Electronic Supplementary Material (ESI) for ChemComm.

Unprecedented Morphology Control of Gas Phase Cocrystal Growth Using Multi Zone Heating and Tailor Made Additives

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Sublimation apparatus

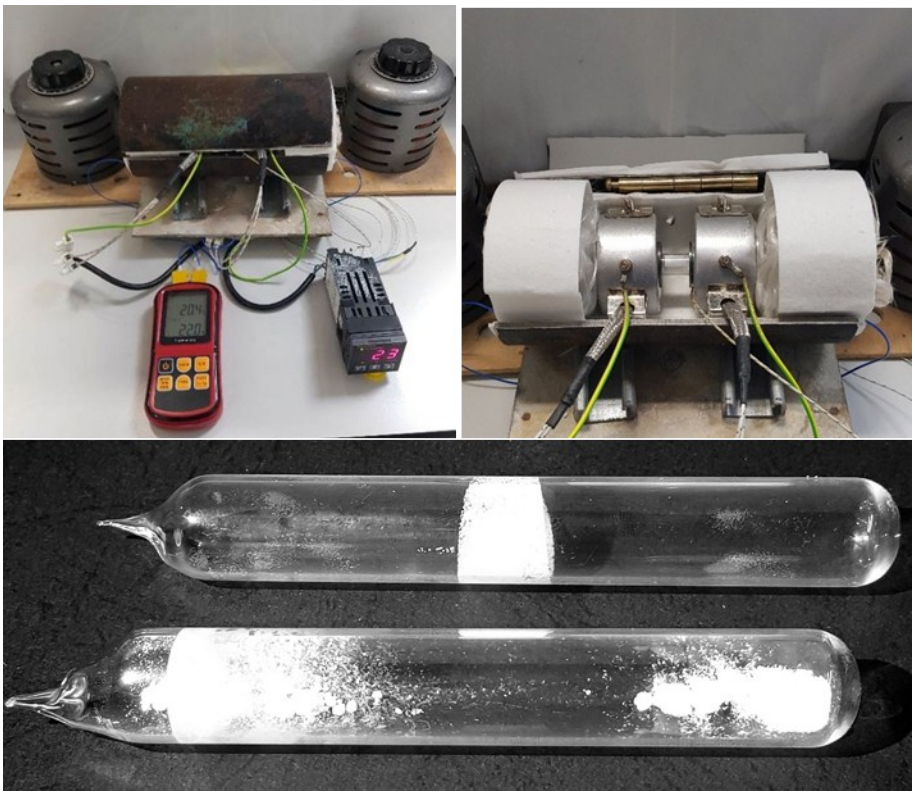

Fig. S1. Sublimation apparatus and (lower) sample before sublimation and (upper) cocrystal after sublimation.

Sublimation apparatus - The sublimation apparatus was constructed using two RS PRO Nozzle Band Heaters, 415 W, 230 V, 60 mm Band Diameter from https://ie.rs-online.com. Two aluminum cylinders, 60 mm od and 15 mm id, were used to conduct heat to the test tube. Two variable voltage transformers were used to operate the heaters and three thermocouple digital thermometers were used to measure the temperatures within the aluminum cylinders close to the test tube and in the centre between the heaters. The enclosure was made from 23 cm of 11.5 cm od gun barrel pipe split in half and lined with calcium magnesium silicate insulation and glass wool.

Crystal structure determination and refinement - An Oxford Diffraction Xcalibur system was used to collect X-ray diffraction data at room temperature. The crystal structures were solved using ShelxT and refined using Shelxl within the Oscail package.[1-3] The Oscail software was also used to obtain the drawings and simulate the PXRD pattern of DIF-EBIPY. CIF files can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, Cambridge, UK with the REF codes 1982619-1982622.

Table S1. Heater Configuration and Temperatures Used for Sublimation

System	Amounts/mg	Gap between heaters/cm	Temperatures/(°C)	Time (hours)
BZA-INA 1:1	BZA 61 INA 61	2	BZA 116.7 INA 151.5 Middle 141	2
BZA-INA 1:1 with 1% BEN	BZA 61 INA 61 Ben 2	2	BZA 116.2 INA 161.4 Middle 150	2
BZA-INA 2:1	BZA 61 INA 30	2	BZA 100 INA 165 Middle 145	2
DIF-INA 2:1 with 10% BEN	50 of a milled sample of (DIF 250.2 + INA 122.1 + BEN 37.2)	0	Heater 1 170.1 Heater 2 160.5	2
DIF-BIPY 2:1	DIF 50 BIPY 15.6	2	DIF 193 BIPY 126.3 Middle 140	2
DIF-EBIPY 2:1	DIF 25 EBIPY 9.1	2	DIF 180 EBIPY 140 Middle 153	2
DIF-EBIPY 2:1 with 1% SPY	DIF 25 EBIPY 18.4 SPY 0.45	2	DIF 176.2 EBIPY 134.7 Middle 149	

