Semi empirical insights into the electronic structure of an isatin derived bis Schiff base

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Abstract: Schiff bases are versatile organic compounds and are widely studied for their broad range of biological applications. Extensive experimental data is available on these compounds but theoretical aspects are not comprehensively studied so far. This paper reports quantum mechanical calculation of a Schiff base to theoretically explore the electronic structure. Semi empirical (Austin Model 1, and Parametric Method 3) methods were employed to predict the optimized geometry and calculate various electronic properties e.g. IR vibrations, frontier molecular energy levels, total energies, dipole moments and some thermo chemical properties.

Keywords: Computational Chemistry, semi empirical calculation, Schiff base.

INTRODUCTION

Schiff bases are remarkable organic compounds and frequently reported for variety of important biological properties including anticancer, antibacterial, antifungal, enzyme inhibition and herbicidal activities (Khan *et al*., 2009). The azomethine group, rich in electron density render these compounds to be promising ligands from coordination chemistry standpoint and a number of coordination complexes have also been reported with broad range of biological applications (Papish*et al*., 2006; Patel, Parekh, & Patel, 2005; Raman, Kulandaisamy, Thangaraja, & Jeyasubramanian, 2003). A theoretical analysis of the candidate compound can so become valuable to predict certain properties and potential binding sites to give supplementary insights into the electronic structures of the candidate compound.

Substantial experimental data is available for these compounds i.e. Schiff bases, but theoretical perspectives are not much explored yet. This fact prompted us to conduct theoretical exploration of the electronic structure of these compounds. In present communication we report the quantum mechanical AM1 and PM3 electronic structure calculations of an isatin derived *bis* Schiff base, "2-hydroxybenzaldehyde-N-(2-oxo-1,2-dihydro-3H-indol-3-ylidene) hydrazone".

The *ab-Initio* methods are computationally very expensive in their application for medium to large sized chemical systems. Semi empirical approach effectively address this limitation of the Hartree-Fock calculation either by omitting or parameter zing some integrals centered on experimental data, such as dipole moments or ionization energies(Arora & Kumar, 2001). Therefore semi empirical calculations are exceedingly fast, applicable to large molecules and often come up with near accurate results when applied to chemical species similar to those used in the process of parameterization (Stewart, 1989a, 1989b). Although semi empirical methods are based upon approximations, yet they are efficiently used to calculate the wave function and energy to predict other properties like heats of formation, force constant, molecular geometry, population analysis, conformational analysis, chemical reaction pathways, prediction of spectral information and transition states etc. (Krossing & Slattery, 2006; McIver & Komornicki, 1971; Stewart, 1989a).

Latest semi empirical models like AM1 and PM3 are based on NDDO (neglect diatomic differential overlap) method which allow the use of a simpler HF equation |H-E|=0 in replacement of secular Hartree-Fock equation |H-ES|=0. These methods are very popular and used by various workers for rapid estimation of molecular properties and have been recently extended to embrace many elements, including some transition metals. The Austin Model 1 (AM1 by Dewar and co-workers) was largely parameterized based on a small number of atomic data, while Parametric Method 3, (PM3 by James Stewart) is parameterized in such a way that it can reproduce a large number of molecular properties (Krossing & Slattery, 2006; McIver & Komornicki, 1971).

MATERIALS AND METHODS

All computations were performed on a 64 bit Intel based computer with 1.7 GHz Quad Core 4005U CPU and 4.0 GB of physical memory. Molecular modeling of six slightly different starting geometries and MM (using Merck Force Field - MMFF94) conformational search was performed using Avogadro version 1.1.1 program (Hanwell *et al*., 2012). The lowest energy conformations for each starting geometry was optimized by semi-empirical AM1 and PM3 Hamiltonians implemented by

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GAMESS software program version 6.3.9600 (Schmidt *et al*., 1993). GAMESS package was also used in the frequency calculation, calculating heat of formation and zero-point energies per particle by AM1 and PM3 quantum chemical methods.

