Electronic Supplementary Material for CrystEngComm

SUPPORTING INFORMATION

Co-crystallisation of benzoic acid derivatives with N-containing bases in solution and by mechanical grinding: stoichiometric variants, polymorphism and twinning

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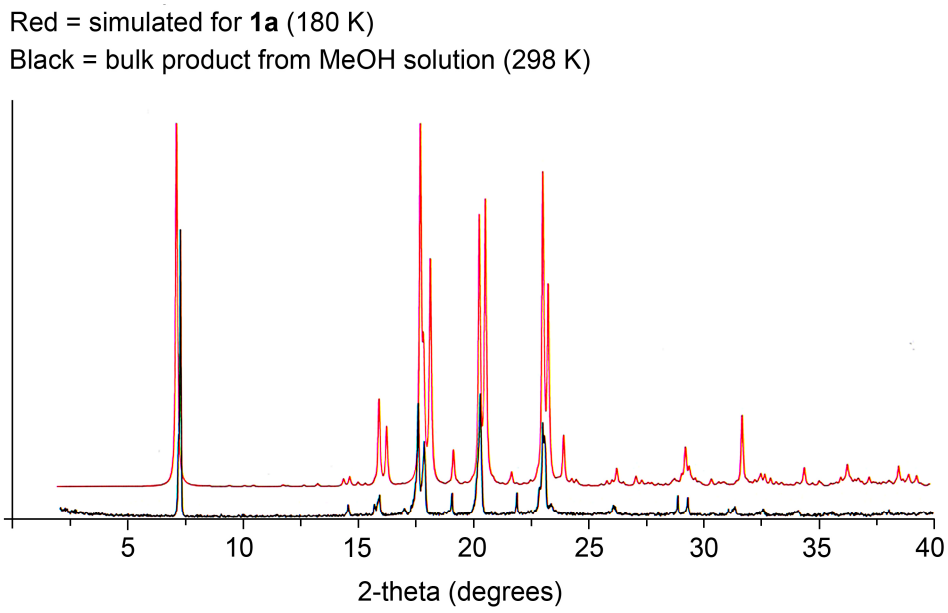
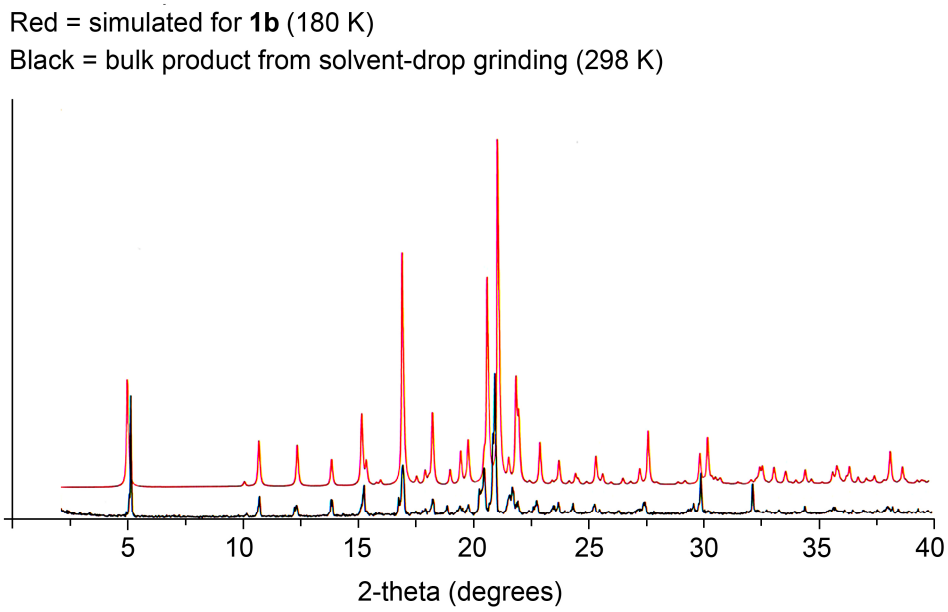
Preparation and PXRD patterns

