STRUCTURAL SCIENCE
CRYSTAL ENGINEERING
MATERIALS

Volume 77 (2021)

Supporting information for article:

Accurate H-atom parameters for the two polymorphs of l-histidine at 5, 105 and 295 K

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Table S1 Crystal-structure determinations of amino acids collected at temperatures ≤ 20 K.

Amino acid	Space group	CCDC Refcode	Temperature (K)	Radiation	Crystal size (mm^3)
***L*-Asparagine monohydrate**	$P2_12_12_1$	ASPARM06	15	Neutron	2.6 × 2.8 × 1.4
		ASPARM08	20	X-ray	0.06 × 0.08 × 0.10
***DL*-Alanine**	$Pna2_1$	DLALNI04	19	X-ray	0.45 × 0.25 × 0.14
***DL*-Aspartic**	$C2/c$	DLASPA03	20	X-ray	0.31 × 0.40 × 0.52
		DLASPA13	20		
***DL*-Serine**	$P2_1/a$	DLSERN15	20	X-ray	0.5 × 0.45 × 0.35
		DLSERN31	20		
		DLSERN35	20		
***L*-serine monohydrate**		LSERMH21	12	X-ray	0.47 × 0.40 × 0.27
Glycine	$P2_1$ (β)	DOLBIR23	10	X-ray	0.30 × 0.30 × 0.05
	$P2_1/n$ (α)	DOLBIR30	18	Neutron	3.0 × 1.3 × 1.3
	$P3_1$ (γ)	DOLBIR35	10	X-ray	0.25 × 0.15 × 0.05
	$P3_1$ (γ)	DOLBIR39	10	X-ray	0.20 × 0.20 × 0.10
	$P2_1/n$ (α)	GLYCIN98	10	X-ray	0.20 × 0.20 × 0.10
***L*-threonine**	$P2_12_12_1$	LTHREO03	12	X-ray	0.58 × 0.36 × 0.33
		LTHREO04	19		

The CCDC search was performed for both neutron and X-ray sources, excluding structures with unresolved errors, structures whose atomic coordinates have not been determined, polymeric structures and ions.

Table S2 Collection strategy on XIPHOS I for each data set for the two polymorphs of the amino acid *L*-histidine, at 5, 105 and 295 K.

	Orientation	Runs	2θ	ω	χ	φ-range	$\Delta\varphi$
Orthorhombic form							
5 K	1	3	45°, 0°, –45°	25°, 0°, –25°	0°	–125° - 215°	0.5°
105 K	1	3	45°, 0°, –45°	25°, 0°, –25°	0°	–125° - 215°	0.5°
295 K	1	3	45°, 0°, –45°	25°, 0°, –25°	0°	–125° - 215°	0.5°
Monoclinic form							
5 K	1	3	35°, 0°, –35°	15°, 0°, –15°	0°	–125° - 215°	0.5°
	2	3	35°, 0°, –35°	15°, 0°, –15°	0°	–125° - 215°	0.5°
105 K	1	3	35°, 0°, –35°	15°, 0°, –15°	0°	–125° - 215°	0.5°
	2	3	35°, 0°, –35°	15°, 0°, –15°	0°	–125° - 215°	0.5°
295 K	1	3	35°, 0°, –35°	15°, 0°, –15°	0°	–125° - 215°	0.5°
	2	3	35°, 0°, –35°	15°, 0°, –15°	0°	–125° - 215°	0.5°

