Quantum Mechanical Modeling of Fluoromethylated-pyrrol Derivatives: A Study on their Reactivities, Structures and Vibrational Properties

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Abstract

In this work, the structural and vibrational properties of 1-5-(difluoromethyl-1H-pyrrol-2-yl)-ethanone (DFPE) were studied by using the hybrid B3LYP/6-31G* method. The properties were analyzed and compared with those obtained for 1-(1H-pyrrol-2-yl)ethanone (PE) and 1-5-(trifluoromethyl)-1H-pyrrol-2-yl)ethanone (TFPE). The theoretical 1H-NMR, 13C-NMR and 19F-NMR spectra and some observed bands in the infrared spectrum in solid phase were published [1]. Here, the initial structures of the different conformers of DFPE were modelled and optimized by using hybrid B3LYP/6-31G* calculations [13,14]. The nature of the interactions present in the structures of DFPE were employed using natural bond orbital (NBO) calculations [15,16] and the atoms in molecules theory (AIM) [17,18] while the reactivities of the more stable conformers were predicted by means of the highest occupied molecular orbital (HOMO)-lowest unoccupied molecular orbital (LUMO) energy gaps [19]. Here, the hydrogen bond donor properties for the CF₂H group of DFPE were also analysed by means of the molecular electrostatic potentials [20-23] and later, they were compared with those obtained for the same group of ZnDFMS [3] and 5-difluoromethyl-1,3,4-thiadiazole-2-amino [4] and, for those obtained in this work for 1-(1H-pyrrol-2-yl)ethanone (PE) and 1-5-(trifluoromethyl)-1H-pyrrol-2-yl)ethanone (TFPE) [24,25]. The harmonic frequencies for DFPE and TFPE were also calculated and, at the same level of theory the detailed assignments of all the infrared bands were performed taking into account the scaled quantum mechanics force field methodology (SQMFF) [26] and the corresponding internal normal coordinates. The Raman spectra for DPE and TFPE were predicted by using the hybrid B3LYP/6-31G* method. The theoretical 1H-NMR, 13C-NMR, 19F-NMR spectra were calculated by using the Gauge-Independent Atomic Orbital (GIAO)

Keywords: 1-5-(difluoromethyl-1H-pyrrol-2-yl)-ethanone; Vibrational spectra; Molecular structure; Force field; DFT calculations

Introduction

The difluoromethyl group (CF₂H) is normally used in areas as pharmacology and medicine because it has hydrogen bond donor properties of great importance in the drug design [1]. The hydrogen bond in this system may be related to the enhanced biological activity of the CF₂H compound over its CF₂ counterpart, as reported by Ericsson and Mc Loughlin [2], allowing this way, their incorporating in a wide variety of organic molecules [1]. In recent times, Fujiwara et al. [1] have reported a new reagent for direct difluoromethylation of organic substrates via a radical process, the zinc difluoro methyl sulfonate salt (ZnDFMS), Zn(SO₂CF₂H)₂, which allows the selective bond in this system may be related to the enhanced biological activity of the compounds containing both, difluoromethyl and pyrrol groups are useful and necessary to predict their properties and metabolic and thermal stability [11,12]. In these contexts, the knowing of the structures of compounds containing both, difluoromethyl and pyrrol groups are useful and necessary to predict their properties and behaviours in the different media in which they are involved and, also to perform the complete assignments of the corresponding vibrational spectra. Hence, these derivatives in any system can be easily identified by means of vibrational spectroscopy. In this work, we studied from theoretical point of view the structure, the vibrational spectra and the structural properties of 1-5-(difluoromethyl-1H-pyrrol-2-yl)-ethanone (DFPE), a new fluoro methylated-pyrrol derivative synthesized by Fujiwara et al. [1] by using ZnDFMS as reagent and a unreported synthetic procedure. So far, the experimental structure of this compound, reported as a white solid, was not determined and only the experimental 1H-NMR, 13C-NMR, 19F-NMR spectra and some observed bands in the infrared spectrum in solid phase were published [1]. Here, the initial structures of the different conformers of DFPE were modelled and optimized by using hybrid B3LYP/6-31G* calculations [13,14]. The nature of the interactions present in the structures of DFPE were employed using natural bond orbital (NBO) calculations [15,16] and the atoms in molecules theory (AIM) [17,18] while the reactivities of the more stable conformers were predicted by means of the highest occupied molecular orbital (HOMO)-lowest unoccupied molecular orbital (LUMO) energy gaps [19]. Here, the hydrogen bond donor properties for the CF₂H group of DFPE were also analysed by means of the molecular electrostatic potentials [20-23] and later, they were compared with those obtained for the same group of ZnDFMS [3] and 5-difluoromethyl-1,3,4-thiadiazole-2-amino [4] and, for those obtained in this work for 1-(1H-pyrrol-2-yl)ethanone (PE) and 1-5-(trifluoromethyl)-1H-pyrrol-2-yl)ethanone (TFPE) [24,25]. The harmonic frequencies for DFPE and TFPE were also calculated and, at the same level of theory the detailed assignments of all the infrared bands were performed taking into account the scaled quantum mechanics force field methodology (SQMFF) [26] and the corresponding internal normal coordinates. The Raman spectra for DPE and TFPE were predicted by using the hybrid B3LYP/6-31G* method. The theoretical 1H-NMR, 13C-NMR, 19F-NMR spectra were calculated by using the Gauge-Independent Atomic Orbital (GIAO)

