DL-3-Aminoisobutyric acid: vibrational, NBO and AIM analysis of N–H⋯O bonded-zwitterionic dimer model

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1. Introduction

Amino acids are the building blocks of polypeptides and proteins with diverse structural and functional properties. They have been and still are of fundamental importance because of their vital role in the vast biological landscape. Lately non-proteinogenic amino acids, also called unnatural amino acids, have also aroused interest for similar reasons including pharmaceutical applications [1, 2]. Biochemical activities in biological species primarily involve non-covalent interactions, say, among amino acids and other molecular fragments, for example, in bases in DNA and RNA; the interactions include H-bonding and stacking. The common H-bonds are O–H⋯O, N–H⋯O, C–H⋯O, and so on [3]. Invariably the amino acids are the building blocks of polypeptides and proteins with diverse structural and functional properties. They have been and still are of fundamental importance because of their vital role in the vast biological landscape. Lately non-proteinogenic amino acids, also called unnatural amino acids, have also aroused interest for similar reasons including pharmaceutical applications [1, 2]. Biochemical activities in biological species primarily involve non-covalent interactions, say, among amino acids and other molecular fragments, for example, in bases in DNA and RNA; the interactions include H-bonding and stacking. The common H-bonds are O–H⋯O, N–H⋯O, C–H⋯O, and so on [3].

Among the non-covalent interactions, namely, H-bonding, x-stacking, van der Waals and electrostatic types, the landscape for H-bonding interactions is vast with implications across diverse supramolecular systems, nanostructures and nano-biomaterials [14, 15]. The nearest competitor to H-bonding is x-stacking interaction. Both H-bonding and x-stacking interactions are proved determinants in DNA-protein interactions for molecular recognition. The van der Waals and hydrophobic interactions, of course, play their role as well but as secondary determinants [16]. In a combined theoretical and experimental study, Krylov et al. have shown that H-bonding, among non-covalent helices, turns and pleated sheets [7, 8, 9, 10].

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interactions, influence ionization energies (IEs) of the dimers of nucleic acid bases: adenine-adenine, thymine-thymine and adenine-thymine dimers [17]. In a detailed theoretical and experimental study on the nine possible 2-pyridone-n-fluorobenzene dimer species, Leutwyler et al. have shown that H-bonding and π-stacking compete with small energy differences, both of which being accounted satisfactorily by the coupled-cluster model comprising single and double excitations with a perturbative corrections for triple excitations (CCSD(T)) [18]. In constructing 2D supramolecular networks, the role of multiple H-bonds has been ascertained in the structural polymorphism at the solid-liquid interface [19, 20, 21, 22, 23, 24]. In particular, the role of multiple H-bonds in inducing chirally different morphologies in a series of self-assembled nanostructures of 2-hydroxy-1,7-pentadecyloxy-fluorone has been demonstrated by Wenli Deng et al. [25]. Some experimental vibrational studies and electronic structure calculations have also been reported for NE and ZW species of amino acids and amino- phosphates [26, 27, 28].

Experimental and theoretical vibrational spectroscopy are proved teak for investigating structural and/or conformational aspects of H-bonded molecular systems and their complexation with other molecules with potential implications for understanding the role of H-bonding in diverse material and biological phenomena [29, 30, 31, 32]. In the present work we study the role of inter-molecular –N–H–O bonding in building dimer species of 3AIBA and characterize dimerization on the basis of the structural, spectral and electronic properties. H-bond-induced dimer structures are of interest in decoding molecular vibrational structures since it is reasonable to assume the dimer species as basic units of intermolecular association in condensed phases [33, 34]. It is profitable to correlate structural, electronic and vibrational characterization with observed vibrational IR and Raman spectral features. Electronic structure calculations from density functional theory (DFT) codes provide an opportunity to model electronic and vibrational properties corresponding to different stable NE conformers in gas phase and ZW conformers in solvent media which are otherwise experimentally difficult to realize. Experimental IR spectrum of 3AIBA shows a very broad composite band structure across 3500–2000 cm⁻¹, making assignments of the bands untenable. It calls for the construction for possible ZW dimer species defined by H-bonding between –NH₂ and –CO₂ groups and such dimer species would yield vibration modes for the satisfactory characterization of the observed IR and Raman spectral features and provide enhanced understanding of the involvement of electronic molecular orbital in –N–H–O bonding. We have carried out this proposed work using DFT modeling and NBO analysis. The NBO provides a satisfactory understanding of the stability of the H-bonded dimer species in terms of perturbative interaction energies resulting from the overlap integral between the lone-pair orbital of the donor and the anti-bonding orbital of the acceptor in the –N–H–O bonding. All these aspects constitute the principal aim of the present work.

