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DFT Study of Kinetic and Thermodynamic Parameters of Tautomerism in 4–acyl Pyrazolone

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ABSTRACT

In the present work, DFT calculations are employed to obtain the optimized structures of 4-acyl pyrazolone tautomers (19 tautomers) using B3LYP/6-311++G** calculations. In addition, molecular parameters, IR frequencies and relative energies are extracted for all tautomers. The existence of aromatic ring, keto tautomer (versus enol tautomer), N-H bond (versus C-H bond) and C=N double bond (versus N=N double bond) are stabilizing factors in relative stabilities of tautomers. Calculation of vibrational frequencies showed that, in accordance with reported values, intramolecular hydrogen bond (existed in some tautomers) decreased the value of OH frequency. The solvent effects on relative stabilities of tautomers are calculated. The relative stabilities of all the tautomers in acetone, tetrahydrofurane and chloroform (in all solvents, except water) were relatively the same as those in the gas phase. In addition, a nearly good relationship is found between dipole moments of tautomers and their ΔG_{solv} in chloroform. This relation shows that by increasing the dipole moment, the absolute amount of ΔG_{solv} in chloroform increases.

Keywords: Pyrazolone, DFT, Tautomer, Solvent effect.

1. INTRODUCTION

Calculations based on density functional theory (DFT) have been employed extensively to study of chemical systems and determination of compound's structures and properties. These methods are more precise than simple HF methods and less time-consuming than post-SCF methods like MP2 or CCSD without major loss in accuracy of obtained data. Therefore, DFT calculation is the best method to study of simple systems without large intermolecular interactions. Moreover, over the past centuries, the chemistry of heterocycles has been a great of interest for scientists. Among various heterocyclic compounds, pyrazolones and their derivatives [1] have been mostly studied because they belong to area of compounds which serve as products and intermediates in chemical,

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analytical, agricultural, biological and pharmaceutical chemistry [2]. Pyrazolone derivatives have been used as TNF-α inhibitor to prevent cancer and in other applications [3-5]. More importantly, pyrazolone is consisted of hydrazide moiety that possesses biological activities, such as potential inhibitors for enzymes [6].

An important derivative of pyrazolone is 4-acyl pyrazolone. Because of its β-diketone structures, 4-acyl-pyrazolone derivatives have been widely used in analytical chemistry [7]. They are widely used in biological and coordination chemistry, catalysis and metal extraction [8].

Because of these useful applications, 4-acyl-pyrazolone has been investigated in this work. One of the most interesting aspects of 4-acyl pyrazolone is its tautomeric diversity. By reviewing the literature, some reports about synthesis, structures, conformations, biological properties and complexation properties [9,10] of 4-acyl pyrazolone were observed. However, only a few reports about study of tautomerism in pyrazolones and 4-acyl pyrazolones [11,12] were reported that all of them have proposed three to five tautomers for 4-acyl pyrazolones. Therefore, to continue our interest on theoretical study of tautomerism in organic compounds [13] and because tautomerism in 4-acyl pyrazolones affects on its chemical and biological activities, especially their complexation and inhibitory properties, it is very important to learn about the complete scheme of tautomerism in 4-acyl-pyrazolone. In this line, the effects of solvent should be also be worked out clearly.

In this study, molecular parameters (Table 1 and Figure 1), relative energies (Table 2 and Figure 4) and vibrational frequencies (Table 3) of 4-acyl pyrazolone tautomers (Figure 3) were calculated using B3LYP/6-311++G** level of theory. Furthermore, the effects of solvent (Table 4 and Figures 5,6) on the relative stabilities were investigated using chloroform, tetrahydrofurane, acetone and water as solvents. The details of computations and the results obtained from this research are presented below.

2. METHODS

Density functional theory (DFT) and second ordered Møller–Plesset perturbation theory (MP2) [14] were employed to obtain the optimized structures and molecular parameters. These methods have been widely used in theoretical chemistry for studying chemical systems during past 30 years. Møller–Plesset perturbation theory (MP) is one of several quantum chemistry post-Hartree–Fock ab initio methods in the field of computational chemistry. It improves on the Hartree–Fock method by adding electron correlation effects by means of Rayleigh–Schrödinger perturbation theory (RS-PT), usually to second (MP2), third (MP3) or fourth (MP4) order. The fundamental mathematics of this theory is based on the expression of Hamiltonian operator based on one-electron fock (from HF theory) operator:

$$\hat{H}_{HF} = \sum_{i=1}^{n} f_i \tag{1}$$

This operator will be equal to:

$$\hat{H}^{(1)} = \hat{H} - \hat{H}_{HF} = \hat{H} - \sum_{i=1}^{n} f_i \tag{2}$$

