

Synthesis, NMR, DFT, GRD, MEP, FMO's analysis and comparison of E and Z-isomer of N'-((4-bromothiophen-2-yl)methylene)naphthalene-2-sulfonylhydrazide

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Abstract

A novel Schiff base N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonylhydrazide ligand was prepared by condensation of equivalents amount of naphthalene -2-sulfonylhydrazide with 4-bromo-2-thiophenecarboxaldehyde. The newly synthesized ligand was isolated in excellent yield. CHN-EA, UV-Vis., GC/MS, FT-IR, ¹H and ¹³C NMR were used to determine the structure of the desired ligand. Density functional theory DFT B3LYP/6-311G(d,p) was performed to optimize the E and Z-structural isomerization process. Several quantum calculations parameters like optimized bond length, angles and torsional angles in addition to HOMO/LUMO, GRD and MEP map, for both E and Z isomers have been calculated and compared under the same level of theory.

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1. Introduction

Schiff base is regarded as one of the most important azomethine such as R-HC = N-R in-group organic compounds acted as an intermediate for many processes [1]. In general, these compounds synthesized by reacting substituted primary amines with several types of ketones or aldehyde in neutral alcoholic or acidic/ basic media [2-4]. Through the passage of dehydration reaction, the oxygen of carbonyl C=O is changed by an imine functional group resulting in the desired Schiff base [2-5]. These ligands have various potentials in several fields of chemistry and pharmacy; they exhibited a number of biological applications as antibacterial anti-inflammatory, anti-depressant antioxidant, anticancer, antifungal and anti-plasmodial, activities [5-9]. DFT computations have become a very useful method of theoretical aspects [10, 11]. In recent years, DFT studies become popular as theoretical Quantum chemical computational for many chemical reactions because it is simple to use and it provides many information such as (optimization of molecular structure, energies of chemical reactions, etc.) that agree well with their experimental relative part [12, 13]. DFT has been used to determine several physical parameters of desired products, which is very helpful in solving their molecular structures. Several physical measurements like FTIR, UV-vis, HOMO-LUMO, MPE, Mull and NPA, DOS, electronic transition, and thermal parameters can be DFT-computed [14, 15], and these parameters are obtained from optimization of the structure by using Gaussian software [16]. As an extension of our continuous work in this field [17-22], condensation of naphthalene-2-sulfonylhydrazide, with 4-bromo-2-thiophenecarboxaldehyde as starting material was carried out resulting in the formation of the desired Schiff base ligand in excellent yield. The desired Schiff was spectrally characterized via CHN-EA, UV-Vis., GC/MS, FT-IR, ¹H, and ¹³C NMR analysis. The E/Z-structural isomers of the synthesized compound were optimized through B3LYP/DFT method. Several DFT computed processes like MEP map, GRD, and HOMO-LUMO were performed to comprise between E and Z-isomers.

2. Materials, methods and Computations

2.1 Materials and Instrumentation

All reagents and solvents were used in synthesis and biological parts were purchased from Sigma Aldrich Chemical Company (USA) and used without further purification. Elemental analyses were performed using the Elementar-Vario EL analyzer. The melting point recorded for Schiff bases from Saturates Melting point apparatus SMP-3. FT-IR (Perkin-Elmer Spectrum) spectrometer was used to gain IR spectra. Shimadzu UV-VIS-NIR (UV-3101PC, TCC-260) scanning spectrophotometer was used to control the reaction by absorption measurements. ¹H and ¹³C (JNM-ECZ600R/S1) Spectrometer was performed on 400MHz to acquire NMR data, using CDCl₃ as solvent. All the DFT calculations were performed using Gaussian09 with the level of theory DFT/B3LYP/6-311G(d,p) [23]. Moreover, the outcome result was visualized using Gaussview [24].

2.2 Synthesis

2.2.1 General procedure for synthesis of N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonylhydrazide.

The white solid product was formed by the addition of excess amounts of hydrazine hydrate (NH₂-NH₂.H₂O) to stoichiometric amount of naphthalene-2-sulfonylchloride [1], in a THF solvent. After 2-hours of stirring at room temperature, The THF was evaporated, and then a precipitate was washed with distilled water several times. Then it was left to be dried in a desiccator at room temperature.

