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Theoretical study of the potential energy surface of N-formyl-L-cysteine-amide by using a genetic algorithm multi niche crowding

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ABSTRACT

The generation of molecular structures constituting the conformational space of trans-N-For-L-Cys-NH_2 was accomplished using the genetic algorithm MNC coupled to the semi-empirical AM1 method, AM1/GA-MNC. The structural and energy analysis of the obtained conformational space E=E(φ,ψ) locates 7 regions or minima γ_L, γ_D, β_L, δ_D, δ_L, ε_D and ε_L. The combination of these folds to structuring modes adopted by the side chain CH_2-SH has allowed us to identify 27 stable geometric structures. The regions corresponding to helical folds α_D and α_L are not favorable for the system that is the subject of current study.

Capsule Summary: Molecular structure of trans-N-For-L-Cys-NH_2 was studied using the genetic algorithm MNC coupled to the semi-empirical AM1 method, AM1/GA-MNC and combination of the folds to structuring modes adopted by the side chain CH_2-SH revealed the possibility of 27 stable geometric structures of N-For-L-Cys-NH_2.

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INTRODUCTION

For several years, many theorists and experiments focus their efforts to analyze and understand the topology of the potential energy surfaces of polypeptides and proteins. The Ramachandran Map (Ramachandran et al., 1963) is a theoretical strategy that appeared in the 60 (Ramachandran., 1968) to explain through a simple map of interactions (interatomic repulsion and attraction) the conformations adopted by amino acids in a time when the crystallographic data are limited. It is a graphical representation associated with the behavior of the amino acid residues included in a peptide chain as a function of the φ and ψ angles describing the structure mode of the main chain or backbone peptide. The conformational analysis of potential energy surfaces of diamides models such as R'CONH-CHR-CNOR'H is being developed. Thus, the conformational properties of the polypeptides and proteins can be deduced from those of the blocked or protected units.

In recent years, several theoretical approaches (Baldoni et al., 1999; Head-Gordan et al,1989; 1991; McAllister et al., 1998; Perczel et al.,1991; Rodrıguez et al., 1998;) have been used to study two-dimensional potential energy surface E(φ ,ψ) of CH_3COHN-CHR-CONHCH_3 or HCONH-CHR-$CONH_2$. The multi-dimensional conformational analysis process (MDCA) states (Perczel et al., 1991) the existence of nine minimum, designated by Greek letters attached to L or D to denote the chirality of the conformer. These codes are noted γ_L, γ_D, β_L, δ_L, α_D, α_L, ε_D, ε_D and δ_D (Fig. 1,a). For amino acid residues that have complex side chains, analyzing their conformational space impose conformational study of two sub-spaces; one that describes the mode of backbone rearrangement E (φ ,ψ) and the two-dimensional space E(χ1 , χ2) that defines the structure mode of the side chain and which is governed by χ1 et χ2 angles (torsion angles around Cα-Cβ and Cβ-X bonds respectively).Each twist angle characterizing the side chain should have 3 positions (g+, a, g-).Thus, the potential energy surface E=E(χ1, χ2) will be defined in the ideal case by 9 conformations Figure (1,b).

Serine and cysteine are amino acids which have the simplest side chains. Thus, for the trans-For-L-Ser-NH_2 (Farkas et al., 1995; Perczel et al., 1995; 1996a; 1996b; 1998; 2003), over 81 conformations were defined by the MDCA. This number was reduced to 44 and 36 structures if methods RHF/3-21G and RHF/6-31++G(d,p) respectively are used. In this case, the most favored structure (global minimum) is the γ_L(g+ g+) followed by C5 conformation [β_L (a g+)] which is 2.10 kcal/mol relative to γ_L(g+ g+) (Perczel et al., 2003).
The tetra-dimensional Ramachandran surface of Cysteine.is defined by four variables E = E(φ,ψ, χ1, χ2) . Given its polar character, the functional group SH may be donor as it can be proton acceptor. In fact, several types of intramolecular interactions are going to be at the heart of discussions such as backbone-backbone interaction and/or side-chain backbone.

Ab initio and DFT Studies (Bombasaro et al., 2005; Zamora et al., 2001) have been devoted to the study of the conformational space of N-acétyl-L-Cystéine-N-methylamide, while for N-Formyl-L-Cys-amide and according to our knowledge, the data are still limited (Zamora et al., 2002).

The conformation adopted by the peptide backbone defined by the HCO-NH-HC_α-$CONH_2$ fragment depends on three angles φ, ψ and ω. The peptide angle may be around 0 ° or 180 ° according to Cis or Trans form of the peptide. In addition, it was recognized that the presence of the cis form of the peptide bond is rare because of the unfavorable contact between the amino acid residues (Pauling., 1960; Ramachandran., 1968).Indeed, we are interested in studying the trans form ofN-For-L-Cys-NH_2 by fixing OCNC angle near 0°.

In a previous paper (Bourjila et al., 2016), we were interested in the study of equilibrium structures and acidity in the gas phase of peptides based on Cysteine and Alanine including $AlaCysNH_2$, Ala_2CysNH_2, Ala_3CysNH_2, Ala_4CysNH_2, $CysAlaNH_2$et $CysAla_2NH_2$. Therefore, we concluded that (i) these systems mainly adopt helical forms in their neutral forms, as they are rearranged in globular form in their deprotonated forms (ii) polyalanines acidity increases with increasing the length of the peptide chain (iii) the residue of cysteine is more acidic when it is placed on N-terminal side of the peptide chain. The objective of this work is the structural and energy analysis of minimum constituting the conformational space E=E(φ,ψ) of Trans-N-For-L-Cys-NH_2 in isolated state.

