

Objective 14. Apply acid-base, substitution, and elimination principles to amines.

Skills: Draw structure

ID structural features and reactive sites (alpha C, beta C, LG, etc.)

ID Nu⁻ and E⁺

use curved arrows to show bonds breaking and forming

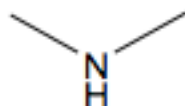
show delocalized electrons with resonance structures.

Key ideas:

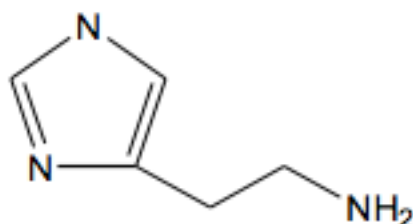
amines are bases and nucleophiles

Amines can be LG – see substitution and elimination

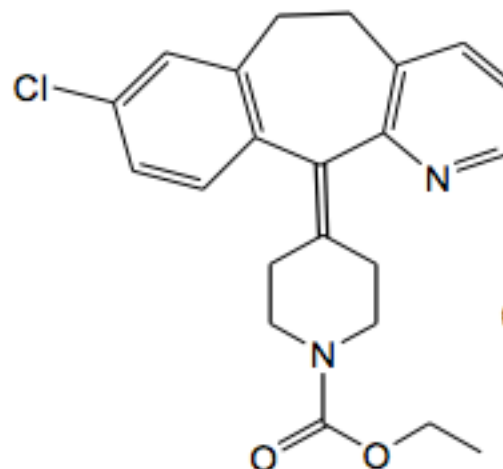
Amines Are Found in Many Natural Products



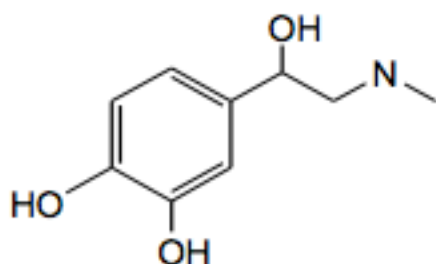
fish odor



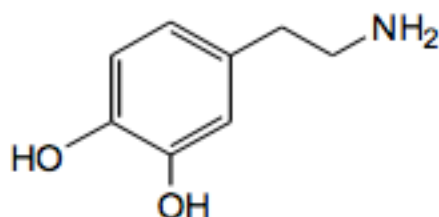
histamine



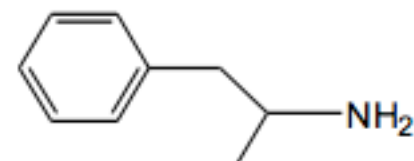
Claritin



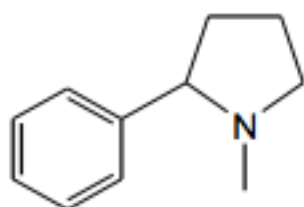
epinephrine (adrenaline)



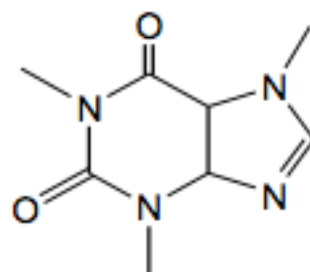
dopamine



benzedrine (amphetamine)



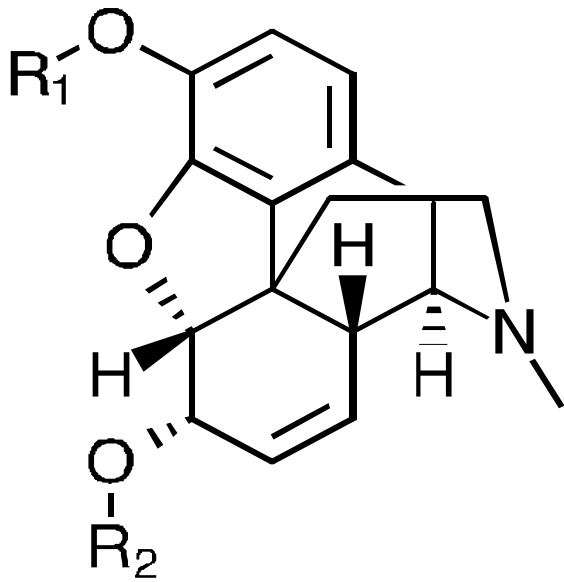
Nicotine



caffeine

Alkaloids are amines found in plants

Morphine - narcotic (analgesic, hypnotic, euphoriant)

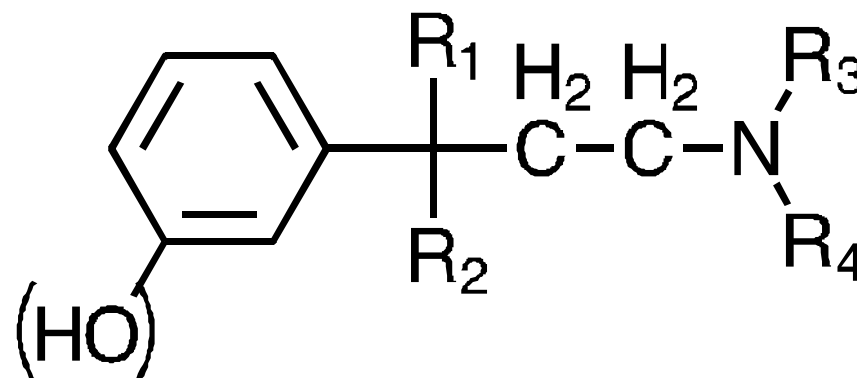


Morphine	$R_1 = H = R_2$
Codeine	$R_1 = CH_3$ $R_2 = H$
Heroin	$R_1 = CH_3CO-$ $R_2 = CH_3CO-$

