Supporting Information for

Continuous Co-crystallization as a Separation Technology: The Study of 1:2 Co-crystals of Phenazine-Vanillin

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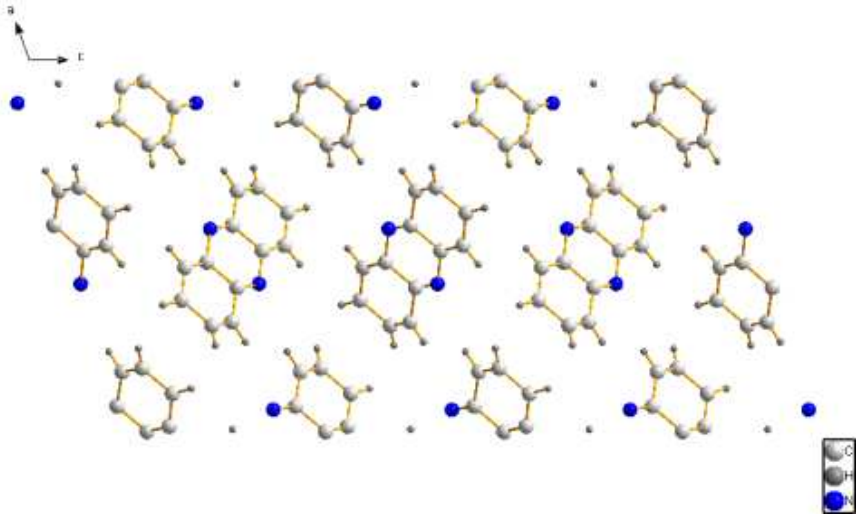
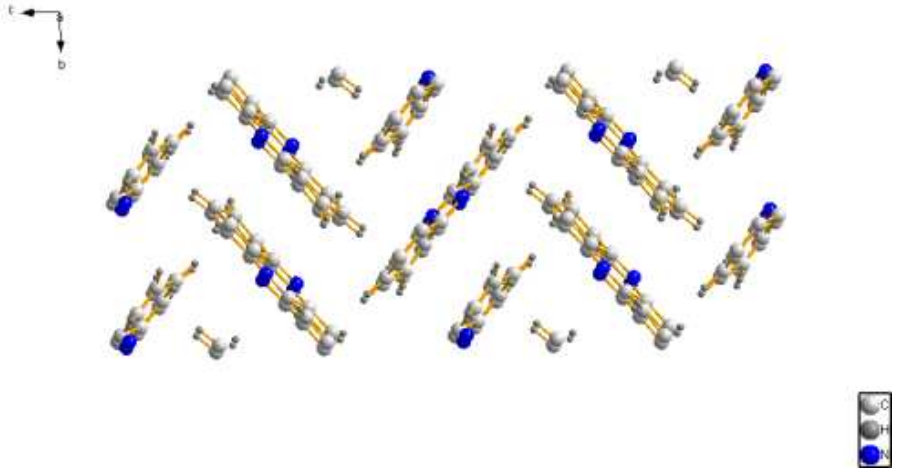
This PDF file includes:

Figures S1 to S2, Tables S1 to S7, and Mixed Suspension, Mixed Product Removal (MSMPR) formalism.

Fig. S1. Lee et al.



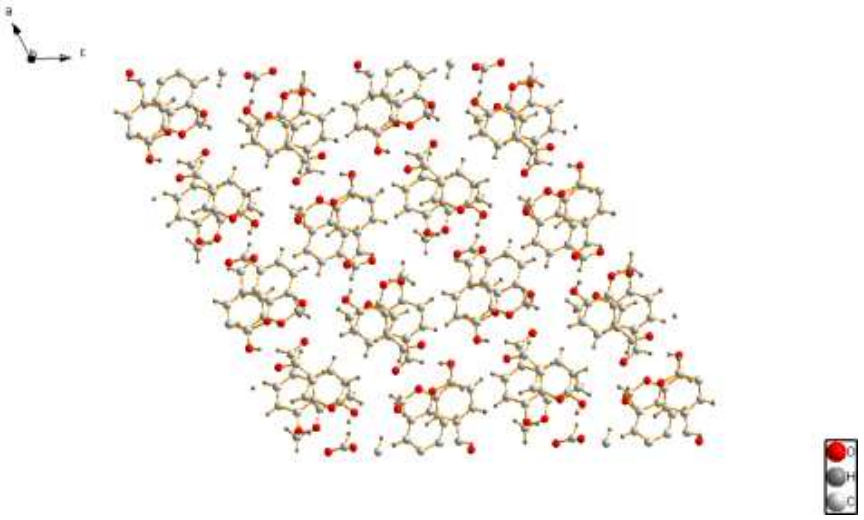
(a)



