Electronic Supplementary Material (ESI) for CrystEngComm.

Supplementary Information

for

"SDPD-SX: combining a single crystal X-ray diffraction setup with advanced powder data structure determination for use in early stage drug discovery"

Kabova et al, 2022

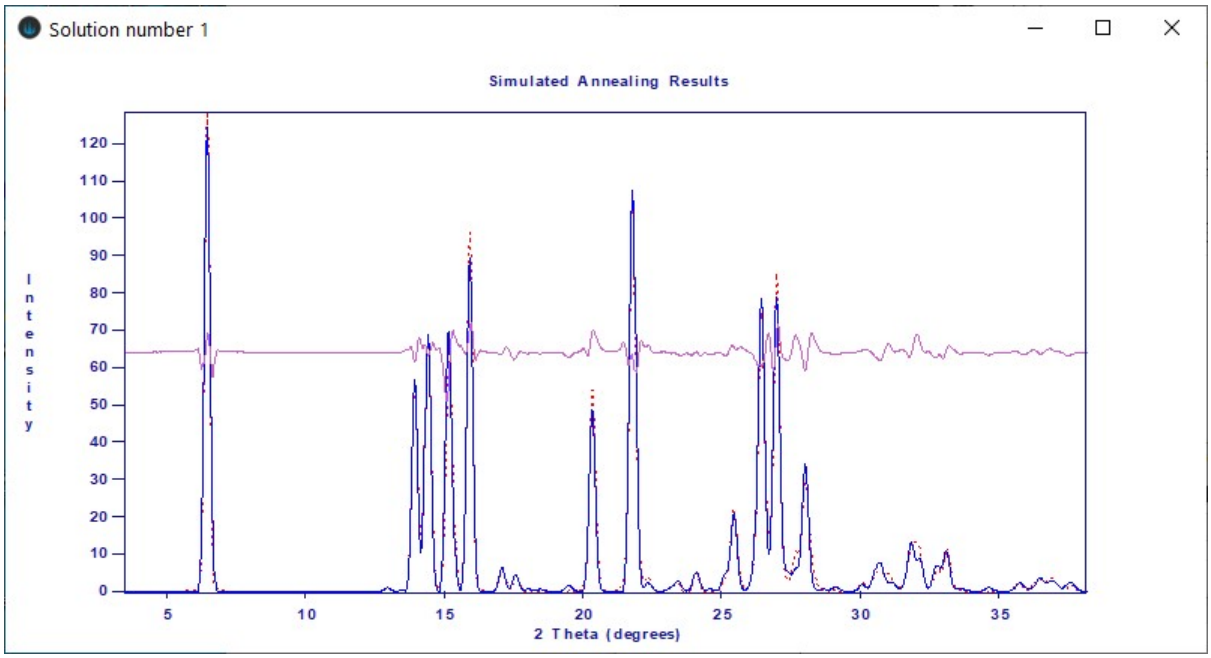


Figure S1: Best DASH fit to mefenamic acid data.

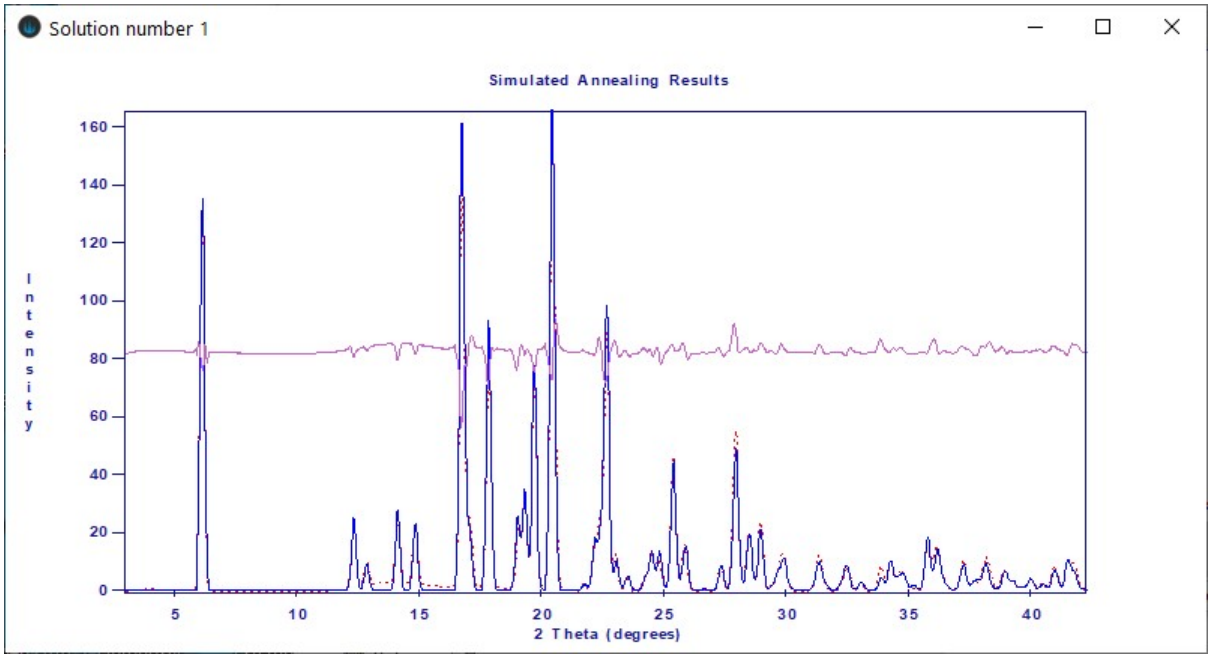


Figure S2: Best DASH fit to ibuprofen data.

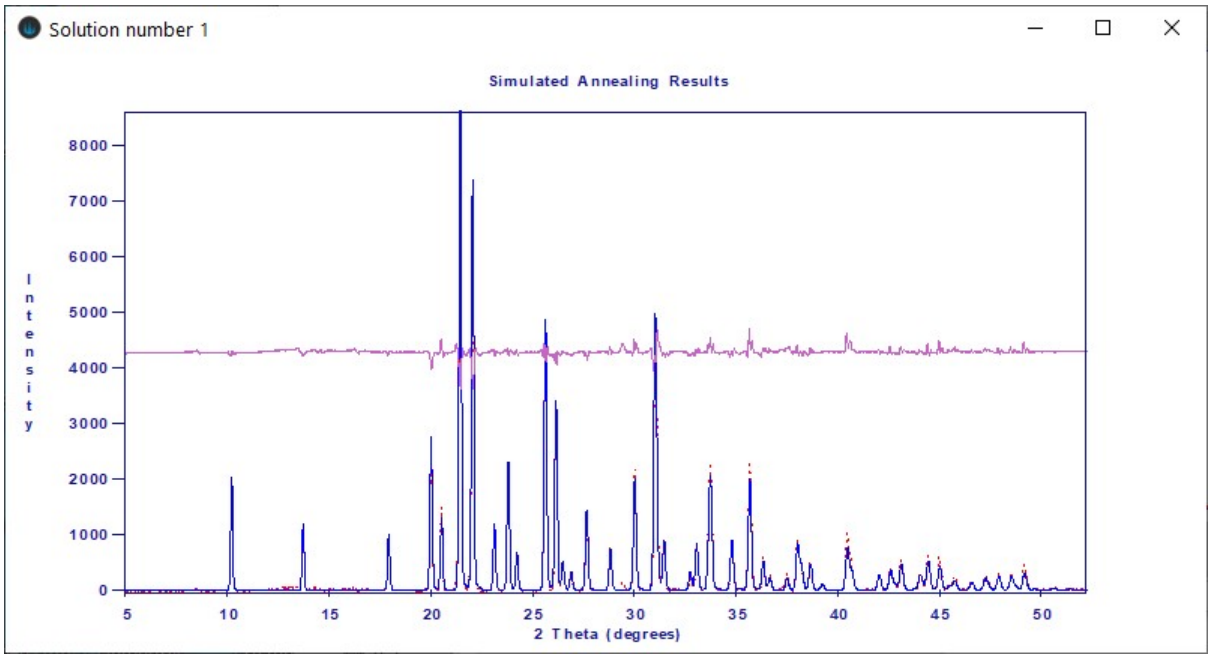


Figure S3: Best DASH fit to L-Glutamic acid data.

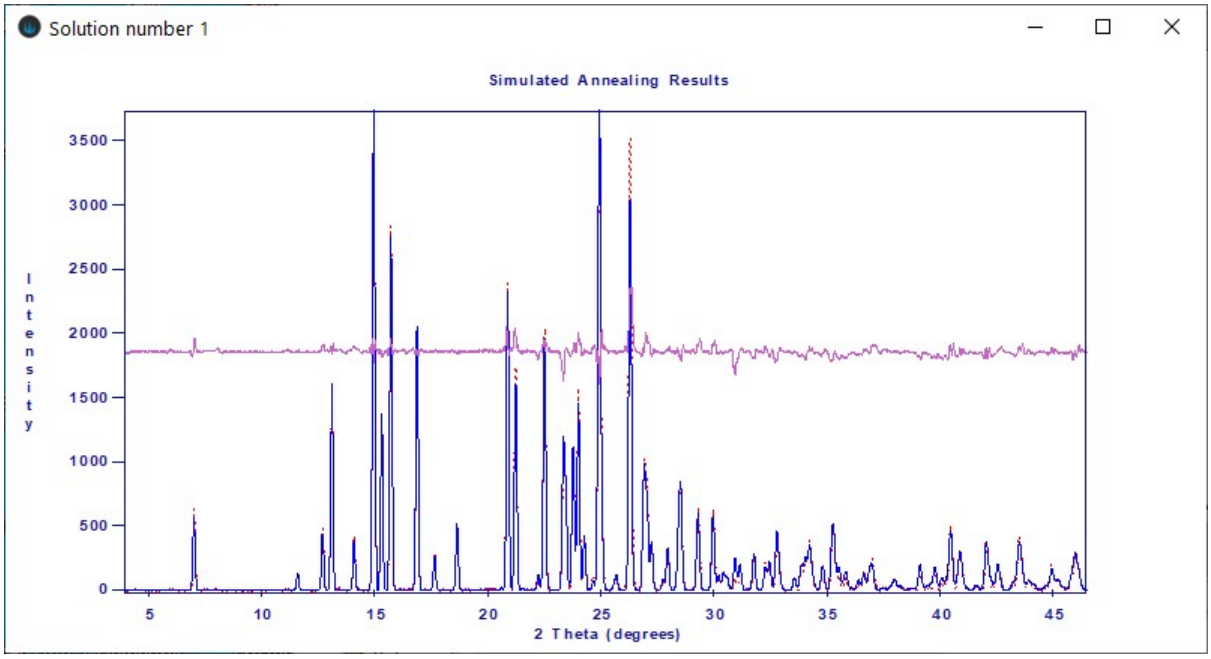


Figure S4: Best DASH fit to sertraline.HCl data.

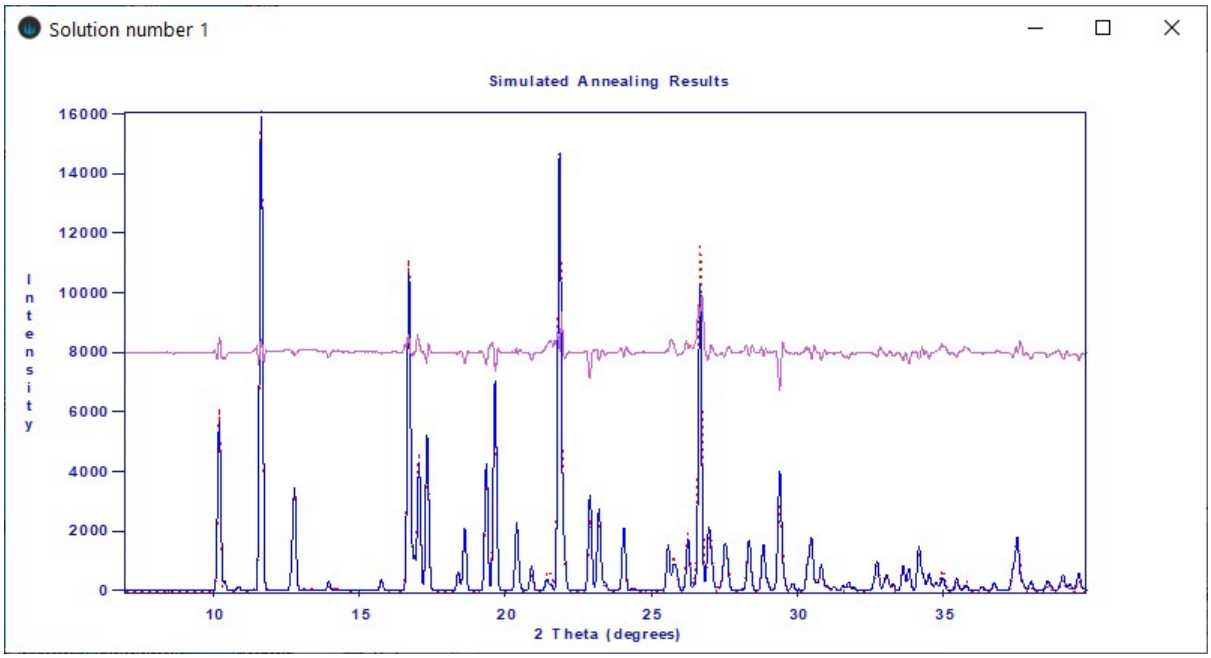


Figure S5: Best DASH fit to indomethacin data.

