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### Highlights:

What are the main findings?

- The L-dopa molecule has 108 stable configurations.
- Vibrational analysis confirms the existence of a dimeric form of L-dopa and a strong IR band peak at 2770 cm<sup>-1</sup> suggests its OH forms.
- L-dopa molecules are found to be chemically soft and biologically active in nature.
- Strong active sites are near the O and H atoms of the OH and COOH groups.

### What is the implication of main findings?

- L-dopa molecule would be a good choice for medicinal application.
- Multiple active sites play significant role for its chemical activities.

Abstract: Structural, conformational and spectroscopic investigations of the L-dopa molecule were made at the b3lyp/6-311++g\*\* level using the Gaussian 09 software. IR, Raman and UV-vis spectra were measured and analyzed in light of the computed spectral quantities. Total energy vs. dihedral angle scans yielded 108 pairs of stable conformers of L-dopa. All the conformers had energies above 500 K relative to the lowest-energy conformer C-I. The observed spectra could be explained in terms of the computed spectra of the lowest-energy dimer of the C-I monomer. MEP and HOMO-LUMO analysis were carried out, and barrier heights and bioactivity scores were determined. The positive bioactive scores represent its higher medicinal and pharmaceutical applications. The present investigation suggests that the molecule has three active sites with moderate bioactivity.

Keywords: DFT; IR and Raman; UV-vis; barrier height; conformational analysis; MEP plots

# 1. Introduction

L-3,4-Dihydroxyphenylalanine (Levodopa  $\equiv$  L-Dopa) is a derivative of one of the essential amino acids, phenylalanine. It is an intermediate in dopamine biosynthesis. There are many herbal extracts containing L-dopa. Some high-yielding natural sources include velvet bean (*Mucuna pruriens* L.) [1] and broad bean (*Vicia faba* L.) [2], while other sources include the genera Phanera-Cassia, Canavalia and Dalbergia.

L-dopa is found to exhibit antioxidant properties which are helpful in the treatment of diseases like cancer, aging, and cardiovascular, neurodegenerative and inflammatory diseases [3,4]. It is a potent drug for the treatment of neurological disorders like Parkinson's disease, characterized by a loss of dopamine in the brain nerve cells. The dopamine molecule cannot cross the blood–brain barrier, whereas L-dopa is able to cross this barrier. Once the L-dopa molecule enters the central nervous system, it is converted into dopamine. As early as 300 BC, Indian Ayurvedic Physicians used to treat Parkinson's disease using



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**Copyright:** © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). the seeds of velvet bean (*Mucuna pruriens* L.), which contain 4–6% of L-dopa [5–8]. It is also useful for food preservation [1,2].

The IR and Raman spectra of L-dopa are available without any spectroscopic interpretation or discussion [9,10]. Siddiqui et al. [11] performed DFT computations at the b3lyp/6-311g(d,p) level and reported partial interpretations of spectral, conformational, structural and thermodynamic data. Chamundeeswari et al. [12] experimentally investigated the IR, Raman, UV-vis and <sup>1</sup>H and <sup>13</sup>C NMR spectra and interpreted the spectral data in light of the DFT calculations performed at the b3lyp/6-31+g(d,p) level. It is to be noted that Chamundeeswari et al. reported only one conformer, which was of higher energy relative to the lowest-energy conformer C-I. However, Siddiqui et al. reported a total of 12 conformers and interpreted the experimental results with the help of the structure of the higher-energy conformer with respect to the lowest-energy conformer. Furthermore, these authors [11,12] have only considered the structures in which the H atom of the hydroxyl group of the COOH moiety is directed towards the O atom of the carbonyl (C=O) group, while the present investigation showed that the lowest-energy conformer corresponds to a structure in which the H atom of the hydroxyl group of the COOH moiety is directed towards the N atom of the amino (NH<sub>2</sub>) group.

The present work deals with the experimental IR, Raman and UV-vis spectra and their analysis in light of the computed spectra and related parameters for the monomeric and dimeric forms of L-dopa using the Gaussian 09, GaussView 5.0 and GAR2PED software. This paper also contains computations and interpretations of the molecular properties of the lowest-energy conformer of the L-dopa molecule, namely optimized geometrical parameters, possible conformers, barrier heights for different top axes, APT charges, MEP, HOMO-LUMO analysis, thermodynamic functions and bioactive scores. The structure of the molecule plays an important role for many physical and chemical properties of the compound. Thus, the present study is helpful for researchers in the chemical, medicinal and pharmacological fields for understanding these molecular properties. Further, we are planning to synthesize this molecule's new Ln complexes and to investigate their antioxidant activity, which is in accordance with the well-known antioxidant potential of L-dopa. This is in continuation of our ongoing work devoted to the pharmacological activity of lanthanide complexes with biologically active ligands.

### 2. Experimental Details

L-dopa forms a white crystalline solid compound. It was purchased from Sigma Chemical Co. (St. Louis, MO, USA) and used as purchased for spectral studies. The IR spectrum was recorded on a Thermo Scientific Nicolet iS5 FTIR spectrometer in the range of 550–4000 cm<sup>-1</sup> and in the ATR mode using the following parameters: scan, 00; gain, 50; and resolution,  $2 \text{ cm}^{-1}$ . The Raman spectrum was recorded on a Renishaw inVia Raman microscope in the region of 50–4000 cm<sup>-1</sup> equipped with a 2400 line/mm grating. The sample was mounted in the sample illuminator using an optical mount without any kind of pre-treatment. A diode laser of  $\lambda$  (532 nm) was used to excite the spectrum. The laser power was set at 50% of 50 mW and with a 50 × objective lens, an acquisition time of 10 s and a spectral resolution of 1.0 cm<sup>-1</sup>. In an ethanol solution at 5 × 10<sup>-4</sup> mole/L concentration, the UV-vis spectrum was recorded on an Eppendorf Bio-spectrometer, model kinetic, in the absorption mode in the range of 200–600 nm.

### 3. Computational Details

All the computations were performed at the B3LYP/6-311++g\*\* level with the Gaussian 09 software [13]. The molecular geometries of all the investigated conformers and the dimeric forms of the lowest-energy conformer of L-dopa were optimized by minimizing the energies with respect to all the geometrical parameters without any molecular symmetry constraints. To search the total number of the possible conformers of L-dopa, the total energy vs. the dihedral angle was scanned for all the tops. The Raman activities  $(S_i)$  calculated by the Gaussian 09 software were converted into Raman intensities using the

relation given elsewhere [14]. The GAR2PED software was used to compute the potential energy distributions (PEDs) for all the normal modes of vibration [15]. HOMO and LUMO analysis and molecular electrostatic potential (MEP) plots were devised using the optimized structure of the L-dopa molecule.

### 4. Results and Discussion

# 4.1. Determination of the Total Number of the Possible Conformers and the Barrier Heights for Different Tops

# 4.1.1. The Number of the Possible Conformers

The L-dopa molecule (Figure 1) has seven tops. To find out its total number of possible conformers, the total energy vs. dihedral angle curves were obtained for different tops. The total energy vs. dihedral angle plots for the seven tops are shown in Figure 2a–c and Figure S1. The L-dopa molecule is a benzene derivative with three substituents at the sites  $C_6$ ,  $C_1$  and  $C_3$ . The substituents at the sites  $C_6$  and  $C_1$  are the OH groups and the substituent at the site  $C_3$  is a 2-aminopropenoic acid group. The 2-aminopropenoic acid skeleton has five top axes, namely  $C_3$ - $C_{14}$ ,  $C_{14}$ - $C_{17}$ ,  $C_{17}$ - $N_{22}$ ,  $C_{17}$ - $C_{19}$  and  $C_{19}$ - $O_{20}$ . The top axes  $C_3$ - $C_{14}$ ,  $C_{17}$ - $C_{19}$  and  $C_{19}$ - $O_{20}$  have two-fold barriers (Figure S1a–c) and the top axis  $C_{14}$ - $C_{17}$  has a three-fold barrier (Figure S2d). When the atom  $H_{24}$  faces towards the atom N<sub>22</sub>, the rotational barrier for the NH<sub>2</sub> group about the C<sub>17</sub>-N<sub>22</sub> axis is two-fold; however, when the atom  $H_{24}$  is directed away from the atom  $N_{22}$ , the barrier about the same axis is one-fold. Hence, the rotation of the NH<sub>2</sub> group about the  $C_{17}$ -N<sub>22</sub> axis produces three different stable configurations. As a result, the total number of the stable configurations of 2-aminopropenoic acid skeleton due to the rotation about the five top axes  $C_3$ - $C_{14}$ ,  $C_{14}$ - $C_{17}$ ,  $C_{17}$ - $N_{22}$ ,  $C_{17}$ - $C_{19}$  and  $C_{19}$ - $O_{20}$  is  $2 \times 2 \times 2 \times 3 \times 3 = 72$ . The rotations of both OH groups give rise to three different stable configurations. Out of these three configurations, there are two configurations in which the H-atoms of both the OH groups are oriented in the same sense of rotation, and in the third configuration both the H-atoms are oriented in the opposite sense of rotation. Hence, the total stable configurations arising due to the rotations about all the seven top axes is found to be  $3 \times 72 = 216$ . Out of these 216 configurations, there are 108 pairs of configurations. In each pair, one configuration is the mirror image of the other configuration. The mirror images of the 108 configurations are generated by a rotation of  $180^{\circ}$  about the top axis C<sub>3</sub>-C<sub>14</sub>. As a result, the total number of different stable configurations of the L-dopa molecule would be 216/2 = 108. The total energies and the energy differences of the first five lowest-energy conformers are given in Table 1. From this Table it is clear that the first higher-energy conformer is found at 388 K relative to the lowest-energy conformer. Different molecular parameters of the lowest-energy monomeric conformer C-I and its lowest-energy dimeric conformer  $D_1$  are collected in Table S1. The optimized structures of the first six lowest-energy conformers of the L-dopa molecule are shown in Figure S2. The energy differences of the five conformers (C-II to C-VI) are found to be below 1000 K relative to the lowest-energy conformer C-I.



Figure 1. Optimized structure of the lowest-energy conformer (C-I) of L-dopa.



**Figure 2.** (**a**–**c**). Variation of the total energies with the dihedral angles for the rotations of the OH groups about their respective axes.

| Gard  | Total Energy |          | ∆E Relativ | <b>ΔE Relative to C-I</b> |  |
|-------|--------------|----------|------------|---------------------------|--|
| Conf. | Hartree      | Hartree  | kcal/mol   | К                         |  |
| C-I   | -705.460596  | 0        | 0          | 0.0                       |  |
| C-II  | -705.459368  | 0.001228 | 0.771      | 388                       |  |
| C-III | -705.458329  | 0.002267 | 1.423      | 716                       |  |
| C-IV  | -705.458148  | 0.002449 | 1.537      | 773                       |  |
| C-V   | -705.457772  | 0.002824 | 1.772      | 892                       |  |
| C-VI  | -705.457510  | 0.003086 | 1.936      | 975                       |  |

Table 1. Total energies and their differences for the first 6 lowest-energy monomeric conformers.

