Poly((4-carboxyphenyl)acetylene) as a Probe for Chirality Assignment of Amines by Circular Dichroism

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Chiral recognition is of particular importance in living systems which often show different pharmacokinetics and pharmacodynamics activities toward a pair of enantiomeric drugs. Therefore, detection and assignment of the chirality of molecules has been studied extensively by using chiral[1] and achiral[2] receptors (hosts) capable of discriminating chiral guests. Here, we report the induced circular dichroism (ICD) based on the helical structure of poly((4-carboxyphenyl)acetylene) (poly-**1**)[3] by complexation with chiral amines. This may be the first example of the prevailing helix formation of an achiral polymer ascribed to an acid−base interaction. The helix exhibited a characteristic ICD in both solution and a solid film, the sign of which reflects the stereochemistry (shape and configuration) of the amines. Therefore, the polyacetylene can be used as a novel probe for determining the chirality of amines. The polyacetylene is an optically inactive polymer. However, it can show an ICD if the twist of the adjacent double bonds around a single bond occurs preferentially in one direction.

Figure 1 shows typical CD and absorption spectra of poly-**1** in the presence of (*R*)-1-(1-naphthyl)ethylamine ((*R*)-**2**) or (*S*)-**2** (Chart 1) in DMSO. The poly-**1**−**2** complexes showed intense split-type ICDs which are mirror images. The intensity of the ICD increased with an increase in the concentration of the chiral amine and reached a constant value ([θ] = *ca.* 23 000 deg cm^2 dmol^{-1} at 375.5 nm) at [**2**]/[poly-**1**] = 20. The results clearly indicate that the complexation involves an acid−base equilibrium, and the poly-**1** having a random twist of the adjacent double bonds around a single bond may be transformed into the helical conformation with a predominant screw sense by interacting with the chiral amine.[6] No ICD signals were observed when the methyl ester of poly-**1** was used with excess (50-fold) (*R*)-**2** in DMSO.

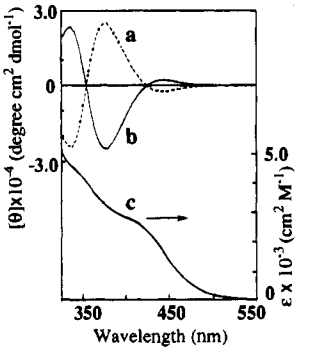
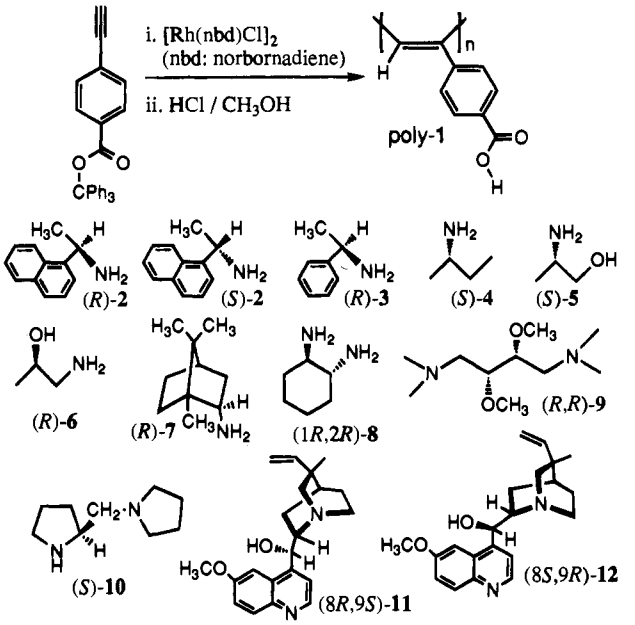


Figure 1. CD spectra of poly-**1** with (*S*)-**2** (a) and (*R*)-**2** (b) and absorption spectrum (c) with (*R*)-**2** in DMSO; molar ratio of **2** to poly-**1** is 50. The CD spectra were measured in DMSO solutions in a 0.05 cm quartz cell at ambient temperature (*ca.* 20−22 °C) with a poly-**1** concentration of 1.0 mg (6.8 mmol of monomer units)/mL. A solution of poly-**1** with (*R*)-**2** (50-fold) gave the same CD spectrum after the sample had been allowed to stand for 8 days at room temperature.

