ion shielding. The stability of the water–polymer interactions observed indicates that they must have an important mediating effect upon the structural possibilities in polymer conformation. It is clear that more experimental work remains to be done in this area.

Acknowledgments. The author is indebted to Professor M. Printz of Rockefeller University for helpful discussions. He also wishes to thank Professors I. M. Klotz and A. Krasna for generous gifts of materials. Some of the measurements were made with the technical assistance of Mrs. J. M. Glasel. This work was supported by Grants No OSW-14-01-0001-1700 and GB-8468 from the U. S. Department of the Interior, Office of Saline Water, and the National Science Foundation, Molecular Biology Division, respectively.

Conformational Studies on Poly-L-cyclohexylalanine and on Poly-L-phenylalanine in Water–Strong Acid Mixtures[1]

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Abstract: The conformation of poly-L-cyclohexylalanine (PCHA) and poly-L-phenylalanine (PLP) in water–methanesulfonic acid mixtures has been studied by circular dichroism (CD) in the far-ultraviolet region. It was found that PCHA assumes the right-handed α-helical conformation in solvent mixtures containing less than 86% acid. This result is in favor of the hypothesis, based on previous investigations, that PLP might also assume the α-helical form. The ordered forms of PCHA and PLP exhibit different conformational stabilities. This result is tentatively explained in terms of different contributions from noncovalent bonds of the side chains.

It is well known that poly-L-phenylalanine (PLP) in solution exhibits some peculiar optical rotatory properties. The CD spectrum of this polymer is different from all known spectra of polypeptides either in the ordered form or in the coiled form.[2–5]

The interpretation of the CD spectrum in terms of conformation is not unequivocal, since possible contributions from the aromatic chromophores can overlap those from the peptide chromophore with consequent complication of the CD pattern.

In a previous investigation carried out on copolymers of L-phenylalanine (Phe) and ϵ-carbobenzoxy-L-lysine (Z-Lys) in tetrahydrofuran (THF) solution, it was found that the progressive introduction of phenylalanine (Phe) residues in the peptide chain perturbs the CD pattern of polycarbobenzoxy-L-lysine, but apparently does not alter the helical sense.[6] No transition appeared to be involved on varying the copolymer composition. On this basis it was tentatively concluded that PLP in THF solution has the same helical conformation as poly-ϵ-carbobenzoxy-L-lysine (PCBL), that is, the right-handed α helix, the actual CD spectrum arising from overlapping of contributions to the optical activity both from the side-chain chromophores and from the peptide chromophores.

Support for this conclusion might be obtained from conformational studies in solution of poly-L-cyclohexylalanine (PCHA) (polyhexahydro-L-phenylalanine). Cyclohexane side chains of PCHA do not absorb in the region of the peptide transitions and the interpretation of the CD spectrum of the polymer in terms of conformation is unequivocal. If it is found that PCHA in solution, in spite of the enhanced bulkness of the side chains (chair or boat conformations of the nonplanar cyclohexane ring are possible), is in the α-helical form, it will be reasonable to assign the same conformation to PLP.

Optical rotatory properties of PCHA in the far-uv have not yet been reported, mainly because the polymer is not soluble in organic solvent transparent in this spectral region.

Very recently it has been found that concentrated strong acids like H_2SO_4 and CH_3SO_3H are good and transparent solvents for polypeptides.[7] In most cases the polymer solutions are stable enough to permit measurements to be made (polymer degradation occurs only after several hours). In these solvents polypeptides are usually in the form of random coils. Addition of water to the acidic solutions causes sharp coil-to-helix transitions in the case of poly-γ-ethyl-L-glutamate[7] and poly-L-glutamic acid.[8]

The present work describes CD and uv properties of PCHA and PLP in CH_3SO_3H–H_2O mixtures. In addition a block copolymer, [γ-benzyl-DL-glutamate]$_{200}$-[L-cyclohexylalanine]$_{35}$, has been prepared, and the optical rotatory properties of the L-cyclohexylalanine sequence in organic solvents are also reported.

(1) A preliminary account of this work has been reported in *Chem. Commun.*, 97 (1969).
(2) W. B. Gratzer and P. Doty, *J. Amer. Chem. Soc.*, **85**, 1193 (1963).
(3) H. G. Sage and G. D. Fasman, *Biochemistry*, **5**, 286 (1966).
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The results are interpreted in terms of conformation of PCHA and PLP either in CH_3SO_3H–H_2O mixtures or in organic solvents.

Experimental Section

Materials. Methanesulfonic acid (Fluka puriss) was distilled under reduced pressure, rejecting the first 10% of the distillate. The final product contained no free sulfate. Potentiometric titration showed an acid content of 98.5% by weight. Concentrated sulfuric acid (Merck puriss) was used directly (the acid content was 95.2% by weight).

