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error. The following gives the choices made for the BDEs.

CH. The CH BDEs of several molecules have been determined.[70] However, Me_3Si-CH_3[71] (BDE of 99.2 kcal/mol) is the most similar to the present systems. Therefore, the value of 99 kcal/mol is used for all CH BDEs.

SiH. The closest analogue to the systems of interest is the $H_3Si-SiH_3$ molecule, which has a BDE of 86.3 kcal/mol.[71] The value of 86 kcal/mol is used for all SiH BDEs.

GeH. The BDE of Ge–H for CH_3GeH_3 is 83 kcal/mol.[72] The BDE for GeH_4 is given as 84[73] and 89[72] kcal/mol by different experimental researchers. Also, a theoretical value of 84.8 kcal/mol has been determined by Binning and Curtiss.[74] The BDE for Me_3GeH has been determined to be 82 kcal/mol. The value of 82 kcal/mol is chosen for all Ge–H BDEs except for that of CH_3GeH_3, since the electronegativity of Si, Ge, and Sn should have similar effects as that of the bulky methyl groups of Me_3GeH.

SnH. The BDE of SnH_4 is 71.6 kcal/mol.[75] The value for Me_3Sn-H[76,77] and Bu_3Sn-H[78] is 74 kcal/mol. Therefore, the value of 74 kcal/mol is used for all Sn–H BDEs.

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Conformers of Gaseous Glycine

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Abstract: Correlated level ab initio calculations (large basis set MP2, and MP4, CCSD, and CCSD(T) computations) have been performed for 13 conformers of neutral glycine, including all 8 possible conformers with planar heavy-atom arrangements. These calculations resulted in accurate geometric structures, relative energies, harmonic vibrational frequencies, and infrared intensities for all conformers. The structural results obtained support the rotational constants measured for the two lowest-energy forms of glycine, and their high accuracy should be profitable in the search for other conformers by rotational spectroscopy. Energetic, structural, and quadratic force field results indicate possible model improvements for an existing gas-phase electron-diffraction study of the lowest-energy conformer. Predictions, probably accurate to within about 100 cm^{-1}, are made for the order and relative energy of all conformers considered.

Introduction

The simplest amino acid, glycine, H_2NCH_2COOH, has three internal rotational degrees of freedom (ϕ, ψ, and θ, associated with bonds C–N, C–C, and C–O, respectively) in its neutral state, which leads to eight rotational isomers of C_s symmetry (see conformers Ip–VIIIp in Figure 1, where p refers to planar heavy-atom arrangement). In several of these rotamers intramolecular H-bonds, of different strengths, are formed stabilizing that particular form. On the other hand, steric strain and repulsion of lone electron pairs on the N and O atoms in some of the planar forms have a destabilizing effect that can be decreased by small torsional changes; thus, some planar forms might not correspond to local energy minima on the potential energy surface of glycine but rather to saddle points. As a result, rotational isomers of C_1 symmetry should also be considered in a conformational study of glycine (these are designated with the letter n, referring to nonplanar heavy-atom arrangement, in Figure 1). These conformational changes, resulting from the balance of steric and H-bond effects, are expected to be accompanied by very small changes in the total energy of the system. Indeed, theoretical calculations performed by Schäfer,[1-4] Pople,[5] and others[6-12] all indicate that several glycine isomers have relative energies less than 1000 cm^{-1} (the height of the rotational barrier of ethane) and that nonplanar forms are more stable for some low-energy isomers (specifically, for II and III of Figure 1) than the respective planar forms.

It is not surprising that prediction and/or reproduction of these small energy differences pose(s) a serious challenge to computational chemistry. In their comparative study using classical, semiempirical (extended Hückel, PCILO, CNDO), and non-empirical (STO-3G SCF) methods to map the rotational energy surface of glycine Palla et al.[7a] conclude that "if one compares numerical values of the relative depth of the potential holes and of the rotational barriers [of glycine], the accordance among the various methods vanishes almost completely". In a recent study

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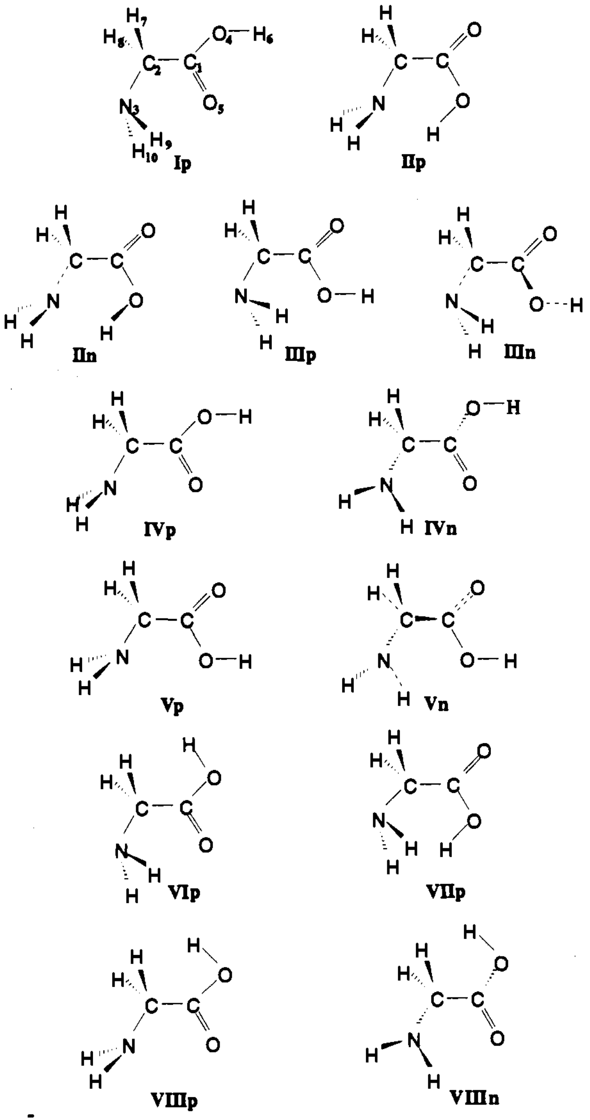

Figure 1. Conformers of glycine considered in this study and their numbering.

