Ternary and quaternary cocrystals of 2,7-dihydroxy naphthalene: Systematic Design with an unusual large modular synthon

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S1. Crystallization details:

A. Materials

2, 7-dihydroxynaphthalene, 2,3,5,6-tetramethyl pyrazine, acridine, quinoxaline and phenazine were purchased from Sigma-Aldrich. Pyrene was purchased from TCI. Phenanthrene was purchased from AVRA chemicals and 1,10-phenanthroline was purchased from SRL. All the chemicals were used without further purification. Crystallization and grinding solvents were purchased from SRL and used as received.

B. Crystallization protocol

*(i) Synthesis of cocrystal **1**:* 2, 7-dihydroxynaphthalene, 2,3,5,6-tetramethyl pyrazine, and phenazine were taken in 1:1:1 ratio and ground with 3-4 drops of ethanol for 15 minutes using mortar and pestle and dissolved in tetrahydrofuran (THF) and kept for slow evaporation. After 1-2 days it forms brown block-shaped good diffraction quality crystals.

*(ii) Synthesis of cocrystal **2**:* 2, 7-dihydroxynaphthalene, 2,3,5,6-tetramethyl pyrazine, and phenanthrene were taken in 1:1:1 ratio in mortar and ground with 3-4 drops of ethanol and the process was repeated for 3 times. Then the mixture was dissolved in acetonitrile and kept for slow evaporation. After 2-3 days, we got good-quality colourless block-shaped crystals from acetonitrile which was subsequently used for data collection.

*(iii) Synthesis of cocrystal **3**:* The three compounds, 2, 7-dihydroxynaphthalene, 2,3,5,6-tetramethyl pyrazine, and acridine, were taken together in a 1:1:1 ratio and ground with 3-4 drops of ethanol for 3-4 times. The ground mixture was dissolved in tetrahydrofuran (THF). Pale yellow needle-shaped crystals were obtained from tetrahydrofuran after 1-2 days.

*(iv) Synthesis of cocrystal **4**:* All the three compounds namely 2, 7-dihydroxynaphthalene, 2,3,5,6-tetramethyl pyrazine, and acridine were taken together in a 1:1:1 ratio and ground with 3-4 drops of ethanol for 3-4 times. The ground mixture was dissolved in nitromethane and colorless block-shaped crystals of 1 were obtained after 3-4 days.

*(v) Synthesis of cocrystal **5**:* 2, 7-dihydroxynaphthalene, 2,3,5,6-tetramethyl pyrazine, and acridine, were taken together in a 1:1:1 ratio and ground with 3-4 drops of ethanol for 3-4 times, dissolved in dioxane and kept for slow evaporation. After 3-4 days colorless block-shaped crystals were obtained.

*(vi) Synthesis of cocrystal **6**:* 2, 7-dihydroxynaphthalene, 2,3,5,6-tetramethyl pyrazine, and pyrene were taken in 1:1:1 ratio and ground with ethanol with 3-4 drops for 12-15 minutes and crystalized the mixture from ethanol. These form colorless plate-shaped hydrated co-crystals after 2- 3 days.

*(vii) Synthesis of cocrystal **7**:* 2, 7-dihydroxynaphthalene, 2,3,5,6-tetramethyl pyrazine, and 1,10-phenanthroline were taken in a 1:1:1 ratio in mortar and ground with 3-4 drops of ethanol and the process was repeated for 3 times. Then the mixture was dissolved in different solvents and kept for slow evaporation. Depending on the solvents after 2-3 days we got colorless block-shaped crystals, from almost all solvents we have used, data were collected using the very good quality crystals formed from nitromethane.

*(viii) Synthesis of cocrystal **8**:* 2, 7-dihydroxynaphthalene, 2,3,5,6-tetramethyl pyrazine, and Quinoxaline were taken in 1:1:1 ratio and ground with 3-4 drops of ethanol for 15 minutes using mortar and pestle and dissolved in nitromethane and kept for slow evaporation. After 3-4 days it forms brown block-shaped good diffraction quality crystals.

*(ix) Synthesis of cocrystal **9**:* 2, 7-dihydroxynaphthalene, 2,3,5,6-tetramethyl pyrazine, acridine, and pyrene were taken in 1:1:1:1 ratio in a mortar and ground with the pestle with 3-4 drops of ethanol and dissolved in different solvents. And got similar morphological crystals from tetrahydrofuran and nitromethane respectively after 1-2 days and 3-4 days.

*(x) Synthesis of cocrystal **10**:* 2, 7-dihydroxynaphthalene, 2,3,5,6-tetramethyl pyrazine Quinoxaline, and pyrene were taken in a 1:1:1:1 ratio and ground with ethanol for 20-25 minutes and dissolved in different solvents. The dissolved solutions were kept for slow evaporation, after 3-4 days colorless block-shaped crystal forms from nitromethane solvent and mounted for single crystal data collection.

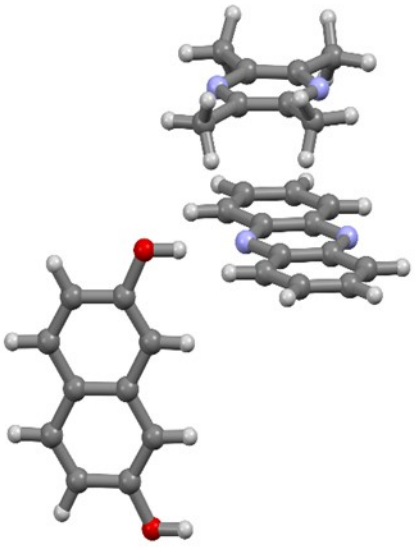
S2.Hydrogen bonding table

structure	interaction	D-H	H···A (Å)	D...A (Å)	<(DHA) (deg)
1	O1-H1...N2	0.94(2)	1.88(2)	2.8133(13)	173.8(17)
2	O1-H1...N3	0.91(3)	1.88(3)	2.772(2)	170(3)
	O2-H2...N4	1.03(4)	1.78(4)	2.789(2)	175(3)
3	O1-H1...N4	0.968(18)	1.801(18)	2.7654(11)	174.3 (15)
4	O1-H1...N5	1.02(4)	1.73(4)	2.751(2)	172(3)
	O2-H2...N7	0.99(3)	1.73(3)	2.7193(19)	176(3)
	O2-H2...N7	0.90(3)	1.94(3)	2.768(2)	151.5
	O4-H4...N8	0.93(3)	1.89(3)	2.783(2)	161(3)
5	O3-H3...N12	0.90(2)	1.86(2)	2.7465(15)	169.5(19)
	O1-H1...N9	0.91(3)	1.86(3)	2.7619(16)	170(2)
	O4-H4...N13	0.92(3)	1.86(3)	2.7554(16)	174(2)

	O2-H2...N10	0.92(2)	1.84(2)	2.7692(16)	173(2)
6	O2-H2...N8	0.949(18)	1.790(19)	2.7377(12)	176.9(16)
	O4-H4...O5	0.96(2)	1.72(2)	2.6707(12)	175.9(17)
	O5-H5A...O2	0.905(19)	1.958(19)	2.8504(12)	168.2(17)
	O5-H5B...O4	0.91(2)	1.91(2)	2.8204(12)	174.5(17)
	O3-H3...N9	0.916(19)	1.852(19)	2.7591(12)	170.1(16)
	O1-H1...N6	0.952(19)	1.857(19)	2.7895(12)	165.9(16)
7	O2-H2...N7	0.95(2)	1.74(2)	2.6795(14)	171(2)
	O2-H2...N7	0.97(2)	1.82(2)	2.7878(16)	175(2)
	O3-H3...O2	0.93(2)	1.75(2)	2.6734(14)	171(2)
8	O1-H1...N5	0.95(2)	1.81(2)	2.7537(16)	171(2)
	O2-H2...N7	0.92(2)	1.76(2)	2.6809 (14)	173(19)
	O3-H3...O2	0.86(2)	1.85(2)	2.7004(14)	170(2)
	O4-H4...N10	0.97(2)	1.81(2)	2.7754 (16)	174(2)
9	O1-H1...N3	0.88(3)	1.86(3)	2.7319(17)	169(2)
	O1-H1...N3	0.83(3)	1.91(3)	2.7368(19)	165(2)
10	O1-H1...N9	0.81(5)	2.02(5)	2.823(4)	172(5)
	O2-H2...N11	1.06(6)	1.74(6)	2.792(4)	174(5)
	O3-H3...N13	0.84	1.94	2.771(4)	171.1
	O4-H4...N15	0.89(5)	1.95(5)	2.829(4)	171(4)
	O5-H5...N18	0.79(5)	2.03(5)	2.823(4)	173(4)
	O6-H6...N19	1.04(6)	1.78(6)	2.796(4)	164(5)
	O7-H7...N21	1.01(7)	1.79(7)	2.788(4)	172(6)
	O8-H8...N23	0.94(5)	1.89(5)	2.820(4)	172(4)

S3. ORTEP Diagrams:

ORTEP diagrams are created using Mercury version 4.2.0 with probability level 50%.



