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The Conformers of Phenylglycine

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Abstract: The neutral form of the unnatural amino acid phenylglycine was vaporized by laser ablation, and the presence of two conformers was detected in a supersonic expansion by Fourier transform microwave spectroscopy. Both conformers were unequivocally identified by comparison of their experimental rotational and quadrupole coupling constants with those calculated ab initio. The most stable conformer is stabilized by intramolecular hydrogen bonds N−H···O=C, N−H···π (with the closest C−C bond in the aromatic ring), and a *cis*-COOH interaction. The other conformer exhibits a O−H···N hydrogen bond between the hydrogen atom of the hydroxyl group and the lone pair at the nitrogen atom.

Keywords: ab initio calculations · amino acids · conformation analysis · hydrogen bonds · laser ablation · rotational spectroscopy

Introduction

Unnatural amino acids are of considerable and increasing interest. They can be incorporated as new building blocks into the genetic codes of both prokaryotic and eukaryotic organisms to facilitate studies of protein structure and function. Over 30 unnatural amino acids with modified side chains have been genetically encoded in response to unique triplet and quadruplet codons.[1] In addition, these compounds are required for peptide-based supramolecular devices.[2] The synthesis of unnatural amino acids, in particular phenylglycines, is of great interest for their use in medicinal chemistry[3] and prompted the development of several procedures to synthesize phenylglycine.[4]

Unnatural amino acids, like natural ones, are expected to exist in a variety of conformations; this aspect, combined with the enantiomeric shape, will determine their properties. While discrimination between enantiomeric forms is routinely performed in condensed phases or in solution, this is not possible for the various conformational species. Intermolecular interactions or interactions with the solvent can overcome the forces which drive the conformational equilibrium in isolated molecules. The only way to quantify the factors which lead to conformational stability is to investigate the isolated molecules in the gas phase.

Unequivocal identification of the various conformers displayed by an amino acid can be provided by a rotationally resolved investigation. Such a description of the gas-phase conformational shape has been reported for several aliphatic amino acids through pure rotational spectroscopy. The rotational spectra of the simplest natural α- and β-amino acids, glycine,[5] alanine[6] and β-alanine,[7] were observed after vaporization by thermal heating. Extension of these studies to other amino acids with high melting points became possible only recently by combining laser ablation with molecular-beam Fourier transform microwave (LA-MB-FTMW, see Experimental Section)[8] spectroscopy. With this technique the problems of thermal instability and low vapour pressure are overcome. A short laser pulse impinges onto a solid rod, made by pressing the amino acid sample, and vaporizes the molecules. The ablated molecules are subsequently dragged into a vacuum chamber by a pulse of inert gas and probed by FTMW spectroscopy. This technique has been successfully applied to the conformational study of the natural amino acids proline[9] and valine[10] among others,[11,12] and has provided very accurate geometries of all conformers of alanine.[13] This kind of investigation is not available for unnatural amino acids. For this reason, we decided to under-

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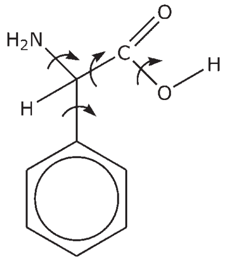
take a conformational investigation of the unnatural α-amino acid phenylglycine (PG) using LA-MB-FTMW spectroscopy.

Phenylglycine (m.p. 290 °C) is a glycine derivative in which a proton of the CH_2 group has been replaced by a phenyl ring (see Scheme 1). Natural amino acids bearing a chromophoric group in their structure, namely, tyrosine, tryptophan, and phenylalanine, have been widely studied in the gas phase with various techniques which combine electronic and vibrational spectroscopy with supersonic expansions.[14–19] However, for none of them has been repotrted a rotationally resolved investigation capable of providing structural information on the various conformers. Hence, this study is the first gas-phase investigation of the unnatural α-amino acid PG, the simplest one bearing a chromophoric group. It can be considered a first step towards the analysis of the rotational spectrum of α-amino acids with more torsional degrees of freedom, such as those mentioned above.



Scheme 1. Sketch of phenylglycine showing the hindered single-bond rotations which govern the conformational equilibrium.

