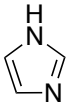
Heterocycles In Biological Chemistry

from chapter(s) _____ in the recommended text

A. Introduction

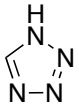
B. Names

pyrrole



imidazole

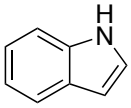
pyrrazole



tetrazole

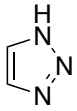
pyridine

1,3-pyrimidine

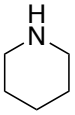


indole

thiophene



1,2,3-triazole



piperidine

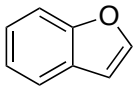
pyrrolidine

aziridine

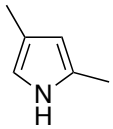
oxirane

oxetane

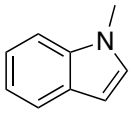
furan



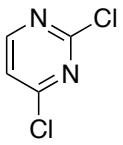
benzofuran



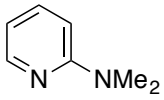
2,4-dimethylpyrrole



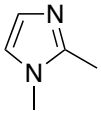
1-methylindole



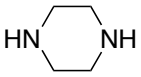
2,4-dichloropyrimidine



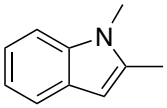
2-dimethylaminopyridine



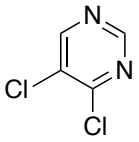
1,2-dimethylimidazole



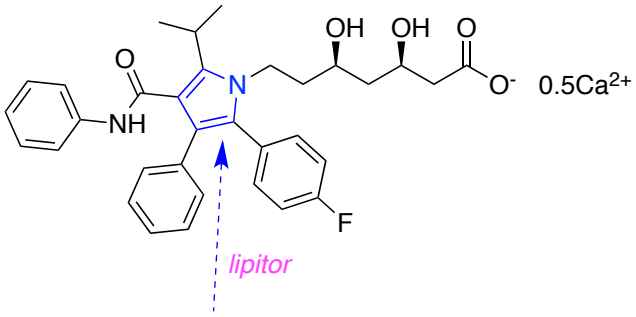
piperazine



1,2-dimethylindole

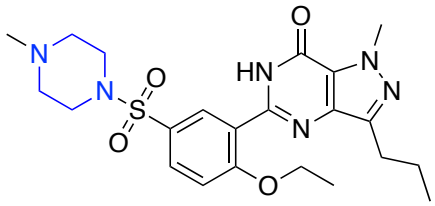


4,5-dichloropyrimidine



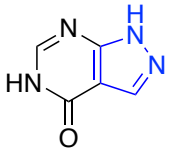
lipitor

pyrrole



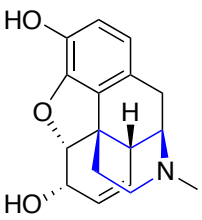
viagra

piperazine



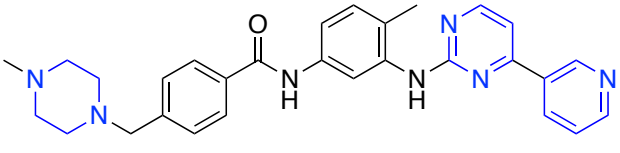
allopurinol

pyrrazole



morphine

piperidine



imatinib

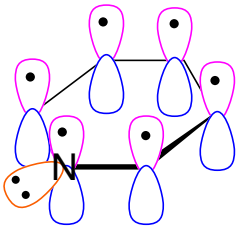
piperazine *and* *pyrimidine* *and* *pyridine*

C. Aromaticity And Basicity Of Heterocycles

Pyridines And Pyrimidines

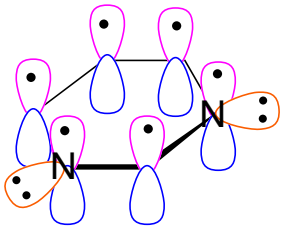
sp^2 hybridized with *a lone pair*
1 electron
aromatic.

pyridine

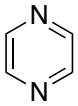


sp^2 hybridized with *a lone pair*
1 electron
aromatic.

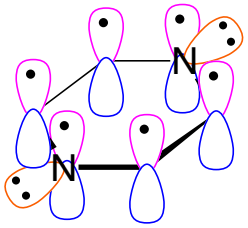
1,3-pyrimidine



sp^2 hybridized with *a lone pair*
1 electron
aromatic.

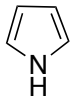


1,4-pyrimidine

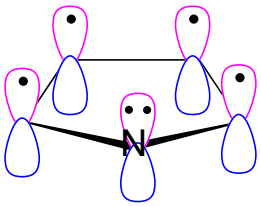


Pyrrole

sp^2 hybridized with *0*
can
aromatic.

