

Sensing Activity of a New Generation of Thiourea-based Receptors; A Theoretical Study on the Anion Sensing

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A theoretical density functional theory (DFT) study was performed on a series of the neutral N-phenylthiourea substituents (*p*-OC₂H₅, *p*-CH₃, *m*-CH₃, H, *p*-Cl, *p*-Br, *m*-Cl, and *p*-NO₂) as the sensor of acetate and fluoride anions. The hydrogen bond character was analyzed as a scale of the sensing activity. It was confirmed that hydrogen bond between the *p*-NO₂ derivatives of N-phenylthiourea and fluoride anion is stronger than acetate in CH₃CN as a solvent. Therefore, N-(*p*-nitrophenyl) thiourea acts as a better chemical sensor in fluoride detection. For the investigation of the N-H bond properties, donor-acceptor interaction energy through the natural bond orbital analysis was obtained. Topology analysis by estimation of the kinetic and potential energy densities of the hydrogen bonds was done. Finally, some correlations between the quantum chemistry descriptors and sensing characters of the studied compounds were obtained and analyzed.

Keywords: Hydrogen bond, Chemosensor, Fluoride, Thiourea, Substituent effect

INTRODUCTION

Chemosensors, biosensors and nanosensors are of the most interesting subjects in chemistry, due to the new needs in the medical diagnostics, biological and environmental processes such as detection of the unapproved drugs, toxic substances and chemical warfare agents [1]. Anionic species involved in the most of the biological phenomena and many organic sensors have been designed to detect the anions such as fluoride, cyanide, phosphate, nitrate, acetate, *etc.* [2-6]. Purposeful design and synthesis of the various molecules (or macromolecules) which can be used as the efficient chemosensors are important [7-11].

Hydrogen bonding is the most popular and important interaction in biological and chemical systems [12-14]. Anions can be selectively identified by the strong hydrogen bond formation. Therefore, in designing the anionic sensors, having an active site to form hydrogen bonds with anions is a principal purpose. An acceptable selectivity is observed for the chemosensors which have the proton donor

groups such as N-H and O-H. These electronegative atoms establish stronger hydrogen bond interactions with anions such as, fluoride and acetate [15-17]. Among the numerous anions, fluoride plays an essential role in a broad range of the biological, medical and chemical processes and has dental care application [18-21]. Moreover, acetate anion is a usual anion in biology, which is seen in the form of acetyl coenzyme A in organisms [22]. Therefore, detection of these ions by a chemosensor has a high degree of importance. To this end, numerous molecules such as urea [23,24], thiourea [25,26], amides [27-29], indole [30], pyrrole [31,32] and thioamides [33,34] have been synthesized and their chemosensing behavior through the hydrogen bond analysis were confirmed.

Since urea and thiourea functional groups act as hydrogen bond donors, they have been extensively utilized in chemosensors [35-37]. Indeed, they are able to form two hydrogen bonds with the anions to get a Y-shaped orientation [38-40]. On the other hand, by incorporation of the N-H unit into an aromatic subunit, it is reasonable to have a charge transfer due to the anion bindings. The presence of an electron-withdrawing substituent such as

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NO_2 causes an increase in the sensibility of the chemosensor. As the mentioned substituents induce more acidic character on the binding subunit and polarize the N-H bond, they facilitate the hydrogen bond interaction. However, because of more acidic nature, thiourea ($\text{pK}_a = 21.1$ in DMSO) has stronger interaction with anions than urea ($\text{pK}_a = 26.9$) [41] and its interaction with very strong basic anions like F^- increases the N-H deprotonation.

Our purpose of this study is the investigation of the hydrogen bond properties as a key factor in the sensing of the substituted N-phenylthiourea (Fig. 1). Fluoride and acetate anions have been considered for this aim. In this work, we theoretically studied the formation of hydrogen bonds between the various derivatives of N-phenylthiourea (**1**) including thiourea unit with acetate and fluoride anions in acetonitrile as the solvent. The presence of electron withdrawing nitro substituent at the phenyl moiety causes the formation of anionic charged species due to more polarization of the N-H bond. Moreover, various analyses such as natural bond orbital (NBO), and atoms in molecules (AIM) help us to have an insight into the hydrogen bond as a scale of the anion sensing.

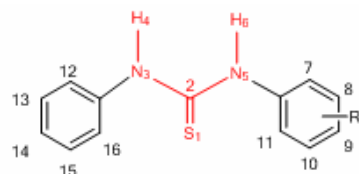
COMPUTATIONAL DETAILS

The structures of the **1(a-h)**, with/without acetate and fluoride as the guest species have been optimized using two kinds of hybrid functionals, M06-2X and ωB97XD [42], by employing the 6-311++G(d,p) basis set [43] as implemented in the Gaussian 09 program [44]. The complexation of the various derivatives of N-phenylthiourea with acetate and fluoride anions was investigated in order to evaluate the sensing properties of these compounds. The interaction energies of these complexes have been computed according to Eq. (1).

$$\Delta E = E(\mathbf{1}@\text{Anion}) - E(\mathbf{1}) - E(\text{anion}) \quad (1)$$

Where $E[\mathbf{1}@\text{anion}]$ is the total energy of the N-phenylthiourea derivatives-acetate and fluoride anions complexes and $E(\mathbf{1})$ and $E(\text{anion})$ are the total energy of the isolated (**1**) and fluoride or acetate anions, respectively.

