Macromolecules **1996,** *29,* 3545−3551 **3545**

Fluorinated Poly(α,L-glutamate)s

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Received July 24, 1995; Revised Manuscript Received December 20, 1995[⊗]

ABSTRACT: Poly(α,L-glutamate)s carrying C_8, C_{10}, and C_{12} fluorinated side chains were synthesized by polymerization of the corresponding amino acid *N*-carboxyanhydrides. Contact angle measurements with water were used to assess the effects of fluorination on the surface energies of films of the resulting polypeptides. The wettability of the polymers was found to decrease with increasing fluorine content, as expected. A remarkably high contact angle (121°) was measured for the homopolymer carrying C_{12} fluorinated side chains, indicating a surface consisting of closely packed trifluoromethyl groups. Side chain crystallization, consistent with the formation of such a surface, was suggested by the results of X-ray diffraction and calorimetric measurements.

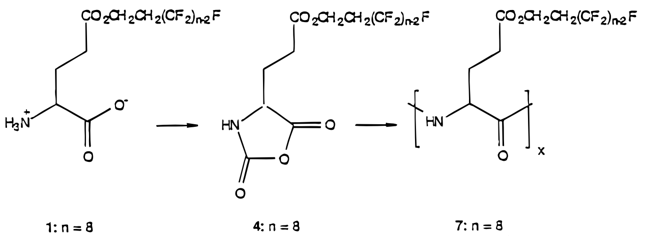
Introduction

Fluorinated polymers exhibit special properties, including stability at high temperatures, toughness and flexibility at very low temperatures, nonadhesiveness, insolubility, chemical inertness, and, in some cases, biocompatibility.[1] Incorporation of fluorinated amino acids has been proposed as a means to impart some of these properties to polypeptides.

The synthesis of polypeptides containing D,L-trifluoroalanine (TFA) has been reported in a previous paper,[2] and we have found that the surface energies of films of copolypeptides of TFA and γ-benzyl L-glutamate (BLG) are significantly reduced compared to that of the PBLG homopolymer only when the fluorinated monomer is present at a significant level (>20%). In some circumstances, it would be desirable to use fluorinated comonomers that would alter polymer properties even when present in very small amounts. Möller and co-workers have shown that copolymers of styrene with monomers carrying C_4F_9 and C_8F_{17} substituents have very low surface energies, even when only a few percent of the fluorinated comonomer is incorporated.[3] An extremely low critical surface tension of 6 mN/m was found for the homopolymer with the perfluorooctyl side chain. This value is as low as that reported for monolayers of perfluorocarbon acids or thiols[4] and is indicative of a surface composed of closely packed trifluoromethyl groups. Differential scanning calorimetry on the *p*-(((perfluorodecylethylene)oxy)methyl)styrene homopolymer showed a first-order phase transition at 82 °C, which was attributed to melting of side chain crystals. It seems likely that in such systems, surface energy is influenced by side chain crystallization, which leads to highly ordered fluorocarbon surfaces. Similar very low surface energies have been reported for acrylate and methacrylate polymers[4−6] and for polysiloxanes with long fluorinated side chains.[7,8] These results prompted us to undertake synthesis of polypeptides prepared from γ-esters of glutamic acid with long fluorinated alcohols.

Poly(α,L-glutamate)s have attracted attention both as model polymers for theoretical studies and as products for potential commercial applications.[9] Their most interesting feature is their ability to exist in a well-defined α-helical conformation independent of the side chain substitution and to maintain that structure in solution. PBLG is the most thoroughly studied of such polymers, but various poly(γ-alkyl α,L-glutamate)s with long paraffinic chains (PALGs) have been of increasing interest, owing to their ability to form thermotropic liquid crystals and ordered Langmuir−Blodgett films.[10−14] The liquid crystalline properties of such polymers are a result of the combination of the rigid-rod character imparted by the α-helical structure and the flexible aliphatic side chains, which melt and act as a solvent for the backbone. PALGs with side chains varying from 1 to 18 carbon atoms have been synthesized and their thermal and structural properties have been reported.[10] It has been suggested that the α-helical conformation is not affected by the side chains even when the latter are long enough to crystallize. In that case, the spatial arrangement of the backbone chains is dictated by the packing of the side chains, and as a result, the typical hexagonal lattice is replaced by a layered structure.[12]

PALGs can be prepared either by polymerization of the corresponding amino acid *N*-carboxyanhydrides (NCAs) or by ester interchange reactions with PBLG or poly(γ-methyl α,L-glutamate) (PMLG).[9,10] Poly(α,L-glutamate)s containing fluorinated side chains have been synthesized from PMLG by ester interchange reactions with fluorinated alcohols,[15] and the N_2 and O_2 permeabilities of films of these compounds have been measured. We report herein the synthesis of γ-esters of glutamic acid with alcohols of the general formula $F(CF_2)_{n-2}(CH_2)_2OH$, with n = 8, 10, and 12 (**1−3** respectively), conversion to the corresponding NCAs, polymerization of the NCAs, and copolymerization with γ-benzyl L-glutamate NCA. The effects of side chain length on the structure, crystallinity, and surface properties of the polypeptides[16] are described.



1: n = 8
2: n = 10
3: n = 12

4: n = 8
5: n = 10
6: n = 12

7: n = 8
8: n = 10
9: n = 12

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[⊗] Abstract published in *Advance ACS Abstracts*, April 1, 1996.

S0024-9297(95)01070-9 CCC: $12.00

Experimental Section

Materials. 1*H*,1*H*,2*H*,2*H*-Perfluorodecanol, 1*H*,1*H*,2*H*,2*H*-perfluorododecanol, and 1*H*,1*H*,2*H*,2*H*-perfluorooctanol were used as received from PCR, Inc. γ-Benzyl L-glutamate was obtained from Fisher Scientific Co. and used without purification. Tetrahydrofuran (THF, Fisher) was distilled (bp 65−67 °C) from Na/benzophenone. Triethylamine (Aldrich Chemical Co.) was distilled (bp 89 °C) from calcium hydride. Triphosgene was used as received from Aldrich.

