Therefore

$$U_0'(1) = \phi_0 + \frac{2}{m}\left[\sum_{j=1}^{m-1}(U_{1(j,j-1)}' + \frac{2\alpha}{m}U_{1(m,m-1)}' \quad \text{(A16)}\right.$$

Inserting eq A14 and collecting terms with same number of sums this results in eq 26

$$U_0'(1) = \phi_0 + \frac{2}{m}\sum_{j=1}^{m}(m - j + \alpha) \times \sum_{i_1=1}^{\infty}\alpha^{i_1-1}\sum_{i_2=1}^{\infty}\alpha^{i_2-1}\ldots\sum_{i_j=1}^{\infty}\alpha^{i_j-1}\phi_{i_1+i_2+\ldots i_j} \quad (26)$$

Comparison of the Conformational Map for Poly(L-proline) with Conformational Maps for Polysarcosine and Poly(*N*-methyl-L-alanine)[1]

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ABSTRACT: The presence of the four minima in the conformational map reported by Mark and Goodman for poly(*N*-methyl-L-alanine) has been confirmed. The conformational map reported by Tanaka and Nakajima for polysarcosine, however, is found to be incorrect due to their failure to consider several crucial interatomic contacts. The conformational maps for both polysarcosine and poly(*N*-methyl-L-alanine) are found to be sensitive to the orientation selected for the methyl groups. If the geometry of these polypeptides is made similar to that of poly(L-proline), the computations at $\phi = 120°$ reveal two regions of low energy, separated by approximately 180° rotation about ψ. The relative energies of these two minima are extremely sensitive to the geometry selected for the polypeptide, as has previously been found to be the case for poly(L-proline).

A recent treatment[2] of the internal dipeptide unit in poly(L-proline) containing peptide bonds in the planar-trans conformation is in agreement with the characteristic ratio observed for this polypeptide[3] and allows for flexibility of the pyrrolidine ring, which has been demonstrated experimentally by proton[4] and ^{13}C[5] magnetic resonance studies. Energy minima are obtained near ϕ, ψ = 110°, 350° and ϕ, ψ = 120°, 130°.[2,6] The precise location and energy of the minimum near ϕ, ψ = 120°, 130° is sensitive to the geometry of the pyrrolidine ring.[2,7] The energy at this minimum may be as little as ~1 kcal/mol greater than the energy at ϕ, ψ = 110°, 350° if the pyrrolidine ring geometry is suitably chosen.[2]

Conformational maps reported for the internal dipeptide unit in polysarcosine[8] and poly(*N*-methyl-L-alanine),[9] computed with $\chi_N = 0°$,[6] report a low energy for ϕ, ψ = 110°, 350°, but do not exhibit a region of low energy near ϕ, ψ = 120°, 130°. These results[8,9] might appear to be in conflict with the conformational maps for poly(L-proline),[2] since it is difficult to understand why a conformation should be available to poly(L-proline) but not to polysarcosine. Consequently the conformational maps for polysarcosine and poly(*N*-methyl-L-alanine) have been recomputed. The results previously reported for poly(*N*-methyl-L-alanine)[9] were confirmed, but it was not possible to reproduce the conformational map reported for polysarcosine.[8] In each case the conformational map is sensitive to the selection of the χ_N. If χ_N and χ_1 are assigned so that the orientation of the methyl groups is similar to that of C$^\beta$ and C$^\delta$ in poly(L-proline), the computed energy *vs.* ψ for ϕ near 120° does exhibit minima close to the locations found in the internal dipeptide of poly(L-proline).[2]