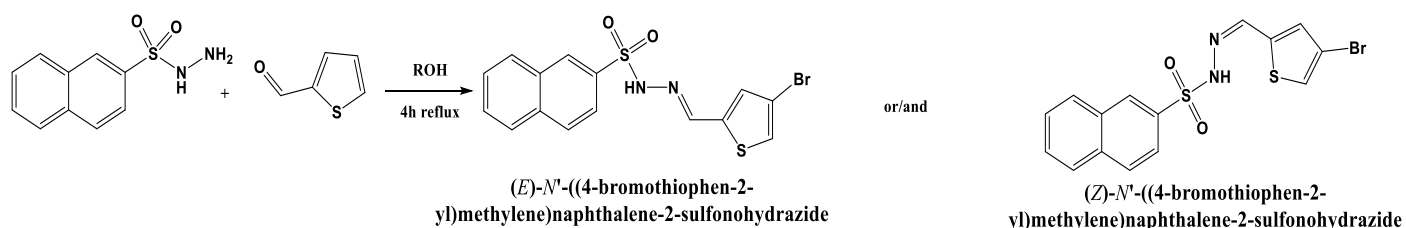
N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonylhydrazide, Yield 91%, white solid, m.p. = 185°C; white solid; molecular formula C₁₅H₁₁BrN₂O₂S₂; FT-IR: 3154.5 cm⁻¹ ν_(N-H), 1648 cm⁻¹ ν_(C=N), 1557 cm⁻¹ ν_(C=C), 1327.5 cm⁻¹ ν_(S=O), 762 cm⁻¹ ν_(C-S). ¹H-NMR(600MHz, CDCl₃, J=7.5 Hz, ppm): 9.8 (s, 1H, NH), 7.7 (s, 1H, N=C-H) azomethine group, thiophen group has 6.9 (s, 1H, BrC=CH-S), 7.1(s, 1H, Br-C=CH-C-S), in naphthalene ring 7.6 and 7.5(t, 2H,

CH=CH-C), 8.1(s,1H, C=CH-C-SO₂), 7.9(d, 1H, C-CH=CH-C-SO₂) and 8.03(d, 2H, CH=C-CH=CH-C-SO₂), 8.3 and 8.8(CH-CH=C); ¹³C-NMR (600MHz,CDCl₃,ppm): 110, 124, 125, 125.7, 127, 128.5, 129, 131, 132,133.4, 134.1, 135.3, 136.7, 138.3, 140.1(azomethine); [M⁺]= 393.9 m/z; UV-Visible (THF): 238 and 308.5 nm.

2. Results and Discussion

3.1 Synthesis and NMR

New N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonylhydrazide Schiff base ligand was prepared via condensation of naphthalene -2-sulfonylhydrazide with 4-bromo-2-thiophenecarboxaldehyde in methanol open reflux condition for 4hours as seen in Scheme 1. The 91% yield was recorded, the final product was isolated as a pure solid white powder with m.p. = 185°C. Moreover, the product is soluble in chlorinated solvents like DCM, slightly soluble in alcohol, and insoluble in water or n-hexane.



Scheme 1. Synthesis of the ligand.

