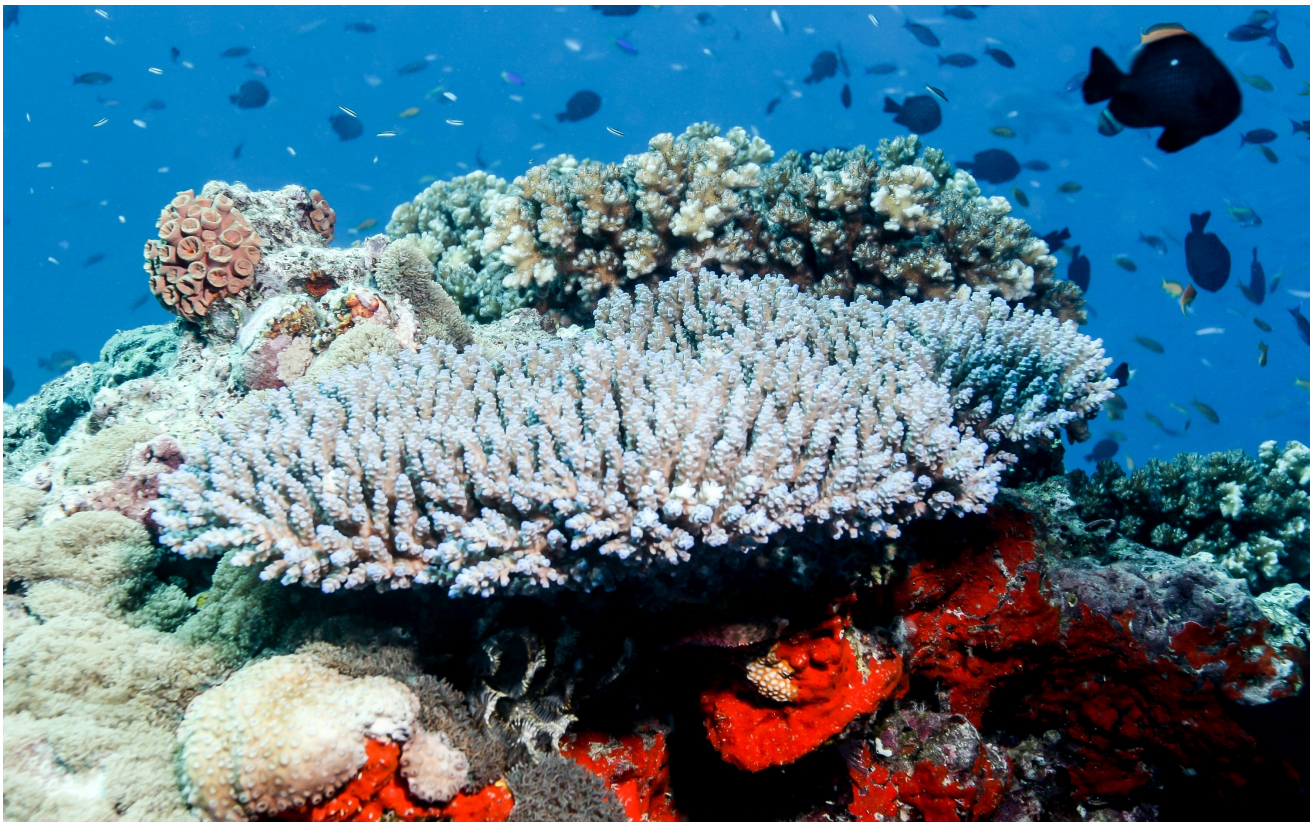
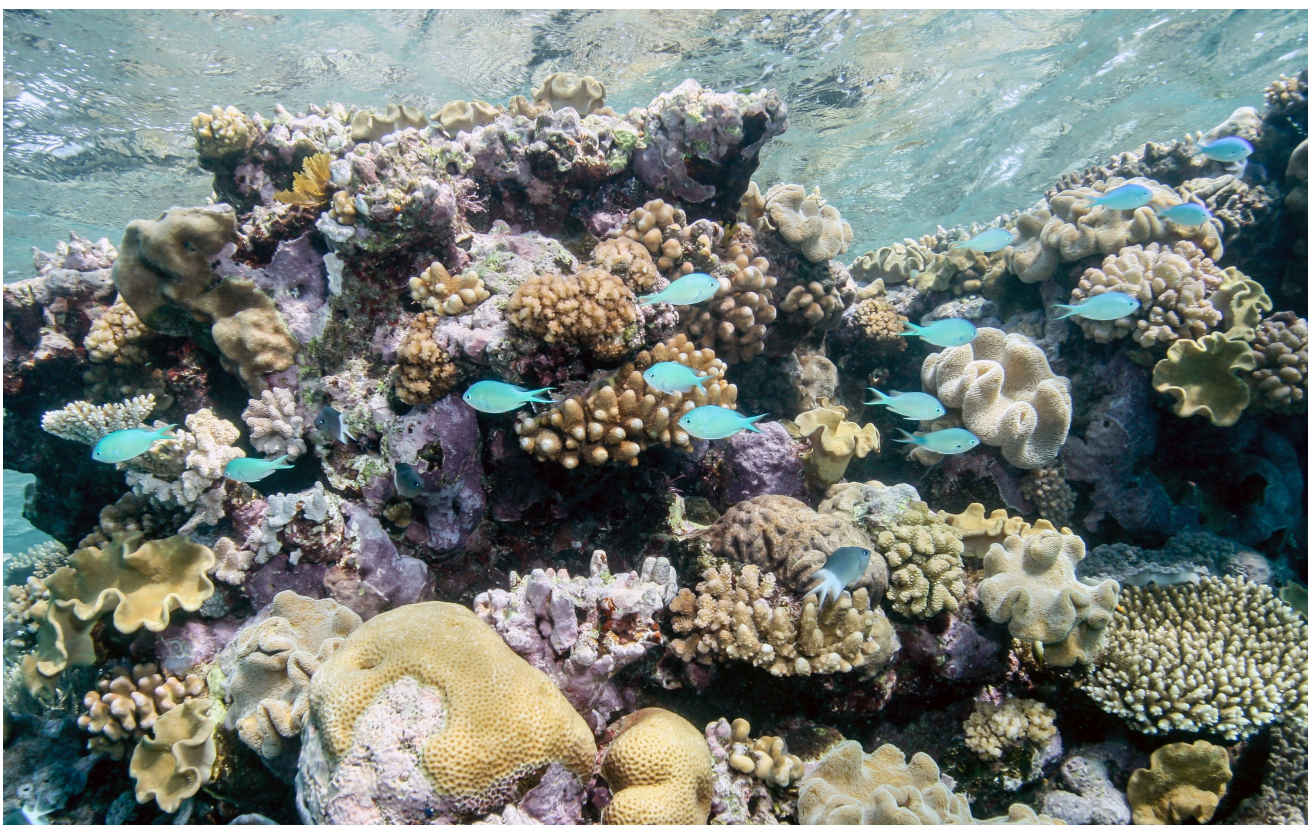
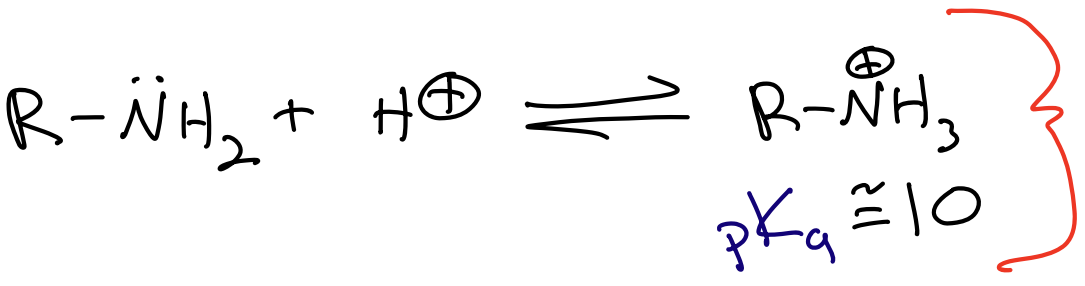




