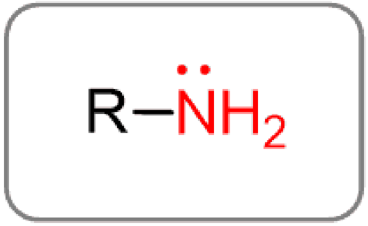
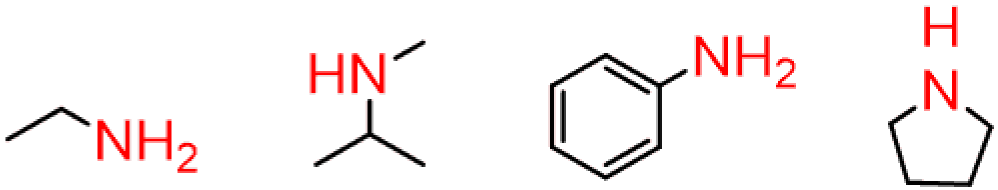
Functional Groups

Functional groups are specific groupings of atoms within molecules that have their own characteristic properties, regardless of the other atoms present in a molecule.

Amines

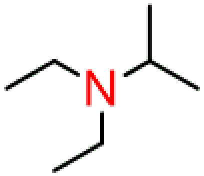


$R-\ddot{N}H_2$



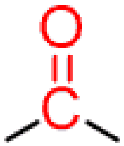
1°

2°



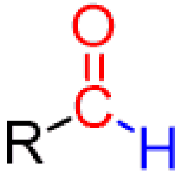
3°

Carbonyl-containing functional groups



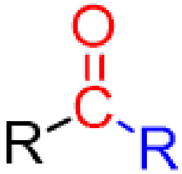
$\overset{O}{\overset{\|}{C}}$

Carbonyl



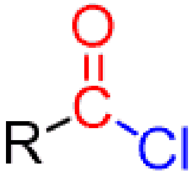
$R-\overset{O}{\overset{\|}{C}}-H$

Aldehydes



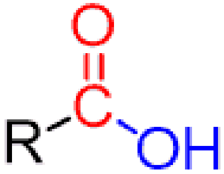
$R-\overset{O}{\overset{\|}{C}}-R$

Ketones



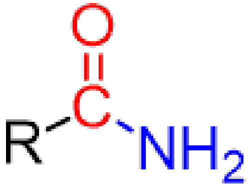
$R-\overset{O}{\overset{\|}{C}}-Cl$

Acid chlorides



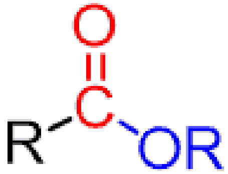
$R-\overset{O}{\overset{\|}{C}}-OH$

Carboxylic acids



$R-\overset{O}{\overset{\|}{C}}-NH_2$

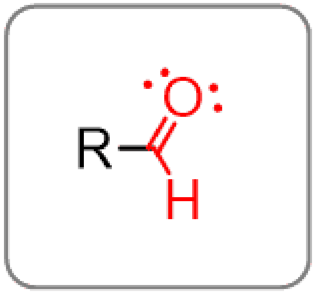
Amides

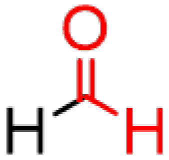


$R-\overset{O}{\overset{\|}{C}}-OR$

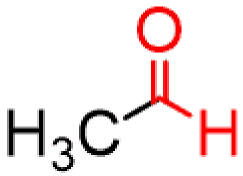
Esters

Aldehydes

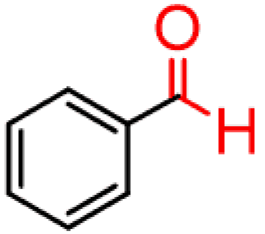




Formaldehyde

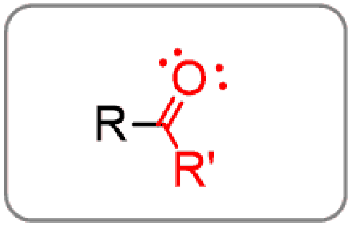


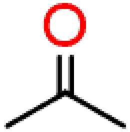
Acetaldehyde



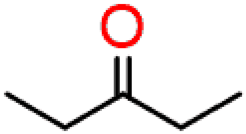
Benzaldehyde

Ketones

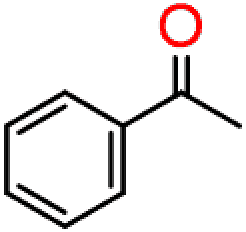




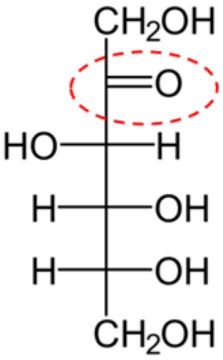
Acetone



Diethyl ketone



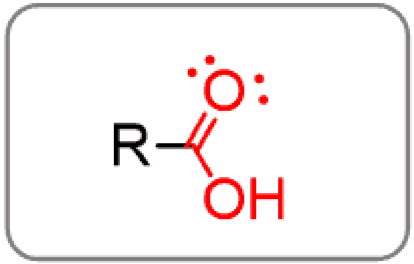
Acetophenone

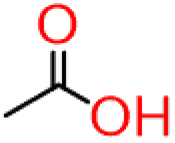


Fructose

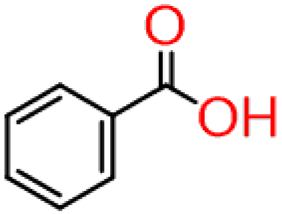
Acetone

Carboxylic acids

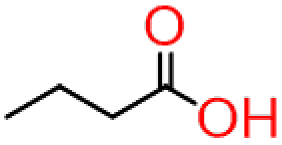




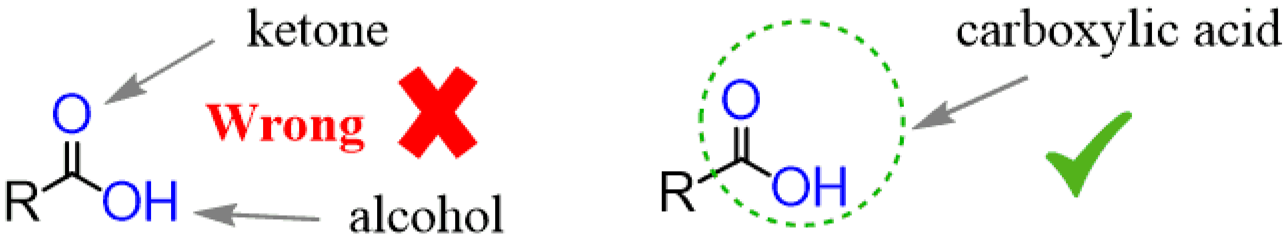
Acetic acid



Benzoic acid



Butanoic acid

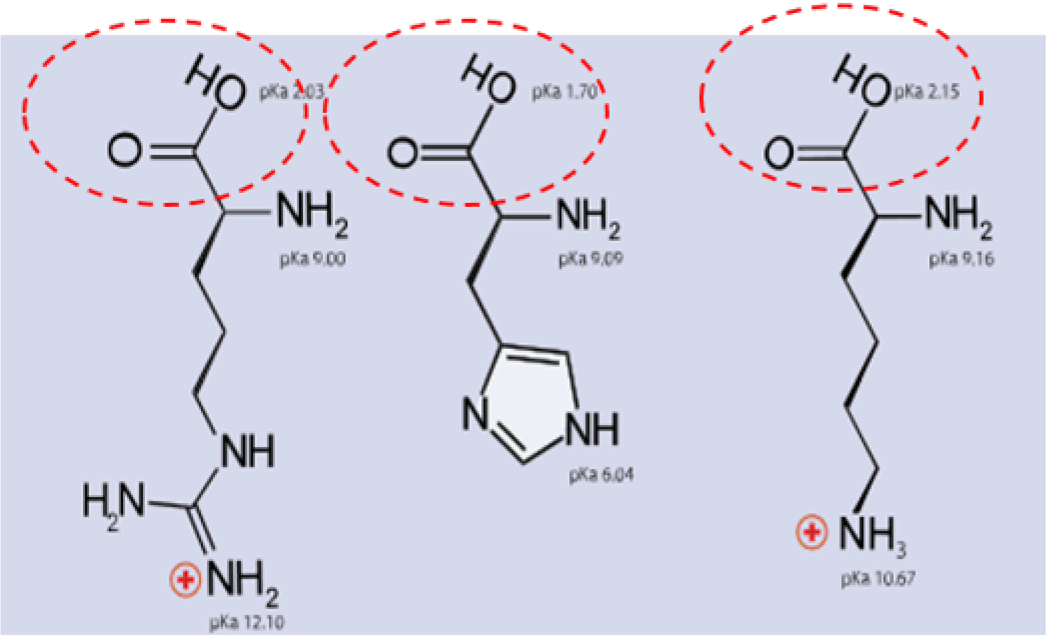


ketone

Wrong ✗

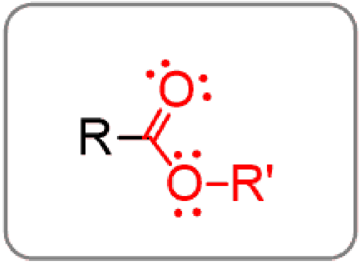
alcohol

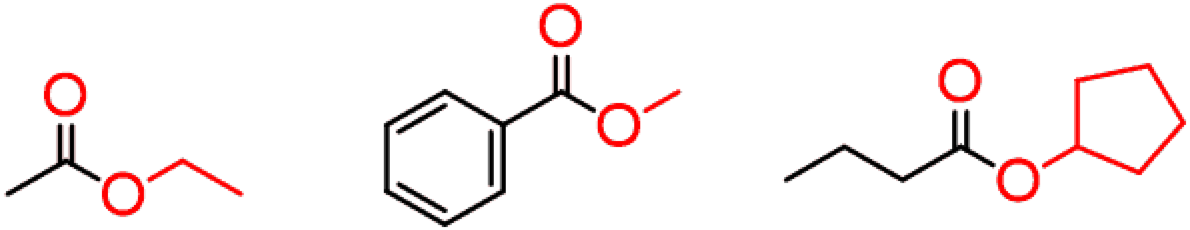
carboxylic acid ✓



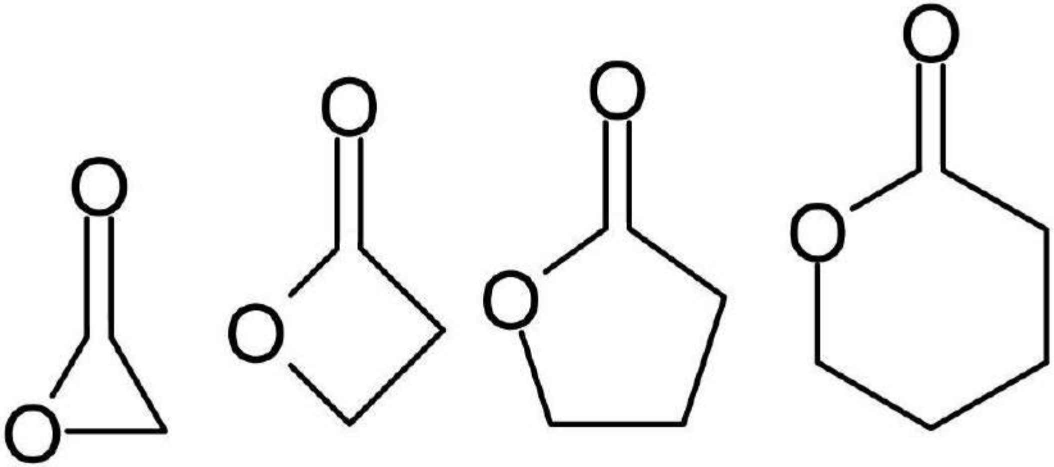
Arginine **Histidine** **Lysine**

Esters



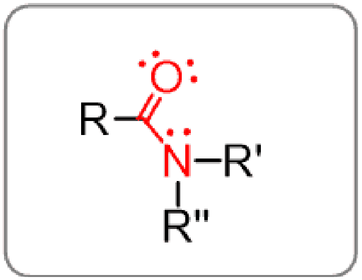


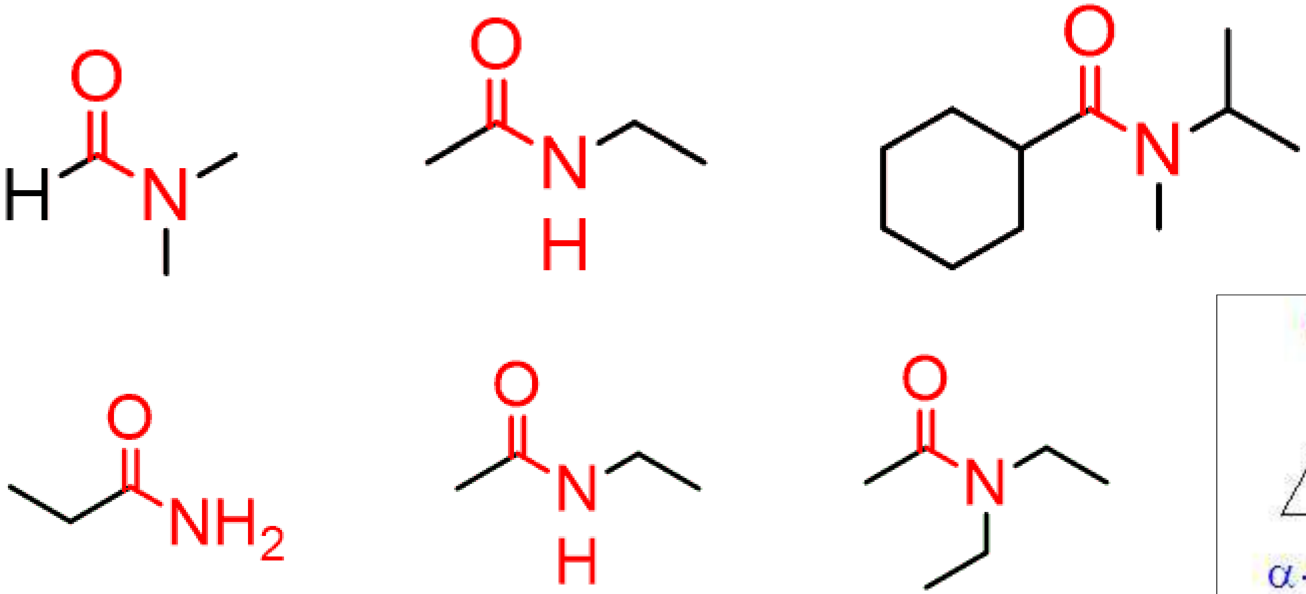
Cyclic esters
“ Lactone”



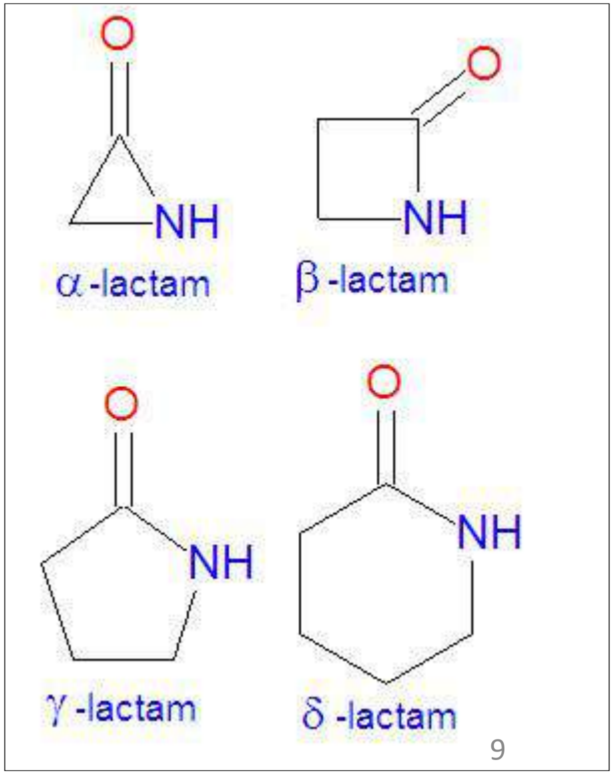
Left-to-Right: α-acetolactone, β-propiolactone, γ-butyrolactone, and δ-valerolactone

Amides

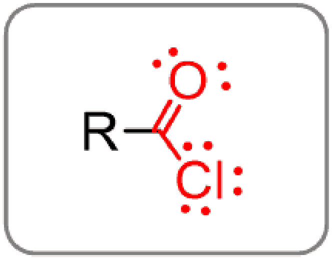

R
O
N
R'
R''

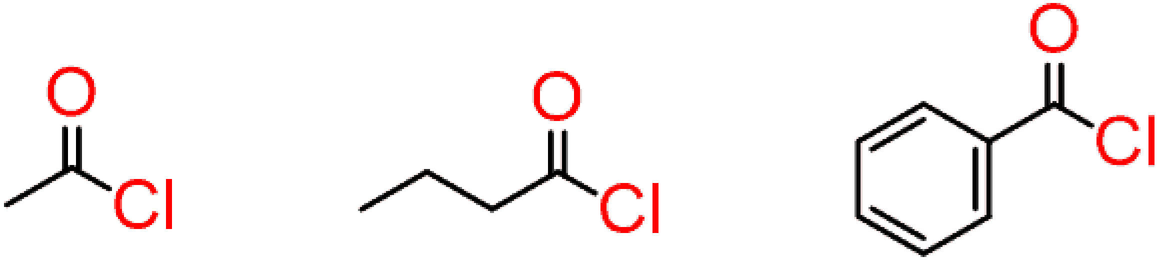

O
H
N
O
N
H
O
N
O
NH2
O
N
H
O
N

1°   2°   3°

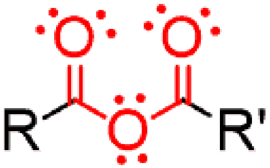

O
NH
α -lactam
O
NH
β -lactam
O
NH
γ -lactam
O
NH
δ -lactam

Acid Chlorides

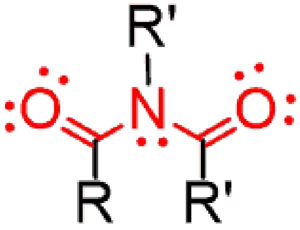




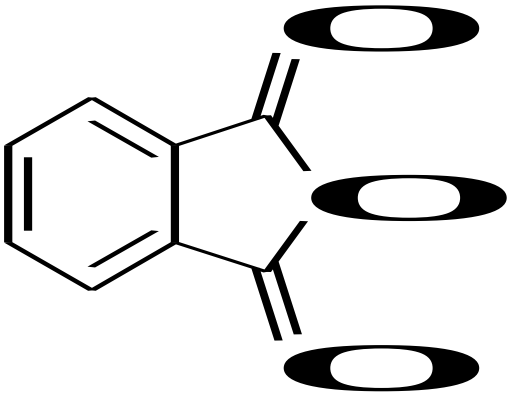
Functional groups with two carbonyls



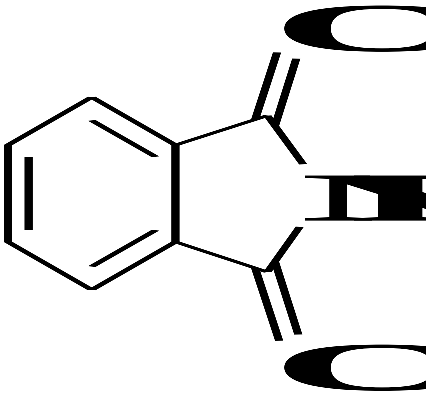
Anhydride



Imide



[illegible]

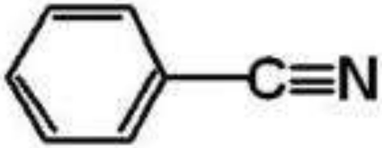


[illegible]

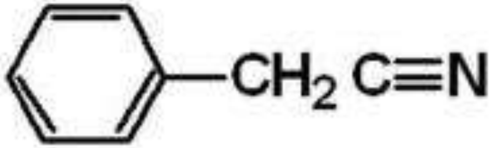
Nitrile

$CH_3C\equiv N$

Ethanenitrile
(Acetonitrile)

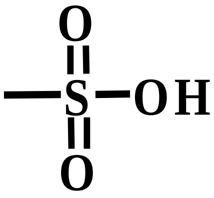


Benzonitrile

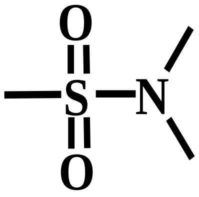


Phenylethanenitrile
(Phenylacetonitrile)

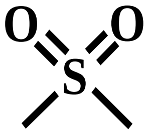
Sulfonic acid, Sulfonamide Sulfone and sulfoxide



