# Crystallisation of organic salts by sublimation: salt formation from the gas phase

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# **Supplementary Information**

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## Materials and methods

All chemicals and solvents were obtained from Sigma Aldrich South Africa and used without further purification.

## Solution crystallisation

Solution crystallisation experiments were carried out in small 10 ml vials using the slow-evaporation method. Starting materials were dissolved in the appropriate solvent or solvent system, with heating, and the resultant solution left to crystallise at room temperature in the capped vial. Crystals formed within a few days.

### Mechanochemistry

Mechanochemical milling experiments were carried out using a FTS1000 Shaker Mill from Form-tech Scientific. Samples were loaded into 15 ml steel SmartSnap<sup>TM</sup> grinding jars containing two 6 mm steel grinding balls (~900 mg each). Samples were milled for 20 minutes at a frequency of 20 Hz (1200 rpm). A total sample mass of roughly 100 mg was used with solvent volume (where applicable for LAG) corresponding to  $\eta = 0.25 \ \mu l \ mg^{-1}$  (approximately 25  $\mu l$ ).

### Sublimation

Sublimation experiments were carried out in thin Schlenk tubes under either static or dynamic vacuum (0.6 mbar line pressure). Tubes were inserted in an oil bath pre-heated to the desired temperature, and sublimation took place onto the sides of the tube within a few hours. For comparison, these experiments were also carried out in a larger Schlenk tube fitted with a water-cooled cold finger as crystallisation surface. To determine the role played by the heat applied during sublimation, select experiments were repeated in a test tube with similar dimensions as a thin Schlenk tube. Here the starting materials were heated in an oil bath and the powder tested to determine how the composition changes due to heat. Finally, sublimation experiments were also carried out in a flat-bottomed Schlenk tube fitted with a cold finger which allowed placement of the starting materials into separate cut-off glass vials. This was done to ensure the starting materials would not come into contact with each other while in the solid state (Figure S1).



**Figure S1** Visual representation of the methods/glassware used in this study. Photographs have been converted to line drawings for clarity, but the images are accurate representations. The methods used include (a) solution crystallisation in small vials, (b) mechanochemistry using a mechanical mill (the grinding jar is shown here), (c) sublimation in a thin Schlenk tube, (d) sublimation in a thick Schlenk tube equipped with a cold finger, (e) heating the starting materials in a test tube, and (f) sublimation without the starting materials being in contact.

#### Characterisation

Single-crystal X-ray Diffraction (SCXRD) was carried out using a Bruker DUO Apex II CCD area detector diffractometer. The instrument is equipped with an Incoatec I $\mu$ S microsource coupled with a multilayer mirror optics monochromator. MoK $\alpha$  radiation of wavelength 0.71073 Å was used for data collections. An Oxford Cryosystems Cryostat (700 Series Cryostream Plus) was used for low temperature data collections at 100 K.

Gas cell SCXRD experiments were carried out using a Bruker D8 Venture diffractometer with a Photon II CPAD detector. The instrument is equipped with an Incoatec I $\mu$ S microsource coupled with a multilayer mirror optics monochromator. MoK $\alpha$  radiation of wavelength 0.71073 Å was used for data collections. An Oxford Cryosystems Cryostream 800 series was used for data collections at elevated temperatures and reduced pressure (0.9 mbar).

Data collection and data reduction were carried out using the Bruker software package SAINT<sup>1</sup> through the Apex3 software. This was followed by an absorption correction using SADABS,<sup>2,3</sup> which also corrects for other systematic errors. SHELXT-18,<sup>4</sup> operated through the graphical user interface X-Seed,<sup>5,6</sup> was used to solve the structures using direct methods. The structures obtained were subsequently refined using SHELXL-18.<sup>7</sup> Hydrogen atoms on sp<sup>3</sup>- and sp<sup>2</sup>-hybridised carbon atoms were placed in calculated positions using riding models, while O–H and N–H hydrogen atoms were placed on maxima in the electron density difference maps. Images were created using POV-ray,<sup>8</sup> as visualised using X-Seed,<sup>5,6</sup> except for the images of the electron density difference maps ( $F_{obs} - F_{calc}$ ; level of detail: 0.118 Å<sup>-3</sup>) (Figure S28 – S31), which were created using Olex2.<sup>9</sup>

Powder X-ray diffraction (PXRD) data were collected on a Bruker D2 Phaser benchtop powder diffractometer equipped with a copper source (1.54183 Å radiation). Data were collected from  $2\theta = 4$  to  $40^{\circ}$  at a speed of 0.5 seconds per scan (0.016° step size).

