Supporting Information for

A rare case of mesomorphic behaviour – molecular reorientation of itraconazole liquid crystal induced by a hygrothermal treatment

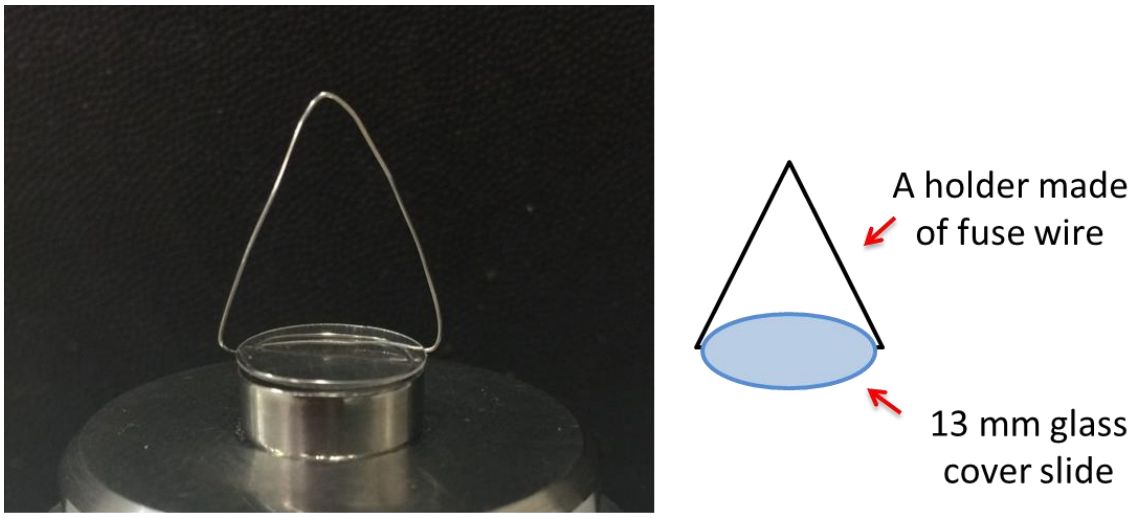


Figure SI.1. An in-house made cover slide holder composed of fuse wire, which was used to hold the cover slide for the hygrothermal treatment in DVS presented in Figure 6. Two holders were used, one for the sample and one for the reference, with masses of 44.1 mg and 42.5 mg, respectively.

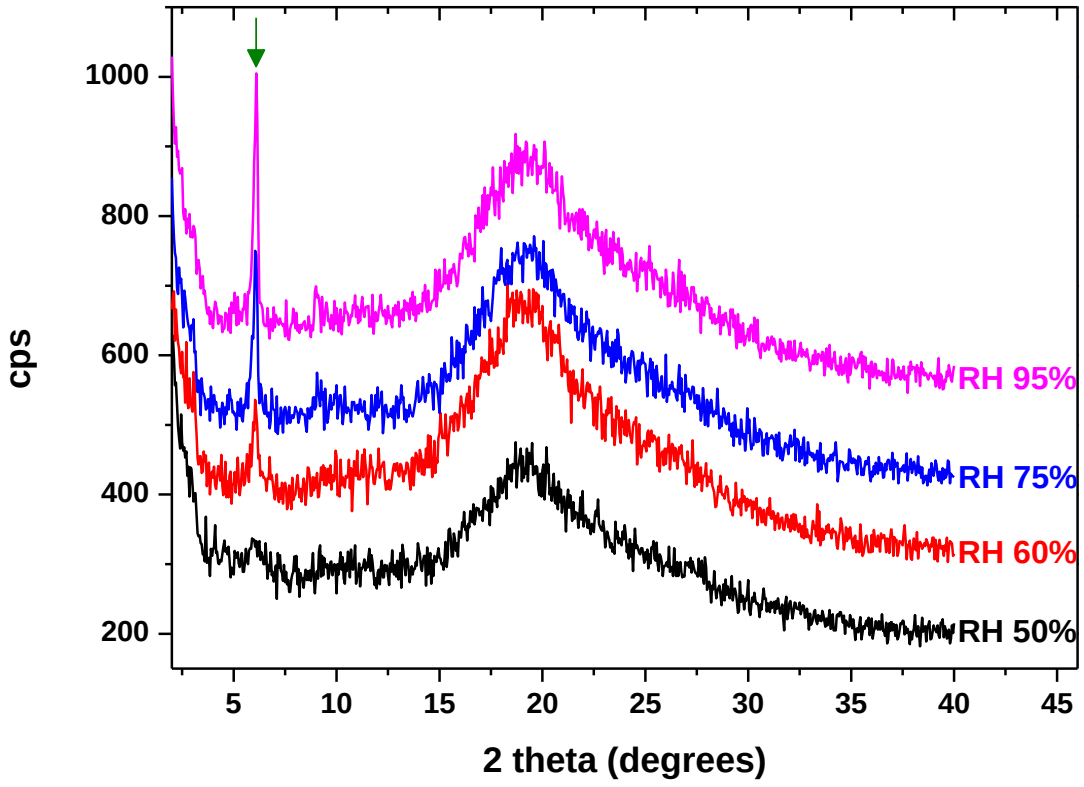
Investigation of ITR-N ordering using saturated salt solutions in an oven

