Electronic Supplementary Material (ESI) for CrystEngComm.

Supporting Information – Crystal-Energy Landscapes of Active Pharmaceutical Ingredients Using Composite Approaches

Luc M. LeBlanc* and Erin R. Johnson*

Department of Chemistry, Dalhousie University, 6274 Coburg Rd, Halifax, Nova Scotia, B3H 4R2, Canada

E-mail: luc.leblanc@dal.ca; erin.johnson@dal.ca

Contents: Relative energies and densities of crystal structures from the CSP studies of 5-fluorouracil, naproxen, carbamazepine, and olanzapine.

Table 1: Relative energies, in kJ/mol per molecule, and unit-cell densities, ρ, in g/cm^3, of the lowest-energy crystal structures of 5-fluorouracil determined by a force field from a previously conducted CSP study [1] (FF; A), and fully relaxed/reranked using B86bPBE-XDM as implemented in Quantum ESPRESSO (PAW; A), B86bPBE-XDM/DZP (SIESTA; A), and sHF-3c (CRYSTAL17; A). Single-point energy calculations performed on low-cost geometries using plane-wave B86bPBE-XDM/PAW or small-basis B86bPBE-XDM/DZP are also tabulated (B//A and C//A, respectively). Energies and densities are relative to OPT_eo1, i.e., the CPOSS [2] database structure identified to be equivalent to the experimental Form-I polymorph; this structure and the other identified to be equivalent to the experimental Form-II polymorph (OPT_am75) are highlighted.

