



Chapter 20: Carboxylic Acids and Nitriles

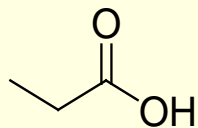


The Importance of Carboxylic Acids (RCO_2H)

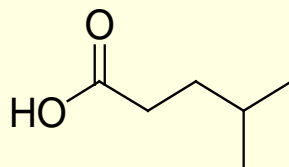
- Starting materials for *acyl derivatives* (esters, amides, and acid chlorides)
- Abundant in nature from oxidation of aldehydes and alcohols in metabolism
 - Acetic acid, $\text{CH}_3\text{CO}_2\text{H}$, - vinegar
 - Butanoic acid, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$ (rancid butter)
 - Long-chain aliphatic acids from the breakdown of fats

Naming Carboxylic Acids and Nitriles

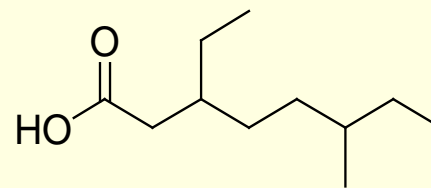
- Carboxylic Acids, RCO_2H
- If derived from open-chain alkanes, replace the terminal *-e* of the alkane name with *-oic acid*
- The carboxyl carbon atom is always the first carbon



Propionic Acid



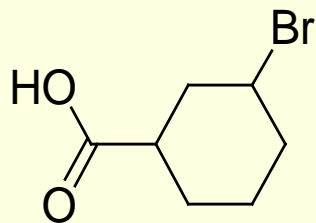
4-methyl-pentanoic acid



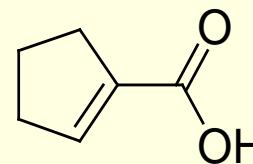
3-ethyl-6-methyl-octanoic acid

Alternative Names

- Compounds with $\text{—CO}_2\text{H}$ bonded to a ring are named using the suffix *-carboxylic acid*
- The CO_2H carbon is not itself numbered in this system



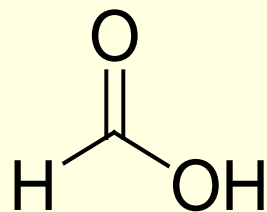
3-bromo-cyclohexane carboxylic acid



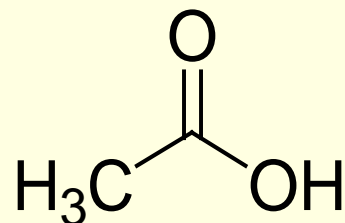
1-cyclopentene carboxylic acid

Common Acids

- Formic acid (HCOOH)
- Acetic acid (CH₃COOH)



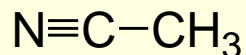
Formic Acid



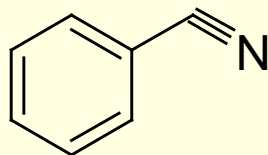
Acetic Acid

Nitriles, $\text{RC}\equiv\text{N}$

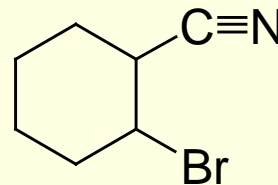
- Closely related to carboxylic acids named by adding *-nitrile* as a suffix to the alkane name, with the nitrile carbon numbered C1
- Complex nitriles are named as derivatives of carboxylic acids.
 - Replace *-ic acid* or *-oic acid* ending with *-onitrile*



Acetonitrile



Benzonitrile



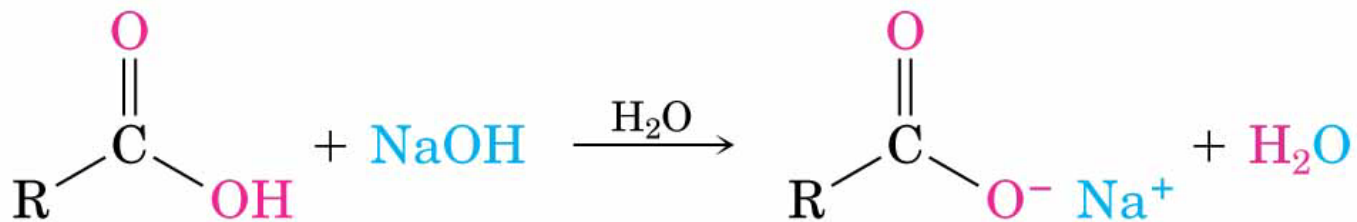
2-Bromo-cyclohexanecarbonitrile

Structure and Physical Properties of Carboxylic Acids

- Carboxyl carbon sp^2 hybridized: carboxylic acid groups are planar with C–C=O and O=C–O bond angles of approximately 120°
- Carboxylic acids form hydrogen bonds, existing as cyclic dimers held together by two hydrogen bonds
- Strong hydrogen bonding causes much higher boiling points than the corresponding alcohols

