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Investigation on Molecular Structure, Vibrational Analysis and Thermodynamic Properties of 1-(2,6-dimethylmorpholine-4-yl-methyl)-3-methyl-4-[3-ethoxy-(4-benzenesulfonyloxy)-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one

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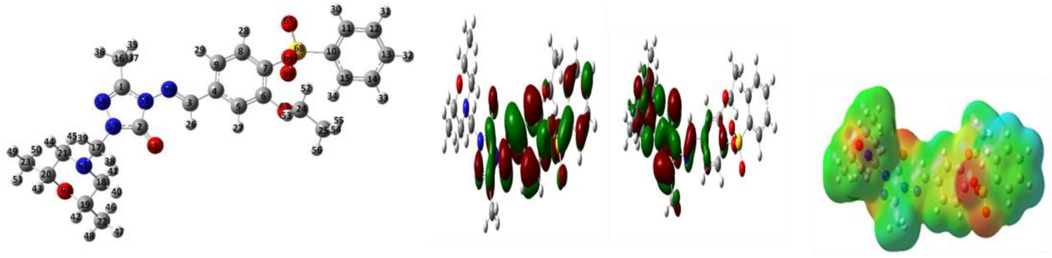
Abstract: In this article, 1-(2,6-dimethylmorpholine-4-yl-methyl)-3-methyl-4-[3-ethoxy-(4-benzenesulfonyloxy)-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one has been theoretically studied. The ^{1}H and ^{13}C NMR chemical shifts of the title molecule were calculated by the GIAO method and compared with experimental results. The vibrational frequency values of this compound have been calculated. The polarizability (α), hyperpolarizability (β), dipole moment along with molecular electrostatic potential surface of the title compound have been performed. The molecular electrostatic potential (MEP) map was calculated to assign reactive site on the surface of the molecule. The calculated electronic, structural and thermodynamic parameters of the title molecule were examined by using the density functional method (DFT/B3LYP) with 6-31G(d,p) basis set.

Keywords: *Mannich base, GIAO, DFT(B3LYP), 6-31G(d,p) basis set*

Graphical Abstract:



Compound HOMO LUMO ESP

Highlights:

- The stable structures of the title compound were performed by DFT/B3LYP method and 6-31G(d,p) basis set.
- The spectroscopic values of the title compound were determined with the same basis set.
- The physicochemical properties were predicted to found the chemical stability behavior of the title compound.
- The electronic and thermodynamic parameters were calculated to predict the reactivity behavior.
- MEP diagrams were visualized to show the reactive site of this compound.

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1. Introduction

Mannich bases play an essential role in organic chemistry. The 1,2,4-triazole derivated-Mannich bases rings systems exhibit a wide range of biological activities such as antibacterial [1], anticancer [2-5], antifungal [6], antitubercular [7], anti-inflammatory [8], antiviral [9,10], antidiabetic [11,12], antiarrhythmic [13] activities. Recently, many studies on the synthesis, biological activity, and computational chemical calculations of Mannich bases were reported [14-16]. The computational chemical calculations have been commonly used the prediction of many properties in the chemical systems. That's why these calculations have widely used the design of functional materials. To elucidate the spectroscopic, electronic and thermodynamic parameters of many organic compounds have been developed by using theoretical calculations methods [17-21].

Mannich bases because of their high biological activities have been able to draw the attention of many researchers. For this reason, the papers on the computational chemical calculations of Mannich bases and their derivatives in the literature were reported [22-25]. Our goal analyzed by using the theoretical method in determination of structural, spectroscopic, electronic and thermodynamic properties of the title compound. Firstly, all quantum chemical calculations of the title compound have been carried out by using B3LYP(DFT)/6-31G(d,p) basis set. The ^{1}H and ^{13}C-NMR chemical shift values, vibrational frequencies, structural, electronic, thermodynamic parameters, HOMO-LUMO energies and molecular electrostatic potential maps (MEP) of the title molecule were calculated by using the optimized structure with B3LYP/6-31G(d,p) level. The vibrational frequencies of the title molecule were related with the spectral data obtained with DFT/B3LYP and 6-31G(d,p) basis set. All calculated spectroscopic values were compared with their experimental values

