

CH 318 N

LECTURE 12

Textbook Assignment: Chapter 16

Homework (for credit): POW 6 posted

Today's Topics: Aldehydes & Ketones-Begin Carboxylic Acids

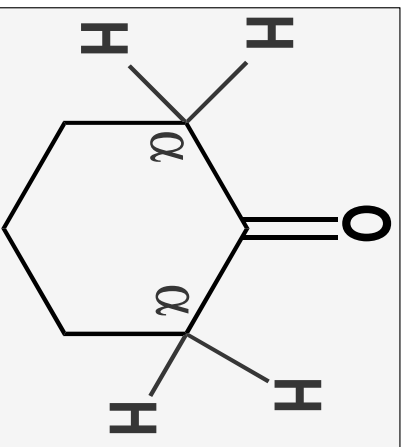
Notice & Announcements:

ORGANIC LECTURE SERIES

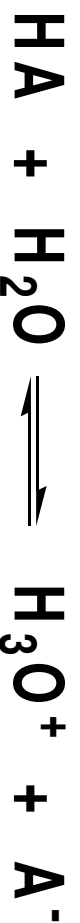
Aldehydes And Ketones

Acidity of α -Hydrogens

Hydrogens alpha to a carbonyl group are more acidic than hydrogens of other hydrocarbons (e.g. alkanes, alkenes, aromatic). The acidity is measured as K_a



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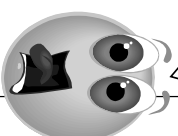
$$K_{\text{eq}} = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}][\text{H}_2\text{O}]}$$

Note: ℓ and s are not used in K

$$[\text{H}_2\text{O}] K_{\text{eq}} = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]}$$

$$K_a = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]}$$

Freshman
Flashback!!



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Acidity of α -Hydrogens

Hydrogens alpha to a carbonyl group are more acidic than hydrogens of alkanes, alkenes, and alkynes but less acidic than the hydroxyl hydrogen of alcohols

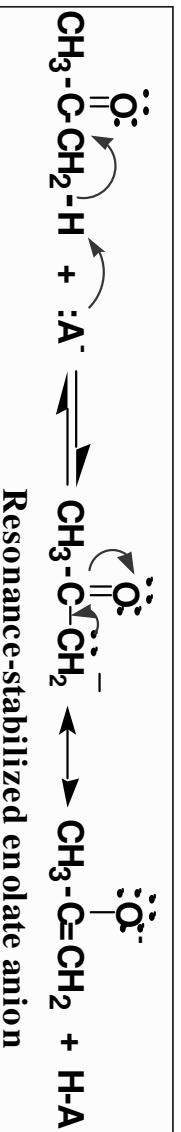
Type of Bond	pK _a
$\text{CH}_3\text{CH}_2\text{O-H}$	16
$\text{CH}_3\overset{\text{O}}{\parallel}\text{CCH}_2\text{-H}$	20
$\text{CH}_3\text{C}\equiv\text{C-H}$	25
$\text{CH}_2=\text{CH-H}$	44
$\text{CH}_3\text{CH}_2\text{-H}$	51

$$\text{pK}_a = -\log K_a$$

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α -Hydrogens are more acidic because the enolate anion is stabilized by:

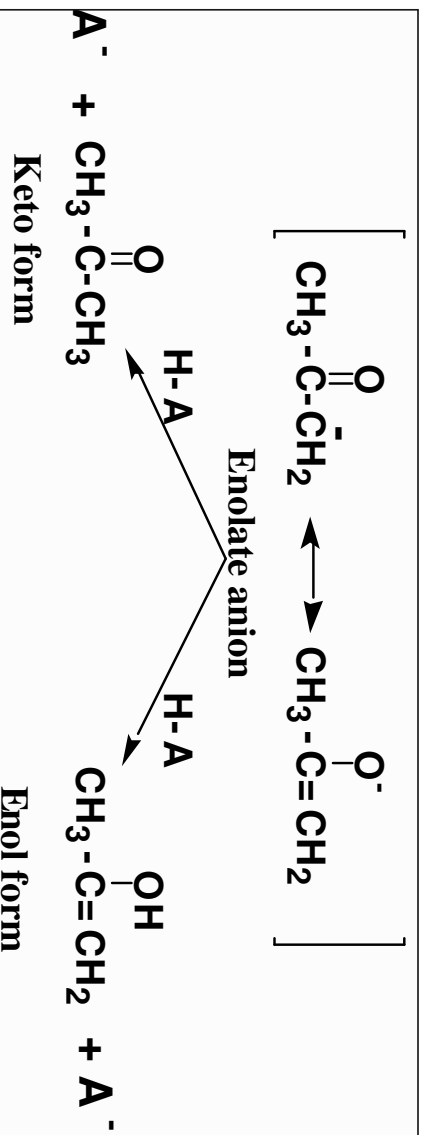
1. delocalization of its negative charge
2. the electron-withdrawing inductive effect of the adjacent electronegative oxygen



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Keto-Enol Tautomerism

– protonation of the enolate anion on oxygen gives the **enol form***; protonation on carbon gives the **keto form**



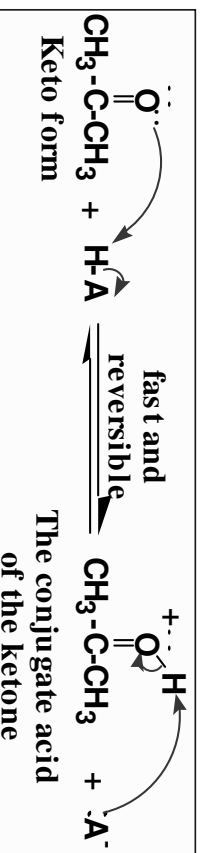
*Enol: made from 2 functional groups-alkene and alcohol

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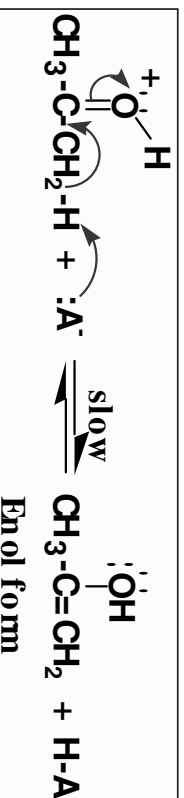
Keto-Enol Tautomerism

– **acid-catalyzed** equilibration of keto and enol tautomers occurs in two steps