Dissociation of Carboxylic Acids

- Carboxylic acids are proton donors toward weak and strong bases, producing metal carboxylate salts, $\text{RCO}_2^- + \text{M}$
- Carboxylic acids with more than six carbons are only slightly soluble in water, but their conjugate base salts are water-soluble



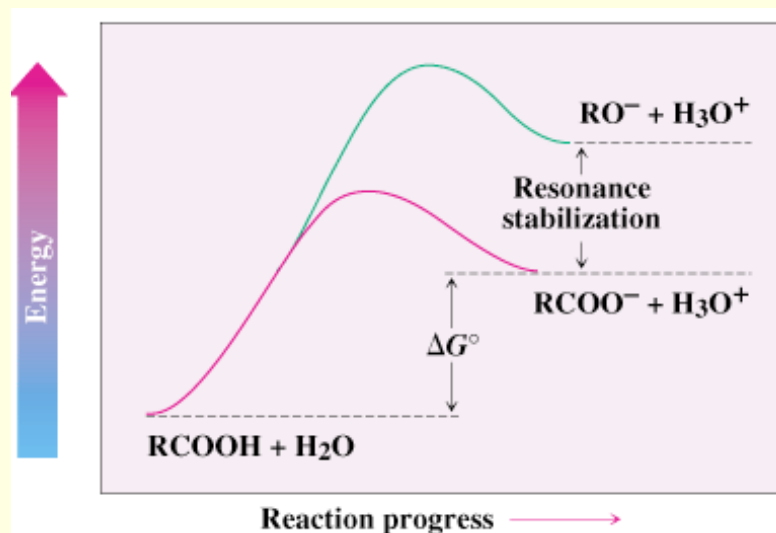
**A carboxylic acid
(water-insoluble)**

**A carboxylic acid salt
(water-soluble)**

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Acidity Compared to Alcohols

- Carboxylic acids are better proton donors than are alcohols (The pK_a of ethanol is ~ 16 , compared to ~ 5 for acetic acid)
- In an alkoxide ion, the negative charge is localized on oxygen while in a carboxylate ion the negative charge is delocalized over two equivalent oxygen atoms, giving resonance stabilization




Substituent Effects on Acidity

Electronegative substituents promote formation of the carboxylate ion

TABLE 20.4 Acidity of Some Carboxylic Acids

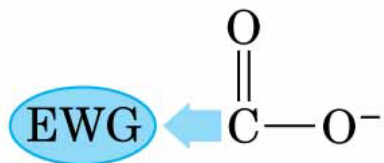
Structure	K_a	pK_a
F_3CCO_2H	0.59	0.23
FCH_2CO_2H	2.6×10^{-3}	2.59
$ClCH_2CO_2H$	1.4×10^{-3}	2.85
$BrCH_2CO_2H$	2.1×10^{-3}	2.68
ICH_2CO_2H	7.5×10^{-4}	3.12
HCO_2H	1.77×10^{-4}	3.75
$HOCH_2CO_2H$	1.5×10^{-4}	3.83
$C_6H_5CO_2H$	6.46×10^{-5}	4.19
$H_2C=CHCO_2H$	5.6×10^{-5}	4.25
CH_3CO_2H	1.76×10^{-5}	4.75
$CH_3CH_2CO_2H$	1.34×10^{-5}	4.87
CH_3CH_2OH (ethanol) ^a	(10^{-16})	(16)

^aValue for ethanol is shown for reference.