no	structure	FF				SIESTA			CRYSTAL17			PAW	
		A	B//A	C//A	ρ	A	B//A	ρ	A	B//A	ρ	A	ρ
1	OPT_ab13	-1.3	4.2	5.8	0.0803	7.9	7.2	0.0443	-4.5	6.2	-0.0531	6.7	0.0198
2	OPT_ab94	-1.7	7.6	9.9	0.0819	10.0	8.9	-0.0036	3.8	10.0	-0.0683	7.7	-0.0208
3	OPT_ab98	-1.4	7.4	10.5	0.0772	12.5	11.0	-0.0125	-4.5	6.3	-0.0538	11.4	-0.0122
4	OPT_ad11	0.9	10.6	12.6	0.0856	19.7	16.1	0.0335	16.8	18.2	-0.0465	16.2	0.0072
5	OPT_af51	0.1	9.8	12.4	0.1317	16.8	13.3	0.0779	8.9	16.2	-0.1632	13.1	0.0198
6	OPT_af57	0.2	7.4	8.9	0.0516	9.2	9.5	0.0069	-3.1	8.9	-0.1183	9.8	-0.0334
7	OPT_ai46	1.3	8.2	9.7	0.0733	13.3	10.8	0.0698	4.3	11.5	-0.0278	11.2	0.0395
8	OPT_ai61	1.5	10.6	15.7	0.0512	16.5	12.7	-0.0067	2.9	11.5	-0.1405	11.0	-0.0925
9	OPT_ai86	-1.2	5.8	8.0	0.0828	8.7	7.0	0.0244	2.2	7.1	-0.0150	6.6	0.0038
10	OPT_aj38	0.4	8.8	10.0	0.0467	11.0	10.9	-0.0096	1.6	12.6	-0.1457	10.6	-0.0494
11	OPT_ak24	-3.1	4.4	8.2	0.0668	9.8	7.6	0.0086	-4.5	6.3	-0.0687	6.7	-0.0329
12	OPT_ak3	-0.1	8.9	11.6	0.0866	13.8	11.4	0.0116	3.6	10.4	-0.1196	9.2	-0.0430
13	OPT_ak39	-1.2	6.8	8.0	0.0633	7.9	8.0	0.0273	-1.1	7.7	-0.0465	7.7	-0.0123
14	OPT_ak90	-2.7	4.3	7.0	0.0567	8.1	6.7	0.0209	-4.5	6.8	-0.0784	6.7	-0.0215
15	OPT_am108	-3.8	6.9	8.9	0.0771	9.7	7.7	-0.0462	-1.3	4.2	-0.0221	4.2	-0.0365
16	OPT_am115	-0.2	6.4	7.4	0.0660	12.3	10.9	0.0119	8.1	10.9	0.0388	11.5	-0.0041
17	OPT_am36	-2.2	4.1	4.2	0.0965	8.3	7.8	0.0496	7.3	8.5	0.0625	8.3	0.0390
18	OPT_am51	-2.5	3.6	6.2	0.0963	7.0	4.9	0.0323	0.4	4.6	0.0278	5.3	0.0184
19	OPT_am56	-5.8	-1.0	2.4	0.1051	4.1	2.2	0.0698	0.5	2.1	0.0678	2.7	0.0480
20	OPT_am64	-1.8	7.5	7.8	0.1210	12.2	11.4	0.0571	6.0	9.5	0.0660	11.2	0.0311
21	OPT_am69	1.0	4.2	8.0	-0.064	7.6	4.5	-0.1024	-0.9	4.0	-0.1024	4.0	-0.1134
22	OPT_am75	-5.9	-0.6	2.2	0.0940	4.3	1.9	0.0436	0.0	2.6	0.0557	2.4	0.0369
23	OPT_am76	1.2	10.0	13.1	0.1179	19.1	14.8	0.0732	5.4	10.2	-0.1605	7.6	-0.0894
24	OPT_am79	0.8	10.8	11.9	0.1371	16.1	14.0	0.0707	-0.9	4.0	-0.0997	4.0	-0.1131
25	OPT_am87	-1.2	3.9	5.6	0.0398	7.0	6.1	0.0086	0.4	4.7	0.0286	6.5	-0.0109
26	OPT_am93	-3.6	2.3	4.5	0.0662	7.1	3.7	-0.0076	-1.2	3.8	-0.0205	4.2	-0.0335
27	OPT_aq103	0.6	8.8	10.6	0.0317	12.1	11.0	-0.0258	-2.9	5.4	-0.0203	6.8	-0.0343
28	OPT_aq116	0.3	7.0	9.4	0.0858	14.2	11.0	0.0268	3.1	10.0	-0.0464	9.3	-0.0080
29	OPT_aq61	-2.4	5.1	8.0	0.0539	8.6	6.2	-0.0094	-2.8	7.8	-0.0710	6.8	-0.0358
30	OPT_aq62	1.6	9.0	12.0	0.1162	15.8	12.0	0.0797	11.2	13.3	-0.0635	11.5	0.0579
31	OPT_aq90	-2.0	5.5	7.9	0.0429	8.4	7.3	-0.0143	-2.2	8.4	-0.0926	7.0	-0.0282
