Supplementary Material for Deposition

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Abstract
Supplementary material to the main paper is provided comprising the following;

- Derivation of ideal solubility equations and relationship to enthalpy of dissolution and solvation
- Examples of raw turbidometric data collected for the poly-thermal cooling crystallisations in three solvents, ethanol, acetonitrile and water. An example from 1 concentration per solvent at a range of cooling rates is provided
- A complete table of dissolution and crystallisation temperatures extracted from the turbidometric data is provided with standard deviations and calculations of equilibrium dissolution temperature and critical under cooling for each solvent system and concentration
- Plots of solubility and super-solubility curves from extrapolation of the equilibrium dissolution and crystallisation temperatures as a function of concentration for each solvent system

1. **Assessment of Solution Thermodynamics**

To assess the solubility of PABA, the concept of ideality together with the activity model were applied. The general expression for the solid-liquid equilibrium derived in terms of activity can be defined as:

$$ln\frac{\gamma_i^L x_i}{\gamma_i^S z_i} = \frac{\Delta H_{fus,i}}{R}\left[\frac{1}{T} - \frac{1}{T_{m,i}}\right] + \frac{\Delta C_{P,i}}{R}\left[\frac{T - T_{m,i}}{T}\right] - \frac{\Delta C_P}{R} ln\frac{T_{m,i}}{T} \quad \textbf{\textit{(Equation 1)}}$$

Where γ is the activity coefficient, ΔC_P is the specific heat capacity and x_i and z_i the molar fractions in liquid and solid phase respectively, R is the gas constant, ΔH_{fus} is the enthalpy of fusion, T is temperature and T_m is the melting temperature of the solid. i stands for a single component in the solution and L and S for liquid and solid phase of the components respectively. This expression relates the composition of solute in liquid and solid phases at a given temperature to thermo-physical properties of the pure solute and activity coefficients in solution for both phases.

In an ideal solution the activity coefficients will be unity, for a "single solute solution" the solid phase will contain only one compound and therefore z_i will be also one. In this work $\Delta C_p, i$ was assumed to be very small and this was neglected with Equation 1 reducing to

$$\ln (x) = \frac{\Delta H_{fus}}{R}\left[\frac{1}{T} - \frac{1}{T_m}\right] \quad \textbf{\textit{(Equation 2)}}$$

This equation is known as the Hildebrand equation and is taken as the "ideal solubility model".

In a non-ideal solution solubility can be expressed as

$$\ln(\gamma x) = -\frac{\Delta H_{fus}}{RT} + \frac{\Delta S_{fus}}{R}$$ ***(Equation 3)***

Where x is the solubility in mole fraction and γ is the activity coefficient that accounts for the deviation from ideality due to differences between solvent-solvent and solute-solute interactions. If the deviation from ideality is accounted for on the right side of the van't Hoff expression the solubility can be also expressed as

$$\ln(x) = -\frac{\Delta H_{diss}}{RT} + \frac{\Delta S_{diss}}{R}$$ ***(Equation 4)***

Where ΔH_{diss} and ΔS_{diss} are the enthalpy and entropy of dissolution respectively. Thus, if the experimentally determined solubility of a "single solute" solution is plotted in the form $\ln x$ vs $1/T$, then this allows calculation of $\Delta H_{diss}$and ΔS_{diss} at solution saturation from the slope and intercept of this line respectively. The enthalpy reported in this study refers to the enthalpic change on dissolving a mole of a substance in an infinite amount of saturated solution. In an ideal solution $\gamma = 1$ and therefore Equation 3 becomes

$$\ln(x) = -\frac{\Delta H_{fus}}{R}\left[\frac{1}{T} - \frac{1}{T_m}\right]$$ ***(Equation 5)***

From the plot in the same coordinate plane of the ideal solubility and the solubility in the form of the van't Hoff expression, the difference between the concentration at saturation (solubility) and that expected for ideality in the same range of temperature (T) will deliver the dependence of activity coefficient (γ) on T, by the iterative calculation of (γ) through Equation 6.