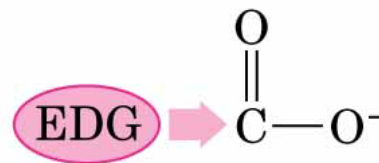
Substituent Effects

- An electron-withdrawing group will drive the ionization equilibrium toward dissociation, increasing acidity
- An electron-*donating* group destabilizes the carboxylate anion and decreases acidity



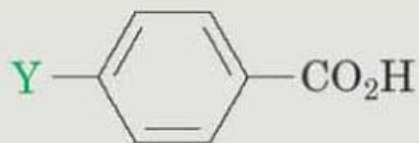
**Electron-withdrawing group
stabilizes carboxylate
and strengthens acid**

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**Electron-donating group
destabilizes carboxylate
and weakens acid**

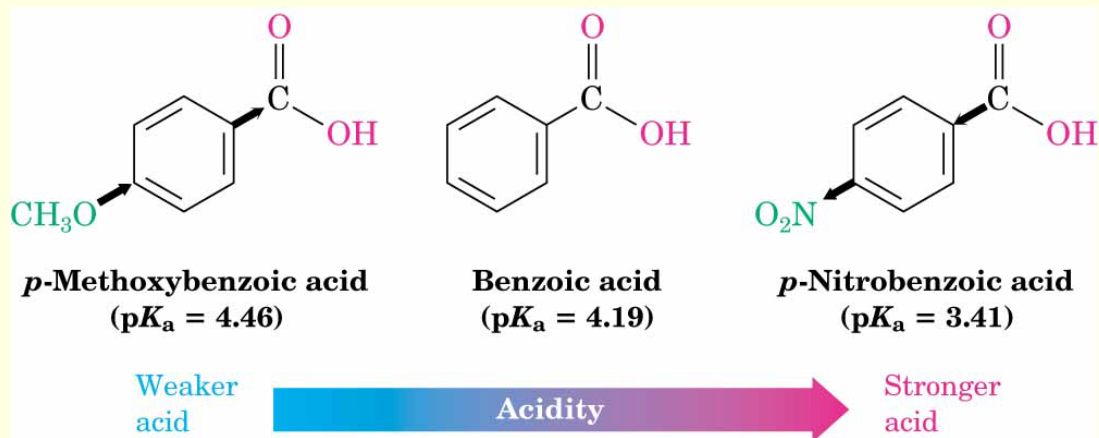
Substituent Effects in Substituted Benzoic Acids



	Y	K_a	pK_a		
<p>Weaker acid</p> <p>Stronger acid</p>	—OH	3.3×10^{-5}	4.48	} Activating groups	
	—OCH ₃	3.5×10^{-5}	4.46		
	—CH ₃	4.3×10^{-5}	4.34		
		—H	6.46×10^{-5}	4.19	
		—Cl	1.0×10^{-4}	4.0	} Deactivating groups
		—Br	1.1×10^{-4}	3.96	
		—CHO	1.8×10^{-4}	3.75	
		—CN	2.8×10^{-4}	3.55	
		—NO ₂	3.9×10^{-4}	3.41	

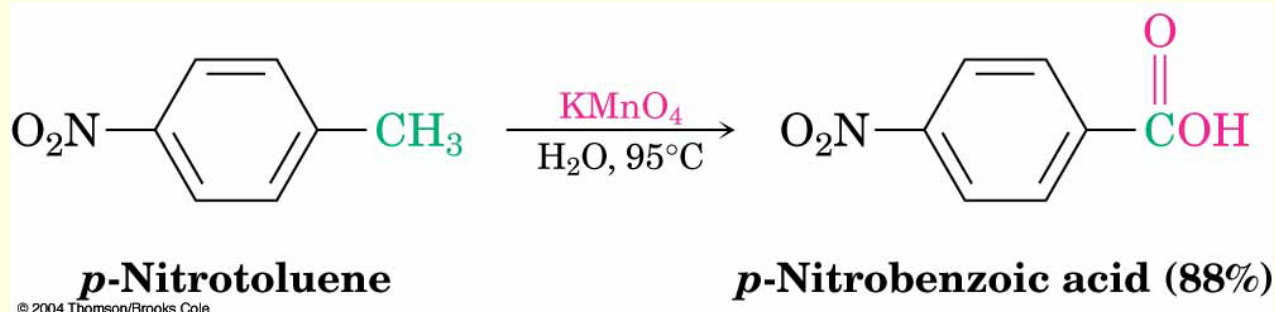
Aromatic Substituent Effects

- An electron-withdrawing group ($-\text{NO}_2$) increases acidity by stabilizing the carboxylate anion, and an electron-donating (activating) group (OCH_3) decreases acidity by destabilizing the carboxylate anion
- We can use relative pK_a 's as a calibration for effects on relative free energies of reactions with the same substituents