Jensen and Gordon[11] also conclude that the potential energy surface of glycine is "not well reproduced by STO-2G, AM1, or PM3 [methods], since the former predicts too many, and the two latter too few, minima". The detailed studies of Schäfer and co-workers[1-4] show that at the self-consistent-field (SCF), restricted Hartree–Fock (RHF) level, which is the only ab initio level that could be afforded, at present, for conformational studies of peptides up to about 60–70 atoms, disconcertedly large fluctuations can be observed in the relative energies of the different conformers and in several cases choice of the basis set affects whether a planar configuration corresponds to a saddle point or a local energy minimum on the potential energy surface. (Note, however, that the basis sets used by Schäfer are all rather small by today's standards but represent likely choices for calculations on oligopeptides.) To our best knowledge, correlated level calculations on the conformers of glycine are rather limited: (a) Dykstra et al.[8] used their SCEP method to calculate the energy difference between conformers Ip and IIp and showed that electron correlation stabilizes conformer IIp substantially more than it does Ip; (b) Ramek, Schäfer, and their co-workers,[2,4] based on 6-311G** MP2 and SCF geometry optimizations for conformers Ip, IIp, and IIn, concluded that geometries optimized at the SCF level sometimes display torsional angles which lead to incorrect estimates of nonbonded interactions, and thus "geometry optimization at the correlated level can have a significant effect on calculated [relative] energies", and that "SCF conformational energy maps [for single amino acids and peptide analogs] are intrinsically inaccurate"; thus, they recommend correlated level calculations both for geometry optimization and for single-point energy calculations for this class of compounds; (c) Jensen and Gordon[11] performed 6-31G* MP2 energy calculations for several glycine conformers whose geometries were optimized at the 6-31G* SCF level and erroneously concluded, based on their unfortunate choice of theoretical methods, that "correlation appears to have little effect on the relative energies [of glycine conformers]". The obvious lack of high-quality theoretical data on the conformers of gaseous glycine prompted the present study since it is expected (and was shown, for example, in the case of the inversion barrier height of cyclopentene[13]) that correlated level calculations with extended basis sets are necessary to converge theoretical results and obtain accurate quantum chemical predictions. In this paper we report for the first time high-level correlated calculations employing extended basis sets for all major conformers of glycine in the hope that the theoretical methods employed finally reached the level where quantitatively correct results are expected. For large systems of biological interest conformational studies can only be performed at much lower levels of theory than employed here; therefore a check of their reliability is of extreme importance. The benchmark results presented in this paper should serve this purpose as well.

Although glycine is known to exist as a zwitterion in the crystalline state and in solution (stabilized by strong electrostatic and polarization interactions with its environment), entry level ab initio[5b,6,7,12] and semiempirical[7a,10] calculations suggest the energy difference between the two forms to be in the order of 30–100 kcal/mol, with the neutral species being more stable. The large differences among the calculated values warrant a more detailed, high-level theoretical investigation, but that is not the object of the present study. The important result for the present study is that glycine exists in its neutral form in the gas phase (this is supported, of course, by experimental studies, see, e.g., refs 14–17), so calculations can and are limited in this study to neutral glycine conformers.

Due to the simplicity of its structure glycine has been the subject of several experimental[14-17] structural studies. Rotational constants were deduced from microwave investigations[14,15] for two forms of glycine, probably of lowest energies among its conformers, while the complete molecular structure of the lowest energy form of glycine in the gas phase was determined from a joint analysis of electron diffraction data and rotational constants.[16] X-ray and neutron diffraction structural studies of the glycine crystal have also been reported[17] but are considered to be not relevant for the present study.

Computational Details

After some preliminary studies employing basis sets of different size two basis sets have been selected for this study. The smaller one is the 6-311++G** basis of Pople et al.,[18] it contains 145 contracted Gaussian functions (CGFs) for glycine and will be designated as B1. (The need for including diffuse functions in the basis set for calculations on hydrogen-bonded systems has long been recognized.[18d]) The core part of the larger basis set, designated as B2, was constructed from the 13s8p primitives of Partridge[19] according to (6,3,1,1,1,1) and (4,1,1,1,1) schemes for the s and p functions, respectively, of the C, N, and O atoms and by a (6s/4s) contraction of the unscaled exponents of Huzinaga[20]

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Table I. Total Energies of Glycine Conformers[a]

method[b]	Ip	IIp	IIn	IIIp	IIIn	IVp	IVn	Vp	Vn	VIp	VIIp	VIIIp	VIIIn
B1 SCF	.921 719	.916 122	.916 325	.918 483	.918 542	.913 754	.919 018	.912 740	.917 373	.911 208	.908 070	.901 948	.908 332
B1 MP2	.787 085	.786 153	.786 247	.784 547	.784 785	.779 633	.785 072	.778 515	.783 580	.777 994	.775 989	.769 260	.775 795
B1 MP2(full)	.883 499	.882 587	.882 680	.880 960	.881 182	.876 040	.881 489	.874 924	.879 980	.874 396	.872 427	.865 653	.872 205
B1 MP3	.797 788	.795 838	.795 973	.794 896	.795 163	.790 195	.795 625	.788 934	.794 020	.788 956	.786 205	.780 080	.786 653
B1 MP4	.850 071	.848 921	.849 022	.847 615	.847 855	.842 640	.847 980	.841 558	.846 590	.841 320	.839 044	.832 663	.839 039
B1 MP∞	.854 121	.852 999	.853 099	.851 703	.851 940	.846 702	.852 028	.845 638	.850 661	.845 392	.843 132	.836 755	.843 109
B1 CCSD	.811 719	.809 611		.808 974		.804 224		.803 043		.802 678	.800 014	.793 926	
B1 CCSD(T)	.844 464	.843 089		.841 865						.835 630			
B2 SCF	.952 342	.946 939	.947 148	.948 905	.948 920	.944 675	.949 816	.943 900	.947 760	.943 277	.940 229	.934 421	.940 590
B2 MP2	.009 528	.008 823	.008 927	.006 871	.006 857	.002 286	.007 643	.001 476	.005 483	.001 645	.000 247	.993 277	.999 627

[a] Results of this study only. All energies in hartrees. Numbers before the decimal point in the total energies were omitted (−282 in the SCF and −283 in all MP*n* and CC cases except B2 MP2 (Ip–VIIp) where it is −284). [b] All calculations were performed at the B1 (6-311++G**) MP2(full) optimized geometries. In all post-SCF calculations the five lowest energy core orbitals and five highest energy virtual orbitals were kept frozen, except in the B1 MP2(full) calculations where all orbitals were correlated. The B1 and B2 basis sets consist of 145 and 350 CGFs, respectively (for details, see text). Correlation energies leading to MP∞ energies were obtained by the extrapolation formula $E_{corr} = (E_2 + E_3)/(1 - E_4/E_2)$, where E_n represents the *n*th-order correction to the electronic energy.[28]