32	OPT_av24	1.4	7.8	10.5	0.0631	11.8	9.0	-0.0141	8.8	8.6	-0.0591	8.8	-0.0541
33	OPT_av32	0.2	6.7	6.8	0.1050	12.2	10.5	0.0748	4.3	10.0	-0.1199	11.4	0.0550
34	OPT_av64	-0.8	5.5	7.8	0.0315	8.9	7.2	-0.0414	-2.5	8.1	-0.0840	7.9	-0.0710
35	OPT_av86	1.9	10.8	12.0	0.0917	15.5	13.3	0.0229	8.8	8.5	-0.0537	8.8	-0.0501
36	OPT_ay76	1.2	11.0	14.0	0.1107	18.2	14.2	0.0767	10.1	19.9	-0.2487	13.2	0.0302
37	OPT_az50	1.4	11.9	14.6	0.1250	18.3	14.8	0.0669	9.1	17.0	-0.1760	12.9	0.0301
38	OPT_ca13	-3.9	6.2	8.9	0.1152	9.1	8.3	0.0238	-4.5	6.2	-0.0561	8.7	0.0078
39	OPT_ca23	0.1	9.0	12.0	0.1032	15.7	12.8	0.0443	3.7	9.4	-0.0610	12.3	-0.0178
40	OPT_ca33	-3.6	2.9	6.3	0.0634	7.1	5.2	0.0314	-4.5	6.2	-0.0544	5.6	0.0119
41	OPT_cd3	0.6	9.6	11.8	0.0824	18.1	14.5	0.0398	4.3	16.2	-0.2525	13.6	0.0263
42	OPT_cd39	0.2	9.6	10.4	0.0712	13.9	12.5	0.0133	9.6	10.2	0.0343	11.4	0.0155
43	OPT_ce23	0.3	7.3	9.4	0.0499	11.3	9.9	0.0082	1.9	14.9	-0.2917	10.1	-0.0317
44	OPT_dc71	-2.2	3.2	6.6	0.0409	8.0	5.4	0.0257	-2.0	5.8	-0.0365	5.8	-0.0071
45	OPT_dd13	0.6	9.6	10.5	0.0345	12.8	12.7	-0.0434	23.2	33.2	-0.2542	13.0	-0.0865
46	OPT_dd26	-0.5	8.5	11.7	0.0662	17.0	13.2	0.0131	15.2	19.5	-0.1515	12.8	-0.0353
47	OPT_dd73	-0.8	7.1	8.1	0.0861	10.3	10.0	0.0258	2.2	12.1	-0.1229	10.1	-0.0185
48	OPT_de24	-0.5	8.2	7.9	0.0668	9.1	10.1	-0.0049	1.3	11.2	-0.1225	10.1	-0.0188
49	OPT_de33	-1.2	8.0	10.1	0.0751	14.7	12.2	0.0064	3.5	15.8	-0.2637	11.7	-0.0277
50	OPT_de93	-0.8	7.0	6.7	0.0601	8.3	9.6	0.0010	0.4	11.6	-0.1357	9.0	-0.0257
51	OPT_eo1	0.0	0.0	0.0	0.0000	0.0	0.0	0.0000	0.0	0.0	0.0000	0.0	0.0000
52	OPT_fa20	-1.9	7.0	9.6	0.0793	14.5	11.4	0.0387	1.6	14.9	-0.2885	11.0	-0.0010
53	OPT_fa30	0.0	6.5	8.8	0.0765	11.5	9.7	0.0420	1.2	14.2	-0.2860	9.9	-0.0150
54	OPT_fa47	-2.4	4.0	5.6	0.0390	6.4	5.0	-0.0163	-3.4	4.5	-0.0070	5.6	-0.0339
55	OPT_fa5	-0.1	7.5	9.0	0.0877	12.3	11.2	0.0564	1.5	15.3	-0.4084	10.4	0.0085
56	OPT_fa56	1.0	12.3	14.5	0.1066	22.2	18.5	0.0452	8.2	14.7	-0.2657	10.7	0.0235
57	OPT_fc19	-1.9	4.4	7.9	0.0447	9.0	6.9	0.0061	-4.5	6.7	-0.0723	7.1	-0.0248
58	OPT_fc25	-0.5	4.0	7.1	0.0989	8.9	6.3	0.0862	3.3	6.4	0.0643	7.0	0.0595
59	OPT_fc34	-0.2	7.4	10.6	0.1082	15.4	11.3	0.0975	3.4	14.2	-0.2525	10.2	-0.0028
60	OPT_fc59	-0.1	4.3	7.2	0.0833	11.0	7.9	0.0282	3.2	10.2	-0.0424	8.2	0.0356
61	OPT_fc65	-0.6	8.9	11.0	0.1109	16.0	13.4	0.0873	3.5	15.0	-0.3693	11.2	-0.0451
62	OPT_fc86	-0.2	6.6	7.1	0.0670	9.2	9.5	0.0230	-2.6	9.5	-0.1241	9.6	-0.0258

