Theoretical Thermodynamic Study of Solvent Effects on Serine and Threonine Amino Acids at Different Temperatures

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ABSTRACT

The thermodynamic functions such as enthalpy (H), Gibbs free energy (G) and entropy (S) of Serine and Threonine amino acids were theoretically studied at different condition (solvents and temperatures) by using Gussian o3, software. First, the structural optimization of isolated Serine and Threonine were done in the gas phase by using the Hartree-Fock (HF) level of theory with 3-21G, 6-31G and 6-311G basis sets. Moreover, vibrational frequencies were calculated in gas phase on the optimized geometries at the same level of theory to obtain enthalpy (H) Gibbs free energy (G) and entropy (S) at 7 different temperatures such as (25, 27, 29, 31, 33, 35 and 37°C).Then, the solvent effects are taken into via the self-consistent reaction field (SCRF=PCM) model. Therefore, all of the calculations were repeated in various solvents (Water, Methanol and Ethanol) and 7 different temperatures (25, 27, 29, 31, 33, 35 and 37°C). Thermodynamically analysis shows the relative enthalpy changes (ΔH) Gibbs free energy changes (ΔG) are negative values but the entropy changes (ΔS) are positive values for Serine and Threonine molecules. Also, the results shows, with increasing dielectric constant of solvent and increasing of temperature the stability of considered molecules increases.

Keywords: Amino acids; Serine; Threonine; HF-calculations; Thermodynamic functions

INTRODUCTION

Amino acids have central role in biochemistry such as, in nutration, food technology and industry. In dustry applications include, the production of biodegradable plastics, medicines and chiral catalysis. Amino acids can be linked together in varying sequences toform a vast variety of proteins. Aliphatic hydroxyl groups of amino acids are one of the impotant type of them containing, Serine and Threonine. The hydroxyl groups in these two amino acids are subject to an important type of posttranslational modification: phosphorylation. Serine is classified as an nonessential amino acid for mammals. Serine can synthesize it from glucose and do not require dietary sources. Serine and some of its derivaties are also important components of a class of lipids (phospholipids) found in biological membrancs. Threonine is classified as an essential amino acid since it can not be synthesized by the human body from other compounds through chemical reactions and thus has tobe taken in with the diet. Threonine, like Serine has a short group

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ended with a hydroxyl group. The hydroxyl group attached makes it a polar amino acid.

Its hydrogen is easy to remove, so Threonine and Serine often act as hydrogen donors in enzyms.

However, while Serine has a repulation as being involved in catalytic functions in enzymes such as in trypsin and chymotrypsin. Both Threonine and Serine are very hydrophilic, therefore the outer regions of soluble proteins tend to be rich with them. Threonine also reflects an element of human responsibility. Kinases is the enzyme that phosphorylate proteins, Serine and Threonine kinases are the two most common [1a-d].

Theoretical study on the solvation thermodynamics properties of amino acids become very important in developing a molecular view of how different residues interact with each other and with solvent. Since, amino acids are building blocks of protein and are using in human body. That is way, the temperature ranges from 25 to 37°C selected based on the temperature of the human body [2-3]. In this study, the structural optimization of the two amino acids Serine and Threonine were investigated. The optimization results of the isolated Serine and Threonine molecules in the gas phase, at the Hartree-Fock level with 3-21G, 6-31G and 6-311G basis sets have also been carried out. The calculation about solvent effects (Water, Methanol and Ethanol) at 7 different temperatures (25, 27, 29, 31, 33, 35 and 37°C) on the thermodynamic functions such as enthalpy, H, Gibbs free energy, G, and enthropy, S, with using PCM model and vibrational frequencies method at HF/6-311G level of Serine and Threonine molecules were performed and then the solvent effects and the temperature effects of surrounding were analyzed.

