Theoretical Study of (RS) - (4-fluorophenyl) (pyridine-2yl) methanol using Density Functional Theory

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Abstract: The theoretical study of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol has been carried out using DFT at B3LYP/6-31++G (d, p) level. Theoretical IR and normal mode analysis of title compound has also been calculated. The structure activity relationship based on the study of frontier orbital gap and molecular electrostatic potential map of the (RS)-(4-fluorophenyl) (pyridine-2yl) methanol has been used to understand the active sites of the molecule under study.

Keywords: Density functional theory, Vibrational analysis, HOMO-LUMO, MESP

1. Introduction

The diphenyl methanols, RPh2COH, exhibit a very rich diversity of supramolecular arrangements, including isolated molecules, hydrogen-bonded dimers, trimers, tetramers and hexamers as well as continuous hydrogen-bonded chains [1]. It is therefore of considerable interest to investigate the influence of an addition potential acceptor of hydrogen bonds as achieved. The vibrational spectroscopic analysis is known to provide immensely invaluable molecular structure elucidation in synergy with quantum chemical calculations. In order to obtain a complete description of molecular dynamics, vibrational wavenumber calculations along with the normal mode analysis have been carried out at the DFT level employing the basis set 6-311++G(d, p). The optimized geometry of molecule under investigation and its molecular properties such as equilibrium energy, frontier orbital energy gap and molecular electrostatic potential energy map, have also been used to understand the properties and active sites of the molecule.

2. Computational Details

Quantum chemical study of the (RS)-(4-fluorophenyl) (pyridine-2yl) methanol has been performed within the framework of the density functional theory [2] with Becke’s three-parameter hybrid exchange functional [3] with Lee–Yang–Parr correlation functionals (B3LYP) [4,5] and employing 6-311++G(d, p) basis set using the Gaussian 09 program package [6].

As the DFT hybrid B3LYP functional tends to overestimate the fundamental normal modes of vibration, a scaling factor of 0.9679 has been applied [7, 8]. The vibrational wavenumber assignments have been carried out by combining the results of the Gaussian 5 program [9], symmetry considerations and the VEDA 4 program [10]. The calculated IR spectra has been shown in Fig. 2.

3. Result and Discussion

3.1. Molecular Geometry Optimization and Energies

The geometry of the title compound has been optimized for the calculation of its molecular properties using DFT at the B3LYP level, with the 6-311++G(d,p) basis set. The optimized geometry of molecule (Fig. 1) under study is confirmed to be located at the local true minima on potential energy surface, as the calculated vibrational spectra contains no imaginary wavenumber. The optimized structural parameters (bond lengths, bond angles, dihedral angles) of title compound have been shown in Table 1. The C - O bond lengths 1.427 Å is found to be close to the standard C - O bond lengths [11,12]. These calculated bond length, bond angles are in full agreement with those standard bond lengths and bond angles.

![Figure 1: Optimized geometry of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol](image)

Table 1: Optimize parameters (bond length and bond angle) of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol calculated at B3LYP/6-311++G(d,p) level

| Parameter       | Bond length (Å) | Parameter       | Bond Angle (Degree) |
|-----------------|-----------------|-----------------|---------------------|
| C1-H2           | 1.0957          | O3-C1-C5        | 108.3696            |
| C1-O3           | 1.4272          | O3-C1-C17       | 111.7021            |
| C1-C5           | 1.5224          | C5-C1-C17       | 111.3161            |
| C1-C17          | 1.5281          | C1-O3-C4        | 108.3242            |
| O3-H4           | 0.9625          | C1-C5-C6        | 121.5308            |
| C5-C6           | 1.3951          | C1-C5-C14       | 119.4787            |
| C5-C14          | 1.3988          | C6-C5-C14       | 118.9899            |
| C6-H7           | 1.0819          | C5-C6-H7        | 119.5374            |
The optimized molecular structure belongs to the C₁ point group as it does not display any special symmetry. The overestimation of the vibrational wave numbers in ab-initio and DFT methods is corrected either by computing anharmonic correlations explicitly or by introducing a scaled field, even directly scaling the calculated wavenumbers with a proper factor. The vibrational wave numbers are calibrated according to the scaling factor of 0.9679 for DFT at B3LYP/6-311+G(d,p) level. The vibrational assignments have been done on the basis of relative intensities, line shape, the VEDA 4 program and the animation option of Gaussview 5.