Dioxane (Carlo Erba RP) was refluxed over sodium metal for several hours and then distilled. The distillate was treated with potassium anthracene[9] and finally redistilled immediately before use.

Tetrahydrofuran (THF) (Carlo Erba RP) was refluxed over potassium anthracene until the blue complex potassium anthracenate was formed. It was then distilled immediately before use.

Dimethylformamide (DMF) (Carlo Erba RP) was dried over phosphorus pentoxide and then fractionally distilled under reduced pressure. The product was subsequently treated with γ-benzyl-L-glutamate N-carboxyanhydride in order to eliminate all traces of amines.[10] The final product was distilled in the dark and under reduced pressure immediately before use.

Ethyl ether and petroleum ether (bp 40–70°; 30–60°) (both Carlo Erba RP) were dried over sodium metal and then distilled. Methylene chloride and ethyl acetate (both Carlo Erba RP) were dried over calcium chloride and then distilled. Highest purity hexafluoro-2-propanol (HFIP) was kindly supplied as a gift from du Pont Chem. Co., and it was used without further purification.

L-Cyclohexylalanine hydrochloride CHA-HCl) was prepared by catalytic hydrogenation of L-phenylalanine according to the procedure described by Sela and Arnon,[11] but using 5% Rh on charcoal (Baker catalysts) instead of platinum black. The reaction was followed by the decreasing of the hydrogen pressure in the Parr bomb. The crude material was recrystallized twice from water. The final product was completely free from phenyl groups (as checked by uv absorption measurements at 258 mμ); mp 234–235° (lit.[11] 234°); $[\alpha]^{20}D$ +10.9° (*c* 0.7, 1 *N* HCl).

L-Cyclohexylalanine N-carboxyanhydride (CHA-NCA) was prepared from CHA-HCl and phosgene according to the literature;[11] mp 123–124° (lit. 123°).

L-Phenylalanine N-carboxyanhydride (Phe-NCA) was prepared from L-Phe and phosgene according to the literature.[12] The product was recrystallized several times from ethyl acetate and *n*-hexane; mp 90°.

γ-Benzyl-L-glutamate and γ-Benzyl-D-glutamate NCA's. These monomers have been prepared from the corresponding γ-benzyl-D- and γ-benzyl-L-glutamates[13] and phosgene according to the literature.[14] Equal amounts of the two NCA's were then mixed and the racemic mixture was obtained. The direct preparation of the racemic monomer by phosgenation of γ-benzyl-DL-glutamate is troublesome especially at the stage of purification, since the DL-NCA exhibits solution properties which are completely different from those of the optically pure NCA.

Poly-L-cyclohexylalanine (PCHA). This polymer was prepared by polymerization of the corresponding CHA-NCA according to the following procedure. To a solution of monomer (0.500 g) in DMF (15 ml), 7.15×10^{-5} mol of *n*-butylamine was added by a Metrohm precision microburet (the monomer to initiator molar ratio was 35). The solution was allowed to stand at room temperature for 2 days. The polymer separated from the solution as a white powder. At the end of the reaction (checked by the disappearance of the monomer ir band at 1840 cm^{-1} in the clear supernatant solution) PCHA was isolated by filtration, abundantly washed with ethyl ether, and finally dried under vacuum at 50°.

Poly-L-phenylalanine (PLP) was prepared by polymerization of the corresponding NCA, according to the following procedure. To a solution of Phe-NCA (10.057 g) in THF (150 ml), 4.55×10^{-4} mol of sodium methoxide (solution in 1:1 methanol–benzene) was added. The solution was allowed to stand at room temperature for 2 days. The polymer separated from the solution as a white powder. At the end of the polymerization (checked by ir) the polymer was isolated by filtration, washed abundantly with ethyl ether, and finally dried *in vacuo* at 50°. *Anal.* Calcd: C, 73.4; H, 6; N, 9.5. Found: C, 72.5; H, 6.1; N, 9.3.

Block Copolymer [γ-Benzyl-DL-glutamate]$_m$[L-cyclohexylalanine]$_n$. γ-Benzyl-L-glutamate NCA (1.88 g, 7.15×10^{-3} mol) was mixed with an equal amount of γ-benzyl-D-glutamate NCA. The $[\alpha]D$ of the mixture was checked to be zero. The racemic monomer mixture (3.76 g equal to 14.30×10^{-3} mol) was dissolved in freshly purified DMF; then 7.15×10^{-5} mol of *n*-butylamine was added (the total monomer to initiator molar ratio was 200). At the end of the reaction (again checked by ir) 0.500 g (2.54×10^{-3} mol) of CHA-NCA was added. It is very important to add the CHA-NCA only when the polymerization of the first monomer is absolutely complete; in fact, if some unreacted γ-benzyl-DL-glutamate NCA is still present at the point of CHA-NCA addition, the CHA sequence in the block copolymer will be contaminated by γ-benzyl-DL-glutamate residues. At the end of the polymerization (checked by ir) the copolymer was precipitated by pouring the solution into ethyl ether. The copolymer was then isolated by filtration, redissolved in methylene chloride, and reprecipitated by pouring the solution into petroleum ether (bp 40–70°; 30–60°).

