Electronic Supplementary Information (ESI)

Influence of crystal packing on the thermal properties of cocrystals and cocrystal solvates of olanzapine drug: insights from computations.

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Table S1. Prominent hydrogen bonds and non-covalent interactions in olanzapine cocrystals and cocrystal solvates.

S.No	H-bond	D–H /Å	H···A / Å	D···A / Å	∠ D–H···A /°	Symmetry code
	OLZ-RES (1:1)					
1	N1–H1N···O2^{i}	0.82(2)	2.334(17)	3.1180(16)	159 (2)	x,1+y,z
2	O1–H1O···N2^{ii}	0.89(2)	1.832(19)	2.7219(16)	177 (2)	1-x,-1/2+y,1/2-z
3	O2–H2O···N4	0.88(2)	1.92(2)	2.7777(15)	166 (2)	
4	C2–H2···O2^{i}	0.95	2.58	3.3627(17)	140	x,1+y,z
5	C4–H4···O1^{iii}	0.95	2.49	3.1437(18)	126	-1+x,1+y,z
6	C13–H13A···O1^{iv}	0.99	2.58	3.2673(19)	126	1-x,1/2+y,1/2-z
7	C17–H17C···S1^{v}	0.98	2.84	3.4496(15)	121	x,-1+y,z
8	C12–H12C···π(Cg3)^{vi}	0.98	2.99	3.7169(17)	132	x,3/2-y,1/2+z
9	C15–H15B···π(Cg1)^{vii}	0.99	2.98	3.7382(14)	134	1-x,1-y,1-z
Cg1 is the centroid of five membered ring atoms S1-C9-C8-C11-C10 Cg3 is the centroid of six membered ring atoms C1-C2-C3-C4-C5-C6						
	OLZ-CAT (1:1)					
1	N1–H1N···O2^{i}	0.86(5)	2.13(6)	2.983(5)	170(5)	1-x,1-y,1-z
2	O1–H1O···N2^{ii}	0.78(8)	1.98(8)	2.755(5)	172(8)	1-x,y,3/2-z
3	O2–H2O···N4	0.81(5)	1.94(6)	2.717(6)	163(5)	
4	C15–H15B···N1^{i}	0.99	2.51	3.263(7)	133	1-x,1-y,1-z
5	C3–H3··· π(Cg8)^{iii}	0.949	3.00	3.636(6)	126	-1/2+x,3/2-y
6	C12–H12A···π(Cg8)^{iv}	0.98	2.60	3.452(6)	145	x,1-y,-1/2+z
Cg8 is the centroid of six membered ring atoms C18-C19-C20-C21-C22-C23						
	OLZ-HQ-BEN (1:1:2)					
1	N1–H1N···O2^{i}	0.904(16)	2.073(16)	2.9483(13)	162.8(14)	1-x,1-y,1-z

2	O1−H1O···N2	0.80(2)	1.96(2)	2.7486(12)	170(2)	
3	O2−H2O···N4	0.876(18)	1.823(18)	2.6779(12)	164.6(18)	
4	C15−H15B···N1^{i}	0.99	2.59	3.4071(15)	140	1-x,1-y,1-z
5	C12−H12C···π(Cg8)^{ii}	0.98	2.93	3.7014(14)	137	x,-1+y,z
6	C12−H12C···π(Cg8)^{iii}	0.98	2.93	3.7014(14)	137	1-x,1-y,1-z
7	C14−H14A···π(Cg1)^{iv}	0.99	2.75	3.6605(12)	153	-x,1-y,1-z
Cg1 is the centroid of five membered ring atoms S1-C9-C8-C11-C10 Cg8 is the centroid of five membered ring atoms C18-C19-C20-18a-C19a-C20a						
	OLZ-HQ-BEN (1:1:1)					
1	N1−H1N···O2^{i}	0.80(4)	2.15(4)	2.922(5)	163(4)	1-x,1-y,1-z
2	O1−H1O···N2	0.84	1.91	2.727(5)	162	
3	O2−H2O···N4	0.84	1.90	2.709(6)	160	
4	C4−H4···O1^{ii}	0.95	2.47	3.217(6)	136	2-x,-y,1-z
5	C15−H15B···N1^{i}	0.99	2.58	3.398(7)	140	1-x,1-y,1-z
6	C12−H12C···π(Cg8)^{iii}	0.98	2.82	3.596(6)	136	x,1+y,z
7	C12−H12C···π(Cg8)^{iv}	0.98	2.82	3.596(6)	136	1-x,1-y,1-x
8	C14−H14A···π(Cg1)^{v}	0.99	2.82	3.688(6)	147	2-x,1-y,1-z
9	C16−H16B···π(Cg3)^{v}	0.99	2.90	3.825(6)	156	2-x,1-y,1-z
10	C25−H25···O1	0.99	2.69	3.410(7)	132	
Cg1 is the centroid of five membered ring atoms S1-C9-C8-C11-C10 Cg3 is the centroid of six membered ring atoms C1-C2-C4-C4-C5-C6 Cg8 is the centroid of six membered ring atoms C18-C19-C20-C18a-C19a-C20a						
	OLZ-HQ-XYL (1:1:1)					
1	N1−H1N···O2^{i}	0.870(18)	1.988(18)	2.8164(16)	158.9(16)	1-x,1-y,1-z
2	O1−H1O···N2	0.89(2)	1.88(2)	2.7596(15)	175(2)	
3	O2−H2O···N4	0.90(3)	1.72(3)	2.5983(15)	163(2)	
4	C5−H5···O1^{ii}	0.95	2.53	3.2486(17)	132	-x,-y,1-z
5	C12−H12B···π(Cg8)^{iii}	0.98	2.90	3.6135(17)	131	x,1+y,z
6	C12−H12B···π(Cg8)^{i}	0.98	2.90	3.6135(17)	131	1-x,1-y,1-z
7	C14−H14A···π(Cg1)^{iv}	0.99	2.75	3.6342(14)	148	-x,1-y,1-z
8	C17−H17C···π(Cg10)	0.98	2.52	3.4449(16)	157	
9	C17−H17C···π(Cg10)^{v}	0.98	2.52	3.4449(16)	157	-x,1-y,2-z
10	C23−H23···π(Cg11)	0.95	2.91	3.8296(16)	163	
11	C23−H23···π(Cg11)^{vi}	0.95	2.91	3.8296(16)	163	1-x,-y,2-z
12	C26−H26···π(Cg9)^{vii}	0.95	2.87	3.5249(15)	127	-1+x,y,z
13	C26−H26···π(Cg9)^{viii}	0.95	2.87	3.5249(15)	127	-x,1-y,2-z
Cg1 is the centroid of five membered ring atoms S1-C9-C8-C11-C10 Cg8 is the centroid of six membered ring atoms C18 -C19-C20-C18a-C19a-C20a Cg9 is the centroid of six membered ring atoms C21-C22-C23-C21b-C22b-C23b Cg10 is the centroid of six membered ring atoms C24-C25-C26-C24c-C25c-C26c Cg11 is the centroid of six membered ring atoms C28-C29-C30-C28d-C29d-C30d						
	OLZ-HQ-ETBEN (1:1:1)					
1	N1−H1N···O2^{i}	0.83(3)	2.10(3)	2.895(3)	160(2)	1-x,1-y,1-z
2	O1−H1O···N2	0.89(3)	1.85(3)	2.736(3)	174(3)	
3	O2−H2O···N4	1.00(2)	1.73(2)	2.700(3)	162(3)	
4	C5−H5···O1^{ii}	0.93	2.59	3.222(3)	125	2-x,-y,1-z
5	C12−H12C···π(Cg8)^{iii}	0.96	2.76	3.486(3)	133	x,1+y,z
6	C12−H12C···π(Cg8)^{i}	0.96	2.76	3.486(3)	133	1-x,1-y,1-z
7	C14−H14A···π(Cg1)^{iv}	0.97	2.73	3.615(3)	152	2-x,1-y,1-z
Cg1 is the centroid of five membered ring atoms S1-C9-C8-C11-C10 Cg8 is the centroid of six membered ring atoms C18-C20-C19-C18a-C20a-C19a						
	OLZ-HQ-XYL-H_2O (1:0.5:0.5:2)					
1	O1−H1OD···O2	0.81(4)	2.00(4)	2.8074(15)	173(3)	

2	N1−H1N···O3^{i}	0.86(2)	2.03(2)	2.8786(13)	168.3(16)	3/2-x,1/2+y,3/2-z
3	O1−H1O···O1^{ii}	0.81(3)	1.99(3)	2.7802(14)	166(4)	1-x,y,1/2-z
4	O2−H1W···N2^{iii}	0.88(2)	2.02(2)	2.8933(13)	175.3(19)	3/2-x,1/2-y,1-z
5	O2−H2WD···O3	0.84(2)	2.00(2)	2.8266(12)	172(2)	
6	O2−H2W···O1	0.85(2)	1.97(2)	2.8074(15)	168(2)	
7	O3−H3WD···O3^{iii}	0.87(3)	2.10(3)	2.9682(12)	175.8(18)	3/2-x,1/2-y,1-z
8	O3−H3W···N4	0.91(2)	1.86(2)	2.7688(12)	176.3(17)	
9	O3−H4W···O2	0.86(2)	1.99(2)	2.8266(12)	166(2)	
10	C14−H14A···π(Cg1)^{iv}	0.99	2.98	3.6942(12)	130	3/2-x,3/2-y,1-z
Cg1 is the centroid of five membered ring atoms S1-C9-C8-C11-C10						

Table S2. Quantum topological properties at (3;-1) critical points corresponding to hydrogen bonds in OLZ multicomponent crystals participating in various heterosynthons.

Synthon	Interaction	ρ_b/ a.u.	$\nabla^2\rho_b$/ a.u.	G_b/ a.u.	E_{int}^{*} / kJ·mol^{-1}
Phenol···piperazine synthon A					
OLZ-RES (1:1)	O2-H2O···N4	0.054	0.112	0.034	38.2
OLZ-CAT (1:1)	O2-H2O'···N4	0.051	0.106	0.031	35.1
	C14-H14B···O1	0.007	0.024	0.005	5.1
	C17-H17B···O2	0.005	0.021	0.004	4.6
OLZ-HQ-BEN (1:1:2)	O2-H2O···N4'	0.060	0.105	0.035	39.5
OLZ-HQ-BEN (1:1:1)	O2-H2O···N4	0.056	0.107	0.034	38.0
OLZ-HQ-XYL (1:1:1)	O2-H2O···N4	0.069	0.111	0.042	47.5
OLZ-HQ-ETBEN (1:1:1)	O2-H2O···N4	0.057	0.105	0.034	38.3
OLZ-HQ-TOL (1:1:1) form I	O2-H2O···N4	0.057	0.108	0.035	38.9
OLZ-HQ-TOL (1:1:1) form II	O2-H2O···N4	0.058	0.105	0.034	38.5
	C15-H15B···O2	0.005	0.023	0.005	5.3
Phenol···diazepine synthon B					
OLZ-RES (1:1)	O1-H1O···N2	0.045	0.092	0.026	29.8
	C13-H13A···O1	0.009	0.033	0.007	8.1
	C23-H23···N2	0.008	0.025	0.005	5.9
	C23-H23···N1	0.007	0.020	0.004	5.0
OLZ-CAT (1:1)	O1-H1O···N2	0.050	0.102	0.031	34.4
	C23-H23···N2	0.007	0.024	0.005	5.7
OLZ-HQ-BEN (1:1:2)	O1-H1O···N2	0.049	0.108	0.031	34.7
	C20-H20···N2	0.008	0.025	0.005	5.9
	C20-H20···N1	0.004	0.012	0.002	2.7
OLZ-HQ-BEN (1:1:1)	O1-H1O···N2	0.051	0.111	0.033	36.6
	C20-H20···N2	0.008	0.025	0.005	5.9
	C20-H20···N1	0.004	0.014	0.003	3.2
OLZ-HQ-XYL (1:1:1)	O1-H1O···N2	0.047	0.104	0.029	33.1
	C20-H20···N2	0.007	0.023	0.005	5.6
	C20-H20···N1	0.004	0.014	0.003	3.3
OLZ-HQ-ETBEN (1:1:1)	O1-H1O···N2	0.050	0.109	0.032	35.6
	C20-H20···N2	0.007	0.023	0.005	5.5
	C20-H20···N1	0.007	0.020	0.004	4.9
OLZ-HQ-TOL (1:1:1) form I	O1-H1O···N2	0.046	0.105	0.029	33.0
	C20-H20···N2	0.007	0.023	0.005	5.4
	C20-H20···N1	0.005	0.017	0.004	4.0
OLZ-HQ-TOL (1:1:1) form II	O1-H1O···N2	0.046	0.104	0.029	32.8
	C20-H20···N2	0.006	0.020	0.004	4.6
	C20-H20···N1	0.005	0.017	0.004	4.0
Diazepine···phenol synthon C					
OLZ-RES (1:1)	N1-H1N···O2	0.019	0.052	0.014	15.7
	C2-H2···O2	0.012	0.037	0.009	9.9
OLZ-CAT (1:1)	N1-H1N···O2	0.026	0.074	0.019	21.8

	O2···S1	0.008	0.030	0.007	7.4
OLZ-HQ-BEN (1:1:2)	N1-H1N···O2	0.024	0.070	0.018	20.4
OLZ-HQ-BEN (1:1:1)	N1-H1N···O2	0.032	0.090	0.024	26.5
OLZ-HQ-XYL (1:1:1)	N1-H1N···O2	0.033	0.100	0.025	28.5
	C22-H22···S1	0.005	0.017	0.003	3.5
	O2···S1	0.007	0.026	0.006	6.2
OLZ-HQ-ETBEN (1:1:1)	N1-H1N···O2	0.030	0.087	0.022	25.3
	O2···S1	0.010	0.033	0.007	8.4
OLZ-HQ-TOL (1:1:1) form I	N1-H1N···O2	0.030	0.088	0.023	25.5
	O2···S1	0.006	0.022	0.005	5.2
OLZ-HQ-TOL (1:1:1) form II	N1-H1N···O2	0.030	0.088	0.023	25.4
	O2···S1	0.009	0.031	0.007	7.8

*Interaction energies were estimated using the Espinosa-Mata equation: E_{int} (a.u.) = 0.429 ·G_b (a.u.).

ρ_b - the electron density, $\nabla^2\rho_b$ - the Laplacian of the electron density, Gb - local electronic kinetic energy density at the bond critical point.