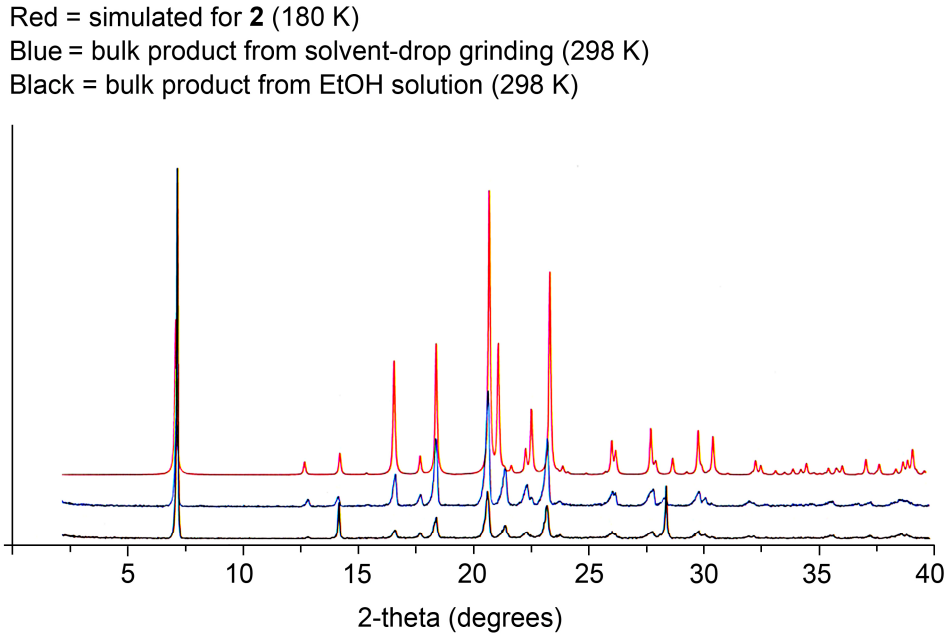
- **Benzoic acid/DABCO (2:1). Polymorph 1a**. Separate saturated solutions of benzoic acid (0.300 g, 0.0025 mmol) and DABCO (0.140 g, 0.0012 mmol) in warm methanol were combined and refluxed with stirring for 1 h. The flask was insulated and left to cool under ambient conditions, giving colourless needles of **1a** after *ca* 1 h. On evaporation to dryness, the uniformity of the bulk product was confirmed by PXRD. m.p. 141–142°C.



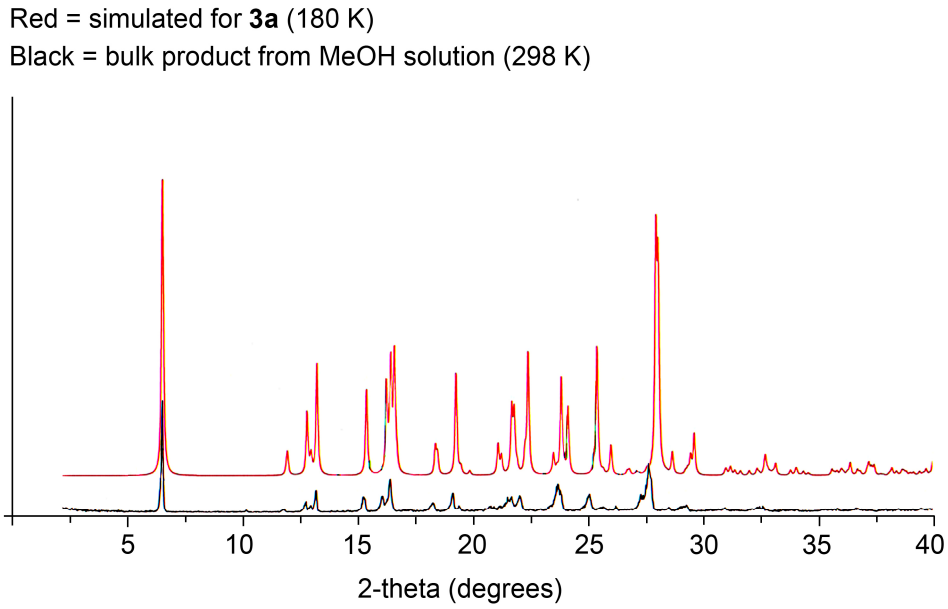
- **Benzoic acid/DABCO (2:1). Polymorph 1b**. Benzoic acid (1.220 g, 0.010 mol), DABCO (0.550 g, 0.005 mol) and two drops of methanol were placed in the ball mill, rotating at 650 rpm for 20 min. Single crystals were obtained by using this powder to seed a saturated methanol solution of benzoic acid and DABCO in a 2:1 molar ratio. After single-crystal analysis, the product obtained directly from the ball mill was confirmed by PXRD to be a uniform phase of **1b**. m.p. 141–142°C.



