

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

Sanjeev Kumar Trivedi¹, C. K. Dixit²

¹Department of Physics, Mumtaz P. G. College, Lucknow University, Lucknow-226007.

²Professor, Department of Physics, Dr. Shakuntala Misra National Rehabilitation University, Lucknow-226017

Abstract: The theoretical study of (RS)-(4-fluorophenyl) (pyridine-2-yl) 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-2-yl) 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-2-yl) 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-2-yl) methanol

Table 1: Optimize parameters (bond length and bond angle) of (RS)-(4-fluorophenyl) (pyridine-2-yl) 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
C8-H9	1.0827	H7-C6-C8	119.7884
C8-C10	1.3891	C6-C8-H9	120.5581
C10-C11	1.7614	C6-C8-C10	119.3087
C10-C12	1.3919	H9-C8-C10	120.1328
C12-H13	1.0825	C8-C10-C11	119.5459
C12-C14	1.3912	C8-C10-C12	121.0331
C14-H15	1.0844	C11-C10-C12	119.4206
N16-C17	1.3374	C10-C12-H13	120.1997
N16-C24	1.3379	C10-C12-H14	119.0957
C17-C18	1.3982	H13-C12-C14	120.7044
C18-H19	1.0828	C5-C14-C12	120.9019
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-C11	-179.9191		
C6-C8-C10-C12	-0.1534		
H9-C8-C10-C11	-0.1622		
H9-C8-C10-C12	179.6035		
C8-C10-C12-H13	-179.6559		
C8-C10-C12-C14	0.1675		
C11-C10-C12-H13	0.1102		
C11-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		

C24-N16-C17-C1	-178.6085
C24-N16-C17-C18	0.4165
C17-N16-C24-C22	-0.5173
C17-N16-C24-H25	179.9234
C1-C17-C18-H19	-1.1175
C1-C17-C18-C20	178.9089
N16-C17-C18-H19	179.9077
N16-C17-C18-C20	-0.0659
C17-C18-C20-H21	179.9832
C17-C18-C20-C22	-0.1988
H19-C18-C20-H21	0.0101
H19-C18-C20-C22	179.8281

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.

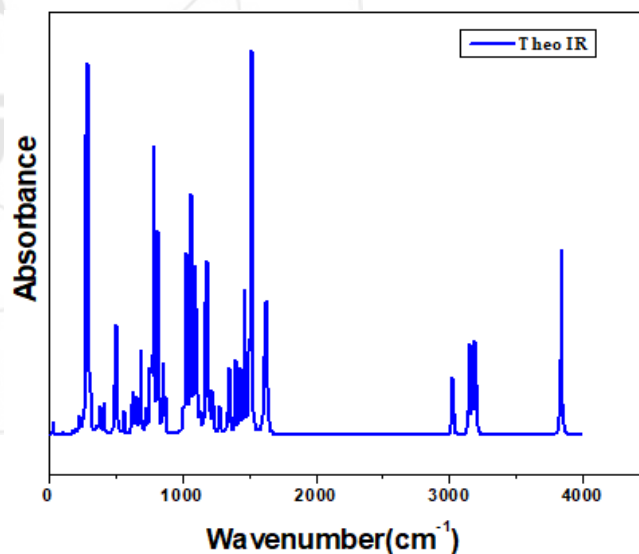


Figure 2: Theoretical IR spectrum of (RS)-(4-fluorophenyl)(pyridine-2yl) methanol,