Calculational Procedure

The atoms considered in the computation for poly(*N*-methyl-L-alanine) are shown in Figure 1. The bond lengths and bond angles for poly(*N*-methyl-L-alanine) were the same as those used by Mark and Goodman[9] except when specifically stated to the contrary. In the computation for polysarcosine the three C$^\beta$ atoms and attached hydrogen atoms were replaced by three hydrogen atoms. The bond lengths and bond angles for polysarcosine were the same as those used by Tanaka and Nakajima.[8] The nonbonded interaction was evaluated for each pair of atoms in Figure 1 whose distance of separation depends upon $\chi_{1,i-1}$, $\chi_{1,i}$, $\chi_{1,i+1}$, $\chi_{N,i}$, $\chi_{N,i+1}$, ϕ_i, or ψ_i utilizing the same functions used in the previous work.[8,9] The total number of interatomic distances used in the evaluation of the nonbonded energy was 171 for polysarcosine and 383 for poly(*N*-methyl-L-alanine). The torsional potentials about ϕ_i and ψ_i were also the same as those used previously.[8,9] The torsional barrier about χ_N was assumed to be identical with that about ϕ_i. A barrier height of 3 kcal/mol was used for torsion about χ_1.[10] Minima occur at ±60 and 180° for torsion about χ_N and χ_1. The electrostatic interaction of the peptide groups was computed by the same procedure used by Tanaka and Nakajima,[8] which assigns partial charges to C′, O, N, and C^N and assumes a dielectric constant of 3.5. The dihedral angles ω_{i-1}, ω_i, and ϕ_{i+1} were held constant at 0°; ψ_{i-1} was also held constant at 0° except when specifically stated to the contrary.

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[1] Supported by Grant No. GB-36055 from the National Science Foundation.

[2] W. L. Mattice, K. Nishikawa, and T. Ooi, *Macromolecules*, **6**, 443 (1973).

[3] W. L. Mattice and L. Mandelkern, *J. Amer. Chem. Soc.*, **93**, 1769 (1971).

[4] D. A. Torchia, *Macromolecules*, **4**, 440 (1971).

[5] D. A. Torchia, private communication.

[6] The convention used is described in J. T. Edsall, P. J. Flory, J. C. Kendrew, A. M. Liquori, G. Nemethy, G. N. Ramachandran, and H. A. Scheraga, *Biopolymers*, **4**, 130 (1966); *J. Biol. Chem.*, **241**, 1004 (1966); *J. Mol. Biol.*, **15**, 339 (1966). In addition C_i^N will signify the carbon atom of the methyl group attached to the nitrogen atom of residue i and $\chi_{N,i}$ will refer to rotation about the N_i–C_i^N bond, which is zero when the C_{i-1}'–N_i and C_i^N–H bonds are eclipsed. The direction of rotation is identical for $\chi_{1,i}$ and $\chi_{N,i}$

[7] N. Gō and H. A. Scheraga, *Macromolecules*, **3**, 188 (1970).

[8] S. Tanaka and A. Nakajima, *Polym. J.*, **1**, 71 (1970).

[9] J. E. Mark and M. Goodman, *Biopolymers*, **5**, 809 (1967).

[10] K. Nishikawa and T. Ooi, *Progr. Theor. Phys.*, **46**, 670 (1971).

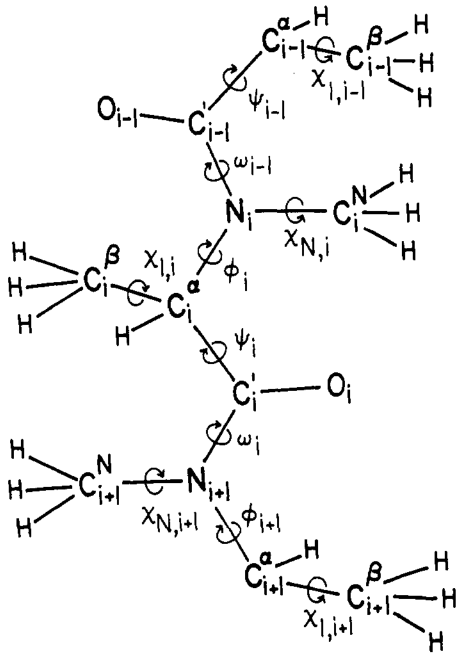

Figure 1. Atoms considered in the computation for poly(*N*-methyl-L-alanine).

