Organic Chemistry II: CHEM 247

Amine (NH_2) and Heterocycles (Aromatic):

Chapter 24

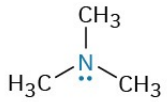
Dr. Xiaodong Michael Shi

MWF, 10:00 am – 10:50 am

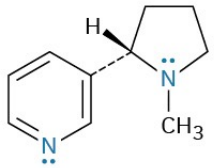
General Topics

- Nomenclature (amine vs aniline)
- Physical property (Basicity! and H-bond);
- Preparation of amine (addition and reduction)
- Preparation of aniline (Ar-NO_2 reduction)
- Reactions of amine (Nu; oxidation; substitution);
- Something special (diazonium: formation and reaction: very important)

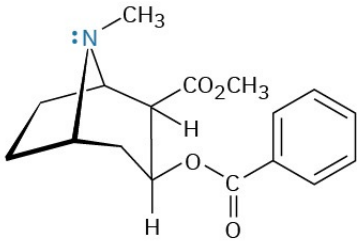
Nomenclature



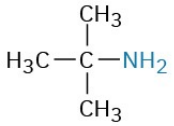
Trimethylamine



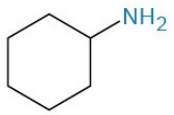
Nicotine



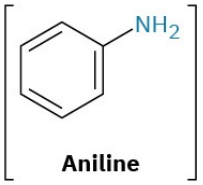
Cocaine



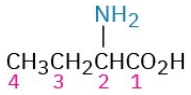
tert-Butylamine



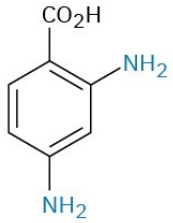
Cyclohexylamine



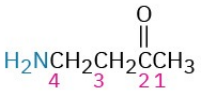
Aniline



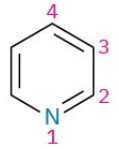
2-Aminobutanoic acid



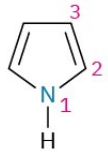
2,4-Diaminobenzoic acid



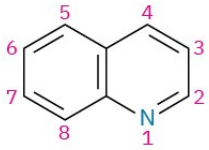
4-Amino-2-butanone



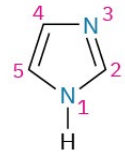
Pyridine



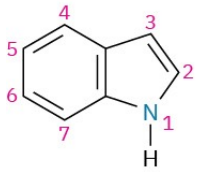
Pyrrole



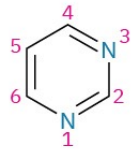
Quinoline



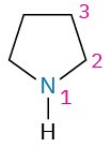
Imidazole



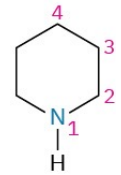
Indole



Pyrimidine



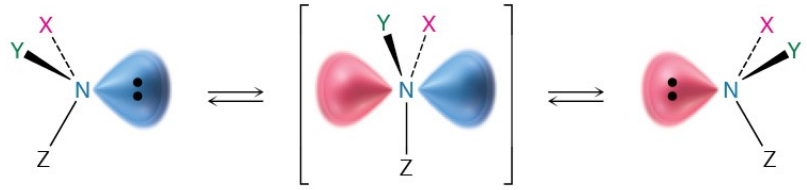
Pyrrolidine

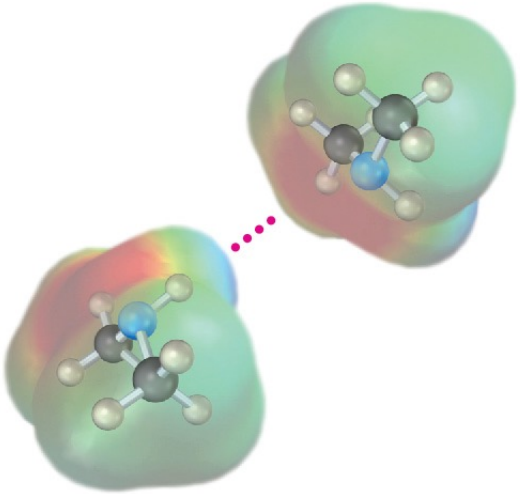


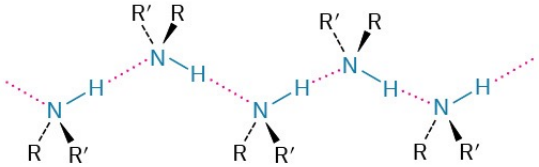
Piperidine

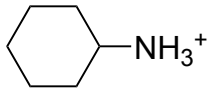
Need to know. Sorry

Amine: Basicity, H-bond and Chiral









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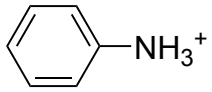

