Conformational Energy and Unperturbed Chain Dimension of Polypeptide Copolymers

Seiji TANAKA and Akio NAKAJIMA*

Department of Polymer Chemistry, Kyoto University, Sakyo-ku, Kyoto Japan.

(Received March 20, 1971)

ABSTRACT: Copolypeptides composed of two components among L-alanine, glycine, N-methylglycine, and N-methyl-L-alanine, and D, L-copolypeptides composed either of D-alanine and L-alanine or of N-methyl-D-alanine, N-methyl-L-alanine were theoretically investigated for conformational energies and unperturbed average chain dimensions, assuming *trans* conformation both for amide and imide bonds.

The characteristic ratios of copolymers were calculated as a function of sequence probability that a residue of the minor component is followed by a residue of the same kind at varied copolymer compositions. For equimolar copolymers, the effect of the degrees of polymerization was also investigated. In racemic D, L-copolymers, the chain dimensions are predicted as markedly dependent on the isotacticity of the polymer. The remarkable effect of N-methylalanine residue on the chain dimension was also discussed.

KEY WORDS Copolymer / Polypeptide / D, L-Copolypeptide / Racemic Copolymer / Glycine / Alanine / N-methylglycine / N-methylalanine / Characteristic Ratio / Chain Conformation /

In our preceding paper,^{1,14} the characteristic ratios of polypeptide homopolymers such as poly(L-alanine), polyglycine, poly(N-methyl-L-alanine) and poly(N-methylglycine), were theoretically investigated.

With regard to polypeptide copolymers, so far, theoretical calculations on the chain dimension have been performed on random glycine-alanine-type copolymers,^{2,3} D, L-copolymers^{2,3} having alanine-type side chains, and copolymers^{2,3} containing proline residues.

The advantage in conformation calculations of polypeptides is that the chain can be treated as a semiindependent rotation model chain,³⁻⁵ whose conformation is described by a function only of ϕ and ψ , the rotational angles around $N_i-C_i^\alpha$ and $C_i^\alpha-C_{i+1}^\alpha$ bonds adjoining C_i^α (see Figure 1). The semiindependent rotation model is also valid for copolypeptides, and enables us to calculate explicitly the characteristic ratio based on configurational and conformational considerations on the copolypeptide chains, without using the Monte Carlo calculation.

In this paper, we shall deal with the characteristic ratios for copolypeptides composed of

two components out of L-alanine (abbreviated as Ala), glycine (Gly), N-methylglycine (NMG), and N-methyl-L-alanine (NMA), and for D, L-copolypeptides composed either of D-alanine (D-Ala) and L-alanine (L-Ala) or of N-methyl-D-alanine (D-NMA) and N-methyl-L-alanine (L-NMA), by assuming *trans* conformation for all the amide and imide bonds and employing the same parameters and potential functions as used in a preceding paper.¹

With regard to N-methyl-L-alanine, the characteristic ratio of the homopolymer obtained in a preceding paper¹ was as small as *ca.* 0.6. Moreover, the conformational energy contour diagram obtained there also suggests that the NMA sequence in homopolymer and copolymer chains is treated as a helix rather than a random coil, though the experimental result is not known. For these reasons, in this paper, the NMA sequence is treated not only as a random coil but also as a helix.

CONFORMATIONAL ENERGY

Molecular Structure and Configuration of Copolypeptides

* To whom correspondence should be addressed.

Figure 1. Fully extended copolypeptide chain. Either R^N or R^α represents a hydrogen atom or a methyl group. The broken lines denote virtual bonds.

In Figure 1, a portion of a polypeptide chain, including the i -th amino acid residue and parts of both the $(i-1)$ -th and the $(i+1)$ -th amino acid residues, is represented in its fully extended *trans* conformation, where R_i^N and R_i^α denote, respectively, the substituents attached to the nitrogen atom N_i and to the α -carbon atom C_i^α of the i -th residue. This figure, which is the same as in a preceding paper,¹ is also adopted for copolypeptides by regulating the kind of the substituents assigned for R_i^N , R_i^α , R_{i+1}^N , etc. As is obvious from Figure 1, the conformational energy $V(\phi_i, \psi_i)$ of the i -th residue in a copolymer chain depends on the kind of the $(i+1)$ -th residue but not on that of the $(i-1)$ -th residue. Concretely, in the $(i+1)$ -th residue the substituent R_{i+1}^N participates to determine $V(\phi_i, \psi_i)$, but in the $(i-1)$ -th residue only the atom O_{i-1} plays the role. Thus, the kind of the $(i-1)$ -th residue does not affect $V(\phi_i, \psi_i)$. In conclusion, the conformational energy $V(\phi_i, \psi_i)$ of copolypeptides is explicitly defined by R_i^N , R_i^α , and R_{i+1}^N . If we represent $-\text{CH}_3$ group and the hydrogen atom attached either to the nitrogen or to the α -carbon atom by R and H, respectively, then all the copolypeptide chains composed of two components out of Ala, Gly, NMG, and NMA are constructed by taking into account the eight kinds of combination of $(R_i^N \cdot R_i^\alpha \cdot R_{i+1}^N)$ shown in Table I. For example, the configurations given either by Ala—NMG or by Ala—NMA are equally represented by (H·R·R). As mentioned in a previous paper,¹³ R may be regarded as not only the $-\text{CH}_3$ group but also the $-\text{CH}_2\text{—R}'$ group.

Hereafter, the conformational energy $V(\phi_i, \psi_i)$ defined as a function of ϕ_i and ψ_i is designated for copolypeptides as $V_{(R_i^N, R_i^\alpha, R_{i+1}^N)}(\phi_i, \psi_i)$.

