crystals

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Article

Impact of a Partial Solid Solution and Water Molecules On The Formation of Fibrous Crystals and Fluid Inclusions

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Supplementary Information:

1. XRPD Confirming the Presence of the Partial Solid Solution

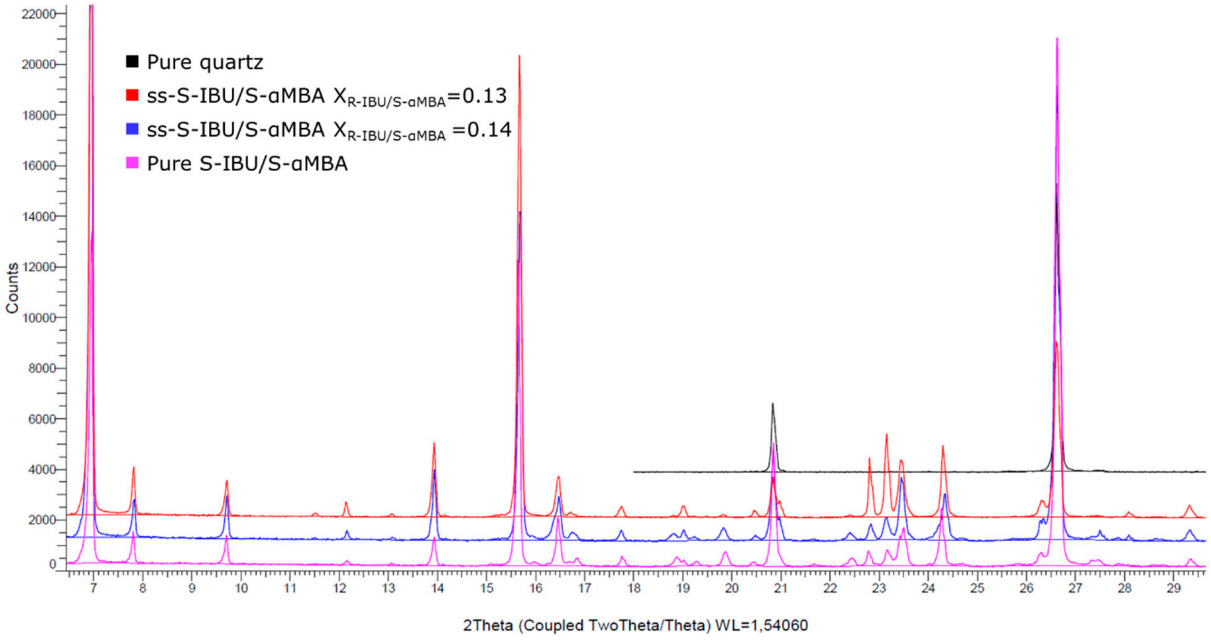

Figure S1. XRPD overlay of two products ss-S-IBU/S-αMBA with the highest chiral purity obtained by chiral resolution of rac-IBU, compared with pure S-IBU/S-αMBA. Quartz was added in the sample preparation to ensure an internal calibration of the diffractograms on the peak 26.6°2θ.

The peak at 24.3°2θ clearly shows a shift in Bragg angle consistent with the partial solid solution.

2. Binary Phase Diagram and Tammann Graph from DSC Measurements in Pierced Pans

The binary phase diagram obtained with pierced pans is presented in Figure S2. The blue curve represents the liquidus, the black one is for the eutectic invariant. The dotted lines represent the estimated limits of the solid solution. The eutectic invariant is found at 134 °C.

Thanks to a Tammann graph (Figure S3), the solid solution is estimated at a molar fraction of R-IBU/S-αMBA equals to 0.12.