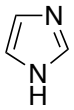


pyrrole

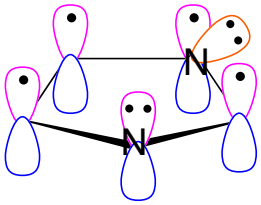


Imidazole

can
are both sp^2 hybridized, and *one*
is



imidazole

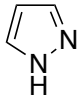


does influence

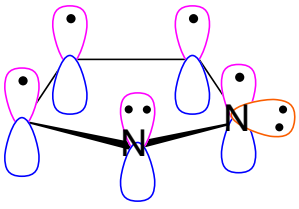
Pyrazole

cannot
are
one

Pyrazole *is*



pyrazole



aromatic stabilization.

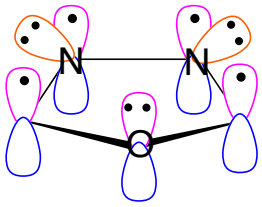
1,3,4-Oxadiazole

sp^2 hybridized and each contributes *1*

sp^2 hybridized and contributes *2*

aromatic.

1,3,4-oxadiazole

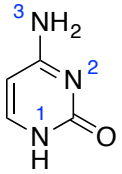


does not

good base

is not lost.

Heterocycles In Nature

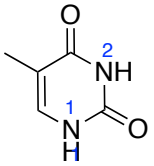


cytosine

N^3: 0

N^2: 1

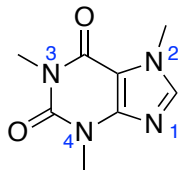
N^1: 2



thymine

N^2: 2

N^1: 2



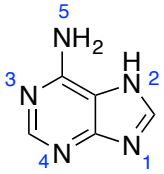
caffeine

N^4: 2

N^3: 2

N^2: 2

N^1: 1



adenine

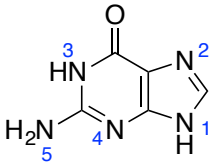
N^5: 0

N^4: 1

N^3: 1

N^2: 2

N^1: 1



guanine

N^5: 0

N^4: 1

N^3: 2

N^2: 1

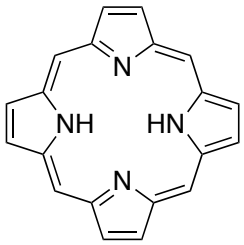
N^1: 2

2 pyridine-like nitrogen atoms, *2*

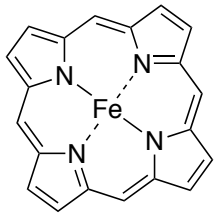
26 π-electrons

are aromatic.

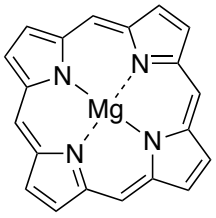
2



porphyrin



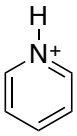
Fe^{2+} complex overall charge 0



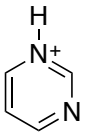
Mg^{2+} complex overall charge 0

Hemoglobin
chlorophyll
): *strongly UV absorbing / fluorescent / capable of redox chemistry*.

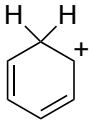
Aromatic Characteristics Of Protonated Heterocycles



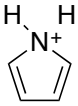
aromatic because it has 6 πe⁻.



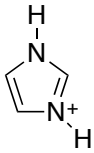
aromatic because it has 6 πe⁻.



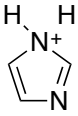
not aromatic because it has 4 πe⁻.



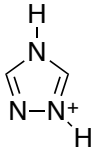
not aromatic because it has 4 πe⁻.



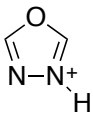
aromatic because it has 6 πe⁻.



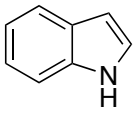
not aromatic because it has 4 πe⁻.



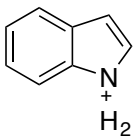
aromatic because it has 6 πe⁻.



aromatic because it has 6 πe⁻.

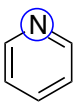


aromatic because it has 10 πe⁻.

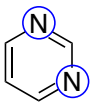


not aromatic because it has 8 πe⁻.