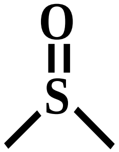
Sulfonic acid



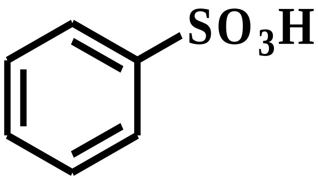
Sulfonamide

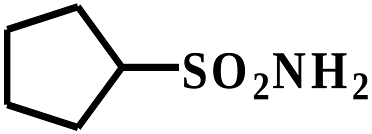


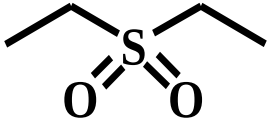
Sulfone

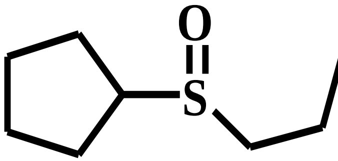


Sulfoxide

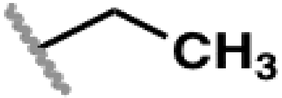




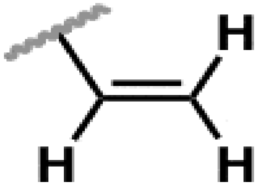




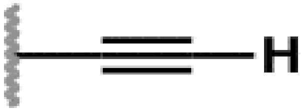
Functional Groups - The Main Players



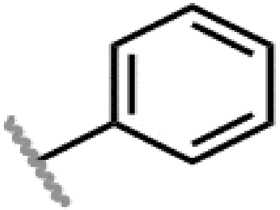
alkane



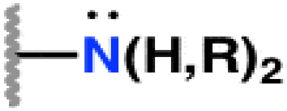
alkene



alkyne



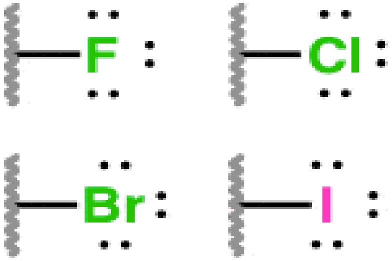
benzene ring (phenyl)



amine

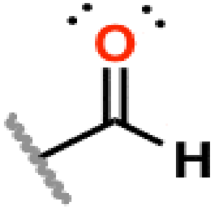
alcohol

ether

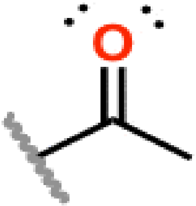


alkyl halide

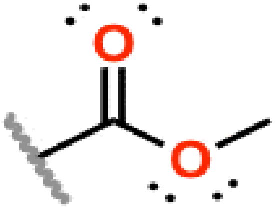
thiol



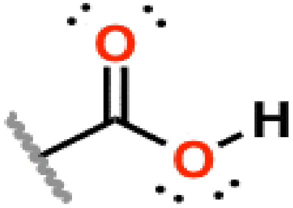
aldehyde



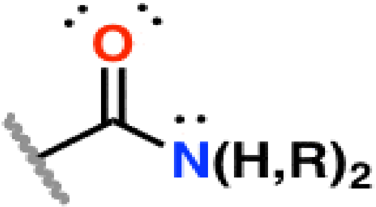
ketone



ester

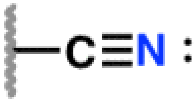


carboxylic acid

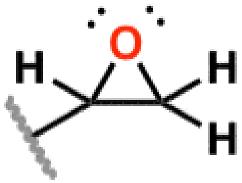


amide

Functional Groups - Supporting Actors

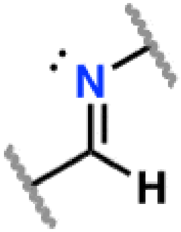


nitrile

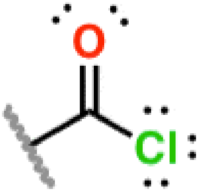


epoxide

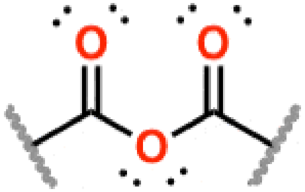
disulfide



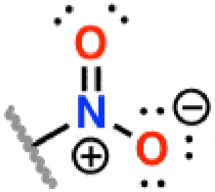
imine



acid chloride

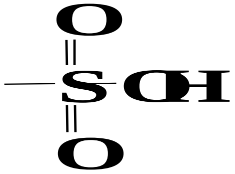


anhydride

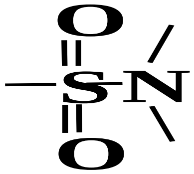


nitro

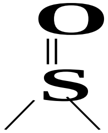
sulfide (thioether)



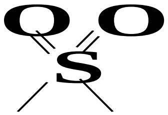
Sulfonic acid



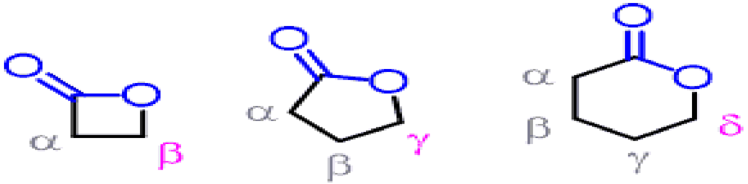
Sulfonamide



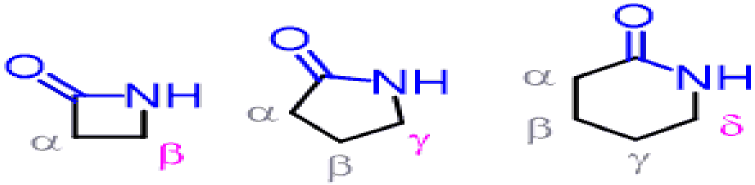
Sulfoxide



Sulfone

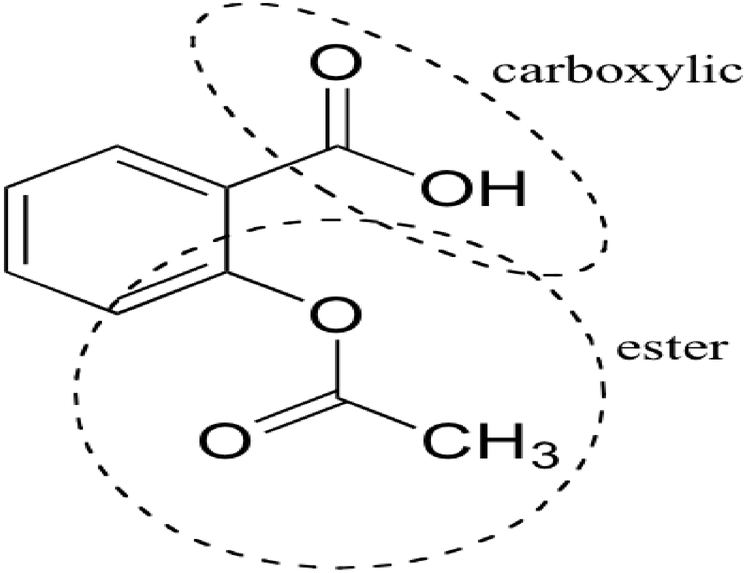


Lactones

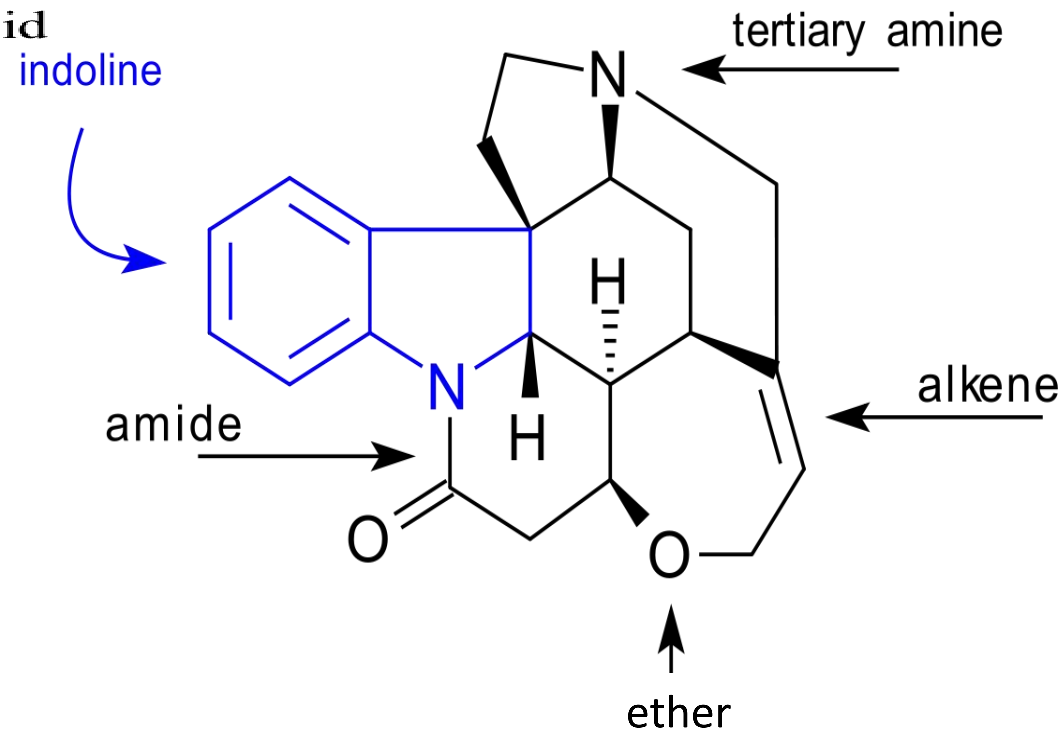


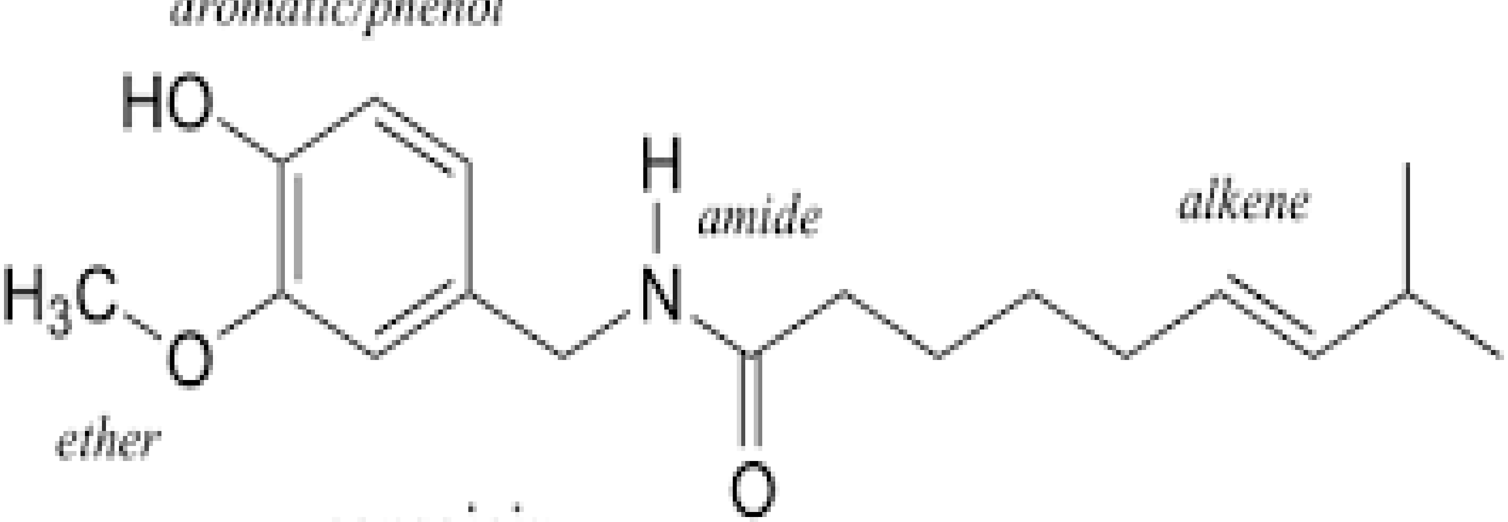
Lactams

Depending on the position of the hydroxyl group, **four, five, and six-membered rings** can be prepared. These are classified as **β–lactones, γ–lactones, and δ–lactones** respectively.

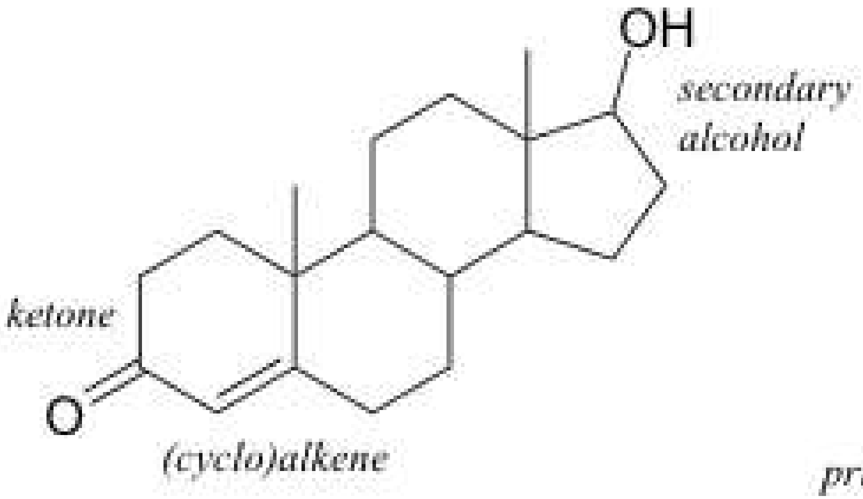


acetylsalicylic acid
(aspirin)



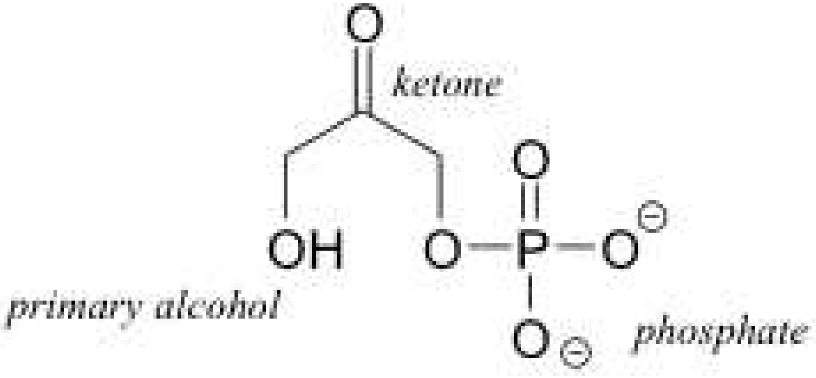


capsaicin

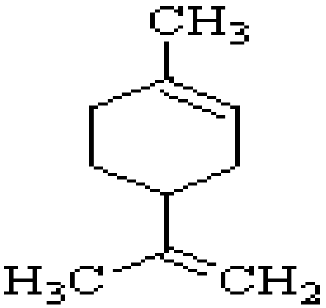


testosterone

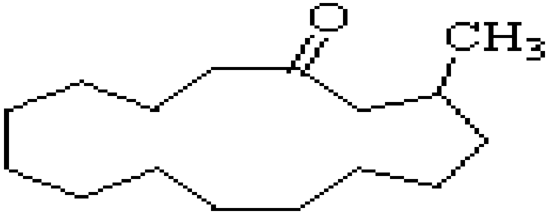
phenylalanine



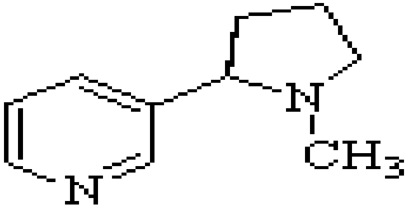
dihydroxyacetone phosphate
(DHAP)



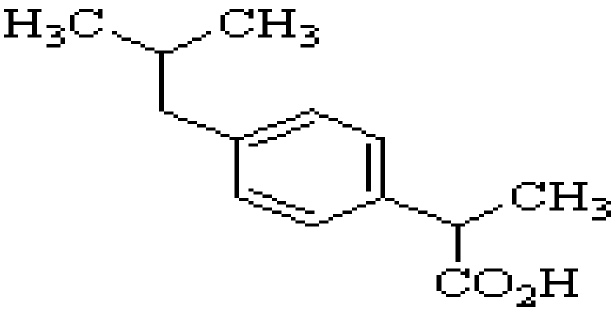
1. limonene



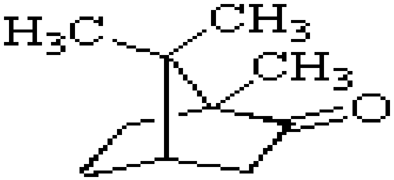
2. muscone



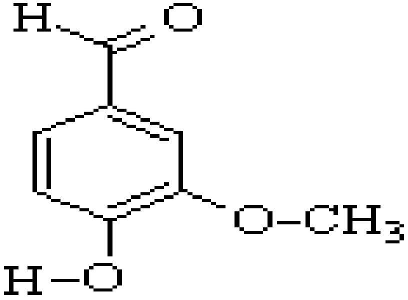
3. nicotine



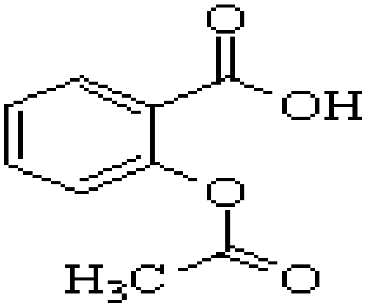
4. ibuprofen



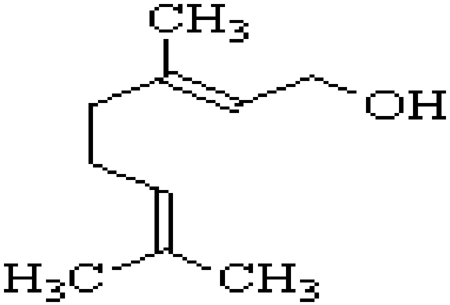
5. camphor



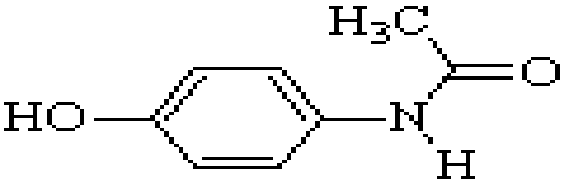
6. vanillin



7. aspirin

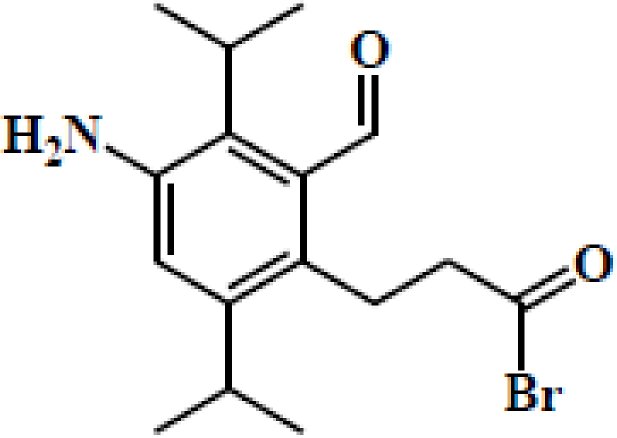


8. geraniol



9. acetaminophen

a]



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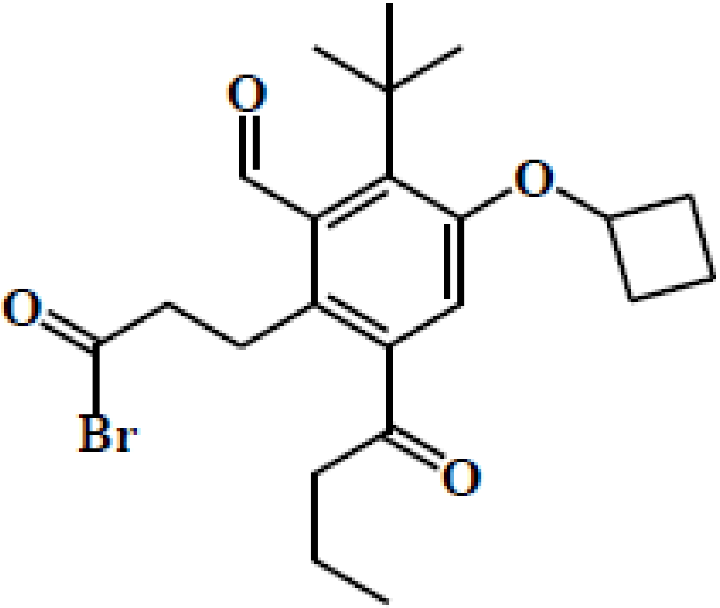

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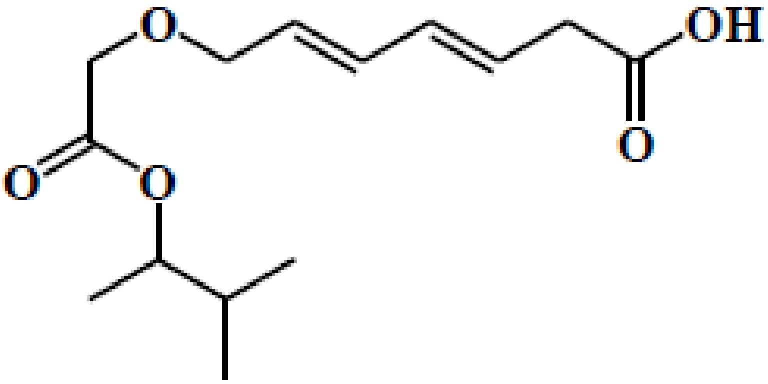