Thermogravimetric analysis (TGA) was carried out using a TA Q500 instrument. Samples of roughly 5 - 10 mg were placed in an aluminium pan and heated at  $10 \text{ °C min}^{-1}$  until after decomposition, and the mass loss recorded. The samples were kept under a constant flow of nitrogen gas (50 ml min<sup>-1</sup>) to purge decomposition products.

Differential Scanning Calorimetry (DSC) was carried out using a TA Q20 instrument. Powdered samples (3 - 10 mg) were placed in closed aluminium pans vented with a pinhole. An empty reference pan was prepared in the same way. Heat flow in the sample and reference pans were measured as they were heated under a flow of nitrogen gas (50 ml min<sup>-1</sup>) until just before decomposition, and subsequently cooled to -20 °C. This cycle was repeated once to determine the reproducibility of any observed phenomena.

Fourier Transform Infrared spectroscopy (FTIR) was carried out on powdered samples using a Bruker Alpha P spectrometer with a Platinum ATR attachment.

Mass spectrometric measurements were carried out using a Waters Synapt G2 Time-of-Flight (TOF) MS instrument equipped with an ESI probe, operated in negative ion mode with a cone Voltage of 15 V. The sample was dissolved in methanol before analysis.

#### Crystallisation of succinic acid with hexamethylenetetramine (1a, 1b, 1c, 1d)

The 2:1 salt of succinic acid and hexamethylenetetramine (1a) was formed by combining succinic acid (0.063 g, 0.53 mmol) with hexamethylenetetramine (0.037 g, 0.26 mmol) in 7 ml acetone and stirring them together at 55 °C until the components had completely dissolved. The vial was then capped and left on a shelf to crystallise at room temperature. Colourless plate-like crystals formed after a few hours. A powder of this salt could also be obtained by grinding a 2:1 molar ratio of the two components together for 20 minutes in a ball mill (neat or with the addition of MeOH, THF or water).

The 1:1 co-crystal of succinic acid and hexamethylenetetramine (**1b**) was formed by combining succinic acid (0.045 g, 0.38 mmol) with hexamethylenetetramine (0.053 g, 0.38 mmol) in 7 ml acetone and stirring them together at 55 °C until the components had completely dissolved. The vial was then capped and left on a shelf to crystallise at room temperature. Colourless plate-like crystals formed within a few hours. A powder of this co-crystal could also be obtained by grinding a 1:1 molar ratio of the two components together for 20 minutes in a ball mill (neat or with the addition of MeOH, THF or water).

The 1:2 co-crystal of succinic acid and hexamethylenetetramine (1c) was made by combining succinic acid (0.030 g, 0.25 mmol) with hexamethylenetetramine (0.071 g, 0.51 mmol) in 8 ml acetone and stirring them together at 55 °C until the components had completely dissolved. The vial was then capped and left on a shelf to crystallise at room temperature. Colourless plate-like crystals formed after a day. A powder of this co-crystal could also be obtained by grinding a 1:2 molar ratio of the two components together for 20 minutes in a ball mill (neat or with the addition of MeOH, THF or water). Grinding for shorter amounts of time (e.g. 5 - 15 minutes) lead to formation of the intermediate co-crystal, 1d, which converts to 1c upon further grinding. Co-crystal 1d is therefore suspected to be a kinetic form. No single crystals of 1d could be obtained, but the FTIR pattern is identical to that of 1c, indicating that it is also a co-crystal (Figure S26).

Crystals of both **1a** and **1b** were also formed by sublimation. The co-crystal **1b** was made by subliming a 1:1, 2:1 or 3:1 molar ratio of the starting materials at 90 °C under dynamic vacuum for 2 hours, followed by heating for 16 hours under static vacuum. **1b** was also made by subliming a 1:1, 2:1, 1:2 or 1:3 molar ratio of the starting materials at 110 °C under dynamic vacuum for 2 hours. When sublimation was continued for two more hours under static vacuum, **1a** started to form in a band underneath **1b**. All sublimation experiments were carried out at least three times to ensure reproducibility. The co-crystals **1c** and **1d** were never obtained by sublimation, even when component ratios and temperatures were varied.