In addition, the various energy data can be obtained from the below equations:

$$E_{HF} = \left\langle \phi_0 \left| \hat{H}_{HF} + \hat{H}^{(1)} \right| \phi_0 \right\rangle \tag{3}$$

$$E^{(0)} = \left\langle \phi_0 \left| \hat{H}_{HF} \right| \phi_0 \right\rangle \tag{4}$$

$$E_{HF} = E^{(0)} + E^{(1)} \tag{5}$$

Finally, the second correction of perturbation energy (MP2) is:

$$E^{(2)} = \sum_{j \neq 0} \frac{\left\langle \phi_j \left| \hat{H}^{(1)} \right| \phi_0 \right\rangle \left\langle \phi_0 \left| \hat{H}^{(1)} \right| \phi_j \right\rangle}{E_0^{(0)} - E_j^{(0)}} \tag{6}$$

Density functional theory (DFT) is precise method put on a firm theoretical footing by the two Hohenberg–Kohn theorems (H–K). The original H–K theorems held only for non-degenerate ground states in the absence of a magnetic field, although they have since been generalized to encompass these. Based on this theory (defined by Kohn), the precise energy of system can be calculated by:

$$E[\rho] = -\frac{\eta^2}{2m_e} \sum_{i=1}^{n} \int \psi_i^*(r_1) \nabla_1^2 \psi_i(r_1) dr_1 - \sum_{I=1}^{N} \int \frac{z_I e^2}{4\pi\varepsilon_0 r_{I1}} \rho(r_1) dr_1 + \frac{1}{2} \int \frac{\rho(r_1)\rho(r_2)e^2}{4\pi\varepsilon_0 r_{12}} dr_1 dr_2 + E_{XC}[\rho] \tag{7}$$

In addition, the density of charged is:

$$\rho(r) = \sum_{i=1}^{n} |\psi_i(r)|^2 \tag{8}$$

The energy of orbitals is also can be obtained using the below expression:

$$\left\{ -\frac{\eta^2}{2m_e} \nabla_1^2 - \sum_{I=1}^{N} \frac{Z_I e^2}{4\pi\varepsilon_0 r_{I1}} + \int \frac{\rho(r_2)e^2}{4\pi\varepsilon_0 r_{12}} dr_2 + V_{XC}(r_1) \right\} \psi_i(r_1) = \varepsilon_i \psi_i(r_1) \tag{9}$$

The Gaussian 03 program package [15] was employed for optimizing the structures and calculation of molecular properties. The IR frequencies and energies obtained from the frequency calculations were used after correction was done by an appropriate scaling factor. Free energies of solvation were calculated for all tautomers using SCRF keyword

with Tomasi's polarized continuum (PCM) model [16]. To perform calculations, the commands "B3LYP/6-311++G** fopt=calcall scf=verytight" were typed in the route section for optimization of structures, obtaining energies and frequencies and "B3LYP/6-311++g** scrf=(solvent=!,pcm) scf=verytight" (instead of !, the name of solvent was inserted) were typed in the route section to calculate salvation effects. It is noticeable that when we use two diffuse functions (++ after 6-311), the "scf=verytight" keyword is necessary to obtain exact data.

3. RESULTS AND DISCUSSION

In the previous reports [31-35], maximum five tautomeric forms were presented for 4-acyl pyrazolone while 19 different tautomers can be shown for this molecule (Figure 1). This number of possible tautomers for such a small molecule is exclusive therefore, this may be very interesting for chemists. In Figure 1, the general structures of the presented tautomers are shown.