$$\gamma = \frac{x_{ideal}}{x}$$ (***Equation 6)***

If $\gamma > 1,$ the activity is higher than the concentration and therefore the "effective concentration" will be lower than for an ideal solution (or less than ideal) this is also known as a positive deviation from Raoult's law. When $\gamma < 1$ the activity is lower than concentration and therefore the "effective concentration" will be higher than for an ideal solution (or more than ideal), this is also known as a negative deviation from Raoult's law. This information can describe the solvation of a solute in a solvent as for $\gamma > 1$ a significant amount more association of the solute molecules would be expected. For $\gamma < 1$ solute-solvent interactions are favourable relative to solute-solute interactions.

For each solvent

$$\Delta H_{solv} = \Delta H_{diss} - \Delta H_{sub}$$ ***(Equation 7)***

Where ΔH_{solv} is the heat of solvation and ΔH_{sub} is the enthalpy of sublimation

ΔH_{sub} was estimated from the calculated lattice energy E_{latt} since

$$E_{latt} = \Delta H_{sub} - 2RT$$ ***(Equation 8)***

A lower enthalpy of solvation will indicate a more favourable solvation (dissolution) process[1, 2]. Calculation of ΔH_{diss} from the van't Hoff analysis allows estimation of the enthalpy of solvation, ΔH_{solv} at a harmonic mean temperature of T_e, by relating the calculated E_{Latt} to

ΔH_{sub} using Equations 7 and 8, for example E_{Latt} for the alpha polymorph was found to be 102.6 KJ/mol[3].

2. Raw Turbidometric Data from Poly-Thermal Crystallisation Experiments

Figures 1, 2 and 3 present examples of raw turbidometric data collected on the Crystal 16 apparatus for the 6 g/kg concentration aqueous PABA solution at a range of cooling rates; 0.1, 0.3, 0.5, 0.7 and 1.0 °C/min. These plots allow extrapolation of the crystallisation and dissolution temperatures T_{crys} and T_{dis}.

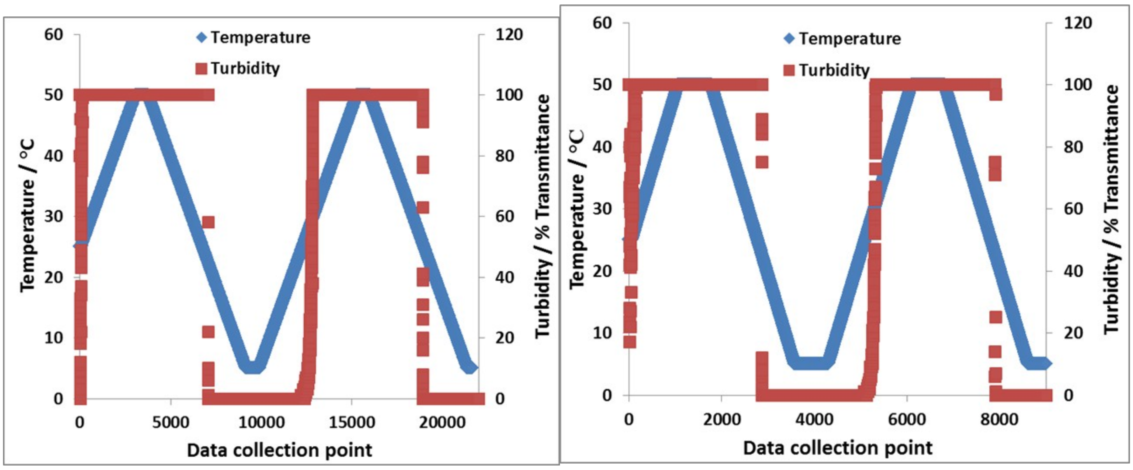


Figure 1: Turbidity vs temperature plot for crystallisation of PABA from 6 g/kg aqueous solution at 0.1left and 0.3 °C / min right