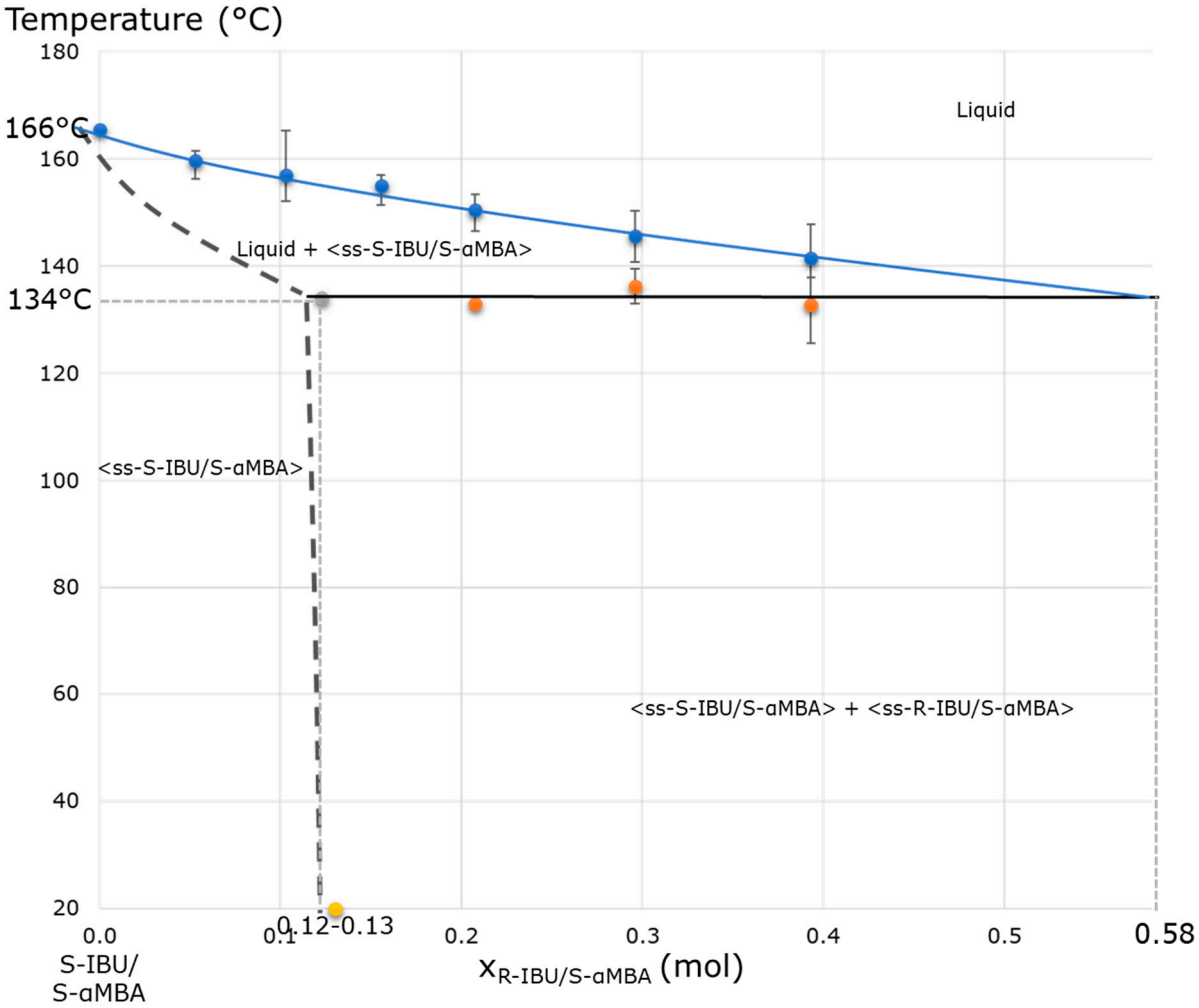

Figure S2. Binary phase diagram obtained with DSC measurements in pierced pans from 20 °C to 200 °C at a heating rate of 2K/min. Blue curve = Liquidus; Black line = Eutectic; Dotted line = solid solution. The solvus has been extrapolated with the following points: (T = 134 °C; $X_{R\text{-}IBU/S\text{-}\alpha MBA}$ = 0.12) and (T = 20 °C; $X_{R\text{-}IBU/S\text{-}\alpha MBA}$ = 0.13). NB: the authors assume that there is also a partial solid solution close to R-IBU/S-αMBA, which is why the second component of the biphasic domain is labelled ss-R-IBU/S-αMBA.

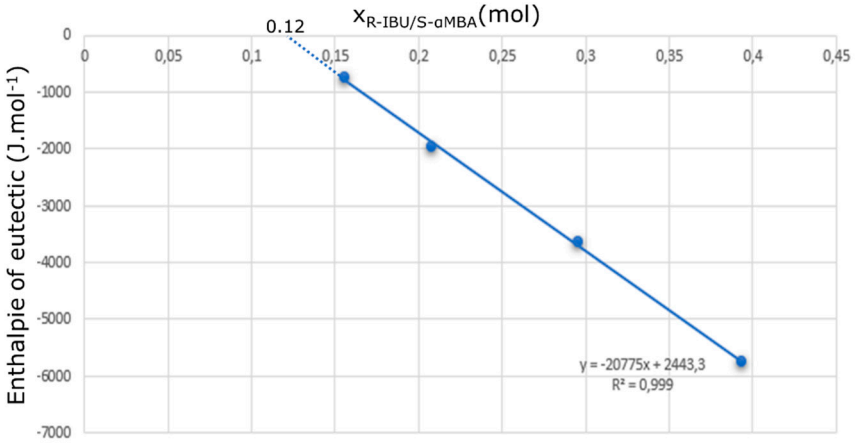

Figure S3. Tammann graph obtained with DSC measurements in pierced pan from 20°C to 200°C at a heating rate of 2K/min.

