stirring at 95 °C until it became homogeneous. This required less than 1 h. Freshly cut sodium metal (0.40 g, 0.018 mol) was then added, and the resulting pink reaction mixture was heated at 95 °C and stirred for 1.5 h. Approximately one-half of the excess phenol was then removed by vacuum distillation. The concentrated reaction mixture was allowed to cool to 40 °C and concentrated HCl (10 mL) was added, slowly, with stirring. The resulting suspension was poured into 20 volumes of methanol to precipitate the polymer, which was then washed with methanol and dried in vacuo. The yield was 0.54 g. Most of this sample was rephenylated, using the procedure described above, but a portion of it was reprecipitated from acetone into methanol, and then dried in vacuo. The infrared spectrum of this portion contained a strong absorption band at 1702 cm^{-1}. A portion of this sample was methylated with diazomethane.[1] The ^1H NMR spectrum of the resulting product contained a strong resonance at ~3.5. Its intensity indicated that approximately 11.5% of the units were methyl methacrylate units.

Characterization of the Completely Phenylated Polymer (V). The $POCl_3$–phenol and $NaOC_6H_5$–phenol reactions were conducted once more to obtain a material that analyzed satisfactorily for poly(phenyl methacrylate).

Anal. Calcd for $(C_{10}H_{10}O_2)_n$: C, 74.06; H, 6.22; Cl, 0.00; P, 0.00. Found: C, 74.12; H, 6.34; Cl, <0.05; P, <0.05.

The infrared spectrum of atactic poly(phenyl methacrylate) derived from atactic poly(methacrylic acid) is compared in Figure 1 with the spectrum of poly(phenyl methacrylate) derived directly from the monomer.

Reaction of Completely Phenylated Polymer with Sodium Methoxide. Finely divided product obtained from the phenylation of the atactic phenyl methacrylate–methacrylic acid copolymer (0.16 g, 0.0010 mol) was added to degassed dioxane (30 mL) under nitrogen, and the mixture was heated with stirring at 50 °C until it became homogeneous. This required 1 h. Degassed methanol (3.2 g, 0.10 mol) was added dropwise during 1 h. Freshly cut sodium metal (0.25 g, 0.01 mol) was then added, and the resulting reaction mixture was heated at 50 °C, under nitrogen and stirred for 24 h. The reaction mixture was allowed to cool to room temperature and was poured into 20 volumes of methanol to precipitate the polymer as a white powder. The yield was essentially quantitative (0.093 g, 0.00093 mol). The polymer was reprecipitated from acetone into methanol, and then dried in vacuo. The ^1H NMR spectrum of this polymer contained no resonances assignable to aromatic protons.

Viscosity Measurements. Intrinsic viscosities were determined in acetone solution at 25 °C using a Ubbelohde dilution viscometer. The viscosity-average molecular weights were calculated by the relationships given for poly(methyl methacrylate) by Meyerhoff and Schulz[19] and for poly(phenyl methacrylate) by Hadjichristidis and co-workers.[20] Degrees of polymerizations were calculated by dividing the viscosity-average molecular weights of the polymers by the molecular weights of the respective monomers.

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N-Substituted Poly(α-amino acids). 1. Synthesis and Characterization of Poly(*N*-methyl-γ-methyl L-glutamate) and Poly(*N*-methyl-γ-ethyl L-glutamate)[1]

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ABSTRACT: The synthesis of high molecular weight poly(*N*-methyl-γ-methyl L-glutamate) and poly(*N*-methyl-γ-ethyl L-glutamate) has been performed by permethylation of poly(γ-methyl- and γ-ethyl L-glutamate). Among the various techniques known for low molecular weight materials, only the procedure introduced by Lederer's group[2a] proved workable in the case of high molecular weight substrates. The degree of methylation was always higher than 95% as shown by elemental analysis, amino acid analysis, and IR techniques. Attempts to obtain polymers starting from N-substituted NCAs other than proline NCA, sarcosine NCA, and *N*-methylalanine NCA failed in all cases. The N-methylated polymers are readily soluble in dimethylformamide, 2,2,2-trifluoroethanol, tetrahydrofurane, and methylene chloride, while they sparingly dissolve in water and methanol. Preliminary CD measurements suggest that the above N-methylated polypeptides adopt an all-trans conformation in solvents such as TFE, methanol, and water.

