

From serendipity to supramolecular design: assessing the utility of computed crystal form landscapes in inferring the risks of crystal hydration in carboxylic acids

Sharmarke Mohamed,^{*a} and Liang Li^b

^a Department of Chemistry, Khalifa University of Science and Technology, PO Box 127788, Abu Dhabi, United Arab Emirates.

^b Central Technology Platforms, New York University Abu Dhabi, PO BOX 129188, Abu Dhabi, United Arab Emirates.

^{*}Corresponding author. E-mail: sharmarke.mohamed@ku.ac.ae

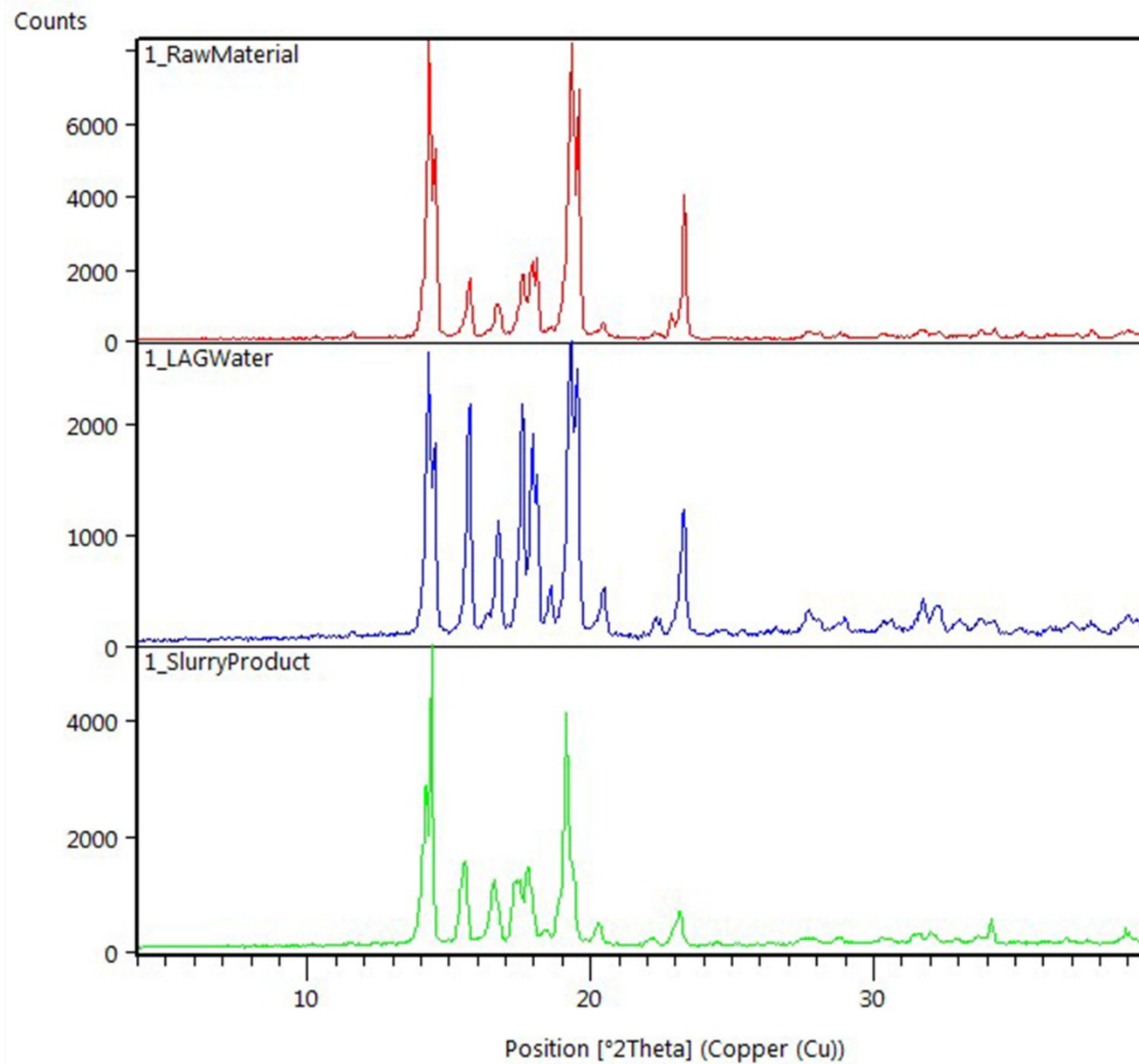


Figure S1: Comparison of the Powder X-Ray Diffraction (PXRD) patterns for the 1-adamantaneacetic acid (**1**) raw material (red, top) against the solid product obtained following liquid assisted grinding (LAG) using catalytic volume of water (blue, middle) or following slurring of **1** in excess water (green, bottom).

