Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 153 (2016) 496–504

Contents lists available at ScienceDirect

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy

journal homepage: www.elsevier.com/locate/saa

Experimental and theoretical study of ornidazole

P. Rajesh [a,e,*], S. Gunasekaran [b], T. Gnanasambandan [c], S. Seshadri [d]

[a] Department of Physics, Pachaiyappa's College, Chennai 600030, India
[b] Research & Development, St. Peter's University, Avadi, Chennai 600 054, India
[c] Department of Physics, Pallavan College of Engineering, Kanchipuram 63150, India
[d] Department of Physics, L.N. Govt. Arts College, Ponneri 601204, India
[e] Department of Physics, Meenakshi Academy of Higher Education & Research, Faculty of Humanities and Science, Meenakshi University, Chennai-600078, India

ARTICLE INFO

Article history:
Received 11 August 2014
Received in revised form 8 August 2015
Accepted 14 August 2015
Available online 22 August 2015

Keywords:
FT-IR
FT-R
DFT
NBO

ABSTRACT

The Fourier transform infrared (FT-IR) and the Fourier transform Raman (FT-Raman) spectra of the title molecule in solid phase were recorded in the region 4000–400 cm^{-1} and 4000–100 cm^{-1} respectively. The geometrical parameters and energies were investigated with the help of Density Functional Theory (DFT) employing B3LYP method and 6-31G (d, p) basis set. The analysis was supported by electrostatic potential maps and calculation of HOMO–LUMO. UV, FT-IR and FT-Raman spectra of ornidazole were calculated and compared with experimental results. Thermodynamic properties like entropy, heat capacity, have been calculated for the molecule. The predicted first hyperpolarizability also shows that the molecule might have a reasonably good non-linear optical (NLO) behavior. The intramolecular contacts have been interpreted using natural bond orbital (NBO) and natural localized molecular orbital (NLMO) analysis.

1. Introduction

Ornidazole is a nitroimidazole which is an antibacterial and antiprotozoal drug used to treat anaerobic enteric protozoa. Also used in the treatment of prophylaxis susceptible anaerobic infections in dental and gastrointestinal surgery. Chemically, ornidazole is 1-Chloro-3-(2-methyl-5-nitroimidazol-1-yl) propan-2-ol. The molecular formula is $C_7H_{10}ClN_3O_3$. Ornidazol is available in the brand name of Avrazor, Biteral, Mebaxol, Oniz, Orni, and Ornid.

The ornidazole and its derivatives are studied by several authors. Investigation of the formation process of in vivo and real time determination of ornidazole and tinidazole and pharmacokinetic study by capillary electrophoresis with microdialysis was done by Zhang et al. [1]. A comparative study of the use of ornidazole hemihydrate was investigated by Deng et al. [2]. Toxicity of ornidazole and its analogues to rat spermatozoa as reflected in motility parameters were studied by Bone et al. [3]. Thermodynamic characteristics of solutions of ornidazole in different organic solvents at different temperatures was done by Bhesaniya et al. [4] Enantioselective determination of ornidazole in human plasma by liquid chromatography–tandem mass spectrometry on a Chiral-AGP column was investigated by Jiangbo Du et al. [5] Synthesis and characterization of P_H-sensitive hydrogel composed of carboxymethyl chitosan for colon targeted delivery of ornidazole were studied by Vaghaniet et al. [6].

Literature survey reveals that so far there is no complete experimental and theoretical study for the title compound ornidazole. In this work, we mainly focus on the detailed spectral assignments and vibrational thermodynamic properties based on the experimental Fourier transform infrared (FT-IR) and Fourier transform Raman (FT-Raman) spectra as well as DFT/B3LYP calculations for ornidazole. The redistribution of electron density (ED) in various bonding, antibonding orbitals and E (2) energies have been calculated by the natural bond orbital (NBO) analysis to give clear evidence of stabilization originating from the hyper conjugation of various intra-molecular interactions. Conformational analysis is the examination of the position of a molecule and the energy changes it undergoes as it converts among the different conformations. The study of HOMO and LUMO analysis has been used to elucidate the information regarding the charge transfer within the molecule. Finally, the UV–vis spectra and the electronic absorption properties were explained and illustrated from the frontier molecular orbitals. Here, the calculated results have been reported in the text. The experimental and theoretical results supported each other and the calculations are valuable for providing insight into the vibrational spectra and molecular properties.