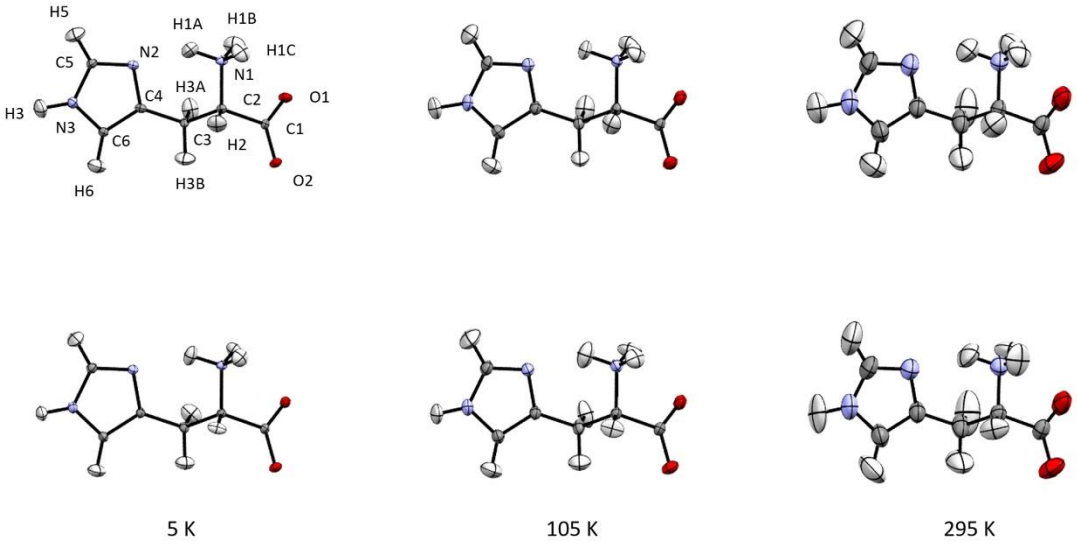


Figure S1 Molecular structures and anisotropic displacement parameters (70% probability surface) for the monoclinic polymorph of the amino acid *L*-histidine at 5 K, 105 K and 295 K. The top series was obtained from the neutron data, while the corresponding structures obtained from X-ray data and refined using HAR in *NoSpherA2* (M062X / x2c-TZVpp and cluster of neighbouring molecules, with a RIGU restraint of 0.004 and 0.003 Å^2 applied to the 105 K and 5 K structures, respectively) are shown in the bottom row.

Table S3 Crystallographic information for the IAM refinements of the two polymorphs of the amino acid *L*-histidine from X-ray data collections performed at 5, 105 and 295 K.

Temperature	**5 K**	**105 K**	**295 K**
Orthorhombic form			
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a, *b*, *c* (Å)	5.1498(2), 7.1902(2), 18.8503(6)	5.1521(10), 7.2228(2), 18.8440(6)	5.1690(3), 7.3430(5), 18.8317(13)
V (Å^3)	697.99(4)	701.23(3)	714.78(8)
Radiation type	Mo *K*α, λ = 0.7107 Å	Mo *K*α, λ = 0.7107 Å	Mo *K*α, λ = 0.7107 Å
Diffractometer	XIPHOS I	XIPHOS I	XIPHOS I
No. of measured, unique and observed [$I > 2\sigma(I)$] reflections	13 781, 2928, 2768	13 858, 2942, 2706	14 149, 3008, 2569
R_{int} / Completeness	0.0274 / 0.962	0.0303 / 0.964	0.0327/ 0.968
d_{min} (Å)	0.60	0.60	0.60
R_1 [$F_o > 4\sigma(F_o)$], wR_2 (F^2), *S*	0.0309, 0.0779, 1.081	0.0337, 0.0856, 1.082	0.0409, 0.1036, 1.078
Weighting scheme param.	*a* = 0.0481, *b* = 0.0464	*a* = 0.0532, *b* = 0.0116	*a* = 0.0571, *b* = 0.0365
No. of parameters	127	127	127
No. of restraints	0	0	0
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.451, –0.223	0.420, –0.220	0.320, –0.190
NPP *m*, *c*, r^2	0.959, 0.034, 0.996	1.004, 0.056, 0.996	0.979, 0.077, 0.997
Monoclinic form			
Space group	$P2_1$	$P2_1$	$P2_1$
a, *b*, *c* (Å)	5.1651(2), 7.2324(2), 9.4957(3)	5.1656(2), 7.2761(3), 9.4978(3)	5.1854(8), 7.3998(10), 9.4976(12)
β (°)	97.065(2)	97.316(3)	98.182(10)
V (Å^3)	352.03(2)	354.07(2)	360.72(9)
Radiation type	Mo *K*α, λ = 0.7107 Å	Mo *K*α, λ = 0.7107 Å	Mo *K*α, λ = 0.7107 Å
Diffractometer	XIPHOS I	XIPHOS I	XIPHOS I
No. of measured, unique and observed [$I > 2\sigma(I)$] reflections	11 140, 2138, 2087	11 215, 2148, 2032	11 388, 1806, 1683
R_{int} / Completeness	0.0254 / 0.997	0.0329 / 0.996	0.0240 / 0.869
d_{min} (Å)	0.70	0.70	0.70
R_1 [$F_o > 4\sigma(F_o)$], wR_2 (F^2), *S*	0.0288, 0.0727, 1.101	0.0324, 0.0807, 1.044	0.0346, 0.0876, 1.060
Weighting scheme param.	*a* = 0.0413, *b* = 0.0573	*a* = 0.0474, *b* = 0.0421	*a* = 0.0436, *b* = 0.0717
No. of parameters	127	127	127
No. of restraints	1	1	1
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.400, –0.180	0.370, –0.180	0.220, –0.160
NPP *m*, *c*, r^2	1.089, 0.054, 0.997	1.028, 0.048, 0.998	1.149, 0.062, 0.999