## Crystallisation of oxalic acid with 4,4'-bipyridine (2a, 2b)

The 2:1 salt of oxalic acid and 4,4'-bipyridine (2a) was made by combining oxalic acid dihydrate (0.030 g, 0.24 mmol) with 4,4'-bipyridine (0.037 g, 0.24 mmol) in 5 ml water and 5 ml ethanol and stirring them together at 75 °C until the components had completely dissolved (about 30 minutes). The vial was then capped and left on a shelf to crystallise at room temperature. Small, colourless plate-like crystals formed after a day. A powder of this salt could also be obtained by grinding a 2:1 molar ratio of the two components together for 20 minutes in a ball mill (neat or with a few drops of MeOH, THF or water).

The 1:1 co-crystal of oxalic acid and 4,4'-bipyridine (**2b**) was made by combining oxalic acid dihydrate (0.030 g, 0.24 mmol) with 4,4'-bipyridine (0.037 g, 0.24 mmol) in 8 ml water and 6 ml methanol and stirring them together at 60 °C until the components had completely dissolved (about 30 minutes). The vial was then capped and left on a shelf to crystallise at room temperature. Large, striated crystals formed within 24 hours. A powder of this co-crystal could also be obtained by grinding a 1:1 molar ratio of the two components together for 20 minutes in a ball mill (neat or with a few drops of MeOH, THF or water), although some **2a** is also formed concomitantly, so that a pure sample is never obtained.

Both **2a** and **2b** could also be formed by sublimation of a 1:1 molar ratio of the starting materials. Oxalic acid dihydrate (0.030 g, 0.24 mmol) and 4,4'-bipyridine (0.037 g, 0.24 mmol) were added to a thin Schlenk and heated in a 125 °C oil bath for 1 hour under dynamic vacuum, followed by heating for 3 hours under static vacuum. Co-crystal **2b** formed a band of polycrystalline material, while salt **2a** formed crystals in a band below that, right above the oil line. Crystals of BPY were also formed much higher up in the tube (Figure S2). A variety of sublimation experiments were carried out where conditions were varied, but the outcome remained the same.



Figure S2 Product distribution on the sides of the tube during the co-sublimation of oxalic acid with BPY.

### **Crystal structures**

Crystal structures for six different multicomponent crystals were obtained. All structural data were collected both at room temperature and at 100 K because temperature has been known to change the ionisation state of molecules, affecting whether a material is a salt or a co-crystal.<sup>9</sup> No major changes in the structures due to temperature were observed, but minor variations will be indicated where applicable. Although the structures of **1b**, **2a** and **2b** have been reported previously (CSD refcodes: TOZTIN01<sup>10</sup>, EZECOC<sup>11</sup> & XEZDIQ<sup>12</sup>), their structures were re-determined as the position of the acidic hydrogen atom is central to this study. In all cases, IR spectroscopy was used in combination with careful assessment of the C–O bond lengths in order to confirm whether a particular structure is a salt or a co-crystal. It was difficult to determine

whether **2b** is a salt or a co-crystal. Acidic hydrogen atoms were placed according to the difference map. The IR indicates this material may contain carboxylate groups. However, carbon-oxygen bond lengths, as well as angles at the heterocyclic nitrogen atom, indicate that this material is a co-crystal, and hydrogen atoms have therefore been placed accordingly in the structure. This results in some long N–H bonds due to very strong hydrogen bonds between the acid and the base.

Crystallographic data are summarised in Table S1 and hydrogen-bond distances and angles in Table S2.

## Structures from HMT and SA

Salt **1a** crystallises in the triclinic space group  $P\bar{1}$ , with one singly protonated HMT cation, one molecule of hydrogen succinate, and two half molecules of neutral succinic acid in the asymmetric unit (ASU) (Figure S3). The succinic acid molecules and succinate ions hydrogen bond to one another to form grid-like layers (Figure S4). Each grid has alternating rows of R4,4(28) and R8,8(44) hydrogen-bonded motifs. The larger of the two hydrogen-bonded rings is filled by two HMT cations that are hydrogen bonded to the carboxylate groups of hydrogen succinate. The layers stack on top of each other in an offset manner to form a close-packed 3D structure (Figure S4), such that the smaller hydrogen-bonded rings are covered at the top and bottom by HMT molecules of adjacent layers.



**Figure S3** Asymmetric unit of **1a**. Atoms highlighted in green are symmetry generated, (-x, 1-y, 1-z) and (-x, -y-1, -z), and not part of the ASU.



Figure S4 (a) A single hydrogen-bonded layer of 1a viewed perpendicular to (001). (b) Packing diagram for 1a viewed along [0-11].

