# One-Dimensional Aromatic Crystals in Solution. 5. Empirical Energy and Theoretical Circular Dichroism Calculations on Helical Poly(L-1-pyrenylalanine)

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ABSTRACT: Empirical energy calculations were performed on helical poly(L-1-pyrenylalanine) to determine stable conformations. Side-chain energy contour maps for the four typical main-chain helical conformations of polypeptides, i.e., right- and left-handed α-helices and $3_{10}$ helices, were obtained. The local minimum-energy conformations found in the energy maps were subjected to the total energy minimization by varying the main-chain ($\phi$, $\psi$) and side-chain ($\chi_1$, $\chi_2$) rotational angles simultaneously. Eight minimum-energy conformations were found in the energy minimization. Quantum-mechanical calculations were carried out for the eight conformations to predict the circular dichroism (CD) of the helical polymer. The calculation was based on the exciton model, taking only π electrons of the amide and the pyrenyl groups into account. Comparison of the profile of the calculated CD spectra with the experimental one suggested that the most probable helical conformation of poly(L-1-pyrenylalanine) is a left-handed one with an α-helix-like main chain.

## Introduction

In search of the best aromatic poly(α-amino acid) which works as a molecular conductor, we have prepared poly(L-1-pyrenylalanine) (poly(L-1-PyrAla)) as a block copolymer with poly(γ-benzyl DL-glutamate).[1,2] The polymer was soluble in polar solvents and its electronic properties have been investigated by chiroptical spectroscopy, such as circular dichroism (CD), circularly polarized fluorescence (CPF), and fluorescence-detected circular dichroism (FDCD). Since the interpretation of the spectroscopic results is intimately related to the conformation of the polymer, we have undertaken conformational energy and theoretical CD calculations to determine the helical conformation of poly(L-1-PyrAla).

The CD intensity of poly(L-1-PyrAla) was much larger than that of the monomeric model compound. Moreover, a strong exciton splitting was observed at the $^1B_a$ absorption band of the polymer.[1,2] These results suggest that poly(L-1-PyrAla) takes a helical conformation, along which the pyrenyl groups are arranged regularly. There are, however, some observations which indicate the presence of some irregularities or thermal fluctuation in the helix. The fluorescence spectrum of the polymer showed a considerable amount of excimer fluorescence and the CD spectrum showed a temperature dependence: the lower the temperature, the stronger the CD intensity. The CD intensity also depended on solvent and the chain length. However, the profile of the CD spectrum including peak positions was independent of these factors. Therefore, the change in the CD intensity was ascribed to a small conformational fluctuation in a single regular helix structure.[2]

In this study we attempted to predict the helical conformation of poly(L-1-PyrAla). An empirical conformational energy was calculated by assuming that the polymer is in a helical conformation. The total energy minimization predicted eight minimum-energy conformations as the candidates. Theoretical CD spectra were compared for the eight candidates taking 2 amide transitions (nπ* and ππ*) and 16 pyrenyl vibronic transitions (5 for $^1L_b$, 5 for $^1L_a$, 3 for $^1B_b$, and 3 for $^1B_a$) into account. Three conformations of the eight candidates afforded reasonable CD spectra, which are compatible with the experimental one. Among the three, a left-handed helix with the total minimum energy (LH-ME-A) was most likely.

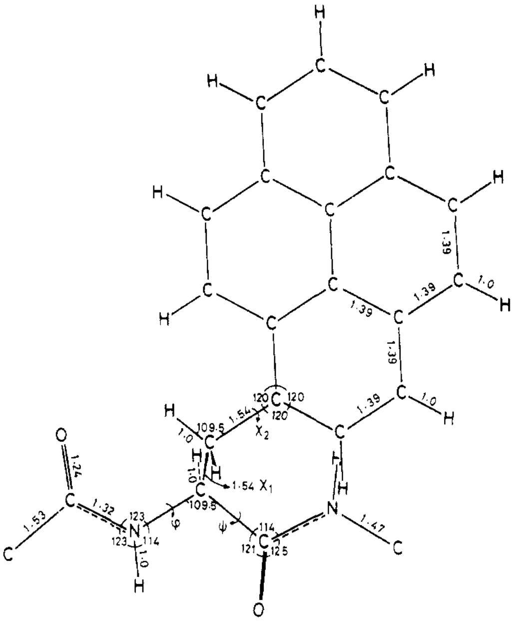

Figure 1. Geometrical parameters of L-1-pyrenylalanine unit.

