



STRUCTURAL SCIENCE  
CRYSTAL ENGINEERING  
MATERIALS

**Volume 75 (2019)**

**Supporting information for article:**

**Comparison of the crystal structures and physicochemical properties of novel resveratrol cocrystals**

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**Table S1** The cocrystal screening experiments of RSV cocrystallized with BPE, DPE or AZPY.

Sample	Solvent	Condition	Results
RSV:4,4'-ethylenedipyridine (BPE)=2:3	ACN	25 °C Evaporation Slowly	RSV-1.5BPE
RSV:4,4'-ethylenedipyridine (BPE)=2:3	ACE:IPA=1:1	25 °C Evaporation Slowly	RSV-1.5BPE
RSV:4,4'-ethylenedipyridine (BPE)=2:3	ACE	25 °C Evaporation Slowly	RSV-1.5BPE
RSV:4,4'-ethylenedipyridine (BPE)=2:3	THF	25 °C Evaporation Slowly	RSV-1.5BPE
RSV:4,4'-ethylenedipyridine (BPE)=2:3	ACE:MIBK=1:1	25 °C Evaporation Slowly	RSV-1.5BPE
RSV:4,4'-ethylenedipyridine (BPE)=2:3	ACE:Tol:Hep=1:1:1	50°C Evaporation Slowly	RSV-1.5BPE
RSV:4,4'-ethylenedipyridine (BPE)=2:3	ACE:Tol=1:1	25 °C Evaporation Slowly	RSV-1.5BPE
RSV:4,4'-ethylenedipyridine (BPE)=2:3	i-PrOH	25 °C Evaporation Slowly	RSV-1.5BPE
RSV:4,4'-ethylenedipyridine (BPE)=2:3	MEK	25 °C Evaporation Slowly	RSV-1.5BPE
RSV:4,4'-ethylenedipyridine (BPE)=2:3	MeOH	25 °C Evaporation Slowly	RSV-1.5BPE
RSV:4,4'-vinylenedipyridine (DPE)=1:2	ACE	25 °C Evaporation Slowly at P <sub>2</sub> O <sub>5</sub> Desiccator	RSV-2DPE Form I
RSV:4,4'-vinylenedipyridine (DPE)=1:2	ACE:EA=1:1	25 °C Evaporation Slowly at P <sub>2</sub> O <sub>5</sub> Desiccator	RSV-2DPE Form I
RSV:4,4'-vinylenedipyridine (DPE)=1:2	ACE:i-PrOH=1:1	25 °C Evaporation Slowly	RSV-2DPE Form I

RSV:4,4'-vinylenedipyridine (DPE)=1:2	THF	25 °C Evaporation Slowly	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	ACE	25 °C Evaporation in an open glass vial	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	ACE:ACN=1:1	25 °C Evaporation Slowly	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	MEK	25 °C Evaporation Slowly	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	ACE:EA=1:1	25 °C Evaporation in an open glass vial	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	MeOH	4°C Cooling	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	ACE:MTBE=1:1	25 °C Evaporation Slowly	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	ACE:IPA=1:1	25 °C Evaporation Slowly	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	ACE:MIBK=1:1	25 °C Evaporation Slowly	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	EtOH	25 °C Evaporation Slowly	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	i-PrOH	25 °C Evaporation Slowly	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	ACE:Tol=1:1	25 °C Evaporation Slowly	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:2	ACE:Tol:Hep=1:1:1	50°C Evaporation Slowly	RSV-2DPE Form II
RSV:4,4'-vinylenedipyridine (DPE)=1:1	MeOH:Hep=1:1	25 °C Evaporation Slowly	RSV-DPE
RSV:4,4'-vinylenedipyridine (DPE)=1:1	MeOH:Hex=1:1	25 °C Evaporation Slowly	RSV-DPE

RSV:4,4'-vinylenedipyridine (DPE)=2:3	ACE:Hep=2:1	25 °C Evaporation Slowly	RSV-1.5DPE•0.5ACE
RSV:4,4'-vinylenedipyridine (DPE)=2:3	MeOH	4 °C Cooling	RSV-1.5DPE•MeOH
RSV:4,4'-azobispyridine (AZPY)=1:2	ACE	70 °C Evaporation	RSV-2AZPY
RSV:4,4'-azobispyridine (AZPY)=1:2	ACE	50 °C Evaporation	RSV-2AZPY
RSV:4,4'-azobispyridine (AZPY)=1:2	ACE	25 °C Evaporation Slowly	RSV-2AZPY
RSV:4,4'-azobispyridine (AZPY)=1:2	EtOH	25 °C Evaporation Slowly	RSV-2AZPY
RSV:4,4'-azobispyridine (AZPY)=1:2	ACE:EA=1:1	25 °C Evaporation Slowly	RSV-2AZPY
RSV:4,4'-azobispyridine (AZPY)=1:2	ACE:THF=1:1	25 °C Evaporation Slowly	RSV-2AZPY
RSV:4,4'-azobispyridine (AZPY)=1:2	MeOH:Hex=1:1	25 °C Evaporation Slowly	RSV-2AZPY
RSV:4,4'-azobispyridine (AZPY)=1:2	MEK:IPA=1:1	25 °C Evaporation Slowly	RSV-2AZPY
RSV:4,4'-azobispyridine (AZPY)=1:2	THF	25 °C Evaporation Slowly	RSV-2AZPY
RSV:4,4'-azobispyridine (AZPY)=1:2	MeOH:Hex=1:1	25 °C Evaporation Slowly	RSV-2AZPY
RSV:4,4'-azobispyridine (AZPY)=1:2	MeOH	25 °C Evaporation Slowly	RSV-2AZPY

**Table S2** List of intermolecular and intramolecular hydrogen bond lengths and angles for RSV cocrystals.

Crystal form	Interactions	H···A (Å)	D···A (Å)	<D-H···A (°)	Symmetry code
RSV-1.5BPE	O <sub>1</sub> -H <sub>1</sub> ···N <sub>3</sub> (Inter)	1.82 (4)	2.685 (3)	144 (3)	1+x, y, z
	O <sub>2</sub> -H <sub>2</sub> ···N <sub>1</sub> (Inter)	1.82 (3)	2.711 (3)	172 (3)	-1+x, y, z
	O <sub>3</sub> -H <sub>3</sub> ···N <sub>2</sub> (Inter)	1.78 (3)	2.715 (2)	172 (3)	-x, -y, 1-z
	C <sub>10</sub> -H <sub>10</sub> ···O <sub>2</sub> (Inter)	2.48	3.410 (3)	169	1-x, 1-y, 1-z
	C <sub>21</sub> -H <sub>21A</sub> ···O <sub>1</sub> (Inter)	2.50	3.437 (4)	161	2-x, 1-y, 1-z
	C <sub>32</sub> -H <sub>32A</sub> ···O <sub>3</sub> (Inter)	2.57	3.441 (3)	148	1-x, 1-y, -z
RSV-2DPE Form I	O <sub>1</sub> -H <sub>1</sub> ···N <sub>4</sub> (Inter)	1.89 (2)	2.744 (3)	177 (3)	1-x, -1/2+y, 3/2-z
	O <sub>2</sub> -H <sub>2</sub> ···N <sub>3</sub> (Inter)	1.82 (2)	2.712 (3)	176 (2)	x, y, z
	O <sub>3</sub> -H <sub>3</sub> ···N <sub>1</sub> (Inter)	1.98 (3)	2.804 (3)	166 (3)	x, y, z
RSV-2DPE Form II	O <sub>1</sub> -H <sub>1</sub> ···N <sub>3</sub> (Inter)	1.91 (4)	2.670 (5)	148 (4)	1+x, -1+y, z
	O <sub>2</sub> -H <sub>2</sub> ···N <sub>2</sub> (Inter)	1.85 (4)	2.715 (5)	173 (4)	-1+x, 1+y, z
	O <sub>3</sub> -H <sub>3</sub> ···N <sub>1</sub> (Inter)	1.93 (4)	2.810 (4)	175 (4)	-x, 1-y, 1-z
	C <sub>33</sub> -H <sub>33</sub> ···O <sub>1</sub> (Inter)	2.33	3.251 (6)	165	-1+x, y, z
RSV-DPE	O <sub>1</sub> -H <sub>1</sub> ···N <sub>2</sub> (Inter)	1.87 (2)	2.7453 (19)	169 (2)	1-x, 1/2+y, 1/2-z
	O <sub>2</sub> -H <sub>2</sub> ···O <sub>3</sub> (Inter)	2.54 (2)	3.0504 (17)	120 (2)	x, -1+y, z
	O <sub>3</sub> -H <sub>3</sub> ···N <sub>1</sub> (Inter)	1.84 (2)	2.7357 (18)	171.8 (19)	x, 3/2-y, 1/2+z
RSV-1.5DPE•0.5ACE	O <sub>1</sub> -H <sub>1</sub> ···N <sub>1</sub> (Inter)	1.80 (5)	2.662 (4)	169 (5)	1-x, -y, 1-z
	O <sub>2</sub> -H <sub>2</sub> ···N <sub>6</sub> (Inter)	1.89 (4)	2.735 (4)	172 (4)	-x, 1-y, 1-z
	O <sub>3</sub> -H <sub>3</sub> ···N <sub>4</sub> (Inter)	1.94 (5)	2.783 (4)	178 (6)	-x, 1-y, -z
	O <sub>4</sub> -H <sub>4</sub> ···N <sub>2</sub> (Inter)	1.80 (6)	2.672 (5)	174 (6)	x, y, z
	O <sub>5</sub> -H <sub>5</sub> ···N <sub>3</sub> (Inter)	1.88 (4)	2.740 (4)	179 (5)	x, 1+y, z
	O <sub>6</sub> -H <sub>6</sub> ···N <sub>5</sub> (Inter)	1.85 (5)	2.740 (4)	178 (6)	x, 1+y, -1+z
	C <sub>32</sub> -H <sub>32</sub> ···O <sub>5</sub> (Inter)	2.51	3.443 (5)	175	x, -1+y, z
	C <sub>37</sub> -H <sub>37</sub> ···O <sub>2</sub> (Inter)	2.37	3.254 (4)	157	1-x, 1-y, 1-z
	C <sub>54</sub> -H <sub>54</sub> ···O <sub>7</sub> (Inter)	2.39	3.303 (5)	163	x, y, z
RSV-1.5DPE•MeOH	O <sub>1</sub> -H <sub>1</sub> ···O <sub>4</sub> (Inter)	1.76 (4)	2.627 (3)	175 (3)	1+x, y, z
	O <sub>2</sub> -H <sub>2</sub> ···N <sub>1</sub> (Inter)	1.89 (4)	2.766 (5)	176 (3)	-1+x, 1+y, z

	O <sub>3</sub> -H <sub>3</sub> ···N <sub>2</sub> (Inter)	1.88 (4)	2.754 (4)	175 (3)	1-x, 1-y, 1-z
	O <sub>4</sub> -H <sub>4</sub> ···N <sub>3</sub> (Inter)	1.89 (4)	2.771 (4)	172 (3)	x, y, z
	C <sub>15</sub> -H <sub>15</sub> ···O <sub>1</sub> (Inter)	2.49	3.272 (4)	141	2-x, -y, -z
RSV-2AZPY	O <sub>1</sub> -H <sub>1</sub> ···N <sub>5</sub> (Inter)	1.80 (4)	2.671 (5)	170 (4)	1-x, y, 3/2-z
	O <sub>2</sub> -H <sub>2</sub> ···N <sub>1</sub> (Inter)	1.95 (4)	2.766 (5)	166 (5)	1/2-x, 1/2-y, 1-z
	O <sub>3</sub> -H <sub>3</sub> ···N <sub>8</sub> (Inter)	1.95 (2)	2.789 (5)	175 (3)	1-x, -y, 1-z

**Table S3** The torsion angles of RSV conformation in RSV-1.5BPE, RSV-2DPE Form I, RSV-2DPE Form II, RSV-DPE or RSV-2AZPY.

