Mechanochemistry of magnesium oxide revisited: facile derivatisation of pharmaceuticals using coordination and supramolecular chemistry

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Supplementary Material

Experimental

Mechanochemical experiments All chemicals were commercially available from the Sigma-Aldrich Company. Magnesium oxide was calcined at 600 °C before use, and the crown ether **15c5** was kept over molecular sieves. In a typical mechanochemical experiment, 0.5 mmol (20 mg) of MgO or $Mg(OH)_2$ (29 mg) was ground with the apropriate amount of the ligand, in the presence of water and/or organic solvent. For the construction of $Mg(H_2O)_6(ibu)_2 \cdot 2H_2O$, 206 mg (1 mmol) of ibuprofen were used, along with 70 μL water (3.9 mmol). For the construction of $Mg(H_2O)_4$(**sal**)$_2$, 138 mg **Hsal** (1 mmol) was used along with 40 μL H_2O (2.2 mmol), while the synthesis of compound **1** involved additional 93 μL **15c5**, 10 μL H_2O and 30 μL acetonitrile. In each case the reaction mixture was placed in a stainless steel jar of 10 mL volume along with a pair of stainless steel balls of 7 mm diameter, and ground using a Retsch MM200 mill operating at a frequency of 30 Hz. The temperature of the reaction mixture measured immediately after grinding never exceeded 30 °C.

Powder X-ray diffraction PXRD data were collected on a Philips X'Pert Pro diffractometer, equipped with an X'celerator RTMS detector, using Ni-filtered CuKα radiation, using a flat plate configuration.

Single crystal X-ray diffraction Single crystal diffraction data were collected on a Nonius Kappa CCD diffractometer equipped with a graphite monochromator and an Oxford cryostream, using Mo*K*α radiation. Structure solution and refinement was perfromed using SHELX available with the WinGX package of crystallographic tools, running on a Pentium-based PC under MS Windows XP.

Thermogravimetric analysis Thermogravimetric measurements were performed on a Mettler Toledo TGA/SDTA851^e thermobalance, using samples of 10-15 mg weight placed in 100 μL pierced lid aluminium pans. All measurements were peformed in a dynamic atmosphere of air (100 cm^3/min), and at a heating rate of 20 K min^{-1}.

FT-IR reflectance spectroscopy Spectra were recorded on a ThermoNicolet NEXUS spectrometer with the Golden Gate ATR accessory, in the range 4000-600 cm^{-1}.

