

STRUCTURE OF ORGANIC
COMPOUNDSSynthesis, Molecular Structure and Quantum Chemical Studies
of *N*-(2-Fluorophenyl)-1-(5-Nitrothiophen-2-yl)methanimineHasan Tanak^{a,*}, Şadiye Karataş^a, Seher Meral^b, and Ayşen Alaman Ağar^b^a Department of Physics, Faculty of Arts and Sciences, Amasya University, Amasya, 05100 Turkey^b Department of Chemistry, Faculty of Arts and Sciences, Ondokuz Mayıs University, Samsun, Turkey

*e-mail: hasantanak@gmail.com

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Abstract—*N*-(2-Fluorophenyl)-1-(5-nitrothiophen-2-yl)methanimine has been synthesized and characterized by single-crystal X-ray determination. Molecular geometry from X-ray determination of the title compound have been compared using the Hartree-Fock (HF) and density functional theory (B3LYP) method with 6-311++G(*d,p*) basis set. Calculated results show that density functional theory (DFT) at B3LYP/6-311++G(*d,p*) level can well reproduce the structure of the title compound. Besides, Mulliken atomic charges, molecular electrostatic potential, and chemical reactivity descriptors (chemical hardness, chemical softness, electronegativity) were also predicted theoretically.

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INTRODUCTION

Schiff bases compounds are used as starting materials in the synthesis of important drugs, such as antibiotics and antiallergic, antiphlogistic, and antitumor substances [1–4]. They are of great interest in many fields of chemistry and biochemistry because of their versatile metal binding ability [5, 6]. Moreover, Schiff bases also have biological activities such as antimicrobial, antifungal, antitumor activities, and herbicidal properties [7–11]. On the industrial scale, they have a wide range of applications, such as in dyes and pigments [12].

Recently, fluoro-containing organic compounds play an important role for the pharmaceutical as well as agrochemical industries, because of their often unique biological properties, such as the increased membrane permeability, enhanced hydrophobic binding and stability against metabolic oxidation [13–16].

Owing to the biological and industrial significance of the Schiff bases, we have synthesized derivatives of Schiff base, *N*-(2-fluorophenyl)-1-(5-nitrothiophen-2-yl)methanimine (Fig. 1), for the first time. The aim

of this study is to investigate the structural and physico-chemical properties of the title compound using density functional theory (DFT) and Hartree-Fock (HF) calculations. In this work, the molecular structure, atomic charges, molecular electrostatic potential (MEP), chemical reactivity descriptors (chemical hardness, chemical softness, electronegativity) have been investigated on the title compound.

EXPERIMENTAL
AND COMPUTATIONAL METHODS*Synthesis*

N-(2-Fluorophenyl)-1-(5-nitrothiophen-2-yl)methanimine (Fig. 1) was prepared by refluxing a mixture of a solution containing 5-nitrothiophene-2-carboxyaldehyde (20.1 mg, 0.128 mmol) in ethanol (20 mL) and a solution containing 2-fluoroaniline (14.2 mg, 0.128 mmol) in ethanol (20 mL). The reaction mixture was stirred for 5 h under reflux. Single crystals of the title compound for X-ray analysis were obtained by slow evaporation of an ethanol solution (yield 60%; m.p. 402–404 K).

Crystal Data and Structure Determination

All measurements were performed at room temperature (296 K) using a BRUKER APEX II diffractometer with the graphite monochromated MoK_α radiation ($\lambda = 0.71073 \text{ \AA}$). Correction for absorption, by comparison of the intensities of equivalent reflections, was applied using Bruker SAINT software [17]

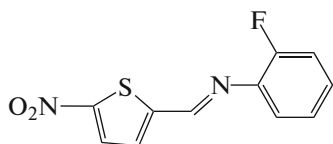


Fig. 1. Chemical diagram of *N*-(2-fluorophenyl)-1-(5-nitrothiophen-2-yl)methanimine.