2. Computational Approaches

The quantum chemical calculations are commonly method used to predict many properties of the molecule. Recently, computational studies have been widely used. In this study, the input files of this compound were viewed with GaussView [26] software and then all calculations were performed with Gaussian 09W Program [27]. All quantum chemical calculations were provided with the B3LYP(DFT) method and 6-31G(d,p) basis set. The structural, spectroscopic (the ^{1}H and ^{13}C-NMR chemical shift values and vibrational frequencies), total energies, molecular electrostatic potential (MEP) maps, Mulliken atomic charges, HOMO–LUMO energies, electronic chemical potential (μ), global hardness (η), electrophilicity (ω), energy gap (ΔE), the mean polarizability ($<\alpha>$), the anisotropy of the polarizability ($\Delta\alpha$), the mean first-order hyperpolarizability ($<\beta>$), electronegativity (χ) of the title molecule were calculated with B3LYP(DFT)/6-31G(d,p) level. The ^{1}H and ^{13}C-NMR shifts values (according to TMS) were calculated using the Gauge-Independent Atomic Orbital (GIAO) method [28]. The veda4f program was used to determine the vibration frequencies [29].

3. Results and discussion

In this study, quantum chemical methods have been significantly employed to get an understanding of the electronic properties of the molecule and to explain experimental spectroscopic features. The optimization of molecular geometries of 1-(2,6-dimethylmorpholine-4-yl-methyl)-3-methyl-4-[3-ethoxy-(4-benzenesulfonyloxy)-benzylidenamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one was carried out by using Density Functional Theory (DFT/B3LYP) method and 6-31G(d,p) basis set. The optimized molecular geometries of 1-(2,6-dimethylmorpholine-4-yl-methyl)-3-methyl-4-[3-ethoxy-(4-benzenesulfonyloxy)-benzylidenamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one is shown in Figure 1. The geometric parameters (bond angles and bond lengths), Mulliken atomic charges of this compound were calculated through use of DFT(B3LYP)/6-31G(d,p) method. The calculated molecular values (bond angles, bond lengths and Mulliken atomic charges) are given in Table S1 (Supplementary Metarials) and Figure 2.

The calculated Ar(C)-Ar(C) bond lengths in benzene rings of this compound are recorded 1.42-1.39 A^0 at B3LYP/6-31G(d,p). The Ar(C)-Ar(C) bond lengths of benzene rings are generally observed at 1,34-1,53 A^0 in literature [33,34]. The calculated N-C bond length in 1,2,4-triazole-5-one ring is recorded as 1.35-1.38 A^0 due to the resonance effect. The bond length for same systems in literature is recorded as 1,29-1,47A^0 [30,31]. The results indicate that the calculated bond lengths are closer to the reported bond lengths for similar compounds.

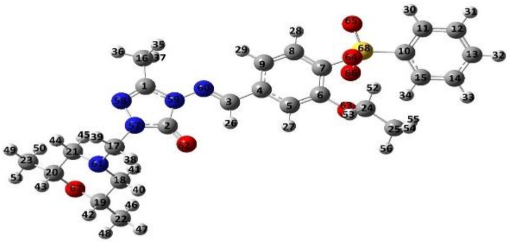

Figure 1. The computed geometric structure of 1-(2,6-dimethylmorpholine-4-yl-methyl)-3-methyl-4-[3-ethoxy-(4-benzenesulfonyloxy)-benzylidenamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one (DFT (B3LYP)/6-31G(d,p)

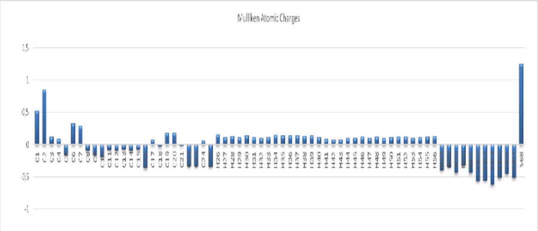

Figure 2. Graph of the calculated Mulliken atomic charges of the title compound.

