

Shape of Glycine

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Abstract: Using our Stark-modulated free-expansion jet spectrometer, we have measured and subsequently analyzed the rotational spectra of the two ¹³C, the ¹⁵N, and the methylene-d₂ isotopomers of the amino acid glycine conformers **1** and **2** and of the *N,O*-d₃ isotopomer for conformer **2**. The structural implications of the derived rotational constants, in light of published geometric parameters from elaborate post-Hartree–Fock *ab initio* calculations, have led to the conclusion that both of these conformers have *r_p* structures of C_s symmetry. A twisted C₁ symmetry modification of conformer **2**, designated **3**, is the favored prediction of elaborate *ab initio* calculations, but the effect of the zero-point twisting vibration would give either conformation an *r_p* geometry of C_s symmetry. Thus there is no discrepancy between theory and experiment. From a sensitive survey scan of the spectrum of the main isotopomer, an upper limit of 1/5 has been set for the abundance of the theoretical conformer **4** relative to **2**. This result appears to be in conflict with the most elaborate *ab initio* calculations, which give **4** as energetically similar to **2** and may point to the importance of conformational relaxation during the jet expansion for higher energy conformers that have suitably low barriers to isomerization.

Introduction

The geometry and conformations of glycine (NH₂CH₂-COOH), the simplest amino acid and the prototype structural unit of other biologically important amino acids and proteins, have been the subject of much theoretical study.^{1a–i} Some experimental microwave spectroscopy^{2a–d} and electron diffraction studies³ have also been made. Of the original microwave studies, one^{2a–c} reported the spectroscopic rotational constants and dipole moment data for one conformer and from these identified it as conformer **2** of Figure 1. The other study^{2d} included the identification of a vibrational satellite and presented a more extensive structural discussion that again reached the conclusion, based on rotational constants, that the observed conformer was **2**. Some time later, stimulated by further discussion of the glycine conformers based on *ab initio* theoretical calculations,^{1b} an additional microwave spectral study was reported^{2e,f} in which another conformer was detected and, again on the basis of its rotational constants, was identified as conformer **1**. On the basis of observed line intensities and approximate estimates of dipole moment components, it was concluded that conformer **1** is about 6 kJ mol⁻¹ more stable than conformer **2**, in moderate agreement with the then theoretical value of 9 kcal mol⁻¹.

The notation for labeling the conformers follows the established convention as in, e.g., a recent theoretical study¹ⁱ and is

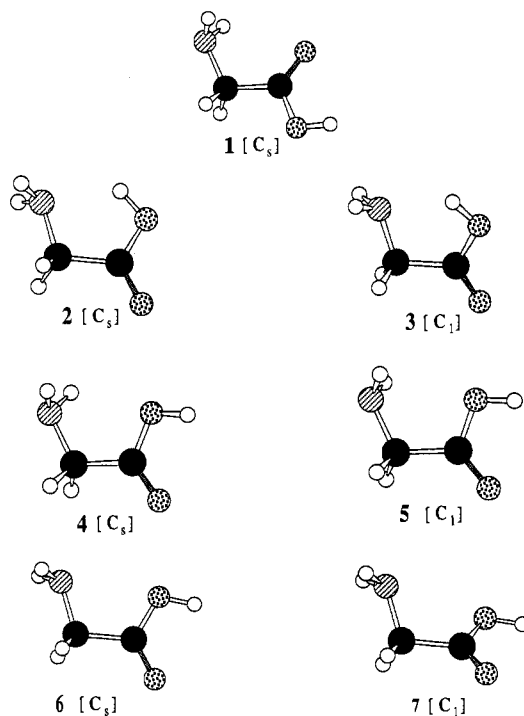


Figure 1. The conformers of glycine predicted to be of lowest energy.

shown in Figure 1. Conformational arrangements permitting three different intramolecular hydrogen-bonding situations distinguish the lower energy conformers, **1** having a bifurcated interaction linking the amino hydrogens to the carbonyl oxygen, **2** with an interaction linking the hydroxyl hydrogen to the amino nitrogen lone pair, and **4** with a bifurcated interaction linking the amino hydrogens to the hydroxyl oxygen lone pairs. By convention, theoretical conformers **1**, **2**, and **4** are defined as having C_s symmetry. A general consensus has emerged that conformer **1** is the most stable and that **2** is probably next in stability. The most elaborate theoretical computations indicate that **1** and **2** have the lowest electronic energies. The two species identified by analysis of the microwave spectrum also have rotational constants in excellent agreement with those predicted by the quantum mechanical calculations on **1** and **2**.