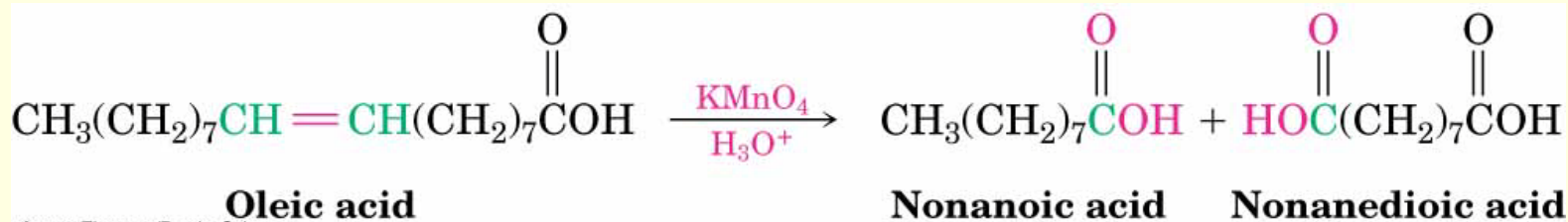
Preparation of Carboxylic Acids

- Oxidation of a substituted alkylbenzene with KMnO_4 or $\text{Na}_2\text{Cr}_2\text{O}_7$ gives a substituted benzoic acid (see Section 16.10)
- 1° and 2° alkyl groups can be oxidized, but tertiary groups are not



From Alkenes

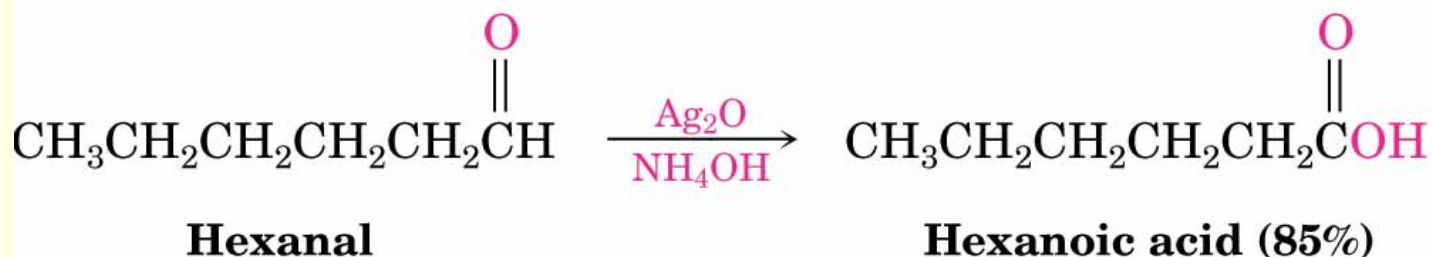
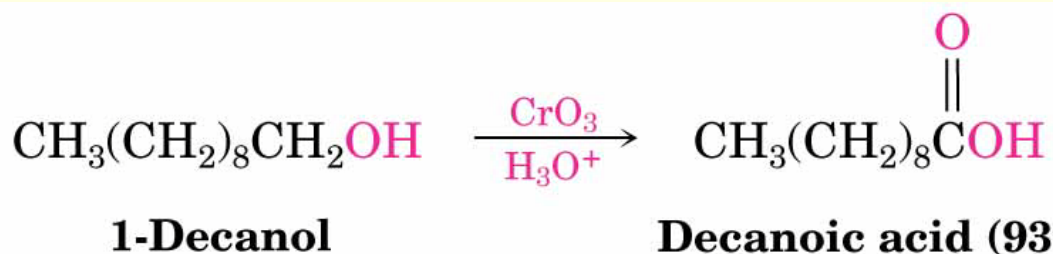
- Oxidative cleavage of an alkene with KMnO_4 gives a carboxylic acid if the alkene has at least one vinylic hydrogen (see Section 7.8)



