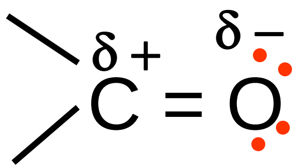
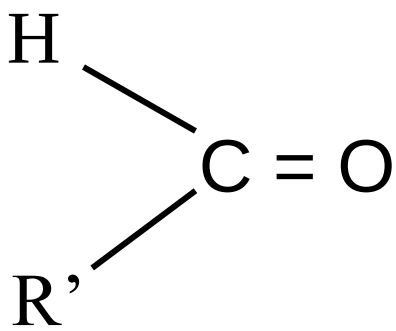
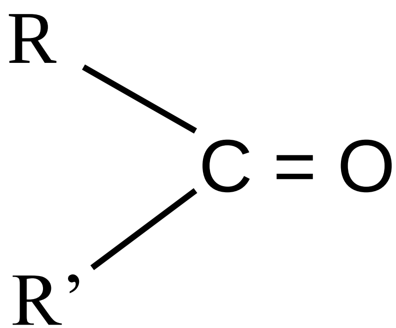
The carbonyl

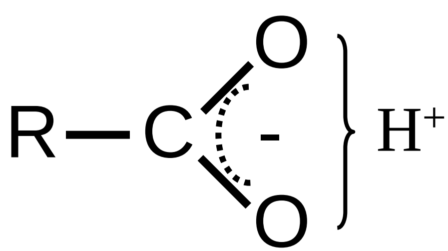




aldehyde

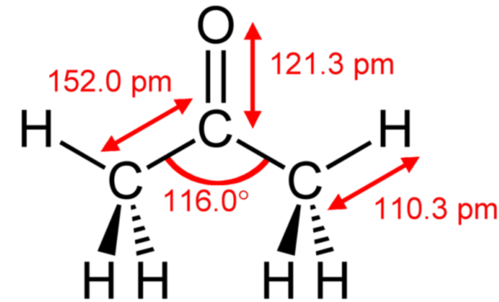


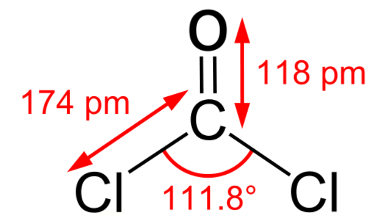
ketone

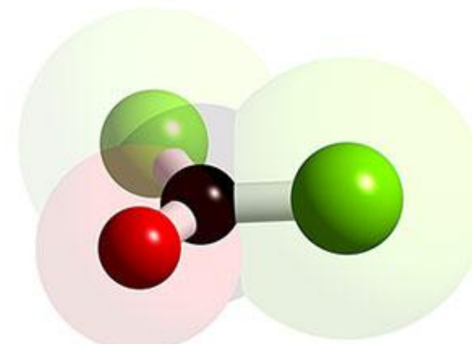


Carboxylic acids

acetone







Phosgene…!
$COCl_2$
Chemical weapon

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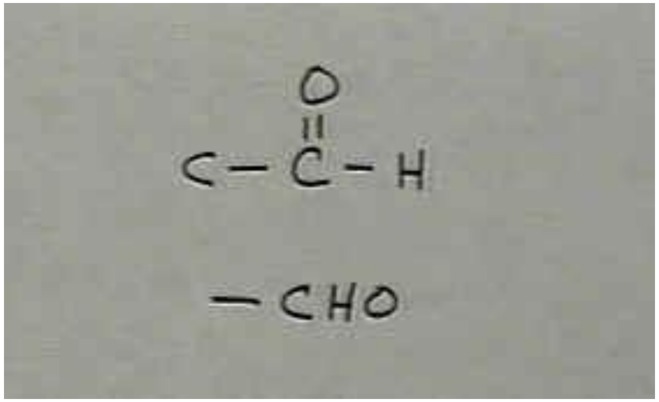
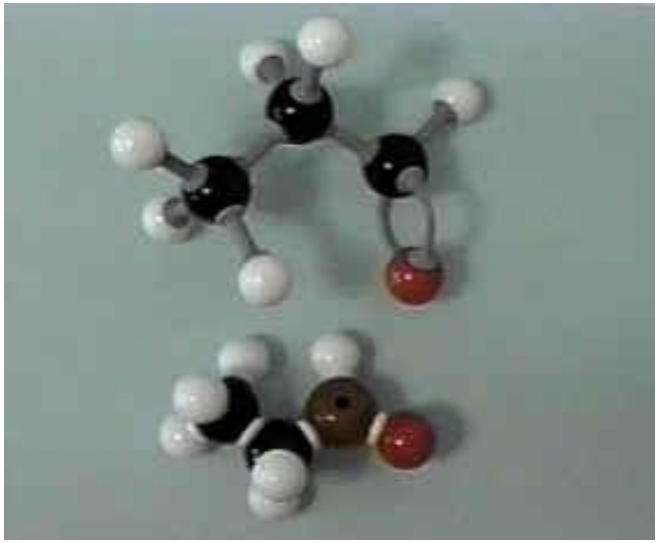
Aldehydes structure





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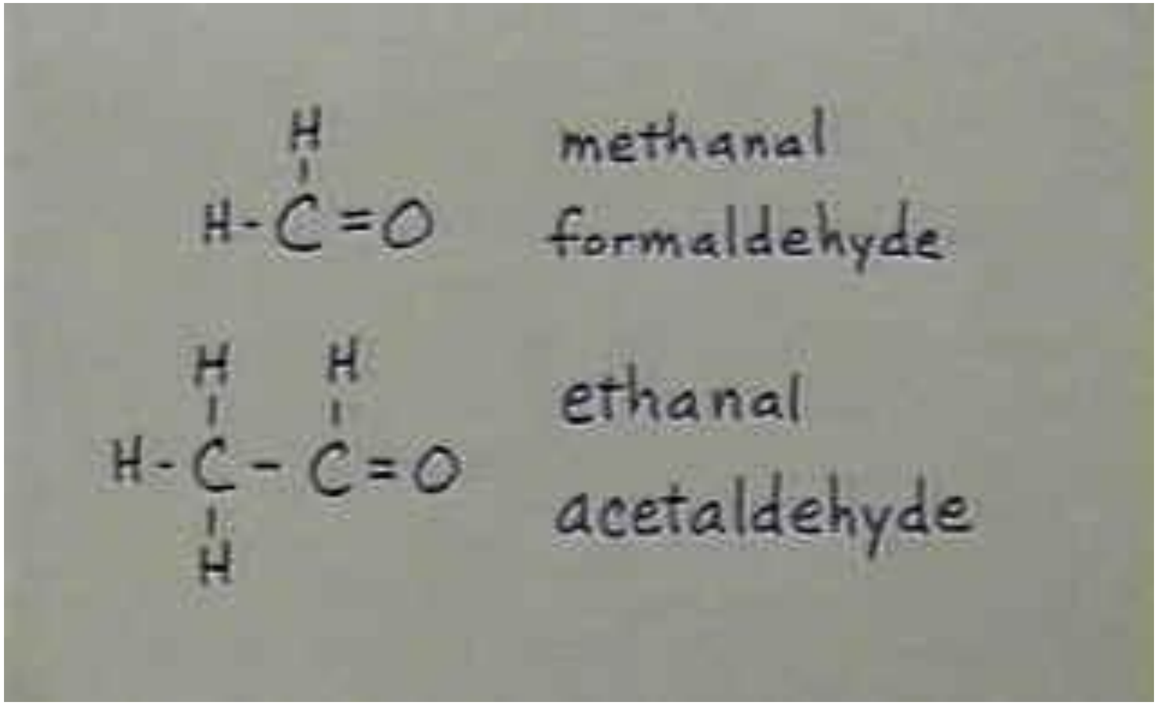
Familiar names & IUPAC



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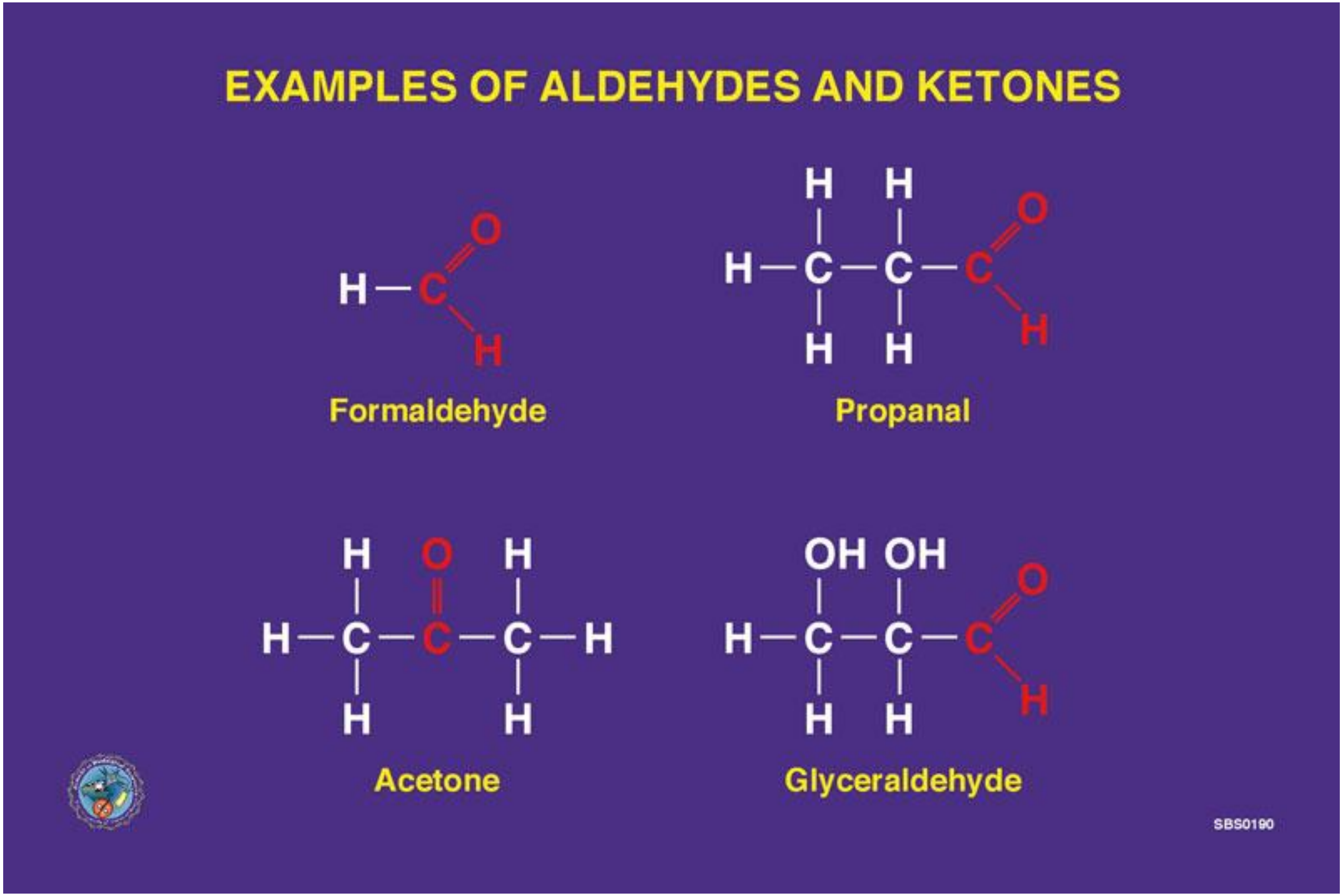
Aldehydes & Ketons



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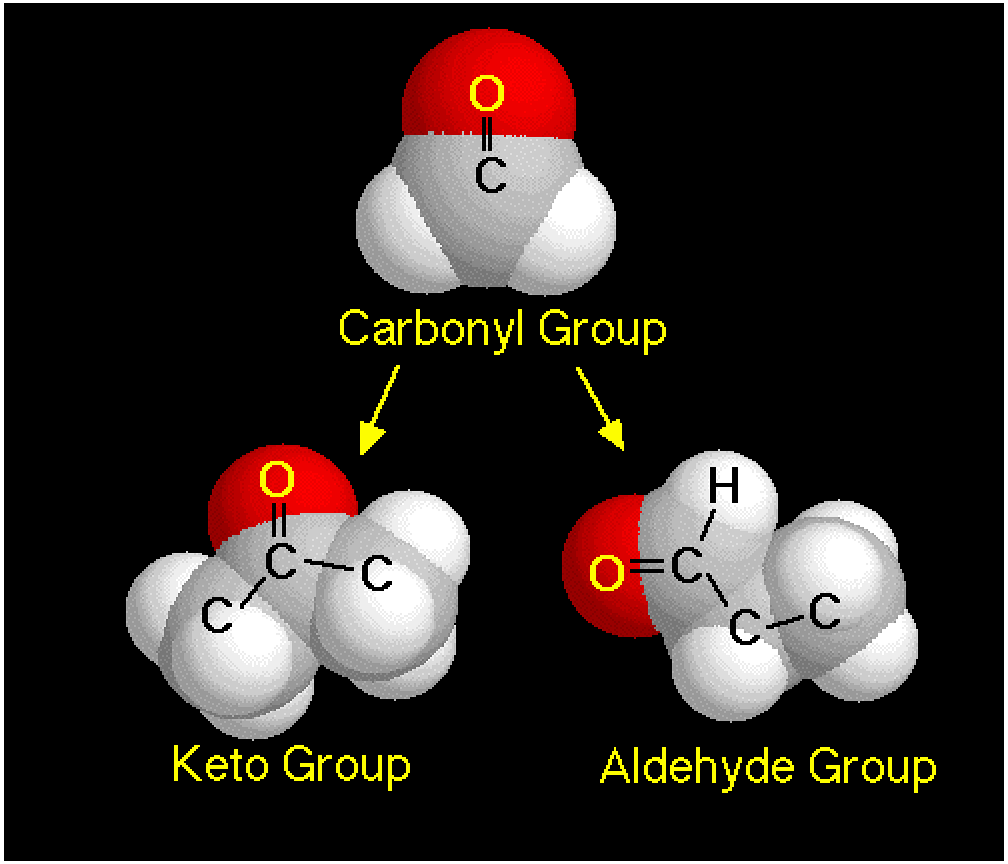
The carbonyl



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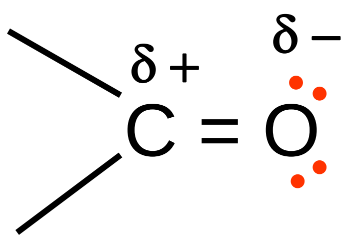
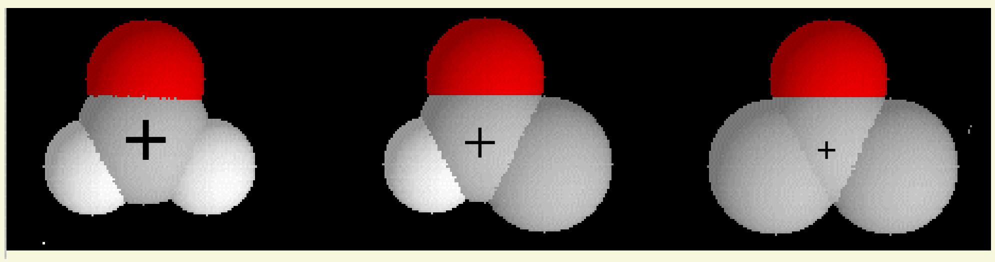