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(2) (a) Storey, J. W. V. Ph.D. Thesis, Monash University, Australia, 1976. (b) Brown, R. D.; Godfrey, P. D.; Storey, J. W. V.; Bassez, M. P. *J. Chem. Soc., Chem. Commun.* **1978**, 547–548. (c) Bassez, M. P. Ph.D. Thesis, Monash University, Australia, 1980. (d) Suenram, R. D.; Lovas, F. J. *J. Mol. Spectrosc.* **1978**, *72*, 372–382. (e) Schäfer, L.; Sellers, H. L.; Lovas, F. J.; Suenram, R. D. *J. Am. Chem. Soc.* **1980**, *102*, 6566–6568. (f) Suenram, R. D.; Lovas, F. J. *J. Am. Chem. Soc.* **1980**, *102*, 7180–7184.

(3) Iijima, K.; Tanaka, K.; Onuma, S. *J. Mol. Struct.* **1991**, *246*, 257.

Table 1. Spectroscopic Parameters (MHz) for Isotopomers of Glycine 1

| constant | main | ¹³ C(1) | ¹³ C(2) | C(2)-d ₂ | ¹⁵ N |
|-----------------|------------------|--------------------|--------------------|---------------------|-----------------|
| A | 10 341.521(89) | 10 340.943(29) | 10 227.084(88) | 9318.452(23) | 10 341.45(12) |
| B | 3876.1785(12) | 3869.1142(57) | 3859.051(21) | 3799.2353(23) | 3762.457(53) |
| C | 2912.3509(10) | 2908.3166(26) | 2893.596(20) | 2832.3222(15) | 2847.639(29) |
| D ₁ | 0.000 743 4(33) | 0.000 736(16) | 0.000 64(14) | 0.000 736 0(71) | 0.001 19(23) |
| D _{JK} | 0.003 986(17) | 0.004 06(16) | 0.003 98(43) | 0.002 53(16) | 0.0031(11) |
| D _K | | 0.0048(22) | 0.0110(67) | | |
| d ₁ | -0.000 190 1(28) | -0.000 188(14) | -0.000 225(56) | -0.000 184 2(50) | -0.000 41(13) |
| d ₂ | -0.000 015 8(17) | -0.000 020 1(64) | | 0.000 005 7(37) | |
| transitions | 73 | 21 | 16 | 23 | 16 |
| rms residual | 0.117 | 0.0227 | 0.0580 | 0.013 | 0.177 |

The electron diffraction data were interpreted in terms of the presence of a single conformer, **1**, but relied upon the adoption of values of lengths and angles for the N–H, C–H, and O–H bonds obtained from moderate-level (4-21G basis) molecular orbital computations, deriving lengths and angles for the N–C, C–C, C–O, and C=O bonds. Hu *et al.*¹¹ (HSS) point out that their much more elaborate computations yield predicted lengths and angles for the bonds to H that typically differ by 5% from those assumed for the electron diffraction analysis, making the conclusions less reliable.⁴

However, two unresolved issues remain: (a) some high-quality computations imply that another conformer, **3**, a twisted version of **2**, is very similar in energy to **2** and may indeed be somewhat more stable (if so, **2** is a saddle point between two equivalent minima that represent **3**); (b) it is only at the most elaborate levels of theory so far employed¹¹ (e.g., DZP CCSD) that conformer **2/3** falls below **4** in computed electronic energy, and some calculations predict that **5** is the stable arrangement rather than **4**, the latter being a transition state between the two minima that represent **5**.

The rotational spectroscopy study of the shapes of molecules need not always constitute a complete determination of structure. Rather it may depend upon starting with a collection of possible shapes (conformers, tautomers, etc.) based on chemical experience or, nowadays, *ab initio* quantum chemical calculations of potential energy surfaces, or at least the calculation of equilibrium molecular structures corresponding to the energy minima on such surfaces. For the theoretical molecular structure at each such energy minimum the relevant spectroscopic parameters are computed. Then the identification of a species observed experimentally with one of the theoretically predicted minima depends upon the different shapes having distinctly different spectroscopic parameters. Although the spectroscopic identification of conformers for other biologically significant molecules has relied on the agreement between theoretically predicted and experimentally derived rotational constants,^{5a–h} these identifications have been supported by additional, independent evidence, such as dipole moment components and nuclear quadrupole hyperfine patterns, the latter being an especially powerful diagnostic for identifying tautomers involving N.

