Deucravacitinib (BMS-986165)

Background

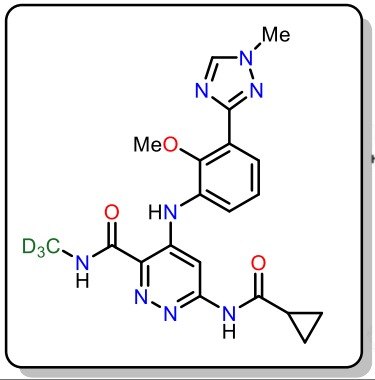
- To mitigate the symptoms of several autoimmune diseases (psoriasis, lupus, etc…)
- High-affinity inhibitor of TYK2 that selectively binds to its pseudokinase (JH2) domain
- D_3-methyl group improved metabolic stability to prevent metabolic demethylation

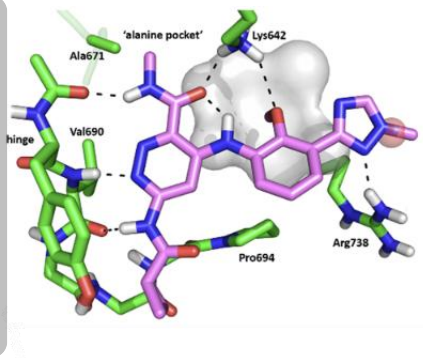
(free amide has also potent bioactivity but lacks selecticity, which induce side effects)

- Approved by FDA in 2022 and considered to be first-in-class medicine.

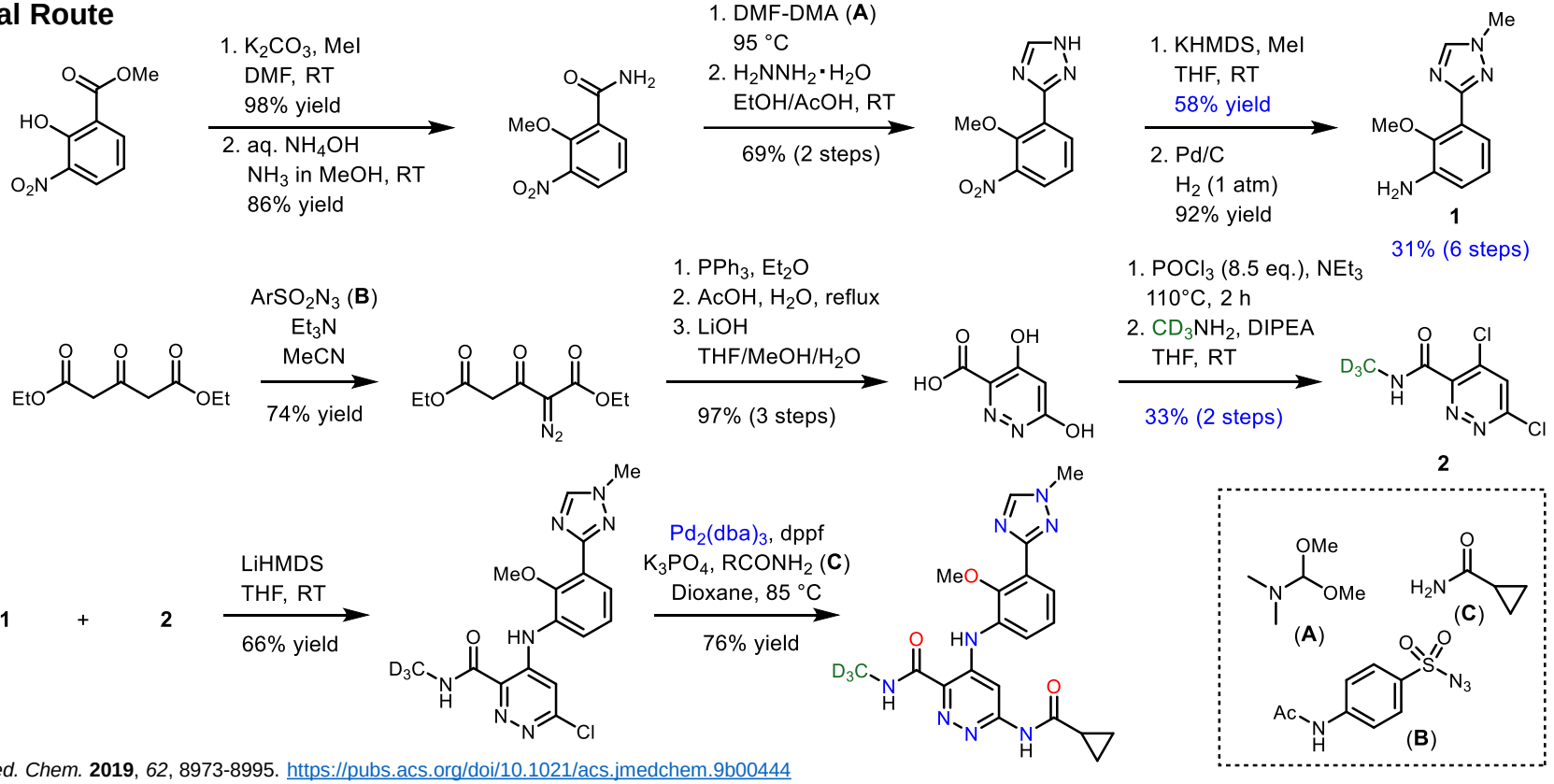
Structural feature

2 heterocycles (1,2,4-triazole, pyridazine) and 2 amides (D_3-methyl, cyclopropyl)





