FOUNDATIONS
ADVANCES

Volume 76 (2020)

Supporting information for article:

A combined model of electron density and lattice dynamics refined against elastic diffraction data. Thermodynamic properties of crystalline l-alanine

Ioana Sovago, Anna A. Hoser and Anders Ø. Madsen

Experimental methods

Crystallization

L-alanine was purchased from Sigma-Aldrich and used without further purification. L-alanine suitable single crystals for X-ray diffraction were produced by slow evaporation from an aqueous solution.

High resolution X-ray diffraction 123 K

A single crystal was mounted on a Bruker D8 Venture diffractometer equipped with Mo tube and Photon 100 CMOS detector. Data collection was performed at 123 K, with the temperature maintained using an open-flow nitrogen cooling device (CIA LN2). Diffraction data were collected in shutterless mode and to ensure a complete dataset without detector overload three different exposure times of 2, 10 and 120 seconds per degree were collected. The data were scaled to a common dataset using the SORTAV program(*1*) in the DREADD package by Blessing. Spherical atom refinement was performed initially using SHELXL-2014(*2*) with full-matrix least-squares on F^2 and using all the unique data. The non-H atoms were refined by allowing anisotropic thermal motion. All calculations were carried out using the WinGX package(*3*) of crystallographic programs. A summary and statistics of the collected data are given in Table S1.

Multipole refinement - 23K and 123K data

The refinements using aspherical form factors against the 23K (*4*) and 123 K data of L-alanine were performed using the formalism of Hansens and Coppens (*5*) as implemented in the XD-2006 software(*6*):

$$\rho(\mathbf{r}) = P_{\text{core}}\rho_{\text{core}}(r) + P_{\text{val}}\kappa^3\rho_{\text{val}}(\kappa r) + \sum_{l=0}^{l_{\max}} \kappa'^3 R_l(\kappa' r) \sum_{m=0}^{l} P_{lm\pm} d_{lm\pm}(\Omega)$$

The multipole expansion was truncated at the octupole level for the O, N and C atoms and the quadrupole level for the H atoms. The ADPs for H atoms in the multipole refinements were estimated using SHADE3(*7*). The core and spherical-valence scattering factor for each pseudoatom were derived from the relativistic Dirac-Fock wavefunctions of Su and Coppens(*8*) expanded in terms of the single-ζ functions of Bunge, Barrientos and Bunge(*9*). The valence deformation functions for the atoms used a single-ζ Slater-type radial function multiplied by the density-normalized spherical harmonics. The radial fits for each atoms were optimized by refinement of their expansion-contraction parameters κ, κ'.

Theoretical methods

Ab-initio periodic calculations were performed in order to obtain the vibrational frequencies using the CRYSTAL09 software(*10*) at different basic sets and levels of theory for 23K as presented in Table 1 and 123 K (Table 3). Empirical dispersion corrections were applied and tested on the NoMoRe refinement, as proposed by Grimme(*11*) and modified for crystals. (*12*)

Table SP1. Crystallographic data for l-alanine 123K

Compound formula	$C_3H_7NO_2$
M_r	89.1
Space group	$P2_12_12_1$
Crystal system	Orthorhombic
a/ Å	5.9534(5)
b/Å	12.2772(10)
c/Å	5.7882(5)
V/Å^{-3}	423.07(1)
Z	4
D_{calc}/g cm^{-3}	1.4
λ/Å	0.71073
μ/mm^{-1}	0.117
Temperature/K	123
Crystal size/mm	0.31×0.24×0.14
θ range/deg	3.3-58
Max sin(θ)/ λ	1.19
No. of data	118409
No. of unique data	5997
hkl range	$0 \le h \le 14$
	$0 \le k \le 29$
	$0 \le l \le 13$
R_{int}	0.046
R_σ	0.027
Spherical atom refinement	
No. of data in refinement	5997
No. of refined parameters	84
Final *R* [$I > 2\sigma(I)$]	0.023
R_w^2	0.063
Goodness of fit *S*	1.144
Extrema in residual map/ e Å^{-3}	0.376→ -0.266
Max shift/esd in last cycle	0.001
Multipole refinement	
No. of data in refinement	6000
No. of refined parameters	131
Final *R* [$I > 3\sigma(I)$]	0.0178
R_w all data	0.0381
Goodness of fit *S*	1.146
Extrema in residual map/ eÅ^{-3}	
(all data)	0.15→ -0.134

Max shift/esd in last cycle	0.57×10^{-4}

Table S2. Correlation matrices from the least squares refinement of selected NoMoRe models.

