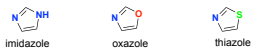
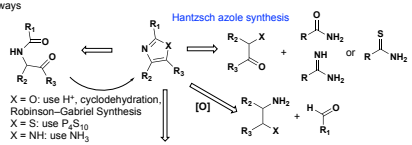
Lecture 13: 1,3-Azoles



General nomenclature:

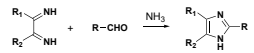
azolidine	increase
azoline	[O] state/
azole	unsaturation

general pathways



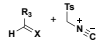
Hantzsch azole synthesis

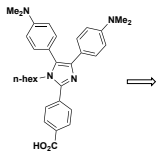
Debus imidazole synthesis



See the PCC book's imidazole starburst (p.470) for even more approaches to the imidazole core.

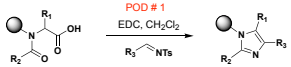
van Leusen synthesis





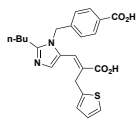
PGP mediator
Ontogen, *BMCL*, **2000**, 2599

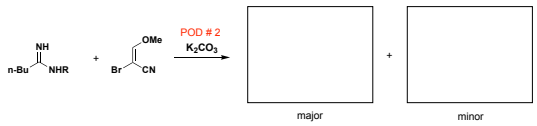
Imidazole case studies:

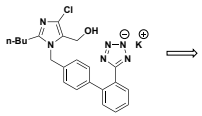


Eprosartan
SmithKline, *JOC* **1997**, *62*, 8449

Med. Chem. ⟸ ⟹ Process:

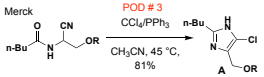


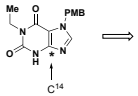




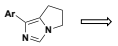
Cozaar (losartan)
Merck, *J. Org. Chem.* **1994**, *59*, 6391;
Org. Lett. **2004**, *6*, 929

Merck

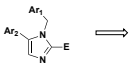




JOC, **2000**, 1516

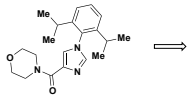


Consulting Corner

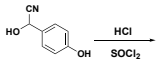


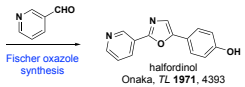


Late stage Ar_1 incorporation

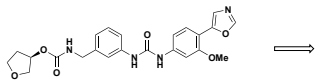


Oxazole case studies:

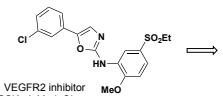




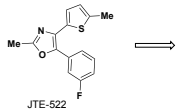
halfordinol
Onaka, *TL* **1971**, 4393



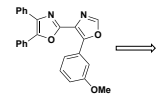
merimepodib (VX-497)
Albany Molecular, *OPRD* **2002**, *6*, 677



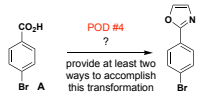
VEGFR2 inhibitor
GSK, *J. Med. Chem.* **2005**, *48*, 1610

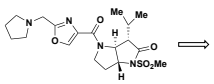


JTE-522

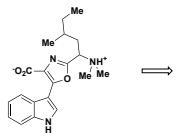


prostacyclin mimic
BMS, *JMC* **1993**, *36*, 3884



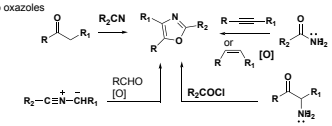


GW475151
GSK, *OPRD* **2001**, *5*, 37

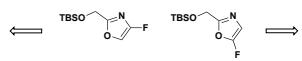


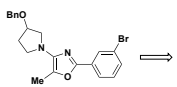
martefragin A
Nakagawa, *TL* **1998**, *39*, 5983

misc routes to oxazoles

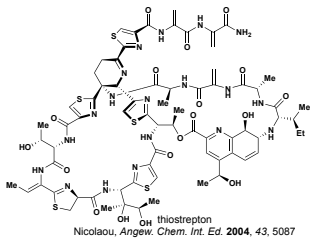


Consulting Corner



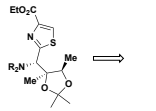


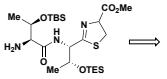
Thiazole case studies:

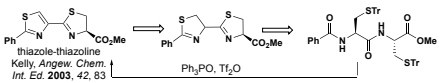


thiostrepton

Nicolaou, *Angew. Chem. Int. Ed.* **2004**, *43*, 5087

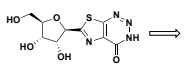






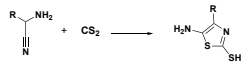
thiazole-thiazoline

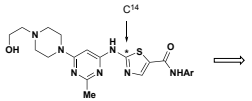
Kelly, *Angew. Chem. Int. Ed.* **2003**, *42*, 83



JOC **1985**, *50*, 1741

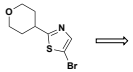
Cook-Heilbron Synthesis

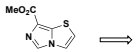




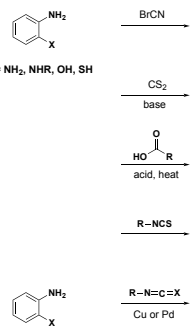
Dasatinib

Consulting Corner





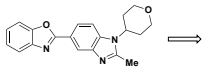
Benzannulated Systems:



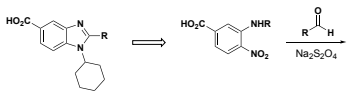
X = NH_2, NHR, OH, SH

X = Halide

POD #5



OPRD, **2016**, *20*, 1053.



OPRD, **2012**, *16*, 96.

Consulting Corner

late stage R incorporation

