Electronic Supplementary Material (ESI) for CrystEngComm.

Electronic Supplementary Information

Isoniazid cocrystallisation with dicarboxylic acids: vapochemical, mechanochemical and thermal methods

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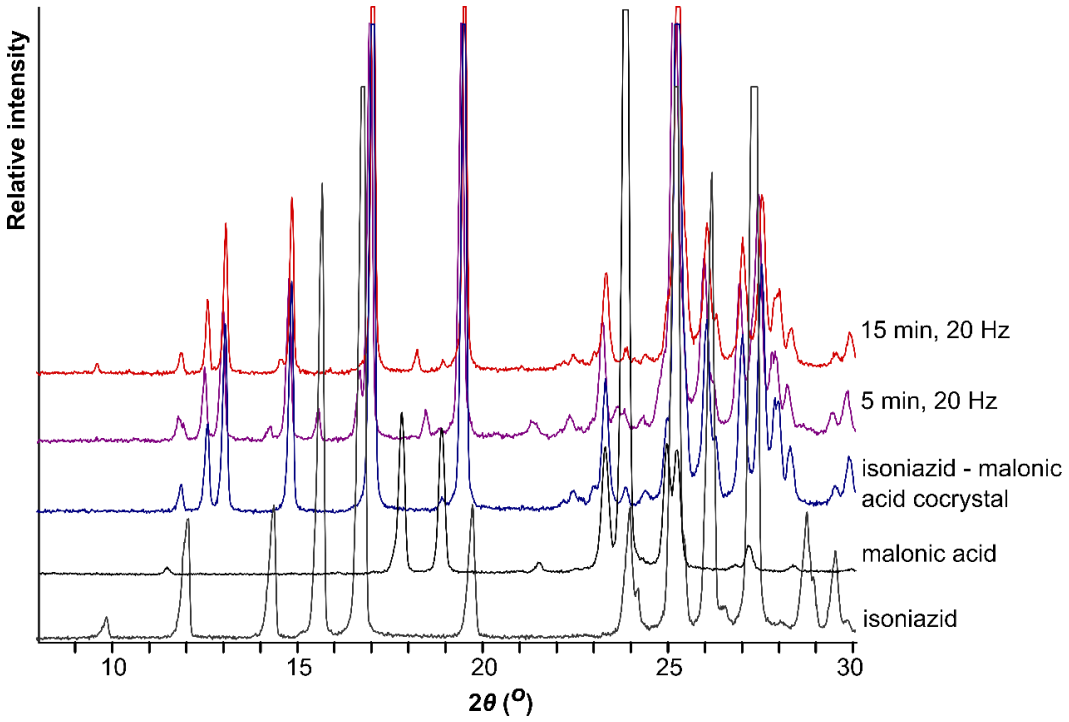

Figure S1. PXRD patterns of isoniazid and malonic acid milling products in comparison to PXRD patterns of isoniazid, malonic acid and their cocrystal.

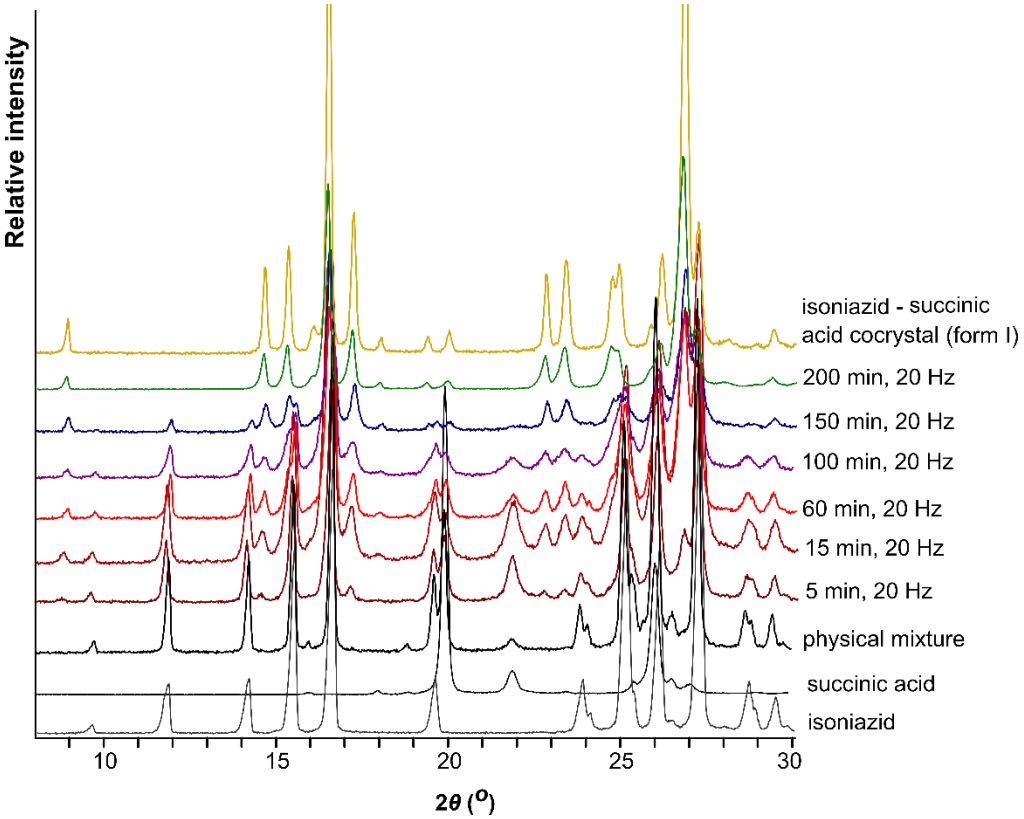

Figure S2. PXRD patterns of isoniazid and succinic acid milling products in comparison to PXRD patterns of isoniazid, succinic acid and their cocrystal form I.

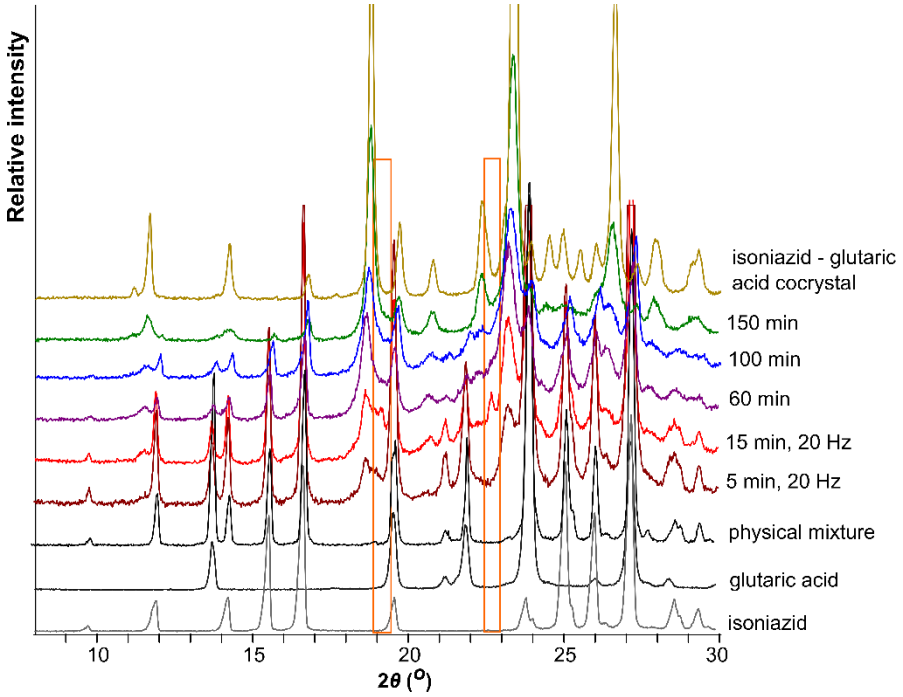

Figure S3. PXRD patterns of isoniazid and glutaric acid milling products in comparison to PXRD patterns of isoniazid, glutaric acid and their cocrystal. The orange frames show peaks of the unidentified phase formed during milling (after 15 min).

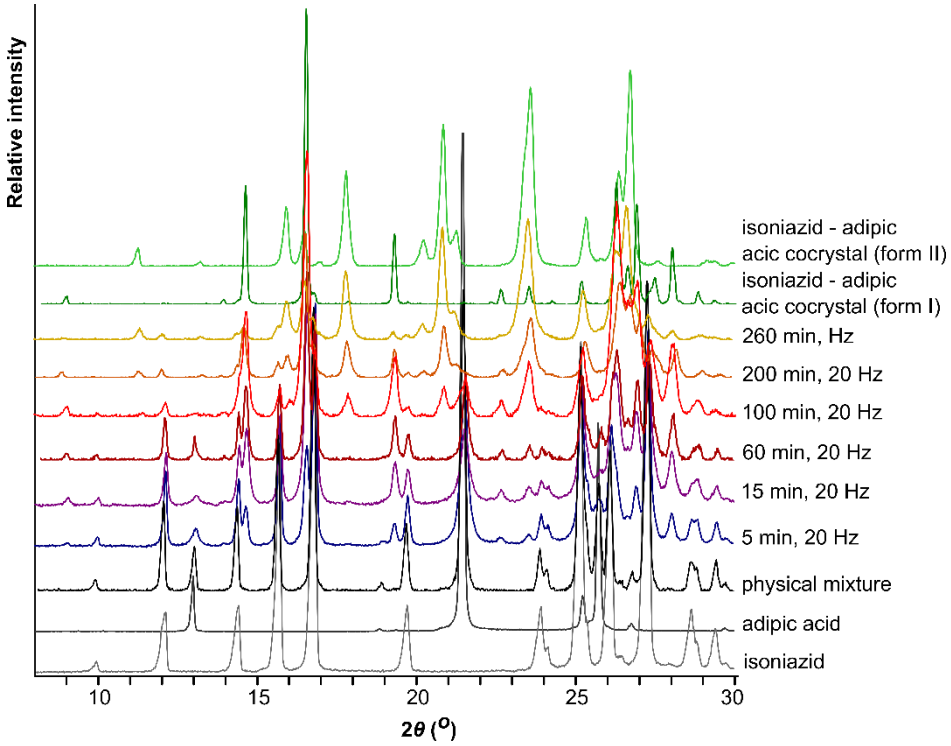

Figure S4. PXRD patterns of isoniazid and adipic acid milling products in comparison to PXRD patterns of isoniazid, adipic acid and their cocrystal (form I and form II).