MATERIAL AND METHODS

The molecular potential energy surface PES was explored automatically by the multi-niche crowding genetic algorithm (MNC GA) programmed in our laboratory (El Merbouh et al., 2014). It's a stochastic techniques based on the simulation of a biological system. These are based on the mechanisms of natural selection and genetic recombination. This algorithm is implemented in a package of program interfaced with MOPAC (Stewart, 1989) (version 6.0) in order to evaluate the quality of the individual to insert into the population in each iteration.

RESULTS AND DISCUSSION

The exploitation and exploration of the conformational space of the blocked diamide of cysteine HCO-NH-L-CH(CH_2-SH)CO-NH_2 using the genetic algorithm, based on the MNC method, coupled with the semi-empirical AM1 method, allows to graphically represent the two-dimensional sub-space E = E(φ,ψ) as shown in Figure 3. The representation is done in two-dimensional space [-180°, 180°] according to the convention of the IUPAC-IUB.

An initial examination of the obtained conformational surface (Fig. 3) shows that the 500 conformations of the final population is grouped in 7 niches or permitted regions. Each of these regions corresponds to a type of folding or minimum (γ_L, γ_D, α_L,) based on the values of φ and ψ angles that describe the structure mode adopted by the main chain or backbone.

The first region (γ_L) is a region where a large number of conformations is grouped as a niche, and it is favored with 29% of 500 conformations constituting the final population. In this region, the backbone of N-For-L-Cys-NH_2 diamide adopts a structure ɣ-turn by forming a C_7^{eq} conformation. The second region occupies 14% of 500 conformations constituting the population, it is denoted (γ_D). In this case, the side chain-CH_2-SH, denoted C_7^{ax}, is in axial position relative to the backbone. The third area denoted (β_L) occupies 38% in the two edges of the left side of the obtained Ramachandran surface. In this region the peptide backbone adopts an extended structure denoted C5. The fourth and the fifth region denoted ε_L and ε_D occupy 8% and 4.8% respectively. The last regions denoted δ_D and δ_L, occupy 5.2% and 1% respectively. The backbones of the two conformations are stabilized mainly by hydrogen bonds involving the two amide functions $O_6C_5N_4H_{12}$ and $O_7C_2N_1H_9$. Each identified minimum is associated with the rearrangement mode adopted by the groups of the side chain -CH_2-SH since each torsional mode (χ1 and χ2) is expected to have three minima (g+, a, g-).

The γ_L backbone conformation

The backbone γ_L(φ ≈ -82.8°, ψ ≈ 64.4°) is stabilized by two hydrogen bonds such backbone/backbone involving the two amide functions $O_6C_5N_4H_{12}$ and $O_7C_2N_1H_9$.

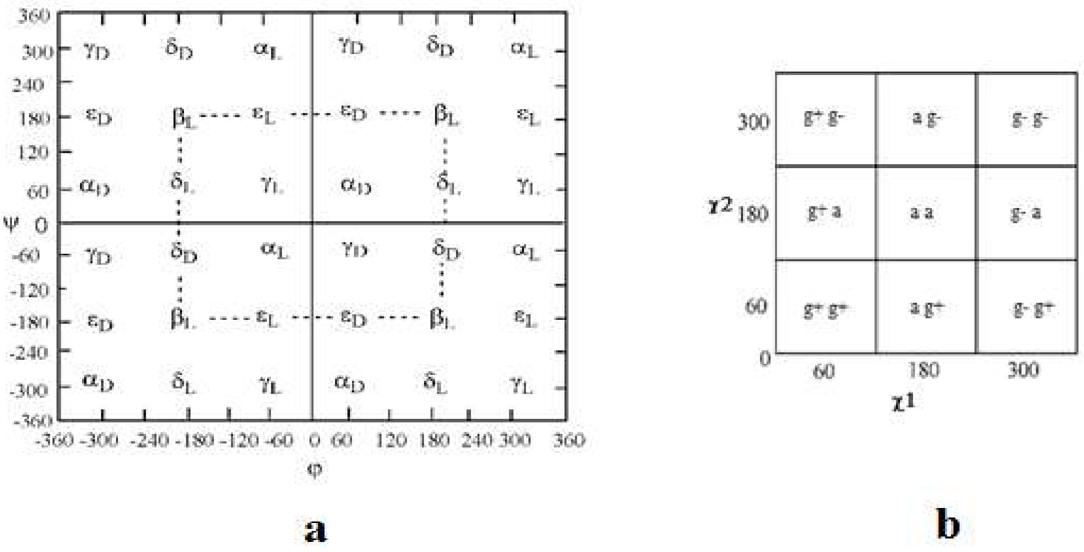
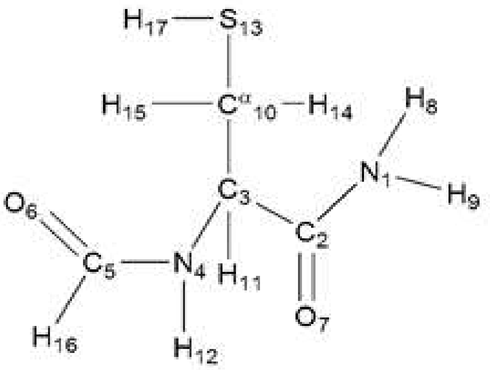


Fig. 1: (a,b) : Idealized PES topology for a single amino acid residue PCO-NH-CHR-CO-NHQ (MDCA). The central square, marked by broken lines, specifies the cut of the PES accepted by IUPAC convention: - 180º ≤ φ ≤+ 180º and - 180º ≤ ψ≤ + 180º (Perczel et al., 1991).



