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Helicity Induction and Conformational Dynamics of Poly(bis(4-carboxyphenoxy)phosphazene) with Optically Active Amines

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Polyphosphazenes have drawn considerable interest as technologically valuable, new polymeric materials because various kinds of poly(organophosphazenes) can be easily prepared from a single polyphosphazene, the poly(dichlorophosphazene), by the macromolecular substitution reaction with nucleophiles such as alkoxides and primary amines, and their properties can be widely tuned by proper selection of the introducing substituents.[1] Although conformation of the polyphosphazenes has been extensively studied using X-ray diffraction analyses[2,3] and computational calculations based on empirical, semiempirical, and the ab initio method,[3e,4,5] there are controversies about these results, and both the helical[2,4] and *cis*−*trans* planar[3,5] conformations have been proposed for the polyphosphazenes. Moreover, a large number of polyphosphazenes bearing optically active side groups, such as amino acid esters and steroidal and glucosyl groups, have been prepared in order to develop biomedical materials because they are bioerodible,[6] but their conformations have not yet been discussed in detail.[7]

Here we show that an achiral polyphosphazene, poly(bis(4-carboxyphenoxy)phosphazene) (poly-**1**),[8] forms a predominantly one-handed helical conformation in solution by responding to the chirality of the optically active amines. This finding will contribute to understanding the significant nature of the poly(organophosphazenes) structure under debate.

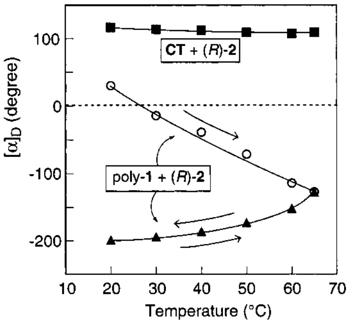
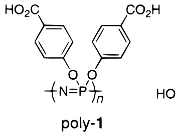
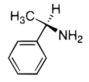
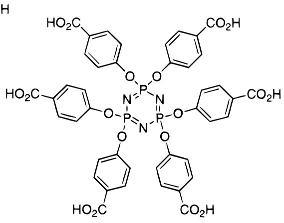


Figure 1. Optical rotation changes in the poly-**1**− (○, ▲) and **CT**−(*R*)-**2** (■) complexes ([(*R*)-**2**]/[carboxy residues of poly-**1** or **CT**] = 5) in DMSO at various temperatures. The rotations were first measured at 20, 30, 40, 50, 60, and 65 °C after annealing the samples at these temperatures for ∼2 h (first-annealing (○); for rotational changes with time at the temperatures, see Supporting Information). During the first-cooling and further annealing and cooling processes (▲), the rotations were measured after allowing the sample to stand for ∼10 min at these temperatures.


poly-**1**


(*R*)-**2**


CT

The chiroptical properties of poly-**1** complexed with an optically active amine, (*R*)-1-phenylethylamine ((*R*)-**2**), were investigated using a polarimeter, and the changes in the optical rotation of the complex in DMSO ([poly-**1**] = 0.5 g/dL, [(*R*)-**2**]/[carboxy residues of poly-**1**] = 5) were followed in the temperature range of 20−65 °C (Figure 1).[10] The optical rotation values were calculated based on the poly-**1** concentration. The optical rotation gradually changed from a positive value to a negative one and increased in the negative direction with an increase in temperature (the optical rotational changes in the complex in the temperature range with time are available in Supporting Information).[11] After annealing the poly-**1**−(*R*)-**2** complex at 65 °C for ∼2 h, the optical rotation of the complex exhibited a large negative value ($[\alpha]^{65}_{D}$ −127°), the sign of which was opposite to that of (*R*)-**2** ($[\alpha]^{25}_{D}$ +33° in DMSO). This first-annealing process was irreversible, but after the solution was once annealed at 65 °C, the poly-**1** then became reversible with further rapid optical

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(7) Recently, Carriedo et al. reported that the poly(organophosphazene) bearing an optically active binaphthyl group might adopt a helicoidal secondary structure in solution based on their optical rotation measurements. Carriedo, G. A.; García-Alonso, F. J.; González, P. A.; García-Alvarez, J. L. *Macromolecules* **1998**, *31*, 3189−3196.

(8) Poly-**1** was prepared according to the reported method developed by Allcock et al.[9] (For detailed experimental procedures, see Supporting Information). The molecular weight (M_n) and the distribution (M_w/M_n) of poly-**1** were estimated to be 1.4 × 10^5 (degree of polymerization, ∼370) and 1.2, respectively, by size exclusion chromatography (SEC) as its ethyl esters.