Methods. Nuclear magnetic resonance spectra were recorded on a Bruker AC-200 (200 MHz ^{1}H, 188 MHz ^{19}F) spectrometer. ^{1}H chemical shifts are reported as parts per million downfield from tetramethylsilane; ^{19}F NMR shifts are reported as parts per million downfield from trifluoroacetic acid. Melting points were measured on a Fisher-Johns melting point apparatus and are uncorrected. Films for contact angle measurements were molded on a Carver Model C laboratory press. The samples were kept at 130 °C (115 °C for polymers with C_{12} side chains) for 1 min and then compressed at 1500 psi for an additional minute at the same temperature. Contact angle measurements with double-distilled water were done using a Ramé-Hart goniometer. Five measurements were made on each film at different locations. Differential scanning calorimetric measurements were performed on a Perkin-Elmer DSC 7 analyzer. Samples were in powder form. After the first run (25 to 200 °C, 80 °C/min), the samples were quenched to 25 °C. The second and third runs (25 to 250 °C, 40 °C/min) were followed by cooling (40 °C/min) to 25 °C. Infrared spectra were obtained on a Perkin-Elmer 1600 Fourier transform spectrophotometer. Samples were either KBr pellets or films prepared by evaporation of THF solutions on NaCl plates. X-ray diffraction photographs were obtained with Ni-filtered Cu Kα (1.54 Å) radiation from a sealed tube source. Wide-angle patterns were recorded using an evacuated flat-plat Statton camera with a specimen to film distance of 53 mm; a Rigaku-Denki X-ray camera, with a specimen to film distance of 230 mm, was used to record low-angle patterns. Powder samples were examined in the form in which they were isolated from the polymerization reaction. Intrinsic viscosity measurements in dichloroacetic acid were performed with a Cannon 100 Ubbelohde viscometer. A water bath with a Lauda temperature controller was used to regulate the temperature to within 0.1 °C. Elemental analyses were performed by the Microanalytical Laboratory, Office of Research Services, University of Massachusetts, Amherst, MA.

Preparations. Esterification of L-Glutamic Acid. A typical esterification procedure was as follows. A 250-mL three-neck round-bottom flask equipped with an addition funnel and a reflux condenser charged with 3A molecular sieves was charged with L-glutamic acid (13.23 g, 0.09 mol), *tert*-butyl alcohol (100 mL), concentrated sulfuric acid (7.8 mL, 0.14 mol), and benzene (18 mL). The mixture was stirred and heated to ca. 70 °C until complete dissolution occurred (typically 20−30 min). 1*H*,1*H*,2*H*,2*H*-Perfluorooctanol (39 mL, 0.18 mol) was added dropwise, and the solution was stirred and maintained at 65−70 °C for 24 h. The initially clear solution became cloudy within an hour after addition of the fluorinated alcohol. The final mixture, which looked like an emulsion, was evaporated to dryness. *tert*-Butyl alcohol (50 mL) was added and the product was stirred until completely dissolved. Triethylamine (7.2 mL, 0.05 mol) was added dropwise to neutralize the excess sulfuric acid and was followed by the addition of water (22.5 mL) and 95% ethanol (315 mL). Additional triethylamine (27.0 mL, 0.19 mol) was added dropwise. The mixture was stirred for 30 min to allow complete precipitation of the ester and then centrifuged until the supernatant became clear. The recovered precipitate was slurried for 20 min at 65 °C with 240 mL of water and recentrifuged hot. The supernatant was decanted, and the precipitate was washed with 60 mL each of methanol and ethyl ether and then dried in a vacuum oven (50 °C) overnight. The crude ester (**1**), obtained in the form of a white powder (24.2 g, 54.4% yield), was recrystallized from an isopropyl alcohol/water (2/1) mixture (80 °C), washed again with methanol and ether, and dried to give 15.1 g (0.031 mol, 34% yield) of the pure ester. Similar yields were obtained from reactions run without stoichiometric excesses of the fluorinated alcohol. ^{1}H NMR (DMSO-d_6/trifluoroacetic acid): δ 2.13 (m, 2H, β-CH$_2$), 2.65 (m, 4H, γ-CH$_2$ and CH$_2$CF$_2$), 4.03 (m, 1H, α-CH), 4.42 (triplet, 2H, OCH$_2$), 8.33 (s, 3H, NH$_3^+$). Esters **2** and **3** were obtained in 44% and 32% yields, respectively, and afforded ^{1}H NMR spectra identical to that of **1**.

Synthesis of Amino Acid *N*-Carboxyanhydrides. A typical procedure for the synthesis of the NCAs of the fluorinated esters was as follows. A 100 mL three-neck round-bottom flask equipped with a reflux condenser and a dropping funnel was charged with **1** (3.93 g, 8 mmol) and dry THF (30 mL). The suspension was stirred and heated to 50 °C. A solution of triphosgene (0.87 g, 8.8 mequiv) in 10 mL of THF was added dropwise, and the mixture was stirred under nitrogen for ca. 3 h. During that time, the initial suspension became almost completely clear. The small amount of remaining precipitate was removed by centrifugation. The supernatant was transferred to a 100 mL round-bottom flask, purged with nitrogen, and concentrated to ca. half the initial volume. Hexane (ca. 50 mL) was added and the mixture was placed in the freezer overnight to allow complete precipitation of the anhydride. The product was filtered under nitrogen, washed with hexane, and dried to give 3.50 g (84% yield) of crude anhydride in the form of a white powder. Recrystallization from THF/hexane (1/3) gave 2.97 g (5.7 mmol, 71% yield) of **4**. ^{1}H NMR (DMSO-d_6): δ 2.15 (m, 2H, β-CH$_2$), 2.6−2.9 (m, 4H, γ-CH$_2$ and CH$_2$CF$_2$), 4.52 (triplet, 2H, OCH$_2$), 4.67 (triplet, 1H, α-CH), 9.20 (singlet, 1H, NH). Anal. Calcd for $C_{14}H_{10}NO_5F_{13}$: C, 32.4; H, 1.94; N, 2.70; F, 47.6. Found: C, 32.4; H, 1.73; N, 2.86; F, 47.8.