The theoretical IR spectrum of the title compound is shown in Figure 2. The scaled calculated wave numbers along with their respective dominant modes are presented in Table 2.

![Theoretical IR spectrum of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol](image)

**Figure 2:** Theoretical IR spectrum of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol.

### 3.4 Vibrational Assignments

- **O-H vibrations**

  The O-H stretching vibration is very sensitive to hydrogen bonding. A free hydroxyl group or a non-hydrogen bonded hydroxyl group absorbs in the range 3700-3500 cm⁻¹. The intra-molecular hydrogen bonding present in the system reduces the hydroxyl stretching band to 3559-3200 cm⁻¹ region [13]. The scaled wavenumber calculated at 3741 cm⁻¹ is identified as O-H stretching with 100% contribution to P.E.D.
C-C and C-H vibrations

C-C stretching wavenumbers are observed as mixed modes in the range 1100 cm\(^{-1}\) to 800 cm\(^{-1}\) and agree well with the general appearance of C-H and C-C stretching modes. The C-C pure stretching are calculated to be 1583, 1575 and 1559 cm\(^{-1}\) which are also in good agreement with previous studies. The C-H stretching vibration of (RS)-(4-fluoro phenyl) (pyridine-2yl) methanol has been observed in the range 3110-2929 cm\(^{-1}\).

**Table 2:** Vibrational analysis of some selected modes of the title compound calculated at the B3LYP/6-311++G (d, p) level.

| Calculated Freq (cm\(^{-1}\)) | Scaled Freq (cm\(^{-1}\)) | IR Intensity | Assignment |
|------------------------------|--------------------------|--------------|------------|
| 3838                         | 3714                     | 44.7         | V\(_2\)[O3-H4(100)] |
| 3213                         | 3110                     | 1.4          | V\(_2\)[C6-H7(85)] |
| 3200                         | 3097                     | 3.8          | V\(_2\)[C18-H19(76)] |
| 3199                         | 3096                     | 2.1          | V\(_2\)[C12-H13(90)] |
| 3193                         | 3091                     | 1.2          | V\(_2\)[C8-H9(85)] |
| 3192                         | 3090                     | 14.9         | V\(_2\)[C18-H19(16)+C22-H23(74)] |
| 3175                         | 3073                     | 1.4          | V\(_2\)[C14-H15(90)] |
| 3172                         | 3070                     | 7.4          | V\(_2\)[C20-H21(77)] |
| 3151                         | 3050                     | 17.6         | V\(_2\)[C24-H25(93)] |
| 3026                         | 2929                     | 13.7         | V\(_2\)[C1-H2(100)] |
| 1635                         | 1583                     | 12.5         | V\(_2\)[C14-C12(30)] |
| 1627                         | 1575                     | 37.7         | V\(_2\)[C18-C20(25)]+C24-C22(23)] |
| 1611                         | 1559                     | 20.6         | V\(_2\)[N16-C17(21)+C22-C20(18)] |
| 1520                         | 1471                     | 71.0         | a\(_2\)[C8-C9(37)]+a\(_1\)[H1(13)-C14(19)] |
| 1464                         | 1417                     | 26.7         | a\(_2\)[C21-C20(25)]+a\(_1\)[H22-C21(24)+C24(32)] |
| 1400                         | 1355                     | 13.8         | a\(_2\)[H4-H3-C1(27)]+a\(_1\)[H2-C1(34)] |
| 1351                         | 1308                     | 13.1         | a\(_2\)[H25-C24-H16(24)+a\(_1\)[H2-H1-C1(27)] |
| 1294                         | 1252                     | 0.8          | V\(_2\)[N16-C24(47)] |
| 1237                         | 1197                     | 7.4          | V\(_2\)[N16-C17(21)+V\(_2\)[C1-C17(19)] |
| 1181                         | 1143                     | 51.9         | V\(_2\)[C5-C1(19)]+a\(_1\)[H4-H3-C1(29)] |
| 1172                         | 1134                     | 6.1          | a\(_2\)[H19-C18-C20(19)]+a\(_1\)[H21-C20-C21(33)]+a\(_1\)[H22-C22-C24(22)] |
| 1116                         | 1080                     | 4.5          | a\(_1\)[H22-C22-C24(23)] |
| 1099                         | 1064                     | 52.5         | V\(_2\)[C12-C10(26)]+V\(_2\)[C11-C10(18)] |
| 1063                         | 1029                     | 34.9         | V\(_2\)[O3-C1(47)] |
| 1031                         | 998                      | 36.2         | a\(_2\)[C18-C20-C21(19)]+a\(_1\)[C12-C10(8)]+a\(_1\)[C12-C10(40)] |
| 1013                         | 980                      | 0.1          | a\(_2\)[C12-C10(3)]+a\(_1\)[C12-C10(3)]+a\(_1\)[H19-C18-C19(19)]+a\(_1\)[H21-C20-C21(33)]+a\(_1\)[H22-C22-C24(22)] |
| 983                          | 951                      | 0.2          | a\(_2\)[H25-C24-N16-C17(52)] |
| 915                          | 886                      | 0.6          | a\(_2\)[H19-C18-C20-C22(45)]+a\(_1\)[H23-C22-C24-N16(20)] |
| 840                          | 813                      | 0.1          | a\(_2\)[C6-C8-C10(19)]+a\(_1\)[H9-C8-C10-C12(21)]+a\(_1\)[H15-C14-C12-C10(18)] |
| 763                          | 739                      | 18.4         | a\(_2\)[H23-C22-C24-N16(27)]+a\(_1\)[C17-C16-C24-C22(23)] |
| 732                          | 708                      | 7.9          | a\(_2\)[C10-C8-C6-C3(34)] |
| 645                          | 624                      | 0.4          | a\(_2\)[C18-C6-C5(20)]+a\(_1\)[C14-C12-C10(22)] |
| 507                          | 491                      | 31.1         | V\(_2\)[C11-C10(26)] |
| 414                          | 401                      | 6.5          | a\(_2\)[C7-C16-C24-C22(19)]+a\(_1\)[C18-C20-C22-C24(28)] |
| 284                          | 275                      | 122.7        | a\(_2\)[H4-H3-C1(34)] |
| 228                          | 221                      | 5.1          | a\(_1\)[C7-C16-C17(37)] |
| 178                          | 172                      | 1.1          | a\(_2\)[C6-C5-C1(44)] |