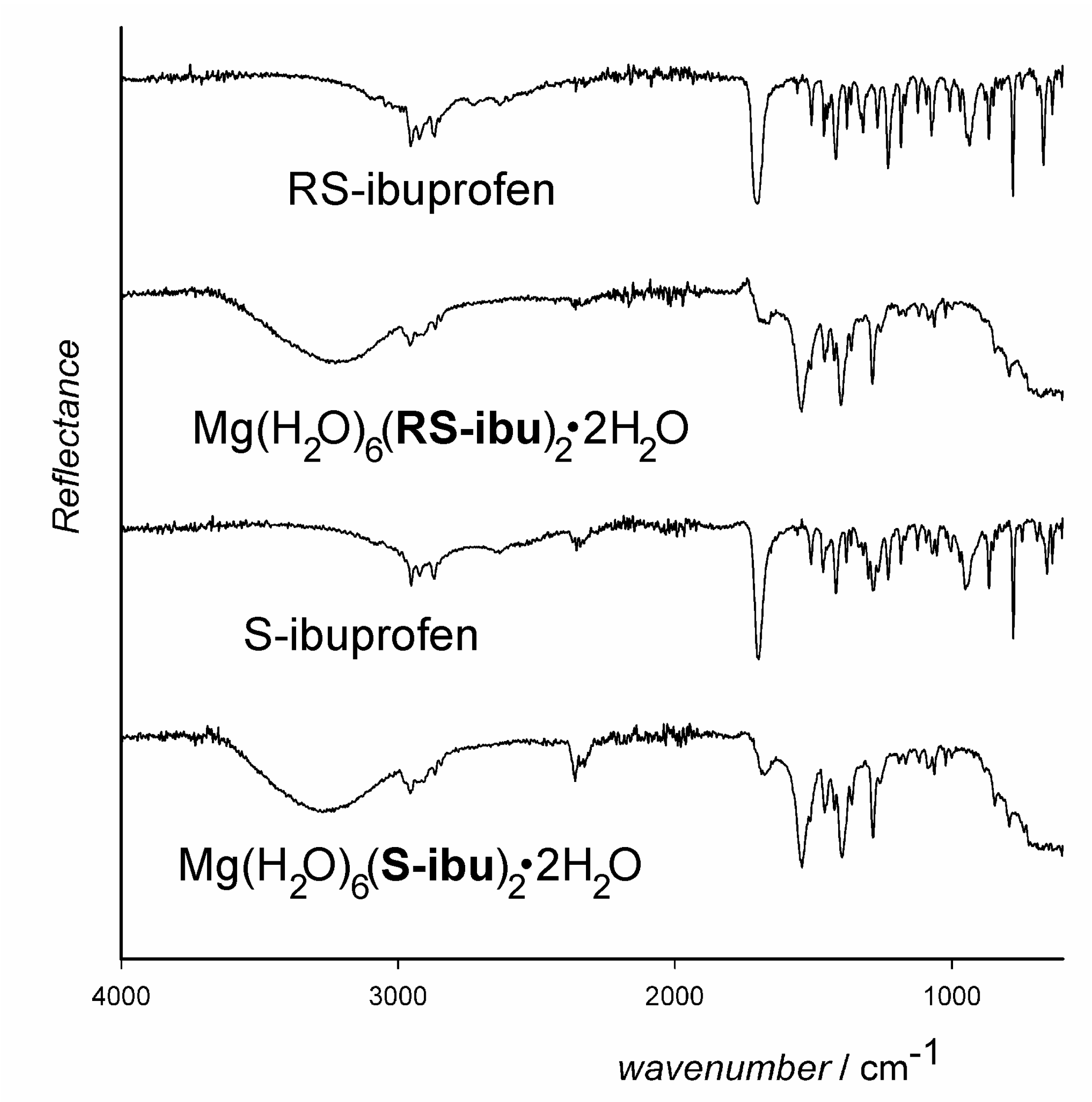

Figure S1. Reflectance FTIR spectra (from top to bottom): $Mg(H_2O)_6(\mathbf{RS\text{-}ibu})_2{\cdot}2H_2O$; commercial **RS-Hibu**, $Mg(H_2O)_6(\mathbf{S\text{-}ibu})_2{\cdot}2H_2O$; commercial **S-Hibu**.

