Electronic Supplementary Material (ESI) for CrystEngComm.

SUPPLEMENTARY INFORMATION

Drug solid solutions – a method for tuning phase transformations

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Contents

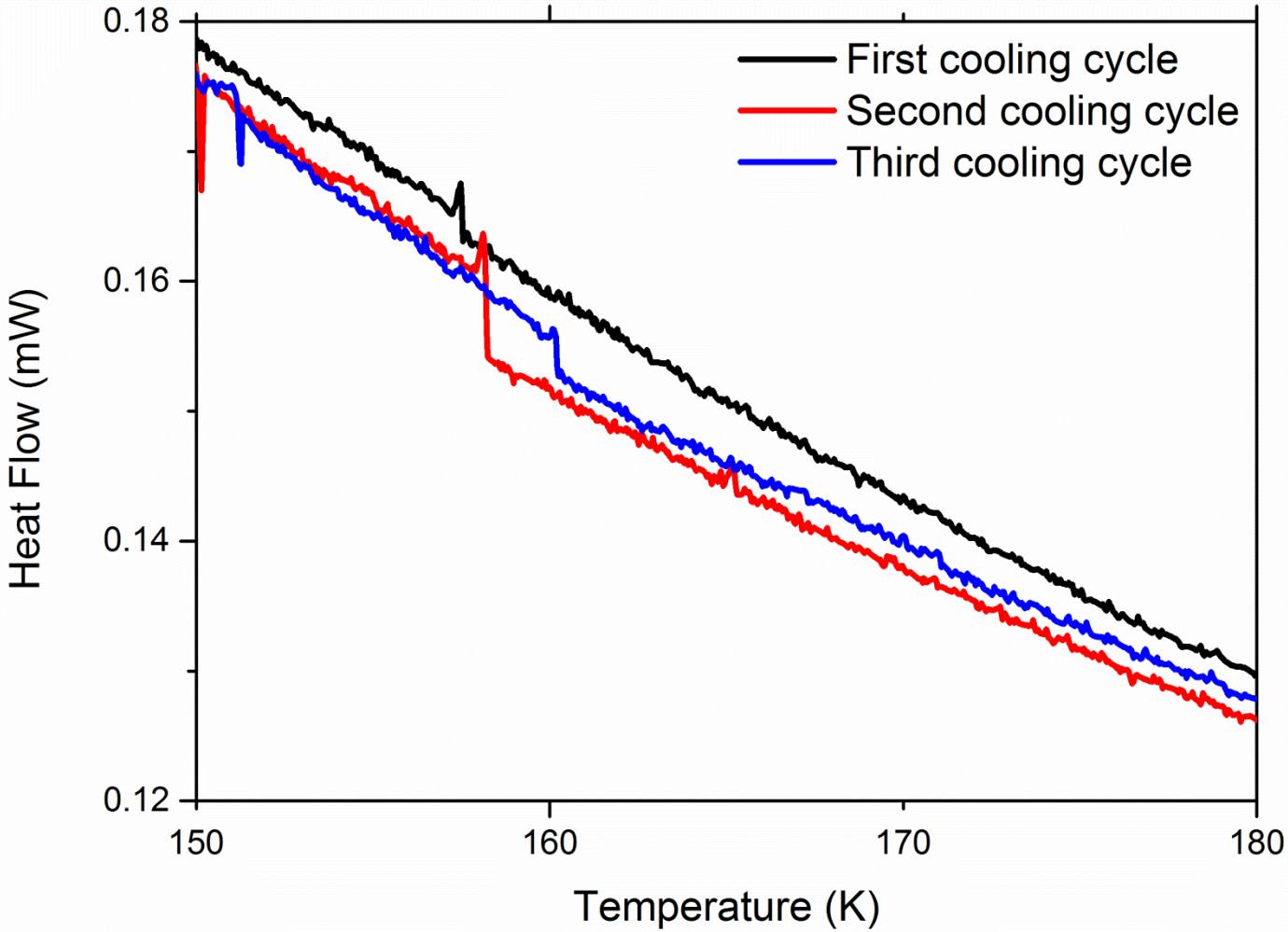

Figure S1. The Differential Scanning Calorimetry traces for (±)-4′-methylmethcathinone hydrochloride on cooling. The change in heat flow is very small and so only a section of the ramp is shown in order to highlight the change. The cooling traces show the transition between the low and high temperature form occurring at ~160 K.

