A Theoretical Study on the Origin of Cooperativity in the Formation of 3_{10}- and α-Helices

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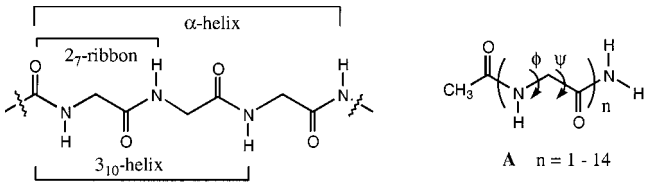
Abstract: By using a simple repeating unit method, we have conducted a theoretical study which delineates the preferences for β-strand, 2_7-ribbon, 3_{10}-helix, and α-helix formation for a series of polyglycine models up to 14 amino acid residues (Ac-$(Gly)_n$, $n = 0, 1, 2, ..., 14$). Interactions among residues, which result in cooperativity, are clearly indicated by variations in calculated energies of the residues. Whereas no cooperativity is found in the formation of β-strands and 2_7-ribbons, there is a significant cooperativity in the formation of 3_{10}- and α-helices, especially for the latter. In the case of α-helices, the 14th residue is more stable than the 3rd by about 3 kcal/mol. A good correlation between calculated residue energy and residue dipole moment was uncovered, indicating the importance of long-range electrostatic interactions to the cooperativity. The results of our calculations are compared with those of the AMBER and PM3 methods, and indicate that both methods, AMBER and PM3, need further development in the cooperative view of electrostatic interactions. The result should be of importance in providing insight into protein folding and formation of helical structures in a variety of polymeric compounds. This also suggests a strategy for the development of more consistent molecular mechanics force fields.

Elements of secondary structures (some of these are shown in the diagram below) such as α- and 3_{10}-helices, β-strands, and β- and γ-turns are ubiquitous in proteins.[1] However, a simple physicochemical theory accounting for these secondary structural features in peptides and proteins is currently immature.[2] Most α-helices in proteins contain 10−15 amino acid residues. At least 15 residues are required for formations of the helix to be observed in protic solvents such as methanol and water.[3] Recent gas-phase studies of polyalanines suggest that formation of the α-helix cannot be realized for peptides with up to 20 alanine residues, but can be promoted by a lysine residue at the C-terminus.[4] Polyglycine models do not form helical structures in the gas phase even with a C-terminal lycine.[4c] On the other hand, the 3_{10}-helix usually forms for short sequences of 4−6 residues.[5] Recent studies on β-peptides, γ-peptides, and oxa-peptides indicate that various helical structures can be formed with short sequences.[6−12] Helical structures can even be formed with polypeptoids that lack the ability to form hydrogen bonds.[13,14]



It is well-known that the coil−helix transition is cooperative.[15] Several molecular mechanisms have been proposed to rationalize the cooperativity of α-helix formation. First, the formation of the first 13-m-r hydrogen-bonded structure conformationally restricts six backbone dihedral angles, and forces three carbonyl groups to adopt a parallel orientation. Subsequent formation of hydrogen bonds between nearby residues (i, $i+3$) only restricts two dihedral angles.[16] Second, in an α-helix, the amide dipoles are roughly parallel to the axis of the helix. While any two adjoining amide dipoles (i, $i+1$) are repulsive, an individual dipole experiences attractive interactions with more distant dipoles. Brant has estimated that in a long α-helix, the total dipole interaction of a given residue with all succeeding residues is attractive by about −1 to −2 kcal/mol.[17] Third, the side chains of peptides also influence the propensity toward helix formation and cooperativity.[18]

Recently Vargas et al. suggested the importance of the C^{α}−H···O═C hydrogen bond in protein folding.[19] Here we present a quantum mechanics study of a series of polyglycine models with up to 14 residues. The results suggest that induced long-

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range electrostatic interactions are important to the formation of certain helical structures of polymeric compounds.

Calculation Methodology

Our study is based on a simple repeating unit approach. That is, we built peptide models with identical repeating units so as to obtain geometric coordinates for the lengthening peptides. This is based on the fact that when a helical peptide chain grows, the inner amino acid residues will adopt very similar geometries. To derive the repeating units for the β-strand and 3_{10}-helix, an *N*-acetylated heptapeptide Ac-$(Gly)_7$ model was optimized with the HF/6-31G* method using the GAUSSIAN 98 program,[20] and with a constraint applied for each amino acid residue with the same geometry. The repeating units for the 2_7-ribbon and α-helix were derived in the same way by using an *N*-acetylated undecapeptide Ac-$(Gly)_{11}$ model.[21] The energies of the peptide models were calculated with both the HF/6-31G* and B3LYP/6-31G* methods.[22] We have shown that these methods give satisfactory results for the conformational features of unnatural peptides such as β-peptides and oxa-peptides.[23,24]