Correlation matrices of AAM Γ 50

```
[ 1.   -0.07 -0.03  0.12  0.13 -0.15  0.07  0.06  0.08 -0.24 -0.01  0.46 -0.28  0.21
0.27 -0.04 -0.16 -0.03 -0.38 -0.   -0.01]
 [-0.07  1.    0.03 -0.92 -0.23  0.04  0.12 -0.48  0.36  0.15  0.31  0.18 -0.41  0.35
0.06 -0.3  -0.34 -0.21 -0.28 -0.17  0.41]
 [-0.03  0.03  1.   -0.15 -0.53 -0.57 -0.7   0.03 -0.09  0.03 -0.24 -0.15  0.39 -0.21 -
0.17  0.22  0.15  0.35  0.19  0.01 -0.03]
 [ 0.12 -0.92 -0.15  1.    0.43 -0.05 -0.09  0.24 -0.36  0.02 -0.25 -0.19  0.18 -0.18 -
0.13  0.02  0.19  0.14  0.15  0.11 -0.32]
 [ 0.13 -0.23 -0.53  0.43  1.   -0.07  0.02 -0.19  0.    0.29 -0.03 -0.03 -0.41  0.27 -
0.12 -0.44 -0.21 -0.28 -0.23 -0.05  0.1 ]
 [-0.15  0.04 -0.57 -0.05 -0.07  1.    0.26  0.02 -0.04 -0.   -0.02 -0.   -0.01 -0.04 -
0.03  0.12  0.1   0.05  0.06 -0.07 -0.02]
 [ 0.07  0.12 -0.7  -0.09  0.02  0.26  1.    0.14  0.17 -0.34  0.46  0.29 -0.26  0.12
0.44 -0.02 -0.1  -0.36 -0.15  0.1  -0.14]
 [ 0.06 -0.48  0.03  0.24 -0.19  0.02  0.14  1.   -0.31 -0.68  0.04  0.15  0.5  -0.51
0.49  0.67  0.55 -0.11  0.37 -0.03 -0.44]
 [ 0.08  0.36 -0.09 -0.36  0.   -0.04  0.17 -0.31  1.   -0.08  0.38  0.24 -0.42  0.61
0.21 -0.25 -0.5  -0.33 -0.64  0.03  0.31]
 [-0.24  0.15  0.03  0.02  0.29 -0.   -0.34 -0.68 -0.08  1.   -0.46 -0.49 -0.27  0.16 -
0.85 -0.48 -0.5   0.22  0.01 -0.05  0.34]
 [-0.01  0.31 -0.24 -0.25 -0.03 -0.02  0.46  0.04  0.38 -0.46  1.    0.33 -0.36  0.37
0.61 -0.21 -0.14 -0.55 -0.39  0.01  0.04]
 [ 0.46  0.18 -0.15 -0.19 -0.03 -0.    0.29  0.15  0.24 -0.49  0.33  1.   -0.49  0.17
0.45  0.01  0.22 -0.04 -0.29  0.01 -0.09]
 [-0.28 -0.41  0.39  0.18 -0.41 -0.01 -0.26  0.5  -0.42 -0.27 -0.36 -0.49  1.   -0.61
0.04  0.63  0.48  0.25  0.58  0.01 -0.35]
 [ 0.21  0.35 -0.21 -0.18  0.27 -0.04  0.12 -0.51  0.61  0.16  0.37  0.17 -0.61  1.
0.09 -0.72 -0.68 -0.39 -0.96  0.05  0.44]
 [ 0.27  0.06 -0.17 -0.13 -0.12 -0.03  0.44  0.49  0.21 -0.85  0.61  0.45  0.04  0.09
1.    0.2   0.16 -0.55 -0.23 -0.27 -0.04]
 [-0.04 -0.3   0.22  0.02 -0.44  0.12 -0.02  0.67 -0.25 -0.48 -0.21  0.01  0.63 -0.72
0.2   1.    0.56  0.28  0.58  0.02 -0.53]
 [-0.16 -0.34  0.15  0.19 -0.21  0.1  -0.1   0.55 -0.5  -0.5  -0.14  0.22  0.48 -0.68
0.16  0.56  1.    0.37  0.61  0.05 -0.53]
 [-0.03 -0.21  0.35  0.14 -0.28  0.05 -0.36 -0.11 -0.33  0.22 -0.55 -0.04  0.25 -0.39 -
0.55  0.28  0.37  1.    0.37  0.16 -0.41]
 [-0.38 -0.28  0.19  0.15 -0.23  0.06 -0.15  0.37 -0.64  0.01 -0.39 -0.29  0.58 -0.96 -
0.23  0.58  0.61  0.37  1.   -0.05 -0.35]
 [-0.   -0.17  0.01  0.11 -0.05 -0.07  0.1  -0.03  0.03 -0.05  0.01  0.01  0.01  0.05 -
0.27  0.02  0.05  0.16 -0.05  1.   -0.37]
 [-0.01  0.41 -0.03 -0.32  0.1  -0.02 -0.14 -0.44  0.31  0.34  0.04 -0.09 -0.35  0.44 -
0.04 -0.53 -0.53 -0.41 -0.35 -0.37  1.  ]
```