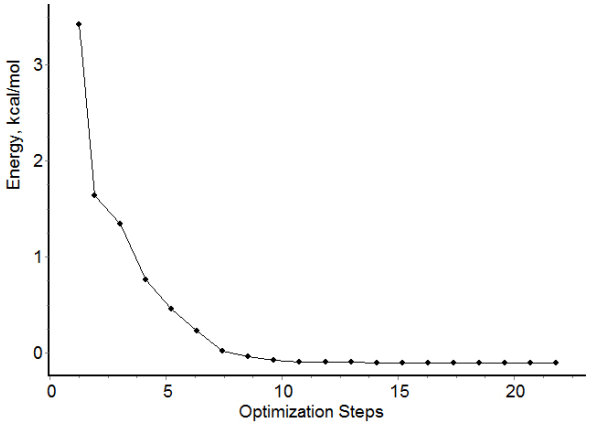

Fig. 1a: Optimization steps-AM1 method

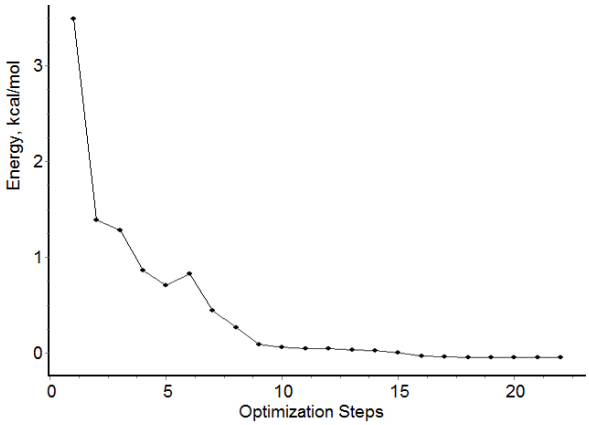

Fig. 1b: Optimization steps PM3 method

Optimized geometry, MO energy levels and IR modes were visualized by ChemCraft 2005 program (Zhurko & Zhurko, 2005) which also aided in animating IR modes and rendering high resolution images of 3D structure of the molecule. Population analysis and dipole moments were computed using Argus Lab 4.0.1 program (Thompson, 2004).

RESULTS

The optimization process went readily to reach to a local minimum for all starting geometries. Since all six starting conformers converged to the same geometry, it was believed that the global minimum was achieved. PM3 calculation produced best geometry with minimum energy (-69603.26 kcal/mol). This conformation was considered to be at the global minimum at the level of theory tested and all calculations were performed on this lowest energy conformer.

DISCUSSION

Figs. 1a and 1b show the optimization steps and fig. 2a and 2b show optimized geometries with calculated bond lengths.

