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The Shape of *β*-Alanine

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Abstract: The combination of Fourier transform microwave spectroscopy in a pulsed supersonic jet with laser ablation has made *β*-alanine amenable to a structural study in the gas phase. Two new conformers of *β*-alanine have been identified together with the two previously observed by McGlone and Godfrey [*J. Am. Chem. Soc.* **1995**, *117*, 1043]. The comparison between the experimental rotational and ^{14}N nuclear quadrupole coupling constants and those calculated ab initio provide a definitive test for molecular structures and confirm unambiguously the identification of all conformers. For the two most abundant conformers, an intramolecular hydrogen bond between the amino group and carbonyl oxygen (N−H···O=C) is established, and the COOH adopts a *cis*-COOH configuration. The next conformer in order of abundance presents an O−H···N intramolecular hydrogen bond with a *trans* configuration for the COOH group. The high sensitivity of the experiment has allowed us to detect for the first time a conformer uniquely stabilized by an n−π^* hyperconjugative interaction between the nucleophile N: of the amino group and the π^* orbital at the carbonyl group. Partial conformational relaxation has been observed in the supersonic expansion.

Introduction

A great part of the success of natural amino acids as building blocks of proteins relies on their high torsional flexibility which results in a large number of low energy conformers in the gas phase. Investigation of the conformational behavior of amino acids and the forces that model their shape, free from intermolecular interactions, must be accomplished in gas phase. However, most studies of amino acids have been conducted in a condensed medium because it is the natural environment for biological processes to occur. This approach has the drawback of providing a picture in which it is difficult to distinguish between the properties that are inherent to amino acids and those arising from interactions with the medium. In addition, amino acids appear as zwitterions in condensed phases ($^+H_3N-CH(R)-COO^-$), in contrast to the neutral form they adopt in proteins and polypeptides.[1]

Microwave spectroscopy is the most powerful technique to distinguish unambiguously between different conformers and provide accurate structural information of a molecular system. Until recently, amino acids have been elusive to gas-phase rotational studies due to their elevated melting points and their thermal unstability. Hence, only glycine,[2] alanine,[3] and *β*-alanine[4] could be investigated in gas phase by rotational spectroscopy using heating methods for vaporization. We have recently developed an experimental method that combines the benefits of laser ablation to efficiently vaporize the solids without substantial decomposition with the high resolution of Fourier transform microwave spectroscopy in supersonic jets to probe the molecules in a collisionless environment.[5] Our laser ablation molecular beam Fourier transform microwave (LA-MB-FTMW) spectrometer has been successfully applied to date to the investigation of proline,[6] valine,[7] alanine,[8] 4-hydroxyproline,[9] *N,N*-dimethylglycine,[10] and isoleucine.[11]

β-alanine ($NH_2-CH_2-CH_2-COOH$), the simplest and only natural *β*-amino acid, has a role in a variety of biological processes. It is believed to be a neurotransmitter in the central nervous system, binding to receptor sites common to glycine and *γ*-aminobutyric acid (GABA)[12] and acting in the visual system.[13] It is one of the amino acids constituting the naturally

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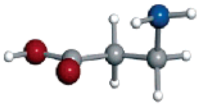
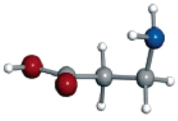
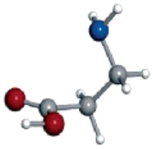
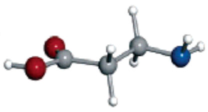
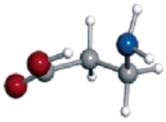
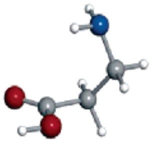
Table 1. Calculated Spectroscopic Parameters and Relative Energies for the Lower-energy Conformers of β-alanine from MP2/6-311++G(d,p) Computations