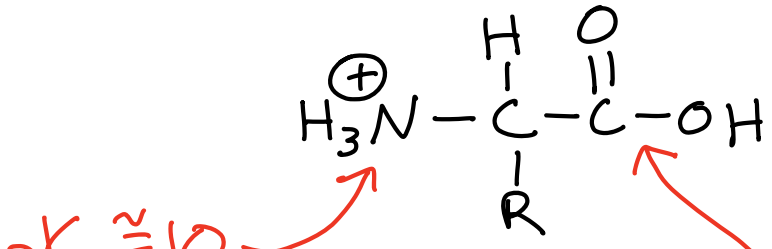
Amines → Relatively strong bases and relatively strong nucleophiles



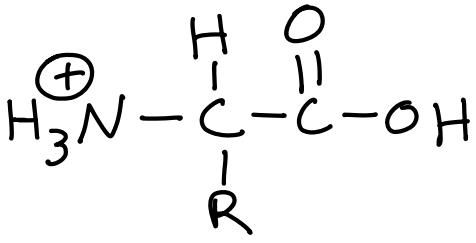
Major form present at neutral pH (pH ≅ 7)

Amines are protonated and positively-charged at neutral pH ⇒ Very important in biochemistry!

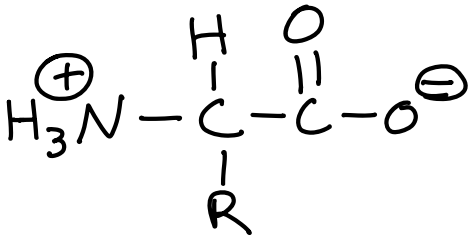
Amino Acids



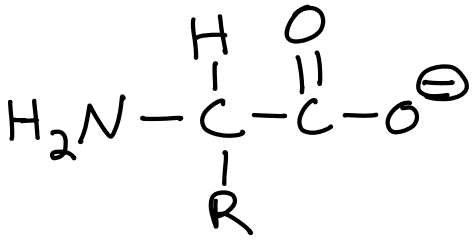
pH 1.0



pH 7.0

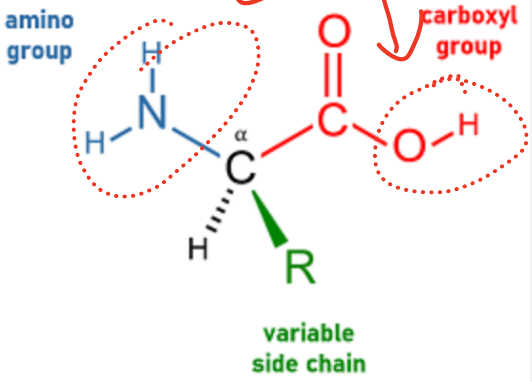


pH 11.0



These are the only possible different forms of an amino acid! (No other forms are possible because of the pKa values!)

Wikipedia

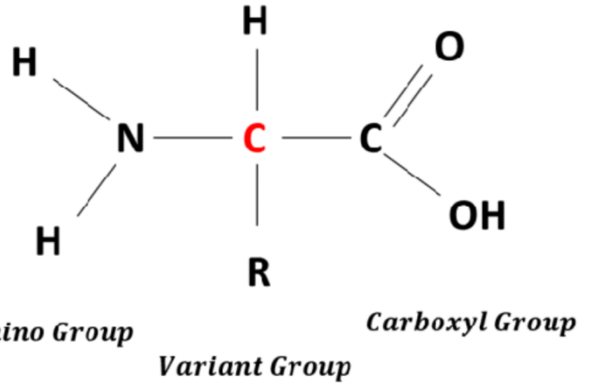


File:Amino acid generic structure.png - Wikipedia

Visit >

These are all wrong! There is no pH possible in which the carboxylic acid is protonated but the amine is not!!

ResearchGate



amino acid structure | Download Scientific Diagram

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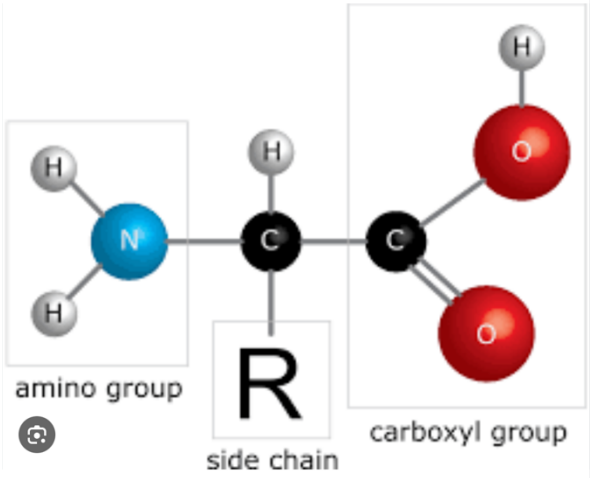

Protein > Amino Acids

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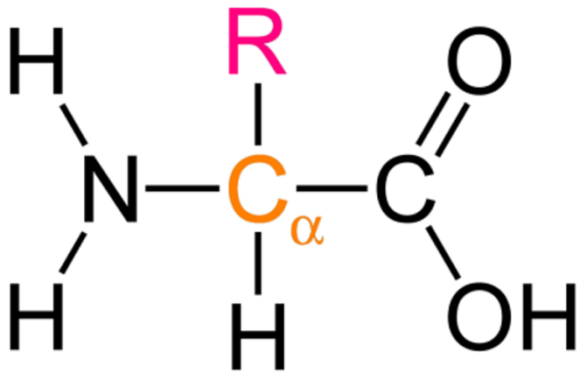