### 4.1.2. Barrier Heights for Different Tops

Barrier heights are determined from the plots of the total energy vs. dihedral angle curves for different tops. Every local minimum of each curve corresponds to a stable configuration of the molecule and a maximum between two adjacent minima corresponds to the transition state configuration of the molecule. The energy difference between a minimum and one of the adjacent maxima is the barrier height. The barrier heights of the seven top axes are listed in Table 2. The rotation of the  $O_{12}H_{13}$  group when the  $H_{11}$  atom of the  $O_{10}$ H11 group faces towards the  $O_{12}$  atom gives rise to a one-fold barrier with the height of 9.35 kcal/mol (Figure 2a) and does not yield any new stable structure. The points A and C in Figure 2a represent the same stable configuration in which both the H atoms of the two OH groups are directed towards the atom H<sub>7</sub>. The rotation of the  $O_{12}H_{13}$  group, when the  $H_{11}$  atom of the  $O_{10}H_{11}$  group is directed away from the atom O<sub>10</sub>, yields a two-fold barrier (Figure 2b). The transition  $A/E \rightarrow C$  via the barrier maxima B/D requires 2.588/2.854 kcal/mol energies, and for the reverse transition the required energies are 6.314/6.517 kcal/mol. The total energy vs. dihedral angle curve for the rotation of the  $O_{10}H_{11}$  group yields a two-fold barrier as shown in Figure 2c. In this case, the point C corresponds to the configuration in which the H atoms of the  $O_{12}H_{13}$  and  $O_{10}H_{11}$  groups are directed away from each other. The barrier heights for the forward and reverse transitions  $C \rightarrow A/E$  via B/D are 2.232 and 9.223 kcal/mol. The barrier heights for the OH groups attached to the phenyl ring of the L-dopa molecule are found to be in agreement with the OH group in dopamine [16] and one order higher than the OH group in phenol (3.8 kcal/mol) [17]. However, the barrier height for the OH group of the carboxylic group is found to be 3-5 times higher than the OH group of phenol due to strong intra-molecular H-bonding (O20-H22 ... NH2) in the L-dopa molecule.

| <b><i>ubic a</i></b> , <i>buillet</i> neights for an the topb of <i>b</i> dopt | Table 2. | Barrier | heights # | for all | the to | ps of | L-dopa. |
|--|----------|---------|-----------|---------|--------|-------|---------|
|--|----------|---------|-----------|---------|--------|-------|---------|

| Тор                              | Foldness | $\Delta E_{AB}$ | $\Delta E_{BC}$ | $\Delta E_{CD}$ | $\Delta E_{DE}$ | $\Delta E_{EF}$ | $\Delta E_{FG}$ |
|----------------------------------|----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| С <sub>19</sub> -ОН              | 2        | 20.565          | 11.340          | 11.340          | 20.565          | -               | -               |
| C <sub>1</sub> -OH               | 1        | 9.775           | -               | -               | -               | -               | -               |
| C <sub>6</sub> -OH               | 2        | 9.223           | 2.232           | 2.232           | 9.223           | -               | _               |
| C <sub>14</sub> -C <sub>17</sub> | 3        | 5.992           | 2.936           | 3.140           | 0.126           | 5.580           | 10.890          |
| C <sub>3</sub> -C <sub>14</sub>  | 2        | 2.301           | 1.544           | 1.945           | 2.710           | -               | -               |
| C-CO <sub>2</sub> H              | 2        | 6.013           | 6.395           | 2.988           | 2.606           | -               | -               |
| C <sub>1</sub> -OH <sup>\$</sup> | 2        | 2.588           | 6.314           | 6.517           | 2.854           | -               | -               |

<sup>#</sup> The barrier heights reported here are approximate because the accurate determination of barrier height requires energy of the structure corresponding to the transition point. Furthermore, corresponding to a minimum in the scan curve, the structure has to be minimized for the exact energy and position. <sup>\$</sup> Rotation of  $O_{12}H_{13}$  group about  $C_1$ - $O_{12}$  axis when  $H_{11}$  is directed away from  $O_{12}$  (Figure 1).

As mentioned earlier, the total energy vs. dihedral angle scan curves for all five tops of the 2-aminopropenoic acid moiety are shown in Figure S1. The rotations about the

top axes C<sub>3</sub>-C<sub>14</sub>, C<sub>17</sub>-C<sub>19</sub> and C<sub>19</sub>-O<sub>19</sub> have two-fold barriers (Figure S1a–c). The barrier heights for the forward and reverse transitions  $A/E \rightarrow C$  for the three rotations were found to be 2.301/2.710, 6.013/2.606 and 20.565/20.565 and 1.544/1.945, 6.395/2.988 and 11.340 kcal/mol, respectively. Referring to Figure S1b, the point A corresponds to the situation when the OH group of the carboxylic moiety faces towards the N-atom, while the point C corresponds to the situation when the carbonyl O atom faces towards the N atom. The barrier height for the transition  $A \rightarrow C$  during which the H atom of the OH group passes through the space closer to the phenyl ring is much higher (6.013 kcal/mol) than that when the H atom of the OH group passes through the space farther from the phenyl ring (2.606 kcal/mol). The rotation about the top axis C<sub>14</sub>-C<sub>17</sub> has a three-fold potential barrier (Figure S1d). It has a very shallow minimum (point E), with the energy 0.123 kcal/mol for the transition  $E \rightarrow C$  and 2–10 kcal/mol for the transitions  $A \rightarrow C$ .

The rotation of the NH<sub>2</sub> group in different orientations of the neighboring carboxylic group has a two-fold barrier (Figure S1e). The scan curve for the rotation of the NH<sub>2</sub> group when the H<sub>24</sub> atom of the COOH group faces towards the NH<sub>2</sub> group is shown in Figure S1e. The local minima points A/C correspond to the configuration when the NH<sub>2</sub> group is directed away from/faces towards the H<sub>24</sub> atom of the carboxylic group. The barrier heights for the forward and reverse transitions A/E  $\rightarrow$  C via the points B/D are 17.103 and 18.986 compared to 7.336 and 9.219 kcal/mol.

### 4.2. Geometrical Parameters

The geometrical parameters, namely, bond lengths, bond angles and dihedral angles for C-I and its dimer  $D_1$ , are collected in Tables 3 and S2. The C-C bond lengths of the phenyl ring are found in the range 1.388–1.408 Å, in conformity with the C-C bond lengths (1.396 Å) in benzene. The two N-H bond lengths of the  $NH_2$  group are not equal due to the different surroundings of the two H-atoms. The C-O(H) bond length of the carboxylic group was found to be smaller as compared to the other two C-O(H) bond lengths. However, the O-H bond length of the carboxylic group was found to be larger than the other two O-H bond lengths due to strong N...H interaction. In the monomeric form, the H<sub>11</sub> atom is involved in the intra-molecular hydrogen bonding (O<sub>10</sub>- $H_{11}$ ... $O_{12}$ ), while, in the dimeric form, the  $H_{13}$  atom is involved in the inter-molecular hydrogen bonding ( $O_{12}$ - $H_{13}$ ... $O'_{46}$ ) (where  $O'_{46}$  is the O atom in the second molecule  $M_2$ , corresponding to the  $O_{21}$  atom of the first molecule  $M_1$ , Figure 3). Hence, the bond length  $O_{10}H_{11}$  was found to be larger than the bond length  $O_{12}H_{13}$  bond in monomeric form. However, in the dimeric form, the  $O_{12}$ - $H_{13}$  was found to be larger than the  $O_{10}$ - $H_{11}$ bond. In going from the monomer to the dimer, the  $C_1$ - $O_{12}$  bond length is reduced by 0.015 Å due to enhancement of the APT charge at the site  $O_{12}$ , which results in a strong attracting force between the  $C_1$  and  $O_{12}$  atoms. The inter-molecular H-bonding enhances the C=O bond length in the dimeric form as compared to the monomeric form. In going from the monomer to the dimer, the bond length N22-H23 is increased, whereas the other bond length N<sub>22</sub>-H<sub>25</sub> remains unchanged.

The C-C-C bond angles of the phenyl ring were found to lie in the range 118.3–121.1° in both the monomeric and dimeric forms. In going from the monomer to the dimer, the bond angles  $C_1-O_{12}-H_{13}$  and  $C_{17}-C_{19}-O_{21}$  were found to reduce by  $1.7^{\circ}$  and  $-1.4^{\circ}$ . The bond angles reported by earlier authors [11,12] show noticeable changes from the present values in several cases (Table S2), causing considerable changes in the vibrational frequencies (Table S4). The geometrical parameters reported previously [11,12] differ from the present values. This is due to the fact that the conformers reported by them differ from each other and also differ from the presently reported conformer C-I.

| Bond                                 | C-I   | D     | 91    | Ref. [10] | Ref. [11] | (0) $(1)$ | (2) $(1)$ | (A) (1) | (5) (1) |
|--------------------------------------|-------|-------|-------|-----------|-----------|-----------|-----------|---------|---------|
| Lengths <sup>#</sup>                 | (1)   | (2)   | (3)   | (4)       | (5)       | (2)-(1)   | (3)-(1)   | (4)-(1) | (5)-(1) |
| r(C <sub>1</sub> -C <sub>2</sub> )   | 1.389 | 1.390 | 1.390 | 1.385     | 1.390     | 0.001     | 0.001     | -0.004  | 0.001   |
| $r(C_1 - C_6)$                       | 1.404 | 1.408 | 1.408 | 1.415     | 1.408     | 0.004     | 0.004     | 0.011   | 0.004   |
| $r(C_2 - C_3)$                       | 1.404 | 1.404 | 1.404 | 1.401     | 1.409     | 0.000     | 0.000     | -0.003  | 0.005   |
| $r(C_3-C_4)$                         | 1.398 | 1.398 | 1.398 | 1.394     | 1.402     | 0.000     | 0.000     | -0.004  | 0.004   |
| $r(C_4 - C_5)$                       | 1.397 | 1.398 | 1.398 | 1.396     | 1.400     | 0.001     | 0.001     | -0.001  | 0.003   |
| $r(C_5-C_6)$                         | 1.388 | 1.386 | 1.386 | 1.389     | 1.391     | -0.002    | -0.002    | 0.001   | 0.003   |
| $r(C_1 - O_{12})$                    | 1.373 | 1.358 | 1.358 | 1.386     | 1.377     | -0.015    | -0.015    | 0.013   | 0.004   |
| $r(C_6 - O_{10})$                    | 1.368 | 1.362 | 1.362 | 1.363     | 1.362     | -0.006    | -0.006    | -0.005  | -0.006  |
| $r(O_{10}-H_{11})$                   | 0.967 | 0.968 | 0.968 | 0.965     | 0.969     | 0.001     | 0.001     | -0.002  | 0.002   |
| $r(O_{12}-H_{13})$                   | 0.965 | 0.982 | 0.982 | 0.964     | 0.967     | 0.017     | 0.017     | -0.001  | 0.002   |
| $r(C_{14}-H_{15})$                   | 1.092 | 1.092 | 1.092 | 1.095     | 1.097     | 0.000     | 0.000     | 0.003   | 0.005   |
| $r(C_{14}-H_{16})$                   | 1.092 | 1.094 | 1.094 | 1.095     | 1.095     | 0.002     | 0.002     | 0.003   | 0.003   |
| $r(C_{14}-C_{17})$                   | 1.549 | 1.551 | 1.551 | 1.562     | 1.555     | 0.002     | 0.002     | 0.013   | 0.006   |
| $r(C_3 - C_{14})$                    | 1.514 | 1.513 | 1.513 | 1.510     | 1.517     | -0.001    | -0.001    | -0.004  | 0.003   |
| $r(C_{17}-C_{19})$                   | 1.542 | 1.541 | 1.541 | 1.517     | 1.547     | -0.001    | -0.001    | -0.025  | 0.005   |
| $r(C_{17}-N_{22})$                   | 1.470 | 1.471 | 1.471 | 1.458     | 1.456     | 0.001     | 0.001     | -0.012  | -0.014  |
| $r(C_{19}-O_{20})$                   | 1.333 | 1.323 | 1.323 | 1.355     | 1.355     | -0.01     | -0.01     | 0.022   | 0.022   |
| $r(C_{19}-O_{21})$                   | 1.212 | 1.216 | 1.216 | 1.201     | 1.209     | 0.004     | 0.004     | -0.011  | -0.003  |
| r(O <sub>20</sub> -H <sub>24</sub> ) | 0.996 | 0.992 | 0.992 | 0.969     | 0.974     | -0.004    | -0.004    | -0.027  | -0.022  |

Table 3. Some important geometrical parameters of L-dopa.

<sup>#</sup> Bond lengths are in unit of Å.



