Conformational analysis and vibrational spectroscopic investigation of L-alanyl-L-glutamine dipeptide

Serda Kecel^{a,*}, Aysen E. Ozel^a, Sevim Akyuz^b and Sefa Celik^c

^a Faculty of Sciences, Department of Physics, Istanbul University, Istanbul, Turkey

^b Faculty of Science and Letters, Department of Physics, Istanbul Kultur University, Atakoy Campus, Istanbul, Turkey

^c Engineering Faculty, Department of Electrical-Electronics Engineering, Istanbul University, Avcilar, Istanbul, Turkey

Abstract. In this study conformational behavior of anticancer chemotherapy dipeptide Ala-Gln and its dimers have been investigated by molecular mechanic and ab-initio calculations. The calculations on Ala-Gln dipeptide as a function of side chain torsion angles, enable us to determine their energetically preferred conformations. The relative positions of the side chain residues of the stable conformations of dipeptide were obtained, depending on the obtained conformational analysis results. The lowest energy conformation of the dipeptide has been determined by using the Ramachandran maps (*Biopolymers* **6** (1963), 1494; *J. Mol. Biol.* **7** (1963), 95) and compared with the quantum chemical ab-initio results. The geometry optimization, vibrational wavenumbers and intensity calculations of Ala-Gln dipeptide were carried out with the *Gaussian03* program by using DFT with B3LYP functional and 6-31++G(d,p) basis set. The IR (4000–400 cm^{−1}) and Raman spectra of the Ala-Gln dipeptide have been reported in solid phase, and compared with the theoretical vibrational data.

Keywords: Conformational analysis, IR and Raman spectra, DFT calculations, L-alanyl-L-glutamine dipeptide

1. Introduction

It is known that the biological functions of the peptides in living systems are related with their three-dimensional structures. Conformational properties of the biologically active peptides are very important for investigation of their functional structure. Besides, electronic and vibrational properties of a molecule are related with its conformational structure.

Glutamine plays an important role in the immune system. It is essential for cell proliferation, that it can act as a respiratory fuel and that it can enhance the function of stimulated immune cells [3]. Oral supplementation with glutamine can significantly decrease the severity of chemotherapy-induced stomatitis, an important cause of morbidity in the treatment of patients with cancer [14]. On the other hand, glutamine supplementation may reduce the incidence of gastrointestinal, neurologic and possibly cardiac complications of cancer therapy [2,13]. Moreover, glutamine depletion has been observed in acute pancreatitis and may contribute to the morbidity of this disease [9].

*Corresponding author: S. Kecel, Faculty of Sciences, Department of Physics, Istanbul University, Vezneciler 34134, Istanbul, Turkey. E-mail: skecel@istanbul.edu.tr.

L-alanyl-L-glutamine (Ala-Gln) dipeptide is known to reduce chemotherapy-induced side-effects, and has demonstrated immunomodulatory, anticatabolic/anabolic, gastrointestinal mucosal protective and antioxidant activities [15]. It is used to prevent of mucositis in patients with head-and-neck cancer [1]. In spite of the above-mentioned importance, up to our knowledge, no study on conformational analysis and quantum chemical calculations on Ala-Gln dipeptide reported yet. In this work, the results of conformational analysis and the experimental and theoretical IR and Raman data of Ala-Gln dipeptide are reported. The theoretical conformational analysis methods allow us to determine whole sets of energetically preferred conformers of peptide molecule. The vibrational wavenumbers of dimers of L-alanyl-L-glutamine dipeptide have also been calculated.

2. Experimental and computational details

The solid Ala-Gln dipeptide was purchased from Sigma Aldrich Co. Ltd. (Cas: 39537-23), and used as received. The IR spectra of KBr discs were recorded on a Jasco 300E FT-IR spectrometer (2 cm^{-1} resolution) between $400\text{--}4000\text{ cm}^{-1}$ spectral region. The Raman spectra of the samples were taken with a Jasco NRS-3100 micro-Raman spectrometer (1800 lines/mm grating and high sensitivity cooled CCD). The spectrometer was calibrated with the silicon phonon mode at 520 cm^{-1} . Either 532 or 785 nm lines of the diode lasers was used for excitation. The exposure time was taken as 2 s and 100 spectra were accumulated. Spectral resolution was better than 4 cm^{-1} .

The conformational analysis of dipeptide was carried out by sequential method with combining all low-energy conformations of constitutive residues. The conformational potential energy of a molecule is given as the sum of the independent contributions of nonbonded (E_{nb}), electrostatic (E_{el}), torsional interactions (E_{tors}) and hydrogen bonds (E_{hb}) energies and then the conformational energy was minimized using program proposed by Godjaev et al. in FORTRAN [6]. The obtained results for the global conformation were used as initial values for geometry optimization performed by DFT/B3LYP.

Due to the success in calculating the electronic structure and energy, the calculations were carried out by using the hybrid density functional theory (DFT/B3LYP) method, either with the complete basic sets {6-31G(d), 6-31G(d,p) and 6-31G++(d,p)} (for monomer) or with only 6-31G(d,p) (for dimer). All computational studies were carried out with the *Gaussian03* package program [4].

The Total Energy Distribution (TED) of the vibrational modes of the molecules was calculated by using Parallel Quantum Mechanics Solutions (PQS) program [10] and the fundamental vibrational modes were characterised by their total energy distribution. The differences between the calculated and the corresponding experimental values are often attributed to the neglect of anharmonicity and incomplete inclusion of electronic correlation effects. In order to correct overestimation between unscaled wavenumbers and observed wavenumbers, dual scaling factors were used. The wavenumbers under 1800 cm^{-1} , were scaled either with 0.967 (for B3LYP/6-31G(d,p)) or 0.977 (for B3LYP/6-31++G(d,p)), and for over 1800 cm^{-1} the scale factor 0.955 were used for both B3LYP/6-31G(d,p), B3LYP/6-31++G(d,p) levels of theory.

3. Result and discussion

The objective of the first part of this study is to report the result of the theoretical conformational studies on alanine–glutamine dipeptide, in order to determine the stable conformers. In the second part of this study, the geometry optimization of the global conformation was performed and after then the

vibrational wavenumbers were calculated. The same calculations were repeated for the dimeric forms of the dipeptide.

The molecular model of the neutral form of Ala-Gln dipeptide with the atom numbering was given in Fig. 1(a). The starting conformations of the dipeptide Ala-Gln were obtained by combining the low energy structures of constitutive residues. The theoretical conformational analysis methods allow us to determine the whole sets of energetically preferred conformers of the dipeptide molecule. The obtained values of the dihedral angles of the side chains of the global conformation of neutral Ala-Gln dipeptide are tabulated in Table 1(a). The conformational potential energy of global conformation of Ala-Gln molecule ($E_{\text{tot}} = -0.18$ kcal/mol) is given as the sum of the van der Waals ($E_{\text{vdW}} = -6.06$ kcal/mol), electrostatic ($E_{\text{el}} = 4.41$ kcal/mol), and torsional interactions ($E_{\text{tor}} = 1.47$ kcal/mol) energies. Knowledge of the conformations of peptides mainly concerns the study of their biological functions and has very significant role on their interactions and their chemical activities. To provide a guide for the assignment of the vibrational spectra, geometry optimization studies were performed for non-zwitterionic form of the lowest energy conformer of Ala-Gln. Calculated bond distances, interbond angles and torsion angles of mono Ala-Gln and dimer I are tabulated in Table 1(b). On the basis of the calculation results, two possible intra H-bonding interactions between H(3) and O(23) (1.95 Å), H(13) and O(23) (2.25 Å) were predicted for the global conformation of monomeric Ala-Gln dipeptide. The dimeric forms of Ala-Gln dipeptide were constructed by bringing together two identical Ala-Gln monomers in possible configurations, as a result of geometry optimization studies, four low energy dimeric structures were obtained. The possible four different configurations (I–IV) of dimeric forms of the dipeptide were given in Fig. 1(d, e, f, g), respectively, together with their total energies. The geometric parameters of Dimer I are given in Table 1(b), in comparison to those of global conformation of mono Ala-Gln. The intra and inter hydrogen bonds, of the dimeric forms (I–IV) of the four low energy conformations, were given in Table 2. The number of inter H-bonds in Dimer I is the highest, in comparison to those of the II–IV dimers. Thus the results indicate that inter hydrogen bonding interaction plays important role in determining the stable dimers. The intra H-bonds of mono Ala-Gln and inter and intra H-bonds of Dimer I are shown in Fig. 1(b, c), respectively.

