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Supplementary Information for

Polymorphism observed in dapsone-flavone cocrystals that present pronounced differences in solubility and stability

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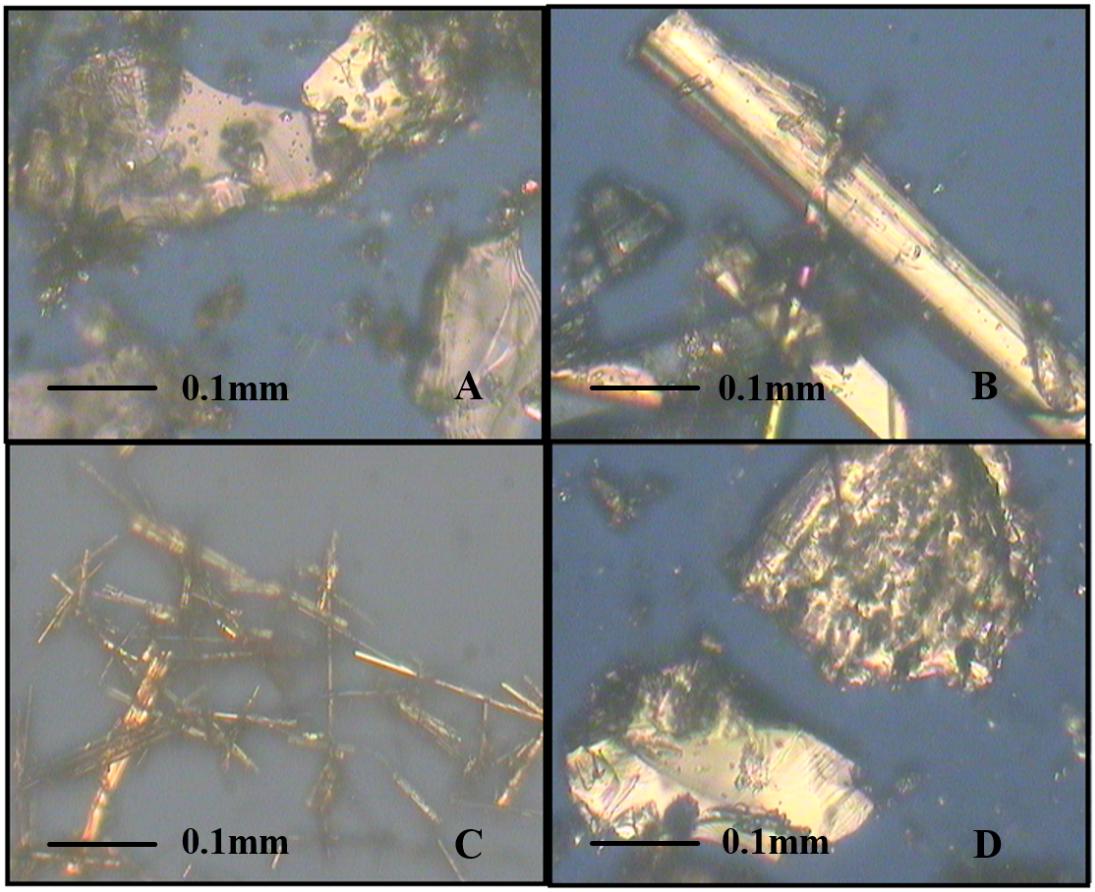

Figure S1. Polarized light microscopies for the cocrystal **A**, **B**, **C** and **D**

