Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 189 (2018) 473–484

Contents lists available at ScienceDirect

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy

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

Structural and vibrational study of a neurotransmitter molecule: Dopamine [4-(2-aminoethyl) benzene-1,2-diol]

Omkant Jha, T.K. Yadav, R.A. Yadav *

Laser and Spectroscopy Laboratory, Department of Physics, Institute of Science, Banaras Hindu University, Varanasi 221005, India

ARTICLE INFO

Article history:
Received 27 October 2016
Received in revised form 30 June 2017
Accepted 30 July 2017
Available online 2 August 2017

Keywords:
DFT
HOMO-LUMO
Molecular structure
NBO
Vibrational
IR and Raman spectra

ABSTRACT

Structural and vibrational studies for the most stable conformer of dopamine {4-(2-Aminoethyl) benzene-1, 2-diol} have been carried out at the DFT/B3LYP/6-311++G** level using the Gaussian 09 software. The IR and Raman spectra have been recorded and analyzed in light of the computed vibrational parameters using the DFT and the PEDs computed with the help of the GAR2PED software. Some of the fundamentals have considerably changed frequencies in going from benzene to dopamine. Except the rocking and wagging modes of the NH_2 group the other four modes are pure group modes. The rocking and wagging modes of the NH_2 group show mixing with the other modes. The two O—H stretching vibrations are highly localized modes. The Kekule phenyl ring stretching mode is found to remain almost unchanged. The HOMO-LUMO study suggests the existence of charge transfer within the molecule and the energy gap supports the pharmacological active property of the dopamine molecule. The NBO analysis has been carried out to understand the proper and improper hydrogen bonding.

1. Introduction

Neurotransmitters help in the transmission of signals between nerve-cells (neurons) throughout human brain and body. The neurotransmitters are of two types (i) inhibitory and (ii) excitatory. The excitatory neurotransmitters stimulate the brain whereas the inhibitory neurotransmitters quiet the brain and create balance. Dopamine is a special type of neurotransmitter as it plays the role of both the excitatory and inhibitory neurotransmitters. The elevated or reduced dopamine level in human body may result in memory loss, daydreaming and not being able to stay on task. Dopamine is also responsible for motivation or drive or desire to get things done. It helps in regulating daily behavior, cognition, appetite, aggression, anger, memory, and sleep [1–3]. Dysfunction of the dopamine system may cause a number of diseases such as Parkinson's disease, schizophrenia, Attention Deficit, Hyperactivity Disorder and so on [4–7]. Dopamine molecule is an amino derivative of 4-ethyl, 1, 2- dihydroxybenzene in which an H atom at the C_2 position of the C_2H_5 group is replaced by an NH_2 group. It is a hormone molecule and is important monoamine neurotransmitter occurring in a wide variety of animal organs with physiological functions connected with the neurotransmission in the central nervous system [8]. Dopamine induces cellular and biochemical effects by interacting with cell surface receptors [9,10]. The dopamine molecule is synthesized by L-tyrosine in the synapse at the end of axon. The neurotransmitter molecule is released on the synaptic cleft and disseminates towards the postsynaptic membrane. The dopamine is synthesized from L- di-hydroxy phenylalanine in neurons and cells, in the adrenal glands. Unlike L-DOPA (L-3,4dihydroxyphenylalanine), dopamine is ineffective to cross the barrier between the brain tissues and circulating blood; serves to protect the central nervous system [11]. Dopamine is attached to the receptors in the postsynaptic membrane due to the excitatory or inhibitory postsynaptic potentials and transmission of information.

In order to investigate the relationship between pharmacological activities and conformational isomers of dopamine, X-ray crystallographic and theoretical investigations have been carried out extensively [12–23]. Using the DFT method Alagona et al. [17] have investigated the trans-perpendicular and gauche-perpendicular conformers stability in aqueous solution. Barreto et al. [20] and Singh et al. [21] have carried out extensive work on FTIR, Raman and UV-Visible spectra of dopamine. Park et al. [22] have presented the spectroscopic analysis of dopamine at the B3LYP/6-31G (d, p) level. Gunasekaran et al. [23] have studied the IR and Raman spectra of the dopamine molecule and performed normal coordinate analysis considering CH_2NH_2 group as a mass point. Moreover, they have considered only 28 modes.

To the best of our knowledge, no work appears to have been reported on the complete vibrational assignment for the lowest energy conformer of dopamine. Therefore, investigation of the complete vibrational spectrum of the dopamine molecule seems pertinent. In the present paper, we have investigated theoretically the optimized molecular geometries, and fundamental vibrational modes along with their IR intensities, Raman activities and depolarization ratios of the

* Corresponding author.
E-mail addresses: kant.omkant@gmail.com (O. Jha), rayadav@bhu.ac.in (R.A. Yadav).

http://dx.doi.org/10.1016/j.saa.2017.07.067
1386-1425/

Raman bands of the most stable energy conformer at the B3LYP/6-311++G(d, p) level. We have also calculated the potential energy distributions (PEDs) for the normal modes of the dopamine molecule to make more reliable vibrational assignments. We have also investigated experimentally the IR and Raman spectra of dopamine, analysed these in light of the computational parameters and presented complete vibrational assignments of the observed spectra, and correlated the calculated and observed frequencies. APT, Mulliken atomic and natural charges were also computed. Change in the electron density (ED) in the antibonding orbitals and energies have been computed by the natural bond orbital (NBO) analysis method to provide definite proof of stabilization of the dopamine molecule.