Torsion angle	RSV-1.5BPE	RSV-2DPE Form I	RSV-2DPE Form II	RSV-DPE	RSV-2AZPY
I					
$\tau_1$ (C3-C4-C7-C8)/°	25.8 (3)	-8.2 (4)	-22.6 (5)	-173.7 (2)	173.3 (4)
$\tau_2$ (C7-C8-C9-C14)/°	17.8 (3)	-8.3 (4)	2.3 (6)	171.3 (2)	-170.3 (4)

**Table S4** Structural parameters and melting points of RSV cocrystals.

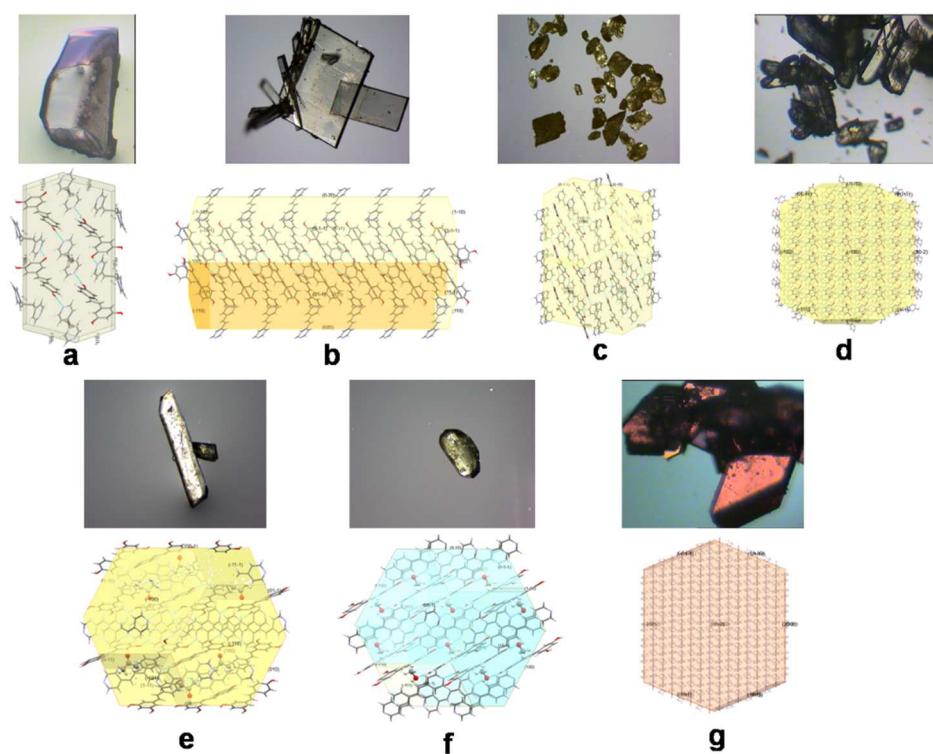
Sample	Melting point (°C)	Packing coefficient (%)	Density (g/cm <sup>3</sup> )
RSV-1.5BPE	202.3	71.03	1.245
RSV-2DPE Form I	239.0	71.28	1.262
RSV-2DPE Form II	235.7	71.25	1.261
RSV-DPE	248.1	75.06	1.341
RSV-1.5DPE•0.5ACE	-	70.69	1.243
RSV-1.5DPE•MeOH	-	72.28	1.266
RSV-2AZPY	204.2	72.79	1.337

**Table S5** The absorbing water content of RSV cocrystals at 80% RH.

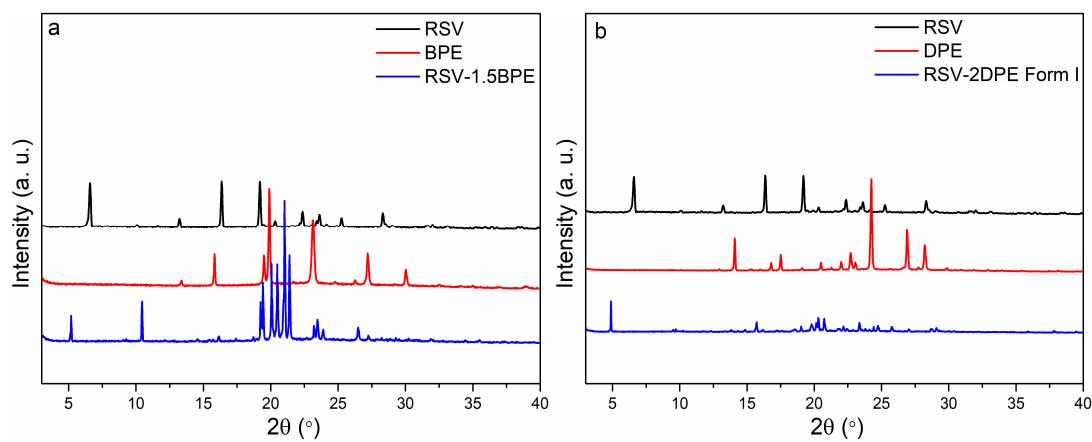
Sample	Water content
RSV	0.099%
RSV-1.5BPE	0.556%
RSV-2DPE Form I	0.098%
RSV-2DPE Form II	0.007%
RSV-DPE	0.172%
RSV-1.5DPE•0.5ACE	1.138%
RSV-1.5DPE•MeOH	4.771%
RSV-2AZPY	0.134%

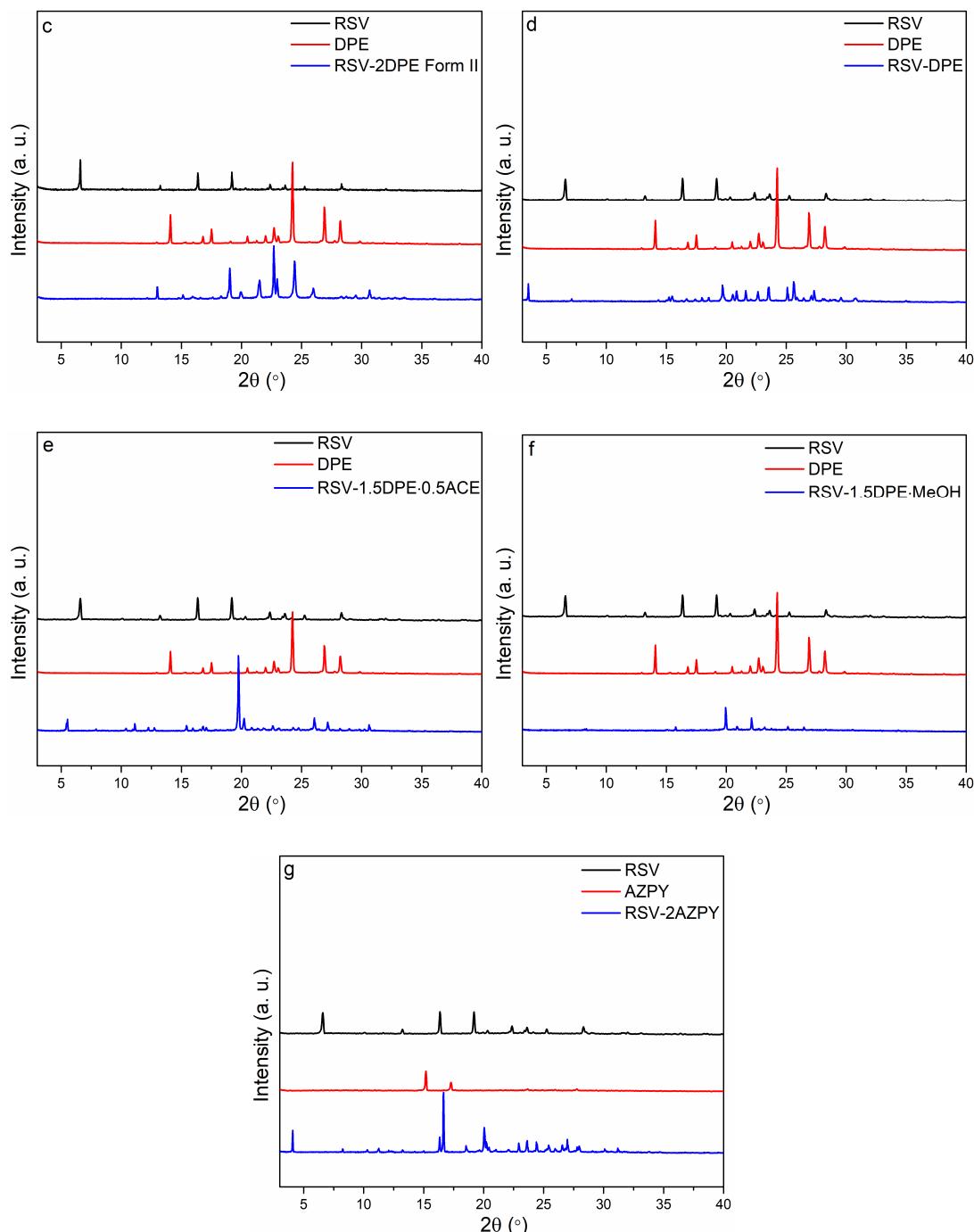
**Table S6** Gradient HPLC system for the determination of RSV content.

