



Gaussian Calculations of 1-(Morpholine-4-yl-methyl)-3-ethyl-4-(4-hydroxybenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-one Molecule

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Abstract 1-(Morpholine-4-yl-methyl)-3-ethyl-4-(4-hydroxybenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-one was optimized by using Density Functional Theory (DFT/B3LYP) and Hatree Fock (HF) methods. Then, from this the most stable structure of the molecule, dipole moments, the HOMO-LUMO energy, total energy of the molecule, bond lengths and mulliken charges were calculated with B3LYP/631G (d,p) and HF/631G (d,p) basis sets. ¹H-NMR and ¹³C-NMR isotropic shift values were calculated by the method of GIAO using the program package Gaussian G09. Theoretical and experimental values were inserted into the graphic according to equation of $\delta_{\text{exp}} = a + b \cdot \delta_{\text{calc}}$. The standard error values were found via SigmaPlot program with regression coefficient of a and b constants. Furthermore, the veda4f program was used in defining of IR data theoretically. Theoretically calculated IR data are multiplied with appropriate adjustment factors and the data obtained according to DFT and HF method are formed using theoretical infrared spectrum.

Keywords 1,2,4-Triazol-5-one, Gaussian G09, HOMO-LUMO, DFT, HF

Introduction

Mannich bases are very significant compounds. Because, these bases widely used in the syntheses of many biologically active and natural products [1-5]. Heterocyclic Mannich bases have various useful properties, most of which were shaped in their pharmacological activities, such as antimicrobial [6-8], anticancer [9], antitumor [10] and antituberculous [11] activities. Also, few Mannich bases invented from 1,2,4-triazoles carrying Morpholine substituent have biologically active [12, 13]. The 1,2,4-triazole and its derivatives were reported to indicate diverse pharmacological activities such as antimicrobial, analgesic, anti-inflammatory, anticancer and antioxidant properties [14-17]. In the last year, theoretical properties of Mannich bases were investigated on a computer. In this study, we examined theoretical features of 1-(Morpholine-4-yl-methyl)-3-ethyl-4-(4-hydroxybenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-one molecule. All theoretical calculations for the target compound were with the Gaussian 09 quantum chemistry program [18] on a personal computer. For this, firstly, molecule were optimized by using the Density Functional Theory (DFT) and Hatree Fock (HF) methods with the restricted B3LYP [18, 19] level of theory, 6-31G(d,p) basis set, for all atoms. Optimized structure is the most stable structure of the molecule. Then from this form, dipole moments, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO), total energy of the molecule, bond lengths and mulliken charges, electronic properties; $E_{\text{LUMO}} - E_{\text{HOMO}}$ energy gap (ΔE_g), electronegativity (χ), electron affinity (A), global hardness (η), softness (σ), ionization potential (I), thermodynamics properties; (thermal energies (E), thermal capacity (CV), entropy (S) were calculated. In addition, The theoretical calculations ¹H-NMR and ¹³C-NMR were performed by using DFT and HF



with the B3LYP/6-31G(d,p) level. ^1H -NMR and ^{13}C -NMR isotropic shift values were calculated by the method of GIAO using the program package Gaussian G09 [19]. Experimental data obtained from the literature [20]. Theoretical and experimental values were inserted into the graphic according to equation of $\delta_{\text{exp}} = a + b \cdot \delta_{\text{calc}}$. The standard error values were found via SigmaPlot program with regression coefficient of a and b constants. Finally, the theoretical vibrational spectra were calculated at the B3LYP/DFT/HF 6-31G(d,p) basis set in the gas phase and these data are scaled with 0.9617 and 0,8992 factors [21]. The data obtained according to DFT and HF method are formed using theoretical infrared spectrum. The experimental and theoretical IR spectra are given in Fig. 3. The veda4f program was used in defining IR data [22].

