Crystal structure landscape of Ethenzamide: their physicochemical property study

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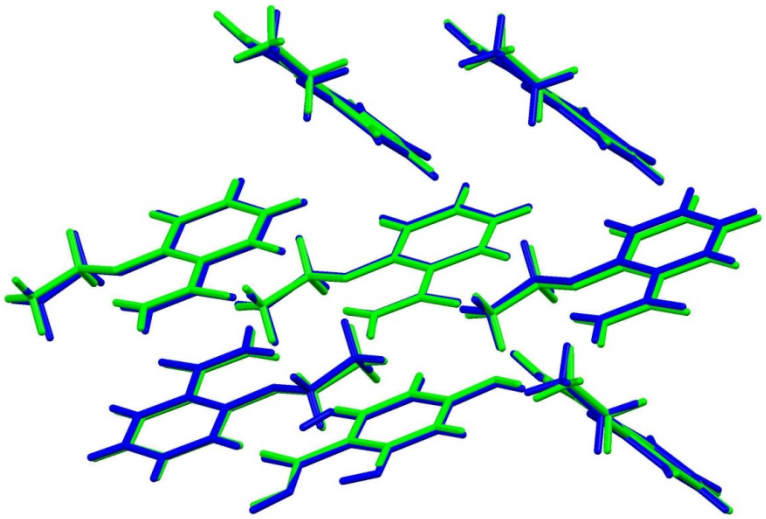


Figure S1. Comparison of crystal packing overlay of ETZ•24DHBA and ETZ•4HBA shown with different colors (green for ETZ•4HBA and blue for ETZ•24DHBA). PXRD similarity value of 0.957305 and rms value of 0.316331 comparing 7 out of 15 molecules with rotation matrix (-1.000, 0.001, 0.016; 0.002, 1.000, 0.024; -0.016, 0.024, -1.000) and translation vector (5.419, 0.208, 24.186) calculated using licensed version of Murcury CSD 3.8 software.

1. ETZ•24DHBA cocrystal (1:1):

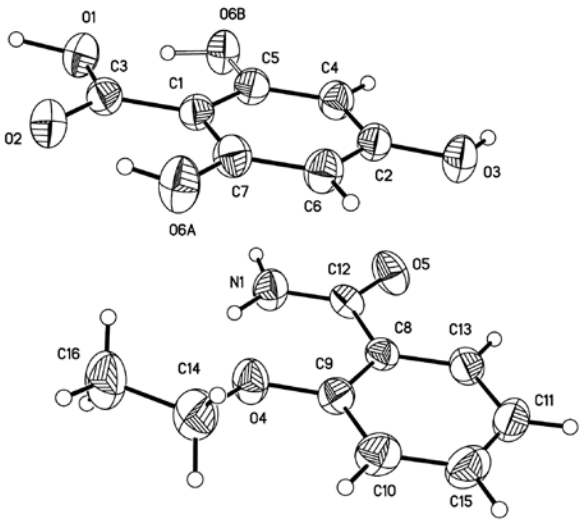


Figure S2. ORTEP diagram of ETZ•24DHBA cocrystal with 35 % probability ellipsoid.

2. ETZ•35DHBA cocrystal (1:1):

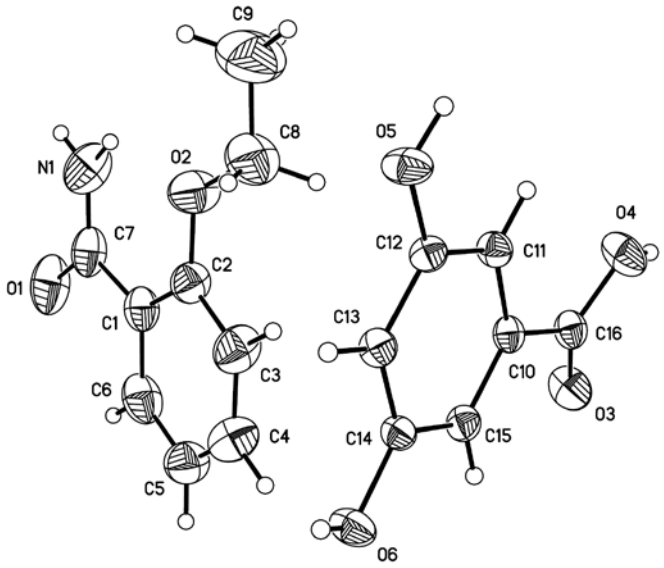


Figure S3. ORTEP diagram of ETZ•35DHBA cocrystal with 35 % probability ellipsoid.