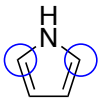
C^3



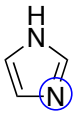
pyridine



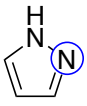
pyrimidine



pyrrole



imidazole



pyrrazole

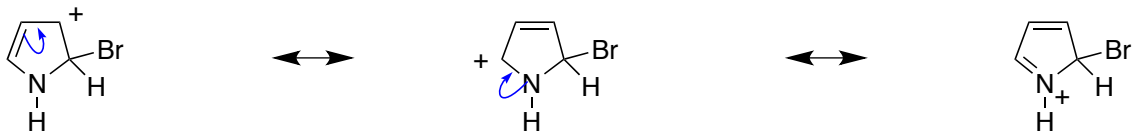
oxazole

D. Electrophilic Attack On Pyrrole And Indole Compared

Pyrrole

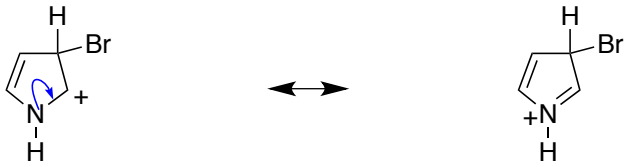
low

in the 2-position



complete diagrams and show arrows

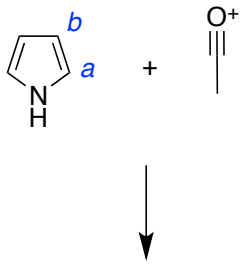
in the 3 position

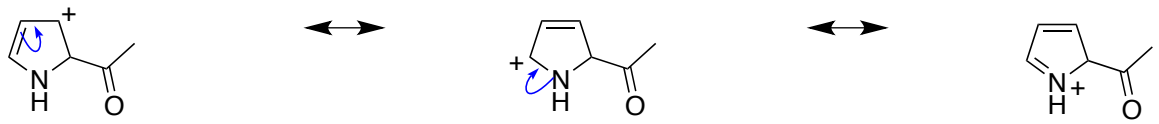


complete diagrams and show arrows

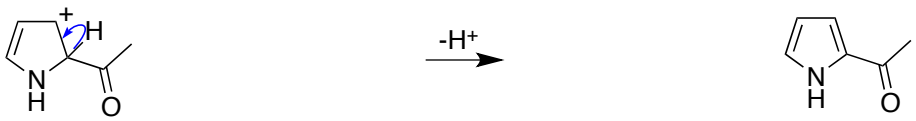
2-position
thermodynamic

Hammond's postulate.





choose correct regiochemistry, show resonance structures, and electron flow that relates them using curly arrows

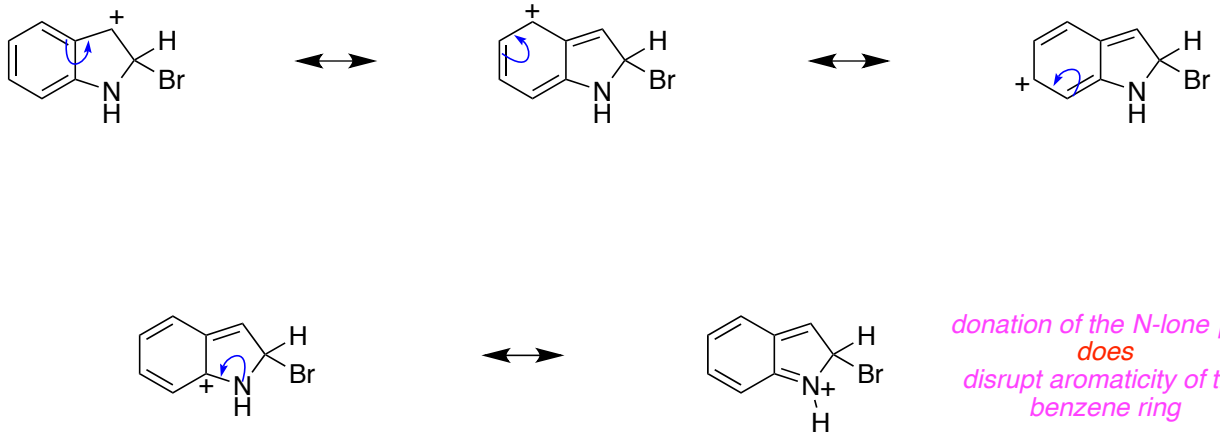


more electron rich than benzene, hence it reacts *faster*

least reactive *most reactive*

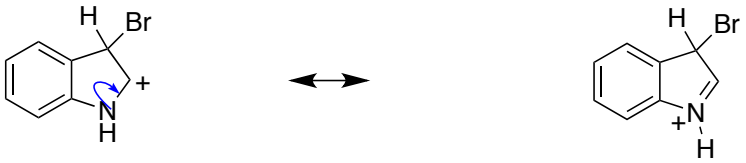
Indole

in the 2-position



donation of the N-lone pair
does
disrupt aromaticity of the benzene ring

in the 3 position



donation of the N-lone pair
need not
disrupt aromaticity of the benzene ring

3-position

because the positive charge can be delocalized onto the nitrogen without disrupting the aromaticity of the benzene, whereas for attack at the 2-position the aromaticity of the benzene must always be disrupted.