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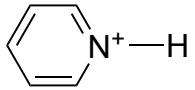

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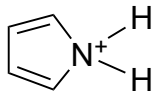

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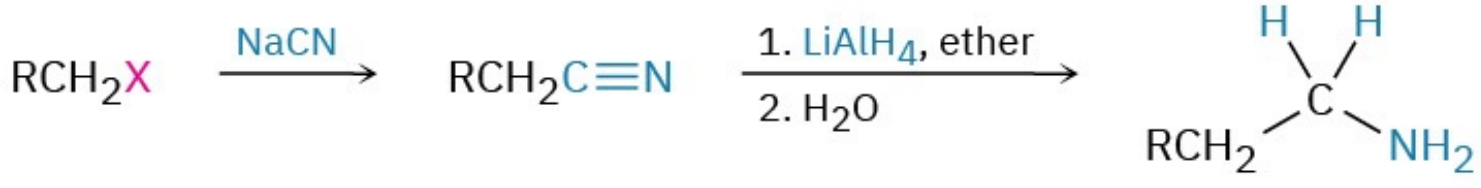
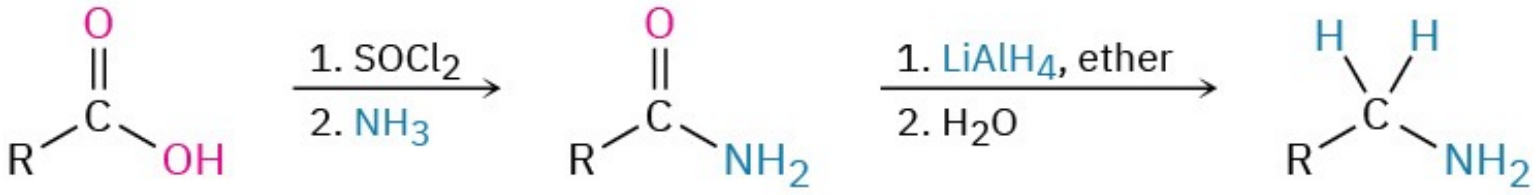
Synthesis of Amine (I): CN and amide reduction



