Does Stoichiometry Matter? Cocrystals of Aliphatic Dicarboxylic Acids with Isonicotinamide: Odd-even Alternation in Melting points

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Section S1: Cocrystals synthesis

All starting materials were purchased from Sigma Aldrich and used without purification.

Pimelic acid: isonicotinamide 1:2 cocrystal (**1**). Pimelic acid and isonicotinamide were taken in a 1:2 molar ratio and ground after adding 2-3 drops of EtOH (solvent drop grinding). The ground sample was dissolved in a minimum amount of two solvent systems, THF and a combination of $CHCl_3$ and MeOH. These solutions were kept at room temperature for slow evaporation. Good quality crystals, suitable for diffraction, were obtained after three days.

Suberic acid: isonicotinamide 1:2 cocrystal (**2**). Suberic acid and isonicotinamide were taken in a 1:2 molar ratio and ground after adding 2-3 drops of EtOH (solvent drop grinding). The ground sample was dissolved in a minimum amount of hot MeOH. Good quality crystals, suitable for diffraction, were obtained after four days.

Azelaic acid : isonicotinamide 1:2 cocrystal (**3**). Azelaic acid and isonicotinamide were taken in a 1:2 molar ratio and ground after adding 2-3 drops of EtOH. The ground sample was dissolved in a minimum amount of hot acetone. Good quality crystals, suitable for diffraction, were obtained after three days.

Sebacic acid : isonicotinamide 1:2 cocrystal (**4**). sebacic acid and isonicotinamide were taken in a 1:2 molar ratio and ground after adding 2-3 drops of EtOH. The ground sample was dissolved in a minimum amount of hot *i*-PrOH. Good quality crystals, suitable for diffraction, were obtained after three days.

Section S2: Instrumental details

Single crystal X-ray crystallography. Single crystal X-ray data for **1** cocrystals was collected Bruker SMART APEX II single crystal X-ray CCD diffractometer having graphite-monochromatised (Mo-Kα = 0.71073 Å) radiation at 100 K. The X-ray data acquisition was monitored by APEX2 program suit. The data was processed by APEX2 package. **2** and **4** cocrystal was collected on a Rigaku Mercury 375/M CCD (XtaLAB mini) diffractometer using graphite monochromated Mo−Kα radiation at 150 K. Rigaku crystal clear software was used for processing the data. Crystals **3** was collected with a Super Nova Dual source X-ray Diffractometer system (Agilent Technologies) having a CCD area detector at 300 K. CrysAlisPro software was used for data processing. Structure solution and refinements were executed using SHELX-97[1] using the WinGX[2] suite or SHELXS[1] through OLEX2[4] software. PLATON[1] was used to prepare material for publication, and Mercury software was utilized for molecular representations and packing diagrams. Refinement of coordinates and anisotropic thermal parameters of nonhydrogen atoms were performed with the full-matrix least-squares method. In most of the cases, the hydrogen atoms in NH_2 and OH groups were located from the difference in Fourier maps. In some certain cases, the CH hydrogen atoms were calculated using the riding model.

Powder X-ray diffraction (PXRD) data was collected using a Rigaku, MicroMax-007HF with high-intensity Microfocus rotating anode X-ray generator. All the crystals were recorded and the data was collected with the help of Control Win software. in the 2θ range between 2–40 The radiation used was Cu Kα (α = 1.54 Å) with a Ni filter, and the data collection was carried out using an Aluminium holder at a scan speed of 1° min^{-1} and a step size of 0.02°.

Fourier transform infrared (FT-IR) spectra was obtained using a Bruker Optics ALPHAE spectrometer with a universal Zn-Se ATR (attenuated total reflection) accessory. IR data are reported with a wave number (cm^{-1}) scale.

Differential scanning calorimetry DSC was performed on DSC Q100 V8.2 Build 268 instrument. All cases <5 mg sample was taken in aluminum pan closed with lid and then run from 27°C to 200 with 10° per min was performed

CSD analysis : Cambridge Structural Database, CSD version 5.39 updates (Nov **2017**). www.ccdc.cam.ac.uk

Section S3: PXRD Comparison of single component crystals and cocrystals

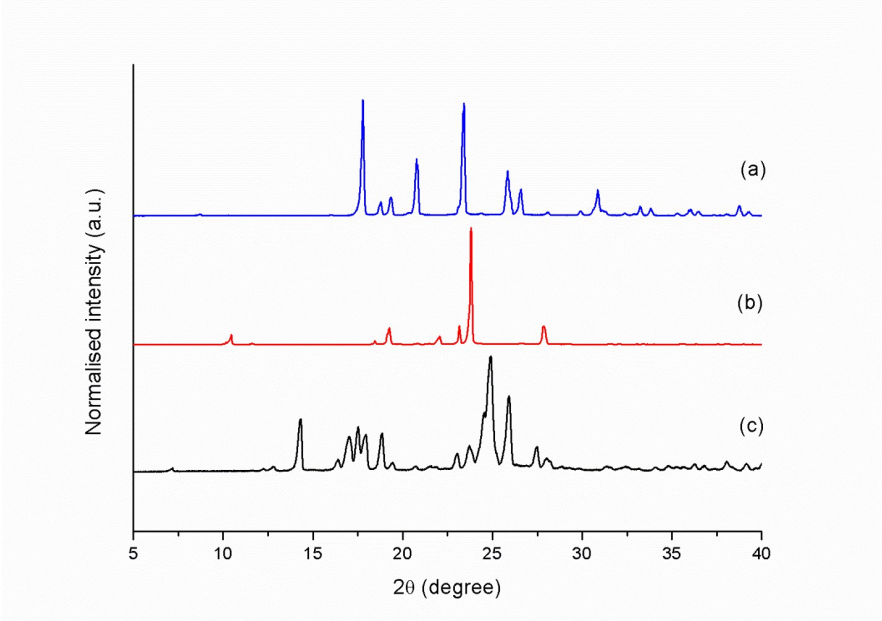


Figure S1: PXRD of (a) Isonicotinamide (b) Pimelic acid (c) Bulk powder of the binary Pimelic acid: Isonicotinamide (1:2) cocrystal obtained after grinding.

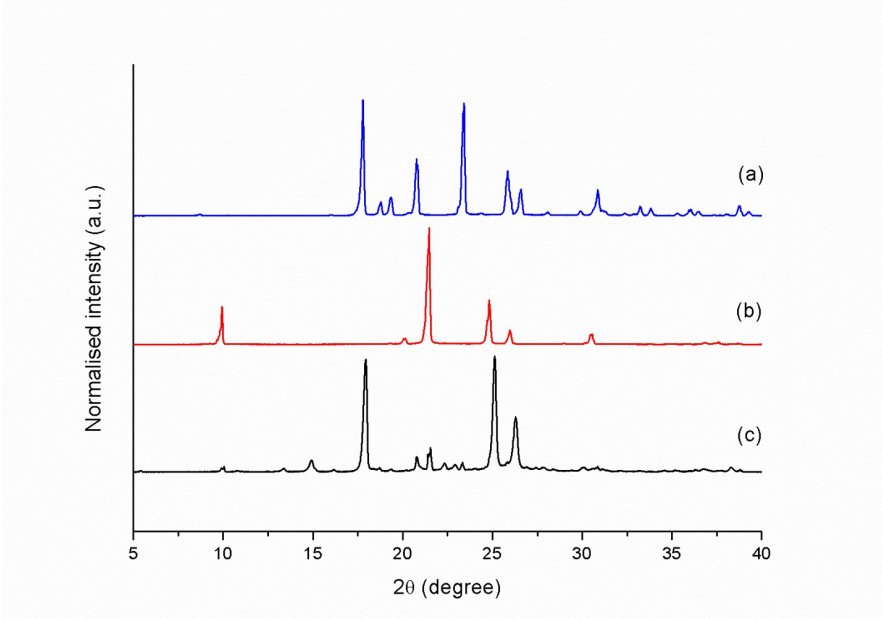


Figure S2: PXRD of (a) Isonicotinamide (b) Suberic acid (c) Bulk powder of the binary Suberic acid: Isonicotinamide (1:2) cocrystal obtained after grinding.