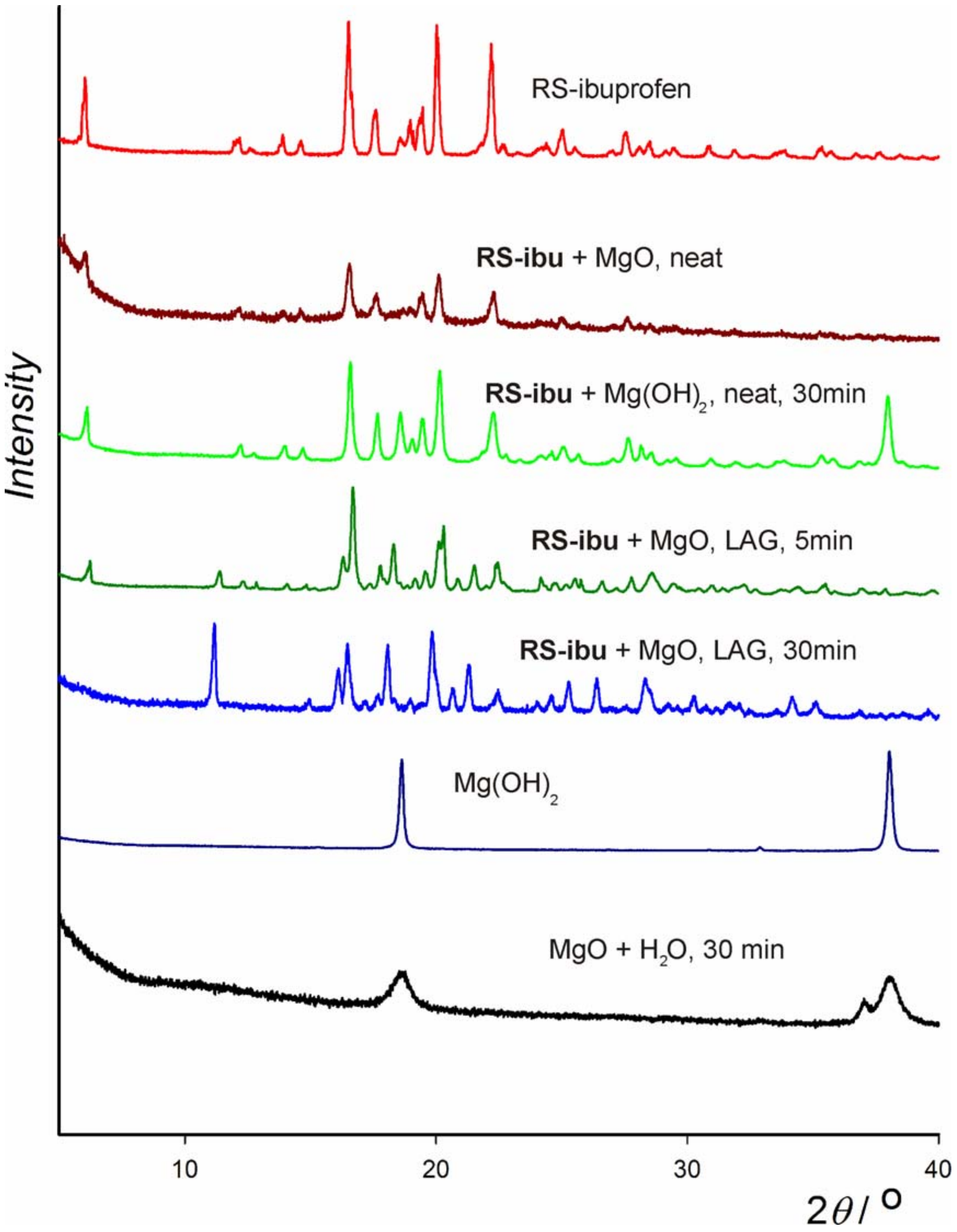

Figure S2. Powder diffraction patterns (from top to bottom): **RS-Hibu**; product of 30 min neat grinding of MgO and **RS-Hibu**; product of 30 min neat grinding of $Mg(OH)_2$ and **RS-Hibu**; product of 5 min LAG of MgO and **RS-Hibu**; product of 30 min LAG of MgO and **RS-Hibu**; commercial $Mg(OH)_2$ and the product of 30 min grinding of MgO and water in 1:1 stoichiometric ratio.