ITR-N samples (50 mg) were equilibrated at 50 °C over solutions of saturated salts at 50 °C. Saturated solutions of salts were used to provide certain relative humidities as described by Nyqvist [1], with slight modifications when necessary to achieve the desired values as shown in Table SI.1 below. The relative humidities were monitored using a Sensirion SHT75 sensor (Sensirion, Switzerland).

Table SI.1. Saturated salt solutions with the corresponding relative humidities at 50 °C.

Salt	$NaCl:MgCl_2$ (1:2 w/w)	NaBr:KBr (1:1 w/w)	NaCl	K_2SO_4
RH (%)	50%	60%	75%	95%

The phase change following 1 hr incubation of ITR-N at the above conditions was examined using WAXS and the results are displayed in Figure SI. 2.



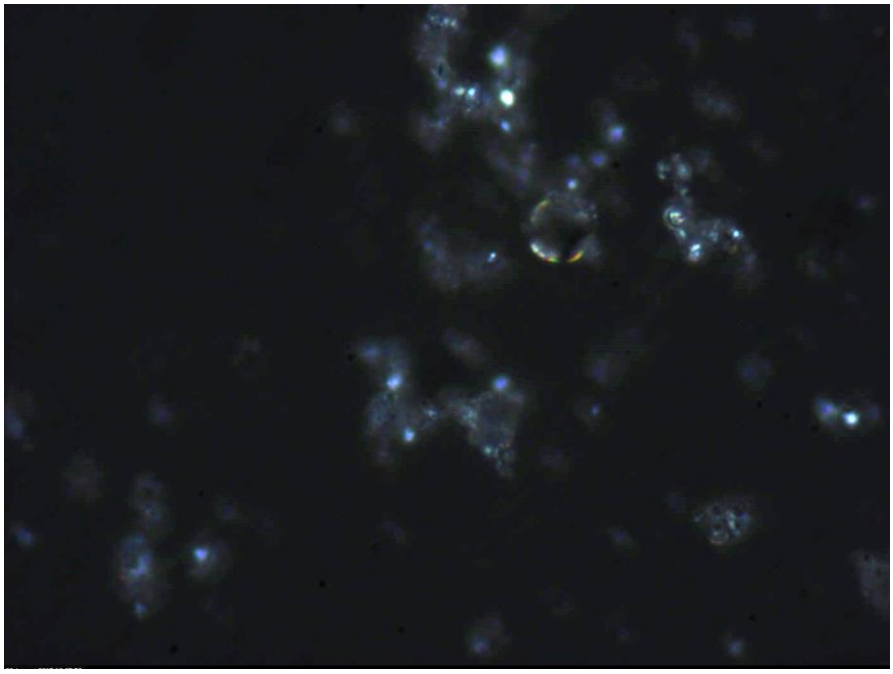


Figure SI.2. WAXS diffractograms illustrating phase changes following incubation of ITR-N at different RH for one hour (upper panel). The arrow indicate a quasi-diffraction peak at 6.05° 2theta of smectic ITR, cps – counts per second. PLM of ITR-N at 25 °C (as recovered from the spray dryer) (500 magnification) (lower panel).

