Electronic properties of 2-(4-methoxyphenyl)-4,5-dimethyl-1h-imidazole 3-oxide: a hartree-fock approach

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Review Report

Your article gives a detailed HF study on the electronic properties of 2-(4-METHOXYPHENYL)-4,5-DIMETHYL-1H-IMIDAZOLE 3-OXIDE. As the DFT studies of the similar compound has been reported, this novel HF study of the title compound seems to be worth publishing.

KEY WORDS:

Imidazole; MEP; HF; FF

ABSTRACT

The computations were performed at Hartree-Fock (HF) levels of theory to get the optimized geometry and electronic properties of the title compound using Gaussian09 software package. The calculated geometrical parameters are in agreement with that of similar derivatives. Fukui Function is one of the widely used local density functional descriptors, to model chemical reactivity and selectivity. The HOMO and LUMO analysis is used to determine the charge transfer within the molecule. MEP was performed by the HF method.

1. Introduction

Imidazole is a colourless solid that dissolves in water to give mildly alkaline solution. It is an aromatic heterocycle, classified as a diazole and as an alkaloid.The imidazole scaffold is an accepted pharmacophore and represents an important synthetic precursor in new drug discovery [Kucukbay et al., 2003]. It is also of considerable interest as a ligand towards transition metal ions in a variety of biological molecules [Venkatesan et al., 2008]. Many imidazoline derivatives possess antidiabetic, antihypertensive, antiinflammatory, anticancer , antiparasitic, antimicrobial and antiviral actions [Hamada et al., 2013; Labarber et al., 2005; Servusovaet al., 2013; Congiu et al., 2008]. Apart of its use for pharmaceutical purpose, it also has variety of applications

in industries[Leahyet al., 2012; Cheng et al., 2005]. Imidazole and its derivatives are reported to be physiologically and pharmacologically active and find applications in the treatment of several diseases [Ucucu et al., 2001]. Such simulations are indispensable tools to perform normal coordinate analysis, so that modern vibrational spectroscopy is unimaginable without involving them. In the present study, the Molecular Electrostatic Potential, Frontier Molecular Orbitals and Fukui Function analysis are reported.

2. Experimental details

2-(4-methoxyphenyl)-4,5-dimethyl-1H-imidazole 3-oxide was synthesized via a solvent free procedure. 1 mmole (0.101 g) of 3-(hydroxyimino) butan-2-one was mixed with 1 mmole (0.136 g) of 4-methoxybenzaldehyde and 5 mmole (0.385 g) of ammonium acetate in an agate mortar and grinded thoroughly with a pestle into an intimate mixture. The mixture was then transferred to a test tube and heated to 115-120°C in an oil bath for 20 mins with constant shaking. Reaction progress was monitored by thin-layer chromatography (TLC) using 0.25 mm Merck Aluminium silica gel 60-F254 precoated plates. After 20 mins, a black solution resulted, which on cooling formed a black sticky precipitate. To the black precipitate, then added a small volume of diethyl ether, when a brown precipitate is separated. The precipitate was washed with 15 ml of ethyl acetate to yield the pure product. The electrospray mass spectrum was recorded on a MICROMASS QUATTRO II triple quadruple mass spectrometer. The ESI capillary was set at 3.5 kV and cone voltage was 40V. Melting Point (uncorrected) 138-140°C. ESI m/z found for ($C_{12}H_{14}N_2O_2$): 218.2 (M+1).

3. Computational details

Calculations of the title compound were carried out with Gaussian09 [Frisch et al., 2010] program using the Hartree-Fock (HF) method to predict the molecular structure and vibrational wave numbers. Molecular geometry was fully optimized by Berny's optimization algorithm using redundant internal coordinates. Harmonic vibrational wave numbers are calculated using the analytic second derivatives, to confirm the convergence to minima on the potential surface. The wave number values computed at the Hartree-Fock level contain known systematic errors due to the negligence of electron correlation [Foresman 1996]. Parameters corresponding to optimized geometry (HF) of the title compound are shown in Fig. 1 The animation option of GAUSSVIEW program, which gives a visual presentation of the vibrational modes [Dennington et al., 2009].
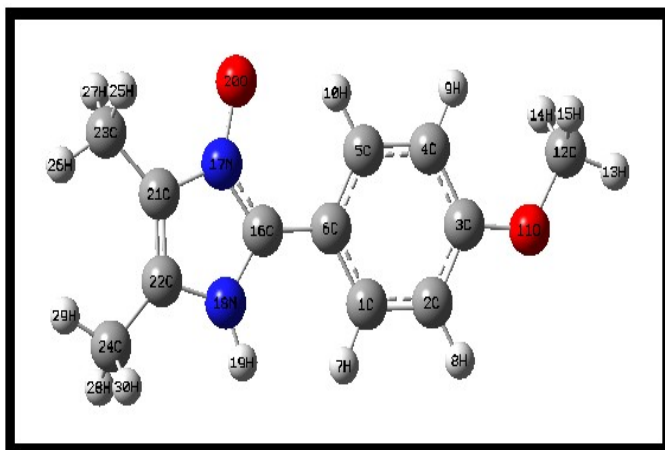
Fig.1 Optimized geometry Hartree-Fock (HF)of 2-(4-methoxyphenyl)-4,5-dimethyl-1H-imidazole 3-oxide.