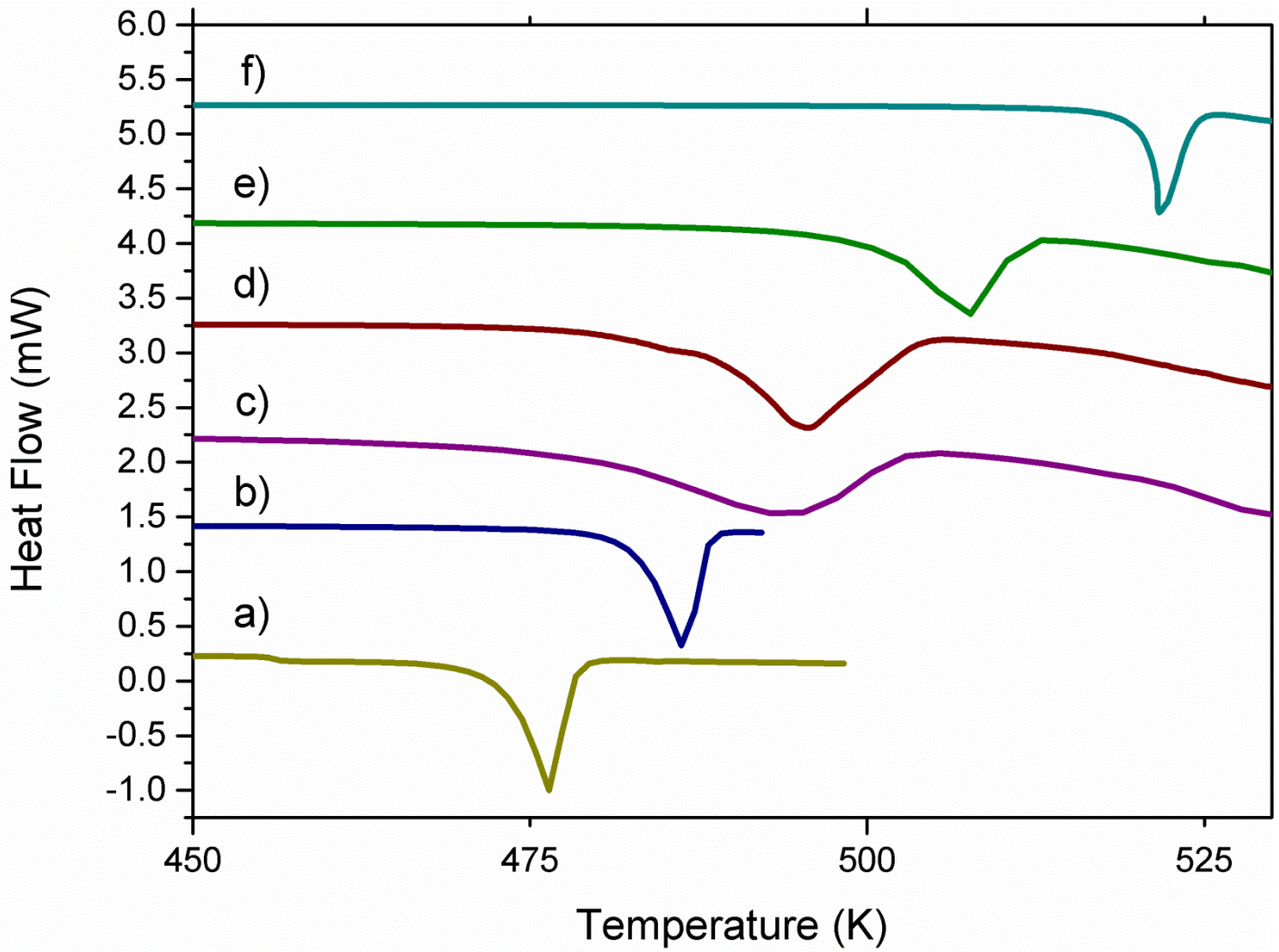

Figure S2. The Differential Scanning Calorimetry traces for compounds a) **1b_I**; b) **1b_II**; c) **1c_3070**; d) **1c_6040**; e) **1c_7030**; f) **1a**. The variation of melting point with %Cl composition is clearly visible.