(4) Hu *et al.* (ref 11) note that “there might exist some uncertainty in the experimental results” because the assumed values change substantially when higher level molecular orbital calculations are used.

(5) (a) Uracil: Brown, R. D.; Godfrey, P. D.; McNaughton, D.; Pierlot, A. *J. Am. Chem. Soc.* **1988**, *110*, 2329–2330. (b) Adenine: Brown, R. D.; Godfrey, P. D.; McNaughton, D.; Pierlot, A. *Chem. Phys. Lett.* **1989**, *156*, 61–63. (c) Cytosine: Brown, R. D.; Godfrey, P. D.; McNaughton, D.; Pierlot, A. *J. Am. Chem. Soc.* **1989**, *111*, 2308–2310. (d) Thymine: Brown, R. D.; Godfrey, P. D.; McNaughton, D.; Pierlot, A. *J. Chem. Soc., Chem. Commun.* **1989**, 37–38. (e) Nicotinamide: Vogelsanger, B.; Brown, R. D.; Godfrey, P. D.; Pierlot, A. *J. Mol. Spectrosc.* **1991**, *145*, 1–11. (f) Histamine: Vogelsanger, B.; Godfrey, P. D.; Brown, R. D. *J. Am. Chem. Soc.* **1991**, *113*, 7864–7869. (g) 2-Pyridinone/2-hydroxypyridine: Hatherley, L. D.; Brown, R. D.; Godfrey, P. D.; Pierlot, A.; Caminati, W.; Damiani, D.; Favero, L. B.; Melandri, S. *J. Phys. Chem.* **1993**, *97*, 46–51. (h) Alanine: Godfrey, P. D.; Flrth, S.; Hatherley, L. D.; Brown, R. D.; Pierlot, A. *J. Am. Chem. Soc.* **1993**, *115*, 9687–9691.

In view of the importance of understanding the structure and shape of the glycine molecule, it is unfortunate that it has not previously been possible to provide additional experimental confirmation of the nature of the conformers, apart from some approximate measurements of dipole moment components. Iijima *et al.*³ are confident that the glycine vapor issuing from their heated nozzle at 219 °C was predominantly conformer **1** but with a small component of another conformer, presumed to be **2** and perhaps a third component, surmised from the theoretical predictions to be conformer **4**. However, as pointed out above, there are some uncertainties⁴ associated with their analysis. The residual uncertainties about the identification of the glycine conformers perhaps have stimulated considerable discussion of conformer structures in the theoretical literature.¹

Here we report some studies of the rotational spectra of several isotopomers of glycine, which strengthen the confidence in the identification of the two conformers so far detected and offer further insight into details of their shape. We also report on the upper limit of concentration of the third conformer, **4**, in glycine vapor.

Experimental Section

The free-jet expansion, Stark-modulated spectrometer used in the present study has been described previously.⁶ Samples of glycine enriched with ¹⁵N (98%), methylene ¹³C (99%), carboxyl ¹³C (99%), and dideuteromethylene (98%) were obtained from Aldrich and used as supplied. The N,O-d₃ sample involving complete deuteration of the readily exchangeable hydrogens was made by treating normal glycine with D₂O. Samples were vaporized at 235 °C in a stream of argon at about 30 kPa before expansion. A number of strong lines was observed in the range 48–72 GHz. Tables of measured frequencies are available as supplementary material.

Results and Discussion

Spectra were assigned from comparisons of the experimental frequencies with those predicted by using the theoretically computed geometry of glycine¹¹ for conformers **1** and **2**. All lines observed down to a S/N level of about 2/1 were attributable to these two conformers, indicating that no other conformer of glycine producing lines of at least this level of intensity was present in the vapor.

The spectroscopic constants derived from analyses of the spectra for the isotopomers are presented in Tables 1 and 2. We have also reanalyzed the spectra of the two known conformers of the parent molecule, incorporating all previously published line frequencies and some additional lines measured both with our current spectrometer and in our earlier glycine studies^{2b,c} as well as line frequencies not previously published (new lines are listed in the supplementary material accompanying this paper). This has led to improved confidence limits for the derived spectroscopic parameters of all those isotopomers (both conformers of the parent molecule and N,O-d₃ for conformer **2**) for which data have previously been published.²

(6) Brown, R. D.; Crofts, J. G.; Godfrey, P. D.; McNaughton, D.; Pierlot, A. *P. J. Mol. Struct.* **1988**, *190*, 185–193.

Table 2. Spectroscopic Parameters (MHz) for Isotopomers of Glycine 2

| constant | main | ¹³ C(1) | ¹³ C(2) | C(2)-d ₂ | ¹⁵ N | O,N-d ₃ |
|-----------------|----------------|--------------------|--------------------|---------------------|-----------------|--------------------|
| A | 10 129.86(34) | 10 130.688(99) | 9996.12(15) | 9080.513(21) | 10 129.145(92) | 9484.76(12) |
| B | 4071.497(11) | 4059.800(13) | 4055.092(17) | 3989.0363(86) | 3961.878(12) | 3680.065(12) |
| C | 3007.485(11) | 3001.157(11) | 2986.793(11) | 2917.5423(52) | 2947.1893(65) | 2777.951(11) |
| D _I | 0.000 665(38) | 0.000 659(51) | 0.000 735(61) | 0.000 728(26) | 0.000 668(40) | 0.000 679(34) |
| D _{IK} | 0.004 81(24) | 0.004 78(21) | 0.004 33(37) | 0.004 00(20) | 0.005 01(17) | |
| D _K | -0.028(25) | | | -0.004 894 8(60) | | 0.007 77(24) |
| d ₁ | -0.000 167(19) | -0.000 130(41) | -0.000 201(46) | -0.000 155(24) | -0.000 175(30) | -0.000 171(29) |
| d ₂ | 0.000 039(25) | | | 0.000 034 5(99) | | |
| transitions | 78 | 15 | 18 | 26 | 21 | 25 |
| rms residual | 0.314 | 0.0289 | 0.0558 | 0.0835 | 0.0766 | 0.066 |

Table 3. Kraitchman Coordinates for Glycine Conformers

| coordinate | C(1) ^a | C(2) ^b | N | H ^c |
|------------|-------------------|-------------------|---------|----------------|
| Glycine 1 | | | | |
| a | -49.03 | 76.17 | 200.15 | 72.78 |
| b | ±5.23 | -74.55 | ±3.97 | -140.42 |
| c | ±0.59 | ±1.97 | 0.03i | (+&-)87.80 |
| Glycine 2 | | | | |
| a | 60.13 | -70.70 | -186.82 | -69.05 |
| b | 6.12i | 82.21 | ±6.12 | 147.18 |
| c | 1.97i | ±5.30 | ±0.19 | (+&-)88.48 |

^a Carboxyl carbon. ^b Methylene carbon. ^c Methylene hydrogen.

Substitution Geometry. From the rotational constants we can compute the changes in the principal moments of inertia for each isotopomer and then, using Kraitchman's equations,⁷ derive the squares of the *a*, *b*, and *c* coordinates of the isotopically substituted atoms. These are listed in Table 3. The sign ambiguity for the larger values of coordinates is resolved by inspection of chemically plausible structures based on even crude values of bond lengths and angles. However, for the small values of coordinates, other considerations have to be brought to bear, and so the uncertainties are indicated in Table 3.

Bond Lengths. From the Kraitchman coordinates summarized in Table 3 we can obtain the *r_s* N-C, C-C, and C-H bond lengths. These have some ambiguity because the *b* coordinates for N and the carboxyl C are small. Moreover it is well-known that, for an atom that lies near an inertial axis, the significance of the substitution coordinate is diminished by the effects of zero-point vibrations, so that it is better to make use of first and second moments, if feasible, to minimize such geometrical uncertainties. Since we did not have access to sufficient additional isotopomers, we are left with the uncertainties associated with such small substitution coordinates. Of the several alternative choices of signs of coordinates, those leading to the most plausible bond lengths yield, for glycine 1, C-C = 148.5 pm and C-N = 146.8 pm and, for glycine 2, C-C = 154.5 pm and C-N = 145.9 pm. The error bars to be attributed to these values come primarily from the influence of zero-point vibrations rather than propagation of errors from the experimental input data. Typically they would be several tenths of a picometer.

The difference in C-C lengths in the two conformers is unexpected and probably must be attributed to the effects of using the small substitution coordinates for C(1). The experimental values differ rather more from the theoretical predictions than would be expected, given the high level of theoretical treatment involved. For comparison, the analogous C-C length reported for glycolic acid⁸ is 149.5 pm (147.5 from Kraitchman coordinates) and, for propionic acid,⁹ 150.9 pm.

