Journal of Physical and Theoretical Chemistry
of Islamic Azad University of Iran, 4 (3) 181-185**:** Fall 2007
(J.Phys.Theor.Chem.IAU Iran: Fall 2007)
ISSN: 1735-2126

Ab initio potential energy surface and second virial coefficient for Asp-His-Ser trimer

R.Faham[1,2] ,M.Monajjemi[1,*], F.Mollaamin[1,3] and M.Khaleghian[1,4]

1. Department of Chemistry, Science and Research Campus, Islamic Azad University, Iran, P.O.Box:14155-775
2. Islamic Azad University, Marand Branch, Marand, Iran
3. Department of Chemistry, Qom Branch, Islamic Azad University, Qom, Iran
4. Department of Chemistry, Young Researcher Club, Varamin Pishva Branch, Islamic Azad University, Tehran, Iran

ABSTRACT

HF level of ab initio calculations with basis-set 6-31G including full counterpoise correction has been applied to compute the AspHis potential with the Ser and HisSer potential with the Asp in AspHisSer trimer. The potential energy surface has a minimum of -16.765 kcal/mol in R_1=1.912 nm and R_2=2.719 nm. The optimum computed curves for two interactions were fitted with intermolecular pair potential models, including of Lennard-Jones, Kihara, Buckingham Exp-6 and Buckingham Exp-6-8 potentials. The Buckingham exponential potentials gave the best fit. These potentials have been used to calculate the second virial coefficient for AspHis-Ser and Asp-HisSer interactions. As we expected B2 for Asp-HisSer interaction was more negative from AspHis-Ser interaction.

INTRODUCTION

The equation of state of a low density gas can be described by the virial expansion. The virial expansion expresses the compressibility factor as a function of density, with temperature dependent coefficients known as virial coefficients [1, 2].

$$Z = \frac{\beta P}{\rho} = 1 + B_2\rho + B_3\rho^2 \qquad (1)$$

Z is the compressibility factor, β is the reciprocal temperature, $\beta = 1/k_BT$, where k_B is Boltzmann's constant and T is the temperature, P is the pressure, ρ is the density, B_2 is the second virial coefficient, and B_3 is the third virial coefficient.

The virial coefficients are basic thermodynamic properties that represent the nonideal behavior of real gases. The importance of the virial coefficients lies in the fact that they are related directly to the interactions between molecules. The second virial coefficient represents the departure from ideality due to interactions between pairs of molecules, the third virial coefficient gives the effects of interactions of molecular triplets, and so on.

If u, the intermolecular potential between two particles, only depends on the relative separation, r, between them, the second virial coefficient B at temperature T was given by the following expression [3]:

---

[*] . Corresponding author:m_monajjemi@yahoo.com

$$B(T) = -2\pi N_A \int_0^\infty \left(e^{-u(r)/k_BT} - 1\right) r^2 dr \qquad (2)$$

where u(r) is the potential energy of two body interactions at an intermolecular separation of r, N_A is the avogadro's number. One way to utilize Eq. (2) is to express u(r) as some of potential functions, hence B (T) is simply obtained by the numeric integral calculation.

In this work, we model Aspartatic acid (Asp), Histidine (His) and Serine (Ser) amino acids in which they are in chymotrypcin active site as reported in the literature[4]. The active site of chymotrypsin consists of Asp102 positioned close to His 57 and Ser 195. A three-dimensional surface energy for interactions between Asp-HisSer and AspHis-Ser was constructed, then for two optimum interactions, potential energy function was obtained by fitting with intermolecular pair potential models and second virial coefficients were calculated. All this calculations were performed by GAUSSIAN 98 package.

2. The intermolecular potentials

In order to calculate the second virial coefficients, the intermolecular potential is needed. Results with different potentials can be fitted with computed data to assess the quality of the potential. In this study we consider the following potentials.

2-1. Lennard-Jones (12–6) potential

This model assumes the familiar form [5],

$$u(r) = 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right] \qquad (3)$$

where ε is the potential depth and σ is the distance for which $u(r) = o$.