Table I. Configurations in copolypeptide chains

	$\begin{array}{c} R_i^N \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ R_i^\alpha \quad R_{i+1}^N \end{array}$	$R_i^N \cdot R_i^\alpha \cdot R_{i+1}^N$
Gly—Gly}	$\begin{array}{c} H \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ H \quad H \end{array}$	H · H · H
Gly—Ala}	$\begin{array}{c} H \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ H \quad H \end{array}$	H · H · H
Ala—Ala}	$\begin{array}{c} H \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ CH_3 \quad H \end{array}$	H · R · H
Ala—Gly}	$\begin{array}{c} H \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ CH_3 \quad H \end{array}$	H · R · H
NMG—NMG}	$\begin{array}{c} CH_3 \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ H \quad CH_3 \end{array}$	R · H · R
NMG—NMA}	$\begin{array}{c} CH_3 \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ H \quad CH_3 \end{array}$	R · H · R
NMA—NMA}	$\begin{array}{c} CH_3 \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ CH_3 \quad CH_3 \end{array}$	R · R · R
NMA—NMG}	$\begin{array}{c} CH_3 \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ CH_3 \quad CH_3 \end{array}$	R · R · R
NMA—Ala}	$\begin{array}{c} CH_3 \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ CH_3 \quad H \end{array}$	R · R · H
NMA—Gly}	$\begin{array}{c} CH_3 \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ CH_3 \quad H \end{array}$	R · R · H
Ala—NMG}	$\begin{array}{c} H \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ CH_3 \quad CH_3 \end{array}$	H · R · R
Ala—NMA}	$\begin{array}{c} H \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ CH_3 \quad CH_3 \end{array}$	H · R · R
NMG—Ala}	$\begin{array}{c} CH_3 \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ H \quad H \end{array}$	R · H · H
NMG—Gly}	$\begin{array}{c} CH_3 \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ H \quad H \end{array}$	R · H · H
Gly—NMG}	$\begin{array}{c} H \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ H \quad CH_3 \end{array}$	H · H · R
Gly—NMA}	$\begin{array}{c} H \quad O \\ \quad \\ -N-CH-C-N- \\ \quad \\ H \quad CH_3 \end{array}$	H · H · R

taking into account the combinations shown in Table I; e.g., $V_{(RRR)}(\phi_i, \psi_i)$ for either the NMA—NMA or the NMA—NMG configuration.

As mentioned in a preceding paper,¹ the conformational energy for each combination is given by eq 1, where $V_{(T)}(\phi_i)$ and $V_{(T)}(\psi_i)$ are the intrinsic torsional potentials energy $V_{(W)jk}(\phi_i, \psi_i)$ is the van der Waals interaction energy between nonbonded atoms j and k , and the last term concerns the dipole—dipole interaction energy between amide and amide, amide and imide, imide and amide, or imide and imide dipoles.

$$\begin{aligned} V_{(R_i^N, R_i^A, R_{i+1}^N)}(\phi_i, \psi_i) \\ = V_{(T)}(\phi_i) + V_{(T)}(\psi_i) + \sum_{jk} V_{(W)jk}(\phi_i, \psi_i) \\ + \sum_{jk} V_{(D)jk}(\phi_i, \psi_i) \end{aligned} \quad (1)$$

Numerical values of molecular parameters, appear in the Lennard—Jones function, and the partial charges on amide and imide groups, and the bond coordinate systems, used in this calculation, are the same as those used in a preceding paper.¹

The contribution from the term $\sum V_{(D)jk}(\phi_i, \psi_i)$ to the total conformational energy $V(\phi_i, \psi_i)$ is shown in Figures 2 and 3, respectively, for the amide—imide and imide—amide dipole interaction. Those for the imide—imide¹ and amide—amide⁶ dipole interactions are not reproduced here, because they have already been mentioned

Figure 2. Contour diagram of nearest neighbor imide—amide dipole interaction energy, $\sum V_{(D)jk}(\phi, \psi)$, for configuration (RRH) or (RHH). Numerals on the contours are the absolute energy values.

Figure 3. Contour diagram of nearest neighbor amide—imide dipole interaction energy, $\sum V_{(D)jk}(\phi, \psi)$, for configuration (HRR) or (HHR). Numerals on the contours are the absolute energy values.

elsewhere. The numerals on the contours in Figures 2 and 3 denote the absolute energy values. To calculate $V_{(HRR)}(\phi_i, \psi_i)$ or $V_{(HHR)}(\phi_i, \psi_i)$ Figure 2 should be used, while Figure 3 is to be used for calculation of $V_{(RRH)}(\phi_i, \psi_i)$ or $V_{(RHH)}(\phi_i, \psi_i)$.

Conformational Energy Contour Diagrams

From eq 1, the conformational energy $V_{(R_i^N, R_i^A, R_{i+1}^N)}(\phi_i, \psi_i)$ was calculated at 20° intervals from 0° to 340° for ϕ_i and ψ_i . The contour diagram of $V_{(RRR)}(\phi_i, \psi_i)$ for the combination NMA—NMG (i.e., NMA succeeded by NMG) is the same as that for NMA—NMA (Figure 6 in ref 1) which has already been obtained¹ NMA-homopolymer. Analogously, the contour diagrams for Gly—Ala, Ala—Gly, and NMG—NMA are, respectively, the same as those for Gly—Gly, Ala—Ala, and NMG—NMG; those for $V_{(HHH)}(\phi_i, \psi_i)$, $V_{(HRR)}(\phi_i, \psi_i)$ and $V_{(RRH)}(\phi_i, \psi_i)$ are, respectively, represented in Figures 5, 4, and 7 in ref 1.

The conformational energies for NMA succeeded by either Ala or Gly, for Ala succeeded by either NMG or NMA, for NMG succeeded by either Ala or Gly, and for Gly succeeded by either NMG or NMA are, respectively, represented by $V_{(RRH)}(\phi_i, \psi_i)$, $V_{(HRR)}(\phi_i, \psi_i)$, $V_{(RHH)}(\phi_i, \psi_i)$, and $V_{(HHR)}(\phi_i, \psi_i)$, as is obvious from Table I.

Figure 4. Contour diagram of total conformational energy $V_{(RRH)}(\phi, \psi)$ for NMA—Ala, or NMA—Gly. The absolute minimum at $\times$ corresponds to -0.39 kcal/mol; the contour interval is 1 kcal/mol of peptide units relative to the minimum.

Figure 6. Contour diagram of total conformational energy $V_{(RHH)}(\phi, \psi)$ for NMG—Ala, or NMG—Gly. The absolute minima at $\times$ correspond to -4.14 kcal/mol; contours are drawn as in Figure 4.

Figure 5. Contour diagram of total conformational energy $V_{(HRR)}(\phi, \psi)$ for Ala—NMG, or Ala—NMA. The absolute minimum at $\times$ corresponds to 1.25 kcal/mol; contours are drawn as in Figure 4.

Figure 7. Contour diagram of total conformational energy $V_{(HHR)}(\phi, \psi)$ for Gly—NMG, or Gly—NMA. The absolute minima at $\times$ correspond to -1.34 kcal/mol; contours are drawn as in Figure 4.

The conformational energy contour diagrams for $V_{(RRH)}(\phi_i, \psi_i)$, $V_{(HRR)}(\phi_i, \psi_i)$, $V_{(RHH)}(\phi_i, \psi_i)$, and $V_{(HHR)}(\phi_i, \psi_i)$ are, respectively, indicated in Figures 4–7. The lowest energy positions are denoted by the symbol $\times$, and the contours are drawn by the energy levels relative to the lowest energy value. Relatively stable regions

in each diagram are designated as regions I, II, III, etc. In Table II are shown the most stable conformations as given by (ϕ, ψ) in each region and their energy absolute value. The conformational energies, without dipole interaction terms [*i.e.*, $\sum V_{(D)jk}(\phi_i, \psi_i) = 0$, $\epsilon = \infty$], are shown in column 6. Comparison of column 6 with column 5 may afford data on the dipolar interaction.

