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Unusual Conformational Change of Optically Active Poly(3-((*S*)-*sec*-butoxycarbonyl)phenyl isocyanate)

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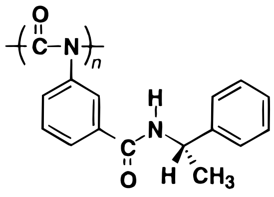
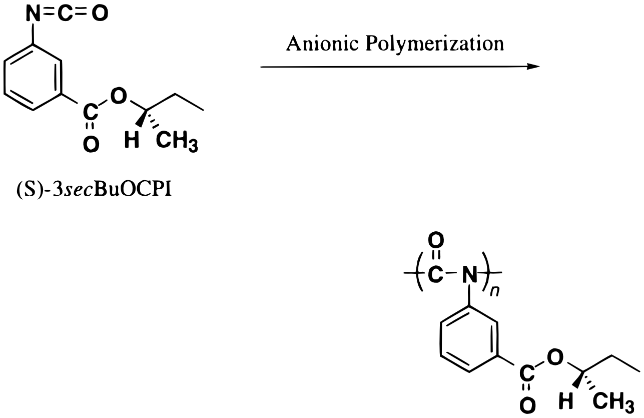
Introduction. Poly(alkyl isocyanate)s are known to exist as a dynamic helix with a long persistence length and helix reversal points due to rigid amide bonds.[1−3] On the other hand, poly(aryl isocyanate)s had been considered to be more flexible and not have a helical structure.[1] However, we recently demonstrated that poly(aryl isocyanate)s exhibit clear optical activity due to a prevailing one-handed helical structure when a chiral group is introduced at an initial polymer end.[4] We also reported that optically active poly(3-((*S*)-α-methylbenzylcarbamoyl)phenyl isocyanate) (poly((*S*)-3MBCPI)) with an amide group has an almost completely one-handed helical conformation and can discriminate enantiomers during NMR measurement.[5] This is the first example of chiral discrimination by polyisocyanates. In the present study, we synthesized a novel optically active poly(aryl isocyanate), poly(3-((*S*)-*sec*-butoxycarbonyl)phenyl isocyanate) (poly((*S*)-3*sec*BuOCPI)), with an ester group and found that this polymer undergoes an unusual conformational change accompanied by inversion of the helical structures with changing temperature.



Poly((S)-3MBCPI)



(S)-3*sec*BuOCPI

Poly((S)-3*sec*BuOCPI)

Experimental Section. Optical rotation was measured using a JASCO DIP-181 polarimeter. Circular dichroism (CD) spectra were taken with a JASCO J-720 spectrometer. ^{1}H NMR spectra were measured on a Varian VXR-500 (500 MHz) or Gemini-2000 (400 MHz) spectrometer using tetramethylsilane (TMS) as the internal standard in $CDCl_3$. IR spectra were recorded on a JASCO FT/IR-7000 spectrometer. The molecular weight of the polymer was determined by SEC (GPC) measurement on a Shodex System-21 SEC system equipped with a Shodex RI-71S detector and a Wyatt Technology DAWN DSP−F multiangle light scattering detector using THF as the eluent at 40 °C. Two SEC columns, Shodex KF-803 and KF-806L, were connected in series.

Tetrahydrofuran (THF) used for the polymerization was distilled from Na wire and then distilled again from $LiAlH_4$ under high vacuum just before use. The lithium amide of piperidine was prepared from piperidine in THF by adding an equimolar amount of *tert*-butyllithium in pentane at room temperature.

