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QUANTUM CHEMICAL STUDY ON THE INTERACTION OF ARGININE WITH SILICA SURFACE

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The structure and energy characteristics of structures formed during arginine adsorption on silica surface from aqueous solution were studied by the density functional theory (B3LYP) method using a valence-split basis set 6-31++G(d,p) within the continuous solvent model (PCM) and supermolecular approximation. The equilibrium structural and energy parameters of the protonated arginine molecule in the gas phase dependent on the location of the hydrogen atom are considered including those of two possible zwitterions. The structure of the arginine ion H_2A^+*, which is formed when a proton attaches to a molecule or zwitterion of a given amino acid, has been elucidated. To determine the deprotonation constant of the carboxyl group in an acidic medium, the complexes of the arginine molecule (*AH_3^{2+}*) in the state with undissociated and deprotonated carboxyl groups are considered. The simulation of the acid medium was performed by taking into account the interaction with two hydrated HCl ion pairs, which provided the protonation of the α-amino group and the nitrogen atom of amino group within the guanidine group.*

In the study on the interaction of an arginine molecule with silica surface in an aqueous medium, complexes containing a $Si_8O_{12}(OH)_7O^-$ *ion with a deprotonated silanol group, six water molecules, and an arginine molecule with a deprotonated carboxyl group were considered. It has been found that the arginine molecule is most likely to be adsorbed on slica surface with formation of hydrogen bonds between the hydrogen atoms of the α-amino group and the oxygen atom of the deprotonated silanol group. In this case, the formation of a hydrogen bond between the oxygen atom of the carboxyl group and the hydrogen atom of the neighboring silanol group is possible. Slightly less likely is adsorption of arginine molecules due to interaction of the guanidine group with silanol groups of the surface. According to the calculated data, the adsorption of the zwitterionic form of the arginine molecule from the aqueous solution is equally likely to occur due to interaction of silanol groups of silica surface with both the carboxyl group and the guanidine group.*

***Keywords**: arginine, silica surface, adsorption, cluster approach, density functional theory method*

INTRODUCTION

Highly dispersed silica has become widely used as a sorbent and carrier of drugs in various fields of medicine, biotechnology, *etc*. [1]. Since most toxins are proteins in nature, the development of new sorbents based on silica requires data on the mechanism of its interaction with the structural elements of proteins - amino acids. Amino acid molecules contain both amine and carboxyl groups. It is not known enough which of them is capable of forming hydrogen bonds with silanol groups on silica surface. Since the vast majority of processes in the biological environment take place in aqueous solutions, the question of the influence of water molecules on the interaction of amino acids with surface groups ≡Si–OH also remains open. It should be noted that the use of sorbents based on silica is expected in a wide range of pH (from pH = 2 in the stomach to pH = 9 in the intestinal environment). The choice of arginine molecule was due to the fact that it contains three proton attachment centers – *α*-amine, carboxyl, and when protoning an additional positive charge is distributed between the three nitrogen atoms of the guanidine group of the arginine molecule, due to which this amino acid has strong basic properties [2]. In acidic solutions (pH < 2) the mentioned amino acid carries a double positive charge. As the pH increases, the carboxyl group is ionized (pK = 2) and a particle with a single positive charge is formed. The ionization constant of the α-amino group and the amino group of the side chain is 9 and 12, respectively [3].

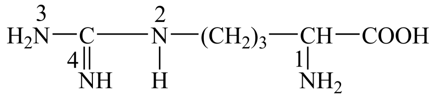
The authors [4, 5] performed modeling of the interaction of glycine in its zwitterionic state with the isolated silanol group of the silicon dioxide surface. The effect of the solvent was taken into account in the supermolecular approximation. The simulation results have shown that in complexes containing one molecule of water, two cases can be realized. In the first, the interaction of the hydrogen atom of the amino group of glycine with the oxygen atom of the silanol group was considered, while the carboxyl group interacted with the hydrogen atom of the silanol group through a water molecule. Conversely, in the second case, the direct interaction of the carboxyl group with the hydrogen atom of the silanol group was considered, and the amino group was in contact with the surface through a water molecule. According to the calculated energy parameters, both states can exist simultaneously.