Correlation matrices of AAM Γ60

```
 [ 1.   -0.25  0.21  0.24  0.13 -0.29  0.05  0.36 -0.23 -0.06 -0.48  0.49  0.24 -0.45
0.07  0.22  0.16  0.26 -0.05 -0.48 -0.39]
 [-0.25  1.    0.09 -0.96 -0.42  0.32  0.02 -0.32  0.39  0.21  0.09 -0.18 -0.11  0.   -
0.19  0.21 -0.24 -0.    0.07  0.23  0.24]
 [ 0.21  0.09  1.   -0.1  -0.51 -0.34 -0.18  0.1  -0.17 -0.07 -0.17  0.1   0.26 -0.23 -
0.    0.35  0.06  0.4  -0.01 -0.22 -0.41]
 [ 0.24 -0.96 -0.1   1.    0.48 -0.35 -0.02  0.16 -0.4  -0.21 -0.01  0.11  0.01  0.03
0.19 -0.33  0.21 -0.04  0.03 -0.09 -0.25]
 [ 0.13 -0.42 -0.51  0.48  1.   -0.51  0.14 -0.14 -0.03 -0.3   0.16  0.04 -0.14  0.14
0.29 -0.4   0.   -0.17 -0.05  0.15 -0.07]
 [-0.29  0.32 -0.34 -0.35 -0.51  1.   -0.37  0.06  0.15  0.46 -0.05 -0.18 -0.16  0.15 -
0.31  0.09 -0.08 -0.24  0.03  0.05  0.43]
 [ 0.05  0.02 -0.18 -0.02  0.14 -0.37  1.    0.01  0.14 -0.14 -0.01  0.2   0.11 -0.14
0.08 -0.25 -0.04 -0.08  0.14  0.01 -0.  ]
 [ 0.36 -0.32  0.1   0.16 -0.14  0.06  0.01  1.   -0.3   0.03 -0.38  0.49  0.34 -0.23
0.01  0.32  0.28  0.03 -0.28 -0.66 -0.12]
 [-0.23  0.39 -0.17 -0.4  -0.03  0.15  0.14 -0.3   1.    0.29  0.11 -0.1  -0.31  0.08 -
0.27 -0.13 -0.42 -0.32 -0.03  0.35  0.4 ]
 [-0.06  0.21 -0.07 -0.21 -0.3   0.46 -0.14  0.03  0.29  1.   -0.37  0.03 -0.4   0.12 -
0.76 -0.07 -0.17 -0.09 -0.03  0.07  0.32]
```

```
 [-0.48  0.09 -0.17 -0.01  0.16 -0.05 -0.01 -0.38  0.11 -0.37  1.   -0.4  -0.43  0.41
0.25 -0.34 -0.13 -0.39  0.05  0.61  0.26]
 [ 0.49 -0.18  0.1   0.11  0.04 -0.18  0.2   0.49 -0.1   0.03 -0.4   1.    0.3  -0.58 -
0.14 -0.05  0.4   0.06  0.08 -0.66 -0.09]
 [ 0.24 -0.11  0.26  0.01 -0.14 -0.16  0.11  0.34 -0.31 -0.4  -0.43  0.3   1.   -0.51
0.15  0.41  0.47  0.43  0.06 -0.73 -0.45]
 [-0.45  0.   -0.23  0.03  0.14  0.15 -0.14 -0.23  0.08  0.12  0.41 -0.58 -0.51  1.
0.05 -0.11 -0.21 -0.33 -0.61  0.55  0.29]
 [ 0.07 -0.19 -0.    0.19  0.29 -0.31  0.08  0.01 -0.27 -0.76  0.25 -0.14  0.15  0.05
1.    0.02 -0.33  0.02 -0.04 -0.   -0.36]
 [ 0.22  0.21  0.35 -0.33 -0.4   0.09 -0.25  0.32 -0.13 -0.07 -0.34 -0.05  0.41 -0.11
0.02  1.    0.14  0.51 -0.45 -0.45 -0.34]
 [ 0.16 -0.24  0.06  0.21  0.   -0.08 -0.04  0.28 -0.42 -0.17 -0.13  0.4   0.47 -0.21 -
0.33  0.14  1.    0.13 -0.05 -0.49 -0.04]
 [ 0.26 -0.    0.4  -0.04 -0.17 -0.24 -0.08  0.03 -0.32 -0.09 -0.39  0.06  0.43 -0.33
0.02  0.51  0.13  1.   -0.07 -0.45 -0.69]
 [-0.05  0.07 -0.01  0.03 -0.05  0.03  0.14 -0.28 -0.03 -0.03  0.05  0.08  0.06 -0.61 -
0.04 -0.45 -0.05 -0.07  1.    0.09  0.04]
 [-0.48  0.23 -0.22 -0.09  0.15  0.05  0.01 -0.66  0.35  0.07  0.61 -0.66 -0.73  0.55 -
0.   -0.45 -0.49 -0.45  0.09  1.    0.42]
 [-0.39  0.24 -0.41 -0.25 -0.07  0.43 -0.   -0.12  0.4   0.32  0.26 -0.09 -0.45  0.29 -
0.36 -0.34 -0.04 -0.69  0.04  0.42  1.  ]]
```