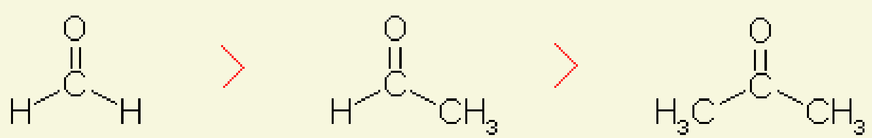
Carbonyl properties:
- both C & O are sp2 hybrids
- polarized bond
- ~165 Kcal/mol stabilized
- average bond length 1.22 Å

•Depending on R ed R’: different *inductive effects*
•Reactivity of aldheydes and ketons



(2)

Steric hindrance of carbonyl carbon



Electrophilic character of carbonyl carbon

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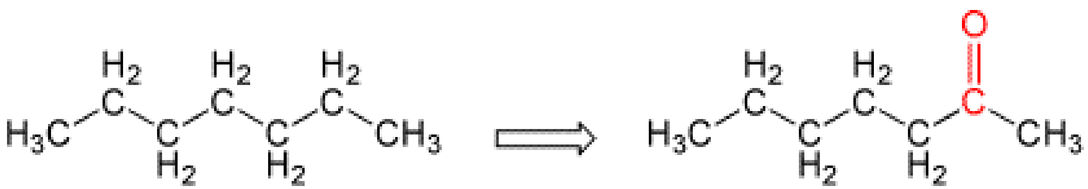
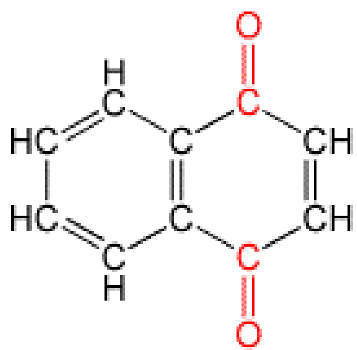
Ketones Nomenclature

alk…ane → …one

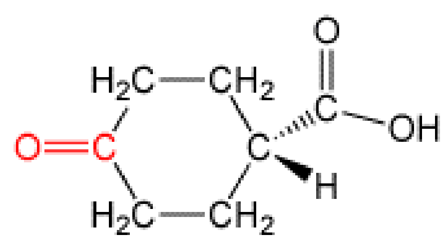


heptane

heptan-2-one
(methyl pentyl ketone)



1,4-naphthoquinone



4-oxocyclohexane-1-carboxylic acid

Again, try to figure out the 3D organization of the molecule !

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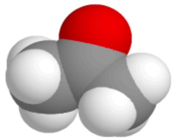
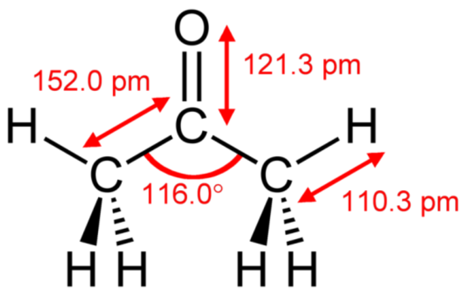
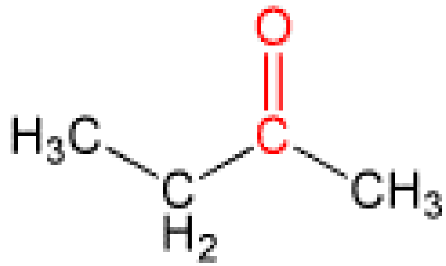
Ketones

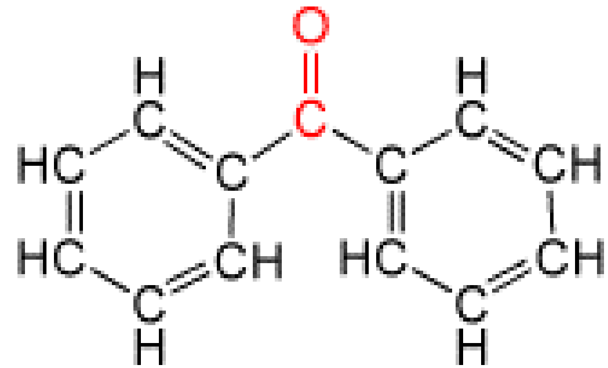




- acetone
- dimethyl ketone
- 2-propanone



- methyl ethyl ketone
- MEK
- 2-butanone



- benzophenone
- diphenyl ketone

R ed R' = alkyl- or aryl-derivatives/substituents

Nomenclature: IUPAC & familiar/common

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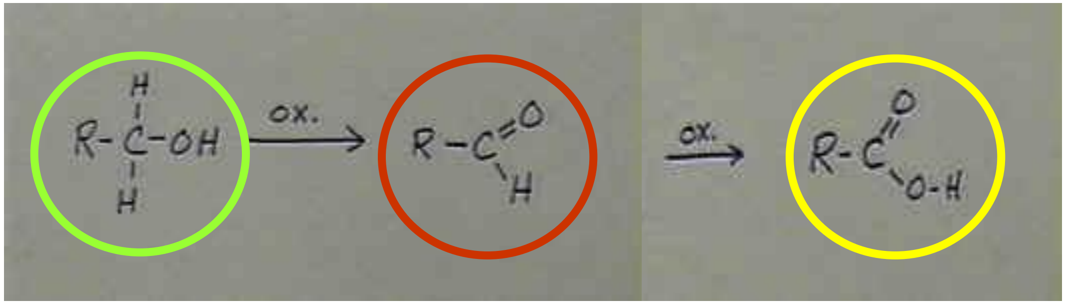
Aldehydes common reactions

oxidation



alcohol aldehyde acid

reduction

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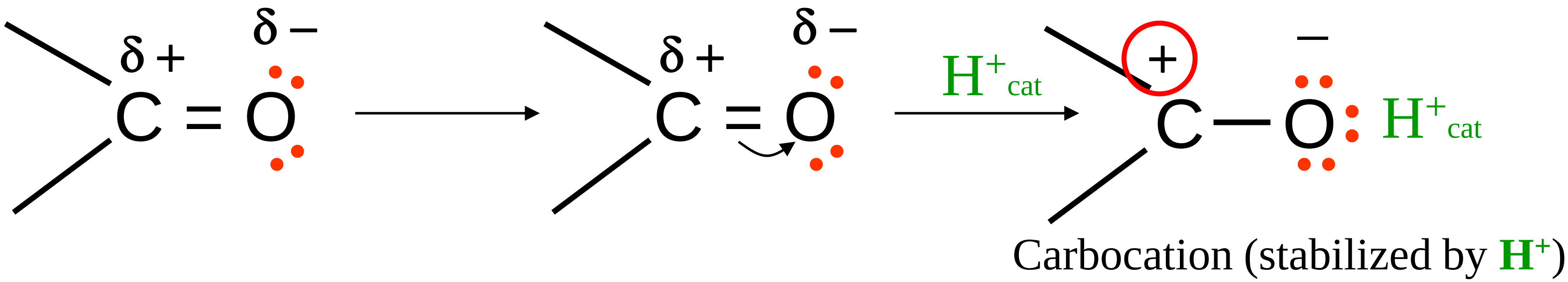
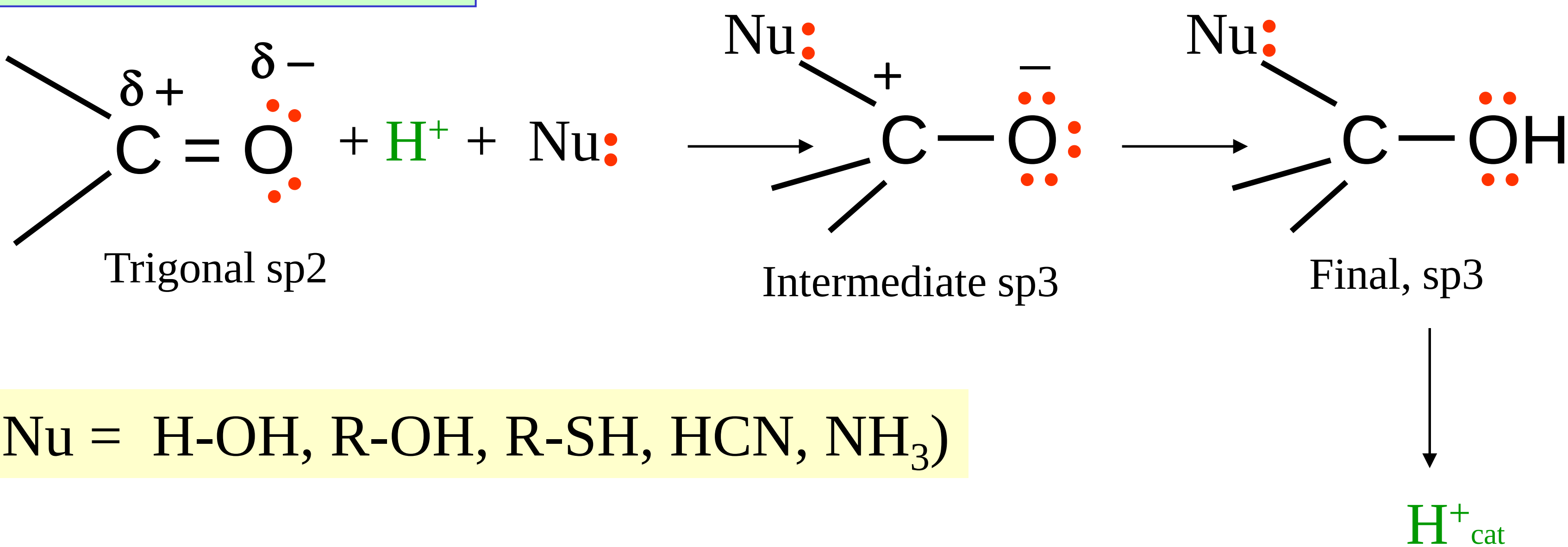
Carbonyl reactivity (aldehydes & ketones)



Addition to double bond



(Ex. Nu = H-OH, R-OH, R-SH, HCN, NH_3)

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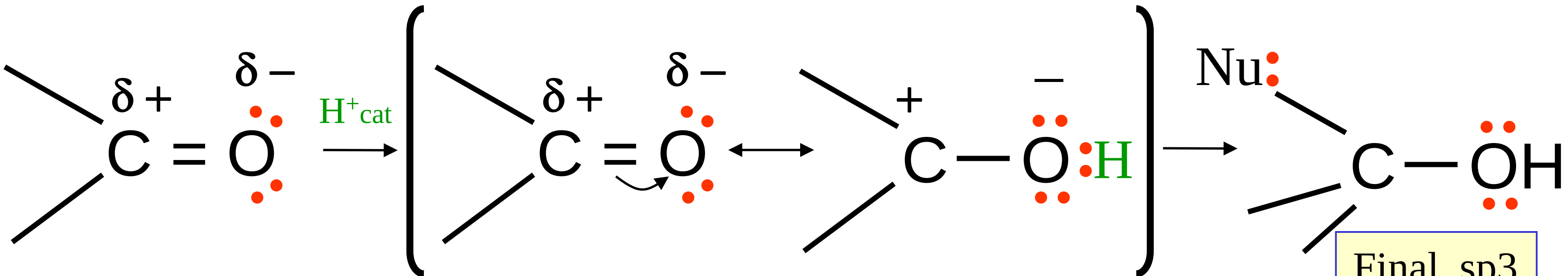
Double bond, nucleophylic addition



Final, sp3

Carbo-cation (stabilized by resonance)

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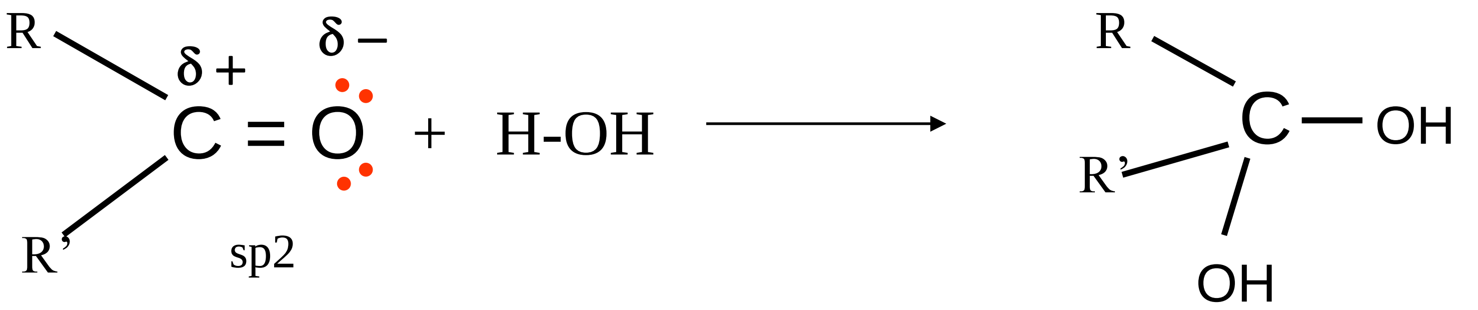
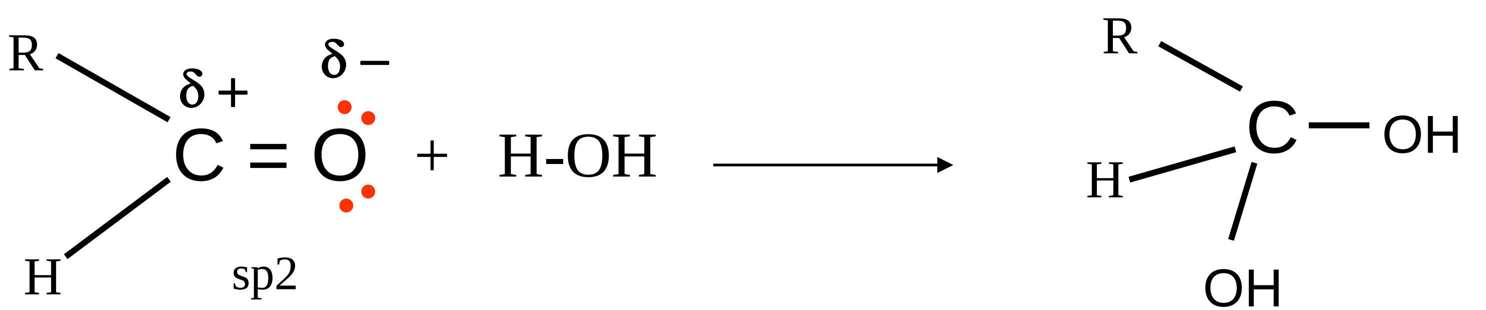
H_2O addition



