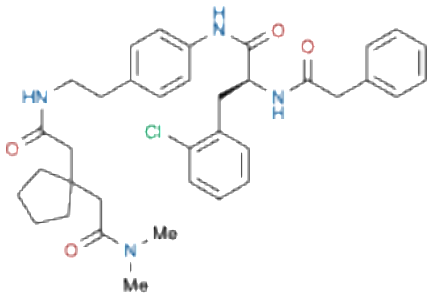
IL-17A Inhibitor Analog 26

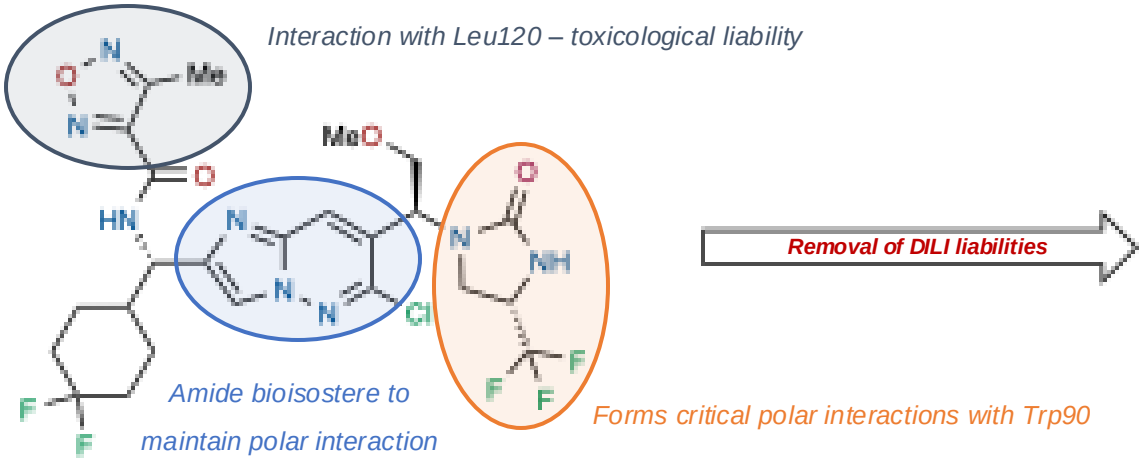
Background

- Interleukin-17A is a pro-inflammatory cytokine whose dysregulation is implicated in the development of autoimmune and inflammatory diseases (rheumatoid arthritis, transplant rejection, asthma, psoriasis, neurological disorders, cancer).
- initially, FDA approved monoclonal antibodies (i.e. secukinumab and ixekizumab) for treatment of psoriasis, psoriatic arthritis, and ankylosing spondylitis which displayed IL-17 was involved in the pathology of these diseases.
- Issues such as skin irritation, infections, and bruising caused the need for small molecule drugs for the inhibition of IL-17A to avoid repeat injections of antibodies.



Ensemble

First reported small molecule of IL-17A



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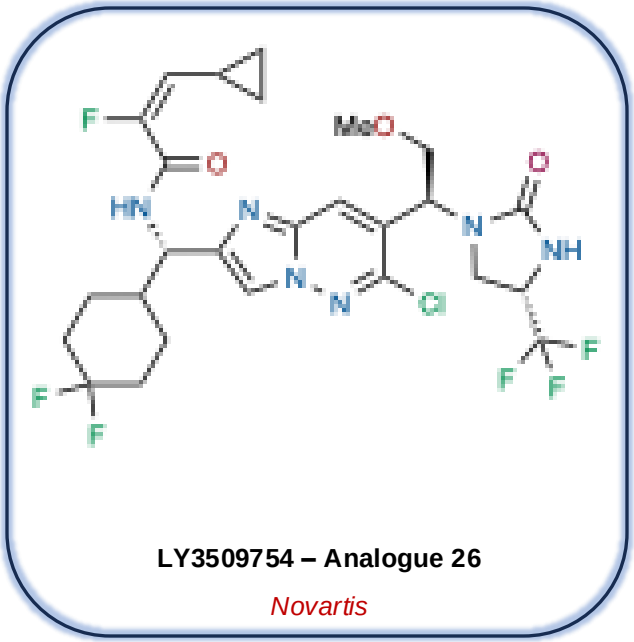
Eli Lilly