Table S2. Crystal data and structure refinement

Identification code	ben_ina_2_1	dif_ina_s1	dif_bipy	dif_ebipy_sub_2
Empirical formula	C20 H18 N2 O5	C64 H44 F8 N4 O14	C36 H24 F4 N2 O6	C19 H13 F2 N O3
Formula weight	366.36	1245.03	656.57	341.30
Temperature	300.0(2) K	149.9(3) K	299.0(1) K	299.0(1) K
Wavelength	0.71073 Å	0.71073 Å	0.71073 Å	0.71073 Å
Crystal system	Triclinic	Monoclinic	Monoclinic	Monoclinic
Space group	P-1	$P2_1/c$	$P2_1/n$	$P2_1/c$
Unit cell dimensions				
a/Å	10.0493(6)	27.197(5)	3.7762(4)	3.8999(2)
b/Å	12.6674(11)	3.7093(4)	29.2094(16)	34.7661(18)
c/Å	14.6060(13)	26.924(4)	13.5261(9)	11.4896(7)
α/°	79.358(7)			
β/°	80.034(6)	94.626(16)	96.309(7)	94.404(5)
γ/°	89.938(6)			
Volume /Å^3	1798.9(3)	2707.3(7)	1482.9(2)	1553.21(15)
Z	4	2	2	4
Density (calc.)/Mg/m^3	1.353	1.527	1.470	1.460
Absorption coefficient	0.098 mm^{-1}	0.126 mm^{-1}	0.117 mm^{-1}	0.115 mm^{-1}
F(000)	768	1280	676	704
Crystal size/ mm^3	0.50 x 0.40 x 0.20	0.50 x 0.20 x 0.05	0.50 x 0.40 x 0.20	0.50 x 0.10 x 0.04
Theta range for data collection	3.573 to 29.259°.	3.495 to 29.105°.	3.683 to 29.151°.	3.516 to 27.499°.
Reflections collected	15274	20495	6756	6841
Completeness to theta = 25.242°	99.7 %	99.6 %	99.7 %	99.8 %
Final R indices [I>2sigma(I)]	R1 = 0.0786, wR2 = 0.1727	R1 = 0.16.78, wR2 = 0.3146	R1 = 0.0521, wR2 = 0.0957	R1 = 0.0509, wR2 = 0.1120
R indices (all data)	R1 = 0.2271, wR2 = 0.2530	R1 = 0.2978, wR2 = 0.3715	R1 = 0.1097, wR2 = 0.1175	R1 = 0.0769, wR2 = 0.1293
Largest diff. peak and hole/ e.Å^{-3}	0.394 and -0.251	0.580 and -0.693	0.155 and -0.193	0.183 and -0.155

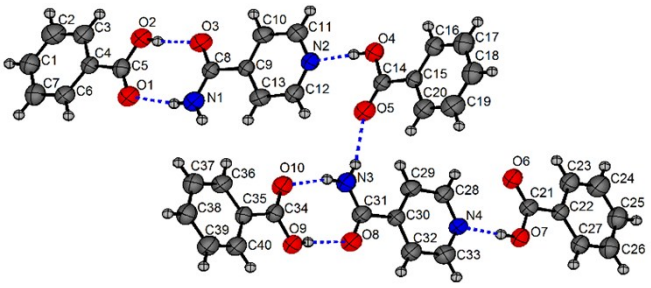

Fig. S2. Asymmetric unit of the crystal structure of the BZA-INA 2:1 cocrystal.