Step 1: proton transfer to the carbonyl oxygen



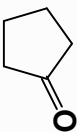
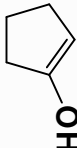
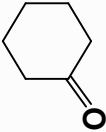
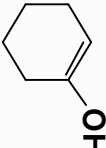
Step 2: proton transfer to the base A⁻



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Keto-Enol Tautomerism

Keto-enol equilibria for simple aldehydes and ketones lie far toward the keto form

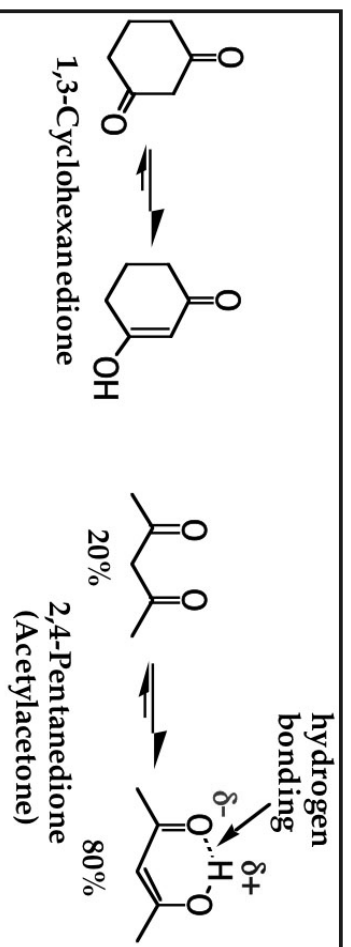
Keto form	Enol form	% Enol at Equilibrium
$\text{CH}_3\overset{\text{O}}{\parallel}\text{CH}$	$\text{CH}_2=\overset{\text{OH}}{\text{C}}\text{H}$	6×10^{-5}
$\text{CH}_3\overset{\text{O}}{\parallel}\text{CCH}_3$	$\text{CH}_3\overset{\text{OH}}{\text{C}}=\text{CH}_2$	6×10^{-7}
		1×10^{-6}
		4×10^{-5}

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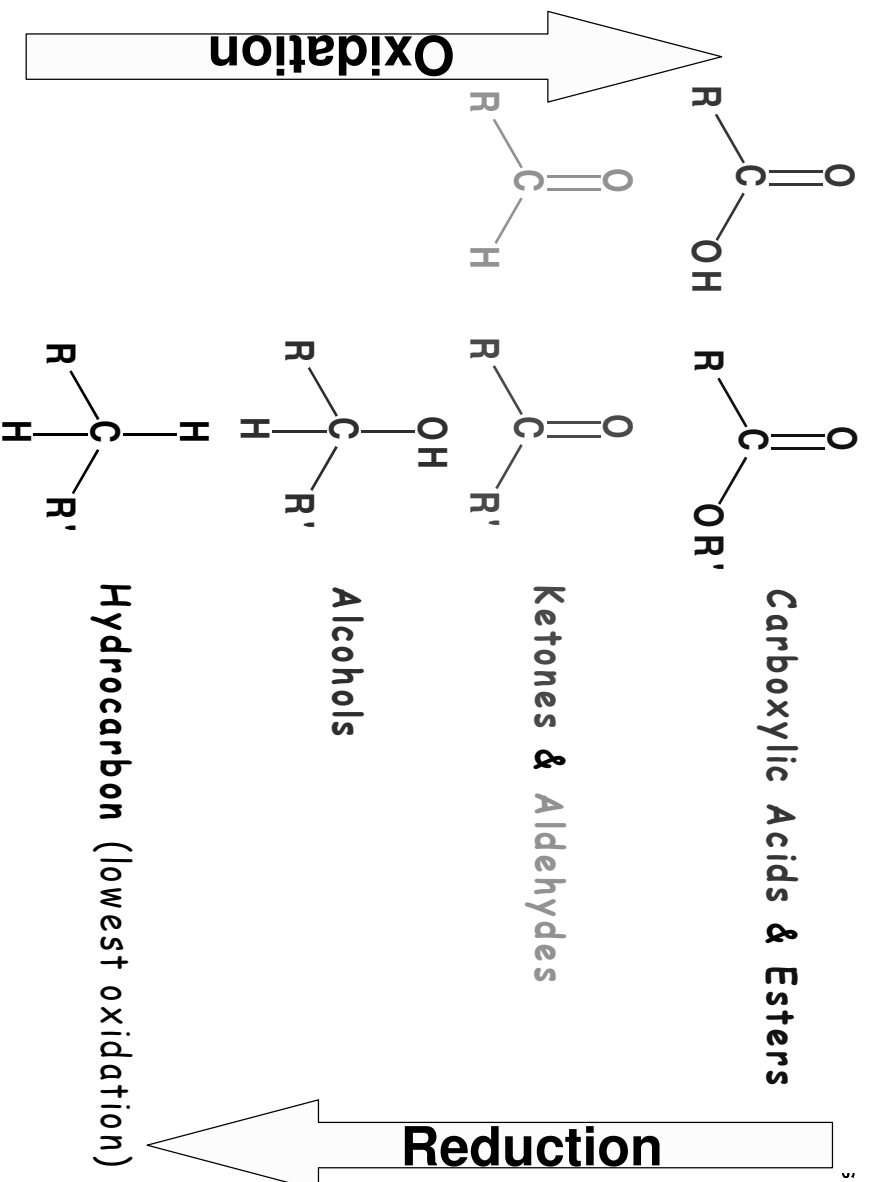
Keto-Enol Tautomerism

For certain types of molecules, however, the enol is the major form present at equilibrium

- for β -diketones, the enol is stabilized by conjugation of the pi system of the carbon-carbon double bond and the carbonyl group
- for acyclic β -diketones, the enol is further stabilized by hydrogen bonding (i.e. 1,3 diones)



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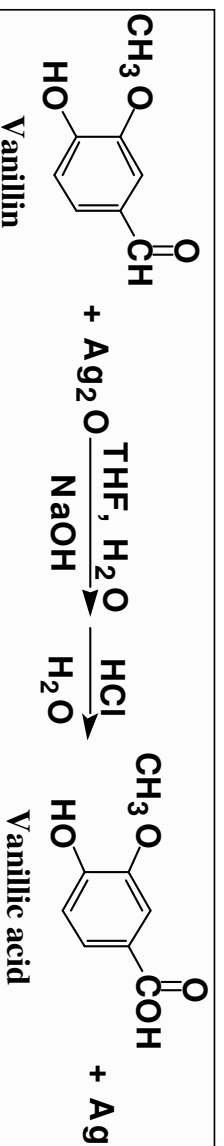