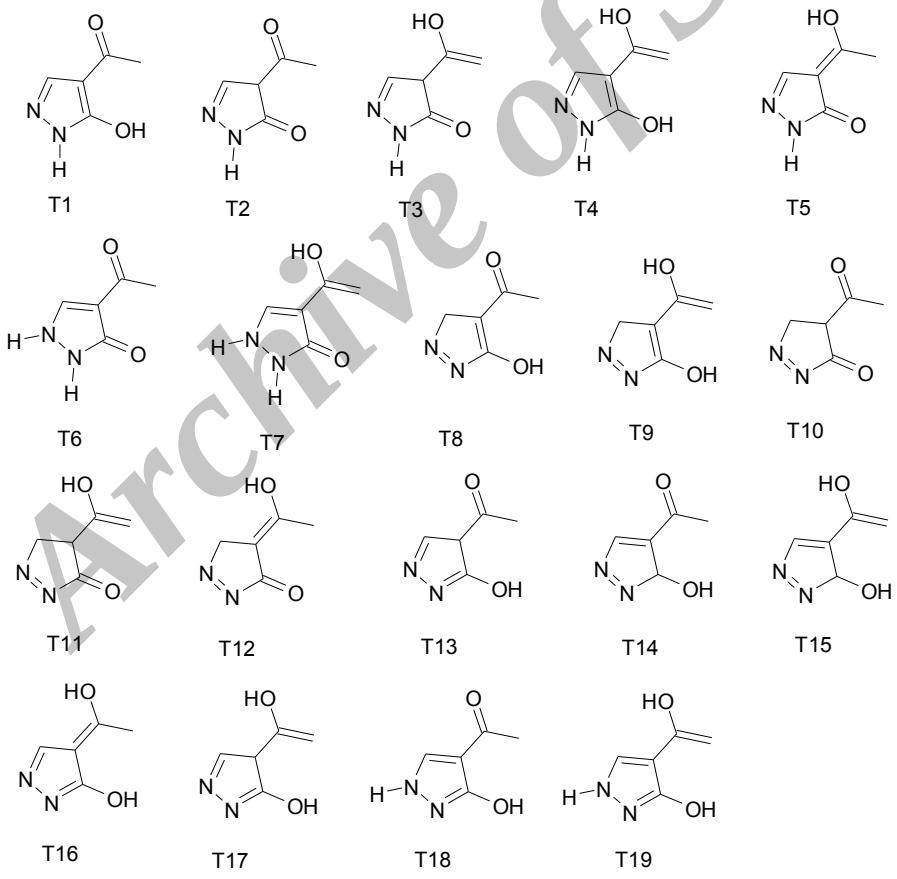

Figure 1. General structures of all tautomers of 1-(5-hydroxy-1H-pyrazol-4-yl) ethanone.

For more simplicity, geometrical and conformational tautomers were neglected in this study. All tautomers were optimized without any symmetric restriction or pre-defined conformational structures and the C1 symmetry was assumed for all the structures.

3.1. Optimized Structures and Parameters

The optimized structures, obtained from B3LYP/6-311++G** calculations, are shown in Figure 2 and the numbering scheme for all tautomers is shown in Figure 3. This numbering scheme was applied identically for all tautomers.

After optimization of all structures, molecular parameters of each structure were extracted and the results were listed in Table 1. To save space, only the most important molecular parameters were shown.

The Figure 2 optimized structures of all tautomers extracted from outputs of our calculations

The Table 1 presents nine bond lengths, four bond angles and two dihedral angles for all the tautomeric forms of 4-acyl pyrazolone. Because of the difference between bond orders in different tautomers, they may have different values. For example, N1-N2 bond was single in tautomers 1-7, 13 and 16-19 and its value was located between 1.36 Å and 1.44 Å. In other tautomers, it was double bond with the value between 1.23 Å and 1.26 Å. Like this bond, the values of other bond lengths reported in Table 1 were consistent with their natures (C-C, C-N or C-O bond) and their bond orders. Briefly, the value of average calculated bond lengths was found to be in this order: C-C>C-N,N-N>C-O>C=C>C=N,N=N>C=O. These bond lengths' orders are normal because they have inverse relationship with the order of each bond (4 larger bond lengths were single bonds). Moreover, the smaller value of NN bond length versus CC was related to the smaller value of nitrogen atomic radius.

By observation of bond angles, it will be possible to obtain some information such as hybridization of central atom, effect of ring and mobility of free lone pairs. N1-N2-C3 angle was the endocyclic bond with sp^2 hybridization in central atom (N2) for T1-T5 and T8-T17. In all the tautomers, its value was in the range of 104.4 to 114.1 degrees while it was about 120 degrees when it had sp^2 hybridization. That was because the endocyclic nature of this bond prevented from having angles larger than those in the geometric angle have. However, other prevented from having angles larger than those in the geometric angle have. However, other reported angles were exocyclic angles and their values were corresponded with the hybridization of their central atoms. From the last two columns of molecular parameters, dihedral angles, the planarity of structures can be followed, especially from N1-N2-C3-C4, which was completely placed in the ring. According to the calculated dihedral angles, in all the tautomers except T6 and T7, the main ring of molecule was totally or nearly planar, which showed an effective resonance in the π-system of tautomer's rings.

