Supporting information

POLYMORPHS AND HYDRATES OF SEQUIFENADINE HYDROCHLORIDE: CRYSTALLOGRAPHIC EXPLANATION OF OBSERVED PHASE TRANSITIONS AND THERMODYNAMIC STABILITY

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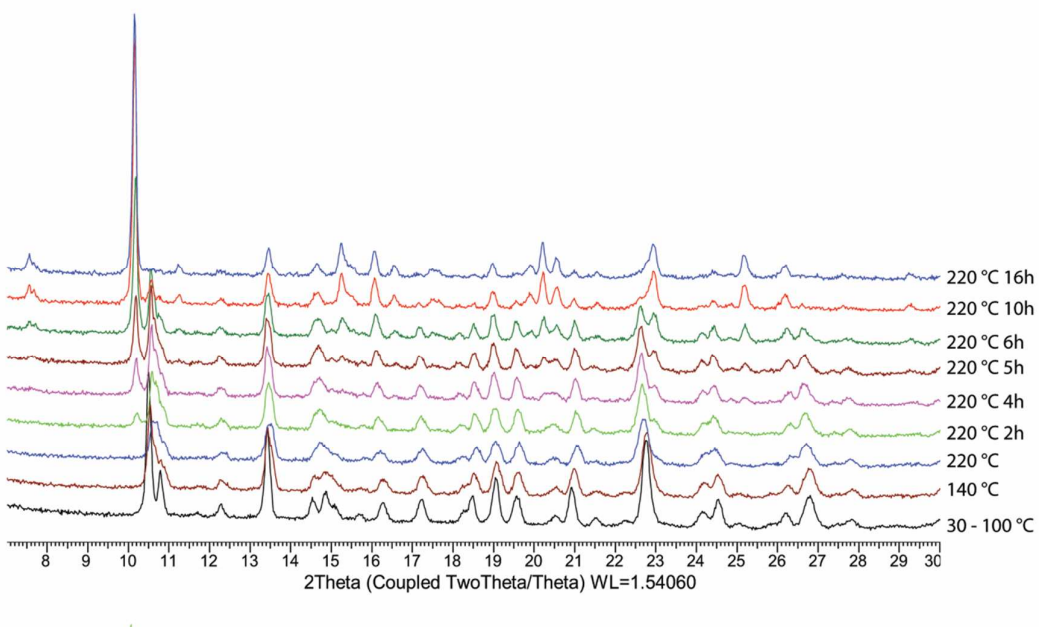

Figure S1. VT-XPRD patterns of polymorph A.

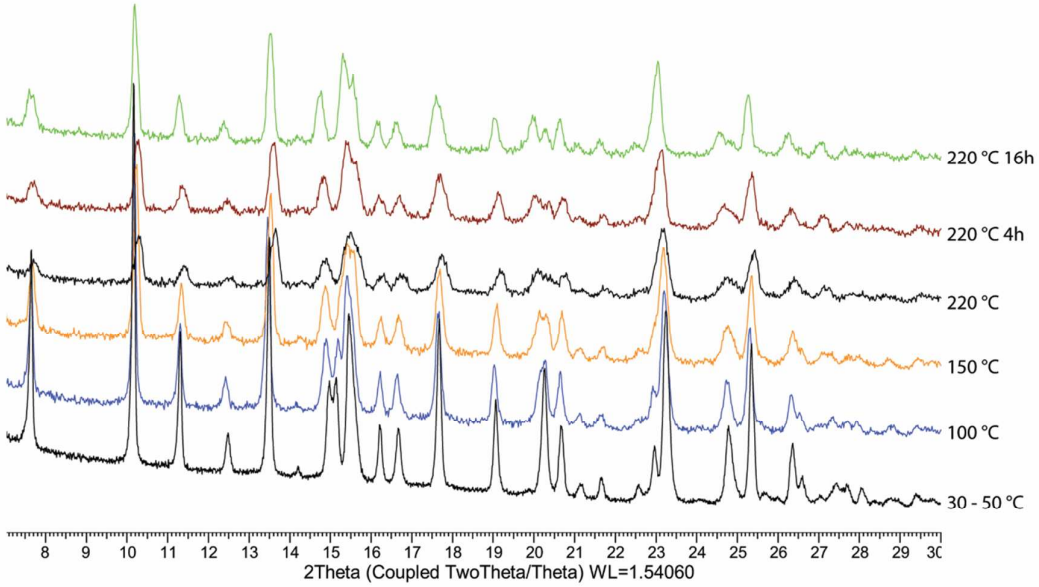

Figure S2. VT-XPRD patterns of polymorph B.

