Supporting information for "Salts, Cocrystals and Ionic Cocrystals of a "Simple" Tautomeric Compound"

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Supporting Information

1. Experimental Details

1.1 Solid form screening via LAG

In LAG experiments, outcomes of the LAG experiments were identical regardless of the solvent used, except for saccharin and malonic acid. For saccharin and malonic acid, the complexes were found to be in different forms when grinding with water and organic solvents (methanol, ethanol, acetone, acetonitrile, etc.). In addition, for pABA and oxalic acid, pXRD indicated that the forms obtained by LAG and evaporation were distinct; however, we failed to produced single crystals of LAG complexes suitable for single crystal XRD.

All the single crystals were crystallized in either water or methanol. The initial ratio (AHMP:coformer) of the compounds added to the solution and the method was listed in Table S1.

1.2 Experimental details on cocrystallisation from solution.

Table S1. Solvents and initial ratio used in crystallization of AHMP complexes single crystals.

Compound No. in article	Species	Coformer	Initial ratio	Solvent	Method
-	Salt	HCl*	-	water	Slow evaporation under ambient temperature (7 days)
-	IC hydrate	HCl*	-	water	Slow evaporation under ambient temperature (7 days)
(1)	Cocrystal	Benzoic acid	1:1	water	Slow evaporation under ambient temperature (7 days)
(5)	Cocrystal	pABA	1:1	water	Slow evaporation under ambient temperature (7 days)
(7)	Salt	Phthalic acid	1:1	water	Slow evaporation under ambient temperature (7 days)
(9a)	IC hydrate	Malonic acid	1:2	water	Slow evaporation under ambient temperature (7days)
(9b)	IC	Malonic acid	1:1	methanol	Slow evaporation under ambient temperature (7days)
(10)	Cocrystal	Glutaric acid	1:1	methanol	Slow evaporation under ambient temperature (7 days)
(11)	Salt	Oxalic acid	1:1	water	Slow evaporation under ambient temperature (7days)
(15a)	Salt hydrate Form I	Saccharin	1:1	water	Slow evaporation under ambient temperature (7days)/cooling at 0.5□/ h (from 40□ to 10□)
(15b)	Salt hydrate Form II	Saccharin	1:1	water	Slow evaporation under ambient temperature (7 days)
(15c)	IC	Saccharin	1:1	methanol	Cooling at 0.5 °/h (from 40□ to 10□)

- For AHMP-HCl complexes, AHMP-HCl salt could be obtained when the pH of the solution is below 2, while its IC could be obtained when the pH is about 4.

For AHMP-HCl salt, 0.1023 g AHMP was dissolved in 30 mL water under ambient temperature (c.a. 25 □). HCl solution (1 mol/L) was added into the solution until the pH is 2 (or below 2). Then the solution was sealed with film with several holes on it and put for slow evaporation. After about 7 days crystals were crystalized from the solution.

For AHMP-HCl ionic cocrystal, 0.1023 g AHMP was dissolved in 30 mL water under ambient temperature (c.a. 25 □). HCl solution (1 mol/L) was added into the solution until the pH is about 4. Then the solution was sealed with film with several holes on it and put for slow evaporation. After about 7 days single crystals suitable for XRD were crystalized from the solution.

For AHMP-benzoic acid cocrystal, about 0.15 g AHMP as well as benzoic acid (about 1:1 in molar ratio) were dissolved in 50 mL water under ambient temperature (c.a. 25 □). The solution was filtered and the filter liquor was sealed with film with several holes on it and put for slow evaporation. After about 7 days single crystals suitable for XRD were crystalized from the solution.

For AHMP-pABA cocrystal, 0.14 g AHMP and 0.15 g pABA (about 1:1 in molar ratio) were dissolved in 50 mL water under ambient temperature (c.a. 25 □). The solution was sealed with film with several holes on it and put for slow evaporation. After about 7 days single crystals suitable for XRD were crystalized from the solution.

For AHMP-phthalic acid salt, about 0.1 g AHMP and 0.13 g phthalic acid (about 1:1 in molar ratio) were dissolved in 50 mL water under ambient temperature (c.a. 25 □). The solution was filtered and the filter liquor was sealed with film with several holes on it and put for slow evaporation. After about 7 days single crystals suitable for XRD were crystalized from the solution.

For AHMP-malonic ionic cocrystal hydrate, about 0.12 g AHMP and 0.2 g malonic acid (about 1:2 in molar ratio) were dissolved in 40 mL water at ambient temperature (c.a. 25 □). The solution was sealed

with film with several holes on it and put for slow evaporation. After about 7 days single crystals suitable for XRD were crystalized from the solution.

For AHMP-malonic ionic cocrystal, about 0.12 g AHMP as well as 0.1 g malonic acid (about 1:1 in molar ratio) were dissolved in 50 mL methanol at 35 □. Then the solution was cooled down to ambient temperature and sealed with film with several holes on it and put for slow evaporation. After about 7 days single crystals suitable for XRD were crystalized from the solution.

For AHMP-glutaric acid cocrystal, about 0.12 g AHMP and 0.13 g glutaric acid (about 1:1 in molar ratio) were dissolved in 50 mL methanol at 35 □. Then the solution was cooled down to ambient temperature and sealed with film with several holes on it and put for slow evaporation. After about 7 days single crystals suitable for XRD were crystalized from the solution.

For AHMP-oxalic acid salt, about 0.1 g AHMP and 0.09 g oxalic acid (about 1:1 in molar ratio) were dissolved in 30 mL water. The solution was slightly warmed to ensure that all of the crystals were dissolved. Then, the solution was sealed with film with several holes on it and put for slow evaporation. After about 7 days single crystals suitable for XRD were crystalized from the solution.

For AHMP-saccharin salt form I, about 0.4 g AHMP and 0.6 g saccharin were dissolved in 15 mL water at 40 □. Then the solution was cooled down to 10 □ at the rate of 0.5 □/h. After 60 hours single crystals suitable for XRD were crystalized from the solution.

For AHMP-saccharin salt form II, it could only crystalize with form I in water. About 0.16 g AHMP and 0.2 g saccharin were dissolved in 50 mL water. The solution was slightly warmed to dissolve all of the crystals. Then the solution was put under ambient temperature and sealed with film with holes on it for slow evaporation. After about 7 days single crystals of form II were crystalized and floated on the surface of the solution. The crystals then were dried for 1 day and were suitable for XRD.

For AHMP-saccharin ionic cocrystal, 0.1 g AHMP as well as 0.18 g saccharin were dissolved in 50 mL methanol at 50 □. Then the solution was cooled down to 40 □ in an hour and were cooled down to 10 □ at the rate of 0.5 □/h. After 60 hours single crystals suitable for XRD were crystalized from solution.

2. PXRD of AHMP and AHMP complexes

The PXRD patterns for all newly discovered forms, as well as pure AHMP are reported in Figure S1.