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From Alcohols

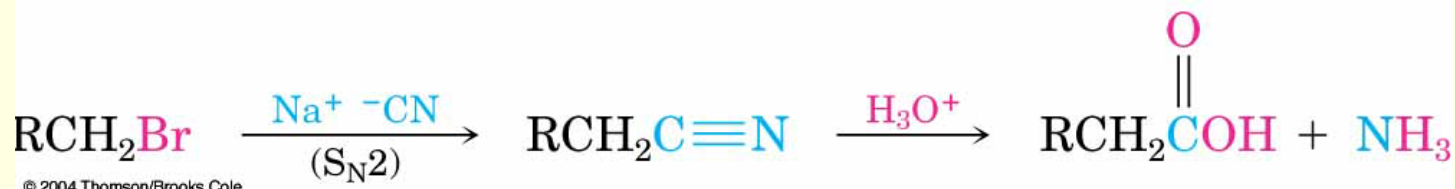
- Oxidation of a primary alcohol or an aldehyde with CrO_3 in aqueous acid



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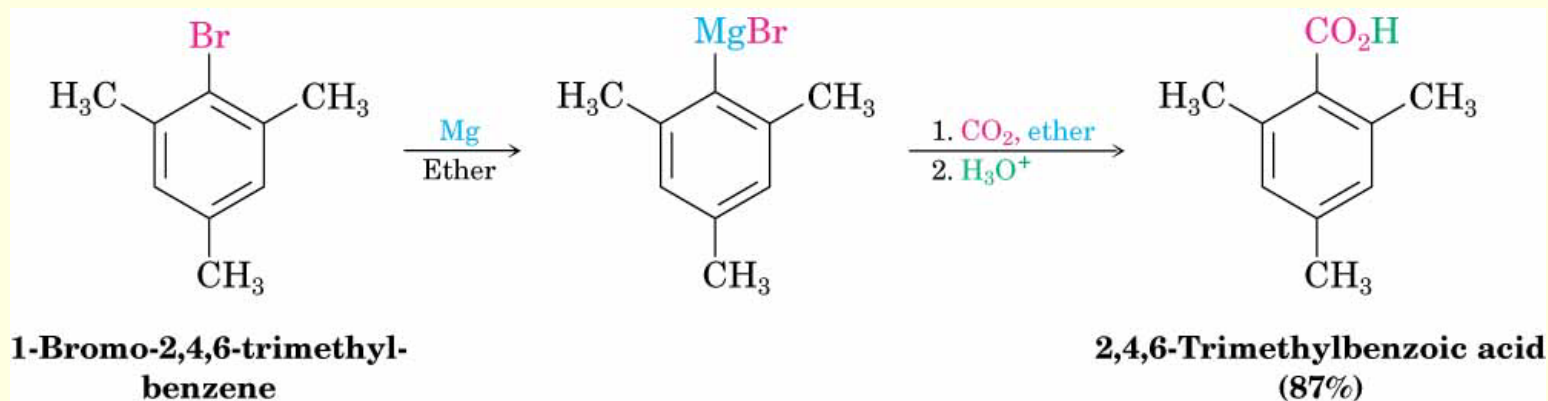
Hydrolysis of Nitriles

- Hot acid or base yields carboxylic acids
- Conversion of an alkyl halide to a nitrile (with cyanide ion) followed by hydrolysis produces a carboxylic acid with one more carbon ($\text{RBr} \rightarrow \text{RC}\equiv\text{N} \rightarrow \text{RCO}_2\text{H}$)
- Best with primary halides because elimination reactions occur with secondary or tertiary alkyl halides



Carboxylation of Grignard Reagents

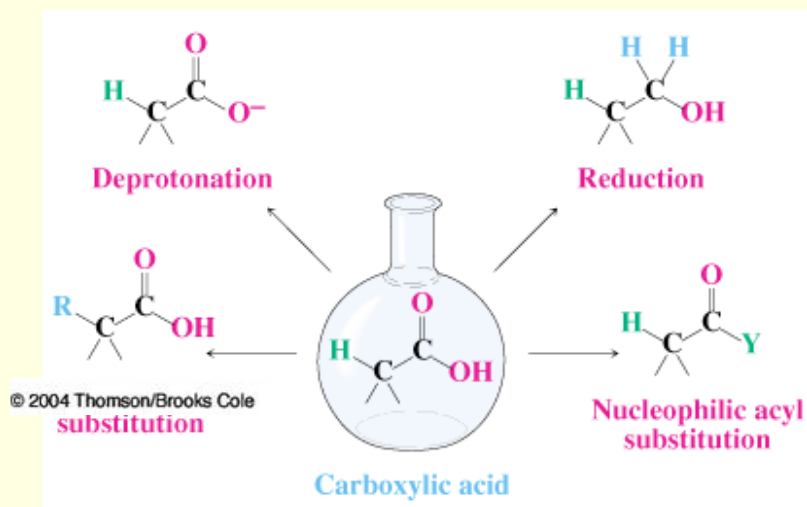
- Grignard reagents react with dry CO_2 to yield a metal carboxylate
- Limited to alkyl halides that can form Grignard reagents (see 17.6)



