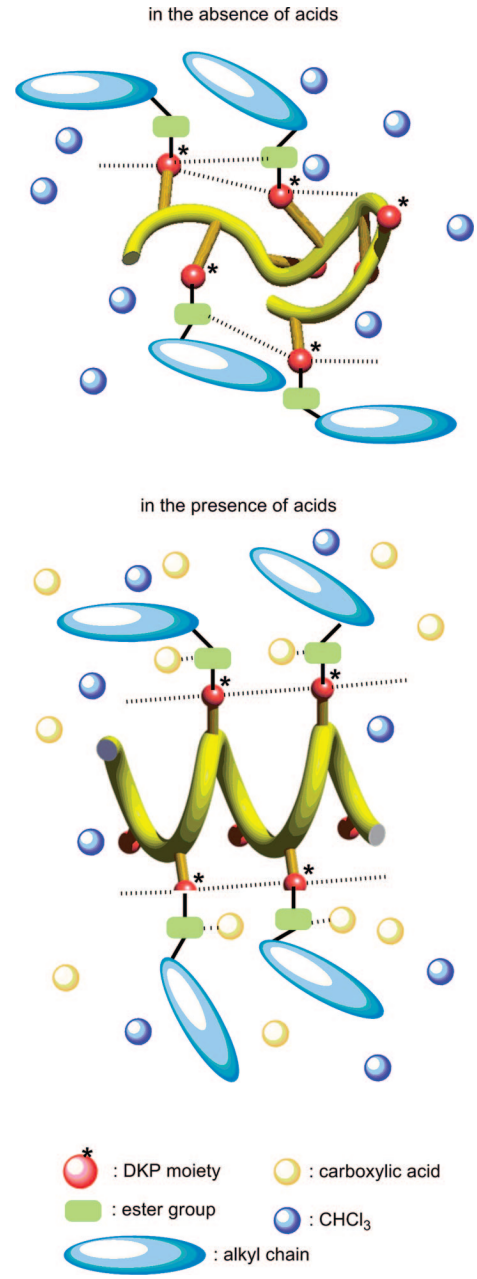


Figure 6. Proposed models of the manner of hydrogen bonding between the DKP moieties, ester groups, and carboxylic acids in $CHCl_3$.

Figure 1 depicts the CD and UV−vis spectra of poly(**1c**) and poly(**1d**) measured in DMF at 0−90 °C. At 0 °C, both polymers exhibited intense Cotton effects at a UV-absorption area based on the conjugated main chain, suggesting that the polymers took helical structures with predominantly one-handed screw sense in the solvent. By raising the temperature, the intensity of the Cotton effects gradually decreased, while the UV−vis absorption peak slightly changed, indicating that the bias of the helical sense was reduced at higher temperature. When the temperature was lowered from 90 to 0 °C, the CD spectroscopic pattern almost returned to the one before heating, indicating the thermal reversibility of the conformational change.

Figure 2 shows the CD and UV−vis spectra of poly(**1d**) measured in DMF/$CHCl_3$ with various compositions. The CD signal gradually decreased in conjunction with the UV−vis absorption upon raising $CHCl_3$ content. The Cotton effects almost disappeared in $CHCl_3$ only. These spectral changes could also be monitored by color change of the solution from yellow to nearly no color. These facts indicate that the conjugation

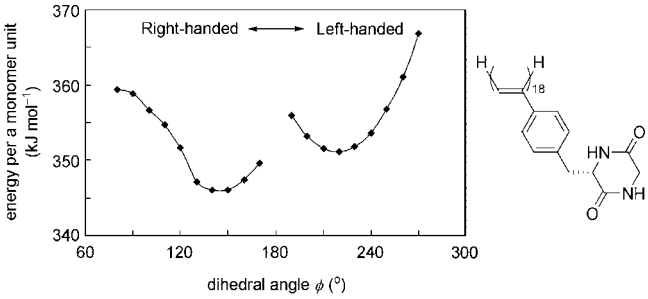


Figure 7. Relationship between the dihedral angle ϕ at the single bond of the main chain of poly(**1a**) (18-mer) and the energy calculated by MMFF94.

length of the main chain is shorter in $CHCl_3$ than that in DMF. Helical substituted polyacetylenes are more conjugated than are randomly coiled ones.[14a] Consequently, it is considered that the conformation of the present polymer is not a helix but a random coil in $CHCl_3$. In a similar manner, poly(**1c**) also seems to take a random structure in $CHCl_3$.