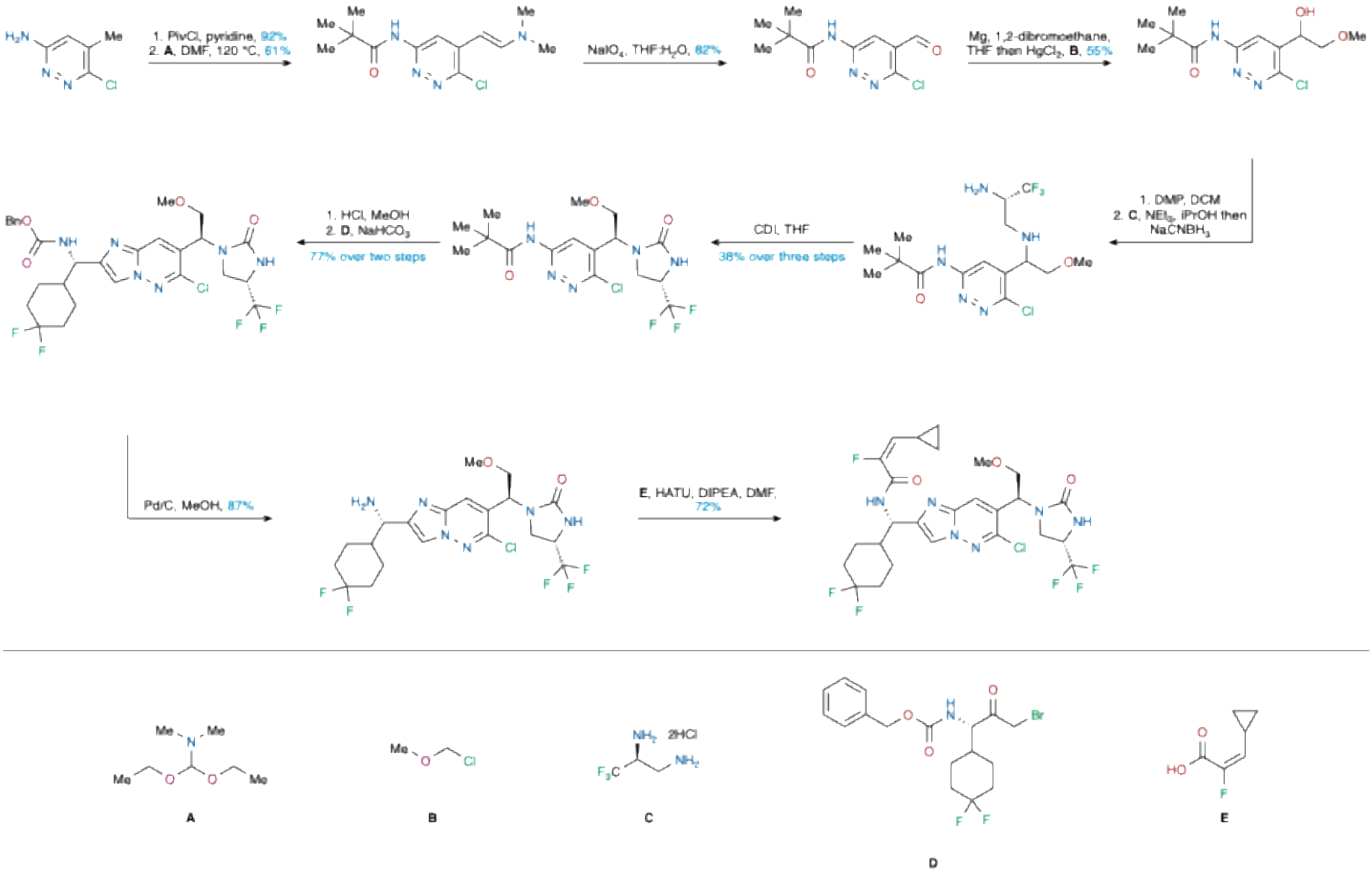


LY3509754 – Analogue 26

Novartis

Ishihara, K. *J. Med. Chem* **2024**, XXX, XXX-XXX. https://doi.org/10.1021/acs.jmedchem.4c01520, WO 2020/146194 A1