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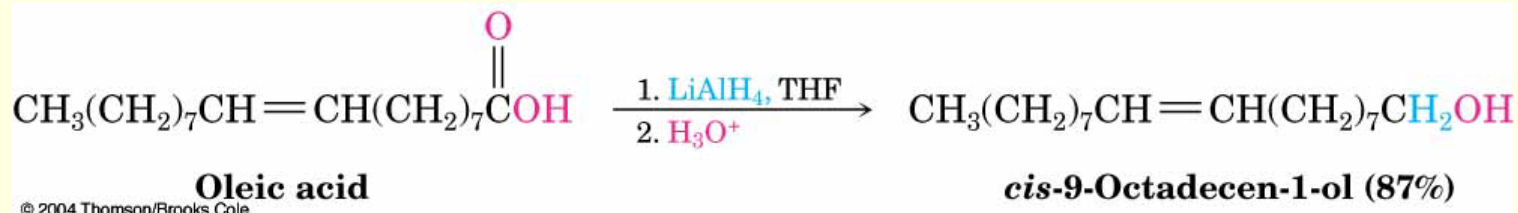
Reactions of Carboxylic Acids: An Overview

- Carboxylic acids transfer a proton to a base to give anions, which are good nucleophiles in S_N2 reactions
- Like ketones, carboxylic acids undergo addition of nucleophiles to the carbonyl group
- In addition, carboxylic acids undergo other reactions characteristic of neither alcohols nor ketones



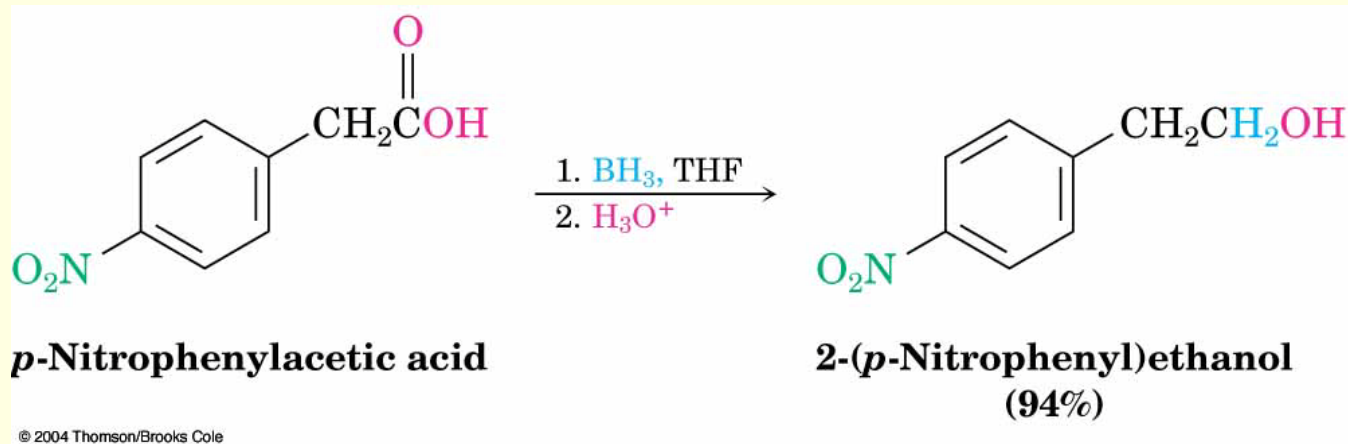
Reduction of Carboxylic Acids

- Reduced by LiAlH_4 to yield primary alcohols
- The reaction is difficult and often requires heating in tetrahydrofuran solvent to go to completion



Reduction with Borane

- Borane in tetrahydrofuran (BH_3/THF) converts carboxylic acids to primary alcohols selectively
- Preferable to LiAlH_4 because of its relative ease, safety, and specificity
- Borane reacts faster with COOH than it does with NO_2