Results

Preliminary model calculations: The molecular system under investigation is relatively rich from the viewpoint of conformational behaviour, because the four possible hindered rotations around single bonds shown in Scheme 1 can generate a plethora of species. For this reason, theoretical calculations were performed to guide the spectral search. The computationally inexpensive semiempirical method AM1 was first used to drive a conformational search and locate the possible minima on the potential hypersurface. In this search, no restrictions were imposed on the torsions of the dihedral angles of the molecule. The structures of the lower-energy conformers found in this way were then fully optimized by using the MP2 method with the 6-311++G-(d,p) basis set,[20] a level of calculation that has proved to give satisfactory predictions of the structures and spectroscopic parameters of similar molecules.[9–13] The six conformers of Figure 1 were localized on the potential energy surface with relative energies below 700 cm^{-1}. The parameters relevant to the rotational spectrum, namely, the rotational constants, the components of the electric dipole moment, and the ^{14}N quadrupole coupling constants are reported, together with the relative conformational energies, in Table 1. The predicted low-energy conformers have been labelled according to the nomenclature previously used for glycine,[6] alanine,[7,13] and valine,[10] which refers to the existence of N−H···O=C (type I), O−H···N (type II) and N−H···OH (type III) hydrogen bonds in combination with *cis*-COOH (types I and III) and *trans*-COOH (type II) configurations.

Abstract in Spanish: *El aminoácido no natural fenilglicina, en su forma neutra, ha sido vaporizado mediante ablación láser, detectándose por espectroscopía de microondas con transformación de Fourier la existencia de dos confórmeros en la expansión supersónica. Su identificación se ha realizado de forma inequívoca comparando las constantes de rotación y cuadrupolo nuclear experimentales con las calculadas teóricamente. El confórmero más estable está estabilizado mediante los enlaces de hidrógeno intramoleculares N−H···O=C, N−H···π con el enlace C−C más próximo del anillo aromático y la interacción* cis*-COOH. El otro confórmero presenta un enlace O−H···N entre el átomo de hidrógeno del grupo hidroxilo y el par electrónico no enlazante del átomo de nitrógeno.*

Rotational spectra and conformational assignment: Initial spectroscopic searches were directed to the identification of the lower-energy conformers, which are predicted to be near-prolate asymmetric rotors. After a wide frequency scan around 5.5 GHz, where the R-branch μ_a-type transitions $J = 4 \leftarrow 3$ were predicted, it was possible to assign two sets of ^aR-type transitions with $K_{-1} = 0$, 1 and 2 to the spectra of two conformers of PG, hereafter referred to as X and Y. All transitions presented the typical pattern of a molecule containing one nitrogen atom: they were split into several component lines due to ^{14}N quadrupole coupling with the overall rotation (Figure 2). The experimental measurements were completed with R-branch transitions of μ_b- and μ_c-type. All measured rotational transitions are listed in Table 2. Deep searches over wide frequency intervals with Ar and Ne as carrier gases were performed to detect other possible conformers, but no lines were observed that could be attributable to them.

The measured rotational frequencies for the X and Y conformers of Table 2 were fitted[21] to a Hamiltonian given by $H = H_R^{(S)} + H_Q$ where $H_R^{(S)}$ is the Watson S-reduced semirigid rotor Hamiltonian in the I^r representation[22] and H_Q is the nuclear quadrupole coupling interaction term.[23] The obtained spectroscopic parameters for the observed conformers are presented in Table 3.

At first glance, the degree of consistency between the rotational constants of species Y with those predicted for conformer **II** in Table 1 indicated that conformer **II** is present in the supersonic expansion. More conclusive evidence to identify species Y with conformer **II** came from the excellent agreement between the experimental and predicted values of the nuclear quadrupole coupling constants χ_{aa}, χ_{bb} and χ_{cc}.