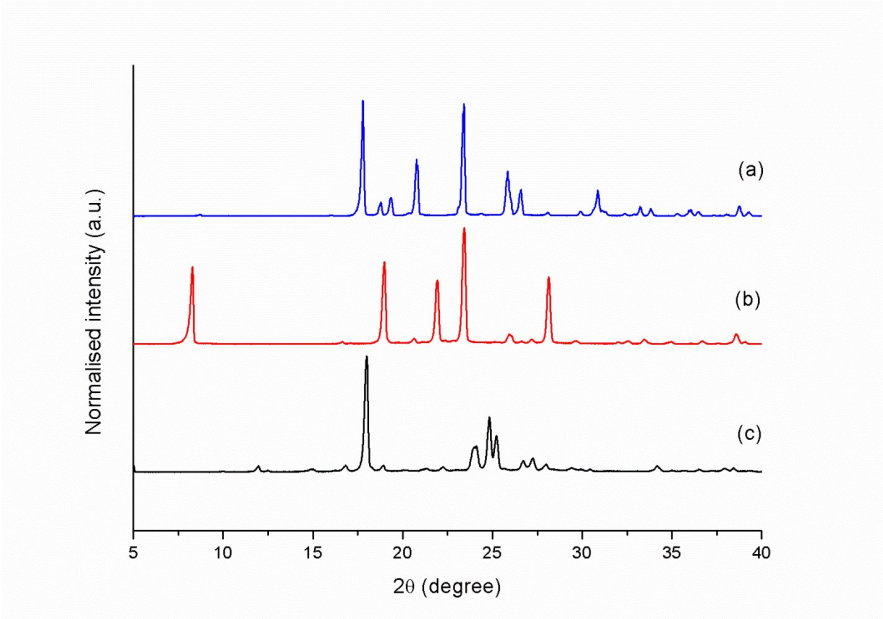
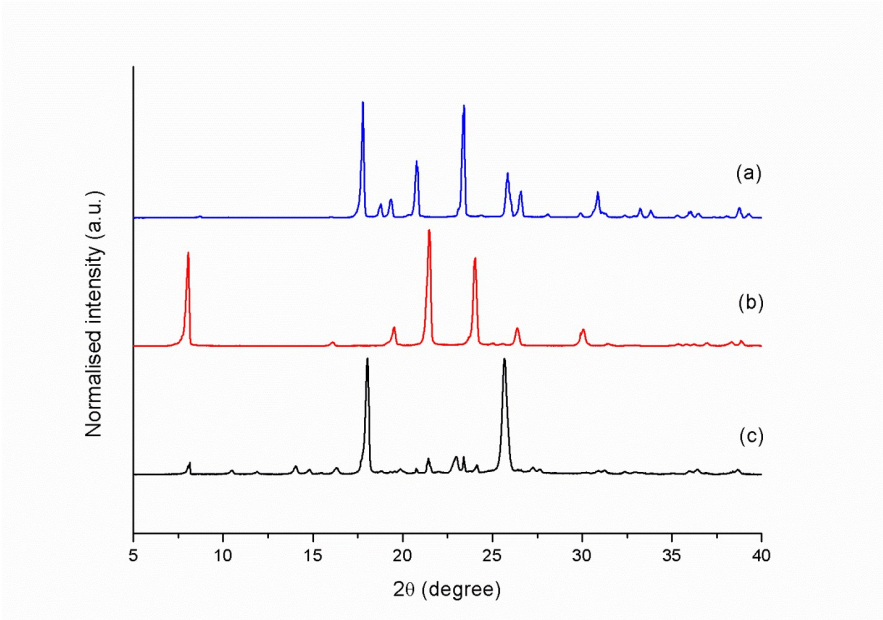


Figure S3: PXRD of (a) Isonicotinamide (b) Azelaic acid (c) Bulk powder of the binary Azelaic acid: Isonicotinamide (1:2) cocrystal obtained after grinding.



Firgure S4: PXRD of (a) Isonicotinamide (b) Sebacic acid (c) Bulk powder of the binary Sebacic acid: Isonicotinamide (1:2) cocrystal obtained after grinding.

Section S4: PXRD Comparison of 1:2 dicarboxylic acids: isonicotinamide cocrystals, bulk material and simulated pattern

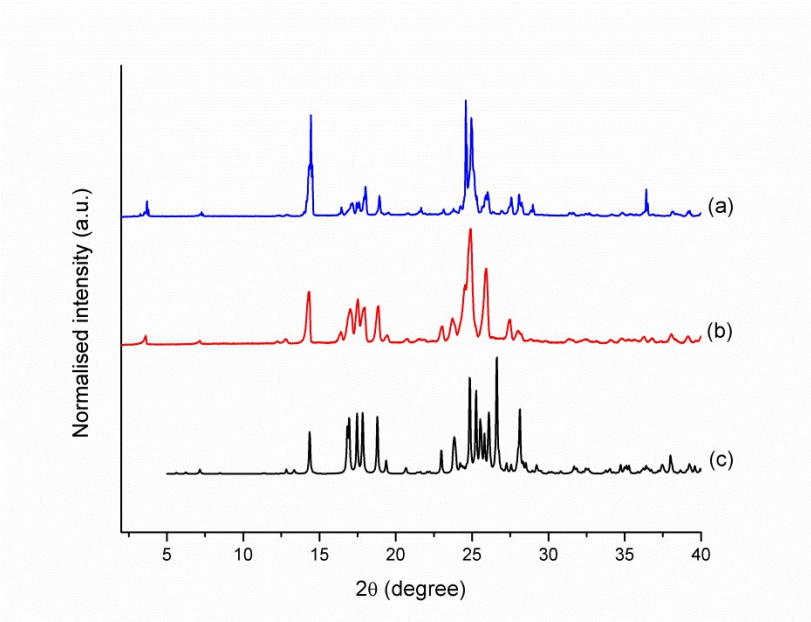


Figure S5: PXRD of Pimelic acid: Isonicotinamide (1:2) (a) Crystals (b) Bulk powder (c) Simulated pattern obtained from single crystal structure

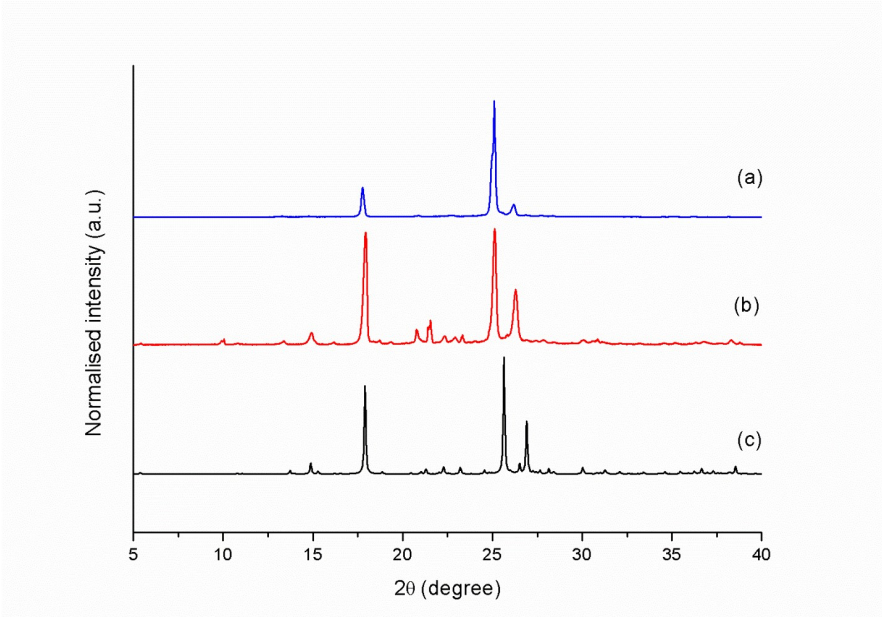


Figure S6: PXRD of Suberic acid: Isonicotinamide (1:2) (a) Crystals (b) Bulk powder (c) Simulated pattern obtained from single crystal structure