Chart 1. Structures of Poly-**1** and Chiral Amines (**2**−**12**)



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(2) For examples of chirality recognition of sugars and alcohols with achiral hosts, see: (a) Kikuchi, Y.; Kobayashi, K.; Aoyama, Y. *J. Am. Chem. Soc.* **1992**, *114*, 1351−1358. (b) Deng, G.; James, T. D.; Shinkai, S. *J. Am. Chem. Soc.* **1994**, *116*, 4567−4572. (c) Mikami, M.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1995**, 153−154. For examples of chirality recognition of amines and ammonium salts with achiral hosts, see: (d) Morozumi, T.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1994**, 1219−1220. (e) Morozumi, T.; Shinkai, S. *Chem. Lett.* **1994**, 1515−1518.

(3) Poly-**1** was obtained by polymerization of (4-((triphenylmethoxy)-carbonyl)phenyl)acetylene with [Rh(nbd)Cl]$_2$ (nbd: norbornadiene),[4] followed by hydrolysis of the ester group. The resulting orange polymer was soluble in dimethyl sulfoxide (DMSO) and insoluble in chloroform and tetrahydrofuran. The molecular weight (M_n) of poly-**1** was estimated to be more than 1 × 10^6 as determined by gel permeation chromatography (GPC) (polystyrene standards using tetrahydrofuran as the eluent) as its triphenylmethyl or methyl esters. The higher molecular weight region exceeded the exclusion limit of GPC columns used (exclusion limit *ca.* 1 × 10^7), and therefore, the exact M_n of poly-**1** could not be determined. The extraordinarily high molecular weight may be due to aggregations of the polymer. The ^{1}H NMR spectra of poly-**1** in DMSO-d_6 and its methyl ester in CDCl$_3$ showed a sharp singlet centered at 5.83 and 5.77 ppm, respectively, due to the main chain protons, indicating that these polymers possess a highly cis−transoidal, stereoregular structure.[5]

(4) (a) Furlani, A.; Napoletano, C.; Russo, M.; Camus, A.; Marsich, N. *J. Polym. Sci., Polym. Chem. Ed.* **1989**, *27*, 75−86. (b) Tabata, M.; Yang, W.; Yokota, K. *Polym. J.* **1990**, *12*, 1105−1107. Very recently, a living, stereospecific polymerization of phenylacetylenes using a well-defined rhodium catalyst has been reported: Kishimoto, Y.; Eckerle, P.; Miyake, T.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1994**, *116*, 12131−12132.

(5) (a) Furlani, A.; Napoletano, C.; V. Russo, M. V.; Feast, W. J. *Polym. Bull.* **1986**, *16*, 311−317. (b) Furlani, A.; Licoccia, S.; Russo, M. V. *J. Polym. Sci., Part A, Polym. Chem.* **1986**, *24*, 991−1005.

(6) These ICDs were similar in pattern and magnitude to those of optically active, cis−transoidal poly(phenylacetylenes) bearing a chiral substituent, for instance the (*R*)-((1-phenylethyl)carbamoyl)oxy group, at the para position. Moreover, the same poly(phenylacetylene) derivative with stereoirregular structure prepared by a different synthetic route did not show any significant CD bands in the 300−500 nm range; see: Yashima, E.; Huang, S.; Matsushima, T.; Okamoto, Y. *Macromolecules* **1995**, *28*, 4184−4193. These results suggest that a regular main chain structure may be essential for the observation of the ICD due to a helical conformation. For references of CD studies on other optically active polyacetylenes, see: (a) Ciardelli, F.; Lanzillo, S.; Pieroni, O. *Macromolecules* **1974**, *7*, 174−179. (b) Moore, J. S.; Gorman, C. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1991**, *113*, 1704−1712. (c) Yamaguchi, M.; Omata, K.; Hirama, M. *Chem. Lett.* **1992**, 2261−2262. (d) Aoki, T.; Kokai, M.; Shinohara, K.; Oikawa, E. *Chem. Lett.* **1993**, 2009−2012.