On the basis of the added amounts of initiator, DL monomer, and CHA-NCA, the composition of the block copolymer should be the following: [γ-benzyl-DL-Glu]$_{200}$[CHA]$_{35}$. This copolymer composition has been checked by elemental analysis. *Anal.* Calcd: C, 66.5; H, 6.36; N, 6.59. Found: C, 66.6; H, 6.44; N, 6.56.

Preparation of PCHA and PLP Solutions in Acid Mixtures. A known amount of polymer was introduced into a 25-ml volumetric flask. A weighed quantity of pure methanesulfonic acid (title 98.5%) was added and the mixture was shaken to complete solution. (The time required to get the material into solution was in the order of 15 min.) Then the desired amount of water was added to the ice-cooled solution. After it came to room temperature, dilution was made to the mark by adding a separately prepared solvent mixture of the same composition as that in the flask (the composition of the water-acid solutions prepared separately has been checked by potentiometric titration). The CD spectra of these solutions were recorded immediately after the preparation, in order to avoid polymer degradation.

Measurements. CD measurements were performed on a Roussel-Jouan 185 Model II° Dichrograph. The original CD patterns directly recorded by the instrument have been reported in the present paper. The ordinate of these CD curves represents the so-called dichroic optical density,[15] $A_l - A_r$ (A_l is the absorbance of the left-handed circularly polarized light and A_r is the absorbance of the right-handed circularly polarized light). From the ordinates of Figures 1–8, the molar circular dichroism $\Delta\epsilon$ was calculated according to the usual equation

$$A_l - A_r = \frac{\Delta\epsilon \times M}{c \times d}$$

where M is the molecular weight per residue, c is the concentration (grams/liter), and d is the cell path in centimeters.

Uv absorption measurements were made on a Perkin-Elmer Hitachi-EPS 3t spectrophotometer or on a Perkin-Elmer Hitachi 124 spectrophotometer, using 1-mm and 5-mm quartz cells.

Potentiometric titrations were performed by a Metrohm Model 388 precision potentiometer equipped with a Metrohm UX combined electrode, and using a Metrohm E 457 microburet.

Results and Discussion

Conformation of PCHA in Methanesulfonic Acid–Water Mixtures. PCHA easily dissolved in pure methanesulfonic acid. The CD spectrum of the polymer in such a solvent (Figure 1) is typical of polypeptides in the random coil conformation, with a weak positive band located at 220 mμ ($\Delta\epsilon$ = 0.44) and a negative band located at 196 mμ ($\Delta\epsilon$ = −3.8). One can observe that the molar dichroic absorption of the negative band is lower than that observed for polypeptides in the

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(14) E. Blout and R. H. Karlson, *J. Amer. Chem. Soc.*, **78**, 941 (1956).
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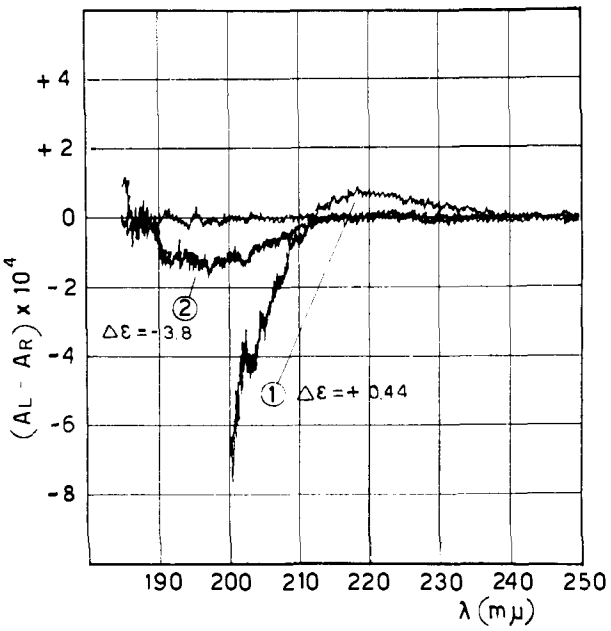

Figure 1. CD spectrum of PCHA in pure methanesulfonic acid. Curve 1 has been obtained in a 0.5-mm cell and curve 2 in a 0.1-mm cell. The polymer concentration was 1.114 g/l. The $\Delta\epsilon$ values have been calculated according to the equation given in the Experimental Section.

