Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting information for "Terminal Crystalline Solid Solutions and T-X Phase Diagrams of Salicylic acid - 4-Hydroxybenzoic acid"

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Table 1. DSC results for SA-4HBA. Average values and standard deviations in parenthesis

X(4HBA)	DSC endotherms	Low temperature endotherm					High temperature endotherm				
mol AA/mol SA+4HBA		T_{inset}	T_{onset}	T_{peak}	T_{offset}	Enthalpy	T_{inset}	T_{onset}	T_{peak}	T_{offset}	Enthalpy
		°C	°C	°C	°C	J/g	°C	°C	°C	°C	J/g
0.00	One endotherm						154.07 (0.08)	158.64 (0.006)	159.16 (0.09)	160.98 (0.23)	189.56 (4.21)
0.00062	One endotherm						154.25 (0.56)	158.57 (0.02)	159.14 (0.04)	161.92 (0.79)	187.66 (1.56)
0.0011	One endotherm						152.11 (0.18)	158.53 (0.01)	159.18 (0.11)	161.15 90.23)	182.65 (3.81)
0.0022	One endotherm						153.49 (0.41)	158.46 (0.05)	159.21 (0.12)	161.56 (0.22)	179.59 (4.47)
0.0036	Two separated endotherms	141.07 (0.50)	142.73 (0.10)	143.76 (0.06)	144.72 (0.12)	0.79 (0.22)	151.43 (0.87)	158.07 (0.09)	159.04 (0.14)	160.80 (0.35)	172.00 (2.87)
0.0062	Two separated endotherms	140.97 (0.47)	142.14 (0.06)	143.20 (0.08)	144.78 (0.18)	1.76 (0.21)	148.87 (0.43)	157.69 (0.03)	158.73 (0.06)	160.58 (0.13)	167.83 (1.33)
0.0153	Two partially overlapping endotherms	141.53 (0.13)	142.72 (0.12)	143.65 (0.04)	145.08[1] (0.14)	7.08 (0.57)	149.12 (1.03)	154.88 (2.13)	158.13 (0.12)	161.39 (2.26)	161.49 (8.28)
0.0303	Two partially overlapping endotherms	140.98 0.34)	143.00 (0.05)	143.87 (0.02)	145.87[1] (0.19)	21.49 (1.97)		154.28 (0.40)	157.26 (0.09)	159.14 (0.24)	153.28 (0.47)
0.0398	Two partially overlapping endotherms	140.35 (0.62)	143.68 (1.15)	143.87 (0.13)	145.66[1] (0.06)	30.91 (3.84)		152.80 (0.73)	156.34 (0.33)	158.64 (0.35)	144.72 (6.36)
0.0516	Two partially overlapping endotherms	141.05 (0.79)	143.00 (0.04)	143.95 (0.09)	145.60[1] (0.27)	38.91 (2.80)		152.46 (1.95)	155.49 (0.61)	157.62 (0.27)	132.90 (9.23)
0.0964	Two partially overlapping endotherms	141.30 (0.04)	143.16 (0.04)	144.37 (0.05)		74.30 (1.05)			153.65 (0.68)	156.18 (0.31)	97.74 (2.29)
0.2069	Two endotherms mostly overlapping	141.65 (0.20)	143.27 (0.01)	144.68 (0.22)		132.31 (1.40)			148.58 (1.72)	149.99 (1.58)	42.45 (1.11)
0.2241	Two endotherms mostly overlapping	141.59 (0.47)	143.34 (0.06)	144.68 (0.29)		138.96 (2.54)				150.28 (1.18)	25.68 (16.40)
0.2496	Two endotherms mostly overlapping	140.22 (0.16)	143.40 (0.21)	144.48 (0.17)		164.54 (12.04)				151.59 (2.21)	12.47 (2.99)
0.2745	Two endotherms mostly overlapping	141.20 (0.24)	143.32 (0.09)	144.58 (0.20)		161.29 (0.71)				148.65 (0.80)	4.18 (5.12)

