

Theoretical thermodynamic study on the interaction between Fe²⁺ ion and Pyrazole

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ABSTRACT

The interaction of Fe²⁺ ion with Pyrazole was theoretically studied by Gaussian 03, software at HF/ (LanL2DZ+6-31G) and HF/ (LanL2DZ+6-31G (d)) levels in gas phase and solution. In this study a comparison between optimized structures of Pyrazole molecule in aspect of thermodynamic parameters such as enthalpy (H[°]), Gibbs free energy (G[°]) and entropy (S[°]) in presence of metallic ion (Fe²⁺), was performed. Thermodynamically analysis indicate that the relative enthalpy (H[°]) and Gibbs free energy (G[°]) are negative values but entropy (S[°]) is positive value for Pyrazole-Fe²⁺ complex, suggesting thermodynamic favorability for covalent attachment of Pyrazole into Fe²⁺ ion. Also, the results show with increasing dielectric constant of solvent the stability of Pyrazole-Fe²⁺ complex increases.

Keywords: Pyrazole-Fe²⁺ complex; Thermodynamic parameters; Solvent effects

INTRODUCTION

Pyrazole, a 5-membered heterocyclic diazole alkaloid composed of three carbon atoms and two nitrogen atoms in adjacent positions, is a prevalent scaffold in drug discovery programs. They have also found use as bifunctional ligands for metal catalysis, and in various building blocks for pharmaceutical and agricultural research. Derivatives of Pyrazole are used for their analgesic, anti-inflammatory, anti-pyretic, anti-arrhythmic, tranquilizing, muscle relaxing, psychoanalepic, anti-convulsant, mono amineoxidase inhibiting, anti-diabetic and anti-hypertensive drugs [1-4].

Coordination of a ligand to a metal ion, such as Fe²⁺, can make appreciable in

thermodynamic parameters, formation constant and reactivity of the ligand, which may be important to understanding of certain biological processes.

We perform a full geometrical, energetical and vibrational analysis of Pyrazole-Fe²⁺ complex with different basis set to elucidate the effect of site specific of these systems. The aim of this study was to investigate the stability of Pyrazole-Fe²⁺ at different conditions (solvent) and examine the effect of dielectric constant on stability of Pyrazole-Fe²⁺ complex.

COMPUTATIONAL METHODS **Geometries**

In this investigation, the Quantum

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chemical study was carried out by applying Gaussian 03, software package [19]. First, geometries of Pyrazole-Fe²⁺ complex were full optimized at HF/(LanL2DZ+6-31G) and HF/(LanL2DZ+6-31G(d)) levels of theory in the gas phase. The minimum energy was obtained to basis set HF/(LanL2DZ+6-31G(d)) level. Then, vibrational frequencies were calculated in gas phase on the optimized geometries at the same level of theory to obtain the enthalpy, Gibbs free energy and entropy of this molecule in standard condition (t=25 °C, P=1atm).

Solvent model

A Self Consistent Reaction-Field (SCRF=PCM) model with three solvents including: (Water, Methanol and Ethanol) were used in these calculations. First, best molecular geometries were obtained by HF/ (LanL2DZ+6-31G (d)) level of optimization in gas phase, then Pyrazole-Fe²⁺ complex separately placed in three solvents and the results were compared with each other and gaseous phase.

RESULTS AND DISCUSSION

In first step, we found the Pyrazole-Fe²⁺ complex to be stable in the optimized gas phase at HF/ (LanL2DZ+6-31G (d)) level. The results are summarized in Table1.

According to this results, the minimum energy was related to basis set HF/(LanL2DZ+6-31G(d)) level. Therefore, here the basis set of 6-31G (d) was selected for determining thermodynamic functions by using vibrational frequencies calculations. This calculations were performed in standard condition (t=25 °C, P=1atm). The results are presented in Table2.

A Self Consistent Reaction-Field (SCRF=PCM) model were used for obtain an estimation of the solvent effects on the gas phase optimized geometries. This

calculations were repeated in various solvents such as Water ($\epsilon=78.39$), Methanol ($\epsilon=32.63$) and Ethanol ($\epsilon=24.55$). The enthalpy changes are identified by: $\Delta H^\circ = H^\circ_{\text{solut}} - H^\circ_{\text{gas phase}}$; Gibbs free energy changes are identified by: $\Delta G^\circ = G^\circ_{\text{solut}} - G^\circ_{\text{gas phase}}$ and entropy changes are identified by: $\Delta S^\circ = S^\circ_{\text{solut}} - S^\circ_{\text{gas phase}}$. The thermodynamic parameters such as, enthalpy changes (ΔH°), Gibbs free energy changes (ΔG°) and entropy changes (ΔS°) in kcal mol⁻¹ for Pyrazole-Fe²⁺ complex as a function of dielectric constant, ϵ , of considered solvents are shown in Table3. The results show the stability of Pyrazole-Fe²⁺ complex reduces by decreasing polarisability of the solvents. The most stability is observed for Water with $\epsilon=78.39$ and the lowest one is for Ethanol with $\epsilon=24.55$.