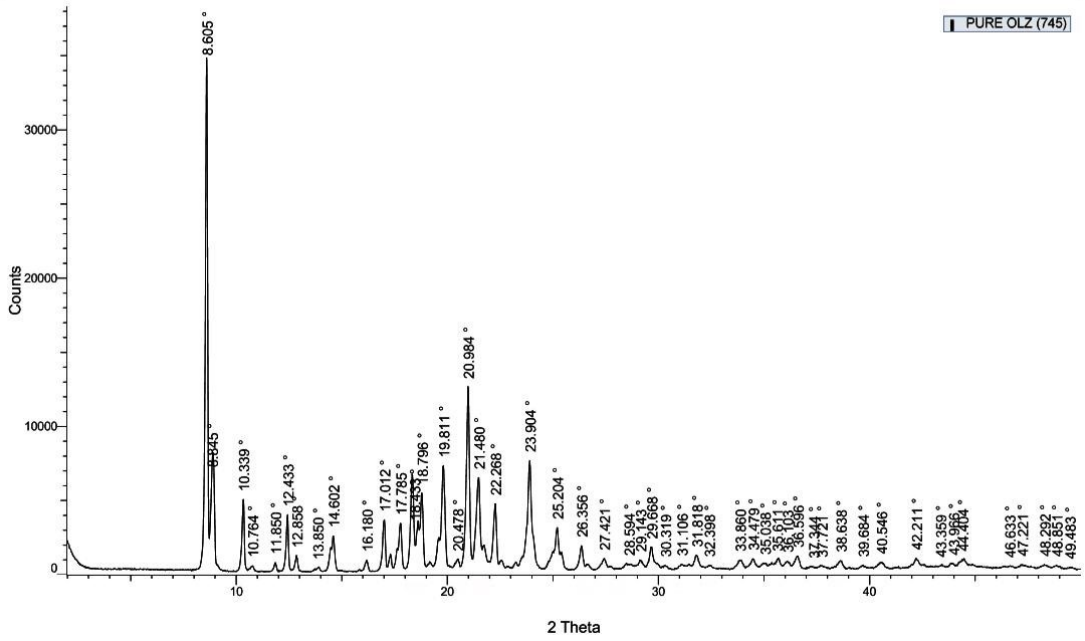
Table S3. List of two- and three-component OLZ crystals showing 2D packing similarity with OLZ-HQ-XYL-H_2O (1:0.5:0.5:2)

Refcode	coformer	Water	Organic Solvent
AQOMAU01	-	H_2O	-
AQOMEY	-	H_2O	-
CAYTUS	-	H_2O	dimethylsulfoxide
ELEVOG	-	H_2O	methanol
GEZKUU	-	-	1-propanol
HELDUZ	nicotinamide	H2O	isopropyl acetate
HELFAH	salicylamide	H_2O	isopropyl acetate
HIRZUF	-	H_2O	-
HISBAO	-	H_2O	ethanol
MICHEN	-	-	ethyleneglycol
MICHIR	-	-	ethanol
MICHOX	-	H_2O	2-methoxy-2-methylpropane
MICHUD	-	H_2O	2-pentanol
MICJAL	-	H_2O	triethylamine
MICJEP	-	H_2O	t-butanol
MICJIT	-	H_2O	3-methyl-1-butanol
MICJOZ	-	H_2O	1,4-butanediol
MICJUF	-	H_2O	DMF
MICKAM	-	H_2O	pyridine
MICKEQ	-	H_2O	tetrahydrofuran
MICKIU	-	H_2O	1,4-dioxan
MICKOA	-	H_2O	acetone
MICKUG	-	H_2O	1-butanol
MICLAN	-	H_2O	acetonitrile
MICLER	-	H_2O	nitromethane
MICLIV	-	H_2O	1,2-dimethoxyethane
MICLOB	-	H_2O	2-methoxyethanol
MICLUH	-	H_2O	methyl acetate
MICMAO	-	H_2O	1,2-propanediol
MICMES	-	H_2O	1-propanol
MIQDUO	-	H_2O	acetonitrile
QEPWOZ	-	H_2O	isopropanol
QEPWUF	-	-	acetic acid
QEPXAM	-	H_2O	acetone
UNOGOT	-	-	methanol
WEXQEW	-	H_2O	ethanol

Table S4. Root-mean-square deviations (%) in atomic positions of OLZ molecules extracted from crystal structures considered in this work.

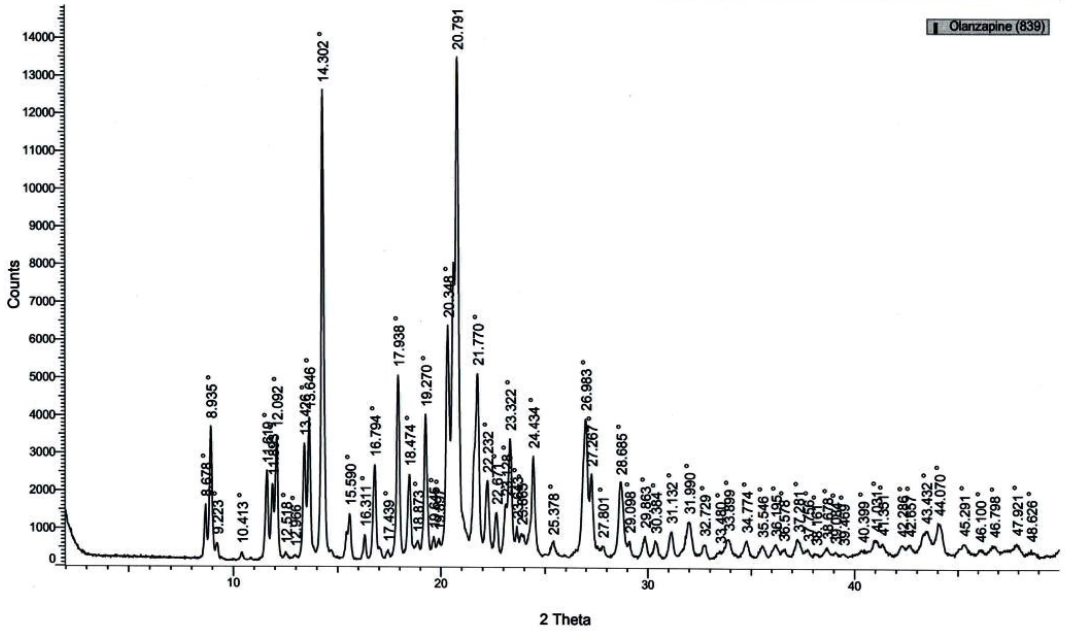
Structure	OLZ-HQ-TOL (1:1:1) I	OLZ-HQ-TOL (1:1:1) II	OLZ-HQ-BEN (1:1:2)	OLZ-HQ-BEN (1:1:1)	OLZ-HQ-XYL (1:1:1)	OLZ-HQ-BEN (1:1:1)	OLZ-HQ-XYL-H_2O (1:1:1:2)	OLZ-RES (1:1)	OLZ-CAT (1:1)
OLZ-HQ-TOL (1:1:1) F.I		4.68	5.82	7.15	10.53	5.37	17.96	22.89	15.11
OLZ-HQ-TOL (1:1:1) F.II	4.68		5.00	4.74	7.90	5.17	14.18	20.53	13.13
OLZ-HQ-BEN (1:1:2)	5.82	5.00		8.12	7.19	4.69	16.16	21.75	12.40
OLZ-HQ-BEN (1:1:1)	7.15	4.74	8.12		11.16	6.28	12.78	18.11	13.70
OLZ-HQ-XYL (1:1:1)	10.53	7.90	7.19	11.16		6.25	14.34	20.66	9.48
OLZ-HQ-BEN (1:1:1)	5.37	5.17	4.69	6.28	6.25		14.41	20.42	12.08
OLZ-HQ-XYL-H_2O (1:1:1:2)	17.96	14.18	16.16	12.78	14.34	14.41		11.60	16.02
OLZ-RES (1:1)	2.89	20.53	21.75	18.11	20.66	20.42	11.60		18.12
OLZ-CAT (1:1)	15.11	13.13	12.40	13.70	9.48	12.08	16.02	18.12	

PURE OLZ



(a)

Olanzapine



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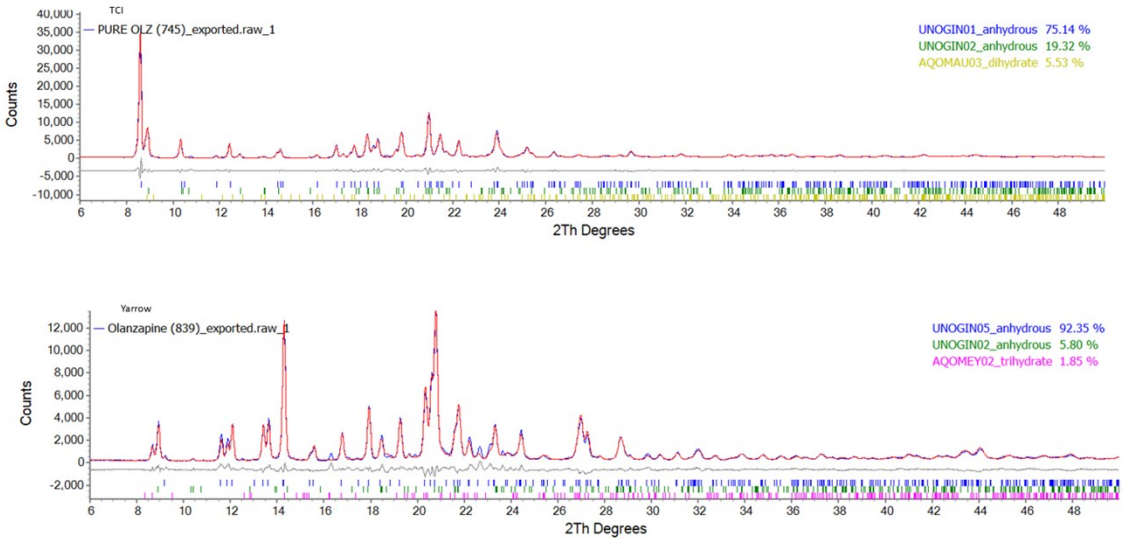


(c)

Figure S1. (a) Powder X-ray diffraction pattern of olanzapine material (source 1: TCI) (b) Powder X-ray diffraction pattern of olanzapine material (source 2: Yarrow). (c) Profile fitting of XRD patterns with known crystal structures of olanzapine in TOPAS software for quantitative analysis of phases. Both sources of olanzapine materials were indicated to be predominantly anhydrous polymorphs of olanzapine (although polymorphs differ in the two batches) with traces of di or trihydrated phases.

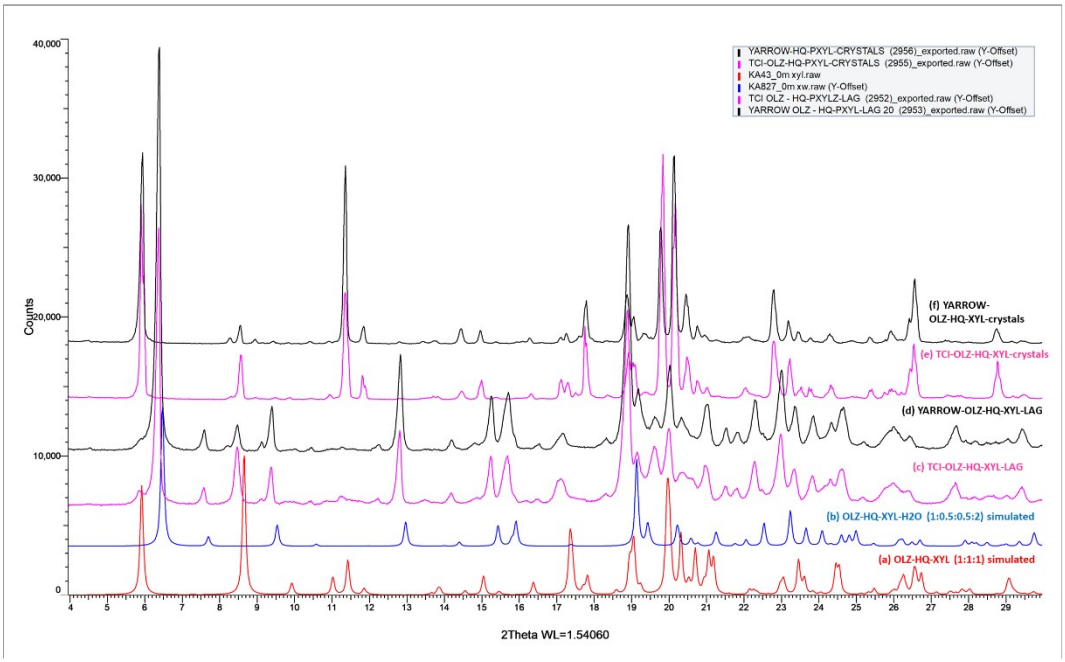
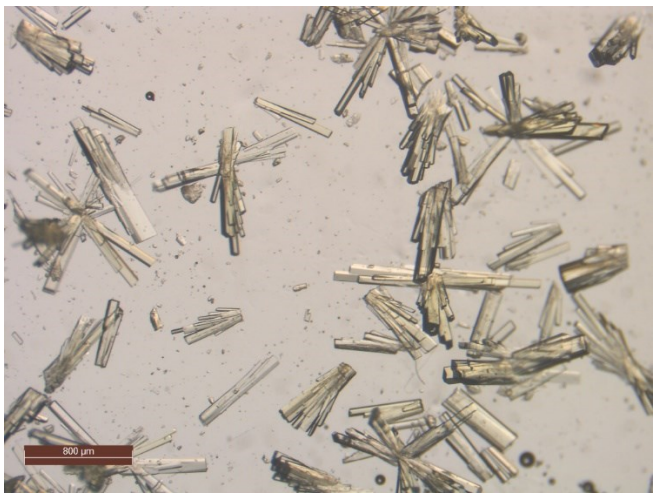
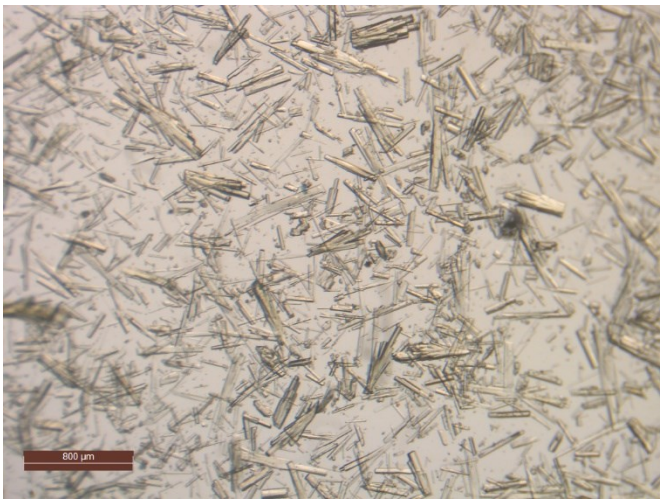


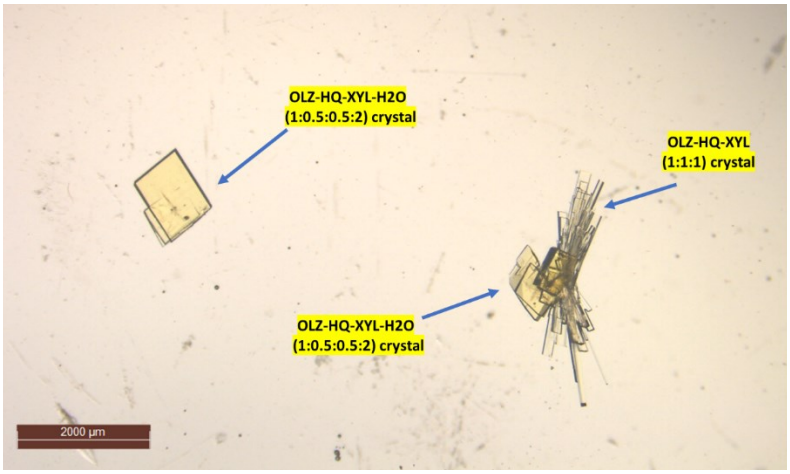
Figure S2. Comparison of simulated PXRD patterns of **(a) OLZ-HQ-XYL (1:1:1) (b) OLZ-HQ-XYL-H2O (1:0.5:0.5:2)** with experimental XRD patterns of cocrystal solvates prepared in the liquid assisted grinding (LAG) independently conducted on two different sources of olanzapine materials with hydroquinone in the presence of xylene solvent **(c) LAG OLZ-HQ-XYL (source1:TCI) (d) LAG OLZ-HQ-XYL (source2: Yarrow)** and with the XRD patterns of cocrystal solvates grown using the slow evaporation method by dissolving respective liquid assisted ground material in xylene **(e) OLZ-HQ-XYL crystals (source1:TCI) (f) OLZ-HQ-XYL crystals (source2:Yarrow)**.



