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Conformational Analysis of N- and C-Terminally Protected Tripeptide Model Glycyl-Isoleucine-Glycyl: An *ab initio* and DFT Study

B. Chahkandi[a,]*, M. Chahkandi[b] and B. Ashrafi[a]
[a]*Department of Chemistry, Shahrood Branch, Islamic Azad University, Shahrood, Iran*
[b]*Department of Chemistry, Hakim Sabzevari University, Sabzevar 96179-76487, Iran*

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An *ab initio* and density functional theory (DFT) study on conformational analysis of tripeptide model HCO-GLY-L-ILE-GLY-NH_2 is presented. The tripeptide was scanned around initial, central, and final residues, separately while for every scanning procedure the two other residues had been kept in the β conformation and side chain (SC) dihedral angles were maintained on the gauche$^-$ (g^-) state (χ_1, χ_2 = -60). Conformers (β_L, γ_L, γ_D, α_D, ε_D), (β_L, γ_L, γ_D), and (β_L, γ_L, γ_D, ε_L) were found through scanning of the tripeptide around initial, central, and the last amino acids, respectively. The geometry optimization and frequency calculation were performed at the HF/6-31G(*d*) and B3LYP/6-31G(*d*) levels of theory. In followings, comparison of the calculated thermodynamic data presents $\beta_L\beta_L\beta_L$ as the most stable conformer among the tripeptide minima on Ramachandran map.

Keywords: Tripeptide structures, *Ab initio* calculations, DFT, Ramachandran map, Conformers

INTRODUCTION

All of the reversible interactions in the biological systems could be controlled by hydrogen bonds (H-bonds), electrostatic, and van der Waals interactions. H-bonding between the CO and NH groups of the amino acid residues stabilizes the 3-D protein structure [1]. Among these non-covalent interactions, H-bonds play diverse roles including catalytic activation [2], constructing and control of crystalline network growing in crystal engineering point of view [3-5], progress the proton transfer reaction in water assisted tautomerism conversions [6-8], protein folding [9-11], and holding complementary strands of DNA together [1]. The protein folding has received intense study due to its fundamental importance in living organism [12,13]. Protein chemists have simplified their approach to the study of the protein folding by separating the problem of backbone (BB) from side-chain (SC) conformation [14]. The proteins are categorized with respect to their primary, secondary, and tertiary structures. As we know, the secondary and tertiary structures of proteins are derived from the primary one [15]. Today, most peptide and protein chemists are using one of the empirical force fields varieties to study the peptide and protein conformations [16]. For this purpose, folding reaction/energy was investigated *via* potential energy surfaces (PES), titled as “2 or 3-D Ramachandran map” [17-20]. A Ramachandran map, originally developed in 1963 by G. N. Ramachandran, *et al.* [21], is a way to visualize ψ against φ the backbone dihedral angles of amino acid residues. Since the partial-double-bond character keeps the peptide planar, ω angle at the peptide bond is normally 180° [22]. Figure 1 illustrates the definition of these dihedral angles [23]. Some of Ramachandran’s researches in the field of biophysics resulted in the elucidation of the collagen structure [24]. Therefore, Ramachandran map could be useful method within investigation of protein structures. The map should be kept in the peptide units and the BB of the protein chain can be described in the terms of Ramachandran angles (ϕ, ψ) (see Fig. 1) [25]. Protein folding is represented by the following partitioning of the potential energy function: E(polypeptide) = $f(\psi_0, \omega_0, \phi_1, \psi_1, \chi_1, \omega_1,..., \omega_{i-1}, \phi_i, \psi_i, \chi_i, \omega_i,..., \omega_{n-1}, \phi_n, \psi_n, \chi_n, \omega_n, \phi_{n+1})$. The

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*Corresponding author. E-mail: bchahkandi@gmail.com

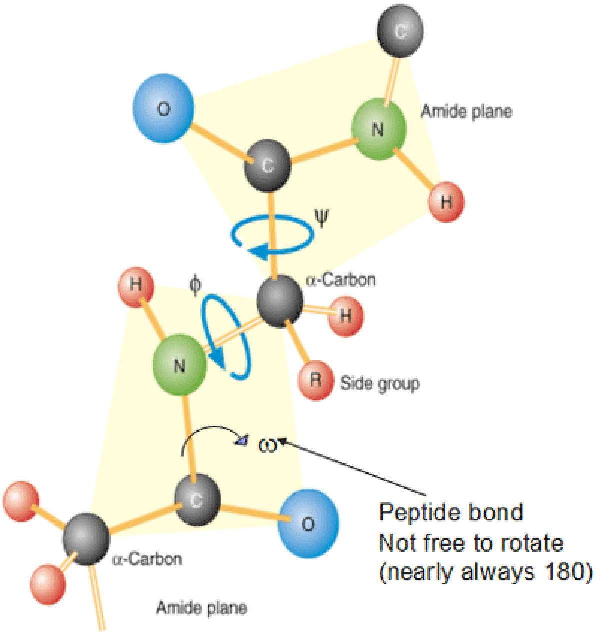


Fig. 1. Protein backbone dihedral angles ϕ, ψ, and ω [22].