φ = C5-N4-C3-C2

ψ = N4-C3-C2-N1

χ1 = S-C10-C3-N4

χ2 = H17-S-C10-C3

Fig. 2: Numbering atoms of N-Formy-L-Cys-amide

The oxygen (O_6) of carbonyl bonded to the amide nitrogen N_4 interacts with one of the hydrogens carried by the heteroatom N_1.Thus, an hydrogen bond O_6...H_9 with a medium length of 2.18 Å was formed, On the other hand, nitrogen N_4 comes into interaction of weak character (2.94 Å) with the same hydrogen N_4...H_9 (Fig. 4).

By analyzing the different conformations γ_L(Fig. 4) , three hydrogen bonds such side-chain backbone are conceivable depending on the values of χ1 and χ2 angles. By combining the type of rearrangement adopted by the side chain -CH_2-SH in the peptide backbone γ_L, 5 conformations were identified namely γ_L[g+g+], γ_L[g-g-], γ_L[ag-], γ_L [g-g+] and γ_L[g-a] (Table 1). Geometrically, in addition to the two deterministic hydrogen bonds (O_6....H_9, N_4...H_9) of backbone γ_L, the sulfur can be an atomic center donor and / or proton acceptor.

In terms of energy, as shown in Table 1 where are represented energy differences between different structures γ_L, we find that the γ_L[g+g+]is the most favored by representing the global minimum from the AM1 of N-For-L-Cys-NH_2 in the isolated state. The structures γ_L[g-g-], γ_L[a g-], γ_L[g-g+] and γ_L[g-a] are less stable and are 1.6,1.9,2.3 et 2.5 kcal/mol respectively, compared to the global minimum. This order of stability can be justified in discussing the hydrogen bonds involving the functional groups of the side chain-CH_2-SH in each structure (Fig. 4).

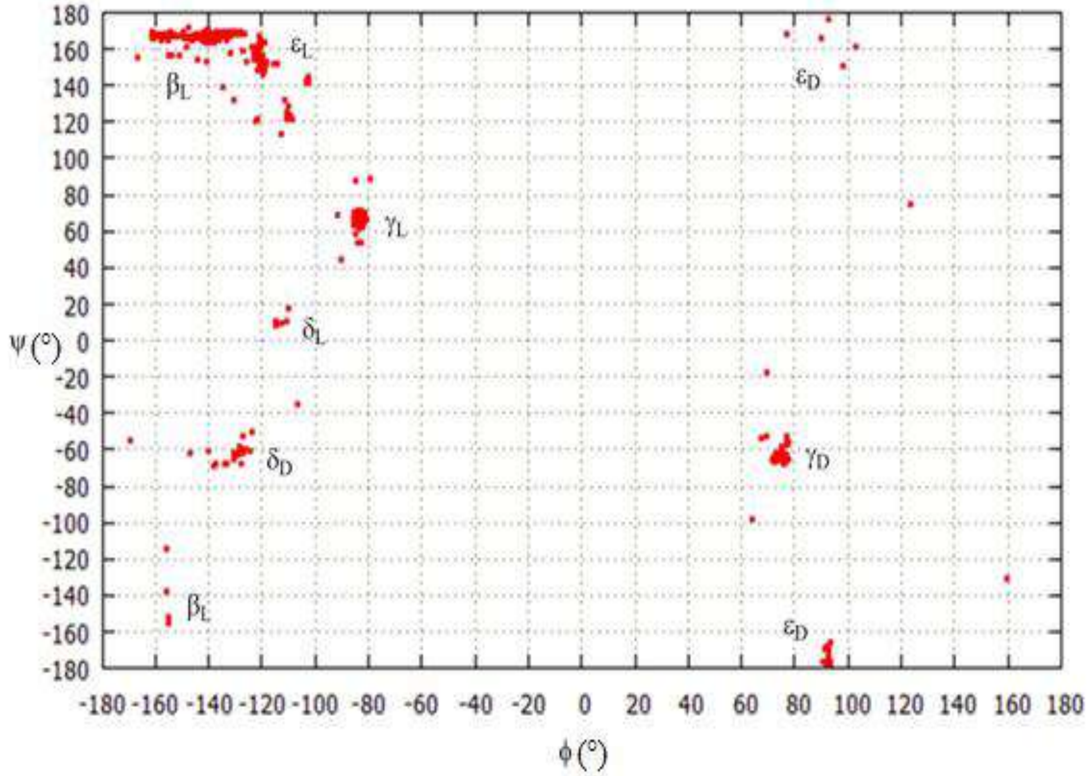
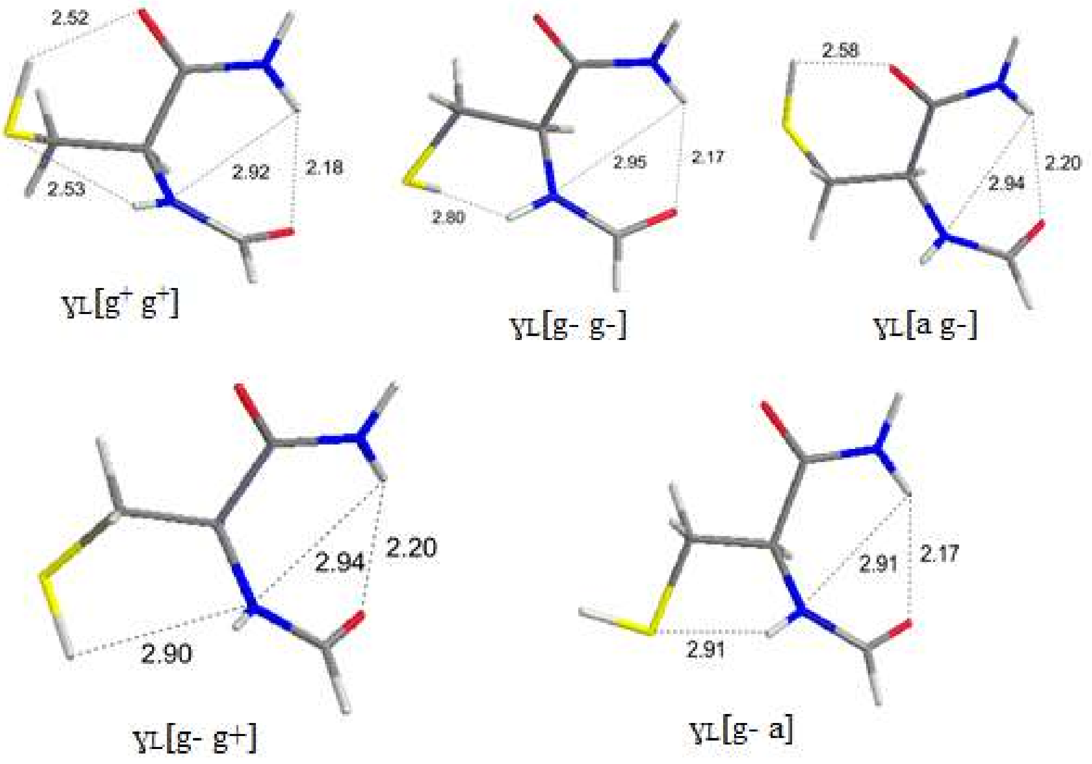