The co-crystal **1b** has been reported previously.<sup>10</sup> It crystallises in the monoclinic space group  $P2_1/c$  with one molecule of succinic acid and one molecule of HMT in the ASU. At 100 K, the succinic acid backbone is disordered over two positions in an approximately 50:50 ratio due to rotation in the C–C chain, but the atoms involved in hydrogen bonding are on the same positions for both parts, so the overall packing and hydrogen bonding network is not affected. At room temperature the disorder ratio shifts to 60:40, and the conformation of the whole molecule changes slightly, but again, this does not greatly affect the overall packing. Succinic acid molecules are hydrogen bonded to HMT molecules, resulting in zig-zag acid-base-acid-base hydrogen-bonded chains running along the *b*-axis (Figure S5a). Chains pack next to each other to form layers, which stack directly on top of one another along [100] (Figure S5b).



Figure S5 (a) Hydrogen-bonded chain in 1b viewed along [001], and (b) the packing diagram of 1b viewed along [100]. The disorder has been omitted in both images for clarity.

Co-crystal **1c** crystallises in the monoclinic space group C2/c with one molecule of succinic acid and two molecules of HMT in the ASU. The succinic acid backbone is disordered over two positions in an approximately 50:50 ratio due to rotation in the C–C chain, similar to the disorder observed in **1a**. Each molecule of acid hydrogen bonds to two molecules of base so that base-acid-base trimers are formed (Figure S6a). Pairs of trimers pack together in a brick wall pattern, which can be seen when viewed along [010] (Figure S6b).



Figure S6 (a) Hydrogen-bonded trimer of 1c, and (b) the packing diagram viewed along [010]. Disordered parts of SA have been omitted for clarity.

## Structures from BPY and OA

The previously-reported salt<sup>11</sup> **2a** crystallises in the triclinic space group  $P\overline{1}$  with one molecule of hydrogen oxalate and half a molecule of 4,4'-bipyridinium in the ASU. Two hydrogen oxalate anions hydrogen bond to one another to form an R2,2(10) ring motif (Figure S7). The carboxylate group of each of anion forms an additional hydrogen bond to the NH<sup>+</sup> of 4,4'-bipyridinium, resulting in chains where each molecule of BPY is separated by a pair of anions. Chains stack to form the 3D structure (Figure S7), with offset face-to-face  $\pi$ - $\pi$  interactions between the BPY aromatic rings (centroid to centroid distance of 3.3146(9) Å).



Figure S7 Packing diagram for 2a viewed along [100].

Co-crystal **2b** crystallises in the triclinic space group  $P\bar{1}$  with two molecules of oxalic acid and two molecules of 4,4'-bipyridine in the ASU (Figure S8a). The hydrogen bonds in **2b** are all relatively short (Table S2). The FTIR spectrum we obtained for **2b** has C=O stretching frequencies corresponding to both carboxylic acid and carboxylate groups, indicating that it is a salt (Figure S27), however, the C–O bond lengths and angles between the interacting groups indicate that this is indeed a co-crystal. The peak seemingly indicating a carboxylate group could be due to some **2a** contaminating the sample (Figure S14).

The structure of **2b** is based on acid-base-acid-base chains formed *via* hydrogen bonds. There are two types of hydrogen-bonded chains, type 1 and type 2 (Figure S8a). The BPY molecules in the latter deviate more from planarity; the angle between the planes formed by the two aromatic rings is  $22.25(5)^{\circ}$  in type 2 chains, while the deviation is only  $9.00(4)^{\circ}$  in chains of type 1. Chains pack alongside one another to form sheets of either Type 1 or Type 2 chains. Sheets stack on top of each other to give a bilayer-type 3D structure (Figure S8b).



**Figure S8** (a) Hydrogen-bonded chains of type 1 (top), and type 2 (bottom), of co-crystal **2b** showing the slight changes in angles. (b) The packing diagram for **2b** viewed along [100] showing how the two types of chains stack (blue = type 1, green = type 2).

### Further details regarding re-sublimation

A powdered sample of **1a**, obtained from mechanochemical co-crystallisation, was added to a thin Schlenk and heated in a 110 °C oil bath for 2 hours under dynamic vacuum, followed by heating under static vacuum for a further 6 hours. Single-crystal diffraction-quality, colourless crystals of **1a** were obtained, as well as crystals of HMT, which formed higher up in the Schlenk.

A powdered sample of **1a** and one equivalent of HMT was added to a thin Schlenk and heated in a 110 °C oil bath for 2 hours under dynamic vacuum, followed by heating under static vacuum for a further 4 hours. Single-crystal diffraction-quality, colourless crystals of **1b** were obtained, as well as crystals of HMT, which formed higher up in the Schlenk.

