Electronic Supplementary Material (ESI) for CrystEngComm

Electronic Supplementary Information

Two polymorphs and one hydrate of a molecular salt involving phenazopyridine and salicylic acid

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Experimental Section

Phenazopyridine hydrochloride (PAP·HCl) was purchased from Wuhan Yuancheng Chemical Co. Ltd. Phenzaopyridine (PAP) was obtained by neutralizing PAP·HCl with aqueous NaOH. Salicylic acid (SA) was purchased from Aladdin reagent Inc. All of the other chemicals and solvents were commercially available and used as received.

Differential scanning calorimetry (DSC) was recorded on a Netzsch STA 409 PC instrument and aluminium sample pans in nitrogen atmosphere, with a heating rate of 10 °C/min.

Co-grinding experiment was completed by a Retsch MM200 Mixer Mill.

Single crystal X-ray diffraction data were collected on an Agilent Xcalubur Nova CCD diffractometer with graphite monochromated Cu-Kα radiation (λ = 1.54178 Å). Cell refinement and data reduction were applied using the program of CrysAlis^{PRO}.[1] The structures were solved by the direct method using the SHELXS-97 programs[2] and refined by the full-matrix least-squares method on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms of protonated pyridine N2 of phenazopyridine and the water molecules in **MH** were located in the difference Fourier maps and refined isotropically. Other hydrogen atoms were placed in calculated positions with fixed isotropic thermal parameters and included in the structure factor calculation in the final stage of full-matrix least-squares refinement. Crystallographic data and details of refinements are listed in Table S1, and the hydrogen bonding distances and angles are given in Table S2.

X-ray powder diffraction data were recorded using a Bruker D8 Advanced diffractometer (Bruker, Madison, WI). The diffractometer was operated with Cu Kα radiation (λ = 1.54180 Å) at 40 kV and 40 mA. Data were collected over an angular range of 3 ^{o}-40 ^{o} (2θ) in continuous scan mode using a step size of 0.02 ^{o} (2θ) and a step time of 0.12 s. Approximately 20 mg samples were weighed into glass sample holders, taking care not to introduce a preferential orientation of crystals.

Dynamic vapour sorption (DVS) study was performed on a DVS Intrinsic instrument (Surface Measurment Systems, UK). All samples were initially dried for several hours under a stream of nitrogen to establish the equilibrium dry mass under 25 ^{o}C. Then the

relative humidity (RH) was then increased in 10% RH steps to 95% RH. Finally, the RH was decreased in a similar fashion for the desorption phase. The temperature was maintained at a constant 25± 0.1 ºC. The sorption/desorption isotherms were calculated from the equilibrium mass values.

Powder dissolution experiments: Concentrations of PAP in water were determined by a Cary 50 UV/Vis spectrophotometry at 427 nm, the absorbance values were related to solution concentrations using a calibration curve. SA has no absorbance at 427 nm and, therefore, does not interfere with the determination of the concentration of PAP·SA. All the solids were milled to powders and sieved using standard mesh sieves to provide samples with approximate particle size ranges of 65-150 μm. In a typical experiment, a flask containing 100 mg of powder was added 100 mL of water, and the resulting mixture was stirred at 25 °C and 500 rpm. At each time interval, the solution was withdrawn from the flask and filtered through a 0.22 μm nylon filter. A 0.1 mL portion of filtered aliquot was diluted to 1.0 mL with water, and measured with UV/Vis spectrophotometry. After 3 hours, the remaining solids were collected by filtration, dried and analyzed by XRPD.