It has been reported that electronegative N and O atoms without S atom have negative atomic charge values in the gas phase. But the S atom which is linked to three electronegative atoms has the highest positive charge value. The C1 atom which is linked to two electronegative atoms, C2 atom surrounded with three electronegative atoms (N, N, O) have one of the highest positive charges values. All hydrogen atoms of the title compound have positive atomic charge values (Figure 2). The results indicate that the calculated structural parameters are closer to the reported parameters for corresponding systems [32-34].

It has been recorded that electronegative N and O atoms except for S atom have negative atomic charge values in gas phase. But the S atom which is surrounded with three electronegative atoms (O, O, O) has the highest positive charge value. The C1 atom which is surrounded with two electronegative atoms (N, N), C2 atom surrrounded with three electronegative atoms (N, N, O) have one of the highest positive charges values. All hydrogen atoms of the title compound have positive atomic charge values (Table S1 (Supplementary Metarials) and Figure 2).

The ^{1}H and ^{13}C-NMR chemical shift values in the gas phase/DMSO solvent (to TMS) with GIAO method of the title compound were calculated using DFT (B3LYP)/6-31G(d,p) method. The calculated and experimental values are given in Table 1.

The calculated ^{1}H-NMR chemical shift values are observed to be 1.61-11.07 ppm in the gas phase and 1.78-11.03 ppm in DMSO solvent at DFT (B3LYP) method and with 6-31G(d,p) basis set, while the experimental parameters are calculated 1.03-9.66 ppm. Aromatic C-H signals were seen at 7.31-7.85 ppm. These signals were calculated 8.07-9.42 ppm in the gas phase and 8.27-9.32 ppm in DMSO solvent at B3LYP/6-31G(d,p) level.

The ^{13}C-NMR chemical shift values of the title compound are observed to be 20.93-153.61 ppm in the gas phase and 20.74-154.05 in DMSO solvent at DFT(B3LYP)/6-31G(d) method, while the experimental parameters are calculated 10.94-151.00 ppm. As a result of the R^2 values of the title compound were assessed and the correlations graphics of ^{13}C and ^{1}H-NMR chemical shift values of the title compound were plotted. Theoretical and experimental between ^{13}C and ^{1}H-NMR chemical shifts ratios of the title compound were regarded as a linear correlation. It is such a relationship between R^2 values of the title compound; B3LYP(DFT) 6-31G(d,p)$_{\text{Vacum}}$: ^{1}H: 0.9905, ^{13}C: 0.9954, B3LYP(DFT) 6-31G(d,p)$_{\text{DMSO}}$: ^{1}H: 0.9938, ^{13}C: 0.9962 (Figure 3).

Table 1. The calculated ^1H and ^{13}C NMR isotropic chemical shifts of the title compound (with respect to TMS, all values in ppm) (6-31G(d,p))