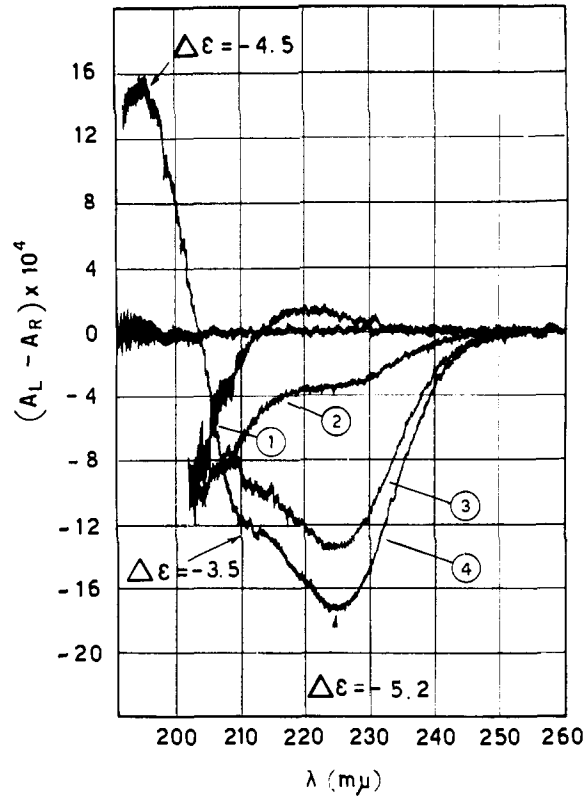

Figure 2. CD spectra of PCHA in various methanesulfonic acid–water mixtures: curve 1, 0.542 g/l. in pure CH_3SO_3H; curve 2, 0.510 g/l. in 89.6% CH_3SO_3H; curve 3, 0.433 g/l. in 74.6% CH_3SO_3H; curve 4, 0.503 g/l. in 67.0% CH_3SO_3H. In all cases a 1-mm pathlength cell was used.

coiled form.[16] This behavior, which is typical of polypeptides dissolved in methanesulfonic and sulfuric acid,[7,8] is probably due to solvent effects on the $\pi \rightarrow \pi^*$ peptide transition.

When water is added to the acidic solution of PCHA a sharp conformational transition takes place in the polymer. Figure 2 shows CD spectra of PCHA in various water–methanesulfonic acid mixtures. It can be observed that the typical spectrum of the right-handed α helix becomes more and more evident as the water content in the solvent mixture is increased. The plot of the $\Delta\epsilon$ values at 225 mμ *vs.* solvent composition (Figure 3) makes evident that the coil-to-helix transition is very sharp and occurs between 89 and 86% acid in the solvent mixtures. As pointed out in the introductory statement to the present paper, the interpretation of the CD spectrum in terms of conformation is unequivocal, since the situation is not complicated by the presence of chromophores in the side chains, whose contributions to the total optical activity could overlap those from the peptide transitions.

The spectrum of PCHA in the helical form requires further comment. We can observe that, even when the water content in the solvent mixture is the highest possible, the amplitudes of the two negative dichroic bands and of the positive one are lower than those expected for the pure α-helical form. In addition a red shift by 2–3 mμ is observed for the two negative bands. The reason for these discrepancies could be twofold. First, the polymer could be not completely in the helical form even in 59.1% methanesulfonic acid. Unfortunately it was impossible to decrease the acid content below 59.1% since extensive polymer precipitation does occur. Second, the presence of very small precipitated polymer particles might cause distortions of the CD

