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Synthesis, Characterization and Theoretical Calculations of Schiff Base Containing Thiophene Ring System

Ayla BALABAN GÜNDÜZALP[1], Naki ÇOLAK[2,*], Saliha ALTINER[2], Zarife Sibel ŞAHİN[3]

[1] *Department of Chemistry, Faculty of Science, Gazi University, 06600 Ankara, Turkey*

[2]*Department of Chemistry, Faculty of Art and Science, Hitit University, 19040 Çorum,Turkey*

[3] *Department of Energy Systems Engineering, Faculty of Engineering and Architecture, Sinop University, 57000, Sinop, Turkey*

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Abstract

Schiff base titled as 2-[(2-methoxybenzylidene)amino]-6-methyl-4,5,6,7-tetrahydrobenzo [b]thiophene-3-carbonitrile was obtained by condensation of amine with 2-methoxybenzaldehyde. Imine compound was characterized by using elemental analysis, FT-IR (fourier transform infrared), NMR (nuclear magnetic resonance)-APT (attached proton test) techniques and X-ray diffraction analysis. X-ray studies reveal that singly crystals were obtained in triclinic system. The optimized structure, chemical shifts (^{1}H and ^{13}C- NMR) and geometrical parameters (bond lenghts and angles) of Schiff base were obtained by DFT (densital functional theory) with B3LYP (Becke's three parameter hybrid functional combined with the Lee-Yang-Parr correlation functional) using 6-311+G(2d,p) level of theory in Gaussian 09W software. The FMOs (frontier molecular orbitals) levels were also determined by this quantum set.

1. INTRODUCTION

In recent years, 2-aminothiophene derivatives have been seen increasing importance in heterocycles with privileged structures. These compounds are known to have demonstrated broad spectrum of applications as antimicrobial, antibacterial [1], antioxidant [2], antifungal [3] anti-inflammatory [4-6] activators, antipromastigoter [7] and antianxietor [8] etc. For example; Tinoridine is known as nonsteroidal anti-inflammatory drug, olanzepine is an atypical anti-psychotic drug for the medicinal treatment of schizophrenia and bipolar disorder [9-12], thiophene-3-carboxamide is also used as small molecule kinase inhibitor [13,14] and adenosine agonist [15] and decrease hypersensitivity in carageenin-inflamed rats by a central mechanism [16]. Aminothiophene derivatives are used for dye chemistry and agrochemicals [17-19]. Especially, aminothiophenes including azo group have many advantages containing color deeping effect as an intrinsic property leading to better dye ability [20,21]. In addition, the alternative activation methodologies such as mechanochemical mixing [22,23], ultrasonic irradiation [24] and using solar thermal energy [25] have been reported for the synthesis of substituted 2-aminothiophene derivatives.

In this work, we synthesized 2-amino-6-methyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile by one-pot cyclocondensation of 4-methylcyclohexanone with malononitrile and elemental sulphur [26] and then heteroaromatic imine compound by the reaction of amine with 2-methoxybenz aldehyde. The structure of Schiff base was determined using ^{1}H,^{13}C/APT-NMR, FT-IR and X-ray methods. The experimental results were combined with theoretical data which describes molecular features [27-32]. In computational studies, DFT method was also used to compute NMR chemical shifts, geometrical parameters, HOMO and LUMO energy levels by DFT/B3LYP basis set in Gaussian 09 [33].

*Corresponding author, e-mail: nakicolak@hitit.edu.tr

2. EXPERIMENTAL

2.1. Methods

Elemental percentages (C,H,N,S) and melting points were taken by LECO-CHNS-O 932 and Gallenkamp instruments. Vibrational spectra was taken using a Thermo Nicolet 6700 FT-IR spectrometer. ^{1}H,^{13}C/APT-NMR spectra were taken by Bruker AVANCE III using $CDCl_3$ (chloroform). X ray data were obtained by using D8-QUEST diffractometer.