0.2939	Two partially overlapping endotherms	140.54 (0.14)	143.23 (0.01)	144.65 0.02)		173.34 (6.29)				162.88 (1.57)	16.78 (5.86)
0.3966	Two partially overlapping endotherms	140.08 (0.85)	143.28 (0.15)	144.58 (0.07)	147.84[1] (0.08)	146.62 (10.33)			165.46 (8.98)	174.54 (6.18)	28.93 (13.14)
0.4995	Two mostly separated endotherms	140.92 (0.13)	143.15 (0.05)	144.40 (0.21)	146.42[1] (0.41)	107.74 (2.26)		180.44 (10.25)	189.78 (8.68)	194.24 (7.93)	34.76 (4.74)
0.6062	Two mostly separated endotherms	140.96 (0.41)	143.09 (0.02)	144.16 (0.06)	146.23[1] (0.13)	88.35 (3.12)		186.45 (8.66)	193.83 (3.44)	200.62 (2.59)	63.17 (8.37)
0.7081	Two mostly separated endotherms	140.30 (0.16)	143.10 (0.01)	144.13 (0.10)	146.24[1] (0.29)	73.31 (3.39)		185.61 (3.68)	195.18 (1.01)	201.16 (0.86)	82.24 (2.35)
0.8011	Two mostly separated endotherms	139.96 (0.11)	143.10 (0.01)	144.01 (0.08)	146.01[1] (0.06)	43.49 (1.59)		205.98 (5.52)	209.68 (3.50)	213.40 (2.00)	139.68 (13.71)
0.9040	Two separated endotherms	139.50 (0.51)	142.64 (0.02)	143.54 (0.04)	145.09 (0.22)	15.60 (1.84)	205.24 (0.62)	211.94 (0.66)	213.44 (0.28)	215.20 (0.30)	189.91 (3.21)
0.9505	Two separated endotherms	139.87 (0.58)	142.94 (0.59)	143.79 (0.17)	144.95 (0.17)	5.92 (0.47)	208.12 (0.90)	213.76 (0.22)	214.88 (0.18)	216.88 (0.16)	207.97 (3.18)
0.9704	Two separated endotherms	140.53 (0.16)	142.18 (0.09)	143.54 (0.14)	144.64 (0.12)	2.75 (0.42)	207.68 (0.57)	213.31 (0.13)	214.52 (0.11)	216.40 (0.20)	212.75 (0.46)
0.9812	One endotherm						206.54 (1.09)	212.85 (0.40)	214.40 (0.21)	216.36 (0.19)	210.51 (8.24)
0.9845	One endotherm						209.43 (1.24)	214.15 (0.14)	214.95 (0.15)	216.99 (0.26)	214.89 (5.31)
0.9911	One endotherm						208.24 (0.48)	213.77 (0.11)	214.67 (0.02)	216.46 (0.24)	217.24 (2.21)
0.9952	One endotherm						210.61 (0.57)	214.36 (0.28)	215.16 (0.13)	216.95 (0.27)	223.91 (5.34)
1.000	One endotherm						213.29 (0.54)	215.22 (0.02)	215.49 (0.07)	217.33 (0.30)	222.87 (6.78)

1. Estimated offset temperature as the endotherm never returns to the baseline. The mid-point between endotherms is used as an approximation of the baseline offset temperature of the low-temperature endotherm when the endotherms increasingly overlap. This separation also provides the calculation of the enthalpy of both the low- and high-temperature endotherms

