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Conformational effects of one glycine residue on the other glycine residues in the Ac-Gly-Gly-Gly-NHMe tripeptide motif: an ab initio exploratory study

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Abstract

Ab initio molecular computations were carried out on the tripeptide model, Ac-Gly-Gly-Gly-NHMe at the RHF/3-21G ab initio level of theory. Two of the glycine residues were chosen at a time to be in the fully extended, or β (C_5) conformation, in order to monitor the effects on the third residue with varying the backbone conformation. The topologies of each of the three Ramachandran type conformational potential energy surfaces were analyzed and five minima (β, γ_L, γ_D, δ_L, δ_D) associated with each one of the three glycine residues, were located for each surface. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Ab initio; Peptides; Glycine; Gly–Gly–Gly

1. Introduction

In a tripeptide, three amino acid residues are bound together at their amide groups, forming a short oligopeptide chain. This work presents the smallest possible tripeptide motif: C- and N-protected triglycine, Ac-Gly-Gly-Gly-NHMe. All other residues exist as pairs of enantiomers (L and D stereoisomers), since they have stereo centers at their α carbons. As glycine has a hydrogen (H) atom as side chain, it is thought to be achiral, that is, it has no stereoisomers. Consequently, glycine can also be regarded as an honorary D-amino just like an honorary L-amino acid.

Glycine occupies very little space and thus allows different polypeptide strands to easily come together in restricted spaces. Thus, it plays a major role in protein folding, such as in beta turns or hairpin conformations, which are among the simplest secondary structural elements occurring at the short loop regions between anti-parallel hydrogen bonded beta-strands. Glycine may be labeled as an insignificant amino acid due to its side chain consisting of only a H atom, however, in protein structure simplicity is of great significance [1].

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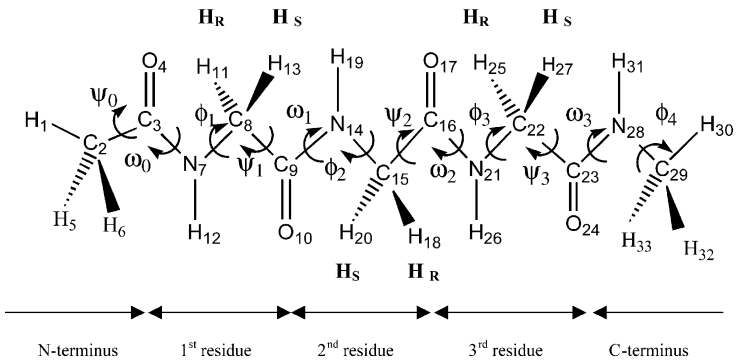

Structure 1.

It has become customary to classify proteins in their primary, secondary, and tertiary structures. The DNA molecule can predetermine only the sequence or the primary structure of the amino acids in a protein. The secondary and tertiary structures are not coded directly by the DNA; therefore it is assumed that they must be a consequence of the primary structure. These higher order structures can be defined in terms of a set of torsional angels (ϕ, ψ, ω) (Structure 1), associated with the peptide backbone making up the oligopeptide or polypeptide chain [2–4]. The detailed study of the backbone conformations of glycine can be used to simplify and provide information for future studies of longer polypeptide chains. From this 'symmetric' glycine standard, other tripeptide combinations may be better evaluated and understood. Following this, different tripeptide blocks could then be put together in selected combinations and optimized more efficiently.

Protein chemists have simplified their approach to the study of protein folding by separating the problem of backbone conformation from side-chain conformation, as well as from the problems of nearest neighbors and long-range interactions. According to this approach, the backbone conformational problems of a protein might be viewed in terms of corresponding conformational potential energy surfaces (PESs) in which long-range interactions are not present.

The simplest amino acids, such as glycine [5–10] and alanine [5–9,11–13] were among the first studied, followed by valine [7,14], which has one side-chain torsional angle was next. Subsequently, *N*-formylserinamide [15–21], which has two side-chain torsional angles, was investigated in considerable detail. Phenylalanine [22–24], which also has two side-chain torsional angles, was also subjected to conformational study even though the side-chain of phenylalanine is considerably larger than that of serine. In addition, conformational studies have been performed on proline [25], aspartate [26], aspargine [27], cystine and selenocystine [28]. Ab initio studies have not been exclusively limited to monoglycine. Conformational studies have been performed on dialanine [11,29–32], trialanine [33], tetra-alanine [34–37], as well as oligoalanine [38].

In order to completely characterize the topologically probable set of the conformers of a glycine tripeptide, it may be divided into three separate segments, as represented in Structure 1 whereby sequence specific dihedral angles are specified by ω_I, ϕ_I, ψ_I (the subscript refers to residue in position I). The prochiral hydrogens (H_R and H_S) are also marked in Structure 1.

