

Photochemical Properties of Phenylalanine-based Helical Conjugated Poly(isocyanide) bearing Azobenzene moiety.

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ABSTRACT: Co-poly(isocyanide) of *rac*-carbazophenoxy-2-phenylethylisocyanide (Az) and (*S*)-1-ethoxycarbonyl-2-phenylethylisocyanide (Et) derived from L-phenylalanine showed large specific rotation based on the one-handed helical conformation. *E*→*Z* photoisomerization of azobenzene moiety upon UV irradiation caused not only enhanced ϵ value at the long wavelength region on the UV spectra, indicating the extended effective conjugation length, but simultaneously reduced value of specific rotation. These spectroscopic changes were reversibly recovered by *Z*→*E* isomerization upon visible light irradiation. This observation indicates that the helical conformation of the main-chain of the copolymers is reversibly controlled by the geometrical change in the photo-isomerization of azobenzene moiety.

Keyword: helical conjugated polymer, poly(isocyanide), amino acid, azobenzene.

1. INTRODUCTION.

Recently, photoresponsive helical polymers have been active in a research line focused on the helical conformational control¹ and the photo-switchable functionalization directed toward ability of chiral recognition,² liquid crystal phases,³ and transcriptional regulator complexes of genes.⁴ On the other hand, conformational control of a conjugated helical polymer has been attracted increasing interest, which has a strong correlation between the conformation and the electronic interactive pathways along the main chain. Exploitation of conformational controllable conjugated polymer can be expected consisting of the tilted p_z orbitals of the sp^2 carbons, unlike natural helical polymers such as DNA, RNA, and α -helices of oligopeptides, and other non-conjugated helical synthetic polymers.⁵

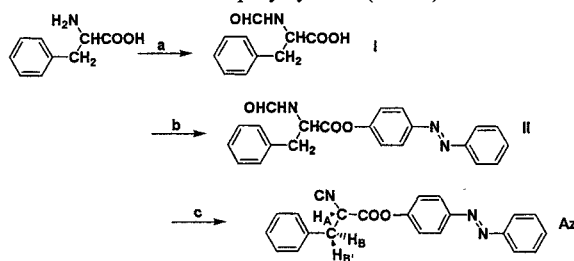
Much interest has been focused on poly(isocyanide) derived from amino acid because of its helical conjugated backbone since Millich and co-workers' first preparation⁶ and the nickel-catalyzed polymerization by Drenth and Nolte.⁷ In our work⁸, helical conjugated poly(isocyanide) derived from phenylalanine-based chiral isocyanides have been elucidated to take various types of helical conformation by tuning the size of the side chain, of which bulkiness can be finely tuned by the size of amino acid residue and ester unit introduced. Especially, in the case of poly(isocyanide) consisting of phenylalanine ethyl ester unit, the helical conformation of the main chain has also been thermodynamically controlled.

Azobenzene is a well-known photoresponsive chromophore, and versatile tool for the creation of light controllable function. The aim of the present work is the reversible control of the helical conformation of poly(isocyanide) by utilizing *E-Z* isomerization of azobenzene. We therefore prepared an isocyanide monomer derived from phenylalanine bearing azobenzene in the ester moiety, as shown in Scheme 1. Here we hope to report about the synthesis and its chiroptical properties of the novel phenylalanine-based poly(isocyanide) bearing azobenzene units, and the

results of reversible controlling the helical conformation under isothermal condition by using photochemical stimuli.

2. EXPERIMENTAL.

Measurement. Optical rotation was measured on a Union PM-101 polarimeter. Elemental Analyses were performed on a Perkin-Elmer 2400 CHN Elemental Analyzer. CD spectra were measured with a JASCO J-720 spectrometer. UV-vis spectra were taken on a Shimadzu UV-3100S. Chloroform for spectrometry (Wako) was used as solvent for CD and UV spectral measurements. ¹H NMR spectra were taken on a JEOL JNM-EX270 spectrometer with tetramethylsilane (TMS) as the internal standard in CDCl₃ at room temperature. IR spectra were recorded on a BIO-RAD FTS-3000MX spectrometer. The molecular weight of the polymer was determined by GPC measurement on a JASCO equipped with an ELMER UV detector and GPC columns serially connecting a Shodex KF-802 and a JAIGEL 3H-AF, using THF as the eluent at 30 °C. The molecular weight of the polymer was determined using a calibration curve obtained with standard polystyrenes (Tosoh).