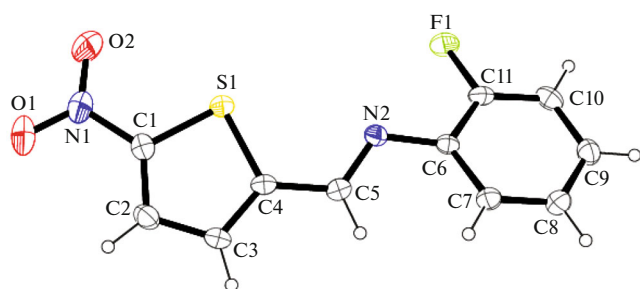


Fig. 2. Ortep-3 diagram of the *N*-(2-fluorophenyl)-1-(5-nitrothiophen-2-yl)methanimine. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

and cell parameters were determined by using Bruker SAINT software [17]. Calculations to solve the structure and to obtain derived results were carried out with the SHELXS 97 computer program [18]. The refinement carried out by full matrix least squares method on the positional and anisotropic temperature parameters of nonhydrogen atoms. All hydrogen atoms were placed in calculated positions and treated using a rid-

ing model ($C-H = 0.93 \text{ \AA}$, fixing the bond lengths). The figures have prepared by using the program ORTEP-3 for windows [19]. The crystallographic data and refinement parameters for the structural analyses are as follows: $C_{11}H_7FN_2O_2S$, $M_r = 250.25$, block and yellow, size $0.12 \times 0.16 \times 0.19 \text{ mm}$, space group *Fdd2*, orthorhombic, $a = 13.173(2) \text{ \AA}$, $b = 51.417(8) \text{ \AA}$, $c = 6.4553(11) \text{ \AA}$, $V = 4372.2(12) \text{ \AA}^3$, $Z = 16$, $D_x = 1.521 \text{ Mg m}^{-3}$, $\mu = 0.30 \text{ mm}^{-1}$, $3.2^\circ \leq \theta \leq 26^\circ$, measured reflections = 7897, reflections with $I > 2\sigma(I) = 1931$, $R_{int} = 0.041$, $GOF = 1.13$, $R_1 (I > 2\sigma(I)) = 0.0544$, $wR_2 (I > 2\sigma(I)) = 0.1296$, number of refined parameters = 154, $-16 \leq h \leq 16$, $-62 \leq k \leq 62$, $-7 \leq l \leq 7$, $T_{min}/T_{max} = 0.5408/0.7457$, $\Delta\rho_{max}/\Delta\rho_{min} = 0.34/-0.36 \text{ e/\AA}^3$.

CCDC no. 1899068 contains the supplementary crystallographic data for the compound reported in this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223-336033; e-mail: deposit@ccdc.cam.ac.uk].

Computational Methods

The DFT/B3LYP and HF calculations have been performed using the Gaussian 09W [20] program package. The output files were visualized by means of GaussView 5.0 program [21]. For searching the reactive sites of the title compound, the MEP was performed using the B3LYP/6-311++G(*d,p*) method.

RESULTS AND DISCUSSION

Crystal Structure

The Schiff base compound, an Ortep-3 view of which is shown in Fig. 2, crystallizes in the orthorhombic space group *Fdd2* with $Z = 16$ in the unit cell. Although the molecule structure is not planar, the ring systems are planar. The dihedral angle between the thiophene and phenyl rings is $21.5(2)^\circ$. The imino group is coplanar with the nitro-thiophene ring as it can be shown by the $N2-C5-C4-C3$ torsion angle is $176.7(4)^\circ$. The length of the $C5=N2$ double bond is $1.275(5) \text{ \AA}$, it is slightly shorter than standard $1.28 \text{ \AA}$ value of $C=N$ double bond and consistent with the related structures [22, 23]. Selected bond lengths, bond angles and torsion angles are given in Table 1. They are within normal ranges and are comparable with those in related structures [24–26].

In the crystal structure, molecules are linked together by $C-H \cdots F$ intermolecular hydrogen bonds, namely $C5-H5 \cdots F1$ (symmetry code: $x, y, z - 1$). The $C5-H5 \cdots F1$ (symmetry code: $x, y, z - 1$) hydrogen bond links the molecules into a $C(6)$ [27] chain along the c axis (Fig. 3). The crystal structure also features $\pi-\pi$ stacking interactions with distance of $Cg1 \cdots Cg2 = 3.721(3) \text{ \AA}$ (symmetry code = $1/2 - x, -y, -1/2 + z$),

