Indian Journal of Chemistry
Vol. 58A, December 2019, pp. 1311-1318

# Theoretical study of structural effects on reactivity and stability of isomeric pyrano-, thiopyrano- and selenopyranopyrroles

Mohammad Mehdi Khodaei*, Abdolhamid Alizadeh & Parvin Ghanbari
Department of Organic Chemistry, Faculty of Chemistry, Razi University, Kermanshah 67149-67346, Iran
Email: mmkhoda@razi.ac.ir

*Received 1 January 2019; revised and accepted 22 November 2019*

In this study we have calculated global and local DFT reactivity descriptors for isomeric pyrano-, thiopyrano- and selenopyranopyrroles. The geometric optimization of the obtained structures have been realized with the density functional theory (DFT, B3LYP) at the level of 6-311G(d,p) and show these isomers have planar configurations. The structural properties such as dipole moments, bond lengths and bond angles of these isomers have been calculated. The heats of formation have also been calculated based on the optimized geometry. The energies of HOMO and LUMO molecular orbitals have been used to determine several global descriptors as a measure of their electronic properties, relative stabilities and chemical reactivities. These include total energy (E), ionization potential (I), electron affinity (A), chemical hardness ($\eta$), chemical softness (S), electronic chemical potentials ($\mu$) and electrophilicity ($\omega$). Selenopyrano[2,3-c]pyrrole possesses the highest electrophilicity and minimum chemical hardness among the calculated isomeric structures. The largest calculated dipole moment belongs to pyrano[2,3-c]pyrrole, while thiopyrano[3,4-b]pyrrole has the lowest.

**Keywords:** DFT calculations, Fused pyrrole, Electrophilicity, Energy gap, Azaheterocycle, Global descriptor

Pyrrole and its derivatives have been reported to be associated with interesting pharmacological properties[1]. Derivatives of pyrrole fused to pyran, thiopyran and selenopyran are important compounds and the developments of new synthetic methods for these heterocycles are of current interest[2-4]. Several derivatives of the pyran, thiopyran and selenopyran or fused these ring systems are endowed to different types of biological activities[5,6]. Compounds containing these moieties have many pharmacological properties and play important roles in biochemical processes. Some of these compounds have proved to possess antibacterial[7,8], growing gilts[9], antioxidative[10,11], and anticancer activities[12,13]. There are six possible isomeric structures for each of these nitrogen heterocycles characterized by different positions of N, O, S, and Se atoms (Fig. 1). For example, the six isomeric structures for Thiopyranopyrrole are: Thiopyrano[2,3-b]pyrrole, Thiopyrano[3,4-b]pyrrole, Thiopyrano[4,3-b]pyrrole, Thiopyrano[3,2-b]pyrrole, Thiopyrano[2,3-c]pyrrole and Thiopyrano[4,3-c]pyrrole (Fig. 1).

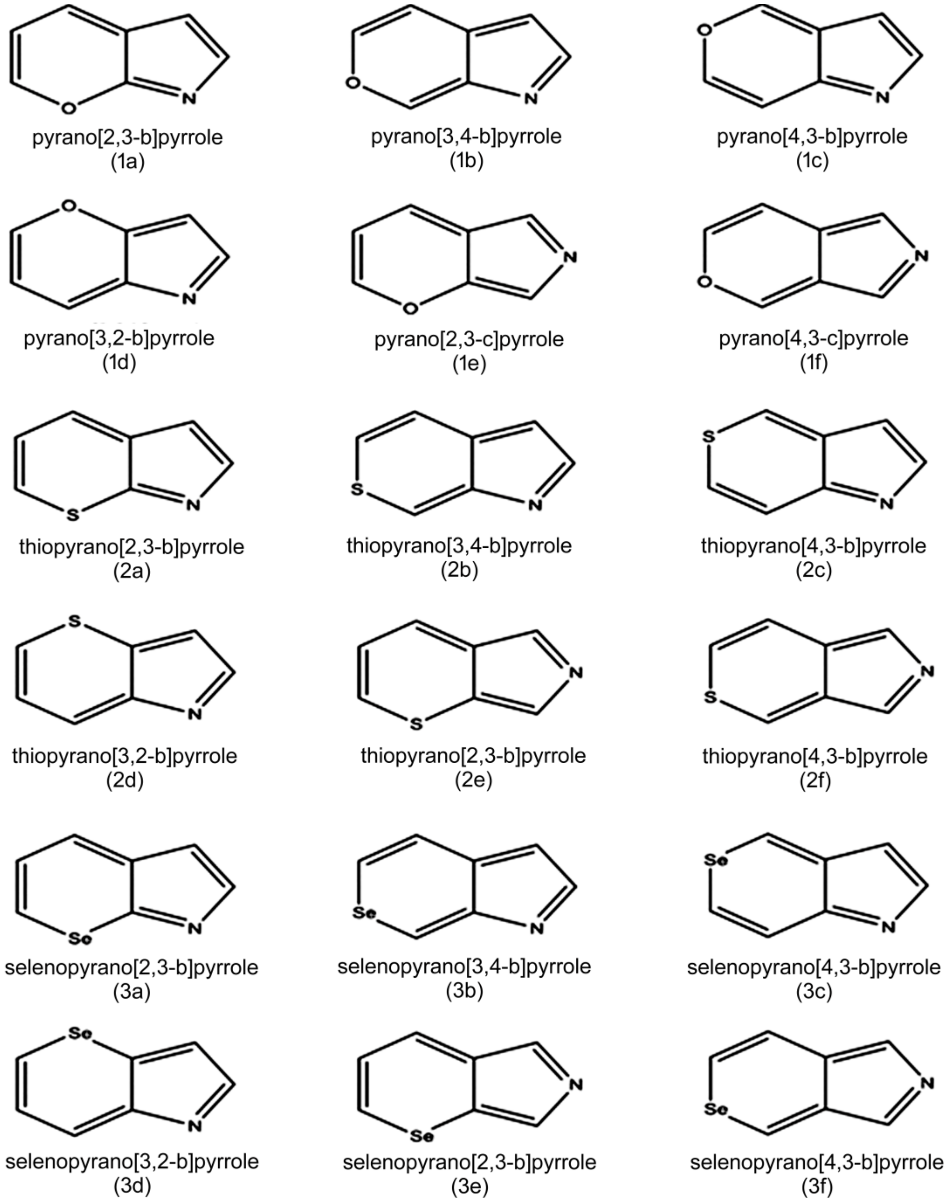
The aim of this study is to rationalize the consequences of the change in position of heteroatoms (N, O, S, and Se) on the electronic structure, stability and reactivity of the isomeric pyrano-, thiopyrano- and selenopyranopyrroles 1a–3f. The density functional theory (DFT) is recognized by the chemistry community as a reliable and effective approach for computing molecular structures, vibrational frequencies and energetics of chemical systems[14,15]. Also, it constitutes a solid support to reactivity models[16].

