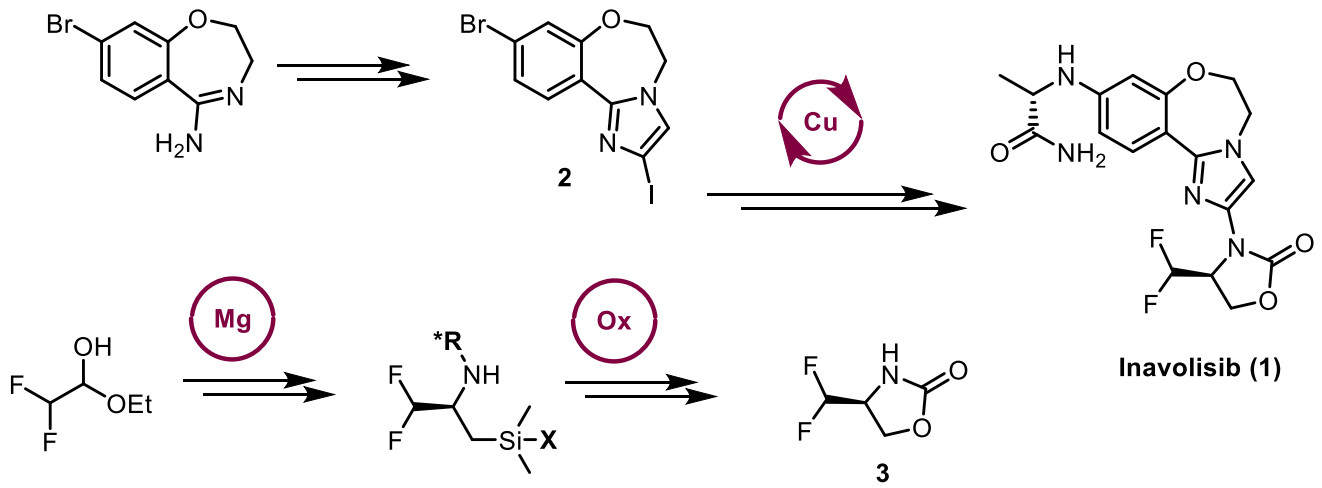
Development of the Commercial Manufacturing Process for Inavolisib

S. Rummelt[I], T. Brütsch[II]

[I] *Process Chemistry & Catalysis, F. Hoffmann-La Roche Ltd., Grenzacherstrasse 124, CH-4070 Basel, Switzerland, stephan.rummelt@roche.com*
[II] *Route and Process Design, Dottikon Exclusive Synthesis AG, Hembrunnstrasse 17, CH-5605 Dottikon, Switzerland, tobias.bruetsch@dottikon.com*



Scheme 1: Synthesis of Inavolisib (1)

Inavolisib (1) is a highly potent and selective PI3Kα inhibitor, which is currently in clinical development for the treatment of HR+, HER2- breast cancer and has recently been approved by the FDA.[1]
Herein we present the development of a robust and scalable manufacturing process for Inavolisib (1). A route scouting case study and process design for the oxazolidinone 3 is presented. The selected route for 3 features a diastereoselective Grignard addition followed by a Tamao-Fleming oxidation.[3] At the core of the synthesis of Inavolisib (1) are two consecutive Cu-catalyzed CN-coupling reactions with one of them connecting the two key building blocks dihalide 2 and oxazolidinone 3 (Scheme 1).[2]

References

[1] N. C. Turner, et al. *NEJM* 2024, 1584; E. J. Hanan, et al. *J. Med. Chem.* 2022, 16589.
[2] C. Han, S. M. Kelly, T. Cravillion, S. Savage, T. Nguyen, F. Gosselin. *Tetrahedron* 2019, 4351.
[3] R. Angelaud, T. Brütsch, F. Gosselin, C. Han, A. Stutz, *WO2022251567* 2022.