Supplementary Information.

1. Profile fitting of NPD data from anhydrous α-lactose

With a large triclinic unit cell and 48 atoms full refinement of the structure against moderate resolution NPD data would lead to instabilities. Therefore only a check of the published structure in fitting the NPD profile was undertaken. The profile fitting included variation of only profile parameters (lattice parameters, zeropoint, profile peak shape parameters and background parameters until the refinement converged.

R_{wp} (fitted) 0.89 % R_{wp}(-background) 0.96% Dwd 0.272
χ^2 = 11.1 R_F2 = 9.79% for 24 variables

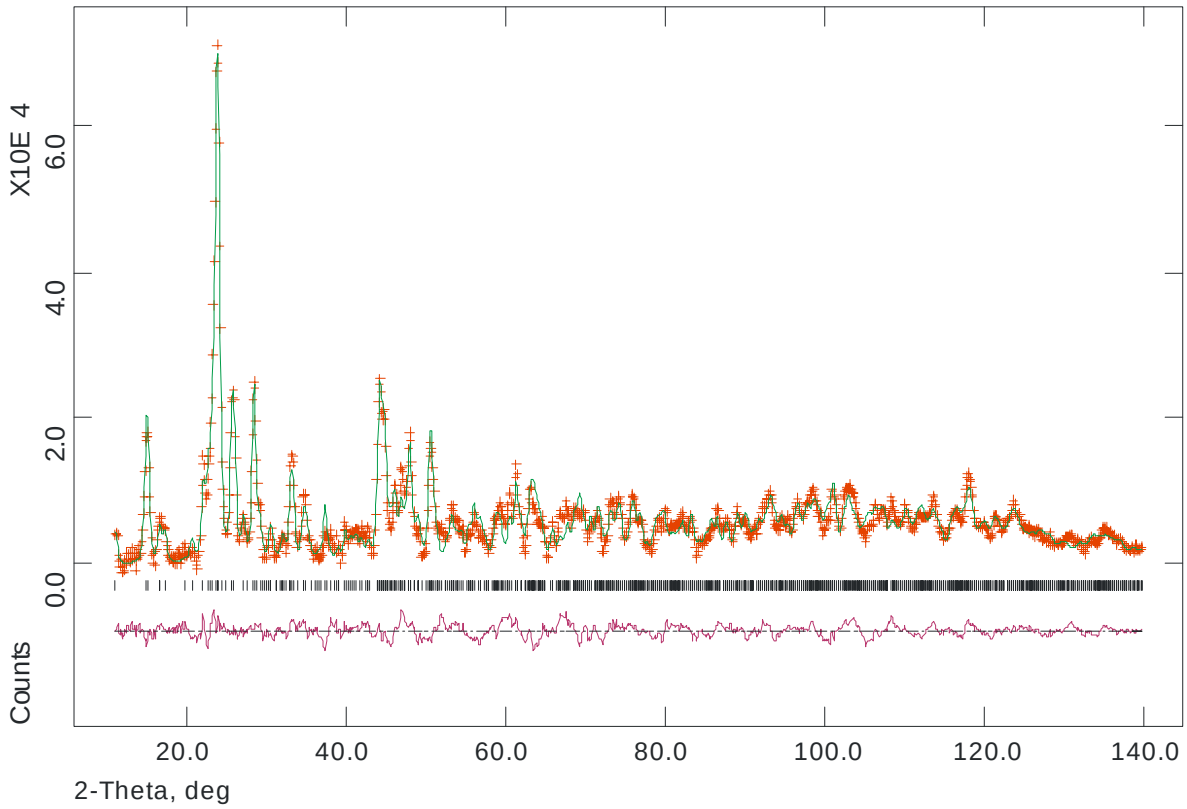

Figure SI.1 Final profile fit achieved to NPD collected from anhydrous alpha lactose. Profile fitted using literature crystallographic model of C. Platteau, J.Lefebvre, F. Affouard, P. Derollez. *Acta Cryst. B*. 2004, **60**, 453. Crosses are experimental data. Upper green line the calculated profile and lower magneta line the difference; tick marks show reflection positions

2. Structure refinement of α-lactose monohydrate against NPD data.

Refinement was undertaken using the published coordinate structures as a starting model (.Beevers, C. A. & Hansen, H. N. (1971). Acta Cryst. B27, 1323–1325., Fries, D. C., Rao, S. T. & Sundaralingham, M. (1971). Acta Cryst. B27, 994–1005. Noordik, J. H., Beurskens, P. T., Bennema, P., Visser, R. A. & Gould, R. O. (1984). Z. Kristallogr. 168, 59–65. J. H. Smith, S. E. Dann, M. R. J. Elsegood, S. H. Dale and C. G. Blatchford. *Acta Cryst E.* 2005, **61(8)**, 2499.) . Initial stages of the refinement included variation of only profile parameters (lattice parameters, zeropoint, profile peak shape parameters and background parameters until the refinement converged. Significant differences in the observed and calculated profiles at this stage derive from differences in modelling positions of hydrogen as a result of the difference in scattering centres of the published structure (single crystal X-ray diffraction – electron density) and the NPD technique (nuclear density); this results in derived hydrogen positions that are shifted closer towards the bond centres and especially towards more electronegative centres (oxygen). Totally free refinement of all atomic coordinates for α-lactose against NPD led to instabilities in the refinement so soft constraints were applied to all C-H and OH bond of 1.10 and 1.00 Å ±0.02 Å respectively. Atomic displacement parameters were constrained to be equal for all sites occupied by the same atom type. Refinement converged smoothly to give the following crystallographic model.