Conformational maps were first computed at intervals of 30° for ϕ_i and ψ_i. Selected areas were then reexamined at intervals of 15, 10, or 5°. Contour lines were calculated by linear interpolation of the energies obtained at adjacent points.

Results and Discussion

Polysarcosine. The conformational map obtained for polysarcosine when $\chi_{N,i} = \chi_{N,i+1} = 0°$ is shown in Figure 2. The contours are drawn relative to the energy minimum, which is 2.4 kcal/mol and occurs at ϕ, ψ = ±105°, 0°. Another region of low energy occurs at ϕ, ψ = 45°, 255° and 315°, 105°. This map differs dramatically from the result reported for $\chi_{N,i} = \chi_{N,i+1} = 0°$ by Tanaka and Nakajima (their Figure 3).[8] The reason for the discrepancy becomes apparent upon comparing the results obtained at ϕ, ψ = 120°, 240°. Tanaka and Nakajima[8] find their lowest energy, −0.28 kcal/mol, at this conformation. We compute an energy well in excess of 100 kcal/mol for this conformation as a consequence of several close interatomic contacts. The most severe contacts are between O_{i-1} and $C_{i+1}{}^N$ (separation of 1.12 Å) and between O_{i-1} and two of the hydrogen atoms attached to $C_{i+1}{}^N$ (separations of 0.92 and 1.03 Å). Inspection of Dreiding models verifies the closeness of these interatomic contacts at ϕ, ψ = 120°, 240°. It is impossible to construct a Corey–Pauling–Koltun (CPK) model of the internal dipeptide unit of polysarcosine with ϕ, ψ = 120°, 240°. In contrast, the CPK model can easily be made to have ϕ, ψ = 105°, 0° or 45°, 255°, corresponding to the regions of low energy in Figure 2. The listing of interatomic distances considered by Tanaka and Nakajima[8] (their Table VI) does not include any of the three distances cited above as being unreasonably small Consequently it is concluded that the conformational map computed by Tanaka and Nakajima[8] is in error due to the neglect of several important interatomic contacts.

The conformational map computed for polysarcosine is highly dependent upon $\chi_{N,i}$ and $\chi_{N,i+1}$, as is shown in Figure 3. The lowest energy (−4.7 kcal/mol) is found at ϕ, ψ = ±90°, 0° in the map with $\chi_{N,i} = \chi_{N,i+1} = 60°$. Another minimum of nearly identical energy is obtained at ϕ, ψ = 45°, 255° and 315°, 105° on the same map. The contours on all four maps in Figure 3 are drawn relative to the minimum in the map with $\chi_{N,i} = \chi_{N,i+1} = 60°$. Equivalent energies for ϕ, ψ and $-\phi$, $-\psi$ are obtained only when the χ_N are either 0 or 60°.

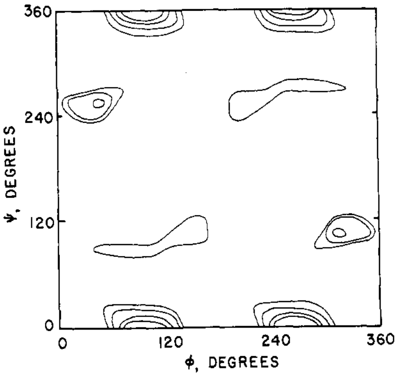

Figure 2. Conformational map for polysarcosine when $\chi_{N,i} = \chi_{N,i+1} = 0°$. Contours are drawn at 1, 2, 5, and 10 kcal per mol relative to the energy minimum, which occurs at ϕ, ψ = ±105°, 0°.