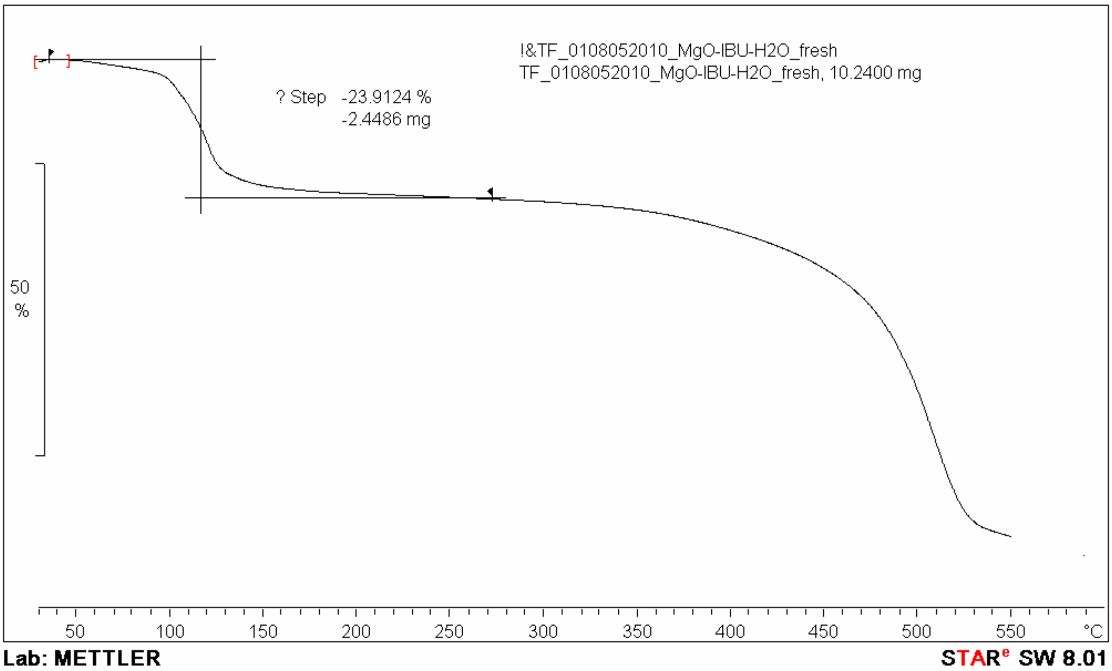

Figure S3. Thermogram of thermal decomposition of $Mg(H_2O)_6$(**RS-ibu**)$_2$·$2H_2O$. Calculated percentage of water is 24.9%, observed loss is 23.9%.

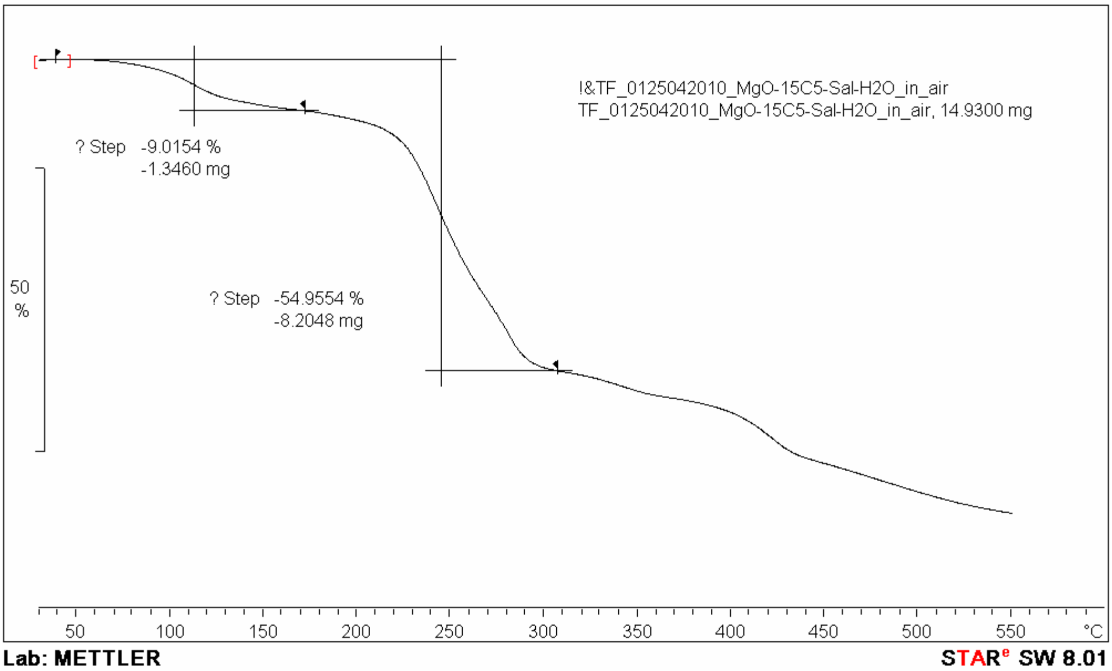

Figure S4. Thermogram of thermal decomposition of compound **1**. The first step (9.0%) roughly corresponds to the loss of acetonitrile (7.9%) and is probably also accompanied by partial loss of water.

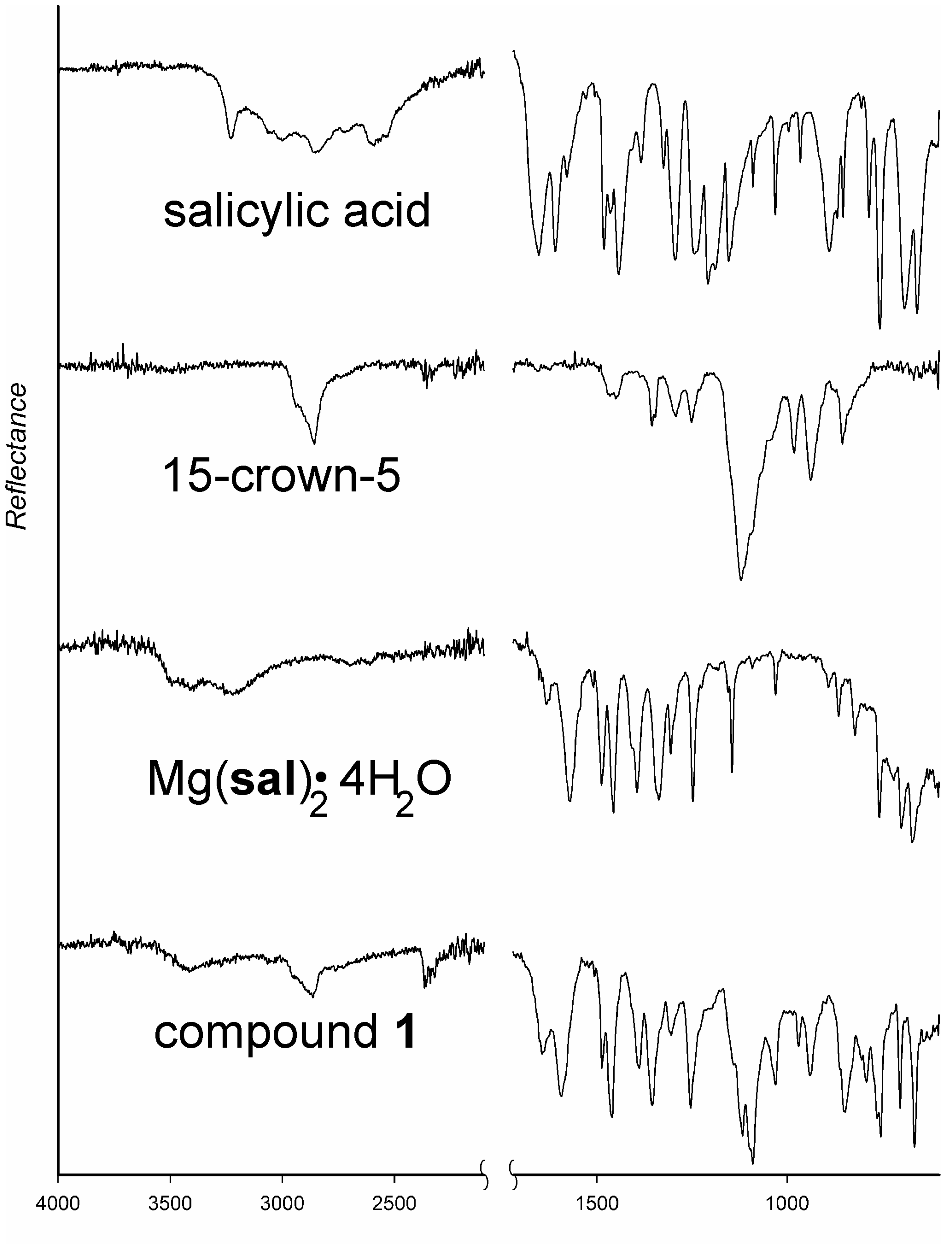

Figure S5. Reflectance FTIR spectra (from top to bottom): commercial salicylic acid, commercial **15c5**, synthesised Mg(**sal**)$_2$(H$_2$O)$_4$; Compound **1**. Compound **1** clearly contains **15c5** and is different than the known magnesium salicylate tetrahydrate.

