

Spontaneous Solid-State Co-Crystallization of Caffeine and Urea

Pól MacFhionnghaile,¹ Clare M. Crowley,² Patrick McArdle,^{*,1} and Andrea Erxleben^{*,1}

¹ Synthesis and Solid State Pharmaceutical Centre and School of Chemistry, National University of Ireland Galway, Galway, H91 TK33, Ireland

² Synthesis and Solid State Pharmaceutical Centre and Department of Chemical Sciences, Bernal Institute, University of Limerick, Limerick, V94 T9PX, Ireland

Supporting Information

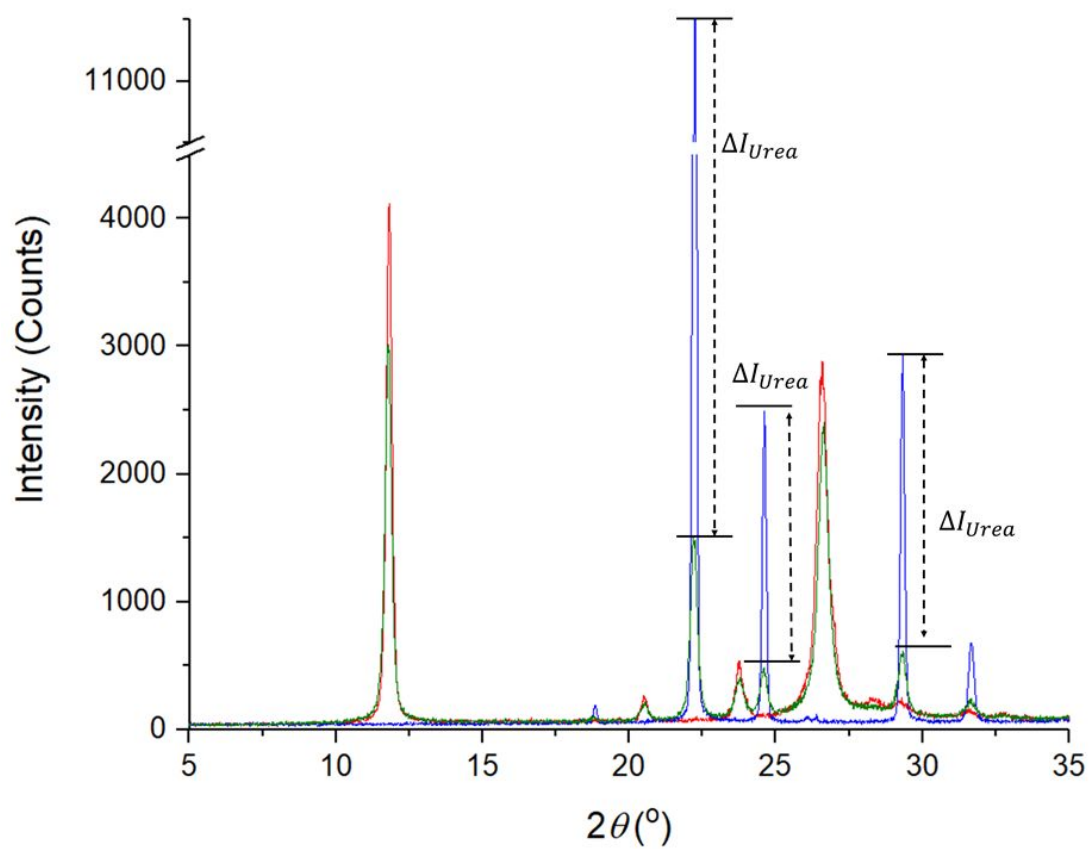


Figure S1. PXRD patterns of commercial caffeine (red), commercial urea (blue), and a milled equimolar caffeine-urea mixture (green).