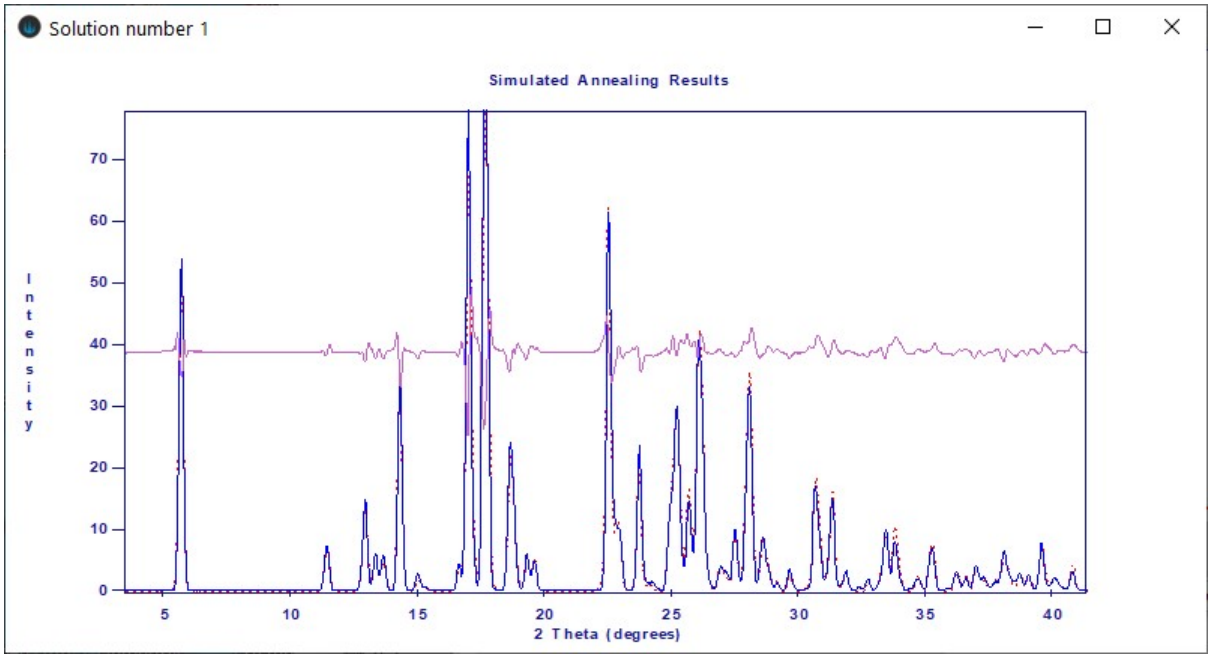


Figure S6: Best DASH fit to lansoprazole data.

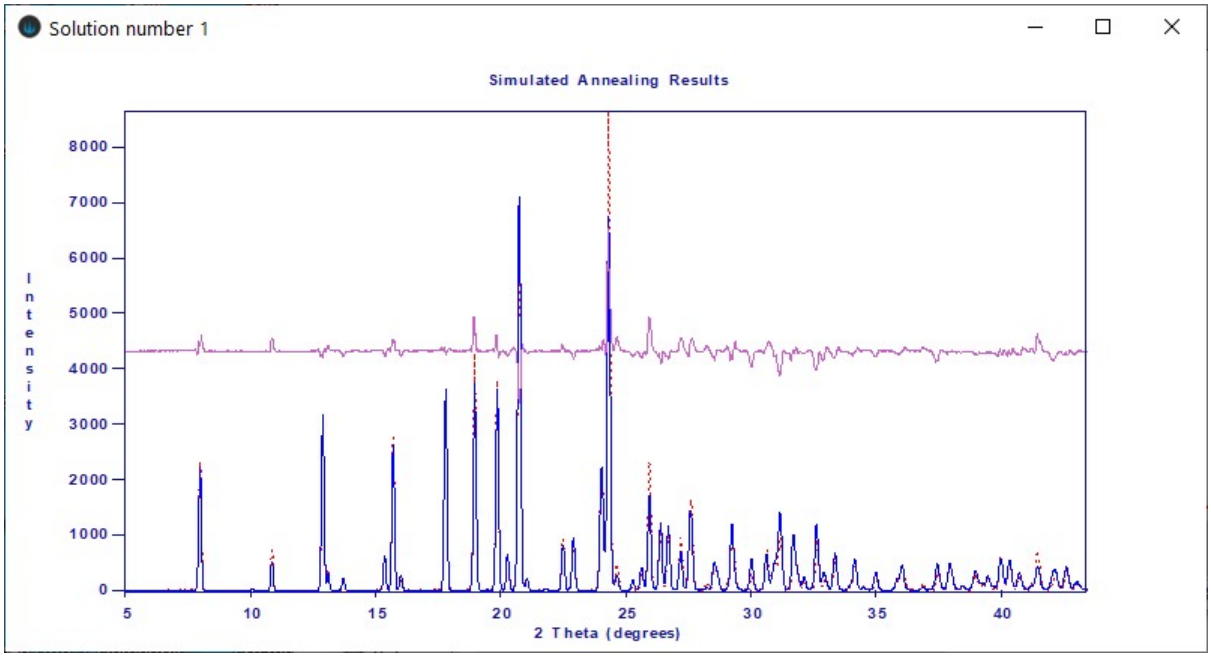


Figure S7: Best DASH fit to chloramphenicol data.

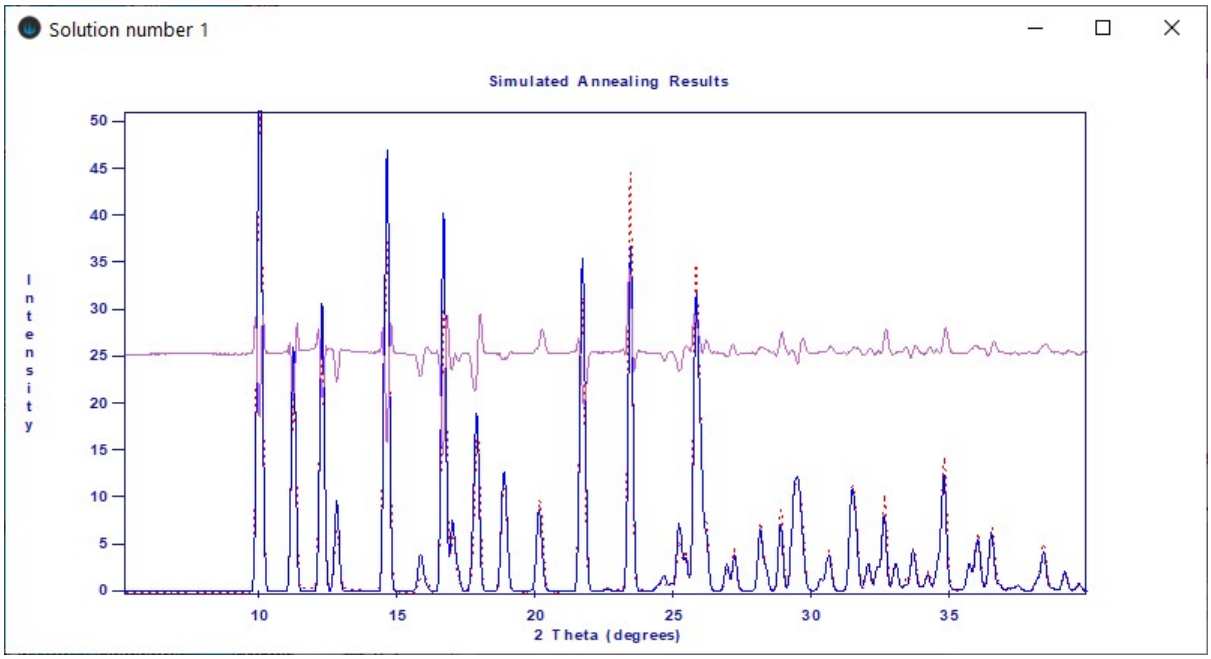


Figure S8: Best DASH fit to cefadroxil.H_2O data.

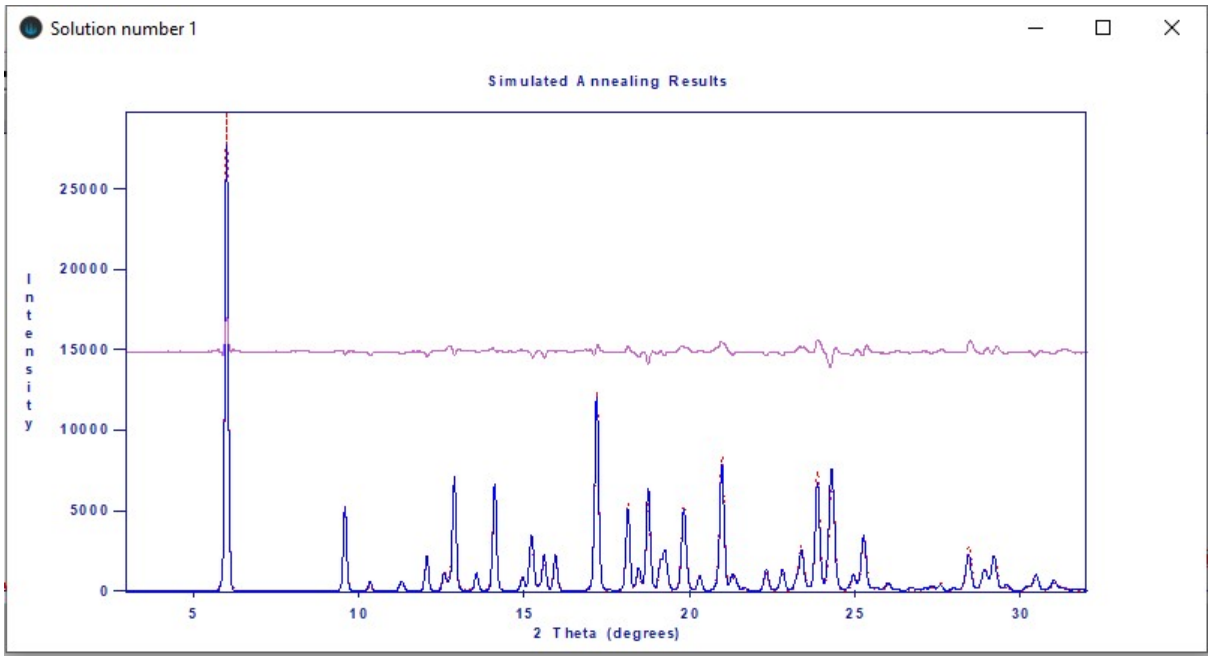


Figure S9: Best DASH fit to imatinib data.

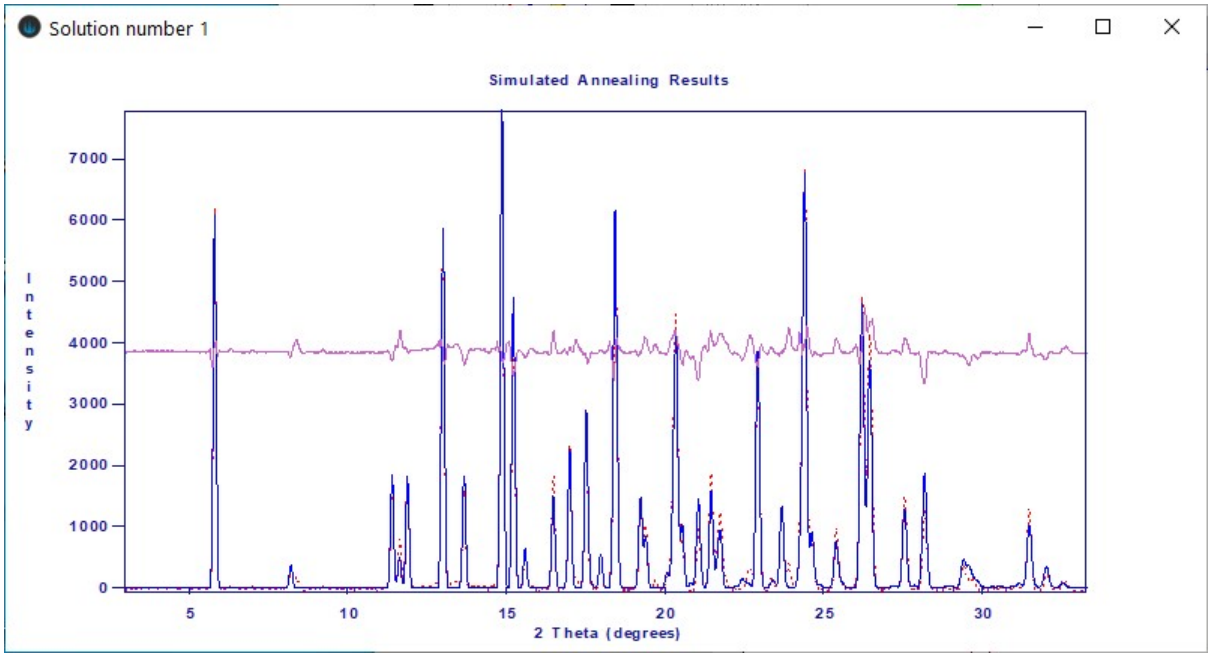


Figure S10: Best DASH fit to carvedilol data.