As illustrated in Structure 1, *N*-acetyl and *N*-methylamide were used as protecting end groups to mimic the steric effects of the neighboring amino acid residues. In this study, the tripeptide was scanned about each of its residues, while keeping the other two residues in the β (C_5) conformation. Multi-dimensional conformational analysis (MDCA)—a systematic method to predict the location of all minima as input for ab initio calculations—was used to predict all topologically probable conformers. The Ramachandran PESs associated with a single amino acid has nine discrete possible conformations labeled as α_L, α_D, β, γ_L, γ_D, δ_L, δ_D, ε_L, ε_D. The topological arrangement of these minima and their defined dihedral angles are shown in Fig. 1.

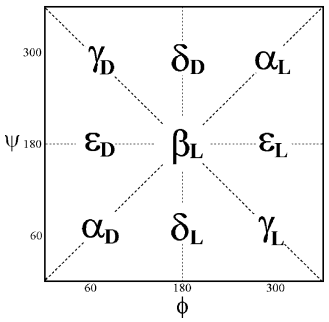

Fig. 1. Topological features of the Ramachandran map, $E = E(\phi, \psi)$, associated with an amino acid residue.

2. Method

Ab initio molecular orbital computations were carried out on the selected conformations of the tripeptide model Ac-Gly-Gly-Gly-NHMe at the RHF/3-21G ab initio level of theory, in order to determine the location of selected minima on the conformational potential energy hyper surface (PEHS). In addition to the dihedral angles, associated with the *trans* peptide bonds (ω_0, ω_1, ω_2, ω_3), a number of torsional angles (ϕ_1, ψ_1, ϕ_2, ψ_2, ϕ_3, ψ_3) were used as independent variables of the energy function:

$$E = f(\phi_1, \psi_1, \phi_2, \psi_2, \phi_3, \psi_3)$$

Ac-Gly-Gly-Gly-NHMe was first modeled with each residue and protecting group segments being numbered separately and in their entirety along the peptide chain. Thus, a 'modular' numbering system has been formed (Structure 1) which made it possible for the model to be extended or truncated at any comprising unit for further studies of longer or shorter peptides.

Hence, each of the amino acids, as well as the *N*-acetyl and *N*-methylamide portions were exclusively defined, using the *z*-matrix internal coordinate system.

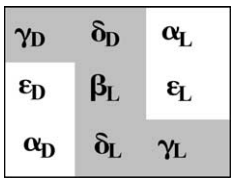

Fig. 2. Topological features of the Ramachandran map, $E = E(\phi, \psi)$, associated with an amino acid residue (the highlighted region represents the five existing minima associated with Ac-Gly-Gly-Gly-NHMe.

The molecular structure, stereochemistry, and genomic conformation were thus uniquely defined. The GAUSSIAN94 [39] and GAUSSIAN98 [40] programs were used to bring about a geometry optimization of the conformers predicted from the analysis of the three-dimensional PES cross-sections of the overall $(3N - 6) + 1$ dimensional PEHS. The optimizations were performed initially using the semi-empirical AM1 method. These were followed by ab initio HF computations at RHF/3-21G level of theory. Tight convergence criteria were carried out on selected conformations, with convergence thresholds for the gradient of the maximum force, RMS force, maximum displacement, and RMS displacement vectors, respectively.

Double scans were run at 30° intervals, from 0 to 360°, involving both ϕ_i and ψ_i for each of the three Gly residues at a time, while keeping the other two Gly resides restrained in their β (C_5) conformations. The graphical presentations of the Ramachandran type PESs were generated using the program AXUM 5.0, plotting the total energy values as a dependent variable generated by the double scans over the independent variables ϕ_i and ψ_i. The optimum coordinates of ϕ and ψ for all possible minima were then visually estimated from the landscape and contour diagrams of the three PESs and used as input variables for the geometry optimization calculations. The existence of these minima was confirmed by optimizing the estimated coordinates at the RHF/3-21G level of theory.

3. Results and discussion

In a previous study on conformational PESs of *N*-formylglycinamide (For-Gly-NH_2), five minima (β, γ_L, γ_D, δ_L, δ_D) were located (Table 1 and Fig. 2) [5]. In the present study, *N*-acetyl and *N*-methyl protective groups were used, which are expected to be superior models of neighboring peptide residues to the formyl and the free amine groups. It is hoped that these larger protecting groups simulate the α-carbon of the neighboring amino acid residues. The same five minima have been located for Ac-Gly-NHMe as were found in the case of For-Gly-NH_2. The conformations and energies are summarized in Table 2 and selected geometrical parameters are

Table 1
Ab initio SCF (3-21G) results for For-Gly-NH_2 conformation

Backbone conformation	ϕ	ψ	E (hartree)	ΔE (kcal/mol)
α	Not found			
β	180.0	180.0	−373.647749	0.653
γ	±83.3	±64.7	−373.648790	0.000
δ	±121.9	±25.2	−373.643579	3.270
ε	Not found			

given in Table 3. The (ϕ_i, ψ_i) torsional angles for the For-Gly-NH_2 and those obtained for Ac-Gly-NHMe are quite close. A correlation of their values is shown in Fig. 3.