Proteins & Amino Acids | Formation, Structures & Sources - Lesson | Study.com

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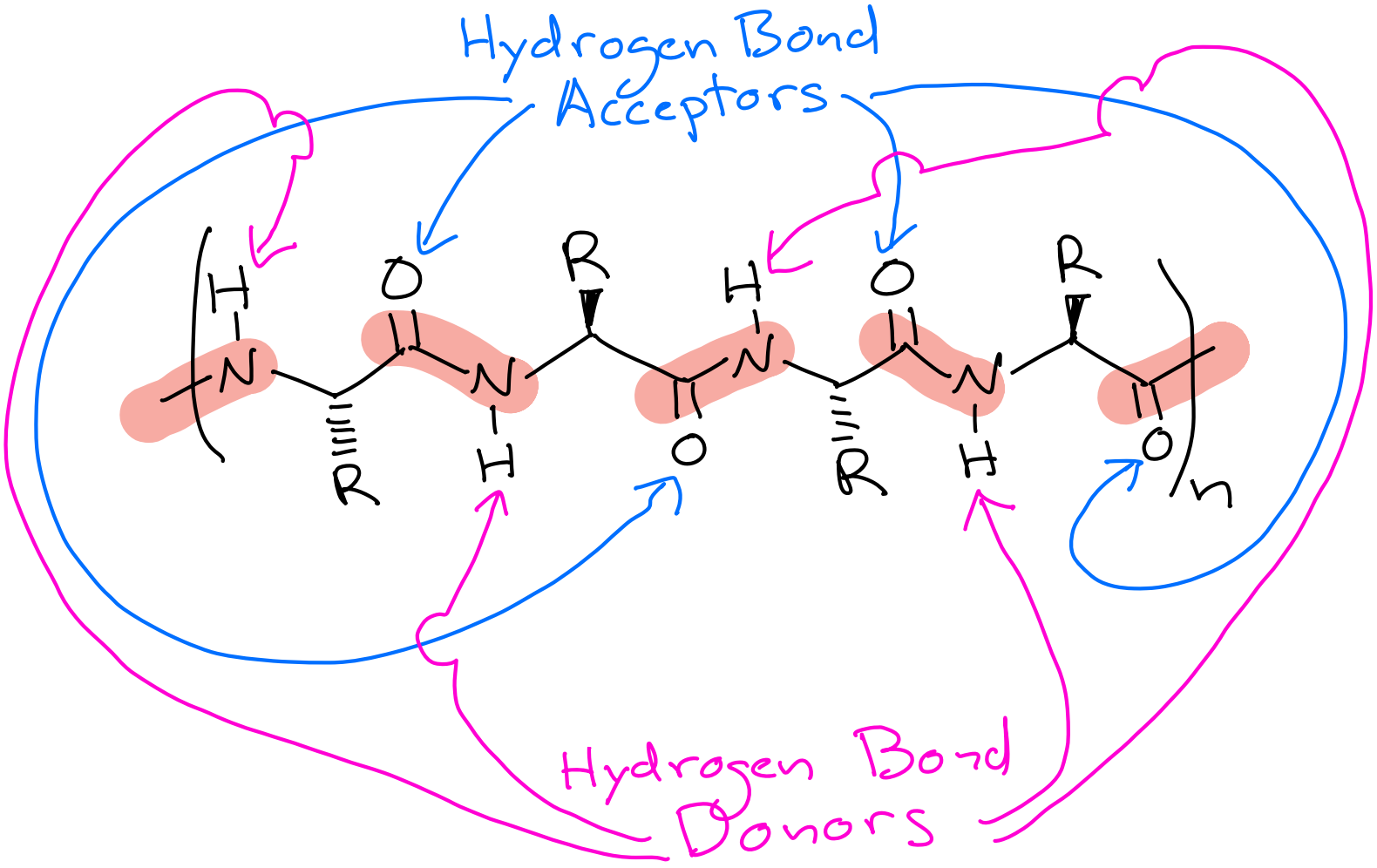
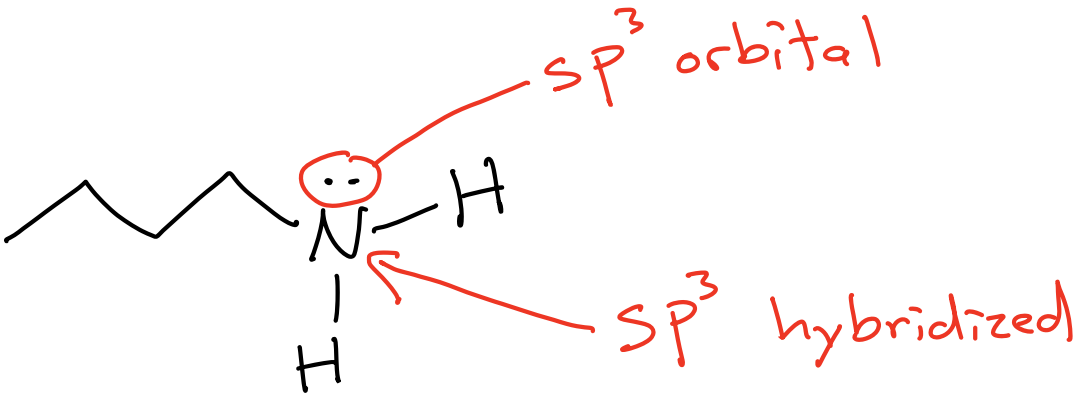
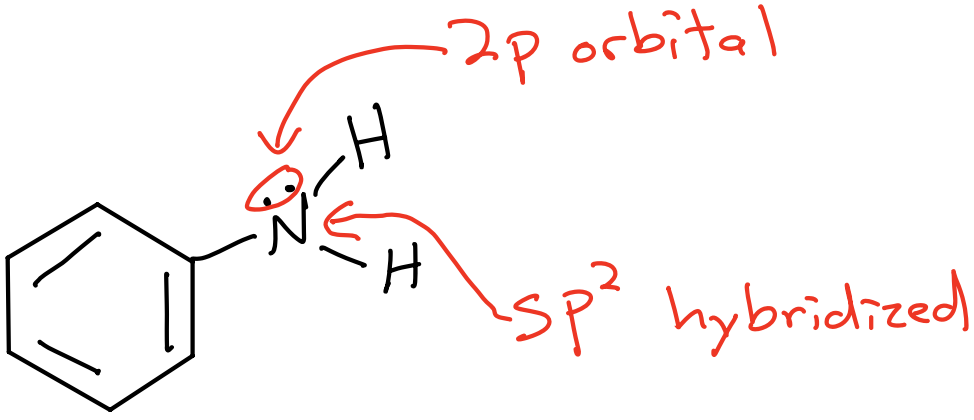
What does this means for amides:

1) The amide group can make strong hydrogen bonds

2) The C–N bond does not rotate at room temperature



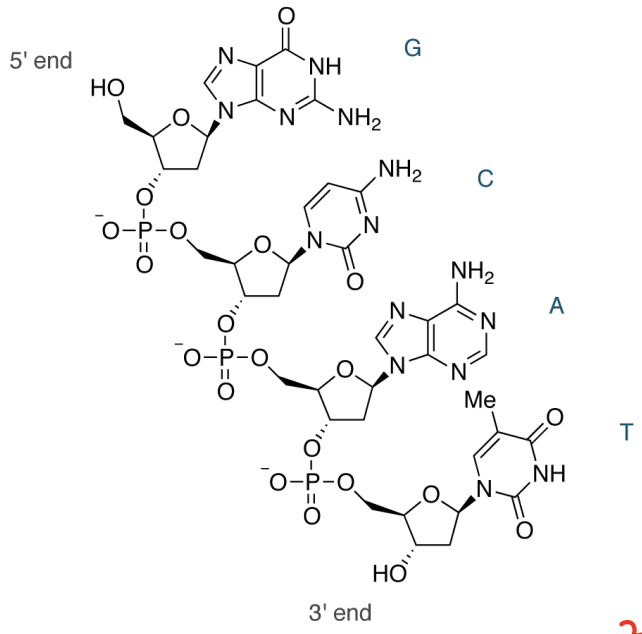


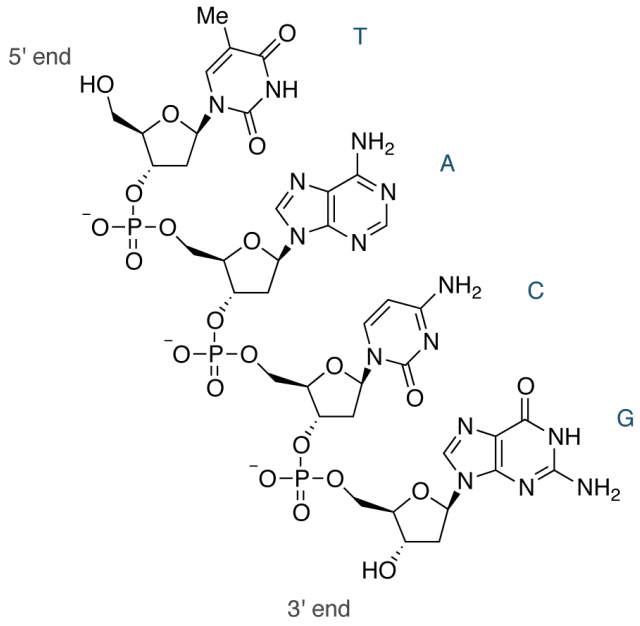


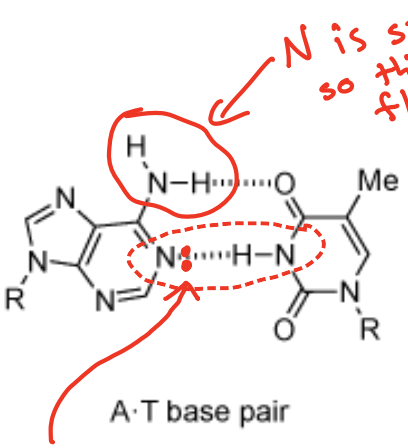
Golden rule: π electrons are more stable when delocalized

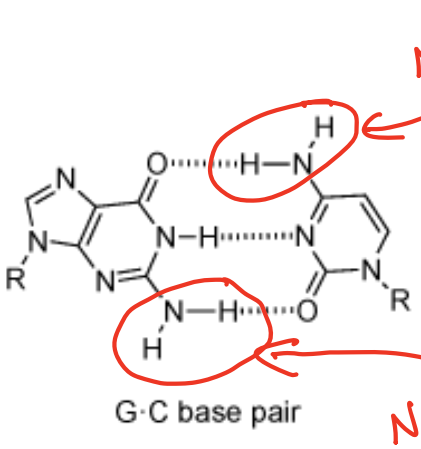
The lone pair is delocalized into the aromatic π system! The lone pair needs to be is a 2p orbital so N must sp^2 hybridized

This is critical to DNA and RNA structure: DNA bases are aromatic and the $-NH_2$ groups on the bases are sp^2 and flat



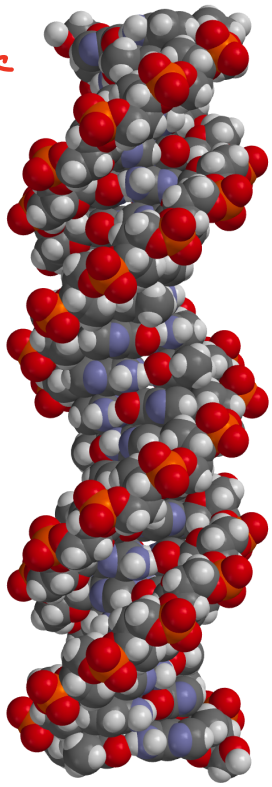


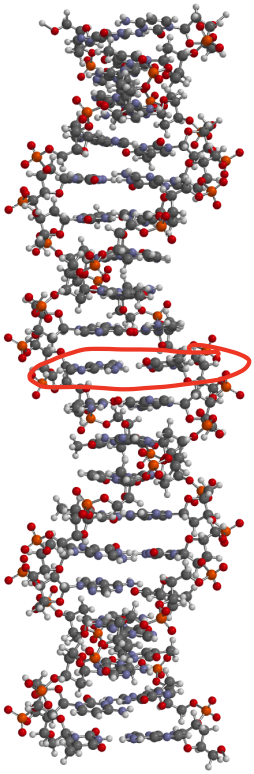




Analogous to pyridine

Lone pair is in an sp^2 orbital and available to make a strong hydrogen bond



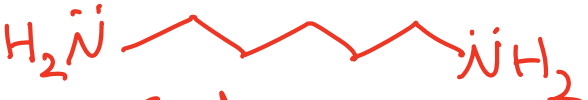


base pairs are flat because N atoms are sp^2

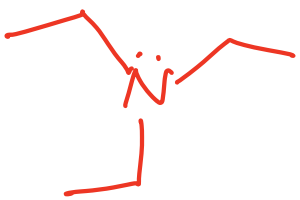
Our sense of smell is highly sensitive to certain molecules that are the result of decomposition of mammal and fish flesh among other things. Not only can we detect very small amounts of these "signal" molecules, we are hard wired to be highly nauseated when we smell them → evolutionary protection to keep us from eating what might look OK, yet would make us sick.

