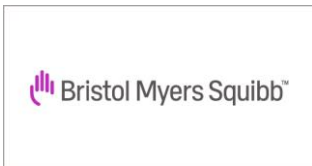
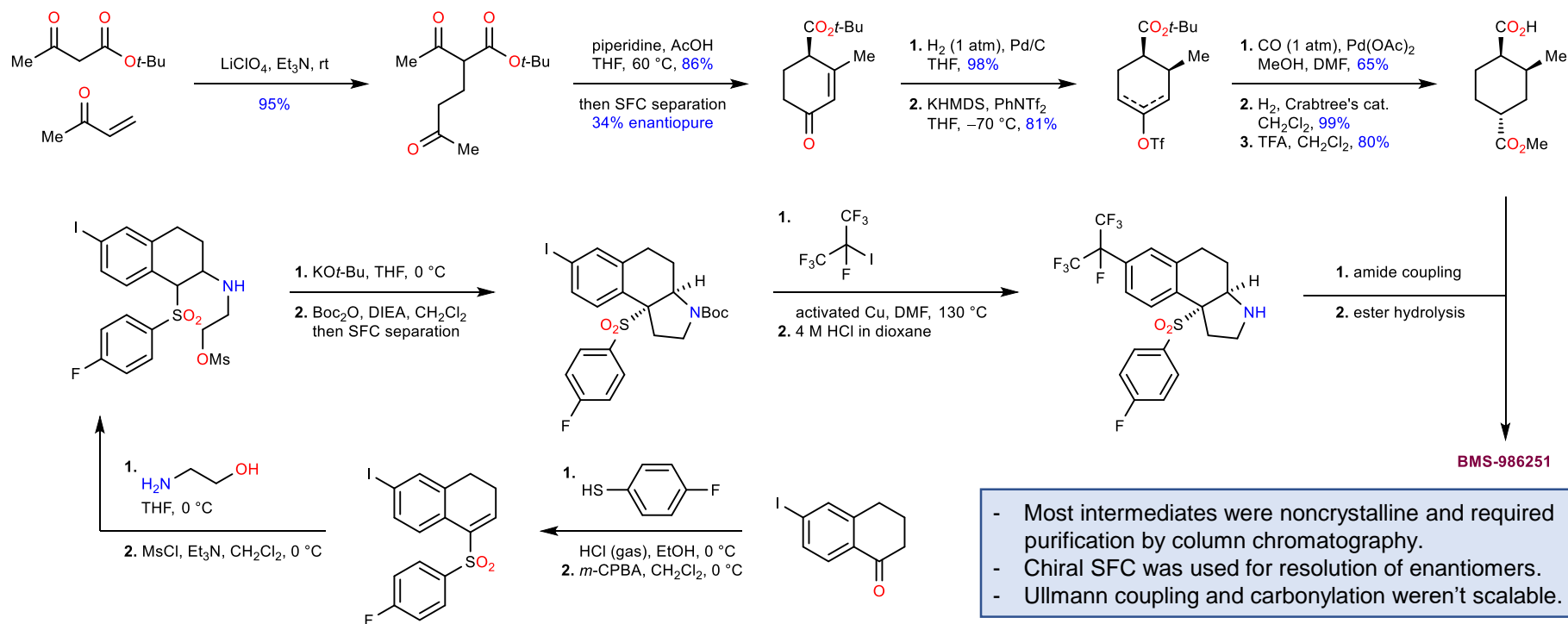


- BMS-986251 is a potent small molecule retinoic acid-related orphan receptor γ (ROR γ t) inverse agonist.
- ROR γ t is expressed in the thymus and is responsible for the differentiation of CD4⁺T cells into Th17 cells which produce pro-inflammatory cytokine IL-17.
- Anti-IL-17 agents are effective against autoimmune diseases.
- A process route for BMS-986251 was required to produce enough material for preclinical and early-phase clinical studies.