Initial Route



J. Med. Chem. **2019**, *62*, 8973-8995. https://pubs.acs.org/doi/10.1021/acs.jmedchem.9b00444

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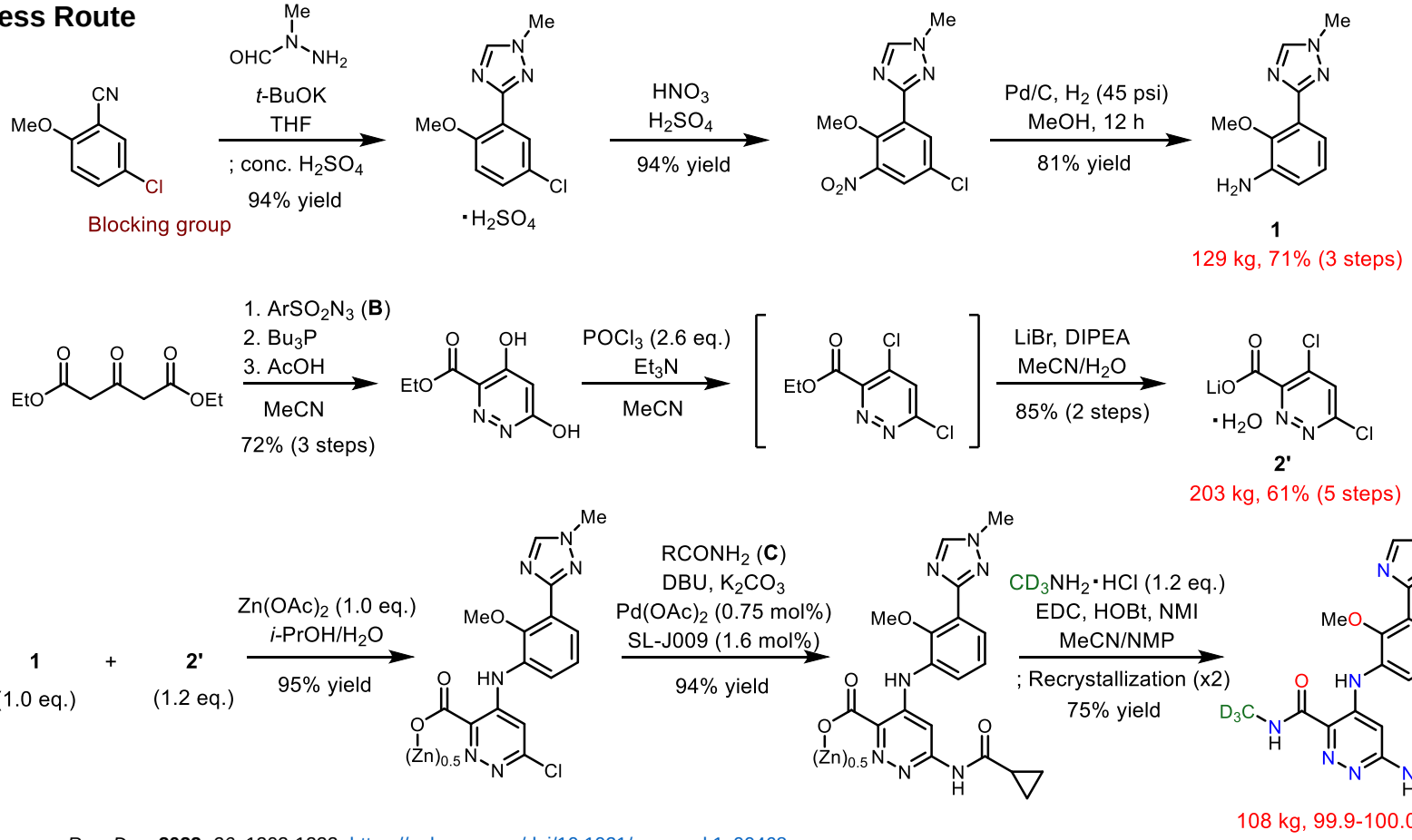
Process Route



Org. Process. Res. Dev. **2022**, *26*, 1202-1222. https://pubs.acs.org/doi/10.1021/acs.oprd.1c00468