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Relationes

Approximated Potential Functions of Non-Bonded Interactions of Methyl Group

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The constants of Lennard-Jones potential functions $E=A/r^{12}-C/r^6$ describing $CH_3...CH_3$, $CH_3...H$, $CH_3...C$, $CH_3...O$, $CH_3...N$ non-bonded interactions were derived using the energy minimization procedure. The effective diameter of CH_3 group separated from the other one by four bonds is 3.7Å and corresponding constants of $CH_3...CH_3$ interactions are $A=7.31\cdot10^5$ Å^{12} kcal/mol and $C=570$ Å^6 kcal/mol. The potentials found are compatible with those of Scott and Scheraga [1–3].

Key words: Methyl group, non-bonded interactions

Theoretical conformational analysis of complex compounds often requires that the number of the pairwise atom interactions be reduced. This can be achieved by replacing some groups in a molecule by effective atoms. The paper deals with potential function parameters of non-bonded interactions of the peptide chain with a methyl group approximated by the effective radius sphere.

The empirical potentials of two types are commonly used for the description of the non-bonded interactions. These are the Buckingham function $E=A\cdot\exp(-br)-C/r^6$("6-exp"), and the Lennard-Jones function $E=A/r^{12}-C/r^6$("6–12") [1, 2] (r is the distance between two interacting atoms). Though these potentials lead to fairly similar results, and neither has essential advantages, the calculational procedure with the function "6–12" is more convenient, than that with the function "6-exp". The Buckingham function involves a greater number of empirical parameters, has an unrealistic minimum when $r\to0$, and requires more computing time. Therefore to calculate the energy of the non-bonded interactions of an effective atom approximating a methyl group we found the parameters A and C for the Lennard-Jones potential.

As the first step we obtained a conformational map for N-acetyl-L-alanine methylamide with the four-atom methyl groups (Fig. 1) calculating the non-bonded interactions of all atoms with the "6–12" potential with Scott and Scheraga parameters [3] and the torsional energy as described elsewhere [4]. The map was constructed at 20° intervals of Φ and Ψ angles, and the total energy was minimized with respect to the methyl group rotational angles χ_1, χ_2, and χ_3 at every point. After this all methyl groups were replaced by effective atoms, and

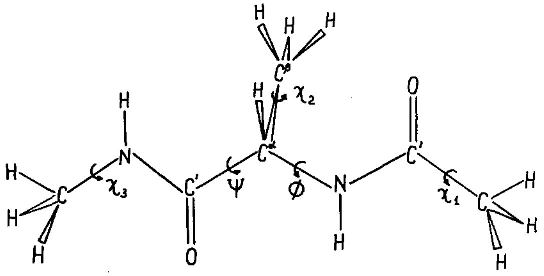

Fig. 1. Calculational model for N-acetyl-L-alanine methylamide. Geometric parameters are the same as those in Ref. [4]. The positions of methyl groups correspond to the minima of the torsional potentials [4]

an approximated conformational map was constructed and compared with the reference map for N-acetyl-L-alanine methylamide. The sum of squared differences of the relative energies at every point of both maps $\Sigma(E_i^0 - E_i)^2$ was minimized over the parameter $C(CH_3\ldots CH_3)$. In the process of minimization only points of the high-energy region in the centre of the map ($\Phi = \Psi = 0°$ according to the nomenclature [5]) were not taken into account. During the iteration process the value of $A(CH_3\ldots CH_3)$ was determined assuming that the potential function has a minimum at $r = r_0$, i.e., $A = 0.5 C \cdot r^6$. At the same time the parameters A and C for the pairwise interactions $CH_3\ldots H$, $CH_3\ldots C$, $CH_3\ldots O$ and $CH_3\ldots N$ were obtained assuming that $C_{ij} = \sqrt{C_{ii} \cdot C_{jj}}$, and $A_{ij} = 0.5 \cdot C_{ij}\left(\frac{r_{ii} + r_{jj}}{2}\right)^6$ at $r = r_0$. The initial value of $C(CH_3\ldots CH_3) = 1125\,\text{Å}^6 \cdot \text{kcal/mol}$ was determined from the Slater-Kirkwood equation using the parameters of Brant *et al.* [6]. The calculations were carried out with the following values of the CH_3 group effective diameters: $r_0(CH_3) - 3.5$, 3.6, 3.7, 3.8, and 3.9 Å (this range includes the values most frequently used in the literature [2, 6–12]).

The Table 1 presents parameters A and C for the "6–12" function with r_0 in the range 3.5–3.9 Å obtained by the above method; they may be used together with the A, C parameters of Scott and Scheraga atom-atom potentials [1, 3]. The absolute values of $\Sigma(E_i^0 - E_i)^2$ which are given in the last line of the table indicate that the range of r_0 selected for the CH_3 group is quite reasonable. The

Table 1. Methyl group parameters for the function "6–12"