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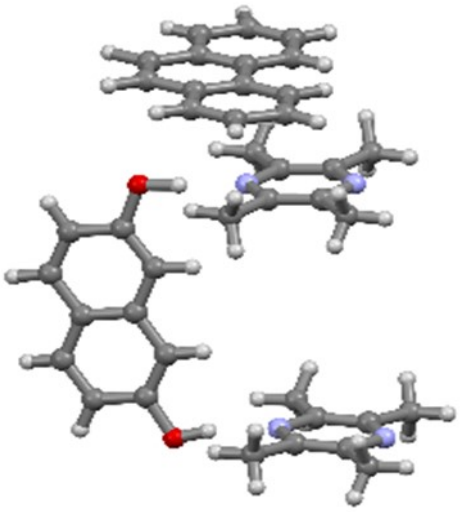

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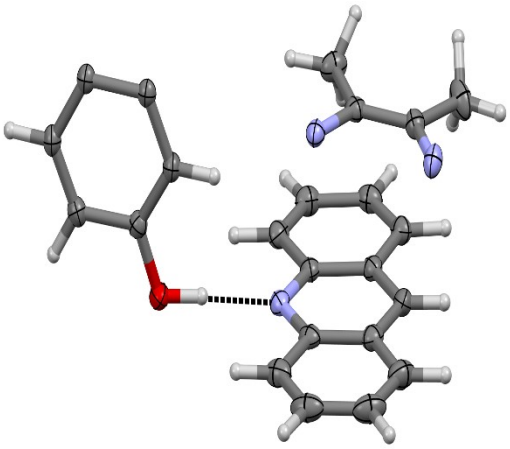

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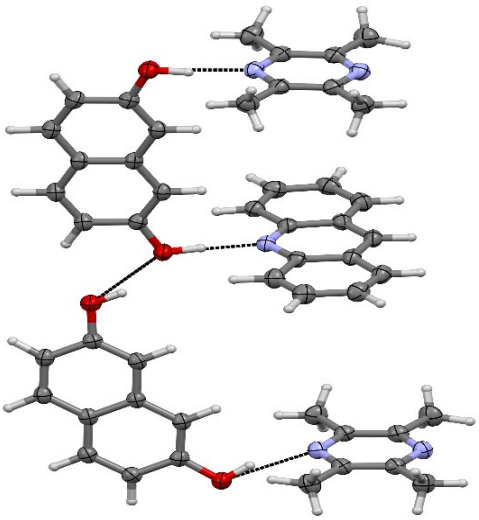

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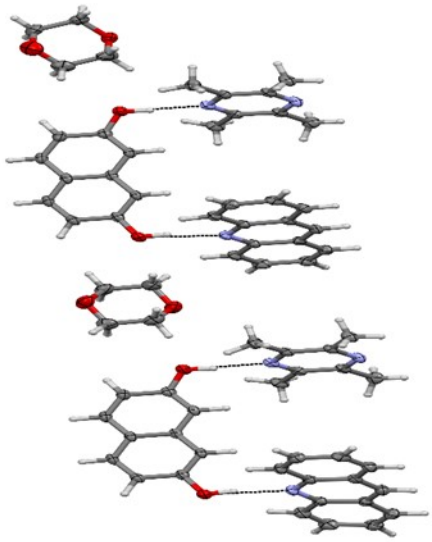

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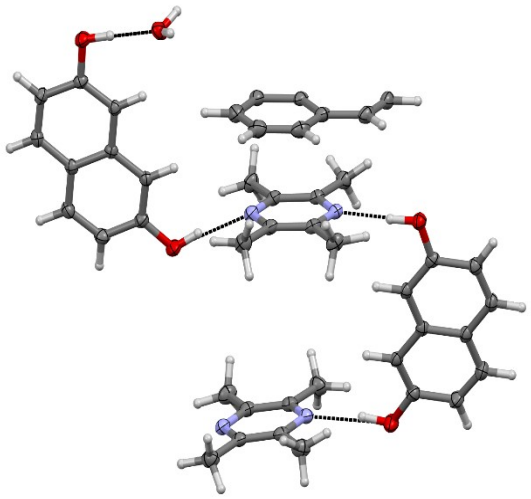

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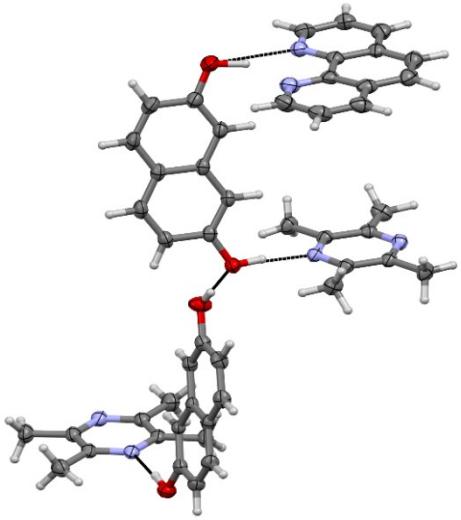

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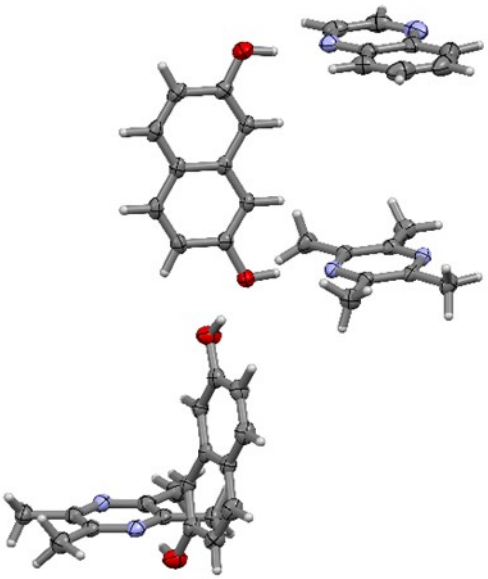

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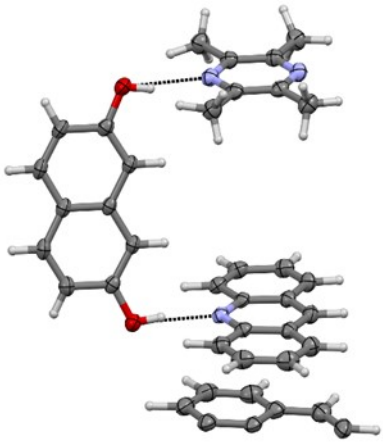
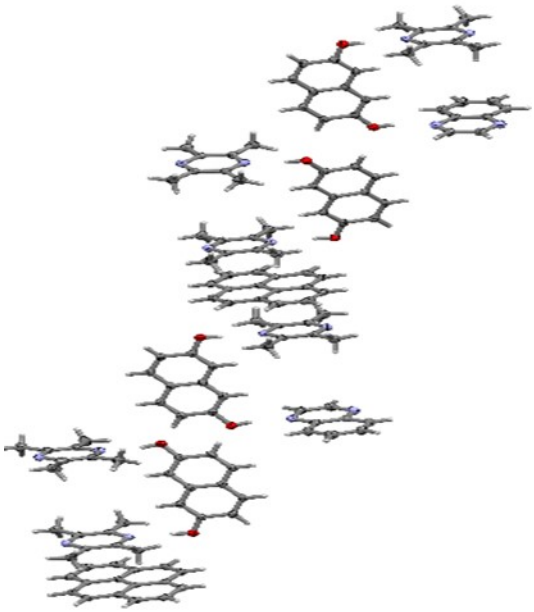




9 **10**

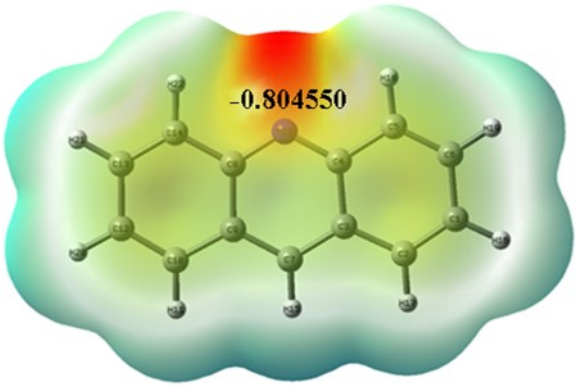
S4. Electrostatic potential energy surface-based charges (ESP) calculation

Electrostatic surface potential (ESP) maps were calculated for different pyridine bases by DFT in Gaussian 09[2] software, using B3LYP, 6-311g (d,p) basis set. ESP maps are obtained for molecular electron density 0.0004 electron/Å. Colour codes denote the locations of positive charge (green) and negative charge (red) surfaces.