Figure 3. Optimized structure of the lowest-energy dimer  $(D_1)$  of the lowest-energy monomer (C-I).

### 4.3. APT Charges

Atomic polar tensor (APT) charges at different sites of the L-dopa molecule are collected in Table 4. The APT charges are the derivatives of the dipole moment with respect to the coordinates of the atomic sites [18]. In the present case, the APT charges at different sites retain their respective polarities in going from the monomer to the dimer. However, the magnitudes of the APT charges were found to decrease at all the atomic sites, except at the sites  $C_3$ ,  $H_{13}$ ,  $H_{15}$  and  $H_{18}$ . The APT charge at the most positive site  $C_{19}$  was found to be +1.419 e in the monomer and +1.106 e in the dimer. However, the atoms  $O_{21}$  and  $O_{20}$  have the APT charges -1.019 and -1.021 e in the monomeric form and -0.938 and -0.737 e in the dimeric form. The magnitude of the APT charge at the site  $H_{13}$  was found

to be reduced in going from the monomeric to the dimeric forms due to inter-molecular H-bonding. The sites  $H_{11}$  and  $H_{24}$  have higher values of the APT charges as compared to the  $H_{13}$  atom of the  $O_{12}H_{13}$  group due to intra-molecular H-bonding.

| Atomic Site     | C-I    | D      | 1      |
|-----------------|--------|--------|--------|
| C <sub>1</sub>  | 0.616  | 0.502  | 0.502  |
| C <sub>2</sub>  | -0.141 | -0.100 | -0.100 |
| C <sub>3</sub>  | -0.021 | -0.044 | -0.044 |
| $C_4$           | -0.110 | -0.099 | -0.099 |
| $C_5$           | -0.074 | -0.050 | -0.050 |
| $C_6$           | 0.657  | 0.485  | 0.485  |
| $H_7$           | 0.077  | 0.061  | 0.061  |
| H <sub>8</sub>  | 0.052  | 0.027  | 0.027  |
| H9              | 0.068  | 0.048  | 0.048  |
| O <sub>10</sub> | -0.981 | -0.762 | -0.762 |
| $H_{11}$        | 0.400  | 0.332  | 0.332  |
| O <sub>12</sub> | -0.966 | -0.930 | -0.930 |
| H <sub>13</sub> | 0.380  | 0.583  | 0.583  |
| C <sub>14</sub> | 0.156  | 0.139  | 0.139  |
| H <sub>15</sub> | -0.017 | 0.001  | 0.001  |
| $H_{16}$        | -0.033 | -0.034 | -0.034 |
| C <sub>17</sub> | 0.274  | 0.192  | 0.192  |
| $H_{18}$        | -0.021 | -0.026 | -0.026 |
| C <sub>19</sub> | 1.419  | 1.106  | 1.106  |
| O <sub>20</sub> | -1.021 | -0.737 | -0.737 |
| O <sub>21</sub> | -1.019 | -0.938 | -0.938 |
| N <sub>22</sub> | -0.697 | -0.530 | -0.530 |
| H <sub>23</sub> | 0.247  | 0.195  | 0.195  |
| H <sub>24</sub> | 0.554  | 0.429  | 0.429  |
| H <sub>25</sub> | 0.202  | 0.149  | 0.149  |

Table 4. APT charges (in e unit) at different atomic sites of L-dopa.

### 4.4. Vibrational Analysis

L-dopa is a 25atomic molecule with 69 normal modes of vibration (Table S3). The computed IR and Raman frequencies along with their relative intensities, depolarization ratios of the Raman bands, PEDs and the corresponding observed IR and Raman frequencies and their intensities and the normal mode assignments are given in Table 5. The computed vibrational frequencies for the lowest-energy monomeric conformer C-I and its lowest-energy dimeric conformer D<sub>1</sub> are compared in Table S4. The observed IR and Raman spectra with the corresponding computed spectra are shown in Figure 4. The complete observed IR spectrum of L-dopa could be explained in terms of the computed spectra of the lowest-energy dimer (D<sub>1</sub>) of the lowest-energy monomer C-I.

The experimental IR spectrum of L-dopa contains a broad intense envelope in the range  $2200-3500 \text{ cm}^{-1}$ , which could not be explained in terms of the computed spectral data of the C-I monomer. In order to explain the origin of this envelope, the related parameters for the dimers of the C-I monomer were computed. In terms of the dimeric spectral data, the complete observed IR and Raman spectra could be explained satisfactorily.

The lowest-energy monomeric conformer C-I forms five dimers ( $D_1$ - $D_5$ ), out of which three dimers ( $D_1$ ,  $D_2$ ,  $D_3$ ) involve two inter-molecular H-bonds and two dimers ( $D_4$ ,  $D_5$ ) involve only one inter-molecular H-bond. The dimers involving two inter-molecular Hbonds have much lower energies as compared to those with one inter-molecular H-bond. As the dimers  $D_2$  and  $D_3$  have much higher (~1200 and ~3500 K) energies relative to the dimer  $D_1$ , the L-dopa molecule would exist in the dimeric form  $D_1$  only.

Vibrational assignments can be discussed under the following three sub-sections: (i) the 2-aminopropenoic acid (CH<sub>2</sub>-CH-NH<sub>2</sub>CO<sub>2</sub>(H)) moiety modes (30), (ii) the phenyl ring moiety modes (30) and (iii) the OH group modes (9).

| <sup>#</sup> Dimer D1             | <sup>+</sup> IR | <sup>+</sup> Raman | PEDs   | Assignments                              |
|-----------------------------------|-----------------|--------------------|--|--|
| 39(0,19)0.75<br>51(0,11)0,75      | -               | 52 s               | $\tau(C_3-C_{14})(53)+\tau(C_{14}-C_{17})(29)-\tau(C_{17}-N_{22})(6)$  | τ(C <sub>3</sub> -C <sub>14</sub> )      |
| 54(0,7)0.66<br>62(0,4)0.75        | -               | 64 m               | $\tau(C_{17}-C_{19})(44)-\tau(C_{17}-N_{22})(11)-\tau(C_{19}-O_{20})(8)-\alpha(C_{3}-C_{14}-C_{17})(7)-\gamma(C_{23}-C_{14}$  | γ(C <sub>3</sub> -C <sub>14</sub> ) 17 a |
| 75(0,3)0.75                       | -               | 75 m               | $\tau(C_{17}-C_{19})(27)+\tau(C_{14}-C_{17})(26)-\tau(C_{3}-C_{14})(21)-\tau(C_{17}-N_{22})(8)-\tau(C_{17}-C_{19})(27)+\tau(C_{17}-C_{19})(27)-\tau(C_{17}-$   | $\tau(C_{14}-C_{17})$                    |
| 89(0,0)0.66                       | -               | 88 w               | $\tau(C_{17}-C_{19})(51)-\tau(C_{17}-N_{22})(14)-\tau(C_{19}-O_{20})(10)+\gamma(C_{3}-C_{19})(51)-\tau(C_{19}-C_{19})(2)+\tau$  | $\tau(C_{17}-C_{19})$                    |
| 95(0,4)0.75<br>170(0.1,2)0.75     | -               | 96 m               | $\phi(R)(49)-\alpha(C_3-C_{14}-C_{17})(11)-\delta1(CNCH)(7)-\tau(C_{17}-C_{19})(6)-\tau(C_{17}-C_{19})(4)=\tau(C_{17}-C_{19})(4)$  | $\alpha(C_3-C_{17}-C_{14})$              |
| 207(0.6,0)0.75                    | _               | 192 w              | $\delta 1(\text{CNCH})(3) - \beta(\text{C}_3 - \text{C}_{14})(3) + \tau(\text{C}_{17} - \text{N}_{22})(3)$<br>$\delta 1(\text{CNCH})(3) - \beta(\text{C}_3 - \text{C}_{14})(25) + \phi(\text{R})(8) + \rho(\text{CO}_2\text{H})(5) - \rho(\text{C}_3 - \text{C}_{14})(3) + \rho(\text{CO}_2\text{H})(5) - \rho(\text{C}_3 - \text{C}_{14})(3) + \rho(\text{CO}_2\text{H})(5) - \rho(\text{C}_3 - \text{C}_{14})(3) + \rho(\text{CO}_3\text{H})(3) + \rho(\text{CO}_3$ | $\beta(C_3-C_{14})$                      |
| 214(0.1,1)0.39<br>237(0.1,1)0.75  | _               | 211 vw<br>251 m    | $\delta^2(\text{CNCH})(4) + \omega(\text{CO}_2\text{H})(3) - \tau(\text{C}_1-\text{O}_{12})(3)$<br>$\tau(\text{C}_1-\text{O}_{12})(30) - \phi(\text{R})(19) + \gamma(\text{C}_1-\text{O}_{12})(10) + \gamma(\text{C}_2-\text{H}_7)(7)$ -   | $\gamma(C_1 - O_{12}) = 10 \text{ h}$    |
| 240(0.1,1)0.72<br>321(1.1,0)0.75  |                 | 212 14             | $ \begin{split} & \delta_2(\text{CNCH})(6) + \tau(\text{C}_6 - \text{O}_{10})(5) - \alpha(\text{C}_3 - \text{C}_{14} - \text{C}_{17})(5) \\ & \beta(\text{C}_1 - \text{O}_{12})(34) - \beta(\text{C}_6 - \text{O}_{10})(34) + \alpha(\text{C}_6 - \text{O}_{10} - \text{H}_{11})(10) - \alpha(\text{C}_1 - \text{O}_{12} - \text{O}_{12}) \\ \end{split} $   | $\beta(C, \Omega) = \beta(0, 2)$         |
| 322(0,0)0.73<br>327(0.7,0)0.75    | -               | 312 W              | $H_{13})(7) + \alpha(R)(8)$<br>$\tau(C_{17}-N_{22})(36)-\tau(C_{19}-O_{20})(14)+\delta3(CNCH)(9)-\beta s(CO_2H)(8)-$   | p(C-O)op(ya)                             |
| 327(0.1,0)0.50<br>341(0.2)0.40    | -               | 327 sn             | $\beta(C_3-C1_4)(7)-\rho(CO2H)(4)+\beta(C_6-O_{10})(4)-\nu(O_{20}-H_{24})(4)$<br>$\tau(C_{17}-N_{22})(44)-\tau(C_{19}-O_{20})(11)-\delta3(CNCH)(9)+\beta(C_{2}-C_{10})(11)-\delta3(CNCH)(11)-\delta3(C$  | $\tau(C_{19}-O_{20})$                    |
| 342(0.8,0)0.75                    | -               | 340 w              | $C_{14}(8) + \rho(CO_2H)(4.)$<br>$\gamma(C_{12}O_{12})(17) + \delta_4(CO_2H)(8) + \gamma(C_{12}O_{12})(8) + \gamma(C_{$  | $\tau(C_{17}-N_{22})$                    |
| 350(0,1)0.41<br>352(0,1)0.75      | -               |                    | $\delta_3(\text{CNCH})(6) + \phi(\text{R})(16) + \gamma(\text{C}_3 - \text{C}_{12})(6) + \delta_3(\text{CNCH})(6) + \phi(\text{R})(16) + \gamma(\text{C}_5 - \text{H}_9)(5) + \delta_2(\text{CNCH})(4) - \tau(\text{C}_{14} - \text{C}_{17})(3,)$  | $\gamma(C_6-O_{10})$ (10 a)              |
| 375(0,0)0.71<br>377(0.3,1)0.75    | -               | 360 w              | $\delta 3(\text{CNCH})(16) - \delta 2(\text{CNCH})(15) - \tau(C_{14} - C_{17})(6) + \delta 1(\text{CNCH})(6) + t(\text{CH}_2)(6) - \gamma(C_6 - O_{10})(6) + \beta(C_3 - C_{14})(5) - \beta s(\text{CO}_2\text{H})(5)$   | δ(CNCH)                                  |
| 420(0,3)0.21<br>422(0.2,1)0.75    | 416 w           | 402 w br           | $\tau(C_6-O_{10})(81)-\tau(C_1-O_{12})(8)-\gamma(C_1-O_{12})(6)$   | $\tau(C_6-O_{10})$                       |
| 449(0.4,0)0.75<br>450(1.5,0)0.72  | 451 m           | 457 m              | $ \alpha(R)(25) - \delta_2(CNCH)(17) + \alpha(R)(16) + \nu(C_3 - C_{14})(9) - \omega(CO_2H)(4) + \tau(C_{19} - O_{20})(3) $  | α(R) 6 a                                 |
| 474(0.6,1)0.75<br>474(4.7,0)0.62  | 472 m           | -                  | $\phi(R)(37)-\gamma(C_1-O_{12})(21)-\gamma(C_6-O_{10})(18)-\phi(R)(14)$  | φ(R) 16 b                                |
| 486(0.1,0)0.75<br>490(0.1,2)0.23  | 509 w           | -                  | $ \begin{aligned} &\alpha(R)(19) + \beta(C_1 - O_{12})(17) + \beta(C_6 - O_{10})(10) + \beta(C_3 - C_{14})(8) - \alpha(C_1 - O_{12} - H_{13})(6) + \phi(R)(3) - \nu(C_2 - C_3)(3) \end{aligned} $  | β(C-O)ip (9 b)                           |
| 527(0.5,0)0.75<br>531(0,3)0.70    | 525 ms          | 523                | $\rho(\text{CO}_{2}\text{H})(43) + \nu(\text{C}_{17}\text{-}\text{C}_{19})(16) + \delta 1(\text{CNCH})(6) + \delta 3(\text{CNCH})(4) - \omega(\text{CO}_{2}\text{H})(4) + \nu(\text{C}_{17}\text{-}\text{N}_{22})(3)$  | $\rho(CO_2H)$                            |
| 546(0.1,1)0.02<br>551(0.5,0)0.75  | 550 w           | 548 m              | $\delta_2(CNCH)(13)-\phi(R)(25)+\alpha(R)(8)-\alpha(C_3-C_{14}-C_{17})(8)+\omega(CO_2H)(9)-\gamma(C_3-C_{14})(4)$<br>-β(C <sub>1</sub> -O <sub>12</sub> )(3)+γ(C <sub>1</sub> -O <sub>12</sub> )(3)  | δ2(CNCH)                                 |
| 575(0.2,1)0.51<br>576(0,0)0.75    |                 |                    | $\beta s(CO_2H)(29) + \delta 3(CNCH)(22) - \nu (C_{14} - C_{17})(10) + \omega (CO_2H)(8) - \phi (R)(9) + \alpha (R)(3) - \nu (C_{17} - C_{19})(3)$   | $\beta_{s}(CO_{2}H)$                     |
| 597(0.6,0)0.75<br>597(0,3)0.41    | 588 m           | 585 m              | $ \alpha(R)(30) - \beta(C_6 - O_{10})(23) - \beta(C_1 - O_{12})(10) - \nu(C_5 - C_6)(8) + \alpha(C_6 - O_{10} - H_{11})(6) - \nu(C_1 - O_{12})(6) - \beta(C_3 - C_{14})(6) $   | α(R) 6 b                                 |
| 653(0.3,0)0.75<br>654(0.3,0)0.60  | 663             | 591 sh             | $\begin{array}{l} \gamma(C_3-C_{14})(20)-\varphi(R)(23)-\gamma(C_1-O_{12})(15)+\gamma(C_6-O_{10})(8)-\alpha(C_3-C_{14}-C_{17})(7)-\beta s(CO_2H)(6)-\delta 3(CNCH)(4)+\omega(CO_2H)(3) \end{array}$  | φ(R) 16 a                                |
| 702(2,1)0.05<br>706(0.5,0)0.75    | -               | 683 w              | $\tau(C_1-O_{12})(51)+\tau(C_6-O_{10})(18)+\phi(R)(18)-\gamma(C_2-H_7)(4.)$  | $\tau(C_1-O_{12})$                       |
| 722(0.1,0)0.75<br>723(0,5)0.15    | 717 m           | 716 s              | $ \begin{aligned} \varphi(\mathbf{R})(21) + \alpha(\mathbf{R})(23) &- \nu(\mathbf{C}_3 - \mathbf{C}_{14})(10) + \gamma(\mathbf{C}_1 - \mathbf{O}_{12})(10) - \gamma(\mathbf{C}_6 - \mathbf{O}_{10})(8) - \omega(\mathbf{CO}_2 \mathbf{H})(6) - \nu(\mathbf{C}_3 - \mathbf{C}_4)(3) \end{aligned} $   | α(R)-12                                  |
| 731(0.1,0)0.75<br>739(0.4,0)0.47  | 731 m           | -                  | $\begin{array}{c} \varphi(R)(50) + \gamma(C_1 - O_{12})(15) - \gamma(C_6 - O_{10})(15) + \gamma(C_3 - C_{14})(4) + \omega(CO_2H)(4) \end{array}$   | Φ(R)-4                                   |
| 774(0.6,5)0.02<br>776(0.2,0)0.75  | 777 m           | 777 vs             | $ \begin{array}{l} \beta s(CO_2H)(18) + \nu(C_{17}-C_{19})(14) + \varphi(R)(8) + \nu(C_{14}-C_{17})(7) - \alpha(C_3-C_{14}-C_{17})(7) - \rho(CO_2H)(6) + \nu(C_{19}=O_{20})(6) - \omega(CO_2H)(5) + \gamma(C_3-C_{14})(5) + \nu(C_{17}-N_{22})(5) \end{array} $  | $\nu(C_{17}-C_{19})$                     |
| 792(0.1,11)0.06<br>792(1.4,1)0.75 | 808 s           | 808 s<br>vs        | $\nu(C_1-C_6)(25)+\nu(C_6-O_{10})(22)-\alpha(R)(10)+\nu(C_5-C_6)(9)+\nu(C_1-C_2)(6)+\nu(C_1-O_{12})(6)+\alpha(R)(5.)$  | ν(R) 1                                   |
| 813(2,1)0.53<br>813(0.3,0)0.75    | -               | 813 sh             | $\gamma(C_5-H_9)(22)+\gamma(C_4-H_8)(19)-\nu(C_{17}-C_{19})(12)+\omega(NH_2)(7)-\gamma(C_6-O_{10})(5)+t(CH_2)(5)-\omega(CO_2H)(4)$   | γ(C-H) 10 a                              |