SC dihedral angles of proteins are denoted as χ_1-χ_5, depending on the distance up the SC. The χ_1 dihedral angle is defined by atoms N-C^α-C^β-C^γ, the χ_2 dihedral angle is defined by atoms C^α-C^β-C^γ-C^δ, and so on [26]. As we know, Ramachandran map is used to determine the most stable BB conformers of peptides. Therefore, first of all, obtaining the most stable state of the SC is not avoidable. For any given amino acid, up to nine BB, stable conformers are topologically probable through 0 to 360° rotation of the ϕ_i and ψ_i the BB dihedral angles [27]. The most stable structures of different amino acids such as glycine and alanine have been studied in theoretical point of view [28,29]. Moreover, glycine and isoleucine amino acids could attract research interests because they were found to be prominent in stimulating protein production [30]. The detailed investigations about valine bearing one SC dihedral angles [31] and N-formylserinamide bearing two SC dihedral angles [32] could be found in the literature.

This work presents the conformational study of N- and C-terminal protected tripeptide "HCO-GLY-L-ILE-GLY-NH_2" within the variations of BB and SC. The initial step for generating PES for the studied tripeptide was a scan of SC about χ for the central amino acid, isoleucine, being varied, with two terminal amino acids maintained in β_L conformation. It led to finding the most stable conformers bearing respective SC dihedral angles χ_1 and χ_2. The same procedure was followed to find the most stable conformers within two terminal amino acids (glycine). This research aims at recognition of the most stable conformer among the tripeptide minima on Ramachandran map.

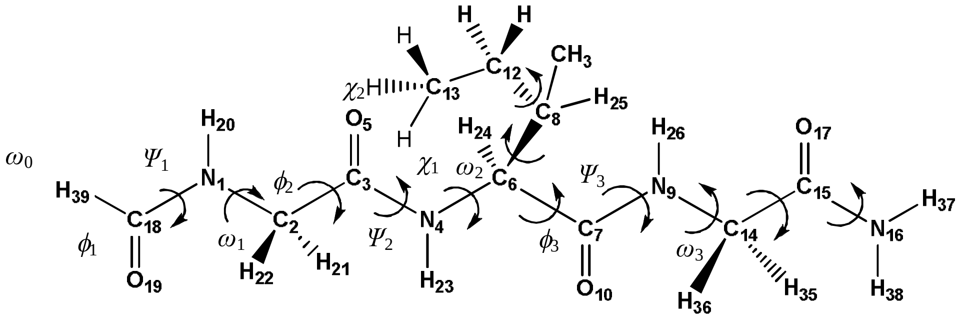
THEORETICAL METHODS

The optimization and frequency calculations of all conformers of tripeptide model HCO-GLY-L-ILE-GLY-NH_2 were carried out in the gas phase using Gaussian 98 [33] at the *Ab initio/*HF/6-31G (*d*) and DFT/B3LYP/6-31G (*d*) [34,35] levels of theory. The tripeptide divided into 5 sections: the N-terminal protecting group, the Gly residue, the ILeu residue, the Gly residue, and the C-terminal protecting group (Fig. 2). First of all, PES scans using the variable SC dihedral angle were made on the tripeptide. In order to determine the energy of BB conformations and obtaining the most stable one, these scans were run at 30° intervals, from 0° to 360° for SC dihedral angles χ_1 and χ_2. In following, the different conformers of the tripeptide HCO-GLY-L-ILE-GLY-NH_2 were optimized through restraining the two residues on the β_L conformation and varying the third residue within all of the nine possible forms on Ramachandran map (see Fig. 3). It would be noted that 25 most probable conformers were examined. At the end, potential energy, enthalpy, Gibbs free energy, and entropy of each conformer were calculated at the HF/6-31G (*d*) and B3LYP/6-31G (*d*) levels which resulted in identifying the most stable conformer.

RESULTS AND DISCUSSION

SC Dihedral Angles

To investigate the proper stability for the chosen conformers of tripeptide, SC dihedral angles (χ_1, χ_2) were changed from 0° to 360° using 30° increments. First of all, using χ_1 changing, optimization and frequency calculations for each pertinent conformer were performed at the HF/6-31G (*d*) and B3LYP/6-31G (*d*) levels that resulted in three minima with the sequence of state stabilizations -60° (g^-) > +60° (g^+) > 180 (anti) (see Table 1). In following, χ_1 was



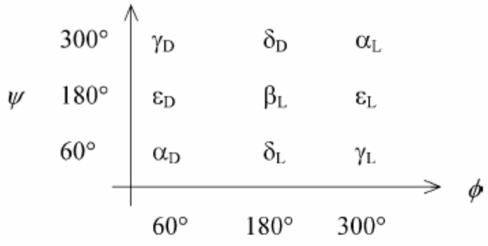
$\omega_0 =< H_{39}C_{18}N_1C_2$ $\quad \phi_1 =< C_{18}N_1C_2C_3$ $\quad \psi_2 =< N_4C_6C_7N_9$

$\omega_1 =< C_2C_3N_4C_6$ $\quad \phi_2 =< C_3N_4C_6C_7$ $\quad \psi_3 =< N_9C_{14}C_{15}N_{16}$

$\omega_2 =< C_6C_7N_9C_{14}$ $\quad \phi_3 =< C_7N_9C_{14}C_{15}$ $\quad \chi_1 =< N_4C_6C_8C_{12}$

$\omega_3 =< C_{14}C_{15}N_{16}H_{37}$ $\quad \psi_1 = < N_1C_2C_3N_4$ $\quad \chi_2 =< C_6C_8C_{12}C_{13}$

Fig. 2. Topological f of Ramachandran map E = f (ϕ_i , ψ_i), associated with an amino acid residue.