3.3. Electronic properties

The highest occupied molecular orbital (HOMO) is the orbital that primarily acts as an electron donor and the lowest unoccupied molecular orbital (LUMO) is the orbital that largely acts as the electron acceptor. The frontier orbital energy gap helps characterize the chemical reactivity and kinetic stability of the molecule. The 3D plots of the frontier orbitals HOMO, LUMO and the Molecular electrostatic potential map (MESP) figures for title compound are shown in Fig. 3 and Fig. 4 respectively. The frontier orbital energy gap is found to be 5.302 eV.

The value of the electrostatic potential (the energy of interaction of a positive test point charge with the nuclei and electrons of a molecule) mapped onto an electron iso-density surface may be employed to distinguish regions on the surface which are electron rich (subject to electrophilic

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attack) from those which are electron poor (subject to nucleophilic attack). When the two molecules are structurally very similar, molecular electrostatic potential surfaces make clear that this similarity does not carry over into their electrophilic/nucleophilic reactivities. The resulting surface simultaneously displays molecular size, shape and electrostatic potential in terms of colour grading and is very useful tool in investigation of correlation between molecular structure and the physicochemical property relationship of molecules including biomolecules and drugs [14-21]. The variation in electrostatic potential produced by a molecule is largely responsible for the binding of a drug to its receptor binding sites, as the binding site in general is expected to have opposite areas of electrostatic potential. The MESP plot of the title compound clearly suggests that the potential swings wildly hydrogen atoms attach with oxygen atom and carbon, which bear most the brunt of positive charge (blue).

**Figure 3:** HOMO-LUMO plots of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol.

![MESP plot of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol](image)

**Figure 4:** MESP plot of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol.

4. Conclusions

We have performed a detailed quantum chemical studies on (RS)-(4-fluorophenyl) (pyridine-2yl) methanol using density functional theory at B3LYP/6-311++G(d,p) level Vibrational spectroscopic analysis has been performed and prominent modes of vibration are assigned and discussed. The HOMO-LUMO gap provides a measure of charge transfer interaction. These finding may stimulate further observations on the biological activity of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol and related natural products.

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