3. Schröder Van Laar (Eutectic Temperature and Composition):

3.1 Pierced pans

Data obtained with DSC measurements in pierced pans give a melting point of the pure salt at 166 °C and the eutectic invariant temperature at 134 °C. In this case, the eutectic composition is estimated at a molar fraction of S-IBU/S-αMBA equals to 0.40 thanks to the Schröder Van Laar equation.

In the literature, the eutectic composition is 0.34 (molar fraction), which gives a eutectic temperature at 127 °C with Schröder van Laar calculation.

3.2 Sealed pans

Data obtained with DSC measurements in sealed pans give a melting point of the pure salt at 176 °C and the eutectic invariant temperature at 145 °C. In this case, the eutectic composition is estimated at a molar fraction of S-IBU/S-αMBA equals to 0.35 thanks to the Schröder Van Laar equation.

In the literature, the eutectic composition is 0.34 (molar fraction), which gives a eutectic temperature at 145 °C with Schröder van Laar calculation.

In Table S1 are displayed the eutectic composition calculated for pierce pans and sealed pans thanks to the Schröder van Laar equation.

Table S1. Eutectic composition calculated with Schröder van Laar equation.

	ΔHf (J/g)	**ΔHf (J/mol)**	**Tf (°C)**	**Tf (K)**	**Composition (Molar Fraction of S-IBU/S-αMBA)**
Pierced Pans	124. 7	40834	166	134	0.418
Sealed Pans	165.0	54039	176	145	0.346

The data obtained with DSC measurements in sealed pans fit much more with the literature data. It can be explained by the sublimation observed when using pierced pans.

4. Evaluation of the Existence of the Solid Solution from the Single Crystal Analysis Point Of View

The Fourier difference map highlights the presence of a residual electronic density in the neighborhood of the asymmetric carbon C2 (Figure S4). Nevertheless, there is no electronic density observable directly on the Fo mapview [20] (Figure S5). If we consider that the C13 carbon atom could be partially replaced by a hydrogen atom, so the hydrogen atom H2 should be also partially replace by a carbon atom. This residual electronic density could be an evidence of the putative presence of a heaviest atom.

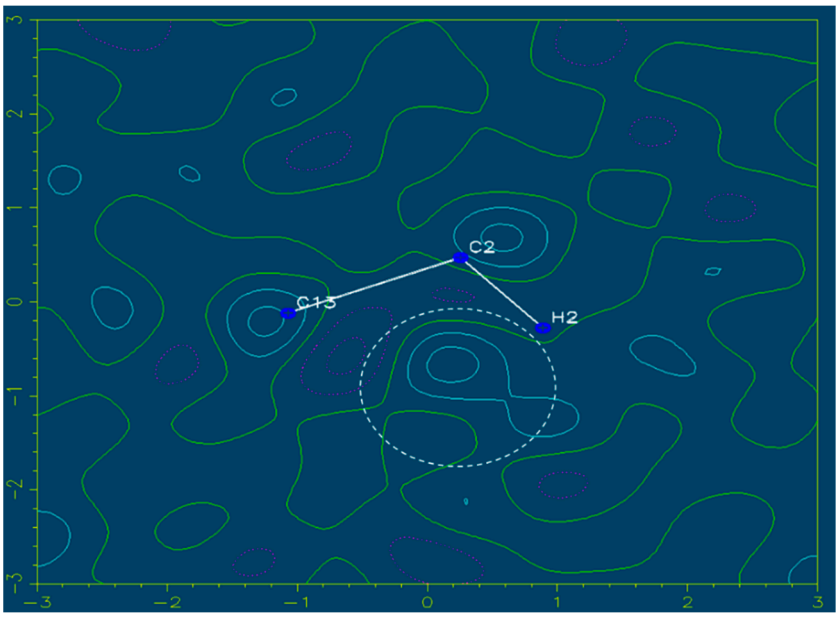

Figure S4. Mapview of the Fobs-Fcalc through C13-C2-H2 plane. In dotted white lines, the highest residual electronic density of the Fourier map.