For the amide plane five bond lengths and six bond angles considered and listed in Table 1(b), those are 4C–10C, 10C–11O, 10C–12N, 12N–14C, 12N–13H, $\angle\text{CCO}$ (4, 10, 11), $\angle\text{CCN}$ (4, 10, 12), $\angle\text{OCN}$ (11, 10, 12), $\angle\text{CNC}$ (10, 12, 14), $\angle\text{CNH}$ (10, 12, 13) and $\angle\text{HNC}$ (13, 12, 14), as indicated in Fig. 1(a). These five bond lengths and six bond angles are found to be in agreement with those of valine and phenylalanine containing dipeptides [5,7]. The geometry around alpha-carbon atom plays very important role in the structure of proteins. Ideally bond angle around carbon atom is 109.5° . But due to the stereogenic nature of C_α atom the ideal nature is not expected. For mono Ala-Gln unit, $\angle\text{CC}_\alpha$ plane (2N, 4C, 10C) is predicted as 111.17° , and for Dimer I, the corresponding angles (2N, 4C, 10C and 35N, 33C, 32C) are 111.47° and 111.45° , respectively. The $\angle\text{CC}_\alpha$ planes were found in 111.9° – 115.0° ranges for valine containing dipeptides [5]. Thus our calculated results are compatible with those of previous findings [5,7].

The dihedral angle of the dipeptide bond can give some information about the planarity of the peptide molecules, it should be 180° if the amide plane is planar. The dihedral angles between (4C, 10C, 12N, 14C) atoms (peptide bond: 10C–12N) of mono and Dimer I structures are -174.40° and -179.40° , respectively. The other dihedral angle between (33C, 32C, 34N, 39C) atoms (peptide bond: 32C–34N) of Dimer I structure is -179.5° . The results indicate that in Dimer I structure, the deviation of the peptide plane from planar structure is less than that of the monomer structure, probably due to the fact that inter hydrogen bonding interactions involving the O atoms on the amide planes forced the amide

Fig. 1. The neutral form of Ala-Gln with the atom numbering and the dihedral angles used in Table 1 (a), the intra H-bonds of monomer Ala-Gln (b), inter and intra H-bonds of Dimer I (c), the geometrical structures of four low energy dimeric forms of Ala-Gln the energies obtained by DFT/B3LYP/6-31G(d,p) level of theory are $E = -977,809.95496405$ kcal/mol Dimer I (d), $E = -977,809.60516250$ kcal/mol Dimer II (e), $E = -977,809.52818043$ kcal/mol Dimer III (f), $E = -977,809.08389576$ kcal/mol Dimer IV (g).

Table 1(a)
The torsional angles for the global conformation of the neutral Ala-Gln

Angles	PHI ₁	CH ₁₁	PSI ₁	W ₂	PHI ₂	CH ₂₁	CH ₂₂	CH ₂₃	PSI ₂
Initial values	50.00	-60.00	60.00	180.00	-150.00	60.00	-60.00	90.00	150.00
Optimized values	50.27	-60.28	71.74	180.87	-150.31	58.25	-76.21	101.43	156.78

Table 1(b)

Geometry of mono Ala-Gln and Dimer I, calculated at the DFT level of theory using the standart 6-31G(d,p) basis set (distance in Å, angles in degrees)

Bond	Mono	Dimer I	Bond	Mono	Dimer I	Angle	Mono	Dimer I	Dihedral	Mono	Dimer I
H ₁ -N ₂	1.0197	1.0212	O ₂₉ -H ₃₀	0.9725	0.9725	N ₂ -C ₄ -C ₆	110.00	109.80	H ₁ -N ₂ -C ₄ -C ₆	-70.02	-64.84
H ₃ -N ₂	1.0202	1.0174	N₁₂-C₁₄	1.4474	1.4475	N ₂ -C ₄ -C ₁₀	111.17	111.47	H ₃ -N ₂ -C ₄ -C ₆	174.90	174.96
C ₄ -N ₂	1.4680	1.4686	C ₁₄ -H ₁₅	1.0949	1.0934	C₄-C₁₀-O₁₁	121.74	121.63	H ₁ -N ₂ -C ₄ -C ₁₀	51.49	56.88
C ₆ -C ₄	1.5305	1.529	C ₁₄ -C ₁₆	1.5539	1.5528	C₄-C₁₀-N₁₂	116.17	115.73	N ₂ -C ₄ -C ₆ -H ₇	-53.75	-53.50
C ₆ -H ₇	1.0926	1.0927	C ₁₆ -H ₁₇	1.0933	1.0934	O₁₁-C₁₀-N₁₂	122.07	122.61	C₄-C₁₀-N₁₂-C₁₄	-174.40	-179.40
C ₆ -H ₈	1.0926	1.0927	C ₁₆ -H ₁₈	1.0933	1.0934	C₁₀-N₁₂-H₁₃	119.91	120.23	C₁₀-N₁₂-C₁₄-C₂₇	-167.64	-139.37
C ₆ -H ₉	1.0926	1.0927	C ₁₆ -C ₁₉	1.5499	1.5506	C₁₀-N₁₂-C₁₄	121.37	122.19	C ₁₀ -N ₁₂ -C ₁₄ -C ₁₆	68.95	97.15
C₄-C₁₀	1.5377	1.5396	C ₁₉ -H ₂₀	1.0933	1.0938	N ₁₂ -C ₁₄ -C ₁₆	114.55	114.53	N ₁₂ -C ₁₄ -C ₁₆ -C ₁₉	57.99	59.06
C₁₀-O₁₁	1.2319	1.2326	C ₁₉ -H ₂₁	1.0957	1.0954	H₁₃-N₁₂-C₁₄	116.42	117.17	N ₂ -C ₄ -C ₁₀ -N ₁₂	115.61	113.07
C₁₀-N₁₂	1.3635	1.3620	C ₁₉ -C ₂₂	1.5269	1.5252	C ₁₄ -C ₁₆ -C ₁₉	115.36	115.32	H ₁₃ -N ₁₂ -C ₁₀ -O ₁₁	166.95	171.62
N₁₂-H₁₃	1.0114	1.0119	C ₂₂ -O ₂₃	1.2273	1.2418	C ₁₆ -C ₁₉ -C ₂₂	113.33	113.74	C ₁₆ -C ₁₉ -C ₂₂ -N ₂₄	-87.43	-87.31
N ₂₄ -H ₂₅	1.0069	1.0081	C ₂₂ -N ₂₄	1.3637	1.3494	C ₁₉ -C ₂₂ -C ₂₃	123.11	121.63	C ₁₉ -C ₂₂ -N ₂₄ -H ₂₅	4.35	5.08
N ₂₄ -H ₂₆	1.0089	1.0275				C ₁₉ -C ₂₂ -N ₂₄	114.98	116.00	C ₁₉ -C ₂₂ -N ₂₄ -H ₂₆	174.41	171.70
C ₁₄ -C ₂₇	1.5198	1.5231				O ₂₃ -C ₂₂ -N ₂₄	121.89	122.35	C ₁₆ -C ₁₄ -C ₂₇ -O ₂₉	-70.26	-72.43
C ₂₇ -O ₂₈	1.2122	1.2114				C ₂₂ -N ₂₄ -H ₂₅	122.42	120.18	C ₁₆ -C ₁₄ -C ₂₇ -O ₂₈	107.49	104.98
C ₂₇ -O ₂₉	1.3503	1.3519				C ₂₂ -N ₂₄ -H ₂₆	118.28	120.19	N ₁₂ -C ₁₄ -C ₂₇ -O ₂₉	163.81	161.38