Table II. Relative Energies of Glycine Conformers[a]

method	Ip^m	IIp	IIn^m	IIIp	IIIn^m	IVp	IVn^m	Vp	Vn^m	VIp^m	VIIp^m	VIIIp	VIIIn^m
B1 SCF	0.0	1228.4	1183.8	710.2	697.3	1748.1	592.8	1970.7	953.8	2306.9	2995.6	4339.2	2938.1
B1 MP2	0.0	204.5	183.9	557.0	504.8	1635.5	441.8	1880.9	769.3	1995.2	2435.3	3912.1	2477.9
B1 MP2(full)	0.0	200.2	179.7	557.2	508.7	1637.1	444.1	1882.0	772.3	1997.9	2430.5	3916.7	2478.7
B1 MP3	0.0	428.0	398.3	634.7	576.1	1666.5	474.7	1943.2	827.0	1938.4	2542.2	3886.5	2443.9
B1 MP4	0.0	252.4	230.2	539.0	486.4	1630.9	458.9	1868.4	764.0	1920.6	2420.1	3820.6	2421.2
B1 MP∞	0.0	246.1	224.4	530.7	478.7	1628.3	459.4	1866.2	759.3	1915.8	2411.8	3811.4	2416.9
B1 CCSD	0.0	462.6		602.5		1645.0		1904.2		1984.3	2569.0	3905.1	
B1 CCSD(T)	0.0	301.8		570.4						1938.8			
B2 SCF	0.0	1185.8	1140.0	754.3	751.0	1682.7	554.4	1852.8	1005.6	1989.5	2658.5	3933.2	2579.3
B2 MP2	0.0	154.7	131.9	583.1	586.2	1589.4	413.7	1767.2	887.8	1730.1	2036.9	3566.7	2173.0
6-311G** SCF[b]	0.0	1128.5	1036.5										
6-311G** MP2[b]	0.0	295.1	244.1										
final predictions[c]	0	196	172	557	(560)[d]	1582	431	1752	878	1651	2013	3466	2112

[a] All energies in cm^{-1}. The conformers which correspond to minima on the B1 MP2 potential energy surface of glycine are marked with the letter m. For further details see footnote *b* to Table I. [b] From ref 4b, calculated at the respective optimized geometries. [c] The relative energy predictions are based on B2 MP2 relative energies, adding to them, as corrections, the (B1 MP∞ − B1 MP2) values. It is rather uncertain what error limits should be attached to these values, a somewhat conservative estimate would be ±100 cm^{-1} (probably smaller for the low-energy conformers). Note that no zero-point vibrational energy (ZPVE) corrections have been added to obtain these values. [d] It is not obvious from the present calculations whether IIIn corresponds to a minimum on the true potential energy surface of glycine; it seems, however, that it might not.

for hydrogen and was augmented by three sets of d and two sets of f functions (3d2f) on C, N, and O atoms, by two sets of p and one set of d functions (2p1d) on hydrogens, and by one set of diffuse functions on each atom resulting in 350 CGFs. All polarization function exponents were taken from Dunning,[21] all diffuse function exponents were chosen to be one-third of the lowest related exponents. All d and f sets of both basis sets included only the five and seven true spherical harmonics, respectively.

Electronic wave functions were determined by the single-configuration, self-consistent-field (SCF), restricted Hartree–Fock (RHF) method,[22-24] by perturbative methods for the incorporation of electron correlation, including second-, third-, and fourth-order Møller–Plesset theory,[25] i.e., MP2, MP3, and MP4(SDTQ),[26] and by coupled cluster (CC) methods including all single and double excitations (CCSD) and in cases, additionally, a perturbative correction for contributions from connected triple excitations (CCSD(T)).[27] Extrapolation of the perturbation series to estimate the infinite-order energy (MP∞, obtained by estimating the exact correlation energy within a given one-particle basis set) was performed using a formula suggested by Pople and co-workers.[28] The t_1 diagnostic values of coupled cluster theory[27e] are around 0.015 for the different conformers, suggesting that glycine can adequately be described by single-reference-based electron-correlation methods. The five lowest energy 1s core orbitals and the corresponding five highest energy 1s* virtual orbitals were kept frozen in all MP*n* and CC treatments except B1 MP2 geometry optimizations.

The geometrical structures of the conformers of glycine were optimized at the B1 MP2(full) level. The residual Cartesian gradients were in all cases less than 3 × 10^{-4} hartree/bohr and substantially less for conformers for which second-derivative calculations have been performed. In all high-level, single-point energy calculations these optimum geometries were employed. The B1 MP2(full) level Cartesian quadratic force constants were determined at the respective optimized geometries from finite difference calculations employing analytic first derivatives.

All electronic structure computations were performed with the program packages GAUSSIAN90[29] and PSI.[30]

Results and Discussion

Tables I and II contain total energies (in hartrees) and relative energies (in cm^{-1}), respectively, obtained in this study for 13 conformers of glycine. Geometry parameters, rotational constants, and dipole moments of all the conformers of glycine investigated are presented in Table III. Harmonic vibrational frequencies, infrared intensities, and zero-point vibrational energies (ZPVEs) of some glycine conformers are presented in Table IV. The numbering of the conformers (I–VIII) reflects the increasing

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Table III. Geometry Parameters, Rotational Constants, and Dipole Moments of Glycine Conformers[a]

