# Poly(phenylacetylene)s Bearing a Peptide Pendant: Helical Conformational Changes of the Polymer Backbone Stimulated by the Pendant Conformational Change

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**Abstract:** Optically active, *cis-transoid* poly(phenylacetylene) derivatives bearing a poly(γ-benzyl-L-glutamate) [poly-(PBGA$_m$)] or poly(L-glutamic acid) [poly(PGA$_m$)] chain as the pendant were prepared by polymerisation of the corresponding macromonomer with a rhodium catalyst followed by hydrolysis of the pendant ester groups. Their conformational changes in solution, induced by a helix–coil transition of the pendant polypeptides, were investigated using circular dichroism (CD) and absorption spectroscopies. A series of macromonomers with a different peptide chain lengths was synthesised by the polymerisation of the N-carboxyanhydride of γ-benzyl-L-glutamate with a phenylacetylene bearing an alanine residue as the initiator. The obtained macromonomers (PBGA$_m$) were further polymerised with a rhodium catalyst in *N*,*N*-dimethylformamide (DMF) to yield novel poly(phenylacetylene)s [poly(PBGA$_m$)] with a poly(γ-benzyl-L-glutamate) pendant. The poly(PBGA$_m$) exhibited an induced circular dichroism (ICD) in the UV/Vis region of the polymer backbone in dimethyl sulfoxide (DMSO), probably due to the prevailing one-handed helix formation. The Cotton effect signs of a DMSO solution of the poly(PBGA$_m$) were inverted and accompanied by a visible colour change in the presence of an increasing amount of chloroform or DMF containing lithium chloride. The results suggest that poly(PBGA$_m$) may undergo a conformational change such as a helix–helix transition with a different helical pitch responding to a change in the α-helix content of the poly(γ-benzyl-L-glutamate) pendant. Moreover, a water-soluble poly(PGA$_m$) also showed a similar, but dramatic change in its helical conformation with a visible colour change stimulated by a helix–coil transition of the pendant poly(L-glutamic acid) chains by changing the pH in water.

**Keywords:** circular dichroism · helical structures · peptides · poly(phenylacetylene) · polymerisation

## Introduction

Constructing a helical structure with a controlled helix sense has become one of the most attractive issues in the fields of polymer and supramolecular chemistries. Optically active helical polymers and helical assemblies with an excess helical sense possess interesting properties and functions based on their helical chirality, such as chiral and chirality recognition and enantioselective catalysis.[1] Another unique feature of helical polymers is a helix inversion (helix–helix transition) between the right- and left-handed helical conformations. Up to now, several synthetic[2] and biological[3] polymers are known to exhibit macromolecular helicity inversion regulated by external, achiral stimuli, such as a change in pH, temperature, solvent, salt concentration, or by irradiation. These switchable helical polymeric materials have potential applications in data storage, optical devices, and liquid crystals for displays. On the other hand, switching of the macromolecular helicity by chiral stimuli still remains rare, but can be used to sense the chirality of chiral guests.[1o]

In earlier studies, we reported that macromolecular helicity with an excess of helical sense could be induced in optically inactive poly(phenylacetylene)s bearing various functional groups such as carboxy,[4] amino,[5] boronate,[6] and phosphonate[7] groups or the bulky crown ether as the pendant.[8] Upon noncovalent complexation with optically active compounds capable of interacting with the functional groups, the polymers formed a predominantly dynamic one-handed helix and the complexes exhibited a characteristic induced circular dichroism (ICD) in the polymer backbone region. Moreover, the macromolecular helicity of the poly(phenylacetylene) bearing a carboxy group induced by opti-

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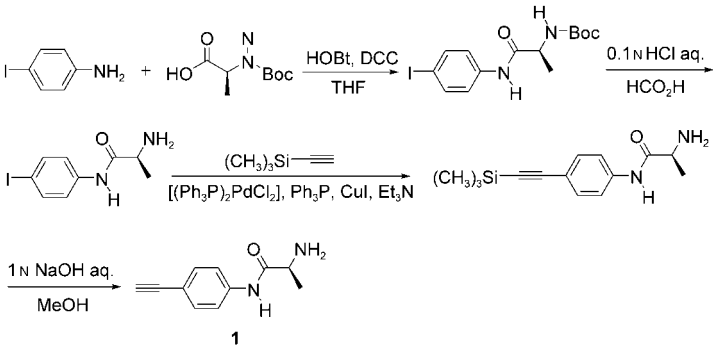
cally active amines can be memorised when the optically active amines are replaced by achiral amines in DMSO.[9]

Similar helical poly(phenylacetylene)s with optical activity can also be prepared by the polymerisation of phenylacetylenes bearing an optically active pendant through covalent bonding.[10] The helical structures of the poly(phenylacetylene)s are dynamic in nature,[4d,11] that is, an equilibrium exists between the helices separated by the helix reversal points.[1c,o] Thus the polymers have a chance to exhibit helix inversion by changing the external chiral and achiral conditions, because the right- and left-handed helices of the optically active poly(phenylacetylene)s are not enantiomers, but diastereomers. Either of the helices may therefore have a helical structure with a different helical pitch and can be predominant under a particular condition. In fact, we found that poly(phenylacetylene)s bearing an optically active (1*R*,2*S*)-norephedrine,[12] β-cyclodextrin,[13] or (1-(1-naphthyl)-ethyl)carbamoyl group[14] as the substituent underwent a helix–helix transition induced by diastereomeric complexation with small chiral molecules as well as by achiral stimuli. These results demonstrate that the helical structures of optically active poly(phenylacetylene)s are dynamic and the helix sense can be controlled not only by the chirality of the pendant, but also by delicate intermolecular and/or intramolecular interactions at the side chains.[11]

On the basis of these observations, we have designed and synthesised a series of optically active, stereoregular poly(phenylacetylene)s bearing a polypeptide chain as the pendant. Some polypeptides are known to undergo conformational changes regulated by a change in pH and solvent.[3] Therefore, we anticipated that the ordered structural change in the polypeptide pendants is transmitted to the polyacetylene backbone, resulting in a further conformational change in the main chain of the poly(phenylacetylene)s. Here we show the detailed results of our investigations of such a dynamic conformational change of the poly(phenylacetylene) backbone. This occurs as a response to conformational change in the pendant polypeptides induced by the external stimuli, such as a change in pH and solvent composition.

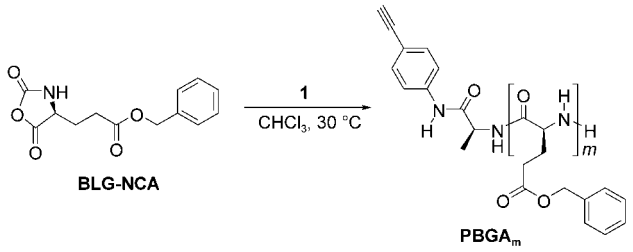
## Results and Discussion

**Synthesis and polymerisation of poly(γ-benzyl-L-glutamate)-based macromonomers bearing an acetylene residue (PBGA) at the C-terminal end**: Ring-opening polymerisation of the N-carboxyanhydride of amino acids (NCA) with a primary amine as the initiator is the most common and straightforward method for the preparation of polypeptides with a controlled molecular weight in which the initiator residue is introduced at the C-terminal end.[15] In order to synthesise macromonomers bearing a polymerisable phenylacetylene residue at the chain end composed of polypeptide (or oligopeptide) chains with various degrees of polymerisations (DPs), we prepared a novel phenylacetylene bearing a primary amino group starting from L-alanine (**1**) (Scheme 1). This was used as the initiator for the polymerisation of the *N*-carboxyanhydride of γ-benzyl-L-glutamate (BLG-NCA). We selected poly(γ-benzyl-L-glutamate) (PBLG) as the pendant polypeptide because PBLG has been found to undergo a helix–random coil conformational change depending on the solvent composition,[16] and the poly(L-glutamic acid) derived from the PBLG also exhibits a similar helix–random coil transition in water by changing the solution pH.[17] The target phenylacetylene bearing a primary amino group (**1**) was prepared starting from 4-iodoaniline and *N*-(*tert*-butoxycarbonyl)-L-alanine in four steps as outlined in Scheme 1.