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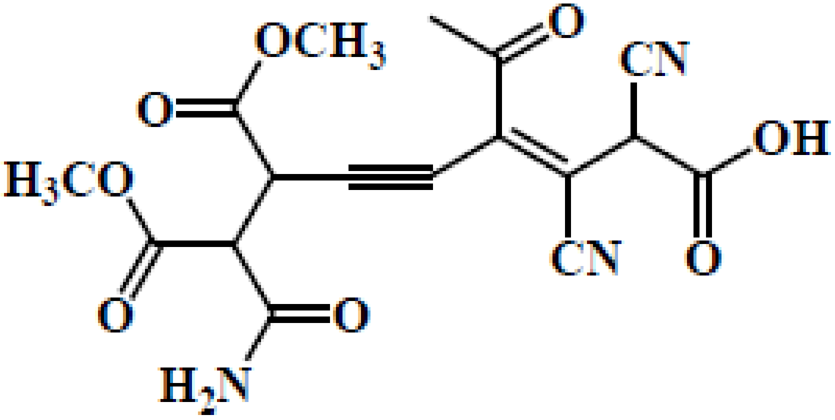
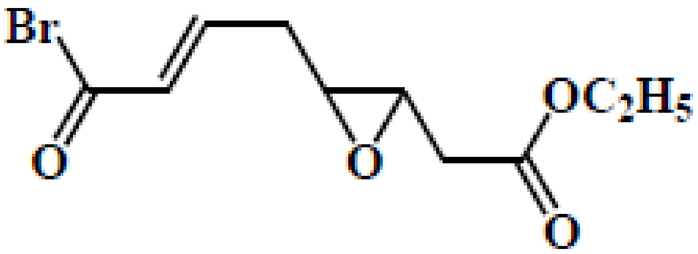
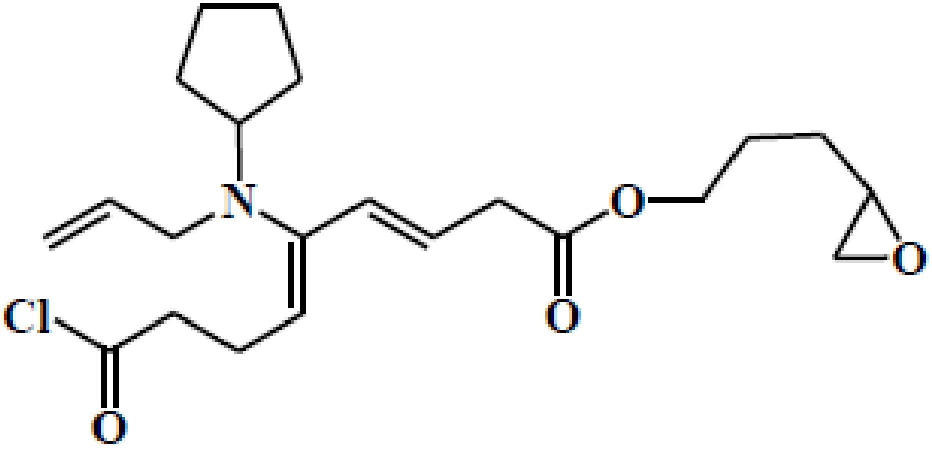


e]



a]



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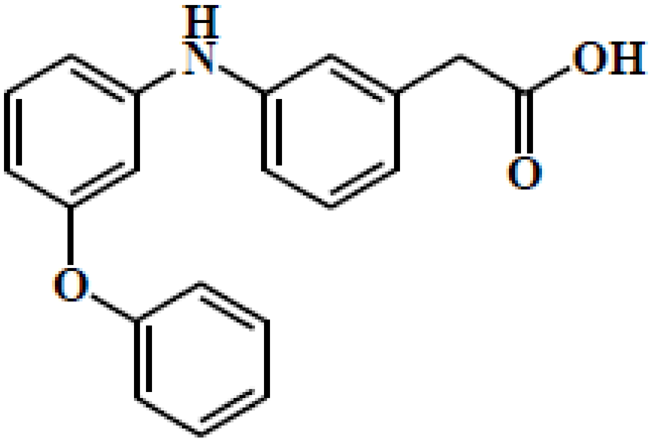

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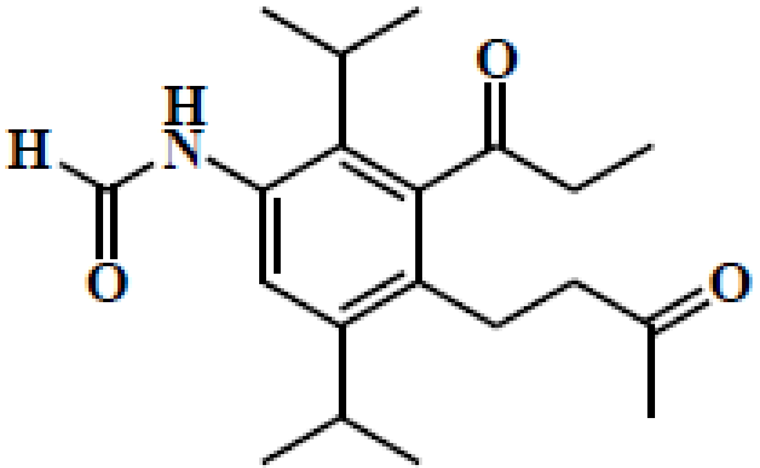

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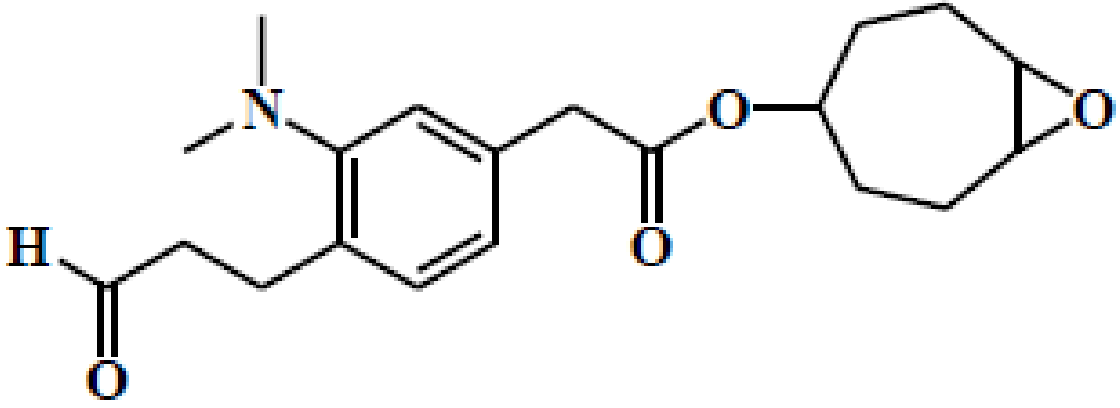
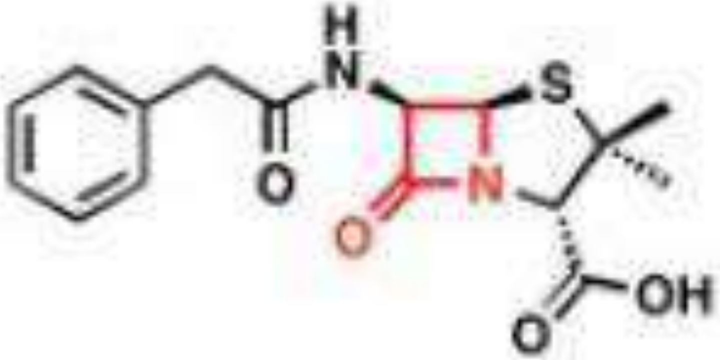
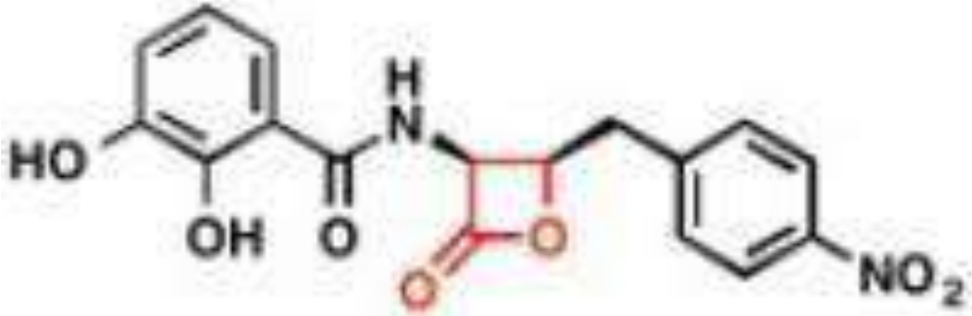
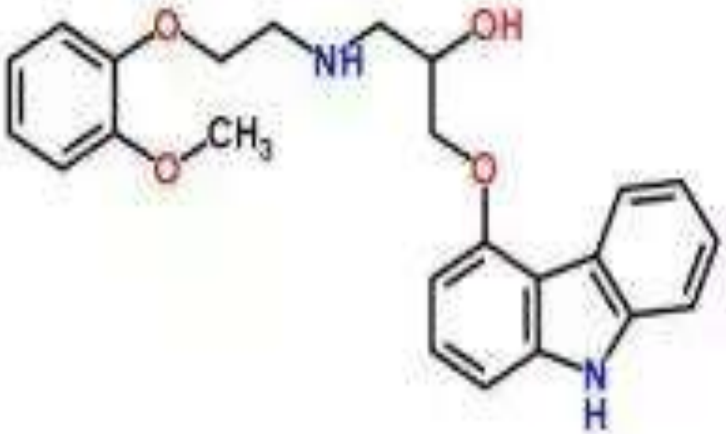




penicillin β-lactam



obafluorin β-lactone

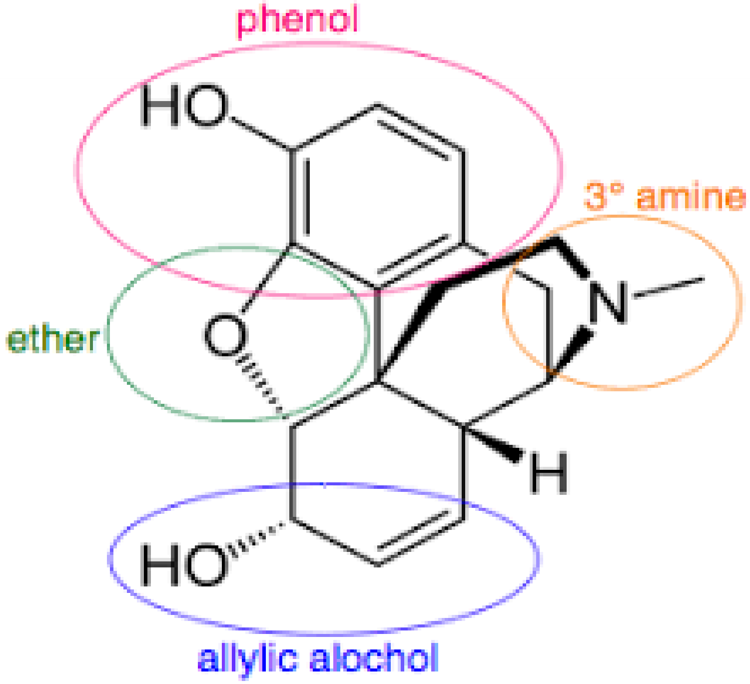


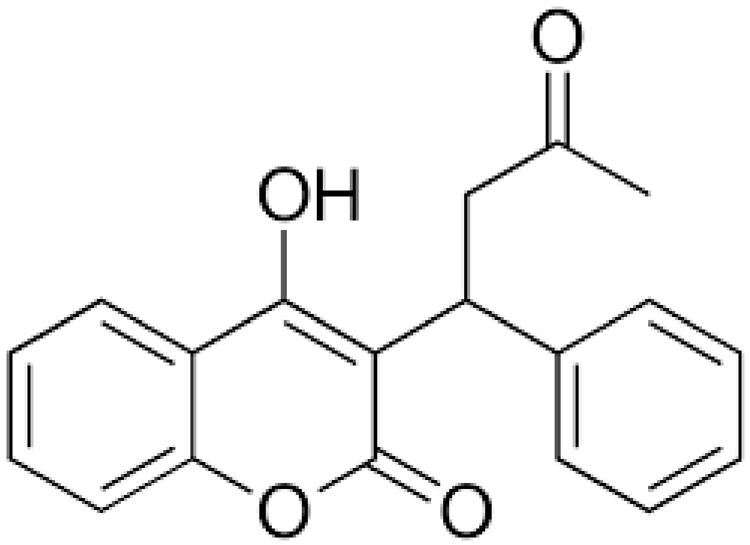
Carvedilol

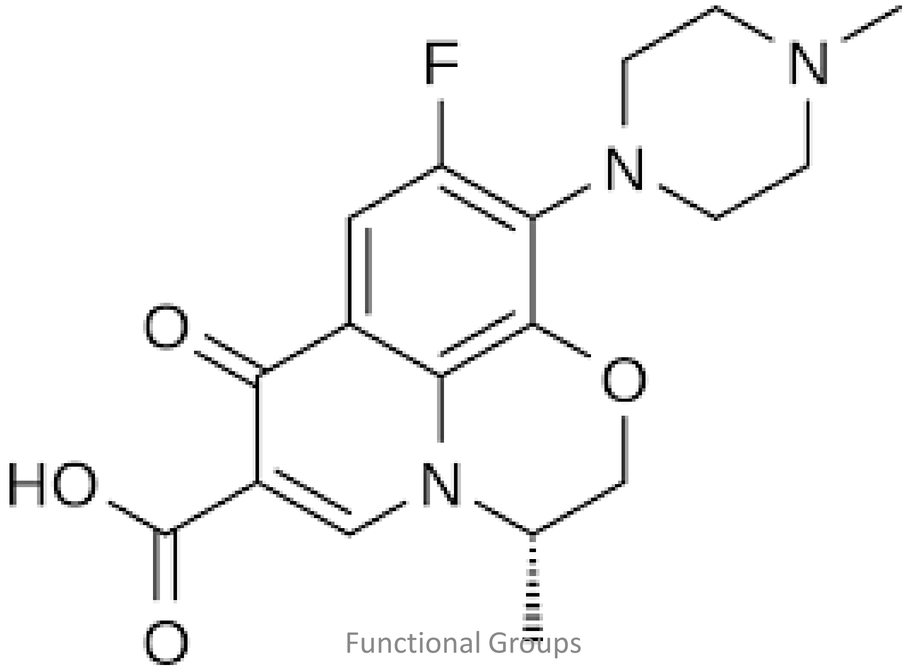
Molecular Formula: $C_{24}H_{26}N_2O_4$

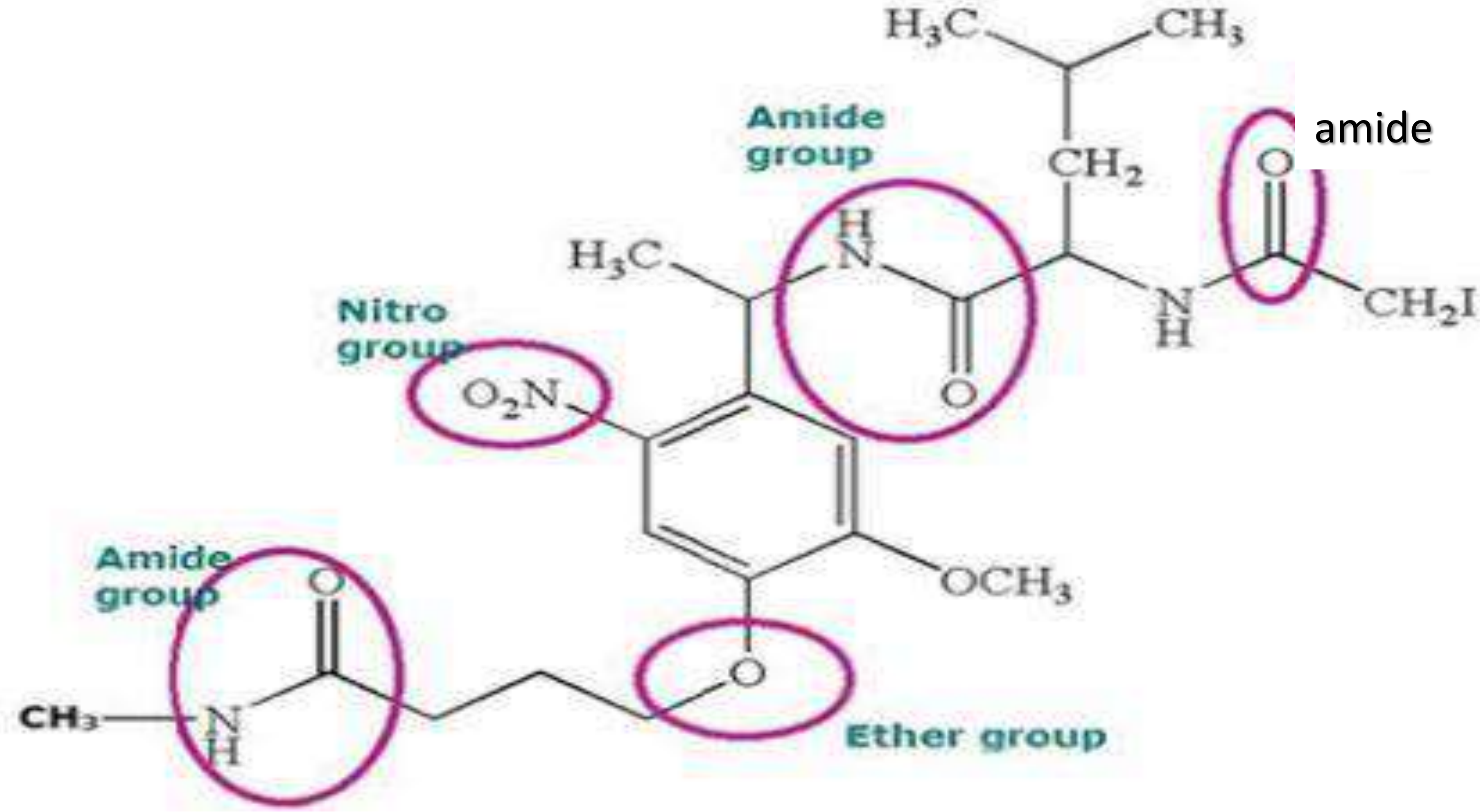
Average mass: 406.474 Da

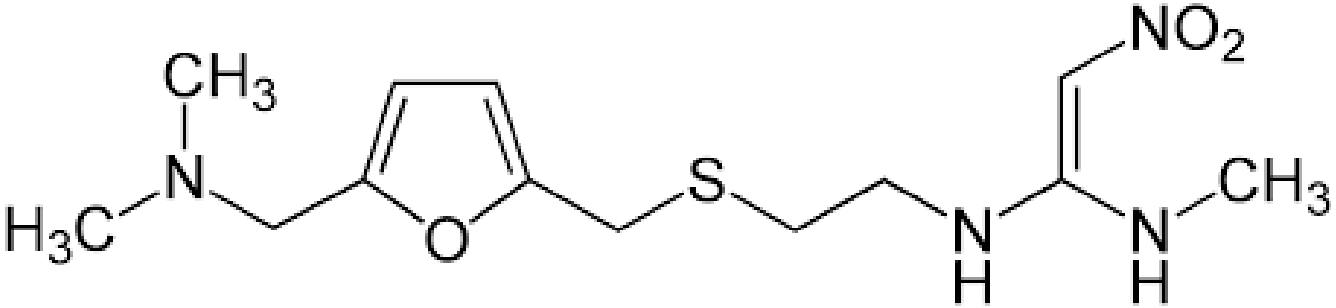
Chemical name: 1-(9H-carbazol-4-yloxy)-3-{[2-(2-methoxyphenoxy) ethyl] amino} propan-2-ol.


phenol
3° amine
ether
allylic alochol






H3C
CH3
Amide group
amide
CH2
O
H
N
H3C
N
H
CH2I
Nitro group
O2N
O
OCH3
Amide group
O
CH3
N
H
O
Ether group


CH3
N
H3C
O
S
N
H
N
H
CH3
NO2

Resonance
الطنين

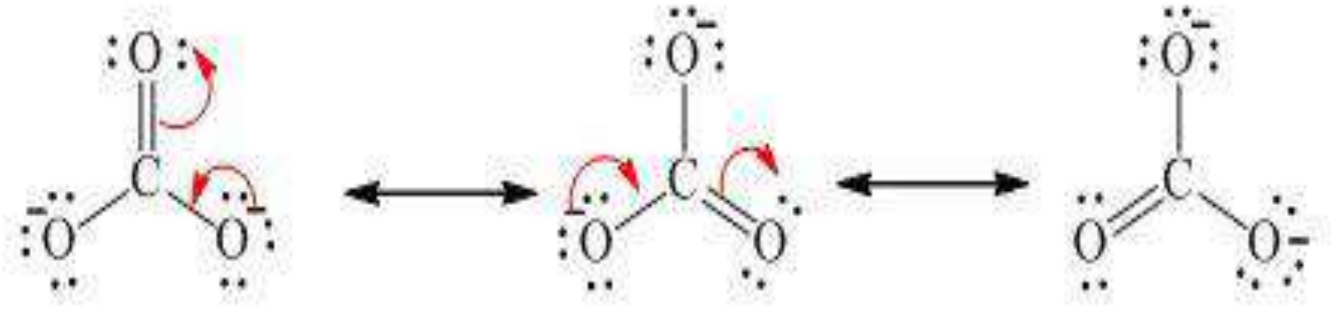
What is Resonance ?