COMPUTATIONAL METHODS
Geometries
Guassian 03[22], suit of programs can be used in many field of science, engineering, statistics and mathematics in order to determine the structural and thermodynamics properties of molecules and complex systems at the atomic level. In other hands, all calculations were done with the Guassian 03, ab initio packages at the Hartree-Fock (HF) level of theory. The geometry of Serine and Threonine molecules were optimized at the HF/3-21G, 6-31G and 6-311G levels in gas phase. The molecular geometries were obtained by HF/6-311G level of optimizations for Serine and Threonine molecules in the gas phase. Then, vibrational frequencies were calculated at7 different temperatures 25, 27, 29, 31, 33, 35 and 37°C.

Solvent model
A Self Consistent Reaction-Field (SCRF=PCM) model with three solvents including: (Water, Methnol and Ethanol) at 7 different temperatures (25, 27, 29, 31, 33, 35 and 37°C) were used in these calculations. First, molecular geometries were obtained by HF/6-311G level of optimization in the gas phase, then each of them separately placed in three solvents at 7 different temperatures and the results were compared with each and gaseous phase.

RESULTS AND DISCUSSION
At the first, the geometries optimization of Serine and Threonine molecules were selected in the gase phase. These molecules were found to be stable in the optimized gas phase at HF/3-21G, 6-31G and 6-311G level. The optimized HF/6-311G structures for Serine and Threonine molecules are displayed in Fig.1. Also the

calculation results relative energy (kcal mol^{-1}) in gas phase are shown in Table1.

(a)

(b)
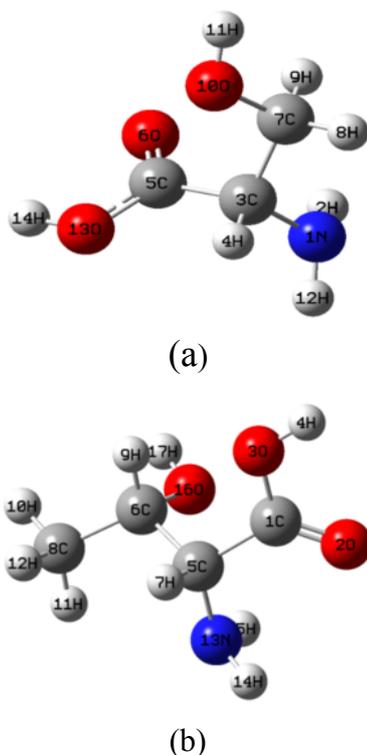
Fig. 1. Optimized geometries of the Serine (a) and Threonine (b) obtained at the HF/6-311G level.

In accordance with the obtained results, the minimum energy were related to basis set 6-311G level. Therefore, here the basis set of 6-311G were selected for other calculations. Vibrational frequencies calculations were applied in the gas phase for the determining thermodynamics functions of Serine and Threonine molecules at7 different temperatures. The results are presented in Table 2.

A Self Consistent Reaction-Field (SCRF=PCM) model were used for obtain an estimation of the solvent effects on the optimized geometreies gasous phase in various solvents such as (Water, Methanol and Ethanol) at 7 different temperatures (25, 27, 29, 31, 33, 35 and 37°C). Then, calculations about vibrational frequencies for determining themodynamic parameters

such as enthalpy, H, Gibbs free energy, G, and entropy, S, were applied of considered solvents and temperatures. The enthalpy changes at the same temperatures are identified by: $\Delta H = H_{solut} - H_{gas\ phase}$ Gibbs free energy changes at the same temperatures are identified by: $\Delta G = G_{solut} - G_{gas\ phase}$ and entropy changes at the same temperatures are identified by: $\Delta S = S_{solut} - S_{gas\ phase}$. The thermodynamic parameters such as, enthalpy changes,ΔH, Gibbs free energy changes, ΔG and entropy changes, ΔS, in kcal mol^{-1} for Serine and Threonine as a function of dielectric constant,ε, of considered solvents and temperatures are shows in Table3 and Table4. The results shows the stability of these molecules reduces with decreasing polarisibility of solvents and decreasing of temperatures. The most stabilities are observed for Water with $\varepsilon = 78.39$ at high temperatures with t=37°C and the lowest stabilities are for Ethanol with $\varepsilon = 24.55$ at low temperatures t=25°C.

