Pharmaceutical cocrystals of ethenzamide: structural, solubility and dissolution studies

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Electronic Supplementary Information

(9 Pages)

Contents

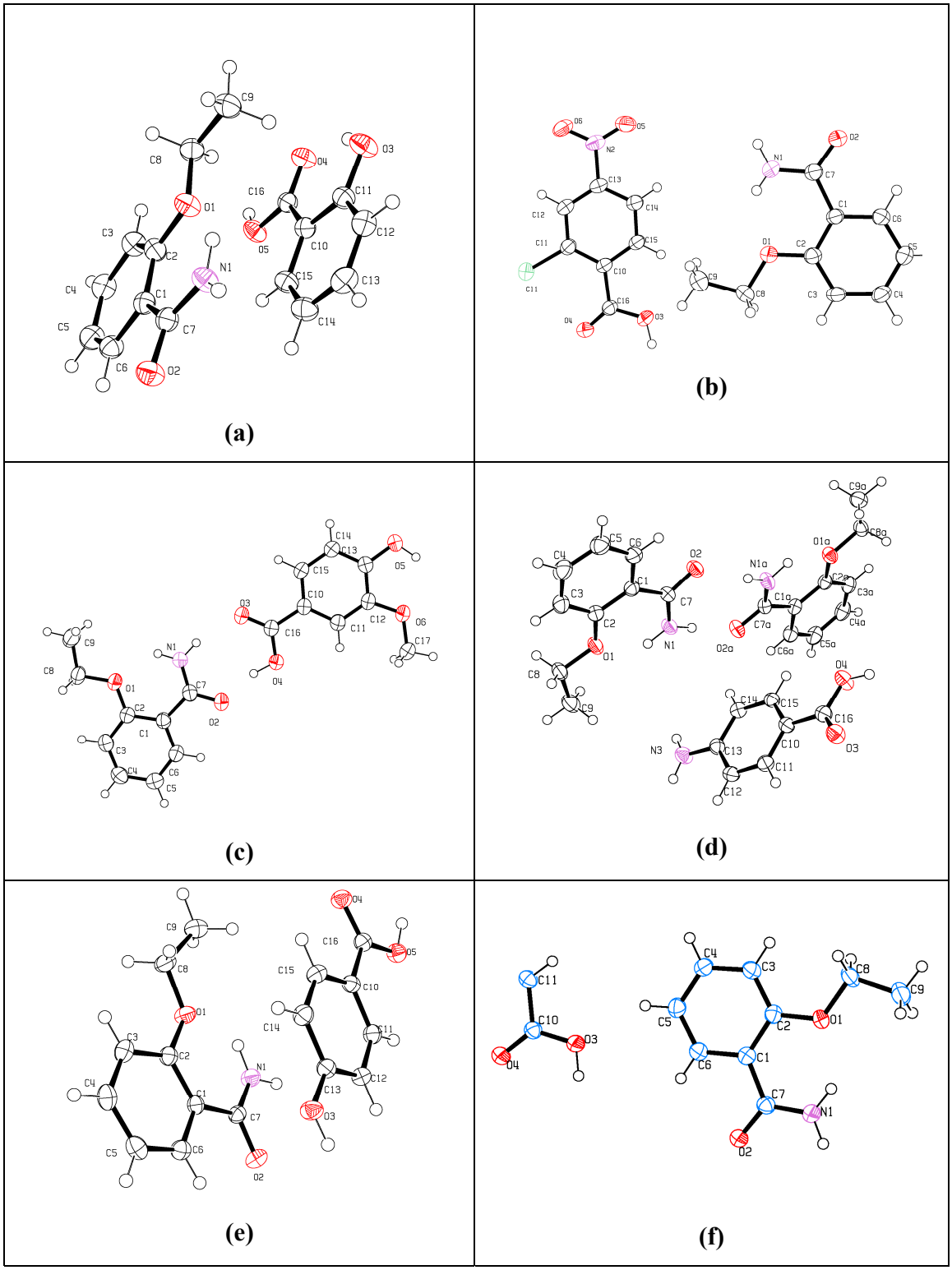

Fig. S1 ORTEP diagrams of the cocrystals discussed in this paper (a) EA•SA, (b) EA•CNBA, (c) EA•VA, (d) EA•ABA, (e) EA•HBA, and (f) EA•FA cocrystal. Thermal ellipsoids were drawn at 50 % probability.