Scheme 1. Synthesis of **1**.

The polymerisation of BLG-NCA with **1** as the initiator was carried out at different molar ratios of [BLG-NCA]/[**1**] in chloroform at 30 °C to yield a macromonomer with a narrow molecular weight distribution (Scheme 2). The polymerisation results are summarised in Table 1. After the polymerisation, the products ($PBGA_m$: *m* represents DP) were separated into a high molecular weight, methanol-insoluble fraction and a low molecular weight, methanol-soluble fraction that was recovered by precipitation in diethyl ether.




Scheme 2. Synthesis of macromonomer ($PBGA_m$).

The DPs of the obtained $PBGA_m$ were estimated by $^1H$ NMR analysis. The $^1H$ NMR spectrum of $PBGA_{57}$ in [$D_7$]*N*,*N*-dimethylformamide (DMF) (methanol-insoluble part of run 6 in Table 1) is shown in Figure 1. The peak intensity of the methylene proton resonances of the benzyl group of $PBGA_m$ segment relative to that of the methyl proton resonances of the initiator **1** attached to the chain end was used to determine the DPs of the $PBGA_m$ macromonomers. In the aromatic region, the two doublet peaks of the initiator residue ($H_D$ and $H_E$ in Figure 1) were separately observed from the aromatic peaks of the $PBGA_m$ pendants. The DPs of the $PBGA_m$ were estimated from their rel-

Table 1. Polymerisation of BLG-NCA with **1** in chloroform at 30 °C.[a]

| Run | [BLG-NCA]/[**1**] | $t$ [h] | MeOH-insoluble part | | | | | | MeOH-soluble and $Et_2O$-insoluble part | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Yield [%] | DP[b] | Helix content [%] in DMSO[b] | Helix content [%] in DMF[c] | $M_n$ (DP)[d] | $M_w/M_n$[d] | Yield [%] | DP[b] | $M_n$ (DP)[d] | Helix content [%][b] | $M_w/M_n$[d] |
| 1 | 5 | 17 | 41 | 11 | 42 | 53 | 5700 (25) | 1.24 | 41 | 3 | 2800 (12) | – | 1.53 |
| 2 | 10 | 17 | 65 | 16 | 58 | 79 | 7000 (31) | 1.12 | 23 | 5 | 3500 (15) | – | 1.16 |
| 3 | 15 | 40 | 75 | 20 | 67 | 81 | 7600 (34) | 1.09 | 17 | 5 | 3900 (17) | – | 1.15 |
| 4 | 20 | 40 | 82 | 26 | 74 | 87 | 7900 (35) | 1.07 | 12 | 7 | 4400 (20) | – | 1.13 |
| 5 | 30 | 45 | 80 | 34 | 82 | 90 | 8500 (38) | 1.06 | 12 | 10 | 5900 (26) | 45 | 1.15 |
| 6 | 50 | 45 | 79 | 57 | 90 | 96 | 9800 (44) | 1.05 | 18 | 21 | 7900 (36) | 72 | 1.14 |

[a] Polymerised under nitrogen, [BLG-NCA] = 0.25 M. [b] Degree of polymerisation (DP) determined by $^1$H NMR in [$D_6$]DMSO. [c] Determined by $^1$H NMR in [$D_7$]DMF. [d] Determined by SEC using DMF containing 10 mM LiCl as the eluent.

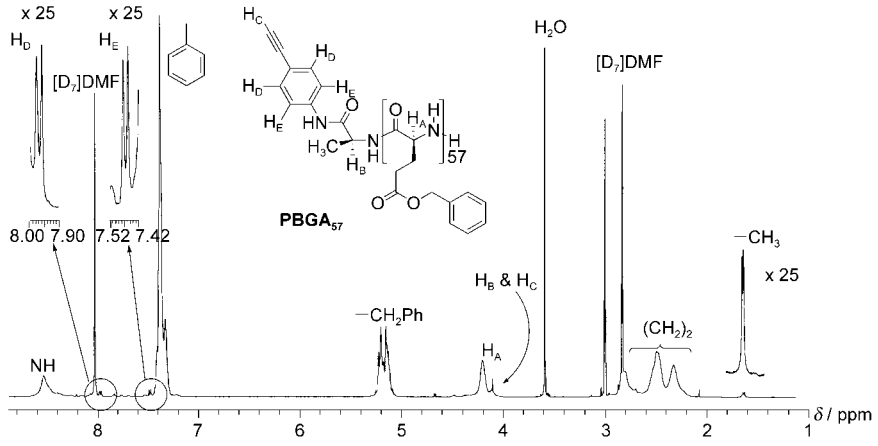



Figure 1. $^1$H NMR (500 MHz) spectrum of $PBGA_{57}$ (run 6 in Table 1) in [$D_7$]DMF at room temperature.

ative peak intensities and agreed well with the above-mentioned DP values. However, the DPs estimated by size-exclusion chromatography (SEC) were different from those estimated by $^1$H NMR and the difference was remarkable for the $PBGA_m$ with a low DP. The $PBGA_m$ obtained has a narrow molecular weight distribution ($M_w/M_n < 1.1$) and the DPs determined experimentally by $^1$H NMR analysis are well correlated with those expected from the macromonomer/initiator ratio ([BLG-NCA]/[**1**]) in the feed except for the $PBGA_m$ obtained at low [BLG-NCA]/[**1**] feed ratios (runs 1 and 2 in Table 1).

The helix content of the $PBGA_m$ was determined by $^1$H NMR analysis. It has been reported that PBLG exhibits two separate peaks due to the α-helix and random coil forms in the α-CH resonance region and the up-field peak was assigned to the α-helix.[18] The $^1$H NMR spectra of the α-CH ($H_A$) regions of the $PBGA_m$ with $m =$ 11 and 26 in [$D_6$]DMSO and [$D_7$]DMF are shown in Figure 2. The $PBGA_m$ exhibited two separate peaks assigned to the α-helix and random coil forms at around $\delta = 3.92$ and 4.26 in [$D_6$]DMSO[19a] and at $\delta = 4.12$ and 4.42 in [$D_7$]DMF, respectively.[18b] The up-field peak assigned to the α-helix partly overlapped the peaks from the ethynyl proton ($H_C$) and the α-CH ($H_B$) proton resonances derived from the initiator. As shown in Table 1, the helix contents of the methanol-insoluble $PBGA_m$ in DMSO were smaller than those in DMF, but increased with an increase in the DP in both solvents. These results agreed with those reported in the literature.[19,20]

The macromonomers with a different peptide length ($PBGA_m$) were then polymerised with a rhodium complex

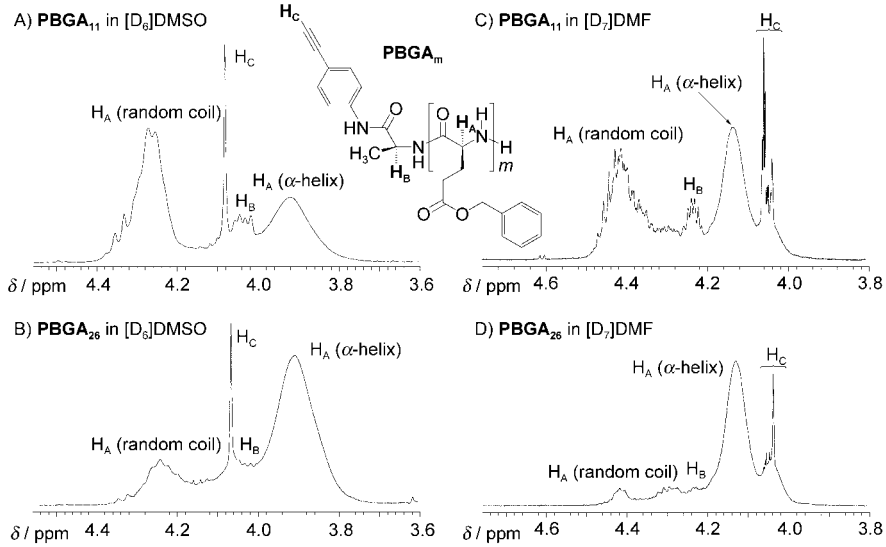



Figure 2. $^1$H NMR (500 MHz) spectra of selected region of $PBGA_{11}$ and $PBGA_{26}$ in [$D_6$]DMSO (A and B) and [$D_7$]DMF (C and D) at room temperature.