N-substituted polypeptides exhibit very interesting conformational properties, due to the lack of hydrogen bonding and to the possibility of cis and trans isomerism around the peptide bond. It is well known that poly(L-proline) can exist in two forms. Form I is a rather compact right-handed helical structure containing all cis peptide bonds.[2b-4] Isomerization to trans amide configuration leads to poly(L-proline) II, whose structure is a rather extended

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left-handed helix.[2b-4] The interconversion between the two forms has been investigated by several methods, and it was shown that ^{13}C magnetic resonance is a powerful method for an unambiguous assignment of trans or cis configuration of the peptide bond.[5] It has also been shown that in concentrated salt solutions there is a random distribution of cis and trans peptide bonds, with consequent disordering of poly(L-proline) chains.[6-9] In the case of the simplest polyimino acid, polysarcosine, it has been found that in dimethyl sulfoxide there is a nearly random distribution of cis and trans peptide configurations, and that the trans configuration becomes strongly preferred in trifluoroethanol,[10] in trifluoroacetic acid,[10,11] and in water.[10] Cis–trans isomerization has been observed in a series of N-substituted polyglycines.[11] On increasing the bulkiness of the N substituents from ethyl to propyl and butyl groups the cis configuration becomes increasingly preferred.[11]

Another example of a widely investigated polymer is poly(*N*-methyl L-alanine), first synthesized by Goodman and co-workers.[12] Contrary to polysarcosine, this polymer assumes a helical conformation in solution with only trans peptide bonds.[12] Potential energy calculations show that the most probable conformation is a threefold, right-handed helix with φ and ψ dihedral angles of 30 and 250°, respectively.[12,14] In the presence of trifluoroacetic acid a random mixture of cis and trans peptide bonds is observed and the polymer undergoes conformational transition to a disordered state.[15] Moreover, the existence of cis peptide bonds is well established for N-methylated amino acid and proline residues in linear and cyclic peptides and in proteins, in solution[16-23] and in the solid state.[26-28]

Two different patterns can be followed in order to obtain N-substituted polypeptides: (i) polymerization of the appropriate NCA; and (ii) N-alkylation of a unsubstituted polypeptide.

Ballard and Bamford[29] investigated the stereochemical aspects of the reaction between substituted glycine NCAs and primary and secondary bases. In the case of bulky secondary bases they found that the reaction rate is always very slow when N substitution or C and N disubstitution at the glycine residues occurs. The only exception is proline NCA since the fused rings reduce the steric interference between the monomer and the attacking base. As a consequence, polymerization of bulky N-substituted or N- and C-disubstituted NCAs should be in general very difficult. The few examples reported in the literature,[12,30] which deal with the polymerization of *N*-methyl-L-alanine NCA and *N*-phenylglycine NCA, strongly support the above conclusion.

On the other hand, N-methylation of natural and synthetic amino acid derivatives and of small peptides can be achieved by several procedures.[2a,31-38] In all cases methylation is performed in the presence of various bases, using methyl iodide as the alkylating agent.

In the present paper we extend the above techniques to high molecular weight materials. In particular we report the synthesis and preliminary conformational studies of poly(N-methyl-γ-methyl L-glutamate) as well as of poly(*N*-methyl-γ-ethyl L-glutamate). The synthesis of new N-substituted NCAs and several attempts of polymerization under various experimental conditions are also reported.

Experimental Section

Materials. Reagents and Solvents. Reagent grade dioxane and dimethylformamide (DMF) were dried according to the literature.[39] Reagent grade ethyl acetate and dimethyl sulfoxide (Me_2SO) were dried over molecular sieves and distilled. Reagent grade acetonitrile was dried over P_2O_5 and recovered by distillation. Ethyl ether and petroleum ether were distilled over sodium metal. Primary, secondary, and tertiary amines were purified according to the literature.[39] Ag_2O was obtained by precipitation from a solution of $AgNO_3$ with NaOH. Reagent grade L-glutamic acid, L-alanine, L-phenylalanine, glycine, CH_3J, NaH, $NaBH_4$, KO-*t*-Bu, and 2,2,2-trifluoroethanol (TFE) were purchased from Fluka Chem. Co.