Correlation matrices of AAM Γ 70

```
 [ 1.   -0.37 -0.04  0.44  0.35  0.06 -0.21  0.07 -0.06 -0.   -0.16  0.63 -0.35 -0.44 -
0.33 -0.26 -0.64  0.13 -0.05 -0.01  0.18]
 [-0.37  1.   -0.14 -0.94 -0.48  0.03  0.46 -0.58  0.33  0.28  0.29 -0.16 -0.21  0.33
0.04 -0.2   0.1  -0.09  0.52 -0.23  0.  ]
 [-0.04 -0.14  1.    0.04 -0.28 -0.14 -0.7   0.23  0.15  0.18 -0.49  0.1   0.2  -0.29 -
0.24  0.16  0.32  0.37 -0.16  0.01  0.19]
 [ 0.44 -0.94  0.04  1.    0.47 -0.02 -0.33  0.39 -0.27 -0.28 -0.23  0.24  0.09 -0.25 -
0.06  0.04 -0.15  0.06 -0.36  0.24 -0.09]
 [ 0.35 -0.48 -0.28  0.47  1.   -0.07 -0.36  0.32 -0.1  -0.04 -0.2   0.14  0.09 -0.23 -
0.15  0.07 -0.2  -0.18 -0.25  0.15  0.11]
 [ 0.06  0.03 -0.14 -0.02 -0.07  1.   -0.15  0.08  0.24  0.32 -0.32  0.01  0.05 -0.12 -
0.38 -0.07 -0.02 -0.07  0.22 -0.07  0.09]
 [-0.21  0.46 -0.7  -0.33 -0.36 -0.15  1.   -0.46 -0.13 -0.27  0.74 -0.19 -0.29  0.51
0.46 -0.21 -0.17 -0.28  0.25 -0.08 -0.33]
 [ 0.07 -0.58  0.23  0.39  0.32  0.08 -0.46  1.   -0.28  0.11 -0.24 -0.14  0.24 -0.28 -
0.19  0.3  -0.03 -0.16 -0.55 -0.07  0.29]
 [-0.06  0.33  0.15 -0.27 -0.1   0.24 -0.13 -0.28  1.    0.52 -0.25  0.21 -0.17 -0.02 -
0.46 -0.28 -0.15 -0.05  0.37 -0.3   0.06]
 [-0.    0.28  0.18 -0.28 -0.04  0.32 -0.27  0.11  0.52  1.   -0.33  0.15 -0.26 -0.03 -
0.75 -0.33 -0.21 -0.09  0.33 -0.6   0.5 ]
 [-0.16  0.29 -0.49 -0.23 -0.2  -0.32  0.74 -0.24 -0.25 -0.33  1.   -0.01 -0.45  0.51
0.47 -0.21 -0.28 -0.37 -0.08 -0.11 -0.2 ]
 [ 0.63 -0.16  0.1   0.24  0.14  0.01 -0.19 -0.14  0.21  0.15 -0.01  1.   -0.64 -0.13 -
0.34 -0.53 -0.64  0.04  0.05 -0.17  0.18]
 [-0.35 -0.21  0.2   0.09  0.09  0.05 -0.29  0.24 -0.17 -0.26 -0.45 -0.64  1.   -0.19
0.29  0.45  0.59  0.13 -0.16  0.21 -0.03]
 [-0.44  0.33 -0.29 -0.25 -0.23 -0.12  0.51 -0.28 -0.02 -0.03  0.51 -0.13 -0.19  1.
0.26 -0.23 -0.04 -0.29 -0.14 -0.13 -0.09]
 [-0.33  0.04 -0.24 -0.06 -0.15 -0.38  0.46 -0.19 -0.46 -0.75  0.47 -0.34  0.29  0.26
1.    0.29  0.29 -0.09 -0.18  0.17 -0.34]
 [-0.26 -0.2   0.16  0.04  0.07 -0.07 -0.21  0.3  -0.28 -0.33 -0.21 -0.53  0.45 -0.23
0.29  1.    0.53  0.18 -0.44  0.37 -0.26]
 [-0.64  0.1   0.32 -0.15 -0.2  -0.02 -0.17 -0.03 -0.15 -0.21 -0.28 -0.64  0.59 -0.04
0.29  0.53  1.    0.25  0.11  0.36 -0.42]
 [ 0.13 -0.09  0.37  0.06 -0.18 -0.07 -0.28 -0.16 -0.05 -0.09 -0.37  0.04  0.13 -0.29 -
0.09  0.18  0.25  1.   -0.02  0.18 -0.19]
 [-0.05  0.52 -0.16 -0.36 -0.25  0.22  0.25 -0.55  0.37  0.33 -0.08  0.05 -0.16 -0.14 -
0.18 -0.44  0.11 -0.02  1.   -0.16 -0.14]
 [-0.01 -0.23  0.01  0.24  0.15 -0.07 -0.08 -0.07 -0.3  -0.6  -0.11 -0.17  0.21 -0.13
0.17  0.37  0.36  0.18 -0.16  1.   -0.48]
```

Table SP3 Comparison of mean square displacement matrices for models IAM and SAMΓ. The values are explained in the paper.

Atom	RMS_{eigvec}	R_{eigval}	S_{12}%	*FOM*
O1	6.58	0.026	99.90	0.031
O2	6.50	0.049	99.83	0.039

N1	25.29	0.027	99.83	0.094
C1	10.96	0.027	99.89	0.046
C2	6.25	0.017	99.96	0.027
C3	3.75	0.036	99.92	0.025

Mean S12 99.89%

Table SP4 Comparison of mean square displacement matrices for models IAM and SAMPD. The values are explained in the paper.