	$\delta_{Exp.}$	**$\delta_{cal.}$ B3LYP (Vacum)**	**$\delta_{cal.}$ B3LYP (DMSO)**	**Different**	**Different (DMSO)**
C1	143.13	146.55	148.33	-3.42	-5.20
C2	151.00	153.61	154.05	-2.61	-3.05
C3	150.15	153.40	154.02	-3.25	-3.87
C4	134.85	139.34	139.60	-4.49	-4.75
C5	124.30	132.66	133.59	-8.36	-9.29
C6	150.87	158.19	158.33	-7.32	-7.46
C7	139.58	150.63	150.02	-11.05	-10.44
C8	120.08	130.63	130.23	-10.55	-10.15
C9	112.91	124.63	124.68	-11.72	-11.77
C10	135.12	147.92	146.23	-12.80	-11.11
C11	129.48	132.01	131.67	-2.53	-2.19
C12	128.14	130.93	132.20	-2.79	-4.06
C13	133.59	135.99	138.38	-2.40	-4.79
C14	128.14	131.41	132.79	-3.27	-4.65
C15	129.48	132.41	131.51	-2.93	-2.03
C16	10.94	20.93	20.74	-9.99	-9.80
C17	65.60	74.08	73.90	-8.48	-8.30
C18	55.57	63.63	62.82	-8.06	-7.25
C19	71.02	80.31	80.34	-9.29	-9.32
C20	71.02	80.38	80.36	-9.36	-9.34
C21	55.57	63.08	63.22	-7.51	-7.65
C22	18.92	28.28	27.85	-9.36	-8.93
C23	18.92	28.16	27.93	-9.24	-9.01
C24	64.05	78.11	78.76	-14.06	-14.71
C25	14.04	25.22	24.93	-11.18	-10.89
H26	9.66	11.07	11.03	-1.41	-1.37
H27	7.31	8.07	8.27	-0.76	-0.96
H28	7.47	8.45	8.50	-0.98	-1.03
H29	7.83	9.00	9.08	-1.17	-1.25
H30	7.85	9.01	9.01	-1.16	-1.16
H31	7.67	8.43	8.69	-0.76	-1.02
H32	7.47	8.53	8.86	-1.06	-1.39
H33	7.67	8.55	8.82	-0.88	-1.15
H34	7.85	9.42	9.32	-1.57	-1.47
H35	2.31	3.18	3.30	-0.87	-0.99
H36	2.31	2.87	2.95	-0.56	-0.64
H37	2.31	3.21	3.30	-0.90	-0.99
H38	4.54	5.69	5.70	-1.15	-1.16
H39	4.54	5.00	5.13	-0.46	-0.59
H40	2.01	3.54	3.55	-1.53	-1.54
H41	2.01	3.06	3.06	-1.05	-1.05
H42	3.53	4.54	4.60	-1.01	-1.07
H43	3.52	4.50	4.55	-0.98	-1.03
H44	2.75	3.38	3.54	-0.63	-0.79
H45	2.75	3.38	3.32	-0.63	-0.57
H46	1.03	1.67	1.84	-0.64	-0.81
H47	1.03	1.89	1.84	-0.86	-0.81
H48	1.03	2.12	2.07	-1.09	-1.04
H49	1.03	1.66	1.86	-0.63	-0.83
H50	1.03	1.91	1.86	-0.88	-0.83
H51	1.03	2.14	2.08	-1.11	-1.05
H52	3.83	4.85	4.86	-1.02	-1.03
H53	3.83	4.32	4.49	-0.49	-0.66
H54	1.10	1.61	1.78	-0.51	-0.68
H55	1.10	2.27	2.32	-1.17	-1.22
H56	1.10	2.39	2.37	-1.29	-1.27