Polymorphic molecular salts retrieved from CSD (May 2013 update)

BEWNAT，CHAPEP，DIVHOF，EJUQIK，HAZFAP，HEYQOR，JUHLUT，KULSOA，MANMUJ，MOLGIE，MUFBOE，NEYLEI，NMACEP，NUYDER，OLUPAM，PEZLOV，PYRPIC，QIQLIL，RIDFOA，TABCAC，TIFLAV，UJOGUW，YAVRIW，YEPCAY，ZEDPON，ALUQEE，WOBQEK，AWIHOE

Table S1. Crystallographic data and detail of refinements for PAP·SA

compound	**AH-I**	**AH-II**	**MH**
formula	$C_{18}H_{17}N_5O_3$	$C_{18}H_{17}N_5O_3$	$C_{18}H_{19}N_5O_4$
formula weight	351.37	351.37	369.38
crystal system	monoclinic	monoclinic	monoclinic
space group	$P2_1/c$	$P2_1$	$C2$
T/K	150(2)	293(2)	293(2)
a/Å	13.2907(10)	4.7841(2)	26.8925(7)
b/Å	5.1776(4)	9.3170(3)	5.1332(1)
c/Å	25.343(2)	18.9162(3)	13.0371(4)
α/ °	90	90	90
β/ °	110.038	92.498(2)	100.854(3)
γ/ °	90	90	90
Z	4	2	4
V/Å^3	1638.4(2)	842.36(5)	1767.50(8)
Dc/g cm^{-3}	1.424	1.385	1.388
μ/mm^{-1}	0.832	0.809	0.840
refln collected	5434	3140	3387
unique reflns	2829	2233	2493
R_1 [I >2σ(I)][a]	0.0482	0.0543	0.0478
wR_2 [all data][b]	0.1400	0.1659	0.1085
GOF	1.017	1.064	1.076

[a] $R_1 = \Sigma \,||F_o| - |F_c||/\Sigma\,|F_o|$. [b] $wR_2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma w(F_o^2)^2]^{1/2}$, $w = 1/[\sigma^2 (F_o)^2 + (aP)^2 + bP\,]$, where $P = [(F_o^2) + 2F_c^2]/3$.

Table S2. Hydrogen bonding distances and angles for PAP·SA.

compound	H bond	H···A/Å	D···A/Å	∠D-H···A/ °
AH-I[a]	N1-H1B···O3#1	2.32	2.922(5)	128
	N2-H2···O2	1.88	2.734(2)	170
	N3-H3B···O1	1.90	2.857(2)	174
	N3-H3A···O1#2	1.99	2.797	155
	O3-H4···O2	1.90	2.592(2)	144
AH-II[b]	N2-H2···O1	1.90	2.717(5)	159
	N1-H1B···O1	2.26	2.983(4)	142
	N3-H3B···O2	1.98	2.813(5)	165
	N3-H3A···O3#1	2.11	2.959(5)	171
	O3-H4···O2	1.77	2.499(5)	148
MH[c]	N3-H3B···O2	1.74	2.778(3)	179
	N1-H1B···O4	1.85	2.861(3)	168
	N2-H2···O1	1.75	2.747(3)	174
	N3-H3A···O3#1	2.07	2.933(3)	173
	O3-H3···O2	1.79	2.514(3)	147
	O4-H4B···O1	1.70	2.631(3)	163
	O4-H4A···O4#2	2.01	2.874(2)	171

Symmetry codes: [a] #1 –x+1, y+0.5, -z+0.5; #2 -x, y+0.5, -z+0.5; [b] #1 -x, y-0.5, -z; [c] #1 -x+2, y+1, -z+2, #2 -x+1.5, y-0.5, -z+2

