Electronic Supplementary Information

to accompany

A quantitative study of vapor diffusions for crystallizations: rates and solvent parameter changes.

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Figure 1: Movie showing standard apparatus used in these studies (one dram inner, 20 mL outer) for three solvent combinations over 60 h. Photos were taken at 1-h intervals, and the playback rate is six hours per second. Note the color changes of the solvatochromic dye; the center vial becomes colorless due to precipitation of the dye.

						Hansen Parameters[2]			
solvent	**relative polarity[1]**	**BP (°C)**	**density (g/mL)**	**20 °C vapor press (torr)**	**viscosity (cp)**	**δ_{disp}**	**δ_{pol}**	**$\delta_{H\text{-}bond}$**	**Molar[2] vol (mL)**
pentane	0.009	36.1	0.626	430	0.24	14.5	0.0	0.0	116.2
triethylamine (TEA)	0.043	88.8	0.723	59	0.36	17.8	0.4	1.0	138.6
toluene	0.099	111	0.867	22	0.59	18.0	1.4	2.0	106.8
benzene	0.111	80.1	0.876	76	0.65	18.4	0.0	2.0	89.4
ether	0.117	34.5	0.713	440	0.24	14.5	2.9	5.1	104.8
2-methyltetrahydrofuran 2-Me-THF	0.179	80.2	0.854	102	0.60	16.9	5.0	4.3	100.2
THF	0.207	66.0	0.889	150	0.55	16.8	5.7	8.0	81.7
ethyl acetate (EtOAc)	0.228	77.2	0.897	73	0.46	15.8	5.3	7.2	98.5
chloroform	0.259	61.2	1.490	158	0.58	17.8	3.1	5.7	80.7
pyridine	0.302	116	0.982	15	0.95	19.0	8.8	5.9	80.9
dichloromethane (DCM)	0.309	39.6	1.330	356	0.45	18.2	6.3	6.1	63.9
1,2-dichloroethane (DCE)	0.327	83.5	1.235	~70	0.79	19.0	7.4	4.1	79.4
DMPU	0.352	247	1.06	<0.3	1.94	17.8	9.5	9.3	120.9
acetone	0.355	56.1	0.791	180	0.32	15.5	10.4	7.0	74
NMP	0.355	203	1.03	0.3	1.65	18.0	12.3	7.2	96.5
DMF	0.386	153	0.944	3	0.92	17.4	13.7	11.3	77
DMSO	0.444	189	1.10	<0.5	2.24	18.4	16.4	10.2	71.3
acetonitrile	0.460	81.6	0.786	73	0.37	15.3	18.0	6.1	52.6
acetic acid	0.648	118	1.05	12	1.31	14.5	8.0	13.5	57.1
ethanol	0.654	78.3	0.789	44	1.10	15.8	8.8	19.4	58.5
methanol	0.762	64.5	0.792	96	0.55	15.1	12.3	22.3	40.7
2,2,2-trifluoroethanol (TFE)	0.898	78.0	1.39	53	0.90	15.4	8.3	16.4	72.3
water	1.000	100	1.00	13	1.00	18.1	17.1	16.9	18

Table 1: Relevant properties of solvents used in these diffusion studies at 20 °C, ranked by increasing polarity.[1]