2-2. Kihara potential

The core model of Kihara [6] allows a convex core of any shape to be assigned to a molecule while the potential energy of interaction is assumed to depend only on the shortest distance between core surfaces and to be of the Lennard-Jones form

$$u(r) = \begin{cases} \infty, & r \le 2a \\ 4\varepsilon\left[\left(\dfrac{\sigma - 2a}{r - 2a}\right)^{12} - \left(\dfrac{\sigma - 2a}{r - 2a}\right)^{6}\right], & r > 2a \end{cases} \qquad (4)$$

where a is the core radius.

2-3. Exp-6 potential

The modified Buckingham or exp-6 [7] has been used in the calculations:

$$u(r) = \begin{cases} \infty, & r \le r_m \\ \dfrac{\varepsilon}{1 - 6/\alpha}\left[\dfrac{6}{\alpha}\exp\left(\alpha\left(1 - \dfrac{r}{r_m}\right)\right) - \left(\dfrac{r_m}{r}\right)^{6}\right], & r > r_m \end{cases} \qquad (5)$$

where ε the repulsive-wall steepness parameter, and r_m is that value of r for which Eq. (5) goes through a false maximum.

2-4. Exp-6-8 potential

The Buckingham exponential-6-8 potential [8],

$$u(r) = b\exp(-\alpha\bar{r}) - c[\bar{r}^{-6} + \beta\bar{r}^{-8}] \qquad (6)$$

where α, β ,b and c are Exp-6-8 parameters.

3. Computational details:

Serine, Histidine and Aspartatic acid amino acids model to form chymotrypcin active site (Fig.1).

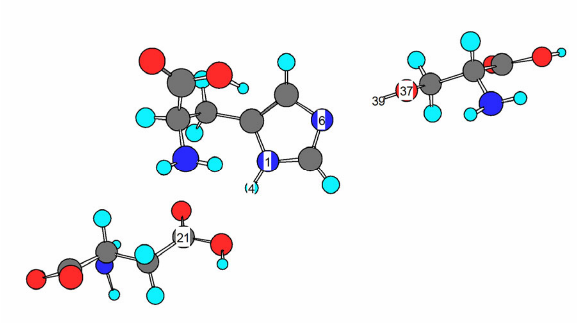

Fig.1. Asp,His and Ser model used in the calculations.

The structures of three amino acid are primary full optimized, and then they are brought together to form model and full optimized again. The Asp-COOH --- HN-His and His-N---HO-Ser conformation must be as model. Then all angles, dihedrals and distances were kept constant near the binding site except R_{37} (distance between N_1 and O_{37}) and R_{21} (distance between N_1 and C_{21}). These distances were changed manually, thus various R_1 (N_6-H_{39} distance for interaction between AspHis and Ser) and R_2 (C_{21}-H_4 distance for interaction between Asp and HisSer) obtained. 441 energy points were calculated with the supermolecular approach on HF level of theory with basis-set 6-31G including full counterpoise correction. For counterpoise correction, three ab initio calculations had to be done for each point of the potential surface: E_{AB}(G, AB), the total energy of the trimer AB calculated with the full basis set AB at geometry G and E_A(G,AB) and E_B(G,AB), the total energies of monomer A and dimer B, respectively, computed with the trimer basis set AB at geometry G, where G denotes the coordinates that specify the geometry of the trimer[9]. Then potential energy can be calculated in the following expression:

$$V_{AB}^{cc}(G) = E_{AB}(G,AB) - E_A(G,AB) - E_B(G,AB) \quad (7)$$

Hence, for 21 distances R_{21} between 2.5 and 8.0 nm, 21 different distances R_{37} have been selected between 4.0 and 8.0 and V (G) calculated. Thus a three-dimensional intermolecular potential energy surface for interactions between Asp-HisSer and AspHis-Ser in AspHisSer trimer on the basis of ab initio calculations is obtained. All calculations have been carried out with the GAUSSIAN 98 package program.

For two Asp-HisSer and AspHis-Ser interactions, optimum potential curves were determined. These curves are fitted by above mentioned intermolecular pair potential models. The Exp-6 and Exp-6, 8 potential gave very good fit and parameters obtained. By replacing two latter potential functions in Eq. 2, interaction second virial coefficient were calculated by numeric integral by maple 9.5.

For drawing the graphs of results, we used the Microsoft office Excell-2003 program and matlab 7.0.4.

4. Results and Discussions

An intermolecular potential energy surface for interactions between Asp-HisSer and AspHis-Ser in AspHisSer trimer on the basis of HF level of ab initio calculations with basis-set 6-31G including full counterpoise correction as a function of R_1 and R_2 are shown in figure 2**.** The data of intermolecular potential energies are given in table 1.

