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# Evaluation the origin of conformational and tautomeric preferences in N-acetylacetamide- a quantum chemical study

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# Abstract

Quantum chemical study of N-acetylacetamide was carried out at various theoretical levels such as HF, B3LYP and MP2 methods with the most popular basis set, 6-311++G (d, p). The computational results reveal that the amide resonance and intramolecular hydrogen bonding are two superior factors in determining the most stable conformation of diamide and amide–imidic acid tautomers, respectively. The evaluation of hydrogen bond energies predicts that the hydrogen bond strength of N-acetylacetamide is weaker than acetylacetamide. But the results of atoms in molecules, natural bond orbital, and geometrical parameters are given a different order, EHB (N-acetylacetamide) > EHB (acetylacetamide). Although the bond average energies of tautomerization process emphasized on more stability of amide–imidic acid tautomer, but our theoretical calculations reveal that the diamide conformers are more stable than the amide–imidic ones. The population analyses of equilibrium conformations by natural bond orbital method also predict that the origin of tautomeric preference is mainly because of the electron delocalization of amide functional group, especially LP(N) $\rightarrow \pi^*_{C=0}$  charge transfer.

Key words: N-acetylacetamide; Intramolecular hydrogen bond; Amide resonance; AIM and NBO





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# **1. Introduction**

Hydrogen bonding is one of the most important concepts in chemistry due to its profound influences on the chemistry of life, crystal packing, solvation, catalysis, chelation, and a host of other important phenomena [1, 2]. Resonance assisted hydrogen bond (RAHB) is a particular subject of hydrogen bond which frequently observed in various complex biological systems. Gilli and coworkers have been proposed the RAHB model as linking the strength of the hydrogen bond to the resonance in chelated systems [3-5]. The chelated enol form of  $\beta$ -dicarbonyl compounds is one of the most significant RAHB structures with O-H…O hydrogen bond which most widely studied, theoretically and experimentally [6-10]. The consequences of the  $\pi$ -electron delocalization within the chelated enol forms of  $\beta$ -dicarbonyl compounds, are as follows: (I) the shortening of O…O distance; (II) the strengthening of hydrogen bond; (III) the equalization of the corresponding single and double bonds.

The amide functional group is the fundamental unit of proteins, peptides, and other biologically important molecules and has been traditionally characterized by a restricted C-N bond rotation, coplanarity of the attached atoms, short C-N bond lengths, red-shifted carbonyl stretching frequencies, relative stability toward nucleophilic attack and protonation at oxygen rather than nitrogen [11]. By substitution an acetyl group on the nitrogen atom of amide compounds, the new class of compounds which called  $\beta$ -diacetamides, was introduced. N-acetylacetamide (NAA) as the simplest member of  $\beta$ -diacetamides compounds can participate in the amide $\leftrightarrow$ imidic acid equilibrium (Fig. 1). At this equilibrium, there are two type of tautomer, diacetamide (DA) and amide-imidic acid (AI) which interconvert to each other by tautomeric equilibriums. The appropriate arrangement of acetamide and imidic acid functional groups in AI-11 is caused that a symmetric and simple RAHB system with a heteroatom (N) is formed. The small molecules, can be used as a model for characterizing the properties of complex biological molecules and therefore potentially interest.

In the present study the characterization of the equilibrium conformations, especially global minimum, and estimation of the intramolecular hydrogen bond (IHB) and  $\pi$ -electron





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delocalization strength were carried out. Furthermore, a detailed population analysis for all the conformational equilibrium of NAA was performed by natural bond orbital (NBO) methods [12] and quantum theory of atoms in molecules (QTAIM) [13] to evaluate the origin of conformational and tautomeric preferences. NBO and QTAIM are powerful data collecting methods at microscopic level on the systems being examined [14-24].



