Carboxylic acids and **Nitriles**

Part A

B. Pharm. Semester-1
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Learning Outcomes

At the end of this lesson, students will be able to describe

Carboxylic acids

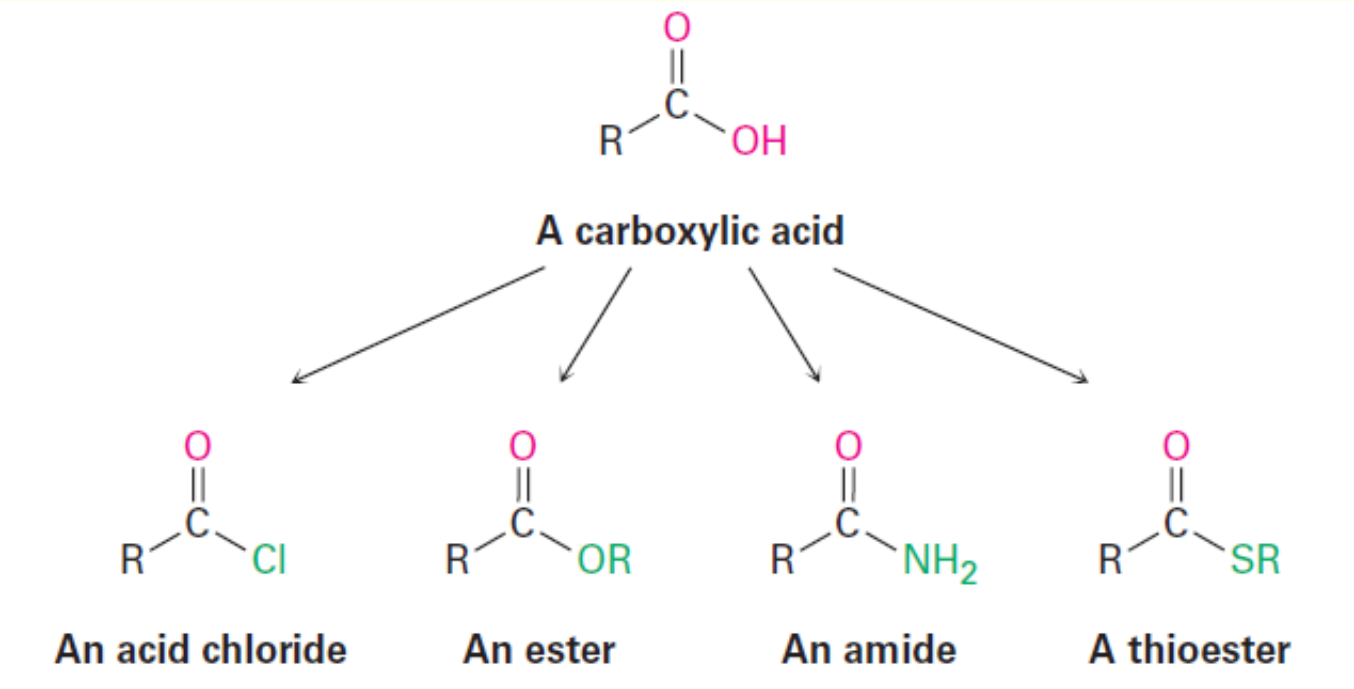
- **Nomenclature of Carboxylic acids**
- **Structure and properties of Carboxylic acids**
- **Acidity of Carboxylic acids**
- **Effect of substituents on acidity of Carboxylic acids**

Objective

The objective of this course is to give to the students of pharmacy the basic knowledge about the organic chemistry.

The Importance of Carboxylic Acids (R-COOH)

Carboxylic acids, R-COOH are valuable compounds and serve as starting materials for the preparation of numerous carboxylic acid derivatives such as acid chlorides, esters, amides, and thioesters.



