Electronic Supporting Information

Tuning mechanical behaviour by controlling structure of a series of theophylline co-crystals

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Table S1. Crystallographic Data and structure refinement parameters of THP co-crystals.

	THP-PIC (2:1)	**THP-DCB (1:2)**	**THP-4Cl3NB (1:1)**	**THP-4F3NB (1:1)**	**THP-HBEN (1:1)**	**THP-ACZ (1:1)**
Chemical Formula	$2(C_7H_8N_4O_2)$, $C_6H_6N_2O$	$C_7H_8N_4O_2$, $2(C_7H_4Cl_2O_2)$	$C_7H_4ClNO_4$, $C_7H_8N_4O_2$	$C_7H_4FNO_4$, $C_7H_8N_4O_2$	$C_7H_8N_4O_2$, $C_7H_7NO_2$	$C_4H_6N_4O_3S_2$, $C_7H_8N_4O_2$
Formula weight	482.48	562.18	381.74	365.29	317.31	402.42
Cryst sys	Triclinic	Triclinic	Triclinic	Triclinic	Orthorhombic	Monoclinic
Space group	*P-1*	*P-1*	*P-1*	*P-1*	*Pbcn*	*C2/c*
a (Å)	8.0597(7)	10.191(3)	7.0637(4)	7.203(4)	8.0218(9)	42.668(6)
b (Å)	9.6051(9)	10.459(3)	15.1470(8)	14.913(9)	14.3076(15)	4.9516(8)
c (Å)	14.2402(13)	12.777(3)	15.4381(8)	16.014(10)	25.258(3)	16.838(3)
α (°)	96.817(2)	98.980(5)	69.6240(10)	63.098(10)	90	90
β (°)	99.412(2)	108.898(5)	81.8190(10)	86.349(12)	90	106.575(6)
γ (°)	103.672(2)	108.434(5)	86.3240(10)	84.677(12)	90	90
Vol (Å^3)	1042.40(16)	1170.6(5)	1532.48(14)	1527.0(16)	2898.9(5)	3409.5(9)
D_{calcd} (g/cm^3)	1.537	1.595	1.655	1.589	1.454	1.568
μ (mm^{-1})	0.116	0.553	0.297	0.134	0.110	0.356
θ range (°)	2.21-27	1.76-27	2.34-27	1.43-27	2.85-26.99	1.0-26.99
Z	2	2	4	4	8	8
range *h*	–8 to +10	–13 to +12	–9 to +9	–9 to +9	–10 to +10	–54 to +54
range *k*	–12 to +12	–13 to +12	–13 to +19	–19 to +19	–18 to +16	–6 to +6
range *l*	–18 to +18	–16 to +16	–16 to +19	–20 to +20	–26 to +32	–21 to +21
Reflns collected	17506	14470	20410	24045	13720	25984
Independent reflns	4557	4908	6677	6643	3170	3728
Obsd reflns	3992	2893	5873	3135	2466	2642
T (K)	100 (K)	296 (K)	100 (K)	296	100 (K)	296 (K)
*R*1	0.0359	0.0442	0.0328	0.1225	0.0425	0.0403
*wR*2	0.0897	0.1041	0.0866	0.2934	0.0902	0.1107
GOF	1.038	1.013	1.053	1.065	1.020	1.074
CCDC	915067	915068	915066	915070	915071	915069

Table S2. Geometrical Parameters of H bonds in all co-crystals

D—H···A (Å)	D—H (Å)	H···A(Å)	D···A (Å)	D—H···A (deg)
THP-PIC				
D—H···A (Å)	**D—H (Å)**	**H···A(Å)**	**D···A (Å)**	**D—H···A (deg)**
N5—H1···O3	0.86	1.95	2.7991(13)	170
N11—H4···O2	0.75	2.11	2.8249(15)	159
N11—H5···N10	0.886(17)	2.293(17)	2.6750(16)	105.9(13)
N11—H5···N9	0.886(17)	2.556(18)	3.1774(16)	127.8(13)
N8—H23···O6	0.86	1.94	2.7886(14)	167
C5—H5B···O1	0.96	2.32	2.7310(17)	105
C6 —H6C···N4	0.96	2.52	2.9502(17)	107
C8 —H8···O3	0.93	2.45	3.2800(16)	148
C10—H10···O1	0.93	2.60	3.2682(17)	129
C12 —H12···N4	0.93	2.53	3.4457(17)	168
C19 —H19···O2	0.93	2.28	3.1241(16)	150
C21—H21C···O7	0.96	2.34	2.6928(17)	101
C24—H24A···N9	0.96	2.55	2.9543(16)	106
THP-DCB				
D—H···A (Å)	**D—H (Å)**	**H···A(Å)**	**D···A (Å)**	**D—H···A (deg)**
N4—H4···O5	0.88(3)	1.91(3)	2.779(5)	170(2)
O4—H5···O3	0.82	1.84	2.645(3)	168
O6—H6···N2	0.82	1.89	2.708(4)	175
C4—H4B···O2	0.96	2.29	2.688(5)	104
C7—H7A···O2	0.96	2.30	2.728(5)	106
C7—H7C···O7	0.96	2.52	3.394(5)	151
C18—H18···O2	0.93	2.24	3.137(4)	163