Chemical hardness, η , electronic chemical potential, μ_e , and electrophilicity, ω , have been calculated. For investigation of the electronic charge distribution and



R= H(1a), *m*-Me(1b), *m*-Cl(1c), *m*-OEt(1d),
p-Me(1e), *p*-Cl(1f), *p*-Br(1g), *p*-NO₂(1h)

Fig. 1. Structure, atom numbering and the position of the substituent in the substituted N-phenylthiourea derivatives.

hydrogen bond (H-bond) formation, NBO analysis was applied [45]. Through this analysis, donor-acceptor interactions between the thiourea units and anions have been studied. The topological properties [46,47], electron location function (ELF) [48-52], localized orbital locator (LOL) [53,54] and quantum theory of atoms in molecules (QTAIM) analyses were performed using the MultiWFN 3.1 software [55].

RESULTS AND DISCUSSION

Structural and Energy Analyses

The substituted N-phenylthiourea acts as a ligand in this complexation reaction. Figure 2 shows the optimized structures of the complexes at the $\omega\text{B97XD}/6\text{-311++G(d,p)}$ level of theory. Thermodynamic properties of the complexation reaction have been calculated and reported in Table 1.

The energies of complexation are different in various substituents. This may be interpreted by their different electron withdrawing properties on the N-phenylthiourea. In Table 1, from top to down, the electron withdrawing character of the substituents and $\Delta E_{\text{complexation}}$ has been increased. *p*-OEt and *p*-NO₂ groups show the minimum and maximum values of the electron withdrawing character and $\Delta E_{\text{complexation}}$, respectively. As a result, the complexation causes a development in the positive charge of H4 and H6 atoms which has a synergy effect on the strong complexation. This effect is more remarkable when the substituents have more electron withdrawing character. Accordingly, the complexation of *p*-NO₂ substituent with the studied anions is more probable than other derivatives.

Table 1 shows the calculated complex formation

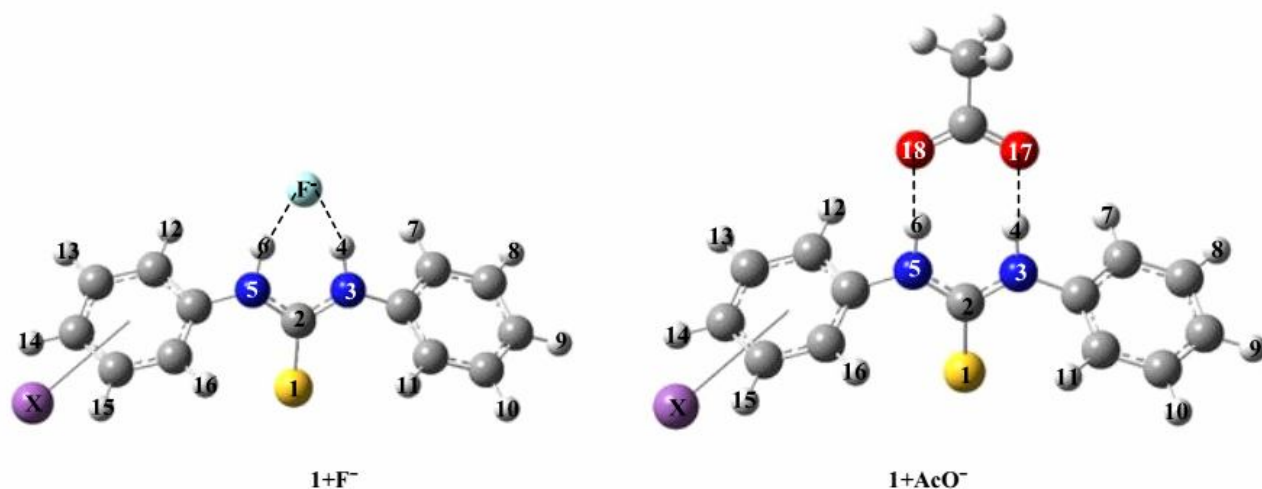


Fig. 2. Optimized structures and atom numbering of the complexes of the N-phenylthiourea derivatives with acetate and fluoride anions at the ω B97XD/6-311++G(d,p) level of the theory.

Table 1. Calculated Thermodynamic Properties and Binding Constants of the Complexation Reactions