Atom	RMS_{eigvec}	R_{eigval}	S_{12}%	*FOM*
O1	7.73	0.031	99.84	0.037
O2	1.09	0.039	99.97	0.017
N1	7.54	0.040	99.91	0.039
C1	6.05	0.041	99.94	0.034
C2	4.83	0.049	99.88	0.033
C3	6.92	0.028	99.85	0.033

Mean S12 99.897%

Table SP5 Comparison of mean square displacement matrices for models AAM standard vs AAMΓ.

Atom	RMS_{eigvec}	R_{eigval}	S_{12}%	*FOM*
O1	4.94	0.038	99.90	0.030
O2	3.65	0.035	99.93	0.024
N1	21.17	0.032	99.92	0.081
C1	6.92	0.034	99.96	0.035
C2	5.04	0.013	99.98	0.021
C3	2.90	0.044	99.92	0.025
H11	23.49	0.086	99.20	0.110
H12	4.60	0.112	99.20	0.055
H13	35.85	0.088	99.40	0.151
H21	6.26	0.067	99.75	0.044
H31	1.80	0.061	99.75	0.027
H32	3.56	0.131	99.10	0.059
H33	12.00	0.082	99.31	0.070

Mean S12 99.64%

Table SP6 Comparison of mean square displacement matrices for models AAM vs AAMPD.

Atom	RMS_{eigvec}	R_{eigval}	S_{12}%	*FOM*
O1	5.13	0.020	99.94	0.024
O2	2.77	0.021	99.97	0.016
N1	8.06	0.026	99.96	0.036
C1	2.35	0.001	99.99	0.008
C2	4.79	0.020	99.98	0.023
C3	5.14	0.041	99.88	0.031
H11	18.11	0.073	99.47	0.086
H12	5.30	0.114	99.30	0.058
H13	19.67	0.076	99.49	0.092
H21	8.00	0.075	99.66	0.053
H31	2.42	0.070	99.54	0.033

H32	10.96	0.144	98.730	0.089
H33	4.72	0.061	99.24	0.039

Mean S12 99.627%

Table SP7 AAM Representative Distances of Bond Critical Points for Nuclei, density and Laplacian of Density at bcp and Eigenvalues of Hessian at bcp's

bond	d_1[a]	d_2[a]	$\rho(r_b)$[b]	$\nabla\rho(r_b)$[c]	λ_1[c]	λ_2[c]	λ_3[c]
C(1)-O(1)	0.4823	0.7645	2.89	-37.65	-28.57	-23.33	14.25
C(1)-O(2)	0.4871	0.7766	2.76	-35.53	-26.91	-22.43	13.8
C(2)-N(1)	0.6492	0.8381	1.7	-8.78	-12.04	-11.72	14.97
C(1)-C(2)	0.7573	0.7762	1.74	-11.86	-12.85	-11.54	12.53
C(3)-C(2)	0.7325	0.7923	1.67	-9.25	-11.09	-10.37	12.21

[a]In units of Å, [b]In units of e Å^{-3} [c]In units of e Å^{-5}.

Table SP8 AAMPD Representative Distances of Bond Critical Points for Nuclei, density and Laplacian of Density at bcp and Eigenvalues of Hessian at bcp's

bond	d_1[a]	d_2[a]	$\rho(r_b)$[b]	$\nabla\rho(r_b)$[c]	λ_1[c]	λ_2[c]	λ_3[c]
C(1) -O(1)	0.4762	0.7706	2.89	-37.5	-28.96	-22.95	14.4
C(1)-O(2)	0.4919	0.7722	2.77	-35.12	-26.81	-22.23	13.93
C(2)-N(1)	0.6568	0.8305	1.7	-8.47	-12.09	-11.8	15.42
C(1)-C(2)	0.7621	0.7716	1.78	-12.71	-13.31	-12.05	12.65
C(3)-C(2)	0.7363	0.7887	1.68	-9.98	-11.63	-10.47	12.12

[a]In units of Å, [b]In units of e Å^{-3} [c]In units of e Å^{-5}.

Table SP9 AAMΓ Representative Distances of Bond Critical Points for Nuclei, density and Laplacian of Density at bcp and Eigenvalues of Hessian at bcp's

bond	d_1[a]	d_2[a]	$\rho(r_b)$[b]	$\nabla\rho(r_b)$[c]	λ_1[c]	λ_2[c]	λ_3[c]
C(1)-O(1)	0.5003	0.7478	2.96	-36.16	-28.64	-23.6	16.07
C(1)-O(2)	0.5045	0.7598	2.82	-34.65	-26.53	-23.06	14.94
C(2)-N(1)	0.6714	0.8164	1.66	-6.85	-11.55	-11.22	15.92
C(1)-C(2)	0.7622	0.7712	1.75	-11.86	-12.77	-11.77	12.67
C(3)-C(2)	0.7313	0.7949	1.66	-9.43	-11.42	-10.23	12.22

[a]In units of Å, [b]In units of e Å^{-3} [c]In units of e Å^{-5}.