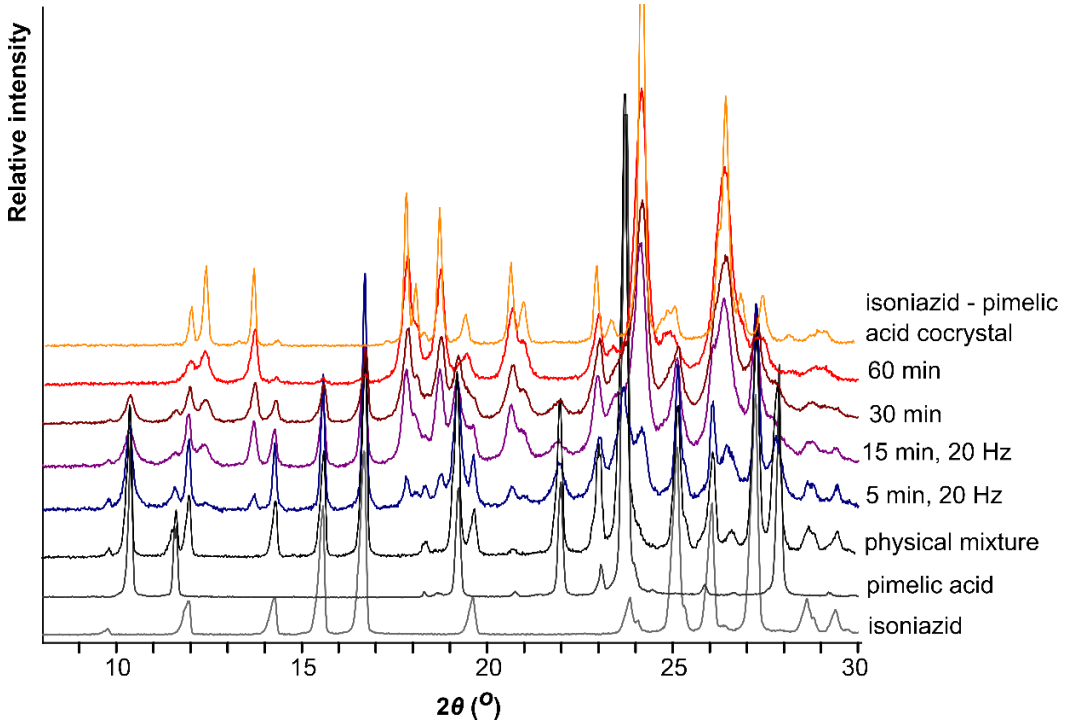

Figure S5. PXRD patterns of isoniazid and pimelic acid milling products in comparison to PXRD patterns of isoniazid, pimelic acid and their cocrystal.

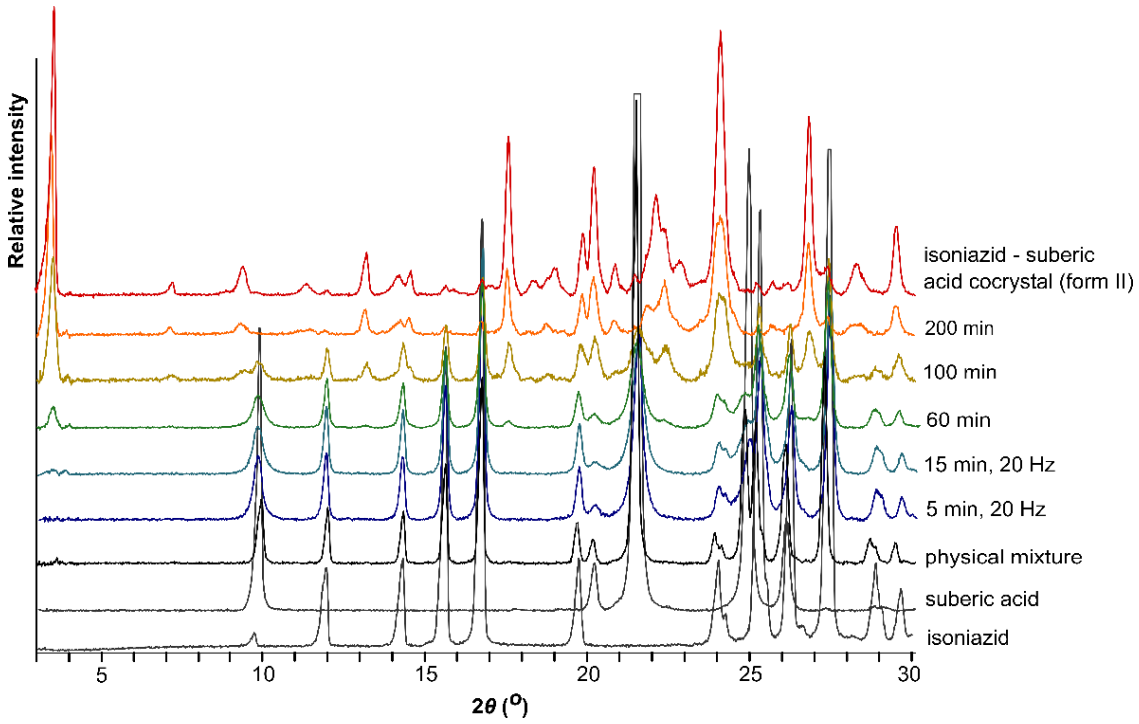

Figure S6. PXRD patterns of isoniazid and suberic acid milling products in comparison to PXRD patterns of isoniazid, suberic acid and their cocrystal.

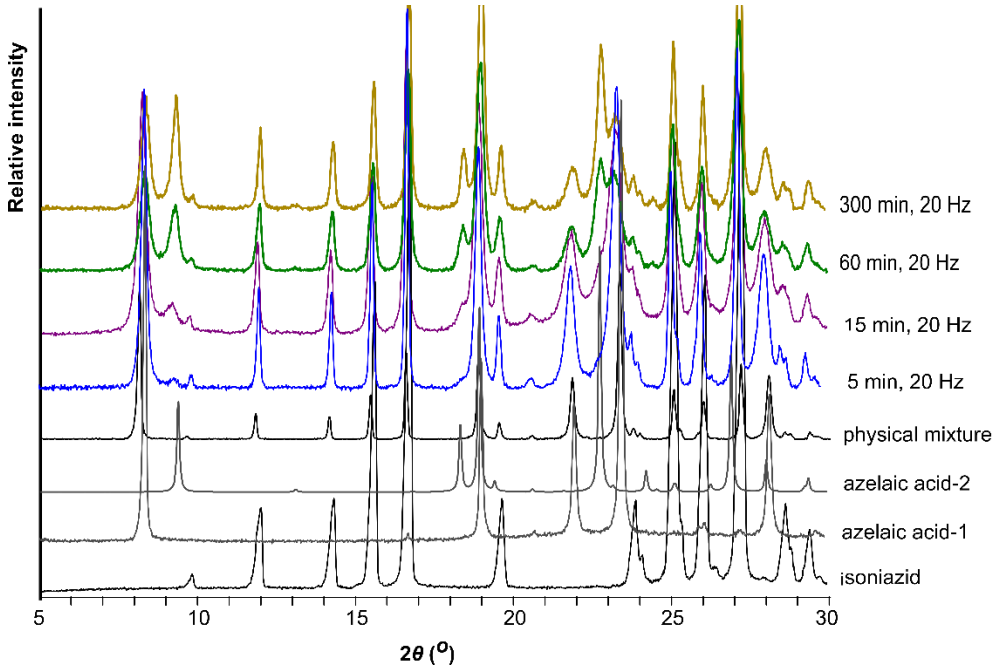

Figure S7. PXRD patterns of isoniazid and azelaic acid milling products in comparison to PXRD patterns of isoniazid and azelaic acid. The azelaic acid-1 is the polymorph used to prepare the physical mixture; azelaic acid-2 is the polymorph formed during mechanochemical treatment.

