

Supplementary Material

TAAM: A reliable and user friendly tool for hydrogen atom location using routine X-Ray diffraction data

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Table S1: Information on the compounds used for TAAM refinement

S. No.	Chemical formula (common name)	Original REFCODE [reference]	CCDC no. of new deposition	max. $\sin(\theta)/\lambda$ [Å ⁻¹]	R(F) [%] - TAAM			
					iso max	iso 0.8 Å	anis max	anis 0.8 Å
1	C ₂ H ₅ N ₃ OS	SOJNAG03 ¹	1961930-33	1.08	1.87	1.14	1.86	1.11
2	C ₈ H ₈ NO ₂ (1-nitroindoline)	QIJDAO01 ²	1961934-37	1.32	2.49	1.67	2.47	1.56
3	C ₆ H ₃ N ₅ O ₆	OMIWIQ01 ³	-	1.15	-	-	-	-
4	C ₆ H ₈ O ₂	SEFSIF11 ⁴	1961938-41	1.52	2.50	1.75	2.45	1.77
5	C ₅ H ₉ N ₄ O ₃ P + H ₂ O	MOBYIL ⁵	1961942-45	1.09	3.54	1.34	3.52	1.31
6	C ₉ H ₆ OS (2-thiocoumarin)	CABYAG01 ⁶	1961946-49	1.08	2.65	2.00	2.65	1.96
7	C ₄ H ₃ N ₃ O	NEDXID ⁷	1961950-53	0.91	2.68	1.80	2.65	1.76
8	CH ₆ NO ₃ P (aminomethylphosphonic acid)	AMEPOS01 ⁸	1961954-57	1.37	1.92		1.91	1.12
9	C ₆ H ₆ (benzene)	N/A ⁹	-	1.11	-	-	-	-
10	C ₂ H ₂ N ₄ O ₃	QOYJOD ¹⁰	1961958-61	1.23	3.15	1.47	3.15	1.46
11	C ₁₆ H ₁₁ NO ₃	UKODEE ¹¹	1961962-65	1.11	3.16	2.05	3.10	1.95
12	C ₁₇ H ₁₈ FN ₃ O ₃ + 6H ₂ O (ciprofloxacin)	COVPIN05 ¹²	1961966-69	1.16	2.16	1.26	2.14	1.21
13	C ₈ H ₆ N ₁₂ O ₁₂ (CL-20)	PUBMUU22 ¹³	1961970-73	1.11	3.03	2.03	3.03	2.03
14	C ₁₆ H ₁₇ NO ₂ (coumarin 102)	VEGMAV03 ¹⁴	1961974-77	1.10	2.30	1.39	2.25	1.29
15	C ₂₂ H ₃₆ N ₆ O ₇ (PRO-PRO-ALA-ALA-ALA-ALA-)	CAMVES ¹⁵	1961978-81	1.32	2.73		2.71	1.65
16	C ₈ H ₁₆ N ₂ O ₃ S (ALA-MET)	ALAMET01 ¹⁶	1961982-85	1.00	2.64	1.26	2.59	1.15
17	C ₄ H ₇ NO ₄ (DL-ASP)	DLASPA03 ¹⁷	-	1.37	-	-	-	-
18	C ₃ H ₇ NO ₃ (DL-SER)	DLSERN15 ¹⁸	1961986-89	1.18	1.95	1.48	1.93	1.45
19	C ₉ H ₁₄ N ₂ O ₂ S*	FEDROW01 ¹⁹	1961990-91	1.16	1.74	2.56	-	-
20	C ₃₃ H ₂₃ NO	WUFJOW01 ²⁰	1961992-95	1.08	2.49	1.15	2.45	1.04
21	C ₂ H ₄ N ₄ O ₄ (FOX-7)	SEDTUQ09 ¹³	1961996-99	1.11	2.49	1.95	2.64	1.38
22	C ₆ H ₁₀ N ₂ O ₅ + 2H ₂ O (GLY-ASP)	BEVXEFO1 ²¹	1962000-3	1.20	2.73	1.42	2.67	1.33
23	C ₅ H ₁₀ N ₂ O ₃ (GLY-ALA)	GLYALB05 ²²	1962004-7	0.77	1.63	1.35	1.58	1.31
24	C ₅ H ₁₀ N ₂ O ₃ (GLY-ALA)	GLYALB06 ²²	1962008-11	0.76	1.75	1.32	1.73	1.25
25	C ₅ H ₁₀ N ₂ O ₃ (GLY-ALA)	GLYALB07 ²²	1962012-15	0.76	1.76	1.52	1.71	1.44
26	C ₆ H ₁₂ N ₂ O ₄ + 2H ₂ O (GLY-THR)	GLYTRE03 ²³	1962016-19	1.15	2.73	1.36	2.69	1.28
27	C ₈ H ₁₈ N ₂ O ₄ S (HEPES)*	WIRMOZ03 ²⁴	1962020-23	1.16	2.72	1.49	2.70	1.43
28	C ₁₄ H ₁₁ NO ₂	ZZZAWJ13 ²⁵	1962024-27	1.22	2.69	1.75	2.64	1.66
29	C ₁₃ H ₁₀ N ₂ O ₂	ODIBUA ²⁵	1962028-31	1.22	2.16	1.18	2.16	1.07

30	C ₁₉ H ₁₄ N ₂ O ₂	ODICAH ²⁵	1962032-35	1.22	2.09	1.55	2.03	1.49
31	C ₈ H ₁₅ N ₃ O ₄ + H ₂ O (ALA-GLY-ALA)	TAPYEP ²⁶	1962036-39	1.25	1.54	1.41	1.46	1.31
32	C ₁₂ H ₁₉ N ₅ O ₄ + C ₃ H ₈ O + H ₂ O (ALA-HIS-ALA)	DUCMAQ ²⁷	1962040-42, 1962299	1.16	2.48	1.13	2.38	1.06
33	C ₁₅ H ₂₁ N ₃ O ₄ + C ₃ H ₇ NO (ALA-PHE-ALA)	DUCMEU ²⁷	1962043-46	1.16	2.59	1.14	2.50	0.88
34	C ₁₁ H ₁₉ N ₃ O ₄ + H ₂ O (ALA-PRO-ALA)	SILTUD ²⁸	1962047-50	1.36	2.61	0.86	2.58	0.78
35	C ₁₅ H ₂₁ N ₃ O ₅ + C ₂ H ₆ O (ALA-TYR-ALA)	KELYOQ ²⁹	1962051-54	1.11	1.75	1.36	1.73	1.29
36	C ₁₅ H ₂₁ N ₃ O ₅ + 2H ₂ O + 0.634H ₂ O (ALA-TYR-ALA)*	KELYIK ²⁹	1962055-58	1.24	3.27	1.14	3.25	1.06
37	C ₃ H ₇ NO ₂ (L-ALA)	LALNIN03 ³⁰	1962059-62	1.08	1.92	1.01	1.90	0.96
38	C ₄ H ₉ NO ₃ (L-homoserine)	BUHGOA01 ³¹	1962063-66	1.19	2.59	1.59	2.56	1.52
39	C ₆ H ₁₅ N ₂ O ₃ + Cl (L-hydroxylysine)	ROLCOL ³²	1962067-69	1.35	3.29	1.53	-	1.45
40	C ₆ H ₁₆ N ₂ O ₃ + 2Cl (L-hydroxylysine)	ROLCUR ³²	1962070-73	1.00	2.48	1.65	2.46	1.59
41	C ₆ H ₁₆ N ₂ O ₃ + H ₂ O + 2Cl (L-hydroxylysine)	ROLDAY ³²	1962074-77	1.11	2.15	2.15	1.72	1.66
42	C ₅ H ₁₃ N ₂ O ₂ + Cl (L-ornithine)*	ORNHCL12 ³³	1962078-81	1.12	1.39	0.72	1.38	0.65
43	C ₄ H ₉ NO ₃ (L-THR)	LTHREO03 ³⁴	-	1.35	-	-	-	-
44	C ₁₁ H ₁₂ N ₂ O ₂ + CH ₂ O ₂ (L-TRP)	MUGKAA01 ³⁵	1962086-89	1.38	2.55	2.08	2.53	2.01
45	C ₁₇ H ₁₉ NO ₃ + H ₂ O (morphine)	MORPHM01 ³⁶	1962090-93	1.15	2.31	1.47	2.30	1.48
46	C ₄ H ₄ N ₂ OS (2-thiouracil)	TURCIL02 ³⁷	1962094-97	1.10	1.73	1.31	1.71	1.28
47	C ₄ H ₅ N ₃ O + H ₂ O (cytosine)	CYTOSM12 ³⁷	1962098-101	1.08	2.27	1.66	2.25	1.57
48	C ₇ H ₆ O ₃ (salicylic acid)	SALIAC16 ³⁷	1962102-5	1.08	2.40	1.84	2.39	1.83
49	C ₇ H ₁₁ NO ₄ + H ₂ O (N-acetyl-L-hydroxyproline)	POKKAD05 ³⁸	1962106-9	1.13	2.49	1.10	2.46	1.03
50	C ₇ H ₁₁ NO ₄ + H ₂ O (N-acetyl-L-hydroxyproline)	POKKAD06 ³⁸	1962110-13	1.00	2.65	1.35	2.63	1.31
51	C ₇ H ₁₁ NO ₄ + H ₂ O (N-acetyl-L-hydroxyproline)	POKKAD07 ³⁸	1962114-17	1.00	2.50	1.31	2.47	1.26
52	C ₇ H ₁₁ NO ₄ + H ₂ O (N-acetyl-L-hydroxyproline)	POKKAD08 ³⁸	1962118-21	1.00	2.70	1.22	2.67	1.15
53	C ₇ H ₁₁ NO ₄ + H ₂ O (N-acetyl-L-hydroxyproline)	POKKAD09 ³⁸	1962122-25	1.02	3.00	1.03	2.96	0.92
54	C ₁₃ H ₁₇ NO ₄ + H ₂ O (N-Acetyl-L-TYR ethyl ester)	ATYREE02 ³⁹	1962126-29	1.09	2.72	1.24	2.61	1.01
55	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH53 ⁴⁰	1962130-33	1.18	1.85	1.21	1.79	1.2
56	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH43 ⁴⁰	1962134-37	1.00	2.37	1.29	2.35	1.23
57	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH42 ⁴⁰	1962138-39,43,44	1.03	1.68	1.61	1.32	1.23
58	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH41 ⁴⁰	1962145-48	1.17	1.89	1.23	1.85	1.16
59	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH40 ⁴⁰	1962149-52	1.13	2.05	1.72	2.01	1.67
60	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH52 ⁴⁰	1962153-56	1.16	1.79	1.61	1.75	1.56
61	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH50 ⁴⁰	1962157-60	1.15	2.05	1.38	2.01	1.31
62	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH49 ⁴⁰	1962161-64	1.15	2.23	1.78	2.20	1.76
63	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH48 ⁴⁰	1962165-68	1.17	2.07	1.50	2.03	1.41
64	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH46 ⁴⁰	1962169-72	1.15	1.48	1.38	1.45	1.32
65	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH45 ⁴⁰	1962173-76	1.20	1.61	1.43	1.57	1.39
66	C ₂ H ₂ O ₄ + 2H ₂ O	OXACDH44 ⁴⁰	1962177-80	1.20	1.79	1.44	1.75	1.39
67	C ₁₀ H ₁₀ N ₄ O ₂	LIXDAY01 ⁴¹	1962181-84	1.10	3.41	1.48	3.36	1.34
68	C ₁₀ H ₁₀ N ₄ O ₂	LIXDAY02 ⁴²	1962185-88	1.10	3.37	1.58	3.35	1.52
69	C ₁₀ H ₁₀ N ₄ O ₂	LIXDAY03 ⁴²	1962189-92	0.88	2.71	1.95	2.68	1.89