The Importance of Carboxylic Acids (R-COOH)

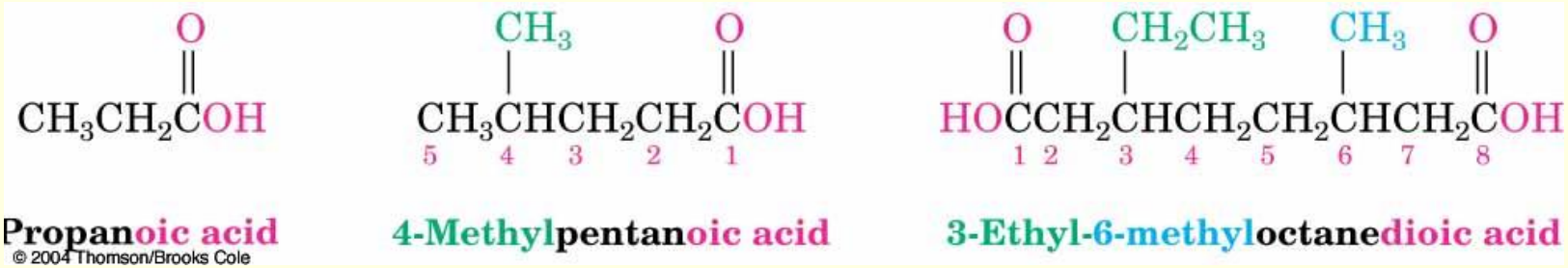
A great many carboxylic acids are found in nature:

1. Acetic acid, CH_3COOH, is the chief organic component of vinegar
2. Butanoic acid, $CH_3CH_2CH_2COOH$, is responsible for the rancid odor of sour butter
3. Hexanoic acid (caproic acid), $CH_3(CH_2)_4COOH$, is responsible for the unmistakable aroma of goats and dirty gym socks (the name comes from the Latin caper, meaning “goat”).

Naming of Carboxylic Acids- RCOOH

Carboxylic Acids, RCOOH

If derived from open-chain alkanes, replace the terminal -e of the alkane name with -oic acid, the carboxyl carbon atom is given C1.



Compounds having -COOH group bonded to a ring are named using the suffix -carboxylic acid.

The COOH carbon is attached to C1 in this system and is not itself numbered. As a substituent, the COOH group is called a carboxyl group.

