

## Quaternary phase diagrams as a tool for ionic cocrystallization: the case of a solid solution between a racemic and enantiopure ionic cocrystal

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### Experimental data for phase diagrams

Table S1. Experimental data for the suspensions of the ternary system ETI-CaCl<sub>2</sub>·2H<sub>2</sub>O-H<sub>2</sub>O at 25 °C.

Initial composition ETI:CaCl <sub>2</sub> (mole)	Initial components			Initial components (mol%)			solid phase at equilibrium
	ETI (mg)	CaCl <sub>2</sub> (mg)	H <sub>2</sub> O (μL)	ETI	CaCl <sub>2</sub>	H <sub>2</sub> O	
9 :1	93.24	6.76	75	0.115	0.013	0.872	ETI
8 :2	85.98	14.02	75	0.105	0.026	0.868	ETI
7 :3	78.16	21.84	75	0.095	0.041	0.864	ETI+ICC1
6 :4	69.7	30.3	75	0.085	0.056	0.859	ICC1
5 :5	60.53	39.47	75	0.073	0.073	0.854	ICC1
4 :6	50.56	49.44	75	0.061	0.091	0.849	ICC1
3 :7	39.66	60.34	75	0.047	0.110	0.843	ICC1
2 :8	27.72	72.28	75	0.033	0.131	0.836	ICC1
1 :9	14.56	85.44	75	0.017	0.153	0.830	ICC1+CaCl <sub>2</sub>

Table S2. Experimental data for the dissolution points of suspensions of table S1 at 25 °C.

Initial composition ETI:CaCl <sub>2</sub> (mole)	Total amount of H <sub>2</sub> O (μL)	Composition at dissolution point			Composition at dissolution point (mol%)		
		ETI (mg)	CaCl <sub>2</sub> (mg)	H <sub>2</sub> O (μL)	ETI	CaCl <sub>2</sub>	H <sub>2</sub> O
10 :0	120	100	0	120	0.081	0.000	0.919
9 :1	133	93.24	6.76	133	0.069	0.008	0.924
8 :2	133	85.98	14.02	133	0.063	0.016	0.921
7 :3	127	78.16	21.84	127	0.060	0.026	0.915
6 :4	119	69.7	30.3	119	0.056	0.037	0.906
5 :5	146	60.53	39.47	146	0.040	0.040	0.919
4 :6	167	50.56	49.44	167	0.030	0.045	0.926
3 :7	186	39.66	60.34	186	0.021	0.049	0.930
2 :8	208	27.72	72.28	208	0.013	0.053	0.934
1 :9	214	14.56	85.44	214	0.007	0.061	0.933
0 :10	99	0	100	99	0.000	0.141	0.859

Table S3. Experimental data for the suspensions of the system LEV-CaCl<sub>2</sub>·2H<sub>2</sub>O-H<sub>2</sub>O at 25 °C

Initial composition LEV:CaCl <sub>2</sub> (mole)	Initial components			Initial components (mol%)			solid phase at equilibrium
	LEV (mg)	CaCl <sub>2</sub> (mg)	H <sub>2</sub> O (μL)	LEV	CaCl <sub>2</sub>	H <sub>2</sub> O	

9 :1	93.24	6.76	60	0.139	0.015	0.845	LEV
8 :2	85.98	14.02	60	0.128	0.032	0.841	LEV
7 :3	78.16	21.84	60	0.115	0.049	0.835	LEV+ICC2
6 :4	69.7	30.3	60	0.102	0.068	0.830	ICC2
5 :5	60.53	39.47	60	0.088	0.088	0.824	ICC2
4 :6	50.56	49.44	60	0.073	0.109	0.818	ICC2
3 :7	39.66	60.34	60	0.057	0.132	0.811	ICC2
2 :8	27.72	72.28	60	0.039	0.157	0.804	ICC2+CaCl <sub>2</sub>
1 :9	14.56	85.44	60	0.020	0.184	0.796	ICC2+CaCl <sub>2</sub>

Table S4. Experimental data for the dissolution points of suspensions of Table S3 at 25 °C.