Experimental and computational studies of NE form of β-alanine crystals and its ZW form in the aqueous media have been reported [35, 36]. The XRD structural studies of H-bonding in a series of aminosubstituted carboxylic acids have been investigated [37, 38, 39]. The first among the series is γ-aminobutyric acid (GABA). The room and low temperatures structural studies of monoclinic phase of GABA have been carried out by different workers [40, 41, 42]. In monoclinic phase, the molecule is observed as partially folded zwitterion in meso conformation while the tetragonal form three strong H-bonds as in the monoclinic phase, but there is additional fourth weaker H-bond resulting in a two-centre bifurcated bond. Also the evidence suggests that there is an intramolecular –N–H–O bridge bond. The three strong H-bonds are similar in both monoclinic and tetragonal phases. There are infinite chains of H-bonded molecules running in one dimension that are cross-linked by the remaining H-bonds to form a three dimensional network. The major difference in both phases is that monoclinic structure shows gauche confirmation while the tetragonal structure shows trans conformation of CH₂–CH₂ groups. Subsequent XRD study on another member of the series, 8-Aminocaproic acid (8ACA) has been shown to crystallize in centro-symmetric space group P2₁/n in the extended ZW form upon dissolving in water [38]. It forms five intermolecular H-bonds, two of which are bifurcated. Each molecule is linked to six neighbouring molecules by a total of ten H-bonds in the monoclinic phase. DL-3-Aminoisobutyric acid monohydrate (DL-3-AIBA-H₂O) whose structure is comparable with the afore-mentioned molecules crystallizes in the orthorhombic with centro-symmetric space group Pca₂1 as a partially folded ZW. With this structure each acid molecule and its associated water molecule are directly H-bonded to five acid molecules and two water molecules. The three hydrogens of the –NH₂ group form inter-molecular H-bonding with the two –CO₂ groups of the neighboring molecules and one water molecule. The N–O distances range from 2.758 to 2.809 Å and –N–H–O angles from 149 to 171°. It is therefore reasonable to assume that the 3AIBA has also ZW form with affinity for inter-molecular –N–H–O bonding as it is true for DL-3-Aminoisobutyric acid monohydrate. This is borne out by the fact that in the present work, some strong IR absorptions in the region 1675-1400 cm⁻¹ are presumably produced by the –NH₂ and –CO₂ groups as characteristic vibrational modes and a medium weak but highly characteristic band at 2139 cm⁻¹ is the signature of the sum of the frequencies of asymmetric bending and torsional modes of –NH₂ group. This sum mode is the most reliable characteristic band for the identification of the –NH₂ cation in all the amino acids with ZW structure [43, 44]. In our previous study, it was satisfactorily explained the observed vibrational spectral features of L-β-Homoserine in terms of ZW dimer structures characterized by inter-molecular –N–H–O and –O–H–O bonding [45]. To account for the vibrational structure of 3AIBA, we computed seven –N–H–O bonded ZW dimer structures, of which the most stable one has produced a molecular structure and vibrational bands, namely, due to the –NH₂ –CO₂ groups and –N–H–O bonding, in fair agreement with the experimental IR and Raman spectral features. Overall, the computed structural parameters of this dimer species are in fair agreement with the experimental crystal structure of 3AIBA monohydrate within 4%. A detailed NBO analysis has provided such properties as molecular orbital occupancies, charges on the atoms and the second order perturbative energies which support the strong –N–H–O bonding in the most stable dimer species (D₁) referred to above. Further, topological AIM and NCI analyses have been performed to characterize the H-bonding in D₁ and its MEP surface has been plotted to understand the reactivity of the molecule.

2. Experimental

2.1. Experimental measurements

The solid sample of DL-3-Aminoisobutyric acid was purchased from Sigma Aldrich Chemical Company and used without further purification. FT-IR spectra of the pellets made up of solid sample were recorded on a Nicolet 6700 FT-IR spectrometer that uses an Alum standard ETC Ever- Glo IR source, Deuterated Triglycine Sulphate (DTGS) detector equipped with KBr window. Pellets were prepared by taking the sample and KBr in 1:100 ratio and the spectra were recorded with 4 cm⁻¹ resolution in the region 4000 – 400 cm⁻¹ for 50 scans. Raman spectra of solid sample were recorded without sample preparation on the Nicolet NXR FT- Raman Module spectrometer that uses a Nd:YVO₄ (1064 nm) laser as a source of excitation, CaF₂ beam splitter and liquid nitrogen cooled Ge detector. The spectra were recorded with 4 cm⁻¹ resolution in the region 4000–100 cm⁻¹ for 500 scans.

2.2. Computational modeling

The electronic structure calculations have been performed using the Gaussian 09W and GaussView5 suite of programs [46, 47]. In order to minimize the computational cost, we did two jobs in tandem, firstly...
Restricted Hartree-Fock (RHF)/3-21G level of calculation followed by a second calculation at B3LYP/6-311++G(d,p) level [48]. To reduce the computational cost, the most stable NE conformers in gas phase were searched by a relaxed potential energy surface (PES) scan at the RHF/3-21G level. Initially, the dihedral angles, $\tau_1$ (16H–3O–1C–2O) and $\tau_2$ (14H–9C–4N–6H) were varied simultaneously with 10° interval from -180° to 180° and from 0° to 360° (refer Fig. 1 for $\tau_1, \tau_2, \tau_3$ and 2(b) for atom numbering). During the relaxed scan, all the internal coordinates were relaxed while the dihedral angles $\tau_1$ and $\tau_2$ were fixed at the specified values. The PES for this scan shows three minimum energy structures (Fig. 2(a)). The full optimization of these structures followed by frequency calculation was performed at B3LYP/6-311++G(d,p) level. Among the optimized structures, the one with lowest energy is considered to be more stable. This stable structure in NE form is shown in Fig. 4 and its geometrical parameters are given in Table 2. Next among the optimized structures, say, D1, D2, ..., D7, that are collected in Fig. 5. The Gibbs free energies and Boltzmann populations of all the dimers are presented in Table 3. Consecutive differences in Boltzmann populations of D1 to D7 show that structurally and energetically D1 is the most stable structure. Further, the five dimer species, D1–D5, are close to one another with respect to their energies and vibrational frequencies and all of their Boltzmann populations add up to 98%. Accordingly, as a reasonable approximation, we chose D1 as a representative species for further optimization, harmonic frequency calculation and NBO analysis at B3LYP/6-311++G(d,p) level and its results will be used in the forthcoming discussion. The resultant geometrical structure of D1 is shown in Fig. 4 and H-bonding parameters are presented in Table 2. In order to include Grimme’s dispersion correction associated with the –N–H⋯O interaction, we ran calculation at B3LYP/D3/6-311++G(d,p) level. We found that both the optimized dispersion-corrected energies and frequencies hardly differed from the results without dispersion correction [51, 52]. We have based vibrational mode analysis on potential energy distributions (PED) computed from VEDA program [54]. The AIM analysis has been carried out using Multiwfn software and the isosurfaces are visualized using VMD software package [55, 56].