Oxidation of Aldehydes

- Aldehydes are oxidized to carboxylic acids by a variety of oxidizing agents, including H_2CrO_4



- They are also oxidized by $\text{Ag}(\text{I})$
 - in one method, a solution of the aldehyde in aqueous ethanol or THF is shaken with a slurry of silver oxide

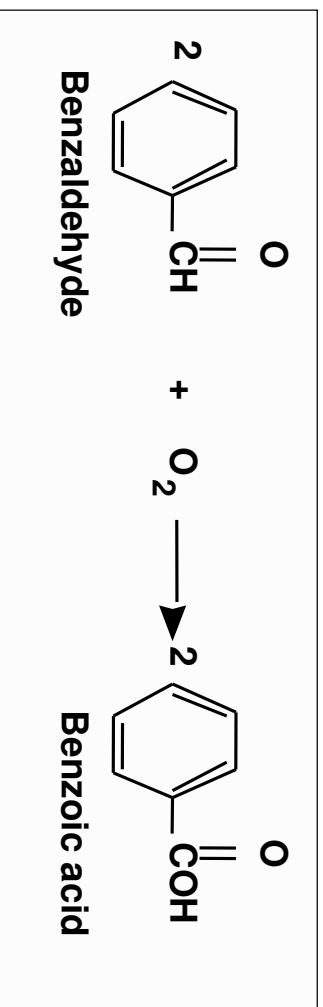


* See 10 for Jones reagent & PCC: pyridine $^+$ ClCrO $_3^-$

Oxidation of Aldehydes

Aldehydes are oxidized by O_2 in a radical chain reaction

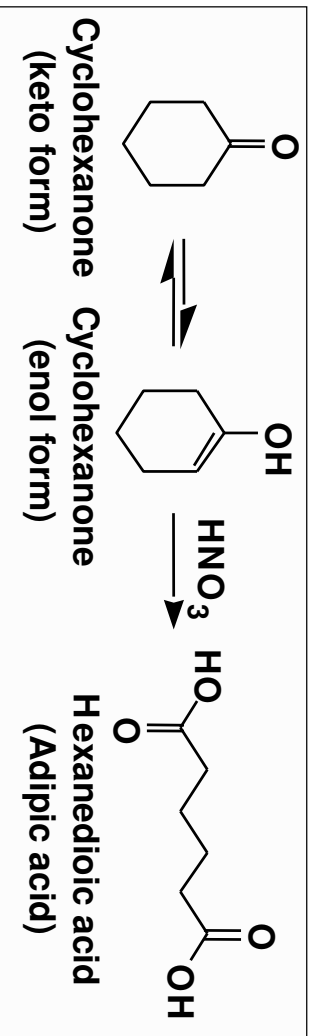
- liquid aldehydes are so sensitive to air that they must be stored under N_2



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Oxidation of Ketones

- ketones are **not** normally oxidized by chromic acid (H_2CrO_4)
- they are oxidized by powerful oxidants at high temperature and high concentrations of acid or base

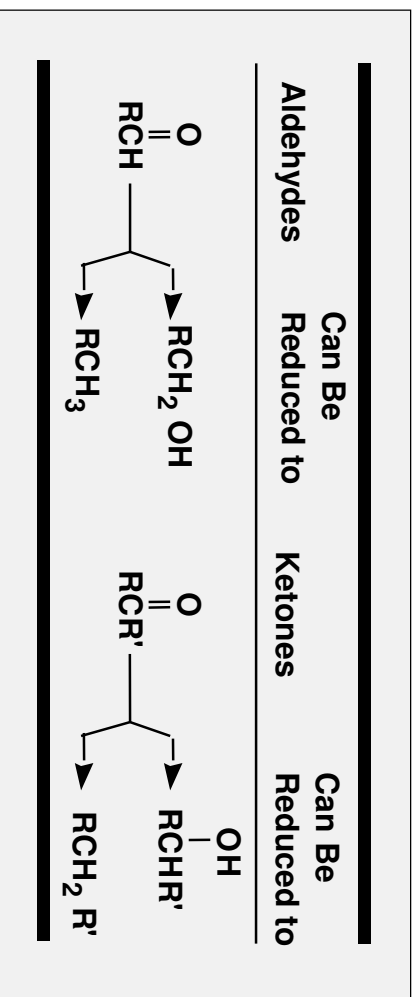


One of the starting materials for Nylon 6,6

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Reduction

- aldehydes can be reduced to 1° alcohols
- ketones can be reduced to 2° alcohols
- the C=O group of an aldehyde or ketone can be reduced to a -CH₂- group

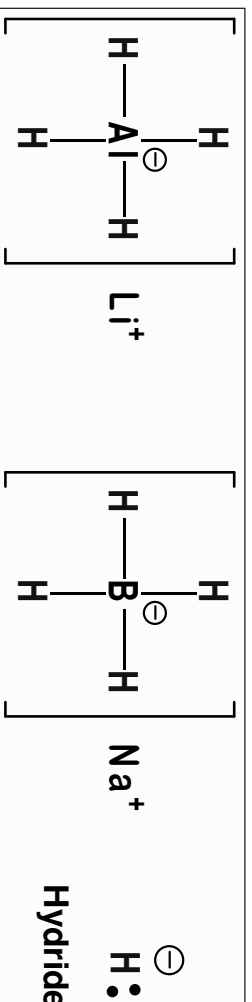


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Metal Hydride Reduction

The most common laboratory reagents for the reduction of aldehydes and ketones are NaBH₄ and LiAlH₄

- both reagents are sources of hydride ion, H:⁻ a very powerful nucleophile

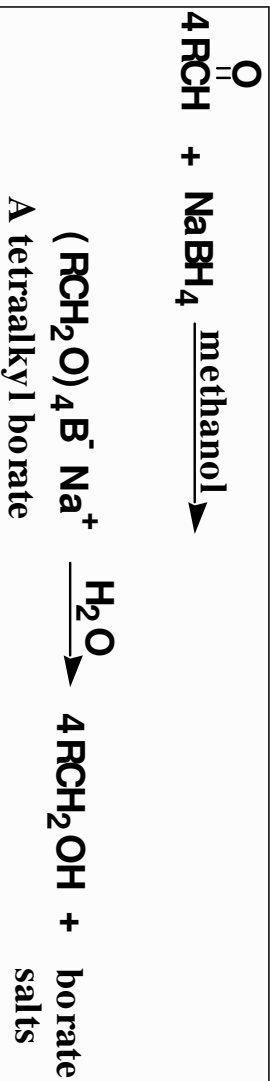


Lithium Aluminum Hydride Sodium Borohydride
LAH NaBH₄

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Sodium Borohydride Reduction