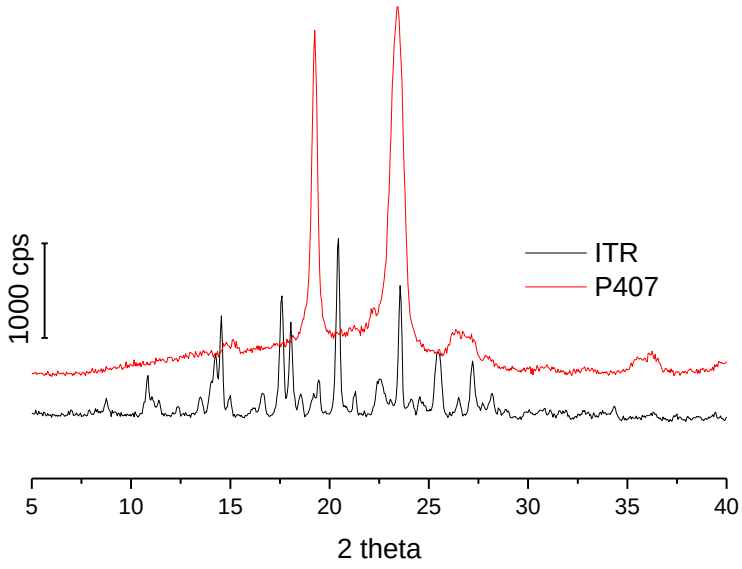


Figure SI.3. Powder X-ray diffractograms of itraconazole (ITR) starting material powder and Poloxamer 407 (P407) starting material powder.