Table 2

The intra and inter hydrogen bonds of the dimeric forms (I-IV) of the four low energy conformations

Atoms	Bond (Å)	Atoms	Bond (Å)	Atoms	Bond (Å)	Atoms	Bond (Å)
Dimer I Intra-molecular		Dimer II Intra-molecular		Dimer III Intra-molecular		Dimer IV Intra-molecular	
H-bonds		H-bonds		H-bonds		H-bonds	
51O...56H	2.28917	13H...23O	1.98321	41H...57O	2.24862	3H...23O	2.24913
28O...30H	2.28921	38H...57O	1.98469	13H...28O	2.25369	41H...57O	2.24972
13H...23O	2.37558	41H...57O	2.14085	38H...51O	2.28370	38H...51O	2.33653
38H...57O	2.38039	3H...23O	2.14085	1H...11O	2.36494	13H...28O	2.34236
		28O...30H	2.28584	31O...40H	2.61083	23O...26H	2.49819
		51O...56H	2.28585			57O...60H	2.49892
						31O...40H	2.72488
						1H...11O	2.73040
Inter-molecular		Inter-molecular		Inter-molecular		Inter-molecular	
H-bonds		H-bonds		H-bonds		H-bonds	
23O...60H	1.87079	35N...26H	1.89284	23O...56H	1.60939	28O...56H	1.63684
26H...57O	1.87155	2N...60H	1.89293	26H...51O	1.88003	30H...51O	1.63825
11O...40H	2.33151						
1H...31O	2.33838

Fig. 2. The experimental micro Raman (a) and FT-IR spectra (b) of Ala-Gln dipeptide, and calculated IR spectra of monomeric (c) and dimeric forms (I–IV) the dipeptide (d–g); Dimer I (d), Dimer II (e), Dimer III (f) Dimer IV (g).

planes of Dimer I structure to be more planar structure; in the Dimer I structure, one of the hydrogens of the N-terminal group of Alanine involves hydrogen bonding interaction with the oxygen atom of the C=O group of Alanine of the other pair (1H...31O), on the other hand the N-terminal group of Alanine molecule of the other pair involves hydrogen bonding interaction with the oxygen atom of the C=O group of Alanine of the first pair (40H...11O) (see Table 2).

The calculated wavenumbers and the total energy distribution of the vibrational modes of mono Ala-Gln dipeptide are given in Table 3, in comparison with the experimental IR and Raman spectra of the investigated dipeptide and the calculated wavenumbers of Dimer I. On the other hand, the calculated vibrational wavenumbers of Ala-Gln dimers (I–IV) were tabulated in Table 4. According to the frequency data in Tables 3 and 4, no imaginary frequency has been observed at the optimized structures of the title molecule and its dimers, proving that a true minima on the potential surfaces were found. The experimental micro Raman and FT-IR spectra of Ala-Gln, in comparison with the calculated IR spectrum of global conformation of mono Ala-Gln and Dimer I units are given in Fig. 2(a, b, c, d), respectively. The calculated IR spectra of low energy conformers of Ala-Gln dimers (Dimers I–IV) are given in Fig. 2(d, e, f, g), respectively.

The C–H stretching vibrations of alifatic structures often occur in the region of 2936–2843 cm^{-1} [8]. In our work, the weak band observed at 2965 cm^{-1} in IR spectra and the very strong band at 2932 cm^{-1} in Raman spectra have been assigned as methylene group of glutamine asymmetric and symmetric stretching, respectively. In theoretical calculations, these stretching modes are predicted at 2969 cm^{-1} {with 6-31G++(d,p)} and 2931 cm^{-1} {with 6-31G++(d,p)}, respectively after scaling with

Table 3

Calculated and experimental wavenumbers (cm^{-1}) and the total energy distribution of the vibrational modes of the Ala-Gln and calculated wavenumbers of Dimer I