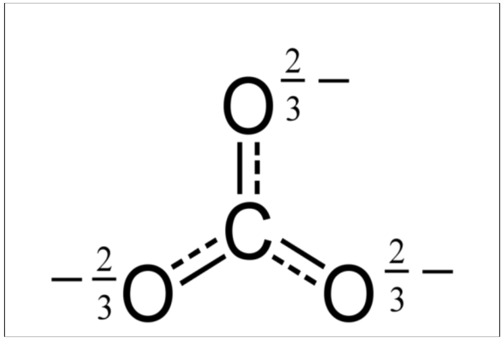
Resonance structures are sets of Lewis structures that describe the delocalization of electrons in a polyatomic ion or a molecule.

What is the benefit of Resonance ?

Resonance is a molecule's way of spreading out its electron density, and that helps to **minimize its ground-state energy.**

Resonance of Carbonate



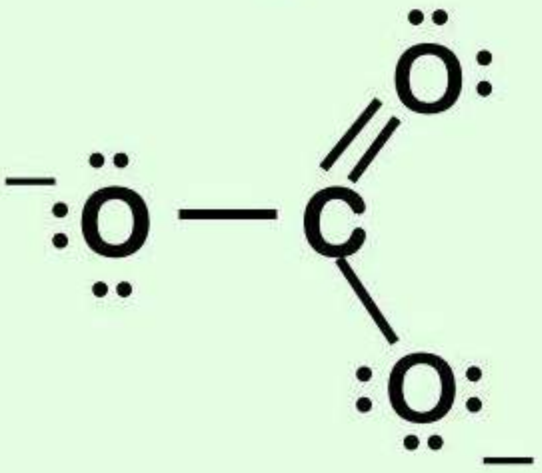


Hybrid

The different resonance structures of the carbonate ion (CO_3^{2-}) are illustrated above. The delocalization of electrons is described via fractional bonds (which are denoted by dotted lines) and fractional charges in a resonance hybrid.

Typical bond lengths

The behavior of a real carbonate ion does not match the Lewis diagram.



C=O	1.22 Å	short
C−O	1.43 Å	long

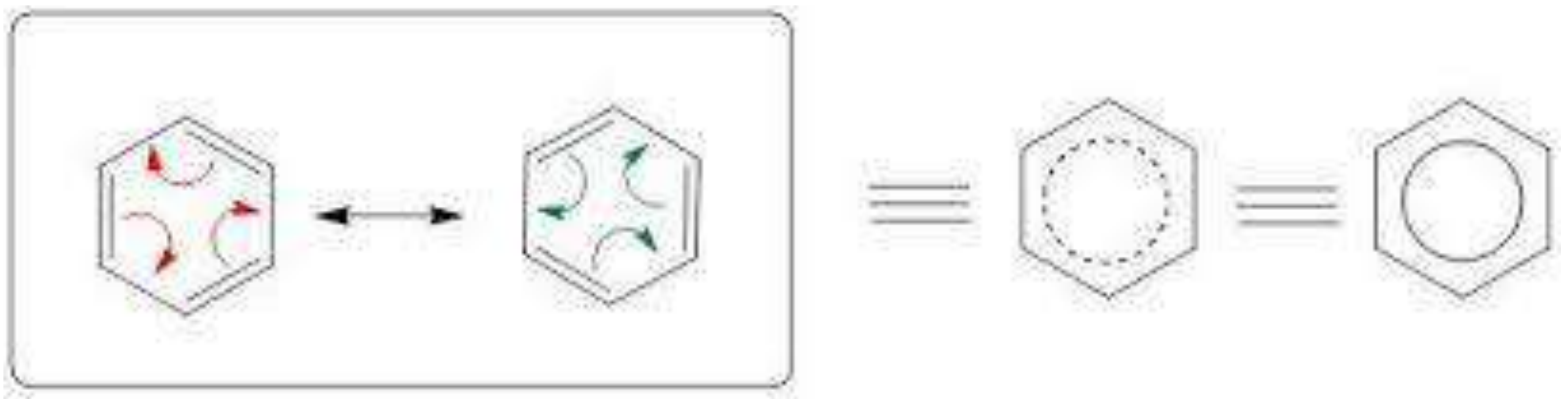
but .....

All bond lengths are equal in carbonate ion, at about 1.30 Å

determined by x-ray crystallography of $CaCO_3$ crystals

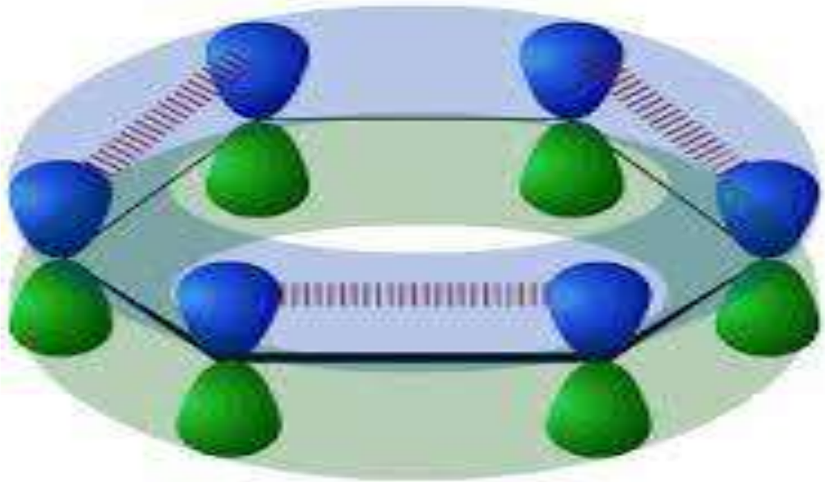
Charge is evenly distributed to the three oxygen atoms

Resonance of Benzene



Benzene 2 Resonance forms

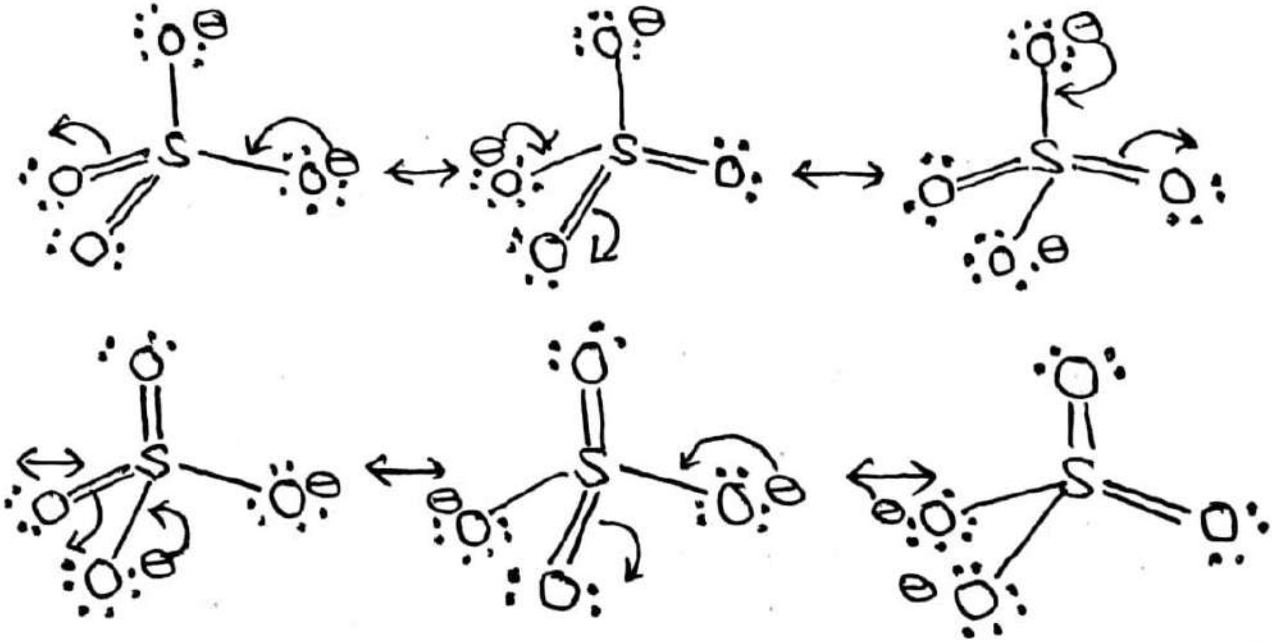
Hybrid Forms

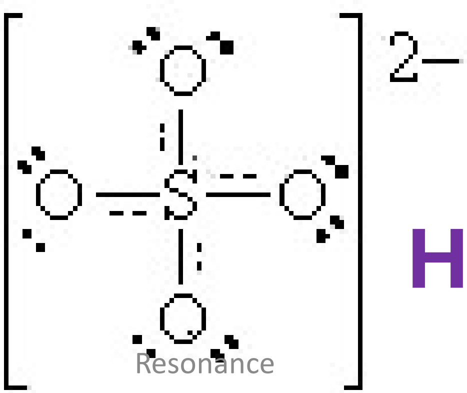


a Kekulé resonance structure

Resonance of Sulfate

The resonance structure of sulfate (SO_4^{2-}) ion is



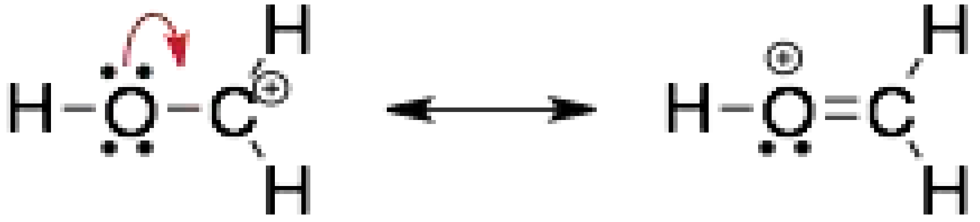


Hybrid

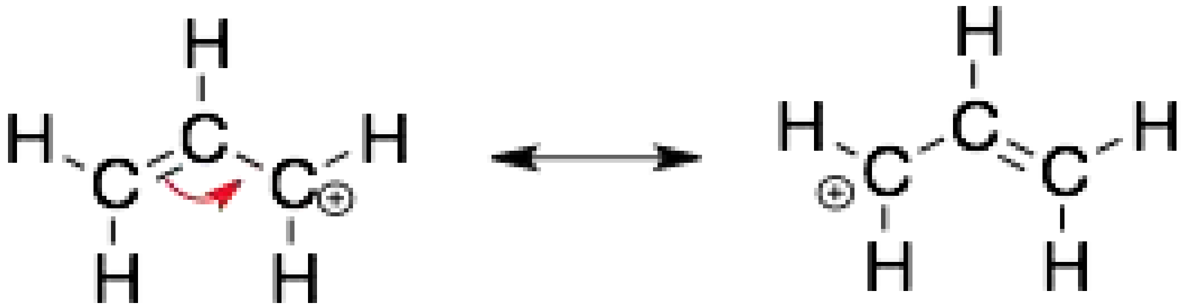
Cases of resonance:-

Curved arrow formalism to show the movement of a pair of electrons. The ‘basic’ on arrow moves are:

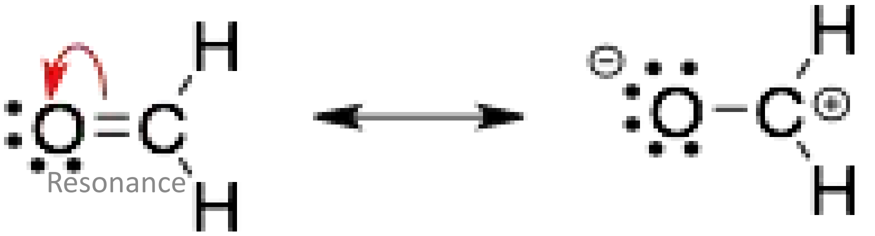
lone pair to bond

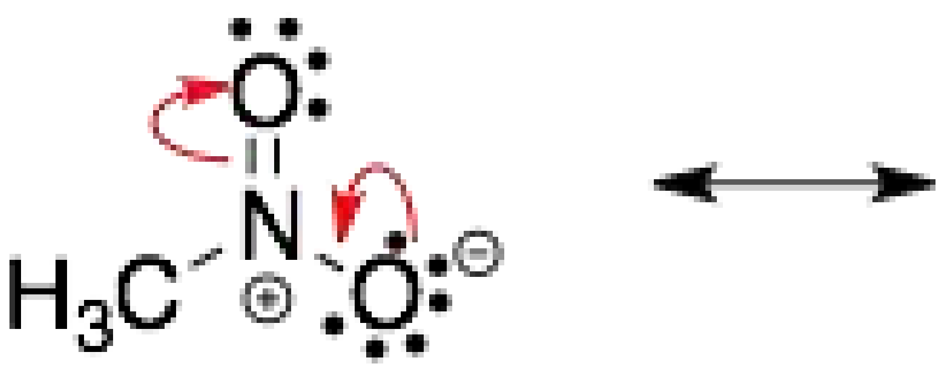


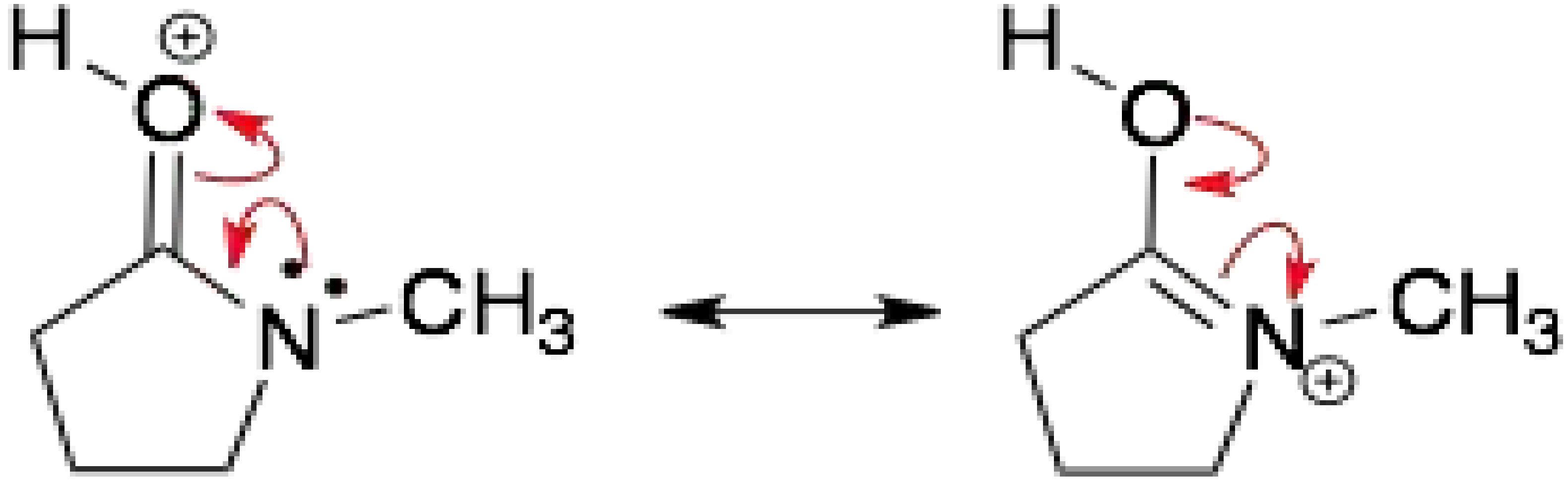
bond to bond



bond to lone pair

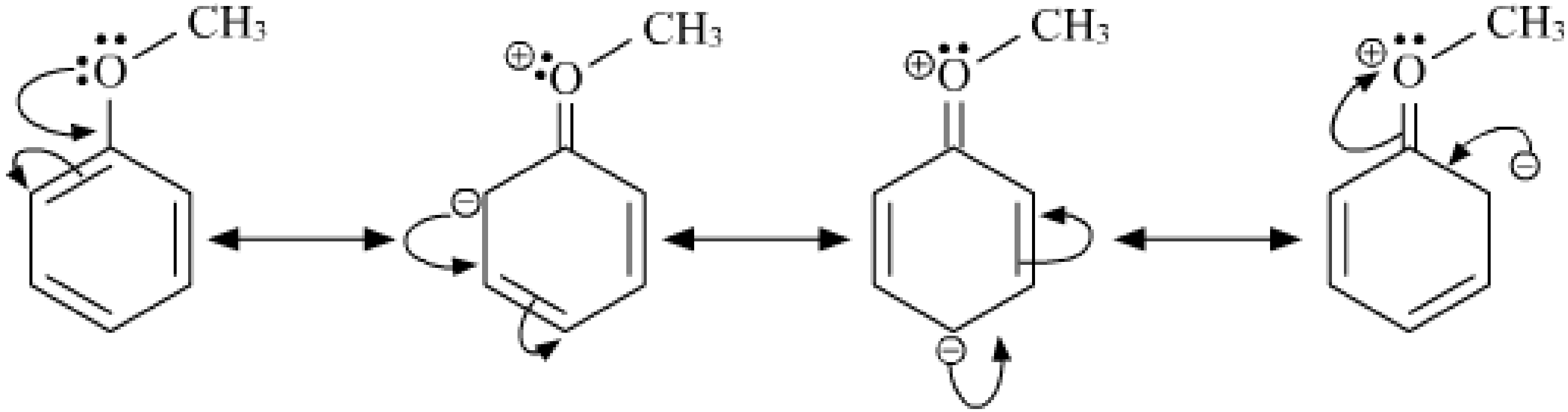



H3C
N
O
O
⊕
⊖
H3C
N
O
O
⊕
⊖


H
O
⊕
N
CH3
H
O
N
⊕
CH3

Hints and rules while performing resonance

1. **It is delocalization of electrons not atoms (if atoms then it is called tautomerization).**

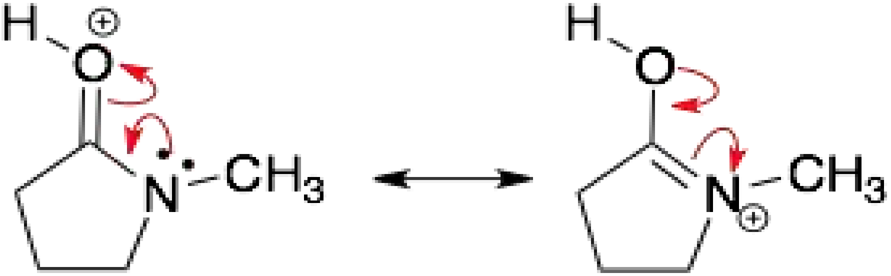


2. **Resonance forms are known as canonical or contributed or resonance structures with a closed arrows among them**

Hybrid
“actual form”

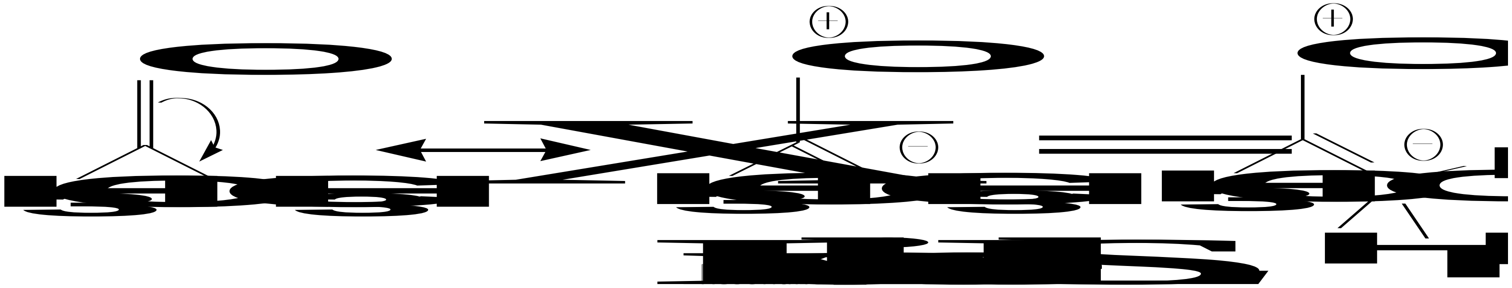
3. The resonance forms are imaginary forms (Not True) the actual one is the hybrid.