Time (min)	0.1% TFA (%)	ACN (%)	Flow rate (mL/min)
0	75	25	1.0
1	75	25	1.0
6	50	50	1.0
7	50	50	1.0
7.01	75	25	1.0
9	75	25	1.0

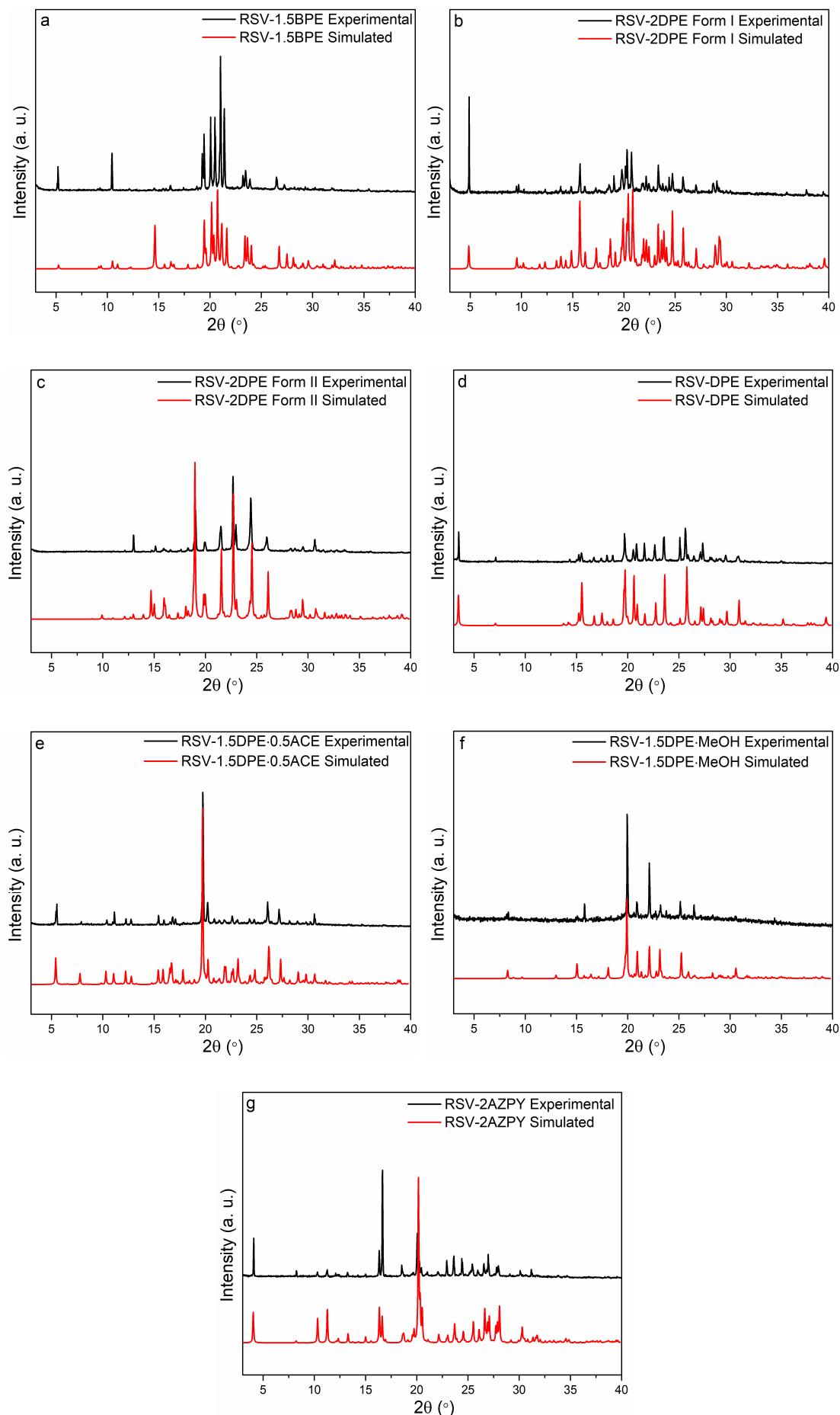


**Figure S1** Polarized light microscopies (upper) and BFDH predictions (below) of RSV cocrystals: (a) RSV-1.5BPE, (b) RSV-2DPE Form I, (c) RSV-2DPE Form II, (d) RSV-DPE, (e) RSV-1.5DPE•0.5ACE, (f) RSV-1.5DPE•MeOH, (g) RSV-2AZPY.

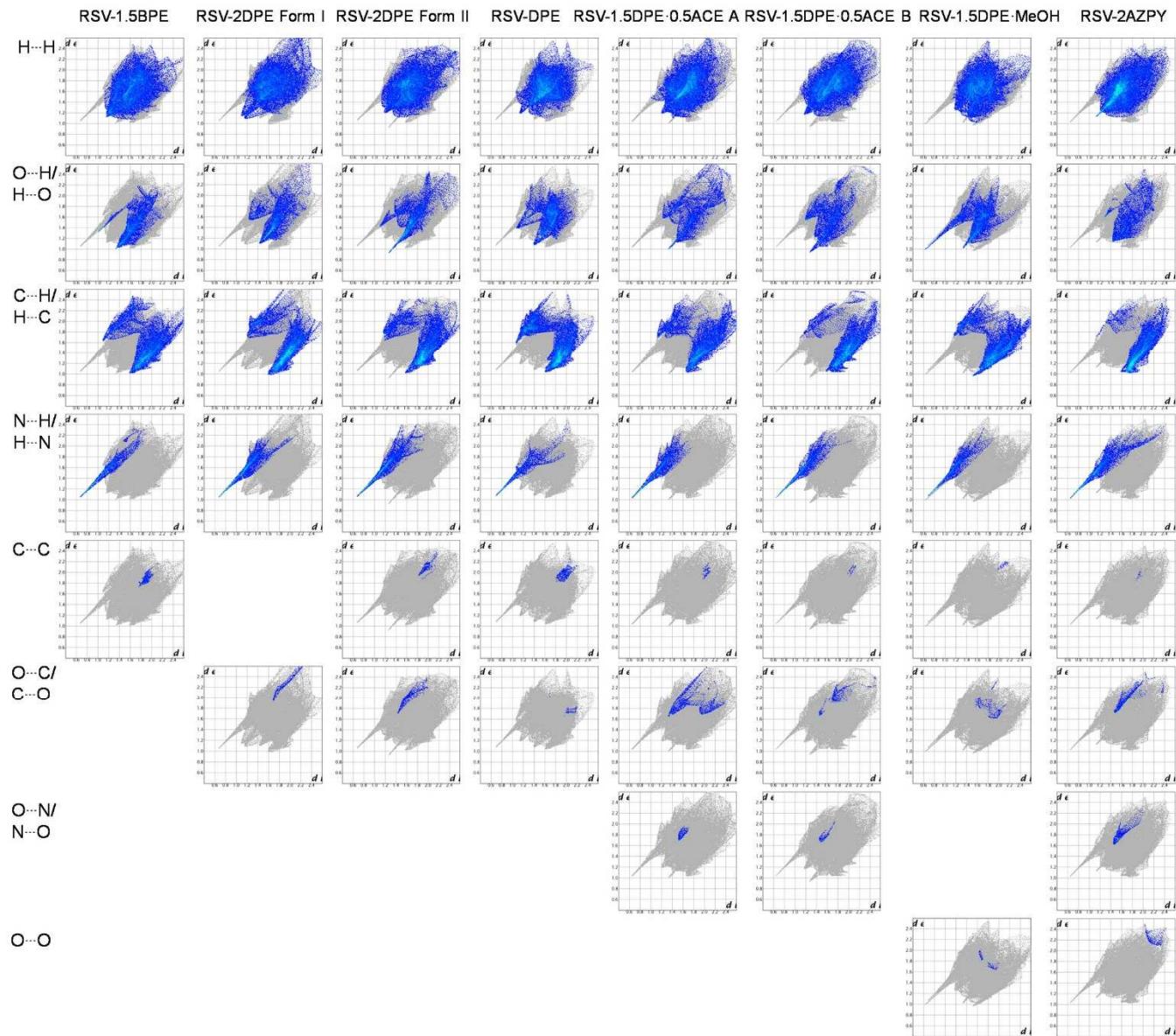




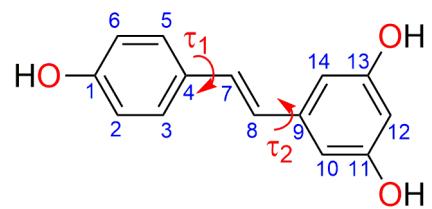
**Figure S2** The experimental PXPD patterns of (a) RSV-1.5BPE, (b) RSV-2DPE Form I, (c) RSV-2DPE Form II, (d) RSV-DPE, (e) RSV-1.5DPE•0.5ACE, (f) RSV-1.5DPE•MeOH, (g) RSV-2AZPY, RSV and corresponding CCFs.