Regular alternations were observed concerning thermodynamic functions *versus* dielectric constant. With increasing dielectric constant of the solvents the stability of Pyrazole-Fe²⁺ complex were increased.

Thermodynamic analysis

Table2 displays the calculated relative enthalpies (H°), Gibbs free energies (G°) and entropy (S°) in both gas phase and in solution, for Pyrazole-Fe²⁺ complex at standard condition. In addition the plots of calculated relative enthalpy changes (ΔH°), Gibbs free energy changes (ΔG°) and entropy changes (ΔS°) versus the dielectric constant, ϵ , of solvents are drawn in Figs.1a-c respectively. From Table 2 it can be seen that Pyrazole-Fe²⁺ complex has negative values of relative enthalpy (H°) and Gibbs free energy (G°) in both gas phase and in solution. Also, our result in Table2 shows entropy (S°) for Pyrazole – Fe²⁺ complex has positive values. These observations can be related to the structural

stability of the Pyrazole-Fe²⁺ complex in both gas phase and in solution. The results in Fig. 1 shows with increasing of

dielectric constant, ϵ , from gas phase to water, the stability of Pyrazole-Fe²⁺ complex increases.

Table1. Calculation results relative energy (kcal mol⁻¹) of the Pyrazole-Fe²⁺ complex obtained at the (LanL2DZ+6-31G) and (LanL2DZ+6-31G (d)) levels

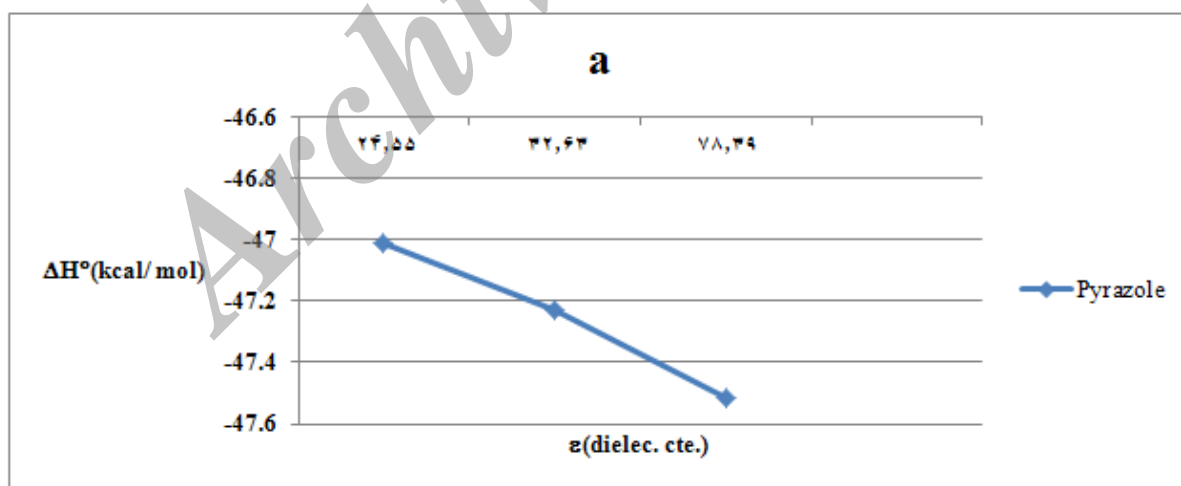
Basis set	E(kcal molK ⁻¹)
6-31G	-1524273.395
6-31G(d)	-1552801.071

Table2. Calculation results relative thermodynamic functions (kcal mol⁻¹) in gas phase and solution phase

	H°(kcal molK ⁻¹)	G°(kcal molK ⁻¹)	S°(kcal molK ⁻¹)
Gas phase	-1552744.610	-1552773.276	0.0981
Water	-1552792.129	-1552827.556	0.1208
Methanol	-1552791.841	-1552824.847	0.1127
Ethanol	-1552791.621	-1552822.315	0.1049

Table3. The solvent effect on the thermodynamic functions changes (kcal mol⁻¹) of Pyrazole-Fe²⁺ complex under the dielectric constant by (LanL2DZ+6-31G (d)) method

Solvents	ϵ	ΔH° (kcal molK ⁻¹)	ΔG° (kcal molK ⁻¹)	ΔS° (kcal molK ⁻¹)
Water	78.39	-47.519	-54.280	0.0227
Methanol	32.63	-47.231	-51.571	0.0146
Ethanol	24.55	-47.011	-49.039	0.0068