In the case of each of the three PESs generated for Ac-Gly-Gly-Gly-NHMe (Fig. 4), five of the nine possible minima were found on the Ramachandran map (Tables 4–6). The approximate location of these five existing minima was β, γ_L, γ_D, δ_L, δ_D as illustrated in Fig. 2. Results were consistent with those of monoglycine in For-Gly-NH_2 and Ac-Gly-NHMe, whose five minima were also found on the PES, as illustrated in Tables 1 and 2, as well as Fig. 2.

From the optimized ab initio (RHF/3-21G) geometries and energies for Ac-Gly(X)Gly(β)Gly(β)-NHMe, Ac-Gly(β)Gly(β)Gly(X)-NHMe and Ac-Gly(β)Gly(X)Gly(β)-NHMe (Tables 4–6), it can be observed that the conformational behavior of the central achiral glycine is influenced by its neighboring glycine residue. The calculations on Ac-Gly(β)-Gly(β)Gly(β)-NHMe, showed that all backbone dihedral angles have the ideal values of almost 180°. Also in the βββ backbone conformation, both C–H bonds of each of the glycine residues have equal lengths, representing a symmetrical model (Tables 7–9) analogous to monoglycine (Table 3). By changing the conformation of either of the terminal glycine residues, the value of the central C–H bond lengths deviated from their ideal values. However, the difference between the C–H bonds, as a function of dihedral values was found to be quite small. The identical C–H bond lengths means that the triglycine molecule in its β–β–β conformation is symmetrical (i.e. it has a plane of symmetry) and is thus achiral. However, different C–H bond lengths of Ac-Gly-Gly-Gly-NHMe in conformations other than its β–β–β conformation shows that the central glycine is no longer achiral. Since the clockwise or counterclockwise twist about ϕ and ψ leads to axis chirality, point chirality of the central glycine residue is induced by the conformation of the terminal glycine residues. Changing the conformation of either of terminal glycine residues results in an asymmetric electron distribution, which is the basis of axis chirality. Axis chirality induces point chirality on the neighboring prochiral residue. Such induction of point chirality by

Table 2
(RHF/3-21G) geometries and energies for Ac-Gly-NHMe

Conformations, Gly	E (hartree)	ΔE (kcal/mol)	ϕ_0	ω_0	ϕ_1	ψ_1	ω_1	ϕ_2
β_L	−451.2931883	0.662	180.000	179.999	−179.999	179.999	179.999	119.364
γ_L	−451.2942437	0.000	179.369	−176.124	−84.7769	66.356	−179.215	−121.467
γ_D	−451.2942437	0.000	−179.370	176.123	84.7770	−66.354	179.215	−117.591
δ_L	−451.2893563	3.067	−174.981	−174.049	−121.855	24.331	176.827	−115.712
δ_D	−451.2893563	3.067	174.977	174.048	121.855	−24.332	−176.827	−122.999
ε_L	N/F	N/F	N/F	N/F	N/F	N/F	N/F	N/F
ε_D	N/F	N/F	N/F	N/F	N/F	N/F	N/F	N/F
α_L	N/F	N/F	N/F	N/F	N/F	N/F	N/F	N/F
α_D	N/F	N/F	N/F	N/F	N/F	N/F	N/F	N/F

Table 3
$C_\alpha-H$ bond lengths and $N-C_\alpha-CO$ bond angles in Ac-Gly-NHMe, computed at the RHF/3-21G level of theory

Conformations	Bond length of C–H		Angle of $N-C_\alpha-CO$
	$C_\alpha-H_R$	$C_\alpha-H_S$	
β	1.084342	1.084342	107.809
γ_L	1.080548	1.077241	112.366
γ_D	1.077241	1.080548	112.367
δ_L	1.081386	1.080611	114.274
δ_D	1.080612	1.081386	114.274
ε_L	N/F	N/F	N/F
ε_D	N/F	N/F	N/F
α_L	N/F	N/F	N/F
α_D	N/F	N/F	N/F

axis chirality may be defined as 'dynamic chirality' (Table 10).