Computational Details

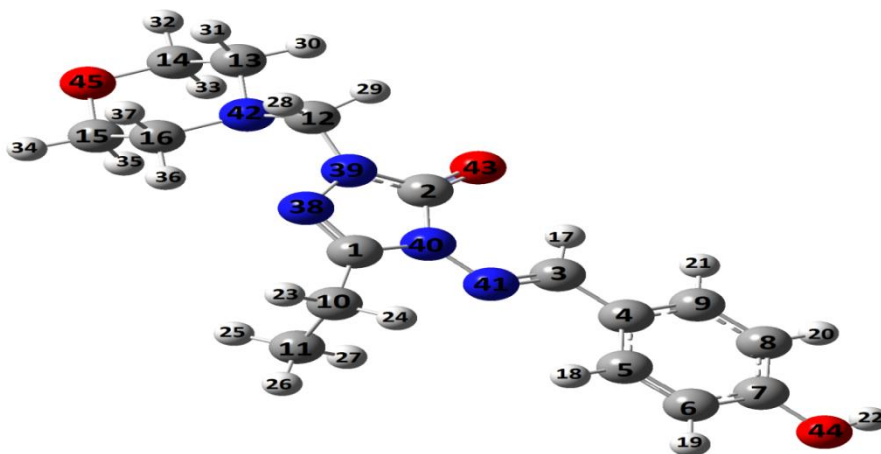


Figure 1: The Gauss view structure of the molecule

Table 1: ^{13}C and ^1H -NMR (DMSO) isotropic chemical shifts (δ /ppm)

No	Exp.	DFT/ dms0	Differ/DFT	HF/ dms0	Differ/HF	No	Exp.	DFT/ dms0	Differ/ DFT	HF/ dms0	Differ/ HF
C1	146.76	152.16	-5.40	147.18	-0.42	H20	6.90	7.67	-0.77	7.35	-0.45
C2	150.50	153.05	-2.55	146.75	3.75	H21	7.69	8.27	-0.58	8.29	-0.60
C3	155.29	154.71	0.58	149.84	5.45	H22	10.20	5.60	4.60	4.67	5.53
C4	124.24	130.54	-6.30	118.66	5.58	H23	2.70	3.31	-0.61	2.65	0.05
C5	129.72	129.41	0.31	127.21	2.51	H24	2.70	3.86	-1.16	3.09	-0.39
C6	115.83	119.19	-3.36	109.79	6.04	H25	1.24	1.89	-0.65	1.37	-0.13
C7	160.78	161.78	-1.00	154.85	5.93	H26	1.24	2.15	-0.91	1.66	-0.42
C8	115.83	117.86	-2.03	106.49	9.34	H27	1.24	2.47	-1.23	1.88	-0.64
C9	129.72	139.46	-9.74	134.00	-4.28	H28	4.54	4.66	-0.12	3.82	0.72
C10	18.46	30.86	-12.40	17.39	1.07	H29	4.54	5.21	-0.67	4.36	0.18
C11	9.79	22.36	-12.57	9.74	0.05	H30	2.59	3.43	-0.84	2.48	0.11
C12	66.12	73.97	-7.85	56.34	9.78	H31	2.59	3.34	-0.75	2.48	0.11
C13	49.89	58.86	-8.97	41.59	8.30	H32	3.57	4.59	-1.02	3.81	-0.24
C14	66.15	74.55	-8.40	55.67	10.48	H33	3.57	4.45	-0.88	3.52	0.05
C15	66.15	73.71	-7.56	55.24	10.91	H34	3.57	4.55	-0.98	3.76	-0.19
C16	49.89	58.27	-8.38	40.75	9.14	H35	3.57	4.32	-0.75	3.35	0.22
H17	9.52	11.02	-1.50	10.27	-0.75	H36	2.59	3.18	-0.59	2.32	0.27
H18	7.69	9.20	-1.51	9.10	-1.41	H37	2.59	3.76	-1.17	2.68	-0.09
H19	6.90	7.90	-1.00	7.62	-0.72						

The relation between R^2 values of the compound



B3LYP/DFT 631G(d,p) (DMSO): ^{13}C : 0.9987, ^1H : 0.8884; HF 631G(d,p) (DMSO): ^{13}C : 0.9962, ^1H : 0.8737

There is such a relationship between R^2 -values of the compound. Found standard error rate and a, b constants regression values were calculated according to formula $\exp = a + b \cdot \delta$ calc Eq. These values for compound were shown in the table 2. Theoretical and experimental carbon and proton chemical shifts ratios between according to a, b vs R^2 values, liner a correlation were observed.