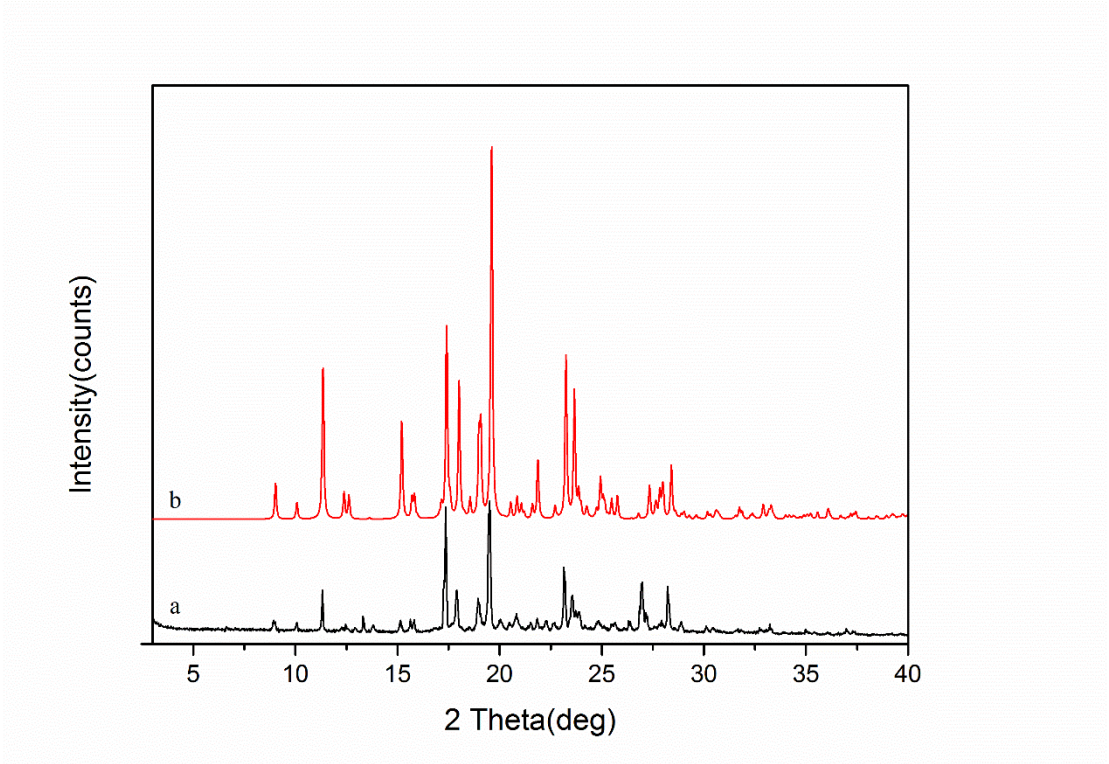

Figure S2. Powder X-ray diffraction of form **A** (a) experimental (b) simulated

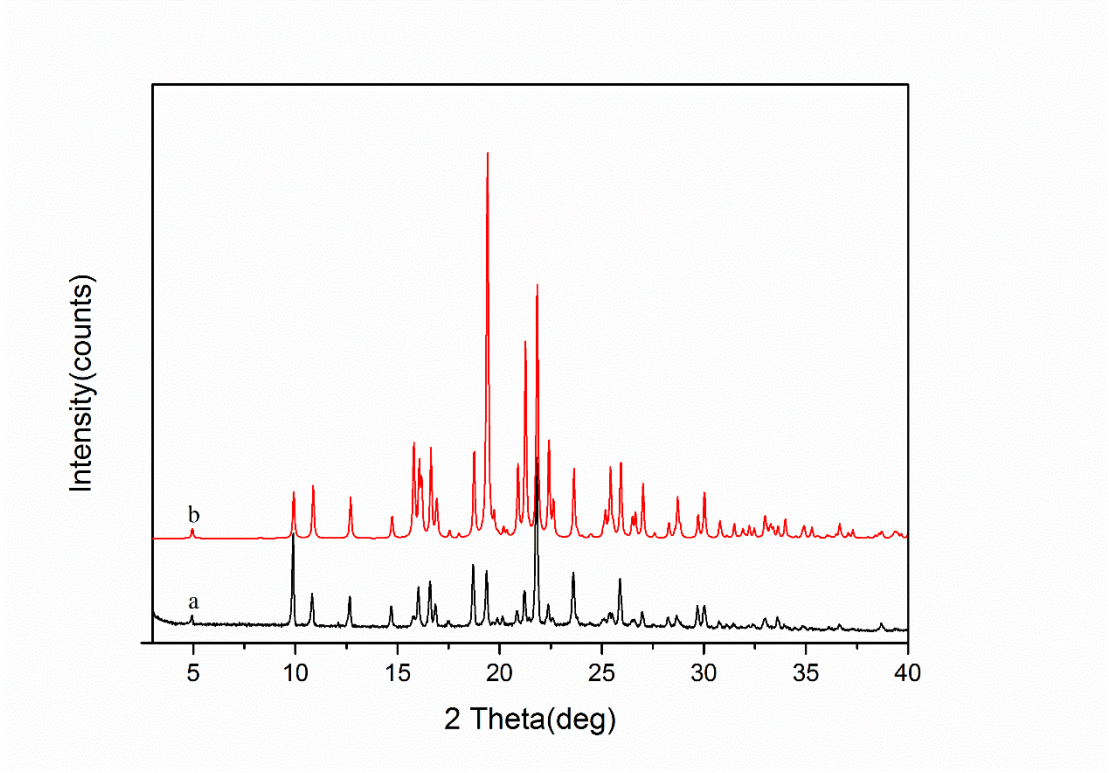

Figure S3. Powder X-ray diffraction of form **B** (a) experimental (b) simulated

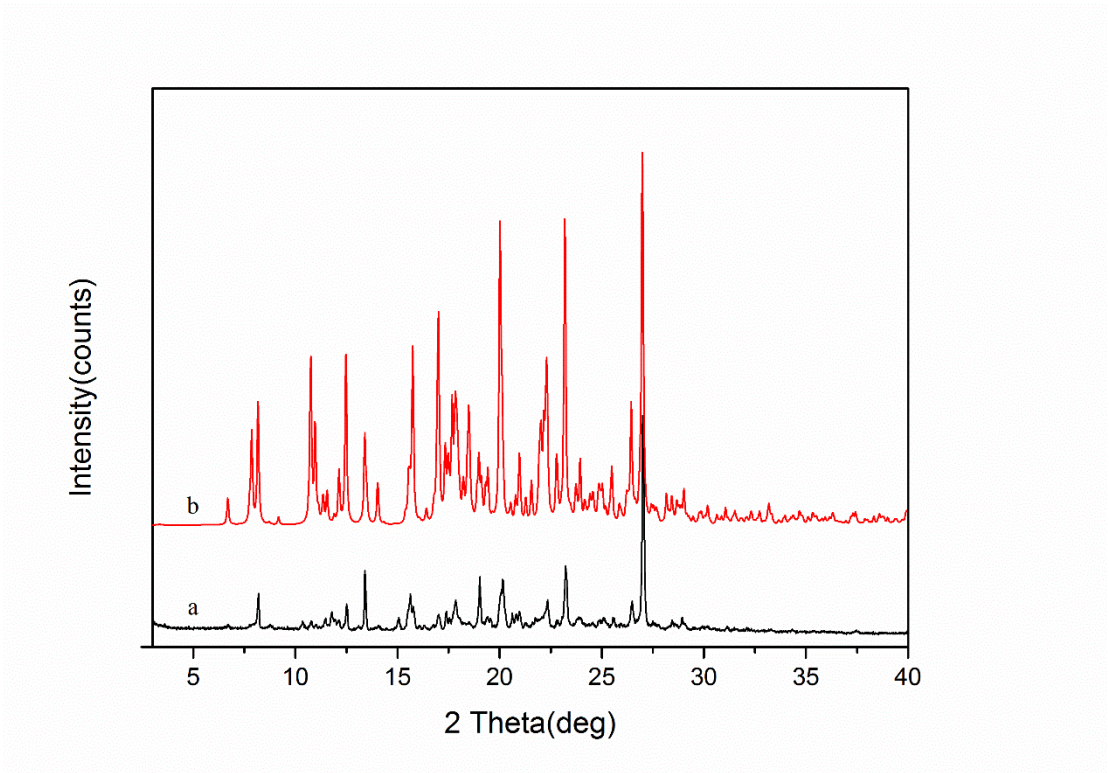

Figure S4. Powder X-ray diffraction of form **D** (a) experimental (b) simulated

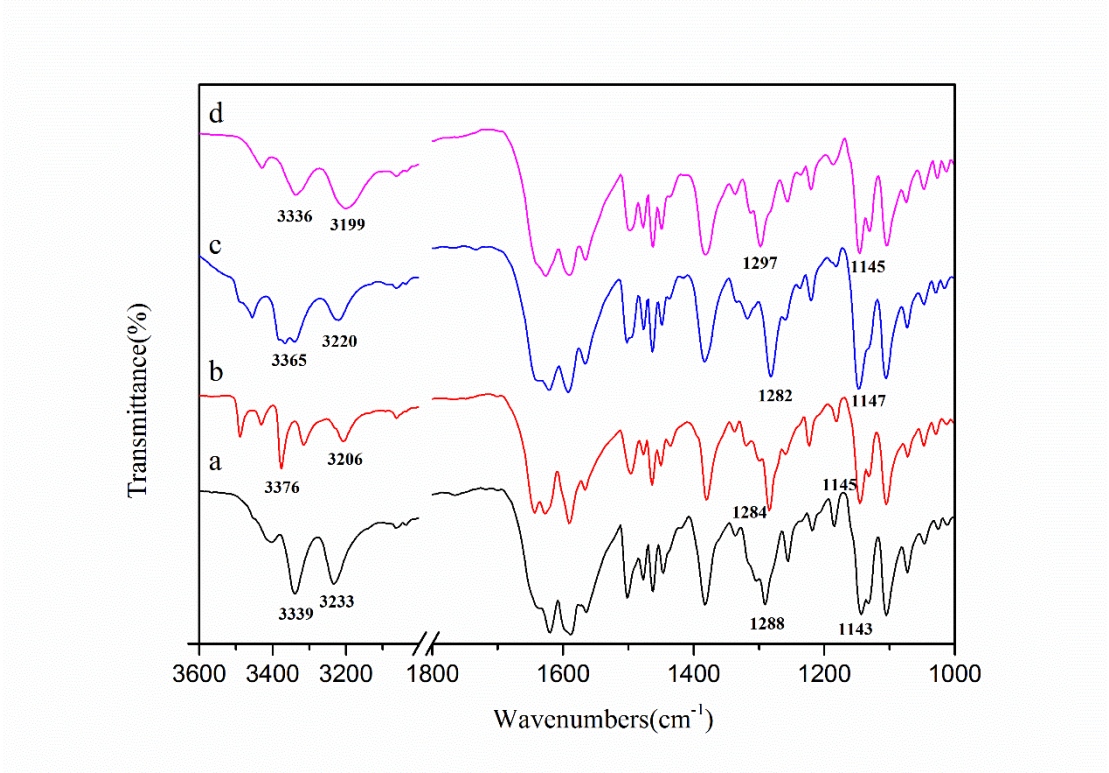

Figure S5. FT-IR spectra of cocrystal (a) **A** (b) **B** (c) **C** and (d) **D**