Scheme 1. Synthetic route of isocyanide monomer bearing azobenzene chromophore derived from L-phenylalanine. (a) acetic formic anhydride in formic acid, r.t. (b) 4-phenylazo-phenol, DCC in ethyl acetate containing pyridine, -20 °C; r.t., overnight. (c) bis(trichloromethyl)carbonate, triethylamine in CH₂Cl₂, 0°C.

Chemicals. Isocyanide monomer was derived from L-phenylalanine in the synthetic route, as Scheme 1 shows. Phenylalanine was obtained from Wako. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ as the polymerization catalyst was purchased from Kojundo Chemical laboratory. Unless otherwise indicated, other chemicals were commercially available and used without further purification.

Acetic formic anhydride.⁹ Into a solution of acetyl chloride (45 ml) in dry ether (25 ml), sodium formate (50 g) was added in several portions in such a way that the temperature did not exceed 27 °C. The mixture was kept from moisture and vigorously shaken. After the shaking had been continued for 5.5 h at 25–27 °C, the salt was filtered off. The filtrate was then evaporated under vacuum below 20 °C in order to remove the ether and the remaining reagent. The residual liquid weighed 46.9 g. Yield 93 %.

***N*-Formyl-L-phenylalanine.**⁹(I) To a solution of L-phenylalanine (5.0 g, 30 mmol) in 8 ml of formic acid, acetic formic anhydride (3.4 g, 39 mmol) was added. The reaction mixture was stirred at a temperature maintained below 10 °C. After 40 min, stirring was continued for further 80 min. at r.t. The first crop of *N*-formyl-L-phenylalanine was taken out by filtration from the reaction mixture, while the second crop was obtained from the mother liquor. They were then washed with water, dried and combined. Yield, 4.8 g (80 %); $[\alpha]_{589}^{20} +75.2$ (c 4.0, EtOH). IR (KBr, cm^{-1}) ν 1752 (C=O of carbonyl), 1613 (C=O of formamide); Calcd. for 61.97; H, 5.84; N, 7.15. Found: C, 61.67; H, 5.81; N, 7.10.

***N*-Formyl-L-phenylalanine-(4-phenylazo)-phenylester.**¹⁰(II) *N*-formyl-L-phenylalanine (4 g, 21 mmol), pyridine (1.7 ml, 21 mmol) and 4-phenylazo-phenol (4.0 g, 21 mmol) were dissolved in ethyl acetate (60 ml) and cooled to -20 °C, *N,N'*-dicyclohexyl-carbodiimide (4.4 g, 22 mmol) was added and the stirred solution allowed attaining r.t. overnight. A few drops of glacial acetic acid were then added and after 0.5 h the DCU was removed by filtration. The filtrate was washed with 5 % NaHCO_3 , 5 % citric acid and water. The solution was dried and evaporated to give a crude oil. Pure powder product was reprecipitated from ethyl acetate. $[\alpha]_{589}^{20} -61.3$ (c 1.0, CHCl_3). IR (KBr, cm^{-1}) ν 3323 (N-H), 1753 (C=O of carbonyl), 1655 (C=O of formamide); ^1H NMR (270 MHz, CDCl_3) δ 3.32(dd, 1H, $^3J_{\text{AB}} = 7.59$ Hz, $^2J_{\text{BB}'} = 13.7$ Hz, $\text{CH}_\text{B}\text{H}_\text{B}-\text{Ph}$)(dd, 1H, $J_{\text{AB}'} = 4.95$ Hz, $J_{\text{BB}'} = 13.7$ Hz, $\text{CH}_\text{B}\text{H}_\text{B}-\text{Ph}$), 5.23 (dd, 1H, $J_{\text{AB}} = 7.59$ Hz, $J_{\text{AB}'} = 4.95$ Hz, CH_A), 6.23 (br, H, NH), 7.24 (m, 7H, H-1,2,3,6), 7.53 (m, 3H, aromatic H-11,12), 7.93 (m, 4H, H-7,10), 8.26 (s, 1H, CHO) ppm. Calcd. for $\text{C}_{22}\text{H}_{19}\text{N}_3\text{O}_9$: C, 70.76; H, 5.13; N, 11.25. Found: C, 70.64; H, 5.18; N, 11.13.

