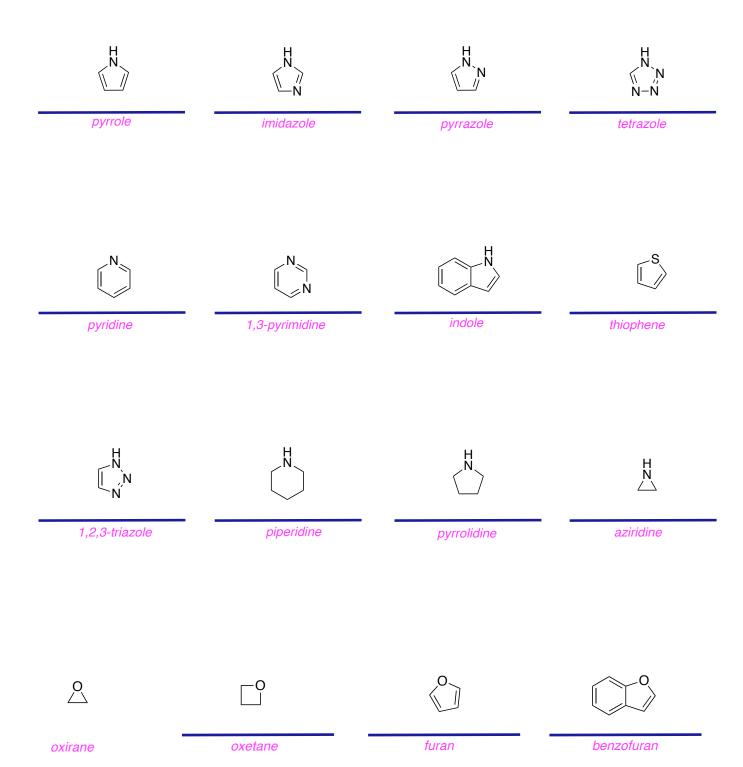
# Heterocycles In Biological Chemistry

## A. Introduction

# B. Names





2,4-dimethylpyrrole

1-methylindole

2,4-dichloropyrimidine

2-dimethylaminopyridine

$$\sqrt[N]{N}$$

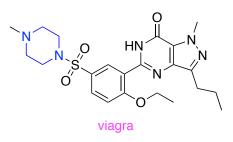
1,2-dimethylimidazole

piperazine

1,2-dimethylindole

4,5-dichloropyrimidine

pyrrole



piperazine

allopurinol

piperidine

morphine



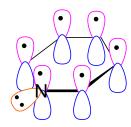
piperazine and pyrimidine and pyridine

pyrrazole

# C. Aromaticity And Basicity Of Heterocycles

Pyridines And Pyrimidines sp<sup>2</sup> hybridized with a lone pair aromatic.

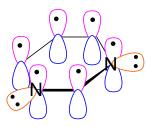




sp<sup>2</sup> hybridized with a lone pair

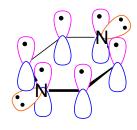
aromatic.





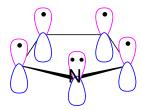
sp<sup>2</sup> hybridized with a lone pair aromatic.





### Pyrrole sp<sup>2</sup> hybridized with 0 can aromatic.



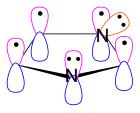


#### Imidazole

can

are both sp<sup>2</sup> hybridized, and one





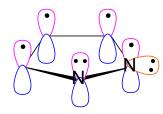
#### does influence

#### Pyrazole

cannot are one

#### Pyrazole is





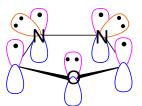
aromatic stabilization.

#### 1,3,4-Oxadiazole

sp<sup>2</sup> hybridized and each contributes 1 sp<sup>2</sup> hybridized and contributes 2 aromatic.



1,3,4-oxadiazole



does not good base is not lost.

#### Heterocycles In Nature

N<sup>3</sup>: 0 N<sup>2</sup>: 1

N¹: 2

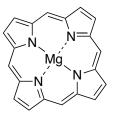
cytosine

$$\begin{array}{c|cccc}
O & N^4: 2 \\
N^3: 2 & N^3: 2 \\
N^4: 1 & N^2: 2 \\
N^1: 1 & Caffeine
\end{array}$$

$$N^{5}$$
: 0  $N^{5}$ : 0  $N^{5}$ : 0  $N^{5}$ : 0  $N^{5}$ : 0  $N^{4}$ : 1  $N^{4}$ : 1  $N^{3}$ : 1  $N^{2}$ : 2  $N^{2}$ : 1  $N^{2}$ : 2  $N^{2}$ : 1  $N^{2}$ : 1  $N^{2}$ : 2  $N^{2}$ : 1  $N^{2}$ : 2

2 pyridine-like nitrogen atoms, 2 **26**  $\pi$ -electrons are aromatic. 2





Fe<sup>2+</sup> complex overall charge 0

Mg<sup>2+</sup> complex overall charge 0

Hemoglobin chlorophyll

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

#### **Aromatic Characteristics Of Protonated Heterocycles**



aromatic because it has



aromatic because it has



not aromatic because it has



not aromatic because it has



aromatic because it has  $6 \pi e^{-}$ .



not aromatic because it has  $4 \pi e^{-}$ .



aromatic because it has  $6 \pi e^{-}$ .



aromatic because it has



aromatic because it has  $10 \text{ } \pi\text{e}^{-}$ .



not aromatic because it has 8 πe<sup>-</sup>.

 $C^3$ 



pyridine



pyrimidine









oxazole

# D. Electrophilic Attack On Pyrrole And Indole Compared

## **Pyrrole**

low

in the 2-position

complete diagrams and show arrows

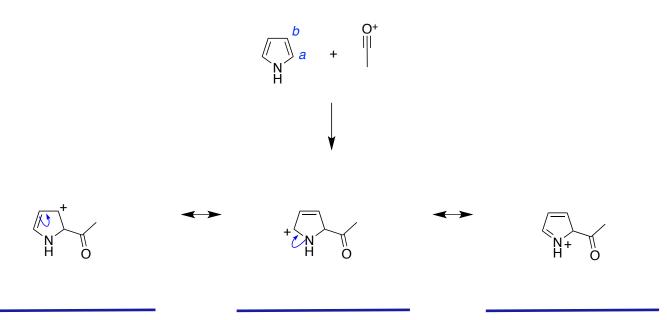
#### in the 3 position

$$H$$
 $B$ 
 $+N$ 
 $H$ 
 $H$ 
 $H$ 
 $H$ 
 $H$ 

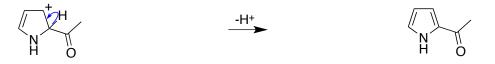
complete diagrams and show arrows

2-position thermodynamic

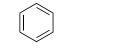
Hammond's postulate.



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

in the 3 position

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

#### 2-position

because it has four resonance structures to delocalize the charge without disrupting aromaticity of the benzene ring while substitution at the 3-position doesn't have resonance structure to delocalize the charge without disrupting aromaticity.