| Table 5. Compute | ed and observed | IR and Raman | frequencies | of L-dopa |
|------------------|-----------------|--------------|-------------|-----------|
| able 5. Compute  |                 | in and Raman | inequencies | or L uopa |

# Table 5. Cont.

| <sup>#</sup> Dimer D1                | <sup>+</sup> IR | <sup>+</sup> Raman | PEDs  | Assignments                |
|--------------------------------------|-----------------|--------------------|---|----------------------------|
| 834(0.1,0)0.75<br>835(0.1,0)0.17     | 839 m           | 836 m              | $\begin{array}{l} \gamma(C_{5}\text{-}H_{9})(24) + \gamma(C_{4}\text{-}H_{8})(12) - \gamma(C_{2}\text{-}H_{7})(7) + \nu(C_{17}\text{-}C_{19})(6) \\ + \omega(CO_{2}H)(5) + \alpha(C_{3}\text{-}C_{14}\text{-}C_{17})(5) - \gamma(C_{6}\text{-}O_{10})(4) \text{-}t(CH_{2})(4) - \nu(C_{17}\text{-}N_{22})(4) - \delta 1(CNCH)(3) \end{array}$   | α(R)                       |
| 862(3,2)0.17<br>862(3.5,0)0.75       | 865 m           | 864 m              | $\omega(NH_2)(37) + \nu(C_{17}-N_{22})(17) + \nu(C_{14}-C_{17})(10) + \omega(CO_2H)(6) + \tau(C_{19}-O_{20})(5) - \delta 3(CNCH)(5) + \alpha(R)(4) - \delta 2(CNCH)(4)$   | $\omega(\mathrm{NH}_2)$    |
| 876(0.3,0)0.75<br>879(0.3,0)0.59     | 865 m           | 864 m              | $\gamma(C_2-H_7)(63)-\phi(R)(18)-\gamma(C_3-C_{14})(5)-\gamma(C_1-O_{12})(4)+\gamma(C_4-H_8)(3)$  | γ(C-H) 5                   |
| 908(0.6,0)0.74<br>909(1.3,2)0.03     | 905 w           | -                  | $\begin{array}{c} t(CH_2)(30) - \omega(NH_2)(16) - \tau(C_{19} - O_{20})(15) + \nu(C_3 - C_4)(4) - \\ \delta 1(CNCH)(4) + \alpha(R)(4) + \nu(C_{14} - C_{17})(3) - \alpha(R)(3) \end{array}$  | t(CH <sub>2</sub> )        |
| 933(2.4,0)0.75<br>934(1,0)0.71       | 943 s           | 943 ms             | $\tau(C_{19}-O_{20})(72)-\omega(NH_2)(12)+t(CH_2)(7)$   | τ(C-OH)                    |
| 924(0.3,0)0.75<br>925(0,0)0.39       | 918 m           | 917 ms             | $\gamma(C_4 - H_8)(46) - \gamma(C_5 - H_9)(37) - \phi(R)(10)$   | γ(C-H) 17 b                |
| 963(0,1)0.20<br>963(0.6,0)0.75       | -               | 960 vw             | $\nu(C_3-C_{14})(12)-\nu(C_1-O_{12})(11)+\alpha(R)(14)+ \\\nu(C_2-C_3)(9)-t(CH_2)(8)+ \\\nu(C_3-C_4)(6)+\beta(C_5-H_9)(5)-\nu(C_{17}-N_{22})(4)$  | v(Cph-C)                   |
| 1006(0.5,0)0.75<br>1006(2,1)0.28     | 982 s<br>1016 w | 982 s              | $\nu(C_{14}-C_{17})(25)-t(CH_2)(12)-\omega(NH_2)(11)-\nu(C_{19}=O_{20})(10)-\nu(C_{17}-C_{19})(8)+\delta 3(CNCH)(7)-\nu(C_3-C_4)(4)-\rho(CH_2)(4)$  | $\nu(C_{14}-C_{17})$       |
| 1075(0.1,100)0.57<br>1075(0.3,0)0.75 | 1063 ms         | 1060 s             | $\begin{split} \nu(C_{17}-N_{22})(39) &- \nu(C_{14}-C_{17})(11) - \rho(CH_2)(6) + \nu(C_2-C_3)(5) - \\ \rho(NH_2)(5) - \delta(C_{17}-H)(4) - t(CH_2)(4) - \rho(CO_2H)(4) + \delta 1(CNCH)(3) \end{split}$   | ν(C <sub>17</sub> -N)      |
| 1117(1.6,0)0.75<br>1117(0,1)0.56     | 1119 vs         | 1119 m             | $ \begin{array}{l} \alpha(C_1-O_{12}-H_{13})(19)-\alpha(R)(17)-\nu(C_1-O_{12})(13)-\beta(C_4-H_8)(12)-\nu(C_1-C_2)(6)+\nu(C_4-C_5)(5)-\nu(C_3-C_4)(4)+\nu(C_6-O_{10})(3) \end{array} $  | β(C-H) 18 b                |
| 1143(1,0)0.75<br>1143(0.1,4)0.20     | 1137 w          | 1135 w             | $\beta(C_5-H_9)(19) + \nu(C_4-C_5)(11) - \nu(C_3-C_{14})(10) - \rho(NH_2)(8) + \nu(C_1-O_{12})(7) - \alpha(C_1-O_{12}-H_{13})(7) - \beta(C_4-H_8)(5) - \nu(C_{19}=O_{20})(3)$   | β(C-H) 18 a                |
| 1156(0.2,0)0.75<br>1156(0,0)0.07     | 1160 w          | 1158 m             | $\rho(\text{NH}_2)(28)-\alpha(\text{C}_1-\text{O}_{12}-\text{H}_{13})(8)+\delta(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(\text{C}_{17}-\text{H})(7)+\delta^{-1}(1$ | ρ(NH <sub>2</sub> )        |
| 1192(0,2)0.08<br>1196(2.3,0)0.75     | 1188 sh         | 1181 w             | $ \begin{array}{l} \alpha(C_1-O_{12}-H_{13})(21)-\beta(C_2-H_7)(15)-\alpha(C_6-O_{10}-H_{11})(11)-\nu(C_3-C_{14})(7)+\nu(C_2-C_3)(6)+\nu(C_1-C_6)(5)-\nu(C_5-C_6)(5)-\nu(C_1-C_2)(4)+\nu(C_4-C_5)(4)+\nu(C_{19}=O_{20})(3)-\rho(CH_2)(3) \end{array} $  | α(С-О-Н)                   |
| 1202(1.3,0)0.69<br>1202(0.5,2)0.14   | -               | 1197 w             | $\nu(C_{19}=O_{20})(33)+\rho(CO_2H)(11)-\nu(C_{17}-C_{19})(10)-\rho(NH_2)(7)+\alpha(C_{19}-O_{21}-H_{22})(6)+\delta3(CNCH)(5)-\rho(CH_2)(4)+\alpha(C_6-O_{10}-H_{11})(3)$   | ν(C <sub>19</sub> -O(H))   |
| 1222(6,0)0.75<br>1223(0,4)0.25       | 1202 m          | -                  | $\alpha(C_6-O_{10}-H_{11})(33)-\beta(C_2-H_7)(13)-\beta(C_5-H_9)(12)+\nu(C_5-C_6)(12)-\nu(C_3-C_{14})(7)+\nu(C_3-C_4)(5)$   | α(С-О-Н)                   |
| 1233(0.4,2)0.69<br>1233(3.5,1)0.75   | 1229 ms         | 1227 w             | $\rho(CH_2)(24) + \delta(C_{17}-H)(16) - \delta'(C_{17}-H)(12) + \nu(C_{19}=O_{20})(7) + \nu(C_{3}-C_4)(5) + \nu(C_{17}-N_{22})(5) - \omega(CH_2)(5) - \nu(C_2-C_3)(4)$   | $\rho(CH_2)$               |
| 1261(0.5,5)0.71<br>1262(5.8,0)0.75   | 1249 s          | 1246 w             | $\nu(C_6-O_{10})(41)-\alpha(R)(19)+\beta(C_4-H_8)(6)-\alpha(C_1-O_{12}-H_{13})(5)-\nu(C_4-C_5)(5)-\nu(C_1-C_6)(4)+\beta(C_5-H_9)(3)$  | ν(C-OH)                    |
| 1274(3.8,0)0.72<br>1274(0.4,8)0.10   |                 |                    | $\delta(C_{17}-H)(23)-\omega(CH_2)(13)-\rho(CH_2)(12)-\rho(NH_2)(10)-\nu(C_{14}-C_{17})(9)-\delta'(C_{17}-H)(6)+\nu(C_{17}-C_{19})(5)+\delta^2(CNCH)(5)$  | δ(C <sub>17</sub> -H)      |
| 1288(0.8,13)0.04<br>1289(7.2,0)0.74  | 1281            | -                  | $\nu(C_1-C_6)(9) + \nu(C_2-C_3)(7) - \nu(C_3-C_{14})(6) - \nu(C_6-O_{10})(4) - \alpha(R)(4) - \omega(CH_2)(3)$  | ν(C-OH)                    |
| 1373(0.1,4)0.10<br>1374(1.7,1)0.75   | -               | -                  | $ \nu(C_2-C_3)(11) - \alpha(C_1-O_{12}-H_{13})(11) + \omega(CH_2)(9) - \beta(C_5-H_9)(8) - \nu(C_3-C_4)(8) + \rho(CH_2)(7) + \nu(C_4-C_5)(6) + \nu(C_1-C_6)(5) - \nu(C_1-C_2)(4) - \beta(C_2-H_7)(4) - \nu(C_5-C_6)(4) - \delta'(C_{17}-H)(4) - \nu(C_5-C_6)(4) - \delta'(C_5-C_6)(4) - \delta'(C_5-C$  | β(C-H) (3)                 |
