Supplementary Information for the article by Artem Golomolzin, Evgeniy Losev, and Elena Boldyreva "Unlocking the reversibility of the mechanochemical synthesis of a pharmaceutical cocrystal"

Examples of Rietveld refinement of the powder X-ray diffraction pattern used for quantitative phase analysis

GSAS-II program is used.

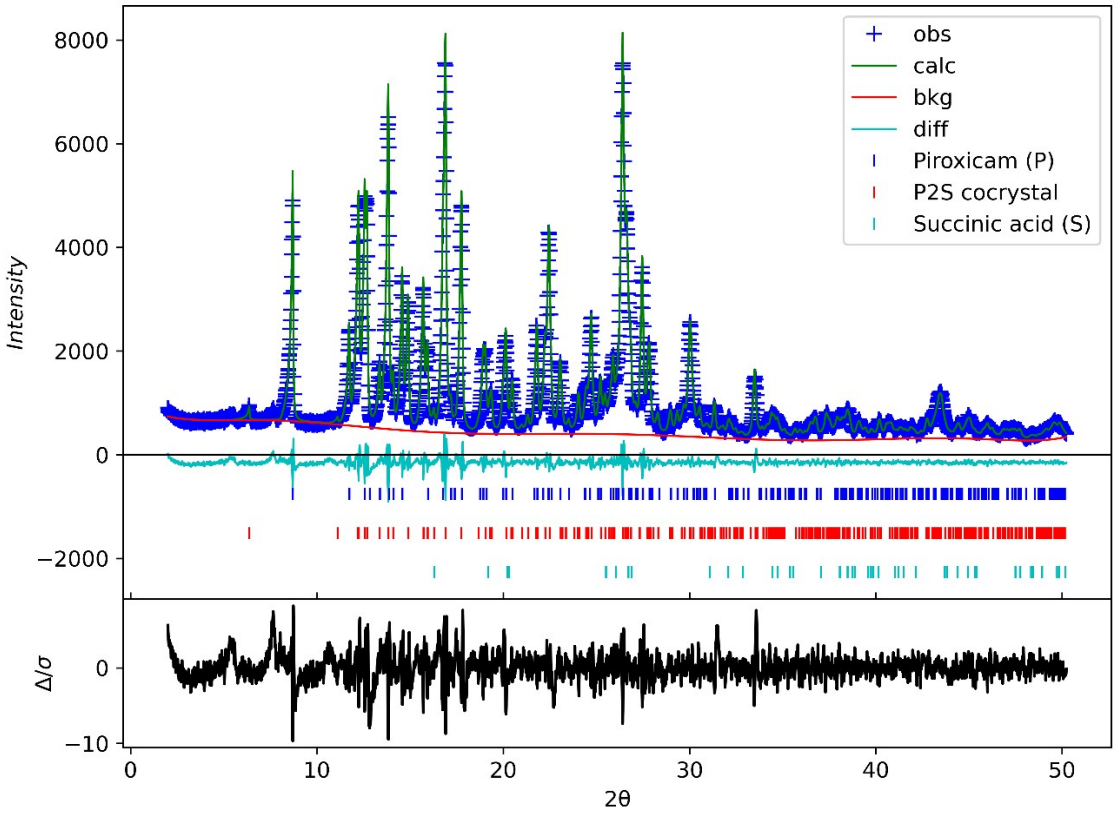

Figure S1. Reaction mixture (initially 85 mg β-piroxicam and 15 mg succinic acid with a 75 µl ethanol added) after 30 minutes of treatment at 25 Hz milling jar oscillations frequency, yielding **P_2S** cocrystal which here has approx. 50 mol.% fraction; wR = 5.573%, GOF = 1.75.