A study of lysine adsorption on the surface of highly dispersed silica was performed using the method of ^{1}H NMR spectroscopy, the results of which are presented in [6]. The data obtained were compared with the results of calculations by the method of density functional theory (B3LYP/6-31G+(d,p)). According to the data obtained by the authors [6], the hydrogen atom of silanol group forms a hydrogen bond with the nitrogen atom of the ε-amino group of lysine.

Therefore, the forms and quantitative parameters of adsorption of some amino acids on silica surface revealed by experimental and theoretical methods require detailed analysis of the obtained information with the involvement of methods of theoretical modeling at the molecular level, in particular, quantum chemical calculations. Therefore, the aim of this work was to investigate the structure and energy characteristics of the structures formed during the adsorption of arginine on silica surface in aqueous solution.

OBJECTS AND METHODS OF RESEARCH

The equilibrium structural and energy parameters of the protonated arginine molecule dependent on the location of the hydrogen atom in the gas phase are considered. Thus, the hydrogen ion can form a bond with the N3 and N4 atoms of the guanidine group. There may be cases when the hydrogen ion belongs to the carboxyl group, or interacts with the N1 atom of the α-amino group:



$$H_2N-\overset{3}{\underset{\overset{4\|}{NH}}{C}}-\overset{2}{\underset{\overset{|}{H}}{N}}-(CH_2)_3-\underset{\overset{1|}{NH_2}}{CH}-COOH$$.

The model for silica surface was a cell of $Si_8O_{12}(OH)_8$ composition. It has the shape of a cube, on top of which are eight silicon-oxygen tetrahedra. Since silica surface at pH < 7 acquires a negative charge, complexes containing an arginine ion with a single positive charge (H_2A^+), which interacts with an ion of the composition $Si_8O_{12}(OH)_7O^-$ with a deprotonated silanol group, were investigated. Thus, the whole system remained electroneutral.

The calculations were performed by the density functional (DFT) method [7] with the exchange-correlation functional B3LYP [8, 9] and the valence-split basis with diffuse functions 6-31++G(d,p), the involvement of which is necessary when considering negatively charged systems. The influence of the aqueous medium was taken into account in the framework of the continuous model of solvent (PCM) [10, 11]. All the calculations were performed using the software package US GAMESS [12]. The deprotonation constants pK_a are calculated by the formula: $pK_a = \Delta G_{react}/2.303RT$ [13], where R is the universal gas constant, T is the temperature, and ΔG_{react} is the free Gibbs energy of the deprotonation process.

RESULTS AND DISCUSSIONS

Since it is known from the literature [2, 14] that arginine forms a zwitter-ion in aqueous solution, the three proton-accepting capacity of the guanidine group is much higher than the α-amino group, so first it was necessary to test the selected calculation method to reproduce this property. Equilibrium spatial and energy parameters of arginine in the molecular (Fig. 1 *a*) and two zwitterionic states were calculated, without the involvement of water molecules, but only with the influence of the solvent in the continuous approximation. In the first of the zwitterionic states, the α-amino group (Fig. 1 *b*) was protonated, and in the second, the imine (=NH) group of the guanidine group (Fig. 1 *c*) was protonated. In this case, for the gas phase, the equilibrium structure of the zwitterion with a protonated α-amino group could not be localized. In the Fig. 1 the following values of the total energy (E) are plotted on the ordinate axis, and the lowest total energy is the lowest is taken as the zero level. The relative energies of all other structures with the highest value of total energy were defined as the difference between the total energy of each considered structure and the minimal total energy in kJ/mol.