3. ETZ•35DHBA•H_2O cocrystal hydrate (1:3:2):

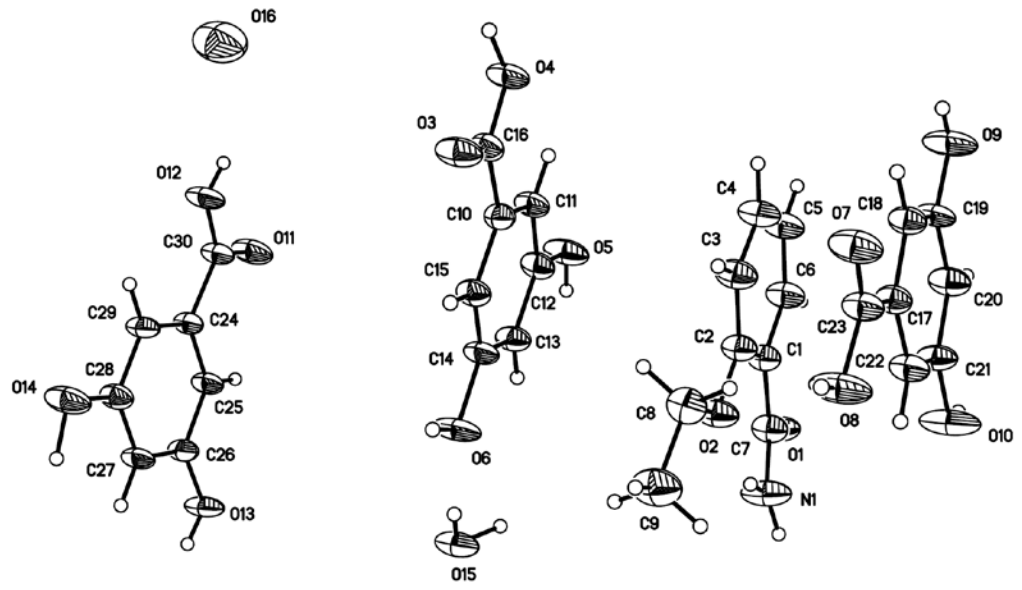


Figure S4. ORTEP diagram of ETZ•35DHBA•H_2O cocrystal hydrate with 35 % probability ellipsoid.

4. ETZ•FRA cocrystal (1:1):

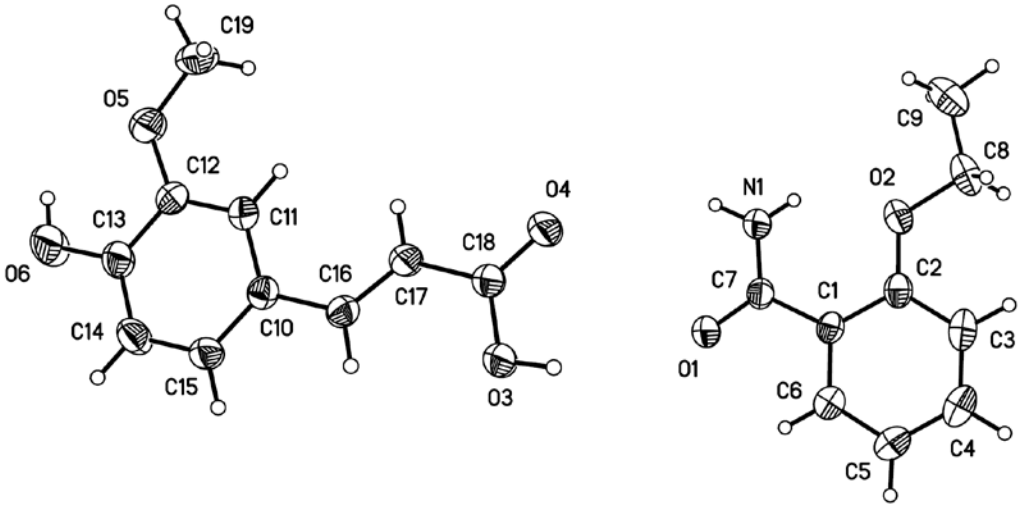


Figure S5. ORTEP diagram of ETZ•FRA cocrystal with 35 % probability ellipsoid.

Table S1: List of various co-formers and solvents used for co-crystallization with ethenzamide.