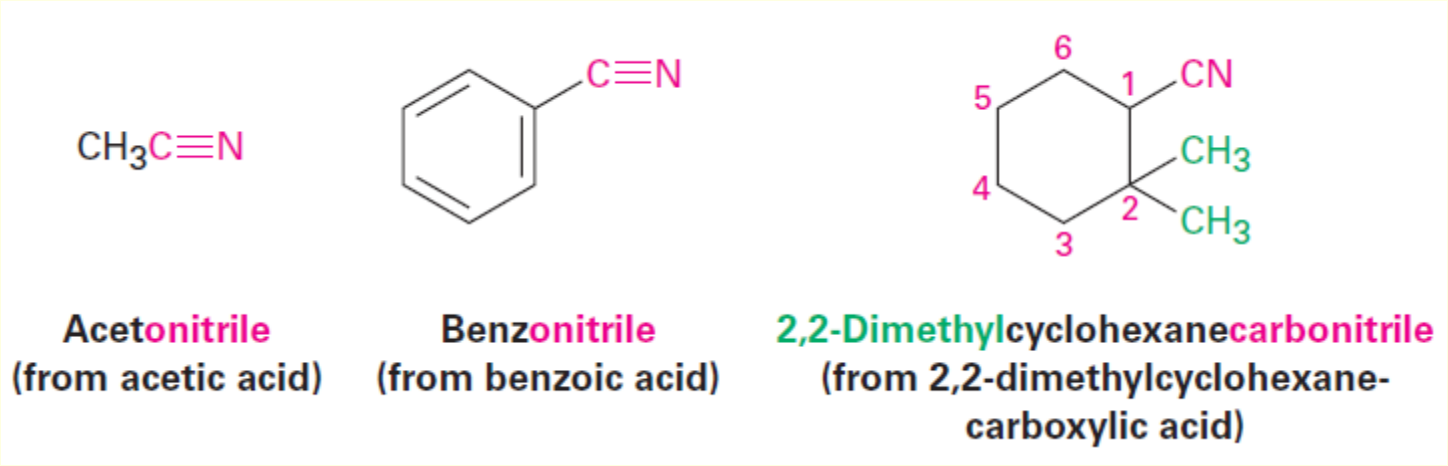
Common Names of Carboxylic Acids

Structure	Name	Acyl group
HCO_2H	Formic	Formyl
CH_3CO_2H	Acetic	Acetyl
$CH_3CH_2CO_2H$	Propionic	Propionyl
$CH_3CH_2CH_2CO_2H$	Butyric	Butyryl
HO_2CCO_2H	Oxalic	Oxalyl
$HO_2CCH_2CO_2H$	Malonic	Malonyl
$HO_2CCH_2CH_2CO_2H$	Succinic	Succinyl
$HO_2CCH_2CH_2CH_2CO_2H$	Glutaric	Glutaryl
$HO_2CCH_2CH_2CH_2CH_2CO_2H$	Adipic	Adipoyl
$H_2C{=}CHCO_2H$	Acrylic	Acryloyl
$HO_2CCH{=}CHCO_2H$	Maleic (cis)	Maleoyl
	Fumaric (trans)	Fumaroyl
$HOCH_2CO_2H$	Glycolic	Glycoloyl

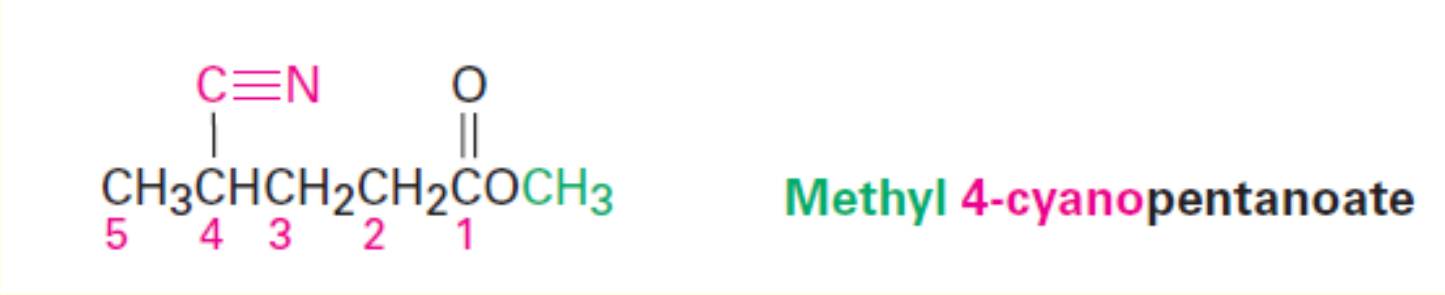
Naming of Nitriles – R-CN

- Compounds containing the –C≡N functional group are called nitriles.
- Simple open-chain nitriles are 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,
- The nitrile carbon atom is attached to C1 but is not itself numbered.

Naming of Nitriles – R-CN



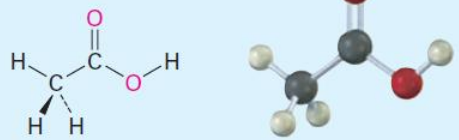
If another carboxylic acid derivative is present in the same molecule, the prefix cyano- is used for the nitrile group.



Structure and 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.