Fig. 3: Distribution of conformations constituting the conformational space of Trans-N-For-L-Cys-NH_2 according to the angles φ and ψ of the backbone, AM1/GA-MNC



$\gamma_L[g^+ g^+]$ $\gamma_L[g- g-]$ $\gamma_L[a g-]$

$\gamma_L[g- g+]$ $\gamma_L[g- a]$

Fig. 4: γ_L minima of N-For-L-Cys-NH_2 obtained by AM1/GA-MNC, hydrogen bonds length are in Å

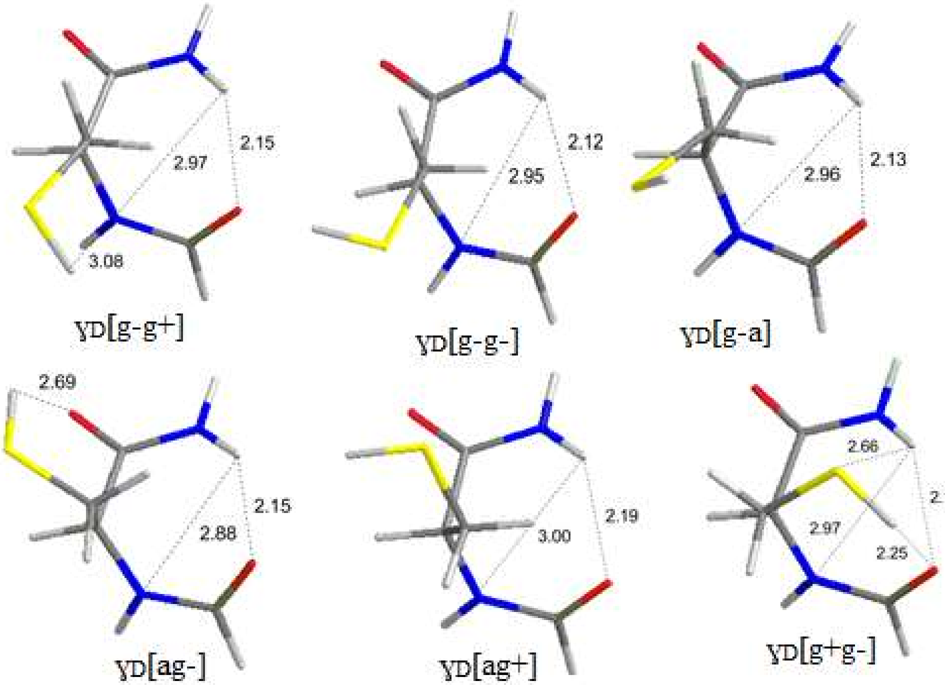


Fig. 5: γD minima of N-For-L-Cys-NH2 calculated by using AM1/GA-MNC, hydrogen bonds length are in Å

