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**Optimization of Enaminone structures
and investigation of substituent effects on molecular stability
using HF and DFT soft computational methods**

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ABSTRACT

Enaminones are chemical compounds consisting of an amino group ($-N=$) linked through a $C=C$ to a $C=O$ group. In this research, four various enaminone structures were theoretically optimized. These enaminone structures have been studied for substituent effect on hydrogen bond, method and basic set effects on the geometrical parameters, vibrational frequencies and etc. Drawing molecular structures and computer calculations were performed with Gauss view (5.0) and Gaussian (09) softwares, respectively. The utilized methods in the paper were the HF and DFT and of DFT methods of basic functions B3LYP and B3P86. Also Basis sets of 6-311G, 6-311G*, 6-311G**, 6-311+G** and 6-311++G** have been utilized. Generally the results of computer calculations and comparing them with experimental equivalents indicate that theoretical procedures could well be helpful and effective in enaminone studies and offer

reasonable and well results. Enaminone structure was studied for tautomerism and it was revealed that Ketamine form is more stable than Enolimine form.

Keywords: Enaminone; HF; DFT; Geometry; Hydrogen bonding.

Introduction

The term Enaminone is used to indicate any chemical compound containing the conjugated system $N-C=C-C=O$ in its structure [1]. Enaminones have shown synthetic utility in therapeutic and biological agents such as ciprofloxacin, taxol, ducarmycin, quinoline, anticonvulsant, anti-malarial, anti-inflammatory, anti-fungal, anti-bacterial and anti-tumor [2-10]. In the Figure 1, basic structure of enaminones has been illustrated where from R^1 to R^5 functional groups and different substituents could be placed in that. Enaminones contain a wide range of chemical compounds because of possibility of placing different substituents on their conjugated system. The conjugated carbonyl group with enaminone generates one stable system for enaminones which cause to make easy synthesizing these compounds at atmospheric conditions and ambient temperature [11, 12].

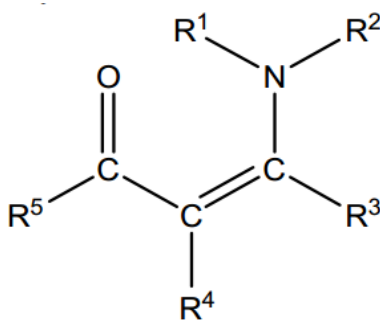


Figure 1. The general structure of Enaminones.

With regarding to Figure 1, if $R^1=H$ then condition for forming hydrogen bond among H and O atoms will be provided. This hydrogen bond which is intramolecular, lead to become stables the enaminone system and subsequently its properties. Moreover, hydrogen bond forming in enaminones lead to generate one six-member ring in the center of enaminone which provide the condition for tautomerism (Figure 2). Enolimine and Ketamine are two structures of enaminone tautomer which may be formed depending on medium condition and molecular stability (Figure 3) [13]. The substituent effect on hydrogen bond strength of enaminones is served as one of the

major issues in their stability which has been paid attention to it from both theoretical and experimental aspects in the recent years [14]. Placing substituents with various electron effects in R^2 to R^5 positions contribute on hydrogen bond strength and subsequently enaminone molecule stability that it causes to form the preferred tautomer.

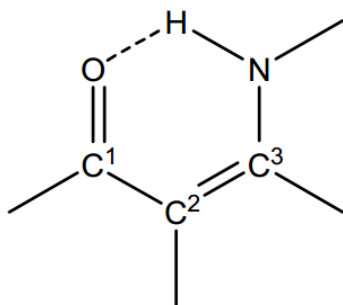


Figure 2. The central ring of Enaminones.

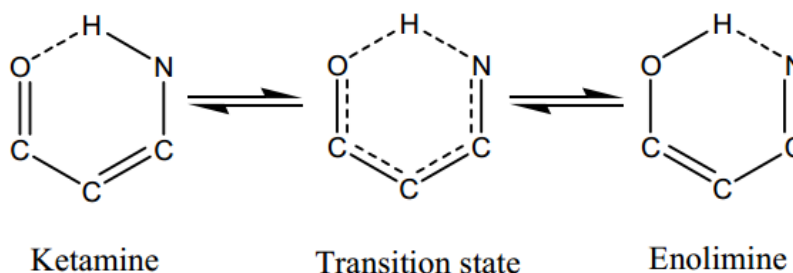


Figure 3. Enaminone tautomers.

