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Solvent Effect Study on the Stability Energies of Glycine, Alanine and Valine Amino Acides

F. Keshavarz Rezaei[1,*], A. Taherpour[1] and M. Aghaie[2]

[1] Chemistry Department, Arak Branch, Islamic Azad University, Arak, Iran
[2] Department of Chemistry, North Tehran Branch, Islamic Azad University,Tehran, Iran

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ABSTRACT

Glycine, Alanine and Valine are taken as amino acids with an equal polar head and with the difference in the length of hydrocarbon chains. The structural optimizations show the results of the isolated Glycine, Alanine and Valine in the gases phase, at the Hartree-Fock level by means of STO-3G,3-21G, 6-31G and 6-31+G basis sets. The calculations were performed for the ten (**1-10**) solvents using PCM model method at HF/6-31+G and then the dielectric effects of the surrounding were analyzed. The solvent effect on the stability of Glycine, Alanine and valine molecules was discussed.

Keywords: Glycine; Alanine; Valine, Solvent effects; PCM model; HF-calculations; Molecular modeling

INTRODUCTION

Amino acids are critical to life, and have many functions in metabolism. One particularly important function is to serve as the building blocks of proteins, which are linear chains of amino acids. Due to their central role in biochemistry, amino acids are important in nutrition and are commonly used in food technology and industry. In industry, applications include the production of biodegradable plastics, medicines, and chiral catalysts. Amino acids can be linked together in varying sequences to form a vast variety of proteins [1a-d]. Twenty-two amino acids are naturally incorporated into polypeptides and are called proteinogenic or standard amino acids. Eight standard amino acids are called "essential" for humans because they cannot be created from other compounds by the human body, and so must be taken in as food. Glycine (Gly or G) is not essential to the human diet, as it is biosynthesized in the body from the amino acid serine, which is in turn derived from 3-phosphoglycerate[1a-d]. In most organisms, the enzyme Serine hydroxymethyltransferase catalyses this transformation *via* the cofactor pyridoxal phosphate. In the liver of vertebrates, glycine synthesis is catalyzed by glycine synthase (also called glycine cleavage enzyme). Glycine is degraded *via* three pathways. The predominant pathway in animals involves the catalysis of glycine cleavage enzyme, the same enzyme also involved in the biosynthesis of glycine. In the second pathway, glycine is degraded in two steps [1a-d]. The first step is the reverse of glycine biosynthesis from serine with serine hydroxymethyl transferase. Serine is then converted to pyruvate by serine dehydratase. In the third pathway of glycine degradation, glycine is converted to glyoxylate by *D*-amino acid oxidase. Glyoxylate is then oxidized by hepatic lactate dehydrogenase to oxalate in an NAD^+-dependent reaction. The half-life of glycine and its elimination from the body varies significantly based on dose. In one study, the half-life was between 0.5 and 4.0 hours [1a-d]. Alanine (Ala or A) is a nonessential amino acid, meaning that

*Corresponding author: f-rezaee@iau-arak.ac.ir

it can be manufactured by the human body, and does not need to be obtained directly through the diet. Alanine is found in a wide variety of foods, but is particularly concentrated in meats. Alanine can be manufactured in the body from pyruvate and branched chain amino acids such as valine, leucine, and isoleucine. Alanine is most commonly produced by reductive amination of pyruvate. Because transamination reactions are readily reversible and pyruvate pervasive, alanine can be easily formed and thus has close links to metabolic pathways such as glycolysis, gluconeogenesis, and the citric acid cycle. It also arises together with lactate and generates glucose from protein *via* the alanine cycle [1a-d]. Valine (abbreviated as Val or V) is an essential amino acid; hence it must be ingested, usually as a component of proteins. It is synthesized in plants *via* several steps starting from pyruvic acid. The initial part of the pathway also leads to leucine. The intermediate α-ketoisovalerate undergoes reductive amination with glutamate [1a-d].