ψ \ φ	60°	180°	300°
300°	γ_D	δ_D	α_L
180°	ε_D	β_L	ε_L
60°	α_D	δ_L	γ_L

Fig. 3. Tripeptid model HCO-GLY-L-ILE-GLY-NH$_2$. The tripeptid divided into 5 sections: the N-terminal protecting group, the Gly residue, the Ileu residue, the Gly residue, and the C-terminal protecting group, with each numbered separately according to a standardized modular numbering system.

kept at -60° and related conformers were found through rotation of χ_2 around chain C6-C8-C12-C13 from 0° to 360° in increments of 30°. Finally, the optimization and frequency calculations of the conformers at the above mentioned levels were carried out. It was resulted in three minima with the stabilization energy order of -60° (g$^-$) > 180° (anti) > 210° (see Table 1). It can be concluded that the most stable conformer bear χ_1 and χ_2 = -60°. Therefore, these two SC dihedral angles were restrained at -60° (Fig. 4).

Topographical Scan of BB

For each scanning step, two residues of tripeptide "HCO-GLY-L-ILE-GLY-NH$_2$" were fixed at the β_L conformation and the third one was varied for the nine possible minima present on Ramachandran map. Up to nine minima is expected in each of these three scans. This would lead to the 3 × 9 = 27 total possible conformers for β_L. Since the fully extended $\beta_L\beta_L\beta_L$ conformer would occur three times, only 25 unique conformers could be established. In this stage, the most stable conformer was determined through the change of dihedral angles of initial, second, and third amino acids. For this purpose, the dihedral angles of initial (ϕ_1, ψ_1), central (ϕ_2, ψ_2), and last amino acid residues (ϕ_3, ψ_3) were separately changed *via* three steps (1th to 3th steps, respectively), while for every step the two rest amino acids had been kept in the β_L conformation. In followings, performing the optimization and frequency calculations led to finding the minima conformers. As a result, three, five, and four stable conformers for 1th to 3th steps have been found, respectively. The $\beta_L\beta_L\beta_L$, $\beta_L\beta_L\gamma_D$, $\beta_L\beta_L\gamma_L$, and $\beta_L\beta_L\varepsilon_L$ are the most stable conformers, while conformer having the second and the last amino acids with the β_L conformation ($\varepsilon_L\beta_L\beta_L$) was not obtained. Another interesting feature is the absence of $\alpha_L\beta_L\beta_L$, $\alpha_L\beta_L\beta_L$, $\delta_L\beta_L\beta_L$, $\delta_D\beta_L\beta_L$, $\varepsilon_D\beta_L\beta_L$, $\beta_L\beta_L\alpha_L$, $\beta_L\beta_L\alpha_D$, $\beta_L\beta_L\delta_L$, $\beta_L\beta_L\delta_D$, and $\beta_L\beta_L\varepsilon_D$ conformers on Ramachandran map. Five minima $\beta_L\beta_L\beta_L$, $\beta_L\gamma_L\beta_L$, $\beta_L\gamma_D\beta_L$, β_L $\alpha_D\beta_L$, and $\beta_L\varepsilon_D\beta_L$ were found for the tripeptide HCO-GLY$_{[\beta L]}$-L-ILE$_{[x]}$-GLY$_{[\beta L]}$-NH$_2$, while conformers $\beta_L\alpha_L\beta_L$, $\beta_L\delta_L\beta_L$, $\beta_L\delta_D\beta_L$, and $\beta_L\varepsilon_L\beta_L$ did not correspond to minima. Calculation results at both employed levels are similar (Table 2). It can be concluded that the $\beta_L\beta_L\beta_L$ conformer has the lowest energy among the all possible models x-$\beta_L\beta_L$,

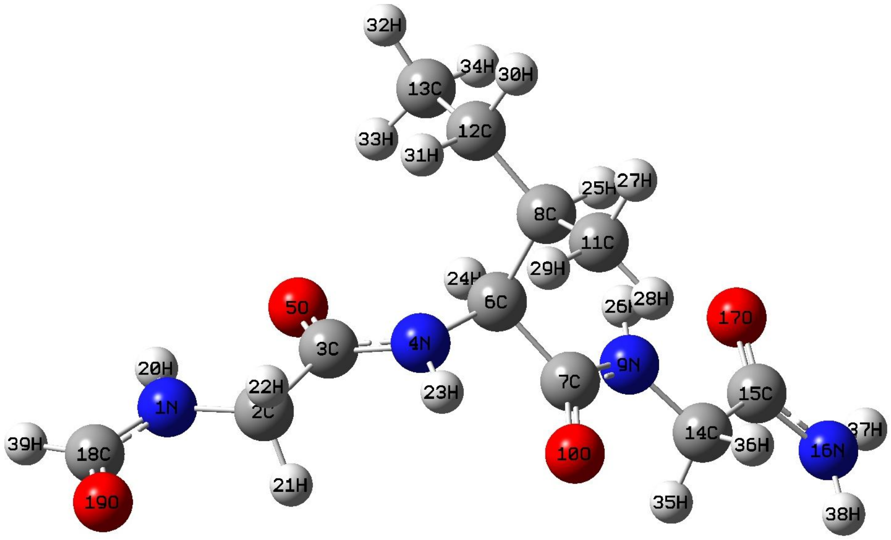


Fig. 4. Model of the most stable tripeptide conformer bearing χ_1 and χ_2 = -60°.