70	$C_{10}H_{10}N_4O_2$	LIXDAY04 ⁴²	1962193-96	1.20	3.22	2.03	3.19	1.92
71	$C_5H_{12}O_4$ (pentaerythritol)	PERYTO12 ⁴³	1962197-200	1.32	1.47	1.11	1.46	1.06
72	$C_9H_{12}NO_2 + C_4H_3O_4$ (L-PHE-ALA hydrogen maleate)	EDAXIQ03 ⁴⁴	-	1.10	-	-	-	-
73	$C_3H_6N_6O_6$ (RDX)	CTMTNA10 ⁴⁵	1962201-4	1.29	2.19	1.70	2.19	1.7
74	$C_3H_6N_6O_6$ (RDX)	CTMTNA11 ⁴⁵	1962205-8	1.32	2.75	1.77	2.75	1.75
75	$C_{41}H_{76}N_2O_{15} + 0.88H_2O$ (roxithromycin)*	KAHWAT ⁴⁶	1962209-12	1.11	2.30	1.15	2.17	0.99
76	$C_3H_7NO_2$ (sarcosine)	YIHHON ⁴⁷	1962213-16	1.19	1.82	0.87	1.77	0.75
77	$C_{12}H_{22}O_{11}$ (sucrose)	SUCROS14 ⁴⁸	-	1.15	-	-	-	-
78	$C_{10}H_{14}N_2O_5$ (thymidine)	THYDINO4 ⁴⁹	1962217-20	1.10	1.90	1.24	1.76	1.19
79	$C_{13}H_{17}N_3O_5 + H_2O$ (TYR-GLY-GLY)	LTYRGG01 ²¹	1962221-24	1.15	3.56	1.19	3.55	1.13
80	CH_4N_2O (urea)	UREAXX25 ⁵⁰	1962225-28	1.44	1.79	1.31	1.71	1.08
81	$C_5H_{12}O_5$ (xylitol)	XYLTOL03 ⁵¹	1962229-32	1.22	2.25	1.00	1.70	0.91

* weakest reflections (outliers) were omitted (similar to HAR).

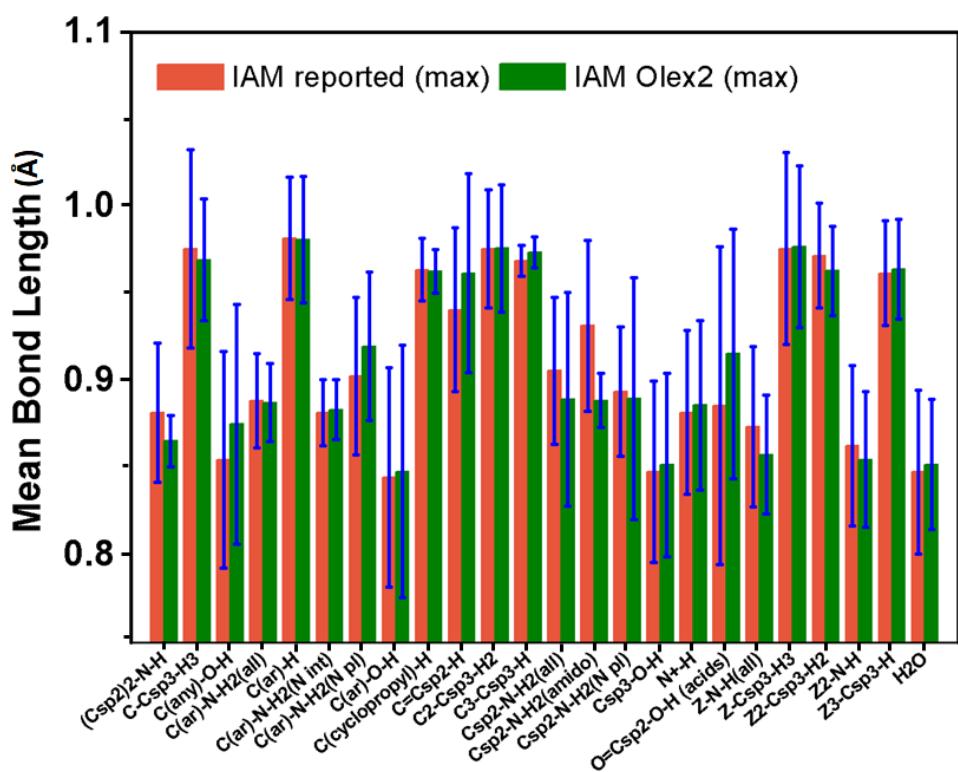


Figure S1: Comparison of IAM results for different Bond types (Bruno & Allen) obtained using (shelxl) and olex2.refine with their respective sample standard deviations (SSDs).

Table S2: 24 Bond types (Bruno & Allen) and water with neutron, X-ray IAM and TAAM average bond lengths including resolution cutoffs and isotropic/anisotropic treatment of hydrogen atom displacements. *MD :- difference between means of X-ray and neutron results *SSDs:- Sample standard deviations

1 $(Csp^2)_2-N-H$	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
			Iso	Aniso	Iso	Aniso		
	no. of observations	43	14	13	14	13	14	14
	mean bond length [Å]	1.030	1.005	1.004	1.009	1.006	0.864	0.882
	population standard deviation [Å]	0.013	0.026	0.015	0.017	0.014	0.018	0.041
	SSDs[Å]	0.013	0.027	0.016	0.017	0.015	0.019	0.043
	standard deviation of the mean [Å]	0.002	0.007	0.004	0.005	0.004	0.005	0.011
	MD [Å]		-0.025	-0.026	-0.021	-0.024	-0.166	-0.148

2 $C-Csp^3-H_3$	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
			Iso	Aniso	Iso	Aniso		
	no. of observations	827	131	125	131	125	131	131
	mean bond length [Å]	1.077	1.076	1.072	1.074	1.073	0.969	0.977
	population standard deviation [Å]	0.029	0.038	0.025	0.033	0.022	0.034	0.036
	SSDs[Å]	0.029	0.038	0.025	0.033	0.022	0.035	0.036
	standard deviation of the mean [Å]	0.001	0.003	0.002	0.003	0.002	0.003	0.003
	MD [Å]		-0.001	-0.005	-0.003	-0.004	-0.108	-0.100

3 $C(\text{any})-O-H$	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
			Iso	Aniso	Iso	Aniso		
	no. of observations	230	43	43	43	43	43	43
	mean bond length [Å]	0.980	0.945	0.943	0.974	0.973	0.871	0.878
	population standard deviation [Å]	0.021	0.044	0.048	0.053	0.053	0.068	0.054
	SSDs[Å]	0.021	0.045	0.048	0.054	0.053	0.068	0.054
	standard deviation of the mean [Å]	0.001	0.006	0.006	0.007	0.007	0.009	0.007
	MD [Å]		-0.035	-0.037	-0.006	-0.007	-0.109	-0.102

