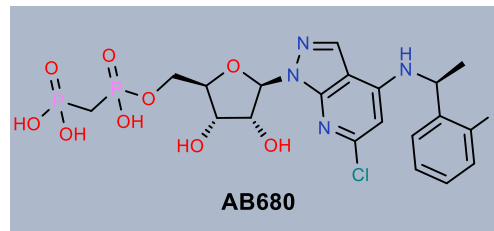
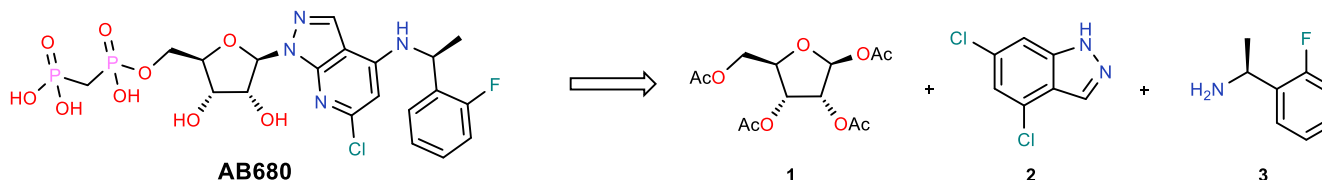


Background

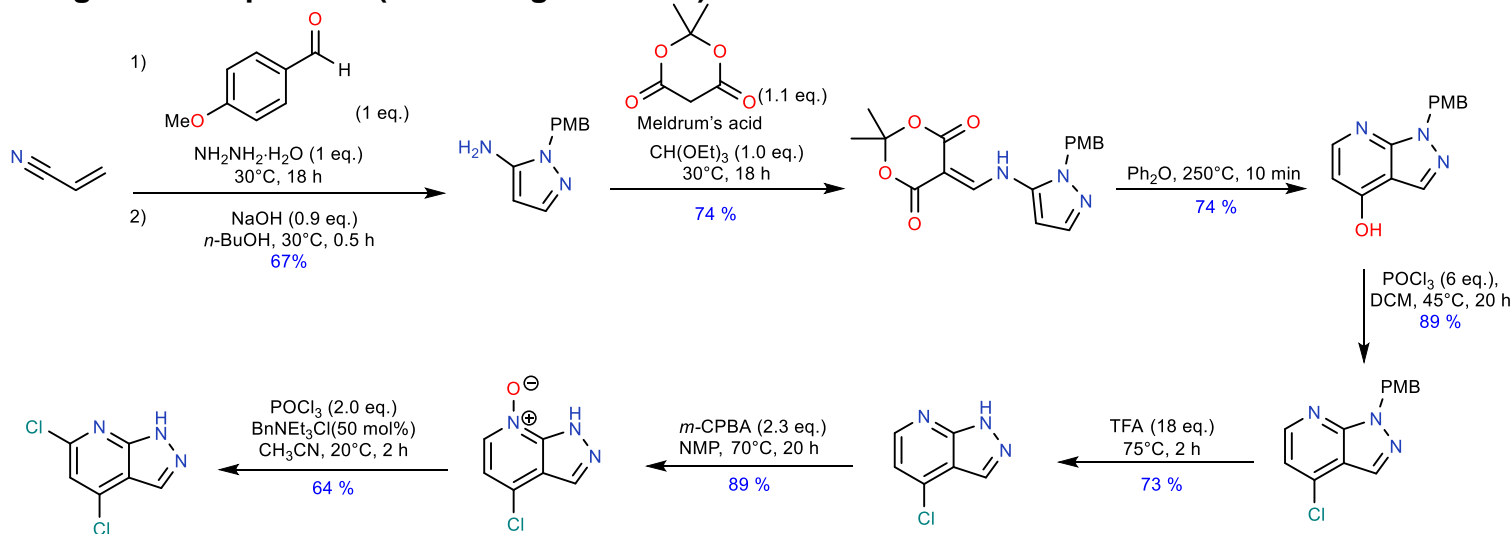
- CD73 is the enzyme that produce immunosuppressive adenosine in tumor microenvironment
- CD73 has been identify as new therapeutic target for various solid tumors
- AB680 is selective CD73 inhibitor ($K_i = 5 \text{ pM}$) under clinical trial toward pancreatic cancer