4. Molecular Electrostatic Potential (MEP)

MEP is related to the ED and is a very useful descriptor in understanding sites for electrophonic and nucleophilic reactions as well as hydrogen bonding interactions [Scrocco et al., 1978; Luque et al., 2000]. The electrostatic potential V(r) is also well suited for analyzing processes based on the "recognition" of one molecule by another, as in drug-receptor, and enzyme-substrate interactions, because it is through their potentials that the two species first "see" each other [Politzer and Murray 1991; Scrocco and Tomasi 1973]. To predict reactive sites of electrophilic and nucleophilic attacks for the investigated molecule, MEP at the HF/6-31G optimized geometry was calculated. The different values of the electrostatic potential at the MEP surface are represented by different colours: red, blue and green which represents the regions of most negative, most positive and zero electrostatic potential respectively. The negative electrostatic potential corresponds to an attraction of the proton by the aggregate electron density in the molecule (shades of red), while the positive electrostatic potential corresponds to the repulsion of the proton by the atomic nuclei (shade of blue). The negative (red and yellow) regions of MEP were related to electrophilic reactivity and the positive (blue) regions to nucleophilic reactivity (Fig.2). From the MEP it is evident that the negative charge covers the nitro group and the positive region is over the NH part of the imidazole ring. The more electro negativity in the nitro group makes it the most reactive part in the molecule.
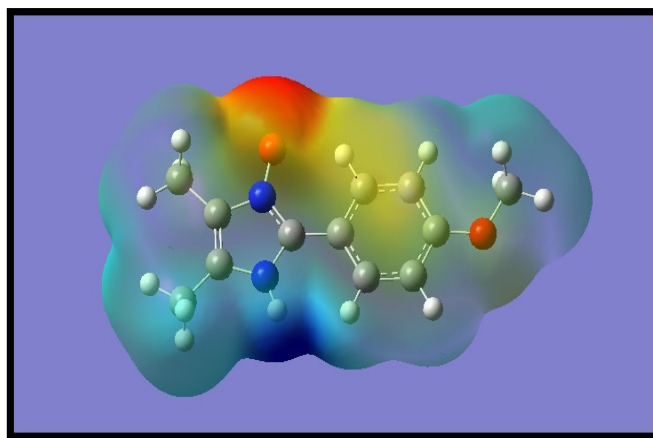
Fig.2 MEP plot of 2-(4-methoxyphenyl)-4,5-dimethyl-1H-imidazole 3-oxide.

5. Frontier Molecular Orbitals

The Frontier molecular orbitals can offer a reasonable qualitative prediction of the excitation properties and the ability of electron transport [Belletete et al., 2005; Zhenminga et al., 2011] The energies of the HOMO (Highest Occupied Molecular Orbital) and LUMO (Lowest Unoccupied Molecular Orbital) orbitals of the title compound are calculated using HF/6-31G basis set and shown in Fig.3 The energies of HOMO and LUMO are negative, which indicates that the studied compound is stable [Xia et al., 2006]. Conceptual HF based descriptors have helped in many ways to understand the structure of the molecules and their reactivity by calculating the chemical potential, global hardness and electrophilicity. HOMO and LUMO are the very important parameters for quantum chemistry. The conjugated molecules are characterized by a HOMO–LUMO separation, which is the result of a significant degree of intra-molecular charge transfer (ICT) from the end-capping electron-donor groups to the efficient electron-acceptor groups through π-conjugated path. The strong charge transfer interaction through π-conjugated bridge results in substantial ground state donor–acceptor mixing and the appearance of a charge transfer band in the electronic absorption spectrum for the title compound, EHOMO =-7.970 eV, ELUMO= -5.115 eV, the HOMO-LUMO gap is found to be 2.855eV
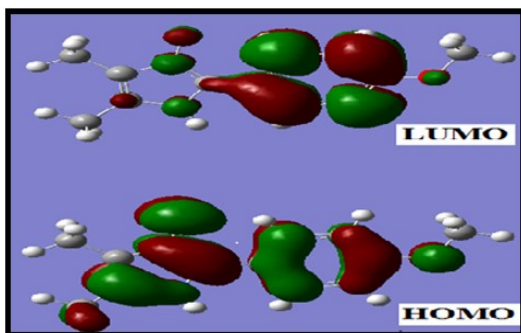
Fig.3 HOMO and LUMO Plots