Initial composition LEV:CaCl <sub>2</sub> (mole)	Total amount of H <sub>2</sub> O (μL)	Composition at dissolution point			Composition at dissolution point (mol%)		
		LEV (mg)	CaCl <sub>2</sub> (mg)	H <sub>2</sub> O (μL)	LEV	CaCl <sub>2</sub>	H <sub>2</sub> O
10 :0	95	100	0	95	0.100	0.000	0.900
9 :1	103	93.24	6.76	103	0.087	0.010	0.903
8 :2	103	85.98	14.02	103	0.080	0.020	0.900
7 :3	97	78.16	21.84	97	0.076	0.033	0.891
6 :4	85	69.7	30.3	85	0.076	0.051	0.873
5 :5	109	60.53	39.47	109	0.053	0.053	0.894
4 :6	125	50.56	49.44	125	0.039	0.058	0.903
3 :7	145	39.66	60.34	145	0.026	0.062	0.912
2 :8	165	27.72	72.28	165	0.016	0.065	0.918
1 :9	175	14.56	85.44	175	0.008	0.073	0.919
0 :10	99	0	100	99	0.000	0.141	0.859

Table S5. Experimental data for suspensions of system ETI-LEV-H<sub>2</sub>O system at 25 °C

Initial composition ETI: LEV (mole)	Initial components			Initial components (mol%)			solid phase at equilibrium
	ETI (mg)	LEV(mg)	H <sub>2</sub> O (μL)	ETI	LEV	H <sub>2</sub> O	
9 :1	90	10	50	0.157	0.017	0.825	ETI
8 :2	80	20	50	0.140	0.035	0.825	ETI
7 :3	70	30	50	0.122	0.052	0.825	ETI
6 :4	60	40	50	0.105	0.070	0.825	ETI
5 :5	50	50	50	0.087	0.087	0.825	ETI
4 :6	40	60	50	0.070	0.105	0.825	ETI+LEV
3 :7	30	70	50	0.052	0.122	0.825	ETI+LEV
2 :8	20	80	50	0.035	0.140	0.825	ETI+LEV
1 :9	10	90	50	0.017	0.157	0.825	LEV

Table S6. Experimental data for the dissolution points of suspensions of Table S5 at 25 °C.

Initial composition ETI: LEV (mole)	Total amount of H <sub>2</sub> O (μL)	Composition at dissolution point			Composition at dissolution point (mol%)		
		ETI (mg)	LEV(mg)	H <sub>2</sub> O(μL)	ETI	LEV	H <sub>2</sub> O

10 :0	120	100	0	120	0.081	0.000	0.919
9 :1	118	90	10	118	0.074	0.008	0.918
8 :2	116	80	20	116	0.067	0.017	0.916
7 :3	111	70	30	111	0.061	0.026	0.913
6 :4	103	60	40	103	0.056	0.037	0.907
5 :5	96	50	50	96	0.050	0.050	0.901
4 :6	84	40	60	84	0.045	0.067	0.888
3 :7	79	30	70	79	0.035	0.083	0.882
2 :8	76	20	80	76	0.024	0.098	0.878
1 :9	85	10	90	85	0.011	0.100	0.889
0 :10	95	0	100	95	0.000	0.100	0.900

Table S7. Experimental data for cut planes using a fixed mole ratio of organic compound/CaCl<sub>2</sub> at 25 °C

Initial components				Initial components (mol%)				solid phase at equilibrium
ETI (mg)	LEV (mg)	CaCl <sub>2</sub> (mg)	H <sub>2</sub> O (μL)	ETI	LEV	CaCl <sub>2</sub>	H <sub>2</sub> O	
(ETI+LEV): CaCl <sub>2</sub> is 5:1								
100	0	13.04	70	0.128	0.000	0.026	0.846	ETI
90	10	13.04	70	0.115	0.013	0.026	0.846	ETI
80	20	13.04	70	0.102	0.026	0.026	0.846	ETI
70	30	13.04	70	0.090	0.038	0.026	0.846	ETI
60	40	13.04	70	0.077	0.051	0.026	0.846	ETI
50	50	13.04	70	0.064	0.064	0.026	0.846	ETI
40	60	13.04	70	0.051	0.077	0.026	0.846	ETI+LEV
30	70	13.04	70	0.038	0.090	0.026	0.846	ETI+LEV
20	80	13.04	70	0.026	0.102	0.026	0.846	LEV
10	90	13.04	70	0.013	0.115	0.026	0.846	LEV
0	100	13.04	70	0.000	0.128	0.026	0.846	LEV
(ETI+LEV): CaCl <sub>2</sub> is 4:1								
100	0	16.30	70	0.127	0.000	0.032	0.841	ETI
90	10	16.30	70	0.114	0.013	0.032	0.841	ETI
80	20	16.30	70	0.102	0.025	0.032	0.841	ETI
70	30	16.30	70	0.089	0.038	0.032	0.841	ETI
60	40	16.30	70	0.076	0.051	0.032	0.841	ETI
50	50	16.30	70	0.064	0.064	0.032	0.841	ETI
40	60	16.30	70	0.051	0.076	0.032	0.841	ETI+LEV
30	70	16.30	70	0.038	0.089	0.032	0.841	ETI+LEV
20	80	16.30	70	0.025	0.102	0.032	0.841	LEV
10	90	16.30	70	0.013	0.114	0.032	0.841	LEV
0	100	16.30	70	0.000	0.127	0.032	0.841	LEV
(ETI+LEV): CaCl <sub>2</sub> is 3:1								
100	0	21.73	70	0.126	0.000	0.042	0.832	ETI+ICC1
90	10	21.73	70	0.113	0.013	0.042	0.832	ETI+ICC3
80	20	21.73	70	0.101	0.025	0.042	0.832	ETI+ICC3

