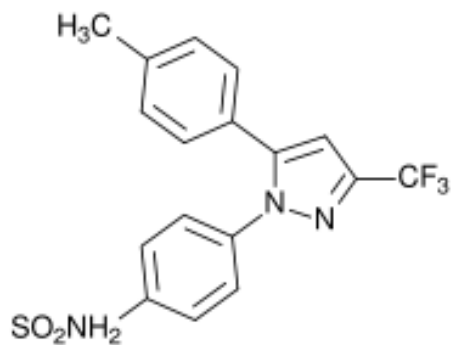


## ***Chapter 43 — Aromatic heterocycles: structures and reactions***

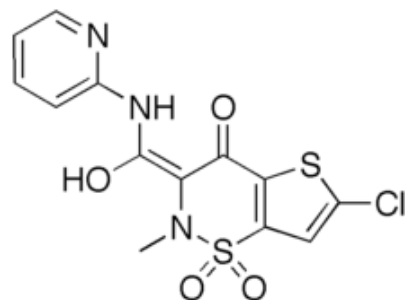
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- Introduction to heterocycles
- Pyridine basicity and reactivity, and DMAP catalysis of acylations (1147–53)
- Pyrrole and furan: where's the lone pair? (1157–61)
- Imidazoles, pyrazoles, triazoles, tetrazoles (1165–69)
- Benzo-fused heterocycles: indoles (1169–71), quinolines (1174–75)
- *FOOD: coffee skullduggery and decaffeination processes*

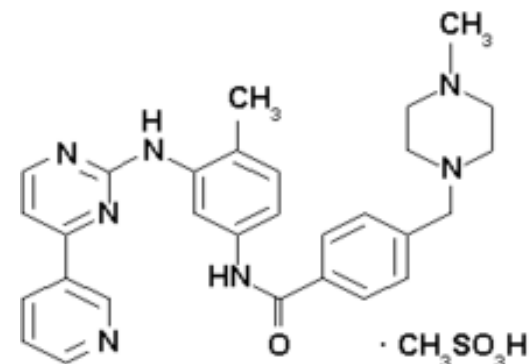
# Heterocyclic drugs



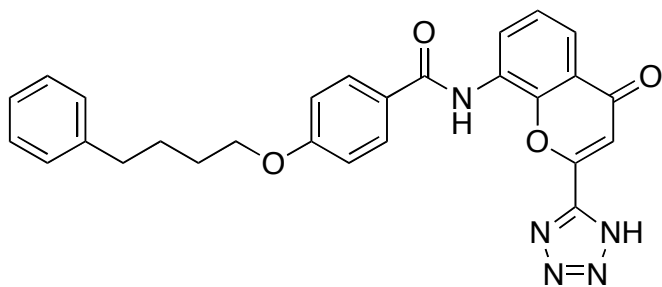
Celebrex (Pfizer)



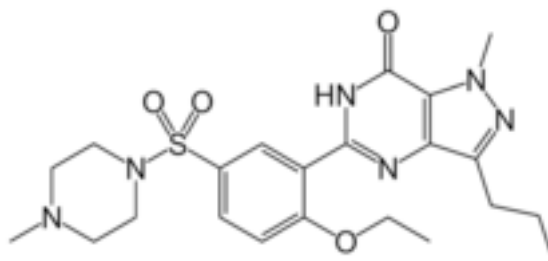
Lornoxicam (Pozen)



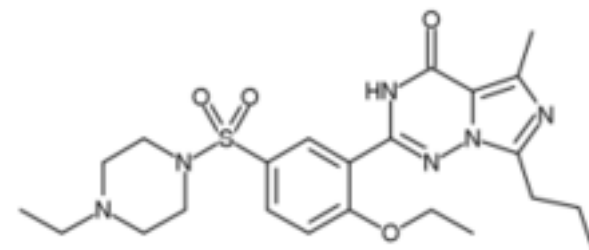
Gleevec (Novartis)



Pranlukast (Ono Japan)



Viagra (Pfizer)