2.2. Synthesis of 2-amino-6-methyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile

Amine compound was synthesized as reported by Gewald [34] in which malononitrile (0.66 g, 0.01 mol), 4-methylcyclohexanone (1.12 g, 0.01 mol) and sulphur (0.32 g, 0.01 mol), morpholine (0.87 g, 0.05 mol) in 15 mL EtOH (ethanol) were mixed at 50 °C until solid product was precipitated. The pure water was added over solution, then crude crystals were picked and purified with EtOH. Yield: 63 %, mp: 138-140 °C [35].

2.3. Synthesis of Schiff base

Schiff base titled as 2-[(2-methoxybenzylidene)amino]-6-methyl-4,5,6,7-tetrahydrobenzo[b] thiophene-3-carbonitrile was obtained by the reaction of amine (1.92 g, 0.010 mol) with 2-methoxybenzaldehyde (1.36 g, 0.01 mol) in 15 mL EtOH for 2 hours reflux at 50 ^{o}C and then left in room conditions. The precipitated crude product was collected, washed and recrystallized with EtOH. The reaction steps of Schiff base is demonstrated in Figure 1. Yield (%): 71, Mp: 169-170 °C. FW: 310.11 g/mol. Anal. calc. for $C_{18}H_{18}N_2OS$(%): C 69.65, H 5.84, N 9.02, S 10.33. Found: C 68.97, H 5.19, N 8.80, S 10.07. FT-IR absorptions (ATR, cm^{-1}) : 3047 cm^{-1}, 2917, 2871 cm^{-1} and 2827 C-H, 2219 CN, 1622 C=N. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): 8.89 (s, 1H, CH=N), 8.26 (d, 1H, Ar-H), 7.46 (t, 1H, Ar-H), 7.04 (t, 1H, Ar-H), 6.92 (d, 1H, Ar-H), 3.91 (s, 3H, OCH_3), 2.64-2.81 ppm and 2.35 (m, 4H, CH_2CH_2), 1.98 (m, 2H, CH_2), 1.48 (m, 1H, CH), 1.13 (d, 3H, CH_3). ^{13}C/APT-NMR (100 MHz, $CDCI_3$, ppm): Positive amplitude: 23.92, 30.25, 33.15, 106,24, 114.65, 123.59; 131.85, 134.49, 159.73, 161.01. Negative amplitude: 21.07; 29.61, 55.83, 110.86, 121.08, 128.06, 133.63, 154.95.

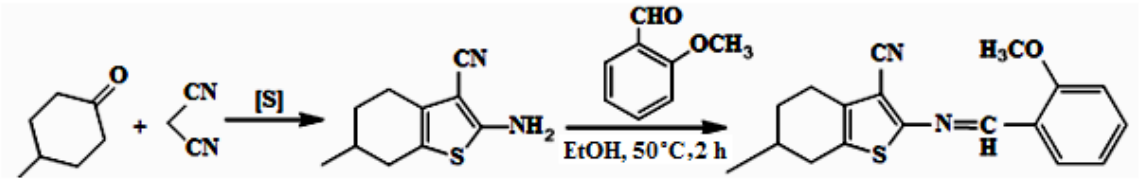


Figure 1. *Reaction steps of Schiff base*

2.4. X-Ray method

In crystal studies, the graphite-monochromatic Mo-K_α radiation was used. The structure of molecule was solved using SHELXS-97 [36,37] and refined by full-matrix least-squares methods on F^2 using SHELXL-97 from within the WINGX [38]. The single crystals in triclinic system with space group P-1 were improved by slowly evaporation of the ethanol used as solvent. The disorder of the benzothiophene group was modeled as two different orientations with occupancy factors of 0.605(5) and 0.395(5), respectively. Molecular and supramolecular diagram was created using MERCURY and PLATON [39,40].

2.5. Computational section

All quantum chemical calculations for Schiff base were performed by 6-311+G(2d,p) level of theory using DFT/B3LYP method in Gaussian 09 software program . DFT calculations were computed to fully optimize

the ground-state structure of the molecule [41-43]. The geometry of Schiff base was optimized to minimize the molecular energies. NMR (^{1}H and ^{13}C) chemical shifts, geometrical parameters (bond lengths and angles) [44] and FMOs (HOMO-2, HOMO-1, HOMO and LUMO, LUMO+1, LUMO+2) levels were calculated by basis set pointed before [45,46].