Effect of Additives. It has been reported that TFA interrupts hydrogen bonding between DKPs to disrupt the association.[3] In the present study, hydrogen bonding also seems to play an important role in forming the secondary structure of the polymers. Thus, we measured the CD and UV−vis spectra of poly(**1d**) in $CHCl_3$ upon addition of TFA (Figure 3) to check the effect on the secondary structure. As described above, the polymer showed no intense CD signal in $CHCl_3$. The addition of 300 equiv of TFA to the monomer unit brought about the appearance of CD signals and UV−vis absorption based on the polyacetylene main chain. A further increase in TFA amount (600 equiv) raised the intensities of the Cotton effect and UV−vis absorption. These results indicate that the addition of TFA promoted the helix formation of the polymer in $CHCl_3$, in which the polymer did not take a helical structure in the absence of TFA. Interestingly, the Cotton effect disappeared when 1200 equiv of TFA was added. The possibility of main chain fission of the polymer is negligible, which was confirmed by GPC measurement after TFA addition. In contrast, TFA addition to a polymer solution in DMF did not affect the spectra.

Figure 4 depicts the CD and UV−vis spectra of poly(**1d**) measured in $CHCl_3$ upon addition of carboxylic acids with various pK_a values: acetic acid (AcOH, pK_a = 4.76), chloroacetic acid ($CH_2ClCOOH$, pK_a = 2.87), dichloroacetic acid ($CHCl_2COOH$, pK_a = 1.48), and trichloroacetic acid (CCl_3COOH, pK_a = 0.70). The intensity of the CD signals increased together with that of UV-absorption based on the conjugated main chain with addition of the carboxylic acids in all cases. It was suggested that these carboxylic acids induced the helical structure of the polymers in $CHCl_3$ in a manner similar to TFA (pK_a = 0.30). The additive amount, which induced the maximum intensity of the Cotton effects, depended on the acidity of the carboxylic acids (AcOH > $CH_2ClCOOH$, $CHCl_2COOH$ > CCl_3COOH > TFA).

The addition of other carboxylic acids such as propionic and *tert*-butylic acid showed the same tendency. In contrast, the addition of tetra-*n*-butylammonium fluoride and δ-valerolactam to a solution of poly(**1d**) in $CHCl_3$ did not induce CD signals and change the UV−vis spectra at all. As noted above, addition of TFA to a polymer solution in DMF did not promote the helix formation of the polymers. These results brought us the idea that the side chain took a conformation inducing a helix efficiently by some interaction such as hydrogen bonding between the side chain and either DMF or carboxylic acids such as TFA. The helical structures induced by addition of carboxylic acids are regarded as the same in form judging from the shapes of the CD signals. It seems that the addition of more than a certain amount of CCl_3COOH and $CHCl_2COOH$ destroys the helical structures (Figure 5). It is assumed that the carboxylic acids below a certain amount form hydrogen bonding with the ester moieties of the DKP side chains to suppress the formation of random hydrogen bonding between the ester and amide groups of DKPs, leading to the formation of helical structure efficiently as illustrated in Figure 6. This assumption agrees with the fact that the CD and UV−vis spectra were inactive for addition of δ-valerolactam, which has an *s-cis*-amide group. However, too much carboxylic acid causes the collapse of the helical structure, presumably due to the formation of hydrogen bonding between the acids and amide groups of the DKP moieties, which disturbs the formation of regulated intramolecular hydrogen bonding between the DKP moieties. Meanwhile, it is considered that, in DMF, the ester moieties mainly form intermolecular hydrogen bonding with DMF, and the DKP moieties form intramolecular hydrogen bonding between the side chains.