Table SP10 Mid-range frequencies of vibrations of L-alanine obtained from Periodic DFT (B3LYP-d*/6/-31G(d,p) calculations compared with experimental solid state Raman measurements (*13*). The first column gives the sequential number of the normal mode in the DFT calculation, the second to fourth columns shows the calculated frequencies of these modes at the k-points (0.5 0 0), (0 0.5 0) and (0 0 0.5) as used in the Normal Mode Refinements. The fifth column gives the experimental values. The assignment of experimental measurements to calculated frequencies is suggestive.

Mode number in calc.	KPOINT 0 0 1	KPOINT 0 1 0	KPOINT 1 0 0	RAMAN EXP
25- 26	218.4439	215.9248	208.9037	290
27- 28	220.4080	257.9759	222.3345	
29- 30	294.4044	274.3803	271.2210	264
31- 32	298.1618	290.9241	275.6435	
33- 34	330.1457	295.3677	293.6654	

35-	36	343.1729	298.1307	318.7140	
37-	38	350.9263	339.0380	327.0205	329
39-	40	359.3118	380.3005	381.8282	398
41-	42	410.1430	418.2455	424.0561	398
43-	44	413.2632	433.3609	430.8963	
45-	46	535.4561	542.7367	542.8731	480
47-	48	540.5782	548.0192	546.5821	
49-	50	590.7659	575.8682	578.2606	532
51-	52	591.7424	589.6167	583.3482	
53-	54	663.6111	659.9290	664.9738	653
55-	56	672.1981	669.2236	666.9681	
57-	58	774.3552	773.4334	771.3712	774
59-	60	776.2931	777.9070	778.7321	
61-	62	851.6051	859.4490	856.1485	852
63-	64	852.8603	861.8917	859.7368	
65-	66	926.6098	926.9985	932.5494	917
67-	68	932.0900	933.2461	937.7103	
69-	70	1035.9963	1040.7034	1040.6878	1010
71-	72	1041.0746	1043.7775	1041.8031	
73-	74	1049.8180	1048.7519	1048.2177	
75-	76	1051.8786	1053.4992	1053.3962	1025
77-	78	1135.6343	1133.0380	1133.2118	1114
79-	80	1139.2753	1137.4650	1136.0826	1146
81-	82	1191.1474	1188.7335	1188.0024	1239
83-	84	1194.6399	1199.3389	1198.7268	
85-	86	1282.6813	1284.3124	1287.2369	1306
87-	88	1285.4730	1286.0138	1288.2113	
89-	90	1346.0135	1347.8461	1351.2319	1359
91-	92	1356.0504	1353.3675	1351.9109	
93-	94	1408.0326	1403.9456	1405.5464	1410
95-	96	1417.9420	1407.8926	1408.9319	
97-	98	1428.0263	1426.7085	1426.5221	
99-	100	1430.3671	1430.6897	1430.2613	
101-	102	1458.1123	1454.6462	1457.9930	1460
103-	104	1469.0710	1462.6088	1465.8966	
105-	106	1512.6088	1507.7942	1508.6049	1502
107-	108	1514.3612	1521.8660	1516.7862	
109-	110	1533.3562	1524.2173	1520.6665	
111-	112	1535.4597	1540.2281	1539.3299	

113- 114	1569.3206	1577.3560	1578.0051	1598
115- 116	1576.4922	1598.5909	1596.1679	
117- 118	1649.4372	1668.7927	1669.0912	1622
119- 120	1668.7368	1675.9520	1676.9957	
121- 122	1712.2979	1683.5969	1685.4780	1650
123- 124	1725.3972	1695.5534	1704.9719	
125- 126	1734.1109	1736.8710	1734.9715	
127- 128	1739.0112	1737.5056	1735.4309	