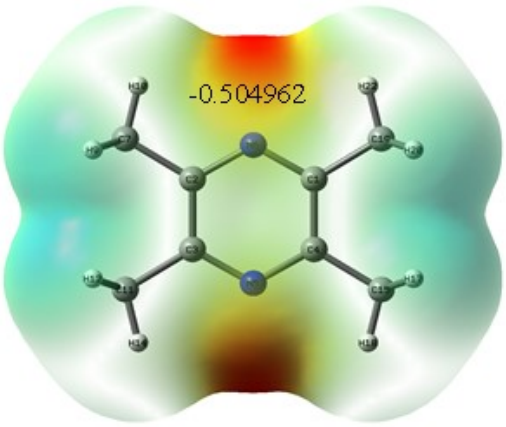
ESP charges with hydrogens summed into heavy atoms:

ACR		TMP		PHN		QUIN		PHENAN	
C1	-0.051610	**C1**	0.251058	**C1**	0.014181	**C1**	0.222697	**C1**	-0.196845
C2	0.017172	**C2**	0.251086	**C2**	-0.127500	**C2**	0.362326	**C2**	0.126227
C3	-0.221069	**C3**	0.251087	**C3**	0.428324	**C3**	0.362335	**C3**	-0.063096
C4	0.750255	**C4**	0.251058	**C4**	0.428320	**C4**	0.222696	**C4**	0.342831
C5	-0.214570	**N5**	0.504962	**C5**	-0.127496	**C7**	-0.116125	**C5**	0.399956
C6	0.077433	**N6**	0.504962	**C6**	0.014179	**C8**	-0.116137	**C6**	-0.043136
C7	0.097038	**C7**	0.001404	**C7**	0.392831	**C10**	0.029098	**C7**	0.342830
C8	0.731978	**C8**	0.001404	**C8**	0.392834	**C11**	0.029089	**C8**	-0.063095
C9	-0.222490	**C9**	0.001414	**C9**	-0.098174	**N15**	0.497992	**C9**	-0.043137
C10	0.020392	**C10**	0.001414	**C11**	0.006051	**N16**	0.497988	**C10**	0.126227
C12	-0.050465	----	----------	**C12**	0.006050	----	----------	**C12**	-0.196845
C13	0.073481	----	----------	**C13**	-0.098170	----	----------	**C13**	0.399957
C14	-0.203426	----	----------	**N21**	-0.615714	----	----------	**C21**	-0.565937

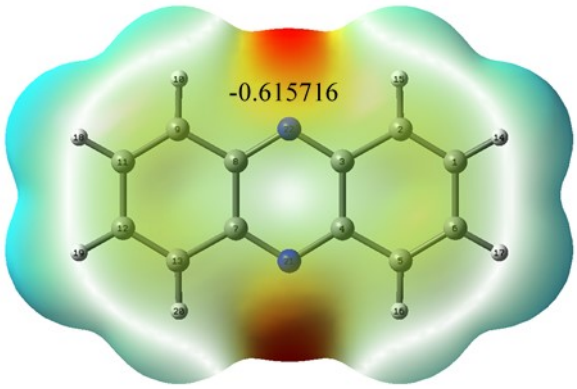
N23	-0.804118	----	----------	**N22**	-0.615716	----	----------	**N22**	-0.565937



(a)



(b)



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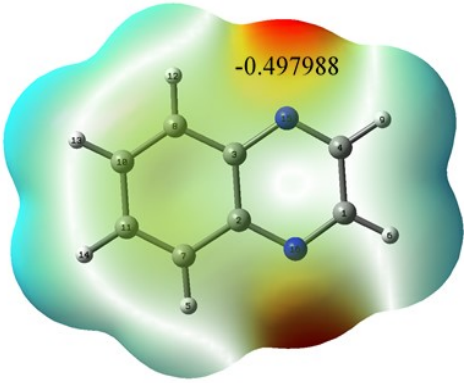

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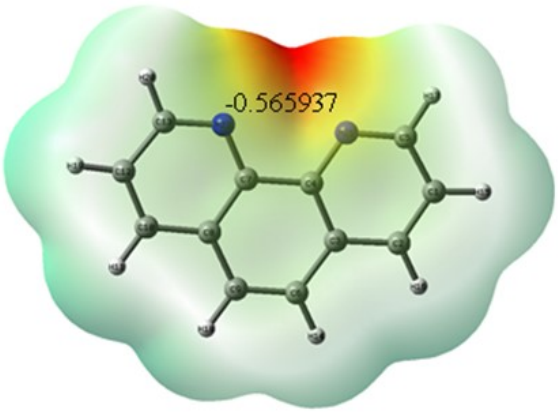


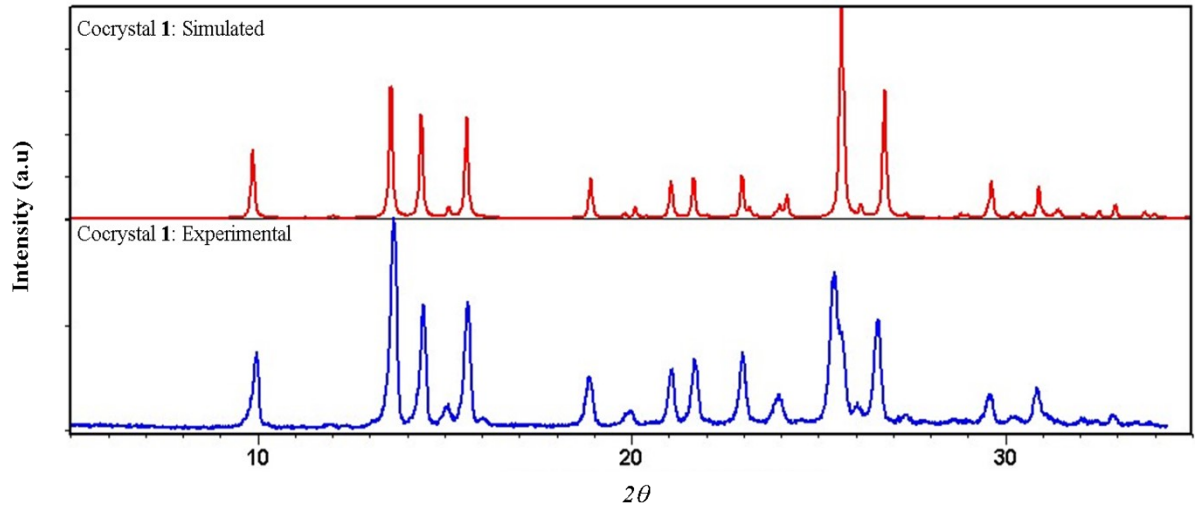
(e)

Figure S1. ESP values of different pyridine bases: (a) ACR, (b) TMP, (c) PHN, (d) QUIN, (e) PHENAN.

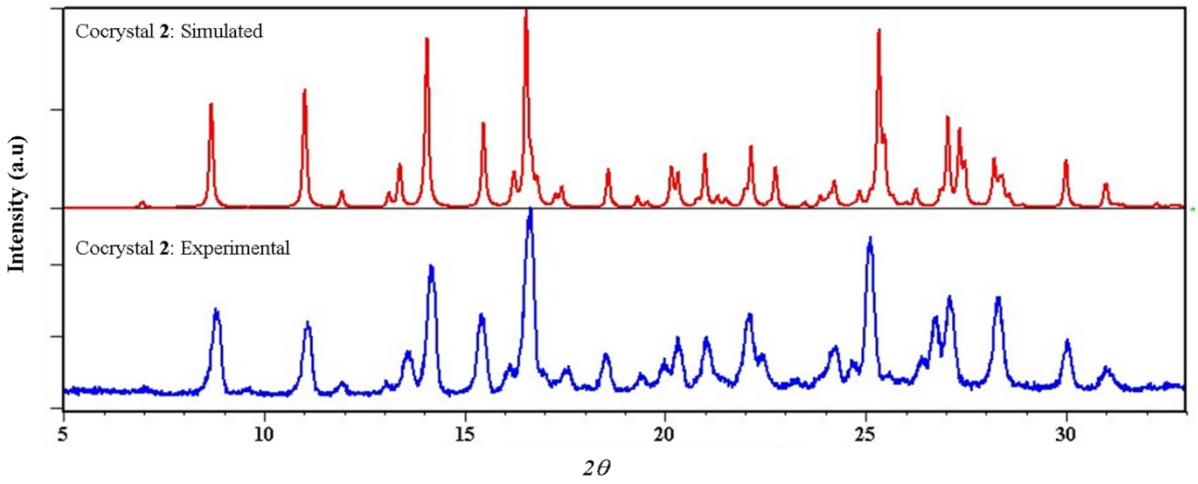
S5. Powder X-Ray Diffraction (PXRD) characterization