Table 2: The correlation data for chemical shifts of the molecule

	^{13}C				^1H			
	R	S. hata	a	b	R	S. hata	a	b
DFT	0.9987	5.5015	1.6392	0.0145	0.8884	1.2704	0.6415	0.1158
HF	0.9962	4.4517	2.3524	0.0225	0.8737	1.3463	0.5777	0.1154

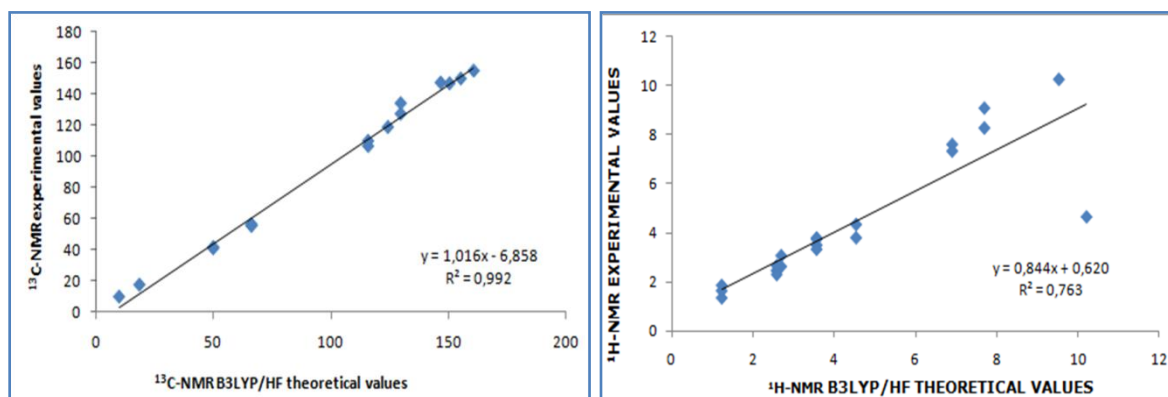


Figure 2: The correlation graphs for B3LYP/HF 631G(d,p) chemical shifts of the molecule

The vibration frequency of the compound

Theoretically IR values were calculation veda 4f programme and scala values were obtain. Theoretically calculated IR data are multiplied with appropriate adjustment factors respectively 0.9617, 0.8992 for DFT/631G(d,p), HF/631G(d,p) basis sets. The negative frequency in the data was not found. This result, structure of compound were shown stable. IR spectrums were drawn with obtained values according to HF and DFT method. Theoretically IR values were compared with experimentally IR values. The result of this compare were found corresponding with each other of values.

Table 3: Significant vibrational frequencies (cm^{-1})

Vibration	Experimental	Theoretical
ν (OH)	3164	3672
ν (C=O)	1694	1732
ν (C=N)	1595	1614

Table 4: The calculated frequencies values of the molecule

Frequencies Values	DFT631G	HF6-31G	Frequencies Values	DFT631	HF6-31G
τ CCNN(33)	13	15	ν CC(10), δ HCC(61)	1089	1097
τ CNNC(33), τ NCCC(11), τ CCNN(25)	27	27	ν OC(58)	1102	1125
τ CNNC(10), τ NCCC(16), τ	36	34	ν NC(28)	1116	1142