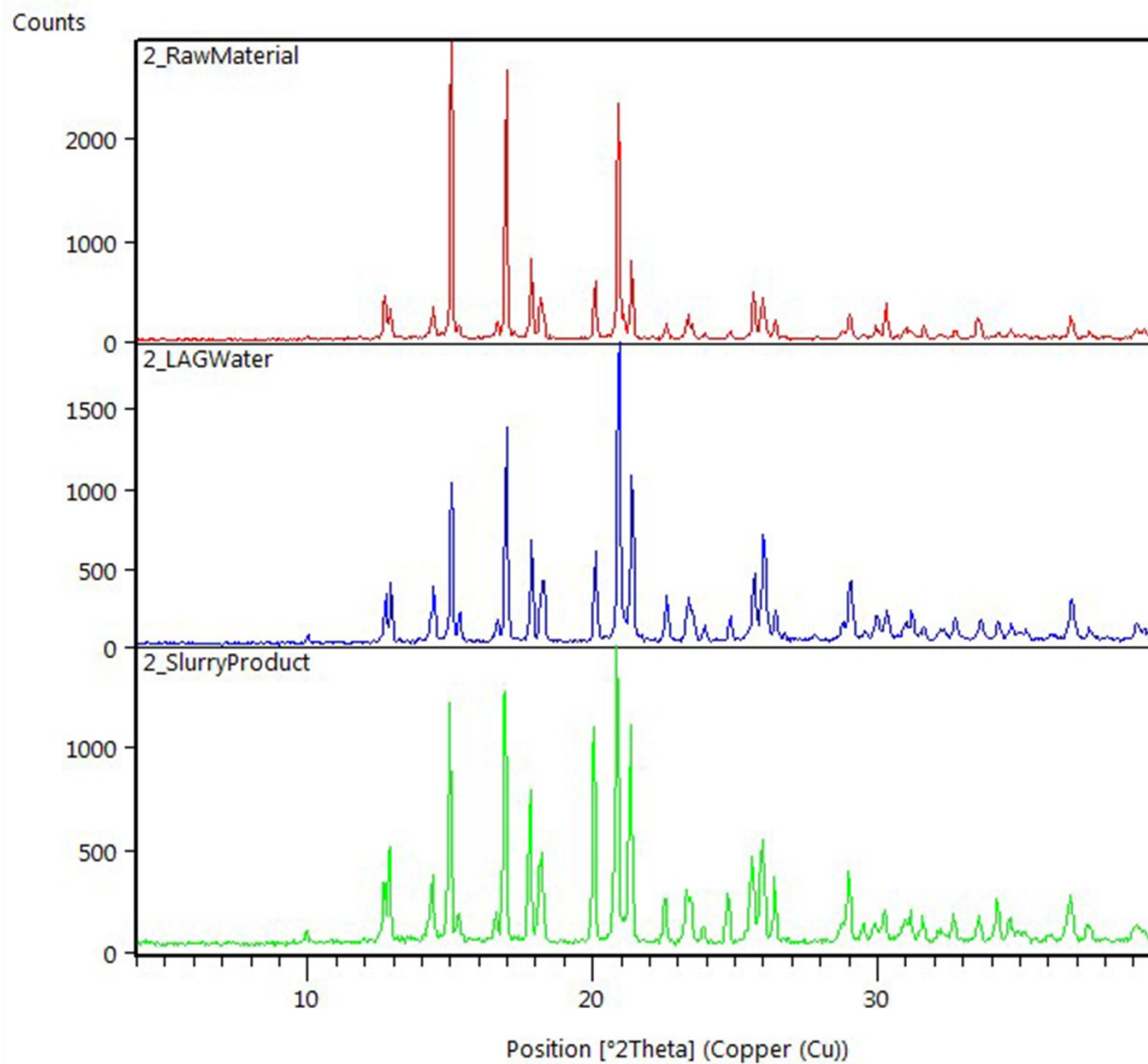


Figure S2: Comparison of the Powder X-Ray Diffraction (PXRD) patterns for the 3-bromoadamantane-1-acetic acid (**2**) raw material (red, top) against the solid product obtained following liquid assisted grinding (LAG) using catalytic volume of water (blue, middle) or following slurring of **2** in excess water (green, bottom).

CSD Refcode	Water Volume in unit cell / Å ³	Cell Volume / Å ³	% Water Volume in Unit Cell	Calculated density / g cm ⁻³	No. Unique Water Molecules
QIWVEZ	9.70	1775.29	0.55	1.24	0.5
JEYKUT	14.14	1317.51	1.07	1.40	0.5
QIVTUK	14.54	709.50	2.05	1.53	0.5
QIVTUK01	18.39	708.15	2.60	1.53	0.5
BIMFUY10	22.42	1607.49	1.39	1.29	0.5
HORKEF	36.56	1434.76	2.55	1.30	0.5
YUJNUM01	107.16	3355.67	3.19	1.47	0.5
UGOWUJ	137.17	3903.38	3.51	1.22	0.5
INOEX	5.35	401.88	1.33	1.32	1
CIZWEN	6.16	998.23	0.62	1.23	1
VUKJIU	6.55	1677.65	0.39	1.51	1
POKKAD09	6.57	931.06	0.71	1.36	1
POKKAD10	6.61	936.55	0.71	1.36	1
POKKAD02	6.72	936.55	0.72	1.36	1
YITKUI	10.46	2337.79	0.45	1.58	1
POKKAD03	12.49	941.99	1.33	1.35	1
POKKAD	12.58	949.32	1.33	1.34	1
PEFBOT	12.85	489.37	2.63	1.50	1
GARPUK	13.17	2033.93	0.65	1.47	1
DIWNON01	13.20	1742.20	0.76	1.42	1
DIPKGA	13.33	1472.09	0.91	1.32	1
DAYGUG	13.41	902.66	1.49	1.40	1
HALNEP	15.29	465.94	3.28	1.53	1
YUXGUV	19.93	381.73	5.22	1.50	1
TUBWAQ	21.66	686.75	3.15	1.69	1
YACNEV	22.24	1306.18	1.70	1.25	1
KUZYIO	25.66	755.18	3.40	1.53	1
NAXXOA	26.23	2992.93	0.88	1.32	1
DUNFAU	27.05	724.03	3.74	1.35	1

BXALPR10	28.12	1640.57	1.71	1.23	1
YOWDOF	28.89	962.57	3.00	1.32	1
JOSWAP	29.09	1786.41	1.63	1.42	1
VOBDOF	30.70	1546.33	1.99	1.52	1
NAHYPL	32.42	959.74	3.38	1.32	1
ZEZLEV	32.87	520.97	6.31	1.70	1
POXCIP	34.76	1364.70	2.55	1.40	1
VEMHOM	36.60	1540.85	2.38	1.18	1
PILVEN	39.48	1520.81	2.60	1.34	1
EVIHEW	40.35	920.59	4.38	1.55	1
HORRIR	40.93	1948.77	2.10	1.25	1
SEZGUA	41.05	828.16	4.96	2.01	1
POXCEL	41.62	1361.76	3.06	1.41	1
TIYLOE	43.42	826.06	5.26	1.40	1
PONREQ	44.57	1499.42	2.97	1.87	1
VAPRUA	48.44	2294.58	2.11	1.39	1
RELROR	49.71	2069.80	2.40	2.20	1
JODPIC	50.82	890.30	5.71	1.55	1
RUKEVAW	57.71	3684.79	1.57	1.37	1
SAQLEC	58.16	1751.15	3.32	1.33	1
SOGGUR	61.25	2727.99	2.25	2.81	1
COSYAM	67.01	2761.04	2.43	1.17	1
WOCREL	68.08	704.91	9.66	1.64	1
PIPCIL	70.69	2563.59	2.76	1.39	1
WOCREL01	73.24	707.70	10.35	1.63	1
WOVWIN	75.91	4372.29	1.74	1.16	1
BANGON	76.53	2186.87	3.50	1.42	1
SOBDOC10	77.72	1666.65	4.66	1.33	1
HATWOO	77.81	2191.63	3.55	1.30	1
EVODOI	79.62	1942.72	4.10	1.20	1
FIZDOH	83.48	717.43	11.64	1.53	1
EHASUC	90.18	2159.62	4.18	1.22	1