***N*-Benzyl-L-alanine** was prepared by reductive alkylation of L-alanine according to previous literature,[40] mp 255–256 °C (lit. mp 255 °C). Anal. Calcd: C, 67.02; H, 7.26, N, 7.82. Found: C, 67.00; H, 7.25; N, 7.83.

***N*-Benzyl-*N*-methyl-L-phenylalanine** was prepared according to the literature,[40] mp 220 °C (lit. mp 220–222 °C). Anal. Calcd: C, 75.83; H, 7.06; N, 5.20. Found: C, 75.03; H, 6.79; N, 5.32.

***N*-Methyl-L-phenylalanine** was prepared by hydrogenation of *N*-benzyl-*N*-methyl-L-phenylalanine according to the literature,[40] mp 260–261 °C (lit. mp 260 °C). Anal. Calcd: C, 67.02; H, 7.26; N, 7.82. Found: C, 66.42; H, 7.20; N, 7.22.

***N*,*N*-Dibenzylglycine** was obtained by reductive alkylation of glycine according to the method of Quitt et al.,[40] mp 198–200 °C (lit. mp 198–200 °C). Anal. Calcd: C, 75.29; H, 6.67; N, 5.50. Found: C, 75.07; H, 6.65; N, 5.34.

***N*-Benzylglycine** was prepared as the hydrochloride according to Haas,[41] mp 223–226 °C (lit. mp 223–228 °C). Anal. Calcd: C, 53.60; H, 5.96; N, 6.94. Found: C, 53.25; H, 5.94; N, 6.81.

γ-Methyl L-glutamate was prepared according to Hanby et al.,[42] mp 182 °C (lit. mp 182 °C). Anal. Calcd: C 44.72; H, 6.83; N, 8.69. Found: C, 44.55; H, 6.64; N, 8.70.

γ-Ethyl L-glutamate was prepared as previously reported,[43] mp 193 °C (lit. mp 194 °C). Anal. Calcd: C, 48.00; H, 7.42; N, 8.00. Found: C 47.91; H, 7.50; N, 7.98.

***N*-Benzyl-L-alanine NCA.** *N*-Benzyl-L-alanine (10 g) was suspended in 300 mL of dry dioxane. $COCl_2$ was bubbled under vigorous stirring for 1 h at 70 °C. Nitrogen was then bubbled through the clear solution for 2 h. The solvent was removed under reduced pressure and the product was dissolved in ethyl ether. The solution was decolored with charcoal and the pure NCA was precipitated with petroleum ether: yield 85%; mp 72 °C. Anal. Calcd: C, 64.4; H, 5.36; N, 6.83. Found: C, 64.7; H, 5.48; N, 6.65.

***N*-Methyl-L-phenylalanine NCA.** *N*-Methyl-L-phenylalanine (10 g) was suspended in 300 mL of dry dioxane. $COCL_2$ was bubbled under vigorous stirring for 1 h at 70 °C. Nitrogen was then bubbled through the clear solution for 2 h. The solvent was removed under reduced pressure and the crude product was recrystallized from methylene chloride/ethyl ether: yield 70%; mp 137–138 °C. Anal. Calcd: C, 64.39; H, 5.36; N, 6.83. Found: C, 64.22; H, 5.41; N, 6.78.

***N*-Benzylglycine NCA.** *N*-Benzylglycine (10 g) was suspended in 300 mL of dry dioxane. $COCl_2$ was bubbled under vigorous stirring for 1 h at 70 °C. Nitrogen was then bubbled through the clear solution for 2 h. The solvent was removed under reduced pressure and the crude product kept under high vacuum for 2 h at 60 °C and recrystallized from ethyl ether: yield 40%; mp 114–115 °C. Anal. Calcd: C, 62.80; H, 4.72; N, 7.33. Found: C, 62.34; H, 4.72; N, 7.15.

γ-Ethyl L-glutamate NCA was prepared as previously reported,[44] mp 71–72 °C. Anal. Calcd: C, 47.76; H, 5.47; N, 6.96. Found: C, 47.59; H, 5.57; N, 6.88.