3. Results and discussion

3.1. Structural analysis

The computed CZW and D1 species with the –N–H⋯O bonding are shown in Fig. 4. The optimised geometrical parameters of NE monomers CNE, C'NE, C''NE, ZW monomer CZW and dimer D1 compared with the XRD data of DL-3-Aminoisobutyric acid monohydrate by means of root-mean-square-deviation (RMSD) values are presented in Table 2. The low RMSD values of CZW and D1 for bond lengths (0.0163 and 0.0231 Å) and bond angles (0.8093 and 0.3905°) show the good agreement with XRD data than NE monomers (0.0487–0.0498 Å for bond lengths and 5.0272–5.1152° for bond angles). From Table 2, we note that the –N–H bond lengths are 1.023 Å in CZW as well as in D1 where the –N–H bonds are free. But the $r = N$–H bond length at the H-bonded region is 1.063 Å showing the elongation of the bond up to 4%. The bond angle $\Theta = N$–H⋯O is 173°. The $d = H$–O distance is 1.663 Å, being shorter than the sum of the van der Waals radii of H and O, $D = 2.721$ Å and the –N⋯O distance is 2.726 Å, apparently indicating rather a strong H-bonding [3, 57]. Elongation in $r$ causes decrease in both force constant and stretching frequency in $D_1$. For example, the 20N–21H bond vibrates at the frequency, 2612 cm$^{-1}$, which is lower than the frequencies, 3399 and 3349 cm$^{-1}$ of the 20N–22H and 20N–32H bonds. The bonds adjacent to the –N–H⋯O, namely, the –C=O corresponding to the 1C–30 bond and the –C–N corresponding to the 25C–20N bond have respectively also shown a small increase and decrease in their values from CZW to D1. These changes...
are consistent with NBO analysis to be discussed in the following sections.

### 3.2. NBO analysis

NBO analysis has originated as a method for studying hybridization and covalency effects in polyatomic wave functions associated with, among other factors, intermolecular associations [58, 59, 60, 61, 62]. NBO analysis was performed for the monomer Czw and dimer D1 of 3AIBA using NBO Version 3.1 implemented in the Gaussian 09 package at B3LYP/6–311+G(d,p) level and the results are presented in Tables 4 and 5. The Tables show the occupancies, description of NBOs, polarization coefficients \( c_A^2, c_B^2 \) (in %) and the contribution of \( s \) character (in %) on each atom forming a bond in the monomer Czw and dimer D1. The following features are observed from the NBO results:

(i) The \( \sigma(1C–2O), \pi(1C–2O) \) and \( \sigma(1C–3O) \) are strongly polarized towards the oxygen atom in both the Czw and D1. The occupancies of these bond orbitals are less in the D1 compared to those in the Czw.

(ii) Again in both Czw and D1, the \( \sigma^*(1C–2O) \) and \( \sigma^*(1C–3O) \) are polarized towards the carbon atom while \( \pi^*(1C–2O) \) is still more polarized towards the carbon atom. Occupancies of \( \sigma^* \) and \( \pi^* \) orbitals of the 1C–2O bond are less in the D1 whereas that of \( \sigma^*(1C–3O) \) is large.

(iii) In both Czw and D1 for \( \sigma(1C–2O), \sigma(1C–3O), \sigma^*(1C–2O) \) and \( \sigma^*(1C–3O) \), natural hybrids on the carbon and oxygen atoms are \( sp^2 \) hybridized as expected with sufficiently large \( p \) character on both the atoms compared to the \( s \) character (in Tables 4 and 5, only \( s \) contributions on the atoms are given). The hybrid orbitals of \( \pi \) and \( \pi^* \) of 1C–2O exhibit \( p \) character.

(iv) The \( \sigma(N–H) \) bond orbitals are polarized more towards the nitrogen atom and \( \sigma^*(N–H) \) are polarized towards hydrogen. In \( \sigma^*(N–H) \) orbitals, the NHO on N are \( sp^3 \) hybridized and NHO on H is completely of \( s \) character.

(v) The nonbonding type of NBOs which are due to lone-electron pair orbitals, \( n_{1}(2O), n_{1}(3O) \) are of \( sp^0.65, sp^0.64 \) hybridized in Czw and \( sp^0.64, sp^0.62 \) in D1. The remaining lone pair orbitals, \( n_{2}(2O), n_{2}(3O) \) and \( n_{3}(3O) \) exhibit pure \( p \) character both in Czw and D1 thus favoring the \( \pi \) delocalization at \(-CO_2\) site.

According to the NBO procedure, the strength of concerned bonds is computed by considering the difference in occupancies of bonding and nonbonding orbitals.
antibonding NBOs. From Tables 4 and 5, it is evident that in D1, the IC-2 bond is strong and in the C$_{2w}$ stronger bond is IC-30. The difference in occupancies of bonding and antibonding σ and π components of IC-2 are 1.94647 and 1.61977 in C$_{2w}$, 1.94797 and 1.63194 in D1. The σ component of IC-20 has slightly more occupancy in the D1 than in C$_{2w}$. The total occupancies (σ + π) are 3.566 in C$_{2w}$ and 3.579 in D1 showing that IC-20 carbonyl bond is stronger in the dimer than in the monomer.