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 $3700-3500\text{ cm}^{-1}$. The intra-molecular hydrogen bonding present in the system reduces the hydroxyl stretching band to $3559-3200\text{ cm}^{-1}$ 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	V _[(O3-H4)(100)]
3213	3110	1.4	V _[(C6-H7)(85)]
3200	3097	3.8	V _[(C18-H19)(76)]
3199	3096	2.1	V _[(C12-H13)(90)]
3193	3091	1.2	V _[(C8-H9)(85)]
3192	3090	14.9	V _{as [(C18-H19)(16)+ (C22-H23)(74)]}
3175	3073	1.4	V _[(C14-H15)(90)]
3172	3070	7.4	V _[(C20-H21)(77)]
3151	3050	17.6	V _[(C24-H25)(93)]
3026	2929	13.7	V _[(C1-H2)(100)]
1635	1583	12.5	V _[(C14-C12)(30)]
1627	1575	37.7	V _{as [(C18-C20)(25)+ (C24-C22)(23)]}
1611	1559	20.6	V _{as [(N16-C17)(21)+ (C22-C20)(18)]}
1520	1471	71.0	σ[(H9-C8-C10)(18)]+ σ[(H13-C12-C14)(19)]
1464	1417	26.7	σ[(H21-C20-C22)(25)]+ σ[(H23-C22-C24)(32)]
1400	1355	13.8	σ[(H4-O3-C1)(27)]+ σ[(H2-C1-O3)(49)]
1351	1308	13.1	σ[(H25-C24-N16)(24)]+ τ _i [(H2-C1-O3-H4)(27)]
1294	1252	0.8	V _[(N16-C24)(47)]
1237	1197	7.4	V _{[(N16-C17)(19)]+ V_[(C1-C17)(19)]}
1181	1143	51.9	V _{[(c5-C1)(19)]+ σ[(H4-O3-C1)(29)]}
1172	1134	6.1	σ[(H19-C18-C20)(19)]+ σ[(H21-C20-C21)(33)]+ σ[(H23-C22-C24)(22)]
1116	1080	4.5	σ[(H23-C22-C24)(23)]
1099	1064	52.5	V _{[(C12-C10)(26)]+ V_[(C11-C10)(18)]}
1063	1029	34.9	V _[(O3-C1)(47)]
1031	998	36.2	σ[(C10-C8-C6)(19)]+ σ[(C12-C10-C8)(20)]+ σ[(C14-C12-C10)(40)]
1013	980	1.2	τ _i [(H21-C20-C22-C24)(39)]
987	955	0.1	τ _i [(H7-C6-C8-C10)(30)]+ τ _i [(H9-C8-C10-C12)(21)]+ τ _i [(H15-C14-C12-C10)(18)]
983	951	0.2	τ _i [(H25-C24-N16-C17)(52)]
915	886	0.6	τ _i [(H19-C18-C20-C22)(45)]+ τ _i [(H23-C22-C24-N16)(20)]
840	813	0.1	τ _i [(H7-C6-C8-C10)(19)]+ τ _i [(H9-C8-C10-C12)(29)]+ τ _i [(H13-C12-C14-C5)(30)]+ τ _i [(H15-C14-C12-C10)(19)]
763	739	18.4	τ _i [(H23-C22-C24-N16)(27)]+ τ _i [(C17-N16-C24+C22)(23)]
732	708	7.9	τ _i [(C10-C8-C6-C5)(34)]
645	624	0.4	σ[(C10-C8-C6)(32)]+ σ[(C8-C6-C5)(20)]+ σ[(C14-C12-C10)(22)]
507	491	31.1	V _[(C11-C10)(26)]
414	401	6.5	τ _i [(C17-N16-C24-C22)(19)]+ τ _i [(C18-C20-C22+C24)(28)]
284	275	122.7	τ _i [(H4-O3-C1-C5)(76)]
228	221	5.1	σ[(C1-C17-N16)(37)]
178	172	1.1	σ[(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).

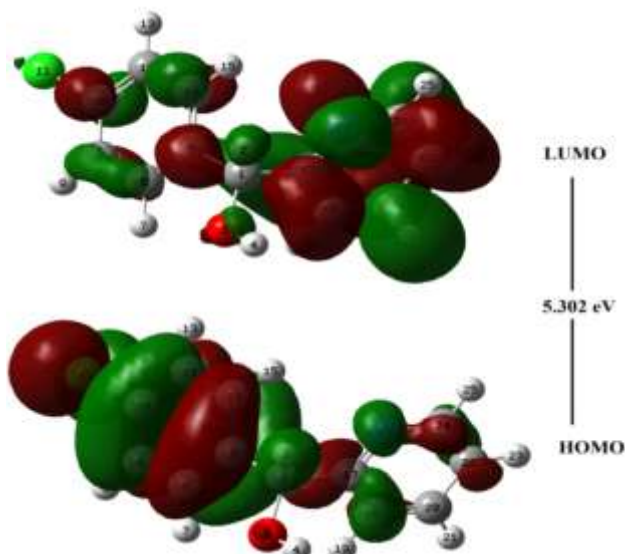


Figure 3: HOMO-LUMO plots of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol,