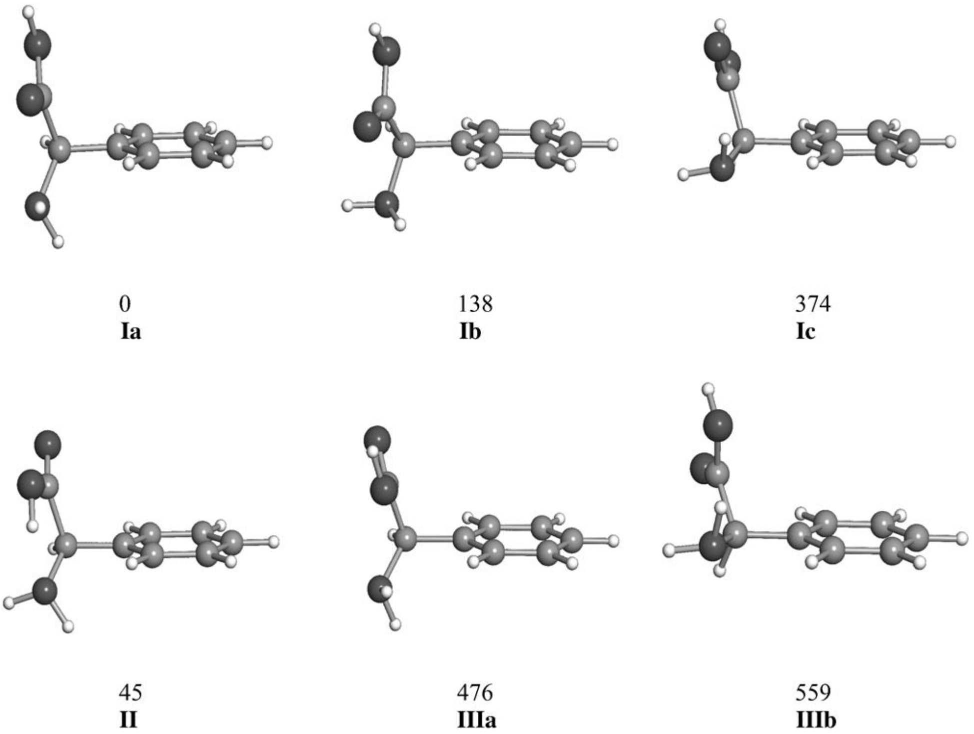


Figure 1. Low-energy conformers of phenylglycine and predicted relative energies [cm^{-1}] from MP2/6-311++G(d,p) calculations.

Table 1. Ab initio (MP2/6–311++G**) molecular properties of the phenylglycine conformers depicted in Figure 1.

	Ia	**Ib**	**Ic**	**II**	**IIIa**	**IIIb**
relative energies						
$\Delta E^{[a]}$ [kJ mol^{-1}]	0	1.6	4.5	0.5	5.7	6.7
ΔE [cm^{-1}]	0	138	374	45	476	559
$\Delta(E$+ZPE$)^{[b]}$ [cm^{-1}]	0	78	372	162	457	583
$\Delta G_{298}{}^{[c]}$ [cm^{-1}]	0	84	264	172	453	499
rotational constants						
A [MHz]	2058.1	2081.3	2005.7	2079.5	2066.1	2048.1
B [MHz]	729.7	723.6	793.6	752.2	730.9	792.9
C [MHz]	704.4	705.8	663.2	688.4	692.1	654.1
^{14}N nuclear quadrupole coupling parameters						
χ_{aa} [MHz]	−2.77	−0.56	−1.43	1.26	−3.69	−1.11
χ_{bb} [MHz]	2.31	−2.24	1.26	1.29	2.35	0.88
χ_{cc} [MHz]	0.47	2.79	0.16	−2.54	1.34	0.23
Electric dipole moments						
μ_a [D]	2.04	−0.24	−0.44	2.18	1.89	−0.40
μ_b [D]	−0.76	0.56	1.29	3.00	1.69	−0.62
μ_c [D]	0.40	−1.10	0.38	−3.43	0.27	−1.31
μ_{total} [D]	2.21	1.26	1.41	5.05	2.55	1.50

[a] Uncorrected for zero-point energy. [b] MP2/6-311++G(d,p) electronic energies corrected with zero-point vibrational energies (ZPE) calculated at B3LYP/6-311++G(d,p) level. [c] Free Gibbs energies at 298 K were calculated by adding the B3LYP/6-311++G(d,p) thermal corrections to the MP2/6-311++G(d,p) electronic energies.