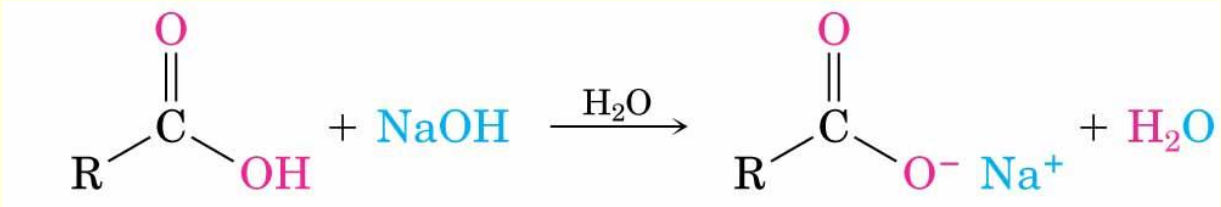
Table 20.2 Physical Parameters for Acetic Acid



Bond angle	(degrees)	Bond length	(pm)
C–C=O	119	C–C	152
C–C–OH	119	C=O	125
O=C–OH	122	C–OH	131

Acidity of Carboxylic Acids

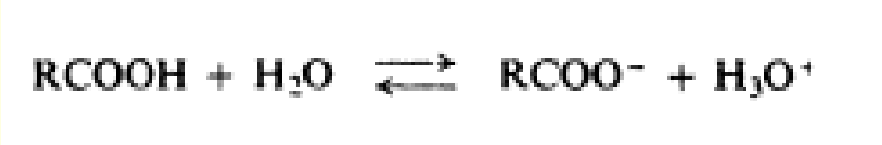
- Carboxylic acids are acidic and are proton donors toward weak and strong bases, producing metal carboxylate salts, $RCOO^- M^+$
- Carboxylic acids with more than six carbons are only slightly soluble in water, but their conjugate base salts are water-soluble.



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

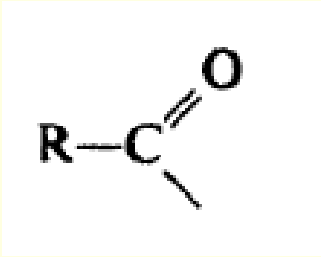
Acidity of Carboxylic Acids

Acidity: It is an important property of carboxylic acids. Their tendency to give up or donate a hydrogen ion in such that in aqueous solution a measurable equilibrium exists between the hydrogen ion and acid.



The –OH group in acid can be replaced by –Cl, -OR, -NH_2 may give the respective derivatives of carboxylic acids such as acid chlorides, esters and amides.

They all contain acyl group:-



Ionization of Carboxylic acids: Acidity constants

In aqueous solution, a carboxylic acid exists in an equilibrium with carboxylate anion and the hydrogen ion (precisely hydronium ion).

As for any equilibrium, the concentrations of the components can be expressed as:-

$$K_a = \frac{[RCOO^-][H_3O^+]}{[RCOOH]}$$

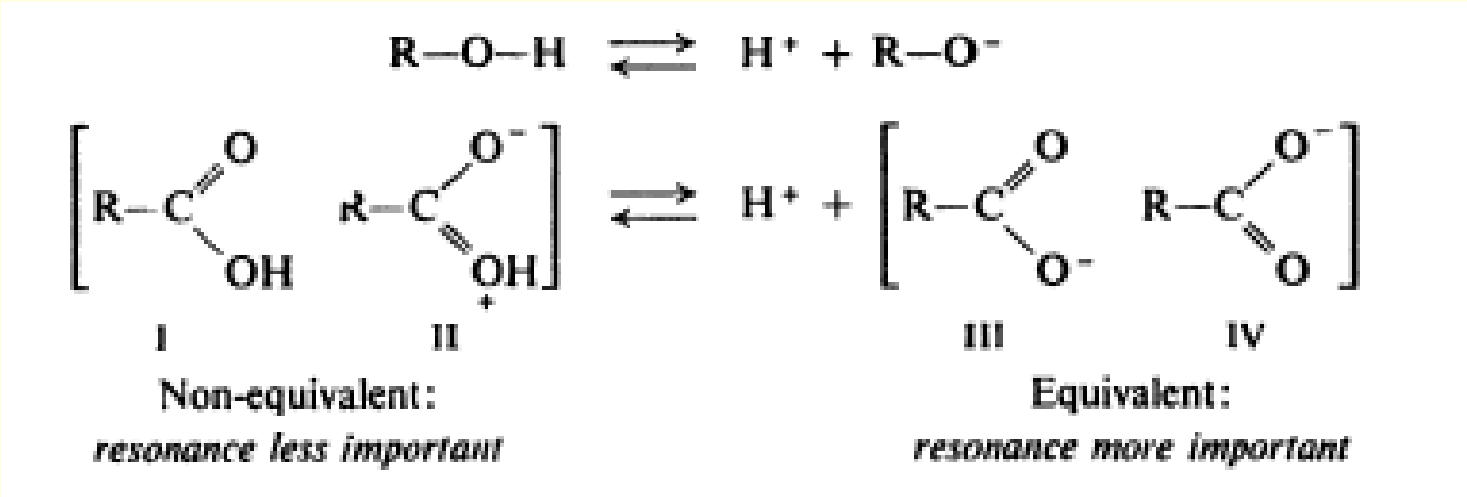
The K_a is the equilibrium constant or Acidity constant. The strength of any acids can be expressed based on the value of K_a. Each carboxylic acids have specific K_a value.