Table 2: Relative energy differences, in kJ/mol per molecule, and unit-cell densities, ρ, in g/cm^3, of the lowest-energy enantiopure and racemate crystal structures of naproxen determined by a force field from a previously conducted CSP study [3] (FF; A), and fully relaxed/reranked using B86bPBE-XDM/DZP (SIESTA; A) and sHF-3c (CRYSTAL17; A). Single-point energy calculations performed on low-cost geometries using plane-wave B86bPBE-XDM/PAW or small-basis B86bPBE-XDM/DZP are also tabulated (B//A and C//A, respectively). Energies and densities are relative to dfCOS1_COS1, i.e., the CPOSS [2] database structure identified to be equivalent to the experimental enantiopure form; this structure and the one identified to be equivalent to the experimental racemate form (dfaf92_af92) are highlighted.

no	structure	FF				SIESTA			CRYSTAL17		
		A	B//A	C//A	ρ	A	B//A	ρ	A	B//A	ρ
1	dfab52_ab52	11.6	10.2	13.2	-0.0735	10.7	8.4	-0.0674	7.4	16.6	-0.0998
2	dfab70_ab70	11.5	10.7	12.2	-0.0546	13.3	13.3	-0.0562	-0.6	16.4	-0.0350
3	dfab99_ab99	11.9	15.0	13.9	-0.0571	11.3	14.1	-0.0792	5.9	17.8	-0.1098
4	dfab9_ab9	6.4	8.1	8.5	-0.0273	7.4	8.2	-0.0540	7.1	11.7	-0.0456
5	dfaf9_af9	8.2	0.6	-1.8	-0.0530	-1.9	-0.7	-0.0345	-2.2	0.8	-0.0348
6	dfai123_ai123	11.4	9.2	8.1	-0.0445	7.3	8.6	-0.0413	9.3	12.6	-0.0500
7	dfai12_ai12	9.5	5.1	3.3	-0.0599	2.9	4.5	-0.0442	-0.7	6.0	-0.0492
8	dfai43_ai43	12.3	9.5	9.4	-0.0864	7.2	8.7	-0.0776	8.8	16.2	-0.0971
9	dfaj49_aj49	22.6	23.1	22.6	-0.1224	22.3	23.6	-0.1266	16.7	26.2	-0.0987
10	dfak24_ak24	6.3	1.5	-0.1	-0.0504	-3.5	-0.3	-0.0369	1.6	2.8	-0.0429
11	dfak35_ak35	1.4	2.2	3.0	-0.0115	1.7	1.4	-0.0096	4.7	5.5	-0.0303
12	dfak52_ak52	11.3	5.9	3.9	-0.0315	0.6	3.6	-0.0301	6.6	12.5	-0.0702
13	dfak57_ak57	0.9	3.2	3.2	0.0035	3.3	3.7	-0.0176	4.0	6.3	-0.0112
14	dfak58_ak58	11.2	5.9	3.8	-0.0317	0.6	3.6	-0.0308	6.6	12.4	-0.0693
15	dfak63_ak63	8.4	2.8	2.3	-0.0718	-1.0	0.2	-0.0538	1.0	4.0	-0.0551
16	dfak86_ak86	12.9	10.9	11.0	-0.0679	8.9	9.3	-0.0687	11.3	14.2	-0.0912
17	dfam133_am133	7.6	13.5	11.2	-0.0628	8.8	12.6	-0.0798	11.2	16.1	-0.0817
18	dfam39_am39	6.1	7.5	9.9	0.0075	12.5	10.1	-0.0061	0.3	12.1	0.0083
19	dfam57_am57	5.9	7.5	9.9	0.0076	12.6	10.1	-0.0071	0.3	12.1	0.0082
20	dfam85_am85	3.8	5.4	4.5	-0.0164	4.3	5.2	-0.0268	7.1	9.3	-0.0375
21	dfaw48_aw48	9.4	10.4	12.3	-0.0008	15.5	13.4	-0.0100	2.1	15.2	0.0037
22	dfbh18_bh18	11.0	3.6	3.6	-0.0579	3.4	2.9	-0.0447	5.1	5.4	-0.0453
23	dfca102_ca102	8.6	8.2	6.8	-0.0481	5.3	8.3	-0.0728	8.1	12.2	-0.0636