	Ip													
parameter	theory	expt[b]	IIp	IIn	IIIp	IIIn	IVp	IVn	Vp	Vn	VIp	VIIp	VIIIp	VIIIn
$r(C_1C_2)$	1.5186	1.529	1.5331	1.5317	1.5218	1.5194	1.5213	1.5083	1.5215	1.5097	1.5289	1.5336	1.5328	1.5198
$r(C_2N_3)$	1.4469	1.466	1.4660	1.4651	1.4491	1.4520	1.4487	1.4535	1.4514	1.4595	1.4452	1.4483	1.4454	1.4513
$r(C_1O_4)$	1.3555	1.354	1.3396	1.3406	1.3559	1.3571	1.3632	1.3531	1.3451	1.3563	1.3612	1.3535	1.3691	1.3576
$r(C_1O_5)$	1.2091	1.204	1.2067	1.2066	1.2095	1.2096	1.2039	1.2090	1.2127	1.2084	1.2030	1.2043	1.1975	1.2030
$r(O_4H_6)$	0.9678	0.966	0.9813	0.9803	0.9682	0.9679	0.9672	0.9679	0.9684	0.9677	0.9640	0.9660	0.9636	0.9633
$r(C_2H_7)$	1.0940	1.081	1.0926	1.0929	1.0938	1.0914	1.0952	1.0921	1.0948	1.0901	1.0963	1.0924	1.0976	1.0959
$r(C_2H_8)$	1.0940	1.081	1.0926	1.0930	1.0938	1.0956	1.0952	1.1019	1.0948	1.1018	1.0963	1.0924	1.0976	1.1024
$r(N_3H_9)$	1.0140	1.001	1.0122	1.0135	1.0135	1.0140	1.0095	1.0146	1.0099	1.0140	1.0145	1.0100	1.0092	1.0152
$r(N_3H_{10})$	1.0140	1.001	1.0122	1.0121	1.0135	1.0136	1.0095	1.0131	1.0099	1.0140	1.0145	1.0100	1.0092	1.0129
$\angle(N_3C_2C_1)$	115.56	113.0	111.28	111.01	118.99	117.89	112.76	109.62	115.63	111.10	115.58	119.61	112.89	109.64
$\angle(C_2C_1O_4)$	110.92	111.5	113.92	113.77	112.95	112.01	109.09	111.40	114.56	110.99	115.05	116.48	113.27	115.57
$\angle(C_2C_1O_5)$	125.73	125.0	122.29	112.56	123.93	124.95	127.68	125.00	122.06	125.75	124.38	121.97	126.25	123.52
$\angle(C_1O_4H_6)$	106.33	110.5	103.89	104.07	105.67	105.93	105.99	106.12	104.91	106.23	109.26	107.05	109.45	109.05
$\angle(H_7C_2C_1)$	107.42		106.82	107.56	105.93	106.71	106.28	108.72	104.94	106.99	107.85	105.95	106.70	105.34
$\angle(H_8C_2C_1)$	107.42		106.82	106.18	105.93	106.12	106.28	105.42	104.94	106.17	107.85	105.95	106.70	109.70
$\angle(H_9N_3C_2)$	110.02		112.03	111.65	110.42	110.37	112.32	109.67	112.13	109.85	109.74	115.34	112.74	109.04
$\angle(H_{10}N_3C_2)$	110.02		112.03	111.83	110.42	110.34	112.32	110.52	112.13	110.20	109.74	115.34	112.74	110.89
$\angle(H_7C_2H_8)$	106.13		107.04	107.34	105.84	106.65	105.79	107.20	105.61	107.90	106.56	106.19	106.25	107.25
$\angle(H_9N_3H_{10})$	106.22		107.64	107.53	106.54	106.80	108.71	108.24	108.40	107.68	106.04	112.04	109.19	108.43
$\tau(N_3C_2C_1O_4)$	180.0	180.00	0.00	11.97	0.00	29.80	180.00	158.22	0.00	44.08	180.00	0.00	180.00	158.96
$\tau(N_3C_2C_1O_5)$	0.0	0.00	180.00	−169.54	180.00	−152.26	0.00	−24.33	180.00	−138.49	0.00	180.00	0.00	−24.67
$\tau(C_2C_1O_4H_6)$	180.0		0.00	−2.76	180.00	177.62	180.00	175.99	180.00	179.28	0.00	0.00	0.00	−8.60
$\tau(H_7C_2C_1O_4)$	56.90		122.86	137.81	123.94	154.04	56.19	37.31	124.47	163.77	57.36	123.73	56.63	38.21
$\tau(H_8C_2C_1O_4)$	−56.90		−122.86	−107.53	−123.94	−92.49	−56.19	−77.36	−124.47	−81.18	−57.36	−123.73	−56.63	−76.92
$\tau(H_9N_3C_2C_1)$	58.34		−119.46	100.25	−58.78	61.00	118.54	45.29	−118.88	178.98	58.08	66.57	117.90	38.77
$\tau(H_{10}N_3C_2C_1)$	−58.34		119.46	−139.22	58.78	−56.80	−118.54	164.55	118.88	−62.53	−58.08	−66.57	−117.90	158.09
A	10279.0	10341.7 (10297.9)[c]	10175.1 (10130.5)[d]	10127.5	9975.0	9744.6	10289.3	10273.0	10052.6	9627.4	10136.1	9866.9	10132.4	10137.0
B	3877.0	3876.2 (3867.5)[c]	4076.3 (4071.5)[d]	4085.3	3989.2	3987.4	3807.2	3979.4	3931.7	4079.5	3885.0	3959.6	3811.2	3992.0
C	2908.1	2912.4 (2911.0)[c]	3010.9 (3007.5)[d]	3024.8	2944.7	2991.6	2870.3	2968.3	2920.5	3072.1	2901.4	2922.1	2861.0	2964.2
μ (SCF)[e]	1.29		6.30	6.20	1.99	1.90	3.16	2.40	2.49	2.85	3.53	4.68	6.21	4.92
μ (MP2)[f]	1.20	1.00		5.59				2.06		2.41	2.95	4.10		4.31

[a] Distances (r) in angstroms, angles ($\angle$ and τ) in degrees, rotational constants (A, B, and C) in MHz, and dipole moments (μ) in debyes. For numbering of atoms and depiction of the different conformers see Figure 1. All theoretical values, if not noted otherwise, were obtained at the B1 (6-311++G**) MP2(full) level. Note that while theoretical rotational constants refer to equilibrium A_e, B_e, and C_e values, available experimental constants do not. [b] Geometry corresponds to r_α^0 parameters (column 5 of Table III of ref 16). For experimental error estimates see original publication. The dipole moment is taken from ref 2. [c] B_z values, i.e., rotational constants corrected for vibrational effects.[16] [d] Experimental rotational constants[2] are given in parentheses. [e] Dipole moments obtained at the B1 (6-311++G**) SCF level. [f] Dipole moments obtained at the BI (6-311++G**) MP2 level.

relative energies of the respective "planar" forms of glycine obtained from B1 MP2 geometry optimizations.[31]