Table 1. Energies and Relative Energies[a] oV various SC Dihedral Angles (χ_1 and χ_2[b]) for HCO-GLY-L-ILE-GLY-NH_2 rieptide at the HF/6-31G (*d*) and B3LYP/6-31G (*d*) Levels of Theory

	χ_1 (4-6-8-12)				**χ_2 (6-8-12-13)**			
	HF/6-31G (*d*)		**B3LYP/6-31G (*d*)**		**HF/6-31G (*d*)**		**B3LYP/6-31G (*d*)**	
χ_i	**E**	**ΔE**	**E**	**ΔE**	**E**	**ΔE**	**E**	**ΔE**
0	-945.5081858	7.28	-951.1715893	6.39	-945.5064626	8.40	-951.1692223	8.21
30	-945.5140924	3.58	-951.1764782	3.32	-945.5081240	7.37	-951.1713299	6.88
60	**-945.5193142**	**0.30**	**-951.1816651**	**0.07**	-945.5130436	4.28	-951.17587778	4.03
90	-945.5170584	1.71	-951.1794976	1.43	-945.5150980	2.99	-951.1775533	2.98
120	-945.5124250	4.62	-951.1757928	3.75	-945.5115580	5.22	-951.1743099	5.01
150	-945.5159176	2.43	-951.1781392	2.28	-945.5137597	3.83	-951.1764255	3.69
180	**-945.5184164**	**0.86**	**-951.1802913**	**0.93**	-945.5191941	0.42	-951.1812499	0.66
210	-945.5155751	2.64	-951.1782442	2.22	-945.5190697	0.50	-951.1810679	0.77
240	-945.5146032	3.25	-951.1771777	3.89	-945.5159370	2.47	-951.1782908	2.52
270	-945.5180946	1.06	-951.1802383	0.96	-945.5178402	1.27	-951.1800740	1.40
300	**-945.5197958**	**0.00**	**-951.1817797**	**0.00**	**-945.5198675**	**0.00**	**-951.1823017**	**0.00**
330	-945.5136780	3.84	-951.1765071	3.30	-945.5142862	3.50	-951.176085	3.90
360	-945.5081858	7.28	-951.175893	6.39	-945.5064626	8.40	-951.1692223	8.21

[a] Energies and relative energies are in hartree and kcal mol^{-1}, respectively. [b] In all calculations for χ_2, the χ_1 SC dihedral angel was set at the most stable state g^-.

Table 2. Summary of Energies, Relative Potential Energies, and Dihedral Angles for HCO-GLY-L-ILE-GLY-NH_2 of the x-$\beta_L\beta_L$[a], β_L-x-β_L[b] and $\beta_L\beta_L$-x[c] States Calculated at the HF/6-31G (*d*) and B3LYP/6-31G (*d*) Levels of Theory

Level	**BB conformation**		***Gly₁***			***IsoLeu***			***Gly₂***				
		ω_0 (18-1)	**Φ_1 (1-2)**	**Ψ_1 (2-3)**	**ω_1 (3-4)**	**Φ_2 (4-6)**	**Ψ_2 (6-7)**	**ω_2 (7-9)**	**Φ_3 (9-14)**	**Ψ_3 (14-15)**	**ω_3 (15-16)**	**Energy (Hartree)**	**ΔE (Kcal mol^{-1})**
HF/ 6-31G (*d*)	**$\beta_L\beta_L\beta_L$**	179.73	-178.00	177.43	170.49	-128.98	160.329	177.97	-178.30	179.39	178.89	-945.5205927	0.00
	$\gamma_L\beta_L\beta_L$	-179.52	-87.42	74.24	176.32	-122.75	158.645	178.50	-179.87	179.03	178.59	-945.516785	2.39
	$\gamma_D\beta_L\beta_L$	-174.16	83.36	-73.90	160.57	-170.54	164.106	-178.42	177.88	177.70	177.33	-945.5182157	1.49
B3LYP/ 6-31G (*d*)	**$\beta_L\beta_L\beta_L$**	179.48	-178.00	176.51	168.72	-123.02	161.769	177.72	179.93	179.67	179.12	-951.1828823	0.00
	$\gamma_L\beta_L\beta_L$	-179.55	-87.42	70.45	177.38	-127.95	156.700	178.37	-177.02	179.71	179.36	-951.1798462	1.90
	$\gamma_D\beta_L\beta_L$	179.58	83.36	-63.22	170.32	-128.84	161.590	177.99	-179.66	178.47	-179.10	-951.1795102	2.12
HF/ 6-31G (*d*)	**$\beta_L\beta_L\beta_L$**	-179.73	-178.02	177.45	-170.50	-128.98	160.327	177.97	-178. 29	179.39	178.89	-945.5205927	0.00
	$\beta_L\gamma_L\beta_L$	-179.97	175.98	-178.79	-175.05	-111.72	6.691	-176.04	-178.82	-178.34	-178.10	-945.5178475	1.72
	$\beta_L\gamma_D\beta_L$	179.52	179.85	173.49	174.40	66.17	-21.088	-179.68	-173.75	173.57	176.93	-945.5075746	8.17
	$\beta_L\alpha_D\beta_L$	-177.58	177.95	-179.74	173.58	49.25	42.547	-174.77	167.28	175.31	176.61	-945.5101695	6.54
	$\beta_L\varepsilon_D\beta_L$	178.91	174.78	-171.31	-163.75	45.92	-150.141	-178.51	-175.07	-177.58	-176.62	-945.507413	8.27
B3LYP/ 6-31G (*d*)	**$\beta_L\beta_L\beta_L$**	-178.84	-178.02	177.20	-168.54	-132.78	161.757	177.51	-178. 51	179.13	179.25	-951.1828804	0.00
	$\beta_L\gamma_L\beta_L$	-179.03	175.98	-171.77	-177.01	-87.84	60.243	-179.65	175.30	-179.34	179.75	-951.1781243	2.98
	$\beta_L\gamma_D\beta_L$	179.76	179.85	175.27	175.92	62.67	-30.172	179.46	-169.82	173.95	176.78	-951.1710089	7.45
	$\beta_L\alpha_D\beta_L$	-177.94	177.95	-176.57	175.37	48.13	42.467	-171.71	157.51	177.80	178.09	-951.1720503	6.80
	$\beta_L\varepsilon_D\beta_L$	178.95	174.78	-169.25	-162.35	44.77	-149.370	179.98	-168.32	-178.48	-176.07	-951.1691846	8.59
HF/ 6-31G (*d*)	**$\beta_L\beta_L\beta_L$**	179.73	-178.00	177.43	170.49	-128.98	160.329	177.97	-178.30	179.39	178.89	-945.5205927	0.00
	$\beta_L\beta_L\gamma_L$	-179.91	-178.54	177.26	170.93	-127.10	159.215	-179.62	-85.40	70.60	-177.98	-945.5186306	1.23
	$\beta_L\beta_L\gamma_D$	-179.95	-179.22	177.92	171.66	-127.67	159.081	175.56	86.48	-69.08	177.17	-945.5186989	1.19
	$\beta_L\beta_L\varepsilon_L$	-179.92	-179.12	177.56	171.40	-127.96	155.974	165.26	-82.09	167.05	-175.04	-945.5185717	1.27
B3LYP/ 6-31G (*d*)	**$\beta_L\beta_L\beta_L$**	179.68	-178.00	177.58	168.99	-132.65	161.584	178.45	-177.35	179.81	179.15	-951.1828869	0.00
	$\beta_L\beta_L\gamma_L$	-179.48	-178.54	176.23	170.26	-130.67	161.836	-179.04	-85.05	67.23	-178.75	-951.1820323	0.54
	$\beta_L\beta_L\gamma_D$	-179.88	-179.22	179.52	171.12	-129.73	160.811	175.55	82.46	-69.69	174.69	-951.1819197	0.61
	$\beta_L\beta_L\varepsilon_L$	-178.98	-179.12	176.38	168.90	-133.39	161.755	178.10	-118.89	178.96	-179.10	-951.1828797	0.0040