	I	II	III	IV/XII[c]	V	VI
A^a /MHz	7150.5	6968.2	5743.5	9195.4	7172.9	5756.2
B /MHz	2363.7	2313.6	2484.7	1858.0	2512.2	2418.6
C /MHz	2012.6	2008.4	2353.7	1584.9	1993.0	2314.4
μ_a /D	-0.1	-1.5	-2.3	-0.4	6.4	0.2
μ_b /D	0.7	1.7	-1.2	0.7	1.5	-0.8
μ_c /D	-0.9	-0.6	-0.8	-1.2	-0.5	-0.8
μ_{TOTAL} /D	1.2	2.4	2.7	1.4	6.6	1.1
χ_{aa} /MHz	1.85	-3.95	-2.69	2.70	-1.30	-3.68
χ_{bb} /MHz	0.95	1.69	2.33	0.78	-0.62	1.58
χ_{cc} /MHz	-2.80	2.26	0.36	-3.48	1.92	2.10
ΔE_{MP2} /cm^{-1}	0	279	398	599	-68	480
$\Delta E_{MP2+ZPC}$/cm^{-1}	0	258	421	522	143	496
$(\Delta E_{HF})^b$ /cm^{-1}	(0)	(259)	(627)	(468)/(978)	(819)	(819)
						

[a] A, B, and C are the rotational constants, μ_a, μ_b, and μ_c are the electric dipole moment components, and χ_{aa}, χ_{bb}, and χ_{cc} are elements of the ^{14}N nuclear quadrupole coupling tensor. [b] HF/6-31G(d,p) relative energies from ref 4. [c] The HF/6-31G(d,p) structures of these conformers converged to the same minimum when calculated at MP2 level.

occurring dipeptides anserine and carnosine,[14] and it also possesses a pharmaceutical interest: derivatives of β-alanine have been proposed for epilepsy treatment.[15] In addition, β-alanine is the most abundant among the amino acids found in CI chondrites (a type of carbonaceous meteorites), exceeding by a factor of 2 the percentage of glycine and β- and γ-aminobutyric acid, and by a factor of 10 that of alanine.[16] Some authors have suggested that the origin of the precursors of meteoritic amino acids, and perhaps the amino acids themselves, could reside in the interstellar medium (ISM).[17] Recent experimental results indicate that β-alanine can be formed in gas phase by ion−molecule reactions of smaller precursors in the ISM and that these reactions preferentially yield β-alanine over alanine.[18] Laboratory experiments demonstrate that β-alanine is formed by UV photolysis of the analogues of icy interstellar grains.[19] Precise laboratory data on its rotational spectrum, comprising the distinctive transition frequencies of all possible conformers, are required for an unambiguous identification of β-alanine in space. The gas-phase rotational data of β-alanine has certainly a direct application in astrochemistry.

The rotational spectrum of β-alanine, a solid at room temperature (mp 202 °C), was studied for the first time in 1995 using a Stark-modulated free-jet absorption spectrometer by heating the sample at 230 °C and entraining it in a stream of argon.[4] Guided by HF/6-31G(d,p) ab initio calculations and partially resolved N-quadrupole coupling, two conformers could be identified corresponding to the structures I and V of Table 1, stabilized by N−H···O and N···H−O hydrogen bonds, respectively. Conformer I was predicted to be the global minimum of β-alanine, and conformer V was calculated to be 9.8 kJ/mol above in energy. Although conformers II−IV were predicted to have intermediate energies between those of conformers I and V, no experimental evidence of other conformers of β-alanine was found. This was explained in ref 4 by an unreliable prediction of the relative energies of the conformers at the level of calculation employed.

It seemed adequate to take advantage of our LA-MB-FTMW technique for a reinvestigation of β-alanine in gas phase. In addition to the previously mentioned advantages of this technique, transition intensity is here proportional to the corresponding electric dipole moment component (in contrast to a Stark-modulated free jet experiment where the transition intensity is proportional to the square of the dipole moment), which makes LA-MB-FTMW spectroscopy more suitable for the study of species with modest dipole moments. In this work, ab initio calculations at a level higher than those reported in the literature[4,20] have been performed. A detailed inspection of the spectra has led to the identification of four conformers through their rotational constants and a fully resolved hyperfine structure (not achievable in the above-mentioned Stark-modulated work) due to the ^{14}N nuclear quadrupole coupling effects.

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Analysis of this hyperfine structure in β-alanine has proved to be an invaluable tool to discriminate between conformers with similar heavy atom backbones that have rotational constants much the same. In addition, conformational relaxation,[21] a process known to occur in supersonic expansions and observed in the jet-cooled studies of other amino acids,[8,22] has been considered.

Methods

1. Experimental. The rotational spectrum of β-alanine in gas phase has been observed and characterized using LA-MB-FTMW spectroscopy.[3] In this technique, a solid rod of β-alanine is vaporized using the green light (532 nm) of a pulsed Nd:YAG laser. The vaporized molecules are subsequently seeded in an inert gas and dragged into a vacuum chamber where they expand adiabatically between the mirrors of a Fabry-Pérot resonator. Microwave radiation is then applied to the molecules in the supersonic beam to macroscopically polarize them. Their decay signals are detected in the time domain and Fourier transformed to the frequency domain to obtain the rotational spectrum.

The samples of β-alanine (Aldrich, 99%) were used without further purification. The target rods were produced by pressing β-alanine (previously ground to obtain homogeneous and fine grains) with small quantities of a commercial binder (methyl cellulose). These rods are placed vertically in front of the exit of a solenoid valve in our desorption nozzle (located in the rear part of one of the Fabry-Pérot mirrors[3]), and they are continuously rotated and translated so that a fresh surface is hit by each laser pulse.

Gas pulses of typically 0.60 ms of neon or argon at backing pressures of 5.5 bar have been used, followed by laser pulses of about 60 mJ/pulse, slightly delayed with respect to the gas pulses, and microwave pulses of 0.3 μs. The delay is adjusted to optimize the signal-to-noise ratio of the rotational transitions. Because the molecular beam and the microwave radiation are parallel in our LA-MB-FTMW spectrometer, each line is split into two due to the Doppler effect. The molecular frequency is the arithmetic mean of the Doppler components. Frequency uncertainty is estimated to be lower than 3 kHz.

2. Computational. There had been previous computational studies of β-alanine,[4,20] but these calculations were carried out using the HF method with the small 6-31G(d,p)[4] and 4-31G[20] basis sets. We therefore sought to carry out higher-level ab initio calculations to improve the quantitative predictions of relative conformational energies and molecular properties, such as rotational constants and ^{14}N nuclear quadrupole coupling parameters, relevant to identify the conformers present in the supersonic expansion of our experiment. Ab initio computations have been conducted on the 20 structures of β-alanine reported in refs 4 and 20 using the second-order Møller−Plesset perturbation theory (MP2) with the 6-311++G(d,p) basis set in the frozen core approximation as implemented in the Gausian03 package.[23] This level of theory behaved satisfactorily in our previous studies of amino acids[6−11] with a remarkable agreement between the experimental and the predicted spectroscopic constants, which supported the assignments of the detected conformers.

All 20 conformers are local minima in the potential energy surface at this level of theory, since there were no negative eigenvalues in their Hessian matrices. The calculation of relative stabilities was improved including the zero-point vibrational contributions within the harmonic approximation. The results are displayed in Table 1 for the lower-energy conformers (with relative energies below 500 cm^{-1}), which have been labeled following the same nomenclature used in ref 4. Molecular properties for the high-energy conformers are available as Supporting Information (Table 1). Conformer I is predicted as the global minimum followed by conformers V, II, and III (see Table 1). According to these predicted relative energies and electric dipole moment components, several conformers should be amenable to experimental observation in the adiabatic expansion of our experiment.

Results and Discussion

1. The N−H···O=C Conformers. Initial scans were directed to search for the rotational transitions of conformer I based on the reported experimental rotational constants of β-alanine.[4] R-branch rotational transitions of μ_b- and μ_c-type for conformer I were readily located and measured. The microwave power needed for optimum polarization of the rotational transitions was consistent with the predicted magnitudes of the components of the electric dipole moment (see Table 1). In addition to the Doppler splitting, all the transitions exhibited fully resolved ^{14}N nuclear quadrupole coupling hyperfine structure (see graphic of β-alanine I in Table 2), thus confirming the presence of a single nitrogen atom in the observed species. Rotational parameters were derived from a final set of six rotational transitions (22 hyperfine components) using a Hamiltonian given by $H = H_R^{(A)} + H_Q$ where $H_R^{(A)}$ represents the Watson A-reduced semirigid rotor Hamiltonian in the I^r representation[24] and H_Q is the nuclear quadrupole coupling interaction term.[25] The determined rotational constants and nuclear quadrupole coupling constants χ_{aa}, χ_{bb}, and χ_{cc} (Table 2) are in excellent agreement with the predicted ab initio values for conformer I in Table 1. The rotational constants are consistent with those previously reported by Godfrey et al. (Table 2 of ref 4).