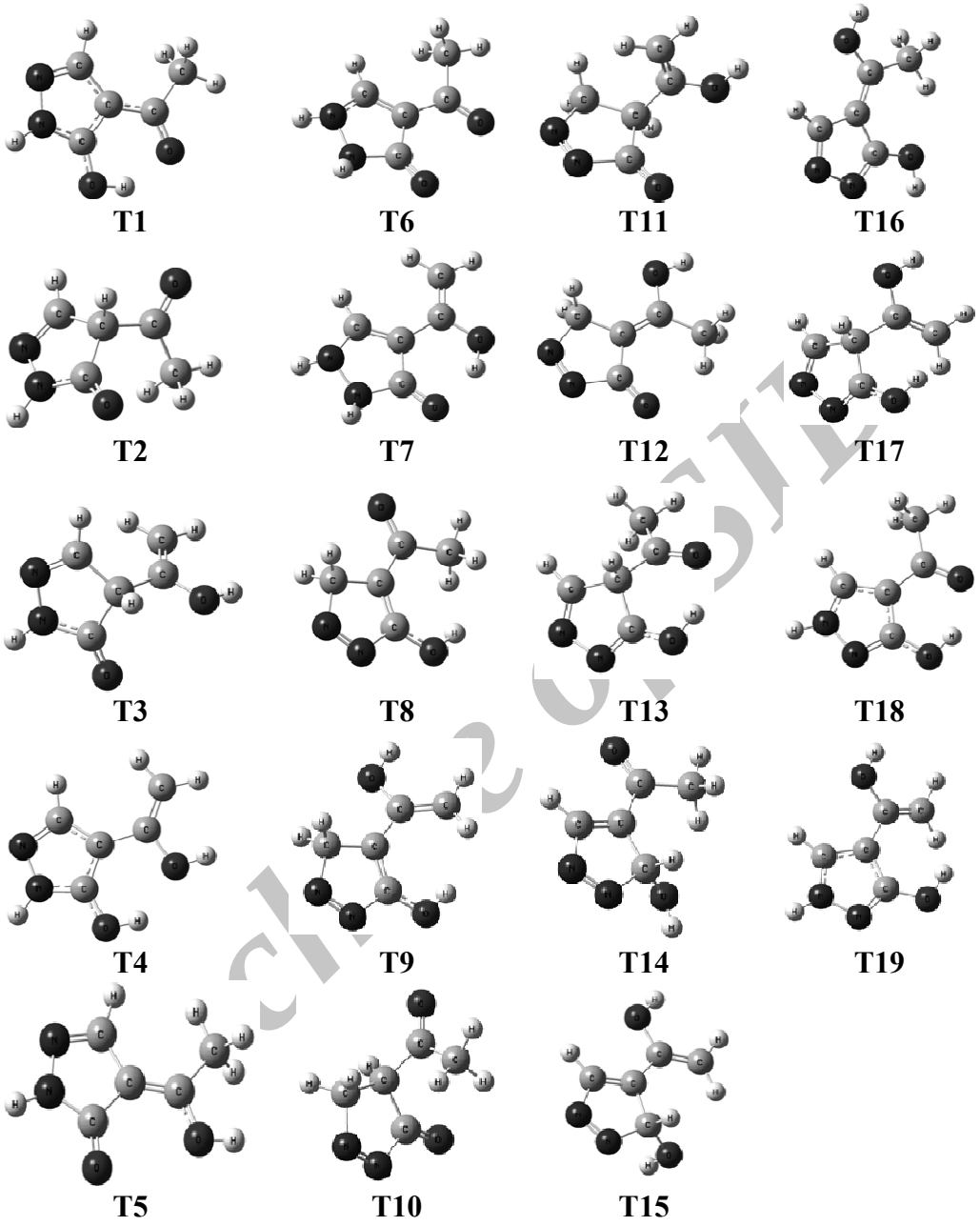

Figure 2. Optimized structures of all tautomers extracted from outputs of our calculations**.**

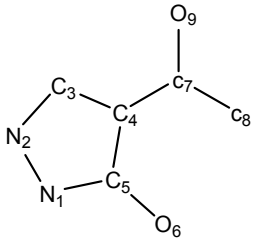

Figure 3. Numbering scheme for the main structure of 1-(5-hydroxy-1H-pyrazol-4-yl) ethanone.

3.2. Energies

As far as the goals of this research was concerned, the most interesting results of these calculations are energy results because via these data, the percent of abundance can be obtained for each tautomer and the stabilizing and destabilizing parameters can be gained in tautomeric systems. Therefore, the relative enthalpies and Gibbs free energies at 298.15 K and one atmosphere pressure were obtained for all the tautomers from the calculations and the results are given in Table 2. Moreover, in order to obtain better insight into the relative stabilities of these tautomers, the graphical representation of sorted relative Gibbs free energies are demonstrated in Figure 4.