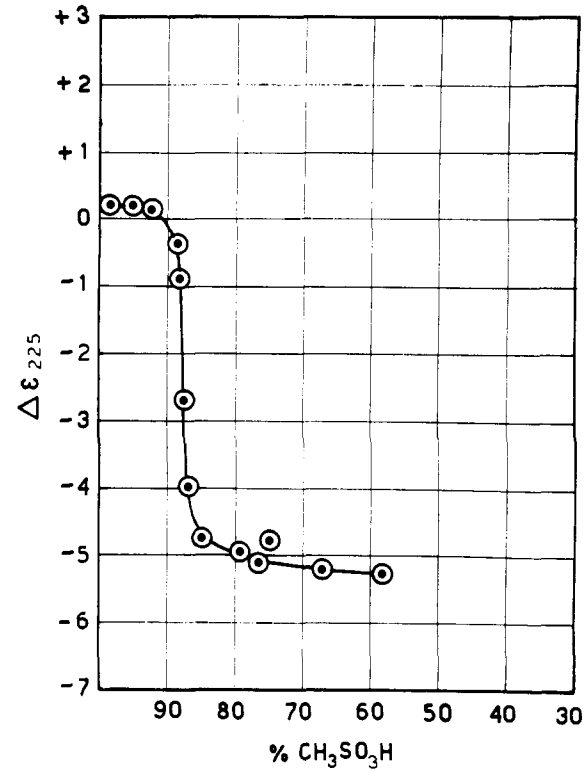

Figure 3. Coil-to-helix transition of PCHA in CH_3SO_3H–H_2O mixtures. $\Delta\epsilon$ values at 225 mμ plotted *vs.* solvent composition.

patterns of helical polymers. In fact Urry and Ji[17]

(16) S. N. Timasheff and M. G. Gorbunoff, *Ann. Rev. Biochem.*, 36, 13 (1967).

(17) D. W. Urry and T. H. Ji, *Arch. Biochem. Biophys.*, 128, 802 (1968).

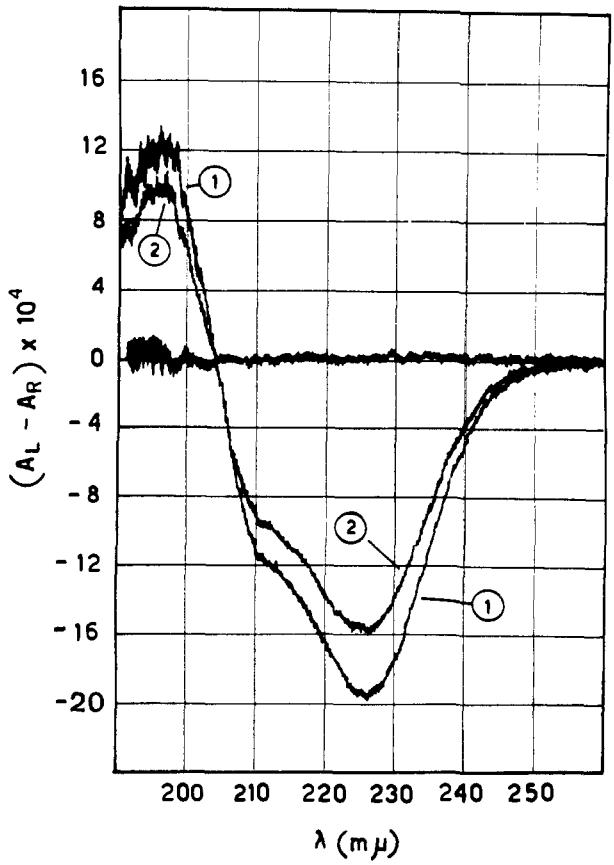

Figure 4. CD spectra of PCHA in 59.1% methanesulfonic acid. Curve 1 has been recorded immediately after the preparation of the solution and curve 2 has been recorded 2 hr later. The polymer concentration was 0.560 g/l. A 1-mm pathlength cell was used.

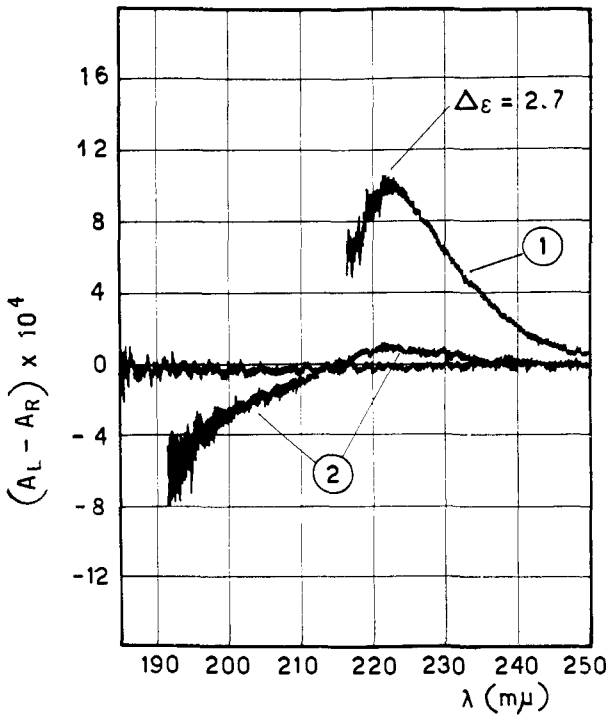

Figure 5. Far-uv CD spectrum of pure PLP in methanesulfonic acid. The polymer concentration was 0.542 g/l.; 1-mm (curve 1) and 0.1-mm (curve 2) pathlength cells.

