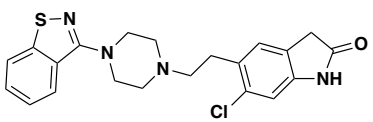
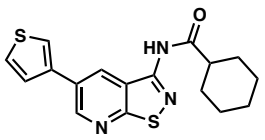
Lectures 15: 1,2-Azoles - Isothiazoles/Case Studies

Study music: Selections from Jascha Heifetz

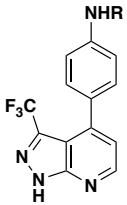
Syntheses discussed:



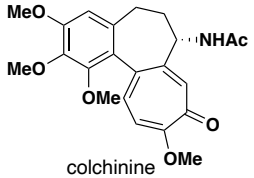
Geodon (ziprasidone)
Pfizer



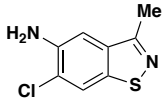
Protein Kinase 1/2 Inhibitor
J. Med. Chem. **2014**, *57*, 7642.



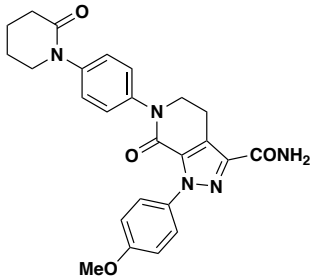
c-KIT/PDGFRα dual inhibitor
J. Med. Chem. **2017**, *60*, 5099.



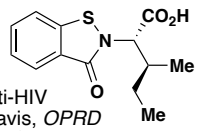
colchinine
Helv. Chim. Acta **1961**, 540.
The Harvey Lecture Series **1963**, 31.
JACS. **1986**, *108*, 6713.



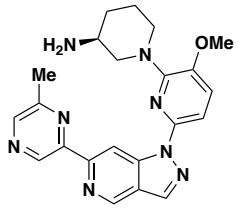
orexin antagonist, Actelion,
Bioorg. Med. Chem. Lett. **2008**, *18*, 5729.



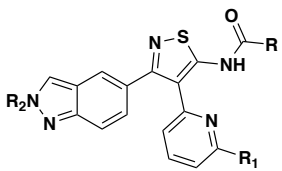
Apixiban (Eliquis), BMS,
J. Med. Chem. **2007**, *50*, 5339.



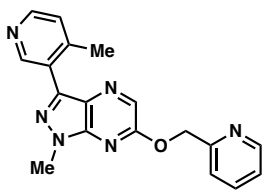
anti-HIV
Parke-Davis, *OPRD* **1998**, *2*, 151



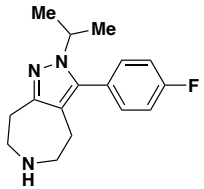
Pan-Pim Inhibitor, Genentech
J. Med. Chem. **2017**, *60*, 4458.



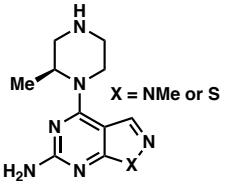
mGlu5 receptor modulator, Lilly
Bioorg. Med. Chem. Lett. **2013**, *23*, 1249.



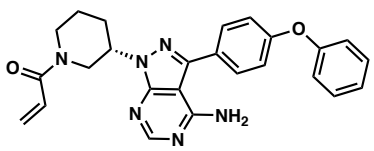
mGluR5 Allosteric Modulator
Pfizer, *Org. Process Res. Dev.* **2014**, *18*, 1145.



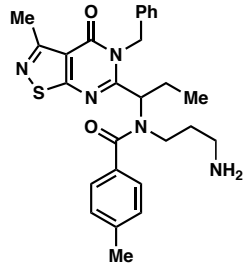
5HT$_7$/5HT$_2$ dual antagonist, J&J
OPRD, **2011**, *15*, 876.
J. Org. Chem. **2014**, *79*, 8800.



UCB9608 (PI4KIIIβ Inhibitor)
UCB Pharma, *J. Med. Chem.* **2018**, *61*, 6705.



Ibrutinib (BTK Inhibitor)
Pharmacyclics/J&J
Org. Process Res. Dev. **2016**, *20*, 1855.

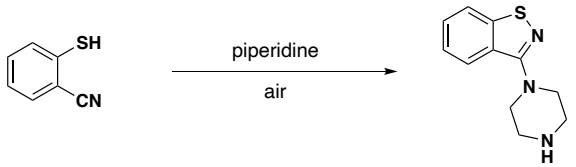


AZD487 (Kinesin Inhibitor)
AstraZeneca, *J. Med. Chem.* **2011**, *54*, 6734.

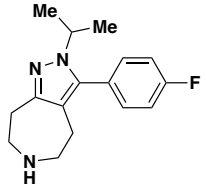
Reading assignment: **HC chapters 25-26; PCC pyrazole, 5/6 Fused Heteroarene**

Problems of the Day:

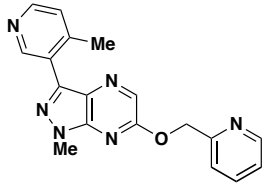
1



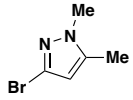
2 Propose three different synthetic routes to the 5HT$_7$/5HT$_2$ dual antagonist



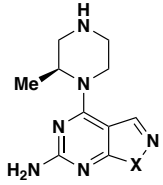
3 Propose medicinal chemistry and process routes to the mGluR5 modulator



4 Propose several different synthetic routes to the following pyrazole



5 Propose a common intermediate for the synthesis of the two compounds below:



X = S, NMe