Relative acidities: RCOOH > HOH > ROH > HC≡CH > NH_3 > RH

Relative basicities: $RCOO^-$ < HO^- < RO^- < $HC{\equiv}C^-$ < NH_2^- < R^-

Acidity of Carboxylic acids in relation with their structures

- Acidity depends on the difference in the stability of the structure of an acid and its corresponding anion structure.
- Alcohol and alkoxide ion can be represented by single structure. But, there is exitance of two resonance structures for an acid (I, II), and correspondingly two resonance structures for a carboxylate anion (III, IV).



Acidity of Carboxylic acids in relation with their structures

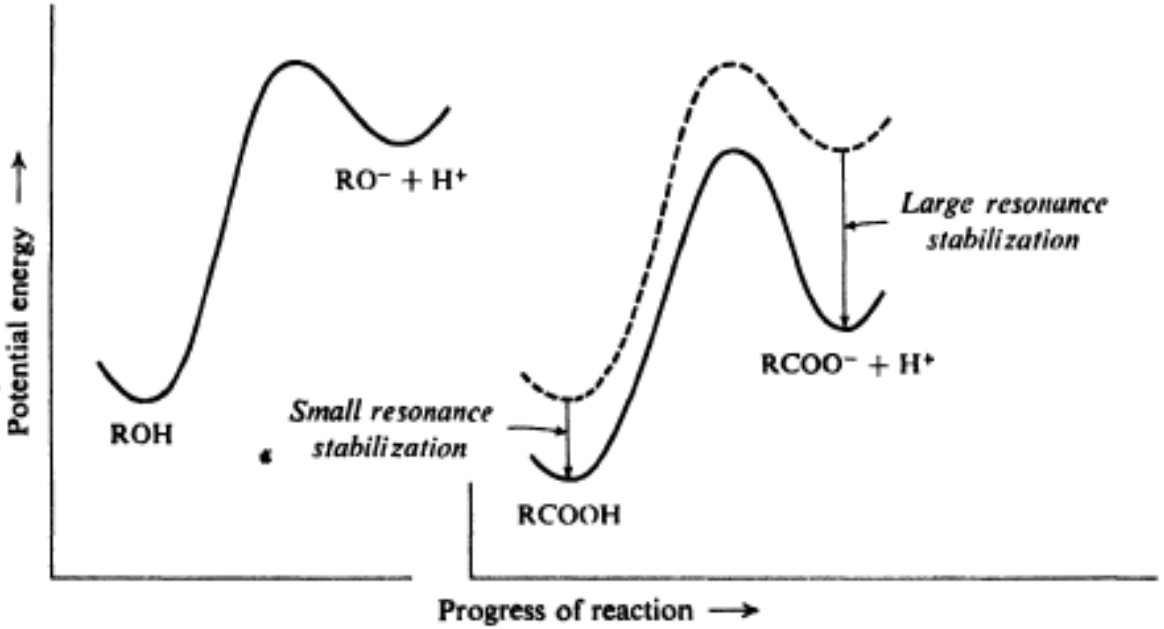
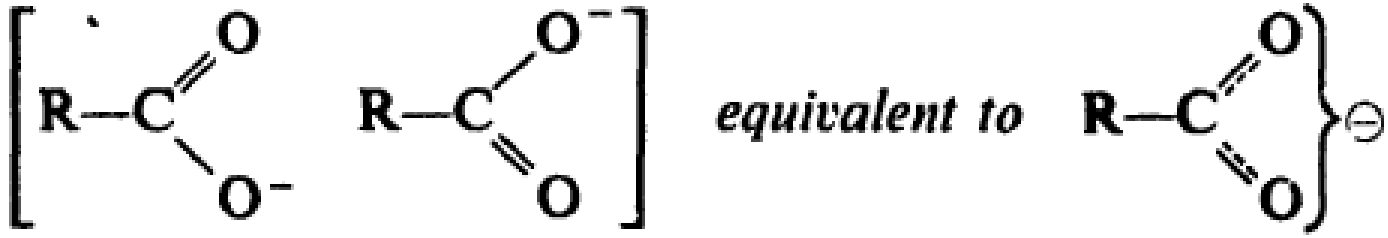