Table 1. Selected molecular structure parameters

Parameters	Experimental	DFT	HF
Bond lengths, $\text{\AA}$			
S1–C1	1.716(4)	1.734	1.722
S1–C4	1.721(4)	1.741	1.725
F1–C11	1.355(5)	1.347	1.321
N2–C5	1.276(6)	1.277	1.250
N2–C6	1.410(5)	1.397	1.404
N1–O1	1.222(6)	1.226	1.187
N1–O2	1.222(6)	1.228	1.187
N1–C1	1.432(6)	1.442	1.440
Bond angles, deg			
C1–S1–C4	89.6(2)	89.33	89.20
C5–N2–C6	118.3(4)	120.66	120.09
C3–C4–S1	111.9(3)	112.33	112.84
C5–C4–S1	121.1(3)	121.18	121.59
N2–C5–C4	121.3(4)	121.65	121.44
F1–C11–C10	118.2(4)	118.74	118.81
F1–C11–C6	118.3(4)	118.82	119.03
Torsion angles, deg			
C6–N2–C5–C4	179.1(3)	176.44	178.08
C8–C7–C6–N2	−179.1(4)	−177.23	−177.80
C5–N2–C6–C11	−154.7(4)	144.78	136.68
F1–C11–C10–C9	178.6(4)	−179.75	−179.93
O2–N1–C1–S1	(4.8(8))°	0.104	−0.047
O1–N1–C1–C2	(6.5(9))°	0.136	−0.002

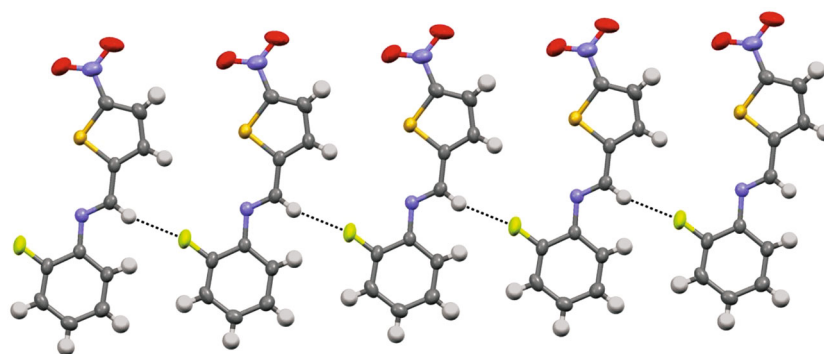


Fig. 3. A view of the intermolecular interactions in the title compound. The intramolecular interactions are shown as dashed lines.

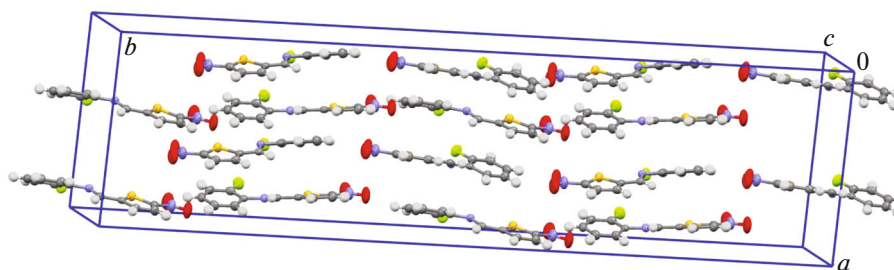


Fig. 4. Packing diagram of *N*-(2-fluorophenyl)-1-(5-nitrothiophen-2-yl)methanimine.

where *Cg*1 and *Cg*2 are the centroids of C1–C4/S1 and C6–C11 rings, respectively. The details of the hydrogen bonds are summarized in Table 2. A packing diagram of the title compound is shown in Fig. 4.

Optimized Geometry

The optimized geometric parameters (bond length, bond angles and torsion angles) of the title compound have been calculated using the DFT/B3LYP and HF methods with the 6-311++G(*d,p*) basis set. Theoretical geometric parameters are listed in Table 1. When the X-ray structure of the title compound is compared with its optimized counterpart, conformational discrepancies are observed between them. The molecular structure of the title compound is not planar. The dihedral angle between the C1–C4/S1 and C6–C11 rings is 21.5(2)° for X-ray, whereas the dihedral angle has been calculated as 40.22° for B3LYP and 46.69° for HF. The orientation of the nitro group is defined by the torsion angles O2–N1–C1–S1 (4.8(8)°) and O1–N1–C1–C2 (6.5(9)°). These torsion angles have been calculated at 0.104° and 0.136° for the B3LYP and at –0.047° and –0.002° for the HF, respectively. The imine C5=N2 bond length is 1.275(5) Å in X-ray structure, whereas the corresponding value in optimized geometries are 1.277 Å for B3LYP and 1.250 Å for HF.