Assignment		IR	Raman	Monomer			Dimer I	TED [†] of mono-Ala-Gln DFT-RB3LYP 6-31G++(d,p)
				DFT 6-31G ++(d,p)	DFT 6-31G (d,p)	DFT 6-31G (d)	DFT RB3LYP 6-31G(d,p)	
		ν_{exp}	ν_{exp}	$^*\nu$	$^*\nu$	$^*\nu$	$^*\nu$	
1	ν_{OH}	—	—	3583	3582	3549	3580–3580	$\nu_{\text{OH}}(100)$
2	$\nu_{\text{NH2}}(\text{asim})$	—	—	3568	3573	3517	3515–3515	$\nu_{\text{NH}}(100)$
3	$\nu_{\text{NH}}(\text{peptid})$	—	—	3459	3460	3446	3453–3453	$\nu_{\text{NH}}(100)$
4	$\nu_{\text{NH2}}(\text{sim})$	—	—	3434	3441	3429	3193–3151	$\nu_{\text{NH}}(100)$
5	$\nu_{\text{NH2}}(\text{asim})$	3400s	3393w	3409	3388	3368	3403–3401	$\nu_{\text{NH}}(100)$
6	$\nu_{\text{NH2}}(\text{sim})$	3332vs	3330s	3321	3303	3284	3314–3312	$\nu_{\text{NH}}(100)$
7	$\nu_{\text{CH3}}(\text{asim})$	3225s	3224w	2993	3001	3002	3002–3002	$\nu_{\text{CH}}(97)$
8	$\nu_{\text{CH2}}(\text{asim})$	—	2991	2979	2985	2986	2979–2979	$\nu_{\text{CH}}(99)$
9	$\nu_{\text{CH3}}(\text{asim})$	2979m	2975s	2977	2983	2985	2990–2990	$\nu_{\text{CH}}(99)$
10	$\nu_{\text{CH2}}(\text{asim})$	2965w	—	2969	2976	2977	2966–2966	$\nu_{\text{CH}}(97)$
11	ν_{CH}	—	—	2940	2946	2955	2968–2968	$\nu_{\text{CH}}(99)$
12	$\nu_{\text{CH2}}(\text{sim})$	2937w	2932vs	2931	2933	2938	2924–2924	$\nu_{\text{CH}}(98)$
13	$\nu_{\text{CH2}}(\text{sim})$	—	—	2917	2919	2923	2919–2919	$\nu_{\text{CH}}(99)$
14	ν_{CH}	2915w	2911m	2913	2916	2921	2903–2902	$\nu_{\text{CH}}(100)$
15	$\nu_{\text{CH3}}(\text{sim})$	2877vw	2874m	2909	2914	2919	2918–2918	$\nu_{\text{CH}}(100)$
16	$\nu_{\text{OC}}(\text{COOH})\text{C}=\text{O}$	1733vw	—	1733	1755	1758	1758–1758	$\nu_{\text{OC}}(85)$
17	$\nu_{\text{OC}}(\text{gln})$	—	—	1715	1725	1727	1705	$\nu_{\text{NC}}(5) + \nu_{\text{OC}}(75)$
18	$\nu_{\text{OC}}(\text{peptid})$	—	1666vw	1684	1693	1695	1691–1688	$\nu_{\text{OC}}(77)$
19	$\delta_{\text{NH2}}(\text{scis})$	1648vs	1636m	1637	1628	1655	1682–1626–1613	$\delta_{\text{HNN}}(51) + \delta_{\text{CNH}}(33)$
20	$\delta_{\text{NH2}}(\text{scis})$	1605m	1600w	1592	1579	1598	1619–1611	$\nu_{\text{NC}}(5) + \delta_{\text{HNN}}(58) + \delta_{\text{CNH}}(30)$
21	$\delta_{\text{CNH}}(\text{peptid})$	1527s	1525m	1510	1495	1503	1511–1510	$\nu_{\text{NC}}(27) + \delta_{\text{CNH}}(54)$
22	δ_{CH3}	—	—	1467	1463	1478	1464–1463	$\delta_{\text{CCH}}(13) + \delta_{\text{HCH}}(50) + \Gamma_{\text{HCCN}}(6) + \Gamma_{\text{HCCC}}(7) + \Gamma_{\text{HCCH}}(10)$
23	$\delta_{\text{CH2}}(\text{scis})$	1456w	1448vs	1462	1455	1470	1463–1463	$\delta_{\text{HCH}}(28) + \Gamma_{\text{HCCN}}(10) + \Gamma_{\text{HCCC}}(13) + \Gamma_{\text{HCCH}}(28)$
24	$\delta_{\text{CH2}}(\text{scis})$	—	—	1461	1453	1469	1455–1454	$\delta_{\text{HCH}}(29) + \Gamma_{\text{HCCN}}(8) + \Gamma_{\text{HCCC}}(10) + \Gamma_{\text{HCCH}}(18)$
25	δ_{CH3}	1416vw	1414m	1458	1451	1466	1451–1451	$\delta_{\text{CCH}}(9) + \delta_{\text{HCH}}(51) + \Gamma_{\text{HCCN}}(11) + \Gamma_{\text{HCCC}}(16) + \Gamma_{\text{HCCH}}(6)$
26	$\delta_{\text{CH3}}(\text{umb})$	1404w	—	1384	1381	1389	1377–1377	$\delta_{\text{CNH}}(17) + \delta_{\text{CCH}}(17) + \delta_{\text{HCH}}(17)$
27	$\delta_{\text{CH3}}(\text{umb})$	1380s	1375w	1376	1372	1380	1371–1370	$\nu_{\text{CC}}(7) + \nu_{\text{OC}}(7) + \delta_{\text{CCH}}(18) + \delta_{\text{HCH}}(17)$
28	$\delta_{\text{CCH}} + \nu_{\text{NC}}$	—	—	1368	1359	1371	1400–1387	$\nu_{\text{NC}}(14) + \nu_{\text{CC}}(7) + \delta_{\text{CCH}}(30)$

Table 3
(Continued)

Assignment	IR	Raman	Monomer			Dimer I DFT RB3LYP 6-31G(d,p)	TED [†] of mono-Ala-Gln DFT-RB3LYP 6-31G++(d,p)
			DFT 6-31G ++(d,p)	DFT 6-31G (d,p)	DFT 6-31G (d)		
29 $\delta_{\text{NCH}} + \delta_{\text{CH3umb}}$	–	1360w	1364	1359	1369	1355–1353	$\delta_{\text{CCH}}(15) + \delta_{\text{NCH}}(31) + \delta_{\text{HCH}}(17) + \Gamma_{\text{HCCN}}(5) + \Gamma_{\text{HCCH}}(8)$
30 δ_{CCH}	1350vw	–	1350	1340	1349	1349–1347	$\nu_{\text{CC}}(5) + \nu_{\text{NC}}(7) + \delta_{\text{CCH}}(28) + \Gamma_{\text{OCCH}}(7)$
31 δ_{CCH}	1319w	1323m	1336	1325	1335	1331–1330	$\delta_{\text{HCN}}(8) + \delta_{\text{CCH}}(15) + \Gamma_{\text{HCCH}}(5) + \Gamma_{\text{HCNH}}(14)$
32 δ_{CCH}	1300w	–	1309	1304	1313	1315–1312	$\nu_{\text{NC}}(8) + \delta_{\text{CCH}}(31) + \delta_{\text{COH}}(7)$
33 δ_{CCH}	1281vw	1279m	1287	1277	1286	1289–1288	$\nu_{\text{NC}}(9) + \delta_{\text{NCH}}(6) + \delta_{\text{COH}}(5) + \delta_{\text{CCH}}(18) + \Gamma_{\text{HCCH}}(9) + \Gamma_{\text{OCCH}}(9)$
34 δ_{COH}	–	–	1256	1252	1262	1254–1254	$\delta_{\text{COH}}(24) + \delta_{\text{CCH}}(21) + \Gamma_{\text{CNCH}}(5)$
35 $\delta_{\text{NCH}} + \delta_{\text{CCH}}$	1232w	1238m	1243	1238	1247	1234–1233	$\delta_{\text{CCH}}(25) + \delta_{\text{CNH}}(27) + \Gamma_{\text{HCCH}}(6)$
36 δ_{CCH}	1214vw	1212m	1233	1219	1254	1221–1221	$\nu_{\text{NC}}(18) + \delta_{\text{HCN}}(6) + \delta_{\text{CCH}}(30) + \Gamma_{\text{HCCH}}(9)$
37 $\nu_{\text{NC}}(\text{peptide})$	1208vw	1180vw	1200	1185	1193	1195–1194	$\nu_{\text{NC}}(29) + \delta_{\text{HCN}}(19)$
38 δ_{CCH}	1165vw	1160vw	1166	1158	1166	1170–1168	$\nu_{\text{OC}}(8) + \delta_{\text{CCH}}(44) + \delta_{\text{CNH}}(8)$
39 $\nu_{\text{OC}} + \delta_{\text{COH}}$	–	–	1149	1142	1148	1140–1139	$\nu_{\text{NC}}(12) + \nu_{\text{OC}}(19) + \delta_{\text{COH}}(16)$
40 ν_{NC}	1110m	–	1114	1112	1117	1114–1110	$\nu_{\text{NC}}(39) + \nu_{\text{CC}}(13) + \delta_{\text{CCH}}(14)$
41 ν_{NC}	1089w	1104s	1104	1100	1104	1097–1096	$\nu_{\text{NC}}(33) + \nu_{\text{CC}}(11) + \nu_{\text{OC}}(21) + \delta_{\text{COH}}(11)$
42 ν_{NH2}	–	–	1071	1067	1074	1107–1101	$\nu_{\text{NC}}(11) + \nu_{\text{OC}}(8) + \delta_{\text{CCH}}(7) + \delta_{\text{CNH}}(44)$
43 $w_{(\text{CH3})}$	1068w	1067w	1061	1060	1068	1056–1053	$\nu_{\text{CC}}(21) + \delta_{\text{CNH}}(5) + \delta_{\text{CCH}}(28) + \Gamma_{\text{HNCH}}(6) + \Gamma_{\text{CCCH}}(8)$
44 ν_{CC}	1044w	1043w	1027	1018	1022	1021–1019	$\nu_{\text{CC}}(64)$
45 ν_{CC}	1022w	1017w	1014	1007	1013	1009–1009	$\nu_{\text{NC}}(6) + \nu_{\text{CC}}(15) + \delta_{\text{CCH}}(7) + \Gamma_{\text{CCCH}}(10)$
46 $\delta_{\text{CCH}} + t_{\text{NH2}}$	1010w	1013vw	1003	998	1004	996–996	$\nu_{\text{CC}}(17) + \delta_{\text{CCH}}(33) + \delta_{\text{CNH}}(6)$
47 δ_{CCH}	961w	958w	939	934	940	941–941	$\nu_{\text{CC}}(14) + \nu_{\text{NC}}(12) + \delta_{\text{CCH}}(14)$
48 Γ_{CCCH}	918vw	916vw	925	921	927	922–920	$\nu_{\text{NC}}(11) + \nu_{\text{CC}}(5) + \Gamma_{\text{CCCH}}(12) + \Gamma_{\text{OCCH}}(6)$
49 $\nu_{\text{C-CH3}}$	893vw	894vs	894	912	921	914–901	$\nu_{\text{CC}}(22) + \delta_{\text{CNH}}(21) + \delta_{\text{CCH}}(8) + \Gamma_{\text{HCNC}}(20) + \Gamma_{\text{HCNH}}(9)$
50 ν_{NC}	860w	858vw	879	875	879	881–880	$\nu_{\text{NC}}(30) + \nu_{\text{CC}}(17) + \delta_{\text{CCH}}(5)$
51 ν_{CC}	–	–	871	864	866	876–875	$\nu_{\text{NC}}(6) + \nu_{\text{CC}}(58)$
52 ν_{CC}	808m	808vw	820	816	817	811	$\nu_{\text{CC}}(29) + \Gamma_{\text{OCNC}}(5)$
53 ν_{CC}	766vw	764vw	776	773	774	785–783	$\nu_{\text{CC}}(35)$
54 $\Gamma_{\text{OCNC}} + \Gamma_{\text{OCNH}}$	–	–	760	755	755	753–752	$\nu_{\text{CC}}(7) + \delta_{\text{CCN}}(6) + \Gamma_{\text{OCCN}}(7) + \Gamma_{\text{OCCC}}(7) + \Gamma_{\text{HCCN}}(6) + \Gamma_{\text{OCNH}}(8) + \Gamma_{\text{OCNC}}(12)$
55 Γ_{OCOH}	–	–	726	725	727	727–727	$\nu_{\text{CC}}(11) + \Gamma_{\text{OCCH}}(11) + \Gamma_{\text{OCNH}}(10) + \Gamma_{\text{NCCO}}(6) + \Gamma_{\text{OCOH}}(13)$
56 ν_{CC}	697vw	696vw	707	706	709	705–698	$\nu_{\text{CC}}(29) + \Gamma_{\text{OCCC}}(5) + \Gamma_{\text{HCCN}}(12) + \Gamma_{\text{OCNH}}(19)$
57 δ_{CCO}	651m	649m	672	672	673	674–671	$\nu_{\text{CC}}(16) + \delta_{\text{CCH}}(9) + \delta_{\text{CCO}}(16) + \delta_{\text{NCO}}(7)$