## Figure 1: Amid↔Imidic acid tautomeric equilibriums in NAA.

## 2. Computational details

All of the computations in the present study were performed by Gaussian 03 series of programs [25]. The geometry optimizations were carried out by HF, B3LYP and MP2 methods with the most popular basis set, 6-311++G (d, p). The optimized structures at MP2/6-311++G (d, p) level of theory were used to obtained the appropriate wave function files for AIM and NBO analyses. The nature of the IHB in the most stable conformers has been studied using the AIM theory of Bader by mean of AIM2000 software [26]. According to this theory, when two neighboring atoms are chemically bonded, a critical point for bond formation appears between them. At the bond critical point (BCP),  $\nabla^2 \rho = 0$ , the charge density is minimum at r<sub>c</sub> along the bond path but maximum along any orthogonal displacement. The sign of Laplacian for electron density at a BCP,  $\nabla^2 \rho$ , reveals whether the charge is concentrated, as in covalent bond ( $\nabla^2 \rho < 0$ ), or depleted, as in closed-shell (electrostatic) interactions ( $\nabla^2 \rho > 0$ ). Additionally, for better understanding the nature of RAHB systems and tautomeric preference, the natural bond orbital (NBO) analysis was performed by using the NBO package included in Gaussian 03 [27]. NBO





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analysis is carried out to understand the orbital interactions and charge delocalization during the course of the reaction.

## 3. Results and discussion

Theoretically, NAA has about 11 different conformers, which systematically arranged in two tautomeric classes, DA and AI with 3 and 8 members, respectively. Theoretical structures and the relative optimized energies of all the possible conformers are shown in Fig. 2 and Table 1. From the relative energies at all of the computational levels, we can easily conclude the following energy order:

DA < HB-AI < non HB-AI

This order readily shows that the DA conformers are more stable than the others which followed by HB-AI and non HB-AI forms. The investigation and interpretation of energy gaps within each group and between these groups are the main goals of the present work.

various levels of	various levels of theory (kcal/mol).						
Conformer	HF	B3LYP	MP2				
DA-1	7.15	6.20	5.67				
DA-2	00.00	00.00	00.00				
DA-3	5.96	4.37	4.24				
AI-11	10.21	8.50	8.83				
AI-12	10.21	8.50	8.83				
AI-13	14.76	14.14	12.98				
AI-14	14.76	14.14	12.98				
AI-21	21.30	19.78	18.47				
AI-22	21.30	19.78	18.47				
AI-23	22.02	20.23	19.32				
AI-24	22.02	20.23	19.32				

Table 1. The relative optimized energies of NAA conformers at various levels of theory (kcal/mol)

<sup>a</sup> at 6-311++G (d, p).







Figure 2: All of the plausible theoretical conformers of NAA.

## **1-3-** Conformational preference

For NAA, three different planar DA conformers (DA1, DA2 and DA3) were proposed and represented in Fig. 2. All of these conformers at HF, MP2 and B3LYP levels with the most popular basis set, 6-311++G (d, p), were fully optimized. The harmonic vibrational frequency calculations predict that all of them have the special local minimum on the potential energy surface and are stable. The bond length of DA conformers and the selected donor-acceptor charge transfer energy of these forms at MP2/6-311++G (d, p) level of theory are collected in Table 2 and 3, respectively. It is obvious from Table 1, all of the computational levels emphasized on DA2 as the most stable form respect to the other conformers. Furthermore, the energy difference between the consecutive forms is relatively small and can be relate to the dipole-dipole interactions or repulsive interactions between the carbonyl functional groups.





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Beside the dipole-dipole interactions, the donor-acceptor charge transfer interactions are probably participate in the determining the most stable diamide form. The total values of charge transfer energies between the nitrogen lone pair and carbonyl antibonds ( $\pi^*_{C=0}$ ) of DA1, DA2 and DA3 are about the 117.06, 126.48 and 129.08 kcal/mol, respectively, which are different from the energy order (see Table 3). Finally, the geometrical parameters of DA forms, for instance C-N, also emphasized on more delocalization in DA3 which followed by DA2 and DA1 and is in line with the previous conclusion. Thus this results show which repulsive interactions in the DA-3 form is greater than other DA forms.

	) == : == (==):		
	DA1	DA2	DA3
R (C=O)	1.211	1.217	1.219
R (C-N)	1.408	1.396	1.403
R (C-N)	1.408	1.410	1.403
R (N-H)	1.011	1.014	1.017
R (C-C)	1.519	1.515	1.510
R (C-C)	1.519	1.504	1.510
R (C=O)	1.211	1.218	1.219

# Table 2. The bond length of DA conformers at MP2/6-311++G(d, p) level (Å).

Table 3. The charge transfer energy of DA forms at MP2/6-311++G (d, p) level (kcal/mol).