The analysis of PXRD of the cocrystal **1** and **2** reveals the cocrystal phase is the major phase in the bulk sample. Cocrystals **3** and **4** were obtained together in the bulk mixture through grinding procedure and is represented by PXRD **Cocrystal 3&4**. The PXRD of Cocrystal **3** was obtained after the ground mixture was crystallized from THF and was checked for PXRD, however slight impurity of cocrystal **4** was still present, indicating towards close energetic relationship between cocrystal **3** and **4**. The PXRD for cocrystal **4** was obtained while the ground mixture was crystallized from nitromethane. Cocrystal **5** was crystallized from the 1,4-dioxane and used for PXRD after grinding thoroughly. Cocrystals **6**, **7** and **9** could be obtained in the bulk. Cocrystals **8** and **10** could also be obtained in the bulk, with excess coformers (QUIN). The PXRD diffractograms are given below:

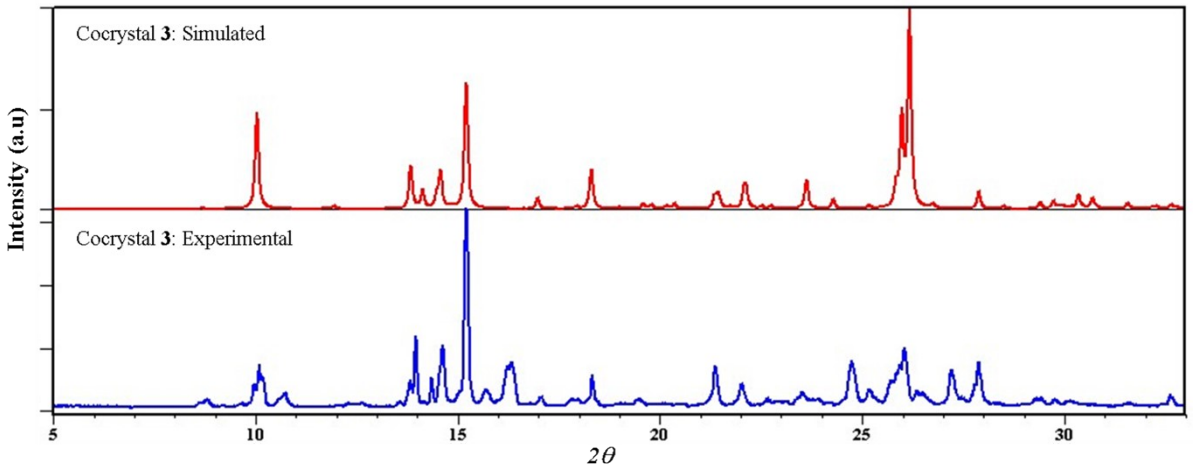
***Cocrystal-1**:*



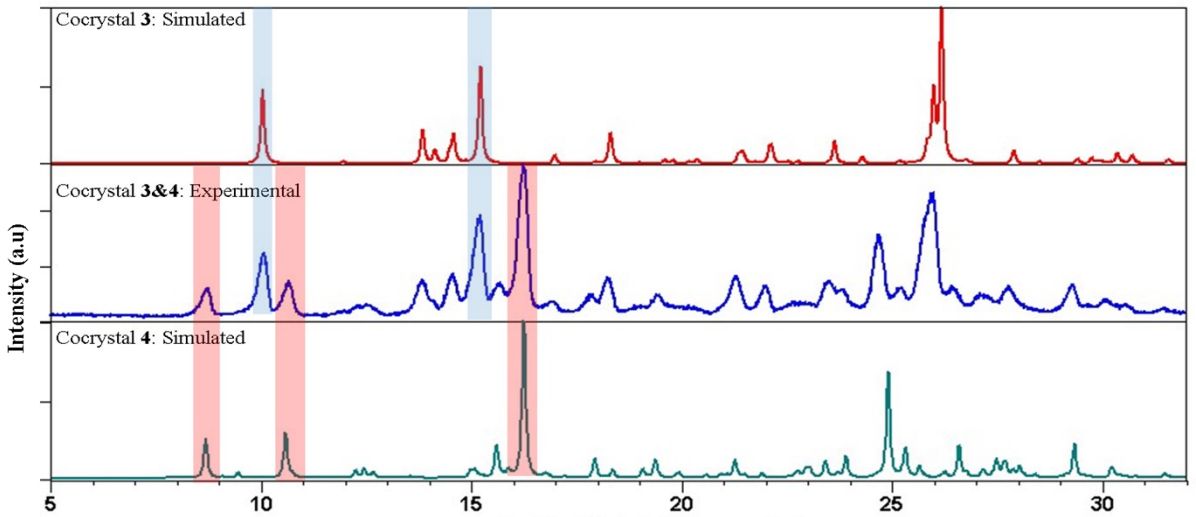
Cocrystal-2:



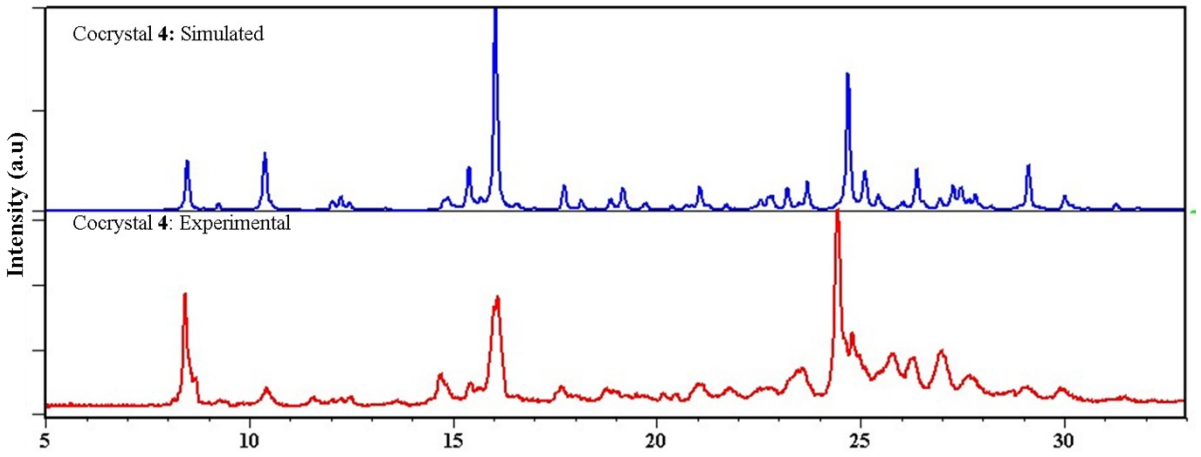
Cocrystal-3:



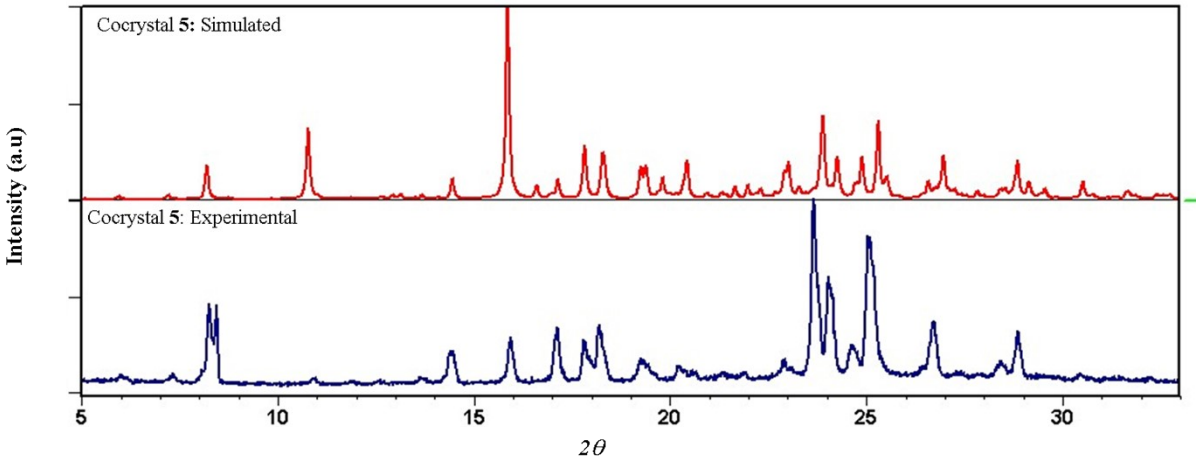
Cocrystal-3 &4:



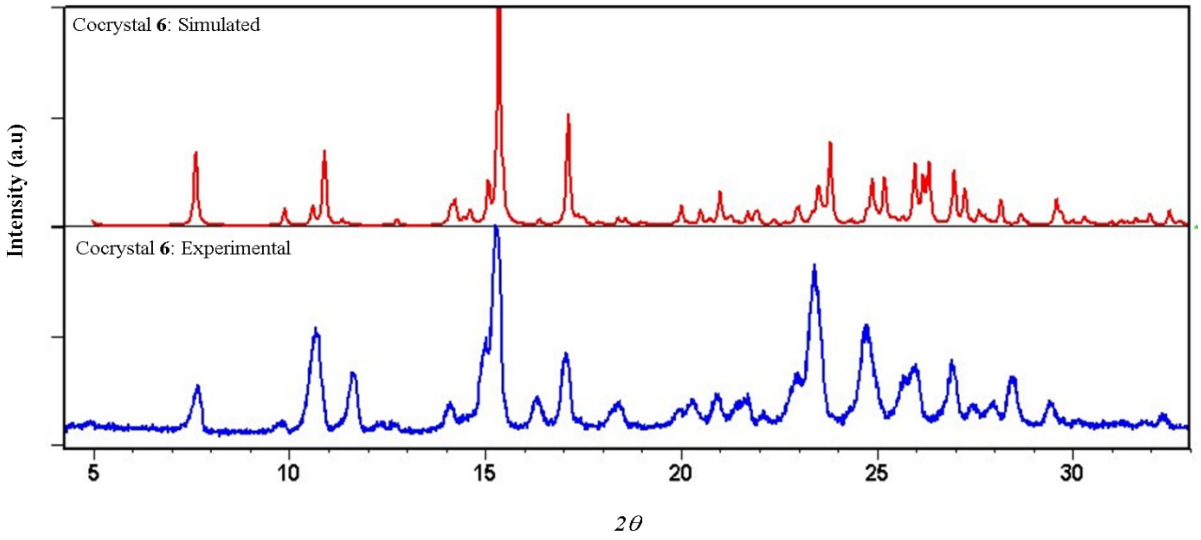
Cocrystal-4:



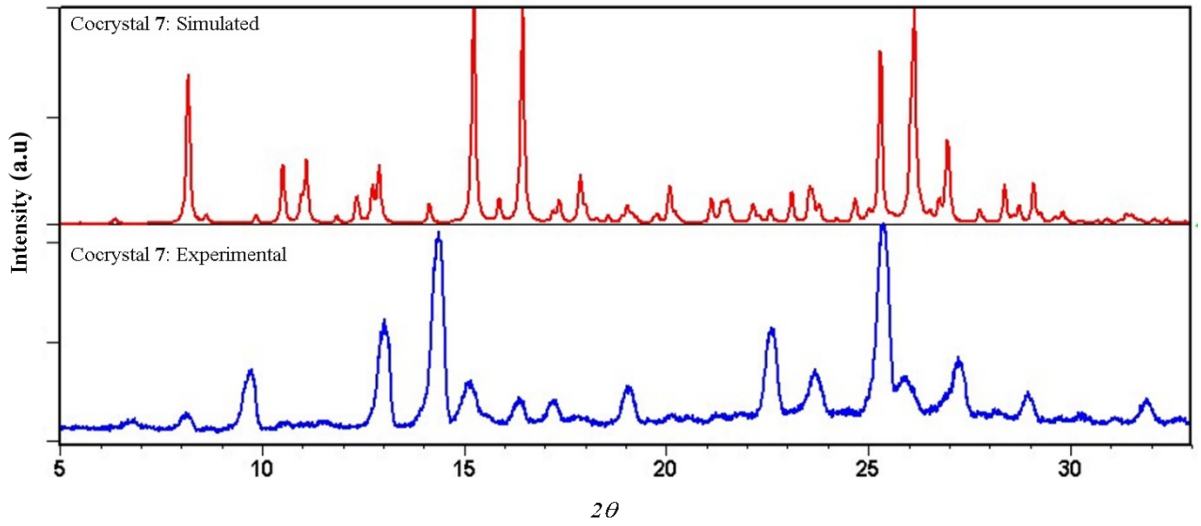
Cocrystal-5:



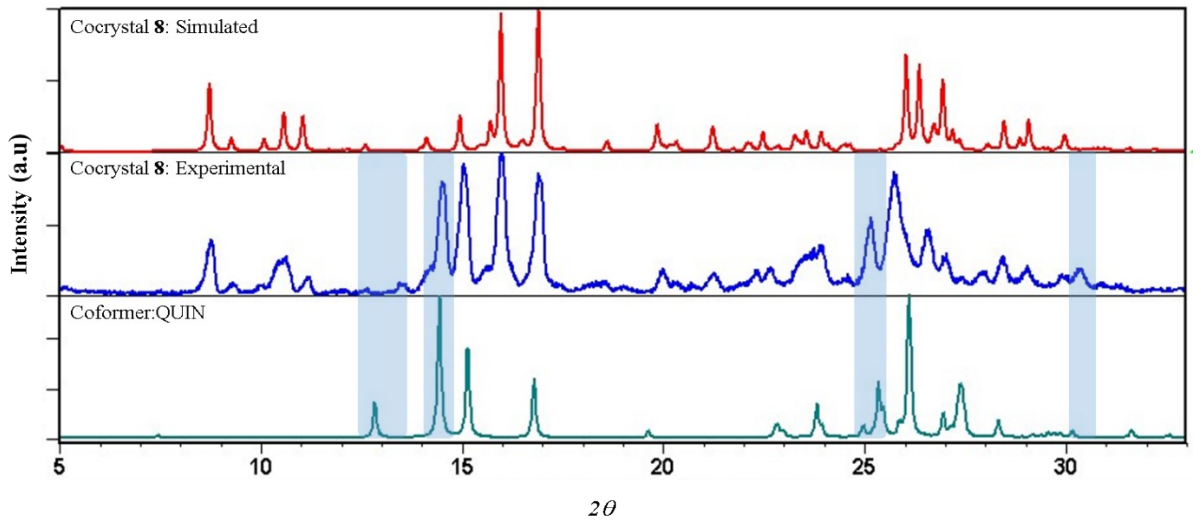
Cocrystal-6:



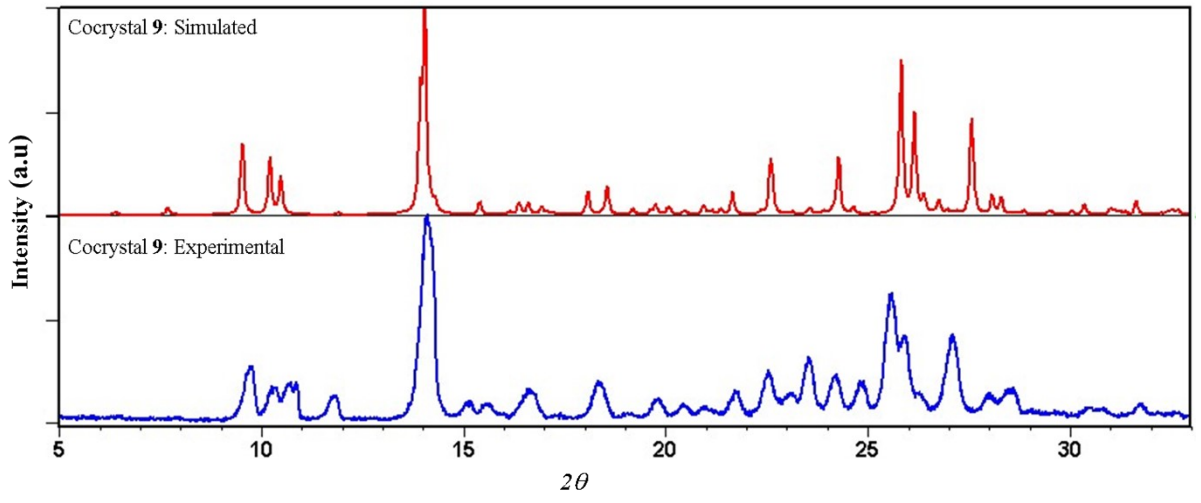
Cocrystal-7:



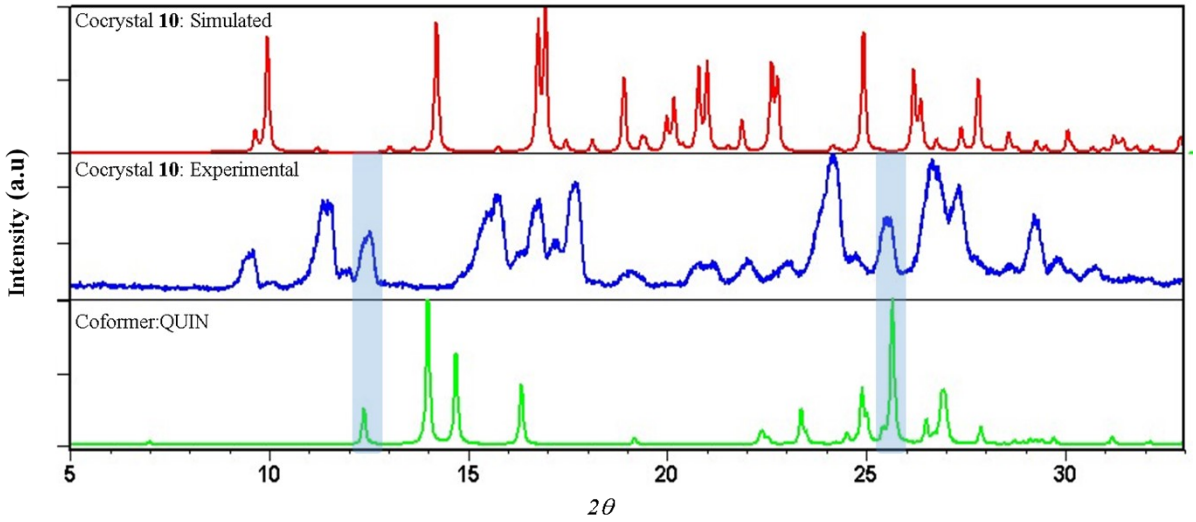
Cocrystal-8:



Cocrystal-9:



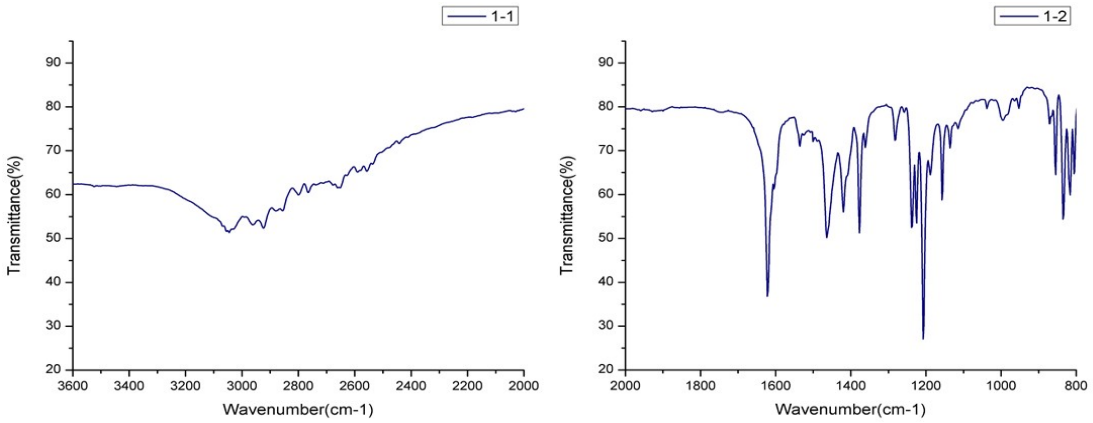
Cocrystal-10:



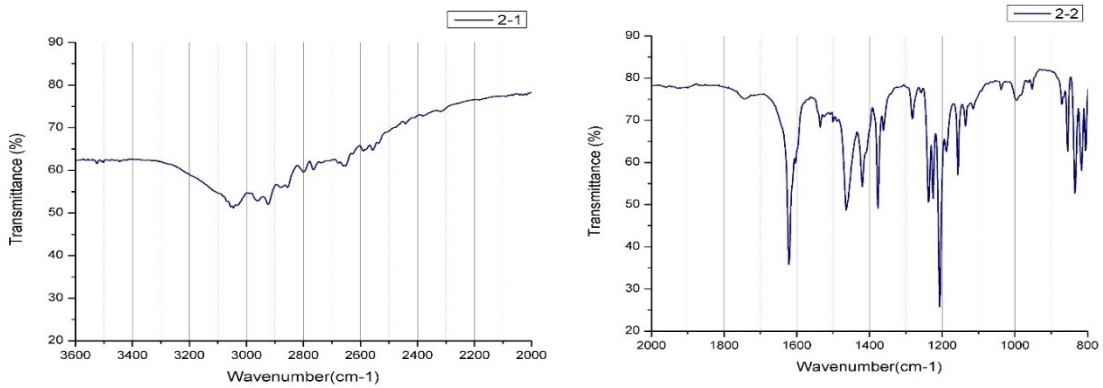
S6. FT-IR characterization

The powder mixtures which were used for PXRD analysis, were employed for FTIR characterization as well. Representatives peaks (e.g. a broad peak near 2500-2600 cm^{-1} for O–H···N) could be observed as shown in the FTIR spectra given below.

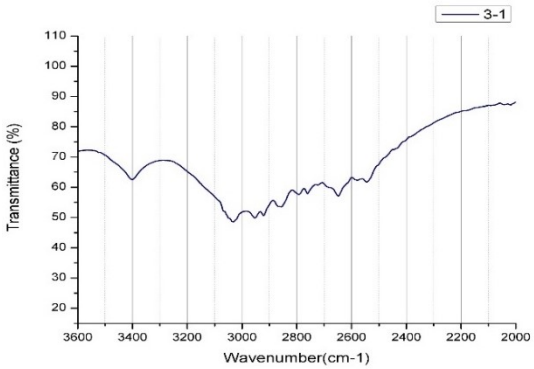
Cocrystal-1

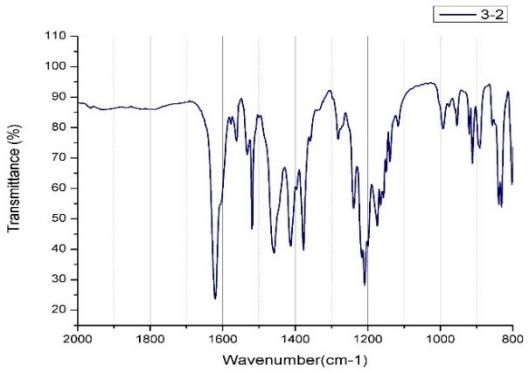


Cocrystal-2

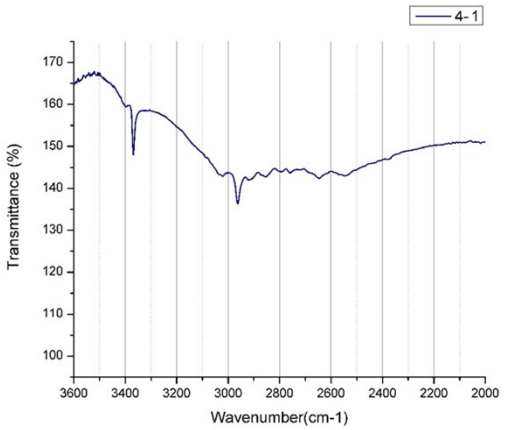


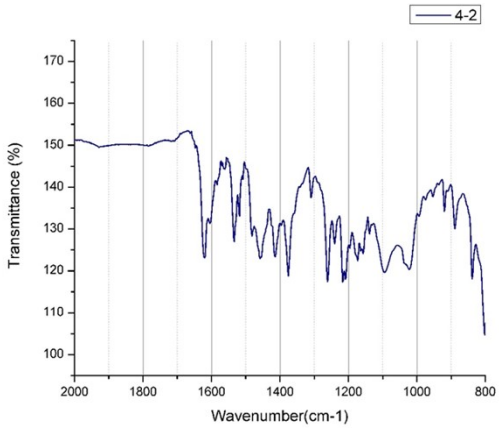
Cocrystal-3&4





Cocrystal-4





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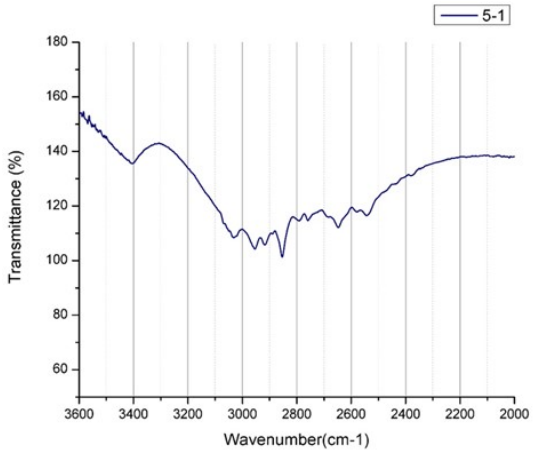

