# SUPPORTING INFORMATION

# From pipemidic acid molecular salts to metal complexes and BioMOFs using Mechanochemistry

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## Structural data

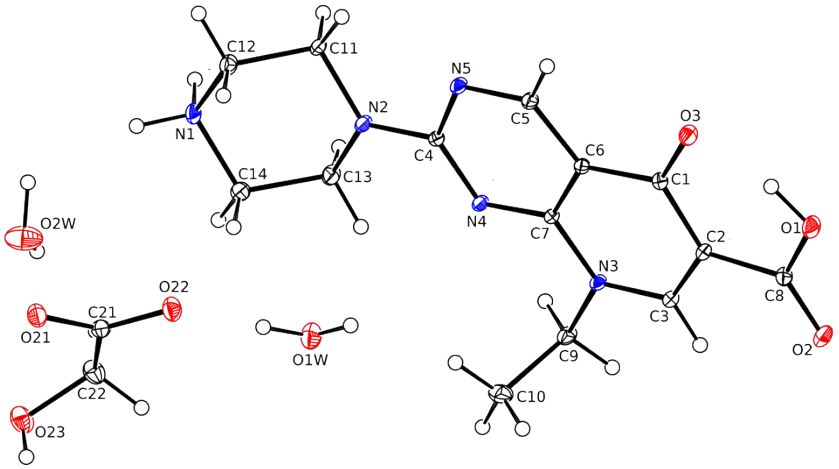


**Figure S1.** Asymmetric unit in **1**·2$H_2O$. Thermal displacement ellipsoids are plotted at 30 % probability level.

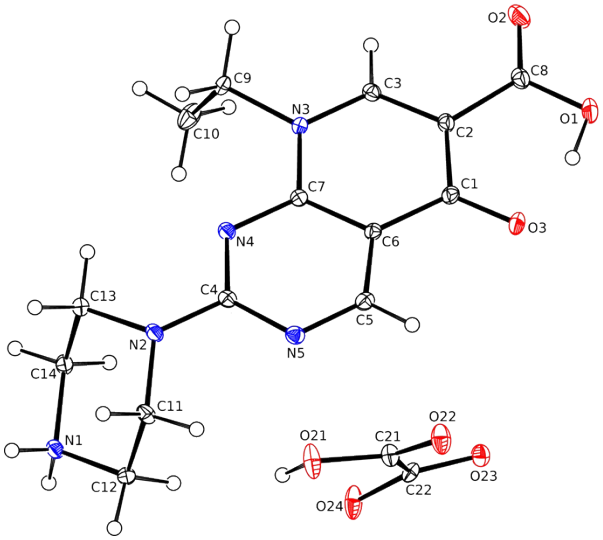


**Figure S2.** Asymmetric unit in **2**. Thermal displacement ellipsoids are plotted at 30 % probability level.

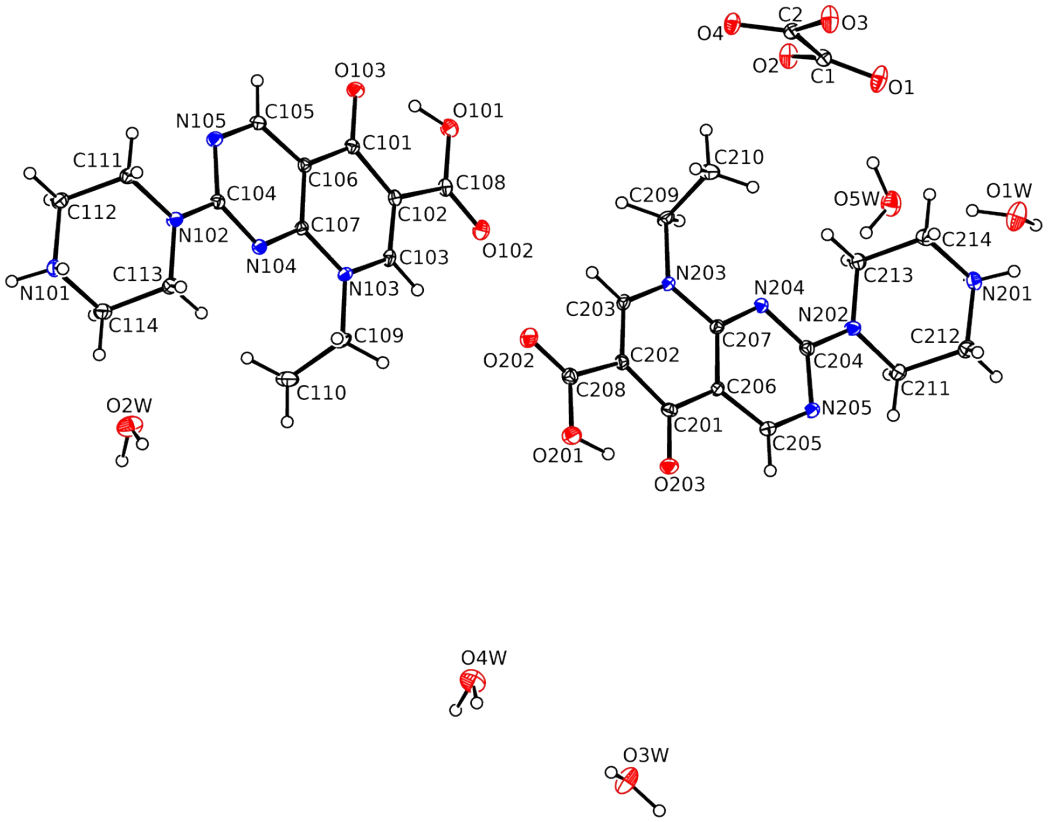


**Figure S3.** Asymmetric unit in **3**·5$H_2O$. Thermal displacement ellipsoids are plotted at 30 % probability level.

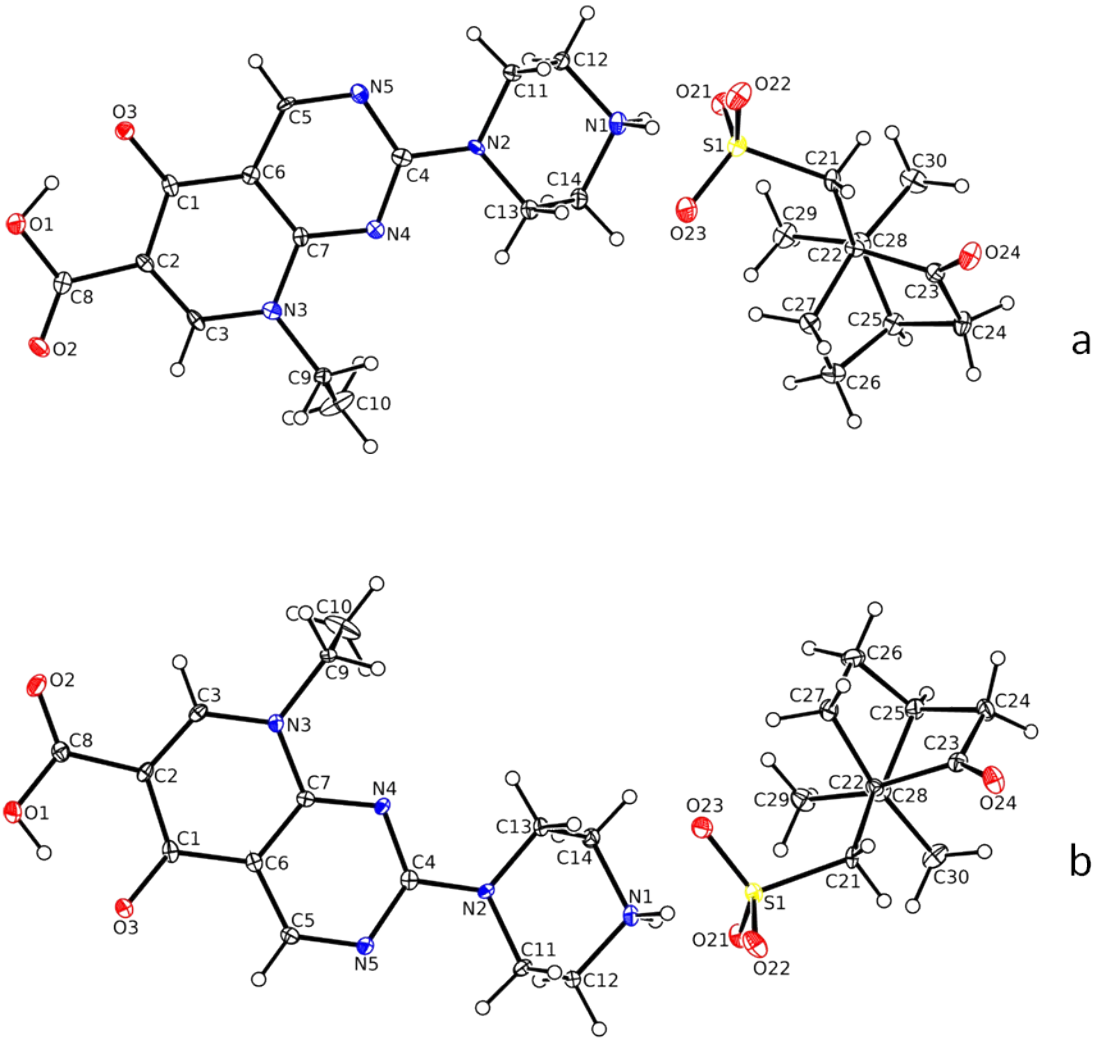


**Figure S4.** Asymmetric units of (a) **4***S* and (b) **4***R*. Thermal displacement ellipsoids are plotted at 30 % probability level.

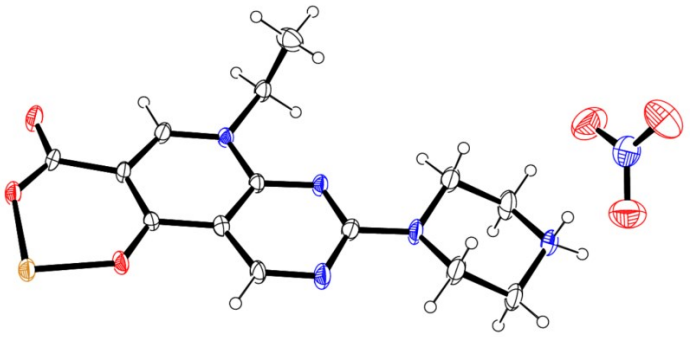

**Figure S5.** Asymmetric units of **5**. Thermal displacement ellipsoids are plotted at 30 % probability level.

**Table S1.** Selected bond lengths (Å) and angles (°) for **1**·$2H_2O$.

| | | | |
|---|---|---|---|
| C1-O3 | 1.269(1) | C2-C1-O3 | 122.5(1) |
| C8-O1 | 1.336(2) | C2-C8-O1 | 114.3(1) |
| C8-O2 | 1.209(2) | C2-C8-O2 | 124.4(1) |
| C21-O21 | 1.252(2) | O1-C8-O2 | 121.3(1) |
| C21-O22 | 1.263(1) | C7-N3-C9-C10 | −76.3(1) |
| C21-C22 | 1.523(2) | C1-C2-C8-O1 | −1.1(2) |
| C22-O23 | 1.412(2) | C1-C2-C8-O2 | 178.5(1) |
| | | O23-C22-C21-O22 | 156.7(1) |

**Table S2.** Selected bond lengths (Å) and angles (°) for **2**.

| | | | |
|---|---|---|---|
| C1-O3 | 1.258(2) | C2-C1-O3 | 122.6(1) |
| C8-O1 | 1.328(2) | C2-C8-O1 | 114.9(2) |
| C8-O2 | 1.214(2) | C2-C8-O2 | 123.5(2) |
| C21-O21 | 1.326(2) | O1-C8-O2 | 121.6(2) |
| C21-O22 | 1.201(2) | C7-N3-C9-C10 | −87.6(2) |
| C22-O23 | 1.242(2) | C1-C2-C8-O1 | 1.1(2) |
| C22-O24 | 1.248(2) | C1-C2-C8-O2 | −178.2(2) |
| C21-C22 | 1.551(2) | O23-C22-C21-O21 | 169.2(2) |

**Table S3.** Selected bond lengths (Å) and angles (°) for **3**·$5H_2O$.

| | | | |
|---|---|---|---|
| C101-O103 | 1.256(2) | C102-C101-O103 | 122.9(2) |
| C108-O101 | 1.323(2) | C102-C108-O101 | 116.0(2) |
| C108-O102 | 1.214(2) | C102-C108-O102 | 123.1(2) |
| C201-O203 | 1.262(2) | O101-C108-O102 | 121.0(2) |
| C208-O201 | 1.327(2) | C202-C201-O203 | 122.9(2) |
| C208-O202 | 1.210(2) | C202-C208-O201 | 114.5(2) |
| C1-O1 | 1.238(2) | C202-C208-O202 | 124.1(2) |
| C1-O2 | 1.260(2) | O201-C208-O202 | 121.5(2) |