From the optimized ab initio calculations on Ac-Gly(β)-Gly(X)-Gly(β)-NHMe, for $X \neq \beta$ (C_5) it can also be observed that the value of dihedral angles ψ_1 and ϕ_3, which are closest to the centrally located residue, deviated the most from the standard value of 180°. This shows that the effect of the conformation of an amino acid residue is greater on the dihedral angles of its closest neighboring residues. This induced effect gets smaller as we move away from the central glycine residue, which has been varied about its dihedrals.

Of all the conformations studied, the β–β–β conformation of Ac-Gly-Gly-Gly-NHMe has the lowest energy value, being the most stable structure. Thus, the energy values of other conformations of Ac-Gly-Gly-Gly-NHMe were compared to the energy value of the symmetrical β–β–β structure, which is the reference conformation. It was observed that the effect of changing either of the terminal residues from β (C_5) to γ_L conformation was less significant than changing the conformation of the central residue (Fig. 4). This might be due to the fact that the central residue can affect the conformation of both terminal residues as it has two nearest neighbors, while the effect of terminal residues can be mostly limited only to their adjacent residue. Since, as discussed earlier, as we move away from a residue, its effect on its neighboring residues gets smaller. The same trend was also observed in the three conformations of β–β–γ_D, γ_D–β–β and β–γ_D–β. But, this trend was not consistent with that of δ_L and δ_D.

The optimized energy values of the enantiomers were further analyzed in the three cases of Ac-Gly(X)-Gly(β)-Gly(β)-NHMe, Ac-Gly(β)-Gly(X)-Gly(β)-NHMe and Ac-Gly(β)-Gly(β)-Gly(X)-NHMe. Although the energy values of the L and D enantiomeric twist of the γ, as well as δ backbone conformations were expected to be equal, they differed slightly in their seventh decimal place (in hartree unit). The C–H bond lengths of these enantiomers were also slightly different in their fourth decimal place (in Å unit). It was also noted that bond lengths of the γ_L and γ_D, as well as δ_L and δ_D enantiomers were opposite. Since the axis chirality changes in these enantiomers, the bond lengths change as well; in fact they become opposite. Tight optimization convergence criteria were used to differentiate method-oriented deviations from real structural ones (Fig. 5).

From the optimized ab initio geometries and energies of Ac-Gly(β)-Gly(X)-Gly(β)-NHMe, it was observed that the dihedral angles of the first and third glycine residues did not twist in the same direction. However, the dihedral angles of the terminal glycine residues in the γ_L and γ_D, as well as δ_L and δ_D enantiomers had opposite twists as expected due to their opposite axis chirality.

Conformational twist changes the relatively achiral distribution to a relatively chiral distribution. The unevenness of such electron distribution makes the two C–H bonds of the glycine residue, which undergoes conformational change, more susceptible to bond length change. Such a difference is gradually decreasing as we go away from the twisted glycine residue thus the nearest neighbor will suffer more and the second nearest neighbor will suffer less (Fig. 6). These changes, however, are opposite to the changes occurring in glycine, which undergoes a conformation change. It may well be that during conformational change, electron density will flow preferentially to the glycine, which undergoes a conformational change making C–H bond shorter and therefore stronger.

4. Conclusions

Five minima were found to be associated with each glycine residue of the triglycine in its protected form: Ac-Gly-Gly-Gly-NHMe. These five minima, which

Table 4
Ab initio (RHF/3-21G) geometries and energies for Ac-Gly(X)-Gly(β)-Gly(β)-NHMe varying the backbone conformation of the first glycine residue, computed under tight convergence criteria

Backbone conformation	ψ_0	ω_0	Gly1			Gly2			Gly3			ϕ_4	E (hartree)	ΔE (kcal/-mol)
			ϕ_1	ψ_1	ω_1	ϕ_2	ψ_2	ω_2	ϕ_3	ψ_3	ω_3			
βββ	59.750	−179.999	179.997	−179.9999	180.000	179.999	180.000	180.000	−179.999	179.999	180.000	0.001	−862.618520492	0.000
γ_Lββ	58.540	−177.067	−87.096	63.799	−179.663	179.460	179.291	−179.737	179.664	−179.747	179.972	0.070	−862.615089405	2.153
γ_Dββ	61.268	177.066	87.097	−63.799	179.662	−179.461	−179.290	179.738	−179.669	179.747	−179.971	−0.076	−862.615089393	2.153
α_Lββ	Not found													
α_Dββ	Not found													
δ_Lββ	59.075	−178.186	−116.969	17.115	178.514	175.124	179.691	−179.509	179.519	−179.694	179.975	0.111	−862.615339250	1.996
δ_Dββ	60.741	178.186	116.972	−17.116	−178.513	−175.130	−179.689	179.510	−179.519	179.693	−179.975	−0.095	−862.615339267	1.996
ε_Dββ	Not found													
ε_Lββ	Not found													