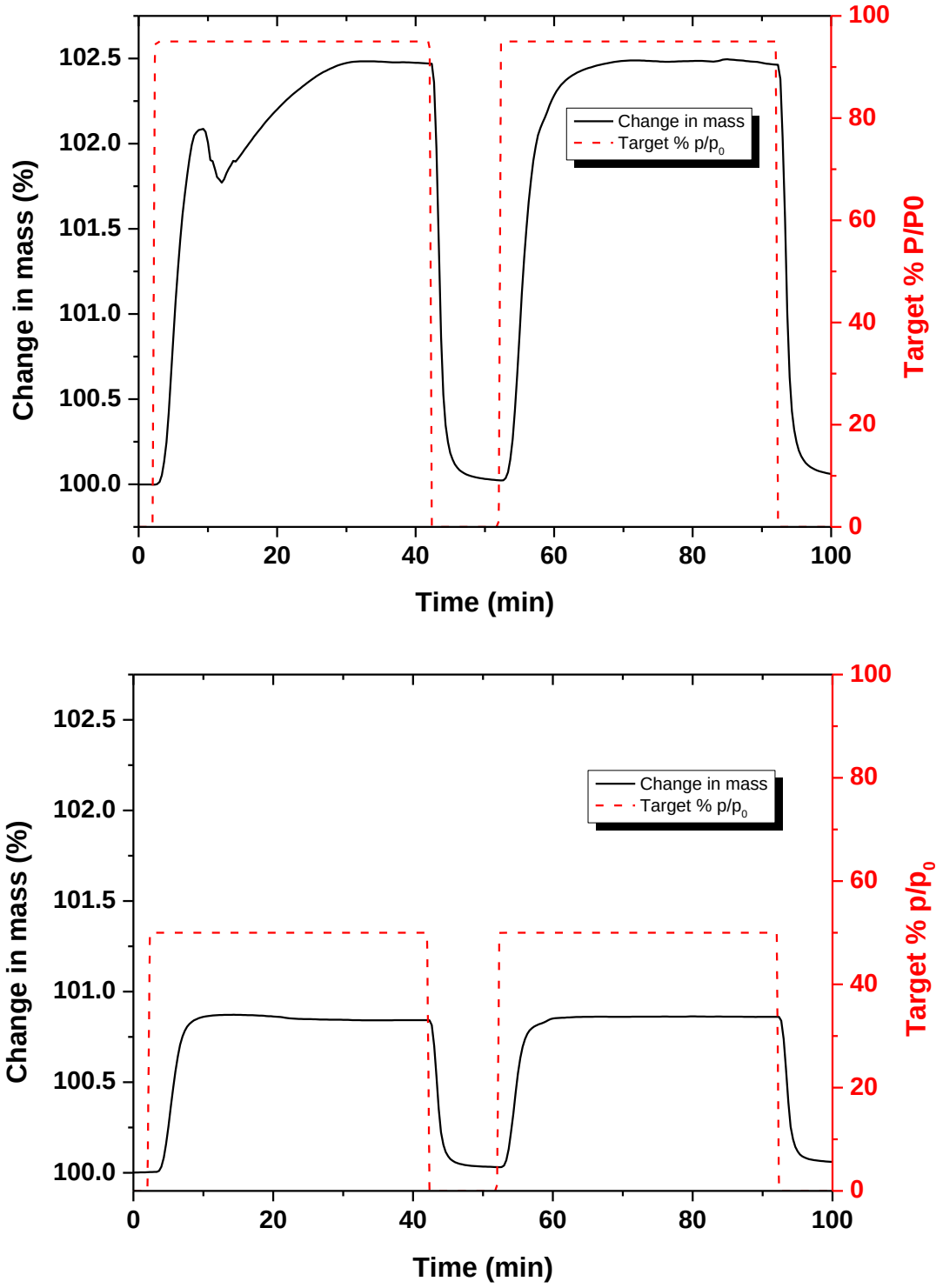


Figure SI.4. Kinetic profiles (by DVS at 50 ºC) of two cycles of water sorption for ITR-N at 95% RH (upper panel) and 50% RH (lower panel).

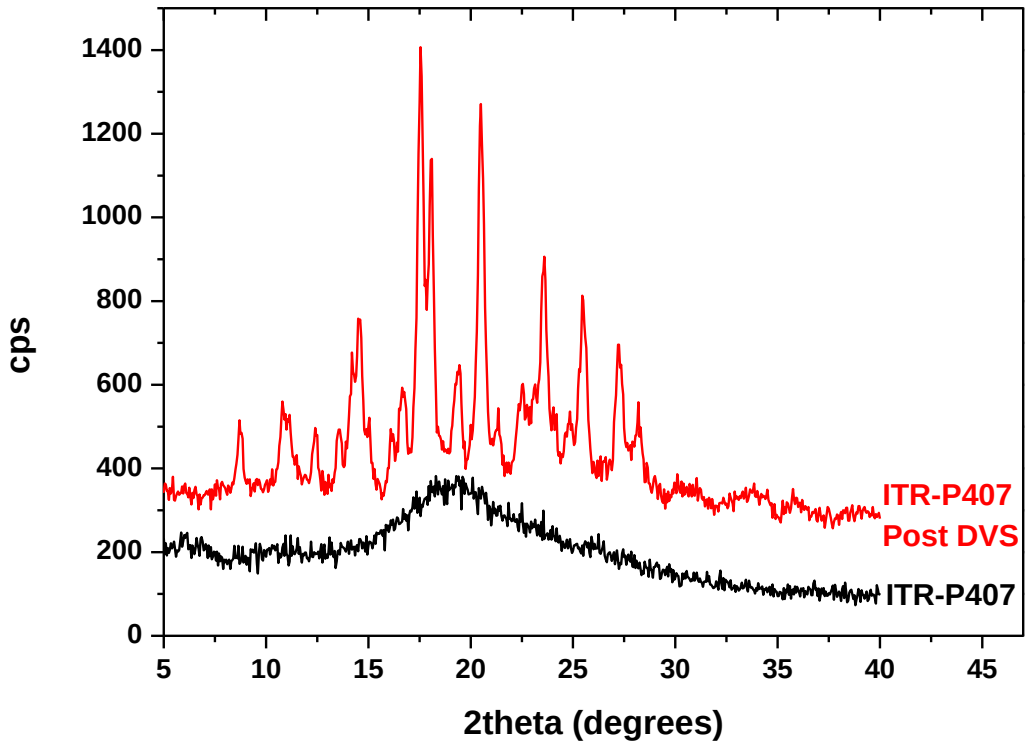


Figure SI.5. WAXS diffractograms of ITR-P407 and the same sample after 5 hr treatment in DVS at 50 °C and 95% RH. cps – counts per second

