Optically Active Oligo- and Polyamides from Optically Active Spiro[3.3]heptane-2,6-dicarboxylic Acid

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ABSTRACT: Optically active (*R*)-spiro[3.3]heptane-2,6-dicarboxylic acid was obtained by optical resolution with brucine. Its optical purity was confirmed by HPLC analysis on optically active stationary phase. The specific optical rotations of model compounds having one and two spiran units increased with increasing the number of spiran unit in sulfuric acid solution. On the contrary, the specific optical rotations showed opposite sign in organic solvents, such as *N,N*-dimethylformamide and *N,N*-dimethylacetamide, and the absolute values decreased with increasing the number of spiran unit. Polycondensation of (*R*)-spiro[3.3]heptane-2,6-dicarboxylic acid chloride and 3,3'-dimethoxybenzidine gave a polymer soluble in common organic polar solvents. This polymer showed a large positive Cotton effect.

KEY WORDS Spiroheptane Dicarboxylic Acid / Optical Resolution / Polycondensation / Polyamide / Optical Rotation / Circular Dichroism / Conformation

It is of interest to control the stereoregularity of polymer backbone from the viewpoint of controlling polymer properties by their structures. We have been studying the properties of stereoregular polymers obtained by polyaddition and ring-opening polymerization of optically active monomers.¹⁻⁴ These polymers were found highly isotactic reflecting the optical purity of the starting monomers.

Some stereoregular polymers produced by addition polymerization were reported to take helical conformation. The helical conformations can be stabilized by the bulky substituents, such as triphenylmethyl⁵ and trichloromethyl⁶ groups, and also by the rigid main chain structure.^{7,8}

Polycondensation of optically active monomers is another effective method to synthesize the polymers with helical structure. Overberger reported that optically active polyamides derived from *trans*-cyclopropanedicarboxylic acid showed some ordered conformations even in solution.⁹ Shulz reported the synthesis of optically active polyamide derived from optically active 2,2'-diamino-1,1'-binaphthyl.¹⁰ Optically active polyamides derived from (*R*)- or (*S*)-6,6'-dimethylbiphenyl-2,2'-dicarboxylic acid chloride or optically active 6,6'-dibromo-2,2'-dimethoxy-1,1'-binaphthyl, CO and azodianiline were reported by Kondo.¹¹ Pu synthesized optically active polymers containing binaphthyl units for catalyst applications.¹² However, since the optical activities of the polymers depend on steric hindrance of the constitutional monomer unit, the twisted angle of helix is not fixed.

It may be possible to control the helix sense by choosing the combination of monomers of rigid structure. Optically active spiro[3.3]heptane-2,6-dicarboxylic acid has two cyclobutane rings twisting 90° each other,¹³ which can be a useful component for a new type of optically active polyamides. Since the polyamides derived from this carboxylic acid inevitably contain rigid cyclobutane rings twisting 90° each other, it is expected that these polyamide chains would twist 90° unit by unit to one direction (Scheme 1), and form some ordered conformation

excess in one helix sense even in solution depending on the structure of the diamine component. As a preliminary result, we reported the synthesis of optically active polyamides derived from optically active spiro[3.3]heptane-2,6-dicarboxylic acid.¹⁴ It was found that the polymer derived from optically active spiran derivative and 1,4-phenylenediamine (**P1**) showed a large optical rotation and a positive Cotton effect in the circular dichroism (CD) spectrum in sulfuric acid. But it was difficult to obtain other molecular characteristics of the polymer because of the low solubility in common organic solvents. We also synthesized a polymer from *trans*-2,5-diamino-4'-dimethylamino-4-nitrostilbene (DDANS) (**P2**) and found that **P2** was soluble in the common organic polar solvents, such as 1-methyl-2-pyrrolidinone (NMP), *N,N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and *N,N*-dimethylacetamide (DMAc). It was

Scheme 1. Molecular structure of **M1** calculated by MM2.

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Scheme 2. Synthesis of **E1**, **M1**, **M2**, and **P3** from (*R*)-SHDAC.

considered that each dye chromophore, DDANS, of side chain is twisted by the existence of spiran unit, and that **P2** showed a larger optical rotation than **P1**.

It is interesting to investigate the effects of the molecular asymmetry of these compounds on the polymer properties. The oligoamides, **M1** and **M2**, containing one and two spiran units, respectively, were synthesized as model compounds to investigate the relationship between the optical properties of these compounds and the number of spiran unit.

It is also interesting to compare the effect of structure of the diamine component in the side chain and in the main chain on the rigidity of the polymer chain and its conformation, especially helical structure.

EXPERIMENTAL

Materials

Optically active spiran derivatives. Spiro[3.3]heptane-2,6-dicarboxylic acid (SHDA) was prepared according to the literature.⁹ Optically active (*R*)-spiro[3.3]heptane-2,6-dicarboxylic acid (*R*)-SHDA was obtained by optical resolution of its complex with brucine. (*R*)-spiro[3.3]heptane-2,6-dicarboxylic acid chloride ((*R*)-SHDAC) was prepared by the reaction of (*R*)-SHDA with excess thionyl chloride.