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Abstract

In this work, the structural and vibrational properties of 1-5-(difluoromethyl-1H-pyrrol-2-yl)-ethanone (DFPE) were studied by using the hybrid B3LYP/6-31G* method. The properties were analyzed and compared with those obtained for 1-(1H-pyrrol-2-yl)ethanone (PE) and 1-(5-(trifluoromethyl)-1H-pyrrol-2-yl)ethanone (TFPE). The theoretical 1H-NMR, 13C-NMR and 19F-NMR chemical shifts for DFPE were predicted by using the B3LYP/6-31++G** approach with the GIAO and CGST methods showing the three spectra good concordances with the corresponding experimental ones. A complete assignment of the vibrational spectra was presented.
and Continuous Set of Gauge Transformations (CSGT) [28] methods employing the optimized structures at B3LYP/6-311++G** level because it size of basis set is recommended for the NMR chemical shift calculations [29,30]. The calculated values show good concordance with the corresponding experimental ones.

**Computational Details**

For DFPE, three stable structures with C3 symmetries were found in the potential energy surface by using the hybrid B3LYP/6-31G* method which are observed in the Figure 1 together with the numbering of all the atoms. These structures were initially modelled with the Gauss View 5.0 program [31] and, then, they were optimized by using the Gaussian 09 program package [32]. The study of the inter- and intra-molecular hydrogen-bonding interactions in DFPE is very important and useful to understand the connection between the structures and activities due to the presence of potentials hydrogen bond donors (N-H and CF2H) and acceptors (C=O) groups, for these reasons, the NBO calculations were performed by using the NBO 3.1 program [16], as implemented in the Gaussian 09 package while for the AIM analysis the AIM2000 program was employed [18].

On the other hand, in this work two different types of charges, such as the natural charges (NPA) and those MK’s charges derived from Merz-Kollman [33] were analyzed. Besides, the bond orders expressed as Wiberg indexes and the stabilization energies for all the studied species were also calculated together with the corresponding molecular electrostatic potentials [20-23]. All the computed properties for the three conformers of DFPE were compared with those obtained at the same level of theory for PE and TFPE. In this work, the more stable structures of PE and TFPE are presented in Figure S1 (Supporting material). The harmonic frequencies and the force fields expressed in Cartesian coordinates for DFPE and TFPE were calculated at B3LYP/6-31G* level and, later, the resulting force fields were transformed to “natural” internal coordinates employing the Molvib program [34]. Tables S1 and S2 (Supporting material) shows the natural internal coordinates defined for all the conformers of DFPE and for the more stable structure of TFPE, in accordance with those obtained for molecules similar [3,4,35-38].

The calculated geometrical parameters for the three theoretical structures of DFPE were compared with those experimental reported for the 2-acetylepyrrol [45] and for 2-(difluoromethyl) isonicotinonitrile [1] by means of the root-mean-square deviation (RMSD) values which are summarized in Table 1.

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The calculated bond lengths and angles for the three conformers of DFPE by using the B3LYP/6-31G* method show a good correlation with those experimental values with rmsds values, for the distances of 0.019 Å and, for the angles between 0.6 and 0.7°. Therefore, these results provide a reliable starting point for the frequency calculations and B3LYP/6-31G* force field of DFPE. Experimentally, 2-acetylepyrrol [45] forms centro symmetric dimers in the solid state, through N-H--O hydrogen bonds involving amine and carbonyl groups, for this reason, in the PE, DFPE and TFPE solids similar structures could be expected.