(a)

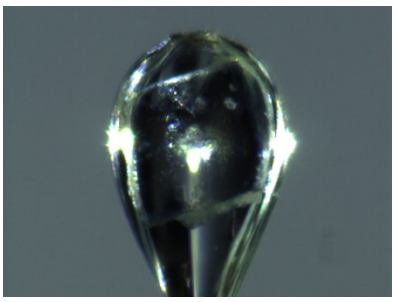


(b)



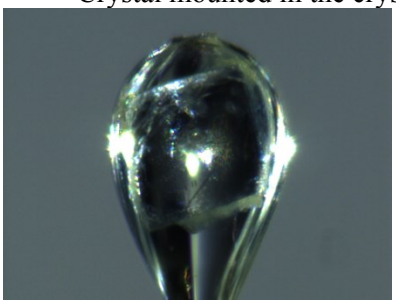
(c)

Figure S3. (a) Crystals of OLZ-HQ-XYL prepared using olanzapine (Source 1:TCI) (b) Crystals of OLZ-HQ-XYL prepared using olanzapine (Source 2: Yarrow) (c) Concomitant growth of both OLZ-HQ-XYL-H2O (1:0.5:0.5:2) and OLZ-HQ-XYL (1:1:1) crystals in the crystallization beaker.



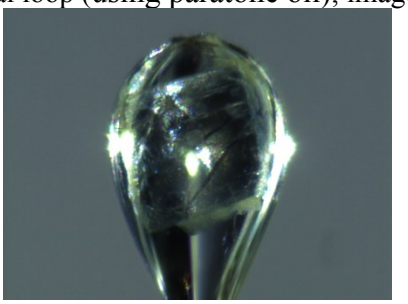
5 minutes

Crystal mounted in the crystal loop (using paratone oil); image recorded prior to fast scan



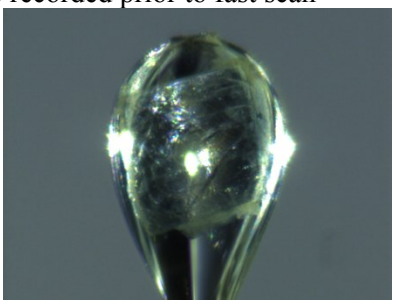
18 minutes

Triclinic	$P\bar{1}$
a = 9.30(2)Å	α = 88.74(3)˚
b = 10.84(2)Å	β = 88.01(5)˚
c = 15.85(4)Å	γ = 82.99(4)˚
V = 1584.72Å^3 ; T = 293K	
OLZ-HQ-BEN (1:1:2)	
Structure solved from fast scan data	



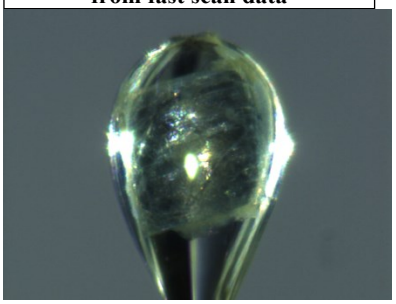
32 minutes

Triclinic	$P\bar{1}$
a = 9.26(3)Å	α = 88.72(4)˚
b = 10.78(4)Å	β = 88.08(5)˚
c = 15.78(6)Å	γ = 83.07(3)˚
V = 1562.55Å^3 ; T = 293K	
OLZ-HQ-BEN (1:1:2)	
Structure solved from fast scan data	



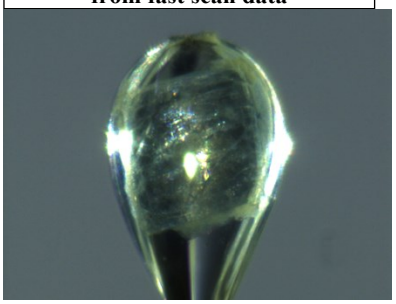
53 minutes

Triclinic	
a = 8.98Å	α = 90.93˚
b = 10.46Å	β = 88.18˚
c = 15.28Å	γ = 96.70˚
V = 1425 Å^3 ; T = 293K	
Only unit cell	
No structure solution	



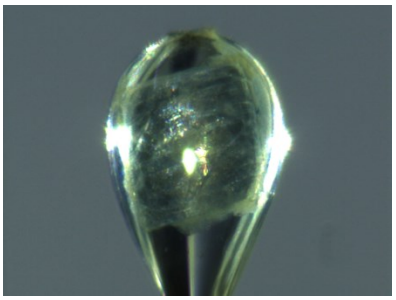
90 minutes

Triclinic	
a = 8.94Å	α = 81.67˚
b = 10.54Å	β = 82.55˚
c = 14.01Å	γ = 83.93˚
V = 1286 Å^3 ; T = 293K	
Only unit cell; difficult to index	
No structure solution	



120 minutes

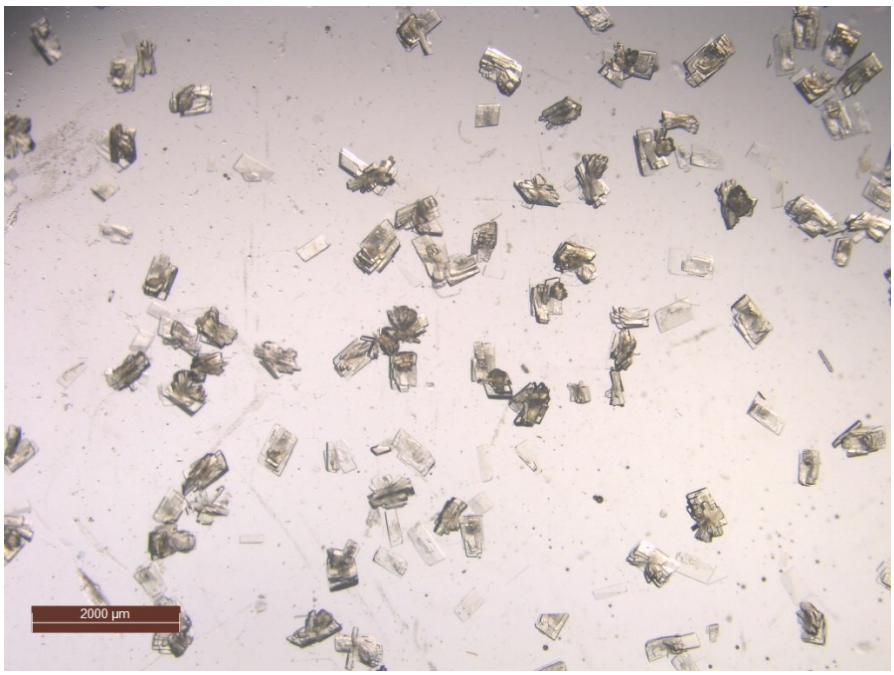
Triclinic	$P\bar{1}$
a = 9.26(10)Å	α = 81.42(9)˚
b = 10.81(11)Å	β = 83.15(9)˚
c = 14.35(16)Å	γ = 84.41(10)˚
V = 1389Å^3 ; T = 293K	
OLZ-HQ-BEN (1:1:1)	
Structure solved from fast scan data	



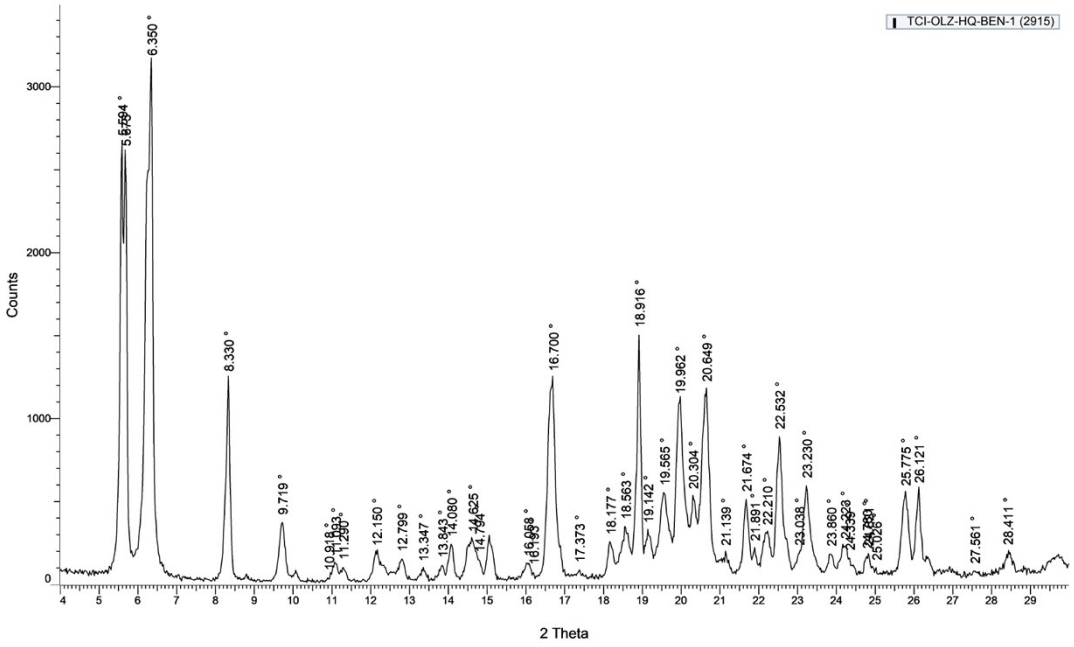
166 minutes

Triclinic	$P\bar{1}$
a = 9.22(5)Å	α = 81.58(5)˚
b = 10.88(6)Å	β = 83.17(6)˚
c = 14.43(8)Å	γ = 84.22(6)˚
V = 1416.64Å^3 ; T = 293K	
OLZ-HQ-BEN (1:1:1)	
Structure solved from fast scan data	

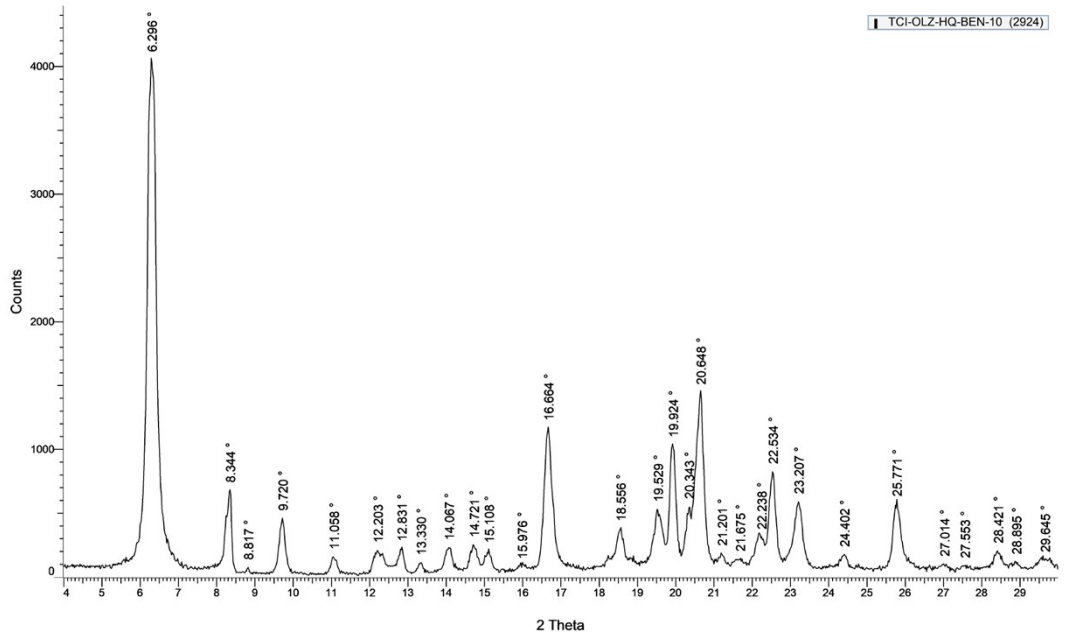
Figure S4. Capturing phase transformation from OLZ-HQ-BEN (1:1:2) to OLZ-HQ-BEN (1:1:1) structure in time-resolved single crystal X-ray diffraction experiments conducted in fast scan mode (180 images - phi scan). Initial fast scan data after 18 minutes indicated unit cell dimensions of structure that matched to OLZ-HQ-BEN (1:1:2). The OLZ-HQ-BEN (1:1:2) crystal was stable up to 32 minutes in the paratone oil, after which it started to transform as indicated by changes in the unit cell dimensions. The transformation to OLZ-HQ-BEN (1:1:1) was complete after 120 minutes. The structure of OLZ-HQ-BEN (1:1:1) was also solved. OLZ-HQ-BEN (1:1:1) remained stable at 166 minutes. Optical images of crystal were also captured at regular time intervals during the phase transition.


2000 µm

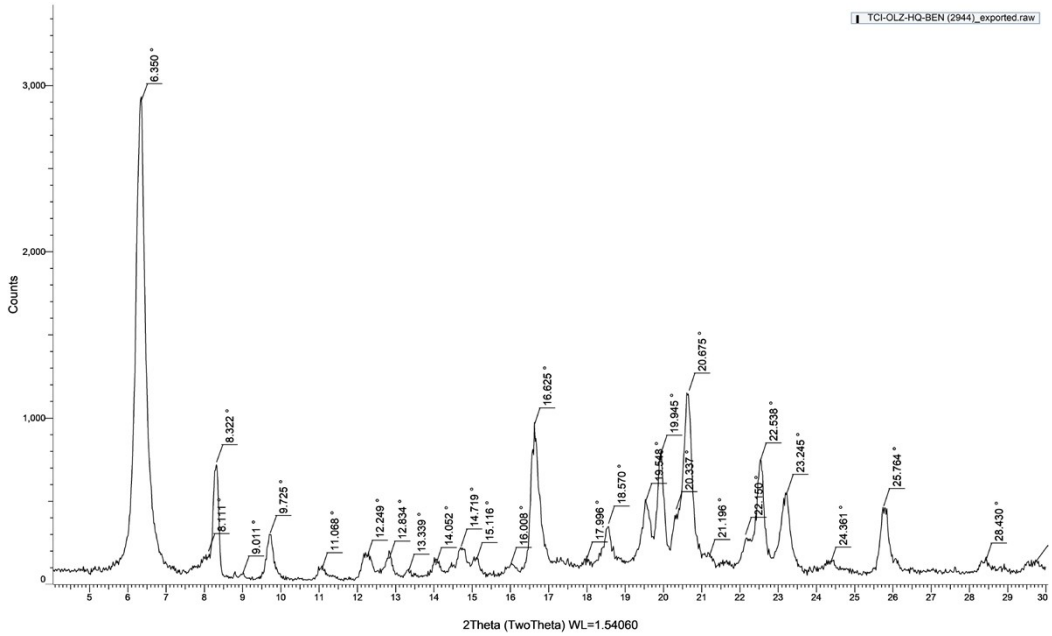
(a)


TCI-OLZ-HQ-BEN-1 (2915)
Counts
2 Theta
6.350 °
8.330 °
9.719 °
12.150 °
12.799 °
13.347 °
13.843 °
14.080 °
16.700 °
17.373 °
18.177 °
18.563 °
18.916 °
19.142 °
19.565 °
19.962 °
20.304 °
20.649 °
21.139 °
21.674 °
21.891 °
22.210 °
22.532 °
23.038 °
23.230 °
23.860 °
25.775 °
26.121 °
27.561 °
28.411 °

(b)



(c)



(d)

Figure S5. (a) Microscope image of freshly grown crystals of OLZ-HQ-BEN (1:1:2) immersed in the benzene liquid. (b) Time-resolved powder X-ray diffraction study at room temperature on OLZ-HQ-BEN (1:1:2) powdered crystals after 3 minutes (c) PXRD data after 30 minutes. The peak at 2θ = 5.67˚ (from 1:1:2 phase) and peak at 2θ = 6.35˚ (from 1:1:1 phase) had approximately similar intensity values and suggested it to be a mixture of two phases at the end of 3 minutes. The OLZ-HQ-BEN (1:1:2) phase completely transformed to OLZ-HQ-BEN (1:1:1) phase at the end of 30 minutes. The phase transformation was indicated by the disappearance of peak at 2θ = 5.67˚ while the intensity of peak at 2θ = 6.35˚ increased. Similarly, the peak at 2θ = 18.92˚ from 1:1:2 crystal was completely disappeared. (d) PXRD data after 24 hours. The transformed OLZ-HQ-BEN (1:1:1) phase was intact.