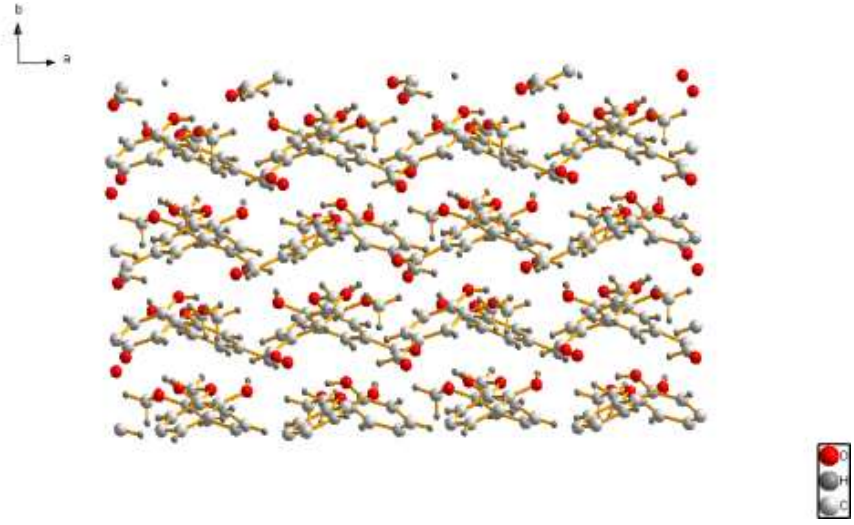
(b)

Figure S1. View of the crystal structure of phenazine Form α (a) along the *b*-axis, and (b) along the *a*-axis.

Fig. S2. Lee et al.



(a)



(b)

Figure S2. View of the crystal structure of vanillin Form I (a) along the *b*-axis, and (b) along the *c*-axis.

Table S1. Lee et al.

Table S1. Materials balance for continuous crystallization with a flow rate of 90 mL/min and batch crystallization of 1:2 co-crystals of phenazine-vanillin in toluene.

	Toluene Volume (ml)	Total Weight Of Starting Materials (g)	Residence Time (s)	Co-crystal Weight Retained on Sieves (g)	Yield (wt%)	Mother Liquor Volume (ml)	Mother Liquor Concentration (g/l)	Co-crystal Weight in Mother Liquor (g)	Total Co-crystal Weight (g)
Continuous	150	24.1±0.1	196	8.5±0.08	51.2±0.7	141.7±0.6	87.8±8.9	12.4±1.2	20.9±1.2.
Batch with no agitation	150	24.1±0.04	196	5.8±0.05	34.9±0.4	145.0±0.1	117.2±4.2	17.0±0.6	22.8±0.6
Batch with stirring	150	24.0± 0.001	196	9.5±1.3	57.7±8.1	141.0±6.8	90.0±7.4	12.6±0.7	22.2±1.5

1. Yield = Solid weight retained on sieves ÷ (Total weight of starting materials – Toluene volume × 50 mg/mL at 25°C) × 100%
2. Co-crystal weight in mother liquor = Mother liquor volume × Mother liquor concentration
3. Total co-crystal weight = Co-crystal weight retained on sieves + Co-crystal weight in mother liquor

Table S2. Lee et al.

Table S2. Mass retained in sieve analysis for continuous crystallization with a flow rate of 90 mL/min of 1:2 co-crystals of phenazine-vanillin in toluene.

Sieve (Mesh)	Size of Mesh (mm)	Cumulative Percent Retained
35	0.5	
50	0.3	26±3.6
60	0.25	44.3±5.0
100	0.15	63.7±2.5
120	0.125	82.3±2.5
200	0.075	100±0

Table S3. Lee et al.

Table S3. Population density distribution data obtained from sieve analysis for continuous crystallization with a flow rate of 90 mL/min of 1:2 co-crystals of phenazine-vanillin in toluene.

Sieve (Mesh)	Average Size Retained (mm)	Difference, ΔL (mm)	ln (Population Density)
50	0.4	0.2	10.6±0.19
60	0.275	0.05	13.5±0.13
100	0.2	0.1	13.8±0.23
120	0.1375	0.025	16.3±0.15
200	0.1	0.05	16.5±0.14

Table S4. Lee et al.

Table S4. Mass retained in sieve analysis for batch crystallization with no agitation of 1:2 co-crystals of phenazine-vanillin in toluene.