The atomic charges are useful in evaluating the electronic structure of bonds [63]. The charge distribution among the atoms in C$_{2w}$ and D1 has also been calculated by the natural population analysis (NPA) and is presented in Table 6. It is noted from Table 6 that, the charges on the atoms 21H, 22H and 32H in D1 are 0.460, 0.435 and 0.435 respectively while on the 20 and 30 are −0.825 suggesting the strong electrostatic interaction between 21H and 30. Charge transfer between the proton donor −NH$_3$ group and the proton acceptor −CO$_2$ group elongate the −N=H bond length and hence weaken the −N=H bond. The difference in natural atomic charges between 5H in C$_{2w}$ and 21H in D1 and proton acceptor 3O are 0.004 and −0.035 respectively, suggesting that the dimer is stabilized by the red-shifted H-bonding. This is consistent with the increase in occupancy (see Tables 4 and 5) from 0.00529 in the monomer (σ*(4N–5H)) to 0.08121 in dimer (σ*(20N–21H)).

The second order perturbation energies (E$_{(2)}^{ij}$) were computed at B3LYP/6–311++G(d,p) level. The energy associated with each donor and acceptor is estimated using second order perturbation theory as,

$$E_{ij}^{(2)} = -\frac{1}{n} \left| F_{ij} \right|^2$$

where n is the population of the donor orbital, F$_{ij}$ is the Fock matrix element between the i and j NBOS, $\epsilon_i$ = $\epsilon_i^D$/$\epsilon_i^A$ and $\epsilon_j = \epsilon_j^D$/$\epsilon_j^A$, where $\epsilon_i^D$ and $\epsilon_i^A$ are donor and acceptor NBOs.

The mixing coefficients λ$_{ij}$ can be estimated as, λ$_{ij}$ = $F_{ij}$/ε$_{ij}$ and the occupancy transfer (charge transfer) Q$_{ij}$ from $\Omega_i$ to $\Omega_j$ as, Q$_{ij}$ = $2\lambda_{ij}$.

Larger the E$_{(2)}^{ij}$ value, more intensive is the interaction between donor and acceptor. Fig. 6 shows the interaction of the filled orbital with the unfilled non-Lewis orbital [64]. The E$_{(2)}^{ij}$ values corresponding to −N=H−O interaction in the dimers D1, D2, D3, D4, D5, D6 and D7 are 35.01, 23.70, 27.42, 20.85, 2.53, 19.08 and 27.13 kcal/mol respectively, suggesting that more charge transfer interactions exist in the case of D1. These intermolecular −N=H−O bonds are formed by the orbital overlap between lone pair (n) of oxygen (O) and antibonding orbital (σ*) of N=H. Lone pair of oxygen and antibonding orbitals of N=H are identified as electron donor and acceptor NBO species. The H-bonding between n(O) and σ*(N=H) results in charge transfer causing stabilization of the dimer species. This −N=H−O intermolecular bonding increases the electron density which leads to the elongation of the N=H bond lengths and hence lowering the corresponding stretching vibrational frequencies in D1. For the D1, the intermolecular interactions between some of the important donor-acceptor NBO pairs such as n(O) and σ*(20N–21H) give rise to the energies 28.46, 6.10 and 0.45 kcal/mol which are presented in Table 7 and the graphical electron density maps of NBOs corresponding to these interactions are presented in Fig. 7.

From this analysis, we can conclude the following. The decreased occupancy of σ component of IC-30 bond from C$_{2w}$ to D1 is consistent with the increase in the 1C–30 bond length value from 1.264 Å in C$_{2w}$ to 1.272 Å in D1. Similarly, the difference in atomic charges 5H in C$_{2w}$, 21H in D1 and 30 suggest that the dimer is stabilized by the red-shifted H-bonding. This is in agreement with the increase in occupancy from 0.00529 in the C$_{2w}$ (σ*(4N–5H)) to 0.08121 in D1 (σ*(20N–21H)). The computed second order perturbative energies also suggest that the strong H-bonding exist in D1.

### Table 2

| Parameters | C$_{NE}$ | C$_{NE}$ | C$_{NE}$ | C$_{NE}$ | D$_1$ | Expt$^a$
|------------|----------|----------|----------|----------|------|-------|
| Bond length (Å) | 1.206 | 1.206 | 1.206 | 1.264 | 1.256 | 1.247 |
| 1C–20 | 1.358 | 1.359 | 1.360 | 1.264 | 1.272/ | 1.251 |
| 1C–30/17C–190° | 1.514 | 1.516 | 1.515 | 1.544 | 1.540 | 1.520 |
| 1C–30 | 0.969 | 0.969 | 0.969 | – | – | – |
| 9C–4N/25C–20° | 1.467 | 1.465 | 1.465 | 1.507 | 1.507/ | 1.484 |
| 9C–7C | 1.538 | 1.530 | 1.544 | 1.527 | 1.527 | 1.522 |
| 9C–1H | 1.098 | 1.099 | 1.100 | 1.088 | 1.088 | 1.000 |
| 9C–15H | 1.092 | 1.093 | 1.092 | 1.088 | 1.088 | 1.020 |
| 4N–5H | 1.015 | 1.014 | 1.015 | 1.023 | 1.022/ | 0.960 |
| 20N–21H | – | – | – | – | 1.063/ | – |
| 4N–6H | 1.013 | 1.013 | 1.013 | 1.023 | 1.023/ | 1.050 |
| 20N–22H | – | – | – | – | 1.022/ | – |
| 4N–4H/6H | – | – | – | 1.023 | 1.023/ | 0.970 |
| 20N–32H | – | – | – | – | 1.022/ | – |
| 8C–7C | 1.542 | 1.530 | 1.538 | 1.539 | 1.539 | 1.528 |
| 8C–1H | 1.091 | 1.092 | 1.092 | 1.092 | 1.092 | 0.970 |
| 8C–12H | 1.090 | 1.090 | 1.090 | 1.094 | 1.094 | 1.060 |
| 8C–13H | 1.093 | 1.092 | 1.092 | 1.093 | 1.093 | 1.010 |
| 7C–1H | 1.095 | 1.094 | 1.093 | 1.094 | 1.094 | 0.980 |
| RMSD | 0.0700 | 0.0704 | 0.0704 | 0.0619 | 0.0619 | 0.0649 |

$^a$ XRD data of DL-3-Aminoiso-butric acid monohydrate [39].