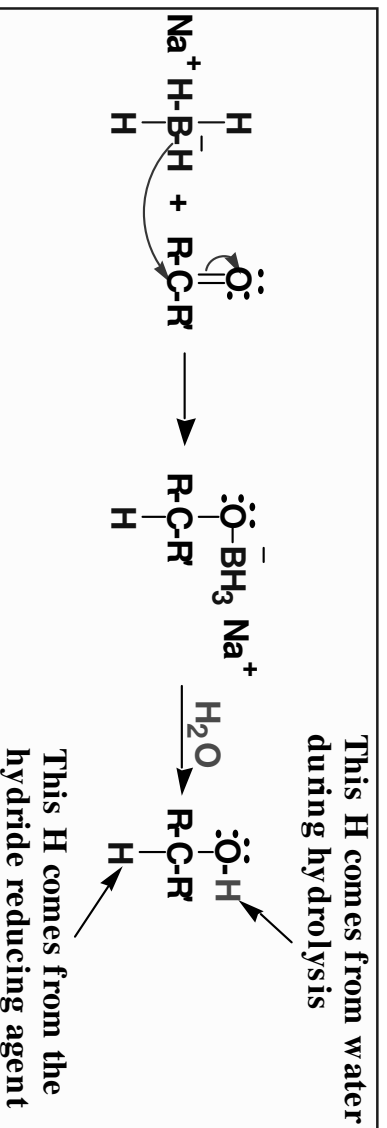
- reductions with NaBH_4 are most commonly carried out in aqueous methanol, in pure methanol, or in ethanol
- one mole of NaBH_4 reduces four moles of aldehyde or ketone



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Sodium Borohydride Reduction

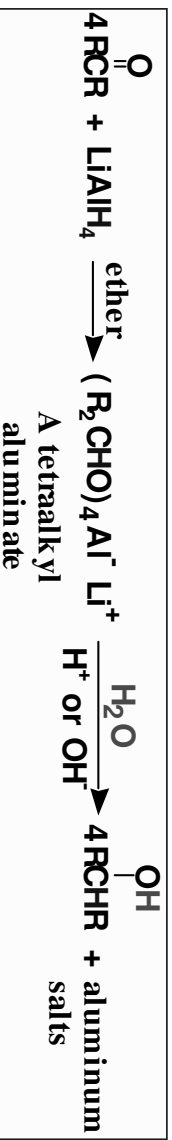
- The key step in metal hydride reduction is transfer of a hydride ion to the $\text{C}=\text{O}$ group to form a tetrahedral carbonyl addition compound



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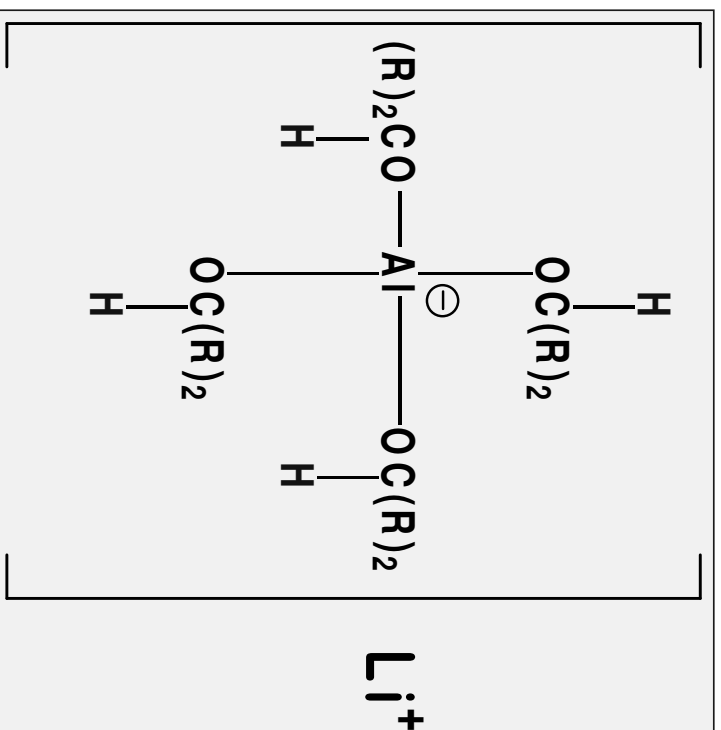
LAH Reduction

- unlike NaBH_4 , LiAlH_4 reacts violently with water, methanol, and other protic solvents
- reductions using it are carried out in dry (anhydrous) diethyl ether or tetrahydrofuran (THF)



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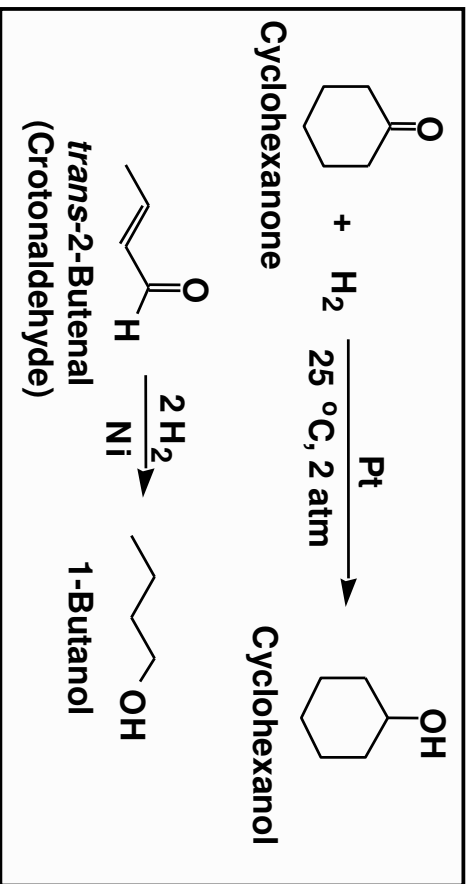
Lithium tetra-alkyl aluminate



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Catalytic Reduction

- Catalytic reductions are generally carried out at from 25 ° to 100 °C and 1 to 5 atm H₂