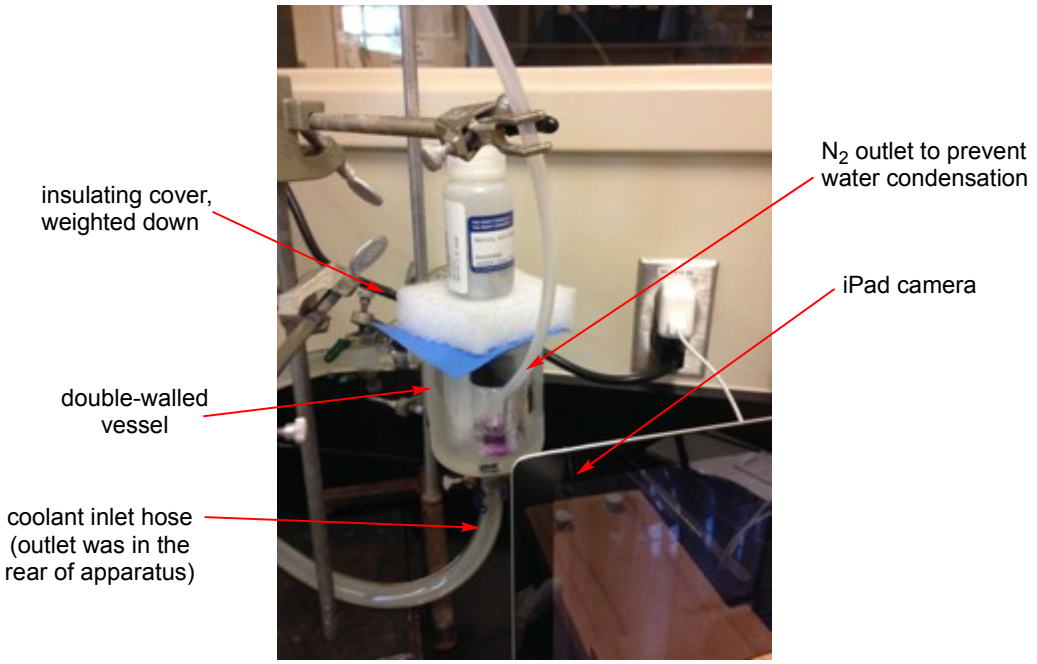


Figure 2: Apparatus for studying variable-temperature diffusions. Note insulating seal above and nitrogen outlet tube to keep the camera access area condensation-free.

Hansen Solubility parameter calculations

The Hansen approach requires the use of volume percents rather than mole percents. The mole percents determined by NMR were converted to the volume percents as follows:

$$\text{volume \% A} = \frac{\text{(mol\% A)*(molar volume A) * 100\%}}{\text{(mol\% A)*(molar volume A) + (mol \% B)*(molar volume B)}}$$

The individual Hansen solubility parameters (D for δ_{disp}, P for δ_{pol}, and H for $\delta_{H\text{-}bond}$) for solvent mixtures are simply the sum of the products of the solubility parameter for each pure solvent[2] times the volume percent of that solvent in the mixture:

$$\delta_{D\ mixture} = (\text{volume \% A})*(\delta_{D,A}) + (\text{volume percent B})*(\delta_{D,B})$$

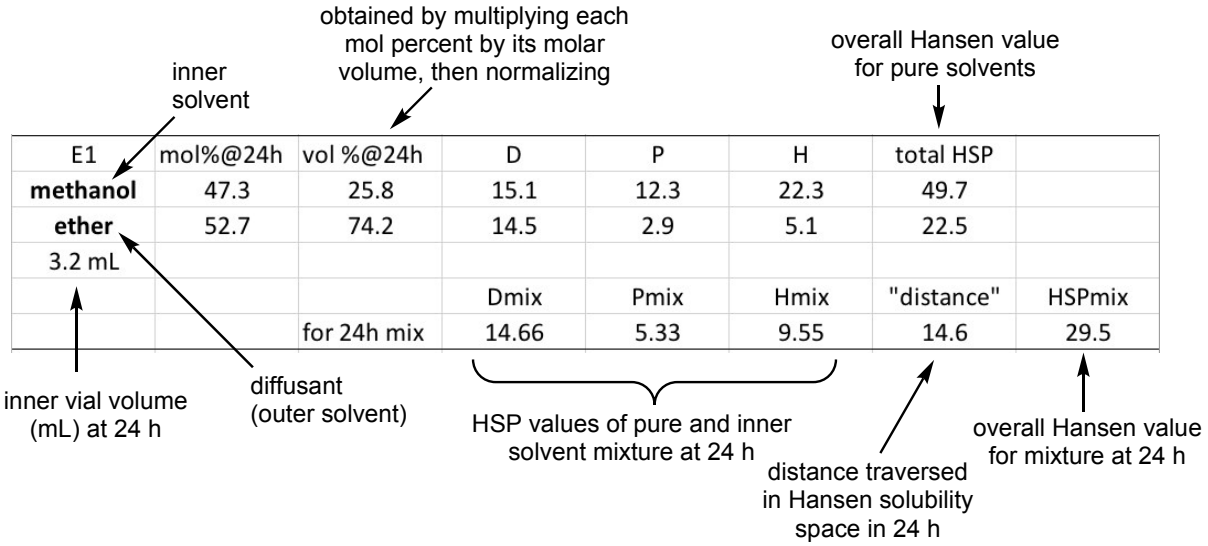
The "distance traversed" from pure solvent to the mixture at 24 h is calculated as follows:

$$\text{distance traversed} = \sqrt{[(4 * (D_{mix} - D_{pure})^2) + (P_{mix} - P_{pure})^2 + (H_{mix} - H_{pure})^2]}$$

Note that the dispersion parameter is favored by a factor of four, a relationship demonstrated empirically and predicted theoretically.

The calculations are given in the format below, with explanations for the various terms. The HSP_{mix} is given, and is analogous to an overall "polarity" or "solvent strength", which roughly correlates with

other polarity scales, but in itself has little quantitative value for the same reasons that polarity values do not (i.e., the various D, P and H contributions must be considered separately).



Calculations for ether diffusions at 24 h diffusion time (ranked by decreasing HSP distance)

E1	mol%@24h	vol %@24h	D	P	H	total HSP	
methanol	47.3	25.8	15.1	12.3	22.3	49.7	
ether	52.7	74.2	14.5	2.9	5.1	22.5	
3.2 mL							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	14.7	5.3	9.5	14.6	29.5

E2	mol%@24h	vol %@24h	D	P	H	total HSP	
ethanol	37.0	24.7	15.8	8.8	19.4	44	
ether	63.0	75.3	14.5	2.9	5.1	22.5	
3.2							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	14.8	4.4	8.6	11.8	27.8

E3	mol%@24h	vol %@24h	D	P	H	total HSP	
acetonitrile	38.6	24.0	15.3	18.0	6.1	39.4	
ether	61.4	76.0	14.5	2.9	5.1	22.5	
3.2							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	14.7	6.5	5.3	11.6	26.6

E4	mol%@24h	vol %@24h	D	P	H	total HSP	
DMF	32.0	25.7	17.4	13.7	11.3	42.4	
ether	68.0	74.3	14.5	2.9	5.1	22.5	
3.4							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.2	5.7	6.7	10.2	27.6

E5	mol%@24h	vol%@24h	D	P	H	total HSP	
2,2,2-TFE	28.0	21.4	15.4	8.3	16.4	40.1	
ether	71.1	78.6	14.5	2.9	5.1	22.5	
4.0							total
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	14.7	4.1	7.5	9.9	26.3

E6	mol%@24h	vol %@24h	D	P	H	total HSP	
NMP	29.8	28.1	18.0	12.3	7.2	37.5	
ether	70.2	71.9	14.5	2.9	5.1	22.5	
3.3							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.5	5.5	5.7	8.6	26.7

E7	mol%@24h	vol %@24h	D	P	H	total HSP	
DMSO	57.6	48.0	18.4	16.4	10.2	45	
ether	42.4	52.0	14.5	2.9	5.1	22.5	
2.2							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	16.4	9.4	7.5	8.5	33.3

E8	mol%@24h	vol %@24h	D	P	H	total HSP	
pyridine	27.5	22.6	19.0	8.8	5.9	33.7	
ether	72.5	77.4	14.5	2.9	5.1	22.5	
3.7							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.5	4.2	5.3	8.3	25.0

E9	mol%@24h	vol %@24h	D	P	H	total HSP	
1,2-DCE	26.7	21.6	19.0	7.4	4.1	30.5	
ether	73.3	78.4	14.5	2.9	5.1	22.5	
3.6							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.5	3.9	4.9	7.9	24.2

E10	mol%@24h	vol %@24h	D	P	H	total HSP	
acetic acid	37.3	24.5	14.5	8.0	13.5	36	
ether	62.7	75.5	14.5	2.9	5.1	22.5	
3.9							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	14.5	4.1	7.2	7.4	25.8