4. The formal charge before and after resonance must be the same.

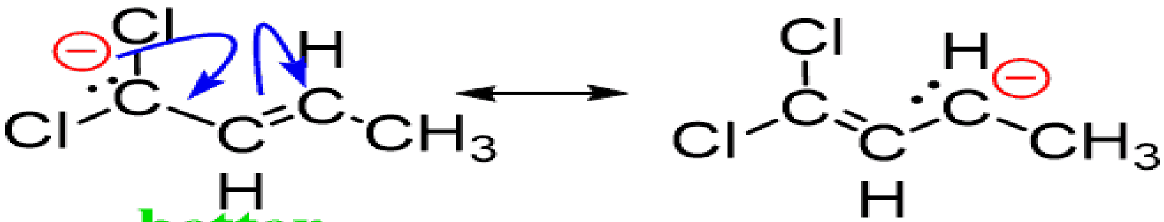


5. Electrons should flow toward positive charges and away from negative charges.

6. Resonance forms obey octet rule.(don’t exceed the octet)



Stability of Resonance forms

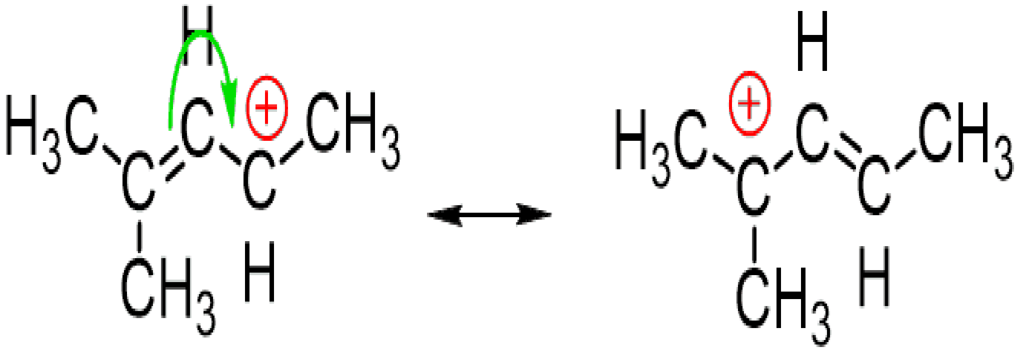


better

Cl's stabilize the negative charge by induction

The more substituted carbon is more stable - major resonance contributor

2^{0} carbocation

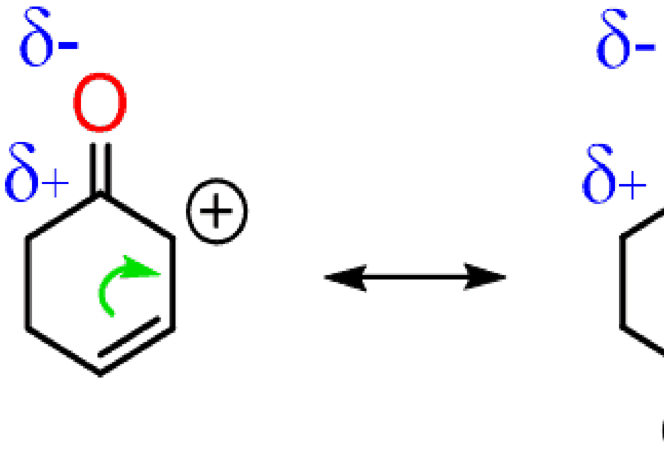


3^{0} carbocation

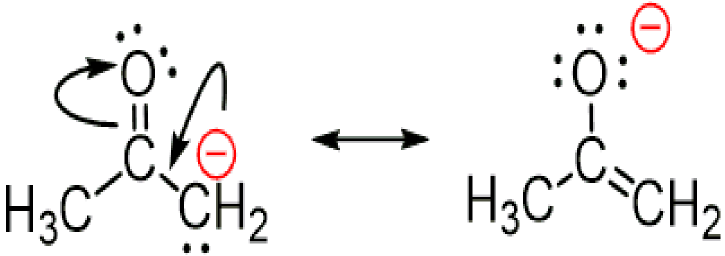
- **better**

minor since

⊕ is next to $\delta+$

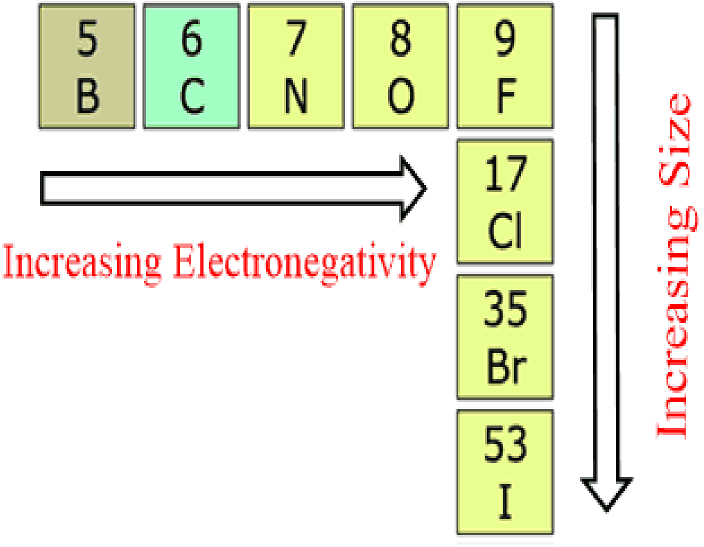


major



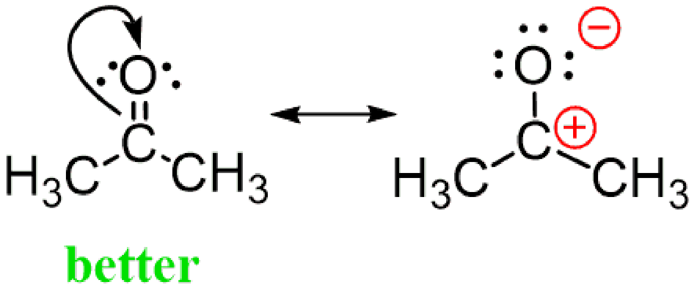
better

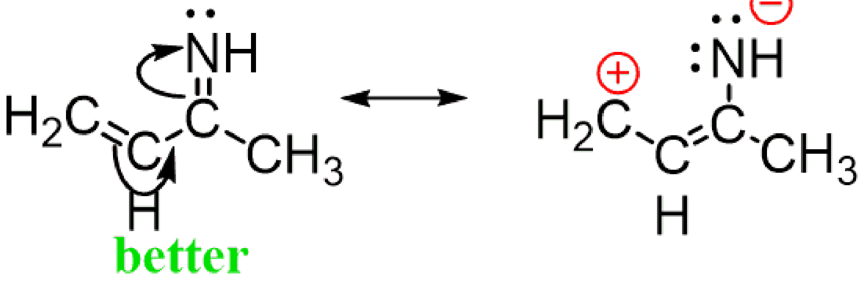
oxygen is more electronegative



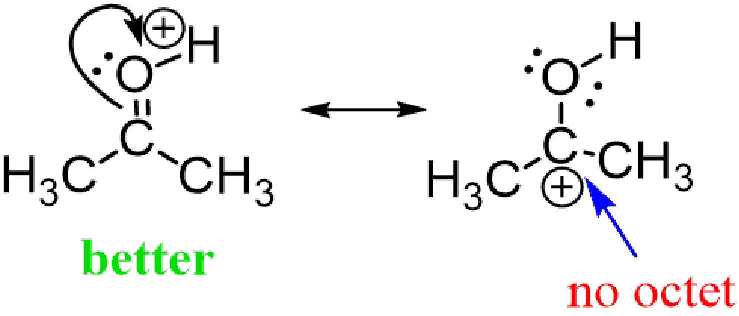
Increasing Electronegativity

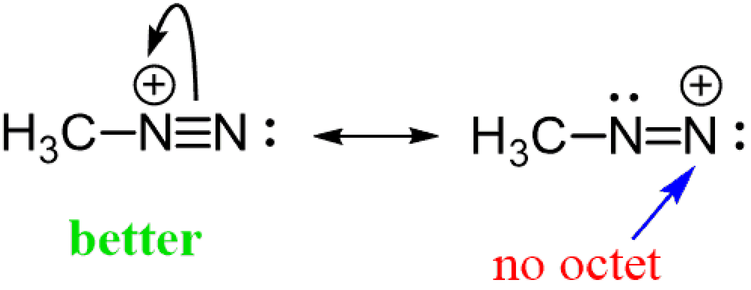
Increasing Size





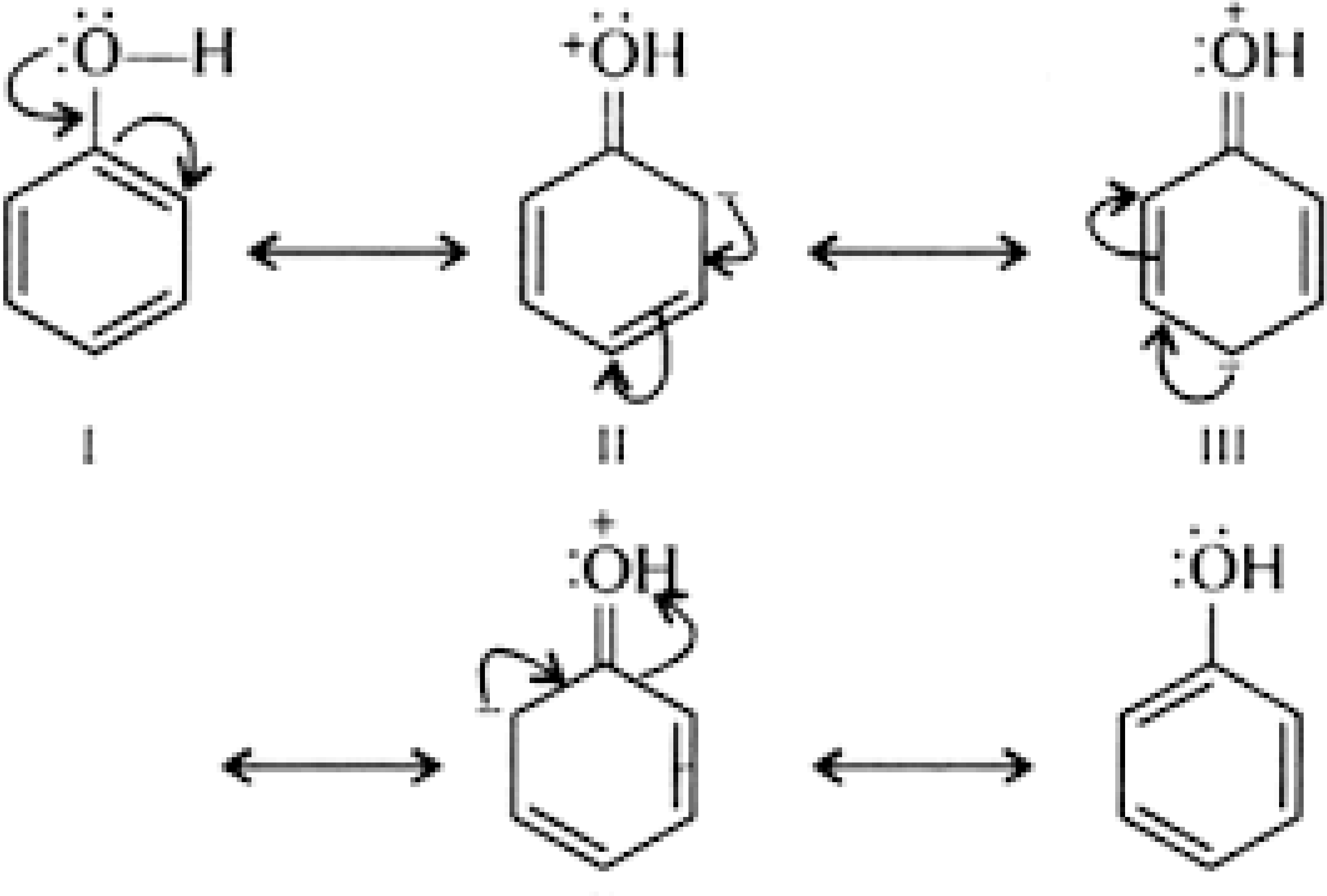
Atoms, in general, “don’t like” charges, so having no charge is better:



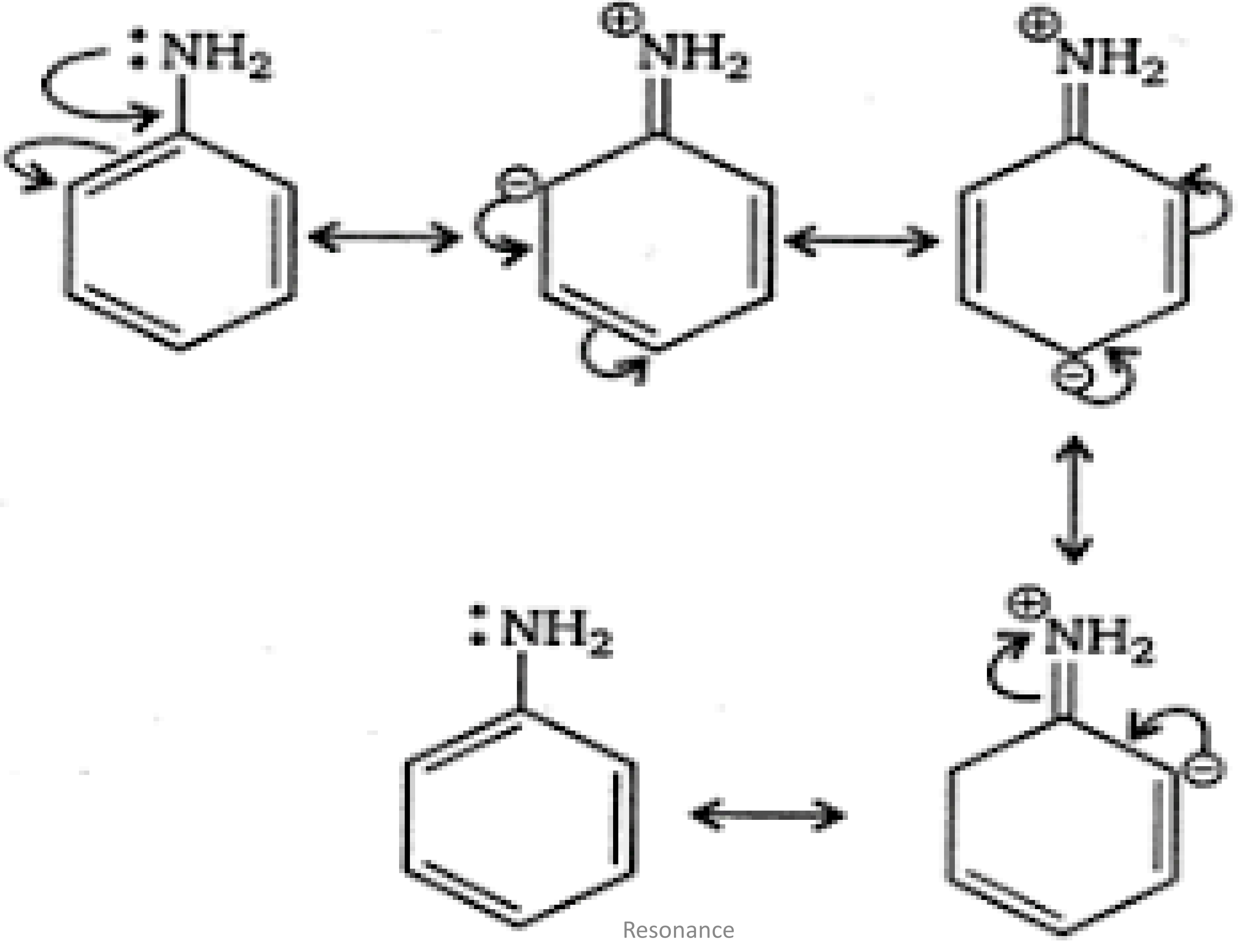


.The resonance structure with a complete octet is more stable:

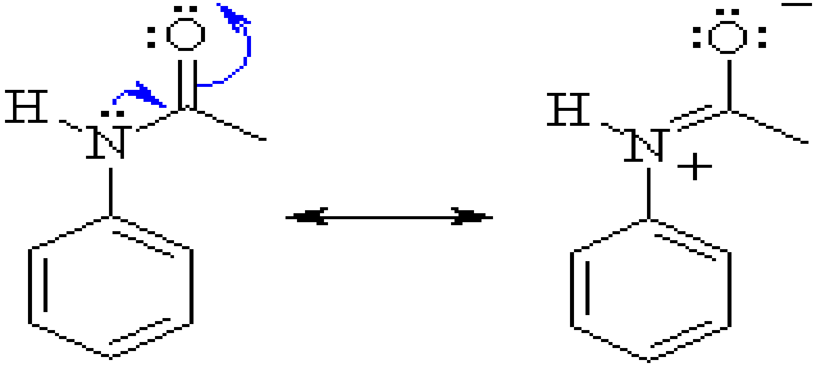
Phenol Resonance forms

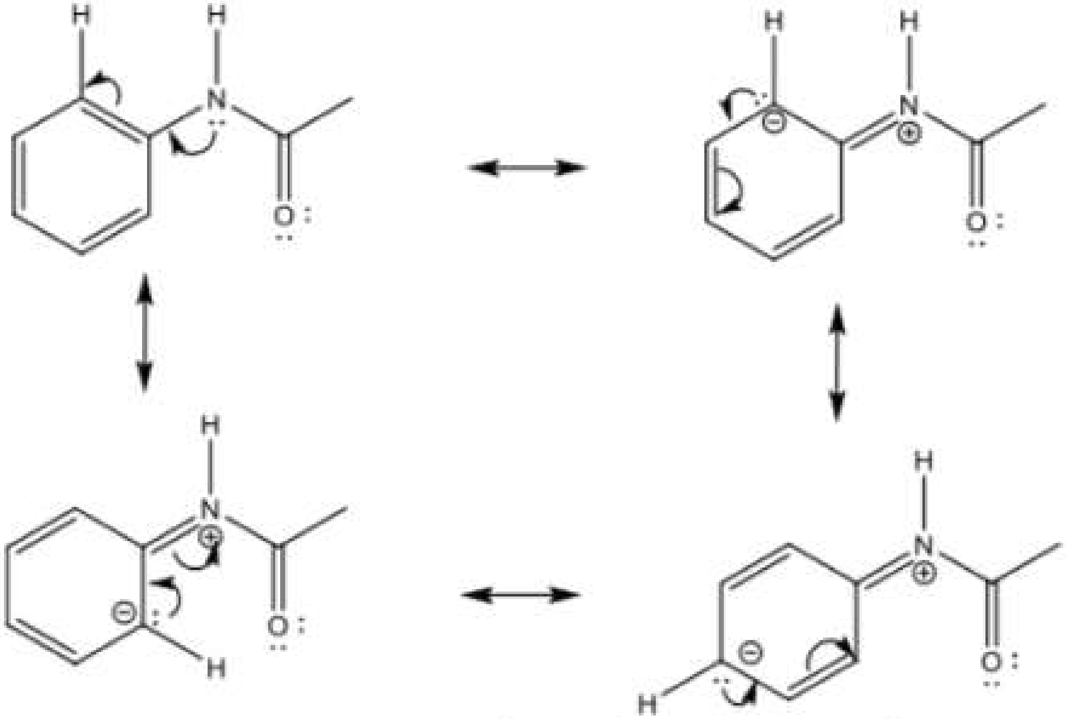


Aniline Resonance forms



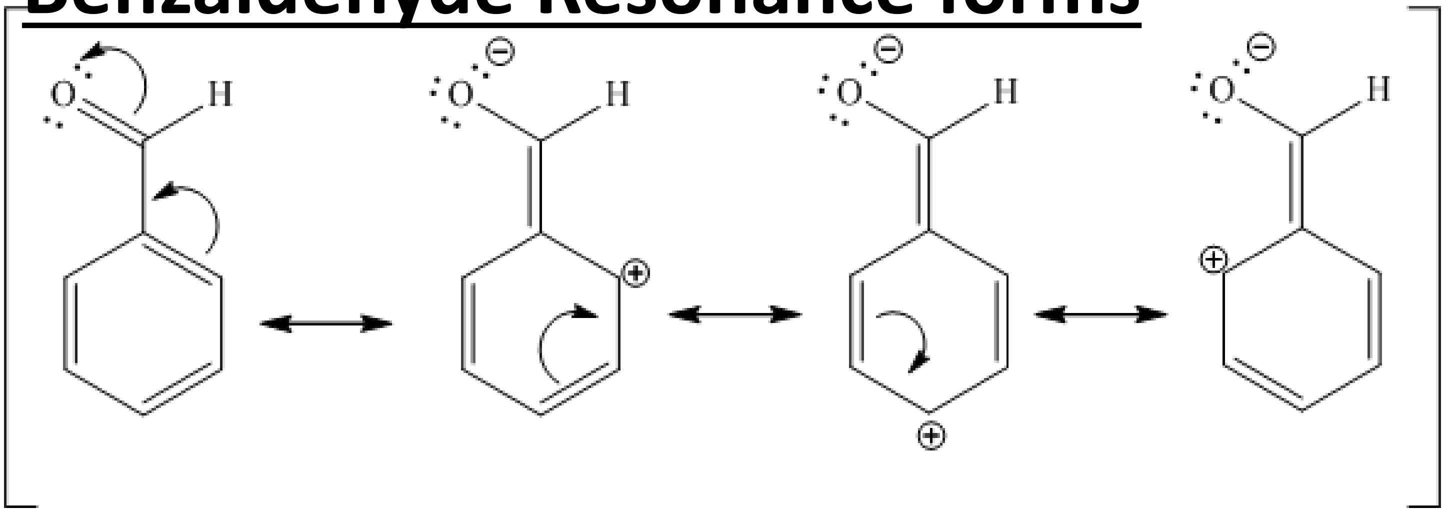
Acetanilide Resonance forms



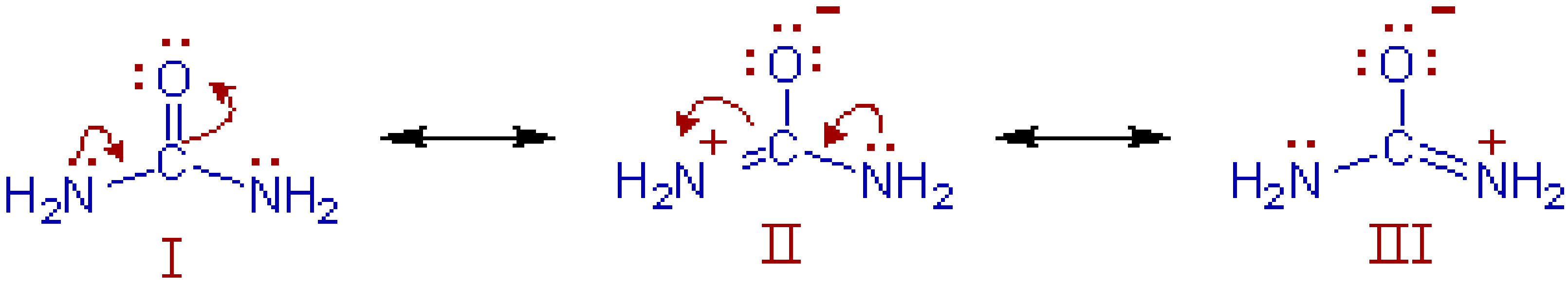


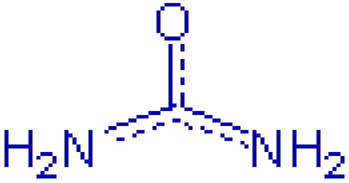
Resonance structures involving the aromatic π-electrons