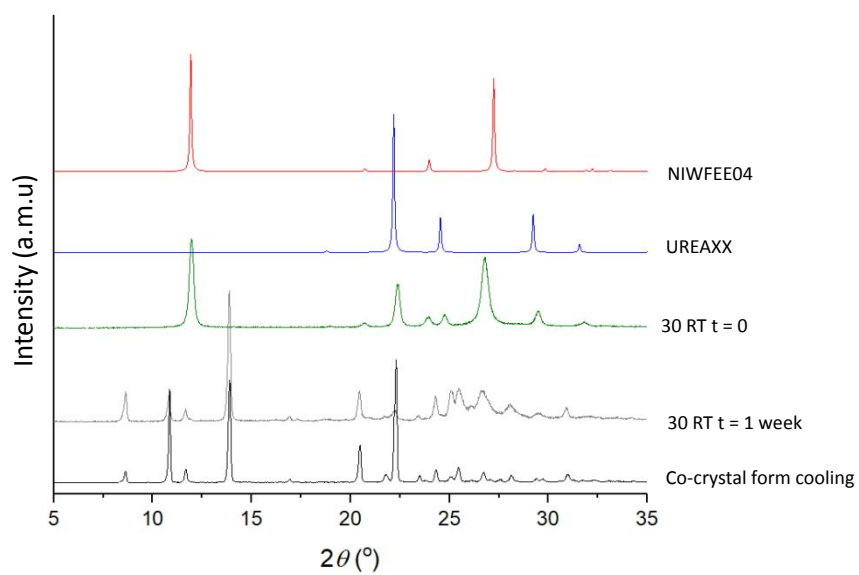


Figure S2. Comparison of the PXRD patterns of a 1:1 caffeine-urea mixture directly after milling (green) and after milling and storage at room temperature (black) with the PXRD patterns of urea (blue; calculated from ref code UREAXX), caffeine (red; calculated from ref code NIWFEE04) and the co-crystal obtained by cooling crystallization from acetonitrile.

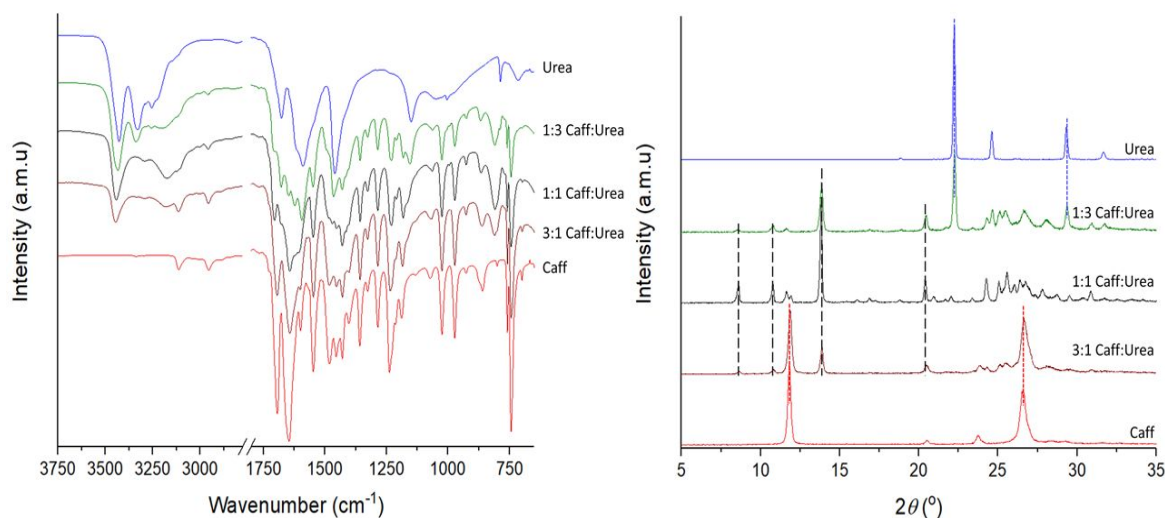


Figure S3. IR spectra (left) and PXRD patterns (right) of urea (blue), caffeine (red), 1:3 (green), 1:1 (black), 3:1 (brown) molar ratios of caffeine and urea after milling and storage at room temperature for 24 h.