	DA1	DA2	DA3
LP (N) $\rightarrow \pi^*_{C=O}$	58.53	57.51	64.54
$LP(N) \rightarrow \pi^*_{C=O}$	58.53	68.97	64.54
Total	117.06	126.48	129.08





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Figure 3: The IR spectrum of DA1 conformer of the Diamide group.

Theoretically, AI group has about 8 different possible conformers which only AI-11 and AI-12 have planar structures (Fig. 2). All of these conformers were fully optimized at HF, MP2 and B3LYP levels with most popular basis set, 6-311++G (d ,p). The optimized structures of AI-12, AI-14, AI-22 and AI-24 clarify that these conformers convert to the similar conformers. Thus these forms has not the special local minimum in potential energy surface. The bond length of AI conformers and donor–acceptor charge transfer interactions are given in Table 4 and 5, respectively.

From the relative energies of enol forms at all of the computational levels, we can find the unique energy order: AI-11 < AI-13 < AI-21 < AI-23

The most stable form (AI-11) has significant energy difference with other conformers. It seems that the more stability of AI-11 with respect to other enol forms is probably due to the IHB formation and  $\pi$ -electron delocalization.





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The IR spectrum of AI-11 conformer of the Amide-imidic acid group have been drawn in Fig. 4. The IR spectrum of A1-11 shows a band at about  $3050 \text{ cm}^{-1}$  which is related to the stretching vibration of the O-H bond. The peaks at 1675 cm<sup>-1</sup> and 1650 cm<sup>-1</sup> can be ascribed to the stretching frequency of carbonyl group (C=O) and the stretching vibration of the C=N group respectively [28, 29]. The absorption bands in the area of 1350-1375 cm<sup>-1</sup> can be attributed to the stretching vibration of the C-N bond. The peak at 1275 cm<sup>-1</sup> is due to the C–O stretching vibrations.

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	AI-11	AI-13	AI-21	AI-23
R(C=O)	1.240	1.219	1.213	1.221
R(C-N)	1.397	1.413	1.422	1.407
R(C-C)	1.503	1.508	1.511	1.509
R(C=N)	1.308	1.283	1.272	1.277
R(C-O)	1.323	1.349	1.368	1.356
R(O-H)	1.001	0.969	0.963	0.963
R(C-C)	1.495	1.499	1.500	1.508
${}^{a}q_{1}$	0.089	0.130	0.150	0.130
$^{b}q_{2}$	0.083	0.130	0.155	0.135
<sup>a</sup> q1	$=R_{C-N}-R_{C=N}$			

Table 4. The bond length of AI conformers at MP2/6-311++G (d, p) level  $(\text{\AA})$ .

 $^{b}q2=R_{C-O}-R_{C=O}$ 

Table 5. The charge transfer energies of AI forms at MP2/6-311++G (d, p) level (kcal/mol).

(								
Charge transfer	AI-11	AI-12	AI-13	AI-14	AI-21	AI-22	AI-23	AI-24
$LP(O) \rightarrow \pi *_{C=N}$	81.77	81.86	54.98	54.98	48.39	48.39	51.04	51.04
$\pi_{C=N} \rightarrow \pi_{C=O}^{*}$	54.15	54.24	22.68	22.66	1.24	1.25	21.05	21.05
$\pi_{C=O} \rightarrow \pi *_{C=N}$	2.03	2.03	2.52	2.52	-	-	2.59	2.60
$\pi^*_{C=N} \longrightarrow \pi^*_{C=O}$	130.58	131.14	22.50	22.48	0.84	0.85	20.58	20.57
Total	268.53	269.27	102.68	102.64	50.47	50.49	95.26	95.26





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Figure 4: The IR spectrum of AI-11 conformer of the Amide-imidic acid group.