([Rh(nbd)Cl]$_2$ (nbd = norbornadiene)) in DMF at 30 °C (Scheme 3). The polymerisation results are summarised in Table 2. The concentrations of PBGA$_m$ in the feed were set to a maximum. The polymerisation proceeded homogeneously, the solution became viscous with time (runs 1–6 in Table 2), and then gelated within a few minutes (runs 1–3 in Table 2). Conversely, an apparent increase in the viscosity was not observed during the polymerisation of PBGA$_m$ with $m>20$ (runs 7 and 8 in Table 2). After the polymerisation reaction, the polymeric products were recovered as the methanol-insoluble fractions. The methanol-insoluble fractions obtained from the polymerisation of the PBGA$_m$ with $m=3$, 5, and 7 were insoluble in common organic solvents, such as THF, chloroform, DMSO and DMF, while those of the PBGA$_m$ with $m>7$ were soluble in DMSO and DMF-containing LiCl (10 mM). The SEC measurements of the methanol-insoluble fractions of the PBGA$_m$ with $m>10$ showed trimodal SEC traces, suggesting that the methanol-insoluble parts consisted of three fractions: high and low molecular weight polymeric fractions (poly(PBGA$_m$)) and the unreacted macromonomer PBGA$_m$. The low molecular weight poly(PBGA$_m$) and the unreacted macromonomer were removed by fractional precipitation using DMF containing 10 mM LiCl as the solvent and methanol as the precipitant to give orange-coloured poly(PBGA$_m$). This showed a unimodal SEC trace. The yield of the high molecular weight polymers significantly decreased with an increase in the DP of the macromonomers. This is probably due to the decrease in the concentration of the macromonomer ([PBGA$_m$]) in the feed because of the solubility limit of the macromonomers.

The helix contents of the pendant PBGA$_m$ in the poly(PBGA$_m$) were determined by $^1$H NMR analysis in the same way as mentioned above for the macromonomers. Figure 3 shows the $^1$H NMR spectra of the poly(PBGA$_m$) ($m=11$, 26: runs 4 and 7 in Table 2) in [D$_6$]DMSO and [D$_7$]DMF. Interestingly, the helix content of the PBGA pendant in the poly(PBGA$_m$) significantly increased in DMF as compared with those of the corresponding macromonomers; for instance, from 53 to 89 % (run 4 in Table 2). This increase in the α-helix content of the pendant peptide after polymerisation of the macromonomer may be ascribed to the formation of a helix-bundle structure in DMF between the pendant PBGA$_m$ chains. A similar enhancement of the α-helix content has been observed for the designed artificial peptides linked to the dendrimer surface, porphyrins, and bipyridyl ligands forming the metal–chelate complexes, when the peptide chains self-assemble to form the helix-bundle structures.[21] These results indicate that the helical polypeptide chains arrange in a one-handed helical array along the helical polyacetylene backbone whose helicity and conformation may be significantly influenced by the pendant polypeptide

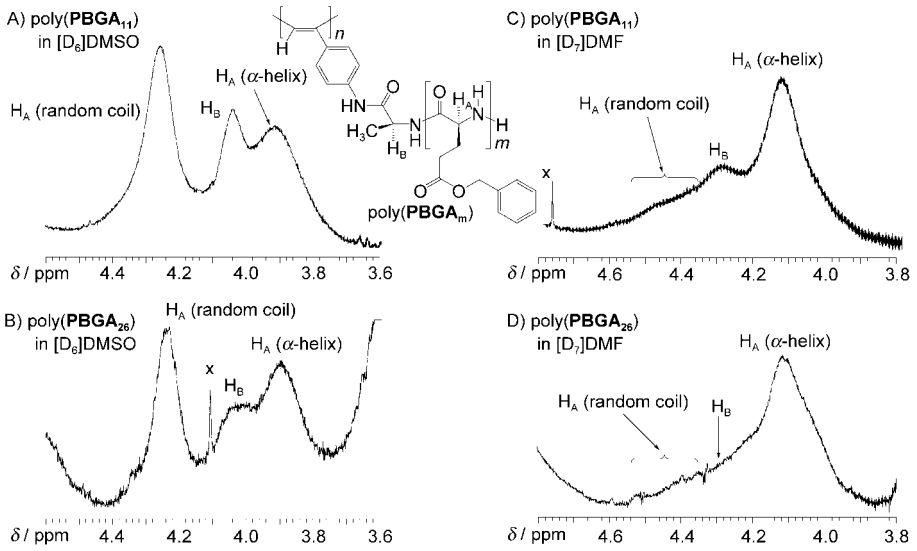



Figure 3. $^1$H NMR (500 MHz) spectra of selected region of poly(PBGA$_{11}$) and poly(PBGA$_{26}$) in [D$_6$]DMSO (a and b) and [D$_7$]DMF (c and d) at room temperature.

Table 2. Polymerisation of macromonomer (PBGA$_m$) with [Rh(nbd)Cl]$_2$ in DMF at 30 °C.[a]

| Run | PBGA$_m$ $m$[b] | Helix content [%][b] in DMSO | in DMF | [PBGA$_m$] [M] | $t$ [h] | Yield[c] [%] | $M_n \times 10^4$[d] | $M_w/M_n$[d] | Helix content [%] in DMSO[e] | in DMF[f] |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 3 | – | – | 0.25 | 15 | 80 | 37.1[g] | 1.91[g] | [h] | [h] |
| 2 | 5 | – | – | 0.25 | 15 | 90 | [h] | [h] | [h] | [h] |
| 3 | 7 | – | – | 0.25 | 15 | 92 | [h] | [h] | [h] | [h] |
| 4 | 11 | 42 | 53 | 0.20 | 17 | 20 | 12.1 | 1.73 | 53 | 89 |
| 5 | 16 | 58 | 79 | 0.15 | 17 | 19 | 25.1 | 2.00 | 55 | 92 |
| 6 | 20 | 67 | 81 | 0.15 | 17 | 20 | 23.2 | 1.97 | 59 | 97 |
| 7 | 26 | 74 | 87 | 0.13 | 40 | 7 | 23.0 | 1.67 | 55 | 95 |
| 8 | 34 | 82 | 90 | 0.10 | 40 | 4[i] | 14.4[j] | – | – | – |

[a] Polymerised under nitrogen, [PBGA$_m$]/[Rh] = 25 and [Et$_3$N]/[Rh] = 50. [b] Degree of polymerisation ($m$) was determined by $^1$H NMR (see Table 1). [c] After removal of oligomers and unreacted PBGA$_m$ by reprecipitation using DMF-LiCl as the solvent and MeOH as the precipitant. [d] Determined by SEC using DMF containing 10 mM LiCl as the eluent. [e] Determined by $^1$H NMR in [D$_6$]DMSO. [f] Determined by $^1$H NMR in [D$_7$]DMF. [g] The polymerisation solution was directly injected into the SEC system after dilution with the eluent. [h] Insoluble in common organic solvents. [i] Containing oligomers. [j] Based on the peak top in the SEC chromatogram.

structure. The helical structure and conformational dynamics of the polyacetylene backbone stimulated by a change in the pendant peptide structure will be discussed later in detail. On the other hand, the helix contents of the pendant of poly(PBGA$_m$) in DMSO were almost constant regardless of the DP of the polypeptides, and rather lower than those of the corresponding macromonomers except for the poly(PBGA$_m$) with $m=11$. As reported in the literature,[16,19] DMF is one of the favourable helix-supporting solvents for PBLG, while DMSO acts as a weak helix supporter. PBLG with low DPs possesses a random coil form in part, but PBLG with high DPs can maintain a full helical structure.[16,19] In DMSO, α-helix formation of the pendant peptides through intramolecular hydrogen bonding is not favourable such that further helix induction in the pendant PBLG chains through the helix bundle formation may not be attained.