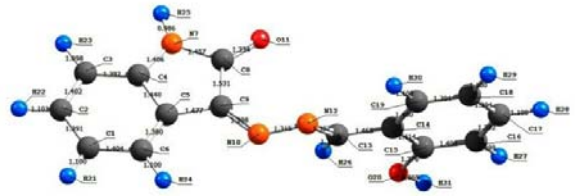

Fig. 2a: Optimized geometry with bond lengths calculated by AM1 method

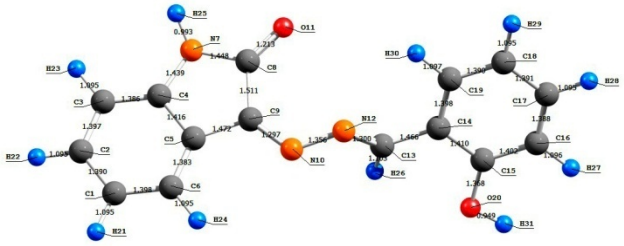

Fig. 2b: Optimized geometry with bond lengths calculated by PM3 method

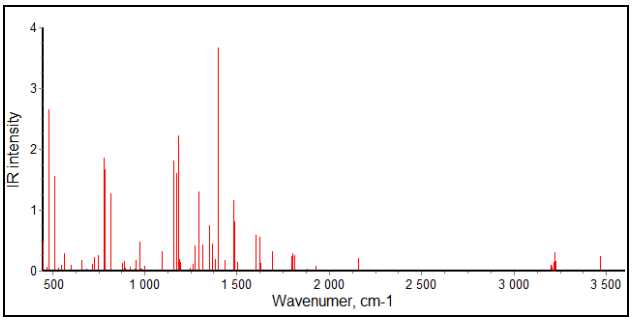

Fig. 3a: Calculated vibrational spectrum by AM1 calculation

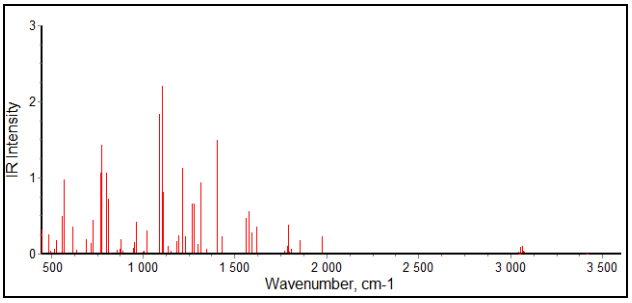

Fig. 3b: Calculated vibrational spectrum by PM3 calculation

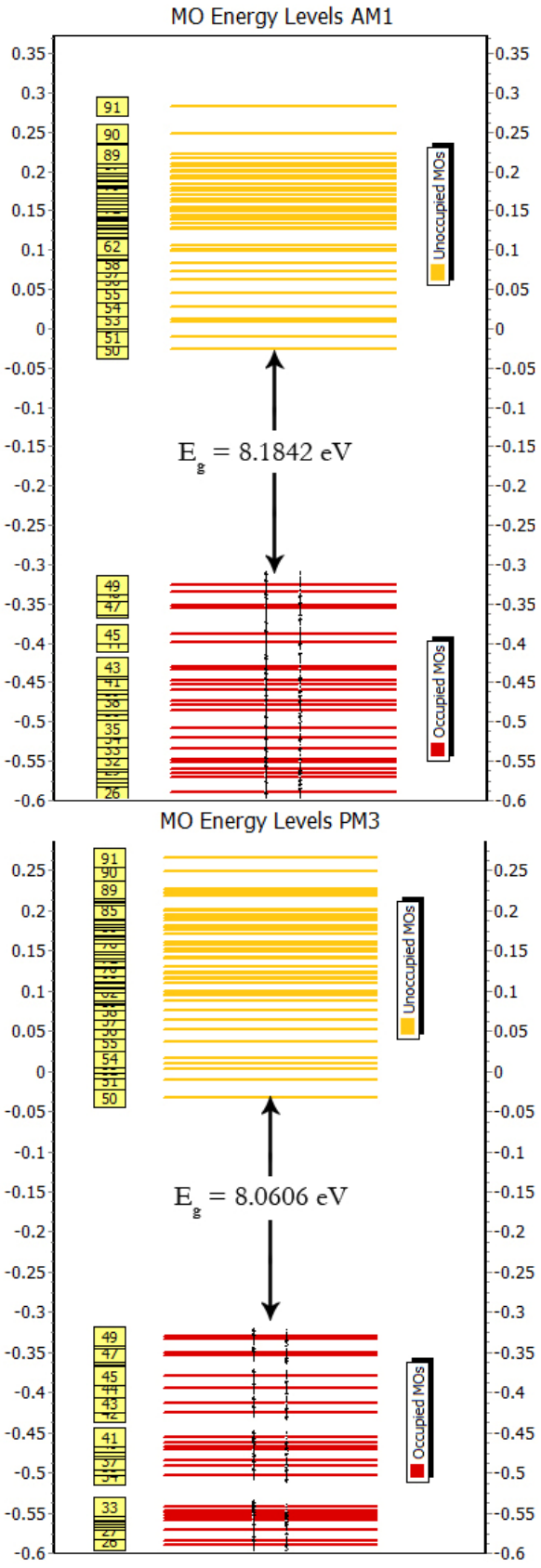

Fig. 4: Calculated MO energy levels

For a ligand to make stable metal complexes, it is a customary requirement to have some binding sites rich in electron densities. The population analysis shows higher electron densities on azomethine moiety (N10 and N12), hydroxyl group (O20) and carbonyl group (O11) of the Schiff base, which can readily donate electrons hence rendering the compound capable of creating coordination bonds. The results of the population analysis i.e. Mulliken and ZDO partial charges are given in tables 2a and 2b.

Table 1: Calculated energies, thermo chemical properties and dipole moments

Calculated Properties	AM1	PM3
Zero Point Energy (kcal/mol)	152.1276	146.6844
Total Energy (kcal/mol)	-76809.20	-69603.26
Heat of Formation (kcal/mol)	47.6	30.30
Dipole Moment (Debye)	1.44	1.21

Generally the frequency calculation by semi empirical methods can deviate from the experimental results by ~200cm^{-1}, the similar behavior was observed in our studies as well. The stretching mode for C=O appeared at 1979cm^{-1} by PM3 method while it appeared at 2073cm^{-1} by AM1 method. Similarly the O-H stretching was observed at 3884cm^{-1} by PM3 methods while it appeared at 3450 cm^{-1} for AM1 method. Other modes also deviated up to the same extent. The calculated vibrational spectra are shown in figs. 3a and 3b.