Regular alterations were observed concerning thermodynamic functions *versus* dielectric constant and temperature. with increasing of the temperature and dielectric constant of the solvents these molecules in gaseous phase and solution phase the thermodynamic functions (ΔG) were decreased and ($\Delta H, \Delta S$) were increased (Fig2a-c) to (Fig3a-c). The Fig.2a show the plot of the enthalpy changes ΔH (in kcal mol^{-1}) of Serine molecule versus the temperature. Obviously, the magnitude of ΔH are increases by increasing the temperature. The Fig.2b show the plot of the Gibbs free energy changes ΔG (in kcal mol^{-1}) of Serine molecule versus the temperature. The results in Fig.2b shows with increase of temperature the Gibbs free energy changes decreases. The Fig.2c show the plot of the enthropy changes ΔS (in kcal

mol^{-1}) of Serine molecule versus the temperature. The entropy changes values are positive and can be related to the structural stability in gas phase and solution phase. The results in Fig.2c shows, with increase of temperature the entropy changes increases. The Fig.3a show the plot of the enthalpy changes ΔH (in kcal mol^{-1}) of Threonine molecule versus the temperature. Obviously, the magnitude of ΔH are increases by increasing the temperature. The Fig.3b show the plot of the Gibbs free energy changes ΔG (in kcal mol^{-1}) of Threonine molecule versus the temperature. The results in Fig.3b shows with increasing of temperature the Gibbs free energy changes decreases. The Fig.3c show the plot of the entropy changes ΔS (in kcal mol^{-1}) of Threonine molecule versus the temperature. The entropy changes values are positive and can be related to the structural stability in gas phase and solution phase. The results in Fig.3c shows, with increasing of temperature the entropy changes increases.

Thermodynamic analysis
Table 2 displays the calculated relative enthalpies (H), Gibbs free energies (G) and entropies (S) in gas phase for Serine and Threonine molecules at 7 different temperatures 25, 27, 29, 31, 33, 35 and 37°C. In addition, the calculated relative enthalpy changes (ΔH), Gibbs free energy changes (ΔG) and entropy changes (ΔS) in kcal mol^{-1} for Serine and Threonine molecules as a function of dielectric constant, ε, and temperatures, T, of considered solvents and temperatures are shown in Table 3 and Table 4. Since, the plots of calculated relative enthalpy changes (ΔH), Gibbs free energy changes (ΔG) and entropy changes (ΔS) versus the 7 different temperatures are drown in Fig. 2a-c to Fig.3a-c respectively. From Table 3 to Table4 and Figs.2a-b to Figs.3a-b it can be seen that Serine and Threonine molecules have negative values of relative enthalpy changes (ΔH) and Gibbs free energy changes (ΔG) in considered solvents and temperatures. Also, our results in Table3 and Table4 and Figs.2c to Fig.3c shows entropy changes (ΔS) for Serine and Threonine molecules have positive values. These observations can be related to the structural stability of Serine and Threonine molecules in solution phase with high dielectric constant (Water, $\varepsilon=78.39$) and at high temperature (t=37°C).

Table1. Absolute calculated results of the conformational energies (E(in kcal mol^{-1})) of Serine and Threonine obtained by geometry optimization at basis set 6-311G, 6-31G and 3-21G levels

E (kcal mol^{-1})		
Basis set	Ser	Thr
3-21G	-248791.5746	-271916.3189
6-31G	-248824.8188	-273314.4968
6-311G	-248892.1351	-273385.7852

Table 2. The determining thermodynamic functions of Serine and Threonine at the 7 different temperatures by using vibrational frequencies calculations in the gas phase

T(K)	H(kcal mol^{-1})	G(kcal mol^{-1})	S(kcal mol^{-1})
		Ser	
298.15	-248810.5722	-248836.6668	0.087523
300.15	-248811.9746	-248838.4275	0.088134
302.15	-248811.9169	-248838.6045	0.088327
304.15	-248811.8586	-248838.7814	0.088519
306.15	-248811.7996	-248838.9584	0.088711
308.15	-248811.7406	-248839.1360	0.088903
310.15	-248811.6816	-248839.3142	0.089094
		Thr	
298.15	-273294.7589	-273322.5948	0.090702
300.15	-273294.6577	-273322.8927	0.094070
302.15	-273294.5849	-273323.0817	0.094313
304.15	-273294.5115	-273323.2698	0.094555
306.15	-273294.4375	-273323.4593	0.094797
308.15	-273294.3634	-273323.6488	0.095038
310.15	-273294.2887	-273323.8396	0.095279