Alkyl halide

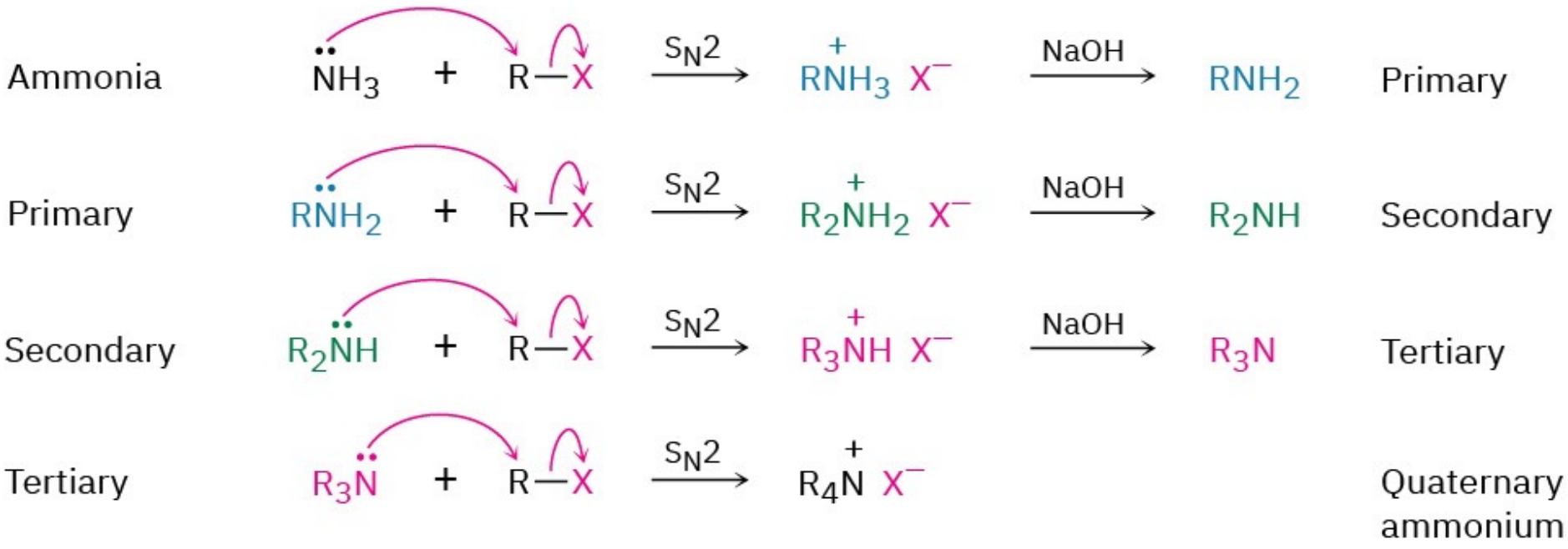
1° amine



Carboxylic acid

1° amine

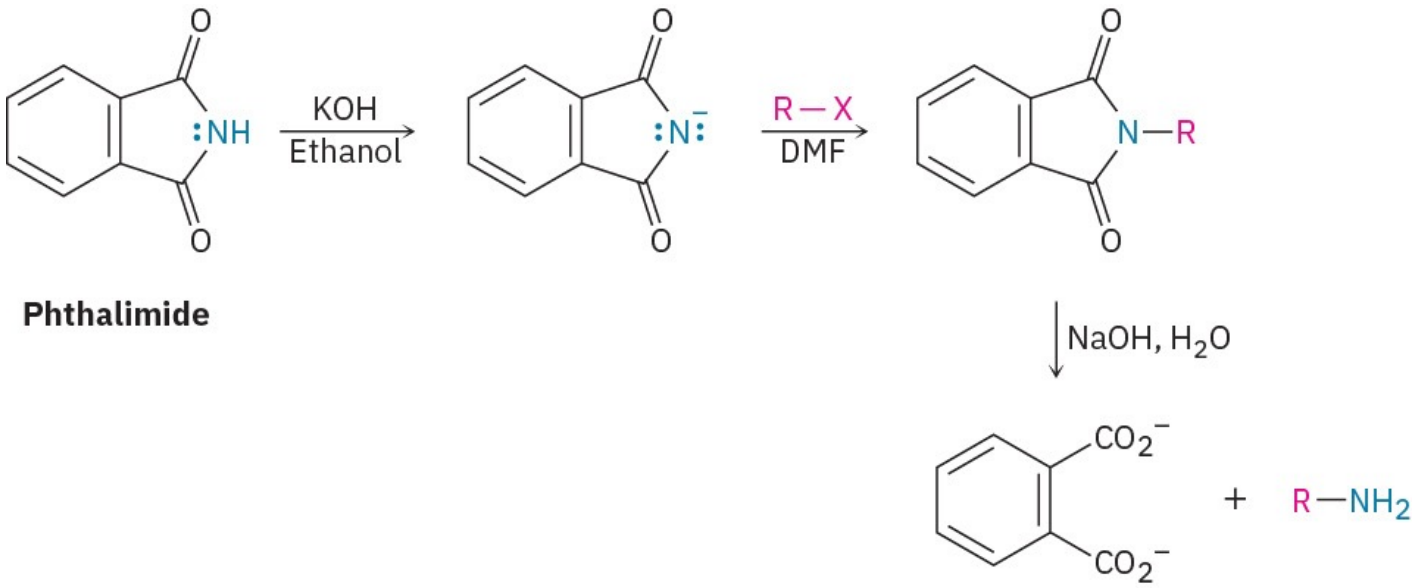
Synthesis of Amine (II): R-NH_2 Nu-addition



NH_2 (or N_3 or CN) as Nucleophile!

Think: stop at primary amine?

Synthesis of Amine (III): Gabriel amine synthesis, RNH_2



Phthalimide

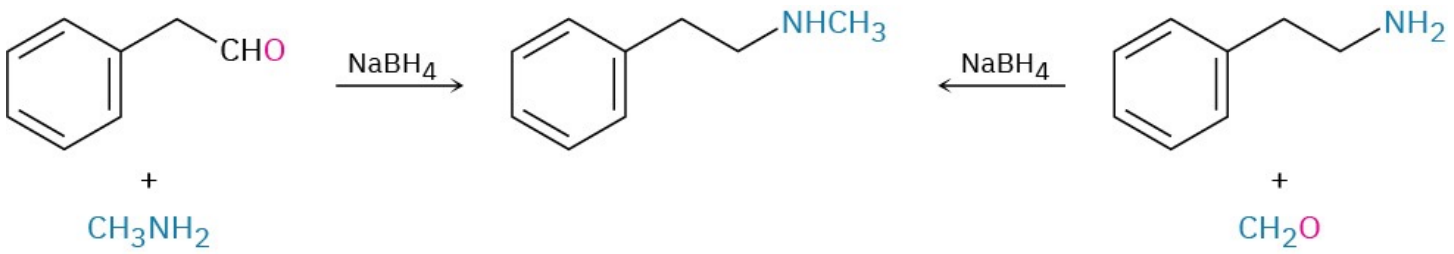
Alternative work-up:

NH_2NH_2

Mechanism?

Synthesis of primary amine!