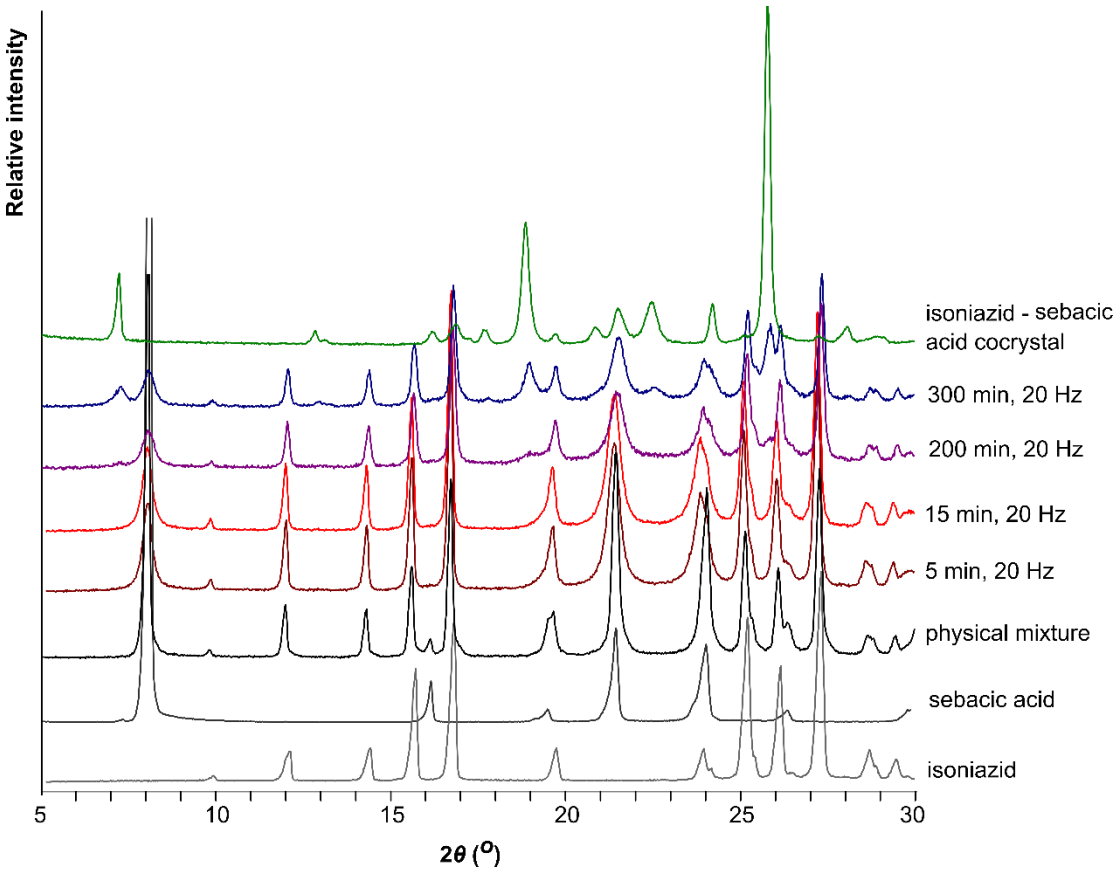

Figure S8. PXRD patterns of isoniazid and sebacic acid milling products in comparison to PXRD patterns of isoniazid, sebacic acid and their cocrystal.

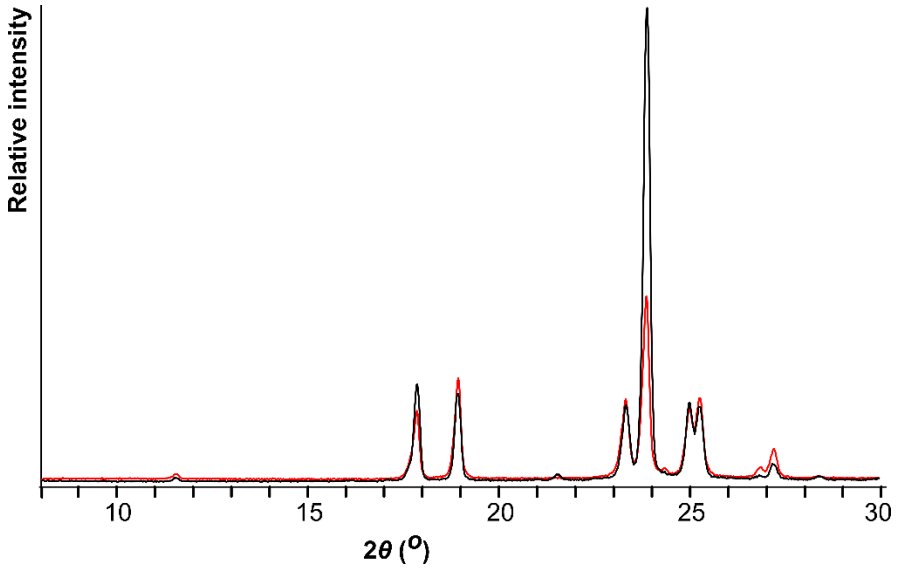

Figure S9. PXRD patterns of the initial sample of malonic acid used in milling experiments (black) and of malonic acid after milling for 60 minutes with 20 Hz (red).

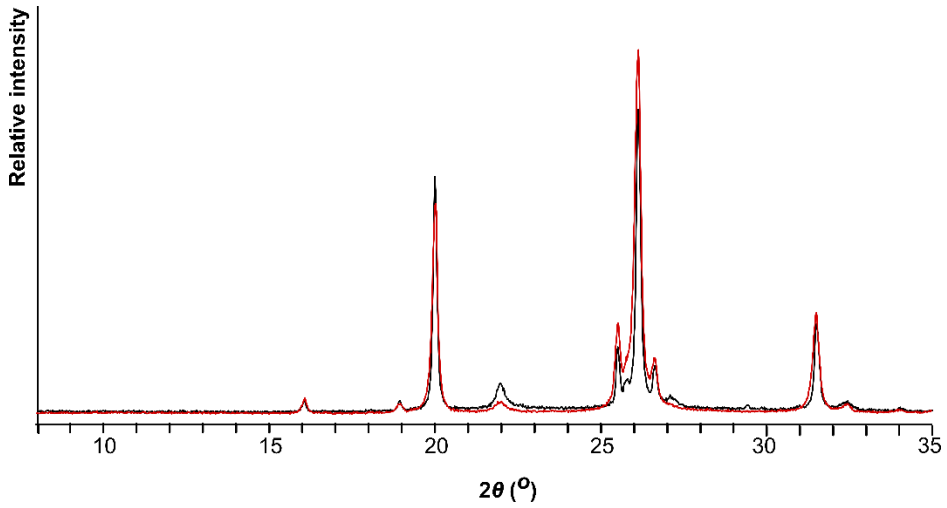

Figure S10. PXRD patterns of the initial sample of succinic acid used in milling experiments (black) and of succinic acid after milling for 60 minutes with 20 Hz (red).

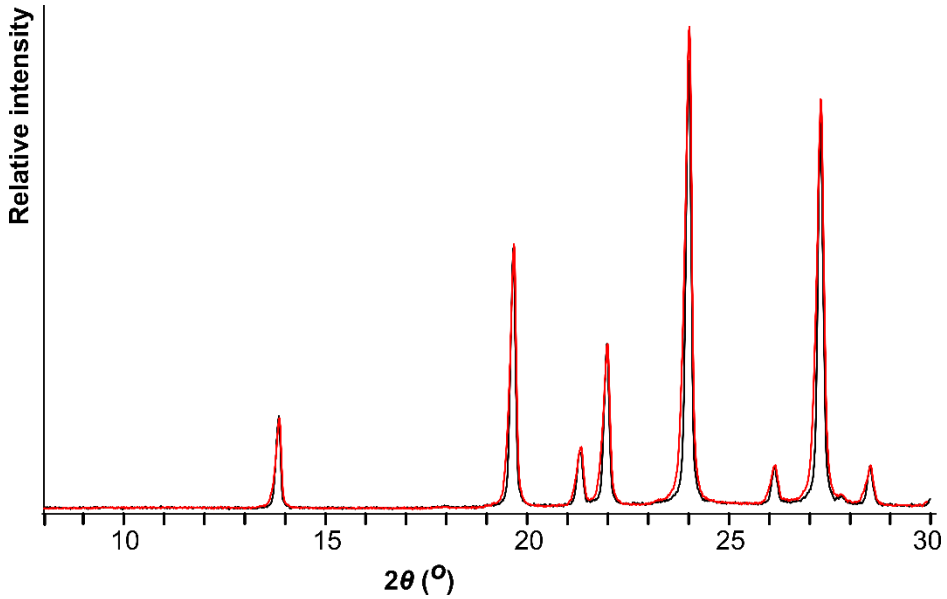

Figure S11. PXRD patterns of the initial sample of glutaric acid used in milling experiments (black) and of glutaric acid after milling for 60 minutes with 20 Hz (red).

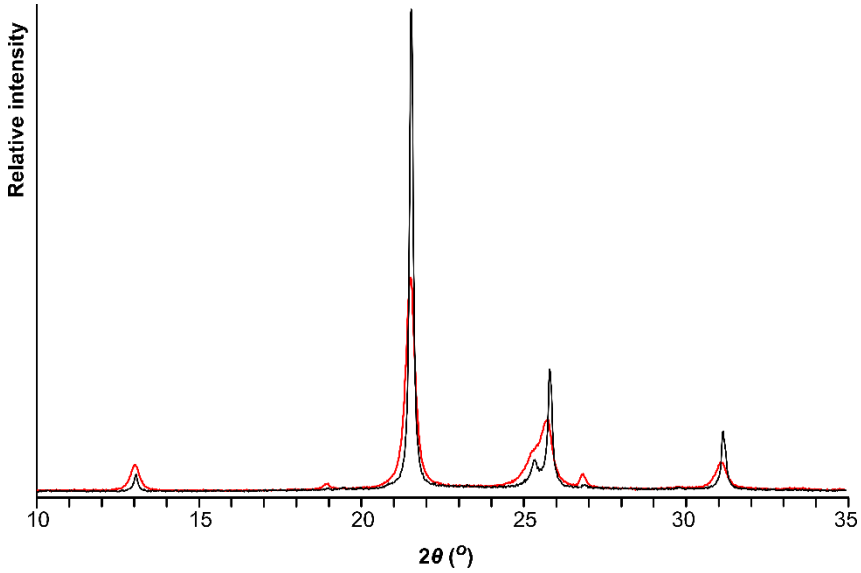

Figure S12. PXRD patterns of the initial sample of adipic acid used in milling experiments (black) and of adipic acid after milling for 60 minutes with 20 Hz (red).

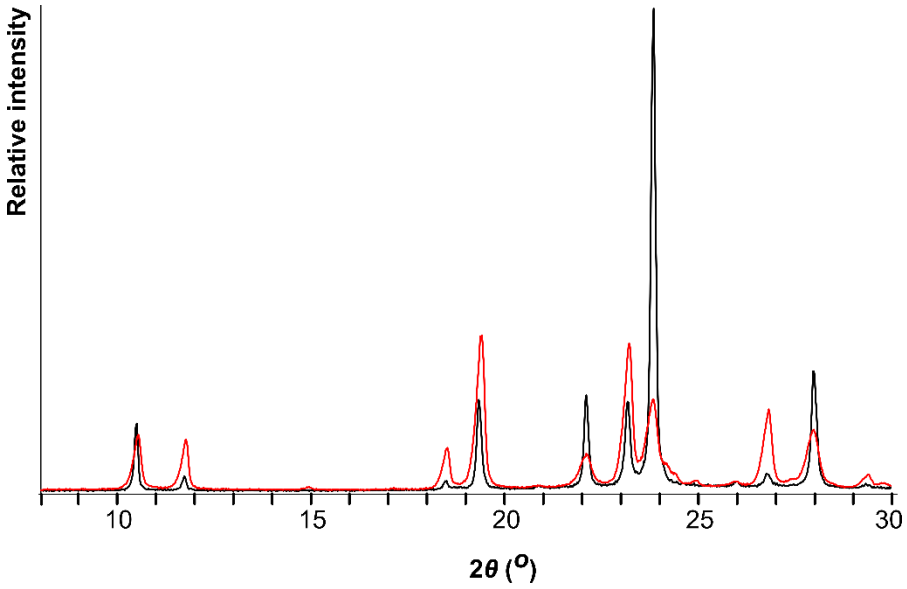

Figure S13. PXRD patterns of the initial sample of pimelic acid used in milling experiments (black) and of pimelic acid after milling for 60 minutes with 20 Hz (red).