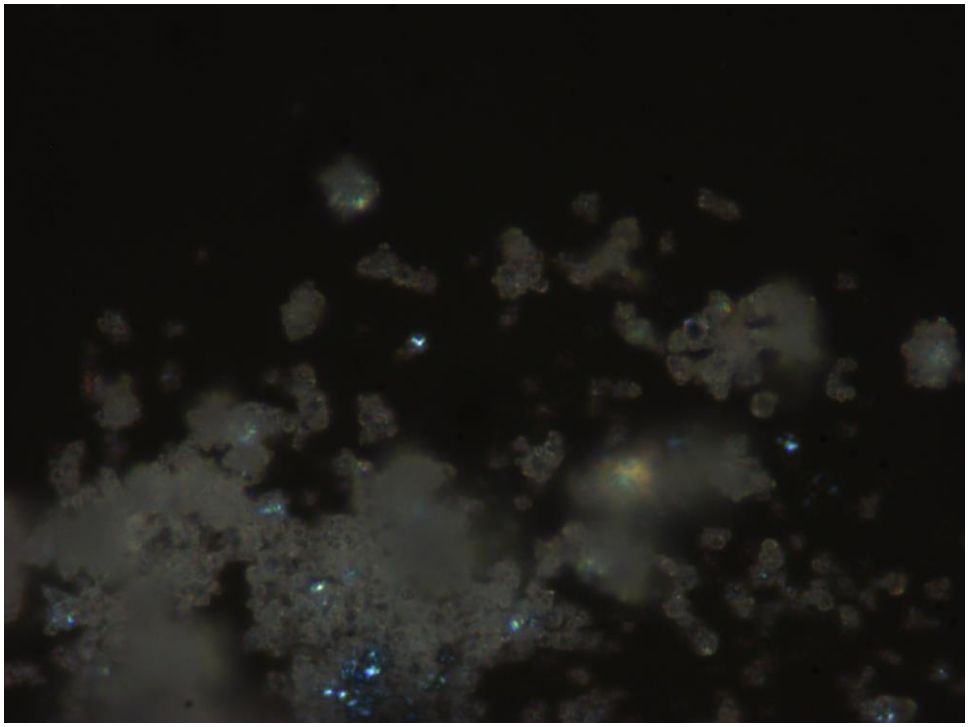


Figure SI.6. PLM of ITR-P407 at 25 °C (as recovered from the spray dryer) (500x magnification).