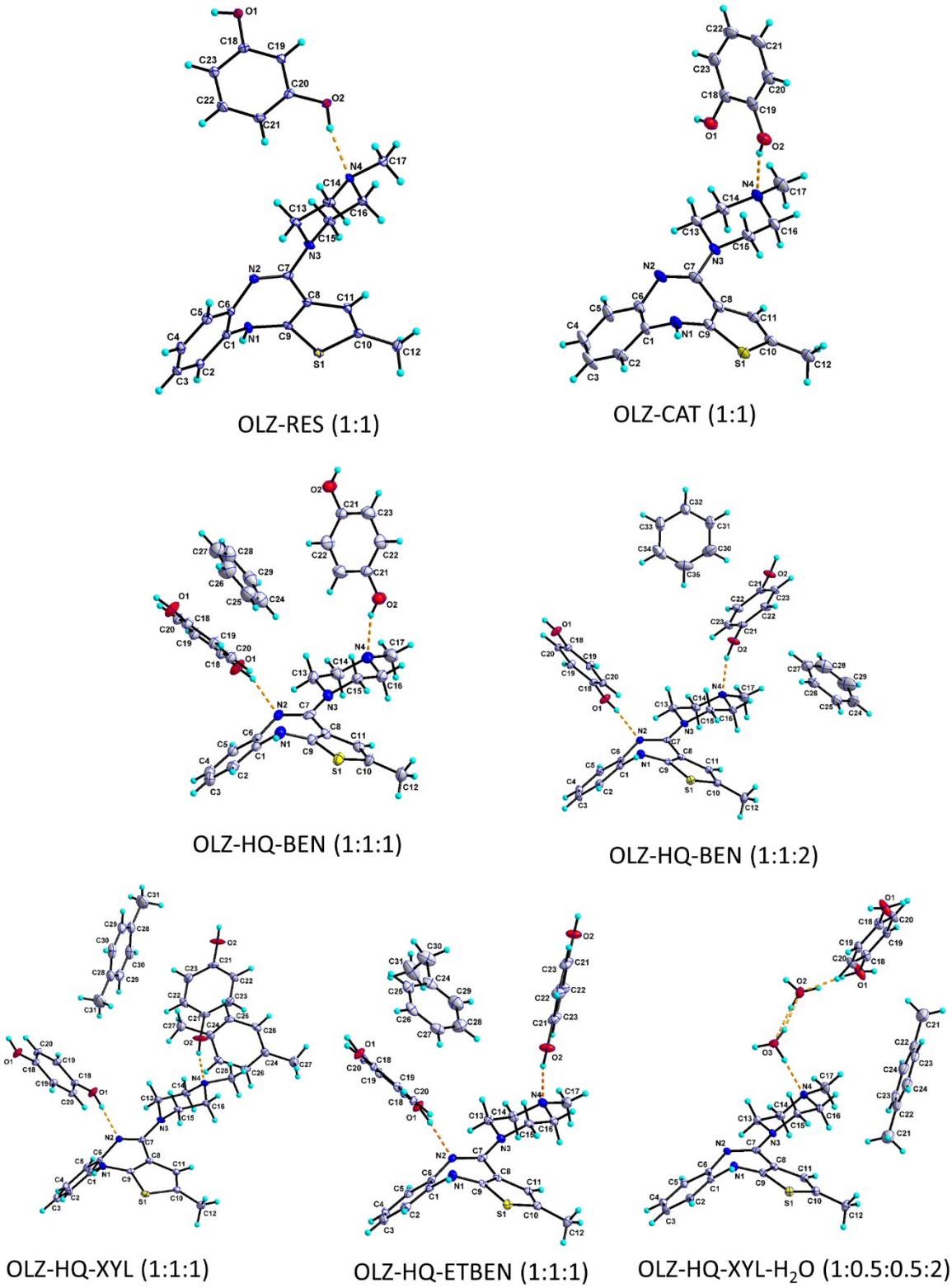


Figure S6. ORTEP diagrams of olanzapine cocrystals and cocrystal solvates. Crystal data were collected at 100K. Atomic displacements are drawn at 50% probability. Hydrogen atoms are shown as spheres of arbitrary radii. Dotted lines represent hydrogen bonds.

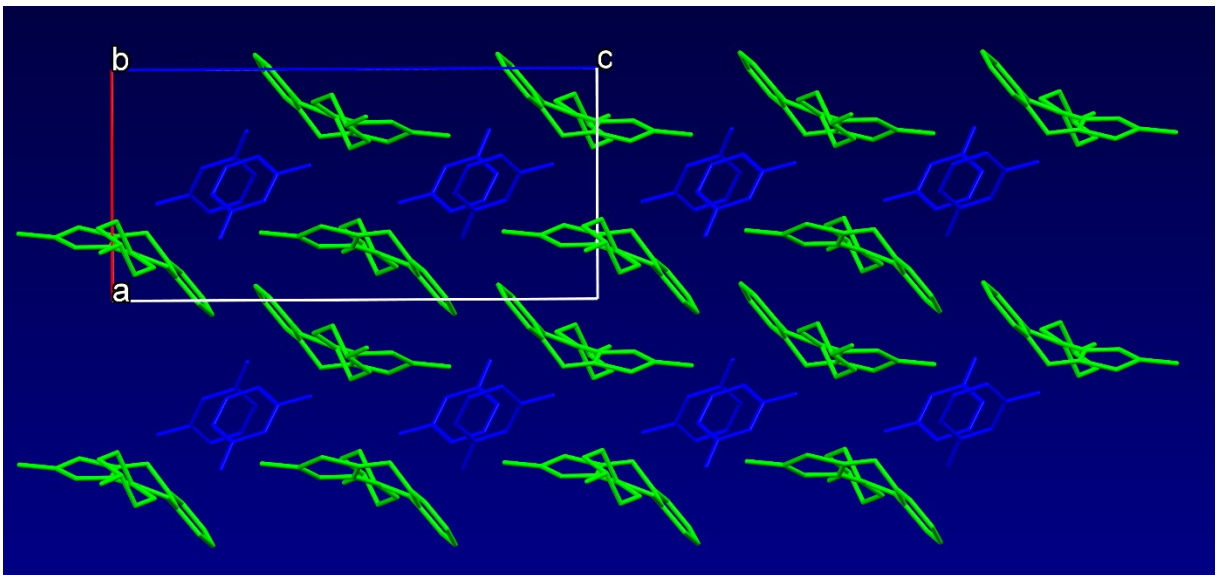


Figure S7. Olanzapine molecules between the adjacent 2D networks are close packed on their concave sides forming a nonbonded centrosymmetric dimers and complete the three dimensional crystal packing.

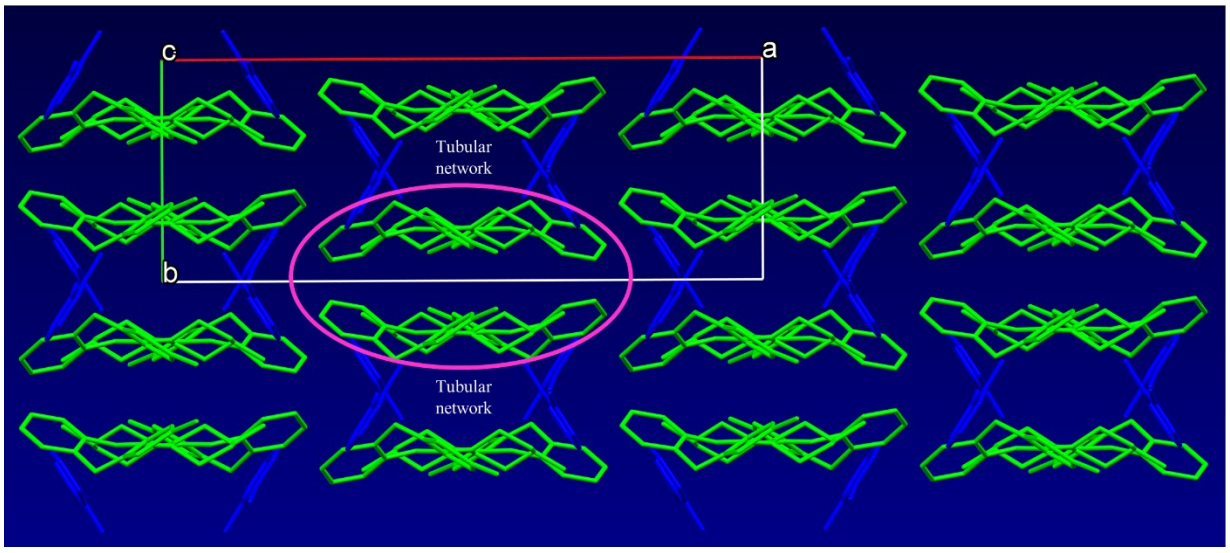


Figure S8. Convex side overlapping of olanzapine molecules (green) facilitates tubular network formation and concave side overlapping of olanzapine molecules connects the adjacent tubular networks and facilitates 3D crystal packing.

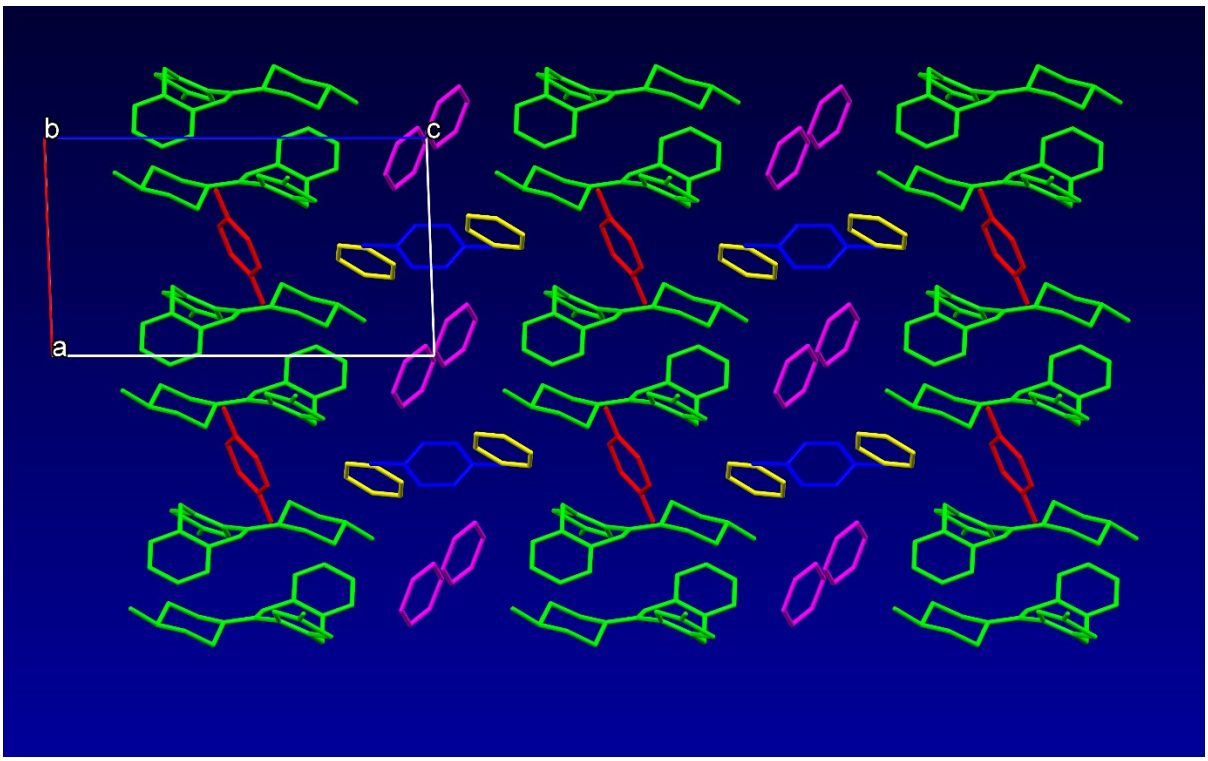


Figure S9. 3D crystal packing of OLZ-HQ-BEN (1:1:2) cocrystal. Concave side overlapping of olanzapine molecules (green) facilitates stacking of 2D networks.

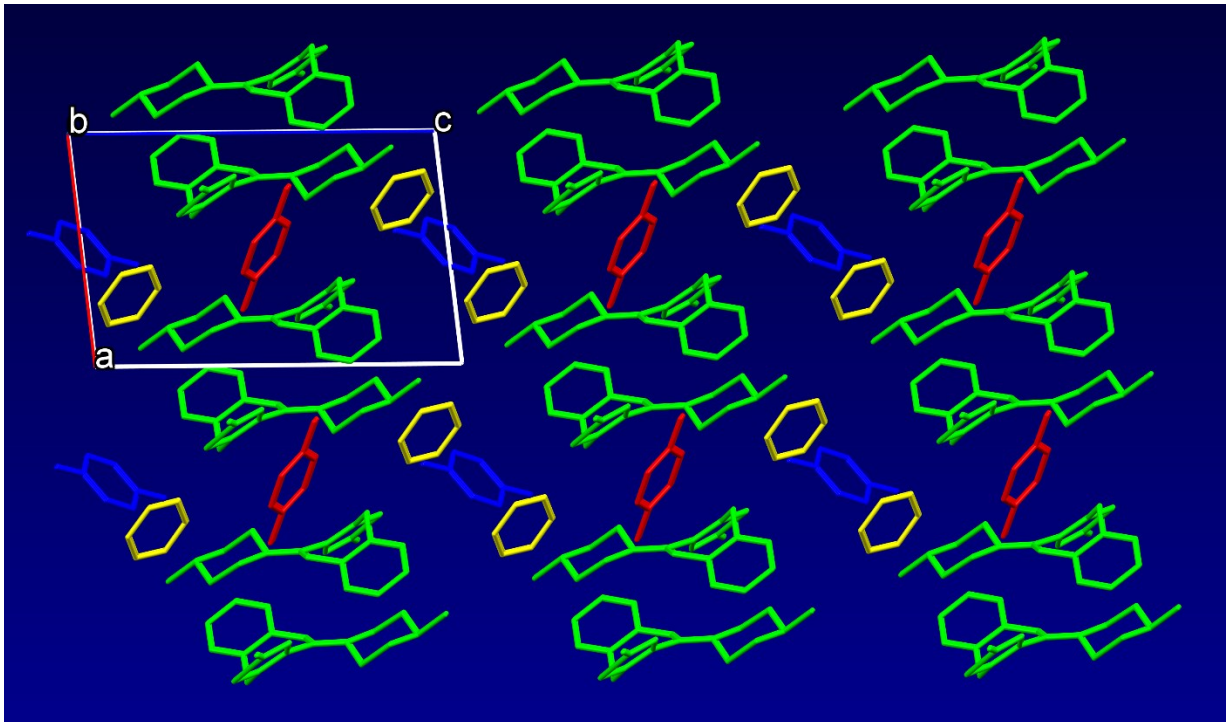


Figure S10. 3D crystal packing of OLZ-HQ-BEN (1:1:1) cocrystal. Concave side overlapping of olanzapine molecules (green) facilitates stacking of 2D networks.