24	dfca114_ca114	9.8	6.2	6.8	-0.0372	5.4	4.7	-0.0393	7.4	10.5	-0.0668
25	dfca13_ca13	8.1	8.3	7.5	-0.0476	5.5	8.0	-0.0764	8.1	12.2	-0.0637
26	dfca39_ca39	6.3	8.1	8.2	-0.0280	6.8	8.0	-0.0549	7.1	11.7	-0.0466
27	dfca69_ca69	9.6	7.1	8.8	-0.0419	7.3	5.6	-0.0391	3.7	10.3	-0.0398
28	dfca79_ca79	9.6	6.2	7.1	-0.0370	5.4	4.7	-0.0396	7.7	10.3	-0.0660
29	dfca84_ca84	9.6	7.0	8.8	-0.0419	7.2	5.6	-0.0398	3.7	10.2	-0.0406
30	dfca87_ca87	11.4	10.5	11.9	-0.0550	13.3	13.3	-0.0568	-0.6	16.4	-0.0352
31	dfca89_ca89	11.9	15.0	14.1	-0.0571	10.8	14.1	-0.0904	5.9	17.8	-0.1092
32	dfcb96_cb96	12.0	8.8	9.2	-0.0346	10.6	10.1	-0.0368	10.9	11.4	-0.0155
33	dfcc56_cc56	11.2	9.5	6.5	-0.0401	7.5	10.3	-0.0459	14.6	10.6	-0.0652
34	dfcd137_cd137	11.7	9.1	6.7	-0.0592	6.5	8.6	-0.0607	10.2	12.8	-0.0701
35	dfCO1_CO1	0.7	0.3	0.2	-0.0020	0.4	0.4	-0.0011	-0.0	0.0	-0.0007
36	dfCO433_CO433	12.3	9.0	9.4	-0.0366	10.4	9.8	-0.0337	10.8	11.4	-0.0158
37	dfCO70_CO70	12.8	10.9	9.2	-0.0553	8.1	10.1	-0.0494	8.2	14.6	-0.0462
38	dfdc96_dc96	12.0	14.5	15.2	-0.0575	14.1	14.3	-0.0756	17.3	25.6	-0.1995
39	dfde139_de139	12.2	14.1	13.0	-0.0613	11.7	12.9	-0.0667	14.6	17.9	-0.0782
40	dfde29_de29	9.9	4.3	2.0	-0.0239	-0.3	4.5	-0.0246	24.7	29.1	-0.1116
41	dfde83_de83	12.0	9.3	7.7	-0.0613	6.1	7.2	-0.0623	27.2	37.5	-0.0986
42	dffa104_fa104	9.8	6.0	6.2	-0.0593	4.3	4.5	-0.0377	6.8	10.2	-0.0982
43	dffa31_fa31	8.0	10.0	8.8	-0.0468	6.8	9.0	-0.0589	8.9	13.2	-0.0629
44	dffb24_fb24	5.7	5.2	4.3	-0.0249	3.6	4.5	-0.0281	6.0	9.1	-0.0462
45	dffb70_fb70	21.7	24.7	24.1	-0.2136	22.8	24.8	-0.2257	18.4	26.7	-0.2210
46	dffc100_fc100	6.6	4.1	3.2	-0.0316	2.2	3.4	-0.0338	5.2	7.3	-0.0444
47	dffc116_fc116	11.5	11.0	9.1	-0.0567	8.2	10.6	-0.0649	10.4	14.7	-0.0711
48	dffc119_fc119	8.2	6.3	5.4	-0.0480	4.5	6.0	-0.0551	6.9	10.1	-0.0576
49	dffc125_fc125	8.2	4.5	5.4	-0.0598	3.0	2.9	-0.0486	3.0	8.5	-0.0660
50	dffc15_fc15	3.3	5.2	5.1	-0.0245	4.6	5.1	-0.0348	4.6	5.8	-0.0524
51	dffc83_fc83	13.6	5.2	5.3	-0.0685	2.9	3.4	-0.0495	9.6	9.3	-0.0880
52	dffd17_fd17	90.3	45.8	48.3	-0.1178	54.7	52.5	-0.1235	46.8	53.4	-0.1206
53	dffd60_fd60	85.2	36.4	35.7	-0.1753	38.5	39.9	-0.1840	33.1	42.1	-0.1841
54	dfCOS1_COS1	0.0	0.0	0.0	0.0000	0.0	0.0	0.0000	0.0	0.0	0.0000
55	dfaq49_aq49	11.7	3.4	1.2	-0.0686	1.7	3.3	-0.0623	-0.6	3.4	-0.0489
56	dfah12_ah12	10.6	4.2	2.0	-0.0717	5.0	6.1	-0.0627	8.2	9.2	-0.0816
57	dfaf41_af41	11.0	14.0	14.7	-0.0137	17.3	17.3	-0.0298	8.0	17.8	-0.0153
58	dfaf92_af92	8.2	0.8	-1.5	-0.0532	-2.0	-0.8	-0.0344	-2.2	0.9	-0.0336

