Electronic Supplementary Information (ESI)

Advantages of mechanochemical cocrystallisation in the solid-state chemistry of pigments: Colour-tuned fluorescein cocrystals

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1. Materials

Fluorescein was obtained from *Fluka Analytical* (*puriss. p.a.*), while acridine (97%), phenanthridine (98%), pyrazine (>99%), ethanol (absolute, *puriss. p.a.*) and nitromethane (>99%) were purchased from *Sigma Aldrich*. All chemicals were used as received.

2. Mechanochemical preparation of the fluorescein cocrystals

The mechanochemical cocrystal syntheses were performed using a *Retsch MM200 Mixer Mill*. In a typical milling experiment, a total of 200 mg of a physical mixture consisting of fluorescein and the cocrystal former (in either 1:1 or 1:2 ratios) was added to 15 ml stainless steel grinding jar, along with 50 μL of nitromethane and two 7 mm stainless steel milling balls. The mixer mill was operated at 30 Hz for 30 minutes. The obtained solids were subsequently analysed by powder X-ray diffraction, differential-scanning calorimetry and thermal gravimetry.

3. Solution-based crystallization of the fluorescein cocrystals

In a typical crystallisation experiment, about 10 mg of a mechanochemically prepared cocrystal was added to 7-15 mL of a hot solvent (*i.e.* acetonitrile, ethanol, dimethylformamide, nitrobenzene, 3-picoline and pyridine) and heated to partially dissolve the solid. The obtained suspension was then sonicated at 25 kHz using an *Elma Transsonic TI-H-20* ultrasonic cleaning bath and a *Ferm FHG-2000* heat gun to facilitate the solubilisation of the cocrystals. The obtained solution was then filtered through a cotton plug and left to evaporate slowly in a partially covered crystallisation vial at ambient conditions. Crystals suitable for single crystal X-ray diffraction experiments were observed in up to four weeks.

4. Crystallographic studies

4.1. Powder X-ray diffraction (PXRD)

PXRD patterns were collected on a *Philips X'Pert PRO MPD* powder X-ray diffractometer (equipped with an *X'Celerator RTMS* detector) using Ni-filtered Cu$K_{\alpha 1}$ radiation ($\lambda = 1.54056$ Å), and operating at 40 kV and 40 mA. The mechanochemically prepared samples (20-50 mg) were mounted on a flat glass bracket (specimen size 10×14×0.5 mm^3) and followed by data collection 298 K (aided by the *X'Pert Data Collector* program) (software version 2.2h, Panalytical B.V.). The scans were performed in the continuous mode (gonio scan axis) in the 2θ range of 3.0-60.0° with counting times of 40 s (for cocrystal screening purposes) and 260 s (for structure solution purposes). The data was analysed using the *X'Pert Highscore Plus* program.[1]

For crystal structure determination from powder X-ray diffraction data, indexing was performed using the *DICVOL06* program.[2] The most probable space group was determined by analysing the individual diffracted intensities extracted using the Pawley refinement[3] procedure implemented in the program *DASH 3.3*.[4] Structure solution and Rietveld refinement[5] were performed in the software *TOPAS Academic*.[6] Molecular geometries were defined by rigid bodies and constraints were used to specify bond lengths, bond angles and most of the torsion angles. Standard uncertainties on atom coordinates were calculated using the bootstrap method. Crystallographic and refinement parameters for crystal structures **A**, **B** and **C** are given in Table 1. The Rietveld plots for crystal structures **A**, **B** and **C** are shown in Fig. S1-S3.

Table 1. Crystallographic and refinement parameters for solids obtained mechanochemically. The crystal structures were solved using powder X-ray diffraction data.