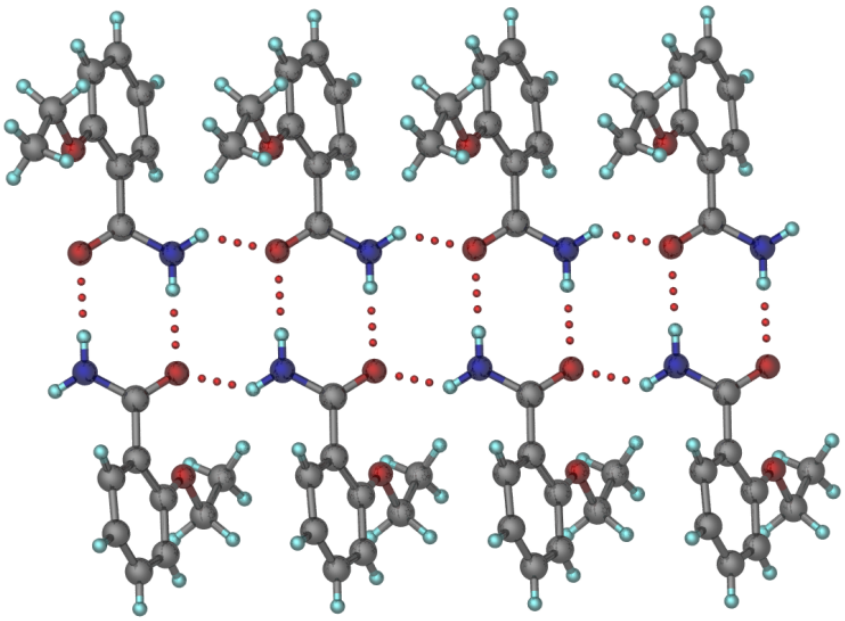

Fig. S2 Packing diagram of crystal structure of EA. Notice the absence of an intramolecular N–H···O hydrogen bond.