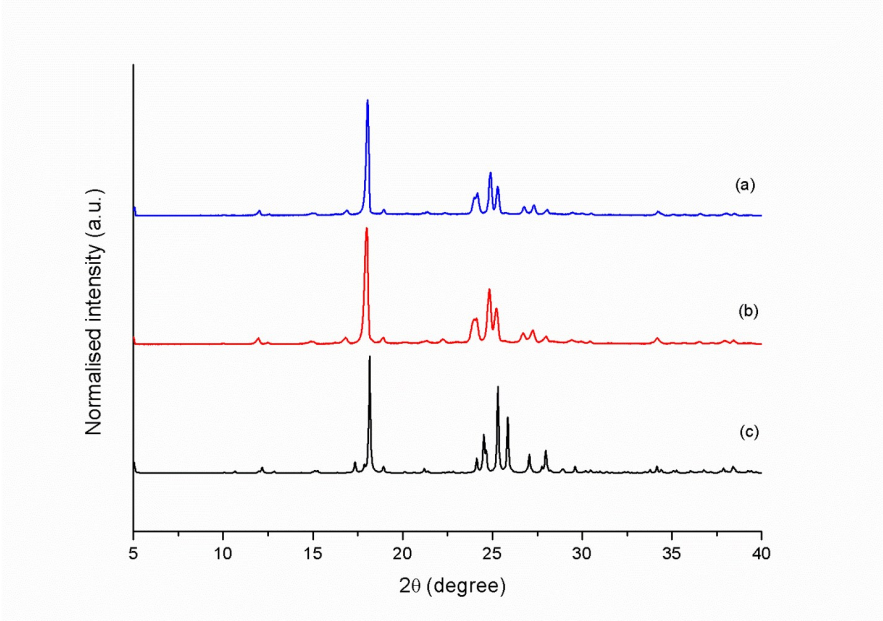


Figure S7: PXRD of Azelaic acid: Isonicotinamide (1:2) (a) Crystals (b) Bulk powder (c) Simulated pattern obtained from single crystal structure

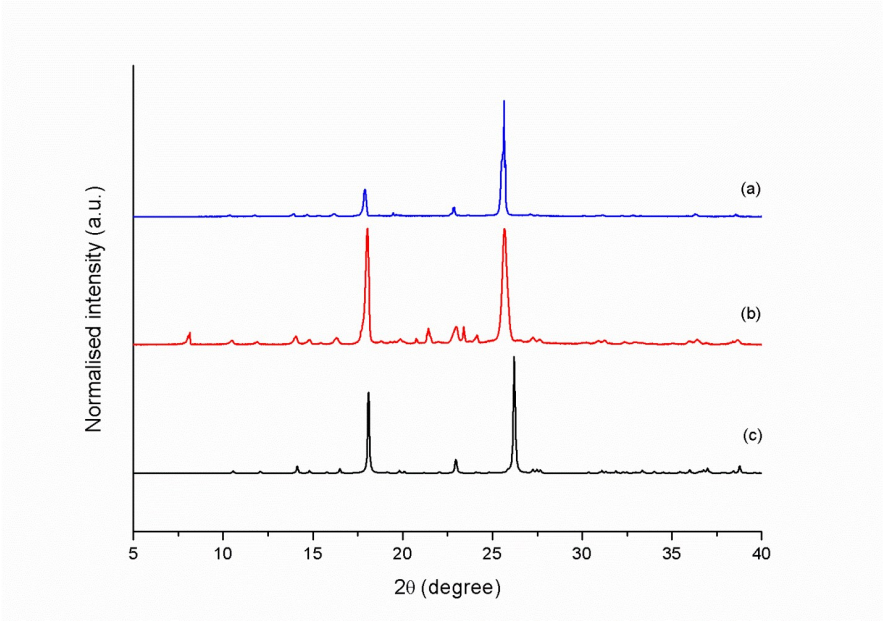


Figure S8: PXRD of Sebacic acid: Isonicotinamide (1:2) (a) Crystals (b) Bulk powder (c) Simulated pattern obtained from single crystal structure

Section S5: PXRD Comparison of 1:2 and 1:1 dicarboxylic acids: isonicotinamide cocrystals

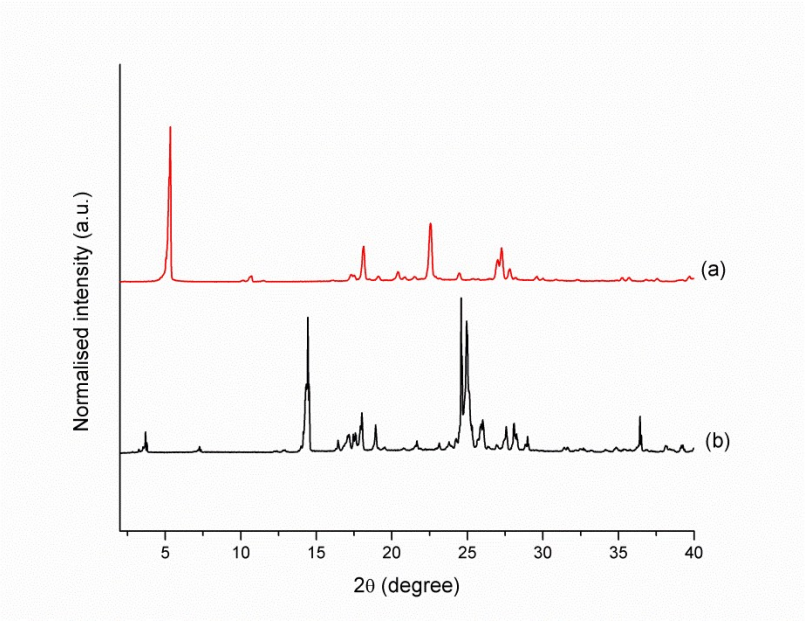


Figure S9: PXRD of Pimelic acid: Isonicotinamide (a) (1:1) Crystals (b) (1:2) Crystals

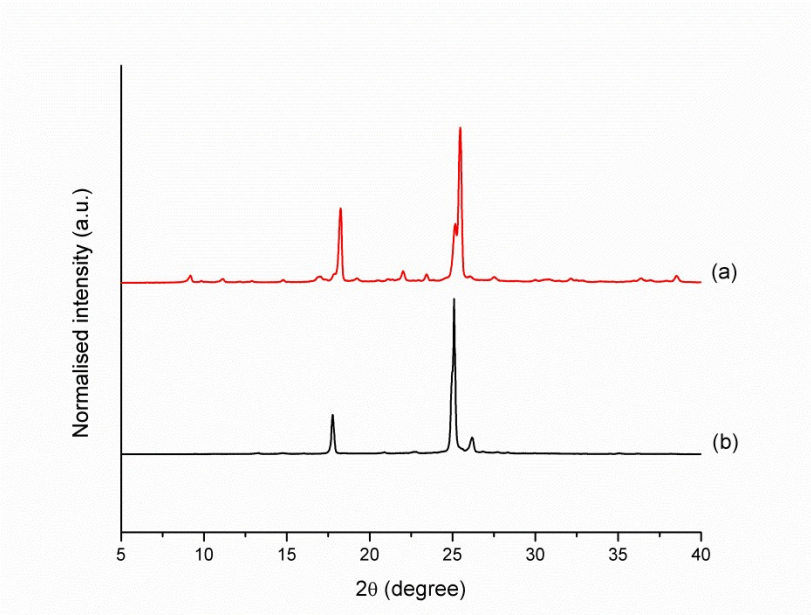


Figure S10: PXRD of Suberic acid: Isonicotinamide (a) (1:1) Crystals (b) (1:2) Crystal