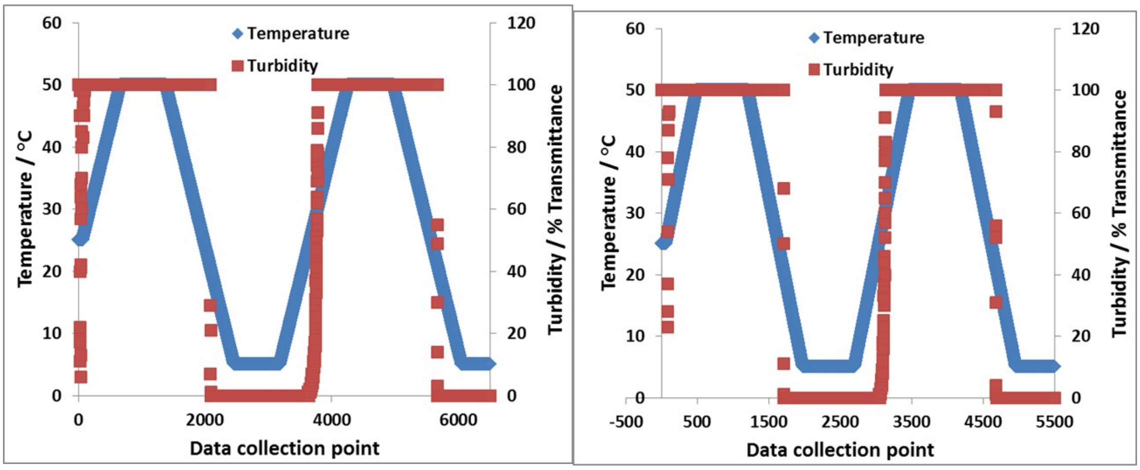


Figure 2: Turbidity vs temperature plot for crystallisation of PABA from 6 g/kg aqueous solution at 0.5 °C / min left and 0.7°C / min right

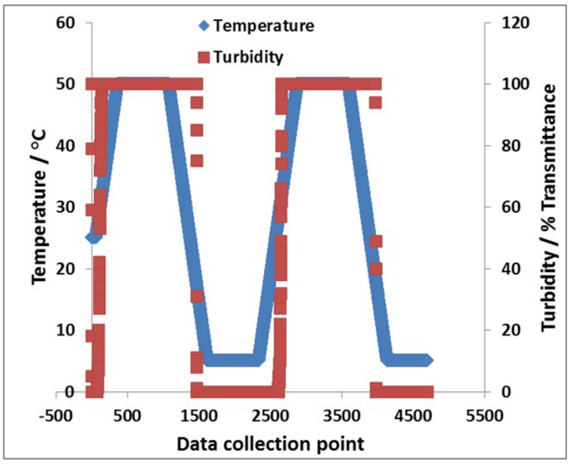


Figure 3: Turbidity vs temperature plot for crystallisation of PABA from 6 g/kg aqueous solution at 1.0°C / min