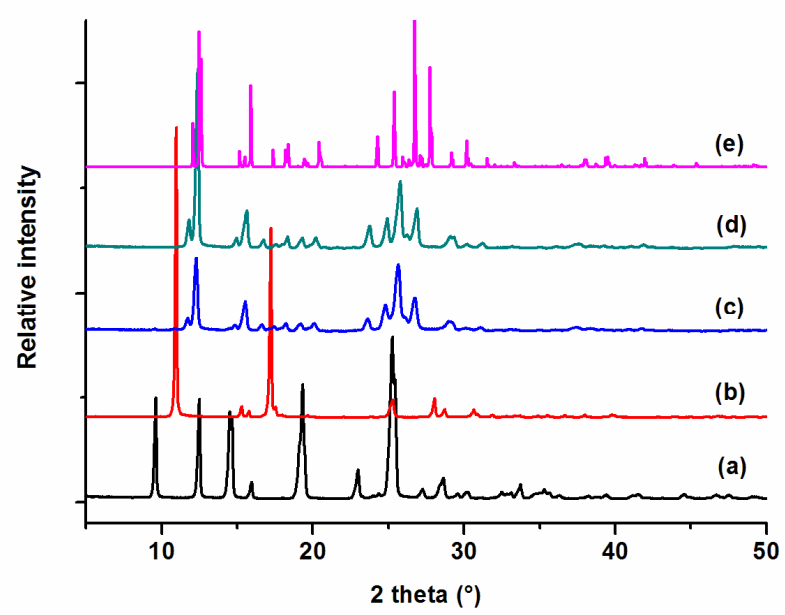

Fig. S3 Comparison of the PXRD patterns of (a) EA, (b) SA, (c) powder obtained from solvent-drop grinding with acetone of 1:1 EA and SA, (d) powder obtained from solvent-drop grinding with methanol on a 1:1 EA and SA, and (e) simulated from X-ray structure of the cocrystal. Notice the close match between the patterns (c) and (d) with (e). Neat grinding of a 1:1 EA and SA resulted a new PXRD pattern that belong to a new polymorph (see the main paper for details).

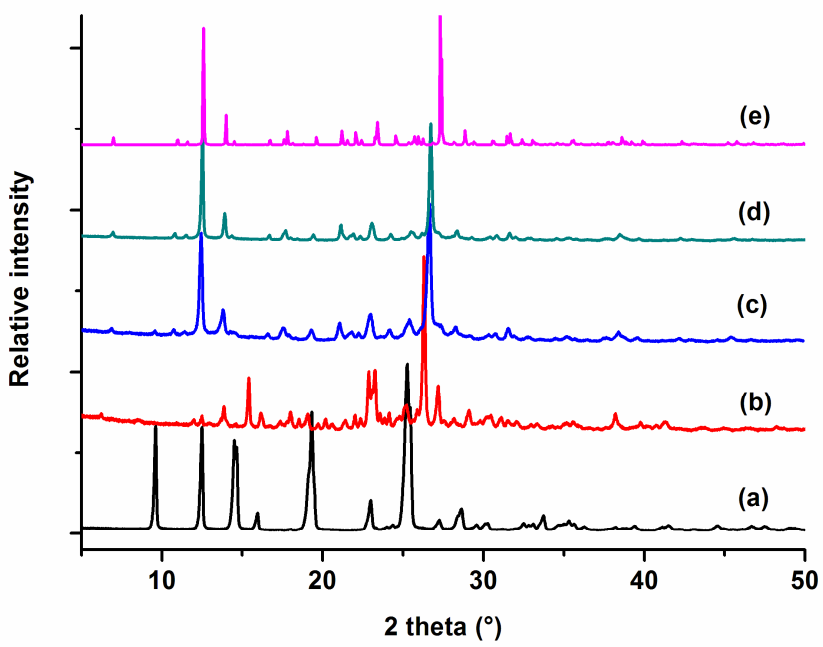

Fig. S4 Comparison of the PXRD patterns of (a) EA, (b) CNBA, (c) powder obtained from neat grinding of 1:1 EA and CNBA, (d) powder obtained from solvent-drop grinding with methanol on a 1:1 EA and CNBA, and (e) simulated from X-ray structure of the cocrystal. Notice the close match between the patterns (c) and (d) with (e).

