Density Functional Theory Study of Contribution of Many-Body Energies to Binding Energy for Alanine-$(Water)_4$ Complex

AJAY CHAUDHARI,* SHYI-LONG LEE

Department of Chemistry and Biochemistry, National Chung-Cheng University, Ming-Hsiung, ChiaYi, 621 Taiwan

Received 29 April 2004; accepted 8 July 2004
Published online 17 November 2004 in Wiley InterScience (www.interscience.wiley.com).
DOI 10.1002/qua.20358

ABSTRACT: The lowest energy conformer of alanine-$(water)_4$ complex (Spectrochim. Acta A, 59, 2619, 2003) was studied in more detail using Density Functional Theory methods B3LYP/6-31+G*. The total energy and binding energy for this complex is −629.514437 hartrees and −41.02 kcal/mol, respectively. Relaxation energy and many-body energies, i.e., two-, three-, four-, and five-body energies, were obtained for this complex using many-body analysis to elucidate their contribution to the binding energy of the complex. It was found that relaxation energy as well as all many-body energies had significant contributions to the total binding energy. The highest contribution is from two-body energies. © 2004 Wiley Periodicals, Inc. Int J Quantum Chem 102: 174–177, 2005

Key words: density functional theory method; (alanine-water)$_4$ complex; many-body interaction

Introduction

Owing to the complexity arising from a direct structural study of protein–water interactions, amino acids have been quite useful as models for understanding structural behavior of proteins and peptides in aqueous solutions. The structural and energetic properties of amino acids play a key role in the optimization and design of both currently used and proposed industrial processes of biochemistry. One useful approach that assists in our understanding of these interactions is to study interactions between basic building blocks of proteins, i.e., amino acids and water, to mimic some aspects of protein structure. There are several investigations on amino acid–water interactions [1–10]. Most of them are on glycine and alanine.

Correspondence to: A. Chaudhari; e-mail: ajaychau5@yahoo.com

*Present address: 104 Davey Lab., PMB 025, Pennsylvania State University, University Park, PA 16802, USA.

Contract grant sponsor: National Science Council, Taiwan.

© 2004 Wiley Periodicals, Inc.

It is now well known that amino acids are known to occur in zwitterionic form in aqueous media [11–13]. Always a subject of interest is: How many water molecules are required to stabilize the zwitterionic form of amino acid? It has been shown that glycine as well as alanine requires at least two water molecules to stabilize the zwitterionic form [2, 10]. Park et al. [10] studied the alanine-$(water)_n$ (n = 1–3) complex using the Density Functional Theory (DFT) method. They predicted the proton transfer pathways between an alanine-$(water)_n$ and zwitterions-$(water)_n$ cluster. Recently, structural and vibrational spectra of the alanine-$(water)_4$ complex were studied experimentally and theoretically [8, 9]. In the theoretical studies, the authors used the DFT/B3LYP method to calculate vibrational frequencies and absorption intensities. They have shown that the calculated vibrational properties were significantly influenced by a very small rearrangement in relative position of the neighboring water molecules.

Here, we extend the earlier study on the alanine-$(water)_4$ complex with the DFT/B3LYP method [14–17] using a basis set that includes both diffuse and polarization functions. We used the 6-31+G* basis set in this study since in the hydrogen-bonded complex both diffuse and polarization functions are expected to be important and are included in the basis set. We considered only the lowest energy conformer for alanine-$(water)_4$ complex optimized in earlier studies. A more detailed study of this structure is done by applying many-body analysis [18–23] to obtain the relaxation energy, many-body (two-, three-, four, and five-body) energies, and their contributions to the binding energy for this complex.

Computational Details

The geometry optimization for alanine-$(water)_4$ was performed using a 6-31+G* basis set at the DFT level. For hydrogen bonding, it is expected that both diffuse and polarization functions may be necessary in the basis set, since the atoms involved in the hydrogen bonding are much more sensitive to the basis sets. DFT with a B3LYP functional [14–17] that consists of the Hartree-Fock and nonlocal exchange and correlation parts was approached along with these basis sets. The relaxation energy and many-body energies (two-, three-, four-, and five-body interaction energies) were calculated as suggested previously [18–23]. All energies are corrected for basis set superposition error (BSSE) by using the counterpoise method and generalized counterpoise method [24–26]. All calculations were performed using the Gaussian 98W program [27].