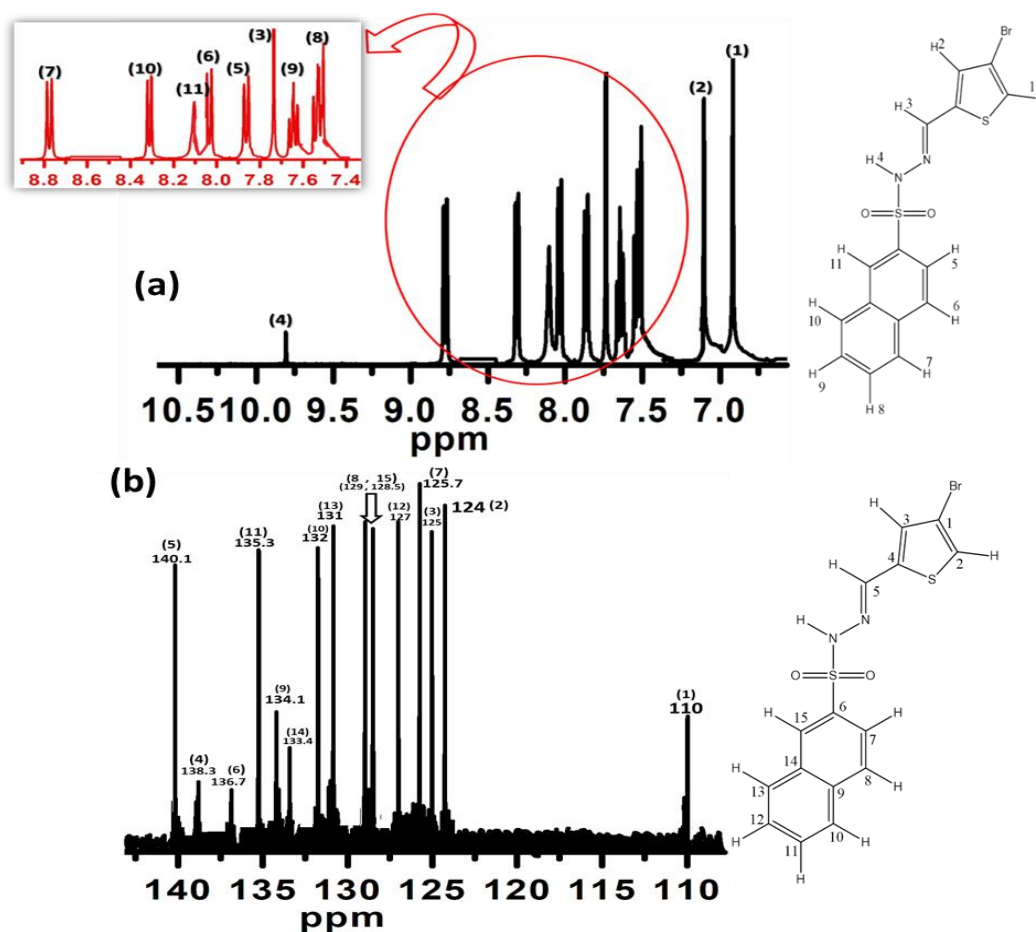


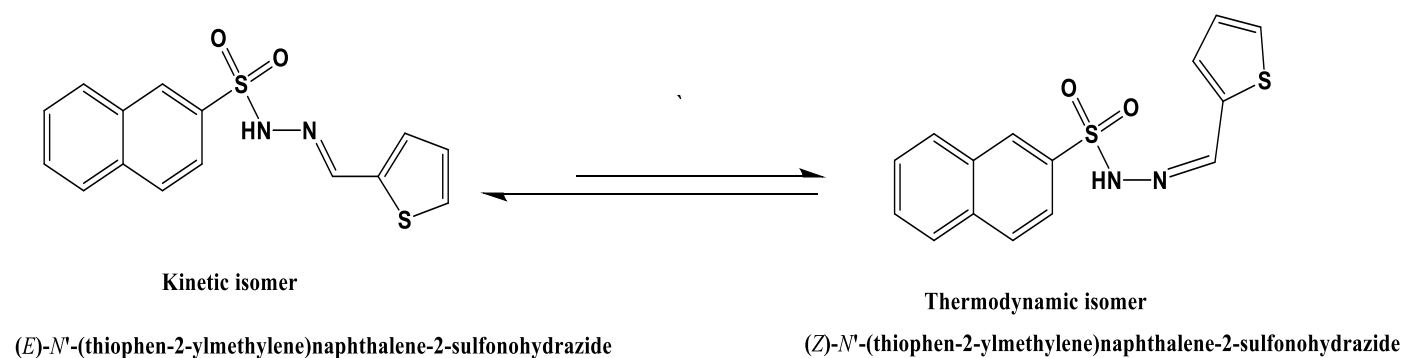
Figure 1: (a) ¹H-NMR spectrum and (b) ¹³C-NMR spectrum the desired ligand dissolved in CDCl₃.

The structure of the desired Schiff base stand out *via* NMR spectra, $^1\text{H-NMR}$ as shown in Figure. 1a represents important peaks for the desired Schiff base compound; singlet at $\delta_{\text{H}}=7.83$ ppm for azomethine group and a singlet for N-H at $\delta_{\text{H}}=9.8$ ppm. Experimentally, $^{13}\text{C-NMR}$ for the investigated compound was shown in Figure 1b, the N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonohydrazide structure was confirmed by $^{13}\text{C-NMR}$ as; azomethine carbon at $\delta_{\text{C}}=140.1$ ppm and the rest of the peaks are clearly appeared in various places in Figure 1b.