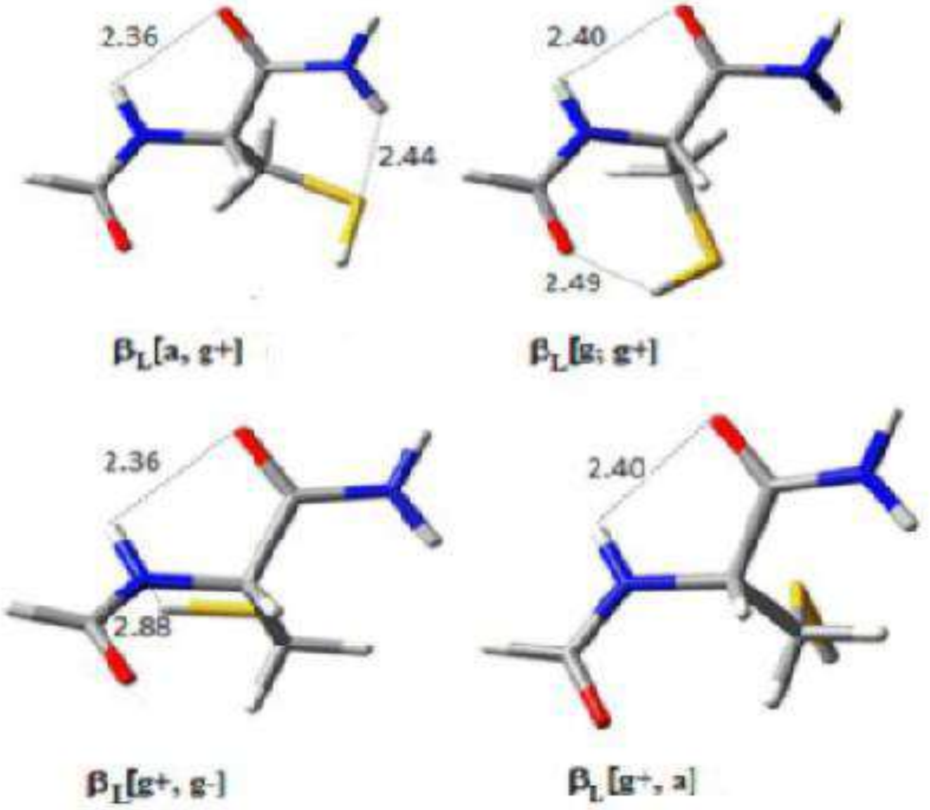
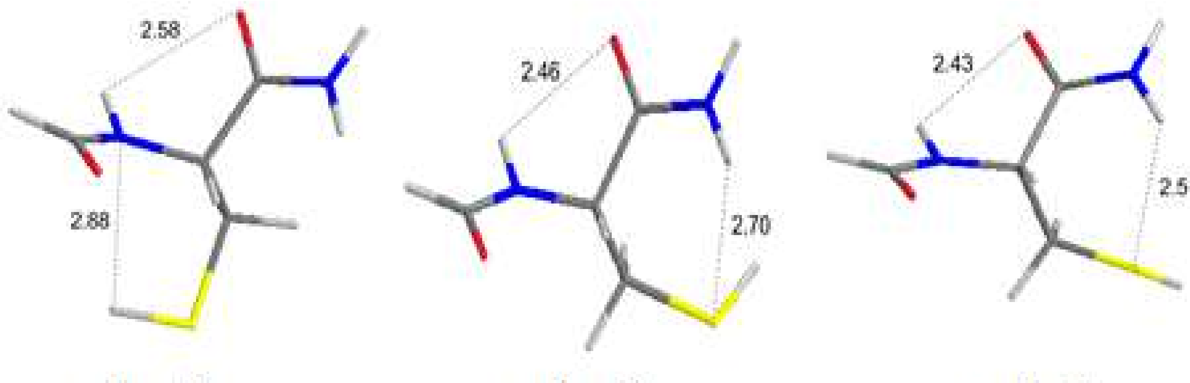
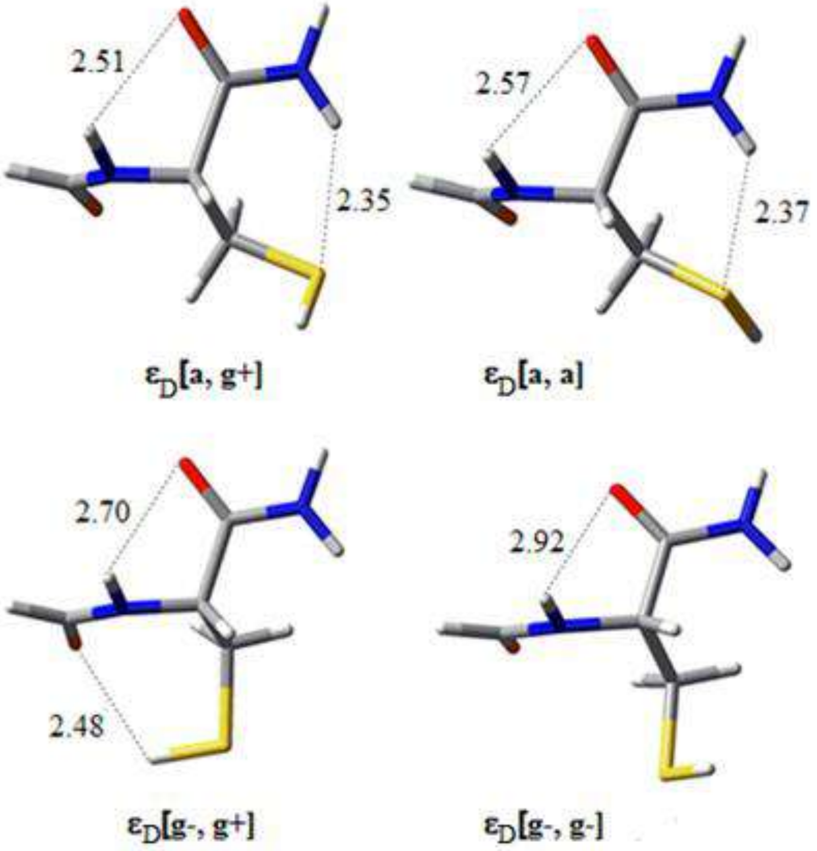


Fig. 6: βL minima obtained forN-For-L-Cys-NH2 by using AM1/GA-MNC, hydrogen bonds length are in Å



ε_L[g-g+] ε_L[a g-] ε_L[a a]