***rac*-1-Carbazophenoxy-2-phenylethylisocyanide.**¹¹(Az) The isocyanide was synthesized by dehydration of the *N*-formamide according to the method of Nolte and Drenth.¹¹ At 0 °C, of bis(trichloromethyl)carbonate (Wako, 0.60 mg, 2 mmol) in 10 ml of dry CH_2Cl_2 was introduced into a 15 ml of dry CH_2Cl_2 containing 1.5 g (6 mmol) of formamide over a period of approximately 1 day with stirring. Just after the reaction was completed for approximately 3 h, 50 ml of water added to the mixture. The organic layer was quickly washed with 150 ml of a 7.5 % NaHCO_3 aqueous solution and dried over MgSO_4 . The crude product was purified by column chromatography on silica gel using CH_2Cl_2 as the eluent.

Yield 64 %. IR (KBr, cm^{-1}) 2148 (N C), 1758 (C=O of carbonyl); ^1H NMR (270 MHz, CDCl_3) δ 3.35 (dd, 1H, $^3J_{\text{AB}} = 7.59$ Hz, $^2J_{\text{BB}'} = 13.94$ Hz, $\text{CH}_\text{B}\text{H}_\text{B}$), 3.44 (dd, 1H, $^3J_{\text{AB}'} = 5.44$ Hz, $^2J_{\text{BB}'} = 13.94$ Hz, $\text{CH}_\text{B}\text{H}_\text{B}$), 4.75 (dd, 1H, $^3J_{\text{AB}} = 7.59$ Hz, $^3J_{\text{AB}'} = 5.44$ Hz, CH_A), 7.16 (m, 2H, aromatic H-3), 7.38 (m, 5H, H-1,2,6), 7.51 (m, 3H, H-11,12), 7.93 (m, 4H, H-7,10) ppm. Calcd. for $\text{C}_{22}\text{H}_{17}\text{N}_3\text{O}_2$: C, 74.35; H, 4.82; N, 11.82. Found: C, 72.75; H, 4.82; N, 11.40.

Polymerization. Methanol and chloroform for polymerization solvent was purified under dry N_2 stream, and then distillation before use. Just prior to the polymerization, the isocyanide monomer was synthesized and purified by column chromatography. The aliquot of methanol containing appropriate amount of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.5 mol % for monomer) was loaded to a reaction vessel and the solvent was flushed up. The polymerization started by the addition of the chloroform solution containing the isocyanide monomer and stirring at room temperatures. After 1.5 day, the reaction solution became viscous and turned dark orange. After solvent evaporation, the concentrated reaction mixture was added dropwise to an excess amount of vigorously stirred chloroform-methanol (1:4 (v/v)). The dark orange precipitate was collected by filtration and dried *in vacuo* at ambient temperature.

Computational Calculations. The minimized geometry and the heat of formation for each molecule was performed using the semi-empirical quantum chemical Austin method (AM1) as provided in the Spartan software version 6.0 (wavefunction Inc.).

Photochemical Measurements. *E*→*Z* photoisomerization of the azobenzene moiety in the copolymers was achieved under UV irradiation with a 150 W Xe-lamp through HOYA U340 and UV34 filters (optical window, $320 < \lambda < 380$ nm), while *Z*→*E* photoisomerization was achieved under visible light irradiation through a HOYA Y50 filter ($\lambda > 480$ nm). The photoisomerization was monitored by UV-vis absorption spectrum and optical rotation.

3. RESULT AND DISCUSSION.

3-1. Mechanism of racemization of isocyanide.