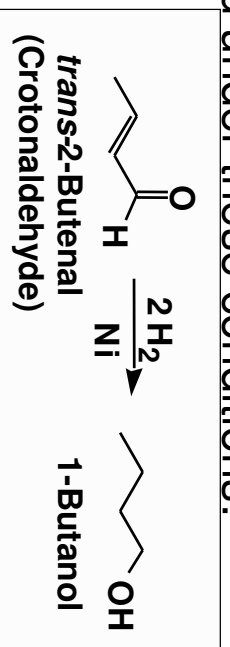


Note: Both the olefin and the carbonyl are reduced

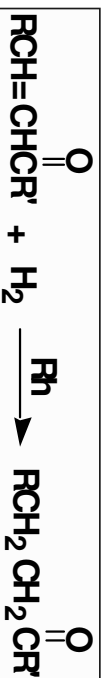
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Catalytic Reduction

- A carbon-carbon double bond may also be reduced under these conditions:



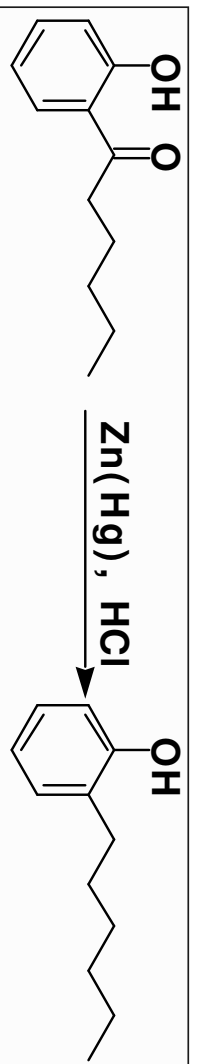
- by careful choice of experimental conditions, it is often possible to selectively reduce a carbon-carbon double in the presence of an aldehyde or ketone



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Clemmensen Reduction

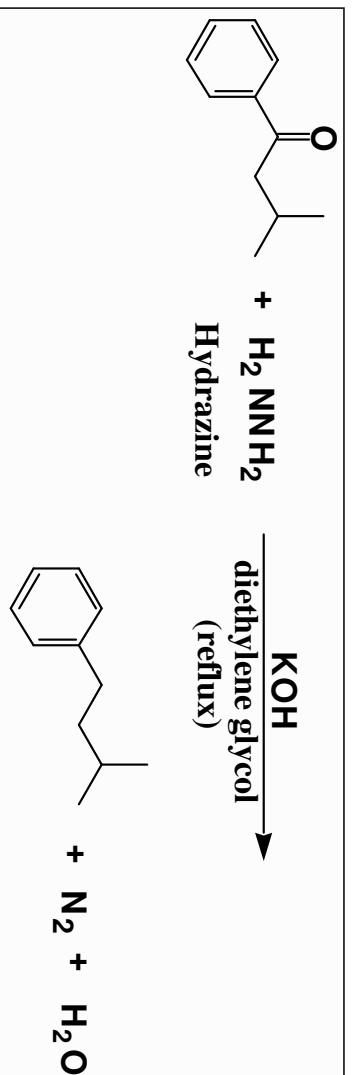
- refluxing an aldehyde or ketone with amalgamated zinc in concentrated HCl converts the carbonyl group to a methylene group
- Classic reaction but harsh conditions limit its use



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Wolff-Kishner Reduction

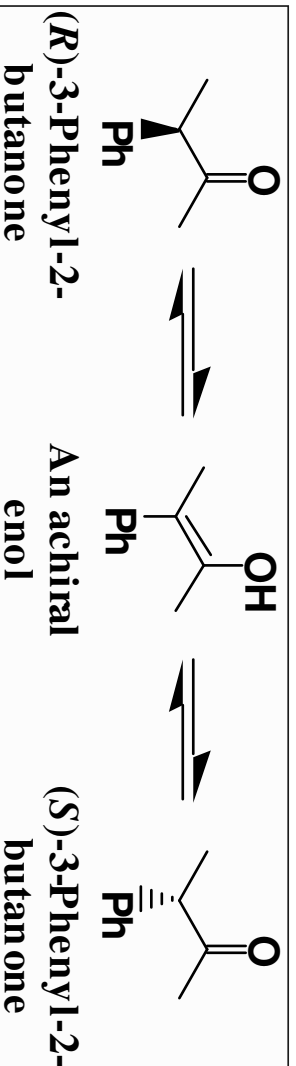
- in the original procedure, the aldehyde or ketone and hydrazine are refluxed with KOH in a high-boiling solvent
- the same reaction can be brought about using hydrazine and potassium *tert*-butoxide in DMSO (Di-methyl sulfoxide)



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Racemization

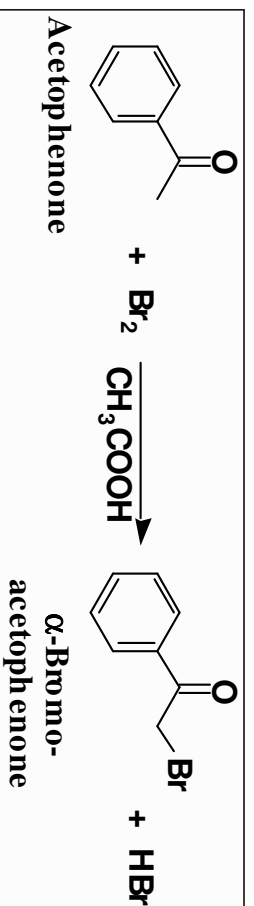
- Racemization at an α -carbon may be catalyzed by either acid or base
- Once stereochemistry is set, this is usually an undesirable side reaction.



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α -Halogenation

- α -Halogenation: aldehydes and ketones with at least one α -hydrogen react at an α -carbon with Br_2 and Cl_2



- reaction is catalyzed by both acid and base
- **Caution!! These are lachrymators**

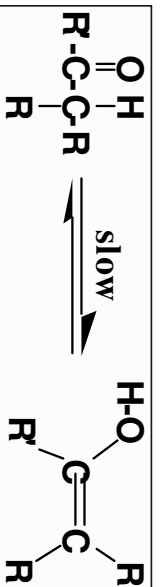


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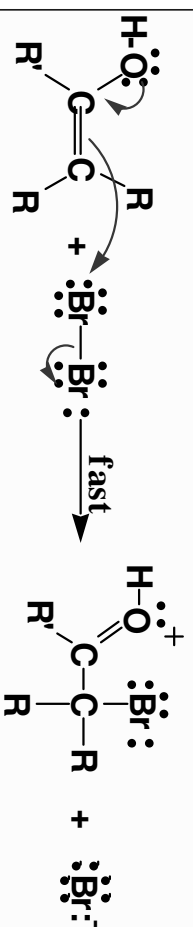
α -Halogenation