3. RESULTS AND DISCUSSION

2-Amino-6-methyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile molecule was reacted with 2-methoxybenzaldehyde to obtain 2-((2-methoxybenzylidene)amino)-6-methyl-4,5,6,7-tetrahydrobenzo[b] thiophene-3-carbonitrile. The general synthetic route used to prepare imine compound is illustrated in Figure 1. The structure of Schiff base was clarified by NMR (^{1}H,^{13}C/APT), FT-IR and X-ray spectroscopies. The geometry optimization, NMR chemical shifts, geometrical parameters and FMO energies were computed using B3LYP level of density functional theory using 6311+G (2d,p) basis set. The computational studies were evaluated by Gaussian 09 software [33].

3.1. FT-IR spectra

In FT-IR spectra of 2-((2-methoxybenzylidene)amino)-6-methyl-4,5,6,7-tetrahydrobenzo [b]thiophene-3-carbonitrile (see Figure 2), the arom. C-H stretching vibration was observed at 3047 cm^{-1}, the aliph. C-H stretching was observed at 2917 cm^{-1}, 2871 cm^{-1} and 2827 cm^{-1}, the CN stretching was observed at 2219 cm^{-1}. The imine (CH=N) vibration corresponding to Schiff base formation was newly observed at 1622 cm^{-1}[47-49].

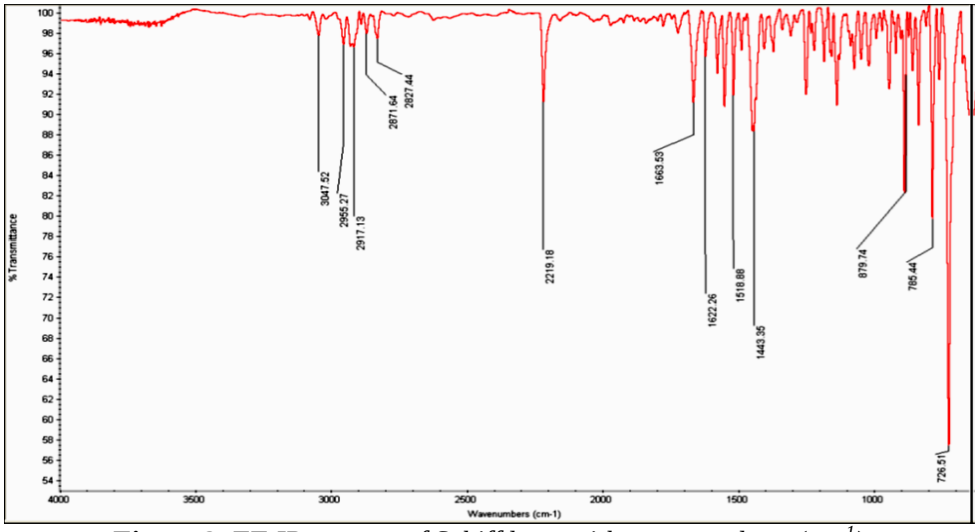
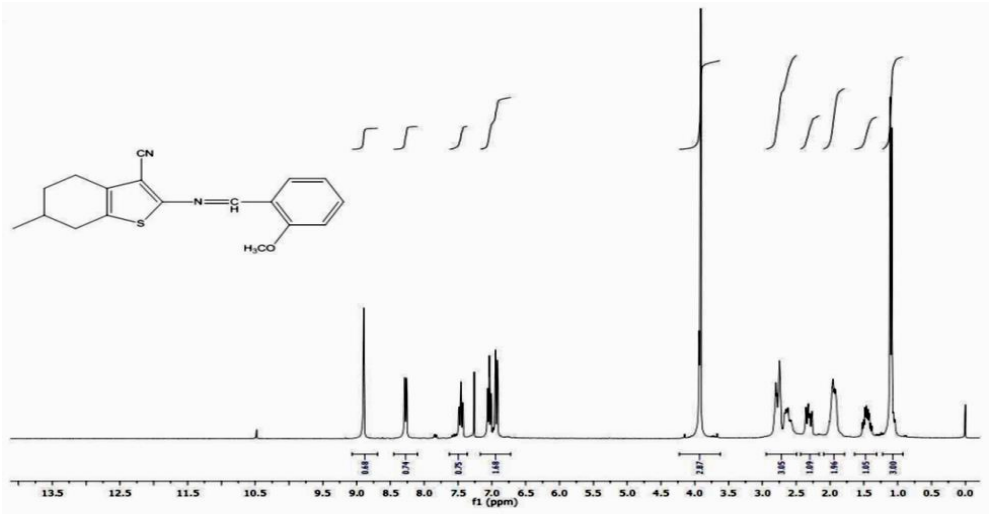