Table 3
(Continued)

Assignment		IR	Raman	Monomer			Dimer I	TED [†] of mono-Ala-Gln DFT-RB3LYP 6-31G++(d,p)
				DFT 6-31G ++(d,p)	DFT 6-31G (d,p)	DFT 6-31G (d)	DFT RB3LYP 6-31G(d,p)	
58	Γ_{CCOH}	620vw	619vw	632	640	643	633–632	$\delta_{\text{CCO}}(8) + \Gamma_{\text{HOCO}}(27) + \Gamma_{\text{HOCC}}(18)$
59	Γ_{CCOH}	596vw	592vw	576	580	583	588–587	$\nu_{\text{CC}}(9) + \delta_{\text{CCO}}(10) + \delta_{\text{OCO}}(14) + \Gamma_{\text{HOCO}}(7) + \Gamma_{\text{HOCC}}(19)$
60	$t_{(\text{NH}_2)} + \Gamma_{\text{CCNH}}$	–	–	565	562	563	849–816	$\delta_{\text{CCO}}(6) + \delta_{\text{OCO}}(14) + \Gamma_{\text{CCNH}}(22) + \Gamma_{\text{OCNH}}(13)$
61	$\Gamma_{\text{CCNH}} + \Gamma_{\text{HOCC}}$	–	–	562	558	562	551–547	$\delta_{\text{CCO}}(9) + \delta_{\text{NCO}}(8) + \Gamma_{\text{CCNH}}(16) + \Gamma_{\text{OCNH}}(11) + \Gamma_{\text{HOCC}}(11)$
62	δ_{NCO}	532vw	531vw	527	524	525	570–566	$\nu_{\text{CC}}(10) + \delta_{\text{CCO}}(16) + \delta_{\text{NCO}}(33)$
63	Γ_{CCNH}	503w	495w	496	492	495	499–494–492	$\Gamma_{\text{OCNH}}(26) + \Gamma_{\text{CCNH}}(47)$
64	δ_{NCC}	454w	452w	467	461	462	464–451–442	$\delta_{\text{NCC}}(18) + \delta_{\text{CCC}}(7) + \Gamma_{\text{OCCC}}(7)$
65	$\delta_{\text{CCO}} + t_{(\text{NH}_2)}$	422vw	–	429	424	424	427	$\delta_{\text{NCC}}(10) + \delta_{\text{CCO}}(25) + \Gamma_{\text{CCNH}}(11)$
66	δ_{NCC}	419vw	–	409	407	407	422–414	$\delta_{\text{CCO}}(27) + \delta_{\text{NCC}}(46)$
67	$r_{(\text{NH}_2)}$	–	359vw	365	380	381	388–337	$\Gamma_{\text{HNCH}}(16) + \Gamma_{\text{HNCC}}(57)$
68	Γ_{CCNH}	–	350w	324	319	320	345–339	$\nu_{\text{CC}}(10) + \delta_{\text{NCC}}(14) + \delta_{\text{CCC}}(12) + \Gamma_{\text{HNCC}}(20)$
69	δ_{NCC}	–	291w	298	301	301	312–304	$\nu_{\text{CC}}(10) + \delta_{\text{NCO}}(8) + \delta_{\text{NCC}}(18) + \delta_{\text{CCC}}(7) + \delta_{\text{OCC}}(11) + \Gamma_{\text{HNCC}}(15)$
70	δ_{CCC}	–	–	280	280	280	293–291	$\delta_{\text{CCC}}(27) + \Gamma_{\text{HNCC}}(15) + \Gamma_{\text{CNCO}}(8) + \Gamma_{\text{HNCO}}(6)$
71	δ_{CCC}	–	–	269	270	269	271–270	$\delta_{\text{NCC}}(16) + \delta_{\text{CCC}}(27) + \Gamma_{\text{HNCC}}(20)$
72	$t_{(\text{NH}_2)} + \Gamma_{\text{CCNH}}$	–	–	255	248	247	475	$\Gamma_{\text{HNCC}}(41) + \Gamma_{\text{HNCO}}(39)$
73	Γ_{CCNH}	–	248vw	244	239	229	248–247	$\nu_{\text{CC}}(7) + \delta_{\text{NCC}}(16) + \delta_{\text{CCC}}(13) + \Gamma_{\text{HNCC}}(33) + \Gamma_{\text{HCCC}}(7)$
74	Γ_{HCCC}	–	229w	223	224	223	224–222	$\Gamma_{\text{HCC}}(16) + \Gamma_{\text{HCCC}}(56)$
75	δ_{CCC}	–	–	205	205	204	216–215	$\delta_{\text{NCC}}(14) + \delta_{\text{CCC}}(29) + \Gamma_{\text{OCCH}}(5) + \Gamma_{\text{NCCO}}(10)$
76	δ_{CCC}	–	–	148	149	151	176–172	$\delta_{\text{CCC}}(41) + \Gamma_{\text{CNCC}}(5) + \Gamma_{\text{HNCC}}(5)$
77	δ_{CNC}	–	–	114	117	118	152–150	$\delta_{\text{NCC}}(34) + \delta_{\text{CNH}}(8) + \delta_{\text{CCC}}(5) + \Gamma_{\text{HCCC}}(10)$
78	Γ_{NCCC}	–	–	105	115	116	135	$\delta_{\text{NCC}}(7) + \Gamma_{\text{HNCC}}(20) + \Gamma_{\text{NCCC}}(24) + \Gamma_{\text{HCCC}}(17) + \Gamma_{\text{CCCC}}(15)$
79	Γ_{NCCC}	–	–	75	89	87	103–83	$\Gamma_{\text{NCCC}}(65) + \Gamma_{\text{OCNC}}(10) + \Gamma_{\text{CNCH}}(11) + \Gamma_{\text{CCCO}}(7)$
80	Γ_{CCNH}	–	–	60	65	66	71–65–40	$\Gamma_{\text{HNCC}}(24) + \Gamma_{\text{OCNH}}(6) + \Gamma_{\text{CNCC}}(21) + \Gamma_{\text{CCCC}}(7) + \Gamma_{\text{OCCC}}(9)$
81	Γ_{OCCN}	–	–	55	60	60	88–87 29–22–20	$\Gamma_{\text{OCCN}}(36) + \Gamma_{\text{OCCH}}(15) + \Gamma_{\text{OCCC}}(9) + \Gamma_{\text{NCCN}}(10) + \Gamma_{\text{NCCH}}(7)$
82	Γ_{OCCC}	–	–	46	47	47	45–47	$\Gamma_{\text{HCCC}}(7) + \Gamma_{\text{OCCH}}(12) + \Gamma_{\text{OCCC}}(52)$
83	Γ_{CCCH}	–	–	26	27	28	55–33	$\Gamma_{\text{NCCN}}(11) + \Gamma_{\text{NCCC}}(15) + \Gamma_{\text{NCCH}}(14) + \Gamma_{\text{HCCC}}(30) + \Gamma_{\text{CCCC}}(13)$
84	Γ_{CCNH}	–	–	19	13	20	97–29	$\Gamma_{\text{HNCC}}(30) + \Gamma_{\text{HNCH}}(7) + \Gamma_{\text{CNCC}}(27) + \Gamma_{\text{CCCH}}(5) + \Gamma_{\text{OCCC}}(7)$