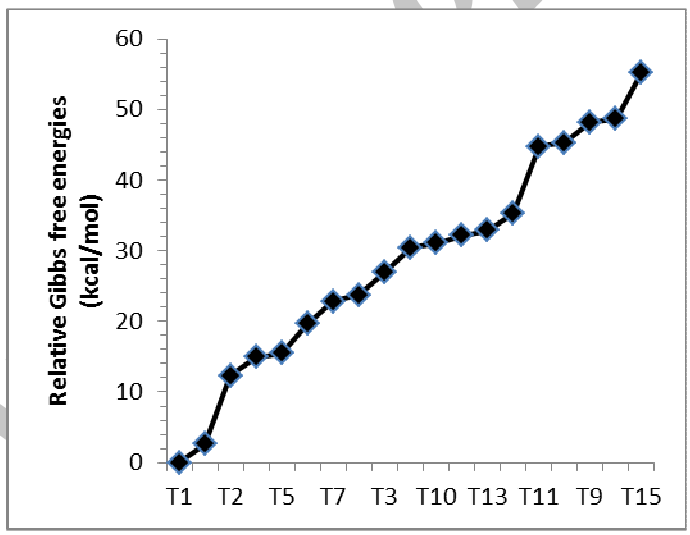

Figure 4. Sorted Relative Gibbs free energies of all tautomers at B3LYP/6-311++G** levels of theory.

The data listed in Table 2 and Figure 4 show that T1 and T15 are the most and least stable tautomers among all 4-acyl pyrazolone tautomers, respectively. Moreover, the relative stabilities of tautomers (in both enthalpies and Gibbs free energies) are T1>T18>T2>T6>T5>T4>T7>T19>T3>T16>T10>T12>T13>T8>T11>T14>T9>T17>T15. The relative Gibbs free energies and enthalpies are nearly the same. Comparing the

optimized structures and their relative energies indicated that the aromatic ring, keto tautomer (versus enol tautomer), N-H bond (versus C-H bond) and C=N double bond (versus N=N double bond) are stabilizing factors for determining the relative stabilities of tautomers. The most stable tautomers are T1 and T19, both of which have all the stabilizing factors such as aromatic ring, keto form (for external acyl group), N-H and C=N bonds. The difference between these tautomers was only 2.60 kcal/mol arising from the immigration of hydrogen from N1 (in T1) to N2 (in T18). Although, T4 and T19 have aromatic rings and their external acyl groups are found as enol tautomer, so that their stabilities' rates were between 6 and 8 among 18 tautomers. This shows the important effect of keto tautomer on the relative stability of tautomer.

Table 1. Molecular parameters of all tautomers at B3LYP/6-311++G** level of theory.*

Molecule	N1-N2	N2-C3	C3-C4	C4-C5	C5-N1	C5-O6	C4-C7	C7-C8	C7-O9	N1-C5-O6	N1-N2-C3	C3-C4-C7	O9-C7-C8	O6-C5-C4-C7	N1-N2-C3-C4
T1	1.38	1.32	1.43	1.40	1.34	1.32	1.45	1.51	1.24	123.8	104.7	135.7	121.0	0.0	0.0
T2	1.38	1.23	1.51	1.53	1.31	1.21	1.55	1.51	1.21	127.0	107.4	112.1	123.6	57.6	0.1
T3	1.38	1.28	1.50	1.55	1.38	1.21	1.51	1.33	1.36	126.9	107.5	116.7	125.0	51.6	0.4
T4	1.36	1.32	1.42	1.39	1.35	1.34	1.45	1.34	1.39	120.2	104.4	130.6	122.2	0.0	0.0
T5	1.38	1.30	1.45	1.49	1.39	1.22	1.36	1.50	1.34	126.1	106.6	128.5	116.3	0.0	0.0
T6	1.41	1.37	1.36	1.48	1.43	1.21	1.48	1.52	1.21	123.0	106.7	126.9	121.1	6.2	9.6
T7	1.41	1.38	1.36	1.46	1.40	1.23	1.47	1.34	1.36	124.6	106.0	131.0	129.6	3.4	9.4
T8	1.26	1.47	1.49	1.36	1.43	1.33	1.46	1.52	1.22	114.4	110.3	124.1	120.8	0.0	0.0
T9	1.26	1.47	1.49	1.35	1.42	1.34	1.45	1.37	1.37	116.2	110.0	127.4	123.3	0.2	1.1
T10	1.23	1.50	1.53	1.53	1.50	1.19	1.54	1.51	1.21	122.6	113.7	114.6	122.6	153.3	1.5
T11	1.23	1.50	1.52	1.55	1.50	1.19	1.51	1.34	1.37	122.6	113.7	117.2	124.6	59.8	2.3
T12	1.24	1.50	1.49	1.46	1.50	1.20	1.35	1.49	1.36	121.5	112.9	127.7	116.8	0.0	0.0
T13	1.43	1.28	1.50	1.52	1.28	1.33	1.53	1.50	1.21	124.0	110.2	122.5	123.0	47.9	2.3
T14	1.24	1.44	1.34	1.50	1.49	1.40	1.49	1.51	1.22	112.4	110.2	126.3	122.6	55.1	0.2
T15	1.25	1.44	1.34	1.51	1.49	1.40	1.45	1.34	1.37	113.0	111.0	128.3	124.0	52.0	0.7
T16	1.42	1.30	1.36	1.46	1.29	1.35	1.36	1.49	1.35	123.1	108.8	129.4	116.5	0.0	0.0
T17	1.44	1.28	1.51	1.51	1.28	1.34	1.51	1.34	1.37	122.1	109.9	116.4	124.8	55.4	1.3
T18	1.37	1.34	1.39	1.44	1.32	1.33	1.45	1.51	1.23	121.9	114.1	132.6	121.0	0.0	0.0
T19	1.36	1.35	1.39	1.43	1.32	1.35	1.46	1.34	1.37	119.5	113.5	127.9	123.0	0.1	1.0