3.2. Optimization structure of (E/Z)-Schiff base compound:

3.2.1. The density functional theory methods (DFT)

The structure of E and Z N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonohydrazide was submitted to DFT- B3LYP optimization, in the gas phase with 6-311G(d,p) level basis set in order to figure out the most stable as kinetically favored isomer and the less as thermodynamically favored isomer as seen in Scheme 1. By neglecting any internal interconnection between molecules for both isomers, in gases state, the less internal steric repulsion factor plays an important role in fixing the E-isomer over Z-isomer, as it is with less internal repulsion. The gaseous state DFT-calculations also showed the energy difference value $\Delta E = 11.6$ kJ/mol between E-isomer (-4187.57381681 a.u.) and Z-isomer (-4187.56990333 a.u.) is very small. Mover, the transition state energy $E_{\text{T.S}} = 63.4$ kJ/mol is also not large as seen in Figure 2. Therefore, the possibility of changing the E-isomer to the Z-isomer easily happens since the energy difference between both isomers is low and the solvent (for example) can prove such energy amount even at RT. Thus, in the solution both isomers can be excess with an equilibrium favored towered the E over Z.



Scheme 2. E-Z isomerization process.

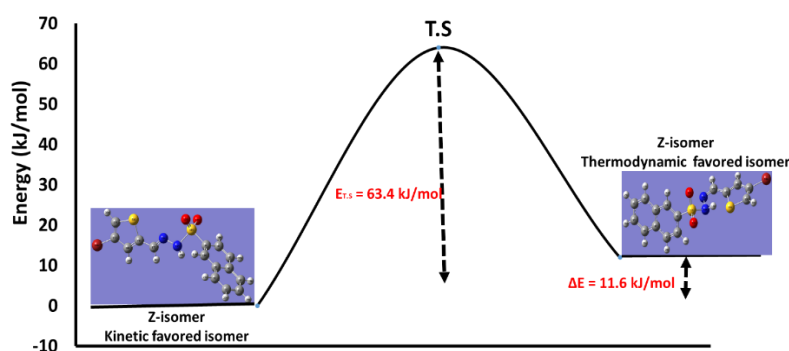


Figure 2. DFT optimized of E/Z isomerization.

The bond lengths, bond angles and torsional angles of both E and Z were calculated upon structure optimization using DFT as listed in Table 1, 2 and 3.

Table 1: Bond length of (E/Z)- N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonohydrazide

Atoms	Bond Length(A)	
	E-isomer	Z-isomer
C1-C2	1.4187	1.4183
C1-C6	1.3755	1.3758
C2-C3	1.376	1.3766
C3-C4	1.4221	1.4216
C4-C5	1.4376	1.4361
C4-C7	1.424	1.4242
C5-C6	1.4225	1.4225
C5-C10	1.4208	1.4191
C7-C8	1.3751	1.3734
C8-C9	1.4046	1.4169
C9-C10	1.3663	1.3752
C9-S11	1.8409	1.762
S11-O12	1.5798	1.4574
S11-O13	1.5898	1.4634
S11-N14	1.8354	1.678
N14-N15	1.406	1.3915
N15-C17	1.293	1.2926
C17-C19	1.4365	1.4435
C19-C20	1.3671	1.377
C19-S23	1.8145	1.7481
C20-C21	1.427	1.4276
C21-C22	1.3551	1.3698
C21-Br24	1.9215	1.8951
C22-23	1.8032	1.7328

Table 2: Angles values of (E/Z)- N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonohydrazide

Atoms	Bond angles (°)	
	E-isomer	Z-isomer
C2-C1-C6	120.36	120.42
C1-C2-C3	120.56	120.42
C2-C3-C4	120.7	119.9
C3-C4-C5	118.65	119.68
C3-C4-C7	122.02	120.64
C5-C4-C7	119.33	119.68
C4-C5-C6	119.21	119.68
C4-C5-C10	118.75	119.68
C6-C5-C10	122.04	120.64
C1-C6-C5	120.52	119.9
C4-C7-C8	120.77	119.9
C7-C8-C9	118.57	120.42
C8-C9-C10	123.57	120.42
C8-C9-S11	116.58	119.79
C10-C9-S11	119.82	119.79
C5-C10-C9	118.99	119.9
C9-S11-O12	113.03	109.47
C9-S11-O13	106.65	109.47
C9-S11-N14	94.31	109.47
O12-S11-O13	120.21	109.47
O12-S11-N14	106.68	109.47
O13-S11-N14	113.02	109.47
S11-N14-N15	111.21	109.47
N14-N15-C17	117.87	120
N15-C17-C19	120.93	120
H18-C17-C19	115.8	120
C17-C19-C20	128.36	124.76
C17-C19-S23	120.26	124.77
C20-C19-S23	111.38	110.46
C19-C20-C21	113.3	113.51
C20-C21-C22	114.87	113.51
C20-C21-Br24	121.79	123.24
C22-C21-Br24	123.34	123.25
C21-C22-S23	111.36	110.46
C19-S23-C22	89.09	90.83