There are 49 filled MO energy levels and the calculated difference between the highest occupied molecular orbital (HUMO) and the lowest unoccupied molecular orbital (LUMO) is 8.1842 eV by AM1 method which corresponds to the UV absorption at 153.9 nm while PM3 method calculated this difference to be 8.0606 eV corresponding to the absorption of UV radiation at 151.4 nm. The MO energy levels are shown in fig. 4.

CONCLUSION

In this communication we studied a Schiff base from theoretical perspective by using semi empirical methods AM1 and PM3. Molecular modeling, geometry optimization, vibrational analysis, MO energy levels, population analysis and some other chemical properties were explored. These methods can further be explored on other similar systems to get faster theoretical insights and can be helpful in identifying potential binding site in a candidate ligand from coordination chemistry standpoint.

Table 2a: Population Analysis AM1 method

Population Analysis by AM1 calculation Charges in Electronic Units					
Atom #	Mulliken Charges	ZDO Charges	Atom #	Mulliken Charges	ZDO Charges
C1	-0.0789	-0.0462	C17	-0.0597	-0.0171
C2	-0.0593	-0.0172	C18	-0.0780	-0.0447
C3	-0.0770	-0.0513	C19	-0.0481	-0.0036
C4	0.1199	0.0918	O20	-0.4684	-0.3415
C5	-0.0080	-0.0183	H21	0.0721	0.0332
C6	-0.0460	-0.0050	H22	0.0741	0.0346
N7	-0.3909	-0.2167	H23	0.0764	0.0370
C8	0.5258	0.4089	H24	0.0878	0.0452
C9	0.2268	0.1607	H25	0.2600	0.1818
N10	-0.2522	-0.1839	H26	0.1147	0.0651
O11	-0.5897	-0.5101	H27	0.0716	0.0338
N12	-0.2959	-0.2339	H28	0.0747	0.0353
C13	0.1721	0.16301	H29	0.0725	0.0335
C4	0.0226	0.0059	H30	0.0914	0.0474
C15	0.1798	0.1441	H31	0.2892	0.2205
C16	-0.0795	-0.0520			

