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Syntheses of Poly[γ-(*l*)-menthyl L- and D-Glutamates] and Their Secondary Structures*

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Synopsis

γ-(*l*)-Menthyl L- and D-glutamates were prepared by a fusion reaction of *N*-phthalyl-L- and D-glutamic anhydrides with *l*-menthol, followed by hydrazinolysis. The monomers were polymerized to poly[γ-(*l*)-menthyl L- and D-glutamates] by the *N*-carboxyanhydride method. These polymers were soluble in many organic solvents, such as ethyl ether, chloroform, tetrahydrofuran, and *n*-hexane. From the results obtained by a study of the infrared absorption spectra, the x-ray photographs, the optical rotatory dispersions and the circular dichroisms, poly[γ-(*l*)-menthyl L-glutamate] was found to be a right-handed α-helix in the solid state and in solution. Similarly, poly[γ-(*l*)-menthyl D-glutamate] was a left-handed α-helix. The helix–coil transition of these polymers was observed in the vicinity of 40% dichloroacetic acid in a chloroform–dichloroacetic acid mixture.

INTRODUCTION

Recently, many investigations of the syntheses and physico-chemical properties of such poly(γ-alkyl glutamates) as γ-methyl, γ-ethyl,[1,2] γ-*n*-propyl, γ-*n*-butyl, γ-isobutyl, γ-isoamyl,[3] and γ-benzyl esters[4,5] have been reported. It has been established by many workers that poly-(γ-alkyl L-glutamate) assumes a helical conformation in a solvent such as chloroform, while it assumes a disordered conformation in a solvent such as dichloroacetic acid (DCA) or trifluoroacetic acid (TFA). In the present study, poly[γ-(*l*)-menthyl L- and D-glutamates] were synthesized, and the effect of the side chain on the secondary structure of these polymers was studied by means of the optical rotatory dispersion (ORD), the circular dichroism (CD), infrared spectroscopy (IR), and x-ray techniques. The route of synthesis of poly[γ-(*l*)-menthyl L- and D-glutamates] is shown in eq. (1).

$$\text{glu} \xrightarrow[\text{phthalimide}]{N\text{-Carboethoxy}} \underset{\text{I}}{\text{Phth-glu}} \xrightarrow[\text{anhydride}]{\text{Acetic}} \underset{\text{II}}{\text{Phth-glutamic anhydride}}$$

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$$\xrightarrow{l\text{-Menthol}} \underset{\text{III}}{\text{Phth-}\gamma\text{-}(l)\text{-menthyl glu}} \xrightarrow{NH_2-NH_2} \underset{\text{IV}}{\gamma\text{-}(l)\text{-menthyl glu}}$$

$$\xrightarrow{COCl_2} \underset{\text{V}}{\gamma\text{-}(l)\text{-menthyl glu NCA}} \xrightarrow{Et_3N} \underset{\text{VI}}{\text{poly-}\gamma\text{-}(l)\text{-menthyl glu}} \qquad (1)$$

where phth denotes phthalyl.

The synthesis of γ-menthyl glutamate (IV) by direct γ-esterification with *p*-toluenesulfonic acid[6] or sulfuric acid was unsuccessful. Optically pure γ-(*l*)-menthyl glutamate (IV) was synthesized through the phthalyl derivative of glutamic acid. The phthalylglutamic acid has already been prepared from glutamic acid and phthalic anhydride by the fusion method.[7] However, the reaction conditions of this method were so drastic that partial racemization took place during the reaction. The optically pure *N*-phthalyl L- and D-glutamic acids (I) were prepared from glutamic acid and *N*-carboethoxyphthalimide as described by Nefkens et al.;[8] we then converted it to *N*-phthalylglutamic anhydride (II) by heating it with acetic anhydride. The product (II) was fused with *l*-menthol to give the monomenthyl ester of phthalylglutamic acid (III) in a 57–67% yield. Both phthalyl D- and L-glutamic anhydrides (II) were fused with *l*-menthol at 135–140°C, until the reaction mixtures became viscous clear solutions. The mixtures were heated for 4 hr in the case of the L-derivative and for 6 hr in the case of the D-derivative. It seems that the D-derivative is less reactive than the L-derivative. Similarly, *N*-phthalyl-γ-(*l*)-menthyl DL-glutamate (III) was prepared from phthalyl DL-glutamic anhydride (II) and *l*-menthol. The fractionation of diastereomers was obtained on recrystallization of the product from ether and *n*-hexane. The crystals separated from the recrystallization solvent were found to be completely composed of the optically pure L-glutamate derivative. From the mother liquor, D-rich crystals were obtained.