ICANEF	93.35	1365.94	6.83	1.51	1
ROLVOF	94.56	946.81	9.99	1.38	1
ZIZHAR	96.99	2117.87	4.58	1.24	1
SILRIP	97.98	2597.35	3.77	1.26	1
TOPRUM	110.31	2252.72	4.90	1.28	1
WIQFOT	172.75	1817.01	9.51	1.32	1
XAFKIY	247.09	5032.82	4.91	1.34	1
RATQAE	364.18	3009.84	12.10	1.35	1
KISJEC	12.58	1840.05	0.68	1.59	2
QITWAS	21.00	743.81	2.82	1.64	2
RIWJEM	23.21	1660.31	1.40	1.58	2
WOBPAA	24.19	792.29	3.05	1.52	2
MUQHOW	26.47	432.32	6.12	1.58	2
DOGSIB	30.25	1071.47	2.82	1.64	2
QALROM	38.30	985.39	3.89	1.35	2
HAXTAD	45.91	1360.89	3.37	1.63	2
NIPLED	48.46	400.21	12.11	1.73	2
OPYQUC	53.27	876.08	6.08	1.61	2
VIKGIG	70.89	912.03	7.77	1.55	2
PIPTAL	77.80	2324.52	3.35	1.33	2
PIPTEP	80.06	2324.21	3.44	1.33	2
BENTAC01	82.31	531.29	15.49	1.54	2
NAMYIJ	86.44	1104.40	7.83	1.25	2
POFROS	91.08	558.89	16.30	2.14	2
SIALAC	94.97	804.41	11.81	1.43	2
DIFPEO	99.69	1096.34	9.09	1.63	2
PUFGUU	101.65	897.35	11.33	2.41	2
FESYIM01	104.85	1028.83	10.19	1.60	2
XIVMIY	108.54	927.62	11.70	1.56	2
NIPLED01	111.68	802.71	13.91	1.72	2
NEFLIT	114.85	1285.72	8.93	1.63	2
ROFGIC	128.55	839.64	15.31	1.40	2

NASTUX	129.33	880.03	14.70	1.31	2
WUZHEG	142.74	2002.21	7.13	1.57	2
SOWJIZ	146.54	3490.12	4.20	1.41	2
GAVMUM	173.45	884.04	19.62	1.56	2
BUWDOO	193.12	1304.71	14.80	1.36	2
DABWOU	209.19	1646.63	12.70	1.45	2
PIKVIO	302.81	2047.89	14.79	1.38	2
ACIWIS	483.40	3968.37	12.18	1.43	2
FAQDIK	125.50	1129.84	11.11	1.52	3
YUKVAB	155.67	1689.26	9.22	1.36	3
VELHAX	257.45	1257.68	20.47	1.49	3
ZZZSSY02	257.47	1960.88	13.13	1.72	3
COWYAP	273.30	1060.30	25.78	1.59	3
LUSWIF	316.02	3653.57	8.65	1.72	3
YARCIE	349.92	2828.46	12.37	1.40	3
ZZZSSY01	380.07	2003.80	18.97	1.69	3

Table S1: Estimated water volumes and calculated cell densities for the set of carboxylic acid hydrates retrieved from the Cambridge Structural Database (see Section 3.2 in the manuscript).

Structure ID	E _{latt} /kJ mol ⁻¹	Relative E _{latt} /kJ mol ⁻¹	Volume /Å ³	Density /g cm ⁻³	Space Group	a / Å	b / Å	c / Å	α / °	β / °	γ / °	Packing Index / %	Solvent Accessible Volume per Unit Cell / %
894	-108.09	0.00	1064.55	1.21	P2 ₁ /c	8.11	12.86	11.32	90.00	64.37	90.00	70.40	0.00
381	-108.04	0.05	534.97	1.21	P-1	8.36	6.61	10.53	87.52	112.56	95.89	70.00	0.00
706	-106.16	1.93	1079.10	1.20	P2 ₁ /c	8.24	12.23	11.31	90.00	71.25	90.00	69.40	0.00
987	-106.16	1.93	2158.85	1.20	Pbca	14.30	12.47	12.11	90.00	90.00	90.00	69.50	0.00
596	-106.12	1.97	1093.90	1.18	P2 ₁ 2 ₁ 2 ₁	6.75	14.66	11.05	90.00	90.00	90.00	68.60	0.00
997	-105.89	2.19	2113.05	1.22	Pbca	7.00	27.38	11.03	90.00	90.00	90.00	71.20	0.00
995	-105.74	2.35	2154.68	1.20	Pbca	12.25	12.31	14.29	90.00	90.00	90.00	69.50	0.00
445	-105.68	2.41	552.84	1.17	P-1	6.84	8.68	11.30	95.80	98.37	121.50	67.70	0.00
795	-105.56	2.53	1057.88	1.22	P2 ₁ /c	14.43	11.05	6.99	90.00	108.25	90.00	71.00	0.00
976	-105.44	2.65	2166.92	1.19	Pbca	11.31	15.07	12.72	90.00	90.00	90.00	69.20	0.00
594	-104.88	3.21	1102.48	1.17	P2 ₁ 2 ₁ 2 ₁	11.50	6.68	14.34	90.00	90.00	90.00	68.00	0.00
742	-104.77	3.32	1104.96	1.17	P2 ₁ /c	6.84	11.98	14.02	90.00	105.79	90.00	67.80	0.00
965	-104.77	3.32	2146.40	1.20	Pbca	25.97	7.34	11.26	90.00	90.00	90.00	69.90	0.00
908	-104.20	3.88	1098.56	1.17	P2 ₁ /c	6.82	19.30	10.41	90.00	53.36	90.00	68.30	0.00
780	-104.20	3.89	1091.59	1.18	P2 ₁ /c	6.53	15.55	12.41	90.00	120.01	90.00	68.70	0.00
759	-104.10	3.99	1108.77	1.16	P2 ₁ /c	17.55	7.11	11.87	90.00	48.43	90.00	67.40	0.00
888	-103.98	4.10	1109.93	1.16	P2 ₁ /c	16.94	6.85	11.50	90.00	56.32	90.00	67.50	0.00
839	-103.86	4.23	1114.53	1.16	P2 ₁ /c	21.87	6.93	11.45	90.00	140.03	90.00	67.20	0.00
601	-103.63	4.46	554.71	1.16	P2 ₁	8.27	6.76	14.74	90.00	137.67	90.00	67.60	0.00
231	-103.49	4.60	565.57	1.14	P-1	13.76	6.85	6.65	78.56	67.68	91.03	66.30	5.00
589	-103.30	4.79	1105.72	1.17	P2 ₁ 2 ₁ 2 ₁	19.73	8.26	6.78	90.00	90.00	90.00	68.00	0.00
11	-103.14	4.95	2236.20	1.15	C2/c	28.41	6.88	11.45	90.00	92.23	90.00	67.00	0.00
306	-103.13	4.96	559.07	1.15	P-1	15.66	6.71	6.55	60.32	86.18	70.42	67.00	0.00
22	-103.12	4.97	2241.89	1.15	C2/c	24.23	6.65	15.31	90.00	65.37	90.00	66.90	6.21
998	-103.03	5.05	2190.95	1.18	Pbca	12.47	11.54	15.22	90.00	90.00	90.00	68.50	0.00
448	-102.96	5.13	554.76	1.16	P-1	6.92	7.92	15.25	45.72	75.99	68.00	67.50	5.01
960	-102.96	5.13	2166.78	1.19	Pbca	23.99	8.42	10.72	90.00	90.00	90.00	69.20	0.00
954	-102.90	5.19	1128.64	1.14	P2 ₁ /c	6.79	22.30	8.66	90.00	59.41	90.00	66.40	0.00
996	-102.71	5.38	2204.11	1.17	Pbca	16.37	11.92	11.29	90.00	90.00	90.00	68.20	0.00
932	-102.65	5.44	1117.52	1.15	P2 ₁ /c	6.80	11.53	16.49	90.00	120.18	90.00	67.00	0.00
531	-102.49	5.60	553.47	1.17	P-1	17.49	8.73	6.61	96.93	105.94	138.42	67.70	0.00

