Old Methods to New Targets: Accessing Highly Functionalized Heterocycles for Drug Development

Christopher Borths

Amgen, Thousand Oaks, CA, USA

The development of a practical and efficient synthesis of an investigational drug candidate will be described. A Vilsmeier-Haak quinolinone synthesis was first developed to support the initial multi-kilo manufactures. Alternative chemistry based on a highly selective Friedlander cyclization was later discovered to provide efficient access to the key quinolinone intermediate. Development of subsequent transformations to access the target molecule including development of a challenging Negishi coupling and selective oxime hydrogenation will also be described. The process development ultimately provided access to the non-racemic drug candidate in 5-step chiral process with a 47% overall yield.