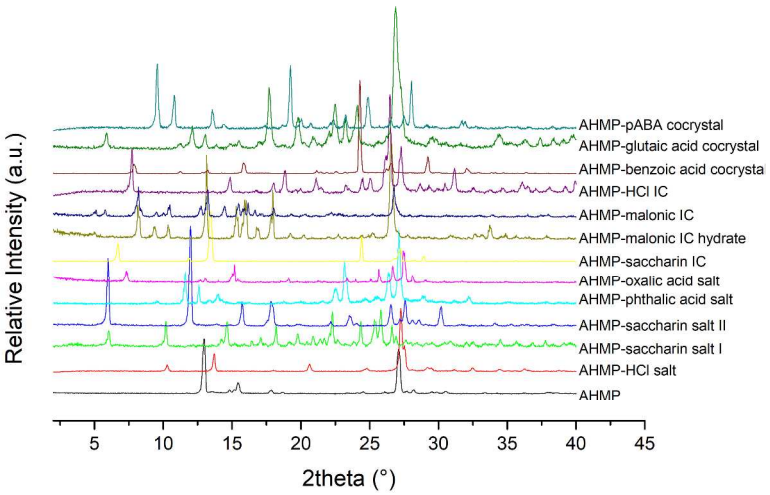
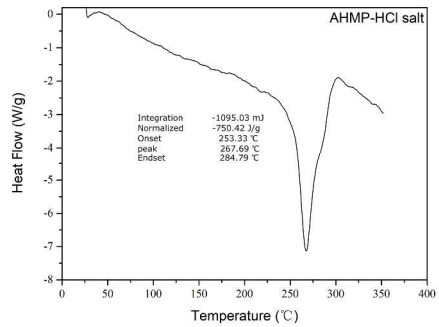
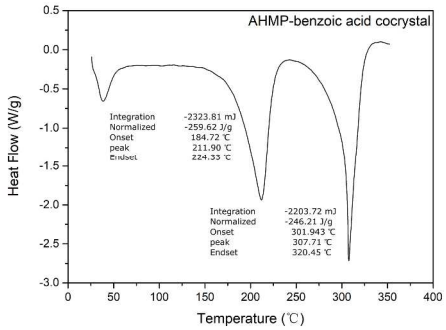


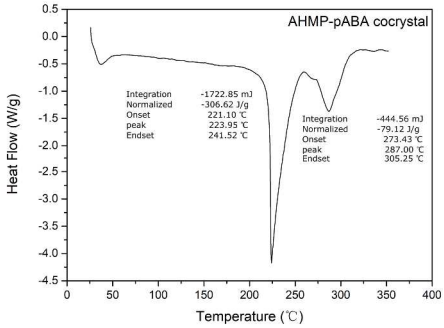
Figure S1. Comparison of PXRD patterns of the new solid forms obtained together with pure AHMP.

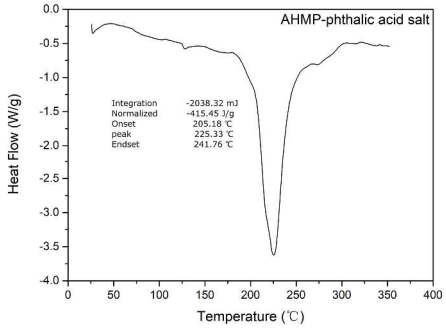
3. DSC Results

DSC patterns for all newly discovered forms are reported in Figure S2 with detail information of the peaks (except AHMP-HCl IC). Nearly all of the patterns show more than one peaks during heating which are distinguished from pure AHMP (about 300 □), except AHMP-HCl salt and AHMP-phthalic acid salt (They all have one peak but different from AHMP). Even though the loss of water molecule may explain the peaks in low temperature for hydrates, there still exist peaks which cannot be identified.









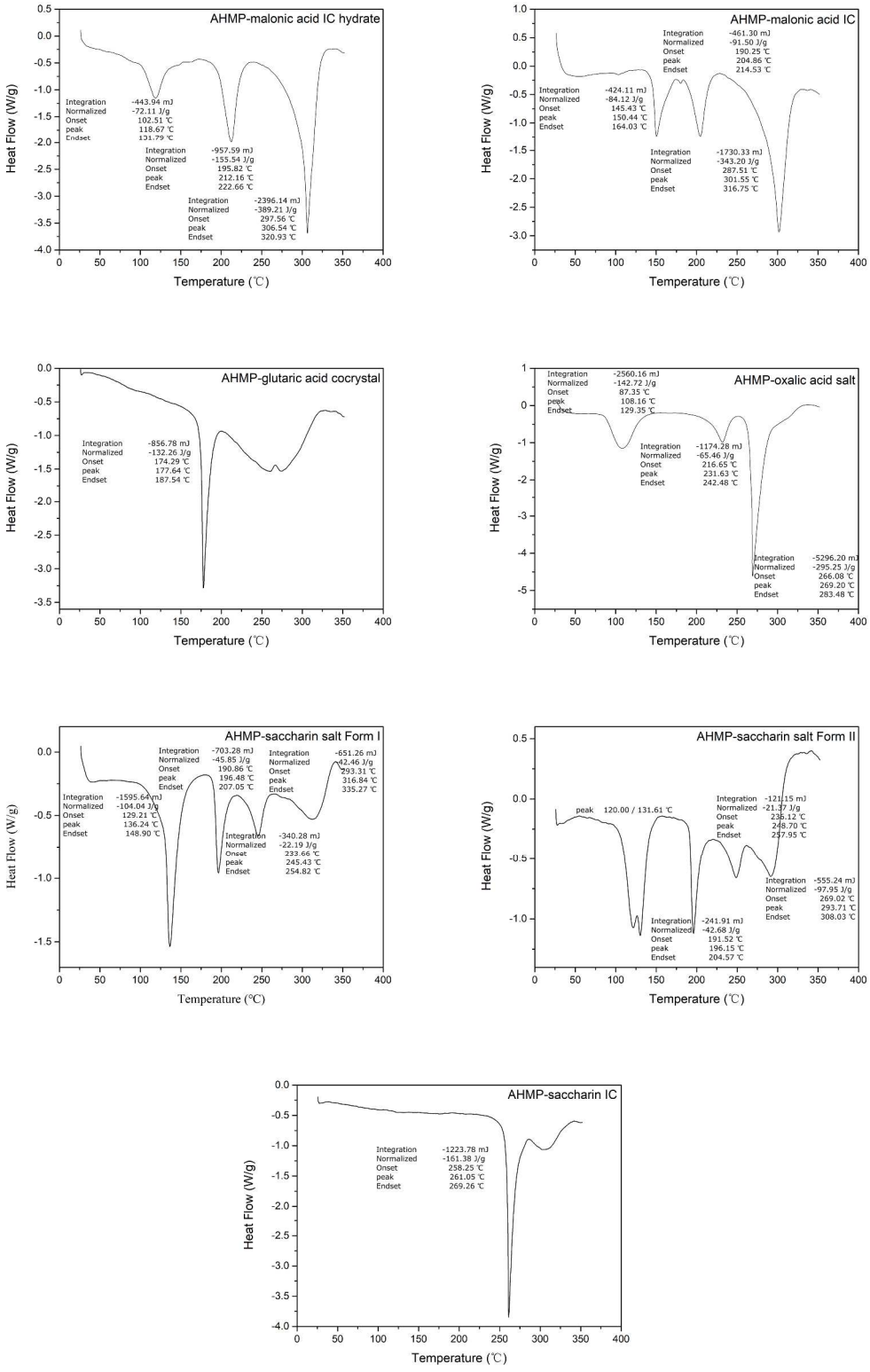
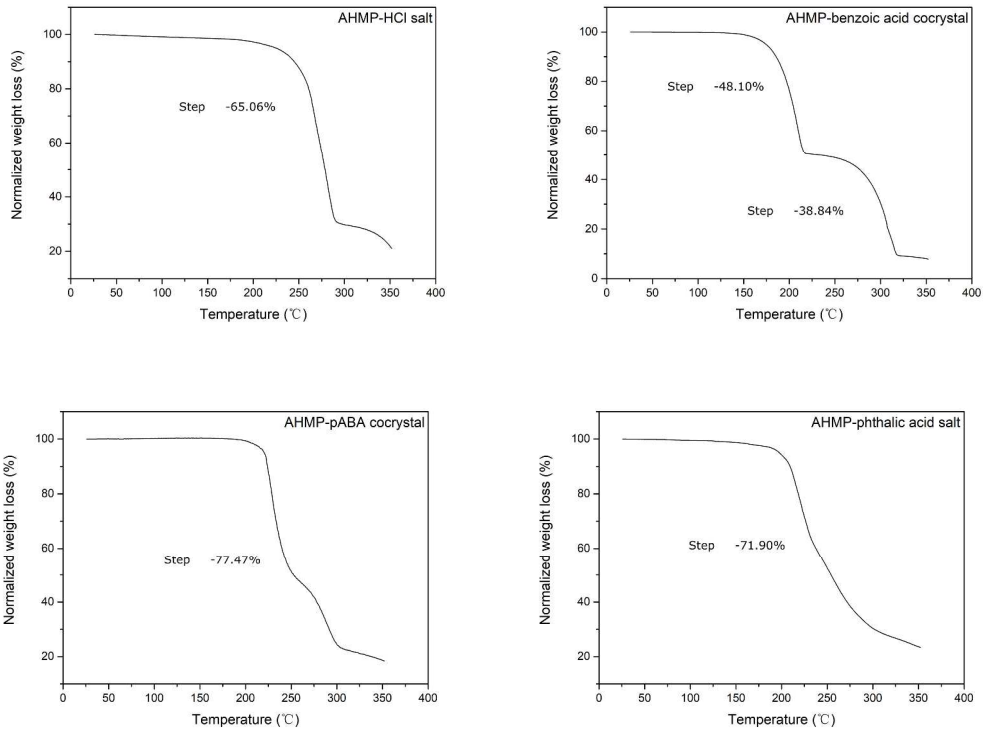