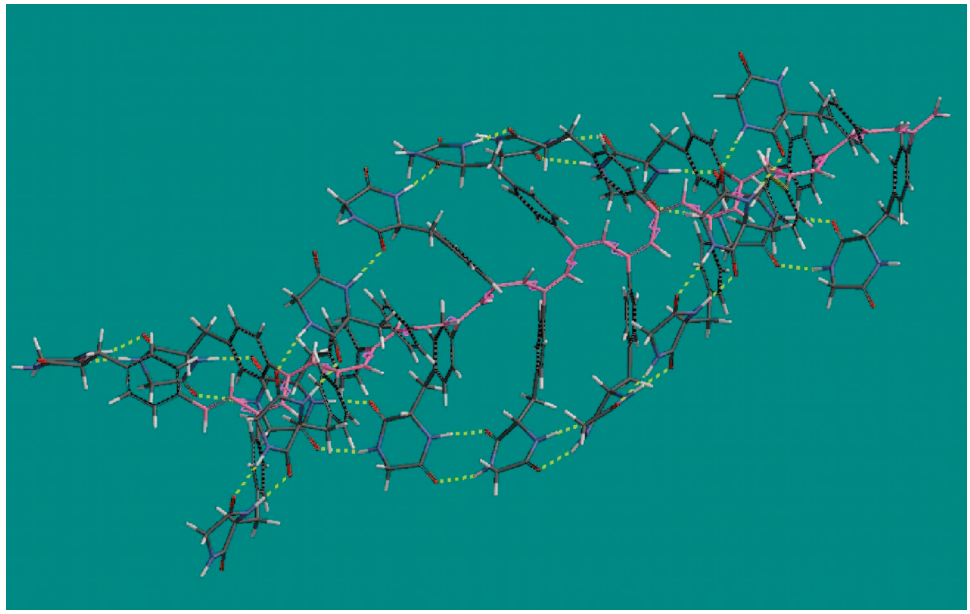


Figure 8. The most stable conformer of poly(**1a**) (18-mer) optimized by MMFF94.

We constructed molecular models of a helical 18-mer of **1a** based on the assumption that hydrogen bonding exists between the amide groups of DKPs. The dihedral angle at the double bond in the main chain was fixed at 0° (*cis*-polyacetylene), and the dihedral angle ϕ at the single bond was varied from 80° to 170° (right-handed helix) and 190° to 260° (left-handed helix) at every 10° increment. The geometries were optimized by the molecular mechanics calculation using the MMFF94 force field[19] to estimate the energy. As illustrated in Figure 7, the right-handed conformer at the energy minimum was 5.11 kJ/mol more stable per monomer unit than the left-handed one. As shown in Figure 8, the right-handed conformer with $\phi = 140°$ was the most stable when hydrogen bonding was doubly formed between *n*th and $(n + 2)$th units. The main chain takes a helical conformation, and the side chains are aligned helically. It should be noted that the helical polyacetylene main chain is right-handed, while the two helical arrays of the DKPs connected with hydrogen bonding strands are left-handed in a manner similar to helical poly(*N*-propargylamide)s.[20]

Yashima and co-workers have determined the helix sense of *cis*-stereoregular poly(phenylacetylene)s from the atomic force microscopy images of the polymers deposited on highly oriented pyrolytic graphite from a dilute solution.[21] They confirmed that the poly(phenylacetylene)s exhibiting a minus Cotton effect around 370 nm show a left-handed helical structure with respect to the pendant arrangements. The main chain of the poly(phenylacetylene)s takes a right-handed helical structure, since the screw sense of helically aligned side chains is opposite to that of the main chain.[20] In the present study, poly(**1c**) and poly(**1d**) showed a minus Cotton effect around 370 nm, as depicted in Figures 1−4. The screw sense of the main chain of the present polymers is right-handed according to the molecular mechanics calculation, which agrees with Yashima's report.[21]

Conclusions

In the present study, we have demonstrated the synthesis and polymerization of novel optically active phenylacetylenes having DKP moieties using a rhodium catalyst to obtain the polymers with moderate molecular weights in good yields. They took helical structures with predominantly one-handed screw sense in DMF, while random one in $CHCl_3$. Addition of various carboxylic acids promoted the formation of helical structures in $CHCl_3$. As far as we know, this phenomenon is the first observation in synthetic helical polymers including polyacetylenes and polyisocyanides. This feature seems to be unique to substituted polyacetylenes whose helical structure is stabilized by the hydrogen-bonding strands doubly formed between the *s-cis*-amide moieties of DKP side chains. The molecular mechanics calculation suggested that the most stable conformer is the right-handed one with $\phi = 140°$ accompanying hydrogen bonding strands formed between *n*th and $(n + 2)$th units.

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Supporting Information Available: ^{1}H NMR spectrum (400 MHz, DMF-d_7) of poly(**1d**) (Figure S1). This material is available free of charge via the Internet at http://pubs.acs.org.

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