MANY-BODY ENERGIES

Many-body energies (two-, three-, four-, and five-body interaction energies) were calculated as follows. The decomposition of the total energy of the complex can be written as:

$$\begin{aligned}\Delta E &= E(ijklm) - \{E_A + 4E_W\} \\ &= \sum_{i=1}^{4} E(i) - \{E_A + 4E_W\} \qquad \text{(relaxation energy)} \\ &\quad + \sum_{i=1}^{n-1}\sum_{j>i}^{n} \Delta^2 E(ij) \qquad \text{(Two-body)} \\ &\quad + \sum_{i=1}^{n-2}\sum_{j>i}^{n-1}\sum_{k>j}^{n} \Delta^3 E(ijk) \qquad \text{(Three-body)} \\ &\quad + \ldots + \Delta^n E(ijk\ldots n) \qquad (n\text{-body})\end{aligned} \tag{1}$$

where $E(i)$, $E(ij)$, $E(ijk)$, $E(ijkl)$ are the energies of the various monomers, dimers, trimers, and tetramer in the complex and E_A, E_W are the energies of isolated alanine and water molecules, respectively. The pairwise two-body interaction energies and higher three-body and four-body interaction energies are defined as the following equations.

$$\Delta^2 E(ij) = E(ij) - \{E(i) + E(j)\} \tag{2}$$

$$\begin{aligned}\Delta^3 E(ijk) &= E(ijk) - \{E(i) + E(j) + E(k)\} \\ &\quad - \{\Delta^2 E(ij) + \Delta^2 E(ik) + \Delta^2 E(jk)\},\end{aligned} \tag{3}$$

$$\begin{aligned}\Delta^4 E(ijkl) &= E(ijkl) - \{E(i) + E(j) + E(k) + E(l)\} \\ &\quad - \{\Delta^2 E(ij) + \Delta^2 E(ik) + \Delta^2 E(il) + \Delta^2 E(jk) \\ &\quad + \Delta^2 E(jl) + \Delta^2 E(kl)\} - \{\Delta^3 E(ijk) + \Delta^3 E(ijl) \\ &\quad + \Delta^3 E(ikl) + \Delta^3 E(jkl)\}\end{aligned} \tag{4}$$

and so on. The BSSE-corrected energy of a subsystem ($ijkl$) is evaluated in the full basis of a larger system ($ijklm$), and denoted by the term $E(ijkl|ijklm)$. Accordingly, the n-body terms are substituted with the BSSE-corrected ones:

$$\Delta^2 E_C(ij) = E(ij|ijklm) - \{E(i|ijklm) + E(j|ijklm)\} \quad (5)$$

$$\Delta^3 E_C(ijk) = E(ijk|ijklm) - \{E(i|ijklm) + E(j|ijklm) + E(k|ijklm)\} - \{\Delta^2 E(ij|ijklm) + \Delta^2 E(ik|ijklm) + \Delta^2 E(jk|ijklm)\} \quad (6)$$

$$\Delta^4 E_C(ijkl) = E(ijkl) - \{E(i|ijklm) + E(j|ijklm) + E(k|ijklm) + E(l|ijklm)\} - \{\Delta^2 E(ij|ijklm) + \Delta^2 E(ik|ijklm) + \Delta^2 E(il|ijklm) + \Delta^2 E(jk|ijklm) + \Delta^2 E(jl|ijklm) + \Delta^2 E(kl|ijklm)\} - \{\Delta^3 E(ijk|ijklm) + \Delta^3 E(ijl|ijklm) + \Delta^3 E(ikl|ijklm) + \Delta^3 E(jkl|ijklm)\} \quad (7)$$

and so on.

The sum of relaxation energy, two-body, three-body, four-body, and five-body energy gives the total binding energy of the complex. The BSSE-corrected total energy is calculated as suggested in ref. 25 and 26.

Results and Discussion

The lowest energy structure of the alanine-(water)$_4$ complex is shown in Figure 1. The total energy of alanine-(water)$_4$ complex in this work obtained at B3LYP/6-31+G* is −629.514437 hartrees.

