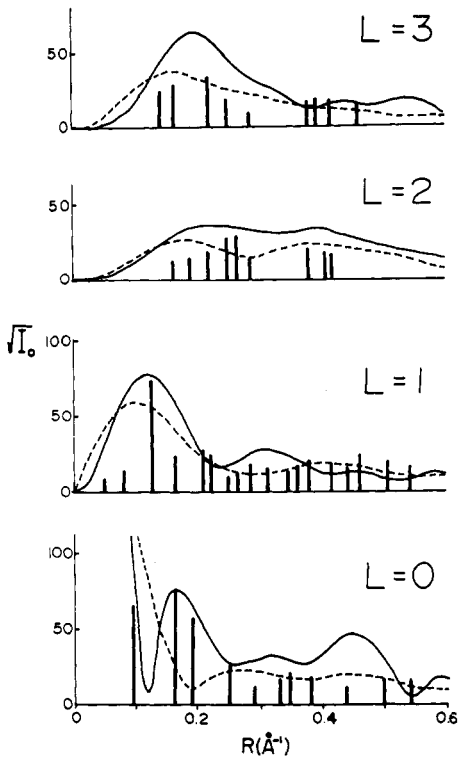

Figure 2. Comparison between the square roots of the observed reflection intensities (vertical rods) and the calculated molecular structure factors for the double helix (solid lines) and for the (5/1) helix (broken lines).

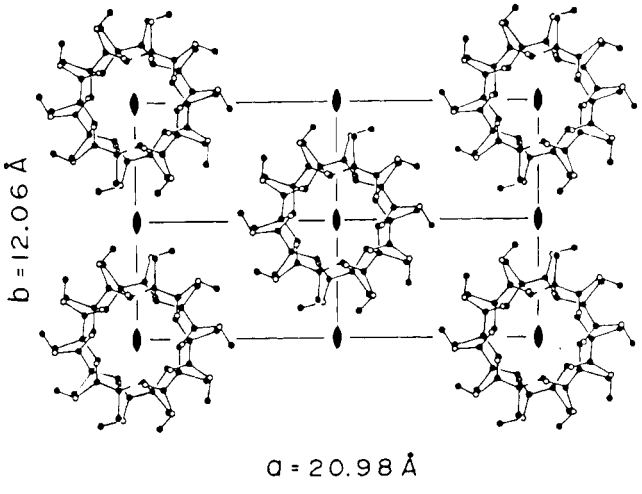

Figure 3. Crystal structure of isotactic poly(methyl methacrylate).

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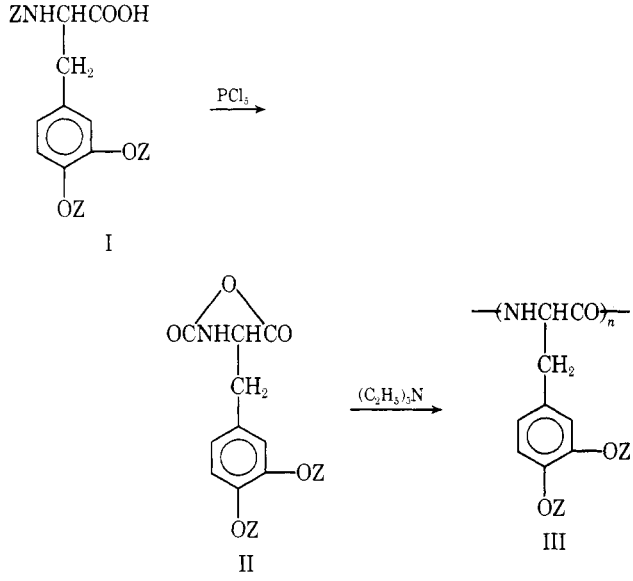
Sense of Helix of Poly-*O,O'*-dicarbobenzoxy-L-DOPA in Solution

We wish to report the helical sense of poly-*O,O'*-dicarbobenzoxy-L-DOPA in helicogenic solvents.[1] The polypeptide was synthesized according to the following scheme:



where Z denotes carbobenzoxy.

Carbobenzoxylation of L-DOPA gave *N,O,O'*-tricarbobenzoxy-L-DOPA (I). Pure crystalline *O,O'*-dicarbobenzoxy-L-DOPA-NCA (II) was prepared from *N,O,O'*-tricarbobenzoxy-L-DOPA and phosphorus pentachloride at 0 to ca. −5 °C in anhydrous ether:[2] yield, 88%; mp 71 °C; ir bands, 1852 and 1788 cm^{-1} (cyclic anhydride). Anal. Calcd for $C_{26}H_{21}O_9N$: C, 63.54; H, 4.31; N, 2.85. Found: C, 63.62; H, 4.59; N, 2.50. The acetone solution of the NCA was passed through a dry charcoal–silver oxide column. After removal of the solvent, poly-*O,O'*-dicarbobenzoxy-L-DOPA (III) was prepared by polymerizing the NCA in 10% dioxane solution using triethylamine as an initiator (A/I = 100): yield, 48%; ir bands (see below). Anal. Calcd for $(C_{25}H_{21}O_7N)_n$: C, 67.11; H, 4.73; N, 3.13. Found: C, 67.50; H, 4.84; N, 3.01. The polypeptide had an intrinsic viscosity $[\eta]$ of 0.26 dl/g in DCA at 25 °C. The molecular weight was estimated to be 28 000 (DP = 60) from an empirical equation for poly-*O*-carbobenzoxy-L-tyrosine in DCA[3] and from the *N*-terminal titration with perchloric acid in chloroform using crystal violet as an indicator.[4]