Hydrated keton



Hydrated aldehyde

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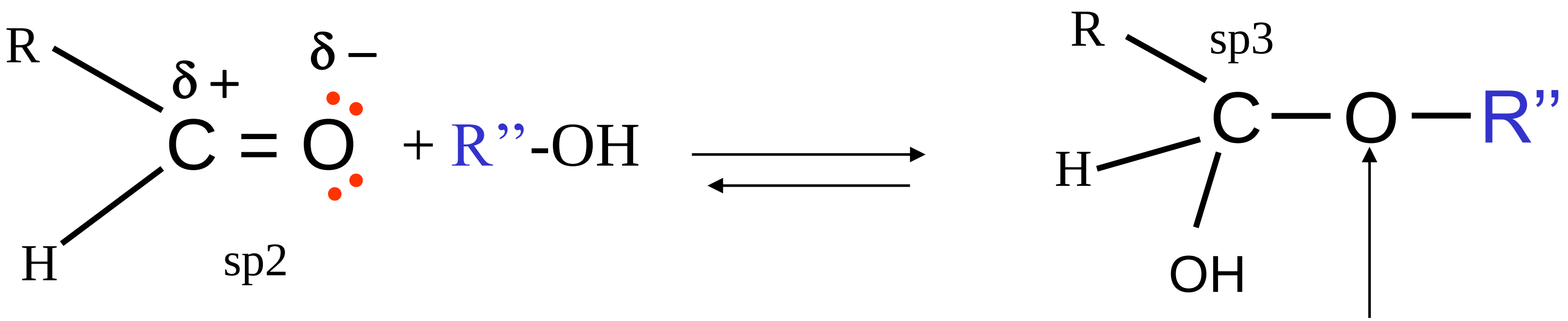
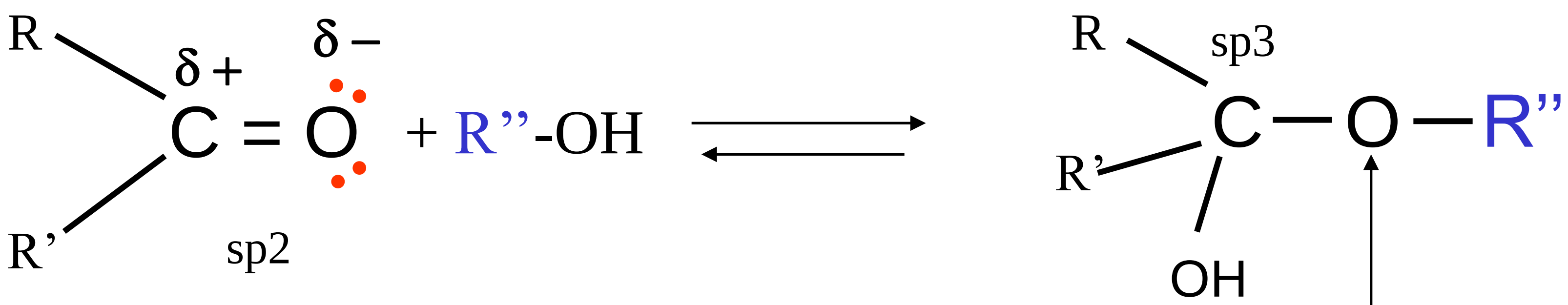
R-OH , R-SH addition



Aldehyde + Alcohol

Hemi-acetal

Glucose cyclization



ketone + Alcohol

Hemi-ketal

Fructose cyclization

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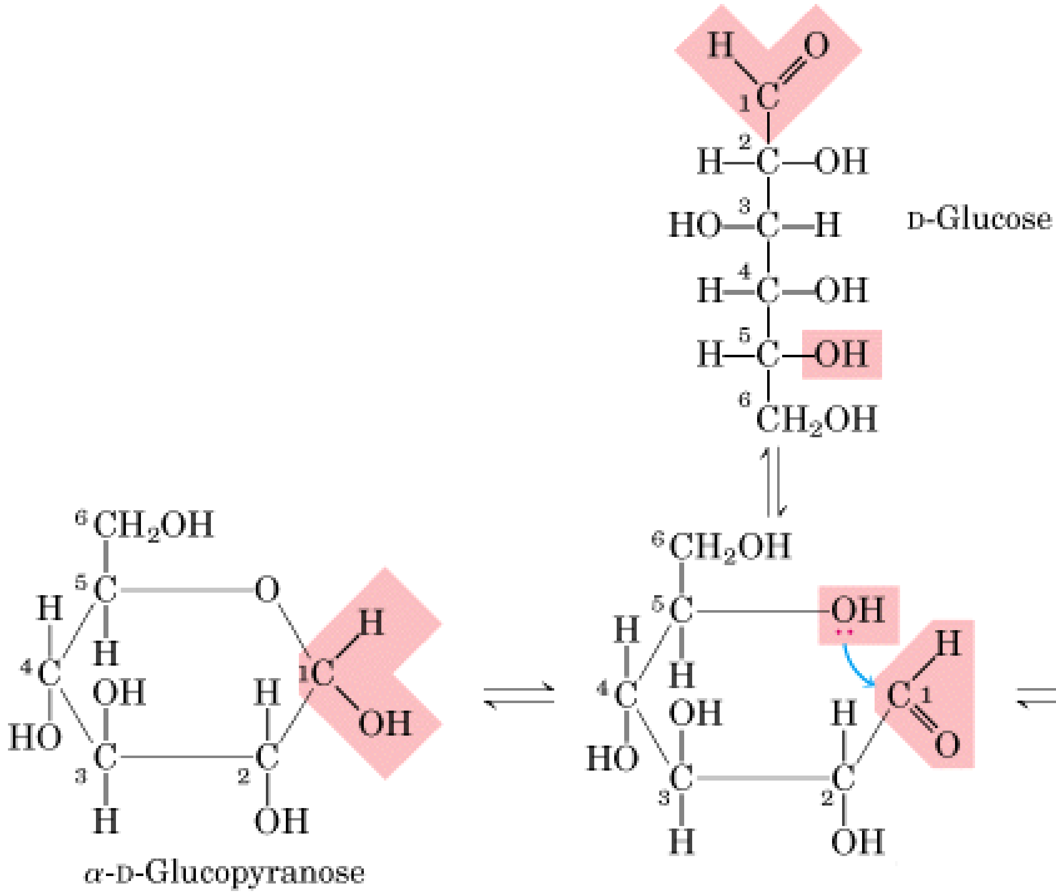
MUTAROTATION (H_2O, 20 °C)

$$\frac{(112-52)}{(112-19)} = 0.64 = 64\%\ \beta$$



α, pure *(crystallized in methanol)*
[α] = 112°

β, pure *(crystallized in acetic ac.)*
[α] = 19°

100 % α (+) 112° ←— +52° —→ (+) 19° 100 % β

β increases →

α increases ←

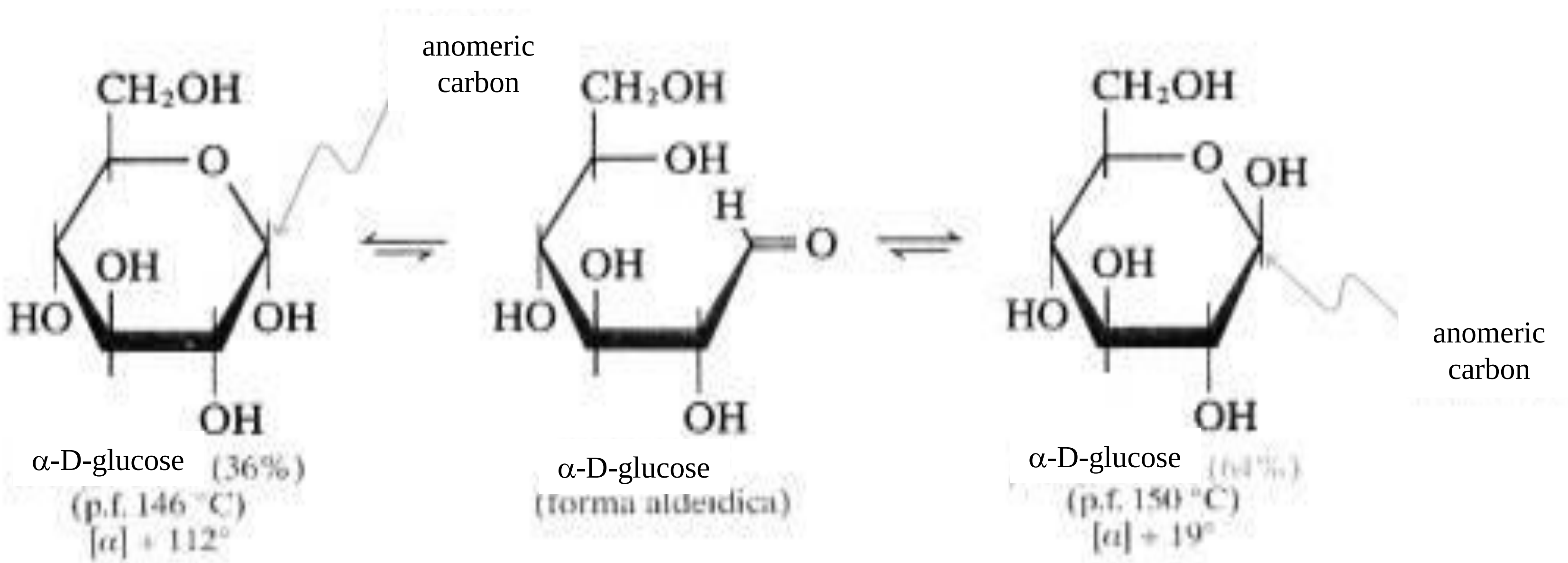
Glucose ; specific optical rotation

α , pure *(in methanol)*
[α] = 112°

β, pure *(in acetic ac.)*
[α] = 19°

Specific optical rotation [α] = +52

time = t_{eq}



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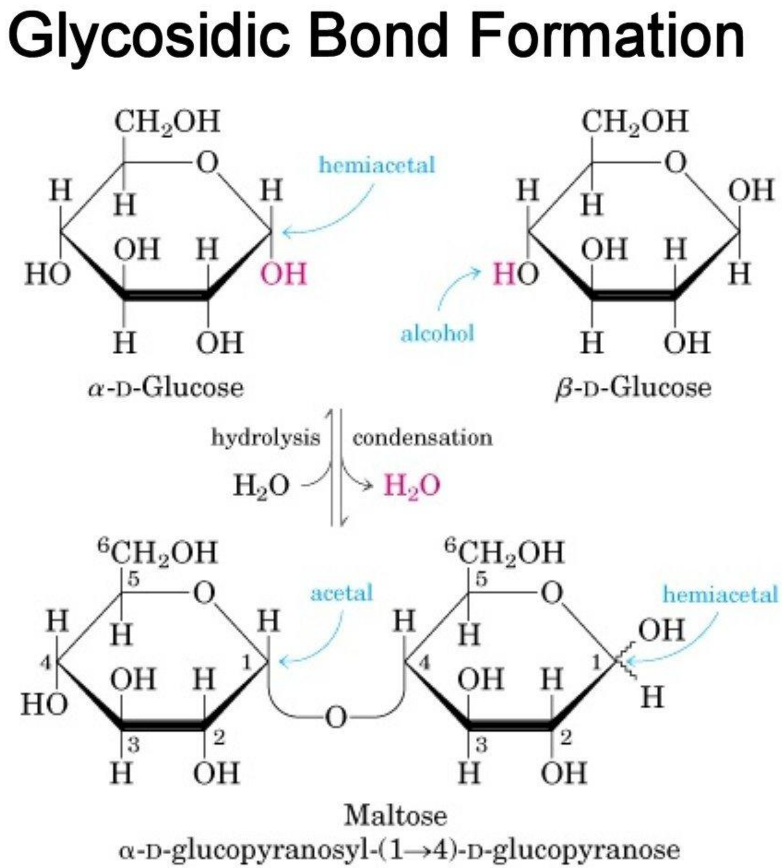
Glucides dimerization - polymerization

hemiacetal + hemiacetal ⇌ acetal + H_2O

O – bond (ether)



keto-enol tautomerization

Definition : two isomers are reciprocal **tautomers** if (within the molecule) there might occur the transfer of:

1) 1 π electron-pair
2) 1 H α

this typically occurs between :

1 *carbonyl* C & 1 α C (keto-enol)
1 *carbonyl* C & 1 α N (nucleic a. bases G, T, U)
1 *imine* N & 1 α N (nucleic a. bases A, C)

Involving

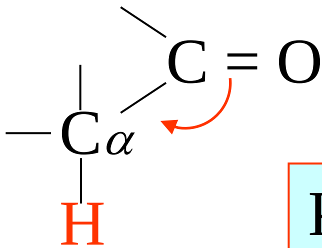
>C = O >C = N-H

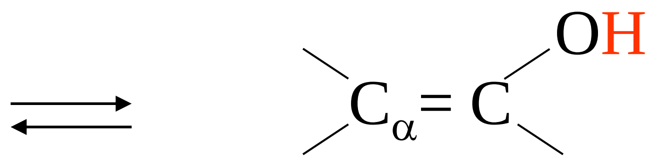
Carbonyl C **imine** N

Keto-enol Tautomerism

Properties of an αC

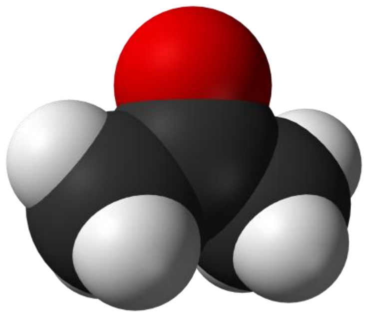
αC displays acidic properties !!





Keto-enol Tautomers

1 carbonilic C & 1 α C



Acetone *(di-methylketone, propanone)*

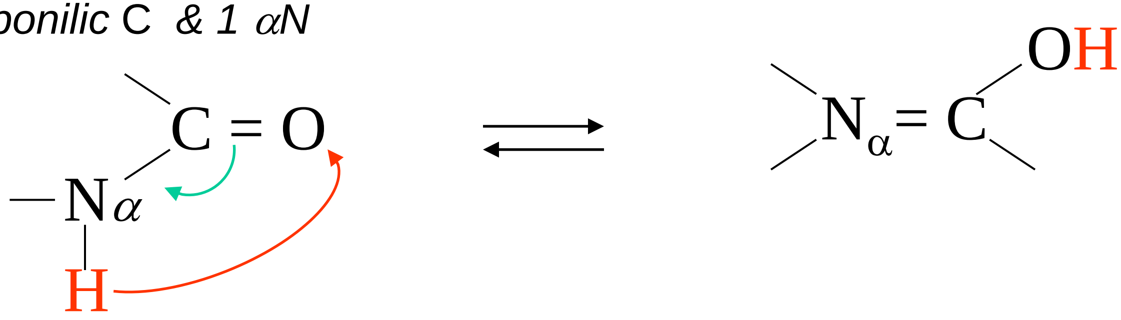
$$CH_3 - \overset{O}{\overset{\|}{C}} - CH_3 \rightleftharpoons CH_2 = \overset{OH}{\overset{|}{C}} - CH_3$$

keto　　　　enol

-NHα, displays acidic properties !