Table II. Low energy conformations on the energy contour diagrams

Configuration ($R_i^N, R_i^\alpha, R_{i+1}^N$)	Regions designated on the contour diagrams, Figures 4—7	Rotational angles (in degree)		Absolute conformational energy, $V_{(R_i^N, R_i^\alpha, R_{i+1}^N)}(\phi, \psi)$ in kcal/mol	
		ϕ	ψ	including $V_{(D)}(\phi, \psi)$ in eq 1	excluding $V_{(D)}(\phi, \psi)$ in eq 1
(RRH)	I	60	260	0.3	0.0
	II	240	240	-0.3	0.1
	III	240	0	-0.4	0.4
(HRR)	I	20	340	1.3	-0.1
	II	240	260	2.4	-0.4
	III	240	340	2.8	0.8
(RHH)	I (I')	100 (260)	260 (100)	-4.1	-3.0
	II (II')	100 (0)	0 (260)	-3.3	-2.8
	III (III')	100 (260)	120 (240)	-3.8	-3.6
(HHR)	I (I')	100 (260)	0 (360)	-1.3	-3.1
	II (II')	0 (360)	260 (100)	-0.5	-2.9
	III (III')	120 (240)	100 (260)	-0.5	-3.3
	IV (IV')	0 (360)	100 (260)	-0.5	-2.9

UNPERTURBED CHAIN DIMENSION

Arrangement of monomer units in a copolypeptide chain is characterized by the polymerization mechanism. Here we are concerned with A,B-copolypeptides constructed according to the Markoffian process. With a Markoffian chain, the reactivity of the i -th monomer unit depends on the kind of the $(i-1)$ -th unit, *i.e.*, the relative reactivities of A and B monomer units depend only on the kind of terminal unit of the growing chain.⁷ Let p_{AB} be the conditional probability that an A unit is succeeded by a B unit, and let us assume that p_{AB} , together with p_{AA} , p_{BA} and p_{BB} similarly defined, are constant in the course of the polymerization process. Then the matrix P of sequence probability is given by eq 2.

$$P = \begin{bmatrix} p_{AA} & p_{AB} \\ p_{BA} & p_{BB} \end{bmatrix} \quad (2)$$

For the 1st amino acid residue ($i=1$), the matrix P_1 written as

$$P_1 = \begin{bmatrix} p_{A;1} & 0 \\ 0 & p_{B;1} \end{bmatrix} \quad (3)$$

where $p_{A;1}$ and $p_{B;1}$ denote, respectively, the *a priori* probabilities that the 1st residue is A and B.

The matrices P and P_1 are stochastic, hence

$$\left. \begin{aligned} p_{AA} + p_{AB} &= 1 \\ p_{BA} + p_{BB} &= 1 \\ p_{A;1} + p_{B;1} &= 1 \end{aligned} \right\} \quad (4)$$

Further, denoting the *a priori* probability that the i -th residue is an A or B unit by $p_{A;i}$ or $p_{B;i}$, we obtain the following relation after the Markoffian process.

$$[p_{A;i} \ p_{B;i}] \begin{bmatrix} p_{AA} & p_{AB} \\ p_{BA} & p_{BB} \end{bmatrix} = [p_{A;i+1} \ p_{B;i+1}] \quad (5)$$

We now assume that the chain is sufficiently long. Then $p_{A;i}$ and $p_{B;i}$ are considered to be independent of i . Let p_A and p_B be *a priori* probabilities for A and B, respectively, averaged over all the units. Then

$$p_A p_{AA} + p_B p_{BA} = p_A \quad (6)$$

These *a priori* probabilities and conditional probabilities are related to such quantities which are experimentally obtained as the monomer frequencies F_A and F_B and the dimer frequencies F_{AA} , F_{AB} , etc.⁸ In other words, the monomer frequencies are equal to corresponding *a priori* probabilities, *i.e.*, $F_A = p_A$ and $F_B = p_B$. The dimer frequencies are related to the conditional probabilities by the relations $F_{AA} = F_A p_{AA}$, $F_{AB} = F_A p_{AB}$, $F_{BA} = F_B p_{BA}$, and $F_{BB} = F_B p_{BB}$. Thus eq 6, for example, is written as

$$F_A p_{AA} + F_B p_{BA} = F_A \quad (7)$$

Further, among dimer frequencies the relations $F_{AB} = F_{BA}$ and $F_{AA} + F_{AB} + F_{BA} + F_{BB} = 1$ are held. Accordingly, Markoffian distribution is described by two independent variables, *e.g.*, if p_A and p_{AA} are known, then other quantities are given by a function of p_A and p_{AA} or if F_A , F_{AA} , etc., are experimentally known, then conditional probabilities are obtained.

The chain conformations of binary copolymers may be classified into two categories, type I and type II; copolymers in which the conformational energy $V(\phi_i, \psi_i)$ for the i -th unit is not varied by the selection of monomers (A or B) for $(i+1)$ -th unit are denoted as type I, while those in which $V(\phi_i, \psi_i)$ for the i -th unit is varied in accordance with the monomer selection for the $(i+1)$ -th unit are denoted as type II. In type I are included the homopolymers as mentioned previously¹ and copolymers composed of either amide—amide or imide—imide sequence. On the other hand, copolymers composed of Ala and NMG, Ala and NMA, Gly and NMG, or Gly and NMA, and copolymers³ including prolyl units, are included in type II.

The statistical average $\langle T \rangle$ of the matrix T which transforms virtual bond vector l_{i+1} to l_i is given by¹

$$\langle T \rangle = \frac{\int_0^{2\pi} \int_0^{2\pi} T(\phi, \psi, \theta''', \xi, \eta) \exp[-V(\phi, \psi)/RT] d\phi d\psi}{\int_0^{2\pi} \int_0^{2\pi} \exp[-V(\phi, \psi)/RT] d\phi d\psi} \quad (8)$$

for the eight kinds of configurations shown in Table I; these are expressed as $\langle T \rangle_{(HHH)}$, $\langle T \rangle_{(HHR)}$, $\langle T \rangle_{(RHR)}$, etc.