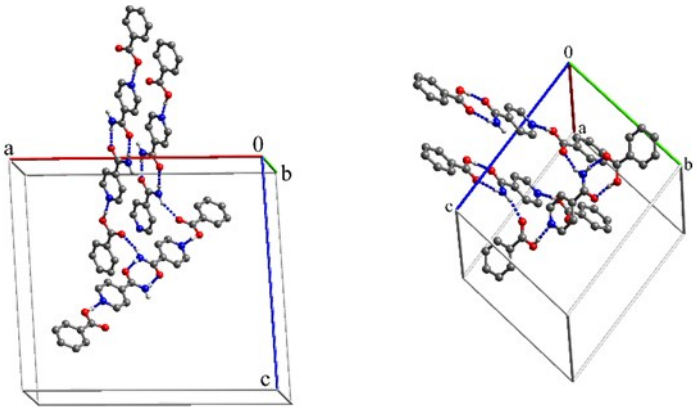

Fig. S3. H-bonding between super molecules of (left) BZA-INA 1:1 and (right) BZA-INA 2:1. H atoms not involved in H-bonds are omitted for clarity.

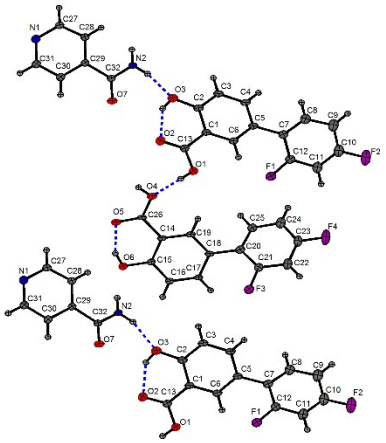

Fig. S4. Crystal structure of DIF INA 2:1 cocrystal (one component of the disorder is shown).

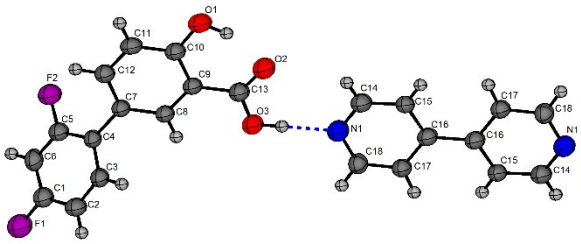

Fig. S5. Crystal structure of DIF-BIPY 2:1 cocrystal (one component of the disorder is shown).

Fig. S6. DIF-BIPY 2:1 cocrystal structure with two unit cells packed along *a* and crystal shape.

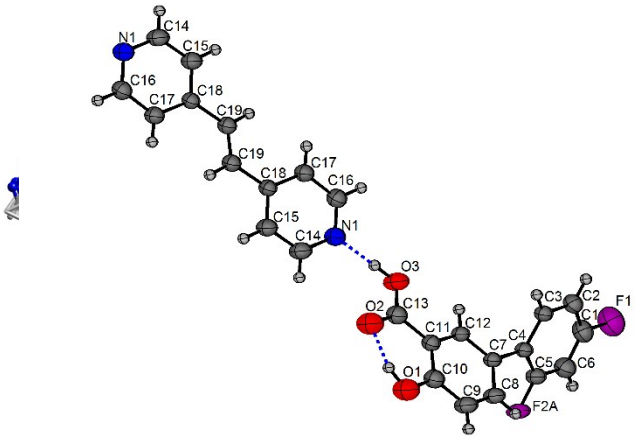

Fig. S7. Crystal structure of DIF-EBIPY 2:1 cocrystal (one component of disorder shown).

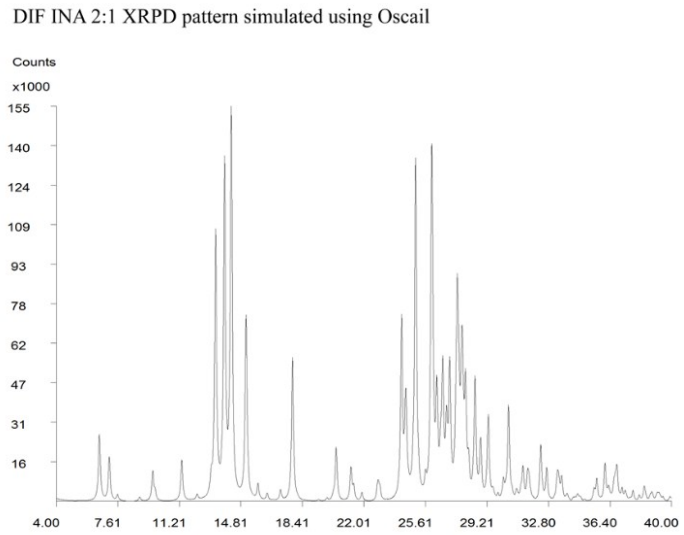

Fig. S8. Simulated XRPD pattern. This pattern is a close match to that reported for powder samples of DIF-INA. [4]

