



Effects of side chains in gas-phase amino acids: Conformational analysis and relative stabilities

Gang Yang^{a,b,*}, Lijun Zhou^a, Yuangang Zu^a, Yujie Fu^a, Rongxiu Zhu^b, Chengbu Liu^{b,*}

^aKey Laboratory of Forest Plant Ecology, Ministry of Education, Northeast Forestry University, 26 Hexing Road, Harbin 150040, PR China

^bInstitute of Theoretical Chemistry, Shandong University, Jinan 250100, PR China

ARTICLE INFO

Article history:

Received 16 October 2008

Received in revised form 6 January 2009

Accepted 6 January 2009

Available online 13 January 2009

Keywords:

Density functional calculations

Conformational analysis

Hydrogen bonds

Relative stability

Side chains

ABSTRACT

B3LYP and MP2 theoretical methods were employed to study the structures and relative stabilities of the Gly, Ala, Val, Aib, F-Gly, I-Gly and dF-Gly conformers. It was found that the relative stabilities of the Gly, Ala, Val and Aib conformers increase in the same orders of $\mathbf{V} < \mathbf{IV} < \mathbf{III} < \mathbf{II} < \mathbf{I}$, due to the similar shapes of the corresponding conformers. Two exceptions exist for the above orders: In Gly, conformer \mathbf{IV} is slightly more stable than conformer \mathbf{III} ; in Aib, conformer \mathbf{II} is more stable than conformer \mathbf{I} . The relative stability of conformer \mathbf{II} vs. \mathbf{I} is gradually enhanced by the substitutions of the lateral H atoms with the alkyl groups, especially in the case of the double substitutions to form Aib. The geometries and relative stabilities of the F-Gly, I-Gly and dF-Gly conformers are quite different from Gly as well as Ala, Aib and Val with the alkyl side chains. The driving forces in the conformers of the halogenated amino acids are mainly the intramolecular hydrogen bonding interactions, at least four hydrogen bonds formed in each dF-Gly conformer. For F-Gly and I-Gly, three conformers $\mathbf{II-IV}$ exist whereas conformers \mathbf{I} and \mathbf{V} are spontaneously transformed into conformers \mathbf{IV} and \mathbf{III} , respectively. It was found that the functional rather than alkyl side chains interact strongly with the NH_2CHCOOH fragments and accordingly have more remarkable influences on the geometries and relative stabilities of the conformers.

© 2009 Elsevier B.V. All rights reserved.

1. Introduction

In crystalline state and aqueous solutions, amino acids exist in the zwitterionic forms [1–3]. In gas phase, however, amino acids are predominated by the canonical isomers. The zwitterions of the gas-phase amino acids are not local energy minima, even for arginine with the extremely basic guanidine group [4–9]. Glycine has been widely used as computational models of proteins and many attempts were made to stabilize the glycine zwitterions [3,6,7,10–18].