Table 5
Ab initio (RHF/3-21G) geometries and energies for Ac-Gly(β)-Gly(X)-Gly(β)-NHMe varying the backbone conformation of the central glycine residue, computed under tight convergence criteria

Backbone conformation	ψ_0	ω_0	Gly1			Gly2			Gly3			ϕ_4	E (hartree)	ΔE (kcal/mol)
			ϕ_1	ψ_1	ω_1	ϕ_2	ψ_2	ω_2	ϕ_3	ψ_3	ω_3			
βββ	59.760	180.000	180.000	180.000	180.000	180.000	180.000	180.000	180.000	180.000	180.000	−0.001	−862.618520493	0.000
$\beta\gamma_L\beta$	59.697	−179.624	179.473	−176.767	−177.113	−86.389	62.205	−179.120	175.572	179.790	−179.834	−0.497	−862.614768430	2.354
$\beta\gamma_D\beta$	59.767	179.622	−179.472	176.721	177.111	86.391	−62.204	179.129	−175.574	−179.791	179.835	−0.508	−862.614768442	2.354
$\beta\alpha_L\beta$	Not found													
$\beta\alpha_D\beta$	Not found													
$\beta\delta_L\beta$	60.604	−179.934	−176.464	178.949	−177.650	−116.280	16.754	178.596	175.940	−179.913	−179.783	0.120	−862.614346430	2.619
$\beta\delta_D\beta$	58.954	179.935	176.464	−178.948	177.651	116.276	−16.750	−178.596	−175.936	179.908	179.782	−0.121	−862.614346430	2.619
$\beta\varepsilon_D\beta$	Not found													
$\beta\varepsilon_L\beta$	Not found													

Table 6
Ab initio (RHF/3-21G) geometries and energies for Ac-Gly(β)-Gly(β)-Gly(X)-NHMe varying the backbone conformation of the last glycine residue, computed under tight convergence criteria

Backbone conformation	ψ_0	ω_0	Gly1			Gly2			Gly3			ϕ_4	E (hartree)	ΔE (kcal/mol)
			ϕ_1	ψ_1	ω_1	ϕ_2	ψ_2	ω_2	ϕ_3	ψ_3	ω_3			
βββ	59.759	−179.999	179.999	−179.999	180.000	179.999	180.000	180.000	−179.999	179.999	180.000	0.001	−862.618520492	0.000
ββγ_L	59.774	179.985	−179.878	179.916	179.927	178.971	−179.274	−176.179	−85.219	66.882	−179.244	−1.375	−862.617112009	0.884
ββγ_D	59.767	−179.986	179.880	−179.916	−179.927	−178.969	179.275	176.180	85.219	−66.883	179.244	1.380	−862.617112021	0.884
ββα_L	Not found													
ββα_D	Not found													
ββδ_L	58.900	−179.969	−179.668	179.862	179.853	178.491	−178.162	−174.724	−122.378	25.150	177.023	4.195	−862.612786787	3.598
ββδ_D	59.644	179.968	179.667	−179.862	−179.852	−178.495	178.162	174.724	122.376	−25.151	−177.022	−4.198	−862.612786786	3.598
ββε_D	Not found													
ββε_L	Not found													

Table 7
C–H bond lengths (Å) of glycine residues in selected conformations of Ac-Gly(X)-Gly(β)-Gly(β)-NHMe varying the backbone conformation of the first glycine residue using tight optimization at the ab initio RHF/3-21G level of theory

Backbone conformation	Gly1	Gly2	Gly3
βββ[a]	H_R 1.08408	1.08358	1.08370
	H_S 1.08408	1.08358	1.08370
γ_Lββ	H_R 1.08029	1.08440	1.08404
	H_S 1.07751	1.08440	1.08398
γ_Dββ	H_R 1.07751	1.08424	1.08398
	H_S 1.08029	1.08440	1.08404
δ_Lββ	H_R 1.08108	1.08373	1.08384
	H_S 1.08115	1.08444	1.08376
δ_Dββ	H_R 1.08115	1.08444	1.08376
	H_S 1.08108	1.08373	1.08384

[a] The equivalent C–H_S and C–H_R bond lengths are computed to be the same for five decimal places. The largest deviation observed was 0.000002 Å.

were the same as those of *N*-formylglycinamide (For-Gly-NH_2) and Ac-Gly-NHMe, were β, γ_L, γ_D, δ_L, δ_D. Conformational behavior of a glycine residue in triglycine is affected by its neighboring glycine residues. This effect is mostly limited to the adjacent bonds and it got smaller as we moved away from the central glycine residue, in either direction.

The triglycine structure in its β–β–β conformation has dihedral angles of exactly 180° and its pairs of C_α–H bond lengths are identical. It also has the lowest energy value and highest stability. Thus, its plane of symmetry represents a completely symmetrical and therefore achiral structure, which can be used as a standard of comparison.