**Charges and molecular electrostatic potentials studies**

As was mentioned above, in DFPE there are two potentials hydrogen bond donors sites, characterized by the N-H and F-C-H groups, for which, it is very important to know which of them is the strongly donor site because the only acceptor site is that determined by the C=O group. Hence, for the three conformers of DFPE, the molecular electrostatic potentials together with the NPA and MK’ charges were analyzed. The calculated molecular electrostatic potentials and the two
Comparison of calculated geometrical parameters with the corresponding experimental values for the conformers of 1-(5-(difluoromethyl)-1H-pyrrol-2-yl) ethane confirming, thus, that the NH bonds are weaker than the F₂C-H bonds. In the three conformers, the bond orders calculated for the O atoms have the same values due to their double bonds character. Note that the C₁ and C₉⁻⁻ conformational energy of the CI conformer, as was also observed in their energies and dipole moment values. The comparison with TFPE values show that the molecular electrostatic potential and the charges values are slightly lower on practically all the atoms of TFPE, as can be seen in Tables S4 and S5, revealing that the presence of a CF₃ group in this compound increases the donor effect of the NH group belonging to the pyrrol ring. Later, in the structure of DFPE solid intermolecular NH···N or CO···H bonds are expected.

NBO study

The above analyses show that the C=O groups are related with nucleophilic sites in DFPE while the N-H and F₂C-H groups with two possible donor sites, being the N-H sites the strongest donor in that molecule. The calculations related with the bond orders, which are expressed as Wiberg indexes, can be seen in Table S6. The values also show that the H₆ atoms have lower bond order values than the H₁₀ atoms confirming, thus, that the NH bonds are weaker than the F₂C-H sites. Additionally, these calculations show practically the same values for the C₉⁻⁻ and C₉⁻⁺ conformational energy of the CI conformer, as was also observed in their energies and dipole moment values. The comparison with TFPE values show that the molecular electrostatic potential and the charges values are slightly lower on practically all the atoms of TFPE, as can be seen in Tables S4 and S5, revealing that the presence of a CF₃ group in this compound increases the donor effect of the NH group belonging to the pyrrol ring. Later, in the structure of DFPE solid intermolecular NH···N or CO···H bonds are expected.

Moreover, taking into account the presence of pyrrol rings in the three conformers of DFPE and, of lone pairs due to the N₅, F₁₁, F₁₂ and O₁₈ atoms, the stabilization energies associated with delocalization energetic by NBO analysis was carried out in order to estimate all possible interactions between “filled” (donor) Lewis-type NBOs and “empty” (acceptor) non-Lewis NBOs [15,16]. Thus, the calculated main delocalization energies can be seen in Table S7. The results show two different interactions related with the C=C bonds belonging to the pyrrol rings and with the lone pairs of the N₅, F₁₁, F₁₂ and O₁₈ atoms. These interactions are the ΔE σ→ σ* and ΔELP→σ* charge transfers, where the latter delocalizations have the higher values, contributing thus in great part to the ΔE Total. Note that the total energies of the CI, CII and CIII conformers are the same and slightly higher than CI, justifying their probable presence at room temperature, as was thermodynamically observed in the section 3.1. In TFPE, the existence of the CF₃ group not shows significant changes in the bond order values, in reference to DFPE.

Types of charges are presented in Table S4 and S5, respectively. In this study, the results for DFPE were compared with those calculated for TFPE. As expected, the higher molecular electrostatic potential values are observed on the F₁₁, F₁₂, O₁₈ and N₅ atoms while the lower values on the H₆ and H₁₀ atoms. Note that the H₆ atoms belonging to the NH groups are the strongest donor sites in relation to the F₂C-H sites because the N atoms are more electronegative than the C ones. On the other hand, analyzing the atomic charges, the H₆ atoms have the most positive NPA and MK charges, in reference to the H₁₀ atoms of the three conformers of DFPE, while the charges on the O₁₈ atoms confirm that these sites are clearly the acceptor sites in DFPE. Note that the MK charges on all the atoms have lower values than the other ones, as observed in other molecules [43,46–49]. Figure S4 show the most negative potential on the O₁₈ atoms and the most positive on the H₆ atoms, thus, the strong red colour is observed on the acceptor C=O sites indicating probable capability of hydrogen bond formation while the strong blue colour is observed on the two donor N-H and F₂C-H sites. Additionally, these calculations show practically the same values for the C₉⁻⁻ and C₉⁻⁺ conformational energy of the CI conformer, as was also observed in their energies and dipole moment values. The comparison with TFPE values show that the molecular electrostatic potential and the charges values are slightly lower on practically all the atoms of TFPE, as can be seen in Tables S4 and S5, revealing that the presence of a CF₃ group in this compound increases the donor effect of the NH group belonging to the pyrrol ring.
AIM analysis