Notes: [†] Only contributions >5% are listed.

*The wavenumbers under 1800 cm^{−1} were scaled with 0.967 and 0.977 for DFT 6-31G(d,p) and DFT 6-31G++(d,p) respectively and for over 1800 cm^{−1} the scale factor 0.955 were used for both DFT 6-31G(d,p) and DFT 6-31G++(d,p) levels of theory.

Table 4
Calculated (B3LYP/6-31G(d,p)) wavenumbers (cm^{-1}) for four conformers of Ala-Gln Dimers (I–IV)

Assign. Dimer I	IR	Raman	I	II	III	IV	Assign. Dimer I	IR	Raman	I	II	III	IV
	ν_{exp}	ν_{exp}	$^*\nu$	$^*\nu$	$^*\nu$	$^*\nu$		ν_{exp}	ν_{exp}	$^*\nu$	$^*\nu$	$^*\nu$	$^*\nu$
1 ν_{OH}			3580	3578	3582	3574	88 ν_{CC}			1019	1029	1018	1020
2 ν_{OH}			3580	3578	3575	3573	89 ν_{CC}	1022w	1017w	1009	1022	1013	1011
3 $\nu_{\text{NH2(asim)}}$			3515	3519	3526	3466	90 ν_{CC}			1009	1016	1010	1011
4 $\nu_{\text{NH2(asim)}}$			3515	3519	3463	3466	91 $\delta_{\text{CCH}} + t_{(\text{NH}_2)}$			996	1014	1003	1000
5 $\nu_{\text{NH(peptid)}}$			3453	3374	3452	3442	92 $\delta_{\text{CCH}} + t_{(\text{NH}_2)}$	1010w	1013vw	996	1011	998	1000
6 $\nu_{\text{NH(peptid)}}$			3453	3374	3442	3441	93 δ_{CCH}			941	993	993	977
7 $\nu_{\text{NH2(asim)}}$			3403	3349	3387	3390	94 δ_{CCH}	961w	958w	941	989	936	938
8 $\nu_{\text{NH2(asim)}}$	3400s	3393w	3401	3348	3386	3389	95 Γ_{CCCH}	918vw	916vw	922	941	935	936
9 $\nu_{\text{NH2(sim)}}$	3332vs	3330s	3314	3282	3311	3303	96 Γ_{CCCH}			920	939	925	936
10 $\nu_{\text{NH2(sim)}}$			3312	3281	3304	3303	97 $\nu_{\text{CC-CH}_3}$	893vw	894vs	914	914	923	921
11 $\nu_{\text{NH2(sim)}}$			3193	3000	3222	3003	98 $\nu_{\text{CC-CH}_3}$			901	913	921	921
12 $\nu_{\text{NH2(sim)}}$			3151	3000	3000	3002	99 ν_{NC}			881	911	915	909
13 $\nu_{\text{CH3(asim)}}$			3002	2995	2999	2997	100 ν_{NC}	860w	858vw	880	910	882	909
14 $\nu_{\text{CH3(asim)}}$			3002	2991	2992	2986	101 ν_{CC}			876	884	882	882
15 $\nu_{\text{CH3(asim)}}$			2990	2991	2985	2985	102 ν_{CC}			875	884	873	881
16 $\nu_{\text{CH3(asim)}}$	2979m	2975s	2990	2980	2984	2985	103 $t_{(\text{NH}_2)} + \Gamma_{\text{CCNH}}$			849	872	872	869
17 $\nu_{\text{CH2(asim)}}$			2979	2977	2982	2985	104 $t_{(\text{NH}_2)}$			816	872	827	869
18 $\nu_{\text{CH2(asim)}}$			2979	2977	2980	2976	105 ν_{CC}	808m	808vw	811	809	814	829
19 ν_{CH}			2968	2967	2977	2976	106 $t_{(\text{NH}_2)}$			806	809	810	826
20 ν_{CH}			2968	2967	2977	2950	107 ν_{CC}			785	779	788	783
21 $\nu_{\text{CH2(asim)}}$			2966	2957	2952	2950	108 ν_{CC}			783	779	784	779
22 $\nu_{\text{CH2(asim)}}$	2965w		2966	2957	2941	2936	109 $\Gamma_{\text{OCNC}} + \Gamma_{\text{OCNHpeptide}}$	766vw	764vw	753	754	755	758
23 $\nu_{\text{CH2(sim)}}$			2924	2936	2935	2936	110 $\Gamma_{\text{OCNC}} + \Gamma_{\text{OCNHpeptide}}$			752	753	741	757
24 $\nu_{\text{CH2(sim)}}$	2937w	2932vs	2924	2936	2929	2920	111 Γ_{OCOH}			727	726	730	728
25 $\nu_{\text{CH2(sim)}}$			2919	2923	2925	2920	112 Γ_{OCOH}			727	726	719	722
26 $\nu_{\text{CH2(sim)}}$			2919	2923	2922	2916	113 ν_{CC}			705	697	708	713
27 $\nu_{\text{CH3(sim)}}$	2877vw	2874m	2918	2920	2917	2915	114 ν_{CC}	697vw	696vw	698	697	692	711
28 $\nu_{\text{CH3(sim)}}$			2918	2920	2913	2913	115 δ_{CCO}	651m	647m	674	668	683	674
29 ν_{CH}	2915w	2911m	2903	2914	2913	2913	116 δ_{CCO}			671	666	676	672
30 ν_{CH}			2902	2914	2840	2885	117 Γ_{CCOH}			633	654	642	623
31 $\nu_{\text{OC(COOH)C=O}}$	1733vw		1758	1762	1761	1724	118 Γ_{CCOH}	620vw	619vw	632	651	632	617
32 $\nu_{\text{OC(COOH)C=O}}$			1758	1762	1718	1724	119 Γ_{CCOH}	596vw	592vw	588	623	591	590
33 $\nu_{\text{OC(gln)}}$			1705	1711	1712	1720	120 Γ_{CCOH}			587	622	575	583