In order to get information on the stereoregularity of poly(PBGA$_m$), the $^1$H NMR measurements were performed for the polymers soluble in organic solvents. However, it was difficult to evaluate the stereoregularity of the polymers by their $^1$H NMR spectra. The peak due to the main chain protons, which are highly useful for assigning the conformation and configuration of the polyacetylene backbone,[22] were broad and their intensities were small relative to those of the protons of the pendant peptides. We then tried to evaluate the stereoregularity of poly(PBGA$_m$) by laser Raman spectroscopy, which has also been utilised to assign the stereoregularity of polyacetylenes.[23] Figure 4 shows the laser Raman spectrum of poly(PBGA$_{20}$) measured in the solid state. The Raman spectrum exhibited intense peaks at 1569, 1332, and 962 cm$^{-1}$, which are characteristic peaks due to the *cis* polyacetylenes and can be assigned to the C=C, C−C and C−H bond vibrations, respectively, while those of the *trans* polyacetylenes were not observed.[24] This indicates that the obtained poly(PBGA$_{20}$) possesses a highly *cis*-transoid structure. Similar Raman spectra were also obtained for the other poly(PBGA$_m$)s, indicating that the poly(PBGA$_m$) is highly *cis-transoid*.

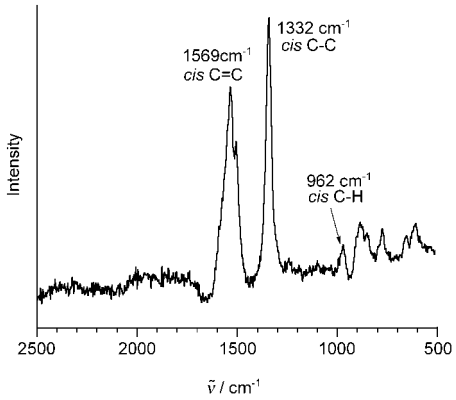



Figure 4. Laser Raman spectrum of poly(PBGA$_{20}$) (run 6 in Table 2) in the solid state at room temperature (ca. 23 °C).

**Chiroptical properties of poly(PBGA$_m$) and their conformational changes**: The CD and absorption spectra of poly(PBGA$_m$) were measured in order to characterise the chiroptical properties of the optically active poly(phenylacetylene)s bearing the PBLG pendant. Figure 5 shows the CD and absorption spectra of poly(PBGA$_m$) (runs 4–7 in Table 2) in DMSO and DMF containing 10 mM LiCl, in which the PBLG pendants favourably form a random coil and α-helix, respectively. These polymers exhibited a characteristic CD in the UV/Vis region of the π-conjugated double bonds of the polyacetylene backbone in both solvents. The macromonomers (PBGA$_m$) showed no CD bands at wavelengths greater than 300 nm. These results indicate that the poly(PBGA$_m$) possesses a predominantly one-handed helical conformation induced by the chirality of the covalently bonded pendant polypeptides. However, the helix sense excess of the poly(PBGA$_m$) backbone in DMSO and DMF-LiCl may not be high judging from their relatively small $[\theta]_{max}$ values compared with those of the previously reported helical poly(phenylacetylene)s.[4–14] In DMF-LiCl, the CD and absorption maxima of poly(PBGA$_m$) shifted to a longer wavelength with increasing DPs of the pendant and the solution colour changed from yellow to red (Figure 5B). By contrast, in DMSO such CD and absorption spectral changes depending on the DPs of the pendant were hardly observed. The colour changes of poly(PBGA$_m$) can be ascribed to a change in the twist angle of the conjugated double bonds of the main chain. The bathochromic shift of the absorption spectra of poly(PBGA$_m$) with the increasing DPs of the pendants suggests that the poly(PBGA$_m$) with high DPs have a rather relaxed helical conformation with an extended π-conjugation in DMF, while the yellow coloured poly(PBGA$_m$) with low DPs has a more tightly twisted helical conformation.[13] Percec et al. recently reported a similar observation that the increase in the steric repulsion between the pendants may result in extending the polyacetylene

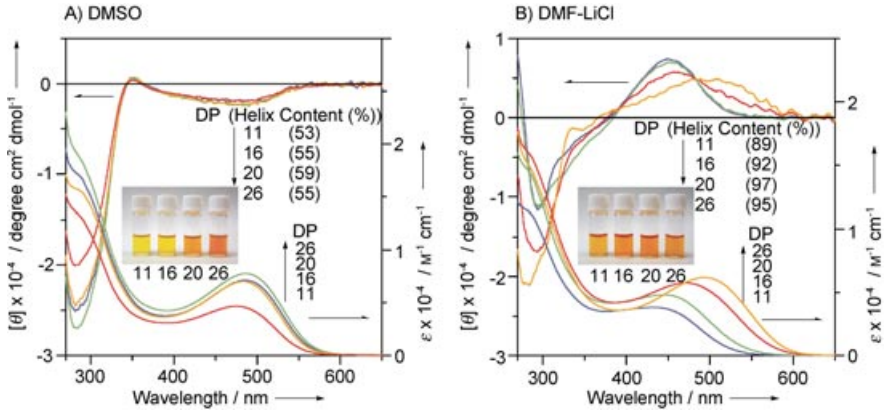



Figure 5. CD and absorption spectra and the visible difference (inset) of poly(PBGA$_m$) with various DPs in A) DMSO and B) DMF containing 10 mM LiCl at room temperature (ca. 23 °C).

backbone.[25] Therefore, it can be presumed that in DMF-LiCl, the steric repulsion between the pendants would increase with an increase in the DPs of the α-helical peptides at the pendant. This, in turn, results in the bathochromic shift of the absorption spectra of poly($PBGA_m$). On the other hand, in DMSO, such a steric repulsion between the pendants seems to be nearly constant regardless of the DPs of the pendant because the helix contents of the pendant $PBGA_m$ chains are low.

More interestingly, the signs of the first Cotton effect of the poly($PBGA_m$) in DMSO were opposite when compared with those in DMF-LiCl. This implies that the predominant helix sense of the polymers in DMSO may be opposite to that in DMF-LiCl. The right- and left-handed helices of the poly($PBGA_m$) are not exactly enantiomers, but diastereomers because of the presence of chiral peptide pendants. Their CD spectra, therefore, differ from one another. However, there may be other possibilities to explain the changes in the CD patterns accompanied by the Cotton effect inversion depending on the solvent; one is a change in the helical pitch of the poly($PBGA_m$) with the same handedness rather than the helix inversion, and the other is aggregations of the poly($PBGA_m$) chains in specific solvent mixtures.[26] It is well known that aggregations are highly sensitive to the polymer concentrations. However, the magnitudes of the ICDs of poly($PBGA_m$) in DMSO- and DMF-LiCl (10 mM) were hardly changed over the concentration range of poly($PBGA_m$) 2–0.08 mg mL$^{-1}$; this indicates that the formation of aggregates could be excluded. The former possibility could not be ruled out because the second Cotton sign was negative in both solvents. We also measured the dynamic light scattering (DLS) of poly($PBGA_{16}$) (run 5 in Table 2) in DMSO and DMF containing 10 mM LiCl; the estimated hydrodynamic radius ($R_h$) values of the polymer were 67 and 88 nm, respectively. Therefore, these DLS results also support this conclusion. The CD spectral changes of poly($PBGA_{16}$) were then measured in DMSO with increasing volumes of DMF (10 mM LiCl) (Figure 6).