E11	mol%@24h	vol %@24h	D	P	H	total HSP	
benzene	24.2	21.4	18.4	0.0	2.0	20.4	
ether	75.8	78.6	14.5	2.9	5.1	22.5	
3.4							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.3	2.3	4.4	7.0	22.1

E12	mol%@24h	vol fr@ 24h	D	P	H	total HSP	
DMPU	29.9	33.0	17.8	9.5	9.3	36.6	
ether	70.1	67.0	14.5	2.9	5.1	22.5	
2.9							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.6	5.1	6.5	6.9	27.1

E13	mol%@24h	vol %@24h	D	P	H	total HSP	
DCM	28.3	19.4	18.2	6.3	6.1	30.6	
ether	71.7	80.6	14.5	2.9	5.1	22.5	
2.3							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.2	3.6	5.3	6.6	24.1

E14	mol%@24h	vol %@24h	D	P	H	total HSP	
acetone	29.0	22.4	15.5	10.4	7.0	32.9	
ether	71.0	77.6	14.5	2.9	5.1	22.5	
2.3							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	14.7	4.6	5.5	6.2	24.8

E15	mol%@24h	vol %@24h	D	P	H	total HSP	
toluene	23.7	24.0	18.0	1.4	2.0	21.4	
ether	76.3	76.0	14.5	2.9	5.1	22.5	
4.0							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.3	2.5	4.4	5.9	22.2

E16	mol%@24h	vol %@24h	D	P	H	total HSP	
chloroform	24.0	19.6	17.8	3.1	5.7	26.6	
ether	76.0	80.4	14.5	2.9	5.1	22.5	
3.7							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.1	2.9	5.2	5.3	23.3

E17	mol%@24h	vol %@24h	D	P	H	total HSP	
ethyl acetate	24.9	23.8	15.8	5.3	7.2	28.3	
ether	75.1	76.2	14.5	2.9	5.1	22.5	
3.3							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	14.8	3.5	5.6	3.1	23.9

Calculations for pentane diffusions at 24 h diffusion time (ranked by decreasing HSP distance)

P1	mol%@24h	vol %@24h	D	P	H	total HSP	
ethanol	61.2	44.3	15.8	8.8	19.4	44	
pentane	38.8	55.7	14.5	0.0	0.0	14.5	
1.9							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.1	3.9	8.6	12.0	27.6

P2	mol%@24h	vol %@24h	D	P	H	total HSP	
pyridine	39.0	30.8	19.0	8.8	5.9	33.7	
pentane	61.0	69.2	14.5	0.0	0.0	14.5	
2.8							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.9	2.7	1.8	9.6	20.4

P3	mol%@24h	vol %@24h	D	P	H	total HSP	
1,2-DCE	39.1	30.5	19.0	7.4	4.1	30.5	
pentane	60.9	69.5	14.5	0.0	0.0	14.5	
2.8							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.9	2.3	1.3	8.6	19.4

P4	mol%@24h	vol %@24h	D	P	H	total HSP	
acetone	44.9	34.2	15.5	10.4	7.0	32.9	
pentane	55.1	65.8	14.5	0.0	0.0	14.5	
1.4							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	14.8	3.6	2.4	8.4	20.8

P5	mol%@24h	vol %@24h	D	P	H	total HSP	
THF	31.2	24.2	16.8	5.7	8.0	30.5	
pentane	68.8	75.8	14.5	0.0	0.0	14.5	
2.7							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.1	1.4	1.9	8.2	18.4

P6	mol%@24h	vol %@24h	D	P	H	total HSP	
ethyl acetate	31.5	28.0	15.8	5.3	7.2	28.3	
pentane	68.5	72.0	14.5	0.0	0.0	14.5	
2.4							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	14.9	1.5	2.0	6.7	18.4

P7	mol%@24h	vol %@24h	D	P	H	total HSP	
chloroform	36.9	28.9	17.8	3.1	5.7	26.6	
pentane	63.1	71.1	14.5	0.0	0.0	14.5	
2.3							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.5	0.9	1.6	6.6	18.0