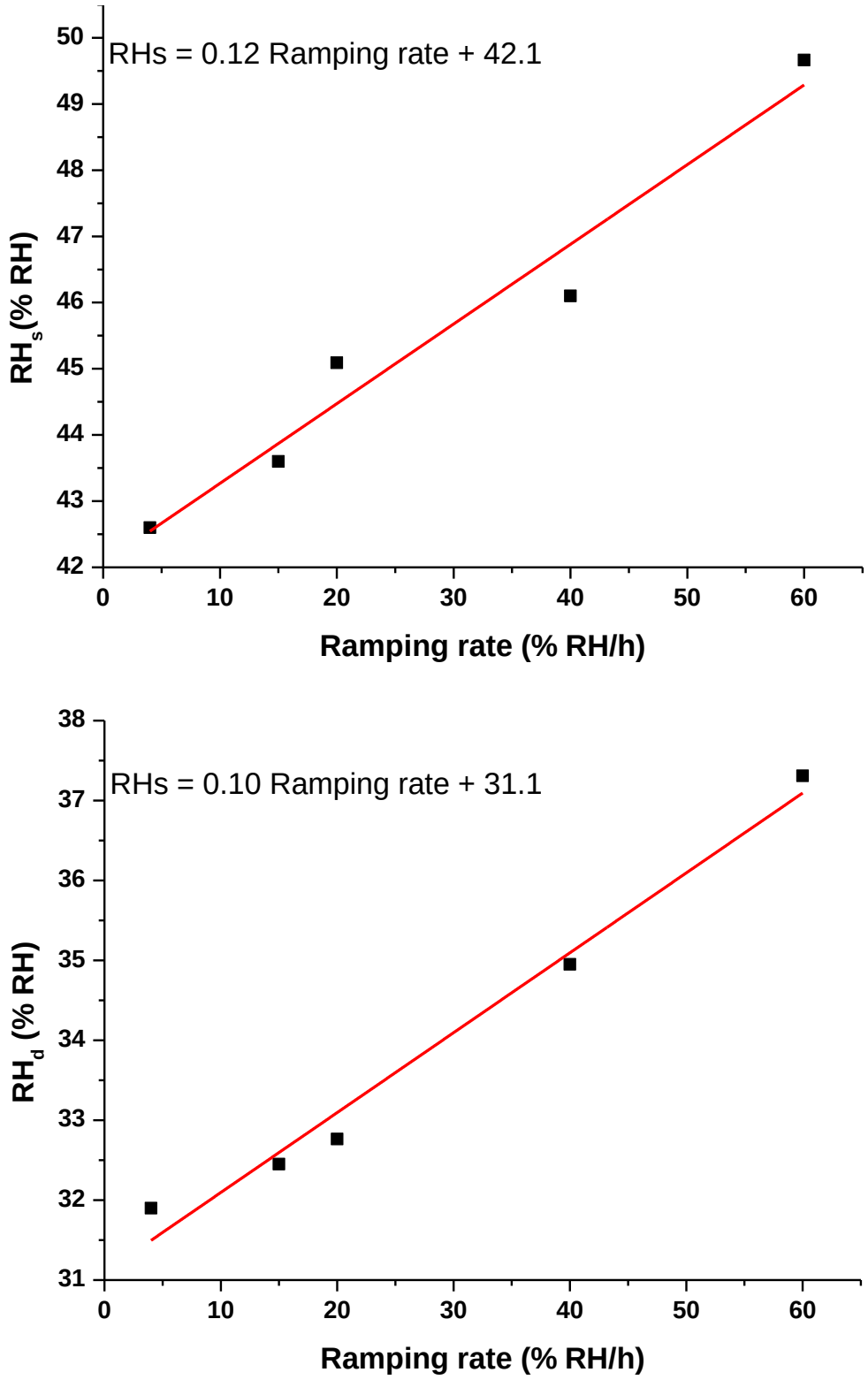


Figure SI.7. Critical relative humidity for ordering in the sorption cycle (RH_s) vs. relative humidity ramping rate (upper panel) and critical relative humidity for deordering in the desorption cycle (RH_d) vs. relative humidity ramping rate (lower panel) for ITR-N at 50 °C.