Table 3: Relative energies, in kJ/mol per molecule, and unit-cell densities, ρ, in g/cm^3, of the lowest-energy crystal structures of carbamazepine determined ranked by a force field [2] (FF; A), and fully relaxed/reranked using B86bPBE-XDM/DZP (SIESTA; A) and sHF-3c (CRYSTAL17; A). Single-point energy calculations performed on low-cost geometries using plane-wave B86bPBE-XDM/PAW or small-basis B86bPBE-XDM/DZP are also tabulated (B//A and C//A, respectively). Energies and densities are relative to dfE1_E1, i.e., the CPOSS [2] database structure identified to be equivalent to the experimental Form-I polymorph; this structure and the others identified to be equivalent to the other experimental polymorphs (Form II: df193_193, Form III: df1_1, Form IV: df54_54, and Form V: df145_145) are highlighted.

no	structure	FF				SIESTA			CRYSTAL17		
		A	B//A	C//A	ρ	A	B//A	ρ	A	B//A	ρ
1	df1045_1045	1.2	4.8	3.9	-0.0388	4.6	5.9	-0.0383	3.6	6.8	-0.0433
2	df1_1	-5.0	-3.9	0.2	0.0421	-1.6	-5.1	0.0548	-6.2	-5.8	0.0300
3	df11_11	-2.5	2.3	4.7	0.0078	5.0	3.1	0.0000	0.4	3.6	-0.0001
4	df12_12	-0.5	5.2	4.7	-0.0159	8.1	7.9	-0.0214	10.9	8.9	-0.0356
5	df1219_1219	0.4	3.5	4.8	-0.0239	5.4	4.5	-0.0287	4.5	5.0	-0.0341
6	df13_13	0.2	5.6	4.3	-0.0032	6.3	7.4	-0.0187	7.1	7.8	-0.0441
7	df141_141	0.7	1.4	0.5	0.0053	2.6	3.3	0.0032	-0.2	3.3	0.0096
8	df14_14	-1.3	6.4	11.6	0.0049	12.0	7.5	-0.0063	17.9	21.0	-0.1326
9	df144_144	1.1	9.9	12.5	0.0194	13.5	11.5	-0.0017	7.5	11.5	-0.0044
10	df145_145	-2.0	0.7	-1.8	-0.0075	0.6	3.0	-0.0192	6.7	2.5	-0.0387
11	df153_153	-0.3	3.8	4.1	0.0010	6.0	5.6	-0.0065	7.5	6.8	-0.0259
12	df1532_1532	0.8	6.3	6.4	-0.0403	7.2	7.7	-0.0459	6.3	9.3	-0.0591
13	df161_161	-1.9	13.0	14.0	0.0084	15.2	14.9	-0.0160	14.0	12.7	-0.0194
14	df17_17	-1.0	2.7	5.0	0.0142	4.0	2.3	0.0142	1.5	2.8	-0.0036
15	df1739_1739	0.5	8.5	13.6	0.0028	14.0	9.4	-0.0126	10.6	9.5	-0.0229
16	df1836_1836	-0.2	5.5	4.8	-0.0277	5.8	6.9	-0.0402	11.5	8.9	-0.0728
17	df193_193	3.6	3.7	4.2	-0.0760	4.4	4.2	-0.0784	3.2	3.6	-0.0741
18	df195_195	1.2	3.6	2.3	-0.0291	1.9	3.0	-0.0319	4.6	4.8	-0.0714
19	df211_211	-0.6	2.8	9.3	-0.0236	9.6	3.6	-0.0253	6.3	8.8	-0.0727
20	df2_2	-2.3	2.0	4.4	-0.0015	5.0	2.8	-0.0096	-0.4	0.1	-0.0316
21	df235_235	0.7	5.2	6.4	-0.0305	6.4	5.9	-0.0316	0.7	5.2	-0.0087
22	df25_25	1.3	7.8	10.1	-0.0017	11.6	9.7	-0.0118	10.3	10.7	-0.0313
23	df26_26	-0.8	1.2	2.8	-0.0038	3.1	2.0	-0.0090	0.3	2.3	-0.0067
24	df269_269	1.2	15.9	16.4	-0.0087	16.8	17.0	-0.0335	17.8	15.0	-0.0461
25	df31_31	-0.3	2.5	3.8	-0.0009	3.2	2.2	-0.0059	2.3	2.8	-0.0279
26	df3_3	-5.9	0.4	0.4	0.0061	2.7	2.7	-0.0106	7.4	2.5	-0.0252
27	df33_33	-1.9	2.5	1.6	-0.0141	2.7	3.4	-0.0249	8.1	2.9	-0.0404
28	df36_36	-1.0	4.8	10.6	0.0131	9.6	4.2	0.0286	6.9	5.9	-0.0094
29	df43_43	1.0	2.5	3.7	-0.0064	4.1	3.4	-0.0121	1.9	3.3	-0.0203
30	df44_44	-0.9	0.4	-0.8	-0.0080	-0.7	0.8	-0.0008	8.7	1.9	-0.0419
31	df444_444	-4.0	1.5	4.2	0.0048	4.5	2.3	-0.0049	0.6	2.7	-0.0024
32	df47_47	0.5	4.5	3.2	-0.0541	4.1	5.5	-0.0552	6.8	5.0	-0.0871
33	df49_49	0.9	6.0	3.7	-0.0799	6.0	8.4	-0.0896	10.8	9.1	-0.1086
34	df51_51	1.1	1.3	1.0	-0.0415	0.5	0.1	-0.0159	2.2	0.3	-0.0680
35	df53_53	-0.7	1.7	10.0	-0.0006	9.0	1.1	0.0102	3.2	2.5	-0.0323
36	df54_54	-1.2	-0.4	4.7	-0.0335	4.2	-0.9	-0.0318	2.4	0.4	-0.0714
37	df60_60	0.6	6.8	8.7	0.0197	9.0	7.2	0.0084	4.5	8.2	0.0031
38	df63_63	0.4	6.6	12.7	0.0211	13.1	7.4	0.0094	4.7	8.1	0.0052
39	df654_654	1.1	5.4	4.7	-0.0508	4.4	6.1	-0.0518	3.0	6.5	-0.0608
40	df65_65	0.5	3.7	7.7	-0.0302	7.2	4.3	-0.0325	0.8	3.6	-0.0570
41	df6_6	-1.1	6.5	6.4	0.0067	6.0	7.0	-0.0116	10.4	9.1	-0.0780
42	df66_66	0.8	9.8	15.1	-0.0174	16.8	11.9	-0.0307	14.8	13.7	-0.0684
43	df68_68	1.2	5.8	12.1	-0.0143	11.4	7.1	-0.0234	10.1	9.5	-0.0675
44	df80_80	-4.0	13.0	15.1	0.0279	15.6	14.5	0.0000	13.0	13.0	-0.0080
45	df809_809	-1.3	4.2	3.2	-0.0093	3.2	4.9	-0.0162	6.6	5.2	-0.0457
46	df838_838	-1.0	1.4	2.2	-0.0254	2.8	2.3	-0.0308	2.1	2.6	-0.0301
47	df853_853	1.1	6.8	7.6	0.0031	10.1	9.4	-0.0093	3.5	9.9	0.0129
48	df863_863	1.2	2.8	1.8	-0.0413	1.1	3.2	-0.0431	0.8	3.5	-0.0572
49	df8_8	-3.5	2.1	-0.7	-0.0350	1.7	4.6	-0.0496	8.7	6.7	-0.0735
50	df90_90	0.6	6.5	6.6	-0.0368	5.5	6.6	-0.0442	2.1	6.2	-0.0662
51	df95_95	0.9	5.6	10.7	-0.0424	9.2	6.2	-0.0465	2.1	6.2	-0.0660
52	dfE1_E1	0.0	0.0	0.0	0.0000	0.0	0.0	0.0000	0.0	0.0	0.0000