According to the theory given by Flory,^{9,10} the characteristic ratio of homopolypeptides with finite chain length is expressed as

$$\frac{\langle R_0^2 \rangle}{nl^2} = \frac{2}{nl^2} [1 \ 0 \ 0 \ 0 \ 0] \prod_{i=1}^n G_i \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{bmatrix} \quad (9)$$

in which

$$G_i = \begin{bmatrix} 1 & l^T \langle T \rangle & l^2/2 \\ 0 & \langle T \rangle & l \\ 0 & 0 & 1 \end{bmatrix} \quad (10)$$

When we substitute $\langle T \rangle_{(RHR)}$ in $\langle T \rangle$, we obtain $\langle R_0^2 \rangle / nl^2$ for NMG-homopolymer.¹

The characteristic ratio for type I copolymers is evaluated by the method reported by Miller, *et al.*² For A,B-copolymers, $\langle T \rangle_A$ and $\langle T \rangle_B$ are evaluated from eq 8 and with the matrices G_A and G_B are constructed. Note that for type I copolymers, $G_A = G_{AA} = G_{AB}$ and $G_B = G_{BA} = G_{BB}$. Now, introducing the matrix G and matrix P_i [which equal to P in eq 2], we construct the matrix K for i -th residue,

$$K = \begin{bmatrix} p_{AA} G_A & p_{AB} G_B \\ p_{BA} G_A & p_{BB} G_B \end{bmatrix} \quad (11)$$

and K_1 for $i=1$.

$$K_1 = \begin{bmatrix} p_{A,1} G_A & 0 \\ 0 & p_{B,1} G_B \end{bmatrix} \quad (12)$$

Thus the characteristic ratio for this type of A,B-copolypeptide chain is given by

$$\frac{\langle R_0^2 \rangle}{nl^2} = \left(\frac{2}{nl^2} \right) [1 \ 0 \ 0 \ 0 \ 0 \ 1 \ 0 \ 0 \ 0 \ 0] K_1 K^{n-1} \begin{bmatrix} 0 \\ 0 \\ 0 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{bmatrix} \quad (13)$$

In eq 13, the bar drawn over $\langle R_0^2 \rangle$ means the average over all the possible configurations of copolymers obtained by polymerization reaction.

With respect to type II copolymers, since the conformational energy of the i -th residue depends on the monomer selection for the $(i+1)$ -th residue, G_i in eq 10 should be individually constructed for AA, AB, BA, and BB, respectively, as G_{AA} , G_{AB} , G_{BA} , and G_{BB} . With these matrices G 's, a matrix K analogous to eq 11 should be constructed. However, for type II copolymers,

the matrices G 's and P introduced should be different from those appearing in eq 11. In this case, the treatment as used by Schimmel, *et al.*,³ is necessary. For type II copolymers, the reactivity of the i -th residue depends on the kind of the $(i-1)$ -th residue, while the conformation of the i -th residue depends on the kind of the $(i+1)$ -th residue. Accordingly, the matrix K for the i -th residue should be constructed after the reaction proceeds to the $(i+1)$ -th residue. In other words, P introduced in K should be P_{i+1} , *i.e.*, P for $(i+1)$ -th residue, instead of P_i , *i.e.*, P for i -th residue.

Thus, for the i -th residue ($1 < i < n$)

$$K = \begin{bmatrix} G_{AA}P_{AA} & G_{AB}P_{AB} \\ G_{BA}P_{BA} & G_{BB}P_{BB} \end{bmatrix} \quad (14)$$

and for the 1st residue ($i=1$)

$$K_1 = \begin{bmatrix} E_5 P_A & 0 \\ 0 & E_5 P_B \end{bmatrix} \quad (15)$$

where E_5 is the unit matrix of the order 5. For the terminal residue ($i=n$), the matrix K_n^* is written as

$$K_n^* = K_{n-1} \begin{bmatrix} G & 0 \\ 0 & G \end{bmatrix} = \begin{bmatrix} G_{AA}P_{AA}G & G_{AB}P_{AB}G \\ G_{BA}P_{BA}G & G_{BB}P_{BB}G \end{bmatrix} \quad (16)$$

Finally, the characteristic ratio is expressed by

$$\frac{\langle R_0^2 \rangle}{nl^2} = \left(\frac{2}{nl^2} \right) [1 \ 0 \ 0 \ 0 \ 0 \ 1 \ 0 \ 0 \ 0 \ 0] K_1 K^{n-2} K_n^* \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{bmatrix} \quad (17)$$

RESULTS ON NUMERICAL CALCULATION

Statistical Mechanical Average of Transformation Matrices

The averaged transformation matrices $\langle T \rangle$'s for eight pairs of configuration were evaluated at an assumed temperature 25°C from eq 8. In practical calculations, the integrals in eq 8 were replaced by summations over ϕ_i and ψ_i from 0° to 330° in 30° intervals. The obtained results are as follows.

$$\langle T \rangle_{(RRR)} = \begin{bmatrix} 0.332 & 0.132 & 0.835 \\ -0.166 & 0.552 & -0.222 \\ -0.557 & -0.027 & 0.223 \end{bmatrix} \quad (18)$$

$$\langle T \rangle_{(RRH)} = \begin{bmatrix} 0.340 & 0.156 & 0.492 \\ -0.250 & 0.366 & -0.277 \\ -0.509 & 0.118 & 0.205 \end{bmatrix} \quad (19)$$

$$\langle T \rangle_{(RRH)} = \begin{bmatrix} 0.578 & 0.653 & 0 \\ -0.267 & -0.032 & 0 \\ 0 & 0 & 0.146 \end{bmatrix} \quad (20)$$

$$\langle T \rangle_{(HRR)} = \begin{bmatrix} 0.579 & 0.328 & 0.646 \\ 0.043 & -0.658 & 0.232 \\ 0.601 & -0.127 & -0.359 \end{bmatrix} \quad (21)$$

$$\langle T \rangle_{(RHH)} = \begin{bmatrix} 0.251 & -0.183 & 0 \\ -0.313 & -0.305 & 0 \\ 0 & 0 & -0.115 \end{bmatrix} \quad (22)$$

$$\langle T \rangle_{(HRR)} = \begin{bmatrix} 0.565 & 0.370 & 0.499 \\ -0.055 & -0.573 & 0.417 \\ 0.566 & -0.417 & -0.330 \end{bmatrix} \quad (23)$$

$$\langle T \rangle_{(HHR)} = \begin{bmatrix} 0.620 & 0.615 & 0 \\ -0.097 & -0.212 & 0 \\ 0 & 0 & -0.047 \end{bmatrix} \quad (24)$$

$$\langle T \rangle_{(HHH)} = \begin{bmatrix} 0.368 & -0.004 & 0 \\ -0.163 & -0.392 & 0 \\ 0 & 0 & -0.140 \end{bmatrix} \quad (25)$$

Eq 18, 20, 23, and 25 are, respectively, the same as eq 11, 10, 8, and 9 in ref 1.