| 1338(0.8,0)0.75<br>1338(0,10)0.44    | 1351 m          | 1345 m             | $ \begin{array}{c} \omega(\text{CH}_2)(46) + \delta(\text{C}_{17}\text{-H})(13) + \beta(\text{C}_4\text{-H}_8)(6) - \nu(\text{C}_3\text{-C}_{14}) \\ (6) + \beta(\text{C}_5\text{-H}_9)(5) - \alpha(\text{C}_{19}\text{-O}_{21}\text{-H}_{22})(4) - \rho(\text{CH}_2)(3) + \\ \alpha(\text{C}_4\text{-O}_{10}\text{-H}_{11})(3) \end{array} $   | ω(CH <sub>2</sub> )        |
| 1361(0,5)0.41<br>1362(3.3,1)0.75     | 1362 sh         | 1358 ms            | $\delta'(C_{17}-H)(29)-\alpha(C_6-O_{10}-H_{11})(10)-\rho(NH_2)(9)+\delta(C_{17}-H_1)(8)+\nu(C_3-C_4)(6)+\nu(C_1-C_2)(5)-\beta(C_4-H_8)(4)+\nu(C_5-C_6)(3)$   | $\delta'(C_{17}\text{-}H)$ |
| 1389(2.3,0)0.51<br>1389(0,12)0.11    | -               | 1386 vw            | $ \begin{split} \delta'(C_{17}-H)(20) &- \nu(C_1-C_2)(12) - \nu(C_3-C_4)(10) + \alpha(C_6-O_{10}-H_{11})(9) - \nu(C_5-C_6)(6) + \beta(C_4-H_8)(6) - \rho(NH_2)(5) + \rho(CH_2)(5) + \nu(C_1-O_{12})(4) + \nu(C_1-C_6)(4) + \nu(C_4-C_5)(3) \end{split} $  | ν(R) 14                    |

# Table 5. Cont.

| <sup>#</sup> Dimer D1               | <sup>†</sup> IR | <sup>+</sup> Raman | PEDs   | Assignments             |
|-------------------------------------|-----------------|--------------------|--|-------------------------|
| 1410(3,1)0.75<br>1414 (21,3)0.11    | 1404 ms         | 1406 m             | $\alpha(C_{19}-O_{21}-H_{22})(60)-\nu(C_{19}=O_{20})(14)+\nu(C_{19}-O_{21})(6)-\rho(CO_2H)(4)$   | α(С-О-Н)                |
| 1448(0.9,4)0.17<br>1449(8.8,0)0.75  | 1439 m          | 1436 m             | $\begin{split} \nu(C_1-C_2)(18) &-\nu(C_4-C_5)(17) - \beta(C_4-H_8)(9) + \nu(C_2-C_3)(8) + \beta(C_5-H_9)(7) - \\ \nu(C_1-O_{12})(7) - \beta(C_3-C_{14})(5) + \rho(CH_2)(5) + \beta(C_6-O_{10})(5) - \\ \beta(CH_2)(4) + \beta(C_1-O_{12})(3) \end{split}$ | v(R) 19 b               |
| 1455(0.1,1)0.75<br>1455(0.8,4)0.74  | 1460 m          | 1458 w             | $\beta(CH_2)(89) + \alpha(C_3 - C_{14} - C_{17})(3)$   | $\beta_s(CH_2)$         |
| 1529(0.6,2)0.71<br>1530(5.5,0)0.75  | 1527 m          | 1531 w             | $\begin{array}{l} \beta(C_2-H_7)(16)-\nu(C_5-C_6)(12)-\beta(C_5-H_9)(11)-\beta(C_4-H_8)(11)-\\ \nu(C_1-C_6)(10)+\nu(C_2-C_3)(9)+\nu(C_6-O_{10})(8)+\nu(C_3-C_4)(7)-\nu(C_3-\\ C_{14})(4)+\beta(C_1-O_{12})(4) \end{array}$                                 | ν(R) 19 a               |
| 1606(1.8,1)0.75<br>1606(0.1,7)0.58  | 1606 w          | 1606 s             | $\nu(C_1-C_6)(20)-\nu(C_5-C_6)(19)+\nu(C_3-C_4)(13)-\nu(C_2-C_3)(10)+\beta_s(NH_2)(10)-\alpha(R)(6)+\beta(C_6-O_{10})(5)$  | v(R) 8 b                |
| 1609(0,0)0.58<br>1610(2.9,0)0.75    | 1606 w          | 1606 s             | $\beta_{s}(NH_{2})(71)+\nu(C_{5}-C_{6})(7)+\nu(C_{2}-C_{3})(4)-1(3)$   | $\beta_{s}(NH_{2})$     |
| 1617(0,1)0.75<br>1617(2.8,0)0.75    | 1606 w          | 1606 s             | $\nu(C_1-C_2)(20)+\nu(C_4-C_5)(16)+\beta_s(NH_2)(11)-\alpha(R)(8)-\nu(C_1-C_6)(7)-\nu(C_3-C_4)(7)-\nu(C_5-C_6)(5)+\beta(C_4-H_8)(4)-\beta(C_2-H_7)(4)-\beta(C_5-H_9)(4)+\beta(C_1-O_{12})(3)-\nu(C_2-C_3)(3)$  | ν(R) 8 a                |
| 1741(4.1,5)0.19<br>1743(29.6,0)0.75 | -               | 1678 w             | $\nu(C_{19}=O_{21})(74)-\beta s(CO_2H)(8)-\alpha(C_{19}-O_{21}-H_{22})(6)-\nu(C_{17}-C_{19})(5)-\nu(C_{19}-O_{20})(3)$   | v(C=O)                  |
| 2927(0.1,11)0.62<br>2927(0.5,1)0.73 | 2928 w          | 2928 s             | $\nu(C_{17}-H_{18})(50)-\nu(C_{14}-H_{16})(30)-\nu(C_{14}-H_{15})(20)$   | $\nu_{s}(CH_{2})$       |
| 2939(1.1,9)0.75<br>2939(0.9,14)0.02 | 2928 w          | 2928 s             | $\nu(C_{17}-H_{18})(50)+\nu(C_{14}-H_{16})(28)+\nu(C_{14}-H_{15})(22)$   | ν(C-H)                  |
| 2979(0.4,3)0.75<br>2979(0,1)0.45    | 2978 w          | 2979 s             | $\nu(C_{14}-H_{15})(58)-\nu(C_{14}-H_{16})(42)$  | $\nu_{as}(CH_2)$        |
| 3038(0.1,4)0.41<br>3038(0.6,1)0.64  | 3042 m          | 3033 ms            | $\nu(C_2-H_7)(59)-\nu(C_4-H_8)(36)+\nu(C_5-H_9)(5)$  | ν(C-H) 7 b              |
| 3059(0.1,0)0.74<br>3059 (0,5)0.27   | 3042 m          | -                  | $\nu(C_4-H_8)(48)+\nu(C_2-H_7)(40)-\nu(C_5-H_9)(11)$   | ν(C-H) 13               |
| 3068(0.5,0)0.72<br>3069(0,13)0.24   | 3061 m          | 3072 m             | $\nu(C_5-H_9)(83)+\nu(C_4-H_8)(16)$  | ν(C-H) 2                |
| 2836(0.5,6)0.12<br>2836(28.2,0)0.73 | 2770 s          | -                  | ν(O <sub>20</sub> -H <sub>24</sub> )(100)  | ν(O-H)                  |
| 3278(2.4,1)0.72<br>3278(0.1,13)0.14 | -               | -                  | $\nu(N_{22}-H_{23})(79)+\nu(N_{22}-H_{25})(20)$  | $\nu_s(\mathrm{NH}_2)$  |
| -                                   | 3216 w          | 3206 w             | -  | 1st overtone of<br>1606 |
| 3374(0,16)0.38<br>3374(2.1,0)0.72   | 3370 m          | 3362 vw            | $\nu(N_{22}-H_{25})(79)-\nu(N_{22}-H_{23})(21)$  | $\nu_{as}(NH_2)$        |
| 3311(0.4,10)0.12<br>3311(6,1)0.75   | -               | -                  | ν(O <sub>10</sub> -H <sub>11</sub> )(100)  | ν(O-H)                  |
| 3051(0,28)0.24<br>3042(100,0)0.75   | 3045 m          | 3046 ms            | ν(O <sub>12</sub> -H <sub>13</sub> )(100)  | ν(O-H)                  |

<sup>#</sup> Number before each bracket is scale frequency (cm<sup>-1</sup>), numbers within the bracket are IR intensity (KM/Mole) and relative Raman intensity and number outside bracket is the depolarization ratio; Scaling factor is 0.99 in the frequency below 1000 cm<sup>-1</sup>; 0.98 for the range 1000–2000 cm<sup>-1</sup>; and 0.956 for the range 3000–3500 cm<sup>-1</sup>, excepting the OH stretching modes for which the used scaling factor is 0.85–0.88 [19,20]. <sup>†</sup> Observed frequencies characterized by the notation w = weak band, sh = shoulder, m = medium, ms = medium strong, vs = very strong, s = strong.



