Supporting Information

Inorganic salts of topiroxostat: Metastable tautomeric form and improved pharmaceutical performance

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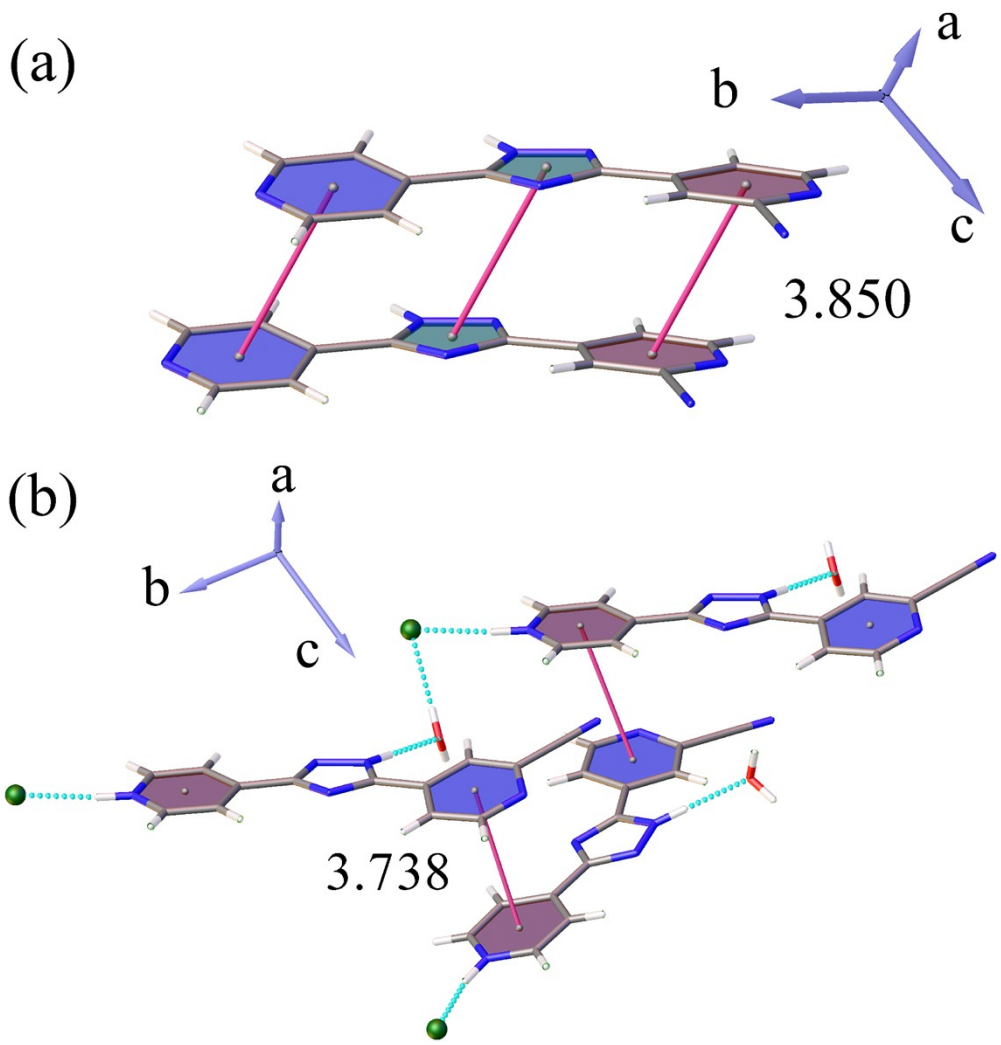

Fig. S1 The π-π stacking interactions in TOP form I (a) and TOP–HCl–H_2O (b).