Putrescine

Rotten Mammal



Cadaverine



Rotten Fish

Triethylamine

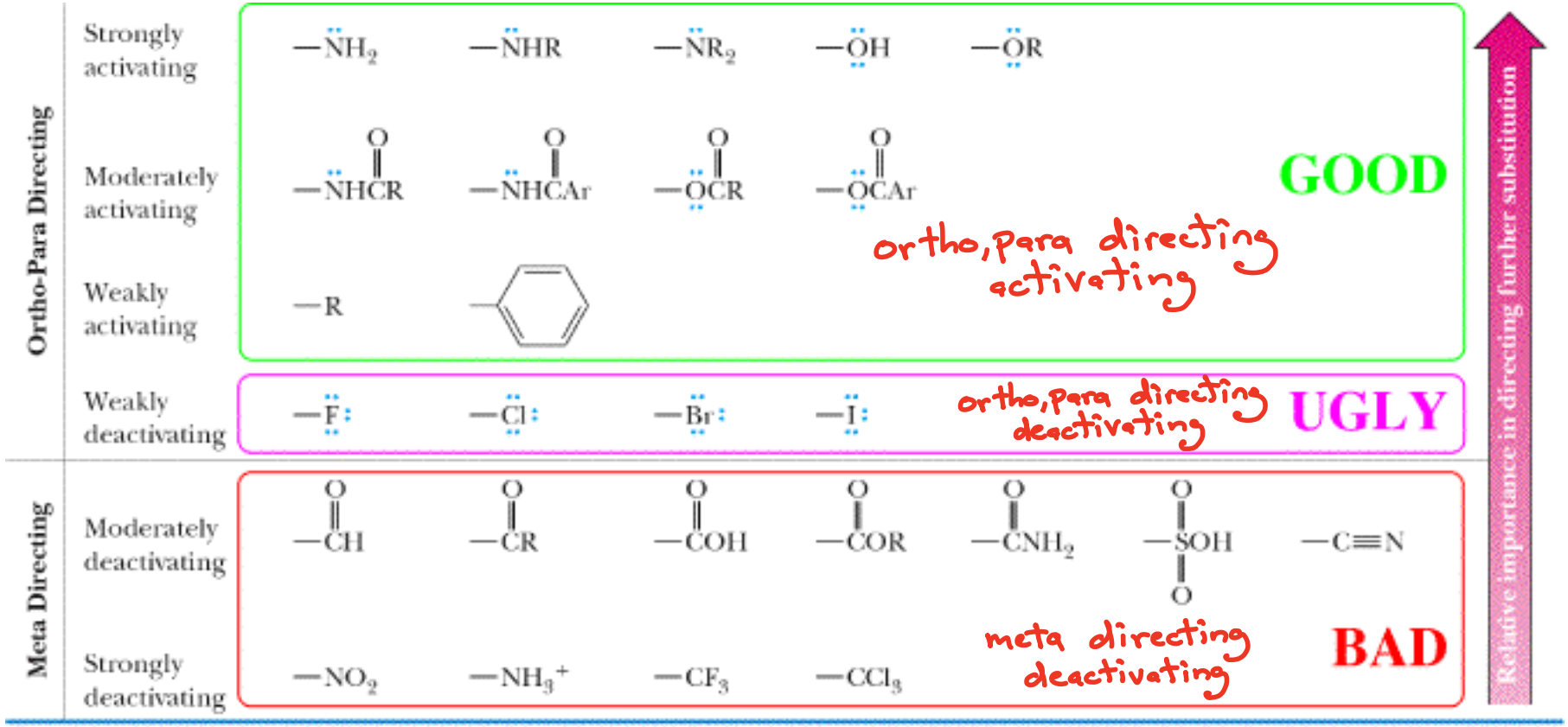
H_2S

Rotten Eggs

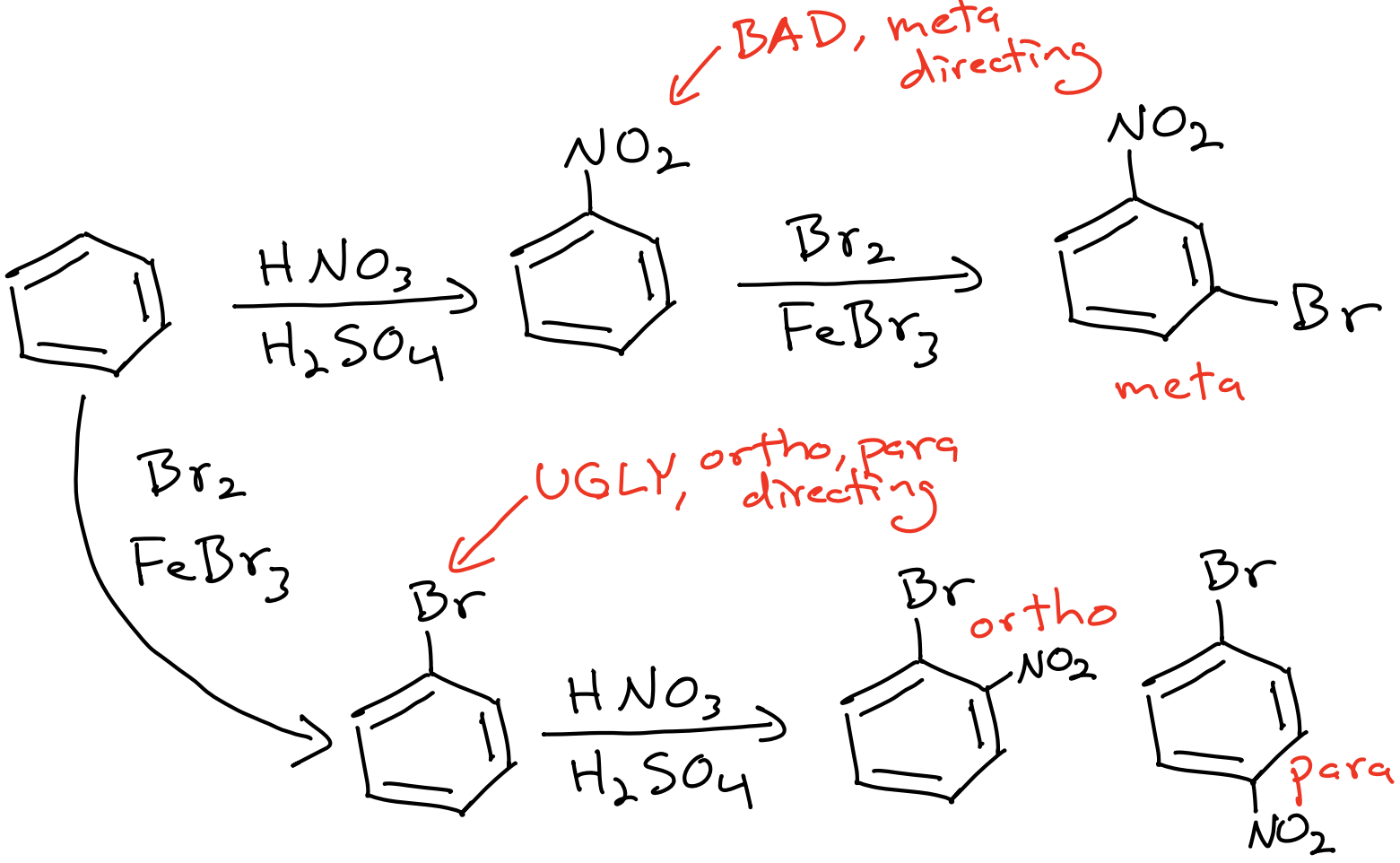
Hydrogen sulfide

Barf

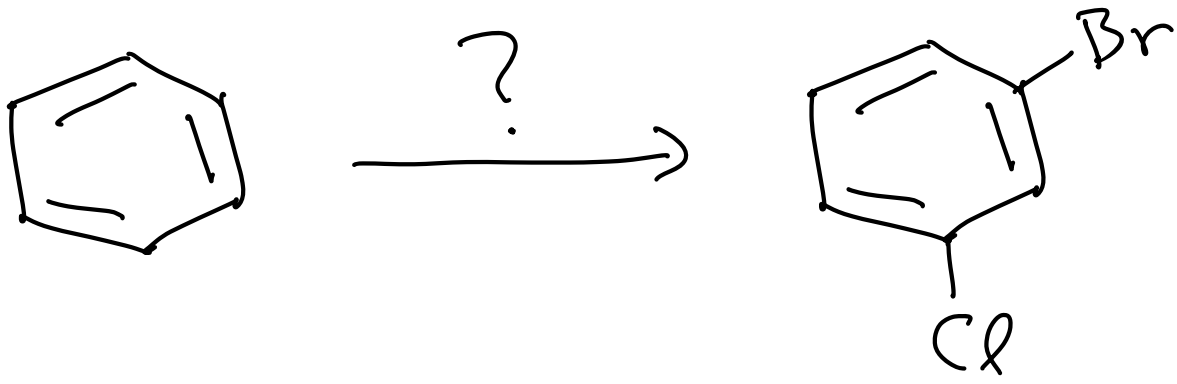
Butyric acid


Ortho-Para Directing
Meta Directing
Strongly activating
Moderately activating
Weakly activating
Weakly deactivating
Moderately deactivating
Strongly deactivating
—NH2
