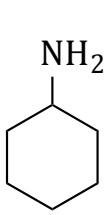
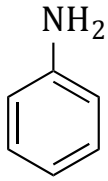
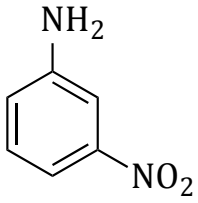
An Introduction to Amines:
Basicity of Nitrogen

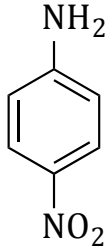
What is an **amine**? Show some examples of amines.

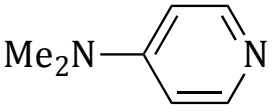
What factors determine the **basicity** of an amine? Rank the following molecules in order of decreasing basicity (1 is the most basic), and explain your reasoning.

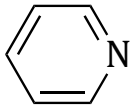


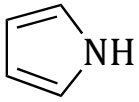












Reading: Section 23.5

S_N2 Reactions of Ammonia and Amines

What happens if you combine ammonia with ethyl bromide? Show the mechanism and product(s) of this reaction.

Reading: Section 23.7

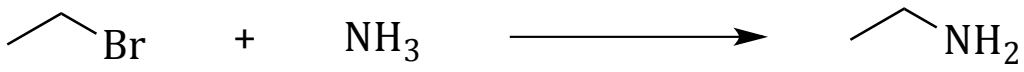
Reactions of Amines with Carbonyl Compounds

You already know some reactions of amines. What reactions do you know in which amines react with carbonyl compounds?

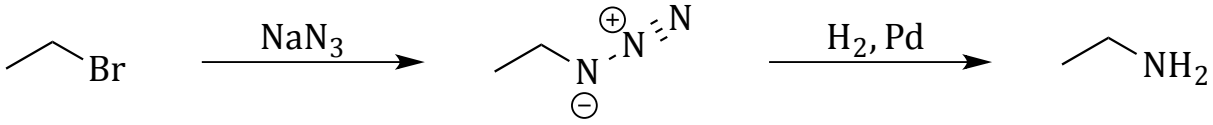
Reading: Section 23.7

Synthesis of 1° Amines

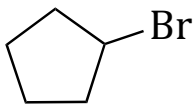
We **cannot** use the following S_N2 reaction to synthesize a primary amine. Why?

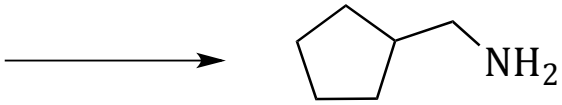


The following sequence of reactions *can* be used to synthesize primary amines through an S_N2 pathway. How does this work?



Primary amines can also be synthesized by the **reduction of nitriles**. Show how this process can be used to synthesize the following amine from bromocyclopentane:



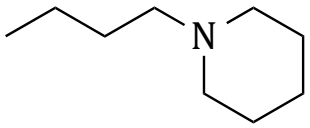


Reading: Section 23.11

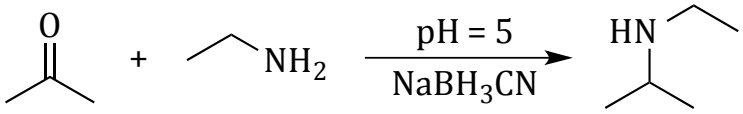
Synthesis of 2° & 3° Amines

Secondary and tertiary amines also cannot be synthesized by a direct S_N2 reaction. Why?

You already know one method for synthesizing 2° or 3° amines. What is that method, and how can it be used to synthesize the following amine?



Another very useful synthesis of 2° or 3° amines is **reductive amination**. Show the mechanism of this reaction. How can it be used in synthesis?



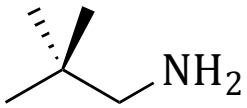
Reading: Section 23.7

Amines from Conjugate Addition

You also know two ways to synthesize amines that involve conjugate addition to an α,β-unsaturated carbonyl compound. What are those methods?

Amines from Nitrile Enolates

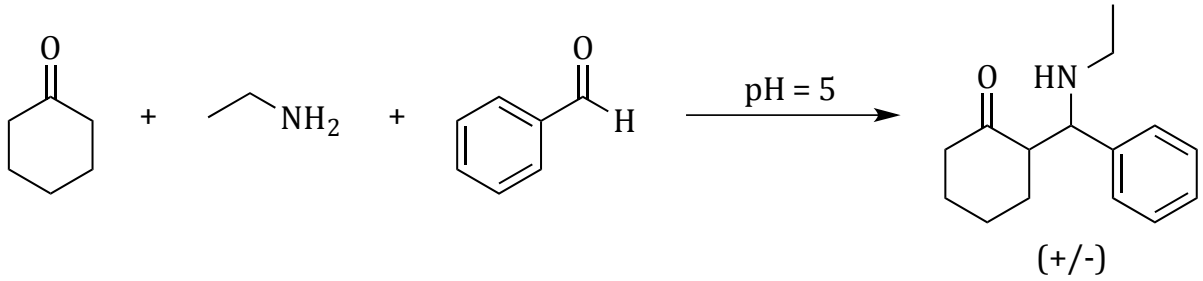
The following amine is fairly challenging to synthesize. Why?



How can that amine be synthesized by a route that involves a **nitrile enolate**?

The Mannich Reaction

The reaction between an enol and an iminium ion is called the **Mannich reaction**; provide a mechanism for this transformation:

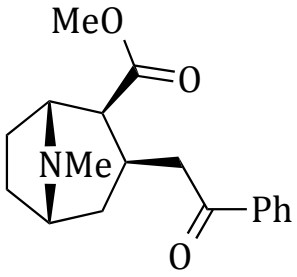


(+/-)

How can the Mannich reaction be used in synthesis?

Making Cocaine:
Part 1 – The Strategy

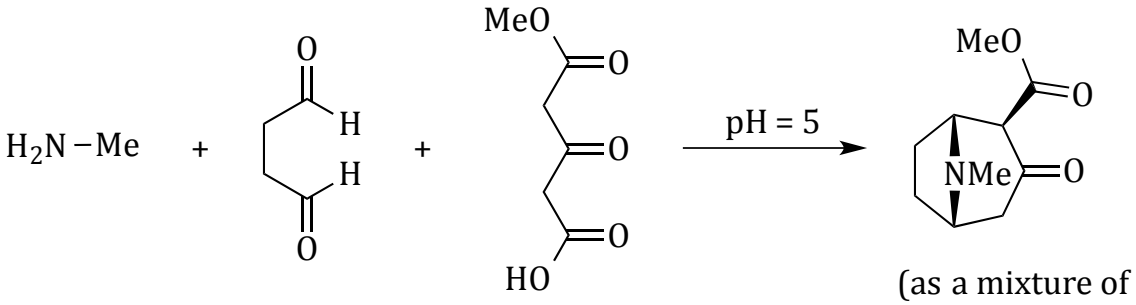
Here is the structure of the natural product **cocaine**. Let's do some retrosynthetic analysis:



How could the Mannich reaction be used in synthesis of cocaine?

Making Cocaine:
Part 2 – The Details

Show the detailed mechanism of the "Mannich synthesis" of this precursor to cocaine:



(as a mixture of stereoisomers)