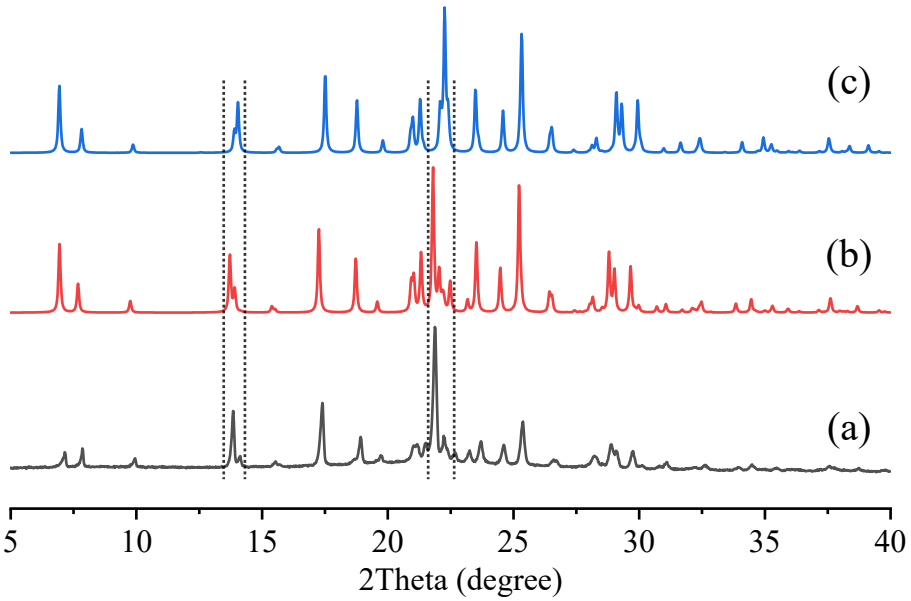

Fig. S2 The powder XRD patterns of TOP–H_2SO_4 form II. Experimental pattern (a) and simulated patterns by using the 273 K structure (b) and 150 K structure (c).

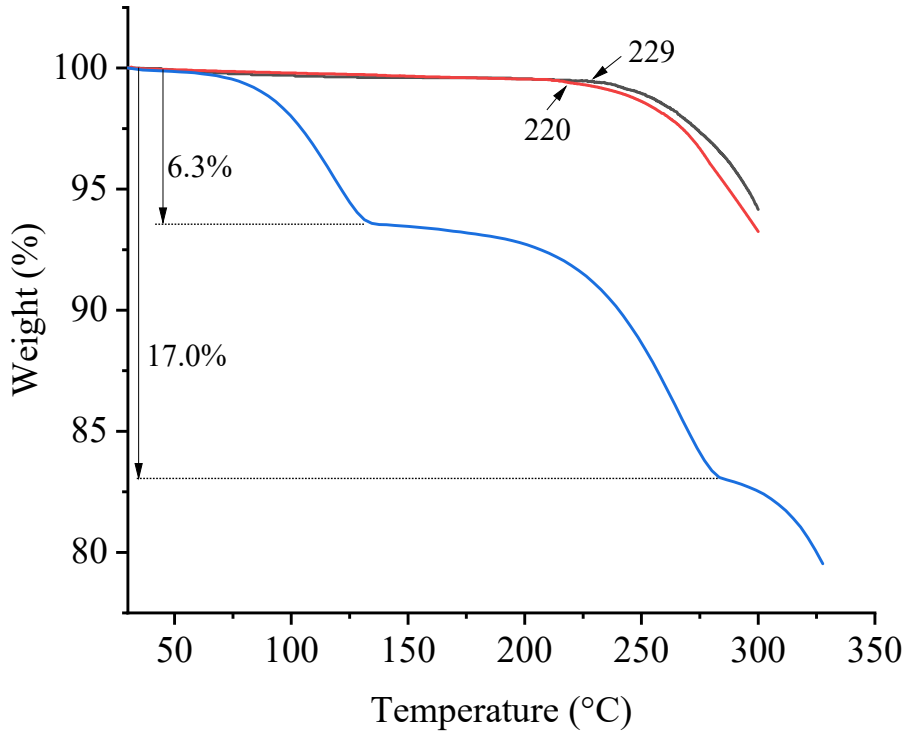

Fig. S3 Thermogravimetric analysis of TOP–HCl–H_2O (blue), TOP–H_2SO_4 form I (red), and TOP–H_2SO_4 form II (black). For TOP–HCl–H_2O, the theoretical contents of H_2O and HCl are 5.95% and 12.04%, respectively.