Although *N*-formamide (II) was dehydrated according to the Nolte's method,¹¹ the value of optical rotation of the resulting isocyanide monomer showed nearly zero °. Unfortunately, racemization was inevitable even under the much milder conditions, such as the very low temperature (~ -30 °C), low concentration (~0.04 mol/l), and Ugi's milder synthetic method.¹² On the other hand, the case of *N*-formyl-L-phenylalanine bearing alkyl ester or benzyl ester was able to be dehydrated without racemization using the same method as Nolte reported. This racemization behavior was also confirmed by the hydrolysis of the resulting isocyanide to form the corresponding racemic formamide (*rac*-II).

To elucidate the mechanism of this racemization process, semi-empirical AM1 molecular orbital calculation was conducted for the model compounds, tolyl and benzyl esters. Heat of formation of tolyl ester shows a larger energy gap between the *enol* (a) and *carboxyl* (b) forms than that of benzyl ester, suggesting that *enol form* (a) has the larger contribution on the *carboxyl-enol* equilibrium in tolyl ester in comparison

with the benzyl one. The electron density on the oxygen of carboxyl group of tolyl ester (a) is larger than that of benzyl ester (c). In the tolyl ester, the hydrogen on the chiral center may be therefore more readily transferred to the oxygen of carboxyl group, to afford the *enol form*. In this context, the azobenzene ester, in which the carboxyl group directly connected to the azobenzene moiety, may be racemized by the participation of such an *enol form*.

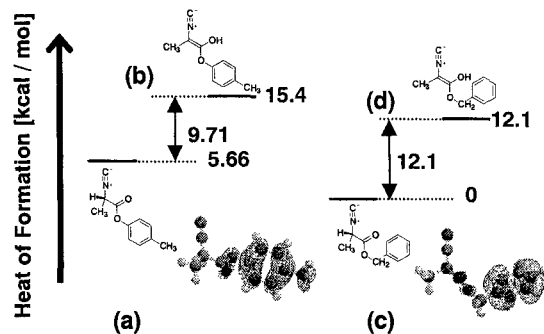


Figure 1 Heat of formation on the basis of the *carboxyl form* of benzyl (c) and optimized geometry with HOMO calculated by semi-empirical AM1.

3-2. Copolymerization of Az monomer and (S)-1-Ethoxycarbonyl-2-phenylethylisocyanide (Et).

Random copolymerization of racemic Az monomer with a chiral (S)-1-ethoxycarbonyl-2-phenylethylisocyanide (Et) monomers⁸ gave the poly(isocyanide) bearing azobenzene moiety. Copolymerization underwent within 1.5 days to give the dark orange powder in about 75 % of the isolated yield. Copolymerization ratio of Az and Et was 3:10 (89 % ee for the chiral center on the phenylalanine residue).¹³ Weight average molecular weight was 6,820 and polydispersity was 1.34, calculated from the GPC measurements (polystyrene standards). Specific rotation showed +802° [ml/cm g] (c 0.2, CHCl₃) which was much larger than the value of monomer, suggesting that the polymers that adopt one-handed helical conformations.^{5,14} Similar increase of specific rotations ranging into the hundreds or even the thousands of degrees have been reported for a number of chiral helical polymers prepared via screw-sense polymerization techniques, including such as poly(isocyanate),¹⁵ poly(silane),¹⁶ poly(methacrylate).¹⁷ As Nolte and co-workers demonstrated previously,¹⁸ even copolymers of achiral and chiral monomers should take the almost single handed helical conformation. So we concluded the resulting polymer had helical conjugated conformation. Unfortunately, due to low S/N ratio, circular dichroism (CD) based on the formation of helical conformation could not be detected here. Normally $\Delta\epsilon$ of poly(alkylisocyanide) shows small value compared with poly(aryl isocyanide) because of more thermally fractured helical conformation due to the low rigidity.^{1(b),11,19} Furthermore, for the large ϵ value of Az moiety, we cannot detect CD signal induced by the helical main chain separately.