## 2-3- Hydrogen Bond

The intramolecular hydrogen bond plays a significant role in conformational preference and its energy is the most important characteristic of this interaction, which strongly depend on the choice of the reference state. Many authors have devised various methods to estimate the energy of intramolecular hydrogen bond [30-34]. In Schuster method, it is assumed that the energy difference between the close (with IHB) and open (without IHB) conformers to be equal with IHB energy [30]. Although, the IHB energy of OH···O systems, such as MA and NFF, can be easily calculated by the Schuster method, but this result would be handled carefully, since the estimated energy are perturbed by the conformational interactions. In the previous study we evaluate the energy of IHB of NFF by Schuster method, related rotamers method (RRM) and Grabowski method. The results of extensive studies show that in the presence of any stabilizing and destabilizing factors the RRM is not useful [31]. Thus we evaluate the energy of IHB of NAA and AA at all of the computational levels were obtained which signify the





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Schuster energy of hydrogen bond in NAA is lower than the corresponding value of AA. In other word, it can be concluded that the presence of a heteroatom (N) significantly decreased the IHB strength. The geometrical parameters can be applied for qualitative description of IHB strength. As we know, with strengthening the O-H···O hydrogen bond,  $R(O \cdots O)$  and  $R(H \cdots O)$ decrease and R(O-H) increase. For example, the values of  $R(O \cdots O)$  for chelated enol forms of NAA is about 2.495 (Table 7). The QTAIM is a powerful tool for characterization and qualitative narration of IHB strength. Poplier [35] proposed a set of criteria for the characterization of hydrogen bond within the AIM formalism. Two criteria are connected with electron density,  $\rho_{BCP}$  and its Laplacian,  $\nabla^2 \rho_{BCP}$ , at BCP of two hydrogen bonded atoms and the other are related to the integrated properties of the H atom. In order to have a deeper knowledge of the nature of the possible hydrogen bonds in NAA conformers, a topological analysis of electronic charge density,  $\rho_{BCP}$ , and its Laplacian,  $\nabla^2 \rho_{BCP}$  were performed. The topological parameters of chelated enol form of AA and NAA at the MP2/6-311++G (d, p) level were evaluated and the results were collected in Table 8. Unlike the HB energies, the electron densities and its Laplacian at BCPs signify that the IHB in NAA is stronger than the AA.

The existence of hydrogen bond implies that a certain amount of electronic charge is transferred from the proton acceptor to the proton donor and a rearrangement of electron density within each part of molecule is occurred. Electron delocalization or charge transfer effects can be identified from the presence of off diagonal elements of the Fock matrix in the NBO basis. The strength of these delocalization interactions,  $E^{(2)}$ , are well estimated by second order perturbation theory. The NBO occupation numbers for the proton donor antibonds, lone pairs and their respective orbital energies ( $\epsilon$ ) are reported in Table 8. Furthermore, some significant donor-acceptor interactions of enol form of AA and NAA and their energies at MP2/6-311++G (d, p) level of theory, are also given in Table 8.

In NBO analysis of HB systems, the charge transfer between the lone pairs of proton acceptor and proton donor antibond ( $\sigma^*$ ) is most significant. As we know, the hydrogen bond charge





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transfer greatly changes the occupation number of the molecular orbital's which involved in IHB interaction. The occupation number of proton donor antibond ( $\sigma^*_{OH}$ ) in non HB conformers is very small and near zero, while the corresponding value for proton acceptor lone pairs is near to the standard value of 2, and the corresponding values in HB enol form show greatly changed. These results can qualitatively predict the IHB strength, which is consistent with the AIM analysis conclusion. The results of NBO analysis also show that in chelated forms, one or two lone pairs of proton acceptor and the proton donor antibonds are involved and the corresponding stabilization energies of NAA and AA are about 42.17, 35.85 kcal/mol, respectively. These results again emphasized on the conclusion of geometrical parameters and AIM analyses.

Table 6. The hydrogen band energy by the Schustermethod at various level of theory (kcal/mol).

	HF	B3LYP	MP2
NAA	11.08	11.27	9.63
AA	14.07	15.86	14.78

Table 7. The selected structural parameters of HB forms of NAA and AA at MP2/6-311++G (d, p) level of theory (Å and degree).

	NAA(open)	NAA(close)	AA(open)	AA(close)
R(OO)	3.204	2.495	2.782	2.547
R(OH)	-	1.590	-	1.631
R(O—H)	0.963	1.000	0.963	0.998
O(OHO)	159.481	147.89	167.71	150.49

Table 8.	The selected results of AIM and NBO analyses at MP2/6-311++G (d, p)
level.	