| C2-O3 | 1.255(2) | C107-N103-C109-C110 | 76.1(2) |
| C2-O4 | 1.243(2) | C101-C102-C108-O101 | 1.0(2) |
| C1-C2 | 1.552(2) | C101-C102-C108-O102 | −178.6(1) |
| | | C207-N203-C209-C210 | −83.3(2) |
| | | C201-C202-C208-O201 | −0.4(2) |
| | | C201-C202-C208-O202 | 179.5(1) |
| | | O1-C1-C2-O4 | −164.1(2) |

**Table S4.** Selected bond lengths (Å) and angles (°) for **4***S*.

| | | | |
|---|---|---|---|
| C1-O3 | 1.256(7) | C2-C1-O3 | 122.2(5) |
| C8-O1 | 1.326(7) | C2-C8-O1 | 114.7(5) |
| C8-O2 | 1.204(7) | C2-C8-O2 | 123.7(5) |
| S1-O21 | 1.458(4) | O1-C8-O2 | 121.6(5) |
| S1-O22 | 1.459(4) | C22-C21-S1 | 122.7(4) |
| S1-O23 | 1.450(4) | C7-N3-C9-C10 | −90.2(6) |
| | | C1-C2-C8-O1 | −0.9(8) |
| | | C1-C2-C8-O2 | 179.7(5) |
| | | C23-C22-C21-S1 | −168.8(4) |

**Table S5.** Selected bond lengths (Å) and angles (°) for **4***R*.

| | | | |
|---|---|---|---|
| C1-O3 | 1.259(6) | C2-C1-O3 | 123.0(4) |
| C8-O1 | 1.322(6) | C2-C8-O1 | 115.1(4) |
| C8-O2 | 1.212(6) | C2-C8-O2 | 123.3(5) |
| S1-O21 | 1.462(4) | O1-C8-O2 | 121.6(4) |
| S1-O22 | 1.458(4) | C22-C21-S1 | 122.5(4) |
| S1-O23 | 1.447(4) | C7-N3-C9-C10 | 90.3(6) |
| | | C1-C2-C8-O1 | 0.6(7) |
| | | C1-C2-C8-O2 | −179.4(5) |
| | | C23-C22-C21-S1 | 168.8(4) |

**Table S6.** Selected bond lengths (Å) and angles (°) for **5**.

| | | | |
|---|---|---|---|
| C(1)-O(3) | 1.284(5) | O(3)-C(1)-C(2) | 126.2(4) |
| C(1)-C(2) | 1.407(6) | O(3)-C(1)-C(6) | 117.6(4) |
| C(1)-C(6) | 1.439(5) | C(2)-C(1)-C(6) | 116.2(4) |
| C(2)-C(3) | 1.385(5) | C(3)-C(2)-C(1) | 118.8(4) |
| C(2)-C(8) | 1.489(5) | C(3)-C(2)-C(8) | 117.4(4) |
| C(3)-N(3) | 1.335(5) | C(1)-C(2)-C(8) | 123.8(4) |
| C(4)-N(4) | 1.331(5) | N(3)-C(3)-C(2) | 124.5(4) |
| C(4)-N(2) | 1.355(5) | N(4)-C(4)-N(2) | 117.6(4) |
| C(4)-N(5) | 1.364(5) | N(4)-C(4)-N(5) | 126.6(4) |
| C(5)-N(5) | 1.309(5) | N(2)-C(4)-N(5) | 115.8(4) |
| C(5)-C(6) | 1.380(5) | N(5)-C(5)-C(6) | 124.8(4) |
| C(6)-C(7) | 1.394(5) | C(5)-C(6)-C(7) | 114.9(4) |
| C(7)-N(4) | 1.334(5) | C(5)-C(6)-C(1) | 123.3(4) |
| C(7)-N(3) | 1.371(5) | C(7)-C(6)-C(1) | 121.7(4) |
| C(8)-O(2) | 1.235(5) | N(4)-C(7)-N(3) | 117.4(3) |
| C(8)-O(1) | 1.279(5) | N(4)-C(7)-C(6) | 123.3(4) |
| C(9)-N(3) | 1.487(5) | N(3)-C(7)-C(6) | 119.3(3) |
| C(9)-C(10) | 1.495(6) | O(2)-C(8)-O(1) | 122.4(4) |
| C(11)-N(2) | 1.454(5) | O(2)-C(8)-C(2) | 118.8(4) |
| C(11)-C(12) | 1.510(6) | O(1)-C(8)-C(2) | 118.8(4) |
| C(12)-N(1) | 1.477(6) | N(3)-C(9)-C(10) | 112.4(3) |
| C(13)-N(2) | 1.461(6) | N(2)-C(11)-C(12) | 110.1(4) |