2. Experimental details

The compound under investigation was obtained from the Lancaster Chemical Company of UK with a stated purity of greater than 98% and it was used as such for the spectral measurements. In room temperature the Fourier transform infrared spectra of ornidazole was recorded in the region 4000–400 cm^{-1} at a resolution of ± 1 cm^{-1} using BRUKER IFS-66V Fourier transform spectrometer equipped with a MCT detector, a KBr beam splitter and global source. The FT-Raman spectrum was recorded with FRA-106 Raman accessories in the region 4000–100 cm^{-1}

---

[*] Corresponding author.
E-mail address: rajesh.ncc5coy@gmail.com (P. Rajesh).

http://dx.doi.org/10.1016/j.saa.2015.08.032
1386-1425/

Nd: YAG laser operating at 200 mW power with 1064 nm excitation was used as a source. The UV–visible absorption spectrum of the sample was recorded using a Shimadzu UV-1800 PC, UV–vis spectrophotometer in the range of 200–400 nm using water as solvent.

3. Methods of analysis

The molecular geometry optimization and vibrational frequency calculations were carried out for ornidazole, with GAUSSIAN 03W software package [7] Becke's three parameter exchange functional (B3) [8,9], and combination with the correlation functional of Lee, Yang and Parr (LYP) [10] with standard 6-31G (d, p) basis sets. The potential energy distribution (PED) corresponding to each of the observed frequencies is calculated using VEDA 4 program [11] and it shows the reliability and accuracy of the spectral analysis. The atomic charge, electric dipole moment, polarizability, first hyperpolarizability, HOMO, LUMO and other thermodynamic parameters were also calculated theoretically. The natural bonding orbital (NBO) calculation were performed using NBO 3.1 program as implemented in the GAUSSIAN 03W package at the DFT level in order to understand the various second-order interactions between the filled orbital of subsystem and the vacant of another subsystem, which is a measure of the intermolecular delocalization or hyperconjugation. Finally, the calculated normal mode of vibrational frequencies will provide the thermodynamic properties through the principle of statistical mechanics.

4. Results and discussion

4.1. Geometrical structure

In order to find the most optimized geometry, the energies were carried out for ornidazole using B3LYP/6-31G (d, p) method for various possible conformers. There are three conformers for ornidazole. The possible conformers of ornidazole have been calculated using the B3LYP/6-31G (d,p) method. The total energies obtained for these conformers were listed in Table 1. It is clear in Table 1, the structure optimizations have shown that the conformer C3 have produced the global minimum energy of −2,947,736.83 kJ/mol. Therefore, C3 form is the most stable conformer than the other conformers. The optimized molecular structure with the numbering of atoms of the ornidazole is shown in Fig. 1. The most optimized structure parameters of ornidazole calculated by DFT-B3LYP levels with the 6-31G (d, p) basis set are listed in the Table 2 in accordance with the atom numbering scheme given in Fig. 2. The optimized molecular structure of ornidazole belongs to C_1 point group symmetry. Table 2 compares the calculated bond lengths and angles for ornidazole with those experimentally available from literature value [12]. The C–N bond length is 1.33 Å, which is shorter than that of normal C–N bond (1.417 Å). The calculated bond length values for C–C and C–H in the nitroimidazole ring vary from 1.3804 to 1.522 Å and 0.9658 to 1.0964 Å by B3LYP/6-31G (d, p) basis set, respectively and well agreed with the experimental values [12]. In this study the optimized bond length of C–Cl are high and for C–C is low (0.965 Å), with the electron donating and withdrawing substituent on the nitroimidazole ring, the symmetry of the ring is distorted, yielding variation in bond angles at the point of substitution. It is clearly shown that the angles at the point of substitution C–C–C, C–C–H, C–C–O, H–C–H O–N–O are 112 Å, 126 Å, 111 Å, 109 Å and 124 Å respectively. The small difference between experimental and theoretical bond lengths and bond angles may be due to presence of intermolecular hydrogen bonding or the experimental results belong to solid phase and theoretical calculations belong to gaseous phase.

Table 1
Total energies of different conformations of ornidazole.