Table 1. Calculated Geometrical Parameters in Comparison with Average Values (in parentheses)

structure	residues/turn	rise (Å)	ψ	Ψ
β-strand	2(2.0)	3.6(3.2 syn, 3.4 anti)	180°	180°
2_7-ribbons	1.86	2.84	−86°	63°
3_{10}-helix	3.05(3.0)	2.20(2.0)	−68° (−71°)	−17° (−18°)
α-helix	3.72(3.6)	1.51(1.5)	−67° (−62°)	−40° (−41°)

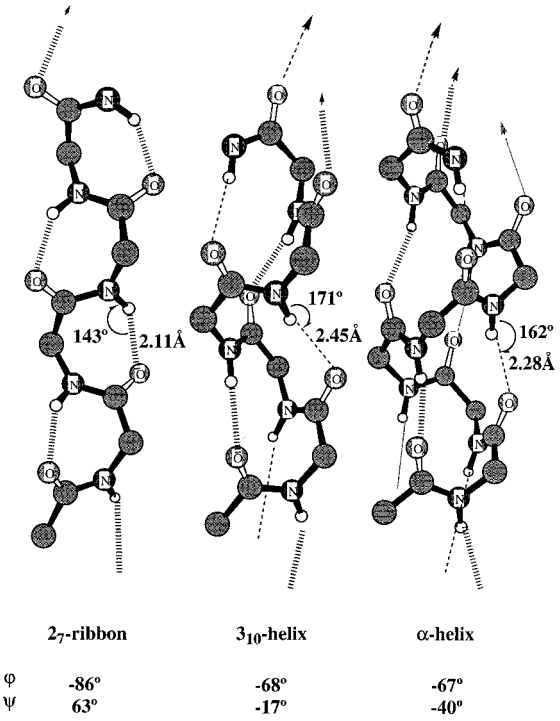

Figure 1. Structures of the 2_7-ribbon, 3_{10}-helix, and α-helix of polyglycine.

Results and Discussion

Geometry. Some calculated geometrical parameters for the four types of structures are given in Table 1, along with reported experimental values. In general, the calculated values are in good agreement with the experimental data. The mean values for the backbone torsions ϕ and ψ were reported as −62° and −41° for the α-helix and −71° and −18° for the 3_{10}-helix, respectively.[25] The corresponding values obtained by the current calculations are −67° and −40° for the α-helix and −68° and −17° for the 3_{10} helix. The β-strand possesses two torsion angles of about 180°. For the 2_7-ribbon, the two values are −86° and

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Table 2. Dipole Moment and Relative Energy of 2_7-Ribbon (**A**), β-Strand (**B**), 3_{10}-Helix (**C**) and α-Helix (**D**) of Polyglycine Models Calculated by the HF/6-31G* and B3LYP/6-31G* Methods

	HF/6-31G*								B3LYP/6-31G*							
	dipole moment (D)				relative energies (kcal/mol)				dipole moment (D)				relative energies (kcal/mol)			
n	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**
0[a]	4.2	4.2	4.1	4.1	0.0	−0.7	−0.6	−0.6	3.8	3.8	3.7	3.7	0.0	−0.3	−0.3	−0.3
1	4.1	2.8	6.9	7.5	0.0	−1.0	3.7	4.9	3.4	3.2	6.0	6.6	0.0	0.4	4.5	5.9
2	7.1	6.1	9.9	10.6	0.0	−1.3	3.2	9.7	6.1	6.3	8.6	9.3	0.0	1.0	4.6	10.9
3	8.8	6.4	13.7	14.6	0.0	−1.4	2.5	10.1	7.4	7.3	12.1	12.9	0.0	1.6	4.6	11.6
4	11.4	9.1	17.6	18.9	0.0	−1.5	1.3	10.0	9.6	10.1	15.5	16.8	0.0	2.2	4.2	11.8
5	13.6	10.1	21.3	23.2	0.0	−1.5	−0.3	9.4	11.5	11.6	18.8	20.7	0.0	2.9	3.5	11.7
6	16.0	12.5	25.2	27.5	0.0	−1.5	−2.0	8.1	13.5	14.3	22.3	24.6	0.0	3.6	2.6	11.0
7	18.5	13.7	29.2	32.0	0.0	−1.5	−3.9	6.3	15.7	16.0	25.9	28.8	0.0	4.2	1.6	9.9
8	20.7	16.1	33.1	36.5	0.0	−1.5	−6.0	4.3	17.6	18.5	29.4	33.0	0.0	4.9	0.5	8.5
9	23.3	17.4	37.1	41.1	0.0	−1.4	−8.1	2.0	19.9	20.4	33.0	37.1	0.0	5.6	−0.7	7.0
10	25.5	19.7	41.1	45.6	0.0	−1.4	−10.2	−0.5	21.7	22.8	36.7	41.3	0.0	6.3	−1.9	5.2
11	28.2	21.2	45.1	50.3	0.0	−1.3	−12.4	−3.1	24.1	24.7	40.2	45.6	0.0	6.9	−3.2	3.3
12	30.4	23.3	49.0	54.9	0.0	−1.3	−14.6	−5.8	25.9	27.1	43.8	49.9	0.0	7.6	−4.4	1.4
13	33.0	24.9	53.1	59.5	0.0	−1.2	−16.9	−8.6	28.2	29.1	47.5	54.1	0.0	8.3	−5.7	−0.7
14	35.3	27.0	57.1	64.2	0.0	−1.2	−19.2	−11.4	30.2	31.5	51.1	58.4	0.0	9.0	−7.1	−2.9