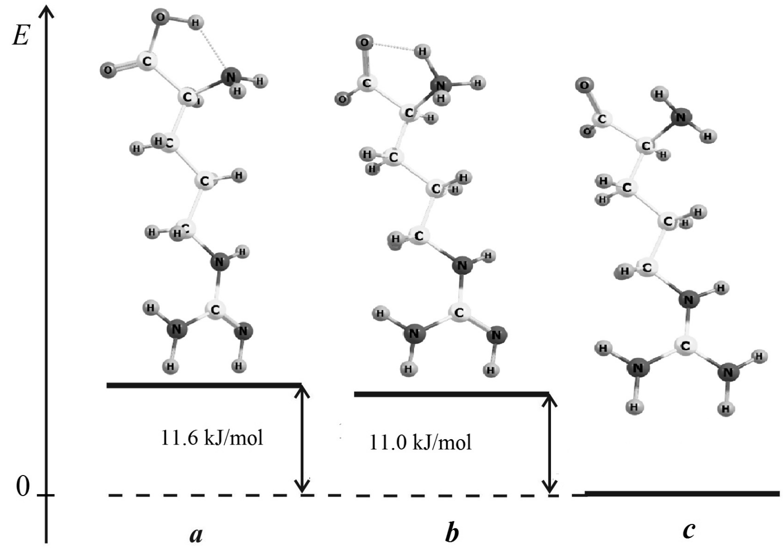


Fig. 1. Equilibrium structures and relative total energy of the arginine molecule (*a*) and the corresponding possible zwitterions (*b*, *c*)

Fig. 1 shows that the lowest energy is for the zwitterion ion in which the guanidine part of arginine is protonated, and they differ by 11.6 kJ/mol from the molecular form and by 11.0 kJ/mol from the alternative zwitterion ion (Fig. 1 *b*), which confirms literature data [14]. This in turn allows the use of further comparisons of the total energies of probable structures calculated by this method. It should be noted that the energy effect of proton transfer from the carboxyl group of the molecular form of arginine to the α-amino group is only 0.6 kJ/mol.

The next step in the study was to determine the structure of the arginine ion H_2A^+, which is formed when a proton attaches to a molecule or zwitterion of a given amino acid, as in the previous case, without the involvement of water molecules, but only in the PCM approximation. Fig. 2 shows the equilibrium structure and total energy of a protonated arginine molecule (H_2A^+) with a protonated α-amino group and a nitrogen atom of the amino group of the guanidine group (*a*), a protonated α-amino group and a nominal group (Fig. 2 *a*), a protonated carboxy or the amino group of the guanidine group (Fig. 2 *c*), the protonated carboxyl group and the nitrogen atom of the nominal group (Fig. 2 *d*). An analysis of the calculated values of total energies for these four structures has shown that the most probable is formation of a structure with protonated α-amino group and nitrogen atom of the amino group of the guanidine group (Fig. 1 *d*).

To calculate the deprotonation constant of the carboxyl group in an acidic environment, complexes of the arginine molecule (AH_3^{2+}) in the state with an undissociated carboxyl group (Fig. 3 *a*) and a deprotonated carboxyl group (Fig. 3 *b*) were constructed. The acid medium was simulated by adding of two hydrated HCl ion pairs to the model considered, so providing the protonation of the α-amino group and the nitrogen atom of the guanidine group imine group. The energy of formation of the complex with the deprotonated carboxyl group is 18.8 kJ/mol higher than that of the complex with the carboxyl group in the ground state. The calculated value of the dissociation constant of the carboxyl group is 3.9, which is close to the experimental value (~ 2) obtained in [15].

To determine the most probable path of interaction of the arginine molecule with the silanol group of silica surface, the electroneutral complexes of the negatively charged $Si_8O_{12}(OH)_7O^-$ ion with the positively charged arginine molecule (AH_2^+) were considered. Fig. 4 *a–d*) The arginine molecule in the zwitterionic state was placed in different positions relative to the deprotonated cluster $Si_8O_{12}(OH)_8$, as well as in the case of direct contact of the zwitterion with the deprotonated silanol group $Si_8O_{12}(OH)_8$ (Fig. 4 *e*).

Based on the calculated interaction energies between the silanol group of silica and the arginine molecule, the most probable is the formation of the hydrogen bond between the oxygen atom of deprotonated silanol group and the hydrogen atom of the α-amino group.