—NHR
—NR2
—OH
—OR
—NHCR
—NHCAr
—OCR
—OCAr
—R
—F:
—Cl:
—Br:
—I:
—CH
—CR
—COH
—COR
—CNH2
—SOH
—C≡N
—NO2
—NH3+
—CF3
—CCl3
GOOD
ortho, para directing activating
ortho, para directing deactivating
UGLY
meta directing deactivating
BAD
Relative importance in directing further substitution

The order in which you add groups matters!



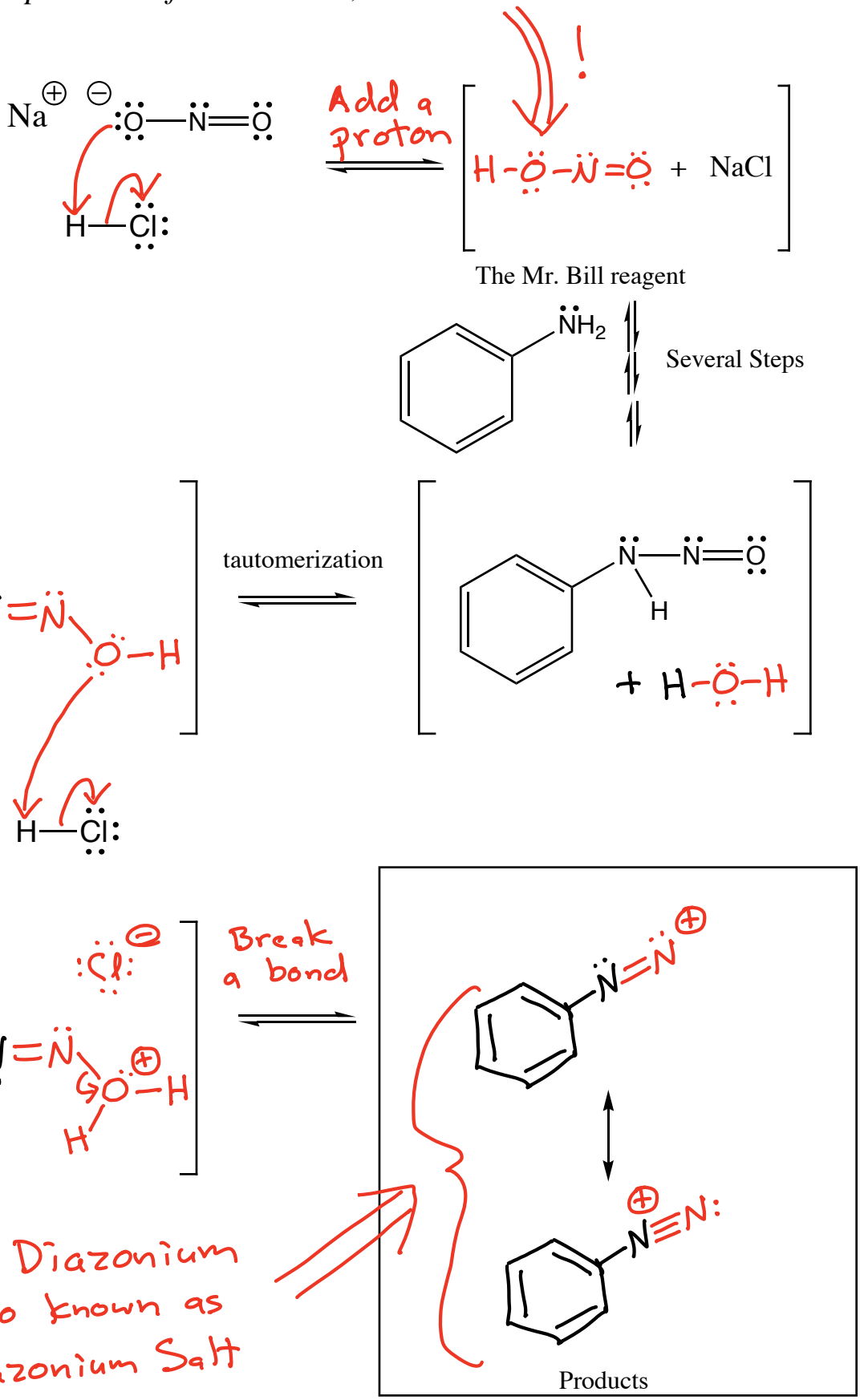
How do we carry out the following synthesis?