| | | | |
|---|---|---|---|
| C(13)-C(14) | 1.508(6) | N(1)-C(12)-C(11) | 110.8(4) |
| C(14)-N(1) | 1.487(6) | N(2)-C(13)-C(14) | 109.9(4) |
| N(6)-O(4) | 1.219(5) | N(1)-C(14)-C(13) | 109.5(4) |
| N(6)-O(5) | 1.225(5) | C(12)-N(1)-C(14) | 111.3(4) |
| N(6)-O(6) | 1.235(5) | C(4)-N(2)-C(11) | 120.7(4) |
| O(1)-Cu(1) | 1.918(3) | C(4)-N(2)-C(13) | 121.4(4) |
| O(3)-Cu(1) | 1.891(3) | C(11)-N(2)-C(13) | 113.1(4) |
| Cu(1)-O(3)#1 | 1.891(3) | C(3)-N(3)-C(7) | 119.5(3) |
| Cu(1)-O(1)#1 | 1.918(3) | C(3)-N(3)-C(9) | 120.9(3) |
| | | C(7)-N(3)-C(9) | 119.2(3) |
| | | C(4)-N(4)-C(7) | 115.4(3) |
| | | C(5)-N(5)-C(4) | 114.9(4) |
| | | O(4)-N(6)-O(5) | 121.4(5) |
| | | O(4)-N(6)-O(6) | 120.5(5) |
| | | O(5)-N(6)-O(6) | 118.0(5) |
| | | C(8)-O(1)-Cu(1) | 131.3(3) |
| | | C(1)-O(3)-Cu(1) | 126.9(3) |
| | | O(3)#1-Cu(1)-O(3) | 180.0 |
| | | O(3)#1-Cu(1)-O(1) | 87.45(12) |
| | | O(3)-Cu(1)-O(1) | 92.55(12) |
| | | O(3)#1-Cu(1)-O(1)# | 92.55(12) |
| | | O(3)-Cu(1)-O(1)#1 | 87.45(12) |
| | | O(1)-Cu(1)-O(1)#1 | 180.0 |

Symmetry transformations used to generate equivalent atoms: #1-x,-y+2,-z+1

**Table S7.** Cremer-Pople θ angle values [°] and puckering amplitudes Q [Å] of piperazine rings in **1-6**.

| Compound | Q [Å] | θ [°] |
|---|---|---|
| **1**·2$H_2O$ | 0.5563(13) | 176.64(13) |
| **2** | 0.5678(17) | 174.18(17) |
| **3**·5$H_2O$ | 0.5608(17), 0.5494(17) | 0.60(17), 177.94(17) |
| **4*S*** | 0.561(6) | 178.7(5) |
| **4*R*** | 0.564(5) | 3.4(5) |
| **5** | 0.566(5) | 177.9(5) |
| **6** | 0.570(6), 0.566(6) | 163.7(6), 171.8(6) |