44	-102.29	5.80	2193.68	1.18	C2/c	25.20	7.72	11.45	90.00	79.88	90.00	68.40	0.00
955	-102.20	5.89	2226.39	1.16	Pbca	11.51	22.12	8.74	90.00	90.00	90.00	67.30	0.00
952	-102.00	6.09	1170.49	1.10	P2 ₁ /c	12.14	6.83	14.24	90.00	97.29	90.00	64.00	9.75
956	-101.99	6.10	2254.57	1.14	Pbca	28.69	6.86	11.46	90.00	90.00	90.00	66.50	0.00
824	-101.89	6.20	1130.88	1.14	P2 ₁ /c	8.09	12.13	16.85	90.00	136.87	90.00	66.30	0.00
152	-101.72	6.37	568.97	1.13	P-1	13.09	7.76	6.99	71.77	62.91	65.50	65.80	2.90
380	-101.70	6.39	565.03	1.14	P-1	7.22	15.74	8.35	50.19	60.43	89.27	66.30	4.00
923	-101.60	6.49	1144.82	1.13	P2 ₁ /c	6.68	25.41	8.70	90.00	129.19	90.00	65.30	7.19
959	-101.59	6.50	2144.34	1.20	Pbca	26.20	7.30	11.21	90.00	90.00	90.00	70.10	0.00
391	-101.56	6.53	562.96	1.15	P-1	7.14	14.97	6.91	83.43	54.94	69.65	66.60	0.00
65	-101.55	6.53	2256.53	1.14	C2/c	12.24	6.50	33.33	90.00	121.65	90.00	66.30	0.00
16	-101.48	6.61	2249.49	1.15	C2/c	15.22	6.87	23.32	90.00	112.80	90.00	66.50	3.50
957	-101.46	6.63	2283.38	1.13	Pbca	25.47	8.82	10.17	90.00	90.00	90.00	65.60	7.46
899	-101.44	6.64	1075.90	1.20	P2 ₁ /c	13.65	7.08	11.36	90.00	101.54	90.00	69.90	0.00
817	-101.39	6.70	1116.18	1.16	P2 ₁ /c	14.24	6.78	11.56	90.00	90.86	90.00	67.20	0.00
5	-101.38	6.71	2287.33	1.13	C2/c	15.80	6.61	22.55	90.00	76.37	90.00	65.50	4.06
2	-101.37	6.72	2262.82	1.14	C2/c	11.94	8.71	22.59	90.00	105.52	90.00	66.30	0.00
513	-101.31	6.78	546.96	1.18	P-1	8.40	10.29	8.88	81.55	46.25	81.71	68.50	0.00
968	-101.04	7.05	2228.48	1.16	Pbca	13.54	11.72	14.04	90.00	90.00	90.00	67.10	0.00
902	-101.04	7.05	1137.18	1.13	P2 ₁ /c	6.83	29.54	6.67	90.00	122.27	90.00	65.90	0.00
593	-100.97	7.12	1172.01	1.10	P2 ₁ 2 ₁ 2 ₁	6.98	6.74	24.93	90.00	90.00	90.00	64.00	11.46
969	-100.74	7.34	2240.50	1.15	Pbca	6.78	11.48	28.80	90.00	90.00	90.00	67.00	0.00
7	-100.69	7.40	2236.77	1.15	C2/c	17.76	14.70	10.94	90.00	51.59	90.00	67.10	3.92
68	-100.57	7.52	2195.35	1.18	C2/c	18.46	8.36	14.25	90.00	87.60	90.00	68.40	0.00
26	-100.46	7.63	2262.38	1.14	C2/c	15.17	6.82	22.60	90.00	104.67	90.00	66.20	5.27
619	-100.37	7.72	587.61	1.10	P2 ₁	12.57	6.95	6.73	90.00	86.87	90.00	63.80	11.40
891	-100.35	7.74	1120.23	1.15	P2 ₁ /c	7.02	14.74	11.63	90.00	111.49	90.00	66.90	0.00
746	-100.30	7.79	1143.70	1.13	P2 ₁ /c	6.63	11.85	16.63	90.00	118.92	90.00	65.60	6.67
15	-100.21	7.88	2199.36	1.17	C2/c	15.86	6.78	20.74	90.00	80.61	90.00	68.10	2.67
872	-100.11	7.98	1130.05	1.14	P2 ₁ /c	6.58	10.91	15.88	90.00	97.32	90.00	66.30	0.00
963	-100.03	8.06	2254.15	1.14	Pbca	10.30	22.23	9.84	90.00	90.00	90.00	66.50	0.00
921	-100.01	8.08	1145.31	1.13	P2 ₁ /c	6.64	14.58	13.40	90.00	62.04	90.00	65.60	6.84
772	-99.87	8.21	1155.57	1.12	P2 ₁ /c	20.01	7.18	12.05	90.00	138.12	90.00	64.80	11.66
733	-99.83	8.26	1127.69	1.14	P2 ₁ /c	8.35	12.77	11.22	90.00	70.65	90.00	66.40	0.00
425	-99.83	8.26	570.74	1.13	P-1	8.71	15.49	6.69	133.04	63.99	118.60	65.70	9.69