- **Acid-catalyzed** α -halogenation

Step 1 : acid-catalyzed enolization - forms the **enol**



Step 2: nucleophilic attack of the enol on halogen



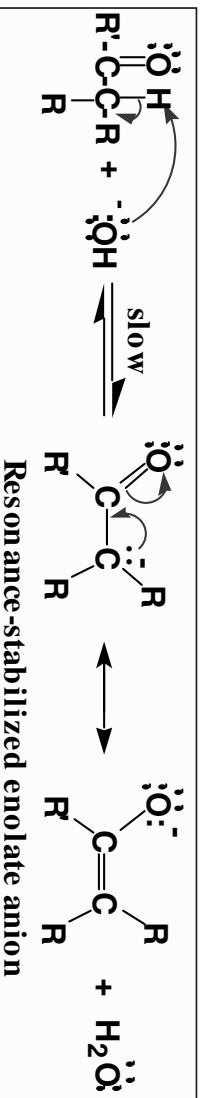
Step 3: (not shown) proton transfer to solvent completes the reaction

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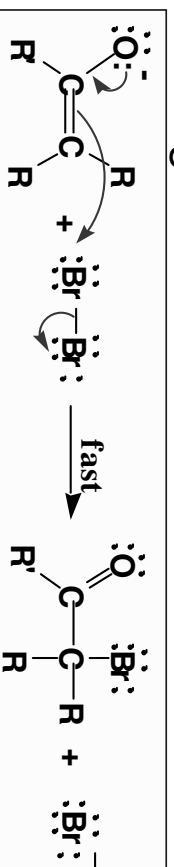
α -Halogenation

- **Base-promoted** α -halogenation

Step 1 : formation of an **enolate anion**



Step 2: nucleophilic attack of the enolate anion on halogen



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α -Halogenation

- **Acid-catalyzed α -halogenation:**
 - introduction of a second halogen is slower than the first
 - introduction of the electronegative halogen on the α -carbon decreases the basicity of the carbonyl oxygen toward protonation
- **Base-promoted α -halogenation:**
 - each successive halogenation is more rapid than the previous one
 - the introduction of the electronegative halogen on the α -carbon increases the acidity of the remaining α -hydrogens and, thus, each successive α -hydrogen is removed more rapidly than the previous one

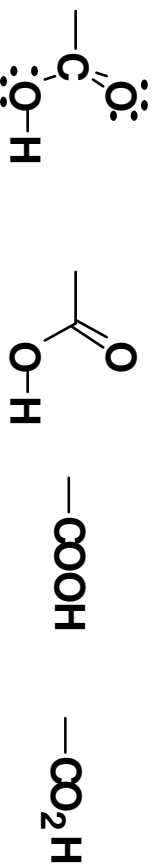
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Carboxylic Acids

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Structure

- The functional group of a carboxylic acid is a carboxyl group



Alternative representations for a carboxyl group

- the general formula for an aliphatic carboxylic acid is RCOOH; that for an aromatic carboxylic acid is ArCOOH

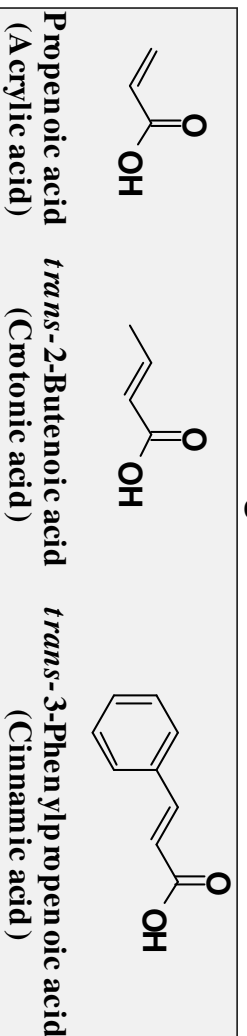
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Nomenclature

- IUPAC names: drop the -e from the parent alkane and add the suffix -oic acid

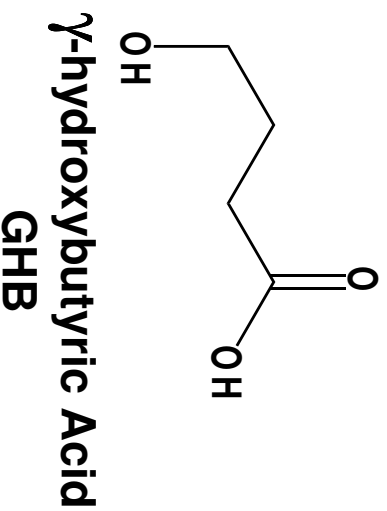
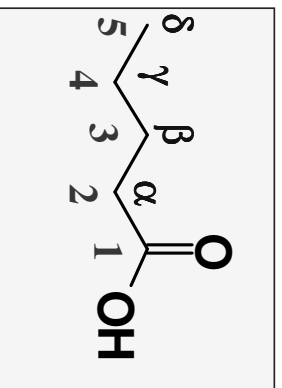
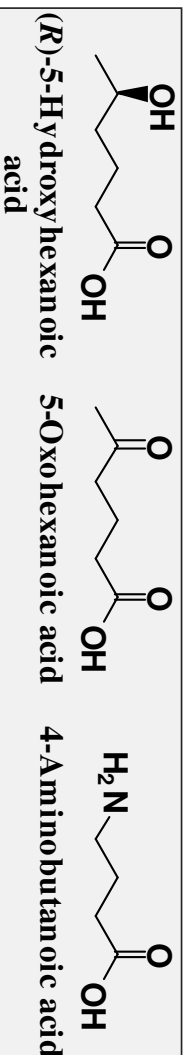


- if the compound contains a carbon-carbon double bond, change the infix -an- to -en-