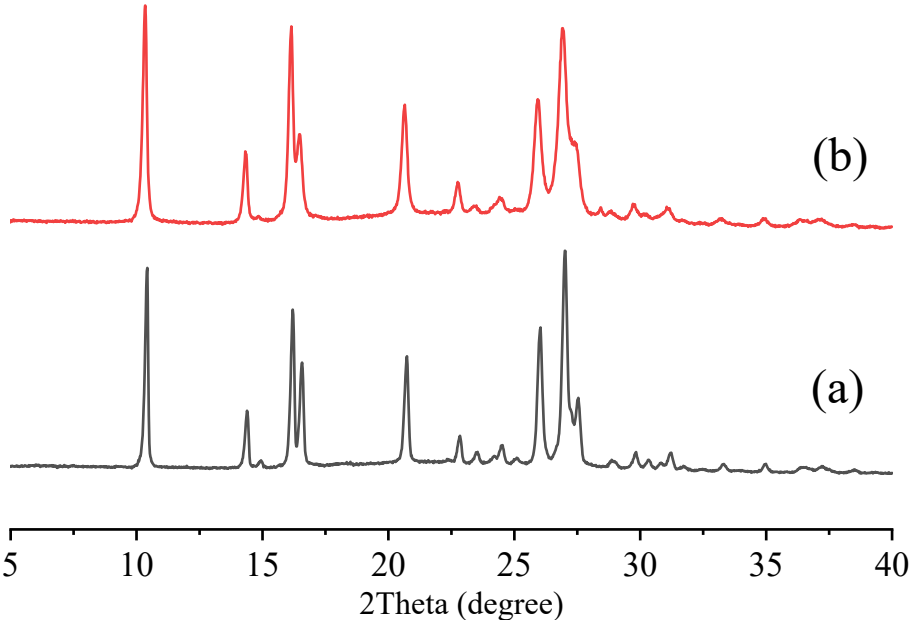

Fig. S4 The powder XRD patterns of TOP–HCl–H_2O after *in situ* heating in DSC pan at 300 °C for 20 min (a). The experimental TOP form I (b) was also given for comparison.