## Powder X-ray diffraction data – bulk purity

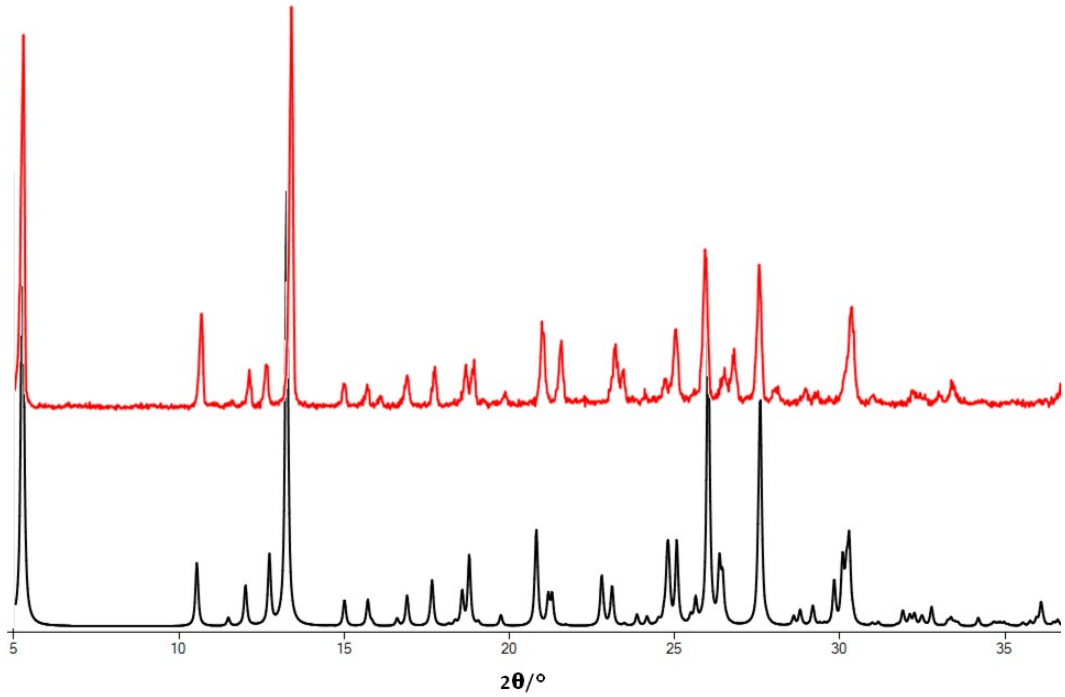


**Figure S6.** Experimental (red) and simulated (black) powder X-ray diffractograms of **1**·$2H_2O$.

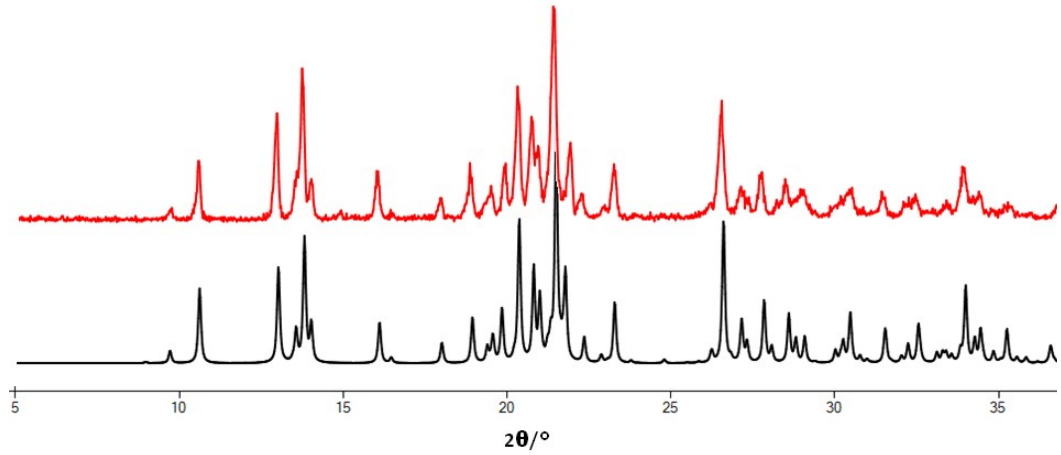


**Figure S7.** Experimental (red) and simulated (black) powder X-ray diffractograms of **2**.

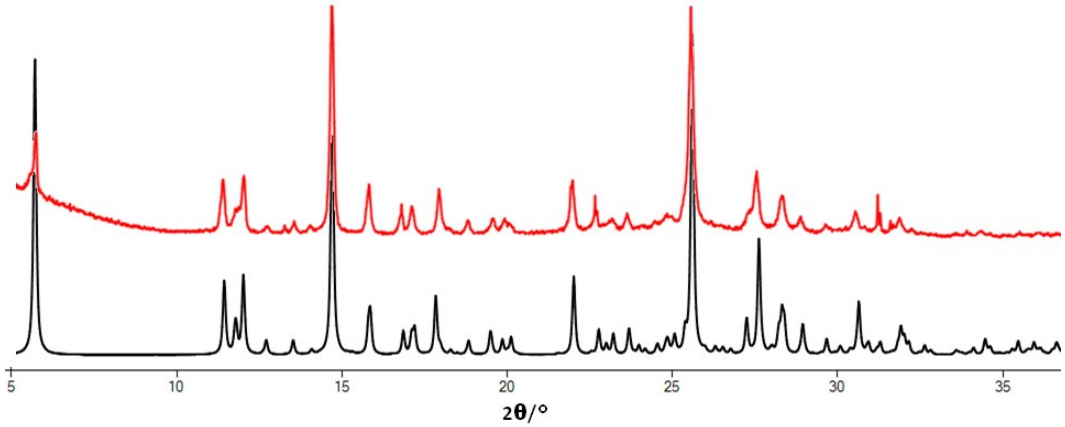


**Figure S8.** Experimental (red) and simulated (black) powder X-ray diffractograms of **3**·5$H_2O$.

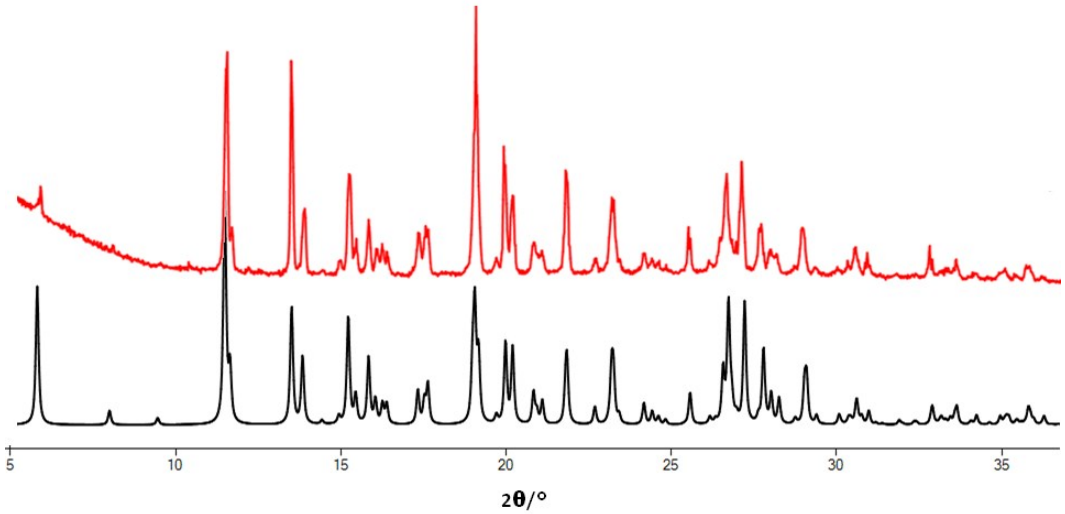


**Figure S9.** Experimental (red) and simulated (black) powder X-ray diffractograms of **4***S*.

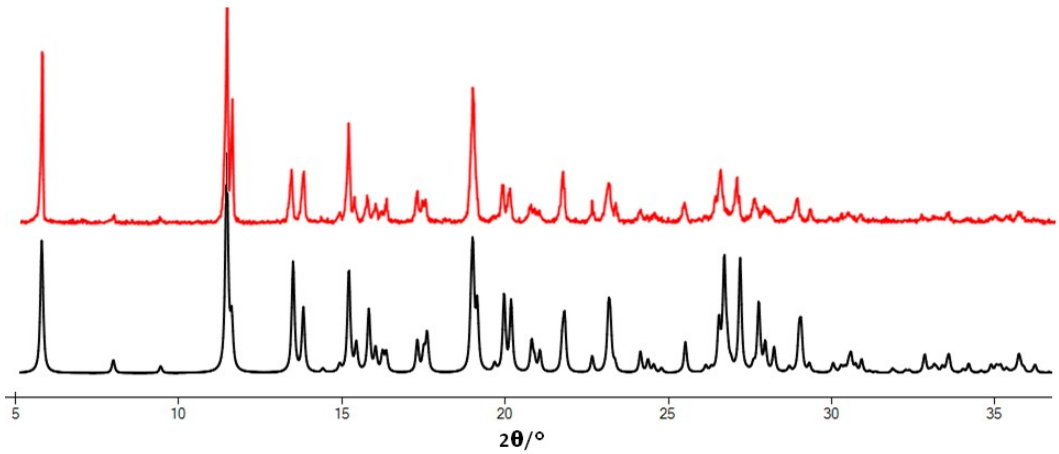


**Figure S10.** Experimental (red) and simulated (black) powder X-ray diffractograms of **4***R*.

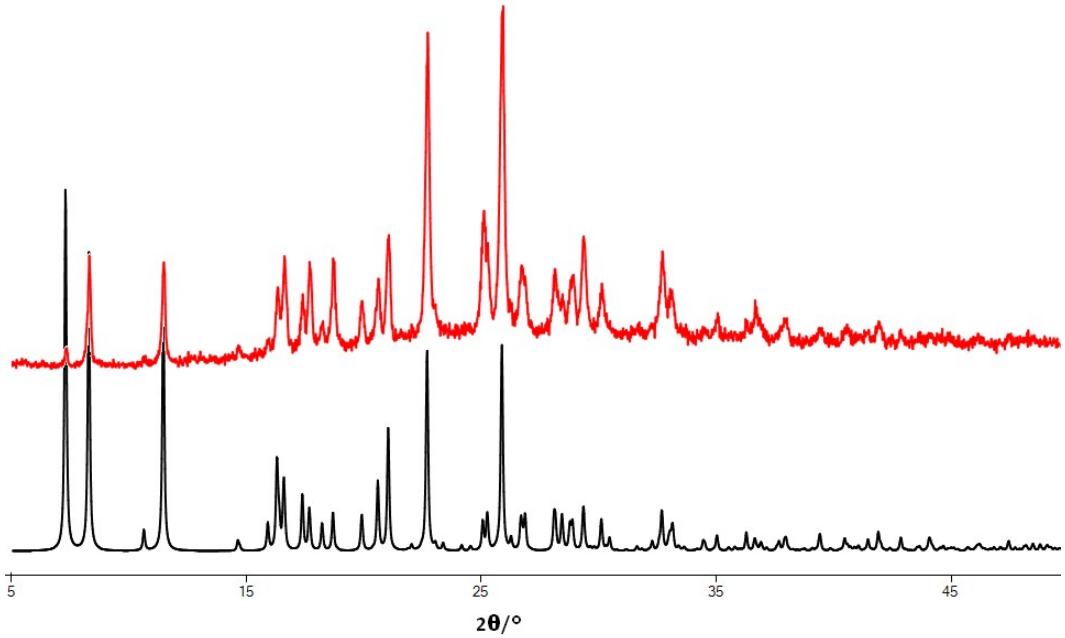