The Gaussian 03 program was applied, which is induded the popular electronic structure necessary modules for performing calculations in a solvated environment using the continuum models approximations [7]. Among such models, the polarizable continuum model (PCM) is one of the most widely used methods since it meets a good compromise between accuracy and computation time. Never the less, Gaussian programs may not be the best option for performing such calculations, but it still can be very useful when used properly [7]. In particular PCM model program does not provide any information on the solvent structure. In addition, the size and shape of cavity have no rigorous definitions. However, there are also several important advantages [7]. First, one can select a designed level of quantum mechanical theory from a wide range of ab initio molecular orbital (MO) and density functional theory (DFT) levels that are sufficiently accurate for modeling bond breaking and forming processes. Second, the reaction coordinate is uniquely defined because solvent effects from the continuum medium are effectively included in the solute Hamiltonian and do not increase the dimensionality of the system. Although these self-consistent reaction field studies provide useful insight, their accuracy is often questionable, due to the uncertainty in the cavity size and shape for variable geometry of the reacting system [7].

The solvent effect is taken into account *via* the self-consistent reaction field (SCRF) method. The solute is placed in to a cavity within the solvent. SCRF approaches differ in how they define the cavity and the reaction field. Properties measured in low-pressure gases and those derived from measurements in the liquid phase differ as molecular interactions perturb the intrinsic polarizabilities, in the so-called solvent effect [2-3]. A dielectric continuum model with the solvated molecule placed in a spherical cavity and surrounded by a linear, homogeneous, polarizable dielectric medium was employed for the description of the condensed phase. The system (usually indicated as a solute) is described as a quantum mechanical charge distribution within a volume, the so-called solute cavity, modeled on the molecular shape of the solute and the environment (or the solvent) as a continuum dielectric. The solute polarizes the dielectric and dielectric polarization in turn generates an electrostatic field at the solute which modifies the original charge distribution [4-6].

In this study, the structural optimizations of the three amino acids Gly, Ala and Val have been investigated. The optimization results of the isolated Glycine, Alanine and Valine molecules in the gas phase, at the Hartree-Fock level by means of STO-3G,3-21G, 6-31G and 6-31+G basis sets have also been carried out. The calculations were performed for the ten solvents [(Water **1**, DMSO **2**, Acetonitrile **3**, Methanol **4**, Ethanol **5**, Dichloroethane **6**, Dichloromethane **7**, Aniline **8**, Dietheleter **9**, and Heptane **10**)] using PCM model method at HF/6-31+G and then the dielectric effects of surrounding were analyzed.

COMPUTATIONAL METHODS

Geometries

All calculations were done with the Gaussian 03 [9], ab initio packages at the Hartree-Fock (HF) level of theory. Four basis sets were used, STO-3G,3-21G,6-31Gand6-31+G. First, the geometry of Glycine, Alanine and Valine were full optimized at the RHF/ STO-3G, 3-21G,6-31G and 6-31+G levels of theory in the gas phase.

Solvent Model

Polarized Continuum Model (PCM) with ten solvents including: (water **1**, DMSO **2**, acetonitrile **3**, methanol **4**, ethanol **5**, dichloroethane **6**, dichloromethane **7**, aniline **8**, diethylether **9**, and heptane **10**) were used in the calculations. First, molecular geometry obtained by HF/6-31+G level of optimization in the gas phase, then each of them separately placed in ten solvents and the results were compared with each other and gaseous phase.

RESULTS AND DISCUSSION

The geometry optimization of Glycine, Alanine and Valine molecules were chosen as starting structures for the gas phase. The Glycine, Alanine and Valine were found to be stable in the optimized gas phase at HF/STO-3G, 3-21G, 6-31G and 6-31+G level. The results are summarized in Table1.