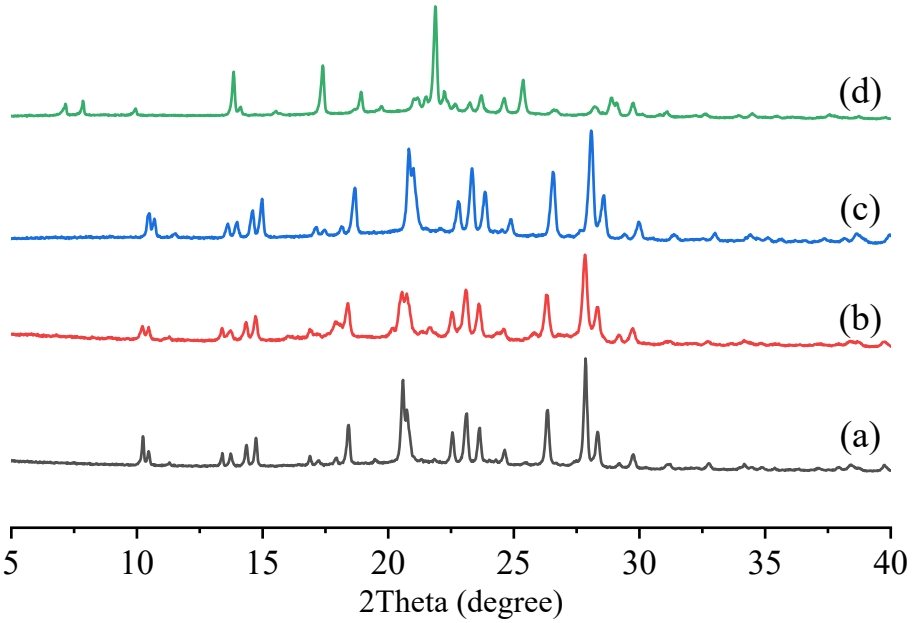

Fig. S5 The powder XRD patterns of the result solid after co-slurry experimental in acetonitrile–*n*-octane (40/60, v/v) (a) and ethyl acetate–*n*-octane (40/60, v/v) (b). Experimental XRD patterns of TOP–H_2SO_4 form I (c) and TOP–H_2SO_4 form II (d) were also provided for comparison.

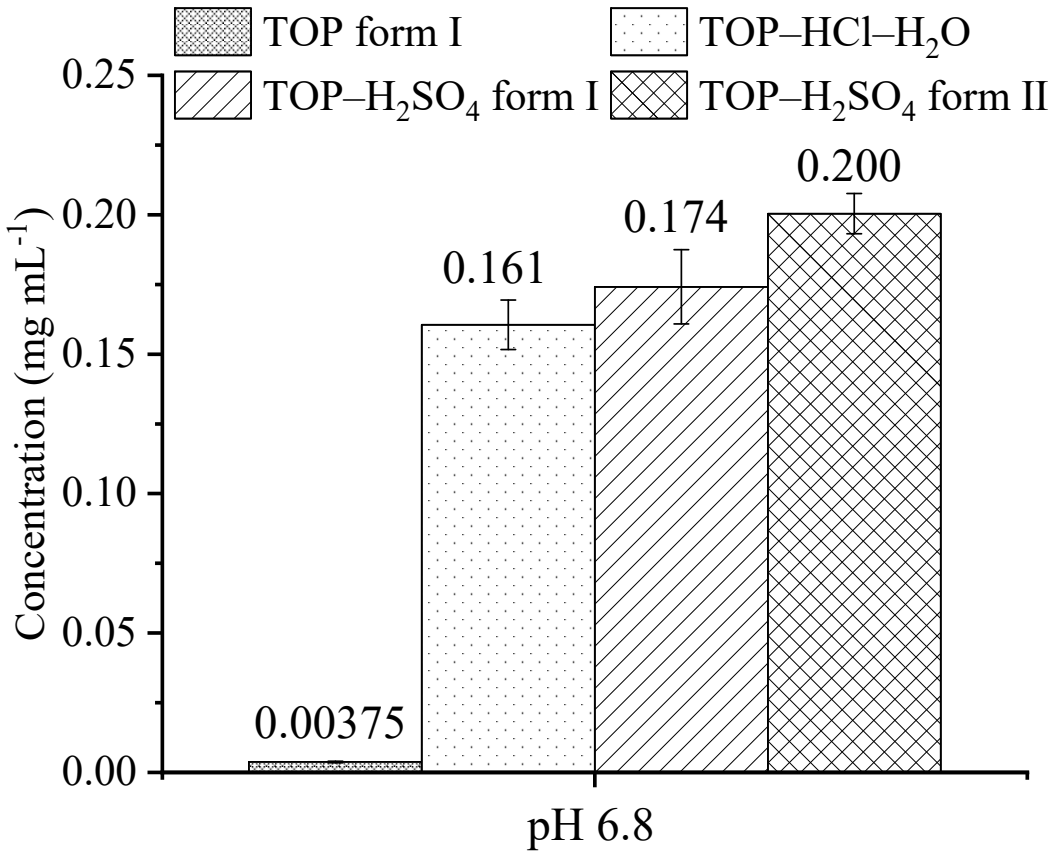

Fig. S6 The apparent equilibrium solubility of TOP, TOP–HCl–H_2O, TOP–H_2SO_4 form I, and TOP–H_2SO_4 form II in pH 6.8 buffer at 37 °C.