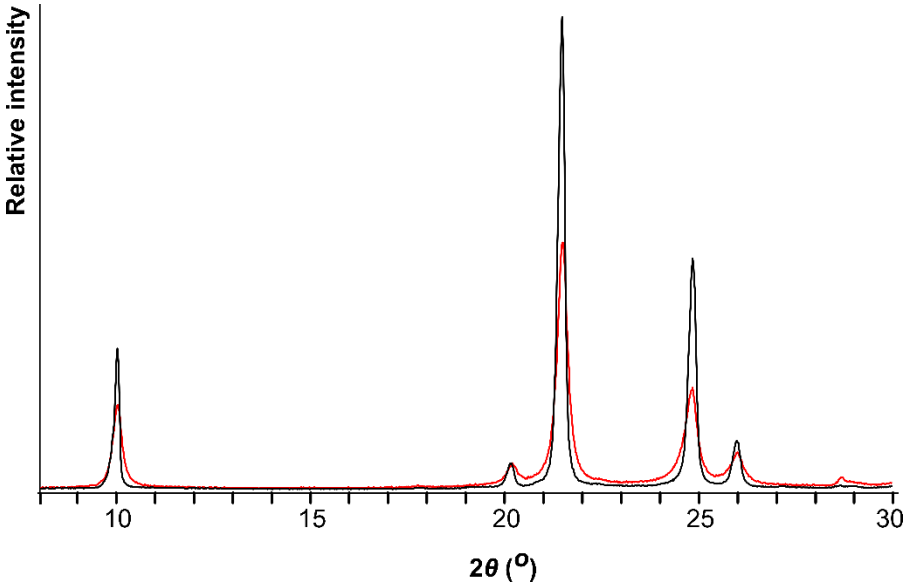

Figure S14. PXRD patterns of the initial sample of suberic acid used in milling experiments (black) and of suberic acid after milling for 60 minutes with 20 Hz (red).

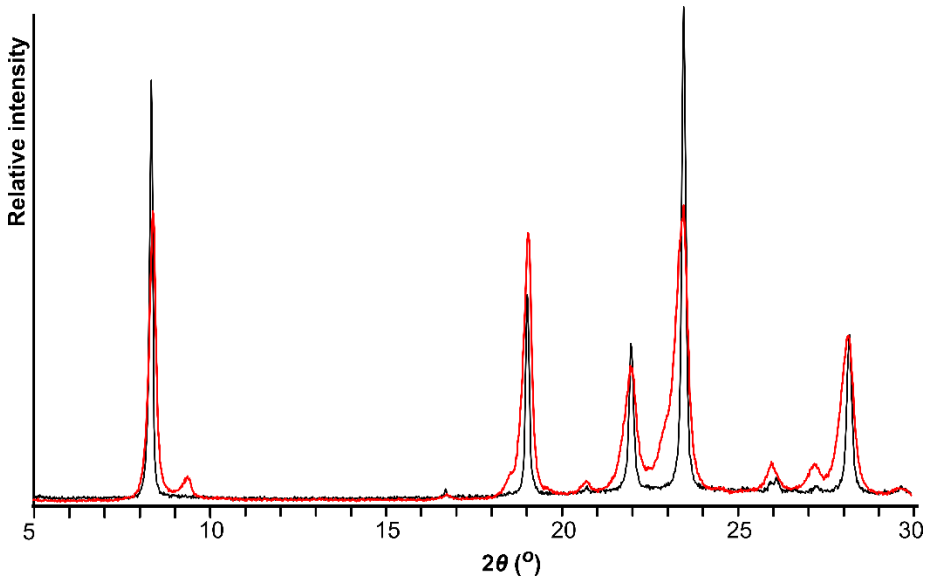

Figure S15. PXRD patterns of the initial sample of azelaic acid used in milling experiments (black) and of azelaic acid after milling for 60 minutes with 20 Hz (red). Polymorph transition was observed during the mechanochemical treatment as implied by formation of new peaks at 2θ=9,2; 18,5; 23°.

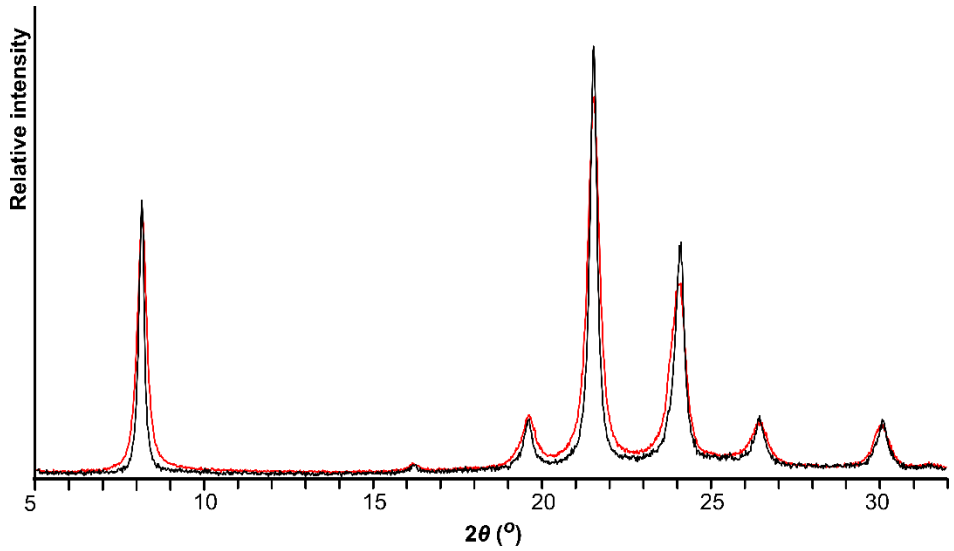

Figure S16. PXRD patterns of the initial sample of sebacic acid used in milling experiments (black) and of sebacic acid after milling for 60 minutes with 20 Hz (red).

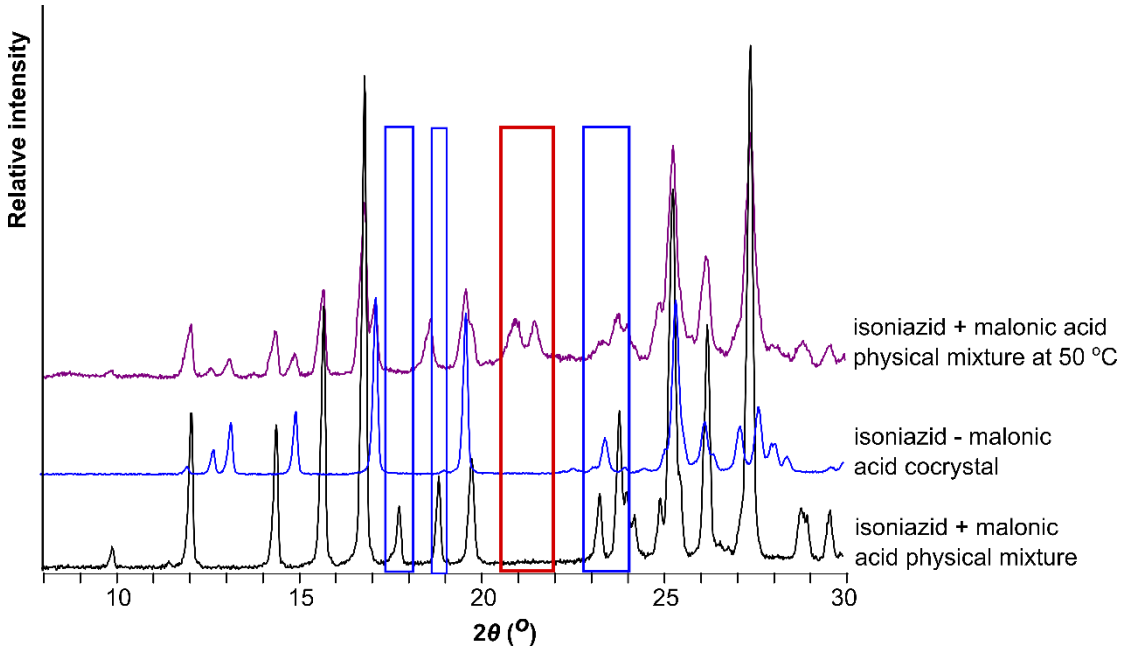

Figure S17. PXRD patterns of isoniazid and malonic acid thermal cocrystallisation products in comparison to PXRD patterns of isoniazid and malonic acid physical mixture and their cocrystal. The red frame shows the peaks of an unidentified phase and the blue frames show the positions of malonic acid peaks.