* bond lengths are in Å and angles are in degrees

Table 2. Relative enthalpies and Gibbs free energies of all tautomers.*

Tautomer	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Relative H	0.00	13.02	26.87	19.47	15.65	15.28	22.17	35.18	47.72	31.78
Relative G	0.00	12.34	26.87	19.64	15.52	14.92	22.78	35.32	48.22	31.06
Tautomer	T11	T12	T13	T14	T15	T16	T17	T18	T19	
Relative H	45.03	32.13	32.69	45.86	55.00	30.40	48.23	2.51	23.11	
Relative G	44.74	32.17	32.90	45.29	55.25	30.46	48.61	2.60	23.72	

* All energies are reported in kcal/mol

The third tautomer (in stability) was T3 which had two carbonyl groups and N-H and C=N bonds. T5, the enol tautomer of T3 and T6, the enamine tautomer of T3, were the following tautomers (4^{th} and 5^{th}). Interestingly, in these tautomers, the double bond between C4 and C5 increased the stability of the tautomer. All the three least stable tautomers (T9, T17 and T15) were non-aromatic ring in enol form without N-H bond. As a result, it can be deduced from the relative stabilities of the applied tautomers that the N-H, C=O and C=N bonds are stronger and are preferred over C-H, C=C and N=N bonds. These preferences and the existence of aromatic rings are determining for the stability of each tautomer.

3.3. Frequencies

In Table 3, the most important calculated frequencies of optimized structures are reported after correction by appropriate scaling factor. To save space, only NH, OH, C=C, C=N, C=O and N=N frequencies were reported, which can be used for obtaining some structural information about tautomers. In this table, T10 had no NH or OH bonds so that it did not have any frequency in the NH or OH areas (3100 to 3700 cm^{-1}) and T2, T8, T11, T12, T13 and T14 had only one NH or OH bonds. In addition, OH bond frequencies were about 200 cm^{-1} higher than NH bond frequencies because of the stronger bond in OH versus NH. In accordance with our knowledge, intramolecular hydrogen bond decreases the value of OH frequency. For example, the free OH frequencies were in the range of 3600-3700 cm^{-1} while, in T1, T7 and T13, which had intramolecular hydrogen bonds, the values of OH bond frequencies were, respectively, 3549, 3486 and 3524 cm^{-1}.

The next part of Table 3 consists of frequency values for double bonds (C=C, C=N, C=O or N=N). All tautomers had three double bonds and three related frequency values. Since it was found in the previous section that the orders of bond lengths were C=C>C=N,N=N>C=O, the related frequencies followed this order with a reverse relationship. Therefore, the highest frequencies in this section are C=O frequencies (1633-1822 cm-1). In addition, conjugation between carbonyl group and π-system, especially aromatic ring, decreases its value. For example, in T1 and T18 in which the carbonyl group conjugated with the aromatic ring, the frequencies of carbonyl groups were 1633 and 1642

cm^{-1}, respectively, while its value was more than 1699 cm^{-1} in other tautomers the same observations can be found in the frequency of other conjugated double bonds.

Table 3. Important IR frequencies (in cm^{-1}) of tautomers.