	NAA(open)	NAA(close)	AA(open)	AA(close)
$\rho_{BCP}$	-	0.06311	-	0.05702
$\nabla^2 \rho_{BCP}$	-	-0.03958	-	-0.0371
$LP(O) \rightarrow \sigma^*_{OH}$	-	42.17	-	35.85





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ON <sub>(LP)</sub>	1.903	1.883	1.918	1.895
$ON_{(\sigma^*)}$	0.0047	0.0616	0.0067	0.055
$E_{(LP)}$ (kcal/mol)	-4.44×10 <sup>-22</sup>	-5.36×10 <sup>-22</sup>	-4.36×10 <sup>-22</sup>	-5.29×10 <sup>-22</sup>
$E_{(\sigma^*)}$ (kcal/mol)	6.78×10 <sup>-22</sup>	6.55×10 <sup>-22</sup>	6.81×10 <sup>-22</sup>	6.76×10 <sup>-22</sup>
ΔΕ	1.12×10 <sup>-21</sup>	1.19×10 <sup>-21</sup>	1.11×10 <sup>-21</sup>	1.20×10 <sup>-21</sup>

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# 3-3- $\pi$ -electron delocalization

The  $\pi$ -electron delocalization is very well known phenomenon that exist in simple and complex molecules and influences on the chemical reactivity, chemical reactions and other characteristic of systems [36, 37]. Although, Grabowski advised a simple method for evaluation the difference in  $\pi$ -electron delocalization energy between the open and close enol forms in  $\beta$ -dicarbonyl compounds [38], but unfortunately, there is no exact method for estimating its energy.

In RAHB systems, the equalization of corresponding bonds is a direct geometrical consequence of  $\pi$ -electron delocalization and can be regard as a resonance criterion. From the Gillis parameters,  $q_1 = R_{C-N} - R_{C=N}$  and  $q_2 = R_{C-O} - R_{C=O}$ , we can qualitatively estimate the greatness of resonance. The bond lengths,  $q_1$  and  $q_2$  for AI conformers are given in Table 4. These results reveal that the  $\pi$ -electron delocalization of AI-11 is much greater than the other AI conformers.

Additionally, the existence of  $\pi$ -electron delocalization implies that a certain amount of electric charge is transferred between the donors and acceptors and a rearrangement of electron density is occurred. These electronic charge transfers are well estimated by NBO approach at MP2/6-311++G (d, p) level of theory and collected in Table 5. These results readily show that the  $\pi$ electron delocalization in HB-AI form (AI-11), are very greater than the non HB-AI ones which support the Gilli's results.

# **4-3-** Tautomeric preference

Theoretical and experimental studies about the  $\beta$ -dicarbonyl compounds explicitly show that the HB enol form has extra stability with respect to the other forms, keto and non HB enol, and is global minimum [39]. Furthermore, the relative energies of NAA conformers (Table 1) reveal





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that in presence or absence of IHB, the DA conformers are usually more stable than AI ones. This extra stability can be related to tautomeric process and amide resonance effect.

In the simplest member of  $\beta$ -diamide compounds (NFF), the bonds average energies predict that the tautomeric process of amide functional group stabilize the molecule, about 4.78 kcal/mol, because C=O, C-N and N-H bonds are broken and C-O, C=N and O-H bonds are formed [40]. It is obvious that the presence of  $\pi$ -electron delocalization and intramolecular hydrogen bond more stabilized the chelated AI form (AI-11) and we expect that this form is recognized as global minimum. But unexpectedly, DA tautomer have extra stability with respect to the AI tautomer, even its hydrogen bonded form. Hence, we conclude that the average bond energies result cannot rationalize the extra stability of DA tautomer.

As previously mentioned, the amide functional group is characterized by some specific properties which are readily rationalized with the most popular concept of amide resonance. The most general definition of amide resonance is the ability of the nitrogen atom to delocalize its lone pair over the  $\pi$  system of carbonyl functional group. This delocalization implies that the planar amide group has to be represented by a set of resonance structures which justify the NAA treatment (see Fig. 5). The simplest feature of amide resonance is the lengthening of C=O and shortening of C-N skeletal bonds of amide functional group (see Table 2). It is obvious that these values are much different from the corresponding values in the small molecules, such as methyl amine with R<sub>C-N</sub>=1.465 Å and formaldehyde with R<sub>C=O</sub>=1.213 Å which are calculated at MP2/6-311++G (d, p) level of theory.