Figure 18.2. Molecular structure and position of equilibrium. Carboxylic acid yields resonance-stabilized anion; is stronger acid than alcohol. (Plots aligned with each other for easy comparison.)

Resonance stabilization of carboxylate anion is greater than the corresponding carboxylic acid, thus increasing *K*a value.

Structure of carboxylate ions

- According to the resonance theory, carboxylate ion is a hybrid of two resonance structures of equal stability and contributing equally to form the resonance hybrid.
- Carbon is joined to each of the oxygen by one-and-half bond.
- The negative charge is evenly distributed to both of the oxygen.

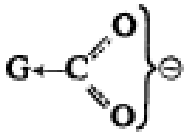


Effect of Substituents on Acidity

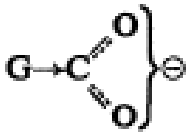
- Any factor stabilizes the anion will increases the acidity, or in other words any factor that makes the anion less stable will decreases the acidity.
- The factor or the substituent may withdraw electrons or donate electrons to the carboxylic acid group.
- If electron-withdrawing substituent group attached to the structure of the carboxylic acid, then it disperses the negative charge and stabilizes the anion thereby increases the acidity.
- If electron-donating substituent group attached to the structure of the carboxylic acid, then it intensifies the negative charge and destabilizes the anion thereby decreases the acidity.

Effect of Substituents on Acidity

Acid Strength



G withdraws electrons: *stabilizes anion, strengthens acid*



G releases electrons: *destabilizes anion, weakens acid*

Table 18.2 Acidity Constants of Carboxylic Acids

	K_a		K_a
HCOOH	17.7×10^{-5}	$CH_3CHClCH_2COOH$	8.9×10^{-5}
CH_3COOH	1.75 ,,	$ClCH_2CH_2CH_2COOH$	2.96 ,,
$ClCH_2COOH$	136 ,,	FCH_2COOH	260 ,,
$Cl_2CHCOOH$	5530 ,,	$BrCH_2COOH$	125 ,,
Cl_3CCOOH	23200 ,,	ICH_2COOH	67 ,,
$CH_3CH_2CH_2COOH$	1.52 ,,	$C_6H_5CH_2COOH$	4.9 ,,
$CH_3CH_2CHClCOOH$	139 ,,	$p\text{-}O_2NC_6H_4CH_2COOH$	14.1 ,,