γ-Methyl L-glutamate NCA was prepared as reported by Hanby et al,[42] mp 99–100 °C. Anal. Calcd: C, 44.92; H, 4.81; N, 7.48. Found: C, 44.69; H, 4.90; N, 7.52.

Poly(γ-methyl L-glutamate). γ-Methyl L-glutamate NCA (3 g) was polymerized in dioxane (100 mL) using triethylamine as the initiator (M/I = 30). The polymer was recovered by precipitation with ethyl ether $[\eta]$ = 0.62 dL/g in dichloroacetic acid. Anal. Calcd: C, 50.35; H, 6.29; N 9.79. Found: C, 50.20; H, 6.32; N, 9.71.

Poly(γ-ethyl L-glutamate). γ-Ethyl L-glutamate NCA (3 g) was polymerized in 100 mL of dioxane using diisopropylamine as the initiator (M/I = 40), $[\eta]$ = 2.25 dL/g in dichloroacetic acid. Anal. Calcd: C, 53.50; H, 7.00, N, 8.92. Found: C, 53.39; H, 7.21; N, 8.90.

Methylation Procedures. Poly(*N*-methyl-γ-methyl L-glutamate). Poly(γ-methyl L-glutamate) (1 g) was dissolved in 50 mL of dry DMF. Ag_2O (10 g) and CH_3J (15 mL) were then

Table I
Analytical Results for the N-Methylation of Poly(γ-ethyl L-glutamate) in Three Experiments Run under the Same Conditions, Using the CH_3J/Ag_2O System as Reported in the Experimental Section

expt no.	yield,[d] %	elemental anal.,[a] % C	N	H	C/N	% of N-methylation[b]	% of trans esterification[c]
1	47	54.27	8.10	7.38	6.70	94.2	11.8
2	36	54.75	8.07	7.43	6.78	96.6	4.8
3	42	54.24	8.08	7.31	6.71	95.8	12.2

[a] Theoretical elemental analysis for poly(*N*-methyl-γ-ethyl L-glutamate): C, 56.14; N, 8.19; H, 7.60; C/N 6.85. [b] From free glutamic acid determination by amino acid analysis of the hydrolyzed polymer. [c] Obtained by combined elemental analysis and amino acid analysis data. [d] Percent of the starting material recovered as completely N-methylated product according to the procedure described in the Experimental Section.

added. The reaction mixture was stirred for 3 days at room temperature. The solid material was separated by centrifugation and the clear solution was exhaustively dialyzed against DMF. The solvent was removed under reduced pressure and the polymer obtained as a white powder, yield 13%. Anal. Calcd: C, 53.50; H, 7.00; N, 8.92. Found: C, 52.30; H, 6.81; N, 8.73.

Poly(*N*-methyl-γ-ethyl L-glutamate). Poly(γ-ethyl L-glutamate) (1 g) was dissolved in 50 mL of dry DMF. Ag_2O (10 g) and CH_3J (15 mL) were then added. The reaction mixture was stirred 24 h at 45 °C. The solid material was separated by centrifugation and the clear solution was exhaustively dialyzed against DMF. The N-methylated polymer was precipitated as a white powder pouring the DMF solution into ethyl ether. The precipitate was filtered off and dried under vacuum. The analytical data relative to various preparations are reported in Table I.

Measurements. The amino acid analyses of the hydrolized N-methylated polymers were performed on a Carlo Erba 3A 27 amino acid analyzer. Acid hydrolyses were made in 6 N HCl for 22 h at 110 °C in evacuated vials.

IR measurements were performed on a Perkin-Elmer 580 spectrometer. Films of the polymeric materials were obtained by evaporating a concentrated TFE solution on KBr disks. After evaporation of the solvent the films were accurately dried under vacuum at 35 °C.

Circular dichroism measurements were carried out with a Cary 61 recording spectropolarimeter. Fused quartz optical cells with Suprasil windows were used.

Results and Discussion

Polymerization of N-Substituted NCAs. A very large number of polymerization attempts have been performed starting from the following N-substituted NCAs: *N*-benzylglycine, *N*-benzyl-L-alanine, and *N*-methyl-L-phenylalanine. The solvents used for our experiments were dioxane, DMF, and acetonitrile. Initiators such as primary and secondary amines and strong bases (sodium methoxide and sodium *p*-nitrophenoxide) were employed, with widely ranging monomer to initiator ratios.