**Figure S11.** Experimental (red) and simulated (black) powder X-ray diffractograms of complex **5.**

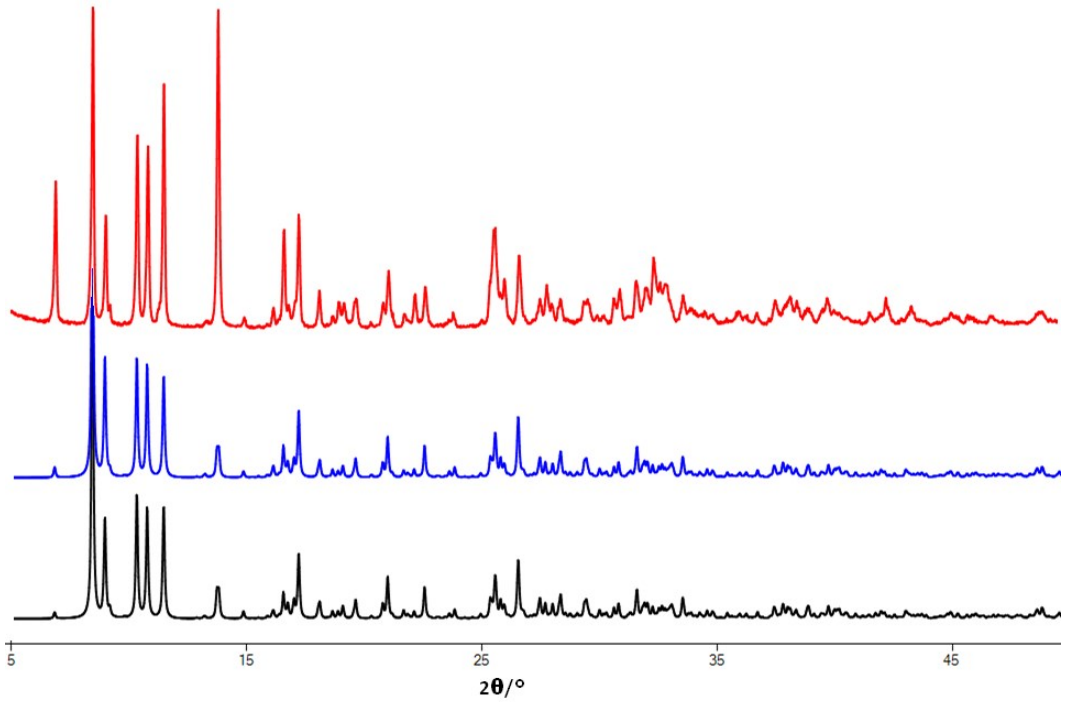


**Figure S12.** Experimental (red) and simulated powder X-ray (black- GIWNOR; blue- PICWUV) diffractograms of MOF **6**.

## Powder X-ray diffraction data – shelf stability

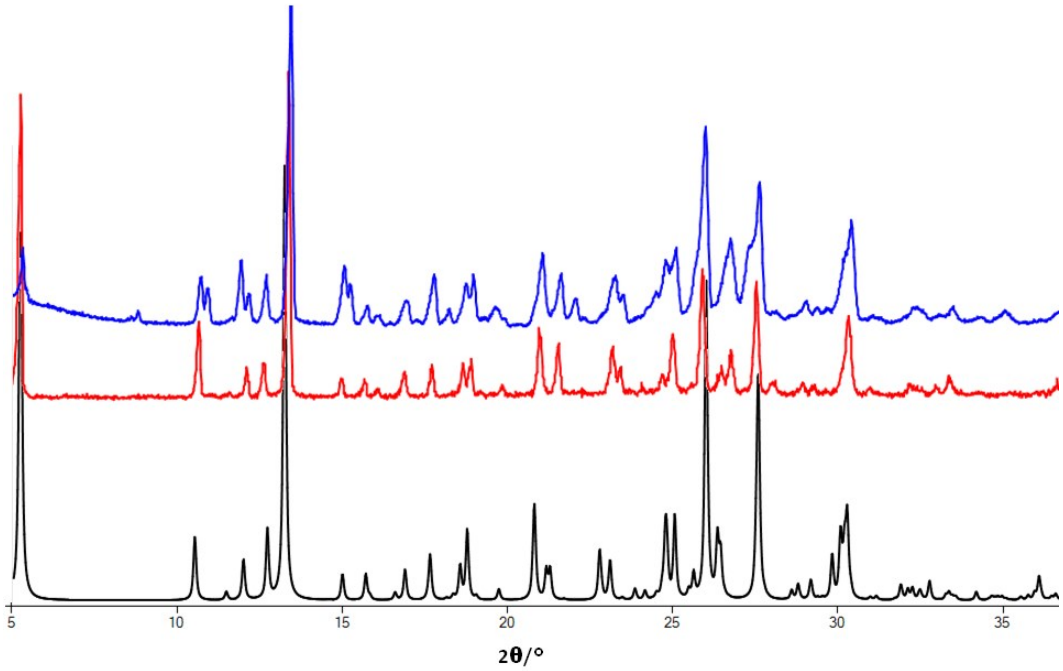


**Figure S13.** Simulated (black) and experimental (red) powder X-ray diffractograms of **1**·$2H_2O$ after 15 months (blue) on shelf at room temperature.

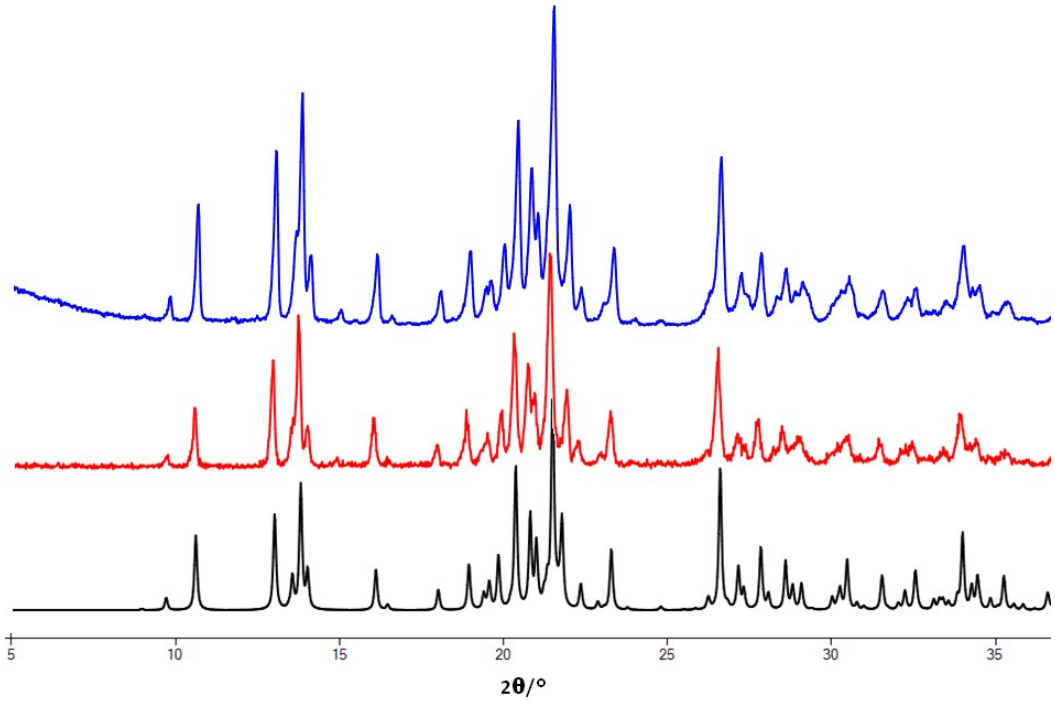


**Figure S14.** Simulated (black) and experimental (red) powder X-ray diffractograms of **2** after 15 months (blue) on shelf at room temperature.

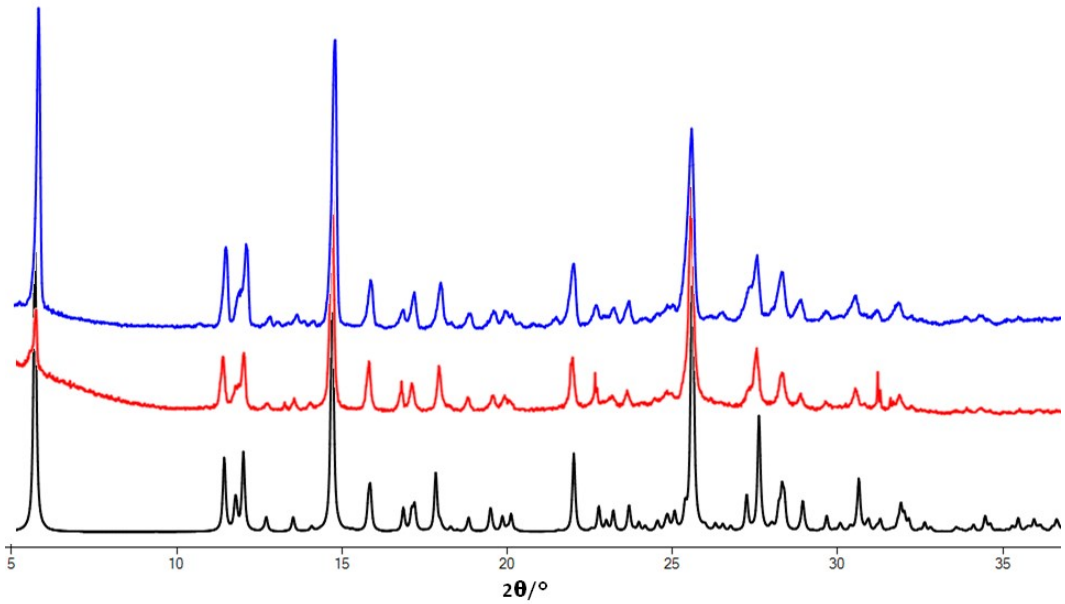


**Figure S15.** Simulated (black) and experimental (red) powder X-ray diffractograms of **3**·5$H_2O$ after 15 months (blue) on shelf at room temperature.