| Derivative | $-\Delta E_{\text{intra}}_{\text{ction}}$ (kcal mol ⁻¹) | | $-\Delta G_{\text{intra}}_{\text{ction}}$ (kcal mol ⁻¹) | | $-\Delta S_{\text{intra}}_{\text{ction}}$ (cal mol ⁻¹ K ⁻¹) | | K_f | |
|---------------------------|------------------------------------------------------------------------|----------------|------------------------------------------------------------------------|----------------|---------------------------------------------------------------------------------------|----------------|----------|----------------|
| | M062X | ω B97XD | M062X | ω B97XD | M062X | ω B97XD | M062X | ω B97XD |
| <i>p</i> -OEt | 17.01 | 14.83 | 10.40 | 7.42 | 23.76 | 24.62 | 42.12E+6 | 27.83E+4 |
| <i>p</i> -Me | 17.53 | 16.10 | 11.26 | 6.88 | 19.50 | 30.26 | 18.01E+7 | 11.04E+4 |
| <i>m</i> -Me | 18.71 | 16.17 | 10.71 | 9.47 | 27.41 | 23.28 | 71.70E+6 | 87.97E+5 |
| H | 18.78 | 16.53 | 12.49 | 7.53 | 22.53 | 29.23 | 14.55E+8 | 33.11E+4 |
| <i>p</i> -Br | 18.96 | 16.86 | 13.32 | 8.54 | 21.60 | 27.39 | 58.25E+8 | 18.20E+5 |
| <i>p</i> -Cl | 19.42 | 16.80 | 12.68 | 8.72 | 24.30 | 26.63 | 19.89E+8 | 24.85E+5 |
| <i>m</i> -Cl | 19.80 | 17.30 | 11.34 | 9.40 | 30.71 | 26.20 | 20.75E+7 | 78.87E+5 |
| <i>p</i> -NO ₂ | 20.92 | 18.51 | 16.43 | 10.20 | 23.29 | 27.76 | 1.12E+12 | 30.01E+6 |
| <i>p</i> -OEt | 13.31 | 15.13 | 3.03 | 3.13 | 32.73 | 36.48 | 16.82E+1 | 19.81E+1 |
| <i>p</i> -Me | 16.00 | 15.27 | 5.40 | 3.16 | 30.23 | 37.27 | 91.87E+2 | 20.66E+1 |
| <i>m</i> -Me | 16.27 | 15.29 | 4.37 | 4.11 | 37.20 | 34.02 | 16.09E+2 | 10.36E+2 |
| H | 16.40 | 15.48 | 4.89 | 3.27 | 36.14 | 37.32 | 38.61E+2 | 24.87E+1 |
| <i>p</i> -Br | 16.74 | 15.97 | 4.57 | 3.81 | 38.05 | 36.92 | 22.63E+2 | 61.88E+1 |
| <i>p</i> -Cl | 17.17 | 15.90 | 4.60 | 5.21 | 38.95 | 32.36 | 23.84E+2 | 65.87E+2 |
| <i>m</i> -Cl | 17.45 | 16.32 | 3.94 | 4.25 | 42.22 | 36.94 | 77.46E+1 | 13.13E+2 |
| <i>p</i> -NO ₂ | 18.33 | 17.64 | 7.42 | 4.85 | 34.96 | 39.04 | 27.74E+4 | 36.31E+2 |

constants (K_f), too. Comparison between the K_f values shows that fluoride has larger K_f than acetate anion, may be due to strong H-bond interaction. Moreover, among of different derivatives of N-phenylthiourea, **1h** with *p*-NO₂ substituent has the largest K_f . These observations confirm that N-phenylthiourea with *p*-NO₂ substituent is the best

chemosensor for fluoride anion. Figure 3 shows changes in K_f of the fluoride and acetate anions with all derivatives of diphenylthiourea.

NBO Analysis

Table 2 shows the natural charge distribution on H4 and

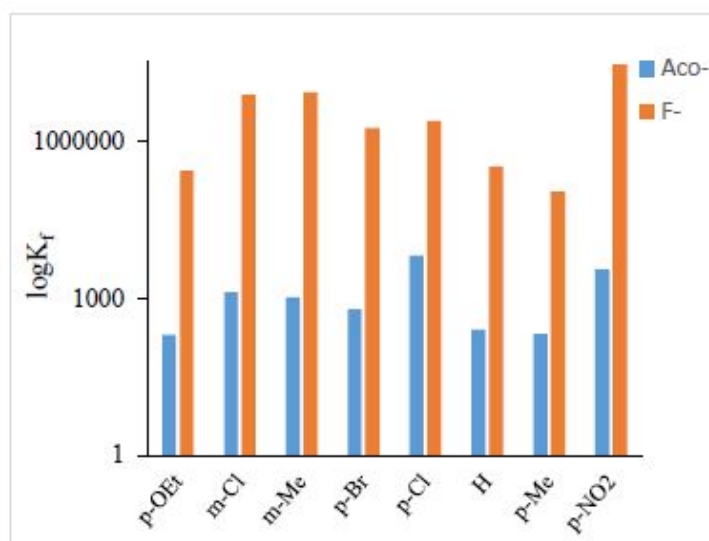


Fig. 3. Calculated K_f for the different N-phenylthiourea derivatives with acetate and fluoride anions calculated by the ω B97XD functional.

Table 2. Natural Atomic Charges of the Complexes on H4 and H6 Atoms at the ω B97XD/6-311++G(d,p) level of the theory

| | 1 | | 1+AcO⁻ | | 1+F⁻ | |
|---------------------------|----------------|----------------|--------------------------|----------------|------------------------|----------------|
| | H ₄ | H ₆ | H ₄ | H ₆ | H ₄ | H ₆ |
| <i>p</i> -OEt | 0.4290 | 0.424 | 0.450 | 0.450 | 0.457 | 0.456 |
| <i>p</i> -Me | 0.4290 | 0.425 | 0.452 | 0.451 | 0.456 | 0.455 |
| <i>m</i> -Me | 0.4290 | 0.426 | 0.450 | 0.450 | 0.456 | 0.456 |
| H | 0.4300 | 0.425 | 0.450 | 0.450 | 0.456 | 0.456 |
| <i>p</i> -Br | 0.4300 | 0.427 | 0.451 | 0.450 | 0.456 | 0.458 |
| <i>p</i> -Cl | 0.4300 | 0.427 | 0.451 | 0.450 | 0.458 | 0.458 |
| <i>m</i> -Cl | 0.4302 | 0.428 | 0.452 | 0.451 | 0.457 | 0.458 |
| <i>p</i> -NO ₂ | 0.4310 | 0.427 | 0.453 | 0.452 | 0.456 | 0.457 |

H6 atoms. In the case of fluoride anion, H4 and H6 atoms show more positive character than acetate anion, where H6 supports a more positive charge.