Structure and Shape Determine Interaction between Drug Receptor and Pharmacophore

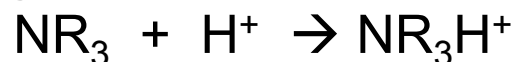
“Morphine Rule” - 4 structural features of strong narcotic analgesics

1. Ring
2. Quaternary C
3. Ethylene bridge
4. 3° amine

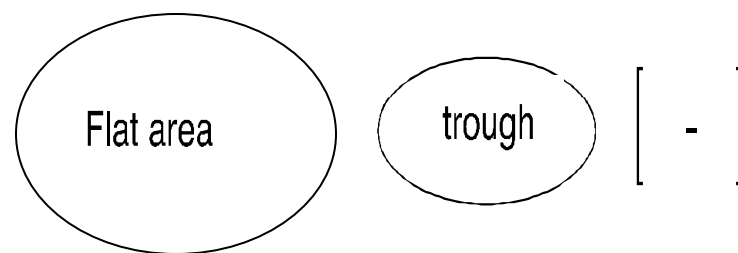


3 essential receptor features:

1. Flat area that binds to ring, probably by van der Waals interaction.
2. an anionic site that attracts the 3° amine. Amine is usually protonated and (+) charged. See pH and pK of amine.



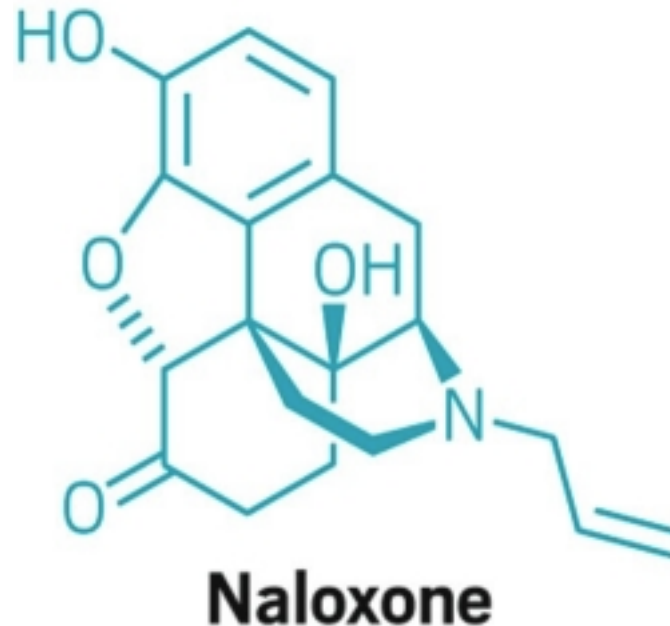
3. a suitably oriented trough between ring and amine to accommodate -CH₂-CH₂- bridge.



Opioid overdose treatment

<http://cen.acs.org/articles/94/i20/Improving-old-tool-treat-opioid.html>

Heroin, oxycodone (Oxycontin), hydrocodone (Vicodin)



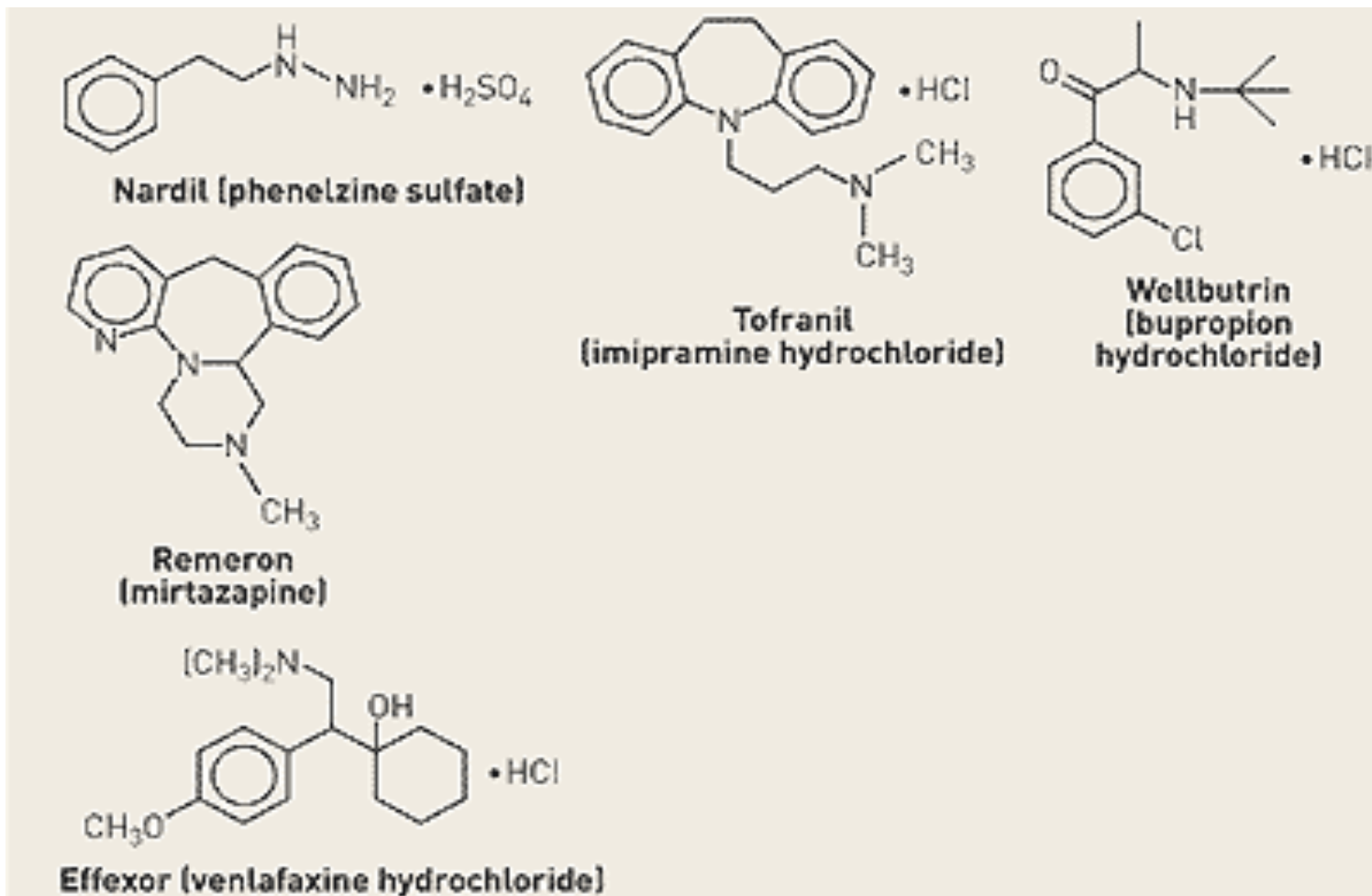
How does Naloxone work?