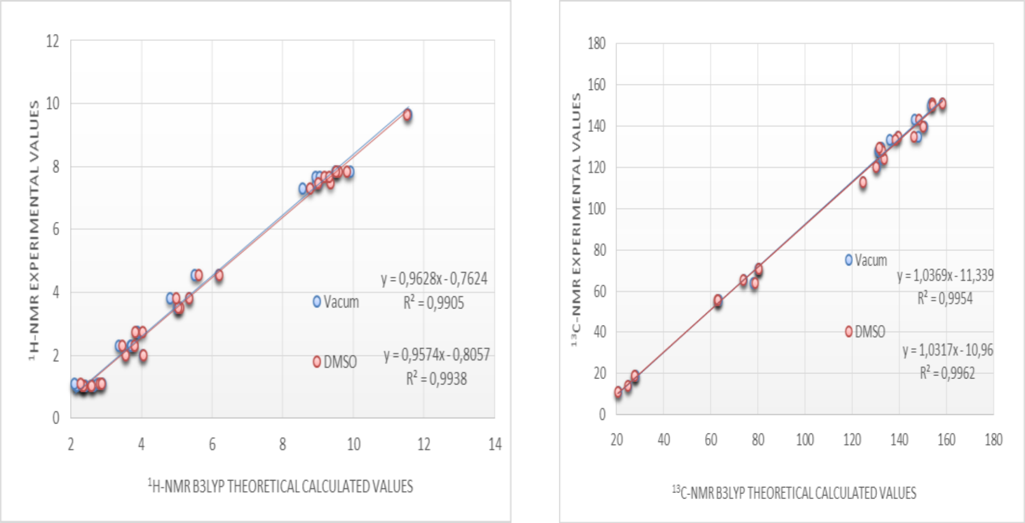

Figure 3. Comparison of experimental and theoretical ^{1}H and ^{13}C-NMR chemical shifts values of the title compound with B3LYP/6-31G(d,p) (Vacum/DMSO) method.

All vibrational frequencies (in cm^{-1}) of the title compound were calculated at B3LYP(DFT) method and the results were presented in Table S1 (Supplementary Materials). The experimental frequencies and simulated IR spectrum of this compound are displayed in Figure 4. There is a slight difference between theoretical vibration and experimental frequencies. Theoretical vibration frequencies for the title compound are generally closer to the experimental frequencies. The $\nu(C=O)_{experimental}$ band is observed at 1705 cm^{-1} and theoretically calculated as 1724 cm^{-1} at DFT (B3LYP)/6-31G(d,p) level.

Moreover, the $\nu(C=N)$ bands were observed at 1603 and 1575 cm^{-1} and calculated at 1611 and 1592 cm^{-1} (DFT/B3LYP) is a close adjustment to the experimental values. The $\nu(SO)$ bands in the experimental IR spectrum were remarked at 1375 and 1171 cm^{-1} whereas were theoretically calculated at 1386 and 1114 cm^{-1}, respectively. The bands at 754 and 605 cm^{-1} in the experimental IR spectrum were assigned to C=C out-of-plane bending vibration modes of the aromatic ring, whereas its calculated value was at 826 and 671 cm^{-1}, respectively. The R^{2} values of the title compound were shown in Figure 5. The R^{2} value is 0.9922 at the B3LYP(DFT)/6-31G(d,p) level.

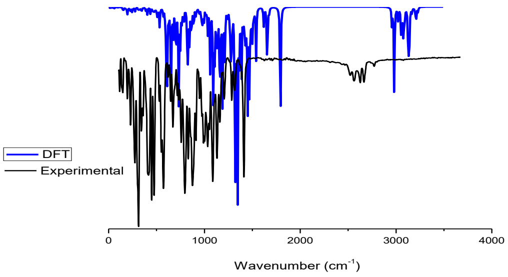

Figure 4. Experimental and theoretical (6-31G(d,p) DFT) IR spectra of the title compound.

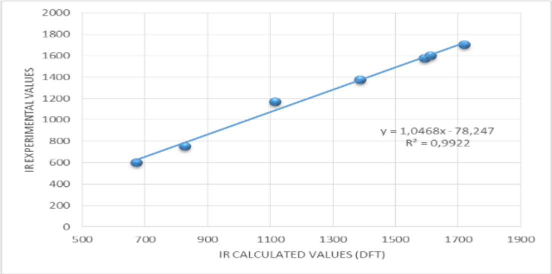

Figure 5. Comparison of experimental - theoretical vibrational frequencies of the title compound with 6-31G(d,p) B3LYP method

The energy levels and combinations of HOMO and LUMO were measured at DFT(B3LYP) 6-31G(d,p) level. Energies of HOMO and LUMO were reported as E_{HOMO}: -5.795, E_{LUMO}: -1.755 eV B3LYP/6-31G(d,p), respectively. Furthermore, the molecular softness (S), hardness (η), electronegativity (χ), chemical potential (Pi), ionization potential (I), electron affinity (A), electrophilic (ω) and nucleophilic index (IP) were determined by using HOMO and LUMO energies

(Table 2). The $\Delta E_{H\text{-}L}$ (energy gap) energy is 4.040 eV at B3LYP/(6-31G(d,p)) level (Figure 6).