The total energy (E) and global chemical reactivity descriptions such as electronic chemical potentials ($\mu$), chemical hardness ($\eta$) and electrophilicity ($\omega$) can be calculated by this method[17-19]. DFT provides an efficient method to include correlation energy in electronic calculations[20,21]. In this paper, the structural properties, energetic data and classification of the chemical properties of these azaheterocycles were studied by DFT method. The important and proper indices were applied in this investigation. The electronic structures of 18 isomeric pyrano-, thiopyrano- and selenopyranopyrroles have been determined and analyzed by DFT level employing the 6-311G(d,p) basis set.

## Materials and Methods

### Computational method

The structural properties have been determined and analyzed at DFT level employing the 6-311G(d,p)



pyrano[2,3-b]pyrrole (1a)
pyrano[3,4-b]pyrrole (1b)
pyrano[4,3-b]pyrrole (1c)
pyrano[3,2-b]pyrrole (1d)
pyrano[2,3-c]pyrrole (1e)
pyrano[4,3-c]pyrrole (1f)
thiopyrano[2,3-b]pyrrole (2a)
thiopyrano[3,4-b]pyrrole (2b)
thiopyrano[4,3-b]pyrrole (2c)
thiopyrano[3,2-b]pyrrole (2d)
thiopyrano[2,3-b]pyrrole (2e)
thiopyrano[4,3-b]pyrrole (2f)
selenopyrano[2,3-b]pyrrole (3a)
selenopyrano[3,4-b]pyrrole (3b)
selenopyrano[4,3-b]pyrrole (3c)
selenopyrano[3,2-b]pyrrole (3d)
selenopyrano[2,3-b]pyrrole (3e)
selenopyrano[4,3-b]pyrrole (3f)

Fig. 1 — Isomers for pyrano-, thiopyrano- and selenopyranopyrroles.

basis set. The Becke 3 Lee-Yang-Parr (B3LYP) functional with 6-311G(d,p) basis set was used in this study to optimize the geometries of isomeric pyrano-, thiopyrano- and selenopyranopyrroles 1a–3f. Geometry optimization is one of the most important steps in the theoretical calculations. Becke's three parameter exact exchange functional (B3) combined with gradient corrected correlation functional of Lee-Yang-Parr (LYP) of DFT method has been employed to optimize the molecules using the standard 6-311G(d,p) Pople's basis sets[22-24]. The graphing and mathematical operations were performed using Microsoft Office Excel-2007 programs. The structural energetic results are obtained by the single point calculations at high levels of theory, including B3LYP/6-311G(d,p). All calculations were carried out using the Gaussian 03 and GaussView suite of quantum chemical programs[25,26].

The optimized geometry of isomeric pyrano-, thiopyrano- and selenopyranopyrroles 1a–3f and their molecular properties such as bond length, bond angle, dipole moment and several global descriptors have been used to understand their structural properties and chemical reactivities.

## Results and Discussion

### Global reactivity description

Chemical descriptors and their application can be used as useful tools for structural studies, prediction of reactivity and stabilities, and study of the biological and toxicological properties of molecules. Here, we have elaborated some variety of the useful indices concerned with the subject of this study. The chemical structures of the isomeric pyrano-, thiopyrano- and selenopyranopyrroles 1a–3f were optimized with B3LYP method employing 6-311G(d,p) basis set. The results are given in Tables 1–4. According to the Koopmans' theorem for closed-shell molecules, ionization potential (I) and electron affinity (A) can be expressed in terms of $E_{HOMO}$ and $E_{LUMO}$, the highest occupied molecular orbital energy and the lowest unoccupied molecular orbital energy, respectively[27].

$$I = -E_{HOMO} \qquad \ldots (1)$$

$$A = -E_{LUMO} \qquad \ldots (2)$$

The values of chemical potential (μ) and absolute hardness (η) can be determine through the following expressions[28,29].

