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DFT Studies on Physicochemical Properties and Spectral Data of 2-Thiophene Carboxylic Acid Thiourea Derivatives †

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Abstract: This study focused on examining five synthesized 2-thiophene carboxylic acid thiourea derivatives that have significant pharmaceutical applications. These compounds exhibit antibacterial properties against both bacterial and fungal strains. In this study, Density Functional Theory (DFT) calculations were performed, and the electronic properties of the investigated compounds, such as ionization potential, electron affinity, and electronic excitation energies, were calculated and compared to determine the beneficial features of these potential future medications. A vibrational analysis of the considered structures was performed, and the experimental FT-IR ATR spectra of the solid powders are presented.

Keywords: thiourea derivative; DFT; FT-IR

1. Introduction

The emergence of drug-resistant microorganisms has become a severe public health problem nowadays. Due to evolutionary adaptation of bacteria and fungi to actual medication, the treatment of the infectious diseases has become inefficient, leading to higher doses of drugs usage. The urgent need for new antimicrobial compounds has turned on the interest in thioureides of 2-thiophene carboxylic acid which are considered ones of the most promising drugs for application in future therapeutic schemes. In this work, five synthesized thiourea derivatives compounds with pharmaceutical important applications was studied. The general chemical formula of the 2-thiophene carboxylic acid thiourea derivative is down below presented.

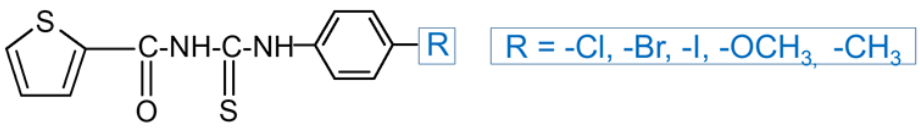

Figure 1. Base chemical structure of 2-thiophene carboxylic acid thiourea derivative with the substitute group marked in blue color.

Such compounds have antimicrobial activity against bacterial and fungal strains. Moreover, they come to offer significant advantages in future treatment strategies [1,2]. In this research, Density Functional Theory (DFT) calculations was used and the five molecules was described in 6-311G(d,p) basis set, [3]. The optimized molecular structure and the energy of individual molecular orbitals were predicted for thioureide derivatives. For studied molecules, electronic properties such as ionization potential, electron affinity, and

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electronic excitation energies were calculated and compared in order to establish the beneficial traits of this possible future pharmaceuticals. Also, by DFT the vibrational frequencies, thermodynamic properties and NMR Chemical Shifts of molecules were obtained. To show how this calculation method matches well with the experimental data, we compared the FT-IR experimental data of the thioureide derivatives with the calculated frequencies of the proposed molecules. We found the candidates of which experimental FT-IR spectra are well matched with DFT calculation. Based on these computations, we obtained properties and key molecular descriptors related to chemical reactivity and spectral behavior.

2. Materials and Methods

2.1. Materials

In Table 1 are presented the name of the chemical structures considered in this study accordingly with IUPAC (International Union of Pure and Applied Chemistry) nomenclature and the corresponding abbreviation used in plots and in the text of the manuscript.

Table 1. The IUPAC name and the corresponding abbreviation used for the chemical structures considered in this work.

IUPAC Name	Abbreviation
1-(4-chlorophenyl)-3-(thiophene-2-carbonyl) thiourea	1-Cl
1-(4-bromophenyl)-3-(thiophene-2-carbonyl) thiourea	2-Br
1-(4-iodophenyl)-3-(thiophene-2-carbonyl) thiourea	3-I
1-(4-methoxyphenyl)-3-(thiophene-2-carbonyl) thiourea	4-OCH3
1-(4-methylphenyl)-3-(thiophene-2-carbonyl) thiourea	5-CH3