Table S1 The pH values after the apparent equilibrium solubility experiments

Identification code	pH
TOP form I	7.34±0.35
TOP–HCl–H_2O	2.02±0.16
TOP–H_2SO_4 I	1.92±0.02
TOP–H_2SO_4 II	1.85±0.02

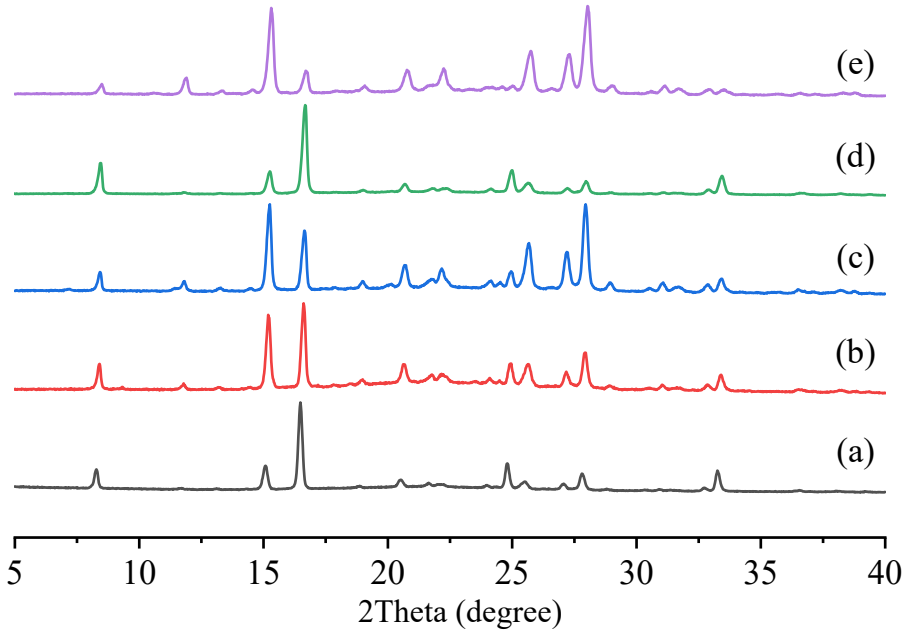

Fig. S7 The powder XRD patterns of resulting solids after the equilibrium solubility experiments. TOP form I (a), TOP–HCl–H_2O (b), TOP–H_2SO_4 form I (c), and TOP–H_2SO_4 form II (d). Experimental pattern of TOP–H_2O (e) was given for comparison.