4 $C(ar)-N-H_2(\text{all})$	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
			Iso	Aniso	Iso	Aniso		
	no. of observations	30	6	6	6	6	6	6
	mean bond length [Å]	1.011	0.976	0.973	0.978	0.979	0.888	0.887
	population standard deviation [Å]	0.013	0.011	0.025	0.011	0.012	0.022	0.016
	SSDs[Å]	0.013	0.011	0.025	0.011	0.013	0.022	0.016
	standard deviation of the mean [Å]	0.002	0.003	0.006	0.003	0.003	0.005	0.004
	MD [Å]		-0.035	-0.038	-0.033	-0.032	-0.123	-0.124

5 $C(ar)-H$	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
			Iso	Aniso	Iso	Aniso		
	no. of observations	721	128	128	128	128	128	128
	mean bond length [Å]	1.083	1.074	1.075	1.071	1.074	0.980	0.971
	population standard deviation [Å]	0.017	0.023	0.022	0.018	0.017	0.036	0.022
	SSDs[Å]	0.017	0.023	0.022	0.018	0.017	0.036	0.022
	standard deviation of the mean [Å]	0.001	0.002	0.002	0.001	0.001	0.003	0.002
	MD [Å]		-0.009	-0.008	-0.012	-0.009	-0.103	-0.112

6	C(ar)-N-H ₂ (N int)	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
				Iso	Aniso	Iso	Aniso		
		no. of observations	7	4	4	4	4	4	4
		mean bond length [Å]	1.010	0.976	0.969	0.977	0.977	0.884	0.889
		population standard deviation [Å]	0.010	0.010	0.025	0.010	0.011	0.017	0.015
		SSDs[Å]	0.011	0.010	0.026	0.011	0.012	0.017	0.015
		standard deviation of the mean [Å]	0.004	0.003	0.006	0.003	0.003	0.004	0.004
		MD [Å]		-0.034	-0.041	-0.033	-0.033	-0.126	-0.121

7	C(ar)-N-H ₂ (N pl)	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
				Iso	Aniso	Iso	Aniso		
		no. of observations	18	2	2	2	2	2	2
		mean bond length [Å]	1.010	0.984	0.986	0.989	0.994	0.920	0.875
		population standard deviation [Å]	0.014	0.015	0.015	0.009	0.009	0.030	0.015
		SSDs[Å]	0.014	0.021	0.021	0.013	0.013	0.042	0.021
		standard deviation of the mean [Å]	0.003	0.015	0.015	0.009	0.009	0.030	0.015
		MD [Å]		-0.026	-0.024	-0.021	-0.016	-0.090	-0.135

8	C(ar)-O-H	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
				Iso	Aniso	Iso	Aniso		
		no. of observations	23	7	7	7	7	7	7
		mean bond length [Å]	0.992	0.941	0.942	0.967	0.964	0.857	0.882
		population standard deviation [Å]	0.017	0.042	0.034	0.044	0.039	0.061	0.044
		SSDs[Å]	0.017	0.045	0.036	0.048	0.041	0.066	0.048
		standard deviation of the mean [Å]	0.004	0.017	0.011	0.018	0.013	0.025	0.018
		MD [Å]		-0.051	-0.050	-0.025	-0.028	-0.135	-0.110

9	C(cyclopropyl)-H	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
				Iso	Aniso	Iso	Aniso		
		no. of observations	9	4	4	4	4	4	4
		mean bond length [Å]	1.080	1.052	1.055	1.057	1.060	0.963	0.958
		population standard deviation [Å]	0.008	0.012	0.010	0.004	0.002	0.011	0.008
		SSDs[Å]	0.008	0.014	0.011	0.004	0.002	0.013	0.010
		standard deviation of the mean [Å]	0.003	0.007	0.006	0.002	0.001	0.006	0.005
		MD [Å]		-0.028	-0.025	-0.023	-0.020	-0.117	-0.122

10	C=Csp ² -H	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
				Iso	Aniso	Iso	Aniso		
		no. of observations	109	2	2	2	2	2	2
		mean bond length [Å]	1.082	1.075	1.045	1.075	1.065	0.925	0.950
		population standard deviation [Å]	0.013	0.015	0.015	0.005	0.015	0.055	0.010
		SSDs[Å]	0.013	0.021	0.021	0.007	0.021	0.078	0.014
		standard deviation of the mean [Å]	0.001	0.015	0.015	0.005	0.015	0.055	0.010
		MD [Å]		-0.007	-0.037	-0.007	-0.017	-0.157	-0.132

11 C₂-Csp³-H₂	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
			Iso	Aniso	Iso	Aniso		
	no. of observations	308	78	78	78	78	78	78
	mean bond length [Å]	1.092	1.077	1.075	1.079	1.081	0.981	0.978
	population standard deviation [Å]	0.017	0.020	0.020	0.017	0.016	0.032	0.027
	SSDs[Å]	0.017	0.021	0.020	0.017	0.016	0.033	0.027
	standard deviation of the mean [Å]	0.001	0.002	0.002	0.002	0.002	0.004	0.003
	MD [Å]		-0.015	-0.017	-0.013	-0.011	-0.111	-0.114
12 C₃-Csp³-H₂	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
			Iso	Aniso	Iso	Aniso		
	no. of observations	82	5	5	5	5	5	5
	mean bond length [Å]	1.099	1.096	1.088	1.094	1.086	0.974	0.976
	population standard deviation [Å]	0.009	0.014	0.007	0.010	0.008	0.008	0.024
	SSDs[Å]	0.009	0.015	0.008	0.011	0.009	0.009	0.027
	standard deviation of the mean [Å]	0.001	0.007	0.004	0.005	0.004	0.004	0.012
	MD [Å]		-0.003	-0.011	-0.005	-0.013	-0.125	-0.123
13 Csp²-N-H₂(all)	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
			Iso	Aniso	Iso	Aniso		
	no. of observations	141	10	10	10	10	10	10
	mean bond length [Å]	1.013	0.992	0.988	0.982	0.987	0.890	0.872
	population standard deviation [Å]	0.009	0.025	0.026	0.028	0.024	0.058	0.054
	SSDs[Å]	0.009	0.026	0.028	0.030	0.025	0.061	0.057
	standard deviation of the mean [Å]	0.001	0.008	0.009	0.009	0.008	0.019	0.018
	MD [Å]		-0.021	-0.025	-0.031	-0.026	-0.123	-0.141
14 Csp²-N-H₂(amido)	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8		IAM max	IAM 0.8
			Iso	Aniso	Iso	Aniso		
	no. of observations	84	2	2	2	2	2	2
	mean bond length [Å]	1.010	1.000	0.980	0.965	0.970	0.889	0.875
	population standard deviation [Å]	0.008	0.001	0.001	0.005	0.010	0.011	0.005
	SSDs[Å]	0.008	0.001	0.001	0.007	0.014	0.016	0.007
	standard deviation of the mean [Å]	0.001	0.001	0.001	0.005	0.010	0.011	0.005
	MD [Å]		-0.010	-0.030	-0.045	-0.040	-0.121	-0.135
15 Csp²-N-H₂(N pI)	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
			Iso	Aniso	Iso	Aniso		
	no. of observations	129	6	6	6	6	6	6
	mean bond length [Å]	1.012	0.975	0.975	0.975	0.981	0.865	0.850
	population standard deviation [Å]	0.008	0.012	0.013	0.026	0.017	0.052	0.055
	SSDs[Å]	0.008	0.013	0.014	0.028	0.018	0.057	0.060
	standard deviation of the mean [Å]	0.001	0.005	0.006	0.012	0.008	0.023	0.025
	MD [Å]		-0.037	-0.037	-0.037	-0.031	-0.147	-0.162

16	Csp^3-O-H	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
				Iso	Aniso	Iso	Aniso		
		no. of observations	169	27	25	27	25	27	27
		mean bond length [Å]	0.970	0.927	0.923	0.951	0.949	0.850	0.861
		population standard deviation [Å]	0.012	0.038	0.053	0.045	0.049	0.052	0.044
		SSDs[Å]	0.012	0.038	0.054	0.046	0.050	0.057	0.045
		standard deviation of the mean [Å]	0.001	0.007	0.010	0.008	0.009	0.010	0.008
		MD [Å]		-0.043	-0.047	-0.019	-0.021	-0.120	-0.109

17	N^+-H	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
				Iso	Aniso	Iso	Aniso		
		no. of observations	187	80	80	80	80	80	80
		mean bond length [Å]	1.036	1.026	1.021	1.037	1.034	0.883	0.899
		population standard deviation [Å]	0.016	0.033	0.026	0.034	0.032	0.046	0.035
		SSDs[Å]	0.016	0.033	0.026	0.034	0.032	0.047	0.036
		standard deviation of the mean [Å]	0.001	0.004	0.003	0.004	0.003	0.005	0.004
		MD [Å]		-0.010	-0.015	0.001	-0.002	-0.153	-0.137

18	$O=Csp^2-O-H$ (acids)	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
				Iso	Aniso	Iso	Aniso		
		no. of observations	37	8	8	8	8	8	8
		mean bond length [Å]	1.018	0.979	0.970	1.017	1.011	0.916	0.906
		population standard deviation [Å]	0.022	0.034	0.031	0.041	0.042	0.070	0.057
		SSDs[Å]	0.022	0.035	0.032	0.042	0.043	0.071	0.059
		standard deviation of the mean [Å]	0.004	0.007	0.007	0.009	0.009	0.015	0.013
		MD [Å]		-0.039	-0.048	-0.001	-0.007	-0.102	-0.112