3-((*S*)-*sec*-Butoxycarbonyl)benzoic Acid ((*S*)-3*sec*BuOCBA). To a solution of isophthaloyl dichloride (30.2 g, 149 mmol) in THF (200 mL) was added dropwise a mixture of (*S*)-*sec*-butyl alcohol (11.0 g, 149 mmol) and pyridine (12.9 g, 164 mmol). The reaction mixture was stirred for 1 h at room temperature. Pyridine (12.9 g, 164 mmol) and H_2O (50 mL) were added to the reaction mixture, which was then stirred for 4 h at 90 °C. After the reaction was cooled to room temperature, 200 mL of 0.2 N HCl was added. The organic layer was separated, washed with 200 mL of water, and dried over magnesium sulfate. After filtering, the solvent was evaporated with a rotary evaporator, and the residual white solid was dissolved in 300 mL of chloroform. Insoluble isophthalic acid resulting from unreacted isophthaloyl dichloride was removed by filtration with a glass filter packed with Celite. After the solvent was evaporated, the residue was recrystallized twice from hexane to give pure (*S*)-3*sec*BuOCBA (13.8 g) in 39% yield: $[\alpha]_{365}^{25}$ +90°, $[\alpha]_D^{25}$ +29° (*c* 0.8, THF); IR (KBr, cm^{-1}) 1718 (C=O of ester), 1687 (C=O of carboxylic acid); ^{1}H NMR ($CDCl_3$) δ 1.00(t, 3H, CH_3), 1.36(d, 3H, CH_3), 1.67−1.83(m, 2H, CH_2), 5.13(m, 1H, CH), 7.6−8.7(m, 4H, aromatic).

3-((*S*)-*sec*-Butoxycarbonyl)phenyl Isocyanate ((*S*)-3*sec*BuOCPI). (*S*)-3*sec*BuOCBA (13.0 g, 58.5 mmol) was dissolved in acetone (200 mL), and the solution was cooled in an ice bath. To this solution were added Et_3N (7.1 g, 70.2 mmol) and then ethyl chloroformate (7.6 g, 70.2 mmol). After the reaction mixture was stirred for 1.5 h at 0 °C, sodium azide (6.7 g, 102.6 mmol) in H_2O (30 mL) was slowly added. The mixture was stirred for 1.5 h at 0 °C and poured into a mixture of ice water (300 mL) and toluene (200 mL). The organic layer was separated, washed with water, and dried over magnesium sulfate. After filtration, the toluene solution was refluxed for 3 h and then cooled to room temperature.[6] The solvent was evaporated in vacuo, and the residue was distilled under reduced pressure (90 °C/0.25 mmHg) to give (*S*)-3*sec*BuOCPI (8.6 g, 39.2 mmol) in 67% yield: $[\alpha]_{365}^{25}$ +87°, $[\alpha]_D^{25}$ +29° (*c* 0.7, THF); IR ($CHCl_3$ solution on NaCl plate, cm^{-1}) 2266 (N=C=O), 1721 (C=O of ester); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97(t, 3H, CH_3), 1.33(d, 3H, CH_3), 1.64−1.79(m, 2H, CH_2), 5.1(m, 1H, CH), 7.2−7.9(m, 4H, aromatic).

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Table 1. Polymerization of 3-((*S*)-*sec*-Butoxycarbonyl)phenyl Isocyanate ((*S*)-3*sec*BuOCPI) with Li−Piperidine in THF at −98 °C[a]

run	[M]/[I]	time (s)	yield (%)[b]	$[\alpha]_{365}^{25}$ [c] (deg)	M_n [d] ($\times 10^{-4}$)	M_w/M_n [d]
1	50	0.5	53	+1298	2.5	1.1
2	50	4	40	+1272[e]	2.6	1.1
3	500	0.5	58	+1474	22	1.3

[a] Conditions: monomer, 0.5 g; THF, 5 mL. [b] MeOH-insoluble part. [c] In THF. [d] Determined by GPC with LS. [e] $[\alpha]_D^{25}$ +286° (THF).