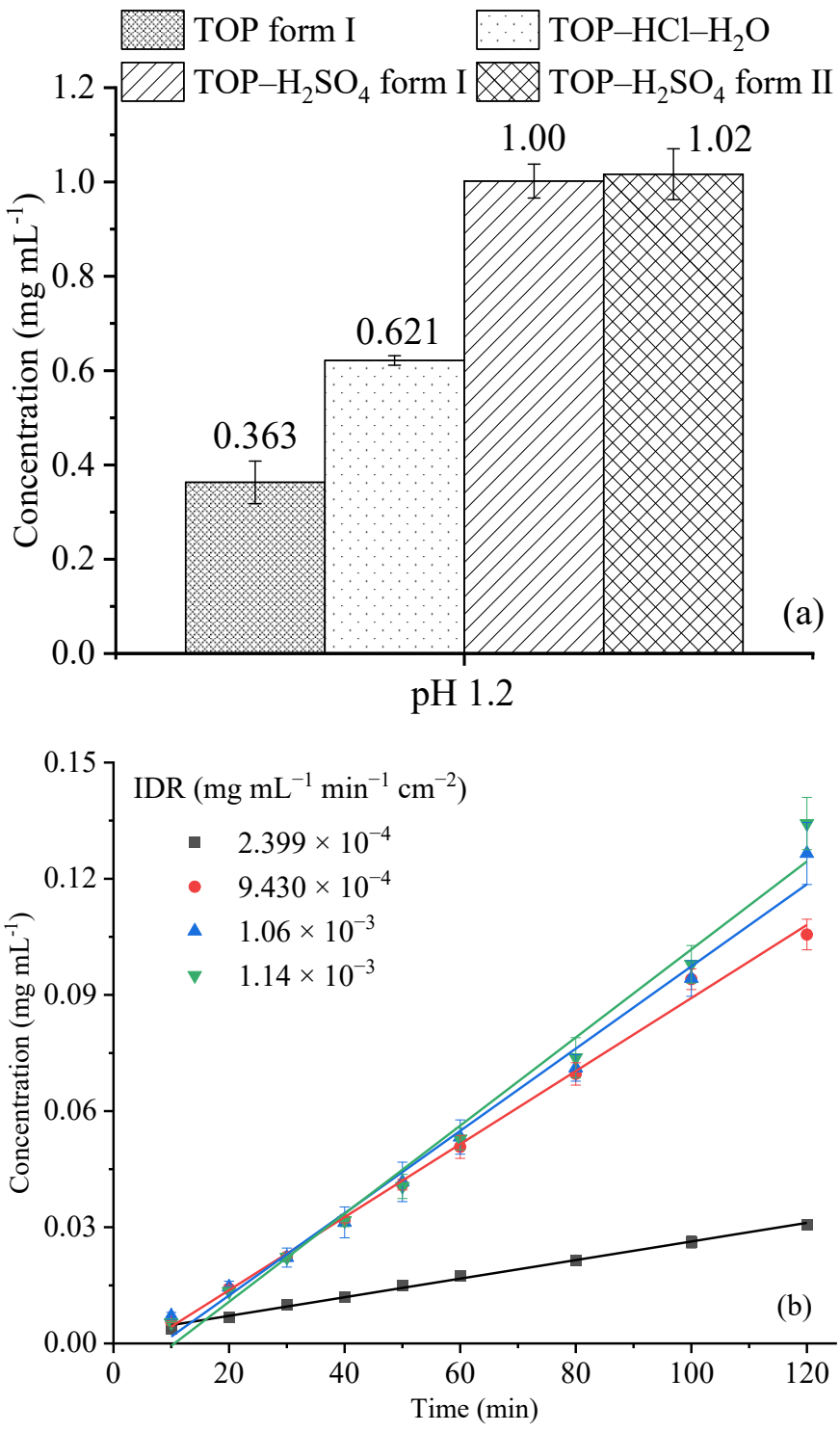

Fig. S8 (a) The apparent equilibrium solubility of TOP form I, TOP–HCl–H_2O, TOP–H_2SO_4 form I, and TOP–H_2SO_4 form II in pH 1.2 HCl solution at 37 °C. (b) IDR profiles of TOP form I (■), TOP–HCl–H_2O (●), TOP–H_2SO_4 form I (▲), and TOP–H_2SO_4 form II (▼) in pH 1.2 HCl solution at 37 °C.