Table 4
(Continued)

Assign. Dimer I	IR	Raman	I	II	III	IV	Assign. Dimer I	IR	Raman	I	II	III	IV
34 $\nu_{\text{OC}}(\text{peptide})$			1691	1710	1700	1697	121 δ_{NCO}			570	585	567	566
35 $\nu_{\text{OC}}(\text{peptide})$		1666vw	1688	1693	1693	1692	122 δ_{NCO}	532vw	531vw	566	584	566	564
36 $\delta_{\text{NH}_2}(\text{scis})$			1682	1692	1671	1663	123 $\Gamma_{\text{CCNH}} + \Gamma_{\text{HOCC}}$			551	575	547	526
37 $\delta_{\text{NH}_2}(\text{scis})$	1648vs	1636m	1626	1623	1627	1627	124 $\Gamma_{\text{CCNH}} + \Gamma_{\text{HOCC}}$			547	565	529	525
38 $\delta_{\text{NH}_2}(\text{scis})$			1619	1620	1626	1627	125 Γ_{CCNH}			499	546	505	487
39 $\delta_{\text{NH}_2}(\text{scis})$			1613	1609	1584	1579	126 Γ_{CCNH}	503w	495w	494	538	503	485
40 $\delta_{\text{NH}_2}(\text{scis})$	1605m	1600w	1611	1609	1576	1578	127 Γ_{CCNH}			492	504	468	473
41 $\delta_{\text{CNH}}(\text{peptide})$	1527s	1525m	1511	1543	1507	1498	128 $t_{(\text{NH}_2)} + \Gamma_{\text{CCNH}}$			475	503	463	468
42 $\delta_{\text{CNH}}(\text{peptide})$			1510	1541	1493	1496	129 δ_{NCC}	453w	452w	464	470	449	459
43 δ_{CH_3}			1464	1461	1464	1473	130 Γ_{CCNH}			451	455	442	438
44 δ_{CH_3}			1463	1461	1462	1463	131 δ_{NCC}			442	443	423	409
45 $\delta_{\text{CH}_2}(\text{scis})$	1456w	1448vs	1463	1451	1460	1462	132 $\delta_{\text{CCO}} + t_{(\text{NH}_2)}$	422vw		427	428	420	409
46 $\delta_{\text{CH}_2}(\text{scis})$			1463	1451	1454	1459	133 δ_{NCC}	419vw		422	422	407	393
47 $\delta_{\text{CH}_2}(\text{scis})$			1455	1445	1453	1456	134 δ_{NCC}			414	415	382	388
48 $\delta_{\text{CH}_2}(\text{scis})$			1454	1445	1453	1452	135 $r_{(\text{NH}_2)}$			388	400	345	348
49 δ_{CH_3}	1416vw	1414m	1451	1444	1450	1452	136 Γ_{CCNH}		359vw	345	393	329	334
50 δ_{CH_3}			1451	1444	1450	1452	137 Γ_{CCNH}		350w	339	349	326	325
51 $\nu_{\text{NC}} + \delta_{\text{CCH}}$			1400	1402	1449	1452	138 $r_{(\text{NH}_2)}$			337	342	311	309
52 $\nu_{\text{NC}} + \delta_{\text{CCH}}$			1387	1402	1403	1436	139 δ_{NCC}			312	314	299	287
53 $\delta_{\text{CH}_3}(\text{umb}) + \delta_{\text{CCH}}$	1404w		1377	1384	1388	1375	140 δ_{NCC}			304	312	287	286
54 $\delta_{\text{CH}_3}(\text{umb}) + \delta_{\text{CCH}}$			1377	1383	1377	1375	141 δ_{CCC}			293	294	285	282
55 $\delta_{\text{CH}_3}(\text{umb})$	1380s	1375w	1371	1377	1370	1362	142 δ_{CCC}			291	289	274	278
56 $\delta_{\text{CH}_3}(\text{umb})$			1370	1377	1363	1361	143 Γ_{CCNH}			271	276	270	268
57 $\delta_{\text{NCH}}\delta_{\text{CH}_3}(\text{umb})$		1360w	1355	1362	1361	1360	144 Γ_{CCNH}			270	272	254	252
58 $\delta_{\text{NCH}} + \delta_{\text{CH}_3}(\text{umb})$			1353	1362	1357	1359	145 Γ_{CCNH}			248	246	242	250
59 δ_{CCH}	1350vw		1349	1348	1348	1354	146 Γ_{CCNH}		248vw	247	244	238	245
60 δ_{CCH}			1347	1348	1342	1351	147 Γ_{CCCH}			224	226	223	235
61 δ_{CCH}			1331	1333	1338	1339	148 Γ_{CCCH}		229w	222	222	221	233
62 δ_{CCH}	1319w	1323m	1330	1333	1320	1338	149 δ_{CCC}			216	218	212	206
63 δ_{CCH}	1300w		1315	1311	1318	1325	150 δ_{CCC}			215	206	207	206
64 δ_{CCH}			1312	1311	1312	1324	151 δ_{CCC}			176	197	170	172
65 δ_{CCH}			1289	1285	1298	1302	152 δ_{CCC}			172	188	163	163
66 δ_{CCH}	1281vw	1279m	1288	1284	1288	1301	153 δ_{CNC}			152	155	161	147
67 δ_{COH}			1254	1257	1273	1275	154 δ_{CNC}			150	145	150	145

Table 4
(Continued)

