

The structure and energetics of glycine polymorphs based on first principles simulation using density functional theory

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Density functional theory (DFT) calculations for the crystal structures of polymorphs of the glycine zwitterion are reported; with unit cell parameters constrained at experimentally determined values, energy minimized configurations for three known glycine polymorphs are in good agreement with crystallographically determined structures, and the calculated energies are in qualitative agreement with observed lattice stabilities.

Molecular orbital calculations, employing Hartree–Fock,¹ density functional theory (DFT),² or even an appropriate combination of both methods³ are standard techniques for the structural and energetic description of molecular systems. Significant developments have also recently taken place in the use of first principles methods to represent ionic and covalently bound periodic systems, such as silicon and zeolites, typically employing plane-wave and plane-wave/pseudo-potential approaches.^{4–7} However, the simulation of molecular solids using first-principles methods has received considerably less attention⁸ and the use of such methods to address the relative energies of crystal polymorphs less still. The lack of suitably refined protocols underlies this comparatively low level of application. Nevertheless, the results presented here show that such calculations are now within the compass of contemporary quantum mechanical methods and computational resources.

To explore the ability of periodic DFT method calculations to describe molecular crystals, calculations were conducted targeting the known polymorphic structures of the glycine zwitterion and using DMol³.^{9–11} The level of theory employed has been shown to be effective in the description of isolated molecules.^{12†}

Initial investigations addressed the selection of a suitable quantum mechanical Hamiltonian and basis set. These calculations employed the β -glycine polymorph, which possesses a unit cell containing two symmetry related molecules and a total of 20 atoms.¹³ Here results for the BLYP^{14–17} functional are summarized. A minimal basis resulted in a 0.34 Å RMS deviation between minimized and observed structures, a double numeric basis (0.33 Å), a double numeric basis with polarization functions on heavy atoms (0.22 Å) and double numeric basis with polarization functions on all atoms (0.21 Å). Of the basis sets sampled then, optimal structural agreement is achieved on full geometry optimization with a so-called double numeric basis set with polarization functions on all atoms (DNP). The DNP basis set has been demonstrated to provide an efficient route to molecular polarizabilities and charge distributions as a result of its reasonable representation of the tail of the wavefunction.¹⁰ However, the ability of this computational approach to describe the relative energetics of polymorphic crystal structures is perhaps of more interest.

To address the calculation of such relative polymorph energies, crystallographically determined structural starting models for α - and γ -glycine were employed.^{18,19} As an additional test of the simulation protocol two incorrectly packed arrangements of glycine molecules were used as starting points; S1, containing four molecules in the unit cell dimensions of the α -polymorph, and S2, containing two molecules with cell dimensions of the β -polymorph.

Table 1 The relative BLYP energies, per glycine molecule, of the α -, β - and γ -glycine polymorphs. Also tabulated are the relative energies of hypothetical packing arrangements S1 and S2 and the root mean squared (RMS) displacements between the experimental structure and energy minimized structure

	Polymorph				
	α	β	γ	S1	S2
Energy/kcal mol ⁻¹	0.0	2.3	2.0	5.8	15.9
RMS/Å	0.19	0.21	0.30	0.33 ^a	1.20 ^a

^a RMS between starting and energy minimized structure.

Energetic results for the systems considered are collected in Table 1. The similarity of the relative energies obtained in the DFT calculations for the α -, β - and γ -polymorphs is mirrored in the experimental observation that all polymorphs are formed at temperatures close to room temperature, with the α -polymorph having the greatest observed stability.¹⁸ The energy differences obtained in the simulations are small and entropic contributions to the lattice stability have not been considered in the present calculations. The inclusion of vibrational entropy would, of course, be possible with increased computation times through calculation of the system's dynamical matrix and appropriate integration of the resulting phonon spectrum. However, the fact that the relative energies of incorrectly packed molecular arrangements S1 and S2 are higher than the observed polymorph energies is of significant interest. For the polar β - and γ -polymorph crystals such a procedure assumes that the macroscopic dipolar energy of the structures is not significant.^{20,21} This appears to be a reasonable approximation.²²

Fig. 1 shows starting structures and optimized structures for each of the polymorphs investigated. Good agreement is

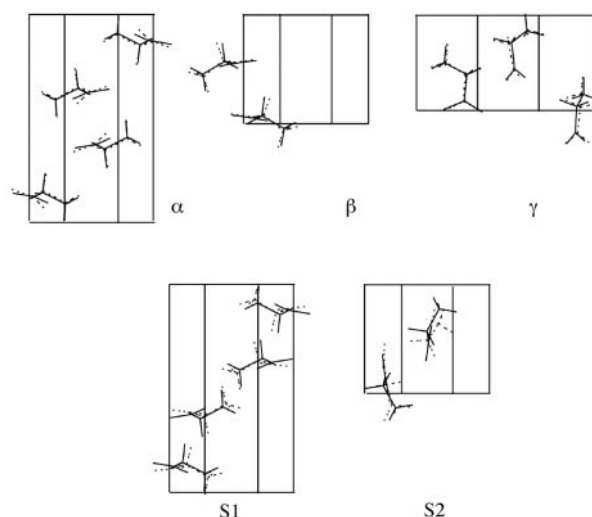
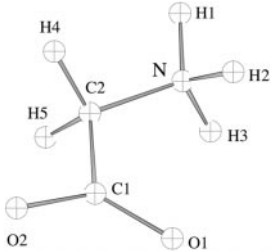


Fig. 1 Structural agreement between energy minimized (dashed line) and experimental structures (solid line) for α -, β - and γ -glycine polymorphs. Hypothetical packing arrangements S1 and S2 (dashed line) show comparison with starting points (solid line).