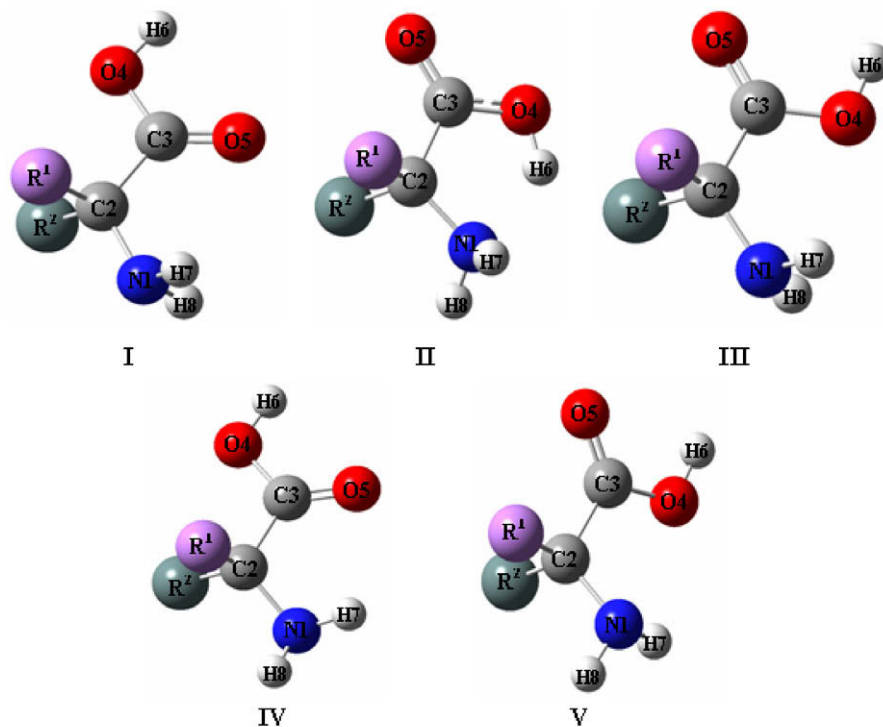
Besides the stabilization of amino acid zwitterions, the conformational studies of gas-phase amino acids are also a recent research focus [4,19–26]. As the landmark contributions of Császár indicated [3,19], eight conformers exist on the potential energy surface (PES) of the gas-phase glycine molecule. The five top populated conformers of glycine were shown in Fig. 1 ($R^1 = R^2 = \text{H}$) [4,13,27]. It is generally believed that conformer \mathbf{I} is stabilized by the two intramolecular N–H hydrogen bonds; however, Wang et al. [28] insisted that the superior stability of this conformer should be due to the hyperconjugation. As to alanine ($R^1 = \text{CH}_3$, $R^2 = \text{H}$, see Fig. 1), the rotational and quartic centrifugal distortion constants of its two conformers were determined with the microwave and millimeter wave spectra [29]. Using theoretical calcula-

tions, Gao et al. [30] and Császár [21] obtained thirteen conformers for the gas-phase alanine molecule. The relative energies indicated that five of them have observable populations, corresponding exactly to the conformers of glycine. Note that only the natural L-valine was counted here. Owing to the presence of the lateral isopropyl group, the conformational behavior of valine becomes more complicated ($R^1 = \text{CH}(\text{CH}_3)_2$, $R^2 = \text{H}$, see Fig. 1). Three most stable valine conformers were provided by Lesarri et al. [22], using laser-ablation molecular-beam Fourier transform microwave (LA-MB-FTMW) technique and *ab initio* calculations.

As is well-known, the side chains of amino acid residues in proteins are of special importance to the formation and maintenance of the three-dimensional (3D) structures [31–33]. In this work, the effects of side chains were discussed on the basis of the conformational studies of seven amino acids. Apart from glycine, alanine and valine described above, another four amino acids were considered; i.e., Aib, F-Gly, I-Gly and dF-Gly (Fig. 1). 2-Aminoisobutyric acid (Aib, $R^1 = R^2 = \text{CH}_3$) is a non-protein amino acid; however, it plays an important role in the transports of cultured McCoy cells and conformational transformations of peptides and proteins [34,35]. The other three are halogenated amino acids: F-Gly ($R^1 = \text{F}$, $R^2 = \text{H}$), I-Gly ($R^1 = \text{I}$, $R^2 = \text{H}$) and dF-Gly ($R^1 = R^2 = \text{F}$). The introduction of the halogen elements into the biologically active molecules bring about profound changes in the physical, chemical and biological properties, and therefore their synthesis has recently received much atten-

* Corresponding authors. Tel.: +86 0451 82192223; fax: +86 0451 82102082 (G. Yang).

E-mail addresses: thebiochem@gmail.com (G. Yang), cblu@sdu.edu.cn (C. Liu).