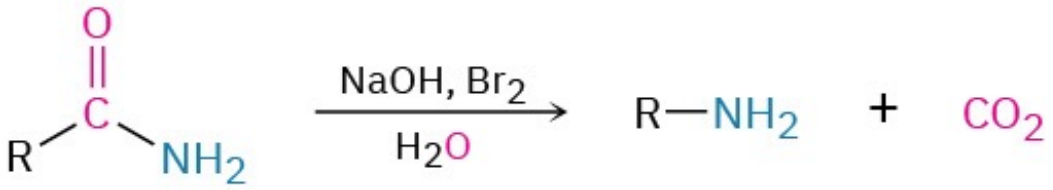
Synthesis of Amine (IV): Reductive Amination



Mechanism, reagents and practical synthesis

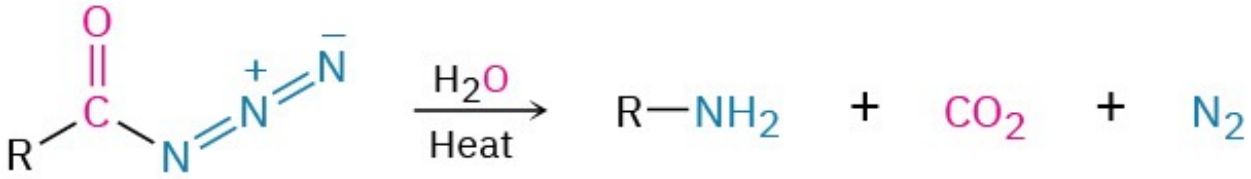
Synthesis of Amine (V): The rearrangements!!!