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Laplacian ($0.1326$ a.u), potential energy density ($V(r) = -0.0486$ a.u). Interaction energy ($E_{int} = 15.2$ kcal/mol) of the $–N–H⋯O$ bond has been calculated at BCP using the relation $E_{int} = V(r)/2$. The low value of $\rho(r)$ and positive value of $\nabla^2 \rho(r)$ and the value of interaction energy satisfy the criteria for existence of medium H-bond according to Rozas et al [70].

With all these values we can conclude that, a medium strong $–N–H⋯O$ inter-molecular bond exist in $D_1$.

Non-covalent interactions (NCI) in the molecular systems can be visualized using reduced density gradient (RDG) [71, 72]. The RDG is given by:
The NCI isosurface for the D1 species is shown in Fig. 8. A blue patch surfaces illustrate the nature of the interactions in real space through colour codes. Blue, green, red colours are used to represent attractive hydrogen bond, weak van der Waals and steric interactions respectively. The NCI isosurface for the D1 species is shown in Fig. 8. A blue patch between the hydrogen atom of –NH3+ group from one ZW monomer and oxygen atom of –CO2− group from another ZW monomer unit in Fig. 8 is attributed to –N–H−O− bonding. Green and red patches between –NH3+, CH3 and –CO2−, CH2 groups within the monomer units represent the van der Waals and repulsive steric interactions respectively.

### Table 3

| Dimer | Gibbs free energy G(Hartree) | ΔG (kcal/mol) | Population (%) |
|-------|-----------------------------|---------------|----------------|
| D1    | -717.601533                | 0             | 35.56          |
| D2    | -717.609996                | 0.337         | 20.20          |
| D3    | -717.609917                | 0.387         | 18.59          |
| D4    | -717.605994                | 0.589         | 13.23          |
| D5    | -717.603118                | 0.762         | 9.89           |
| D6    | -717.598533                | 1.883         | 1.51           |
| D7    | -717.598126                | 2.138         | 0.98           |

### Table 4

| NBOs Ω/Ω* (A-B) | Occupancy q | Polarization coefficients (%) | Description of NBO | Contribution of σ character (%) | ΔGΩΩ* |
|-----------------|-------------|---------------------------------|---------------------|----------------------------------|-------|
| (1C-20)         | 0.99624     | 34.31                           | σ                  | 65.69                            | 0.5858 (σ^2.20) | 32.23 |
| (1C-20)         | 0.94977     | 65.69                           | σ                  | 34.31                            | 0.8105 (σ^2.20) | 32.23 |
| (1C-20)         | 1.99334     | 22.75                           | σ                  | 77.25                            | 0.4769 (σ^2.20) | 32.23 |
| (1C-20)         | 0.37357     | 77.25                           | σ                  | 22.75                            | 0.8789 (σ^2.20) | 32.23 |
| (1C-30)         | 0.99484     | 34.15                           | σ                  | 65.85                            | 0.5843 (σ^2.20) | 32.23 |
| (1C-30)         | 0.66381     | 65.85                           | σ                  | 34.15                            | 0.8115 (σ^2.20) | 32.23 |
| (4N-5H)         | 0.99316     | 72.96                           | σ                  | 27.04                            | 0.8542 (σ^2.20) | 32.23 |
| (4N-5H)         | 0.00529     | 27.04                           | σ                  | 72.96                            | 0.5200 (σ^2.20) | 32.23 |
| (1N-4H)         | 0.99371     | 72.96                           | σ                  | 27.04                            | 0.8533 (σ^2.20) | 32.23 |
| (1N-4H)         | 0.00836     | 27.18                           | σ                  | 72.82                            | 0.5214 (σ^2.20) | 32.23 |
| (1N-4H)         | 0.99380     | 72.81                           | σ                  | 27.19                            | 0.8533 (σ^2.20) | 32.23 |
| (1N-4H)         | 0.00831     | 27.19                           | σ                  | 72.81                            | 0.5214 (σ^2.20) | 32.23 |

### Table 5

| NBOs Ω/Ω* (A-B) | Occupancy q | Polarization coefficients (%) | Description of NBO | Contribution of σ character (%) | ΔGΩΩ* |
|-----------------|-------------|---------------------------------|---------------------|----------------------------------|-------|
| (1C-20)         | 1.99575     | 34.37                           | σ                  | 65.63                            | 0.5862 (σ^2.20) | 31.64 |
| (1C-20)         | 0.04778     | 65.63                           | σ                  | 34.37                            | 0.8101 (σ^2.20) | 31.64 |
| (1C-20)         | 1.98812     | 23.06                           | σ                  | 76.94                            | 0.4802 (σ^2.20) | 31.64 |
| (1C-20)         | 0.35618     | 76.94                           | σ                  | 23.06                            | 0.8772 (σ^2.20) | 31.64 |
| (1C-30)         | 0.98748     | 32.45                           | σ                  | 67.55                            | 0.5697 (σ^2.30) | 31.64 |
| (1C-30)         | 0.10611     | 67.55                           | σ                  | 32.45                            | 0.8219 (σ^2.30) | 31.64 |
| (2C-20H)        | 1.99041     | 72.26                           | σ                  | 27.74                            | 0.8730 (σ^2.40) | 31.64 |
| (2C-20H)        | 0.99277     | 72.26                           | σ                  | 27.74                            | 0.8489 (σ^2.40) | 31.64 |
| (2C-20H)        | 0.00951     | 72.26                           | σ                  | 27.74                            | 0.5286 (σ^2.40) | 31.64 |
| (2C-20H)        | 0.00892     | 72.93                           | σ                  | 27.07                            | 0.5286 (σ^2.40) | 31.64 |
| (2C-32H)        | 1.99708     | 72.93                           | σ                  | 27.07                            | 0.8584 (σ^2.50) | 31.64 |
| (2C-32H)        | 0.10325     | 72.93                           | σ                  | 27.07                            | 0.5286 (σ^2.50) | 31.64 |
| (2C-32H)        | 0.99243     | 72.93                           | σ                  | 27.07                            | 0.8584 (σ^2.50) | 31.64 |
| (2C-32H)        | 1.86544     | 72.93                           | σ                  | 27.07                            | 0.5286 (σ^2.50) | 31.64 |
| (2C-32H)        | 1.61485     | 72.93                           | σ                  | 27.07                            | 0.8584 (σ^2.50) | 31.64 |