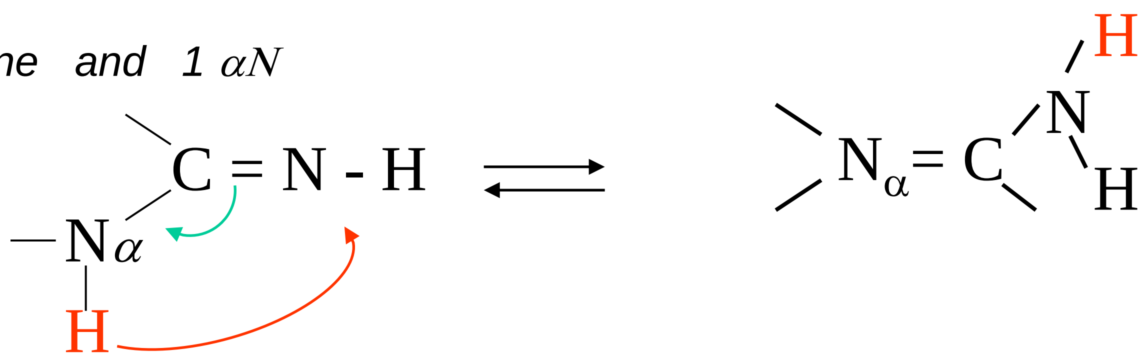
α position (C,N)
definition & properties

1 *carbonilic* C *& 1 αN*



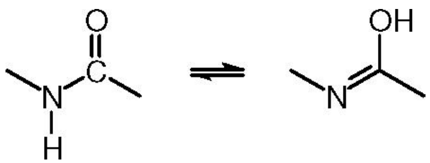
keto   enol

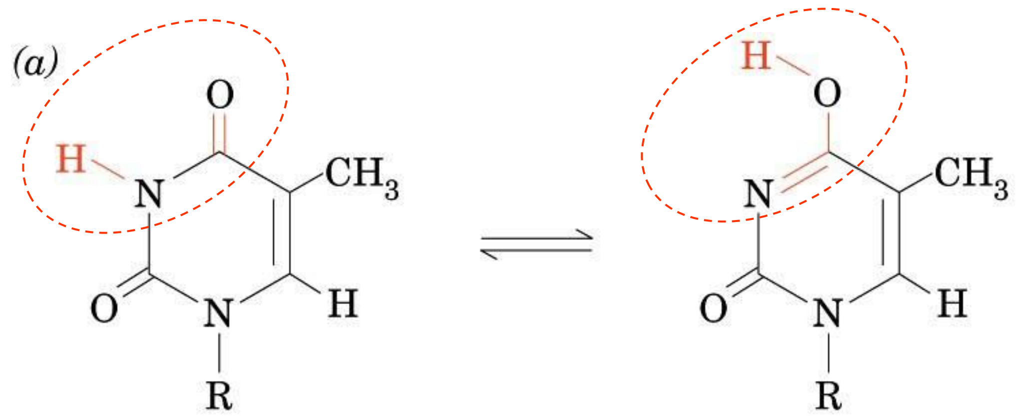
1 imine and 1 αN



imine *keto, lactam form*   amine *enol, lactim form*

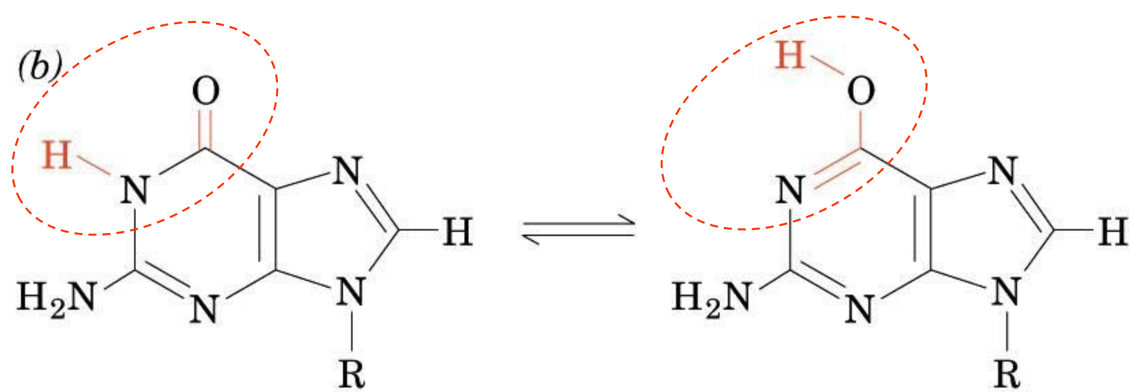
$>C=O$ & αN





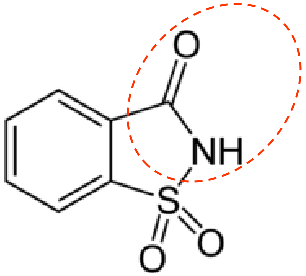
Thymine
(keto *or* lactam form)

Thymine
(enol *or* lactim form)



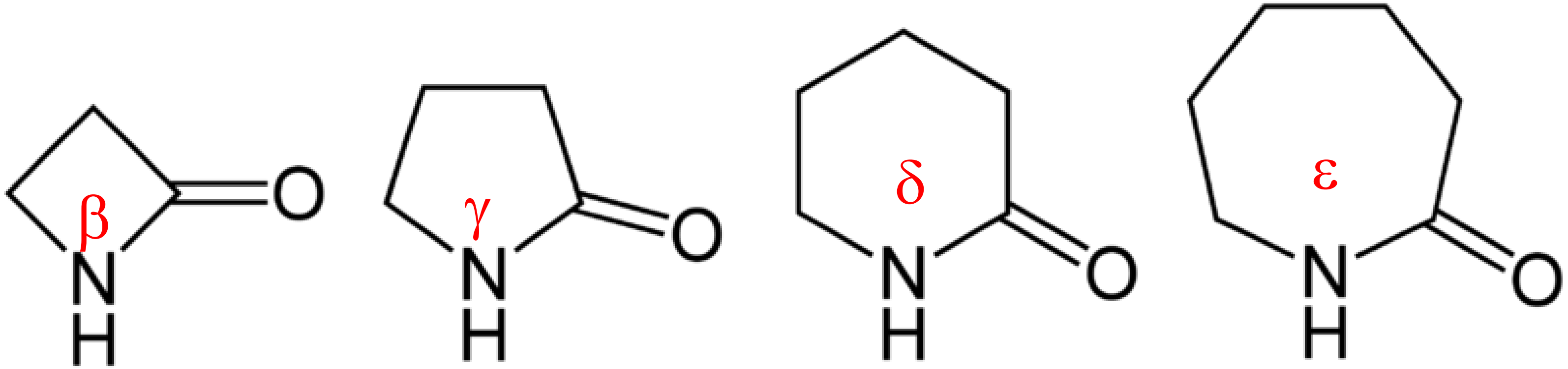
Guanine
(keto *or* lactam form)

Guanine
(enol *or* lactim form)



curiosity…
saccharin

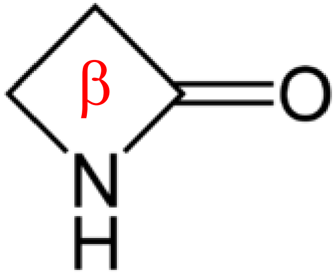
A curiosity… lactams

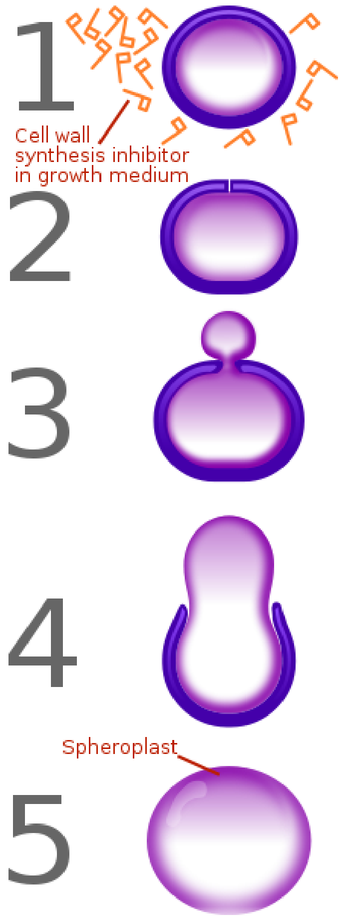


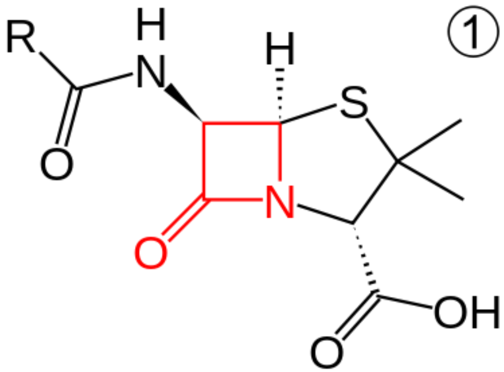
greek letter = n° of C in the ring out of carbonyl