Hint: Does Naloxone fit the “Morphine Rule”?

Drugs to treat depression are Amines: Classify the amine type

CENEAR 82 06 pp. 33-40, February 9, 2004

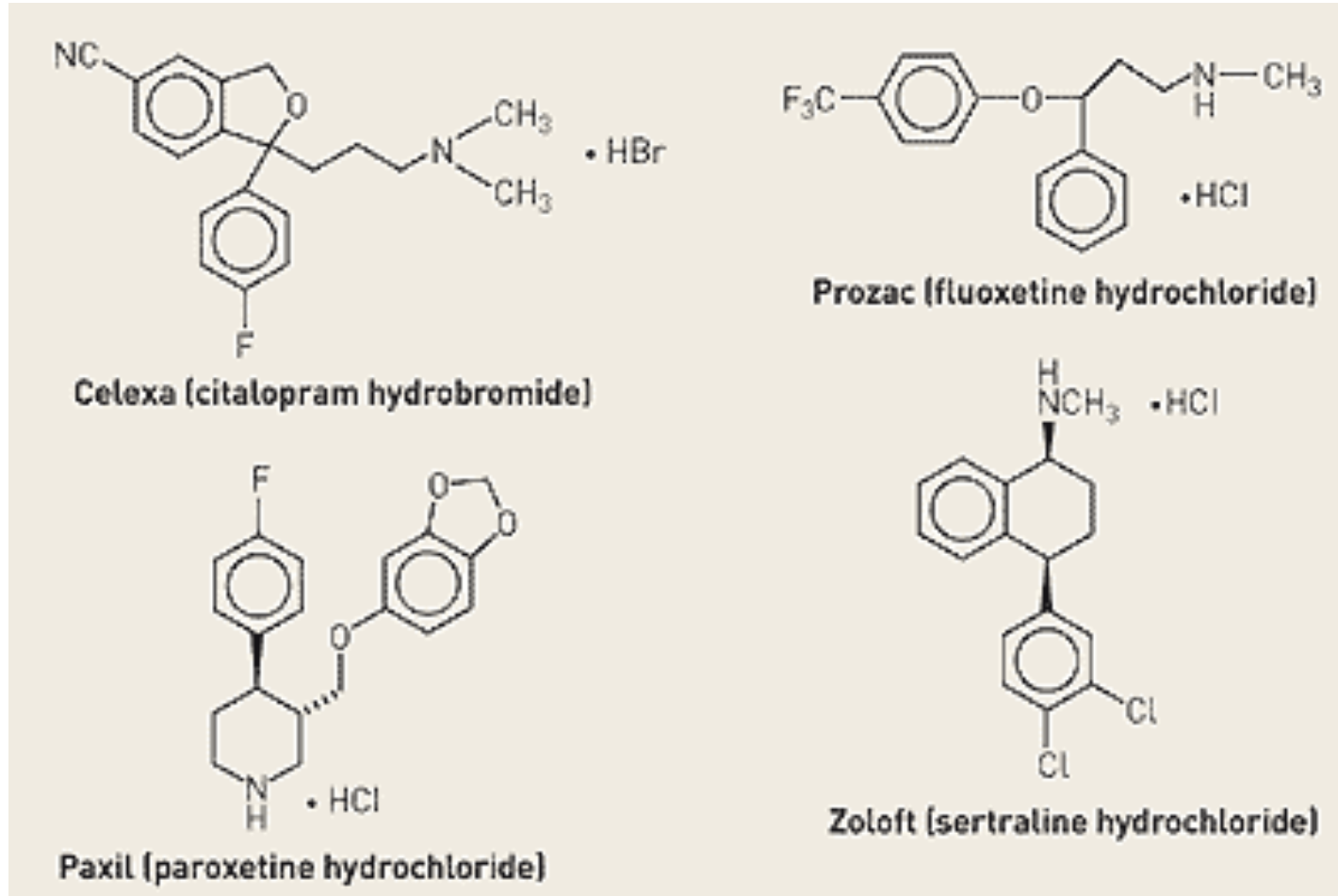
(1°, 2°, 3°)



Early treatments for depression included monoamine oxidase inhibitors such as Nardil and tricyclics such as Tofranil. They have been succeeded by compounds with fewer side effects such as Wellbutrin, Remeron, and Effexor, as well as selective serotonin reuptake inhibitors.