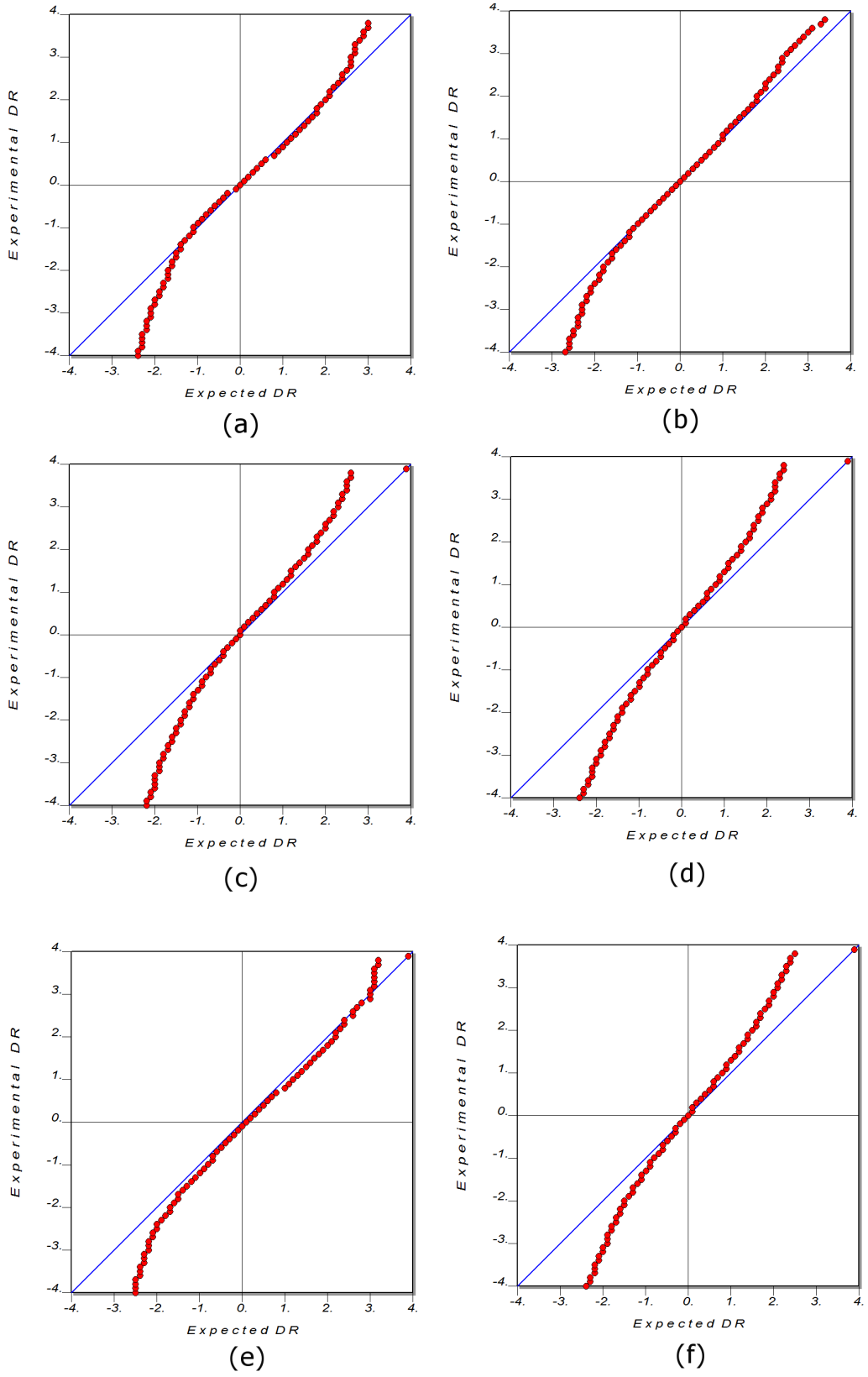

Figure SP1. Residual density normally probability plots of L-alanine 123K (a) standard spherical, (b) standard aspherical, (c),(d) spherical and aspherical NoMoRe Γ point, (e),(f) spherical and aspherical NoMoRe more points in the Brillouin zone