On the other hand, the evaluation of the donor-acceptor interaction of the N3-H4 and N5-H6 bonds shows the interesting results. The comparison of $E(2)$ values of the N-H bond interaction with the anions shows that each N-H bond displays a different behavior. In the case of acetate, electron releasing groups such as *p*-OEt, *p*-Me and *m*-Me decrease the interaction of the $Lp_{O18} \rightarrow \sigma^*_{N5-H6}$, while electron withdrawing groups such as *p*-NO₂, *m*-Cl, *p*-Cl and *p*-Br strengthen it. In the fluoride complexes, similar to acetate, the same treatment can be seen for $Lp_{F17} \rightarrow \sigma^*_{N5-H6}$ interaction, while a regular behavior cannot be observed for $Lp_{O17} \rightarrow \sigma^*_{N3-H4}$ interaction. The interaction of $Lp_{F17} \rightarrow \sigma^*_{N3-H4}$ shows an exactly opposite behavior respect to $Lp_{F17} \rightarrow \sigma^*_{N5-H6}$, therefore fluoride anion shows a more regular and predictable behavior than acetate anion.

It is well worth to answer this question that why $Lp_{F17} \rightarrow \sigma^*_{N3-H4}$ and $Lp_{F17} \rightarrow \sigma^*_{N5-H6}$ interactions show an opposite response to the electron releasing and withdrawing groups? H6 is closer to the substituents than H4 atom, as indicated in

Table 2, in the presences of the electron withdrawing groups, H6 supports a more positive charge (about 0.001e). Therefore, electron transfer from $Lp_{F17} \rightarrow \sigma^*_{N5-H6}$ is significant. On the other hand, an increase in this transfer causes a decrease in the $Lp_{F17} \rightarrow \sigma^*_{N3-H4}$ interaction. However, positive charge of H6 in the presences of electron donating groups is lower, showing an opposite behavior (Table 3).

Band Gap Analysis

In order to evaluate and compare the sensing activity of the studied N-phenylthiourea derivatives, change in the band gap for the proposed sensors and their complexes with the anions have been calculated. The calculated data have been shown in Table 4. Based on the obtained values, the difference between the HOMO and LUMO levels, band gap energy, of the substituents have been decreased after complexation with the anions, confirming their sensing activity. Since the calculated values of ΔE_g for *H*, *m*-Cl, *p*-NO₂ and *m*-Me are lower than the other substituents, it can be concluded that their corresponding compounds act as a better chemosensors in AcO⁻ and F⁻ sensing.

Table 3. Calculated Perturbation Energy of the Donor-acceptor Interactions (kcal mol⁻¹) between the Lone Pair of the Anions and σ^*_{N-H} at the ω B97XD/6-311++G(d,p) Level

| | 1+AcO ⁻ | | 1+F ⁻ | |
|---------------------------|-----------------------------------------|-----------------------------------------|-----------------------------------------|-----------------------------------------|
| | $Lp_{O17} \rightarrow \sigma^*_{N3-H4}$ | $Lp_{O18} \rightarrow \sigma^*_{N5-H6}$ | $Lp_{F17} \rightarrow \sigma^*_{N3-H4}$ | $Lp_{F17} \rightarrow \sigma^*_{N5-H6}$ |
| <i>p</i> -OEt | 27.01 | 25.64 | 22.76 | 14.98 |
| <i>p</i> -Me | 26.20 | 26.95 | 20.91 | 17.96 |
| <i>m</i> -Me | 26.66 | 26.99 | 20.12 | 19.21 |
| H | 27.44 | 27.05 | 19.68 | 19.68 |
| <i>p</i> -Br | 27.34 | 28.26 | 17.19 | 23.26 |
| <i>p</i> -Cl | 27.33 | 28.14 | 17.46 | 22.87 |
| <i>m</i> -Cl | 28.48 | 27.97 | 16.11 | 24.91 |
| <i>p</i> -NO ₂ | 29.12 | 30.45 | 13.60 | 31.96 |

Table 4. HOMO and LUMO Analysis of the N-phenylthiourea Derivatives and their Band Gap Before and After Complexation with the Anions at the ω B97XD/6-311++G(d,p) Level of Theory (in a.u.)

| | 1 | | | 1+AcO⁻ | | | | 1+F⁻ | | | |
|---------------------------|-------------------|-------------------|----------------|--------------------------|-------------------|----------------|--------------|------------------------|-------------------|----------------|--------------|
| | E _{HOMO} | E _{LUMO} | E _g | E _{HOMO} | E _{LUMO} | E _g | ΔE_g | E _{HOMO} | E _{LUMO} | E _g | ΔE_g |
| <i>p</i> -OEt | -30.06 | 2.65 | 32.70 | -28.42 | 3.87 | 32.29 | -0.41 | -28.44 | 3.91 | 32.35 | -0.35 |
| <i>p</i> -Me | -30.40 | 2.43 | 32.83 | -28.52 | 3.61 | 32.14 | -0.70 | -28.50 | 3.34 | 31.84 | -1.00 |
| <i>m</i> -Me | -30.41 | 2.68 | 33.09 | -28.57 | 3.67 | 32.24 | -0.85 | -28.57 | 3.09 | 31.66 | -1.43 |
| H | -30.35 | 2.84 | 33.19 | -28.58 | 3.34 | 31.92 | -1.27 | -28.65 | 3.13 | 31.78 | -1.41 |
| <i>p</i> -Br | -30.53 | 1.53 | 32.06 | -28.70 | 2.78 | 31.48 | -0.58 | -28.75 | 2.58 | 31.33 | -0.73 |
| <i>p</i> -Cl | -30.56 | 1.59 | 32.16 | -28.69 | 2.89 | 31.58 | -0.58 | -28.76 | 2.70 | 31.45 | -0.70 |
| <i>m</i> -Cl | -30.52 | 2.42 | 32.94 | -28.83 | 2.89 | 31.73 | -1.22 | -28.86 | 2.49 | 31.35 | -1.60 |
| <i>p</i> -NO ₂ | -30.99 | 4.19 | 26.80 | -29.25 | -3.53 | 25.72 | -1.08 | -29.25 | -3.60 | 25.65 | -1.15 |