By treating the phthalyl glutamate (III) with hydrazine,[7,9] the corresponding γ-(*l*)-menthyl L- and D-glutamates were obtained. In order to compare the physical properties of the γ-ester with those of the α-ester, α-menthyl L-glutamate was prepared by the *N*-carboxyanhydride (NCA) method.[10] The α- and the γ-esters were found to be considerably different. On paper chromatography, the α-ester showed R_f 0.90 and the γ-ester showed R_f 0.33 in the *n*-butanol–acetic acid–water (4:1:5, v/v) system. The condensation of phthalylglutamic anhydride with *l*-menthol seemed to lead almost exclusively to formation of the γ-ester derivative.[11–13] γ-Menthyl L- and D-glutamate NCA's (V) were prepared from γ-menthyl L- and D-glutamates and phosgene in dry dioxane. The NCA's were polymerized in dioxane, tetrahydrofuran (THF), and dimethylformamide (DMF) with triethylamine as an initiator for 3 days at 15°C, for 2 days at 30°C, and 5 hr at 100°C. The polymerization reaction proceeded in a clear solution in THF; however, the polymers were precipitated in dioxane and in DMF. The relationship between the solvent and the degree of polymerization is shown in Table I.

TABLE I

Molecular weight of Poly[γ-(*l*)-Menthyl L- and D-Glutamates][a]

	L-Polypeptide				D-Polypeptide			
Solvent	Monomer NCA, mg[b]	Yield, mg	Molecular weight (DP)[c]	η_{sp}/c[d]	Monomer NCA, mg[b]	Yield, mg	Molecular weight (DP)[c]	η_{sp}/c[d]
Dioxane	500	437	18,300(69)	0.22	500	315	29,500(110)	0.28
THF	600	541	5,500(21)	0.08	800	701	8,700(33)	0.12
DMF	600	548	12,500(47)	0.10	800	684	12,000(45)	0.15

[a] Polymerized for 3 days at 15°C, for 2 days at 30°C, and for 5 hr at 100°C.
[b] 10% concentration and molar ratio of anhydride to initiator, A/I, of 100.
[c] By titration of the amino endgroup with 0.02*N* perchloric acid.
[d] c = 0.5% in DCA at 25°C.

The number-average molecular weight was determined by the titration of the amino endgroup with 0.02*N* perchloric acid in THF, crystal violet being used as the indicator. The solubilities of the D- and L-polymers were similar in many solvents. However, their solubilities were different from those of the usual polypeptides. Poly(γ-(*l*)-menthyl glutamates) were soluble in THF, diethyl ether, *n*-hexane, chloroform, benzene, toluene, dimethylacetamide, pyridine, benzyl alcohol, *m*-cresol, DCA, and TFA. They were slightly soluble in methylene chloride, carbon tetrachloride, DMF, xylene, petroleum ether, *n*-butanol, dimethyl sulfoxide, *tert*-amyl alcohol, and isopropyl ether, and were insoluble in acetone, ethyl alcohol, methyl alcohol, acetic acid, dioxane, acetonitrile, formic acid, 2-chloroethanol, and water.

EXPERIMENTAL

Materials

The elemental analyses are carried out with a Yanagimoto CHN corder, the results are listed in Table II.

***N*-Phthalyl-L-glutamic Acid (I_L).** *N*-Phthalyl-L-glutamic acid was prepared from L-glutamic acid and *N*-carboethoxyphthalimide as described by Nefkens et al.;[8] mp, 160°C; $[\alpha]_D^{22} = -48.3°$ (c = 3, dioxane).