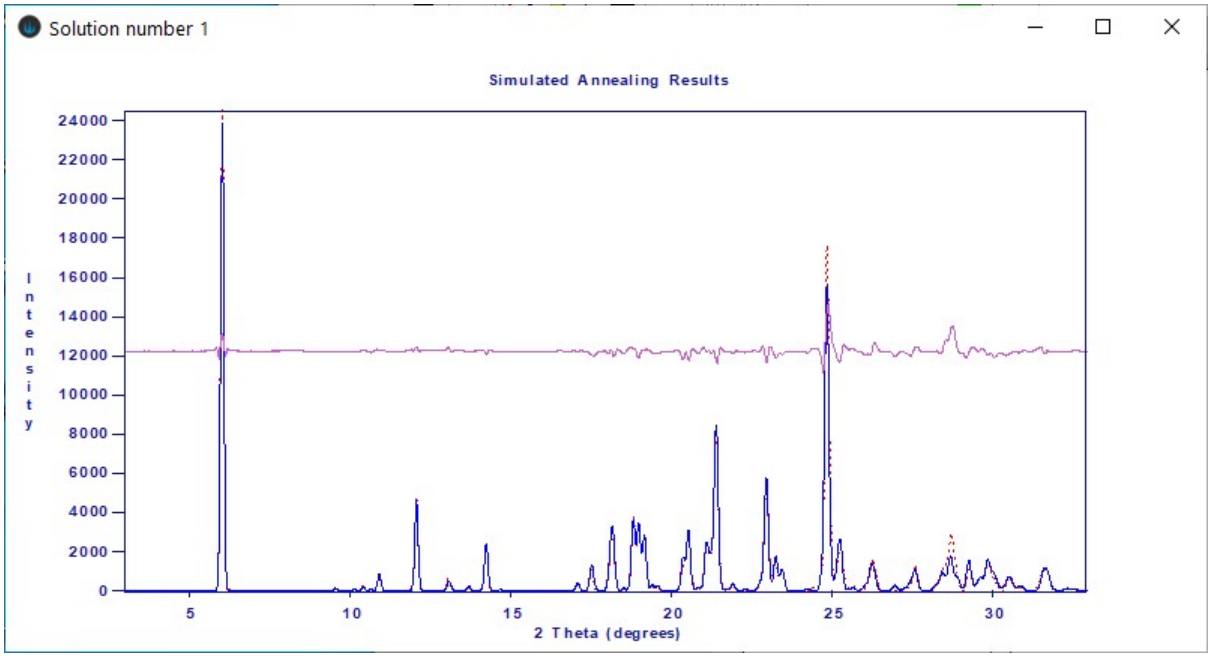


Figure S11: Best DASH fit to furosemide data.

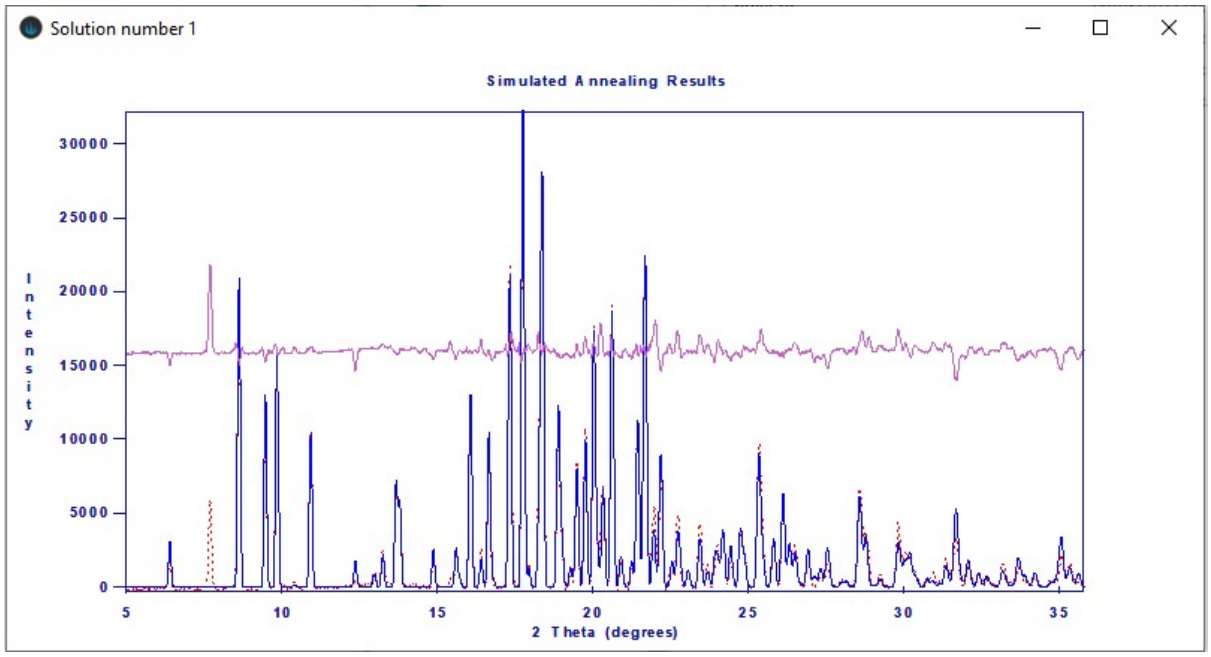


Figure S12: Best DASH fit to ritonavir data.

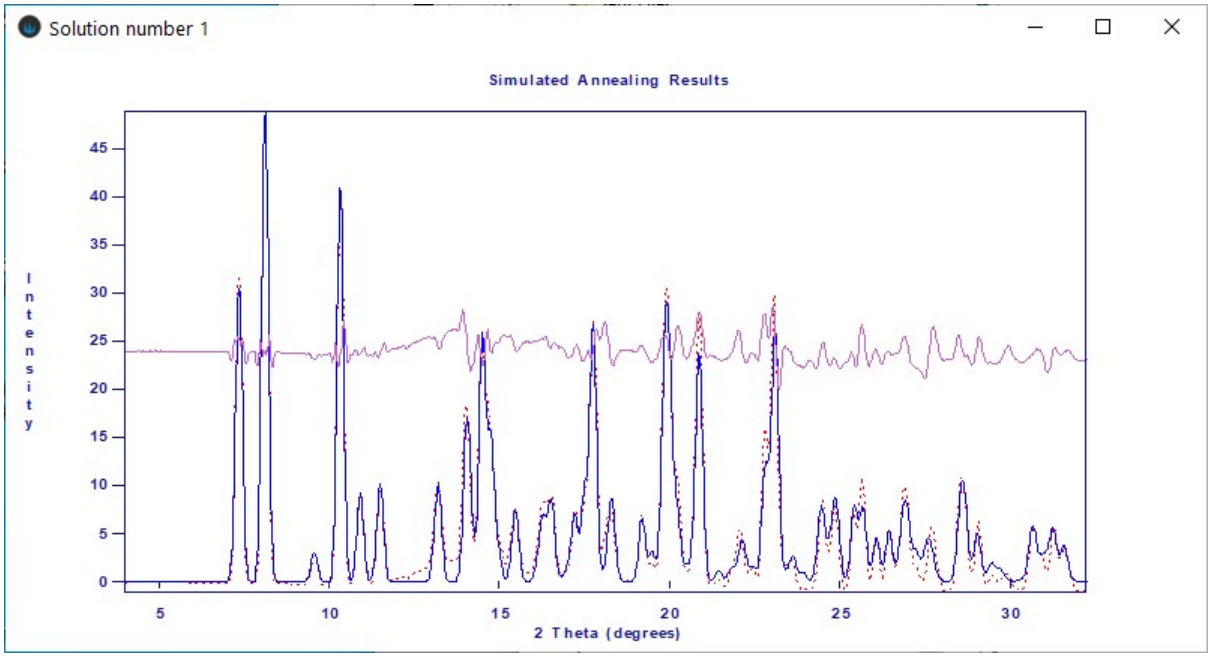


Figure S13: Best DASH fit to sildenafil citrate.H_2O data.

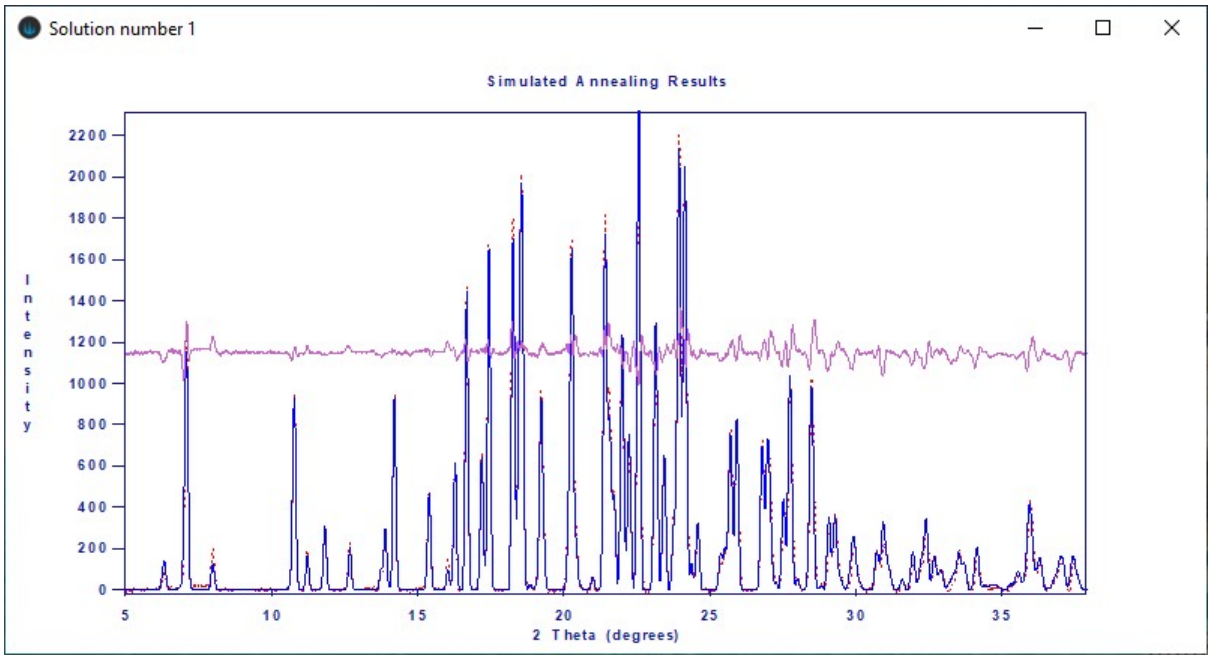
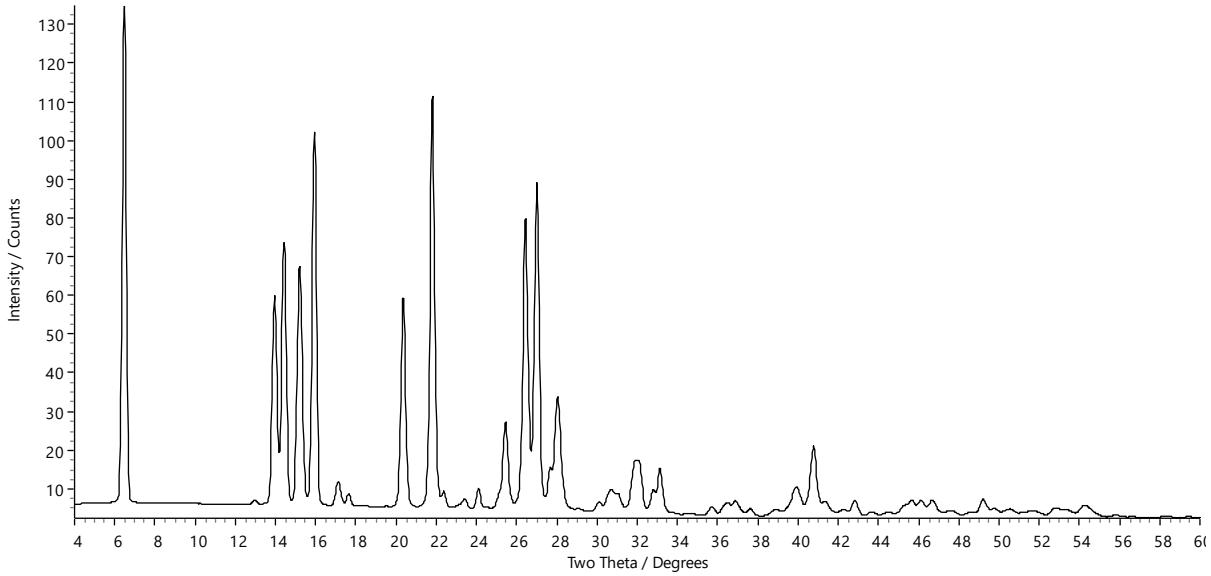
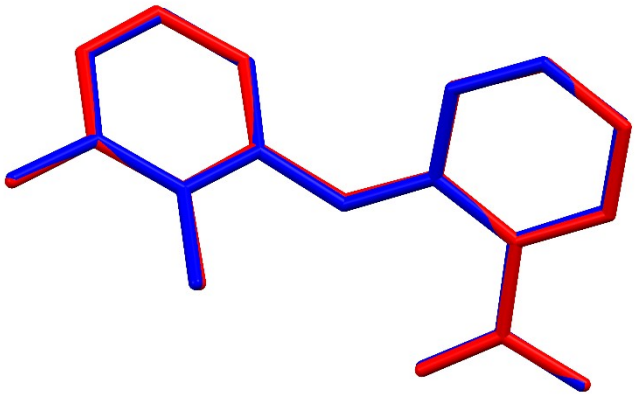


Figure S14: Best DASH fit to paroxetine.HCl.½H_2O data.