## Methods for Calculations

The empirical conformational calculations and the theoretical CD calculation were carried out by essentially the same procedure as described before for poly(L-1- and 2-naphthylalanines).[3,4] The details of the procedure are described therein.

## Results and Discussion

**Calculation of Empirical Conformational Energy.** Figure 1 shows the geometrical parameters used for the calculation. The amide bond was fixed in a planar trans ($\omega$ = 180°) conformation. Four rotational variables ($\phi$, $\psi$, $\chi_1$, $\chi_2$) remain to determine the entire atomic coordinates of a helical heptamer of L-1-PyrAla. All pairs of nonbonded atoms of the heptamer were considered and the empirical functions of potential energy reported by Mom-

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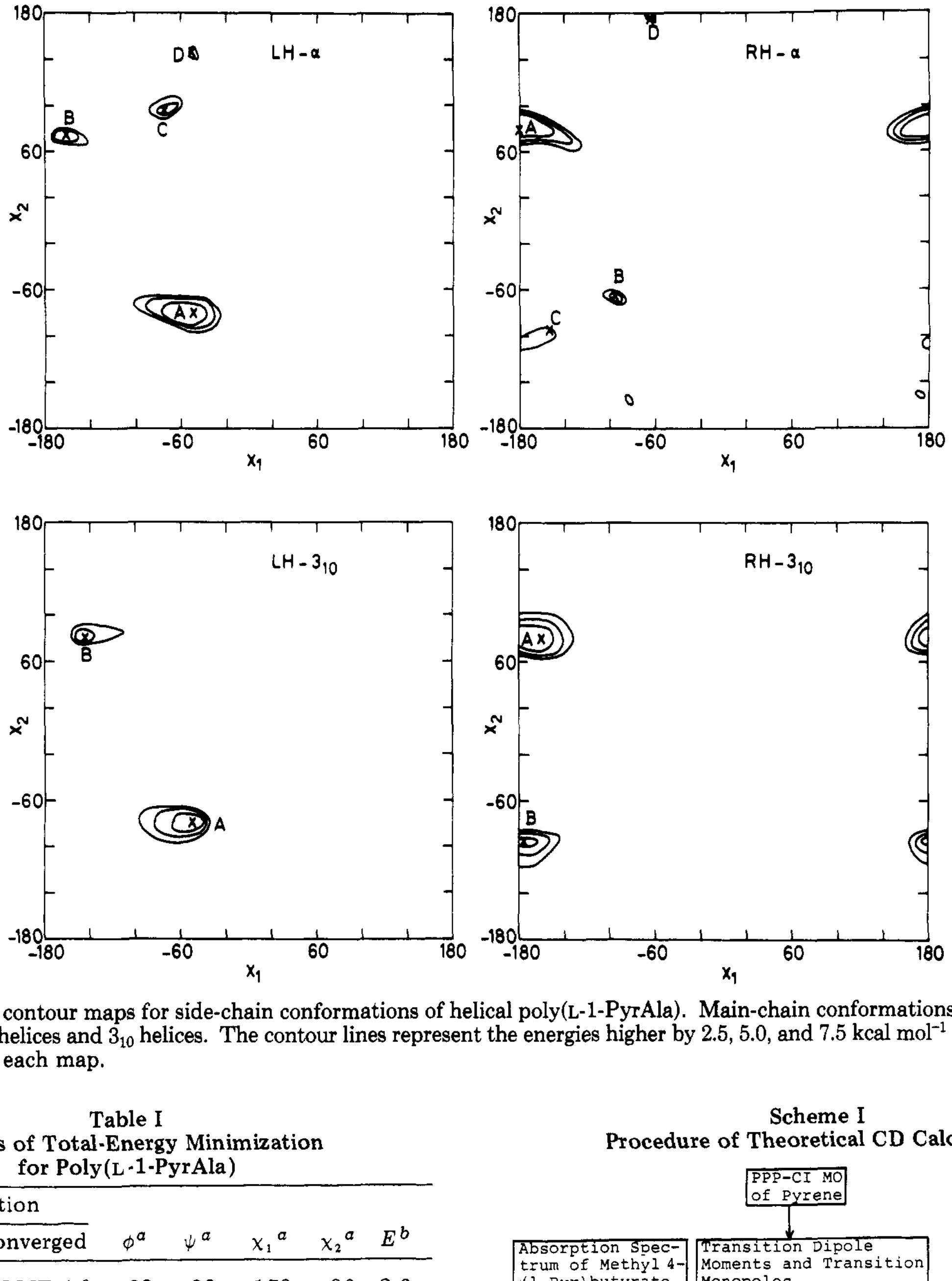