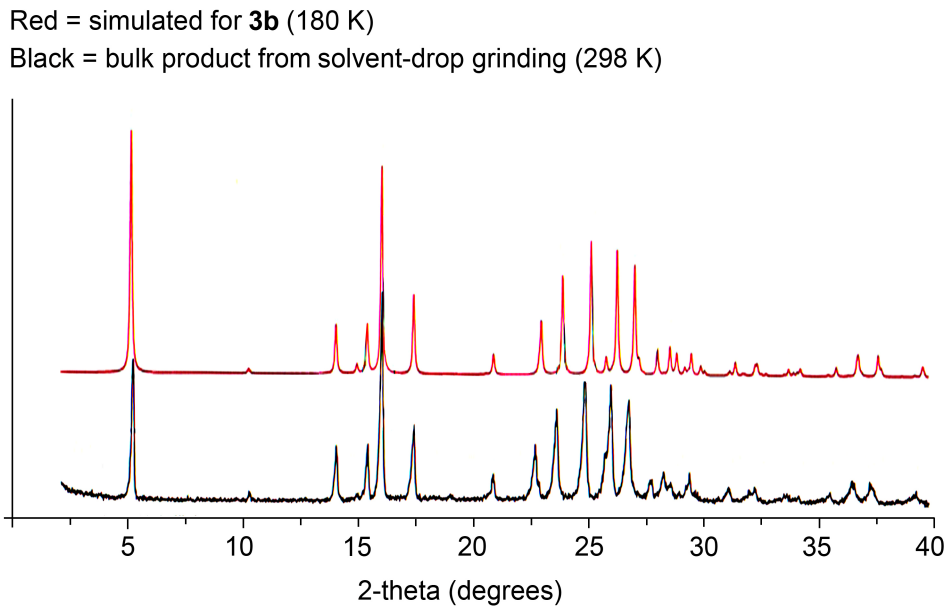
- **Benzoic acid/piperazine (2:1)**. **2**. Separate saturated solutions of benzoic acid (0.200 g, 0.0017 mmol) and piperazine (0.070 g, 0.00083 mmol) in warm ethanol were combined and refluxed with stirring for 1 h. The flask was insulated and left to cool under ambient conditions, giving colourless needles of **2** after *ca* 1 h. After evaporation to dryness, the uniformity of the bulk product was confirmed by PXRD. Alternatively: benzoic acid (1.220 g, 0.010 mol), piperazine (0.420 g, 0.0050 mol) and two drops of methanol were placed in the ball mill, rotating at 650 rpm for 20 min. The product was shown by PXRD to be a uniform phase of **2**. m.p. 184–186°C.



- **Benzoic acid/2-aminopyrimidine (2:1). Polymorph 3a**. Separate saturated solutions of benzoic acid (0.061 g, 0.500 mmol) and 2-aminopyrimidine (0.024 g, 0.250 mmol) in warm methanol were combined and refluxed with stirring for 1 h. The flask was insulated and left to cool under ambient conditions, giving colourless needles of **3a** after *ca* 1 h. On evaporation to dryness, PXRD showed the bulk to be a uniform phase. m.p. 95–97°C.