Compound	**Solvent**	**Inference**

ETZ:24DHBA (1:1)	Acetone	ETZ•24DHBA Cocrystal obtained
	CH_3NO_2	ETZ•24DHBA Cocrystal obtained
	CH_3CN	ETZ•24DHBA Cocrystal obtained
	EtOAc	Precipitate obtained
	Dioxane	ETZ•24DHBA Cocrystal obtained
ETZ:35DHBA (1:1)	EtOH	Precipitate obtained
	EtOAc	ETZ•35DHBA cocrystal
	Hexane-Acetone-EtOH	ETZ•35DHBA•H_2O cocrystal hydrate
	Hexane-toluene-EtOH	ETZ•35DHBA cocrystal
ETZ:Ferulic acid (1:1)	CH_3CN	ETZ•FRA cocrystal
ETZ:*p*TSA (1:1)	CH_3CN	Precipitate obtained
ETZ:Caffeic acid (1:1)	CH_3CN-EtOH	Precipitate obtained
ETZ:Cinnamic acid (1:1)	CH_3CN	Precipitate obtained
	EtOH	Precipitate obtained
	THF	Precipitate obtained
ETZ:Orotic acid (1:1)	CH_3CN-EtOH	Precipitate obtained
ETZ:Nicotinic acid (1:1)	CH_3CN-THF	Precipitate obtained
ETZ:Nicotinamide (1:1)	CH_3CN-THF	Precipitate obtained
ETZ:4-aminopyridine (1:1)	CH_3CN	Precipitate obtained

Table S2. The geometric parameters for the intermolecular interactions in the ETZ cocrystals

Compound	**Interaction**	**Donor···Acceptor**	**H···Acceptor**	**Donor–H···Acceptor**	**Symmetry code**
ETZ•24DHBA	N1–H15···O4	2.649(2)	1.84(2)	134	x,y,z

	O6A–H4···O2	2.520(2)	1.69(3)	158(3)	x,y,z
	O6B–H2···O1	2.445(4)	1.53(3)	165(7)	x,y,z
	N1–H14···O5	2.954(2)	2.05(2)	162	-x+3/2, y+1/2, -z+3/2
	O3–H16···O5	2.6523(18)	1.67(2)	169	-x+3/2, y-1/2, -z+3/2
	O1–H17···O2	2.6452(18)	1.59(3)	175(2)	-x+2, -y+2, -z+2
	C14–H8···O6A	3.056(3)	2.50	116	-x+1, -y+1, -z+2
	C14–H9···O6B	3.541(5)	2.61	161	x-1, y, z
ETZ•35DHBA	N1–H1A···O6	3.092(3)	2.31(4)	163(3)	x, -y+3/2, z-1/2
	N1–H1B···O2	2.665(3)	2.06(4)	129(3)	x,y,z
	O4–H4A···O5	2.6681(19)	1.83(3)	162(3)	x-1/2, -y+1, z
	O5–H5A···O1	2.569(2)	1.66(3)	165(3)	x, y-1/2, -z
	O6–H6A···O3	2.805(2)	1.97(4)	178(3)	x+1/2, y, -z+1/2
ETZ•35DHBA•H_2O	C9 H9A O11	3.498(6)	2.65	148	x, y-1, z
	N1–H1A···O2	2.652(5)	1.83(6)	148(5)	x,y,z
	O4–H4A···O1	2.644(4)	1.68(6)	167(5)	x, y, z+1
	O6–H6A···O9	2.678(4)	1.88(5)	165(5)	x-1, y, z
	O8–H8A···O3	2.682(4)	1.94(6)	153(6)	-x+1, -y, -z+1
	O10–H10A···O13	2.745(4)	1.97(5)	172(5)	-x+1, -y+1, -z
	O14–H14A···O5	2.800(4)	1.81(5)	159(4)	x-1, y, z
	N1–H1B···O3	3.020(5)	2.14(6)	160(4)	x, y, z-1
	O9–H9D···O7	2.689(5)	1.91(6)	160(5)	-x+2, -y, -z+1
	O5–H5A···O16	2.746(4)	1.93	173	-x+1, -y+1, -z+1
	O12–H12···O11	2.645(4)	1.84	169	-x+1, -y+2, -z+1
	O13–H13A···O15	2.753(4)	1.95	166	-x, -y+1, -z
	O15–H15A···O6	2.816(4)	1.87(3)	163(6)	x,y,z
	O15–H15B···O16	2.824(4)	1.85(5)	159(11)	x, y, z-1
ETZ•FRA	N1–H1A···O2	2.642(3)	2.00(3)	137(3)	x,y,z
	N1–H1B···O4	2.913(3)	2.02(3)	168(2)	x, y-1, z
	O3–H3A···O1	2.578(2)	1.70(4)	166(3)	x, y+1, z
	O6–H6A···O5	2.656(3)	2.21(4)	114(4)	x,y,z
	O6–H6A···O4	2.821(3)	2.07(4)	150(4)	x+1/2, -y+3/2, -z+1
	C17–H17···O6	3.193(3)	2.46	135	x-1/2, -y+3/2, -z+1

Powder materials obtained after liquid assisted grinding are used for FT-IR spectroscopy to characterize formation of the corresponding cocrystals of ethenzamide.