Table 5. Calculated Topological Properties of the Hydrogen Bonds between the Anions and N-phenylthiourea Derivatives (in a.u.)

| | AcO⁻ | | | | | | F⁻ | | | | | |
|---------------------------|------------------------|----------------|-------------------|----------------|--------|----------------|----------------------|----------------|-------------------|----------------|--------|----------------|
| | ρ | | $-\nabla^2(\rho)$ | | $-V/G$ | | ρ | | $-\nabla^2(\rho)$ | | $-V/G$ | |
| | M062X | ω B97XD | M062X | ω B97XD | M062X | ω B97XD | M062X | ω B97XD | M062X | ω B97XD | M062X | ω B97XD |
| <i>p</i> -OEt | 0.0440 | 0.0420 | 0.0326 | 0.0308 | 1.1112 | 1.0871 | 0.0408 | 0.0438 | 0.0377 | 0.0349 | 1.0492 | 1.0946 |
| <i>p</i> -Me | 0.0437 | 0.0431 | 0.0325 | 0.0313 | 1.1082 | 1.0966 | 0.0467 | 0.0451 | 0.0410 | 0.0380 | 1.0919 | 1.0846 |
| <i>m</i> -Me | 0.0437 | 0.0428 | 0.0325 | 0.0312 | 1.1076 | 1.0941 | 0.0429 | 0.0460 | 0.0390 | 0.0385 | 1.0642 | 1.0899 |
| H | 0.0441 | 0.0426 | 0.0326 | 0.0310 | 1.1122 | 1.0928 | 0.0474 | 0.0463 | 0.0413 | 0.0387 | 1.0976 | 1.0915 |
| <i>p</i> -Br | 0.0454 | 0.0438 | 0.0329 | 0.0316 | 1.1267 | 1.1035 | 0.0768 | 0.0486 | 0.0489 | 0.0400 | 1.3050 | 1.1058 |
| <i>p</i> -Cl | 0.0453 | 0.0438 | 0.0329 | 0.0316 | 1.1259 | 1.1029 | 0.0739 | 0.0483 | 0.0486 | 0.0399 | 1.2864 | 1.1043 |
| <i>m</i> -Cl | 0.0460 | 0.0439 | 0.0330 | 0.0316 | 1.1332 | 1.1049 | 0.0773 | 0.0495 | 0.0490 | 0.0406 | 1.3082 | 1.1113 |
| <i>p</i> -NO ₂ | 0.0485 | 0.0459 | 0.0334 | 0.0323 | 1.1623 | 1.1249 | 0.1525 | 0.0553 | -0.0096 | 0.0410 | 2.0844 | 1.1663 |

QTAIM Analysis

Topological analysis by QTAIM method was carried out for the hydrogen bonds at the center of the complexation and the corresponding results are reported in Table 5.

Calculated electron density values of the H4-X and H6-X (X = F⁻, AcO⁻) bonds (0.03 a.u.), indicate a strong hydrogen bonding. On the other hand, the amounts of -V/G ratios, the ratio of the potential energy density to the kinetic energy

density, are larger than one, confirming a non-covalent character of these bonds. The electron density of the fluoride is higher than that of acetate anion, showing that the H...F bond can be stronger than H...O bond in acetate. Higher degree of electron density and -V/G ratio of the H6-F bond are obtained for **1h** than the other substituents, which are compatible with the larger amount of K_f for the F⁻

in comparison to AcO⁻.

It is reasonable to consider the electron density of NH...F bond as a function of the interaction energy of $LP_{F17} \rightarrow \sigma^*_{N5-H6}$, as shown in Fig. 4. According to this figure, an increase in the electron withdrawing character of the substituents elevates gradually, the electron density of the H6...F17 and interaction energy of the $LP_{F17} \rightarrow \sigma^*_{N5-H6}$,

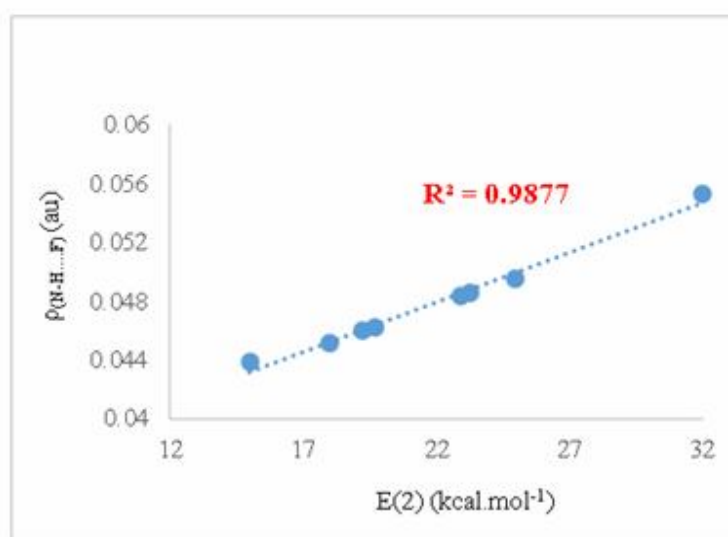


Fig. 4. Linear correlation of the electron density of the H6...F17 bond and the interaction energy of $LP_{F17} \rightarrow \sigma^*_{N5-H6}$.