Table 3. The solvent effect on the thermodynamic functions changes (kcal mol^{-1}) of Serine under the temperature by HF/6-311G method

T(K)	ΔH(kcal mol^{-1})	ΔG(kcal mol^{-1})	ΔS(kcal mol^{-1})
		Water	
298.15	-22.5479	-78.0162	0.1960
300.15	-22.2814	-79.7769	0.2016
302.15	-22.0456	-81.5376	0.2068
304.15	-21.7695	-83.2983	0.2122
306.15	-21.4184	-85.0590	0.2178
308.15	-21.0817	-86.8197	0.2233
310.15	-20.7734	-88.5804	0.2286
		Methanol	
298.15	-21.7751	-75.2786	0.1794
300.15	-21.4952	-77.0456	0.1851
302.15	-21.2553	-78.8063	0.1905
304.15	-20.9642	-80.5670	0.1959
306.15	-20.6461	-82.3277	0.2014
308.15	-20.3654	-84.0884	0.2067
310.15	-19.9879	-85.8491	0.2123
		Ethanol	
298.15	-21.0169	-73.8576	0.1678
300.15	-20.7485	-75.6183	0.1736
302.15	-20.5286	-77.3790	0.1787
304.15	-20.2218	-79.1397	0.1845
306.15	-19.8769	-80.9004	0.1899
308.15	-19.5539	-82.6611	0.1953
310.15	-19.2334	-84.4218	0.2008

Table 4. The solvent effect on the thermodynamic functions changes (kcal mol^{-1}) of Threonine under the temperature by HF/6-311G method