The NCAs of **2** and **3** were prepared according to the same procedure and afforded ^{1}H NMR spectra identical to those of **4**. For **5**: yield 63%. Anal. Calcd for $C_{16}H_{10}NO_5F_{17}$: C, 31.0; H, 1.63; N, 2.26; F, 52.2. Found: C, 30.8; H, 1.35; N, 2.42; F, 51.9. For **6**: yield 56%. Anal. Calcd for $C_{18}H_{10}NO_5F_{21}$: C, 30.0; H, 1.40; N, 1.95; F, 55.5. Found: C, 29.8; H, 1.14; N, 2.06; F, 55.1.

Polymerizations. A typical polymerization procedure was as follows. A 25 mL round-bottom flask equipped with a drying tube was charged with **4** (1.04 g, 2 mmol). THF (5 mL) was added via cannula, and after dissolution of the anhydride, triethylamine (2.8 μL, 0.02 mmol) was added. A precipitate was noted shortly after addition of the initiator. The polymerization was monitored by infrared spectroscopy until complete disappearance of the bands corresponding to the anhydride carbonyl stretching vibrations (1780 and 1855 cm^{-1}). Methanol (ca. 20 mL) was added to the reaction mixture, and the precipitate was filtered, washed with methanol and ether, and dried in a vacuum oven (50 °C) overnight. In the case of copolymerizations, both monomers were charged at the onset, and the same procedure was followed.

Results and Discussion

Esterification of L-Glutamic Acid. The γ-esters of glutamic acid (**1**−**3**) with long fluorinated alcohols were prepared by direct esterification under acidic conditions.[17] Three fluorinated alcohols were used: 1*H*,1*H*,2*H*,2*H*-perfluorooctanol (n = 8), 1*H*,1*H*,2*H*,2*H*-perfluorodecanol (n = 10), and 1*H*,1*H*,2*H*,2*H*-perfluorododecanol (n = 12).

The esterification was initially performed as described for aliphatic alcohols.[17] Free glutamic acid was suspended in *tert*-butyl alcohol, sulfuric acid was added, and the suspension was heated to 65 °C until complete dissolution of the amino acid. A fourfold excess of the alcohol was added to the clear solution. Although all of the fluorinated alcohols are soluble in *tert*-butyl alcohol, each of the reaction mixtures became heterogeneous, with emulsions appearing ca. 20 min after addition of the alcohol. Termination of the reaction after 1 h led to no detectable product, and workup after 1 day afforded yields of fluorinated esters of less than

10%. Phase separation, which is not observed in esterifications with aliphatic alcohols, may continue to the low yields. The use of hexafluoroisopropyl alcohol as a substitute for *tert*-butyl alcohol did not eliminate the emulsion.

The low yields of the esters may also reflect the unfavorable equilibrium for reaction of the fluorinated alcohol. In order to remove water efficiently, the reaction flask was equipped with a condenser charged with molecular sieves. The temperature of the reaction was kept at 65−70 °C, and a small amount of benzene was added. *tert*-Butyl alcohol, water, and benzene form an azeotrope with a boiling point of 67.3 °C.[18] This method afforded yields of 30−45% after recrystallization, without the need for large excesses of the fluorinated alcohol. The main product of the esterification in all cases was the γ-ester, but small amounts (5−10%) of the α-ester were also observed by ^{1}H NMR spectroscopy. Recrystallization from isopropyl alcohol water (2/1) resulted in enrichment in the γ-ester; after two recrystallizations, no α-ester was detectable.

The reaction was also performed at higher temperatures and in the absence of *tert*-butyl alcohol. In each case, we found 50−60% α-ester and diester byproducts as estimated by ^{1}H NMR spectroscopy. Reaction times longer than 1 day did not increase the reaction yield.

Evaporation of the solvent before termination by addition of triethylamine appeared to be necessary to allow subsequent precipitation of the ester. After the reaction mixture was evaporated to dryness, addition of *tert*-butyl alcohol led to clear solutions. Excess sulfuric acid was neutralized by addition of triethylamine, and water and ethanol were added. Excess triethylamine was then added to precipitate the free glutamate ester. The precipitate was collected by centrifugation, slurried with water, and recentrifuged hot. This procedure was found to be necessary and sufficient to remove free glutamic acid. Further washings with methanol and ethyl ether removed any residual alcohol.

Synthesis of Amino Acid *N*-Carboxyanhydrides. Synthesis of the NCAs of the fluorinated esters was performed in tetrahydrofuran with use of triphosgene.[19] The amino acid esters are insoluble in THF, but their NCAs are soluble. Solutions of triphosgene in THF were added to suspensions of the amino acids in THF at 50 °C. Phosgenation reaction was most efficient when the amino acid suspensions were heated to 50 °C before addition of triphosgene. Gelation and formation of an unidentified byproduct were observed upon addition of triphosgene to the suspension of the amino acid at room temperature and subsequent heating. The initial suspensions became almost clear ca. 3 h after addition of triphosgene. The NCAs were obtained in high yields (56−71%) after precipitation with hexane and recrystallization. Phosgenation can be monitored by infrared spectroscopy; as the reaction proceeds, the anhydride bands at 1780 and 1855 cm^{-1} increase in intensity relative to the ester absorption at 1730 cm^{-1}. Purging with N$_2$ during the phosgenation is generally recommended for removal of the excess of HCl[19] but it was avoided in this case because of the surface activity of the fluorinated NCAs, which caused foaming.