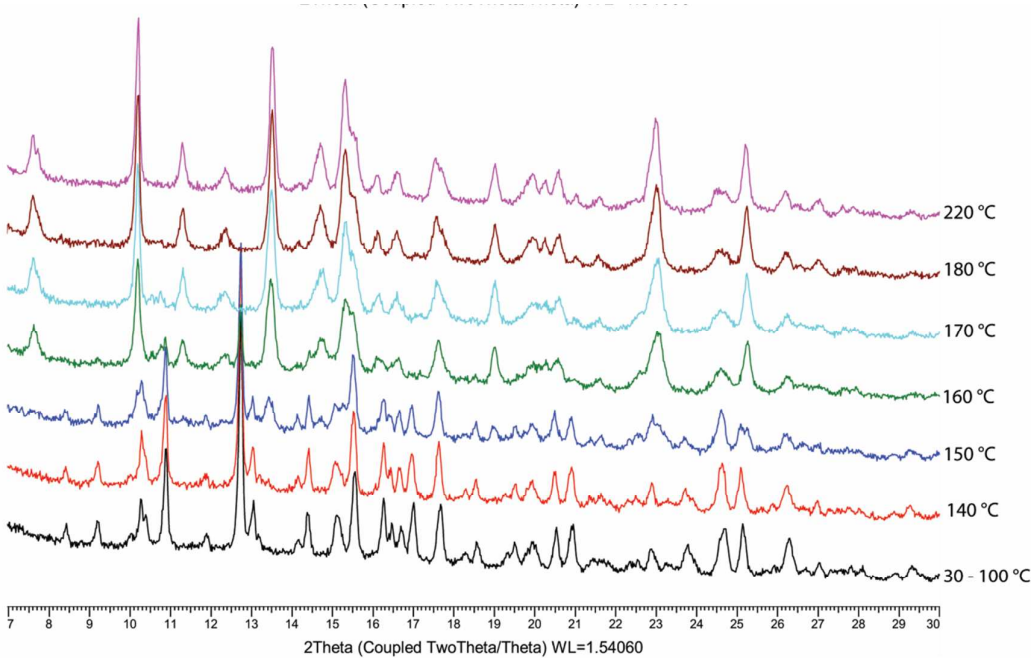

Figure S3. VT-XPRD patterns of polymorph C.

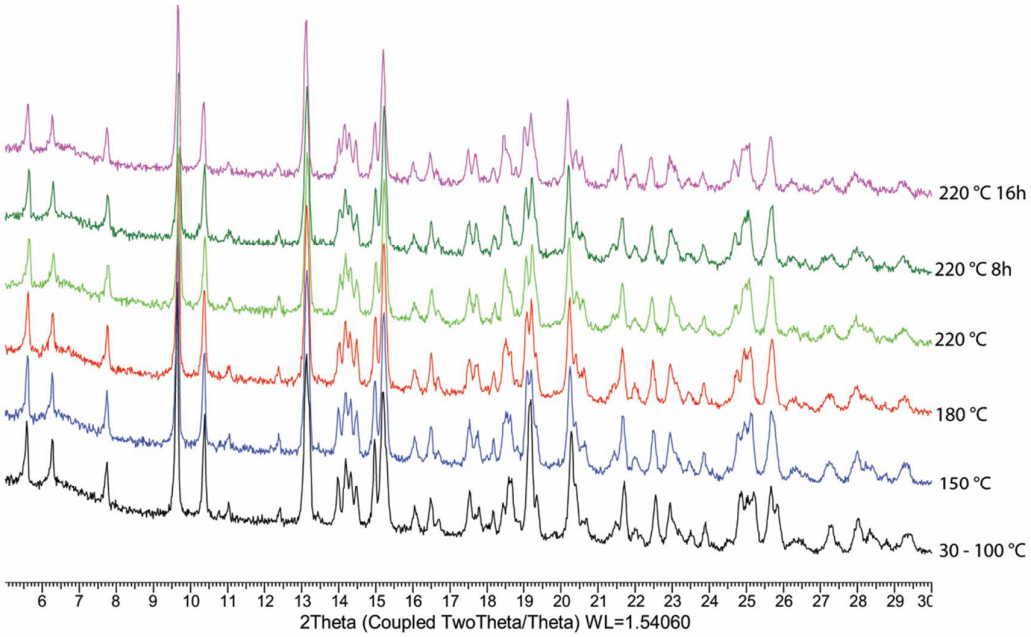

Figure S4. VT-XPRD patterns of polymorph D.