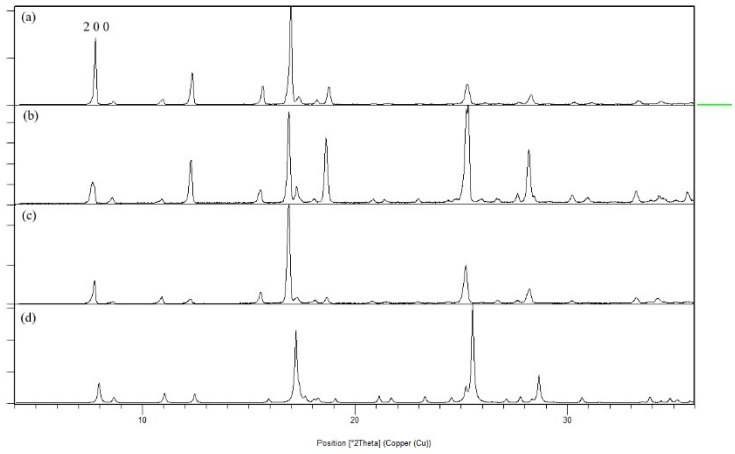

Fig. S9. XRPD patterns of (a) BZA-INA cocrystals, (b) BZA-INA cocrystals grown with 1% BEN, (c) BZA-INA cocrystals grown with 1% BEN ground and (d) pattern calculated using CSD code BUDWEC.

The patterns of the ground sample grown in the presence of 1% BEN and the calculated one are in excellent agreement. The pattern for the needle crystals shows the largest preferred orientation effects. The 2 0 0 reflection has enhanced intensity due the needles grown along 0 k 0 lying down.

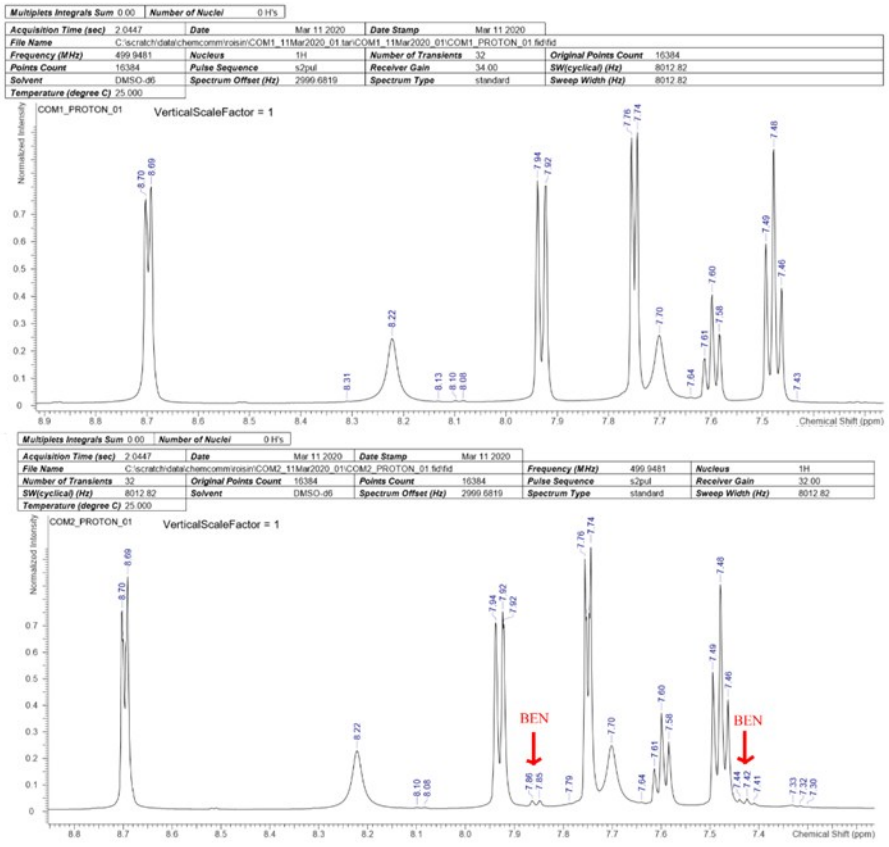

Fig. S10. ^{1}H NMR spectra in d6 acetone of upper BZA-INA cocrystals grown in the absence of BEN and lower BZA-INA cocrystals grown in the presence of 1% BEN. The latter sample has small peaks at 7.855 and 7.42 ppm which show incorporation of BEN into the crystals.