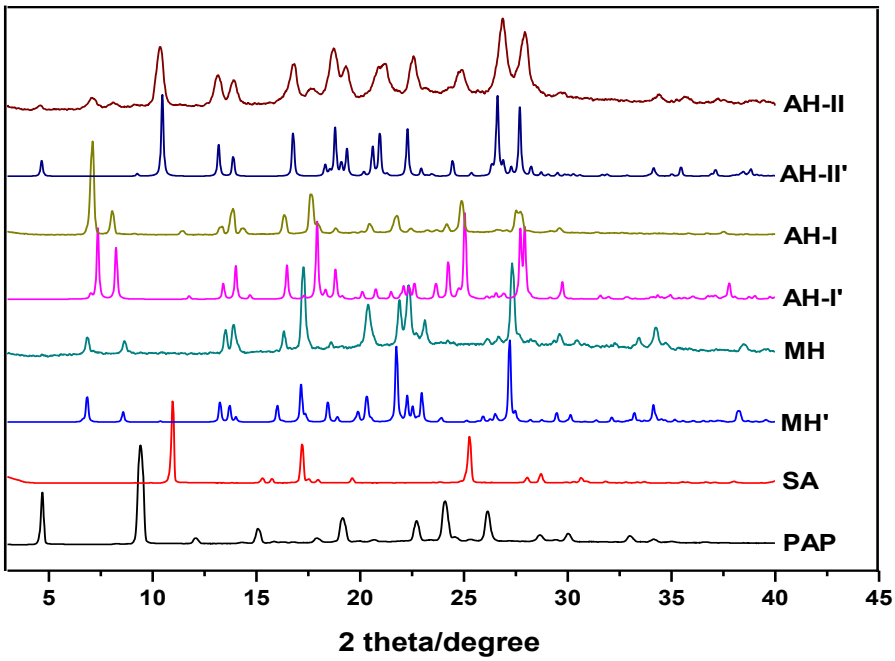

Fig. S1 The measured XRPD patterns (**AH-I**, **AH-II** and **MH**) and simulated patterns (**AH-I′**, **AH-II′**, **MH′**) of PAP·SA.

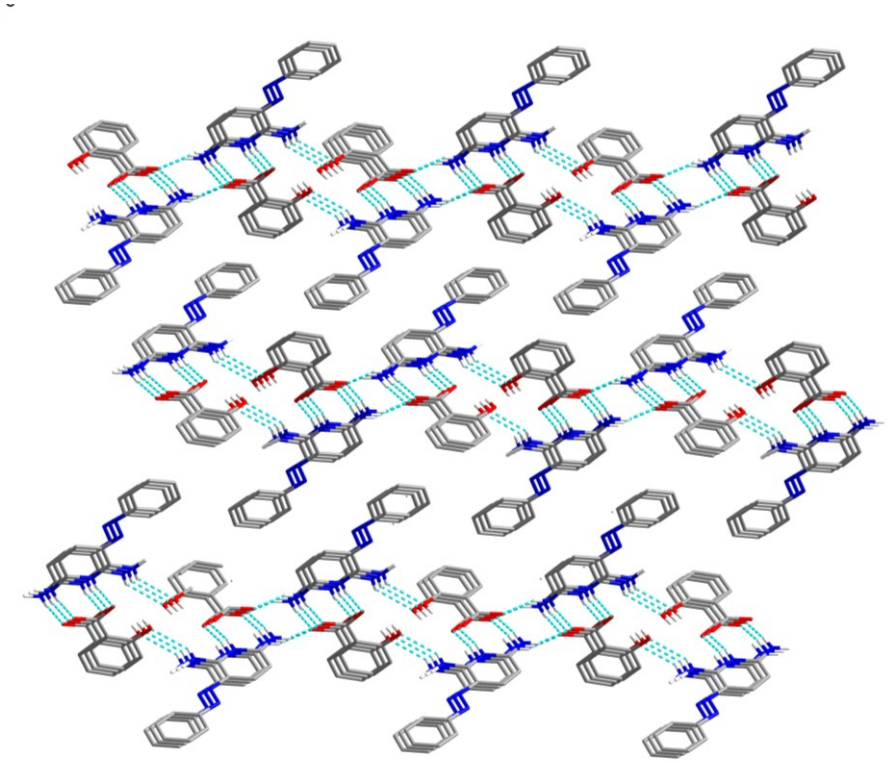

Fig. S2 The 3D packing structure of **AH-I** from *b*-axis view.