***N*-Phthalyl-D-glutamic Acid (I_D).** To a suspension of D-glutamic acid (5 g) in 40 ml of water, 8.8 g of sodium carbonate were added. The mixture was cooled to 0°C, and then 10.4 g of *N*-carboethoxyphthalimide was added. The mixture was stirred at room temperature for about 1.5 hr. After filtration, the filtrate was acidified to pH 3 with 6*N* hydrochloric acid. An oily product was crystallized upon cooling or by scratching; yield, 6.5 g (69%). It was recrystallized from water; yield, 6.1 g (65%); mp, 159–160°C; $[\alpha]_D^{22} = +52.1°$ (c = 1.03, dioxane).

***N*-Phthalyl-L-glutamic Anhydride (II_L).** *N*-Phthalyl-L-glutamic anhydride was prepared from phthalyl-L-glutamic acid and acetic anhydride as

TABLE II
Elemental Analysis of Glutamic Acid Derivatives

Sample	Molecular formula	Calcd			Found		
		C, %	H, %	N, %	C, %	H, %	N, %
Phth-D-glu	$C_{13}H_{11}O_6N$	56.32	4.00	5.05	56.47	3.91	5.17
Phth-D-glu anhydride	$C_{13}H_9O_5N$	60.23	3.50	5.40	60.11	3.24	5.43
Phth-γ-menthyl L-glu	$C_{23}H_{29}O_6N$	66.49	7.04	3.39	66.85	6.97	3.40
Phth-γ-menthyl D-glu	$C_{23}H_{29}O_6N$	66.49	7.04	3.39	66.42	6.98	3.64
γ-Menthyl L-glu	$C_{15}H_{27}O_4N$	63.13	9.54	4.91	63.54	9.29	4.95
γ-Menthyl D-glu	$C_{15}H_{27}O_4N$	63.13	9.54	4.91	63.24	10.01	5.10
γ-Menthyl L-glu NCA	$C_{16}H_{25}O_6N$	61.72	8.09	4.50	61.13	8.29	4.42
γ-Menthyl D-glu NCA	$C_{16}H_{25}O_6N$	61.72	8.09	4.50	61.63	8.30	4.42
Poly-γ-menthyl L-glu	$C_{15}H_{25}O_3N$	67.38	9.42	5.24	67.38	10.09	5.29
Poly-γ-menthyl D-glu	$C_{15}H_{25}O_3N$	67.38	9.42	5.24	67.10	10.09	5.23
α-Menthyl-γ-methyl L-glu hydrochloride	$C_{16}H_{30}O_4NCl$	57.22	9.00	4.17	57.18	9.01	4.17
α-Menthyl L-glu	$C_{15}H_{27}O_4N$	63.13	9.54	4.91	63.40	9.53	4.91

has been described by King and Kidd;[14] mp, 197–198°C; $[\alpha]_D^{22} = -42.0°$ (c = 0.99, dioxane).

***N*-Phthalyl-D-glutamic Anhydride (II_D).** *N*-Phthalyl-D-glutamic acid (4.5 g) in 20 ml of acetic anhydride was heated for 5 min at 110°C until the solution became clear. The reaction mixture was concentrated to dryness under reduced pressure. The crystalline product was washed with ether, filtered, and dried; yield, 4.1 g (98%); mp, 198–200°C; $[\alpha]_D^{15} = +45.8°$ (c = 1.01, dioxane).

***N*-Phthalyl-γ-(*l*)-menthyl L-Glutamate (III_L).** A mixture of finely pulverized phthalyl-L-glutamic anhydride (15 g, 0.058 mole) and *l*-menthol (10 g, 0.064 mole) was fused at 135–140°C for 4 hr with stirring until a clear solution was obtained. After cooling, the reaction mixture was dissolved in ether and the solution was extracted with a saturated sodium bicarbonate solution (2 equivalent mole). After filtration, the filtrate was acidified to Congo red with 6*N* hydrochloric acid. The crystals thus precipitated were filtered and dried; yield, 15.8 g. This was recrystallized from ether and *n*-hexane; yield, 13.7 g (57%); mp, 188°C; $[\alpha]_D^{22} = -73.4°$ (c = 1.0, dioxane).