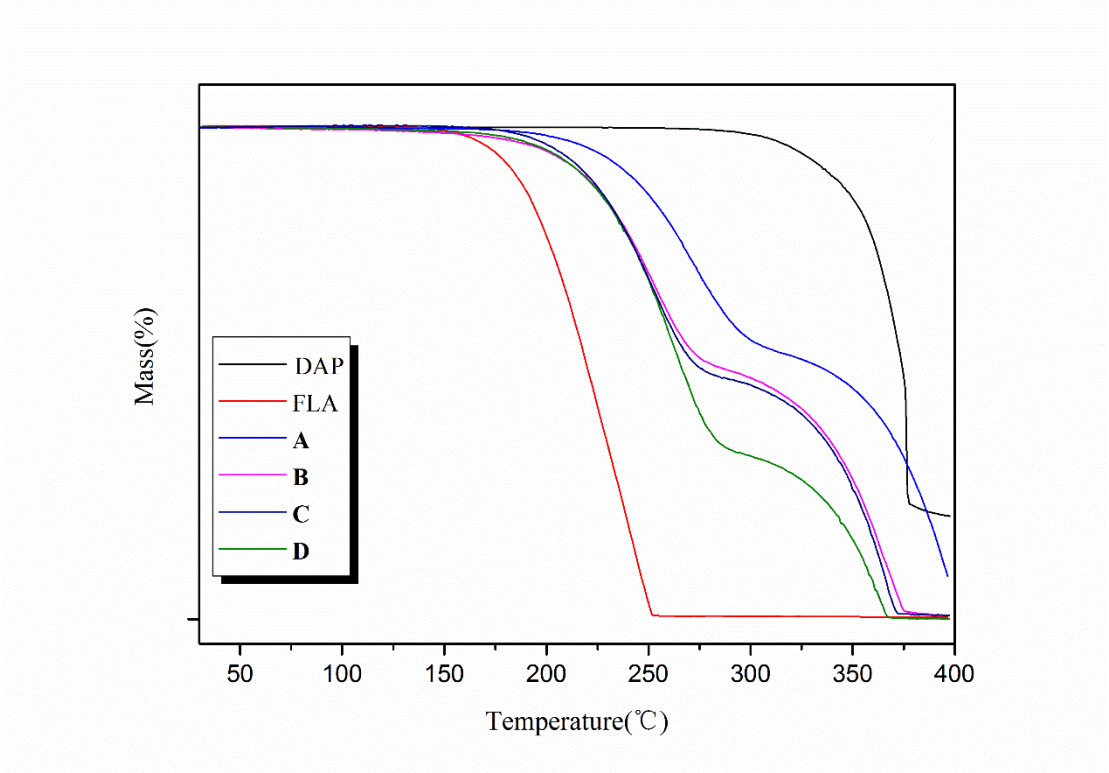

Figure S6. Comparison of TGA thermograms of DAP, FLA, **A**, **B**, **C** and **D**.

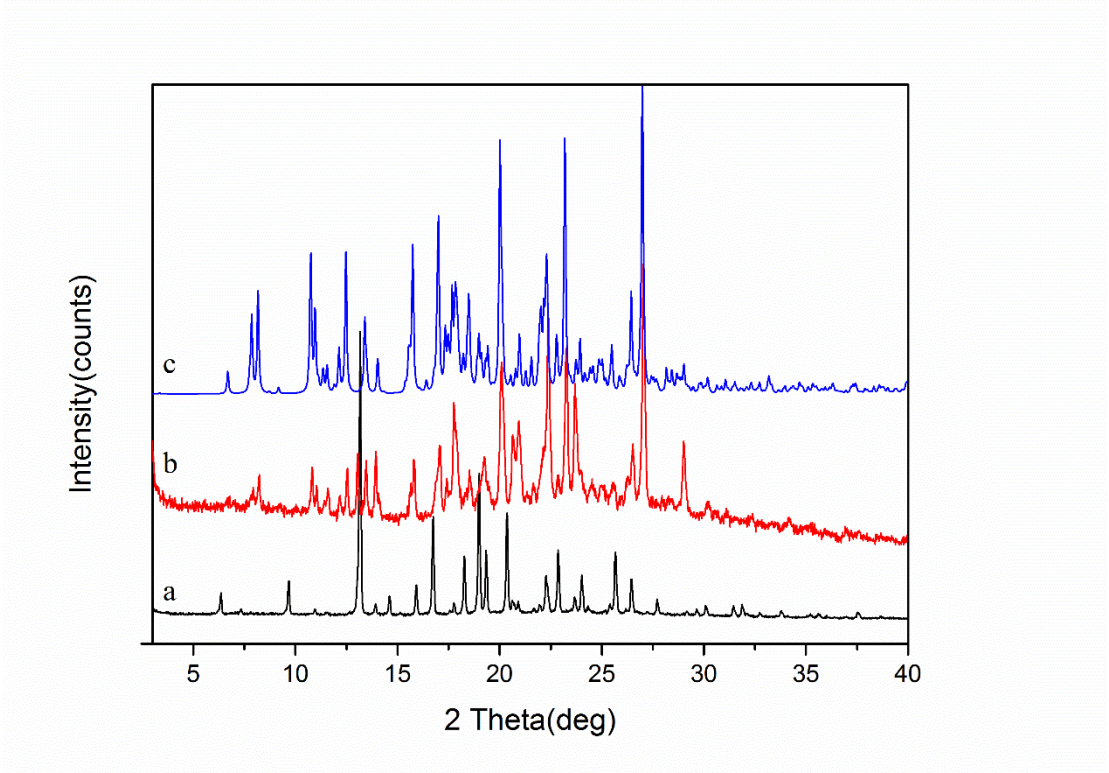

Figure S7. Comparison of PXRD patterns of (a) form **C** (b) form **C** heating for 2h at 90 ℃ (c) form **D** simulated