70	30	21.73	70	0.088	0.038	0.042	0.832	ETI+ICC3
60	40	21.73	70	0.076	0.050	0.042	0.832	ETI+ICC3
50	50	21.73	70	0.063	0.063	0.042	0.832	ETI+LEV+ICC3
40	60	21.73	70	0.050	0.076	0.042	0.832	ETI+LEV+ICC3
30	70	21.73	70	0.038	0.088	0.042	0.832	ETI+LEV+ICC3
20	80	21.73	70	0.025	0.101	0.042	0.832	LEV+ICC3
10	90	21.73	70	0.013	0.113	0.042	0.832	LEV+ICC3
0	100	21.73	70	0.000	0.126	0.042	0.832	LEV

(ETI+LEV): CaCl<sub>2</sub> is 2:1

100	0	32.60	70	0.123	0.000	0.062	0.815	ETI+ICC1
90	10	32.60	70	0.111	0.012	0.062	0.815	ETI+ICC3
80	20	32.60	70	0.099	0.025	0.062	0.815	ETI+ICC3
70	30	32.60	70	0.086	0.037	0.062	0.815	ETI+LEV+ICC3
60	40	32.60	70	0.074	0.049	0.062	0.815	ETI+LEV+ICC3
50	50	32.60	70	0.062	0.062	0.062	0.815	ETI+LEV+ICC3
40	60	32.60	70	0.049	0.074	0.062	0.815	ETI+LEV+ICC3
30	70	32.60	70	0.037	0.086	0.062	0.815	ETI+LEV+ICC3
20	80	32.60	70	0.025	0.099	0.062	0.815	LEV+ICC3
10	90	32.60	70	0.012	0.111	0.062	0.815	LEV+ICC3
0	100	32.60	70	0.000	0.123	0.062	0.815	LEV+ICC2

(ETI+LEV): CaCl<sub>2</sub> is 3:2

100	0	43.47	80	0.108	0.000	0.072	0.819	ICC3
90	10	43.47	80	0.098	0.011	0.072	0.819	ICC3
80	20	43.47	80	0.087	0.022	0.072	0.819	ICC3
70	30	43.47	80	0.076	0.033	0.072	0.819	ICC3
60	40	43.47	80	0.065	0.043	0.072	0.819	ICC3
50	50	43.47	80	0.054	0.054	0.072	0.819	ICC3
40	60	43.47	80	0.043	0.065	0.072	0.819	ICC3
30	70	43.47	80	0.033	0.076	0.072	0.819	ICC3
20	80	43.47	80	0.022	0.087	0.072	0.819	ICC3
10	90	43.47	80	0.011	0.098	0.072	0.819	ICC3
0	100	43.47	80	0.000	0.108	0.072	0.819	ICC3

(ETI+LEV): CaCl<sub>2</sub> is 1:1

100	0	65.20	120	0.075	0.000	0.075	0.850	ICC3
90	10	65.20	120	0.067	0.007	0.075	0.850	ICC3
80	20	65.20	120	0.060	0.015	0.075	0.850	ICC3
70	30	65.20	120	0.052	0.022	0.075	0.850	ICC3
60	40	65.20	120	0.045	0.030	0.075	0.850	ICC3
50	50	65.20	120	0.037	0.037	0.075	0.850	ICC3
40	60	65.20	120	0.030	0.045	0.075	0.850	ICC3
30	70	65.20	120	0.022	0.052	0.075	0.850	ICC3
20	80	65.20	120	0.015	0.060	0.075	0.850	ICC3
10	90	65.20	120	0.007	0.067	0.075	0.850	ICC3
0	100	65.20	120	0.000	0.075	0.075	0.850	ICC3