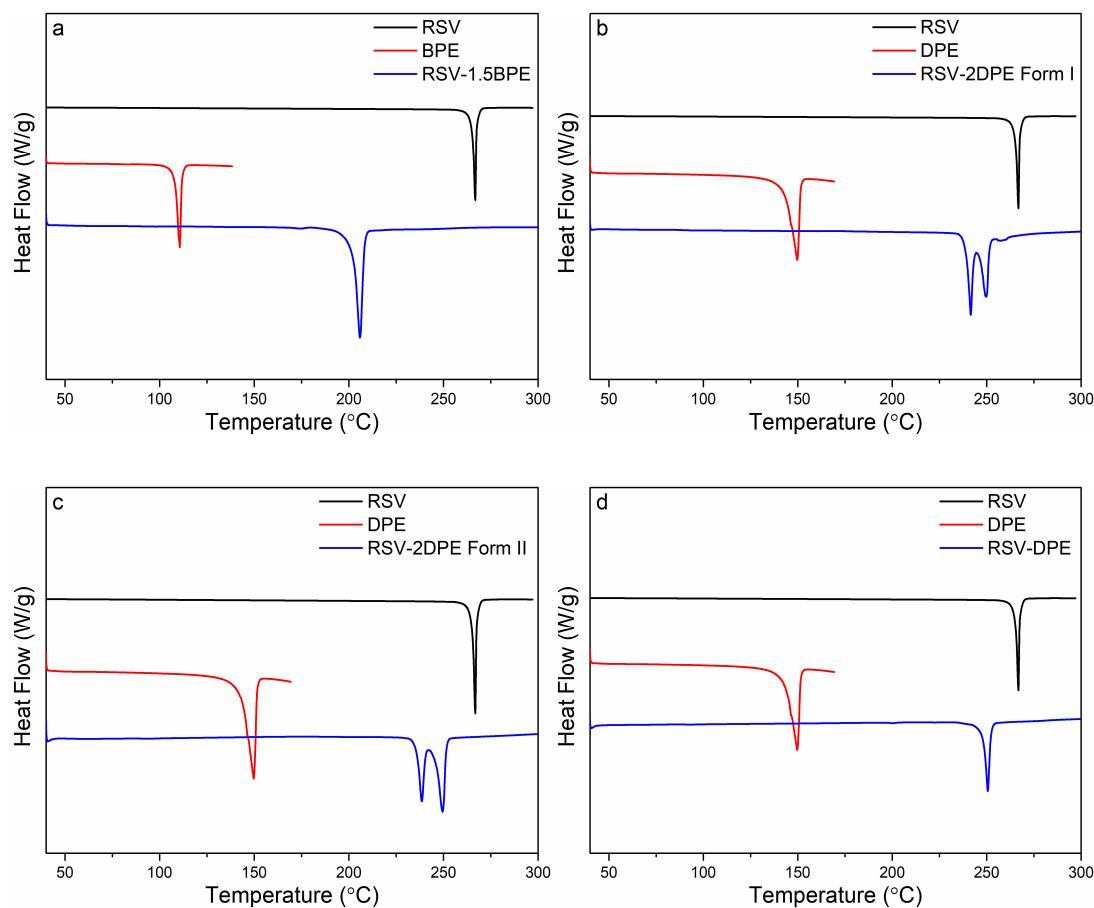
**Figure S3** Comparison between experimental and simulated PXRD patterns of cocrystals: (a) RSV-1.5BPE, (b) RSV-2DPE Form I, (c) RSV-2DPE Form II, (d) RSV-DPE, (e) RSV-1.5DPE•0.5ACE, (f) RSV-1.5DPE•MeOH, (g) RSV-2AZPY.

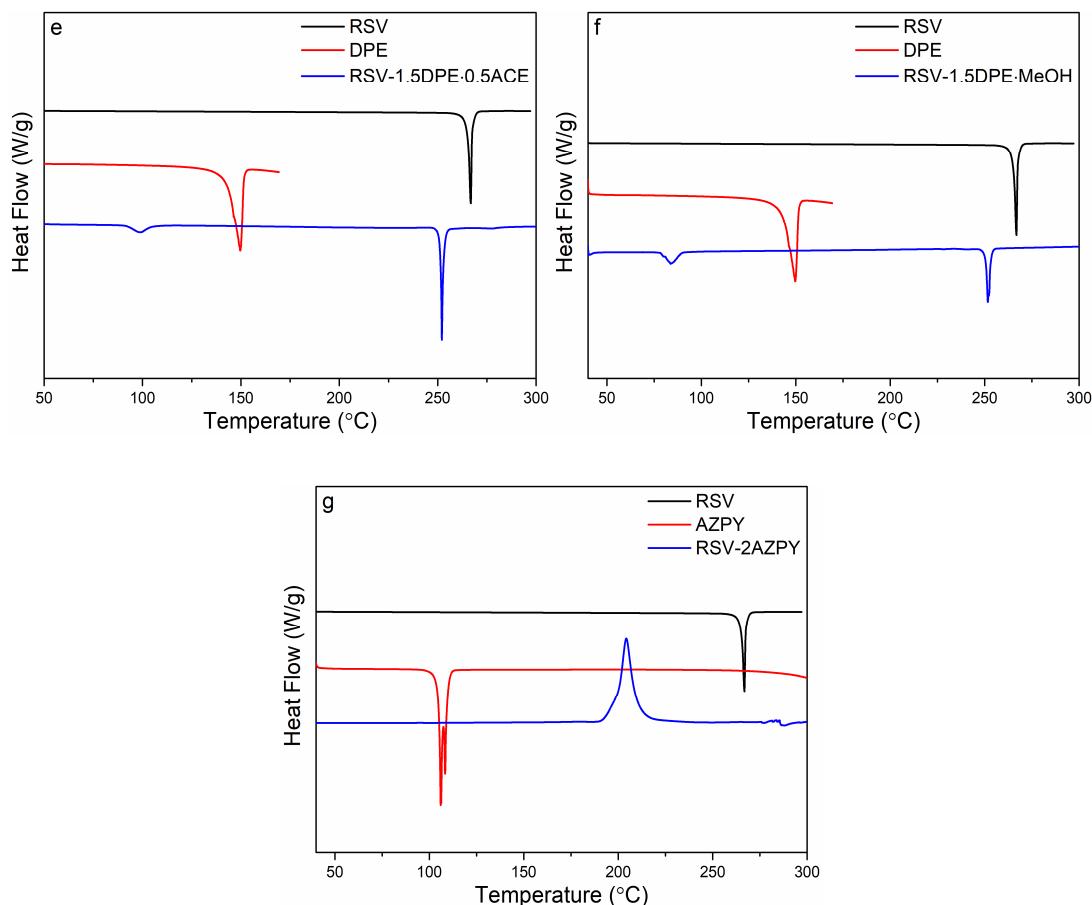


**Figure S4** 2D fingerprint plots of RSV in RSV cocrystals.

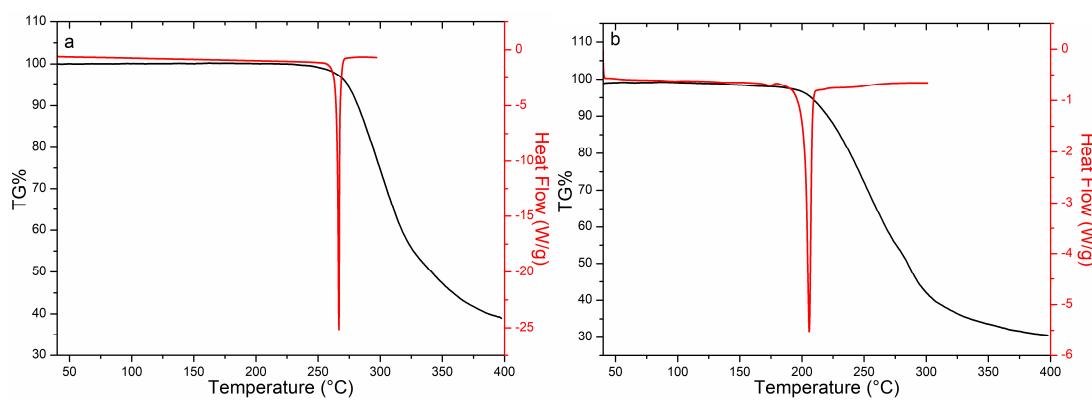


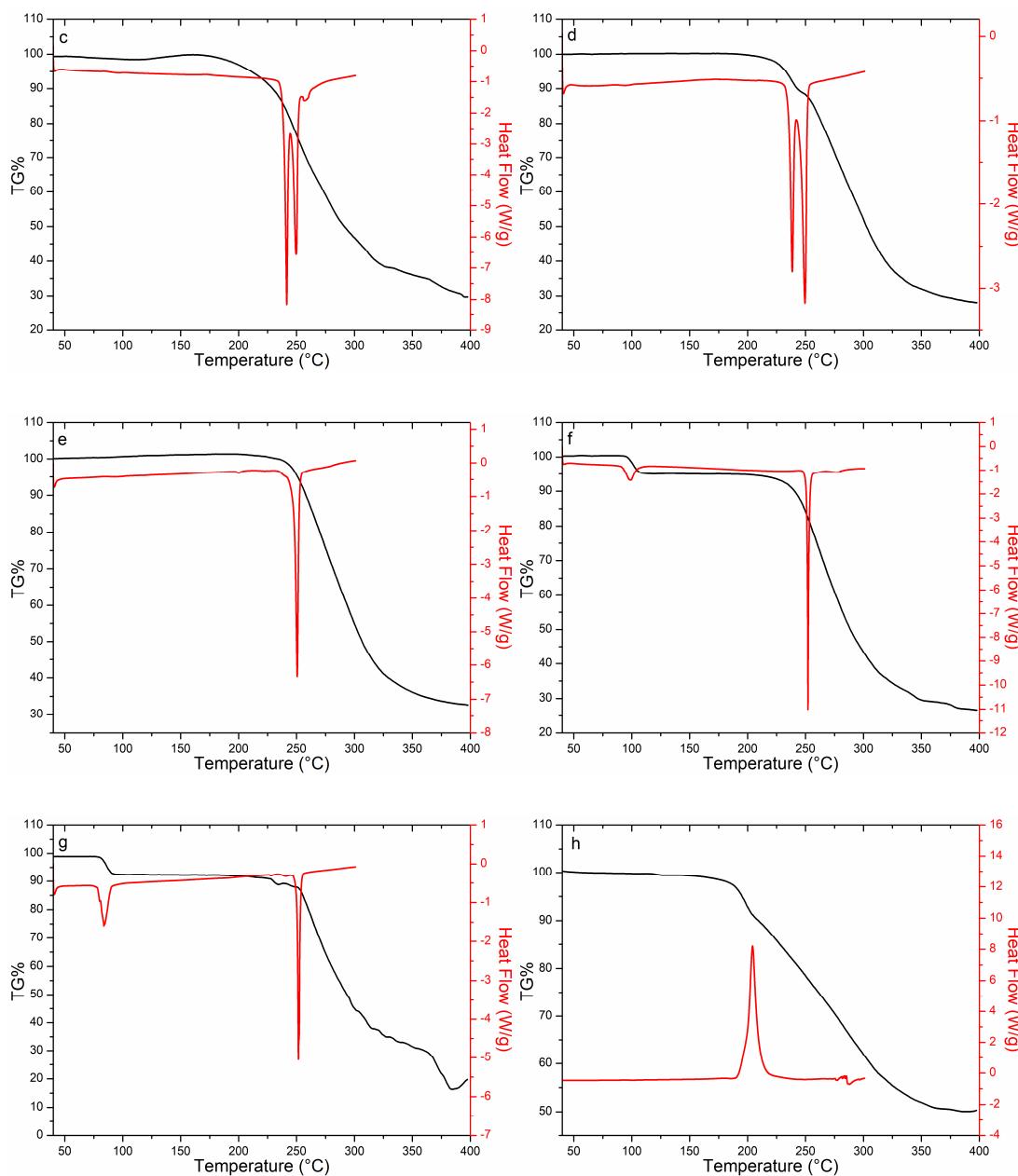
**Figure S5** Molecular structure of *trans*-RSV presenting torsion angles  $\tau_1$  (C3-C4-C7-C8) and  $\tau_2$  (C7-C8-C9-C14).