β-lactames inhibit bacterial cell wall synthesis

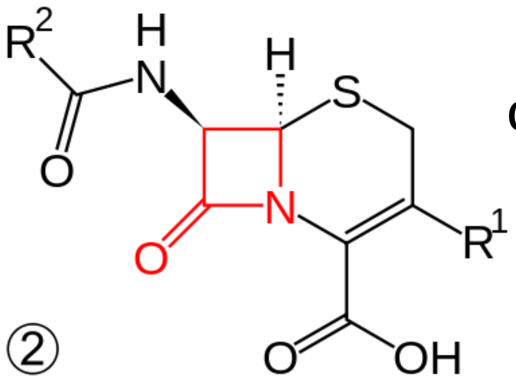
β-lactam ring







penicillins



cephalosporins

DNA bases: keto-enol tautomerism

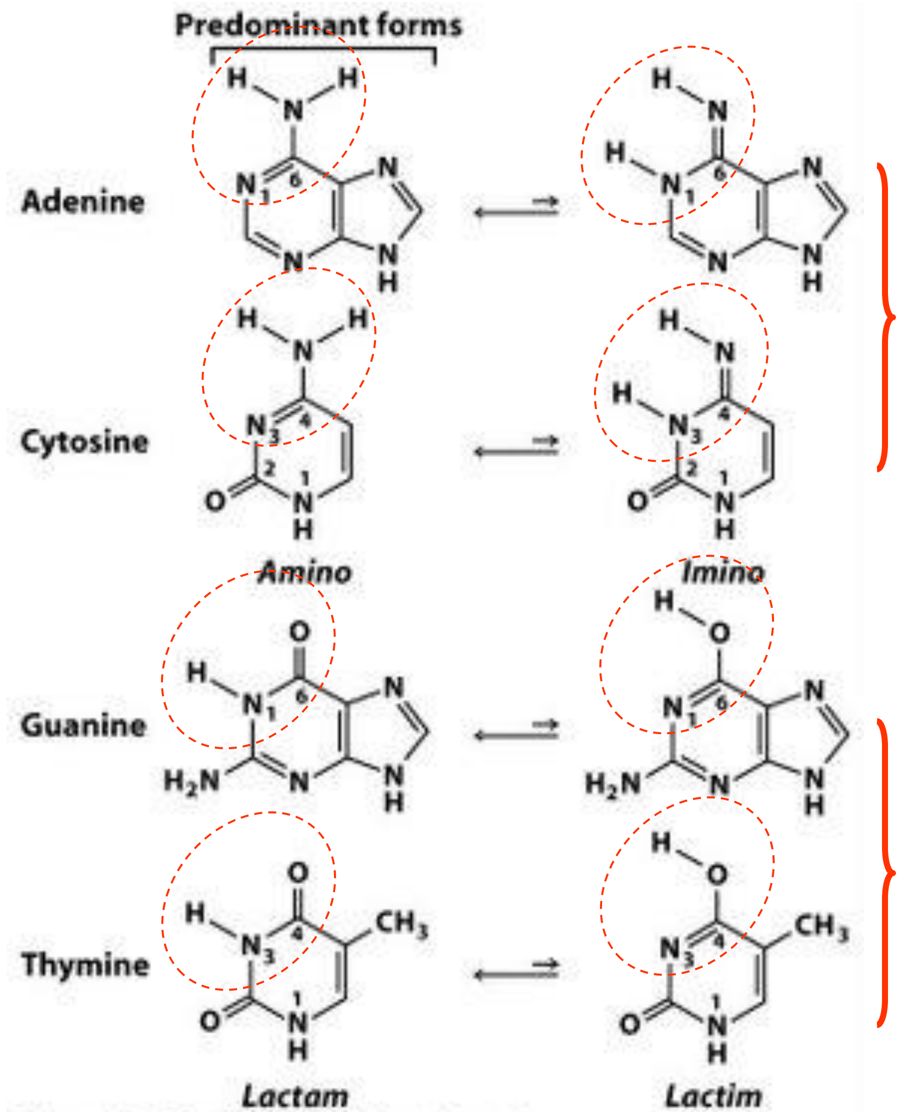


Figure 19-5 Principles of Biochemistry, 4/e

1 iminic N and 1 N α

1 carbonilic C and 1 N α

DNA bases : keto-enol tautomerism & H-bonds

a = H bond acceptor

d = H bond donor

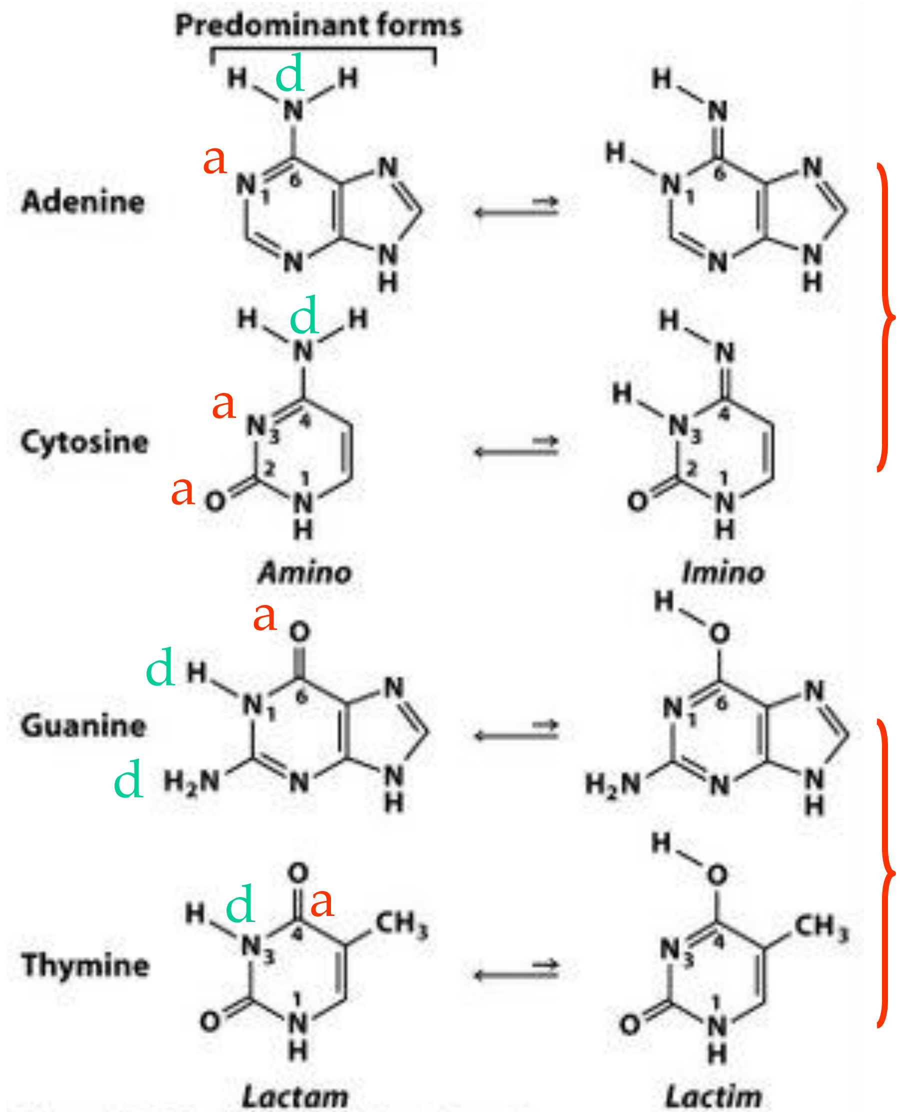
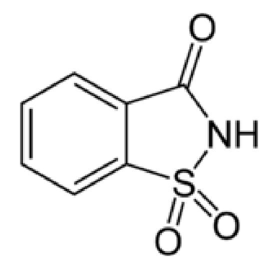


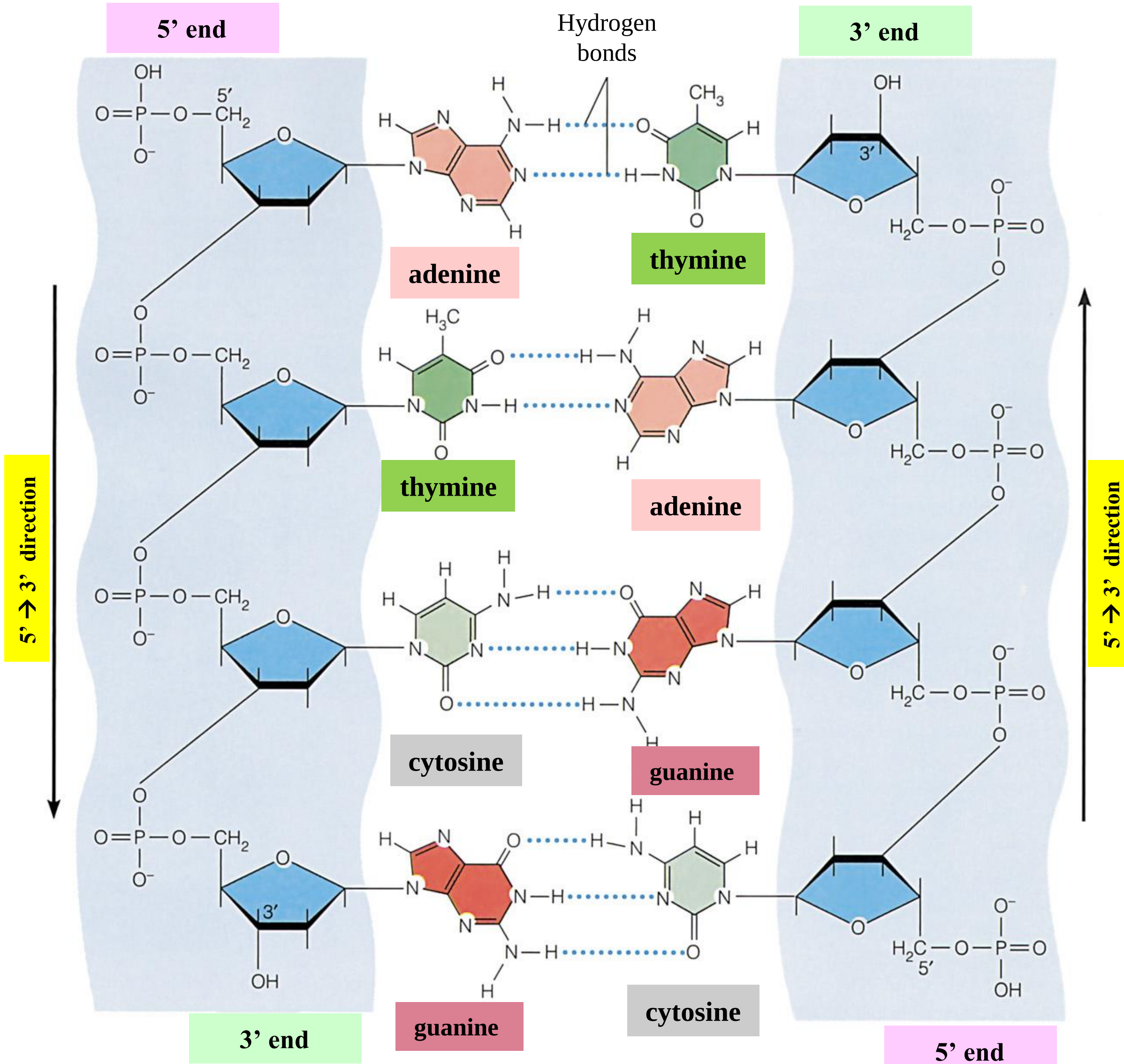
Figure 19-5 Principles of Biochemistry, 4/e

1 N iminic and 1 N α

1 C carbonylic and 1 N α

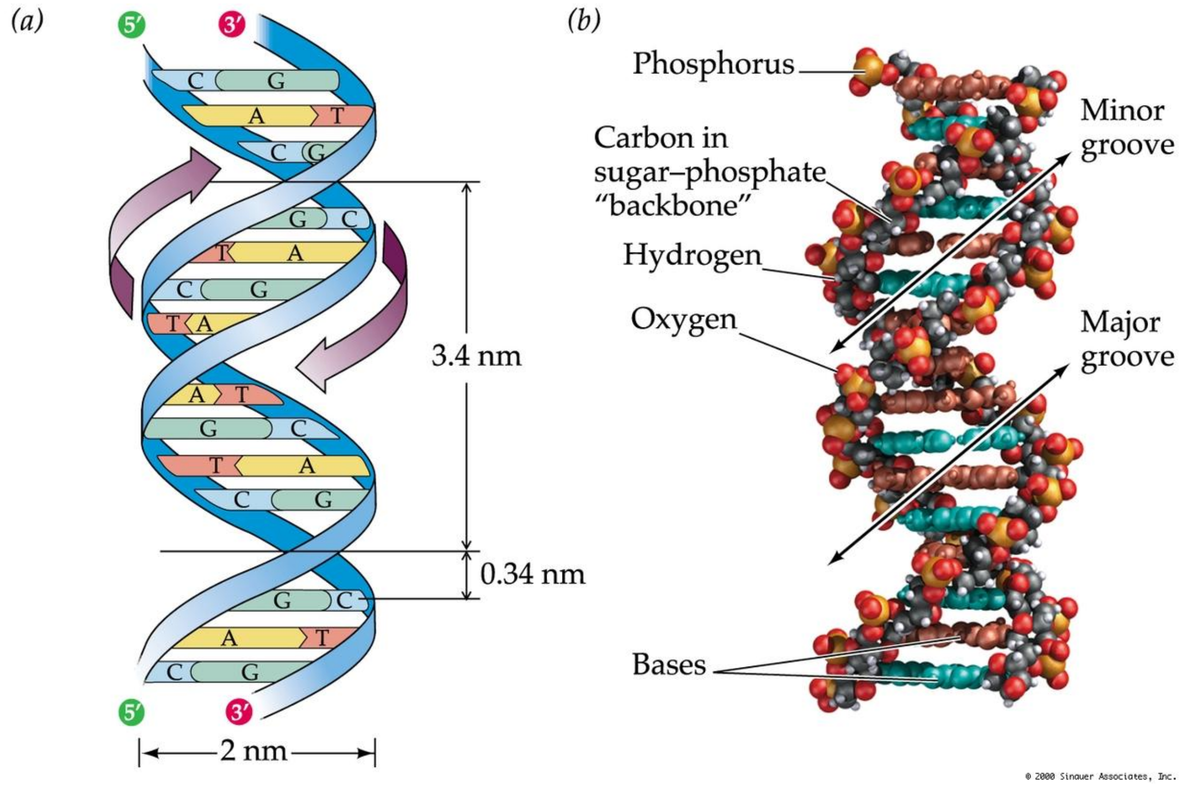


saccharin



5’ end
Hydrogen bonds
3’ end
adenine
thymine
thymine
adenine
cytosine
guanine
guanine
cytosine
3’ end
5’ end
5’ → 3’ direction
5’ → 3’ direction

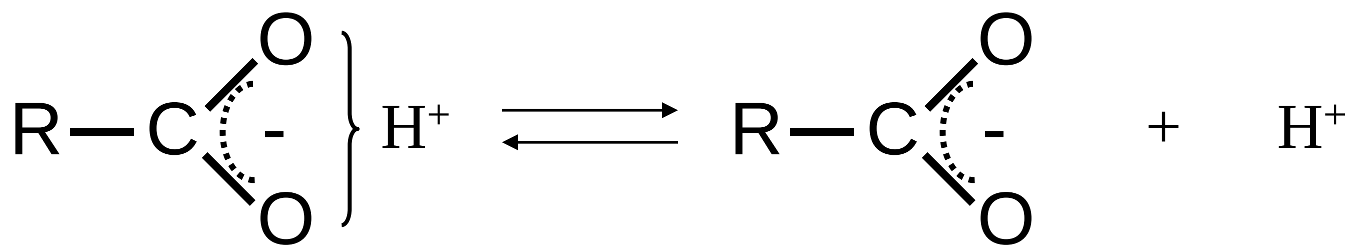
double helix (DNA)
OVERALL PICTURE



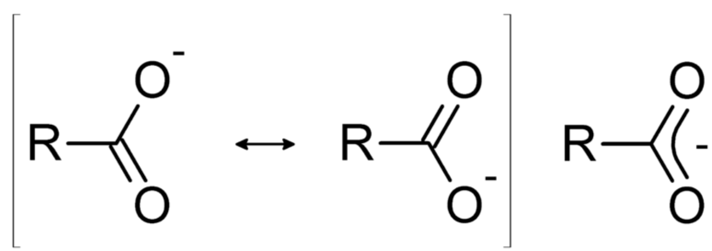
CARBOXYLIC ACIDS

CARBOXYLIC ACIDS

mono- di- poly-

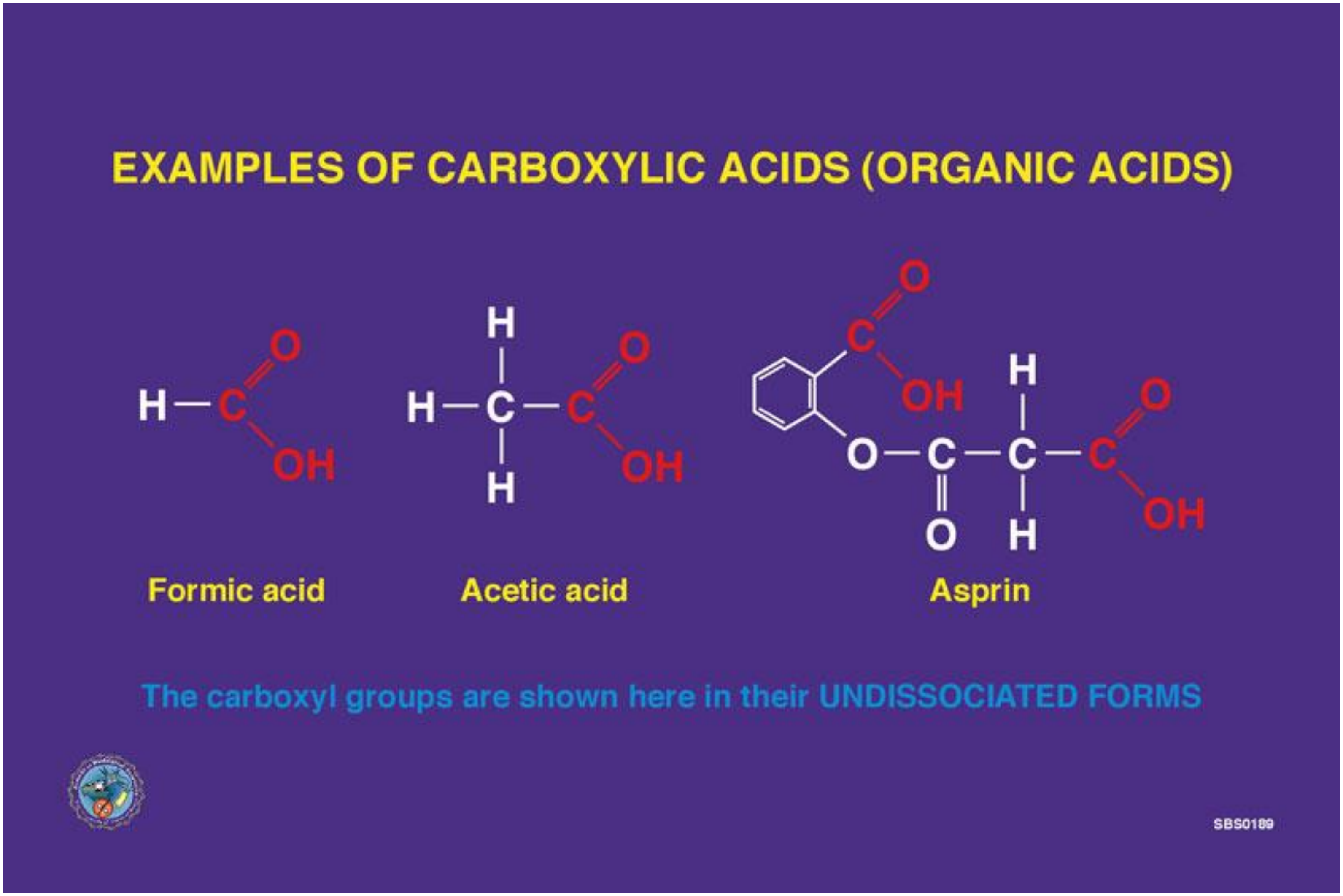


Carboxyl group Carboxylate ion



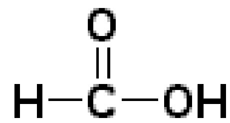
π bond resonance

Some organic acids



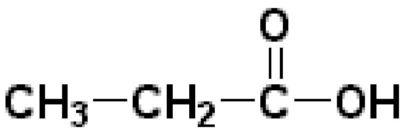
Others : watch R…! (inductive effects)