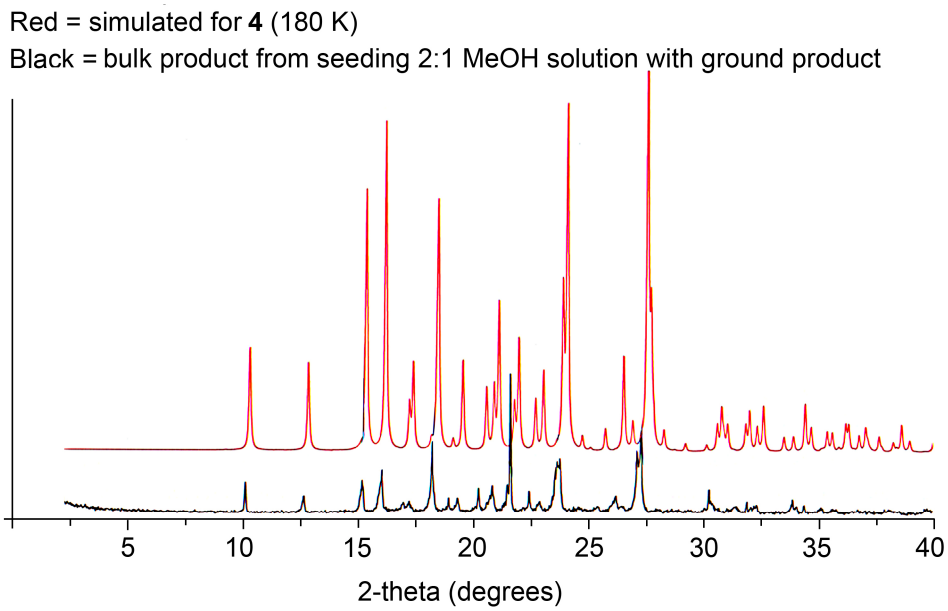


- **Benzoic acid/2-aminopyrimidine (2:1). Polymorph 3b** and **benzoic acid/2-aminopyrimidine (1:1) 4**. Benzoic acid (1.220 g, 0.010 mol), 2-aminopyrimidine (0.480 g, 0.005 mol) and two drops of methanol were placed in the ball mill, rotating at 650 rpm for 20 min. After obtaining single-crystal structures, the product obtained directly from the ball mill was shown to be a uniform phase of **3b**. m.p. 99–101°C.

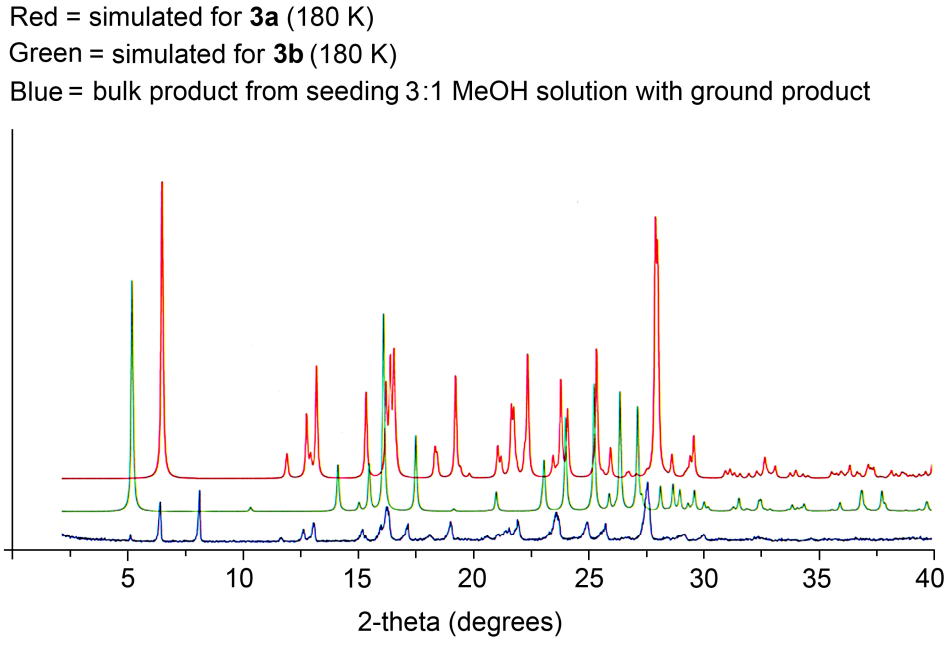


Several seeding experiments were undertaken using the grinding product:

(i) Seeding in a saturated methanol solution of benzoic acid and 2-aminopyrimidine in a 1:1 molar ratio or 2:1 molar ratio produced single crystals of the 1:1 co-crystal **4**. After evaporation to dryness, both bulk products were confirmed to be uniform phases of **4**. m.p. 103–105°C.

