Supersaturation-dependent polymorphic outcome and transformation rate of L-glutamic acid

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**Experimental Section:**

**Materials**

L-glutamic acid (L-Glu, >99%) was purchased from Sinopharm Chemical Reagent Co. Ltd. (China), and ultrapure water (ELGAPURELAB classic, 18.2 MΩ·cm) was used for solution preparation in the crystallization experiment.

1. **FTIR**

A supersaturated L-Glu aqueous solution ($\sigma = (c-c_{eq}) / c_{eq}$), where $c$ is the actual solution concentration, and $c_{eq}$ is the solubility of $\alpha$ form at 25 °C, was prepared by completely dissolving appropriate amounts of L-Glu into ultrapure water in a crystallizer which was kept inside a constant temperature bath (CTB) maintained at 80 °C. The hot solution was filtered through a warmed 0.22 μm syringe filter, and the filtrate was collected into another crystallizer maintained at 80 °C for 1 h. Then the crystallizer was swiftly transferred into another CTB maintained at 25 °C. The solution sample was withdrawn immediately for FTIR (Nicolet 7500, United State).

All experiments were duplicated to check the reproducibility.

2. **In-situ observation of crystallization process**

A supersaturated L-Glu aqueous solution was prepared by completely dissolving appropriate amounts of L-Glu into ultrapure water in a crystallizer which was kept inside a constant temperature bath (CTB) maintained at 80 °C. The hot solution was filtered through a warmed 0.22 μm syringe filter, and the filtrate was collected into another crystallizer maintained at 80 °C for 1 h. Then the crystallizer was swiftly transferred into another CTB maintained at 25 °C. The events in the solution were recorded with time using an optical microscope (ECLIPSE E200, Nikon, Japan).

3. **XRD**

The polymorphic forms of the crystals were determined by using powder X-ray diffraction (RINT2000, Rigaku, Japan).

Three relatively high supersaturated L-Glu aqueous solutions ($\sigma = 1.0, 2.0$ and $3.0$) were respectively prepared by completely dissolving appropriate amounts of L-Glu into ultrapure water in crystallizers which were kept inside a constant temperature bath (CTB) maintained at 80 °C. The hot solution was filtered through a warmed 0.22 μm syringe filter, and the filtrate was collected into another crystallizer maintained at
80°C for 1 h. Then the crystallizer was swiftly transferred into another CTB maintained at 25 °C. In each experiment, samples of crystal slurry were taken from the crystallizer at different intervals during the transformation process, and then the dried crystals were characterized using PXRD to determine the polymorphic composition.

All experiments were duplicated to check the reproducibility.

Reference:
Fig. S1 The unit cell of L-glutamic acid (a) α form and (b) β form.
Fig. S2 Molecular structure of L-glutamic acid (a) α form and (b) β form.
Fig. S3 FTIR spectra for (a) α and β form of L-Glu and (b) water.
Fig. S4 Nucleation observed in different supersaturated solutions with time \( t=0 \).
Fig. S5 (a) PXRD profiles of L-Glu with various compositions and (b) the calibration line.
Green squares represent the characteristic peak of α form, and orange balls represent the characteristic peak of β form.
Fig. S6 PXRD profiles of crystals obtained from lower supersaturated solutions. Orange balls represent the characteristic peak of β form.
Fig. S7 PXRD profile of crystals obtained from supersaturated solution with $\sigma_\alpha=0.7$. Green squares represent the characteristic peak of $\alpha$ form, and orange balls represent the characteristic peak of $\beta$ form.