Ka = 1.77 x 10^{-4} pKa= 3.75



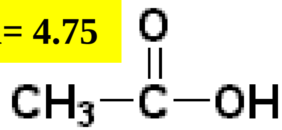
formic acid

Ka = 1.34 x 10^{-5} pKa= 4.87

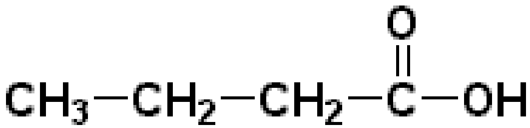


propionic acid

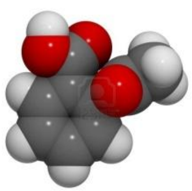
Ka = 1.8 x 10^{-5} pKa= 4.75

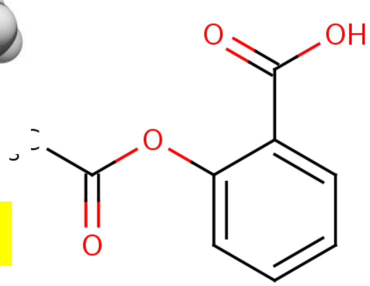


acetic acid

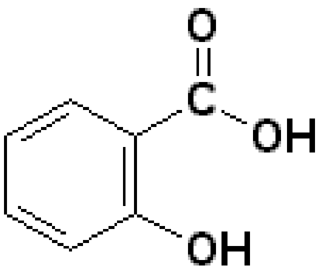


butyric acid



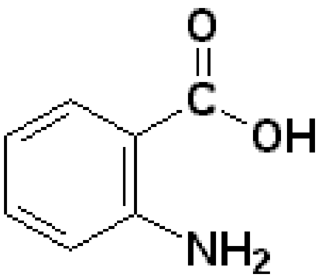


pKa= 3.5



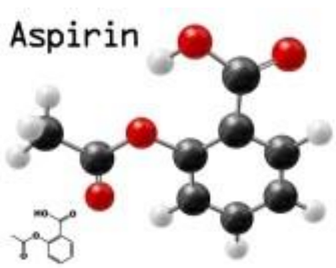
salicylic acid

Ka = 1.07 x 10^{-3} pKa= 1.96



anthranilic acid

Ka = 7,24 x 10^{-3} pKa= 2.14



aspirin (acetyl-salicylic acid)

Ka = 1.4 x 10^{-5} pKa= 4.84

Table 5-3

Dissociation Constants of Some Acids at 25 °C[a]

Acid[b]	HA	A^-	K_a	pK_a
Perchloric	$HClO_4$	ClO_4^-	$\sim10^{+8}$	~-8
Permanganic	$HMnO_4$	MnO_4^-	$\sim10^{+8}$	~-8
Chloric	$HClO_3$	ClO_3^-	$\sim10^{+3}$	~-3
Nitric	HNO_3	NO_3^-		
Hydrobromic	HBr	Br^-		
Hydrochloric	HCl	Cl^-		
Sulfuric (1)	H_2SO_4	HSO_4^-		
Hydrated proton or protonated solvent	H^+	H_2O(solvent)	1.00	0.00
Trichloroacetic	CCl_3COOH	CCl_3COO^-	2×10^{-1}	0.70
Oxalic (1)	HOOC—COOH	$HOOC—COO^-$	5.9×10^{-2}	1.23
Dichloroacetic	$CHCl_2COOH$	$CHCl_2COO^-$	3.32×10^{-2}	1.48
Sulfurous (1)	H_2SO_3	HSO_3^-	1.54×10^{-2}	1.81
Sulfuric (2)	HSO_4^-	SO_4^{2-}	1.20×10^{-2}	1.92
Phosphoric (1)	H_3PO_4	$H_2PO_4^-$	7.52×10^{-3}	2.12
Bromoacetic	$CH_2BrCOOH$	CH_2BrCOO^-	2.05×10^{-3}	2.69
Malonic (1)	$HOOC—CH_2—COOH$	$HOOC—CH_2—COO^-$	1.49×10^{-3}	2.83
Chloroacetic	$CH_2ClCOOH$	CH_2ClCOO^-	1.40×10^{-3}	2.85
Nitrous	HNO_2	NO_2^-	4.6×10^{-4}	3.34
Hydrofluoric	HF	F^-	3.53×10^{-4}	3.45
Formic	HCOOH	$HCOO^-$	1.77×10^{-4}	3.75
Benzoic	C_6H_5COOH	$C_6H_5COO^-$	6.46×10^{-5}	4.19
Oxalic (2)	$HOOC—COO^-$	$^-OOC—COO^-$	6.4×10^{-5}	4.19
Acetic	CH_3COOH	CH_3COO^-	1.76×10^{-5}	4.75
Propionic	CH_3CH_2COOH	$CH_3CH_2COO^-$	1.34×10^{-5}	4.87
Malonic (2)	$HOOC—CH_2—COO^-$	$^-OCC—CH_2—COO^-$	2.03×10^{-6}	5.69
Carbonic (1)	$CO_2 + H_2O$	HCO_3^-	4.3×10^{-7}	6.37
Sulfurous (2)	HSO_3^-	SO_3^{2-}	1.02×10^{-7}	6.91
Hydrogen sulfide (1)	H_2S	HS^-	9.1×10^{-8}	7.04
Phosphoric (2)	$H_2PO_4^-$	HPO_4^{2-}	6.23×10^{-8}	7.21
Ammonium ion	NH_4^+	NH_3	5.6×10^{-10}	9.25
Hydrocyanic	HCN	CN^-	4.93×10^{-10}	9.31
Silver ion	$Ag^+ + H_2O$	AgOH	9.1×10^{-11}	10.04
Carbonic (2)	HCO_3^-	CO_3^{2-}	5.61×10^{-11}	10.25
Hydrogen peroxide	H_2O_2	HO_2^-	2.4×10^{-12}	11.62
Hydrogen sulfide (2)	HS^-	S^{2-}	1.1×10^{-12}	11.96
Phosphoric (3)	HPO_4^{2-}	PO_4^{3-}	2.2×10^{-13}	12.67
Water[c]	H_2O	OH^-	1.8×10^{-16}	15.76

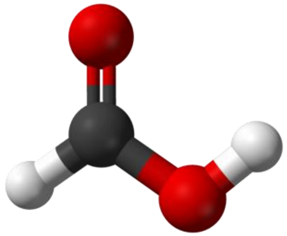
[a]HA is the acid form, with acid strength decreasing down the table. A^- is the conjugate base, with base strength increasing down the table. The equilibrium is $HA \rightleftarrows H^+ + A^-$ and the equilibrium-constant expression is

$$K_a = \frac{[H^+][A^-]}{[HA]} \qquad pK_a = -\log_{10} K_a$$

[b]The notation (1) indicates a first dissociation or proton-transfer reaction; (2) indicates a second dissociation; and (3) indicates a third dissociation.

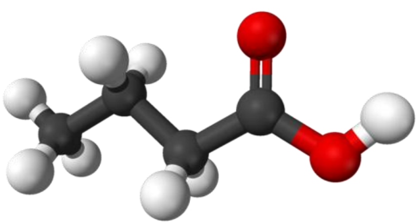
[c]This K_a value for water explicitly uses $[H_2O] = 55.6$ moles liter^{-1} in the denominator, for the sake of consistency with the other entries in the table. The standard K_w is obtained by noting that $55.6 \times 1.8 \times$

Methanoic *vs* butanoic acid



pKa = 3.74

$Ka = 10^{-3.74} = 1.8 \times 10^{-4}$

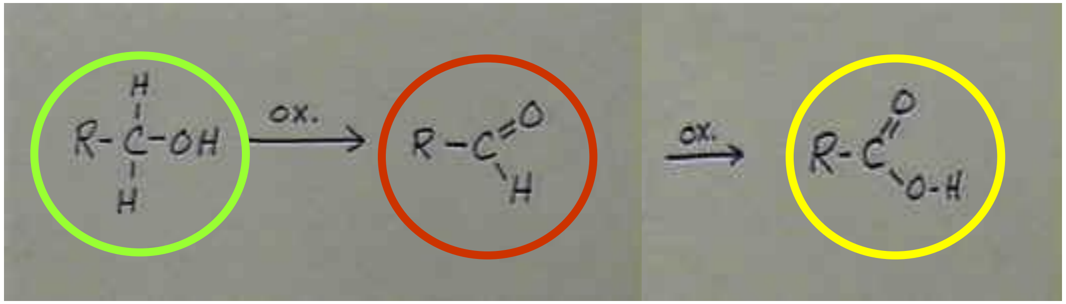


pKa = 4.82

$Ka = 10^{-4.82} = 1.5 \times 10^{-5}$

Most common reactions

Oxidation



alcohol aldehyde acid

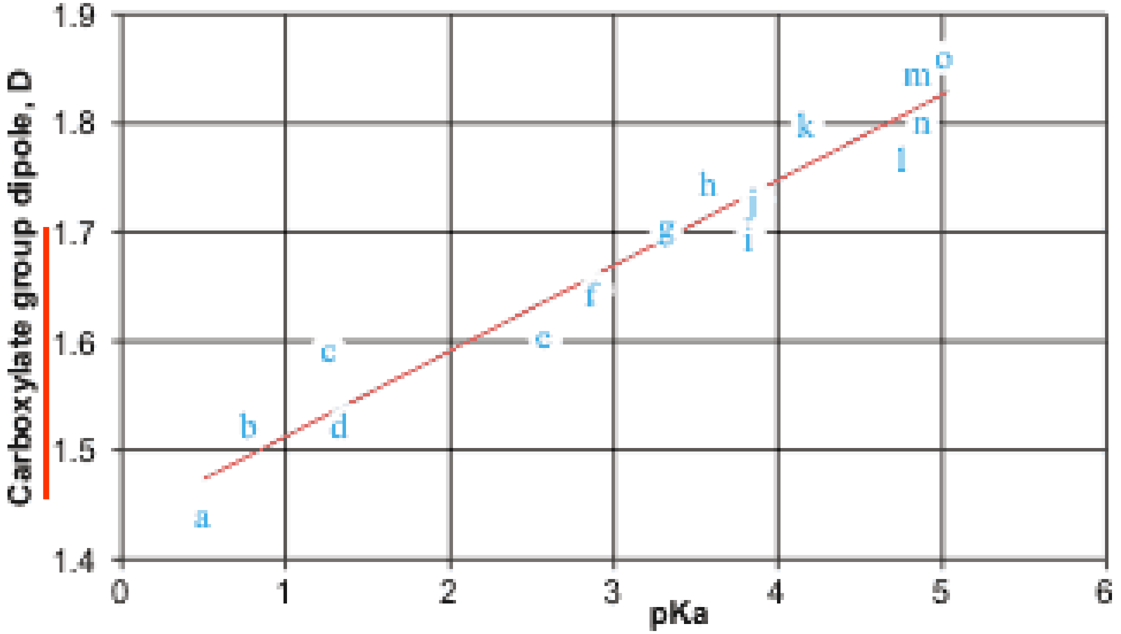
Reduction

mono-carboxylic acids

HCOOH	formic acid	methanoic acid
CH_3COOH	acetic	ethanoic
CH_3CH_2COOH	propionic	propanoic
$CH_3CH_2CH_2COOH$	butyric	butanoic
$CH_3(CH_2)_4COOH$	hexanoic	capronic
$CH_3(CH_2)_6COOH$	octanoic	caprylic
$CH_3(CH_2)_8COOH$	decanoic	caprynic
C_6H_5COOH	benzoic	

Inductive effects & acidity (*mono-carboxylic*)

Carboxylic Acid	**Structure**	**pKa**
Ethanoic acid	CH_3-COOH	4.7
Propanoic acid	CH_3CH_2-COOH	4.9
Fluoroethanoic acid	CH_2F-COOH	2.6
Chloroethanoic acid	CH_2Cl-COOH	2.9
Dichloroethanoic acid	$CHCl_2$-COOH	1.3
Trichloroethanoic acid	CCl_3-COOH	0.9
Nitroethanoic acid	O_2NCH_2-COOH	1.7



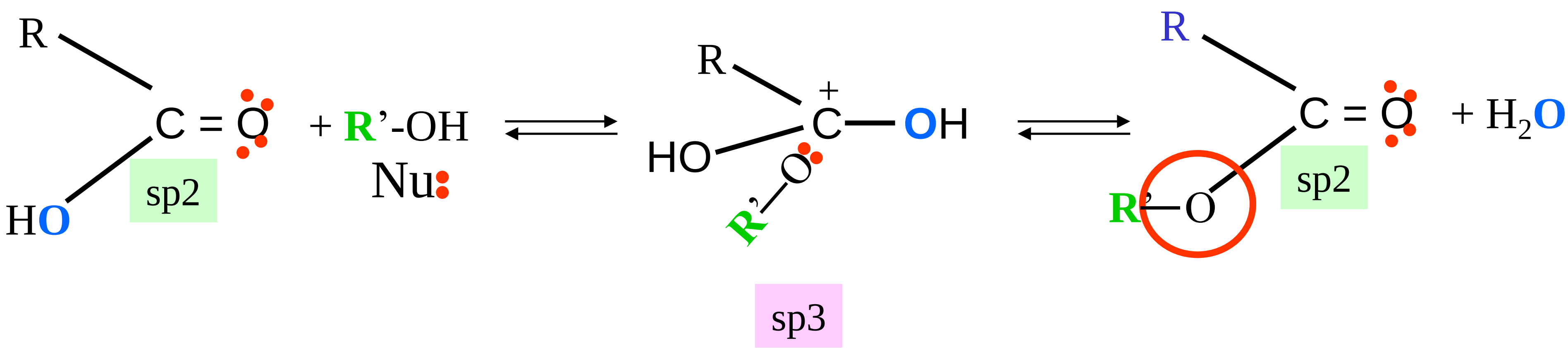
acidity high

acidity low

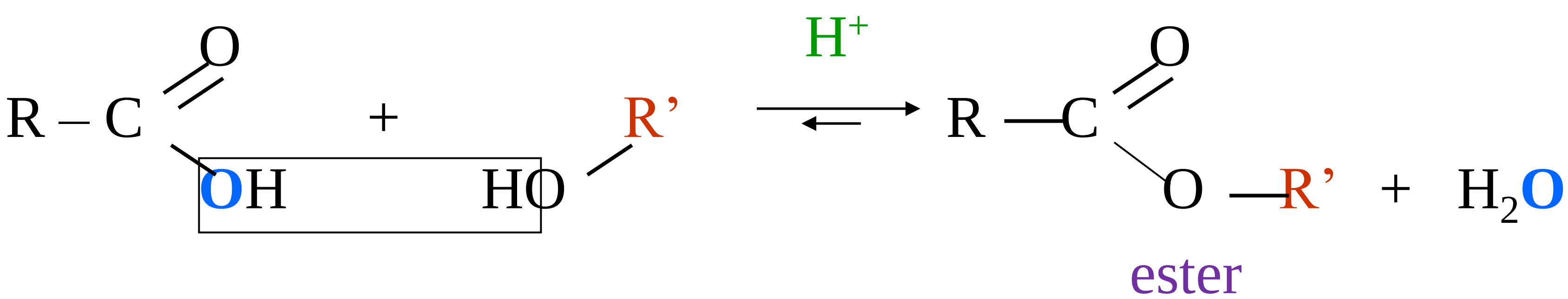
di-carboxylic acids (K_{a1} *vs* K_{a2}!)