Although, the magnitude of resonance phenomenon in amides can be evaluated by various methods such as geometrical parameters, rotational barrier of C-N and AIM analyses, but the significant of this charge transfer can be carefully calculated by the second order perturbation theory in NBO analyses. The population analyses of equilibrium conformations by the natural bond orbitals method also predict that the origin of tautomeric preference is mainly due to the electron delocalization of amide functional group, especially LP(N) $\rightarrow \pi^*_{C=O}$  charge transfer. The electron charge transfers between the donor and acceptor orbitals of DA forms are collected





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in Table 3. It is evident that the significance of resonance in DA3 is much greater than the other DA forms that followed by DA2 and DA1.



Figure 5: Schematic representation of amide resonance.

## 4. Conclusion

Quantum chemical calculations, based on HF, B3LYP and MP2 methods, are applied to conformational study of NAA. The results of these ab-initio calculations were employed to evaluation the origin of conformational and tautomeric preferences in NAA. Additionally, the results of NBO and AIM analyses were used in order to estimation of IHB strength.

- At all of the theoretical levels, the DA forms have more stability with respect to the AI conformers. - DA-2 forms have greater stability with respect to the other forms and known as global minimum.

- Theoretical calculations at all of the computational levels show that the IHB in AA is stronger than the NAA, however AIM and NBO analyses and geometrical parameters give the opposite result,  $E_{HB}(NAA) > E_{HB}(AA)$ .

- A detail investigation of tautomeric equilibrium, hydrogen bond and resonance, explicitly show that the origin of tautomeric preference is mainly due to the electron delocalization in diamide tautomer, especially LP(N) $\rightarrow \pi^*_{C=O}$  charge transfer.

# References

[1] Jeffrey GA, An Introduction to Hydrogen Bonding, Oxford University Press: New York, 1997.





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[2] Grabowski SJ, Hydrogen Bonding – New Insights, Springer: Berlin, 2006.

[3] Gilli P, Belluchi F, Ferretti V, Bertolasi V, Evidence for resonance-assisted hydrogen bonding from crystal-structure correlations on the enol form of the .beta.-diketone fragment, J. Am. Chem. Soc., 111: 1023-1028,1989.

[4] Bertolasi V, Gilli P, Ferretti V, Gilli G, Evidence for resonance-assisted hydrogen bonding. 2. Intercorrelation between crystal structure and spectroscopic parameters in eight intramolecularly hydrogen bonded 1,3-diaryl-1,3-propanedione enols, J. Am. Chem. Soc., 113: 4917-4925 (1991).

[5] Gilli P., Bertolasi V., Ferretti V., Gilli G., Evidence for resonance-assisted hydrogen bonding. 4. Covalent nature of the strong homonuclear hydrogen bond. Study of the O-H--O system by crystal structure correlation methods, J. Am. Chem. Soc., 116: 909-915 (1994).

[6] Nowroozi A., Jalbout AF., Roohi H., E Khalilinia E., Sadeghi M., A De Leon A., Raissi H., Hydrogen Bonding in Acetylacetaldehyde: Theoretical Insights from the Theory of Atoms in Molecules, Int. J. Quan. Chem., 109: 1505-1514 (2009).

[7] Nowroozi A., Sheibaninia M., Roohi H., Sadeghi Ghoogheri MS., Raissi H., Conformational and tautomeric preferences in 3-aminoacrylaldehyde: A theoretical study, Int. J. Quan. Chem., 111: 586-595 (2011).

[8] Nowroozi A., Roohi H., Poorsargol M., Mohammadzadeh Jahani P., Hajiabadi H., Raissi H., N-H...S and S-H...N Intramolecular Hydrogen Bond in  $\beta$ -Thioaminoacrolein: A Quantum Chemical Study, Int. J. Quan. Chem., 111: 3008-3016 (2011).

[9] Nowroozi A., Raissi H., Strong intramolecular hydrogen bond in triformylmethane ab-initio, AIM and NBO study, J. Mol. Struct: THEOCHEM, 759: 93-100 (2006).