The results show the minimum potential energy in R_1=1.912 nm and R_2=2.719 nm equal to -16.765 kcal/mol. Potential energy curve as a function of R_1 in R_2=2.719 nm, and potential energy curve as a function of R_2 in R_1=1.912 nm are optimum potential curves for two interactions. These curves were fitted with the different above mentioned pair potential functions by matlab 7.0.4. Table 2 presents R-square and RMSE, for examine the goodness of fits. A value of R-square closer to 1 and a RMSE value closer to 0 indicates a better fit, thus the Buckingham exponential potentials give the best fit (Fig 3). Knowing the form of *u*, the second virial coefficient will be calculated by solving equation (2). Table.3 shows the fitting parameters of these potentials and calculated second virial coefficients.

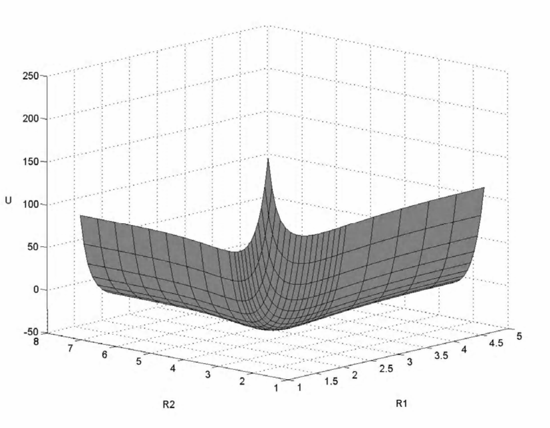

Fig.2. The potential energy surface for interactions between Asp-HisSer and AspHis-Ser in AspHisSer trimer

The results show the minimum potential energy in R_1=1.912 nm and R_2=2.719 nm, thus for R_2=2.719 nm, potential energy curve as a function of R_1 and for R_1=1.912 nm, potential energy curve as a function of R_2 are optimum potential curves for two interactions. These curves were fitted with the different above mentioned pair potential functions by matlab 7.0.4. Table 2 presents R-square and RMSE, for examine the goodness of fits. A value of R-square closer to 1 and a RMSE value closer to 0 indicates a better fit, thus the Buckingham exponential potentials give the best fit (Fig 2). Knowing the form of *u*, the second virial coefficient will be calculated by solving equation (3). Table.3 shows the fitting parameters of these potentials and calculated second virial coefficients.

Table 1. The data of potential energies for interactions between Asp-HisSer and AspHis-Ser in AspHisSer trimer at the HF/6-31G level in various R_1 and R_2.

R1 R2	**1.008**	**1.144**	**1.318**	**1.413**	**1.513**	**1.612**	**1.712**	**1.812**	**1.9125**	**2.013**	**2.213**	**2.414**	**2.914**	**3.914**	**4.913**
1.57	204.24	145.1	118.18	111.31	107	104.4	102.96	102.3	102.157	102.36	103.32	104.57	107.46	110.84	111.96
1.768	146.12	86.981	60.001	53.09	48.737	46.103	44.628	43.934	43.7656	43.942	44.864	46.077	48.904	52.196	53.283
1.965	113.9	54.775	27.744	20.797	16.409	13.743	12.239	11.521	11.3289	11.485	12.371	13.554	16.321	19.542	20.603
2.064	104.14	45.024	17.97	11.008	6.6042	3.9244	2.4084	1.679	1.47747	1.6244	2.495	3.6645	6.4057	9.596	10.645
2.163	97.307	38.191	11.117	4.1407	-4E-4	-2.969	-4.496	-5.235	-5.4456	-5.307	-4.45	-3.293	-0.575	2.5875	3.6259
2.262	92.66	33.547	6.4559	-0.533	-4.963	-7.666	-9.203	-9.952	-10.17	-10.04	-9.195	-8.048	-5.352	-2.214	-1.185
2.362	89.633	30.524	3.4167	-3.584	-8.024	-10.74	-12.28	-13.04	-13.266	-13.14	-12.31	-11.17	-8.494	-5.379	-4.358
2.461	87.788	28.681	1.5594	-5.451	-9.901	-12.62	-14.18	-14.94	-15.174	-15.05	-14.23	-13.1	-10.44	-7.349	-6.336
2.56	86.787	27.682	0.5475	-6.472	-10.93	-13.66	-15.22	-15.99	-16.231	-16.12	-15.3	-14.18	-11.54	-8.461	-7.456
2.719	86.331	27.23	0.0771	-6.955	-11.43	-14.17	-15.74	-16.52	**-16.76**	-16.66	-15.86	-14.75	-12.13	-9.072	-8.076
3.058	87.529	28.433	1.2502	-5.802	-10.29	-13.05	-14.64	-15.44	-15.695	-15.6	-14.82	-13.73	-11.14	-8.128	-7.148
4.055	92.397	33.307	6.075	-1.012	-5.536	-8.327	-9.943	-10.76	-11.043	-10.97	-10.23	-9.163	-6.629	-3.683	-2.731
5.053	94.506	35.419	8.164	1.0619	-3.478	-6.282	-7.91	-8.74	-9.0322	-8.967	-8.239	-7.189	-4.681	-1.764	-0.824
6.051	95.127	36.041	8.7745	1.6645	-2.883	-5.695	-7.329	-8.165	-8.4621	-8.402	-7.682	-6.639	-4.144	-1.243	-0.31
7.05	95.398	36.313	9.0391	1.9243	-2.628	-5.444	-7.082	-7.922	-8.2221	-8.165	-7.45	-6.411	-3.924	-1.033	-0.104