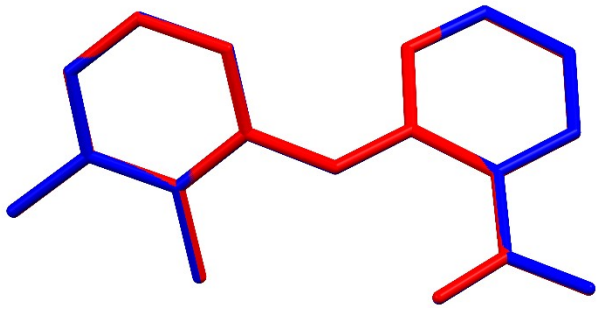


Figure S15: **Top**: Powder diffraction data for mefenamic acid. **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.

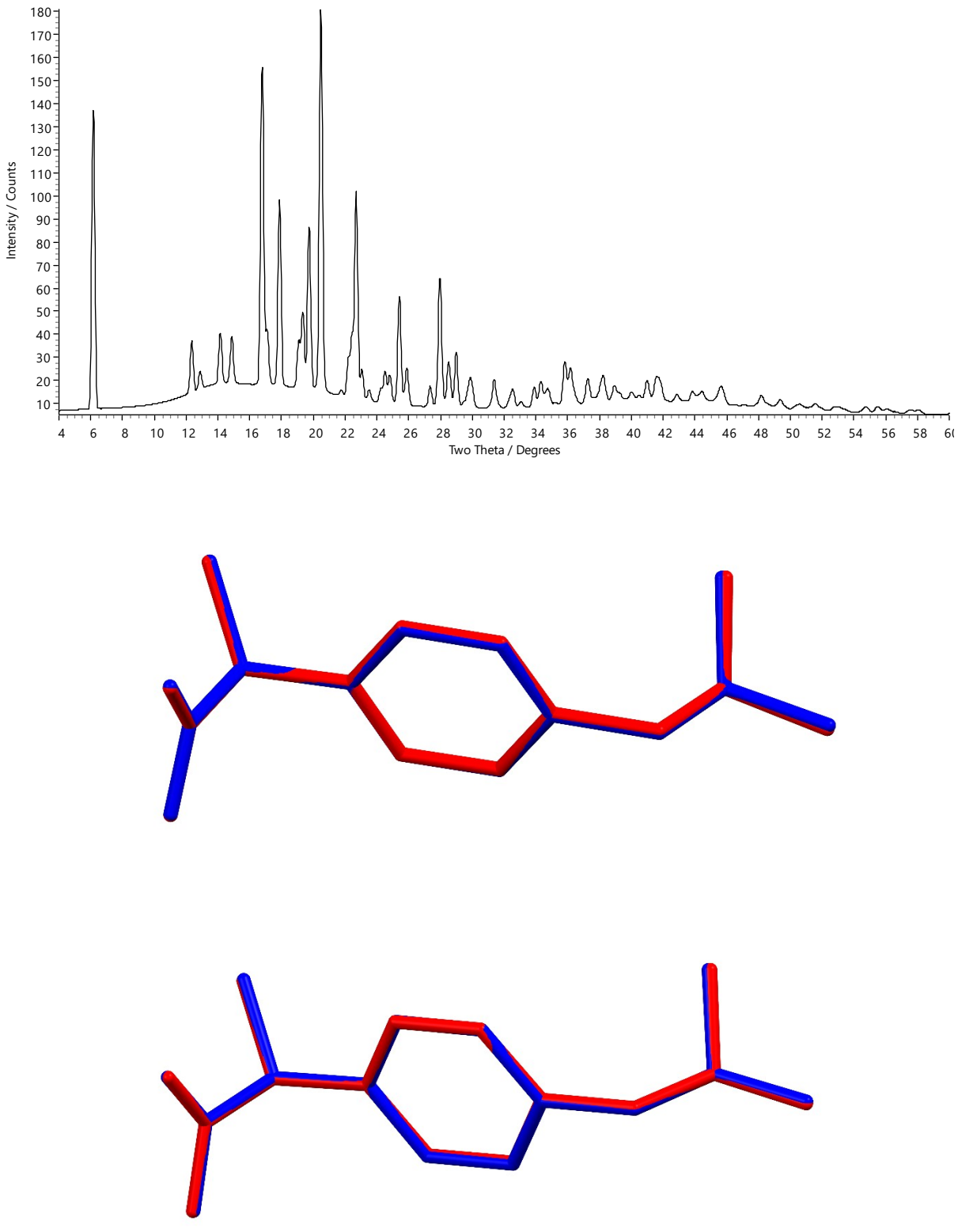


Figure S16: **Top**: Powder diffraction data for ibuprofen. **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.

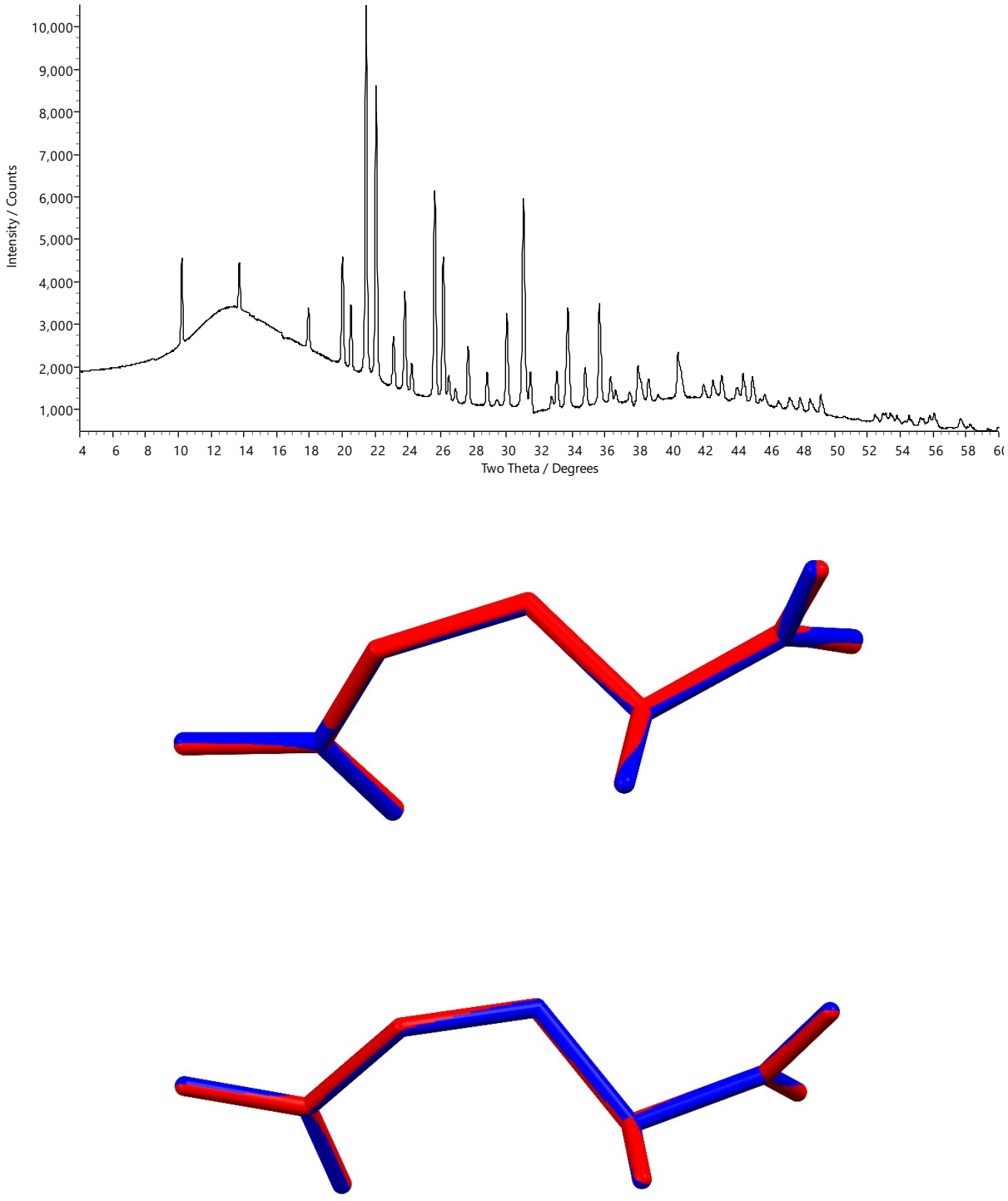
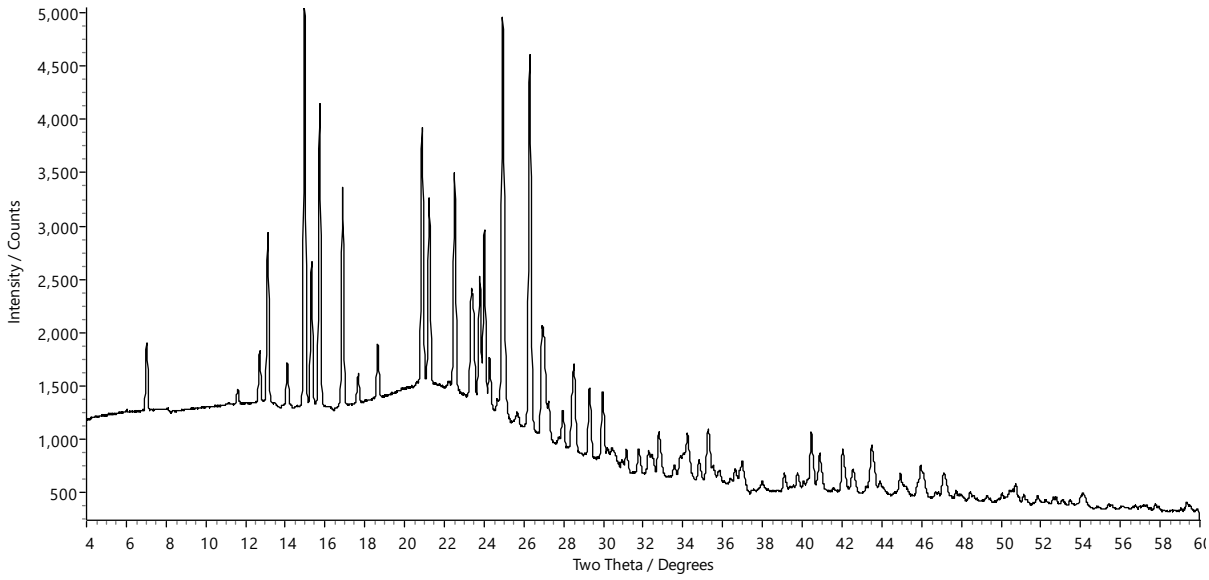


Figure S17: **Top**: Powder diffraction data for L-Glutamic acid. **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.



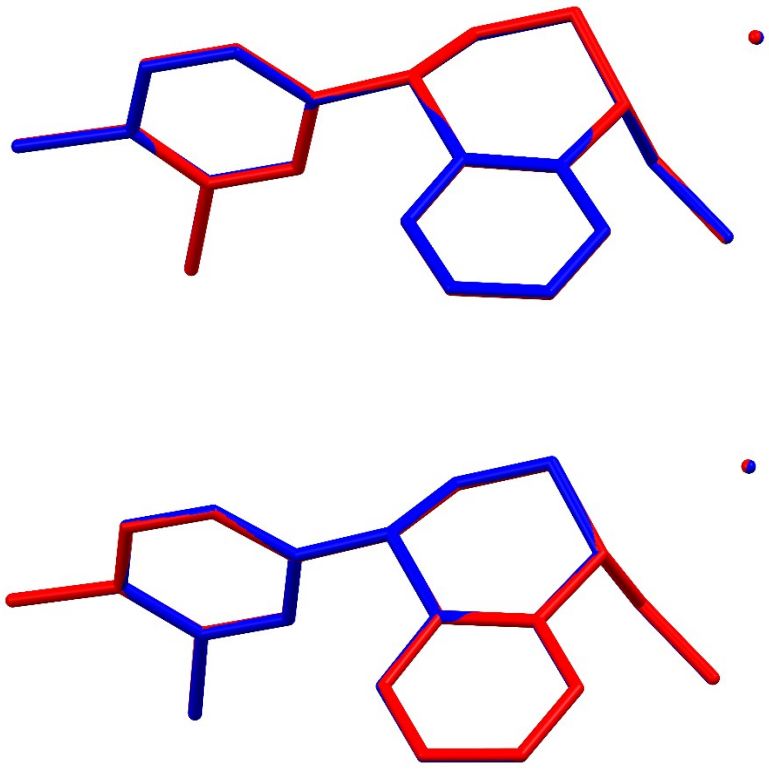
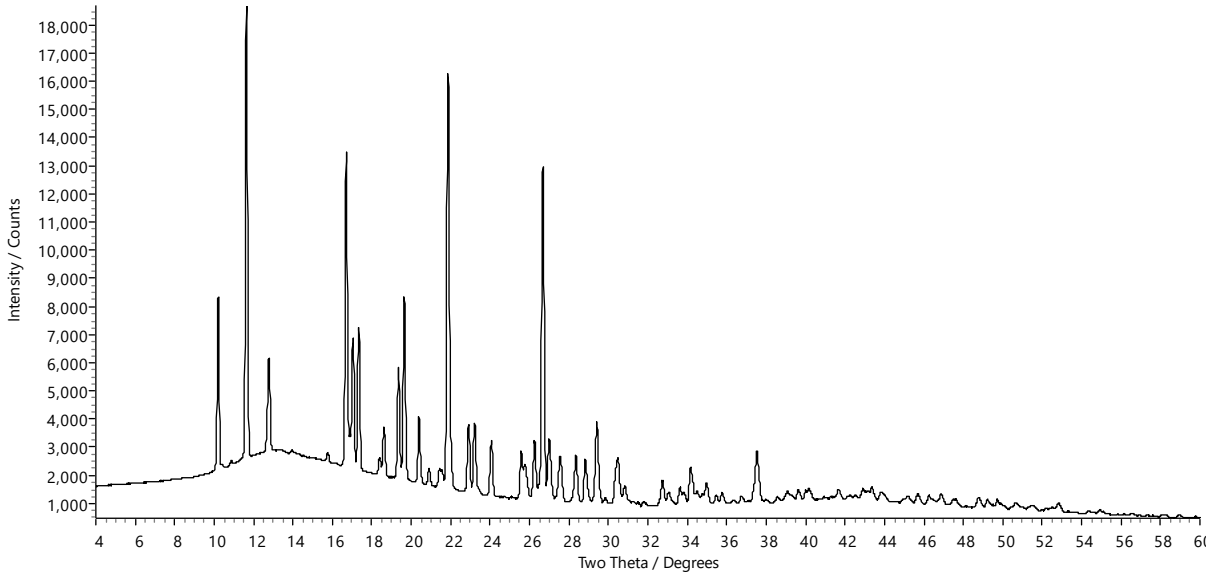


Figure S18: **Top**: Powder diffraction data for sertraline.HCl. **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.