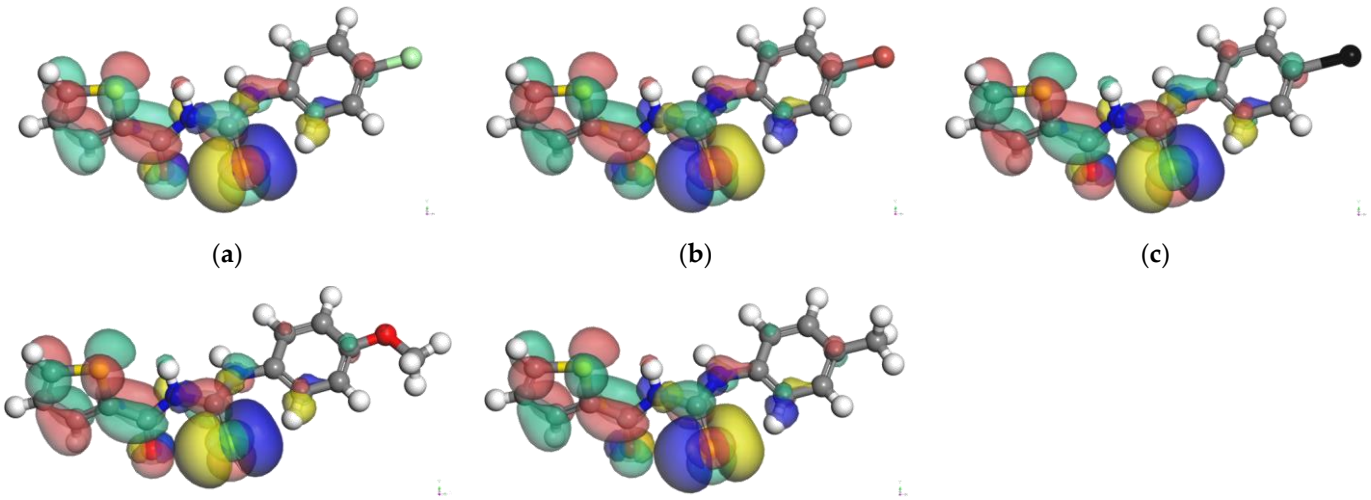
2.2. Methods

Density Functional Theory (DFT) calculations was used to calculate various properties of studied chemical structures, including electronic structure, energies, and geometries. For packing analysis, DFT was used to accomplish vibrational analysis and predict IR spectra.

Fourier-transform infrared spectroscopy (FT-IR) spectra were obtained at room temperature by Nicolet iS10 FT-IR spectrometer in the range from 4000 cm^{-1} to 600 cm^{-1}. The spectra were acquired by fast average of 32 scans with spectral resolution of 4 cm^{-1} in attenuated total reflectance, (ATR) mode.

3. Results

The analysis of the frontier orbitals, the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO), indicates the shapes and distributions of these orbitals, showing where the electron density is concentrated in the considered molecules. This graphical representation is presented in Figure 2. Some reactivity descriptors resulting from HOMO-LUMO analysis are given in Table 1.



(**a**) (**b**) (**c**)

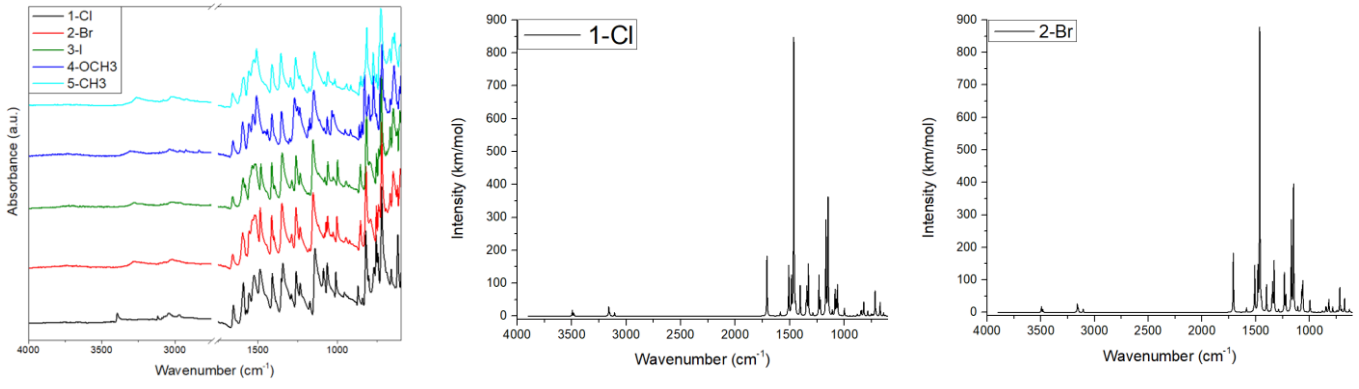
(**d**) (**e**)

Figure 2. The plot of the frontier orbitals HOMO and LUMO (for an isovalue of 0.03) for the studied chemical structures. The surfaces are drawn by yellow/blue and green/red colors for HOMO and LUMO, respectively, where the negative/positive blobs are represented by light and dark colors. The grey, red, blue, yellow and white spheres represent the carbon, oxygen, nitrogen, sulfur and hydrogen atoms, respectively. Light-green, brown and black sphere are chlorine, bromine and iodine halogen atoms.