[a] The model with $n = 0$, acetamide, in the corresponding secondary structure.

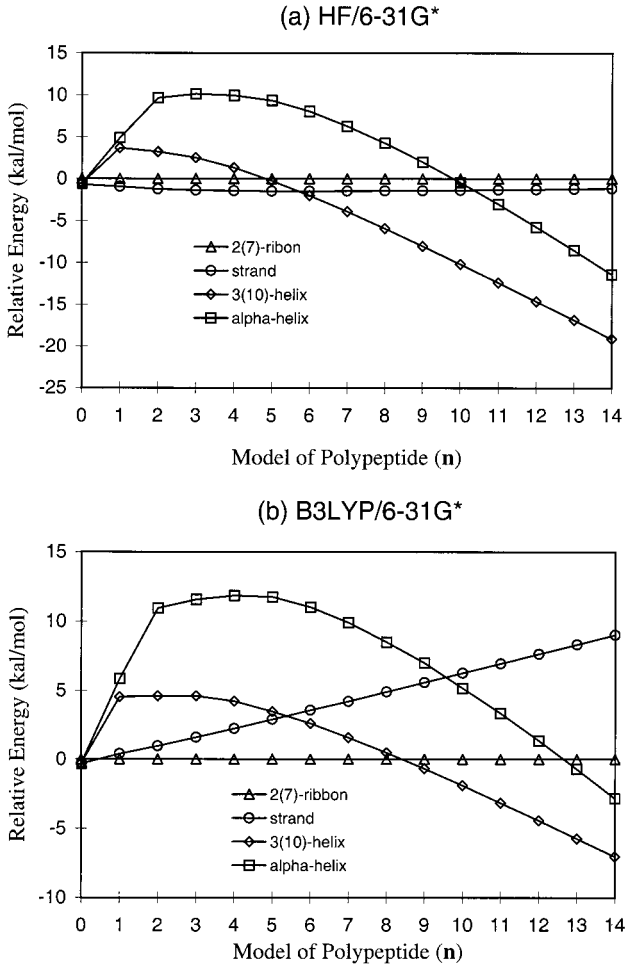

Figure 2. Plot of calculated relative energies (kcal/mol) of the β-strand, 2_7-ribbon, 3_{10}-helix, and α-helix of polyglycine models by (a) HF/6-31G* and (b) B3LYP/6-31G* methods.

63°, respectively. While the 2_7-ribbon has the shortest hydrogen bond (Figure 1), the hydrogen bond in the 3_{10}-helix is quite long (2.45 Å).

Relative Stabilities. The calculated total dipole moments and relative stabilities of the four types of secondary structures are collected in Table 2. For clarity, Figure 2 gives the plot of relative energies with respect to the 2_7-ribbon structure against residue number (n) in the Ac-$(Gly)_n$ model. The results obtained by the HF and B3LYP methods are very similar, but the latter method is known to generate more accurate energy for systems involving hydrogen bonds.[26] Several features are apparent. (1) The relative energy of the β-strand linearly increases with respect to the 2_7-ribbon. Each unit of the former is about 0.7 kcal/mol less stable than that in the latter. This is close to the best value of 0.9 kcal/mol obtained for a dipeptide model.[27] (2) The 3_{10}-helical structure is about 4.5 kcal/mol higher in energy than the 2_7-ribbon when $n = 1$, but this difference decreases for increasing n. When n is larger than 9, the 3_{10}-helical structure becomes more stable than others and holds until n is too big to be beaten by the α-helical structure. (3) The α-helix is least stable when $n = 3-5$. However, when n becomes larger than 5, its stability quickly increases. Our projection is that it matches the stability of the 3_{10}-helix when n reaches about 20. This strongly supports the idea that the 3_{10}-helix is an intermediate in the formation of the α-helix.[5,28]