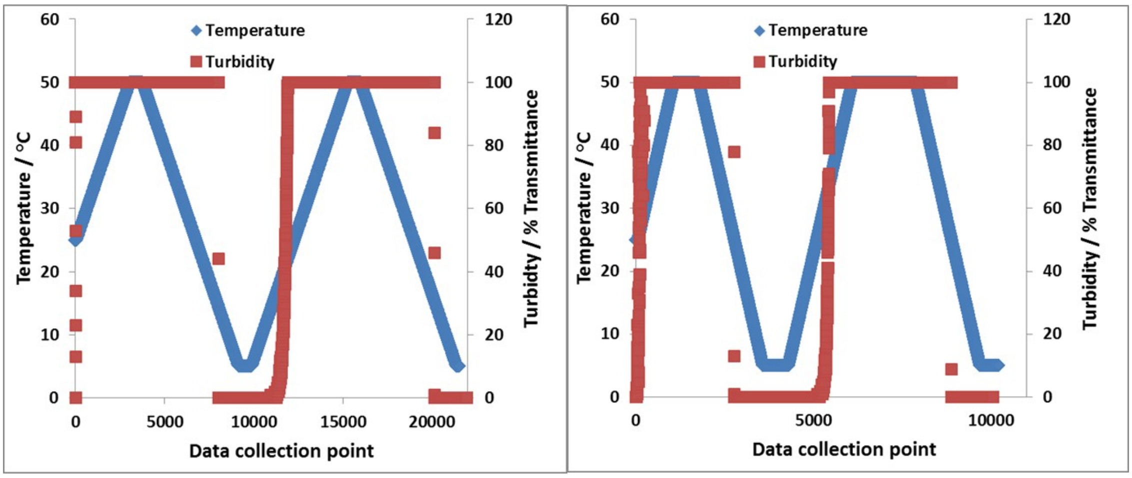


Figure 4: Turbidity vs temperature plot for crystallisation of PABA from 64.8 g/kg acetonitrile solution at 0.1 °C / min left and 0.3°C / min right

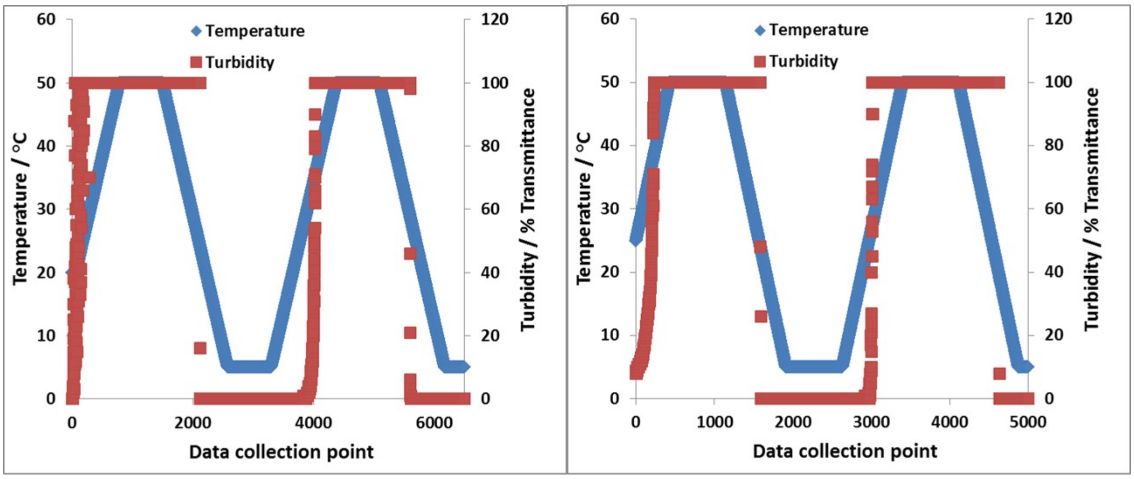


Figure 5: Turbidity vs temperature plot for crystallisation of PABA from 64.8 g/kg acetonitrile solution at 0.5 °C / min left and 0.7°C / min right

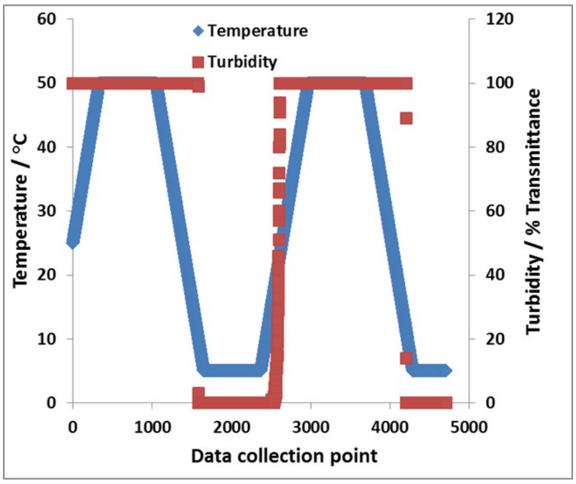


Figure 6: Turbidity vs temperature plot for crystallisation of PABA from 64.8 g/kg acetonitrile solution at 1.0 °C / min

