

# Synthetic Chemistry Case Study: Initial Scale-up and Process Improvements for the Preparation of a Lead Antibacterial Macrolone Compound

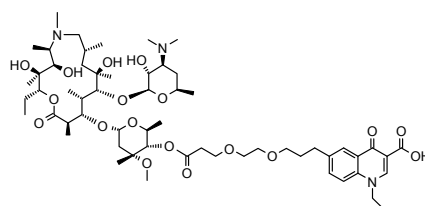
## Objective:

- Modification of a 13-step route to a lead compound
- Development of a synthetic procedure suitable for the preparation of several hundred gram quantities with at least 98 % purity

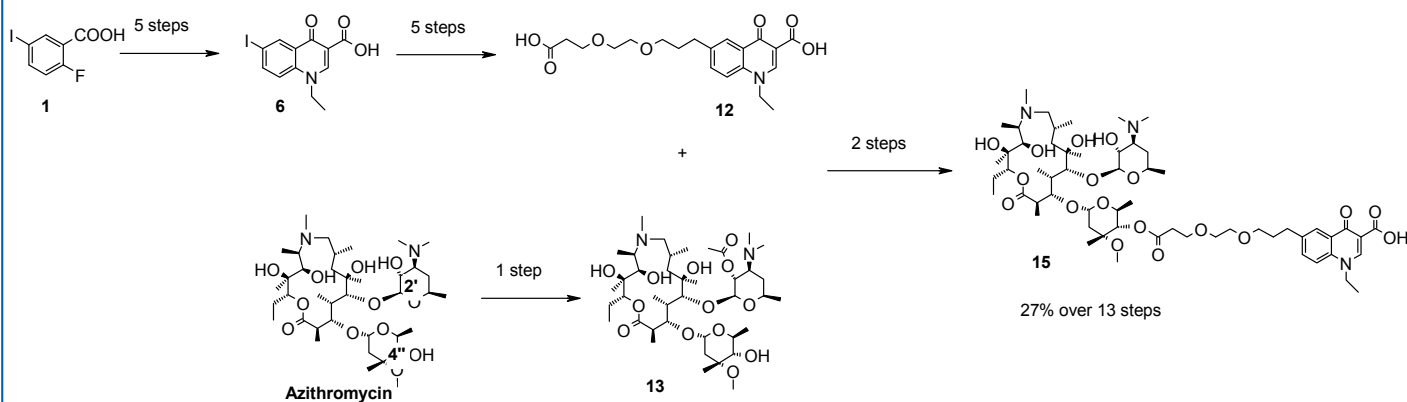
## Challenge:

- To prepare sufficient material to support preclinical *in vivo* studies within limited time frame

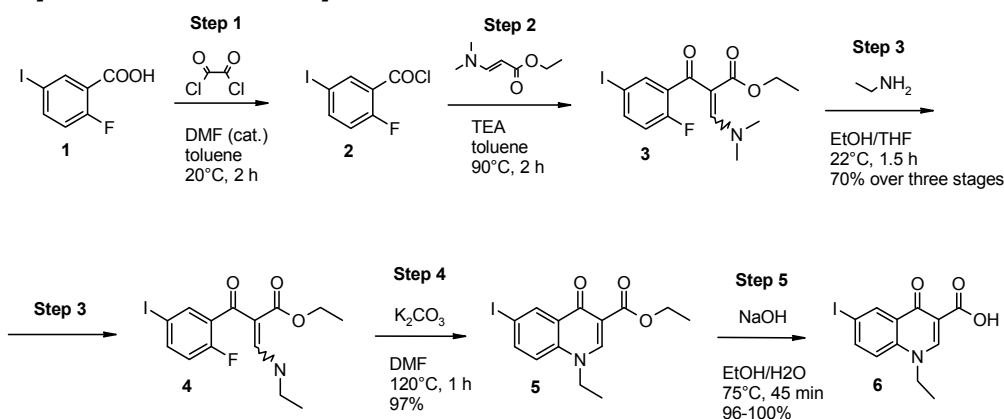
Modified synthetic procedure was successfully applied using laboratory 5L reactor to prepare an initial 350 g of lead compound



## Synthetic route to lead compound and key building blocks

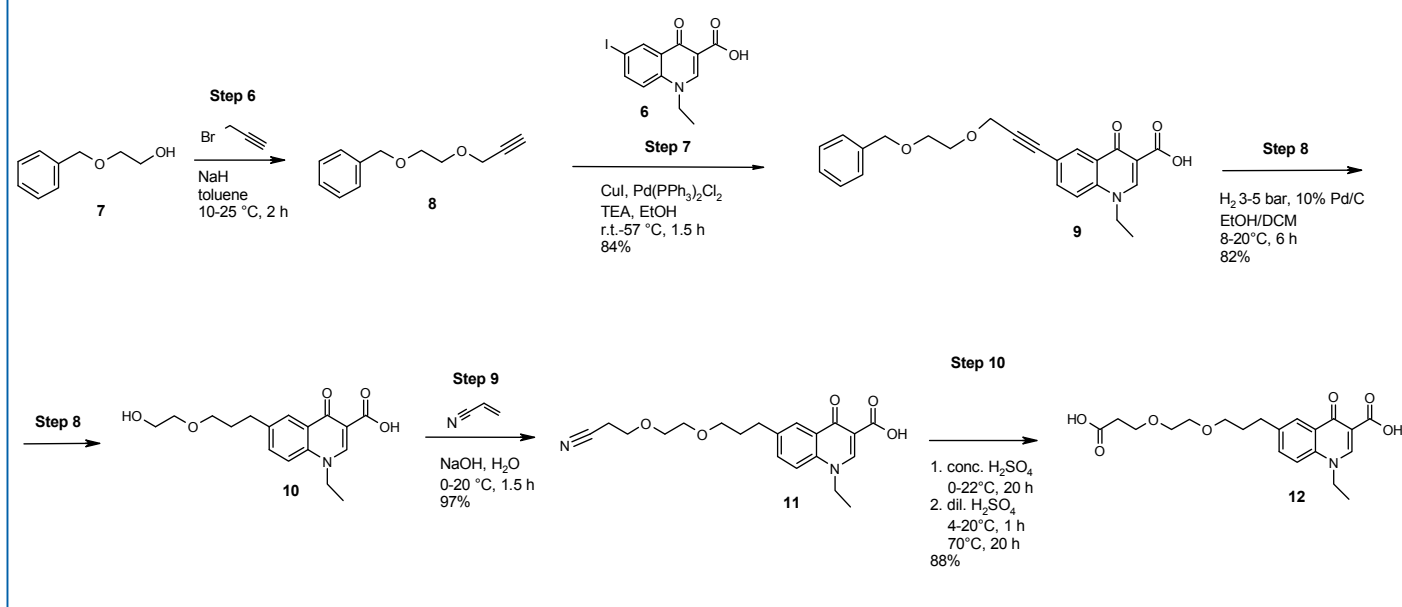


## Synthesis of the key intermediate



Minor modifications in the workup, isolation and purification were required to furnish 2.0 kg of intermediate **6** in 66% overall yield with >99.5% purity

### Optimised synthetic route - multigram scale synthesis



### Summary:

- Critical reaction steps in the medicinal chemistry route were modified for an initial scale up process
- Synthetic procedure for several hundred gram quantities of the final product with over 98% purity was developed
- The new procedure does not require any purification by column chromatography
- Total of 350 g of lead compound was prepared

### References:

V. Štimac et al., *OPRD* **14** (2010) 1393-1401.