	NH , OH			C=C, C=N and C=O		
T1	3549	3247		1633	1556	1533
T2	3541			1748	1732	1583
T3	3703	3541		1759	1650	1597
T4	3723	3592	3555	1654	1565	1551
T5	3704	3555		1728	1643	1536
T6	3472	3438		1757	1711	1563
T7	3486	3441	3418	1687	1643	1591
T8	3697			1669	1608	1495
T9	3702	3643		1628	1612	1483
T10				1814	1732	1576
T11	3702			1822	1649	1577
T12	3698			1757	1665	1563
T13	3524			1709	1603	1544
T14	3691			1699	1593	1474
T15	3712	3695		1631	1578	1469
T16	3702	3652		1669	1540	1496
T17	3698	3682		1649	1606	1556
T18	3555	3431	3154	1642	1577	1473
T19	3702	3667	3565	1638	1563	1483

3.4. Solvation Effect

Four different solvents (chloroform, tetrahydrofurane, acetone and water) were used to compute free energies of solvation for all the tautomers. The variations of ΔG solvations (ΔG_{solv}) in each solvent versus tautomers are shown in Figure 5. This figure shows that the order of absolute value of ΔG_{solv} in all the tautomers was found to be as follows: water>acetone>tetrahydrofurane>chloroform. In this figure, the water's curve is different from the others. It was known that water's dielectric constant is much higher than that in the other solvents (ε=78 for water, 20 for acetone, 7 for tetrahydrofurane and 5 for chloroform). Therefore, the absolute amount of ΔG_{solv} of all polar compounds in water is much higher than that in the other solvents. Moreover, since water is protic solvent and the other solvent used in this study is aprotic, the value of ΔG_{solv} of each compound in water is related to its ability to making hydrogen bonding with water. Therefore, some irregulations can be observed in the water curves versus the other curves arises from difference in existence and quantity of hydrogen bonding between each tautomers with water. For example, T15 has two OH group in its structure and it can be strongly make hydrogen bond via these groups with water. These bonds stabilize T15 more than other tautomers.

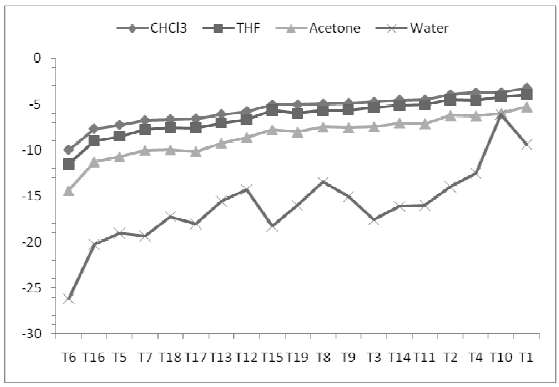

Figure 5. Sorted free e nergies of solvation of all tautomers in different solvent.

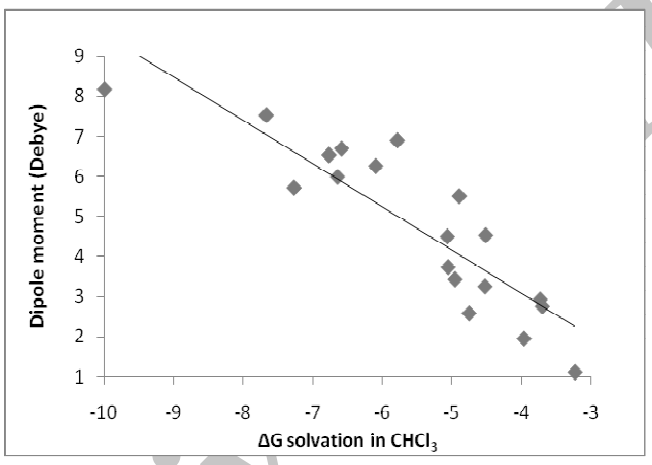

Figure 6. The relation between calculated ΔG solvations (in chloroform) and dipole moments.

In other words, by the increase of solvent's dielectric constant, the absolute amount of ΔG_{solv} of each tautomer increased. In this figure, the variations of ΔG_{solv} of tautomers in acetone, tetrahydrofurane and chloroform were in better order compared with those of the water solvent because the solvation energy of water may differ extensively when the hydrogen bonding is possible between the structures and solvent. Since it may be possible to find a relationship between dipole moments of each tautomer and its ΔG_{solv}, the authors investigated and found a partly good relationship between dipole moments of tautomers and its ΔG_{solv} in chloroform. This relation is depicted in Figure 6, which shows that, by the increase of dipole moment of each tautomer, the absolute amount of ΔG_{solv} in chloroform increases. Because chloroform is a polar solvent, the increase of dipole moment of tautomer affects its interaction with the solvent.

ΔG solvations were applied for calculating relative Gibbs free energies of tautomers in different solvents. The complete results of these calculations (ΔG_{solv} and relative Gibbs free energies in solvents) are given in Table 4.