The C-H lengths in both conformers are 109.8 pm. They are not derived from small substitution coordinates and so should

be relatively uninfluenced by vibrational effects. They are almost identical with the analogous lengths (109.7 pm) reported for glycolic acid⁹ and propionic acid¹⁰ and also agree with the lengths predicted by HSS. The values of the HCH angle in glycine 1 (106.2°) and in glycine 2 (107.4°) are comparable with the HSS calculations (106.3° and 107.1°) and are also close to those in glycolic acid (106.7°) and propionic acid (106.4°).

Conformer Shapes. The *c* components of the coordinates of the nuclei are most informative in relation to debates about the shapes of the glycine conformers because they indicate how far the substituted atoms are from the inertial *ab* plane. If each conformer of glycine has the symmetrical C_s symmetry (all heavy atoms in one plane), then each *c* should be 0 except for the methylene hydrogens (and the amino hydrogens, for which substitution coordinates have not been determined).

It can be seen that in both cases the *c* coordinates of the heavy atoms are 0 to within the bounds dictated by zero-point vibrational effects (which can lead to small positive or negative values of *c*² for these atoms). The methylene hydrogen coordinate is close to the value expected on the basis of the location predicted by the molecular orbital calculations. The preliminary conclusion therefore is that the heavy atom frameworks of both glycine 1 and glycine 2 are planar.

It is also instructive to consider the planar moment *P_c* (*P_c* = Σ*m_ic_i²*) of the various isotopomers. Figures 2 and 3 show plots of *P_c* for six isotopomers of conformers 1 and 2/3, respectively, computed using geometries predicted by HSS (DZP CCSD) except for deviations of NCCO from planarity, against the torsional angle, *θ*, about the C-C bond, *θ* = 0° representing conformer 1 or 2, respectively. For glycine 1 the experimental values of *P_c*, plotted at the left of the graphs, closely correspond to the theoretical values predicted for *θ* = 0°, while for glycine 2/3 the experimental values correspond to values of *θ* around 5°. It is tempting to conclude that this implies that 1 has C_s symmetry and that 2 is very slightly distorted from C_s symmetry.

However, it must be asked what degree of uncertainty is introduced by the effect of the zero-point vibrations. Past spectroscopic studies of the ground vibrational states of triatomic and other small planar molecules have yielded values of *P_c* of perhaps 0.02–0.13 uÅ². If such uncertainties were applicable in the present case, then our experimental values would imply that the twist angle *θ* is uncertain by up to 4–5°. If the amplitude of the twisting vibration is large, we should probably increase this uncertainty to, say, 10°, but it is hard to quantify the possible error because the theoretical predictions of "inertial defects" have proved intractable for all but very small molecules. The most reasonable interpretation of the *P_c* values is therefore that both 1 and 2/3 are of C_s symmetry but that, in light of the theoretical studies of 2/3 (see below), the amplitude of the twisting vibration is large amplitude for the latter.

(7) Kraitchman, J. *Am. J. Phys.* **1953**, *21*, 17.

(8) Blom, C. E.; Bauder, A. *J. Am. Chem. Soc.* **1982**, *104*, 2993–2996.

(9) Stiefvater, O. L. *J. Chem. Phys.* **1975**, *62*, 244–256.

(10) (a) Brown, R. D. *Chem. Br.* **1988**, *24*, 770. (b) Brown, R. D. In *Structures and Conformations of Non-Rigid Molecules (Proceedings of NATO Advanced Workshop)*; Kluwer Academic: Dordrecht, 1992; pp 99–112 and references therein.