Table 2b: Population Analysis PM3 method

Population Analysis by PM3 calculation Charges in Electronic Units					
Atom #	Mulliken Charges	ZDO Charges	Atom #	Mulliken Charges	ZDO Charges
C1	-0.2238	-0.1327	C17	-0.1225	-0.0383
C2	-0.1505	-0.0644	C18	-0.2460	-0.1530
C3	-0.2079	-0.1180	C19	-0.1023	-0.0160
C4	-0.0756	-0.0754	O20	-0.2464	-0.2328
C5	-0.1158	-0.1042	H21	0.1979	0.1067
C6	-0.1039	-0.0195	H22	0.1918	0.1020
N7	-0.0270	0.0451	H23	0.2070	0.1144
C8	0.2905	0.2591	H24	0.2123	0.1174
C9	-0.0825	-0.0852	H25	0.1483	0.0904
N10	0.0125	0.0259	H26	0.2046	0.1137
O11	-0.3214	-0.3096	H27	0.1997	0.1120
N12	-0.0972	-0.078	H28	0.1909	0.1013
C13	-0.0649	0.0048	H29	0.2017	0.1096
C14	-0.1345	-0.119	H30	0.2195	0.1226
C15	0.1225	0.1265	H31	0.2304	0.2041
C16	-0.0795	-0.0520			

REFERENCES

Arora K and Kumar D (2001).Semi-Empirical AM1 and PM3 Calculations for Electronic Structure of a Pyrazolone.*Asian J. Chem.***13**(4): 1325-1329.

Hanwell MD, Curtis DE, Lonie DC, Vandermeersch T, Zurek E and Hutchison GR (2012). Avogadro: An advanced semantic chemical editor, visualization, and analysis platform. *J. Cheminformatics*, **4**(1): 17.

Khan KM, Khan M, Ali M, Taha M, Rasheed S, Perveen S and Choudhary MI (2009). Synthesis of *bis*-Schiff bases of isatins and their antiglycationactivity. *Bioorg. Med. Chem.***17**(22): 7795-7801.

Krossing I and Slattery JM (2006). Semi-empirical methods to predict the physical properties of ionic liquids: An overview of recent developments. *Zeitschrift.für. Physikalische.Chemie.*,**220**(10): 1343-1359.

McIver J and Komornicki A (1971).Rapid geometry optimization for semi-empirical molecular orbital methods.*Chem. Phys. Lett.* **10**(3): 303-306.

Papish ET, Taylor MT, Jernigan FE, Rodig MJ, Shawhan RR, Yap GP and Jové FA (2006). Synthesis of zinc, copper, nickel, cobalt and iron complexes using Tris (pyrazolyl) methane sulfonate ligands: A structural model for N, N, O binding in metalloenzymes.*Inorg. Chem.* **45**(5): 2242-2250.

Patel NH, Parekh HM and Patel MN (2005). Synthesis, characterization and biological evaluation of manganese (II), cobalt (II), nickel (II), copper (II) and cadmium (II) complexes with monobasic (NO) and neutral (NN) Schiff bases. *Transition Met. Chem*,**30**(1): 13-17.

Raman N, Kulandaisamy A, Thangaraja C and Jeyasubramanian K (2003). Redox and antimicrobial studies of transition metal (II) tetradentate Schiff base complexes. *Transition Met. Chem*, **28**(1): 29-36.

Schmidt MW, Baldridge KK, Boatz JA, Elbert ST, Gordon MS, Jensen JH and Su S (1993).General atomic and molecular electronic structure system. *J. Comput. Chem.***14**(11): 1347-1363.

Stewart JJ (1989a). Optimization of parameters for semiempirical methods I. Method. *Journal of Computational Chemistry*, **10**(2): 209-220.

Stewart JJ (1989b). Optimization of parameters for semiempirical methods II. Applications. *Journal of Computational Chemistry*, **10**(2): 221-264.

Thompson MA (2004). Argus Lab 4.0. 1. Planaria Software LLC, Seattle, WA http://www.arguslab.com.

Zhurko G and Zhurko D (2005).Chem Craft: Tool for treatment of chemical data. Lite version build,p.**8**.