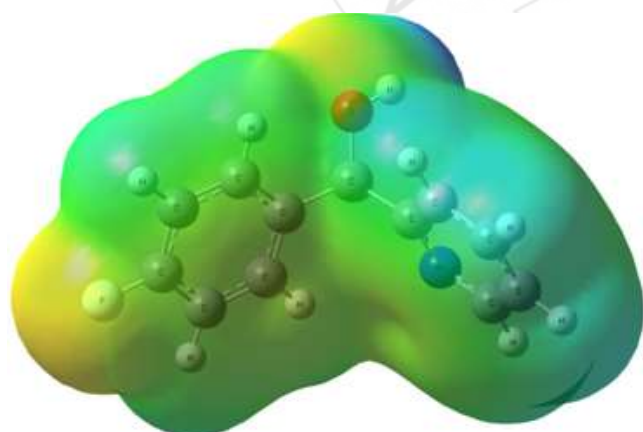


Figure 4: MESP plot of (RS)-(4-fluorophenyl) (pyridine-2yl) methanol,

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) 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.

References

- [1] G. Ferguson, C. D. Carroll, C. Glidewell, C. M. Zakaria, A. J. Lough, (1995). *Acta Cryst. B* 51, 367-377.
- [2] W. Kohn, L.J. Sham, *Phys. Rev.* 140 (1965) A1133.
- [3] A.D. Becke, *J. Chem. Phys.* 98 (1993) 5648.
- [4] C. Lee, W. Yang, R.G. Parr, *Phys. Rev. B* 37 (1988) 785.
- [5] B. Miehlich, A. Savin, H. Stoll, H. Preuss, *Chem. Phys. Lett.* 157 (1989) 200.
- [6] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G.A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H.P. Hratchian, A.F. Izmaylov, J. Bloino, G. Zheng, J.L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J.A. Montgomery Jr., J.E. Peralta, F. Ogliaro, M. Bearpark, J.J. Heyd, E. Brothers, K.N. Kudin, V.N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J.C. Burant, S.S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J.M. Millam, M. Klene, J.E. Knox, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, R.L. Martin, K. Morokuma, V.G. Zakrzewski, G.A. Voth, P. Salvador, J.J. Dannenberg, S. Dapprich, A.D. Daniels, Ö. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski, D.J. Fox, *Gaussian 09, Revision A.1*, Gaussian, Inc., Wallingford CT, 2009.
- [7] A.P. Scott, L. Random, *J. Phys. Chem.* 100 (1996) 16502.
- [8] P. Pulay, G. Fogarasi, G. Pongor, J.E. Boggs, A. Vargha, *J. Am. Chem. Soc.* 105 (1983) 7037.
- [9] M.J. Frisch, H.P. Hratchian, R.D. Dennington II, T.A. Keith, John Millam, A.B. Nielsen, A.J. Holder, J. Hiscocks. *Gaussian, Inc. GaussView Version 5.0.*, June 2009.
- [10] M.H. Jamroz, *Vibrational Energy Distribution Analysis: VEDA 4 Program* Warsaw, Poland, 2004.
- [11] M. Ladd, *Introduction to Physical Chemistry*, third ed., Cambridge University Press, Cambridge, 1998.
- [12] F.H. Allen, O. Kennard, D.G. Watson, L. Brammer, A.G. Orpen, R. Taylor, *J. Chem. Soc., Perkin Trans. II* (1987) S1-S19.
- [13] M. Jag. *Organic Spectroscopy –Principles and Applications (2nd Edition)* Narosa Publishing House: New Delhi, 2001.
- [14] I. Fleming, *Frontier Orbitals and Organic Chemical Reactions*, John Wiley and Sons, New York, 1976.
- [15] J.S. Murray, K. Sen, *Molecular Electrostatic Potentials, Concepts and Applications*, Elsevier, Amsterdam, 1996.
- [16] I. Alkorta, J.J. Perez, *Int. J. Quant. Chem.* 57 (1996) 123.
- [17] E. Scrocco, J. Tomasi, in: P. Lowdin (Ed.), *Advances in Quantum Chemistry*, Academic Press, New York, 1978.

- [18] F.J. Luque, M. Orozco, P.K. Bhadane, S.R. Gadre, J. Phys. Chem. 97 (1993) 9380.
[19] J. Sponer, P. Hobza, Int. J. Quant. Chem. 57 (1996) 959.
[20] R.K. Pathak, S.R. Gadre, J. Chem. Phys. 93 (1990) 1770.
[21] S.R. Gadre, I.H. Shrivastava, J. Chem. Phys. 94 (1991) 4384.