A logical method for globally comparing the structures obtained from the calculations is by superimposing the molecular skeleton on that obtained from X-ray diffraction, giving an root mean square error (RMSE) of 0.286 Å for B3LYP and 0.343 Å for HF (Fig. 5). According to results, it is seen that the B3LYP calculation well reproduce the geometry of the title compound.

Atomic Charges

The Mulliken atomic charges of the title compound were calculated using the DFT/B3LYP and HF methods with 6-311++G(*d,p*) basis set. Calculated results are presented in Table 3. The Mulliken atomic charges show that the C1 atom attached to nitro group have bigger negative atomic charges. This behavior can be the result of the electronegativity of the nitro group. Besides, the atomic charge values of the N1, N2, S1, and F1 atoms have negative atomic charges. On the other hand, all hydrogen atoms have positive atomic charges.

Table 2. Hydrogen-bond geometry (Å, deg)

D–H...A	D–H	H...A	D...A	D–H...A
C5–H5...F1 ⁱ	0.93	2.37	3.277(5)	164

Symmetry codes: (i) *x*, *y*, *z* – 1.

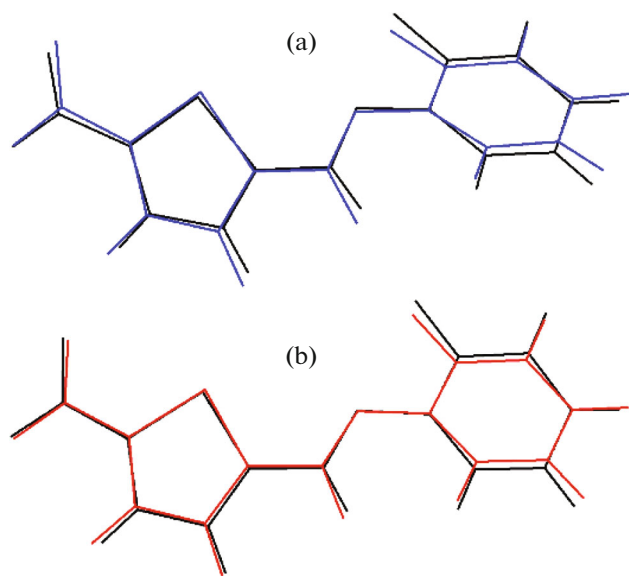


Fig. 5. Atom-by-atom superimposition of the structures calculated (a) DFT (blue); (b) HF (red) over the X-ray structure (black) for the title compound.

Molecular Electrostatic Potential

MEP is related to the electronic density and is a very useful descriptor in understanding sites for electrophilic and nucleophilic reactions [28]. To predict reaction path ways for electrophilic and nucleophilic process for the title compound, MEP surface was obtained at the B3LYP/6-311++G(*d,p*) optimized geometry.

The negative potential regions (red colour) of MEP were related to electrophilic reactivity and the positive potential regions (blue colour) to nucleophilic reactivity shown in Fig. 6. The negative regions are found around the O1 and O2 atoms of nitro group, N2 atom

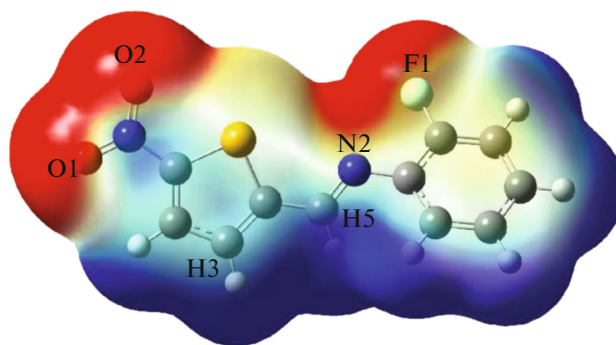


Fig. 6. Molecular electrostatic potential map calculated at B3LYP/6-311++G(*d,p*) level.

and F1 atom. The MEP values are -0.053 a.u. for O2, -0.051 a.u. for O1, -0.032 a.u. for N2, and -0.028 a.u. for O2. Thus, it can be predicted that an electrophile would preferentially attack of the title molecule at O1 and O2 positions. However, a maximum positive MEP value is $+0.053$ a.u. for the region between H3 and H5 atoms.

