Characterization of Spray-Dried Lactose Using StepScan DSC and Temperature XRPD

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EXPERIMENTAL

With StepScan DSC, heating (10°C/min or **5°C/min**) is applied over small temperature increments (1°C - **2°C**) after which the temperature is held for a short time interval (30 s - **60 s**) allowing the heat flow to equilibrate. From the repeated temperature steps the specific heat is calculated (**Thermodynamic C_p**, reversible) together with the curve indicating the kinetically controlled effects (**IsoK Baseline**, irreversible), which is obtained from the heat flows at the end of the isothermal equilibrations.

With temperature XRPD, the diffractograms are measured at various temperatures by means of the temperature controlled sample table in the goniometer.

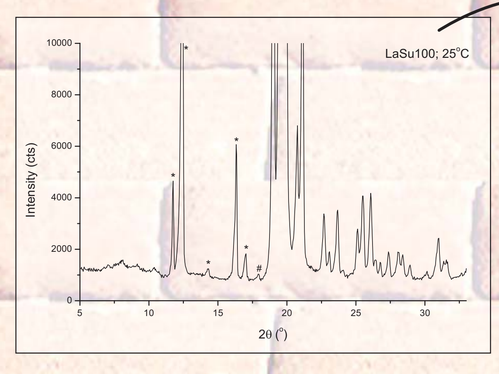
The samples used in the present study were prepared by spray drying. By changing the ethanol/water concentration of the feed solution, lactose samples with various amorphous degrees were obtained. The amorphiness of the lactose samples was determined with isothermal microcalorimetry (IMC).

RESULTS

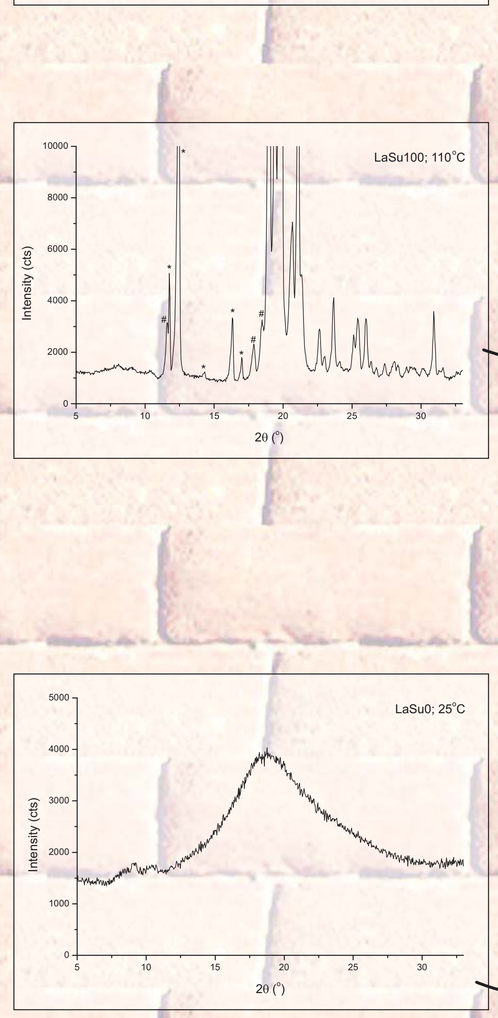
Conventional DSC (2 °C/min) and StepScan DSC curves are coupled with TXRPD curves in the collage below. The crystalline spray dried lactose (LaSu100) contains mainly α-lactose monohydrate and a minor amount of α-lactose anhydrate. Before the dehydration takes place at 140°C, the amount of α-lactose anhydrate is increased. After the dehydration endotherm, the sample consists of β-lactose and two different α-lactose anhydrates. During the small exotherm at 170°C, the second α-lactose anhydrate (unstable) vanishes bringing up the portions of α-lactose anhydrate and α-lactose.

The amorphous spray dried lactose (LaSu0) undergoes recrystallization at 160°C after the glass transition temperature T_g at 115°C. The corresponding change in C_p has only small effect on the diffractogram, but after the recrystallization the sample is mainly α-lactose anhydrate.

