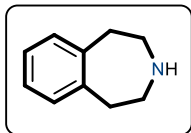
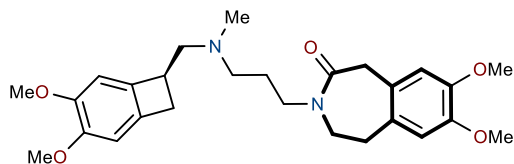


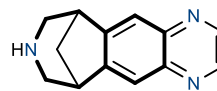
2,3,4,5-tetrahydro-1H-benzo[d]azepines



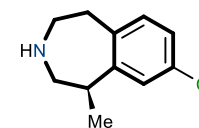
privileged scaffold in medicinal chemistry



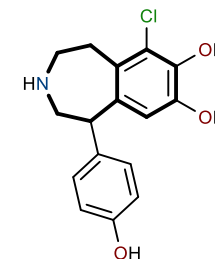
ivabradine
HCN channel blocker



varenicline
nicotinic ACh partial agonist

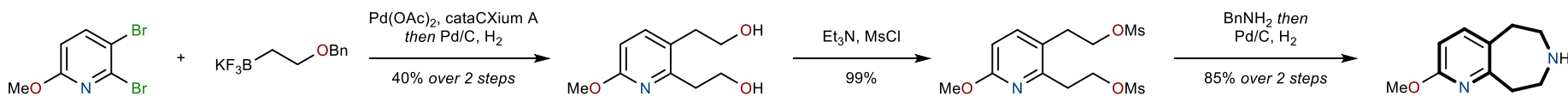


locaserin
5HT_{2c} agonist

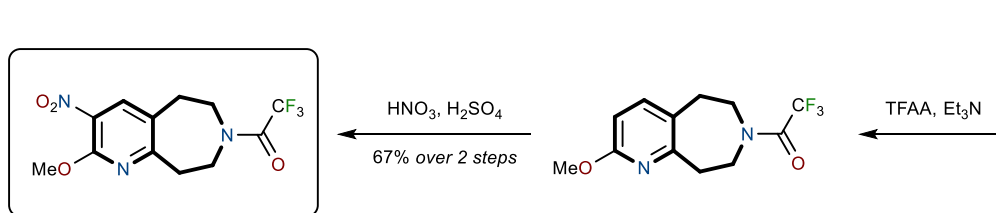


fenoldopam
D₁ partial agonist

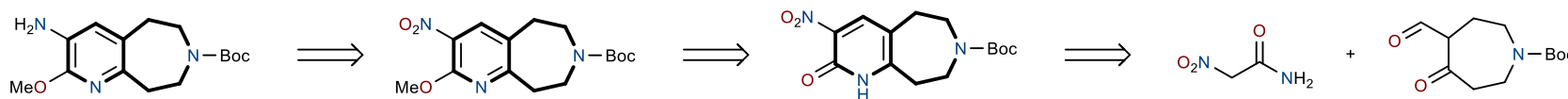
Discovery route



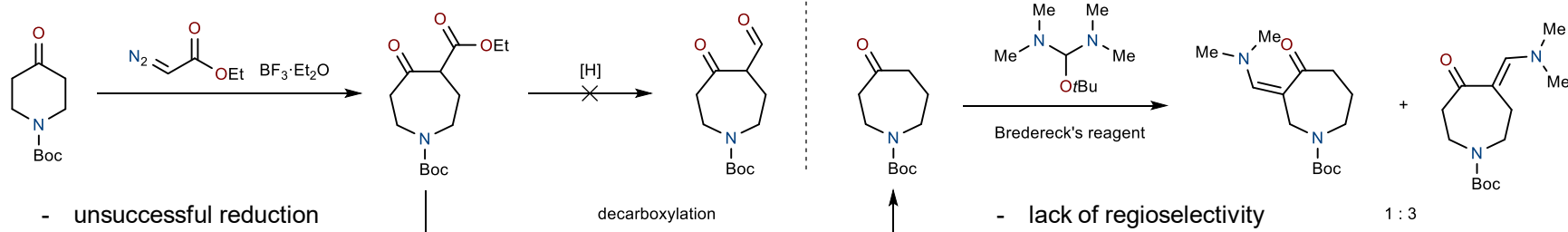
- low yielding Molander coupling
- requires a lot of solvents
- high waste generation
- challenging access to trifluoroborate
- large scale nitration not ideal



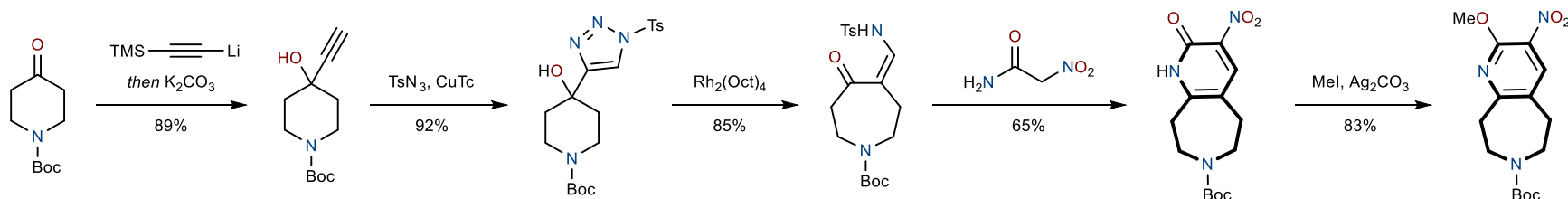
Alternative retrosynthetic proposal



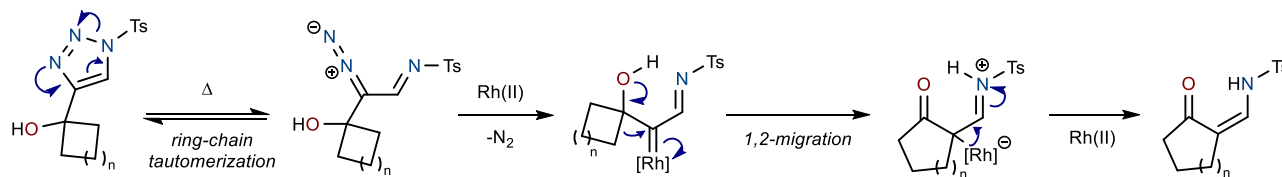
Humphery J. M. *Org. Process Res Dev.* **2023**, *27*, 248. <https://doi.org/10.1021/acs.oprd.2c00145>



Second generation route



Mechanism, scope and applications



| n | ref 1 | ref 2 |
|---|-------|-------|
| 1 | 80 % | / |
| 2 | 90 % | 91 % |
| 3 | 95 % | 93 % |
| 4 | 74 % | 94 % |
| 5 | 78 % | / |