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Table 1. Signs of Split Cotton Effects and Molar Ellipticities ([θ]) for Poly-**1**−Amine Complexes[a]

	first Cotton		second Cotton		third Cotton	
amine	sign	$[\theta] \times 10^{-3}$ (λ)	sign	$[\theta] \times 10^{-4}$ (λ)	sign	$[\theta] \times 10^{-4}$ (λ)
(*R*)-(+)-**2**	+	1.93 (447.0)	−	2.52 (375.5)	+	2.35 (334.0)
(*S*)-(−)-**2**	−	2.60 (447.0)	+	2.49 (375.5)	−	2.44 (334.0)
(*R*)-(+)-**2**[b]	+	0.36 (447.0)	−	0.44 (375.5)	+	0.40 (334.0)
(*R*)-(+)-**2**[b,c]	+	1.40 (447.0)	−	1.33 (375.0)	+	0.88 (316.0)
(*R*)-(+)-**3**	+	0.84 (440.5)	−	1.03 (376.5)	+	0.95 (334.0)
(*S*)-(+)-**4**			+	0.14 (377.5)	−	0.14 (330.0)
(*S*)-(+)-**5**	−	2.00 (438.5)	+	2.47 (373.0)	−	2.81 (330.0)
(*R*)-(−)-**6**	−	1.28 (447.0)	+	1.63 (373.0)	−	2.00 (334.0)
(*R*)-(+)-**7**	+	3.48 (441.0)	−	2.36 (372.0)	+	2.38 (334.0)
(*R,R*)-(−)-**8**			−	0.30 (378.0)	+	0.28 (330.0)
(*R,R*)-(−)-**9**			+	0.06 (386.0)	−	0.12 (334.0)
(*S*)-(+)-**10**	+	0.83 (435.0)	−	1.20 (374.0)	+	1.21 (341.0)
(8*R*,9*S*)-(+)-**11**	−	4.53 (442.0)	+	2.45 (376.0)		*d*
(8*S*,9*R*)-(−)-**12**	+	4.57 (447.0)	−	2.12 (385.0)		*d*

[a] All spectra were measured on a Jasco J-720 L spectropolarimeter in DMSO with a poly-**1** concentration of 1.0 mg/mL; molar ratio of chiral amine to poly-**1** is 50; [θ] (degree cm^2 dmol^{-1}) and λ (nm). [b] Molar ratio of chiral amine to poly-**1** is 1. [c] In the film. The film was prepared by coating a DMSO solution of poly-**1** (1.0 mg) and (*R*)-**2** (6.8 mmol) on a cylindrical quartz cell (0.5 cm thick) followed by evaporation of the solvent under reduced pressure. The ellipticity was estimated by calculation to the same molar concentration on the basis of the absorption measurements. [d] It could not be measured because of overlap with the guests.

