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 6-31++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 6-31++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 Gaussview 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 ester 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

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-H4	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

C6-C8	1.3948	C5-C6-C8	120.67	C24-N16-C17-C1	-178.6085
C8-H9	1.0827	H7-C6-C8	119.7884	C24-N16-C17-C18	0.4165
C8-C10	1.3891	C6-C8-H9	120.5581	C17-N16-C24-C22	-0.5173
C10-Cl11	1.7614	C6-C8-C10	119.3087	C17-N16-C24-H25	179.9234
C10-C12	1.3919	H9-C8-C10	120.1328	C1-C17-C18-H19	-1.1175
C12-H13	1.0825	C8-C10-Cl11	119.5459	C1-C17-C18-C20	178.9089
C12-C14	1.3912	C8-C10-C12	121.0331	N16-C17-C18-H19	179.9077
C14-H15	1.0844	Cl11-C10-C12	119.4206	N16-C17-C18-C20	-0.0659
N16-C17	1.3374	C10-C12-H13	120.1997	C17-C18-C20-H21	179.9832
N16-C24	1.3379	C10-C12-H14	119.0957	C17-C18-C20-C22	-0.1988
C17-C18	1.3982	H13-C12-C14	120.7044	H19-C18-C20-H21	0.0101
C18-H19	1.0828	C5-C14-C12	120.9019	H19-C18-C20-C22	179.8281
C18-C20	1.3897	C5-C14-H15	119.6989		
C20-H21	1.0844	C12-C14-H15	119.3986		
C20-C22	1.3935	C17-N16-C24	118.0385		
C22-H23	1.0834	C1-C17-N16	115.9829		
C22-C24	1.3915	C1-C17-C18	121.2471		
C22-H25	1.0863	N16-C17-C18	122.7627		
H2-C1-O3	110.4387	C17-C18-H19	119.8617		

C18-C20-H21	120.437
C18-C20-C22	118.9111
H21-C20-C22	120.6516
C20-C22-H23	121.4195
C20-C22-C24	118.2013
H23-C22-C24	120.3791
N16-C24-C22	123.4441
N16-C24-H25	116.0027
C22-C24-H25	120.5517
H2-C1-O3-H4	-55.0146
C5-C1-O3-H4	-173.6015
C17-C1-O3-H4	63.4141
H2-C1-C5-C6	-129.8172
H2-C1-C5-C14	50.454
O3-C1-C5-C6	-9.9395
O3-C1-C5-C14	170.3317
O17-C1-C5-C6	113.2782
O17-C1-C5-C14	-66.4506
H2-C1-C17-N16	-22.7389
H2-C1-C17-C18	158.2201
O3-C1-C17-N16	-143.4455
O3-C1-C17-C18	37.5135
C5-C1-C17-N16	95.263
C5-C1-C17-C18	-83.778
C1-C5-C6-H7	1.2869
C1-C5-C6-C8	-179.4635
C14-C5-C6-H7	-178.983
C14-C5-C6-C8	0.2666
C1-C5-C14-C12	179.4832
C1-C5-C14-H15	-0.2326
C6-C5-C14-C12	-0.2525
C6-C5-C14-H15	-179.9683
C5-C6-C8-H9	-179.823
C5-C6-C8-C10	-0.0672
H7-C6-C8-H9	-0.5753
H7-C6-C8-C10	179.1805
C6-C8-C10-Cl11	-179.9191
C6-C8-C10-C12	-0.1534
H9-C8-C10-Cl11	-0.1622
H9-C8-C10-C12	179.6035
C8-C10-C12-H13	-179.6559
C8-C10-C12-C14	0.1675
Cl11-C10-C12-H13	0.1102
Cl11-C10-C12-C14	179.9335
C10-C12-C14-C5	0.0384
C10-C12-C14-H15	179.7551
H13-C12-C14-C5	179.8608
H13-C12-C14-H15	-0.4225