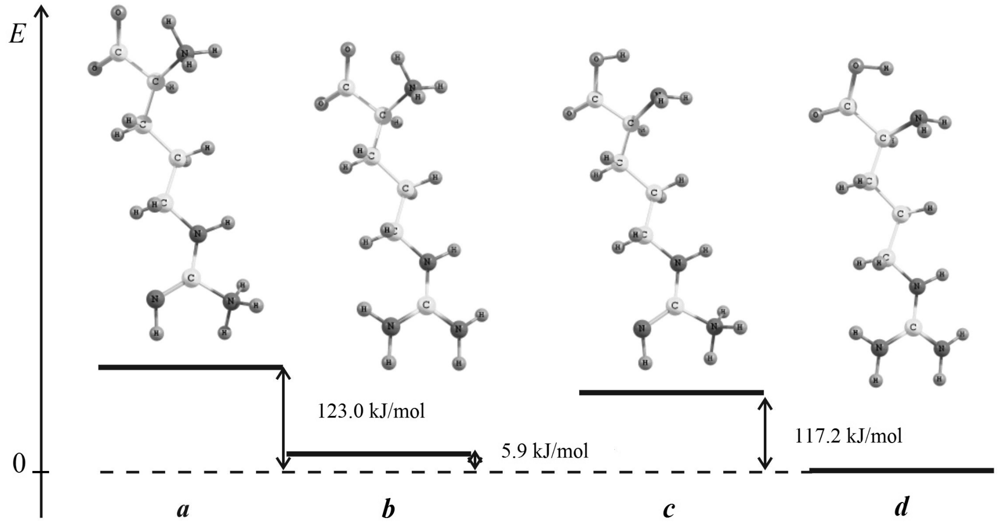


Fig. 2. Equilibrium structures and relative total energies of the protonated arginine molecule (H_2A^+): with the protonated α-amino group and the nitrogen atom of the amino group of the guanidine group (*a*); a protonated α-amino group and a nitrogen atom of the imine group (*b*); a protonated carboxyl group and a nitrogen atom of amine group of the guanidine group (*c*); a protonated carboxyl group and a nitrogen atom of the imine group (*d*)

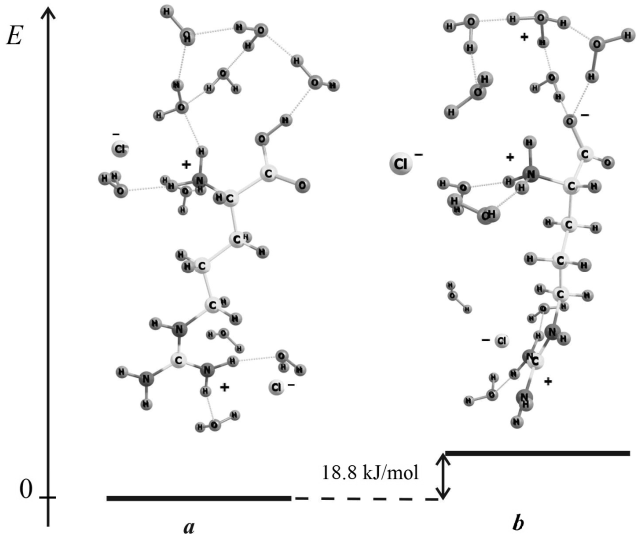


Fig. 3. Equilibrium structures and relative energies of the complexes of an arginine molecule with a carboxyl group in the molecular state (*a*) and a deprotonated carboxyl group (*b*) upon contact with two hydrated HCl ion pairs