30	-99.68	8.41	2174.58	1.19	C2/c	31.34	7.07	11.40	90.00	120.53	90.00	69.10	0.00
346	-99.67	8.42	567.01	1.14	P-1	7.02	15.04	6.57	74.12	58.11	81.25	66.00	0.00
962	-99.63	8.46	2245.60	1.15	Pbca	22.79	8.51	11.57	90.00	90.00	90.00	66.80	0.00
859	-99.53	8.56	1105.11	1.17	P2 ₁ /c	12.44	12.55	12.75	90.00	33.70	90.00	67.90	0.00
53	-99.42	8.66	2280.03	1.13	C2/c	17.01	12.84	11.84	90.00	61.78	90.00	65.70	5.43
999	-99.40	8.69	2242.35	1.15	Pbca	10.78	22.06	9.43	90.00	90.00	90.00	66.80	0.00
883	-99.39	8.70	1146.46	1.13	P2 ₁ /c	11.90	6.69	15.70	90.00	113.45	90.00	65.50	9.33
938	-99.38	8.71	1132.30	1.14	P2 ₁ /c	6.86	22.50	8.36	90.00	118.54	90.00	66.10	0.00
33	-99.36	8.73	2235.43	1.15	C2/c	29.54	6.52	11.62	90.00	92.67	90.00	67.10	0.00
328	-99.36	8.73	573.51	1.13	P-1	7.98	11.39	6.65	77.89	91.99	76.73	65.40	5.25
710	-99.31	8.77	1126.23	1.15	P2 ₁ /c	11.34	9.65	10.78	90.00	107.28	90.00	66.60	0.00
961	-99.27	8.81	2260.64	1.14	Pbca	12.84	11.05	15.94	90.00	90.00	90.00	66.30	0.00
882	-99.24	8.85	1148.70	1.12	P2 ₁ /c	6.50	28.25	7.15	90.00	118.84	90.00	65.20	0.00
17	-99.19	8.90	2280.70	1.13	C2/c	11.12	7.03	33.98	90.00	120.88	90.00	65.60	3.02
904	-99.16	8.93	1199.03	1.08	P2 ₁ /c	6.93	15.44	13.33	90.00	57.28	90.00	62.40	12.58
735	-99.11	8.97	1130.94	1.14	P2 ₁ /c	14.57	11.26	16.12	90.00	25.32	90.00	66.20	0.00
273	-98.93	9.15	571.50	1.13	P-1	7.85	6.67	11.92	80.56	68.33	87.24	65.50	4.93
66	-98.93	9.16	2239.86	1.15	C2/c	22.85	8.65	11.36	90.00	86.15	90.00	67.00	1.31
966	-98.88	9.21	2337.89	1.10	Pbca	15.98	12.08	12.11	90.00	90.00	90.00	64.10	5.94
4	-98.79	9.30	2300.02	1.12	C2/c	11.27	6.78	30.91	90.00	76.95	90.00	65.10	3.06
184	-98.78	9.31	564.00	1.14	P-1	6.61	11.67	14.34	136.02	123.36	83.18	66.40	6.44
12	-98.74	9.35	2330.18	1.11	C2/c	28.86	7.09	12.12	90.00	109.94	90.00	64.30	10.71
911	-98.63	9.46	1173.56	1.10	P2 ₁ /c	16.19	7.07	12.82	90.00	53.13	90.00	63.80	7.42
10	-98.60	9.49	2324.98	1.11	C2/c	30.58	6.73	11.58	90.00	102.73	90.00	64.50	5.15
887	-98.54	9.55	1162.95	1.11	P2 ₁ /c	15.13	6.73	11.58	90.00	80.78	90.00	64.40	5.05
950	-98.51	9.58	1124.78	1.15	P2 ₁ /c	7.76	21.55	7.04	90.00	72.98	90.00	66.50	0.00
13	-98.51	9.58	2299.62	1.12	C2/c	15.73	6.68	23.89	90.00	113.62	90.00	65.20	9.97
19	-98.39	9.70	2338.96	1.10	C2/c	27.37	7.22	12.14	90.00	77.25	90.00	64.00	11.44
386	-98.38	9.71	579.18	1.11	P-1	14.88	8.40	6.99	113.43	109.44	115.12	64.70	5.32
983	-98.24	9.85	2179.48	1.18	Pbca	15.92	20.24	6.76	90.00	90.00	90.00	68.90	0.00
428	-97.89	10.20	572.58	1.13	P-1	6.75	13.87	8.70	51.51	64.02	73.28	65.40	2.27

Table S2: Predicted lattice energy minima for 1-adamantaneacetic acid (**1**) within a relative lattice energy range of 10 kJ mol⁻¹ with respect to the global minimum structure.