Final Crystallographic model
Space group $P2_1$ a = 7.9125(4) b = 21.5137(12) c = 4.78382(32) Å ß = 109.620(4) Cell volume = 767.05(8) $Å^3$

Atom	x	y	z	Ui/Ue*100
C1	0.2374(30)	0.3373(10)	0.418(4)	1.43(10)
C2	0.1862(30)	0.1002(9)	0.112(4)	1.43(10)
C3	0.3640(32)	0.3877(11)	0.410(4)	1.43(10)
C4	-0.0027(33)	0.1412(11)	0.119(4)	1.43(10)
C5	0.3144(34)	0.4553(9)	0.578(4)	1.43(10)
C6	0.0392(34)	0.2089(10)	0.070(4)	1.43(10)
C7	0.1193(29)	0.4662(10)	0.414(4)	1.43(10)
C8	0.2213(34)	0.2216(9)	0.276(4)	1.43(10)
C9	-0.0081(32)	0.4135(10)	0.405(5)	1.43(10)
C10	0.3914(31)	0.1901(12)	0.238(4)	1.43(10)
C11	-0.2083(32)	0.4285(9)	0.218(5)	1.43(10)
C12	0.5628(31)	0.2078(8)	0.482(4)	1.43(10)
H1	0.2206(47)	0.3193(14)	0.614(5)	3.17(18)
H2	0.1179(46)	0.5259(8)	0.111(7)	3.17(18)
H3	-0.3758(39)	0.3527(15)	-0.020(5)	3.17(18)
H4	0.2113(43)	0.0540(10)	0.191(7)	3.17(18)
H5	-0.0146(51)	0.1300(15)	0.327(5)	3.17(18)
H6	0.0487(49)	0.2276(14)	-0.129(5)	3.17(18)
H7	0.2464(45)	0.2274(17)	0.507(4)	3.17(18)
H8	0.4121(48)	0.2011(16)	0.035(5)	3.17(18)
H9	0.5938(45)	0.1898(14)	0.700(4)	3.17(18)
H10	0.5725(57)	0.2561(8)	0.447(8)	3.17(18)
H11	0.3204(32)	0.0932(14)	-0.168(8)	3.17(18)
H12	0.3813(47)	0.3978(15)	0.204(5)	3.17(18)
H13	-0.1364(47)	0.1352(14)	-0.259(5)	3.17(18)
H14	-0.0099(39)	0.2772(10)	0.101(8)	3.17(18)
H15	0.7667(47)	0.2085(11)	0.325(8)	3.17(18)
H16	-0.3717(42)	0.0931(14)	-0.004(7)	3.17(18)
H17	-0.5080(49)	0.0301(13)	-0.270(5)	3.17(18)
H18	0.2959(54)	0.4345(14)	0.767(5)	3.17(18)

H19	0.0692(42)	0.4995(13)	0.530(7)	3.17(18)
H20	-0.0159(52)	0.4092(15)	0.620(6)	3.17(18)
H21	-0.2031(51)	0.4511(15)	0.024(6)	3.17(18)
H22	-0.3075(42)	0.4592(14)	0.240(7)	3.17(18)
H23	0.6164(43)	0.3802(16)	0.481(6)	3.17(18)
H24	0.4579(47)	0.5226(13)	0.740(5)	3.17(18)
O1	0.2901(37)	0.3002(12)	0.204(6)	1.27(10)
O2	0.1946(29)	0.1060(13)	-0.177(5)	1.27(10)
O3	0.5600(36)	0.3741(11)	0.642(5)	1.27(10)
O4	-0.1480(39)	0.1213(14)	-0.062(5)	1.27(10)
O5	0.4489(41)	0.4939(9)	0.566(5)	1.27(10)
O6	-0.0919(34)	0.2404(9)	0.098(6)	1.27(10)
O7	0.1104(37)	0.4787(8)	0.095(5)	1.27(10)
O8	0.0598(35)	0.3642(13)	0.217(6)	1.27(10)
O9	0.3462(33)	0.1208(11)	0.312(6)	1.27(10)
O10	-0.2982(34)	0.3760(12)	0.164(4)	1.27(10)
O11	0.7009(39)	0.1711(9)	0.370(6)	1.27(10)
O12	-0.4651(33)	0.0594(9)	-0.092(5)	1.27(10)

R_{wp} (fitted) 0.36 % R_{wp}(-background) 0.37% DwD 0.491

$\chi^2 = 7.47$ $R_F2 = 4.59\%$ for 163 variables

Figure S2.1 Final profile fit achieved to NPD collected from alpha lactose monohydrate. Crosses are experimental data. Upper green line the calculated profile and lower magneta line the difference; tick marks show reflection positions