Table 8
C–H bond lengths (Å) of glycine residues in selected conformations of Ac-Gly(β)-Gly(X)-Gly(β)-NHMe varying the backbone conformation of the central glycine residue using tight optimization at the ab initio RHF/3-21G level of theory

Backbone conformation	Gly1	Gly2	Gly3
βββ	H_R 1.08408	1.08358	1.08370
	H_S 1.08408	1.08358	1.08370
βγ_Lβ	H_R 1.08444	1.07715	1.08415
	H_S 1.08437	1.08030	1.08491
βγ_Dβ	H_R 1.08437	1.0803	1.08491
	H_S 1.08444	1.07715	1.08414
βδ_Lβ	H_R 1.08413	1.08071	1.08386
	H_S 1.08482	1.08077	1.08453
βδ_Dβ	H_R 1.08482	1.08077	1.08453
	H_S 1.08414	1.08071	1.08386

Table 9
C–H bond lengths (Å) of glycine residues in selected conformations of Ac-Gly(β)-Gly(β)-Gly(X)-NHMe varying the backbone conformation of the last glycine residue using tight optimization of the ab initio RHF/3-21G level of theory

Backbone conformation	Gly1	Gly2	Gly3
βββ	H_R 1.08408	1.08358	1.08370
	H_S 1.08408	1.08358	1.08370
ββγ_L	H_R 1.08416	1.08396	1.08020
	H_S 1.08419	1.08380	1.07688
ββγ_D	H_R 1.08419	1.08380	1.07688
	H_S 1.08416	1.08396	1.08020
ββδ_L	H_R 1.08412	1.08375	1.08106
	H_S 1.08420	1.08434	1.08003
ββδ_D	H_R 1.08420	1.08434	1.08003
	H_S 1.08412	1.08375	1.08106

The central glycine residue can affect the conformation of its two adjacent terminal residues. However, each of the terminal glycine residues can most significantly affect their one adjacent residue. The effect of one terminal glycine residue on the other terminal glycine residue is minimal. Therefore, the effect of changing either of the terminal residues from β to γ_L or to γ_D conformation is less significant than

Table 10
N–Cα–C bond angles

Backbone conformation	Gly1	Gly2	Gly3
(a) Ac-Gly(X)-Gly(β)-Gly(β)-NHMe			
βββ	107.61	107.26	107.29
γ_Lββ	112.28	108.66	107.60
γ_Dββ	112.28	108.66	107.60
δ_Lββ	114.06	107.33	107.39
δ_Dββ	114.06	107.33	107.39
(b) Ac-Gly(β)-Gly(X)-Gly(β)-NHMe			
βββ	107.61	107.26	107.29
βγ_Lβ	107.82	112.27	108.61
βγ_Dβ	107.83	112.27	108.60
βδ_Lβ	107.90	114.16	107.29
βδ_Dβ	107.90	114.16	107.29
(c) Ac-Gly(β)-Gly(β)-Gly(X)-NHMe			
βββ	107.61	107.26	107.29
ββγ_L	107.72	107.69	112.10
ββγ_D	107.72	107.69	112.10
ββδ_L	107.70	107.66	114.17
ββδ_D	107.72	107.69	112.10

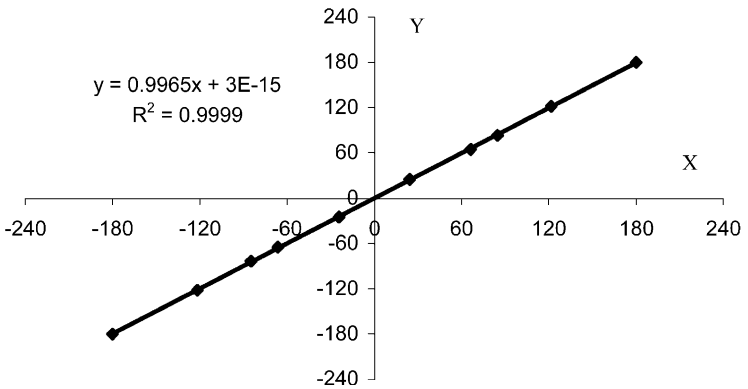

Fig. 3. Correlation of torsional angles obtained for For-Gly-NH_2 with those optimized for Ac-Gly-NHMe. Note that the *X*-axis represents the torsional angles (ϕ and ψ) obtained for Ac-Gly-NHMe and the *Y*-axis represents the torsional angles (ϕ and ψ) obtained for For-Gly-NH_2.

changing the conformation of the central residue. This trend is not true for the δ_L and δ_D conformers.