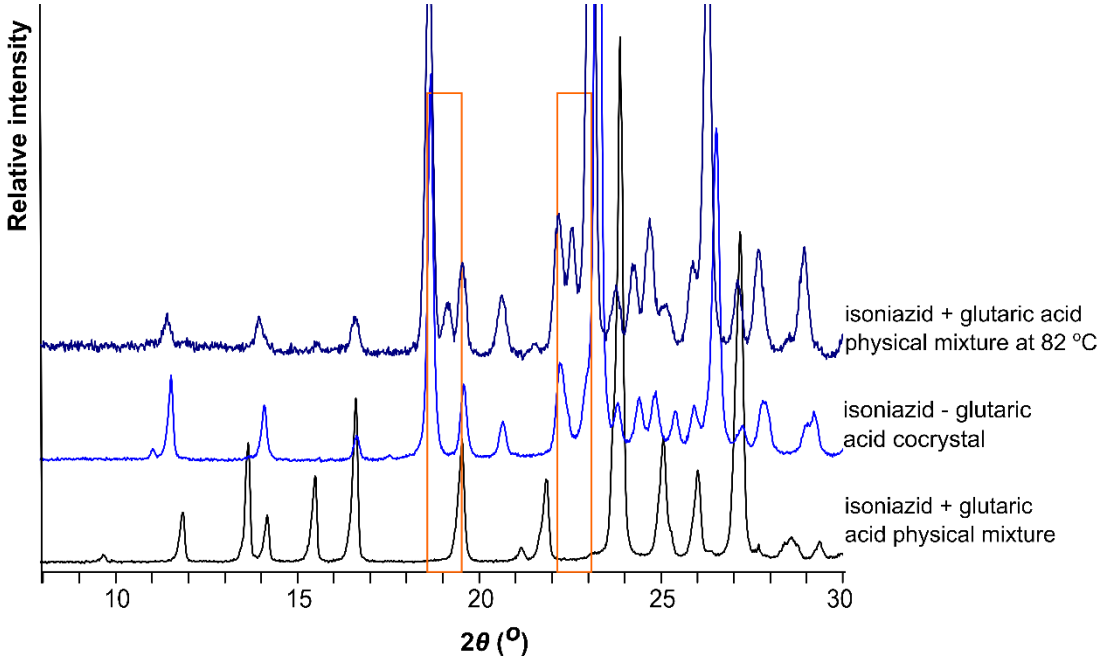

Figure S18. PXRD patterns of isoniazid and glutaric acid thermal cocrystallisation products in comparison to PXRD patterns of isoniazid and glutaric acid physical mixture and their cocrystal. The orange frame shows peaks of an unidentified phase.

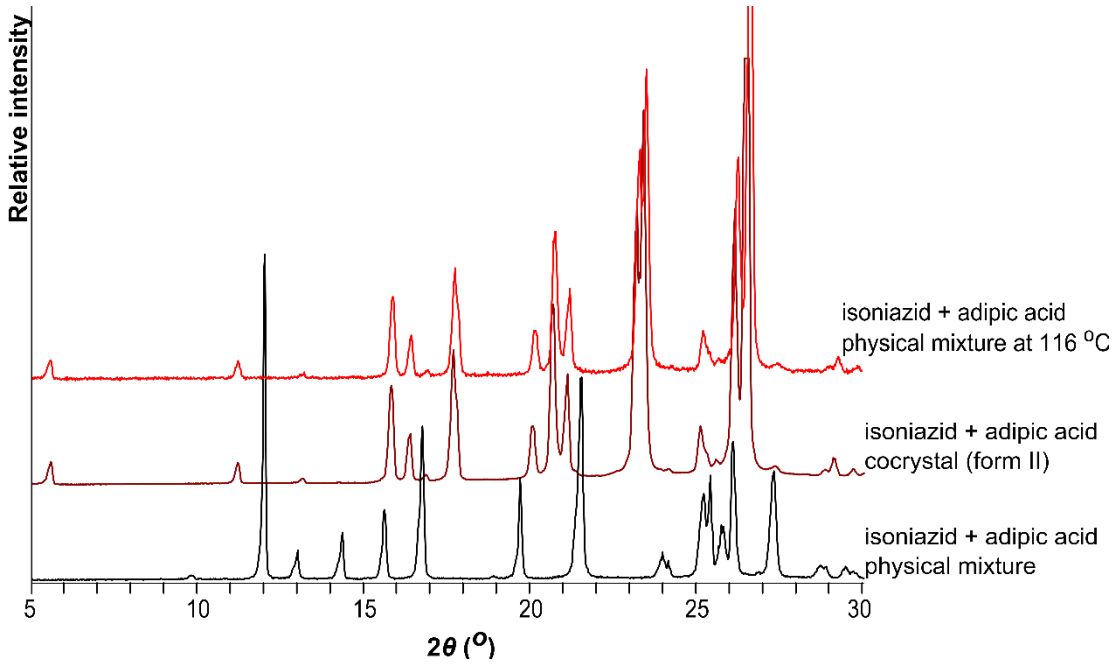

Figure S19. PXRD patterns of isoniazid and adipic acid thermal cocrystallisation products in comparison to PXRD patterns of isoniazid and adipic acid physical mixture and their cocrystal.

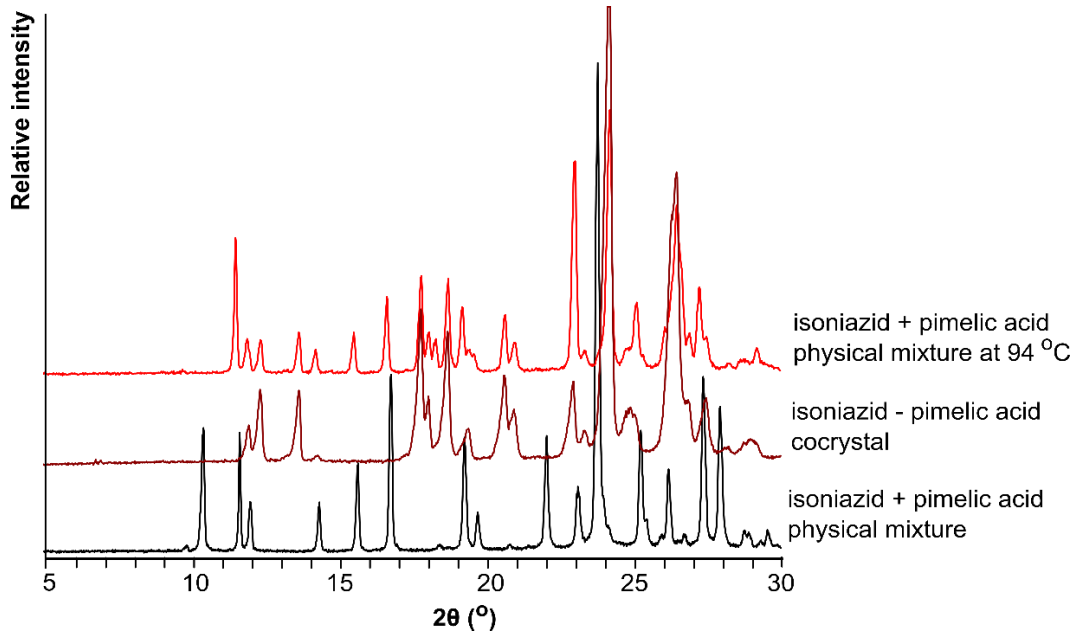

Figure S20. PXRD patterns of isoniazid and pimelic acid thermal cocrystallisation products in comparison to PXRD patterns of isoniazid and pimelic acid physical mixture and their cocrystal.

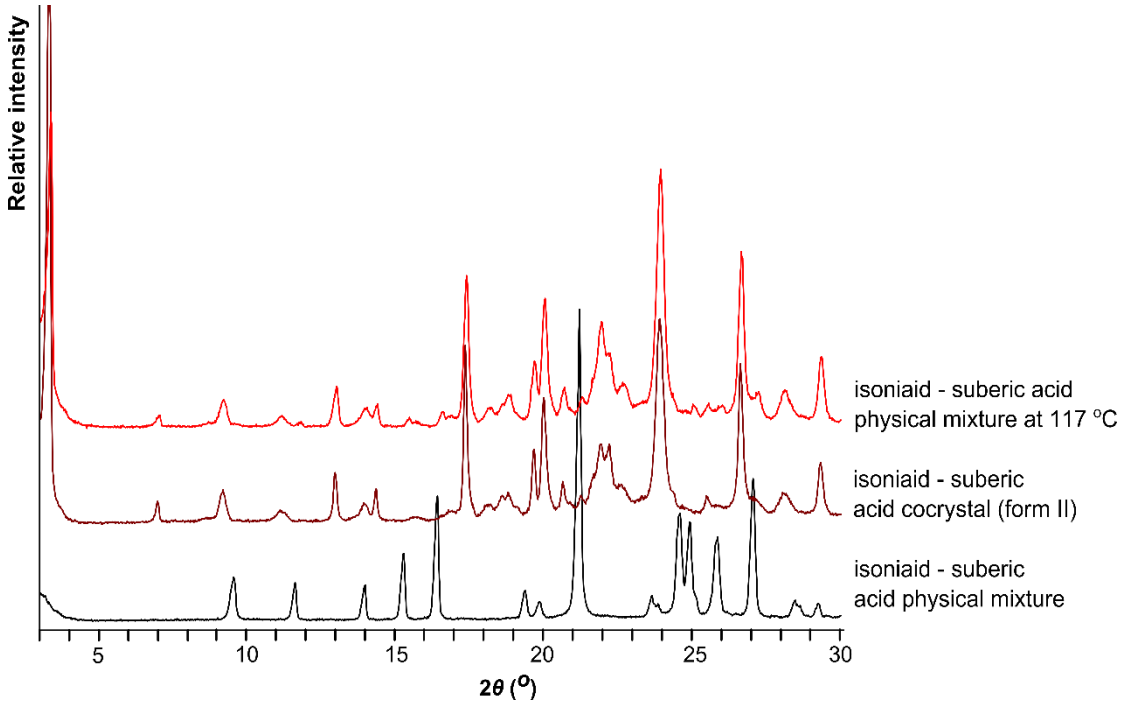

Figure S21. PXRD patterns of isoniazid and suberic acid thermal cocrystallisation products in comparison to PXRD patterns of isoniazid and suberic acid physical mixture and their cocrystal.