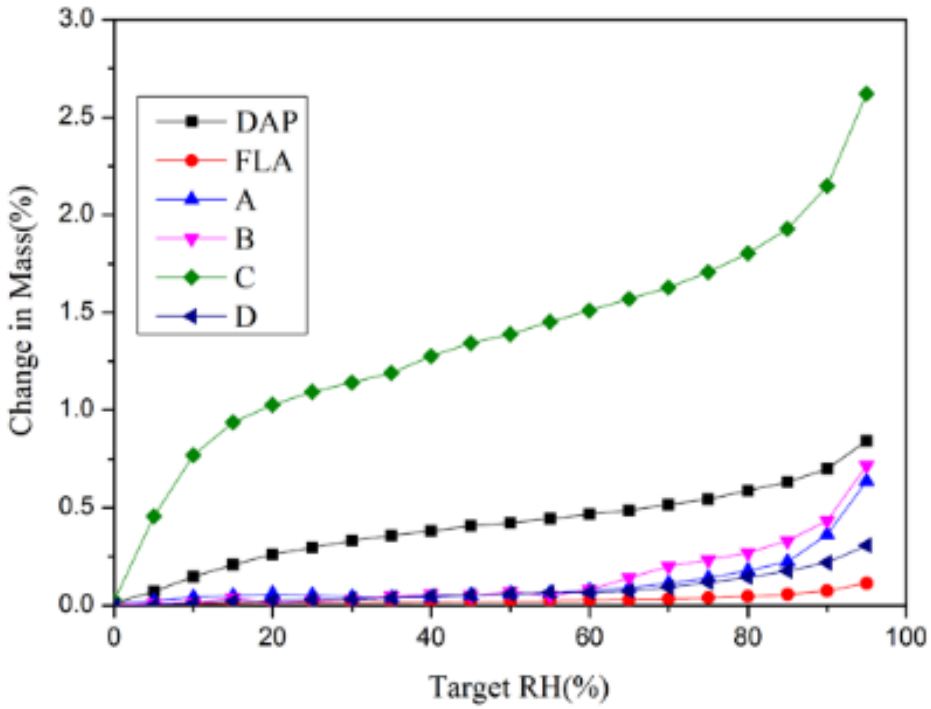

Figure S8. DVS diagrams of DAP, FLA, **A**, **B**, **C** and **D**

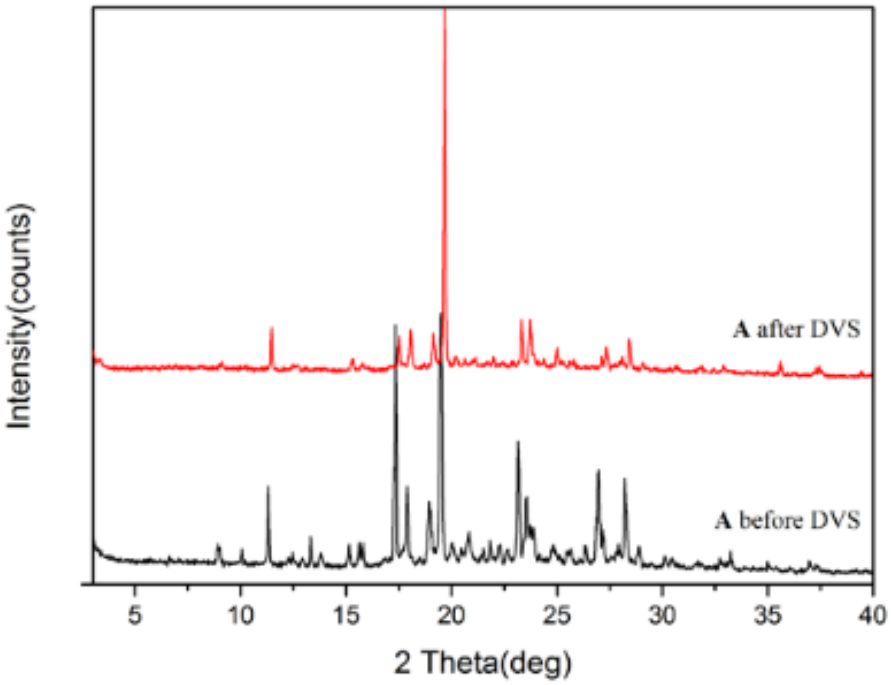

Figure S9. Comparison of PXRD patterns for form **A** before and after DVS.

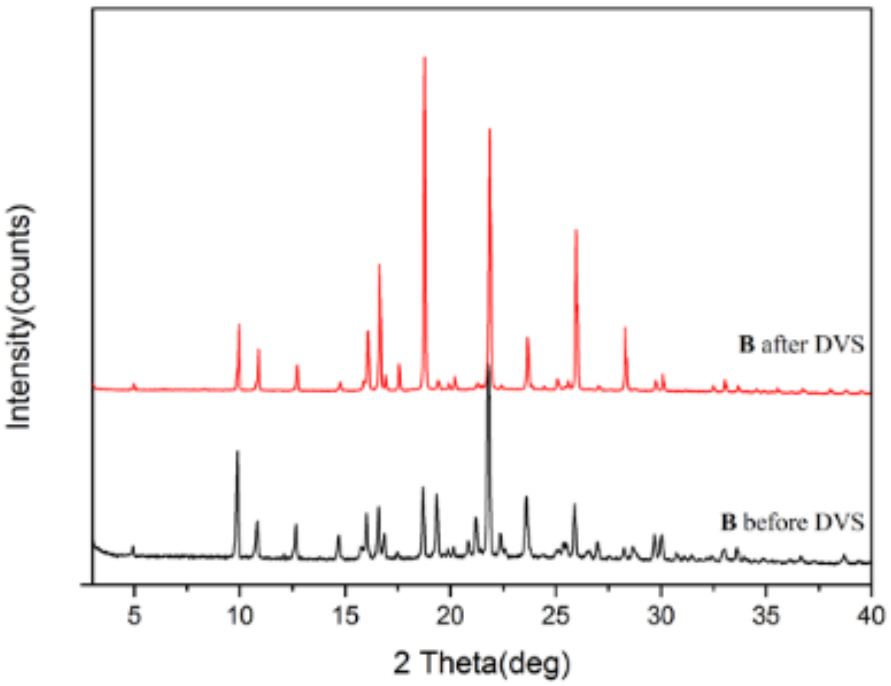

Figure S10. Comparison of PXRD patterns for form **B** before and after DVS.

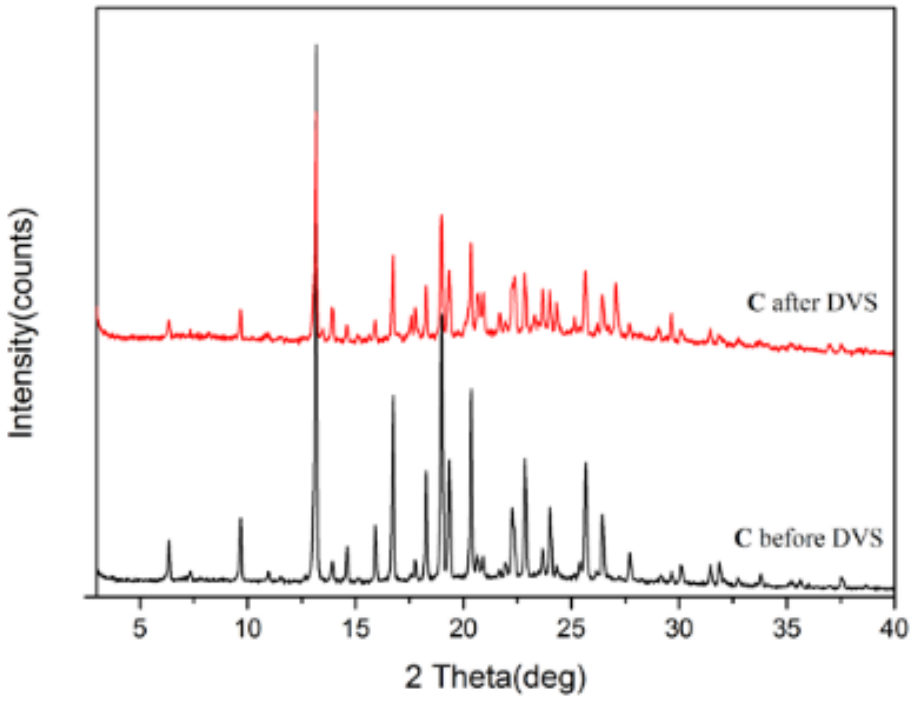

Figure S11. Comparison of PXRD patterns for form **C** before and after DVS.