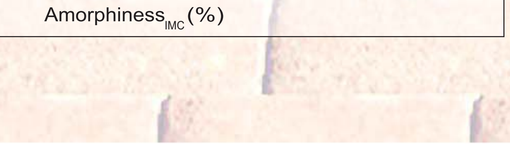
The values of ΔC_p at T_g and the recrystallization enthalpy calculated from the StepScan DSC data are represented in Fig. 1. The linearity of the $\Delta H_{cryst.}$ values are poor due to the overlapping of the dehydration endotherm and the recrystallization exotherm. On the basis of the confidence bands for ΔC_p, the precision and the sensitivity of the method can be estimated.



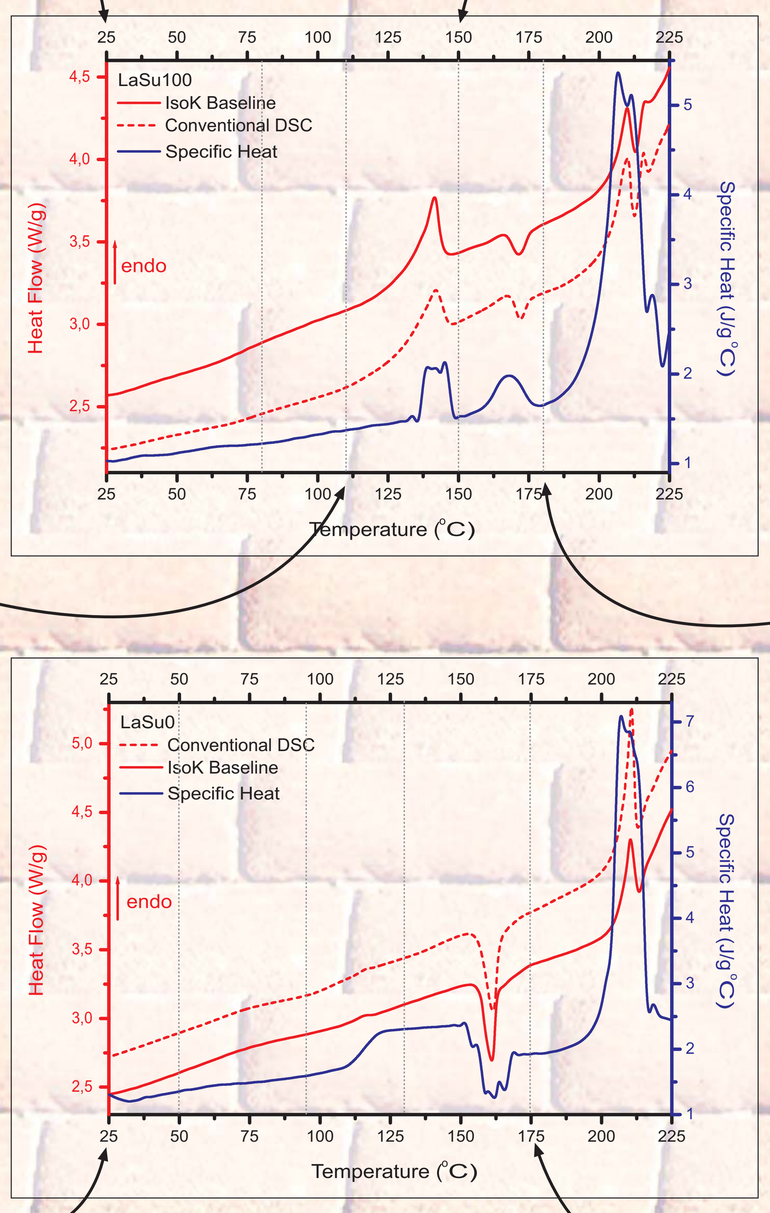
LaSu100, 25°C:
Mainly α-lactose monohydrate (*) + minor α-lactose anhydrate (unstable) (#).

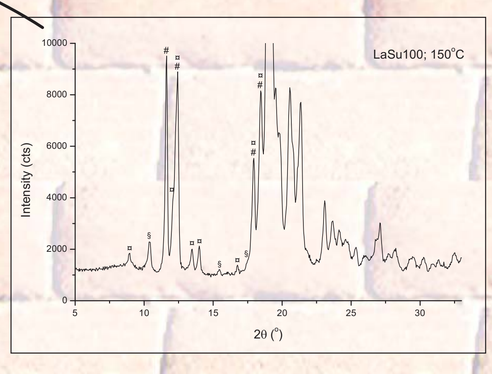


LaSu100, 110°C:
α-lactose monohydrate (*) + increased amount of α-lactose anhydrate (unstable) (#), no β-lactose.