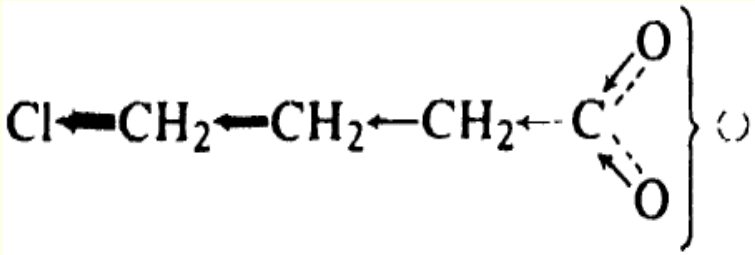
Acidity Constants of Substituted Benzoic Acids

K_a of benzoic acid = 6.3×10^{-5}

	K_a		K_a		K_a
$p\text{-}NO_2$	36×10^{-5}	$m\text{-}NO_2$	32×10^{-5}	$o\text{-}NO_2$	670×10^{-5}
p-Cl	10.3 ,,	m-Cl	15.1 ,,	o-Cl	120 ,,
$p\text{-}CH_3$	4.2 ,,	$m\text{-}CH_3$	5.4 ,,	$o\text{-}CH_3$	12.4 ,,
$p\text{-}OCH_3$	3.3 ,,	$m\text{-}OCH_3$	8.2 ,,	$o\text{-}OCH_3$	8.2 ,,
p-OH	2.6 ,,	m-OH	8.3 ,,	o-OH	105 ,,
$p\text{-}NH_2$	1.4 ,,	$m\text{-}NH_2$	1.9 ,,	$o\text{-}NH_2$	1.6 ,,

Inductive Effect of Substituents on Acidity

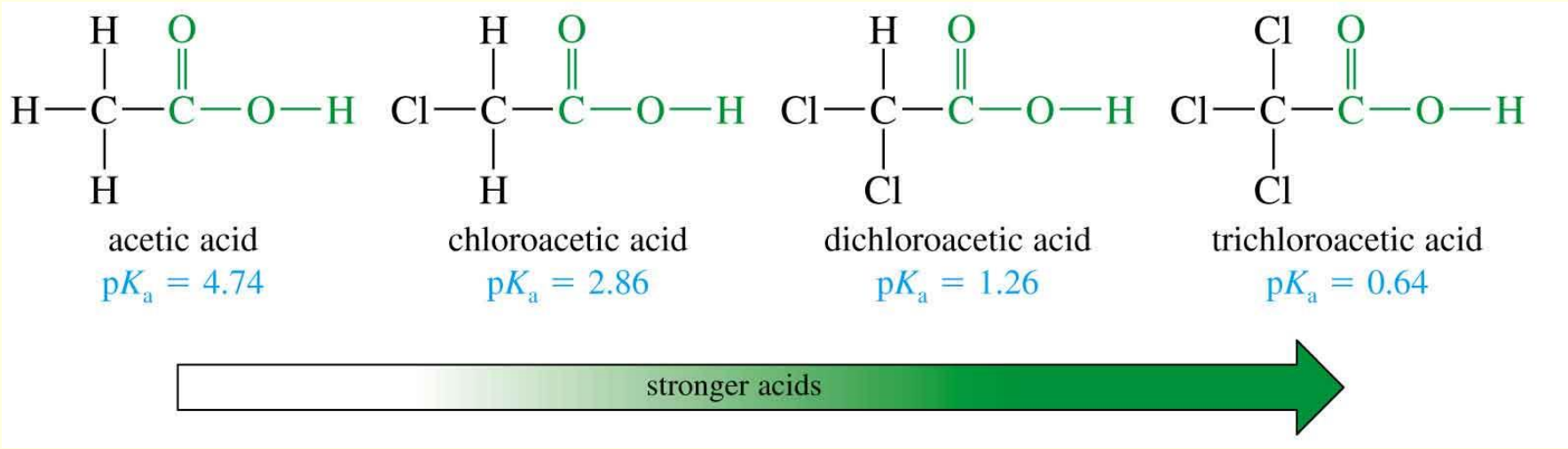
- α-chlorobutyric acid is as strong as chloroacetic acid. Because the chlorine atom is moved away in α-chlorobutyric acid.
- β-chlorobutyric acid is six times as strong as butyric acid.
- γ-chlorobutyric acid is only two times as strong as butyric acid.
- This is due to inductive effects that they decrease rapidly with distance of about four atoms.