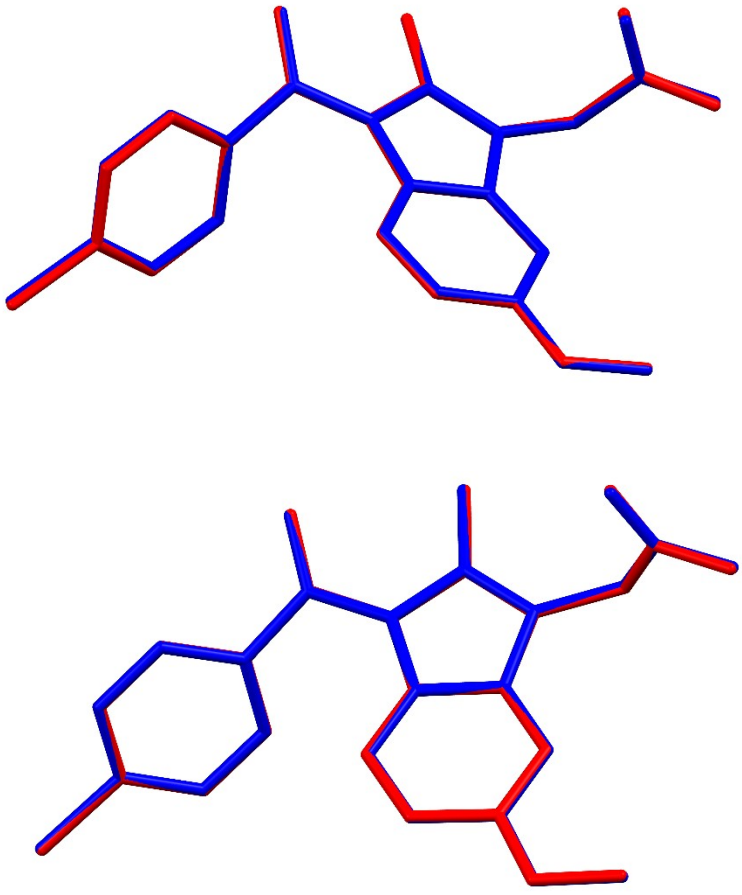
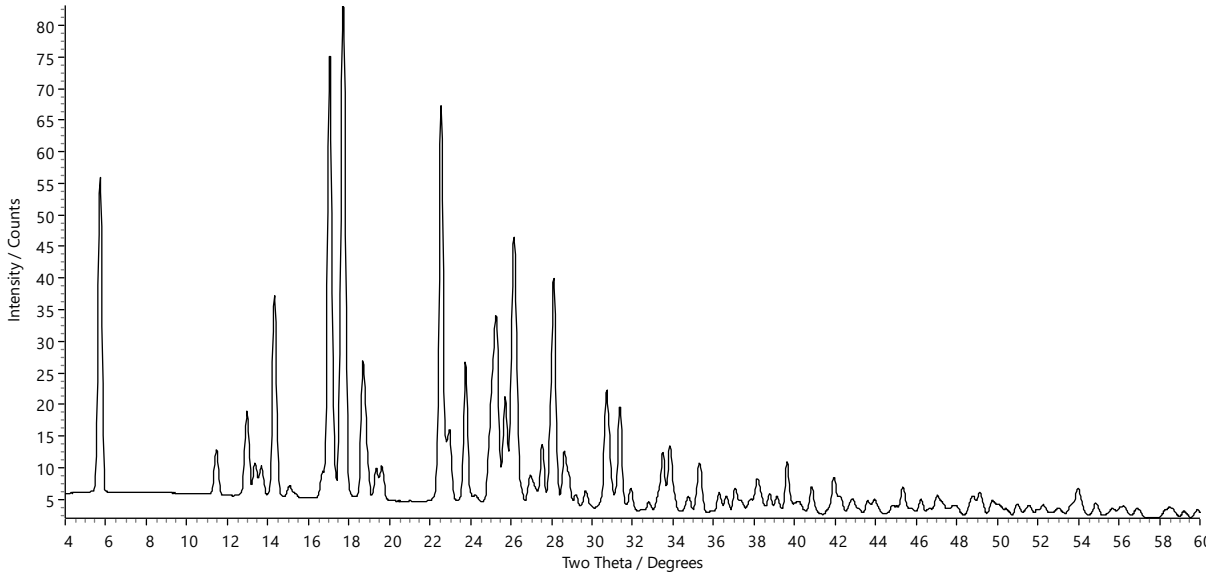
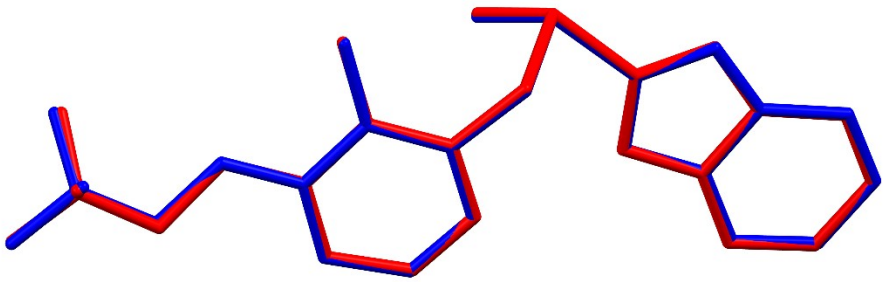


Figure S19: **Top**: Powder diffraction data for indomethacin. **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.





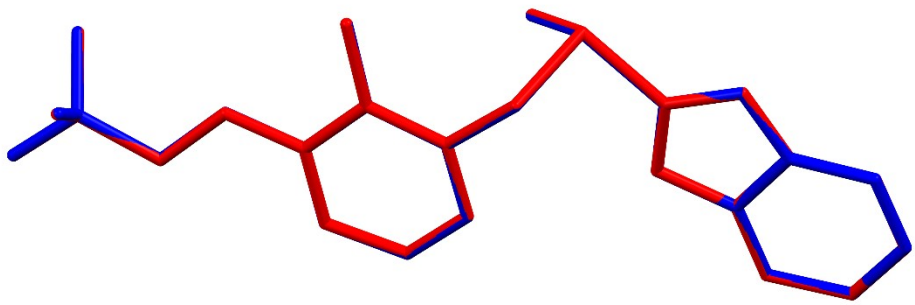
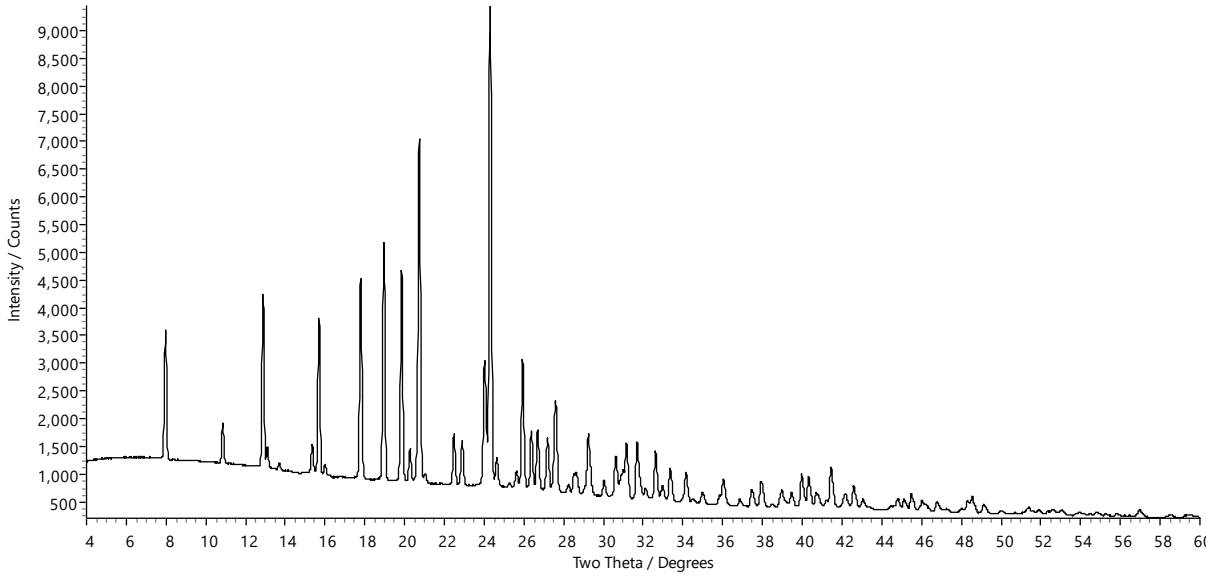


Figure S20: **Top**: Powder diffraction data for lansoprazole. **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.



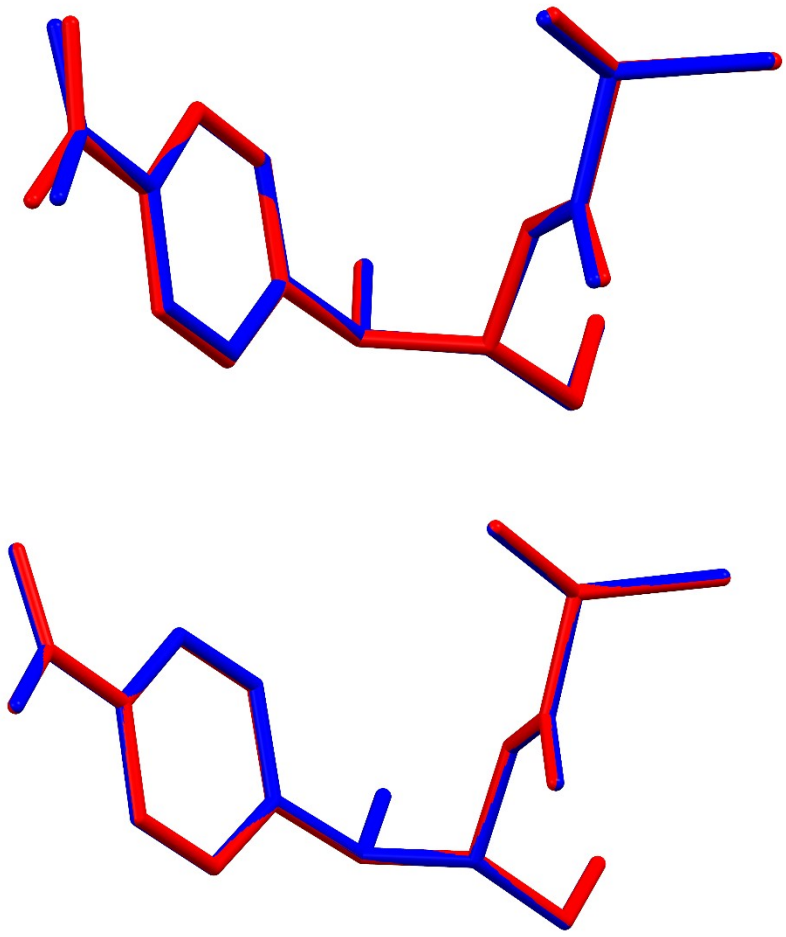


Figure S21: **Top**: Powder diffraction data for chloramphenicol. **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.