The relative stabilities of all tautomers in acetone, tetrahydrofurane and chloroform (in all solvents, except water) were nearly the same. These relative stabilities were found to be in the following way: T18>T1>T6>T5>T2>T4>T7>T19>T3>T16>T12>T13>T10>T8>T11>T14>T17>T9>T15). The comparison of these results with the gas phase results (T1>T18>T2>T6>T5>T4>T7>T19>T3>T16>T10>T12>T13>T8>T11>T14>T9>T17>T1) demonstrates four differences. In these solvents, the relative Gibbs free energies of T18 versus T1, T5 and T6 versus T2, T12 and T13 versus T10 and T17 versus T9 had the upper position (or more stable position) because their ΔG_{solv} (T18, T5, T6, T12, T13 and T17) was very higher than that of others (T1, T2, T10 and T9). The relative energies in water do not obey the meaningful order and cannot be interpreted.

Table 4. ΔG solvation ($\mathbf{\Delta G_{solv}}$) of all tautomers and their related energies.* In each column, relative energies were calculated versus the most stable tautomer.

	ΔG solvations				Relative Gibbs free energies				
	CHCl3	THF	Acetone	Water	Gas	CHCl3	THF	Acetone	Water
T1	-3.24	-3.96	-5.25	-9.41	0.00	0.81	0.96	2.11	5.20
T2	-3.97	-4.47	-6.22	-13.96	12.34	12.42	12.79	13.48	12.99
T3	-4.76	-5.34	-7.44	-17.59	26.87	26.16	26.45	26.79	23.89
T4	-3.74	-4.54	-6.25	-12.52	19.64	19.95	20.02	20.75	21.73
T5	-7.27	-8.51	-10.71	-19.02	15.52	12.30	11.93	12.17	11.11
T6	-9.99	-11.49	-14.39	-26.16	14.92	8.98	8.35	7.89	3.37
T7	-6.77	-7.76	-10	-19.35	22.78	20.06	19.94	20.14	18.04
T8	-4.96	-5.68	-7.48	-13.46	35.32	34.41	34.56	35.20	36.47
T9	-4.9	-5.62	-7.54	-15.08	48.22	47.37	47.52	48.04	47.75
T10	-3.71	-4.17	-5.97	-6.1	31.06	31.39	31.80	32.44	39.56
T11	-4.52	-5.06	-7.11	-16.02	44.74	44.26	44.59	44.98	43.32
T12	-5.79	-6.63	-8.58	-14.27	32.17	30.43	30.46	30.95	32.51
T13	-6.1	-7.02	-9.22	-15.53	32.90	30.84	30.79	31.03	31.97
T14	-4.53	-5.1	-7.03	-16.12	45.29	44.81	45.11	45.62	43.78
T15	-5.07	-5.66	-7.77	-18.29	55.25	54.22	54.50	54.83	51.56
T16	-7.67	-8.99	-11.25	-20.26	30.46	26.84	26.39	26.57	24.81
T17	-6.59	-7.57	-10.13	-18.04	48.61	46.07	45.96	45.84	45.18
T18	-6.65	-7.52	-9.96	-17.21	2.60	0.00	0.00	0.00	0.00
T19	-5.06	-6.00	-8.00	-16.04	23.72	22.70	22.63	23.07	22.28

* All energies are reported in kcal/mol

These data showed that, although the relative energies in the solvent changed toward those in the gas phase, these changes did not have extensive effects on the order of relative energies of tautomers. In other words, the stability orders of most tautomers in various solvents were similar to those in the gas phase and only the stability orders of four tautomers in the solvent were different from the ones in the gas phase. The differences between the values of ΔG solvations of other tautomers were too small to change their stability orders.

4. CONCLUSION

Nineteen tautomers for 4-acyl pyrazolone were found, which showed its interesting tautomeric versatility. The optimized structures, molecular parameters, IR frequencies and relative energies of these tautomers were obtained using DFT calculations. Moreover, the relative stabilities were calculated in different solvents (acetone, chloroform, tetrahydrofurane and water) in order to obtain solvent effects. The relative Gibbs free energies of tautomers are T1>T18>T2>T6>T5>T4>T7>T19>T3>T16>T10>T12>T13 >T8>T11>T14>T9>T17>T15 and the relative stabilities of all the tautomers in acetone, tetrahydrofurane and chloroform (in all solvents, except water) were the same and found to be as follows: T18>T1>T6>T5>T2>T4>T7>T19>T3>T16>T12>T13>T10>T8>T11>T14> T17>T9>T15. These data show that although the relative energies in solvents changed toward those in the gas phase, these changes did not have extensive effects on the order of relative energies of tautomers. Interestingly, a relationship was found between dipole moments of tautomers and their ΔG_{solv} in chloroform for in the applied tautomeric system. These relations show that, by the increase of dipole moment of each tautomer, the absolute amount of its ΔG_{solv} in chloroform increases.

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