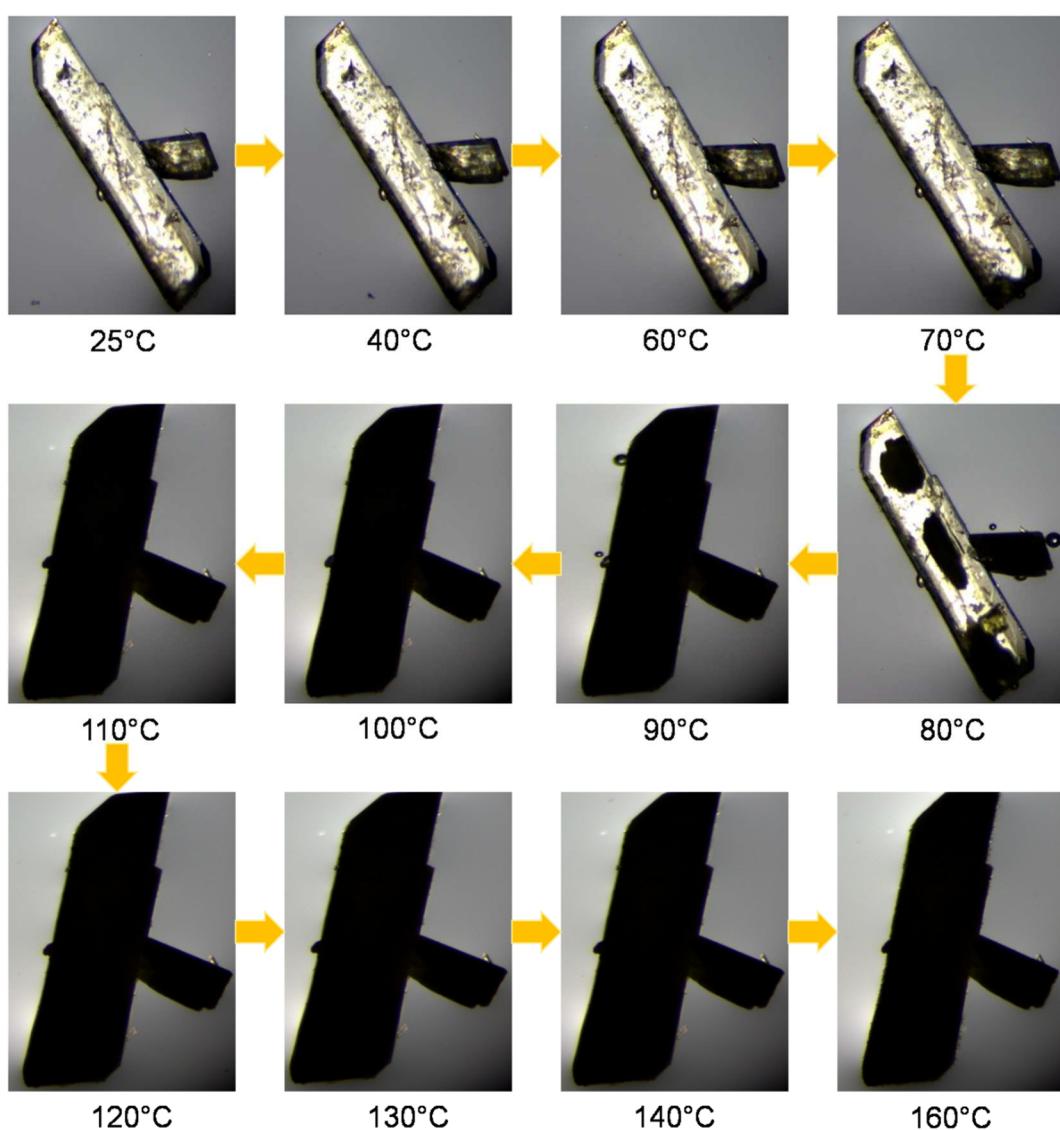


**Figure S6** Comparison of DSC curves among RSV, corresponding CCFs and cocrystals: (a) RSV-1.5BPE, (b) RSV-2DPE Form I, (c) RSV-2DPE Form II, (d) RSV-DPE, (e) RSV-1.5DPE•0.5ACE, (f) RSV-1.5DPE•MeOH, (g) RSV-2AZPY.

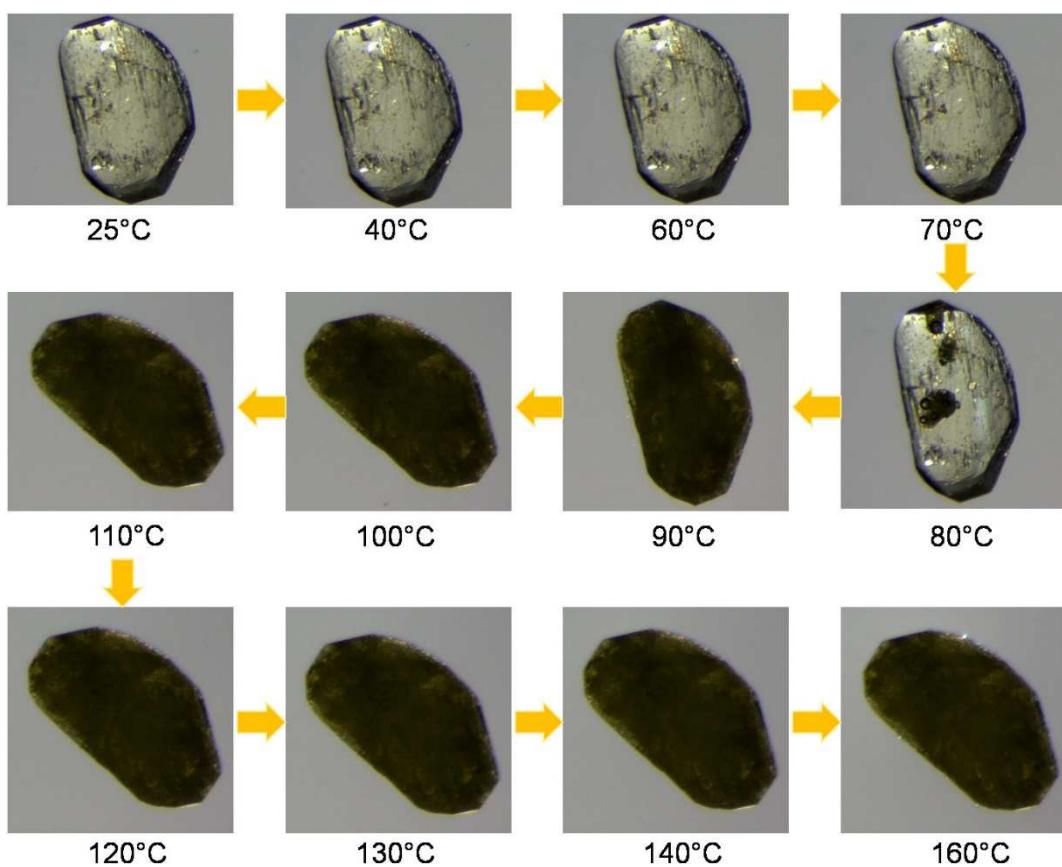




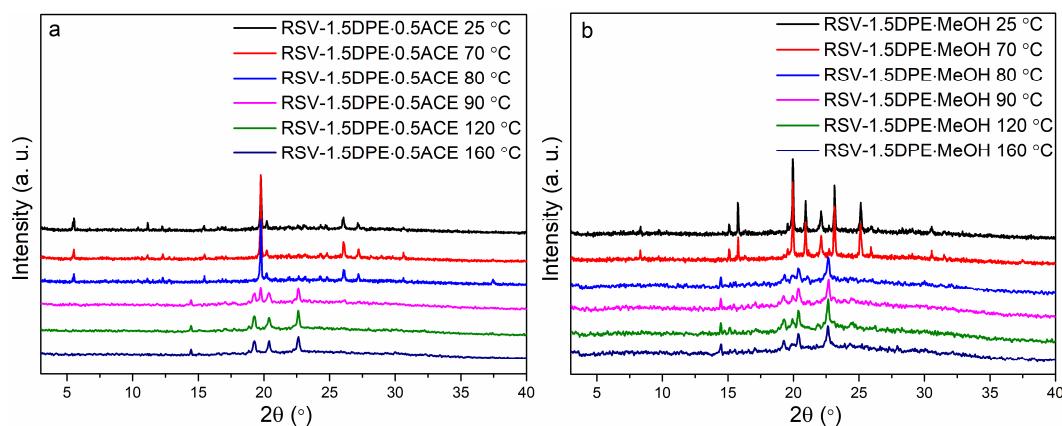
**Figure S7** TG and DSC curves of (a) RSV, (b) RSV-1.5BPE, (c) RSV-2DPE Form I, (d) RSV-2DPE Form II, (e) RSV-DPE, (f) RSV-1.5DPE•0.5ACE, (g) RSV-1.5DPE•MeOH, (h) RSV-2AZPY.



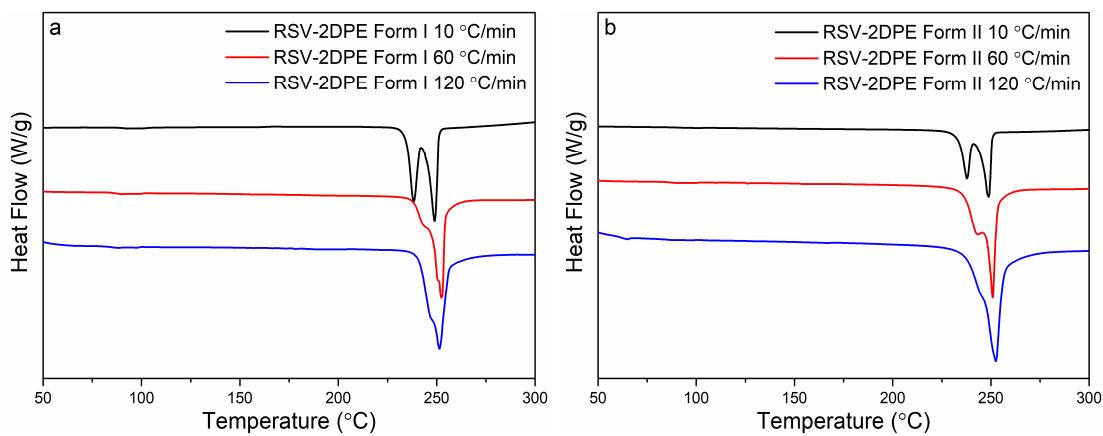
**Figure S8** Polarized light microscopies of RSV-1.5DPE•0.5ACE with different temperature.