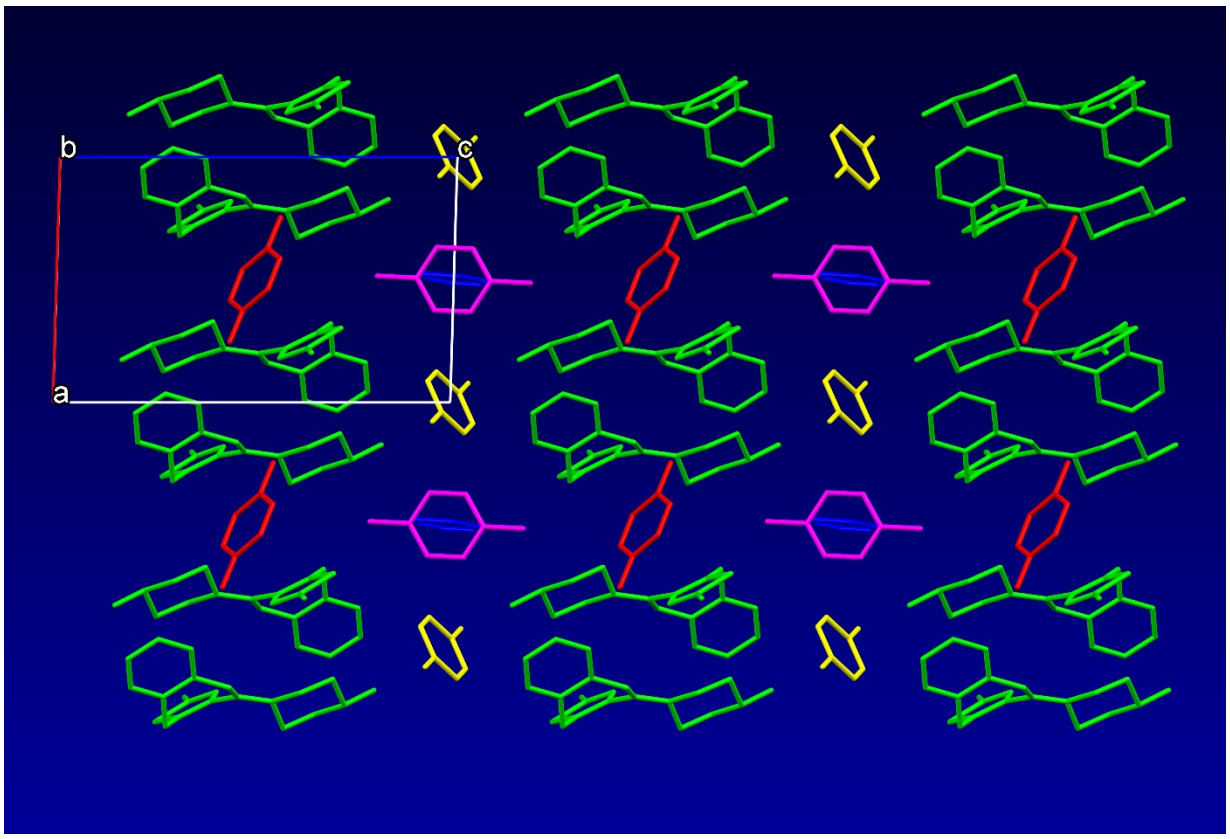


Figure S11. 3D crystal packing of OLZ-HQ-XYL (1:1:1) cocrystal. Concave side overlapping of olanzapine molecules (green) facilitates the stacking of 2D networks.

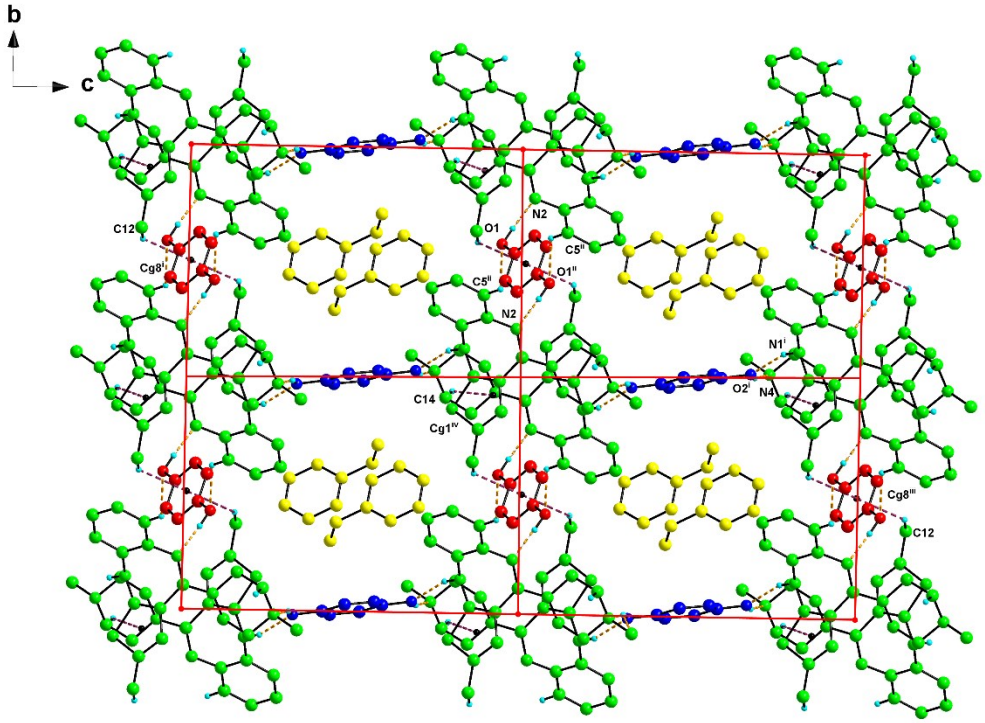


Figure S12. Representation of rectangular grid network in 3D-crystal packing in OLZ-HQ-ETBEN (1:1:1). Symmetry codes: (i) 1-x,1-y,1-z;(ii) 2-x,-y,1-z;(iii) x,1+y,z;(iv) 2-x,1-y,1-z.

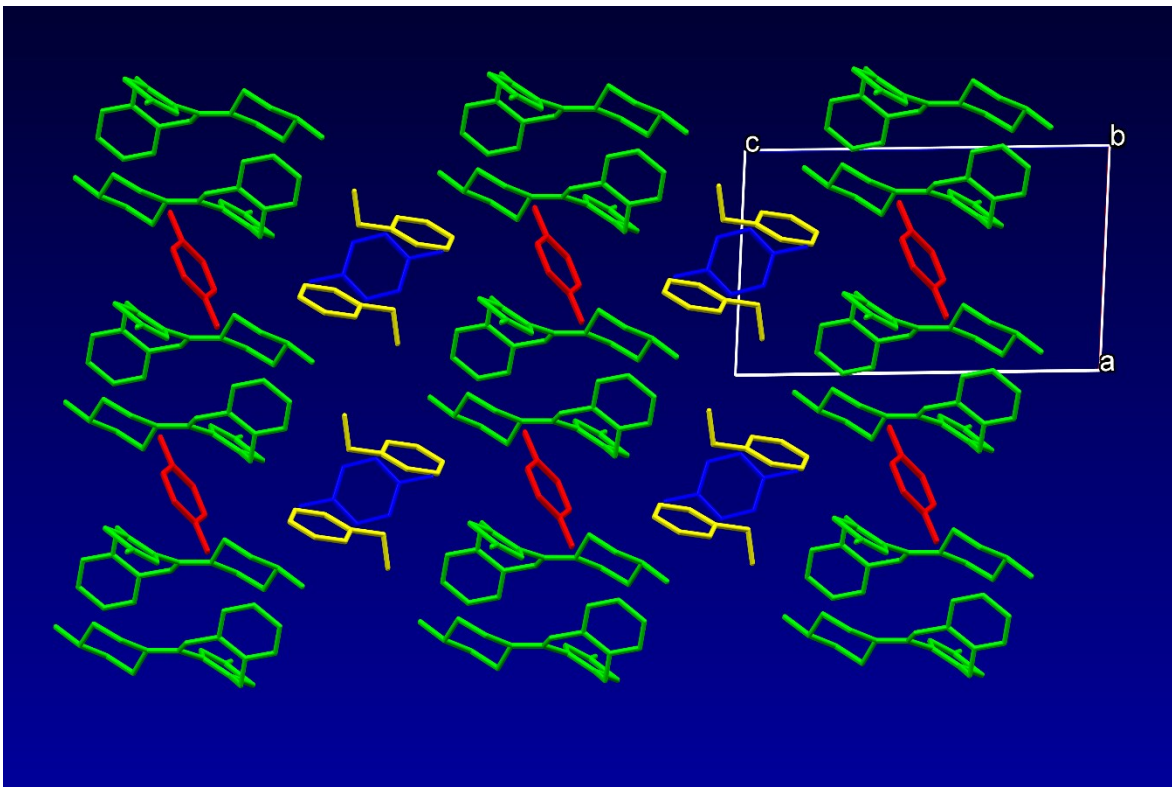


Figure S13. Three dimensional crystal packing of OLZ-HQ-ETBEN (1:1:1) cocrystal. Overlapping of olanzapine molecules (green) on their concave sides facilitates stacking of 2D networks.

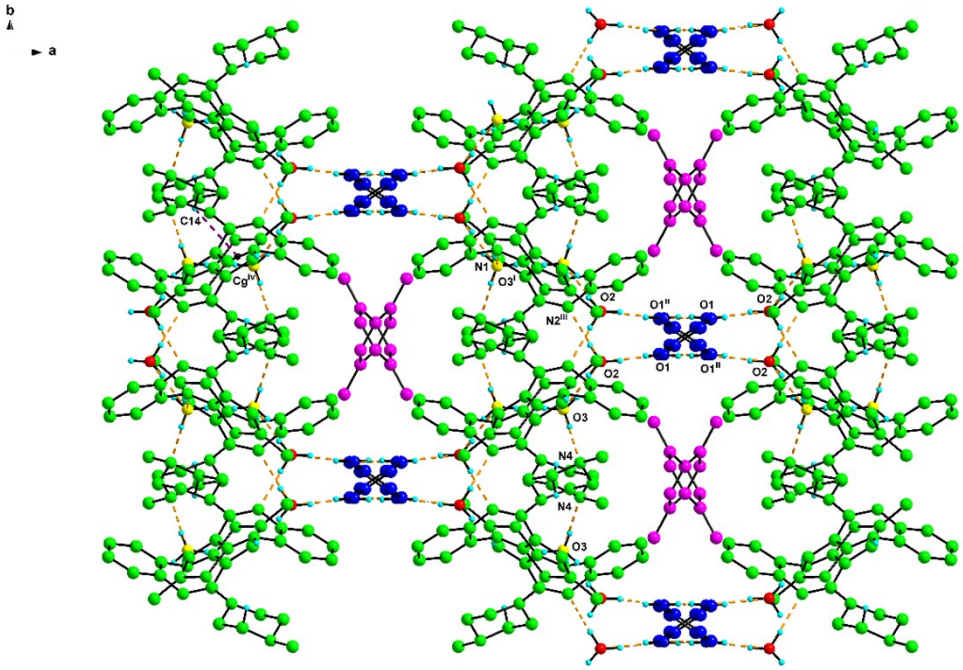


Figure S14. 3D-crystal packing of OLZ-HQ-XYL-H_2O (1:0.5:0.5:2). Voids were observed in the hydrogen bonded network of OLZ (green), HQ (blue) and water (red) molecules, which were occupied by solvent molecule p-xylene (magenta colored molecules). Symmetry codes: (i)3/2-x,1/2+y,3/2-z;(ii)1-x,y,1/2-z;(iii)3/2-x,1/2-y,1-z;(iv)3/2-X,3/2-Y,1-Z.

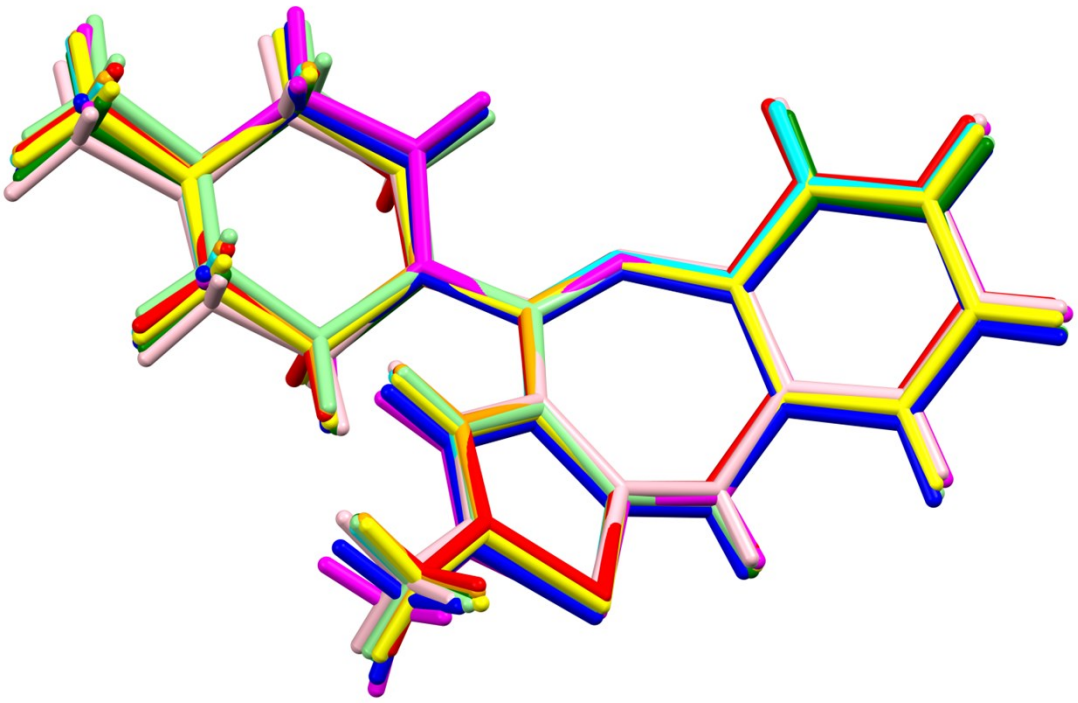
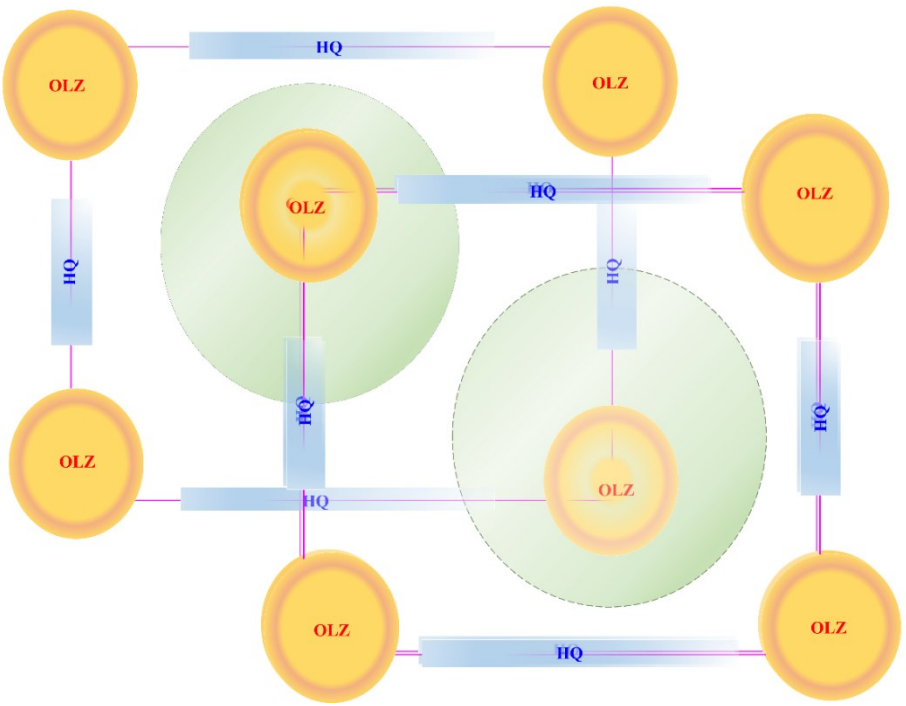
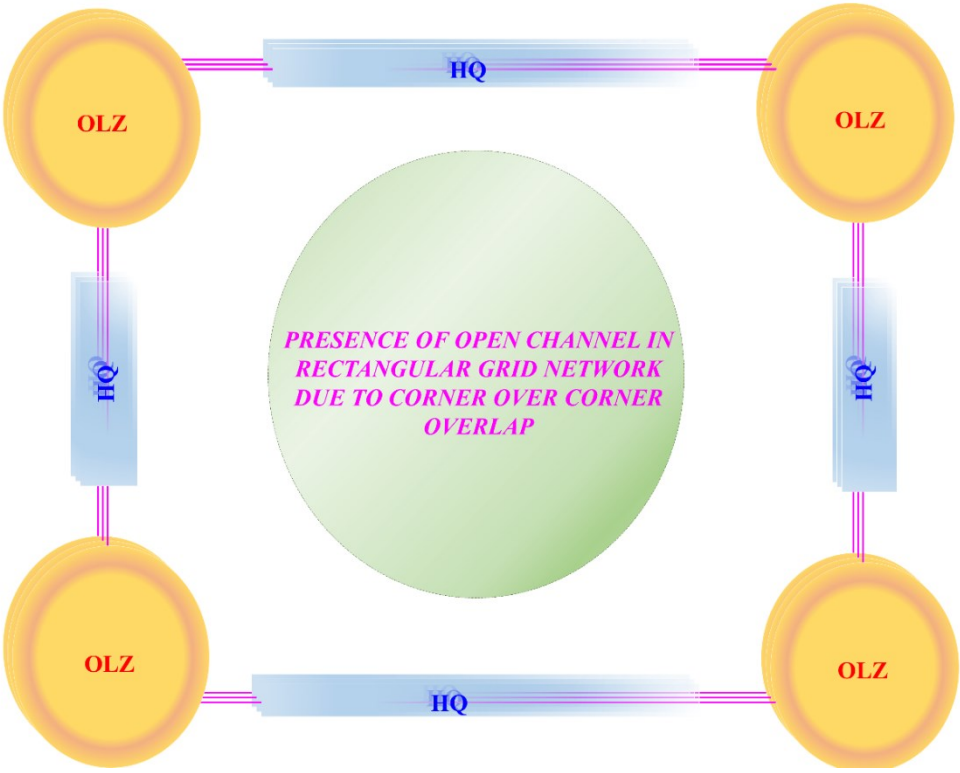


Figure S15. Overlay of OLZ molecules extracted from different crystal structures considered in this work. Color codes: OLZ-HQ-TOL (1:1:1) Form I – red, OLZ-HQ-TOL (1:1:1) Form II – orange, OLZ-HQ-BEN (1:1:2) – yellow, OLZ-HQ-BEN (1:1:1) – light green, OLZ-HQ-XYL (1:1:1) – dark green, OLZ-HQ-ETBEN (1:1:1) – cyan, OLZ-HQ-XYL-H_2O (1:1:1:2) – blue, OLZ-RES(1:1) – magenta, OLZ-CAT (1:1) – pink.