Energies. As has been determined both experimentally[1b,16] and theoretically,[1-12] the lowest energy form of neutral glycine in the gas phase is Ip, i.e., a conformer with a planar heavy-atom structure and two equal N–H···O H-bonds. It is important to emphasize that not only the present high-level calculations but all semiempirical and nonempirical theoretical methods studied[4,7] previously did predict Ip to be the lowest energy form of glycine. On the other hand, as mentioned in the Introduction, for the separation energy between this conformer and the rest of the conformers the different theoretical methods provided confusingly different results. For example, IIp is an energy minimum at some SCF levels (e.g., 4-31G and 6-31+G), but a slightly nonplanar form of II (IIn) is predicted to have a lower energy at several other (lower and higher) theoretical levels, most notably at the 6-311G** MP2[2,4] and at the present 6-311++G** MP2 levels. Furthermore, at the SCF level "there is considerable scatter in calculated energy differences and in the optimized values of the nonplanar N–C–C=O torsions".[4] These observations are confirmed by the present study as far as some large deviations between B1 SCF and B1 MP2 and MP4 relative energies are concerned. Most notably, conformation II is predicted at the B1 SCF level of theory to be only the sixth most stable conformer of glycine whereas all high-level calculations predict it to be the second most stable form of glycine. Still, although for most high-energy conformers B1 SCF relative energies are larger than the corresponding B1 MP2 results by 90–560 cm^{-1}, the energy order of the conformers is not changed. Since for large systems (e.g., oligopeptides) it is the SCF level of ab initio theory which can be routinely applied, it is of considerable interest to see whether the observed problems are connected to the incompleteness of the one-particle basis sets employed or are inherent consequences of the limitations of the Hartree–Fock approach. The present B2 SCF calculations employing 350 CGFs should definitely be very close to the Hartree–Fock limit, and thus they can answer this question (even though the B2 basis set does not contain g functions on the heavy atoms and effects of geometry relaxation on the relative energies cannot easily be assessed). As can be seen in Table II the B2 SCF relative energies are rather close to those obtained employing much smaller basis sets (the average deviation between B1 SCF and B2 SCF relative energies is only 144 cm^{-1}), and thus one can conclude that the simplifications leading to the Hartree–Fock level of theory prevent one from obtaining quantitative results for the relative energies of the isomers of glycine. It seems very likely that this problem exists for most other amino acids, as well. On the other hand, for most conformers B2 MP2 relative energies are quite similar to those obtained from B1 MP2 calculations, the average deviation being 152 cm^{-1}, while the maximum deviation is still less than 400 cm^{-1} (large deviations are observed only for conformers V–VIII). An equally important observation is that the changes accompanying extension of the one-particle basis from B1 (145 CGFs) to B2 (350 CGFs) more or less compensate for the changes accompanying extension of the electron-correlation treatment from MP2 to MP∞ (using the B1 basis). As a result, the final theoretical predictions for the relative energies of the isomers of glycine (see Table II) are close to the results obtained directly from B1 MP2 calculations, with the exception of conformers V–VIII. The relative energies determined at the B1 CCSD level of theory are rather close to those obtained by perturbation theory; in particular, they do not deviate more than 50 cm^{-1} from B1 MP3 values. The effect of triple substitutions, judged from the limited B1 CCSD(T) results available, seems to be rather small, suggesting that the theoretical values obtained in this study for the relative energies of the glycine conformers are well converged. In summary, although the Hartree–Fock level of theory seems insufficient to provide quantitative results for the relative energies of the isomers of glycine (and probably for most other amino acids), the only slightly more expensive MP2 level of theory, when employed with a reasonably large basis set (including both polarization and diffuse functions, like the present B1 basis, 6-311++G**), seems to perform well. Still, it should be pointed out that in the cases of the conformer pairs IIIp–IIIn and Vp–VIp there is disagreement in the ordering between the B1 MP2 (MP4) and B2 MP2 levels of theory. The energy differences involved are, however, very small (less than 100 cm^{-1}, i.e., 0.3 kcal/mol). Further enlargement of the one-particle basis set or extension of the level of correlation treatment is not expected to alter the above conclusions in any substantial way.

As mentioned several times, one striking result of earlier theoretical studies was the fact that at certain levels of SCF theory some "nonplanar" (C_1 symmetry) glycine isomers (basically those of conformers II and III) had lower total energies than their "planar" (C_s) counterparts and that these differences were extremely sensitive to the choice of the basis set. Existence of a small energy difference between conformers IIp and IIn, and IIIp and IIIn is basically confirmed in the present study. In both cases the equilibrium energy differences between planar and nonplanar conformers are very small at all levels studied, varying between 3 and 58 cm^{-1}. There is, however, a significant difference between conformers II and III: while for conformer II all theoretical levels of this study indicate that the nonplanar form has the lower energy, for conformer III the planar form is more stable at the B2 MP2 level, although by only 3 cm^{-1}. Thus, one can argue that for conformer III even more and even higher level theoretical calculations would be needed to decide which form corresponds to a minimum on the potential energy surface, although the B2 MP2 results indicate that it might be the planar form.[32] Because no higher level calculations can be done at present, this problem is left for future studies. The calculated values for the bare barrier heights are actually so small that one has to wonder whether the theoretical predictions should be accepted. Even if one trusts theory, i.e., accepts that a slightly distorted, nonplanar conformer of II is indeed a minimum energy conformer while IIp is a saddle point on the potential energy surface of glycine,[33] the effect of zero-point vibrations on the effective barrier height has to be addressed. Second-derivative calculations at the B1 MP2 level were performed to answer this question (see Table IV). The zero-point vibrational energy (ZPVE) value obtained raises the predicted equilibrium energy difference, 172 cm^{-1}, between conformers Ip and IIn by 140 cm^{-1}, arriving at a value of 312 cm^{-1}. Still, II remains the second lowest energy conformer. On the other hand, the ZPVE corrections calculated for conformer II result in a very significant change in the relative energies of IIp and IIn: while the final prediction for the bare barrier height for conformer II (see Table II) is 24 cm^{-1}, the ZPVE values decrease this height by 24 cm^{-1}, resulting in a final effective barrier height of about 0 cm^{-1}. This value, although it may change by several wave numbers up and down given the uncertainties in the theoretical values, indicates that the effective ground-state structure is probably planar for conformer II (this prediction is supported by the extremely good agreement between the measured and calculated rotational constants of conformer IIp) and that the splitting, if any, of the rotational levels is extremely small. Note that scaling the theoretical B1 MP2 frequencies should not change these conclusions.

