Organic solid-state chemistry mainly deals with crystalline materials; their synthesis, structures, properties and applications. In the pharmaceutical area, altering the solid state chemistry of materials can lead to improvements in desired physicochemical properties, such as solubility, bioavailability, stability etc.1-3 Cocrystallization is one method to achieve these improvements.4 Crystallisation of diastereomeric salts derived from a racemic compound with an enantiopure resolving agent (e.g. chiral amine base with a racemic carboxylic acid) is a very effective and well-established method for the resolution of enantiomers from racemic mixtures. In contrast, the use of cocrystallisation with an enantiopure coformer as a strategy for resolution has been reported only very rarely, despite the obvious benefit of broader applicability, for example not requiring an ionisable functional group in the compound. This work has investigated chiral cocrystallization by examining two series of phenylalkanamides. The size of the alkyl groups on the chiral carbon and the position of the amide functional group relative to the chiral centre (either α or β) has been varied. During this work, it became evident that the use of cocrystallisation to effect resolution is very challenging, in keeping with the small differences in energy between different forms.5 Unanticipated rare phenomena were observed including kryptoracemic cocrystals, in which both enantiomers crystallize in Sohncke space group.6 We also found that non-classical kryptoracemic cocrystals present another potential hurdle during chiral resolution trials using cocrystallization. These results provide fascinating insights into the ways in which enantiomers of chiral racemic materials interact in the solid state.


Keywords: Cocrystallization, classical and non-classical kryptoracemates, chiral resolution