Structure ID	E _{latt} /kJ mol ⁻¹	Relative E _{latt} /kJ mol ⁻¹	Volume /Å ³	Density /g cm ⁻³	Space Group	a / Å	b / Å	c / Å	α / °	β / °	γ / °	Packing Index / %	Solvent Accessible Volume per Unit Cell / %
126	-103.78	0.00	369.22	1.28	P-1	12.34	7.08	5.92	100.69	99.74	128.59	69.80	0.00
498	-103.40	0.38	366.32	1.29	P-1	12.75	6.85	5.52	67.00	116.73	119.18	70.50	0.00
40	-103.37	0.41	1478.96	1.28	C2/c	12.62	5.50	22.41	90.00	71.81	90.00	69.80	0.00
945	-102.66	1.11	718.54	1.31	P2 ₁ /c	6.89	6.64	28.48	90.00	146.53	90.00	72.00	0.00
992	-101.85	1.93	1487.49	1.27	Pbca	16.41	8.25	10.99	90.00	90.00	90.00	69.50	0.00
790	-101.62	2.15	753.28	1.25	P2 ₁ /c	15.53	5.81	12.09	90.00	136.40	90.00	68.40	0.00
920	-101.50	2.28	743.16	1.27	P2 ₁ /c	5.46	21.71	6.85	90.00	66.35	90.00	69.40	0.00
380	-101.32	2.46	372.13	1.27	P-1	11.04	6.24	6.92	126.96	87.86	100.74	69.40	0.00
110	-101.08	2.70	362.68	1.30	P-1	7.14	12.71	5.48	65.99	53.10	78.29	71.20	0.00
953	-100.87	2.91	729.98	1.29	P2 ₁ /c	6.13	12.23	10.11	90.00	74.52	90.00	70.70	0.00
913	-100.58	3.20	775.89	1.22	P2 ₁ /c	7.02	10.29	10.92	90.00	100.58	90.00	66.40	0.00
561	-100.56	3.21	355.00	1.33	P2 ₁	10.80	6.25	6.38	90.00	55.58	90.00	72.90	0.00
441	-100.44	3.34	375.26	1.26	P-1	6.31	10.28	6.26	79.37	109.67	94.90	68.80	0.00
797	-100.18	3.59	749.38	1.26	P2 ₁ /c	5.17	22.81	6.64	90.00	106.85	90.00	68.90	0.00
642	-100.11	3.66	721.65	1.31	P2 ₁ 2 ₁ 2 ₁	22.93	6.63	4.75	90.00	90.00	90.00	71.70	0.00
915	-100.08	3.70	779.70	1.21	P2 ₁ /c	6.16	23.26	5.95	90.00	66.14	90.00	66.10	8.94
269	-100.05	3.73	387.64	1.22	P-1	5.83	6.22	12.17	91.90	82.54	117.45	66.60	4.51
940	-100.00	3.77	750.47	1.26	P2 ₁ /c	6.51	22.49	6.10	90.00	57.06	90.00	68.80	0.00
1	-99.90	3.88	1556.10	1.21	C2/c	11.01	5.82	24.29	90.00	91.75	90.00	66.30	5.80
993	-99.88	3.90	1550.42	1.22	Pbca	22.75	5.90	11.56	90.00	90.00	90.00	66.50	0.00
396	-99.75	4.03	383.86	1.23	P-1	6.59	6.60	11.68	116.68	111.02	101.06	67.30	4.35
916	-99.73	4.05	759.64	1.24	P2 ₁ /c	7.63	12.60	10.21	90.00	50.65	90.00	68.10	0.00
43	-99.43	4.35	1478.65	1.28	C2/c	12.56	5.46	27.46	90.00	51.69	90.00	70.00	0.00
994	-99.42	4.35	1568.27	1.20	Pbca	5.84	24.42	10.99	90.00	90.00	90.00	65.80	0.00
128	-99.11	4.66	375.39	1.26	P-1	6.47	7.13	9.02	85.92	112.23	102.73	68.80	0.00
763	-98.99	4.79	778.81	1.21	P2 ₁ /c	6.74	9.69	13.19	90.00	115.31	90.00	66.30	0.00
12	-98.96	4.82	1530.69	1.23	C2/c	23.05	5.29	28.83	90.00	25.84	90.00	67.40	0.00
5	-98.94	4.84	1565.44	1.21	C2/c	11.53	6.73	20.45	90.00	99.70	90.00	65.90	3.99
600	-98.90	4.88	376.49	1.25	P2 ₁	5.51	7.01	11.69	90.00	56.46	90.00	68.90	0.00