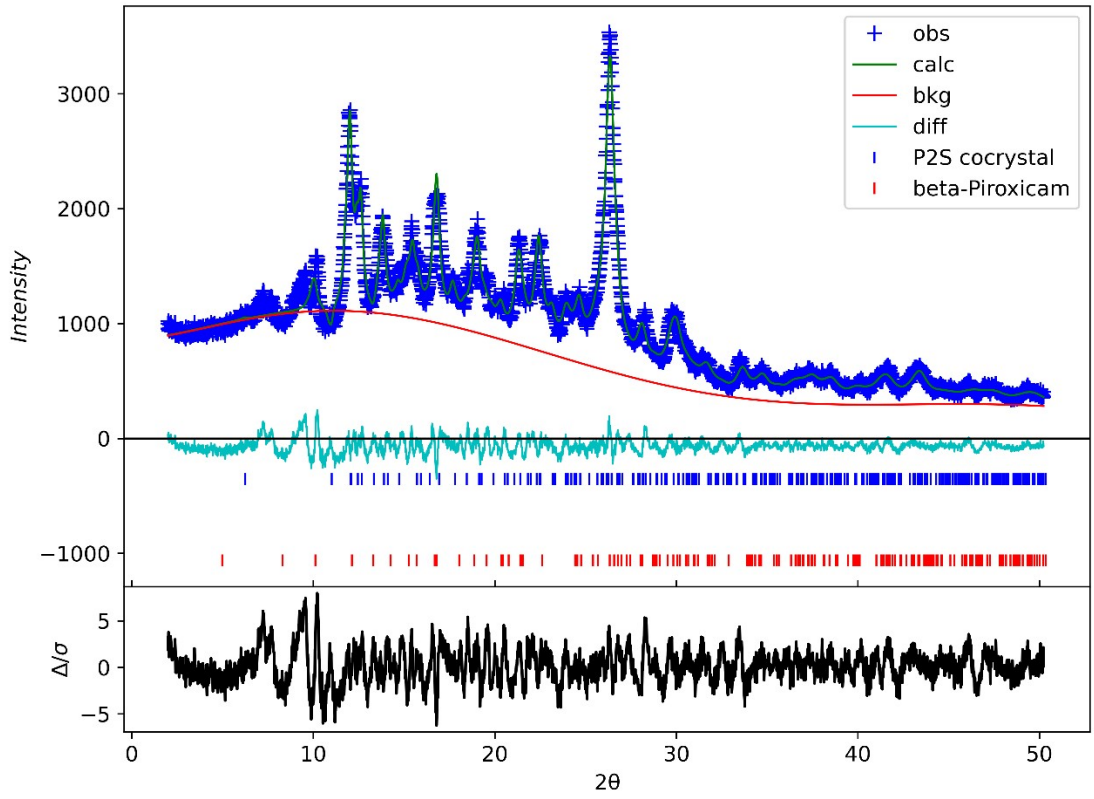

Figure S2. Reaction mixture (initially 100 mg solution-crystallized **P_2S**, no liquid added) after 30 minutes of treatment at 25 Hz, leading to decomposition and yielding approx. 50 mol.% α-piroxicam; wR = 5.756%, GOF = 1.84.

Representative visualizations used in the process of milling sound analysis. Audacity program was used