In most experiments a white powder was obtained after long periods of time (1 week or longer). The presence of typical amide bands was observed by IR measurements. The elemental analyses exactly correspond to the N-substituted amino acid residue. Molecular weight determinations suggest the formation of diketopyperazines. In no case were we able to isolate polymeric materials.

Synthesis of Poly(*N*-methyl-γ-methyl glutamate). (1) Experiments Using the Procedure Introduced by Lederer's Group.[2a] Various attempts of N-methylation have been made starting from poly(γ-methyl L-glutamate), using CH_3J as the methylating agent and Ag_2O as the base in DMF solution.[2a] The polymer, Ag_2O and CH_3J concentrations and relative amounts have been varied over a wide range. The reaction has also been studied as a function of time and temperature. The best results have been obtained using the conditions reported in the Experimental Section. In all experiments performed at room temperature no more than 13% of the theoretical amount of polymer was obtained. Loss of polymer during the dialysis process cannot be responsible for this fact since the starting polymer does not pass through the membrane and extensive degradation during methylation is not to be expected. On the other hand by treatment of a polymer solution in DMF (0.1 g in 5 mL) with Ag_2O (1 g) in the absence of CH_3J, we observed precipitation of the polymer on the metal oxide. In no way could we recover the polymer which remains adsorbed on the oxide surface. The reason for the low yields of N-methylated polymer should therefore rest on the poor solubility of the starting polymer in the reaction medium. The solubility is further decreased by addition of methyl iodide. Experiments performed at higher temperatures (45 °C) gave much better yields (up to 40%), but in all cases we obtained N-methylated samples with very poor analysis.

(2) Experiments Using Alternative N-Methylation Methods. Attempts have been made of performing N-methylation of poly(γ-methyl L-glutamate) using strong bases, soluble in the reaction medium, instead of Ag_2O. The system CH_3J–potassium terbutylate in Me_2SO has been reported to provoke very fast N-methylation of peptide groups.[38] All our attempts failed since the polymer is much less reactive than small peptides, and direct methylation of the base by methyl iodide becomes by far the predominant reaction. Under our experimental conditions total methylation of the base is complete within a few minutes, with very little, if any, N-methylation of the polymer.

Substantially the same results have been obtained using sodium hydride and CH_3J in Me_2SO.[32,33,37]

Synthesis of Poly(*N*-methyl-γ-ethyl L-glutamate). Since the main reason for low yields obtained in N-methylation of poly(γ-methyl L-glutamate) was the low solubility of the polymer in the reaction medium, methylation experiments have been carried out using poly(γ-ethyl L-glutamate), which is much more soluble in DMF. Contrary to poly(γ-methyl L-glutamate), as far as yield, elemental analysis, and time of reaction are concerned, the best results have been obtained at temperatures of the order of 45 °C.

Table I summarizes the results of three different experiments. The above data indicate that the yield of N-methylated polymer is always better than 35% and the extent of N-methylation, as determined by amino acid analysis and infrared spectroscopy, is always higher than 94%.

From the extent of N-methylation and from elemental analysis data the percent of trans methylation of polymer side chains was also estimated. In our case about 10% of the ethyl groups have been substituted by methyl groups, the final product being actually a random copolymer of *N*-methyl-γ-ethyl glutamate and *N*-methyl-γ-methyl glutamate. We will see in the next section that this fact

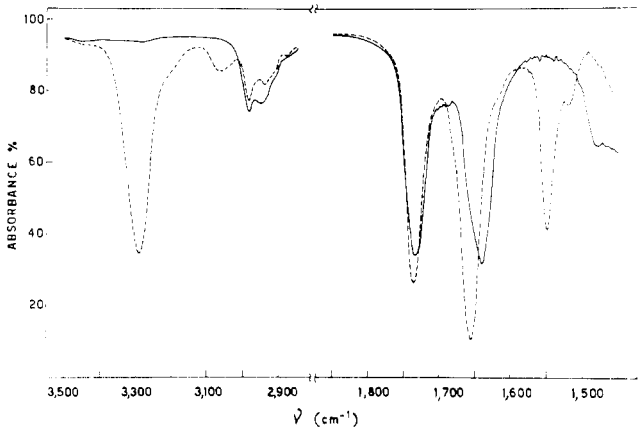

Figure 1. IR spectra of poly(*N*-methyl-γ-ethyl L-glutamate) (solid line) and of poly(γ-ethyl L-glutamate) (dashed line) in the 3500–2800 and 1800–1400 cm^{-1} regions. For both polymers films were cast from TFE solutions.

does not influence the conformational properties of the polymer.