Figure 4. Computed and experimental IR and Raman spectra of L-dopa.

4.4.1. -CH<sub>2</sub>-CH-NH<sub>2</sub>CO<sub>2</sub>(H) Moiety Modes (30)

The 2-aminopropenoic acid (CH<sub>2</sub>-CH-NH<sub>2</sub>CO<sub>2</sub>(H)) moiety can be further sub-divided into five sub-groups: (i)  $^{-14}$ CH<sub>2</sub> group modes-6, (ii) $^{-17}$ CH modes-3, (iii) -NH<sub>2</sub> group modes-6, (iv) CO<sub>2</sub>(H) group modes-6 and (v) side chain skeleton C<sub>14</sub>-C<sub>17</sub>(N<sub>22</sub>) -C<sub>22</sub> modes-9.

# <sup>14</sup>CH<sub>2</sub> and <sup>17</sup>CH Group Modes (6+3)

The -CH<sub>2</sub> group has six modes, namely  $v_s$ (-CH<sub>2</sub>),  $v_{as}$ (-CH<sub>2</sub>),  $\beta_s$ (CH<sub>2</sub>),  $\omega$ (CH<sub>2</sub>),  $\rho$ (CH<sub>2</sub>) and t(CH<sub>2</sub>). The mode  $v_s({}^{14}CH_2)$  was found to be strongly coupled with the  $v({}^{17}C-H)$ mode. From their PEDs, one mode could not be distinguished from the other mode, since each has 50% contributions to the computed frequencies 2929 and 2938 cm<sup>-1</sup>. However, the  $\nu_s(^{14}CH_2)$  mode is expected to be more intense in the Raman spectrum as compared to the  $v(^{17}C-H)$  mode. The frequency 2938 cm<sup>-1</sup> is more intense than 2929 cm<sup>-1</sup> in the Raman spectrum, and hence it is correlated to the  $v_s({}^{14}CH_2)$  mode and the frequency 2929 cm<sup>-1</sup> to the  $v({}^{17}C-H)$  mode. The  $v_{as}(CH_2)$  is a pure mode with the computed frequency 2975 cm<sup>-1</sup>, observed at 2964 cm<sup>-1</sup> in both the IR and Raman spectra. The  $\beta_s$ <sup>(14</sup>CH<sub>2</sub>) mode seems to be a pure mode and it was computed to be 1449  $cm^{-1}$  with medium IR and Raman intensities, and was correlated with a medium-strong band 1439 cm<sup>-1</sup> observed in the IR and Raman spectra. The remaining three modes,  $\omega(^{14}CH_2)$ ,  $\rho(^{14}CH_2)$  and  $t(^{14}CH_2)$ , were found to be coupled with the other modes and are computed to be 1339, 1217 and 902  $cm^{-1}$ , respectively. The computed IR and Raman intensities for these modes were found to be weak. Out of these three modes, only the twisting mode could be observed at 901  $cm^{-1}$ in the IR spectrum. The two <sup>17</sup>C-H deformation modes were computed to be 1263 and 1217 cm<sup>-1</sup> and were correlated to the observed frequencies 1249(IR)/1247(R) and 1202 (IR, R)  $cm^{-1}$ . These assignments were found to be in conformity with the assignments of the corresponding modes of the L-dopa molecule reported earlier [12].

# -NH<sub>2</sub> Group Modes (6)

Similar to the -CH<sub>2</sub> group, the -NH<sub>2</sub> group also has the six modes  $v_s$ ,  $v_{as}$ ,  $\beta_s$ ,  $\omega$ ,  $\rho$  and  $\tau$ . The modes  $v_s$  and  $v_{as}$  for the NH<sub>2</sub> group were observed in the range 3200–3500 cm<sup>-1</sup> [21]. For the two NH<sub>2</sub> stretching modes  $v_s$  and  $v_{as}$  of the NH<sub>2</sub> group, with two identical N-H bonds, Bellamy et al. [22] proposed an empirical relation:  $v_s = 345.5 + 0.876 v_{as}$ . For

a given observed frequency corresponding to one  $(v_s/v_{as})$  of the two modes  $v_s$  and  $v_{as}$ , the computed frequency for the other  $(v_{as}/v_{s})$  mode would differ from its observed frequency within  $\pm 5 \text{ cm}^{-1}$  only. For the L-dopa molecule, the computed frequencies for the  $v_s$  and  $v_{as}$  modes were found to be 3290 and 3378 cm<sup>-1</sup>. Considering these two frequencies, 3290 and 3378 cm<sup>-1</sup>, as the observed frequencies for the  $v_s$  and  $v_{as}$  modes, the computed frequency using the above empirical relation was found to differ from the observed frequency within  $\pm 17 \text{ cm}^{-1}$ , indicating that the two N-H bonds are not identical. This is also evident from the two significantly differing bond lengths (N<sub>22</sub>-H<sub>23</sub>) 1.018 and (N<sub>22</sub>-H<sub>25</sub>) 1.014 Å. The computed  $v_s$  and  $v_{as}$  modes were found to be much weaker in IR and Raman spectra and seem to be buried under the broad and strong/weak IR/Raman bands originating due to the OH stretching modes. Chamundeeswari et al. [12] assigned the  $v_s$  mode at 3209 cm<sup>-1</sup> for L-dopa, while Siddiqui et al. [10] assigned these two modes at 3355 and 3433 cm<sup>-1</sup> for L-dopa and L-tyrosine molecules.

The mode  $\beta_s(NH_2)$  appears in the range 1600–1700 cm<sup>-1</sup> with medium to strong IR intensities. The observed frequency 1606 (IR, R) cm<sup>-1</sup> could be assigned to the  $\beta_s(NH_2)$ mode of L-dopa. The computed IR and Raman intensities for this mode were found to be lower than the ring stretching modes 8(a/b) which were also observed around 1600 cm<sup>-1</sup>. In the present case, the  $\beta_s(NH_2)$  mode was found to have slightly lower magnitude (20 cm<sup>-1</sup>) as compared to the corresponding mode of aniline. The  $\rho(NH_2)$ ,  $\omega(NH_2)$  and  $\tau(NH_2)$  modes have higher magnitudes than the corresponding modes of the aniline molecule. The mode  $\rho(\text{NH}_2)$  appears in the range 1000–1200 cm<sup>-1</sup> with weak to medium intensity in aniline and its derivatives [21]. In the present case, this mode was computed to be 1148 cm<sup>-1</sup> and was observed at 1135 cm<sup>-1</sup> with weak IR and Raman intensities. The  $\omega(NH_2)$  mode of the L-dopa molecule was computed to be 855 cm<sup>-1</sup> and was correlated with the observed frequencies 864(IR)/865(R) cm<sup>-1</sup>. The lowest-frequency mode  $\tau$ (NH<sub>2</sub>) of the NH<sub>2</sub> group was computed to be 328 cm<sup>-1</sup> and was observed only in the Raman spectrum at 327 cm<sup>-1</sup>. The present assignments for the  $\beta_s(NH_2)$ ,  $\rho(NH_2)$ ,  $\omega(NH_2)$  and  $\tau(NH_2)$ modes agree with the assignments of these modes earlier proposed by Chamundeeswari et al. [12] for the L-dopa molecule.

### -CO<sub>2</sub>(H) Group Modes (6)

Out of the six CO<sub>2</sub>(H) group modes, the modes v(C=O) and v(C-O(H)) do not couple with each other. The v(C=O) mode was computed to be 1741 cm<sup>-1</sup> and was correlated to the strong IR band at 1649 cm<sup>-1</sup> in agreement with the assignment of this mode in L-dopa [11,12]. The computed frequency for the mode v(C-O(H)) was found to be 1177 cm<sup>-1</sup> with weak IR and Raman intensities and could not be observed experimentally. For the remaining four modes, the COO(H) group behaves like a CO<sub>2</sub> group and its four modes were found to arise due to coupling between the C=O and C-O(H) modes. These modes are  $\beta_s \{CO_2(H)\}$ ,  $\omega \{CO_2(H)\}$ ,  $\rho \{CO_2(H)\}$  and  $\tau \{CO_2(H)\}$  with the respective computed frequencies 572, 542, 528 and 88 cm<sup>-1</sup>, all with weak Raman intensities. These modes are strongly coupled with the 2-anilinepropene moiety modes. From the GaussView 5.0 animation software, the rocking mode of the COO(H) group seems to arise due to the major deformation of the C=O and minor deformation of the C-O(H) bonds. However, the other three modes were found to arise due to almost equal contributions from the angular deformations of the C=O and C-O(H) bonds.

## Side Chain Skeleton C<sub>14</sub>-C<sub>17</sub> N<sub>22</sub>-C<sub>19</sub> Modes (9)

The side chain skeleton  $C_{14}$ - $C_{17}$   $N_{22}$ - $C_{19}$  has nine normal modes of vibration. Assuming the entire mass (except the <sup>14</sup>CH<sub>2</sub> moiety) of the 2-aminopropenoic acid moiety to be concentrated at the center of the atom  $C_{17}$  and labeling it as  $C'_{17}$ , the  $C_{14}$ - $C'_{17}$  bond has three normal modes:  $\nu(C_{14}$ - $C'_{17})$ ,  $\alpha(C_3$ - $C_{14}$ - $C'_{17})$  and  $\tau(C_3$ - $C_{14})$ . Similarly, assuming the mass of the <sup>22</sup>NH<sub>2</sub> and <sup>19</sup>COOH groups to be concentrated at the centers of the atoms  $N_{22}$  and  $C_{19}$  and denoting these mass points as  $N'_{22}$  and  $C'_{19}$ , one has the  $C'_{17}N'_{22}C'_{19}$  group. This group has two stretching modes:  $\nu(C'_{17}$ - $N'_{22})$  and  $\nu(C'_{17}$ - $C'_{19})$ . The mode  $\nu(C_{14}$ - $V'_{14}$ -V'

 $C'_{17}$ ) was found to be coupled with the two stretching modes  $\nu(C_{17}-N'_{22})$  and  $\nu(C_{17}-C'_{19})$ , whereas the modes  $\nu(C_{17}-N'_{22})$  and  $\nu(C_{17}-C'_{19})$  couple with each other. The computed frequencies for the modes  $\nu(C_{14}-C'_{17})$ ,  $\nu(C_{17}-N'_{22})$  and  $\nu(C_{17}-C'_{19})$  were found to be 1064, 995 and 779 cm<sup>-1</sup> and correlated to the observed frequencies 1063(IR)/1060(R), 982(IR, R) and 777(IR, R) cm<sup>-1</sup>, respectively. The modes  $\alpha(C_3-C_{14}-C'_{17})$  and  $\tau(C_3-C_{14})$  were computed to be 170 and 67 cm<sup>-1</sup> with the observed Raman bands 166 and 64 cm<sup>-1</sup>.