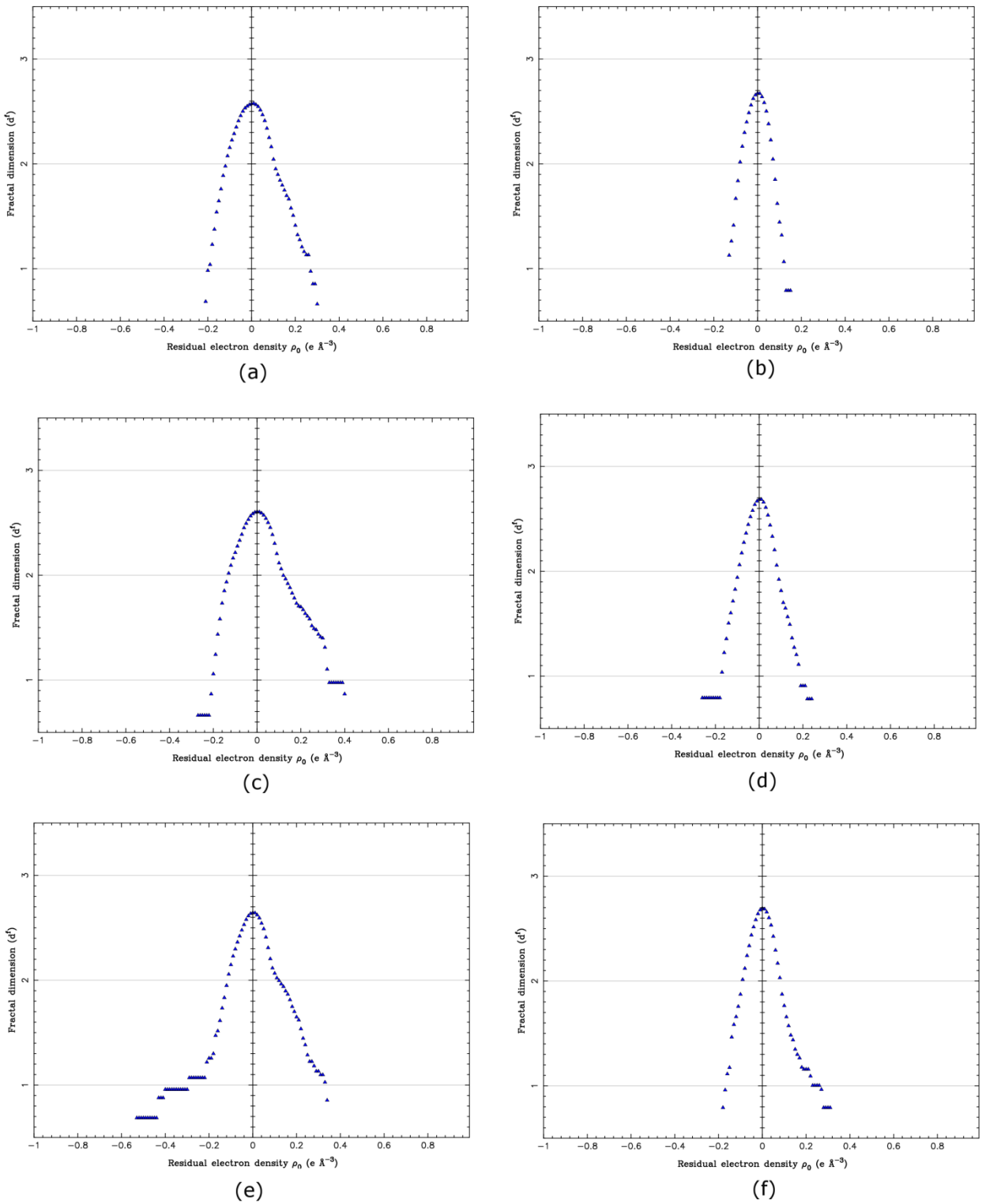

Figure SP2. Residual density fractal dimension plots of L-alanine 123K (a) standard spherical, (b) standard aspherical, (c),(d) spherical and aspherical NoMoRe Γ point, (e),(f) spherical and aspherical NoMoRe more points in the Brillouin zone

1. R. H. Blessing, An empirical correction for absorption anisotropy. *Acta Crystallogr., A, Found. Crystallogr.* **51 (Pt 1)**, 33–38 (1995).

2. G. M. Sheldrick, A short history of *SHELX*. *Acta Crystallographica Section A Foundations of Crystallography*. **64**, 112–122 (2008).

3. L. J. Farrugia, WinGX suite for small-molecule single-crystal crystallography. *J Appl Cryst*. **32**, 837–838 (1999).

4. R. Destro, R. E. Marsh, R. Bianchi, A low-temperature (23 K) study of L-alanine. *The Journal of Physical Chemistry*. **92**, 966–973 (1988).

5. N. K. Hansen, P. Coppens, Testing aspherical atom refinements on small-molecule data sets. *Acta Crystallographica Section A: Crystal Physics, Diffraction, Theoretical and General Crystallography*. **34**, 909–921 (1978).

6. T. Koritsanszky, S. Howard, Z. Su, P. R. Mallinson, T. Richter, N. K. Hansen, XD-A computer program package for multipole refinement and analysis of electron densities from diffraction data. *Free University of Berlin, Berlin, Germany* (1997).

7. A. Ø. Madsen, A. A. Hoser, *SHADE3* server: a streamlined approach to estimate H-atom anisotropic displacement parameters using periodic *ab initio* calculations or experimental information. *Journal of Applied Crystallography*. **47**, 2100–2104 (2014).

8. P. Coppens, Z. Su, P. J. Becker, in *International Tables for Crystallography Volume C: Mathematical, physical and chemical tables*, E. Prince, Ed. (Springer Netherlands, 2006; http://link.springer.com/referenceworkentry/10.1107/97809553602060000615), *International Tables for Crystallography*, pp. 713–734.

9. C. F. Bunge, J. A. Barrientos, A. V. Bunge, Roothaan-Hartree-Fock Ground-State Atomic Wave Functions: Slater-Type Orbital Expansions and Expectation Values for Z = 2-54. *Atomic Data and Nuclear Data Tables*. **53**, 113–162 (1993).

10. R. Dovesi, R. Orlando, B. Civalleri, C. Roetti, V. R. Saunders, C. M. Zicovich-Wilson, CRYSTAL: a computational tool for the ab initio study of the electronic properties of crystals. *Zeitschrift für Kristallographie-Crystalline Materials*. **220**, 571–573 (2005).

11. S. Grimme, Accurate description of van der Waals complexes by density functional theory including empirical corrections. *J. Comput. Chem.* **25**, 1463–1473 (2004).

12. B. Civalleri, C. M. Zicovich-Wilson, L. Valenzano, P. Ugliengo, B3LYP augmented with an empirical dispersion term (B3LYP-D*) as applied to molecular crystals. *CrystEngComm*. **10**, 405–410 (2008).

13. K. Machida, A. Kagayama, Y. Saito, T. Uno, Polarized Raman spectra and intermolecular potential of l-alanine crystal. *Spectrochimica Acta Part A: Molecular Spectroscopy*. **34**, 909–914 (1978).