The rotational constants of species X are consistent with those predicted for conformers **Ia**, **Ib**, and **IIIa**. However, the experimental quadrupole coupling constants of this species are closer to those predicted for conformer **Ia**. The quadrupole coupling constants are very sensitive to the orientation of the amino group in the molecule. Hence, the disagreement between the experimental and ab initio values of these constants for conformer **Ia** may indicate a slightly different position of the amino group from that predicted ab initio. We calculated the values of the quadrupole coupling constants at different values of the dihedral angle ∢HNCC (see Figure 3). The results shown in Figure 3 and Table 4 indicate that the ab initio quadrupole coupling constants χ_{aa} and χ_{cc} of conformer **Ia** match the experimental ones if the amino group is rotated counterclockwise by about 9° with respect to the value initially predicted for ∢HNCC (76.5°). Species X can thus be conclusively identified with conformer **Ia**. The rotation of the amino group shortens the distance

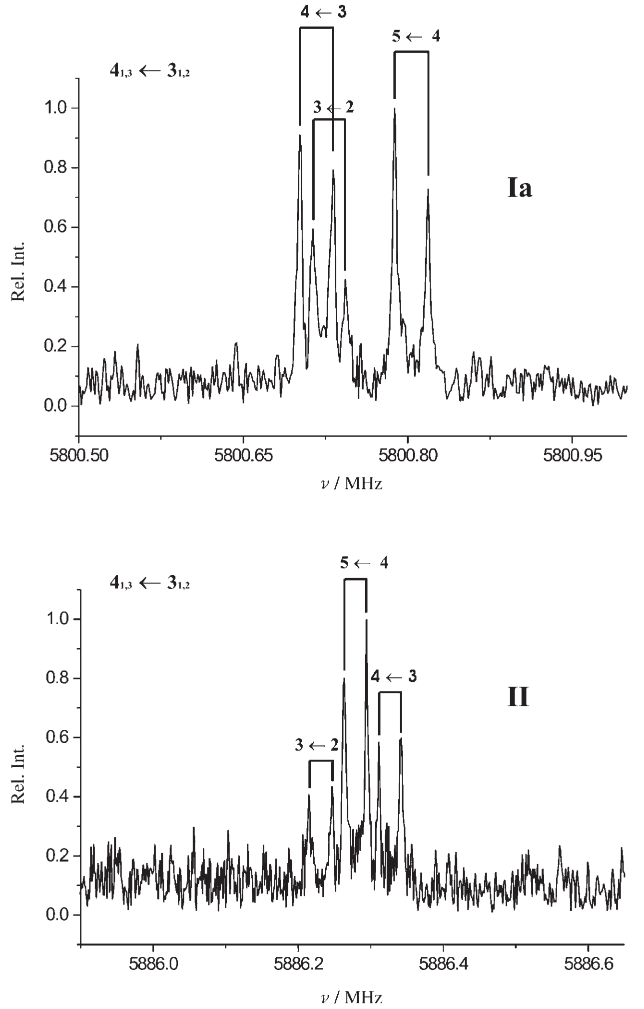


Figure 2. The $4_{1,3}{\leftarrow}3_{1,2}$ rotational transition of conformers **Ia** (upper trace) and **II** (lower trace) of phenylglycine. The hyperfine components due to ^{14}N nuclear quadrupole coupling interactions are labeled with the quantum numbers $F'{\leftarrow}F''$. Each component appears as a doublet (Π) due to the Doppler effect.

between one of the H atoms of NH_2 and the carbonyl oxygen in the COOH group. The distance of the other H atom of the amino group to the nearest C–C bond in the aromatic ring is also shortened to 2.8 Å, and thus it is possible to establish an N–H⋅⋅⋅π interaction such as those shown for phenylethylamine[24,25] and efedrine[26] and inferred for phenylalanine.[18]

The predicted magnitude of the electric dipole-moment components for conformers **Ia** and **II** in Table 1 is also consistent with the microwave power needed for optimal polarization of *a*-, *b*- and *c*-type transitions. Similar microwave power was used for the *a*-type transitions of both conformers, in agreement with the almost equal values predicted for μ_a (see Table 1). For the *b*- and *c*-type transitions of conformer **Ia**, higher microwave powers were necessary, compatible with the smaller values of μ_b and μ_c calculated for conformer **Ia** with respect to those of conformer **II**.

The relative populations of the observed **Ia** and **II** conformers of PG were estimated by comparing the intensities of six selected *a*-type R-branch transitions with Ar or Ne as carrier gases. Assuming that cooling in the adiabatic expansion brings all conformers to their ground vibrational state, the intensities of the lines for each conformer are proportional to $\mu_a \cdot N$, that is, the electric dipole-moment component along the *a* principal inertial axis and the number density in the supersonic jet. Taking into account the ab initio electric dipole moments of Table 1, an estimated population ratio of $N_{\mathbf{Ia}}:N_{\mathbf{II}}=4$ was obtained in both Ar and Ne, which indicates that conformer **Ia** is the most abundant species in the supersonic expansion (see Figure 2).