Figure S2. DSC curves of complexes obtained in the experiment.

4. TGA Results

Thermogravimetric analysis curves are reported in Figure S3 for all newly discovered forms (except AHMP-HCl IC). It can be concluded that all of the complexes experienced at least one weigh loss during the heating, indicating that some complicated decomposition processes have happened, in addition to desolvation. While there is a one-to-one correspondence between the weight loss and almost all of the DSC peaks, melting point is difficult to identify because of the decomposition processes.



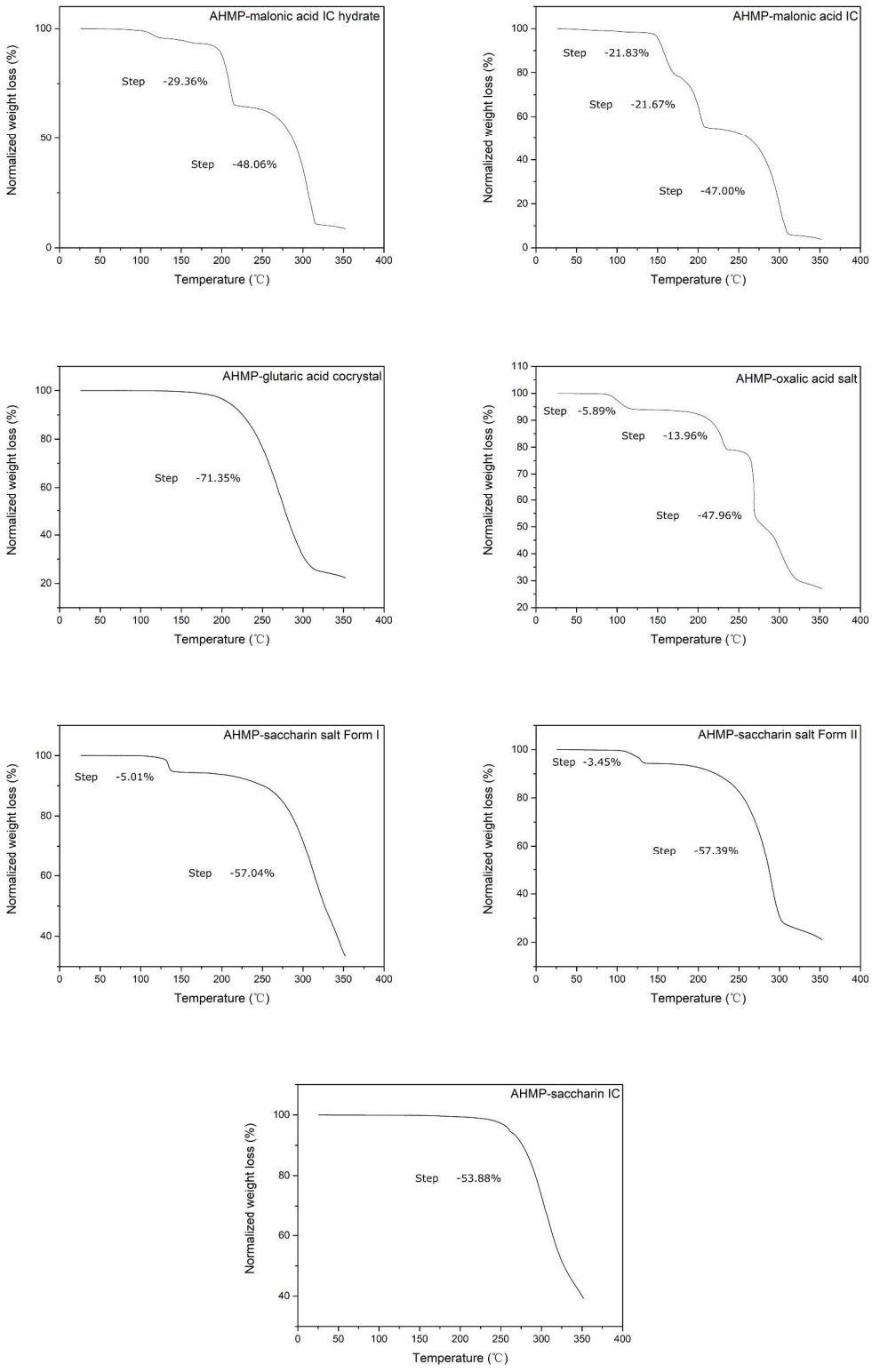


Figure S3. TGA curves of complexes obtained in the experiment.

5. Titration of aqueous AHMP solution with hydrochloric acid

About 1 g of AHMP powder was dissolved in 300 mL water to which HCl (1 mol/L) was added in 0.2 mL increments. A pH meter (Mettler Toledo, Five Easy) was used to detect the pH of the solution. The titration was stopped when the pH nearly stopped decreasing. Figure S4 shows the pH against the volume of HCl solution added.

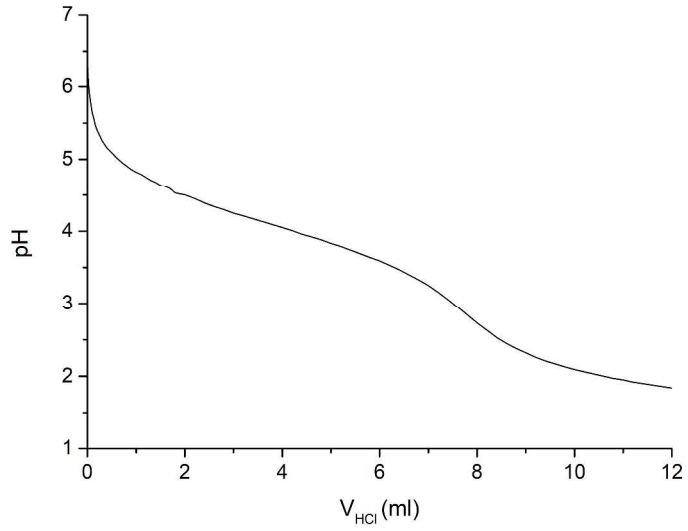


Figure S4. AHMP's pH variation with the addition of HCl in aqueous solution.

