



Spectroscopic and chemical reactivity analysis of D-Myo-Inositol using quantum chemical approach and its experimental verification

DEVENDRA P MISHRA, ANCHAL SRIVASTAVA and R K SHUKLA*

Department of Physics, University of Lucknow, Lucknow 226 007, India

*Corresponding author. E-mail: rajeshkumarshukla_100@yahoo.co.in

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Abstract. This paper describes the spectroscopic (^1H and ^{13}C NMR, FT-IR and UV–Visible), chemical, nonlinear optical and thermodynamic properties of D-Myo-Inositol using quantum chemical technique and its experimental verification. The structural parameters of the compound are determined from the optimized geometry by B3LYP method with 6-311++G(d,p) basis set. It was found that the optimized parameters thus obtained are almost in agreement with the experimental ones. A detailed interpretation of the infrared spectra of D-Myo-Inositol is also reported in the present work. After optimization, the proton and carbon NMR chemical shifts of the studied compound are calculated using GIAO and 6-311++G(d,p) basis set. The search of organic materials with improved charge transfer properties requires precise quantum chemical calculations of space-charge density distribution, state and transition dipole moments and HOMO–LUMO states. The nature of the transitions in the observed UV–Visible spectrum of the compound has been studied by the time-dependent density functional theory (TD-DFT). The global reactivity descriptors like chemical potential, electronegativity, hardness, softness and electrophilicity index, have been calculated using DFT. The thermodynamic calculation related to the title compound was also performed at B3LYP/6-311++G(d,p) level of theory. The standard statistical thermodynamic functions like heat capacity at constant pressure, entropy and enthalpy change were obtained from the theoretical harmonic frequencies of the optimized molecule. It is observed that the values of heat capacity, entropy and enthalpy increase with increase in temperature from 100 to 1000 K, which is attributed to the enhancement of molecular vibration with the increase in temperature.

Keywords. FT-IR; NMR; density functional theory; D-Myo-Inositol.

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1. Introduction

D-Myo-Inositol, a compound isolated from pinaceae and leguminosae plants, has been reported to possess insulin-like properties. Although the hypoglycemic activity of D-Myo-Inositol was recognized in recent years, the molecular mechanism of D-Myo-Inositol in the treatment of diabetes mellitus remains unclear. Diabetes mellitus is a complex disease that is called ‘the silent killer’ due to the number of patients and many chronic complications. Around 90% of the diabetes cases are type-2 diabetes mellitus (t2dm), which is known as non-insulin-dependent diabetes mellitus [1]. t2dm patients mostly are characterized by insulin resistance and impaired insulin secretion because of the dysfunction of β -cells caused by the high levels of blood glucose [2]. Irregularly increasing adipose

body tissues lead to obesity, raising the risk of insulin resistance and then impairing insulin-stimulated glucose uptake in the peripheral tissues [3,4]. D-Myo-Inositol, the 3-O-methyl form of D-chiro-Inositol, is one of the naturally occurring Inositol derivatives [5]. Pinaceae plants are rich in this compound and has already been found in leguminosae plants [6]. D-Myo-Inositol is regarded as a bioactive compound as it can be used for treatments connected with diabetes mellitus and its chronic complications. Many studies have shown the favourable effect of D-Myo-Inositol on the treatment of disorders associated with insulin because of its insulin-like function [7–10]. D-Myo-Inositol have an inherent understanding of biology space, and its synthetic derivatives have played significant roles in the discovery and development of drugs. Owing to the importance listed above, D-Myo-Inositol scaffolds are of prime

interest to researchers in the field of drug design and discovery.

2. Experimental method

The compound D-Myo-Inositol was isolated from alcoholic fraction of *anthocephalus chinensis* leaves. It was purified over silica gel (flash 230–400 mesh) column using gradient elution with mobile phase $\text{CHCl}_3:\text{MeOH}$ (85:15). Similar fractions were combined after monitoring the TLC. D-Myo-Inositol was obtained as white solid, MP 225–227°C. The molecular formula of the compound is found to be $\text{C}_6\text{H}_{12}\text{O}_6$ by ESI-MS and the analysis of its ^1H , ^{13}C , DEPT 90 and 135 spectra. ESI-MS showed the molecular ion peak $[\text{M} + \text{H}]^+$ at $m/z = 181$. The IR (in KBr) spectrum showed bands ν_{max} at 3428 cm^{-1} for hydroxyl group. The Fourier transform infrared spectra were recorded in the range $4000\text{--}400\text{ cm}^{-1}$ using a Thermo Nicolet Avatar, 370 FT-IR spectrometer. The sample was prepared in the form of a pellet by mixing KBr and D-Myo-Inositol. The UV absorption spectra of D-Myo-Inositol were examined in the range $200\text{--}500\text{ nm}$ using the Shimadzu 1800, UV-Visible recording spectrometer. The UV pattern was taken from a 10^{-5} M solution of D-Myo-Inositol in methanol. The ^1H and ^{13}C NMR spectra were recorded on a Bruker DRX-300 spectrometer operating at 300 MHz. The measurements were done in dimethyl sulphoxide (DMSO) solution. The solution was prepared by dissolving about 2 mg of the sample in 0.6 ml of DMSO. The spectra have the following experimental parameters: number of scans = 32; spectral width = 9615.385 Hz; acquisition time = 3.40 s. Chemical shifts were reported in ppm relative to TMS.