$$\mu = (I+A)/2 \qquad \ldots (3)$$

$$\eta = (I-A)/2 \qquad \ldots (4)$$

The inverse values of the global hardness are designated as the softness (S), as follows:

$$S = 1/\eta \qquad \ldots (5)$$

The electrophilicity is a descriptor of chemical reactivity that allows a quantitative data categorizing of the global electrophilic nature of a molecule within a relative scale. Parr proposed electrophilicity index as a measure of energy lowering due to maximal electron flow between donor and acceptor and defined electrophilicity index (ω) as follows[30]:

$$\omega = \mu^2/2\eta \qquad \ldots (6)$$

A good reactive electrophile is characterized by higher value of ω, and conversely a more reactive nucleophile is characterized by a lower value of ω. The global reactivity descriptors such as ionization potential (I), electron affinity (A), chemical hardness (η), chemical softness (S), chemical potential (μ) and electrophilicity index (ω) values were examined with DFT / B3LYP / 6-311G(d,p) level to have information about the chemical reactivity and relative stability of the these azaheterocycle isomers. The electronic structures of isomeric pyrano-, thiopyrano- and selenopyranopyrroles 1a–3f have been investigated, in order to assess the effect of changing the position of N and other heteroatoms (O, S, and Se) in the 5,6-fused ring systems on their electronic structures and properties. Reactivity parameters are defined by the equations (1–6).

Table 1 — B3LYP/6-311G(d,p) calculated bond lengths (Å) for isomeric 1a-3f

| | Bond length (Å) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Molecule | 1-2 | 2-3 | 3-3a | 4-3a | 4-5 | 5-6 | 6-7 | 7-7a | 3a-7a | 1-7a |
| 1a | 1.40 | 1.38 | 1.43 | 1.37 | 1.42 | 1.36 | 1.34 | 1.35 | 1.46 | 1.30 |
| 1b | 1.33 | 1.43 | 1.38 | 1.42 | 1.35 | 1.36 | 1.35 | 1.36 | 1.46 | 1.37 |
| 1c | 1.39 | 1.38 | 1.43 | 1.36 | 1.35 | 1.36 | 1.35 | 1.42 | 1.47 | 1.32 |
| 1d | 1.33 | 1.44 | 1.37 | 1.35 | 1.35 | 1.36 | 1.43 | 1.37 | 1.46 | 1.37 |
| 1e | 1.40 | 1.32 | 1.43 | 1.36 | 1.43 | 1.36 | 1.34 | 1.36 | 1.46 | 1.36 |
| 1f | 1.32 | 1.39 | 1.37 | 1.42 | 1.35 | 1.37 | 1.34 | 1.35 | 1.47 | 1.44 |
| 2a | 1.39 | 1.36 | 1.43 | 1.37 | 1.42 | 1.37 | 1.72 | 1.73 | 1.47 | 1.31 |
| 2b | 1.33 | 1.43 | 1.38 | 1.42 | 1.36 | 1.74 | 1.72 | 1.36 | 1.47 | 1.38 |
| 2c | 1.38 | 1.38 | 1.43 | 1.36 | 1.72 | 1.73 | 1.36 | 1.41 | 1.48 | 1.32 |
| 2d | 1.33 | 1.43 | 1.38 | 1.72 | 1.72 | 1.37 | 1.42 | 1.37 | 1.47 | 1.37 |
| 2e | 1.39 | 1.32 | 1.43 | 1.37 | 1.42 | 1.37 | 1.72 | 1.73 | 1.47 | 1.37 |
| 2f | 1.31 | 1.39 | 1.37 | 1.42 | 1.36 | 1.74 | 1.72 | 1.36 | 1.47 | 1.44 |
| 3a | 1.40 | 1.37 | 1.43 | 1.37 | 1.42 | 1.36 | 1.87 | 1.87 | 1.47 | 1.31 |
| 3b | 1.32 | 1.43 | 1.38 | 1.42 | 1.35 | 1.88 | 1.87 | 1.36 | 1.44 | 1.38 |
| 3c | 1.39 | 1.37 | 1.43 | 1.36 | 1.87 | 1.88 | 1.36 | 1.42 | 1.48 | 1.32 |
| 3d | 1.32 | 1.44 | 1.37 | 1.87 | 1.87 | 1.36 | 1.42 | 1.37 | 1.47 | 1.38 |
| 3e | 1.40 | 1.31 | 1.44 | 1.36 | 1.43 | 1.36 | 1.87 | 1.88 | 1.47 | 1.36 |
| 3f | 1.31 | 1.39 | 1.37 | 1.42 | 1.35 | 1.89 | 1.87 | 1.35 | 1.47 | 1.45 |

Table 2 — Selected bond angles (°) for fused systems 1a-3f, using the B3LYP/6-311G(d,p) method