The remaining four modes of the  $C'_{17}N'_{22}C'_{19}$  group result due to coupling between the corresponding angular deformations involving the atoms  $C_{17}$ ,  $N'_{22}$  and  $C'_{19}$ . These modes can be approximately described as the scissoring ( $\beta_s$ ), rocking ( $\rho$ ), wagging ( $\omega$ ) and twisting ( $\tau$ ) modes of the  $C_{17}N'_{22}C'_{19}$  group. These four modes were found to be strongly coupled with the other angle deformation modes. The computed frequencies for these modes were found to be 568, 420, 210 and 92 cm<sup>-1</sup>, respectively. All these modes were observed in the Raman spectrum with weak intensities (Table 5).

### 4.4.2. Phenyl Ring Moiety Modes (30)

The phenyl ring has six ring stretching modes {1, 8a, 8b, 14, 19a and 19b}, three planar ring deformation modes {6a, 6b and 12} and three non-planar ring deformation modes {4, 16a and 16b}. In benzene derivatives, the assignments of the modes 8a, 8b, 19a and 19b are well established [16,23,24]. The two modes 8a and 8b were found to be localized and were observed slightly above and below 1600 cm<sup>-1</sup>. In tri-light substituted benzenes, the mode 19a was observed around 1500 cm<sup>-1</sup>, while the component 19b was observed in the range  $1400 \pm 50$  cm<sup>-1</sup> [20].

The frequency corresponding to the ring breathing mode-1 varies considerably and appears with varying IR intensity and good intensity in the Raman spectrum. Varsanyi [20] has assigned this mode based on the concept of the light (mass < 25 amu) and heavy (mass > 25 amu) substituents and suggested different frequency ranges for this mode depending upon the number, nature and positions of the substituents. The L-dopa molecule is of the 1,2,4-thri-light substituted benzenes category, for which the frequency range for the ring breathing mode as suggested by Varsanyi [20] is 630–740 cm<sup>-1</sup>. Presently, the ring breathing mode was observed at 777 cm<sup>-1</sup>, a frequency slightly higher than the upper limit of the proposed range for the 1, 2, 4-thri light substituted benzenes. The observed frequency 777 cm<sup>-1</sup> of L-dopa has medium IR and strong Raman intensities, which is also supported by the computed intensity pattern for this mode. The Kekule ring stretching mode-14 was presently observed at 1362 (sh, IR) cm<sup>-1</sup> in L-dopa, which is in good agreement with the assignment of this mode in substituted benzenes proposed by the earlier works [20,23,24].

Out of the three planar ring deformation modes 12, 6a and 6b, the mode 12 showed considerable variation in the form and frequency of substituted benzenes. However, the modes 6a and 6b retained their forms in benzene derivatives and appeared with variable frequencies. The computed frequencies for the modes 12, 6b and 6a were found to be 723, 597 and 426 cm<sup>-1</sup>, corresponding to the benzene frequencies 1010, 606 and 606 cm<sup>-1</sup>, respectively. The reduction of the magnitude of the trigonal angle bending mode 12 is a result of the loading of both the triangles formed by the alternate C-atoms of the ring. Similarly, the loading of the pair of para positions  $C_3$  and  $C_6$  of the phenyl ring is responsible for the lowering of the frequency of the mode 6a. During the vibration in the mode 6b, the ring atoms  $C_3$  and  $C_6$  are practically stationary and the atoms  $C_1$ ,  $C_2$ ,  $C_4$  and  $C_5$  participate equally. Hence, the loading of the OH group at the site  $C_1$  has little effect on the vibrational frequency corresponding to the mode 6b. The assignment of the mode 6b is corroborated the earlier assignment for this mode by Chamundeeswari et al. [12].

The three non-planar ring deformation modes 4, 16a and 16b retain their forms of vibration in the substituted benzenes. The mode 4 involves motion of the alternative C-atoms in opposite directions and showed small frequency variation in the benzene derivatives. Contrary to the above, the modes 16a and 16b showed considerable variation in the magnitudes of the frequencies in the benzene derivatives. The computed frequencies for the modes 4, 16a and 16b were found to be 735, 653 and 449 cm<sup>-1</sup>. The modes 4 and

16b show small variation in the magnitudes of the computed frequencies for the L-dopa as compared to the corresponding mode of benzene. However, the mode 16a is considerably enhanced as compared to the corresponding mode of benzene ( $404 \text{ cm}^{-1}$ ).

For the L-dopa molecule, the three C-H stretching modes were computed to be 3043, 3043 and 3062 cm<sup>-1</sup> with the corresponding observed frequencies 3046, 3046 and 3072 cm<sup>-1</sup>, which could be, respectively, correlated to the modes 20a, 20b and 2 of benzene. The three planar C-H bending modes were computed to be 1325, 1133 and 1100 cm<sup>-1</sup> and were correlated to the observed frequencies 1325 (R, w), 1119 (IR, R) and 1097 (IR)/1095 (R) cm<sup>-1</sup>. These modes were identified as the C-H planar bending modes corresponding to the benzene modes 3, 18a and 18b, respectively. The three non-planar C-H bending modes were assigned to the observed frequencies 943, 878 and 808 cm<sup>-1</sup> with the corresponding respective computed frequencies 942, 879 and 814 cm<sup>-1</sup>. These three non-planar C-H bending modes could be identified as the modes corresponding to the respective modes 17b, 5 and 10a of the benzene molecule. The assignments of these planar and non-planar C-H bending modes are in agreement with the corresponding assignments in the 1,2.4-tri light substituted benzene derivative [23,24].

The remaining nine modes of the phenyl ring moiety arise due to the bonds  $C_3$ - $C_{14}$ ,  $C_1$ - $O_{10}$  and  $C_6$ - $O_{12}$  and correspond to  $\nu(C_3$ - $C_{14}$ ),  $\nu(C_1$ - $O_{10}$ ) and  $\nu(C_6$ - $O_{12}$ );  $\beta(C_3$ - $C_{14}$ ),  $\beta(C_1-O_{10})$  and  $\beta(C_6-O_{12})$ ;  $\gamma(C_3-C_{14})$ ,  $\gamma(C_1-O_{10})$  and  $\gamma(C_6-O_{12})$ . The modes  $\nu(C_6-O_{12})$ ,  $v(C_1-O_{10})$  and  $v(C_3-C_{14})$  were computed to have frequencies 1289, 1261 and 961 cm<sup>-1</sup> and correlated to the observed frequencies 1281, 1249 and 960  $cm^{-1}$ , respectively. These modes correspond to the modes 7a, 13 and 7b of the benzene molecule. The modes  $\beta(C_3$ - $C_{14}$ ,  $\beta(C_1-O_{10})$  and  $\beta(C_6-O_{12})$  were found to have computed frequencies 210, 346 and  $488 \text{ cm}^{-1}$  with the corresponding observed frequencies 192(R), 325(R) and 527(IR)/531(R) $cm^{-1}$ , respectively. These modes, respectively, correspond to the modes 15, 9a and 9b of the benzene molecule. The three non-planar bending modes  $\gamma$ (C<sub>3</sub>-C<sub>14</sub>),  $\gamma$ (C<sub>1</sub>-O<sub>10</sub>) and  $\gamma$ (C<sub>6</sub>-O<sub>12</sub>) were found to have computed frequencies 58, 248 and 375 cm<sup>-1</sup> and these are corelated to the observed Raman frequencies 64, 251 and 360  $\text{cm}^{-1}$ , respectively. These modes correspond, respectively, to the 17a, 10a and 10b modes of the benzene molecule. The assignments of these modes were found to be in good agreement with those proposed by earlier works [20,23,24] excepting the mode  $\gamma$ (C<sub>3</sub>-C<sub>14</sub>), which was found to have a considerably lower frequency of 64 cm<sup>-1</sup> as compared to the lower limit of the proposed range 200-400  $\rm cm^{-1}$ .

### 4.4.3. O-H Group Modes (9)

The v(O-H) mode of the COOH group was observed in the range 2500–3050 cm<sup>-1</sup> [20,25,26]; however, the v(O-H) mode for the OH group(s) attached to the phenyl ring was observed in the range  $2900-3660 \text{ cm}^{-1}$  in different surroundings [17,22]. Generally, the OH stretching appears with medium to strong intensity and a broad band signature in the IR spectra, while it is weak or even may not be observed in the Raman spectra. The experimental IR spectrum of L-dopa contains a broad intense envelope in the range 2200–3500 cm<sup>-1</sup>, which was deconvoluted to yield four bands: 3378, 3216, 3045 and 2770 cm<sup>-1</sup> (Figure 5). The computed vibrational frequencies of the three OH stretching modes of the lowest energy monomer C-I and its three lowest-energy dimers  $D_1$ ,  $D_2$  and  $D_3$  are given in Table 6, which also includes the corresponding deconvoluted IR bands. A perusal of this Table suggests that considering the lowest-energy monomeric conformer C-I, out of the four deconvoluted bands only two bands could be assigned, whereas when considering the dimers D1 and D2 all the four deconvoluted bands could be assigned. However, only one deconvoluted band could be assigned considering the dimer  $D_3$ . The dimers  $D_2$  and  $D_3$  have much higher ( $\sim$ 1200 and  $\sim$ 3500 K) energies than the dimer D<sub>1</sub>, suggesting that at room temperature, the L-dopa molecule exists in the dimeric form  $D_1$  only.



Figure 5. Deconvolution of the broad and intense IR envelope in the range 2200–3400 cm<sup>-1</sup>.

| Obs    | served |      | Com            | nputed         |                |
|--------|--------|------|----------------|----------------|----------------|
| IR     | Raman  | C-I  | D <sub>1</sub> | D <sub>2</sub> | D <sub>3</sub> |
| 2770 s | -      | 2870 | 2942/2943      | 2939/2919      | 2758/2949      |
| 3045 m |        | -    | 3048/3052      | 3045           | 3174           |

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3378/3326

 $2 \times 1606$ 

3366/3366

3226

3326/3326

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3381/3336/3325

3216

3370 m

3206 m

3362 vw

Table 6. Deconvoluted IR bands and computed frequencies of monomer and dimer of L-dopa.

The v(O<sub>12</sub>-H<sub>13</sub>), v(O<sub>10</sub>-H<sub>11</sub>) and v(O<sub>20</sub>-H<sub>21</sub>) modes were found to have the computed frequencies 3378, 3327 and 2870 cm<sup>-1</sup>, whereas for the dimer D<sub>1</sub>, the computed frequencies for these modes were found to be 3366/3366, 3048/3052 and 2942/2943 cm<sup>-1</sup>, respectively. Considering the monomer C-I, only the two deconvoluted bands 3378 and 2770 cm<sup>-1</sup> could be assigned, whereas with the dimer D<sub>1</sub> the three deconvoluted bands 3378, 3045 and 2770 cm<sup>-1</sup> could be correlated to the three OH stretching modes. The considerably lower observed frequency 2770 cm<sup>-1</sup> for the v(O<sub>20</sub>-H<sub>21</sub>) mode as compared to its computed value 2942 cm<sup>-1</sup> is a result of the strong H...N intra-molecular interaction. The remaining fourth deconvoluted IR band 3216 cm<sup>-1</sup> could be assigned as the first overtone of the NH<sub>2</sub> scissoring mode observed at 1606 cm<sup>-1</sup>.