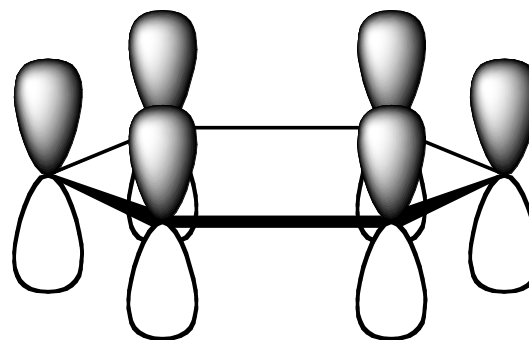
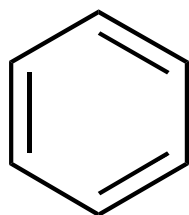


Levitra (GSK/Bayer)

## Reminder on orbitals

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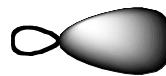
Atoms in small aromatic rings are almost always  $sp^2$  hybridized



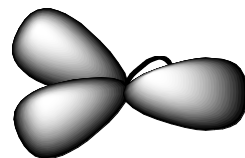
1 s  
3 p



3  $sp^2$



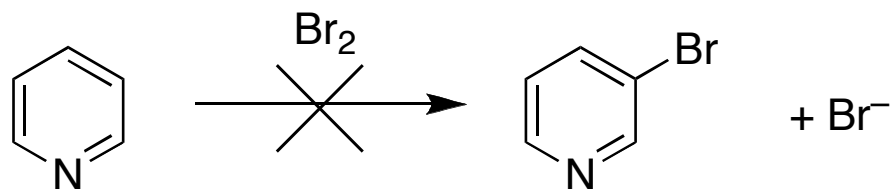
1 p



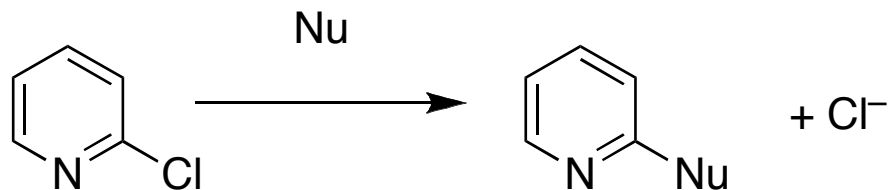
## ***Pyridine's nitrogen is an imine-type functional group***

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- Bad at stabilizing positive charges by resonance donation



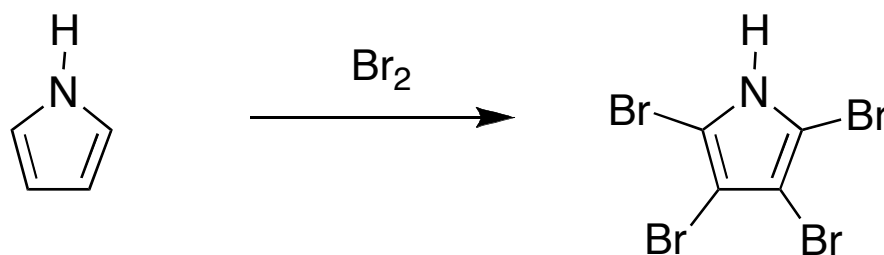
- Good at stabilizing negative charges by resonance accepting



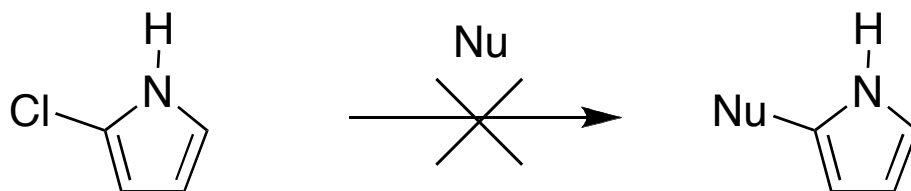
## ***Pyrrole's nitrogen is an enamine-type functional group***