Table 2. Solid-Liquid Equilibria for SA-4HBA Anhydrate in ACN at 20°C

Solid phase	Liquid	Solid	Liquid	Solid	Conc. of SA	Conc. of 4HBA	X(SA)	A(4HBA)	X(solvent)
	w% 4HBA in SA	w% 4HBA in SA	mol% 4HBA in SA	mol% 4HBA in SA	mg SA/g solvent	mg 4HBA/ g solvent	mmol SA/ (mol total)	mmol 4HBA/ (mol total)	mol solvent/ (mol total)
SA	0.000%	0.000%	0.000%	0.000%	92.27	0.00	26.6910	0.0000	0.9733
α	0.392%	0.012%	0.392%	0.012%	86.15	0.34	24.9620	0.0982	0.9749
α	1.611%	0.017%	1.611%	0.017%	102.09	1.67	29.4337	0.4820	0.9701
α	3.953%	0.038%	3.953%	0.038%	93.36	3.84	26.9689	1.1098	0.9719
α	8.605%	0.046%	8.605%	0.046%	107.19	10.09	30.7852	2.8984	0.9663
α	6.778%	0.071%	6.778%	0.071%	110.52	8.04	31.7294	2.3070	0.9660
α	16.426%	0.100%	16.426%	0.100%	105.34	20.70	30.1776	5.9311	0.9639
α	26.630%	0.159%	26.630%	0.159%	115.86	42.05	32.8906	11.9376	0.9552
α	26.459%	0.166%	26.459%	0.166%	117.28	42.20	33.2788	11.9735	0.9547
α	28.293%	0.171%	28.293%	0.171%	99.80	39.38	28.4835	11.2384	0.9603
α	20.458%	0.193%	20.458%	0.193%	112.91	29.04	32.1998	8.2815	0.9595
α + β	34.387%	0.555%	34.387%	0.555%	128.29	67.24	36.0356	18.8857	0.9451
α + β	34.019%	20.038%	34.019%	20.038%	126.10	65.02	35.4643	18.2852	0.9463
α + β	34.182%	22.717%	34.182%	22.717%	129.35	67.18	36.3226	18.8634	0.9448
α + β	34.504%	56.387%	34.504%	56.387%	127.89	67.38	35.9255	18.9263	0.9451
α + β	34.466%	76.699%	34.466%	76.699%	119.30	62.74	33.6356	17.6898	0.9487
α + β	34.517%	99.336%	34.517%	99.336%	126.07	66.45	35.4418	18.6818	0.9459
β	40.829%	99.648%	40.829%	99.648%	86.09	59.41	24.5267	16.9239	0.9585
β	43.870%	99.725%	43.870%	99.725%	88.94	69.52	25.2458	19.7314	0.9550
β	49.685%	99.790%	49.685%	99.790%	58.55	57.81	16.8194	16.6085	0.9666
β	77.932%	99.938%	77.932%	99.938%	14.20	50.16	4.1421	14.6272	0.9812
β	93.321%	99.964%	93.321%	99.964%	3.34	46.63	0.9772	13.6545	0.9854
4HBA Anhydrate	100.00%	100.00%	100.00%	100.00%	0.00	44.97	0.0000	13.1890	0.9868

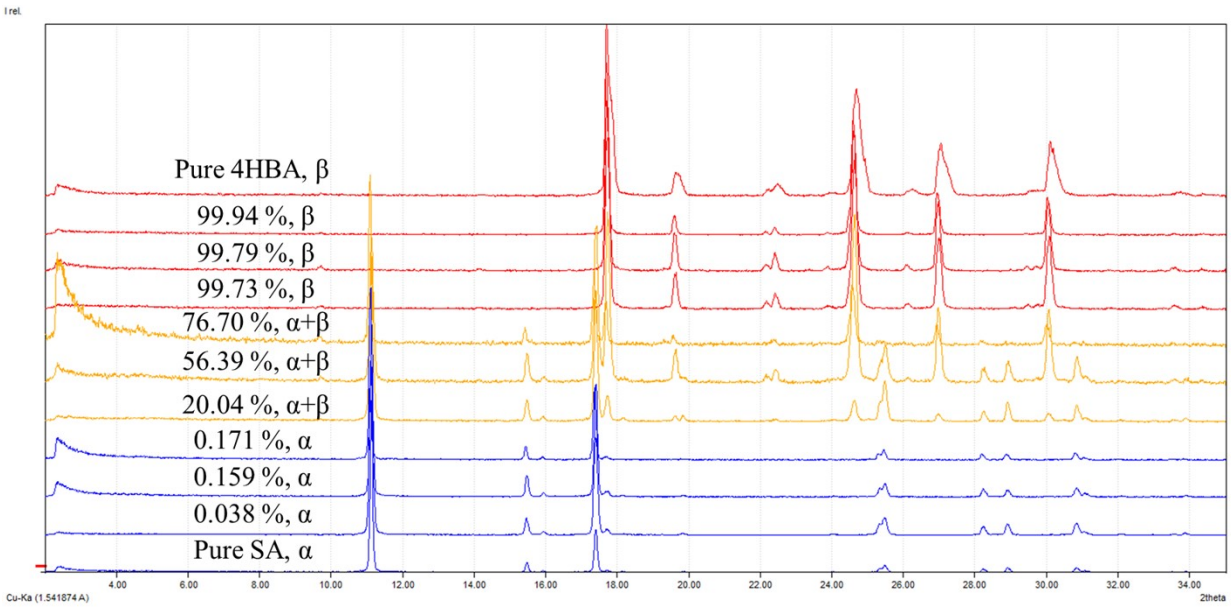

Figure 1. XRPD of SA-4HBA (Anhydrate) of (select) solid phase samples from SLE study in ACN