Table 6. Vibrational Frequencies (cm⁻¹) of the N-H Bonds of the N-phenylthiourea Derivatives Before and After Complexation

| | 1 | | 1+AcO⁻ | | 1+F⁻ | |
|---------------------------|----------|---------------------|--------------------------|---------------------|------------------------|---------------------|
| | M062X | ωB97XD ^a | M062X | ωB97XD ^a | M062X | ωB97XD ^a |
| <i>p</i> -OEt | 3585.1 | 3601.4 | 2952.1 | 3112.2 | 3092.6 | 3163.6 |
| <i>p</i> -Me | 3577.6 | 3601.2 | 2959.0 | 3031.2 | 3027.9 | 3135.5 |
| <i>m</i> -Me | 3584.1 | 3604.9 | 2962.0 | 3103.7 | 3060.0 | 3126.9 |
| H | 3592.4 | 3598.6 | 2968.2 | 3093.7 | 2994.7 | 3124.1 |
| <i>p</i> -Br | 3560.3 | 3598.9 | 2928.8 | 3080 | 3218.8 | 3120.6 |
| <i>p</i> -Cl | 3566.3 | 3602.8 | 2925.8 | 3100.9 | 3206.6 | 3120.2 |
| <i>m</i> -Cl | 3592.8 | 3601.8 | 2929.6 | 3069.1 | 3225.7 | 3123.2 |
| <i>p</i> -NO ₂ | 3551.1 | 3594.5 | 2864.6 | 3031.2 | 3421.9 | 3126.2 |

^aWithout correction factor

making the hydrogen bond stronger.

Spectral Analysis

The study of the vibrational frequencies and absorption properties are important in the hydrogen bond evaluation and sensing activity. According to Table 6, the stretching vibration frequency of the N-H bonds of thiourea functional group has been decreased after complexation. This trend has been experienced by both of the electron donating and withdrawing groups. For example, when R = *p*-NO₂, the vibration frequency at the ω B97XD method is 3594.5 cm⁻¹

which has been reduced after the complexation to 3031.2 and 3126.2 cm⁻¹ for acetate and fluoride anion, respectively. Indeed, the anion electronegativity in the complexes causes a decrease in the electron density of the N-H bonds and stretching vibration frequency. Also, this trend has been confirmed by QTAIM analysis. For instance, when R = *p*-NO₂, the electron density of NH bond is 0.3344 a.u. which has been decreased to 0.0459 and 0.0553 a.u. in the presence of the acetate and fluoride anions, respectively.

A red shift in the absorption spectra has been observed from 241 nm to 327 nm and 330 nm in the presence of the

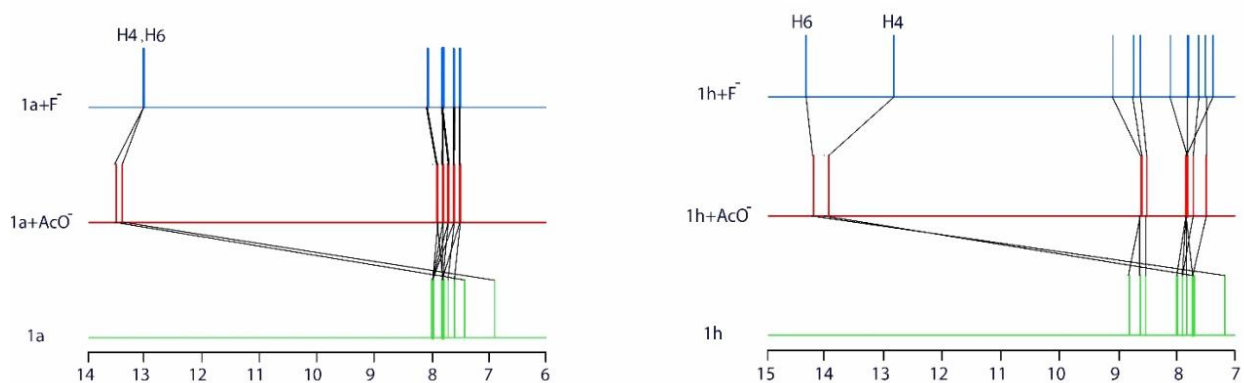


Fig. 5. The comparison of the proton chemical shifts of **1a** and **1h** before and after the complexation with acetate and fluoride anions at the ω B97XD/6-311++G(d,p) level.