Fig. 7: εL minima calculated forN-For-L-Cys-NH$_2$ by using AM1/GA-MNC, hydrogen bonds length is in Å

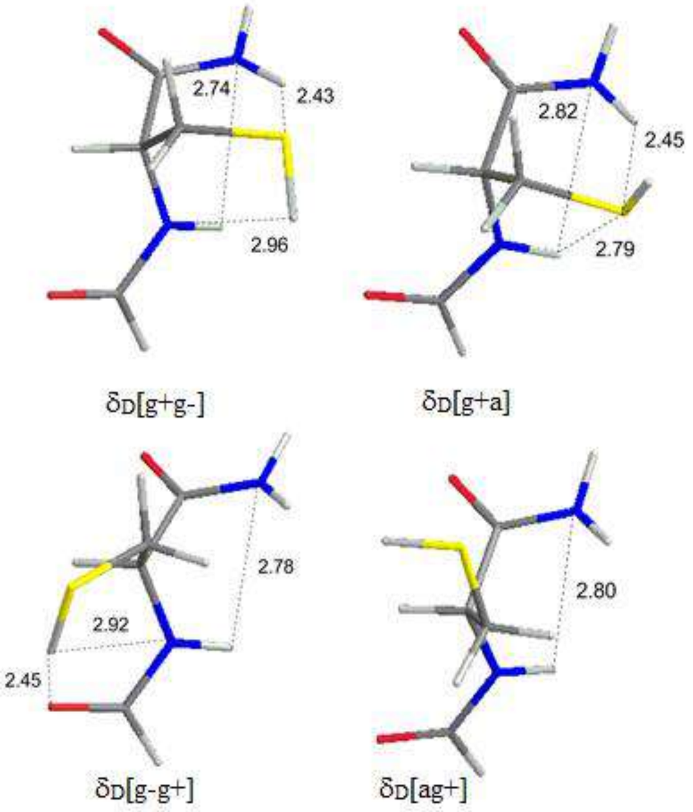


ε_D[a, g+] ε_D[a, a]

ε_D[g-, g+] ε_D[g-, g-]

Fig. 8: ε_D minima calculated for the N-For-L-Cys-NH$_2$ using AM1/GA-MNC, hydrogen bonds length are in Å

The comparison of mean values of angles φ and ψ of backbone γ_L found in this study with their counterparts from other theoretical calculation methods and for other diamides (Table 2) shows that the used research technique (AM1/GA-MNC) well locates γ_L conformation at values of angles that are in perfect agreement with those found either by the same method AM1 or those from the ab initio. Moreover, we can say that the increase in the size of the side chain -R linked to the alpha carbon does not lead to a geometric modification of the backbone γ_L.



δ_D[g+g-] δ_D[g+a]

δ_D[g-g+] δ_D[ag+]

Fig. 9: δ_D conformations obtained for the N-For-L-Cys-NH_2 using AM1/GA-MNC, hydrogen bonds length are in Å

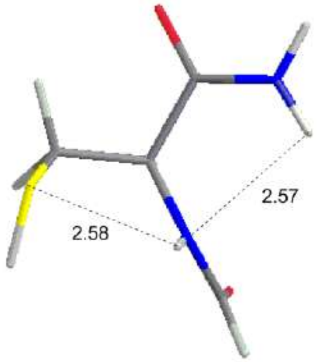


Fig. 10: The δ_L[g+ g-] conformation calculated for N-For-L-Cys-NH_2, AM1/GA-MNC, hydrogen bonds length are in Å

The γ_D backbone conformation

The second allowed region characterizing the conformational space of N-For-L-Cys-NH_2 is denoted γ_D($\varphi \approx 73.8$,$\psi \approx -61.5$) (C_7^{ax}). Structurally, the peptide backbone of γ_D conformation is stabilized by the same bonds of backbone-backbone type as those of γ_L (N_4...H_9 et O_6...H_9).The corresponding lengths are of the order of 2.15 and 2.95 Å, respectively. The backbone γ_D wherein the side chain is in the axial position is less stable than γ_L where the –CH_2-SH is in the equatorial position relative to the peptide backbone. By analyzing the space Eγ_D(χ1, χ2),6 conformations were located, γ_D[g-g+], γ_D[g-g-], γ_D[g-a], γ_D[ag-], γ_D[ag+] and γ_D[g+g-] (Fig. 5).

The energies barriers noticed between γ_D structures result in small geometric changes. In a previous paper (Bourjila et al., 2017), We carried out a conformational study on the preferred minima γ_D (C^7_{ax}) of trans N-For-L-Cys-NH_2 in isolated state by AM1/GA-MNC calculation. All conformations located were subjected to geometry optimization at the HF/3-21G and the HF/6-31G++ (d, p) levels of theory. The three levels of theory provide the same results.

The β_L backbone conformation

The third area populated by the diamideN-For-L-Cys-NH_2 is located in both sides of the left side of the obtained Ramachandran surface ($\varphi \approx$-150.1and$\psi \approx$ 177.2) (figure 3). In this region denoted β_L, were gathered conformations which have an expanded geometry C_5 where the peptide backbone arranges in a manner to create interaction between hydrogen amide carried by the nitrogen N4 and oxygen of carbonyl bonded to the alpha carbon (O_7...H_{12}).The length of the hydrogen bond thus formed (deterministic folding β_L) is around 2.41 ± 5 Å. By analyzing the three possible positions of functional groups SH of the side chain according to the values of the corresponding angles χ1 and χ2, 4 conformations β_L may be adopted. In Table 3, we have grouped the energies gaps of β_L structures relative to the global minimum γ_L[g+g+] and the values of the corresponding angles φ, ψ, χ1 and χ2. The β_L structures are less stable than the global minimum γ_L[g+g+]. The energy gap increases from one conformation to another Table 3. This can be explained by analyzing the intramolecular interactions stabilizing each structure of Figure 6. As regards the conformationβ_L[a g+], the functional group SH is arranged in a way to make its acceptor atomic center S in interaction of strong character (2.44 Å) with the hydrogen carried by the nitrogen N_1 (S...H_9). The conformation β_L[g+a], no binding is provided by the side chain -CH_2-SH which reduces its stability of 6.7 kcal/mol relative to the global minimum.