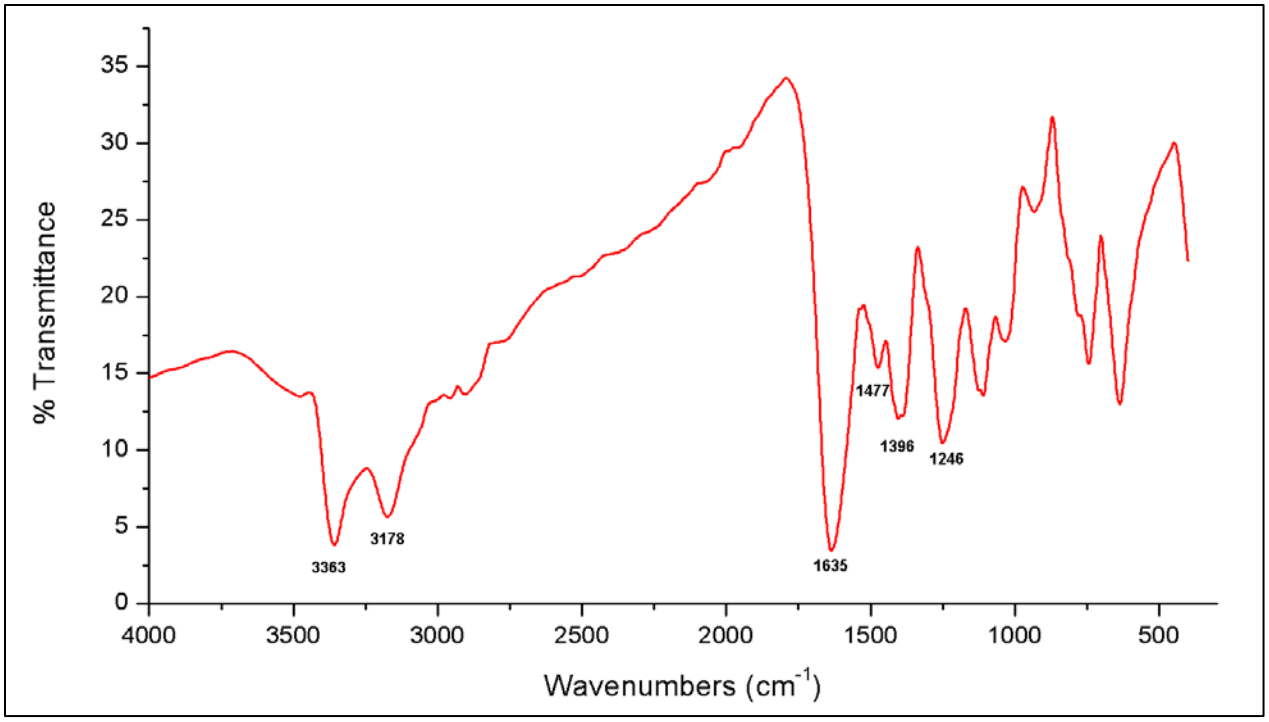


Figure S6 FT-IR spectrum of ETZ.

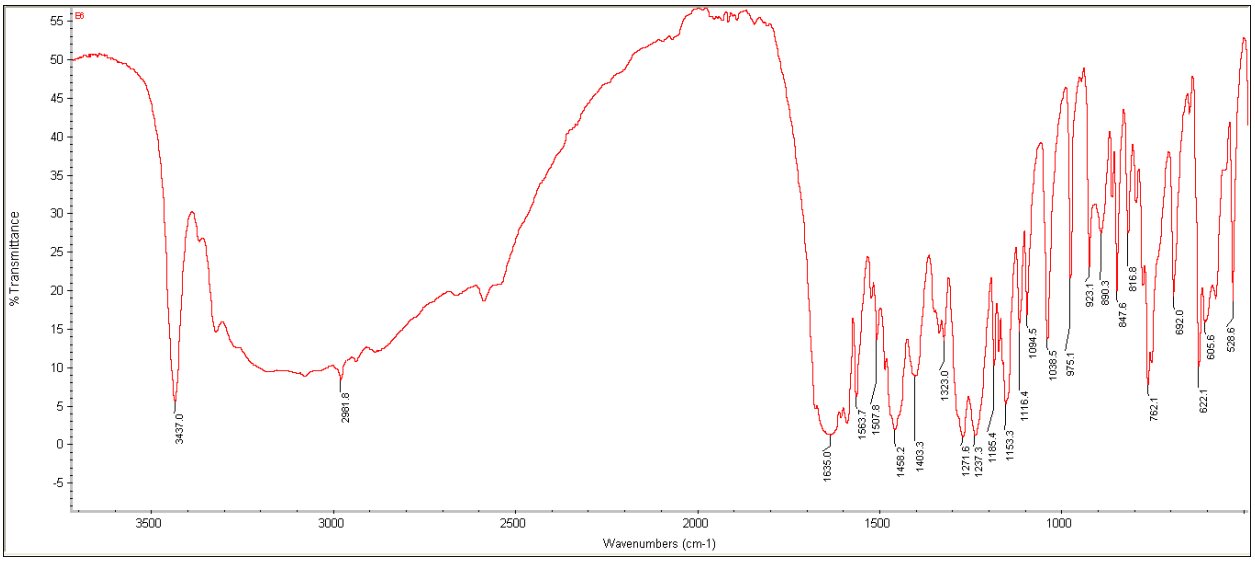


Figure S7 FT-IR spectrum of ETZ•24DHBA.