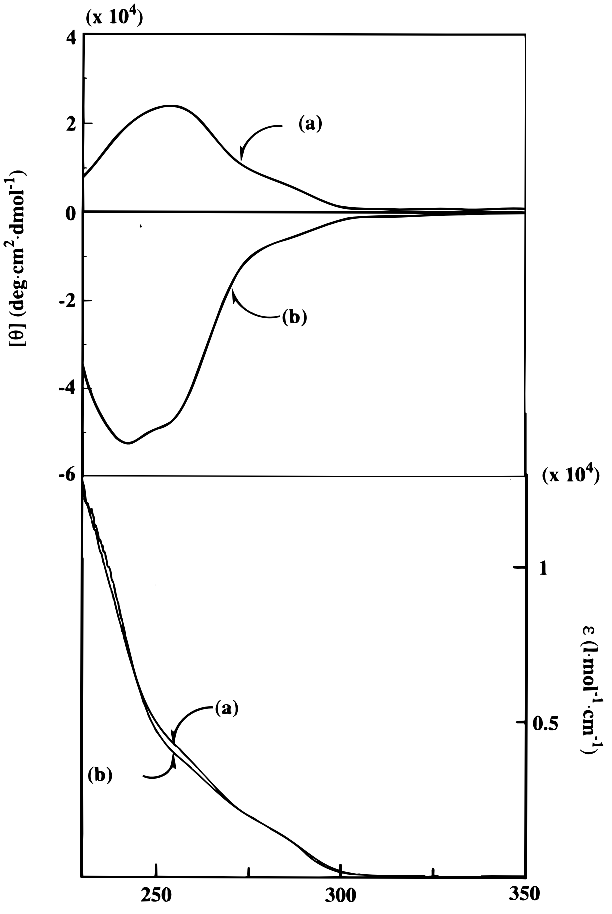


Figure 1. CD (top) and UV (bottom) spectra of poly((*S*)-3*sec*BuOCPI) (run 2 in Table 1) at +25 °C (a) and at −45 °C (b) in THF.

The polymerization of (*S*)-3*sec*BuOCPI was carried out with the lithium amide of piperidine in THF at −98 °C under a dry nitrogen atmosphere. The reaction was terminated by adding a 10-fold excess of HCl in methanol to the initiator. The polymer was precipitated in a large amount of methanol, collected by centrifugation, and dried in vacuo.

Results and Discussion. The results of the polymerization of (*S*)-3*sec*BuOCPI are summarized in Table 1. The obtained polymers showed very large positive specific rotations compared with that of the monomer ($[\alpha]_{365}^{25}$ +87°). The CD and UV spectra of poly((*S*)-3*sec*BuOCPI) (run 2 in Table 1) in THF at 25 °C are shown in Figure 1a. The polymer showed a very intense positive CD absorption around 255 nm, while the monomer (*S*)-3*sec*BuOCPI had almost no absorption in the range 220−350 nm. The spectral pattern of the polymer is similar to that of the predominantly one-handed helical, optically active poly(alkyl isocyanate)s,[7] indicating that the poly((*S*)-3*sec*BuOCPI) has a predominantly one-handed helical conformation in solution.

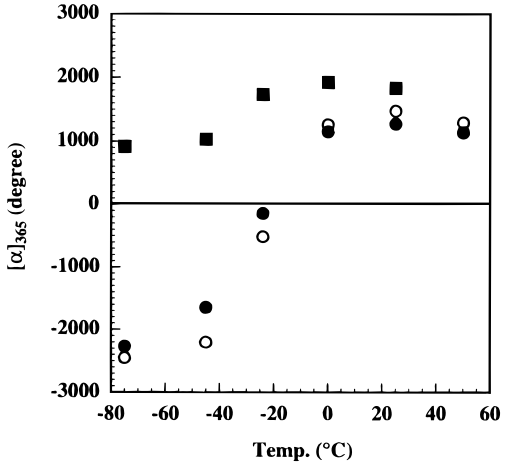
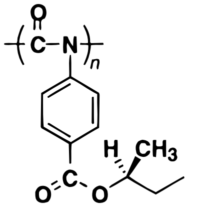


Figure 2. Temperature dependence of the specific rotation of poly((*S*)-3*sec*BuOCPI): run 2 in Table 1 in THF (●), run 3 in Table 1 in THF (○), and run 2 in Table 1 in toluene (■).