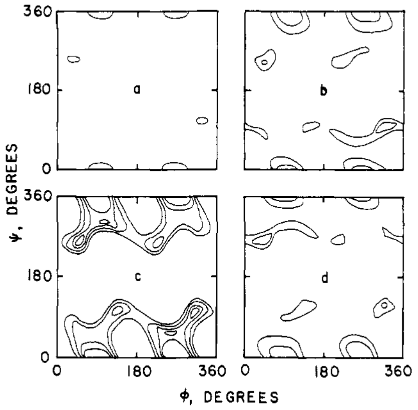

Figure 3. Conformational maps for polysarcosine for the following values of $\chi_{N,i}$ and $\chi_{N,i+1}$: (a) 0°, 0°; (b) 30°, 30°; (c) 60°, 60°; (d) 90°, 90°. The lowest energy (−4.7 kcal/mol) occurs at ϕ, ψ = ±90°, 0° in part c. Contours are drawn at 1, 2, 5, and 10 kcal per mol relative to the minimum in part c.

There is some uncertainty regarding the form of the torsional potential for rotation about ϕ,[11] and therefore also about χ_N. This uncertainty will not affect the relative energies at various ϕ, ψ in a particular conformational map in Figures 2 and 3, since they were each computed at constant χ_N. It will, however, produce an uncertainty in the relative energies of the different conformational maps in these figures. If the locations of the minima for the torsional potential about χ_N were all displaced by 60°, the lowest energy in Figure 3 would still occur at the same location in Figure 3c. The lowest energy in Figure 3a, located at ϕ, ψ = ±105°, 0°, would then be only 1.1 kcal/mol above the minimum in Figure 3c.

Poly(*N*-methyl-L-alanine). The conformational map computed for poly(*N*-methyl-L-alanine) when all χ_1 = 60° and all χ_N = 0° exhibits four minima at locations very close to the four minima previously found by Mark and Goodman for this polypeptide.[9] These authors did not include electrostatic interactions in their computation. Deletion of the electrostatic interaction from our computation yields a minimum energy of 57.6 kcal/mol at ϕ, ψ = 35°, 245°. This energy is substantially higher than the minimum energy of −0.9 kcal/mol found previously at ϕ, ψ = 30°, 250°.[9] The difference in energy at the minimum

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(11) D. A. Brant and P. J. Flory, *J. Amer. Chem. Soc.*, 87, 2791 (1965).

Table I

Comparison of the Locations and Relative Energies of the Minima for Poly(*N*-methyl-L-alanine) When All χ_1 = 60° and All χ_N = 0°

Mark and Goodman[a]			This Work		
ϕ (deg)	ψ (deg)	Energy (kcal/mol)	ϕ (deg)	ψ (deg)	Energy (kcal/mol)[b]
30	250	0.0	35	245	0.0
210	250	0.6	210	245	0.9
240	345	2.4	245	345	3.3
80	345	3.4	90	345	4.8

[a] J. E. Mark and M. Goodman, *Biopolymers*, **5**, 809 (1967). [b] Electrostatic interaction of peptide units deleted.

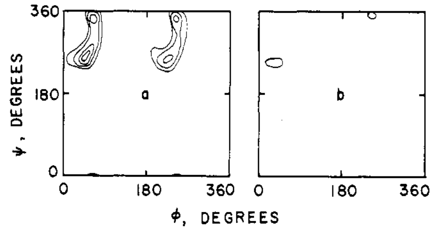

Figure 4. Conformational maps for poly(*N*-methyl-L-alanine) for the following values of χ_1 and χ_N: (a) 0°, 60°; (b) 0°, 0°. The lowest energy (7.3 kcal/mol) occurs at ϕ, ψ = 50°, 260° in part a. Contours are drawn at 1, 2, 5, and 10 kcal per mol relative to the minimum in part a.