As far as the relative energies of conformers IV–VIII are concerned no experimental data are available. In their elec-

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(31) For the sake of simplicity, the IUPAC–IUB nomenclature (*Biochemistry* **1970**, *9*, 3471), which recommends designation of amino acids and peptides by torsion angles N–C$^{\alpha}$ (ϕ), C$^{\alpha}$–C (ψ), C–N (ω) and C–O″ (θ) is not followed in this paper.

(32) That the potential energy curve of glycine is extremely flat around IIIp has already been demonstrated by Siam et al. at the 4-21G SCF level (see Table III and Figure 3 of ref 3).

(33) It is important to point out that the higher the level of the perturbational treatment is the lower its contribution becomes to the energy difference between conformers IIp and IIn: using the B1 basis set, the energy-difference contributions are −23.9, −9.0, +7.5, and +0.2 cm^{-1} at the MP2, MP3, MP4, and MP∞ levels, respectively. These numbers suggest that the perturbational series is reasonably well converged at the MP4 level, and even more importantly they show that very large basis set MP2 calculations (like the B2 MP2 calculations of the present study) should result in answers very close to the exact one as the higher-order contributions seem to cancel out.

Table IV. Harmonic Vibrational Frequencies, Infrared Intensities, and Zero-Point Vibrational Energies (ZPVEs) of Some Low-Energy Glycine Conformers[a]

	Ip			IIp			IIn			IVn			Vn			VIp			VIIp			VIIIn		
ν_i	sym	freq	int	sym	freq	int	sym	freq	int	sym	freq	int	sym	freq	int	sym	freq	int	sym	freq	int	sym	freq	int
1	A′	3808	75.9	A′	3585	8.0	A	3670	20.0	A	3808	80.9	A	3811	82.2	A′	3854	60.7	A′	3810	100.8	A	3867	63.8
2		3562	2.8		3531	336.9		3578	15.0		3661	13.4		3657	10.5		3558	4.6		3599	7.7		3659	17.4
3		3106	13.5		3115	9.2		3549	301.6		3559	3.4		3558	1.8		3078	23.0		3118	9.2		3555	6.7
4		1825	264.7		1848	329.9		3170	4.9		3152	8.2		3178	5.9		1849	216.3		1845	253.1		3103	21.7
5		1680	22.5		1660	37.0		3111	10.6		3028	38.9		3027	42.0		1681	26.1		1660	31.1		3021	43.7
6		1474	14.4		1477	4.8		1848	323.1		1831	257.6		1832	288.7		1484	7.4		1464	4.9		1853	207.7
7		1422	22.7		1440	378.0		1660	36.0		1646	58.1		1655	36.9		1399	35.3		1373	26.4		1644	60.6
8		1318	19.1		1362	14.7		1484	4.9		1512	9.0		1511	3.7		1299	345.3		1347	356.5		1513	6.7
9		1191	56.2		1243	27.5		1437	374.2		1472	32.1		1451	46.0		1190	4.7		1202	8.8		1455	31.6
10		1147	264.1		1104	16.6		1382	6.3		1340	36.7		1363	52.6		1142	49.8		1142	15.2		1318	332.2
11		949	124.5		929	144.4		1338	9.1		1294	0.3		1313	6.3		949	169.4		853	44.8		1287	60.9
12		845	76.8		846	13.0		1242	24.7		1231	74.0		1245	70.8		851	25.3		661	99.2		1233	4.1
13		642	5.9		648	5.7		1171	2.3		1159	209.5		1154	136.7		652	15.1		514	176.5		1157	13.5
14		472	31.5		517	1.9		1102	13.3		1130	45.2		1098	46.4		473	2.1		507	3.9		1136	31.2
15		260	9.4		325	18.0		960	85.9		1042	9.6		1035	19.3		263	27.3		281	20.7		1035	12.4
16	A″	3652	9.3	A″	3677	23.0		911	62.9		869	72.0		868	79.2	A″	3647	11.5	A″	3717	20.8		871	70.3
17		3158	4.8		3175	3.7		867	101.2		858	95.3		846	70.4		3131	8.5		3173	2.7		863	93.1
18		1401	0.3		1353	0.05		850	15.4		670	59.4		709	71.3		1408	0.5		1382	0.6		663	10.4
19		1192	0.9		1169	2.1		656	7.0		625	58.9		595	73.6		1184	0.1		1166	0.2		575	7.0
20		927	1.0		925	1.3		551	7.0		523	36.9		551	38.0		929	0.2		908	3.9		471	11.8
21		626	85.5		880	97.5		511	2.4		465	13.0		452	6.1		562	5.9		590	20.3		439	99.4
22		497	53.7		543	5.7		322	18.2		289	7.6		293	23.7		376	99.1		508	25.0		290	8.0
23		237	49.7		240	11.9		274	13.3		220	48.4		251	29.1		234	69.7		337	88.0		223	56.4
24		54	3.4		−68	0.01		79	2.3		96	2.5		75	2.0		62	6.9		52	4.2		100	3.9
ZPVE[b]		50.67	[50.59]		[50.88]			51.07	[50.94]		50.72	[50.58]		50.79	[50.66]		50.40	[50.31]		50.33	[50.25]		50.51	[50.36]

[a] Frequencies (ν_i; freq) in cm^{-1}, intensities (int) in km/mol, zero-point vibrational energies (ZPVE) in kcal/mol. All theoretical values were obtained at the B1 (6-311++G**) MP2(full) level at the respective fully optimized reference geometries. The scale factor of 0.97 might be a reasonable estimate for frequency (and consequently ZPVE) corrections. [b] Values in square brackets were obtained by neglecting the contribution from ν_{24}.

tron-diffraction study Iijima and co-workers[16] arrive at the value of 595 cm^{-1} for the energy difference between conformers Ip and III. When the several pitfalls associated with the use of the electron-diffraction technique to obtain energy differences between rotational conformers in general[34] and some deviations (vide infra) between results of the present study and that of Iijima et al.[16] in particular (most importantly the complete neglect of the second most stable conformer of glycine, II, in their analysis) are considered, the agreement between the theoretical value of 560 cm^{-1} and the experimental value of 595 cm^{-1} is fortuitous. The energy difference between conformers Ip and IIp was estimated to be 490 ± 150 cm^{-1} by Suenram and Lovas,[15b] based on intensity measurements on the $13_{5,8}$–$12_{5,7}$ transitions of both conformers. Suenram and Lovas assumed in their model calculations that the vibrational partition function was equal for the two conformers. This approximation does not seem to be the best possible in light of the present B1 MP2 harmonic frequencies. When other sources of error in the relative energy measurements, which have already been emphasized by Suenram and Lovas, are considered, it seems possible that the discrepancy between the theoretical estimate (about 310 cm^{-1}) and the experimental value (490 ± 150 cm^{-1}) of the energy difference between Ip and II is related, at least partly, to larger than assumed experimental model errors and uncertainties and that the experimental estimate of the energy difference should be revised downward. It is evident that further experimental studies are necessary to judge the quality of the final theoretical predictions for the relative energies of the conformers of glycine (see Table II for the equilibrium values; these should, of course, be corrected for vibrational effects (see Table IV) to make them comparable to experimental values).