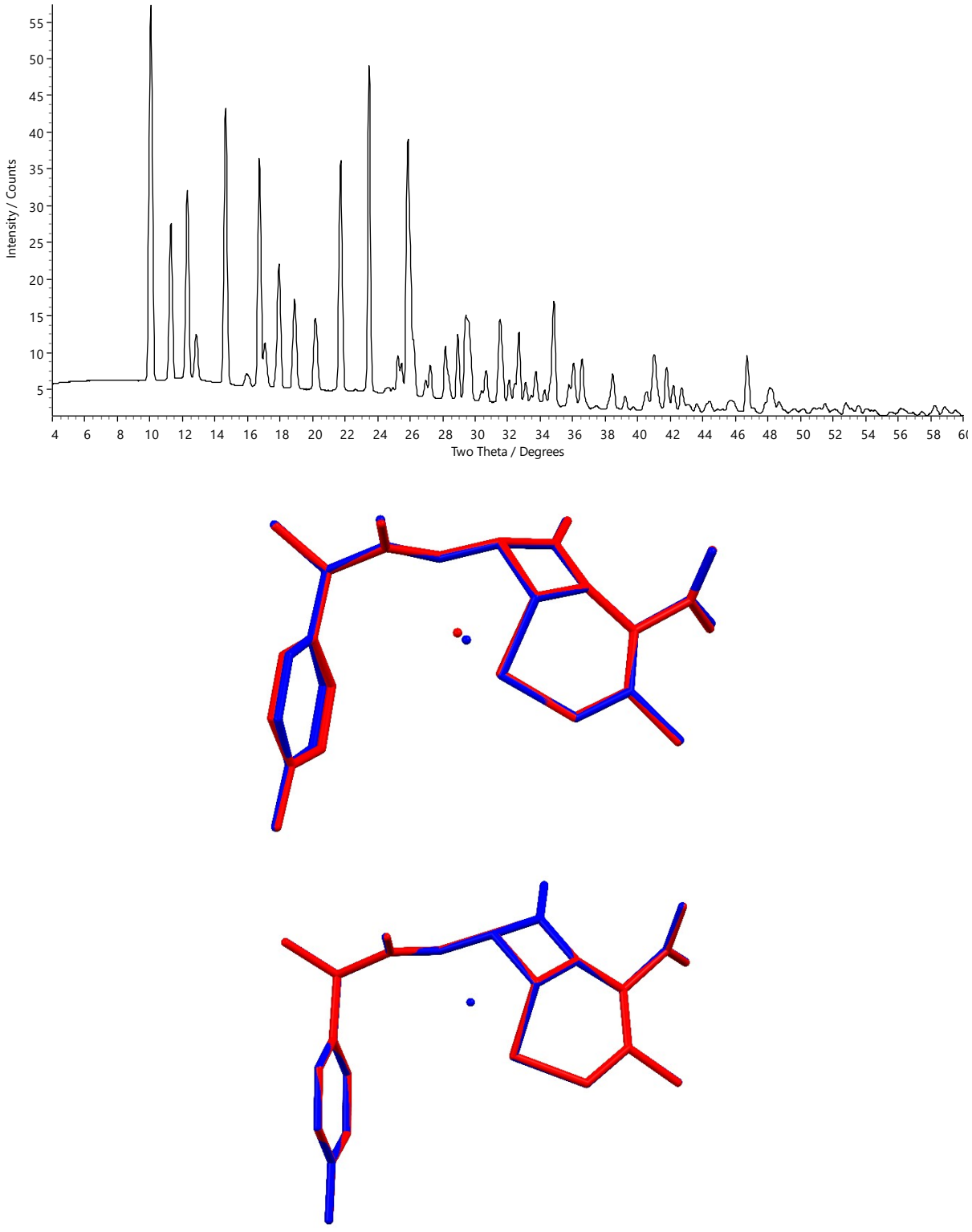
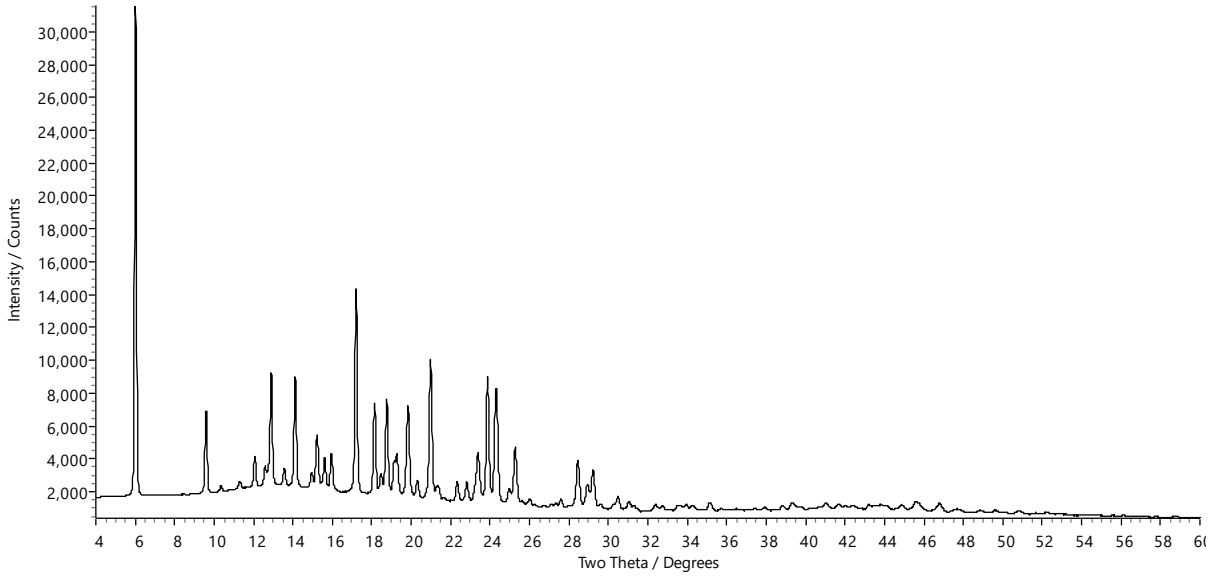


Figure S22: **Top**: Powder diffraction data for cefadroxil.H_2O. **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.



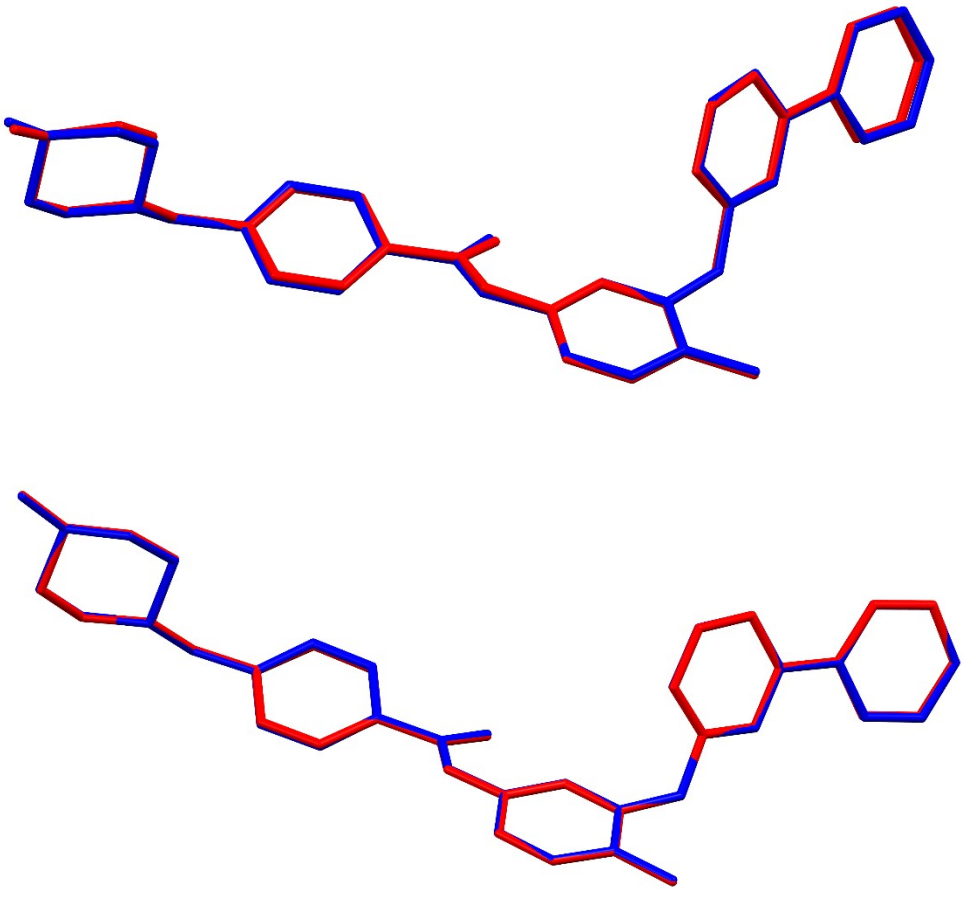


Figure S23: **Top**: Powder diffraction data for imatinib. **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.

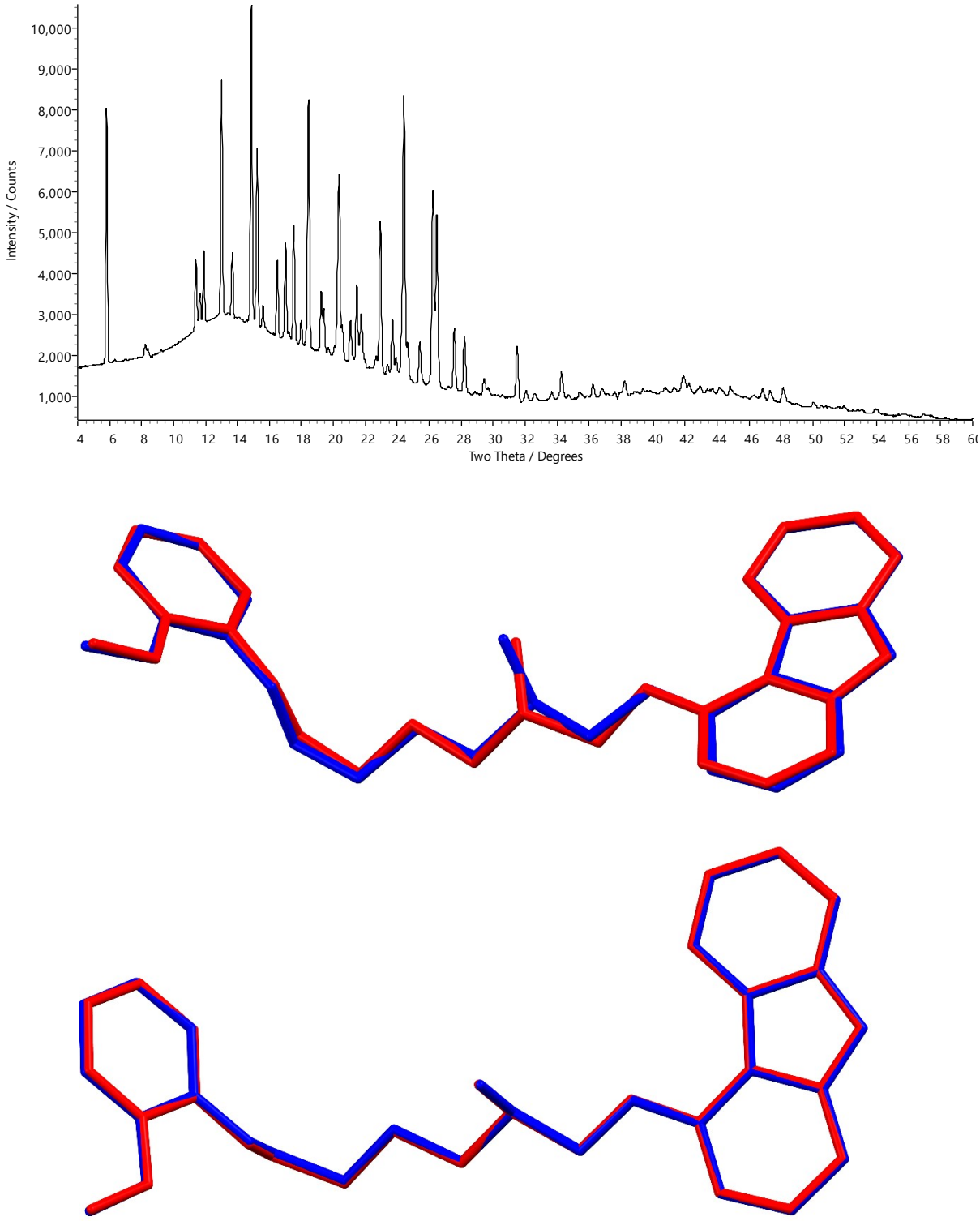


Figure S24: **Top**: Powder diffraction data for carvedilol. **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.