Polymerization. Homopolymers and statistical copolymers of **1**−**3** with γ-benzyl L-glutamate were prepared by polymerization of the respective NCAs in THF using triethylamine as initiator (Tables 1−3). All of the polymerizations were monitored by infrared spectroscopy and were terminated (after complete conversion of the NCAs) by addition of methanol. The reaction mixtures became inhomogeneous shortly after addition of the initiator. Infrared spectra taken during the course of the polymerization indicated initial formation of polypeptides in predominantly β-sheet conformations. Figure 1 shows characteristic infrared spectra recorded during the copolymerization of **5** and γ-benzyl L-glutamate NCA (**10**) (Table 2, run 3). As the copolymerization proceeds, the absorptions at 1852 and 1783 cm^{-1} assigned to the carbonyl groups of the anhydrides decrease in intensity. Two amide I vibrations of the polypeptide are seen, one at 1624 cm^{-1} assigned to a β-sheet conformation[20] and one at 1651 cm^{-1} assigned to the α-helical conformation.[20] The percentage of α-helical content increases with time, in agreement with the literature on the polymerization of L-alanine NCA.[21]

Table 1. Copolymerization of 4 with 10

run	**4** (g)	**10** (g)	mol % **4** (feed)	reacn time (days)	mol % **1** (polymer)[a]	[η] (dL/g)	% yield
1	1.036	0	100	11	100[b]		87.6
2	0.509	0.258	50.0	9	52.4[c]	0.07	85.2
3	0.271	0.528	20.6	8	21.9[d]	0.08	81.4
4	0.260	0.921	12.5	5	13.4[e]	0.10	60.7
5	0.138	1.263	5.3	5	5.7[f]	0.17	84.8

[a] Copolymer compositions were estimated on the basis of elemental analysis. Fluorine contents were determined by Schöniger flask decomposition of the compound in an oxygen atmosphere. The resulting F$^-$ was analyzed using an ion selective electrode. [b] Anal. Calcd: C, 32.8; H, 2.12; N, 2.95; F, 52.0. Found: C, 32.0; H, 2.20; N, 2.98; F, 51.9. [c] Anal. Calcd: C, 42.6; H, 3.26; N, 3.96; F, 36.6. Found: C, 42.0; H, 3.39; N, 3.76; F, 36.5. [d] Anal. Calcd: C, 53.3; H, 4.52; N, 5.09; F, 19.6. Found: C, 52.9; H, 4.44; N, 5.02; F, 19.4. [e] Anal. Calcd: C, 57.5; H, 5.01; N, 5.52; F, 13.1. Found: C, 57.1; H, 5.03; N, 5.41; F, 12.1. [f] Anal. Calcd: C, 61.9; H, 5.53; N, 5.99; F, 6.0. Found: C, 61.9; H, 5.57; N, 6.93; F, 5.5.

Table 2. Copolymerization of 5 with 10

run	**5** (g)	**10** (g)	mol % **5** (feed)	reacn time (days)	mol % **2** (polymer)[a]	[η] (dL/g)	% yield
1	0.423	0	100	16	100[b]		68.7
2	0.615	0.277	48.6	10	54.5[c]		62.3
3	0.314	0.556	19.4	7	19.5[d]	0.09	76.8
4	0.315	1.170	10.3	5	10.3[e]	0.13	86.8
5	0.155	1.250	5.0	4	5.9[f]	0.15	84.5

[a] Copolymer compositions were estimated on the basis of elemental analysis. Fluorine contents were determined by Schöniger flask decomposition of the compound in an oxygen atmosphere. The resulting F$^-$ was analyzed suing an ion selective electrode. [b] Anal. Calcd: C, 31.3; H, 1.75; N, 2.44; F, 56.1. Found: C, 30.4; H, 1.72; N, 2.61; F, 52.2. [c] Anal. Calcd: C, 39.6; H, 2.77; N, 3.39; F, 42.6. Found: C, 39.6; H, 2.73; N, 3.20; F, 41.5. [d] Anal. Calcd: C, 52.4; H, 4.34; N, 4.85; F, 21.8. Found: C, 51.8; H, 4.10; N, 4.56; F, 21.0. [e] Anal. Calcd: C, 57.8; H, 5.00; N, 5.48; F, 13.0. Found: C, 57.3; H, 5.08; N, 5.51; F, 12.7. [f] Anal. Calcd: C, 60.9; H, 5.38; N, 5.83; F, 8.0. Found: C, 60.9; H, 5.46; N, 5.79; F, 7.5.

Table 3. Copolymerization of 6 with 10

run	**6** (g)	**10** (g)	mol % **6** (feed)	reacn time (days)	mol % **3** (polymer)[a]	[η] (dL/g)	% yield
1	0.423	0	100	11	100[b]		81.4
2	0.196	0.754	8.7	3	8.7[c]	0.14	83.8

[a] Copolymer composition was estimated on the basis of elemental analysis. Fluorine contents were determined by Schöniger flask decomposition of the compound in an oxygen atmosphere. The resulting F$^-$ was analyzed using ion selective electrode techniques. [b] Anal. Calcd: C, 30.4; H, 1.49; N, 2.07; F, 59.1. Found: C, 29.5; H, 1.41; N, 2.42; F, 58.2. [c] Anal. Calcd: C, 57.4; H, 4.92; N, 5.37; F, 13.9. Found: C, 57.0; H, 4.77; N, 5.37; F, 12.9.