Characteristic Ratios of Copolypeptides

(a) *Copolymers of Alanine and N-methylglycine.* This type of copolymer belongs to type II. The characteristic ratio is obtained from eq 17, in which K is constructed by

denoting Ala and NMG as A and B, respectively, and writing as

$$\begin{bmatrix} G_{AA} & G_{AB} \\ G_{BA} & G_{BB} \end{bmatrix} = \begin{bmatrix} G_{(HRH)} & G_{(HRR)} \\ G_{(RHH)} & G_{(RHR)} \end{bmatrix} \quad (26)$$

where, $G_{(HRH)}$, $G_{(HRR)}$, $G_{(RHH)}$, and $G_{(RHR)}$ indicate the matrices G 's obtained eq 10 with $\langle T \rangle$ expressed by eq 23, 21, 22, and 20, respectively.

In the first place, let A(*i.e.*, Ala) be the minor component (*i.e.*, $0 < p_A < 0.5$) of the copolymer. The sequence probability p_{AA} can take values of $0 < p_{AA} < 1$. Thus p_A and p_{AA} are given. Then the numerical values of p_B , p_{AB} , p_{BA} , and p_{BB} are explicitly determined from eq 4 and 6. In Figure 8, the characteristic ratios for Ala(A)—NMG(B) copolymers, in which A is the minor component and $n=153$, are shown as a function of the sequence probability p_{AA} . Next, letting B(*i.e.*, NMG) be the minor component, we obtain the results as shown in Figure 9. The numerals appearing in these figures denote mole% of Ala (Figure 8) and of NMG (Figure 9).

The characteristic ratios of equimolar Ala—NMG copolymers with different chain lengths are shown in Figure 10 as a function of the sequence probability p , by assuming $p=p_{AA}=p_{BB}$. The numerals in the figure indicate the

Figure 8. Plot of the characteristic ratio against the sequence probability p_{AA} for Ala(A)—NMG(B) copolymers ($n=153$). The numerals on the curves denote the mol% of A(minor component).

Figure 9. Plot of the characteristic ratio against the sequence probability p_{BB} for Ala(A)—NMG(B) copolymers ($n=153$). The numerals on the curves denote the mol% of B(minor component).

Figure 10. Plot of the characteristic ratio against the sequence probability $p(=p_{AA}=p_{BB})$ for equimolar Ala(A)—NMG(B) copolymers. The numerals on the curves denote the number of virtual bonds, n , in the chain.

number n of the virtual bonds in the chain. The characteristic ratios at $p=0$, $p=0.5$, and $p=1$ correspond, respectively, to those for the alternative copolymer, the equimolar random copolymer, and the equimolar mixture of Ala- and NMG-homopolymer.

(b) *Copolymers of Alanine and N-methyl-L-alanine.* This type of copolymer also belongs to type II. Representing Ala and NMA by A and B, respectively, we have

$$\begin{bmatrix} G_{AA} & G_{AB} \\ G_{BA} & G_{BB} \end{bmatrix} = \begin{bmatrix} G_{(HRH)} & G_{(HRR)} \\ G_{(RHH)} & G_{(RHR)} \end{bmatrix} \quad (27)$$

The characteristic ratios of Ala(A)—NMA(B)

Figure 11. Plot of the characteristic ratio against the sequence probability p_{AA} or p_{BB} for Ala(A)—NMA(B) copolymers ($n=153$).

Solid curves: NMA(B) is the minor component; numerals on the curves are mol% of NMA(B); abscissa is p_{BB} . Broken curves: Ala(A) is the minor component; numerals on the curves are mol% of Ala(A); abscissa is p_{AA} .

Figure 12. Plot of the characteristic ratio against the sequence probability p ($p=p_{AA}=p_{BB}$) for equimolar Ala(A)—NMA(B) copolymers. The numerals on the curves denote the number of virtual bonds, n , in the chain.

copolymers ($n=153$) as a function of the sequence probability are shown in Figures 11 and 12. In Figure 11, the minor components are A

and B, respectively; Figure 12 refers to equimolar copolymers with different chain lengths.

(c) *Copolymers of Alanine and Glycine.* Copolymers composed of Ala(A-component)—Gly(B-component) belong to type I. The characteristic ratio is obtained from eq 13, by using K [eq 11] constructed with $[G_A \ G_B] = [G_{(HHH)} \ G_{(HHH)}]$. In Figure 13, the characteristic ratios of Ala(A)—Gly(B) copolymers ($n=153$) are plotted against p_{AA} (A is the minor component) or p_{BB} (B is the minor component). For equimolar copolymer with $n=151$, the characteristic ratio is also shown in Figure 13 as a function of p on the assumption of $p=p_{AA}=p_{BB}$.

Figure 13. Plot of the characteristic ratio against the sequence probability for Ala(A)—Gly(B) copolymers.

Solid curves: Gly(B) is the minor component and $n=153$; numerals on the curves are mol% of B (Gly); abscissa is p_{BB} . Chain curve: equimolar copolymer ($n=151$); abscissa is $p_{AA}=p_{BB}$. Broken curves: Ala(A) is the minor component and $n=153$; numerals on the curves are mol% of A (Ala); abscissa is p_{AA} .

(d) *Copolymers Composed of Glycine and L-alanine, of Glycine and N-methyl-L-alanine, and of N-methylglycine and N-methyl-L-alanine.* Gly(A)—NMG(B) and Gly(A)—NMA(B) copolymers belong to type II, while NMG(A)—NMA(B) copolymer belongs to type I. For Gly(A)—NMG(B) copolymer

$$\begin{bmatrix} G_{AA} & G_{AB} \\ G_{BA} & G_{BB} \end{bmatrix} = \begin{bmatrix} G_{(HHH)} & G_{(HHR)} \\ G_{(RHH)} & G_{(RHR)} \end{bmatrix} \quad (28)$$

for Gly(A)—NMA(B) copolymer

Figure 14. Plot of the characteristic ratio against the sequence probability $p (=p_{AA}=p_{BB})$ for equimolar NMA-NMG copolymers (curve I), equimolar Gly-NMA copolymers (curve II), and equimolar Gly-NMG copolymers (curve III).

$$\begin{bmatrix} G_{AA} & G_{AB} \\ G_{BA} & G_{BB} \end{bmatrix} = \begin{bmatrix} G_{(HHH)} & G_{(HHR)} \\ G_{(RRH)} & G_{(RRR)} \end{bmatrix} \quad (29)$$

and for NMG(A)-NMA(B) copolymer

$$[G_A \quad G_B] = [G_{(RHR)} \quad G_{(RRR)}] \quad (30)$$

The characteristic ratios for corresponding copolymers are obtained from eq 17 with eq 28 or 29 and from eq 13 with eq 30.