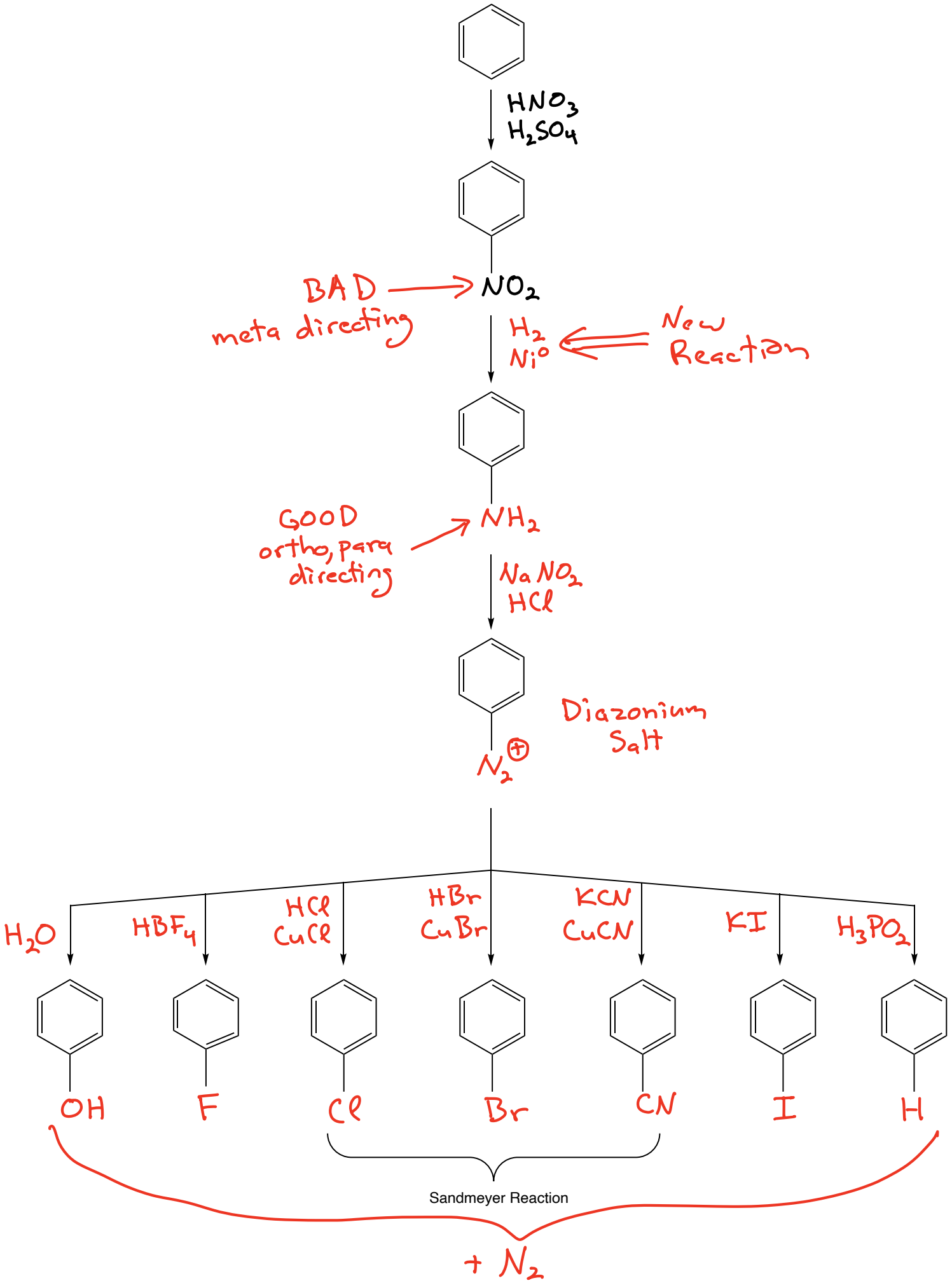
Time to call "Mr. Bill"

Both of these are UGLY so they are ortho, para directing. How do we introduce both of them meta to each other?

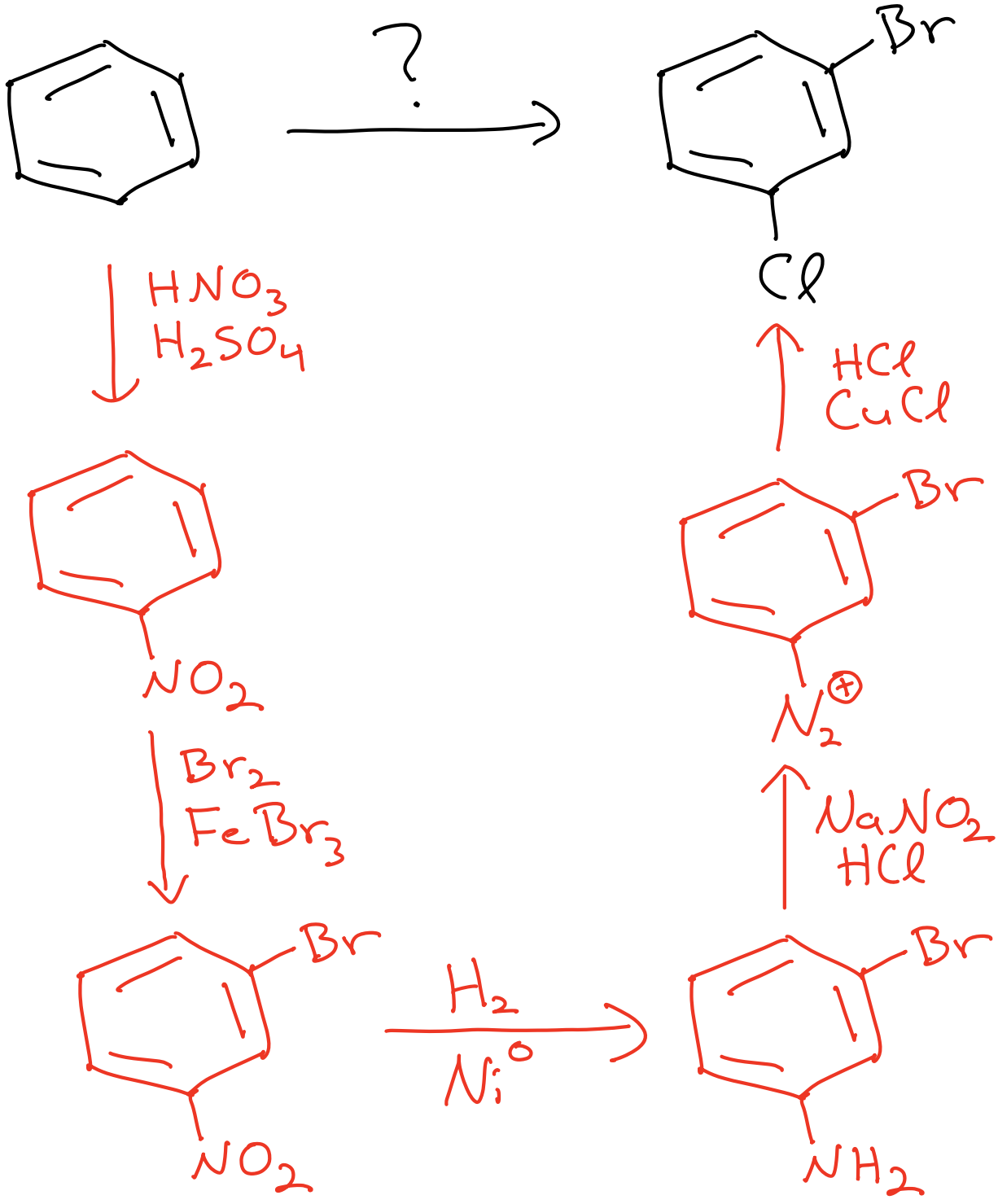
Preparation of Diazoniums, The "Mr. Bill" Reaction



N_2 leaves and is replaced by a variety of reagents → Not responsible for mechanisms

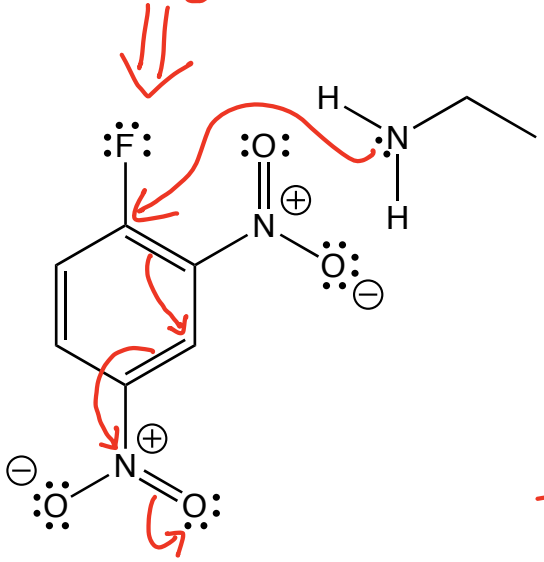

HNO3
H2SO4
BAD
meta directing
NO2
H2
Ni°
New
Reaction
GOOD
ortho, para
directing
NH2
NaNO2
HCl
Diazonium
Salt
N2⊕
H2O
HBF4
HCl
CuCl
HBr
CuBr
KCN
CuCN
KI
H3PO2
OH
F
Cl
Br
CN
I
H
Sandmeyer Reaction
+ N2

How do we carry out the following synthesis?