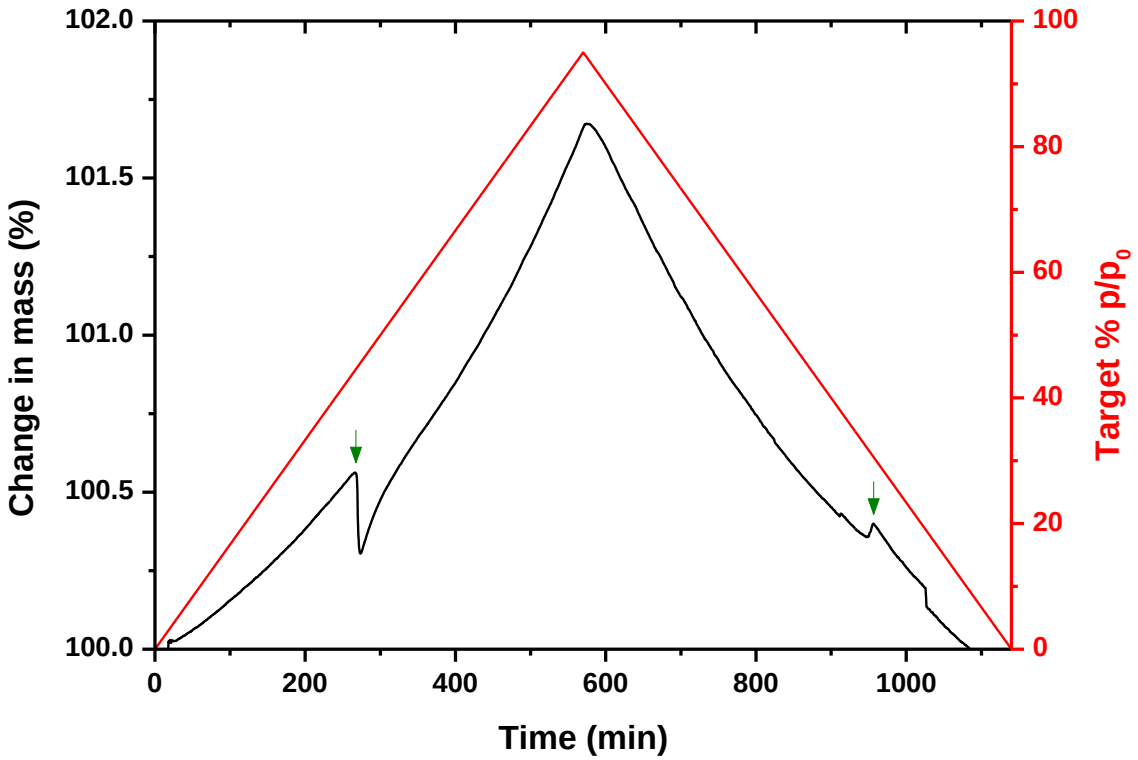


Figure SI.8. Kinetic profile of ITR-N sample upon changing the relative humidity from 0 to 95% at a ramping rate of 10% RH/h (50 °C).

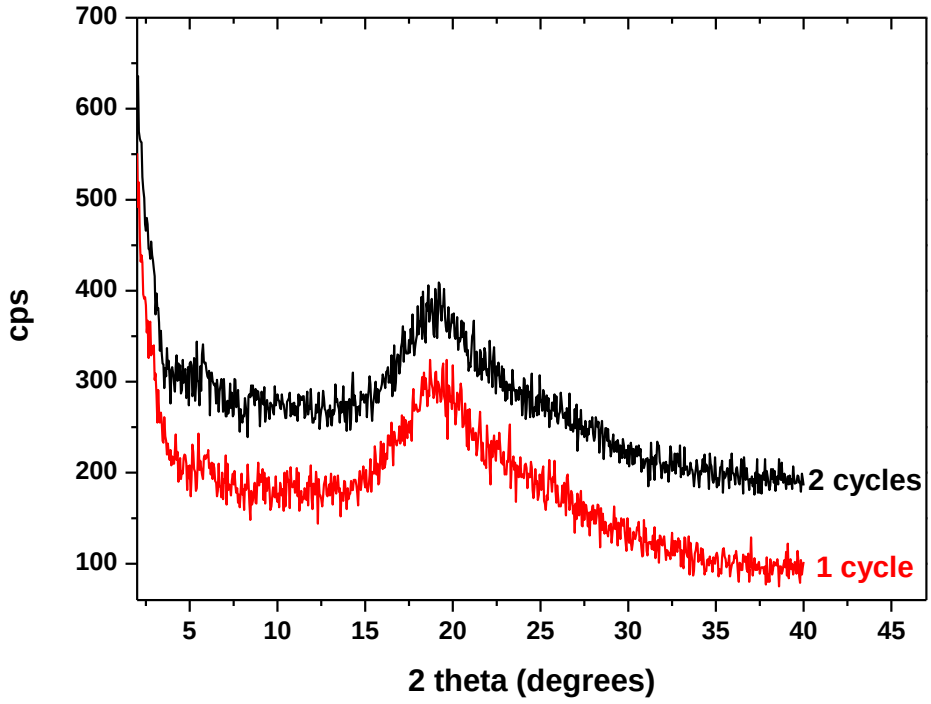


Figure SI.9. WAXS diffractograms of samples following one or two DVS cycles using dm/dt of ≤ 0.002 in DVS at 50 °C. cps – counts per second.