In Figure 14 are shown the characteristic ratios of equimolar copolymers ($n=150$) composed of Gly and NMG, of Gly and NMA, and of NMG and NMA, as functions of sequence probability p , by assuming $p=p_{AA}=p_{BB}$.

(e) *Racemic Copolymers of N-methyl-D-alanine and N-methyl-L-alanine.* The averaged transformation matrix $\langle T \rangle_{L-(RRR)}$ for N-methyl-L-alanine is already given by eq 18. The conformational energy $V_{L(RRR)}(\phi, \psi)$ of L-isomer is related to that of D-isomer by

$$V_{L(RRR)}(\phi, \psi) = V_{D(RRR)}(-\phi, -\psi)$$

Thus, the matrix $\langle T \rangle_{D-(RRR)}$ for N-methyl-D-alanine is derived, from the relation just mentioned above, as

$$\langle T \rangle_{D-(RRR)} = \begin{bmatrix} 0.332 & 0.132 & -0.835 \\ -0.166 & 0.552 & 0.221 \\ 0.557 & 0.027 & 0.223 \end{bmatrix} \quad (31)$$

The racemic NMA copolymers belong to type I; hence the characteristic ratio is obtained from eq 13 by letting

Figure 15. Plot of the characteristic ratio against the isotacticity, f , for racemic D,L-NMA copolymers. The numerals on the curves denote the number of virtual bonds, n , in the chain.

$$[G_A \quad G_B] = [G_{L-(RRR)} \quad G_{D-(RRR)}]$$

in eq 11. In the polymerization of D and L units, for the present system, the probability p_{AA} that a D-residue follows a D-residue is assumed to be equal to that p_{LL} for an L-residue to follow an L-residue, and represented as $p_{LL}=p_{DD}=f$. f is regarded as a measure of isotacticity of the chain. The results of calculations are shown in Figure 15, in which the numerals denote the number n of the virtual bonds in the chain. The characteristic ratios at $f=0$, $f=0.5$, and $f=1$ correspond to those for completely syndiotactic polymer, random D,L-copolymer, and an equimolar mixture of D- and L-homopolymers.

(f) *D,L-copolymers of Alanine or of N-methyl-alanine.* In this section, we are concerned with copolymers containing D- and L-enantiomorphs in different molar ratios. The case where the symmetry principle, i.e., $p_{LL}=p_{DD}$ and $p_{LD}=p_{DL}$, holds in the polymerization process, has already been discussed in section (e). In the copolymerization of D- and L-N-carboxyanhydrides, the relative reactivities of the components may depend not only on the terminal residue of the growing chain but also on a particular residue preceded by a few (two or three) residues from the terminal residue. In such a case, the chain may be treated⁷ as a Markoffian chain which satisfies given conditions. In principle, this may be performed by increasing the order of the

matrix P . However, in the present treatment, D,L-copolymers are regarded as obeying the simple Markoffian process in which reactivities of the components depend only on the terminal residue of the growing chain. The copolymers referred to here are regarded as those polymerized under conditions in which the symmetry principle is broken, *i.e.*, $p_{LL} \neq p_{DD}$.

D,L-Ala-copolymers and D,L-NMA-copolymers belong to type I. The averaged transformation matrix $\langle T \rangle_{D-(\text{HRRH})}$ for D-alanine is derived from

eq 23 for L-alanine:

$$\langle T \rangle_{D-(\text{HRRH})} = \begin{bmatrix} 0.565 & 0.370 & -0.499 \\ -0.055 & -0.573 & -0.417 \\ -0.566 & 0.417 & -0.330 \end{bmatrix} \quad (32)$$

The characteristic ratios are calculated from eq 13 by using K constructed from

$[G_A \ G_B] = [G_{L-(\text{HRRH})} \ G_{D-(\text{HRRH})}]$ for Ala,
and

$[G_A \ G_B] = [G_{L-(\text{RRR})} \ G_{D-(\text{RRR})}]$ for NMA.

The characteristic ratio, as a function of the sequence probability p (*i.e.*, p_{LL} or p_{DD}) that a residue of the minor component is succeeded by the same kind of residue, is shown in Figure 16 for D,L-Ala-copolymers, and in Figure 17 for D,L-NMA-copolymers. Note that $p_{LL} \neq p_{DD}$. The numerals on the curves indicate the mole% of the minor component; for example, the abscissa gives p_{LL} for D:L=80:20 copolymer, while it gives p_{DD} for D:L=20:80 copolymer. These figures lead to the plots of characteristic ratio against the stereocomposition (say %L-isomer) of randomly sequenced D,L-Ala- or D,L-NMA-copolymer which give a symmetrical curve about an axis at %L=50.

Figure 16. Plot of the characteristic ratio against the sequence probability p that a residue of the minor component is succeeded by the same kind of residue for D,L-Ala copolymers ($n=150$). The numerals on the curves denote the mol% of the minor component.

Figure 17. Plot of the characteristic ratio against the sequence probability p that a residue of the minor component is succeeded by the same kind of residue for D,L-NMA copolymers ($n=150$). The numerals on the curves denote the mol% of the minor component.

Effect of Helical Parts on $\langle R_0^2 \rangle / nl^2$ of Binary Copolymers Containing N-Methylalanine

In a preceding paper,¹ we pointed out that the poly(*N*-methylalanine) chain is extremely restricted for rotations about the N—C $^\alpha$ and C $^\alpha$ —C' bonds. In a contour diagram, four conformationally available regions, I, II, III, and IV, were found. In particular, the contribution of the region III containing the left-handed α -helix, is very large.¹ The calculated characteristic ratio for infinite chain is unusually as small as 0.6. Neither the circumstances where the NMA chain portion exists either in helix or in coil conformation, nor information about the helix—coil transition for NMA chains has been ascertained experimentally as yet. However, there is a possibility that the NMA chain portion in homopolymers and copolymers takes a helix conformation. If the NMA chain takes a crystalline structure even in solution, then the probable conformation is assumed to be left-handed α -helix.

In this section we shall discuss the effect of the rod-like portion of the helix conformation on the characteristic ratio. Such considerations are similar to those reported by Nagai¹¹ on the change of the characteristic ratio in the helix-coil transition region. Nagai's treatment is based on the equilibrium theory. On the other hand, in the present treatment, the NMA residue is treated as contributing only to the helix.