---

- Good at stabilizing positive charges by resonance donation

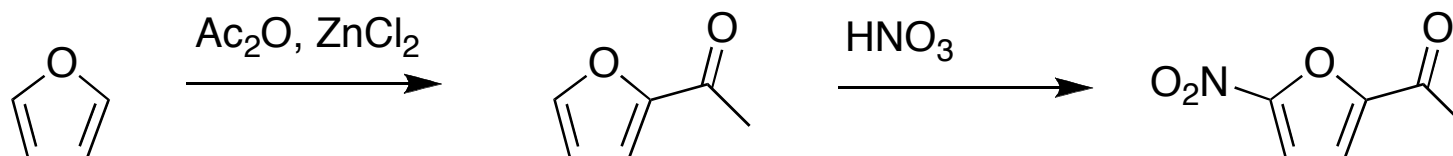
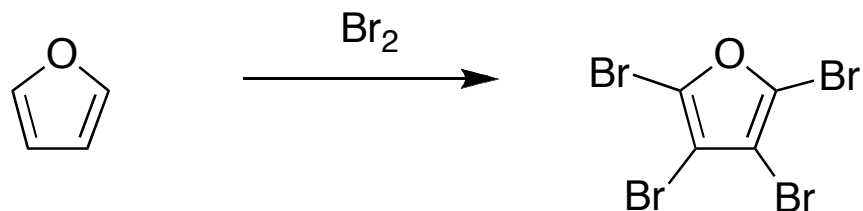


- Bad at stabilizing negative charges by resonance accepting



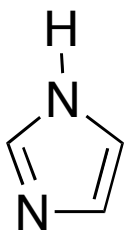
***Furans are electron-rich, and are good nucleophiles like pyrroles***

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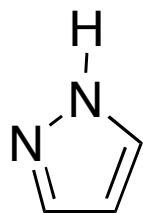


## ***Azoles: 5-membered nitrogen rings with 2, 3, 4, or 5 heteroatoms***

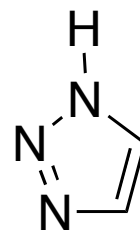
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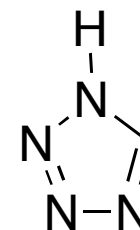
imidazole



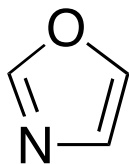
pyrazole



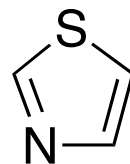
1,2,3-triazole



tetrazole



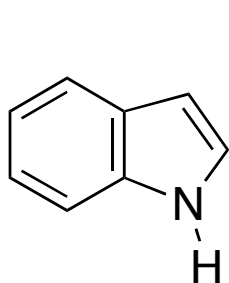
oxazole



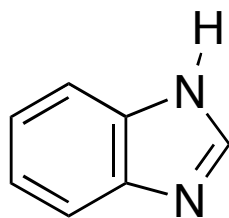
thiazole

## Benzo-fused heterocycles

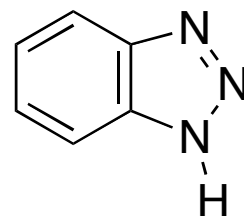
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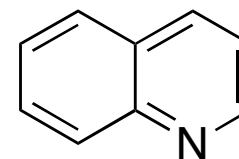
Indole



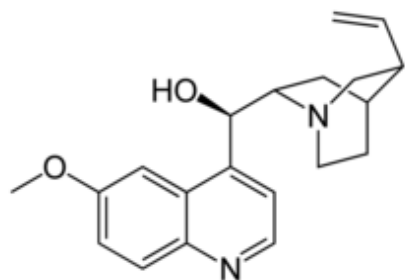
Benzimidazole



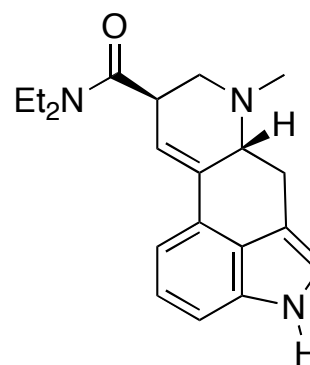
Benzotriazole



Quinoline



Quinine



Lysergic acid diethylamide