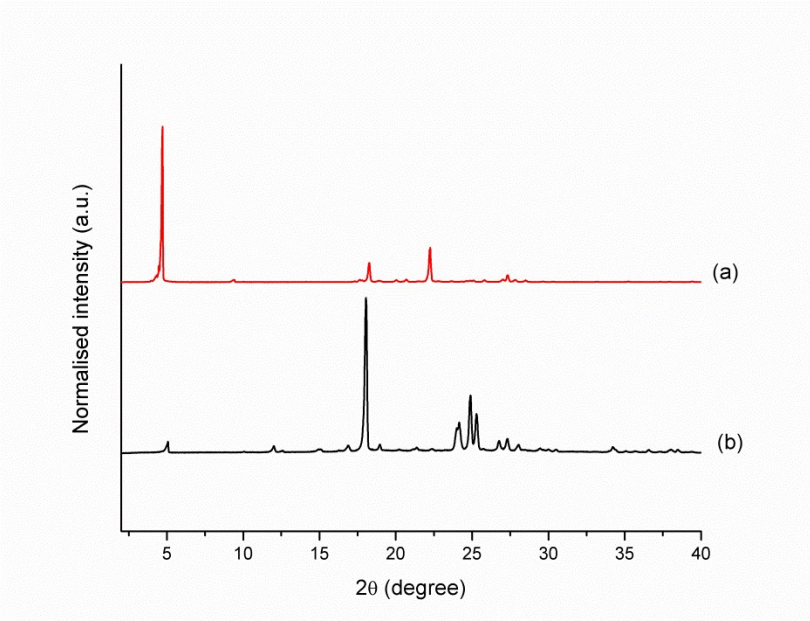


Figure S11: PXRD of Azelaic acid: Isonicotinamide (a) (1:1) Crystals (b) (1:2) Crystals

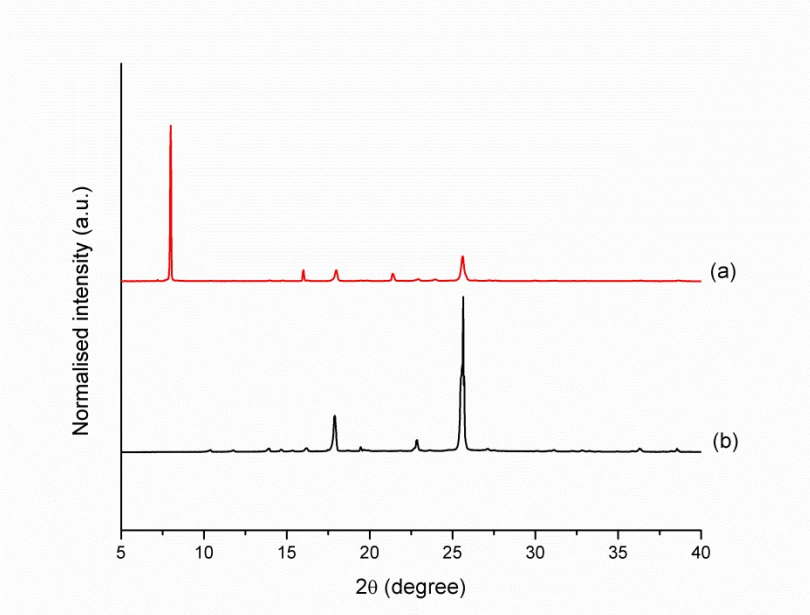


Figure S12: PXRD of Sebacic acid: Isonicotinamide (a) (1:1) Crystals (b) (1:2) Crystals

Figures S9-S12 indicate that the obtained cocrystals of different stoichiometry have distinct phases. The individual components react in the stoichiometry chosen and do not yield a mixture of phases

Section S6: Simulated PXRD patterns of 1:1 and 1:2 of dicarboxylic acids and nicotinamide/picolinamide

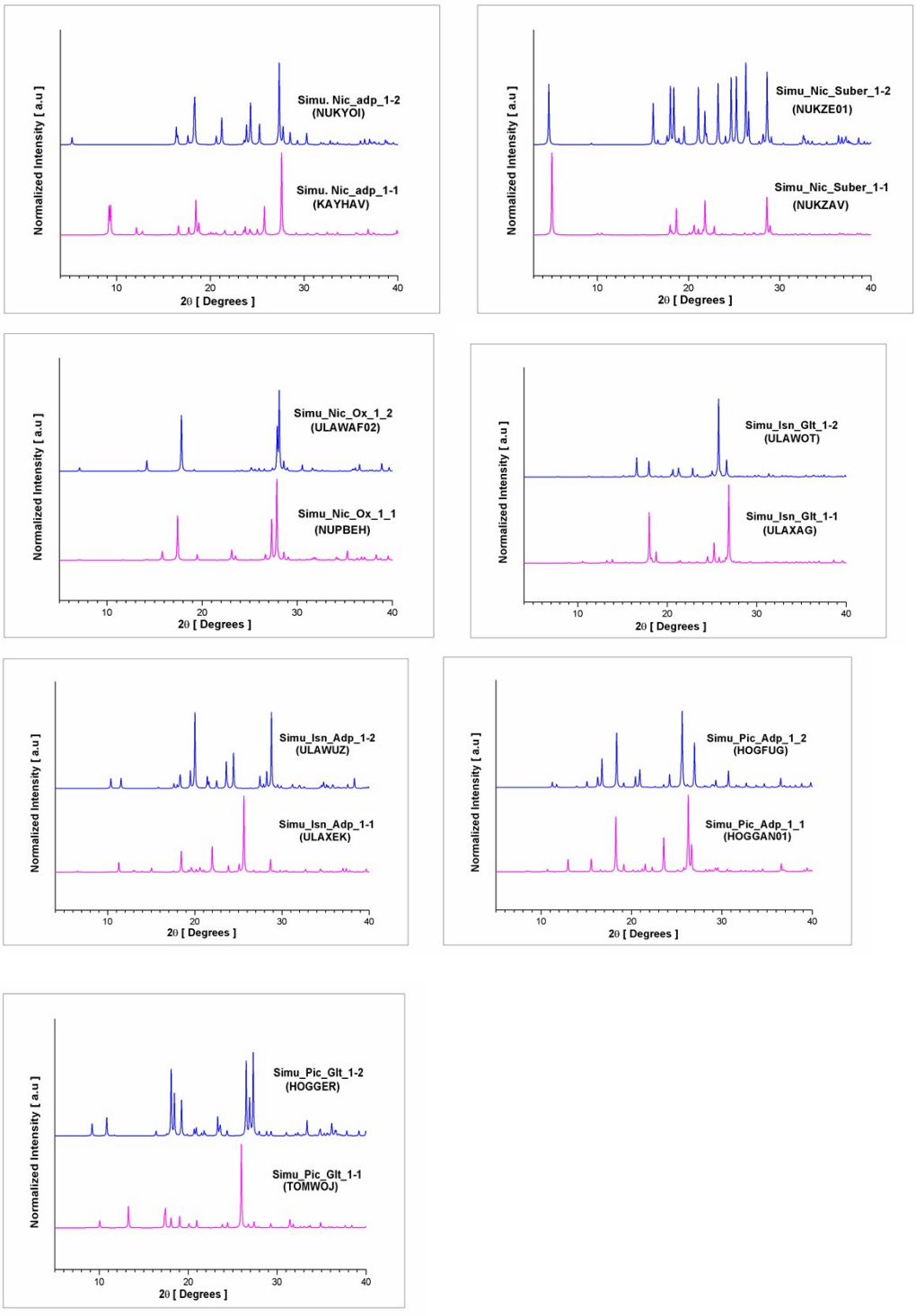


Figure S13 : Simulated PXRD patterns of 1:1 and 1:2 of dicarboxylic acids and nicotinamide/picolinamide. Refcodes are given in the brackets.

