

Conformational Analysis of 1,2-Dichloroethane in Implicit Solvent (SMD) through Solvation Thermodynamics

Diego J. Raposo, Ricardo L. Longo

Universidade Federal de Pernambuco, Departamento de Química Fundamental, Recife, PE, Brazil (email: sherlockmang@yahoo.com.br)

Abstract: Solvation Thermodynamics is a theory that properly defines the concept of solvation fromstatistical thermodynamics and provides insights into how to calculate, interpret, and obtain experimentally solvation thermodynamic quantities (Gibbs energy, entropy, enthalpy, etc.) [1]. Although it allows us to study the effects of the population of different conformers on the Gibbs solvation energy of the flexible molecule and the equilibrium constants of conversion between the conformers in different fluid phases, so far this level of information within the solvation thermodynamics domain has not been obtained by computational methods. The molecule 1,2-dichloroethane (1,2-DCE) is a prototype for studying conformational equilibrium in gas and in solution by different computational techniques and theoretical approaches [2]. It is well known that the relative abundance of the two major conformers of 1,2-DCE, gauche (g) and anti (a), characterized by the dihedral angle between chlorine atoms of the molecule, changes in different phases. In pure gas, the *anti* conformer is more abundant (79 %) compared to gauche [3], whereas in polar solutions there is a population inversion, and gauche is more likely to be found in solution (64.6 % in 1,2-DCE pure liquid, for instance [4]). To test the effectiveness of the solvation thermodynamics in predicting qualitative and quantitatively such population changes, we calculated the so called Conformational Probability Density (CPD) of 1,2-DCE in ideal gas and in water. It quantifies, among other things, the probability of a selected molecule to be within certain dihedral angle (or, more generally, certain volume in conformational space) in a given phase, and also the influence of each conformer on the resulting Gibbs solvation energy, with more abundant conformers have more influence on such energy. We have estimated the CPD function from the internal partition functions of each conformer, restricting the dihedral angle to a given value during the geometry optimizationcalculated at the MP2/ccpVTZlevel and using solvation energies from SMD implicit solvent model (B3LYP/6-31g(d)). We have found that the population of theanti conformer changes from 91% (greater than experimental value) to 52% from the ideal gas 1,2-DCE to 1,2-DCE in water, considering anti conformers those with dihedral angle between 120° and 240° [5]. The solvation energies of each conformer ranged from -4.0 to -2.5 kcal/mol, and the total solvation energy was -2.81 kcal/mol, which can be compared with the experimental value of -1.7 kcal/mol [6]. There are two possible gauche conformers, with dihedral angles $\sim 70^{\circ}$ (g+) and $360^{\circ}-70^{\circ} = 290$ degrees (g-), and we calculated the conversion energies from both gauche conformers to anti $(g+ \text{ and } g- \rightarrow a)$, which is



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related to the total population of gauche conformers, and the conversion energy of a specific gauche conformer to anti $(g+ \text{ or } g- \rightarrow a)$, both in ideal gas and in implicit solvent model of solution. Therefore, the conversion energy of $g(+ \text{ and } -) \rightarrow a$ process (the conversion of both gauche conformers is accounted) is 6.10 kcal/mol in gas and 5.44 kcal/mol in solution, and the conversion energy of $g(+ \text{ or } -) \rightarrow a \text{ process}$ (referring to the conversion of one specific gauche conformer to anti) is -1.79 kcal/mol in gas and -0.47 kcal/mol in solution. The experiments shows that $g(+ \text{ or } -) \rightarrow a$ is -1.20 kcal/mol in ideal gas [7], and -0.57 kcal/mol in aqueous solution [8], which compare reasonably well with the calculatedvalues. The relationship between the equilibrium constants of conversion amongst the conformers and the CPD of 1,2-DCE in each phase allows us to estimate equilibrium constants (and conversion energies) even in cases when conformers have the same structure, and therefore with the same Gibbs solvation energy, and to determine the relative population and the conformational equilibrium through probabilistic reasoning. We notice the SMD implicit solvent gives a preference to theanti conformer and a larger stability than experimentally verified in gas phase, which increases its population over the gauche conformer, even in aqueous solution, were it is expected be less abundant. The decrease in population from gas to polar solvent due to dipole-dipole interactions with water is, however, verified in our results. The importance of this work resides in the first application of the solvation thermodynamics formalism to conformational equilibrium by using well known computational tools, which might be fundamental to deeper understanding of some reactions in solution, such as antiperiplanar eliminations and electrocyclic reactions, from both thermodynamicsand kinetics (transition state theory) perspectives. We also verified the consistency of the mathematical formalism of such theory in the predictions of some molecular aspects that drives the solvation process, but the reliability of the computational technique or model used can lead to predictions that need improvement. Other forms of calculating the Gibbs energy of solvation (Monte Carlo simulations, analytical approximations, numerical integrations) to each conformer can lead to more satisfactory results and we are pursuing these approaches.

Key-words: Solvation Thermodynamics, conformer distributions, implicit solvent **Support:**This work has been supported by CAPES, CNPq, FACEPE, PRONEX. **References:**

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