T(K)	ΔH(kcal mol^{-1})	ΔG(kcal mol^{-1})	ΔS(kcal mol^{-1})
	Water		
298.15	-21.3576	-82.8262	0.2061
300.15	-21.1453	-84.5869	0.2114
302.15	-20.9426	-86.3476	0.2165
304.15	-20.6721	-88.1083	0.2217
306.15	-20.3952	-89.8690	0.2269
308.15	-20.1158	-91.6297	0.2321
310.15	-19.8632	-93.3904	0.2371
	Methanol		
298.15	-20.7256	-74.0886	0.1790
300.15	-20.5145	-75.8556	0.1844
302.15	-20.2783	-76.9063	0.1874
304.15	-19.9895	-79.3770	0.1952
306.15	-19.7935	-81.1377	0.2004
308.15	-19.5216	-82.8984	0.2056
310.15	-19.2934	-84.6591	0.2107
	Ethanol		
298.15	-19.9643	-68.6676	0.1633
300.15	-19.7459	-70.4283	0.1688
302.15	-19.5184	-72.1890	0.1743
304.15	-19.2829	-73.9497	0.1797
306.15	-19.0425	-75.7104	0.1851
308.15	-18.7582	-78.4711	0.1928
310.15	-18.5029	-79.2318	0.1968
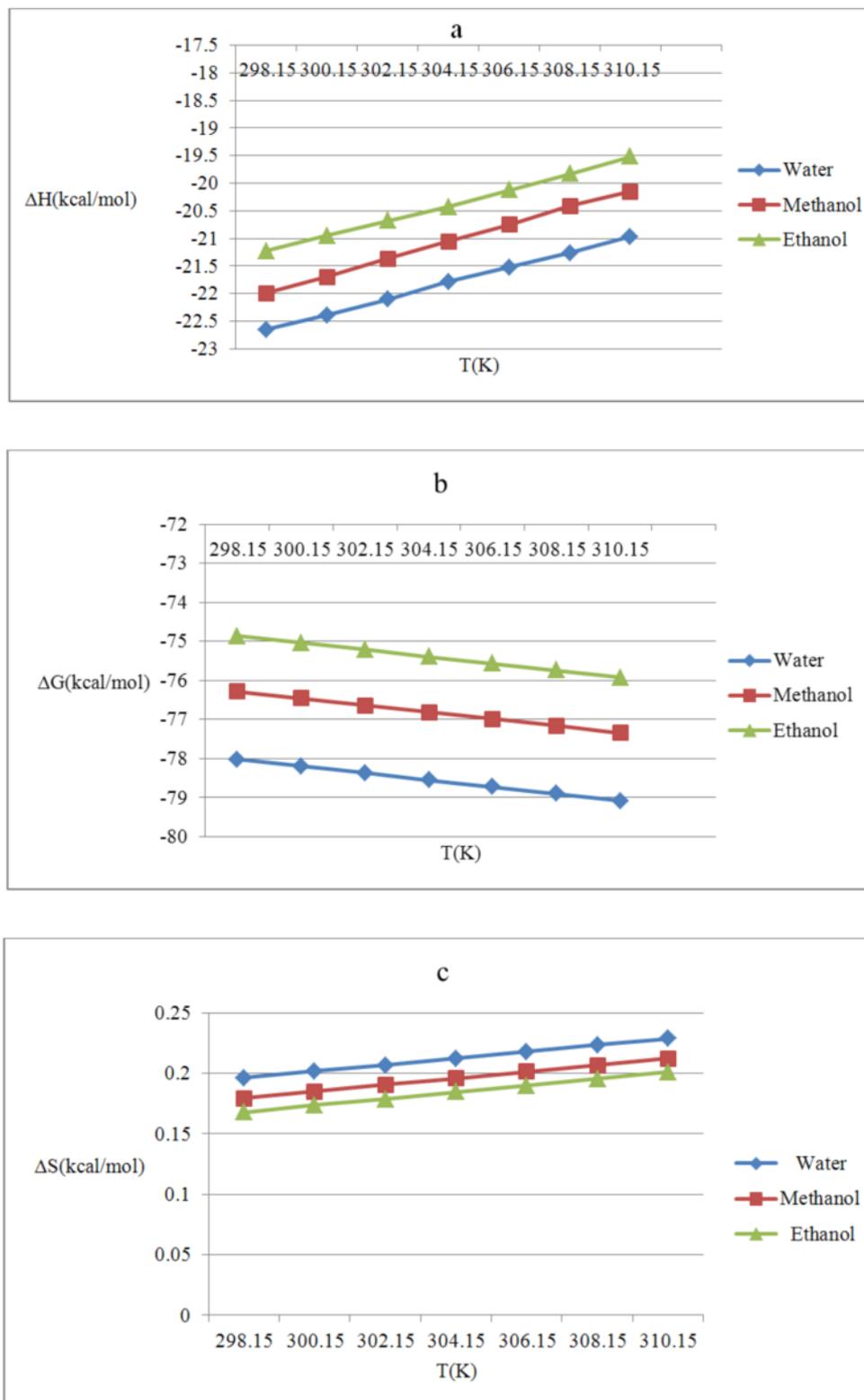
Fig. 2. Plots of the Enthalpy changes ΔH (in kcal mol^{-1}) of versus temperature, K, (a), Gibbs free energy changes ΔG (in kcal mol^{-1}) versus temperature, K, (b) and Entropy changes ΔS (in kcal mol^{-1}) versus temperature, K, (c) of Serine in various solvents.