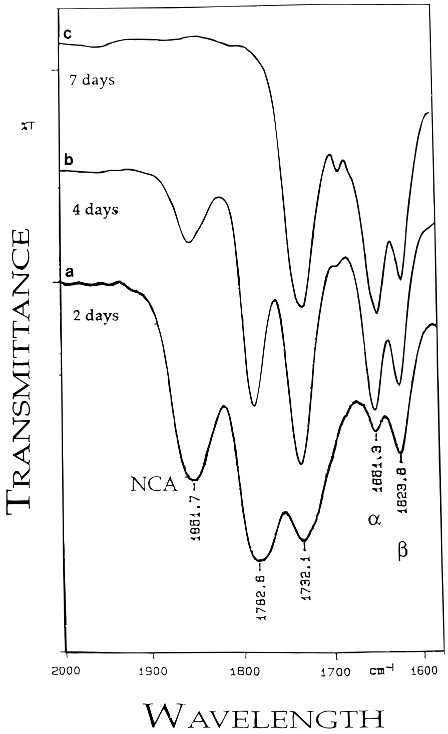

Figure 1. IR spectra recorded during the copolymerization of **5** with **10**: (a) 2, (b) 4, and (c) 7 days after the addition of initiator. Samples were in the form of films prepared by evaporation of a reaction aliquot (in THF) on a NaCl plate.

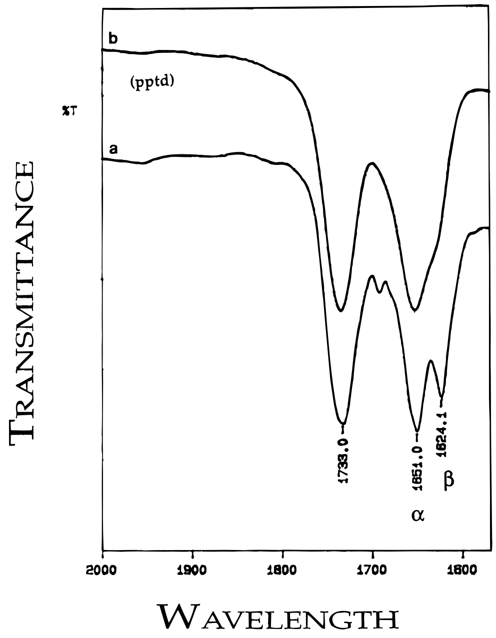

Figure 2. (a) IR spectra recorded during the copolymerization of **5** with **10**, 7 days after the addition of initiator (film on NaCl plate). (b) IR spectrum of the precipitated copolypeptide (KBr pellet).

Solid-state spectra of the precipitated polypeptide, recorded subsequently, show considerable enrichment in α-helical content as shown in Figure 2.

Copolymers were prepared to allow determination of the dependence of surface energy on percent fluorination; thus conversions were high and feed ratios were chosen to give a useful range of fluorine contents. Elemental analysis of the copolypeptides showed that the copolymer compositions were close to the feed compositions (as expected at high conversion), favoring slightly the fluorinated amino acid. On the other hand, since the recovered yields were not 100%, the appearance of enhanced reactivity of **4**–**6** may have resulted from preferential precipitation of chains enriched in fluorinated units. The solubility of these copolypeptides in different organic solvents varies with fluorine content. Polymerization products with 5 mol % of any of the fluorinated comonomers are soluble in the solvents that solubilize PBLG, e.g., THF, DMF, and chloroform. This indicates that they are indeed copolymers, since the homopolymers of the fluorinated esters are not soluble in these solvents. The fluorinated homopolymers are soluble in trifluoroacetic acid and hexafluoroisopropyl alcohol but not in dichloroacetic acid; the latter is a solvent for the copolymers.

Table 4. Contact Angles of Water on Films of Copolymers of 1 and 10[a]

			contact angle (deg)	
run	**1** mol %	% F	advancing	receding
1	100	51.9	107 ± 2	90 ± 3
2	52	36.5	101 ± 10	66 ± 9
3	22	19.4	88 ± 3	54 ± 7
4	13	12.1	90 ± 5	56 ± 7
5	6	5.5	73 ± 7	55 ± 5

[a] Contact angles on PBLG: $\theta_{adv} = 71 \pm 4°$, $\theta_{rec} = 56 \pm 4°$.

Table 5. Contact Angles of Water on Films of Copolymers of 2 and 10[a]

			contact angle (deg)	
run	**2** mol %	% F	advancing	receding
1	100	52.2	107 ± 4	72 ± 10
2	55	41.5	101 ± 2	72 ± 4
3	19	21.0	89 ± 2	64 ± 10
4	10	12.7	90 ± 4	60 ± 7
5	6	7.5	91 ± 2	56 ± 3

[a] Contact angles on PBLG: $\theta_{adv} = 71 \pm 4°$, $\theta_{rec} = 56 \pm 4°$.

Table 6. Contact Angles of Water on Films of copolymers of 3 and 10[a]

			contact angle (deg)	
run	**3** mol %	% F	advancing	receding
1	100	58.2	121 ± 3	89 ± 2
2	9	12.9	87 ± 6	58 ± 6

[a] Contact angles on PBLG: $\theta_{adv} = 71 \pm 4°$, $\theta_{rec} = 56 \pm 4°$.

Contact Angle Measurements. Films for contact angle measurements were prepared by pressing powder samples between Kapton films at 130 °C (115 °C in the case of polymers of **3**) in a melt press. This method proved convenient and effective in the preparation of films with smooth surfaces.