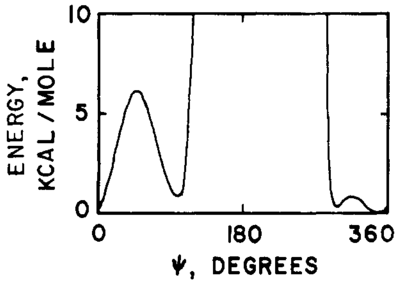

Figure 5. Slice through Figure 3c at ϕ = 120°. The energy scale has been shifted to yield a minimum energy of 0 kcal/mol.

arises primarily from the interaction of hydrogen atoms attached to $C_{i-1}{}^{\beta}$ and $C_i{}^{N}$. One pair of hydrogen atoms is separated by only 1.44 Å. Mark and Goodman did not include the substituents attached to $C_{i-1}{}^{\alpha}$ and $C_{i+1}{}^{\alpha}$ in their computation. The close contact of the hydrogen atoms could be relieved by a small rotation about $\chi_{1,i-1}$ or ψ_{i-1}. Since the separation of these atoms is constant so long as $\chi_{1,i-1}$, ψ_{i-1}, and $\chi_{N,i}$ are constant, it is anticipated that our inclusion of the substituents on $C_{i-1}{}^{\alpha}$ and $C_{i+1}{}^{\alpha}$ will have an important effect on the energy at the minimum but only a minor effect on the manner in which the energy varies with ϕ_i and ψ_i.

The results obtained with all χ_1 = 60° and all χ_N = 0°, and the electrostatic interaction deleted, are compared to the results obtained by Mark and Goodman[9] in Table I. The four minima are seen to occur at nearly the same positions as those found previously.[9] Slight differences in the relative energies of the minima can be attributed to the effect of the substituents on $C_{i-1}{}^{\alpha}$ and $C_{i+1}{}^{\alpha}$. Therefore our computations confirm the existence of the four minima found previously for poly(*N*-methyl-L-alanine).[9]

The conformational maps for poly(*N*-methyl-L-alanine) when all the χ_1 = 0° and all χ_N = 0 or 60° are shown in Figure 4. The minimum energy (7.3 kcal/mol) is found at ϕ, ψ = 50°, 260° in the map where the χ_1 = 0° and the χ_N = 60°. All contours are drawn relative to this minimum. If all χ_1 are at 60° the energy is always more than 10 kcal/mol above the minimum energy in Figure 4. As mentioned in the section on polysarcosine, the relative energies of the conformational maps in Figure 4 would be affected by a different choice of the torsional potential about χ_N.

Figures 3 and 4 demonstrate that the conformational maps for polysarcosine and poly(*N*-methyl-L-alanine) are sensitive to the values of χ_N and $\chi_{N,i+1}$. It has been previously demonstrated that the conformational maps for poly(L-proline) depend upon the orientation of the pyrrolidine ring.[2,7] These results lead to the generalization that the conformational map calculated for any polypeptide in which the peptide hydrogen atom is replaced by an alkyl group will be sensitive to the orientation selected for the alkyl group.

In the computation of the dimensional properties of polyglycine[12] and poly(L-alanine)[12] it could be assumed that rotations about ϕ_i and ψ_i were independent of the rotational angles in residues $i - 1$ and $i + 1$. This assumption is no longer valid if the peptide hydrogen atoms are replaced by alkyl groups. In the case of polysarcosine, rotation about ϕ_i and ψ_i is affected not only by $\chi_{N,i}$ but also by $\chi_{N,i+1}$. The rotation about $\chi_{N,i}$ is influenced by rotation about ψ_{i-1}. These same considerations apply to poly(*N*-methyl-L-alanine). In this latter case, however, rotation about $\chi_{N,i}$ is influenced not only by ψ_{i-1} but also by $\chi_{1,i-1}$. Attempts to predict the characteristic ratio observed for polysarcosine would be further complicated by the presence of peptide bonds in the cis conformation.[13]

Interdependence of rotations exists also in poly(L-proline), where the energy for rotation about ψ_i at constant ϕ_i depends upon the conformation of the pyrrolidine ring of both residues i and $i + 1$.[7] However, it is possible to correctly predict the characteristic ratio of poly(L-proline) containing peptide bonds in the trans conformation without taking detailed account of this interdependence.[2]