The CD curves of poly-*O,O'*-dicarbobenzoxy-L-DOPA are shown in Figure 1A. The CD values are $[\theta]_{225}$ = −13 600 in chloroform, $[\theta]_{225}$ = −18 900 in methylene dichloride, $[\theta]_{228}$ = 24 800 in THF, and $[\theta]_{228}$ = 24 000 in dioxane. A model compound, *N,O,O'*-tricarbobenzoxy-L-DOPA-glycine ethyl ester, exhibits the same positive CD band in dioxane or chloroform (see Figure 1A). Thus, the CD behavior of the polypeptide is anomalous.

The solution ir spectra of poly-*O,O'*-dicarbobenzoxy-L-

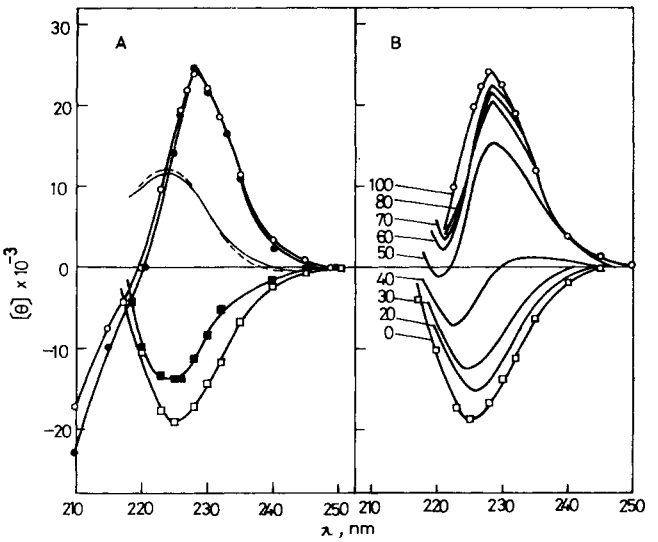


Figure 1. CD spectra in the far-ultraviolet region at 25 °C. (A) poly-*O,O'*-dicarbobenzoxy-L-DOPA: ○, in dioxane; ●, in THF; □, in methylene dichloride; ■, in chloroform. *N,O,O'*-Tricarbobenzoxy-L-DOPA-glycine ethyl ester: —, in dioxane; - - -, in chloroform. (B) Poly-*O,O'*-dicarbobenzoxy-L-DOPA in dioxane–methylene dichloride mixed solvents: numerals, volume percents of dioxane in methylene dichloride.

DOPA shows amide I and II bands at 1665 and 1545 cm^{-1} in chloroform and at 1670 and 1550 cm^{-1} in dioxane. The frequencies for the left-handed helix are higher by 8–9 cm^{-1} for the amide I band and 3–6 cm^{-1} for the amide II band than for the right-handed helix.[5,6] These higher frequencies support the normal coordinate calculations of Miyazawa et al. for the differences in frequencies between the left- and right-handed helices of poly-L-alanine.[7]

Figure 2 shows the 60-MHz NMR spectra of poly-*O,O'*-dicarbobenzoxy-L-DOPA in three solvents at 25 °C. In dioxane-d_8 solution (spectrum a), the α-CH resonance appears at 3.95 ppm, whereas in chloroform-d_1 (spectrum b) this proton appears at 4.13 ppm. Spectrum c in TFA shows the α-CH peak at 4.85 ppm (random coil). These chemical shift trends agree with those reported by Bradbury[8] for left-handed helical poly(β-benzyl L-aspartate) and right-handed helical poly(β-ethyl L-aspartate) and copolymers of β-benzyl L-aspartate with L-alanine.

The CD, solution ir, and NMR results suggest that the conformation of poly-*O,O'*-dicarbobenzoxy-L-DOPA depends greatly on the solvent taking the right-handed helical sense in alkyl halides and the left-handed helix in cyclic ethers. In TFA the polypeptide assumes a random coil structure.