Our results are in agreement with the gas-phase experimental results;[4] each residue in the β-strand is expected to be about 3−4 eu higher in entropy than each residue in the helical structure where hydrogen bonding reduces degrees of freedom. This corresponds to about 0.9−1.2 kcal/mol stabilization in the β-strand. Therefore, it can be estimated that the β-strand is more stable than the helical structures for polyglycine in the gas phase, when n is less than 15. However, since a globular structure of polyglycine is even more stable than the β-strand structure,[4c] helical structures are not observed for polyglycines in the gas phase.

Residue Energy and Cooperativity. To analyze the electrostatic interactions along the peptide frame, we calculated the residue energy (ϵ) in each secondary structure, which is defined as the increment of total energy provided by each amino acid residue, as shown in Scheme 1. Since each residue has the same geometry in each secondary structure, ϵ_n should be a constant if there is no interaction among amino acid residues. If each amino acid residue has an attractive interaction with the other

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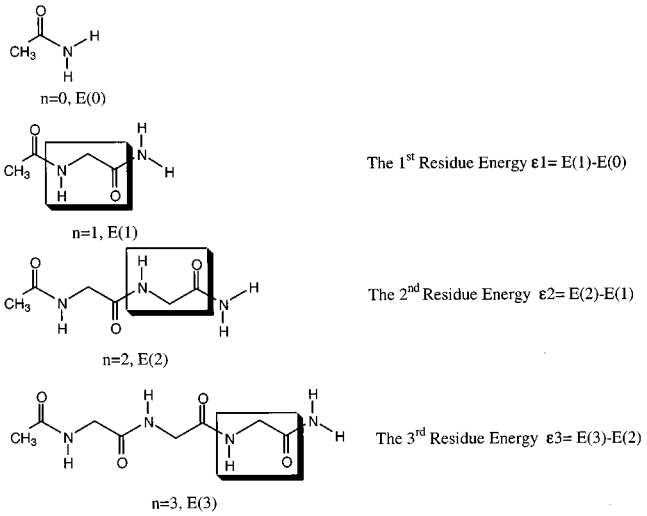
Scheme 1



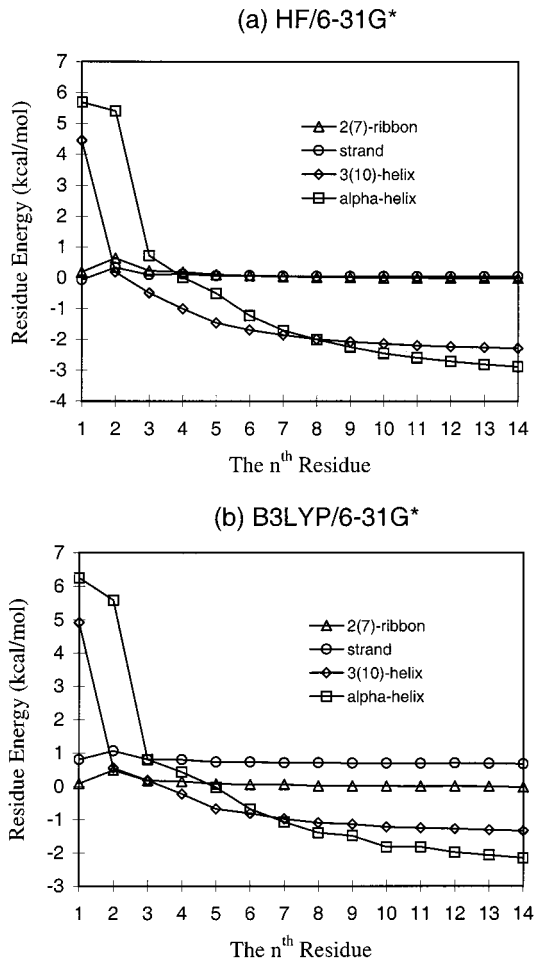


Figure 3. Plot of calculated residue energies of the *n*th residue $\epsilon_n = E(n) - E(n-1)$. The zero energy equals −206.8177 au for HF/6-31G* and −208.0119 au for B3LYP/6-31G*, respectively: (a) HF/6-31G* and (b) B3LYP/6-31G*.

residues, then ϵ_n becomes more negative when *n* increases. The value of $\epsilon_n - \epsilon_{n-1}$ roughly represents the interaction between the first residue and the terminal residue. This value will tend to be zero when *n* becomes very large.

