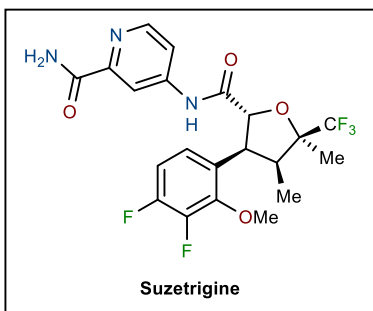
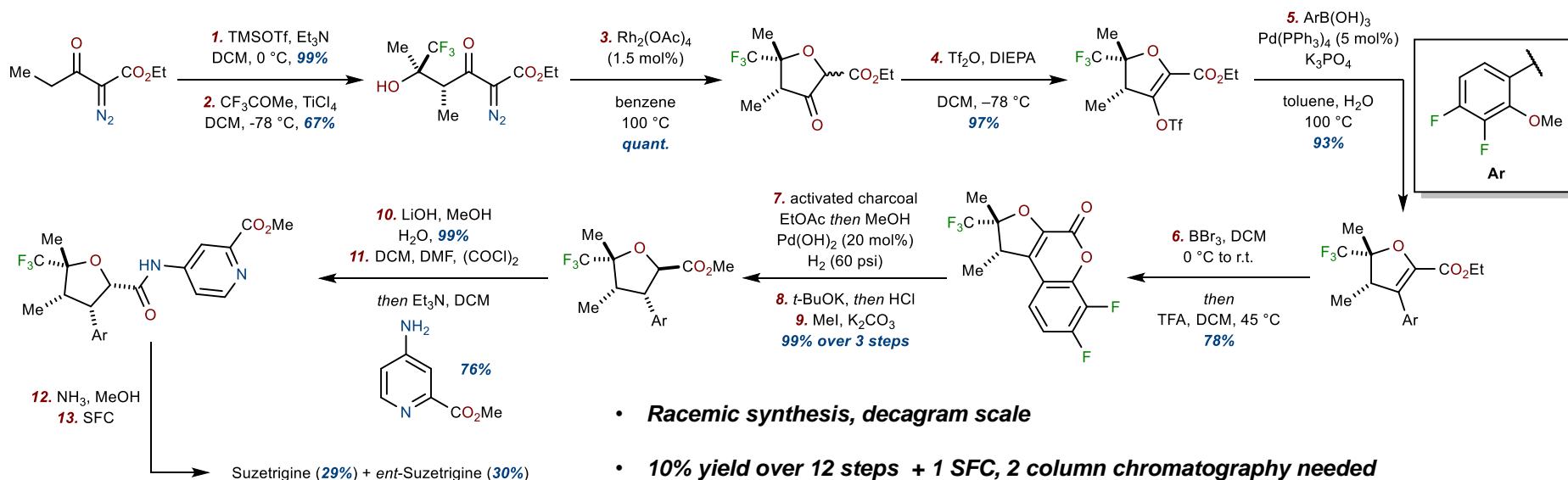