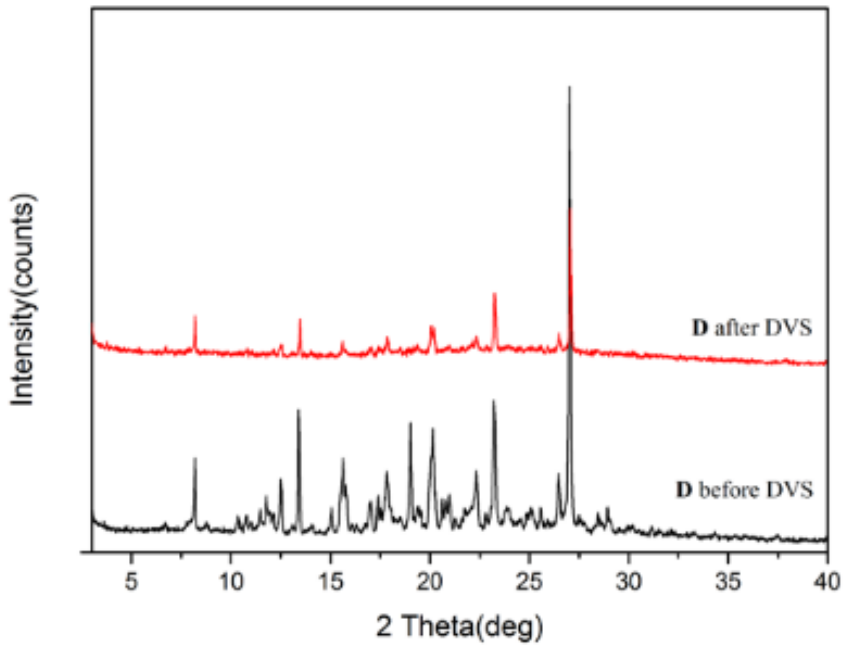

Figure S12. Comparison of PXRD patterns for form **D** before and after DVS.

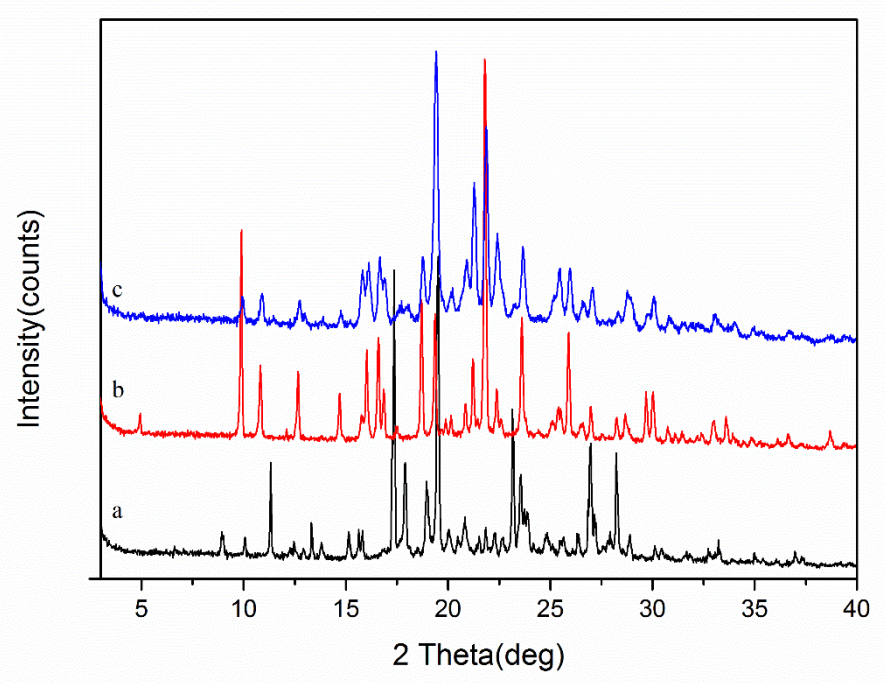

Figure S13. Comparison of PXRD patterns of (a) **A** (b) **B** (c) **A** and **B** slurry in hexane for 24 h

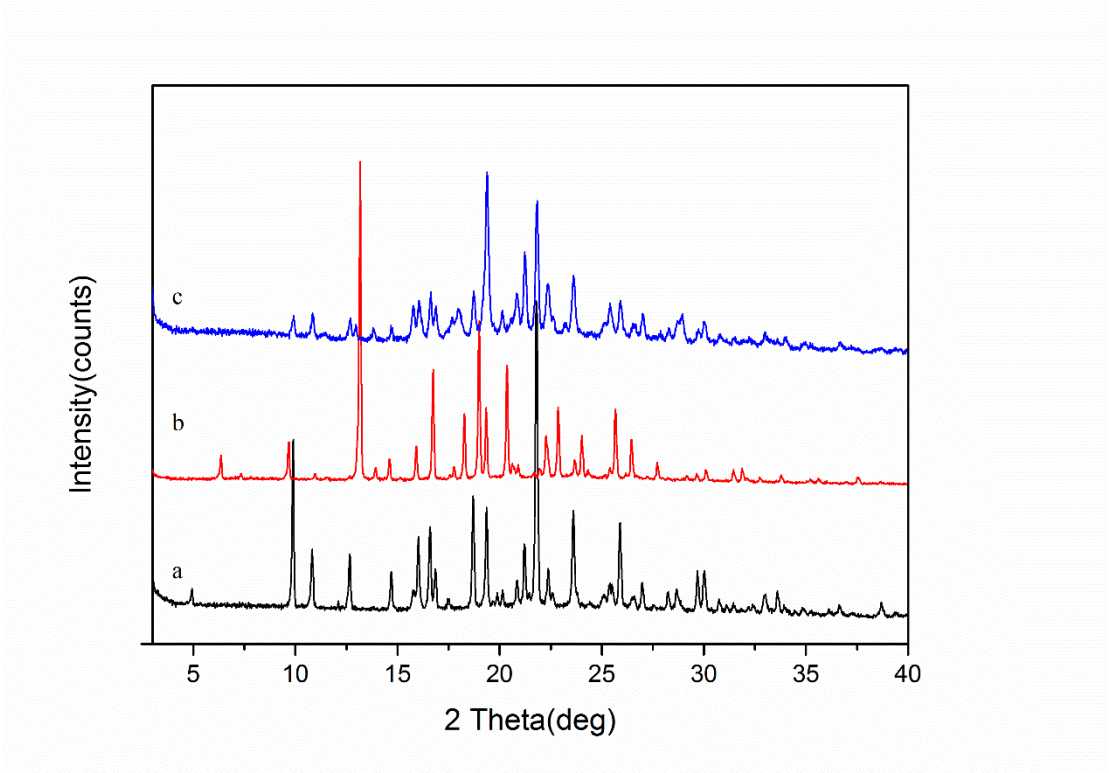

Figure S14. Comparison of PXRD patterns of (a) **B** (b) **C** (c) **B** and **C** slurry in hexane for 24 h