THP-4Cl3NB

D—H···A (Å)	D—H (Å)	H···A(Å)	D···A (Å)	D—H···A (deg)
N1—H1···O11	0.86	1.91	2.7583(16)	167
O5—H5···N4	0.82	1.84	2.6547(17)	177
O8—H8···N9	0.82	1.88	2.6602(17)	158
N10—H10···O1	0.86	1.86	2.7036(16)	168
C4—H4A···O1	0.96	2.30	2.7102(19)	105
C4—H4B···O10	0.96	2.58	3.279(2)	130
C7—H7B···O2	0.96	2.37	2.7825(19)	105
C7—H7B···O7	0.96	2.55	3.465(2)	160
C13—H13···O12	0.93	2.46	3.067(2)	123
C14—H14···O5	0.93	2.39	2.7142(18)	100
C14—H14···O12	0.93	2.54	3.1067(19)	119
C17—H17···O2	0.93	2.43	3.3585(19)	172
C20—H20···O8	0.93	2.39	2.714(2)	100
C21—H21···O4	0.93	2.39	3.290(2)	163
C22—H22B···O12	0.96	2.37	2.7069(19)	100
C22—H22C···Cl2	0.96	2.80	3.5901(16)	140
C26—H26A···N9	0.96	2.58	2.984(2)	105
C26—H26C···O7	0.96	2.51	3.4202(19)	159
C27—H27···O6	0.93	2.59	3.478(2)	161

THP-4F3NB Co-crystal

D—H···A (Å)	D—H (Å)	H···A(Å)	D···A (Å)	D—H···A (deg)
N3—H3···O3	0.86	1.86	2.714(2)	174
O4—H4···O2	0.82	1.87	2.6833(18)	175
N5—H5A···N2	0.91(2)	2.29(2)	3.170(2)	162(2)
N5—H6A···O1	0.90(2)	2.07(2)	2.963(2)	173(2)
C4—H4B···N2	0.96	2.55	2.964(3)	106
C6—H6···O1	0.93	2.25	3.070(2)	146
C7—H7B···O1	0.96	2.34	2.737(2)	104

C10—H10···O3	0.93	2.44	2.761(2)	100

THP-4F3NB

D—H···A (Å)	**D—H (Å)**	**H···A(Å)**	**D···A (Å)**	**D—H···A (deg)**
N1—H3···O7	0.86	1.88	2.732(7)	169
O3—H3A···N2A	0.82	1.86	2.659(7)	166
O10—H10···N9	1.09(4)	1.62(5)	2.665(6)	160(4)
N10—H22···O2	0.86	1.87	2.719(7)	168
C2—H2B···O1	0.96	2.27	2.673(8)	104
C2—H2B···O12	0.96	2.58	3.400(7)	144
C3—H3C···O1	0.96	2.39	2.773(7)	104
C3—H3C···O8	0.96	2.43	3.354(8)	161
C13—H13···O6	0.93	2.54	3.134(7)	122
C14—H14···O6	0.93	2.50	3.118(8)	124
C18—H18···O4	0.93	2.48	3.383(6)	164
C20—H20C···O6	0.96	2.22	2.674(8)	108
C21—H21B···N9	0.96	2.55	2.976(8)	107
C26—H26···O1	0.93	2.40	3.328(7)	176
C28—H28···O10	0.93	2.40	2.715(7)	100
C29—H29···O5A	0.93	2.46	3.386(8)	172