The refinement of the crystal structures at 295 K started from the ambient-conditions atomic coordinates of the structural models obtained by Novelli and colleagues (Novelli, *et al.*, 2020). Otherwise, refinements started from the atomic coordinates of the preceding temperature point.

Table S4 Results of HARs of the two polymorphs of *L*-histidine at 105 K and 295 K.

Method - Cluster	R_1	wR_2 (F^2)	*S*	$\Delta\rho_{min/max}$	**n. p. d. ADPs**	**Time (min)**

				(e Å^{-3})		
Orthorhombic form 105 K						
M062X / x2c-TZVpp-✓	0.0226	0.0371	1.114	–0.143 / 0.170	H1C, H3	136
***RIGU** 0.005*	*0.0226*	*0.0374*	*1.100*	*–0.151 / 0.167*		
***RIGU** 0.004*	*0.0226*	*0.0375*	*1.103*	*–0.151 / 0.167*		
***RIGU** 0.003*	*0.0227*	*0.0377*	*1.108*	*–0.151 / 0.167*		
***RIGU** 0.002*	*0.0228*	*0.0388*	*1.103*	*–0.153 / 0.168*		
Monoclinic form 105 K						
M062X / x2c-TZVpp-✓	0.0217	0.0311	1.172	–0.118 / 0.147	H1B, H2	106
***RIGU** 0.005*	0.0218	0.0314	1.151	*–0.119 / 0.148*		
***RIGU** 0.004*	0.0218	0.0315	1.155	*–0.119 / 0.148*		
***RIGU** 0.003*	0.0219	0.0317	1.161	*–0.120 / 0.148*		
***RIGU** 0.002*	0.0221	0.0321	1.173	*–0.120 / 0.148*		
Orthorhombic form 295 K						
M062X / x2c-TZVpp-✓	0.0287	0.0539	1.114	–0.170 / 0.164		113
***RIGU** 0.005*	*0.0289*	*0.0543*	*1.104*	*–0.163 / 0.162*		
***RIGU** 0.004*	*0.0290*	*0.0576*	*1.071*	*–0.162 / 0.163*		
***RIGU** 0.003*	*0.0291*	*0.0579*	*1.078*	*–0.163 / 0.163*		
***RIGU** 0.002*	*0.0294*	*0.0585*	*1.091*	*–0.163 / 0.164*		
Monoclinic form 295 K						
M062X / x2c-TZVpp-✓	0.0247	0.0486	1.349	–0.098 / 0.104		96
***RIGU** 0.005*	*0.0252*	*0.0515*	*1.289*	*–0.099 / 0.112*		
***RIGU** 0.004*	*0.0254*	*0.0528*	*1.280*	*–0.097 / 0.116*		
***RIGU** 0.003*	*0.0256*	*0.0540*	*1.277*	*–0.099 / 0.117*		
***RIGU** 0.002*	*0.0261*	*0.0560*	*1.276*	*–0.103 / 0.117*		