Table S1: The solvent used in the solvent screen

Solvent	(**1a**)	(**1b**)
Acetone	I	I/II[b]
Acetonitrile	I	I/II[b]
Benzene	I	I
Benzylalcohol	I	-
1-butanol	I	I
Chloroform	I	I
Cyclopentane	-	-
Dichloromethane	I	I
Diethyl ether	I	I
Dimethylsulfoxide	I	-
Ethanol	I	II
Ethyl acetate	I	I
Methanol	I	II
Nitromethane	I	I
nn-Dimethylformamide	I	-
Pentane	-	-
2-octanol	-	-
2-phenylethanol	I	-
1,2-propanediol	I	-
1-propanol	I	I
2-propanol	I	I
Toluene	I	I
Trichloroethylene	I	I
Water	I	-

[a] Those entries marked with a '-' designate apparent insolubility.

[b]These samples showed variability in phase depending on rate of evaporation.

Table S2: The structural refinement parameters for salts (**1a-b**) and salt solutions (**1c**). (**1a-I**) and (**1a-II**) are the parameters at base temperature for each phase of (**1a**) i.e. 180 K for the high temperature **1a_I** and 100 K for the low temperature **1a_II**. (**1b-I**) and (**1b-II**) are Phase I and II of the hydrobromide (**1b**).

	1a-I	**1a-I**	**1a-I**	**1a-I**
Chemical formula	$C_{11}H_{16}NO{\cdot}Cl$	$C_{11}H_{16}NO{\cdot}Cl$	$C_{11}H_{16}NO{\cdot}Cl$	$C_{11}H_{16}NO{\cdot}Cl$
M_r	213.71	213.71	213.71	213.71
Crystal system, space group	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/n$
Temperature (K)	293	275	250	230
a, b, c (Å)	7.1345 (7), 23.048 (3), 7.4330 (8)	7.1365 (14), 23.041 (5), 7.4304 (15)	7.1314 (14), 23.013 (5), 7.4180 (15)	7.1264 (14), 22.986 (5), 7.4072 (14)
β (°)	90.449 (6)	90.628 (2)	90.803 (2)	90.974 (2)
V (Å^3)	1222.2 (2)	1221.7 (4)	1217.3 (4)	1213.2 (4)
Z	4	4	4	4
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.28	0.28	0.28	0.29
Crystal size (mm)	0.50 × 0.20 × 0.10	0.50 × 0.20 × 0.10	0.50 × 0.20 × 0.10	0.50 × 0.20 × 0.10
Diffractometer	Bruker Kappa Apex2 diffractometer	Bruker Kappa Apex2 diffractometer	Bruker Kappa Apex2 diffractometer	Bruker Kappa Apex2 diffractometer
Absorption correction	Multi-scan *SADABS* (Siemens, 1996)	Multi-scan *SADABS* (Siemens, 1996)	Multi-scan *SADABS* (Siemens, 1996)	Multi-scan *SADABS* (Siemens, 1996)
T_{min}, T_{max}	0.88, 0.97	0.88, 0.97	0.86, 0.97	0.86, 0.97
No. of measured, independent and observed [$I > 2.0\sigma(I)$] reflections	13589, 2311, 1388	7911, 2431, 1378	7889, 2425, 1443	7848, 2415, 1616