Compound reference	**A**	**B**	**C**
Chemical formula	$(C_{20}H_{12}O_5)\cdot 2(C_{13}H_9N)$	$(C_{20}H_{12}O_5)\cdot 2(C_{13}H_9N)$	$(C_{20}H_{12}O_5)\cdot(C_4H_4N_2)$
M_r	690.75	690.75	412.40
Crystal system	orthorhombic	orthorhombic	monoclinic
a/Å	25.2967(29)	27.7695(27)	7.81238(87)
b/Å	16.8422(26)	15.4243(20)	19.0241(17)
c/Å	7.88909(77)	7.98361(73)	12.7880(14)
α/°	90	90	90
β/°	90	90	91.1378(67)
γ/°	90	90	90
V/Å^3	3361.17(72)	3419.58(64)	1900.22(34)
T/K	293(2)	293(2)	293(2)
Space group	$Cmc2_1$	$Cmc2_1$	$P2_1/c$
Z	4	4	4
Radiation type	CuK_α	CuK_α	CuK_α
R_{wp}	0.048	0.047	0.052
R_p	0.038	0.036	0.040
R_{Bragg}	0.018	0.012	0.028
χ^2	2.073	3.755	1.692
No. of parameters	42	36	39
CCDC deposition number	908178	908179	908180

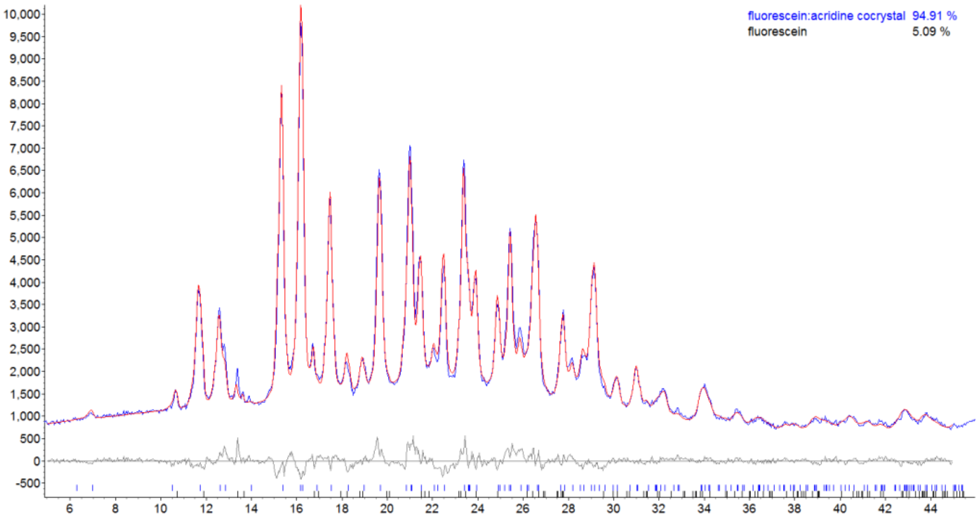

Figure S1. Rietveld plot for cocrystal **A** (*red*: calculated, *blue*: measured, *grey*: difference). The peak position represented with tick marks.

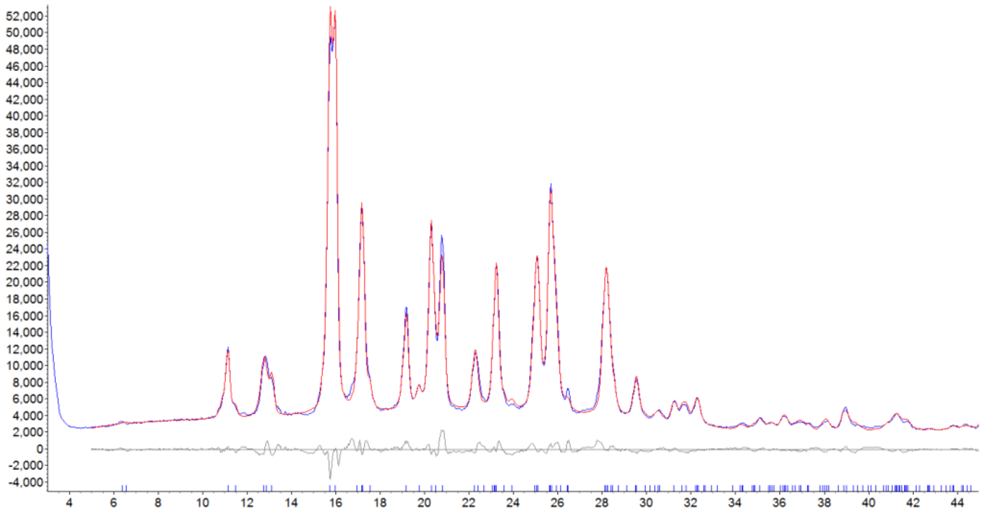

Figure S2. Rietveld plot for cocrystal **B** (*red*: calculated, *blue*: measured, *grey*: difference). The peak position represented with tick marks.

