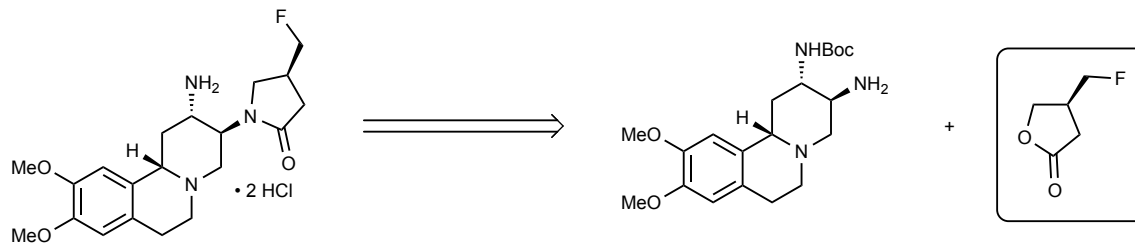
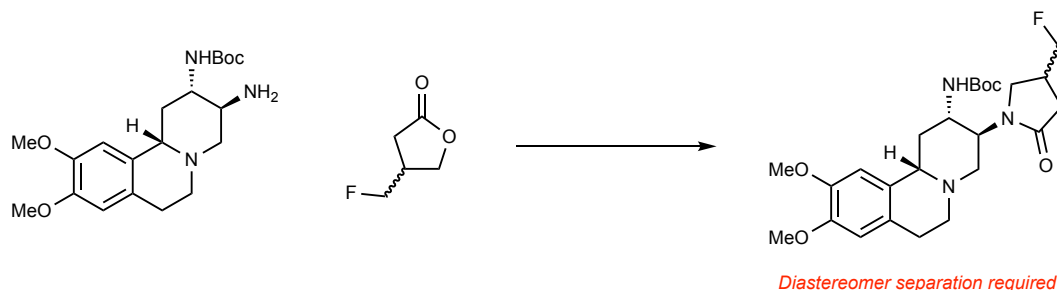
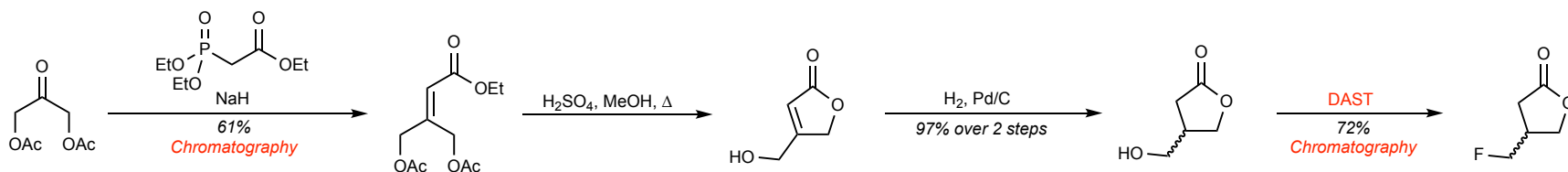


Carmegliptin is a DPP-IV inhibitor used to treat diabetes.
Scalable and enantioselective synthesis of (S)-3-Fluoromethyl-γ-butyrolactone required for API.



Discovery route to fluoromethyl butyrolactone:

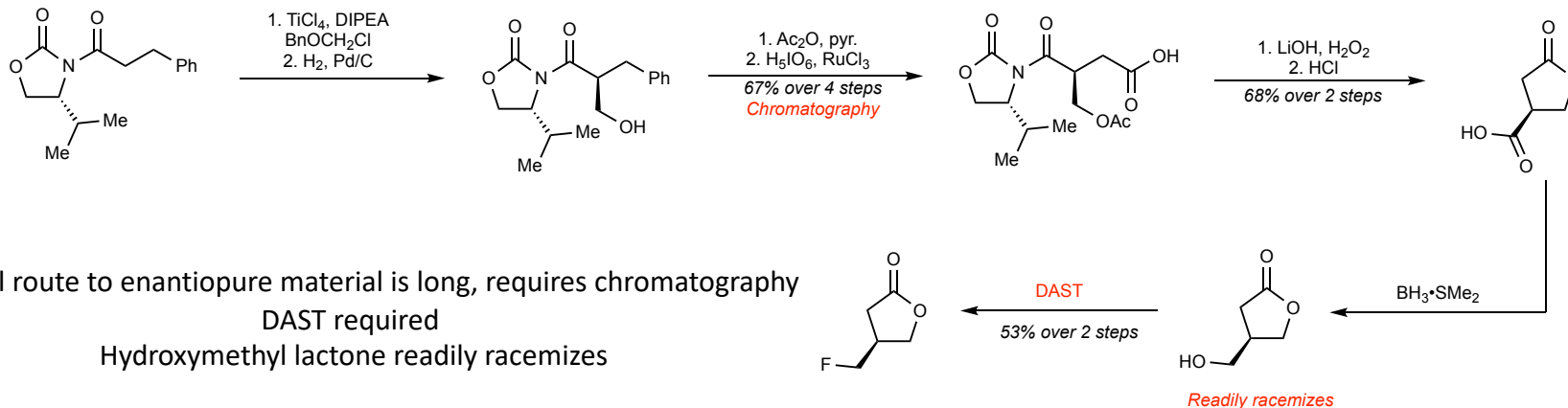


Problems in scaleup:

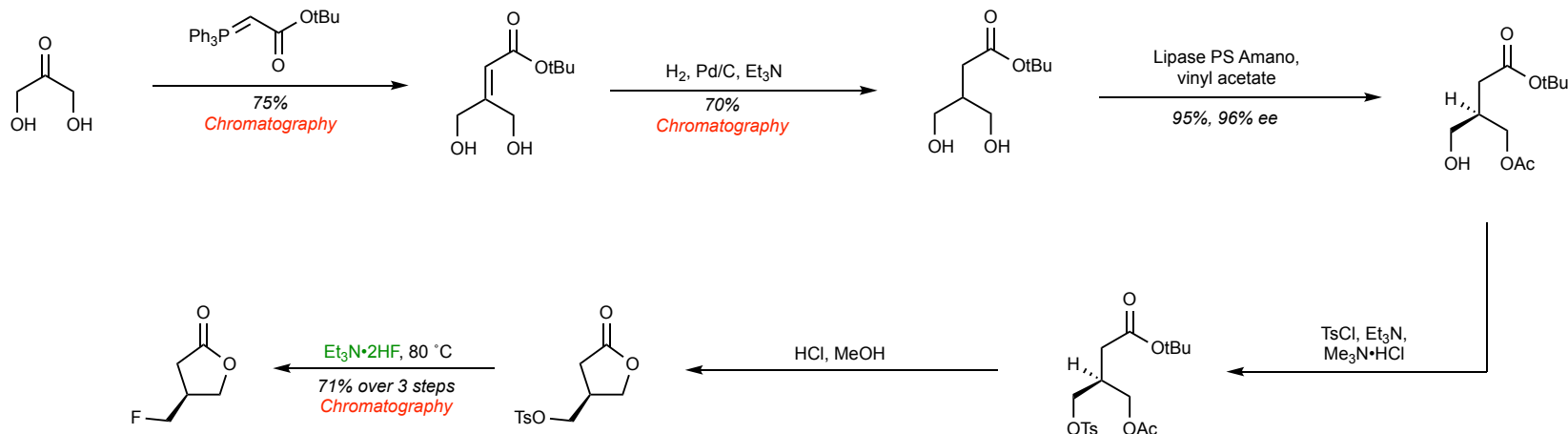
- Racemic synthesis required separation late-stage
- DAST is thermally unstable and expensive
- Column chromatography required

Your Challenge:
Enantioselective synthesis of (S)-3-Fluoromethyl-γ-butyrolactone
Avoid use of DAST

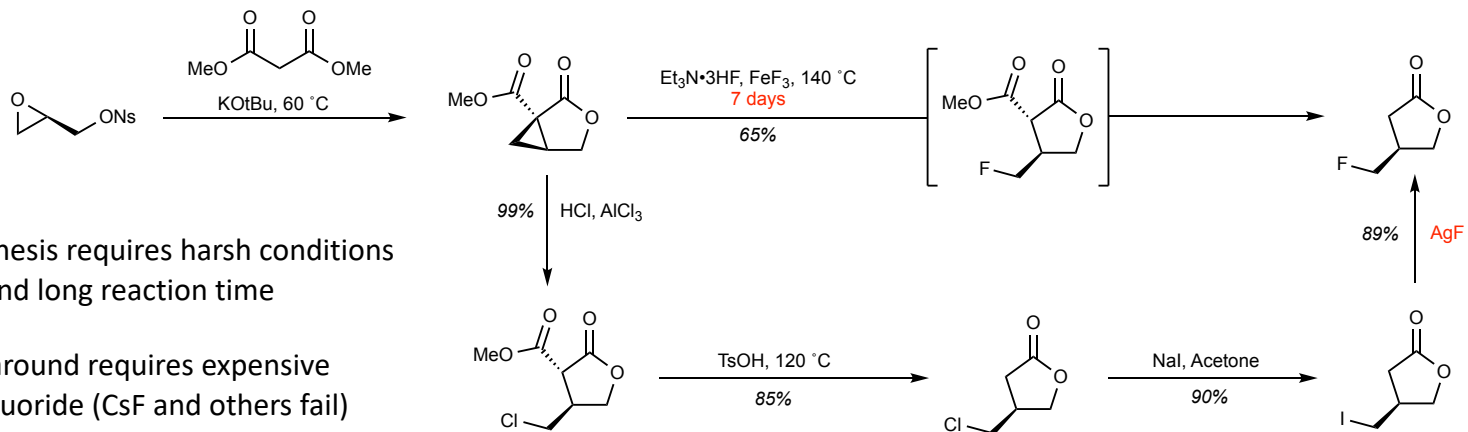
Generation 2 synthesis:



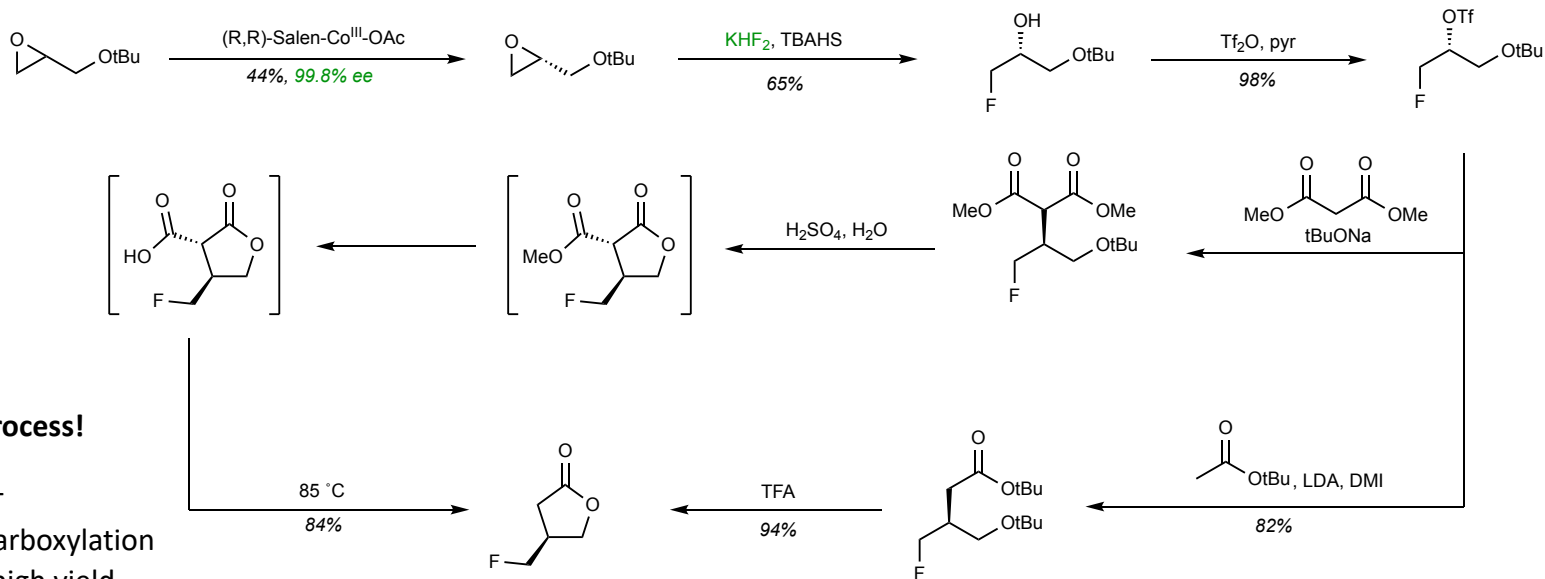
Enzymatic Resolution:



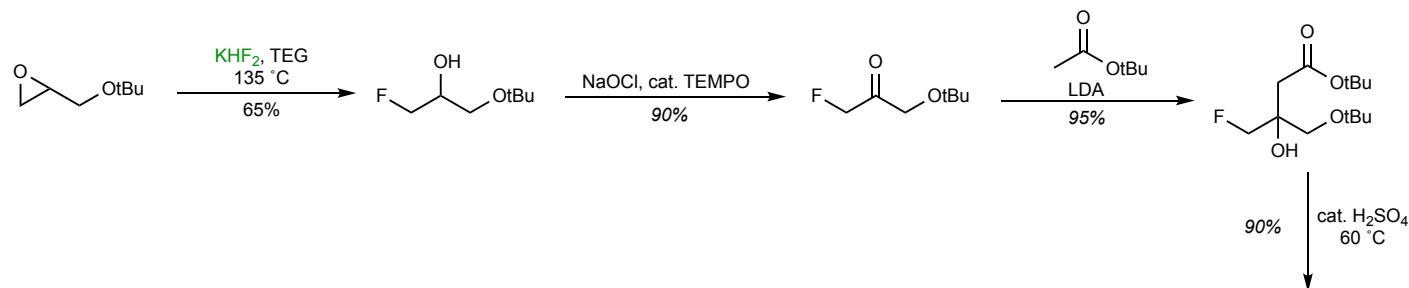
Homo-Michael Route:



Epoxide Opening Route:



Hydrogenation Route:



Candidate 2 for process!
Excellent ee with low [Ru] loading
KHF₂ instead of DAST
Simple removal of impurities after epoxide opening