6. SCXRD results & Structure analysis

Table S2 reports crystallographic information of the newly discovered forms obtained from single crystal XRD. In the remainder of this section, structural features of the newly discovered forms are discussed.

Table S2. Single crystal XRD data of complexes in the experiment.

Compound No. in article	-	-
Coformer	Hydrochloric acid	Hydrochloric acid
Space Group	P c	P -1
Cell Lengths	**a** 4.19835(13) **b** 8.5153(2) **c** 9.8366(2)	**α** 6.7683(5) **b** 8.1761(7) **c** 14.0552(10)
Cell Angles	**α** 90 **β** 90.552(3) **γ** 90	a 104.625(7) **β** 92.203(6) **γ** 103.703(7)
Cell Volume	351.644 Å	727.164 Å
Z,Z'	**Z**: 2 **Z'**: 0	**Z**: 1 **Z'**: 0
R-Factor (%)	2.92	4.47
Temperature (K)	150	100

Compound No. in article	(1)	(5)
Corformer	Benzoic acid	Para aminobenzoic acid (pABA)
Space Group	P 2_1/c	P 2_1/c
Cell Lengths	**a** 6.5502(13) **b** 8.3944(17) **c** 22.215(4)	**a** 9.2771(3) **b** 18.0908(5) **c** 8.2883(4)
Cell Angles	**α** 90.00 **β** 91.51(3) **γ** 90.00	**α** 90 **β** 101.780(4) **γ** 90
Cell Volume	1221.07	1361.73 Å
Z,Z'	**Z**: 4 **Z'**: 0	**Z**: 4 **Z'**: 0
R-Factor (%)	4.65	4.14
Temperture (K)	283-303	149.98

Compound No. in article	(7)	(9a) IC hydrate
Corformer	Phthalic acid	Malonic acid
Space Group	P -1	P 2_1/n

Cell Lengths	**a** 7.9490(6) **b** 12.3337(7) **c** 13.7736(8)	**a** 4.7073(9) **b** 32.916(7) **c** 10.921(2)
Cell Angles	**α** 88.319(5) **β** 74.844(6) **γ** 86.849(5)	**α** 90.00 **β** 97.96(3) **γ** 90.00
Cell Volume	1301.28 Å	1675.86 Å
Z,Z'	**Z**: 2 **Z'**: 0	**Z**: 0 **Z'**: 0
R-Factor (%)	3.93	7.25
Temperture (K)	150	150

Compound No. in article	(9b) IC	(11)
Corformer	Malonic acid	Oxalic acid
Space Group	P 2_1	P -1
Cell Lengths	**a** 11.107(2) **b** 15.996(3) **c** 9.2485(18)	**a** 6.6189(13) **b** 7.2115(14) **c** 11.856(2)
Cell Angles	**α** 90.00 **β** 98.21(3) **γ** 90.00	**α** 82.42(3) **β** 76.00(3) **γ**66.20(3)
Cell Volume	1626.32 Å	502.032 Å
Z,Z'	**Z**: 2 **Z'**: 0	**Z**: 2 **Z'**: 0
R-Factor (%)	5.66	7.34
Temperture (K)	283-303	283-303

Compound No. in article	(15a) salt hydrate Form I	(15b) salt hydrate Form II
Corformer	Saccharin	Saccharin
Space Group	P -1	P -1
Cell Lengths	**a** 6.3096(10) **b** 7.5095(10) **c** 14.836(3)	**a** 7.9794(5) **b** 9.2354(6) **c** 13.1180(11)
Cell Angles	**α** 83.168(12) **β** 86.857(13) **γ** 85.943(12)	**α** 88.652(6) **β** 84.108(6) **γ** 76.900(6)
Cell Volume	695.453 Å	936.573 Å
Z,Z'	**Z**: 2 **Z'**: 0	**Z**: 2 **Z'**: 0
R-Factor (%)	5.65	6.25

Temperture (K)	100	149.9

Compound No. in article	(15c) IC
Corformer	Saccharin
Space Group	P $2_1/n$
Cell Lengths	**a** 9.1545(3) **b** 10.7373(3) **c** 28.9295(8)
Cell Angles	**α** 90 **β** 91.826(2) **γ** 90
Cell Volume	2842.17 Å
Z,Z'	**Z**: 4 **Z'**: 0
R-Factor (%)	2.98
Temperture (K)	100.01

6.1 AHMP·HCl salt (1:1)

Figure S5 illustrates the intermolecular interactions and crystal packing of the new 1:1 AHMP chloride salt. The AHMP molecule is protonated by HCl forming and has a A^+ structure. The chloride ion interacts with two different A^+ molecules through pyrimidine N-H···Cl^- hydrogen bonds (Figure S5a). A^+ molecules also interact with each other via NH_2···O=C hydrogen bonds forming long ribbons which stack in the crystal structure (Figure S5b).

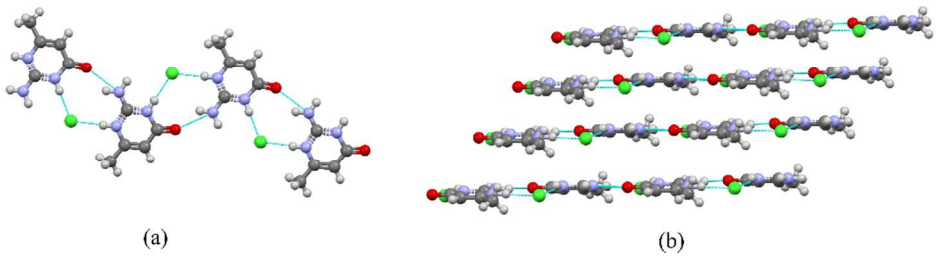
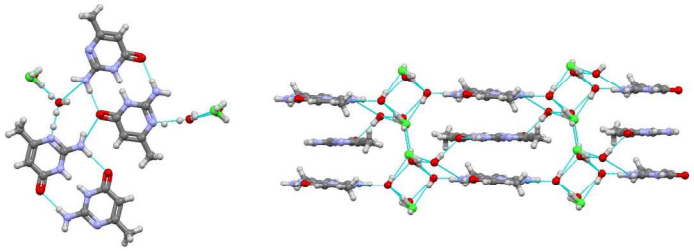


Figure S5. Structure of AHMP·HCl salt (1:1): (a) interactions between Cl^- and AHMP molecule and (b) stacking of the layers. AHMP molecules are protonated in the structure.

6.2 AHMP.HCl ionic cocrystal (3:1:1:5)

AHMP and HCl also crystallise an ionic cocrystal at a higher pH (ca. 4). This is a hydrate with $A:A^{+}:Cl^{-}:H_2O=3:1:1:5$. Unfortunately, there are disorders in the structure. However, as in the other ionic cocrystals, in the idealised model of this structure, robust $A/B\text{-}A^{+}/B^{+}$ dimers can also be identified; these are often to a water molecule, followed by a Cl^{-} (Figure S6a). A ring which is vertical to the dimer planar, is comprised of Cl^{-} as well as water molecules, making the dimers packing together (Figure S6b).



(a) (b)

Figure S6. Structure of AHMP·HCl ionic cocrystal (3:1:1:5): (a) arrangement of dimers and (b) the packing of the layers. The position of hydrogen is somewhat in disorder because of the poor quality of single crystal.

6.3 AHMP·benzoic acid cocrystal (1:1)

AHMP·benzoic acid cocrystal's single crystal was obtained from slow evaporation from water. The cocrystal is in P $2_1/c$ space group with one AHMP and one benzoic acid molecule in the asymmetric unit. No proton transfer happens in the structures and all AHMP molecules are in tautomer A form. AHMP-benzoic acid heterodimers, based on the robust $R_2^2(8)$ array, is further

sustained by two C=O···H-N bonds (Figure S7a). The layers then pack together by weak C=O···H as well as C···H interactions to form a herringbone-like structure (Figure S7b).