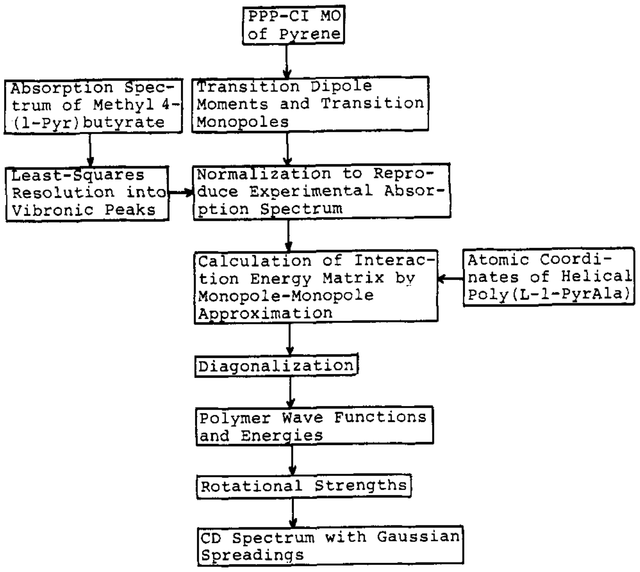
Figure 2. Energy contour maps for side-chain conformations of helical poly(L-1-PyrAla). Main-chain conformations are fixed to right- and left-handed α-helices and $3_{10}$ helices. The contour lines represent the energies higher by 2.5, 5.0, and 7.5 kcal mol$^{-1}$ than the minimum indicated by A in each map.

Table I
Results of Total-Energy Minimization for Poly(L-1-PyrAla)

| conformation | | | | | | |
|---|---|---|---|---|---|---|
| starting | converged | $\phi$[a] | $\psi$[a] | $\chi_1$[a] | $\chi_2$[a] | $E$[b] |
| RH-α-A<br>RH-$3_{10}$-A | RH-ME-A[c] | −69 | −39 | −178 | 80 | 2.6 |
| RH-α-B | RH-ME-B | −57 | −47 | −96 | −73 | 6.6 |
| RH-α-C<br>RH-$3_{10}$-B | RH-ME-C | −74 | −34 | −178 | −95 | 4.9 |
| RH-α-D | RH-ME-D | −68 | −36 | −64 | 175 | 9.1 |
| LH-α-A,<br>LH-$3_{10}$-A | LH-ME-A | 54 | 50 | −49 | −78 | 1.2 |
| LH-α-B<br>LH-$3_{10}$-B | LH-ME-B | 55 | 50 | −160 | 76 | 4.3 |
| LH-α-C | LH-ME-C | 43 | 62 | −63 | 97 | 5.7 |
| LH-α-D | LH-ME-D | 55 | 50 | −50 | 149 | 8.1 |

[a] In degrees. [b] (Empirical potential energy for the heptamer)/7, in kcal mol$^{-1}$. [c] ME indicates minimum-energy conformation.

Scheme I
Procedure of Theoretical CD Calculation



any et al.[5] were applied for each atomic pair. The calculation was started by setting the main-chain conformation to one of the standard helical conformations, i.e., right-handed (RH) and left-handed (LH) α-helices ($\phi$,$\psi$) = (−50°,−56°), (49°,57°), and $3_{10}$ helices (−60°,−30°), (60°,30°). For each main-chain conformation, side-chain rotational angles were varied from 0° to 360°, and the energy contour map was obtained. Figure 2 shows the side-chain contour maps for the four main-chain conformations. The energy minimum in each map is indicated by a point A, and the other local minima are indicated by B–D, in increasing order of the energy. The contour lines connect the points of constant energy higher by 2.5, 5.0, and 7.5 kcal mol$^{-1}$ than the minimum energy at point A.