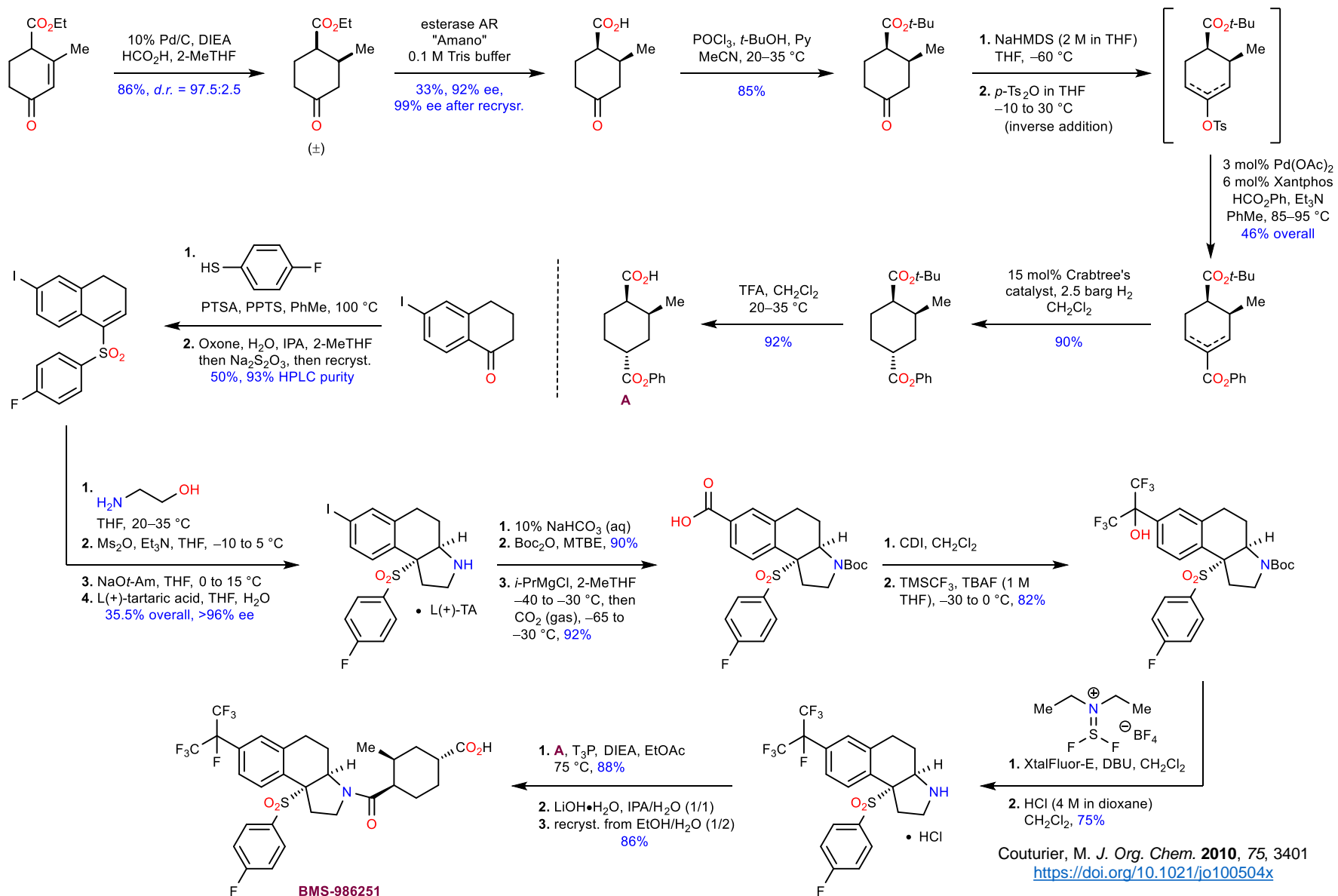
Cherney, R. J. *ACS Med. Chem. Lett.* **2020**, *11*, 1221
<https://doi.org/10.1021/acsmchemlett.0c00063>
 Gonzales-Bobes, F., Vaidyanathan, R. *Org. Process Res. Dev.* **2021**
<https://doi.org/10.1021/acs.oprd.1c00124>
<https://doi.org/10.1021/acs.oprd.1c00125>

Discovery Route:



- Most intermediates were noncrystalline and required purification by column chromatography.
- Chiral SFC was used for resolution of enantiomers.
- Ullmann coupling and carbonylation weren't scalable.

Process Route:



Couturier, M. *J. Org. Chem.* **2010**, *75*, 3401
<https://doi.org/10.1021/jo100504x>