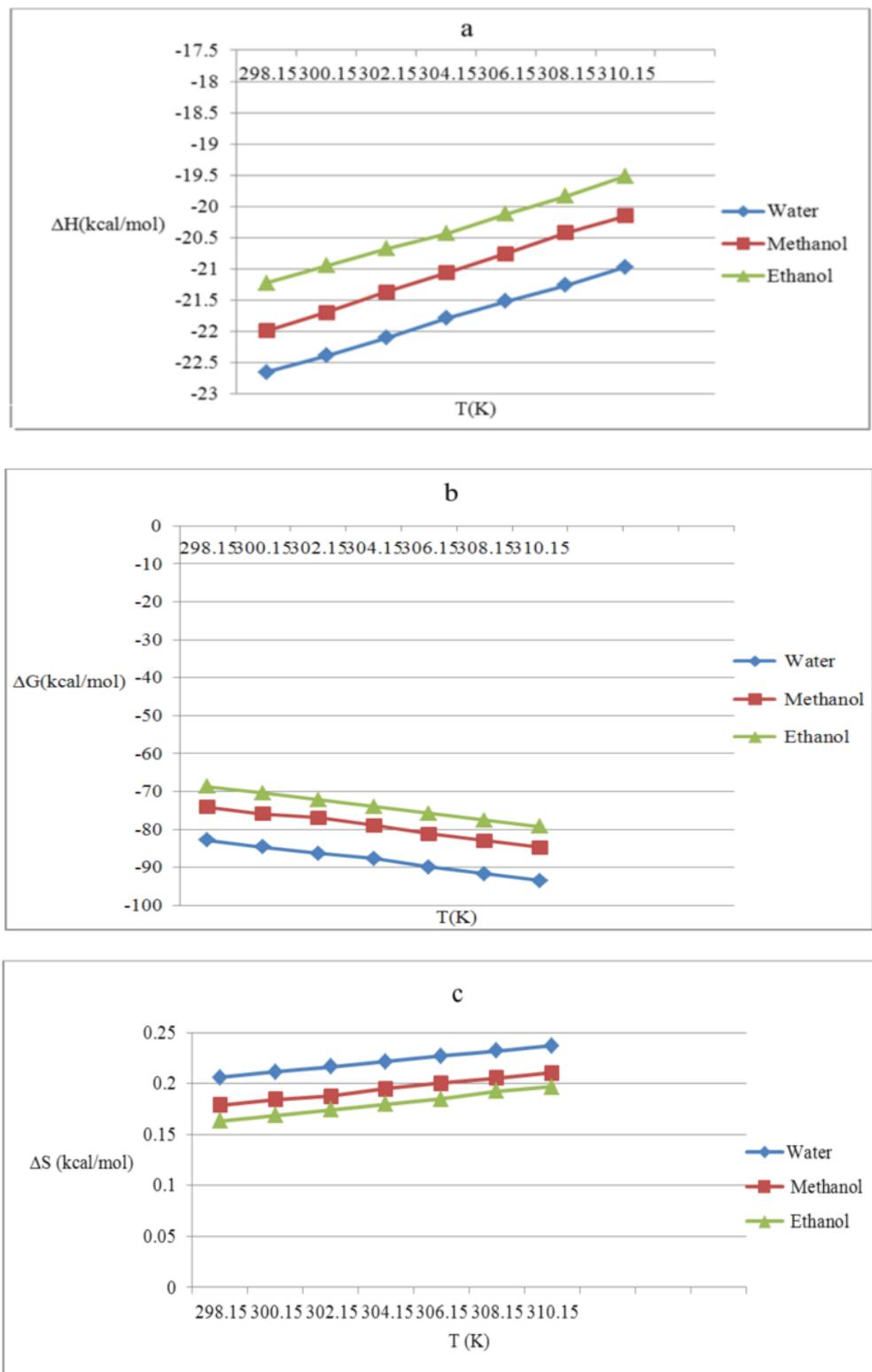
Fig. 3. Plots of the Enthalpy changes ΔH (in kcal mol⁻¹) of versus temperature, K, (a), Gibbs free energy changes ΔG (in kcal mol⁻¹) of versus temperature, K, (b), Entropy changes ΔS (in kcal mol⁻¹) of versus temperature, K, (c) of Threonine in various solvent.

CONCLUSIONS

The thermodynamic analysis shows with increasing dielectric constant from gas phase to water and temperature, the Gibbs free energy changes ΔG (kcal mol^{-1}) of Serine and Threonine decreases and the enthalpy changes ΔH (kcal mol^{-1}) and entropy changes ΔS (kcal mol^{-1}) of Serine and Threonine increases. This means that with increasing dielectric constant from gas phase to water and temperature, the stability of Serine and Threonine increases.

With this information, we can discuss the effect of variable solvent and temperature on Serine and Threonine and whenever special reaction must be done.

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