(Abbreviations: Nic= Nicotinamide, Isn= isonicotinamide, Pic= Picolinamide, Adp= adipic acid, Suber= suberic acid), Ox = oxalic acid, Glt = glutaric acid

Section S7: DSC of Cocrystals

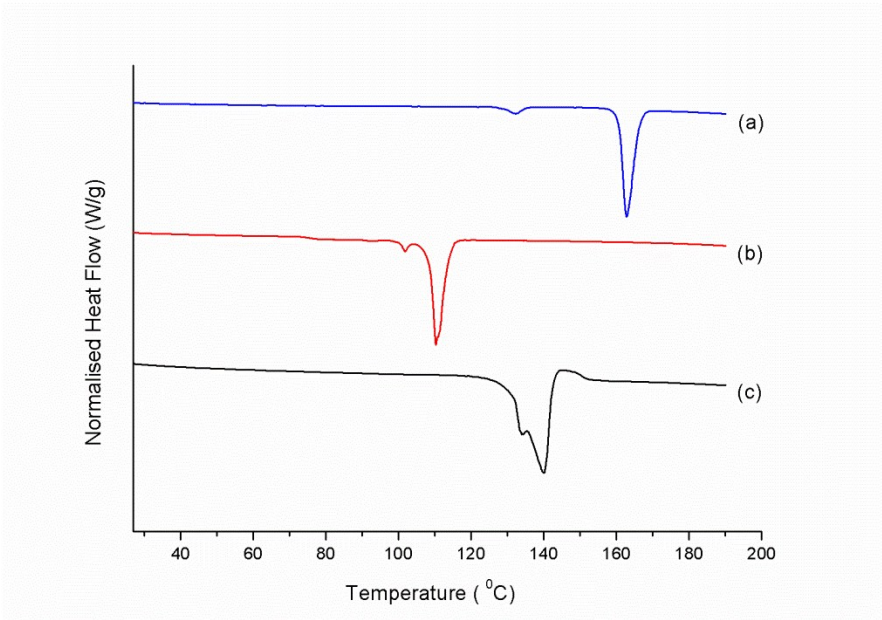


Figure S14: DSC of (a) Isonicotinamide (b) Pimelic acid (c) Crystals of the binary Pimelic acid: Isonicotinamide (1:2) cocrystal obtained after crystallization in THF. (Melting point 140 °C)

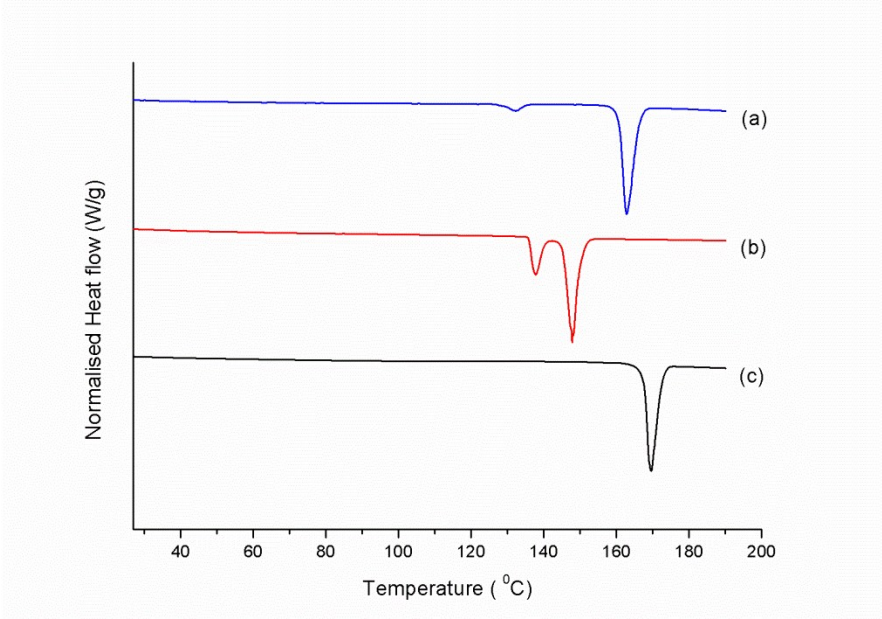


Figure S15: DSC of (a) Isonicotinamide (b) Suberic acid (c) Crystals of the binary Suberic acid: Isonicotinamide (1:2) cocrystal obtained after crystallization in MeOH (Melting point 170 °C)

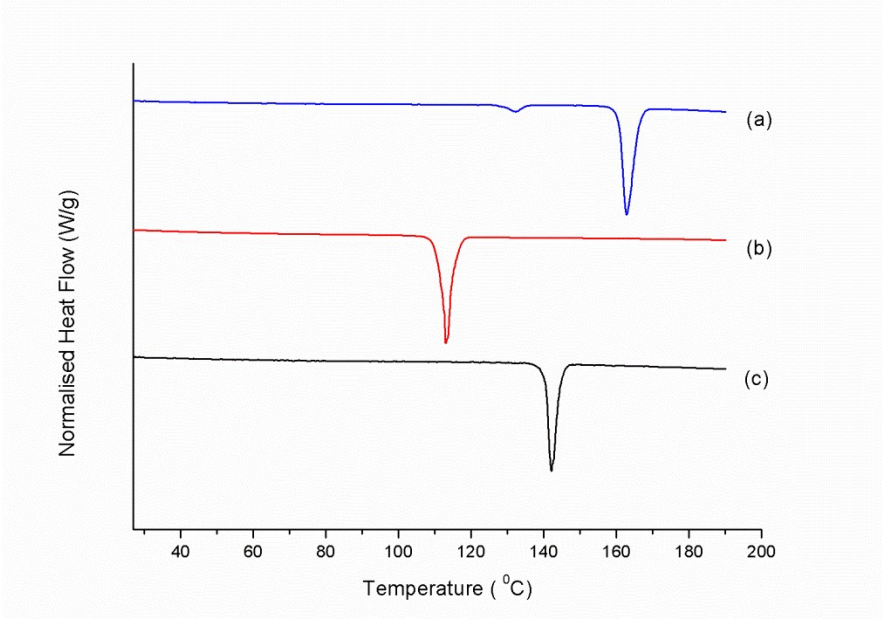


Figure S16: DSC of (a) Isonicotinamide (b) Azelaic acid (c) Bulk powder of the binary Azelaic acid: Isonicotinamide (1:2) cocrystal obtained after crystallization in Acetone (Melting point 141 °C)

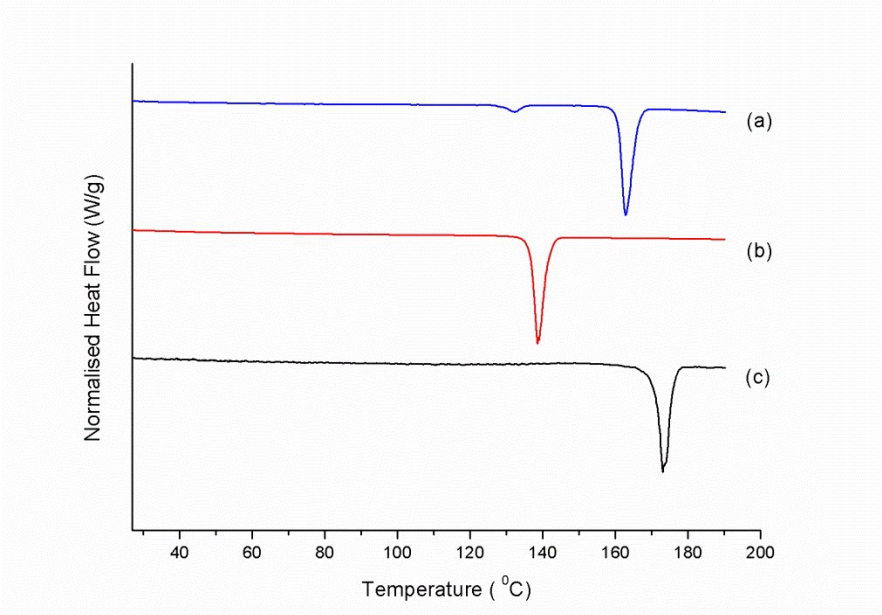


Figure S17: DSC of (a) Isonicotinamide (b) Sebacic acid (c) Bulk powder of the binary Sebacic acid: Isonicotinamide (1:2) cocrystal obtained after crystallization in *i*-PrOH (Melting point 174 °C)