Table S5 Interactions in the first molecular coordination sphere of the polymorphs of the amino acid *L*-histidine, at 295 K. All energies are in kJ mol^{-1}. Calculations were performed on the experimental neutron structures. The symmetry operators relate the central molecule to the other molecules in the first coordination sphere, for a total of 12 intermolecular contacts. H-atom-to-acceptor distances are reported, for each contact, in Ångstrom.

Label	Symmetry	T (K)	Centroid Distance (Å)	Pixel Coulombic	Pixel Polarisation	Pixel Dispersion	Pixel Repulsion	Pixel Total	Intermolecular Contact, direction (Å)
Orthorhombic form									
H-bonds									
A / A′	3/2 – *x*, 1 – *y*, – 1/2 + *z* 3/2 – *x*, 1 – *y*, 1/2 + *z*	295	9.436	–104.3	–33.4	–11.9	53.8	–95.7	N3–H3···O1^{i} = 1.745(8), along **c**
B / B′	– 1 + *x*, *y*, *z* 1 + *x*, *y*, *z*	295	5.169	–16.2	–30.3	–24.5	39.2	–31.8	N1–H1B···O2^{ii} = 1.883(7), along **a**
C / C′	1 – *x*, – 1/2 + *y*, 1/2 – *z* 1 – *x*, 1/2 + *y*, 1/2 – *z*	295	7.092	–116.4	–41.6	–20	50.5	–127.5	N1–H1C···O2^{iii} = 1.788(7), along **b**
Electrostatic Interactions									
D / D′	2 – *x*, – 1/2 + *y*, 1/2 – *z* 2 – *x*, 1/2 + *y*, 1/2 – *z*	295	6.79	–44	–12.9	–11.5	8.6	–59.8	N1H1X···O1 (X = A, B, C) = 2.504 - 3.093
E / E′	1/2 + *x*, 3/2 – *y*, 1– *z* – 1/2 + *x*, 3/2 – *y*, 1– *z*	295	6.394	–15.8	–6	–17.5	13.4	–25.9	C6H6···ring = 2.712
F / F′	– 1/2 + *x*, 1/2 – *y*, 1– *z* 1/2 + *x*, 1/2 – *y*, 1– *z*	295	5.838	21	–6.4	–21.5	11.7	4.8	NH_3^+···NH_3^+ = 7.660, NH_3^+···ring = 5.044
Monoclinic form									
H-bonds									
A / A′	*x*, *y*, – 1 + *z* *x*, *y*, 1 + *z*	295	9.498	–97.8	–33.2	–12.1	53	–90.1	N3–H3···O1^{i} = 1.756(5), along **c**
B / B′	– 1 + *x*, *y*, *z* 1 + *x*, *y*, *z*	295	5.185	–21.5	–31.6	–23.8	42.5	–34.4	N1–H1B···O2^{ii} = 1.846(5), along **a**
C / C′	2 – *x*, 1/2 + *y*, 2 – *z* 2 – *x*, – 1/2 + *y*, 2 – *z*	295	7.143	–118.8	–43.6	–19.9	55.1	–127.2	N1–H1C···O2^{iii} = 1.764(5), along **b**
Electrostatic interactions									
D / D′	1 – *x*, – 1/2 + *y*, 2 – *z* 1 – *x*, 1/2 + *y*, 2 – *z*	295	6.881	–41.5	–11.3	–9.8	5.9	–56.8	N1H1X···O1 (X = A, B, C) = 2.598 - 3.138
E / E′	1 – *x*, 1/2 + *y*, 1 – *z* 1 – *x*, – 1/2 + *y*, 1 – *z*	295	5.712	–6.3	–7.2	–22.5	12.5	–23.5	C6H6···ring = 2.667