The energy values of the γ_L and γ_D, as well as δ_L and δ_D enantiomers, were identical up to seven decimal places as permitted by the accuracy of geometry optimization. The C−H bond lengths of the enantiomers were also slightly different. The bond lengths were opposite in the γ_L and γ_D, as well as δ_L and δ_D enantiomers due to the opposite axial chirality. Also the dihedral angles of the first and third glycine residues did not twist in the same direction. However, the dihedral angles of the terminal glycine residues in the γ_L and γ_D, as well as δ_L and δ_D enantiomers had opposite twists as expected due to their opposite axial chirality.

A conclusion may appear form the present study namely that terminal glycine residues may represent the best protective groups. Thus, single amino acid (Xxx) conformations may be best studied in tripeptides, such as Ac-Gly(β)-Xxx-Gly(β)-NHMe.

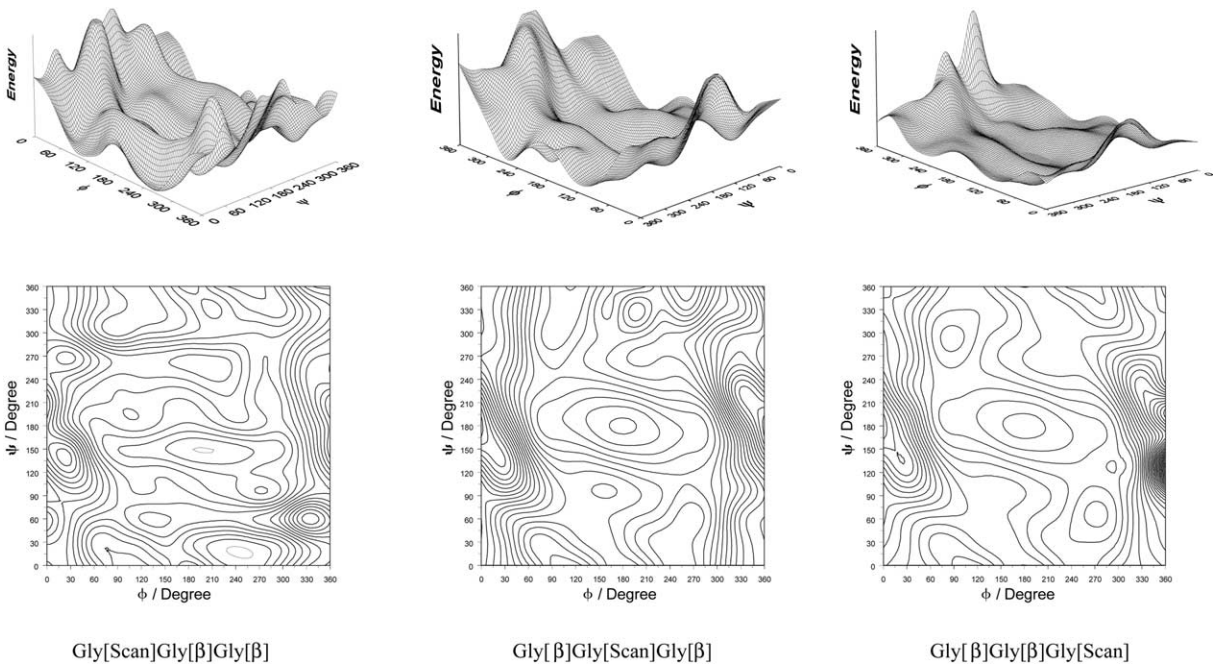

Fig. 4. Landscape (top) and contour (bottom) representations of Ramachandran type PESs of Ac-Gly-Gly-Gly-NHMe.