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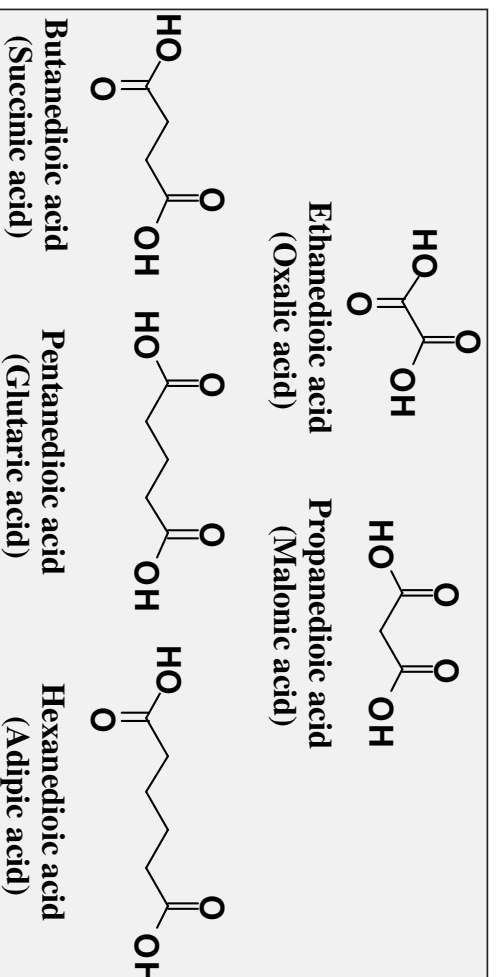
- The carboxyl group takes precedence over most other functional groups



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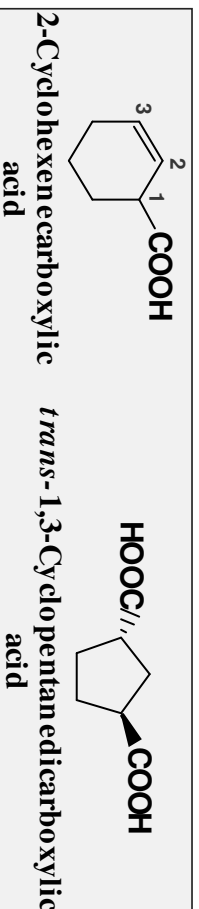
Nomenclature

– dicarboxylic acids: add the suffix -dioic acid to the name of the parent alkane containing both carboxyl groups



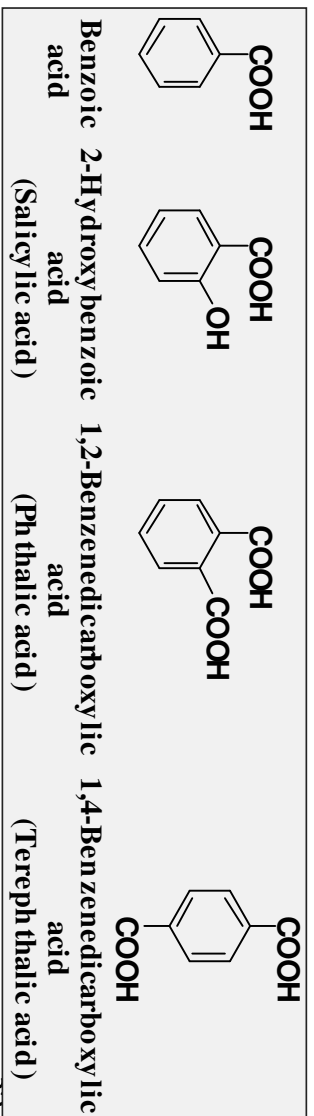
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– if the carboxyl group is bonded to a ring, name the ring compound and add the suffix -carboxylic acid



– benzoic acid is the simplest aromatic carboxylic acid

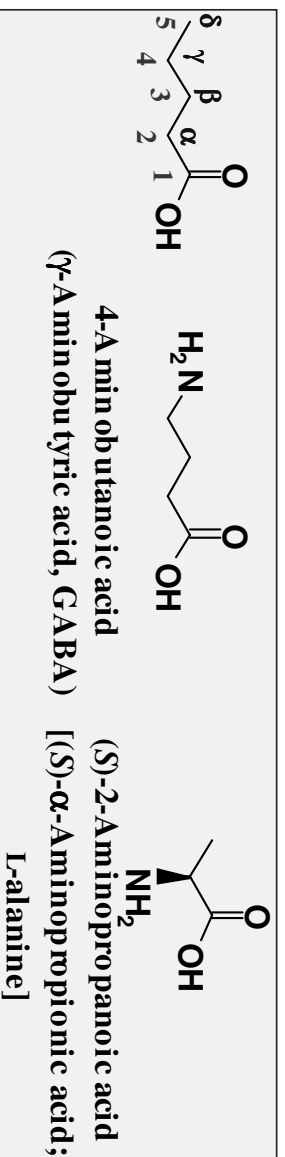
– use numbers to show the location of substituents



Nomenclature

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– when **common names** are used, the letters α , β , γ , δ , etc. are often used to locate substituents



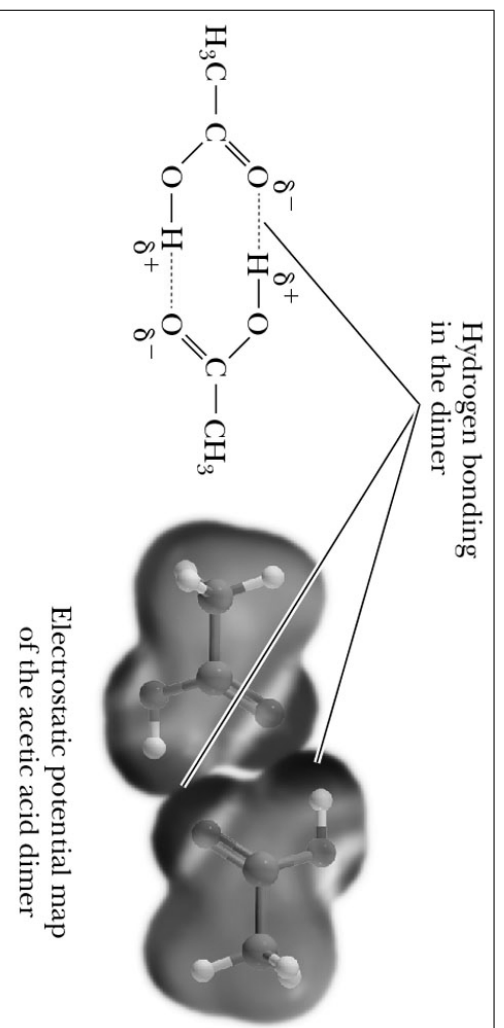
Spectral Properties

- **IR:** Broad O-H stretch (s) 3300-2500 cm^{-1}
Carbonyl (s) 1720-1705 cm^{-1}
C-O (m) 1440-1395 cm^{-1}
- **NMR:** Acidic proton is a singlet δ 10-15
- **^{13}C NMR:** carbonyl carbon 150-185 ppm
- **MS:** Peaks @ M-17 (OH) and M-45 (COOH); these are α cleavage products