[a] $\alpha_L\beta_L\beta_L$, $\alpha_D\beta_L\beta_L$, $\delta_L\beta_L\beta_L$, $\delta_D\beta_L\beta_L$, $\varepsilon_D\beta_L\beta_L$, $\varepsilon_L\beta_L\beta_L$, [b] $\beta_L\alpha_L\beta_L$, $\beta_L\delta_L\beta_L$, $\beta_L\delta_D\beta_L$, $\beta_L\varepsilon_L\beta_L$, and [c] $\beta_L\beta_L\alpha_L$, $\beta_L\beta_L\alpha_D$, $\beta_L\beta_L\delta_L$, $\beta_L\beta_L\delta_D$, $\beta_L\beta_L\varepsilon_D$ conformers not found.

Table 3. Thermodynamic Properties for the Optimized Geometries of HCO-GLY-L-ILE-GLY-NH_2 of the x-$\beta_L\beta_L$[a], β_L- and $\beta_L\beta_L$-x[c] States at the HF/6-31G (*d*) and B3LYP/6-31G (*d*) Levels of Theory

BB conformation	**HF/6-31G (*d*)**						**B3LYP/6-31G (*d*)**					
	ε_0+G_{corr}	ΔG	ε_0+H_{corr}	ΔH	S	ΔS	ε_0+G_{corr}	ΔG	ε_0+H_{corr}	ΔH	S	ΔS
LβLβLβ	-945.222447	0.00	-945.146410	0.00	160.033	0.00	-950.911814	0.00	-950.832565	0.00	166.792	0.00
LβLβLγ	-945.218042	2.76	-945.142246	2.61	159.526	-0.51	-950.906732	3.19	-950.829080	2.19	163.431	-3.36
LβLβDγ	-945.218244	2.64	945.143384-	1.90	157.557	2.48-	-950.907267	2.85	950.828827-	2.35	165.091	-1.70
LβLβLβ	-945.222447	0.00	-945.146410	0.00	160.033	0.00	-950.911667	0.00	-950.832538	0.00	166.542	0.00
LβLγLβ	-945.220327	1.35	-945.143754	2.93	161.162	1.13	-950.908867	1.76	-950.827872	2.93	170.470	3.93
LβDγLβ	-945.209879	7.90	-945.133278	7.46	161.219	1.19	-950.900871	6.77	-950.820651	7.46	168.837	2.29
LβDα Lβ	-945.211755	6.71	-945.136168	6.72	159.086	0.95-	-950.900521	6.99	-950.821837	6.72	165.603	-0.94
LβLεDβ	-945.208551	8.72	-945.133175	8.54	158.643	-1.39	-950.897605	8.82	-950.818920	8.54	165.607	-0.94
LβLβLβ	-945.222447	0.00	-945.146410	0.00	160.033	0.00	-950.911722	0.00	-950.832560	0.00	166.609	0.00
LγLβLβ	-945.219103	0.0033	-945.143867	0.0025	158.347	1.69-	-950.908062	2.30	-950.831028	0.96	162.131	-4.48
DγLβLβ	-945.219294	0.0031	-945.143954	0.0024	158.567	-1.47	-950.907965	2.36	-950.830942	1.01	162.109	-4.50
βLβLεL	-945.219855	0.003	-945.144029	0.0024	159.90	0.44-	-950.911688	0.15	-950.832555	0.04	166.549	-0.37