Table 3. Solid-Liquid Equilibria for SA-4HBA Hydrate in 40 w% MeOH in H2O at 20°C

Solid phase	Liquid	Solid	Liquid	Solid	Conc. of SA	Conc. of 4HBA	X(SA)	A(4HBA)	X(solvent)
	w% 4HBA in SA	w% 4HBA in SA	mol% 4HBA in SA	mol% 4HBA in SA	mg SA/g solvent	mg 4HBA /g solvent	mmol SA/ (mol total)	mmol 4HBA / (mol total)	mol solvent/ (mol total)
SA	0.00%	0.00%	0.00%	0.00%	22.91	0.00	3.6098	0.0000	0.9964
α	11.88%	0.047%	11.88%	0.047%	24.15	3.26	3.8022	0.5126	0.9957
α	16.19%	0.051%	16.19%	0.051%	24.44	4.72	3.8463	0.7430	0.9954
α	19.99%	0.057%	19.99%	0.057%	23.70	5.92	3.7302	0.9318	0.9953
α	28.15%	0.085%	28.15%	0.085%	24.48	9.59	3.8507	1.5087	0.9946
α	28.47%	0.086%	28.47%	0.086%	25.75	10.25	4.0485	1.6117	0.9943
α	36.65%	0.103%	36.65%	0.103%	26.25	15.18	4.1229	2.3853	0.9935
α	35.15%	0.104%	35.15%	0.104%	25.21	13.67	3.9618	2.1476	0.9939
α	51.40%	0.130%	51.40%	0.130%	28.31	29.95	4.4360	4.6922	0.9909
α	54.16%	0.143%	54.16%	0.143%	30.29	35.79	4.7397	5.5998	0.9897
α	58.55%	0.182%	58.55%	0.182%	34.83	49.19	5.4351	7.6759	0.9869
α + βH	71.19%	30.28%	71.19%	30.28%	37.23	92.02	5.7693	14.2585	0.9800
α + βH	70.74%	41.43%	70.74%	41.43%	39.91	96.47	6.1766	14.9312	0.9789
α + βH	70.48%	42.29%	70.48%	42.29%	35.64	85.09	5.5304	13.2022	0.9813
α + βH	70.18%	44.85%	70.18%	44.85%	38.68	91.03	5.9934	14.1046	0.9799
α + βH	70.06%	51.80%	70.06%	51.80%	41.42	96.95	6.4095	15.0010	0.9786
α + βH	70.65%	67.59%	70.65%	67.59%	42.01	101.09	6.4949	15.6309	0.9779
α + βH	71.19%	92.60%	71.19%	92.60%	34.42	85.06	5.3419	13.1996	0.9815
α + βH	71.39%	99.75%	71.39%	99.75%	35.42	88.39	5.4927	13.7077	0.9808
βH	74.80%	99.81%	74.80%	99.81%	30.19	89.63	4.6850	13.9081	0.9814
βH	80.61%	99.90%	80.61%	99.90%	18.66	77.56	2.9064	12.0794	0.9850
βH	89.24%	99.94%	89.24%	99.94%	8.74	72.43	1.3640	11.3075	0.9873
βH	88.63%	99.94%	88.63%	99.94%	10.40	81.12	1.6217	12.6440	0.9857
4HBA-Hydrate	100.00 %	100.00%	100.00%	100.00%	0.00	69.740	0.0000	10.9070	0.9891