Note: ΔGΩΩ* = Difference in occupancies qΩ − qΩ*. Where Ω - bonding and Ω* - antibonding orbitals on A and B.

### 3.4. MEP analysis

The molecular electrostatic potential (MEP) serves as a useful quantity to explain H-bonding and reactivity of molecules [73]. The MEP surface of the D1 species was calculated from the optimized molecular structure discussed in section 2.2 and shown in Fig. 9. The different values of electrostatic potentials at the MEP surface are represented by different colors: red, blue and green represent the regions of most negative, most positive and zero electrostatic potential respectively. The negative region is localized over –CO2− group indicating the most reactive site for electrophilic attack and positive region is localized over –NH3+ group which is reactive site for nucleophilic attack. The loss of red and blue colors on –CO2− and –NH3+ groups in the bonding region of the D1 species is attributed to –N–H−O− donor-acceptor interaction.

### 3.5. Vibrational analysis

The experimental IR and Raman spectra of 3AIBA and their comparison with the simulated spectra of D1 are shown in Figs. 10 and 11.
vibrational analysis of the observed and computed bands of the CZW. The Raman bands are weak in this region. We now present a detailed spectrum has not shown these bands since the Raman modes are gener-

3.5.1. NH₃ modes

In the IR spectrum no absorption is observed in the usual N-H stretching region, 3500 – 3200 cm⁻¹; instead a broad absorption of medium intensity at 3044 cm⁻¹ is identified as asymmetric stretching mode of –NH₃ as against the predicted band at 3391 cm⁻¹ in C₂W and at 3399 cm⁻¹ in D₁ [74,75]. Second asymmetric stretching mode has not been observed near 3383 cm⁻¹ but is computed in C₂W and it is at 3390 cm⁻¹ in D₁ (bonded mode is at 3349 cm⁻¹). The symmetric stretching mode is not seen in the Raman spectrum since this band is apparently obscured by the more intense –C-H stretching band, but is predicted at 3321 cm⁻¹ [76]. As for the bonded mode we identify a medium weak absorption at 2629 cm⁻¹, which is correlated to a predicted band at 2612 cm⁻¹ [77]. Bonded asymmetric bending mode identified as a medium weak absorption at 1675 cm⁻¹ with its Raman band at 1689 cm⁻¹ is correlated to the predicted band at 1599 cm⁻¹; the free mode is predicted at 1568 cm⁻¹. The second bonded mode is assigned to a very strong absorption at 1627 cm⁻¹ (Raman band at 1616 cm⁻¹) is correlated to a predicted band at 1566 cm⁻¹, the free mode is predicted at 1556 cm⁻¹. Another asymmetric mode appearing as a very strong absorption at 1574 cm⁻¹ with its weak Raman band at 1584 cm⁻¹ is correlated to a predicted band at 1482 cm⁻¹. The symmetric bending mode observed as a medium weak absorption at 1400 cm⁻¹ is correlated to a predicted band at 1431 cm⁻¹. As for the rocking modes, weak and medium weak absorptions observed at 995 and 844 cm⁻¹ are correlated to the predicted bands at 970 and 843 cm⁻¹ respectively.

3.5.2. CO₂ modes

As for the –CO₂ modes, the asymmetric stretching bonded mode is identified as a very strong absorption at 1546 cm⁻¹ with its Raman mode at 1544 cm⁻¹ and is computed at 1458 cm⁻¹; the free mode is predicted at 1465 cm⁻¹. The second asymmetric mode predicted at 1450 cm⁻¹ is correlated to a strong absorption and medium strong Raman band near 1468 cm⁻¹. Symmetric stretching mode identified as a medium strong absorption at 1329 cm⁻¹ is computed at 1332 cm⁻¹. Another symmetric stretching mode predicted at 1325 cm⁻¹ is correlated to the medium strong Raman band at 1312 cm⁻¹. Weak to medium absorptions at 782, 642 and 526 cm⁻¹ are identified as deformation modes of –CO₂ and are predicted at 761, 668 and 502 cm⁻¹ respectively.

3.5.3. Combination bands

Further, some bands appeared only in the IR spectrum in the region 2700 – 2000 cm⁻¹ as a substructure on the broad absorption are assigned to a combination of asymmetric bending of –NH₃ with –C-N stretching or torsional modes of –NH₂ [10, 57]. The weak to medium absorptions at 2702 and 2629 cm⁻¹ may arise due to the –N-H-O bonding, and it is reasonable to assign them to a combination of –NH₃ asymmetric stretch and deformation of the –C-N bond [78]. The band at 2139 cm⁻¹ being a combination of –NH₃ asymmetric stretch and –C-N torsional mode is identified as a marker band for the identification of –NH₃ moieties in amino acids [10, 11]. Similarly, the weak absorptions at 2817, 2779 and 2582 cm⁻¹ are combinations of –NH₃ asymmetric stretch with –C-N deformation and stretching vibrations.

3.5.4. C-H, C-C and C-N bands

All the other bands, which are not influenced by the H-bonding, have appeared in their usual region. As for methyl vibrations, the Raman spectra shows distinct, intense bands assigned to asymmetric and symmetric stretching vibrations in the region 3000 – 2850 cm⁻¹ whereas the IR bands in this region appeared as weak bands or sometimes as shoulder to the other bands. The scissoring and deformation modes appear in the region 1450 – 1360 cm⁻¹. The –C-N bending modes are assigned to the coupled vibrations with –C-C bending and stretching vibrations in the region 1300 – 800 cm⁻¹. Medium weak Raman bands at 1033 and 891 cm⁻¹ are identified as –C-C skeletal vibrations suggesting that the carbon

| Atom | Charge (a.u.) | Atom | Charge (a.u.) | Atom | Charge (a.u.) |
|------|--------------|------|--------------|------|--------------|
| 1C   | 0.796        | 1C   | 0.815        | 17C  | 0.795        |
| 2O   | 0.842        | 2O   | -0.825       | 18O  | -0.855       |
| 3O   | -0.860       | 3O   | -0.825       | 19O  | -0.850       |
| 4N   | -0.673       | 4N   | -0.672       | 20N  | -0.707       |
| 5H   | 0.456        | 5H   | 0.456        | 21H  | 0.460        |
| 6H   | 0.450        | 6H   | 0.451        | 22H  | 0.435        |
| 7C   | -0.332       | 7C   | -0.329       | 23C  | -0.329       |
| 8C   | -0.582       | 8C   | -0.582       | 24C  | -0.582       |
| 9C   | -0.167       | 9C   | -0.167       | 25C  | -0.171       |
| 10H  | 0.222        | 10H  | 0.225        | 26H  | 0.219        |
| 11H  | 0.216        | 11H  | 0.217        | 27H  | 0.215        |
| 12H  | 0.206        | 12H  | 0.208        | 28H  | 0.204        |
| 13H  | 0.207        | 13H  | 0.208        | 29H  | 0.206        |
| 14H  | 0.227        | 14H  | 0.227        | 30H  | 0.221        |
| 15H  | 0.224        | 15H  | 0.225        | 31H  | 0.217        |
| 16H  | 0.450        | 16H  | 0.451        | 32H  | 0.425        |

Fig. 6. Second order perturbative donor-acceptor interaction involving a filled orbital i and an unfilled orbital j.

The IR spectrum marked by a broad composite band structure in the region 3500 – 2000 cm⁻¹ with FWHM 700 cm⁻¹ is indicative of inter-
molecular interactions of which we assume H-bonding. A series of mul-
tiple peaks on this broad band and, medium to strong bands in the 1675 – 1400 cm⁻¹ are characteristic modes of –NH₃ and –CO₂ groups, strongly suggesting the ZW nature of the 3AIBA. However, the Raman spectrum has not shown these bands since the Raman modes are generally weak for ionic group vibrations. The strong bands it has shown are due to –CH₂, –CH₃ and –CH₄ groups in the 3000 – 2850 cm⁻¹. In other regions, the 1675 – 1400 cm⁻¹ is marked by very sharp IR bands readily assigned to the stretching and bending modes of –CO₂ and –NH₃ groups. The Raman bands are weak in this region. We now present a detailed vibrational analysis of the observed and computed bands of the C₂W monomer and D₁ dimer species. We refer to modes arising from H-

![Diagram](image)
**Fig. 7.** Electron density maps of selected NBOs involved in –N–H⋯O bonding in D₁. Donor (lone pair orbital of 3O) and acceptor (antibonding orbital of 20N–21H) NBOs are shown separately in left columns and their overlapping due to H-bonding is shown in right columns. Green and yellow colours of the orbitals correspond to positive and negative signs respectively.

**Fig. 8.** Reduced density gradient isosurface for D₁ of DL-3-Aminoisobutyric acid. Blue, green, red colours are used to represent attractive hydrogen bond, weak van der Waals and steric interactions respectively.

**Fig. 9.** Molecular electrostatic potential surface for D₁ of DL-3-Aminoisobutyric acid (in the range between -0.178 to 0.178 a.u.).
Fig. 10. (a) Experimental and (b) simulated dimer (D₁) IR spectra of DL-3-Aminoisobutyric acid. Frequency values corresponding to vibrational modes are given in Table 8. Only the stretching, bending vibrations of –NH₃⁺, –CO₂⁻ and their combinations are assigned in the above spectra. Ordinate in Dimer spectrum (b) is broken to adjust the bands from overshooting because of their largest intensity.

Fig. 11. (a) Experimental and (b) simulated dimer (D₁) Raman spectra of DL-3-Aminoisobutyric acid. Frequency values corresponding to vibrational modes are given in Table 8. Only the stretching, bending vibrations of –NH₃⁺, –CO₂⁻ and their combinations are assigned in the above spectra. Ordinate in Dimer spectrum (b) is broken to adjust the bands from overshooting because of their largest intensity.

chain is not perturbed due to the H-bonding. A detailed assignments of all the modes compared with the assignments of β-alanine are presented in Table 8.