Poly(*N*-methyl-γ-ethyl L-glutamate) is soluble in DMF, chloroform, methylene chloride, TFE, and tetrahydrofuran, while it sparingly dissolves in water (≃0.02 g/L) and methanol (≃0.25 g/L).

Infrared Absorption Measurements. Infrared absorption measurements have been carried out either on films obtained by evaporation of polymer solutions in TFE or in KBr pellets. In the region between 3500 and 3000 cm^{-1} the characteristic amide bands corresponding to the N–H stretching vibrations are virtually absent on N-methylated samples (Figure 1). Furthermore the intensity of the bands corresponding to the C–H stretching vibrations is enhanced consistently with the introduction of one methyl group per structural unit. In the region 1800–1400 cm^{-1} the typical ester band is present at 1735 cm^{-1}, which remains unchanged after N-methylation. Taking this band as internal reference, the extent of nonmethylated residual peptide groups was estimated from the relative intensity of the amide A bands before and after N-methylation. The extent of N-substitution was always in the range 97–99%. This figure is a little higher than the values obtained by determination of free glutamic acid after total hydrolysis of N-methylated polymers in 6 M HCl at 110 °C for 24 h. It is not unlikely that the drastic hydrolysis conditions lead to 2–3% dealkylation of *N*-methylglutamic acid, yielding free glutamic acid.

The amide I band, which is almost entirely due to the C=O stretching vibration, shifts to 1637 cm^{-1} in the N-methylated samples. This figure is consistent with infrared results obtained on poly(*N*-methylalanine)[15] (amide I band at 1635 cm^{-1}) and poly(proline)[45] forms I and II (amide I band at 1639 cm^{-1}). Differently from N-unsubstituted polypeptides,[46] the amide I band seems to be scarcely dependent upon the conformation of the backbone in these cases.

We also observe that the amide II band at 1550 cm^{-1} disappears in N-methylated polymers while a new band is present at 1480 cm^{-1}. Amide II is assigned in part to N–H in-plane bending and in part to the C–N stretching vibration.[46] N-methylation breaks the coupling of the two modes of vibration and causes a red shift of the C–N vibration.

Circular Dichroism Studies. The conformational properties of poly(N-methyl-γ-methyl L-glutamate) and poly(*N*-methyl-γ-ethyl L-glutamate) in TFE have been investigated using CD techniques. The CD patterns of the two N-substituted polymers are shown in Figure 2. A