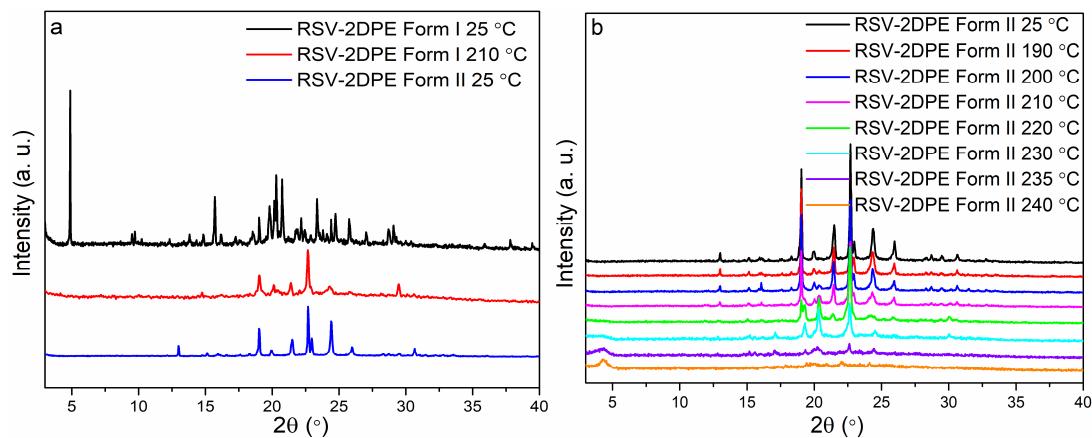
**Figure S9** Polarized light microscopies of RSV-1.5DPE•MeOH with different temperature.



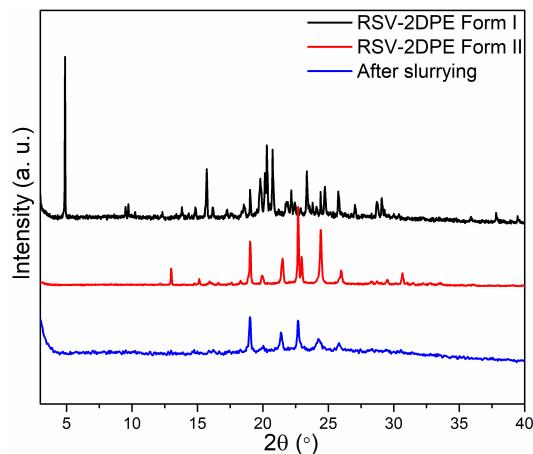
**Figure S10** TD-PXRD patterns of (a) RSV-1.5DPE•0.5ACE, (b) RSV-1.5DPE•MeOH.



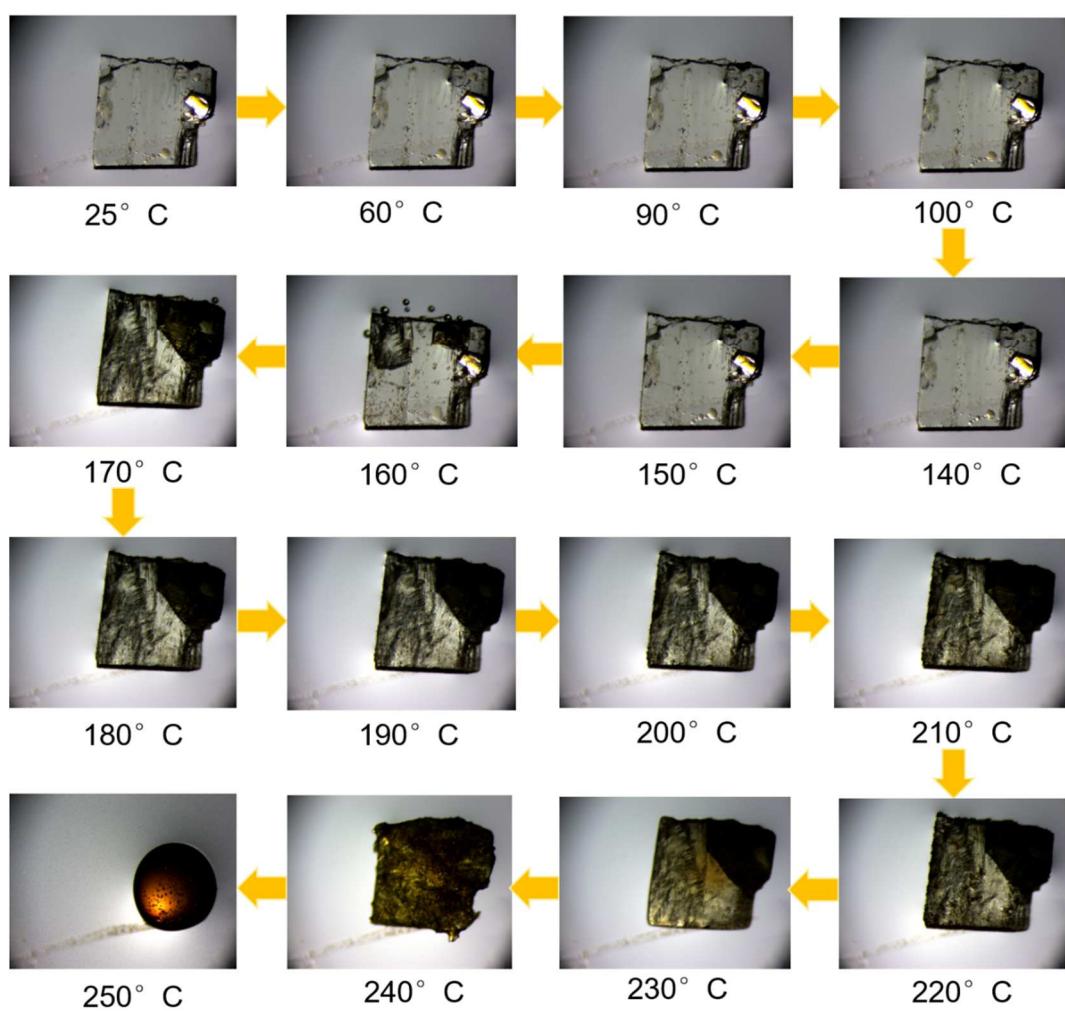
**Figure S11** DSC curves of (a) RSV-2DPE Form I, (b) RSV-2DPE Form II with different DSC heating rates.



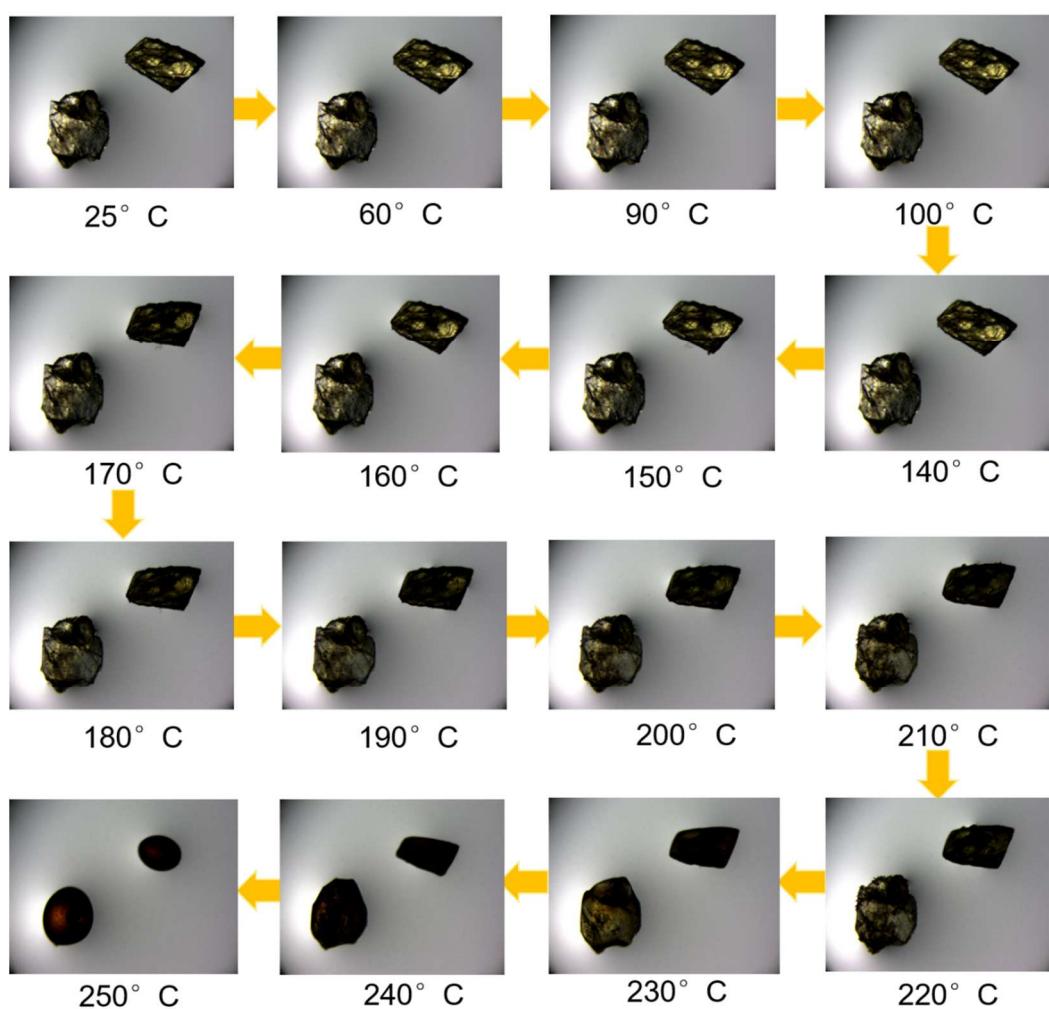
**Figure S12** TD-PXRD patterns of (a) RSV-2DPE Form I, (b) RSV-2DPE Form II.