Sieve (Mesh)	Size of Mesh (mm)	Cumulative Percent Retained
35	0.5	
50	0.3	65.7±5.5
60	0.25	81.3±5.7
100	0.15	91.3±3.8
120	0.125	95.3±2.1
200	0.075	100±0

Table S5. Lee et al.

Table S5. Population density distribution data obtained from sieve analysis for batch crystallization with no agitation of 1:2 co-crystals of phenazine-vanillin in toluene.

Sieve (Mesh)	Average Size Retained (mm)	Difference, ΔL (mm)	ln (Population Density)
50	0.4	0.2	10.6±0.07
60	0.275	0.05	13.0±0.06
100	0.2	0.1	12.7±0.2
120	0.1375	0.025	14.0±0.41
200	0.1	0.05	14.6±0.43

Table S6. Lee et al.

Table S6. Mass retained in sieve analysis for batch crystallization with stirring of 1:2 co-crystals of phenazine-vanillin in toluene.

Sieve (Mesh)	Size of Mesh (mm)	Cumulative Percent Retained
35	0.5	
50	0.3	73.35±5.9
60	0.25	82.84±3.1
100	0.15	95.95±1.5
120	0.125	97.61±0.6
200	0.075	100±0

Table S7. Lee et al.

Table S7. Population density distribution data obtained from sieve analysis for batch crystallization with stirring of 1:2 co-crystals of phenazine-vanillin in toluene.

Sieve (Mesh)	Average Size Retained (mm)	Difference, ΔL (mm)	ln (Population Density)
50	0.4	0.2	17.5±0.17
60	0.275	0.05	17.9±0.36
100	0.2	0.1	18.6±0.10
120	0.1375	0.025	18.9±0.63
200	0.1	0.05	19.6±0.19

The Mixed Suspension, Mixed Product Removal (MSMPR) Formalism for the Population Density

To approximate G and B^0 based on the sieve analysis developed for an MSMPR crystallizer at steady state:

$$\tau \frac{d(Gn)}{dL} + n = 0 \tag{S1}$$

where n is population density, L is characteristic size. If G is not a function of L, the result becomes:

$$\frac{dn}{dL} = -\frac{n}{G\tau} \tag{S2}$$

If the boundary condition of n^0 representing zero-sized particles is employed, i.e., $n(0) = n^0$, the final result is:

$$n = n^0 \exp\left(-\frac{L}{G\tau}\right) \tag{S3}$$

Therefore, the growth rate, G, can be determined from the slope of $\ln(n)$ vs. L:

$$\ln n = -\left(\frac{1}{G\tau}\right)L + \ln n^0 \tag{S4}$$

If B^0 is the rate of appearance of near zero-sized particles,

$$B^0 = \left.\frac{dN}{dt}\right|_{L\to 0} = \left[\frac{dN}{dL}\cdot\frac{dL}{dt}\right]_{L\to 0} = n^0 G$$

(S5)

where N is the number data. The cumulative sieve data are reduced to the population density by:

$$n = \frac{\Delta m}{k_v \rho \overline{L^3} (\Delta L)}$$

(S6)

where Δm is the weight retained on a sieve, k_v is the volumetric shape factor, ρ is the crystal mass density, $\overline{L}$ is the mean size of the sieve on which the particles are retained and the sieve above it in the stack, and ΔL is the size difference between the two sieves just mentioned.

For example, the crystals average size retained on the 60 mesh in Table S2 is calculated to be: average size retained, $\overline{L_{60}} = \frac{0.3 + 0.25}{2} = 0.275$ mm, and the mesh size difference is, ΔL = 0.3 – 0.25 = 0.05 mm for the 60 mesh sieve in Table S3. The cumulative sieve data are then reduced to population density by eq S6. The suspension density, ρ, is calculated from Table S1 as: co-crystal weight retained on sieves ÷ toluene volume = 56 g/l for continuous co-crystallization, and 39 g/l for batch co-crystallization. We will assume $k_v = 10$ for the needle-shaped 1:2 co-crystals of phenazine:vanillin and $\rho = 1.4$ g/cm^3 from the crystal lattice density of co-crystals as determined by SXD in Table 1. The population density, n, for the 60 mesh sieve in Table S3 is calculated as:

$$n = \frac{\Delta m}{k_v \rho \bar{L}^3 \Delta L} = \frac{(0.443 - 0.26) \times 56 \frac{g}{l}}{10 \times 1.4 \frac{g}{cm^3} \times \frac{1 cm^3}{1000 mm^3} \times (0.275 \frac{mm}{no.crystals})^3 (0.05 mm)}$$

Thus, n = 703951.9 no. crystals/mm·l and $ln(n)$ = 13.5. The remaining values are given in Table S3.