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Title: Continuous Flow Synthesis of Chiral Amines

The synthesis of chiral amines is important due to their presence in a range of active pharmaceutical ingredients (APIs). Chiral resolution processes are common in the pharmaceutical industry as they are cheaper and easier than the alternatives; however, the maximum yield is only 50%. Crystallisation induced diastereomeric transformation (CIDT) is a variant of resolution where a racemic amine is converted into a diastereomeric salt pair by reaction with a chiral acid, forming a pair of diastereomers, which have different solubilities. This process allows a single diastereomer to crystallise out whilst the undesired diastereomer remains in solution. The undesired enantiomer can then be racemised by iridium catalysis, forming more of the racemic starting material, which is then available for further crystallisation.

This diastereomeric resolution/racemisation recycling process has been carried out in a continuous flow process. Conventionally, flow systems are unable to handle multiphase systems; however, the AMTech Coflore agitated tube reactor (ATR) addresses this problem. We present a continuous CIDT and racemisation process of a model amine substrate using the Coflore ATR, which gives 100% yield of a single enantiomer. To our knowledge, this is the first time such a process has been successfully achieved in flow.