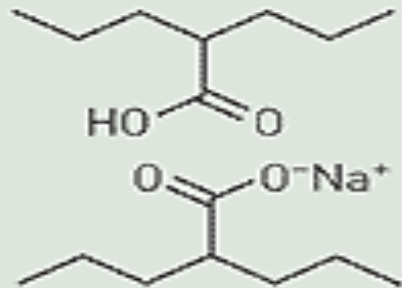
Drugs to treat depression are Amines

CENEAR 82 06 pp. 33-40, February 9, 2004

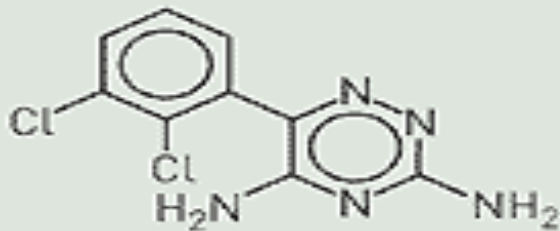


Selective serotonin reuptake inhibitors such as these have less severe side effects than older treatments for depression. This class of drug was introduced in the mid-1980s.

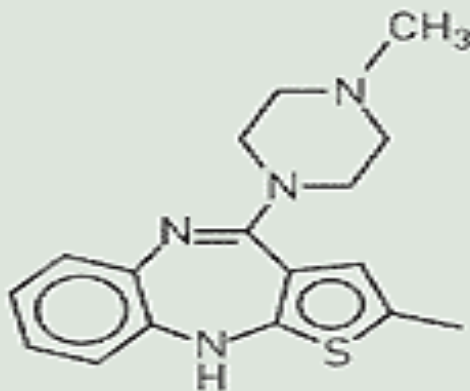
Drugs to treat depression are Amines



Depakote (divalproex sodium)



Lamictal (lamotrigine)



Zyprexa (olanzapine)

The standard treatment for bipolar disorder is lithium carbonate, a mood stabilizer first approved in 1970.

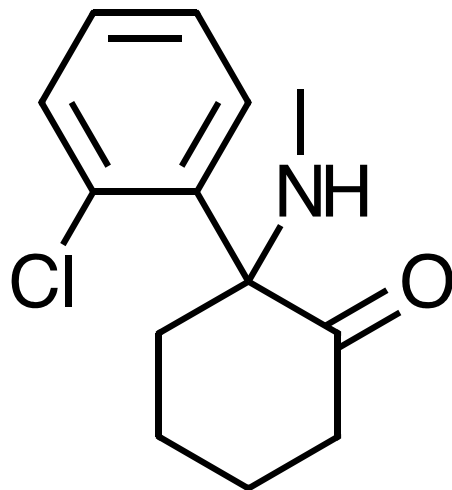
Physicians can use these other compounds that have fewer side effects to treat the condition, though they aren't as effective.

(CENEAR 82 06 pp. 33-40, February 9, 2004)

<http://cen.acs.org/articles/91/i12/Limits-Lithium.html>

3/25/13, CEN, p. 15 “Limits Of Lithium” It helps millions with bipolar disorder, but toxicity problems and side effects have scientists looking for alternatives by analyzing the drug’s mysterious mechanism.

Subanesthetic infusion of **Ketamine** (anesthetic agent) can relieve the symptoms of depression and suicidal urges in a matter of hours. The effect lasts about a week, whereas commonly prescribed antidepressants usually take weeks to work. (C&EN, Aug. 23, 2010, page 8).



Ketamine

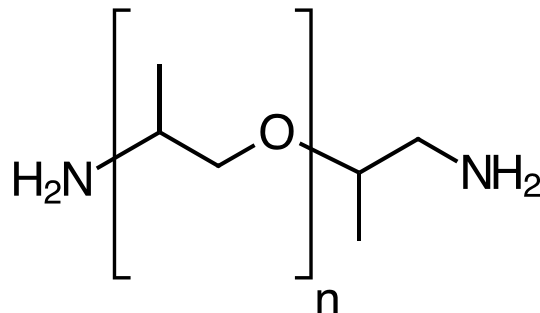


Amines are used as the active cleaning molecule in fuels

In the 1960s and early 1970s, low-molecular-weight amines were used to control carburetor deposits

Polybutene amine detergents arrived in the early 1970s.

In 1980, Chevron patented a next-generation cleaning approach based on polyether amines (PEAs)



polyetheramine D2000

<http://www.hansonco.net/Structures.pdf>

<http://cen.acs.org/articles/87/i14/Gasoline-Wars.html>

4/6/09, CEN, p. 20. Oil companies use additive packages to help their fuels stand out from the crowd

Structure and properties:

Amines are soluble in water.

Gaseous amines often smell like ammonia.

Liquid amines often have a fishy odor.

Nitrogen bases (**Amines**) are stronger bases (better Nu:-) than oxygen bases.

Draw the structures of ammonia, methyl amine, and aniline.

The pK_a of each conjugate acid is 9.3, 10.6, and 4.6.