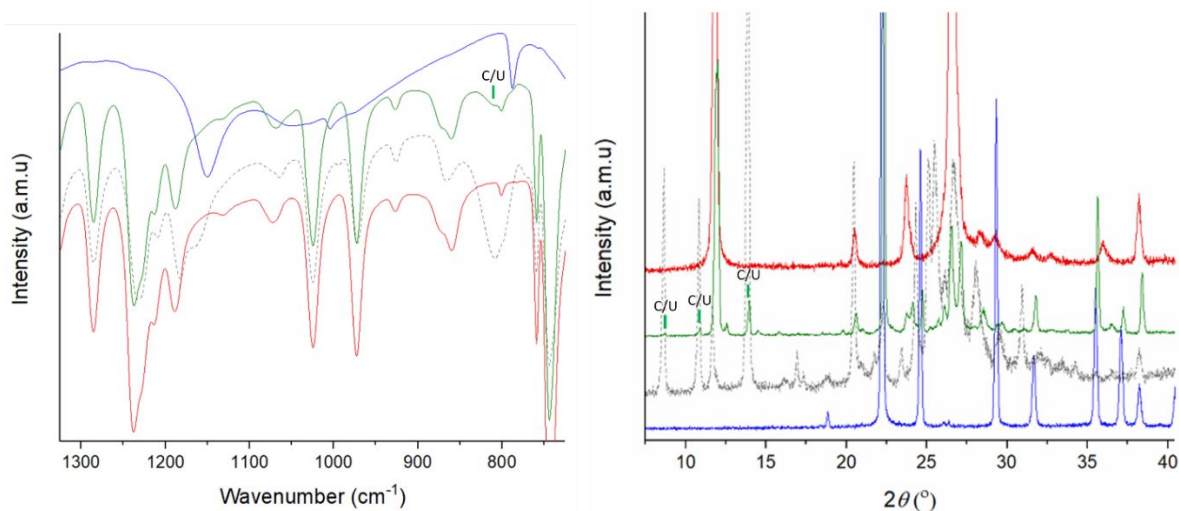


Figure S4. IR spectra and PXRD patterns of urea (blue), caffeine (red), co-crystal (dashed grey), and (un-milled) caffeine and urea mixed for 10 weeks in a low energy mixer at room temperature (green) (C/U indicate peaks characteristic to the co-crystal).