During the analysis of the rotational spectrum a set of weaker μ_a-type R-branch transitions with a characteristic pattern of a nearly prolate asymmetric top was located very close to that of conformer I, leading to the assignment of a new conformer. The assignment was completed with the measurements of μ_b- and μ_c-type R-branch transitions. All the transitions exhibited ^{14}N quadrupole hyperfine structure (see figure in Table 2) and were fitted using the same Hamiltonian described above for conformer I.

At first inspection, the determined spectroscopic constants collected in the second column of Table 2 are in good agreement with those predicted ab initio (see Table 1) for conformers I and II, which have similar rotational constants. However, the predicted differences in the ^{14}N nuclear quadrupole coupling constants χ_{aa}, χ_{bb}, and χ_{cc} provide a conclusive argument to identify unambiguously the new conformer in our supersonic expansion as conformer II. Conformer II is structurally similar to conformer I; the main difference between them is the orientation of the amino group with respect to the carboxylic group (compare structures in Table 2), which dramatically affects the values of their quadrupole coupling constants. The ^{14}N nuclear quadrupole coupling constants depend on the electronic environment around the amino nitrogen atom and are extremely sensitive to the amino group orientation. As a consequence, what appears to be a slight structural difference between conformers I and II—reflected in similar values of their rotational constants—has a huge effect on the values of their ^{14}N nuclear quadrupole coupling constants (see Table 2). It can be concluded that conformers I and II could not have been

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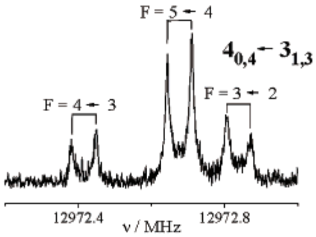
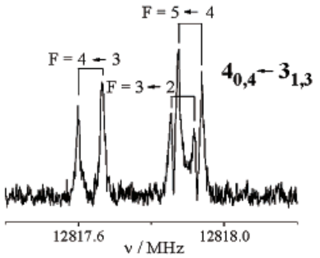
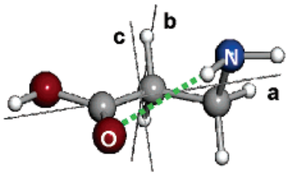
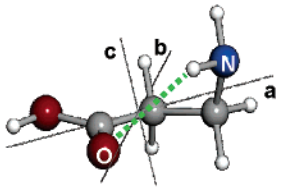
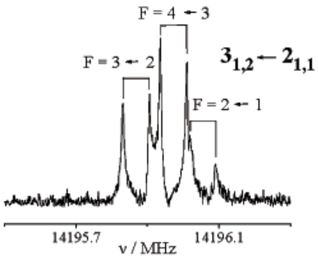
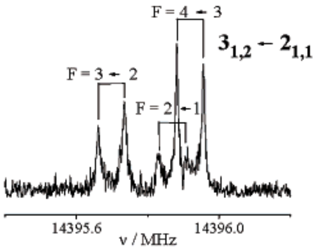
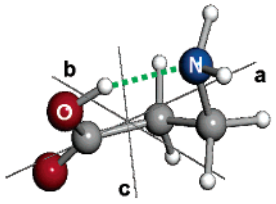
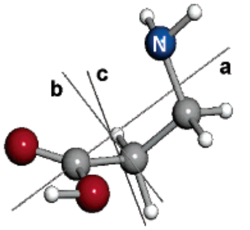
Table 2. Spectroscopic Constants for Conformers I and II of β-Alanine, along with Their Respective $4_{0,4} \leftarrow 3_{1,3}$ Rotational Transitions[a]

	Conformer I		Conformer II	
A^b / MHz	7267.8292(18)[e]		7160.50092(64)	
B / MHz	2335.1700(63)		2298.73029(15)	
C / MHz	1986.77894(69)		1974.35380(22)	
Δ_J / kHz	0.893(31)		0.8973(61)	
Δ_{JK} / kHz	-1.83(39)		-2.074(81)	
χ_{aa} / MHz	1.7295(34)		-3.5076(15)	
χ_{bb} / MHz	0.8860(45)		1.5942(20)	
χ_{cc} / MHz	-2.6155(45)		1.9134(20)	
σ^c / kHz	3.1		1.9	
N^d	22		54	