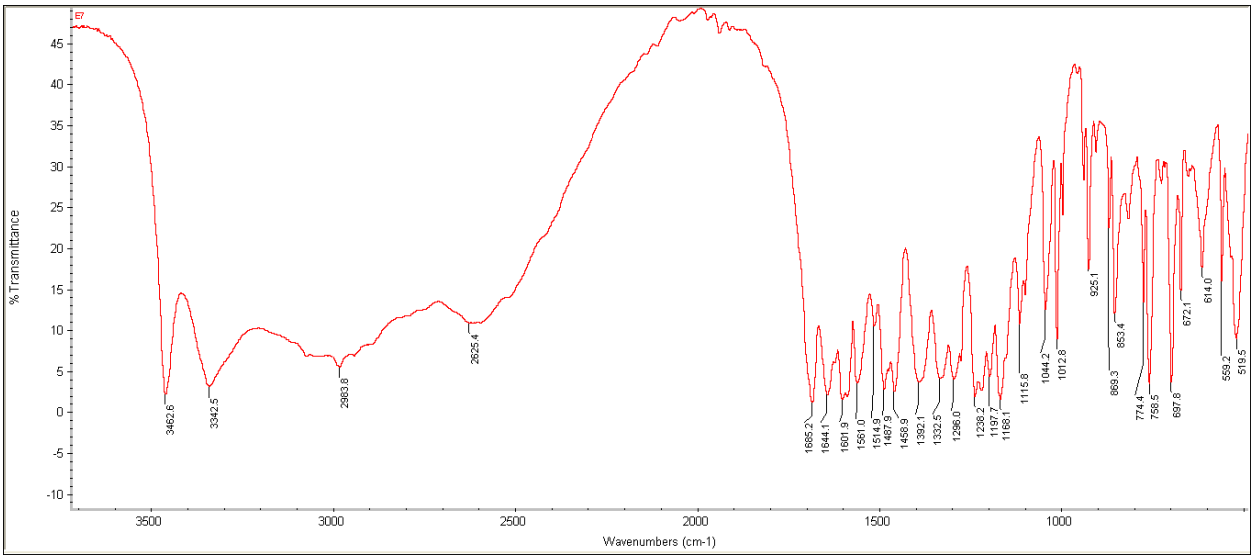


Figure S8 FT-IR spectrum of ETZ•35DHBA.

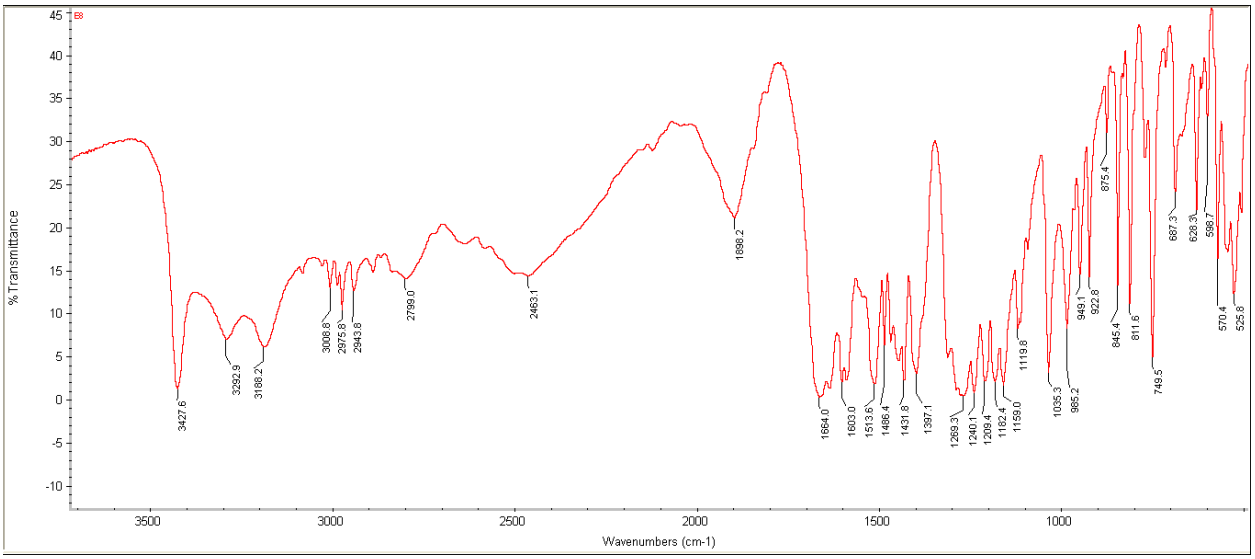


Figure S9 FT-IR spectrum of ETZ•FRA.