661	-98.87	4.91	774.62	1.22	P2 ₁ 2 ₁ 2 ₁	17.42	6.11	7.28	90.00	90.00	90.00	66.70	0.00
956	-98.81	4.96	773.12	1.22	P2 ₁ /c	7.05	10.95	12.79	90.00	51.57	90.00	66.80	0.00
652	-98.76	5.01	755.75	1.25	P2 ₁ 2 ₁ 2 ₁	5.48	19.60	7.03	90.00	90.00	90.00	68.50	0.00
452	-98.73	5.05	396.59	1.19	P-1	6.57	6.63	12.29	63.78	62.52	60.28	65.20	0.00
35	-98.61	5.16	1518.93	1.24	C2/c	16.01	9.40	13.72	90.00	47.38	90.00	68.10	0.00
8	-98.58	5.20	1571.67	1.20	C2/c	11.66	6.62	20.39	90.00	87.02	90.00	65.90	0.00
25	-98.51	5.27	1536.84	1.23	C2/c	10.17	7.23	21.17	90.00	80.78	90.00	67.10	0.00
6	-98.41	5.36	1532.94	1.23	C2/c	10.54	8.38	19.44	90.00	116.77	90.00	67.50	4.58
451	-98.22	5.56	374.29	1.26	P-1	11.57	5.50	6.23	90.57	109.23	89.85	69.00	0.00
809	-98.15	5.63	762.07	1.24	P2 ₁ /c	6.13	12.42	11.05	90.00	64.84	90.00	67.70	0.00
818	-98.13	5.64	751.10	1.26	P2 ₁ /c	6.49	4.97	24.39	90.00	107.28	90.00	68.80	0.00
803	-98.05	5.73	733.58	1.29	P2 ₁ /c	5.46	10.90	15.10	90.00	125.17	90.00	70.40	0.00
831	-97.98	5.80	782.81	1.21	P2 ₁ /c	5.92	20.40	8.36	90.00	50.83	90.00	66.10	0.00
469	-97.94	5.83	379.96	1.24	P-1	5.50	7.02	9.87	85.80	87.51	90.02	68.10	0.00
837	-97.89	5.89	722.37	1.31	P2 ₁ /c	6.35	17.91	6.35	90.00	88.98	90.00	71.70	0.00
9	-97.75	6.03	1565.48	1.21	C2/c	23.56	6.36	10.45	90.00	91.81	90.00	65.90	6.88
998	-97.70	6.08	1603.67	1.18	Pbca	12.59	11.53	11.05	90.00	90.00	90.00	64.40	0.00
860	-97.53	6.24	764.08	1.24	P2 ₁ /c	4.99	23.40	8.32	90.00	51.85	90.00	67.60	0.00
866	-97.49	6.29	767.86	1.23	P2 ₁ /c	5.13	23.59	7.21	90.00	118.34	90.00	67.30	0.00
942	-97.45	6.33	758.52	1.24	P2 ₁ /c	5.54	6.99	22.98	90.00	121.47	90.00	68.30	0.00
929	-97.42	6.36	749.80	1.26	P2 ₁ /c	6.83	14.52	8.61	90.00	118.61	90.00	68.80	0.00
888	-97.27	6.50	765.20	1.23	P2 ₁ /c	4.84	23.86	6.63	90.00	91.21	90.00	67.50	0.00
34	-97.23	6.54	1609.44	1.17	C2/c	23.47	6.57	25.21	90.00	155.54	90.00	64.10	1.80
30	-97.18	6.60	1560.46	1.21	C2/c	11.38	6.80	27.68	90.00	46.74	90.00	66.30	3.51
897	-97.04	6.73	754.20	1.25	P2 ₁ /c	6.83	21.49	6.15	90.00	123.38	90.00	68.50	0.00
784	-96.98	6.79	775.69	1.22	P2 ₁ /c	5.56	22.21	6.97	90.00	115.67	90.00	66.70	0.00
7	-96.78	7.00	1496.96	1.26	C2/c	24.08	5.01	12.70	90.00	77.84	90.00	69.10	0.00
673	-96.75	7.03	386.50	1.22	P2 ₁	12.23	5.46	7.03	90.00	55.32	90.00	67.00	0.00
799	-96.71	7.07	781.16	1.21	P2 ₁ /c	11.53	5.42	12.95	90.00	105.19	90.00	66.20	0.00
13	-96.68	7.10	1501.39	1.26	C2/c	10.62	8.36	17.48	90.00	75.20	90.00	69.00	0.00
987	-96.68	7.10	1558.48	1.21	Pbca	10.49	12.98	11.45	90.00	90.00	90.00	66.20	0.00

656	-96.62	7.15	772.89	1.22	P2 ₁ 2 ₁ 2 ₁	5.50	7.00	20.08	90.00	90.00	90.00	66.90	0.00
996	-96.55	7.23	1582.88	1.19	Pbca	5.91	11.47	23.37	90.00	90.00	90.00	65.10	6.24
930	-96.44	7.34	759.97	1.24	P2 ₁ /c	7.11	8.92	15.23	90.00	128.13	90.00	67.90	0.00
27	-96.24	7.53	1522.90	1.24	C2/c	8.41	11.15	16.86	90.00	105.69	90.00	67.80	0.00
828	-96.15	7.63	743.98	1.27	P2 ₁ /c	11.98	4.82	13.41	90.00	106.32	90.00	69.50	0.00
948	-96.14	7.64	750.04	1.26	P2 ₁ /c	7.20	7.16	15.18	90.00	106.83	90.00	68.90	0.00
909	-96.03	7.75	763.14	1.24	P2 ₁ /c	5.91	11.41	11.34	90.00	86.56	90.00	67.90	3.32
28	-96.02	7.75	1593.49	1.19	C2/c	18.57	6.61	13.17	90.00	80.07	90.00	64.90	5.40
933	-95.89	7.89	748.95	1.26	P2 ₁ /c	9.01	9.19	11.05	90.00	54.94	90.00	69.20	0.00
42	-95.87	7.91	1536.53	1.23	C2/c	11.28	6.87	20.19	90.00	78.96	90.00	67.40	3.09
560	-95.62	8.15	377.41	1.25	P2 ₁	7.50	4.90	12.64	90.00	125.60	90.00	68.60	0.00
810	-95.55	8.22	754.05	1.25	P2 ₁ /c	5.28	13.17	12.32	90.00	118.25	90.00	68.60	0.00
838	-95.47	8.31	805.81	1.17	P2 ₁ /c	6.48	11.41	11.86	90.00	113.32	90.00	64.20	0.00
852	-95.44	8.34	775.84	1.22	P2 ₁ /c	7.00	20.29	8.95	90.00	142.34	90.00	66.70	0.00
19	-95.40	8.37	1570.62	1.20	C2/c	8.28	10.01	19.94	90.00	71.77	90.00	65.90	1.83
686	-95.35	8.43	367.95	1.28	P2 ₁	12.02	4.85	6.52	90.00	75.34	90.00	70.40	0.00
904	-95.34	8.43	750.06	1.26	P2 ₁ /c	11.75	6.05	11.75	90.00	116.09	90.00	69.10	0.00
39	-95.32	8.46	1587.06	1.19	C2/c	10.40	8.92	17.77	90.00	74.28	90.00	65.20	0.00
644	-95.29	8.48	756.39	1.25	P2 ₁ 2 ₁ 2 ₁	20.61	4.90	7.50	90.00	90.00	90.00	68.50	0.00
862	-95.25	8.52	753.76	1.25	P2 ₁ /c	8.99	6.65	12.88	90.00	102.10	90.00	68.70	0.00
24	-95.11	8.67	1633.90	1.16	C2/c	11.37	24.24	5.93	90.00	89.55	90.00	63.10	7.39
658	-95.05	8.73	746.95	1.26	P2 ₁ 2 ₁ 2 ₁	12.33	5.49	11.04	90.00	90.00	90.00	69.20	0.00
947	-94.86	8.91	774.33	1.22	P2 ₁ /c	5.55	19.84	8.99	90.00	51.53	90.00	66.90	0.00
645	-94.86	8.92	732.81	1.29	P2 ₁ 2 ₁ 2 ₁	10.46	11.15	6.29	90.00	90.00	90.00	70.60	0.00
768	-94.80	8.98	789.81	1.20	P2 ₁ /c	6.69	20.22	6.91	90.00	122.37	90.00	65.30	0.00
20	-94.80	8.98	1504.84	1.25	C2/c	11.50	6.09	21.53	90.00	93.93	90.00	68.90	0.00
648	-94.77	9.00	745.13	1.27	P2 ₁ 2 ₁ 2 ₁	14.98	4.83	10.29	90.00	90.00	90.00	69.30	0.00
887	-94.61	9.16	794.54	1.19	P2 ₁ /c	6.98	11.58	11.05	90.00	62.79	90.00	65.00	0.00
894	-94.48	9.29	750.13	1.26	P2 ₁ /c	6.70	8.03	14.14	90.00	99.53	90.00	69.00	0.00
795	-94.30	9.48	774.73	1.22	P2 ₁ /c	12.68	8.74	7.08	90.00	80.64	90.00	66.60	0.00