| Isomer | Bond Angle (°) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2-1-7a | 3-2-1 | 2-3-3a | 3-3a-7a | 1-7a-3a | 5-4-3a | 4-5-6 | 5-6-7 | 6-7-7a | 7-7a-3a | 4-3a-7a |
| 1a | 103.00 | 114.56 | 104.90 | 102.85 | 114.71 | 118.06 | 120.47 | 123.14 | 118.54 | 121.43 | 118.34 |
| 1b | 103.70 | 114.78 | 104.99 | 104.84 | 111.69 | 118.48 | 123.17 | 120.47 | 121.06 | 119.69 | 117.13 |
| 1c | 104.73 | 114.47 | 104.46 | 104.52 | 111.81 | 121.36 | 120.75 | 123.00 | 118.27 | 117.80 | 118.80 |
| 1d | 104.25 | 115.36 | 102.96 | 107.60 | 109.83 | 118.07 | 123.20 | 120.71 | 117.59 | 118.76 | 121.67 |
| 1e | 109.11 | 108.93 | 110.91 | 103.17 | 107.87 | 117.97 | 120.14 | 123.84 | 118.03 | 121.11 | 118.90 |
| 1f | 110.56 | 108.23 | 111.38 | 105.05 | 104.79 | 118.82 | 122.96 | 120.05 | 121.67 | 119.62 | 116.88 |
| 2a | 104.14 | 113.94 | 105.57 | 103.00 | 113.35 | 122.53 | 124.03 | 125.68 | 102.02 | 122.90 | 122.85 |
| 2b | 104.37 | 114.44 | 105.41 | 104.73 | 111.25 | 122.67 | 125.00 | 103.66 | 123.36 | 123.65 | 121.71 |
| 2c | 105.25 | 114.17 | 104.97 | 104.25 | 111.36 | 123.52 | 103.87 | 124.84 | 122.66 | 122.13 | 122.98 |
| 2d | 104.97 | 114.59 | 104.32 | 106.21 | 109.91 | 102.29 | 125.52 | 123.94 | 122.42 | 123.31 | 122.52 |
| 2e | 110.69 | 108.06 | 111.53 | 103.43 | 106.29 | 122.47 | 123.39 | 126.17 | 102.19 | 121.87 | 123.91 |
| 2f | 111.11 | 107.81 | 111.86 | 104.83 | 104.39 | 122.99 | 124.85 | 103.29 | 123.48 | 123.97 | 121.42 |
| 3a | 104.32 | 113.68 | 105.72 | 102.82 | 113.45 | 124.21 | 125.45 | 125.34 | 98.03 | 122.35 | 124.61 |
| 3b | 104.58 | 114.28 | 105.67 | 104.73 | 110.73 | 124.23 | 124.56 | 99.47 | 123.07 | 125.25 | 123.43 |
| 3c | 105.60 | 113.95 | 105.18 | 104.06 | 111.22 | 123.26 | 99.67 | 124.40 | 124.32 | 123.74 | 124.60 |
| 3d | 105.09 | 114.43 | 104.44 | 106.36 | 109.67 | 98.25 | 125.23 | 125.31 | 124.10 | 125.11 | 121.99 |
| 3e | 110.90 | 107.71 | 111.71 | 103.29 | 106.39 | 124.01 | 124.74 | 125.90 | 98.09 | 121.30 | 125.95 |
| 3f | 111.35 | 107.89 | 112.17 | 104.80 | 104.17 | 124.52 | 124.42 | 99.15 | 123.04 | 125.72 | 123.14 |

Table 3 — Calculated values for the energies of frontier orbitals: HOMO, LUMO, energy gap (ΔE), Ionization potential (I), electron affinity (A) and global properties of fused systems 1a-3f

| Molecule | $E_{HOMO}$ (eV) | $E_{LUMO}$ (eV) | ΔE (eV) | I (eV) | A (eV) | η (eV) | S (eV) | μ (eV) | ω (eV) |
|---|---|---|---|---|---|---|---|---|---|
| 1a | –6.217 | –2.274 | 3.943 | 6.217 | 2.274 | 1.971 | 0.507 | 4.245 | 4.571 |
| 1b | –6.146 | –1.799 | 4.347 | 6.146 | 1.799 | 2.173 | 0.460 | 3.972 | 3.630 |
| 1c | –6.047 | –1.816 | 4.231 | 6.047 | 1.816 | 2.115 | 0.473 | 3.931 | 3.653 |
| 1d | –6.270 | –2.245 | 4.025 | 6.270 | 2.245 | 2.012 | 0.497 | 4.257 | 4.503 |
| 1e | –5.784 | –2.490 | 3.294 | 5.784 | 2.490 | 1.647 | 0.607 | 4.137 | 5.196 |
| 1f | –5.739 | –1.947 | 3.792 | 5.739 | 1.947 | 1.896 | 0.527 | 3.843 | 3.895 |
| 2a | –6.136 | –2.485 | 3.651 | 6.136 | 2.485 | 1.825 | 0.548 | 4.310 | 5.089 |
| 2b | –6.068 | –2.091 | 3.977 | 6.068 | 2.091 | 1.988 | 0.503 | 4.079 | 4.185 |
| 2c | –6.032 | –2.137 | 3.895 | 6.032 | 2.137 | 1.947 | 0.514 | 4.084 | 4.283 |
| 2d | –6.119 | –2.447 | 3.672 | 6.119 | 2.447 | 1.836 | 0.545 | 4.283 | 4.996 |
| 2e | –5.697 | –2.654 | 3.043 | 5.697 | 2.654 | 1.521 | 0.657 | 4.175 | 5.730 |
| 2f | –5.694 | –2.252 | 3.442 | 5.694 | 2.252 | 1.721 | 0.581 | 3.973 | 4.586 |
| 3a | –6.094 | –2.552 | 3.542 | 6.094 | 2.552 | 1.771 | 0.565 | 4.323 | 5.276 |
| 3b | –6.014 | –2.181 | 3.833 | 6.014 | 2.181 | 1.916 | 0.522 | 4.097 | 4.380 |
| 3c | –6.005 | –2.241 | 3.764 | 6.005 | 2.241 | 1.882 | 0.531 | 4.123 | 4.516 |
| 3d | –6.060 | –2.520 | 3.540 | 6.060 | 2.520 | 1.770 | 0.564 | 4.290 | 5.199 |
| 3e | –5.678 | –2.704 | 2.974 | 5.678 | 2.704 | 1.487 | 0.672 | 4.191 | 5.906 |
| 3f | –5.537 | –2.316 | 3.221 | 5.537 | 2.316 | 1.610 | 0.621 | 3.926 | 4.787 |