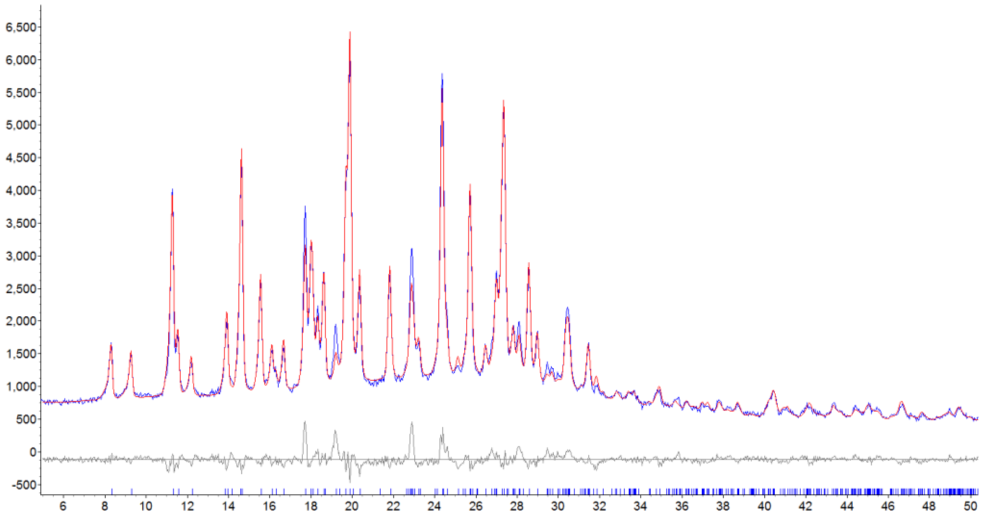

Figure S3. Rietveld plot for cocrystal **C** (*red*: calculated, *blue*: measured, *grey*: difference). The peak position represented with tick marks.

4.2. Single crystal X-ray diffraction (SXRD)

SXRD data was collected using on an *Agilent Gemini Ultra* single crystal X-ray diffractometer equipped with an *Eos CCD* detector. The data were collected at 120 K using Cu$K_{\alpha 1}$ radiation (λ = 1.5418 Å). The data were collected and processed using the *CrysAlis*Pro program.[7] The datasets were corrected for Lorentz and polarization effects. Empirical absorption corrections were performed using spherical harmonics implemented in the *SCALE3 ABSPACK* scaling algorithm.[8] Structure solution and refinement were accomplished using *SHELXS-97* and *SHELXL-97*,[9] respectively. The structures were solved using direct methods. Non-hydrogen atoms missing in the initially obtained model were indentified from the difference Fourier map within several refinement steps. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms associated with carbon atoms were refined in geometrically constrained positions (or in positions identified in the difference Fourier map, if needed to achieve a reasonable model of the investigated compound). Hydrogen atoms associated with oxygen atoms were calculated in an optimal hydrogen bonding geometry. Crystallographic and refinement parameters for crystal structures **1**, **2** and **3** are given in Table 2.

Table 2. Crystallographic and refinement parameters for solids obtained through solution crystallisation. The crystal structures were solved using single crystal X-ray diffraction data.