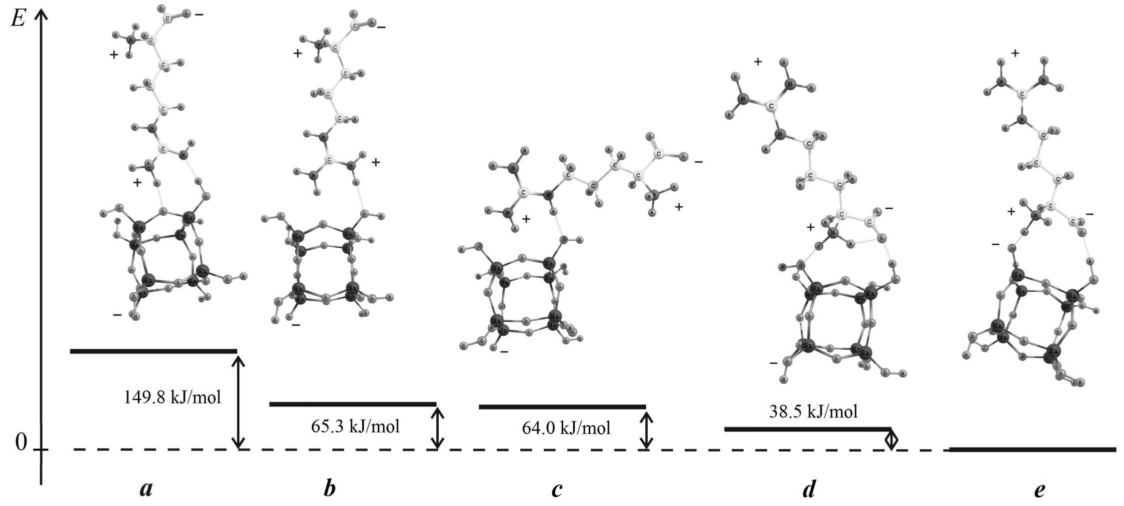


Fig. 4. Equilibrium structures and energies of intermolecular complexes where the deprotonated silanol group of the silica cluster interacts with the guanidine group (*a*, *b*), the side amino group (*c*), the α-amino group (*d*, *e*)

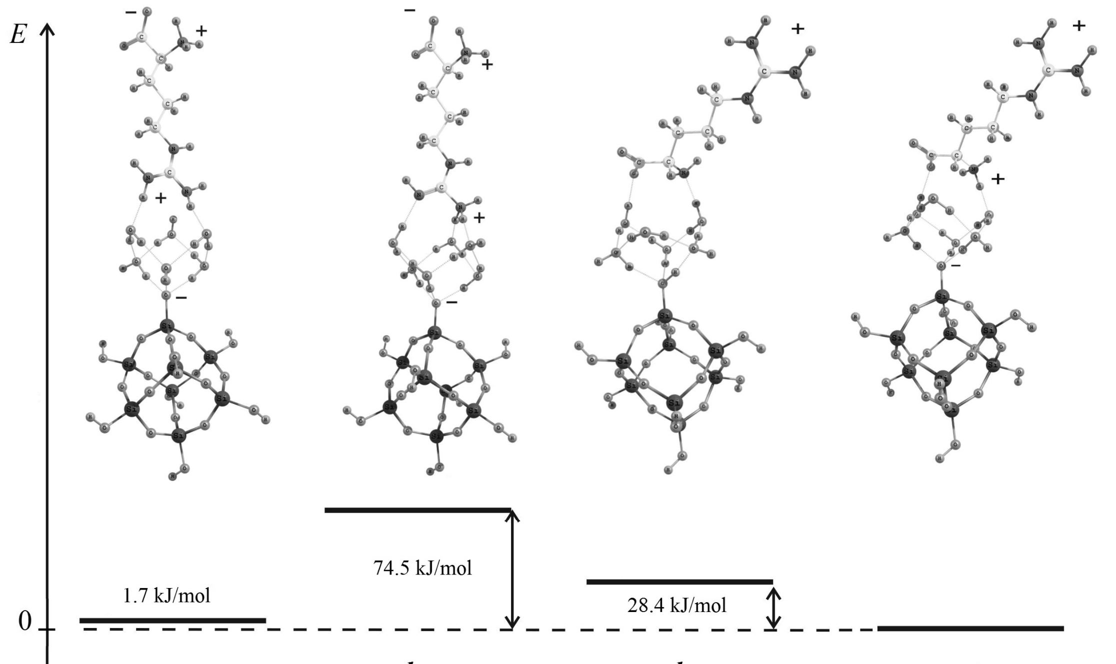


Fig. 5. Equilibrium structures and relative total energies of the complex containing the $Si_8O_{12}(OH)_7O^-$ ion, six water molecules and a molecule of arginine with a protonated carboxyl group placed in different positions relative to the silanol group