Table 2 Mulliken (ref. 23) derived partial electronic charges obtained with the BLYP Hamiltonian and DNP basis sets for α -, β - and γ -glycine polymorphs and hypothetical packing arrangements S1 and S2 (molecules 1 and 2). Also tabulated are partial electronic charges for an isolated molecule in the configuration of the unique molecule of the α -glycine polymorph

	Isolated molecule	Polymorph						
		α	β	γ	S1	S2: 1	S2: 2	
	O1	-0.534	-0.640	-0.618	-0.654	-0.630	-0.687	-0.597
	C1	0.401	0.553	0.555	0.546	0.530	0.550	0.514
	N	-0.222	-0.410	-0.456	-0.425	-0.494	-0.410	-0.447
	C2	-0.167	-0.168	-0.185	-0.146	-0.129	-0.185	-0.183
	H1	0.234	0.352	0.356	0.348	0.357	0.269	0.331
	H3	0.258	0.286	0.334	0.293	0.320	0.402	0.329
	H2	0.265	0.344	0.344	0.353	0.351	0.260	0.283
	H5	0.137	0.133	0.149	0.165	0.118	0.149	0.184
	O2	-0.509	-0.650	-0.654	-0.629	-0.622	-0.538	-0.606
	H4	0.137	0.200	0.174	0.147	0.198	0.196	0.184

obtained between simulation and experiment for the known crystal models. The lowest RMS displacement between optimized and experimental structure (0.19 Å) is obtained for the α -polymorph, a structure determined using neutron diffraction data with the lowest crystallographic R value of the polymorphs ($R = 0.032$).¹⁹ The starting geometries of incorrectly packed arrangements, S1 and S2, are altered by the optimization procedure to a greater extent than the observed polymorphs. In neither case do the resulting structures resemble the experimental polymorph structures.

For S1 the structural deviation has an RMS value of 0.33 Å implying that, in this case, energy minimization is able to locate a stationary point in the vicinity of the starting structure. S1 was generated using the unit cell and asymmetric unit of the α -polymorph and applying the symmetry operations of the $P2_1/c$ spacegroup. This procedure yields a packing configuration similar for half the molecules to that of the α -polymorph (spacegroup $P2_1/n$). For S2 larger structural changes are evident in both the RMS displacement (1.2 Å) and in Fig. 1. This polymorph was generated by randomly placing two molecules within the cell of the β -polymorph.

The present calculations employ the experimental unit cell dimensions as a constraint. This reduces computation times through a reduction in the number of variables used to describe the system. However it is important to note that cell parameter data, through indexed powder diffraction patterns, are among the most readily obtained structural information for solid state materials. The current calculations, which focus on the optimization of the geometry within the unit cell, provide valuable information that augments experimental observation and leads to the full description of the crystal.

The magnitudes of partial charges are key to the accuracy of models employing classical mechanics. Table 2 collects the Mulliken²³ charges for each of the atoms of the glycine molecule in the calculations conducted. The calculations are performed within a $P\bar{1}$ triclinic simulation cell. However, for the α -, β - and γ -polymorphs symmetry is maintained during the optimization, hence charges are reported for a single molecule only. S1 was produced with the $P2_1/c$ spacegroup and also has four equivalent molecules, one of which is listed. For S2, symmetry is not present and charges for both molecules are listed. Interestingly for the experimental polymorphs there is little difference between the atomic partial charges obtained, despite the differences in local environment that each crystal form necessarily imposes on its constituent molecules. For the hypothetical packing arrangements S1 and S2, differing charge distributions are exhibited on several atoms, most notably O1, O2 and N. Also tabulated in Table 2 are gas phase derived atomic charges using the same basis set and Hamiltonian for the structure of the unique molecule of the α -polymorph. The magnitude of charges on oxygen and nitrogen atoms of the isolated molecule are lower than in the crystal structure calculations. The unambiguous definition of atomic partial charges from supplied molecular orbitals is not straightforward.^{24,25} In particular Mulliken analysis is sensitive to the

choice of basis set. However, these findings, using a particular charge definition method²³ and uniform basis set and calculation type, indicate that the practice of transferring partial charges from gas phase calculations to the condensed phase may lead to an inaccurate description of the charge distribution exhibited by molecules in the crystalline state. Of course, no such ambiguity affects the first-principles calculations where charge density and its variation with environment are both consequences of the molecular orbitals obtained in the solution of the Schrödinger equation.

The calculations demonstrate that energy minimization leading to a determination of the relative energetics of molecular crystals is practical using first principles methods.[‡]

Notes and references

† The Brillouin zones of the polymorphs were sampled at the Γ point only. A detailed report on the effect of the choice of Hamiltonian and basis set on the structures and energies for molecular solids is in preparation. Geometry optimization (varying all atomic coordinates within the fixed cell) required calculation times of a few days on a single processor of an Origin 200 SGI (180 MHz) workstation.

‡ The computed structures are available from the authors by email.

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