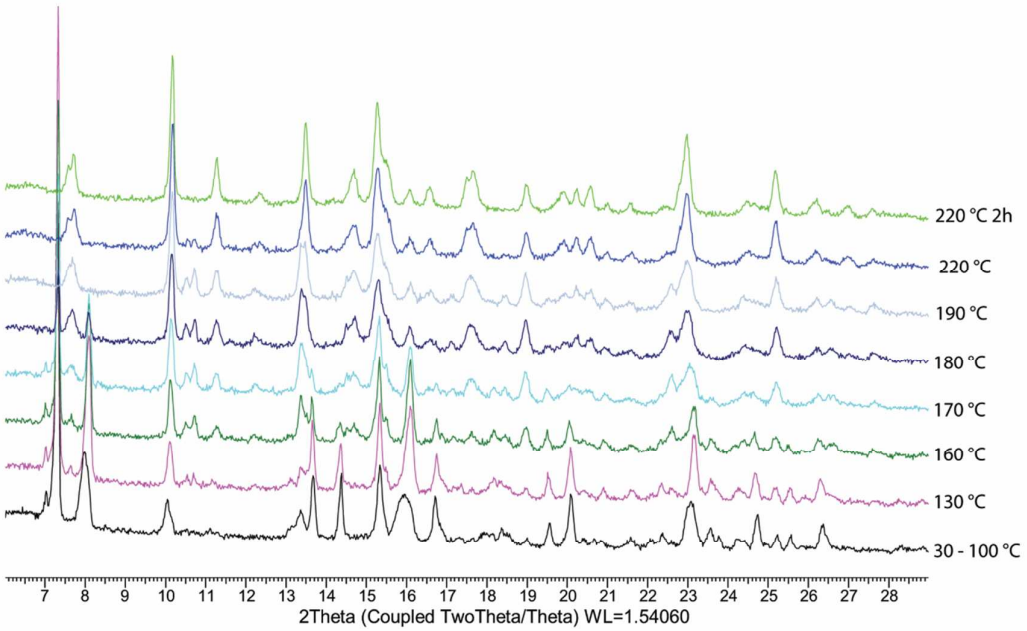

Figure S5. VT-XPRD patterns of polymorph E

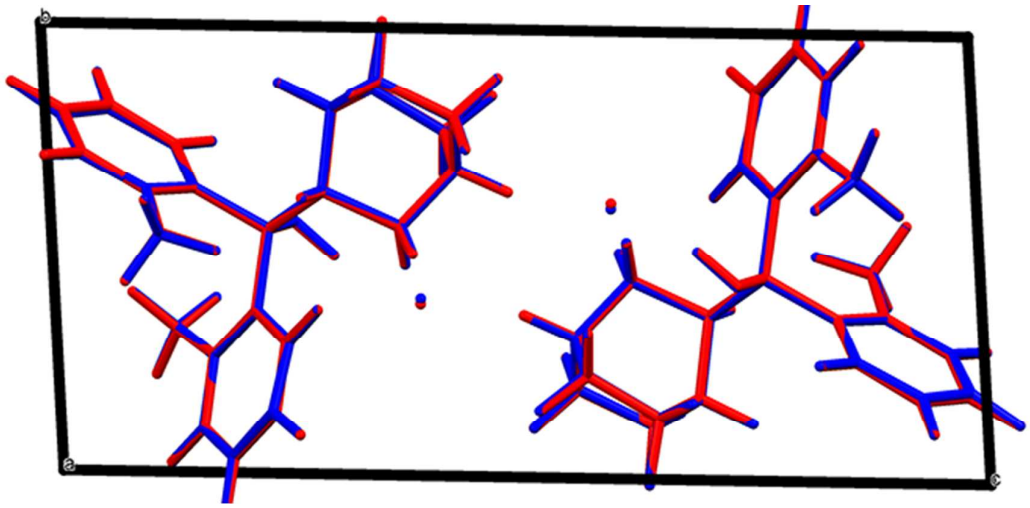

Figure S6. Overlay of the experimentaly determinated (red) and optimized using periodic DFT calculations (blue) crystal structures of form A.

