Lecture 8: Furopyridines, Thienopyridines and Azaindoles

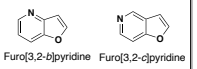
Fused heterocycles…
which ring to break? 🤷‍♀️🤷



Option 1: Annulate B onto A

Option 2: Annulate A onto B

Furopyridines



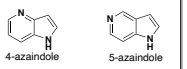
95% of the time: Annulate furan on pyridine

Thienopyridines



80% of the time: Annulate thiophene on pyridine

Azaindoles

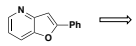


70% of the time: Annulate pyrrole on pyridine

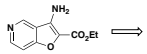
Furopyridine

POD #1

A



B



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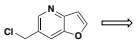

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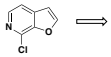

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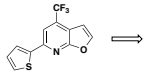
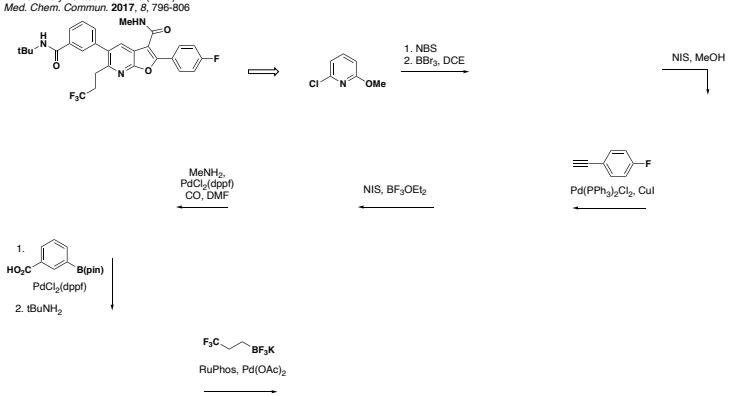


POD #2

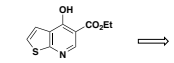
Calling all med chemists! Diversity MUST be installed in the following order: R^1, R^2, R^3

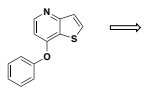


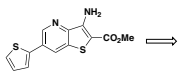
HCV Polymerase Inhibitors (BMS)
Med. Chem. Commun. **2017**, *8*, 796-806

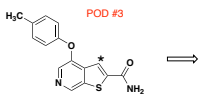


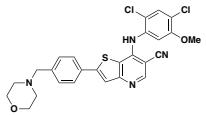
Thienopyridines



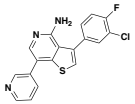








Src Kinase Inhibitor (Wyeth)
J. Med. Chem. **2005**, *48*, 3891



Protein kinase inhibitors
(GSK) BMCL **2007**, *17*, 250

Syntheses of azaindoles by using classic indole syntheses

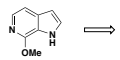
	 4-azaindole	 5-azaindole	 6-azaindole	 7-azaindole
Reissert synthesis	◔	◔	●	◐
Batcho-Leimgruber synthesis	◔	◔	●	◐
Hemetsberger-Knittel Synthesis	◐	◔	●	◔
Bartoli Synthesis	◔	◐	●	○
Fischer Synthesis	●	○	●	○
Madelung Synthesis	◐	◔	◔	●
Lorenz Synthesis	●	◐	◐	●
Larock Synthesis	●	●	●	●
Hegedus-Mori-Heck Synthesis	●	●	●	●



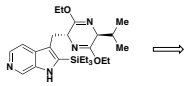
A similar classification has been made in the PCC book's azaindole synthesis report card (p.559).

POD #4

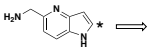
A



D



B



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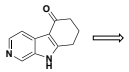

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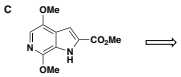
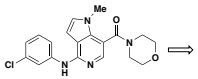
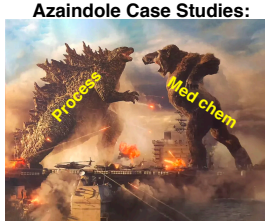
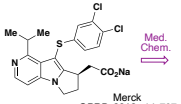




J. Med. Chem. **2009**, *52*, 5785

Azaindole Case Studies:



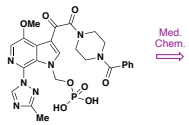


Med. Chem.

Process Chem.

Merck
OPRD, **2010**, *14*, 787

BMS-663068 *OPRD*, **2017**, *21*, 1095



Med. Chem. ⟹

Process Chem. ⇩