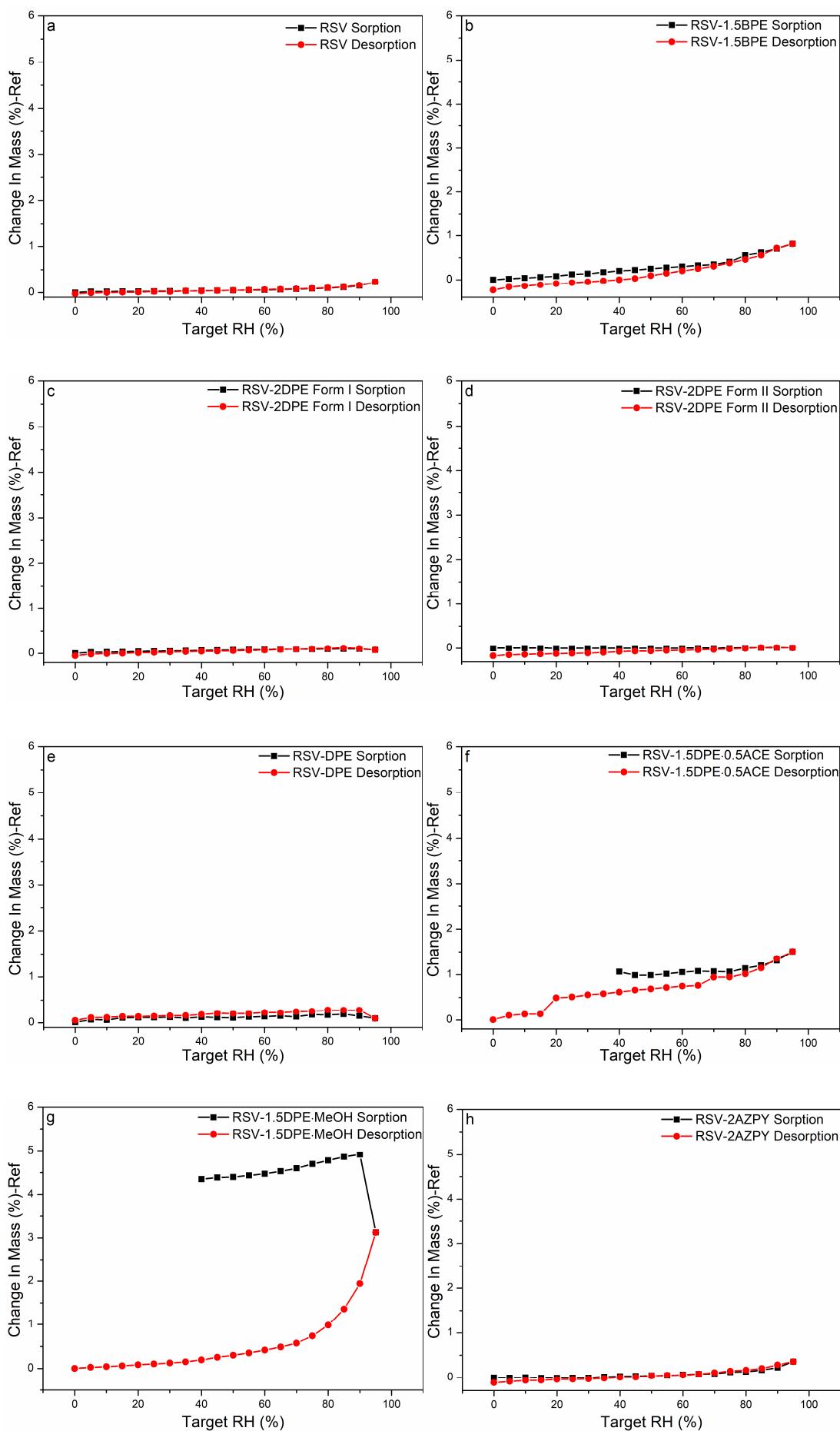
**Figure S13** PXRD patterns of RSV-2DPE Form I, RSV-2DPE Form II and the powder after slurring with equal molar ratio of RSV-2DPE Form I and RSV-2DPE Form II.



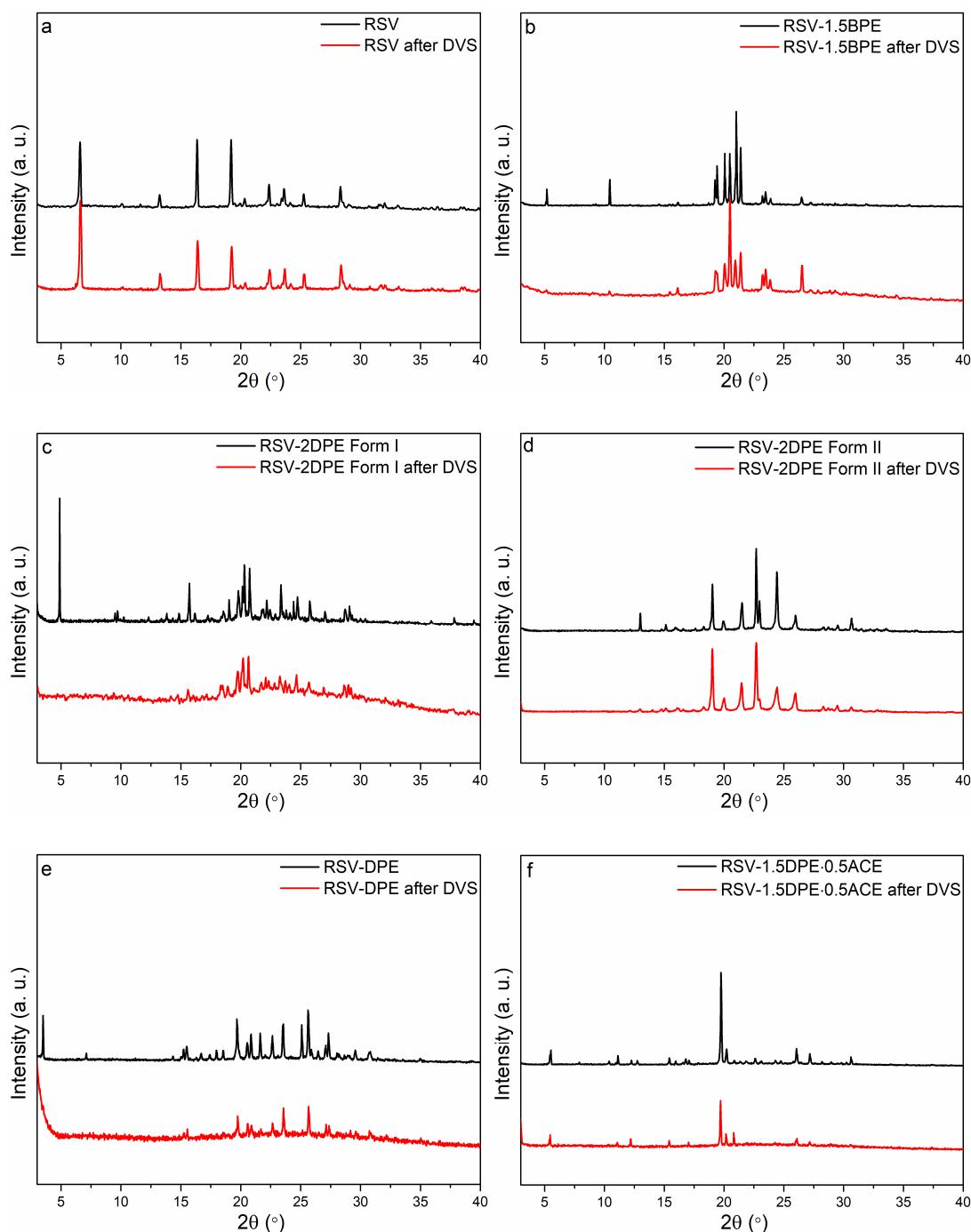
**Figure S14**Polarized light microscopies of RSV-2DPE Form I with different temperature.

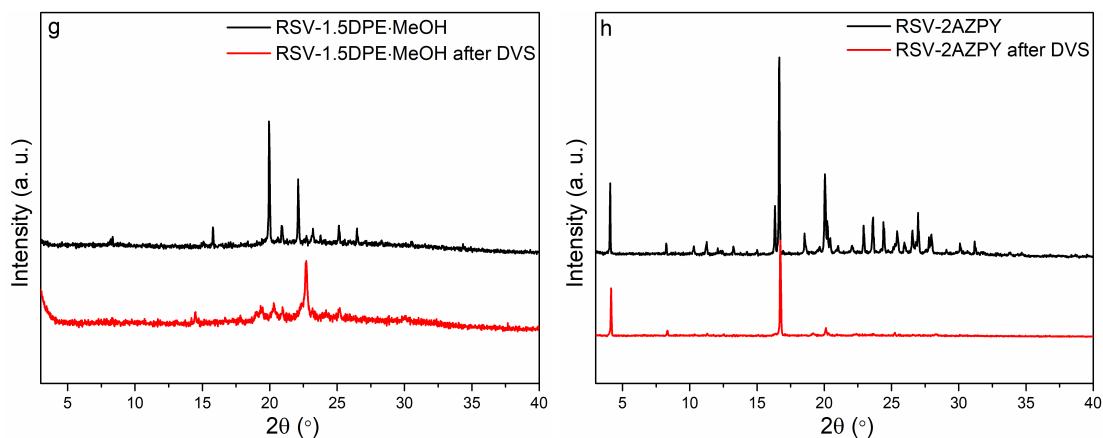


**Figure S15** Polarized light microscopies of RSV-2DPE Form II with different temperature.

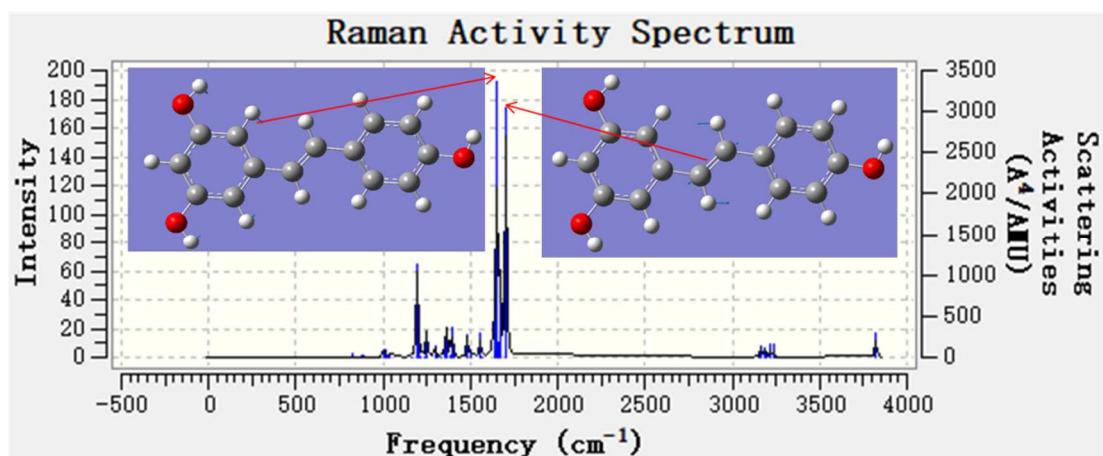


**Figure S16** Water vapour sorption and desorption isotherm curves of (a) RSV, (b) RSV-1.5BPE, (c) RSV-2DPE Form I, (d) RSV-2DPE Form II, (e) RSV-DPE, (f) RSV-1.5DPE•0.5ACE, (g) RSV-1.5DPE•MeOH, (h) RSV-2AZPY.