Diphenyl (*R*)-spiro[3.3]heptane-2,6-dicarboxylate (E1**).** Phenol (239 mg, 2.6 mmol) was added dropwise to the solution of (*R*)-SHDAC (265 mg, 1.2 mmol) in NMP (3 ml) at 0 °C under nitrogen atmosphere. After the reaction mixture was stirred at 0 °C for 1 h and at 100 °C for 2 h, the reaction mixture was poured into 200 ml water. The precipitated white solid was isolated by filtration, and washed with water (200 ml). The crude product was purified by recrystallization from methanol to give a white solid (360 mg, 1.1 mmol, 89 %). ¹H NMR spectrum (500 MHz, δ ppm, DMSO-*d*₆): 2.38 – 2.58 (broad, methylene, 8H), 3.28 (m, methine, 2H), 7.07 (d, phenyl, *o*-H, 4H, *J* = 7.5 Hz), 7.22 (t, phenyl, *p*-H, 2H, *J* = 7.5 Hz), 7.38 (t, phenyl, *m*-H, 4H, *J* = 7.5 Hz). MS (*m/z*): 336 (*M*⁺).

(*R*)-Spiro[3.3]heptane-2,6-dicarboxanilide (M1**).** **M1** was synthesized similarly to **E1** and purified by recrystallization from acetone to give a white solid (170 mg, 0.51 mmol, 71 %, mp 234 °C). ¹H NMR spectrum (500 MHz, δ ppm, DMSO-*d*₆): 2.05 – 2.30 (broad, methylene, 8H), 3.08 (m, methine, 2H), 6.99 (t, phenyl, *p*-H, 2H, *J* = 7.5 Hz), 7.26 (t, phenyl, *m*-H, 4H, *J* = 7.5 Hz), 7.57 (d, phenyl, *o*-H, 4H, *J* = 7.5 Hz), 9.73 (s, amide, 2H). MS (*m/z*): 334 (*M*⁺).

***N,N'*-Bis[(*R*)-6-anilino]carbonylspiro[3.3]heptane-2-carboxylate-1,4-phenylenediamine (**M2**).** To the solution of (*R*)-SHDAC (153 mg, 0.69 mmol) in NMP (2 ml) at 0 °C under nitrogen atmosphere was added dropwise 1,4-phenylenediamine (38 mg, 0.35 mmol). After the reaction mixture was stirred at 0 °C for 1 h and at room temperature for 15 h, aniline (66 mg, 0.70 mmol) was added into the mixture and stirred for further 15 hr. The reaction product was treated similarly to **M1**, and the crude product was dissolved in NMP and recovered by reprecipitation in water (180 mg, 0.31 mmol, 88 %). ¹H NMR spectrum (500 MHz, δ ppm, DMSO-*d*₆): 2.06 – 2.27 (broad, methylene, 16H), 2.90 (m, methine, 4H), 7.00 (t, phenyl, *p*-H, 2H, *J* = 7.3 Hz), 7.26 (dt, phenyl, *m*-H, 4H, *J* = 7.3, 7.8 Hz), 7.46, 7.47 (s, phenylene-H, 4H), 7.57 (d, phenyl, *o*-H, 4H, *J* = 7.8 Hz), 9.68 (s, amide, 2H), 9.74 (s, amide, 2H).

Poly[imino(oxomethylene)]{(*R*)-spiro[3.3]heptane-2,6-diyl}(oxomethylene)imino (3,3'-dimethoxybiphenyl-4,4'-diyl)} (P3**).** To the solution of (*R*)-SHDAC (180 mg, 0.82 mmol) in NMP (3 ml) at 0 °C under nitrogen atmosphere was added dropwise 3,3'-dimethoxybenzidine (38 mg, 0.35 mmol). After the reaction mixture was stirred at 0 °C for 1 h and at room temperature for 20 h, the reaction mixture was poured into 200 ml methanol. The precipitated white solid was separated by filtration, and washed with water (200 ml). Then it was dissolved in NMP and reprecipitated in methanol (three times) (282 mg). ¹H NMR spectrum (500 MHz, δ ppm, DMF-*d*₇): 2.18 – 2.34 (broad, methylene, 8H), 3.97 (s, OCH₃, 6H), 7.29 (d,

phenylene, 5,5'-*H*, 2H, $J = 8.5$ Hz), 7.37 (s, phenylene, 2,2'-*H*, 2H), 8.33 (d, phenylene, 6,6'-*H*, 2H, $J = 8.5$ Hz), 8.99 (s, amide, 2H).

Methods

Size exclusion chromatography (SEC) and HPLC analyses on an optically active stationary phase were performed on a JASCO HPLC on the combination of Shodex KD-802.5 (exclusion limit: $M_n = 2 \times 10^4$, poly(styrene)) and KD-804 (exclusion limit: $M_n = 4 \times 10^5$, poly(styrene)) columns (linear calibration down to $M_n = 100$, poly(styrene)) using DMF as an eluent and on a Daicel CHIRALCELL OD[®] column (cellulose carbamate derivative) with hexane/2-propanol (v/v 10/1) as an eluent, respectively. Mass spectra (MS) were taken on a Shimadzu QP-5000 mass spectrometer. Specific optical rotations were measured with a JASCO DIP-370S digital polarimeter. Electronic absorption and CD spectra were measured in a 0.2 cm quartz cell with a JASCO Ubest-50 UV/vis spectrophotometer and a JASCO J-720W spectropolarimeter. Molar ellipticity, $[\theta]$, was calculated based on spiran unit.