Type of interaction	$r_0(CH_3) = 3.5$ Å		$r_0(CH_3) = 3.6$ Å		$r_0(CH_3) = 3.7$ Å		$r_0(CH_3) = 3.8$ Å		$r_0(CH_3) = 3.9$ Å	
	A	C	A	C	A	C	A	C	A	C
$CH_3\ldots CH_3$	$8.64\cdot10^5$	940	$7.89\cdot10^5$	725	$7.31\cdot10^5$	570	$6.70\cdot10^5$	445	$6.16\cdot10^5$	350
$CH_3\ldots H$	$6.90\cdot10^4$	209.5	$6.71\cdot10^4$	184	$6.57\cdot10^4$	163.2	$6.40\cdot10^4$	144	$6.24\cdot10^4$	127.9
$CH_3\ldots C$	$4.97\cdot10^5$	589.8	$4.76\cdot10^5$	517.9	$4.60\cdot10^5$	459.2	$4.42\cdot10^5$	405.8	$4.25\cdot10^5$	359.9
$CH_3\ldots N$	$3.77\cdot10^5$	584.1	$3.62\cdot10^5$	513	$3.51\cdot10^5$	454.9	$3.39\cdot10^5$	401.9	$3.28\cdot10^5$	356.4
$CH_3\ldots O$	$3.59\cdot10^5$	587.4	$3.45\cdot10^5$	515.8	$3.35\cdot10^5$	457.4	$3.23\cdot10^5$	404.1	$3.13\cdot10^5$	358.4
$\Sigma(E_i^0 - E_i)^2$	190.07		186.61		185.36		185.41		186.45	

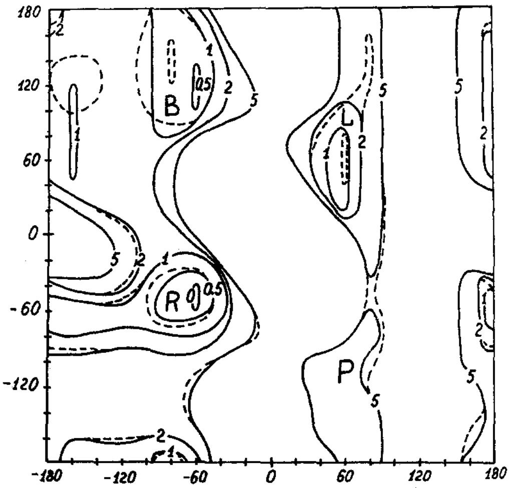

Fig. 2. Reference (solid line) and approximated (dashed line) conformational maps for N-acetyl-L-alanine methylamide

deviation of the approximate map contours from those of the reference map described by the value $\Sigma(E_i^0 - E_i)^2$ taken over a great number of point (~ 300) is small, the error being minimal at $r_0(CH_3) = 3.7$ Å. Therefore, the parameters of the $CH_3 \ldots CH_3$ interaction, $A = 7.31 \cdot 10^5$ Å^{12} kcal/mol and $C = 570$ Å^6 kcal/mol at $r_0 = 3.7$ Å, and the corresponding set for the pairwise interactions of the CH_3 group (Table 1) are most reliable for conformational calculations of the peptide molecules with methyl groups separated by at least four bonds. As methyl groups are conventionally represented by spheres, one may assume that the decrease of the number of bonds between them will require the utilization of the A, C parameters corresponding to the effective values of $r_0 = 3.5$, 3.6 Å. Thus, the results of the conformational analysis of poly-N-methyl-L-alanine [7] indicate that the best approximation to real situation is achieved when the CH_3 groups are replaced by the spheres with $r_0 = 3.5$ Å.

Figure 2 shows reference (solid lines) and the approximated (dashed lines) conformational maps for N-acetyl-L-alanine methylamide. As is seen from the figure, both potential surfaces are fairly close to each other in the most important low-energy regions (R, B, and L). In the upper part of the approximate map at $\Phi \sim -160°$, a slight shift and a broadening of the region within the 1 kcal/mol contour are observed. The error in the energy resulting from this fact does not exceed 0.2–0.3 kcal/mol. The decrease of the barrier at $\Phi \sim 80$, and $\Psi \sim -40$ by 1 kcal/mol makes the approximated map contour smoother, a specific link limited by the 5 kcal/mol contour appearing between the regions L and P.

References

1. Scheraga, H. A.: Advan. Phys. Org. Chem. **6**, 103 (1968)
2. Ramachandran, G. N., Sasisekharan, V.: Advan. Protein Chem. **23**, 283 (1968)
3. Scott, R. A., Scheraga, H. A.: J. Chem. Phys. **45**, 2091 (1966)
4. Pletnev, V. Z., Gromov, E. P., Popov, E. M.: Khim. Prirodn. Soedin. 224 (1973)
5. IUPAC-IUB Comm. Biochem. Nomenclature, Biochem. **9**, 3471 (1970)

6. Brant, D. A., Tonelli, A. E., Flory, P. J.: Macromolecules **2**, 228 (1969)
7. Warvari, H. E., Knaell, K. K., Scott, R. A.: J. Chem. Phys. **56**, 2903 (1972)
8. Brant, D. A., Flory, P. J.: J. Am. Chem. Soc. **87**, 2791 (1965)
9. Ramachandran, G. N., Venkatachalam, C. M., Krimm, S.: Biophys. J. **6**, 849 (1966)
10. Venkatachalam, C. M., Ramachandran, G. N.: Conformation of biopolymers, Vol. 1, p. 83. London and New York: Acad. Press 1967
11. Gibson, K. D., Scheraga, H. A.: Proc. Natl. Acad. Sci. (USA) **58**, 420 (1967)
12. Goebel, C. V., Dimpfi, W. L., Brant, D. A.: Macromolecules **3**, 644 (1970)

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