F / **F**′	2 − *x*, − 1/2 + *y*, 1 − *z* 2 − *x*, 1/2 + *y*, 1 − *z*	295	6.555	8.8	−5.5	−16.8	12.9	−0.6	$NH_3^+\cdots NH_3^+$ = 8.329, $NH_3^+\cdots$ring = 5.095

Table S6 Comparison of element-element and element-H bond lengths (in Å) obtained from the X-ray HAR and neutron refinements for the orthorhombic polymorph of *L*-histidine, at all temperatures.

	5 K			105 K			295 K		
Bond	**Neutron**	**HAR**	**Δ_σ**	**Neutron**	**HAR**	**Δ_σ**	**Neutron**	**HAR**	**Δ_σ**
O1-C1	1.254(3)	1.2550(5)	0	1.247(3)	1.2536(6)	2	1.238(4)	1.2453(8)	2
O2-C1	1.256(2)	1.2585(5)	1	1.257(3)	1.2561(6)	0	1.251(4)	1.2514(7)	0
N1-C2	1.4953(19)	1.4927(6)	1	1.4964(19)	1.4911(7)	3	1.497(2)	1.4892(8)	4
N2-C4	1.3917(18)	1.3910(5)	0	1.3865(19)	1.3891(7)	1	1.382(3)	1.3839(9)	1
N2-C5	1.330(2)	1.3250(7)	2	1.331(3)	1.3252(8)	2	1.325(4)	1.3219(9)	1
N3-C5	1.353(2)	1.3525(6)	0	1.349(2)	1.3514(7)	1	1.346(3)	1.3452(10)	0
N3-C6	1.378(2)	1.3782(6)	0	1.376(3)	1.3784(7)	1	1.379(3)	1.3758(10)	1
C1-C2	1.542(2)	1.5396(5)	1	1.544(3)	1.5398(8)	1	1.542(3)	1.5404(8)	1
C2-C3	1.543(2)	1.5411(7)	1	1.544(2)	1.5386(8)	3	1.532(3)	1.5370(10)	2
C3-C4	1.502(3)	1.5003(5)	1	1.502(3)	1.5001(8)	1	1.500(4)	1.4984(10)	0
C4-C6	1.376(3)	1.3756(5)	0	1.377(3)	1.3737(8)	1	1.374(4)	1.3698(10)	1
N1-H1A	1.042(4)	1.018(9)	2	1.046(6)	1.014(9)	3	1.037(6)	1.007(11)	2
N1-H1B	1.042(4)	1.012(8)	3	1.030(5)	0.997(9)	3	1.005(7)	1.008(11)	0
N1-H1C	1.039(4)	1.009(9)	3	1.037(4)	1.013(10)	2	1.041(6)	1.002(11)	3
N3-H3	1.054(4)	1.018(8)	4	1.059(4)	1.015(9)	4	1.044(8)	1.006(13)	2
C2-H2	1.110(4)	1.087(7)	3	1.100(4)	1.082(8)	2	1.101(6)	1.073(10)	2
C3-H3A	1.105(4)	1.097(8)	1	1.093(5)	1.089(9)	0	1.091(8)	1.062(14)	2
C3-H3B	1.096(4)	1.052(8)	5	1.091(5)	1.050(9)	4	1.081(7)	1.067(11)	1
C5-H5	1.082(4)	1.061(7)	3	1.088(5)	1.062(8)	3	1.086(8)	1.049(11)	3
C6-H6	1.085(4)	1.065(7)	2	1.071(5)	1.068(8)	0	1.084(7)	1.053(11)	2

The neutron bond length are compared with the unrestrained HAR performed with M062X / x2c-TZVpp and a cluster of molecules surrounding the asymmetric unit. Δ_σ is the difference between the neutron and HAR distances in units of the larger σ

Table S7 Comparison of element-element and element-H bond lengths (in Å) obtained from the X-ray HAR and neutron refinements for the monoclinic polymorph of *L*-histidine, at all temperatures.