Table 7. Calculated λ_{\max} (nm) of the N-phenylthiourea Derivatives Before and After Complexation with the Fluoride and Acetate Anions

| | 1 | 1+AcO⁻ | 1+F⁻ |
|---------------------------|----------|--------------------------|------------------------|
| <i>p</i> -OEt | 241.3 | 249.4 | 247.7 |
| <i>p</i> -Me | 244.0 | 243.7 | 244.6 |
| <i>m</i> -Me | 241.0 | 247.7 | 248.0 |
| H | 241.5 | 239.5 | 245.1 |
| <i>p</i> -Br | 253.2 | 259.6 | 249.7 |
| <i>p</i> -Cl | 252.6 | 258.4 | 248.5 |
| <i>m</i> -Cl | 244.4 | 258.1 | 250.4 |
| <i>p</i> -NO ₂ | 296.2 | 327.7 | 330.2 |

acetate and fluoride anions, respectively (Table 7). Considering Table 7, **1h** having the *p*-NO₂ substituent, displays the maximum red shift during the sensing of the fluoride and acetate anions.

The calculated NMR spectra showed that H4 and H6 protons are shifted about 6 ppm to the upfield after the complexation with acetate and fluoride anions, as shown in Fig. 5. According to this figure, chemical shifts of the H4

and H6 protons are nearly equal in the case of **1a**, while in the case of **1h**, H6 is more positive than H4 and it appears in the upper field than H4, especially in the presence of the fluoride anion. The investigation of the natural charges in Table 2 and donor-acceptor interactions of the N3-H4 and N5-H6 bonds in Table 3, verify that the fluoride anion induces a more positive charge on the H4 and H6 atoms of the complexes than the acetate anion.

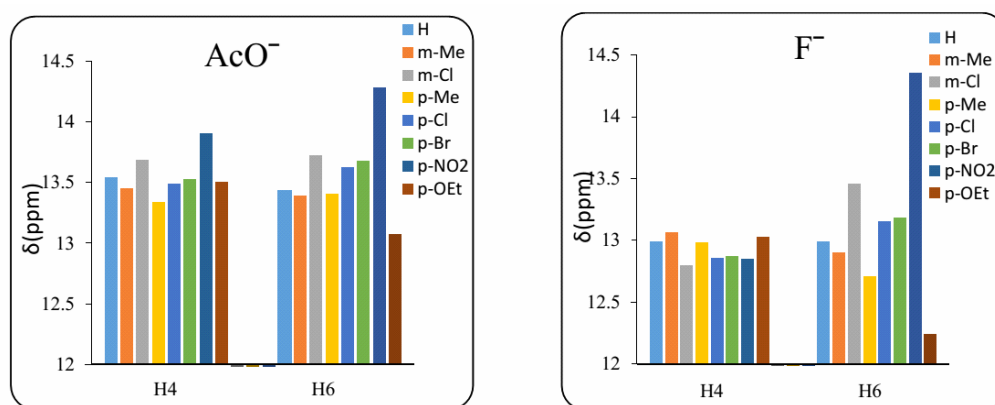


Fig. 6. Theoretical chemical shifts of the H4 and H6 protons in all complexes of N-phenylthiourea derivatives with the acetate and fluoride anions.

Table 8. Calculated Values of the ELF and LOL on the H4/H6 Atoms of the Studied Complexes

| | AcO ⁻ | | | | F ⁻ | | | |
|---------------------------|------------------|--------|--------|--------|----------------|--------|--------|--------|
| | ELF | | LOL | | ELF | | LOL | |
| | H4 | H6 | H4 | H6 | H4 | H6 | H4 | H6 |
| <i>p</i> -OEt | 0.1601 | 0.1575 | 0.3039 | 0.3019 | 0.1542 | 0.1414 | 0.2993 | 0.2887 |
| <i>p</i> -Me | 0.1606 | 0.1614 | 0.3044 | 0.3050 | 0.1401 | 0.1356 | 0.2877 | 0.2837 |
| <i>m</i> -Me | 0.1591 | 0.1606 | 0.3032 | 0.3043 | 0.1393 | 0.1382 | 0.2870 | 0.2860 |
| H | 0.1626 | 0.1603 | 0.3060 | 0.3041 | 0.1391 | 0.1391 | 0.2868 | 0.2868 |
| <i>p</i> -Br | 0.1636 | 0.1648 | 0.3067 | 0.3076 | 0.1366 | 0.1465 | 0.2846 | 0.2930 |
| <i>p</i> -Cl | 0.1634 | 0.1644 | 0.3065 | 0.3074 | 0.1369 | 0.1457 | 0.2849 | 0.2923 |
| <i>m</i> -Cl | 0.1674 | 0.1650 | 0.3097 | 0.3078 | 0.1358 | 0.1494 | 0.2839 | 0.2954 |
| <i>p</i> -NO ₂ | 0.1721 | 0.1739 | 0.3132 | 0.3146 | 0.1461 | 0.1803 | 0.2927 | 0.3193 |

Quantitative analysis of the chemical shifts of the H4 and H6 atoms was also performed. Figure 6 shows that H4 and H6 chemical shifts are approximately similar in the case of the acetate anion, whereas, in the case of the complexation with fluoride anion, especially in **1h**, a larger chemical shift is observed.

