Polymorph screening studies of oxcarbazepine : twisted habit in crystals of the elusive form III

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Crystal structures exhibiting twisted morphology have been observed at the nanoscale, mesoscale, and macroscale and are challenging to characterise structurally because of their lack of long-range translational symmetry [1]. Crystal structure prediction (CSP) studies of an active pharmaceutical ingredient's lattice energy landscape are often utilised for assisting experimentalists in identifying and characterising novel polymorphic forms that are thermodynamically feasible, including ones that crystallise with twisted morphologies [2-4].

Oxcarbazepine (OXCBZ) is a commercially available pharmaceutical used for the treatment of epilepsy and three polymorphic forms have been reported, two of which (form I and form II) are known to crystallise in the monoclinic space groups P21/c and P21 respectively [5]. Form III of OXCBZ was originally prepared by slow evaporation from methanol solutions that contained polymer additives but structure solution was not possible because of the small size and poor quality of the crystals.

Herein, we present experimental protocols for the crystallization of OXCBZ III from both solution and the vapour phase. In our work, we combined CSP studies of OXCBZ with physical vapour deposition studies and solution-based polymorph screening experiments. Needle-like and fibre-like crystals of OXCBZ III exhibiting variable twisted habit emerged from vapour deposition of OXCBZ onto metallic substrates. Scanning electron and atomic force microscopy studies have been carried out to obtain an insight into the mechanism of formation and growth of the twisted OXCBZ III crystals over the course of the deposition process.

References

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