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Physical Properties

- In the liquid and solid states, carboxylic acids are associated by hydrogen bonding into dimeric structures



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Physical Properties

- Carboxylic acids have significantly **higher boiling points** than other types of organic compounds of comparable molecular weight
 - they are polar compounds and form very strong intermolecular hydrogen bonds

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Physical Properties

- Carboxylic acids **are more soluble in water than alcohols**, ethers, aldehydes, and ketones of comparable molecular weight
 - they form hydrogen bonds with water molecules through their C=O and OH groups

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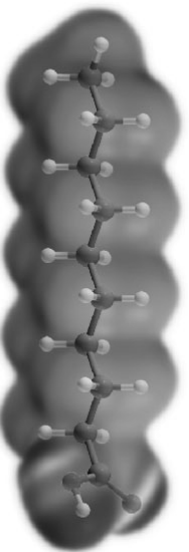
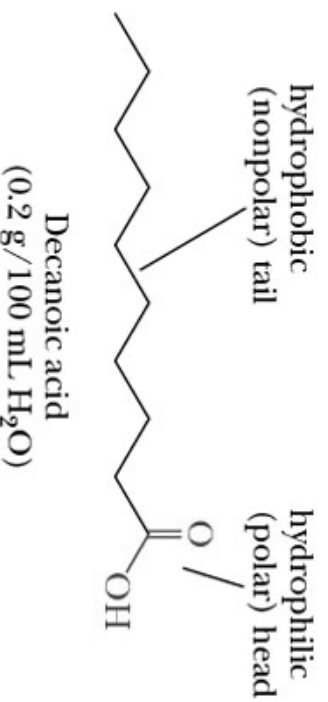
Physical Properties

Structure	Name	Molecular Weight (g/mol)	Boiling Point (°C)	Solubility (g/100 g H ₂ O)
CH ₃ COOH	Acetic acid	60.1	118	Infinite
CH ₃ CH ₂ CH ₂ OH	1-Propanol	60.1	97	Infinite
CH ₃ CH ₂ CHO	Propanal	58.1	48	16
.....				
CH ₃ (CH ₂) ₂ COOH	Butanoic acid	88.1	163	Infinite
CH ₃ (CH ₂) ₃ CH ₂ OH	1-Pentanol	88.1	137	2.3
CH ₃ (CH ₂) ₃ CHO	Pentanal	86.1	103	Slight
.....				
CH ₃ (CH ₂) ₄ COOH	Hexanoic acid	116.2	205	1.0
CH ₃ (CH ₂) ₅ CH ₂ OH	1-Heptanol	116.2	176	0.2
CH ₃ (CH ₂) ₅ CHO	Heptanal	114.1	153	0.1

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Physical Properties

water solubility decreases as the relative size of the hydrophobic portion of the molecule increases

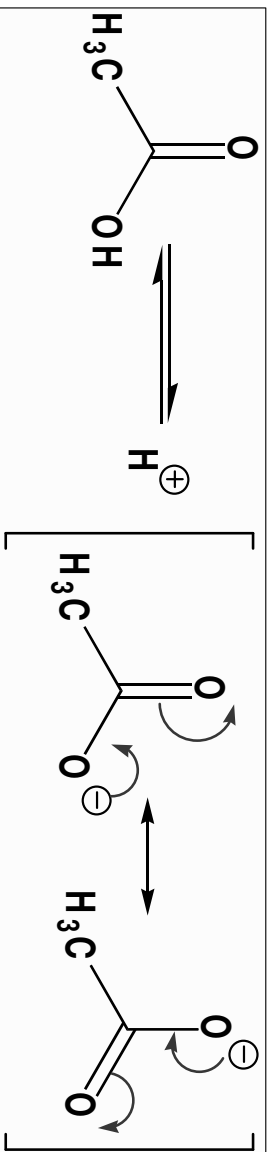


Electrostatic potential map

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Acidity

- Carboxylic acids are **weak acids**
 - values of pK_a for most aliphatic and aromatic carboxylic acids fall within the range 4 to 5
- The greater acidity of carboxylic acids relative to alcohols (both compounds that contain an OH group) is due to resonance stabilization of the carboxylate anion



Acidity

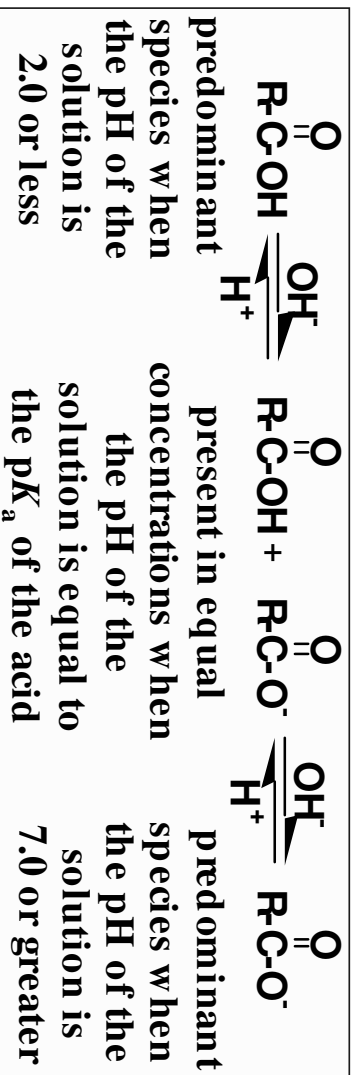
– electron-withdrawing substituents near the carboxyl group increase acidity through their inductive effect

Formula:	CH_3COOH	ClCH_2COOH	Cl_2CHCOOH	Cl_3CCOOH
Name:	Acetic acid	Chloroacetic acid	Dichloroacetic acid	Trichloroacetic acid
pK_a :	4.76	2.86	1.48	0.70
	Increasing acid strength			

F_3CCOOH (TFAA): $pK_a = 0.3$

Note: the pK_a scale is a logarithmic scale

the form of a carboxylic acid present in aqueous solution depends on the pH of the solution:



$$\text{pH} = \text{p}K_a + \log_{10} \frac{[\text{A}^-]}{[\text{HA}]}$$

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For organic acids in equilibrium:



Henderson-Hasselbalch equation:

$$\text{pH} = \text{p}K_a + \log_{10} \frac{[\text{A}^-]}{[\text{HA}]}$$

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Reaction with Bases

Carboxylic acids, whether soluble or insoluble in water, react with NaOH, KOH, and other strong bases to give water-soluble salts