Introduction



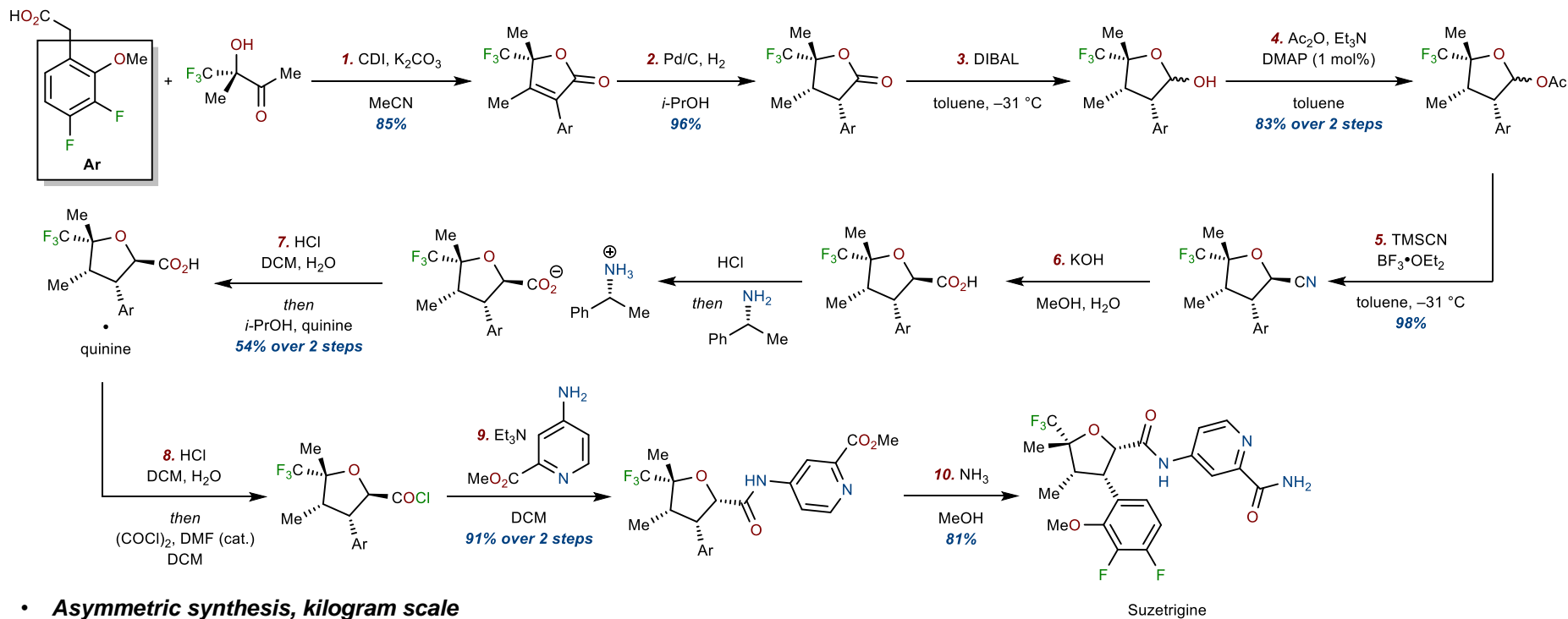
- Non-opioid, small-molecule analgesic, selective inhibitor of sodium ion channel Nav1.8
- For the treatment of moderate-to-severe acute pain, for example, post-surgical pain
- Successfully met several endpoints in its Phase III trials, as claimed by Vertex in Jan. 2024
- Penta-substituted tetrahydrofuran, four contiguous stereocenters

Discovery Route



- **Racemic synthesis, decagram scale**
- **10% yield over 12 steps + 1 SFC, 2 column chromatography needed**
- **High-energy starting material, cryogenic reaction conditions**

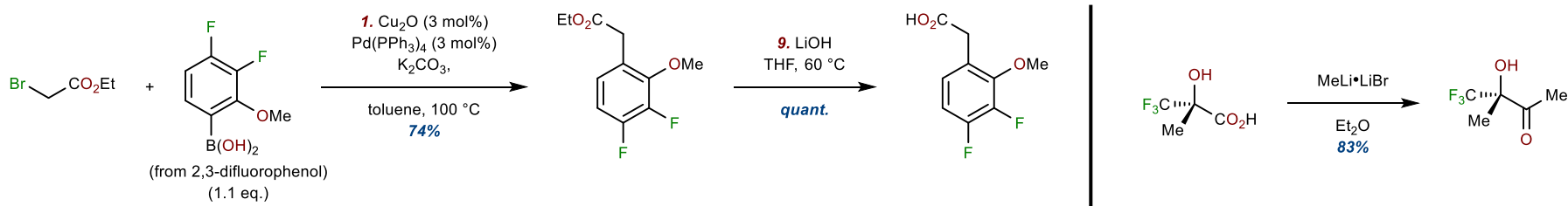
Process Route



• **Asymmetric synthesis, kilogram scale**

• **26% yield over 10 steps, no SFC or column chromatography needed**

Process for the synthesis of substituted tetrahydrofuran modulators of sodium channels, WO2022256660 A1 2022-12-08



Hydroxy and (halo)alkoxy substituted tetrahydrofurans as modulators of sodium channels and their preparation, WO2022256842 A1 2022-12-08