In order to study the interaction of an arginine molecule with silica surface in an aqueous medium, we considered complexes containing a $Si_8O_{12}(OH)_7O^-$ ion, six water molecules and a deprotonated arginine molecule in the position where the guanidine group is located close to the silanol group (Fig. 5 *a, b*) as well as those in the position where the guanidine group of arginine molecule is stationed opposite to the silanol group (Fig. 5 *c, d*).

Fig. 5 shows that the lowest energy relates to an intermolecular complex where the dissociated silanol group interacts through water molecules with the carboxyl and α-amino groups, a slightly higher value (1.7 kJ/mol) of total energy relates to the complex where the dissociated silanol group through water molecules interacts with the protonated guanidine group, what indicates the possibility of the simultaneous existence on silica surface of both these intermolecular complexes.

CONCLUSIONS

Based on the analysis of the results of calculations of structural and energy parameters, it can be concluded that the arginine molecule is most likely adsorbed on silica surface with formation of hydrogen bonds between the hydrogen atoms of the α-amino group and the oxygen atom of the deprotonated silanol group. In this case, a hydrogen bond may be formed between the oxygen atom of carboxyl group and the hydrogen atom of the neighboring silanol group. Slightly lesser adsorption of arginine molecule occurs when the guanidine group interacts with silanol groups. According to the calculated data, the adsorption of the zwitterionic form of the arginine molecule from the aqueous solution is equally likely to occur when the silanol groups of silica surface interact with both the carboxyl group and the guanidine group.

Квантовохімічне дослідження взаємодії аргініну з поверхнею кремнезему

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Методом теорії функціоналу густини (B3LYP) з використанням валентно-розщепленого базисного набору 6-31++G(d,p) в межах континуальної моделі розчинника (PCM) та супермолекулярного наближення досліджено будову та енергетичні характеристики структур, які утворюються при адсорбції аргініну на поверхні кремнезему у водному розчині. Розглянуто рівноважні структурні та енергетичні параметри протонованої молекули аргініну в газовій фазі в залежності від місця розташування атома гідрогену і двох можливих цвітер-іонів. Було з'ясовано будову іона аргініну H_2A^+, який утворюється при приєднанні протона до молекули або цвітеріона даної амінокислоти. Для визначення константи депротонування карбоксильної групи в кислому середовищі розглянуто комплекси молекули аргініну (AH_3^{2+}) в стані з недисоційованою та депротонованою карбоксильною групою. Моделювання кислотного середовища здійснювалося шляхом врахування взаємодії з двома гідратованими іонними парами HCl, які забезпечили протонування α-аміногрупи та атома азоту аміногрупи гуанідінового угрупування.

При дослідженні взаємодії молекули аргініну з поверхнею кремнезему у водному середовищі були розглянуті комплекси, які містять іон $Si_8O_{12}(OH)_7O^-$ з депротонованою силанольною групою, шість молекул води та молекулу аргініну з депротонованою карбоксильною групою. Встановлено, що молекула аргініну, найбільш ймовірно, адсорбується на поверхні кремнезему з утворенням водневих зв'язків між атомами гідрогену α-аміногрупи та атомом кисню депротонованої силанольної групи. При цьому можливе утворення водневого зв'язку між атомом кисню карбоксильної групи та атомом гідрогену сусідньої силанольної групи. Дещо менша ймовірність адсорбції молекул аргініну при взаємодії гуанідінового угрупування з силанольними групами поверхні. Згідно розрахункових даних, адсорбція цвіттеріонної форми молекули аргініну з водного розчину, рівноймовірно, відбувається шляхом взаємодії силанольних груп поверхні кремнезему як з карбоксильною групою, так і з гуанідіновою групою.

Ключові слова: *аргінін, поверхня кремнезему, адсорбція, кластерне наближення, метод теорії функціоналу густини*

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