Investigation of Stability of Caffeine Dimer in Water Clusters: A quantum mechanical study

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Abstract

The most stable conformation of caffeine dimer in gas phase has flat-dimer structure while the most probable (abundance) conformation is anti-parallel. A electronic structure calculation was preformed to investigate the most stable dimer conformation in water medium. It was found that when the number of water molecules increases the anti-parallel structure shows a greater stability and the process was found to be enthalpically driven.

1. Introduction

Caffeine (molecular formula: $C_8H_{10}N_4O_2$) is a sapid molecule that found in coffee, tea, soft drinks, chocolate and some medications. Caffeine is chemically known as 1,3,7-trimethyl-2,6-dioxopurine. It has been found that caffeine aggregates when concentration is greater than 0.1 M in aqueous medium [1].

From previous studies of caffeine dimers in gas phase, it was identified that a flat-dimer structure as the most stable conformation with lowest potential energy while the anti-parallel dimer structure as the most probable conformation with the highest abundance compare to the other observed optimized structures [2].

The objective of this research is to investigate the stable conformation of caffeine dimer in aqueous medium, considering energetically more stable structure (flat dimer structure) and the most probable structure (anti-parallel dimer structure) observed from the gas phase study.

2. Computational Procedures

To find the most stable conformation of caffeine dimer in the aqueous medium, the flat dimer structure and the anti-parallel dimer structure obtained from the gas phase were reoptimized in the aqueous phase, using HF/6-31G basis set. Hydrogen bonding interaction between caffeine dimer and water was modelled by adding water molecules, one by one, to the optimized dimer structures. Gibbs free energy change, enthalpy change and entropy change of caffeine-dimer-water cluster formation were calculated using aqueous phase energies, free energies and enthalpies of the respective species.

A conformational study of the caffeine dimer was carried out by electronic structure calculations using Gaussian98W software running on an Intel(R) Pentium IV, 3.2 MHz processor with 1GB RAM under the Windows XP operating system. GaussView software was used to generate Gaussian input files and to view the output files of optimized geometries.

Keywords “OPT FREQ” were used in the Route section to do the geometry optimization and the frequency calculation. Frequency calculation was performed on each optimized configuration to verify the final geometry is corresponding to a local minima or the global minimum.

3. Results and Discussion

Interactions among water molecules and caffeine dimer have been intensely studied. It is evident that both flat and anti-parallel geometries are slightly changed in the presence of water molecules. The stability of dimers in the aqueous phase is influenced by caffeine-caffeine interactions and caffeine-water hydrogen bonding interactions. However, no hydrogen bonding is possible between two caffeine molecules as the caffeine molecule does not possess hydrogen donar groups. Identification of the structural changes and properties of the optimized geometries are used to predict the most stable structure in the aqueous phase.

Table 1 and Table 2 given below display the values of thermodynamic properties (free energy change, □G, internal energy change, □U, enthalpy change, □H and entropy change, □S, for the aggregate formation process) of the flat and anti-parallel dimer respectively. N_{water} is the number of water molecules added to each dimer configuration.

Table 1: Changes in thermodynamic parameters of aggregation for flat dimer

N_{water}	ΔG	ΔU	ΔH	ΔS
	kJ mol^{-1}			kJ mol^{-1} K^{-1}
1	-1033.89	-1115.15	-1099.96	-0.22158
2	-2074.48	-2199.05	-2174.61	-0.33586
3	-3113.11	-3279.86	-3246.22	-0.44646
4	-4144.99	-4357.71	-4314.40	-0.56819

By considering calculated Gibbs free energy values, it can be concluded that formation of aggregates is thermodynamically favourable in the presence of water molecules. Clearly, it can be seen that when increasing the number of water molecules, Gibbs free energy change of aggregation decreases linearly. Thus, caffeine dimer conformation is more stable than existing as two monomers. Calculated Gibbs free energy values of both anti-parallel and flat dimers clearly indicate that the anti-parallel structure becomes more stable with four water molecules than the flat dimer. Up to the addition of three water molecule, the flat dimer structure showed greater stability.

Table 2: Changes in thermodynamic parameters of aggregation for anti-parallel dimer

N_{water}	ΔG	ΔU	ΔH	ΔS
	kJ mol^{-1}			kJ mol^{-1} K^{-1}
1	-1011.84	-1118.03	-1101.37	-0.30027
2	-2056.76	-2216.60	-2189.19	-0.44419
3	-3108.98	-3320.78	-3283.05	-0.58384
4	-4150.52	-4408.64	-4361.15	-0.70647

New hydrogen bonds were formed in the presence of water molecules with both anti-parallel and flat dimers. Bond formation is an exothermic process, and gives a negative value for enthalpy change. Enthalpy changes were increased gradually with increasing number of water molecules as the number of hydrogen bonds between caffeine dimes and water increases. Anti-parallel dimer structure tends to form more hydrogen bonds compared to the flat dimer. Therefore, favourable enthalpy changes arise from non covalent interactions in anti-parallel dimer

The ordering of water molecules associated with hydrogen bonding causes the entropy of the system to decrease. This resulted a negative entropy change of aggregation. It was evident that the anti-parallel dimer structures accounts for more negative entropy change of aggregation than the flat dimer conformation.

Internal energy of the optimized geometries was decreased as the structures become more stable in the presence of water molecules due to the formation of higher number of attractive interactions.

By considering observed results it can be concluded that formation of dimer structures (flat or anti-parallel) is thermodynamically more stable than existing as monomers. Intermolecular forces, mainly hydrophobic effect and hydrogen bonds affect the stability of two dimer structures in the presence of water molecules.

Further, from free energy change for aggregation process, it is clear that anti-parallel conformation is more stable than flat-dimer with increasing water molecules, conforming the experimental finding. Since the entropic contribution for anti-parallel dimer is more negative than that of for flat dimer it can be suggested that the aggregate formation is enthalpically driven rather than entropically driven and the energy stabilization may come from hydrogen bonding between caffeine and water in the medium.

References

[1] Cesàro, A., Russo, E., Tessarotto, **D.,** ***J. Solution Chem***. 1980, 9(3), 221

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