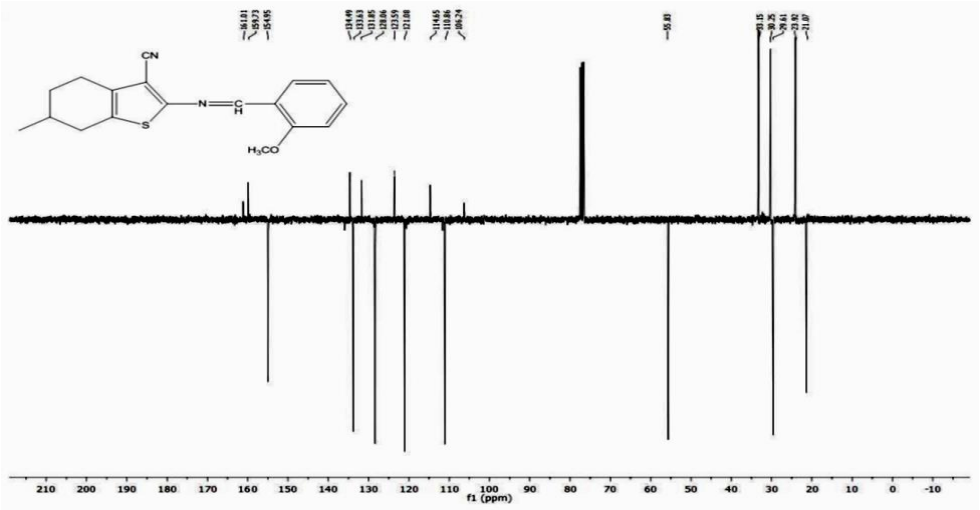
Figure 2. *FT-IR spectra of Schiff base with wavenumbers (cm^{-1})*

3.2. NMR spectra

The ^{1}H-NMR spectra of imine (Figure 3a) have been carried out in $CDCl_3$ at room temperature. The peak at 8.89 distinguishable as a singlet for azomethine (CH=N) proton [50] and aromatic protons resonate at 8.26–6.92 ppm [51], methoxy protons was observed 3.91 ppm as singlet, aliphatic protons are observed at 2.64 ppm and 1.13 ppm, respectively. The attached proton test (APT) experiment that is used as an aid to assignment by separating carbons singals. In the ^{13}C/APT-NMR spectra (Figure 3b), C and CH_2 are observed at positive amplitude, CH and CH_3 are observed at negative amplitude. In order to facilitate the interpretation of the NMR spectra, theoretical calculations were evaluated using B3LYP/6-311+G(2d,p) level of theory with DFT method. The experimental and theoretical NMR data of Schiff base are compared in Table 1.