Poly-**1** responds to the shape and configuration of chiral amines including simple primary amines such as (*R*)- and (*S*)-**2**, (*R*)-**3**, and (*S*)-**4**, aminoethanols ((*S*)-**5** and (*R*)-**6**), a tricyclic primary amine ((*R*)-**7**), a cyclic diaminohexane ((*R,R*)-**8**), and secondary and tertiary amines ((*R,R*)-**9**, (*S*)-**10**, quinidine (**11**), and quinine (**12**)) (Chart 1). The results of the ICD studies for chiral amines (**2**−**12**) are summarized in Table 1. The split type and magnitude of the Cotton effects appear to reflect the configuration, bulkiness, and type (primary, secondary, or tertiary) of chiral amine. Primary amines **2**−**5**, **7**, and **8** but not **6**, which bears an amino group on the carbon adjacent to the asymmetric center, gave the same Cotton effect signs depending on the configuration. However, secondary and/or tertiary amines **9**−**12** showed the opposite signs if the configuration of the asymmetric center bearing an amino group was the same.[7] The magnitude of the ICD likely increased with an increase in the bulkiness of the chiral amines; *i.e.*, the observed ICD increased in the order **9** ≪ **4** < **8** ≪ **3** < **10** < **7**, **12**, **11**, **2**. The bulky groups introduced at the *para* position of poly-**1** appear to contribute more efficiently for the polymer to take a predominant screw sense. However, two less bulky ethanolamines **5** and **6** also exhibited a significantly intense ICD. The chelation effect of the hydroxy group may play a role in the ICD, since (*S*)-**4** and (*S*)-2-butanol gave very weak and no ICD, respectively. An amino group far from the chiral center (**9**) may not work well for inducing a helical conformation. Other chiral amines with a weaker basicity such as the (−)-cotinine and L-tryptophan methyl ester showed no ICD.

In the film state, the poly-**1**−(*R*)-**2** complex (1:1 mol/mol) exhibited an ICD (Table 1) identical in pattern and sign to that shown in Figure 1b, and the intensity was greater than that observed in DMSO solution for the same molar ratio (Table 1).

Interestingly, the complex formation of poly-**1** with **2** exhibits a nonlinear relationship (positive nonlinear effect or asymmetric amplification)[8] between the enantiomeric excess (ee) of the chiral amine and the observed ellipticity of the Cotton effects (see supporting information). The excess enantiomer bound to poly-**1** may induce an excess of a single-handed helix (right- or left-handed helix), which will result in a more intense ICD than that expected from the ee of the amine. Green et al. recently reported a parallel effect in a polyisocyanate with the chiral pendants covalently bound. This was termed "majority rule" by the excess enantiomers.[8a]

We, therefore, conclude that an achiral polyacetylene, poly-**1**, with its random twist around a single bond transforms into a prevailing one-handed helical conformation upon complexation with chiral amines and its helical sense is sensitive to the stereochemistry of the chiral amines. The advantages of the present polyacetylene are its long-wavelength absorption, high sensitivity and response to chiral amines, and easy preparation into a film. We expect that related stereoregular poly(phenylacetylene)s bearing other functional groups such as amino groups will also respond, for example, to chiral acids showing a characteristic ICD depending on the stereochemistry of the acids. This work is in progress.

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Supporting Information Available: Figure exhibiting the nonlinear effect between the absolute values of ICD at 375.5 nm and the % ee of **2** (*R* rich) in the complexation with poly-**1** in DMSO (1 page). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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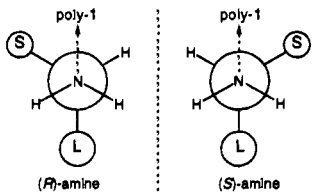
(7) Primary amines may be favorably complexed with poly-**1** as described below, where the bulkiest substituent (L) is placed remote from the poly-**1**, and therefore, the complexes may show an ICD with mirror images depending on the configuration. The relationship between the configuration of secondary and/or tertiary amines and the sign of ICD has not been generalized.



(8) For recent references of the nonlinear effect on helix-sense selective copolymerization, see: (a) Green, M. M.; Peterson, N. C.; Sato, T.; Teramoto, A.; Cook, R.; Lifson, S. *Science* **1995**, *268*, 1860−1866 and references cited therein. (b) Okamoto, Y.; Nishikawa, M.; Nakano, T.; Yashima, E.; Hatada, K. *Macromolecules* **1995**, *28*, 5135−5138. For a review of synthetic helical polymers, see: Okamoto, Y.; Nakano, T. *Chem. Rev.* **1994**, *94*, 349−372.