Retrosynthesis



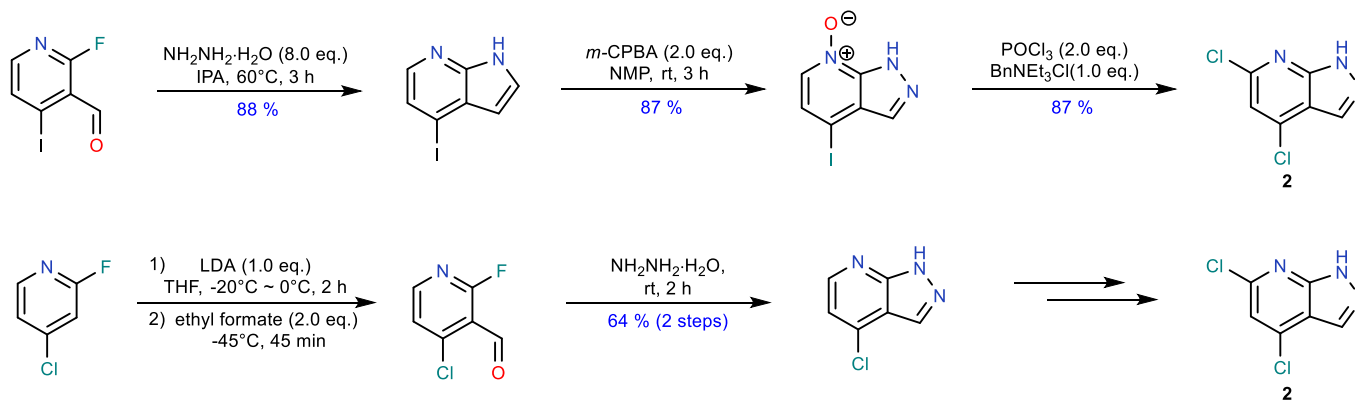
1st generation process (multi-kilogram scale)



Limitation

- High temperature (250° C)
- Polymeric byproduct in PMB deprotection
- Excess amount of *m*-CPBA
- Safety issue (*N*-oxide)
- 14 % overall yield

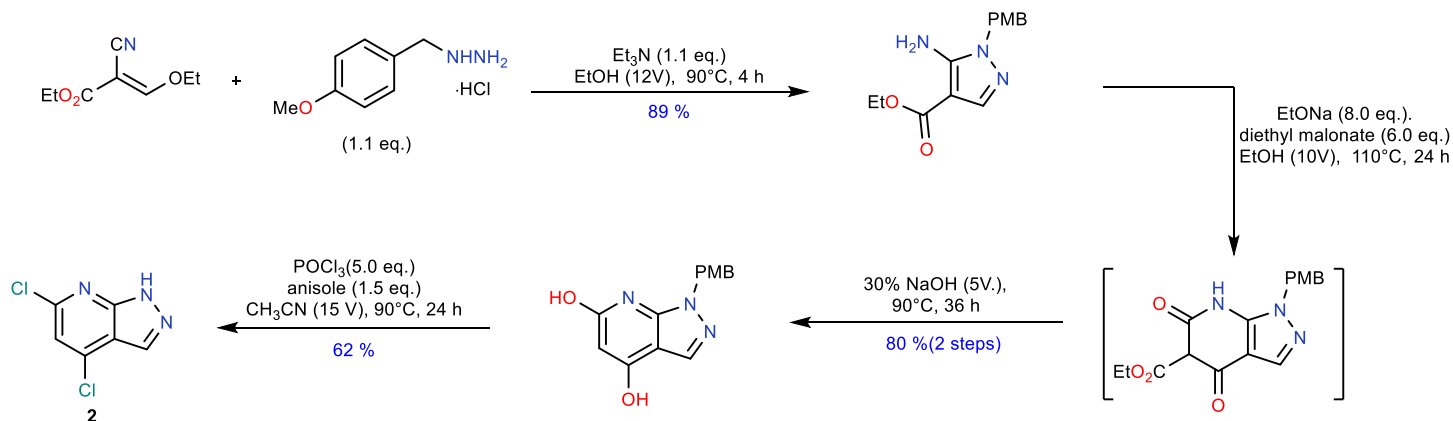
Optimization process for Compound 2



Limitation

- Expensive fluoropyridine starting material

Optimized Process for Compound 2



Optimization

- Step count 7 → 4
- Yield 14 % → 44 %
- Mild conditions
- Safe intermediate
- Cheap starting material
- No polymer formation