A powdered sample of **1a** and one equivalent of SA was added to a thin Schlenk and heated in a 110 °C oil bath for 2 hours under dynamic vacuum, followed by heating under static vacuum for a further 4 hours. Single-crystal diffraction-quality, colourless crystals of **1a** were obtained.

A powdered sample of **1b** was added to a thin Schlenk and heated in a 90 °C oil bath for 2 hours under dynamic vacuum, followed by heating under static vacuum for a further 3 hours. Polycrystalline material of **1b** formed in a band above the oil line, as well as crystals of HMT, which formed higher up in the Schlenk.

A powdered sample of **1c** was added to a thin Schlenk and heated in a 90 °C oil bath for 2 hours under dynamic vacuum, followed by heating under static vacuum for a further 24 hours. Polycrystalline material of **1b** formed in a band above the oil line, as well as crystals of HMT, which formed higher up in the Schlenk.

Similarly, a powdered sample of **1d** was added to a thin Schlenk and heated in a 90 °C oil bath for 2 hours under dynamic vacuum, followed by heating under static vacuum for a further 24 hours. Polycrystalline material of **1b** formed in a band above the oil line, as well as crystals of HMT, which formed higher up in the Schlenk.

The co-crystal **1b** was isolated from a mixture ( $12 \text{ mg } \mathbf{1a} + 12 \text{ mg } \mathbf{1b}$ ). The mixture was added to a thin Schlenk and heated in a 110 °C oil bath for 2 hours under dynamic vacuum. Polycrystalline material of **1b** formed in a band above the oil line, as well as crystals of HMT, which formed higher up in the Schlenk.

A powdered sample of **2a** or **2b** was added to a thin Schlenk and heated in a 170 °C oil bath for 4 hours under static vacuum. Crystals of BPY formed high up in the Schlenk, followed by polycrystalline **2a** below that and then **2b** in a band of powder right at the bottom.

# Crystallographic tables

Table S1 Crystallographic data for the salts 1a and 2a, and the co-crystals 1b, 1c, and 2b (at room temperature and 100 K).

Structure	1	a	1b		1c		2a		2b		
Chemical formula	C14H2	C14H24N4O8		C10H18N4O4		C16H30N8O4		C14H12N2O8		C24H20N4O8	
Formula weight /g mol <sup>-1</sup>	376.37		258.28		398.48		336.26		492.44		
Crystal system	triclinic		monoclinic		monoclinic		triclinic		triclinic		
Space group	$P\overline{1}$		$P2_{1}/c$		C2/c		ΡĪ		$P\bar{1}$		
Temperature /K	298(2)	100(2)	298(2)	100(2)	298(2)	100(2)	298(2)	100(2)	298(2)	100(2)	
a /Å	9.6812(2)	9.6037(4)	6.017(1)	5.8215(8)	21.847(1)	21.654(3)	3.7614(3)	3.6795(7)	8.7731(5)	8.740(1)	
b /Å	9.8923(2)	9.8432(4)	18.340(3)	18.363(2)	6.9981(4)	6.948(1)	9.8932(7)	9.855(2)	9.8652(5)	9.849(1)	
c /Å	10.3777(3)	10.2613(4)	11.778(2)	11.592(2)	26.359(2)	25.748(4)	10.4498(7)	10.425(2)	13.9929(7)	13.663(2)	
α /°	70.346(1)	68.903(1)	90	90	90	90	116.121(1)	116.097(2)	73.741(2)	73.285(2)	
β /°	83.328(1)	83.980(1)	99.387(3)	100.266(2)	102.170(1)	101.148(2)	96.721(1)	97.436(2)	72.890(2)	72.292(2)	
γ /°	67.442(1)	68.045(1)	90	90	90	90	98.409(1)	97.188(2)	72.483(2)	72.343(2)	
Calc. density /g cm <sup>-3</sup>	1.446	1.490	1.338	1.401	1.344	1.393	1.651	1.694	1.515	1.569	
Volume /Å <sup>3</sup>	864.26(4)	838.87(6)	1282.3(4)	1219.3(3)	3939.4(4)	3800.7(1)	338.11(4)	329.5(1)	1079.2(1)	1042.5(2)	
Ζ	2	2	4	4	8	8	1	1	2	2	
Independent reflections	4299	3442	3199	3017	4898	4758	1679	1630	5389	5192	
R <sub>int</sub>	0.0379	0.0213	0.0286	0.0256	0.0344	0.0276	0.0177	0.0292	0.0744	0.0244	
$R_1 \left[ I > 2\sigma(I) \right]$	0.0526	0.0329	0.0718	0.0414	0.0533	0.0473	0.0409	0.0360	0.0936	0.0605	