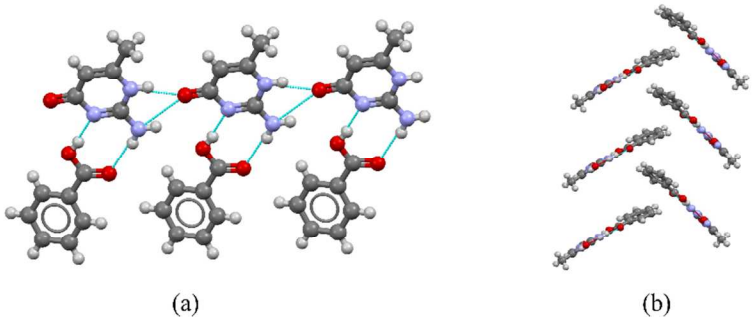


Figure S7. Structure of AHMP·benzoic acid cocrystal (1:1): (a) hydrogen bonds between dimers and (b) the herringbone-like packing. All of the AHMP molecules are in tautomer A state.

6.4 AHMP·pABA hydrate complex (1:1:1)

AHMP and pABA crystallize together as a multi-component product which belongs to P $2_1/c$ space group. Whereas XRD analysis cannot clearly show whether there is proton transfer happening AHMP molecules due to disorder, it still can be found that there exist tautomer B molecules participating in a $R_2^2(8)$ graph set with pABA (Figure S8a). The heterodimers are further sustained by C=O···H-N between AHMP molecules, constructing the 2D structure of the layer. Water molecules connect pABA and AHMP molecules by hydrogen bonds (O-H···O and N-H···O), acting as dominant interactions linking all of the layers (Figure S8b).

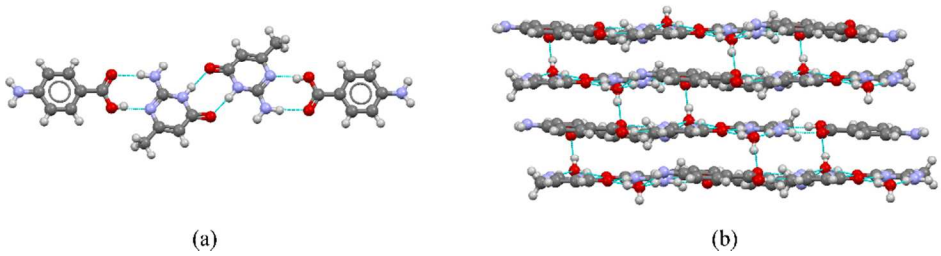


Figure S8. Structure of AHMP·pABA hydrate complex (1:1:1): (a) molecular chains in the structure and (b) stacking of the paralleled layers. Part of AHMP molecules are in tautomer B state while the others cannot be identified by SCXRD.

6.5 AHMP·phthalic acid salt (1:1)

The product obtained from AHMP and phthalic acid aqueous solution turned out to be in P-1 space group. Only one proton transfers from phthalic acid to the N site of pyrimidine ring, and the remaining one is shared by the two carboxylic groups. The deprotonated phthalic acid carboxylic groups participate in constitution of two $R_2^2(8)$ graph set (Figure S9a). The non-coplanar dimers are sustained into a wave-like layer, which stacked together by π···π as well as C=O···C interactions (Figure S9b).

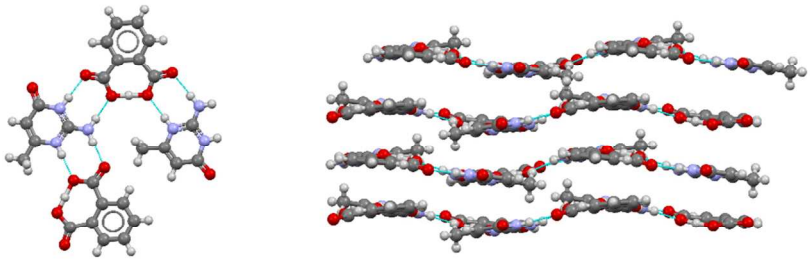


Figure S9. Structure of AHMP·phthalic acid salt (1:1): (a) primary dimers and (b) the packing of wave-like ribbons. AHMP molecules are protonated in the structure.

6.6 AHMP·malonic acid ionic cocrystal hydrate (1:1:1:1)

AHMP together with malonic acid cocrystallised as an ionic cocrystal hydrate from aqueous solution ($A:A^+$:malonic acid:water=1:1:1:1). One of malonic acid's carboxylic groups is deprotonated and proton transfer to one AHMP molecule. Tautomer A and cation A^+ constitute a

typical robust dimer, which also interacts with a malonic acid molecule by C=O···NH. Two water molecules interact with two AHMP dimers as well as a malonic acid, which together comprise a $R_6^4(22)$ ring (Figure S10a). This graph set extends to a 2D net structure, and C=O(AHMP)···NH acts as dominant interactions which pack the layers (Figure S10b).

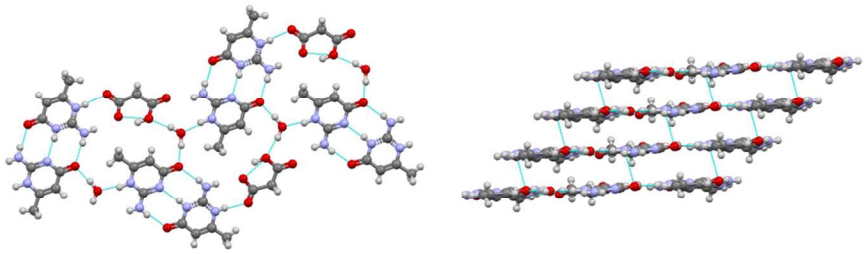


Figure S10. Structure of AHMP·malonic acid ionic cocrystal hydrate (1:1:1:1): (a) net-like arrangement of molecules and (b) the packing of the layers. Half of AHMP molecules are in tautomer A state while the others are protonated.

6.7 AHMP·malonic acid ionic cocrystal (1:1:1)

Besides ionic cocrystal hydrate, AHMP and malonic acid could also crystallise an ionic cocrystal from methanol. Distinguished from its hydrate, it has a ratio of A:A^+:malonic acid = 1:1:1. The $R_2^2(8)$ ring describes the two-point interactions between A and A^+ which affords the dimer, and malonic acid connect two dimers at both ends (Figure S11a). However, the other group acts differently. Tautomer A and A^+ only connect by interactions between amino groups. Two kinds of arrangements are stacked alternately and paralleled with each other (Figure S11b).

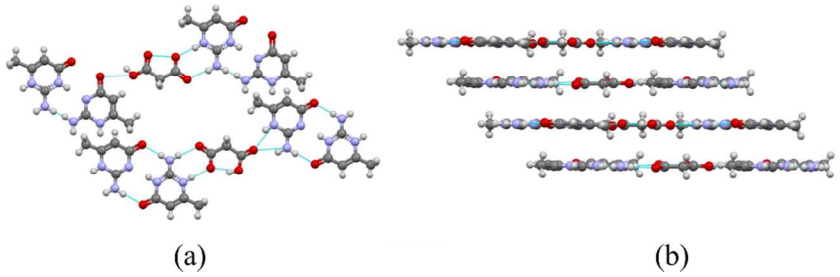


Figure S11. Structure of AHMP·malonic acid ionic cocrystal (1:1:1): (a) two different arrangement of AHMP-malonic acid molecules and (b) the packing of the layers. Half of AHMP molecules are in tautomer A state while the others are protonated.