In the paper, various structures of enaminones has been studied. This research which is as theoretical computations will be given rise to further recognize the enaminones and better investigate their properties.

Computational approach

Density functional theory (DFT) is a computational modelling method used in physics and chemistry sciences to investigate atoms, molecules, and the condensed phases [15, 16]. DFT and Hartree-Fock (HF) calculations were performed with Gaussian. With respect to different enaminone structures in this study, of the various methods in computational chemistry, two methods of HF and DFT and of DFT, two hybrid functions of B3LYP and B3P86 are employed.

In Table 1, the used basis sets (BS) and their codes have been listed. After putting substituent's in R-position, the structures were plotted through Gauss View (version 5.0) software (Figure 4). Then all structures in selected route sections were calculated and optimized through Gaussian (version 09). Finally, all information related to geometric parameters and vibrational frequencies were drawn out from output files.

Table 1. Basis sets and their codes.

Basis set (BS)	Code
6-311G	BS1
6-311G*	BS2
6-311G**	BS3
6-311+G**	BS4
6-311++G**	BS5

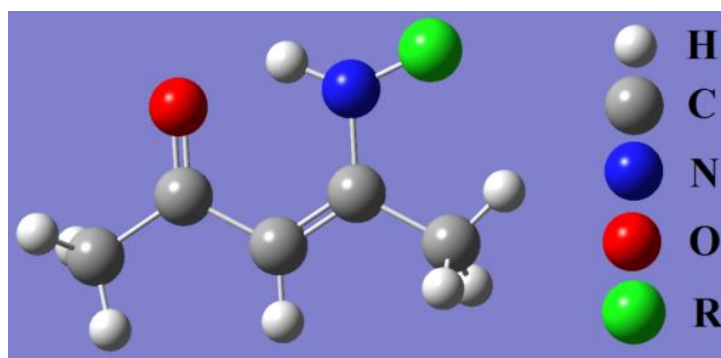
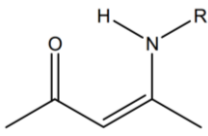


Figure 4. Enaminone structure investigated in this research.

Enaminone structures

In the paper, four structures of enaminone (EN1 to EN4) were investigated for the substituent effect on the geometric parameters such as hydrogen bonding and vibrational frequencies. In Table 2 the formulas EN1 to EN4 and those substituents which are substituted for R group, also have been showed. In each one of EN1 to EN4 structures firstly individual substituents were substituted in R position and then were optimized in all methods and related basis sets.

Table 2. Molecular structure of enaminone and its substituents.

Enaminone	R	Code
	-ph	EN1
	-p-phOCH ₃	EN2
	-p-phCH ₃	EN3
	-p-phCl	EN4

Results and discussion

Considering Table 2, four various substituents were placed in R position related to enaminone structure and then were optimized. It is necessary to note that four structures of substituents replacing in the E1 molecule were experimentally synthesized and have been studied [17]. In Tables 3 through 5 the results of bond lengths in six-member central ring (Figure 2) corresponded to enaminone structure has been reported that in every these tables, method, basis sets, substituents and measured parameters have been given. With regarding to mention results in these tables it could be said that:

- About bond length N-H, DFT methods in compared to HF method has computed more values. Also the results reported in two B3LYP and B3P86 are in relative agreement to each other.
- The computed bond length for N-C by HF and DFT methods does not substantially varied with each other and the results of B3LYP and B3P86 methods have reported the same values.
- About C=C bond length , the results of DFT methods yield higher values than HF results and conversely in the case of C-C bond length, HF results yield higher values than the results of DFT methods.
- The results calculated for C=O bond length does not substantially varies with each other.
- In all three methods of HF, B3LYP and B3P86, -ph and -p-phCl substituents reduce the length of H...O hydrogen bond and cause to increase the its strength while -p-phOCH₃ and -p-phCH₃ increase this bond length and reduce the strength of it.
- In one special method, substituent changes do not have any substantial effect on the N-H, N-C, C=C, C-C and C=O bonds length.