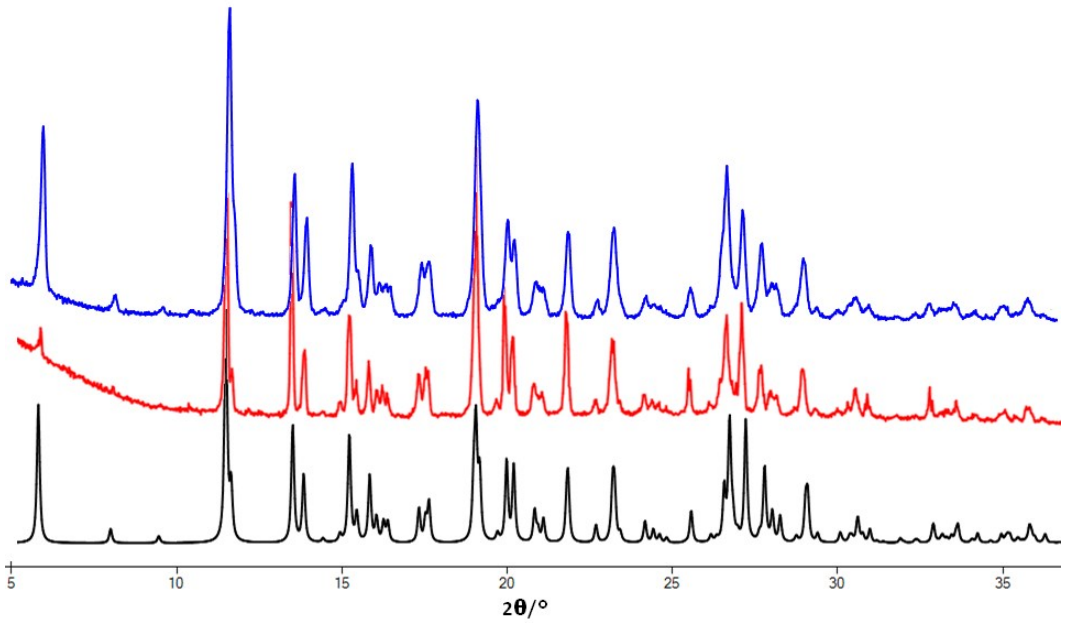


**Figure S16.** Simulated (black) and experimental (red) powder X-ray diffractograms of **4***S* after 15 months (blue) on shelf at room temperature.

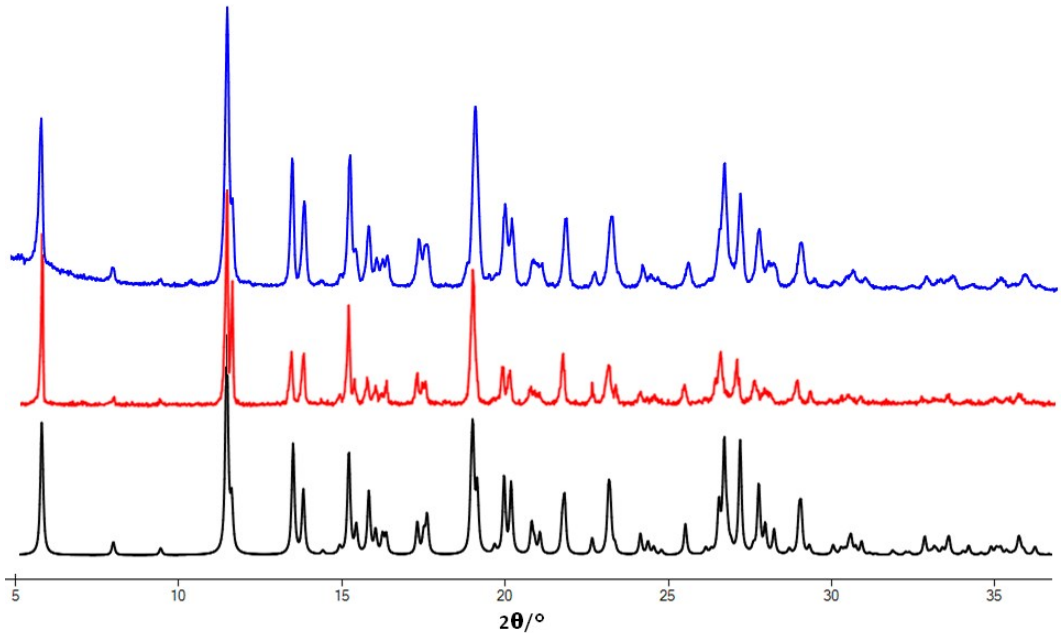


**Figure S17.** Simulated (black) and experimental (red) powder X-ray diffractograms of **4***R* after 15 months (blue) on shelf at room temperature.

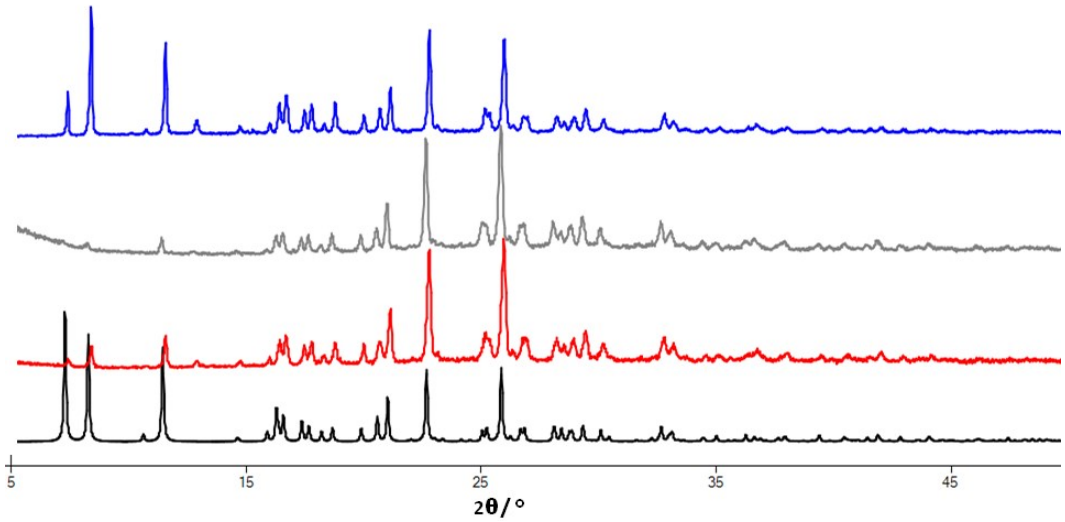


**Figure S18.** Simulated (black) and experimental (red) powder X-ray diffractograms of **5** after 8 (grey) and 15 (blue) months on shelf at room temperature.