### Bond length and bond angle analysis

There are six types of bonds in these isomeric structures: C-O, C-S, C-Se, C-N, C-C and C-H (Fig. 2). The geometries of the isomeric pyrano-, thiopyrano- and selenopyranopyrroles are strongly influenced by the position of nitrogen atoms on their structure, involving a considerable shortening of C–N bonds as compared to C–C, C–S and C–Se bonds. When N is present at position 1 in the 5,6-fused rings, bond length of C-N is shorter than when this atom is placed in position 2 of the pentagonal ring. The shortest C-N bond is observed in the pyrrole ring with the nitrogen atom in position 1 and heteroatoms in position 7 (1a). These calculations show that the shortest bonds in 1a–3f are C7a-N in 1a, while the longest bond is C5-Se in 3f (Table 1).

Since the crystal structures data for these isomers are not available, the optimized structures can only be compared with other similar systems for which crystal structures have been solved. Based on this, a

Table 4 — DFT/B3LYP/6-311G(d,p) Calculated total energy ($E_{total}$) and heats of formation ($\Delta H_f$), relative energies ($\Delta E_{rel}$) and dipole moment for isomeric 1a–3f

| Molecule | $E_{total}$ (a.u.) | $\Delta E_{rel}$ (kcal.mol$^{-1}$) | $\Delta H_f$ (a.u.) | Dipole moment (D) |
|---|---|---|---|---|
| 1a | –399.776976 | 0.000 | –399.665543 | 4.010 |
| 1b | –399.777559 | –0.366 | –399.665834 | 3.031 |
| 1c | –399.776746 | 0.144 | –399.665065 | 3.073 |
| 1d | –399.773817 | 1.982 | –399.662327 | 3.286 |
| 1e | –399.760011 | 10.646 | –399.648724 | 4.903 |
| 1f | –399.766965 | 6.282 | –399.655450 | 3.725 |
| 2a | –722.757315 | 0.000 | –722.648710 | 3.727 |
| 2b | –722.760842 | –2.213 | –722.652322 | 2.988 |
| 2c | –722.759198 | –1.182 | –722.650766 | 3.134 |
| 2d | –722.758572 | –0.789 | –722.649918 | 3.163 |
| 2e | –722.745842 | 7.199 | –722.637383 | 4.605 |
| 2f | –722.750060 | 4.553 | –722.641768 | 3.650 |
| 3a | –2726.084770 | 0.000 | –2725.977019 | 3.538 |
| 3b | –2726.088660 | –2.441 | –2725.981077 | 2.989 |
| 3c | –2726.086640 | –1.173 | –2725.979146 | 3.309 |
| 3d | –2726.086448 | –1.053 | –2725.978611 | 3.200 |
| 3e | –2726.0745759 | 6.397 | –2725.966850 | 4.488 |
| 3f | –2726.078754 | 3.775 | –2725.971340 | 3.707 |

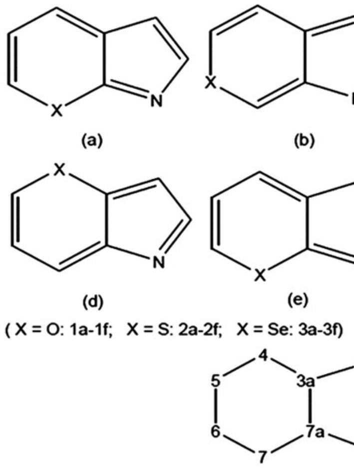


Fig. 2 — The digits of the atoms for the selected structural data of 1a-3f isomers.

satisfactory agreement between calculated values and experimental and other computational findings has been found. However, according to our calculations, the optimized bond lengths obtained by DFT/B3LYP/6-311(d,p) method show the best agreement with experimental values. For example, the optimized bond length of C-Se in selenopyran ring of selenopyranopyrroles falls in the range: 1.87–1.89 Å at B3LYP/6-311(d,p) method which is in good agreement with that of the crystal data of substituted selenopyran ring [1.87–1.90 Å][31]. Also the optimized bond length of C-S falls in the range: 1.72–1.74 Å at B3LYP/6-311(d,p) method which is in good agreement with that of the crystal data of sulfur-containing heterocycles (1.72–1.75 Å)[32,33].

In these isomers, the maximum angle deviation from 120° is observed for the C-X-C (X = O, S, and Se) bond angles. The hexagonal internal angles for pyrano-, thiopyrano- and selenopyranopyrroles are about 116.88–123.84°, 102.02–126.17° and 98.03–125.90°, respectively (Table 2). Thus, increasing the size of atom X in the hexagonal ring, leads to reduced bond angles. The optimized bond angle of C-Se-C in selenopyran ring of selenopyranopyrroles falls in the range: 98.03–99.67° at B3LYP/6-311(d,p) method which is in good agreement with that of the crystal and calculated data of substituted selenopyran ring (97.00–99.80°)[32].