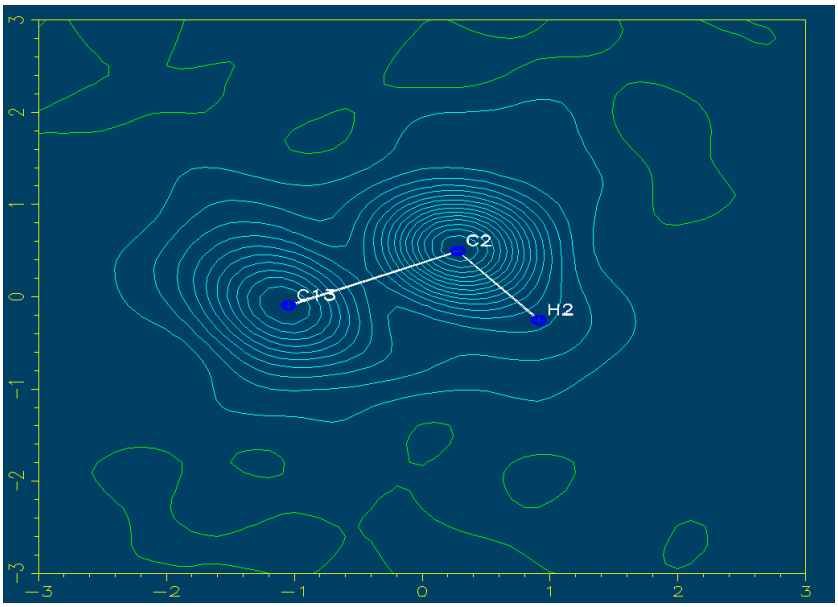

Figure S5. Mapview of Fo through C13 C2 H2 atoms.

Furthermore, if the carbon atom C13 should be partially replaced by a hydrogen atom, so its thermal displacement should be higher than the other terminal carbon atom, to evenly distributed the electronic density of a hydrogen atom and a carbon atom on the same location compared to a pure carbon atom solely.

When comparing the Ueq of the distal CH3 carbons (Table S2) present in the two molecules of the salt, no discrepancy appears between the carbon C13 (hold by the asymmetric carbon C2 on the ibuprofen molecule), and the others terminal carbon atoms. We could have expected that this C13 carbon exhibit a higher thermal displacement to compensate the partial presence of a lightest atom in the same crystallographic position such as a hydrogen atom.

Table S2. Comparison of the Ueqs.

Label	Ueq (x10³ Å²)

C13 (ibuprofen)	150(3)
C11 (ibuprofen)	211(4)
C12 (ibuprofen)	239(4)
C8A (S-αMBA)	94(2)

The last point on this evaluation is the question of the representativity of the crystal analysed. They were exhibiting a lot of surfaced default; many crystals were tested but only one allow us to achieve the structural resolution. So maybe this one was good enough for the resolution because it exhibited the lowest ratio of the counter enantiomer that we cannot detect.

5. Angle between C-CH₃ and 'c' Axis*

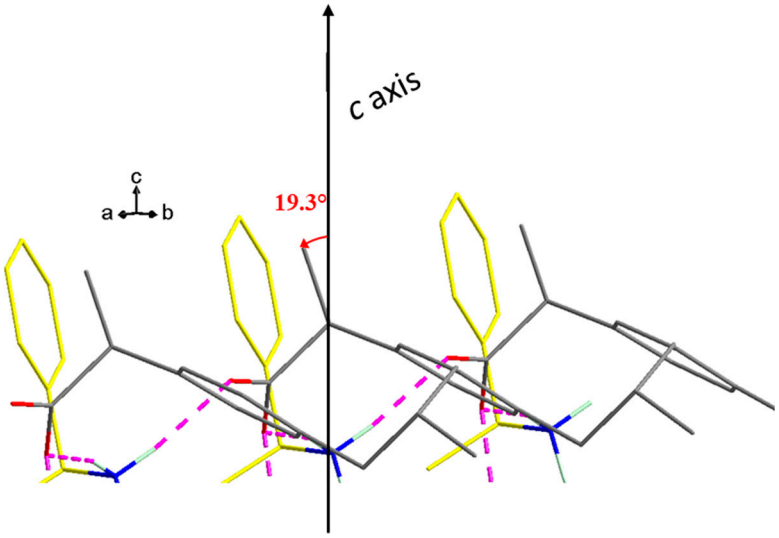

Figure S6. Inclination of the bond C*-C with reference to the 'c' axis.

6. Film

The film of the hot stage microscopy from 20 °C to 120 °C at 1K/min on the inclusions of a crystal of S-Ibu-S-a-MBA X = 0.2 (obtained from a chiral resolution of rac-IBU in EtOH/H_2O 80/20) can be found in a separate file.