[10] Nowroozi A., Tayyari SF., Rahemi H., Fourier transforms infrared spectra and structure of triformylmethane. A density functional theoretical study, Spect. Acta., 59: 1757-1572 (2003).

[11] Kemnitz CR., Loeven JM., "Amide Resonance" Correlates with a Breadth of C-N Rotation Barriers, J. Am. Chem. Soc., 129: 2521-2528 (2007).

[12] Reed AE., Curtis LA., Weinhold FA., Intermolecular interactions from a natural bond orbital, donor-acceptor viewpoint, Chem. Rev., 88: 899-926 (1988).

[13] Bader RFW., " Atoms in Molecules. A Quantum Theory ", Clarendon; Oxford, U. K.

[14] Pandey A.K., Mishra V.N., Singh V., Biological, Electronic, NLO, NBO, TDDFT and Vibrational Analysis of 1-benzyl-4-formyl-1H-pyrrole-3-carboxamide, Iran. J. Chem. Chem. Eng., 39: 233-242 (2020).

[15] Rajaeian E., Kinetic Study of Reactions between Nitrile Oxides with Simple Cycloalkynes with DFT Method, Iran. J. Chem. Chem. Eng., 38: 99-110 (2019).

[16] Singh B., Singh R., Singh B., Kumar D., Computational Investigation of Structure and Reactivity of Methyl Hydrazinecarbodithioate, Iran. J. Chem. Chem. Eng., 37: 117-131(2018).

[17] Hussien S., Ali T.E., Abdel-Kariem S., Synthesis, DFT Calculations to investigate the Structure Electronic, Absorption Electronic Spectra, Antimicrobial Activity Application, and Non-Linear Optical





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**6−8 دی ماه ۲۰۳، دانشگاه هرمزگان** 

Analysis of Pyridinyl and Pyrimidinyl Phosphonates Schemes, Iran. J. Chem. Chem. Eng., Articles in Press.

[18] Seif N., Farhadi A., Badri R., Kiasat A.R., An Experimental and Theoretical Study on Bicyclo-3,4-Dihydropyrimidinone Derivative: Synthesis and DFT Calculation, Iran. J. Chem. Chem. Eng., 39: 21-33 (2020).

[19] Bayach I., Tan T.Y., Achari V.M., Hashim R., Quantum Chemical Investigations on C14C10-Branched-Chain Glucoside Isomers Towards Understanding Self-Assembly, Iran. J. Chem. Chem. Eng., 39: 257-269 (2020).

[20] CHAFAI N., Benbouguerra K., Chafaa S., Quantum chemical study of Hydroxychloroquine and Chloroquine drugs used as a treatment of COVID-19, Iran. J. Chem. Chem. Eng., Articles in Press.

[21] Mohammad Alipour F., Babazadeh M., Vessally E., Hosseinian A., Delir Kheirollahi Nezhad P., A Computational Study on the Some Small Graphene-Like Nanostructures as the Anodes in Na–Ion Batteries, Iran. J. Chem. Chem. Eng., 40: 691-703 (2021).

[22] Pakiari A.H., Farrokhnia M., Theoretical Study of Heteroatom Resonance-Assisted Hydrogen Bond: Effect of Substituent on  $\pi$ -delocalization, Iran. J. Chem. Chem. Eng., 29: 197-210 (2010).

[23] Khashi M., Beyramabadi S.A., Gharib A., Novel Schiff Bases of Pyrrole: Synthesis, Experimental and Theoretical Characterizations, Fluorescent Properties and Molecular Docking, Iran. J. Chem. Chem. Eng., 37: 59-72 (2018).

[24] Ali L.L., Abdel Halim S.A., Hassan Gomaa E.A., Sanad S.G., Theoretical Study of 1,4-Dioxane in Aqueous Solution and Its Experimental Interaction with Nano-CuSO4, Iran. J. Chem. Chem. Eng., 38: 43-60 (2019).