We expected that the Cotton effect inversion of poly($PBGA_m$) might be induced by the change in the α-helix content of the pendant PBGA chains during the change in the solvent composition, since the helix content of the pendant peptides of poly($PBGA_m$) in DMSO was smaller than those in DMF-LiCl by approximately 30%. As shown in Figure 6, the CD intensity significantly decreased with the increasing amount of DMSO. The sign became inverted from the positive to negative direction at DMSO/DMF-LiCl 8:2 (*v*/*v*) with a clear isosbestic-like point at 376 nm, and further increased in the negative direction. These CD spectral changes were accompanied by remarkable changes in the absorption spectra; the absorbance maxima ($\lambda_{max}$) at 448 nm shifted to a longer wavelength by 43 nm with a clear isosbestic point at 435 nm, and the solution colour changed from yellow to reddish orange (Figure 6).[27] The helix contents of the pendant peptides in the DMSO/DMF-LiCl mixtures estimated by $^1$H NMR analyses decreased with an increasing amount of DMSO, and this change in the helix content significantly occurred in DMF-LiCl/DMSO (8:2 *v*/*v*), leading to a possible helicity inversion of the polymer backbone as evidenced by the CD inversion in the long wavelength region. A similar solvent-driven CD spectral inversion accompanied by the visible colour change was also observed in the DMSO-chloroform mixtures. As well as DMF, chloroform is one of the most effective helix supporting solvents for PBLG.[16,18,19]

Figure 7 shows the CD and absorption spectral change of poly($PBGA_{16}$) in the DMSO-chloroform mixtures. The CD pattern dramatically changed with the increasing volumes of chloroform, and the first Cotton sign became inverted at DMSO/chloroform 6:4 (*v*/*v*) accompanied by a large blue shift in the absorption spectra with isosbestic points at 352 and 420 nm. These changes in the CD and absorption spectra caused by the change in the helix content of the pendant peptides lead to the solvatochromism from reddish orange to yellow. These results suggest that the poly($PBGA_{16}$) backbone may undergo a conformational transition such as a helix–helix transition by responding to the change in the conformation of the pendant polypeptides (or oligopeptides) (α-helix to random coil) stimulated by the external stimuli (Figure 8).[28] Although the helix–helix transition regulated by achiral and chiral external stimuli such as solvent, tem-

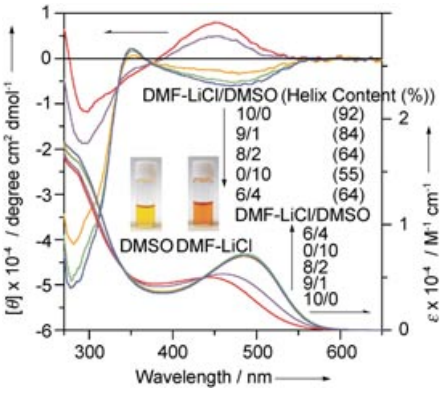



Figure 6. CD and absorption spectral changes of poly($PBGA_{16}$) (run 5 in Table 2) in DMSO-DMF mixtures containing 10 mM LiCl at room temperature (ca. 23 °C). Inset photographs show the visible difference of poly($PBGA_{16}$) in DMSO and DMF-LiCl.

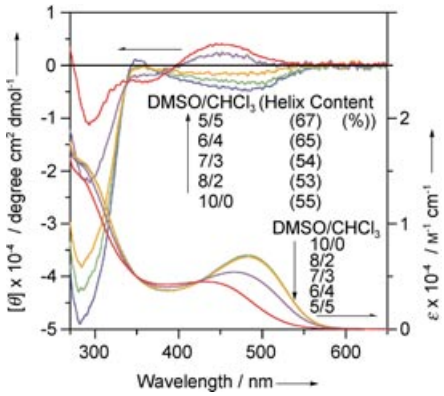



Figure 7. CD and absorption spectral changes of poly($PBGA_{16}$) (run 5 in Table 2) in DMSO-chloroform mixtures at room temperature (ca. 23 °C).

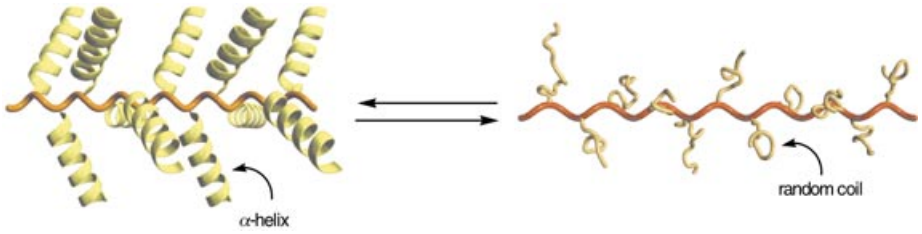



Figure 8. Illustration of interconvertible right- and left-handed helices of poly($PBGA_m$) stimulated by the helix–coil transition of the pendant peptide chains. The helix sense of the main chain is tentative.

perature, pH, and interaction with chiral or achiral guest molecules has been reported for other synthetic helical polymers[2] and biopolymers,[3] the present system is significantly different from those previously reported; that is the inversion of the macromolecular helicity regulated by the change in the ordered structure of the peptides that occurred at the remote side chain.[13]

**Synthesis of water-soluble poly($PGA_m$)s and their chiroptical properties**: Poly(L-glutamic acid) (PGA) undergoes a helix–coil transition by changing the pH of the solution; it forms an α-helix under acidic conditions (low pH) and a random coil under basic conditions (high pH).[17] We then hydrolysed the PBLG side chains of poly($PBGA_m$) in aqueous alkaline solution to obtain a water-soluble poly($PGA_m$) bearing a poly(L-glutamic acid) pendant (Scheme 3), and the effect of the pH on the main chain conformational change induced by the change in the ordered conformation (α-helix–random coil) of the PGA pendants in water was investigated. Poly($PBGA_{20}$) was selected as the typical sample and it was converted to poly($PGA_{20}$) by hydrolysis of the benzyl ester groups of the pendant PBLG in DMF-aqueous NaOH (1 N) (1:6 *v*/*v*) (Scheme 3). The completion of the hydrolysis of the esters was confirmed by IR and $^1$H NMR spectroscopies. The poly($PGA_{20}$) obtained was soluble in water over pH 3.8. The stereoregularity of the poly($PGA_{20}$) was evaluated by using laser Raman spectroscopy. Poly($PGA_{20}$) showed characteristic peaks at 1551, 1342, and 962 $cm^{-1}$, due to the C=C, C–C, and C–H bond vibrations in the *cis* polyacetylenes, respectively, indicating that the poly($PGA_{20}$) derived from the poly($PBGA_{20}$) maintained a highly *cis*-transoid structure after hydrolysis of the ester groups.