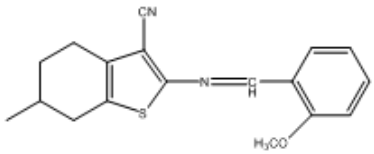
(a)



(b)

Figure 3. *^{1}H-NMR (a) and ^{13}C/APT-NMR (b) spectrum of Schiff base*

Table 1. *The experimental and theoretical NMR (^{1}H and ^{13}C/APT) data of Schiff base*



Schiff base; 2-((2-methoxy benzylidene) amino)-6-methyl-4,5,6,7-tetrahydrobenzo [b]thiophene-3-carbonitrile

Experimental chemical shifts (ppm)

^{1}H-NMR: 8.89 (s, 1H, CH=N), 8.26 (d, 1H, Ar-H), 7.46 (t, 1H, Ar-H), 7.04 (t, 1H, Ar-H), 6.92 (d, 1H, Ar-H), 3.91 (s, 3H, OCH_3), 2.64 (m, 4H, CH_2CH_2), 1.98 (m, 2H, CH_2), 1.48 (m, 1H, CH), 1.13 (d, 3H, CH_3)

^{13}C/APT-NMR: (Positive amplitude) 23.92, 30.25, 33.15, 106.24, 114.65, 123.59, 131.85, 134.49, 159.73, 161.01
(Negative amplitude) 21.07, 29.61, 55.83, 110.86, 121.08, 128.06, 133.63, 154.95

Theoretical chemical shifts (ppm)

^{1}H-NMR: 9.52 (1H, CH=N), 9.04 (1H, Ar-H), 7.83 (1H, Ar-H), 7.41 (1H, Ar-H), 7.04 (1H, Ar-H), 4.03 (3H, O-CH_3), 2.78-3.07 and 2.16 (4H, CH_2CH_2), 1.78 (2H, CH_2), 1.30 (1H, CH), 1.22 (3H, CH_3)

^{13}C/APT-NMR: (Positive amplitude) 28.00, 35.27, 36.89, 111.56, 113.70, 134.514, 137.40, 140.88, 143.32, 153.74, 166.46
(Negative amplitude) 22.64, 34.19, 54.74, 117.64, 124.38, 129.53, 171.91

3.3. Description of the X-ray crystal structure

The crystal structure with atomic numbers is shown in Figure 4. The N2-C16 bond distance [1.148 (3) Å] is typical N≡C triple bond while the N1-C7 bond distance [1.287 (3) Å] is typical N═C double bond.

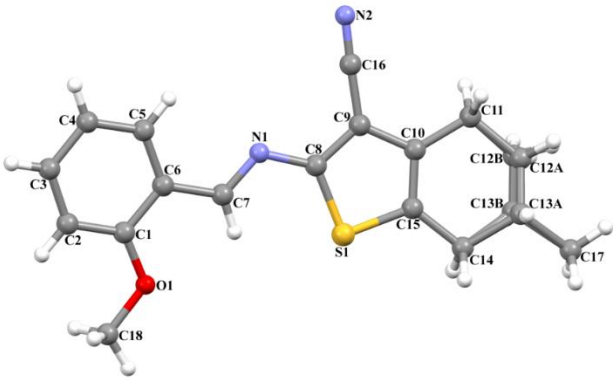


Figure 4. *The optimized structure of Schiff base with the atomic numbers*

Schiff base was singly crystallized in triclinic system with space group P-1. Its molecular geometry possess C_1 point group symmetry. Crystal data of Schiff base are given in Table 2.

Table 2. *Crystal data of Schiff base*

Empirical formula	$C_{18}H_{18}N_2OS$	Z	2
Formula weight(g/mol)	310.40	D_c (g cm^{-3})	1.315
Crystal system	Triclinic	μ (mm^{-1})	0.21
Space group	P-1	T (K)	100
a (Å)	8.6627 (5)	θ range (º)	3.2-28.4
b (Å)	9.3379 (5)	Measured refls.	19191
c (Å)	10.7712 (6)	Independent refls.	3068
α (º)	78.514 (2)	R_{int}	0.027
β (º)	66.684 (3)	S	1.03
γ (º)	86.734 (2)	R1/wR2	0.059/0.139
V (Å^3)	783.89 (8)	$\Delta\rho_{max}/\Delta\rho_{min}$ (eÅ^{-3})	1.16/-1.37

The geometrical parameters (bond lengths and angles) of molecule were obtained by using DFT/B3LYP method with 6-311+G(2d,p) level of theory. The experimental and calculated bond lengthts and angles of compound are presented in Table 3.