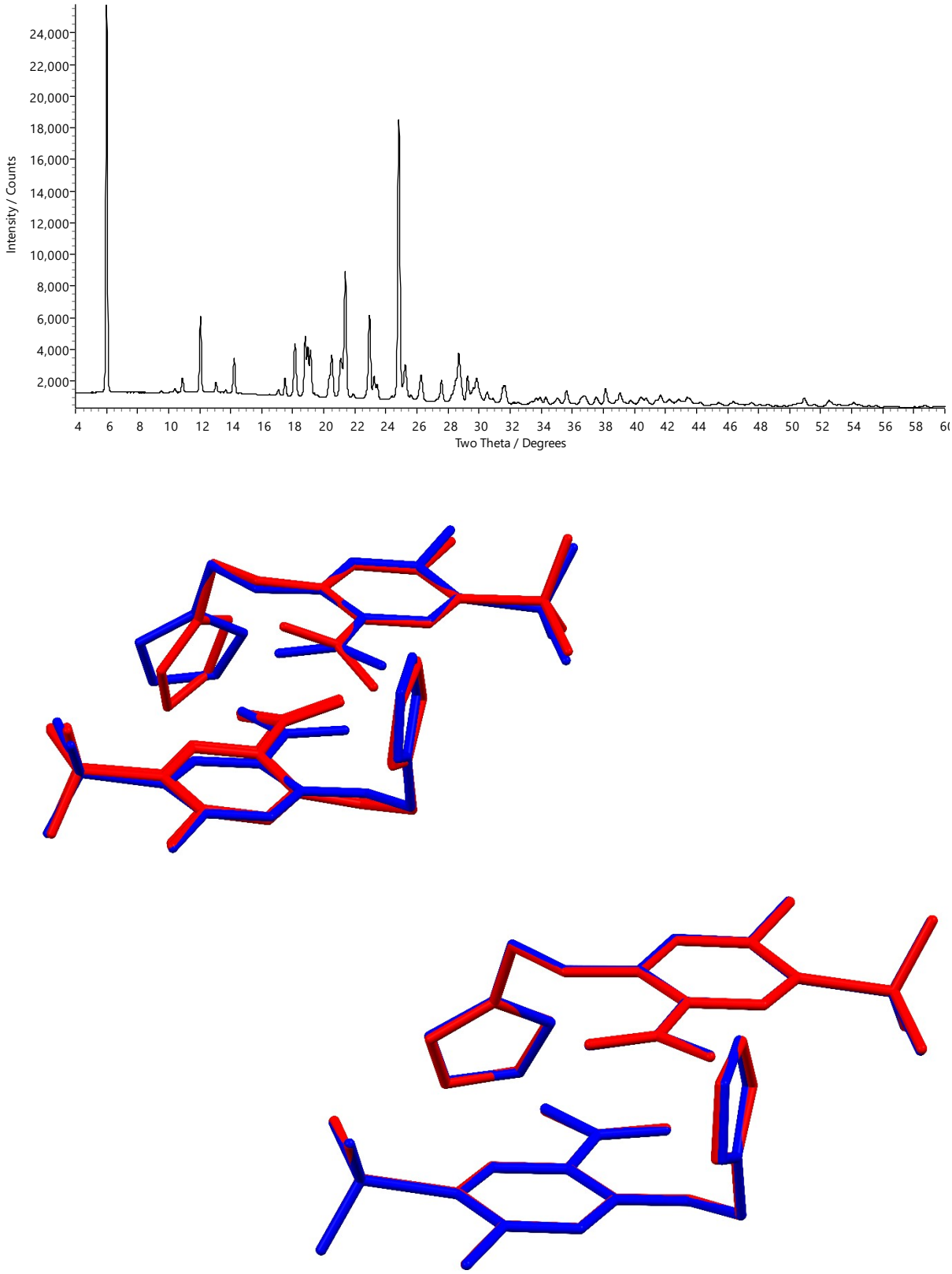


Figure S25: **Top**: Powder diffraction data for furosemide (Z'=2). **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.

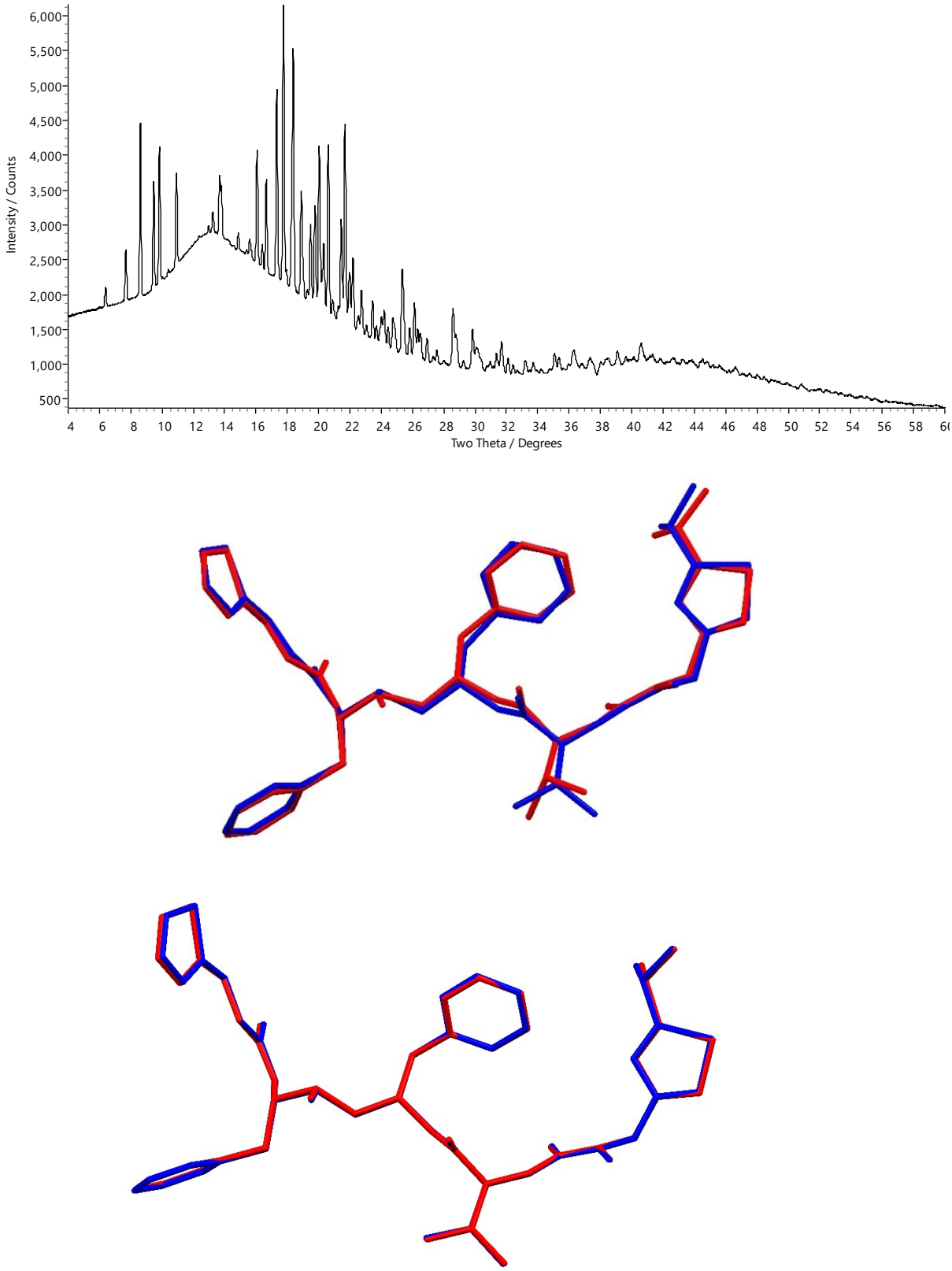


Figure S26: **Top**: Powder diffraction data for ritonavir (form II). **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.

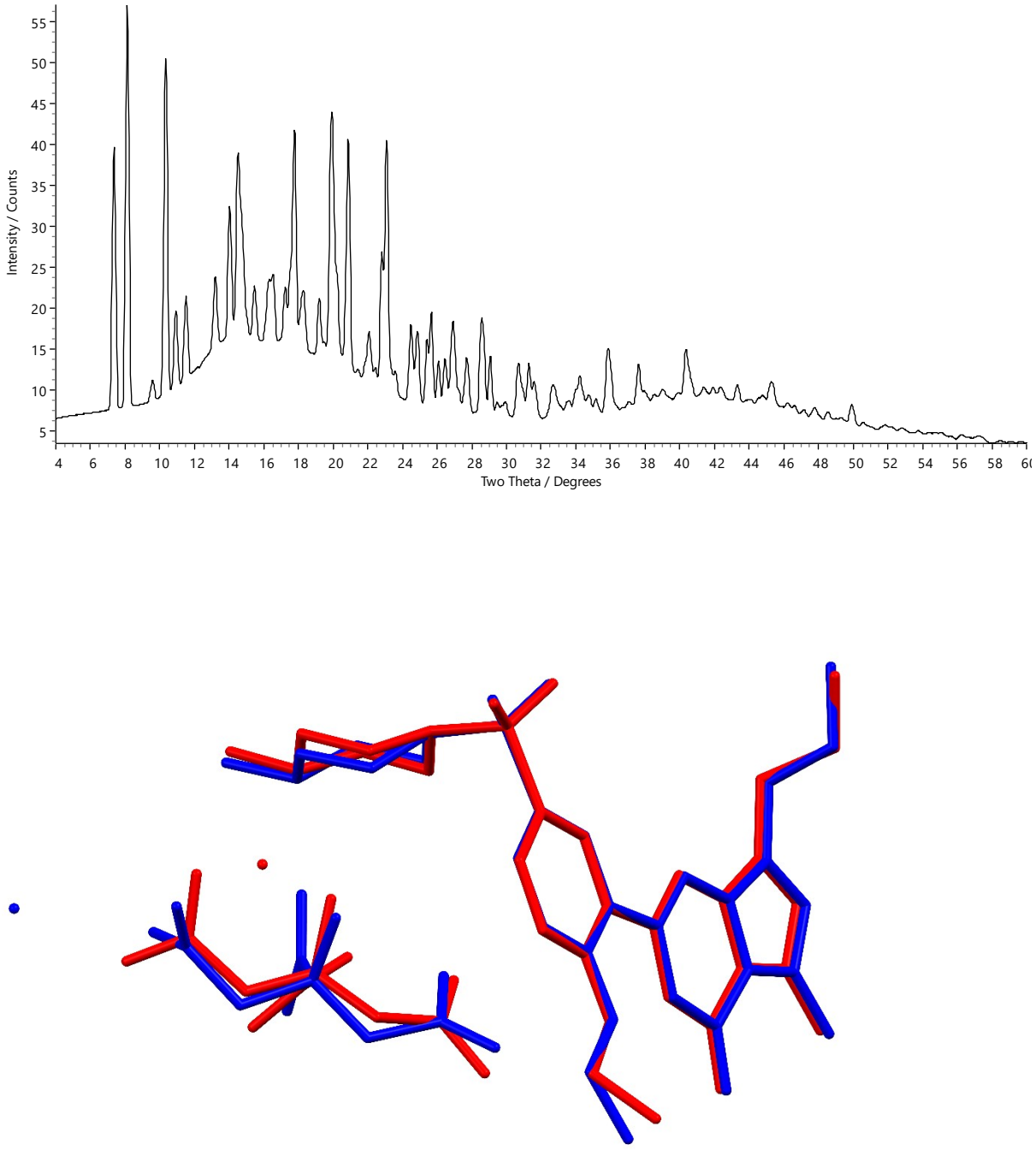
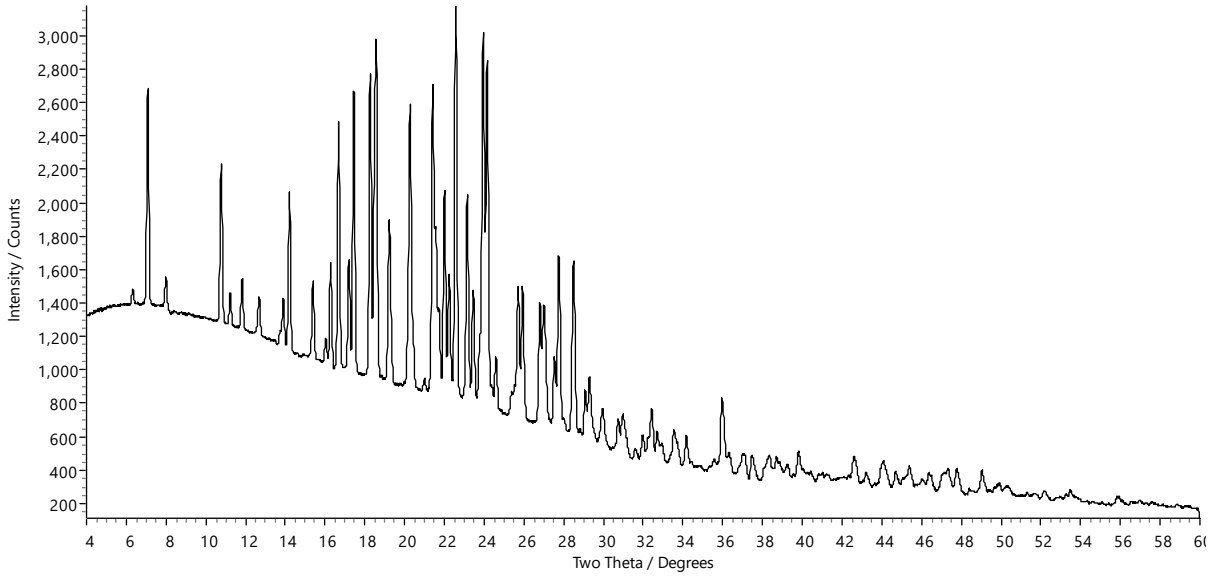
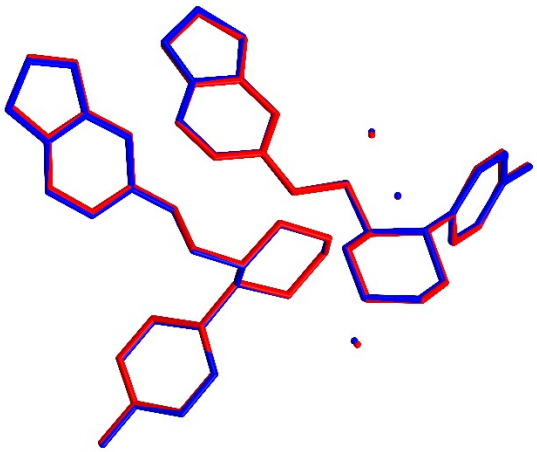


Figure S27: **Top**: Powder diffraction data for sildenafil citrate.H_2O. **Bottom**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity. Note that no DFT-D optimisation was performed for this structure because the location of the water molecule could not be determined with sufficient accuracy from the diffraction data alone.