P8	mol%@24h	vol %@24h	D	P	H	total HSP	
2-Me-THF	26.0	23.3	16.9	5.0	4.3	26.2	
pentane	74.0	76.7	14.5	0.0	0.0	14.5	
3.1							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.1	1.2	1.0	6.3	17.2

P9	mol%@24h	vol %@24h	D	P	H	total HSP	
benzene	28.4	23.4	18.4	0.0	2.0	20.4	
pentane	71.6	76.6	14.5	0.0	0.0	14.5	
3.1							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.4	0.0	0.5	6.2	15.9

P10	mol%@24h	vol %@24h	D	P	H	total HSP	
toluene	25.9	24.3	18.0	1.4	2.0	21.4	
pentane	74.1	75.7	14.5	0.0	0.0	14.5	
3.6							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.4	0.3	0.5	5.6	16.2

Calculations for benzene diffusions at 24 h diffusion time (ranked by decreasing HSP distance)

B1	mol%@24h	vol %@24h	D	P	H	total HSP	
DMF	64.3	60.8	17.4	13.7	11.3	42.4	
benzene	35.7	39.2	18.4	0.0	2.0	20.4	
1.5							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	17.8	8.3	7.7	6.5	33.8
B2	mol%@24h	vol %@24h	D	P	H	total HSP	
DMSO	75.2	70.7	18.4	16.4	10.2	45	
benzene	24.8	29.3	18.4	0.0	2.0	20.4	
1.5							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	18.4	11.6	7.8	5.4	37.8
B3	mol%@24h	vol %@24h	D	P	H	total HSP	
acetic acid	80.1	72.0	14.5	8.0	13.5	36	
benzene	19.9	28.0	18.4	0.0	2.0	20.4	
1.4							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.6	5.8	10.3	4.5	31.6
B4	mol%@24h	vol %@24h	D	P	H	total HSP	
NMP	65.7	67.4	18.0	12.3	7.2	37.5	
benzene	34.3	32.6	18.4	0.0	2.0	20.4	
1.6							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	18.1	8.3	5.5	4.4	31.9
B5	mol%@24h	vol %@24h	D	P	H	total HSP	
DMPU	57.6	64.8	17.8	9.5	9.3	36.6	
benzene	42.4	35.2	18.4	0.0	2.0	20.4	
1.6							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	18.0	6.2	6.7	4.2	30.9
B6	mol%@24h	vol %@24h	D	P	H	total HSP	
pyridine	63.0	60.6	19.0	8.8	5.9	33.7	
benzene	37.0	39.4	18.4	0.0	2.0	20.4	
1.5							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	18.8	5.3	4.4	3.8	28.5

Calculations for miscellaneous diffusions at 24 h diffusion time (ranked by decreasing HSP distance)

M1	mol%@24h	vol %@24h	D	P	H	total HSP	
methanol	45.9	31.8	15.1	12.3	22.3	49.7	
acetone	54.1	68.2	15.5	10.4	7.0	32.9	
1.7							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.4	11.0	11.9	10.5	38.2

M2	mol%@24h	vol %@24h	D	P	H	total HSP	
ethanol	43.5	37.8	15.8	8.8	19.4	44	
acetone	56.5	62.2	15.5	10.4	7.0	32.9	
1.9							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.6	9.8	11.7	7.8	37.1

M3	mol%@24h	vol %@24h	D	P	H	total HSP	
acetonitrile	53.3	42.4	15.3	18.0	6.1	39.4	
THF	46.7	57.6	16.8	5.7	8.0	30.5	
1.5							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	16.2	10.9	7.2	7.4	34.3

M4	mol%@24h	vol %@24h	D	P	H	total HSP	
water	83.1	54.5	18.1	17.1	16.9	52.1	
acetone	16.9	45.5	15.5	10.4	7.0	32.9	
1.7							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	16.9	14.0	12.4	5.9	43.4

M5	mol%@24h	vol %@24h	D	P	H	total HSP	
2,2,2-TFE	45.3	42.3	15.4	8.3	16.4	40.1	
THF	54.7	57.7	16.8	5.7	8.0	30.5	
2.1							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	16.2	6.8	11.6	5.3	34.6