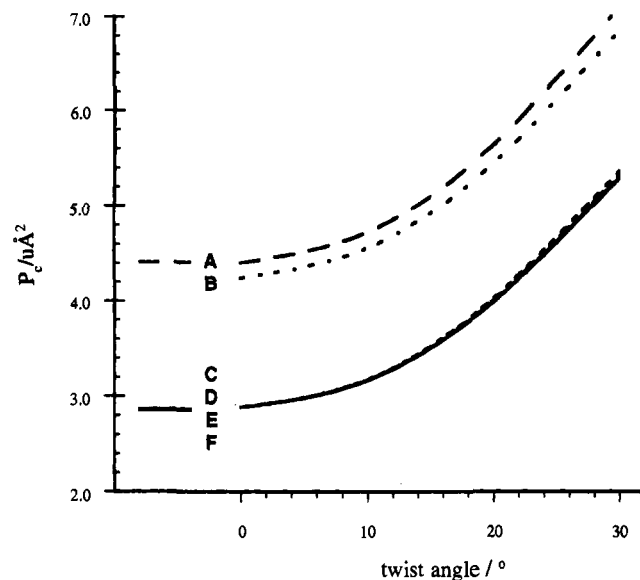


Figure 2. Variation of the planar moment, P_c , with NCCO twist angle for glycine 1: A, glycine-2,2- d_2 ; B, glycine- $N,O-d_3$; C, glycine-2- ^{13}C ; D, glycine- ^{15}N ; E, glycine-1- ^{13}C ; F, main isotopic species of glycine. The experimentally determined values ($\text{u}\text{\AA}^2$) of P_c are as follows: A, 4.4114(2); C, 2.860(1); D, 2.858(4); E, 2.8601(2); F, 2.8600(1); values in parentheses are standard deviations from the nonlinear least squares fit of spectra via the S-reduced Hamiltonian.

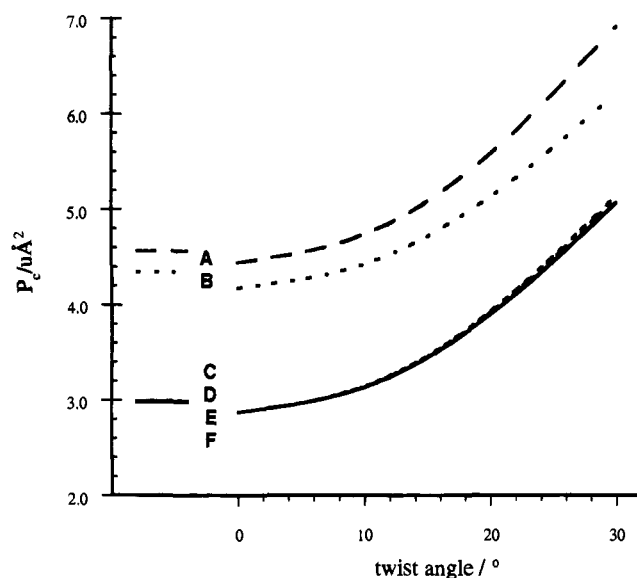


Figure 3. Variation of the planar moment, P_c , with NCCO twist angle for glycine 2/3: A–F as in Figure 1. The experimentally determined values ($\text{u}\text{\AA}^2$) of P_c are as follows: A, 4.5633(3); B, 4.344(1); C, 2.991(1); D, 2.989(1); E, 2.988(1); F, 2.987(1).

The most elaborate *ab initio* calculations for conformer 2/3 predict that the minima do not fall at the symmetric C_s arrangement of nuclei, but at arrangements that represent only small twist angles from planarity (about 13°) for the NCCO. For any plausible potential energy function this implies that the twisting vibration amplitude will be large and that the zero-point level will lie above the slight central maximum. The *ab initio* calculations predict, at the DZP CCSD(T) level, an energy barrier at the symmetrical position of 18 cm^{-1} . The situation is schematically depicted in Figure 4a. Although the r_e geometry in this instance is of symmetry C_1 , it is not possible to distinguish this case from the alternative, Figure 4b, because the small central maximum makes no perceptible difference to the vibrational energy levels if the shape of the remainder of the potential function is the same as in Figure 4a.