Table S3: List of reported crystal structures of ETZ, their CSD ref codes, coformers and primary H bond synthon present therein.

Sl. No.	CSD ref code	Coformer	Primary Hydrogen bond synthon
1.	DUKXAJ	---- (guest free)	amide dimer

2.	GEQXIL	3,5-Dichlorobenzoic acid	acid-amide dimer
3.	KITWOA	Thiourea	No 3D coordinate
4.	NURFOW	2,5-dihydroxybenzoic acid acetic acid	acid-amide dimer
5.	QULLUF	2,5-Dihydroxybenzoic acid (polymorph I)	acid-amide dimer
6.	QULLUF01	2,5-Dihydroxybenzoic acid (polymorph II)	acid-amide dimer
7.	QULLUF02	2,5-Dihydroxybenzoic acid (polymorph III)	acid-amide dimer
8.	REHSAA	2-Hydroxybenzoic acid	acid-amide dimer
9.	REHSEE	2-Chloro-4-nitrobenzoic acid	acid-amide dimer
10.	REHSII	4-Hydroxy-3-methoxybenzoic acid	acid-amide dimer
11.	REHSOO	4-aminobenzoic acid	amide dimer
12.	REHSUU	4-hydroxybenzoic acid	acid dimer, amide catemer
13.	REHTAB	fumaric acid	acid-amide dimer
14.	VAKTOS	ethylmalonic acid (polymorph I)	acid-amide dimer, acid dimer
15.	VAKTOS01	ethylmalonic acid (polymorph II)	acid-amide dimer, acid dimer
16.	VUHFIO	saccharin (polymorph I)	amide dimer
17.	VUHFIO01	saccharin (polymorph II)	amide dimer
18.	WUZHOP	3,5-dinitrobenzoic acid ((polymorph I)	acid-amide dimer
19.	WUZHOP01	3,5-dinitrobenzoic acid ((polymorph II)	amide dimer
20.	WUZJAD	3,5-dinitrobenzoic acid acetone solvate	amide dimer
21.	WUZJEH	3,5-dinitrobenzoic acid dioxane solvate	amide dimer

22.	WUZJIL	3,5-dinitrobenzoic acid diethyl ether solvate	amide dimer
23.	WUZJOR	3,5-dinitrobenzoic acid toluene solvate	amide dimer
24.	WUZJUX	3,5-dinitrobenzoic acid acetonitrile solvate	amide dimer
25.	WUZKAE	3,5-dinitrobenzoic acid ethyl acetate solvate	amide dimer
26.	WUZKEI	3,5-dinitrobenzoic acid p-xylene solvate	amide dimer
27.	WUZKIM	3,5-dinitrobenzoic acid mesitylene solvate	acid-amide dimer
28.	1468148	Gallic acid	amide dimer acid dimer
29.	1468153	2-nitrobenzoic acid	acid-amide dimer
30.	1468154	3-nitrobenzoic acid	acid-amide dimer
31.	1468159	2,4-dinitrobenzoic acid	acid-amide dimer
32.	1468161	3-toluic acid	acid-amide dimer

