CAN MOLECULAR FLEXIBILITY CONTROL CRYSTALLISATION?

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Molecular flexibility has a profound impact on the number of possible ways molecules can pack in the solid state. The phenomenon of *Conformational Polymorphism* has been well-studied (Cruz-Cabeza, 2014) and recognised to be very common in complex pharmaceuticals (Cruz-Cabeza, 2015).

Perhaps what is less well understood is how molecular flexibility impacts crystallisation. In previous works, we studied the nucleation and growth kinetics of a number of rigid benzoic acid derivatives (Cruz-Cabeza, 2017). We have now studied the nucleation and growth kinetics of a number of flexible benzoic acid derivatives asking the fundamental question "Can Molecular Flexibility Control Crystallisation?" (Tang, 2021). Our kinetic data shows that when the energy barriers for conformational change are small, molecular flexibility is not rate controlling in crystallisation. Aromatic stacking was found, again, to be the key controlling step in the kinetics of crystallisation (Tang, 2021).

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