4. Conclusions

A satisfactory zwitterionic dimer model at B3LYP/6-311++G(d,p) level and SCSF-SMD method, constructed of inter-molecular –N–H–O bonding between –NH₃⁺ group of one zwitterionic monomer unit and –CO₂⁻ group of another identical zwitterionic monomer unit, has been proposed for DL-3-Aminoisobutyric acid. The vibration modal features predicted by the model are in fair agreement with the IR and Raman modes in 3040-3000 cm⁻¹ and 1680–1460 cm⁻¹. The Grimme’s dispersion correction associated with the –N–H–O interaction computed at B3LYP-D3/6-311++G(d,p) level which yielded both the optimized dispersion-corrected energies and frequencies hardly differed from the results without dispersion correction. As for the NBO characterization of

| Observed Frequenciesa | β-alanineb | Computed Frequenciesc | Assignmentsc |
|-----------------------|------------|----------------------|--------------|
| IR Raman              | IR Raman   | CZW D₁               |              |
| 3044 s                | –          | 3391 3399            | V₆(NH₃⁺, 90) |
| –                    | –          | 3383 3390            | V₆(NH₃⁺, 98) |
| –                    | (3349)     | 3313 3221            | V₆(NH₂⁺, 100)|
| 2629 mw               | 2612       | 3017 3016            | V₆(CH₂, 99)  |
| 2969 s                | –          | 2936                 | V₆(CH₂, 99)  |
| –                    | 2949       | 3012 3011            | V₆(CH₂, 96)  |
| –                    | 2908 vs    | 3011 3009            | V₆(CH₂, 95)  |
| –                    | 2889 sh    | 2993 2993            | V₆(CH₂, 95)  |
| –                    |            | 2945 2948            | V(CH₆)       |
| 2879 mw               |            | 2936 2935            | V₆(CH₂, 99)  |
| 2817 w                |            | –                    | 1675 + 1136  |
| 2779 w                |            | –                    | 1627 + 1136  |
| 2702 w                |            | –                    | 1627 + 1053  |
| 2629 w                |            | –                    | 1574 + 1053  |
| 2582 w                |            | –                    | 1574 + 923   |
| 2139 w                |            | –                    | 1675 + 447   |
| 1675 1689 w           | 1653 1686  | 1561 1568            | δ₉(NH₂⁺, 86) |
| mw                    |            | (1599)               |              |
| 1627 mw               | 1616 w     | 1554 1556            | δ₉(NH₂⁺, 90) |
| vs                    |            | (1566)               |              |
| 1574 1584 vs          | 1573 1556  | –                    | δ₉(NH₂⁺, 71) |
| vs                    |            | 1482                 |              |
| 1546 vs               | 1544 w     | 1633 1630            | 1463 1465    | V₆(CO₂⁻), 64 |
| vs                    |            | (1458)               |              |
| 1468 s                | 1465       | 1452 1450            | V₆(CO₂⁻), 18 |
| ms                    | 1445       | 1441 1444            | δ₉(CH₆)      |
| 1452 ms               | 1445       | 1466 1473            | δ₉(CH₆, 73)  |
| 1419 s                | –          | 1436 1435            | δ₉(CH₆, 63)  |
| 1400 w                | 1399 w     | 1423 1431            | δ₉(NH₂⁺, 56) |
| 1379 mw               | 1386 w     | 1447 1434            | δ₉(CH₆)      |
| 1360 mw               | 1365 w     | 1371 1371            | δ(CH₃, 34)   |
| w                     |            | (δ(CH₃), 14)         |              |
| 1329 ms               | 1331       | 1403 1395            | 1330 1322    | V(CO₂⁻), 17 |
| mw                    | 1312       | –                    | V(CO₂⁻), 16 |
| 1299 –                |            | 1290 1294            | δ(CH₃, 15)   |
| 1272 w                | 1267 s     | 1248 1251            | δ(CH₃, 15)   |
| w                     |            | 1160 1159            | δ(CH₃, 15)   |
| 1136 mw               | 1134 w     | 1121 1119            | δ(CH₃, 15)   |
| 1108 w                | 1107 w     | –                    | δ(CH₃, 15)   |
| 1053 mw               | 1051       | –                    | δ(CH₃, 15)   |
| 1032 mw               | 1033       | –                    | δ(CH₃, 15)   |
| 995 w                 | 1003 w     | 1061 1068            | 965 970     |
| vw                    |            | (δ(NH₂⁺, 10), δ(CC, |              |
| 923 vw                | 921 w      | 937 943              | (δ(CO), 10) |
| 891 w                 | 891 w      | –                    | V(CO₂⁻), 17 |
| 844 mw                | 837 ms     | 991 998              | V(CO₂⁻), 17 |
| –                    | –          | 838 843              | V(CO₂⁻), 17 |

(continued on next page)
the –N–H⋯O bonding, it has been shown that it is formed by the orbital overlap between lone pair (n) of oxygen (O) as electron donor and antibonding orbital (σ*) of N–H bond as acceptor. The stabilization of the dimer species has been shown from the hyperconjugation interaction between n(O) and σ*(N=H) that has explained both structural aspects of DL-3-Aminoisobutyric acid and its empirical IR red spectral shift. The AIM analysis has shown the intermolecular –N–H⋯O bonding in D1 of 3AIBA. The values of ρ(r) and V^2ρ(r) and hydrogen bond energy at bond critical points indicate a strong intermolecular –N–H⋯O bonding. The same result has been deduced from the NCI analysis as well. Overall all the DFT, NBO, AIM and NCI calculations mutually support each other. It may be said that the stretching modes of –NH2 and –CO2\(^{\ddagger}\) might have been predicted more accurately perhaps for a trimer model.

**Declarations**

**Author contribution statement**

Shashikala Yalagi: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Jagdish Tonannavar: Conceived and designed the experiments; Analyzed and interpreted the data.

Jayashree Tonannavar: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

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**Competing interest statement**

The authors declare no conflict of interest.

**Additional information**

No additional information is available for this paper.

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