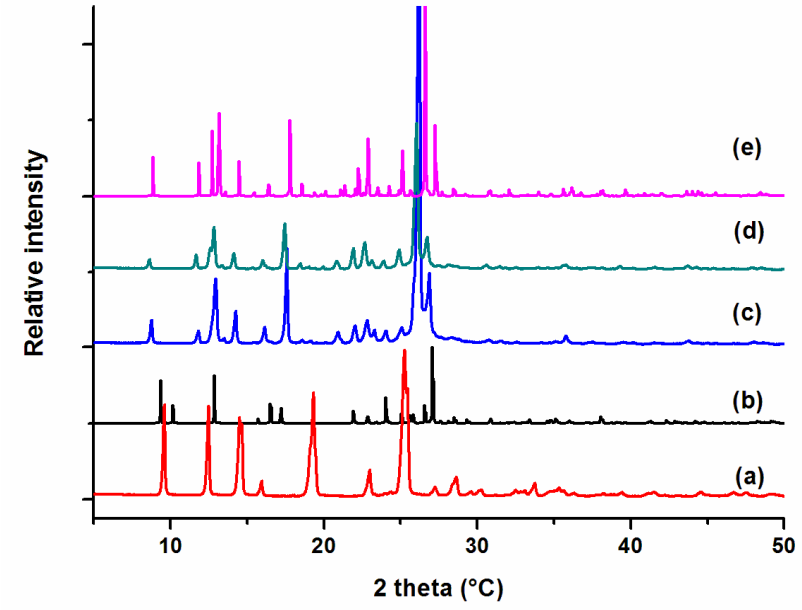

Fig. S5 Comparison of the PXRD patterns of (a) EA, (b) VA, (c) powder obtained from neat grinding of 1:1 EA and VA, (d) powder obtained from solvent-drop grinding with methanol on a 1:1 EA and VA, and (e) simulated from X-ray structure of the cocrystal. Notice the close match between the patterns (c) and (d) with (e).

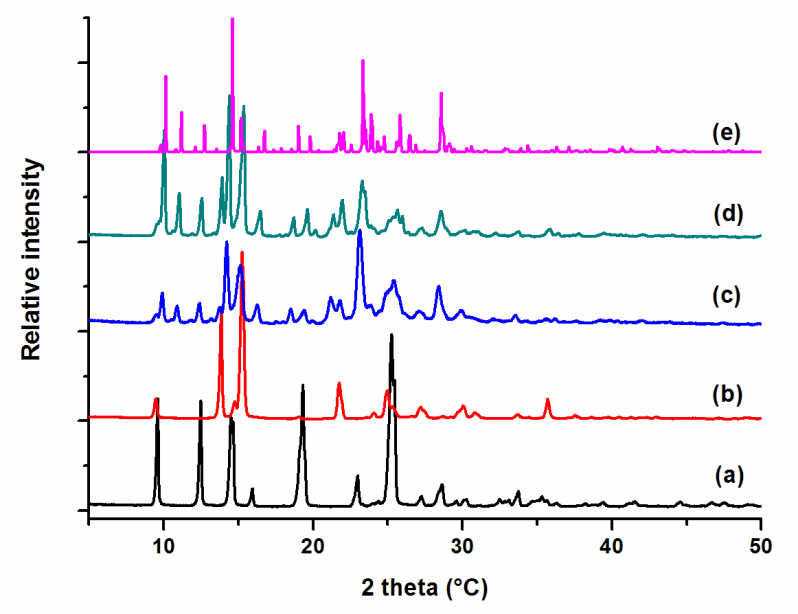

Fig. S6 Comparison of the PXRD patterns of (a) EA, (b) ABA, (c) powder obtained from neat grinding of 2:1 EA and ABA, (d) powder obtained from solvent-drop grinding with methanol on a 2:1 EA and ABA, and (e) simulated from X-ray structure of the cocrystal. Notice the close match between the patterns (c) and (d) with (e).