In order to study the contribution of many-body energies to the binding energy, the alanine-(water)$_4$ complex is divided into alanine and water monomers and 10 two-body, 10 three-body, 5 four-body, and a five-body term. Table I represents the values of these energies. All the energies are in kcal/mol and are BSSE-corrected. The binding energy of the complex obtained is −41.02 kcal/mol. It can be seen that most of the two-body energies have an attractive contribution except W_1-W_2 and W_1-W_3, which have a repulsive contribution. Also, the interaction energy of alanine with individual water molecules is greater than that of water–water interaction. The highest and lowest two-body interaction contribution is from A-W_2 (–12.87 kcal/mol) and W_1-W_2 (0.04 kcal/mol), respectively, but the former is attractive and the latter is repulsive. On comparing the interaction energy between alanine with individual water molecules, A-W_2 has the highest contribution (–12.87 kcal/mol) among A-W_1, A-W_2, A-W_3, and A-W_4. The highest water–water contribution is from W_2-W_3 (−4.18 kcal/mol).

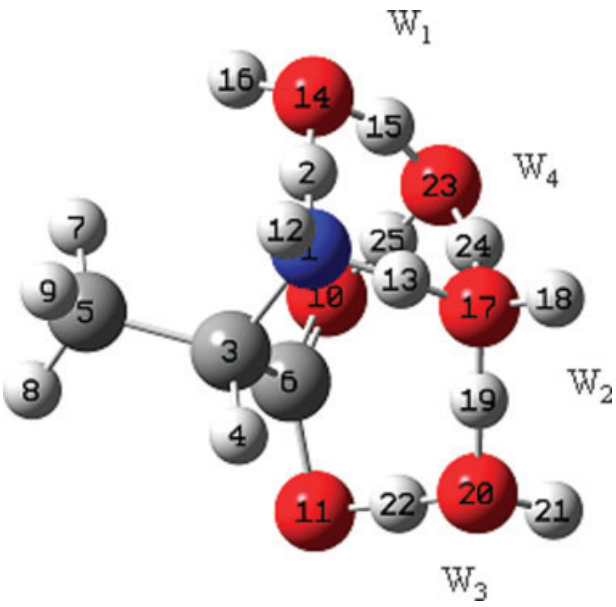

FIGURE 1. Lowest energy conformer of alanine-(water)$_4$ complex optimized using B3LYP/6-31+G* level.

The total two-body interaction energy is attractive and is –50.22 kcal/mol.

The three-body energies also have an attractive contribution except A-W_1-W_2, A-W_2-W_4, and A-W_3-W_4, which have a repulsive contribution. The highest three-body energy is –7.08 kcal/mol for A-W_2-W_3. The highest water–water–water interaction energy is –2.61 kcal/mol for W_1-W_3-W_4. The total three-body energy is attractive and is –17.77 kcal/mol. All the four-body energies are repulsive. The highest four-body energy is 2.62 kcal/mol for A-W_1-W_2-W_3. The water–water–water–water interaction energy also contributes significantly (2.51 kcal/mol) to the total four-body energy. The total four-body energy is repulsive and is 7.96 kcal/mol. Five-body energy is attractive and is –2.51 kcal/mol. The relaxation energy, which is a measure of the degree of distortion in individual molecules in a complex, is 21.52 kcal/mol.

Conclusions

We studied in detail the lowest energy conformer of alanine-(water)$_4$ complex with the DFT/B3LYP method and using a basis set that includes diffuse and polarization functions. The contributions of many-body energies were studied. It was found that relaxation energy as well as many-body energies (two-,

TABLE I

Many-body interaction energies (two-, three-, four-, and five-body) for alanine-(water)$_4$ complexes using B3LYP/6-31+G* level.