3. Computational details

The entire calculation was performed using the Gaussian 09W program package, invoking gradient geometry optimization. The initial geometry was generated from standard geometrical parameters and was minimized without any constraint in the potential energy surface at the B3LYP level, adopting the standard 6-311++G(d,p) basis set. The optimized structural parameters were used in the vibrational frequency calculations to characterize at stationary points as minima. We have utilized the density functional theory (DFT) with the three-parameter hybrid fundamental (B3LP) for the exchange part, and the Lee-Yang-Parr (LYP) correlation function for the computation of the molecular structure, vibrational frequencies and energies of the optimized structure. Strength for D-Myo-Inositol was calculated by TD-DFT using 6-311++G(d,p) basis set and B3LYP functional

after taking into account the configuration interaction between singly excited states. All molecular geometries were visualized using Chemcraft and Gauss-View program. The proton and carbon NMR chemical shifts were calculated with gauge including atomic orbital (GIAO) approach by applying B3LYP/6-311++G(d,p) method on the title molecule and compared with the experimental NMR spectra.

4. Results and discussion

The optimized structure of D-Myo-Inositol with numbering scheme for the atoms is presented in figure 1 and it belongs to C_1 point group symmetry.

4.1 Vibrational analysis

The observed FT-IR spectra of the title molecule were made with the help of Gauss-View program. The O–H band is characterized by a very strong and sharp band appearing approximately at $3800\text{--}3778\text{ cm}^{-1}$. The C–H stretching vibration is allotted for the simulated values from $3082\text{ to }3008\text{ cm}^{-1}$ and its experimental counterpart in IR spectrum exactly coincides with this value. The twisting of H–C–O appears in $1440\text{ to }1358\text{ cm}^{-1}$ range. The bending of H–O–C appears in the range of $1285\text{ to }1199\text{ cm}^{-1}$. The bending of O–C–C and C–C–C appears in the range $408\text{ to }109\text{ cm}^{-1}$.

4.2 NMR analysis

The chemical shifts of the compounds are reported in ppm relative to TMS for ^1H and ^{13}C NMR spectra and are listed in table 1. Data show good agreement between experimental and calculated chemical shifts.

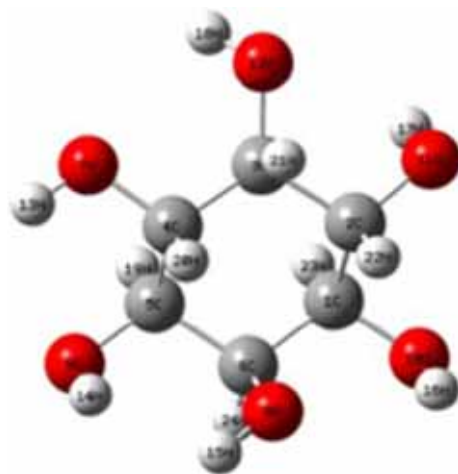


Figure 1. Molecular structure of D-Myo-Inositol with numbering scheme for the atoms.

Table 1. Experimental and theoretical isotropic chemical shifts of the compounds in ppm relative to TMS.