[a] The hyperfine structure of the rotational transition reflects the different orientation of the $-NH_2$ group in both conformers. The ^{14}N nuclear quadrupole coupling hyperfine components ($F' \leftarrow F''$) are labeled by the quantum numbers $F = I + J$. Each component appears as a doublet (++) because of the Doppler effect. [b] A, B, and C are the rotational constants, Δ_j and Δ_{jk} are the quartic centrifugal distortion constants, and χ_{aa}, χ_{bb}, and χ_{cc} are elements of the ^{14}N nuclear quadrupole coupling tensor. [c] rms deviation of the fit. [d] Number of fitted hyperfine components. [e] Standard error in parentheses in units of the last digit.

Table 3. Spectroscopic Constants for Conformer V and III of β-Alanine along with Their Respective $3_{1,2} \leftarrow 2_{1,1}$ Rotational Transitions[a]

	Conformer V		Conformer III	
A^b / MHz	7177.0630(10)[e]		5841.28(44)	
B / MHz	2499.71943(34)		2430.29713(37)	
C / MHz	1982.45703(31)		2307.85654(37)	
Δ_J / kHz	0.352(12)		2.087(19)	
Δ_{JK} / kHz	-		-	
χ_{aa} / MHz	-1.2153(21)		-2.4048(20)	
χ_{bb} / MHz	-0.5740(30)		1.9870(71)	
χ_{cc} / MHz	1.7893(30)		0.4178(71)	
σ^c / kHz	2.6		2.1	
N^d	39		23	

[a] The ^{14}N nuclear quadrupole coupling hyperfine components ($F' \leftarrow F''$) are labeled by the quantum numbers $F = I + J$. Each component appears as a doublet (++) because of the Doppler effect. [b] A, B, and C are the rotational constants, Δ_j and Δ_{jk} are the quartic centrifugal distortion constants, and χ_{aa}, χ_{bb}, and χ_{cc} are elements of the ^{14}N nuclear quadrupole coupling tensor. [c] rms deviation of the fit. [d] Number of fitted hyperfine components. [e] Standard error in parentheses in units of the last digit.

distinguished without the use of quadrupole hyperfine structure, which constitutes a unique identifier for conformers.

Conformers I and II are stabilized by an intramolecular amine-to-carbonyl N−H···O=C hydrogen bond interaction (predicted intramolecular distances for the hydrogen bond N−H···O=C of 2.403 and 2.513 Å, respectively) and a *cis*-COOH functional group interaction as observed in the α-amino acids glycine[2], alanine,[3,8] valine,[7] and isoleucine,[11] except for the non bifurcated character of the N−H···O=C hydrogen bond.

2. The O−H···N Conformer. Once the analysis of conformers I and II was completed, a number of strong unassigned transitions still remained in the spectrum. These belonged to the conformer V previously observed by Godfrey et al.[4] In agreement with the predicted values of the dipole moment components in Table 1 strong μ_a-type R-branch transitions showing totally resolved ^{14}N nuclear quadrupole hyperfine structure (see structure in Table 3) were first located and measured. The experimental measurements were completed with μ_b-type R-branch transitions. No μ_c-type transitions were detected, which is consistent with the very low calculated value of this dipole moment component for conformer V (see Table 1). The 10 measured transitions (39 hyperfine components) were analyzed with the same Hamiltonian used for conformers I and II, and the corresponding rotational parameters are given in Table 3. The comparison with the predicted rotational and quadrupole coupling constants (χ_{aa}, χ_{bb}, and χ_{cc}) of Table 1 is a definitive argument to identify this conformer in the supersonic expansion.

In accordance with the orientation of the amino group (structure of Table 3), conformer V is stabilized by an intramolecular hydrogen bond between the hydrogen atom of the hydroxyl group and the electron lone pair at the nitrogen atom (O−H···N interaction, with an ab initio predicted distance of 1.784 Å). This imposes a *trans* arrangement for the carboxylic group, which implies the loss of a stabilizing energy contribution.