RESULTS AND DISCUSSION

Optical Purity of Spiran

It has been believed that optically active spiro[3.3]heptane-2,6-dicarboxylic acid obtained by the optical resolution with brucine is optically pure ($[\phi]_{405}^{26} = 18.2$ (c 5.3, acetone)).¹³ We also used this method to obtain the optically active acid with $[\phi]_{405}^{26} = 18.8$ (c 5.3, acetone). Although it was difficult to determine the optical purity of the spiran dicarboxylic acid itself, the optical purity of **E1** was successfully determined by HPLC analysis on an optically active stationary phase (Figure 1). It was found that enantiomer excess of **E1**, obtained from SHDA with $[\phi]_{405}^{26} = 18.8$, was approximately 70 %. In this report, SHDA with $[\phi]_{405}^{26} = 18.8$ was used. Caution

Figure 1. HPLC on an optically active stationary phase. a) optically active **E1** synthesized from spiran obtained by optical resolution with brucine. b) racemic **E1** (detected by UV). c) racemic **E1** (detected by ORD).

Table I. Characteristics of optically active polyamides and model compounds

Polymer or Oligomer	Molecular Weight	$[\alpha]_D^{26}$ [degree]		
		conc. H ₂ SO ₄	DMF	DMAc
M1	334 (M ⁺) ^a	+17.0 (c 0.57)	-8.5 (c 0.54)	-15.6 (c 0.55)
M2	-- ^b	+31.1 (c 0.52)	-4.8 (c 0.21)	-7.5 (c 0.54)
P1 ^c	-- ^d	+47.0 (c 0.17)	--- ^d	--- ^d
P2 ^c	2.43×10^4 ^e	--- ^f	---	+278.5 (c 0.0079)
P3	1.14×10^5 ^e	--- ^f	+32.6 (c 0.57)	+29.1 (c 0.40)

^a measured by MS. ^b no signal in MS. ^c reference 14. ^d insoluble in organic solvent. ^e determined by SEC (eluent: DMF containing 0.01 mol dm⁻³ of LiCl, poly(styrene) standard). ^f decomposed.

should be paid to the optical purity of SHDA in the future research.

Optical Properties of Model Compounds

The model compounds, **M1** and **M2**, were soluble in the common organic polar solvents. The specific optical rotations of **M1** and **M2** are listed in Table I. In sulfuric acid, their specific optical rotations tend to increase with increasing the number of spiran unit in the compound. In CD spectra, their molar ellipticities also increased with increasing the number of spiran unit (Figure 2). Since sulfuric acid will protonate the amide groups and makes these compounds take expanded conformation, the number of spiran unit seems to be directly reflected in their optical rotation.

On the other hand, the specific optical rotations of **M1** and **M2** in DMF and DMAc showed negative value, and their absolute values decreased with increasing the number

Figure 2. CD spectra of **M1**, **M2**, and **P1** in sulfuric acid.

CONCLUDING REMARKS

Optical purity of SHDA was determined by HPLC analysis on an optically active stationary phase. The specific optical rotations of model compounds, **M1** and **M2**, in DMF and DMAc showed negative value and their absolute values decreased with increasing the number of spiran unit. On the other hand, their specific optical rotations in sulfuric acid tend to increase with increasing the number of spiran unit. The CD spectrum of **P3** showed a large positive Cotton effect, suggesting that **P3** can take some ordered structure even in organic polar solvents. It is interesting to investigate the relationship between polymer structure and their properties, such as thermal stability and liquid crystallinity. These investigations are under consideration.

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Figure 3. Electronic absorption and CD spectra of **P3** in DMF.

of spiran unit. Since amide groups will be just solvated by these solvents, these compounds are considered not to be able to take any expanded structure.

Characterization of **P3**

Since **P1** was only soluble in sulfuric acid, optical data were taken in sulfuric acid. **P3** was soluble in common organic polar solvents, such as NMP, DMF, DMSO, and DMAc. SEC showed that the molecular weight of **P3** was very high, $M_n = 1.1 \times 10^5$. The characteristics of **P3** are also summarized in Table I. Since **P3** was unfortunately decomposed in sulfuric acid, its optical rotations were measured in DMF (+32.6) and DMAc (+29.1). The CD spectrum of **P3** showed a large positive Cotton effect in the region of the wavelength corresponding to the absorption band of π - π^* transition of biphenylene unit (Figure 3). These results suggest that **P3** has some ordered structure even in these polar solvents.

The optical rotations of **P2** and **P3** in organic solvents were large. The motion of the amide groups might be restricted by their long polymer chain itself.

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