Geometries. Comparing the calculated rotational constants with the experimental ones available for conformers Ip and IIp it is immediately clear that the B1 MP2(full) level geometry optimizations resulted in highly accurate structures. The average deviation between the six measured A_0, B_0, and C_0 and calculated A_e, B_e, and C_e values is a mere 0.24%, for the two smaller rotational constants even the largest deviation is smaller than 5 MHz. Corrections to obtain equilibrium rotational constants from the observed constants corresponding to the vibrational ground state are expected to be several MHz in magnitude. Indeed, vibrational corrections to the rotational constants of Ip calculated by Iijima et al.[16] change the observed values substantially, bringing the original 63 MHz deviation between theory and experiment for rotational constant A just under 20 MHz. Although in the light of the impressive agreement between the previous SCF level theoretical rotational constants and their experimental counterparts the gratifying agreement obtained in this study is not that unexpected, it is still very reassuring. One should feel confident that the calculated rotational constants obtained for the yet unobserved conformers of glycine have similar accuracy; thus, they should guide all future attempts to observe these species using the techniques of rotational spectroscopy. It seems very likely that the nonplanar conformer IVn could be observed experimentally relatively easily, since it has a low relative energy (compared to the most stable conformer Ip it is only around 400 cm^{-1}) and has a sizable dipole moment. Since the highest energy conformers (VIp, VIIp, and VIII) all have fairly large dipole moments (3–6 D), at slightly elevated temperatures they could also be observed by microwave spectroscopy despite their low abundance as intensities of transitions in the microwave region are proportional to the square of the dipole moment.[35]

There is a plethora of information for a comparative study of the calculated geometric structures of the conformers of glycine (see Table III). Probably the most significant piece of information and the only one being discussed here is the calculated dependence of the values of the CCN and CCO angles on the orientation of the NH_2 and OH groups, respectively. The tilt and asymmetry of methyl groups in asymmetric environments (CH_3Z compounds) has been known for many years and was interpreted, based on ab initio molecular orbital calculations, by Boggs et al.[36] as a result of the combination of through-space bond–bond interactions leading to minimum bond–bond repulsions. If Z has a lone pair (L) of electrons (e.g., Z = NH_2, the case we are mainly interested in), although both C–H···N–H and C–H···L interactions are important, the former repulsion is dominant. As a result, in the stable staggered conformation the ZCH angle trans to the lone pair of electrons is considerably different from the "gauche" ZCH angles (according to calculations,[36] the difference is 5.1° in CH_3NH_2). In primary amines and alcohols the same effect will predictably show up. Indeed, based on quantum chemical calculations, Räsänen et al.[37] proposed a so-called trans–angle rule: "if in a conformer of a primary alcohol or amine a CC or CH bond is trans to an XH bond (X = O, N), the corresponding XCC or XCH angle will be considerably smaller than that for other configurations". This rule has been confirmed experimentally.[38–40] As far as the conformers of glycine are concerned the NCC angle in them changes between 109.6° and 119.6°, while the CCO angle changes between 109.1° and 116.5°. While part of this large spread in the bond angles should be attributed to sizable through-space repulsions (e.g., strong H···H repulsions in conformer VIIp), the trans–angle rule is clearly valid for the conformers of glycine. For example, the OCC angle of conformer Ip is 110.9°, while that of IIp (and similarly IIn) is 113.9°, in agreement with the "trans" vs "cis" arrangement of the CC bond as compared to the OH bond.

Although generally there is an excellent agreement between the B1 MP2(full) theoretical r_e structure and the r_α^0 experimental structure of Ip determined by gas electron diffraction (GED),[16] there are some discrepancies worth discussing. Before going into details one should note that Iijima et al.[16] have found that the agreement of the rotational constants calculated from the analysis of the GED data alone with the observed rotational constants "was not very good". Furthermore, although the agreement improved substantially when they performed a joint GED and rotational constants analysis, they then obtained an unreasonable torsion angle for CCOH (it was calculated to be close to 30°). One of the discrepancies between theory and experiment concerns the length of the C–C and C–N bonds. The r_α^0 values of Iijima et al.[16] are much closer to the values obtained for conformer II than to values of conformer Ip, when according to the calculations the differences between the C–C and C–N bond lengths of conformers Ip and IIp (IIn) are sizable, 0.015 (0.013) and 0.019 (0.018) Å, respectively.[41] Another discrepancy concerns the CNN angle, for which the measured value is some 2.6° smaller than the calculated value. Interestingly, the measured value is right in between the calculated CCN angles of Ip and II. Note also that the COH angle was fixed during the structure refinement to a 4-21G SCF optimized value, which turns out to be too large by as much as 4.2° if compared to the present B1 MP2 result. One plausible explanation for all the observed discrepancies is that although during recording of the GED data Iijima et al.[16] measured scattering from both low-energy conformers I and II of

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(34) Hedberg, K. In *Stereochemical Applications of Gas-Phase Electron Diffraction*; Hargittai, I., Hargittai, M., Eds.; VCH: New York, 1988; pp 347–366.

(35) This fact led, in the late 1970s, to some confusion about the lowest energy form of glycine in the gas phase,[1] as first not I but II was observed in the microwave region due to its much larger dipole moment. Fruitful collaboration between theorists and experimentalists resulted in the measurement of the weak rotational lines of Ip.[1b] A subsequent electron diffraction study[16] confirmed unambigously that indeed Ip is the lowest energy form of glycine in the gas phase.

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(40) Császár, A. G.; Hedberg, K. Unpublished results on a joint electron diffraction, microwave spectroscopy, and quantum mechanical investigation of the molecular structures and conformational composition of 2-fluoroethylamine and 2-aminoethanol.