(ETI+LEV): CaCl <sub>2</sub> is 2:3								
100	0	97.80	140	0.064	0.000	0.095	0.841	ICC3
90	10	97.80	140	0.057	0.006	0.095	0.841	ICC3
80	20	97.80	140	0.051	0.013	0.095	0.841	ICC3
70	30	97.80	140	0.045	0.019	0.095	0.841	ICC3
60	40	97.80	140	0.038	0.025	0.095	0.841	ICC3
50	50	97.80	140	0.032	0.032	0.095	0.841	ICC3
40	60	97.80	140	0.025	0.038	0.095	0.841	ICC3
30	70	97.80	140	0.019	0.045	0.095	0.841	ICC3
20	80	97.80	140	0.013	0.051	0.095	0.841	ICC3
10	90	97.80	140	0.006	0.057	0.095	0.841	ICC3
0	100	97.80	140	0.000	0.064	0.095	0.841	ICC3
(ETI+LEV): CaCl <sub>2</sub> is 3:7								
100	0	152.14	160	0.054	0.000	0.126	0.819	ICC3
80	20	152.14	160	0.043	0.011	0.126	0.819	ICC3
60	40	152.14	160	0.033	0.022	0.126	0.819	ICC3
40	60	152.14	160	0.022	0.033	0.126	0.819	ICC3
20	80	152.14	160	0.011	0.043	0.126	0.819	ICC3
0	100	152.14	160	0.000	0.054	0.126	0.819	ICC3
(ETI+LEV): CaCl <sub>2</sub> is 1:4								
100	0	260.81	200	0.045	0.000	0.105	0.850	ICC3
80	20	260.81	200	0.036	0.009	0.105	0.850	ICC3
60	40	260.81	200	0.027	0.018	0.105	0.850	ICC3
40	60	260.81	200	0.018	0.027	0.105	0.850	ICC3
20	80	260.81	200	0.009	0.036	0.105	0.850	ICC3
0	100	260.81	200	0.000	0.045	0.105	0.850	ICC3

Table S8. Experimental data for the dissolution points of suspensions of Table S7 at 25 °C

Composition at dissolution point				Composition at dissolution point (mol%)			relative mole amount of H <sub>2</sub> O
ETI (mg)	LEV(mg)	CaCl <sub>2</sub> (mg)	H <sub>2</sub> O (μL)	ETI	LEV	CaCl <sub>2</sub>	
(ETI+LEV): CaCl <sub>2</sub> is 5:1							
100	0	13.04	145	0.833	0.000	0.167	11.414
90	10	13.04	161	0.750	0.083	0.167	12.673
80	20	13.04	144	0.667	0.167	0.167	11.335
70	30	13.04	134	0.583	0.250	0.167	10.548
60	40	13.04	134	0.500	0.333	0.167	10.548
50	50	13.04	127	0.417	0.417	0.167	9.997
40	60	13.04	109	0.333	0.500	0.167	8.580
30	70	13.04	92	0.250	0.583	0.167	7.242
20	80	13.04	97	0.167	0.667	0.167	7.635
10	90	13.04	108	0.083	0.750	0.167	8.501
0	100	13.04	118	0.000	0.833	0.167	9.288