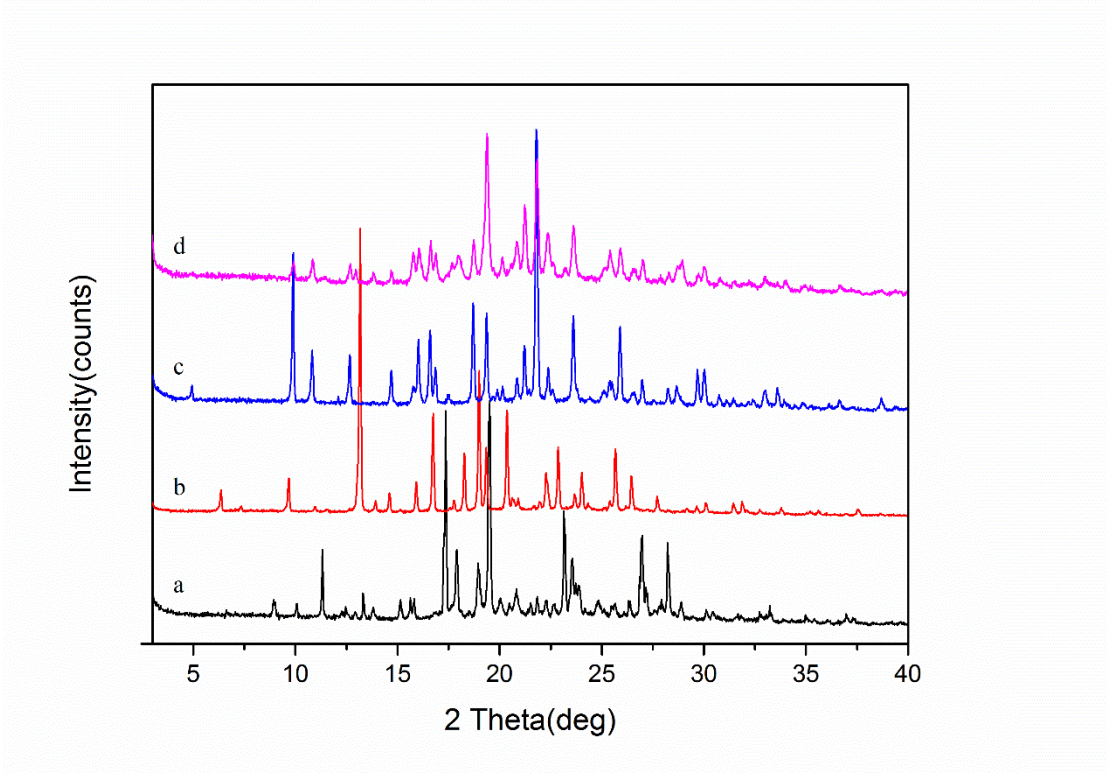

Figure S15. Comparison of PXRD patterns of (a) **A** (b) **C** (c) **B** (d) **A** and **C** slurry in hexane for 24 h

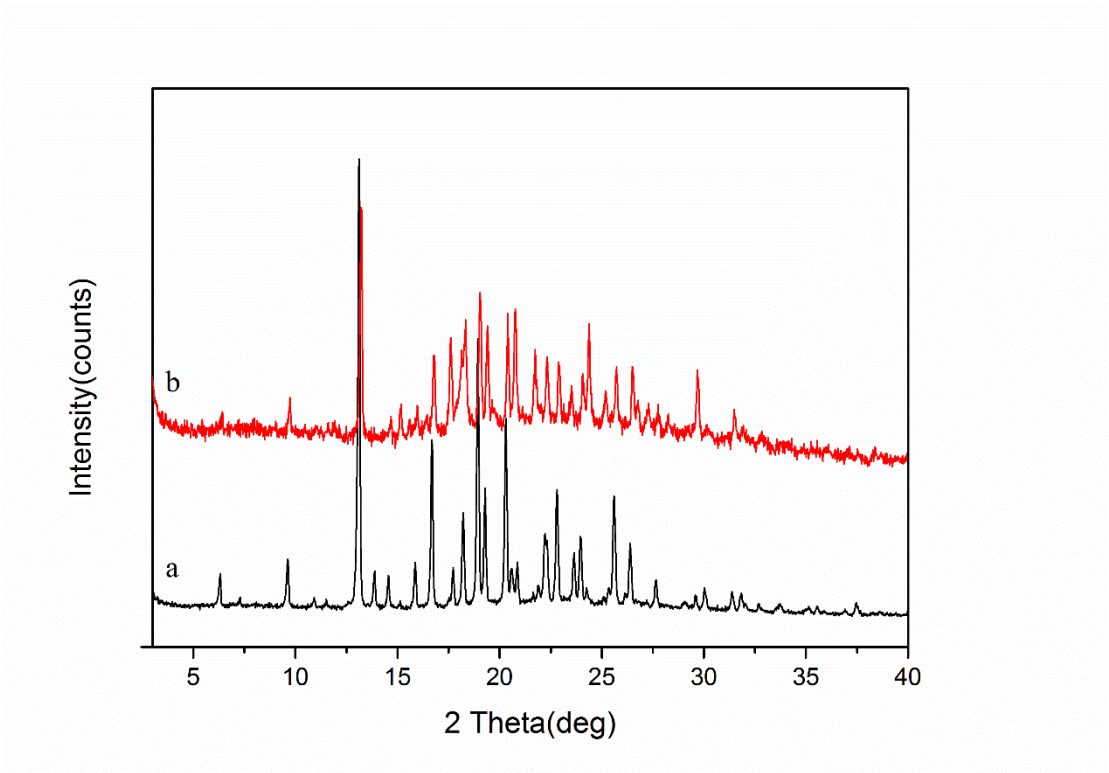

Figure S16. Comparison of PXRD patterns of (a) **C** (b) residual solid of **A** slurry in water

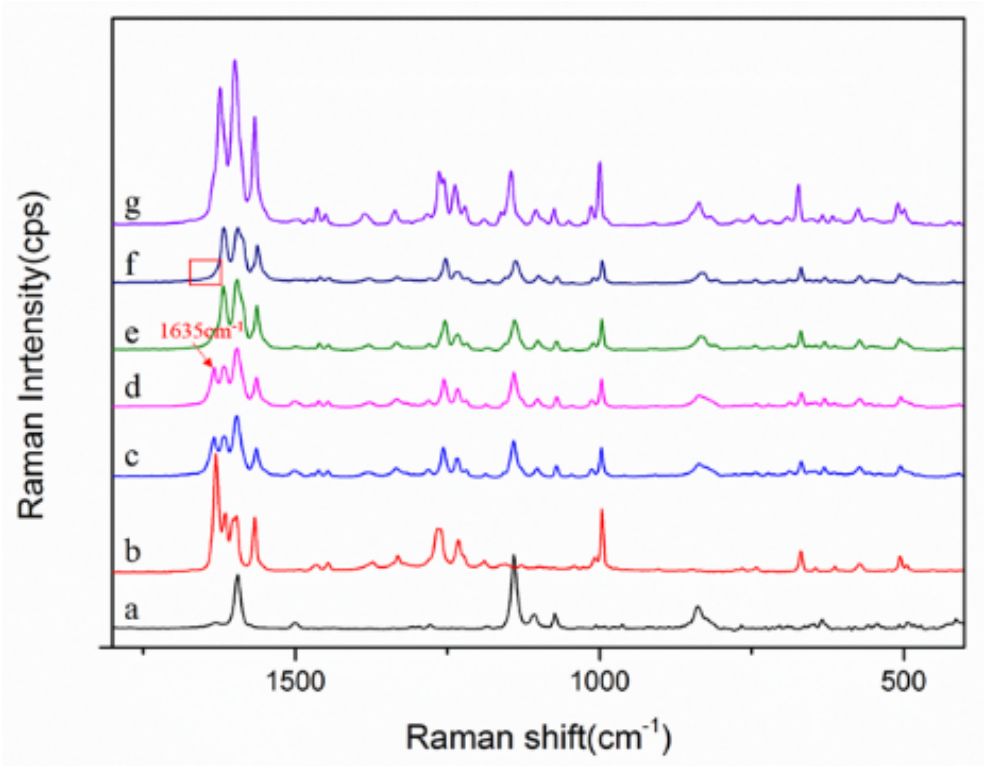

Figure S17. Comparison of Raman spectra for (a) DAP (b) FLA (c) **C** at 25 ℃ (d) **C** at 50 ℃ (e) **C** at 60 ℃ (f) **C** at 95 ℃ (g) **D** between 1800 to 400 cm^{-1}.