	5 K			105 K			295 K		
Bond	**Neutron**	**HAR**	**Δ_σ**	**Neutron**	**HAR**	**Δ_σ**	**Neutron**	**HAR**	**Δ_σ**
O1-C1	1.255(3)	1.2531(6)	1	1.251(3)	1.2505(7)	0	1.244(3)	1.2461(12)	1
O2-C1	1.258(2)	1.2610(7)	1	1.259(3)	1.2595(8)	0	1.249(3)	1.2530(14)	1
N1-C2	1.4970(19)	1.4932(8)	2	1.492(2)	1.4903(9)	1	1.4899(19)	1.4895(15)	0
N2-C4	1.3891(19)	1.3898(7)	0	1.388(2)	1.3877(9)	0	1.384(2)	1.3835(15)	0
N2-C5	1.329(2)	1.3261(6)	1	1.329(3)	1.3271(7)	1	1.331(2)	1.3226(12)	4
N3-C5	1.351(2)	1.3534(7)	1	1.355(2)	1.3519(9)	1	1.344(3)	1.3456(17)	0
N3-C6	1.378(2)	1.3793(7)	1	1.377(2)	1.3778(9)	0	1.379(3)	1.3758(16)	1
C1-C2	1.542(3)	1.5416(7)	0	1.542(3)	1.5435(8)	0	1.544(3)	1.5432(13)	0
C2-C3	1.537(2)	1.5419(8)	2	1.543(3)	1.5408(10)	1	1.538(3)	1.5366(14)	0
C3-C4	1.503(3)	1.5019(7)	0	1.498(3)	1.5027(8)	2	1.500(3)	1.5025(14)	1
C4-C6	1.382(3)	1.3773(7)	2	1.381(3)	1.3762(8)	2	1.374(3)	1.3695(14)	1
N1-H1A	1.046(5)	1.011(9)	3	1.050(5)	1.019(10)	3	1.044(5)	1.018(16)	2
N1-H1B	1.047(4)	1.009(8)	4	1.046(5)	1.015(10)	3	1.030(5)	0.987(16)	3
N1-H1C	1.056(4)	1.017(9)	4	1.049(5)	0.997(11)	4	1.046(5)	0.991(15)	3
N3-H3	1.045(5)	1.002(7)	5	1.055(6)	0.996(8)	6	1.038(5)	1.009(14)	2
C2-H2	1.103(4)	1.088(7)	2	1.102(5)	1.090(8)	1	1.096(4)	1.098(12)	0
C3-H3A	1.098(5)	1.088(8)	1	1.110(6)	1.098(9)	1	1.102(6)	1.086(18)	1
C3-H3B	1.103(4)	1.091(8)	1	1.094(6)	1.088(10)	1	1.098(7)	1.09(2)	0
C5-H5	1.080(5)	1.072(8)	1	1.079(5)	1.087(10)	1	1.086(6)	1.10(2)	1
C6-H6	1.081(5)	1.076(9)	0	1.076(5)	1.069(9)	1	1.077(6)	1.078(18)	0

The neutron bond length are compared with the unrestrained HAR performed with M062X / x2c-TZVpp and a cluster of molecules surrounding the asymmetric unit. Δ_σ is the difference between the neutron and HAR distances in units of the larger σ