Compound reference	**1**	**2**	**3**
Chemical formula	$(C_{20}H_{12}O_5)\cdot 2(C_{13}H_9N)$	$(C_{20}H_{12}O_5)\cdot 2(C_{13}H_9N)$	$(C_{20}H_{12}O_5)\cdot(C_4H_4N_2)\cdot(CH_4O)$
M_r	690.72	690.72	808.76
Crystal system	monoclinic	orthorhombic	triclinic
a/Å	8.6428(3)	27.6912(12)	7.6060(4)
b/Å	19.6270(7)	15.3574(9)	11.1161(9)
c/Å	20.9268(9)	7.8814(4)	12.0927(8)
α/°	90	90	115.965(7)
β/°	98.748(4)	90	93.139(5)
γ/°	90	90	92.811(6)
V/Å^3	3508.6(2)	3351.7(3)	914.80(11)
T/K	120(2)	120(2)	120(2)
Space group	$P2_1/c$	$Cmc2_1$	$P\bar{1}$
Z	4	4	1
Radiation type	CuK_α	MoK_α	MoK_α
μ/mm^{-1}	0.686	0.089	0.107
No. of refl. measured	11932	4864	5815
No. of indep. reflections	6669	2671	3211
R_{int}	0.0237	0.0388	0.0251
R_1 ($I > 2\sigma(I)$)	0.0426	0.0383	0.0521
$wR(F^2)$ ($I > 2\sigma(I)$)	0.1066	0.0756	0.1379
R_1 (all data)	0.0573	0.0521	0.0721
$wR(F^2)$ (all data)	0.1176	0.0808	0.1496
GooF	1.026	0.972	1.078
CCDC deposition number	908181	908183	908184

5. Thermal analyses

5.1. Differential-scanning calorimetry (DSC)

The DSC measurements were performed using the *Mettler-Toledo DSC822e* calorimeter equipped with an autosampler (*Mettler-Toledo TSO801RO*). In a typical experiment, 3-7 mg of the sample was placed in a 40 µl aluminium crucible, covered with a pierced aluminium lid. The sample was then loaded into the calorimeter and heated from 25 to 300 °C at a rate of 10 K min^{-1} in an N2 atmosphere (gas flow). The data was analysed using *STAR^e* software.[10] DSC thermograms of samples **A**-**C** and **1**-**3** are shown in Figures S4-S9.

5.2. Thermal gravimetry (TG)

Thermogravimetric measurements were performed using *the Mettler-Toledo TGA/SDTA851^e* thermal analyser equipped with an autosampler (*Mettler-Toledo*

TSO801RO). In a typical experiment, 6-12 mg of a sample was placed in a 100 µl aluminium crucible, loaded into the furnace, and heated from 30 to 400 °C at a rate of 10 K min^{-1} in an N_2 atmosphere (gas flow). The data was analysed using the *STAR^e* program.[10] TG thermograms of compounds **A**-**C** are shown in Figures S7-S9. TG analyses were not performed on samples **1**-**3**, as these samples could only be prepared in insufficiently small amounts.

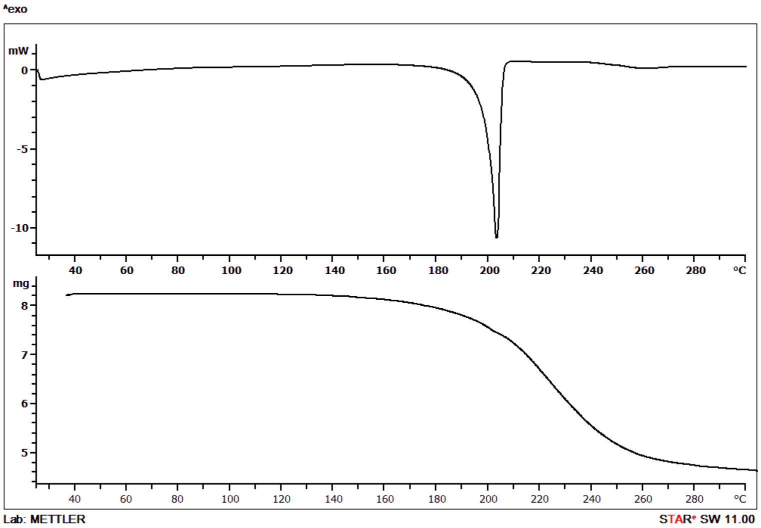

Figure S4. DSC (top) and TG (bottom) thermograms of cocrystal **A** (T_m: 199.3 °C).