(a)



(b)

Figure S16. (a) Corner-over-cavity arrangement in OLZ-HQ-TOL (1:1:1) form I. (b) Corner-over-corner arrangement in OLZ-HQ-TOL (1:1:1) form II.

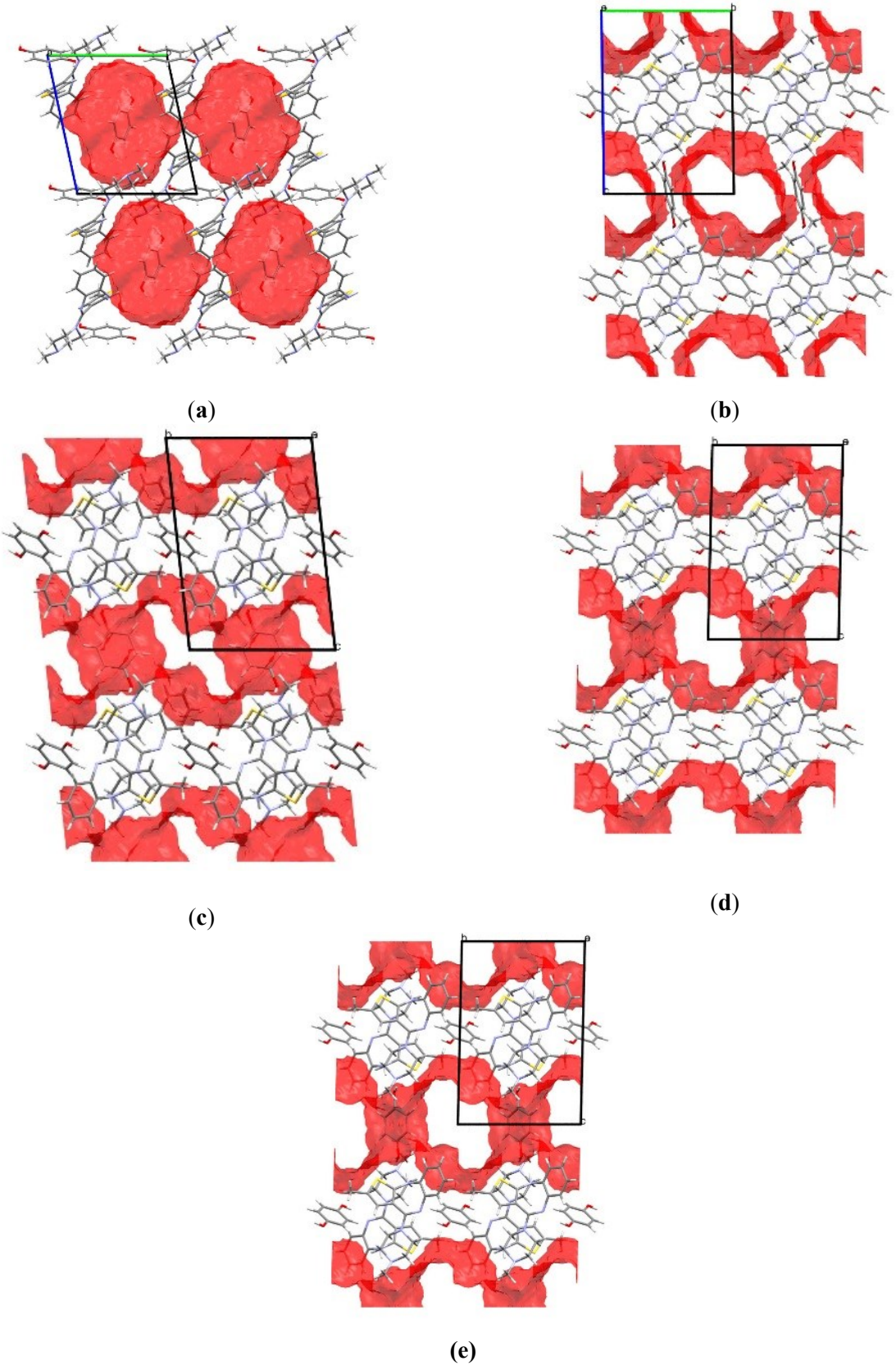


Figure S17. Void maps in the crystal structures of (a) OLZ-HQ-TOL (1:1:1) form I, (b) OLZ-HQ-TOL (1:1:1) form II, (c) OLZ-HQ-XYL (1:1:1), (d) OLZ-HQ-BEN (1:1:1) and (e) OLZ-HQ-BEN (1:1:1).

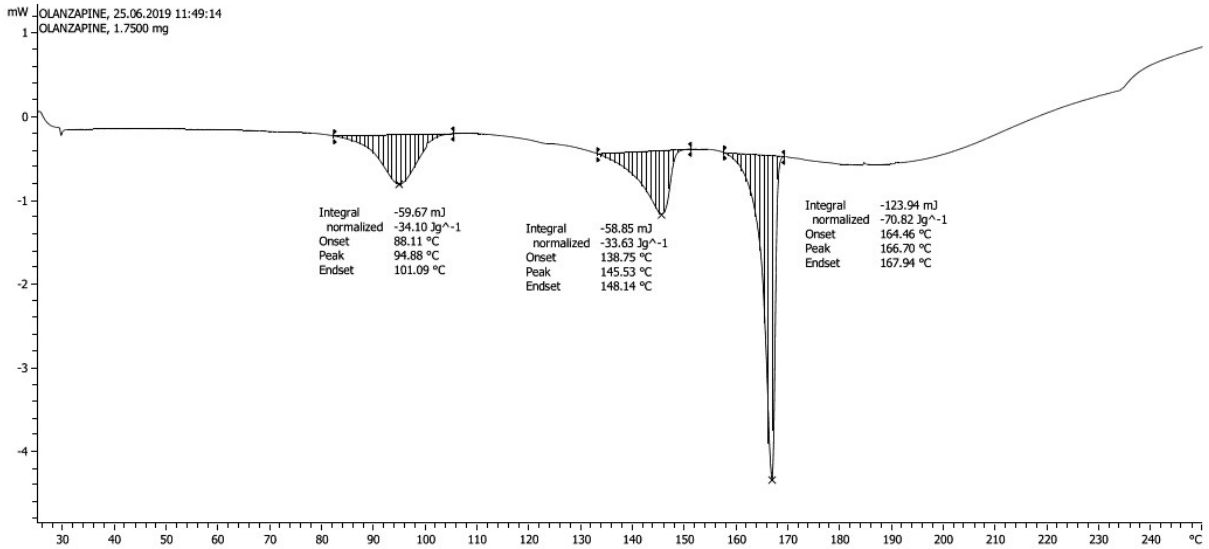


Figure S18. DSC thermogram of OLZ-HQ-XYL (1:1:1) cocrystal solvate. The first endotherm corresponds to the desolvation, followed by the second endotherm of a phase transformation and the third endotherm to the melting of the material.

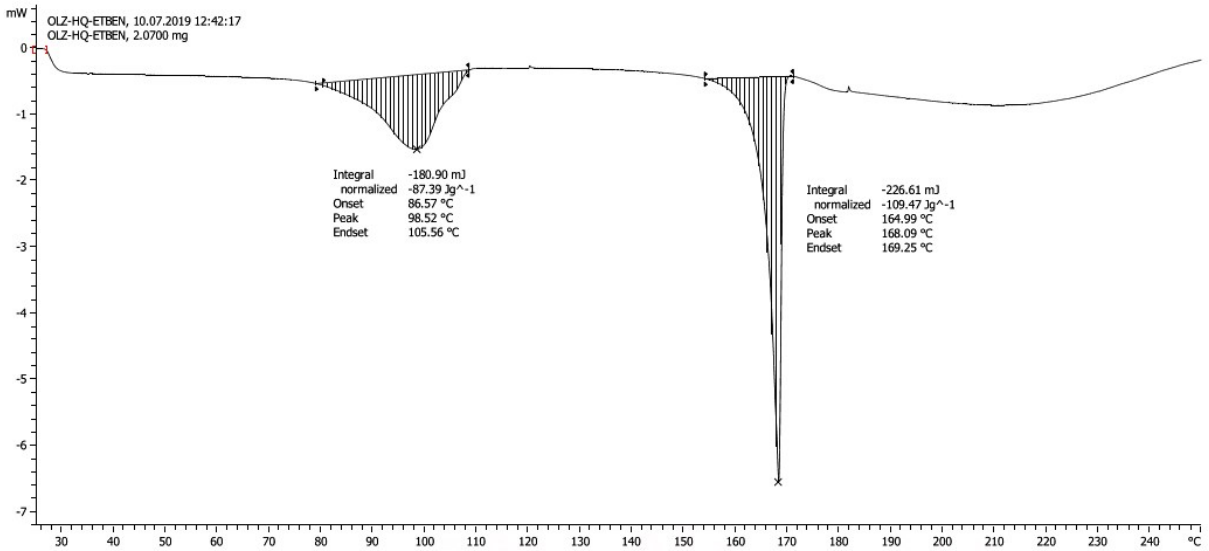


Figure S19. DSC thermogram of OLZ-HQ-ETBEN (1:1:1) cocrystal solvate. The first endotherm corresponds to the desolvation followed by the second endotherm of melting of the material.

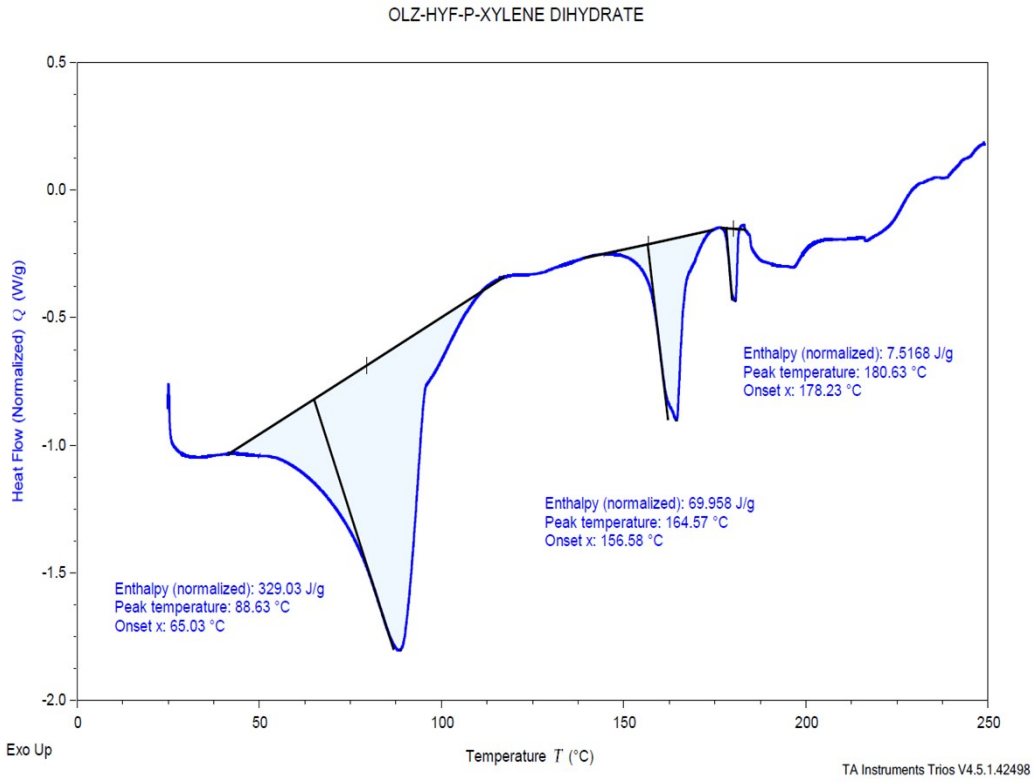


Figure S20. DSC thermogram of OLZ-HQ-XYL-H_2O (1:0.5:0.5:2) cocrystal solvate hydrate. The first endotherm corresponds to the concomitant events of desolvation and melting of cocrystal, and the second endotherm corresponds to the phase transformed olanzapine anhydrous form I material.

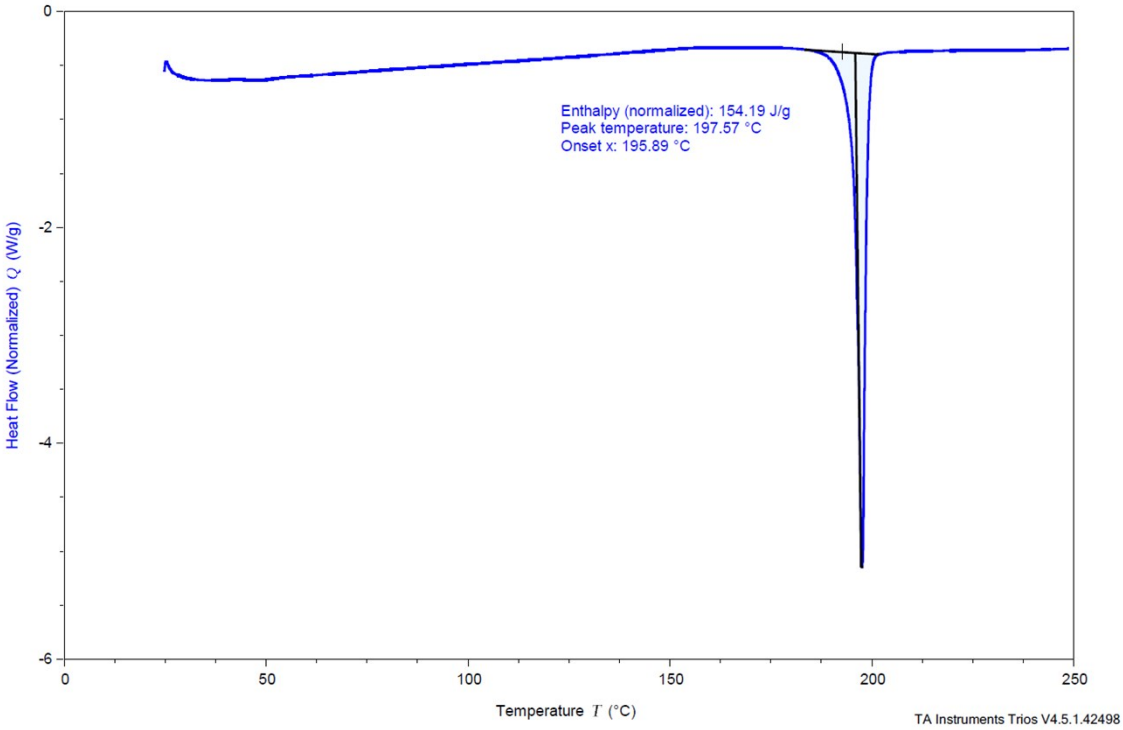


Figure S21. DSC thermogram of OLZ-RES (1:1) cocrystal which showed a single melting endotherm.