## DSC and TGA data

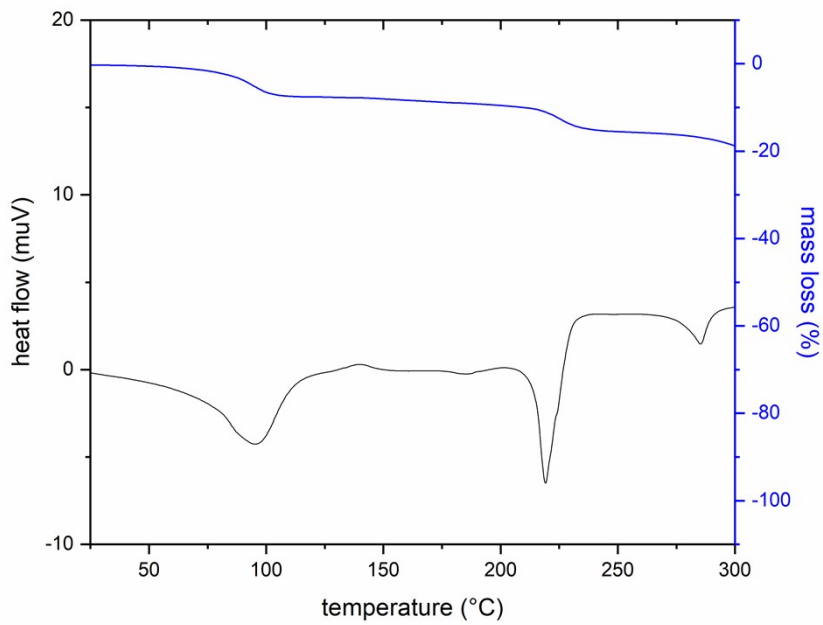


**Figure S19.** DSC and TGA data for **1**·$2H_2O$.

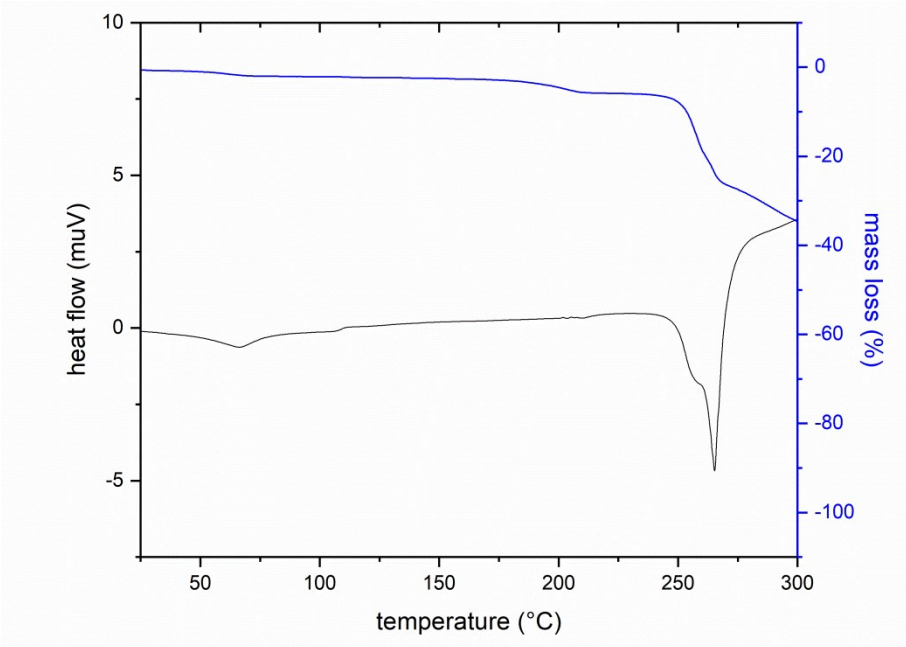


**Figure S20.** DSC and TGA data for **2**.

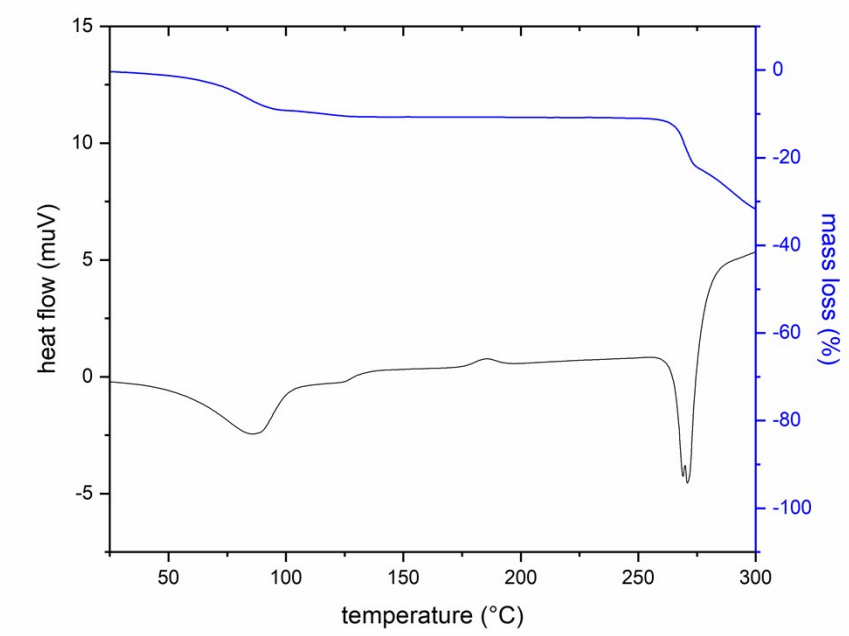


**Figure S21.** DSC and TGA data for **3**·5$H_2O$.

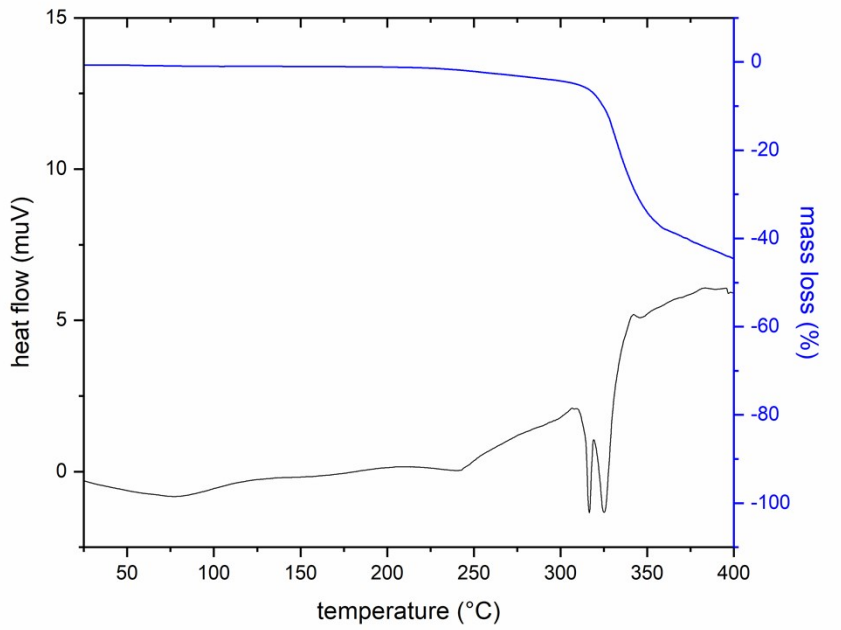


**Figure S22.** DSC and TGA data for **4***S*.

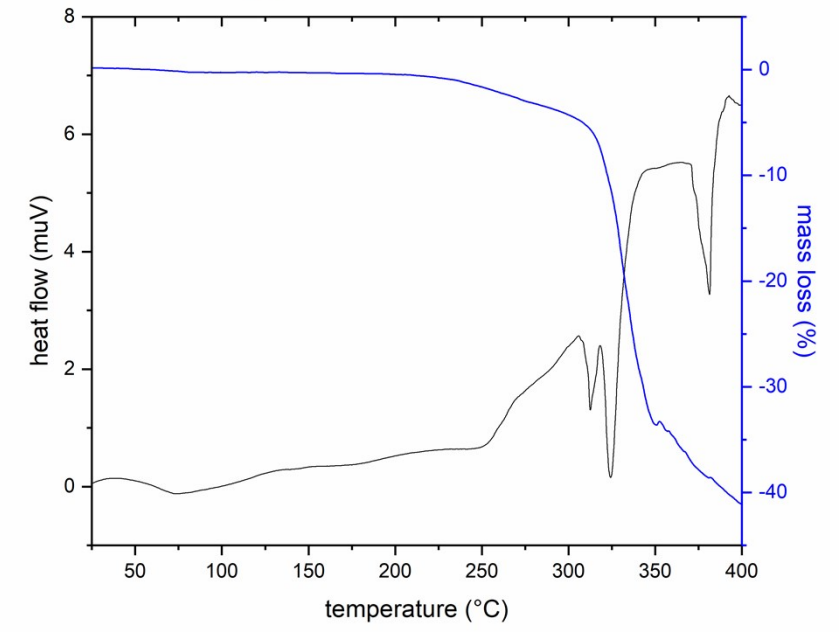


**Figure S23.** DSC and TGA data for **4***R*.

## Hot-stage microscopy data

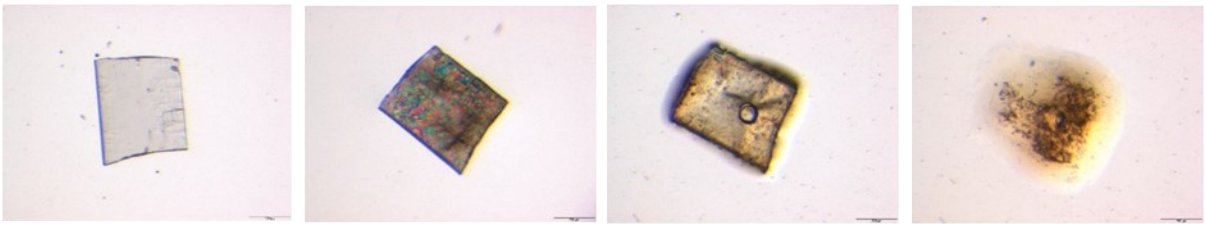

**Figure S24.** Hot-stage images for **1**·2$H_2O$ (pipemidic glycolate dihydrate) at 23, 98, 219 and 237°C (from left to right).

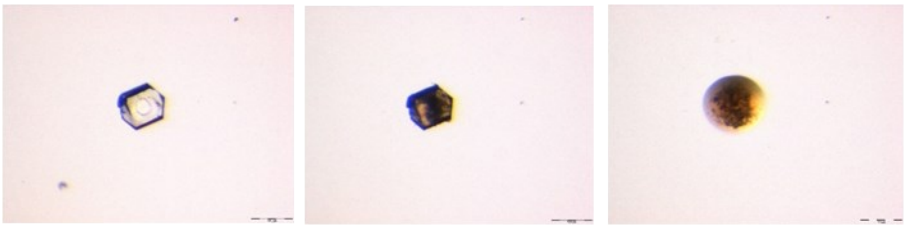

**Figure S25.** Hot-stage images for **2** (pipemidic hydrogenoxalate) at 23, 252 and 272°C (from left to right).

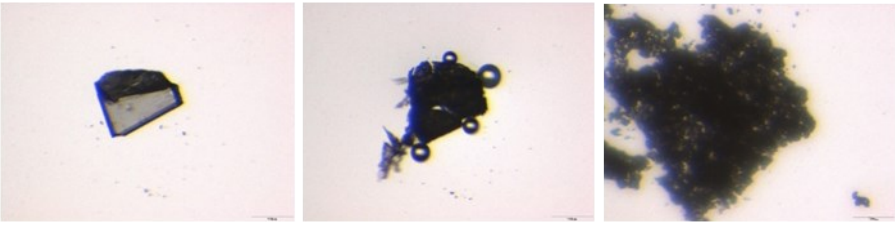