Assign. Dimer I	IR	Raman	I	II	III	IV	Assign. Dimer I	IR	Raman	I	II	III	IV
68 δ_{COH}			1254	1257	1252	1275	155 Γ_{CCCN}			135	126	128	137
69 $\delta_{\text{NCH}} + \delta_{\text{CCH}}$	1232w	1238m	1234	1241	1244	1242	156 Γ_{NCCN}			116	123	120	128
70 $\delta_{\text{NCH}} + \delta_{\text{CCH}}$			1233	1240	1241	1241	157 Γ_{NCCN}			110	108	108	106
71 δ_{CCH}	1214vw	1212m	1221	1235	1229	1234	158 Γ_{CCCN}			103	103	104	103
72 δ_{CCH}	1208vw		1221	1232	1220	1233	159 Γ_{CCNH}			97	96	98	96
73 $\nu_{\text{NC}}(\text{peptide})$			1195	1214	1209	1220	160 Γ_{OCCN}			88	88	80	84
74 $\nu_{\text{NC}}(\text{peptide})$			1194	1213	1190	1219	161 Γ_{OCCN}			87	77	73	82
75 δ_{CCH}			1170	1175	1177	1182	162 Γ_{CCCN}			83	71	59	66
76 δ_{CCH}	1165vw	1160vw	1168	1174	1160	1182	163 Γ_{CCNH}			71	63	58	61
77 $\nu_{\text{OC}} + \delta_{\text{COH}}$			1140	1140	1153	1153	164 Γ_{CCNH}			65	58	55	61
78 $\nu_{\text{OC}} + \delta_{\text{COH}}$			1139	1140	1144	1153	165 Γ_{CCCH}			55	49	48	47
79 ν_{NC}			1114	1111	1122	1118	166 Γ_{OCCC}			47	45	45	45
80 ν_{NC}	1110m		1110	1110	1113	1118	167 Γ_{OCCC}			46	41	40	40
81 r_{NH2}			1107	1104	1103	1107	168 Γ_{OCCC}			45	35	39	36
82 r_{NH2}			1101	1101	1100	1107	169 Γ_{CCNH}			40	35	33	30
83 ν_{NC}	1089w	1105s	1097	1096	1095	1067	170 Γ_{CCCH}			33	26	29	26
84 ν_{NC}			1096	1092	1066	1067	171 Γ_{OCCN}			29	21	21	25
85 $w_{(\text{CH3})}$	1068w	1067w	1056	1068	1063	1058	172 Γ_{OCCN}			29	18	18	21
86 $w_{(\text{CH3})}$			1053	1068	1062	1058	173 Γ_{OCCN}			22	14	13	16
87 ν_{CC}	1044w	1043w	1021	1030	1019	1020	174 Γ_{OCCN}			20	8	8	12

Notes: * The wavenumbers under 1800 cm^{-1} , were scaled either with 0.967 (for B3LYP/6-31G(d,p)) or 0.977 (for B3LYP/6-31++G(d,p)), and for over 1800 cm^{-1} the scale factor 0.955 were used for both B3LYP/6-31G(d,p), B3LYP/6-31++G(d,p) levels of theory.

0.955. The scaled frequencies of Ala-Gln are well consistent with the experimental data. The stretching vibrations of methylene and methine group of Ala-Gln are assigned between 3000 and 2874 cm^{-1} as sharp bands (see Table 3). The symmetrical CH_3 stretching vibration is observed in IR as a weak intense band at 2877 cm^{-1} and in Raman spectrum as a medium band at 2874 cm^{-1} . The asymmetrical CH_3 stretching is assigned as a strong band at 3225 cm^{-1} in the IR spectrum and a weak band at 3224 cm^{-1} in the Raman spectrum.

The inter and intra hydrogen bonding differences between mono Ala-Gln and Dimer I are found to reflect in the calculated wavenumbers of mono and Dimer I structures (Table 3).

4. Conclusion

The monomer and dimer structures of Ala-Gln were studied by using the DFT/B3LYP method with 6-31++G(d,p) basis set. The structural characteristics of these molecules were revealed. Purpose of this work is to investigate vibrational modes of the energetically most stable conformer of mono- and dimer Ala-Gln molecules. We calculated 810 conformers for mono-Ala-Gln dipeptide and four dimer conformers (I–IV) for dimer-Ala-Gln molecule. The mono-Ala-Gln dipeptide are characterized by the extended backbone shape in the LB conformational range [11,12] with the energy -0.18 kcal/mol . The most stable conformers of dimer-Ala-Gln molecule (Dimer I) has $E = -1558.25542661\text{ a.u.}$ This investigation provides a rather satisfactory theoretical description of the monomer and dimer structures of Ala-Gln molecules. The determination of conformational details of biological macromolecules and conformational possibilities of Ala-Gln dipeptide is very important to understand their functions of a drug and may be useful as a base for synthesis of their more effective structural analogs.

Acknowledgement

This study was supported by the Research fund of Istanbul University (project Nos are T/3171 and ONAP-2423).

References

- [1] L.C.A. Cerchietti, A.H. Navigante, M.A. Lutteral, M.A. Castro, R. Kirchuk, M. Bonomi, M.E. Cabalar, B. Roth, G. Negretti, B. Sheinker and P. Uchima, *Int. J. Radiat. Oncol. Biol. Phys.* **65**(5) (2006), 1330.
- [2] C. Decker-Baumann, K. Buhl, S. Frohmüller, A.V. Herbay, M. Dueck and P.M. Schlag, *Eur. J. Cancer* **35** (1999), 202.
- [3] H. Eagle, V.I. Oyama, M. Levy, C.L. Horton and R. Fleischman, *J. Biol. Chem.* **218** (1956), 607.
- [4] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery Jr., T. Vreven, K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez and J.A. Pople, *Gaussian03*, Revision C.02, Gaussian, Inc., Wallingford, CT, 2004.
- [5] S. Ghosh, S. Mondal, A. Misra and S. Dalai, *J. Mol. Struct.* **805** (2007), 133.
- [6] N.M. Godjaev, I.S. Maksumov and I. Ismailoval, *J. Chem. Struct.* **24** (1983), 147.
- [7] S. Mondal, D.S. Chowdhuri, S. Ghosh, A. Misra and S. Dalai, *J. Mol. Struct.* **810** (2007), 81.

- [8] K. Nakamoto, *Infrared Spectra of Inorganic and Coordination Compounds*, Wiley, London, 1970.
- [9] J. Ockenga, K. Borchert, K. Rifai, M. Petermanns and S. Bischoff, Effect of glutamine-enriched total parenteral nutrition in patients with acute pancreatitis, *Clin. Nutr.* **21**(5) (2002), 409.
- [10] PQS Version 3.1, *Parallel Quantum Solutions*, 2013 Green Acres Road, Fayetteville, AR.
- [11] G.N. Ramachandran, *Biopolymers* **6** (1963), 1494.
- [12] G.N. Ramachandran, C. Ramakrishnan and V. Sasisekharan, *J. Mol. Biol.* **7** (1963), 95.
- [13] D.M.F. Savarese, G. Savy, L. Vahdat, P.E. Wischmeyer and B. Corey, Prevention of chemotherapy and radiation toxicity with glutamine, *Cancer Treat. Rev.* **29** (2003), 501.
- [14] K.M. Skubitz and P.M. Anderson, Oral glutamine to prevent chemotherapy induced stomatitis: A pilot study, *J. Lab. Clin. Med.* **127**(2) (1996), 223.
- [15] H.C.T. van Zaanen, H. van der Lelie, J.G. Timmer, P. Fürst and H.P. Sauerwein, *Cancer* **74**(10) (1994), 2879.