observed a strong decrease of the amplitude of the CD bands (50% or more) in not completely homogeneous

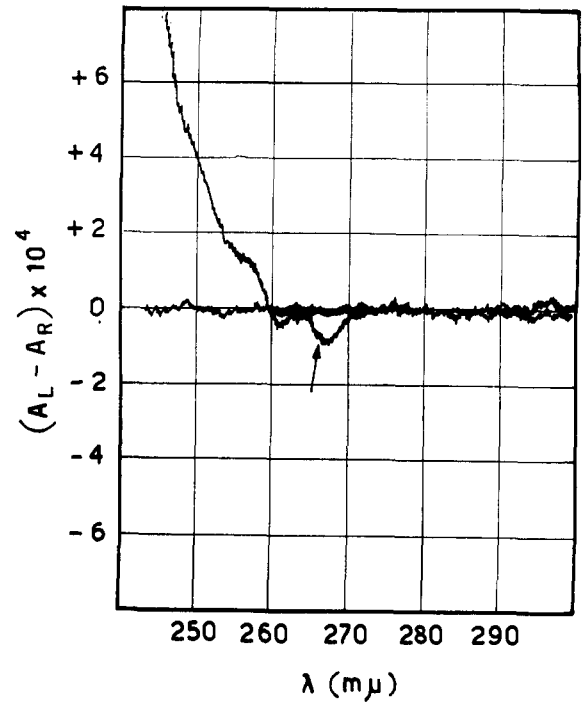

Figure 6. CD spectrum in the aromatic region of PLP in pure methanesulfonic acid. The polymer concentration was 0.596 g/l. in a 1-cm pathlength cell. The arrow indicates $\Delta\epsilon = 0.020$.

solutions of helical polymers. The same authors also observed a red shift by 2–3 mμ of the negative CD bands. According to these authors the observed distortion of the CD patterns arises both from absorption flattening and scattering distortion.[18]

The solutions of PCHA in solvent mixtures containing less than 86% methanesulfonic acid were slightly opalescent immediately after their preparation, and the turbidity increased as the solutions aged. At the same time we observed that the CD spectra of these solutions showed a marked time dependence. This is clearly shown in Figure 4; the CD signal diminishes as the solution ages indicating that the phenomenon is related to the presence of small precipitated polymer particles.

In the light of the observed time dependence and the red shift of the CD spectra it seems reasonable to assume that PCHA in solvent mixtures containing less than 86% methanesulfonic acid is completely in the right-handed α-helical form, the observed distortions of the CD patterns being due to the not complete homogeneity of the polymer solutions.

Conformation of PLP in Water–Methanesulfonic Acid Mixtures. The CD spectrum PLP in pure methanesulfonic acid is shown in Figures 5 and 6. The general shape of the spectrum is similar to that of polypeptides in the coiled form. We assume that this CD pattern describes the random-coil conformation of PLP. Both position and intensity of the positive band are quite unusual. The band is 4–5 mμ red shifted and the intensity is about ten times higher than that expected for typical coiled polymer.[19] Possible contributions from the phenyl chromophores and solvation effects[7] as well

(18) L. N. M. Duysens, *Biochim. Biophys. Acta*, **19**, 1 (1956).
(19) Very similar results have also been obtained by P. Quadrifoglio and D. W. Urry in 1,2-dichloroethane solutions containing 1% (by weight) of TFA.

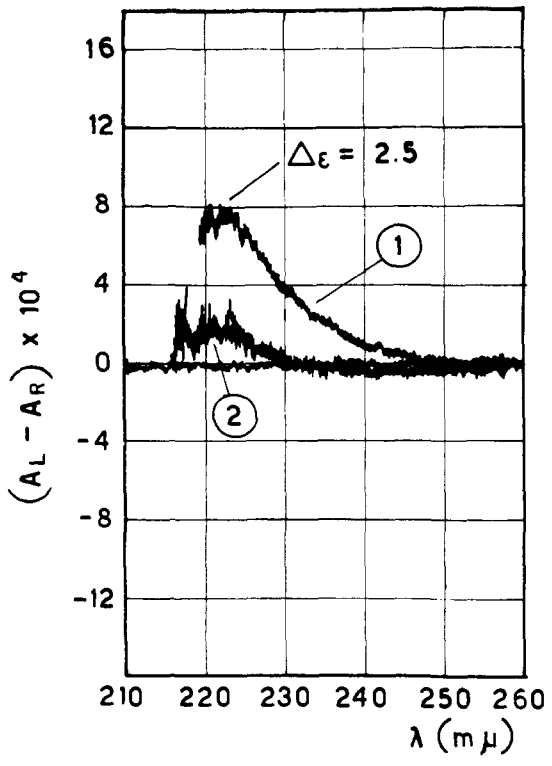

Figure 7. CD spectra of PLP in various methanesulfonic acid–water mixtures: curve 1, 0.44 g/l. in 84% methanesulfonic acid; curve 2, 0.40 g/l. in 82% methanesulfonic acid. In all cases a 1-mm pathlength cell was used.