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(10) A CD spectrum of the poly-**1**−(*R*)-**2** complex in DMSO at shorter wavelength less than ∼270 nm could not be measured because of overlap with the solvent and (*R*)-**2**. However, the cast films, particularly, the film prepared from the annealed solution of the poly-**1**−(*R*)-**2** complex exhibited an intense CD in the aromatic region (see Supporting Information). It should be noted that polyphosphazenes show no UV or visible absorption spectra at wavelength longer than 220 nm due to the main chains. Allcock, H. R. *Chem. Rev.* **1972**, *72*, 315−356.

(11) We tried to estimate the thermodynamic parameters for this process using the standard Arrhenius analysis, but it was difficult due to the nonlinear relation between the kinetics and temperature.

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Table 1. Specific Rotations of Poly-**1** and Cyclic Trimer (**CT**) in the Presence of (*R*)-**2** After Annealing at 65 °C for 2 h[a]

	$[\alpha]^{20}_D$ (*c* 0.5, DMSO) (deg)		
[(*R*)-**2**]/[-CO$_2$H]	poly-**1**[b]	**CT**[b]	(poly-**1**)−(**CT**)[c]
1	−125	+20	−145
5	−197	+117	−314
5[d]	+199	−116	+315
10	−62	+247	−309

[a] Optical rotation was measured on a Jasco P-1030 polarimeter in a 5-cm quartz cell equipped with a temperature controller (EYELA NCB-2100). [b] The specific rotation values were calculated on the basis of the concentrations (g/dL) of poly-**1** and **CT**. [c] Net rotations showing the rotational contribution derived from an induced helical conformation of poly-**1**. [d] (*S*)-**2** was used instead of (*R*)-**2**.

rotational changes in the temperature range of 20−65 °C and showed a larger optical rotation ($[\alpha]^{20}_D$ −197° in DMSO).[12]

On the other hand, the optical rotation of the cyclic trimer (**CT**)−(*R*)-**2** complex, which can be regarded as a model complex of poly-**1**−(*R*)-**2**, hardly changed in the temperature ranges under identical conditions and the sign of optical rotation was the same as that of (*R*)-**2**, but was opposite to that of the annealed poly-**1**−(*R*)-**2** complex (Figure 1).[13] These results indicate that the large negative optical rotation of the poly-**1**−(*R*)-**2** complex may be due to the prevailing, one-handed helicity induction on the polymer main chain upon complexation with the optically active (*R*)-**2** through the acid−base interaction.[14]

Table 1 shows the specific rotations of poly-**1** and **CT** in the presence of increasing amounts of (*R*)-**2** in DMSO at 20 °C after annealing the samples at 65 °C for 2 h; the specific rotation values were calculated based on the poly-**1** and **CT** concentrations. To exclude the rotational contribution of the added (*R*)-**2** to the observed rotation, the net rotations (poly-**1** - **CT** in Table 1) were calculated by subtracting the specific rotations of **CT** from those of poly-**1**, which appear to be the rotational contribution derived from an induced helical conformation of the poly-**1** backbone.[15] The net optical rotation increased with an increase in the (*R*)-**2** concentration and reached an almost constant value ($[\alpha]^{20}_D$ ∼−310°) at [(*R*)-**2**]/[the carboxy residue of poly-**1**] ≥ 5. When the enantiomeric amine, (*S*)-**2**, was employed, the poly-**1**−(*S*)-**2** complex showed mirror image behaviors.

As expected, the optical rotation of the poly-**1**−(*R*)-**2** complex instantly changed to the same value as that of the **CT**−(*R*)-**2** complex when the poly-**1**−(*R*)-**2** complex was exposed to a stronger acid, such as trifluoroacetic acid, which frees the poly-**1** so it reverts to the original, optically inactive polymer. This suggests that the original, free poly-**1** cannot maintain the induced helical conformation in solution.

To investigate the stability of the induced helical conformation of the poly-**1**−(*R*)-**2** complex ($[\alpha]^{20}_D$ −197°; [(*R*)-**2**]/[carboxy residues of poly-**1**] = 5), the solution of the complex was further annealed at temperatures higher than 80 °C for 1 h and then the optical rotations were measured immediately after cooling the samples to 20 °C. After reannealing the poly-**1**−(*R*)-**2** complex at 80, 90, and 110 °C for 1 h, the $[\alpha]^{20}_D$ values decreased to −191°, −158°, and −71°, respectively. However, after further annealing the samples at 65 °C for 2 h again, the specific rotations recovered to the original values ($[\alpha]^{20}_D$ ∼−200°). These results indicate that at higher temperatures (≥80 °C), the induced helical conformation of poly-**1** partially collapses and transforms into a nonhelical conformation.[16]