The hydrogen bonding plays an important role in the design of bioactive molecules and, as in DFPE there are nucleophilic and electrophilic sites it is expected the presence of probable inter and/or intra-molecular interactions and, in additional form, the possibility of it for act as a pharmacologic drug. For these reasons, for the three conformers of DFPE was performed a topological analysis by means the AIM2000 program [18]. The electron charge density, (ρ) and the Laplacian of the electron density, ∇²ρ(r) calculated for the three conformers of DFPE show the presence only of ring critical points (RCPs) whose properties can be seen in Table S8. Here, the topological properties for the C₁ conformer have slightly higher values than C₉ and C₁₀ while the same values are observed in these last two conformers. This analysis clearly shows that the three conformers are expected in the gas phase and that in their structures intra-molecular interactions are not observed. Additionally, the presence of the CF group slightly increases the electron charge density of TFPE, as compared with the three conformers of DFPE (Table S8). The latter result is expected due to the presence of three electronegative F atoms in TFPE. It is important to mention that the AIM analysis for the three conformers of DFPE by using the 6-311++G** neither show bond critical points in their structures and, therefore, intra-molecular interactions are not observed by using this level of theory.

NMR analysis

A comparison of the theoretical ¹H-NMR, ¹³C-NMR, ¹⁹F-NMR chemical shifts for the three conformers of DFPE, calculated employing the GIAO and CGST methods [27,28] at the B3LYP/6-311++G** level, with the corresponding experimental values by means of the root mean square deviations (RMSD) values can be seen in Table 2. In general, the calculated chemical shifts with both methods show higher values than the corresponding experimental ones, as also was observed in other molecules [4,50-54]. In both cases, the results show a good concordance for the H nuclei with rmsd values between 0.8 and 0.9ppm and a slightly lower agreement for the ¹³C nuclei (4.9-4.1 ppm) while the calculated ¹⁹F chemical shifts show the higher rmsd values using the GIAO method (18.2 and 20.8 ppm) and the lower values using the CGST method. These observed higher variations can be attributed in part to the calculations because they were performed in gas phase while the experimental values were obtained for DFPE in solution.

On the other hand, the GIAO method uses basis functions which depend on the field while the CGST method achieves gauge invariance by performing a continuous set of gauge transformations, for each point, obtaining an accurately description of the current density [53]. Additionally, the proximities between the values for the three conformers suggest their presence in solution. A further observation is that the peak belonging to the H atom of the N-H bond appears in furyl compounds at 11.37 ppm [50-53], in this case for the N₅-H₆ bonds are observed at 6.88 ppm, as in the 2-(2'-furyl)-1H-imidazol compound [52,53]

whose crystalline structure is polymeric with N-H---N bonds. Thus, the small shifts of these peaks towards lower fields suggest for DFPE probably the existence of some intermolecular interaction between nonbonding electrons.

Vibrational analysis

In this analysis, we considered the three stable structures of DFPE because they are thermodynamically predicted due to the proximities in their energy values. The three DFPE conformers and the TFPE structure have 48 normal vibration modes and all the modes are active in the IR and Raman spectra. The predicted IR and Raman spectra for the three conformers of DFPE by using B3LYP/6-31G** level can be seen in Figures 2 and 3, respectively compared with the corresponding to TFPE. The experimental bands observed in the infrared spectra in solid phase for DFPE and TFPE were taken from [1] and [24] and they are compared with the corresponding calculated wavenumbers in Table 3. The complete vibrational assignments of the experimental bands to the normal vibration modes were performed by comparison with related molecules [3,4,20-22,49-55] and taking into account the calculations performed here. The PED contributions for the three DFPE conformers can be seen in Tables S9–S11 while for TFPE are observed in Table S12. The comparison between the theoretical IR spectra show principally differences in the bands related to the vibration modes of the CF₂H and CF₃ groups, as observed in Figures 2 and 3 and, in Table 3. The SQM force fields for all the conformers of DFPE and for TFPE can be obtained at request. At continuation a brief discussion of the assignments of the most important groups is presented below.