Which base is stronger, methyl amine or aniline?

Why is lemon juice used on fish?

Amines undergo the typical reactions of nucleophiles:

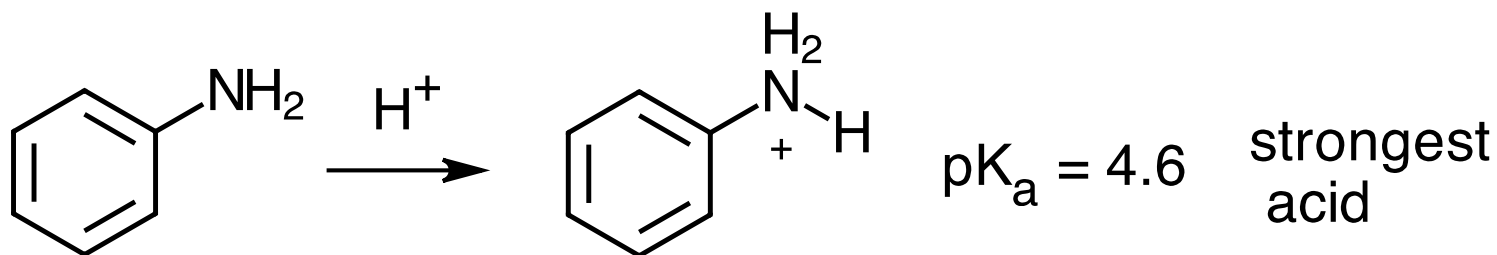
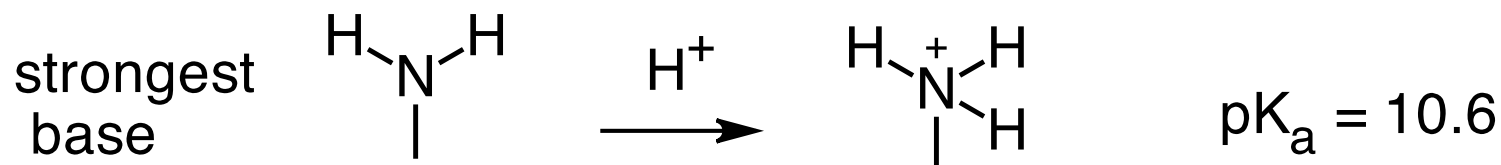
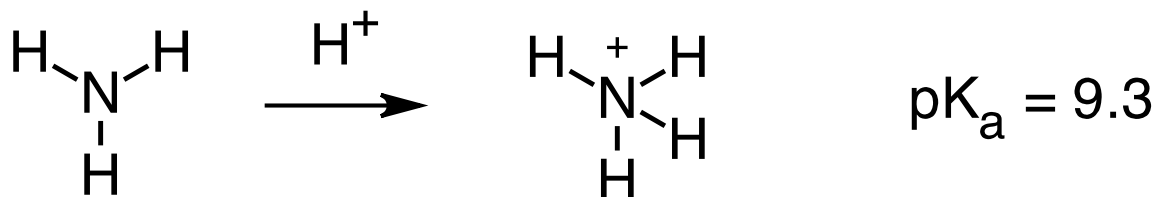
- Substitution
- Addition (or acyl substitution) at carbonyl carbon

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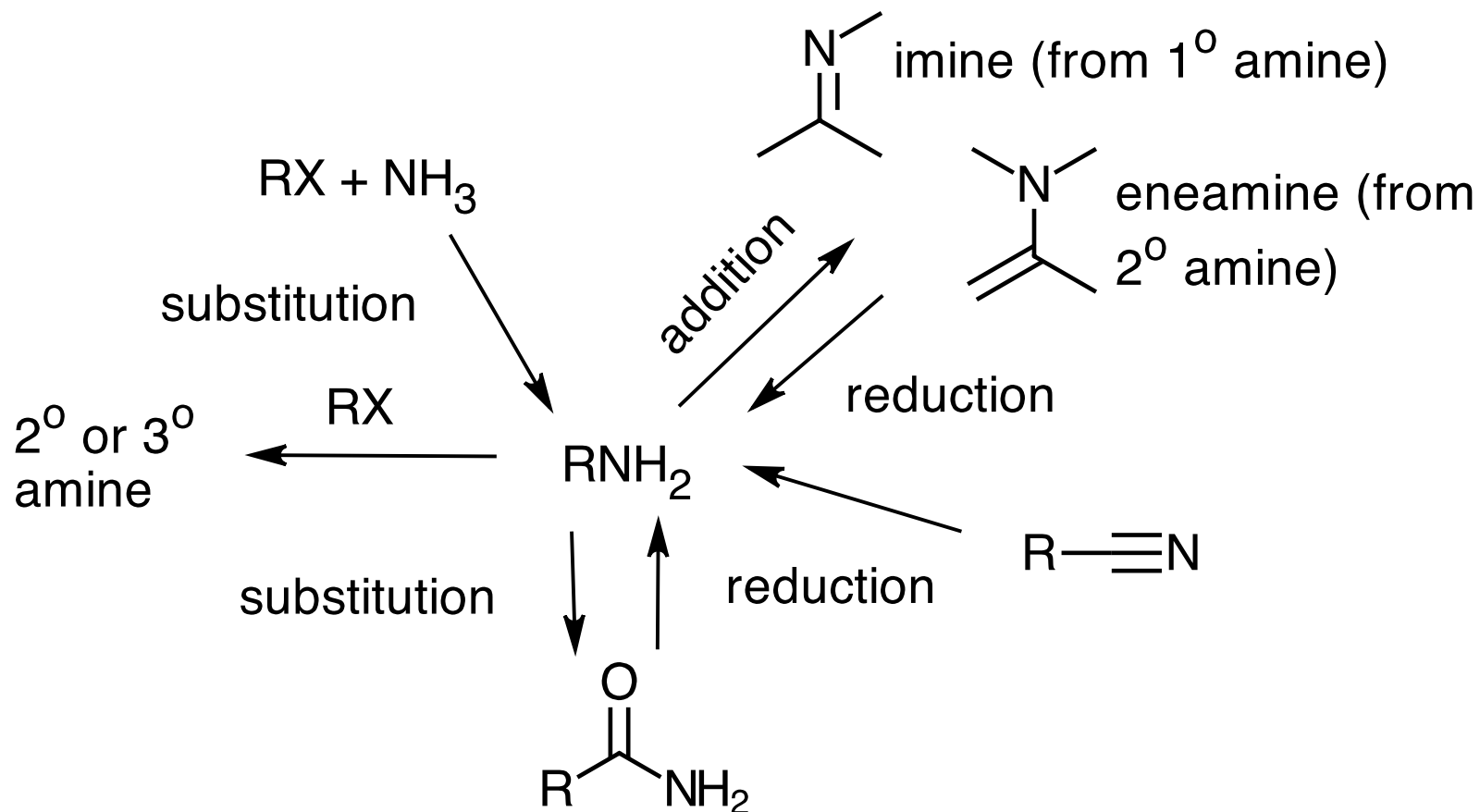
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Amine Roadmap