The  $\alpha$ (C-O-H) modes are generally observed in the range 1170–1250 cm<sup>-1</sup> [20]. In the present case, the computed  $\alpha$ (C-O-H) modes for the O<sub>10</sub>H, O<sub>12</sub>H and O<sub>20</sub>H groups were found to have the frequencies 1192, 1222 and 1412 cm<sup>-1</sup> and these were correlated to the observed frequencies 1188(IR), 1202(IR) and 1404(IR)/1406(R) cm<sup>-1</sup>, respectively. The computed frequency 1412 cm<sup>-1</sup> for the  $\alpha$ (C<sub>19</sub>-O<sub>20</sub>-H) mode has considerably higher IR intensity as compared to the other two  $\alpha$ (C-O-H) modes. A large enhancement in the magnitude (1412 cm<sup>-1</sup>) of the frequency due to the mode  $\alpha$ (C<sub>19</sub>-O<sub>20</sub>-H) as compared to its frequency (1178 cm<sup>-1</sup>) in Phenol [17] is a result of the strong intra-molecular H-bonding.

Similar to the OH stretching mode, the torsional mode of the OH group is strongly affected due to the intra- and inter-molecular H-bonding. The torsional modes of the

 $O_{12}H$  and  $O_{10}H$  groups were found to have computed frequencies of 702 and 420 cm<sup>-1</sup>. These torsional modes could be observed at the frequencies 681 and 416 cm<sup>-1</sup> in the Raman spectrum only. The  $\tau(O_{20}H)$  mode was computed to have a much higher frequency (920 cm<sup>-1</sup>) which could be correlated to the observed frequencies 921(IR)/917(R) cm<sup>-1</sup>. The torsional modes  $\tau(O_{20}H)$  (920 cm<sup>-1</sup>) and  $\tau(O_{12}H)$  (702 cm<sup>-1</sup>) have considerably enhanced frequencies as compared to their magnitude in phenol (~300 cm<sup>-1</sup>) due to strong intra- and inter-molecular H-bonding. The assignment of the  $\tau(O_{12}H)$  mode is in agreement with the assignment of the mode  $\tau(O_{14}H)$  for the kaempferol molecule [22].

### 4.4.4. Effect on Vibrational Parameters in Going from Monomer to Dimer

In going from the C-I monomer to its  $D_1$  dimer, noticeable changes were observed in frequencies, intensities and depolarization ratios for several normal modes. The computed frequencies for the  $\nu(O_{12}-H_{13})$  and  $\tau(O_{12}-H_{13})$  modes were strongly affected in going from the monomer C-I to its dimer  $D_1$ , due to the inter-molecular H-bonding. In going from the conformer C-I to dimer  $D_1$ , the modes  $\nu_s(NH_2)$  and  $\tau(C-OH)$  of the COOH group were found to be enhanced by 20 and 16 cm<sup>-1</sup>.

In the dimeric form  $D_1$ , the modes of the two constituent molecules  $M_1$  and  $M_2$  did not show considerable changes in frequencies except in a few cases, namely  $\tau(C_3-C_{14})$ ,  $\gamma(C_3-C_{14})$ ,  $\beta(C_3-C_{14})$  and  $\Phi(R)$ -4. However, the IR and Raman intensities changed considerably in many cases (first column of Table 5). Considerable changes in the IR and Raman intensities for different modes of the two molecules of  $D_1$  arise due to the in-phase and out-of-phase coupling between the corresponding modes of the two molecules  $M_1$  and  $M_2$ .

#### 4.5. Bioactive Scores

The medicinal/pharmaceutical activity of a molecule is directly connected to its bioactive scores. The bioactive scores are related to the binding preference of the molecule with the biological targets. The bioactive scores of the L-dopa molecule are computed using the online software *Molinspiration* available at the site www.molinspiration.com (accessed on 1 November 2023). The computed bioactive scores of the L-dopa molecule are given in Table 7. Out of the six bioactive scores, two scores, namely ion channel modulator and enzyme inhibitor, were found to be positive and the remaining four were negative and close to zero. These scores suggest that L-dopa is a strong bioactive molecule.

| <b>Bioactive Acceptors</b> | OH Form | ZI Form |
|----------------------------|---------|---------|
| GPCR ligand                | -0.04   | -0.22   |
| Ion channel modulator      | 0.39    | 0.03    |
| Kinase inhibitor           | -0.60   | -0.57   |
| Nuclear receptor ligand    | -0.17   | -0.52   |
| Protease inhibitor         | -0.01   | -0.61   |
| Enzyme inhibitor           | 0.29    | -0.15   |

Table 7. Bioactive scores of L-dopa.

#### 4.6. MEP Plots

The MEP plots of the L-dopa molecule in monomeric and dimeric forms are shown in Figure 6. The red and blue colors over the MEP plots represent the most negative and positive sites. Negative and positive sites are suitable for electrophilic and nucleophilic substitutions. In going from the red to the blue color, the electronegativity (electrophilicity) decreases, while the nucleophilicity increases. The C-I monomer bears good polar nature and it has five active sites for different substitutions. In going from the monomer C-I to the dimer D<sub>1</sub>, the dipole moment is decreased. The sites near H<sub>13</sub> and H<sub>25</sub> are stronger electrophilic sites than the sites near the H<sub>11</sub>, H<sub>23</sub> and H<sub>24</sub> atoms. However, nucleophilic



sites were seen near both the O atoms of the carboxylic group. The atomic site  $O_{21}$  was found to be more strongly nucleophilic than the site  $O_{20}$ . A very weak nucleophilic site near the atom  $O_{10}$  was also seen.

Figure 6. Pictorial representation of the MEP plots of the C-I monomer and the dimer D<sub>1</sub>.

### 4.7. HOMO-LUMO Analysis

The frontier representation of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) of the L-dopa molecule is shown in Figure 7. The energies of these two MOs and their gaps are helpful in calculating the chemical parameters like ionization potential (I), electron affinity (A), chemical hardness/softness (S), chemical potential ( $\mu$ ), electronegativity ( $\chi$ ) and electrophilicity index ( $\omega$ ) [27]. The HOMO, LUMO and their energy difference as well as related parameters are collected in Table 8. The energy difference between the HOMO and LUMO of the L-dopa molecule suggests that the C-I monomer and the dimer D<sub>1</sub> are relatively more chemically soft as compared to the dimer D<sub>2</sub>. From the HOMO plot of L-dopa, it can be seen that the localized charge density is spread over the phenyl ring and both the OH groups attached to the ring, while for the LUMO the charge density is shifted towards the 2-aminopropenoic acid moiety. Perusal of the MEP and LUMO plots shows that the charge density is shifted towards the electron-deficient region. This suggests that in going from the HOMO to the LUMO the charge density is shifted from the electron-rich region to the electron-deficient region.



Figure 7. Frontier representation of the HOMO and LUMO orbitals of L-dopa.

| Carterna     | Er      | nergy in Unit (e | Electronegativity | Chemical       |              |  |
|--------------|---------|------------------|-------------------|----------------|--------------|--|
| Conformers – | НОМО    | LUMO             | ΔΕ                | - ( <u>x</u> ) | Hardness (η) |  |
| C-I          | -5.8276 | -0.9630          | 4.8646            | 3.3953         | 2.4323       |  |
| D1           | -5.7966 | -0.9388          | 4.8578            | 3.3677         | 2.4289       |  |
| D2           | -6.2115 | -0.7170          | 5.4945            | 3.4643         | 2.7473       |  |

Table 8. HOMO-LUMO energies and related quantities for L-dopa.

The observed and computed UV-vis spectra of L-dopa are shown in Figure S3. The computed and observed absorption bands with related parameters and possible transitions are given in Table 9. The computed UV-vis spectrum of L-dopa has three absorption bands peaking at 259, 246 and 241 nm with the major contributions from the transition  $H \rightarrow L$ ,  $H \rightarrow L + 1$  and  $H \rightarrow L + 2$ , respectively. The highest wavelength was observed due to the transition  $H \rightarrow L$ , suggesting that the observed absorption band 271 nm corresponds to the computed wavelength 259 nm. The computed wavelength 246 nm is correlated with the observed band 235 nm reported by Chamundeeswari et al. [12], which arises due to the transitions  $H \rightarrow L + 1$  and  $H \rightarrow L + 2$  with 68% and 32% contributions. The computed absorption band 241 nm is a result of transitions  $H \rightarrow L + 2$  and  $H \rightarrow L + 1$  with contributions 60% and 30%, respectively.

| Absorption Bands     |                      | Excitation    | Oscillator   | * Contributions   |
|----------------------|----------------------|---------------|--------------|---|
| $\lambda_{exp}$ (nm) | $\lambda_{cal}$ (nm) | Energies (eV) | Strength (f) | Contributions   |
| 271.6                | 259.2                | 4.7837        | 0.0636       | H-1→L+1%<br>H-1→L+3 11%<br>H→L86%   |
| 235 <sup>\$</sup>    | 246.7                | 5.0252        | 0.0088       | $\begin{array}{c} H {\rightarrow} L {+}1\ 62\% \\ H {\rightarrow} L {+}2\ 38\% \end{array}$ |
| 225–215 \$           | 241.6                | 5.1327        | 0.0108       | $H \rightarrow L+1 33\%$<br>$H \rightarrow L+2 60\%$<br>$H \rightarrow L+3 7\%$             |

Table 9. UV-vis absorption bands and the corresponding transitions for L-dopa.

\* H stands for HOMO, L stands for LUMO; <sup>\$</sup> observed by Chamundeeswari et al. [12].

### 5. Conclusions

The L-dopa molecule was found to exist in pairs of 108 stable conformers. All the conformers were found to have energies higher than 300 K with respect to the lowest-energy conformer C-I. The broad intense envelop in the range 2200–3500 cm<sup>-1</sup> of the IR spectrum necessitates the presence of L-dopa in the dimeric form. The complete observed IR and Raman spectra could be explained in terms of the computed spectra of the lowest energy dimer (D1) of C-I monomer. A large number of amino acids were found to exist in the Zwitterionic form; however, the intense IR band peaked around  $2800 \text{ cm}^{-1}$ , suggesting the existence of the L-dopa molecule in the OH form. Out of the 69 normal modes of L-dopa, 65 modes were observed experimentally. In going from the C-I monomer to its dimer D<sub>1</sub>, the C-O bond lengths were found to be reduced; on the other hand, the  $O_{10}$ -H<sub>11</sub> and  $O_{12}$ -H<sub>13</sub> bond lengths were considerably enhanced due to inter-molecular hydrogen bonding. The phenyl ring OH groups were found to have nearly two times the barrier heights of the OH group in phenol. However, the OH group of the carboxylic group had nearly five times the barrier height of the phenol OH group due to strong N...H bonding. The MEP plot of the L-dopa molecule suggests that it has multiple active sites. In going from the C-I monomer to the  $D_1$  dimer, the number of active sites increases. From the HOMO-LUMO analysis, the L-dopa molecule was found to be chemically soft in nature. Out of the six bioactive scores

of the L-dopa molecule, two scores were found to be positive, suggesting that the it is a molecule with strong bioactive properties.

**Supplementary Materials:** The following supporting information can be downloaded at: https:// www.mdpi.com/article/10.3390/app132413336/s1, Figure S1: Total energy vs. dihedral angle plots of the different tops of L-dopa; Figure S2: The optimized structures of the first six lower energy conformers; Figure S3: Computed and observed UV-vis spectra of L-dopa; Table S1: Some important parameters of L-dopa; Table S2: Geometrical parameters of the lowest-energy conformer C-I and dimer D1 of L-dopa; Table S3: Normal mode distributions of L-dopa; Table S4: Computed vibrational frequencies and their assignment of L-dopa; Table S5: Geometrical parameters of the first six lower energy conformers of L-dopa.

**Author Contributions:** Conceptualization: R.K.Y.; Experimental (IR, RAMAN and UV-vis spectra) data: R.K.Y.; Software: R.A.Y.; Visualization: R.A.Y. and I.K.; Analysis and investigation: R.K.Y. and R.A.Y.; Writing—original draft preparation: R.K.Y.; Writing—review and editing: R.K.Y., R.A.Y. and I.K.; Supervision: R.A.Y. and I.K. All authors have read and agreed to the published version of the manuscript.

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