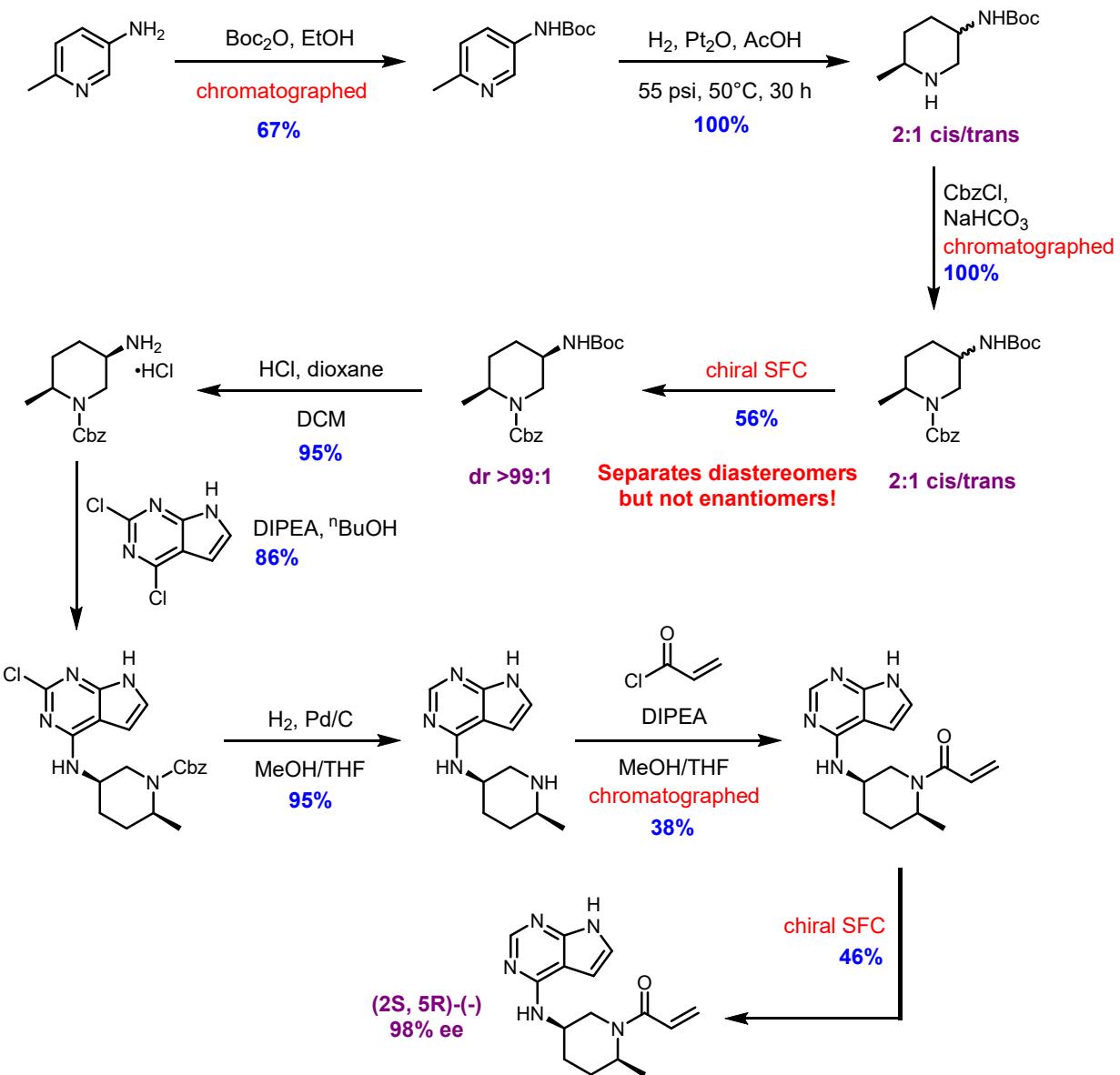
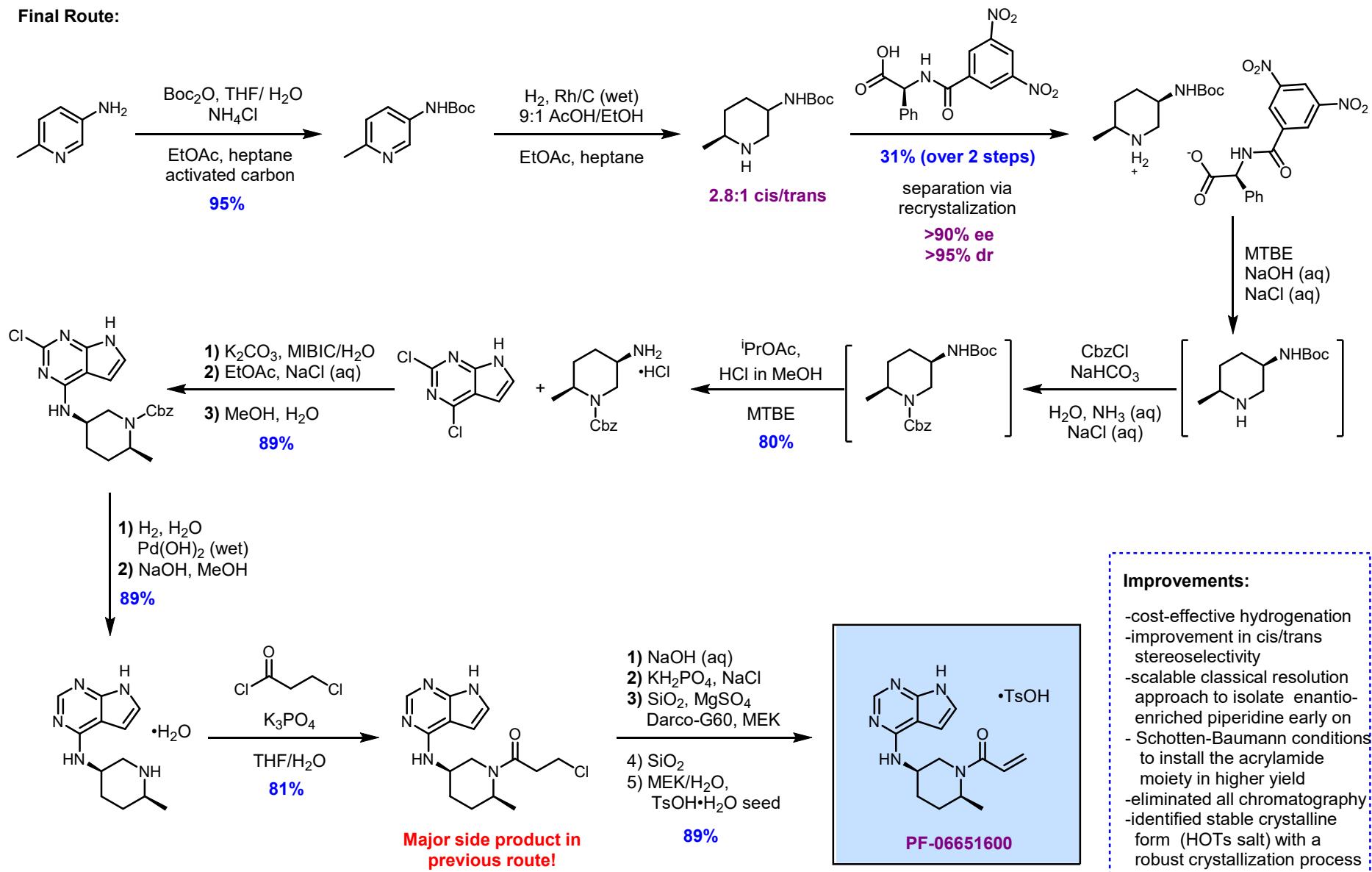


-JAK₃ covalent inhibitor with potent immunomodulatory therapy.
-Under clinical investigation for treatment of alopecia areata, rheumatoid arthritis, Crohn's disease, and ulcerative colitis.
-FDA named breakthrough therapy for alopecia areata.
-API demand increased from kilograms to more than 100 kilograms.

Initial Route:

Final Route:



Improvements:

- cost-effective hydrogenation
- improvement in cis/trans stereoselectivity
- scalable classical resolution approach to isolate enantio-enriched piperidine early on
- Schotten-Baumann conditions to install the acrylamide moiety in higher yield
- eliminated all chromatography
- identified stable crystalline form (HOTs salt) with a robust crystallization process