Hofmann rearrangement



An amide

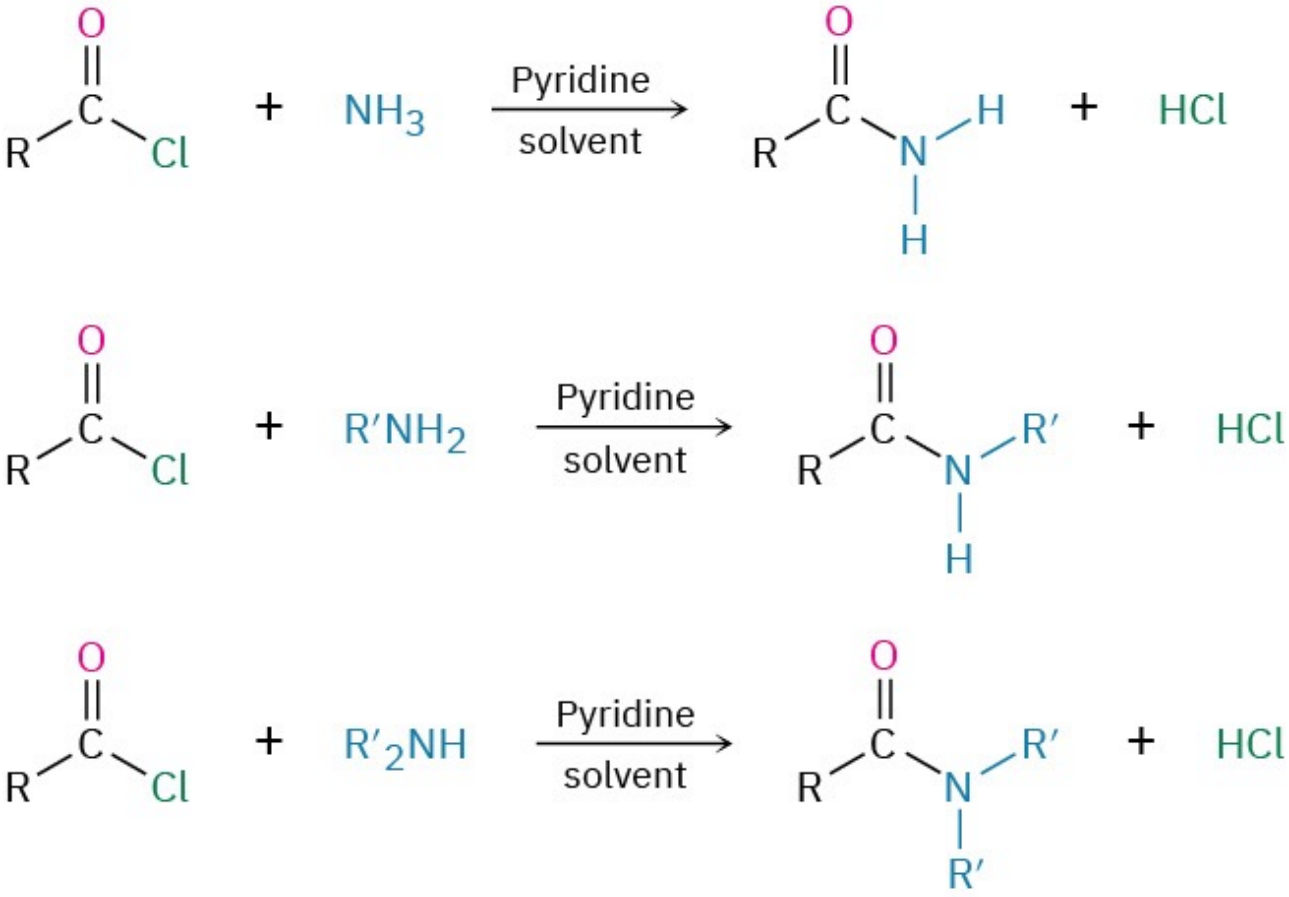
Curtius rearrangement



An acyl azide

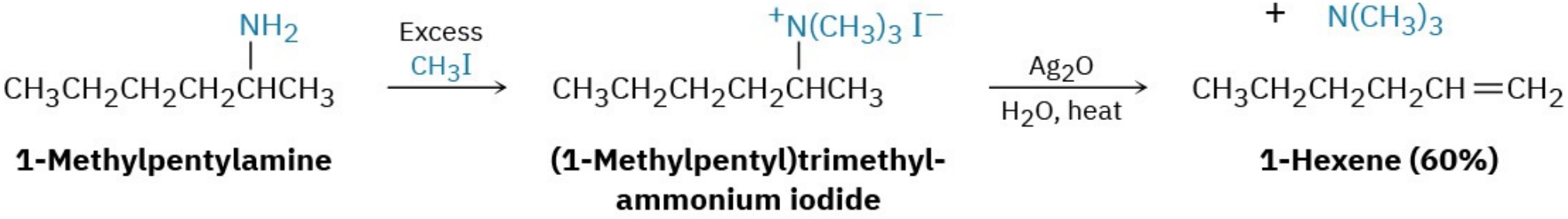
Mechanism, reagents and practical synthesis

Reaction of Amine (I): Alkylation and Acylation

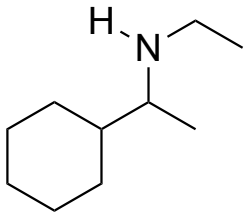


Basicity nothing fancy

Reaction of Amine (I): Alkylation (Hofmann Elimination)



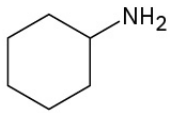
1-Methylpentylamine | **(1-Methylpentyl)trimethyl-ammonium iodide** | **1-Hexene (60%)**

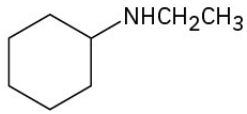


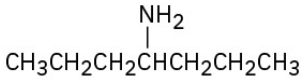
1) CH_3I

2) Ag_2O, H_2O, heat

?

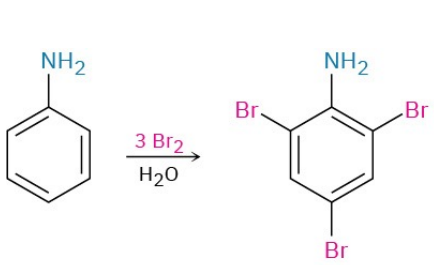




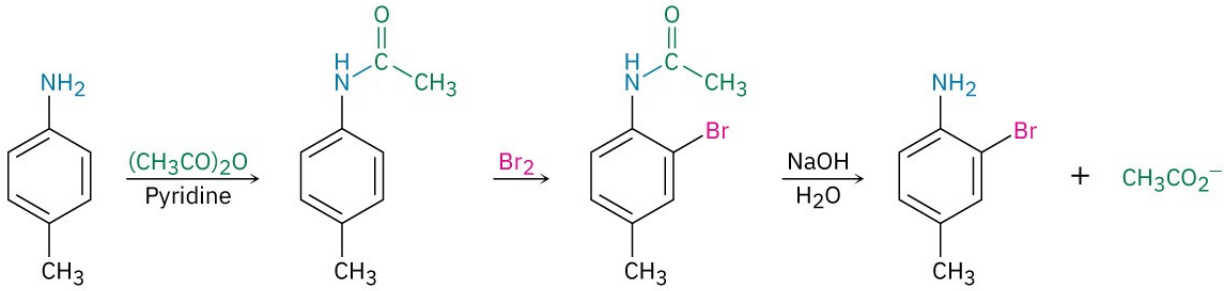


What are the products?