		K_{a1}	K_{a2}
HOOC – COOH	oxalic *ac*	5.4×10^{-2}	5.4×10^{-5}
HOOC-CH_2-COOH	malonic	1.4×10^{-3}	0.2×10^{-5}
HOOC-$(CH_2)_2$-COOH	succinic	6.2×10^{-5}	0.2×10^{-5}
HOOC-$(CH_2)_3$-COOH	glutaric	4.6×10^{-5}	0.4×10^{-5}

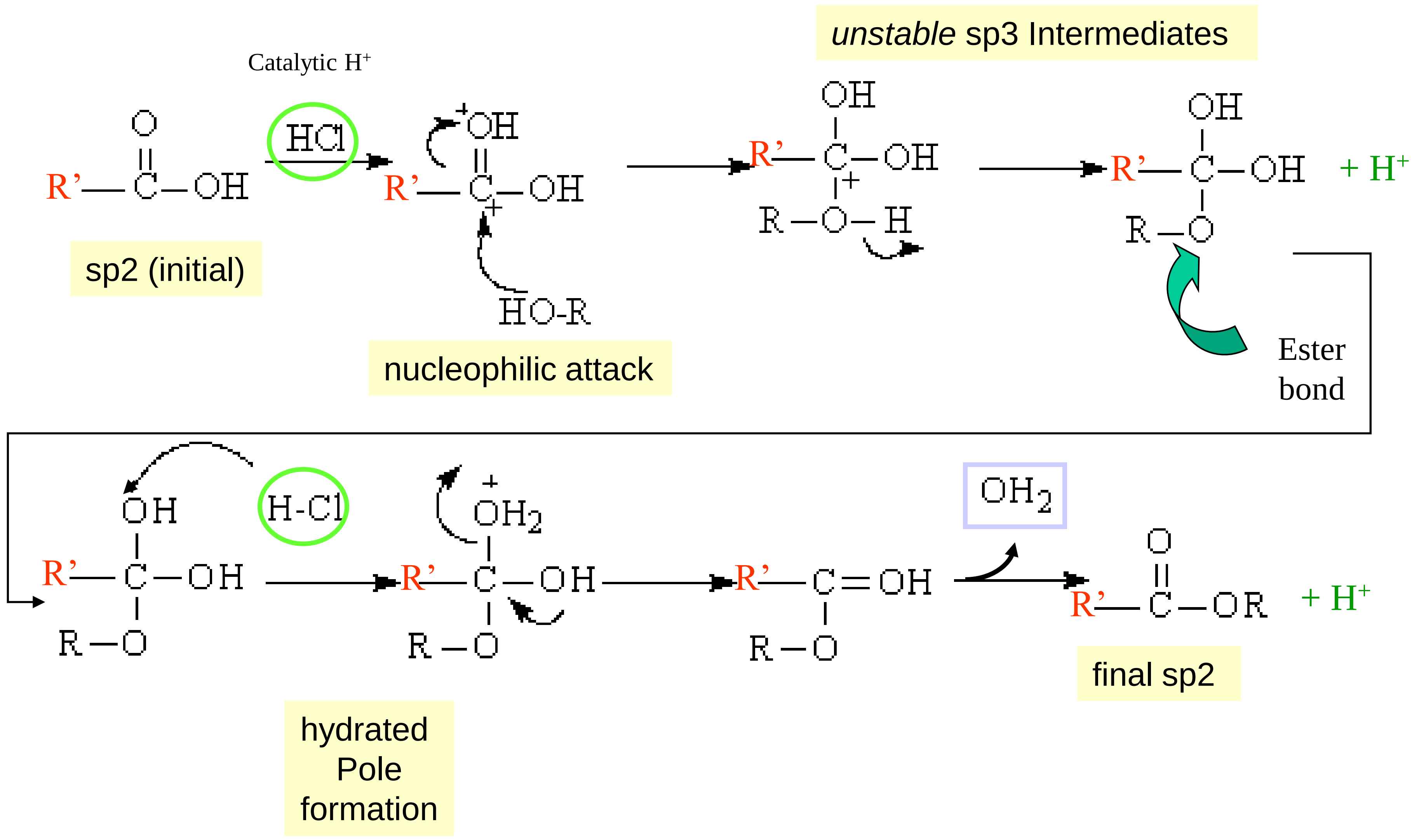
Fischer *Esterification*



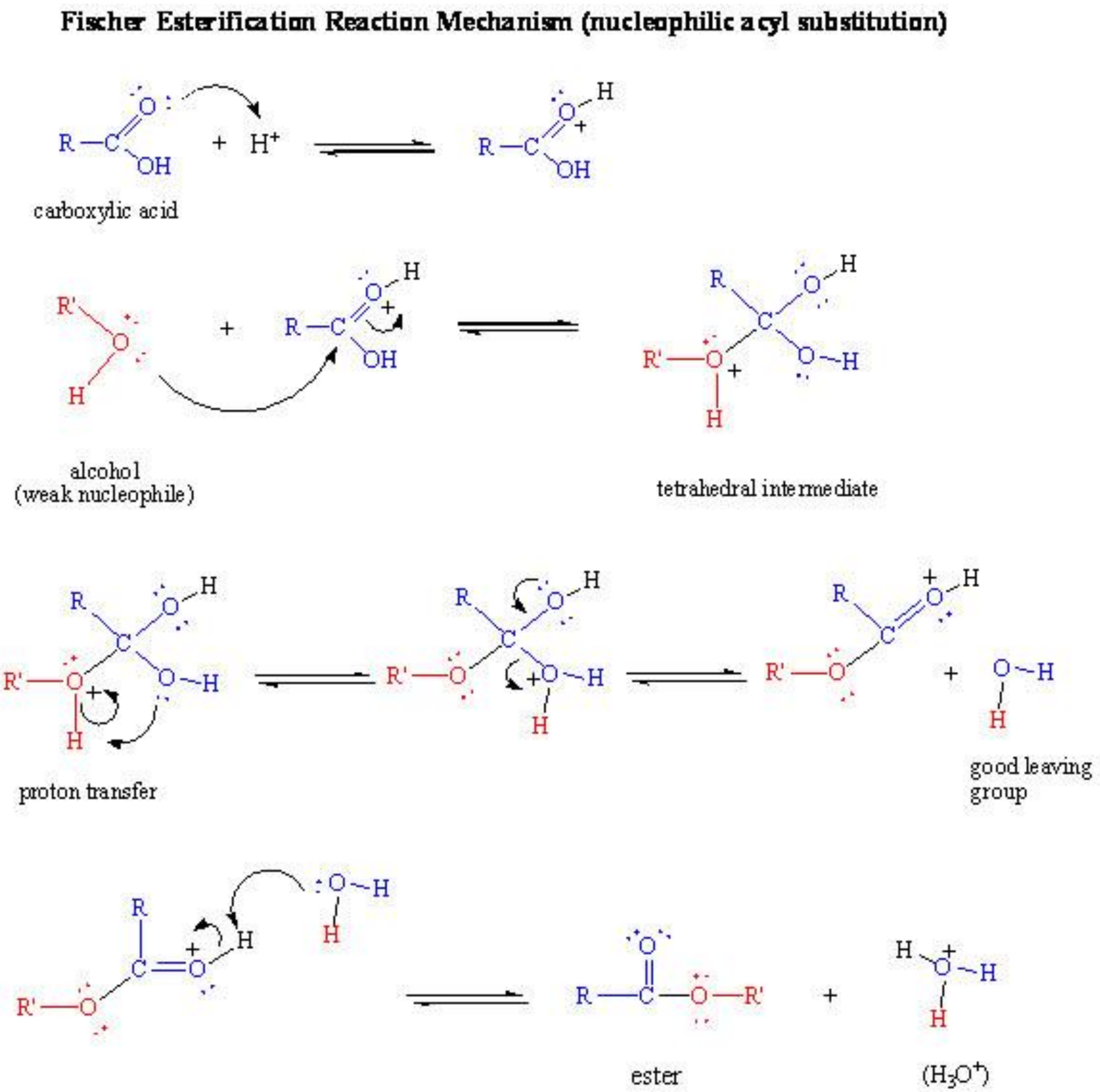
acid + alcohol ⇌ intermediate ⇌ ester + H_2O



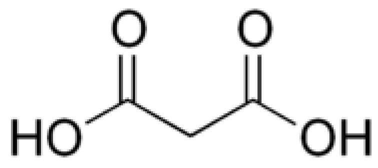
The mechanism (Fischer)

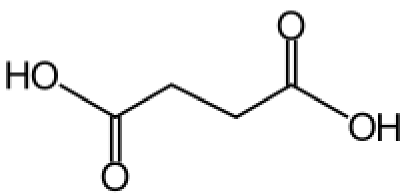


Fischer mechanism : relevant steps



dicarboxylic (*inductive effects*)

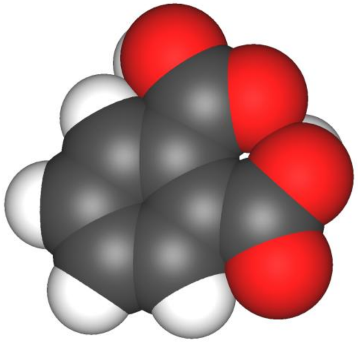


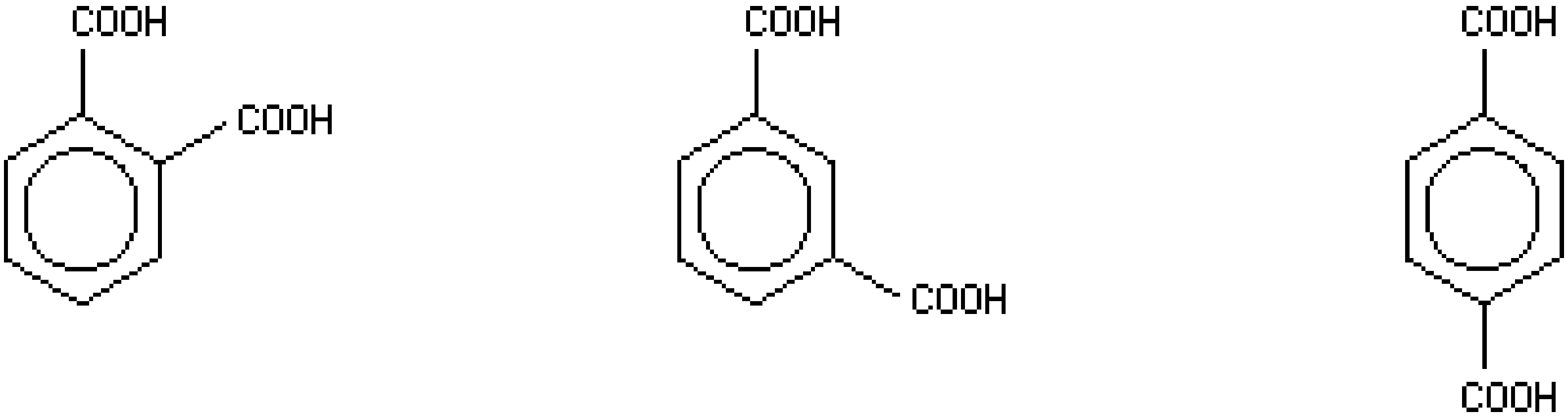


Oxalic ac.	Malonic ac.	Succinic ac.
HOOC – COOH	HOOC – CH_2 – COOH	HOOC – $(CH_2)_2$ – COOH
pK_{a1} 1.27 pK_{a2} 4.26	pK_{a1} 2.87 pK_{a2} 5.70	pK_{a1} 4.25 pK_{a2} 5.64