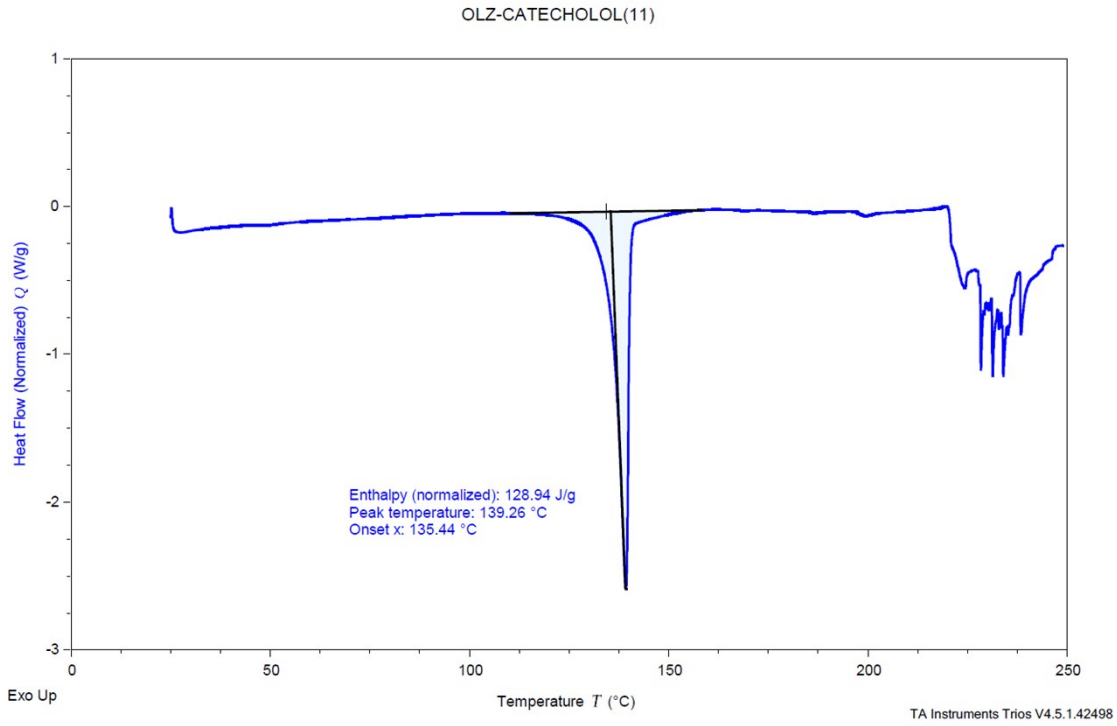


Figure S22. DSC thermogram of OLZ-CAT (1:1) cocrystal which showed a single melting endotherm.

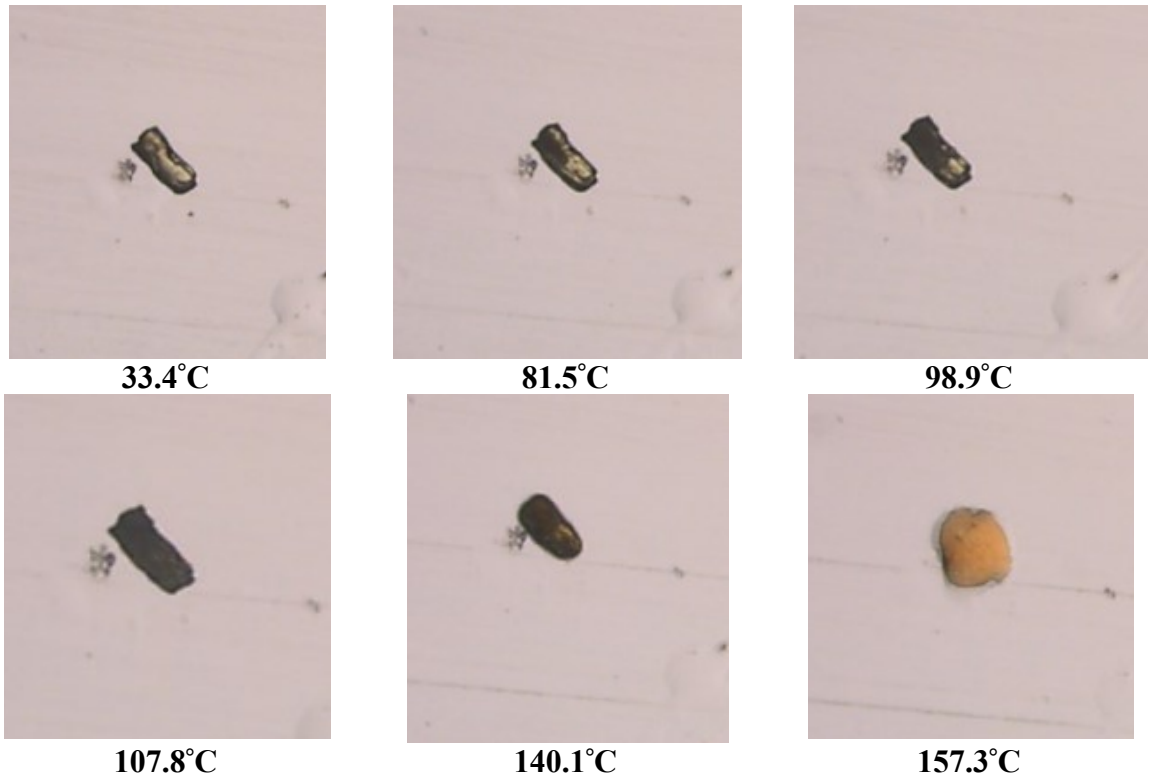


Figure S23. Hot stage images for OLZ-HQ-TOL (1:1:1) form I.

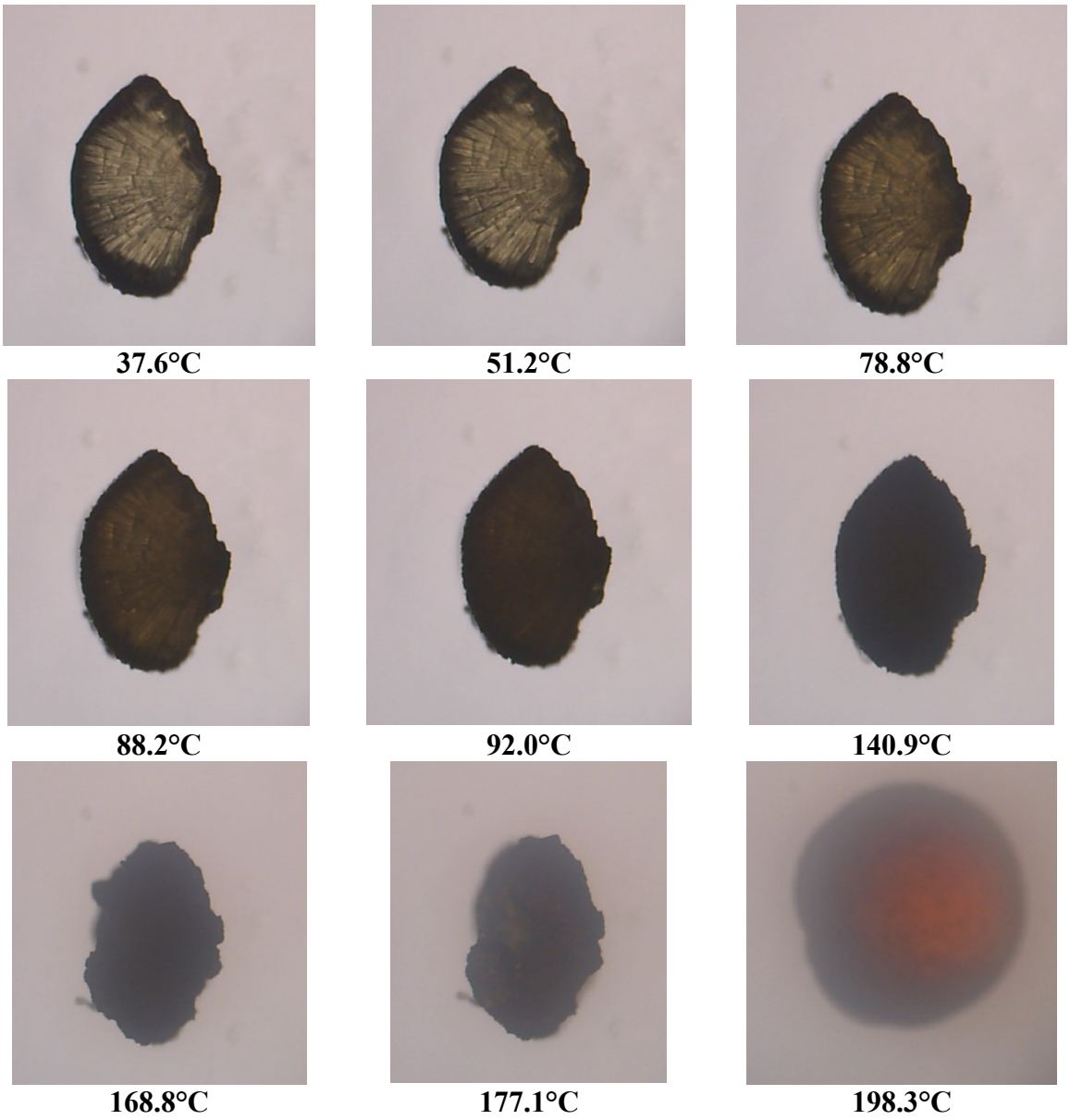


Figure S24. Hot stage images for OLZ-HQ-TOL (1:1:1) form II.

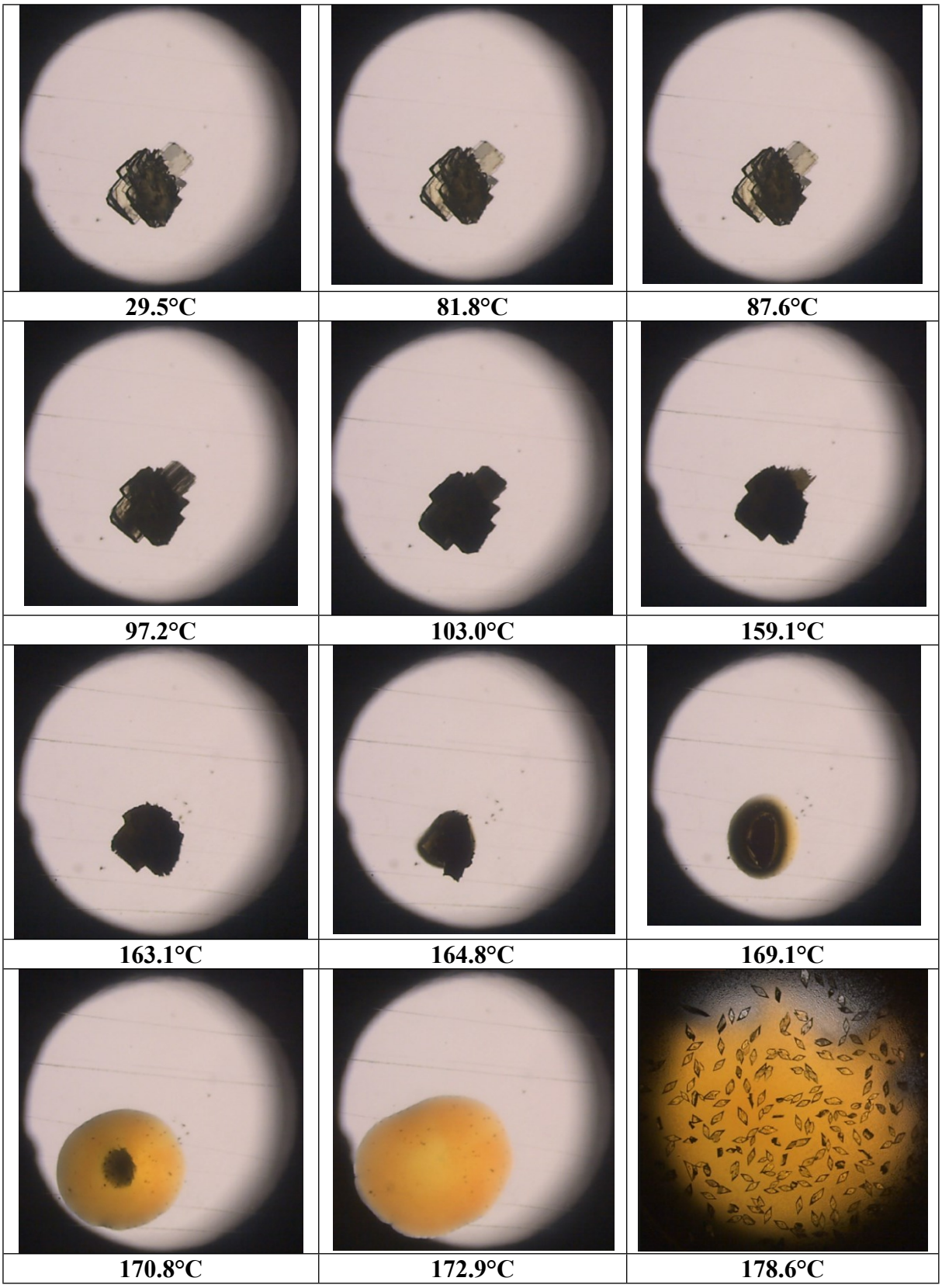


Figure S25. Hot stage images for OLZ-HQ-XYL (1:1:1). The crystals noticed after the cocrystal melting correspond to sublimed crystals of hydroquinone.