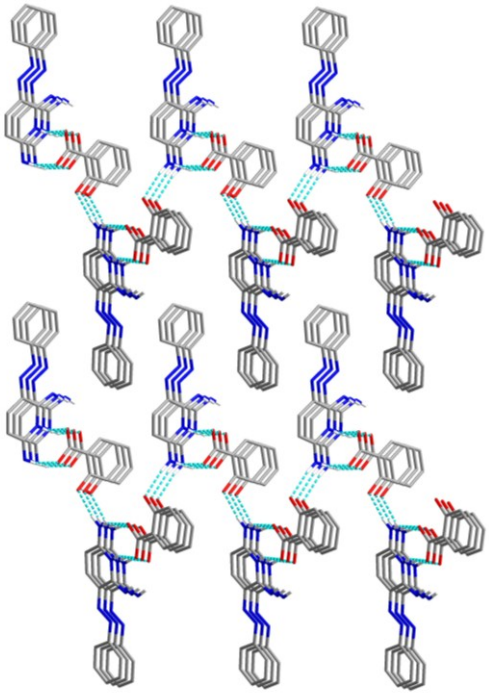

Fig. S3 The 3D structure of **AH-II** from *a*-axis.

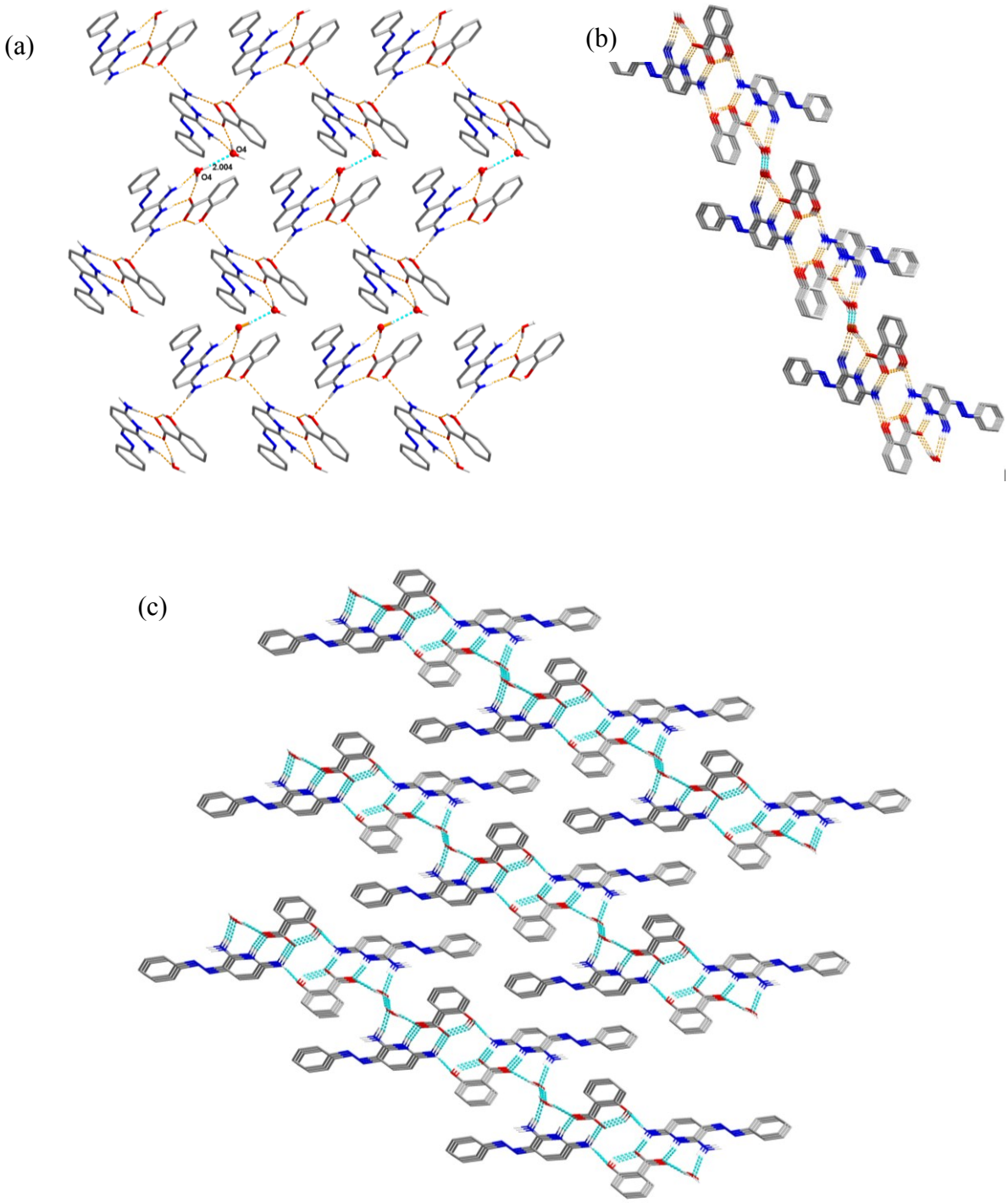

Fig. S4 The 2D structure of **MH** (a), side view of 2D structure (b) and 3D structure of **MH** (c).