6.8 AHMP·glutaric acid cocrystal (1:1)

AHMP and glutaric acid cocrystallized as a cocrystal from methanol. The crystal structure published in other research was used directly for analysis. In this cocrystal, all the AHMP molecules are tautomer B, and two AHMP molecules interact as a homodimer via C=O···H-N (Figure S12a). Two glutaric acid molecules act as bridges connecting AHMP dimers together. But the two carboxylic acid interacts differently. On one side, it forms a dimer with AHMP. On the other side, its OH interacts with AHMP's carbonyl while the C=O forms hydrogen bond with another AHMP's amino group (Figure S12a). Thus, the assemblies are sustained and layers are stacked by π-π and C···H interactions (Figure S12b).

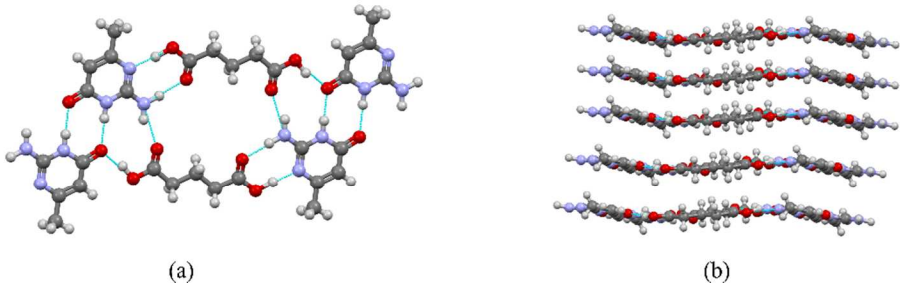


Figure S12. Structure of AHMP·glutaric acid cocrystal (1:1): (a) interactions between AHMP and glutaric acid molecules and (b) stacking of the layers. AHMP molecules are all in tautomer B state.

6.9 AHMP·oxalic acid salt hydrate (1:1:1)

AHMP.oxalic acid crystallised from water turned out to be a salt in P-1 space group, in a ratio of 1:1:1 (AHMP:oxalic acid:water). AHMP was protonated and one proton transfers from oxalic acid to AHMP. A heterodimer contains oxalic acid and AHMP molecules, via interactions between deprotonated carboxylic group and AHMP's NH and amino group. While the side-by-side dimers interact by C=O···NH_2 and C=O···NH bond, the head-to-head assemblies are not coplanar but parallel to each other (Figure S13a). Water molecules stay between the parallel layers and connect them together, and this 2D structures pack through π···π interactions (Figure S13b).

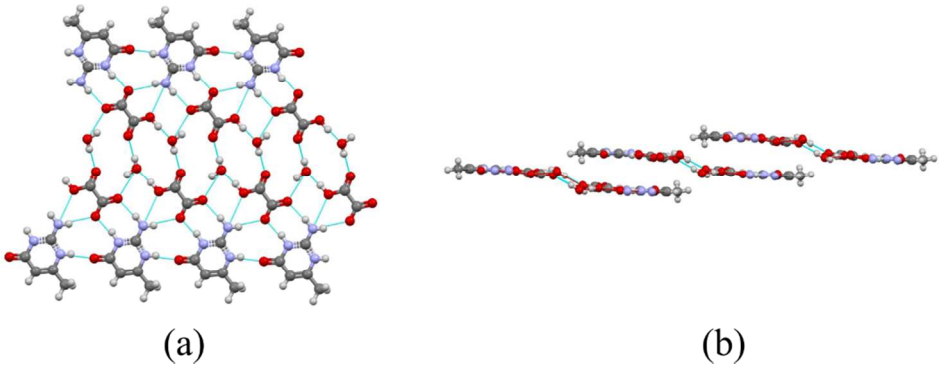


Figure S13. Structure of AHMP·oxalic salt hydrate (1:1:1): (a) interactions between heterodimers and (b) packings of the layers. AHMP molecules are protonated in the structure.

6.10 AHMP·saccharin salt hydrate (1:1:1) form I

The asymmetric unit of the first form obtained for a hydrate of the AHMP-saccharin salt, contains six molecules including two A^+ cations, two saccharin molecules and two water molecules, leading to a 1:1:1 overall ratio. We observe proton transfer from the NH of saccharin to AHMP. A^+ and saccharin ions make strong $R_2^2(8)$ heterodimers through N-H···O and N-H···N hydrogen bonds (Figure S14a). The two remaining NH groups interact with water and a neighbouring A^+:saccharin dimer (Figure S14a).

In addition, water also interact with saccharin of the adjacent layer, through the O-H (water)···O (saccharin) hydrogen bonds (Figure S14b). However, the two layers have totally opposite arrangement of molecules, which repeat vertically by weak C-H···O as well as face-to-face π···π interactions.

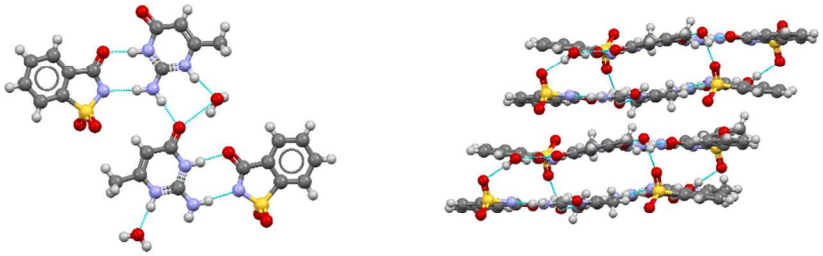


Figure S14. Structure of AHMP·saccharin salt hydrate (1:1:1) form I: (a) dimers in the salt and (b) stacking of the double-layers. AHMP molecules are protonated in the structure.

6.11 AHMP·saccharin salt hydrate (1:1:1) form II

Form II was crystallized simultaneously with Form I from water with a distinguished morphology. It belongs to P -1 space group and has a 1:1:1 (AHMP:saccharin:water) ratio in the asymmetric unit. Similarly, in Form II, AHMP molecule was protonated at the nitrogen site, and also comprises the robust $R_2^2(8)$ heterodimers (Figure S15a) with saccharin molecule. However,

the packing of the dimers is totally different from Form I. A water molecule acts as a bond which links four dimers which are arranged head-to-head and parallel to each other, and the structure is sustained to form a void between them (Figure S15b).

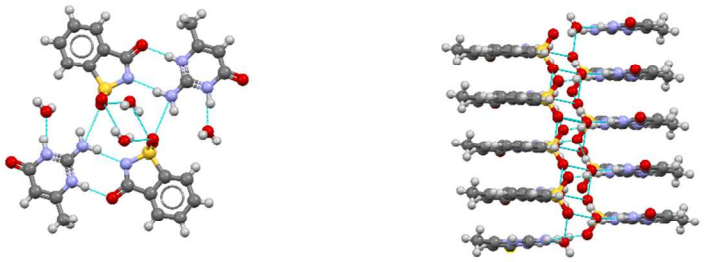


Figure S15. Structure of AHMP·saccharin salt hydrate (1:1:1) form II: (a) AHMP-saccharin dimers and (b) void formed along the layers. AHMP molecules are protonated in the structure.