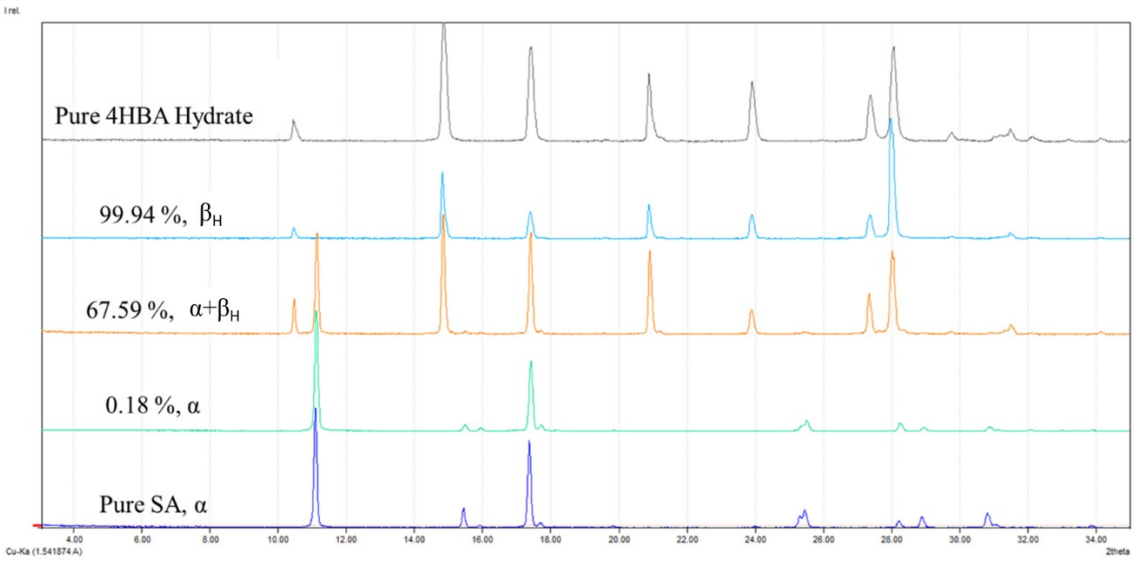

Figure 2. XRPD of SA-4HBA (monohydrate) of (select) solid phase samples from SLE study in 40 w% MeOH in H2O

Fitting the Liquid BIPs Δg_{12}^{L} and Δg_{21}^{L}

For the liquid-state NRTL BIPs of 4-hydroxybenzoic acid (1) and salicylic acid (2), Δg_{12}^{L} and Δg_{21}^{L} were not expressed as functions of temperature due to the sparsity of solid-liquid equilibrium melt data (i.e., the SSLE data at the eutectic temperature).

During the regression of these parameters it was noted that a wide range of parameter values for Δg_{12}^{L} and Δg_{21}^{L} would give decent predictions of the SSLE data. As a result, a more in-depth study was performed to assess the degeneracy of the liquid parameters with respect to the SSLE criteria which must be satisfied simultaneously:

$$\left\{\gamma_i^{\alpha} x_i^{\alpha} f_i^{S}/f_i^{L} = \gamma_i^{L} x_i^{L} = \gamma_i^{\beta} x_i^{\beta} f_i^{S}/f_i^{L}\right\}_{i\,=\,1,\,2} \tag{S1}$$

Numerically, the regression procedure requires determination of the parameters Δg_{12}^{L} and Δg_{21}^{L} to calculate γ_i^{L} (provided known values of Δg_{12}^{S} and Δg_{21}^{S}, which we obtained from regressing the solvus data to the T-dependent expressions described in the text, and hence known values of γ_i^{S}). This was done by driving the objective function shown below to zero:

$$OF = \sum_{i\,=\,1}^{2}\left(\gamma_i^{\alpha} x_i^{\alpha} f_i^{S}/f_i^{L} - \gamma_i^{L} x_i^{L}\right)^2 + \left(\gamma_i^{\beta} x_i^{\beta} f_i^{S}/f_i^{L} - \gamma_i^{L} x_i^{L}\right)^2 \tag{S2}$$

Because there are only two regression parameters in the above equation (Δg_{12}^{L} and Δg_{21}^{L}), one can easily visualize how the OF varies with the parameter values. A contour plot showing this functional dependency is illustrated below:

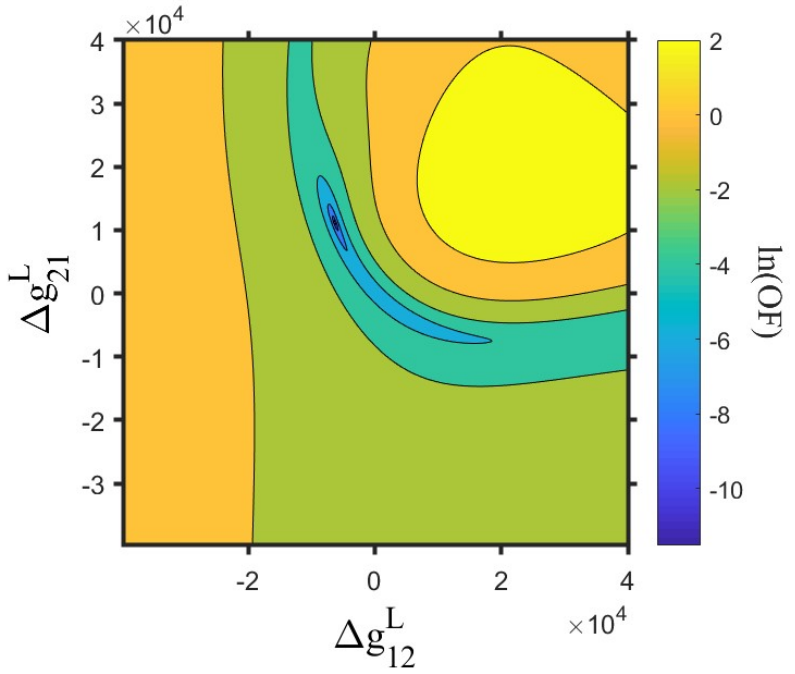

Figure 3: Objective function at SSLE, with varying values of Δg_{12}^{L} *and* Δg_{21}^{L}.

Clearly, there is a wide range of parameter space over which the objective function is quite close to zero (e.g., < e^{-4} = 0.0183). Such degeneracy or relative "flatness" in the parameter space can make it difficult to converge at a single parameter set when different initial guesses are employed. Therefore, we focused-in on the lowest OF region, as shown below, and restricted our initial guesses for the parameters to be sufficiently close to the absolute minimum, thereby allowing the regression algorithm to more-easily converge to the global-minimum. Alternatively, the minimum value can be approximately read off the graph.

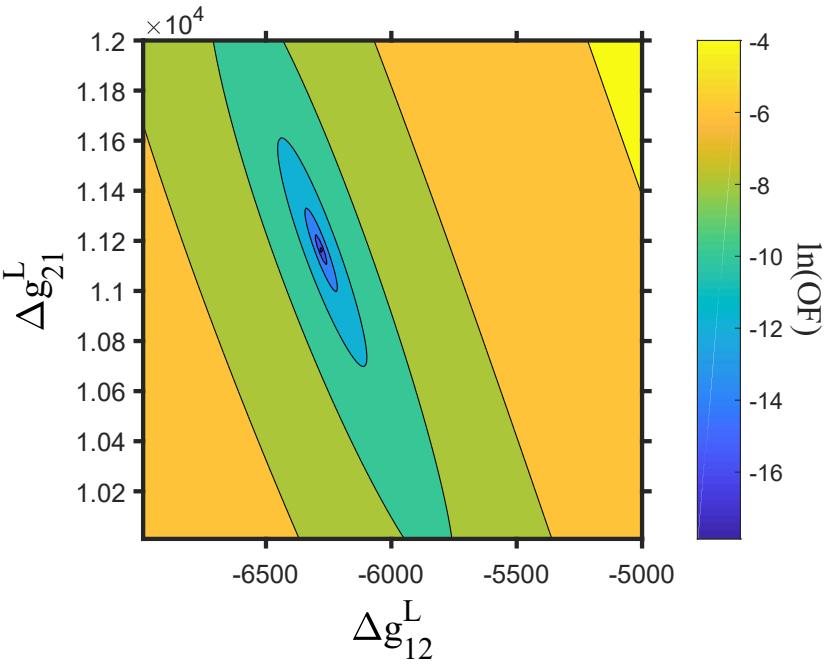

Figure 4: Zoomed-view of Figure 3.