[a] $\alpha_L\beta_L\beta_L$,$\alpha_D\beta_L\beta_L$,$\delta_L\beta_L\beta_L$,$\delta_D\beta_L\beta_L$, $\varepsilon_D\beta_L\beta_L$, $\varepsilon_L\beta_L\beta_L$,, [b] $\beta_L\alpha_L\beta_L$, $\beta_L\delta_L\beta_L$,$\beta_L\delta_D\beta_L$,$\beta_L\varepsilon_L\beta_L$, and [c] $\beta_L\beta_L\alpha_L$,$\beta_L\beta_L\alpha_D$,$\beta_L\beta_L\delta_L$,$\beta_L\beta_L\delta_D$, $\beta_L\beta_L\varepsilon_D$ conformers not found.

Table 4. Resulting Optimized Conformers at HF/6-31G (*d*) and B3LYP/6-31G (*d*) Levels of T. 12 Stable Conformers were Found (Output), 15 were Converged to Different Conformers with Greater Stability (Migration Pattern)

	$x\beta_L\beta_L$			$\beta_Lx\beta_L$			$\beta_L\beta_Lx$		
Input Data	$\gamma_D\beta_L\beta_L$ $\varepsilon_D\beta_L\beta_L$ $\alpha_D\beta_L\beta_L$	$\delta_D\beta_L\beta_L$ $\beta_L\beta_L\beta_L$ $\delta_L\beta_L\beta_L$	$\alpha_L\beta_L\beta_L$ $\varepsilon_L\beta_L\beta_L$ $\gamma_L\beta_L\beta_L$	$\beta_L\gamma_D\beta_L$ $\beta_L\varepsilon_D\beta_L$ $\beta_L\gamma_L\beta_L$	$\beta_L\delta_D\beta_L$ $\beta_L\beta_L\beta_L$ $\beta_L\delta_L\beta_L$	$\beta_L\alpha_L\beta_L$ $\beta_L\varepsilon_L\beta_L$ $\beta_L\alpha_D\beta_L$	$\beta_L\beta_L\gamma_D$ $\beta_L\beta_L\varepsilon_D$ $\beta_L\beta_L\alpha_D$	$\beta_L\beta_L\delta_D$ $\beta_L\beta_L\beta_L$ $\beta_L\beta_L\delta_L$	$\beta_L\beta_L\alpha_L$ $\beta_L\beta_L\varepsilon_L$ $\beta_L\beta_L\gamma_L$
Output Data	$\gamma_D\beta_L\beta_L$ *N.F* *N.F*	*N.F* $\beta_L\beta_L\beta_L$ *N.F*	*N.F* *N.F* $\gamma_L\beta_L\beta_L$	$\beta_L\gamma_D\beta_L$ $\beta_L\varepsilon_D\beta_L$ $\beta_L\alpha_D\beta_L$	*N.F* $\beta_L\beta_L\beta_L$ *N.F*	*N.F* *N.F* $\beta_L\gamma_L\beta_L$	$\beta_L\beta_L\gamma_D$ *N.F* *N.F*	*N.F* $\beta_L\beta_L\beta_L$ *N.F*	*N.F* $\beta_L\beta_L\varepsilon_L$ $\beta_L\beta_L\gamma_L$
Migration Pattern	*F* $\beta_L\beta_L\beta_L$ $\gamma_D\beta_L\beta_L$	$\gamma_D\beta_L\beta_L$ *F* $\gamma_L\beta_L\beta_L$	$\gamma_L\beta_L\beta_L$ $\beta_L\beta_L\beta_L$ *F*	*F* *F* *F*	$\beta_L\delta_L\beta_L$ *F* $\beta_L\gamma_L\beta_L$	$\beta_L\delta_L\beta_L$ $\beta_L\beta_L\beta_L$ *F*	*F* $\beta_L\beta_L\beta_L$ $\beta_L\beta_L\gamma_D$	$\beta_L\beta_L\gamma_D$ *F* $\beta_L\beta_L\gamma_L$	$\beta_L\beta_L\gamma_L$ *F* *F*

β_L-x-β_L, and $\beta_L\beta_L$-x of the studied tripeptide (see Table 2). Thus, the relative energies of the other conformers were compared with the $\beta_L\beta_L\beta_L$ structure. The obtained results of the conformers of β_L-x-β_L model establish the stability order of $\beta_L\beta_L\beta_L > \beta_L\gamma_L\beta_L > \beta_L\alpha_D\beta_L > \beta_L\gamma_D\beta_L > \beta_L\varepsilon_D\beta_L$ (see Table 2). The stability order of x-$\beta_L\beta_L$ model conformers at HF/6-31G (*d*) level is $\beta_L\beta_L\beta_L > \gamma_D\beta_L\beta_L > \gamma_L\beta_L\beta_L$ while, $\gamma_L\beta_L\beta_L$ is more stable than $\gamma_D\beta_L\beta_L$ at the B3LYP/6-31G (*d*) level. For $\beta_L\beta_L$-x model, the sequence of $\beta_L\beta_L\beta_L > \beta_L\beta_L\gamma_D > \beta_L\beta_L\gamma_L > \beta_L\beta_L\varepsilon_L$ at the HF/6-31G (*d*) and $\beta_L\beta_L\beta_L > \beta_L\beta_L\varepsilon_L > \beta_L\beta_L\gamma_L > \beta_L\beta_L\gamma_D$ order at the B3LYP/6-31G (*d*) levels are dominated. The key thermodynamic functions namely ΔH, ΔG, and ΔS were obtained using frequency calculations for all of the found minima in Ramachandran map (Table 3). According to our computational results, Gibbs free energy and enthalpy of $\beta_L\beta_L\beta_L$ conformer of x-$\beta_L\beta_L$ model have minimum and entropy has the maximum values at both employed levels. Ordered stable minima within Gibbs free energy is $\beta_L\beta_L\beta_L > \gamma_D\beta_L\beta_L > \gamma_L\beta_L\beta_L$ at the both used levels. Based on employed levels of calculation, ordering of stable minima within entropy and enthalpy show different trends, as $\beta_L\beta_L\beta_L > \gamma_D\beta_L\beta_L > \gamma_L\beta_L\beta_L$ stands for HF/6-31G (*d*) and $\beta_L\beta_L\beta_L > \gamma_L\beta_L\beta_L > \gamma_D\beta_L\beta_L$ establishes for B3LYP/6-31G (*d*) levels. $\beta_L\beta_L\beta_L$ conformer of β_L-x-β_L model have the minimum values of Gibbs free energy and enthalpy at the both levels of calculations. While $\beta_L\gamma_D\beta_L$ and $\beta_L\gamma_L\beta_L$ conformers of this model have the maximum value of entropy at the both levels. The calculated ΔG and ΔH at the both levels show the same sequence as $\beta_L\beta_L\beta_L > \beta_L\gamma_L\beta_L > \beta_L\alpha_D\beta_L > \beta_L\gamma_D\beta_L > \beta_L\varepsilon_D\beta_L$ but orders of calculated ΔS at HF/6-31G (*d*) and B3LYP/6-31G (*d*) levels are $\beta_L\gamma_D\beta_L > \beta_L\gamma_L\beta_L > \beta_L\beta_L\beta_L > \beta_L\alpha_D\beta_L > \beta_L\varepsilon_D\beta_L$ and $\beta_L\gamma_L\beta_L > \beta_L\gamma_D\beta_L > \beta_L\beta_L\beta_L > \beta_L\varepsilon_D\ \beta_L > \beta_L\alpha_D\ \beta_L$, respectively. Based on our results, $\beta_L\beta_L\beta_L$ conformer is more stable than the other conformers created by change of the last amino acid configuration in $\beta_L\beta_L$-x state. Moreover, calculated ΔG and ΔH values at two employed levels suggest no considerable difference. Regarding to the obtained results, one can conclude that the $\beta_L\beta_L\beta_L$ conformer has the highest S value. Generally, maximum value of S is, minimum values of E, G, and H functions are, and *vice versa*. However, $\beta_L\beta_L\beta_L$ conformer has the lowest total energy among the all possible ones (see Table 3).

Available Conformers of HCO-GLY-L-ILE-GLY-NH$_2$ and Migration Patterns

Based on the optimization calculations of 27 probable conformers at both levels, 15 ones converged by migration and 12 unique intrinsic stable ones exist (Table 4). Moreover, base on the energy calculations at both levels, nine of the all 27 conformers have minima energy. The 15 unstable conformers converged to the other conformations with higher stability (Fig. 3). The $\beta_L\beta_L\varepsilon_D$, $\varepsilon_D\beta_L\beta_L$, and $\beta_L\beta_L\varepsilon_L$ conformers inclined toward more stable $\beta_L\beta_L\beta_L$ conformer. Also, $\beta_L\beta_L\delta_L$, $\beta_L\beta_L\alpha_L$, $\alpha_L\beta_L\beta_L$, $\delta_L\beta_L\beta_L$, and $\beta_L\delta_L\beta_L$ conformers inclined toward $\beta_L\beta_L\gamma_L$, $\gamma_L\beta_L\beta_L$, and $\beta_L\gamma_L\beta_L$ conformers, respectively. An interesting result is that β_L-x-β_L state was recognized as the most stable conformers among all the three states.

CONCLUSIONS

An amino acid residue in a peptide is influenced by its neighbors. This effect is stronger about the adjacent bonds and get weaker as we move away from the central amino acid residue bearing big SC such as Isoleucin. The obtained results of the present work within calculations performed at the HF/6-31G (*d*) and B3LYP/6-31G (*d*) levels of theory indicate that:

1- The most stable conformer bears χ_1 and χ_2 SC dihedral angles equal to -60° (g$^-$ state).
2- On Ramachandran map, 25 BB conformers of tripeptide HCO-GLY-L-ILE-GLY-NH$_2$ were investigated which 12 intrinsic stable ones with maintained SC dihedral angels in g$^-$ states were found and the rest ones were converged to different conformers with higher stability.
3- 12 found stable conformers for x-$\beta_L\beta_L$, β_L-x-β_L, and $\beta_L\beta_L$-x states are (β_L, γ_L, γ_D), (β_L, γ_L, γ_D, α_D, ε_D), and (β_L, γ_L, γ_D, ε_L), respectively.
4- As a general rule, 15 unstable conformers are migrated to conformers having β_L, γ_L, γ_D or δ_L as x residue (see Table 4).
5- The most stable conformer among all of the found stable ones is $\beta_L\beta_L\beta_L$.