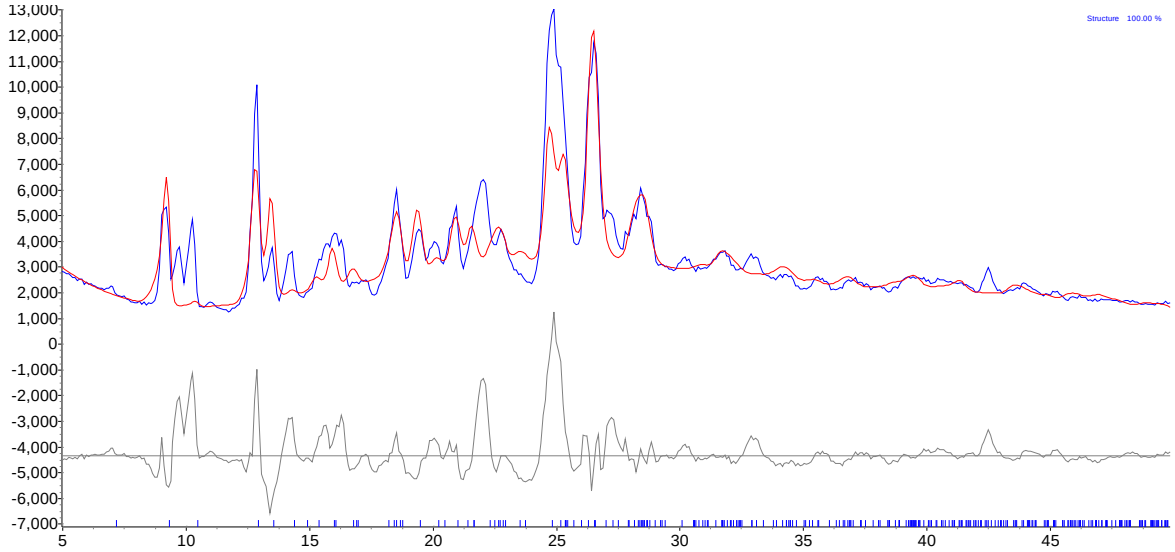


Figure S10 Rietveld refinement of ETZ•24DHBA cocrystal prepared using LAG (R_p 14.1% and R_{wp} 19.9%). The experimental pattern is shown in blue, while the simulated pattern is shown in red. Evidently, the material is not phase-pure. It may be suggested that a solvated cocrystal phase is present in the mixture.

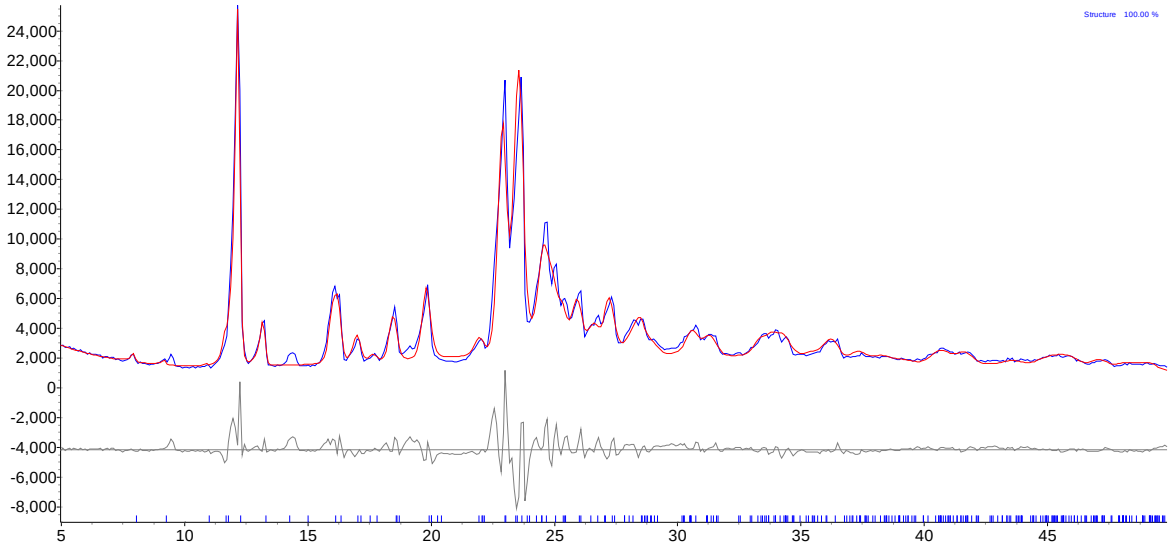


Figure S11 Rietveld refinement of ETZ•35DHBA cocrystal prepared using LAG (R_p 8.9% and R_{wp} 12.1%). The experimental pattern is shown in blue, while the simulated pattern is shown in red.