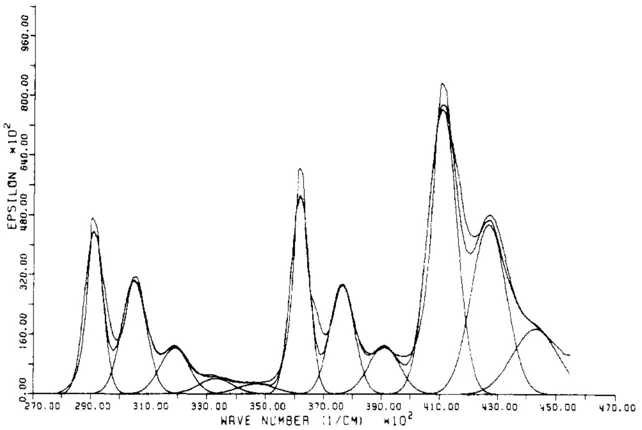


**Figure 3.** Result of least-squares peak resolution of the absorption spectrum of methyl 4-(1-pyrenyl)butyrate in trimethyl phosphate.

**Table II**
**Oscillator Strengths and Peak Positions of the Vibronic Peaks of 4-(1-Pyrenyl)butyric Acid Methyl Ester in Trimethyl Phosphate**[a]

| electronic transition | peak position, cm$^{-1}$ | oscillator strength |
|---|---|---|
| $^1L_b$ | 26539 | 0 |
| | 27939 | 0 |
| | 29339 | 0 |
| | 30739 | 0 |
| | 32139 | 0 |
| $^1L_a$ | 29095 | 0.2088 |
| | 30495 | 0.1936 |
| | 31895 | 0.0917 |
| | 33295 | 0.0353 |
| | 34695 | 0.0258 |
| $^1B_b$ | 36179 | 0.2541 |
| | 37639 | 0.1869 |
| | 39099 | 0.1033 |
| $^1B_a$ | 41102 | 0.5701 |
| | 42702 | 0.4120 |
| | 44302 | 0.2061 |

[a] Refractive index = 1.40.

The maps shown in Figure 2 are much the same as those calculated for poly(L-1-naphthylalanine) (Figure 5 in ref 3), indicating that the two additional aromatic rings fused to the 1-naphthyl group are directed to the outside of the helix and do not affect the stable conformations of the two helical polymers.

Starting from the local minima in the side-chain energy maps, total energy minimization was performed by varying the four rotational angles ($\phi$, $\psi$, $\chi_1$, $\chi_2$) simultaneously. The results are listed in Table I. Conformations found in the side-chain energy maps for the right-handed $\alpha$-helix and $3_{10}$ helix converged into the same right-handed minimum-energy (ME) conformation and those in the left-handed $\alpha$-helices and $3_{10}$ helices converged into the same LH-ME conformation. The main-chain rotational angles of the ME conformations are somewhat affected by the side-chain conformations. The conformation of least energy is the LH-ME-A. However, since other ME conformations have comparable energies, they cannot be discarded solely on the basis of empirical energy considerations.

**Computation of Theoretical Circular Dichroism.** The procedure reported for poly(L-tyrosine) and for poly(L-phenylalanine) by Woody and co-workers[6-8] was followed to calculate the CD for a pentadecamer ($n$ = 15) of helical poly(L-1-PyrAla). The procedure is schematically illustrated in Scheme I.