6 . Fukui Function Analysis

Fukui Function (FF) is one of the widely used local density functional descriptors to model chemical reactivity and selectivity. The Fukui function is a local reactivity descriptor that indicates the preferred regions where a chemical species will change its density when the number of electrons is modified. Therefore, it indicates the propensity of the electronic density to deform at a given position upon accepting or donating electrons [Parr et al., 1989; Ayers et al., 2000; Parr et al., 1984]. Also, it is possible to define the corresponding condensed or atomic Fukui functions on the jth atom site as,

$f_j^- = q_j(N) - q_j(N-1)$
$f_j+ = q_j(N+1) - q_j(N)$
$f_j0 = \frac{1}{2}[q_j(N+1) - q_j(N-1)]$

For an electrophilic $f_j^-(r)$, nucleophilic or free radical attack $f_j+(r)$, on the reference molecule, respectively. In these equations, q_j is the atomic charge (evaluated from Mulliken population analysis, electrostatic derived charge, etc.) at the jth atomic site is the neutral (N), anionic (N + 1) or cationic (N - 1) chemical species. Chattaraj et al., have introduced the concept of generalized philicity. It contains almost all information about hitherto known different global and local reactivity and selectivity descriptor, in addition to the information regarding electrophilic/nucleophilic power of a given atomic site in a molecule. Morell et al., have recently proposed a dual descriptor ($\Delta f(r)$), which is defined as the difference between the nucleophilic and electrophilic Fukui function and is given by,

$\Delta f(r) = [f+(r) - f^-(r)]$

$\Delta f(r) > 0$, then the site is favored for a nucleophilic attack, whereas if $\Delta f(r) < 0$, then the site may be favoured for an electrophilic attack. Under this situation, dual

descriptors Δf(r) provide a clear difference between nucleophilic and electrophilic attack at a particular site with their sign. That is they provide positive value for site prone for nucleophilic attack and a negative value prone for electrophilic attack.

Atoms	fj-	fj+	Δfk
C1	0.01998	0.01037	-0.00960
C2	0.02240	0.02128	-0.00113
C3	0.02215	0.01924	-0.00291
C4	0.06223	0.03043	-0.03180
C5	0.00356	0.01908	0.01552
C6	0.04002	0.02333	-0.01669
H7	0.04056	0.03056	-0.01000
H8	0.06460	0.06789	0.00328
H9	0.08588	0.05174	-0.03414
H10	0.08006	0.04012	-0.03994
O11	0.04530	0.05234	0.00704
H12	0.03274	0.03557	0.00283
C13	0.06318	0.08365	0.02047
N14	0.01426	-0.02344	-0.03770
N15	0.02254	0.01044	-0.01211
H16	0.04423	0.03469	-0.00954
O17	0.07562	0.24867	0.17304
C18	0.02789	0.02811	0.00022
C19	0.00553	0.01139	0.00585
C20	-0.00274	-0.00895	-0.00621
C21	-0.00638	-0.00729	-0.00091
H22	0.01753	0.04255	0.02502
H23	0.03943	0.04360	0.00417
H24	0.03319	0.02756	-0.00563
H25	0.03582	0.03644	0.00062
H26	0.04691	0.04294	-0.00397
H27	0.06341	0.02757	-0.03583

Table 1. Values of the Fukui function considering Mulliken charges.

From the values reported in Table 1, according to the condition for dual descriptor, nucleophilic site for in our title compound is C5, H8, O11, H12, C13, O17, C18, C19, H22, H23, H25(positive value i.e. Δf(r) > 0). Similarly the electrophilic attack site is C1, C2, C3, C4, C6, H7, H9, H10, N14, N15, H16, C20, C21, H24, H26,

H27 (negative value i.e. $\Delta f(r) < 0$). The behaviour of molecules as electrophiles/ nucleophiles during reaction depends on the local behaviour of molecules.

7. Conclusion

The electronic properties of 2-(4-methoxyphenyl)-4,5-dimethyl-1H-imidazole 3-oxide in the ground state were reported. MEP predicts the most reactive part in the molecule. From the MEP it is evident that the negative charge covers the nitro group and the positive region is over the NH part of the imidazole ring. The more electro negativity in the nitro group makes it the most reactive part in the molecule. This along with the lowering of HOMO-LUMO band gap supports for the bioactivity of the molecule. In Fukui Function analysis the title compounds chemical reactivity and selectivity is also reported.

References

1. A.M. Venkatesan, A. Agarwal, T. Abe, H.O. Ushirogochi, D. Santos, Z. Li, G. Francisco, Y.I. Lin, P.J. Peterson, Y. Yang, W.J. Weiss, D.M. Shales, T.S. Mansour, Bioorg. Med. Chem. Lett.16 (2008) 1890-1902.