Figure 9 depicts the changes in the CD and absorption spectra of poly($PGA_{20}$) in water at various pHs. Poly($PGA_{20}$) also exhibited a rather weak, but apparent ICD in the π-conjugated main-chain region (330–600 nm) probably due to a slight excess of the single-handed helical formation of the polyene backbone in water at pH 10.7. However, lowering the pH of the solution caused a series of dramatic changes in the CD pattern from a nonsplit, broad positive

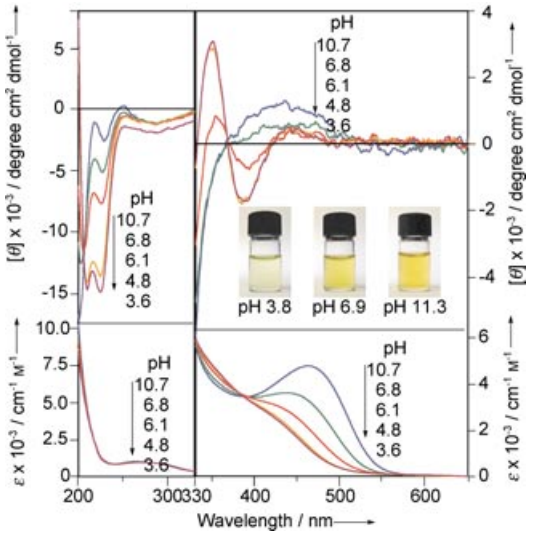
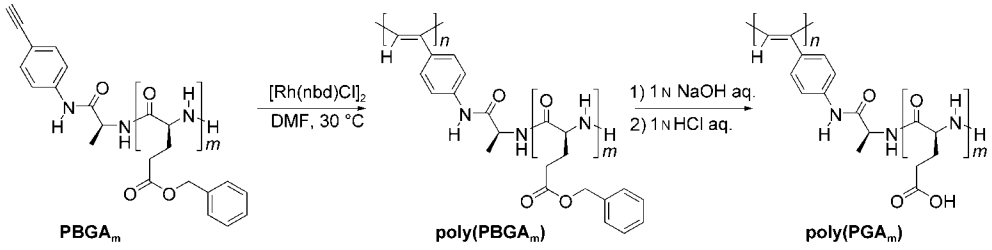



Figure 9. CD and absorption spectral changes of poly($PGA_{20}$) in water at room temperature (ca. 23 °C) with pH. The molar ellipticity ([θ]) and molar absorption coefficient (ε) were calculated using the concentration of the gultamic acid residue (200–330 nm) and the monomer units of poly($PGA_{20}$) (330–650 nm). Inset photographs show the visible difference of poly($PGA_{20}$) in water at different pH.

Cotton effect to a split-type one.[4–9] These CD changes were accompanied by a gradual blue shift in the absorption spectra with a clear isosbestic point at 387 nm and the solution colour changed from deep yellow to light yellow. These CD and absorption spectral changes were reversible. Simultaneously, the CD pattern corresponding to the pendant PGA chains at wavelengths below 250 nm also significantly changed. Poly($PGA_{20}$) exhibited a characteristic CD due to a random coil conformation at pH 10.7, whereas the CD pattern in that region dramatically changed by lowering the pH and exhibited the two negative bands at 210 and 225 nm, a typical right-handed α-helix below pH 4.8,[17,21a,29]




Scheme 3. Synthesis of poly($PBGA_m$) and poly($PGA_m$).

indicating that the pendant PGA chains underwent a random coil to α-helix transition by changing the solution pH. The α-helix content of the pendant PGA chains in the poly($PGA_{20}$) in water at pH 3.6 was estimated to be about 43% on the basis of the reported value of molar ellipticity of a 100% helical PGA at 222 nm ($[\theta]_{222} = -3.4 \times 10^4$).[30] The reason for this rather low α-helicity of the poly($PGA_{20}$) may be due to the low DP of the PGA pendant,[31] and the hydrogen-bonding formation between the pendant carboxy acids may prevent the α-helix formation through the intramolecular hydrogen bonding interaction. However, we believe that the α-helix content may be underestimated and thus be higher, because CDs from the poly(phenylacetylene) overlapped in the region below 250 nm. Consequently, a water-soluble poly($PGA_{20}$) also underwent a conformational change from one helix to another with a different helical pitch of the same or opposite helix sense, and this conformational change can be regulated by the change in the ordered structure of the pendant peptides in water.

## Conclusion

The optically active poly(phenylacetylene)s bearing a series of polypeptide pendants form a predominantly one-handed helical structure in which the helical polypeptide pendants are arranged in a helical array with a predominant screw-sense along the helical poly(phenylacetylene) backbone. A unique conformational change such as a helix–helix transition of the polymer backbone takes place by response to the conformational change of the pendant polypeptides, which can be controlled by external stimuli such as the change in the solvent or pH, although the relationships between the Cotton effect patterns at the polymer backbone regions and the conformations of the polymer remain unknown at present. We expect this methodology to be useful in the construction of novel switchable chiral materials such as chiral sensors and chiral selectors.[1]

## Experimental Section

**Instrumentation**: NMR spectra were measured on a Varian VXR-500 (500 MHz for $^1$H) or Varian Mercury 300 (300 MHz for $^1$H) spectrometer in $CDCl_3$, $D_2O$, [$D_6$]DMSO, or [$D_7$]DMF using tetramethylsilane (for $CDCl_3$), dioxane (for $D_2O$), or a solvent residual peak (for [$D_6$]DMSO and [$D_7$]DMF) as the internal standard. Melting points were measured on a Büchi melting point apparatus and are uncorrected. Optical rotation was measured in a 5 cm quartz cell on a Jasco P-1030 polarimeter. IR spectra were recorded using a Jasco Fourier Transform IR-620 spectrophotometer. Absorption spectra were measured with a Jasco V-570 spectrophotometer in a 0.1 cm quartz cell. CD spectra were measured on a Jasco J-725 spectropolarimeter with a liquid nitrogen-controlled quartz cell (0.5 cm) in a cryostat. The temperature was controlled with a Jasco PTC-348WI apparatus. SEC was performed with a Jasco PU-980 liquid chromatograph equipped with a UV/Vis (254 nm, Jasco UV-970) detector using Tosoh TSK-GEL α-3000 and α-5000 columns connected in series (eluent: DMF containing LiCl (10 mM), standards: poly(ethylene oxide)s and poly(ethylene glycol)s. DLS measurements were performed on a DLS-7070YN (Otsuka Electronics Co. Ltd., Japan) equipped with a 10 mW He/Ne Laser (632.8 nm) at a fixed scattering angle of 90° at 25°C.

**Materials**: THF and hexane were dried over sodium/benzophenone and distilled under nitrogen. Chloroform was dried over calcium hydride and distilled under nitrogen. These solvents were stored under nitrogen over molecular sieves 4 Å (Nacalai Tesque, Kyoto, Japan). Triethylamine was dried over KOH pellets and distilled onto KOH under nitrogen, which was distilled under high vacuum just before use. DMF was dried over calcium hydride and distilled under reduced pressure. Triphosgene, 4-iodoaniline, and Boc-Ala were purchased from Tokyo Kasei (TCI, Tokyo, Japan). *N*,*N*′-Dicyclohexylcarbodiimide (DCC) and bis(triphenylphosphine)palladium dichloride were purchased from Nacalai Tesque and Wako (Osaka, Japan), respectively. Triphenylphosphine, copper(I) iodide, L-glutamic acid, and benzyl alcohol were obtained from Kishida (Osaka, Japan). Bis[(norbornadiene)rhodium(I) chloride] {[Rh(nbd)Cl]$_2$} and 1-hydroxybenzotriazole monohydrate (HOBt) were purchased from Aldrich. (Trimethylsilyl)acetylene (TMSA) was kindly supplied from Shinetsu Chemical (Tokyo, Japan). γ-Benzyl L-glutamate was prepared by the reaction of L-glutamic acid and benzyl alcohol.[32]

**4-{*N*-[*tert*-Butoxycarbonyl]-L-alanylamino}iodobenzene**: HOBt (20.9 g, 155 mmol) was added to a solution of Boc-Ala (12.3 g, 86.0 mmol) in dry THF (50 mL) at 0°C. After the solution was stirred at 0°C for 1 h under nitrogen, DCC (50.0 g, 242 mmol) in THF (50 mL) was added and the mixture was stirred at 0°C for 1 h. 4-Iodoaniline (20.1 g, 92.1 mmol) in THF (50 mL) was then added to the reaction mixture at 0°C and the solution was stirred at room temperature for 17 h. After filtration, the filtrate was evaporated under reduced pressure. The residue was dissolved in ethyl acetate and washed with saturated $NaHCO_3$ aqueous solution, aqueous citric acid (pH 3), and water, and the organic layer was dried over $Na_2SO_4$. After filtration, the solvent was evaporated and the crude product was purified by silica gel chromatography with ethyl acetate/hexane (1:4 *v*/*v*) as the eluent, yielding a yellowish white solid (19.4 g, 57.7%).[33] M.p. 169.1–170.0°C; $[\alpha]_D^{25} = -45°$ ($c = 0.5$ in chloroform); IR (KBr): $\tilde{\nu} = 3297$ (amide NH), 1687 (amide I), 1517 cm$^{-1}$ (amide II); $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.42$ (d, 3H; $CH_3$), 1.45 (s, 9H; $C(CH_3)_3$), 4.31 (q, 1H; CH), 5.18 (d, 1H; NH), 7.26 (d, 2H; aromatic), 7.57 (d, 2H; aromatic), 8.64 (s, 1H; amide NH).