Figure 3 is a plot of the residue energy against residue number for the four types of structures. The residue energy is almost a constant for the 2_7-ribbon and β-strand; this indicates no electronic communication among residues (that is, there is only local interaction between residues *i* and $i + 1$ but no long-range interaction between residues *i* and $> i + 1$) and no cooperative interaction. As expected, there is a large stabilization from $n = 1$ to $n = 2$ for the 3_{10}-helix ($\epsilon 2$) and from $n = 2$ to $n = 3$ for the α-helix ($\epsilon 3$), due to the formation of a hydrogen bond. Most interestingly, for these two types of helices, the residue energy decreases (more negative) with increasing *n*, which demonstrates increasing interresidue attraction in longer peptides. It reaches the minimum for the 3_{10}-helix when *n* is about 10. However, for the α-helix, even if *n* reaches 14, the residue energy still decreases. This means that residue units that are separated by as much as 20 Å in the α-helix can still communicate electronically in the gas phase, causing stabilization.

Thus, the formation of the α- and 3_{10}-helices is highly cooperative. For the α-helix, the 14th residue is about 3 kcal/mol more stable than the 3rd residue. For the 3_{10}-helix, the 14th residue is more stable than the second residue by about 1.8 kcal/mol. As far as we are aware, there is no previous report on such large cooperativity for the helical structures in protein secondary structures. This cooperative effect must be due to long-range electronic interaction,[29] and must play a crucial role in the formation of these helices. Other factors, such as entropy and side-chain effects, also contribute to the cooperative formation of helical structures.[16,30,31] However, it appears that the intrinsic electronic interaction discussed here is likely the most important factor.

Origin of Cooperativity. To better understand the nature of the cooperativity, we analyzed the incremental dipole moment contributed by each amino acid residue, referred to as the residue dipole moment. That is, the residue dipole moment of the *n*th residue is obtained by the vector subtraction of the dipole moment of the peptide model containing $(n - 1)$ residues from the dipole moment of the peptide model containing (*n*) residues. These values are given in Table 3. The residue dipole moment can be projected onto the axis of the helix (axial) and the plane perpendicular to the helix axis (equatorial). As shown in Figure 4, the residue dipole moments are nearly constant for the β-strand and 2_7-ribbon; however, those of the α-helix and 3_{10}-helix increase noticeably as *n* increases. In the case of the α-helix, the residue dipole moment increases by about 40% from the first residue to the 14th residue. This is due mainly to the contribution from the axial component in the direction of the helix axis; the equatorial component of the residue dipole moment is approximately constant for each of the secondary structures (Table S2 in Supporting Information). The calculated dipole moment of acetamide is about 3.8 D, while the residue dipole moment increases to about 4.9 D in a long α-helix. This is in agreement with an early estimate.[32,33]

The adjoining residue dipoles in the β-strand structures are always antiparallel to each other, which result in a large interaction between them. Surprisingly, however, the values of residue energies and residue dipoles are almost constant. This indicates that there is no long-range interaction between residues and no cooperativity at all in the β-strand structures. The residue dipole moment of the β-strand is about 0.2 D larger than that of acetamide, considered being the ideal standard reference.

The residue dipole moments in the 2_7-ribbon structures are

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Table 3. Residue Energy $\epsilon_n = E(n) - E(n-1)$ and Residue Dipole Moments, in the 2_7-Ribbon (**A**), β-Strand (**B**), 3_{10}-Helix (**C**), and α-Helix (**D**) of Polyglycine Models Calculated with the HF/6-31G* and B3LYP/6-31G* Methods[a]