	Gly	Ala	Val	Aib	F-Gly	I-Gly	dF-Gly
R ¹	H9	C9H ₃	C9H(CH ₃) ₂	C9H ₃	F9	I9	F9
R ²	H10	H10	H10	C10H ₃	H10	H10	F10

Fig. 1. Five conformers of the amino acids presently studied.

tion [36,37]. The conformational behaviors of Aib, F-Gly, I-Gly and dF-Gly were explored for the first time. On such basis, the effects of side chains in amino acids were discussed.

2. Computational details

All the calculations were performed with Gaussian 03 software package [38]. The Becke 3-parameter Lee-Yang-Parr exchange-correlation (B3LYP) functional [39,40] was testified by numerous literatures [20,28,41–48] to be suitable to treat the amino acid related systems. The standard 6-311++G(d,p) basis set was used for all the elements except I. Owing to the significant relativistic effects, the inner electrons of the I element were treated with LanL2DZ effective core potentials (ECP) and the valence electrons with LanL2DZ basis set [49]. The NBO charge analysis was accomplished at the same level of theory [50].

As suggested by the referee, the single-point energies of all the structures were evaluated at MP2/Aug-CC-pVDZ level of theory, using the B3LYP/6-311++G(d,p) geometries. In addition, the conformers of Gly, Ala, Aib and F-Gly were also optimized with the MP2/Aug-CC-pVDZ method. It indicated that the MP2/Aug-CC-pVDZ geometries and energies are in excellent agreements with those of B3LYP/6-311++G(d,p) and MP2/Aug-CC-pVDZ//B3LYP/6-311++G(d,p) levels, respectively. Accordingly, the geometric and energetic analysis of this work was based on the latter two theoretical levels, except specially pointed out.

3. Results and discussion

The experimental and computational results [4,13,20–22,25,27] indicated that amino acids such as Gly, Ala, Pro and Val are predominated by not more than five conformers. Accordingly, the five

top populated conformers of amino acids in Fig. 1 were considered in this work. The present geometries and relative energies of Gly, Ala and Val are in excellent agreements with the previous data [4,13,20–23,28].

For the different conformers of amino acids, the direct bond distances are changed within a narrow range and the standard deviations are quite small [4,13,20,21–23,28,51]. Take C3–O5 bonds for example. The C3–O5 bond distances of all the presently studied conformers fall within 1.340–1.362 Å, with the exception of the value 1.333 Å in conformer IV(dF-Gly). The best structural parameters to characterize and distinguish different conformers should be the dihedrals. For all the conformers of the seven amino acids in Fig. 1, the four atoms in the carboxyl groups (C3O5O4H6, see Fig. 1) remain nearly planar. Their deviations from planar are usually less than 2.0°, and in some conformers such as I(Gly), III(Gly), II^A(Val) and I(Aib), the deviations are even below 0.1°. However, larger deviations are observed in conformers II of some amino acids. The $\Psi(O5C3O4H6)$ dihedrals are equal to 176.34° in conformer II^B(Val), 175.53° in conformer II(F-Gly), –176.61° in conformer II(I-Gly) and 176.43° in conformer II(dF-Gly), respectively. Owing to the more deviations from planar, the conjugations in these carboxyl groups are reduced by certain degrees. The structural analysis indicated that the $\Psi(O4C3C2N1)$, $\Psi(O4C3C2R^2)$ and $\Psi(C3C2N1H7)$ dihedrals can finely characterize and distinguish the various conformers of amino acids. The values of the three dihedrals were collected and listed in Table 1. If interested, please find the complete geometric details in Supplementary materials.

3.1. Val

For Val, Lesarri et al. [22] provided the structures and relative energies of conformers I–III. Presently, conformers IV and V were

Download English Version:

<https://daneshyari.com/en/article/5416815>

Download Persian Version:

<https://daneshyari.com/article/5416815>

[Daneshyari.com](https://daneshyari.com)