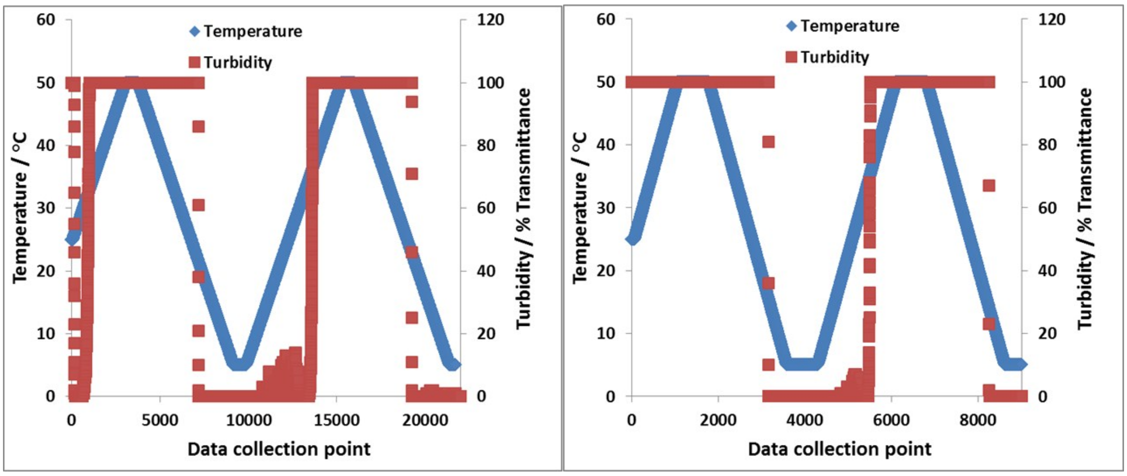


Figure 7: Turbidity vs temperature plot for crystallisation of PABA from 170 g/kg ethanol solution at 0.1 °C / min left and 0.3°C / min right

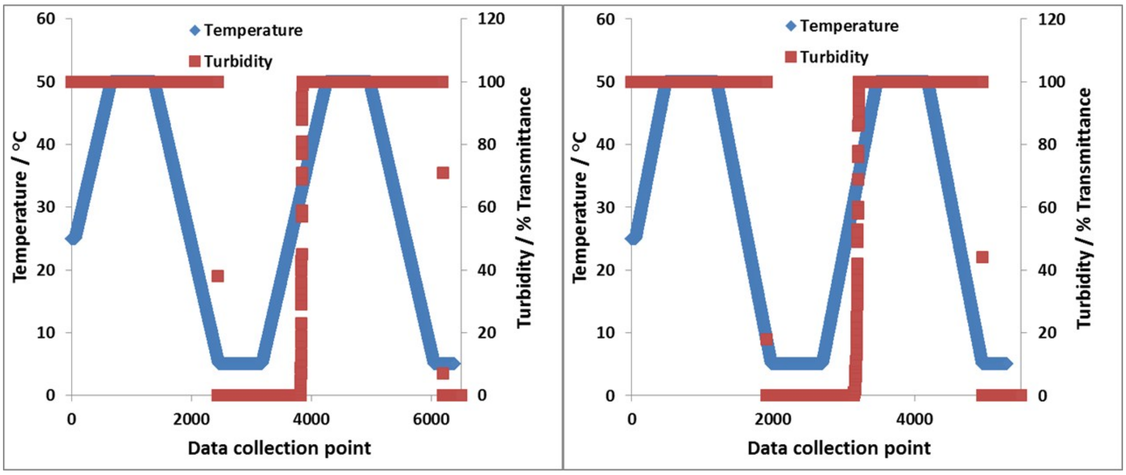


Figure 8: Turbidity vs temperature plot for crystallisation of PABA from 170 g/kg ethanol solution at 0.5 °C / min left and 0.7°C / min right