CCNN(10)					
τ NCNN(12), τ CNCN(12)	46	46	ν OC(11), δ HCC(38)	1126	1156
δ CCN(13), δ CCC(10), τ HCCC(14)	57	57	ν CC(10), δ HCC(65)	1148	1156
τ CNCC(24)	78	78	ν CC(13), δ HCC(70), δ HOC(10)	1153	1169
τ CCCC(13), τ CNNC(27)	93	93	δ HCC(12), δ HNC(10)	1188	1199
τ CCNC(19), τ CNNC(11)	114	118	ν CC(14), δ NCN(10)	1192	1208
τ CNCN(11)	125	126	δ HCC(19)	1198	1231
δ CCC(11)	166	164	ν NC(11), δ HCC(13), δ HCO(16)	1234	1233
δ CCN(35), τ HCCC(20)	178	178	ν NN(12), δ NCN(11)	1250	1251
τ NCCC(22), τ CCCC(33)	194	179	δ HCO(19)	1257	1273
τ COCC(16)	211	210	ν CC(20), ν OC(49)	1267	1281
δ CCN(23)	227	228	δ HCN(19), δ HCO(27)	1271	1288
τ HCCC(30)	240	236	δ HCC(58)	1287	1296
τ COCC(17)	251	69	δ HCO(18)	1292	1311
δ CNN(15)	267	267	ν NC(10), δ HCN(12)	1298	1318
τ NCNN(14), τ NNCC(17), τ CCCC(13)	292	293	τ HCNC(12), τ HCOC(28)	1317	1346
δ CNC(26), τ CCCC(10)	332	315	ν CC(20), δ HCC(13), δ HCO(20)	1332	1351
δ CCN(13), δ CNO(10)	345	335	τ HCOC(36), δ HCN(36)	1345	1379
δ ONC(11), δ OCC(38), δ NNC(10)	364	351	ν NC(10), δ HCN(28), δ HCH(12)	1353	1382
δ CCC(27)	376	381	ν NC(11)	1357	1390
τ OCC(13), τ CCCC(14)	393	399	τ HCOC(20)	1365	1396
δ CNC(34)	400	403	δ HCH(76)	1366	1402
τ CCCC(14)	417	426	τ HCNC(21), τ HCOC(20)	1388	1427
δ NNC(12), δ CCC(21)	440	444	ν NC(10), δ HCN(16)	1417	1435
δ CCN(12)	470	472	δ CCC(11)	1425	1445
δ CCN(10)	478	482	ν CC(27), δ HCC(22), δ CCC(11)	1426	1449
τ CCCC(24), τ ONNC(23)	522	530	δ HCH(53)	1426	1455
δ CCC(15)	529	535	δ HCH(29)	1438	1461
τ HCOC(13)	578	583	δ HCH(39), τ HCCN(14)	1441	1462
δ COC(23), τ HCOC(13)	599	607	δ HCH(29)	1452	1467
δ OCN(14)	609	617	δ HCH(70), τ HCCC(18)	1454	1473
δ CCC(29)	631	636	δ HCH(33), τ HCOC(10)	1460	1479
τ ONNC(20)	661	680	δ HCH(70), τ HCCC(17)	1467	1484
τ ONNC(39)	691	713	ν CC(10), δ HCC(45)	1503	1525
τ CCCC(25), τ ONNC(23)	695	718	ν CC(29), δ CCC(11)	1567	1603
τ CCCC(25), τ ONNC(11), τ NNCC(39), τ OCC(11)	702	758	ν NC(43), ν CC(10)	1584	1632
ν NC(14)	754	765	ν NC(17), ν CC(22)	1599	1676
ν NC(39)	779	785	ν NC(35), ν CC(29)	1614	1709
ν NC(30)	780	794	ν OC(91)	1732	1754
τ HCCC(35)	784	810	ν CH(46)	2817	2789
ν NN(11)	801	822	ν CH(45)	2825	2797