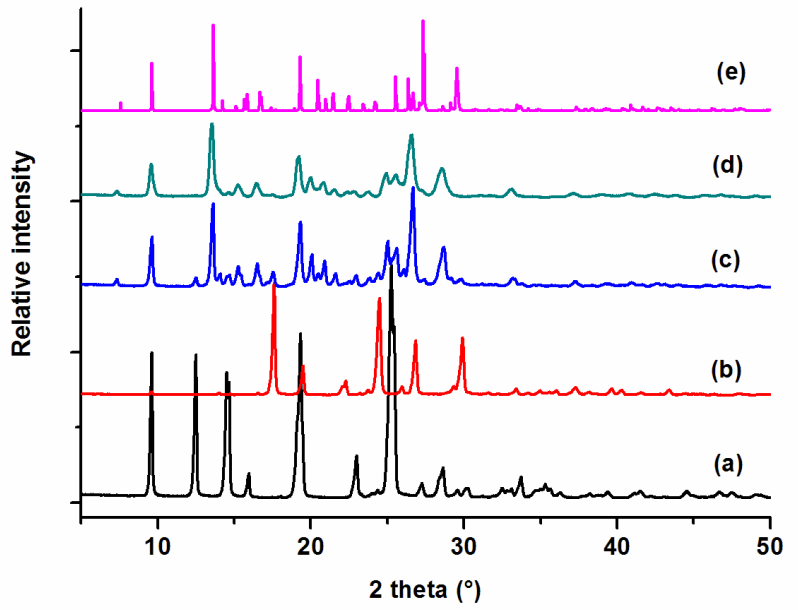

Fig. S7 Comparison of the PXRD patterns of (a) EA, (b) HBA, (c) powder obtained from neat grinding of 1:1 EA and HBA, (d) powder obtained from solvent-drop grinding with methanol on a 1:1 EA and HBA, and (e) simulated from X-ray structure of the cocrystal. Notice the close match between the patterns (c) and (d) with (e). The sample obtained from neat grinding contains a small amount of EA.

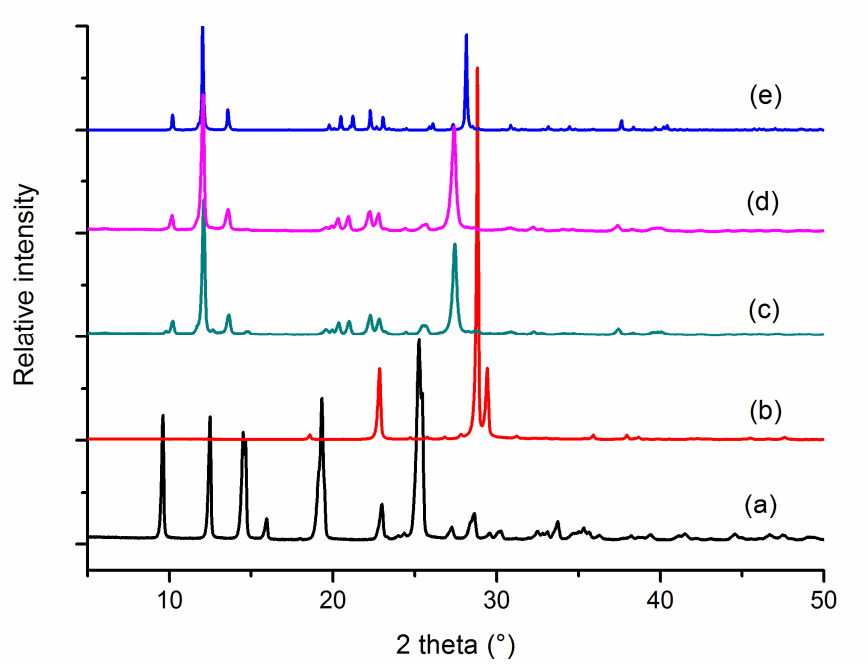

Fig. S8 Comparison of the PXRD patterns of (a) EA, (b) FA, (c) powder obtained from neat grinding of 1:1 EA and FA, (d) powder obtained from solvent-drop grinding with methanol on a 1:1 EA and FA, and (e) simulated from X-ray structure of the cocrystal.