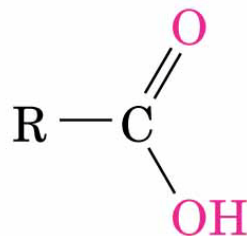
Chemistry of Nitriles

- Nitriles and carboxylic acids both have a carbon atom with three bonds to an electronegative atom, and both contain a π bond
- Both both are electrophiles



**A nitrile—three
bonds to nitrogen**

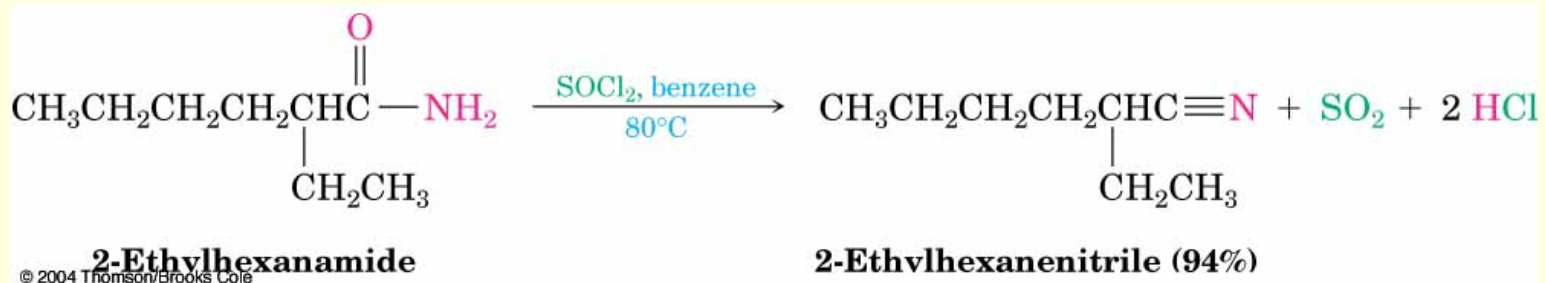
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**An acid—three
bonds to two oxygens**

Preparation of Nitriles by Dehydration

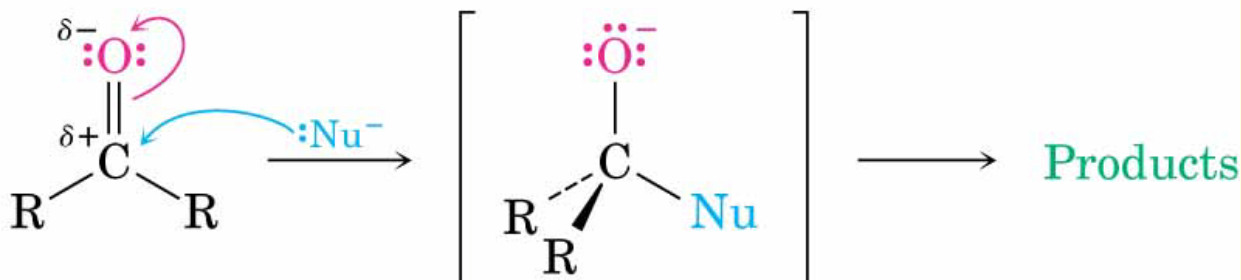
- Reaction of primary amides RCONH_2 with SOCl_2 or POCl_3 (or other dehydrating agents)
- Not limited by steric hindrance or side reactions (as is the reaction of alkyl halides with NaCN)



Reactions of Nitriles

- $\text{RC}\equiv\text{N}$ is strongly polarized and with an electrophilic carbon atom
- Attacked by nucleophiles to yield sp^2 -hybridized imine anions