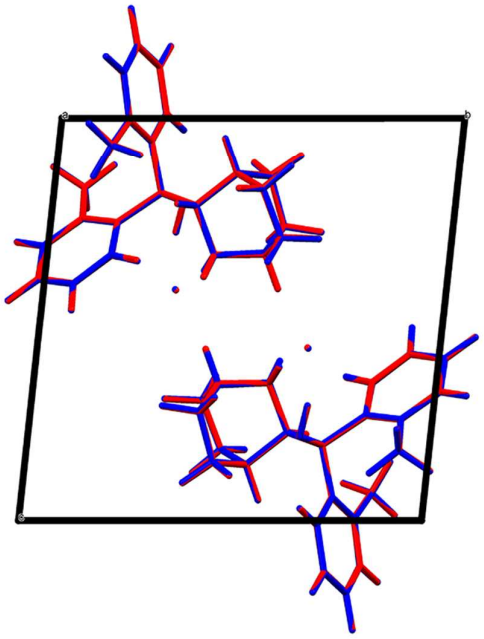

Figure S7. Overlay of the experimentaly determinated (red) and optimized using periodic DFT calculations (blue) crystal structures of form B.

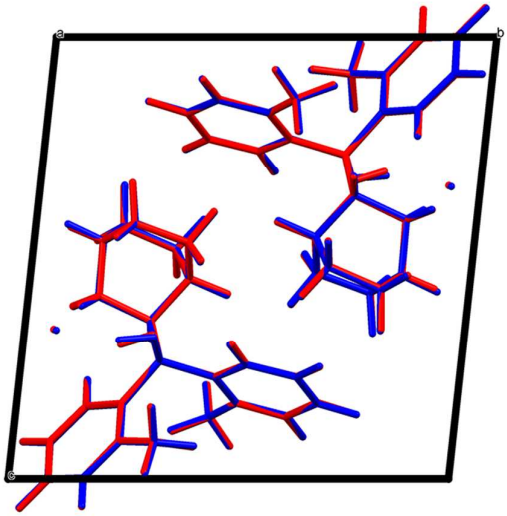

Figure S8. Overlay of the experimentaly determinated (red) and optimized using periodic DFT calculations (blue) crystal structures of form B'.

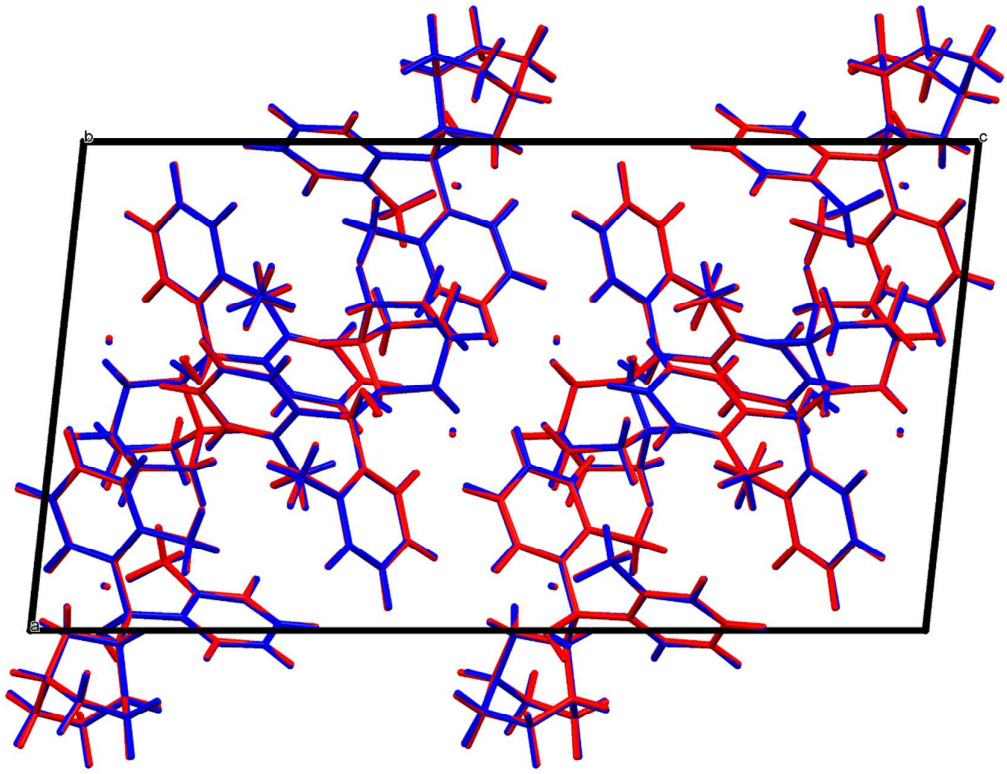

Figure S9. Overlay of the experimentaly determinated (red) and optimized using periodic DFT calculations (blue) crystal structures of form C .