Section S8: FTIR of cocrystals

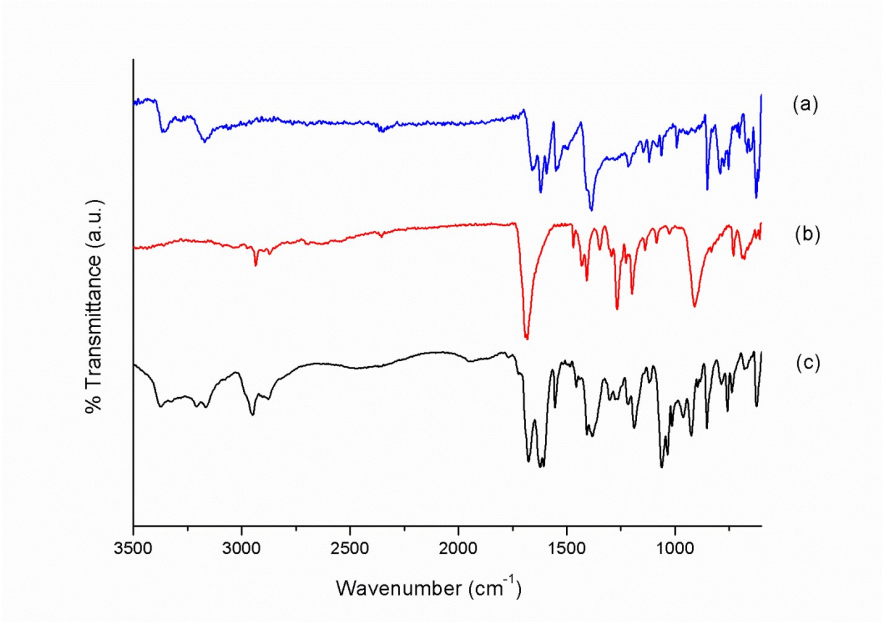


Figure S18: FTIR of (a) Isonicotinamide (b) Pimelic acid (c) Bulk powder of the binary Pimelic acid: Isonicotinamide (1:2) cocrystal obtained after grinding.

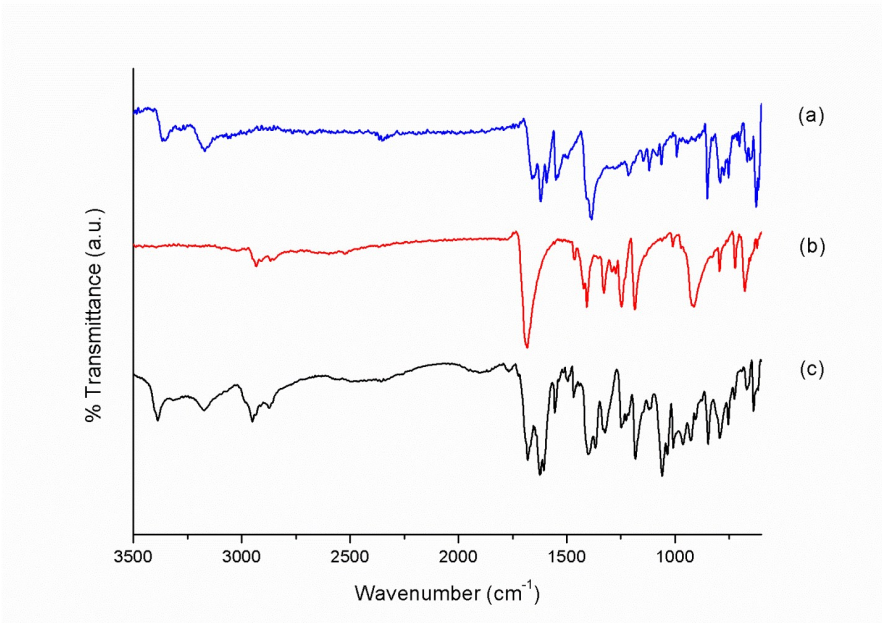


Figure S19: FTIR of (a) Isonicotinamide (b) Suberic acid (c) Bulk powder of the binary Suberic acid: Isonicotinamide (1:2) cocrystal obtained after grinding.

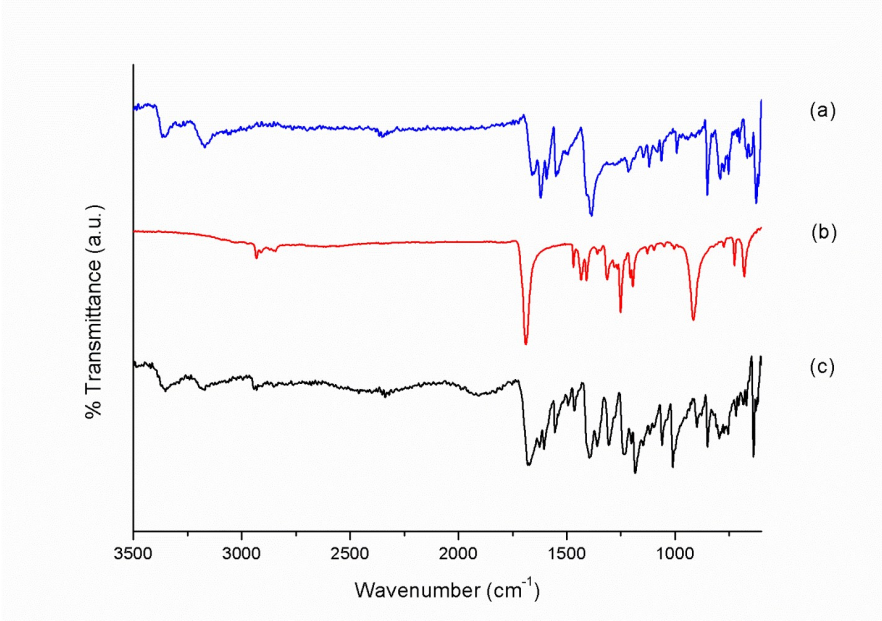


Figure S20: FTIR of (a) Isonicotinamide (b) Azelaic acid (c) Bulk powder of the binary Azelaic acid: Isonicotinamide (1:2) cocrystal obtained after grinding.

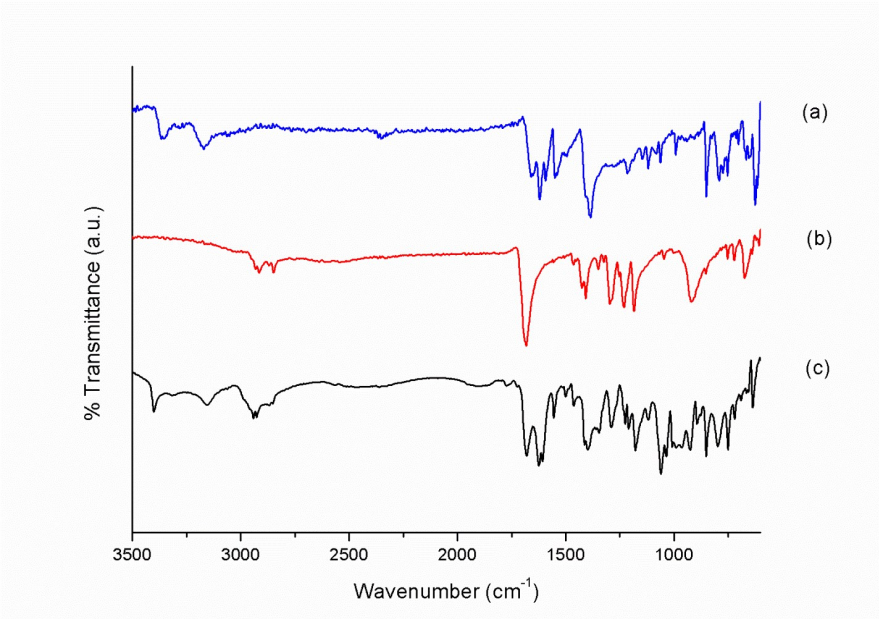


Figure S21: FTIR of (a) Isonicotinamide (b) Sebacic acid (c) Bulk powder of the binary Sebacic acid: Isonicotinamide (1:2) cocrystal obtained after grinding.