DFPE and TFPE Assignments

C-H modes: In furyl imidazole compounds [50-53], the C-H stretches are observed in the 3150-3012 cm⁻¹ region, for this reason, the band observed at 3247 cm⁻¹ is assigned to those vibration modes for the three conformers of DFPE while for TFPE these modes are associated with the band at 3254 cm⁻¹. For the C₁ conformer these modes are calculated as totally pure while for the C₉ and C₁₀ conformers are observed combined between them. The in-plane deformation modes are observed between 1227 and 1018 cm⁻¹ while the corresponding out-of-plane deformations of the C-H group are observed between 753 and 718 cm⁻¹. Hence, the IR bands at 1228 and 1094 cm⁻¹ are assigned to those deformation modes for the three conformers, as observed in

<p>| Table 2: Observed and calculated H, C and F chemical shifts (δ, in ppm) for the three conformers of 1-(5-(difluoromethyl)-1H-pyrrol-2-yl) ethanone. |</p>
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Table 3. For TFPE, only one in-plane deformation mode and one out-of-plane deformation mode were assigned to the bands at 1049 and 795 cm⁻¹, respectively.

Note that the calculated C-H stretchings wavenumbers for C II and C III by using SQM calculations have higher values than C I while the two C-H rocking modes corresponding to the CF₂H groups are predicted at the same wave numbers.

**CH₃ modes:** As observed in molecules containing this group [20,42,49,54,55], both anti-symmetric and symmetric stretchings modes are predicted for the three conformers of DFPE and TFPE as totally pure modes in the expected region. Thus, taking into account this observation, those modes were assigned in the same region. Note that only the symmetric stretching and the bending modes for TFPE were assigned to the bands at 2923 and 1333 cm⁻¹. Furthermore, the rocking and twisting modes of the methyl group for DFPE and TFPE were predicted by the calculations in the same regions and, for these reasons, they were assigned accordingly.

**NH modes:** Note that the presence of the CF₃ group in TFPE produce a shifting of the N-H stretching mode toward lower wavenumbers, thus, the SQM calculations predict this stretching mode at 3480 cm⁻¹.

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*This work
†From Ref. [1]
‡From Ref. [24]
§From B3LYP/6-31G* method
¶From scaled quantum mechanics force field

Table 3: Experimental and calculated frequencies (cm⁻¹) and assignment of the three conformers of 1-(5-(difluoromethyl)-1H-pyrrol-2-yl) ethanone and for 1-(5-(trifluoromethyl)-1H-pyrrol-2-yl) ethanone.
while in the three conformers of DFPE are predicted between 3485 and 3433 cm⁻¹. Moreover, the IR and Raman bands attributed to the N-H stretching mode in the C₁ conformer is predicted with higher intensity than in the other ones, as can be seen in Figures 2 and 3. For DFPE and TFPE, the in-plane and out-of-plane deformation modes are predicted in the regions between 1219-1068 and 873-797 cm⁻¹, respectively.

**C₇F₃ and CF₃ modes**: The more important variations in the IR spectra of DFPE and TFPE are observed for the vibration modes of these groups [55]. Thus, both C₇F₃ stretches modes for the three conformers of DFPE are predicted by SQM calculations between 1048 and 1098 cm⁻¹ and, for this, they were assigned to the band at 1094 cm⁻¹. For TFPE, the three C₇F₃ stretches modes are clearly assigned to the bands at 1164, 1115 and 1096 cm⁻¹. Only, the C₇F₃ symmetric deformation mode was assigned to the band at 738 cm⁻¹ while, the two rocking and twisting modes were predicted respectively at 402, 384 and 22 cm⁻¹. For the three conformers of DFPE, only were assigned the wagging modes at 805 and 780 cm⁻¹ while the rocking and twisting mode are predicted between 479-424 and 34-29 cm⁻¹, as observed in Table 3.