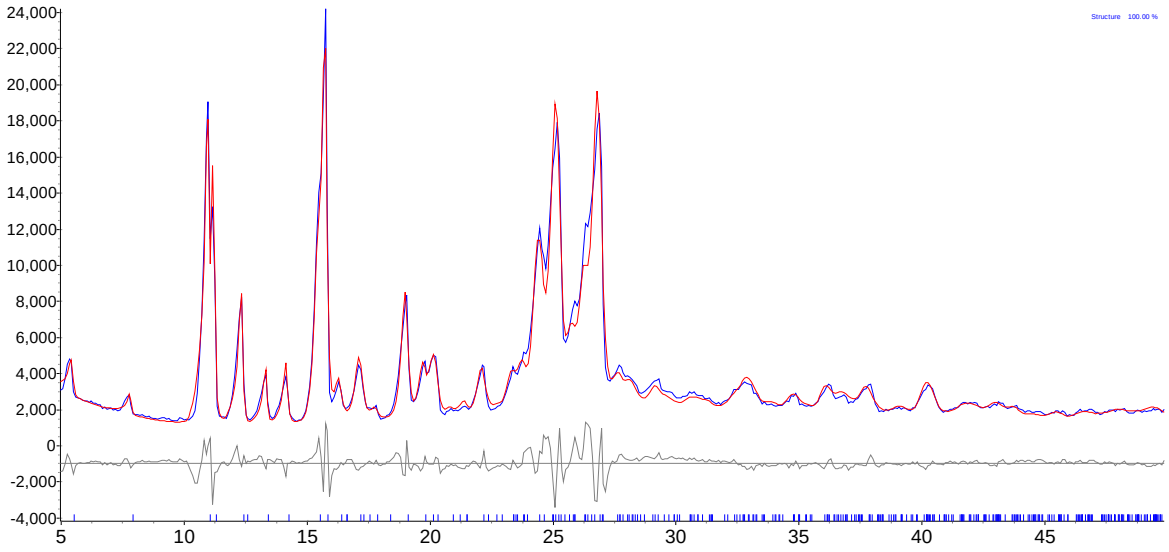
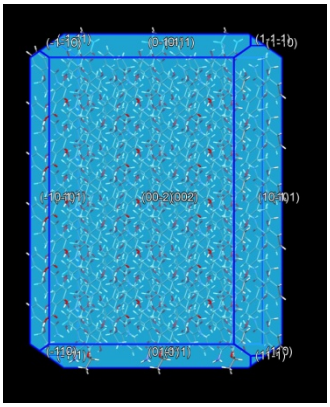
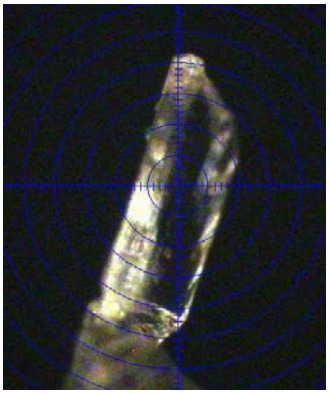
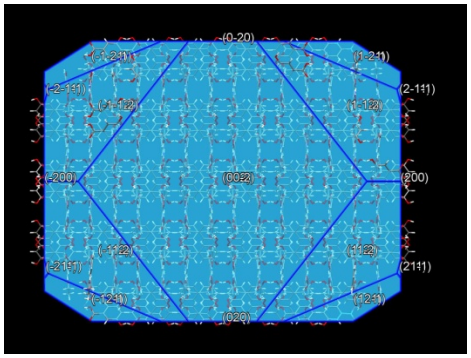


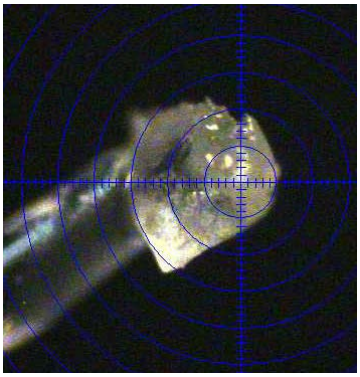
Figure S12 Rietveld refinement of ETZ•FRA cocrystal prepared using LAG (R_p 7.4% and R_{wp} 9.6%.). The experimental pattern is shown in blue, while the simulated pattern is shown in red.



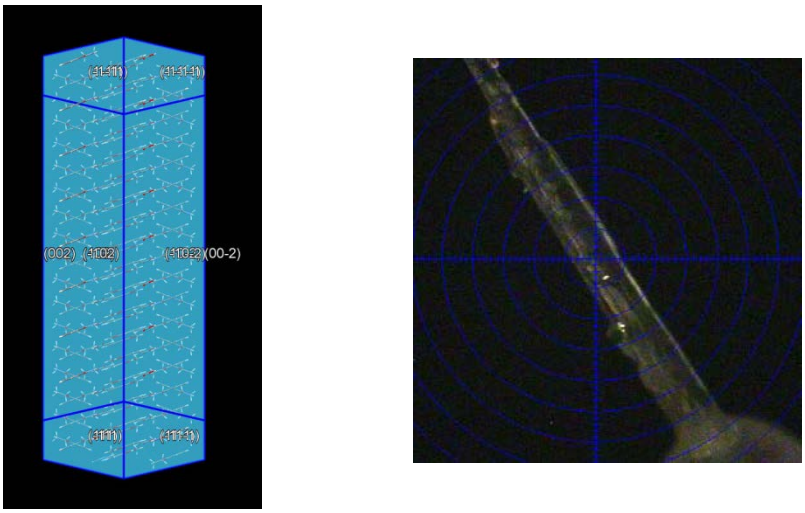


ETZ•24DHBA cocrystal





ETZ•35DHBA cocrystal



ETZ•FRA cocrystal

Figure S13 BFDH morphology predicted using Mercury CSD 3.8 licensed version vs. crystal morphology obtained during crystallisation experiment.