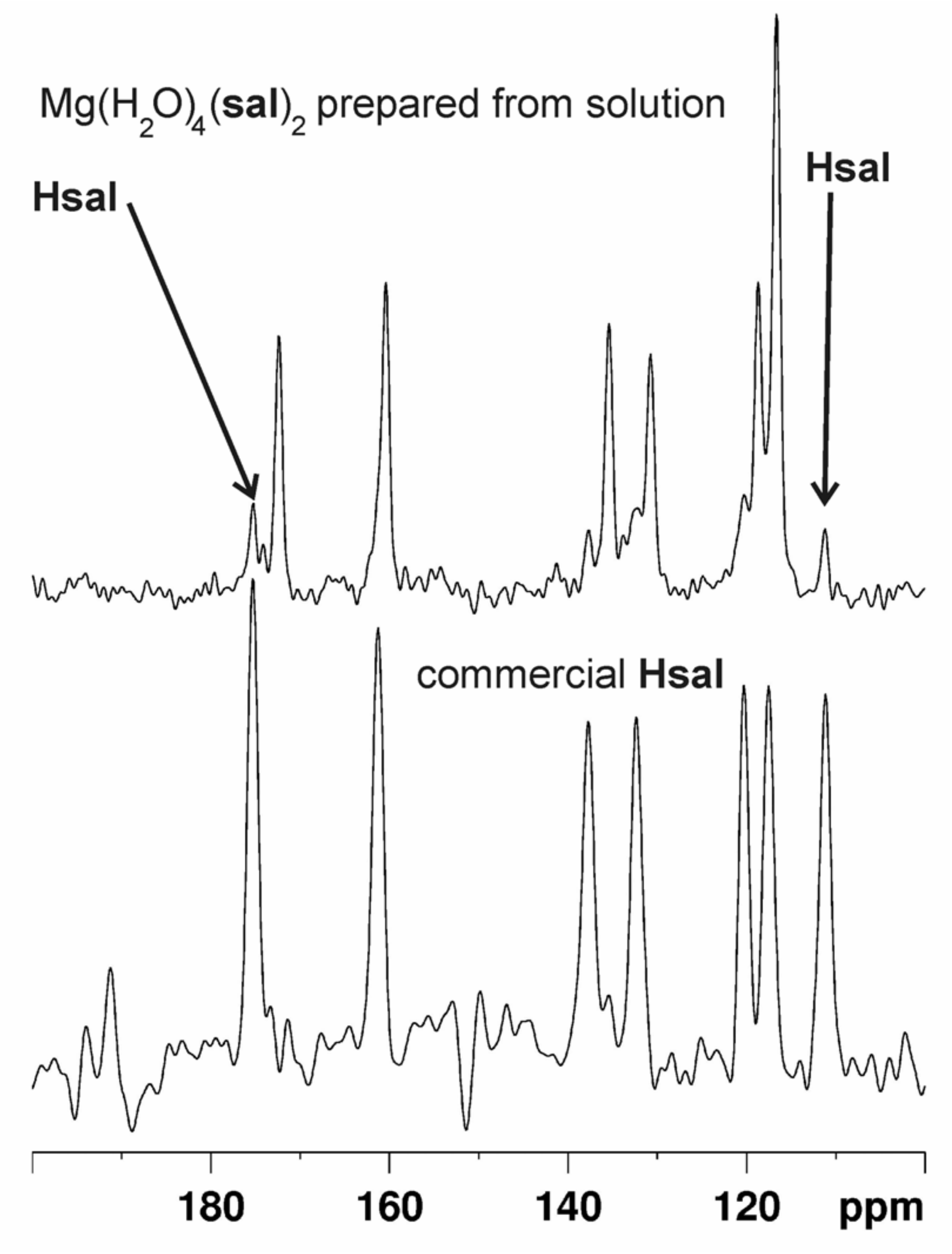

Figure S6. Cross-polarisation magic angle spinning (CP-MAS) solid-state ^{13}C NMR spectra of solution-synthesised $Mg(H_2O)_2$(**sal**)$_2$ (top) and commercial **Hsal** (bottom). The NMR spectra reveal that solution synthesis provides a sample of magnesium salicylate tetrahydrate containing a small amount of starting material salicylic acid.