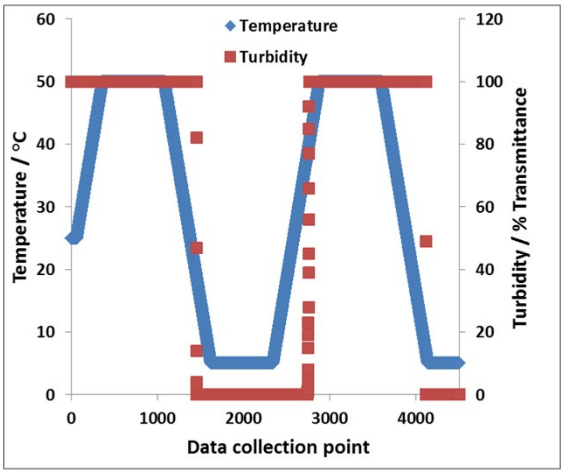


Figure 9: Turbidity vs temperature plot for crystallisation of PABA from 170 g/kg ethanol solution at 1.0 °C / min

3. Recorded Crystallisation Parameters from Turbidometric Data

Table 1 highlights the complete list of all measured crystallisation and dissolution temperatures with standard deviations from repeat measurements in ethanol, acetonitrile and aqueous solutions. The value of the equilibrium dissolution temperature, T_e, is also provided for each concentration from extrapolation of dissolution temperatures to 0°/min cooling rate. The calculated values critical undercooling, *ΔTc,* is also presented in Table 1 for each cooling rate in the specified solvent system.

Table 1: List of the measured crystallisation and dissolution temperatures together with extrapolated values of the equilibrium dissolution temperature Te and the calculated values of critical undercooling ΔTc for PABA solutions in ethanol, acetonitrile and water at varying concentrations and cooling rates

Ethanol Solutions **150g/kg Rate (°C/min^{-1})**	***Tdis (°C)***	***T_C (°C)***	***ΔTc***
0.1	27.8 ±1.09)	11.7 ± 2.22	16.1(0)
0.3	31.3 ± 1.49	9.1 ±1.83	22.2(0)
0.5	31.8 ± 1.39	8.6 ± 3.50	23.1(5)
0.7	29.3 ± 1.16	10.4 ±1.08	18.(9)
1	30.9 ±1.05	5.1 ± 0.05	25.7(8)
	T_e = 29.26		
160g/kg Rate (°C/min^{-1})	***Tdis (°C)***	***T_C (°C)***	***ΔTc***
0.1	30.9 ± 1.02	16.7 ± 4.73	14.2(0)
0.3	34.7 ± 1.73	13.7 ± 5.09	21.0(0)
0.5	33.5 ± 1.17	11.2 ± 1.86	22.3(0)
0.7	35.7 ± 2.29	11.5 ± 3.99	24.1(6)
1	35.6 ± 3.70	5.8 ± 1.19	29.8(0)
	T_e = 31.70		
170g/kg Rate (°C/min^{-1})	***Tdis (°C)***	***T_C (°C)***	***ΔTc***
0.1	32.05 ± 0.78	22.40 ± 1.13	6.9(1)
0.3	32.18 ± 0.87	16.10 ± 1.57	13.2(1)

0.5	33.14 ± 1.10	7.85 ± 2.62	21.4(6)
0.7	35.63 ± 1.10	5.40 ± 0.14	23.9(1)
1	41.90 ± 3.42	-0.67 ± 0.32	29.9(8)
	T_e = 29.31		
180g/kg Rate (°C/min^{-1})			
0.1	33.60 ± 1.71	24.58 ± 1.00	7.1(3)
0.3	34.60 ± 1.26	21.67 ± 2.59	10.0(3)
0.5	39.47 ± 0.78	22.15 ± 2.21	9.5(5)
0.7	38.90 ± 0.4	13.53 ± 1.30	18.1(7)
1	45.40 ± 1.21	10.40 ± 1.85	21.3(0)
	T_e = 31.70		
190g/kg Rate (°C/min^{-1})			
0.1	36.17 ± 0.64	29.08 ± 0.91	5.0(9)
0.3	37.20 ± 2.03	24.53 ± 4.11	9.6(3)
0.5	39.85 ± 1.06	26.98 ± 4.21	7.1(9)
0.7	42.93 ± 2.15	27.00 ± 1.87	7.1(7)
1	46.83 ± 2.47	17.60 ± 0.71	16.5(7)
	T_e = 34.17		
200g/kg Rate (°C/min^{-1})			
0.1	40.43 ± 1.40	35.18 ± 0.29	3.8(1)
0.3	42.20 ± 3.19	31.70 ± 1.10	7.2(8)
0.5	42.77 ± 1.92	33.03 ± 1.23	5.9(5)
0.7	46.00 ± 0.42	33.12 ± 1.07	5.8(6)
1	49.35 ± 0.78	25.55 ± 1.20	13.4(3)
	T_e = 38.98		