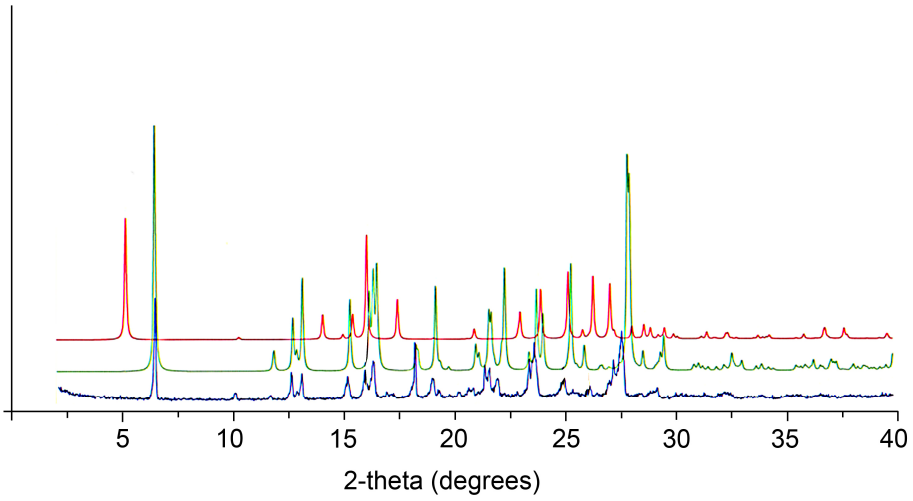


(ii) Seeding in a saturated methanol solution of benzoic acid and 2-aminopyrimidine in a 3:1 molar ratio produced single crystals of the 2:1 co-crystal **3a**. After evaporation to dryness, PXRD showed the bulk product to be principally **3a**, but with peaks that originate from **3b** and from benzoic acid (principally $2\theta \approx 8.1°$).



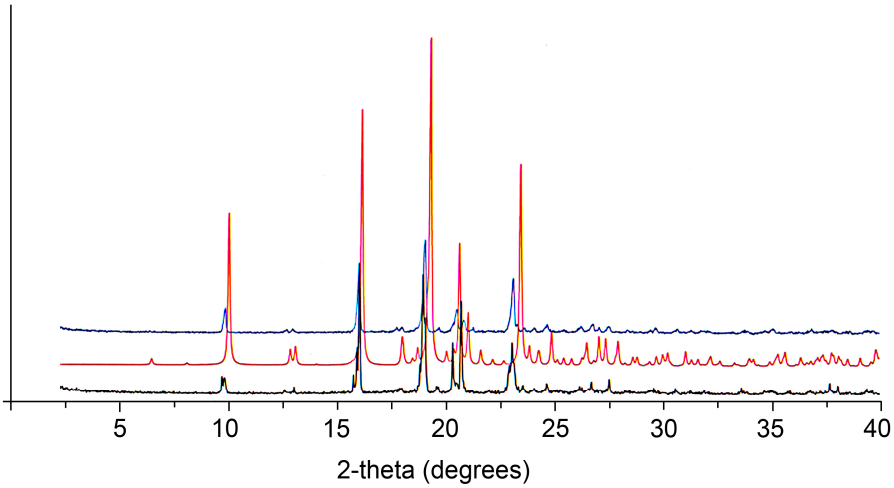
(iii) Seeding in a saturated acetonitrile solution of benzoic acid and 2-aminopyrimidine in a 2:1 molar ratio produced single crystals of the 2:1 co-crystal **3b**. After evaporation to dryness, PXRD showed the bulk material to comprise only **3a**, suggesting that **3b** is metastable in acetonitrile.

Red = simulated for **3b** (180 K)
Green = simulated for **3a** (180 K)
Blue = bulk product from seeding 2:1 MeCN solution with ground product