Table 4: Relative energies, in kJ/mol per molecule, and unit-cell densities, ρ, in g/cm^3, of the lowest-energy crystal structures of olanzapine determined by a force field from a previously conducted CSP study [4] (FF; A), and fully relaxed/reranked using B86bPBE-XDM/DZP (SIESTA; A) and sHF-3c (CRYSTAL17; A). Single-point energy calculations performed on low-cost geometries using plane-wave B86bPBE-XDM/PAW or small-basis B86bPBE-XDM/DZP are also tabulated (B//A and C//A, respectively). Energies and densities are relative to dfeq11_eq11, i.e., the CPOSS [2] database structure identified to be equivalent to the experimental Form-I polymorph; this structure and the others identified to be equivalent to the other experimental polymorphs (Form II: dfeq45_eq45, Form III: [4] dfeq162_eq162, Form IV: dfeq1_eq1) are highlighted.

no	structure	FF				SIESTA			CRYSTAL17		
		A	B//A	C//A	ρ	A	B//A	ρ	A	B//A	ρ
1	dfax16_ax16	7.7	10.0	7.0	-0.0728	11.0	15.3	-0.1159	2.2	14.4	-0.1069
2	dfax1_ax1	7.2	8.0	8.5	0.0047	14.6	15.1	-0.0304	4.4	12.0	-0.0198
3	dfax2074_ax2074	3.9	10.2	5.8	-0.1279	9.0	15.8	-0.1760	3.9	15.3	-0.1624
4	dfax211_ax211	3.8	9.9	5.9	-0.1210	9.1	15.5	-0.1692	3.9	15.2	-0.1611
5	dfax3_ax3	-2.1	11.2	7.8	-0.0859	8.0	14.0	-0.1387	3.9	13.6	-0.1287
6	dfax4_ax4	7.3	14.2	15.4	-0.0096	23.0	23.8	-0.0635	10.8	22.7	-0.0520
7	dfax6763_ax6763	6.2	11.9	14.5	-0.0165	20.3	18.2	-0.0664	6.8	16.4	0.0000
8	dfeq10_eq10	2.3	8.8	8.3	-0.0279	14.7	16.8	-0.0742	24.0	18.9	-0.1031
9	dfeq11_eq11	0.0	0.0	0.0	0.0000	0.0	0.0	0.0000	0.0	0.0	0.0000
10	dfeq126_eq126	7.8	14.5	14.3	-0.0205	21.6	24.0	-0.0726	17.4	22.3	-0.0438
11	dfeq12_eq12	6.6	12.5	13.3	-0.0119	17.7	18.3	-0.0547	6.5	13.2	-0.0025
12	dfeq1392_eq1392	3.3	5.9	5.1	-0.0162	7.1	9.1	-0.0455	4.7	6.6	-0.0301
13	dfeq13_eq13	3.4	5.7	6.5	-0.0060	9.9	10.2	-0.0332	3.7	7.6	-0.0164
14	dfeq157_eq157	6.4	10.7	10.7	-0.0168	18.1	19.7	-0.0602	17.6	19.1	-0.0440
15	dfeq15_eq15	4.0	7.5	6.3	-0.0142	13.4	16.4	-0.0648	26.1	21.5	-0.0759
16	dfeq162_eq162	7.1	4.4	4.1	-0.0203	4.9	5.8	-0.0442	-1.5	-0.3	-0.0139
17	dfeq17_eq17	4.9	10.4	8.5	-0.0399	16.2	19.9	-0.0885	10.2	16.1	-0.0568
18	dfeq1_eq1	-2.0	-1.9	-2.3	-0.0046	-0.8	1.0	-0.0287	-0.2	0.5	-0.0293
19	dfeq206_eq206	4.6	15.6	13.5	-0.0523	13.7	18.3	-0.0977	12.3	16.9	-0.0863
20	dfeq20_eq20	3.3	5.7	4.9	-0.0156	6.8	8.7	-0.0435	4.7	6.6	-0.0301
21	dfeq226_eq226	6.0	18.8	19.0	-0.0034	20.8	22.5	-0.0570	14.5	22.3	-0.0312
22	dfeq23_eq23	7.6	8.0	3.9	-0.0468	6.5	12.0	-0.0783	10.1	12.8	-0.0642
23	dfeq2481_eq2481	5.4	19.8	19.1	-0.0240	13.4	17.5	-0.0657	10.0	18.0	-0.0585
24	dfeq24_eq24	1.6	13.2	11.1	-0.0509	12.6	17.1	-0.0981	14.8	16.0	-0.0919
25	dfeq25_eq25	7.0	13.4	13.5	-0.0353	19.7	21.3	-0.0795	22.3	22.2	-0.0759
26	dfeq2639_eq2639	0.0	0.1	0.1	-0.0017	0.1	0.1	0.0015	0.0	0.0	-0.0002
27	dfeq27_eq27	5.2	7.8	6.1	-0.0636	10.9	14.2	-0.1066	7.9	10.0	-0.0673
28	dfeq28_eq28	4.7	9.8	10.8	-0.0045	17.8	18.2	-0.0459	19.2	16.6	-0.0399
29	dfeq2_eq2	4.9	8.2	5.8	-0.0202	11.5	15.4	-0.0604	7.6	13.1	-0.0208
30	dfeq30_eq30	-0.6	13.1	11.1	-0.0556	12.7	17.2	-0.1033	11.0	16.8	-0.0975
31	dfeq336_eq336	7.1	14.6	17.4	-0.0060	22.1	21.2	-0.0516	19.0	18.5	-0.0179
32	dfeq34_eq34	1.9	10.4	10.2	0.0007	1.8	13.6	-0.0499	9.3	15.0	-0.0573
33	dfeq36_eq36	6.4	9.2	8.2	-0.0447	13.1	15.5	-0.0849	10.5	14.2	-0.0503
34	dfeq3731_eq3731	-2.5	1.2	3.8	0.0362	10.6	9.4	-0.0037	11.7	8.3	0.0076
35	dfeq406_eq406	3.3	4.9	6.4	-0.0057	12.4	11.1	-0.0281	12.5	11.8	-0.0293
36	dfeq42_eq42	5.8	10.0	10.6	-0.0355	16.0	16.5	-0.0604	17.7	16.9	-0.0467
37	dfeq45_eq45	6.2	4.0	4.3	-0.0219	3.5	3.7	-0.0334	0.3	1.5	-0.0362
38	dfeq49_eq49	4.3	13.0	13.2	0.0131	14.8	16.7	-0.0415	11.9	15.7	-0.0308
39	dfeq4_eq4	3.7	5.6	2.5	-0.0467	6.2	10.5	-0.0789	12.9	11.7	-0.1052
40	dfeq539_eq539	-0.6	4.2	6.0	0.0135	12.6	12.2	-0.0253	14.6	11.7	-0.0295
41	dfeq53_eq53	6.4	8.7	10.1	0.0038	15.8	15.4	-0.0324	16.7	12.7	-0.0098
42	dfeq55_eq55	7.6	13.7	14.5	0.0113	20.7	21.9	-0.0443	12.7	20.5	0.00550
43	dfeq56_eq56	7.3	18.2	18.5	-0.0226	22.5	24.1	-0.0792	12.1	21.1	-0.0242
44	dfeq63_eq63	7.1	14.6	12.3	-0.0522	19.6	23.9	-0.1024	17.6	22.5	-0.0950
45	dfeq679_eq679	7.7	12.3	12.9	-0.0177	19.7	20.0	-0.0542	16.2	20.9	-0.0304
46	dfeq6_eq6	2.0	3.7	2.5	-0.0334	5.4	7.9	-0.0638	4.8	5.4	-0.0312
47	dfeq71_eq71	7.7	14.7	14.7	-0.0085	20.2	20.8	-0.0432	16.9	19.7	-0.0389
48	dfeq75_eq75	7.6	22.1	20.4	-0.0425	15.5	18.8	-0.0622	12.3	20.1	-0.0816
49	dfeq7_eq7	-2.5	9.2	6.7	-0.0548	8.8	13.4	-0.0950	9.1	11.3	-0.0837
50	dfeq99_eq99	7.8	13.5	13.2	-0.0249	18.5	19.4	-0.0504	22.9	19.3	-0.0447