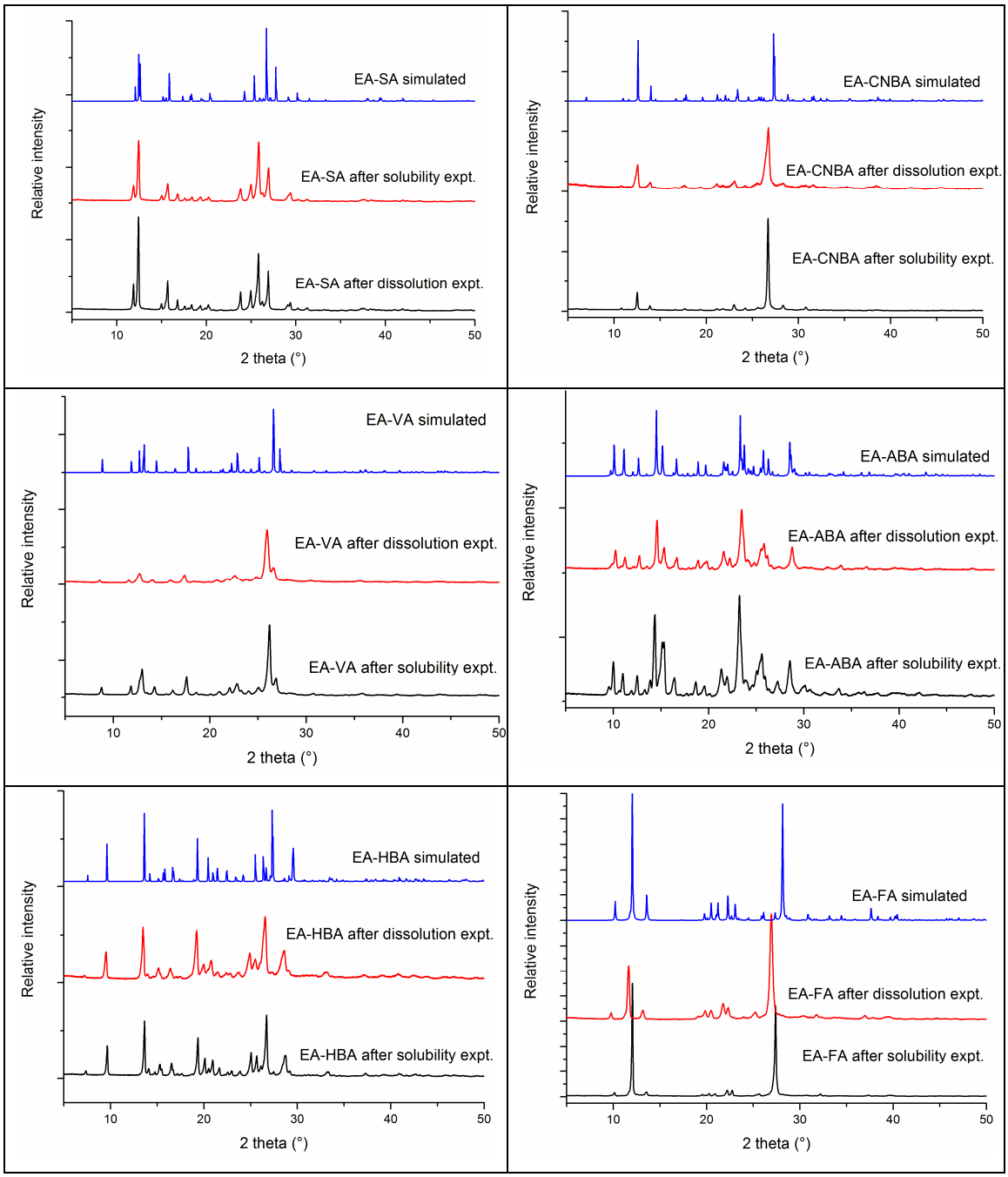

Fig. S9 Comparison of the PXRD patterns of the samples remaining after solubility and dissolution experiments on cocrystals with the simulated patterns of crystal structure of the respective cocrystals.