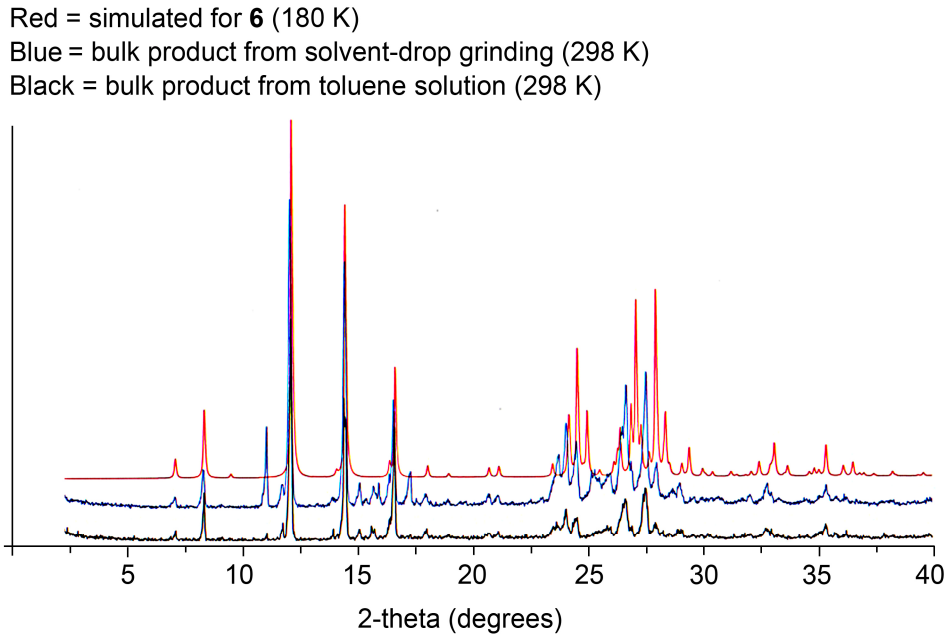


- **Salicylic acid/DABCO (2:1). 5**. Separate saturated solutions of salicylic acid (0.280 g, 0.002 mmol) and DABCO (0.110 g, 0.001 mmol) in warm methanol were combined and refluxed with stirring for 1 h. The flask was insulated and left to cool under ambient conditions, giving colourless needles of **5** after *ca* 1 h. After evaporation to dryness, the uniformity of the bulk product was confirmed by PXRD. Alternatively: salicylic acid (0.700 g, 0.005 mol), DABCO (0.275 g, 0.0025 mol) and two drops of methanol were placed in the ball mill, rotating at 650 rpm for 20 min. The product was a uniform phase of **5**. m.p. 138–139°C.

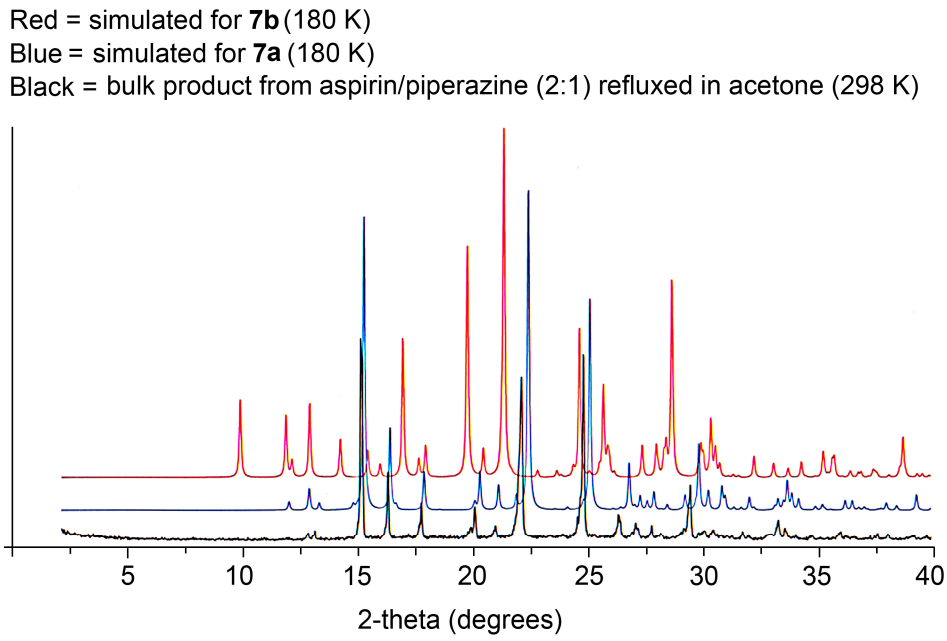
Red = simulated for **5** (180 K)
Blue = bulk product from solvent-drop grinding (298 K)
Black = bulk product from MeOH solution (298 K)