Discussion and Conclusions

Conformers **Ia** and **II** of PG (see Figure 1) have been detected and characterized in the supersonic expansion of a LA-MB-FTMW experiment through the analysis of their rotational spectra. The experimental values of the rotational and quadrupole coupling constants played a conclusive role in identifying the conformers of PG on the basis of ab initio predictions.

The conformational behaviour of PG can be understood in the context of the intramolecular forces that act in each conformer. Conformer **Ia** is stabilized by intramolecular N–H⋅⋅⋅O=C and N–H⋅⋅⋅π hydrogen bonds and a *cis*-COOH interaction, which involves the H atom of OH and the oxygen lone pair of C=O.[27] This contrasts with the intramolecular hydrogen bonds in the type **I** conformers of glycine,[6] alanine,[7,13] valine[10] and isoleucine.[12] In these amino acids, besides the *cis*-COOH interaction, both amino hydrogen atoms interact with the oxygen atom of the C=O group in a bifurcated N–H⋅⋅⋅O=C bond. The corresponding conformer **Ib** was not observed for PG. This indicates that the stabilization energy of a single N–H⋅⋅⋅O=C bond plus a N–H⋅⋅⋅π interaction (as in **Ia**) is larger than that of a bifurcated N–H⋅⋅⋅O=C hydrogen bond (as in **Ib**). Conformer **II** exhibits an intramolecular O–H⋅⋅⋅N hydrogen bond, like those of the type **II** conformers of glycine,[6] alanine,[7,13] valine[10] and isoleucine.[12] A distance of about 2.6 Å between one of the hydrogen atoms of the amino group and the closest C–C bond of the phenyl ring could allow the establishment of a N–H⋅⋅⋅π interaction in conformer **II** like that of conformer **Ia**.

The non-observation of the forms **Ib**, **Ic**, **IIIa** and **IIIb** of PG, predicted to fall in the group of low-energy conformers (see Table 1), deserves some explanation. Certain high-energy conformers may collisionally relax to lower-energy conformers during the supersonic expansion. Hence, it is not a surprise that thermally accessible conformers corresponding to the equilibrium distribution predicted ab initio are missing in the jet.[28] Conformational energy differences and barrier heights determine which species are observable in the expansion.[29] The carrier gas also plays a role: heavier carrier gases enhance conformer interconversion, as evidenced in hydrogen-bonded complexes.[30] In PG, conform-

Table 2. Frequencies of the measured transitions of phenylglycine (MHz).

								PG X		PG Y	
J'	K'_{-1}	K'_{+1}	J''	K''_{-1}	K''_{+1}	F'	F''	ν_{obs}	$\nu_{obs}-\nu_{calcd}$	ν_{obs}	$\nu_{obs}-\nu_{calcd}$
2	2	0	1	1	1	1	0			7022.859	0.001
						2	1			7021.144	0.001
						3	2			7021.982	0.001
3	0	3	2	0	2	2	1	4303.385	−0.001		
						3	2	4303.508	−0.001		
						4	3	4303.514	0.000		
3	1	2	2	0	2	2	1			5894.207	0.001
						3	2			5893.068	−0.002
						4	3			5893.850	0.000
3	1	3	2	0	2	2	1	5567.643	0.000		
						3	2	5568.690	−0.001		
						4	3	5568.011	0.000		
3	1	2	2	1	1	2	1	4351.009	−0.001		
						3	2	4350.922	0.000		
						4	3	4351.114	−0.002		
3	1	3	2	1	2	2	1	4259.562	0.004		
						3	2	4259.308	0.002		
						4	3	4259.462	0.001		
4	0	4	3	0	3	3	2	5735.527	0.000	5726.158	0.000
						4	3	5735.600	0.001	5726.213	0.000
						5	4	5735.587	0.000	5726.134	0.000
4	1	4	3	0	3	3	2	6942.932	0.000	6779.803	0.000
						4	3	6943.774	−0.001	6780.492	0.001
						5	4	6943.152	0.001	6779.908	−0.001
4	1	3	3	0	3	3	2			7476.620	−0.003
						4	3			7475.577	0.000
						5	4			7476.374	0.000
4	1	3	3	1	2	3	2	5800.728	0.000	5886.231	0.000
						4	3	5800.717	−0.001	5886.325	−0.002
						5	4	5800.803	0.000	5886.279	0.000
4	1	4	3	1	3	3	2	5678.672	−0.003		
						4	3	5678.592	−0.001	5608.098	0.001
						5	4	5678.655	0.000	5608.021	0.000
4	2	3	3	2	2	3	2			5750.330	0.001
						4	3			5750.538	0.001
						5	4			5750.372	0.000
5	0	5	4	0	4	4	3	7165.579	0.000	7138.583	0.000
						5	4	7165.639	0.000	7138.663	−0.001
						6	5	7165.617	0.000	7138.573	0.000
5	0	5	4	1	4	4	3			6084.937	−0.002
						5	4			6084.387	0.002
						6	5			6084.797	−0.001
5	1	4	4	0	4	4	3	8763.254	0.000	9102.839	−0.003
						5	4	8762.629	−0.001	9101.805	−0.001
						6	5	8763.179	0.002	9102.643	0.001
5	1	4	4	1	3	4	3	7249.898	−0.002	7352.377	0.001
						5	4	7249.907	0.000	7352.440	0.000
						6	5	7249.951	0.000	7352.401	0.000
5	1	5	4	0	4	4	3	8304.772	0.001	8059.153	0.000
						5	4	8305.508	−0.001	8059.796	−0.002
						6	5	8304.924	0.000	8059.239	0.000
5	1	5	4	1	4	4	3			7005.510	0.003
						5	4	7097.334	0.001	7005.520	0.001
						6	5	7097.361	0.000	7005.464	0.001
5	2	3	4	2	2	4	3	7185.091	0.002		
						5	4	7184.903	0.001	7236.638	0.000
						6	5	7185.073	0.000	7236.626	−0.002
5	2	4	4	2	3	4	3	7174.808	0.001	7184.641	−0.002
						5	4	7174.656	0.000	7184.751	0.002
						6	5	7174.794	0.000	7184.656	0.002
6	0	6	5	0	5	5	4	8593.111	0.000	8539.683	0.001
						6	5	8593.169	0.000	8539.778	0.000
						7	6	8593.137	0.000	8539.676	−0.001
6	0	6	5	1	5	5	4			7619.111	−0.001
						6	5			7618.645	0.001
						7	6			7619.012	0.001
6	1	5	5	0	5	5	4			10778.781	0.002
						6	5			10777.716	−0.001
						7	6			10778.607	0.001
6	1	5	5	1	4	5	4	8698.353	0.000	8814.518	−0.002
						6	5	8698.367	0.000	8814.576	0.000
						7	6	8698.389	−0.001	8814.538	0.001
6	1	6	5	0	5	5	4	9654.661	0.000	9320.774	−0.001
						6	5	9655.327	0.000	9321.354	0.000
						7	6	9654.776	0.001	9320.841	0.001
6	1	6	5	1	5	5	4			8400.201	−0.004
						6	5	8515.457	0.000	8400.220	−0.001
						7	6	8515.469	0.001	8400.176	0.002
6	2	4	5	2	3	5	4	8626.657	−0.002	8705.621	0.003
						6	5	8626.538	−0.001	8705.577	−0.003
						7	6	8626.657	0.001	8705.614	0.003
6	2	5	5	2	4	5	4	8608.760	0.001	8616.713	0.004
						6	5	8608.681	−0.001	8616.774	−0.003
						7	6	8608.760	0.000	8616.713	0.002
7	0	7	6	0	6	6	5	10017.722	0.000	9929.188	−0.002
						7	6	10017.780	−0.001	9929.293	0.000
						8	7	10017.742	0.001	9929.188	0.001
7	0	7	6	1	6	6	5			9148.097	0.001
						7	6			9147.717	0.000
						8	7			9148.024	0.000
7	1	6	6	1	5	6	5	10145.916	0.000	10271.517	−0.003
						7	6	10145.933	0.000	10271.575	−0.002
						8	7	10145.945	0.001	10271.537	0.002
7	1	7	6	0	6	6	5	10994.434	−0.001	10573.032	0.000
						7	6	10995.041	−0.001	10573.534	0.000
						8	7	10994.524	0.000	10573.079	0.000
7	1	7	6	1	6	6	5	9932.886	0.001	9791.937	−0.001
						7	6	9932.886	0.003	9791.957	−0.001
						8	7	9932.886	0.000	9791.918	0.001
8	0	8	7	0	7	7	6			11308.185	−0.001
						8	7			11308.289	−0.002
						9	8			11308.185	0.001
8	0	8	7	1	7	7	6			10664.345	0.001
						8	7			10664.050	0.001
						9	8			10664.293	0.001
8	1	8	7	0	7	7	6			11824.446	0.001
						9	8	11349.533	0.000	11180.586	0.000
9	0	9	8	0	8	8	7			12678.881	−0.001
						9	8			12678.979	0.000
						10	9			12678.881	0.001
9	1	9	8	1	8	10	9	12765.351	0.000		

