Occurrence of spontaneous resolution of ketoprofen with a racemic crystal structure by simple crystallization under nonequilibrium preferential enrichment conditions

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Fig. S1  HPLC chromatograms of ketoprofen. (a) RS (0% ee), (b) S-rich (64% ee), and (c) R-rich (68% ee). The ee values were determined by HPLC analysis using a chiral stationary phase column (Daicel Chiralcel OJ, 0.40 x 25 cm), a mixture of hexane, 2-propanol, and acetic acid (900:100:5) as the mobile phase at a flow rate of 1.0 mL/min at 30°C, and UV-vis spectrometer (254 nm) as the detector.
Fig. S2  Crystal structure of (RS)-ketoprofen. A view down the a-axis.
**Fig. S3** SEM images of the deposited $S$-rich crystals of $1.2\%$ $ee$ after recrystallization of slightly $R$-rich crystal of ketoprofen under the preferential enrichment conditions. The scale bar at the lower left corresponds to (a) $100 \, \mu m$ and (b) $6.6 \, \mu m$. In panel b, the depth of the hollow along the red line was ca. $1 \, \mu m$ by AFM observation.
Fig. S4  Comparison of in situ ATR-IR (ReactIR) spectra of ketoprofen. In the supersaturated H₂O-EtOH (v/v 1:1) solution of (RS)-ketoprofen (solid line) and in the solid state of deposited S-rich crystals of 1.2% ee (dotted line). The spectral region includes (i) the C=O stretching vibrations of the keto group and (ii) the C=O and C-O stretching vibrations and O-H bending vibrations with respect to the carboxylic acid. The band near 920 cm⁻¹ which is observed only in the solid state corresponds to the out-of-plane bending of the bonded O-H, which is characteristic of dimeric carboxylic acids. Arrows indicate the difference in the two spectra.