3-3. Photo-isomerization behavior of poly(Az-Et) on UV-vis spectrum and specific rotation.

UV-vis spectral change of copolymers Az-Et under UV/vis irradiation is shown in Figure 2. Photochemical

E-Z isomerization of azobenzene moiety can be easily observed in UV-vis spectra. *E*→*Z* isomerization was detected by the observation of the absorption region of π - π^* transition at 340 nm shifted to shorter wavelength with the decreased ϵ value, and the increased ϵ value at 450 nm under UV 360 nm irradiation. Simultaneously, the absorption edge in long wavelength region was red-shifted, implying that the effective conjugation length might be extended. These changes caused by UV irradiation were recovered reversibly upon visible light irradiation beyond 480 nm.

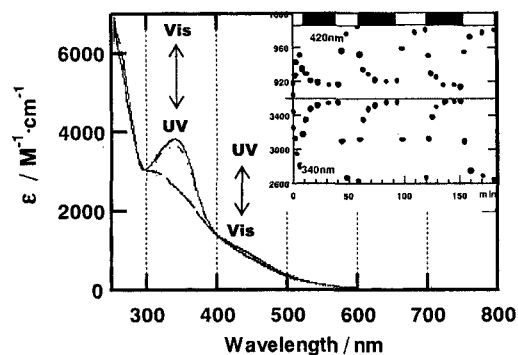


Figure 2 UV-vis. spectral change of copolymer Az-Et upon UV/vis. irradiation in CHCl₃. The inset shows the plot of ϵ value versus UV/vis. irradiation time (min) at 450 nm (π - π^* transition of *trans* azobenzene) (upper) and at 340 nm (π - π^* transition of *cis* azobenzene) (lower), respectively.

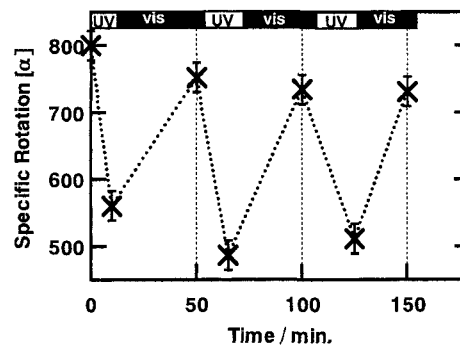


Figure 3 Specific rotation changes of copolymer Az-Et after UV/vis irradiation in CHCl₃.

The influence of *E*→*Z* isomerization on helical conformation of the main chain was examined by monitoring the change of specific rotation. The change of specific rotation after UV/vis irradiation is shown in Figure 3. Specific rotation of copolymer decreased during *E*→*Z* isomerization of azobenzene moiety upon UV irradiation, and then went back to almost original value in the *Z*→*E* isomerization upon visible light irradiation.

Red-shift of the absorption edge in long wavelength region implies that the main-chain of the copolymer is extended to planar conformation, in which the overlap of p_z orbitals between neighboring carbons in the polymer main-chain increased, to extend the effective conjugation length. Since the optical purity of each monomer unit may not be changed by photoirradiation process, the reduction of the optical rotation value after UV irradiation may be therefore solely attributable to the

extended conformation of the helical main chain. This change depending on light irradiation indicates that the conformation of helical main chain can be reversibly switched between the tight helical conformation and the extended one.

4. CONCLUSIONS.

Co-poly(isocyanide) consisting of Az and Et was prepared in the presence of NiCl₂ catalyst. It shows very large specific rotation in comparison with the corresponding Et monomer, indicating one-handed helical conformation. By the UV irradiation, the azobenzene moiety introduced in the copolymer was effectively isomerized from *E*→*Z* isomer, the effective conjugation length was elongated, and simultaneously the specific rotation of the copolymer was dramatically reduced. Furthermore, these changes were almost completely reversible during UV/vis alternative irradiation. These observations imply that the conformation of helical main chain can be reversibly controlled by the photochemical stimuli.

5. ACKNOWLEDGEMENT.

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following equation.

$$\% ee = \frac{([S]-Et) + [Az]/2}{([S]-Et) + [Az]}$$

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