3. The n−π* Interaction Conformer. Additional frequency surveys were carried out in the hope of observing more low-energy conformers. After discarding the lines corresponding to the assigned conformers I, II, and V, very weak transitions of a fourth conformer were identified that showed the characteristic nuclear quadrupole coupling hyperfine structure (see figure in Table 3) due to a single ^{14}N nucleus. Measurements of μ_a-type R-branch transitions and subsequent fits with the same Hamiltonian described above led to the rotational parameters listed in Table 3. The agreement between the experimental rotational and quadrupole coupling constants with those predicted in Table 1 for conformer III provides evidence of its presence in the supersonic expansion.

No intramolecular hydrogen bond is apparent in conformer III; the amino group hydrogens adopt an arrangement pointing away from the carboxylic moiety (see figure in Table 3). Therefore, we must admit that its stabilization should be originated by a factor different from intramolecular hydrogen bonding. Some crystal structure regularities in compounds containing nucleophilic groups N: and electrophilic centers have been interpreted in terms of an n−π* interaction, which arises from the hyperconjugative delocalization of the nonbonding electron pair from the nitrogen to the π* orbital at the carbonyl group of the −COOH, reminiscent of the Bürgi−Dunitz trajectory.[26] The observed distances in crystals between N: and the carbonyl carbon range from about 1.5 to 3 Å, while the typical ∠NCO angles are between 100° and 114°. For the MP2 ab initio structure of conformer III of β-alanine, $r(\mathrm{N^-C}) = 2.85$ Å and $\angle\mathrm{NCO} = 112°$—optimal for such interaction to occur. We have performed an NBO analysis[27] at the B3LYP/6-311++G(d,p) level that further supports the existence of this interaction, which is the only one established between nonvicinal parts of conformer III of β-alanine, and is calculated to provide a stabilizing energy of 580 cm^{-1}.

All measured transition frequencies for the observed conformers are provided as Supporting Information (Tables 2−5).

4. Conformer Abundances. The relative post-expansion abundances of the observed conformers of β-alanine can be studied from comparing the intensity measurements of different rotational transitions, which in turn can be taken as indicative of the conformer stability trend. The "effective population" of the observed conformers in the supersonic jet is a consequence of population owing to their relative energies plus the possible contributions from relaxation of other conformers. Collisions at the onset of the supersonic expansion between the seeded molecules (β-alanine in this case) and the carrier gas may produce the relaxation of high-energy conformers to lower-energy ones. The extension to which relaxation occurs is usually associated with the height of the interconversion barrier between conformers. For systems involving only one degree of freedom, such as torsional isomerism[21] or axial/equatorial equilibrium in hydrogen bond complexes,[28] barriers less than about 400 cm^{-1} have been proposed to allow relaxation. In multiconformational systems, where several degrees of freedom can channel the relaxation, it has been suggested that barrier heights of 1000 cm^{-1} or higher would impede conformational relaxation.[29] The carrier gas used also influences the extent of relaxation: heavier carrier gases are more effective relaxants, and their use may even prevent the observation of the higher-energy forms of isomers or conformers.

Assuming that the intensities of lines for a conformer *i* are proportional to $\mu_i \cdot N_i$, where μ_i is the corresponding electric dipole moment component and N_i is the number density of species *i* in the jet, the relative population ratio obtained with Ne as a carrier gas shows that conformer I is the global minimun and is much more populated than other conformers. Conformer II seems to be slighly more populated than conformer V, while conformer III is the least populated.

It was observed that the intensity ratio II/I increases significantly in going from the heavier (Ar) to the lighter (Ne or He) carrier gas. This is indicative of partial relaxation from conformer II to conformer I in our molecular beam. In β-alanine, interconversion between conformers I and II can occur through the rotation of the amino group around the N−C bond with a barrier of about 1000 cm^{-1} predicted at the MP2/6-311++G(d,p) level. To our knowledge, this is the first case in which incomplete relaxation is observed between conformers separated by a barrier of 1000 cm^{-1}. This result makes it difficult to relate the post-expansion populations to the preexpansion equilibrium populations. However, the II → I relaxation does not change the qualitative energy picture of the conformers. No relaxation effects have been observed for conformers III and V when changing Ar to Ne.