(ETI+LEV): CaCl <sub>2</sub> is 4:1							
100	0	16.30	155	0.800	0.000	0.200	11.713
90	10	16.30	159	0.720	0.080	0.200	12.015
80	20	16.30	155	0.640	0.160	0.200	11.713
70	30	16.30	153	0.560	0.240	0.200	11.561
60	40	16.30	153	0.480	0.320	0.200	11.561
50	50	16.30	125	0.400	0.400	0.200	9.446
40	60	16.30	115	0.320	0.480	0.200	8.690
30	70	16.30	97	0.240	0.560	0.200	7.330
20	80	16.30	101	0.160	0.640	0.200	7.632
10	90	16.30	108	0.080	0.720	0.200	8.161
0	100	16.30	119	0.000	0.800	0.200	8.992
(ETI+LEV): CaCl <sub>2</sub> is 3:1							
100	0	21.73	163	0.750	0.000	0.250	11.548
90	10	21.73	159	0.675	0.075	0.250	11.264
80	20	21.73	155	0.600	0.150	0.250	10.981
70	30	21.73	149	0.525	0.225	0.250	10.556
60	40	21.73	149	0.450	0.300	0.250	10.556
50	50	21.73	129	0.375	0.375	0.250	9.139
40	60	21.73	121	0.300	0.450	0.250	8.572
30	70	21.73	100	0.225	0.525	0.250	7.085
20	80	21.73	116	0.150	0.600	0.250	8.218
10	90	21.73	115	0.075	0.675	0.250	8.147
0	100	21.73	126	0.000	0.750	0.250	8.927
(ETI+LEV): CaCl <sub>2</sub> is 2:1							
100	0	32.60	168	0.667	0.000	0.333	10.548
90	10	32.60	160	0.600	0.067	0.333	10.075
80	20	32.60	160	0.533	0.133	0.333	10.075
70	30	32.60	153	0.467	0.200	0.333	9.603
60	40	32.60	142	0.400	0.267	0.333	8.910
50	50	32.60	125	0.333	0.333	0.333	7.871
40	60	32.60	120	0.267	0.400	0.333	7.557
30	70	32.60	120	0.200	0.467	0.333	7.525
20	80	32.60	113	0.133	0.533	0.333	7.084
10	90	32.60	118	0.067	0.600	0.333	7.399
0	100	32.60	124	0.000	0.667	0.333	7.808
(ETI+LEV): CaCl <sub>2</sub> is 3:2							
100	0	43.47	170	0.600	0.000	0.400	9.634
90	10	43.47	170	0.540	0.060	0.400	9.634
80	20	43.47	166	0.480	0.120	0.400	9.408
70	30	43.47	165	0.420	0.180	0.400	9.351
60	40	43.47	164	0.360	0.240	0.400	9.294
50	50	43.47	164	0.300	0.300	0.400	9.294
40	60	43.47	156	0.240	0.360	0.400	8.841

30	70	43.47	155	0.180	0.420	0.400	8.784
20	80	43.47	152	0.120	0.480	0.400	8.614
10	90	43.47	124	0.060	0.540	0.400	7.027
0	100	43.47	121	0.000	0.600	0.400	6.857
(ETI+LEV): CaCl <sub>2</sub> is 1:1							
100	0	65.20	240	0.500	0.000	0.500	11.335
90	10	65.20	236	0.450	0.050	0.500	11.146
80	20	65.20	234	0.400	0.100	0.500	11.052
70	30	65.20	235	0.350	0.150	0.500	11.099
60	40	65.20	231	0.300	0.200	0.500	10.910
50	50	65.20	231	0.250	0.250	0.500	10.910
40	60	65.20	223	0.200	0.300	0.500	10.532
30	70	65.20	212	0.150	0.350	0.500	10.012
20	80	65.20	207	0.100	0.400	0.500	9.776
10	90	65.20	179	0.050	0.450	0.500	8.454
0	100	65.20	178	0.000	0.500	0.500	8.407
(ETI+LEV): CaCl <sub>2</sub> is 2:3							
100	0	97.80	328	0.400	0.000	0.600	12.393
90	10	97.80	324	0.360	0.040	0.600	12.242
80	20	97.80	323	0.320	0.080	0.600	12.204
70	30	97.80	322	0.280	0.120	0.600	12.166
60	40	97.80	323	0.240	0.160	0.600	12.204
50	50	97.80	310	0.200	0.200	0.600	11.713
40	60	97.80	297	0.160	0.240	0.600	11.222
30	70	97.80	298	0.120	0.280	0.600	11.259
20	80	97.80	280	0.080	0.320	0.600	10.579
10	90	97.80	250	0.040	0.360	0.600	9.446
0	100	97.80	247	0.000	0.400	0.600	9.332
(ETI+LEV): CaCl <sub>2</sub> is 3:7							
100	0	152.14	472	0.300	0.000	0.700	13.375
80	20	152.14	465	0.240	0.060	0.700	13.176
60	40	152.14	450	0.180	0.120	0.700	12.751
40	60	152.14	423	0.120	0.180	0.700	11.986
20	80	152.14	394	0.060	0.240	0.700	11.165
0	100	152.14	370	0.000	0.300	0.700	10.485
(ETI+LEV): CaCl <sub>2</sub> is 1:4							
100	0	260.81	740	0.200	0.000	0.800	13.979
80	20	260.81	731	0.160	0.040	0.800	13.809
60	40	260.81	714	0.120	0.080	0.800	13.488
40	60	260.81	710	0.080	0.120	0.800	13.413
20	80	260.81	653	0.040	0.160	0.800	12.336
0	100	260.81	585	0.000	0.200	0.800	11.051