Conformational Energy for ϕ near 120°. While the pyrrolidine ring exhibits flexibility,[2,4,5,7,10,14] ϕ_i, χ_N, and χ_1 will be restricted to the vicinity of 120, 60, and 0°, respectively. In order to assess the implications of the conformational maps of polysarcosine and poly(*N*-methyl-L-alanine) for poly(L-proline), the conformational maps should be examined where ϕ_i, χ_N, and χ_1 have these values. The result for polysarcosine is the slice through Figure 3c at ϕ = 120°, which is shown in Figure 5. The energy scale in Figure 5 has been adjusted so that the minimum energy occurs at 0 kcal/mol. It is apparent that there is a second region of low energy at ψ = 100° when the conformation of polysarcosine is made analogous to that of poly(L-proline). Inspection of Figure 3c shows that the exact location and depth of this second minimum will be extremely sensitive to the value assigned to ϕ for ϕ in the range 100° to 140°. This situation also occurs in poly(L-proline).[2]

(12) D. A. Brant, W. G. Miller, and P. J. Flory, *J. Mol. Biol.*, 23, 47 (1967).
(13) F. A. Bovey, J. J. Ryan, and F. P. Hood, *Macromolecules*, 1, 305 (1968).
(14) G. N. Ramachandran, A. V. Lakshminarayanan, B. Balasubramanian, and G. Tegoni, *Biochim. Biophys. Acta*, 221, 165 (1970).

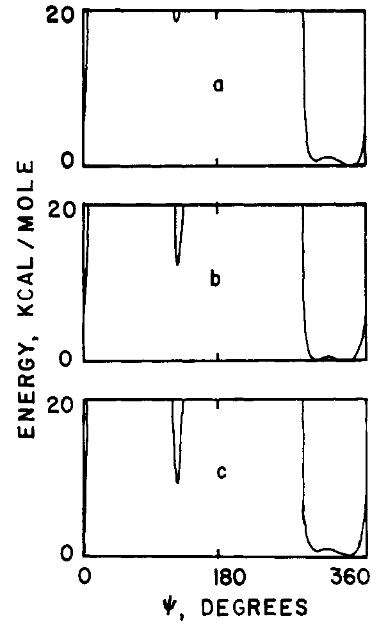

Figure 6. Conformational maps at constant ϕ for poly(N-methyl-L-alanine). The energy scale has been adjusted to yield a minimum energy of 0 kcal/mol. The actual computed energy is in excess of 100 kcal/mol (see text). (a) $\phi_i = 120°$, all $\chi_1 = 0°$, all $\chi_N = 60°$; (b) $\phi_i = 130°$, all $\chi_1 = -5°$, all $\chi_N = 60°$; (c) $\phi_i = 130°$, all $\chi_1 = 0°$, all $\chi_N = 55°$.

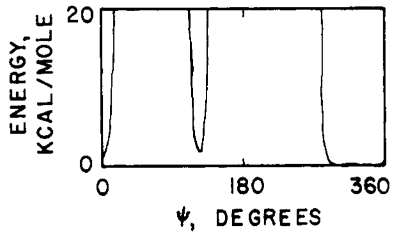

Figure 7. Conformational map for poly(N-methyl-L-alanine) when $\phi = 120°$, all $\chi_1 = 0°$, all $\chi_N = 60°$, and bond angles used in computations for poly(L-proline) are substituted for those previously used for poly(N-methyl-L-alanine). The energy scale has been adjusted to yield a minimum energy of 0 kcal/mol. The actual computed energy is in excess of 100 kcal/mol (see text).