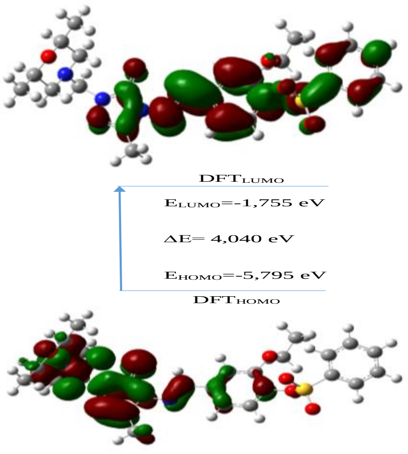

Figure 6. 3D plots of HOMO-LUMO energies of the title compound at the B3LYP 6-31G(d,p).

Table 2. The calculated electronic properties of the title compound (6-31G(d,p) B3LYP)

	Electronic Properties	**DFT (6-31G(d,p)) eV**
	LUMO	-1.755
	HOMO	-5.795
A	**Electron Affinity**	1.755
I	**Ionization Potential**	5.795
ΔE	**Energy Gap**	4.040
χ	**Electronegativity**	3.775
Pi	**Chemical Potential**	-3.775
ω	**Electrophilic Index**	0.019
IP	**Nucleophilic Index**	-0.280
S	**Molecular Softness**	366.573
η	**Molecular Hardness**	2.020

The total dipole moment values of the title compound were estimated as 4.6777 D for DFT(B3LYP) method with the 6-31G(d,p) basis set. The results were presented in Table 4. The highest dipole moment is registered as a μz component at B3LYP method. The mean polarizability (<α>) and the mean first-order hyperpolarizability (<β>) and are calculated -43.138x10^{-24} esu and 12.127x10^{-30} esu for B3LYP, respectively. It was determined that the β values at B3LYP method of the title compound are higher than that of urea (Table 3).

Table 3. The mean polizability (<α>), the anisotropy of the polarizability (Δα), the mean first-order hyperpolarizability (<β>), dipole moment values of the title compound.

	B3LYP (6-31G(d,p))
μ_x	-3.3425 Debye
μ_y	0.8433 Debye
μ_z	3.1619 Debye
μ_{Toplam}	4.6777 Debye
α_{xx}	80.80 a.u.
α_{yy}	48.22 a.u.
α_{zz}	31.87 a.u.
α	53.629x10^{-24} esu
Δα	43.138x10^{-24} esu
βx	12077.64 a.u.
βy	-791.24 a.u.
βz	749.67 a.u.
βxxx	1347.56 a.u.
βxxy	-83.75 a.u.
βxyy	-38.85 a.u.
βyyy	-60.42 a.u.
βxxz	175.49 a.u.
βxyz	38.60 a.u.
βyyz	-20.50 a.u.
βxzz	134.38 a.u.
βyzz	19.65 a.u.
βzzz	-65.42 a.u.
β	12.127x10^{-30} esu

The thermodynamic properties of the title compound are given in Table 4. The MEP maps of the title compound are displayed in Figure 7. Additionally, the MEP map records that the positive potential sites are nearby the hydrogen while the negative potential sites are on electronegative oxygen, nitrogen atoms.