6.12 AHMP·saccharin ionic cocrystal (2:1)

This ionic cocrystal was crystallized from methanol in P-1 space group. Distinguished from Form I and Form II, it has a 2:1 stoichiometry – one saccharin and two AHMP molecules in the asymmetric unit. Proton transfer also happens, but only half of the AHMP molecules are protonated and the other half stay neutral. The same synthon as Form I and Form II could also be found between protonated AHMP and deprotonated saccharin molecules (Figure S16a). The neutral AHMP molecule exists as tautomer A and forms a dimer with the protonated AHMP via robust two N-H···O as well as one N-H···N hydrogen bonds. Four AHMP molecules, among which two are protonated, interact with each other via N-H···O, constituting $R_4^2(8)$ graph set. The assembly is sustained by C-H (saccharin)···O (AHMP), and the layers stack by N-H···O with C=O of saccharin as acceptor and neutral AHMP pyrimidine ring's N-H as donor, as well as face-to-face π-π interactions (Figure S16b).

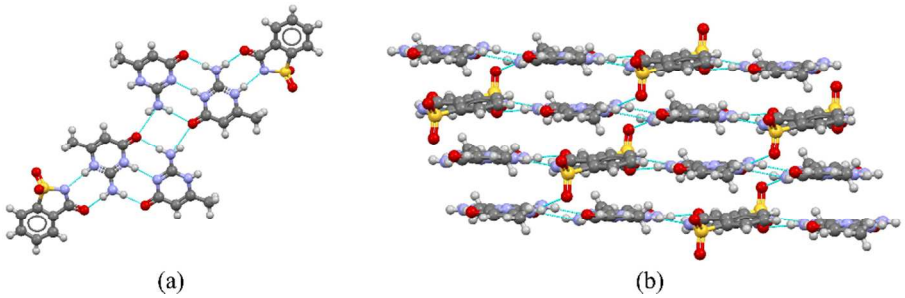


Figure S16. Structure of AHMP·saccharin ionic cocrystal (2:1): (a) interactions between dimers and (b) packing of the layers. Half of AHMP molecules is protonated and half stay in tautomer A.

7. Analysis of the disordered AHMP ionic cocrystal hydrate with HCl

The hydrate of the AHMP ionic Cocrystal with HCl contains significant disorder. The stoichiometry is clearly A:A^+:Cl^-:water 3:1:1:5. An image the asymmetric unit of this crystal structure is given in Figure S17.

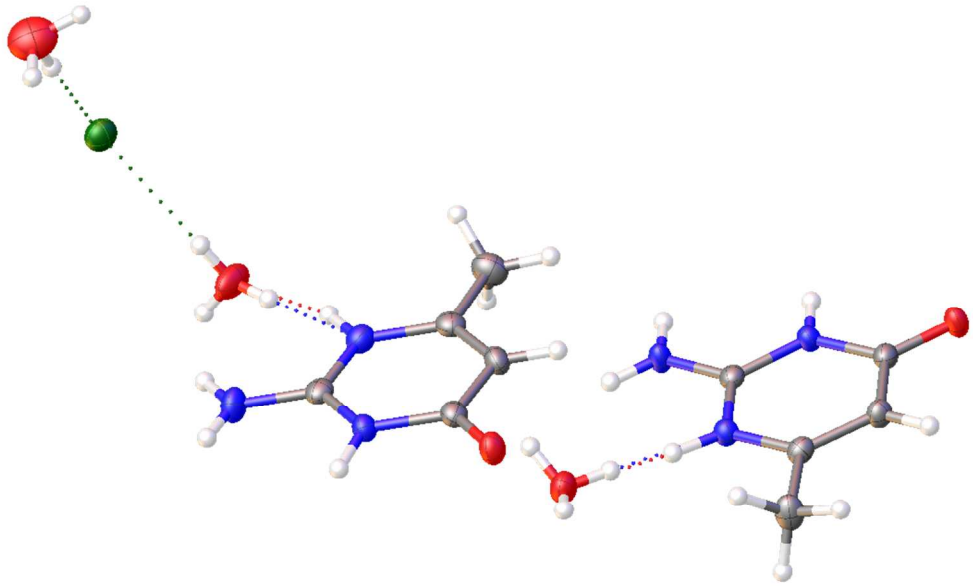
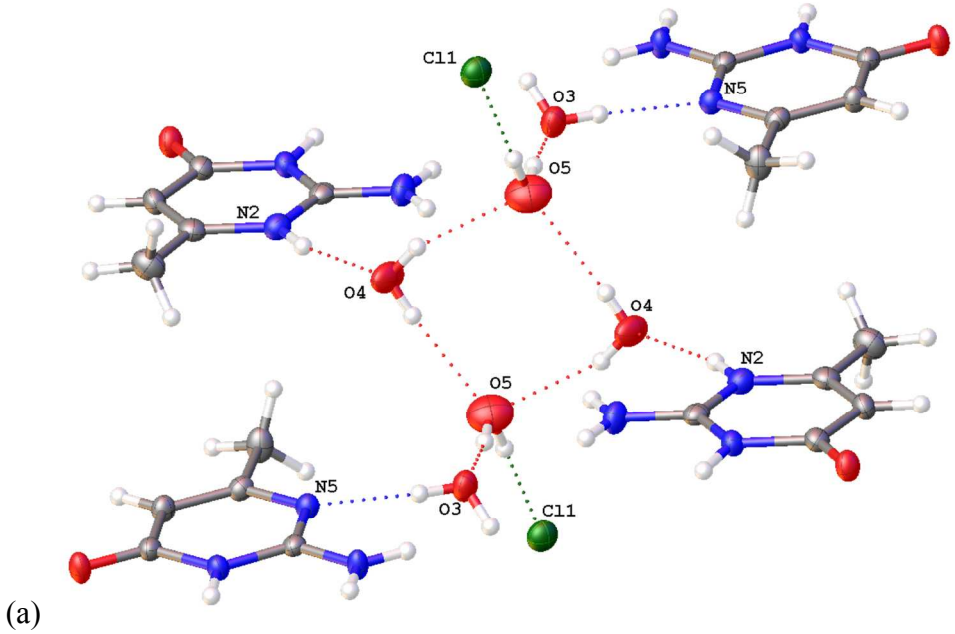


Figure S17. Asymmetric unit of the AHMP hydrated cocrystal with HCl.

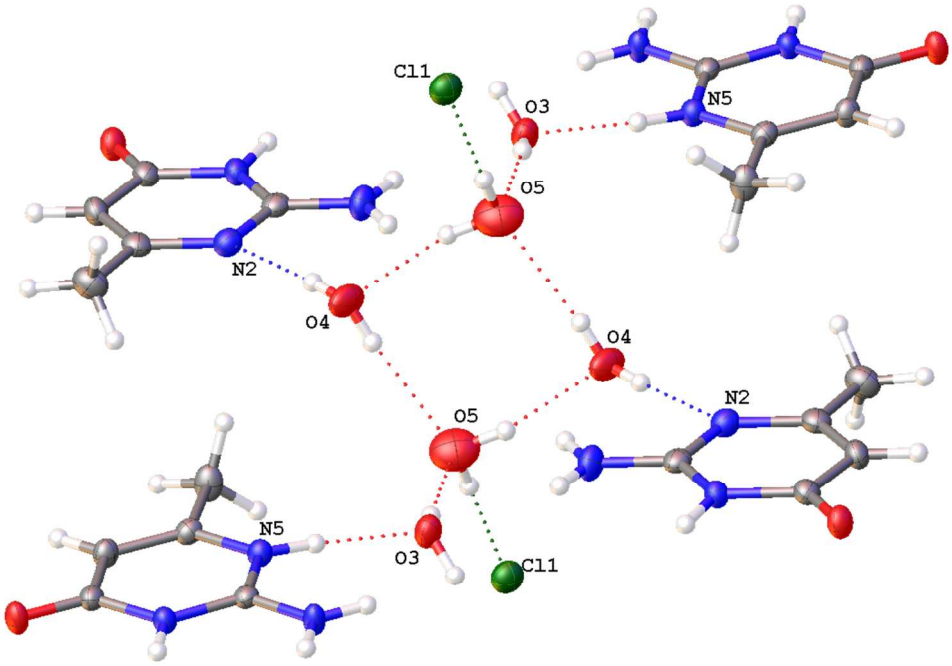
The structure of the AHMP:HCl:H2O ionic cocrystal is highly disordered. All species have been modelled with the correct relative occupancies and atomic positions based on the hydrogen bonding interactions within the structure. It is not possible to generate a model to show all the possible hydrogen bond networks due to the degree of disorder combined with the limitations of modelling the different parts of the disorder. The model should be interpreted in the following way. Firstly, There is always a proton present between the N1 – N1 and N4 – N4 pairs (related by inversion symmetry), modelled with a 50% occupancy as it cannot exist on both nitrogens of the pairs at the same time. Secondly, O5 and Cl1 share a similar location crystallographically within the unit cell, both with 50% occupancy. O5 has been modelled within an adjacent assymetric unit in order to correctly model the hydrogen bonding between O5 and Cl1; when O5 is present it always hydrogen bonds to Cl1 of an adjacent crystallographic site (through H5E). O5 can never be a direct neighbour to another O5. The same is true for Cl1. Thirdly, N2 and N5 are protonated 50% of the time, which results in two different hydrogen bonding pathways in the crystal, depending on which is protonated. Each water molecule (O3, O4 and O5) is modelled with three hydrogens present, two with 50% occupancy, with each of the latter only present depending on which of N2 or N5 are protonated. This results in the following H-bonding networks.