<b>1a</b> O1-H1···O14 0.87 (2) 1.85 (2) 2.668 (1) 157 (2) x+1, y-1, z	
O13-H13···O8 0.97 (2) 1.58 (2) 2.544 (1) 178 (2)	
O9–H9···O7 0.88 (2) 1.73 (2) 2.607 (1) 173 (2)	
N23-H23···O8 0.94 (2) 1.80 (2) 2.728 (1) 174 (2)	
<b>1b</b> O1–H1···N9 0.95 (2) 1.73 (2) 2.678 (1) 176 (2)	
O7A–H7…N13 1.00 (3) 1.73 (3) 2.701 (6) 163 (2) -x+1, y-1/2, -	z+1/2
O7B-H7…N13 0.96 (3) 1.73 (3) 2.652 (6) 161 (2) -x+1, y-1/2, -	z+1/2
C5B-H5B2···O8B 0.99 1.72 2.649 (3) 155.3 -x+1, -y+1, -z	Z
<b>1c</b> O1A-H1···N19 0.99 (2) 1.75 (2) 2.743 (2) 175 (5) -x+1, -y, -z+1	l
O1B-H1···N19 0.93 (2) 1.756 (2) 2.675 (2) 167 (5) -x+1, -y, -z+1	l
O7B-H7B···N9 0.92 (3) 1.82 (3) 2.737 (3) 177 (6) $-x+1/2, -y+3/2$	2, -z+1
O7A–H7A···N9 0.92 (3) 1.72 (3) 2.634 (2) 171 (5) -x+1/2, -y+3/2	2, -z+1
<b>2a</b> O1–H1···O5 0.92 (2) 2.21 (2) 2.694 (1) 112 (2)	
O1-H1···O5 0.92 (2) 1.82 (2) 2.594 (1) 141 (2) $-x+2, -y+2, -z$	z+1
N7-H7···O6 1.03 (2) 1.64 (2) 2.638 (1) 161 (2)	
<b>2b</b> O1–H1…N16 1.34 (4) 1.24 (4) 2.579 (1) 179 (4) x+1, y+1, z	
O6–H6…N7 1.10 (3) 1.46 (3) 2.543 (1) 166 (3)	
O24-H24…N25 1.07 (4) 1.48 (4) 2.535 (1) 167 (4)	
O19–H19…N34 1.07 (4) 1.50 (4) 2.559 (1) 169 (4) x-1, y-1, z	

**Table S2** Hydrogen bond lengths and angles for 1 and 2 at 100 K.

# Gas cell experiments

Structure	1a	1a_RT_vac	1a_323K_vac	1a_343K_vac	1a_363K_vac
Temperature /K	298(2)	297(2)	323(2)	343(2)	363(2)
Pressure /mbar	atmospheric	0.9	0.9	0.9	0.9
<i>a</i> /Å	9.6812(2)	9.6855(5)	9.6936(3)	9.7001(3)	9.709(2)
b /Å	9.8923(2)	9.8968(5)	9.9012(2)	9.9056(3)	9.907(1)
c /Å	10.3777(3)	10.3851(5)	10.3959(3)	10.4083(4)	10.410(2)
α /°	70.346(1)	70.349(2)	70.525(1)	70.699(1)	70.848(5)
β /°	83.328(1)	83.366(2)	83.312(1)	83.300(1)	83.298(5)
γ /°	67.442(1)	67.454(2)	67.369(1)	67.299(1)	67.240(5)
Calc. density /g cm <sup>-3</sup>	1.446	1.444	1.440	1.436	1.433
Volume /Å <sup>3</sup>	864.26(4)	865.74(8)	868.18(4)	870.69(5)	872.2(2)
Ζ	2	2	2	2	2
Independent reflections	4299	4106	4266	4269	4338
R <sub>int</sub>	0.0379	0.0341	0.0241	0.0255	0.0358
$R_1 [I > 2\sigma(I)]$	0.0526	0.0557	0.0526	0.0544	0.0526

 Table S3 Crystallographic data for 1a compared to data collected under vacuum conditions using the gas cell.



Figure S9 Labels for atoms of 1a that are involved in hydrogen bonding.