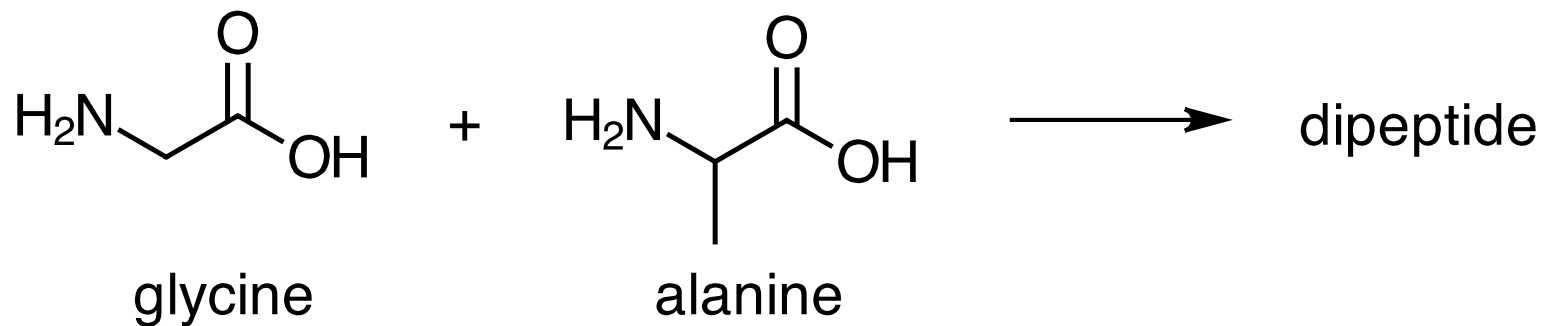
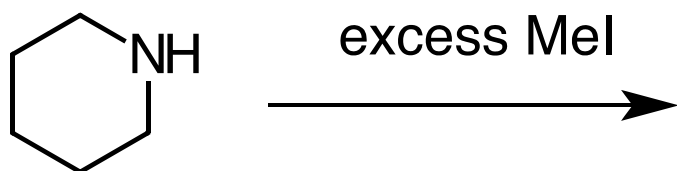
We've seen many of these reactions before!



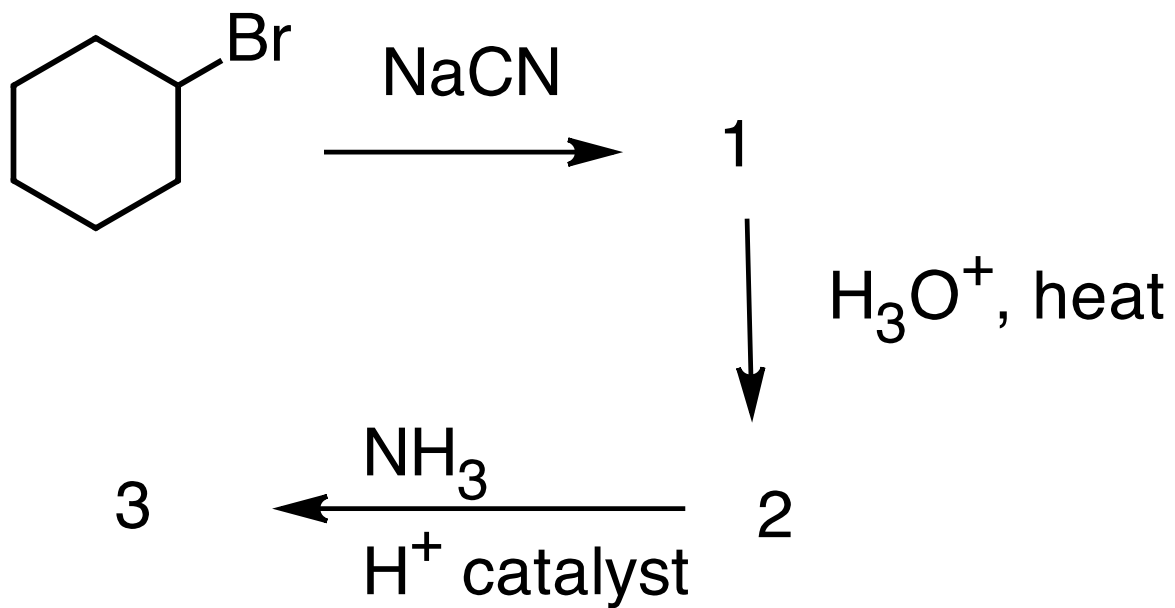
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- Substitution
- Addition or acyl substitution at carbonyl carbon