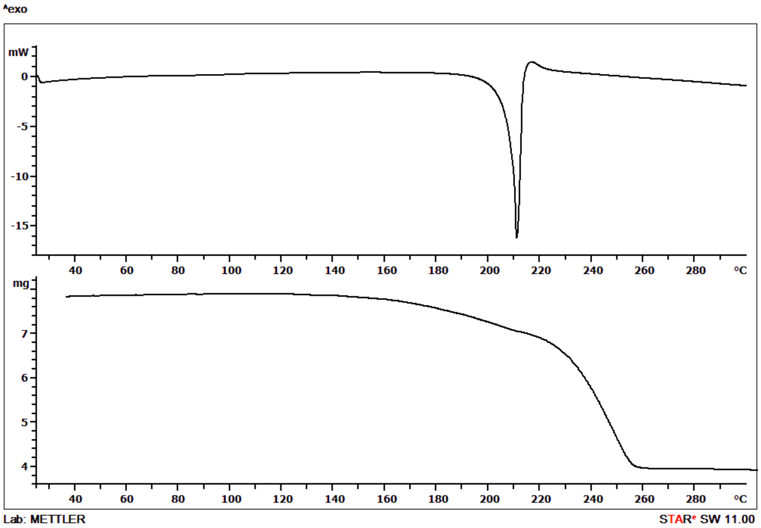

Figure S5. DSC (top) and TG (bottom) thermograms of cocrystal **B** (T_m: 208.4 °C).

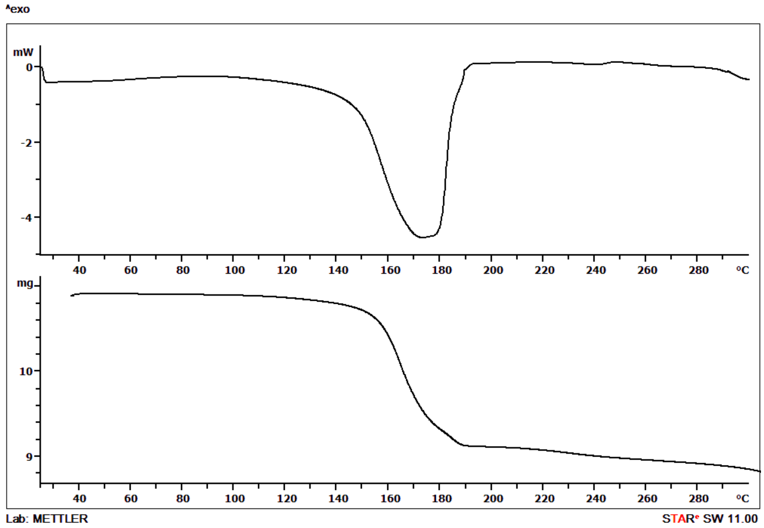

Figure S6. DSC (top) and TG (bottom) thermograms of cocrystal **C** (T_m: 145.3 °C).

Figure S7. DSC thermogram of cocrystal **1** (T_m=177.3 °C; an additional thermal event occurs in the 115-160 °C temperature range).

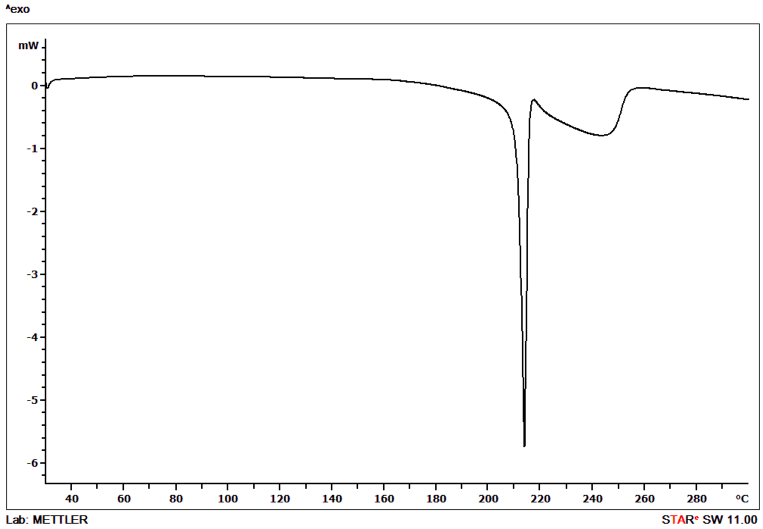

Figure S8. DSC thermogram of cocrystal **2** (T_m: 211.2 °C).