ELF and LOL Analyses

Electron location function and localized orbital locator are analyzed *via* H bonds for all complexes and reported in Table 8. A large value of the ELF is a specific character of the calculated covalent bond (approximately 0.8 to 1.0). The calculated values of the ELF on the H4 and H6 atoms are

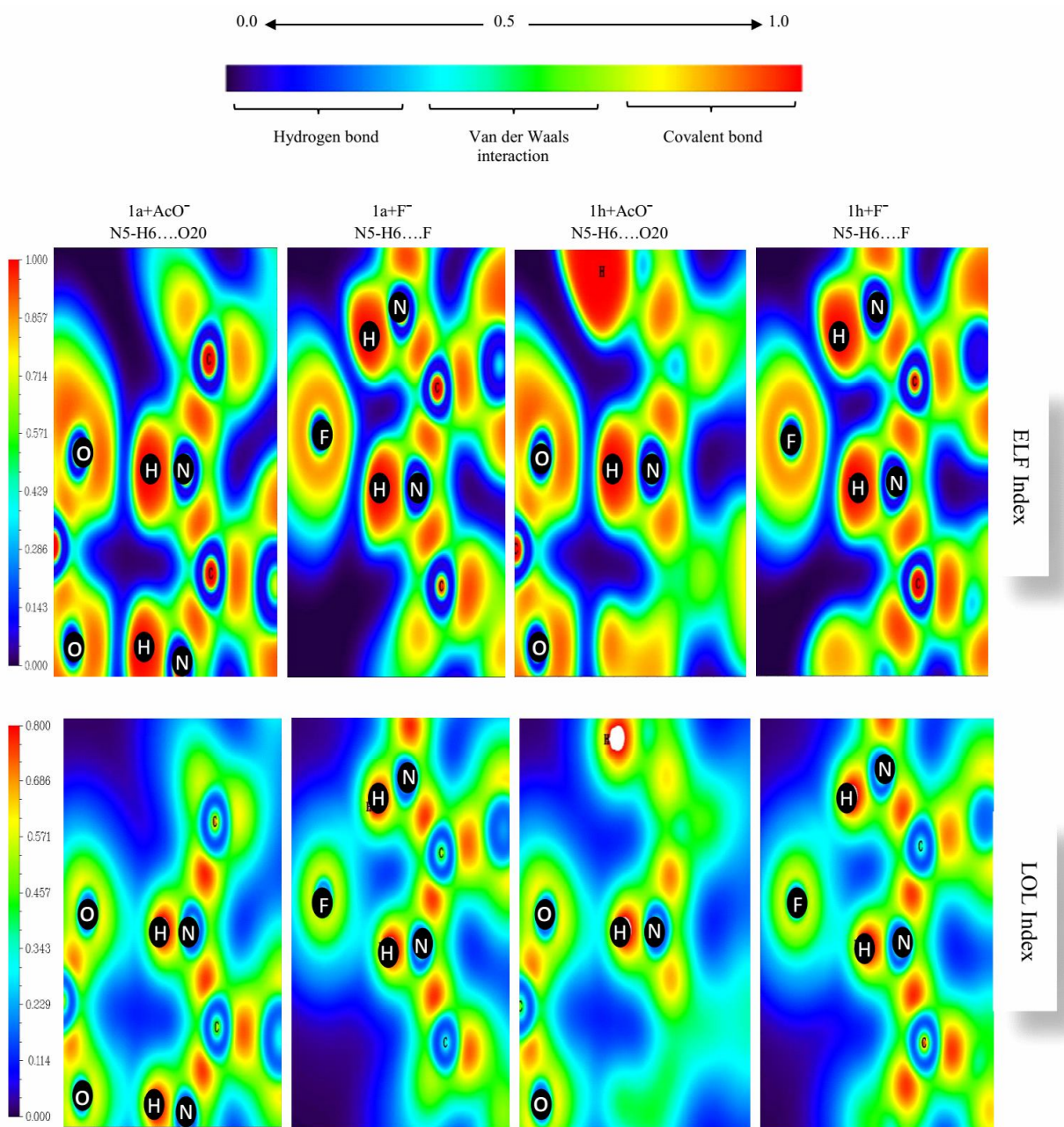


Fig. 7. Electron location function (ELF) and localized orbital locator (LOL) in complexes of **1a** and **1h** with the anions.

smaller than 1, showing the non-covalent interactions. A pictorial representation of the data in Table 8 has been provided in Fig. 7. This color-filled graph helps us to know the weak interaction regions and the type of the interaction. Blue/red colors indicate the regions with higher/lower values of the interactions. High ELF values are colored in red; the series descends through yellow to green in middle ELF values (*ca.* 0.5) [50]. Accordingly, the obtained value of 0.2 for ELF, demonstrates the H-bond formation in these complexes. As an example, ELF and LOL indices for the complexes of **1a** and **1h** in Fig. 7, are low (blue color) in the regions between the anions and H atoms of the urea derivatives, confirming the electrostatic interactions (H-bonding).

CONCLUSIONS

A theoretical DFT study was applied for the investigation of the sensing activity of the N-diphenylthiourea derivatives through the hydrogen bond formation between the anions and the N-H fragment of the thiourea functional group by using the M062X and ω B97XD functionals. ω B97XD functional showed a more reasonable correlation than M062X. During the complexation of the N-diphenylthiourea derivatives with acetate and fluoride anions, leading to an increase in the electron withdrawing character of the substituents, a significant charge transfer occurs from the anion to the N-H. For investigating the hydrogen bond character of these bonds, electron location function and the localized orbital locator were applied. Complex formation constants (K_f) of the different derivatives of N-diphenylthiourea showed a strong complex formation between the fluoride anion and *p*-nitro derivative (3×10^7), showing a stronger hydrogen bond formation in this complex (**1h**) than that of other derivatives. Based on the theoretical data, N-(*p*-nitrophenyl) thiourea receptor has higher selectivity toward F⁻ than acetate anion. Therefore, these results showed that this compound (**1h**) is the best candidate for fluoride sensing which can be used in designing of the chemosensors with an acceptable performance.

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Appendix A. Supplementary Data

Supplementary data associated with this article can be found, in the online version, at physchemres.org.

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