The postexpansion abundances qualitatively agree with the predicted gas-phase relative energy ordering from Table 1, except for the fact that conformer V is predicted to be more stable than conformer II. The use of the MP2 method and large basis sets considerably improves the agreement between the predictions and the experimental results. Conformer V in particular reflects the effect of using higher-level calculations: it was calculated at the HF/6-31G(d,p) level to be at 820 cm^{-1} above conformer I,[4] while the MP2 calculations here predicted it to be 140 cm^{-1} above conformer I after inclusion of the zero-point correction (see Table 1). The relative energies of the conformers seem to be reasonably well predicted now.

No transitions attributable to other conformers remained unassigned in the spectrum. Conformer VI which exhibits an intramolecular hydrogen bond between the amine group and the oxygen atom of the hydroxyl group (N−H···O−H) has not been observed in the supersonic expansion. This conformer is predicted ab initio to lie close in energy to conformer III and corresponds to a conformer similar to conformer II, but with

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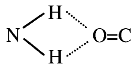
the carboxylic group rotated by ca. 180° (see Table 1). As in the case of aliphatic α-amino acids[2,3,7,8,11] an interconversion barrier VI $\leftrightarrow$ II below 400 cm^{-1} can be expected, which may allow relaxation of this conformer.

Conclusions

The four lowest-energy conformers of β-alanine have been observed and characterized by LA-MB-FTMW spectroscopy, which combines the benefits of laser ablation and molecular beams with the sensitivity and resolution of FTMW spectroscopy. Unequivocal identification of these conformers was achieved by comparing the experimental values of the rotational and nuclear quadrupole coupling constants with those predicted ab initio. The contribution of the hyperfine constants is of particular significance because it allows discrimination between structures with similar rotational constants. The nuclear hyperfine coupling constants provide incomparable structural information on the amino group.

The intramolecular hydrogen bonding exhibited by conformer V (O$-$H$\cdots$N, with a *trans* disposition of the COOH group) is similar to that observed in α-amino acids such as glycine[2], α-alanine,[3,8] valine,[7] or isoleucine.[11] The nature of the hydrogen bonding in conformers I and II is considerably different from the bifurcated arrangement of α-amino acids which gives rise to one conformer. The hydrogen bond is now established between the oxygen atom of the carboxylic group and only one of the hydrogens of the amino group, presumably because a bifurcated interaction imposes too close a distance between the atoms involved. Therefore, two conformers can arise in β-alanine, depending on the H atom involved in the intramolecular interaction. Only the dramatic difference in the quadrupole constants of these two conformers allows one to distinguish between them.



Conformer III is, in contrast, stabilized not by hydrogen bonding but by an n$-\pi^*$ interaction, which has not been observed in aliphatic α-amino acids thus far. Only in the α-imino acid 4-hydroxyproline has a similar interaction been observed between the nonbonding electron of the hydroxyl oxygen and the π^* at the carboxylic carbon.[9] An increase of the number of carbon atoms between the amino group and the carboxylic group confers a higher flexibility to the heavy atom backbone. This gives rise to the appearance of a larger number of low-energy conformers and changes the balance of intramolecular forces, since the stabilizing contributions and the steric constraints are modified. Thus, the prevalence of N$-$H$\cdots$O and O$-$H$\cdots$N hydrogen bonds as main stabilizing contributions in α-amino acids might diminish as the length of the carbon chain between the $-NH_2$ and $-$COOH groups increases. In this context, the study of β-alanine ($NH_2-CH_2-CH_2-COOH$) can be seen as intermediate between those of glycine (NH_2-CH_2-COOH) and γ-aminobutyric acid ($NH_2-CH_2-CH_2-CH_2-COOH$, the next member of the series, traditionally known as GABA), for which a conformer with the same n$-\pi^*$ interaction has been already characterized in our laboratory by LA-MB-FTMW spectroscopy.[30] Comparison between different amino acids will shed more light on the intramolecular forces that influence their preferred configurations and determine their implication in polypeptides or proteins.

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Supporting Information Available: Tables of the rotational frequencies of conformers I, II, III, and V of β-alanine measured in this work together with ab initio structural data for all conformers; complete ref 23. This material is available free of charge via the Internet at http://pubs.acs.org.

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