THP-ACZ

D—H···A (Å)	**D—H (Å)**	**H···A(Å)**	**D···A (Å)**	**D—H···A (deg)**
N1—H1···O5	0.82(3)	2.06(3)	2.860(3)	166(3)
N2—H2···N3	0.86	1.99	2.846(3)	172
N1—H3···O1	0.83(3)	2.04(3)	2.869(3)	174(3)
N6—H6···O4	0.86	1.93	2.773(3)	169
C5—H5A···O4	0.96	2.28	2.733(4)	108
C8—H8···N8	0.93	2.56	3.484(3)	170
C11—H11A···O5	0.96	2.42	2.768(3)	101
C11—H11C···O2	0.96	2.46	3.098(4)	124
C11—H11C···O2	0.96	2.46	3.098(4)	124

PXRD

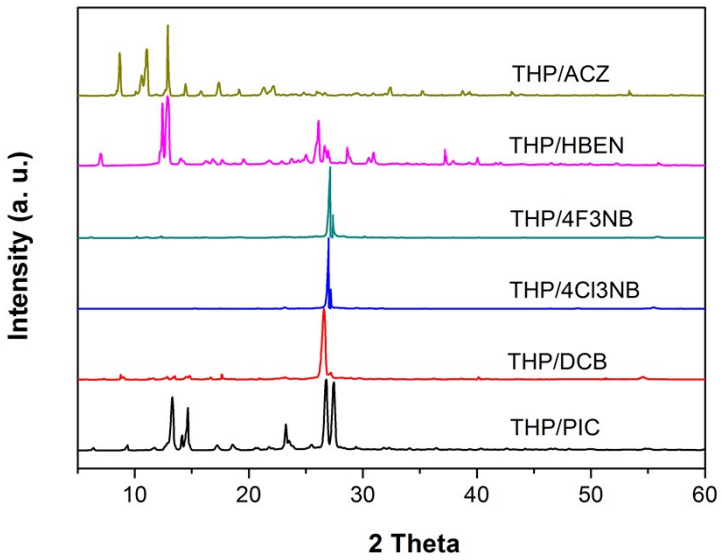

Fig. S1 PXRD profile of THP co-crystals.

FTIR Spectra

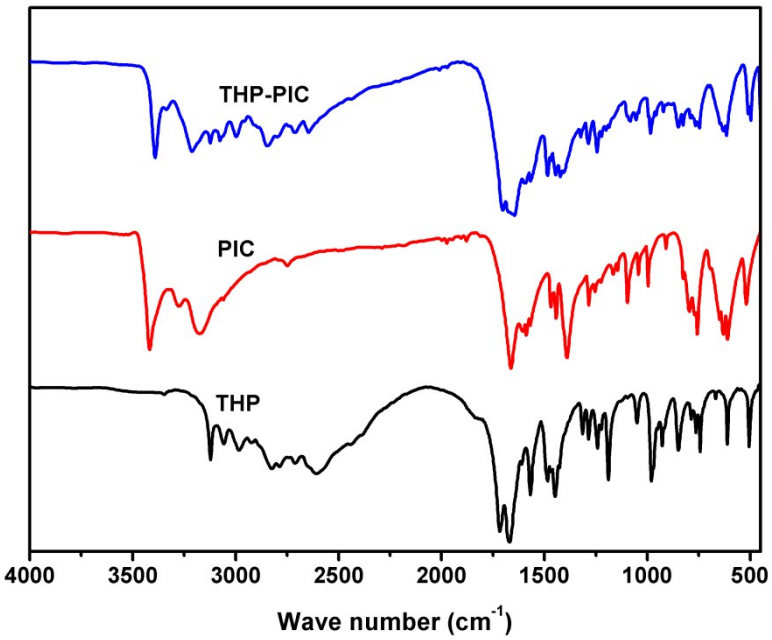

Fig. S2 Comparison of FTIR spectra of THP, PIC and its co-crystal, THP-PIC.