		HF/6-31G*								B3LYP/6-31G*							
n		residue energy (ϵ_n) (kcal/mol)				residue dipole (D)				residue energy (ϵ_n) (kcal/mol)				residue dipole (D)			
former	latter	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**	**A**	**B**	**C**	**D**
0	**1**	0.19	−0.10	4.44	5.68	4.55	4.28	4.05	3.86	0.09	0.80	4.92	6.26	4.13	3.94	3.66	3.51
1	**2**	0.64	0.34	0.18	5.40	4.50	4.30	4.53	4.01	0.49	1.06	0.55	5.59	4.05	4.01	4.18	3.66
2	**3**	0.23	0.10	−0.49	0.72	4.56	4.32	4.64	4.63	0.18	0.80	0.18	0.80	4.11	4.05	4.26	4.33
3	**4**	0.19	0.12	−1.01	0.01	4.56	4.33	4.73	4.78	0.15	0.79	−0.22	0.43	4.12	4.07	4.36	4.44
4	**5**	0.10	0.06	−1.47	−0.50	4.58	4.33	4.80	4.88	0.07	0.73	−0.67	−0.03	4.13	4.08	4.43	4.55
5	**6**	0.07	0.07	−1.70	−1.23	4.58	4.33	4.84	4.98	0.06	0.73	−0.81	−0.67	4.14	4.08	4.46	4.66
6	**7**	0.04	0.05	−1.86	−1.71	4.59	4.34	4.86	5.05	0.06	0.70	−0.97	−1.06	4.15	4.09	4.49	4.73
7	**8**	0.02	0.05	−2.00	−2.01	4.59	4.34	4.89	5.09	0.01	0.70	−1.09	−1.39	4.15	4.09	4.51	4.77
8	**9**	0.01	0.04	−2.09	−2.25	4.59	4.34	4.90	5.13	0.01	0.69	−1.13	−1.48	4.15	4.09	4.53	4.81
9	**10**	0.00	0.05	−2.15	−2.46	4.59	4.34	4.91	5.16	0.01	0.69	−1.22	−1.82	4.15	4.09	4.54	4.84
10	**11**	0.00	0.04	−2.20	−2.60	4.59	4.34	4.92	5.18	0.01	0.68	−1.25	−1.82	4.15	4.09	4.54	4.86
11	**12**	−0.01	0.04	−2.24	−2.72	4.59	4.34	4.92	5.20	0.01	0.69	−1.27	−1.98	4.15	4.09	4.55	4.88
12	**13**	−0.01	0.04	−2.27	−2.81	4.60	4.34	4.93	5.21	0.00	0.68	−1.30	−2.07	4.15	4.09	4.56	4.90
13	**14**	−0.02	0.04	−2.29	−2.89	4.60	4.34	4.93	5.22	−0.02	0.67	−1.33	−2.15	4.15	4.09	4.56	4.91

[a] The zero energy is −206.8177 au for the HF/6-31G* method and −208.0119 au for the B3LYP/6-31G* method, respectively.

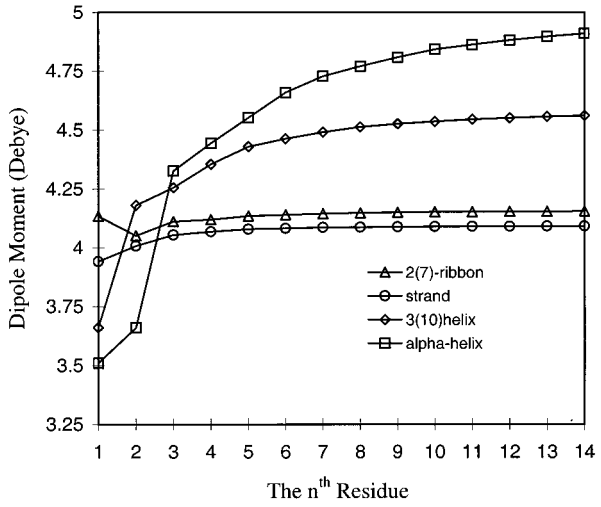

Figure 4. Residue dipole moments of the β-strand, 2_7-ribbon, 3_{10}-helix, and α-helix of polyglycine models, calculated by the B3LYP/6-31G* method, which is derived by vector subtractions of dipole moments of peptide model ($n-1$) from that of peptide model (n).

larger by about 0.1−0.2 D than those in the β-strand structure. This is due to the 7-m-r hydrogen bonding structure polarizing the residue dipole in the 2_7-ribbon. For the 3_{10}- and α-helical structures, the first residue dipole moment is smaller than that of the β-strand structure. This reflects the repulsive nature of adjoining residues, and also is in agreement with the view of cooperativity, that is, the electrostatic characteristic is curtailed if there is an energy penalty. However, there is a large induced dipole moment by the second reside in the 3_{10}-helical structures, or the third residue in the α-helical structures, corresponding to the formation of the first hydrogen bond. Interestingly, for the α-helix, even the second residue causes a considerable induced dipole.

A comparison between Figure 3 and Figure 4 indicates that there is a good correlation between calculated residue energy and residue dipole moment. For the 2_7-ribbon and β-strand, both residue energy and residue dipole moment are nearly constant. For the 3_{10}- and α-helices, both residue energy and residue dipole moment increase as n increases. This suggests that the intrinsic cooperativity and induced residue dipole in the formation of the 3_{10}- and α-helices are caused by long-range electrostatic interaction synchronously. That is, long-range electrostatic interactions among residues produce stabilization intrinsically. This stabilization is amplified by induced charge distributions that result in induced residue dipole.