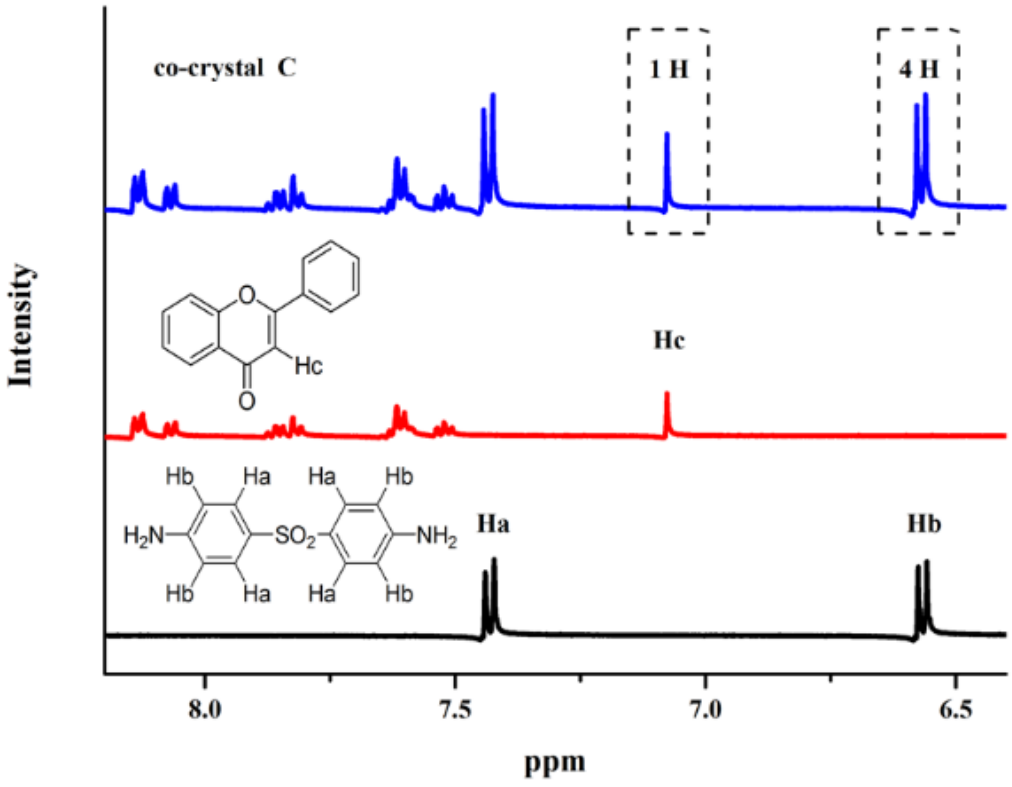

Figure S18. Comparison of ^{1}H-NMR (d_6-DMSO, 400 MHZ) patterns of **C**, DAP and FLA. The integration values suggested that the stoichiometry of DAP:FLA = 1:1.

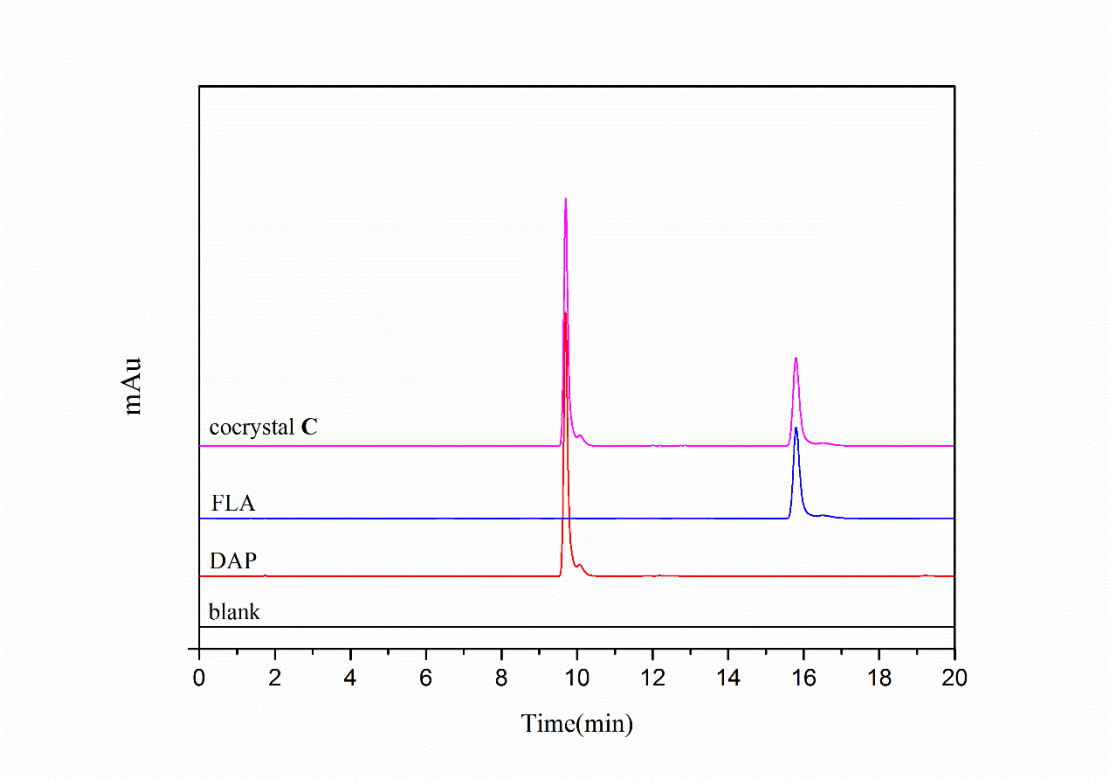

Figure S19. Comparison of HPLC analysis of DAP, FLA and cocrystal **C**. The integration area suggested that the stoichiometry of DAP:FLA = 1:1.

