Is your Crystal Representative of the Bulk?

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Structure analysis by X-ray diffraction is commonly carried out on just **ONE** single crystal. The physical, chemical, pharmaceutical, biological and structural properties of this one crystal can only be characteristic of the bulk under certain circumstances. In particular for bulk samples which are mixtures, or whose purity is questionable, an excellent ploy is to characterize the one single crystal used for the diffraction experiment. However until recently a difficulty has been its small mass *ca*. 1 μg. Thermochemical characterization by way of differential scanning calorimetry (DSC) can provide clear evidence on purity, phase transitions and solid-solution formation. For enantiomeric mixtures both circular dichroism (CD) and enantioselective chromatography, but not optical activity, may be applied to such a single crystal taken into solution.

As a first case study, a determination of absolute configuration was achieved from X-ray diffraction and CD measurements on crystals obtained from a racemate in the bulk by spontaneous resolution to give a tricky racemic conglomerate. Crystals were either enantiopure but twinned by a pure rotation or twinned by inversion in various proportions. In the second case study of an absolute-configuration determination from an enantiopure sample, the optical activity and CD spectrum were far too weak to be useful to characterize the enantiomer. However enantioselective chromat-ography on the single crystal taken into solution provided the necessary characterization.

Keywords: single-crystal, chiral, characterization