R_{int}	0.037	0.046	0.042	0.032
$R[F^2 > 2\sigma□F^2)]$, $wR(F^2)$, S	0.046, 0.140, 1.02	0.039, 0.089, 0.81	0.038, 0.090, 0.85	0.041, 0.115, 0.98
No. of reflections	2299	2427	2421	2411
No. of parameters	127	127	127	127
No. of restraints	0	0	0	0
H-atom treatment	H-atom parameters constrained	H-atom parameters constrained	H-atom parameters constrained	H-atom parameters constrained
$\Delta_{max,}\Delta_{min}$ (e Å^{-3})	0.29, -0.29	0.37, -0.38	0.31, -0.34	0.42, -0.31
	1a-I	**1a-I**	**1a-II**	**1a-II**
Chemical formula	$C_{11}H_{16}NO·Cl$	$C_{11}H_{16}NO·Cl$	$C_{11}H_{16}NO·Cl$	$C_{11}H_{16}NO·Cl$
M_r	213.71	213.71	213.71	213.71
Crystal system, space group	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$
Temperature (K)	210	180	150	123
a, b, c (Å)	7.1234 (14), 22.966 (4), 7.3986 (14)	7.1160 (12), 22.916 (4), 7.3818 (13)	10.0604 (18), 22.876 (4), 10.4041 (19)	10.0093 (3), 22.8207 (8), 10.4016 (4)
β (°)	91.146 (2)	91.415 (2)	91.741 (2)	91.416 (2)
V (Å^3)	1210.1 (4)	1203.4 (4)	2393.3 (7)	2375.20 (14)
Z	4	4	8	8
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.29	0.29	0.29	0.29
Crystal size (mm)	0.50 × 0.20 × 0.10	0.50 × 0.20 × 0.10	0.50 × 0.20 × 0.10	0.50 × 0.20 × 0.10
Diffractometer	Bruker Kappa Apex2 diffractometer	Bruker Kappa Apex2 diffractometer	Bruker Kappa Apex2 diffractometer	Bruker Kappa Apex2 diffractometer
Absorption correction	Multi-scan *SADABS* (Siemens, 1996)	Multi-scan *SADABS* (Siemens, 1996)	Multi-scan *SADABS* (Siemens, 1996)	Multi-scan *SADABS* (Siemens, 1996)
T_{min}, T_{max}	0.85, 0.97	0.86, 0.97	0.87, 0.97	0.88, 0.97

No. of measured, independent and observed [$I > 2.0\sigma(I)$] reflections	7803, 2402, 1663	7763, 2390, 1655	15469, 4743, 2781	26575, 4513, 3110
R_{int}	0.032	0.041	0.052	0.046
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.041, 0.107, 0.99	0.039, 0.099, 0.90	0.038, 0.077, 0.78	0.038, 0.100, 1.10
No. of reflections	2398	2386	4738	4494
No. of parameters	127	127	253	253
No. of restraints	0	0	0	0
H-atom treatment	H-atom parameters constrained	H-atom parameters constrained	H-atom parameters constrained	H-atom parameters constrained
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.43, -0.30	0.33, -0.33	0.62, -0.47	0.39, -0.42
	1a-II	**1b-I**	**1b-II**	
Chemical formula	$C_{11}H_{16}NO{\cdot}Cl$	$C_{11}H_{16}NO{\cdot}Br$	$C_{11}H_{16}NO{\cdot}Br$	
M_r	213.71	258.16	258.16	
Crystal system, space group	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	
Temperature (K)	100	123	123	
a, b, c (Å)	9.9973 (13), 22.788 (3), 10.4078 (14)	5.7804 (4), 19.7971 (14), 10.5967 (6)	10.8355 (19), 10.2030 (17), 11.5425 (19)	
β (°)	91.243 (1)	100.841 (3)	111.839 (8)	
V (Å^3)	2370.5 (5)	1190.99 (14)	1184.5 (4)	
Z	8	4	4	
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	
μ (mm^{-1})	0.29	3.42	3.44	
Crystal size (mm)	0.50 × 0.20 × 0.10	0.40 × 0.30 × 0.10	0.30 × 0.06 × 0.05	
Diffractometer	Bruker Kappa Apex2 diffractometer	Bruker Kappa Apex2 diffractometer	Bruker Kappa Apex2 diffractometer	
Absorption correction	Multi-scan	Multi-scan	Multi-scan	

	SADABS (Siemens, 1996)	*SADABS* (Siemens, 1996)	*SADABS* (Siemens, 1996)
T_{min}, T_{max}	0.85, 0.97	0.45, 0.71	0.68, 0.84
No. of measured, independent and observed [$I > 2.0\sigma(I)$] reflections	15326, 4706, 3354	9953, 2944, 2500	14238, 2426, 2105
R_{int}	0.038	0.029	0.027
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.039, 0.087, 1.01	0.026, 0.071, 0.98	0.020, 0.048, 1.00
No. of reflections	4702	2938	2417
No. of parameters	253	127	127
No. of restraints	0	0	0
H-atom treatment	H-atom parameters constrained	H-atom parameters constrained	H-atom parameters constrained
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.52, -0.48	0.54, -0.52	0.40, -0.33