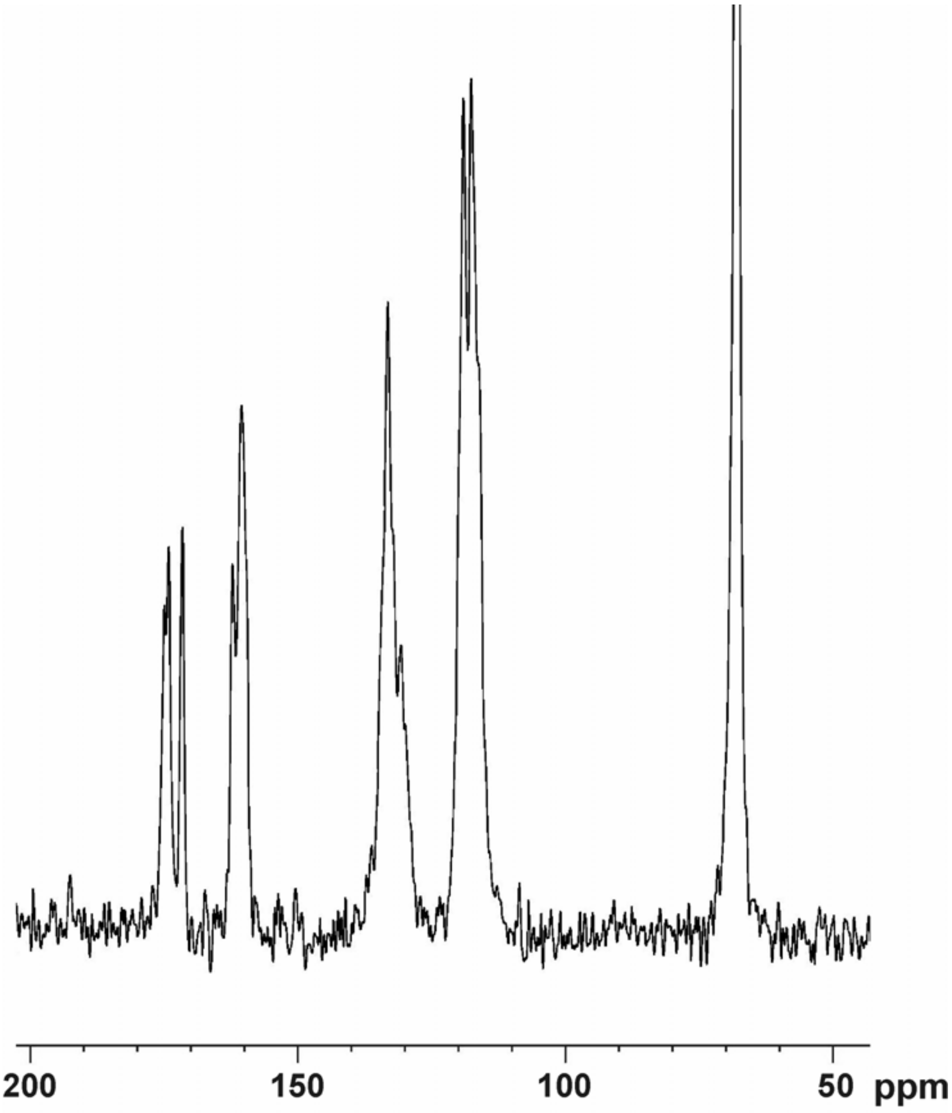

Figure S7. Cross-polarisation magic angle spinning (CP-MAS) solid-state ^{13}C NMR spectrum of Compound **1**. Besides demonstrating a difference from the $Mg(H_2O)_2$(**sal**)$_2$ in the region 100-200 ppm, the spectrum also confirms the presence of **15c5** in the sample by the strong signal around 50 ppm. The absence of signals that could be assigned to acetonitrile suggests the included molecules are dynamic.