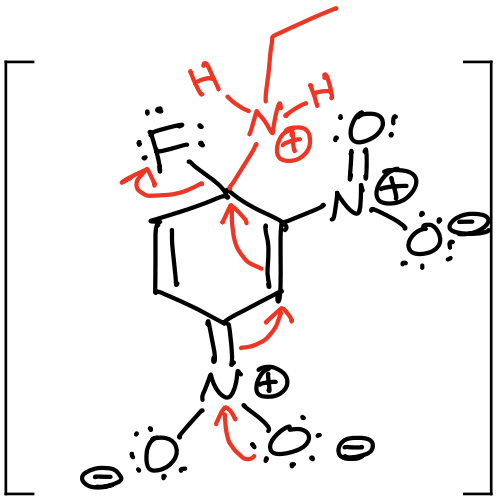


VERY electron deficient aromatic ring because of all the electron withdrawing groups

Nucleophilic Aromatic Substitution



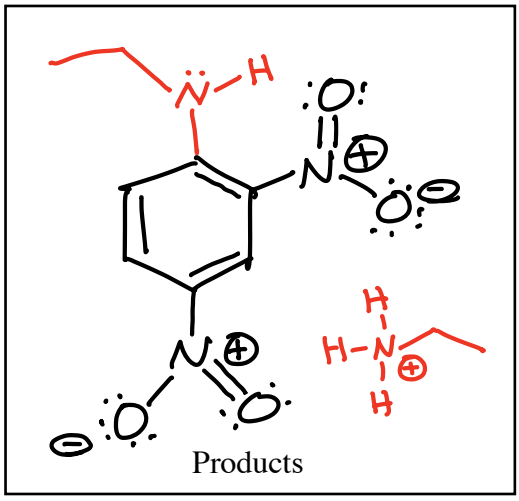
Make a bond



Meisenheimer complex

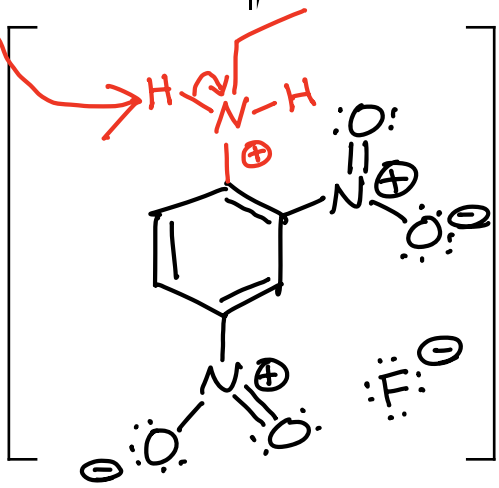
The timing of this last deprotonation step is uncertain

Break a bond



Products

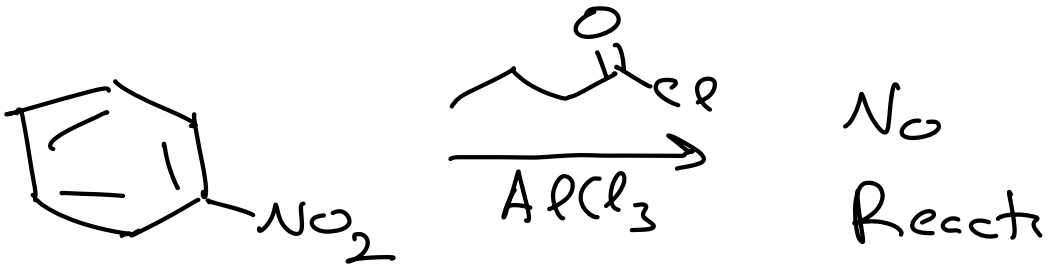
Take a Proton Away



This reaction is relatively rare, and this is the only example you will see in this class

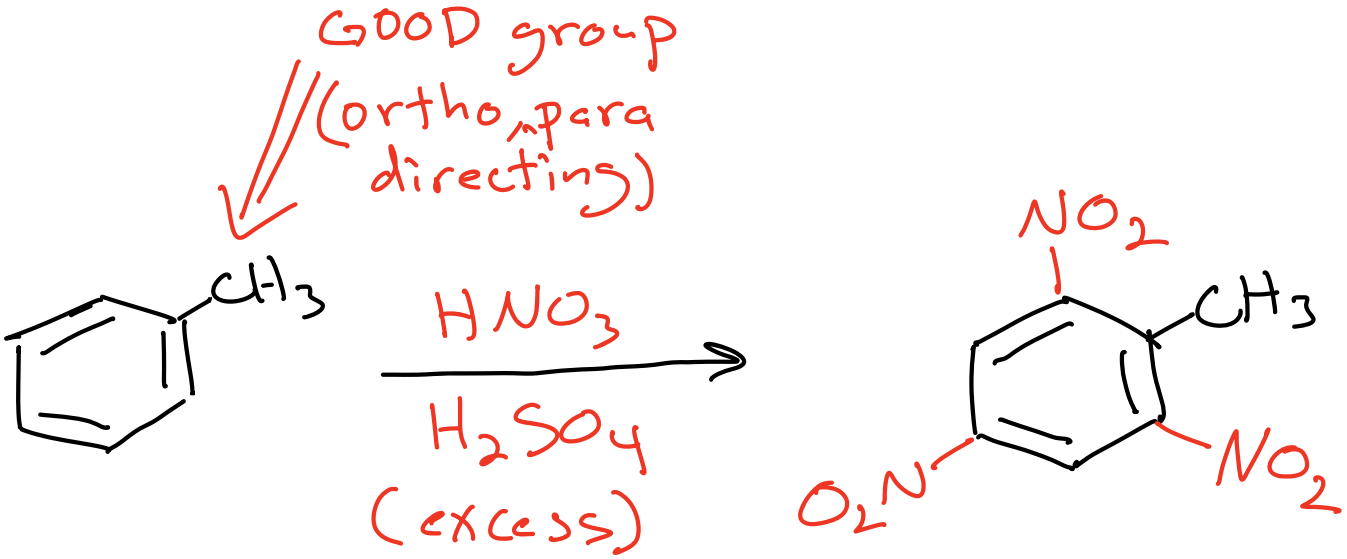
What you need to know about electrophilic aromatic substitution reactions:

1) Friedel-Crafts alkylations and acylations do not work if there is a bad group (i.e. $-NO_2$) on the ring



Conditions are not strong enough to overcome a deactivated ring

However → some reactions with harsh conditions will work:



Toluene

Solvent used in glue for plastic

Trinitrotoluene (TNT)

Boom!