Intensity / Counts
3,000
2,800
2,600
2,400
2,200
2,000
1,800
1,600
1,400
1,200
1,000
800
600
400
200
4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44 46 48 50 52 54 56 58
Two Theta / Degrees



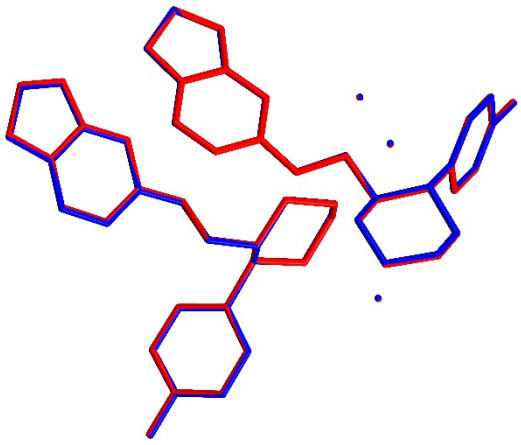


Figure S28: **Top**: Powder diffraction data for paroxetine.HCl.½H_2O. **Middle**: Asymmetric unit of DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). **Bottom**: Asymmetric unit of DFT-optimised DASH solution (red) superimposed upon the asymmetric unit of known structure (blue). Hydrogen atoms are hidden for clarity.

Parameter	Capillary data to 45°	SDPD-SX data to 60°
a / Å	7.9916(2)	7.9887(1)
b / Å	8.3590(3)	8.3567(2)
c / Å	25.0981(9)	25.0896(5)
V / Å^3	1676.60(9)	1674.96(5)

Comparison of Rigid-body refined structures: 15/15 molecules, RMSD = 0.023 Ang

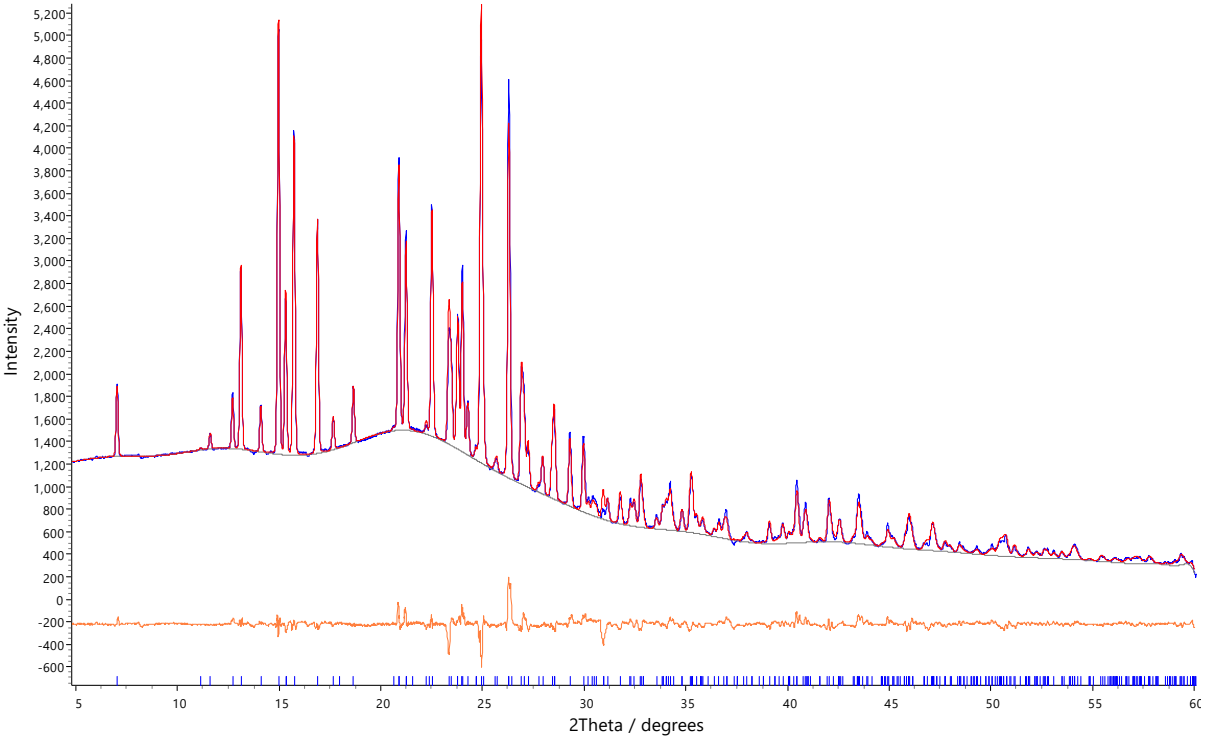


Figure S29: Key profile refinement information for sertraline hydrochloride

Top: A comparison of refined unit cell parameters obtained by Pawley fitting of the capillary and SDPD-SX data sets.

Middle: A comparison, using the Crystal Packing Similarity functionality of Mercury, of output structures from rigid-body Rietveld refinements against SDPD-SX data and capillary data.

Bottom: Observed (blue) and calculated (red) data for the rigid-body Rietveld refined crystal structure of sertraline hydrochloride against the SDPD-SX data. The fitted background is shown in grey and the difference profile is shown in orange. R_{wp} = 1.85

Parameter	Capillary data to 45°	SDPD-SX data to 60°
a / Å	14.4345(4)	14.400(2)
b / Å	11.2039(2)	11.1702(8)
c / Å	11.0501(2)	11.048(1)
V / Å^3	1787.06(7)	1777.1(3)

Comparison of Rigid-body refined structures: 15/15 molecules, RMSD = 0.043 Ang

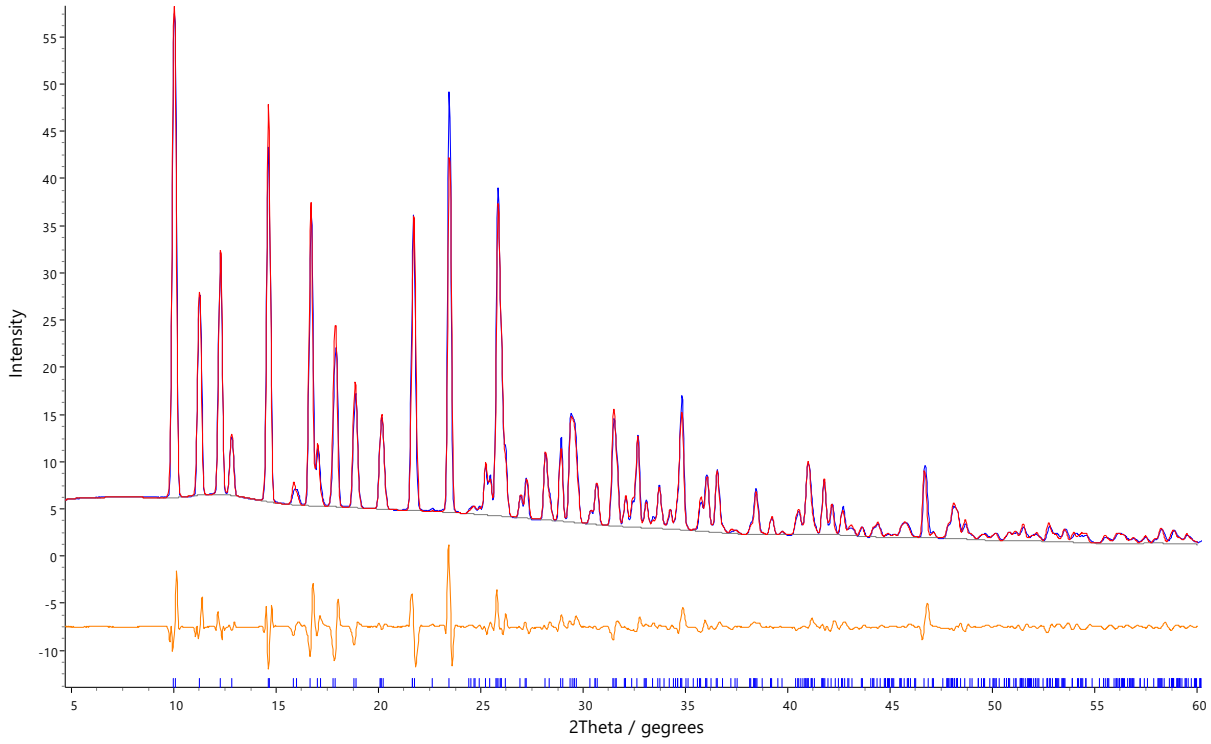


Figure S30: **Key profile refinement information for cefadroxil monohydrate**

Top: A comparison of refined unit cell parameters obtained by Pawley fitting of the capillary and SDPD-SX data sets.

Middle: A comparison, using the Crystal Packing Similarity functionality of Mercury, of output structures from rigid-body Rietveld refinements against SDPD-SX data and capillary data.

Bottom: Observed (blue) and calculated (red) data for the rigid-body Rietveld refined crystal structure of cefadroxil monohydrate against the SDPD-SX data. The fitted background is shown in grey and the difference profile is shown in orange. R_{wp} = 7.67

Parameter	Capillary data to 60°	SDPD-SX data to 60°
a / Å	20.4927(3)	20.4886(8)
b / Å	18.6654(3)	18.6576(8)
c / Å	9.9866(2)	9.9828(4)
V / Å^3	3819.9(1)	3816.1(3)

Comparison of Rigid-body refined structures: 15/15 molecules, RMSD = 0.133 Å

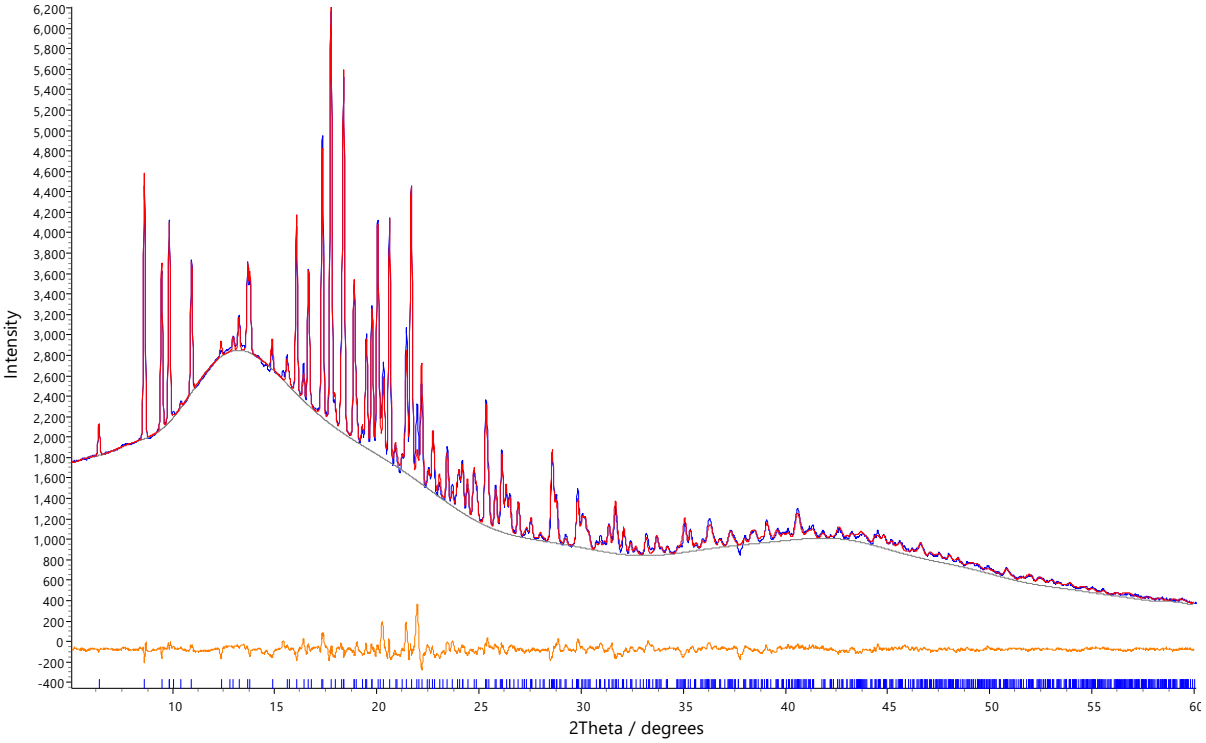


Figure S31: **Key profile refinement information for ritonavir**

Top: A comparison of refined unit cell parameters obtained by Pawley fitting of the capillary and SDPD-SX data sets.

Middle: A comparison, using the Crystal Packing Similarity functionality of Mercury, of output structures from rigid-body Rietveld refinements against SDPD-SX data and capillary data.

Bottom: Observed (blue) and calculated (red) data for the rigid-body Rietveld refined crystal structure of ritonavir against the SDPD-SX data. The fitted background is shown in grey and the difference profile is shown in orange. R_{wp} = 1.83

Notes on some individual structures and DFT-D

Treatment of H atoms

For hydrogen atoms whose positions are not explicitly determined by the geometry of the non-H structures to which they are attached (*e.g.,* the hydrogen of an X-OH group that is free to rotate about the X-O bond) their orientation makes little difference to the fit to the PXRD data but may have a significant impact upon the DFT-D calculation. In the case of cefadroxil (JOSWAP01) several of the H atoms in the published structure are poorly located, and one H atom is missing on the carboxylic acid group; the missing H was added prior to DFT-D.

Furosemide

In the *DASH* answer, the orientation of the SO_2NH_2 group of one of the molecules in the asymmetric unit is out by 120°. This, a consequence of the 'equal scattering' issue, is not surprising and the correct orientation is easily identified from H-bonding considerations prior to DFT-D optimisation.