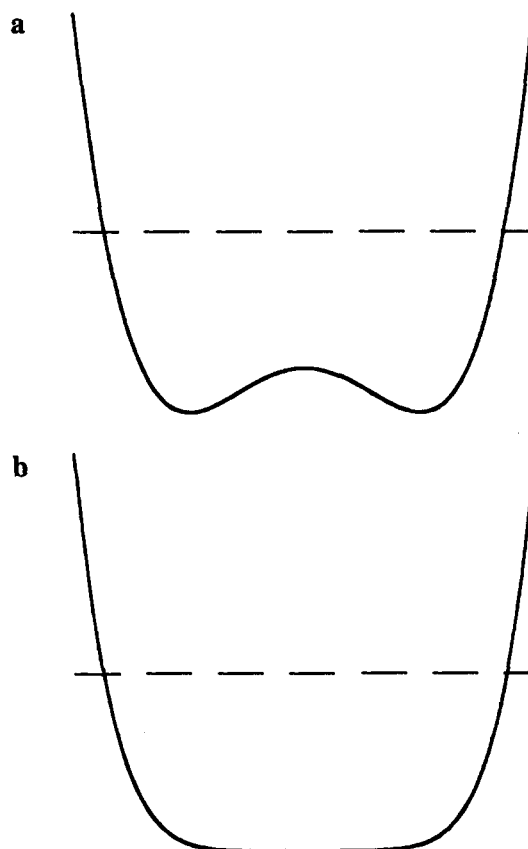


Figure 4. Two possible twisting potentials for glycine 2/3 and their zero-point vibrational levels. Case a represents the predictions of a well with a small double minimum, such as predicted by elaborate *ab initio* calculations. Case b represents an alternative, with only a single minimum. The two will be essentially indistinguishable by spectroscopic means if the double minimum in case a falls well below the zero-point level but case a would correspond to an unsymmetrical r_e geometry and case b to a symmetrical r_e geometry. The most probable geometry, r_P , is symmetrical in both cases.

Such cases for other molecules have been discussed extensively before,¹⁰ leading to the suggestion that it is best to describe the structure in terms of the “most probable” geometry, r_P . The r_P geometry would be symmetrical C_s for glycine 2. Thus for glycine 2/3 there is no discrepancy between a theoretical computation that predicts an equilibrium structure with C_1 geometry and spectroscopic study that corresponds to a most probable geometry with C_s symmetry, and it seems simplest to refer to it as glycine 2.

The existence of a broad potential well giving rise to a low-frequency large-amplitude vibrational mode for the C–C torsion is supported by the observation of a vibrationally excited rotational spectrum with a significantly enlarged value of P_c accompanying the ground state spectrum of conformer 2 in early high-temperature spectroscopy of glycine.^{2d} The absence of this vibrationally excited spectrum from our jet-cooled spectra [despite the use of a higher initial volatilization temperature ($235\text{ }^\circ\text{C}$, cf. $180\text{ }^\circ\text{C}$)] is consistent with the previously observed efficient jet cooling of such large-amplitude vibrational motions, analogous to rotational cooling, while higher frequency smaller amplitude vibrations are not cooled.^{5g}

Other Glycine Conformers. We can estimate an upper limit for the relative abundance of conformer 4 in the vapor as follows: The strongest transition in our spectral region for conformer 2 is the $7_{16}-6_{15}$ transition with an absorption coefficient (for unit mole fraction) of 0.95 cm^{-1} , calculated from the observed rotational constants and the dipole moment components computed by HSS.¹¹ We observed this line in a typical spectral scan at S/N about 40/1. For conformer 4, from

the theoretically predicted rotational constants and dipole moment components, we predict absorption coefficients (for unit mole fraction) in the region we scanned up to 0.12 cm^{-1} for four transitions ($3_{31}-2_{20}$, $3_{30}-2_{21}$, $4_{32}-3_{21}$, $4_{31}-3_{22}$). We conclude that some lines of conformer **4** would have been detected if it had been present with a relative abundance of 1/5 relative to conformer **2**.

If the conformational mole fractions are assumed to be established at the nozzle temperature of $235\text{ }^{\circ}\text{C}$, then the nondetection of **4** is in conflict with predicted relative stabilities of conformers **2** and **4** based on the most elaborate *ab initio* calculations,¹¹ in which their energy separation is predicted (DZP CCSD, 0.66 kJ mol^{-1} ; DZP CCSD(T), 1.9 kJ mol^{-1}) to be smaller than the available thermal energy at $235\text{ }^{\circ}\text{C}$ ($RT = 4.0\text{ kJ mol}^{-1}$). In earlier high-temperature static vapor spectroscopic studies by our own group^{2a,b} and by Suenram and Lovas,^{2d,f} where the conformer abundances were determined by thermodynamic equilibrium at ca. $200\text{ }^{\circ}\text{C}$, no microwave absorption lines except those of **1** and **2** were reported. This does add weight to the view that **4** is, in reality, of significantly higher energy than **2**, but the sensitivity limits of these early studies are problematic, and so, taken with our current significantly more sensitive jet studies, this raises the question as to whether the nonobservance of **4** in the present work could be due to the relaxation of **4** to **1**, or perhaps to **2**, during the rotational and kinetic cooling of glycine in our jet.