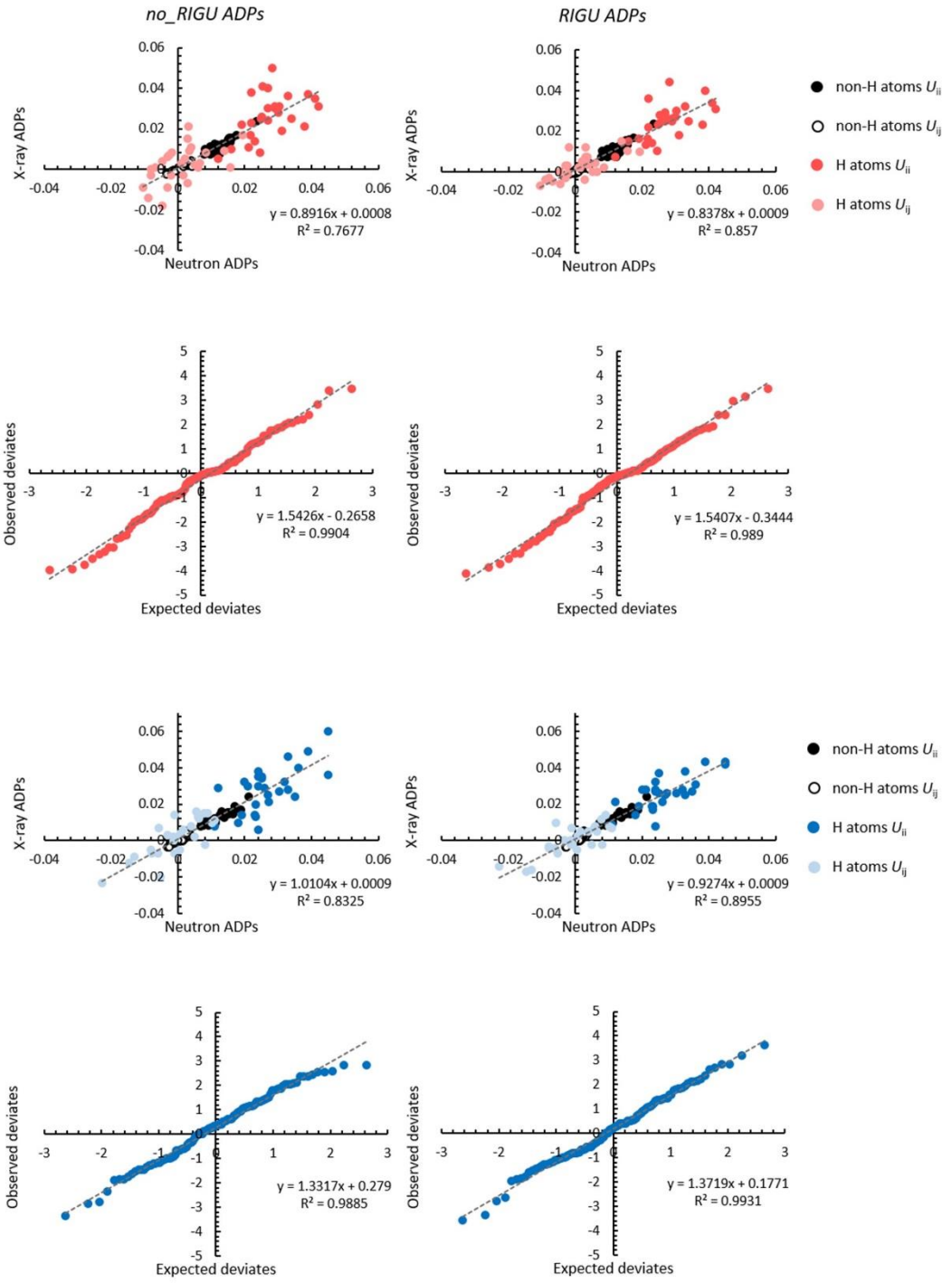
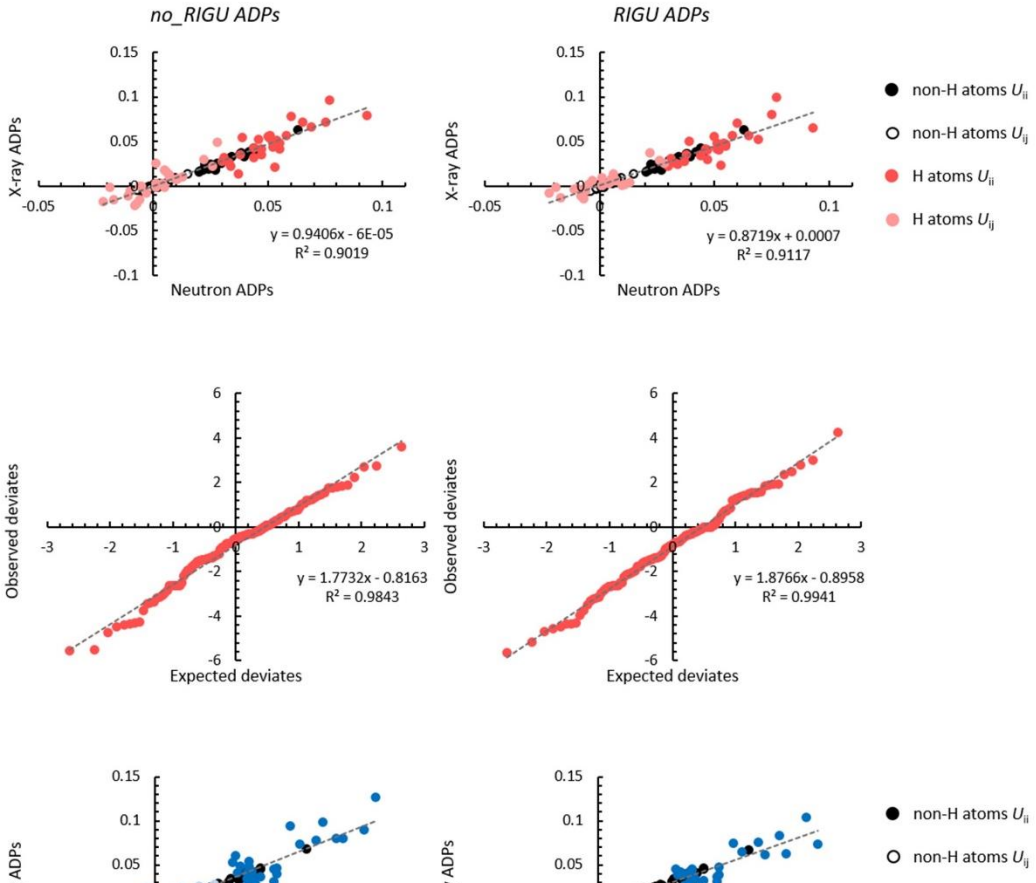


Figure S3 Direct comparison and normal probability plots of the neutron and X-ray ADPs for the orthorhombic (red) and monoclinic (blue) polymorphs of the amino acid *L*-histidine at 105 K. The X-ray model corresponds to unrestrained M062X/x2c-TZVpp/cluster HAR setting. The left side represents unrestrained models, while the right side shows the results for the application of the RIGU restraint equal to 0.004 Å^2. In the direct comparison of equivalent parameters, the three diagonal U_{ii}


no_RIGU ADPs
RIGU ADPs
X-ray ADPs
Neutron ADPs
y = 0.9406x - 6E-05
R² = 0.9019
y = 0.8719x + 0.0007
R² = 0.9117
non-H atoms U_{ii}
non-H atoms U_{ij}
H atoms U_{ii}
H atoms U_{ij}
Observed deviates
Expected deviates
y = 1.7732x - 0.8163
R² = 0.9843
y = 1.8766x - 0.8958
R² = 0.9941