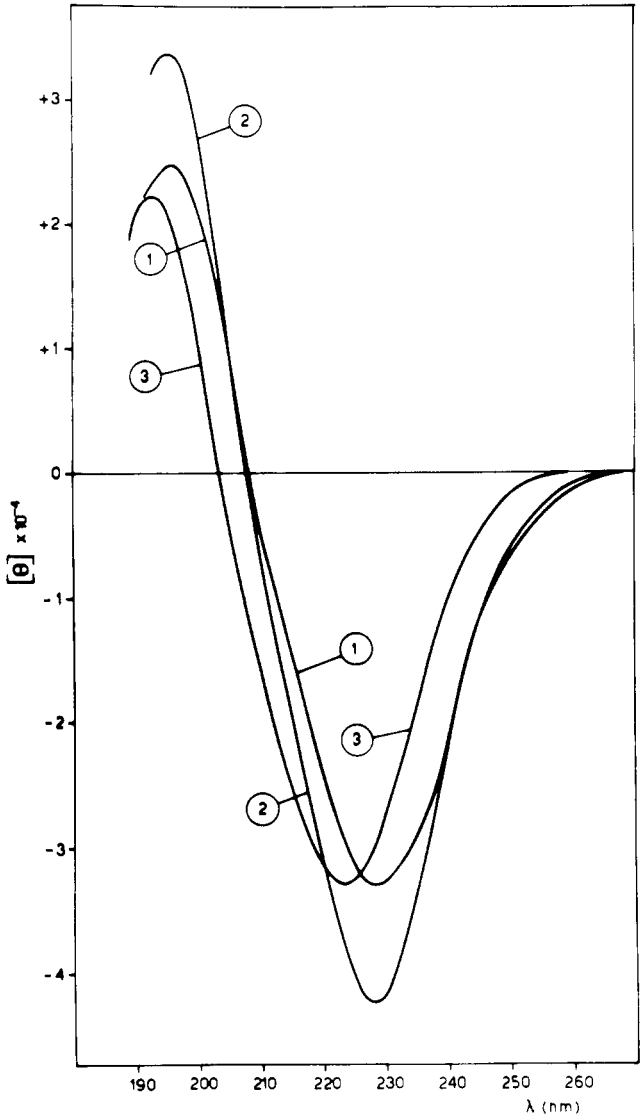

Figure 2. CD spectrum of poly(*N*-methyl-γ-methyl L-glutamate) (1); poly(*N*-methyl-γ-ethyl L-glutamate) (2); and poly(*N*-methyl-L-alanine) (3) (from ref 15) in TFE.

broad asymmetric negative band at 228 nm along with a positive peak at 196 nm are present in both cases. Since no substantial difference between the CD patterns of the methyl and ethyl ester derivatives of poly(*N*-methyl-L-glutamic acid) is evident, it follows that the two polymers exhibit the same conformational properties in TFE solution. The molar ellipticity values were found to be −42 500 and +33 500 at the maximum wavelengths for poly(*N*-methyl-γ-ethyl L-glutamate) and −31 000 and +23 000 for poly(*N*-methyl-γ-methyl L-glutamate). These spectral properties do not match those of poly(L-proline) forms I and II.[47] On the contrary there are strong similarities between our results and the CD pattern of poly(*N*-methylalanine) first reported by Goodman and coworkers.[15]

The shape of the spectrum is identical. However, we observe a red shift by 4–5 nm of both negative and positive bands and higher intensities. These facts are probably related to differences in molecular weight, since our samples were obtained by modification of high molecular weight compounds, while poly(*N*-methyl-L-alanine) was prepared by polymerization of the corresponding NCA,[31] which is known to polymerize with difficulty, yielding low molecular weight materials.

Conformational studies carried out using CD and NMR

techniques showed that poly(*N*-methyl-L-alanine) exists in a helical structure in which all peptide bonds are in a trans configuration.[15] Conformational energy calculations independently carried out by two research groups showed that the lowest energy structure is a right-handed helix, whose φ and ψ dihedral angles are 30 and 250°, respectively.[13,14] On the basis of the CD pattern we propose for our polymers the same conformation as poly(*N*-methyl-L-alanine). Under this hypothesis the negative, asymmetric CD band at 229 nm should arise from the overlapping of $n \rightarrow \pi^*$ peptide transition and the low energy component of the $\pi \rightarrow \pi^*$ transition. The positive band at 196 nm should be assigned to the high energy component of a split $\pi \rightarrow \pi^*$ peptide transition.

CD spectra recorded in water, methanol, and tetrahydrofuran gave substantially the same results. The only appreciable difference is a small red shift of the long wavelength band on decreasing solvent polarity. This trend is consistent with the assignment of this band to a $n \rightarrow \pi^*$ transition.

Conclusions

The synthesis of N-methylated derivatives of methyl and ethyl esters of poly(L-glutamic acid) has been achieved using a procedure initially proposed by Lederer for N-methylation of oligopeptides.[2a] Yields higher than 35% have been obtained using the ethyl ester polymer as starting material in DMF, the modified polymer containing more than 95% of N-methylated residues.

Preliminary CD measurements indicate that the N-substituted polymers in TFE probably assume the same helical conformation as poly(*N*-methyl-L-alanine).[15]

More detailed conformational studies, including IR and ^{13}C and proton magnetic resonance measurements, on poly(*N*-methyl-γ-ethyl L-glutamate) and on poly(*N*-methyl-L-glutamic acid) are in progress in our laboratories and will be reported elsewhere.

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