Section S9: Hydrogen bond table for cocrystals

	Donor -- H···Acceptor	H···A (d)	D…A (D)	D-H···A ()
1 (1:2)	O1–H1···N2^{m}	1.69	2.6169(12)	169
	N1–H1A···O14	2.03	2.8845(13)	175
	N1–H1B···O6	2.18	3.0432(13)	168
	O2–H2···N12^{k}	1.817	2.6980(12)	168.4
	N4–H4C···O15^{b}	2.144	2.9729(13)	169.4
	N4–H4D···O7^{b}	2.116	2.9887(13)	175.6
	O5–H5···N7^{k}	1.824	2.6898(12)	169.0
	N6–H6C···O16	2.014	2.8672(13)	171.9
	N6–H6D···O12^{e}	2.136	2.9909(13)	174.4
	O8–H8···N10^{l}	1.700	2.6280(12)	169.0
	N8–H8A···O17	2.142	2.9731(13)	167.8
	N8–H8B···O11	2.089	2.9485(13)	172.9
	O9–H9···N3^{i}	1.808	2.6852(12)	170.0
	N9–H9C···O4^{c}	2.114	2.9733(13)	171.5
	N9–H9D···O18	2.009	2.8675(13)	174.8

	O10–H10···N5[l]	1.686	2.6240(12)	167.5
	N11–H11C···O3[a]	2.048	2.9474(13)	176.4
	N11–H11D···O13[c]	2.204	3.0273(13)	168.6
	C6–H6A···O18[d]	2.555	3.1939(14)	121.3
	C9 –H9A···O14	2.572	3.2114(14)	121.1
	C16–H16A···O16[b]	2.552	3.1908(14)	121.0
	C24–H24 ···O6	2.284	3.2321(14)	167.3
	C27–H27 ···O10[d]	2.584	3.5088(15)	175.8
	C28–H28···O2	2.523	3.2784(15)	132.3
	C32–H32···O11[i]	2.453	3.2187(15)	134.3
	C33–H33···O7[b]	2.248	3.1543(16)	167.7
	C34–H34···O1	2.527	3.4753(15)	179.1
	C39–H39···O12[e]	2.346	3.2363(14)	156.6
	C40 –H40···O7[k]	2.403	3.1764(15)	133.8
	C41–H41···O11	2.279	3.1812(16)	166.4
	C44 –H44···O5[e]	2.501	3.3096(15)	135.1
	C47–H47···O4[c]	2.563	3.2964(14)	136
	C51–H51···O8	2.561	3.4665(15)	159
	C55–H55···O9[e]	2.513	3.3101(15)	137
	C56–H56 ···O3[a]	2.267	3.1688(16)	170
	C57–H57···O3[k]	2.425	3.2033(15)	132

	Donor -- H···Acceptor	H···A (d)	D…A (D)	D-H···A ()
2 (1:2)	N4–H3··· O3[a]	2.12	2.942(6)	172
	N4–H4···O8[b]	2.06	2.919(6)	170
	O5–H5···N2[c]	1.81	2.665(6)	163
	N3–H1···O6[d]	2.18	3.008(6)	172
	O4–H6···N1[e]	1.93	2.659(6)	163
	N3–H2···O1[f]	1.92	2.877(6)	176
	C15–H14···O1	2.59	3.332(7)	135
	C20–H20···O6[d]	2.40	3.321(7)	163

Equivalent Position Code

[e] = -x,-y,-z
[c] = 2-x,2-y,1-z
[b] = 1+x,1+y,z
[a] = 1-x,1-y,-z
[f.] = -1+x,-1+y,z

[d] = 1-x,1-y,1-z

3	(1:2)	N9–H9A···O17[a]	2.10	2.938(3)	165
		N9–H9B···O19[b]	2.18	3.007(3)	162
		N18–H18A···O8[a]	2.08	2.911(3)	162
		N18–H18B···O30[c]	2.13	2.960(3)	162
		O29–H29···N13[d]	1.86	2.645(3)	161
		O31–H31···N1[e]	1.86	2.657(3)	164
		C3–H3···O19[b]	2.48	3.248(4)	140

Equivalent Position Code

[d]= 1+x,1+y,z
[e]= 1-x,-1-y,-z
[a]= 1-x,1-y,1-z
[b] = x,1+y,z
[c]= -1+x,y,z

4	(1:2)	O2–H2···N4[a]	1.75	2.669(12)	162
		N3–H3A···O5[b]	2.03	2.882(12)	171
		N3–H3B ···O(1)	2.17	3.012(13)	165
		C18–H18···O1[c]	2.42	3.318(14)	161

Equivalent Position Code

[a] = x,1+y,1+z
[b] =1-x,1-y,1-z
[c] = x,-1+y,z

The following symmetry operations are denoted by their codes (a-n) in the table: [1445.] = -1+x,-1+y,z (a), [1455.] = -1+x,y,z (b), [1545.] = x,-1+y,z (c), [1565.] = x,1+y,z (d), [1655.] = 1+x,y,z (e), [1656.] = 1+x,y,1+z (f), [1665.] = 1+x,1+y,z (g), [2555.] = -x,-y,-z (h), [2565.] = -x,1-y,-z (i), [2645.] = 1-x,-1-y,-z (j), [2665.] = 1-x,1-y,-z (k), [2666.] = 1-x,1-y,1-z (l), [2676.] = 1-x,2-y,1-z (m), (n)[2776.] = 2-x,2-y,1-z (n)

Section S10 : Representation molecules in the asymmetric unit and their crystal packing.

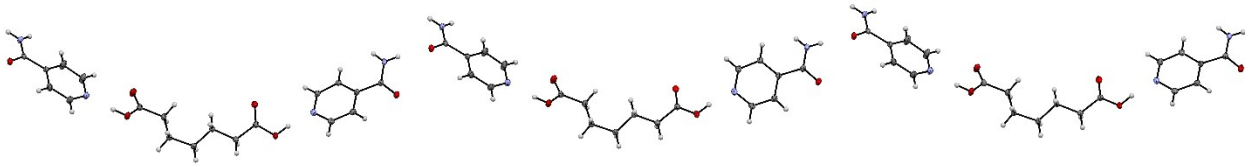


Figure S22: ORTEP diagram shows total number of molecules in the asymmetric unit (6 molecules of isonicotinamide and 3 molecules of pimelic acid) and it corresponds to 1:2 cocrystals of pimelic acid: isonicotinamide (1)

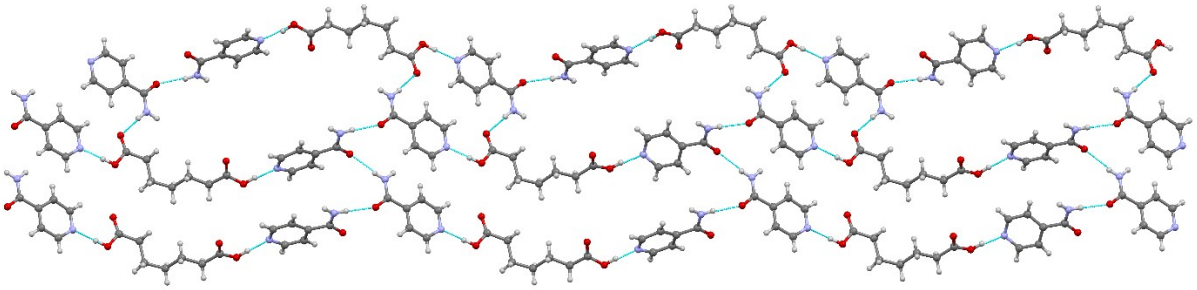


Figure S23: Packing diagram of 1:2 cocrystals of pimelic acid: isonicotinamide (1). Notice there are two types of 6 membered loops are present. Both loops are formed by four molecules of isonicotinamide and two molecules of pimelic acid but the arrangement of molecule order is different. In one loop two molecules of isonicotinamide arranged consecutively where as in another loop three molecules of isonicotinamide are arranged consecutively and the terminals are connected with pimelic acid.