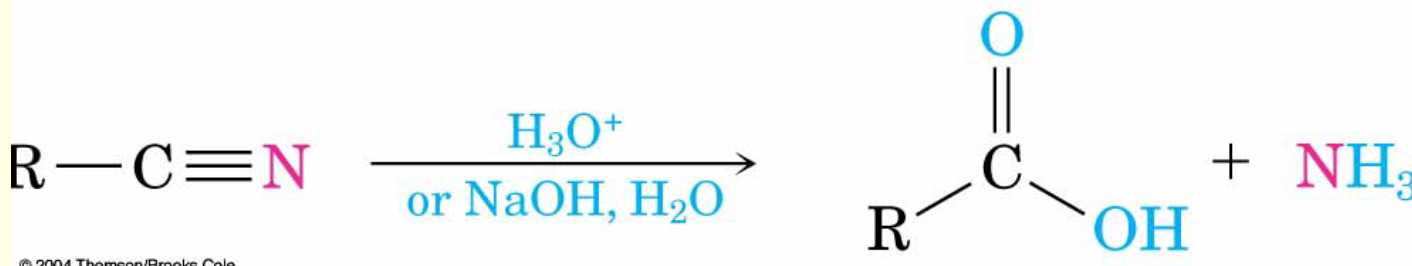
carbonyl
compound



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Hydrolysis: Conversion of Nitriles into Carboxylic Acids

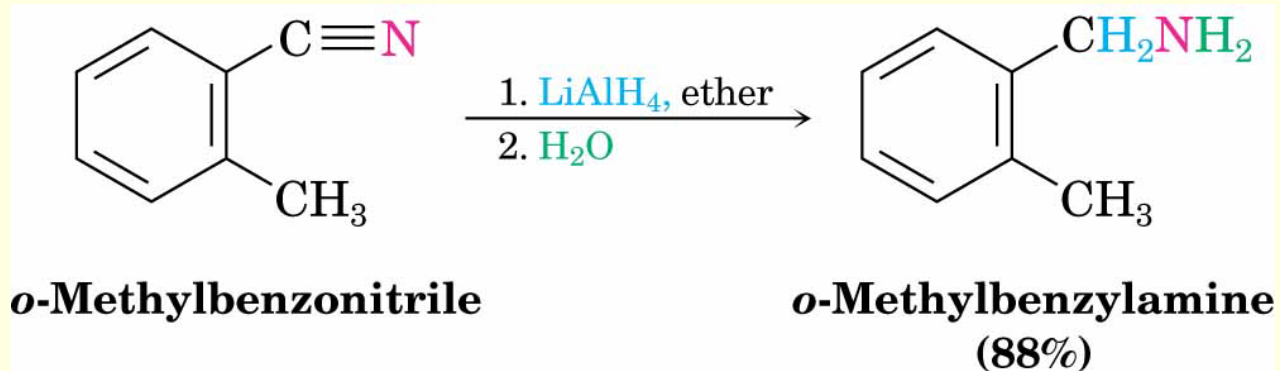
- Hydrolyzed in with acid or base catalysis to a carboxylic acid and ammonia or an amine



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Reduction: Conversion of Nitriles into Amines

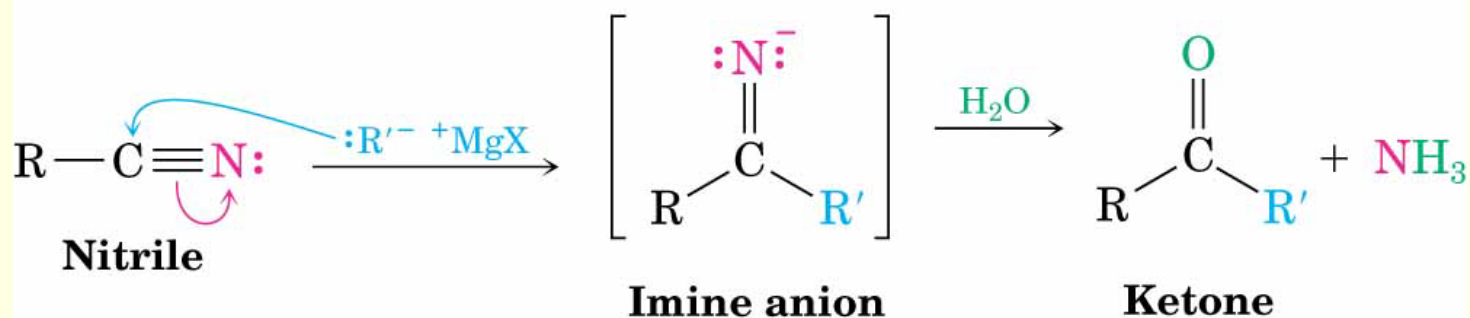
- Reduction of a nitrile with LiAlH_4 gives a primary amine



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Reaction of Nitriles with Organometallic Reagents

- Grignard reagents add to give an intermediate imine anion that is hydrolyzed by addition of water to yield a ketone



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