19	$Z-N-H$ (all)	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
				Iso	Aniso	Iso	Aniso		
		no. of observations	233	52	52	52	52	52	52
		mean bond length [Å]	1.015	0.981	0.976	0.980	0.982	0.879	0.876
		population standard deviation [Å]	0.016	0.023	0.023	0.022	0.018	0.039	0.041
		SSDs[Å]	0.016	0.023	0.023	0.022	0.018	0.039	0.041
		standard deviation of the mean [Å]	0.001	0.003	0.003	0.003	0.002	0.005	0.005
		MD [Å]		-0.034	-0.039	-0.035	-0.033	-0.136	-0.139

20	$Z-O-H$	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
				Iso	Aniso	Iso	Aniso		
		no. of observations	259	44	44	44	44	44	44
		mean bond length [Å]	0.983	0.937	0.939	0.956	0.955	0.876	0.873
		population standard deviation [Å]	0.025	0.044	0.048	0.053	0.052	0.069	0.054
		SSDs[Å]	0.025	0.044	0.048	0.053	0.053	0.070	0.055
		standard deviation of the mean [Å]	0.002	0.006	0.006	0.007	0.007	0.009	0.007
		MD [Å]		-0.046	-0.044	-0.027	-0.028	-0.107	-0.110

21 Z-Csp³-H₃	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8 Å		IAM max	IAM 0.8 Å
			Iso	Aniso	Iso	Aniso		
	no. of observations	1118	158	152	158	152	158	158
	mean bond length [Å]	1.077	1.084	1.068	1.070	1.060	0.977	0.980
	population standard deviation [Å]	0.026	0.036	0.028	0.032	0.025	0.036	0.034
	SSDs[Å]	0.026	0.036	0.028	0.032	0.025	0.036	0.034
	standard deviation of the mean [Å]	0.001	0.003	0.002	0.002	0.002	0.003	0.002
	MD [Å]		0.007	-0.009	-0.007	-0.017	-0.100	-0.097

22 Z₂-Csp³-H₂	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8		IAM max	IAM 0.8
			Iso	Aniso	Iso	Aniso		
	no. of observations	704	174	172	174	172	174	174
	mean bond length [Å]	1.091	1.087	1.082	1.083	1.083	0.964	0.964
	population standard deviation [Å]	0.017	0.024	0.021	0.019	0.018	0.030	0.025
	SSDs[Å]	0.017	0.024	0.021	0.019	0.018	0.030	0.025
	standard deviation of the mean [Å]	0.001	0.002	0.002	0.001	0.001	0.002	0.002
	MD [Å]		-0.004	-0.009	-0.008	-0.008	-0.127	-0.127

23 Z₂-N-H	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8		IAM max	IAM 0.8
			Iso	Aniso	Iso	Aniso		
	no. of observations	74	40	38	40	38	40	40
	mean bond length [Å]	1.027	0.980	0.977	0.985	0.985	0.855	0.863
	population standard deviation [Å]	0.016	0.025	0.019	0.022	0.017	0.033	0.043
	SSDs[Å]	0.016	0.025	0.019	0.022	0.018	0.034	0.043
	standard deviation of the mean [Å]	0.002	0.004	0.003	0.003	0.003	0.005	0.007
	MD [Å]		-0.047	-0.050	-0.042	-0.042	-0.172	-0.164

24 Z₃-Csp³-H	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8		IAM max	IAM 0.8
			Iso	Aniso	Iso	Aniso		
	no. of observations	344	80	79	80	79	80	80
	mean bond length [Å]	1.098	1.075	1.078	1.079	1.082	0.963	0.959
	population standard deviation [Å]	0.011	0.023	0.022	0.020	0.019	0.028	0.023
	SSDs[Å]	0.011	0.023	0.022	0.021	0.019	0.028	0.023
	standard deviation of the mean [Å]	0.001	0.002	0.002	0.002	0.002	0.003	0.002
	MD [Å]		-0.023	-0.020	-0.019	-0.016	-0.135	-0.139

25 H₂O	Method/resolution H treatment	Neutron	TAAM max		TAAM 0.8		IAM max	IAM 0.8
			Iso	Aniso	Iso	Aniso		
	no. of observations	222	52	52	52	52	52	52
	mean bond length [Å]	0.959	0.918	0.916	0.940	0.939	0.851	0.857
	population standard deviation [Å]	0.061	0.028	0.026	0.024	0.025	0.039	0.029
	SSDs[Å]	0.061	0.028	0.026	0.024	0.025	0.039	0.029
	standard deviation of the mean [Å]	0.004	0.003	0.003	0.003	0.003	0.004	0.003
	MD [Å]		-0.041	-0.043	-0.019	-0.020	-0.108	-0.102

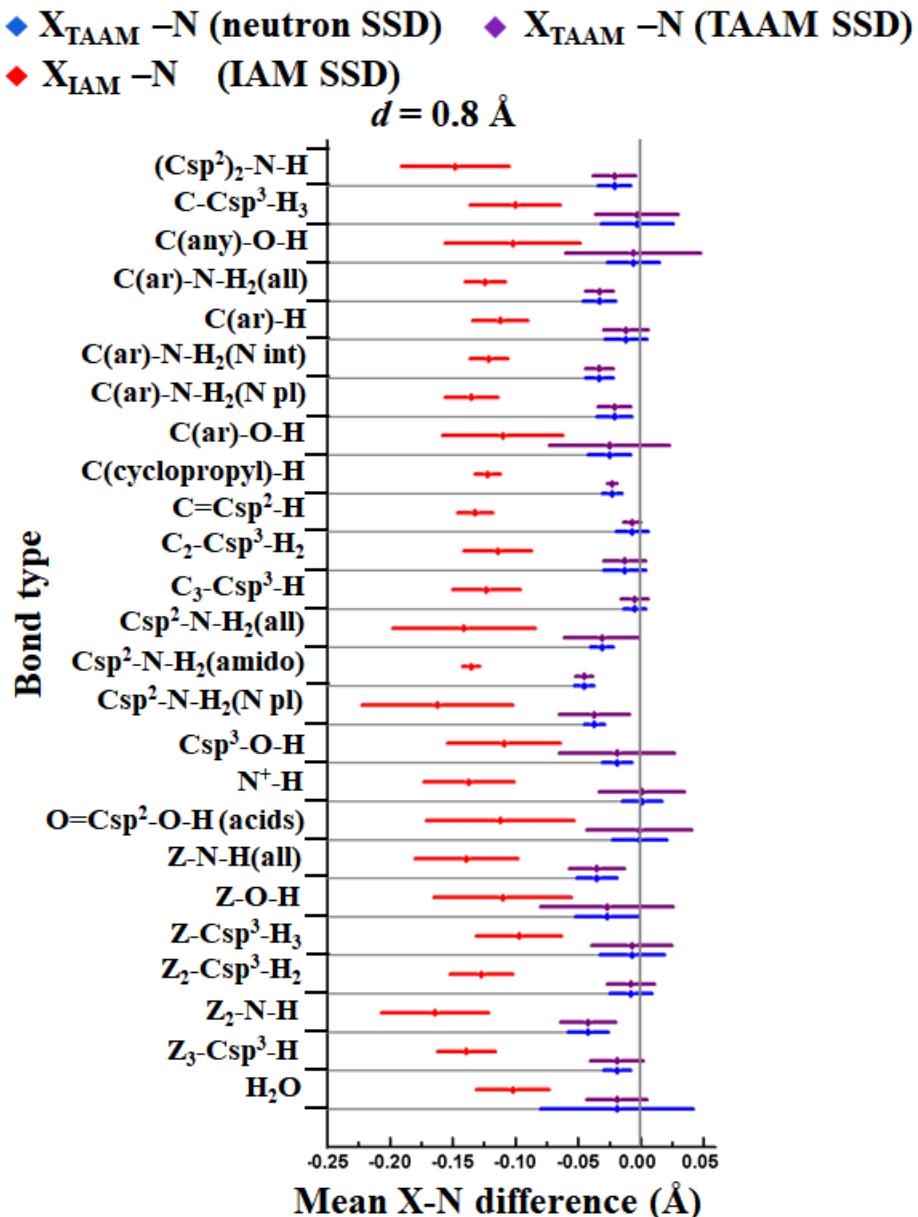


Figure S2: Comparison of mean X-ray and neutron (X-N) bond lengths differences for $d_{\min}=0.8 \text{ \AA}$ resolution with neutron, TAAM and IAM SSDs. Hydrogen atoms were refined with isotropic displacement parameters for X-ray data. The error bar intersecting the vertical line at 0.00 \AA in most of the cases indicates that the TAAM and neutron results agree within a single SSD.