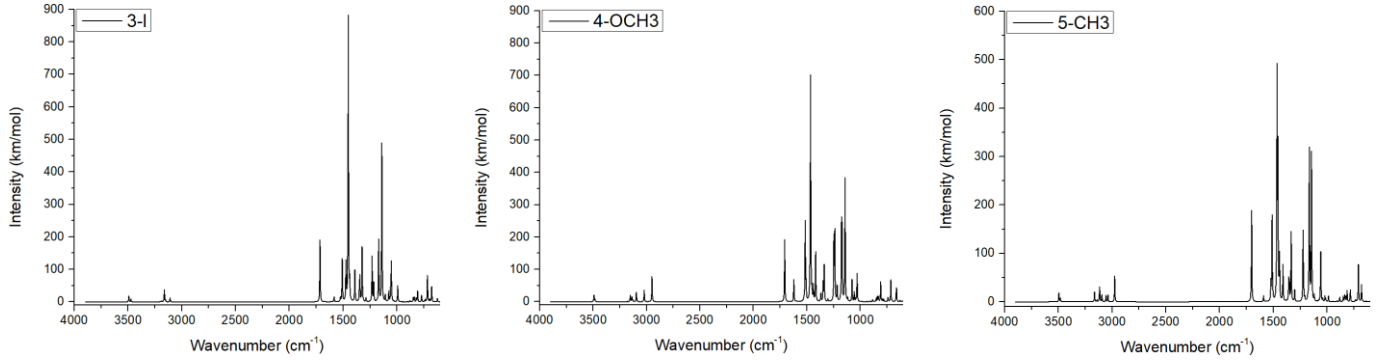
Table 2. The HOMO and LUMO energy, energy gap, chemical potential, chemical hardness, chemical softness, electronegativity and electrophilicity of studied chemical structures in vacuum. The presented values are in eV.

Descriptor	Formula	1-Cl	2-Br	3-I	4-OCH3	5-CH3
E(HOMO)	(−I)	−0.189106	−0.189465	−0.192689	−0.181173	−0.181763
E(LUMO)	(−A)	−0.107816	−0.108136	−0.110981	−0.099413	−0.10192
Band Gap	ΔE = I − A	0.08129	0.081329	0.081708	0.08176	0.079843
Chemical Potential	(I + A)/2 = μ	−0.148461	−0.1488005	−0.151835	−0.140293	−0.1418415
Electronegativity	−(I + A)/2 = χ	0.148461	0.1488005	0.151835	0.140293	0.1418415
Hardness	(I − A)/2 = η	0.040645	0.0406645	0.040854	0.04088	0.0399215
Softness	1/(2*η) = S	12.30163612	12.29573707	12.23870368	12.23091977	12.52457949
Electrophilicity	(μ^2)/(2*η) = ω	0.271136284	0.272247154	0.28214945	0.240730502	0.251982154

Further, for the considered compounds the ATR FT-IR spectra and the simulated vibration paterns are presented in Figure 3.



(**a**) (**b**) (**c**)



(**d**) (**e**) (**f**)

Figure 3. Experimentaly obtained ATR FT-IR spectra for studied chemical structures—(**a**) and corresponding vibration spectra obtained by simulation (**b**–**f**).

4. Conclusions

The energy gap between HOMO and LUMO (referred to as the HOMO-LUMO gap) is significant in predicting a molecule's stability, thus a smaller gap typically indicates higher reactivity. The presented results suggest that the gap decrease in order: 5-CH3 < 1-Cl < 2-Br < 3-I < 4-OCH3, that indicate a greater stability for 4-OCH3. According to Pearson's principle, the structure 4-OCH3 is less reactive, while 5-CH3 is more reactive. Therefore, for the halogenated structures the reactivity of the molecule is influenced by the electronegativity of the halogen attached.

A higher electrophilicity corresponds to a lower energy of the LUMO, which implies a greater ability to accept electrons, so the electrophilicity index (ω) increases following the order: 4-OCH3 < 5-CH3 < 1-Cl < 2-Br < 3-I.

As presented, there are similarities but also many differences between the spectra recorded experimentally and the simulated ones. Simulations often assume a single conformation, while experiments may capture multiple conformers or dynamic effects. Simulations typically use harmonic approximations, while real molecular vibrations can exhibit anharmonic behavior, leading to discrepancies in frequency predictions. Also, the method, the basis set and environment conditions has a strong influence in spectra prediction.

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