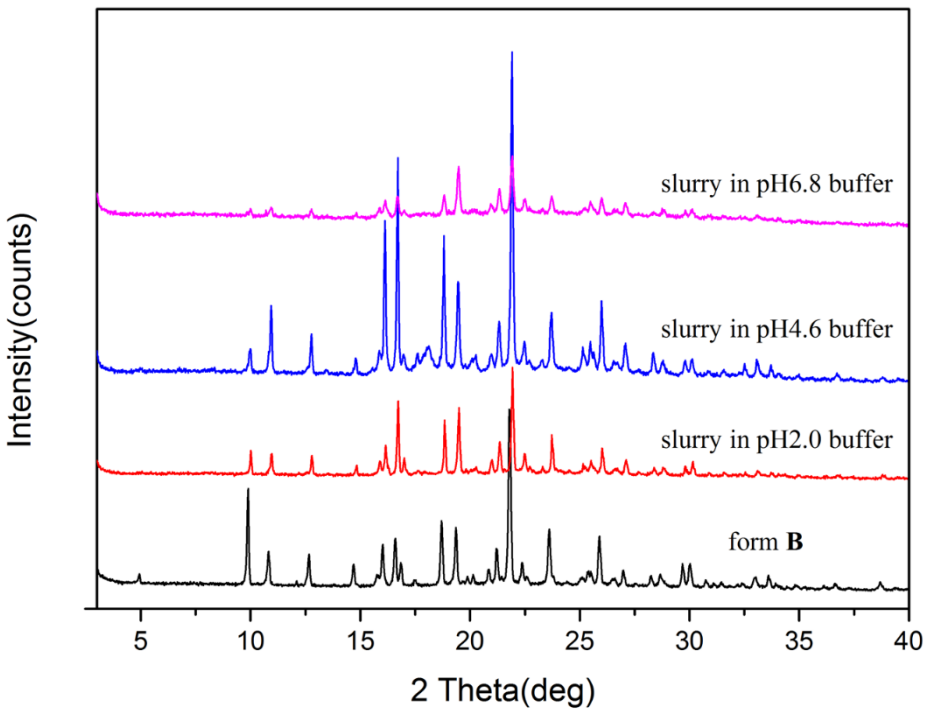

Figure S20. PXRD patterns for residual solids from **B** solubility experiments.

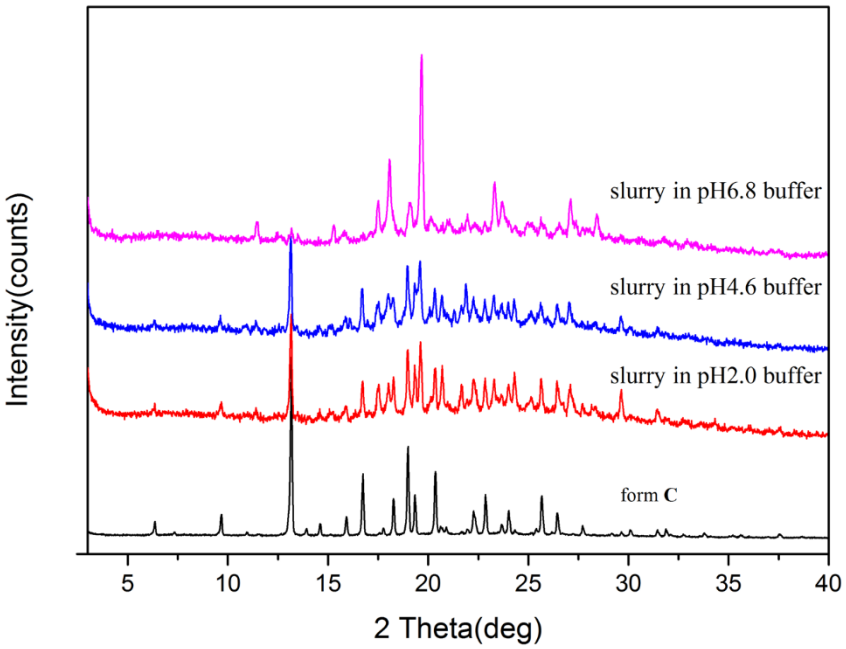

Figure S21. PXRD patterns for residual solids from **C** solubility experiments

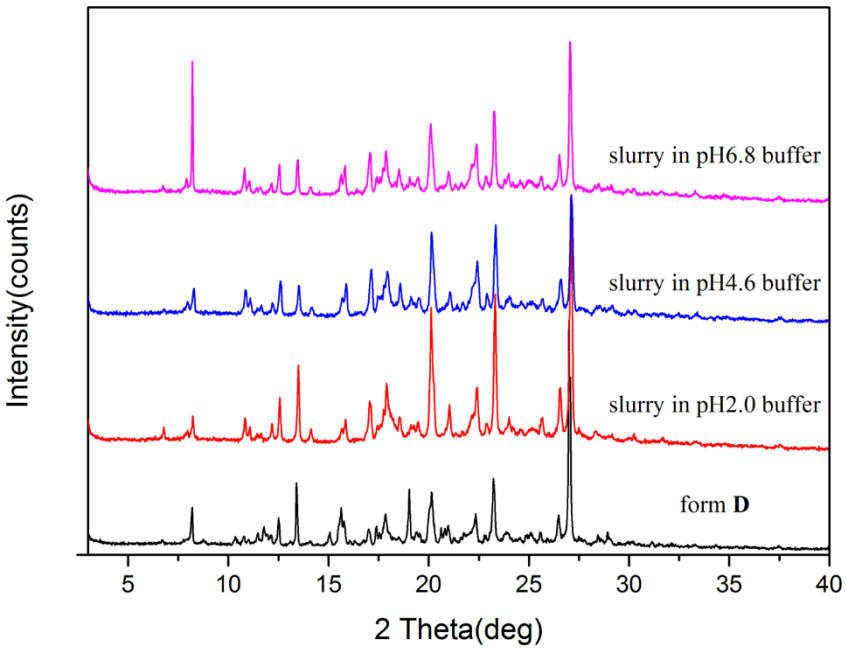

Figure S22. PXRD patterns for residual solids from **D** solubility experiments.

Table S1. Hydrogen bond data for the polymorphic cocrystals

Forms	D-H···A	d(D-H), Å	d(H···A), Å	d(D···A), Å	∠(D-H···A), deg	Symmetry code

A	N1-H1A···N2	0.86	2.38	3.174(2)	153	x+1, y, z
	N1-H1B···O4	0.86	2.21	2.957(6)	146	x+1/2,-y+3/2,z-1/2
	N2-H2A···O1	0.86	2.16	2.969(3)	156	-x+1/2,y-1/2,-z+1/2
	N2-H2B···O4	0.86	2.11	2.918(3)	157	-x+1/2,y-1/2,-z+1/2
B	N1-H1B···O4	0.86	2.13	2.971(9)	164	-x+1/2,-y+2,z+3/2
	N2-H2B···O1	0.86	2.30	3.146(8)	166	x+1/4,-y+7/4,z-1/4
D	N3-H3B···N4	0.86	2.36	3.102(3)	145	x-1,y,z
	N4-H4A···O10	0.86	2.03	2.821(3)	153	x+1,y-1,z
	N4-H4B···O12	0.86	2.11	2.942(3)	163	x+1,y-1,z
	N1-H1A···O6	0.86	2.19	2.990(3)	153	x-1,y,z
	N1-H1B···O8	0.86	2.29	2.979(3)	137	x-1,y,z
	N2-H2A···N1	0.86	2.25	3.082(3)	165	x+1,y,z
	N2-H2B···O4	0.86	2.20	3.055(3)	173	

Table S2. Summary of Equilibrium Solubility of DAP, FLA and DAP-FLA cocrystals

Material	Equilibrium solubility (mg/ml)			Residue after equilibrium
	pH 2.0	pH 4.6	pH 6.8	
DAP	0.40*	0.17*	0.17*	DAP hydrate
A	0.47*	0.20*	0.18*	**C**
B	0.33	0.17	0.17	**B**
C	0.38	0.19	0.15	**C**
D	0.10	0.07	0.09	**D**

*Note: Value are corresponding to the equilibrium solubility of the residue solids.

Table S3. Summary of Intrinsic Dissolution Rates of DAP, FLA and DAP-FLA cocrystals

Material	IDR(ug/min · cm^2)

	pH 2.0	pH 4.6	pH 6.8
DAP	98.9	44.9	31.1
A	46.6	35.6	19.8
B	15.5	10.0	8.7
C	12.9	9.2	2.4
D	8.0	8.1	5.1