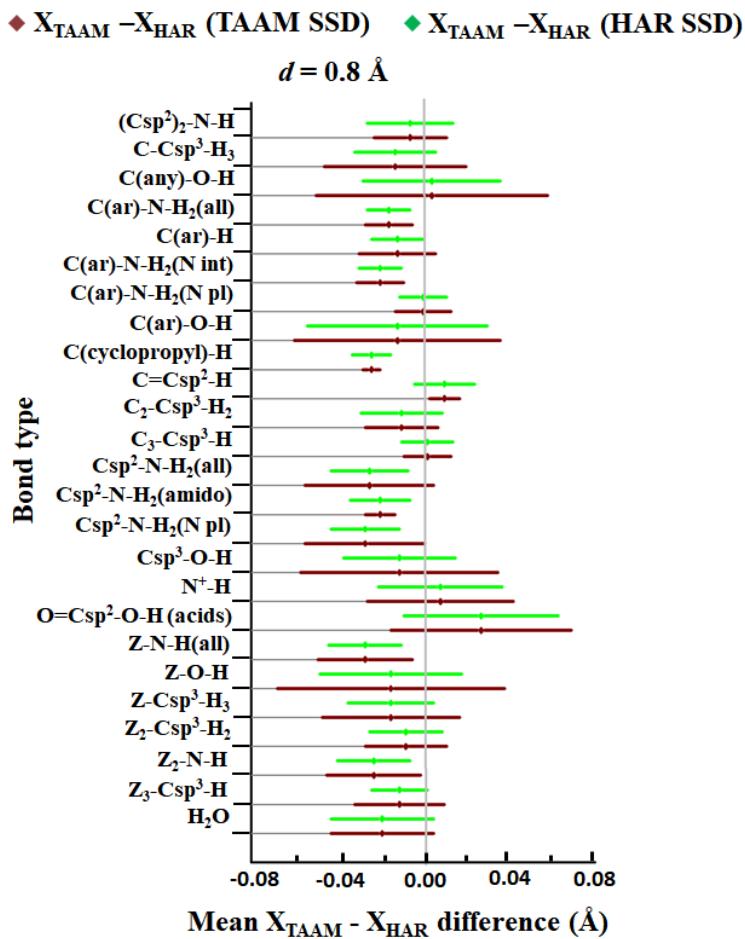


Figure S3: Comparison of mean X-ray, TAAM and X-ray HAR bond lengths differences for $d_{min}=0.8 \text{ \AA}$ resolution with TAAM and HAR SSDs. Hydrogen atoms were refined with isotropic displacement parameters.

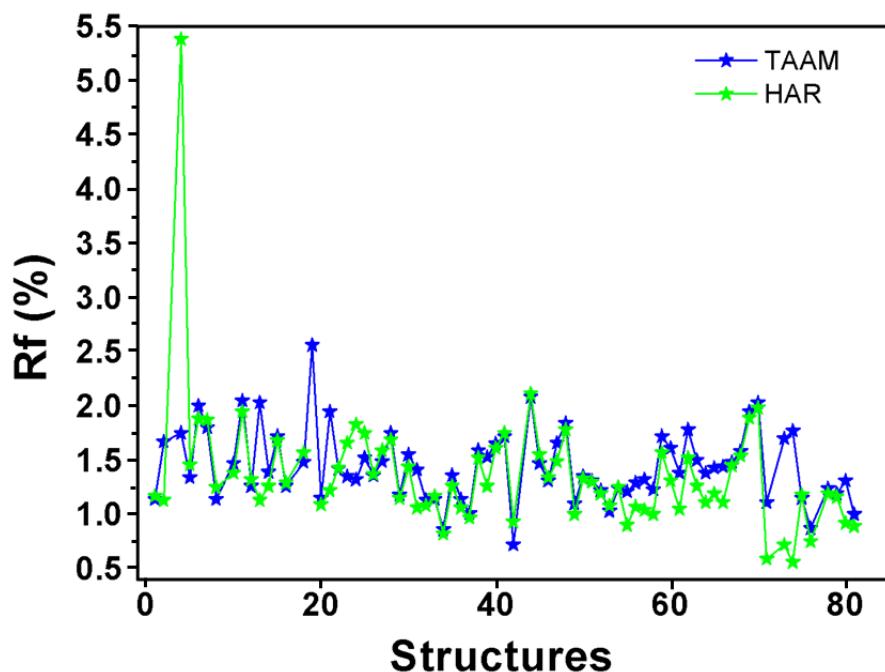


Figure S4: Comparison of the reliability factor (R_f) for the TAAM and HAR refinements at 0.8 \AA resolution. Hydrogen atoms were refined with isotropic displacement parameters.

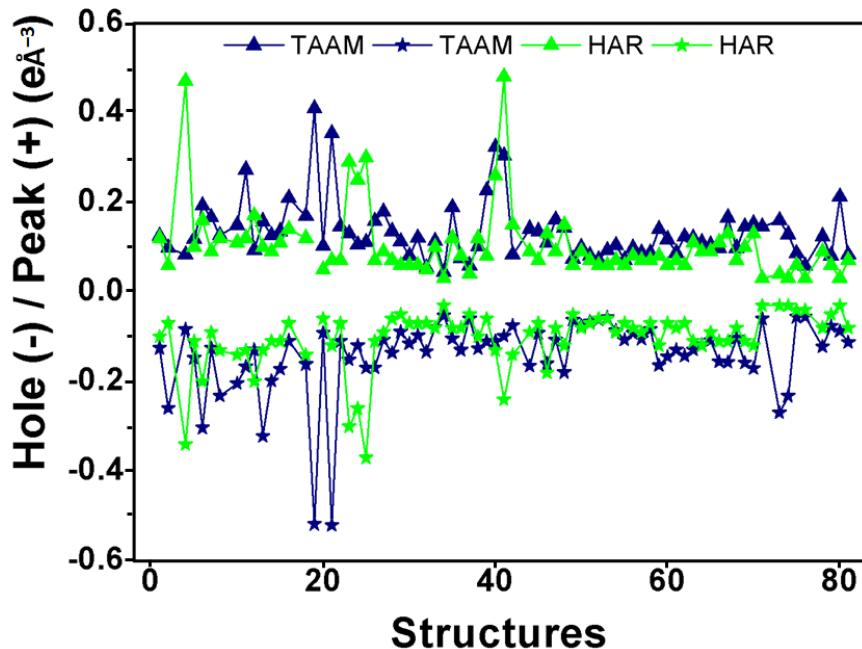


Figure S5: Comparison of residuals (i.e. peak (+) and hole (-)) for the TAAM and HAR refinements at 0.8 Å resolution. Hydrogen atoms were refined with isotropic displacement parameters.

The averaged % difference between U_{eqIAM} and U_{eqTAAM} was calculated by using given below formula in eq. 1

Averaged % difference between U_{eqIAM} and U_{eqTAAM} =

$$\frac{\sum_i[U_{eq_i IAM}] - \sum_i[U_{eq_i TAAM}]}{\sum_i[U_{eq_i IAM}]} \times 100 \quad \text{equation -1}$$

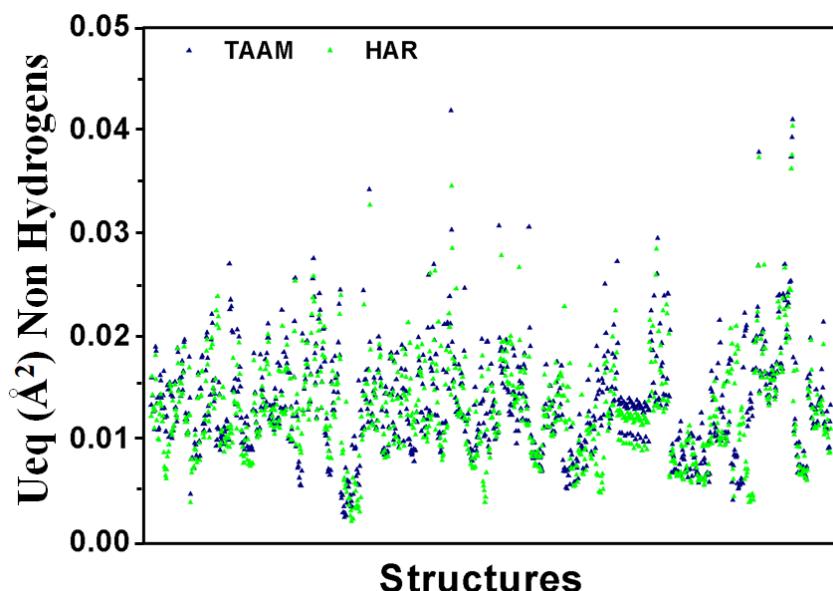


Figure S6: Comparison of U_{eq} (Å²) obtained from TAAM and HAR refinement for non-hydrogen atoms at 0.8 Å resolution. Hydrogen atoms were refined with isotropic displacement parameters.

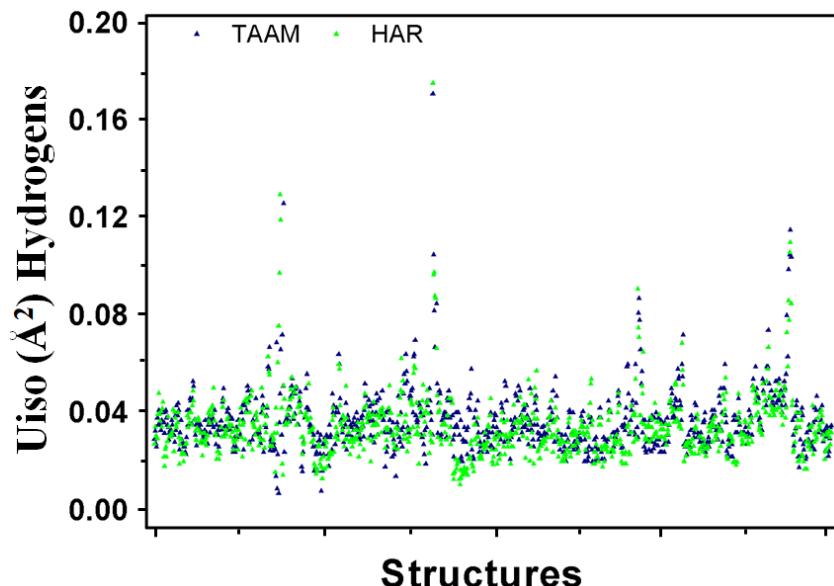


Figure S7: Comparison of U_{iso} (\AA^2) for hydrogen atoms obtained from TAAM and HAR refinements at 0.8 \AA resolution. Hydrogen atoms were refined with isotropic displacement parameters

Table S3: Detailed comparison of refinement parameters between HAR and TAAM for selected structures.