The ε_L backbone conformation

The ε_L conformation results from a rotation around the ─Cα─CO─ bond of β_L backbone. Thus, the obtained folding defines the fourth area occupied by the diamide N-For-L-Cys-NH_2 in an isolated state.

By combining the rearrangement mode of the side chain to ε_L folding, 3 conformations were located namely ε_L[g-g+], ε_L[a g-] and ε_L[a a]. Their corresponding geometric parameters are grouped in the Table 4.

Table 1: Relatives energies in (kcal/mol) and angles values of γ_L minima calculated for N-For-L-Cys-NH_2. AM1/GA-MNC

Backbone [sidechain]	$\Delta\Delta H_f$	φ(°)	ψ(°)	χ1(°)	χ2(°)
γ_Lg+g+]	0.00	-82.4	62.8	44.8	73.2
γ_L[g-g-]	1.6	-82.7	68.0	-45.9	-63.7
γ_L[a g-]	1.9	-82.7	65.5	-160.0	-76.8
γ_L [g-g+]	2.3	-80.8	61.9	-72.8	63.4
γ_L[g-a]	2.5	-85.4	63.8	-57.9	-177.8

Table 2: Comparison of angles values (φ, ψ) of γ_L backbone (obtained in this work) with those of N-For-L-Gly-NH_2, N-For-L-Ala-NH_2 and N-For-L-Ser-NH_2 [a,b]

Systems	φ(°)	ψ(°)
N-For-L-Gly-NH_2 (HF/3-21G)	-83.9	67.8
N-For-L-Ala-NH_2 (AM1)	-82.2	65.7
N-For-L-Ala-NH_2 (HF/3-21G)	-84.5	67.3
N-For-L-Ser-NH_2 (HF/3-21G)	-82.2	67.4
N-For-L-Cys-NH_2 (AM1/GA-MNC)	-82.8	64.4

[a] Rodrıguez et al. (1998), [b] Perczel et al. (1996)

Table 3: Relatives energies and angles values characterizing the minimum β_L obtained from AM1/GA-MNC calculation

Backbone [sidechain]	$\Delta\Delta H_f$(kcal/mol)	φ (°)	ψ(°)	χ1(°)	χ2(°)
β_L[a g+]	2.6	-150.5	167.8	-156.6	73.0
β_L[g- g+]	3.8	-151.0	157.6	-111.3	57.1
β_L[g+g-]	5.1	-134.7	170.2	67.3	-60.1
β_L[g+a]	6.7	-157.5	167.2	64.7	-160.9

The ε_L[g-g+], ε_L[a g-] and ε_L[a a] structures are 3.5, 4.2 and 4.3 kcal/mol, respectively relative to minimum global. Geometrically, in addition to the hydrogen bonding (O_7… H_{12}) common among the three structures, a second interaction is generated by the SH group as shown in Figure 7.

Regarding conformations ε_L[a g-] and ε_L[a a], the same geometrical structure is adopted. However, in ε_L[a a] conformation, the acidic hydrogen of the thiol function is rotated around the S-CH_2 bond. The corresponding dihedral angle χ2 varies from -98.3 ° to -140.5 °.

The ε_D backbone conformation

Symmetrically with ε_L conformation, the minimum denoted ε_D appears in the right side of the obtained Ramachandran surface. The ε_D backbone adopts an extended structure favored by the formation of hydrogen bonds involving hydrogen amide H_{12} and the carbonyl oxygen bonded to the alpha carbon (O_7…H_{12}).

According to the values of χ1 and χ2 angles that define the type of rearrangement adopted by the side chain –CH_2-SH, 4 conformations have been associated with folding ε_D namely ε_D[a g+], ε_D[a a], ε_D[g-g+] and ε_D[g-g-] (Table 5 is shown energy gaps of structures with respect to the global minimum γ_L[g+g+] and the values of corresponding dihedral angles.

The structures of the Table 5 are classed in ascending order of their formation energies. The energy deviation from the global minimum increase of 5.6 kcal/mol for ε_D[a g+] to 9.7 kcal/mol for ε_D[g-g-]. This order of stability may be due to effect (steric or electronic) which can be generated by the functional groups of the side chain. Highlighted minimum ε_D for theN-For-L-Cys-NH_2 are grouped in Figure 8.

Structural analysis of the different conformations of Figure 8 shows that at most both types of intramolecular interactions are possible. In addition to hydrogen bonding (O_7…H_{12}) characterizing the ε_D backbone, the first two conformations ε_D[a g+] and ε_D[a a] are stabilized by a second hydrogen bond (average length of 2.36 Å) which involves the acceptor atomic center S of the thiol group and one of the hydrogens carried by N_1 (S…H_9). These two structures adopt similar geometries. However, the energy barrier of 0.4 kcal/mol is likely due to the redirection of the acidic hydrogen in ε_D[a a].