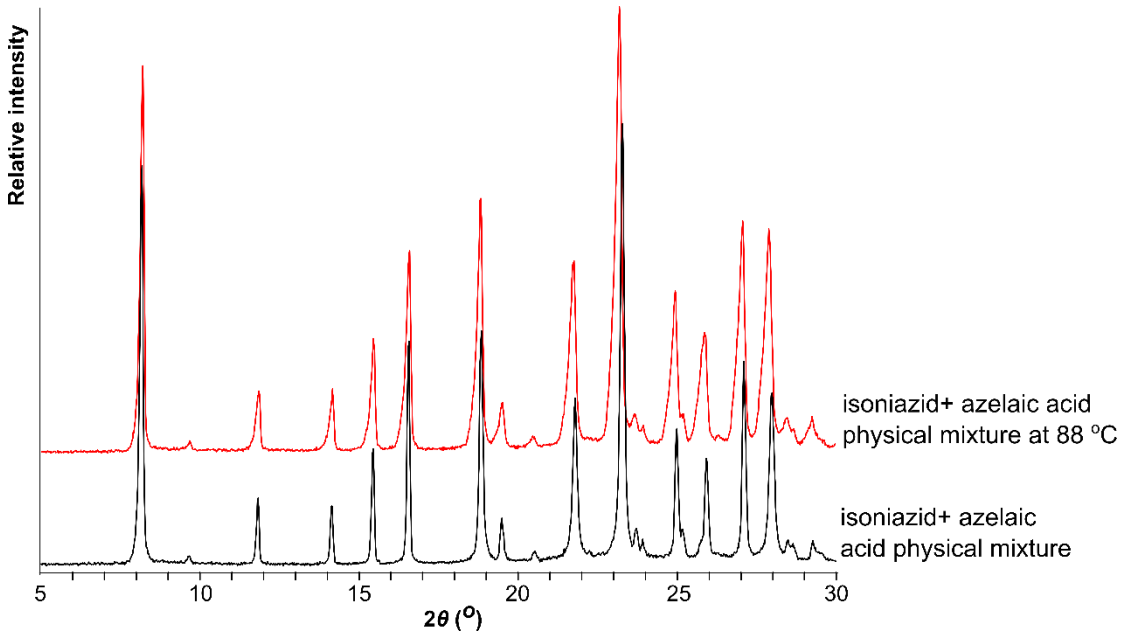

Figure S22. PXRD patterns of isoniazid and azelaic acid thermal cocrystallisation products in comparison to PXRD patterns of isoniazid and azelaic acid physical mixture and their cocrystal.

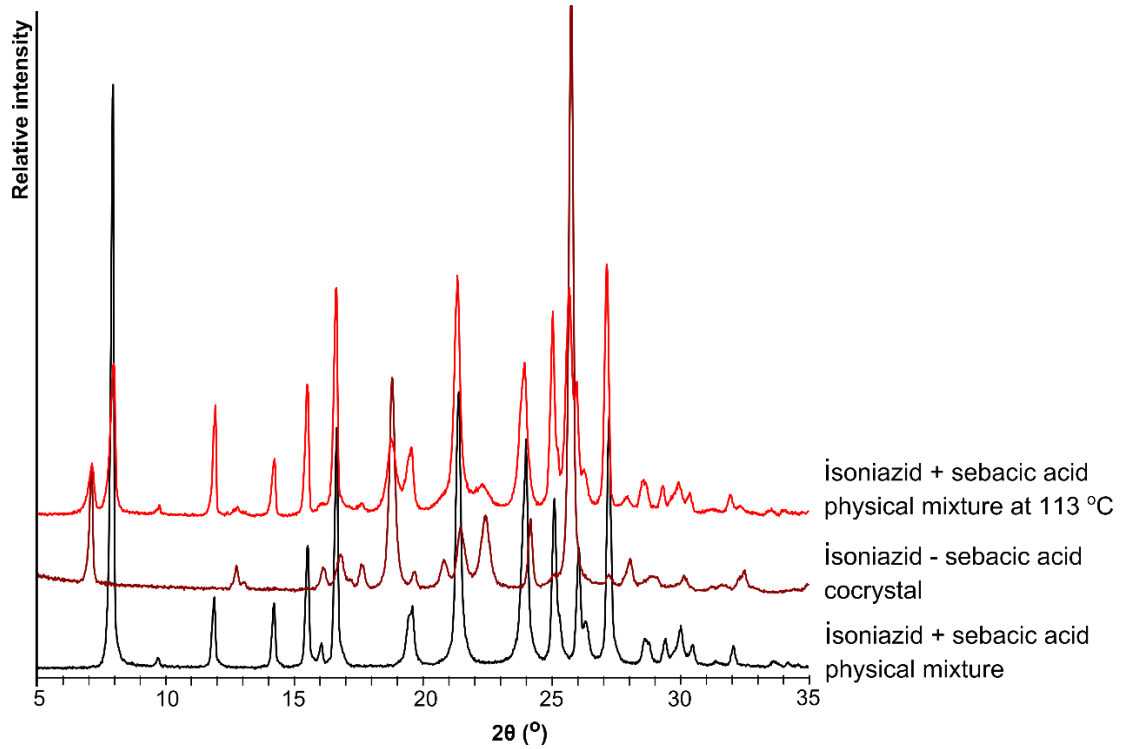

Figure S23. PXRD patterns of isoniazid and sebacic acid thermal cocrystallisation products in comparison to PXRD patterns of isoniazid and sebacic acid physical mixture and their cocrystal.

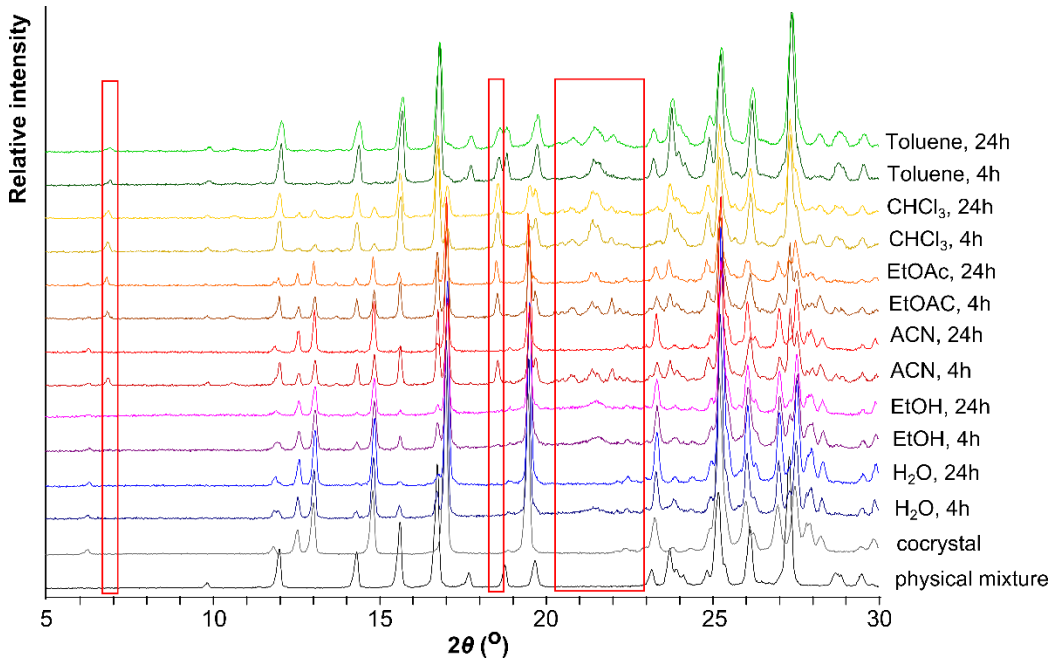

Figure S24. PXRD patterns of isoniazid and malonic acid vapochemical cocrystallisation products in comparison to PXRD patterns of isoniazid and malonic acid physical mixture and their cocrystal. The red frames show the peaks of an unidentified phase.

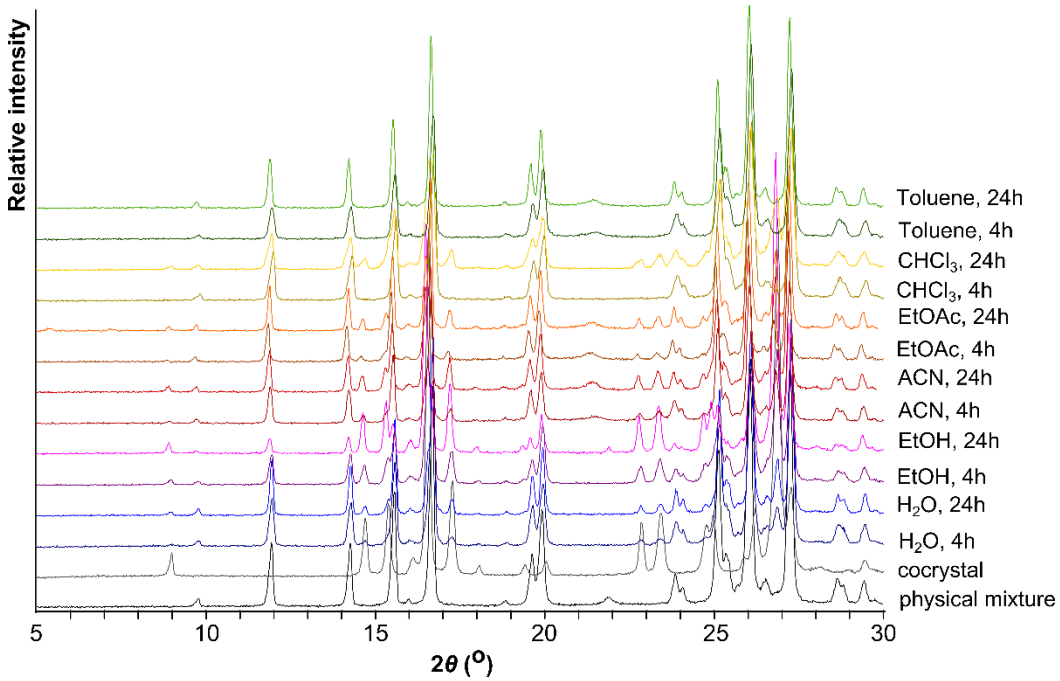

Figure S25. PXRD patterns of isoniazid and succinic acid vapochemical cocrystallisation products in comparison to PXRD patterns of isoniazid and succinic acid physical mixture and their cocrystal.