(41) Naturally, one should not place too much emphasis on the absolute value of the calculated bond lengths, as they might be, even at the level of theory employed in this study, somewhat less accurate than the calculated bond angles for which remaining errors of less than 1° can be assumed.

glycine (this would be especially important if the energy difference between the two conformers is indeed as small as indicated by the present calculations), in the process of structure refinement they basically included parameters of only one of the conformers (that of I). (Note that torsion around the C–C bond has been included in their fit in the form of a simple two-parameter cosine potential, but this rotation leads to conformer III and not to conformer II.) Consequently, the geometry parameters included in their carefully executed fit became basically (weighted) averages of structures Ip and II. It would be interesting to see how a new joint structural refinement of GED and microwave data, biased toward B1 MP2 structural parameters, quadratic force fields,[42] and relative energy differences for conformers Ip and II (and perhaps III) would alter the structural results obtained by Iijima et al.[16]

Vibrational Spectra. The B1 MP2 theoretical vibrational frequencies and infrared intensities presented in Table IV for several glycine conformers would allow interpretation of a carefully executed experimental investigation of the gas-phase vibrational spectrum of glycine. Since we are not aware of such a study this task is left for the future. It is only noted here that the different conformers of glycine have high-intensity infrared bands in different regions of the spectrum; for example, Ip has intensive bands at 1147, 949, and 626 cm^{-1}; IIp at 1440, 929, and 880 cm^{-1}; IVn at 1159 and 858 cm^{-1}, and VIIp at 1347 and 514 cm^{-1}. These considerable shifts in the normal mode vibrations should allow identification of a number of different conformers in the gas-phase vibrational spectrum of glycine. These calculations also reveal that there are some normal modes that do not change substantially from one conformer to another (they predictably include not only ν_4(C=O str) and ν_6(CH$_2$ sci) but also ν_5(NH$_2$ sci) and ν_{12}(C–C str)). Note also that a uniform scale factor of 0.97 might be a reasonable estimate for frequency corrections at the B1 MP2 level of theory.

Conclusions

The following important conclusions can be drawn from the present theoretical study of the conformers of gaseous glycine:

1. Simplifications leading to the Hartree–Fock level of theory prevent one from obtaining quantitative results for the relative energies of the isomers of glycine (and probably for most other amino acids and peptides formed from them), as can be judged from B2 SCF results (employing 350 CGFs) of the present study which should definitely be very close to the Hartree–Fock limit. Given the considerable difficulties observed at the SCF level, the substantially simpler molecular mechanics models must be extremely carefully parametrized to assure that they yield accurate relative energies and thus allow meaningful predictions for the conformational behavior of oligopeptides and peptides.

2. It is shown, employing the t_1 diagnostics of coupled cluster theory, that single-reference-based electron-correlation methods can provide accurate relative energies of glycine conformers. In particular, the MP2 level of theory, when employed with a reasonably large basis set (including both polarization and diffuse functions, like the basis 6-311++G** employed in this study), seems to perform exceptionally well in most respects, partly due to an error cancellation (extension of the one-particle basis more or less compensates for changes accompanying extension of the electron-correlation treatment). It is also observed that in most cases higher order (MP3, MP4, MP∞, CCSD, and CCSD(T)) contributions to the energy differences of conformers seem to cancel out indicating that very large basis set MP2 calculations (like B2 MP2 of this study) might result in highly accurate relative energies, which can be further improved by correcting them with MP3, MP4, and MP∞ contributions obtained using a smaller basis set (these latter corrections vary between −79 and +41 cm^{-1} for the isomers considered). A similar strategy for theoretical computations is recommended for future studies on neutral amino acids (and possibly on their amides). Results obtained at the highest levels of theory employed in this investigation (B2 MP2, B1 MP4, and B1 CCSD(T)) should probably serve as benchmarks for these future calculations.

3. Eight minimum-energy conformers of neutral glycine have been identified in this study, among them there are five distinct conformers whose relative energy is less than 1000 cm^{-1} (the barrier to internal rotation in ethane). Five of the eight minima have a nonplanar heavy-atom structure, which results from a balance between stabilizing intramolecular H-bonds and destabilizing steric strain and lone-pair electron-repulsion effects.

4. The lowest energy form of glycine (Ip) has a planar heavy-atom structure and two equal N–H···O H-bonds, while the second most stable conformer (II) has an O–H···N H-bond and is less stable than Ip by only about 180 cm^{-1} (equilibrium value), which changes to 310 cm^{-1} by inclusion of vibrational effects. At equilibrium, a nonplanar structure is preferred by conformer II according to all correlated level calculations. ZPVE calculations suggest, however, that the effective ground-state structure of II is probably planar. (Note that there is an extremely good agreement between the measured and calculated rotational constants of IIp.) For conformer III the potential energy curve is extremely flat around IIIp, thus even calculations at the highest levels leave the question open as to whether the C_s or the C_1 form is a minimum.

5. Agreement between the B1 MP2 rotational constants and experiment is excellent for the two lowest energy forms of glycine (experimental data are available only for Ip and IIp), even the largest deviations are only a few MHz. The rotational constants calculated for the yet unobserved conformers should have a similar accuracy and thus could help in the search for these conformers by rotational spectroscopy.

6. Within the limits of their chosen model Iijima and coworkers[16] performed a careful joint GED and rotational constants analysis that resulted in the structure of the lowest-energy form of glycine. Their model, however, should be revised based on the newly available theoretical data of this study, and the analysis should be repeated since considerable changes in some structural parameters are expected as the result of model revision.

7. The calculated vibrational spectra of the conformers of glycine reveal that different conformers have some high-intensity bands in different regions of the spectrum. These considerable shifts in normal mode vibrations would probably allow identification of a number of conformers in the gas-phase vibrational spectrum of glycine.

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Supplementary Material Available: Table V listing of the symmetry coordinates for glycine and Table VI containing the B1 (6-311++G**) MP2 quadratic force field of glycine Ip in symmetry coordinates (2 pages). Ordering information is given on any current masthead page.

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[42] The quadratic force field obtained for Ip as part of the present study (see Tables V and VI of the supplementary material) has actually been used to calculate root-mean-square amplitudes for all distances incorporated in the GED analysis of Iijima et al.[16] to check their accuracy. Most calculated values agree reasonably well with the amplitudes assumed and/or measured by Iijima et al., suggesting that their Urey–Bradley force field was as accurate as required for the purposes of a GED study.