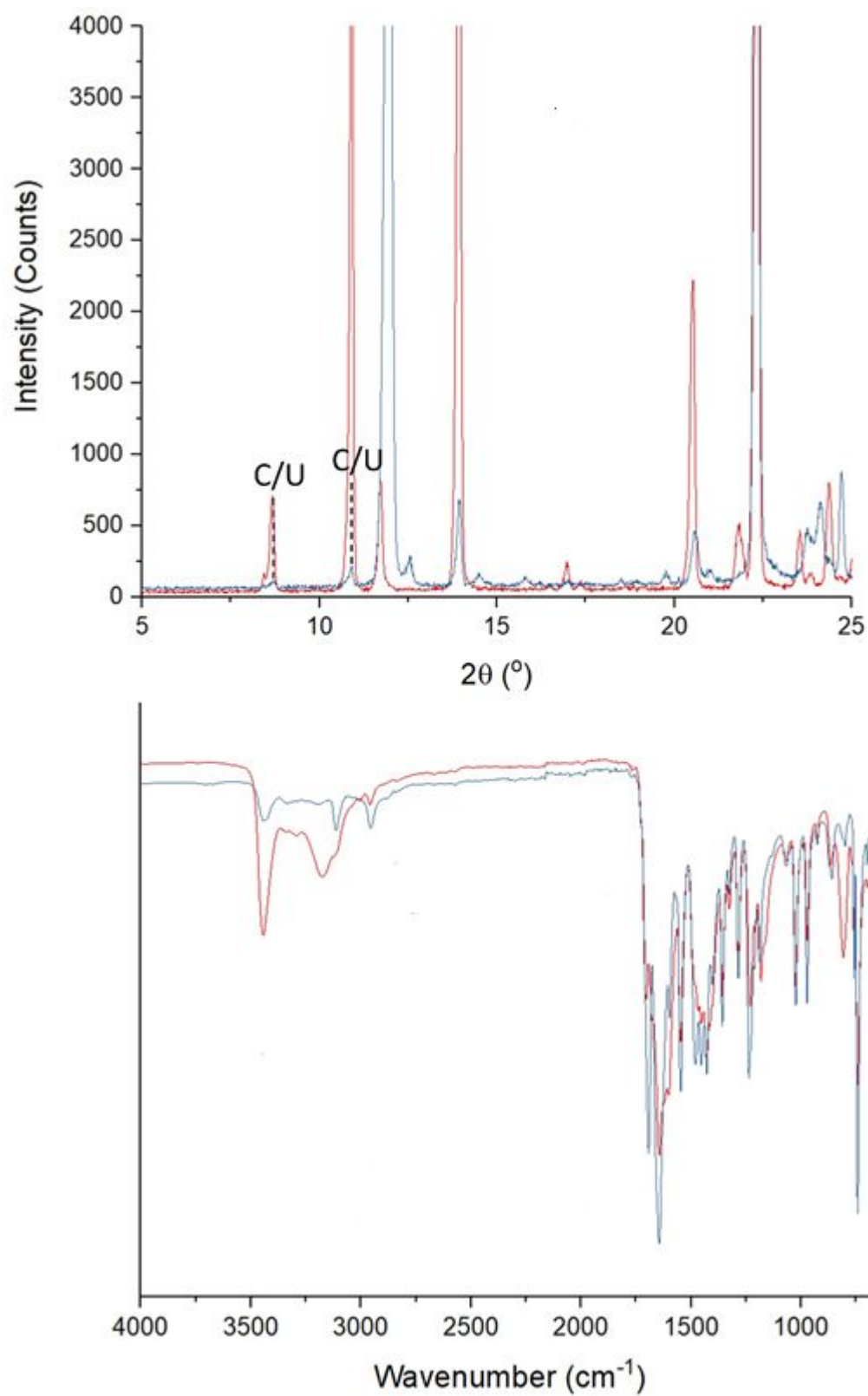


Figure S5. PXRD patterns (top) and IR spectra (bottom) of (unmilled) caffeine and urea mixed for 5 weeks using a magnetic stirrer (blue) and of the co-crystal (red).

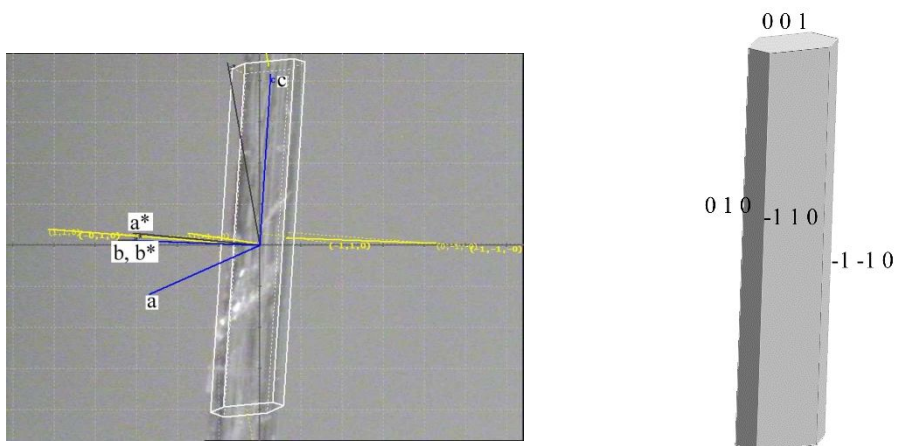


Figure S6. Crystal indexed on the diffractometer and the crystal drawn using the diffractometer face index file.

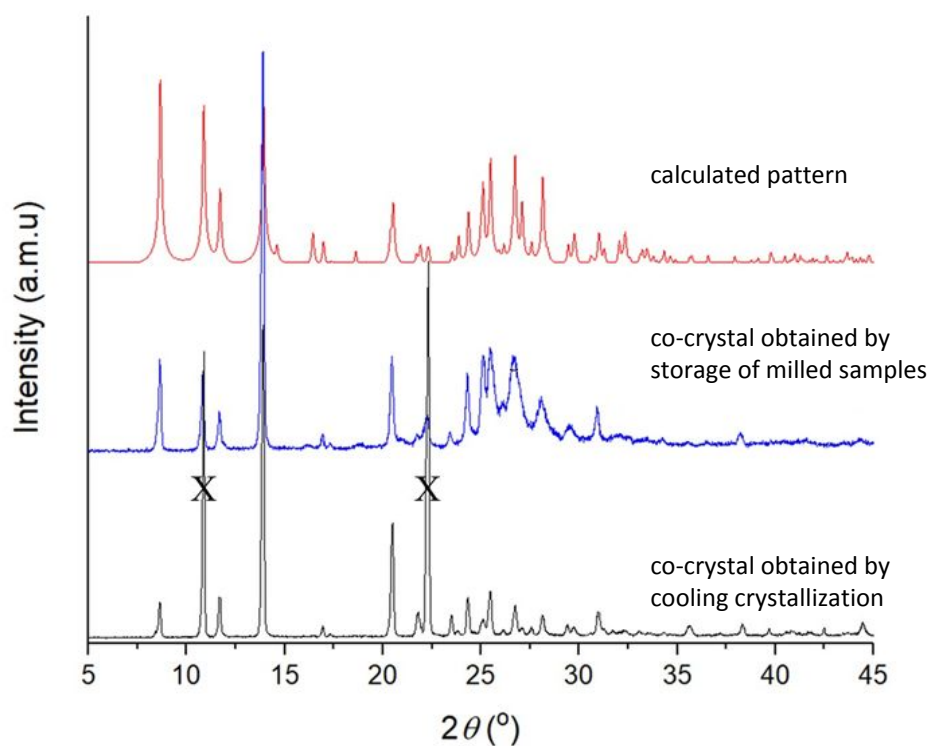


Figure S7. PXRD patterns of the co-crystal obtained by storage of milled samples (blue) and by solution crystallization (black) and the theoretical pattern calculated from the single crystal data. The PXRD pattern of the sample crystallized from solution shows preferred orientation effects (X).