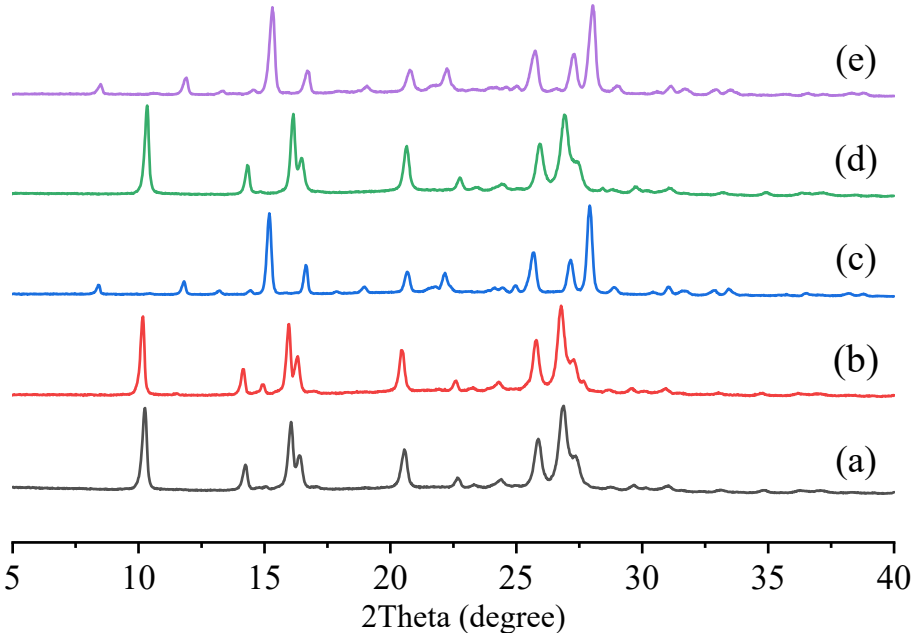

Fig. S9 The powder XRD patterns of TOP form I under 25°C/20% RH (a), 25°C/50% RH (b), and 25°C/90% RH (c) conditions for 2 weeks. Experimental patterns of TOP form I (d) and TOP–H_2O (e) were given for comparison.

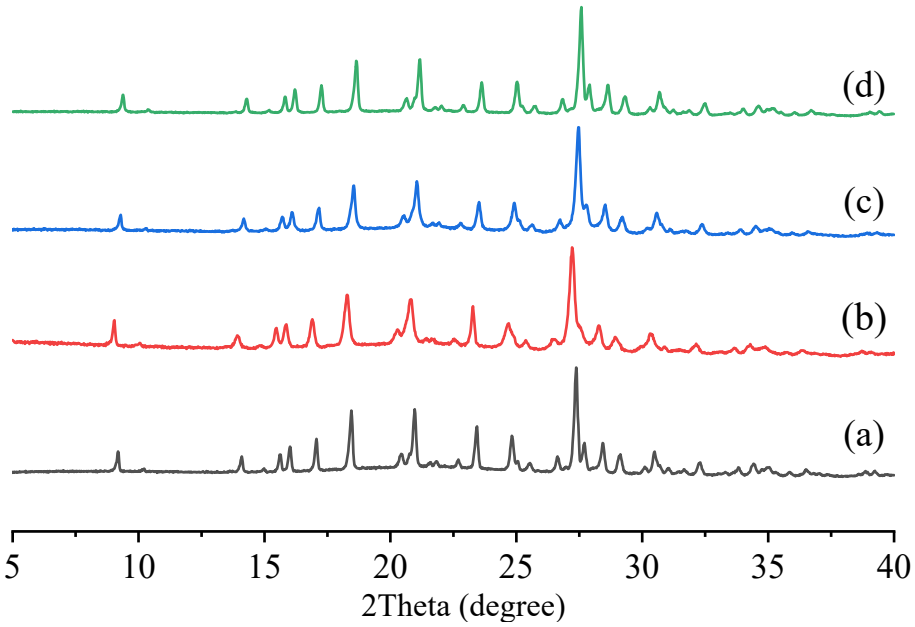

Fig. S10 The powder XRD patterns of TOP–HCl–H_2O under 25°C/20% RH (a), 25°C/50% RH (b), and 25°C/90% RH (c) conditions for 2 weeks. Experimental pattern of TOP–HCl–H_2O (d) was given for comparison.