2. B. Servusova, J. Vobickova, P. Paterova, V. Kubicek, J. Kunes, M. Dolezal, J. Zit ko, Bioorg. Med. Chem. Lett. 23 (2013) 3589-3591.

3. Biochemistry and Molecular Biophysics: A Comprehensive Survey, Protein, Vol. 2, Adenine Press, Schenectady, NY, 1991 (chapter 13).

4. C. Congiu, M.T. Cocco, V. Onnis, Bioorg. Med. Chem. Lett. 18 (2008) 989-993.

5. C. Morell, A. Grand, A. Toro-Labbe, J. Phys. Chem. A 109 (2005) 205-212.

6. D. Zhenminga, S. Hepinga, L. Yufanga, L. Dianshenga, L. Bob, Experimental and theoretical study of 10-methoxy-2-phenylbenzo[h]quinoline, Spectrochim. Acta 78A (2011) 1143-1148..

7. D.V. Labarber, S.B. Skibo, Bioorg. Med. Chem. 13 (2005) 387-395.

8. E. Scrocco, J. Tomasi, Adv. Quantum. Chem. 103 (1978) 115-193.

9. E. Scrocco, J. Tomasi, Top. Curr. Chem. 42 (1973) 95-170.

10. F.J. Luque, J.M. Lopez, M. Orozco, Theor. Chem. Acc. 103 (2000) 343-345.

11. H. Kucukbay, R. Durmaz, E. Orhan, S. Gunal, II Farmaco. 58 (2003) 431-437.

12. J. Cheng, J. Xie, X. Luo, Bioorg. Med. Chem. Lett. 15 (2005) 267-269.

13. J.B. Foresman, in: E. Frisch (Ed.), Exploring Chemistry with Electronic Struc tureMethods: A Guide to Using Gaussian, Pittsburg, PA, 1996.

14. J.W. Leahy, C.A. Buhr, H.W.B. Johnson, B. Gyu Kim, T.G. Baik, J. Cannoy, T.P. Forsyth, J.W. Jeong, M.S. Lee, S. Ma, K. Noson, L. Wang, M. Williams, J.M. Nuss, E. Brooks, P. Foster, L. Goon, N. Heald, C. Holst, C. Jaeger, S. Lam, J.

Lougheed, L. Nguyen, A. Plonowski, J. Song, T. Stout, X. Wu, M. F. Yakes, P. Yu, W. Zhang, P. Lamb, O. Raeber, J. Med. Chem. 55 (2012) 5467-5482.

15. M. Belletete, J.F. Morin, M. Leclerc, G. Durocher, A theoretical, spectroscopic and photophysical study of 2,7-carbazolenevinylene-based conjugated deriva tives, J. Phys. Chem. 109A (2005) 6953-6959.

16. M. Hamada, V. Roy, T.R. McBrayer, T. Whitaker, C.U. Blanco, S.P. Nolan, J. Balzarini, R. Snoeck, G. Andrei, R.F. Schinazi, L.A. Agrofoglio, Eur. J. Med. Chem. 67 (2013) 398-408.

17. M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Chee seman, 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. Sonnen berg, 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, T. Keith, 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, O. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski, D.J. Fox, Gaussian 09, Revision B.01, Gaussian, Inc., Wallingford CT, 2010.

18. P. Politzer, J.S. Murray, in: D.L. Beveridge, R. Lavery (Eds.), Theoretical

19. P.K. Chattaraj, B. Maiti, U. Sarkar, J. Phys. Chem. A 107 (2003) 4973-4975.

20. P.W. Ayers, R.G. Parr, J. Am. Chem. Soc. 122 (2000) 2010-2018.

21. R. Dennington, T. Keith, J. Millam, GaussView, Version 5, Semichem Inc., Shawnee Mission KS, 2009.

22. R.G. Parr, W. Yang, Functional Theory of Atoms and Molecules, Oxford Univer sity Press, New York, 1989.

23. R.G. Parr, W.J. Yang, Am. Chem. Soc. 106 (1984) 511-516.

24. R.J. Parr, L.V. Szentpaly, S. Liu, J. Am. Chem. Soc. 121 (1999) 1922-1924.

25. S.W. Xia, X. Xu, Y.L. Sun, Y.L. Fan, Y.H. Fan, C.F. Bi, D.M. Zhang, L.R. Yang, Density functional theory study of La complex with Schiff base as building block, Chin. J. Struct. Chem. 25 (2006) 197-203.

26. S.W. Xia, X. Xu, Y.L. Sun, Y.L. Fan, Y.H. Fan, C.F. Bi, D.M. Zhang, L.R. Yang, Chin. J. Struct. Chem. 25 (2006) 197-203.

27. U. Ucucu, N. Gundogdu, I. lsikadag, II Farmaco.56 (2001) 285-290.