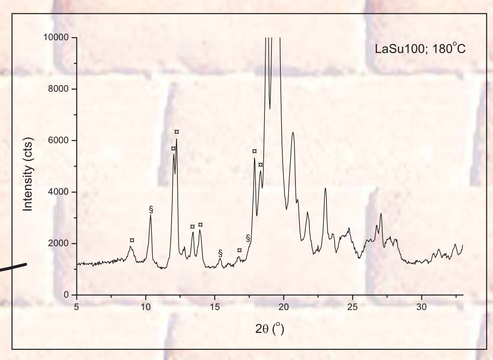


LaSu0, 25°C - 130°C:
Amorphous.

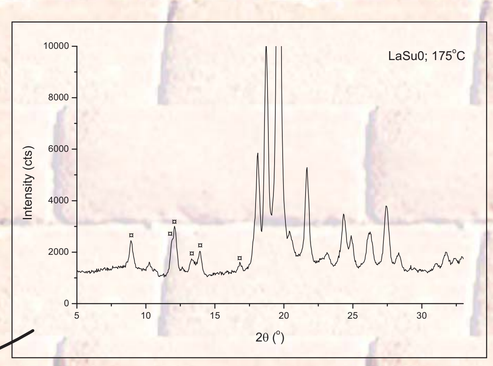




LaSu100, 150°C:
β-lactose (§) + two different α-lactose anhydrates (stable (¤) and unstable (#)).



LaSu100, 180°C:
Increased portions of α-lactose anhydrate (stable) (¤) and β-lactose (§), no α-lactose anhydrate (unstable).



LaSu0, 175°C:
Mainly α-lactose anhydrate (stable) (¤).

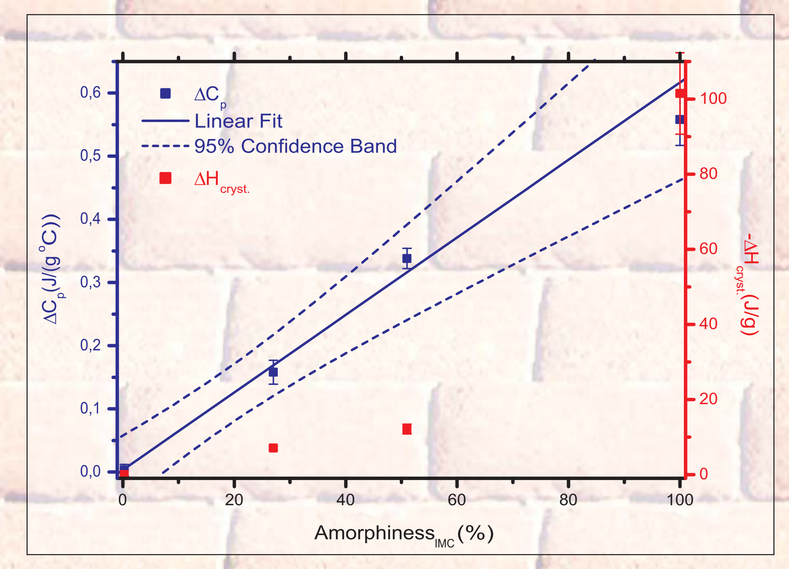


Fig. 1. StepScan results for the lactose samples with different amorphicity. Error bars, solid line and dashed lines denote SDs, the linear fit of ΔC_p and the corresponding confidence band of 95%, respectively.

CONCLUSIONS

- Combination of DSC and temperature XRPD data yields a good insight into the thermal behavior of materials crystal structures.
- StepScan DSC facilitates the measurement of the glass transition, the relaxation endotherm and the heat capacity without temperature modulation and applying Fourier transform.
- The change of specific heat capacity at T_g obtained through StepScan DSC can be used to quantify amorphicity with better precision when compared with the corresponding values obtained by conventional DSC as the endothermic relaxation is eliminated from the **Thermodynamic C_p** curve.