An energy well in excess of 100 kcal/mol is computed for poly(N-methyl-L-alanine) when $\phi_i = 120°$, all $\chi_1 = 0°$, and all $\chi_N = 60°$, regardless of the value of ψ_i. This situation arises because of the extremely close contact of a hydrogen atom attached to C_i^N and a hydrogen atom attached to C_i^β. These hydrogen atoms are each directed toward the position which would be occupied by C_i^γ in poly(L-proline). This contact is constant as long as ϕ_i, $\chi_{1,i}$, and $\chi_{N,i}$ are constant. Therefore it is possible to assess the implications of poly(N-methyl-L-alanine) for poly-L-proline) by examining how the energy varies with rotation about ψ_i when ϕ_i, all χ_1, and all χ_N are specified, even though poly(N-methyl-L-alanine) itself will not be capable of assuming these conformations.

This slice through Figure 4a at $\phi = 120°$, with the energy scale adjusted to yield a minimum energy of 0 kcal/mol, is shown in Figure 6a. A second minimum appears at $\psi = 130°$ when the $\chi_1 = 0°$ and the $\chi_N = 60°$, but it is of substantially higher energy than the minimum at $\psi = 340$–$345°$. The relative energies of these minima in poly(L-proline) are extremely sensitive to the choice of ϕ and the puckering of the pyrrolidine ring.[2] The analogous parameters in poly(N-methyl-L-alanine) are the choice of ϕ and the rotation about the bonds to the methyl groups. Figure 6b,c show the variation of the energy with ψ when $\phi = 130°$ and the orientation of the methyl groups corresponds to the $\gamma 1$ position (Figure 6b) and the $\gamma 2$ position (Figure 6c) for poly(L-proline).[2] The relative energies of the two minima are obviously influenced by the choice of geometry for the polypeptide chain, within the range of geometries available to poly(L-proline). However, the second region of low energy near $\psi = 120°$ is still substantially higher than the energy near $\psi = 340°$.

Table II
Alterations in Bond Angles Used to Compute the Data for Figure 7

Bond Angle	Alteration (Deg)
C'-N-C^α	−2.0
C'-N-C^N	3.0
C^N-N-C^α	−1.0
C^α-C'-O	−2.0
C^α-C'-N	4.0
N-C'-O	−2.0
N-C^α-C^β	−4.5
N-C^α-C'	2.5
C'-C^α-C^β	1.0

Since small changes in geometry markedly affect the relative energies of these minima, it becomes important to assess the effect of the slightly different bond angles used in the computations for poly(N-methyl-L-alanine)[9] and poly(L-proline).[2] Consequently the computation presented in Figure 6a was repeated, but using the bond angles for poly(L-proline).[2] Our purpose here is not to suggest that the poly(L-proline) bond angles should be actually observed in poly(N-methyl-L-alanine), but rather to investigate the effect of the small difference in bond angles upon the conformational energy as a function of ψ for $\phi = 120°$. The bond angles altered, and the alterations themselves, are listed in Table II. The N-C^α-H angle was 109.5°. The result of the computation is shown in Figure 7, where again the energy scale has been adjusted to yield a minimum energy of 0 kcal/mol. The second minimum at $\psi = 125°$ is now of only slightly higher energy than that obtained with $\psi = 350°$.

The results presented here show that the conformational maps for polysarcosine and poly(N-methyl-L-alanine) are consistent with the presence of two regions of low energy, separated by about 180° rotation about ψ, in the conformational map for the internal dipeptide unit in poly(L-proline). The relative energies of these minima are highly sensitive to chain geometry in polysarcosine and poly(N-methyl-L-alanine), as well as in poly(L-proline).[2,7]

Acknowledgments. We thank Dr. Alan Tonelli for bringing our attention to the apparent discrepancy between the conformational maps for polysarcosine, poly(N-methyl-L-alanine), and poly(L-proline), and Dr. Dennis Torchia for providing us with the conclusions from his ^{13}C magnetic resonance study of poly(L-proline).[15]

(15) **Note Added in Proof.** While this manuscript was in press our attention was called to calculations for polysarcosine with $\chi_N = 60°$ in S. Tanaka and A. Nakajima [*Polym. J.*, 2, 717 (1971)], which obtained a conformational energy map very similar to Figure 3c in the present work. They also acknowledge that their previous results for polysarcosine (ref 8) are incorrect.