CASE STUDY

Effective Route Scouting allows Pilot Plant Slot to be met

The challenge

CatSci was tasked with performing route-scouting, route selection and early-phase process development over a 6-month period to meet a pilot plant manufacturing slot.

How?

Collective brainstorming, and the use of SciFinder, identified a range of synthetic strategies. Scouting experiments were performed using model systems to probe structurally simplifying disconnections. After two such iterations, three distinct route options were studied in more detail (see right). A Pugh matrix was used to semi-quantitatively facilitate the route selection exercise.

The achievement

After Route option 1 was selected, reagents, solvents and processing conditions were developed for each of its stages based on solubility data for its intermediates. A key challenge arose at the ultimate step, as the final product resisted crystallisation and oiled out. Use of crystallisation screening systems led to the identification of an optimal solvent system and seeding temperature, ensuring this key risk to the manufacture was eliminated ahead of the transfer to the manufacturing plant. The process was successfully performed 'right first time' on 120 kg scale with reproducible yields, purity and physical form. CatSci is working with the client on a patent application to protect the use of the route intermediates

Rapid R&D: 6-months from PoC to tech transfer

Reproducible solid form: optimised crystallisation method

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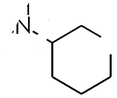
Route-Scouting: 7 Synthetic Strategies Identified
Route Selection: 3 Most-Promising Options with key disconnections

Route Option 1



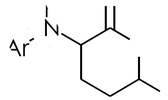
Direct Displacement

Predictive PMI: 108

Number of Steps: 3

Ideality: 66.6%

Route Option 2



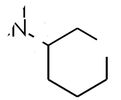
Cross Coupling

Predictive PMI: 590

Number of Steps: 4

Ideality: 50%

Route Option 3



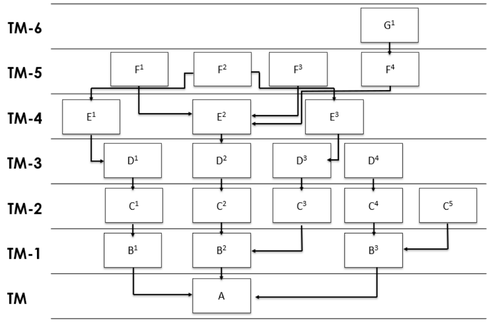
Reductive Amination

Predictive PMI: 677

Number of Steps: 4

Ideality: 40%

Route Map 7: Potential Options



- Visualised synthetic strategies
- Highlighted common intermediates
- Identified most direct routes

Route comparison using the Pugh Matrix

Criteria	Weighting	Route 1	Route 2	Route 3
Limited use of toxic reagents		0	+	+ +
Multiple SM suppliers		0	0	-
Cost of raw materials		0	+	- -
Telescope opportunities		0	-	-
Solid state of intermediates		0	- -	0

- Highlighted strengths & weaknesses of each synthetic route
- Criteria & weighting decided with client

Find out more: catsci.com