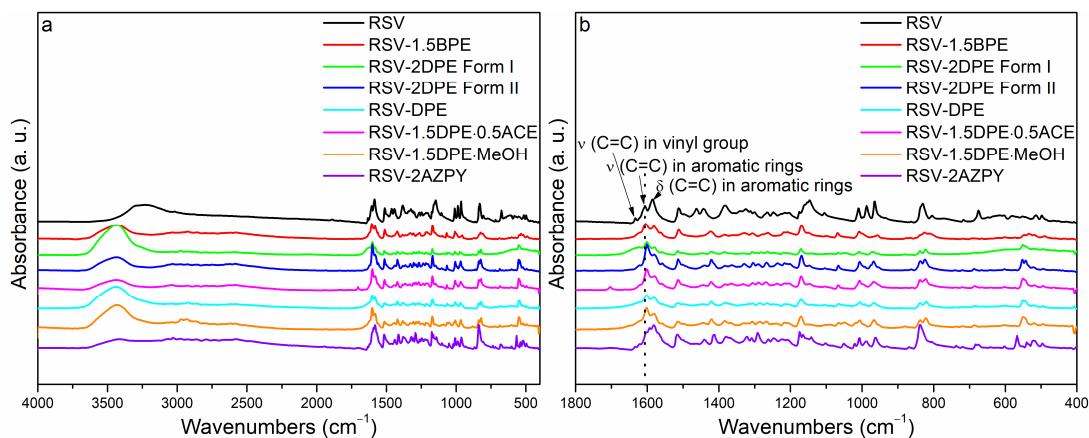




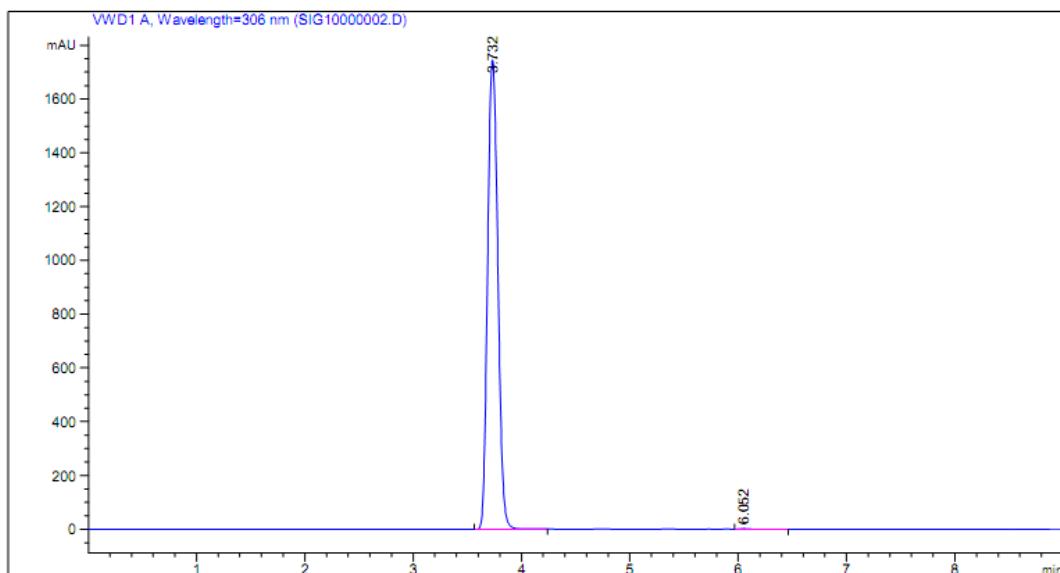
**Figure S17**PXRD patterns of cocrystals after DVS experiments of (a) RSV, (b) RSV-1.5BPE, (c) RSV-2DPE Form I, (d) RSV-2DPE Form II, (e) RSV-DPE, (f) RSV-1.5DPE•0.5ACE, (g) RSV-1.5DPE•MeOH, (h) RSV-2AZPY.



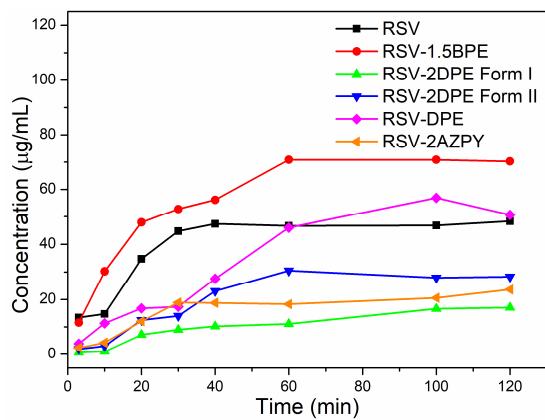
**Figure S18**Calculated Raman spectroscopy of RSV by QM calculations at the B3LYP/6-31G (d, p) level.



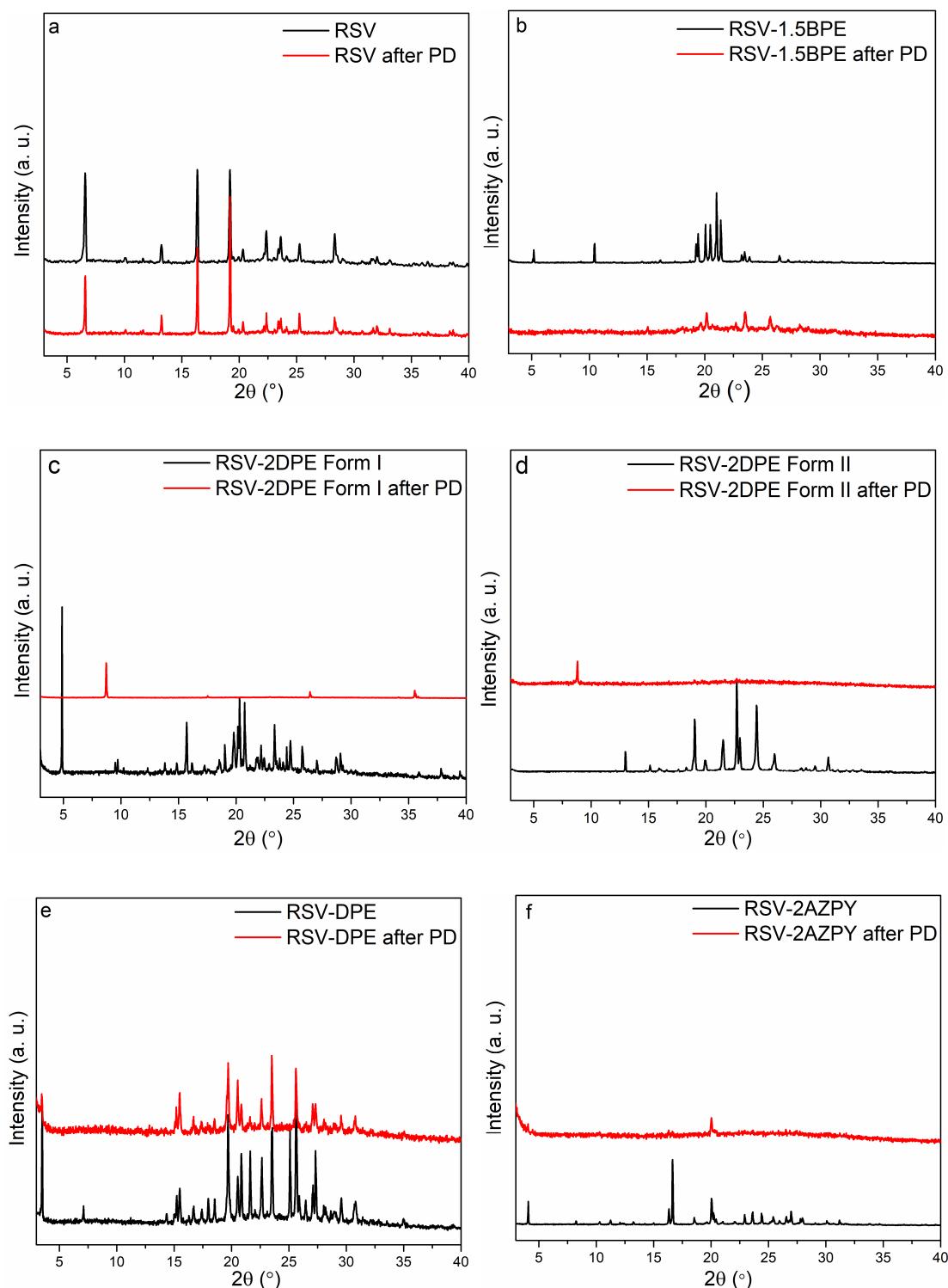
**Figure S19**(a) FTIR spectra of RSV and its cocrystals in the 4000-400  $\text{cm}^{-1}$  region. (b) FTIR spectra of RSV and its cocrystals in the 1800-400  $\text{cm}^{-1}$  region.



**Figure S20** HPLC chromatogram of RSV.



**Figure S21** Powder dissolution profiles of RSV, RSV-1.5BPE, RSV-2DPE Form I, RSV-2DPE Form II, RSV-DPE and RSV-2AZPY in pH 4.6 buffer solution.



**Figure S22** PXRD patterns of RSV and RSV cocrystals before and after PD experiments in pH 4.6 buffer solution of (a) RSV, (b) RSV-1.5BPE, (c) RSV-2DPE Form I, (d) RSV-2DPE Form II, (e) RSV-DPE, (f) RSV-2AZPY.