By changing the heteroatom from position 1 to 2 in the five-membered ring, the C-N-C angle change is much greater for large atoms in the other ring. Thus, the angle difference between the smallest and largest C-X-C angle is 6.08°, 23.98° and 27.81° for pyrano-, thiopyrano- and selenopyranopyrroles, respectively.

### Reactivity analysis

The global reactivity parameters and dipole moment are important electronic parameters which useful to predict the reactivity and polarity of chemical systems. Global reactivity descriptors were evaluated at the level of theory DFT/B3LYP/6-311G(d,p). These obtained data for all studied isomers of 1a-3f are given in Tables 3 and 4.

The basic electronic parameters related to the frontier orbitals (FOs) in a molecule are HOMO, LUMO and their resulting energy gap (ΔE). The HOMO is the orbital that primarily acts as an electron donor and the LUMO is the orbital that largely acts as the electron acceptor. The energy gap (ΔE) is an important stability index. The chemical hardness indicates the resistance towards the deformation or polarization of the electron cloud of the atoms, ions, or molecules under small changes in the reaction conditions. A soft molecule, with a small ΔE, is more polarizable and it is generally associated with a high chemical reactivity and low stability. Soft molecules are more reactive than the hard molecules because they can easily offer electrons to an acceptor. There is direct relationship between hardness and energy gap. When energy gap is more, the molecule is harder and less reactive. A soft molecule has a low energy gap and a hard molecule has a large one (Fig. 3).

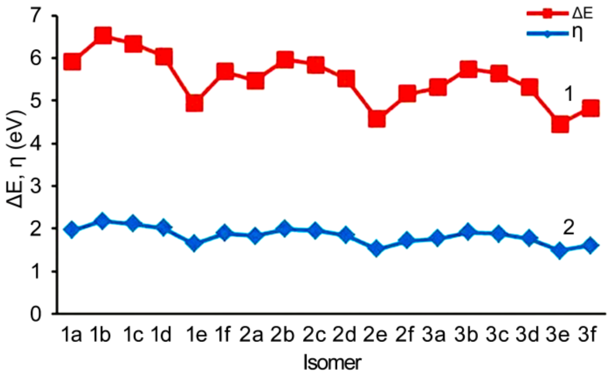


Fig. 3 — The relationship between the ΔE (1) and η (2) of isomeric pyrano-, thiopyrano- and selenopyranopyrroles 1a-3f.

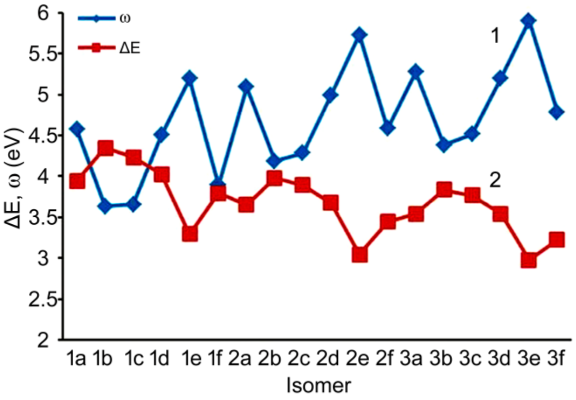


Fig. 4 — The relationship between ω (1) and ΔE (2) of isomeric pyrano-, thiopyrano- and selenopyranopyrroles 1a-3f.

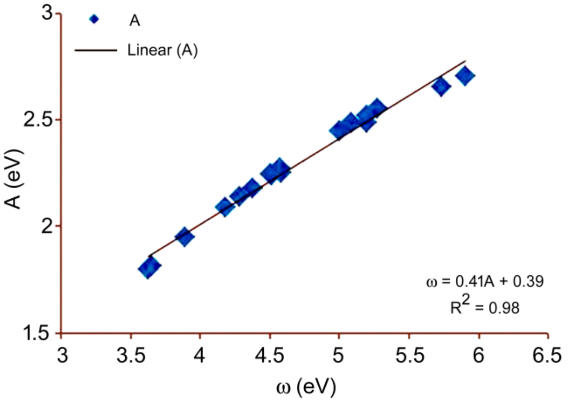


Fig. 5 — The linear relationships between the electron affinity (A) and the electrophilicity (ω) of isomeric pyrano-,thiopyrano- and selenopyranopyrroles 1a-3f. Linear line **(1)**, ☐ **(2)**.

Compared with the hard atom of oxygen in pyranopyrroles, the soft atoms sulfur and selenium in thiopyranopyrroles and selenopyranopyrroles, respectively, cause a greater impact on decreasing the energy gap and therefore reducing the hardness of thiopyranopyrrole and selenopyranopyrrole isomers (Fig. 3). The calculated frontier orbital gaps at B3LYP/6-311G(d,p) method are shown in Table 3. According to these results, selenopyrano[2,3-c]pyrrole (**3e**) has the lowest value of HOMO-LUMO energy gap. This makes **3e** a soft and more polarizable molecule compared to the other isomers. By changing the nitrogen atom from position 1 to 2 in the pyrrole ring, the energy gap will change more than 0.57 eV, while the change of energy gap due to the position of heteroatom in the hexagonal ring is less than 0.25 eV. Thus, the energy-gap order of isomeric 1a–3f, for heteroatoms in similar positions, follows the trend: selenopyranopyrrole < thiopyranopyrrole < pyranopyrrole.