ers **Ib** and **Ic** may relax to conformer **Ia** by simple rotation of the amino group about the C−N bond. These interconversion paths were investigated by ab initio calculations, which led to a barrier to conformer **Ia** of about 300 cm^{-1}, so conformers **Ib** and **Ic** are likely to relax to conformer **Ia**. Type **III** conformers have not been detected for the α-amino acids glycine,[6] alanine,[7,13] valine[10] and isoleucine,[12] and conformational relaxation to type **I** conformers in the supersonic expansion has been proposed to explain this. In our case, conformer **IIIa** may transform into conformer **Ia** by ro-

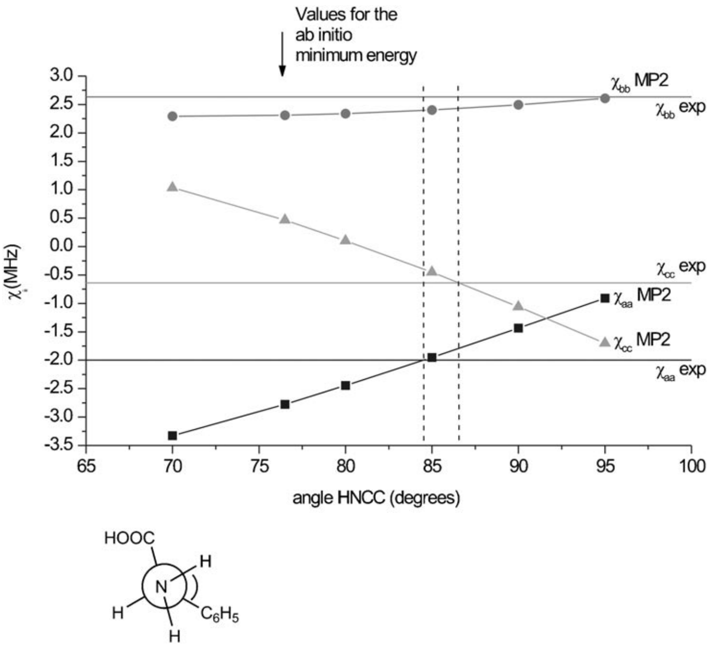


Figure 3. Variation of the quadrupole coupling constants calculated at the MP2/6-311++G(d,p) level with the dihedral angle $\sphericalangle$HNCC. χ_{bb} is practically invariant with the dihedral angle.

Table 3. Spectroscopic constants of the two observed conformers of phenylglycine.

	PG X	PG Y
A [MHz]	2071.62729(35)[a]	2088.42797(24)
B [MHz]	732.866322(60)	753.894720(64)
C [MHz]	702.324222(45)	684.237085(49)
D_J [kHz]	0.10027(47)	0.13825(53)
D_{JK} [kHz]	0.268(9)	0.5011(80)
D_K [kHz]	[0.0][b]	[0.0]
d_1 [kHz]	−0.02311(35)	−0.04578(40)
d_2 [kHz]	−0.01766(50)	−0.02660(62)
χ_{aa} [MHz]	−1.9960(53)	1.1508(52)
χ_{bb} [MHz]	2.6334(42)	1.4517(38)
χ_{cc} [MHz]	−0.6374(42)	−2.6025(38)
N[c]	75	100
σ[d] [kHz]	1.0	1.3

[a] Errors in parentheses are expressed in units of the last digit. [b] Parameters in square brackets were fixed to zero in the fit. [c] Number of fitted hyperfine components. [d] RMS deviation of the fit.