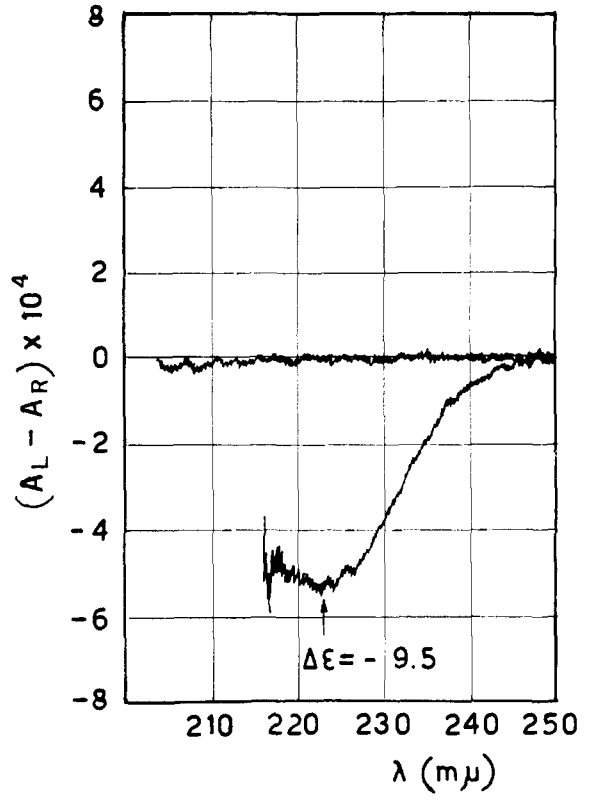

Figure 8. CD spectrum of the block copolymer [γ-benzyl-DL-Glu]$_{200}$-[CHA]$_{35}$ in HFIP. The copolymer concentration was 0.950 g/l. in a 1-mm pathlength cell.

could be invoked in order to explain position and intensity of this band, whose nature is not well understood at the present time.[20]

Addition of water to the polymer solution does not change the shape of the CD pattern between 100 and 85% methanesulfonic acid. This result leads to the conclusion that in this range of solvent composition no conformational transition takes place. In 84% acid the amplitude of the positive band starts to decrease (Figure 7), and between 84 and 82% acid the CD pattern of PLP drastically changes. Negative dichroism appears around 240–230 mμ and the positive band centered at 222 mμ decreases considerably. We conclude that PLP undergoes a conformational transition between 84 and 82% methanesulfonic acid content in the solvent mixture. Unfortunately, polymer precipitation does not allow the transition to follow completely: in 82% methanesulfonic acid the polymer solution is opalescent; in 80% acid PLP comes out from the solution.

All the above data show without ambiguity that the conformational stability of the ordered form of PLP is lower than that of PCHA. In fact in 85% methanesulfonic acid, PCHA is completely in the α-helical form, while PLP is still completely in the coiled form.

Conformational Properties of PCHA in Organic Solvents. The conformation of PCHA has been also studied in HFIP. Since the pure homopolymer does not dissolve in organic solvents, the study has been carried out on the block copolymer [CHA]$_{35}$[γ-benzyl-DL-Glu]$_{200}$. The CD spectrum is shown in Figure 8 and refers obviously to the optically active sequence of the blockcopolymer. Because of strong absorption of the benzyl groups of the optically inactive solubilizing sequence, it was impossible to record the spectrum below 205 mμ. It is clearly evident that PCHA does exist in the α-helical conformation in HPIP, the negative band at 223 mμ having position and amplitude in quantitative agreement with the expected values for this conformation.

(20) S. Beychok in "Poly-α-amino Acids," G. D. Fasman, Ed., Marcel Dekker, Inc., New York, N. Y., 1967, p 306.

Conclusions

The data presented give evidence that PCHA does exist in the right-handed α-helical conformation in water–methanesulfonic acid mixtures containing less than 86% acid, and in HFIP as well. This result supports the hypothesis, based on previous investigations, that PLP exists in the α-helical conformation in water and in organic solvents. The behavior of PCHA and PLP in water–methanesulfonic acid mixtures deserves further comment. It was already pointed out that the α-helical conformation of PCHA is more stable than that of PLP. This result cannot be explained on the basis of the different steric requirements of the side chains.