Tables 4–6 list the advancing and receding contact angles of water placed on films of the various homopolymers and copolymers. All films show hysteresis comparable to but somewhat higher than that reported for a copolymer of tetrafluoroethylene and perfluoropropylene (ca. 25°).[22] In general, differences between advancing and receding contact angles can be result of surface roughness, heterogeneity, and deformability.[22] Figure 3 shows the dependence of the advancing contact angle on the total fluorine content. Results obtained previously on polymers of trifluoroalanine are included. In each case the contact angle increases significantly between 0 and 10% fluorine and levels off. The surface energy correlates better with the total fluorine content than with the molar percent of fluorinated monomer. The homopolymer of **3** shows an exceptionally high water contact angle (121°). Zisman has demonstrated that the surface energy depends on both the constitution

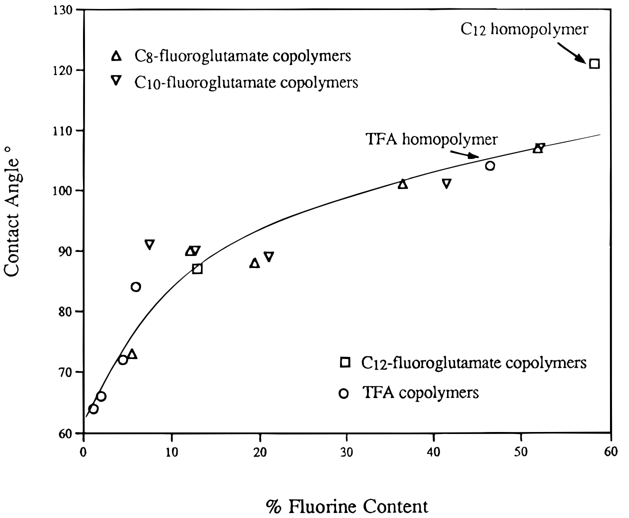

Figure 3. Advancing contact angle for water vs fluorine content for various fluorinated polypeptides.

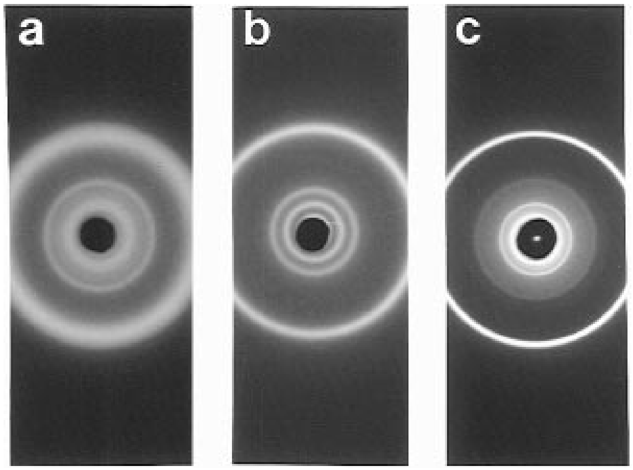

Figure 4. X-ray diffraction patterns of homopolymers of (a) **1**, (b) **2**, and (c) **3**.

and structure of the surface and that the lowest surface energy is that closely packed trifluoromethyl groups.[4,23] Indicative of the effect of packing in lowering the surface energy is the fact that the water contact angle on Teflon is 108°[8] while on self-assembled perfluorinated alkanethiol monolayers it is 118°[24] and on poly(1*H*,1*H*-pentacafluorooctyl methacrylate), 120°.[25] The contact angle for the homopolymer of **3** indicates a highly ordered fluorocarbon surface that can result from side chain crystallization. Side chain crystallization has been further verified by X-ray scattering and differential scanning calorimetry as discussed below. It is interesting that Möller and co-workers also find very low surface energy for the fluorinated homopolymer when side chain crystallization takes place. However, in their work the dispersion force contribution to the surface energy, γ_s^D, varies linearly with fluorine content and is not affected in any apparent way by side chain crystallization.[3]

X-ray Diffraction. Figure 4 shows the X-ray diffraction photographs obtained for the homopolymers of **1**−**3**. Each pattern consists of a set of powder X-ray diffraction rings; a listing of the interplanar spacings and a visual estimate of relative intensities is presented in Table 7. Examination and comparison of all three X-ray diffraction patterns reveal that in each case the low-angle set of diffraction rings varies independently of the wide-angle diffraction. This feature is expected, and found previously,[12] from polymer molecules with this level of complexity, that is, with a high linear density of long side chains decorating a backbone. The low-angle reflections emanate from the packing of whole molecules while the wide-angle diffraction relates to localized crystallization of side chains.

Table 7. X-ray Diffraction Spacings (Å) and Estimates of Observed Relative Intensities for Homopolymers of 1−3[a]

homopolymers of		
1	**2**	**3**
	Low-Angle Region	
16.4 s (100)	36.4 s (100)	43.0 vs (100)
9.3 m (110)	18.0 s (200)	21.5 s (200)
	12.2 s (300)	14.3 s (300)
	9.0 vw (400)	10.8 vw (400)
	7.2 w (500)	8.5 w (500)
		7.2 w (600)
	Wide-Angle Region	
5.1 s, broad (10)	5.1 s (10)	4.9 vs (10)
		2.8 w (11)
		2.5 w (20)

[a] vs = very strong, s = strong, m = medium, w = weak, vw = very weak.

Starting with the homopolymer of **3**, with the longest side chains, the six low-angle reflections are successive *h*00 orders of 43 Å and are characteristic of a layered structure which can be attributed to the lamellar-packing periodicity of the fluoroalkyl side chains. The wide-angle triplet, with a strong and sharp first order, indexes on a two-dimensional hexagonal lattice of side $a = 5.7$ Å, which we interpret as arising from the close packing of the fluorinated segments of the side chains, since it is known that poly(tetrafluoroethylene) crystallizes in a hexagonal lattice of side $a = 5.66$ Å.[26−28] For the homopolymer of **2**, with 20% fewer CF_2 groups in the side chains, the wide-angle pattern noticeably worsens; only a broadened 10 reflection remains and with a 4% increase in spacing, consistent with poorer packing of the shortened fluorinated segments. In addition, the lamellar-packing periodicity reduces to 36 Å. It is more convenient to discuss the results for the homopolymer of **1** latter.