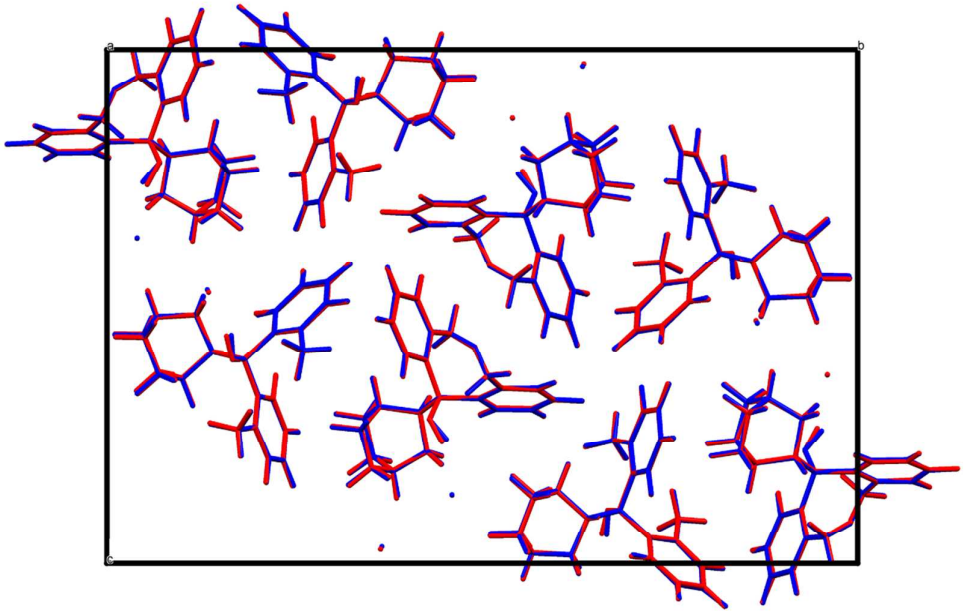

Figure S10. Overlay of the experimentaly determinated (red) and optimized using periodic DFT calculations (blue) crystal structures of form D.

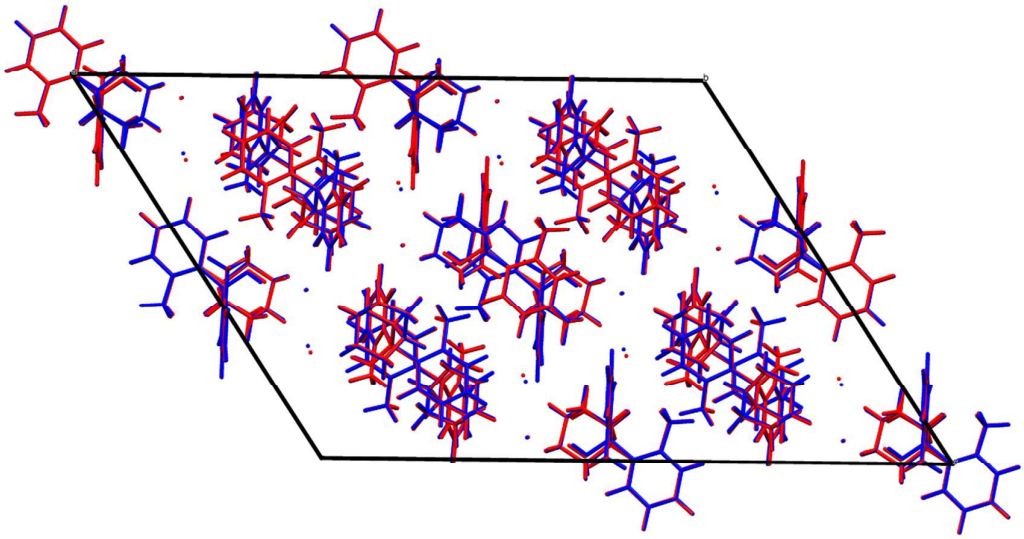

Figure S11. Overlay of the experimentaly determinated (red) and optimized using periodic DFT calculations (blue) crystal structures of form E.