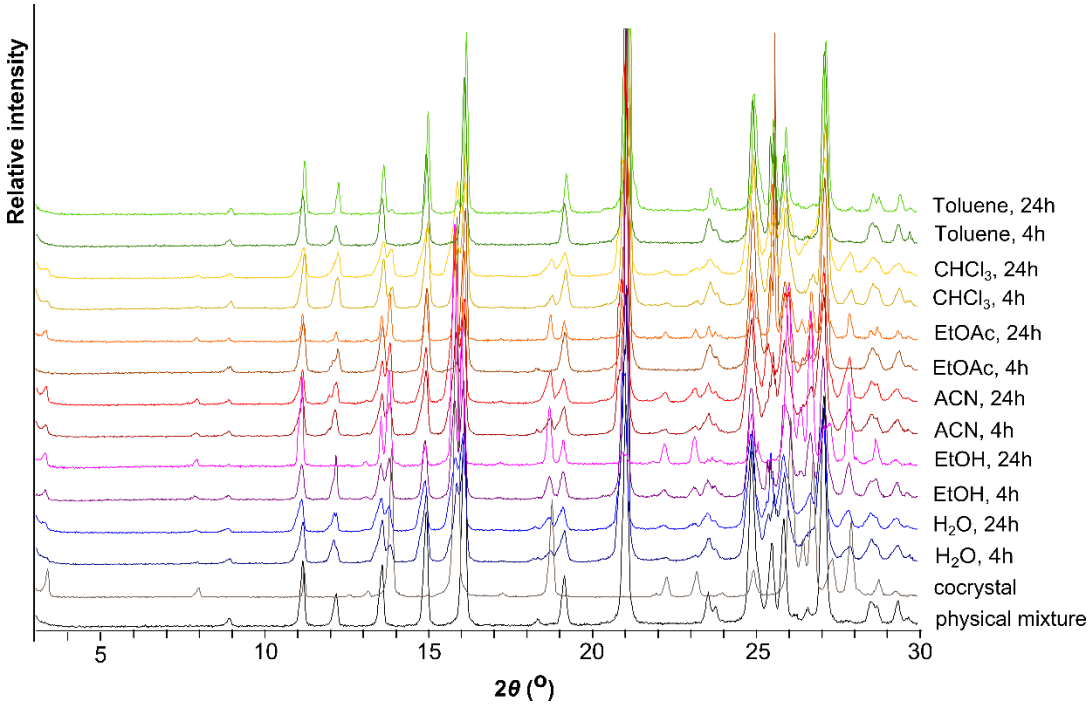

Figure S26. PXRD patterns of isoniazid and glutaric acid vapochemical cocrystallisation products in comparison to PXRD patterns of isoniazid and glutaric acid physical mixture and their cocrystal.

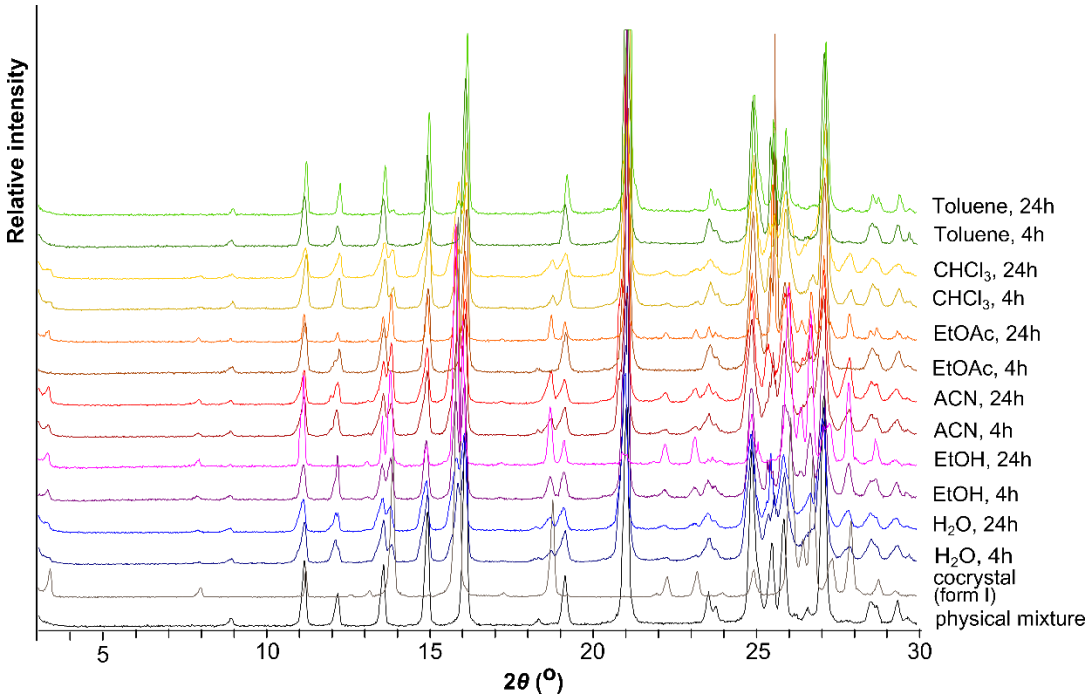

Figure S27. PXRD patterns of isoniazid and adipic acid vapochemical cocrystallisation products in comparison to PXRD patterns of isoniazid and adipic acid physical mixture and their cocrystal.

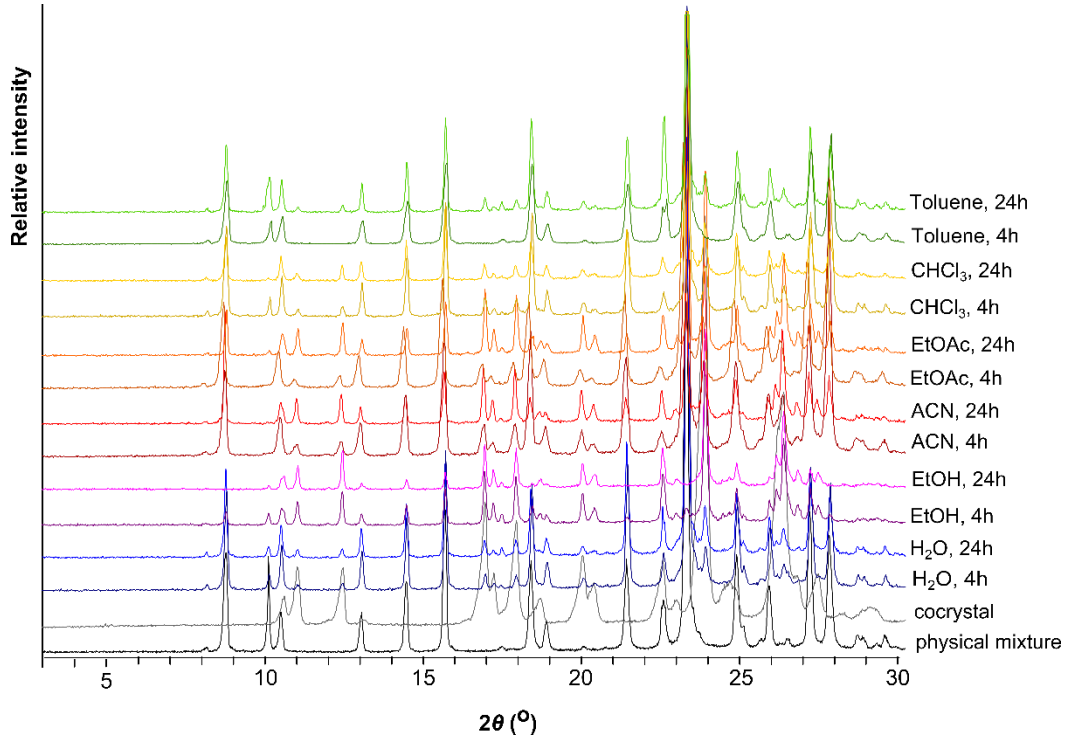

Figure S28. PXRD patterns of isoniazid and pimelic acid vapochemical cocrystallisation products in comparison to PXRD patterns of isoniazid and pimelic acid physical mixture and their cocrystal.