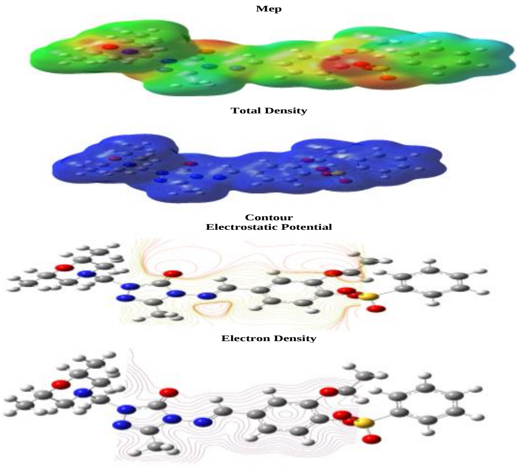

Figure 7. The calculated molecular surfaces of the title compound.

Table 4. The calculated thermodynamics parameters of the title compound (6-31G(d,p) B3LYP).

	DFT (6-31G(d,p))
Rotational temperatures (Kelvin)	
A	0.01074
B	0.00136
C	0.00132
Rotational constants (GHZ)	
A	0.22376
B	0.02842
C	0.02758
Zero-point vibrational energy (Kcal/Mol)	344.62109
Thermal correction to Energy	0.549119
Thermal correction to Enthalpy	0.586164
Thermal correction to Gibbs Free Energy	0.475437
Sum of electronic and zero-point Energies	-2094.009468
Sum of electronic and thermal Energies	-2093.973437
Sum of electronic and thermal Enthalpies	-2093.972493
Sum of electronic and thermal Free Energies	-2094.083219
Thermal Energies E(Kcal/mol)	
Translational	0.889
Rotational	0.889
Vibrational	365.453
Total	367.231
Thermal Capacity CV(Cal/Mol-Kelvin	
Translational	2.981
Rotational	2.981
Vibrational	129.280
Total	135.241
Entropy S (Cal/Mol-Kelvin)	
Translational	44.685
Rotational	38.747
Vibrational	149.613
Total	233.044

4. Conclusion

In this research, the geometric, thermodynamics, spectroscopic, and electronic values of the title compound have been assessed by using DFT (B3LYP)/6-31G(d,p) basis set. The IR, ^{1}H- and ^{13}C-NMR spectral values have been received and matched with the experimental spectroscopic values. The bond lengths obtained DFT/6-31G(d,p) level of the title compound diplayed a close relationships due to slightly exaggerated electron correlation effects. The calculated DFT/6-31G(d,p) vibrational frequencies are generally higher than the corresponding experimental frequencies. The Mulliken atomic charges indicated that the carbon atoms (out C4, C6,C7) of the aromatic rings have negative charges and the heteroatoms in the whole system (excluding S) is negative and the N59 within 1,2,4 triazole ring has the highest negative values of -0.43 a.u. The S68 in the whole system has the highest positive values of 1.25 a.u. That between theoretical and experimental ^{1}H- and ^{13}C-NMR chemical shift values noted a great relationship; B3LYP(DFT)/6-31G(d,p)$_{\text{Vacum}}$ R^2: ^{1}H; 0.9905, ^{13}C; 0.9954, B3LYP(DFT)/6-31G(d,p)$_{\text{DMSO}}$: ^{1}H; 0.9938, ^{13}C; 0,9962, The statistical analysis results of the title compound shown that it was a great correlations (R^2=0.9922) between experimental and calculated vibrational frequencies. The recorded values of $\Delta E_{\text{H-L}}$ confirmed that this compound is considerably stable and reactive. The negative regions of the title compound are nearby S, N and O groups in the whole system and the positive region are nearby aromatic hydrogen atoms.

For all that, the molecular structure, the vibrational frequencies, the HOMO-LUMO, MEP and NLO properties, Mulliken atomic charges and thermodynamic properties of the 1-(2,6-

dimethylmorpholine-4-yl-methyl)-3-methyl-4-[3-ethoxy-(4 benzenesulfonyloxy)-benzylidenamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one molecule should be measured at the B3LYP/DFT/6-31G(d,p) level of the theory for the primary time. Futhermore, it can be clearly declared that the computed vibrational wavenumbers, ^{1}H- and ^{13}C-NMR chemical shift values are in excellent relation to the experimental values.

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