20.9: Nitriles
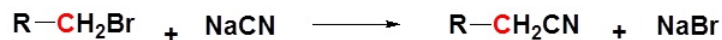
Synthesis of Nitriles

Nitriles are formed by an S_N2 reaction between a bromide and sodium cyanide

$$R-CH_2Br \; + \; NaCN \longrightarrow R-CH_2CN \; + \; NaBr$$

Reactivity of Nitriles

The carbon in a nitrile is electrophilic because a resonance structure can be drawn which places a positive charge on it. Because of this the triple bond of a nitrile accepts a nucleophile in a manner similar to a carbonyl.

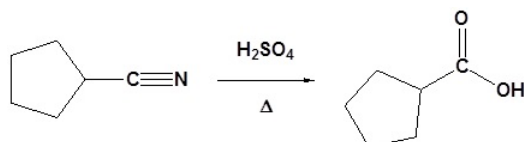**Nitrile**   **Carbonyl**
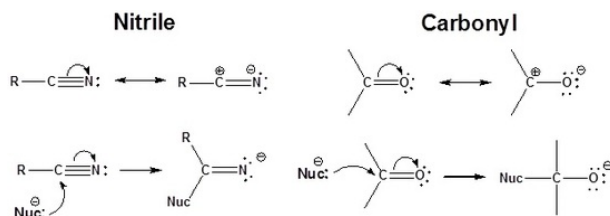
Hydrolysis of Nitriles

Nitriles can be converted to carboxylic acid with heating in sulfuric acid. During the reaction an amide intermediate is formed.
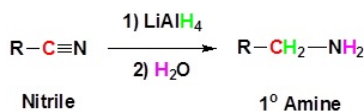
General Reaction

$$R-C\equiv N \xrightarrow[\Delta]{H_2SO_4} \underset{\text{Carboxylic Acid}}{R-\overset{\overset{\textstyle O}{\|}}{C}-OH}$$
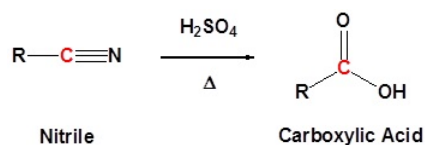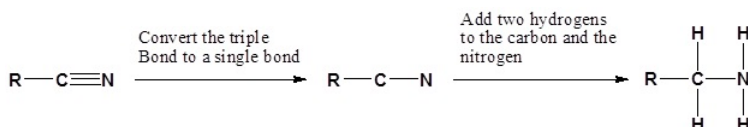
Nitrile

Example

Reduction of Nitriles

Nitriles can be converted to 1° amines by reaction with $LiAlH_4$. During this reaction the hydride nucleophile attacks the electrophilic carbon in the nitrile to form an imine anion. Once stabilized by a Lewis acid-base complexation the imine salt can accept a second hydride to form a dianion. The dianion can then be converted to an amine by addition of water.
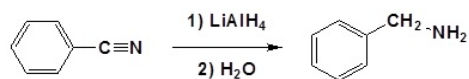
General Reaction

$$\underset{\text{Nitrile}}{R-C\equiv N} \xrightarrow[\text{2) } H_2O]{\text{1) } LiAlH_4} \underset{\text{1° Amine}}{R-CH_2-NH_2}$$

Going from reactants to products simplified

$$R-C\equiv N \xrightarrow{\substack{\text{Convert the triple} \\ \text{Bond to a single bond}}} R-C-N \xrightarrow{\substack{\text{Add two hydrogens} \\ \text{to the carbon and the} \\ \text{nitrogen}}} R-\overset{\overset{\textstyle H}{|}}{\underset{\underset{\textstyle H}{|}}{C}}-\overset{\overset{\textstyle H}{|}}{\underset{\underset{\textstyle H}{|}}{N}}$$

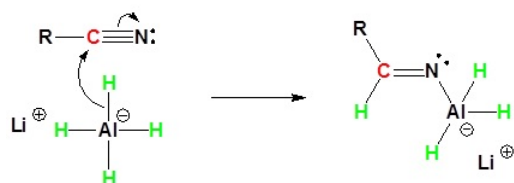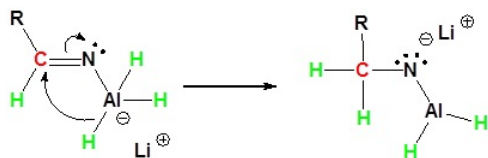## Example
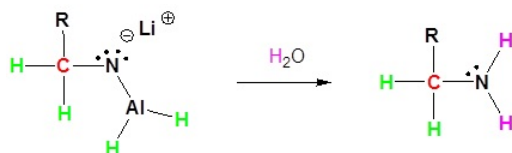

Mechanism

1) Nucleophilic Attack by the Hydride

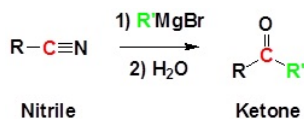

2) Second nucleophilic attack by the hydride.

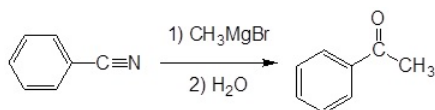3) Protonation by addition of water to give an amine

Addition of Grignard Reagents

Grignard reagents can attack the electophillic carbon in a nitrile to form an imine salt. This salt can then be hydrolyzed to become a ketone.
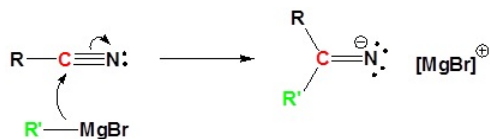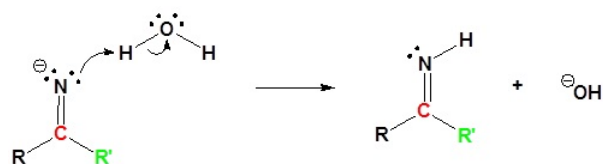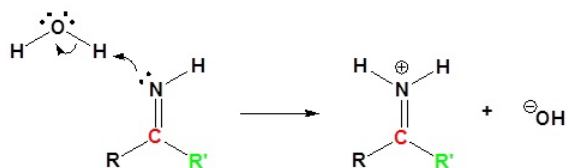
General Reaction

Example

Mechanism

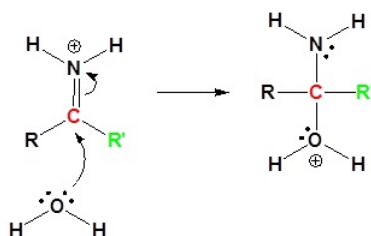1) Nucleophilic Attack by the Grignard Reagent
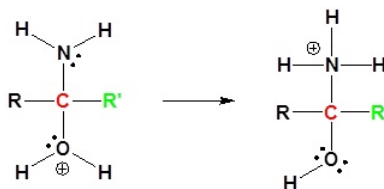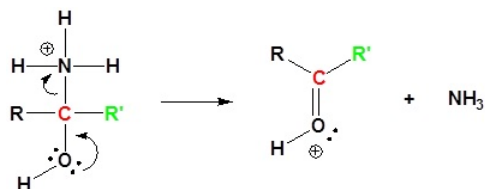

2) Protonation

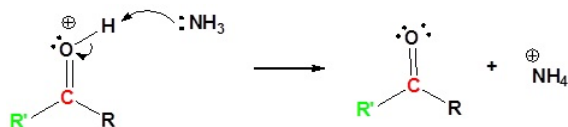3) Protonation

4) Nucleophilic attack by water

5) Proton Transfer

6) Leaving group removal

7) Deprotonation

Contributors

- Prof. Steven Farmer (Sonoma State University)