Table 3: Torsional angles of (E/Z)- N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonohydrazide

Atoms	Torsional angles (°)	
	E-isomer	Z-isomer
C2-C3-C4-C5	179.67	180
C3-C4-C5-C10	179.89	180
C7-C4-C5-C6	-179.64	180
C3-C4-C7-C8	179.99	-180
C10-C5-C6-C1	-179.88	-180
C6-C5-C10-C9	-179.64	-180
C7-C8-C9-S11	179.23	180
S11-C9-C10-S23	-179.31	-180
C8-C9-S11-O12	-135.16	180
C8-C9-S11-O13	-0.91	-60
C8-C9-S11-N14	114.67	60
C10-C9-S11-O13	177.33	120
C10-C9-S11-N14	-67.09	-120
C9-S11-N14-N15	175.87	59.99
O12-S11-N14-N15	60.26	-60
O13-S11-N14-N15	-74	180
S11-N14-N15-C17	157.39	150
N14-N15-C17-C19	177.09	0.01
N15-C17-C19-C20	-179.91	-179.86
N15-C17-C19-S23	0.2	-0.15
C17-C19-C20-C21	-179.84	172.21
S23-C19-S23-C22-C21	0.06	-7.54
C17-C19-S23-C22	179.83	-169.88
C20-C19-S23-C22	-0.08	9.87
C19-C20-C21-Br24	-179.88	-179.29
C20-C21-C22-S23	-0.05	7.54
Br24-C21-C22-S23	179.81	-173.17
C21-C22-S23-C19	0.07	-9.87

3.2.2. The Frontier molecular orbital (FMO) analysis

HOMO/LUMO computation are widely employed to explain the electronic and optical properties of synthesized new inorganic and organic molecules [20]. Interfering of molecular orbitals figured out the bonding orbital as stable MO orbital and non-overlapped antibonding molecular orbital to be destabilized one. Moreover, the Frontier molecular orbital (FMO) analysis help to predict and understand the electronic, reactivity of chemical and optical properties of compounds. FMO analysis was carried out for N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonohydrazide by using the B3LYP method and 6-311G(d,p) level of basis set. The intermolecular charge transfer by an excitation process from the donor (HOMO) to acceptor (LUMO) moiety, and the tendency of the compound with the largest

HOMO that donates an electron to an acceptor with low energy and lowest LUMO that indicate the compound has a tendency to accept electrons [18-20], as shown in Figure 3.

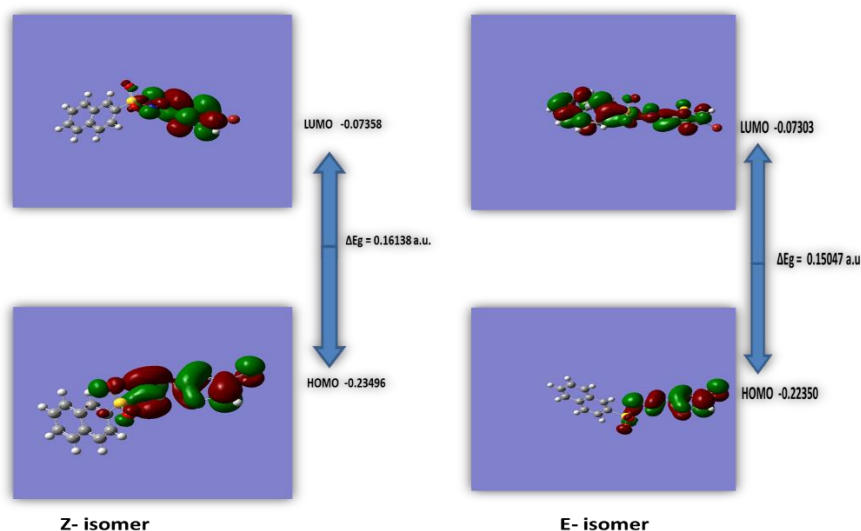


Figure 3. FMO of E and Z - N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonohydrazide

3.2.3. GRD Quantum Parameters

GRD is a theoretical analysis that helps to obtain quantum parameters for the desired molecule like electronegativity (χ), electrophilicity (ω), chemical potential (μ), hardness (η), and softness (σ) indexes. Such parameters can be calculated from HOMO/LUMO energy gap [9-20] as shown in Table 4. The stability of the E-isomer estimated from the chemical potential value, the electronegativity and electrophilicity that describes the electronic attraction, and the hardness value for the compound. Such finding explains that the compound becomes softer with electron transfer.