***N*-Phthalyl-γ-(*l*)-menthyl D-Glutamate (III_D).** A mixture of II_D (12.2 g) and *l*-menthol (8.1 g) was fused at 135–140°C for 6.5 hr. It was then treated in the same way as III_L; yield, 17.8 g. This was recrystallized from ether and *n*-hexane; 13.1 g (67%); mp, 144°C; $[\alpha]_D^{22} = -12.0°$ (c = 1.01, dioxane).

γ-(*l*)-Menthyl L-Glutamate (IV_L). To a solution of *N*-phthalyl-γ-(*l*)-menthyl L-glutamate (6.9 g, 0.017 mole) in 37 ml of ethyl alcohol, 2.57 ml of 90% hydrazine hydrate were added, and then the solution was refluxed for 1 hr. The reaction mixture was allowed to stand overnight at room temperature. This solution was heated at 50°C for 10 min with addition

of 2*N* hydrochloric acid, after which the mixture was allowed to stand at room temperature for 30 min. The phthalylhydrazide was removed by filtration, and the filtrate was concentrated to dryness under reduced pressure. The residual product was redissolved in hot water and neutralized with a sodium bicarbonate solution. The precipitated crystalline was filtered, washed with water, and dried. This was recrystallized from 50% alcohol; yield, 2.2 g (47%); mp, 194–195°C; $[\alpha]_D^{15} = -49.3°$ (c = 1.0, acetic acid). The molecular weight was determined by amino-group titration with 0.02*N* perchloric acid and found to be 287.3 (calculated for $C_{15}H_{27}O_4N$, 286.7).

γ-(*l*)-Menthyl D-Glutamate (IV_D). To a solution of III_D (10 g) in 70 ml of ethyl alcohol, 3.72 ml of 90% hydrazine hydrate was added. It was treated in a same way as IV_L; yield, 4.0 g; mp, 195°C. This was recrystallized from ether and *n*-hexane; yield, 3.65 g (53%); mp, 196°C; $[\alpha]_D^{15} = -73.6°$ (c = 1.06, acetic acid). The molecular weight was determined by amino-group titration and found to be 292.5 (calculated for $C_{15}H_{27}O_4N$, 286.7).

γ-(*l*)-Menthyl L-Glutamate NCA (V_L). Dry phosgene was passed through a suspension of γ-(*l*)-menthyl L-glutamate (2.2 g) in 44 ml of dry dioxane for 30 min at 50°C. Nitrogen was then passed through the reaction mixture for 30 min. The solvent was removed at 40°C under reduced pressure. The residual oily product was crystallized by treating it with *n*-hexane. The crystals were filtered and dried. This crude product was dissolved in dry acetone and was then passed through a dry charcoal column to purify it. The acetone was removed to dryness under reduced pressure. The residue was treated with *n*-hexane, and the crystals were filtered; yield, 1.9 g (80%); mp, 103°C.

γ-(*l*)-Menthyl D-Glutamate NCA (V_D). γ-(*l*)-Menthyl D-glutamate NCA was prepared from IV_D (2.2 g) and dry phosgene in the same way as V_L; yield, 2.1 g (88%); mp, 108°C.

Poly[γ-(*l*)-menthyl L-Glutamate] (VI_L). γ-(*l*)-Menthyl L-glutamate NCA was dissolved in THF, DMF, and dioxane at the concentration of 10%. Triethylamine was added to each solution at NCA/initiator ratios of 100/1. The mixture was polymerized in a sealed tube at 15°C for 3 days, at 30°C for 2 days, and at 100°C for 5 hr according to the procedure described by Blout[14] and Hashimoto.[15] The results are listed in Table I.

Poly[γ-(*l*)-menthyl D-Glutamate] (VI_D). Poly[γ-(*l*)-menthyl D-glutamate] was prepared in the same way as VI_L. The results are listed in Table I.

Hydrolysis of Poly[γ-(*l*)-menthyl L- and D-Glutamates]. A suspension of poly[γ-(*l*)-menthyl L- and D-glutamates] in 6*N* hydrochloric acid was hydrolyzed at 105°C for 37 hr. The hydrolyzate gave only glutamic acid upon paper chromatography. The specific rotation of the hydrolyzate showed $[\alpha]_D^{20} + 31.2°$, which agrees with the value of authentic L-glutamic acid. The same results were obtained in the case of the D derivative.