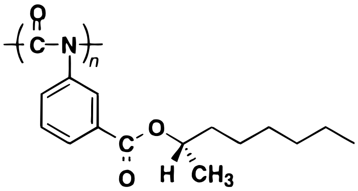
The poly((*S*)-3*sec*BuOCPI) showed a remarkable change in optical activity in THF with changing temperature. The specific rotation of the polymers (runs 2 and 3 in Table 1) varied from a large positive value to a large negative one by decreasing the temperature, and this change was reversible (Figure 2). The CD and UV spectra of the poly((*S*)-3*sec*BuOCPI) (run 2 in Table 1) in THF at −45 °C are shown in Figure 1b. At −45 °C, the polymer shows an intense negative peak with a spectral shape opposite to that at 25 °C in the absorption region due to the main chain. Green et al. reported that in a polypeptide an analogous change in optical activity is observed by changing temperature, and this change has been ascribed to an aggregation of the polymer chains.[8] Furthermore, it has been reported that poly(hexyl isocyanate) aggregates reversibly to form a gel with changing temperature. This also causes the reversible change in optical activity.[3c,9] Therefore, poly((*S*)-3*sec*BuOCPI) may also aggregate at low temperature. To confirm this, the optical activity was measured at a lower concentration (0.04%) in THF. However, the temperature effect was similar to that shown in Figure 2, suggesting the absence of the aggregation. Following results also supported this. ^{1}H NMR spectra became of course broader at lower temperatures, but they were still clearly observable even at −45 °C. The 10% polymer solution in THF was not viscous at all even at −45 °C, and the polymer did not seem to form gel. These results indicate that the aggregation of the polymer chains does not occur in THF. Therefore, it is highly likely that at −45 °C the poly((*S*)-3*sec*BuOCPI) possesses a predominantly one-handed helical conformation with a helical sense opposite to that at 25 °C and the polymer undergoes a reversible helix−helix transition with changing temperature. The polymer with a higher molecular weight showed a clearer change in specific rotation than that of the lower molecular weight one. This may be because the higher mobility of the chain ends reduces the optical activity of the polymer, and this influence is more pronounced in a lower molecular weight polymer.

The temperature effect on the optical activity of poly((*S*)-3*sec*BuOCPI) (run 2 in Table 1) was also examined in toluene (Figure 2). The specific rotation of the polymer decreased with a decrease in temperature, but did not cross 0°. Green et al. reported that the optical activity of the poly(alkyl isocyanate)s increases with a decrease in temperature because the number of helix reversals decreases at low temperature and more units can act in concert.[3,7,10] We also reported that the optical activity of poly(phenyl isocyanate)s with an optically active group at a chain end significantly increased with a decrease in temperature.[4a,b] Therefore, the change in toluene is also unusual.

In two other novel optically active poly(aryl isocyanate)s, poly((*S*)-4*sec*BuOCPI) ($[\alpha]_{365}^{25}$ −1684° (THF)) and poly((*S*)-3OcOCPI) ($[\alpha]_{365}^{25}$ −1510° (THF)),[11] such an inversion of optical activity by changing temperature was not observed, and the absolute value of the specific rotation of these two polymers increased with a decrease in temperature (poly((*S*)-4*sec*BuOCPI) $[\alpha]_{365}^{-45}$ −2490°, poly((*S*)-3OcOCPI) $[\alpha]_{365}^{-45}$ −1833°) as expected from previous reports.[3,4a,b,7,10] These results indicate that the helix−helix transition induced by changing temperature is specific for poly((*S*)-3*sec*BuOCPI). This is probably because the enthalpy of activation and the entropy of activation between the diastereomeric helical senses have the same sign so that the free energy difference will change sign as a function of temperature. The temperature effect on the solvation for the two diastereomer's structure is probably different, and this may be a main factor to induce the unique change of conformation. Green et al. reported an analogous change could occur for poly(deuterio-*n*-hexyl isocyanate) although such a change cannot be actually observed because the temperature predicted for the change is so high that the polymer would decompose.[12]



Poly((S)-4*sec*BuOCPI)



Poly((S)-3OcOCPI)

In conclusion, the polymerization of (*S*)-3*sec*BuOCPI afforded an optically active polymer with a predominantly one-handed helical conformation. As the temperature was decreased, the optical rotation of the polymer in THF was changed from dextrorotatory to levorotatory. This change is attributable to the helicity change (helix−helix transition) of the main chain. Except for poly(α-amino acid)s,[13] this may be the first example of the reversible helix−helix transition induced by temperature change. Further work is now in progress.

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