M6	mol%@24h	vol %@24h	D	P	H	total HSP	
water	93.0	74.5	18.1	17.1	16.9	52.1	
THF	7.0	25.5	16.8	5.7	8.0	30.5	
1.4							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	17.8	14.2	14.6	3.7	46.6

M7	mol%@24h	vol %@24h	D	P	H	total HSP	
water	82.5	67.6	18.1	17.1	16.9	52.1	
methanol	17.5	32.4	15.1	12.3	22.3	49.7	
1.4							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	17.1	15.5	18.7	3.0	51.3

M8	mol%@24h	vol %@24h	D	P	H	total HSP	
water	93.2	82.4	18.1	17.1	16.9	52.1	
acetonitrile	6.8	17.6	15.3	18.0	6.1	39.4	
1.2							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	17.6	17.3	15.0	2.1	49.9

M9	mol%@24h	vol %@24h	D	P	H	total HSP	
water	93.2	80.8	18.1	17.1	16.9	52.1	
ethanol	6.8	19.2	15.8	8.8	19.4	44	
1.2							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	17.7	15.5	17.4	1.9	50.5

M10	mol%@24h	vol %@24h	D	P	H	total HSP	
DMF	72.8	91.4	17.4	13.7	11.3	42.4	
water	27.2	8.6	18.1	17.1	16.9	52.1	
1.1							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	17.5	14.0	11.8	0.6	43.2

M11	mol%@24h	vol %@24h	D	P	H	total HSP	
DMSO	76.0	92.6	18.4	16.4	10.2	45	
water	24.0	7.4	18.1	17.1	16.9	52.1	
1.1							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	18.4	16.5	10.7	0.5	45.5

Calculations for the low-volume-change diffusions at 24 h diffusion time (ranked by decreasing HSP distan

LV1	mol%@24h	vol %@24h	D	P	H	total HSP	
Et3N	36.5	66.2	17.8	0.4	1.0	19.2	
methanol	63.5	33.8	15.1	12.3	22.3	49.7	
1.0							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	16.9	4.4	8.2	8.4	29.5

LV2	mol%@24h	vol %@24h	D	P	H	total HSP	
acetonitrile	71.4	59.5	15.3	18.0	6.1	39.4	
benzene	28.6	40.5	18.4	0.0	2.0	20.4	
1.1							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	16.6	10.7	4.4	7.9	31.7

LV3	mol%@24h	vol %@24h	D	P	H	total HSP	
DCM	49.2	34.8	18.2	6.3	6.1	30.6	
pentane	50.8	65.2	14.5	0.0	0.0	14.5	
1.0							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	15.8	2.2	2.1	7.5	20.1

LV4	mol%@24h	vol %@24h	D	P	H	total HSP	
ether	22.9	21.1	14.5	2.9	5.1	22.5	
pentane	77.1	78.9	14.5	0.0	0.0	14.5	
0.7		100.00					
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	14.5	0.6	1.1	4.6	16.2

LV5	mol%@24h	vol %@24h	D	P	H	total HSP	
2,2,2-TFE	83.7	80.6	15.4	8.3	16.4	40.1	
benzene	16.3	19.4	18.4	0.0	2.0	20.4	
1.1							
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	16.0	6.7	13.6	3.4	36.3

LV6	mol%@24h	vol %@24h	D	P	H	total HSP	
1,2-DCE	68.8	66.2	19.0	7.4	4.1	30.5	
benzene	31.2	33.8	18.4	0.0	2.0	20.4	
1.1		100.00					
			Dmix	Pmix	Hmix	"distance"	HSPmix
		for 24h mix	18.8	4.9	3.4	2.6	27.1

1. From Christian Reichardt, "Solvents and Solvent Effects in Organic Chemistry", Wiley-VCH Publ., 4th Ed, 2011; Weinheim, Germany; pp 453-461.

2. From Charles M. Hansen, "Hansen Solubility Parameters: A User's Handbook", CRC Press 2nd Ed., 2007; Boca Raton, Fl.; pp 345-483.