α-(*l*)-Menthyl L-Glutamate. A mixture of γ-methyl L-glutamate NCA (5 g, 0.027 mole) and *l*-menthol (12.5 g, 0.081 mole) was dissolved in 40 ml of 2*N* hydrogen chloride–dioxane and kept overnight.[10] After the removal of the solvent, the residual oil was dissolved in 100 ml of a saturated sodium bicarbonate solution. Then the solution was extracted with ether to obtain the free ester. The ethereal layer was washed once with water and dried over sodium sulfate. To this dried solution, dry hydrogen chloride was introduced and then evaporated to dryness under reduced pressure. The ester hydrochloride was treated with *n*-hexane and then filtered; yield, 4.3 g. This was recrystallized from ether and *n*-hexane; mp, 114°C. This diester (3.0 g) was dissolved in a mixture of 2*N* hydrochloric acid (30 ml) and glacial acetic acid (30 ml) and heated for 1 hr at 100°C. The solvent was removed to dryness under reduced pressure. The residue was redissolved in water and neutralized with a sodium bicarbonate solution. The precipitate was filtered, washed with water, and dried; yield, 1.6 g; mp, 156–158°C. This was recrystallized from 80% ethanol; $[\alpha]_D^{15} = -54.8°$ (c = 1.04, acetic acid).

Fractionation of Diastereomers of the *N*-Phthalyl-γ-(*l*)-menthyl DL-Glutamate

N-Phthalyl-DL-glutamic acid was prepared from DL-glutamic acid and phthalic anhydride by fusion for 1.5 hr at 140°C ,as has been described by King and Kidd.[16] It was converted to *N*-phthalyl-DL-glutamic anhydride by the same method as above. A mixture of *N*-phthalyl-DL-glutamic anhydride and *l*-menthol was fused for 5 hr at 135–140°C and dissolved in ether, and the solution was extracted with a sodium bicarbonate solution. After filtration, the filtrate was acidified to Congo red with 6*N* hydrochloric acid. The precipitate was filtered and dried; yield, 10.5 g (66%); mp, 143°C; $[\alpha]_D^{18} = -39.3°$ (c = 1.03, dioxane). This product (1.5 g) was dissolved in 10 ml of ether. To this solution, 2 ml of *n*-hexane were added, and the mixture was kept at room temperature for 2 hr. The L-crystals thus obtained weighed 0.30 g; $[\alpha]_D^{25} = -73.2°$ (c = 0.50, dioxane); mp, 180°C. The mother liquor was then concentrated to 1/3 volume. The DL-crystals thus obtained weighed 0.35 g; $[\alpha]_D^{25} = -39.7°$ (c = 0.50, dioxane); mp, 143°C. From the mother liquor, 0.35 g of the D-rich fraction was obtained by evaporation; $[\alpha]_D^{20} = -24.3°$ (c = 0.50, dioxane); mp, 132°C.

METHODS

Optical rotatory dispersion, circular dichroism, and infrared absorption spectra measurements were made on the ORD/UV 5 instrument with the CD attachment and the IR DS-301 instrument, respectively, both made by the Japan Spectroscopic Co., Ltd. The optical rotatory dispersion and circular dichroism were measured with 0.1–10 mm cells for the 195–600 mμ wavelengths. Nitrogen flushing was employed in the far ultraviolet region. The optical rotations were expressed as a reduced molar residue

rotation. As for CD, the measured values of $\epsilon_L - \epsilon_R$ were converted to the molar ellipticity. The concentrations of the samples were in the 0.1–1.0% range. The x-ray diffraction photographs were taken with a Rigakudenki Geigerflex, using a Cu-target.

RESULTS AND DISCUSSION

Infrared Spectra and X-Ray Analyses

The infrared absorption spectra of poly[γ-(*l*)-menthyl L- and D-glutamates] are shown in Figure 1. The L-polymer showed absorptions at 3330, 3080, 2960, 2930, 1735, 1665, and 1548 cm^{-1}, while the D-polymer showed them at 3320, 3070, 2950, 2920, 1737, 1660, and 1550 cm^{-1}. Both of them gave infrared spectra typical of polypeptides and suggest that the polymers have the α-structure.