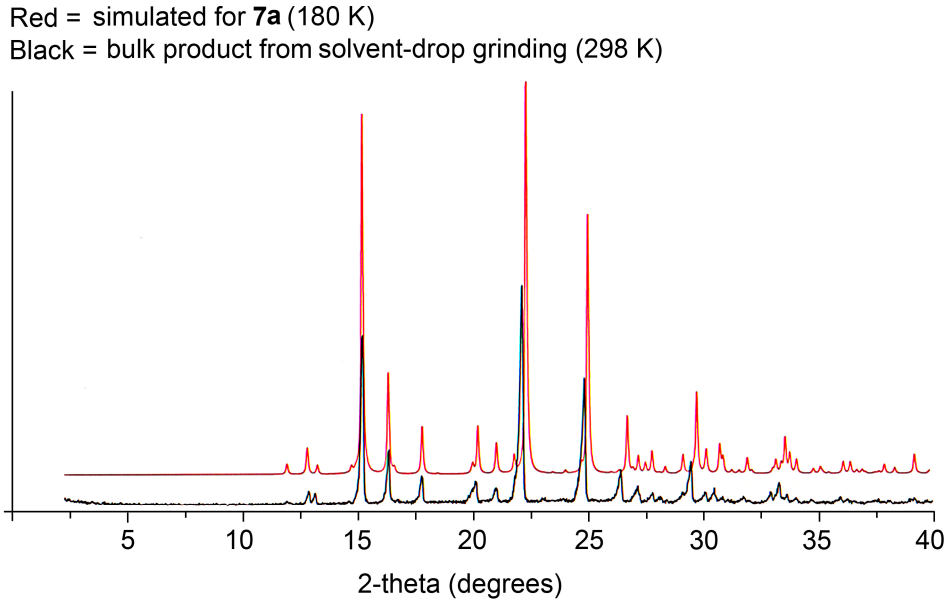
- **Salicylic acid/phenazine (2:1). 6**. Separate saturated solutions of salicylic acid (0.690 g, 0.005 mmol) and phenazine (0.450 g, 0.0025 mmol) in warm toluene were combined and refluxed with stirring for 1 h. The flask was insulated and left to cool under ambient conditions, giving colourless needles of **6** after *ca* 1 h. After evaporation to dryness, PXRD showed the product to comprise principally **6**, with trace salicylic acid remaining ($2\theta \approx 10.8°$). Alternatively, salicylic acid (0.690 g, 0.005 mol), phenazine (0.450 g, 0.0025 mol) and two drops of methanol were placed in the ball mill, rotating at 650 rpm for 20 min. The product was shown by PXRD to comprise **6**, with a larger quantity of salicylic acid remaining compared to the product from solution. m.p. 133–135°C.



- **Salicylic acid/*N*,*N*′-diacetylpiperazine (2:1). Polymorph 7a**. Aspirin (0.60 g, 0.0033 mol), piperazine (0.15 g, 0.0017 mol) and two drops of methanol were placed in the ball mill, rotating at 650 rpm for 20 min. Single crystals of **7a** were obtained by using the resulting powder to seed a saturated acetonitrile solution of aspirin and piperazine in a 2:1 molar ratio, prepared by reflux. After single-crystal analysis, the product obtained directly from the ball mill was confirmed as a uniform phase of **7a**. m.p. 100–101°C.



- **Salicylic acid/*N*,*N*′-diacetylpiperazine (2:1). Polymorph 7b**. Separate saturated solutions of aspirin (0.150 g, 0.800 mmol) and piperazine (0.037 g, 0.40 mmol) in warm acetone were combined and refluxed with stirring for 1 h. The solution was then cooled rapidly in an ice bath, producing single crystals of **7b**. On evaporation to dryness, PXRD showed the bulk product to comprise only **7a**, suggesting that **7b** is metastable in acetone.



- **Aspirin/DABCO (2:1). 8**. Aspirin (0.720 g, 0.004 mol), DABCO (0.275 g, 0.0025 mol) and two drops of methanol were placed in the ball mill, rotating at 650 rpm for 20 min. Single crystals were obtained by using the resulting powder to seed a saturated acetonitrile solution of aspirin and DABCO in a 2:1 molar ratio. After single-crystal analysis, the product obtained directly from the ball mill was confirmed as a uniform phase of **8**. The product proved to be unstable: on standing in air, peaks appear in the PXRD at $2\theta \approx 6.4$ and 10.8° after 24–48 hours, which grow more intense over time, while the peak at $2\theta \approx 10.4°$ in **8** diminishes and eventually disappears.