10	-94.28	9.50	1476.52	1.28	C2/c	24.29	5.81	10.51	90.00	94.97	90.00	70.00	0.00
17	-94.23	9.55	1513.24	1.25	C2/c	10.88	8.43	31.10	90.00	32.05	90.00	68.30	0.00
1000	-94.11	9.67	1543.95	1.22	Pbca	8.62	15.00	11.94	90.00	90.00	90.00	67.10	0.00
657	-94.08	9.70	764.43	1.24	P2 ₁ 2 ₁ 2 ₁	8.92	6.98	12.28	90.00	90.00	90.00	67.90	0.00
864	-94.00	9.77	753.78	1.25	P2 ₁ /c	8.85	10.23	10.36	90.00	126.57	90.00	68.60	0.00
756	-93.86	9.92	768.38	1.23	P2 ₁ /c	5.88	9.91	13.20	90.00	87.19	90.00	67.30	0.00
900	-93.80	9.97	802.64	1.18	P2 ₁ /c	6.69	13.78	11.68	90.00	131.82	90.00	64.40	0.00
863	-93.80	9.97	776.34	1.22	P2 ₁ /c	6.54	19.75	7.04	90.00	121.46	90.00	66.70	0.00
995	-93.68	10.10	1495.93	1.26	Pbca	21.02	6.22	11.44	90.00	90.00	90.00	69.20	0.00

Table S3: Predicted lattice energy minima for 4-oxocyclohexanecarboxylic acid (**3**) within a relative lattice energy range of 10 kJ mol⁻¹ with respect to the global minimum structure.

Structure ID	$E_{\text{latt}}/\text{kJ mol}^{-1}$	Relative $E_{\text{latt}}/\text{kJ mol}^{-1}$	Volume / $\text{\AA}^3$	Density / g cm^{-3}	Space Group	$a / \text{\AA}$	$b / \text{\AA}$	$c / \text{\AA}$	$\alpha / ^\circ$	$\beta / ^\circ$	$\gamma / ^\circ$	Packing Index / %	Solvent Accessible Volume per Unit Cell / %
904	-145.85	0.00	734.66	1.66	P2 ₁ /c	11.09	11.86	5.88	90.00	108.09	90.00	73.50	0.00
993	-144.98	0.87	1485.19	1.65	Pbca	11.84	5.80	21.64	90.00	90.00	90.00	72.50	0.00
43	-144.40	1.45	1485.38	1.65	C2/c	17.10	10.80	11.85	90.00	137.28	90.00	72.70	0.00
312	-144.23	1.62	387.78	1.58	P-1	9.56	8.17	6.17	96.85	57.03	81.44	69.60	10.24
787	-143.41	2.44	744.60	1.64	P2 ₁ /c	5.81	11.87	12.26	90.00	61.71	90.00	72.70	0.00
995	-143.22	2.63	1466.55	1.67	Pbca	15.33	8.93	10.72	90.00	90.00	90.00	73.80	0.00
8	-143.07	2.78	1565.23	1.56	C2/c	16.82	5.95	16.02	90.00	77.34	90.00	68.60	9.85
997	-142.52	3.32	1502.80	1.63	Pbca	10.78	15.56	8.96	90.00	90.00	90.00	71.80	0.00
46	-141.78	4.07	1476.40	1.66	C2/c	28.92	5.60	10.72	90.00	121.68	90.00	73.20	0.00
788	-141.63	4.22	714.52	1.71	P2 ₁ /c	5.60	6.38	25.29	90.00	127.81	90.00	76.00	0.00
762	-141.21	4.64	730.84	1.67	P2 ₁ /c	5.95	15.74	9.17	90.00	58.39	90.00	73.80	0.00
987	-140.67	5.18	732.41	1.67	P2 ₁ /c	5.65	14.36	10.65	90.00	58.02	90.00	73.80	0.00
982	-139.88	5.97	719.81	1.70	P2 ₁ /c	7.90	9.82	10.60	90.00	118.87	90.00	75.10	0.00
763	-139.69	6.16	724.22	1.69	P2 ₁ /c	9.06	5.13	25.73	90.00	37.27	90.00	74.40	0.00
798	-138.99	6.86	757.20	1.61	P2 ₁ /c	8.12	5.82	18.26	90.00	118.78	90.00	71.20	0.00
382	-138.71	7.14	357.27	1.71	P-1	6.96	12.68	4.22	89.49	85.61	74.31	75.60	0.00
420	-138.49	7.35	357.63	1.71	P-1	6.97	13.50	4.23	110.08	85.48	106.65	75.50	0.00
781	-138.32	7.52	737.86	1.66	P2 ₁ /c	7.87	6.38	19.21	90.00	49.96	90.00	73.30	0.00
892	-137.33	8.52	766.09	1.60	P2 ₁ /c	5.79	16.80	7.95	90.00	97.81	90.00	70.30	0.00
409	-136.74	9.10	360.35	1.70	P-1	7.92	8.09	5.67	90.00	89.99	97.05	75.20	0.00
809	-136.70	9.15	720.66	1.70	P2 ₁ /c	8.09	5.67	15.84	90.00	97.05	90.00	75.30	0.00
977	-135.63	10.21	755.07	1.62	P2 ₁ /c	9.60	5.38	16.27	90.00	64.00	90.00	71.80	5.18

Table S4: Predicted lattice energy minima for 2-pyrone-4,6-dicarboxylic acid (**4**) within a relative lattice energy range of 10 kJ mol⁻¹ with respect to the global minimum structure.