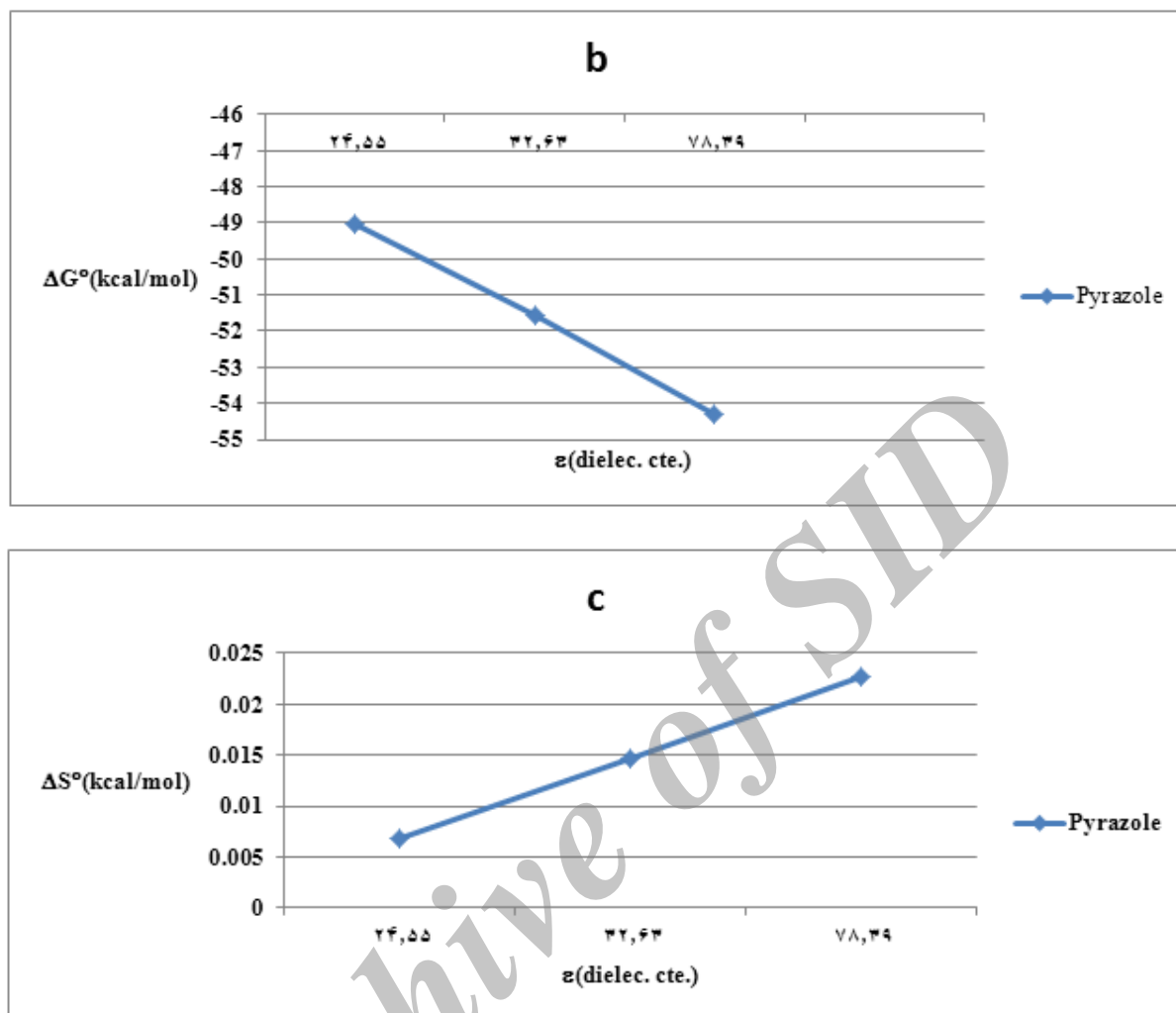


Fig.1. plots of the Enthalpy changes ΔH° (in Kcal mol⁻¹) of versus dielectric constant, ϵ , (a), Gibbs free energy changes ΔG° (in Kcal mol⁻¹) versus dielectric constant, ϵ , (b) and Entropy changes ΔS° (in Kcal mol⁻¹) versus dielectric constant, ϵ , (c) of Pyrazole-Fe²⁺ complex.

CONCLUSIONS

The thermodynamic analysis shows enthalpy (H°) and Gibbs free energy (G°) are negative values but entropy (S°) is positive value for Pyrazole-Fe²⁺ complex, suggesting thermodynamic favorability for

covalent attachment of Pyrazole into Fe²⁺ ion. Also, the results show with increasing of dielectric constant, ϵ , from gas phase to water, the stability of Pyrazole-Fe²⁺ complex increases.

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