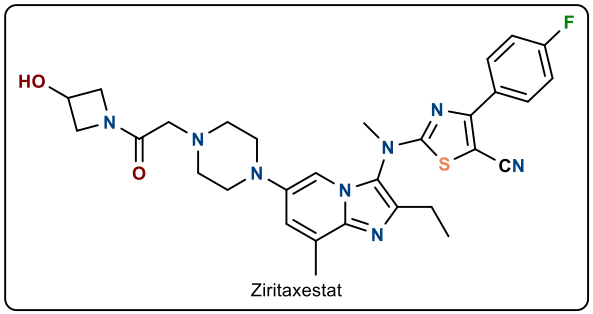
Ziritaxestat

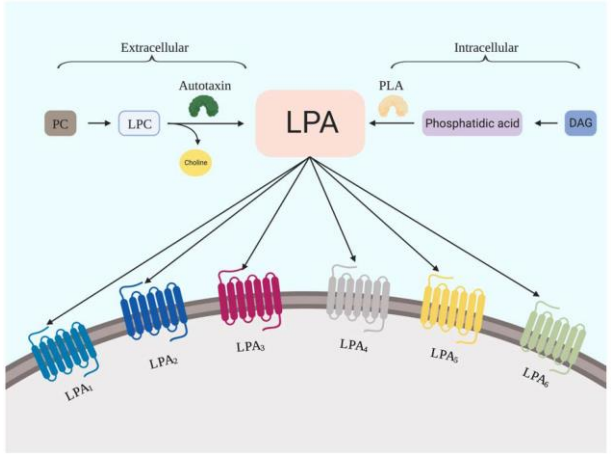


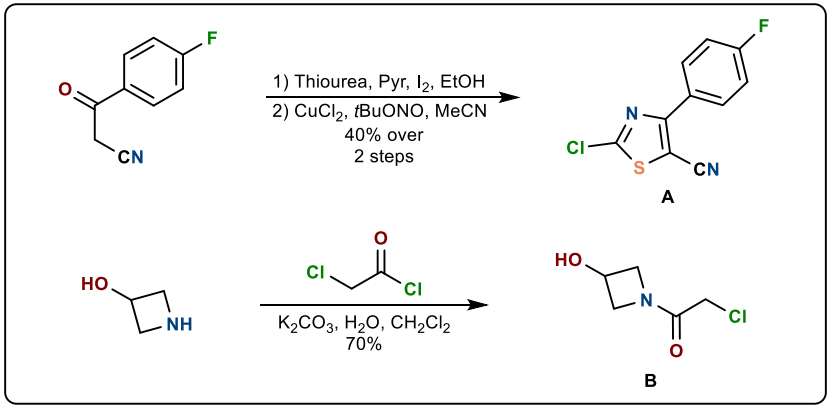
Ziritaxestat

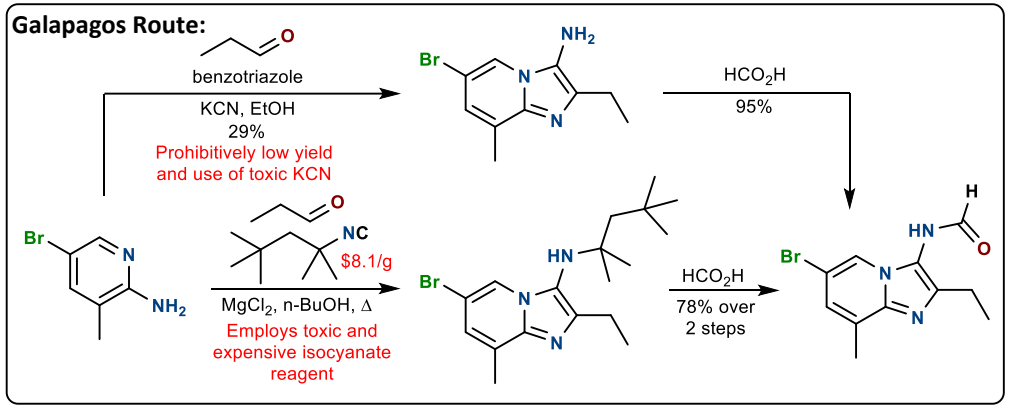
- First-in-class small molecule Autotaxin inhibitor
- Used to treat patients with idiopathic pulmonary fibrosis (IPF) or chronic obstructive pulmonary diseases
- Initially developed by the Galapagos pharmaceutical company
- Started phase III clinical trials in 2018

Galápagos

- Idiopathic pulmonary fibrosis (IPF) is a form of interstitial lung disease that results in scarring (fibrosis) of the lungs for an unknown reason
- There are currently no medications that can cure IPF or decrease the amount of scarring in the lungs, however some medications can help slow the progression of the scaring.
- Autotaxin, a lysophospholipase that cleaves lysophosphatidyl choline (LPC) into the bioactive phospholipid derivative lysophosphatidic acid (LPA) has been implicated in IPF
- Both Autotaxin and LPA have been shown to be upregulated in patients with IPF and autotaxin knockout mice were shown to be less sensitive to experimental models of lung fibrosis.
- Ziritaxestat is a competitive inhibitor of autotaxin that occupies the hydrophobic pocket of the active site, which accommodates the fatty acid chain of LPC, as well as a hydrophobic channel, which is responsible for delivering LPA to its target receptors.