H3AA of O3 always hydrogen bonds to O2, and H4AA of O4 always hydrogen bond to the shared O5 Cl1 shared site; none of the hydrogens of O5 are directed towards O4. When N2 is protonated, with H2 present, it forms a H-bond to O4, which in turn forms a H-bond to the O5/Cl1 shared site through H4C (with H4B not present as H4B and H2 cannot both be present simultaneously). In this case, H5D is present on O5 (with H5F not present), forming an H-bond

to O3, which forms an H-bond to the deprotonated N5 through H3C (with H3BB not present). (Figure S18a)



(a)



(b)

Figure S18 (a) H-Bonding network when N2 is protonated (b) H-bonding network when N5 is protonated.

When N5 is protonated with H5 present, it forms a H-bond to O3, which in turn forms a H-bond to the O5/Cl1 shared site through H3BB (with H3C not present as H3C and H5 cannot both be present simultaneously). In this case H5F is present on O5 (with H5D not present), forming an H-bond to O4, which forms an H-bond to the deprotonated N2 through H4B (with H4C not present). (Figure S18b)

8. XPS results

XPS patterns of part of newly discovered crystals in this study are listed in Figure S19 ~ S23.

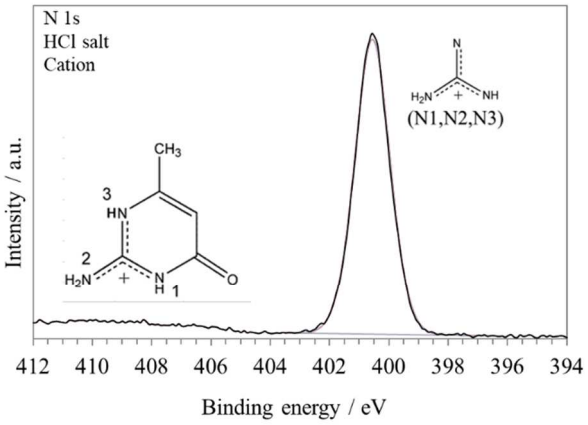


Figure S19. Nitrogen XPS of the AHMP:HCl salt (1:1) .

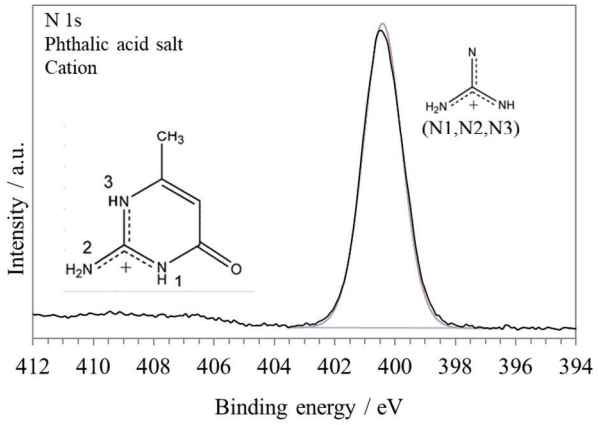


Figure S20. Nitrogen XPS of the AHMP:phthalic acid salt (1:1) .

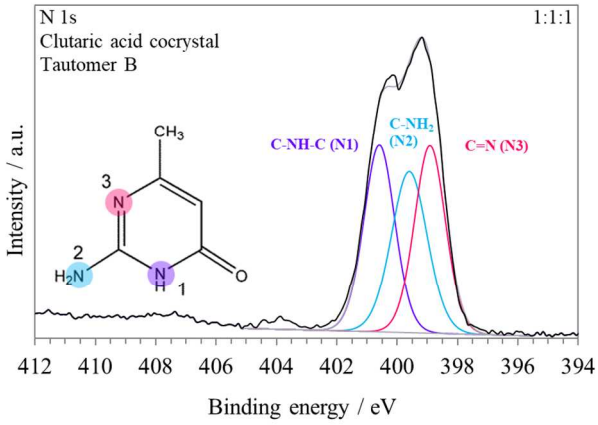


Figure S21. Nitrogen XPS of the AHMP:glutaric acid cocrystal (1:1).

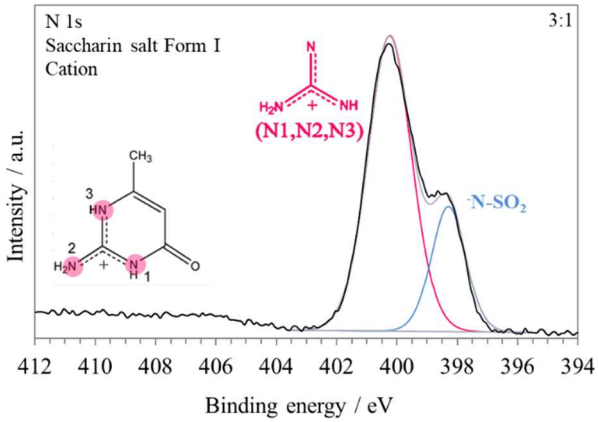


Figure S22. Nitrogen XPS of the AHMP:saccharin salt hydrate (1:1:1) form I.

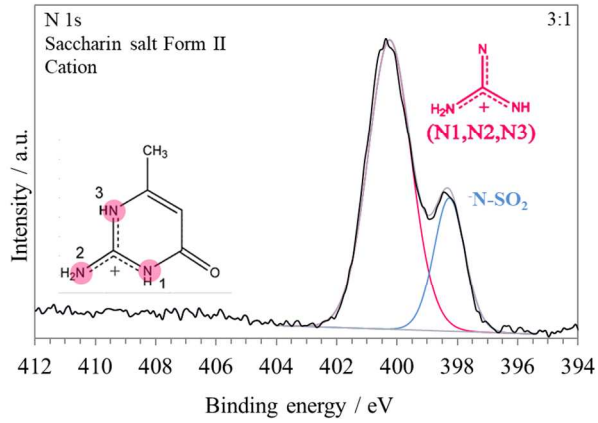


Figure S23. Nitrogen XPS of the AHMP:saccharin salt hydrate (1:1:1) form II.