IL-17A Inhibitor Analogue 26



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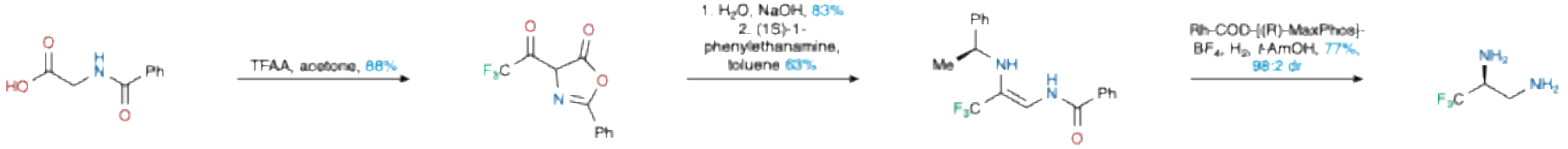
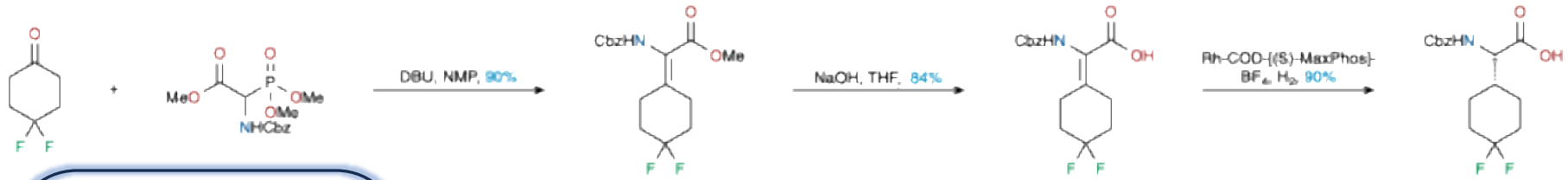
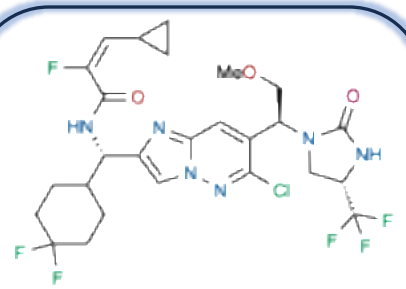
IL-17A Inhibitor Analogue 26





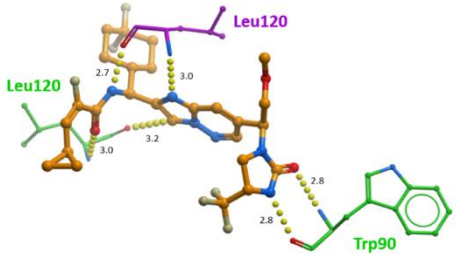


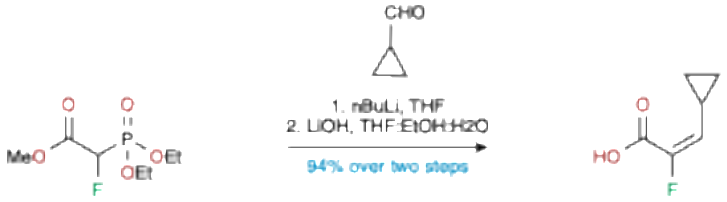
Excellent permeability and initial pharmacokinetic properties

Exceptional off-target profile

Inhibition of swelling in rat antigen-induced arthritis

Toxicity observed in rat and dog in vivo studies





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