REFERENCES

[1] H. Rangwala, G. Karypis (Eds.), Introduction to

Protein Structure Prediction: Methods and Algorithms, J. Wiley, New York, 2011.
[2] H. Eshtiagh-Hosseini, M. Chahkandi, M.R. Housaindokht, M. Mirzaei, Polyhedron 60 (2013) 93.
[3] M. Mirzaei, H. Eshtiagh-Hosseini, M. Chahkandi, N. Alfi, A. Shokrollahi, N. Shokrollahi, A. Janiak, Cryst. Eng. Comm. 14 (2012) 8468.
[4] M. Mirzaei, H. Eshtiagh-Hosseini, M. Mohammadi Abadeh, M. Chahkandi, A. Frontera, A. Hassanpoor, Cryst. Eng. Comm. 15 (2013) 1404.
[5] H. Eshtiagh-Hosseini, M. Mirzaei, M. Biabani, V. Lippolis, M. Chahkandi, C. Bazzicalupi, Cryst. Eng. Comm. 15 (2013) 6752.
[6] B. Chahkandi, S.F. Tayyari, M. Bakhshaei, M. Chahkandi, J. Mol. Graph. Model. 44 (2013) 120.
[7] A. Karton, R.J. O'Reilly, L.J. Radom, J. Phys. Chem. A 116 (2012) 4211.
[8] S. Nachimuthu, J. Gao, D.G. Truhlar, Chem. Phys. 400 (2012) 8.
[9] N. Kobko, J.J. Dannenberg, J. Phys. Chem. A 107 (2003) 10389.
[10] V. Daggett, Chem. Rev. 106 (2006) 1898.
[11] A. Ben-Naim, J. Phys. Chem. 95 (1991) 1437.
[12] C.M. Dobson, J. Trends Biochem. 24 (1999) 329.
[13] C.D. Keefe, K.J. Pearson, J. Theochem. Canada 679 (2004) 65.
[14] C.M. Dobson, Phil. Trans. R. Soc. Lond. B 356 (2001) 133.
[15] A. Perczel, O. Farkas, I.G. Csizmadia, J. Mol. Struct. (Theochem.) 540 (2001) 271.
[16] R.S. Corey, L. Pauling, The Fundamental Dimensions of Polypeptide Chains, London, 1953, p. 10-20.
[17] A.V. Mikhonin, S.V. Bykov, N.S. Myshakina, S.A. Asher, J. Phys. Chem. B. 110 (2006) 1928.
[18] B. Chahkandi, B.S. Hosseini, Wseas Transactions on Biology and Biomedicine 6 (2009) 89.
[19] S. Basu, D. Bhattacharyya, R. Banerjee, Biophysical J. 102 (2012) 2605.
[20] B.E. Bowler, Curr. Opin. Struc. Biol. 22 (2012) 4.
[21] G.N. Ramachandran, C. Ramakrishnan, V. Sasisekharan, J. Mol. Bio. 7 (1963) 95.
[22] L. Pauling, H.R. Corey, H.R. Branson, Proceedings National Academy of Sciences USA 37 4 (1951) 205.
[23] It can be cited as: http://www.molecularsciences.org/book/export/html/128
[24] a) G.N. Ramachandran, V. Sasisekharan, Y.T.T. Hathachari, Structure of Collagen at the Molecular Level in collagen, J. Wiley, New York, 1962, p. 81-115; b) G.N. Ramachandran, M. Bansal, R.S. Bhatnagar, Biochimica et Biophysica Acta (BBA)-Protein Structure 322 (1973) 166.
[25] G.N. Ramachandran, V. Sasisekharan, Adv. Protein Chem. 23 (1968) 283.
[26] E. Hcilbronner, J. Pure. Appl. Chem. 40 (1974) 291.
[27] N.I. Phillipsa, R. Jenness, J. Biochim. Biophys. Acta 229 (1971) 1.
[28] A. Perczel, O. Farkas, I.G. Csizmadia, J. Am. Chem. Soc. 117 (1995) 1653.
[29] H.A. Baldoni, G.N. Zamarbide, R.D. Enriz, E.A. Jauregui, O. Farkas, A. Perczel, S.J. Salpietro, I.G. Csizmadia, J. Mol. Struct. 500 (2000) 97.
[30] S. Miyashiro, H. Enei, Y. Hirose, S. Udaka, Agric. Biol. Chem. 44 (1980) 105.
[31] A. Perczel, M. Kajtar, J.F. Marcoccia, I.G. Csizmadia, J. Mol. Struct. (Theochem.) 232 (1991) 291.
[32] G. Endredi, A. Perczel, O. Farkas, M.A. McAllister, G.I. Csonka, J. Ladik, I.G. Csizmadia, J. Mol. Struct. (Theochem.) 391 (1997) 15.
[33] M.J. Frisch, *et al.* GAUSSIAN 98, RevisionA.9, Gaussian, Inc., Pittsburgh Pople, PA, 1998.
[34] C. Lee, R.G. Parr, W. Yang, Phys. Rev. B 37 (1988) 785.
[35] A.D. Becke, J. Chem. Phys. 98 (1993) 5648.