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Investigation of the most probable structure for caffeine dimer: An *ab initio* study

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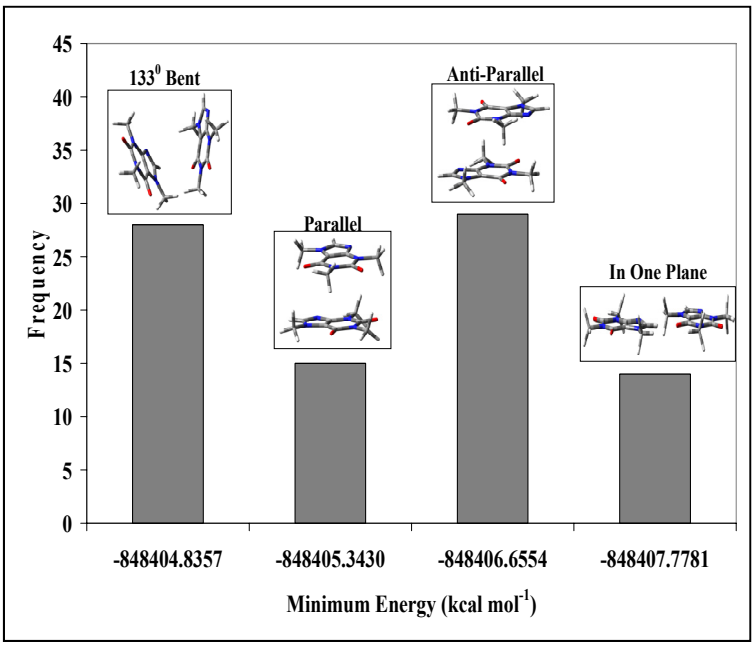
Caffeine (CAF) is a xanthine alkaloid which is considered to be the most widely consumed psychoactive substance in the world. CAF is chemically known as 1,3,7-trimethyl-2,6-dioxopurine having the formula of $C_8H_{10}N_4O_2$. An Aqueous solution of caffeine contains both monomers and molecular aggregates which reveals the fact that CAF has a tendency to stacking self-association, like many aromatic heterocyclic molecules. The reason for this phenomenon is still unknown and it may be due to hydrophobic interactions. Since the stable conformation of these dimmers and higher aggregates are still not accurately known; the objective of this study was to find the most probable conformation of CAF dimer in gaseous phase by carrying out a detailed conformational search.

The strategy was to generate a large number of possible conformations of CAF dimer in gaseous phase and then optimize these structures using Gaussian 98W software to check whether they converge to a common, stable structure. In order to implement this, a series of initial configurations of CAF dimer was generated with different centres of mass (COM) distances and different relative orientations, and those were optimized using the HF/6-31G level calculation using Gaussian 98W. After the analysis four sets of stable conformations of the CAF dimer were identified.



As illustrated in the Figure "In one plane" conformation has the lowest energy, but the "Anti-parallel" conformation is the most abundant. Since all stable conformations have energies in a narrow range of 3 kcal mol^{-1}, all these may exist in gaseous phase. Thus, after examining the structures, potential energy, abundance and COM distance between two CAF molecules, it appears that the best conformation of the CAF dimer is the "Anti-parallel" conformation.