Benzaldehyde Resonance forms



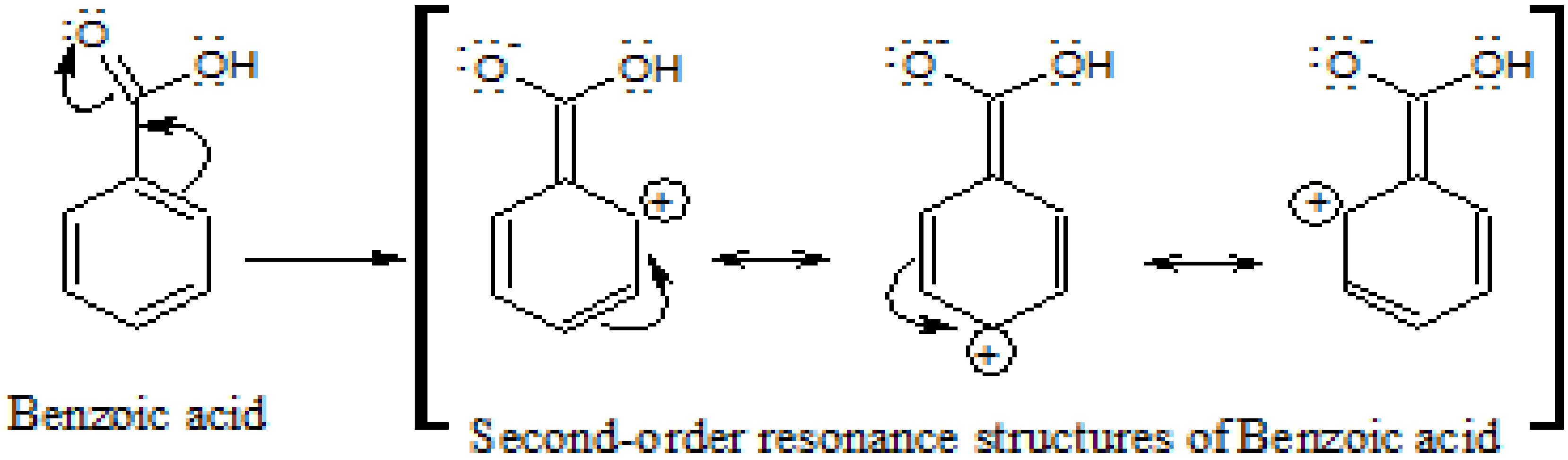
Urea Resonance forms





Resonance hybrid

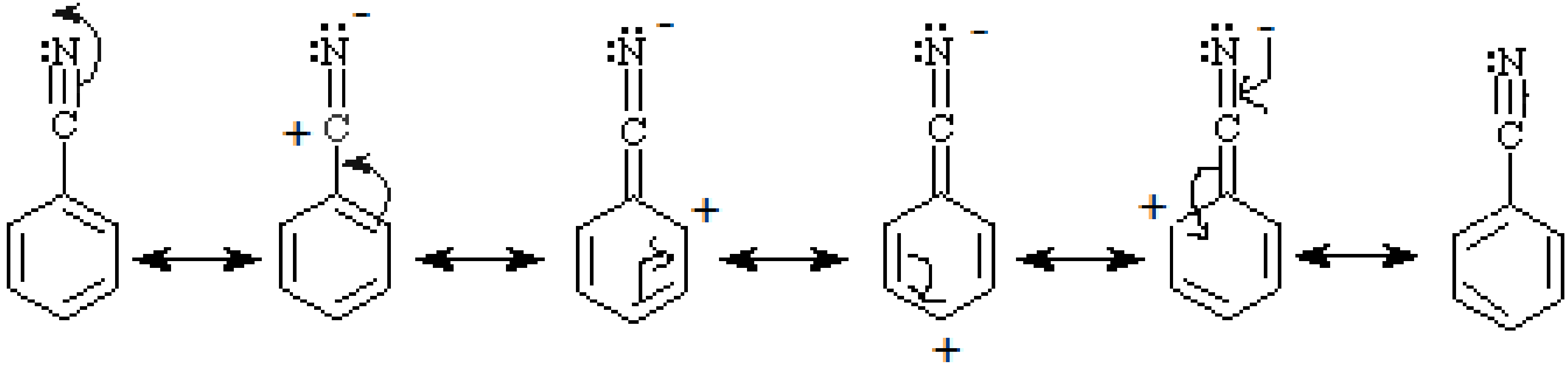
Benzoic acid Resonance forms



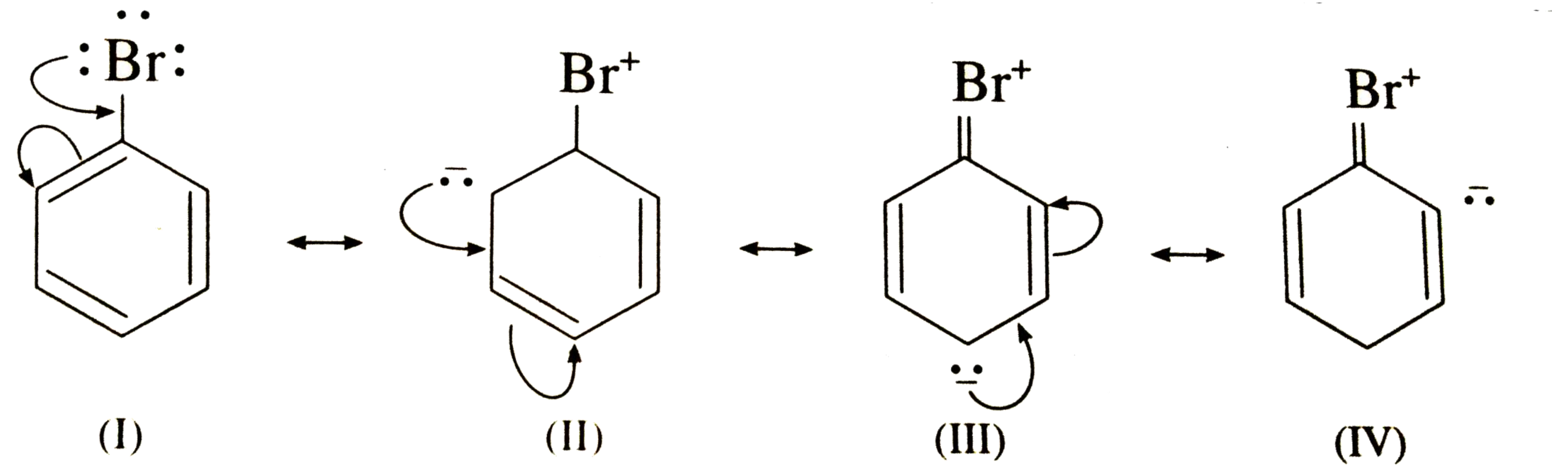
Benzoic acid

Second-order resonance structures of Benzoic acid

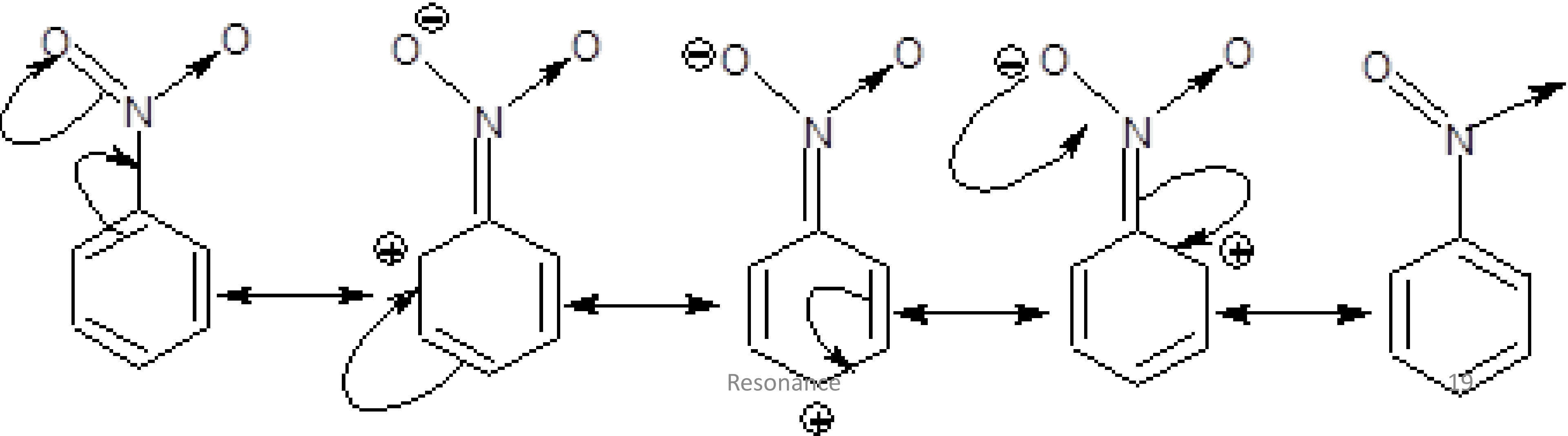
Benzonitrile Resonance forms



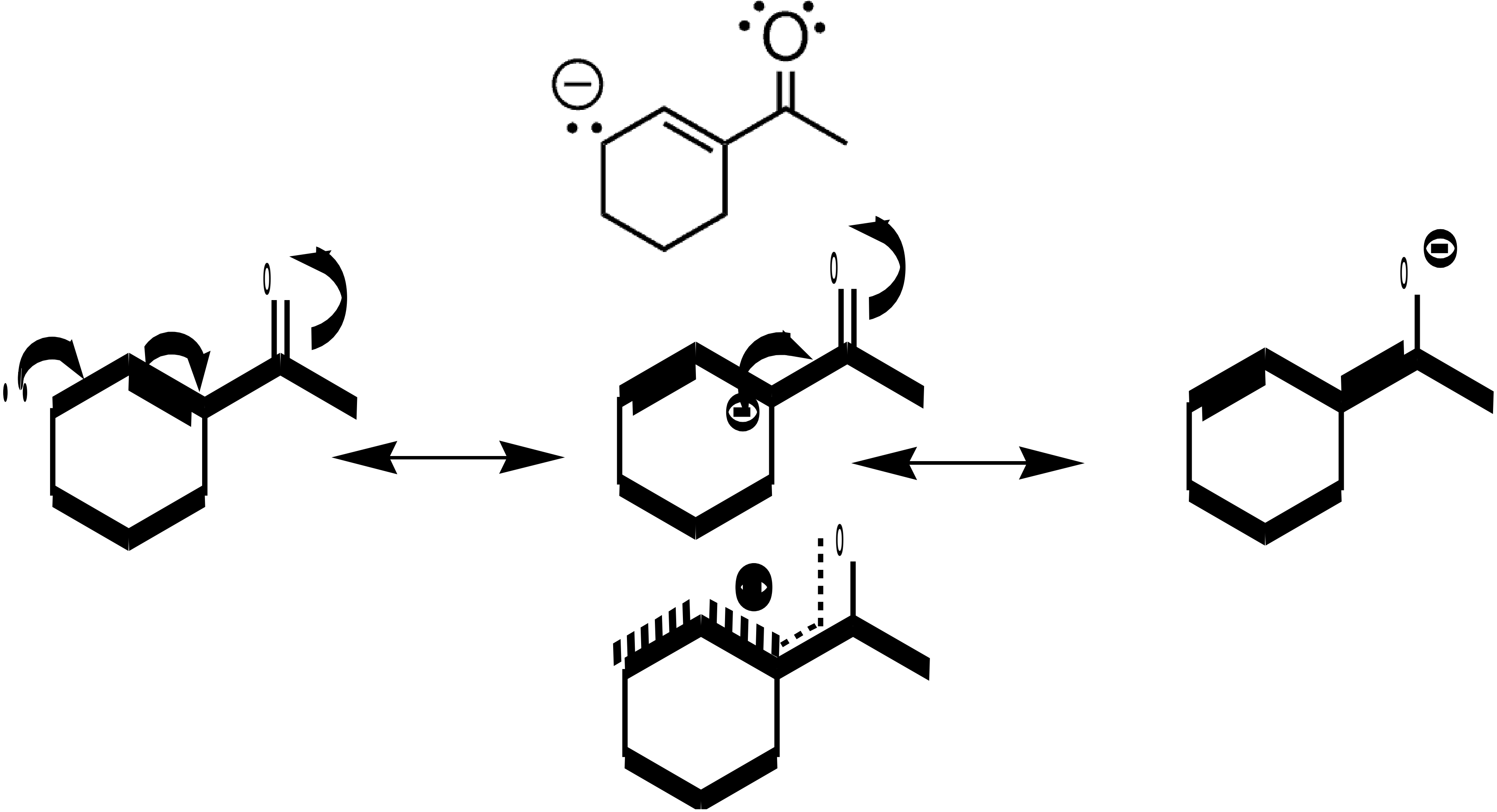
Bromobenzene Resonance forms



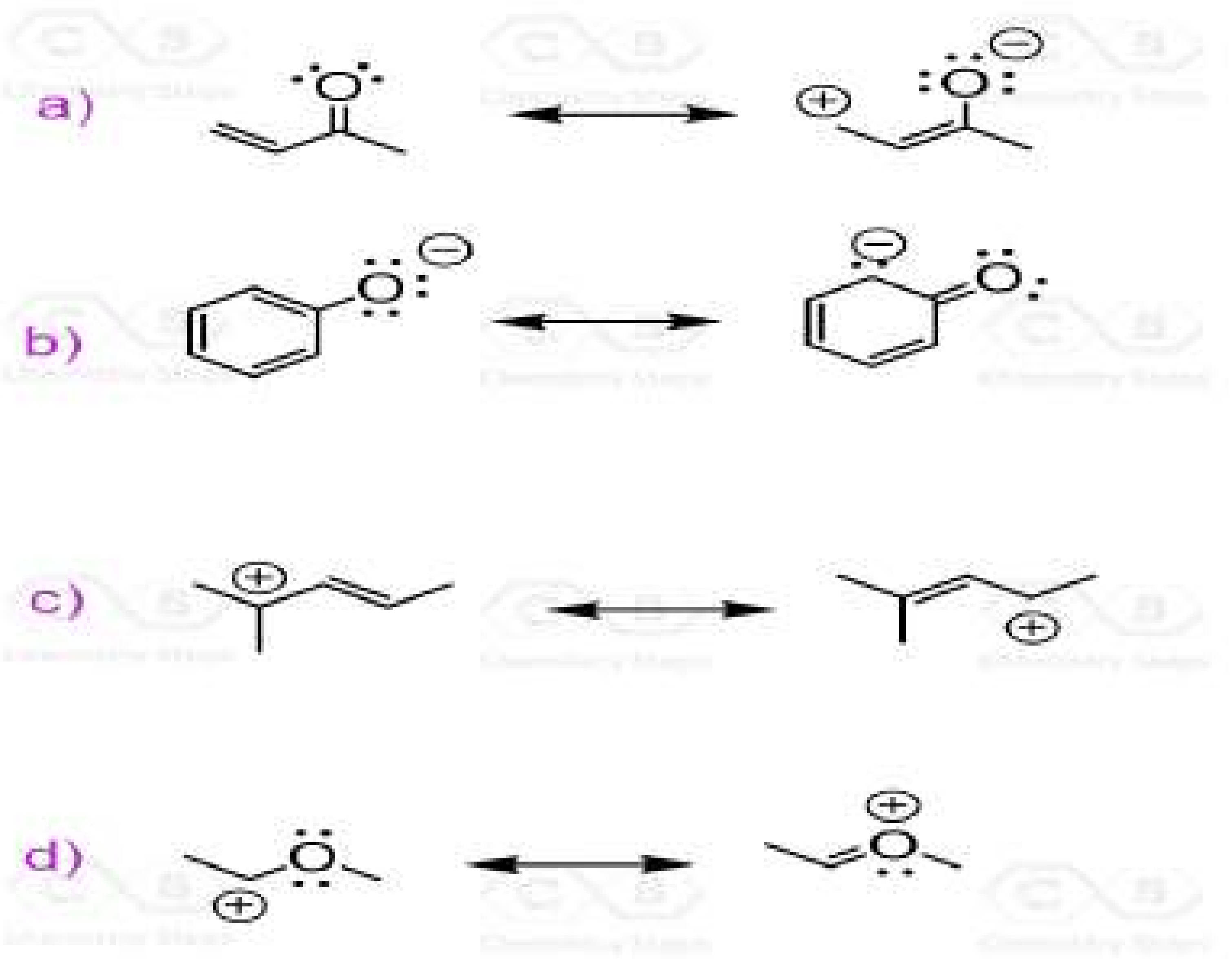
Nitrobenzene Resonance forms



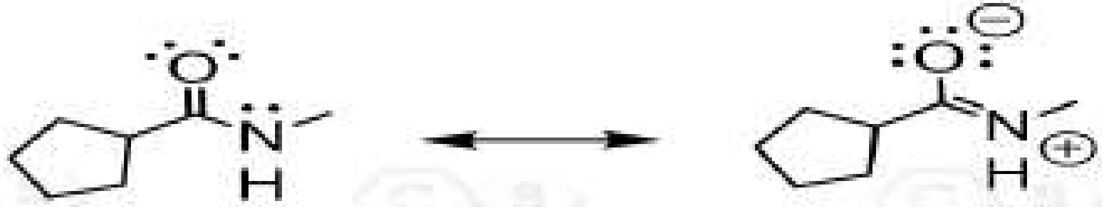
Use curved arrows to draw all the significant resonance structures for the following molecule and determine the major contributor to the resonance hybrid:



Which is more stable resonance forms? Why

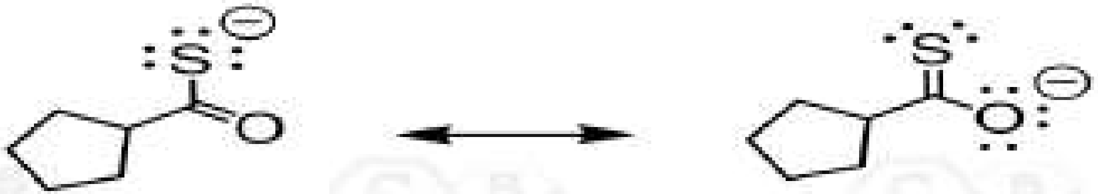


e)

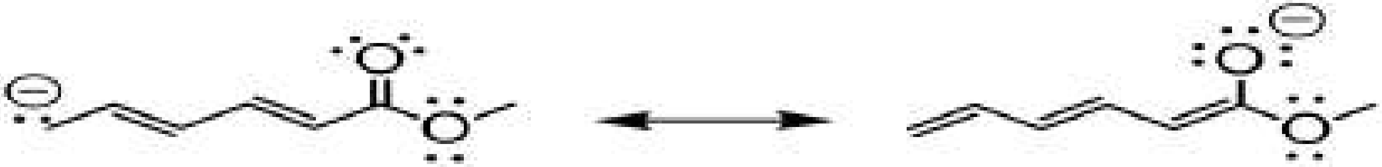


f)

g)