S. No.	Chemical formula (common name)	Method	R(F) [%]				Residuals ($e/\text{\AA}^3$) $\Delta\varrho_{min}/\Delta\varrho_{max}$			
			iso max	iso 0.8 \AA	anis max	anis 0.8 \AA	Iso max	iso 0.8 \AA	anis max	anis 0.8 \AA
27.	$\text{C}_8\text{H}_{18}\text{N}_2\text{O}_4\text{S}$ (HEPES)*	TAAM	2.72	1.49	2.70	1.43	-0.25/0.45	-0.10/0.17	-0.26/0.45	-0.10/0.18
		HAR	2.76	1.59	2.74	1.52	-0.18/0.30	-0.09/0.09	-0.18/0.29	-0.09/0.09
36.	$\text{C}_{15}\text{H}_{21}\text{N}_3\text{O}_5 + 2\text{H}_2\text{O} + 0.634\text{H}_2\text{O}$ (ALA-TYR-ALA)*	TAAM	3.27	1.14	3.25	1.06	-0.33/0.65	-0.12/0.07	-0.33/0.64	-0.12/0.07
		HAR	3.42	1.06	3.40	0.99	-0.33/0.38	-0.08/0.08	-0.33/0.38	-0.08/0.07
42.	$\text{C}_5\text{H}_{13}\text{N}_2\text{O}_2 + \text{Cl}$ (L-ornithine)*	TAAM	1.39	0.72	1.38	0.65	-0.20/0.30	-0.07/0.08	-0.20/0.30	-0.07/0.07
		HAR	1.64	0.93	1.63	0.89	-0.59/0.63	-0.14/0.15	-0.59/0.64	-0.14/0.15
75.	$\text{C}_{41}\text{H}_{76}\text{N}_2\text{O}_{15} + 0.88\text{H}_2\text{O}$ (roxithromycin)*	TAAM	2.30	1.15	2.17	0.99	-0.37/0.28	-0.05/0.08	-0.34/0.18	-0.05/0.08
		HAR	2.22	1.18	2.05	0.98	-0.19/0.16	-0.04/0.06	-0.18/0.17	-0.04/0.05

* weakest reflections (outliers) were omitted (similar to HAR).

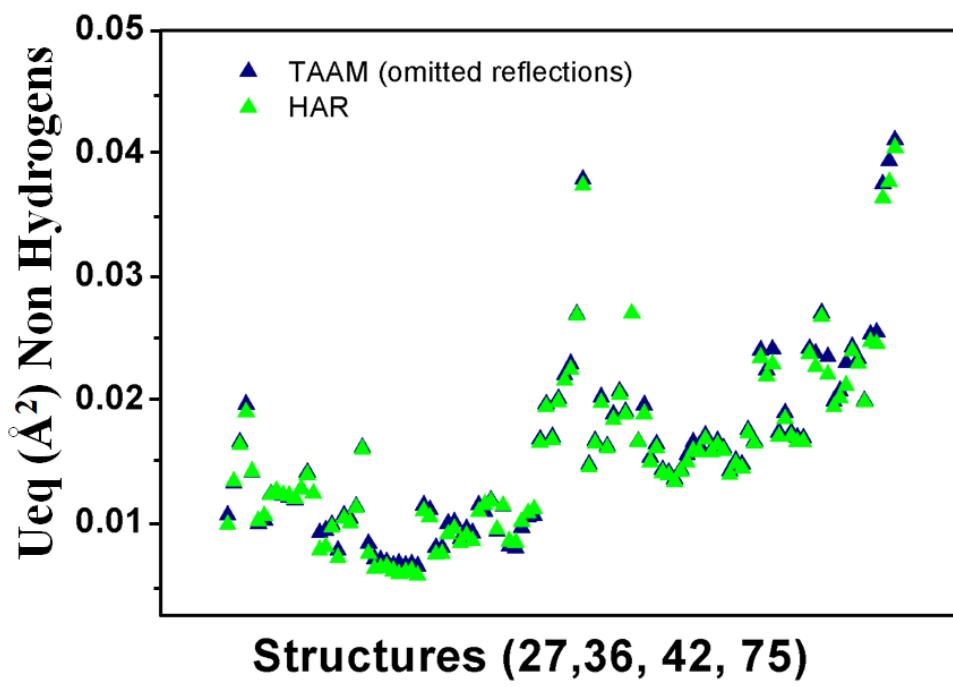


Figure S8: Comparison of U_{eq} (\AA^2) obtained from TAAM (omitted reflection similar to HAR) and HAR refinement for non-hydrogen atoms at 0.8 \AA resolution. Hydrogen atoms were refined with isotropic displacement parameters.

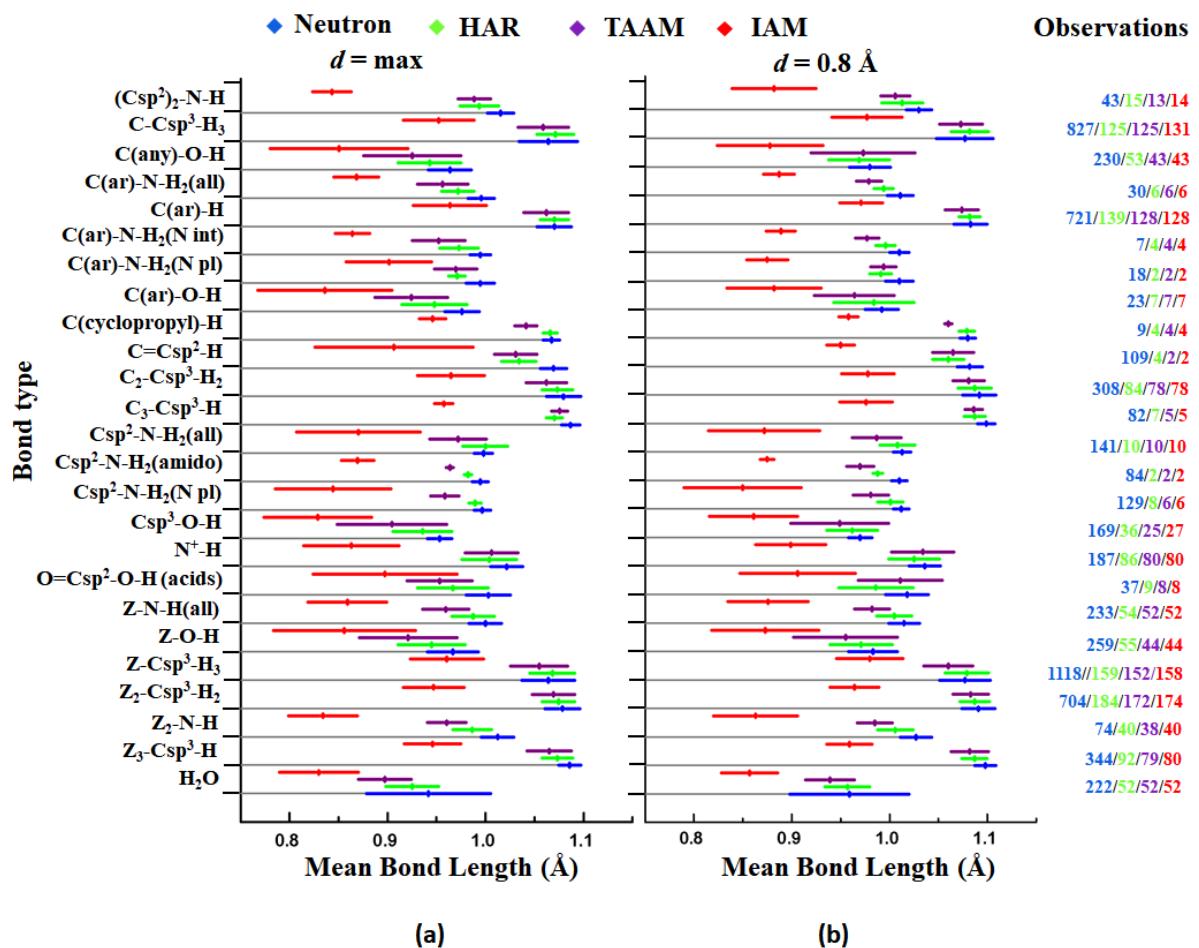


Figure S9: Comparison of the X-H bond distances from X-ray and neutron data refinement for TAAM, HAR and neutron data at (a) max and (b) 0.8 Å resolution for the selected 75 structures with hydrogen atoms refined with anisotropic displacement parameters. The X-H bond distances obtained from 81 structures were categorized and compared with the averaged neutron distances as defined in the paper by Allen and Bruno (Allen & Bruno, 2010). Additionally the O–H bond in water trapped in these structures was also included and the corresponding neutron distances were taken from the paper by Woinska *et. al.*, 2016. The bars in the figure shows the SSDs of each of the associated bond types.(75 from IAM and TAAM, 81 from HAR).