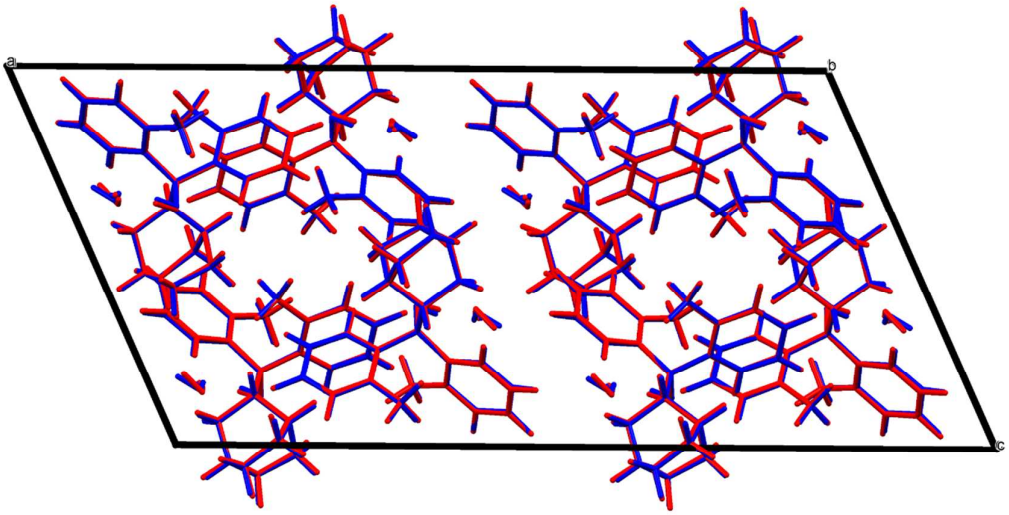

Figure S12. Overlay of the experimentaly determinated (red) and optimized using periodic DFT calculations (blue) crystal structures of form MH .

Table S1. Intermolecular hydrogen bond geometry of A, B, B', C, D, E, NSH, MH and DH

	D–H···A	**H···A/ Å**	**D···A/ Å**	**D–H···A/ °**
A				
	N21–H21···Cl25	2.13	3.14	152
	O4–H4···Cl25	2.32	3.14	162
	C22–H22A···Cl25	2.81	3.76	169
	C22–H22B···Cl25	2.99	3.89	159
	C24–H24A···Cl25	2.94	3.85	155

B				
	N21–H21···Cl25	2.22	3.08	170
	O4–H4···Cl25	2.25	3.04	163
	C22–H22A···Cl25	2.82	3.70	153
	C12-H12···Cl25	2.96	3.88	160
B’				
	N21–H21···Cl25	2.15	2.99	161
	O4–H4···Cl25	2.34	3.09	152
	C22–H22A···Cl25	2.94	3.82	153
	C22–H22B···Cl25	2.99	3.94	168
C				
	N21–H21···Cl25	2.29	3.15	167
	N46–H46···Cl50	2.31	3.16	165
	C20–H20A···Cl50	2.92	3.66	135
	C20–H20B···Cl25	2.95	3.86	158
	C32–H32···Cl50	2.97	3.72	135
	C45–H45A···Cl25	2.91	3.80	155
	C45–H45B···Cl50	2.84	3.60	137
	C47–H47A···Cl50	2.88	3.54	136
D				
	N21–H21···Cl25	2.14	2.95	153
	O4–H4···Cl50	2.40	3.11	145
	N46–H46···Cl50	2.27	3.13	169
	O29–H29···Cl25	2.38	3.15	158
	C45–H45B···Cl25	2.93	3.77	147
	C47–H47A···Cl25	2.90	3.71	142
	C47–H47B···Cl25	2.69	3.60	160
	C49–H49A···Cl25	2.89	3.75	149
E				
	N21–H21···Cl50	2.14	2.99	166
	O4–H4···Cl25	2.50	3.27	157
	N46–H46···Cl25	1.85	2.70	167
	O29–H29···Cl50	2.46	3.18	147
	C20–H20A···Cl50	2.96	3.72	136
	C22–H22A···Cl25	2.74	3.68	166
	C22–H22B···Cl50	2.95	3.74	136
	C19–H19B···O29	2.92	3.87	171
NSH				
	N21–H21···Cl50	2.08	2.94	171
	O4–H4···Cl25	2.26	3.02	152
	N46–H46···Cl25	2.09	2.92	161
	O29–H29···Cl50	2.41	3.16	151
	O51–H51B···Cl25	2.58	3.37	161
	C19–H19B···O29	2.82	3.77	176
	C20–H20A···Cl50	2.94	3.71	138
	C22–H22A···Cl25	2.82	3.73	159