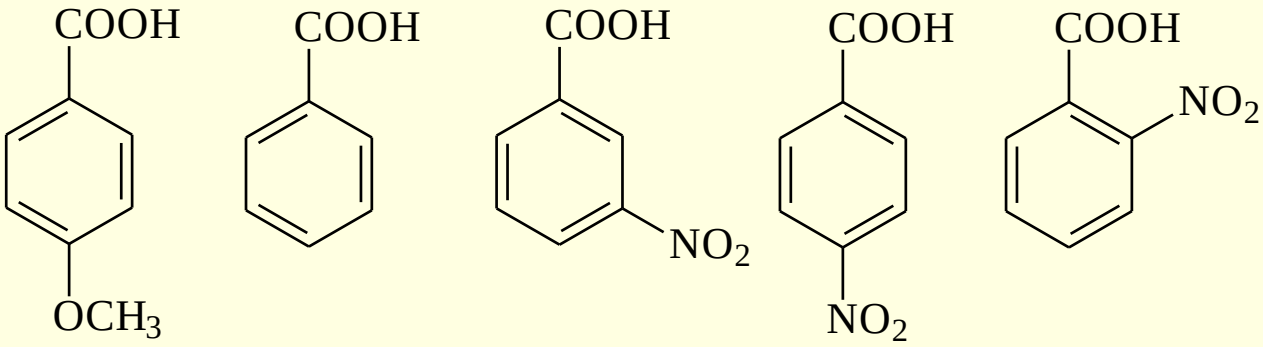
Inductive effect: *decreases with distance*

Inductive Effect of Substituents on Acidity

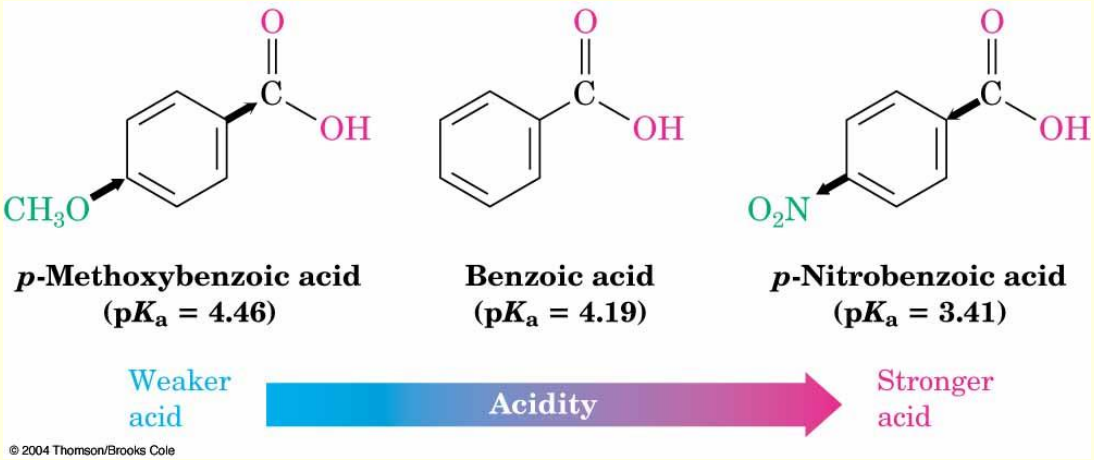
- The acidity of aromatic acids also similarly affected by substituents: -CH_3, -OH, -NH_2 make benzoic acid weaker, and -Cl, -NO_2 makes benzoic acid stronger.
- Thus, both resonance and inductive effects determines the stability of anion and thus determining the acidity of carboxylic acids.



Inductive Effect of Substituents on Acidity



pK_a = 4.46 **pK_a = 4.19** **pK_a = 3.47** **pK_a = 3.41** **pK_a = 2.16**



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