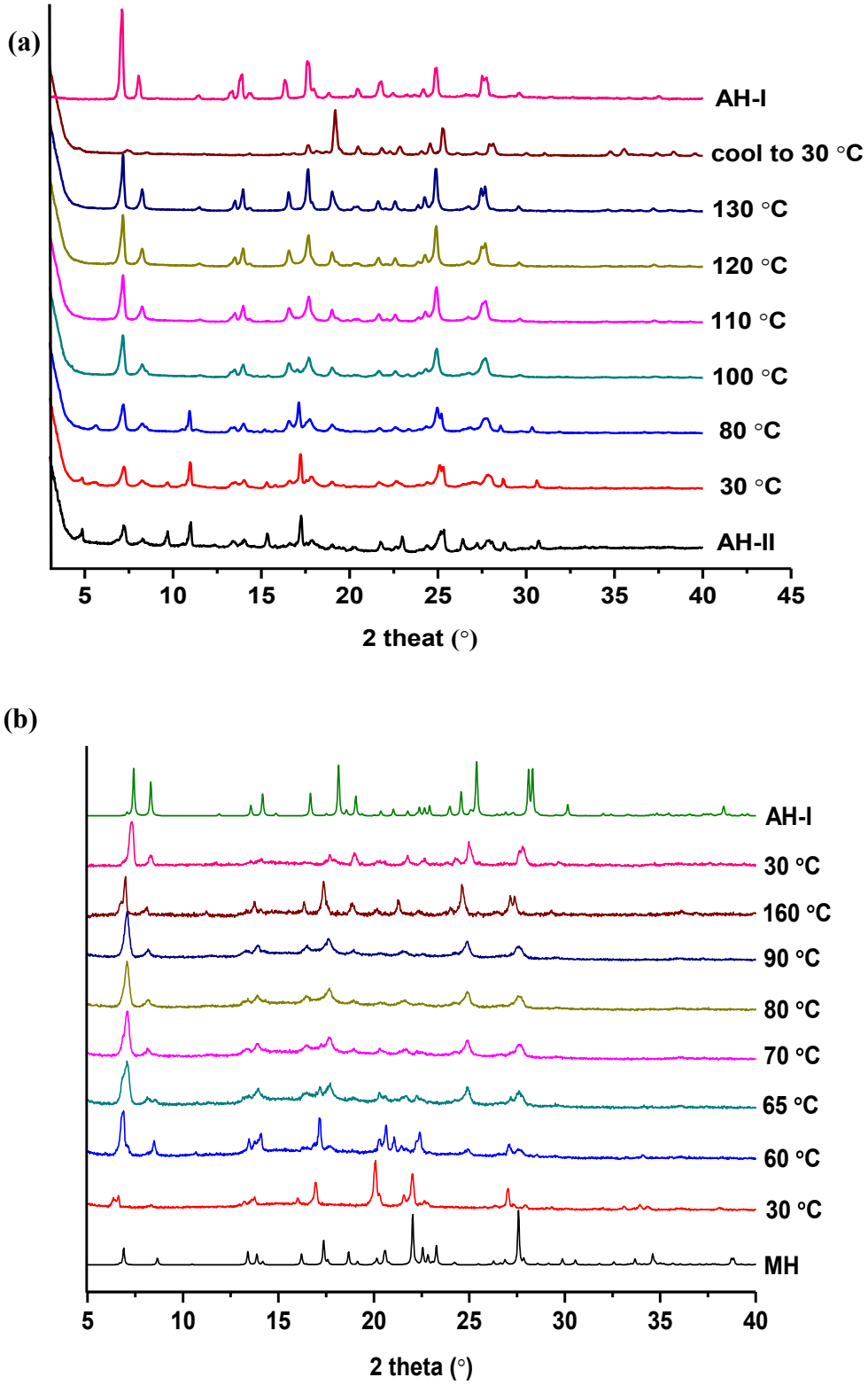

Fig. S5 VT-XRPD pattern of **AH-II** (a) and **MH** (b).

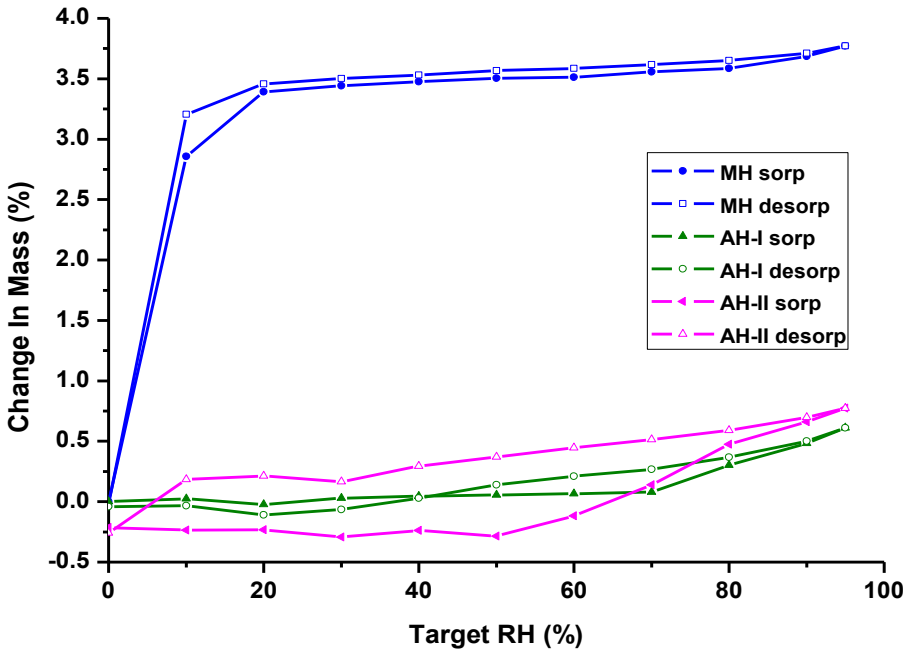

Fig. S6 **W**ater sorption/desorption isotherms on **AH-I** (green), **AH-II** (red) and **MH** (blue) at 25 ºC.

References

1 CrysAlis^{Pro} Version 1.171.35.19. Agilent Technologies Inc. Santa Clara, CA, USA, 2011.

2 G. M. Sheldrick, SHELXS 97, Program for Crystal Structure Refinement, University of Göttingen, Göttingen, 1997.