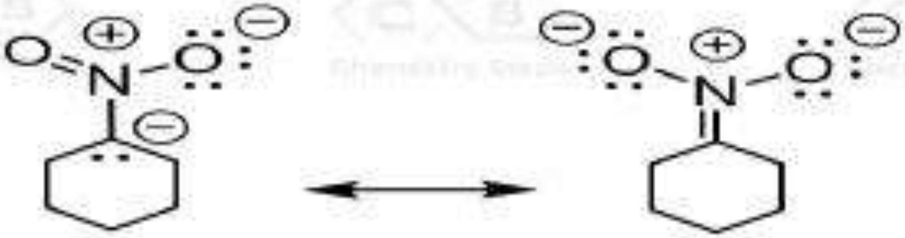


h)



i)

j)

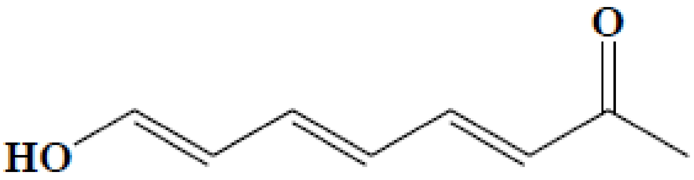


k)

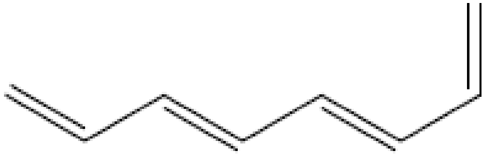
l)

Draw at least one resonance form for each of the following

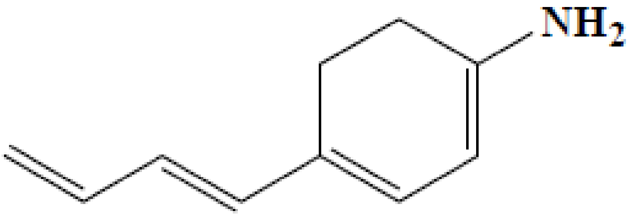
a]



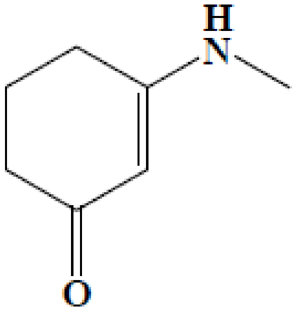
b]



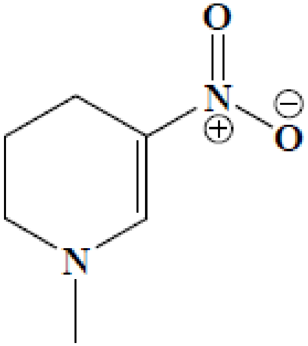
c]



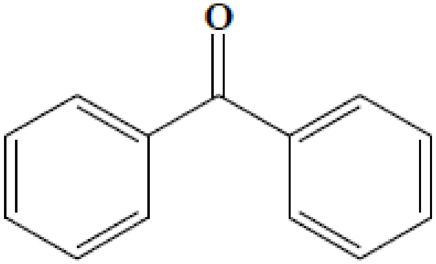
d]



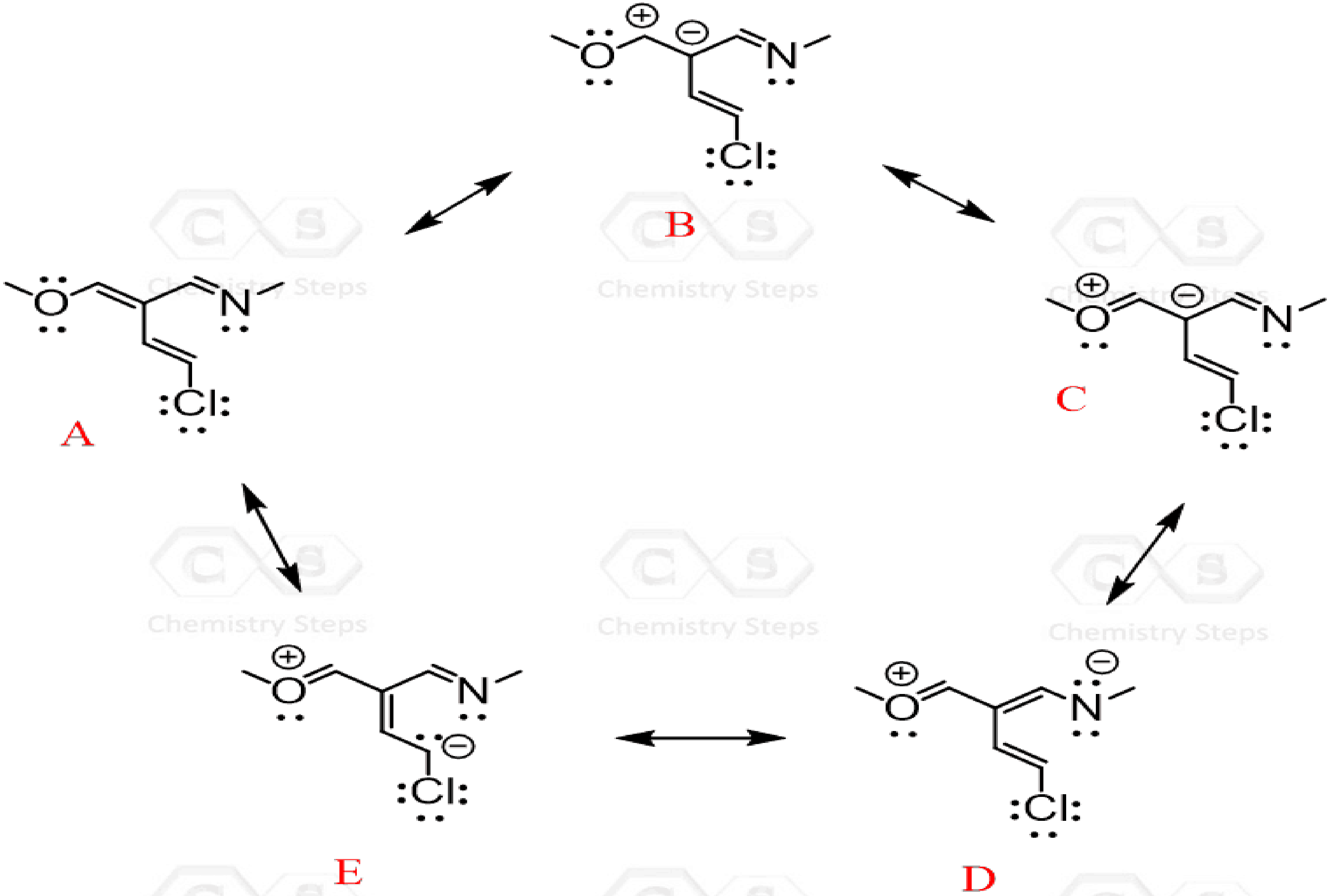
e]



f]



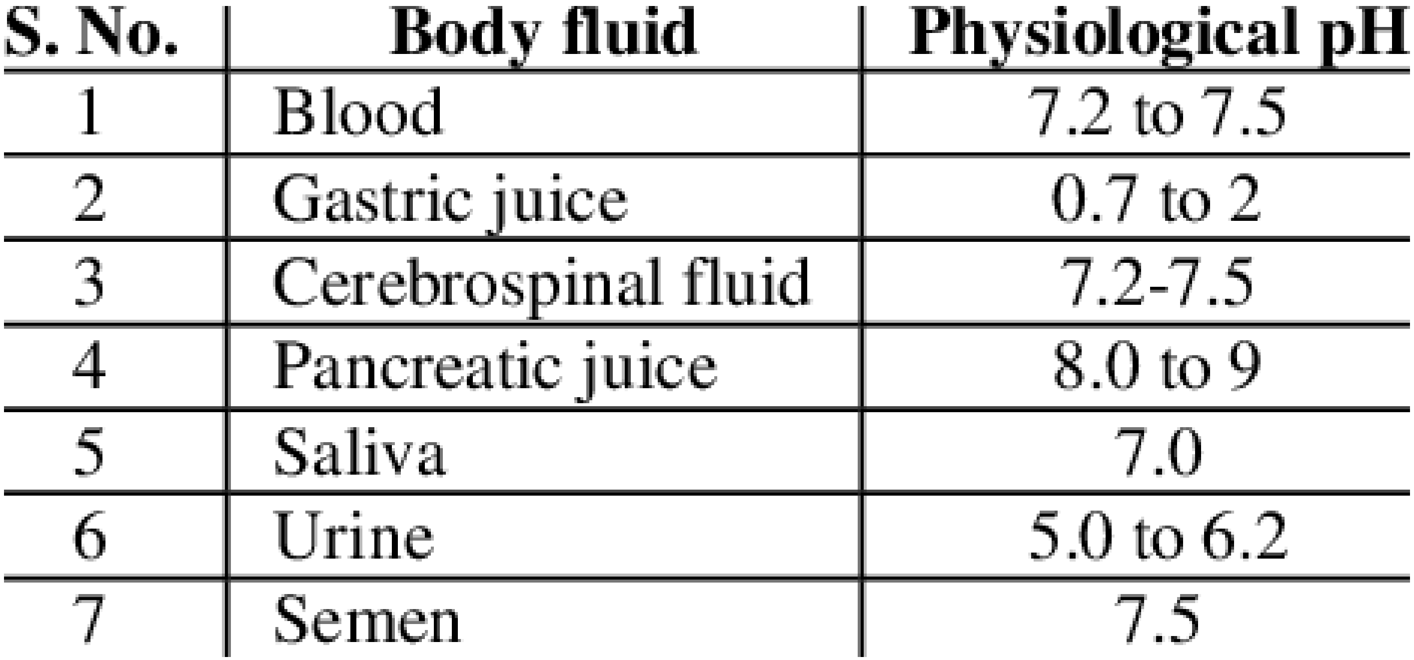
Rank the following resonance structures from the most to the least stable



Acidity & Basicity

1- Acidity

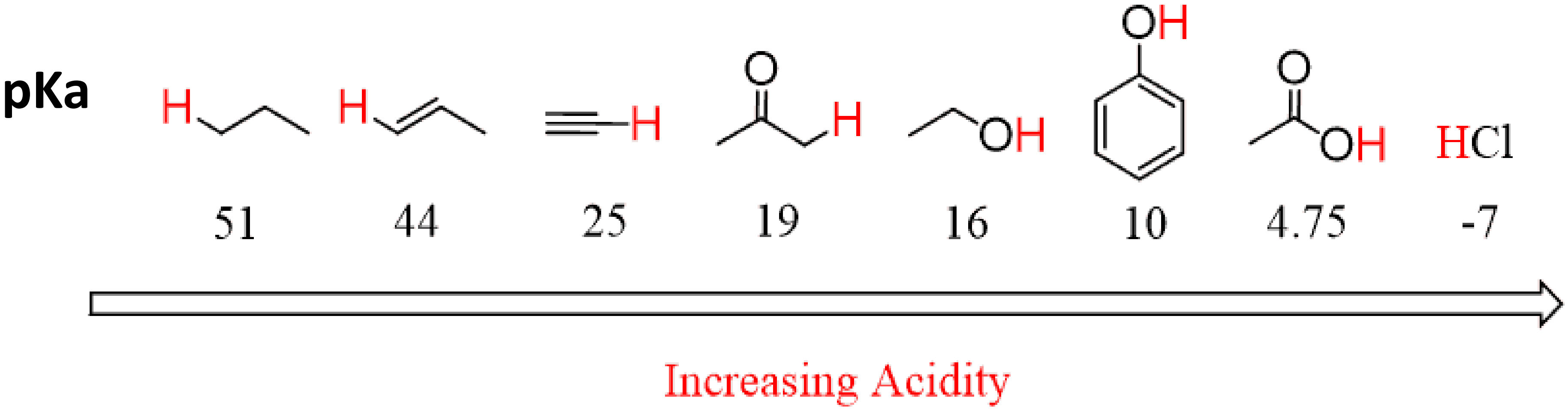
Why acidity and basicity is important in pharmacy?



S. No.	Body fluid	Physiological pH
1	Blood	7.2 to 7.5
2	Gastric juice	0.7 to 2
3	Cerebrospinal fluid	7.2-7.5
4	Pancreatic juice	8.0 to 9
5	Saliva	7.0
6	Urine	5.0 to 6.2
7	Semen	7.5

It is important to understand pH and its influence on drug solubility, stability, and absorption. In an acidic medium, basic drugs are more charged and acidic drugs are less charged. ... This is why weak acids are better absorbed from the stomach and weak bases from intestine where the pH is alkaline

Ka and pKa and Acid Strength



What is the acid ?

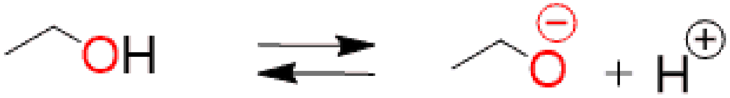
Species that donate proton in easier way or dissociate in faster rate

Weaker conjugate base means a more stable conjugate base because if it was not as stable as it is, it would have reacted with the proton and shift the reaction backward, forming the acid.

$\mathrm{p}K\mathrm{a}_1 = 4.75$

stronger acid

weaker conjugate base



$\mathrm{p}K\mathrm{a}_1 = 16$

weaker acid

stronger conjugate base

$\mathrm{p}K\mathrm{a} = 16$

$\mathrm{p}K\mathrm{a} = 37$

Note:- The acidity mainly relies on the stability of the conjugate base.

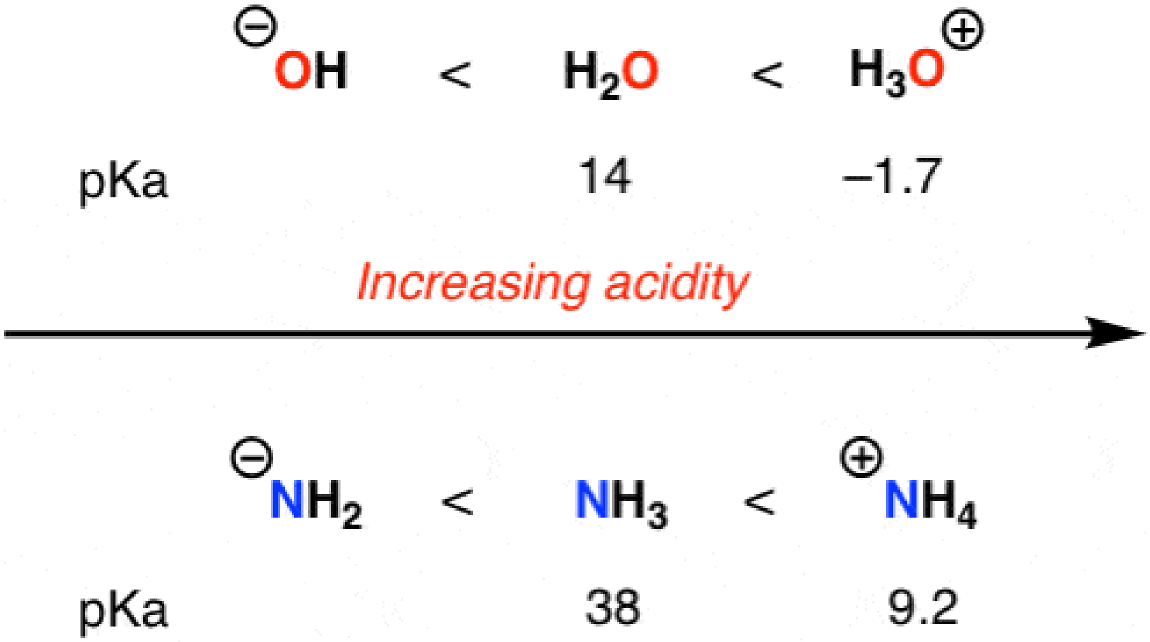
There are five main factors, that affect the stability of the conjugate base:

- **CHARGE**
- **ATOM**
- **RESONANCE**
- **INDUCTION**
- **ORBITAL**

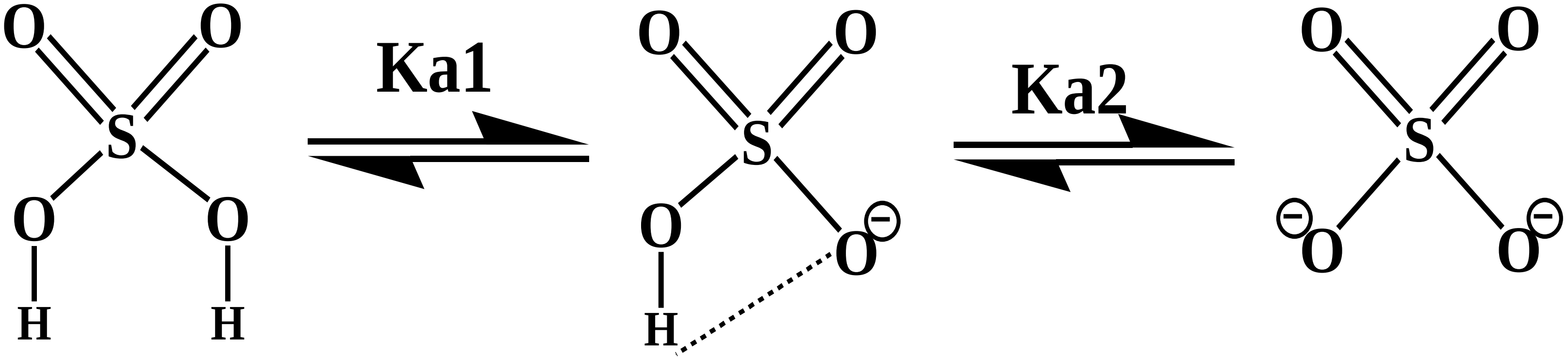
This is often abbreviated and referred to as CARIO.

1] Charge

Removal of a proton, H+ from a positive species, while it is more difficult to remove H+ from neutral compound and it is most difficult to remove H+ when it is negatively charged species.