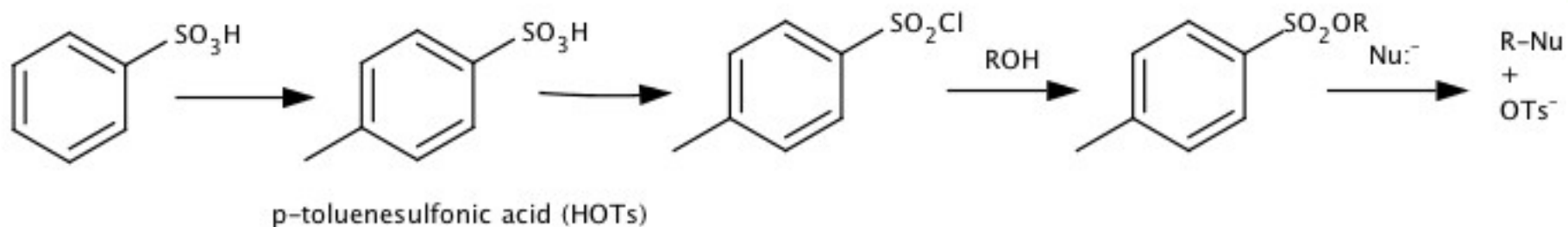
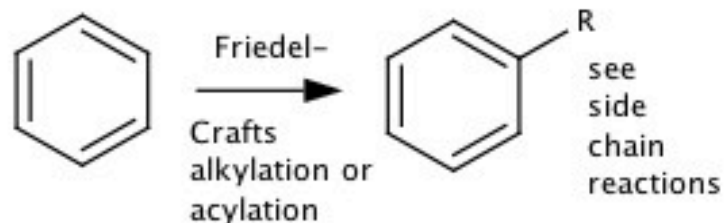
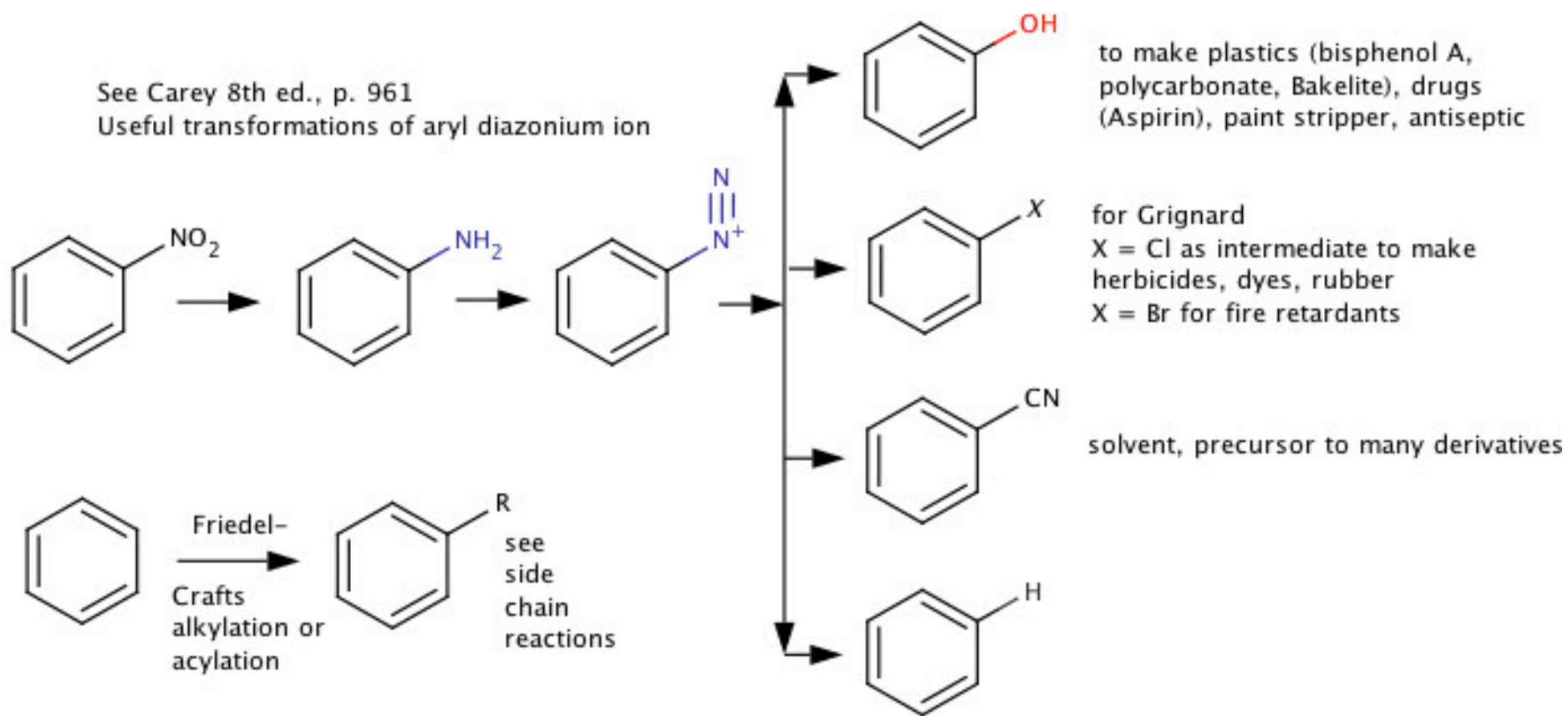
Predict the product:



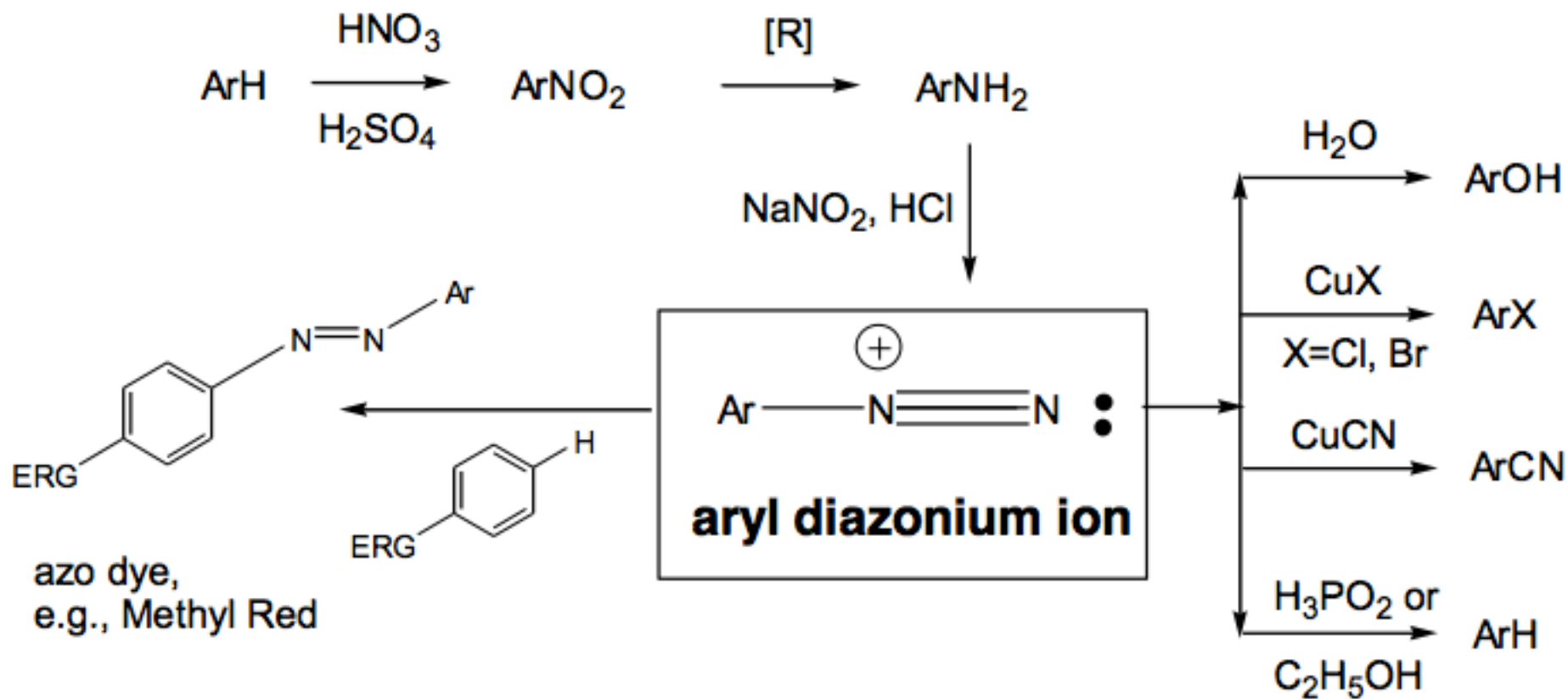
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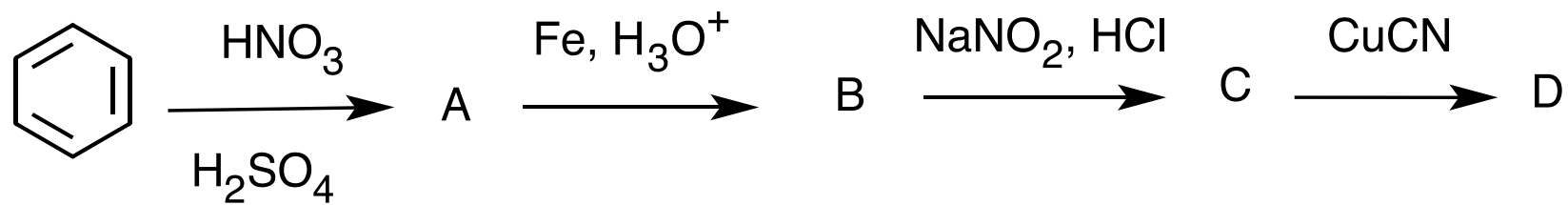
See Carey 8th ed., p. 961
Useful transformations of aryl diazonium ion



The Aryl Diazonium ion makes Substituted Arenes and Azo Dyes



Predict the product:



Propose an efficient synthesis