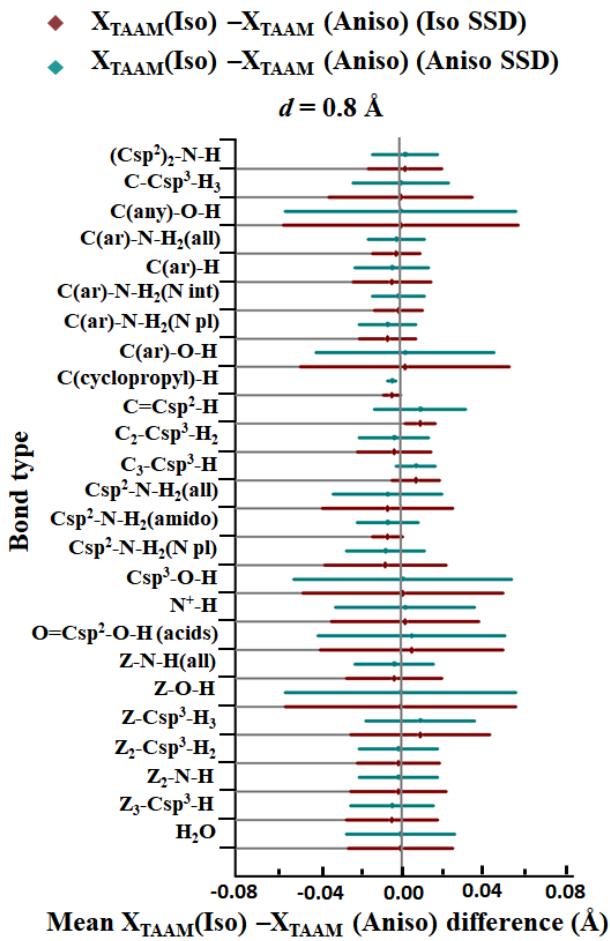


Figure S10: Comparison of Mean X-rayTAAM and X-rayHAR bond lengths differences for $d_{min}=0.8 \text{ \AA}$ resolution with TAAM and HAR SSDs. Hydrogen atoms were refined with anisotropic displacement parameters.

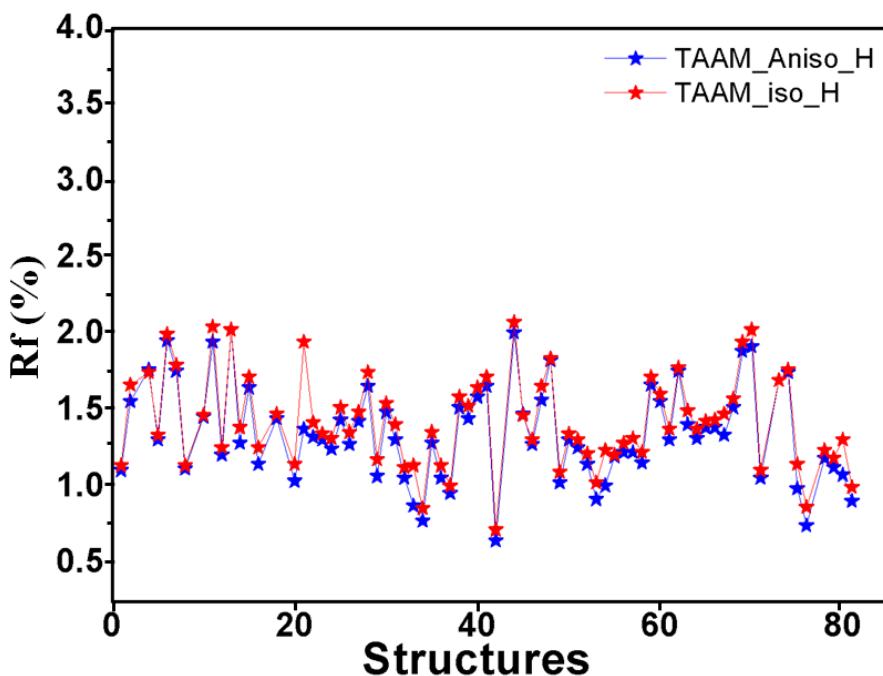


Figure S11: Comparison of reliability factor (R_f) for iso- and anisotropic refinement of hydrogen atoms displacements with TAAM at 0.8 Å resolution.

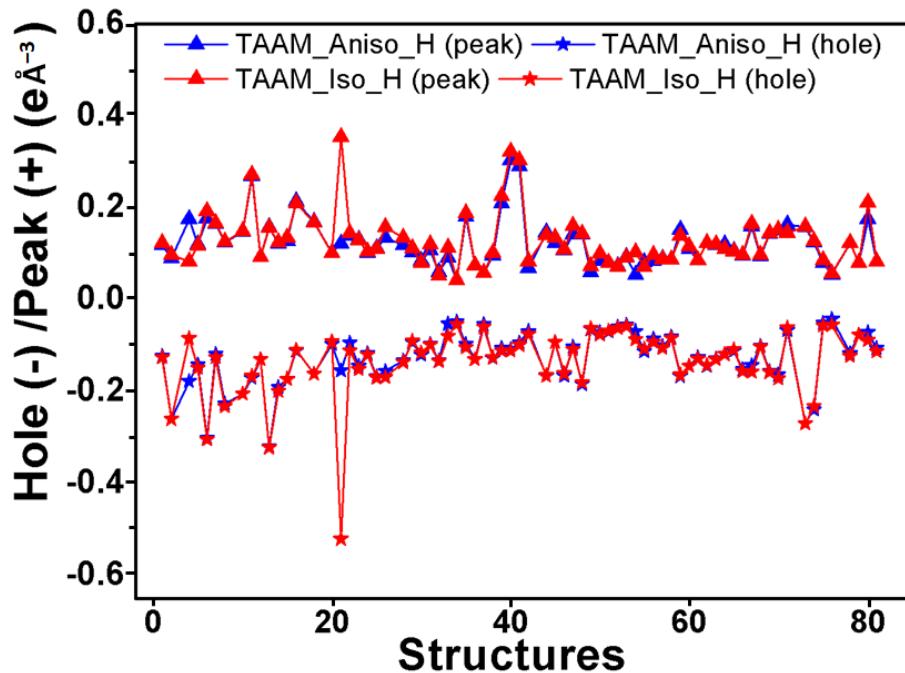


Figure S12: Comparison of residuals (peak(+)) and hole (−)) for iso- and anisotropic refinement of hydrogen atoms displacements with TAAM at 0.8 Å resolution.

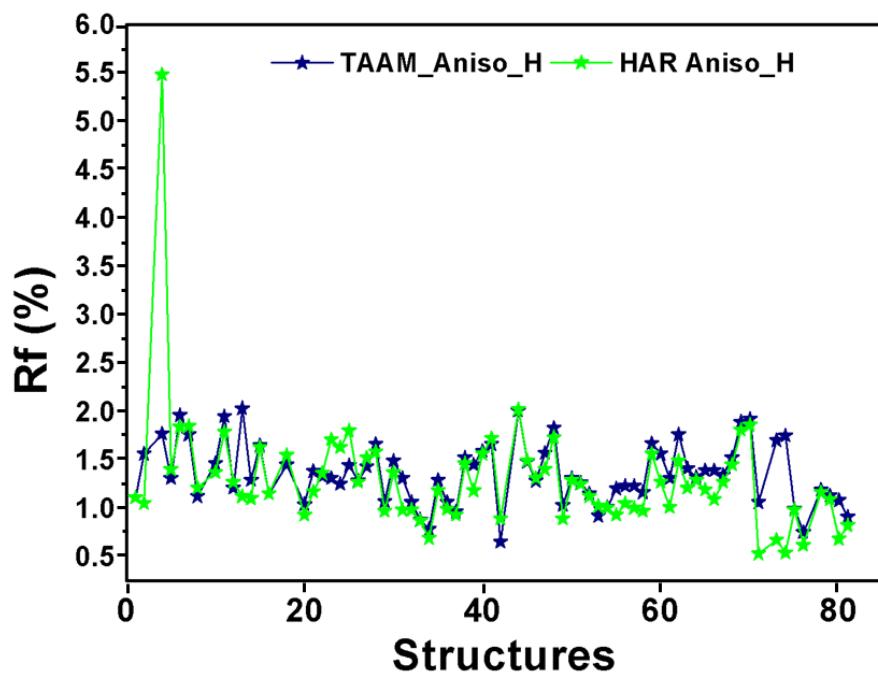


Figure S13: Comparison of the reliability factor (R_f) for TAAM and HAR refinements at 0.8 Å resolution. Hydrogen atoms were refined with anisotropic displacement parameters.