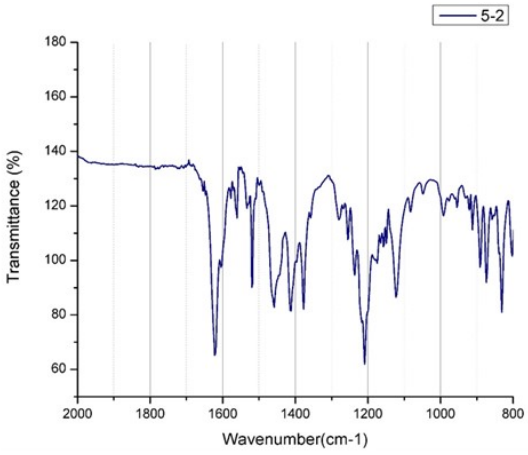

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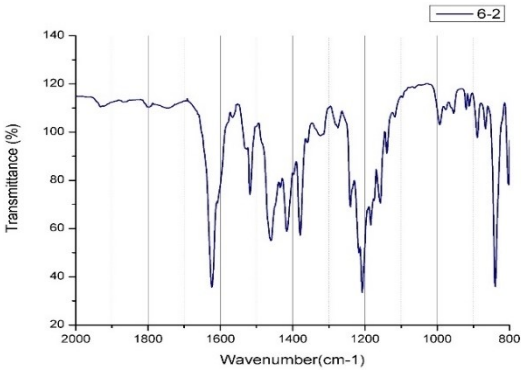

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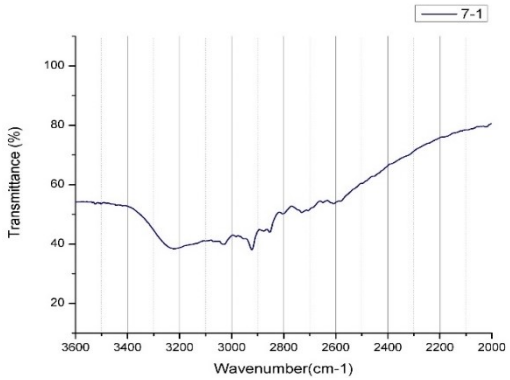
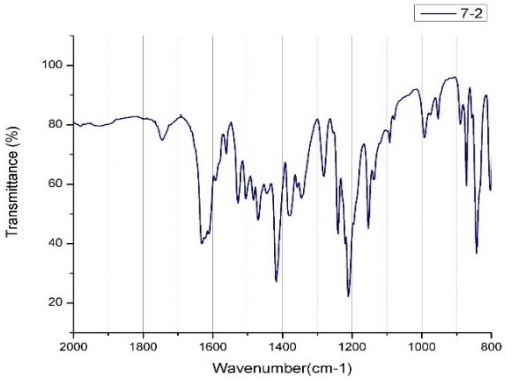
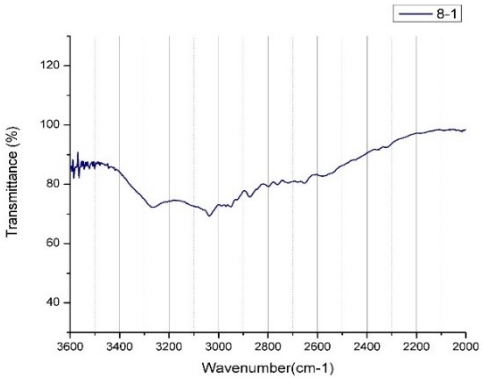
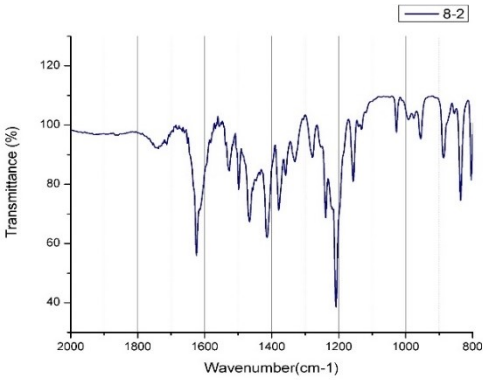


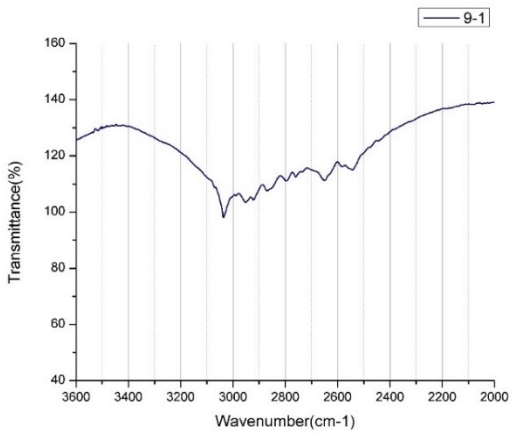


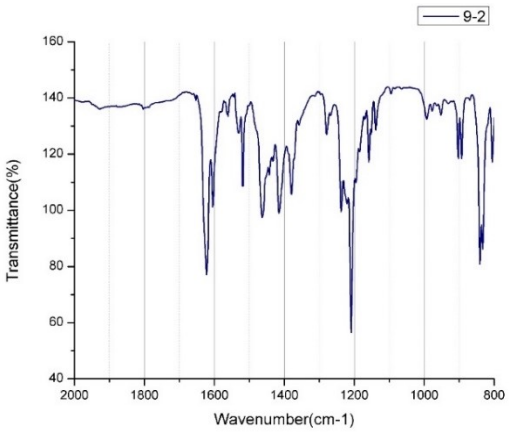
Cocrystal-8



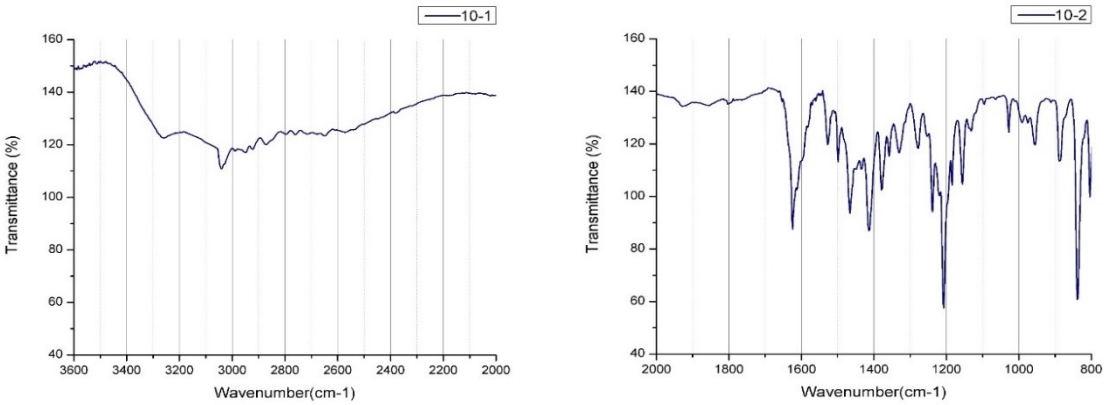


Cocrystal 9





Cocrystal 10



S7. Melting point of the cocrystals*:*

Melting points were checked using the same ground mixtures which were used for PXRD, FTIR and TGA analysis.

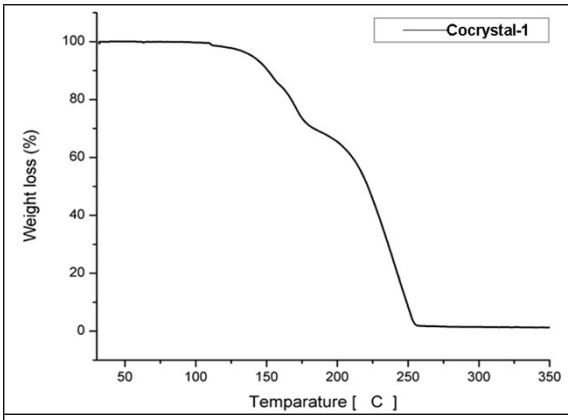
Sl. No.	Compound name	Melting point(°C)
1	*Cocrystal-1:*	*195*
2	*Cocrystal-2:*	*137*
3	*Cocrystal-3:**	*152*
4	*Cocrystal-4:*	*127*
5	*Cocrystal-5:*	*151*
6	*Cocrystal-6:*	*126*
7	*Cocrystal-7:*	*146*
8	*Cocrystal-8:**	*112*
9	*Cocrystal-9:*	*128*
10	*Cocrystal-10:**	*101*

* Cocrystal **3** could not be obtained as a pure phase even after crystallization from THF. Slight impurity of cocrystal **4** was present in the sample tested for melting point. Cocrystal **8** and **10** contains excess of quinoxaline.