Many-body term	Energy (kcal/mol)
Two-body energies	
A-W1	−10.85
A-W2	−12.87
A-W3	−9.78
A-W4	−7.94
W1-W2	0.04
W1-W3	2.61
W1-W4	−3.86
W2-W3	−4.18
W2-W4	−2.77
W3-W4	−0.62
Three-body energies	
A-W1-W2	0.93
A-W1-W3	−2.80
A-W1-W4	−4.66
A-W2-W3	−7.08
A-W2-W4	1.89
A-W3-W4	0.62
W1-W2-W3	−2.43
W1-W2-W4	−0.81
W1-W3-W4	−2.61
W2-W3-W4	−0.82
Four-body energies	
A-W1-W2-W3	2.62
A-W1-W2-W4	0.07
A-W1-W3-W4	2.48
A-W2-W3-W4	0.28
W1-W2-W3-W4	2.51
Five-body energy	
A-W1-W2-W3-W4	−2.51
Relaxation energy	21.52
Total 2-B	−50.23
Total 3-B	−17.77
Total 4-B	7.96
Total 5-B	−2.51
BE	−41.02

A is alanine and W_i denotes i^{th} water molecule in a complex according to Figure 1. All energies are in kcal/mol and are BSSE-corrected.

three-, four-, and five-body) have significant contributions to the binding energy. Total two-body, three-body, and five-body energies are attractive, whereas four-body and relaxation energy is repulsive. This is different from the many-body study on water clusters and ethylenediamine-(water)$_3$ complex [18], in which the authors found that the higher-body energies (four-body and higher) were almost negligible.

References

1. Hall, N. E.; Smith, B. J. J Phys Chem A 1998, 102, 3985.
2. Jensen, J. H.; Gordon, M. S. J Am Chem Soc 1995, 117, 8159.
3. Nagaoka, M.; Yoshida, N. O.; Yamabe, T. J Phys Chem A 1998, 102, 8202.
4. Romano, S.; Clementi, E. Int J Quantum Chem 1978, 14, 839.
5. Alagona, G.; Ghio, C. J Mol Liq 1990, 47, 139.
6. Wang, W.; Pu, X.; Zheng, W.; Wong, N.; Tian, A. J Mol Struct 2003, 626, 127.
7. Alagona, G.; Ghio, C.; Kollman, P. A. J Mol Struct 1988, 166, 385.
8. Ellzy, M. W.; Jensen, J. O.; Hameka, H. F.; Kay, J. G. Spectrochim Acta A 2003, 59, 2619.
9. Tajkhorshid, E.; Jalkanen, K. J.; Suhai, S. J Phys Chem B 1998, 102, 5899.
10. Park, S. W.; Ahn, D. S.; Lee, S. Chem Phys Lett 2003, 371, 74.
11. Albrecht, G.; Corey, R. B. J Am Chem Soc 1939, 61, 1087.
12. Lehninger, A. L. In Principles of Biochemistry; CBS: Delhi, 1987, p 97.
13. Gaffney, J. S.; Pierce, R. C.; Friedman, L. J Am Chem Soc 1977, 99, 4293.
14. Becke, A. D. Phys Rev A 1988, 38, 3098.
15. Becke, A. D. J Chem Phys 1993, 98, 5648.
16. Becke, A. D. J Chem Phys 1997, 107, 8554.
17. Schmider, H. L.; Becke, A. D. J Chem Phys 1998, 108, 9624.
18. Woo, D. W. Bull Kor Chem Soc 2001, 22, 693.
19. Xantheas, S. S. J Chem Phys 1994, 100, 7523.
20. Xantheas, S. S. Chem Phys 2000, 258, 225.
21. Hankins, D.; Moskowitz, J. W.; Stillinger, F. H. J Chem Phys 1970, 53, 4544.
22. Mhin, B. J.; Kim, J.; Lee, S.; Lee, J. Y.; Kim, K. S. J Chem Phys 1994, 100, 4484.
23. Kim, J.; Lee, S.; Cho, S. J.; Mhin, B. J.; Kim, K. S. J Chem Phys 1995, 102, 839.
24. Boys, S. F.; Bernardi, F. Mol Phys 1970, 19, 553.
25. Valiron, P.; Mayer, I. Chem Phys Lett 1997, 275, 46.
26. White, J. C.; Davidson, E. R. J Chem Phys 1990, 93, 8029.
27. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb. M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nakayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian 98: Rev. A.6; Gaussian: Pittsburgh, PA, 1998.