di-benzoic acids

Acido ftalico

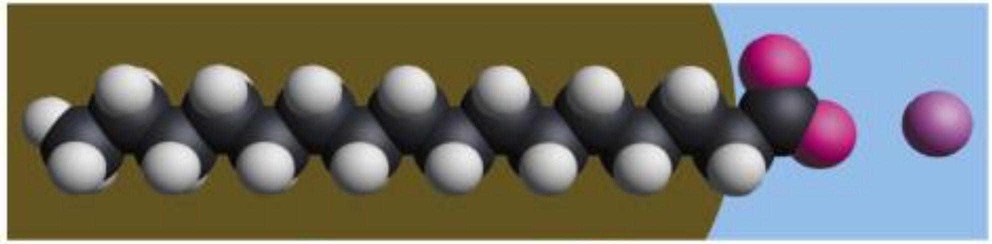


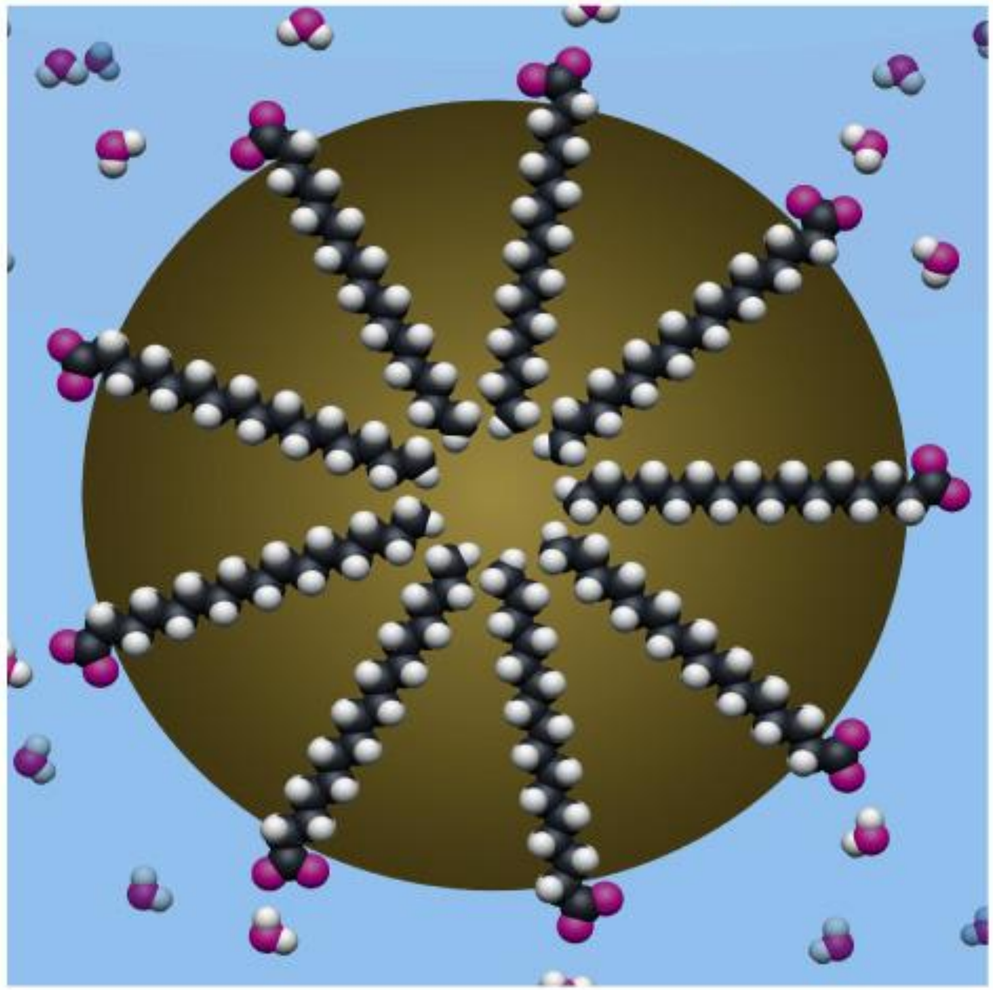


	orto	meta	para
pK_{a1}	2.95	3.62	3.54
pK_{a2}	5.41	4.61	4.45

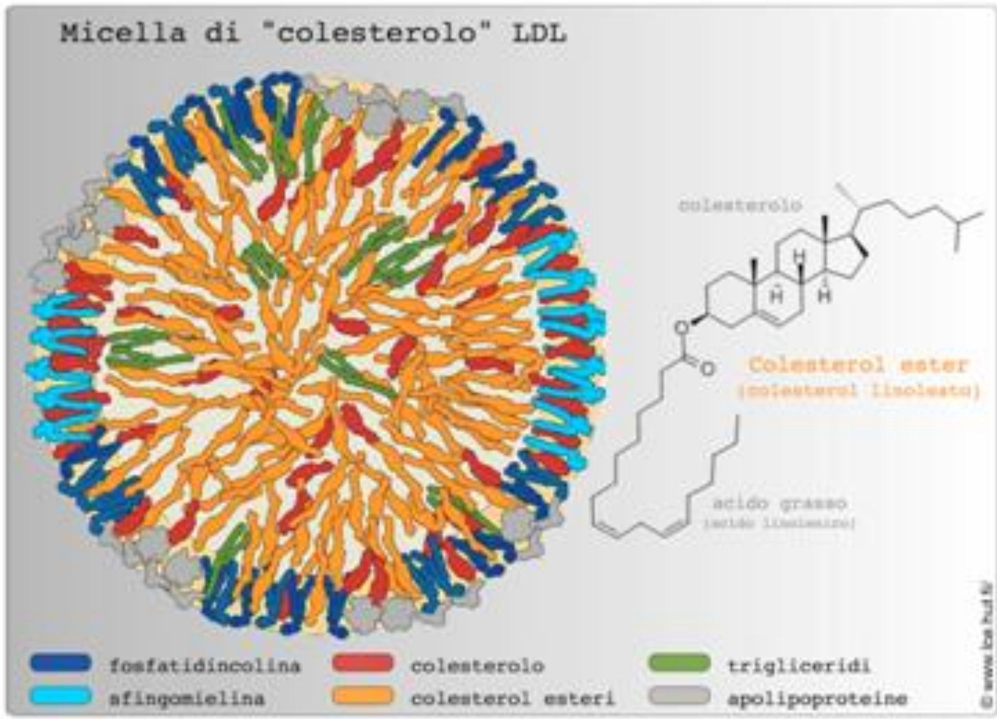
orto meta para

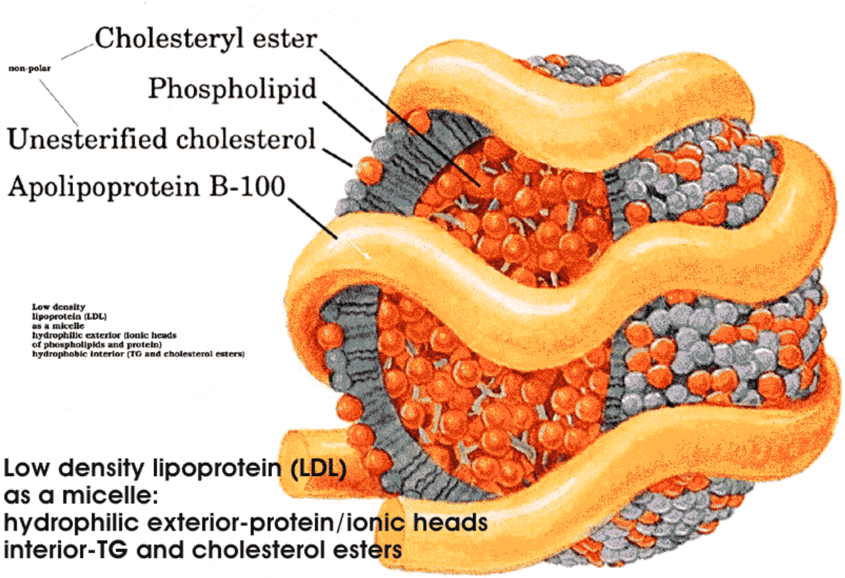
Fatty acid salts & detergents


(a)


(b)

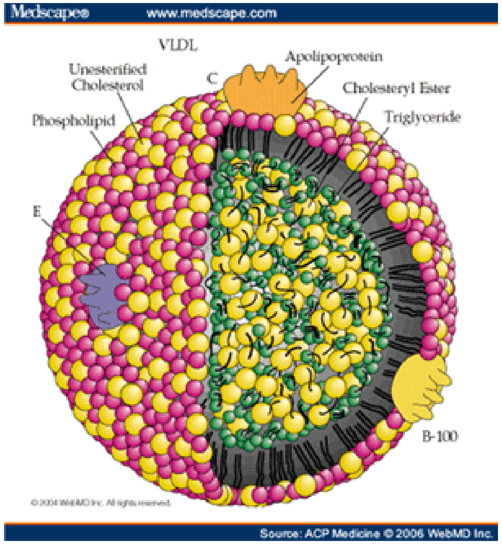
LIPIDI


Micella di "colesterolo" LDL
colesterolo
Colesterol ester
(colesterol linoleato)
acido grasso
fosfatidincolina
sfingomielina
colesterolo
colesterol esteri
trigliceridi
apolipoproteine

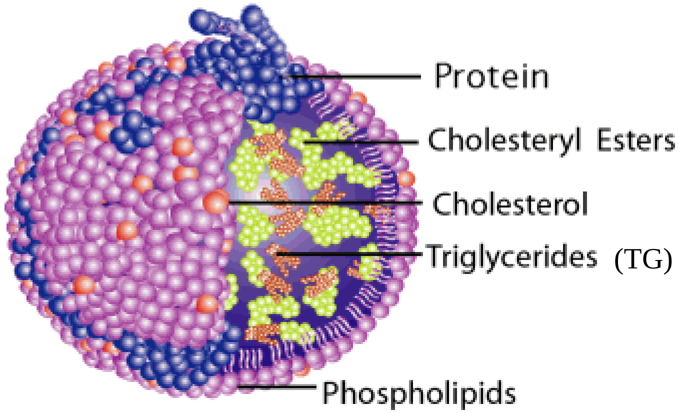


LDL

- All lipoprotein particles are heterogeneous
  - Within classes
  - Within each patient
  - Between patients
- Particle composition, not cholesterol concentration, determines metabolic function



VLDL



HDL

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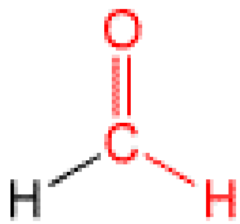
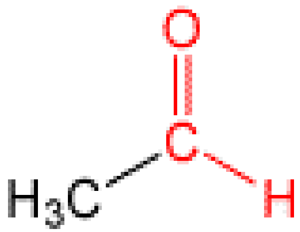
Aldehydes Nomenclature

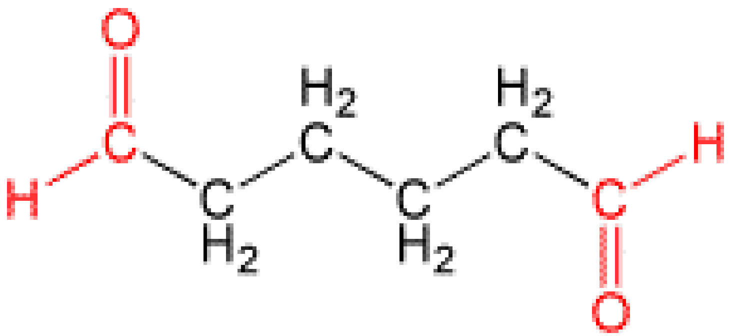
alk…*ane* → *…*anal* (*but see also common/familiar names)*



- formaldehyde
- oxomethane
- methanal



- acetaldehyde
- 1-ethanal



- 1-6-hexandial

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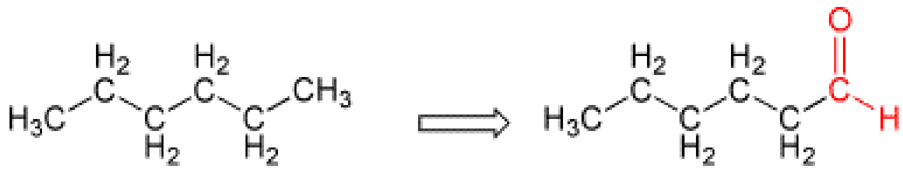
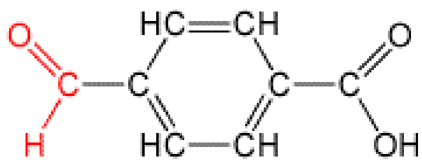
Aldehydes Nomenclature

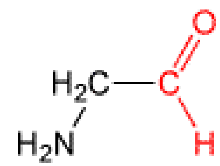
alk…*ane* → *…*anal*   *(but see also common/familiar names)*



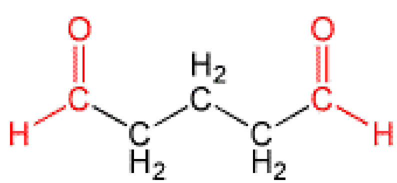
hexane   hexanal



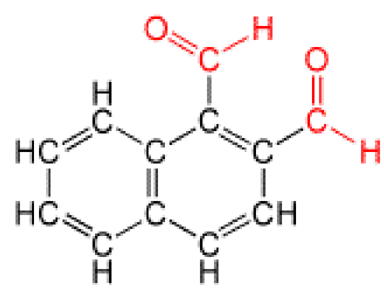
p-formylphenylacetic acid



aminoacetaldehyde



1,5-pentandial
(glutaraldehyde)



1,2-naphthalenedicarbaldehyde

Try to figure out the 3D organization of the molecule !

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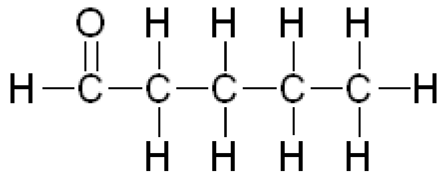
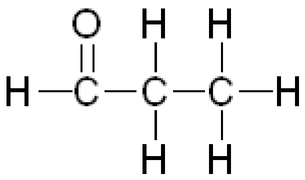
examples

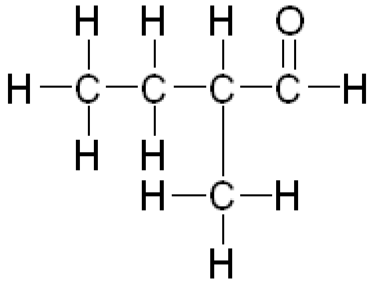
Nomenclature



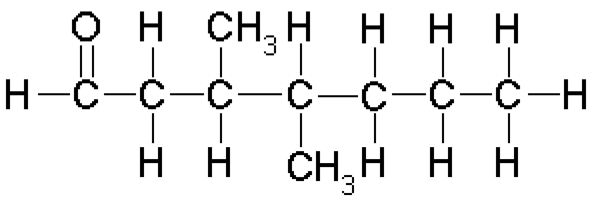
Heptanal



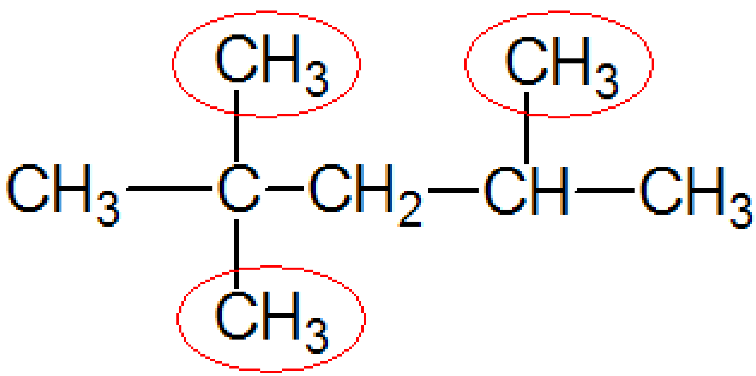
Propanal

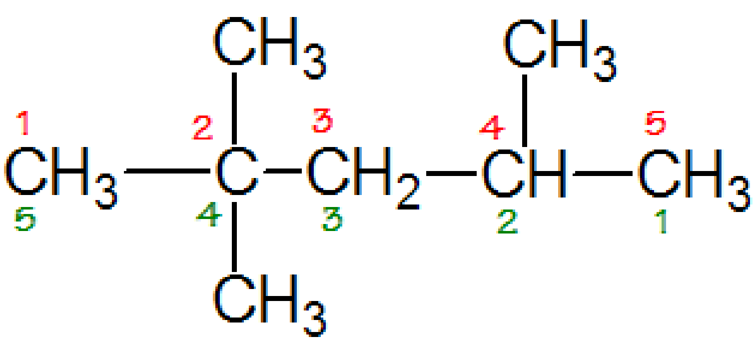


2-methyl-butanal



3,4-di-methyl-heptanal





2,2,4 tri-methyl-pentane OK