References

(1) Hulme, A. T.; Price, S. L.; Tocher, D. A. A New Polymorph of 5-Fluorouracil Found Following Computational Crystal Structure Predictions. *J. Am. Chem. Soc.* **2005**, *127*, 1116–1117.

(2) *The CPOSS (Control and Prediction of the Organic Solid State) database holds details of the hypothetical crystal structures generated in the computational searches carried out at University College London, and is maintained by Dr. Louise S. Price, and led by Prof. Sally L. Price. See http://www.chem.ucl.ac.uk/cposs/index.htm*

(3) Braun, D. E.; Ardid-Candel, M.; D'Oria, E.; anf J.-B. Arlin, P. G. K.; Florence, A. J.; Jones, A. G.; Price, S. L. Racemic Naproxen: A Multidisciplinary Structural and Thermodynamic Comparison with the Enantiopure Form. *Cryst. Growth Des.* **2011**, *11*, 5659–5669.

(4) Bhardwaj, R. M.; Price, L. S.; Price, S. L.; Reutzel-Edens, S. M.; Miller, G. J.; Oswald, I.; Florence, B. F.; Florence, A. J. Exploring the Experimental and Computed Energy Landscape of Olanzapine. *Cryst. Growth Des.* **2013**, *13*, 1602–1617.