Temperature	D–H····A	D—H /Å	H…A /Å	D…A /Å	D—H…A ∕∘	Symmetry codes
297 K	N23-H23…O8	0.94 (3)	1.79 (3)	2.731 (2)	173 (2)	
	O1–H1…O14	0.87 (3)	1.87 (3)	2.694 (2)	158 (2)	x-1, y+1, z
	O13–H13…O8	0.96 (3)	1.60 (3)	2.548 (2)	173 (3)	
	O9–H9…O7	0.91 (3)	1.69 (3)	2.595 (2)	176 (3)	
323 K	N23-H23…O8	0.91 (2)	1.83 (2)	2.731 (2)	172 (2)	
	O1—H1…O14	0.83 (3)	1.91 (3)	2.695 (2)	156 (2)	x-1, y+1, z
	O13–H13…O8	0.94 (3)	1.61 (3)	2.551 (2)	175 (2)	
	O9–H9…O7	0.92 (3)	1.68 (3)	2.593 (2)	171 (3)	
343 K	N23-H23…O8	0.89 (2)	1.85 (2)	2.731 (2)	171 (2)	
	O1—H1…O14	0.84 (3)	1.90 (3)	2.696 (2)	157 (2)	x-1, y+1, z
	O13–H13…O8	0.93 (3)	1.62 (3)	2.551 (2)	175 (2)	
	O9–H9…O7	0.92 (3)	1.68 (3)	2.591 (2)	171 (3)	
363 K	N23-H23…O8	0.89 (2)	1.85 (2)	2.733 (2)	171 (2)	
	O1—H1…O14	0.84 (3)	1.90 (3)	2.696 (2)	158 (2)	x-1, y+1, z
	O13–H13…O8	0.93 (3)	1.62 (3)	2.552 (2)	175 (2)	
	O9–H9…O7	0.93 (3)	1.68 (3)	2.589 (2)	168 (3)	

Table S4 Hydrogen bond lengths and angles for 1a at elevated temperatures under vacuum conditions.

## **Powder X-Ray diffraction patterns**



Figure S10 Comparison of the experimental powder patterns of 1a (obtained from sublimation, LAG using THF, and solution) to the pattern simulated from single-crystal data collected at room temperature.



Figure S11 Comparison of the experimental powder patterns of 1b (obtained from sublimation, LAG using THF, and solution) to the pattern simulated from single-crystal data collected at room temperature.



**Figure S12** Comparison of the experimental powder patterns of **1c** (obtained from LAG using THF and solution) to the pattern simulated from single-crystal data collected at room temperature. These patterns are also compared to the experimentally obtained pattern for **1d**, which clearly differs from **1c**.



Figure S13 Comparison of the experimental powder patterns of 2a (obtained from sublimation, LAG using THF, and solution) to the pattern simulated from single-crystal data collected at room temperature.



**Figure S14** Comparison of the experimental powder patterns of **2b** (obtained from sublimation, LAG using THF, and solution) to the pattern simulated from single-crystal data collected at room temperature. The extra peaks in the mechanochemistry pattern (around 20.5 and 28.2°) are from **2a** forming concomitantly.

## Interconversions between stoichiometries by grinding

All the different forms can be interconverted by grinding each with extra equivalents of starting material for 20 minutes in a ball mill (with 20  $\mu$ l of MeOH;  $\eta = 0.25 \ \mu$ l mg<sup>-1</sup>). A summary of the results follows:

- **1a** (58 mg, 0.15 mmol) + 1 equivalent HMT (22 mg, 0.16 mmol) gives **1b** (Figure S15)
- **1a** (38 mg, 0.10 mmol) + 3 equivalents HMT (42 mg, 0.30 mmol) gives **1d** (converts to **1c** upon longer grinding) (Figure S16)
- 1b (55 mg, 0.21 mmol) + 1 equivalent SA (25 mg, 0.21 mmol) gives 1a (Figure S17)
- **1b** (52 mg, 0.20 mmol) + 1 equivalent HMT (28 mg, 0.20 mmol) gives **1d** (converts to **1c** upon longer grinding) (Figure S16)
- 1c (62 mg, 0.16 mmol) + 1 equivalent SA (18 mg, 0.15 mmol) gives 1b (Figure S17)
- 1c (39 mg, 0.098 mmol) + 3 equivalents SA (35 mg, 0.30 mmol) gives 1a (Figure S17)
- 2a (54 mg, 0.16 mmol) + 1 equivalent BPY (25 mg, 0.16 mmol) gives 2b (Figure S18)
- **2b** (64 mg, 0.13 mmol) + 1 equivalent OA·2H<sub>2</sub>O (16 mg, 0.13 mmol) gives a mixture of **2a** and **2b**, even when milled for 60 minutes (Figure S18)



Figure S15 Salt 1a can be converted to co-crystal 1b when milled with an additional equivalent of HMT, and to 1d when milled with three extra equivalents of HMT. The reference patterns for 1b and 1d shown here were obtained from previous mechanochemistry experiments and can be used to identify the products obtained.