A more interesting phenomenon was observed in the addition experiments of (*S*)-**2** to the solutions of the annealed poly-**1**−(*R*)-**2** (net $[\alpha]^{20}_D$ −309°) and **CT**−(*R*)-**2** complexes. Apparently, the optical activity of the **CT**−(*R*)-**2** solution completely disappeared after the addition of an equivalent amount of (*S*)-**2** ([(*R*)-**2**]/[(*S*)-**2**] = 1), because **2** exists as a racemic mixture in the solution. However, rather surprisingly, the optical activity of the poly-**1**−(*R*)-**2** solution was still observed along with a slight decrease in the rotation value (net $[\alpha]^{20}_D$ −279°) even after the addition of an equivalent amount of (*S*)-**2**. Moreover, the net specific rotation did not disappear after annealing the sample at 65 °C for 3h ($[\alpha]^{20}_D$ −210°) and further annealing at 100 °C for 1 h ($[\alpha]^{20}_D$ −57°). This suggests that the one-handed helical conformation of the poly-**1** induced by (*R*)-**2** may be memorized[17] even after the (*R*)-**2** complexed with poly-**1** could be randomly replaced by (*S*)-**2** or the helical poly-**1** formed by (*R*)-**2** may act as a chiral filter to exclude one enantiomer for racemic amines.[14c]

We, therefore, conclude that an achiral poly-**1** transforms into a prevailing one-handed helical conformation upon complexation with chiral amines.[18] This unique helical poly(organophosphazene) may be used as novel chiral materials in areas such as liquid crystals, membranes, and chiral selectors. We are now making an effort to prepare poly-**1**s with different molecular weights to understand the mechanism and cooperativity of helicity induction.[19]

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Supporting Information Available: Experimental procedures, optical rotation changes in the poly-**1**−(*R*)-**2** complex with time at various temperatures, nonlinear effects between the optical rotation of poly-**1** and percent ee of **2**, CD spectra and X-ray diffractograms of cast films, ^{31}P NMR spectra of poly-**1** with or without (*R*)-**2**, viscosity and light scattering measurements, and chiroptical properties of novel model compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) Recently, Novak et al. reported a similar, but irreversible transformation for an optically inactive polyguanidine complexed with optically active camphorsulfonic acid. Schlitzer, D. S.; Novak, B. M. *J. Am. Chem. Soc.* **1998**, *120*, 2196−2197.

(13) The net specific rotation of the **CT**−(*R*)-**2** complex is almost exactly the same as that of pure (*R*)-**2**.

(14) Similar helicity induction through chiral interactions has been observed for other optically inactive polymers, see ref 12. (a) Yashima, E.; Matsushima, T.; Okamoto, Y. *J. Am. Chem. Soc.* **1995**, *117*, 11596−11597. (b) Yashima, E.; Nimura, T.; Matsushima, T.; Okamoto, Y. *J. Am. Chem. Soc.* **1996**, *118*, 9800−9801. (c) Yashima, E.; Matsushima, T.; Okamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 6345−6359. (d) Yashima, E.; Maeda, Y.; Matsushima, T.; Okamoto, Y. *Chirality* **1997**, *9*, 593−600. (e) Yashima, E.; Goto, H.; Okamoto, Y. *Polym. J.* **1998**, *30*, 69−71. (f) Maeda, K.; Yamamoto, N.; Okamoto, Y. *Macromolecules* **1998**, *31*, 5924−5926. (g) Norris, I. D.; Kane-Maguire, L. A. P.; Wallace, G. G. *Macromolecules* **1998**, *31*, 6529−6533.

(15) The twisted *cis*−*trans* or helical *cis-gauche*−*gauche* conformation[4b] may be specific to the induced helical conformation of the poly-**1**−(*R*)-**2** complex.

(16) Preliminary viscosity measurements were conducted for the poly-**1**−(*R*)-**2** complex ([poly-**1**] = 0.5 g/dL, [(*R*)-**2**]/[carboxy residues of poly-**1**] = 5). The viscosity gradually increased with time. However, once the solution was annealed at 65 °C for 2 h, the viscosity significantly decreased accompanying an increase in the specific rotation, and the viscosity and rotation values did not change further with time. These results indicate that poly-**1** may intermolecularly interact to form a kind of aggregates before annealing. However, once it is annealed in the initial stage or later, the polymer may disaggregate to form an intramolecularly stable conformation, probably a helical conformation, thus showing a large negative optical rotation. Once it's happened, no aggregation may occur so that the viscosity and optical rotation remain unchanged. When the poly-**1**−(*R*)-**2** solution was further annealed at higher temperatures (>80 °C), the induced helical conformation of poly-**1** may partially collapse and the optical rotation decreases. However, after further annealing the sample at 65 °C for 2 h again, the polymer forms a helical conformation and the specific rotation recovers to the original value. For more detailed discussion, see the Supporting Information.

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