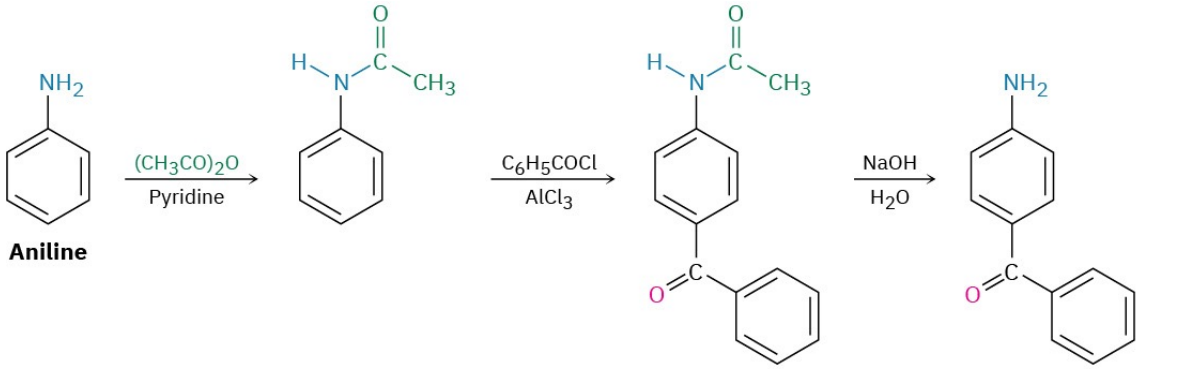
Reaction of Aniline (II):E-Rich Benzene



Aniline **2,4,6-Tribromoaniline (100%)**



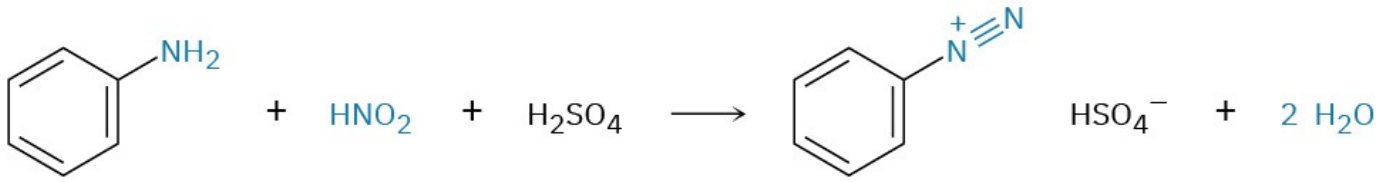
***p*-Toluidine** **2-Bromo-4-methyl-aniline (79%)**



Aniline **4-Aminobenzophenone (80%)**

Old aromatic chemistry

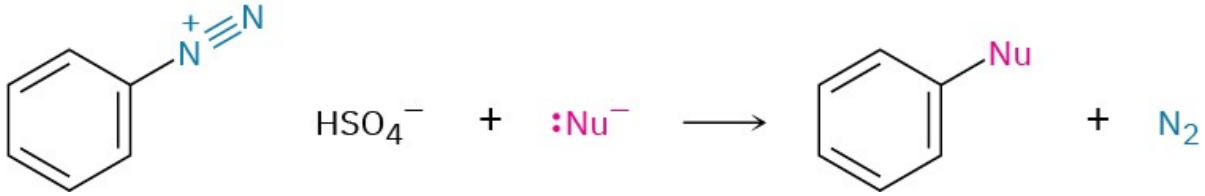
Reaction of Aniline (III): Diazonium $[ArN_2]^+$



Easy synthesis;