τ HCCC(11), τ OCCC(11)	820	847	ν CH(33)	2872	2848
τ HCOC(81), ν OC(12)	836	848	ν CH(91)	2878	2856
ν CC(17), ν OC(15)	848	850	ν CH(91)	2884	2861
ν OC(27)	851	871	ν CH(62)	2938	2872
δ COC(17)	880	892	ν CH(73)	2948	2901
ν CC(10), δ HCC(12)	904	916	ν CH(53)	2955	2905
ν CC(33)	911	958	ν CH(73)	2985	2931
τ CCCC(17), τ HCCC(12)	943	973	ν CH(50)	2986	2931
ν NN(10), ν CC(10)	958	993	ν CH(39)	2988	2934
ν OC(10), ν CC(11)	975	995	ν CH(72)	2995	2939
τ HCNC(81)	981	996	ν CH(16)	2997	2941
ν OC(13), ν CC(17)	987	1005	ν CH(77)	3008	2957
δ CCC(44)	988	1018	ν CH(31)	3024	2963
δ CCC(56), ν NC(16), ν CC(35)	1007	1036	ν CH(53)	3048	2998
τ HCCC(27)	1031	1055	ν CH(47)	3050	3017
δ HCH(14), τ HCCN(50), τ HCCC(10)	1056	1077	ν CH(63)	3070	3033
δ HCO(13), τ HCOC(11)	1059	1079	ν CH(51)	3085	3035
ν NC(17), τ HCCC(10)	1071	1080	ν CH(76)	3099	3049
			ν OH(100)	3672	3770

