CASE STUDY

Designing a Robust Scalable Catalytic Process

The challenge

The client's Phase I process was struggling to deliver API in low kg quantities. In particular, Intermediate B was of variable quality, and residual metals were known to negatively affect the onward chemistry.

How?

CatSci's extensive experience interrogating inherited processes with respect to identifying stable catalytic species, minimising catalyst degradation and leveraging statistical (DoE) knowledge was utilised to design a robust, scalable process with effective metal scavenging and no chromatography.

The achievement

A new isolation procedure for Intermediate B was designed, resulting in effective removal of Cu and Pd from Step 1 by means of treatment with $Na_2S_2O_3$ followed by charcoal filtration. Use of high-purity Intermediate B resolved many of the issues with the Step 2 chemistry, allowing Intermediate C to be telescoped into Step 3 with high purity. A DoE study understanding the reaction space for Step 3 allowed conditions to be selected which minimised impurity formation, removing the need for chromatographic purification of Intermediate E. The client will apply learning to refine flow system for metal removal and generate isotherms for the scavenging processes.



The team: Dr Vargini Thangavadivale, Dr Dan Smith & Dr Siân Forsyth

Old Process	New Process
Struggling to deliver on kilogram scale	Robust & regioselective >99%
Intermediate B variable purity	Homogeneous reaction
Problematic residual metals in intermediate B	5 relative volumes
Unstable intermediate C isolated	Residual Pd: <100 ppm
89 area% intermediate E at the end of reaction	97 area% intermediate E at the end of reaction