Position of the atom	Calculated chemical shifts (in ppm)	Experimental chemical shifts (in ppm)
C-5	104.7448	74.1
C-1	89.0609	71.9
C-2	85.1678	72.3
C-6	78.4419	72.1
C-4	75.1221	69.3
C-3	34.7777	61.1
H-21	9.5135	4.03
H-22	4.9827	3.60
H-20	4.7261	3.51
H-24	4.3679	3.60
H-19	4.3319	3.51
H-13	3.7781	3.25
H-23	2.9125	–
H-14	2.6616	–
H-17	2.3004	–
H-18	2.2933	–
H-16	0.9331	–
H-15	0.7527	–

4.3 UV–Visible spectroscopy

The search for the organic materials with improved charge transfer properties requires precise quantum chemical calculations of space-charge density distribution, stable and transition dipole moments, HOMO and LUMO states. The absorption in the range of UV spectrum has been taken as the main criterion for the verification of the performed quantum chemical calculations. Recently, it has been shown that time-dependent density functional theory (TD-DFT) method reproduces optical susceptibilities very accurately for a wide range of organic systems. The nature of transition in the observed UV–Visible spectrum of the title compound has been studied by the TD-DFT. Frontier molecular orbitals HOMO and LUMO determine the ability of a molecule to absorb light and the molecular reactivity. A combined experimental and theoretical UV–Visible spectrum analysis of the title compound indicates that the observed electronic excitation at $\lambda_{\max} = 270$ nm corresponds to the electronic excitation calculated at $\lambda_{\max} = 276.87$ nm with oscillator strength $f = 0.0016$. The difference between the experimental and calculated values of the band gap was due to the absorbing medium. On the basis of molecular orbital and molecular orbital coefficient analysis, the nature of transition was found to be π to π^* .

4.4 Thermochemical analysis

Thermochemical properties of the title molecule are dominated by molecular vibrations as electronic

contribution becomes negligible due to the absence of free electrons, especially at the room temperature. Various thermal parameters for the title molecule are calculated and reported in table 2.

These parameters are related to one another via standard thermodynamic relations and can be useful for the estimation of chemical reaction paths. From the above table, it can be observed that these thermodynamic functions increase with temperature because the molecular vibrational intensities increase with temperature. The correction equations between heat capacity ($C_{p,m}$), entropy (S_m), enthalpy change (H_m) and temperature (T) are fitted by quadratic formulas. The corresponding fitting equations are as follows:

$$C_{p,m} = -0.077 + 0.184T - 8 \times 10^{-5}T^2 \quad (R^2 = 0.999)$$

$$S_m = 50.14 + 0.195T - 5 \times 10^{-5}T^2 \quad (R^2 = 1.000)$$

$$H_m = 121.90 + 0.021T + 5 \times 10^{-5}T^2 \quad (R^2 = 0.999).$$

4.5 Global reactivity descriptors

The global reactivity descriptors like ionization potential ($= -0.221$ eV), electron affinity ($= -0.441$ eV), chemical potential ($= 0.331$ eV), electronegativity ($= -0.331$ eV), global hardness ($= 0.11$ eV), global softness ($= 9.09090$ eV $^{-1}$) and global electrophilicity index ($= 0.498004$ eV) have been calculated using DFT.

Table 2. Thermodynamical properties of D-Myo-Inositol.

T (K)	H_m (kcal/mol)	$C_{p,m}$ (cal/mol-K)	S_m (cal/mol-K)
100	125.290	17.171	69.017
200	127.849	33.497	87.485
300	131.923	47.842	104.613
400	137.381	61.034	120.795
500	144.059	72.145	136.094
600	151.736	81.054	150.428
700	160.211	88.187	163.784
800	169.330	94.010	176.218
900	178.981	98.866	187.813
1000	189.079	102.989	198.658

4.6 NLO analysis

Dipole moment, polarizability and first-order hyperpolarizability of D-Myo-Inositol were evaluated using B3LYP/6-311++G(d,p) level. The value of dipole moment was 1.51765 D, the mean polarizability (α) = 1.40447×10^{-23} esu, the anisotropy of the polarizability ($\Delta\alpha$) = 178.8362 a.u., $\Delta\alpha = 2.65035 \times 10^{-23}$ esu, the mean first-order hyperpolarizability (β_0) = 196.79026 a.u. = 1.70013×10^{-30} esu. The first-order hyperpolarizability is six times greater than that for urea ($\beta_0 = 0.3728 \times 10^{-30}$ esu). It shows that the title molecule possesses very good non-linear properties.

5. Conclusion

A systematic study has been conducted on the structural and spectral analysis of D-Myo-Inositol molecule by spectroscopy and quantum chemical calculations. The vibrational and studies of D-Myo-Inositol have been conducted using various spectroscopic techniques such as FT-IR, NMR, UV-Visible and thermochemical analyses. The global reactivity descriptors, dipole moment, polarizability and first-order hyperpolarizability were evaluated. D-Myo-Inositol has six times more

pronounced non-linear optical properties than those of urea.

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