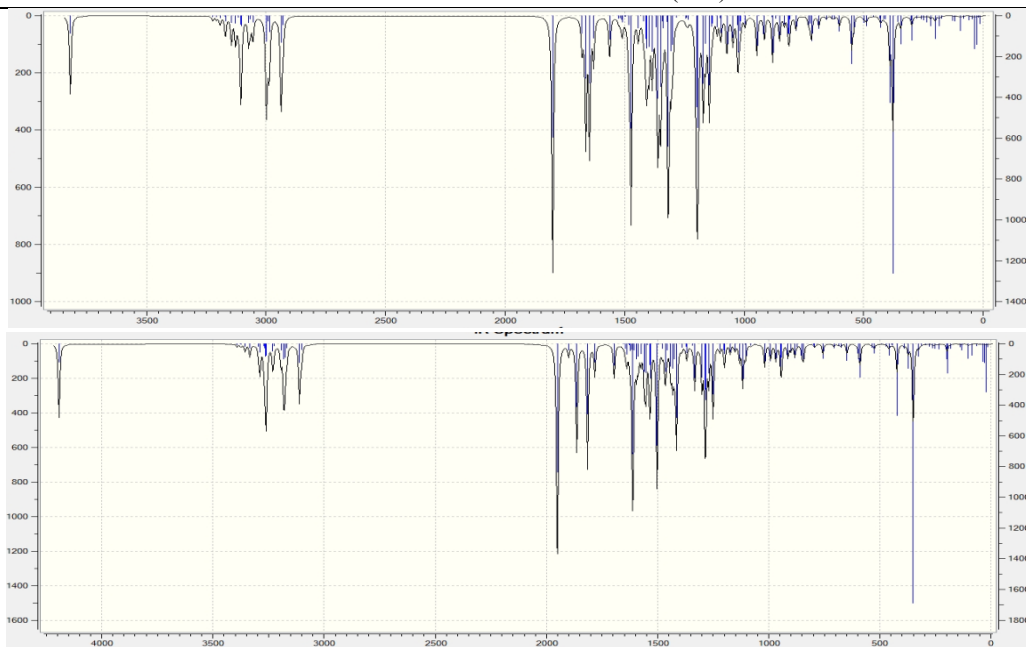


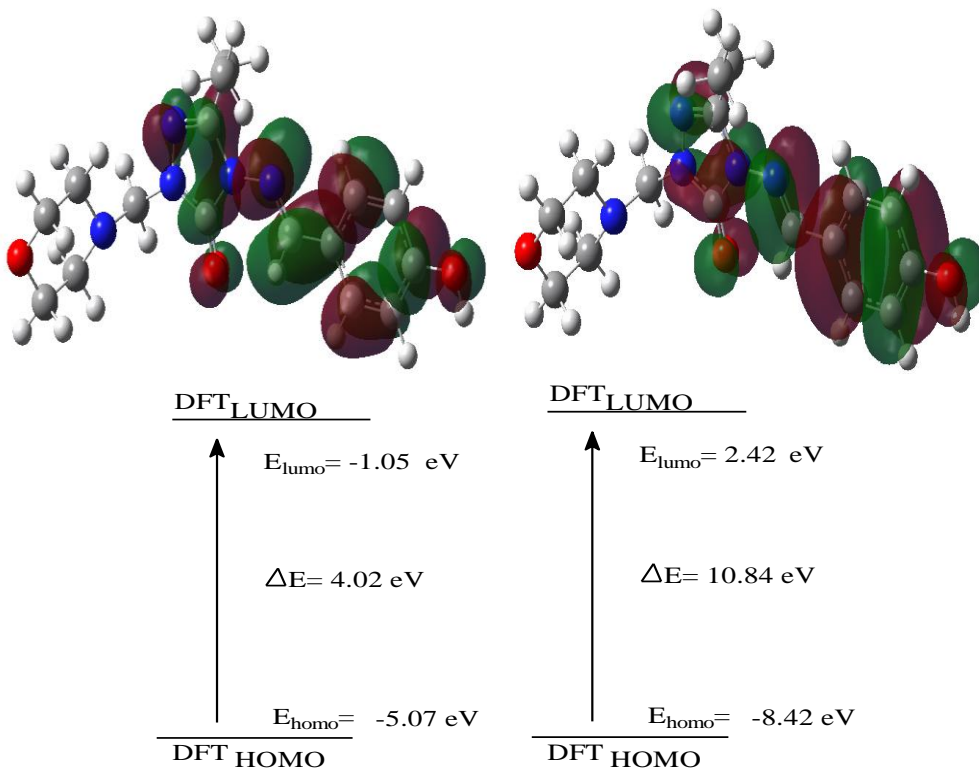
Figure 3: Theoretical IR spectra and simulated with DFT/B3LYP/631G(d,p)(a) and HF/B3LYP/631G(d,p)(b) levels of the molecule

Table 5: The calculated bond lengths with B3LYP/HF 631G(d,p) of the molecule

Bond Lengths	DFT	HF	Bond Lengths	DFT	HF
C(1)-C(10)	1.492	1.494	C(7)-C(8)	1.398	1.383
C(1)-N(40)	1.387	1.377	C(8)-H(20)	1.087	1.076
C(1)-N(38)	1.301	1.269	C(8)-C(9)	1.391	1.386



N(38)-N(39)	1.385	1.374	C(9)-H(21)	1.086	1.076
N(39)-C(2)	1.374	1.349	C(4)-C(9)	1.403	1.386
C(2)-N(40)	1.414	1.385	N(39)-C(12)	1.446	1.438
C(2)-O(43)	1.225	1.204	C(12)-H(28)	1.102	1.088
C(10)-H(23)	1.093	1.082	C(12)-H(29)	1.092	1.080
C(10)-H(24)	1.095	1.083	C(12)-N(42)	1.453	1.441
C(10)-C(11)	1.538	1.532	N(42)-C(13)	1.464	1.453
C(11)-H(25)	1.094	1.084	C(13)-H(30)	1.107	1.085
C(11)-H(26)	1.094	1.084	C(13)-H(31)	1.096	1.095
C(11)-H(27)	1.092	1.083	C(13)-C(14)	1.527	1.519
N(41)-C(3)	1.290	1.261	C(14)-H(32)	1.093	1.082
C(3)-H(17)	1.088	1.075	C(14)-H(33)	1.101	1.089
C(3)-C(4)	1.460	1.470	C(14)-O(45)	1.421	1.399
C(4)-C(5)	1.409	1.398	O(45)-C(15)	1.422	1.400
C(5)-H(18)	1.084	1.073	C(15)-H(34)	1.093	1.082
C(5)-C(6)	1.384	1.373	C(15)-H(35)	1.101	1.089
C(6)-H(19)	1.084	1.074	C(15)-C(16)	1.525	1.518
C(6)-C(7)	1.403	1.393	C(16)-H(36)	1.107	1.082
C(7)-O(44)	1.362	1.346	C(16)-H(37)	1.093	1.094
O(44)-H(22)	0.966	0.943	C(16)-N(42)	1.466	1.454