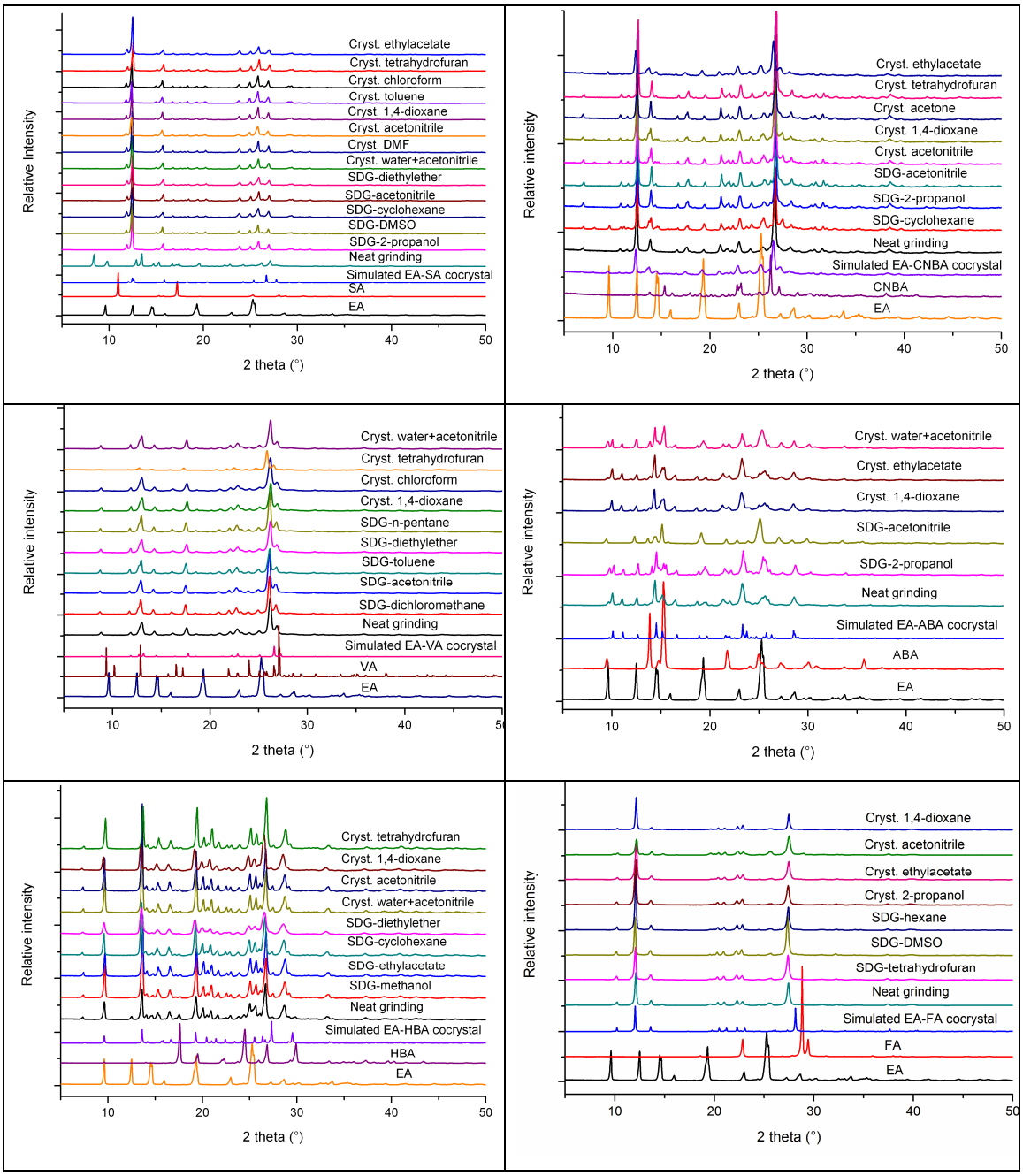

Fig. S10 Comparison of the PXRD patterns of the samples obtained in the polymorph screening experiments (only results of the selected experiments shown).