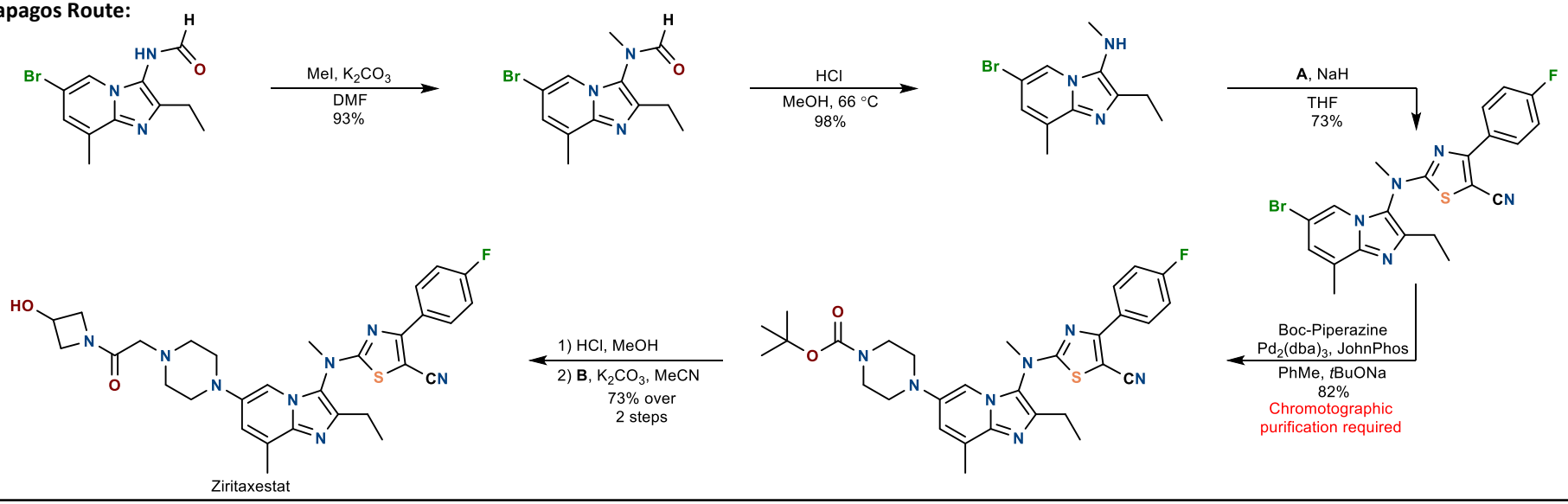




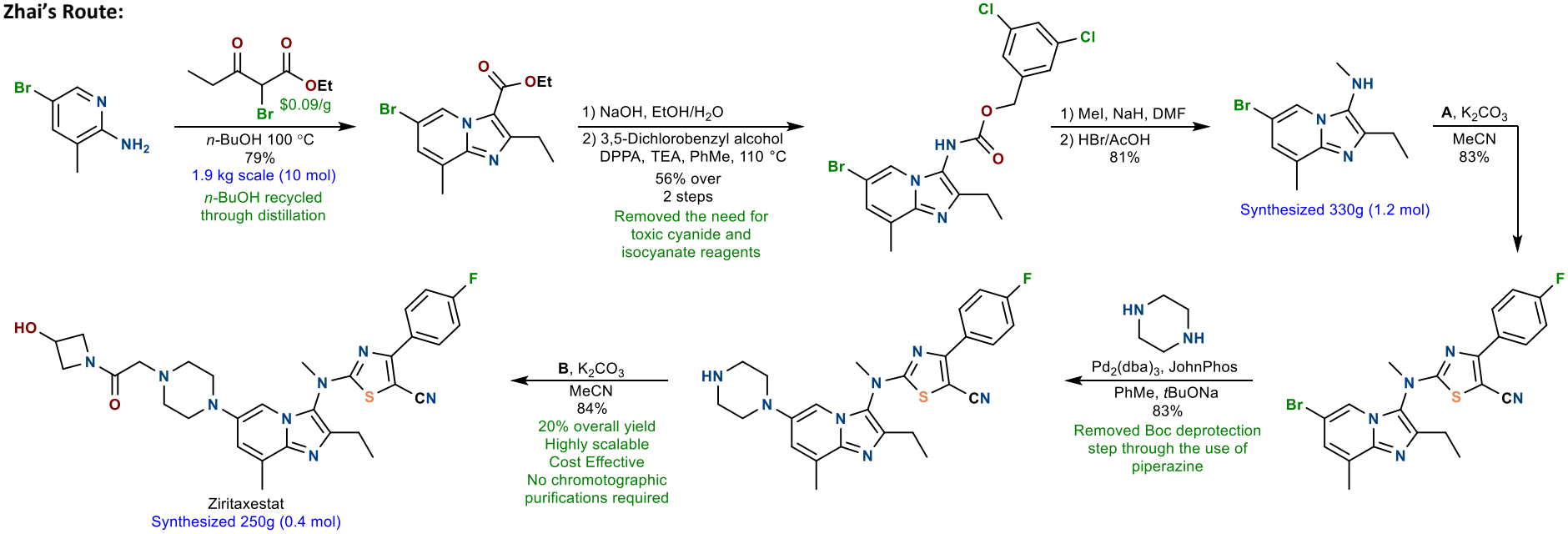
Zhai, X. *Org. Process. Res. Dev.* **2020**, *ASAP*. https://doi.org/10.1021/acs.oprd.9b00511

Ziritaxestat

Galapagos Route:



Zhai's Route:



Zhai, X. *Org. Process. Res. Dev.* **2020**, *ASAP*. https://doi.org/10.1021/acs.oprd.9b00511