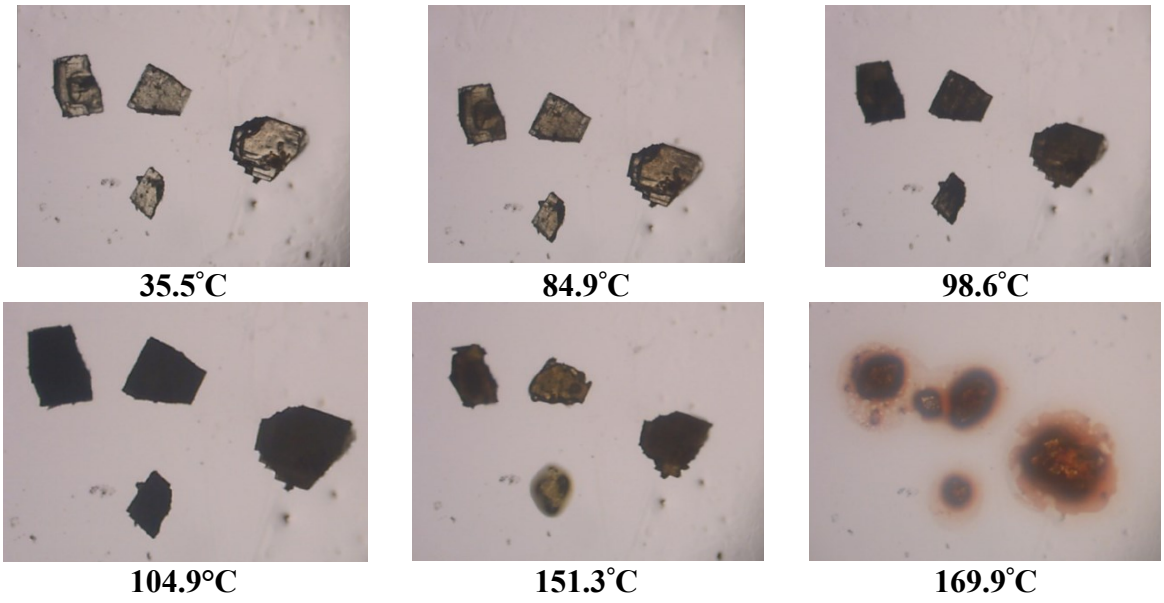


Figure S26. Hot stage images for OLZ-HQ-ETBEN (1:1:1)

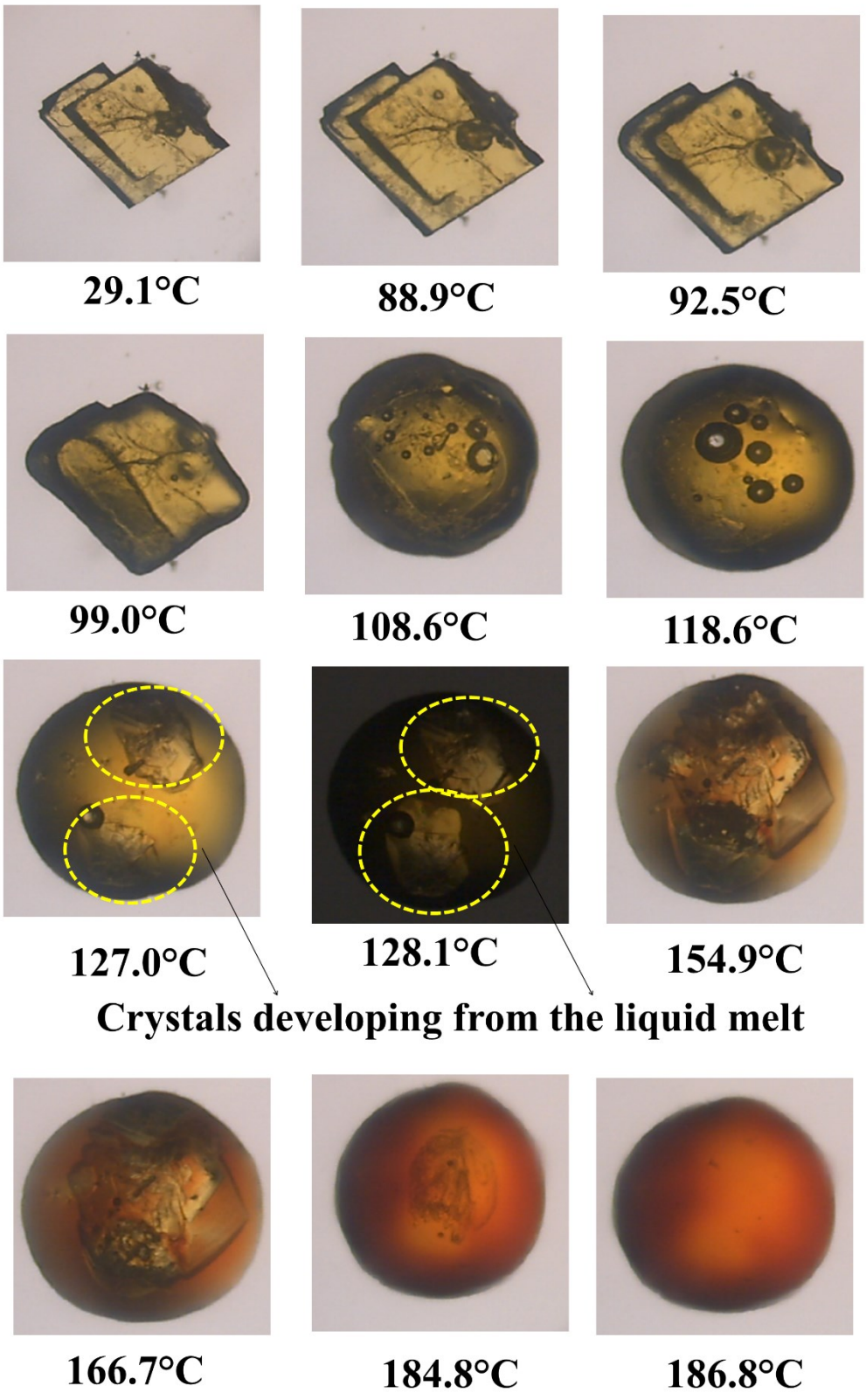


Figure S27. Hot stage images for OLZ-HQ-XYL-H2O (1:0.5:0.5:2). The desolvation and melting were not distinct, but occurred concomitantly from the temperature 92.5°C and extended till the temperature 118.6°C. The crystals were developed from the melt at 127.0°C and those crystals started to re-melted at 166.7°C and ended by 185.0°C. The newly developed crystals were later identified as anhydrous olanzapine form 1.

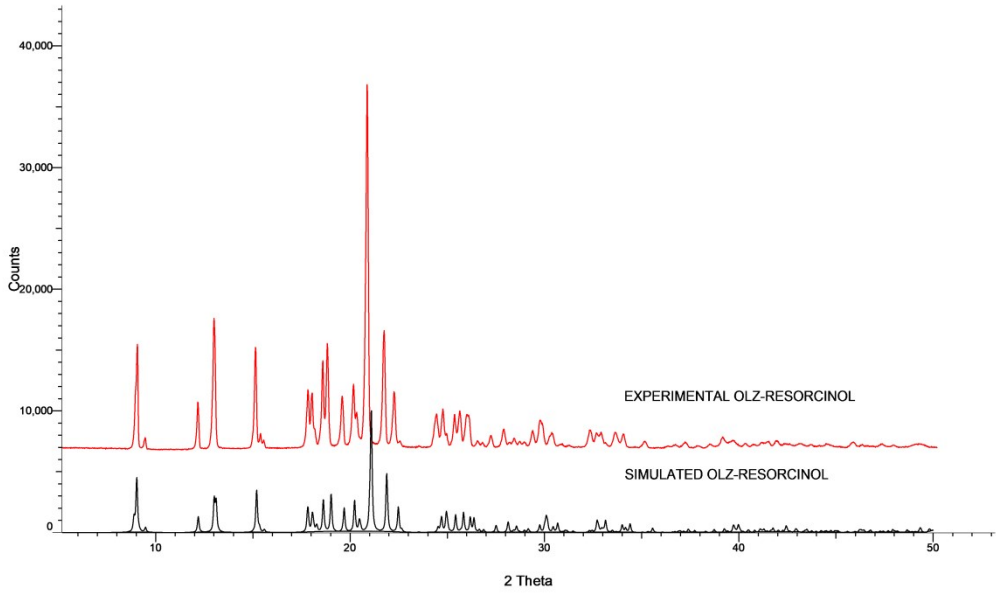


Figure S28. Overlay of experimental and simulated PXRD patterns of OLZ-RES (1:1) cocrystal.

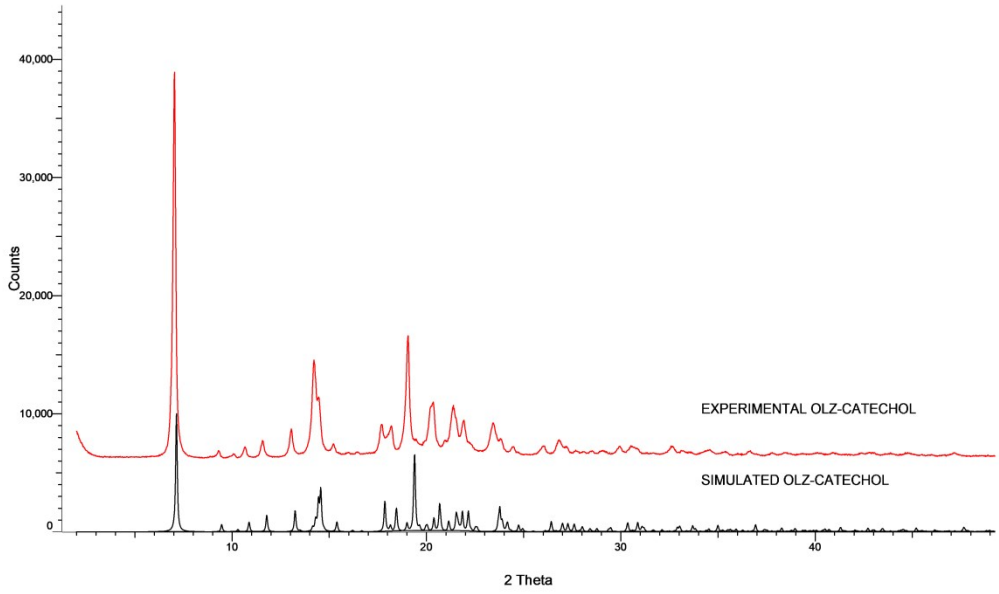


Figure S29. Overlay of experimental and simulated PXRD patterns of OLZ-CAT (1:1) cocrystal.

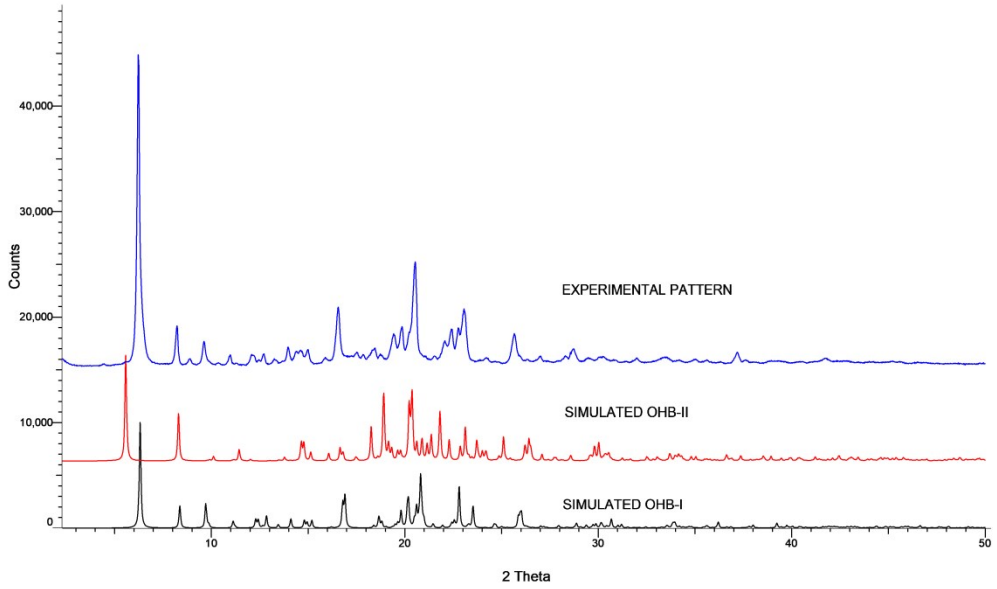


Figure S30. Overlay of experimental and simulated PXRD patterns of OLZ-HQ-BEN cocrystal material. The experimental pattern matches to OHB-I (1:1:1). A 2θ peak at 8.9° indicated the presence of unreacted OLZ in trace amounts.

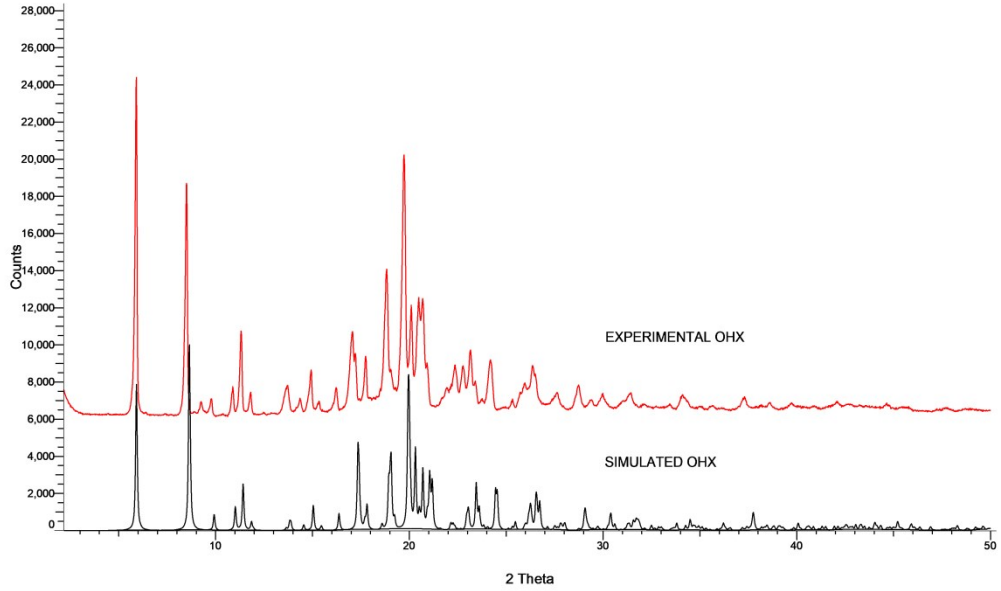


Figure S31. Overlay of experimental and simulated PXRD patterns of OLZ-HQ-XYL (1:1:1) cocrystal material. The experimental pattern nicely matches to the simulated pattern. OHB-I (1:1:1). A 2θ peak at 9.26° in experimental PXRD indicated the presence of unreacted HQ in trace amounts.

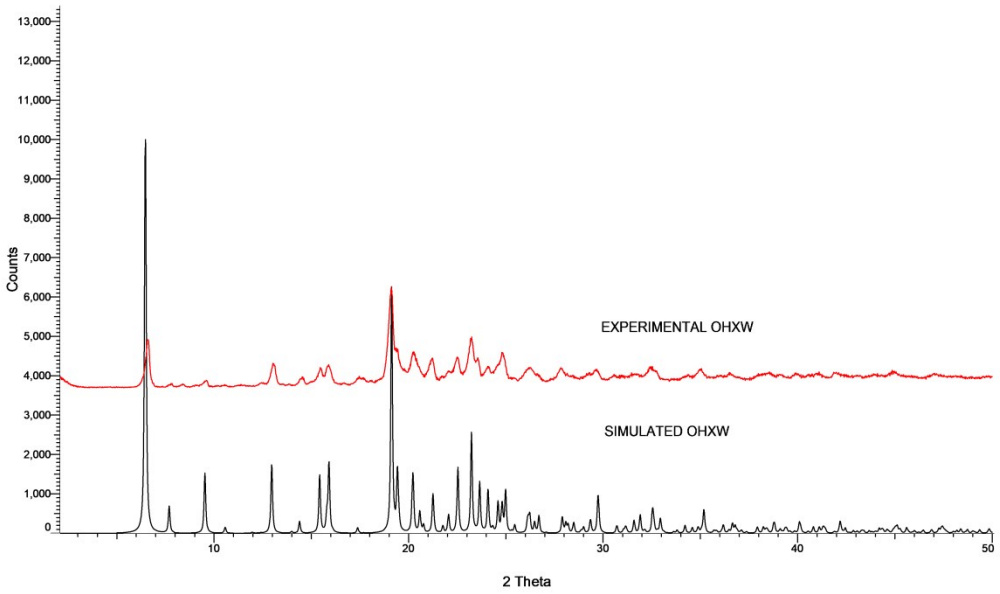


Figure S32. Overlay of experimental and simulated PXRD patterns of OLZ-HQ-XYL-H2O (1:0.5:0.5:1) cocrystal material. The experimental pattern matched well with the simulated pattern. OHB-I (1:1:1).