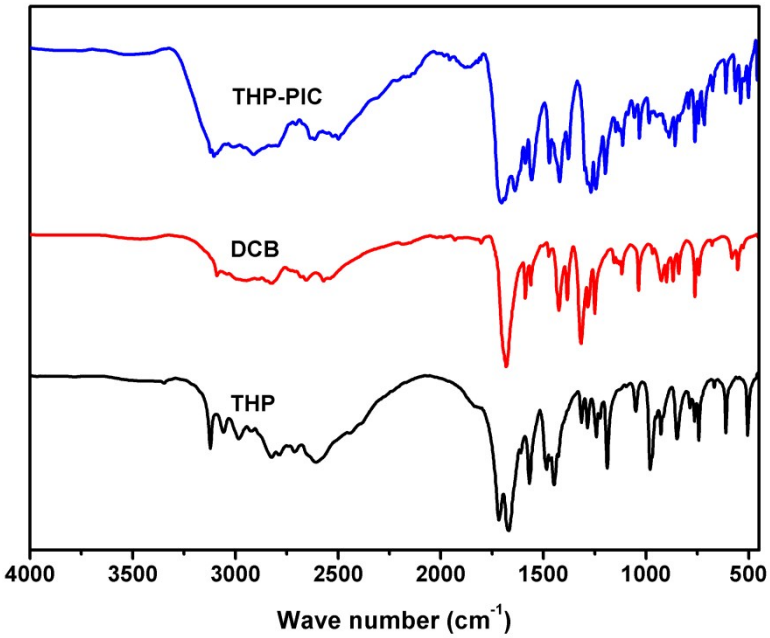

Fig. S3 Comparison of FTIR spectra of THP, DIC and its co-crystal, THP-DIC.

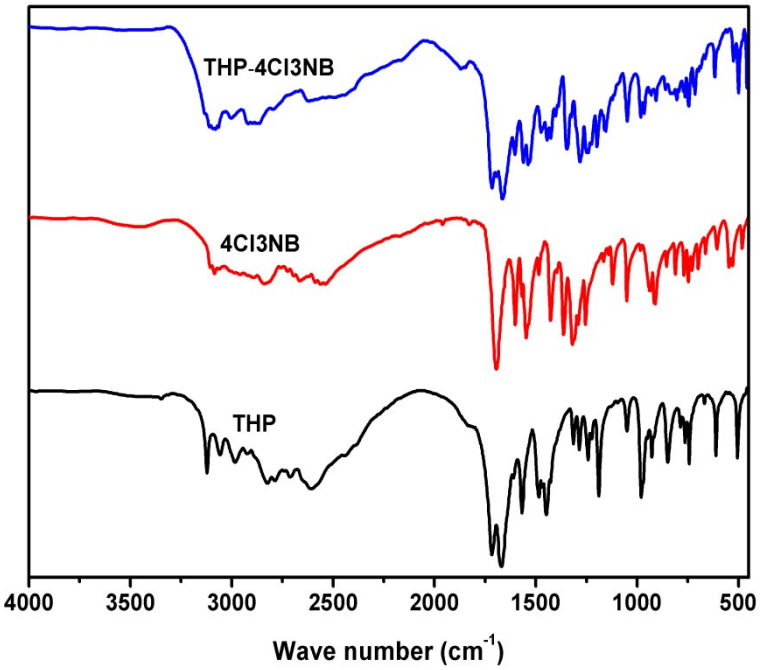

Fig. S4 Comparison of FTIR spectra of THP, 4Cl3NB and its co-crystal, THP-4Cl3NB.

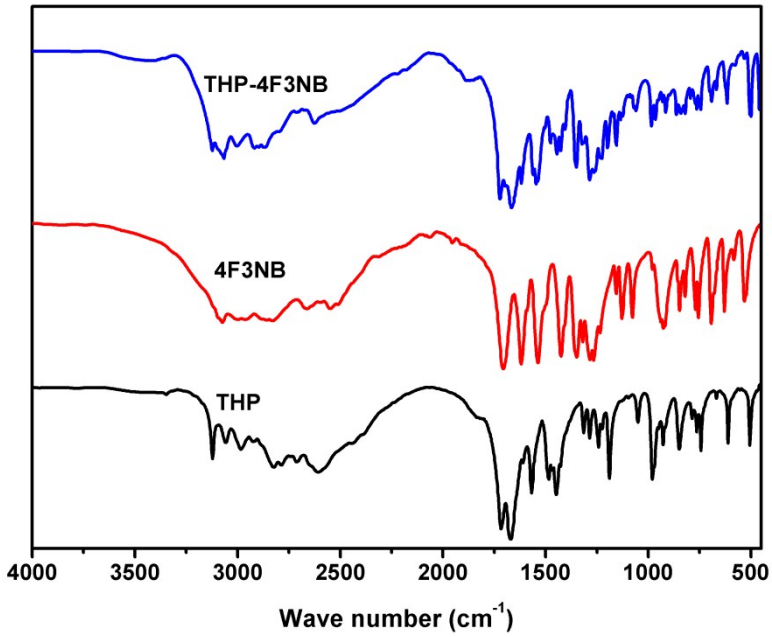

Fig. S5 Comparison of FTIR spectra of THP, 4F3NB and its co-crystal, THP-4F3NB.