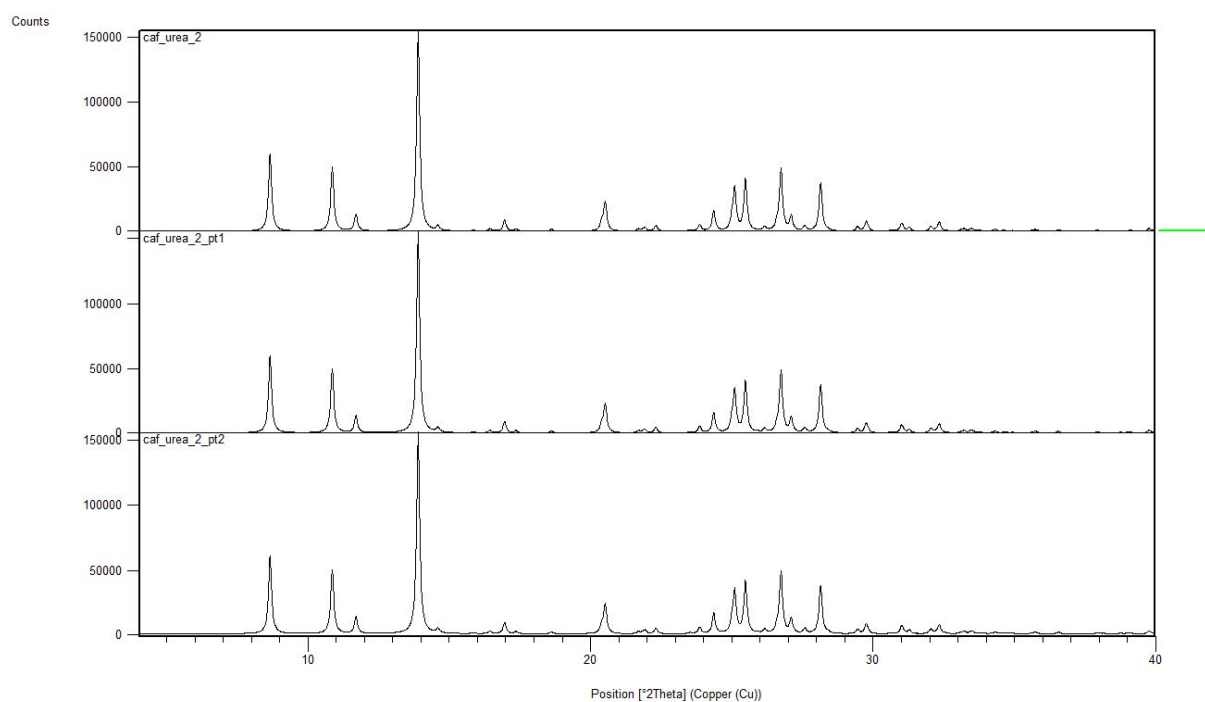


Figure S8. Theoretical PXRD pattern of caffeine-urea calculated from the single crystal structure (top), calculated for the major component of the disordered single crystal structure (middle) and calculated for the minor component of the disordered single crystal structure (bottom).