**Skeletal modes**: The C-C and C-N stretching modes belonging to the pyrrol ring undergoes slightly changes in the intensities and positions of the bands due to the presence of the CF₂ and CF₃ groups while, the C-C and C=O stretching modes belonging to the side chain of DFPE and TFPE are predicted by SQM calculations in the same regions. Hence, the C13-018 stretching modes in DFPE are assigned to the band at 1645 cm⁻¹ while in TFPE that mode is assigned to the band at 1671 cm⁻¹. Figures 2 and 3 shows clearly that the IR and Raman bands attributed to the C=O stretching modes of the three conformers of DFPE are predicted with higher intensities than the corresponding to TFPE. The C1-C2 stretching modes in DFPE are predicted between 1559 and 1556 cm⁻¹ while in TFPE that mode is assigned to the band at 1561 cm⁻¹. The positions of the bands assigned to the two ring deformation and torsion modes corresponding to the pyrrol ring are also slightly modified as consequence of the CF₂ and CF₃ groups, as can be observed in Table 3. Thus, the bands observed in the spectrum of DFPE at 1012 and 931 cm⁻¹ can be assigned to ring deformation modes corresponding to the conformers of DFPE, in accordance with the calculations.

**Force Field**

The force constants for the three conformers of DFPE were calculated at the B3LYP/6-31G* level of theory by using the SQM methodology [26] with the Molvib program [34]. The values for DFPE are observed in Table 4 compared with those calculated for TFPE.

The results show, on one hand, that the force constants related with the C-N, C-C and C-H stretches belonging to the pyrrol rings for the three conformers of DFPE are different from those calculated for TFPE as consequence of the CF₂ and CF₃ groups. On the other hand, these groups have not influence on the side chain because the CH stretching force constants values are not modified while the C=O stretches force constants values are slightly different in DFPE and TFPE, as observed in Table 4. These observations are probably related to the different intensities and positions of the bands associated with the C=O stretches modes in DFPE and TFPE, as explained in the vibrational analysis (Table 3). The presence of three F atoms in TFPE justifies the high C-F stretching force constant value in TFPE, in relation to DFPE.

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**Table 4:** Comparison of scaled internal force constants for DFPE with the corresponding to TFPE.

<table>
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<tr>
<th>Force constant</th>
<th>1-(5-(difluoromethyl)-1H-pyrrol-2-yl) ethanone (DFPE)</th>
<th>1-(5-(trifluoromethyl)-1H-pyrrol-2-yl) ethanone (TFPE)</th>
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<tr>
<td>f(νN-H)</td>
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<tr>
<td>f(νC=O)</td>
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<td>f(δC-F)</td>
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<td>1.759</td>
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Units are mdyn Å⁻¹ for stretching/stretching/stretching interaction and mdyn Å rad⁻² for angle deformations.

*This work at the B3LYP/6-31G* level of theory.
low energy differences among them. The charges and molecular electrostatic potentials analyses predict intermolecular NH−N or CO−H bonds in the structure of 1-(5-(difluoromethyl)-1H-pyrrol-2-yl) ethane solid. The NBO and AIM studies demonstrate that the total stabilization energy and the topological properties increases in 1-(5-(trifluoromethyl)-1H-pyrrol-2-yl) ethane due to the presence of the CF3 group. The SQM force fields for 1-(5-(difluoromethyl)-1H-pyrrol-2-yl) ethane and 1-(5-(trifluoromethyl)-1H-pyrrol-2-yl) ethane were calculated and the complete assignments for the 48 normal modes of vibration corresponding to both compounds are reported together with their corresponding force constants. The comparison among the different descriptors of the 1-(1H-pyrrol-2-yl) ethane, 1-(5-(difluoromethyl)-1H-pyrrol-2-yl) ethane and 1-(5-(trifluoromethyl)-1H-pyrrol-2-yl) ethane compounds show that (i) the gap energies following the trend: ΔEGapPE < ΔEGapDFPE < ΔEGapTFPE, (ii) the electrophilicity index following the trend: PE < DFPE < TFPE and, (iii) the compound with the CF3 group has better capability to accept electrons due to their bigger electrophilicity index and, additionally, it has a low reactivity.

Acknowledgement

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Supporting Information Available

Tables S1-S13 and Figures S1-S4 are included in the Supporting Information.

References

16. Glendening ED, Badenhoop JK, Reed AD, Carpenter JE, Weinhold F (1996) NBO 3.1; Theoretical Chemistry Institute, University of Wisconsin, Madison, WI.