Behavior similar to that observed for the homopolymers of **2** and **3** as a function of increasing side chain length has been reported by Watanabe and co-workers[12] for PALGs with side chains of 14 methylene units or longer, and a lamellar model with interdigitated side chains was proposed to explain both the development of side chain crystallization and the layered arrangement of helices from the low-angle X-ray pattern. Side chain interdigitation was not observed directly, but was proposed because the center-to-center distance between helices (corresponding to the 100 reflection) is substantially less than two fully extended (planar zigzag conformation) alkane side chains. In our case, the value of 43 Å matches the lamellar-stacking periodicity if the side chains are extended (in the helical conformation typical of the hexagonal modification of poly(tetrafluoroethylene)) and *not* interdigitated, as illustrated schematically in Figure 5. The diameter of poly(γ-methyl α,L-glutamate) is reported to be 14 Å.[14] The side chain of the homopolymer of **3** has an additional methylene group (axial projection 1.25 Å)[29] and 10 perfluorinated side chain carbon atoms (10 × 1.3 Å);[26] thus, the diameter of helices bearing fully extended side chains is ca. 42.5 Å. This value is in agreement with the observed periodicity (100 spacing) and suggests that the perfluoroalkyl side chain segments are *not* interdigitated. In the case of the homopolymer of **2**, the lamellar-

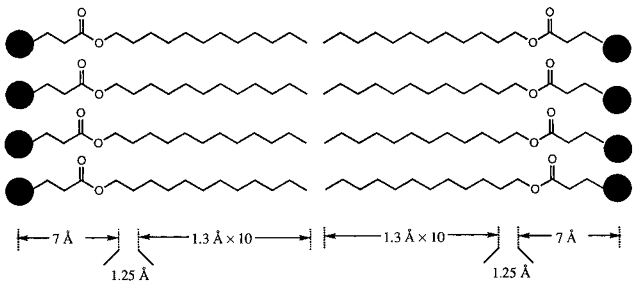

Figure 5. Interhelical distance for the homopolymer of **3** with fully extended side chains.

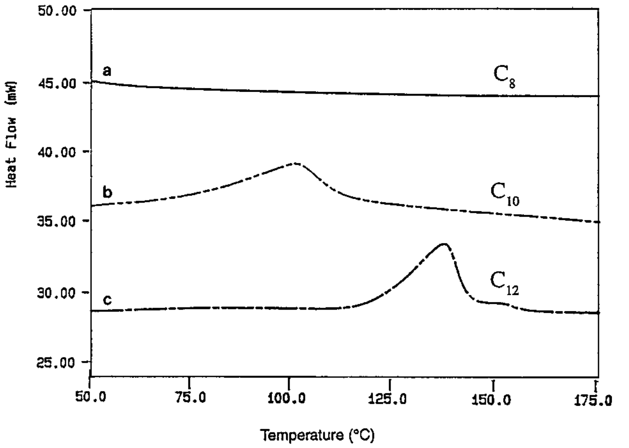

Figure 6. DSC heating traces of the homopolymers of (a) **1**, (b) **2**, and (c) **3** (third heating).

packing periodicity is 36.4 Å, a reduction of 6.6 Å compared with the homopolyer of **3**, a value somewhat larger than the theoretical difference corresponding to 4 CF_2 units ($4 \times 1.3 = 5.2$ Å).

The X-ray diffraction results from the homopolymer of **1**, with the shortest side chains, exhibit a single strong, broad wide-angle diffraction ring similar to the homopolymer of **2** but the low-angle diffraction is different in character. A pair of low-angle reflections index as the 10 and 11 of a two-dimensional hexagonal lattice with $a = 18.9$ Å. For PALGs with side chains shorter than 14 methylene units, the helices pack on hexagonal lattices and it is only at greater side chain lengths that the overall (lamellar) structure is dictated by crystallization of the aliphatic chains. The hydrogenated polyglutamate with 8 methylene units in the side chain (the analog of the homopolymer of **1**) crystallizes in a hexagonal lattice with $a = 17.1$ Å. The slight increase in the lattice spacing is readily explained as a result of the increased bulkiness of the fluorocarbon chain. The side chains cannot form extended crystals, and the wide-angle reflection is much broader than those of the homopolymers of **2** and **3**.

Thermal Analysis. Figure 6 shows DSC heating traces of the homopolymers of **1**–**3**. The homopolymers of **2** and **3** show first-order transitions at 96 and 137 °C, respectively; no corresponding transition is observed in the homopolymer with C_8 side chains. The observed transitions are assigned to melting of side chain crystals, consistent with the X-ray data on each of the homopolymers. Upon cooling at 40 °C/min, crystallization exotherms are observed at 74 and 123 °C, respectively, for the homopolymers of **2** and **3**. The transition enthalpies associated with these endotherms are 1.50 and 6.75 kJ/mol, respectively. Möller et al. report the melting of pure $C_{12}F_{26}$ at 72 °C, with an associated heat of melting of 21 kJ/mol, which corresponds to 1.75 kJ/CF_2.[30] If one assumes that this value holds for the glutamate side chains, the number of “crystalline” CF_2 units can be calculated to be 3.9 (6.75/1.75) for the homopolymer of **3** and 0.9 for that of **2**. The corresponding values for the hydrogenated analogs have been calculated by Watanabe et al. to be 0.4, 1.4, 3.0, 5.9, and 7.7 for the C_{10}, C_{12}, C_{14}, C_{16}, and C_{18} side chains, respectively.[12]

Conclusions

Poly(α,L-glutamate)s carrying long fluorinated side chains have been synthesized by polymerization of the corresponding amino acid *N*-carboxyanhydrides. The surface energies of the fluorinated polypeptides (as indicated by the water contact angle) were found to vary with total fluorine content, independent of the length of the side chain. The very high contact angle (121°) measured for the homopolymer with C_{12} side chains was attributed to the formation of a surface of closely packed trifluoromethyl groups. This explanation is consistent with X-ray diffraction results, which indicate well-developed side chain crystallinity. Crystallization of the fluorinated segments controls the spatial arrangement of the polymer backbone, which organizes into layered arrays for chains bearing C_{10} and C_{12} side chains.