In fact the PCHA side chains (which can assume either boat or chair configurations) are more bulky than those of PLP and, contrary to the observation, they should make the α helix of PCHA less stable.

Neither of the different stabilities can be explained on the basis of differences of the degree of polymerization of the two samples. In fact, PLP, which has been prepared by sodium methoxide initiation, should have a higher molecular weight (and then a higher conformation stability) than PCHA. Furthermore, it has been

recently observed that in methanesulfonic acid–water mixtures the solvent composition at which the coil-to-helix transition of poly-L-glutamic acid occurs does not change upon changing the molecular weight of the polymer over a wide range.[6]

There is an additional factor which may account for the differences between the two polymers. Noncovalent bonds among side chains might contribute differently to the conformational stability of PCHA and PLP. Already it has been shown that noncovalent interactions like hydrophobic bands among side chains are responsible for the enhanced conformational stability of PLP in aqueous solutions.[4] It is presently well known that nonpolar paraffin chains in aqueous solutions form hydrophobic bonds and tend to aggregate, the driving force for aggregation being the increase of entropy or decrease of order of the water structure involved in the process.[21,22]

Strong acids like sulfuric acid do resemble water very closely in the fact that they possess a structure in which acid molecules are very strongly hydrogen bonded.[23,24]

Long-chain fatty acids form micelles in concentrated sulfuric acid and in sulfuric acid–water mixtures. It was shown that this phenomenon is due to the favorable entropy changes going from individual fatty acid molecules with solvent highly organized around the paraffin chain to micelles where the aggregation decreases the order of the solvent structure.[25]

Micelle formation studies in methanesulfonic acid are not reported in the literature, but very probably noncovalent bonds between nonpolar solutes might form in this acid and in acid–water mixtures as well.

Therefore it is possible that the attitude of the cyclohexane side chains of PCHA to form "acidophobic" bonds is different from that of the phenyl groups of PLP. In this respect one might observe that the side chains of PCHA are much less polar than the side chains of PLP. Phenyl groups can in fact be considered nonpolar only when they are viewed parallel to the plane of the ring; both faces of the ring are polar. As a consequence there is the possibility that stronger noncovalent bonds are formed in PCHA than in PLP. This fact could enhance the stability of the α-helical structure of PCHA, with respect to PLP, in spite of the unfavorable steric interference between the side chains and the peptide backbone.

Acknowledgments. The authors express their gratitude to Professor Ernesto Scoffone for continuous and stimulating discussions during this work, and to Professor Joseph Steigman, Polytechnic Institute of Brooklyn, for useful suggestions at the beginning of this research.

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(25) J. Steigman and N. Shane, *J. Phys. Chem.*, 69, 968 (1965).

Crystalline Salt Complexes of Macrocyclic Polyethers

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Contribution No. 209 from the Elastomer Chemicals Department, Experimental Station, E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware 19898. *Received February 19, 1969*

Abstract: The stoichiometry of the crystalline complexes of sodium, potassium, ammonium, rubidium, cesium, and barium salts with the subject polyethers has been investigated in greater detail. Depending on the relative sizes of the "hole" in the cyclic polyether and of the cation, complexes with polyether:cation mol ratios of 1:1, 3:2, or 2:1 are obtained. The 2:1 and 3:2 complexes might possibly be "sandwich" structures. By preferential complex formation in methanol, potassium and cesium ions have been separated almost quantitatively.

The preparation and properties of a number of macrocyclic polyethers have been described previously.[1] Due to the cumbersomeness of the nomenclature of these compounds, a simplified method of naming them,[1] as shown by the examples in Figure 1, will be used.

Certain polyethers, particularly those containing 5 to 10 oxygen atoms each separated from the next by 2 carbon atoms, were shown to form crystalline complexes of alkali and alkaline earth salts, such as chlorides, iodides, and thiocyanates. It was originally reported that the stoichiometry of these complexes is always one molecule of polyether per ion regardless of its valence. It is the purpose of this paper to report that more recent work indicates that the stoichiometry is not as simple as previously assumed.

Some indication that the stoichiometry is not strictly 1:1 is evident in the published data.[1] For example, in Table VII[1] the ratio of moles of XXVIII dissolved per mole of cesium thiocyanate is given as 1.20, indicating that a mole of this salt interacts with more than a mole of the polyether in methanol. In Table XIV,[1] whereas the melting points of the XXVIII complexes of sodium, potassium, ammonium, and rubidium thiocyanates are sharp, that of the cesium salt is unsatisfactory. Also, Pressman found that a rubidium ion can interact in solution with more than a single molecule of dicyclohexyl-18-crown-6.[2]

(1) C. J. Pedersen, *J. Amer. Chem. Soc.*, 89, 7017 (1967).