**4-[L-Alanylamino]iodobenzene**: 4-{*N*-[*tert*-Butoxycarbonyl]-L-alanylamino}iodobenzene (19.4 g, 49.6 mmol) was dissolved in formic acid (350 mL) and 0.1 N HCl (1.2 mL) and the solution was stirred at room temperature for 5 h. The solution was concentrated to ca. 100 mL, the aqueous layer neutralised with saturated aqueous $NaHCO_3$, extracted with chloroform, and the chloroform layer was washed with water and dried over $Na_2SO_4$. After filtration, the solvent was removed by evaporation. The residue was purified by chromatography on silica gel with hexane/ethyl acetate (1:1 *v*/*v*), followed by hexane/ethyl acetate/methanol (2:2:1 *v*/*v*/*v*) as the eluents to give 4-[L-alanylamino]iodobenzene (9.92 g, 34.2 mmol, 69.0%).[33] M.p. 113.2–114.0°C; $[\alpha]_{365}^{25} = +2.6°$ ($c = 0.5$ in chloroform); IR (KBr): $\tilde{\nu} = 3293$ (amide NH), 1670 (amide I), 1521 cm$^{-1}$ (amide II); $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.43$ (d, 3H; $CH_3$), 1.57 (s, 2H; $NH_2$), 3.60 (q, 1H; CH), 7.40 (d, 2H; aromatic), 7.61 (d, 2H; aromatic), 9.53 (s, 1H; amide NH).

**4-[L-Alanylamino]phenylacetylene (1)**: Bis(triphenylphosphine)palladium dichloride (718 mg, 1.02 mmol), triphenylphosphine (266 mg, 1.02 mmol), and copper(I) iodide (195 mg, 1.02 mmol) were added to a solution of 4-[L-alanylamino]iodobenzene (9.90 g, 34.1 mmol) in triethylamine (300 mL) and methanol (30 mL) and the reaction mixture was stirred under nitrogen at room temperature for 1 h. (Trimethylsilyl)acetylene (15 mL, 0.10 mmol) was then added to the reaction mixture, which was stirred under nitrogen at room temperature for 3 h. The solvent was removed under reduced pressure, and the residue was dissolved in ethyl acetate; the insoluble ethyl acetate part was removed by filtration. The filtrate was washed with saturated $NaHCO_3$ aqueous solution and water, and dried over $Na_2SO_4$. After the solvent was evaporated, the crude residue was purified by column chromatography on silica gel with hexane/ethyl acetate (1:4 *v*/*v*) as the eluent to give yellowish white crystals (1-[4-[L-alanylamino]phenyl]-2-[trimethylsilyl]acetylene) (7.48 g, 84.0%). M.p. 138.3–139.3°C; $[\alpha]_{365}^{25} = -7.0°$ ($c = 0.5$ in chloroform); IR (KBr): $\tilde{\nu} = 3275$ (amide NH), 3189 ($-NH_2$), 2154 (C≡C), 1664 (amide I), 1533 cm$^{-1}$ (amide II); $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.23$ (s, 9H; $Si(CH_3)_3$), 1.40 (d, 3H; $CH_3$), 2.03 (s, 2H; $NH_2$), 3.61 (q, 1H; CH), 7.40 (d, 2H; aromatic), 7.54 (d, 2H; aromatic), 9.60 (s, 1H; NH).

NaOH (1 N, 20 mL) was added to a solution of 1-[4-[L-alanylamino]phenyl]-2-[trimethylsilyl]acetylene (6.94 g, 23.9 mmol) in methanol (200 mL) and the solution was stirred at room temperature for 5 h. After the solvent was removed under reduced pressure, the residue was dissolved in chloroform, washed with water, and dried over $Na_2SO_4$. The solvent was evaporated, and the resulting crude product was purified by recrystallisation from hexane/ethyl acetate (1:1 *v*/*v*) to give **1** as a white solid (3.48 g, 72.1%). M.p. 86.1–86.4°C; $[\alpha]_{577}^{25} = +2.9°$ ($c = 5$ in chloroform); IR (KBr): $\tilde{\nu} = 3382$ (amide NH), 3315 ($-NH_2$), 3147 ($\equiv CH$), 1655 (amide I), 1524 $cm^{-1}$ (amide II); $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 1.37$ (d, 3H; $CH_3$), 1.80 (s, 2H; $NH_2$), 3.08 (s, 1H; $\equiv CH$), 3.56 (q, 1H; CH), 7.43 (d, 2H; aromatic), 7.53 (d, 2H; aromatic), 9.61 (s, 1H; NH); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta = 21.5$ ($CH_3$), 51.1 (CH), 76.8, 83.5 (HC≡C), 117.1, 118.9, 132.7, 138.2 (aromatic), 173.8 (C=O); elemental analysis calcd (%) for $C_{11}H_{12}N_2O$ (202.25): C 70.19, H 6.43, N 14.88; found: C 70.19, H 6.58, N 14.64.

**γ-Benzyl L-glutamate *N*-carboxyanhydride (BLG-NCA)**: This was prepared by the reaction of γ-benzyl L-glutamate with triphosgene and purified by repeated recrystallisation from a mixture of hexane and THF according to the literature method (75.1% yield).[34] IR (KBr): $\tilde{\nu} = 3300$ (−NH), 1884, 1786 (C=O of acid anhydride), 1721 $cm^{-1}$ (C=O of ester); $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 2.13$, 2.31 (m, 2H; γ-$CH_2$), 2.61 (m, 2H; β-$CH_2$), 4.37 (m, 1H; −CHNH−), 5.15 (s, 2H; $CH_2Ph$), 6.24 (s, 1H; NH), 7.36 (m, 5H; aromatic).

**Synthesis of macromonomer $PBGA_m$**: $PBGA_m$ was synthesised by the polymerisation of the BLG-NCA with **1** as initiator in chloroform (Scheme 2). A typical polymerisation procedure (run 3 in Table 1) is described below. Polymerisation was carried out in a dry glass ampoule under a dry nitrogen atmosphere. BLG-NCA (3.99 g, 15.1 mmol) was placed in a dry ampoule, which was then evacuated on a vacuum line flushed with dry nitrogen. After this evacuation-flush procedure was repeated three times, a three-way stopcock was attached to the ampoule, and chloroform was added with a syringe. To this was added a solution of **1** in chloroform at 30°C. The concentrations of the monomer and the initiator were 0.25 and 0.017 M, respectively. The polymerisation proceeded homogeneously and the reaction mixture gelated within a few hours. After 40 h, the resulting polymer was dissolved in DMF and precipitated into a large amount of methanol, collected by centrifugation, and dried in vacuo at room temperature over night (2.63 g, 74.5%). The methanol-soluble fraction was concentrated under reduced pressure and reprecipitated into a large amount of ether. The ether-insoluble part was collected by centrifugation, and dried in vacuo at room temperature over night (0.59 g, 16.8%).