Studies by Ruoff *et al.*¹¹ of compounds with several conformers seeded into expanding jets of noble gases, in which their jet conditions were similar to ours except that their jets were operated at room temperature, indicate that, for such jets at room temperature, no relaxation of conformers occurs when barriers to isomerization are greater than about 400 cm^{-1} (5 kJ mol^{-1}). Accepting this criterion for relaxation, then the observation of **1** and **2**, where the predicted energy difference is 4.44 kJ mol^{-1} , implies that the barrier to isomerization must be at least as high as the critical value of 5 kJ mol^{-1} [and probably the critical value for relaxation for our jet at $235\text{ }^{\circ}\text{C}$ will be higher, say 8 kJ mol^{-1} (700 cm^{-1})]. An appreciable barrier would be expected in view of the fact that the making and breaking of internal hydrogen bonds and rotation of carboxyl and amino groups are involved. This is supported by some recent *ab initio* calculations¹² using density functional theory including electron correlation (RB-LYP/6-31G**)¹³ which indicate that the barrier for twisting from conformer **2** to **1** is at least 2000 cm^{-1} .

Relaxation of **4** to **1** involves breaking of hydrogen bonds and rotation of the carboxyl group and so might be expected to involve a barrier similar to the **1**-**2** barrier. However the DFT calculations for the twist to convert **4** into **1** imply that the barrier for this process is no more than 500 cm^{-1} , the calculation also showing that the energy minimum corresponds to **5**, in which the NCC plane is tilted away from that of the OCO. Conformer **4** is, in this situation, a small local maximum separating the two equivalent minima that correspond to the conformational enantiomers of **5**. Indeed, it is this feature surrounding this configuration of nuclei that seems to lead to the lower barrier in this case. It is also relevant to note that at this level of *ab initio* treatment **5** is much higher in energy (15 kJ mol^{-1}) relative to **1** than the expectedly more exact DZP CCSD(T) energy of ca. 6 kJ mol^{-1} for **4** reported by HSS, while for **2** the results of

the two methods are more similar, being ca. 1.5 and 4.5 kJ mol^{-1} , respectively.

The calculations of HSS on conformer **7** indicate that it may be of comparable energy to conformer **4/5**, but HSS did not report energy calculations etc. for this conformer at their highest levels of treatment of electron correlation. The detectability of its spectrum in our spectrometer might also be influenced by the presence of low-barrier pathways for relaxation to either **1** or **2**.

It is at least plausible that a similar relaxation explanation underlies our inability to detect a third conformer of alanine^{5h} analogous to glycine **4**. Likewise, when two or more different conformers were detected in jet spectroscopy of several neurotransmitters containing aminoethyl side chains in their structures,¹⁴ doubts arose as to the reliability of *ab initio* methods for predicting relative stabilities of conformers, but perhaps it is necessary to know the sizes of barriers to relaxation also before we can judge the quality of the theoretical predictions. Certainly quantum chemistry has been very successful in consistently indicating as the lowest energy conformer the most abundant conformer actually detected in the jet spectrum. In this special case no opportunity for relaxation to another species exists.

Conclusion

The results reported here provide strong evidence, in addition to that previously based on rotational constants and *ab initio* calculations, that the previous identifications of conformers **1**^{2d} and **2**^{2b} are correct. We further conclude that both detected conformers of glycine have their heavy atoms in a plane, the shape of conformer **2** being smeared somewhat by a large-amplitude vibration. This conclusion is fully compatible with the most elaborate *ab initio* calculations on glycine.

There is no experimental evidence for the presence of conformer **4**, predicted by the most recent theoretical calculations to be very close in energy to conformer **2**, or of any other conformer, in the vapor in our spectrometer. This could be attributable to the relaxation of **4** to **1** via a low-barrier pathway, no such low-barrier pathway being available for relaxation of **2**. Similar considerations could apply to conformer **7** and perhaps also to the understanding of the conformers detected in jet spectroscopy of alanine and of several neurotransmitters having aminoethyl side chains. It is, however, in the opinion of the authors, still an open question as to whether conformational relaxation is responsible for the nondetection of conformers such as **4** and **7** or whether a lack of reliability in the *ab initio* prediction of their relative conformational energies has led to an erroneous expectation of the detection of these conformers.

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Supplementary Material Available: A listing of the measured microwave transition frequencies used to calculate the parameters presented in Tables 1 and 2 (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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