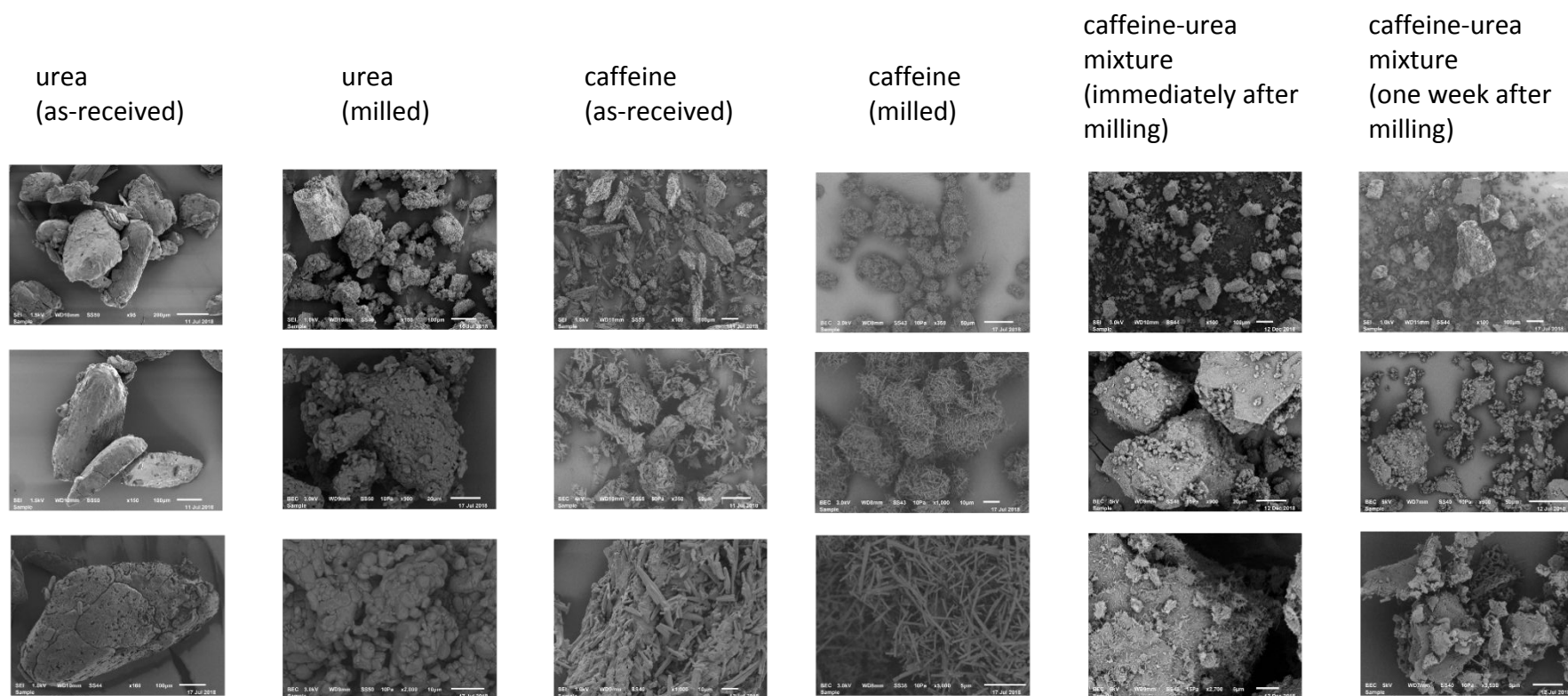


Figure S9. Additional SEM images showing the effects of milling on caffeine and urea, and the transformation of milled caffeine and urea to the co-crystal.

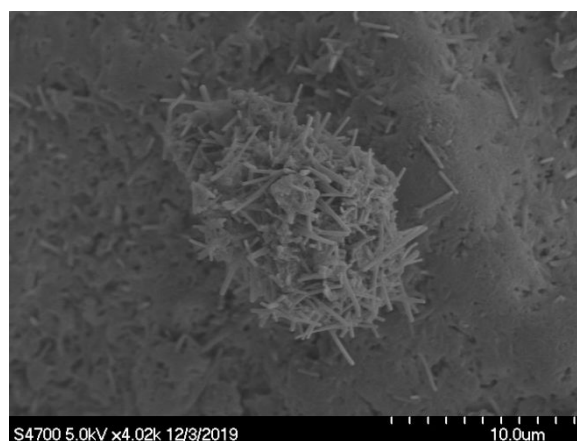


Figure S10. SEM image of milled caffeine and milled urea after 1 d mixing using the low energy mixer.

Table S1. H bonding interactions in the caffeine-urea cocrystal

D-H \cdots A	d(D \cdots H) (Å)	d(H \cdots A) (Å)	d(D \cdots A) (Å)	\angle (DHA) (°)	symmetry code
N(1)-H(1A) \cdots O(1)	0.86	2.06	2.916(4)	172.4	-x-1,-y,-z-1
N(1)-H(1B) \cdots N(4a)	0.86	2.33	3.096(15)	148.6	x, y, z
N(2)-H(1N2) \cdots N(4a)	0.89(2)	2.20(4)	2.991(14)	148(6)	x, y, z
N(2)-H(2N2) \cdots O(1)	0.894(19)	2.03(2)	2.917(5)	174(4)	-x-1,-y,-z