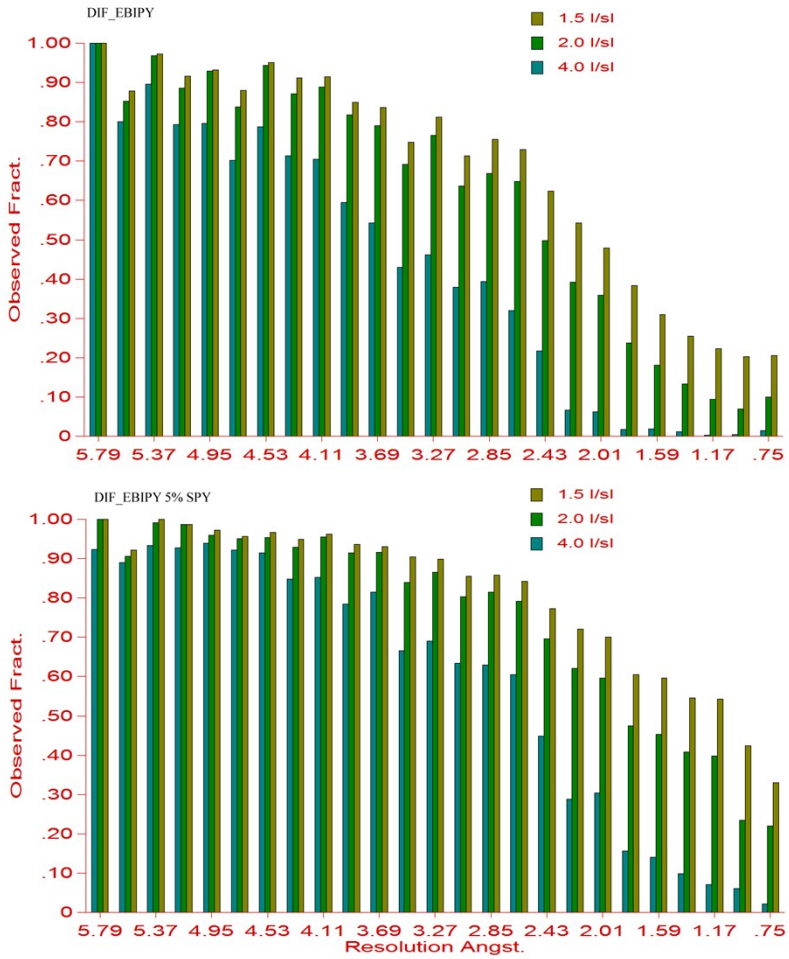

Fig. S11. Diffraction observed from (above) a DIF-EBIPY plate-like crystal grown without SPY and (below) from a needle crystal grown with 5% SPY.

Dissolution and sublimation movies

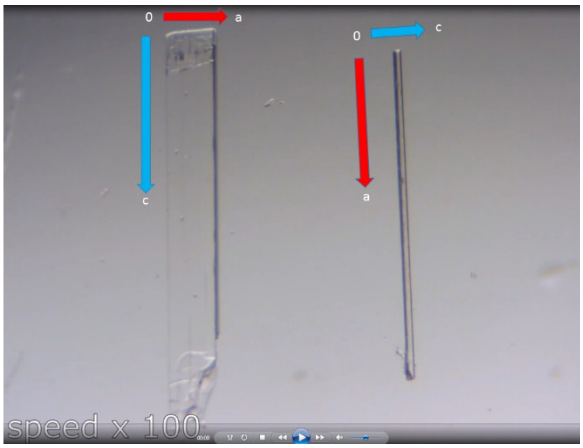

Fig. S12. Axial directions in the DIF-EBIPY crystals used in the ethanol dissolution movie.

In the movie the fastest dissolutions are c for both the plate crystal grown in the absence of SPY and for the needle grown in the presence of SPY.

Sublimation movies of needle crystals DIF-EBIPY and DIF-BIPY. These movies show contrasting behavior. The DIF-EBIPY needle gets thinner fastest and the DIF-BIPY crystal gets shorter fastest.

References

1. P. McArdle, *J. Appl. Crystallogr.*, 2017, **50**, 320-326.
2. G. Sheldrick, *Acta Cryst.,* 2015, **A71**, 3-8.
3. G. Sheldrick, *Acta Cryst.,* 2015, **C71**, 3-8.
4. L. Wang, B. Tan, H. Zhang and Z. Deng, *Org. Process Res. Dev.*, 2013, **17**, 1413-1418.