	C22–H22B···Cl50	2.72	3.56	147
	C49–H49B···O51	2.56	3.34	138
MH				
	N21–H21···O26	2.30	3.14	166
	O4–H4···Cl25	2.20	3.00	165
	O26–H26A···Cl25	2.40	3.11	143
	C24–H24B···Cl25	2.73	3.63	158
	C14-H14···O26	2.87	3.79	159
	C15-H15···O4	2.72	3.64	149
DH				
	N21–H21···O27	1.85	2.73	154
	O4–H4···Cl25	2.30	3.16	155
	O26–H26A···Cl25	2.25	3.20	171
	O26–H26B···Cl25	2.31	3.19	177
	O27–H27A···Cl25	2.29	3.17	179
	O27–H27B···O26	1.90	2.78	162
	C20–H20B···O26	2.54	3.41	149
	C22–H22B···Cl25	2.90	3.84	164

Table S2. Intermolecular hydrogen bond energy of SQ-HCl polymorphs

Structure / conformer	E(NH···Cl), kJ/mol	E(OH···Cl), kJ/mol	Total energy, kJ/mol
A	-532.2	-487.6	-509.9
B	-533.9	-465.8	-499.9
B'	-534.8	-474.9	-504.8
C1	-538.9	-	-269.0
C2	-537.1	-	
D1	-543.8	-488.1	-518.2
D2	-540.9	-500.2	
E1	-532.2	-496.9	-512.1
E2	-532.5	-486.9	