Koopman's notations:-

- Electronegativity (χ) = $-E_{\text{HOMO}} + (-E_{\text{LUMO}}/2)$
- Chemical potential (μ) = $-x$
- Hardness (η) = $E_{\text{LUMO}} + (-E_{\text{HOMO}}/2)$
- Softness (σ) = $1/\eta$
- Electrophilicity (ω) = $\mu^2/2\eta$

Table 4: Calculated energy values by B3LYP/3-21G.

Basis set	B3LYP/3-21G	
	Z-isomer	E-isomer
E (a.u.)	-4187.56990333	-4187.57381681
E_{HOMO} (eV)	-6.393589635	-6.081747035
E_{LUMO} (eV)	-2.002214527	-1.98724826
ΔE (eV)	4.391375378	4.094498775
χ (eV)	7.3946968985	7.075371165
μ (eV)	-7.3946968985	-7.075371165
η (eV)	1.1945802905	1.0536252575
σ (eV)	0.837114096	0.9491040509
ω (eV)	22.8873448924	23.7564906337

3.2.4 MEP Analysis

MEP analysis is a good tool to determine the possible interaction sites and reactivity of the compound. MEP diagram, as shown in Figure 4, shows the distribution of charges that helps to determine the nature of the chemical bond. The positive moiety describes the nucleophilic sites, while the negative area shows the electrophilic site at the MEP diagram. The results are shown in Figure 4 for both isomers (E and Z) to clarify the amounts of negative charge that are above oxygen atoms SO₂ group. The lone pair of electrons is regarded as nucleophilic sites and is ready to attach electrophilic sites that are represented as an acidic reagent to make the protonation step in the reaction. The positive moiety described by the blue color is localized around hydrogens atoms. The green region shows the zero potential of the structure. The attached ribbon contains color in range -6.891×10^{-2} a.u (reddish color) and $+6.891 \times 10^{-2}$ a.u (dark blue) for E-isomer and Z-isomer between $(-6.090$ to $+6.092) \times 10^{-2}$ a.u as seen in Figure 4.

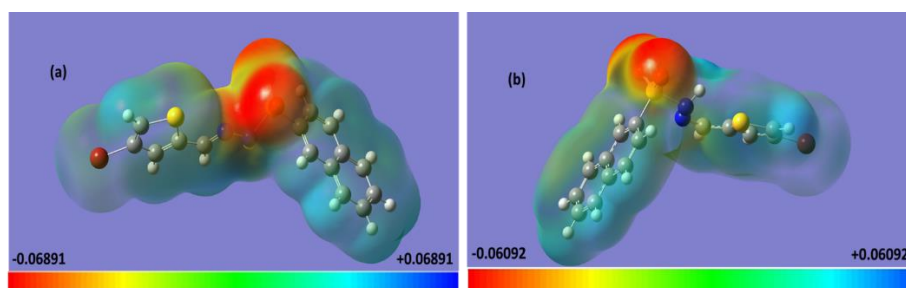


Figure 4. MEP map surface of (a) E, and (b) Z-isomer of the desired ligand.

4. Conclusion

This work involved the synthesis of a new Schiff base compound N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonylhydrazide. The structure of the desired ligand was physicochemical determined via UV-Vis., GC/MS, FT-IR, CHN-EA, ¹H and ¹³C NMR analysis. The E and Z isomers structure of N'-((4-bromothiophen-2-yl) methylene) naphthalene-2-sulfonylhydrazide was subjected successfully to DFT/B3LYP optimization and E/Z-isomerization in the gaseous phase. Several quantum aspects such as HOMO/LUMO, MEP, GRD, and structural parameters (angles, bonds and torsional angles) for both E and Z isomers were calculated and compared. The result supported the E-isomer to be the kinetically favored isomer (less internal repulsion) and Z-isomer as the thermodynamically favored isomer and showed that it is possible to have E to Z isomerization since the energies of formation of each are much closed.

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