Sl. no.	Conformer	Hartrees	KJ/mol	Energy difference (J/mol)
1	C1	−1118.132	−2,935,656.978	0.000000
2	C2	−1118.188	−2,935,803.231	146.2531
3	C3	−1122.733	−2,947,736.836	12,079.85

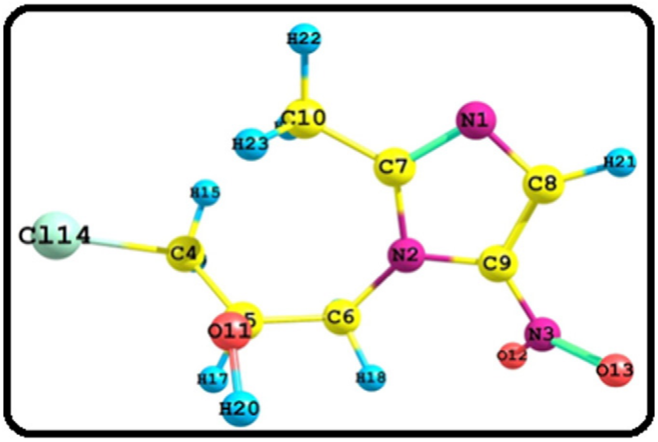

Fig. 1. Optimized structure of ornidazole.

4.2. Vibrational assignments

The title molecule consists of 24 atoms, hence undergoes 66 normal modes of vibrations, all are active in infrared and Raman spectra. The molecule under investigation possesses C_1 point group symmetry. The observed and calculated wavenumbers along with the relative intensities, probable assignments and total energy distribution (PED) are presented in Table 3. The experimental and theoretical FTIR and FT-Raman spectra are shown in Figs. 3 and 4. The scaling factor of 0.963 for B3LYP/6-31G (d, p) is used in the present work.

Table 2
Optimized geometrical parameters like bond length and bond angles of ornidazole.

Bond length	B3LYP	Expt	Bond angle	B3LYP	Expt
C1–C2	1.5226	1.518	C2–C1–Cl14	113.72	112.27
C1–Cl14	1.8174	1.770	C2–C1–H15	110.57	109.86
C1–H15	1.0909	0.970	C2–C1–H16	109.44	109.81
C1–H16	1.0895	0.970	H15–C1–H16	109.89	109,54
C2–C3	1.5385	1.522	C1–C2–C3	112.45	110.50
C2–C4	1.4209	1.354	C1–C2–O4	108.45	110.20
C2–H17	1.0996	0.980	C1–C2–H17	105.40	108.26
C3–H9	1.0467	0.960	C3–C2–O4	111.58	110.69
C3–H18	1.0891	0.960	C3–C2–H17	107.85	108.00
C3–H19	1.0896	0.960	O4–C2–H17	110.92	109.81
C4–H20	0.9658	0.930	C2–C3–N9	111.71	111.71
C5–N6	1.3334	1.340	C1–C2–H18	110.37	109.63
C5–N9	1.3694	1.370	C2–C3–H19	109.45	109.22
C5–C13	1.4932	1.522	N9–C2–H18	108.65	109.01
N6–C7	1.3558	1.351	N9–C2–H19	107.33	108.27
C7–C8	1.3804	1.353	H18–C3–H19	109.23	109.55
C7–H21	1.0798	0.980	C2–O4–H20	108.17	106.76
C8–N9	1.3936	1.414	N6–C5–N9	112.11	111.71
C8–N10	1.4179	1.419	N6–C5–C13	124.03	124.81
N10–O11	1.2327	1.218	N9–C5–C13	123.83	123.64
N10–O12	1.2433	1.224	C5–N6–C7	106.08	106.46
C13–H22	1.0903	0.980	N6–C7–C8	109.91	109.48
C13–H23	1.0935	0.970	N6–C7–H21	123.19	124.20
C13–H24	1.0964	0.970	C8–C7–H21	126.88	125.32
			C7–C8–N10	106.65	107.59
			C7–C8–N10	127.75	127.17
			N9–C8–N10	125.58	125.40
			C3–N9–C8	129.18	129.73
			C5–N9–C8	105.23	106.46
			C8–N10–O11	116.85	117.21
			C8–N10–012	118.77	119.36
			O11–N10–O12	124.36	124.10