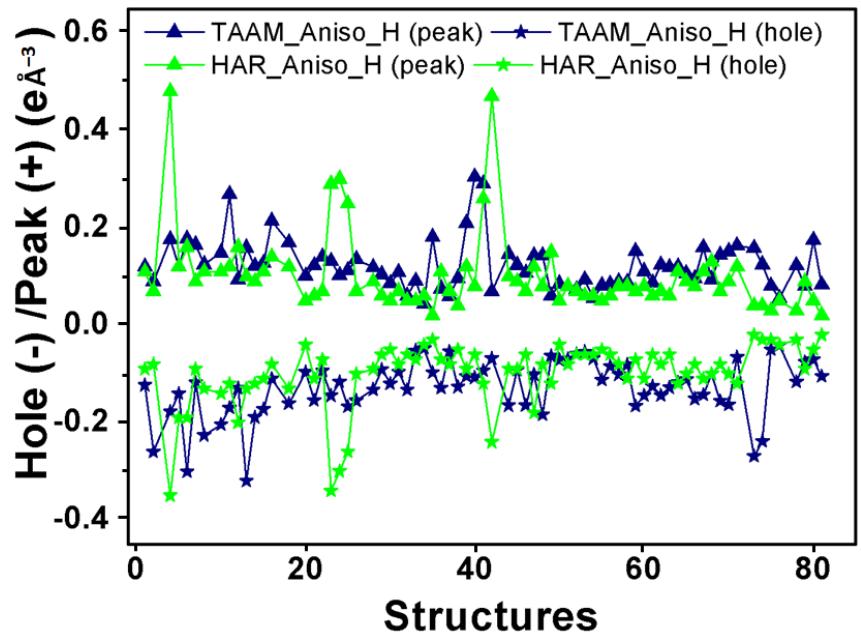


Figure S14: Comparison of residuals (i.e. peak (+) and hole (-)) for TAAM and IAM refinements at 0.8 Å resolution. Hydrogen atoms were refined with anisotropic displacement parameters.

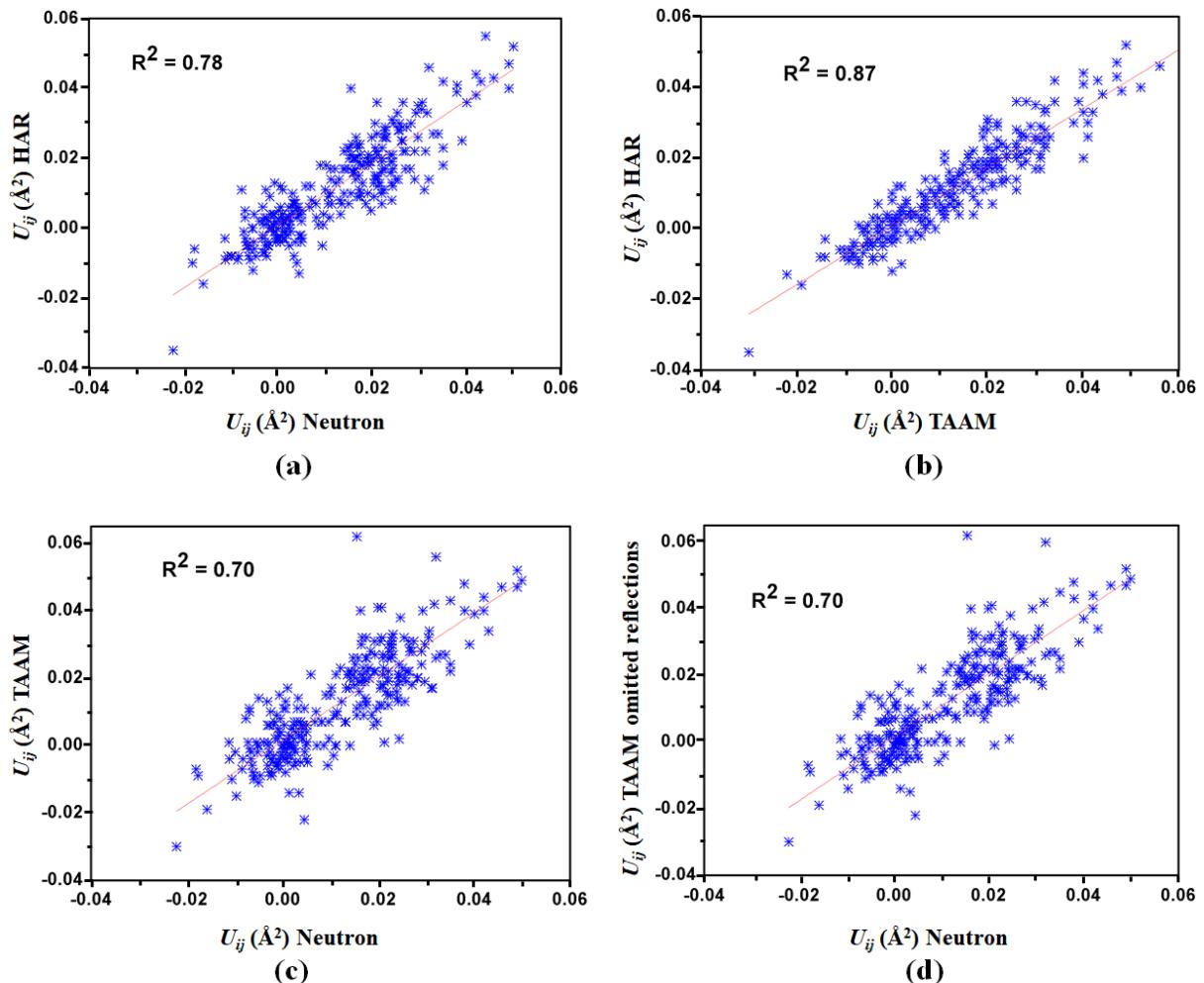


Figure S15: Correlation of U_{ij} values of hydrogens obtained from neutron, HAR, TAAM and TAAM (omitted reflections as in HAR) respectively at 0.8 Å resolution for structures 23, 24, 49, 80, 81.

Table S4: Similarity index (S_{12}) comparison of ADPs of structures 23, 24, 49, 80 and 81 between neutron and TAAM refinements using all data, TAAM refinement with omitted reflections (similar to HAR), HAR results, respectively at 0.8 Å resolution. (CCDC No. 23 = 1962082), (CCDC No. 24 = 1962083), (CCDC No. 49 = 1962084), (CCDC No. 80 = 1962228), (CCDC No. 81 = 1984051)

23_HAR	23_TAAM	23_TAAM_omitted reflections	
C1	15.8	15.1	15.2
C2	13.5	10.2	11.0
C3	7.7	6.9	6.4
C4	11.4	8.4	8.5
C5	7.2	6.4	6.4
O1	9.0	8.1	7.9
O2	11.2	9.6	9.8
O3	5.0	4.7	4.7
N1	11.2	12.1	12.5
N2	9.5	10.0	10.0
H1	8.7 NPD	NPD	
H2	18.1	20.1	20.6
H3	NPD		
H4	18.0	16.9	16.4
H5	9.7	4.8	5.8
H6	8.2	7.4	7.2
H7	10.9	5.2	4.4
H8	6.1	2.9	1.4
H9	7.9	4.9	5.2
H10	NPD	2.4	4.1

24_HAR	24_TAAM	24_TAAM_omitted reflections	
C1	7.3	8.3	8.2
C2	9.1	8.0	8.5
C3	3.3	2.9	2.8
C4	11.4	8.8	9.0
C5	5.2	5.3	5.1
O1	4.2	3.9	4.0
O2	4.8	5.0	5.0
O3	3.9	4.1	4.2
N1	7.4	7.0	7.0
N2	7.9	8.1	8.3
H1	9.6 NPD	NPD	
H2	9.7	12.6	10.4
H3	NPD		
H4	NPD		
H5	5.5	3.4	3.4
H6	3.4	2.3	2.2
H7	3.7	6.9	7.4
H8	1.6	3.3	3.7
H9	17.4	2.5	3.6
H10	NPD	37.6	66.4

49_HAR	49_TAAM	49_omitted reflections	
C1	3.2	2.6	2.5
C2	0.3	0.9	0.9
C3	1.7	2.7	2.6
C4	1.9	1.3	1.3
C5	0.7	1.1	1.1
C6	1.5	1.5	1.6
C7	0.7	0.8	0.8
O1	1.5	1.5	1.5
O2	1.5	1.9	1.9
O3	3.5	3.3	3.3
O4	0.5	0.4	0.4
O5	1.1	1.2	1.2
N1	1.7	1.3	1.3
H1	13.2	17.4	16.6
H2	4.5	7.9	8.5
H3	4.5	4.7	4.7
H4	3.3	6.0	6.4
H5	11.7	7.6	7.6
H6	4.8	4.0	4.5
H7	2.7	5.5	5.6
H8	4.7	2.4	2.6
H9	3.0	3.4	3.5
H10	5.0	5.0	4.7
H11	3.4	2.4	2.5
H12	1.5	11.3	16.7
H13	18.0 NPD	NPD	

	80_HAR	80_TAAM	
H2	2.09	2.09	3.21
H1	2.20	2.20	7.27
O1	0.07	0.07	0.03
N1	0.05	0.05	0.07
C1	0.16	0.16	0.01

	81_HAR	81_TAAM	81_TAAM_omitted	
H1A	4.06	5.95	5.95	
H1B	2.89	7.75	7.75	
H5A	4.22	8.23	8.23	
H5B	1.66	1.82	1.82	
H11	17.06	NPD	NPD	
H12	1.53	7.07	6.89	
H13	7.01	13.56	13.56	
H14	3.83	12.92	12.92	
H15	4.22	14.23	14.23	
H2	1.74	2.71	2.71	
H3	1.92	4.39	4.39	
H4	2.89	2.92	2.92	
O5	0.21	0.37	0.37	
O4	0.31	0.46	0.46	
O3	0.91	1.16	1.17	
O2	0.66	0.84	0.84	
O1	0.55	0.70	0.70	
C3	0.30	0.39	0.39	
C5	0.29	0.39	0.39	
C4	0.91	1.13	1.13	
C2	0.874	0.978	0.978	
C1	0.384	0.493	0.492	

NPD: Non-Positive Definite

*In case of 80 the reflections were not omitted in HAR refinement.

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