Johnson Matthey
Pharma Services

CASE STUDY

Process Research and Development for a Scalable Synthesis of a Natural Product API

Summary
Pharma Division of a large corporation desired a scalable kg synthesis of a complex natural product for pre-clinical studies.

Approach

- Developed scalable 6-step synthesis of complex natural product (5 chiral centers) from original medicinal chemistry route which was done on a mg scale.
- Improved overall yield from 1.4% to 13%.
- Reduced chromatography steps (6) including prep HPLC to a single filtration through silica.
- Sourced a natural product analog as key SM.
- Replaced NaH and L-Selectride with alternative process-friendly base and reduction method.
- Developed biphasic reductive de-protection method as last step to minimize over-reduction.
- Able to generate 1-2 kg of final product, >97% purity.
- Applied as general synthesis to analogues using isomeric natural product SM.

Results
Client was able to progress compound through pre-clinical testing including in-vivo testing finding unexpected target activity of compound.