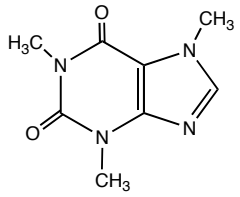
CHEM 109, Lecture 13

Nucleic Acids & Nucleotide Structure

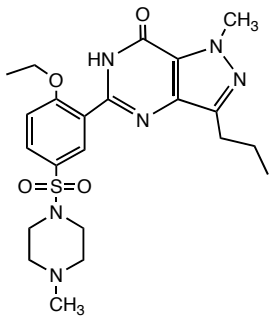
- Heterocycles – Aromaticity & Basicity
- H-Bonding

Heterocycles: *Questions addressed in today's lecture:*

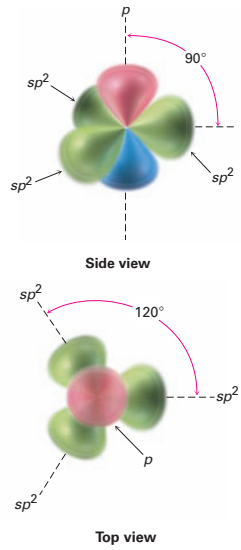
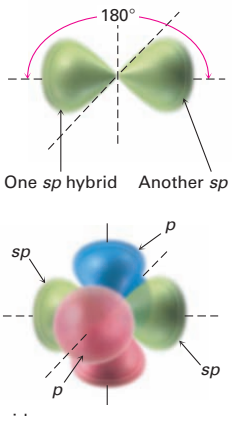
- What is the hybridization of each N atom below?
- Which N lone pairs are involved in resonance?
- Which N atoms are basic?
- Are any N's more basic than others? Which ones?



caffeine



sildenafil

Hybridization	**sp^3**	**sp^2**	**sp**
# charge clouds*	4	3	2
* **Charge cloud** = atom or lone pair around central atom; NOT the number of bonds! *Exception: lone pair next to positive charge or pi bond*			
Molecular Geometry	Tetrahedral	Trigonal Planar	Linear
Bond Angles	109.5°	120°	180°
Atomic Orbitals	 sp^3 carbon sp^3 nitrogen	 Side view / Top view	 One *sp* hybrid / Another *sp*
e-config *add arrows*	sp^3 ___ ___ ___ ___	p ___ sp^2 ___ ___ ___	p ___ ___ sp ___ ___

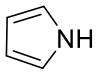
Rules for Aromaticity

1. There must be a ring!
2. All atoms in ring are **sp^2** (conjugated/resonance)
3. Huckel Rule (4n+2)

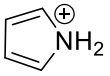
Basicity of N-Heterocycles

You do not need to memorize these pKa's or heterocyclic ring structures-names, but you should develop a general understanding of relative basicity, as determined by conjugate acid stability and other factors.

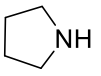
Pyrrole vs. pyrrolidine: Which is the stronger base and why?



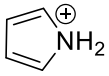
Pyrrole
pKa 17.5



Conjugate acid
pKa 0.4



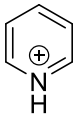
Pyrrolidine
pKa 35ish



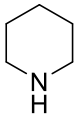
Conj. acid
pKa 11.3

Pyridine vs. piperidine: Which is the stronger base and why?

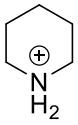
Pyridine
pKa n/a



conj. acid
pKa 5.25

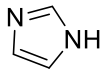


Piperidine
pKa 35ish

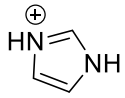


Conj. acid
pKa 11.2

Imidazole: Which *N* is basic and why?



Imidazole
pKa 14.2

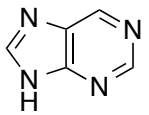


Conj. acid
pKa 6.95

Who's the base?

Pyrimidine

Purine



Nitrogen Basicity Flowchart

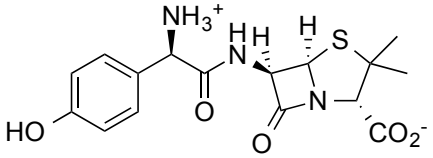
Use the examples on pages 1 and 2 to develop a set of **criteria for N to be basic** and any trends about **relative basicity**.

Devise a **series of questions** you'd ask about a new N-containing molecule to determine **whether each N is basic** and, if possible, **rank those basic N's by basicity**. Format these questions into flow chart format.

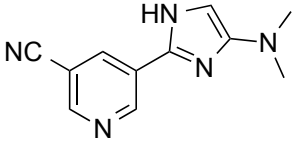
Unrelated flow chart Ex. "Do I feel comfortable in this dress?" –yes→ wear it!

|
No
↓
Don't wear it

Apply your flow chart to each N in these compounds. *Which is the most basic N in each?*



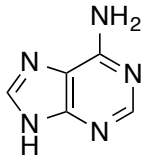
Amoxicillin



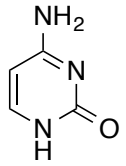
Fictional Molecule

Nucleobases

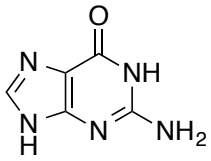
- Which H's are available to serve as H-bond **d**onors?
- Which lone pair are available to serve as H-bond **a**cceptors?



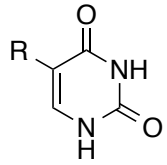
Adenine



Cytosine

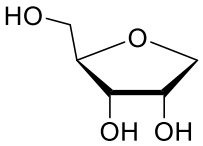


Guanine

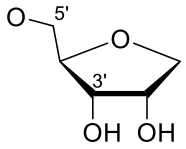


Thymine, R = CH_3
Uracil, R = H

Nucleoside = (Nucleobase + Ribose) - H_2O



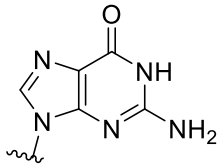
Nucleotide = (Nucleobase + Ribose + Phosphate) – 2 H_2O



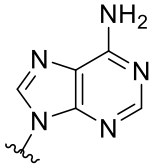
Hydrogen Bonding in DNA / RNA

- Many options for pairing; only one is naturally occurring per pair
- H-bond donor (has the H) = **d**; H-bond acceptor (has the lone pair) = **a**

G-C Base Pair **A-T Base Pair**



Guanine



Adenine

Next time…nucleobase / DNA mutations, introduction to medicinal chemistry