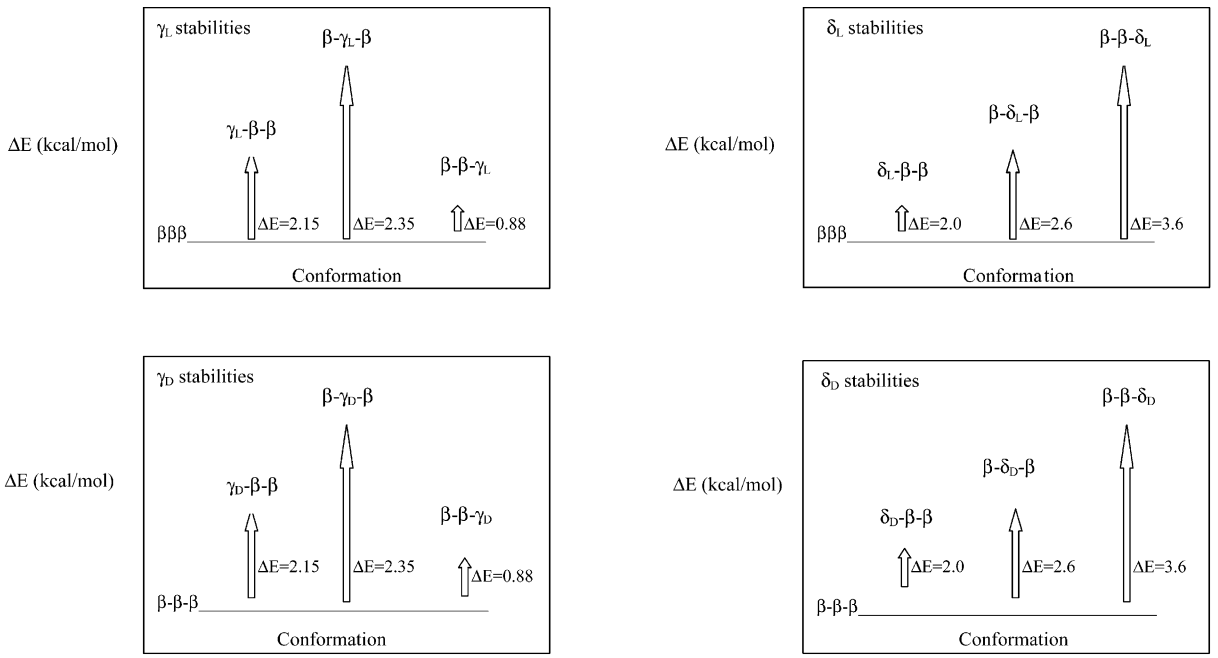

Fig. 5. Relative stabilities (ΔE) of γ_L and γ_D, as well as δ_L and δ_D backbone conformers in triglycine with the following conformational variation: X–β–β, β–X–β and β–β–X with respect to β–β–β.

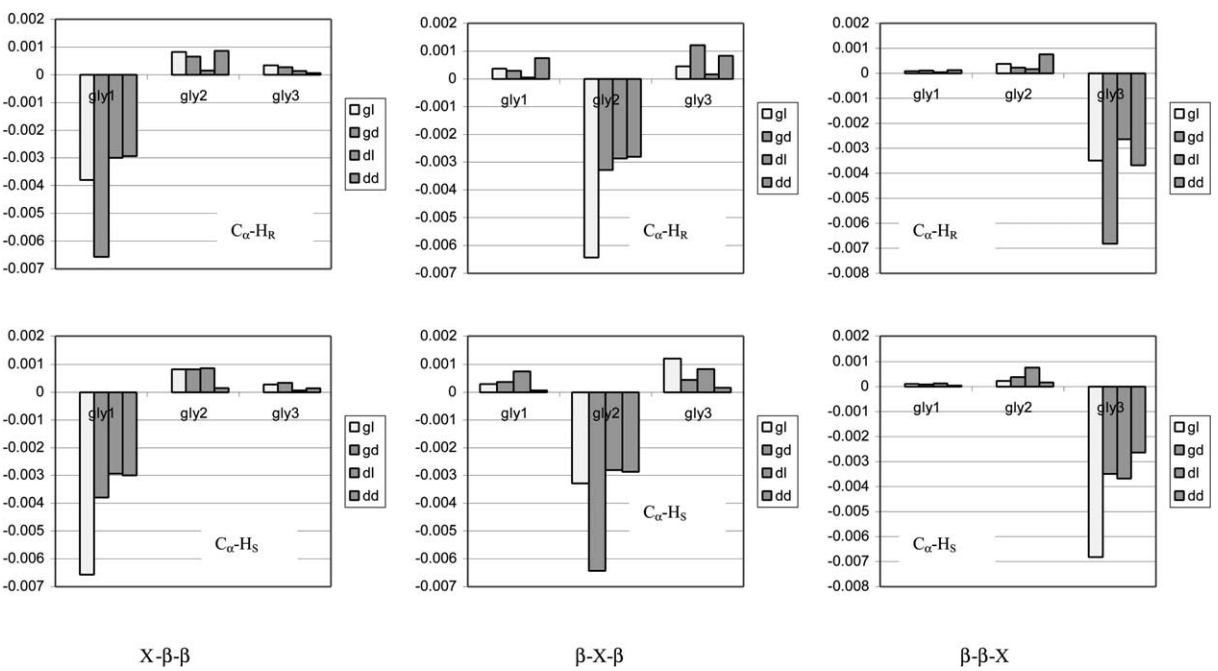

Fig. 6. $C_\alpha–H_R$ and $C_\alpha–H_S$ stretches and contractions in each of the three glycine residues in Ac-Gly-Gly-Gly-NHMe at gl = γ_L, gd = γ_D, dl = δ_L and dd = δ_D backbone conformations.

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