**Graph of XRPD of solid solution**

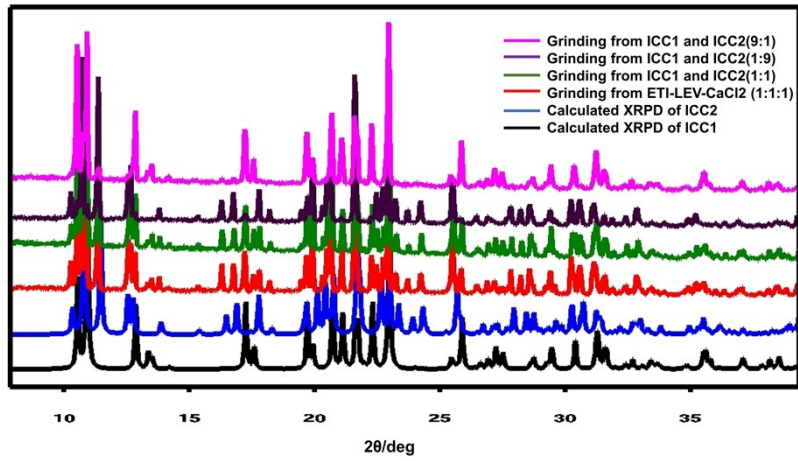


Figure S1. XRPD result of solid solution.

### Full version graphs of phase diagrams

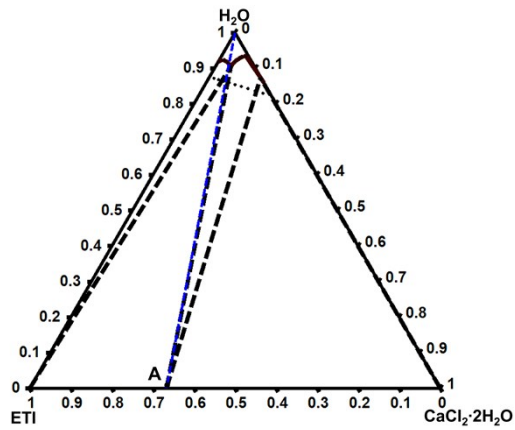


Figure S2. Full version of TPD for ETI- CaCl<sub>2</sub>- H<sub>2</sub>O system.

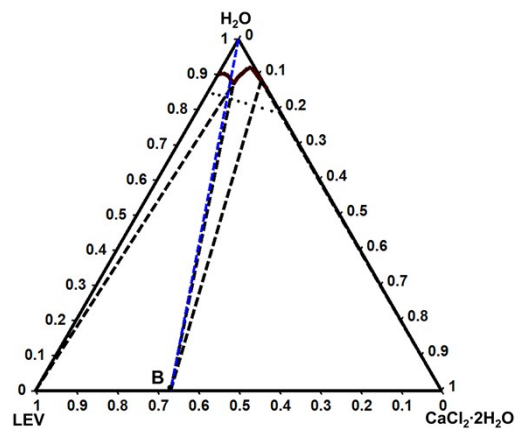


Figure S3. Full version of TPD for LEV- CaCl<sub>2</sub>- H<sub>2</sub>O system.



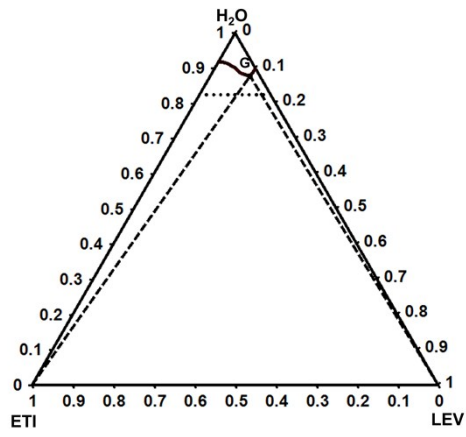


Figure S4. Full version of TPD for ETI- LEV- H<sub>2</sub>O system.