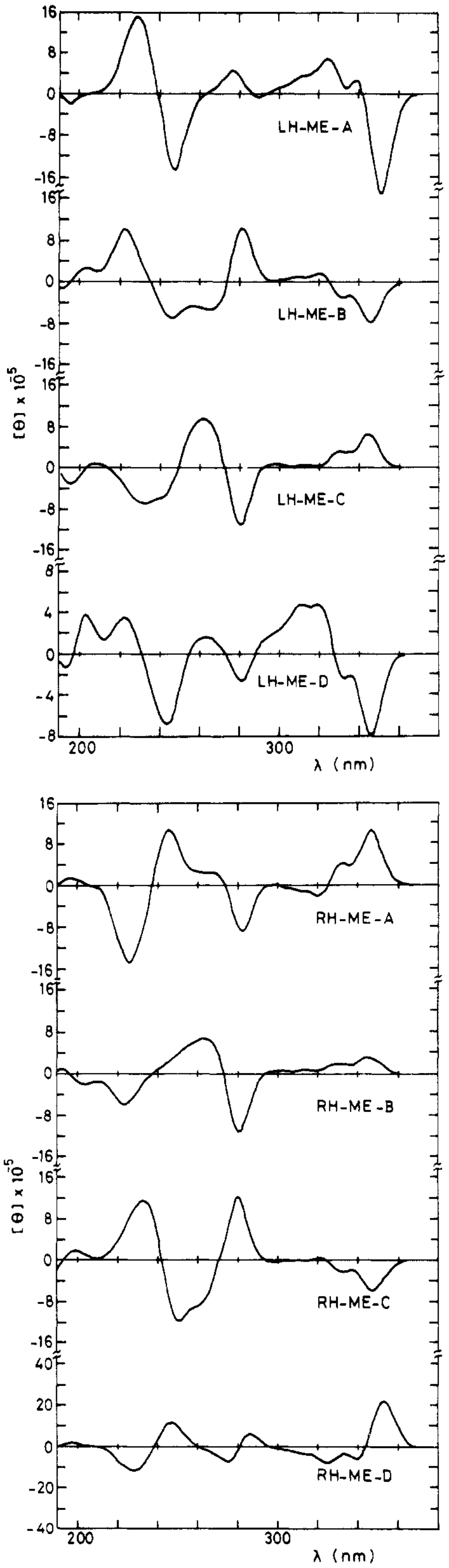


**Figure 4.** Theoretical CD curves for the minimum-energy conformations listed in Table I.

Two amide transitions ($n\pi^*$ and $\pi\pi^*$) and sixteen pyrenyl vibronic transitions (five for $^1L_b$, five for $^1L_a$, three for $^1B_b$, and three for $^1B_a$) were considered for each monomeric unit. The parameters for the $n\pi^*$ and $\pi\pi^*$ transitions were taken from Woody's paper[9] and they have been listed in Tables I and II of ref 3. The parameters for the vibronic transitions of pyrenyl groups were taken from a PPP-CI molecular orbital calculation reported by Hummel and Ruedenberg (TBM geometry).[10,11] The PPP-CI results of the transition dipole moments and the transtion monopoles for the $^1L_a$, $^1B_b$, and $^1B_a$ transitions were cor-