Isomer 1b has the highest energy gap and chemical hardness while 3e has the lowest energy gap and chemical hardness among the isomeric structures of 1a–3f as shown in Table 3 and Fig. 3. The calculated values of global electrophilicity index ω are shown in Table 3. The calculated values of the energy gap and the electrophilicity (ω) are in agreement with trends of electrophilic substitution reactions in these isomers (Fig. 4). The smaller ω of pyranopyrroles, reduces their tendency for electrophilic substitution reactions compared to thiopyranopyrroles. Whereas, in nucleophilic reactions, pyranopyrroles are more reactive. Thus, the larger electrophilicity values calculated for selenopyranopyrroles, predict higher electrophilicity for these isomers. The calculated ω values for selenopyrano[2,3-c]pyrrole (3e) are much higher compared to those obtained for the other isomeric structures of 1a-3f. Thus, 3e with maximum electrophilicity among various isomers of 1a-3f, is the most reactive isomer. The calculated values of the electrophilicity (ω) of isomers 1a-3f are in agreement with the experimental and calculated trends of substitution reactions of furopyridine and thienopyridines as similar fused heterocycles[34,35].

$$\omega = 0.41A + 0.39 \qquad \ldots (7)$$

By calculation of the energy levels of LUMO orbitals, it is possible to calculate the willingness of the electrophilicity (without using μ and η data) for the isomeric structures[35]. The relationship between electrophilicity (ω) and electron affinity (A) among the isomeric structures of pyrano-, thiopyrano- and selenopyranopyrroles is shown in Eqn 7 and Fig. 5. Therefore, the graph shown in Fig. 5 demonstrate the description of linear relationship between these two indices. The $R^2$ values for the graphs are about 0.98 (≈1).

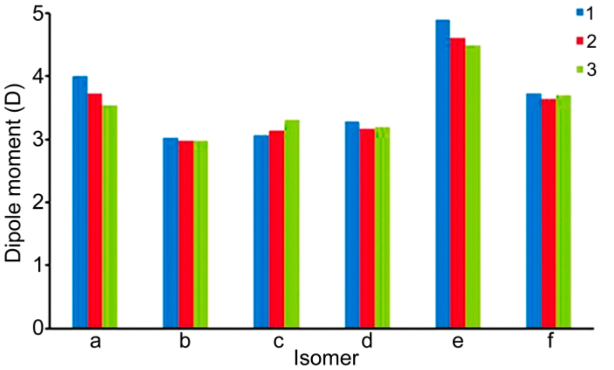


Fig. 6 — Comparison of dipole moments of the pyranopyrrole (1), thiopyranopyrrole (2) and selenopyranopyrrole (3) isomers.

**Dipole moment analysis**

A molecular dipole moment is the dipole moment of the molecule taken as a whole. It is a good indicator of a molecule's overall polarity. The dipole moment of a molecule is an important property mainly used to study the intermolecular interactions involving the bonded type dipole-dipole interactions. The calculated dipole moments of the isomeric pyrano-, thiopyrano- and selenopyranopyrroles are shown in Table 4. Isomers 1e, 2e and 3e have the largest dipole moments in their groups (Fig. 6). The calculated dipole moments for 1b, 2b and 3b are smaller than 3.032 Debye. Thiopyrano[3,4-b]pyrrole (2b) with 2.988 Debye, possesses the smallest dipole moment.

**Relative stability analysis**

Standard enthalpy of formation is a fundamental thermodynamic property. The calculated enthalpies of formation ($\Delta H°_f$) show the relative stabilities of the isomeric structures of 1a–3f. Thus, determination and usage of $\Delta H°_f$ as a quantitatively physiochemical parameter is effective for investigation of the relationship between stabilities related to the heteroatom position in isomeric 1a–3f.

According to the calculated $\Delta H°_f$ and relative energies ($\Delta E_{rel}$) from DFT/B3LYP/6-311G(d,p) method, pyrano[3,4-b]pyrrole (1b), thiopyrano[3,4-b] pyrrole (2b) and selenopyrano[3,4-b]pyrrole (3b) are the most stable isomers in their corresponding isomers (Table 4). The energy differences between these isomers and the most unstable isomer in their groups, namely isomers 1e, 2e and 3e, are 11.01, 9.41 and 8.84 kcal mol$^{-1}$, respectively.

## Conclusions

In this work, DFT/B3LYP/6-311G(d,p) calculations were carried out to study the structures and reactivities for the isomeric structures of pyrano-, thiopyrano- and selenopyranopyrroles 1a-3f. The reactivity indices calculated by DFT method have been successfully applied to the concept of chemical reactivity. Global descriptors such as frontier orbital gap (ΔE), electrophilicity (ω), softness (S) and ionization energy (I) were determined and applied to identify the differences in the reactivity of these heterocycles.

These theoretical calculations indicate that the most reactive isomer with maximum electrophilicity among various isomers of 1-3, is selenopyrano[2,3-c]pyrrole (3e). A linear relationship between electron affinity (A) and electrophilicity (ω) of these isomeric compounds was observed. Selenopyrano[2,3-c] pyrrole (3e) possesses the highest softness and electrophilicity among the calculated isomers. The largest calculated dipole moment belongs to pyrano[2,3-c]pyrrole (1e), while thiopyrano[3,4-b] pyrrole (2b) has the lowest one. According to the total energies ($\Delta E_{total}$), heats of formation ($\Delta H°_f$) and relative energies ($\Delta E_{rel}$) from DFT-B3LYP/6-311G(d,p) calculations, pyrano[3,4-b]pyrrole (1b), thiopyrano [3,4-b]pyrrole (2b) and selenopyrano[3,4-b]pyrrole (3b) are the most stable isomers of pyrano-, thiopyrano- and selenopyranopyrroles, respectively.

