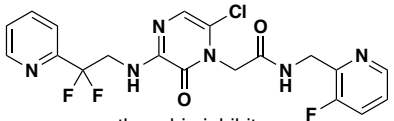
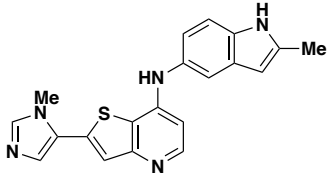
Study music: Grieg, Piano Concerto (suites 1 & 2)

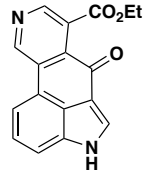
Syntheses discussed:



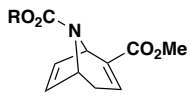
thrombin inhibitor
Merck, *Org. Proc. Res. Dev.* **2004**, *8*, 192



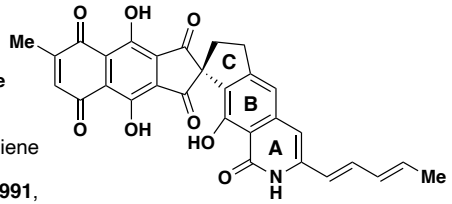
kinase inhibitor
Pfizer, *Org. Proc. Res. Dev.* **2003**, *7*, 676



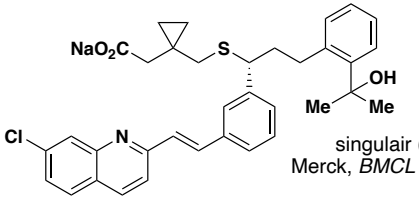
8-azaergoline ring system
Doll, *J. Org. Chem.* **1999**, *64*, 1372



8-azabicyclo[3.2.1]octadiene
(cocaine skeleton)
Davies, *J. Org. Chem.* **1991**, *56*, 5696



fredericamycin A
Boger, *J. Am. Chem. Soc.*, **1995**, *117*, 11839
Kita, *J. Am. Chem. Soc.*, **2001**, *123*, 3214



singulair (montelukast sodium)
Merck, *BMCL* **1992**, 1141 and **1995**, 283

Reading assignment: HC chapters 4, 13, 15, 19, 23, PCC pyridine substitution, Essentials of Heterocyclic Chemistry-I (lamianted handout)

Partial list of concepts/transforms discussed:

Nucleophilic attack on hydrogen (metallation of heterocycles)

Reaction of heterocycles with radicals and electron deficient species

Minisci reaction

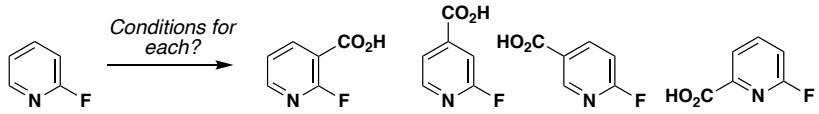
Ciamician-Dennstedt rearrangement

Effect of heterocycles on their substituents:

- By electron withdrawal
- By electron donation

Problems of the day:

(1)



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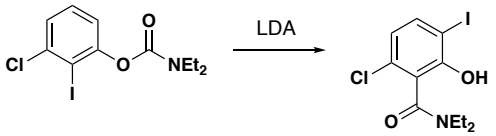

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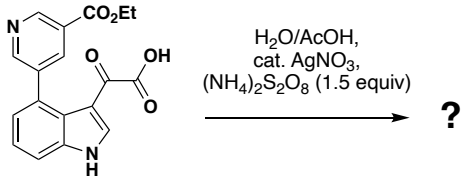
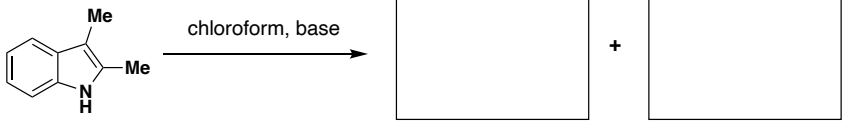


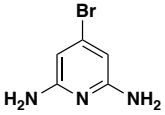
(4)

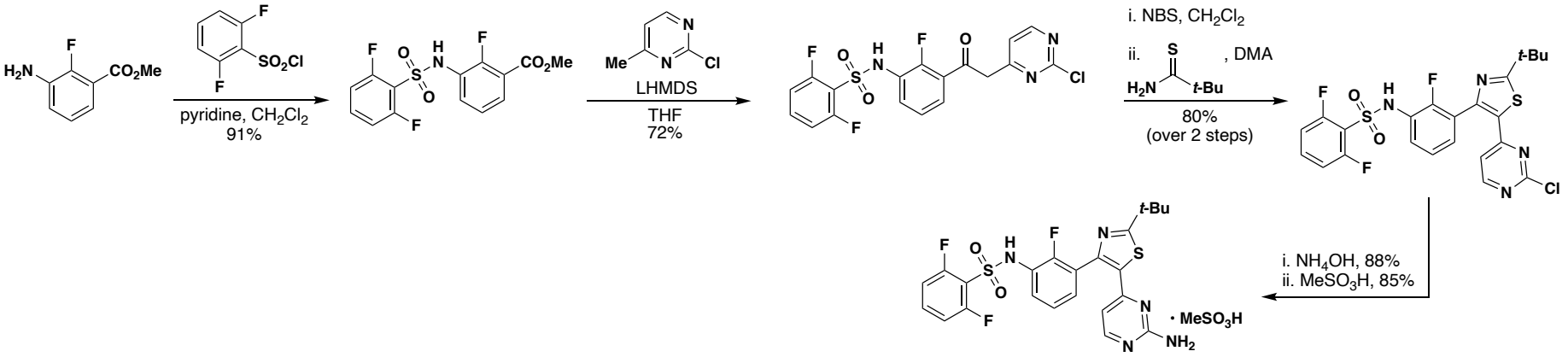


heterocycle with 2 chlorines (46%)

heterocycle with 1 chlorine (32%)

(5) Propose a synthesis of the following compound from a pyridine-based s.m.





Dabrafenib mesylate