Table 3. *Experimental and calculated bond lengths (Å) and angles (º)*

Assign.	Exp.	Calc.*	Assign.	Exp.	Calc.*	Assign.	Exp.	Calc.*
			bond lengths (Å)					
C10—C15	1.357 (3)	1.362	C1—C6	1.410 (3)	1.414	C8—C9	1.379 (3)	1.385
C10—C11	1.502 (3)	1.505	C8—S1	1.739 (2)	1.769	C1—O1	1.363 (3)	1.362
C9—C10	1.434 (3)	1.434	C15—S1	1.731 (2)	1.745	C3—C4	1.392 (4)	1.392
C14—C15	1.502 (3)	1.499	C8—N1	1.381 (3)	1.361	C18—O1	1.437 (3)	1.423
C9—C16	1.433 (3)	1.421	C7—N1	1.287 (3)	1.285	C5—C6	1.404 (3)	1.402
C16—N2	1.148 (3)	1.154	C6—C7	1.454 (3)	1.455	C4—C5	1.381 (3)	1.384
			bond angles (°)					
O1—C1—C2	123.9 (2)	123.6	O1—C1—C6	116.2 (2)	116.4	C2—C1—C6	119.9 (2)	120.1
C3—C2—C1	120.1 (2)	119.9	C2—C3—C4	120.7 (2)	120.8	C5—C4—C3	119.4 (2)	119.4
C4—C5—C6	121.1 (2)	121.3	C5—C6—C7	121.4 (2)	121.1	C1—C6—C7	119.9 (2)	120.2
C5—C6—C1	118.7 (2)	118.6	N1—C7—C6	122.3 (2)	121.9	C9—C8—N1	125.1 (2)	124.0
C9—C8—S1	109.8 (17)	109.5	N1—C8—S1	125.1 (17)	126.5	C10—C15—C14	125.8 (2)	125.2
C8—C9—C16	122.6 (2)	122.7	C8—C9—C10	114.0 (2)	114.2	C16—C9—C10	123.4 (2)	123.1
C15—C10—C9	111.8 (2)	114.2	C14—C15—S1	122.0 (18)	122.6	C15—C10—C11	121.9 (2)	122.2
N2—C16—C9	177.9 (3)	177.4	C9—C10—C11	126.2 (2)	125.4	C7—N1—C8	119.1 (2)	122.6
C1—O1—C18	117.8 (18)	118.9	C15—S1—C8	92.2 (11)	91.7			

Schiff base crystals are connected by intermolecular π···π interactions between thiophene rings of neighbouring molecules and C-H···S hydrogen bonds. C14 atom acts as hydrogen bonding donor, via atom H14B, to atom S1 in the molecule at (-x, -y+1, -z+1), forming centrosymmetric $R_2^2(8)$ ring. The combination of these interactions produces one-dimensional framework which is running parallel to the [100] direction (Figure 5 and Table 4).