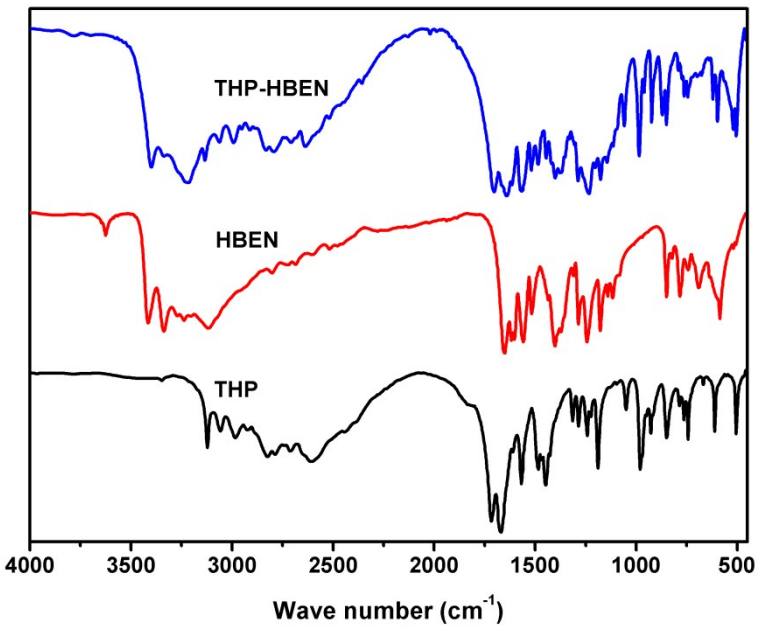

Fig. S6 Comparison of FTIR spectra of THP, HBEN and its co-crystal, THP-HBEN.

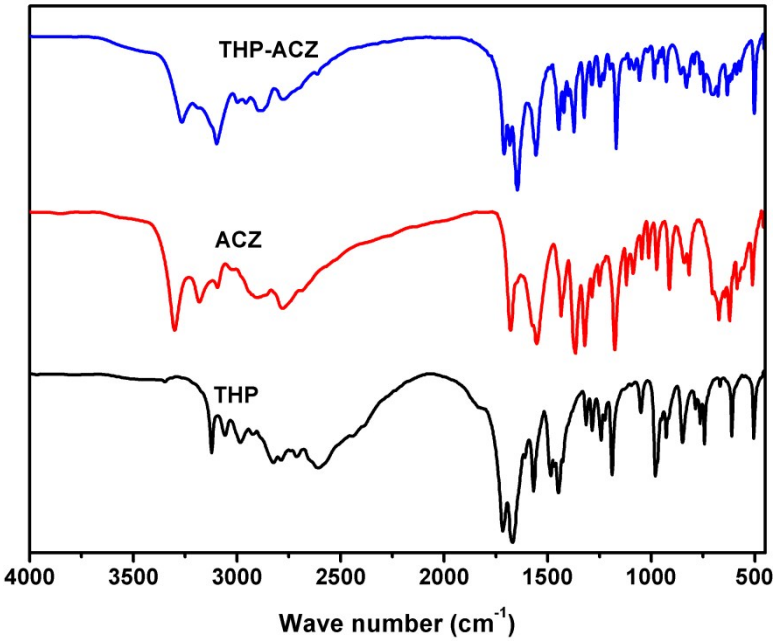

Fig. S7 Comparison of FTIR spectra of THP, ACZ and its co-crystal, THP-ACZ.

Table S3. Melting Points of Theophylline, Co-Crystals with Various Co-Formers.

Sample code	mp (°C) T_{max} from DSC	Co-former mp (°C)[a]
THP	273.2	
THP-PIC	188.0	110
THP-DCB	184.1	204-206
THP-4Cl3NB	211.2	181-184
THP-4F3NB	190.2	123-126
THP-HBEN	233.8	161-162
THP-ACZ	229.2	258-259

[a] Melting point values as reported in Sigma-Aldrich chemical catalog.