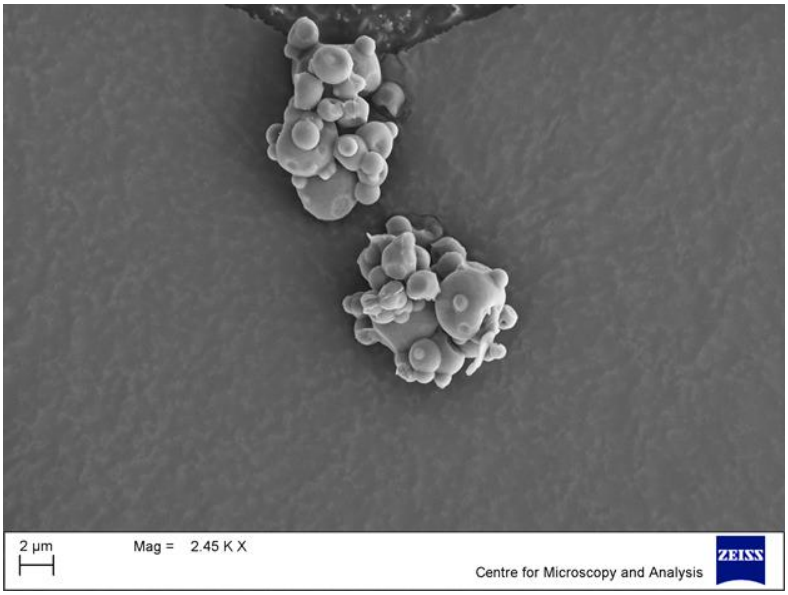


Figure SI.10. SE micrograph of ITR-N particles following resorption in DVS. Particles were collected at 95% RH in the second DVS sorption cycle, as shown in Figure 4.

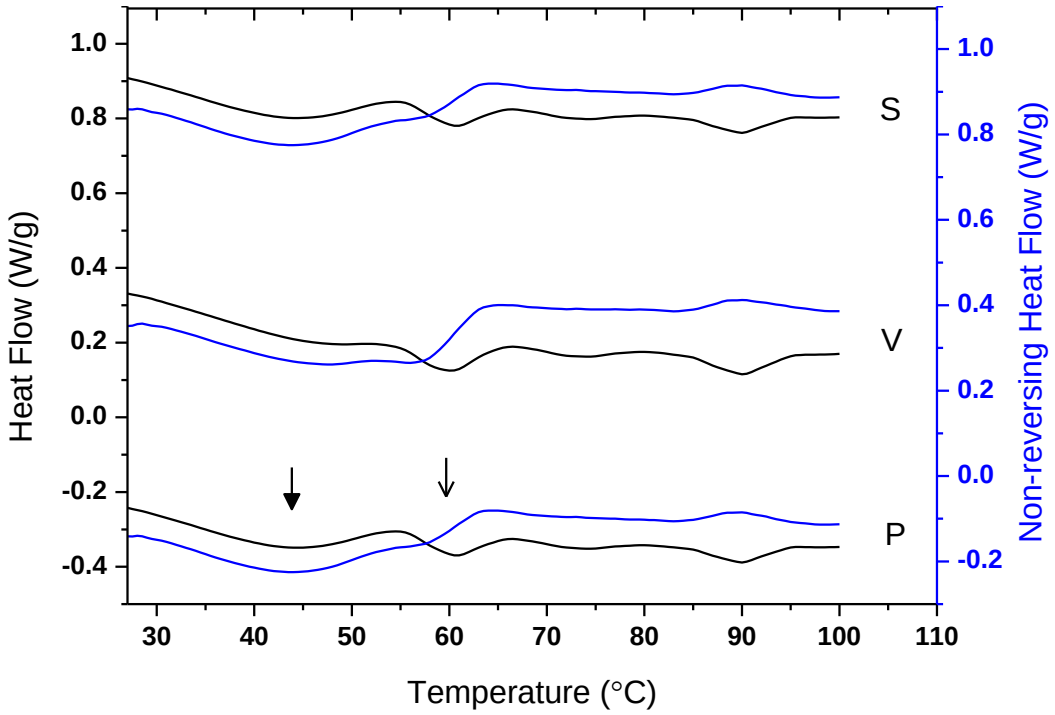


Figure SI.11. MDSC thermograms (total and non-reversing heat flow) of samples P, V and S. The non-reversing heat flow curves illustrate the loss of moisture represented as the broad endotherm at around 43 °C (closed arrow) and the enthalpic relaxation at around 60 °C (open arrow).

References

1. Nyqvist, H. Saturated salt solutions for maintaining specified relative humidities. *Int. J. Pharm. Tech. Prod. Manuf.* **1983,** *4,* 47-48.