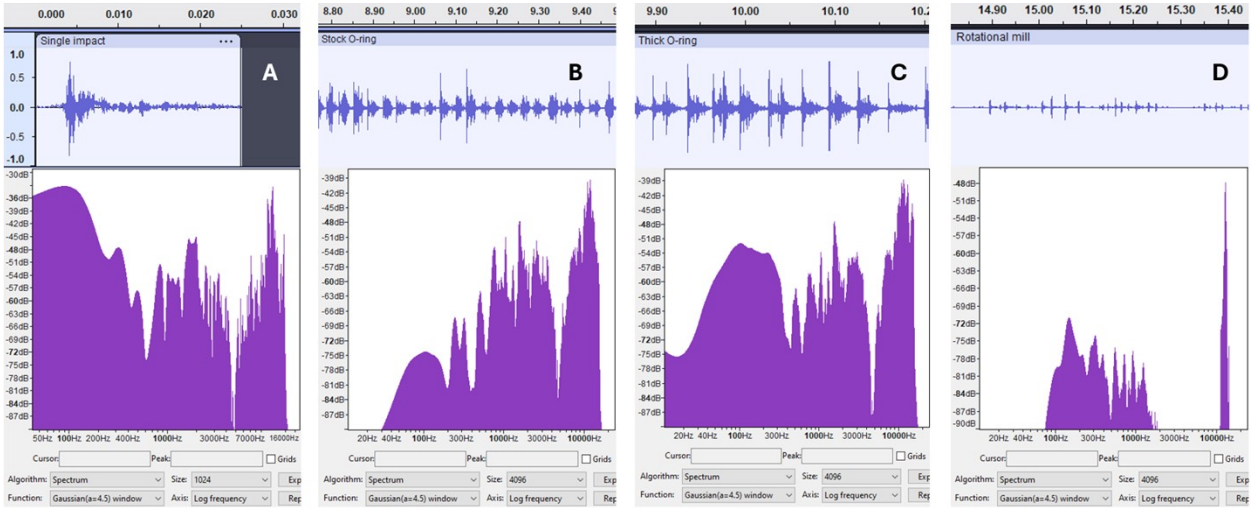

Figure S3. Sound wave shape (top) and spectrum of a longer (~5 s) sample (bottom) for audio records of: A) a single inside impact of a metal milling ball and milling jar walls; B) milling noise in vibrational mill at 15 Hz with stock O-ring; C) same with thicker O-ring; D) milling noise in rotational mill at 15 Hz (900 rpm). Noise is removed with Audacity's noise reduction by noise profile of a mill without any load and milling body.

Samples photos

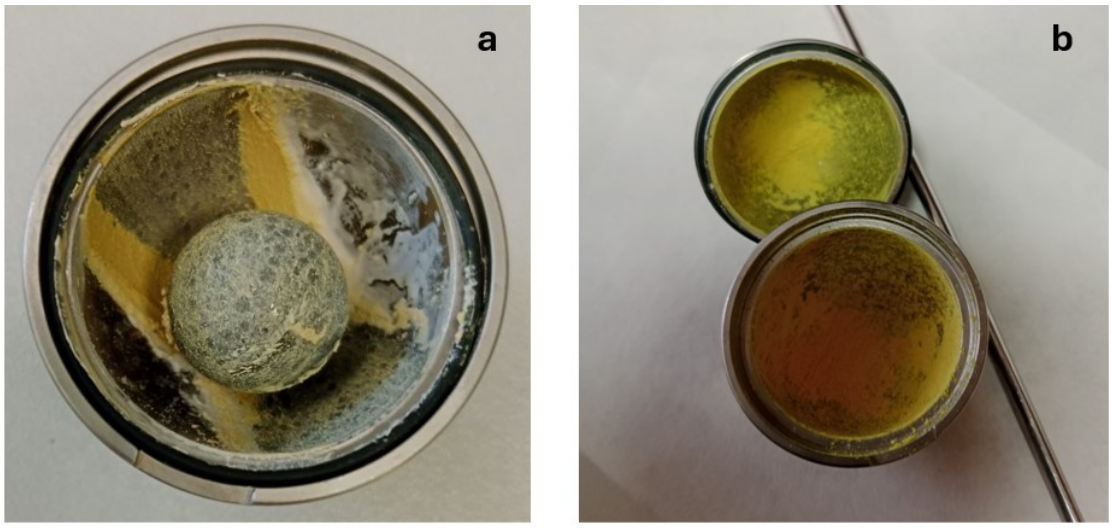

Figure S4. Reaction mixture in the milling jar right after vibrational mill treatment. a) One of the synthesis study samples: stoichiometric **P** and **S** load with EtOH, 30 min treatment at 25 Hz. b) One of the decomposition study samples: $\mathbf{P_2S}$ after 30 min of dry treatment at 25 Hz decomposed partly, to give α-piroxicam.