## Supplementary Data

Supplementary data associated with this article, including the isomers, the digits of the atoms of the selected structural data and cartesian coordinates of pyranopyrrole, thiopyranopyrroles and selenopyrrole Fig. S1–S4 and Table S1–S18, are available in the electronic form at http://www.niscair.res.in/jinfo/ijca/IJCA_58A(12)1311-1318_SupplData.pdf.

## Acknowledgement

This research was partially supported by the Research Council of the Razi University in Iran. We thank our colleagues in Razi University who provided insight and expertise that greatly assisted the research.

## References

1 Bhardwaj V, Gumber D, Abbot V, Dhimana S & Sharma P, *RSC Adv*, 5 (2015) 15233.

2 Damavandi S & Sandaroos R, *Synth React Inorg Met Org Nano Metal Chem*, 42 (2012) 621.

3 Mansoor S S, Aswin K, Logaiya K, Sudhan S P N & Ramadoss H, *J Saudi Chem Soc*, 20 (2016) S393.

4 Gao Q, Hao W J, Liu F, Tu S J, Wang S L, Li G & Jiang B, *Chem Commun*, 52 (2016) 900.

5 Reddy B V S, Medaboina D, Sridhar B & Singarapu K K, *J Org Chem,* 78 (2013) 8161.

6 Jha M, Dhiman S, Cameron T S, Kumar D & Kumar A, *Org Lett,* 19 (2017) 2038.

7 Khafagy M M, Abd El-Wahab A H F, Eid F A & El-Agrody A M, *Farmaco,* 57 (2004) 715.

8 Fouad S A, Hessein S A, Abbas S Y, Farrag A M & Ammar Y A, *Croat Chem Acta,* 91 (2018) 99.

9 Nedeva R, Apostolov A, Marchev Y, Kistanov E, Kacheva D, Shumko E & Borjaev G, *Bulg J Agric Sci*, 15 (2009) 604.

10 Abadjieva D V, Kistanova E K, Marchev Y, Nedeva R, Vaisberg C, Stefanov R G, Boryaev G & Nevitov M, *Mac Vet Rev,* 37 (2014) 165.

11 Naik H R P, Naik H S, Naik T R, Bindu P J, Naika H R, Aravinda T & Lamani D S, *Med Chem,* 5 (2009) 148.

12 Li Y B, Hou W, Lin H, Sun P G H, Lin J & Chen W M, *Med Chem Commun,* 9 (2018) 471.

13 Khiati S, Seol Y, Agama K, Rosa I D, Agrawal S, Fesen K, Zhang H, Neuman K C & Pommier Y, *Mol Pharmacol,* 86 (2014) 193.

14 Beyramabadi S A & Morsali S A, *Int J Phys Sci,* 6 (2011) 1780.

15 Mebi C A, *J Chem Sci,* 123 (2011) 727.

16 Koch W & Holthausen M C, *A Chemist's Guide to Density Functional Theory*, (Wiley–VCH, Weinheim) 2001, p. 239.

17 Pearson R G, *J Chem Sci,* 117 ( 2005) 369.

18 Parr R G & Pearson R G, *J Am Chem Soc,* 105 (1983) 7512.

19 Parr R G, Szentpaly L & Liu S B, *J Am Chem Soc,* 121 (1999) 1922.

20 Vektariene A, Vektaris G & Svoboda J, *ARKIVOC*, 7 (2009) 311.

21 Memarian H R, Kalantari M, Rudbari H A, Sabzyan H & Bruno G, *Theor Chem,* 1099 (2017) 75.

22 Ditchfield R, Hehre W J & Pople J A, *J Chem Phys,* 54 (1971) 724.

23 Becke A D, *J Chem Phys*, 98 (1993) 5648.

24 Lee C, Yang W & Parr R G, *Phys Rev* B, 37 (1988) 785.

25 Gaussian 03, revision D.01 (Gaussian, Inc., Wallingford CT) 2004.

26 GaussView, Version 5.0, Dennington R, Keith T & Millam J, Semichem Inc, Shawnee Mission Ks, GaussView, 2009.

27 Koopmans T, *Physica,* 1 (1933) 104.

28 Pearson R G, *J Am Chem Soc,* 85 (1963) 3533.

29 Becke A D, *J Chem Phys,* 98 (1993) 5648.

30 Lesar A & Milosev I, *Chem Phys Lett,* 483 (2009) 198.

31 Jiri K, Jan C, Stanislav B, Pavel S, Stanislav N, Igor K, Petr S, Petr H, Vladimir H, Bohumil K & Josef K, *J Chem Soc*, 2 (2002) 1909.

32 Nerenz H, Grahn W & Jones E G, *Acta Crystallographica Section C*, 53 (1997) 787.

33 Glaucio B F, Nadia M C, James L W & Eduardo H, *J Braz Chem Soc*, 15 (2004) 951.

34 Sherman A R, Katritzky A R, Rees C W & Scriven E F V, *In Comprehensive Heterocyclic Chemistry II*, (Pergamon Press, Oxford) 1996, p. 167.

35 Aliveisi R, Taherpour A (A) & Yavari I, *Phosphorus Sulfur Silicon Relat Elem*, 192 (2016) 422.