*Spectroscopic data of $PBGA_{20}$*: IR (KBr): $\tilde{\nu} = 3295$ (amide NH), 1736 (C=O of ester), 1655 (amide I), 1543 $cm^{-1}$ (amide II); $^1H$ NMR (500 MHz, [$D_7$]DMF): $\delta = 1.4$–1.6 (m, 3H; $CH_3$ of **1**), 2.0–3.0 (br, 4H×20; $CH_2CH_2$×20), 4.13 (brs, 1H×20; α-CH (α-helix)×20), 4.42 (brs, 1H×20; α-CH (random coil)×20), 5.0–5.3 (m, 2H×20; $CH_2Ph$×20), 7.36 (brs, 5H; aromatic), 7.45 (d, 2H; aromatic of **1**), 7.96 (d, 2H; aromatic of **1**), 8.53 (brs, 1H×20; NH×20); elemental analysis calcd (%) for $(C_{12}H_{13}NO_3)_{20}{\cdot}C_{11}H_{12}N_2O{\cdot}2H_2O$ (4608.99): C 65.41, H 6.04, N 6.69; found: C 65.45, H 6.00, N 6.89.

**Polymerisation of $PBGA_m$**: Polymerisation of the macromonomer $PBGA_m$ was conducted according to Scheme 3. A typical polymerisation procedure (run 6 in Table 2) is described below. Polymerisation was carried out in a similar way for the polymerisation of BLG-NCA in a dry glass ampoule under a dry nitrogen atmosphere with $[Rh(nbd)Cl]_2$ as the catalyst. $PBGA_{20}$ (0.91 g, 0.19 mmol) was placed in a dry ampoule and DMF and triethylamine were added with a syringe. A solution of $[Rh(nbd)Cl]_2$ in DMF was added at 30°C. The concentrations of the monomer and the rhodium catalyst were 0.15 and 0.006 M, respectively. The polymerisation proceeded homogeneously, and the solution became viscous with time. After 17 h, the resulting polymer was precipitated into a large amount of methanol, collected by centrifugation, and dried in vacuo at 50°C for 2 h (0.18 g, 20%). The SEC measurement of the obtained methanol-insoluble fraction showed a trimodal SEC trace, suggesting that the methanol-insoluble part consisted of three fractions with a different molecular weight: high and low molecular weight polymeric fractions, and the unreacted macromonomer $PBGA_{20}$. In order to remove the low molecular weight fraction and the unreacted macromonomer, the methanol-insoluble part was dissolved in DMF containing 10 mM LiCl, and methanol was added to the solution as the precipitant. The resulting yellow precipitate was collected by centrifugation, washed with acetone, and dried in vacuo at 50°C for 2 h to give poly($PBGA_{20}$) showing a unimodal SEC trace (0.18 g, 20% yield). Poly($PBGA_{20}$) was soluble in DMSO and DMF containing LiCl, but insoluble in other usual organic solvents such as toluene, THF, chloroform, acetonitrile, and acetone. The molecular weight ($M_n$) and the distribution ($M_w/M_n$) of the poly($PBGA_{20}$) were estimated to be $2.32 \times 10^5$ and 1.97, respectively, as determined by SEC (poly(ethylene oxide) standards using DMF containing 10 mM LiCl as the eluent).

*Spectroscopic data of poly($PBGA_{20}$)*: IR (KBr): $\tilde{\nu} = 3295$ (amide NH), 1736 (C=O of ester), 1655 (amide I), 1543 $cm^{-1}$ (amide II); elemental analysis calcd (%) for $[(C_{12}H_{13}NO_3)_{20}{\cdot}C_{11}H_{12}N_2O_n{\cdot}4H_2O]_n$: C 64.90, H 6.08, N 6.63; found: C 64.75, H 5.95, N 6.83. For $^1H$ NMR, see Figure S1 (Supporting Information).

**Hydrolysis of PBGA**: Poly($PBGA_{20}$) (28 mg) was dissolved in DMF (10 mL) containing 10 mM LiCl and 1 N NaOH aq.(10 mL) was added at 0°C. After 10 min, 50 mL of water was added at 0°C and the reaction mixture was stirred at 0°C for 1 h. The solution was neutralised with 1 N HCl aq. and freeze-dried. The residue was suspended in 0.3 N NaOH (70 mL) and stirred at room temperature until the suspended compound was completely dissolved (2 h). The solution was then acidified with 1 N HCl aq. and the precipitated poly($PGA_{20}$) was collected by centrifugation, washed with water, and dried in vacuo at room temperature over night. Yield 50.6% (8.6 mg).

*Spectroscopic data of poly($PGA_{20}$)*: IR (KBr): $\tilde{\nu} = 1719$ (C=O of carboxylic acid), 1655 (amide I), 1544 $cm^{-1}$ (amide II); elemental analysis calcd (%) for $[(C_5H_7NO_3)_{19}{\cdot}C_{12}H_{13}NO_3{\cdot}C_{11}H_{12}N_2O{\cdot}2H_2O]_n$: C 48.93, H 5.64, N 10.64; found: C 48.99, H 5.72, N 10.21. For $^1H$ NMR, see Figure S2 (Supporting Information).

**CD measurements—effect of solvent on ICD of poly($PBGA_m$)**: A stock solution of poly($PBGA_{16}$) in DMF (4.7 mg/3 mL) containing 10 mM LiCl was prepared in a 3 mL flask equipped with a stopcock and the initial CD and absorption spectra were recorded. 900, 800, 700, and 600 μL aliquots of the stock solution were transferred to four flasks equipped with a stopcock using a Hamilton microsyringe, and DMSO was added up to mark. Absorption and CD spectra were taken for each flask with the use of a 0.2 or 0.5 cm quartz cell. In a similar manner, the effect of chloroform on ICD of poly($PBGA_{16}$) was investigated.

**Concentration effect of poly(PBGA) on ICD**: A stock solution of poly($PBGA_{16}$) (2 mg $mL^{-1}$) in DMSO was prepared in a 2 mL flask equipped with a stopcock and the initial CD spectrum was recorded with a 0.4 cm quartz cell. A 600 μL aliquot of the stock solution was transferred to a vessel with a screw-cap using a Hamilton microsyringe and the solution was diluted with DMSO, giving a 0.08 mg $mL^{-1}$ solution of poly($PBGA_{16}$). The CD spectrum of this solution was recorded in a 5 cm quartz cell. Similarly, the concentration effect of poly($PBGA_{16}$) on ICD in DMF containing LiCl (10 mM) was also investigated.

**Effect of pH on ICD of poly($PGA_{20}$)**: Deionised, distilled water was used after degassing with nitrogen. A stock solution of poly($PGA_{20}$) in alkaline water (pH 10.7) (1.5 mg/3 mL) was prepared in a 3 mL flask equipped with a stopcock and the initial CD and absorption spectra were recorded with 0.05 (200–330 nm) and 1.0 cm (330–650 nm) quartz cells. The pH of the solution was measured with a B-211 pH meter (Horiba). The pH of the solution was adjusted with 1.0 or 0.5 N HCl aq. The absorption and CD spectra were then taken at pH 6.8, 6.1, 4.8, and 3.6 with 0.05 (200–330 nm) and 1.0 cm (330–650 nm) quartz cells.

**Dynamic light scattering measurements**: In the DLS measurements, we used poly($PBGA_{16}$) (run 4 in Table 1). Solutions of poly($PBGA_{16}$) (2 mg $mL^{-1}$) in DMF containing 10 mM LiCl and in DMSO were separately prepared in 2 mL flasks equipped with a stopcock and the solutions were filtered using a 0.2 μm syringe filter (Toyo Roshi Co. Ltd., Japan). The DLS measurements of the samples were performed at a fixed scattering angle of 90°. The obtained autocorrelation functions were analysed by the method of cumulants to give the translational diffusion coefficients ($D$). The corresponding hydrodynamic radius ($R_h$) was calculated using the Stokes–Einstein equation: $R_h = k_B T/(6\pi\eta D)$, where $k_B$, $\eta$, and $T$ are the Boltzmann constant, the solvent viscosity, and the absolute temperature, respectively.

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