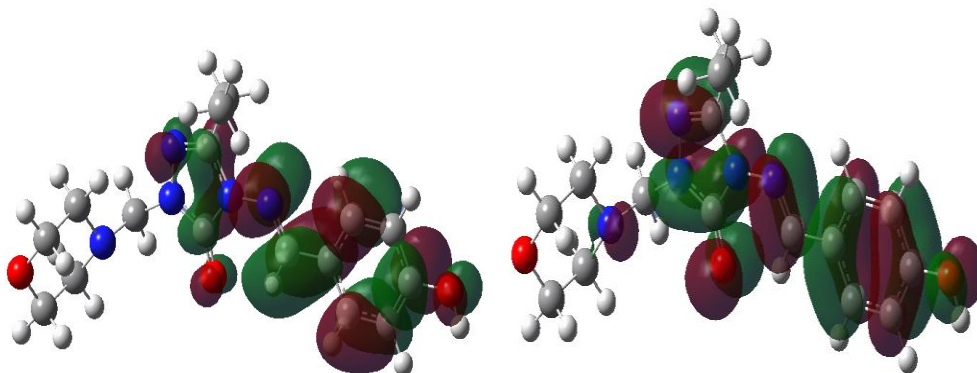


Figure 4: HOMO-LUMO energy of the molecule

Table 6: The calculated electronic structure parameters of the molecule

	Hatree	ev	kcal/mol	KJ/mol
LUMO	-0.03876	-1.05469	-24.322	-101.764
HOMO	-0.18657	-5.0767	-117.073	-489.84
A elektron ilgisi	0.03876	1.05469	24.322	101.764
I İyonlaşma potansiyeli	0.18657	5.0767	117.073	489.84
ΔE energy gap	0.14781	4.02201	92.7512	388.075
χ electronegativity	0.112665	3.06569	70.6976	295.802
Pi chemical potential	-0.112665	-3.06569	-70.6976	-295.802
ω electrophilic index	0.000469053	0.01276	0.29433	1.2315
IP Nucleophilic index	-0.00832651	-0.22657	-5.22491	-21.8612
S molecular softness	13.5309	368.185	8490.67	35525.3
η molecular hardness	0.073905	2.01101	46.3756	194.038

Investigation of thermodynamics properties of compound

Thermodynamics parameters of molecule calculated with B3LYP/DFT631G (d,p) and B3LYP/HF631G (d,p) basis sets and shown in the table 7. Thermodynamic parameters of molecule (such as thermal energy, heat capacity, entropy, zero-point vibrational energies (ZPVE), rotational constants and rotational temperatures) were calculated 233.044 K and 1 atm of pressure (Table 6.) stated the values of some thermodynamic parameters without experimental determinations. These calculated results are consistent with reported works [23-26], which are important to test the reliability of our results. In addition to, the standard thermodynamic functions of heat capacity $CV_{p,m}^0$ entropy S_m^0 and enthalpy H_m^0 were obtained at the B3LYP/DFT/HF6-31G(d,p) level.