Acknowledgment. The authors thank Dr. A. Waddon for helpful discussions of the X-ray data. The help of Kean Hock Yeap in the synthesis of the fluorinated glutamates is greatly appreciated. This work was supported by a grant from the U.S. Army Research Office and by the National Science Foundation Materials Research Science and Engineering Center at the University of Massachusetts.

References and Notes

(1) Mark, H. F.; Bikales, N. M.; Overberger, C. G.; Menzes, G., Eds.; *Encyclopedia of Polymer Science and Engineering*, 2nd ed.; John Wiley & Sons, Inc.: New York, 1987; Vol. 7, pp 256–257.
(2) Dessipri, E.; Tirrell, D. A. *Macromolecules* **1994**, *27*, 5463–5470.
(3) Hoepken, J.; Moeller, M. *Macromolecules* **1992**, *25*, 1461.
(4) Zisman, W. A. In *Contact Angle Wettability and Adhesion*; Gould, R. F., Ed.; American Chemical Society: Washington, DC, 1964; Vol. 43; pp 1–51.
(5) Pittman, A. G.; Sharp, D. L.; Ludwig, B. A. *J. Polym. Sci., Part A-1* **1968**, *6*, 1729–1740.
(6) Johnson, R. E. J.; Dettre, R. H. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1987**, *28*, 48–49.
(7) Doeff, M. M.; Lindner, E. *Macromolecules* **1989**, *22*, 2951–2957.
(8) Kobayashi, H.; Owen, M. J. *Macromolecules* **1990**, *23*, 4929–4933.
(9) Block, H. *Poly(γ-benzyl-L-glutamate) and Other Glutamic Acid Containing Polymers*; Gordon and Breach Science Publishers: New York, 1983; pp 1–29.
(10) Daly, W. H.; Poché, D.; Negulescu, I. I. *Prog. Polym. Sci.* **1994**, *19*, 79–135.
(11) Watanabe, J.; Fukuda, Y.; Gehani, R.; Uematsu, I. *Macromolecules* **1984**, *17*, 1004–1009.
(12) Watanabe, J.; Ono, H.; Uematsu, I.; Abe, A. *Macromolecules* **1985**, *18*, 2141–2148.
(13) Watanabe, J.; Goto, M.; Tatsuya, N. *Macromolecules* **1987**, *20*, 298–304.
(14) Vierheller, T. R.; Foster, M.; Schmidt, A.; Mathauer, K.; Knoll, W.; Wegner, G.; Satija, S.; Majkrzak, C. F. *Macromolecules* **1994**, *27*, 6893–6902.
(15) Hotta, I.; Tsujita, Y.; Takizawa, A.; Kinoshita, T.; Okamata, Y. *Kobunshi Ronbunshu* **1989**, *46*, 487–491.
(16) Ito, Y.; Iwata, K.; Kang, I.-K.; Imanishi, Y.; Sisido, M. *Int. J. Biol. Macromol.* **1988**, *10*, 201–208.
(17) Wassermann, D.; Garber, J. D.; Meigs, F. M. U.S. Patent 3,285,953, 1966.

(18) Gordon, A. J.; Ford, R. A., Ed.; *The Chemistapos Companion: A Handbook of Practical Data, Techniques, and References*; John Wiley & Sons, Inc.: New York, 1972; p 29.

(19) Daly, W. H.; Poche, D. *Tetrahedron Lett*. **1988**, *29*, 5859–5862.

(20) Cantor, C. R.; Schimmel, P. R. *Biophysical Chemistry*; W. H. Freeman and Co.: San Francisco, 1980; Vol. II, pp 470–471.

(21) Kricheldorf, H. R. α-*Amino acid N-Carboxyanhydrides and Related Heterocycles*; Springer-Verlag: Berlin, 1987; pp 188–191.

(22) Johnson, R. E. J.; Dettre, R. H. *Wettability*; Marcel Dekker Inc.: New York, 1993; pp 1–71.

(23) Schulman, F.; Zisman, W. A. *J. Colloid Sci*. **1952**, *7*, 465–481.

(24) Chidsey, C. E. D.; Loiacono, D. N. *Langmuir* **1990**, *6*, 682–691.

(25) Shaffrin, E. G. *Handbook of Adhesives*; Van Nostrand Reinhold: New York, 1977; p 67.

(26) Bunn, C. W.; Howells, E. R. *Nature* **1954**, *174*, 549–551.

(27) Clark, E. S.; Muus, L. T. *Z. Kristallogr*. **1962**, *117*, 119–127.

(28) Clark, E. S.; Muus, L. T. *Z. Kristallogr*. **1962**, *117*, 108–118.

(29) Alexander, L. E. *X-Ray Diffraction Methods in Polymer Science*; John Wiley & Sons, Inc.: New York, 1969; p 365.

(30) Hoepken, J.; Pugh, C.; Richtering, W.; Moeller, M. *Makromol. Chem*. **1988**, *189*, 911–925.

MA9510707