Table 4. Comparison of the predicted quadrupole coupling constants of conformer **Ia** of phenylglycine as a function of the angle $\sphericalangle$HNCC with the experimental values.

	MP2/6-311++G(d,p)						Exptl
$\sphericalangle$HNCC	70°	76.5°	80°	85°	90°	95°	
χ_{aa} [MHz]	−3.33	−2.77	−2.44	−1.95	−1.43	−0.91	−1.9960(53)
χ_{bb} [MHz]	2.29	2.31	2.34	2.40	2.49	2.61	2.6334(42)
χ_{cc} [MHz]	1.04	0.47	0.10	−0.45	−1.06	−1.70	−0.6374(42)

tation of the carboxyl group along the C−C bond through an estimated barrier to interconversion of about 1100 cm^{-1}, which may preclude conformational cooling. On the other hand, this conformer is predicted to lie almost 500 cm^{-1} above conformer **Ia**. This latter factor, or perhaps a combination of the relative energy and partial conformational cooling, can result in rotational transition intensities of conformer **IIIa** that fall below the sensitivity limit of our spectrometer and thus provide a satisfactory explanation for the nonobservation of this conformer. The same reasoning can be applied to conformer **IIIb**, corresponding to a minimum slightly higher in energy than conformer **IIIa**.

In spite of the fact that post-expansion abundances are affected by uncertainties in the reproducibility of laser ablation and in the values of ab initio dipole moments, the experimental population ratio can be tentatively related to the equilibrium distribution of conformers. Assuming that the laser-vaporized molecules are in conformational equilibrium distribution[13] and that no conformer relaxation between **Ia** and **II** occurs (since no detectable alteration in the intensity ratios with the carrier gas (Ar or Ne) was observed), conformer **Ia** must be proposed as the most stable conformer of PG, in agreement with the ab initio predictions of Table 1. Additionally, the ab initio equilibrium populations at 298 K of the lower-energy conformers of PG have been calculated from the ab initio Gibbs energies (see Table 1) to be $N_{\mathbf{Ia}}:N_{\mathbf{Ib}}:N_{\mathbf{Ic}}:N_{\mathbf{II}}:N_{\mathbf{IIIa}}:N_{\mathbf{IIIb}}=39:26:11:17:4:3$. Assuming that all conformers are brought to their lowest vibrational states after the expansion and that the relaxation processes **Ib**,**Ic**→**Ia** take place, a relative population ratio of $N_{\mathbf{Ia}}:N_{\mathbf{II}}=4.5$ is calculated. This value is not substantially changed even when the unlikely complete cooling of conformers **III**→**I** is considered, and it is in very good agreement with the result from relative intensity measurements.

The conformational behaviour displayed by PG, an aromatic unnatural α-amino acid, and that of aliphatic α-amino acids[6,7,10,11,13] in the gas phase is remarkably alike: type **I** conformers are the global minimum in all cases. As mentioned above, PG displays an additional N−H···π hydrogen bond. This study on PG provides the first conformational results for an unnatural α-amino acid with a chromophoric group, and shows the applicability of LA-MB-FTMW spectroscopy to these molecules. Investigations of other aromatic α-amino acids with longer side chains, such as phenylalanine, tryptophan or tyrosine, by this technique are now encouraged. They will provide data on whether and how the balance between different intramolecular forces alters the conformational landscape.

Experimental Section

The details of the LA-MB-FTMW technique have been given elsewhere,[8] and therefore only a brief description of the spectrometer is given here. In this experiment, the PG molecules were vaporized by laser ablation with the second harmonic (512 nm) of a Q-switched pulsed Nd:YAG laser. The green laser pulses were focussed onto the desorption nozzle, where a solid sample rod of roughly 6 mm diameter was held vertically at the exit channel of a commercial solenoid-pulsed valve. The rods were formed by pressing PG powder (Aldrich, D,L-phenylglycine, 99%) mixed with minimum quantities of a commercial binder. The target rod rotated and translated so the laser hit a different point of the sample surface in each successive pulse.

The ablation products, diluted in a light inert carrier gas, were expanded supersonically to form a molecular beam between the mirrors of a Fabry–Pérot resonator where they were probed by FTMW spectroscopy. The collinear arrangement of the supersonic jet and the resonator axis makes all lines appear as doublets, due to the Doppler effect (see Figure 2). The molecular frequency is the arithmetic mean of the Doppler components.

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