	1c_7030	**1c_6040**	**1c_3070**
Chemical formula	$C_{11}H_{16}Br_{0.3}Cl_{0.7}NO$	$C_{11}H_{16}Br_{0.4}Cl_{0.6}NO$	$C_{11}H_{16}Br_{0.72}Cl_{0.28}NO$
M_r	227.16	154.43	245.64
Crystal system, space group	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$
Temperature (K)	123	123	123
a, b, c (Å)	10.1012 (5), 22.5506 (12), 10.4737 (5)	10.1409 (11), 22.488 (3), 10.4979 (11)	10.2017 (6), 22.3376 (13), 10.5639 (6)
β (°)	90.441 (3)	90.359 (8)	90.157 (3)
V (Å^3)	2385.7 (2)	2394.0 (5)	2407.3 (2)
Z	8	8	8
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$

μ (mm^{-1})	1.24	1.55	2.51
Crystal size (mm)	0.90 × 0.30 × 0.11	0.10 × 0.05 × 0.01	0.20 × 0.04 × 0.03
Diffractometer	Bruker Kappa Apex2 diffractometer	Bruker Kappa Apex2 diffractometer	Bruker Kappa Apex2 diffractometer
Absorption correction	Multi-scan *SADABS* (Siemens, 1996)	Multi-scan *SADABS* (Siemens, 1996)	Multi-scan *SADABS* (Siemens, 1996)
T_{min}, T_{max}	0.79, 0.87	0.53, 0.98	0.66, 0.93
No. of measured, independent and observed [$I > 2.0\sigma(I)$] reflections	30693, 4888, 4403	15233, 4353, 2731	4964, 4964, 4051
R_{int}	0.027	0.072	0.048
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.032, 0.075, 1.04	0.119, 0.413, 1.56	0.029, 0.070, 1.01
No. of reflections	4871	4333	4948
No. of parameters	263	263	263
No. of restraints	0	14	0
H-atom treatment	H-atom parameters constrained	H-atom parameters constrained	H-atom parameters constrained
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e $Å^{-3}$)	0.30, -0.31	4.08, -4.75	0.59, -0.50

Computer programs: Apex2 (Bruker AXS, 2006), *SIR92* (Altomare *et al.*, 1994), *CRYSTALS* (Betteridge *et al.*, 2003), *CAMERON* (Watkin *et al.*, 1996).

Table S3: The hydrogen bonding parameters in the variable temperature study. Distances in Å and angles in °.

298K	D…A (Å)	H…A (Å)	D-H…A(°)
N12-H121…Cl1[i]	3.104(2)	2.17	162
N12-H122…Cl1	3.063(2)	2.24	161
273K			
N12-H121…Cl1[i]	3.104(1)	2.24	161
N12-H122…Cl1	3.067(1)	2.17	162
250K			
N12-H121…Cl1[i]	3.100(2)	2.24	161
N12-H122…Cl1	3.064(1)	2.18	162
230K			
N12-H121…Cl1[i]	3.095(2)	2.27	157
N12-H122…Cl1	3.062(2)	2.13	161
210K			
N12-H121…Cl1[i]	3.094(2)	2.27	157
N12-H122…Cl1	3.061(2)	2.13	161
180K			
N12-H121…Cl1[i]	3.089(2)	2.27	157
N12-H122…Cl1	3.057(1)	2.13	161
150K			
N12-H121…Cl2[ii]	3.107(2)	2.21	163
N12-H122…Cl1	3.059(2)	2.13	167
N25-H251…Cl1	3.082(2)	2.21	158
N25-H252…Cl2 [iii]	3.066(1)	2.15	168

123K			
N12-H121...Cl2[ii]	3.054(2)	2.15	168
N12-H122...Cl1	3.104(2)	2.21	163
N25-H251...Cl1	3.079(2)	2.20	162
N25-H252...Cl2 [iii]	3.065(2)	2.14	166
100K			
N12-H121...Cl2[ii]	3.112(2)	2.22	162
N12-H122...Cl1	3.058(2)	2.16	168
N25-H251...Cl1	3.082(2)	2.20	163
N25-H252...Cl2[iii]	3.070(2)	2.16	168