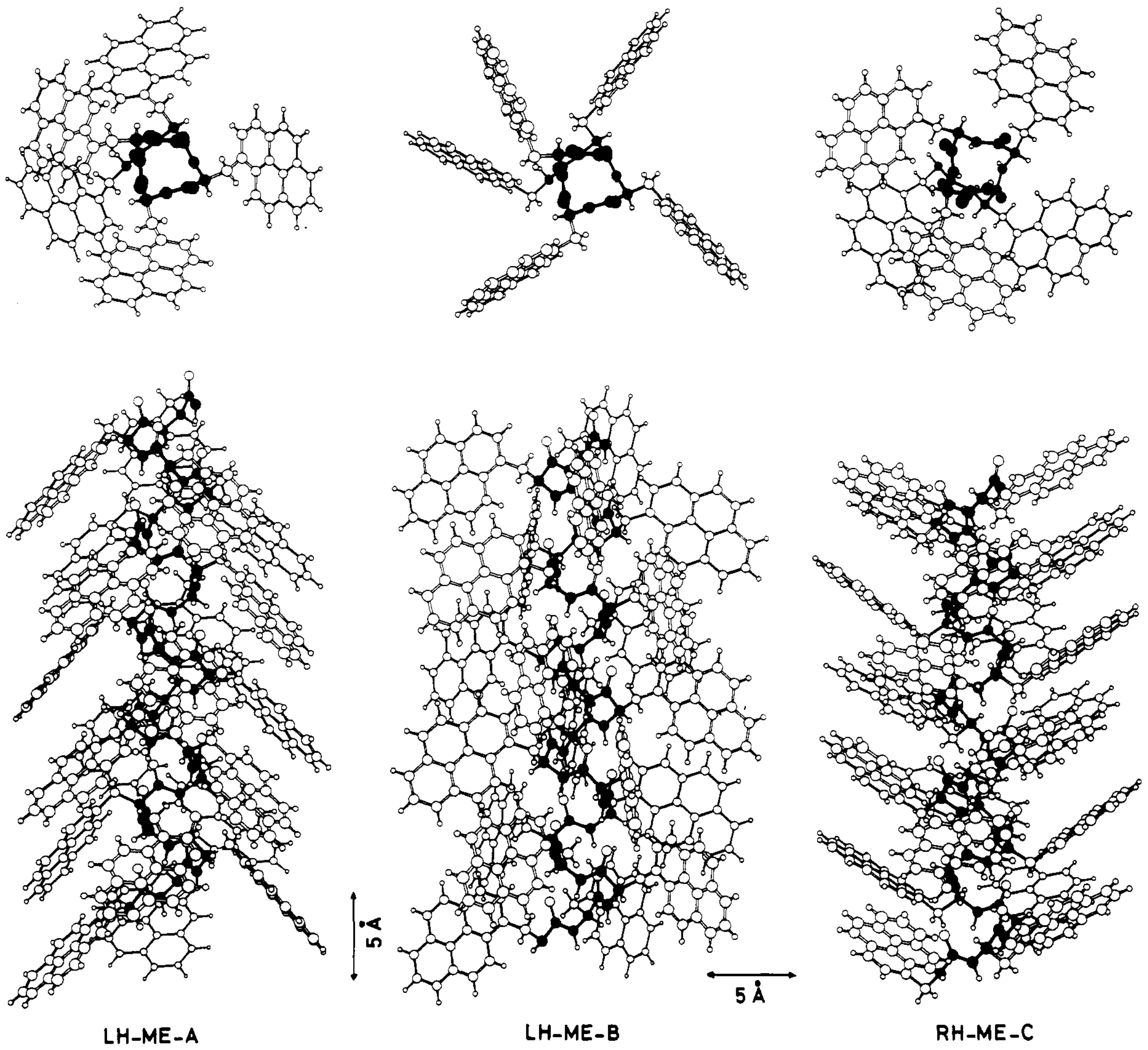
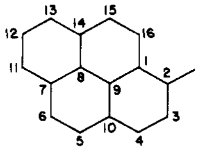


**Figure 5.** Top view and side view of poly(L-1-PyrAla) in LH-ME-A (left), LH-ME-B (center), and RH-ME-C (right) conformations. Solid circles represesnt atoms involved in the peptide main chain. NAMOD molecular display program (ref 12) was used.