The x-ray diffraction patterns indicated the presence of 16.9 (vs), 12.0 (w), 7.4 (s), and 4.9 (w) Å reflections in the L-polymer, and 16.9 (vs), 11.8 (w), 7.5 (s), and 4.9 (w) Å in the D-polymer. The x-ray photograph of poly(γ-benzyl L-glutamate) (PBLG) in the α-helix structure shows the presence of 12.8, 7.4, and 4.9 Å reflections.[17] This could be interpreted as indicating that poly[γ-(*l*)-menthyl D- and L-glutamates] have the α-helix structure and that the helix-helix interval of an α-helical polypeptide is broadened from 12.8 Å to 16.9 Å for γ-(*l*)-menthyl polymers because of the bulky side chain, as is shown in poly-$N^{\omega,\omega'}$-dicarbobenzyloxy-L-arginine, poly-N^{ω}-carbobenyloxy-L-arginine,[18] and poly-L-tryptophan.[19]

Optical Rotatory Dispersion and Circular Dichroism

The ORD and CD curves of poly[γ-(*l*)-menthyl L- and D-glutamates] in THF, in diethyl ether, in chloroform, in *n*-hexane (α-helix), in DCA, and

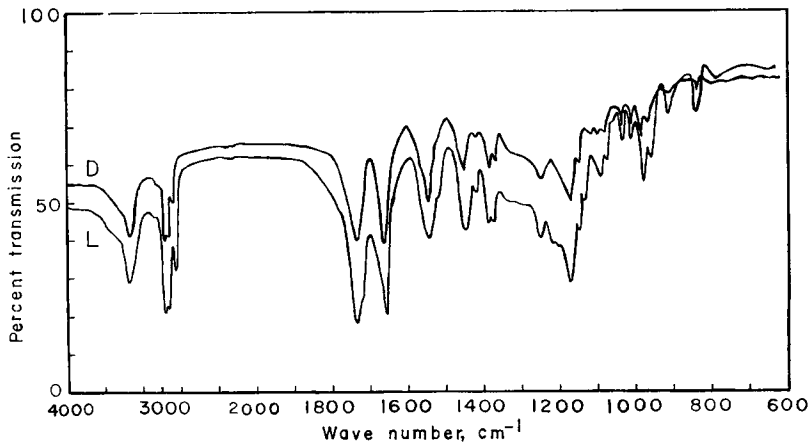

Fig. 1. Infrared absorption spectra of poly[γ-(*l*)-menthyl D- and L-glutamates in the solid state (KBr disk).

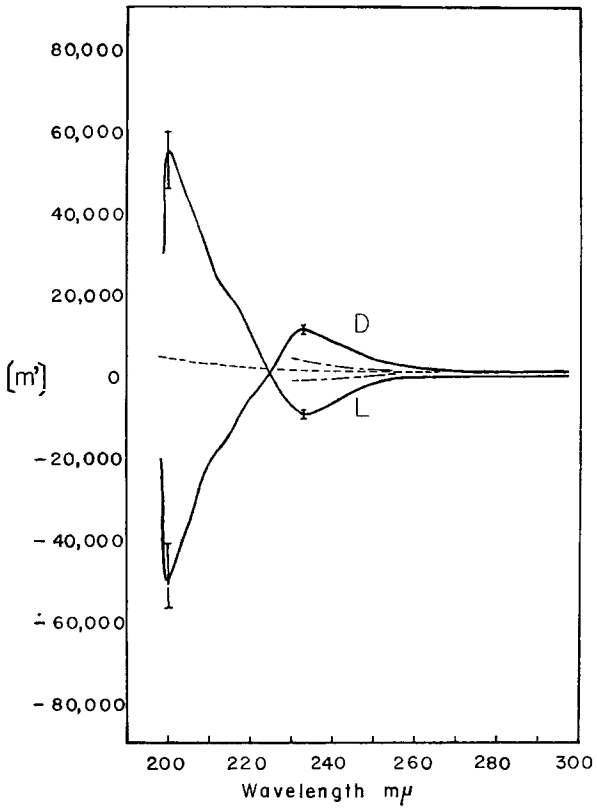

Fig. 2. Optical rotatory dispersions of poly[γ-(*l*)-menthyl D- and L-glutamates] at 25°C: (——) in THF; (- - -) in TFA; (- - -) base line.