In the 2_7-ribbon, there is one hydrogen bond network as shown in Figure 1. Each hydrogen bond, which is formed between adjoining residues, generates a large induced dipole. Since the 2_7-ribbon structure does not have cooperative interaction, this suggests that through-bond resonance effect involving the hydrogen bond network is not important.[34,35] In the 3_{10}- and α-helices, there are two and three hydrogen bond networks, respectively (Figure 1). Induced dipoles are not only caused by hydrogen bonds, but also by through-space electrostatic (or dipole) interactions between adjacent residues, which belong to different hydrogen bond networks.[36] This mechanism allows residues far away from each other to communicate electronically, and results in the through-space resonance-like cooperativity. Since the α-helix allows for the most adjacent dipole interactions, it has the largest cooperativity.

The above cooperativity can be generally applied to other polymeric materials. In the case of β-peptides and γ-peptides, we have found a similar cooperativity for certain helical structures.[37,38] Green et al. have attributed chirality amplification of helical polyisocyanates to a cooperative effect.[39] Since hydrogen bonding is not the origin of the cooperativity, it is expected that the inductive cooperativity also plays an important role in the formation of helical structures of polypeptoids and β-peptides derived from proline.[13,14] It is possible that this cooperativity might cause helix formation of polyketones and other polymeric materials.[40]

While the importance of electrostatic interaction to protein folding and protein functionality has been well recognized,[41,42]

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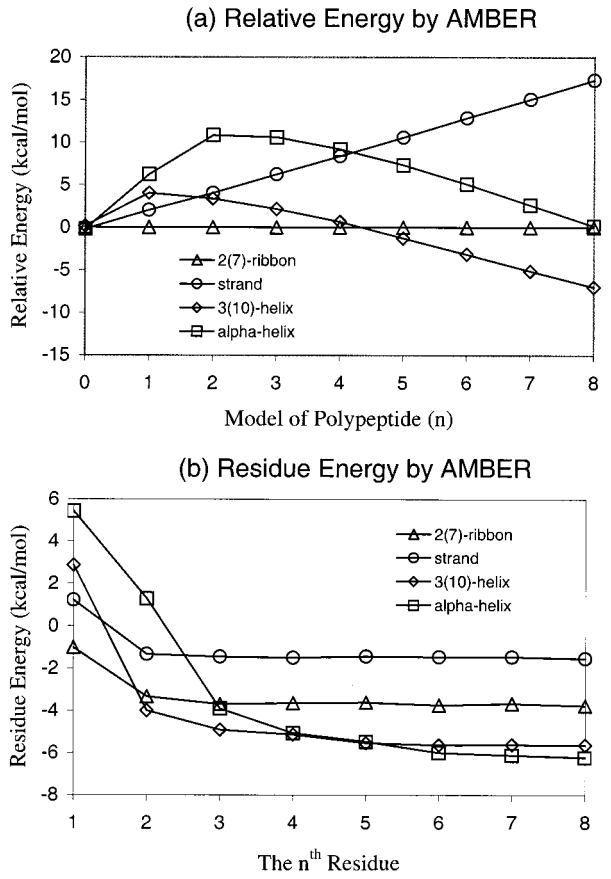

Figure 5. Plot of relative energies and residue energies (kcal/mol) of the β-strand, 2_7-ribbon, 3_{10}-helix, and α-helix of polyglycine models calculated by the AMBER method.