**Table III**
**Monopole Charges for Pyrenyl Transitions**[a,b]

| center[c] | $^1L_b$ | $^1L_a$ | $^1B_b$ | $^1B_a$ | $^1L_b{}^1L_a$ | $^1L_b{}^1B_b$ | $^1L_b{}^1B_a$ | $^1L_a{}^1B_b$ | $^1L_a{}^1B_a$ | $^1B_b{}^1B_a$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 0.0 | 0.1669 | –0.1769 | 0.2974 | –0.1050 | 0.1147 | 0.1091 | –0.0103 | 0.0532 | –0.0755 |
| 2 | 0.0 | –0.4055 | –0.1929 | –0.0924 | 0.1278 | –0.2439 | –0.2056 | –0.0861 | 0.0289 | 0.0463 |
| 3 | 0.0 | 0.1435 | 0.0 | 0.5860 | 0.0 | 0.3122 | 0.0 | 0.0 | –0.0269 | 0.0 |
| 4 | 0.0 | –0.4055 | 0.1929 | –0.0924 | –0.1278 | –0.2439 | 0.2056 | 0.0861 | 0.0289 | –0.0463 |
| 5 | 0.0 | –0.2058 | 0.1077 | 0.0056 | –0.0887 | –0.1161 | 0.1783 | 0.0097 | –0.0721 | –0.0070 |
| 6 | 0.0 | 0.2058 | 0.1077 | –0.0056 | 0.0887 | –0.1161 | –0.1783 | –0.0097 | –0.0721 | 0.0070 |
| 7 | 0.0 | –0.1669 | 0.1769 | –0.2974 | –0.1050 | 0.1147 | 0.1091 | –0.0103 | 0.0532 | –0.0755 |
| 8 | 0.0 | 0.0123 | 0.0 | 0.5811 | 0.0 | 0.1793 | 0.0 | 0.0 | 0.0062 | 0.0 |
| 9 | 0.0 | –0.0123 | 0.0 | –0.5811 | 0.0 | 0.1793 | 0.0 | 0.0 | 0.0062 | 0.0 |
| 10 | 0.0 | 0.1669 | 0.1769 | 0.2974 | 0.1050 | 0.1147 | –0.1091 | 0.0103 | 0.0532 | 0.0755 |
| 11 | 0.0 | 0.4055 | 0.1929 | 0.0924 | 0.1278 | –0.2439 | –0.2056 | –0.0861 | 0.0289 | 0.0463 |
| 12 | 0.0 | –0.1435 | 0.0 | –0.5860 | 0.0 | 0.3122 | 0.0 | 0.0 | –0.0269 | 0.0 |
| 13 | 0.0 | 0.4055 | –0.1929 | 0.0924 | –0.1278 | –0.2439 | 0.2056 | 0.0861 | 0.0289 | –0.0463 |
| 14 | 0.0 | –0.1669 | –0.1769 | –0.2974 | 0.1050 | 0.1147 | –0.1091 | 0.0103 | 0.0532 | 0.0755 |
| 15 | 0.0 | 0.2058 | –0.1077 | –0.0056 | –0.0887 | –0.1161 | 0.1783 | 0.0097 | –0.0721 | –0.0070 |
| 16 | 0.0 | –0.2058 | –0.1077 | 0.0056 | 0.0887 | –0.1161 | –0.1783 | –0.0097 | –0.0721 | 0.0070 |

[a] Monopoles are located 1.0806 Å above and below the aromatic ring. Charges given are those for each monopole in units of $10^{-10}$ esu. [b] Charges for $^1L_a$, $^1B_b$, and $^1B_a$ transitions are the results of PPP-CI calculation normalized to reproduce the observed oscillator strength. For other transitions the PPP-CI results are given. [c] Numbering of the carbon atoms is as follows:



rected to reproduce the oscillator strengths observed for methyl 4-(1-pyrenyl)butyrate in trimethyl phosphate.

Each vibronic peak in the $^1L_b$, $^1L_a$, $^1B_b$, and $^1B_a$ bands of the pyrenyl group was treated as a single independent transition. The direction of the transition moment and the charges of transition monopoles for each vibronic transition were assumed to be the same within vibronic peaks which belong to the same band. The magnitude of the vibronic transition moment and the absolute value of the monopole charges were calculated to reproduce the partial oscillator strength of each vibronic peak, which has been evaluated by a least-squares curve resolution of the experimental absorption spectrum of methyl 4-(1-pyrenyl)butyrate in trimethyl phosphate. The result of the curve resolution is shown in Figure 3. In the figure, the wavenumbers of the 0–0 transitions of the three bands were assumed to be 29 095 ($^1L_a$), 36 179 ($^1B_b$), and 41 102 ($^1B_a$) cm$^{-1}$. No information is available for the peak positions and the spacings of the $^1L_b$ band. The small peak observed at 26 539 cm$^{-1}$ was taken to be the 0–0 peak of the $^1L_b$ band and four other vibronic peaks were positioned with an equal interval of 1400 cm$^{-1}$. The oscillator strength of the $^1L_b$ band was set equal to zero. Therefore, the peak positions of the $^1L_b$ vibronic peaks are not important in the following calculation. The positions and partial oscillator strengths of the vibronic peaks used for the CD calculation are collected in Table II.

To evaluate the nondiagnoal Hamiltonian matrix elements between local exciteted states within the same pyrenyl group, dipole moments and monopole charges for the transitions between excited states, i.e., $^1L_b$–$^1L_a$, $^1L_b$–$^1B_b$, $^1L_b$–$^1B_a$, $^1L_a$–$^1B_b$, $^1L_a$–$^1B_a$, and $^1B_b$–$^1B_a$, are required. These quantities can be evaluated from the PPP-CI result.[10,11] However, the MO calculation does not predict the dipole moments for vibronic transitions between the excited states. We have assumed that only vibronic transitions between the excited states having the same vibrational quantum number possess nonzero dipole moments.[4] The assumption is physically equivalent to assuming the same equilibrium nuclear configurations for the two excited states. It has been shown in the case of poly(L-1- and 2-naphthylalanines) that the above assumption does not affect the final CD curves,[4] because of the negligible contribution of the corresponding Hamiltonian elements. The monopole charges for the pyrenyl transitions thus evaluated are tabulated in Table III.