Acetonitrile Solutions **54g/kg Rate (°C/min^{-1})**	***Tdis (°C)***	***Tcrys (°C)***	***ΔTc***
0.1	14.82 ± 0.49	8.46 ± 0.74	6.8(1)
0.3	16.03 ± 0.21	6.09 ± 1.13	9.1(8)
0.5	18.13 ± 0.54	7.01 ± 1.71	8.2(6)
0.7	17.46 ± 0.27	5.17 ± 0.37	10.1(0)
0.9	17.07 ± 0.23	5.27 ± 0.31	10.0(0)
	T_e = 15.22		
64.8g/kg Rate (°C/min^{-1})			

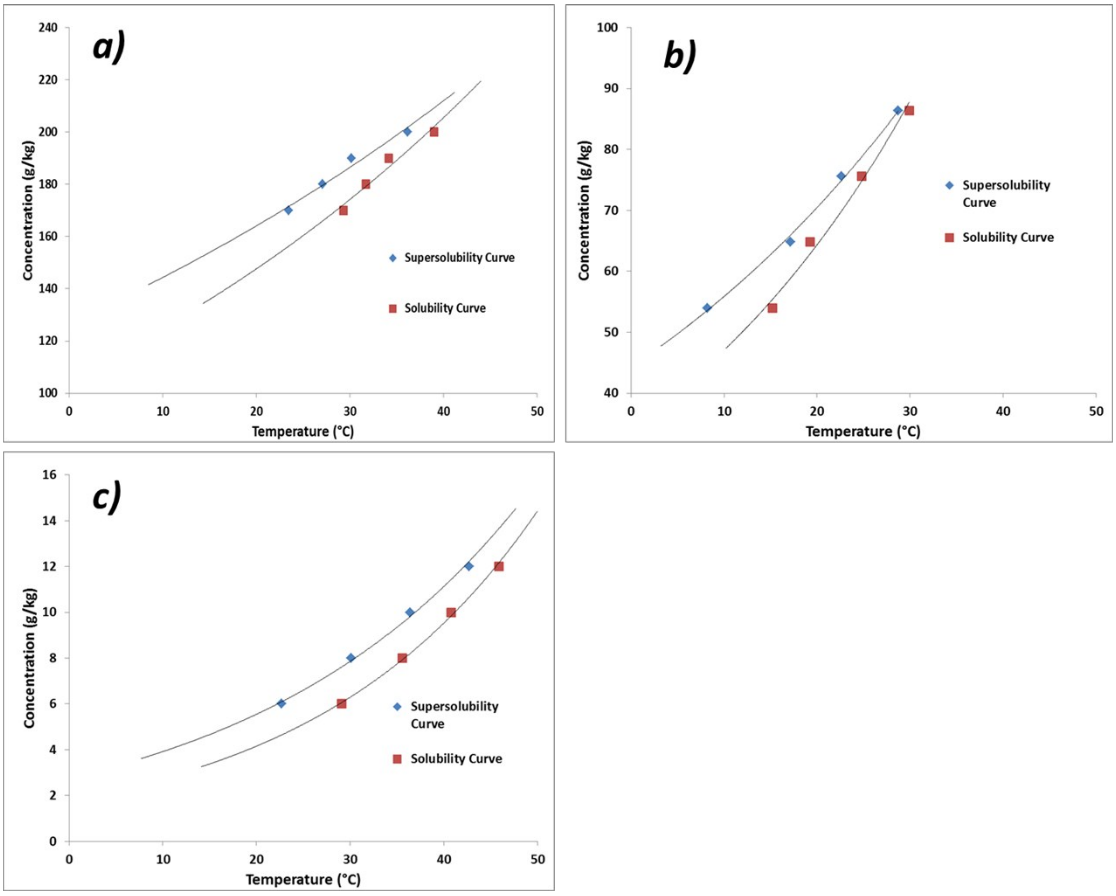
0.1	18.64 ± 0.19	15.53 ± 0.94	3.7(8)
0.3	21.02 ± 1.08	16.12 ± 0.54	3.1(8)
0.5	24.00 ± 0.55	15.73 ± 2.48	3.5(7)
0.7	22.90 ± 0.46	13.85 ± 2.21	5.4(5)
0.9	23.03 ± 0.06	11.55 ± 0.21	7.7(5)
	T_e = 19.25		
75.6g/kg Rate (°C/min^{-1})			
0.1	24.62 ± 0.72	21.87 ± 1.84	2.9(6)
0.3	25.62 ± 1.57	21.86 ± 0.73	2.9(7)
0.5	28.56 ± 0.40	22.40 ± 0.20	2.4(3)
0.7	27.84 ± 1.01	20.00 ± 0.48	4.8(3)
0.9	27.68 ± 1.57	19.98 ± 1.93	4.8(5)
	T_e = 24.78		
86.4g/kg Rate (°C/min^{-1})			
0.1	29.63 ± 0.17	27.77 ± 0.93	2.1(9)
0.3	29.33 ± 1.50	27.00 ± 0.92	2.9(6)
0.5	34.13 ± 0.82	28.79 ± 1.17	1.1(7)
0.7	31.37 ± 0.21	25.53 ± 2.37	4.4(4)
0.9	30.97 ± 0.91	24.45 ± 1.28	5.5(1)
	T_e = 29.91		