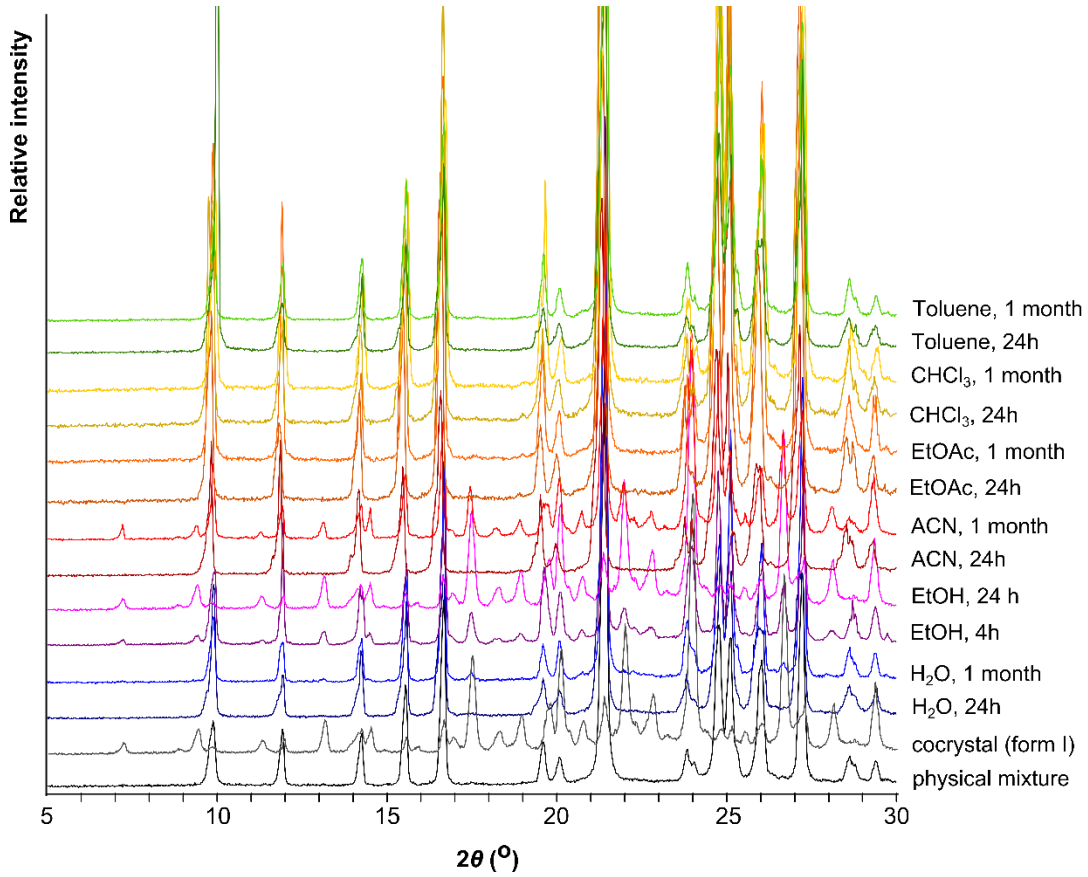

Figure S29. PXRD patterns of isoniazid and suberic acid vapochemical cocrystallisation products in comparison to PXRD patterns of isoniazid and suberic acid physical mixture and their cocrystal.

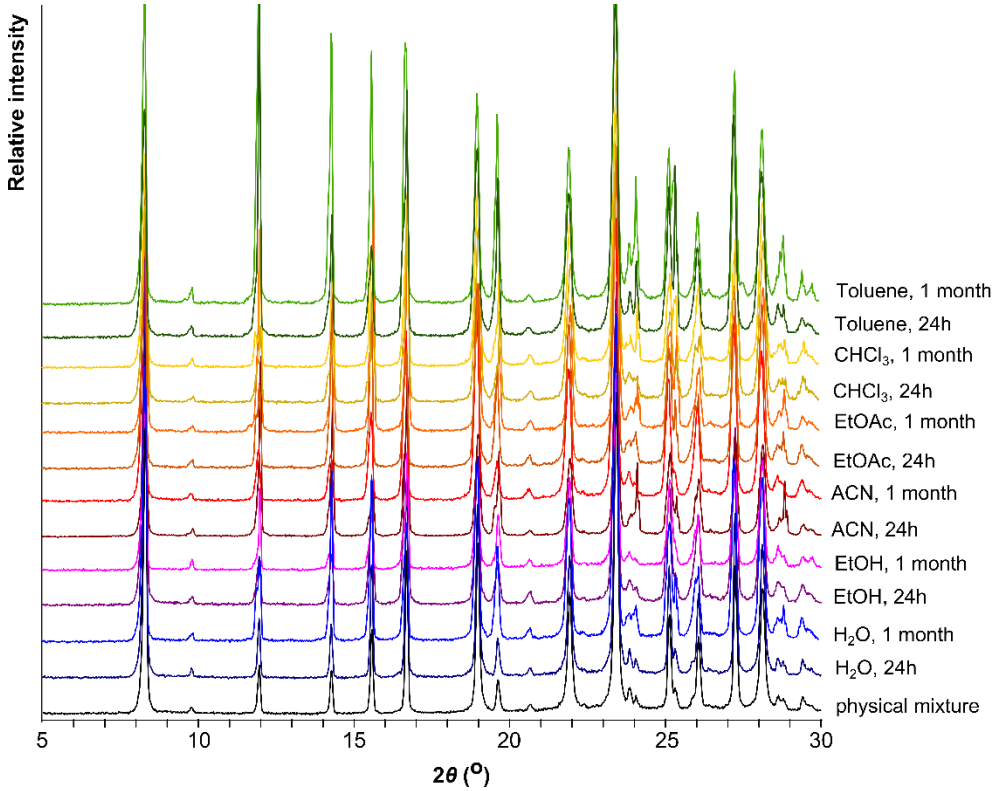

Figure S30. PXRD patterns of isoniazid and azelaic acid vapochemical cocrystallisation products in comparison to PXRD patterns of isoniazid and azelaic acid physical mixture and their cocrystal.

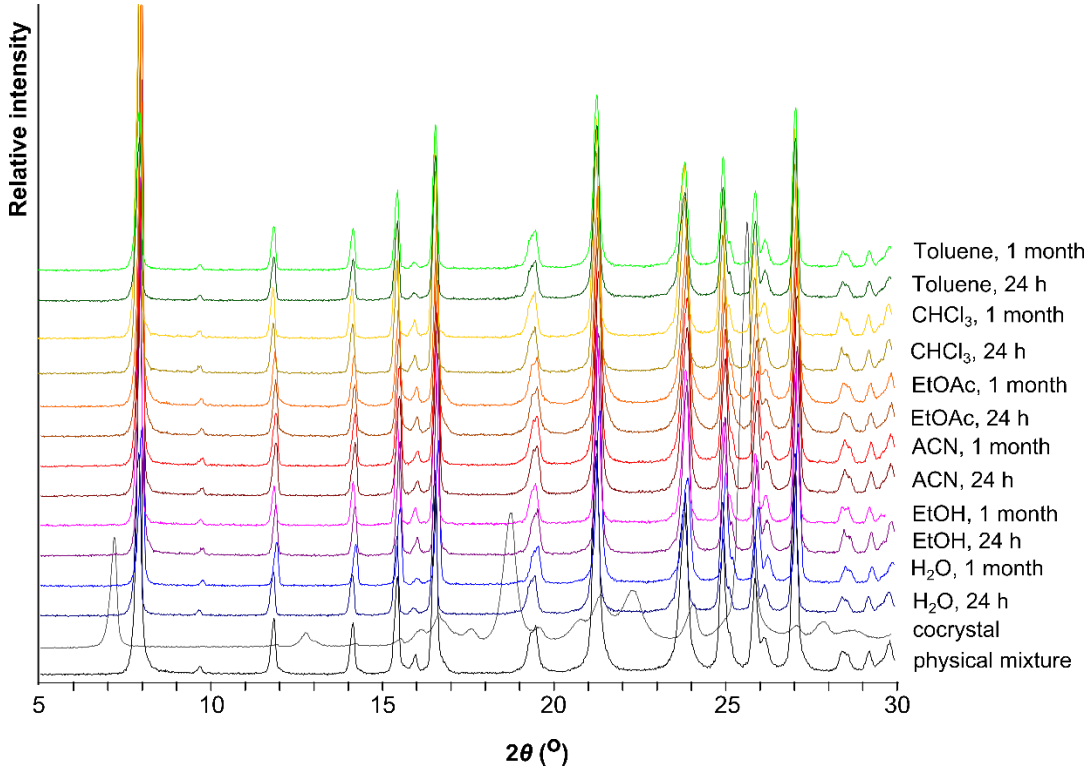

Figure S31. PXRD patterns of isoniazid and sebacic acid vapochemical cocrystallisation products in comparison to PXRD patterns of isoniazid and sebacic acid physical mixture and their cocrystal.

Table S1 Molecular descriptors and physical property parameters of solvents used in vapour-assisted cocrystallisation experiments

Solvent	SIEA-probe[1]	SIED-probe[1]	α^2	β^2	VOL[1]	n^1	π^1	γ^1	ε^1	μ^1	η^1	σ^1	PI[1]	BP[1]
Water	0.0	-45.7	1.17	0.47	136	1.33	0.45	104.7	78.4	1.9	0.9	45.8	8.8	100
Ethanol	-36.4	-11.3	0.37	0.48	267	1.36	0.42	31.6	24.6	1.7	1.1	26.4	4.3	78
Acetonitrile	-18.6	0.0	0.07	0.32	241	1.34	0.90	41.3	37.5	3.9	0.4	24.1	5.8	82
Ethyl acetate	-15.7	0.0	0.00	0.45	394	1.37	0.62	33.7	6.1	1.8	0.4	18.3	4.4	77
Chloroform	-1.2	0.0	0.15	0.02	313	1.45	0.49	38.4	4.8	1.0	0.5	19.0	4.1	61
Toluene	0.0	0.0	0.00	0.14	413	1.50	0.52	40.2	2.3	0.4	0.6	18.4	2.4	111

SIEA-probe – Surface integral for enthalpy values of interactions between acceptor atoms of a molecule and a donor probe on the surface

SIED-probe – Surface integral for enthalpy values for interactions between donor atoms of a molecule and an acceptor probe on the surface

α – Summation of the hydrogen bond donor propensities of the solvent

β – Summation of the hydrogen bond acceptor propensities of the solvent

VOL – Intrinsic volume of the molecule, $Å^3$

N – Refraction index

π – Polarizability

γ – Surface tension

ε – Dielectric constant

μ – Dipole moment, Debye

η – Viscosity, c.p.

σ – Hildebrand solubility, $(J\ cm^{-3})^{0.5}$

PI – Polarity Index, Snyder

BP – Boiling point, °C

[1] D. Xu and N. Redman-Furey, *Int. J. Pharm.*, 2007, **339**, 175–188.
[2] M. H. Abraham, *J. Phys. Org. Chem*., 1993, **6**, 660–684.

Table S2. Crystallographic data of isoniazid – adipic acid cocrystal form II

Empirical formula	$C_6H_{10}O_4 \cdot 2(C_6H_7N_3O)$
Formula weight	420.43
Crystal system	Monoclinic
Space group	$P\,2_1/c$
***a* (Å)**	16.20(1)
***b* (Å)**	7.378(7)
***c* (Å)**	8.793(6)
***β* (°)**	105.08(3)
***V* (Å^3)**	1014.8(13)
Z	2
***ρ* (g cm^{-3})**	1.376
***T* (K)**	293
R_1	0.04334
wR_2	0.05947
GOF	7.9