Table 7: The calculated thermodynamics parameters of the molecule

Rotational temperatures (Kelvin)	DFT	HF
A	0.02441	0.02447
B	0.00418	0.00426
C	0.00384	0.00391
Rotational constants (GHZ)		
A	0.50854	0.50988
B	0.08716	0.08884
C	0.08009	0.08156
Thermal Energies E(kcal/mol)		
Translational	0.889	0.889



Rotational	0.889	0.889
Vibrational	245.136	261.981
Total	246.913	263.759
Thermal Capacity CV(cal/mol-K)		
Translational	2.981	2.981
Rotational	2.981	2.981
Vibrational	78.184	72.091
Total	84.145	78.053
Entropy S(cal/mol-K)		
Translational	43.287	43.287
Rotational	35.758	35.719
Vibrational	84.204	157.922
Zero-point correction (Hartree/Particle)	0.371381	0.399484
Thermal correction to Energy	0.393481	0.420326
Thermal correction to Enthalpy	0.394425	0.421270
Thermal correction to Gibbs Free Energy	0.316860	0.346236
Sum of electronic and zero-point Energies	-1121.392047	-1114.539957
Sum of electronic and thermal Energies	-1121.369946	-1114.519115
Sum of electronic and thermal Enthalpies	-1121.369002	-1114.518171
Sum of electronic and thermal Free Energies	-1121.446567	-1114.593205
Zero-point vibrational energy (Kcal/mol)	233.04480	250.67999

Table 8: The calculated mulliken charges datas B3LYP/HF 631G(d,p) of the molecule

	DFT	HF		DFT	HF
C1	0,528	0,606	H24	0,129	0,153
C2	0,844	1,102	H25	0,115	0,136
C3	0,111	0,184	H26	0,109	0,123
C4	0,083	-0,105	H27	0,131	0,142
C5	-0,105	-0,100	H28	0,105	0,156
C6	-0,104	-0,186	H29	0,129	0,130
C7	0,334	0,400	H30	0,107	0,099
C8	-0,138	-0,226	H31	0,084	0,129
C9	-0,131	-0,130	H32	0,101	0,110
C10	-0,223	-0,252	H33	0,094	0,123
C11	-0,325	-0,347	H34	0,102	0,124
C12	0,121	0,234	H35	0,092	0,107
C13	-0,044	-0,037	H36	0,082	0,099
C14	0,055	0,107	H37	0,123	0,144
C15	0,052	0,106	N38	-0,348	-0,346
C16	-0,048	-0,036	N39	-0,388	-0,599
H17	0,156	0,227	N40	-0,430	-0,638
H18	0,110	0,183	N41	-0,331	-0,338
H19	0,102	0,173	N42	-0,348	-0,622
H20	0,082	0,149	O43	-0,554	-0,669
H21	0,100	0,170	O44	-0,550	-0,649
H22	0,321	0,352	O45	-0,485	-0,639
H23	0,127	0,157			



Table 9: The calculated dipole moments datas of the molecule

	μ_x	μ_y	μ_z	μ_{Toplam}
Dft	-1.8264	0.9772	0.9212	2.2670
Hf	-5.3317	3.1941	-0.1974	6.2183

Table 10: The calculated total energy datas B3LYP/HF of the molecule

Enerji (a.u.)	DFT	HF
	-1121.7634	-1114.9394

Conclusion

In this work, electronic, geometric and spectroscopic parameters of molecule are calculated by Density Functional Theory (DFT) and Hartree-Fock (HF) methods with the 631G(d,p) basis sets of the program package Gaussian G09W. Obtained spectroscopic parameters are compared with experimental data. In addition, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO), bond lengths, mulliken charges, $E_{\text{LUMO}}-E_{\text{HOMO}}$ energy gap (ΔE_g), electronegativity (χ), electron affinity (A), global hardness (η), softness (σ), ionization potential (I), total energy of the molecule, thermodynamics properties, dipole moments were calculated with B3LYP/DFT631G (d,p) and HF/631G (d,p) basis sets. Furthermore, IR vibrational frequencies and IR spectrums were obtained. The IR data was found positive. This result, structure of compound were shown stable. The chemical shifts in the calculations $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ and IR vibrational frequencies are found to be compatible with the experimental data. Theoretical and experimental carbon and proton chemical shifts ratios between according to R^2 ve a, b values, lineer a correlation were observed.

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