Symmetry Operators: i) -1/2+x,3/2-y,-1/2+z, ii) 1+x,1/2-y,1/2+z, iii) x,1/2-y,1/2+z

Table S4: The hydrogen bonding parameters in the solid solutions at 123 K. Distances in Å and angles in °. The counterion changes in the description which reflects the change in the most prevalent counterion in the structure. The positional parameters for the chloride and bromide ion were set to be equal in the refinement of the solutions. *The R-factor for the 60% crystal was ~11.9% using I >2σ.

0% Cl	D…A (Å)	H…A (Å)	D-H…A(°)
N12-H121…Br1	3.257(2)	2.38	168
N12-H122…Br1^{i}	3.302(2)	2.48	154
30% Cl			
N12-H121…Br21^{ii}	3.234(2)	2.37	162
N12-H122…Br11	3.167(2)	2.30	163
N25-H251…Br11	3.182(2)	2.34	157
N25-H252…Br21^{iii}	3.170(2)	2.28	169
60% Cl*			
N12-H121…Br21^{ii}	3.227(8)	2.37	163
N12-H122…Br11	3.139(8)	2.28	164
N25-H251…Br11	3.079(8)	2.24	156
N25-H252…Br21^{iii}	3.110(9)	2.22	169
70% Cl			
N12-H121…Cl20^{ii}	3.182(2)	2.29	159
N12-H122…Cl10	3.104(2)	2.20	162
N25-H251…Cl10	3.131(2)	2.23	164
N25-H252…Cl20^{iii}	3.090(2)	2.17	170
100% Cl			
N12-H121…Cl2^{ii}	3.054(2)	2.15	168
N12-H122…Cl1	3.104(2)	2.21	163
N25-H251…Cl1	3.079(2)	2.20	162
N25-H252…Cl2^{iii}	3.065(2)	2.14	166

Symmetry Operators: i) x,3/2-y,-1/2+z, ii) 1+x,1/2-y,1/2+z, iii) x,1/2-y,1/2+z

Table S5: Identification of the phase transition temperatures. Unit cell parameters and reflections observed at various temperatures for each solid solution. Lengths are in Å and beta angles in °.

30% Cl						
Temp (K)	a (Å)	b (Å)	c (Å)	β (°)	Volume (Å^3)	No. reflections
250	7.332(7)	22.43(4)	7.615(11)	93.23(9)	1251(3)	184
240	7.36(2)	22.48(5)	7.676(19)	93.38(4)	1268(9)	156
240	10.42(2)	22.59(4)	10.61(2)	90.62(3)	2496(14)	384
235	7.310(2)	22.42(2)	7.632(5)	93.3(4)	1248.9(15)	165
235	10.299(8)	22.51(2)	10.567(6)	90.15(5)	2450(3)	581
220	10.286(3)	22.478(7)	10.5846(19)	90.369(17)	2447.1(12)	774
60% Cl						
Temp (K)	a (Å)	b (Å)	c (Å)	β (°)	Volume (Å^3)	No. reflections
216	7.212(16)	22.52(4)	7.568(7)	92.51(10)	1228.0(17)	111
190	7.292(17)	22.27(5)	7.594(12)	92.46(14)	1232(3)	122
190	10.301(13)	22.26(5)	10.61(3)	91.54(15)	2432(6)	198
180	7.318(16)	22.24(4)	7.628(10)	91.91(13)	1241(3)	84
180	10.309(16)	22.33(5)	10.45(3)	92.07(17)	2404(7)	208
70% Cl						
Temp (K)	a (Å)	b (Å)	c (Å)	β (°)	Volume (Å^3)	No. reflections
170	7.233(9)	22.41(6)	7.513(14)	92.45(13)	1217(4)	169
165	7.25(2)	22.50(7)	7.38(4)	92.7(4)	1202(8)	208
165	10.22(2)	22.57(4)	10.50(4)	90.6(2)	2423(10)	126
162	10.108(14)	22.69(2)	10.50(2)	91.02(14)	2408(6)	184
160	10.171(13)	22.62(2)	10.532(18)	91.36(12)	2422(5)	349