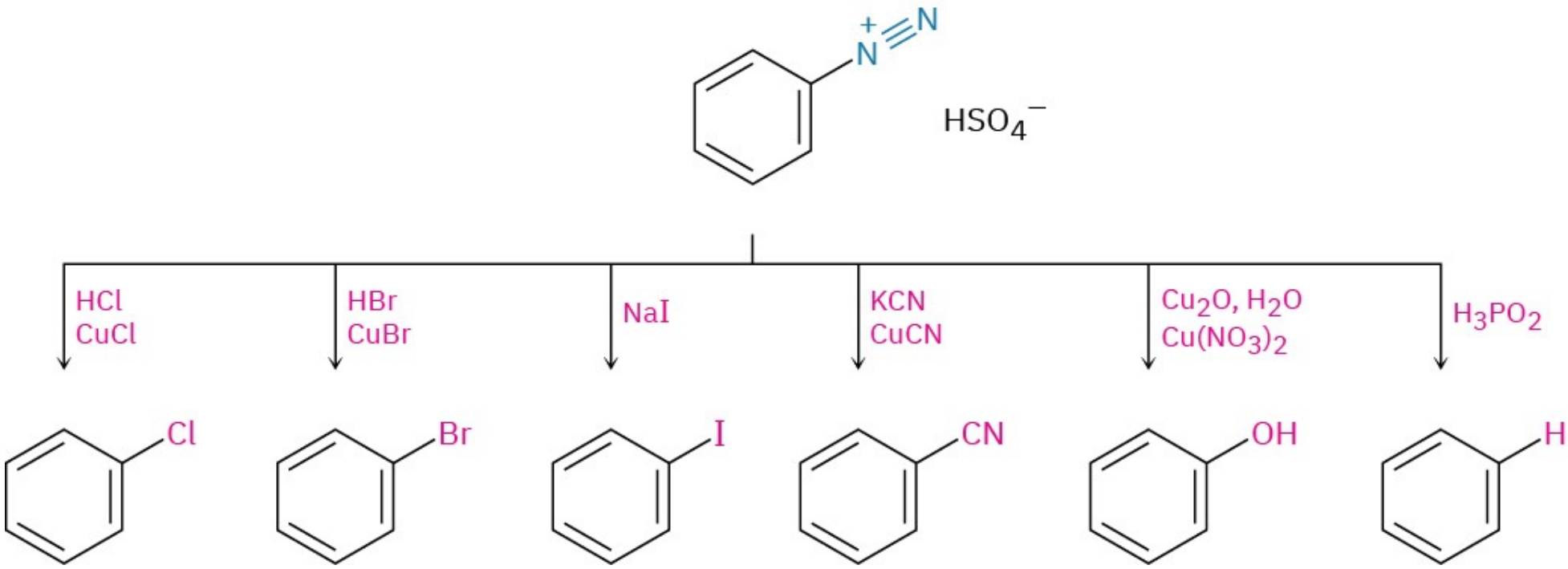
Mechanism?

Condition!

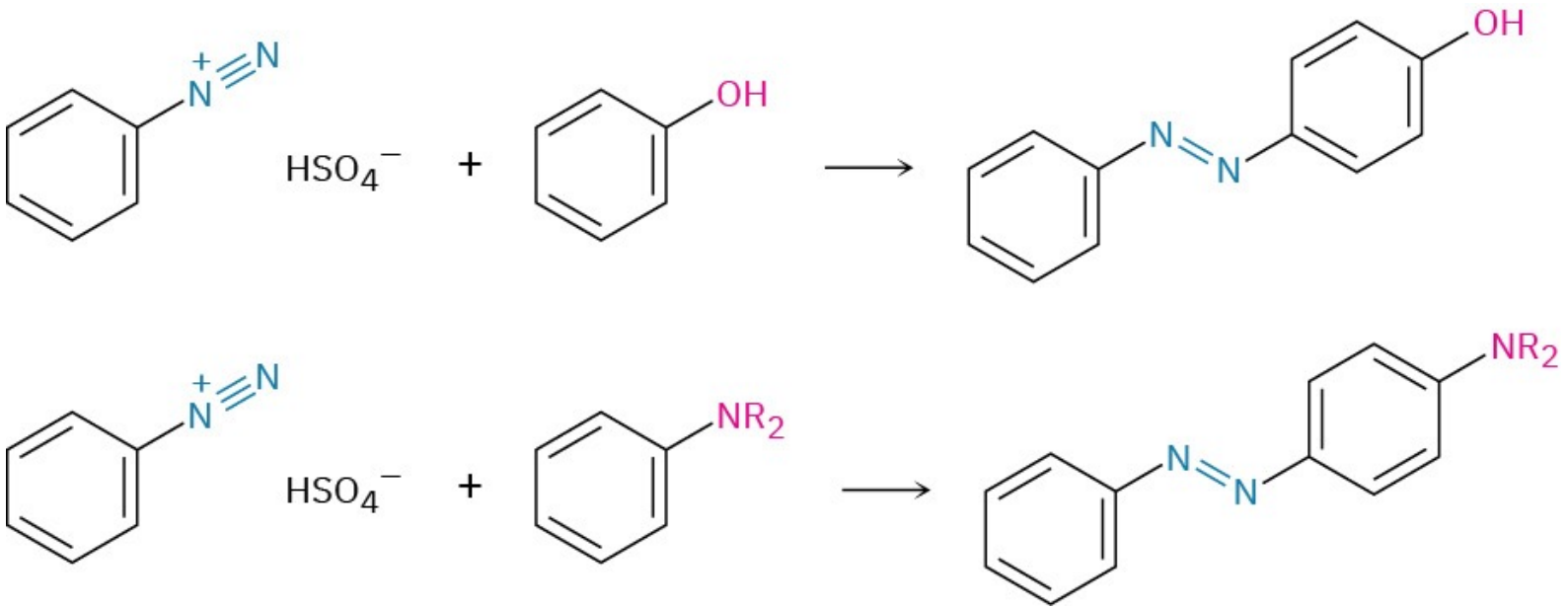


Nucleophilic Aromatic Substitution SN_{Ar} (important new reactivity)

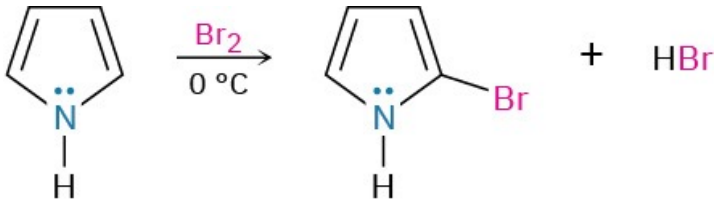
THE Conditions to remember!!!