Chemical Reactivity Descriptors

In order to explore the energetic and chemical reactivity behaviours, some physico-chemical properties such as total molecular energies, HOMO and LUMO energies, HOMO–LUMO gap, the ionization potential (I), the electron affinity (A), the chemical hardness (η), softness (S), and the electronegativity (χ) were calculated using the DFT/B3LYP and HF methods with the 6-311++G(*d,p*) basis set. The calculated results are given in Table 4.

Hard species having a large HOMO–LUMO gap will be more stable and less reactive than soft species having a small HOMO–LUMO gap [29]. By using

Table 3. Mulliken atomic charges (e) of the title compound

Atoms	DFT	HF	Atoms	DFT	HF
C1	−0.755031	−0.859211	H2	0.197505	0.236721
C2	0.667845	0.380171	H3	0.082448	0.130516
C3	0.381180	0.089687	H4	0.164272	0.205976
C4	0.259519	0.187939	H5	0.178751	0.213871
C5	−0.158893	−0.220394	H6	0.168827	0.202658
C6	0.122354	0.038297	H7	0.205201	0.249805
C7	0.061531	0.036322	F1	−0.164027	−0.224663
C8	0.065371	−0.147925	N1	−0.196532	−0.120456
C9	−0.219982	−0.553389	N2	0.149669	0.176082
C10	0.376932	0.163385	O1	0.015328	−0.042529
C11	−0.326870	−0.192182	O2	−0.041023	−0.076912
H1	0.247254	0.293188	S1	−0.237371	−0.166959

Table 4. The calculated total energies, molecular orbital energies, softness, hardness, and electronegativity for the title compound

Parameters	HF	DFT
Total energy, a.u.	−1176.25131367	−1181.47919990
E_{HOMO} , eV	−8.244	−8.172
E_{LUMO} , eV	−5.217	−5.374
HOMO–LUMO gap	−3.027	−2.798
Ionization potential, I , eV	8.244	8.172
Electron affinity, A , eV	5.217	5.374
Electronegativity, χ , eV	−6.7205	−6.773
Chemical softness, S , eV ^{−1}	0.75675	0.6995
Chemical hardness, η , eV	1.5135	1.399

HOMO and LUMO energy values for a molecule, the chemical hardness, chemical softness and electronegativity can be calculated as follows: $\eta = (I - A)/2$, $S = 1/2\eta$, and $\chi = (I + A)/2$. The ionization energy and electron affinity can be expressed through HOMO and LUMO orbital energies as $I = -E_{\text{HOMO}}$ and $A = -E_{\text{LUMO}}$ [30]. The chemical hardness (η), softness (S), and the electronegativity (χ) calculated are 1.399 eV, 0.699 eV^{−1}, and −6.773 eV for B3LYP and 1.513 eV, 0.756 eV^{−1}, and −6.720 eV for HF, respectively. When it is compared to the related Schiff base compound in the literature, the calculated value of η of the title compound is smaller than that of (*E*)-*N*-[4-bromo-2-(trifluoromethoxy)phenyl]-1-(5-nitrothiophen-2-yl)methanimine (1.650 eV) [23]. It is concluded that the title molecule is less stable and more reactive than (*E*)-*N*-[4-bromo-2-(trifluoromethoxy)phenyl]-1-(5-nitrothiophen-2-yl)methanimine.

CONCLUSIONS

N-(2-Fluorophenyl)-1-(5-nitrothiophen-2-yl)methanimine has been synthesized and characterized by single-crystal X-ray determination. The molecular structure, Mulliken atomic charges, molecular electrostatic potential, and chemical reactivity descriptors have been calculated using the DFT/B3LYP and HF methods with 6-311++G(*d,p*) basis set. According to results, it is seen that the DFT/B3LYP calculation well reproduce the geometry of the title compound. The Mulliken charge analysis show that the atomic charge values of the N1, N2, S1, and F1 atoms have negative atomic charges. The MEP map shows that the negative potential sites are on F1, N2, O1, and O2 atoms while the positive potential sites are around the hydrogen atoms. We note that an electrophile would preferentially attack of the title molecule at O1 and O2 positions. The chemical hardness of the title compound have been predicted theoretically.

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