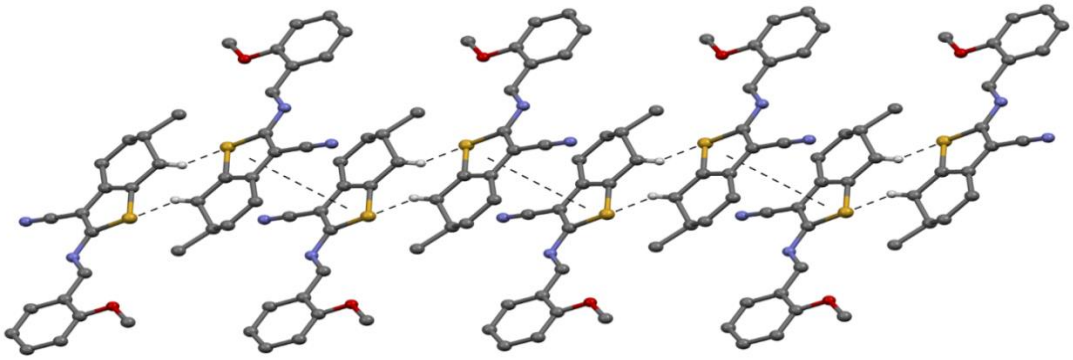


Figure 5. *The crystal structure of molecule with intermolecular interactions*

Table 4. *Intermolecular interaction distances (Å)*

Hydrogen bond distances

D-H···A	D-H	H···A	D···A	D-H···A
C7-H7···S1	0.93	2.56	3.022 (2)	111
C14-H14B···S1^{i}	1.02(3)	2.86 (3)	3.460 (3)	118

π···π interactions distances

Cg(I)	Cg(J)	Cg-Cg	Perpendicular distance
Cg(1)	Cg(1)^{ii}	4.063	3.689

Symmetry codes: (i) −x, −y+1, −z+1, (ii) 1-x, 1-y, 1-z; Cg(1)=S1/C8/C9/C10/C15

3.4. Frontier Molecular Orbitals (FMOs)

FMOs (HOMOs and LUMOs) are the frontier molecular orbitals taking part in the chemical reactions and have importance in electronic and optical properties of compound [52]. The HOMOs are electron donors representing the ability to donate an electron and LUMOs are electron acceptors representing the ability to obtain an electron. The HOMO and LUMO levels are directly related to the ionization potentials and electron affinities [53]. The FMOs surfaces and energies were obtained using DFT method with B3LYP/6-311+G(2d,p) level of theory and presented in Figure 6. The HOMOs (HOMO, HOMO-1, HOMO-2) energies were calculated as -0.302 eV, -0.321 eV, -0.346 eV, respectively and the LUMOs (LUMO, LUMO-1, LUMO-2) energies were also calculated as -0.229 eV, -0.171 eV, -0.161 eV, respectively.

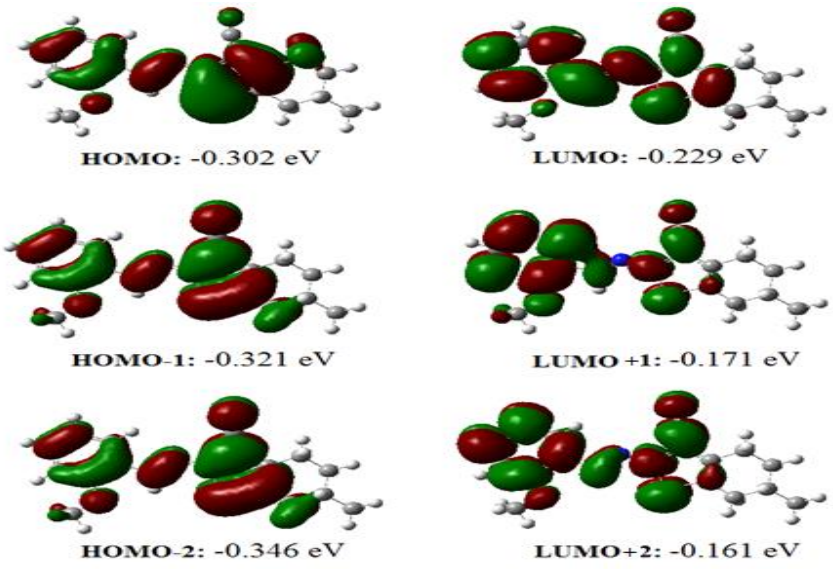


Figure 6. *FMO surfaces and energies of Schiff base*

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SUPPLEMENTARY MATERIAL

X-ray data have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 1420260. Copies of data may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax:+44-1223-336033;e-mail:deposit@ccdc.cam.ac.uk or www:http://www.ccdc. cam.ac.uk).

CONFLICT OF INTEREST

No conflict of interest was declared by the authors

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