Figure S16 Co-crystal 1b can be converted to salt 1a when milled with an additional equivalent of SA, and to 1d when milled with an extra equivalent of HMT. The reference patterns for 1a and 1d shown here were obtained from previous mechanochemistry experiments and can be used to identify the products obtained.



Figure S17 Co-crystal 1c can be converted to co-crystal 1b when milled with an additional equivalent of SA, and to 1a when milled with three extra equivalents of SA. The reference patterns for 1b and 1a shown here were obtained from previous mechanochemistry experiments and can be used to identify the products obtained.



**Figure S18** Salt **2a** can be converted to **2b** when milled with an additional equivalent of BPY. On the other hand, when co-crystal **2b** is milled with an extra equivalent of OA, it only partially converts to **2a**, while some **2b** remains. The reference patterns for **2b** and **2a** shown here were obtained from previous mechanochemistry experiments and can be used to identify the products obtained.

## Test tube heating experiments



Figure S19 When SA and HMT are heated together under ambient conditions (top pattern), HMT sublimes, leaving only succinic acid. On the other hand, OA and BPY combine to form both 2a and 2b when heated together under ambient conditions (bottom pattern).

## Thermal analysis (TGA and DSC)



Figure S20 Thermal analysis results for 1a. TGA trace shown in blue and DSC traces in yellow (cycle 1) and purple dashes (cycle 2).



Figure S21 Thermal analysis results for 1b. TGA trace shown in blue and DSC traces in yellow (cycle 1) and purple dashes (cycle 2).



Figure S22 Thermal analysis results for 1c. TGA trace shown in blue and DSC traces in yellow (cycle 1) and purple dashes (cycle 2).



Figure S23 Thermal analysis results for the unknown co-crystal, 1d. TGA trace shown in blue and DSC traces in yellow (cycle 1) and purple dashes (cycle 2).



Figure S24 Thermal analysis results for 2a. TGA trace shown in blue and DSC traces in yellow (cycle 1) and purple dashes (cycle 2).



Figure S25 Thermal analysis results for 2b. TGA trace shown in blue and DSC traces in yellow (cycle 1) and purple dashes (cycle 2).



**Figure S26** FTIR spectra for the salt, **1a**, and co-crystals, **1b**, **1c** and **1d**, formed from succinic acid and hexamethylenetetramine. For **1a**, the peak at 1717.82 cm<sup>-1</sup> represents the carboxylic acid C=O stretching frequency, while the peak at 1548.92 cm<sup>-1</sup> indicates the presence of a carboxylate group, as is expected for a salt. For the three co-crystals the peak at 1699.28 cm<sup>-1</sup>/1695.16 cm<sup>-1</sup> represents the carboxylic acid C=O stretching frequency for succinic acid. There is no carboxylate peak as **1b**, **1c** and **1d** are co-crystals.

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**Figure S27** FTIR spectra for the salt and co-crystal formed from oxalic acid and 4,4'-bipyridine, **2a** and **2b**. For **2a**, the peak at 1744.60 cm<sup>-1</sup> represents the carboxylic acid C=O stretching frequency, while the peaks around 1605 - 1648 cm<sup>-1</sup> indicates the presence of a carboxylate group, as is expected for a salt. For **2b** the peak at 1705.46 cm<sup>-1</sup> represents the carboxylic acid C=O stretching frequency, while the peak at 1604.53 cm<sup>-1</sup> seems to indicate the presence of a carboxylate group, even though according to the literature this is a co-crystal. This carboxylate frequency could be due to small amounts of **2a** contaminant, as can be seen in the PXRD pattern (Figure S13).

## Difference electron density maps

The position of acidic hydrogen atoms could be determined based on electron density.



Figure S28. Electron density difference map for salt 1a before the O-H and N-H hydrogen atoms were assigned.



Figure S29. Electron density difference map for co-crystal 1b before the O-H and N-H hydrogen atoms were assigned.



Figure S30. Electron density difference map for co-crystal 1c before the O-H and N-H hydrogen atoms were assigned.



Figure S31. Electron density difference map for salt 2a before the O-H and N-H hydrogen atoms were assigned.



Figure S32 Mass spectrum for 1a showing the presence of the hydrogen-bonded adduct SA-HMT at m/z = 257.

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