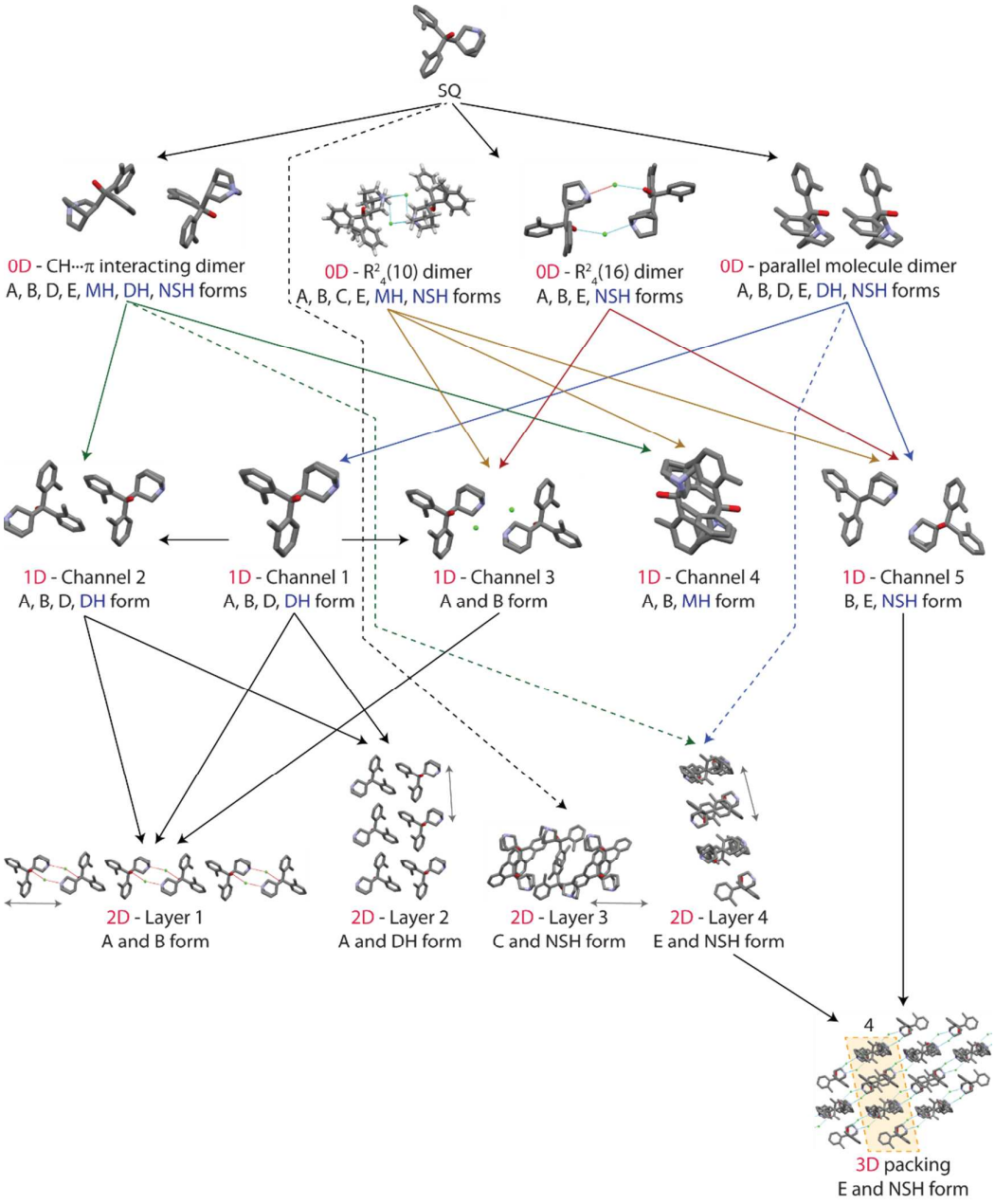

Figure S14. Illustration of the packing similarities of common building blocks in crystal structures of SQ-HCl polymorphs and hydrates. For all channels (1D building blocks) view from the top are shown. For all layers (2D building blocks) view from the top are shown (direction of periodic repetition is indicated by grey arrows).

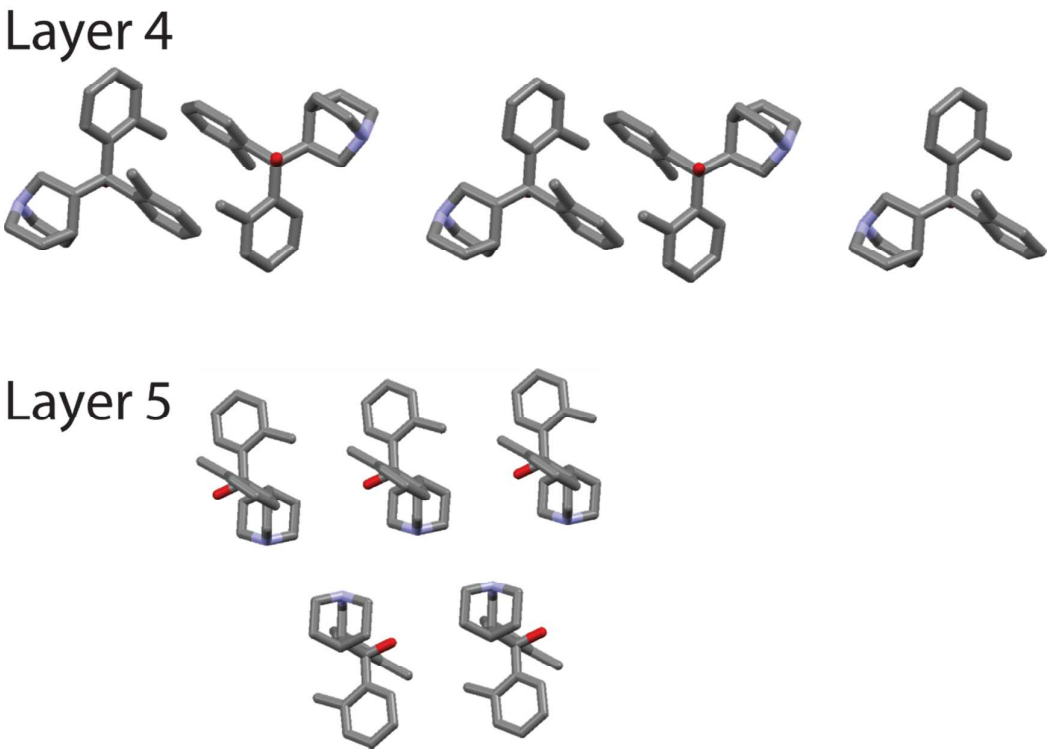

Figure S15. Side-view to the building blocks Channel 4 and Channel 5.