**Figure S26.** Hot-stage images for **3**·5$H_2O$ (pipemidic hydrogenoxalate pentahydrate) at 21, 100 and 210°C (from left to right).

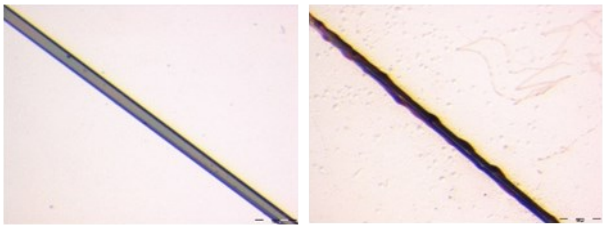

**Figure S27.** Hot-stage images for **4***S* ((*S*)-camphorsulfonate salt) at 23 and 325°C (from left to right).

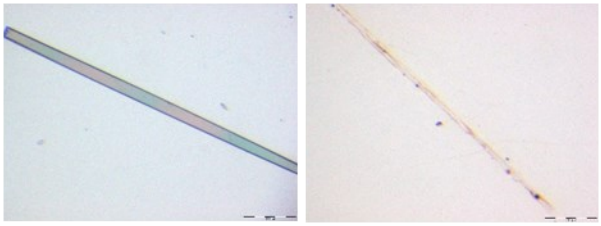

**Figure S28.** Hot-stage images for **4***R* ((*R*)-camphorsulfonate salt) at 23 and 320°C (from left to right).

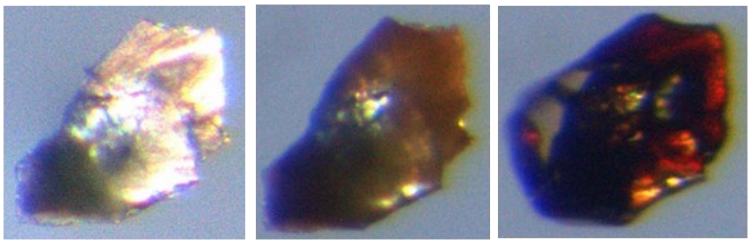

**Figure S29.** Hot-stage images for **5** at 25, 230 and 298°C (from left to right).

## FTIR data

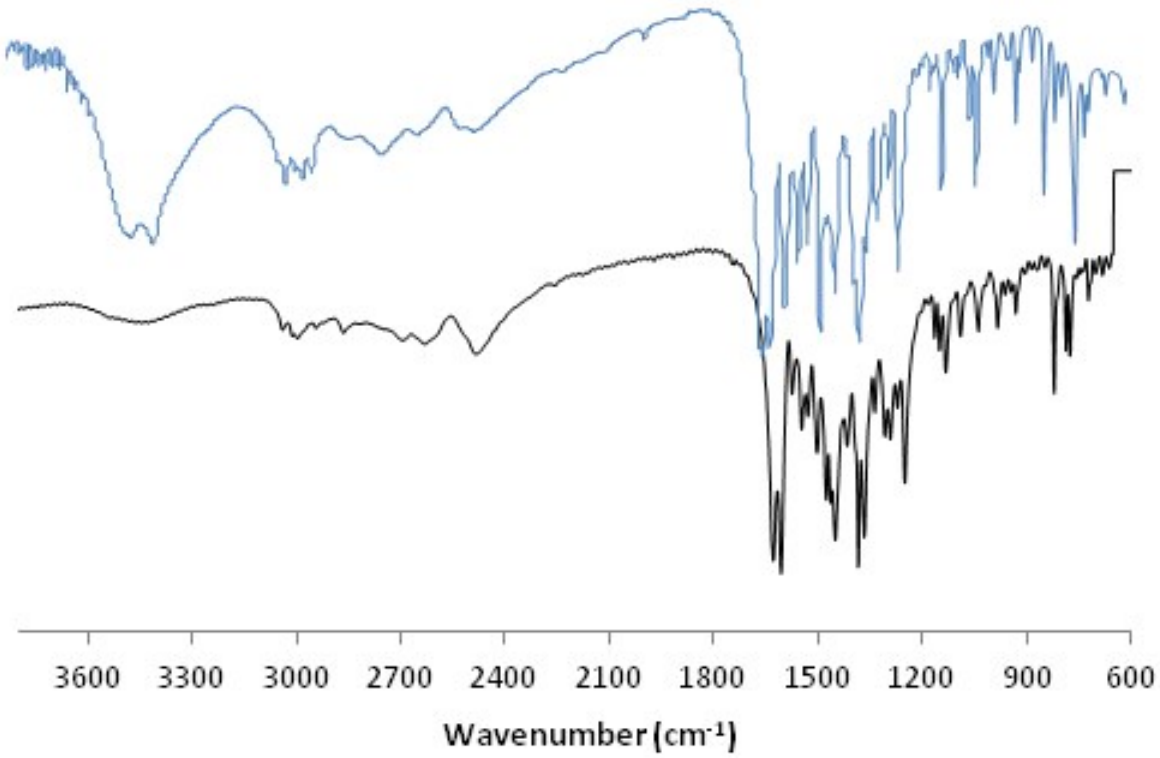


**Figure S30.** Fourier-transform infrared (FTIR) spectra in KBr pellets of **5** (black) and pipemidic acid (blue).