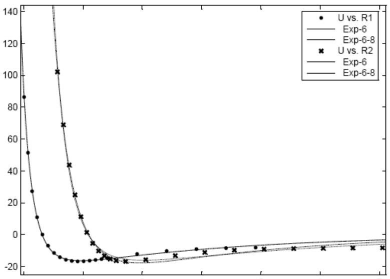

Fig.3. Fitting of calculated data with Buckingham exponential potentials

At the molecular level, B_2 reflects the nature of interactions: a more negative value of B_2, indicating a more attractive interaction, hence as we expected Asp-HisSer interaction (B_2=-4.307 × 10^{10}) is more attractive from AspHis-Ser interaction. (B_2=-6.72 × 10^9).

Table 2. R-Square and RMSE of data fits with four potential models.

Potential Model		**L.J(12,6)**	**Kihara**	**Exp-6**	**Exp-6-8**
U vs. R1	**R-Square**	0.774	0.9816	0.9996	0.9996
	RMSE	12.81	3.76	0.59	0.60
U vs. R2	**R-Square**	0.8496	0.9922	0.9946	0.9964
	RMSE	12.45	2.92	2.43	2.04

Table 3. Fitting parameters of calculated data with Buckingham exponential potentials.

Exp-6	**α**	**ε**	**r_m**	**$B_2(m^3/mol)$**
U vs. R1	0.665	16.3	1.965	-6.72e+9
U vs. R2	0.8531	16.02	3.021	-4.307e+10

Exp-6-8	**α**	**β**	**b**	**c**	**r_m**	**$B_2(m^3/mol)$**
U vs. R1	3.857	-9.522e-5	-35.39	-5.043e-5	11.48	-7.22e+9
U vs. R2	4.564	-6.036e-3	-68.29	-1.119e-3	11.94	-1.41e+10

REFERENCES

1. J.O. Hirschfelder, C.F. Curtiss, R.B. Bird, Molecular Theory of Gases and Liquids, Wiley, 1967.
2. D.A. McQuarrie, Statistical Mechanics, University Science Books, Sausalito, CA, 2000.
3. J.H. Dymond, E.B. Smith, The Virial Coefficients of Pure Gases and Mixtures, Oxford University, Oxford, 1980.
4. Voet's Biochemistry, John Wiley & Sons, Inc, copyright ©1990.
5. Lennard-Jones, J. Proc. Roy. Soc. 106A 463, 1924.
6. Kihara T. Virial coefficients and models of molecules in gases. Rev. Modern Phys. 25 831-843, 1953.
7. Buckingham, R. A. Proc. Roy. Soc. 168A, 264, 1938.
8. Buckingham,R. A. and Corner, J. Proc. Roy. Soc. 189A, 118, 1947.
9. S.F. Boys, F. Bernardi, Mol. Phys. 19, 553, 1970.