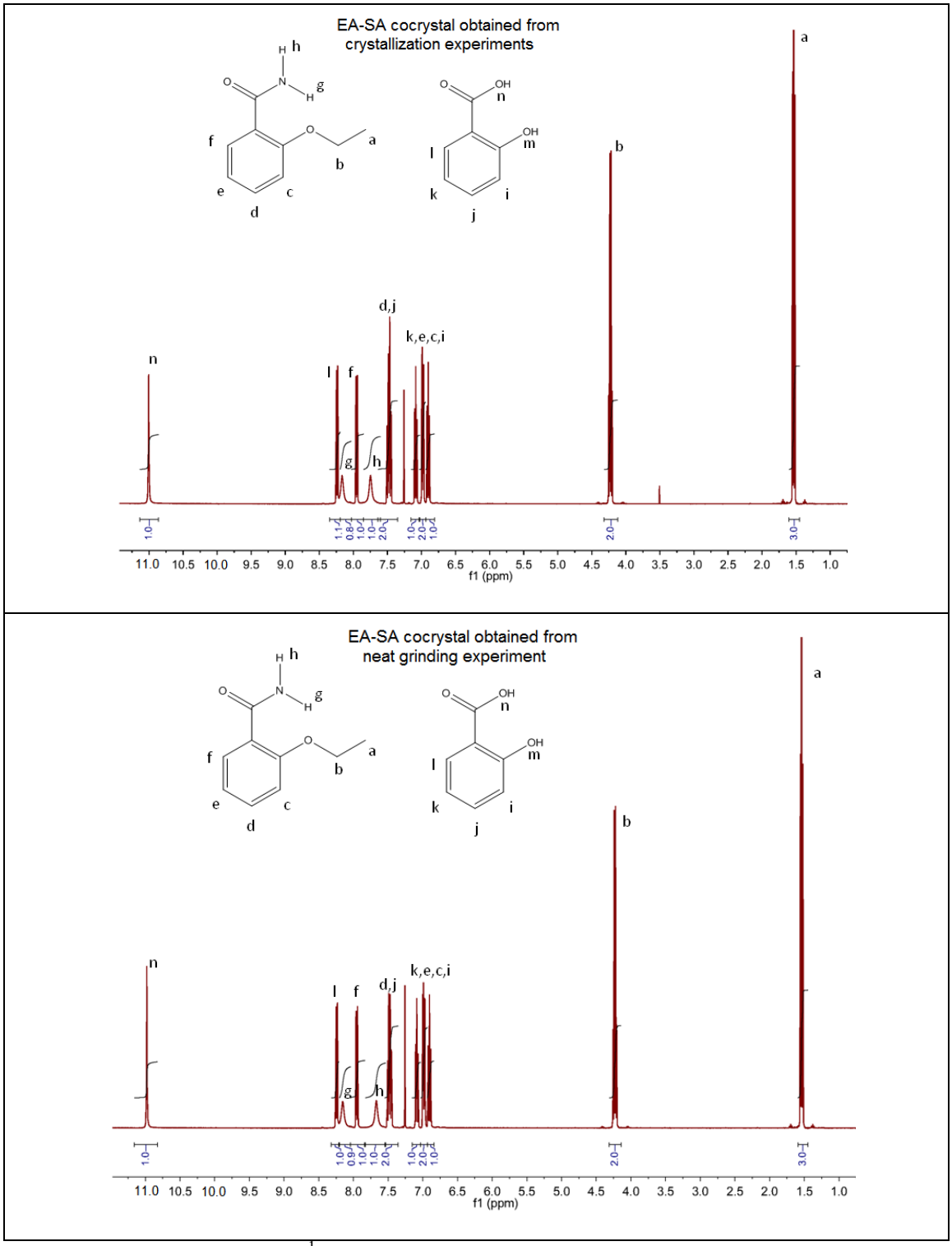

Fig. S11 Comparison of the ^{1}H-NMR spectra of polymorphs of the EA•SA cocrystal. NMR spectra were recorded at 400 MHz on a Bruker instrument in $CDCl_3$ at 25 °C.