Water Solutions **6g/kg Rate (°C/min^{-1})**	***Tdis (°C)***	***Tcrys (°C)***	***ΔTc***
0.1	29.51 ± 0.83	22.54 ± 0.76	6.5(6)
0.3	29.58 ± 1.74	20.96 ± 0.78	8.1(4)
0.5	30.12 ± 0.83	20.44 ± 0.47	8.6(6)
0.7	31.76 ± 1.09	21.04 ± 1.37	8.0(6)
1	31.46 ± 0.96	18.52 ± 0.53	10.5(8)

	T_e = 29.10		
8g/kg Rate (°C/min^{-1})			
0.1	36.10 ± 0.61	30.22 ± 0.89	5.3(8)
0.3	35.92 ± 1.87	28.30 ± 0.93	7.3(0)
0.5	37.12 ± 0.58	27.10 ± 1.17	8.5(0)
0.7	38.02 ± 1.38	29.64 ± 0.94	5.9(6)
1	38.28 ± 0.93	25.62 ± 1.74	9.9(8)
	T_e = 35.58		
10g/kg Rate (°C/min^{-1})			
0.1	41.45 ± 1.11	37.28 ± 0.47	3.5(2)
0.3	40.82 ± 2.00	33.68 ± 1.22	7.1(2)
0.5	42.70 ± 0.67	35.10 ± 0.75	5.7(0)
0.7	43.82 ± 1.03	35.10 ± 1.36	5.7(0)
1	43.74 ± 0.88	33.62 ± 1.04	7.1(8)
	T_e = 40.76		
12g/kg Rate (°C/min^{-1})			
0.1	46.33 ± 0.36	43.30 ± 1.21	2.6(0)
0.3	45.92 ± 1.80	40.82 ± 1.32	5.0(8)
0.5	47.08 ± 1.21	40.54 ± 1.31	5.3(6)
0.7	48.67 ± 1.39	43.48 ± 1.62	2.4(2)
1	47.82 ± 2.40	39.66 ± 2.01	6.2(4)
	T_e = 45.88		

4. Solubility and Supersolubility Curves

Figure 4 provides the solubility and super-solubility curves of alpha PABA in the three solvents by extrapolation of T_{dis} and T_{crys} to the kinetic limit to obtain the equilibrium solubility and crystallisation temperatures as a function of solution concentration.



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