A TEST FOR THE USE OF TWO-FOLD TORSIONAL POTENTIAL FOR Ψ ROTATION—'UNPERTURBED DIMENSIONS OF POLYPEPTIDES'

A. R. SRINIVASAN

Department of Crystallography and Biophysics, University of Madras, Madras 600 025

AND

V. S. R. RAO

Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560 012

RECENTLY, by applying classical energy methods to polypeptides, a number of interesting results have been reported[1-9]. The calculated values[9] of C_α are found to be sensitive to the input peptide geometry. These studies also showed no correlation between C_α and the number of allowed conformations of the peptide unit suggesting that the steric factor σ need not always provide information about the flexibility or freedom of rotation of chain units. In the classical potential energy approximation the energy of a system is divided into several discrete contributions, such as Vander Waals energies, electrostatic interactions, torsional energy, hydrogen bond energy, etc. Though the form and nature of the functions used by different groups[1-5] for computing non-bonded energy differ, to some extent but all of them predict same trends in the energy contours including minima at about the same region. On the other hand, the form of potential functions that have been used by different workers for computing torsional energy differ drastically. For the potential function associated with ϕ (C'—N—C$^\alpha$—C') both the forms $V_0(\phi)/2$ $(1 + \cos 3\phi)$ and $V_0(\phi)/2$ $(1 - \cos 3\phi)$ have been used. Values of 0·6 to 1·5 kcal.mole^{-1} have been used for $V_0(\phi)$. Similarly for the potential function associated with ψ (N—C$^\alpha$—C'—N) the earlier investigators have used a form $V_0(\psi)/2$ $(1 + \cos 3\psi)$, with low values ranging from 0·25 to 1 kcal.mole^{-1} for $V_0(\psi)$. Recently from quantum chemical studies on model compounds Sasisekharan and co-workers[10] have suggested that the potential function associated with ψ should be of the form $V(\psi) = V_0(\psi)/2$ $(1 - \cos 2\psi)$ but not $V_0(\psi)/2$ $(1 + \cos 3\psi)$. These authors suggested a value of 4 kcal.mole^{-1} for $V_0(\psi)$ from theoretical studies, without any experimental confirmation. Infrared studies of amides made by Shimanouchi[11] also support the two fold torsional function for $V(\psi)$. For the potential function associated with ϕ (C'—N—C$^\alpha$—C'), these authors also suggested that there is no need for separately adding the $V(\phi)$ term in empirical potential energy calculations since $V(\phi)$ was found to be very small[12]. The implications of these changes in the form of intrinsic torsional functions have been discussed by Ramachandran[13], while dealing with the ordered polypeptide chains. In this paper, the authors have examined the relevance of

the new form of intrinsic torsional potential functions on the unperturbed dimensions of polypeptides.

Fixing of Atoms and Calculation of Potential Energy

The averaged peptide parameters reported by Ramachandran *et al.*[14] have been used for calculations on poly (L-alanine). The side groups were fixed by the method suggested by Ramachandran and Sasisekharan[1] assuming C$^\alpha$—H$^\alpha$ and C$^\alpha$—C$^\beta$ bond lengths to be 1·0 and 1·54 Å respectively. The —CH$_3$ was treated as an united atom with higher Vander Waals radii.

The conformational energy was computed using the expression,

$$V(\phi_i, \psi_i) = V_0(\phi)/2 (1 + \cos 3\phi_i) + V_0(\psi)/2 \times (1 - \cos 2\psi_i) + \sum_{k,l} V_{k,l}(\phi_i, \psi_i) + \sum_{k,l} V_e k,l \tag{1}$$

Values of 0–1·5 kcal.mole^{-1} for $V_0(\phi)$ and 1–4 kcal. mole^{-1} for $V_0(\psi)$ (in independent calculations) have been used. 6-exp non-bonded potential functions[1] with a set of recently modified constants[15] for H···H and H···X interactions were used to compute the non-bonded interaction energy [$\sum_{k,l} V_{k,l}(\phi_i, \psi_i)$].