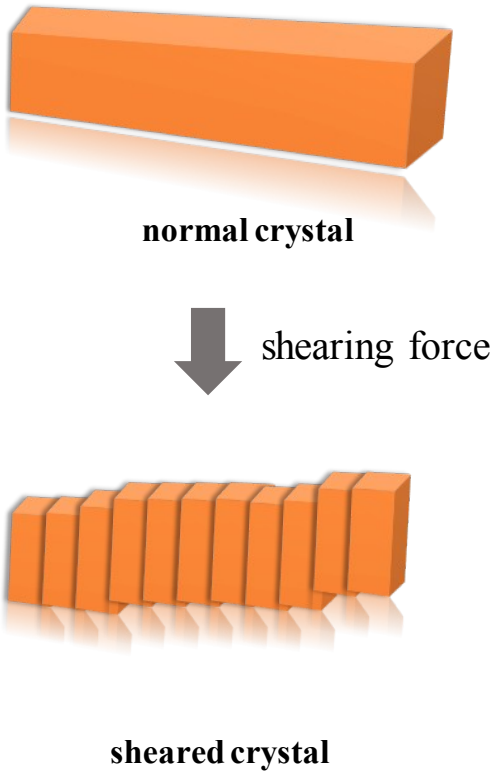

Fig. S8 Schematic representation of shearing of crystal upon applying mechanical force.

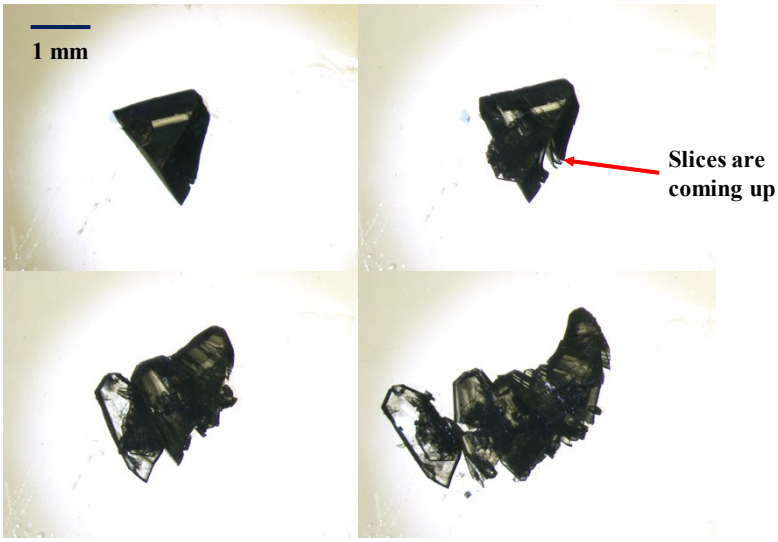

Fig. S9 Stepwise shearing of THP-4Cl3NB crystal.

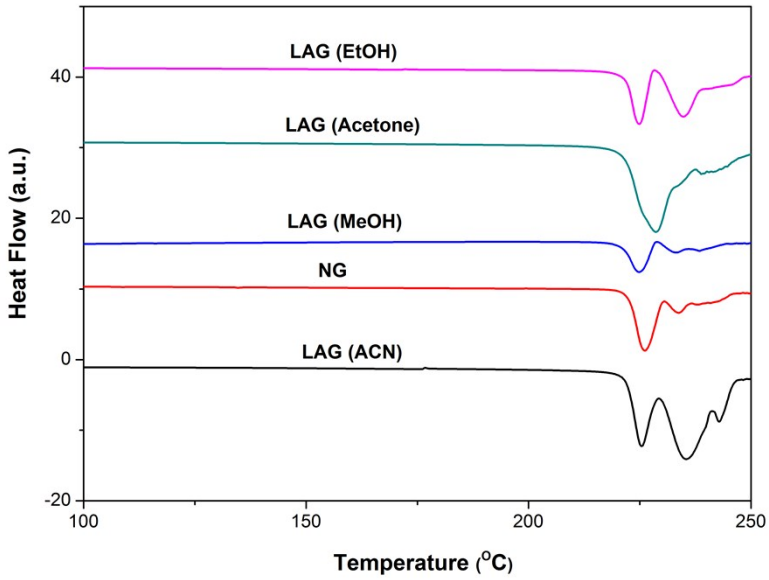

Fig. S10 DSC thermogram of compositions obtained from different solvents (LAG) and neat grinded (NG) samples of THP-ACZ co-crystal.