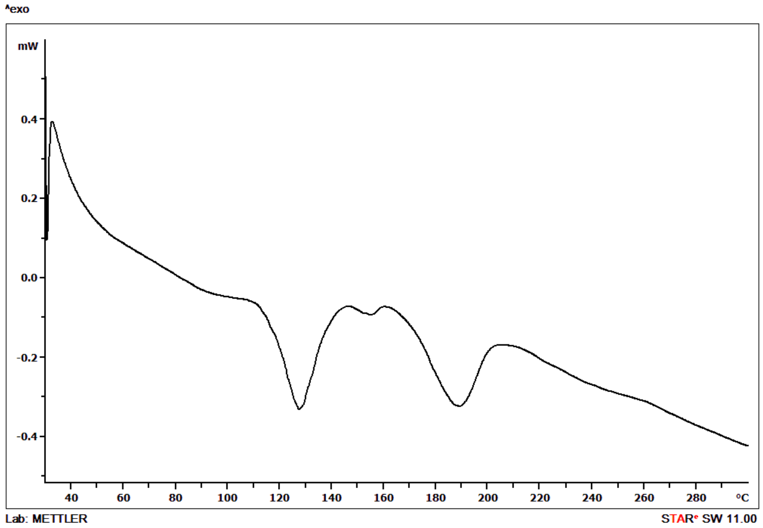

Figure S9. DSC thermogram of cocrystal **3** (T_m: 117.1 °C).

6. Spectroscopic studies

UV-Vis spectra of solids **A**, **B** and **C** were recorded using a *Perkin Elmer Lambda 750* spectrophotometer equipped with an integrating sphere. The obtained data was processed using the *R* software package.[11] The spectra are shown on Figure S10. The UV-Vis spectra of samples **1-3** were not studied, as the samples could only be prepared in insufficiently small amounts.

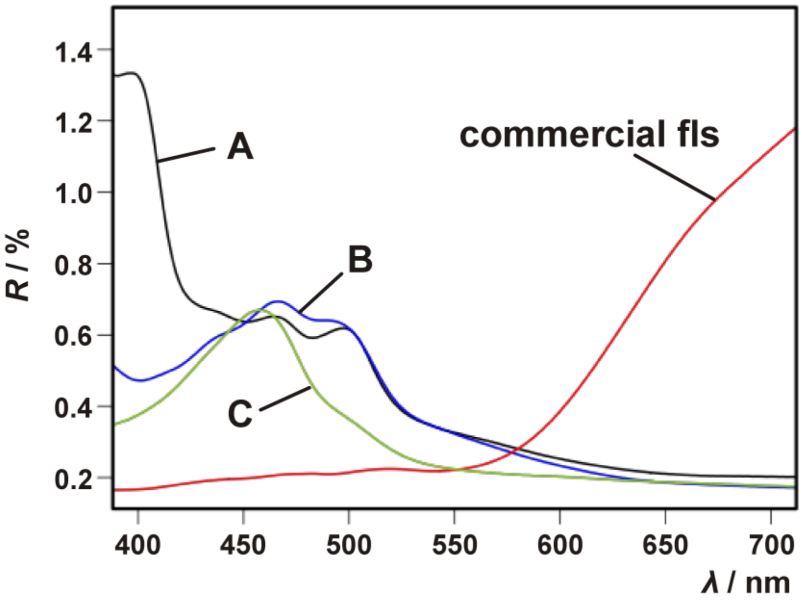

Figure S10. The visible region of the solid-state reflectance spectra of compounds **A** (black), **B** (blue), **C** (green), as compared to the spectrum of commercial **fls** (red).

7. References

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