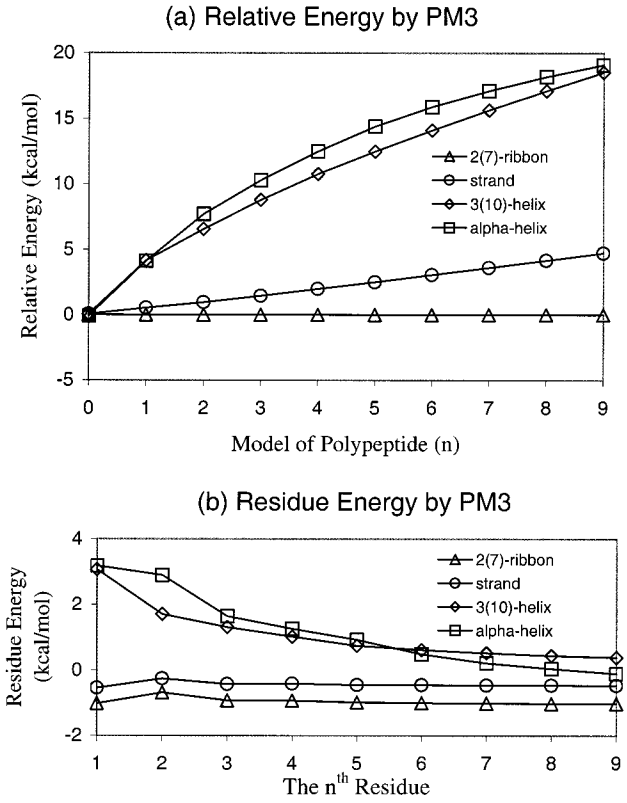

Figure 6. Plot of relative energies and residue energies (kcal/mol) of the β-strand, 2_7-ribbon, 3_{10}-helix, and α-helix of polyglycine models calculated by the PM3 method.

our study provides more detailed mechanistic information on the effect of the electrostatic interaction. For example, since the cooperativity is dependent upon the secondary structure, and the electrostatic interaction that causes the cooperativity is very much dependent upon the dielectric constant of the medium, it is expected that the tendency of helix formation is dependent upon the protein-folding environment. Therefore, our results support the idea that both local and global factors determine the formation of the secondary structures.[44] In addition, the α-helix is mainly destabilized at the C-terminus due to four parallel carbonyl groups that are not involved in hydrogen bonding. It is expected that the best situation for the formation of the α-helix would be with a polar environment at the C-terminus and a nonpolar environment for the inner residues. This will also be true for the formation of a 3_{10}-helix. Indeed, formation of helical structures in a micelle environment such as in membrane proteins is often found in the case of the helical bundles of ion channels.[45]

Comparison with Force Field and the PM3 Methods. Currently, most of the computational studies of protein-related problems employ molecular dynamics methods based on force-field potential energy functions.[46] We used similar geometries and repeated the above calculations with the AMBER force field, which employs fixed atomic charges.[47] As shown in Figure 5, the AMBER relative energies are in quite good agreement with the B3LYP/6-31G* results. But the former displays a faster energy rise for the β-strand and faster energy decrease for the 3_{10}- and α-helices. In terms of residue energy, the AMBER gives a large residue energy drop in the range of $n = 1-5$ for the 3_{10}-helix and $n = 1-7$ for the α-helix. Beyond these ranges, there is essentially no energy change. In particular, there is a large decrease in residue energy from $n = 1$ to $n = 2$ (ϵ_2) for all the four types of secondary structures. Such large electrostatic attractions between adjacent amino acid residues are not found in the ab initio calculations shown in Figure 3. Therefore, it appears that the AMBER overestimates short-range electrostatic interactions (or dipole interaction) but underestimate long-range electrostatic interactions.[48] This further demonstrates the importance of long-range induced electrostatic interaction to the protein structural preference. Our calculations thus suggest a strategy for the improvement of molecular mechanics force-field methods for the study of protein problems.

Recently, semiempirical methods have also been applied to study protein structures.[49] As shown in Figure 6, the PM3 method does not calculate the relative stabilities of the four types of structures correctly. The stabilities of the two helical structures are significantly underestimated. The problem is attributable to the significant underestimation of hydrogen bonding energy, as

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shown in Figure 6b. Thus, the calculated residue energies of the two helical structures are higher than that of the 2_7-ribbon even when *n* reaches about 10. In addition, the method produces only about 60% of the magnitude of the cooperativity obtained by the B3LYP/6-31G* method. Therefore, to apply the PM3 method to the study of protein structures, modification of parameters is necessary.

Summary. Through calculations of a series of polyglycine models, we clearly demonstrate that there is a significant cooperativity for the formation of the 3_{10}- and α-helices. There is an excellent correlation between calculated residue energy and residue dipole moment, indicating the importance of induced dipole to the cooperativity. We propose that the induced dipole is not due to resonance interaction through the hydrogen bond networks, but is mainly caused by through-space dipole/dipole interactions.[35] This cooperativity should be applicable to the helix formation of other types of polymeric materials including those without hydrogen bond networks. The current study should be useful for the understanding of protein folding. It also highlights the deficiency of force field and semiempirical methods, and suggests a possible strategy for the improvement of the methods. In addition, we demonstrate that the repeating unit approach is an efficient method for the study of conformational features of polymeric materials. We are currently applying the method to the study of *β*-sheets and other polymeric systems.

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Supporting Information Available: Calculated total energies and residue dipole (axial and equatorial components) of polyglycine models (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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