3.4 Vibrational Assignments

The optimized molecular structure belongs to the C_1 point group as it does not display any special symmetry. The overestimation of the vibrational wave numbers in ab-initio and DFT methods are corrected either by computing anharmonic correlations explicitly or by introducing a scaled field, even directly scaling the calculated wavenumbers with proper factor. The vibrational wave numbers are calibrated accordingly with 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.
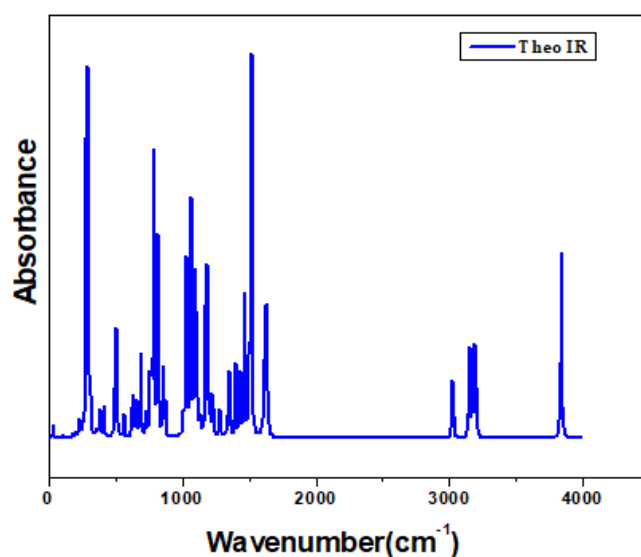

Figure 2: Theoretical IR spectrum of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol,

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-fluorophenyl) (pyridine-2yl) methanol has been observed in the range 3110-2929 cm^{-1}.

Ring vibrations

The thiophene ring spectral region predominantly involves the C–H, C–C, C-Cl, C-S and C=C stretching, and C–C–C as well as H–C–C-bending vibrations. The bands due to the ring C–H-stretching vibrations were observed as a group of partially overlapping absorptions in the region 3110–3069 cm^{-1} with more than 90% potential energy contribution. Vibrations involving C–H in-plane bending are found in the region 1600–825 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	$\nu_{[(O3-H4)(100)]}$
3213	3110	1.4	$\nu_{[(C6-H7)(85)]}$
3200	3097	3.8	$\nu_{[(C18-H19)(76)]}$
3199	3096	2.1	$\nu_{[(C12-H13)(90)]}$
3193	3091	1.2	$\nu_{[(C8-H9)(85)]}$
3192	3090	14.9	$\nu_{as\ [(C18-H19)(16)+\ (C22-H23)(74)]}$
3175	3073	1.4	$\nu_{[(C14-H15)(90)]}$
3172	3070	7.4	$\nu_{[(C20-H21)(77)]}$
3151	3050	17.6	$\nu_{[(C24-H25)(93)]}$
3026	2929	13.7	$\nu_{[(C1-H2)(100)]}$
1635	1583	12.5	$\nu_{[(C14-C12)(30)]}$
1627	1575	37.7	$\nu_{as\ [(C18-C20)(25)+\ (C24-C22)(23)]}$
1611	1559	20.6	$\nu_{as\ [(N16-C17)(21)+\ (C22-C20)(18)]}$
1520	1471	71.0	$\sigma[(H9-C8-C10)(18)]+ \sigma[(H13-C12-C14)(19)]$
1464	1417	26.7	$\sigma[(H21-C20-C22)(25)]+ \sigma[(H23-C22-C24)(32)]$
1400	1355	13.8	$\sigma[(H4-O3-C1)(27)]+ \sigma[(H2-C1-O3)(49)]$
1351	1308	13.1	$\sigma[(H25-C24-N16)(24)]+ \tau_i [(H2-C1-O3-H4)(27)]$
1294	1252	0.8	$\nu_{[(N16-C24)(47)]}$
1237	1197	7.4	$\nu_{[(N16-C17)(19)]}+ \nu_{[(C1-C17)(19)]}$
1181	1143	51.9	$\nu_{[(c5-C1)(19)]}+ \sigma[(H4-O3-C1)(29)]$
1172	1134	6.1	$\sigma[(H19-C18-C20)(19)]+ \sigma[(H21-C20-C21)(33)]+ \sigma[(H23-C22-C24)(22)]$
1116	1080	4.5	$\sigma[(H23-C22-C24)(23)]$
1099	1064	52.5	$\nu_{[(C12-C10)(26)]}+ \nu_{[(Cl11-C10)(18)]}$
1063	1029	34.9	$\nu_{[(O3-C1)(47)]}$
1031	998	36.2	$\sigma[(C10-C8-C6)(19)]+ \sigma[(C12-C10-C8)(20)]+ \sigma[(C14-C12-C10)(40)]$
1013	980	1.2	$\tau_i [(H21-C20-C22-C24)(39)]$
987	955	0.1	$\tau_i [(H7-C6-C8-C10)(30)]+ \tau_i [(H9-C8-C10-C12)(21)]+ \tau_i [(H15-C14-C12-C10)(18)]$
983	951	0.2	$\tau_i [(H25-C24-N16-C17)(52)]$
915	886	0.6	$\tau_i [(H19-C18-C20-C22)(45)]+ \tau_i [(H23-C22-C24-N16)(20)]$
840	813	0.1	$\tau_i [(H7-C6-C8-C10)(19)]+ \tau_i [(H9-C8-C10-C12)(29)]+ \tau_i [(H13-C12-C14-C5)(30)]+ \tau_i [(H15-C14-C12-C10)(19)]$
763	739	18.4	$\tau_i [(H23-C22-C24-N16)(27)]+ \tau_i [(C17-N16-C24+C22)(23)]$
732	708	7.9	$\tau_i [(C10-C8-C6-C5)(34)]$
645	624	0.4	$\sigma[(C10-C8-C6)(32)]+ \sigma[(C8-C6-C5)(20)]+ \sigma[(C14-C12-C10)(22)]$
507	491	31.1	$\nu_{[(Cl11-C10)(26)]}$
414	401	6.5	$\tau_i [(C17-N16-C24-C22)(19)]+ \tau_i [(C18-C20-C22+C24)(28)]$
284	275	122.7	$\tau_i [(H4-O3-C1-C5)(76)]$
228	221	5.1	$\sigma[(C1-C17-N16)(37)]$
178	172	1.1	$\sigma[(C6-C5-C1)(44)]$