in TFA (random coil) were measured. The ORD curves of the polymers in THF and in TFA are shown in Figure 2. In THF the L-polymer exhibits a deep trough at 233 mμ, a zero value of [*m'*] near 225 mμ, a shoulder at 212 mμ, and a strong peak near 198 mμ. This ORD behavior is essentially identical with that of the right-handed α-helical form of the other polyamino acids.[20,21] The [*m'*] value of 233 mμ is about −11,000 deg-cm²/dm. The D-polymer exhibits the same behavior with a deep trough of about +10,100 deg-cm²/dm at the same wavelength (233 mμ); it was found to have the left-handed α-helix structure.

The CD curves of the polypeptides in THF are recorded in order to resolve any possible overlapping of Cotton effects in this region. The CD curves are shown in Figure 3. Two negative dichroism bands at 222 mμ and 206 mμ, with $[\theta]_{222} = -28{,}000$ and $[\theta]_{206} = -25{,}000$, are observed for poly[γ-(*l*)-menthyl L-glutamate] in THF, and a positive dichroism band can be expected below 200 mμ.

The negative ellipticity band at 222 mμ appears to be a n–π^* peptide electronic transition associated with the α-helical conformation of poly-

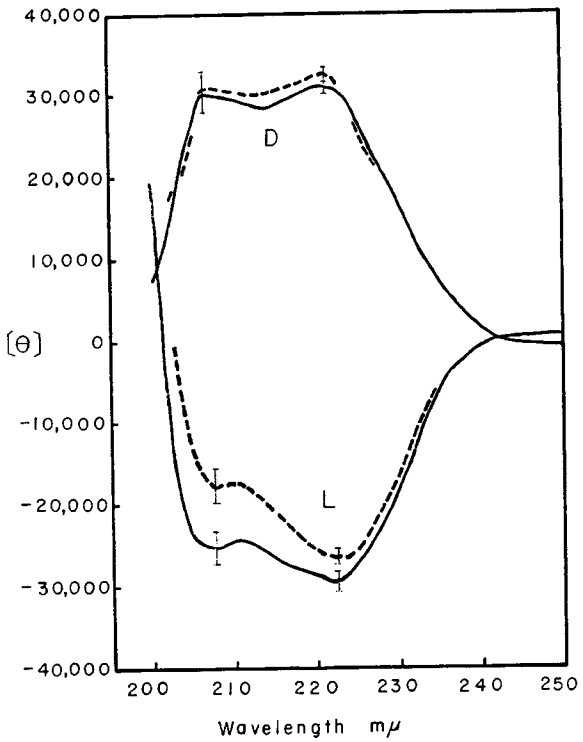

Fig. 3. Circular dichroism of poly[γ-(*l*)-menthyl D- and L-glutamates] at 25°C: (——) in THF; (- -) in diethyl ether.

peptide, and the negative band at 206 mμ and the positive band below 200 mμ are to be assigned to the parallel-polarized and perpendicular-polarized π–π^* exciton transitions of the peptide groups, respectively.[22] These dichroism bands of poly[γ-(*l*)-menthyl L-glutamate] are found in approximately the same positions and have the same signs and magnitudes as has been observed in right-handed α-helical polypeptides. The polymer gave similar curves in diethyl ether, in chloroform, and in *n*-hexane above the 205 mμ region. The values of $[m']_{233}$ and $[\theta]_{222}$ are listed in Table III.

Recently, Toniolo, Falxa, and Goodman[23] reported that ORD measurements of poly(β-*p*-nitrobenzyl L-aspartate) in hexafluoroacetone trihydrate indicated a peptide Cotton effect trough of about −10,000 deg-cm²/dm at 233 mμ. From the same point of view, the lower $[m']_{233}$ and $[\theta]_{222}$ values in Table III indicate that the solvents might destroy the weak helix or that the menthyl group in the side chain may be too bulky to support the complete helical structure. These results suggest that the α-helical polypeptide mingles with some random coil conformation.