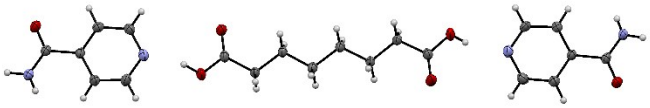


Figure S24: ORTEP diagram shows total number of molecules in the asymmetric unit (1 molecules of suberic acid and 2 molecules of isonicotinamide) and it corresponds to 1:2 Cocrystals of suberic acid: isonicotinamide (2)

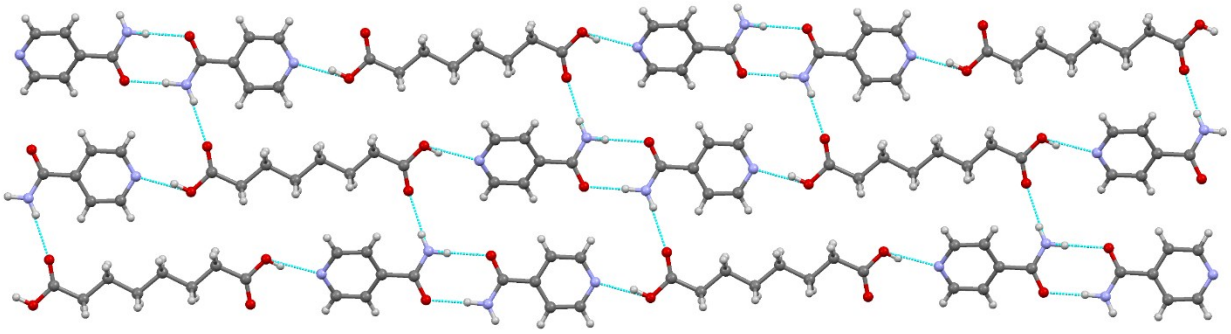


Figure S25: Packing diagram of 1:2 cocrystals of suberic acid: isonicotinamide (2). Molecules are connected via acid-pyridine synthon, amide-amide dimer and N–H···O hydrogen bonds.

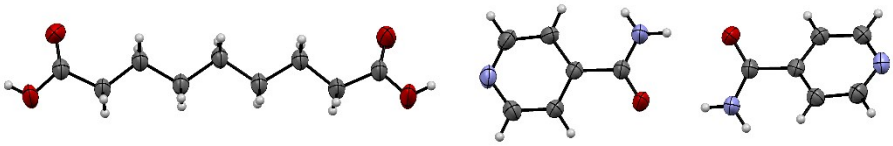


Figure S26: ORTEP diagram shows total number of molecules in the asymmetric unit (1 molecules of azelaic acid and 2 molecules of isonicotinamide) and it corresponds to 1:2 cocrystals of azelaic acid: isonicotinamide (3)

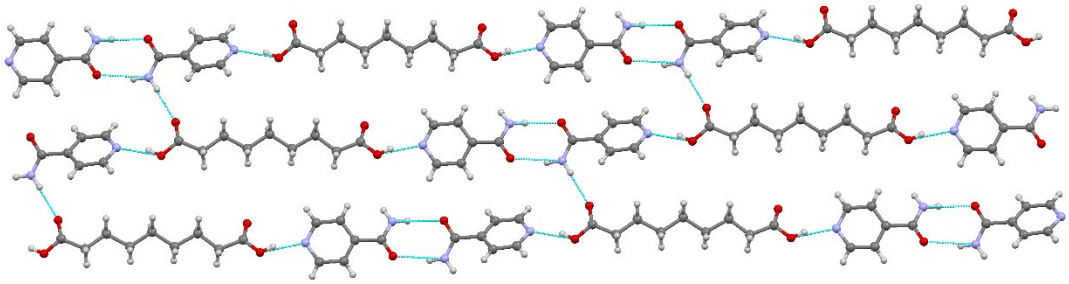


Figure S27: Packing diagram of 1:2 cocrystals of azelaic acid: isonicotinamide (3). Molecules are connected via acid-pyridine synthon, amide-amide dimer and N–H···O hydrogen bonds

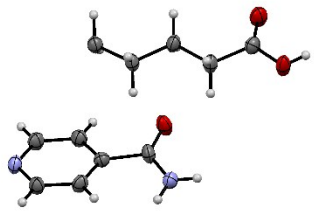


Figure S28: ORTEP diagram shows total number of molecules in the asymmetric unit (1/2 molecules of sebacic acid and 1 molecules of isonicotinamide) and it corresponds to 1:2 cocrystals of sebacic acid : isonicotinamide (4)

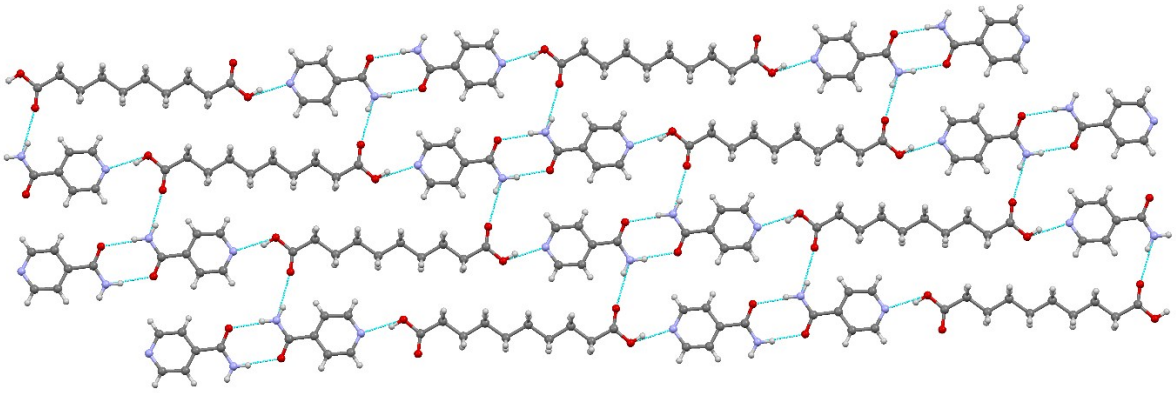


Figure S29: Packing diagram of 1:2 cocrystals of sebacic acid: isonicotinamide (4). Molecules are connected via acid-pyridine synthon, amide-amide dimer and N–H···O hydrogen bonds.

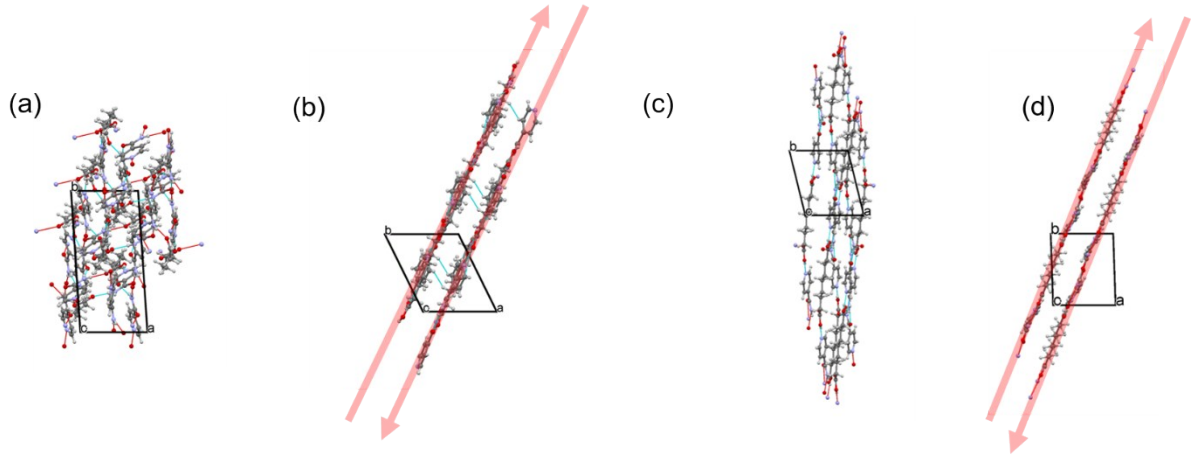


Figure S30: Crystal packing of cocrystals (a) pimelic acid: isonicotinamide (1) (b) suberic acid: isonicotinamide (2) (c) azelaic acid: isonicotinamide (3) (d) sebacic acid: isonicotinamide (4). When two consecutive layers are selected and viewed along c-axis, packing diagrams show zig-zag orientation in (a) and (c); linear orientation in (b) and (d). The diagrams make it pretty obvious that cocrystals were obtained with odd dicarboxylic acids cannot pack efficiently (Zig-zag orientation) and cause loose crystal packing that leads to low melting point. On the other hand even dicarboxylic acids have tight packing hence melt at higher temperature.

Section S11: References

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