[25] Frisch MJ., Trucks GW., Schlegel HB., Scuseria GE., Robb MA., Cheeseman JR., Zakrzewski VG., Montgomery JA., Stratmann RE., Burant JC., Dapprich S., Millam JM., Daniels AD., Kudin KN., Strain MC., Farkas O., Tomasi J., Barone V., Cossi M., Cammi R., Mennucci B., Pomelli C., Adamo C., Clifford S., Ochterski J., Petersson GA., Ayala PY., Cui Q., Morokuma K., Malick DK., Rabuck AD., Raghavachari K., Foresman JB., Cioslowski J., Ortiz JV., Baboul AG., Stefanov B B., Liu G., Liashenko A., Piskorz P., Komaromi I., Gomperts R., Martin RL., Fox DJ., Keith T., Al- Laham MA., Peng CY., Nanayakkara A., Gonzalez C., Challacombe M., Gill PMW., Johnson B., Chen W., Wong MW., Andres JL., Gonzalez C., Head-Gordon M., Replogle E. S., Pople, J. A., Gaussian 03, Revision C.02, Gaussian, Inc.: Pittsburgh (2003).

[26] Biegler-Ko"nig F., Scho"nbohm J., Bayles D., AIM2000-A Program to Analyze and Visualize Atoms in Molecules, J. Comp. Chem., 22: 545-559 (2001).

[27] Glendening DE., Reed AE., Carpenter JE., Weinhold F., NBO, Version 3.1, Theoretical Chemistry Institute, University of Wisconsin: Madison, Wisconsin, USA (1998).

[28] Yan J., XiaoLiang Y., Ying Q., Poly-Amidoamine Structures Characterization: Amide Resonance Structure Imidic Acid (HO-C=N) and Tertiary Ammonium, RSC Adv., 4: 49535-49540 (2014).

[29] Mateo-Marti E., Pradier C.M., UV irradiation study of a tripeptide isolated in an argon matrix: A tautomerism process evidenced by infrared and X-ray photoemission spectroscopies, Spectrochimica Acta Part A: Molecular and





18th National and 3rd International Conference of هجدهمین همایش ملی و سومین همایش Iranian Biophysical chemistry بین المللی بیوشیمی فیزیک ایران

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**۶−۵ دی ماه ۲۰۳، دانشگاه هرمزگان** 

Biomolecular Spectroscopy, 109: 247-252 (2013).

[30] Schuster P., Zundel G., "The Hydrogen Bond. Recent Development in Theory and Experiment", North-Holland: Amesterdam (1976).

[31] Nowroozi A., Raissi H., Farzad F., The presentation of an approach for estimating the intramolecular hydrogen bond strength in conformational study of  $\beta$ -Aminoacrolein, J. Mol. Struc: THEOCHEM, 730: 161-169 (2005).

[32] Buemi G., Ab initio DFT study of the hydrogen bridges in hexafluoro-acetylacetone, trifluoro-acetylacetone and some 3-substituted derivatives, J. Mol. Struct: THEOCHEM, 499: 21-34 (2000).

[33] Rozas I., Alkorta I., Elguero J., Intramolecular Hydrogen Bonds in ortho-Substituted Hydroxybenzenes and in 8-Susbituted 1-Hydroxynaphthalenes: Can a Methyl Group Be an Acceptor of Hydrogen Bonds?, J. Phys. Chem. A, 105: 10462-10467 (2001).

[34] Jablonski M., Kaczmarek A., Sadlej AJ., Estimates of the Energy of Intramolecular Hydrogen Bonds, J. Phys. Chem. A, 110: 10890-10898 (2006).

[35] Popelier PLA., Bader RFW., The existence of an intramolecular C-H-O hydrogen bond in creatine and carbamoyl sarcosine, Chem. Phys. Let., 189: 542-548 (1992).

[36] Schleyer PVR., Introduction: Delocalization Pi and Sigma, Chem. Rev., 105: 3433-3435 (2005).

[37] Krygowski TM., Cyranski M., Structural Aspects of Aromaticity, Chem. Rev., 101: 1385-1420 (2001).

[38] Grabowski SJ.,  $\pi$ -Electron delocalisation for intramolecular resonance assisted hydrogen bonds, J. Phys. Org. Chem., 16: 797-802 (2003).

[39] Emsley J., The composition, structure and hydrogen bonding of the  $\beta$ -diketones, Struct. and Bond., 57: 147-191 (1984).

[40] Pauling L., " The Nature of the Chemical Bond and the Structure of Molecules and Crystals: An Introduction to Modern Structural Chemistry", Cornell University Press: New York (1960).