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

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 physiochemical 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).
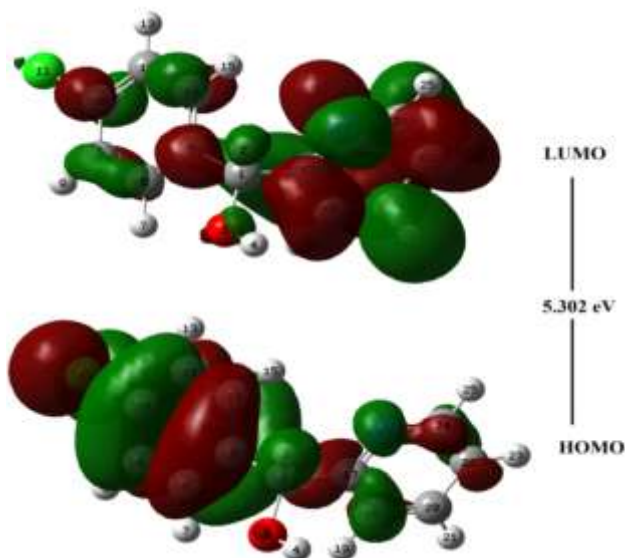

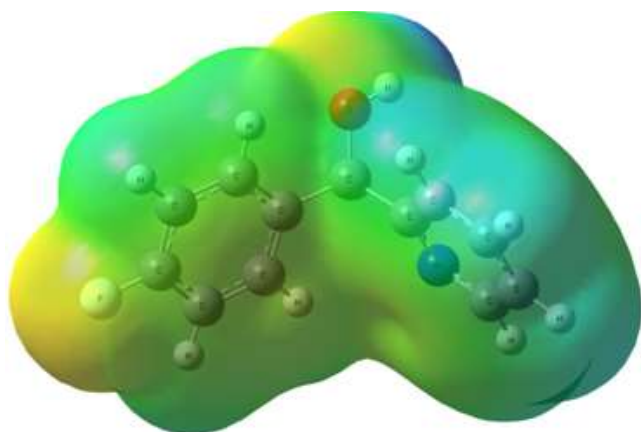**Figure 3:** HOMO-LUMO plots of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol,

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) levelVibrational 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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