2. Experimental Details

The dopamine compound (purity ≥ 98%), purchased from the Sigma Aldrich Co., was used without any further purification for the experimental investigations. At the room temperature it exists as a white solid.

FTIR spectrum of the compound has been recorded in the spectral range 400–4000 cm^{-1} using a Perkin Elmer FTIR spectrometer at the room temperature. In recording the FTIR spectrum the parameters used were: mode- transmission, source- MIR, detector- MIRTGS, resolution ~2 cm^{-1}

Raman spectrum of the compound was recorded in the spectral range 50–3800 cm^{-1}. The Raman spectrum of the dopamine compound was collected at room temperature with a Renishaw inVia Raman spectrometer, equipped with both 532 and 785 nm lasers. To avoid heating, the 532 nm line of a diode pumped solid-state laser bearing a power of 5 mW mm^{-2} was used for excitation in developing the Raman spectrum. The incident laser beam was focused on the dopamine sample by a 50x short distance objective attached to the Leica DM 2500M microscope. The scattered light was gathered in back-scattering geometry by the same objective and a 2400 groove per mm grating was used as the dispersive component. The slit width of 50 μm was kept throughout the measurement.

3. Computational Details

The optimized molecular structures of all the stable conformers of dopamine {4-(2-aminoethyl) benzene-1, 2-diol}, have been computed at the B3LYP/6-311++G(d, p) level using the Gaussian 09 package [24] and molecular visualization program [25]. The computations have been made to determine the APT, Mulliken and natural charges, the bond lengths, bond angles, and vibrational frequencies with their IR intensities, Raman activities, and depolarization ratio of the Raman bands using the optimized molecular geometry of the most stable conformer. The potential energy distributions (PEDs) for each mode have been calculated using the GAR2PED software [26] to help the vibrational assignments of normal modes.

Fausto et al. [27] have proposed six conformers of dopamine and its cation while another group of authors [28] have found only seven conformers of natural dopamine in the gas phase from microwave spectroscopy. To resolve the controversy in the number of conformers of dopamine we have carefully tried to investigate the solution of the problem using DFT computations. For the dopamine molecule, there are large number of conformers, which result due to different orientations of the two-hydroxyl groups (OH) and an ethylamine side chain. To get the minimum energy conformer of the dopamine molecule, the following method has been adopted. We started with the optimized structure of benzene. One of the H atoms of benzene was replaced by an OH group and the structure was optimized. In this structure, an H atom was replaced by another OH group on the C atom in the juxtaposition of the C atom attached to the first OH group and the resulting structures (4 in number due to 2 orientations of each of the OH groups) were optimized. Taking the minimum energy structure and replacing the H atom at the C_4 position (Fig. 1) by a CH_3 group we optimized the structure (4 in number due to the 4 possible orientations of the CH_3 group). Now one of the H atoms of the CH_3 group was replaced by another CH_3 group and with all the possible orientations of this CH_3 group the structures were optimized. Taking the least energy structure an NH_2 group was substituted for one of the H atoms of this CH_3 group and the structures were optimized with different NH_2 orientations. In this way, the optimized structure of the least energy conformer was obtained (Fig. 1). In the present manuscript, the lowest energy conformer is considered. Fig. 1 shows the optimized geometry of the lowest energy conformer C_1.

Assignments of the normal modes of vibration have been made with the help of the assignments made for related molecules and to the computed PEDs for the normal modes of the dopamine molecule. The normal modes of dopamine were compared with the corresponding normal modes of benzene(Bz), phenol(Ph), 1,2-dihydroxy benzene(1,2-DHB), 4-ethyl 1,2-dihydroxy benzene(4-E-1,2-DHB) and butylamine(BA) [29], with the help of animation available with the Gauss-View software [30]. The NBO analysis was carried out in order to understand the intra-molecular charge-transfer interactions (CT), rehybridization, and delocalization of electron density (ED).

4. Result and Discussion

4.1. Molecular Geometries

As mentioned earlier, the optimized structure with the atomic labeling scheme of the lowest energy conformer of dopamine has been shown in Fig. 1. The total and relative energies and other related parameters of spectroscopic importance for the lowest energy conformer are collected in Table 1. All the calculated conformers and the geometric parameters have been included in Supplementary material (ST-1 and ST-2). The optimized energy for the lowest energy conformer is −516.82406 a.u. The lowest energy conformer has the C_1 point group

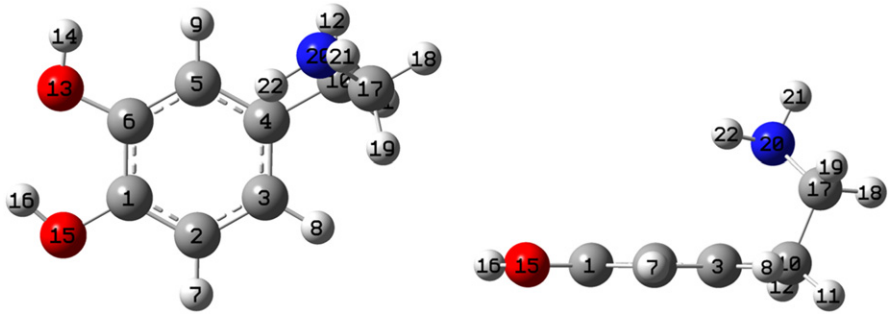

Fig. 1. Front and side views of the lowest energy conformer of dopamine.