Table 4: Energies deviations from the global minimum and angles characterizing the minimum ε_L of N-For-L-Cys-NH_2, AM1/GA-MNC

Backbone [sidechain]	$\Delta\Delta H_f$ (kcal/mol)	φ(°)	ψ(°)	χ1(°)	χ2(°)
ε_L[g-g+]	3.5	-102.5	143.7	-72.8	60.7
ε_L[a g-]	4.2	-120.5	155.0	-165.5	-98.3
ε_L[a a]	4.3	-122.0	159.2	-157.0	-140.5

Table 5: Energies gaps and angles characterizing the minima ε_D of N-For-L-Cys-NH_2, obtained from AM1/GA-MNC calculation

Backbone [sidechain]	$\Delta\Delta H_f$ (kcal/mol)	φ(°)	ψ(°)	χ1(°)	χ2(°)
ε_D[a g+]	5.6	93.5	-167.9	-155.2	65.8
ε_D[a a]	6.0	91.2	-170.5	-149.3	-174.7
ε_D[g-g+]	7.0	99.9	161.2	-71.8	83.0
ε_D[g-g-]	9.7	77.6	170.0	-63.4	-58.8

Table 6: Energies deviations from the global minimum γ_L[g+g+] and the values of the angles φ, ψ, χ1 and χ2 of the 4 minimum δ_D of N-For-L-Cys-NH_2 system. AM1/GA-MNC

Backbone [side chain]	$\Delta\Delta H_f$ cal/mol	φ(°)	ψ(°)	χ1(°)	χ2(°)
δ_D[g+g-]	3.8	-130.2	-60.3	51.9	-76.9
δ_D[g+a]	4.8	-127.8	-57.3	49.2	156.6
δ_D[g-g+]	5.9	-131.8	-65.4	-81.5	25.6
δ_D[ag+]	6.2	-133.3	-67.8	173.3	58.2

The δ_D backbone conformation

The δ_D region constitutes the sixth populated area of the Ramachandran surface E= E(φ , ψ) of N-For-L-Cys-NH_2system. In all δ_D structures, the amide hydrogen of the peptide bond $H_{12}N_4C_5O_6$ is attracted by the acceptor atomic center N_1 of the second amide function. Thus, a hydrogen bond N_1...H_{12} of backbone-backbone type and with an average length 2.78 Å was established. By combining the geometric shape adopted by the –CH_2-SH fragment to fold δ_D 4 conformations are at the heart of discussions as shown in Figure 9.

Structurally, the two structures δ_D[g+g-] and γ_L[g+g+] undergo completely different geometrical rearrangements. Thus, the formation of C7 ring and the equatorial position of the side chain -CH_2-SH make the conformation γ_L[g+g+] less hindered and favor the formation of strong hydrogen bonds by two thiol.

In Table 6 are shown the energies deviations from the global minimum γ_L[g+g+] and the values of the anglesφ, ψ, χ1 et χ2 of the 4 minimum δ_D of N-For-L-Cys-NH_2 system.

In the structure δ_D[g+g-], the position of the -CH_2-SH fragment relative to δ_D backbone leads to the interaction of the thiol with hydrogen H_9 (S...H_9) (2.43 Å) with the lone pair of the nitrogen amide N_4 (N_4...H_{17}) (2.96 Å, which increase the effect of the steric hindrance, and consequently the decrease in stability of 3.8 kcal / mol. From a conformation to another, the energy barrier ΔH_f (δ_D)-ΔH_f (γ_L[g+g+]) increases until it reaches 6.2 kcal / mol.

The δ_L backbone conformation

The least populated region (1%) of Ramachandran surface of N-For-L-Cys-NH_2 is denoted δ_L (φ= -114.7, ψ= 16.7). As for the δ_D conformation, the backbone δ_L is stabilized by hydrogen bonding (N_4...H_9) between the two amide functions. The corresponding length is of the order of 2.57 Å. The side chain -CH_2-SH rearranges in a manner to create interaction of strong character (2.59 Å) between the sulfur and the amide hydrogen (S...H_{12}). The values of χ1 andχ2 angles are of about 37.8 and -91.7°, respectively. Energetically the δ_L[g+ g-]conformation (ΔH_f= -76.2 kcal/mol) is 5.1 kcal / mol relative to the global minimum γ_L[g+g+]. This can be justified by comparing the number of interactions stabilizing each minima (Fig. 10).

The structure γ_L[g+g+] is the most stable found along the surface conformation of N-For-L-Cys-NH_2 .According to our knowledge, a conformational and electronic study of energetically favored conformations of N-For-L-Cys-NH_2diamide at HF/3-21G and B3LYP/6-31G(d,p) (Zamora et al., 2002), shows that the most stable structure (global minimum) of this system adopts the structure γ_L[g+g+].in this work we found the same result with our technical computing AM1/GA-MNC. Results revealed that this techniques is useful for the generation of molecular structures constituting the conformational space of protein and could possibly be extended for the determination of molecular structures of other related molecules (Bora et al., 2019; Custódio et al., 2014; Daeyaert et al., 2005; Fu et al., 2018; Kaur and Kadam, 2018; Lei et al., 2018; Lucasius and Kateman, 1994; Luke, 1996; Song et al., 2018; Tian et al., 2018; Vitela and Castaños, 2012).

CONCLUSIONS

The conformational analysis of trans-N-For-L-Cys-NH_2 using genetic algorithm MNC coupled to the semi-empirical calculation method AM1 was studied and 7 regions or folds were located based on the mode of rearrangement of backbone, namely γ_L,γ_D, β_L, δ_D, δ_L,ε_D and ε_L and 27 have been identified if the rearrangement mode is associated of the side chain to these minima. The minimum corresponding to helical folds α_D and α_L are not favorable for this system.

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