In order to study the method effect on the IR frequencies, in Tables 6 through 8 which everyone relates to one method, vibrational modes corresponded to C=O and N-H stretching have been showed. Reason of selecting these two stretching vibrations was due to higher strength of them in IR range than other vibrations. In respect to the results, it is found that generally those frequencies values calculated in HF method in compared to DFT are higher. Also about stretching vibration N-H, the results show that basis sets of BS2 and BS5 yielded highest values respectively for DFT and HF methods which indicate the effect of basis sets on the IR frequencies.

Table 3. Geometric results (Å) related to HF method.

EN	BS	H-N	N-C	C=C	C-C	C=O	O...H
EN1	BS1	0.99	1.35	1.36	1.43	1.24	1.92
	BS2	0.99	1.35	1.36	1.45	1.21	1.96
	BS3	0.99	1.35	1.36	1.45	1.20	1.95
	BS4	0.99	1.34	1.36	1.45	1.20	1.95
	BS5	0.99	1.35	1.36	1.45	1.20	1.95
EN2	BS1	0.99	1.36	1.36	1.43	1.24	1.92
	BS2	0.99	1.35	1.36	1.45	1.21	1.96
	BS3	0.99	1.34	1.36	1.45	1.20	1.95
	BS4	0.99	1.34	1.36	1.45	1.20	1.96
	BS5	0.99	1.35	1.36	1.45	1.21	1.96
EN3	BS1	0.99	1.36	1.37	1.44	1.24	1.93
	BS2	0.99	1.35	1.36	1.45	1.20	1.97
	BS3	0.99	1.34	1.36	1.45	1.20	1.95
	BS4	0.99	1.35	1.36	1.45	1.21	1.96
	BS5	0.99	1.34	1.36	1.45	1.21	1.96
EN4	BS1	0.99	1.36	1.36	1.44	1.24	1.92
	BS2	0.99	1.35	1.35	1.45	1.20	1.96
	BS3	0.99	1.35	1.36	1.46	1.21	1.95
	BS4	0.99	1.35	1.36	1.45	1.20	1.95
	BS5	0.99	1.35	1.36	1.45	1.21	1.95

Table 4. Geometric results (Å) related to B3LYP method.

EN	BS	H-N	N-C	C=C	C-C	C=O	O...H
EN1	BS1	1.03	1.36	1.39	1.43	1.28	1.76
	BS2	1.02	1.35	1.38	1.44	1.24	1.81
	BS3	1.02	1.35	1.38	1.44	1.24	1.81
	BS4	1.03	1.35	1.38	1.44	1.25	1.77
	BS5	1.02	1.35	1.38	1.43	1.24	1.81
EN2	BS1	1.03	1.36	1.39	1.43	1.28	1.76
	BS2	1.02	1.35	1.38	1.44	1.24	1.80
	BS3	1.02	1.35	1.38	1.44	1.24	1.81
	BS4	1.03	1.35	1.38	1.44	1.24	1.81
	BS5	1.03	1.35	1.38	1.44	1.24	1.82
EN3	BS1	1.03	1.36	1.38	1.43	1.28	1.76
	BS2	1.02	1.36	1.37	1.44	1.24	1.81
	BS3	1.02	1.35	1.38	1.44	1.24	1.81
	BS4	1.03	1.35	1.38	1.43	1.24	1.82
	BS5	1.03	1.35	1.38	1.44	1.24	1.82
EN4	BS1	1.03	1.36	1.38	1.43	1.28	1.78
	BS2	1.02	1.36	1.37	1.44	1.24	1.80
	BS3	1.02	1.36	1.38	1.44	1.24	1.79
	BS4	1.02	1.36	1.38	1.44	1.24	1.81
	BS5	1.03	1.35	1.38	1.44	1.24	1.80

Table 5. Geometric results (Å) related to B3P86 method.