Figure 1B shows the change of helical sense of poly-*O,O'*-dicarbobenzoxy-L-DOPA with change of solvent composition in dioxane–methylene dichloride mixtures at 25 °C. In a 1:1 mixed solvent the CD curve of the polypeptide gave a positive ellipticity band at 228 nm with $[\theta]_{228}$ = 15 800. This suggests that the left-handed helix of the polypeptide is more stable than the right-handed helix.

Poly-*O*-carbobenzoxy-L-tyrosine (DP = 570),[9] which has been demonstrated to have a right-handed α-helical conformation from the change of b_0 with copolymer composition,[3] the CD spectrum in trimethyl phosphate,[10] and the x-ray diffraction pattern in the solid state,[11] shows a similar negative ellipticity band at 231 nm with $[\theta]_{231}$ = −9000 in dioxane or chloroform (see Figure 3). The only difference between the two polypeptides is that poly-*O*-carbobenzoxy-L-tyrosine has one less *O*-carbobenzoxy group at the 3 position in the aromatic side chain. It is possible from this study to suggest that the solvent affects the delicate balance of the stacking of three aromatic groups of poly-*O,O'*-dicarbobenzoxy-L-DOPA and causes a reversal of the helix sense in solution.

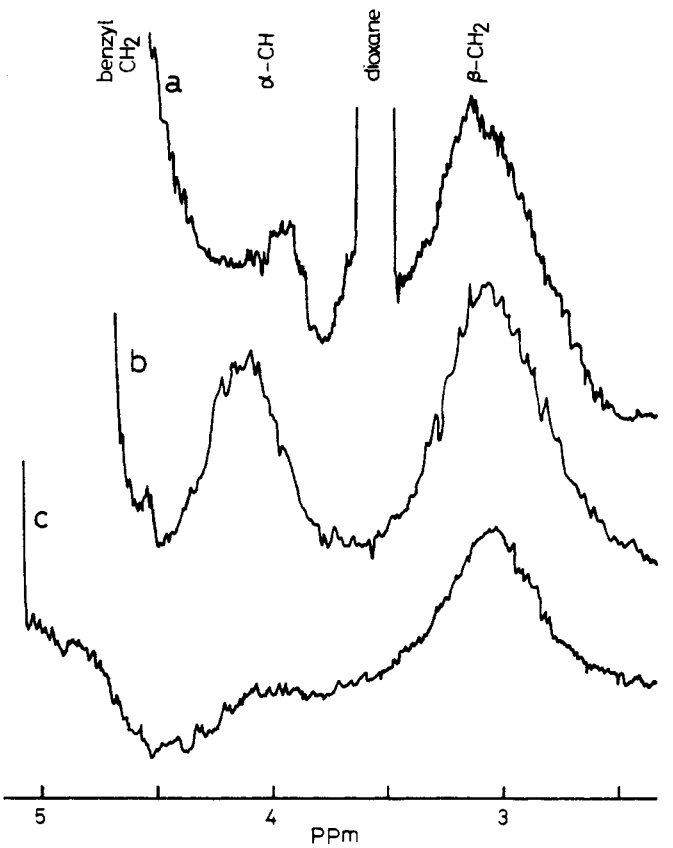


Figure 2. NMR spectra of poly-*O,O'*-dicarbobenzoxy-L-DOPA at 25 °C (no spinning): (a) in dioxane-d_8–5% TFA; (b) in chloroform-d_1–1% TFA; (c) in TFA.

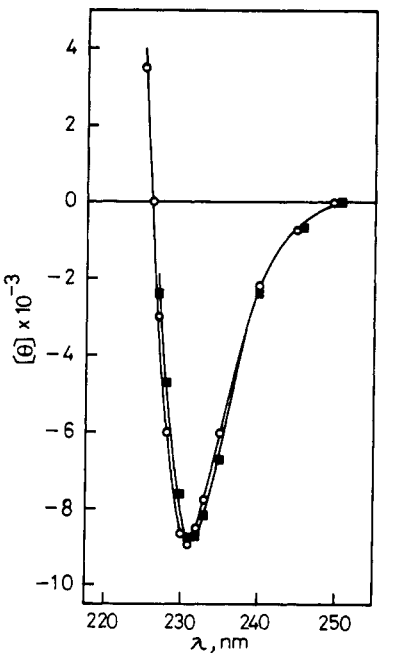


Figure 3. CD spectra of poly-*O*-carbobenzoxy-L-tyrosine in the far-ultraviolet region at 25 °C: ○, in dioxane; ■, in chloroform.

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References and Note

(1) Abbreviations used in this work: DOPA, δ-3,4-dihydroxyphenyl-α-alanine; NCA, *N*-carboxyanhydride; DP, degree of polymerization; DCA, dichloroacetic acid; TFA, trifluoroacetic acid; THF, tetrahydrofuran; ir, infrared; CD, circular dichroism; NMR, nuclear magnetic resonance; the dimension of $[\theta]$ is deg cm^2 dmol^{-1}.
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