Table1. Absolute calculated results of the conformational energies (E(kcal mol^{-1})) of Glycine, Alanine and Valine obtained by geometry optimization at basis set 6-31+G, 6-31G,3-21G and STO-3G levels

Basis set	E(kcal mol^{-1})		
	Gly	Ala	Val
STO-3G	-175041.4245	-199358.0926	-247776.014
3-21G	-176387.203	-200844.719	-249565.156
6-31G	-177391.447	-201878.558	-250846.983
6-31+G	-177398.693	-201885.618	-250854.168

In accordance with the obtained results, the minimum energies were related the basis set 6-31+G level. Therefore, here the basis set 6-31+G have been selected for the calculations.

Most chemical reactions and biological process take place in solutions. A quantum-mechanical analysis of the solvent effect on the stability of Glycine, Alanine and Valine molecules was presented in Table2. Increasing the stability energies were identified by: $\Delta E = E_{gaseous\ phase} - E_{solute}$. Table 2 has shown the reduction of the stability energies ΔE (in kcal mol^{-1}) of Gly, Ala and Val by decreasing the amounts of "ε" of the ten solvents (water **1**, DMSO **2**, acetonitrile **3**, methanol **4**, ethanol **5**, dichloroethane **6**, dichloromethane **7**, aniline **8**, diethylether **9**, and heptane **10**). The calculated values were performed by HF/6-31+G method. The results show that due to the dielectric structures of the amino acids, the stabilities have reduced by decreasing the polarisability of the solvents. The most stability have determined for water with ε = 78.39 and the lowest one is for heptane with ε=1.92.

Table 2. The solvent effect on the stability energies under the dielectric constant by HF/6-31+G method

ΔE(kcal mol^{-1})			
ε (Solvents 1-10)	**Gly**	**Ala**	**Val**
78.39 (**1**)	15.941	15.307	15.131
46.70 (**2**)	15.636	14.927	14.80
36.64 (**3**)	15.492	14.809	14.707
32.63 (**4**)	15.420	14.762	14.650
24.55 (**5**)	15.130	14.456	14.357
10.36 (**6**)	13.625	13.039	12.935
8.93 (**7**)	13.327	12.582	12.606
6.89 (**8**)	12.525	11.896	11.835
4.34 (**9**)	10.674	10.117	10.071
1.92 (**10**)	5.637	5.241	5.189

Regular alterations were observed concerning energy *versus* dielectric constant. With increasing of the dielectric constant of the solvents the stability, of Glycine, Alanine and Valine molecules were increased (Fig .1). The figure 1 has shown the graphs of the relationships between the stability energies ΔE (in kcal mol^{-1}) of Gly, Ala and Val and the amounts of "ε" of the ten solvents (**1-10**). Obviously the amounts of ΔE increased by increasing the amounts of dielectric constant (ε).

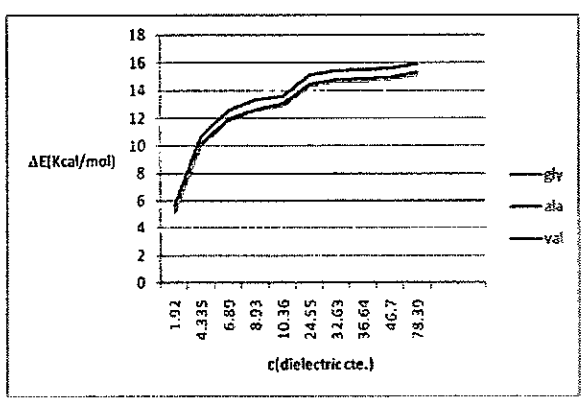

Fig. 1. The curves of the stability energies ΔE (in kcal mol^{-1}) of Gly, Ala and Val and the amounts of the dielectric constant "ε" of the ten solvents (**1-10**).

CONCLUSIONS

Two regions of dielectric constant values were identified ($1<\varepsilon<10$) and ($10<\varepsilon<80$). As it was expected, by increasing the dielectric constant of the solvents the stability energies of Glycine, Alanine and Valine were increased. By using the plot of the calculated energies and dielectric constant of Glycine, Alanine and Valine, we have reached to interesting results. We have proposed an empirical communication between effect of the solvent and length of hydrocarbon chains in the amino acids.

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