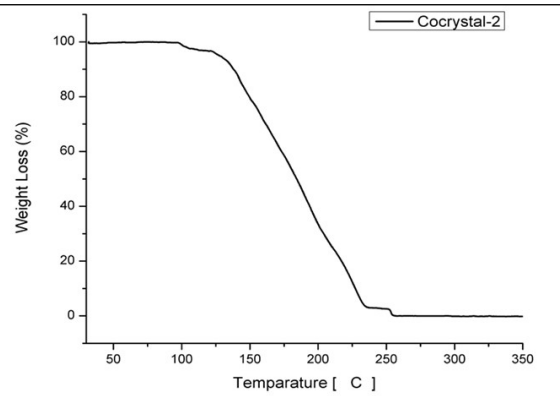
S8. Thermogravimetric analysis (TGA) of Cocrystals:

The weight loss patterns are shown for all the ground mixtures. For cocrystals **3** and **4**, crystallized samples from THF and nitromethane were used. In cocrystal **3**, small amount of cocrystal **4** may be present. In cocrystal **8** and **10**, some of the residual coformers may be present. In the case of cocrystal **5**, first weight loss may happen due to the removal of 1,4-dioxane. The event started near 110˚C and completed at 163˚C, the weight loss percentage calculated from graph is 28.19%, which is close to the theoretical weight loss of 28.41%.

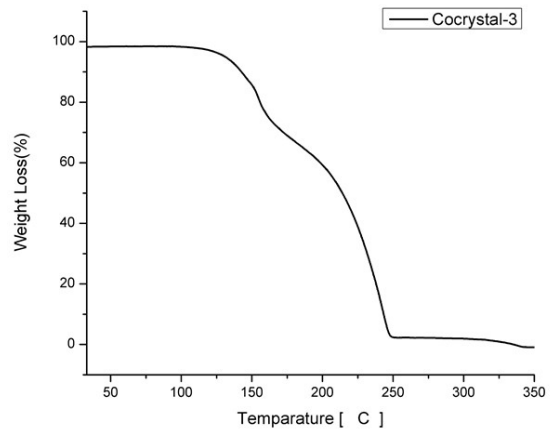
Cocrystal-1	***Cocrystal-2***



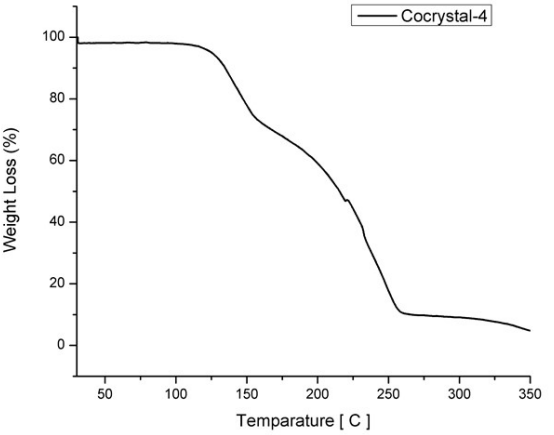
Cocrystal-3



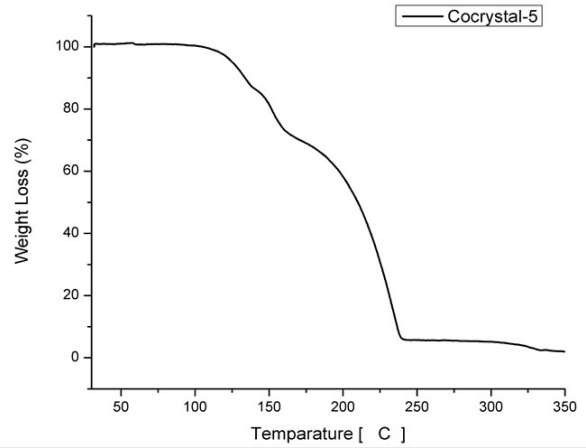
Cocrystal-4



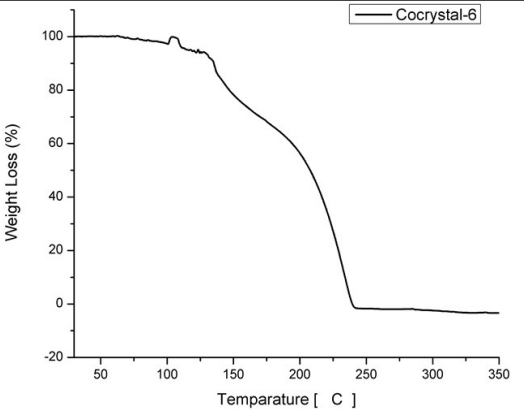
Cocrystal-5



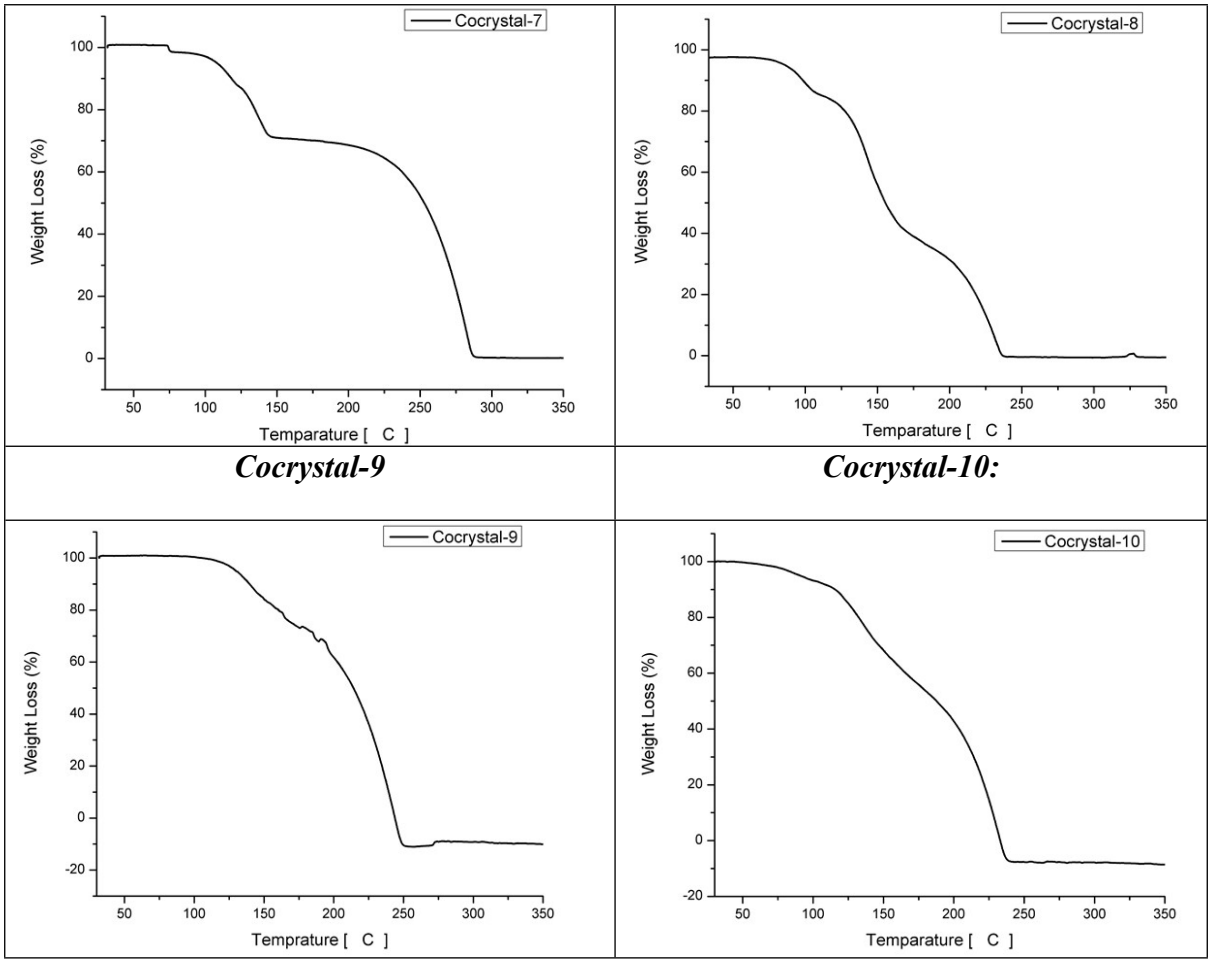
Cocrystal-6



Cocrystal-7



Cocrystal-8:



Cocrystal-9 ***Cocrystal-10:***

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