

a AND b LACTOSE: AB INITIO INDEXING AND STRUCTURAL DETERMINATION USING POWDER X-RAY DIFFRACTION

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The aim of this study was to facilitate identification at room temperature of the four most common crystalline phases of Lactose ($C_{12}H_{22}O_{11}$) by PXRD and to refine the conditions needed to obtain the pure phases. Two unknown crystal structures were solved (α -anhydrates, $L\alpha$ and $L\alpha_H$) with a direct space method and PXRD data. The $L\alpha_{H_2O}$ [1,2,3,4] used exhibited a chemical purity of more than 99.7%. For the $L\beta$ [4,5,6], a purification step by crystallisation in a water solution above 93.5°C [4] was performed. Pure $L\alpha$ was produced by storing $L\alpha_{H_2O}$ for 72 hours under methanol vapours.

Experimental conditions optimized by TGA allowed the isolation of pure $L\alpha_H$ by dehydration of $L\alpha_{H_2O}$ heated up to 132°C at 5K/min under N_2 and maintaining at this temperature during 30 min (open pan is required). Based on our experience and literature, $L\alpha_H$ is always obtained as polycrystalline [4] and for $L\alpha$, no suitable crystals were obtained [4, 5]. X-ray powder data were collected with Panalytical diffractometers (X'Celerator [7] detector and Cu $K\alpha$ 1 radiation were used in all experiments). For pattern indexing, a Bragg-Brentano geometry was used. To reduce effect of transparency, a thin layer of powder was deposited on silicon plates. For structural determination, data were recorded using a Debye-Scherrer geometry. The powder was loaded into a 0.5 mm diameter capillary. To avoid the hydration of $L\alpha_H$, the reflection data were collected in 2 hours under a dry nitrogen flux to reduce kinetic of hydration. Stability of compounds and X-ray sources were checked by recording again data at low angles. Under these conditions, $L\alpha_H$ was stable for few hours. For structural determination, warm powder was used to fill a pre-heated capillary in a 20%RH controlled room. The Capillary was annealed for a few minutes at 100°C and sealed.

Indexation was done using Dicol91[8]. High figures of merit were obtained. Low $\Delta 2\theta$ mean values and pattern matching procedures increased the confidence in the potential solutions for the two unknown phases $L\alpha$ and $L\alpha_H$. The parallel tempering solution calculations were then carried out using *PowderSolve* [9] with the complete α molecule taken as structural fragment. A rigid body Rietveld refinement allowed the optimisation of the models. An analysis of the packings and an excellent matching between observed and calculated data gave confidence in the structural solutions. Results are the following :

$L\alpha_{H_2O}$, monoclinic, $a = 7.945(3)\text{\AA}$, $b = 21.606(4)\text{\AA}$, $c = 4.819(6)\text{\AA}$, $\beta = 109.76(9)^\circ$, $V = 778.6\text{\AA}^3$
[FOM: $M_{20} = 65.5$, $F_{20} = 74.3$ (0.0040, 67)].

$L\beta$, monoclinic, $a = 10.831(7)\text{\AA}$, $b = 13.334(8)\text{\AA}$, $c = 4.964(6)\text{\AA}$, $\beta = 91.44(5)^\circ$, $V = 716.8\text{\AA}^3$
[FOM: $M_{20} = 53.2$, $F_{20} = 106.9$ (0.0057, 33)].

$L\alpha$, triclinic, $P1$, 2 molecules per cell, $a = 7.656(8)\text{\AA}$, $b = 19.880(4)\text{\AA}$, $c = 4.985(8)\text{\AA}$, $\alpha = 91.91(9)^\circ$,
 $\beta = 106.26(8)^\circ$, $\gamma = 97.21(2)^\circ$, $V = 720.9\text{\AA}^3$ [FOM: $M_{20} = 73.2$, $F_{20} = 175.6$ (0.0041, 28)].
Refinements, Pawley $R_{wp} = 0.0372$ and Rietveld $R_p = 0.0288$, $R_{wp} = 0.0402$.

$L\alpha_H$, monoclinic, $P2_1$, 2 molecules per cell, $a = 7.784(5)\text{\AA}$, $b = 19.680(7)\text{\AA}$, $c = 4.908(0)\text{\AA}$,
 $\beta = 103.68(5)^\circ$, $V = 730.6\text{\AA}^3$ [FOM: $M_{20} = 67.2$, $F_{20} = 147.8$ (0.0048, 28)].
Refinements, Pawley $R_{wp} = 0.0771$ and Rietveld $R_p = 0.0678$, $R_{wp} = 0.0912$.

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