These calculations also were repeated with the constants suggested by Flory and co-workers[6] for non-bonded potentials. Electrostatic energy ($\sum_{k,l} V_{ek,l}$) was computed using the expression reported by Brant *et al.*[7] and the charges reported by Srinivasan and Rao[9]. The characteristic ratios (C_α) of an infinitely long chain were obtained by using the expression,

$$C_\alpha = [(E + \langle T \rangle)(E - \langle T \rangle)^{-1}]_{22} \tag{2}$$

where E is the identity matrix of order 3 and $\langle T \rangle$ is the statistical-mechanical averaged matrix. The sub script 22 denotes the (2, 2) element of the final matrix. The averaged matrix $\langle T \rangle$ was evaluated as described by Srinivasan and Rao[9].

RESULTS AND DISCUSSION

Since Ramachandran *et al.*[14] suggested a value of about 110° for the bond angle (τ) at non-glycyl α-carbon atom from crystal structure data, most of the calculations were carried out for this (τ) angle and these results are presented in Table I. It is seen from the table that the magnitude of $V_0(\psi)$ and $V_0(\phi)$ do affect the values C_α significantly. The value C_α

TABLE I

Computed C_α values for Poly (L-alanine) using a two-fold function for $V(\phi)$ with different $V_0(\psi)$ values ($\tau = 110$ and $T = 298$ K has been used)

Nature of functions used	C_α values $V_0(\psi) -$ (in kcal. mole^{-1})			
	1	2	3	4
(N, Z)	9·0	9·3	9·9	10·3
(N, TA)	7·9	8·2	8·6	9·0
(N, TB)	7·0	7·2	7·5	7·9
(N, TC)	6·4	6·3	6·6	7·0
(F, Z)	16·9	16·8	19·6	23·6
(F, TC)	12·0	11·6	12·3	14·0

N—Non-bonded potential functions and constants given in Refs. 1 and 15.

F—Non-bonded potential functions and constants given in Ref. 7.

Z—$V_0(\phi) = 0$

TA—$V(\phi) = 0·25 (1 + \cos 3\phi)$

TB—$0·5 (1 + \cos 3\phi)$

TC—$0·75 (1 + \cos 3\phi)$.

(10·3) obtained assuming $V_0(\phi) = 0$ and $V_0(\psi) = 4$ kcal. mole^{-1} (as suggested by Kolaskar *et al.*[10,12]) is slightly higher than the experimental value of 8·6 ± 0·5[16-18]. On the other hand the value 8·6 obtained with $V_0(\phi) = 0·5$ kcal. mole^{-1} and $V_0(\psi) = 3$ kcal. mole^{-1} in the expression agree well with the experimental data. This suggests that the corrected barrier $V_0(\psi)$ is slightly lower than the 4 kcal. mole^{-1} suggested by Kolaskar *et al*[10]. Similarly the value of $V_0(\phi) = 0·5$ kcal. mole^{-1} suggests that the intrinsic barrier about N—C$^\alpha$ is small in agreement with the recent theoretical results of Kolaskar *et al.*[12]. Though these authors suggested a complete neglect of the $V(\phi)$ term in the empirical potential energy calculations, the present calculations suggest the retention of this term with a low intrinsic barrier. The values of C_α, obtained with the constants suggested by Brant *et al.*[7] for the non-bonded potentials, are very high compared to the experimental value[16-18] of 8·6. The large differences in the computed C_α values arise mainly due to differences in non-bonded potentials involving H-atom. Unlike Brant *et al.*[7] Ramachandran[18] suggested softer potentials for H....H and H....X

interactions from the experimental observations in the solid state. In fact, the observed conformational parameters for the LL-term were explained[12] better with modified non-bonded potentials. The present study also supports the use of new form of potential function for $V(\psi)$, *i.e.*, $V(\psi) = 1·5 (1 - \cos 2\psi)$ together with the softer potentials for H ··· H and H··· X interactions for conformational energy studies on polypeptides.

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