Supplemental Information

Revealing the true crystal structure of L-phenylalanine using solid-state density functional theory

Matthew D. King, Thomas N. Blanton, and Timothy M. Korter

Materials and Methods

Experimental

L-Phenylalanine (purity ≥ 98%) was purchased from Sigma-Aldrich and used without further purification. Samples for powder X-ray diffraction (PXRD) measurements were passed through a 200 mesh (75 micron) sieve and front-packed into a glass sample holder. PXRD measurements were obtained using a Rigaku D2000 Bragg Brentano diffractometer equipped with a copper rotating anode, diffracted beam monochromator tuned to 1.542-Å $Cu_{\kappa\alpha}$ radiation, and a scintillation detector. Data were collected over a range of 2 to 60 degrees 2θ, as a continuous scan of 2 degrees 2θ min^{-1}. The resulting diffraction data were analyzed using MDI Jade 9.0 software.

Theoretical

Calculations were carried out using a desktop workstation equipped with dual six-core 2.8 GHz processors (Intel Xeon X5660) and 24 GB RAM. DFT calculations with periodic boundary conditions were performed using the CRYTAL09 software package.[1, 2] Calculations used the PBE and B3LYP density functionals with the atom-centered 6-31G(d,p) basis set.[3-6] Total energy convergence criteria of $\Delta E < 10^{-7}$ hartree was used for geometry optimizations. A shrinking factor of 3 was used in defining the sampling rate as a function of **k** points for the density matrix and commensurate grid in reciprocal space in order to meet the convergence criteria.[7, 8] The angular and radial distribution of points were defined by a pruned (75,974) integration grid. Truncation tolerances were set to 10^{-6}, 10^{-6}, 10^{-6}, 10^{-6}, and 10^{-12} hartree for the Coulomb and HF exchange integral series.[9]

An empirical energy correction for London-type dispersion forces of form $1/R^6$ was included in all DFT calculations (DFT-D).[10, 11] The dispersion correction is given by the equation

$$E_{disp} = -s_6 \sum_i \sum_j \sum_{\mathbf{g}} \frac{C_6^{ij}}{R_{ij,\mathbf{g}}^6} f_{dmp}\left(R_{ij,\mathbf{g}}\right), \qquad (1)$$

where the energy correction is the summation over all atom pairs and **g** lattice vectors. C_6^{ij} is the dispersion coefficient and R_{ij} is the internuclear separation of atom pair ij, s_6 is a global dispersion scalar, and f_{dmp} is a dampening function included to avoid near-singularities at small values *R*. The dampening function is of the form

$$f_{dmp}\left(R_{ij}\right) = \left[1 + e^{-d(R_{ij}/R_{vdw}-1)}\right]^{-1}, \qquad (2)$$

where R_{vdw} is the sum of the van der Waals radii, and *d* defines the function steepness. A cutoff distance for the dispersion energy term of 25 Å was used to truncate the summation over lattice vectors. Values for C_{ij}^6, R_{vdw}, and *d* were taken from Ref. 9, and the R_{vdw} were scaled for the application of dispersion corrections in molecular crystals.[11, 12] The global dispersion scaling factor, s_6, was modified to adjust for the magnitude of the dispersion forces applied to the calculations. It has been demonstrated in previous studies employing solid-state DFT-D that the proposed s_6 values, originally optimized for molecules in the gas phase, are too large for the accurate reproduction of non-zero temperature crystal structures.[13-15] Therefore, the proposed value of 0.75 for use with the PBE functional was reduced to 0.50 based on the results of these previous studies using the same dispersion correction scheme.

The initial crystal structure of L-phenylalanine was constructed from the published *C*2 structure of D-phenylalanine.[16] These enantiomeric crystal structures are related by an *a*-*c* reflection plane. Full structural optimization of the Z = 8 unit cell was performed with no symmetry constraints, i.e. lattice parameters and all unit cell contents were allowed to freely optimize in *P*1 symmetry. Unit cells optimized in *C*2 symmetry allowed for full optimization of the lattice dimensions and the two molecules of the asymmetric unit with constraints placed only on preservation of space group symmetry.

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Table S1. Lattice parameters for calculated crystal structures of L-phenylalanine.

	*P*2	*C*2
Z	8	8
Z'	4	2
a (Å)	8.74074	8.84062
b (Å)	6.04118	6.21395
c (Å)	31.39407	31.18564
β (°)	97.7452	96.8953
V (Å^3)	1642.62	1700.80
d (g cm^{-3})	1.335	1.289
Rel. Energy (kJ mol^{-1})[a]	0.00	5.31

[a] Relative energy per molecule with respect to *P*2 structure.