Our calculations done on the copolymer composed of Ala and NMA, as an example, assumed that Ala-residues were in random coil and NMA-residues were in left-handed α -helix conformation. The rotational angles ϕ , ψ for NMA were assumed to be $\phi = -122^\circ$, $\psi = -133^\circ$, as assigned to the left-handed α -helix by Pauling and Cory,¹² although the lowest energy point obtained from the contour diagram was located at $\phi = -120^\circ$, $\psi = -100^\circ$ (see Figure 6 in ref 1). Let the transformation matrix for NMA in the left-handed α -helix conformation be T_{helix} . In section (b), Ala-NMA copolymers were treated by assuming that both Ala and NMA are in random coil conformation. For the present model, G_{helix} was constructed from eq 10 by using T_{helix} in place of $\langle T \rangle$. The obtained G_{helix} was inserted in eq 27 in place of $G_{(\text{RRR})}$, to obtain the following equation.

Figure 18. Plot of the characteristic ratio, calculated by assuming NMA residues in helix conformation, against the sequence probability p for equimolar Ala-NMA copolymers. The numerals on the curves denote the number of virtual bonds, n , in the chain.

Figure 19. Plot of the characteristic ratio, calculated by assuming NMA residues in helix conformation, against the number of virtual bonds, n , for Ala-NMA copolymers.

Solid curves: Ala content is 5 mol%. Broken curves: Ala content is 20 mol%. The numerals on the curves denote the sequence probability of Ala-Ala.

$$\begin{bmatrix} G_{AA} & G_{AB} \\ G_{BA} & G_{BB} \end{bmatrix} = \begin{bmatrix} G_{(\text{HRH})} & G_{(\text{HRR})} \\ G_{(\text{RRH})} & G_{\text{helix}} \end{bmatrix} \quad (33)$$

The characteristic ratio for a copolymer with finite chain length was calculated from eq 17 using K derived from eq 33.

In Figure 18, the characteristic ratios for equimolar Ala-NMA copolymers with various n are shown as a function of p . The dependence of the characteristic ratios on n , the number of virtual bonds in the chain, is shown in Figure 19, where solid curves are concerned with 5-mol% Ala and broken curves with 20-mol% Ala content. The numerals on the curves denote the values of sequence probability p_{AA} that an Ala unit is followed by an Ala unit.

The effect of the junction where the helix and coil meet as treated in eq 33, is not taken into consideration. This effect may appear in $G_{(\text{HRR})}$ and $G_{(\text{RRH})}$. But it does not seem large, owing to the absence of the effect of hydrogen bonding.

DISCUSSION

In this paper, the characteristic ratios are investigated on various types of copolypeptides.

In a following paper we shall discuss some characteristic features of the results obtained.

We have referred to the copolymers containing alanine residues, *e.g.*, Ala—NMG copolymers (Figures 8—10), Ala—NMA copolymers (Figures 11 and 12), and Ala—Gly copolymers (Figure 13). To compare these three copolymers, it is convenient to use Figures 10, 12, and 13, obtained for corresponding equimolar copolymers. With respect to the relation between the characteristic ratio and the sequence probability p , the characteristic ratios for both the Ala—NMG (Figure 10) and Ala—Gly (Figure 13) copolymers increase with increasing p , while those for Ala—NMA copolymers (Figure 12) have a minimum at $p=0.5$, *i.e.*, for random copolymers.

The value of $\langle \bar{R}_0^2 \rangle / nl^2$ for Ala—NMA copolymers with $n=200$, in the limit of the perfectly alternating polymer ($p=0$), is as large as 3.5. This fact is understandable from the contour diagrams for $V_{(\text{HRR})}(\phi, \psi)$ (Figure 5) and for $V_{(\text{RRH})}(\phi, \psi)$ (Figure 4). Namely, for $V_{(\text{HRR})}(\phi, \psi)$ the energy minimum locates at $\phi=20^\circ$, $\psi=340^\circ$, so that a rather extended conformation is preferred, on the other hand, for $V_{(\text{RRH})}(\phi, \psi)$ where the minimum locates at $\phi=240^\circ$, $\psi=0^\circ$. In accordance with the three state model (in which *trans*, *gauche*, and another *gauche* conformation are, respectively, denoted by T , G , and G'), it may be said that the contribution of TT is large for $V_{(\text{HRR})}(\phi, \psi)$, and that of $G'T$ is large for $V_{(\text{RRH})}(\phi, \psi)$. These two contributions may reflect on the rather large characteristic ratio for the alternating copolymer. In the range of $0 < p < 0.5$, the characteristic ratios decrease with increasing p . This behavior may be mainly due to the fact that the influence of $V_{(\text{RRH})}(\phi, \psi)$ (see Figure 6 in ref 1) is large. After the minimum is passed, the characteristic ratios in the range of $0.5 < p < 1$ increase with the increased blockness of the chains, which is attributed to the fact that extended conformation is preferred for the Ala—Ala sequence (see Figure 4 in ref 1). Note that the characteristic ratio of the Ala-homopolymer is as high as 8.4.

With respect to Ala—NMG copolymers, it should be noted that the characteristic ratio (1.8) of the alternating copolymer ($p=0$) with $n=200$ (Figure 10) is less than those of 8.4 and

2.97, for the Ala-homopolymer and NMG-homopolymer, respectively. Conformation of the perfectly alternating Ala—NMG copolymer is given by merely $V_{(\text{HRR})}(\phi, \psi)$ and $V_{(\text{RRH})}(\phi, \psi)$ and is no longer affected by such conformations as $V_{(\text{RRH})}(\phi, \psi)$ and $V_{(\text{HRR})}(\phi, \psi)$ which contribute to NMG-homopolymers and Ala-homopolymers. For this reason, the characteristic ratio of the alternating Ala—NMG copolymer stands apart from that of the component homopolymers. From Figures 5 and, in particular, 4, it is known that the conformationally preferred regions I, I', III, and III' for $V_{(\text{RRH})}(\phi, \psi)$ (Figure 6) correspond to the skewed conformations as GG' , $G'G$, GG , and $G'G'$, which result in such a small value as 1.8 for the characteristic ratio of the alternating copolymer. This value 1.8 is very close to 1.9 for a free rotation chain. Such tendency is similar to the case of the Gly-homopolymer.¹ The characteristic ratio in the range of $0.5 < p < 1$ monotonously increased with an increasing p , *i.e.*, with increasing blockness. Such behavior may be caused by the contribution of extended conformation due to Ala—Ala blockness.