EN	BS	H-N	N-C	C=C	C-C	C=O	O...H
EN1	BS1	1.03	1.36	1.39	1.42	1.27	1.70
	BS2	1.02	1.35	1.37	1.43	1.24	1.79
	BS3	1.03	1.35	1.38	1.43	1.24	1.74
	BS4	1.03	1.34	1.38	1.43	1.24	1.71
	BS5	1.03	1.34	1.38	1.43	1.24	1.73
EN2	BS1	1.03	1.35	1.38	1.42	1.28	1.71
	BS2	1.02	1.34	1.38	1.43	1.24	1.79
	BS3	1.02	1.35	1.38	1.43	1.24	1.75
	BS4	1.03	1.35	1.38	1.43	1.24	1.75
	BS5	1.03	1.34	1.37	1.43	1.24	1.75
EN3	BS1	1.03	1.35	1.38	1.43	1.28	1.74
	BS2	1.02	1.35	1.37	1.43	1.23	1.79
	BS3	1.03	1.35	1.38	1.43	1.24	1.75
	BS4	1.03	1.34	1.37	1.43	1.24	1.75
	BS5	1.03	1.35	1.38	1.43	1.24	1.75
EN4	BS1	1.03	1.36	1.38	1.42	1.27	1.73
	BS2	1.02	1.35	1.37	1.44	1.24	1.78
	BS3	1.03	1.35	1.37	1.43	1.24	1.74
	BS4	1.03	1.34	1.38	1.43	1.24	1.74
	BS5	1.03	1.34	1.37	1.43	1.24	1.74

Table 6. Vibrational frequencies (cm⁻¹) related to HF.

Bond (EN)	BS1	BS2	BS3	BS4	BS5
N-H(EN1)	3730.68	3806.92	3761.23	3758.36	3758.40
N-H(EN2)	3732.82	3805.90	3764.06	3761.60	3761.69
N-H(EN3)	3734.42	3809.71	3764.03	3761.63	3761.80
N-H(EN4)	3723.19	3802.57	3757.52	3755.36	3755.54
C=O(EN1)	1771.57	1895.62	1891.93	1874.98	1874.89
C=O(EN2)	1799.41	1895.01	1891.50	1874.46	1874.38
C=O(EN3)	1799.71	1894.89	1891.36	1874.18	1874.12
C=O(EN4)	1803.69	1898.19	1894.32	1877.46	1877.39

Table 7. Vibrational frequencies (cm^{-1}) related to B3LYP.

Bond (EN)	BS1	BS2	BS3	BS4	BS5
N-H(EN1)	3201.70	3330.06	3293.42	3244.13	3300.48
N-H(EN2)	3209.70	3318.37	3299.53	3305.71	3305.89
N-H(EN3)	3204.85	3332.09	3299.98	3307.14	3307.09
N-H(EN4)	3238.83	3319.88	3279.13	3287.92	3288.28
C=O(EN1)	1669.29	1677.83	1675.52	1643.81	1662.84
C=O(EN2)	1689.40	1663.83	1675.58	1662.84	1662.73
C=O(EN3)	1669.52	1675.97	1675.23	1662.79	1662.69
C=O(EN4)	1667.77	1679.89	1676.24	1663.49	1663.41

Table 8. Vibrational frequencies (cm^{-1}) related to B3P86.

Bond (EN)	BS1	BS2	BS3	BS4	BS5
N-H(EN1)	3129.84	3304.85	3224.74	3160.96	3191.73
N-H(EN2)	3141.71	3308.79	3234.34	3239.37	3239.68
N-H(EN3)	3211.43	3311.14	3234.67	3240.48	3240.78
N-H(EN4)	3179.14	3290.88	3206.13	3214.98	3215.39
C=O(EN1)	1605.38	1697.29	1690.35	1660.57	1670.64
C=O(EN2)	1602.98	1697.22	1690.84	1679.88	1679.78
C=O(EN3)	1613.89	1696.95	1690.42	1679.72	1679.70
C=O(EN4)	1615.05	1697.80	1690.85	1680.01	1679.95

Conclusion

In the paper, four enaminone structures have been studied using computational methods. The studied enaminone structures in the paper have been investigated for substituent effect on the hydrogen bond, method and basis sets effect on geometrical parameters and vibrational frequencies. The results of computational calculations indicate that HF and DFT methods could be helpful for enaminone structure. Generally data of calculations for enaminone structures studied in the paper indicated that results in similar sections support each other. In enaminone resulted from R group, tautomerism was studied and results indicated that Ketamine form is more stable than Enolimine form.

Acknowledgments

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