It has been known that many α-helical polypeptides undergo a helix–random coil transition in a chloroform–dichloroacetic acid (or trifluoroacetic acid) mixed solvent.[24] In the case of PBLG, the helix–coil transition

TABLE III

Values of $[m']_{233}$ and $[\theta]_{222}$ for Poly[γ-(*l*)-Menthyl L- and D-Glutamates] in Various Solvents at 25°C[a]

Solvent	Configuration	$[m']_{233}$	$[\theta]_{222}$
Chloroform	D	+9700	+18300
	L	−9400	−17600
Diethyl ether	D	+11900	+32200
	L	−9900	−23100
n-Hexane	D	+3200	+14300
	L	−8900	−19800
THF	D	+10100	+30800
	L	−11000	−28000
Carbon tetrachloride	L	−7900	
TFA	D	+1800	
	L	−1800	

[a] MW 18,300 for L-polymer and 29,500 for D-polymer.

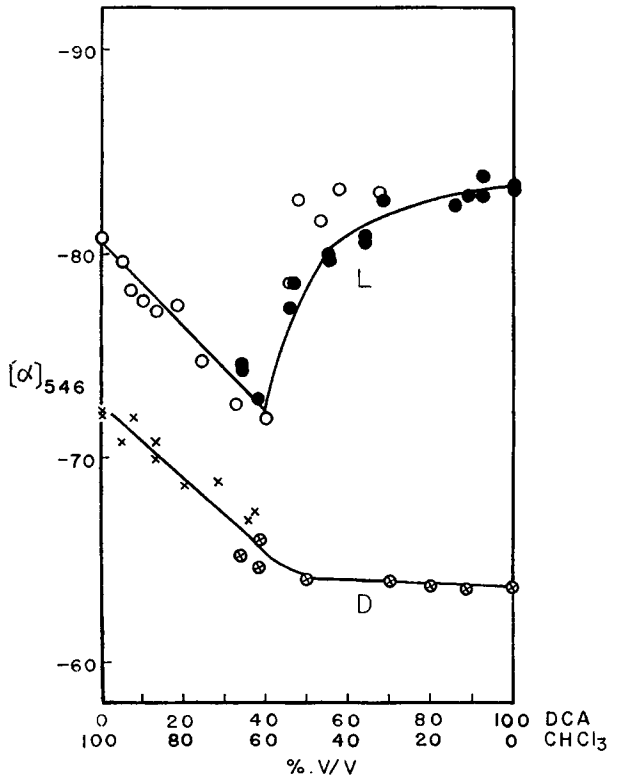

Fig. 4. Specific rotation $[\alpha]_{546}$ values of poly[γ-(*l*)-menthyl D- and L-glutamates] of varying solvent composition: (○) L-polymer and (×) D-polymer dissolved in chloroform (solution diluted with DCA); (●) L-polymer and (⊗) D-polymer dissolved in DCA (solution diluted with chloroform); at room temperature.

occurred at 68% DCA–32% chloroform. Plots of the $[\alpha]_{546}$ values versus the solvent composition of poly[γ-(*l*)-menthyl L- and D-glutamates] are shown in Figure 4.

These polymers cause a gradual helix–coil transition at about 40% DCA. Poly[γ-(*l*)-mentyl L-glutamate] gradually loses its helical structure upon an increase in the DCA, whereupon the specific rotation decreases to a minimal value of $[\alpha]_{546} = -72°$ at 40% DCA, finally reaching $[\alpha]_{546} = -83°$ at above 40% DCA. On the other hand, poly[γ-(*l*)-menthyl D-glutamate] decreases its optical rotation at below 40% DCA and reaches a constant value of $[\alpha]_{546} = -64°$. In comparison with PBLG, the helical structure of poly[γ-(*l*)-menthyl L- and D-glutamates] are made rather unstable by the introduction of the γ-menthyl group.

These poly[γ-(*l*)-menthyl L- and D-glutamates] are thought to have the helical and the random coil conformations as their secondary structures in mixed DCA–chloroform solvents. In the random coil region, the $[\alpha]_{546}$ values of L- and D-polypeptides are different. This result can be considered that the asymmetry of the *l*-menthyl chromophore in the side chain causes an extraordinary optical rotation; that is, this phenomenon arises from interaction between the chromophore in the side chain and the optically active centers in the polypeptide main chain, as has been described by Goodman and Kossay.[25]

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