Diazonium $[ArN_2]^+$ Reaction (B): diazo Compounds

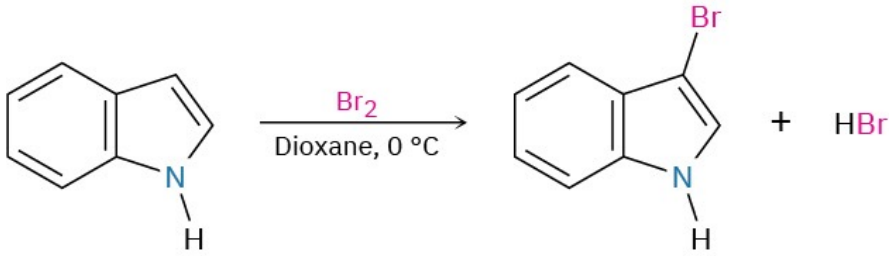


Heterocycles: The *three* important ones to remember

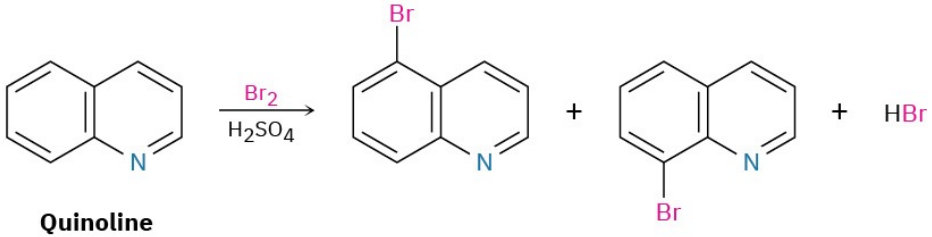


Pyrrole **2-Bromopyrrole (92%)**

Pyridine **3-Bromopyridine (30%)**



Indole **3-Bromoindole**

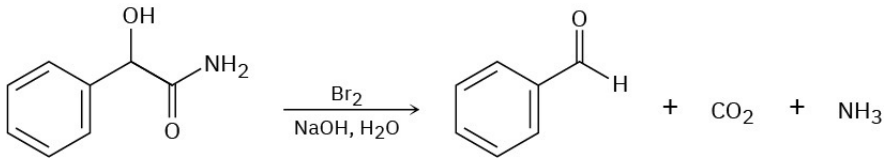


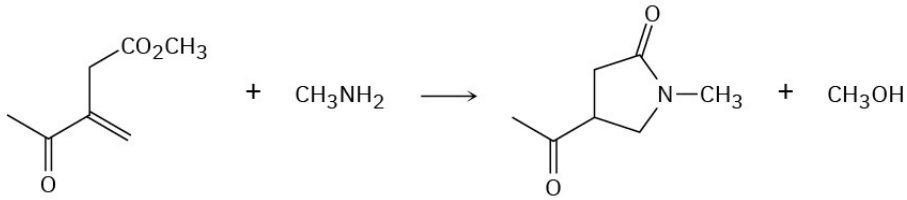
Quinoline

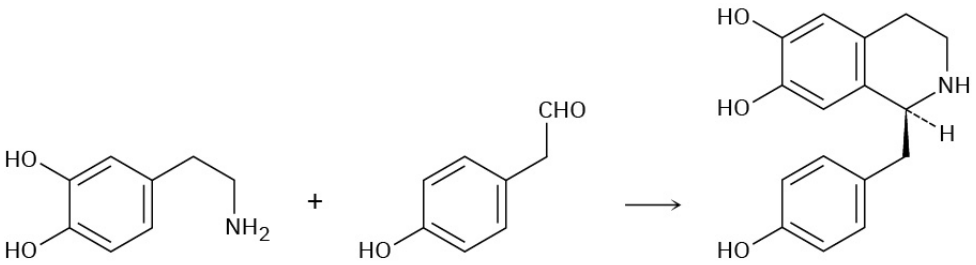
5-Bromoquinoline **8-Bromoquinoline**

A 51 : 49 ratio

Something Special? Not really







Dopamine + ***p*-Hydroxyphenyl-acetaldehyde** → **(*S*)-Norcoclaurine**

Mechanism and Synthesis