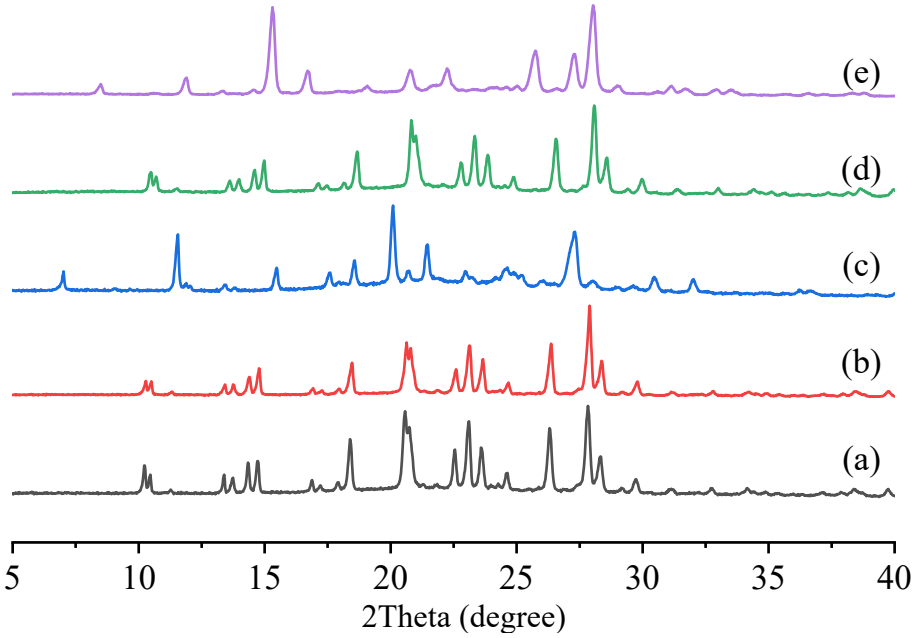

Fig. S11 The powder XRD patterns of TOP–H_2SO_4 form I under 25°C/20% RH (a), 25°C/50% RH (b), and 25°C/90% RH (c) conditions for 2 weeks. Experimental patterns of TOP–H_2SO_4 form I (d) and TOP–H_2O (e) were given for comparison.

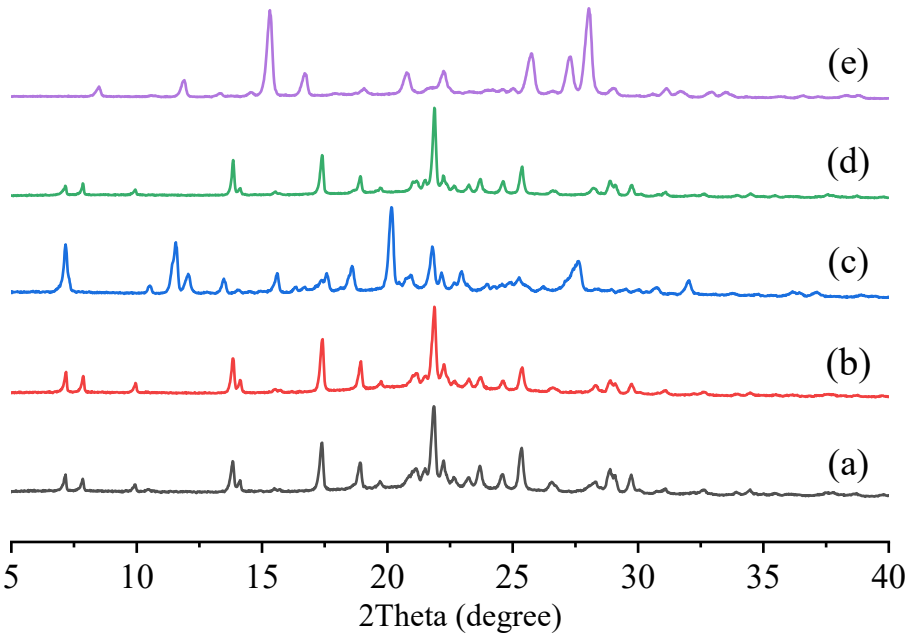

Fig. S12 The powder XRD patterns of TOP–H_2SO_4 form II under 25°C/20% RH (a), 25°C/50% RH (b), and 25°C/90% RH (c) conditions for 2 weeks. Experimental patterns of TOP–H_2SO_4 form II (d) and TOP–H_2O (e) were given for comparison.