Since the number of excited states for a monomeric PyrAla unit is 18, the total number of local excited states for the pentadecamer of L-1-PyrAla is 270. Thus, the Hamiltonian matrix of the dimension of 270 × 270 was constructed and diagonalized to obtain the wave functions and the energies of the polymer. The theoretical CD curves were computed from these data according to the procedure of Woody.[8]

The theoretical CD curves for the ME conformations listed in Table I are shown in Figure 4. These spectra should be compared with the experimental one presented in the accompanying paper (Figure 2 in ref 2).[12] The most reasonable criterion for the fitness of the calculated curve to the experimental one may be the sign of the exciton splitting of $^1B_a$ and $^1B_b$ bands, whose transitions are allowed. Hence, three conformations, i.e., LH-ME-A, LH-ME-B, and RH-ME-C, were found to be acceptable. All three conformations correctly predicted the negative CD observed at the longest wavelength peak of the $^1L_a$ band. We cannot choose one conformation from the three solely on the basis of the theoretical CD. However, the empirical energy calculation suggests that the LH-ME-A conformation has a lower energy of about 3 kcal mol$^{-1}$ than the PyrAla residue (Table I) and has a broader potential minimum (Figure 2) than the other two conformations. Hence, at the present, one may claim that among the three possible conformations of poly(L-1-PyrAla), LH-ME-A, LH-ME-B, and RH-ME-C, the first one is most likely.

In Figure 5 are shown NAMOD molecular display drawings[13] for the three possible conformations. In the three helical conformations, the nearest pair of pyrenyl groups are the first and fifth ones. The center-to-center distances are 7.4 Å for LH-ME-A, 7.5 Å for LH-ME-B, and 6.1 Å for RH-ME-C conformations. The center-to-center distances between the first and second pair of pyrenyl groups are 9.6 Å for LH-ME-A, 11.1 Å for LH-ME-B, and 9.8 Å for RH-ME-C conformations.

## References and Notes

(1) Egusa, S.; Sisido, M.; Imanishi, Y. *Chem. Lett.* **1983**, 1307.
(2) Egusa, S.; Sisido, M.; Imanishi, Y. *Macromolecules*, preceding article in this issue.
(3) Sisido, M; Egusa, S.; Imanishi, Y. *J. Am. Chem. Soc.* **1983**, *105*, 1041.
(4) Sisido, M.; Egusa, S.; Imanishi, Y. *J. Am. Chem. Soc.* **1983**, *105*, 4077.
(5) Momany, F. A.; McGuire, R. F.; Burgess, A. W.; Scheraga, H. A. *J. Phys. Chem.* **1975**, *79*, 2361.
(6) Chen, A. K.; Woody, R. W. w. *J. Am. Chem. Soc.* **1971**, *93*, 29.
(7) Woody, R. W. *Biopolymers*, **1972**, *11*, 1149.
(8) Woody, R. W. *Macromol. Rev.* **1977**, *12*, 181.
(9) Woody, R. W. *J. Chem. Phys.* **1968**, *49*, 4797.
(10) Hummel, R. L.; Ruedenberg, K. *J. Phys. Chem.* **1962**, *66*, 2334.
(11) Hummel, R. L.; Ruedenberg, K. *U.S. At. Energy Committee Rep.* **1964**, *IS450*.
(12) The theoretical CD spectra overestimate the CD intensity roughly by 1 order of magnitude. This is partly due to the fact that the observed spectrum corresponds to an average of thermally fluctuating conformations, especially in the side chains, and also due to an inadequate choice of the Gaussian broadening factor (10 nm) allotted to each rotational strength. The latter parameter was not adjusted to reproduce the observed spectrum, because the absolute intensity of CD spectrum in the absence of thermal fluctuation is unknown.
(13) Beppu, Y. Quantum Chemistry Program Exchange, University of Indiana, Bloomington, IN, No. 370, 1979.