In contrast to type II copolymers, type I copolymers retain the conformations characteristic to the component homopolymers. Hence, for type I copolymers, their behavior was markedly different from that presumed from component homopolymers and was not expected. Such examples are shown for Ala—Gly copolymers in Figure 13. What can be said in common about Ala—NMG, Ala—NMA, and Ala—Gly copolymers, is that the slight increase in the blockness at high p abruptly increases the characteristic ratio, owing to the fact that relatively extended conformation is preferred for the Ala—Ala sequence.

The characteristic ratios of Gly—NMG copolymers, Gly—NMA copolymers, and NMG—NMA copolymers are shown in Figure 14. For NMA—NMG copolymers (curve I) and Gly—NMA copolymers (curve II), the average chain dimensions decrease as the sequence probability p is increased, in contrast to Gly—NMG copolymers (curve III) for which the average chain dimensions invariably increase with p . The skewed conformation of the NMA residue may be re-

sponsible for a decrease in the characteristic ratio with increasing p as exhibited in curves I and II. Further, the result that $\langle \bar{R}_0^2 \rangle / nl^2 = 2.25$ for Gly—NMA alternating copolymer ($p=0$) is higher than those for Gly- and NMA-homopolymers (2.17 for Gly-, and 0.6 for NMA-homopolymer) may be attributed to the fact that this copolymer belongs to type II, so that the conformations for component homopolymers are not reflected in the copolymer. In other words, as is obvious from eq 29, the characteristic ratios of this alternating copolymer are obtained from $V_{(RRH)}(\phi, \psi)$ (see Figure 4) and $V_{(HHR)}(\phi, \psi)$ (see Figure 7) without being affected by $V_{(HHH)}(\phi, \psi)$ and $V_{(RRR)}(\phi, \psi)$. In particular, it is noted that the energy minimum position in Figure 7 locates at $\phi=100^\circ$ and $\psi=0^\circ$.

A feature in $\langle \bar{R}_0^2 \rangle / nl^2$ of the racemic NMA-copolymers is that the characteristic ratio is the largest for alternating D,L-copolymer ($f=0$), and monotonously decreases with an increasing f in the range of $0 < f < 1$ (Figure 15), in contrast to racemic Ala-copolymers where the characteristic ratio, as pointed out by Miller, *et al.*,² monotonously increases with f . As pointed out in a preceding paper,¹ the L-NMA-homopolymer takes compact conformation. This is true also for the D-NMA-homopolymer. However, in the alternating D,L-NMA-copolymer, conformations correspond to the mirror image of each other appearing alternatively in the chain, which leads to a relatively large value such as 4.3 for the characteristic ratio. As the isotacticity f approaches 1, the average chain becomes a compact coil peculiar to L- and D-homopolymers. Such a tendency is still retained for copolymers indicated in Figures 16 and 17.

As mentioned above, NMA residues are also treated as in helix conformation. Figures 18 and 12, obtained for equimolar Ala—NMA copolymers, show the results calculated by assuming, respectively, helix and random coil conformation for NMA residues. A comparison of these two Figures makes us understand the effect of rod-like parts on the average chain dimension. In the range $0 < p < 0.9$, relations between the characteristic ratio and sequence probability are not markedly different for either case in which helix or coil conformation is as-

sumed for NMA residues. This is attributed to the characteristic ratio of the α -helix portion composed of NMA residues less than 60 and is not significantly different from or smaller than that of the random coil chain. However, in the range of high blockness ($0.9 < p < 1$), behaviors of both curves are different; the characteristic ratio in Figure 18 increases abruptly, because the length of the helix portion (number of residues in helix portion) increases. Moreover, as is obvious from Figure 19, the characteristic ratio of NMA—Ala copolymers is largely affected by the sequence probability, p and the degrees of polymerization, $n+1$, when a small amount (5%) of Ala is contained in the copolymer. However, with copolymers of 20% Ala content, the characteristic ratio is not largely affected by the degrees of polymerization even at $p=0.8$. For both cases (5% and 20% Ala-copolymers), the characteristic ratios are, if the degrees of polymerization are less than 60, not largely affected whichever helix or coil conformation is assumed for NMA residues. The reason for their behavior is due to the fact that the characteristic ratio for the shorter helix ($n < 60$) is smaller than that for the corresponding random coil chain. Such a result is similar to that pointed out by Nagai¹¹ with respect to the change of the characteristic ratio in the helix—coil transition region.

In all the calculations mentioned above, the imide bond in NMG or NMA residue was assumed to be in *trans* conformation. As mentioned elsewhere,^{1,14} the presence of *cis* bonds has also been suggested.¹⁵ The effect of *cis* bonds on the characteristic ratio is now under consideration. Along with this, some experimental studies relating to the present paper are also being undertaken by our research group.

The computations were carried out on the KDC-II and the FACOM-60 computers at the Kyoto University Computation Center. This work was presented at the SPSJ Microsymposium 1970-I in Kyoto, on November 21, 1970.

REFERENCES

1. S. Tanaka and A. Nakajima, *Polymer J.*, **2**, 717 (1971).
2. W. I. Miller, D. A. Brant, and J. P. Flory, *J.*

Chain Conformation of Polypeptide Copolymers

- Mol. Biol.*, **23**, 67 (1967); P. R. Schimmel and P. J. Flory, *ibid.*, **34**, 105 (1968).
3. P. J. Flory, "Statistical Mechanics of Chain Molecules" Interscience Publishers, New York, N.Y., 1969, Chap. VII.
4. D. A. Brant and P. J. Flory, *J. Amer. Chem. Soc.*, **87**, 2791 (1965).
5. G. Némethy and H. A. Scheraga, *Biopolymers*, **3**, 155 (1965).
6. D. A. Brant, W. G. Miller, and P. J. Flory, *J. Mol. Biol.*, **23**, 47 (1967).
7. L. Peller, *J. Chem. Phys.*, **43**, 2355 (1965).
8. D. Poland and H. A. Scheraga, "Theory of Helix—Coil Transition in Biopolymers," Academic Press, New York, N.Y., 1970, p 138.
9. P. J. Flory, *Proc. Natl. Acad. Sci.*, **51**, 1060 (1964).
10. P. J. Flory and R. L. Jernigan, *J. Chem. Phys.*, **42**, 3509 (1965).
11. K. Nagai, *J. Chem. Phys.*, **34**, 887 (1961).
12. L. Pauling and R. B. Corey, *Proc. Natl. Acad. Sci. USA.*, **37**, 729 (1951).
13. S. Tanaka and A. Nakajima, *Polymer J.*, **1**, 505 (1970).
14. S. Tanaka and A. Nakajima, *Polymer J.*, **1**, 71 (1970).
15. F. A. Bovey, J. J. Ryan, and F. P. Hood, *Macromolecules*, **1**, 305 (1968).