

niacinamide mw 122.12
solubility
water 1 gm in 1 mL
glycerol 0.1 gm/mL
ethanol 0.667 gm/mL = 66.7%
pH 6 - 7.5 in 5% solution

solubility of niacin in water
18 mg/ml at 77F = 1.8%
pH approx 2.7 at saturation

molecular weights:
niacin 123.11
water 18.0
ethanol
dmso = 78.14
dmso/water = 78.14 / 18 = 4.34
acetone

Temperature dependency of the mole fraction (x_{NA}) equilibrium solubilities of nicotinic acid.^a

Water			Ethanol			DMSO		Acetone		Acetonitrile		Diethyl ether	
T/K	$10^3 \cdot x_{NA}$	pH	T/K	$10^3 \cdot x_{NA}$		T/K	$10^2 \cdot x_{NA}$	T/K	$10^3 \cdot x_{NA}$	T/K	$10^4 \cdot x_{NA}$	T/K	$10^4 \cdot x_{NA}$
283.59	1.721 ± 0.040 (6)	3.604	283.38	2.235 ± 0.004 (3)		293.56	5.966 ± 0.175 (6)	285.46	0.733 ± 0.012 (5)	283.30	0.712 ± 0.168 (7)	283.45	3.224 ± 0.752 (3)
F 68 293.41	2.183 ± 0.030 (9)	3.453	293.46	3.087 ± 0.154 (6)		303.38	7.404 ± 0.060 (6)	292.26	1.139 ± 0.026 (9)	288.51	1.204 ± 0.284 (9)	285.74	3.786 ± 0.490 (3)
303.03	2.805 ± 0.076 (5)	3.373	303.15	4.234 ± 0.018 (3)		313.07	9.106 ± 0.085 (5)	296.80	1.373 ± 0.018 (2)	293.01	1.696 ± 0.192 (14)	290.57	5.386 ± 0.486 (3)
312.97	3.655 ± 0.100 (5)	3.273	312.83	6.052 ± 0.078 (3)		322.84	10.852 ± 0.067 (3)	302.14	1.610 ± 0.058 (3)	297.58	1.850 ± 0.148 (9)	294.02	6.179 ± 0.328 (5)
119F 322.83	4.650 ± 0.032 (3)	3.217	322.64	8.427 ± 0.008 (3)		332.36	13.059 ± 0.015 (3)	307.10	2.314 ± 0.066 (4)	302.63	2.680 ± 0.214 (12)	298.66	8.132 ± 0.530 (6)
332.01	5.859 ± 0.052 (3)	3.119	332.43	11.465 ± 0.052 (3)				317.11	3.180 ± 0.0140 (4)	306.91	3.541 ± 0.158 (6)		
										312.49	4.752 ± 0.200 (9)		
										316.21	5.473 ± 0.166 (6)		
										322.45	7.150 ± 0.342 (6)		
										332.32	10.707 ± 0.300 (3)		

283.6 K = 50.8F
303K = 86 F

^a The indicated uncertainties correspond to twice the standard error of the mean of the number of experiments is given in parenthesis.

at 68F, ethanol/water sol = 3.087/2.183 = 1.4141 * 1.8 % = 2.53%
dmso/water = 74.04/2.183 = 33.92 * 1.8 = 61.05%

process did not lead to changes in the morphology or transparency of the crystals, which could indicate the occurrence of a phase transformation or desolvation. Moreover, no contamination by impurities was detected by GC-MS analysis (see supporting information).

The X-ray powder diffractograms collected at $T = (293 \pm 2)$ K for the starting material and all the products obtained at the end of the solubility experiments (see supporting information) could be indexed as monoclinic space group $P2_1/c$. As shown in table 4 the corresponding cell parameters are in good agreement with the single crystal X-ray diffraction results previously reported for the same crystalline phase [49,50].

The conclusion that all samples refer to the same crystalline phase was also corroborated by the results of Fourier transform infrared spectroscopy analysis. As shown in figure 5 the corresponding infrared spectra were very similar, with no evidence of band shifts or other differences that could indicate the presence of distinct polymorphs, solvates, or mixtures of phases.

Scanning electron microscopy imaging (figure 6) indicated that the materials were essentially formed by prismatic crystalline particles, but with significant differences in average size. Image analysis carried out using the Olympus Cell^D 2.6 software led to the Feret's mean diameters, d_p (the mean value of the distance between pairs of parallel tangents to the projected outline of the particle, like in a measurement with a caliper) [51] indicated in table 5. Each value corresponds to the median result for n particles and should be regarded as a very approximate measurement of Feret's mean diameter due to the small number of particles used in the analysis and to the fact that, as show in figure 6, particle superposition/aggregation was impossible to avoid in the SEM imaging.

The DSC measuring curves of both the starting material and the products of the solubility measurements showed only two thermal events over the temperature range (298 to 525) K: a reversible solid–solid phase transition with onset at $T = \sim 453$ K and fusion with onset at ~ 507 K. The temperatures of the peaks onset (T_{on}) and maximum (T_{max}), and the enthalpies of solid–solid phase transition ($\Delta_{tr}H_m$) and fusion ($\Delta_{fus}H_m$) are summarized in table 6, where the uncertainties quoted represent twice the standard error of the mean of four to seven determinations. These results are in good agreement with the analogous data previously reported for a NIST standard reference sample of nicotinic acid (SRM 2151) [25]. The obtained enthalpies of fusion rank amongst the highest published for nicotinic acid ($\Delta_{fus}H_m = 12.4$ kJ · mol⁻¹ [52], (13.01 ± 0.32) kJ · mol⁻¹ [53], (20.8 ± 0.4) kJ · mol⁻¹ [54], 24.6 kJ · mol⁻¹ [52], (26.7 ± 0.4) kJ · mol⁻¹ [54], 27.57 kJ · mol⁻¹ [55], 30 kJ · mol⁻¹ [56]), indicating that the samples were significantly crystalline, in agreement with the X-ray powder diffraction evidence. From the baseline shifts observed upon fusion of the products resulting from the solubility measurements in water, ethanol, DMSO, acetone, acetonitrile, and diethyl ether it was possible to calculate the molar heat capacity of fusion of nicotinic acid as $\Delta_{fus}C_{p,m} = (39.6 \pm 3.0)$ J · K⁻¹ · mol⁻¹ [32]. This value represents the weighted mean [57] of the average results obtained for each of the five different samples. It was assigned to $T = (507.0 \pm 0.4)$ K which represents the weighted mean of the corresponding T_{on} values. These results are used below to obtain the ideal solubility of nicotinic acid as a function of the temperature. Interestingly, Koop's rule gives for nicotinic acid $\Delta_{fus}C_{p,m} (298.15 \text{ K}) = 38.0$ J · K⁻¹ · mol⁻¹ [58].

The molar enthalpies of solution in DMSO, $\Delta_{sol}H_m$, of the starting material and the products of the solubility measurements, obtained by solution calorimetry, at $T = 298.15$ K, are shown in table 7. Detailed results are given as supporting information. The $\Delta_{sol}H_m$ values correspond to the process:

