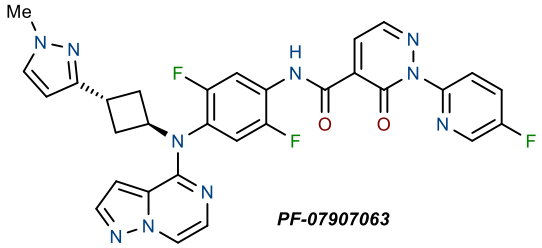
PF-07907063 (Pfizer)

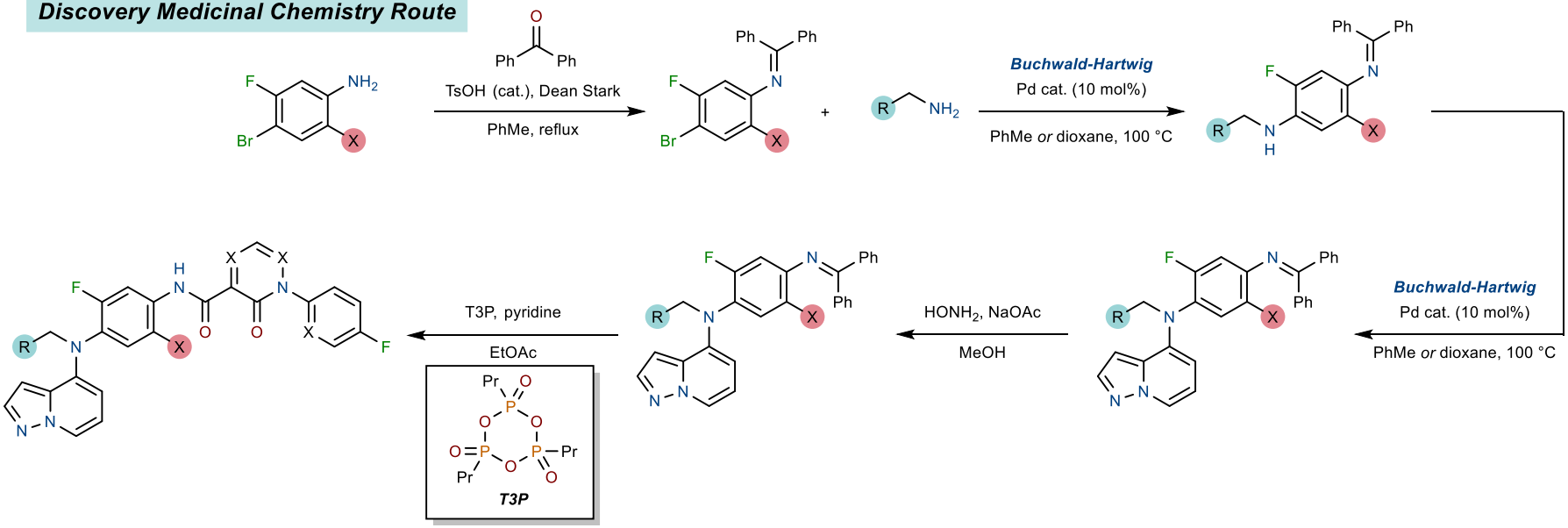
Background

- Mesenchymal-epithelial transition factor (cMET) – receptor tyrosine kinase important for embryogenesis, tissue regeneration, wound healing, etc.
- Aberrant activation of cMET leads to cancers
- Current therapeutics suffer from off-target toxicity and resistance mutations (e.g. crizotinib, cabozantinib, glesatinib, and savolitinib)
- PF-07907063 – a brain penetrant cMET inhibitor that addresses active site mutations & spared cardio-/ocular toxic off-targets



Pfizer

Discovery Medicinal Chemistry Route



McKenna, G.; Cruz, C.; Simmons, B.; Brewster, J. T. I.; Benz-Weeden, A. M.; Brandt, T. A.; Bumpers, Q. A.; Cook, A.; Elsayed, M. S. A.; Golec, D.; Lewandowski, N.; Nguyen, P.; Pipal, R. W.; Savechenkov, P.; Wong, C. E.; Tarlton, E.; Gaudino, J. J.; Hinklin, R. J.; Tang, T. P. *Org. Process Res. Dev.* **2025**, *29*, 1048–1057. https://doi.org/10.1021/acs.oprd.4c00441.

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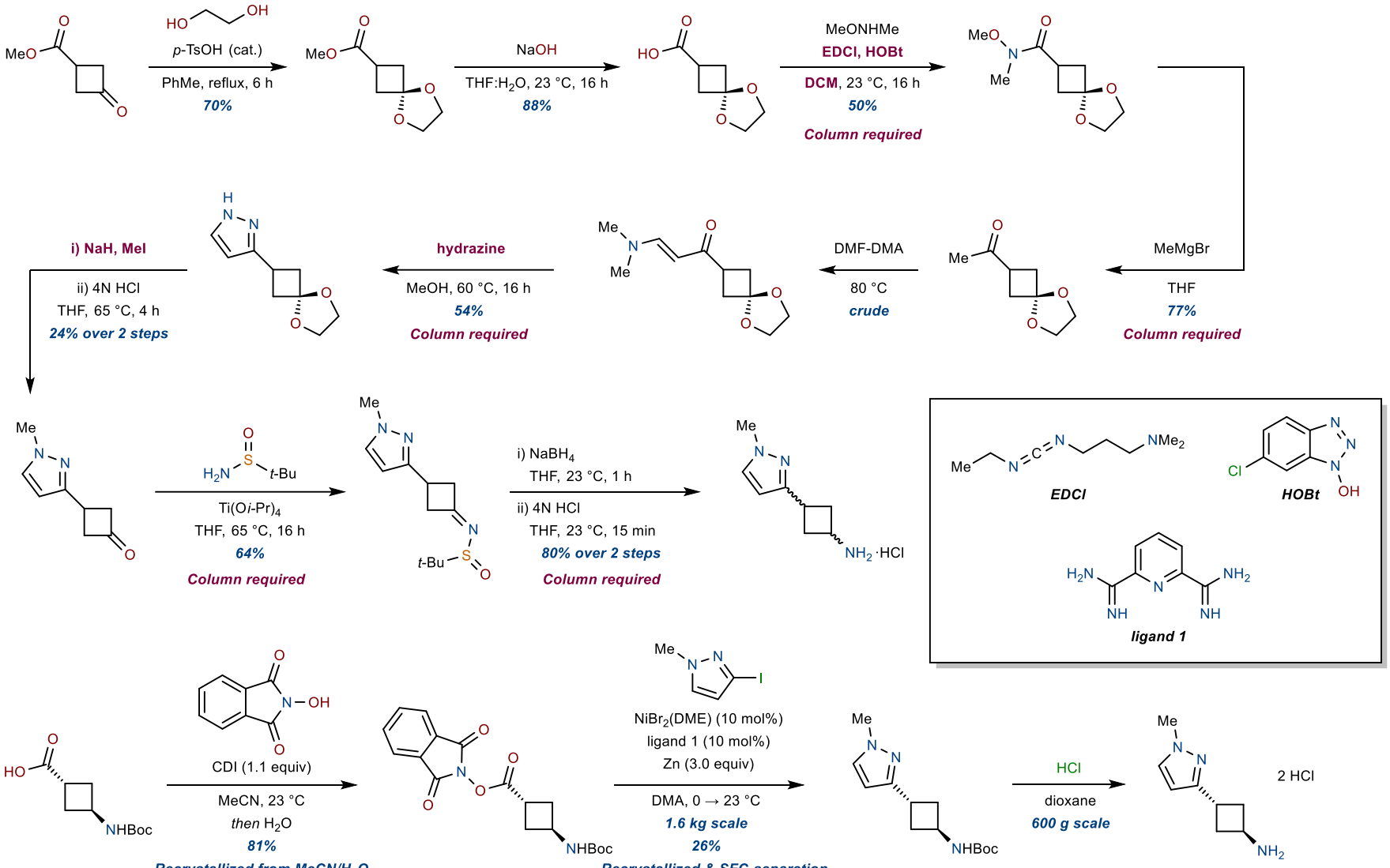
Synthesis of Cyclobutylamine



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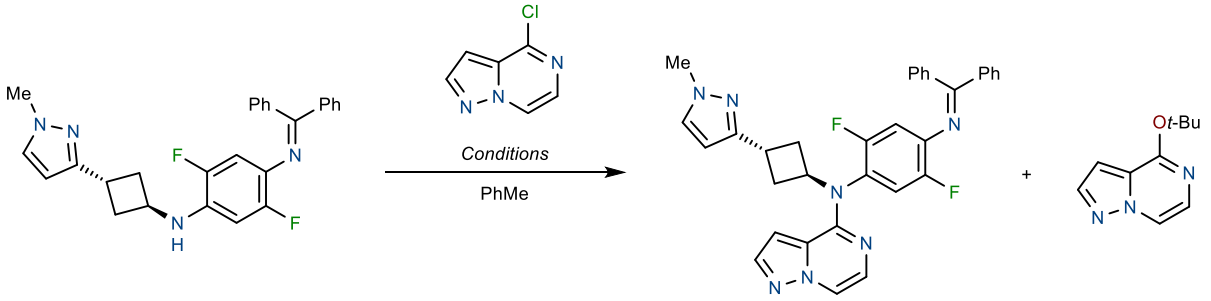
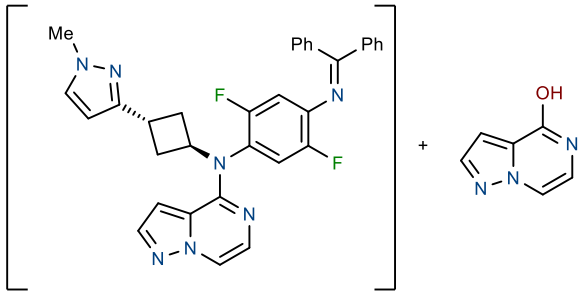
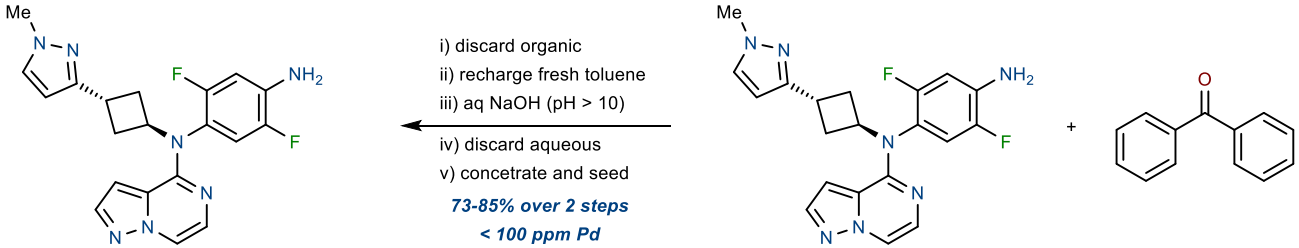


Entry	amine (equiv)	NaO*t*-Bu (equiv)	XPhos Pd G2 (mol%)	Temperature (°C)	Yield
1	2.0	3.0	10	100	> 95
2	**1.5**	3.0	10	100	90
3	1.5	**2.0**	10	100	87
4	**1.25**	**1.5**	10	100	80
5	1.5	3.0	10	**70**	> 95
6	**1.3**	**2.0**	10	70	> 95
7	1.3	**1.3**	**1.25**	**50**	> 95

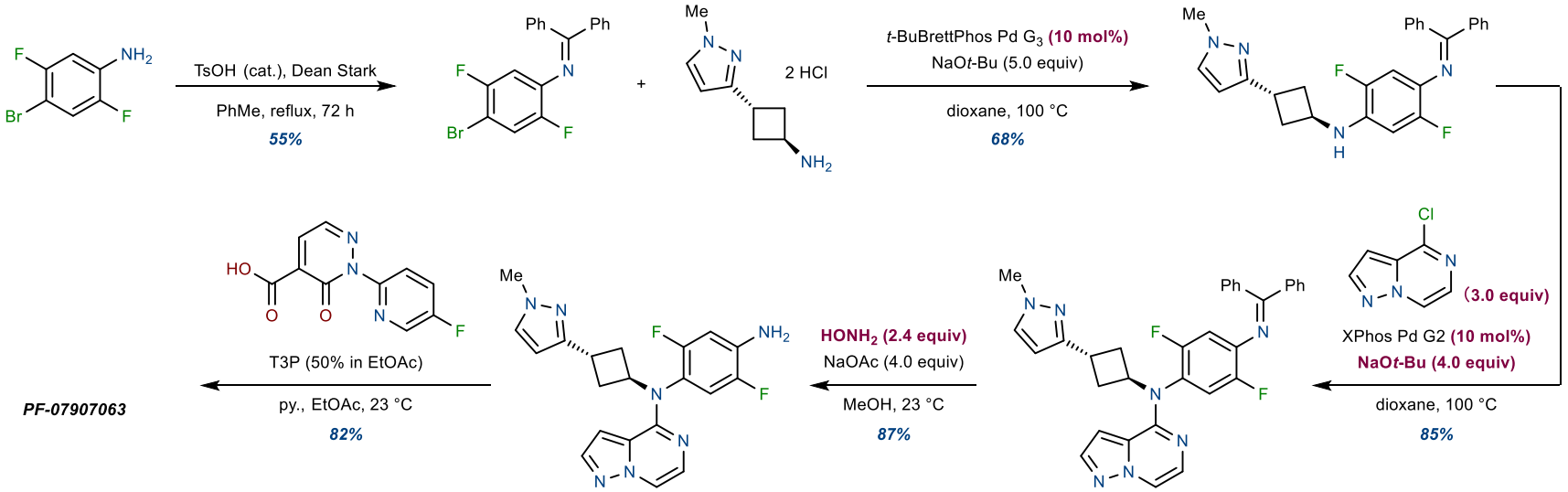


i) discard aqueous
ii) 2M aq. H_2SO_4



PF-07907063 (Pfizer)

Medicinal Chemistry Route



Process Route