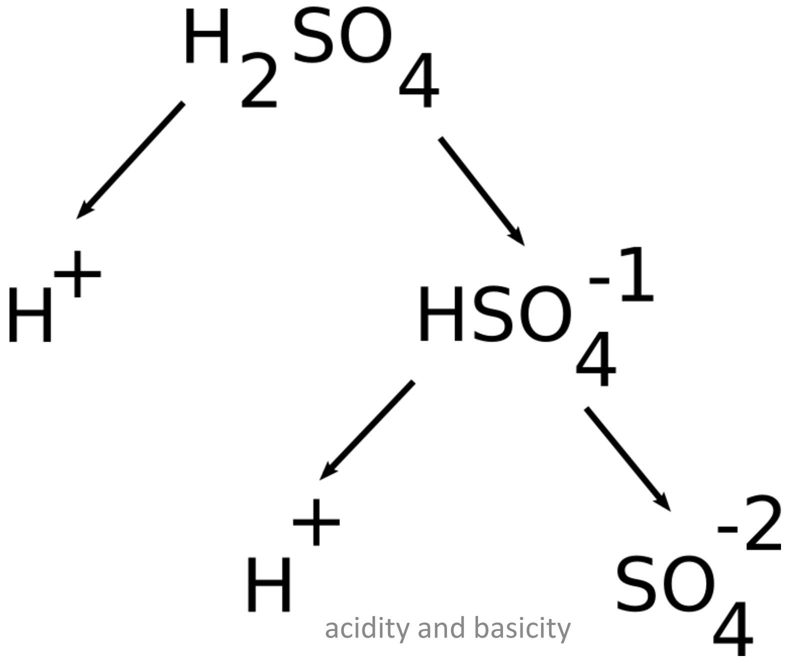


Sulfuric acid acidity



H_2SO_4

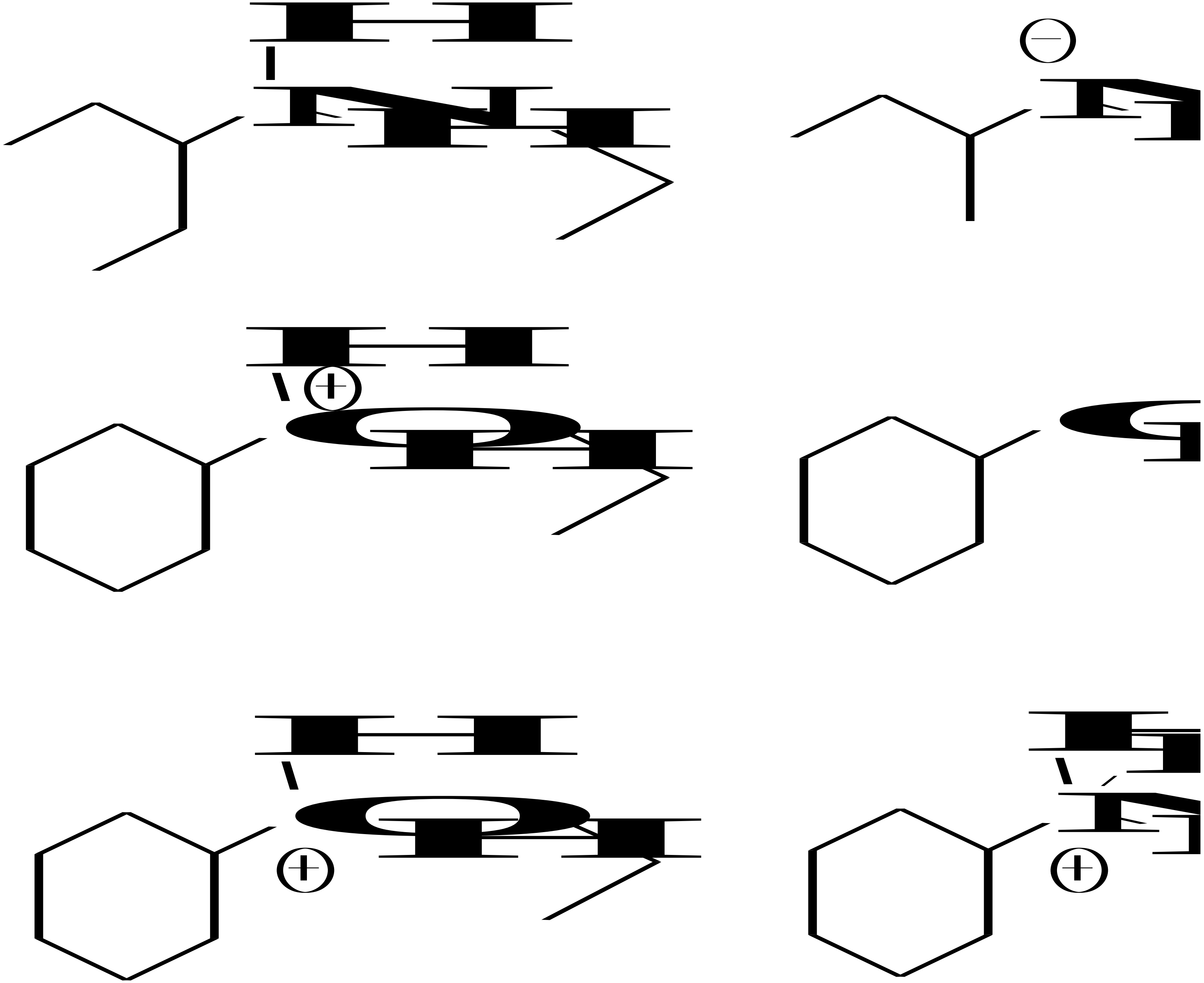
Ka1 ⋙ Ka2



H_2SO_4

H^+ HSO_4^{-1}

H^+ SO_4^{-2}

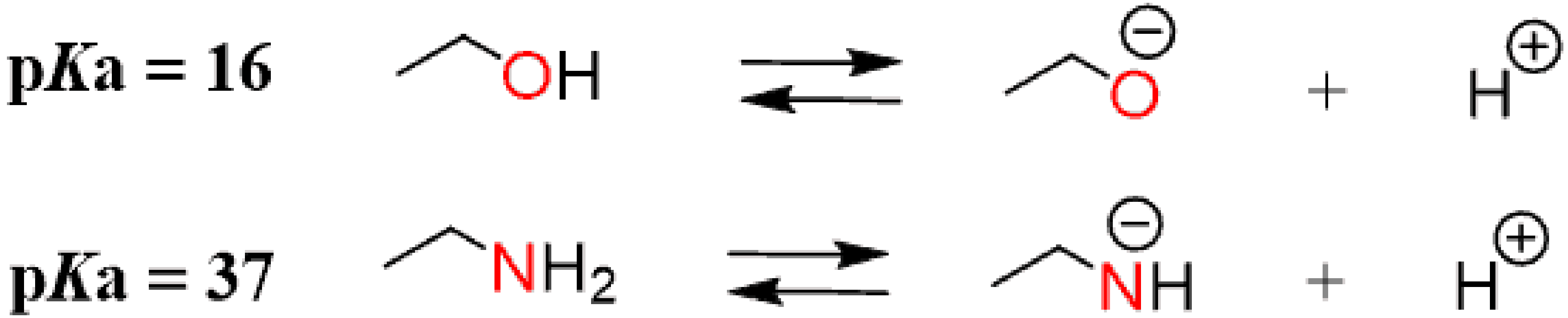


2] Atom:-

i-electronegativity :-

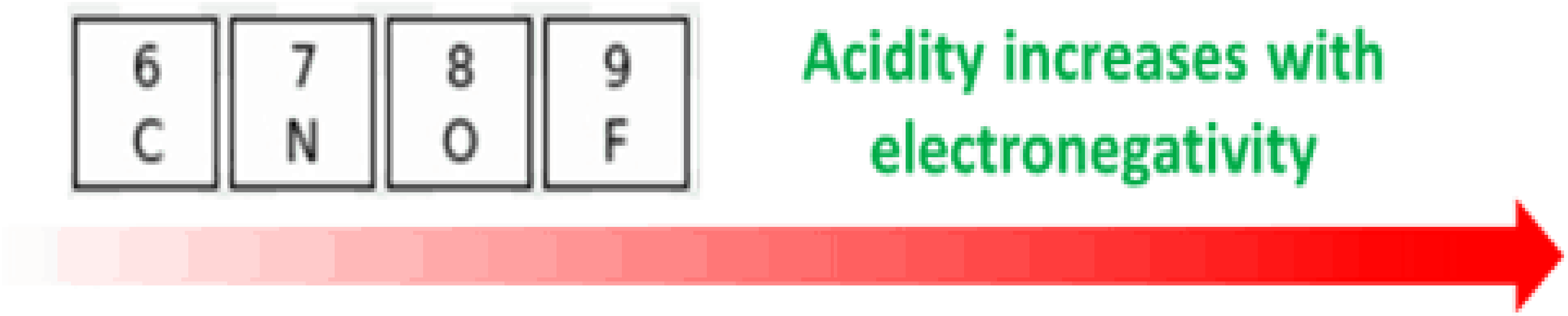
The better it stabilizes the negative charge, the more stable the conjugate base is.

For example, we know that alcohols are more acidic than amines:



The answer is because it is more electronegative than the nitrogen – it likes electrons/negative charge or doesn't mind them as much as nitrogen does.

The acidity of H–A increases as the electronegativity of A increases going from left to the right in the periodic table:

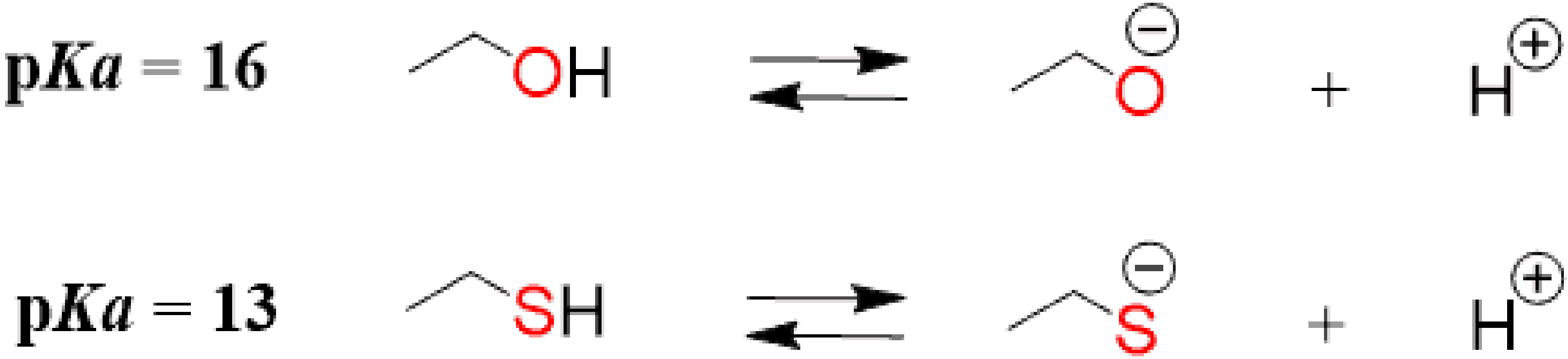


Acidity increases with electronegativity

	$H_3C{-}H$	$H_2N{-}H$	$HO{-}H$	$F{-}H$
p*K*a	50	38	15.7	3.2

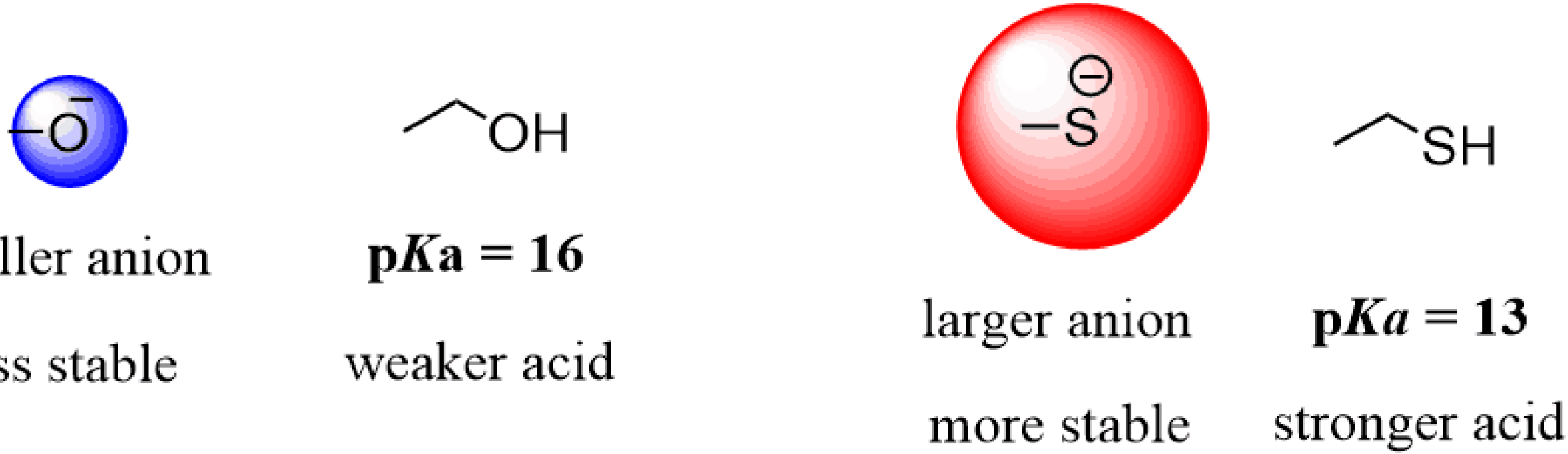
ii- size:-

If you look in the p*K*a table, you will see that thiols (R-SH) are more acidic than alcohols:



This is interesting because oxygen is more electronegative than sulfur, and you'd expect the opposite acidity trend. The reason for this is the ability of larger atoms to better stabilize the negative charge:

The effect of atomic size on the acidity



smaller anion

less stable

pKa = 16

weaker acid

larger anion

more stable

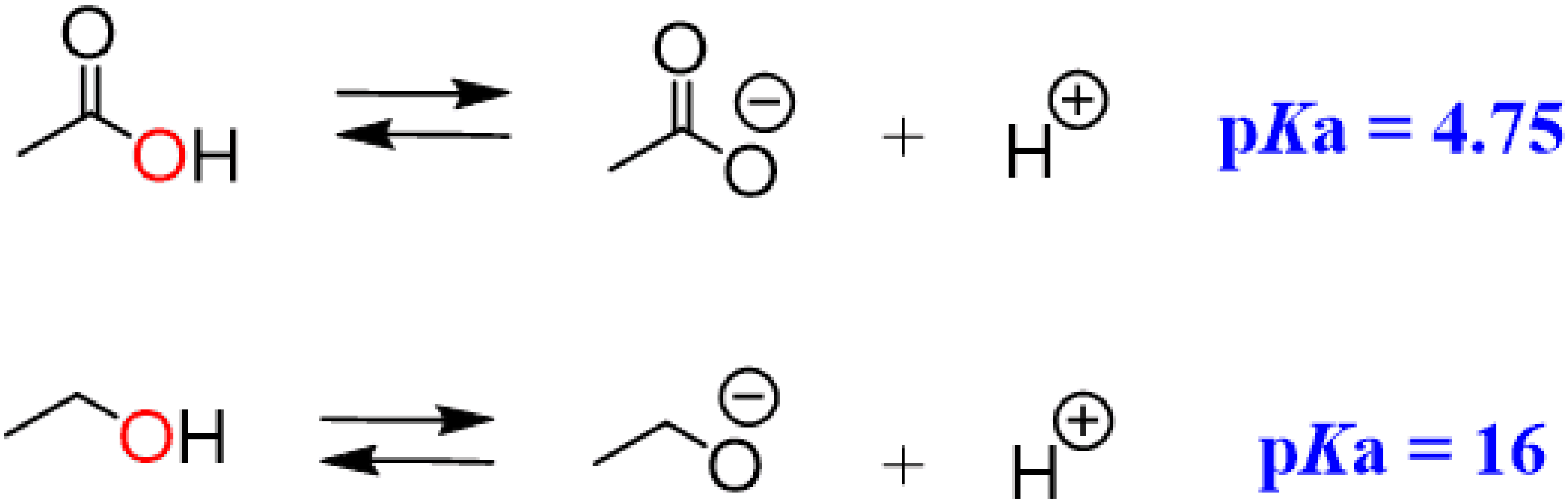
pKa = 13

stronger acid

Therefore, down the periodic table, the atomic size determines the acidity and not the electronegativity.

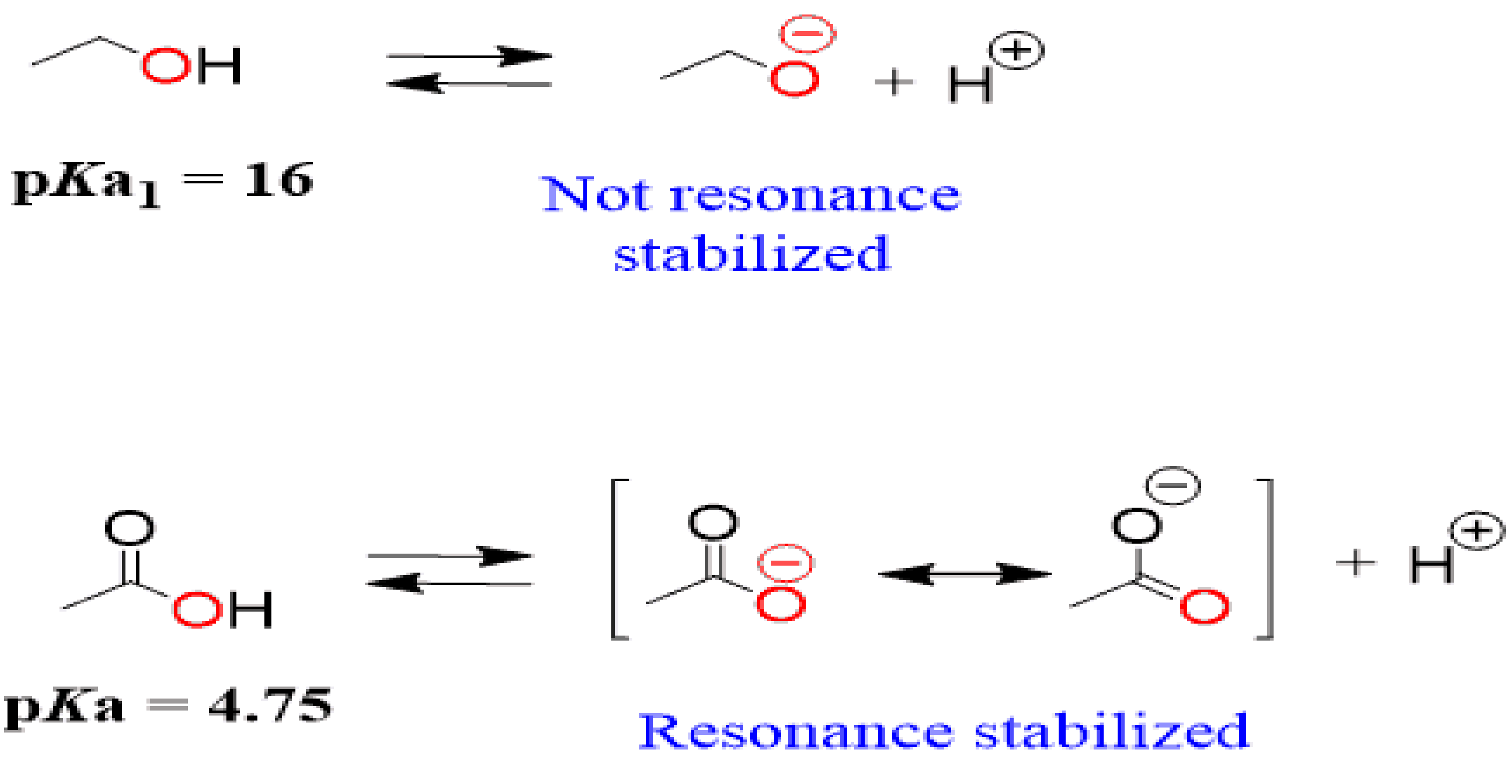
3- Resonance

why carboxylic acids are more than a billion times more acidic than alcohols:



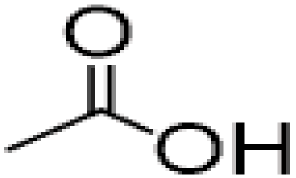
The electrons on the oxygens of a carboxylic acid are delocalized and the negative charge is handled by both atoms, while the oxygen in the alcohol handles the negative charge alone:

The Effect of Resonance-Stabilization on Acidity

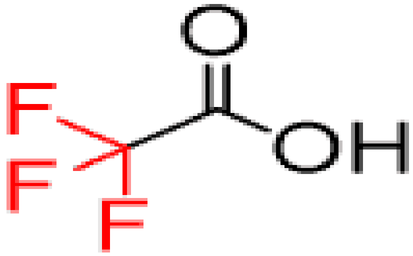


4- Induction

How do we explain the difference in acidity of the following two carboxylic acids?



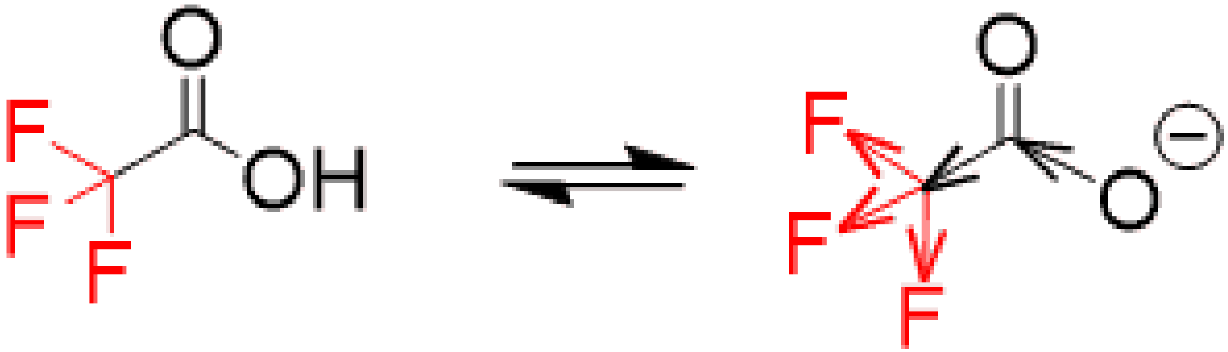
p*K*a = 4.75



p*K*a = 0.23

the question is how the presence of three electronegative atoms increases the acidity of the O-H bond?

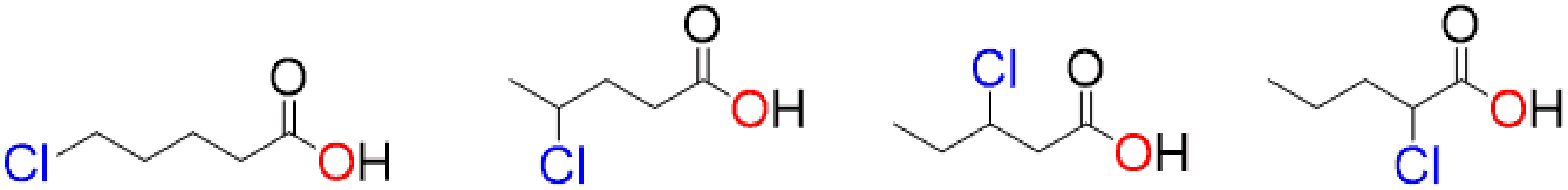
Electronegativity of the fluorine remotely helps the oxygen to handle the negative charge. They are pulling some of the electron density, thus reducing it on the oxygen:



The stronger the electronegativity, the stronger the inductive effect:

p*K*a = 4.75 p*K*a = 2.85 p*K*a = 2.80 p*K*a = 2.65

Another factor is the distance of the electronegative element from the negative charge. The closer it is, the better it helps to stabilize then negative charge:

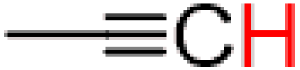


The closer the electronegative atom to the hydrogen, the stronger the acid.

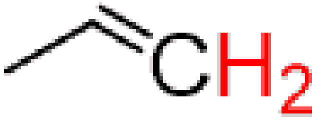
Increasing Acidity

5] Orbital/Hybridization

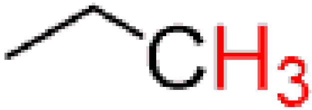
To illustrate this concept, we will consider the acidity of hydrocarbons:



p*K*a = 25

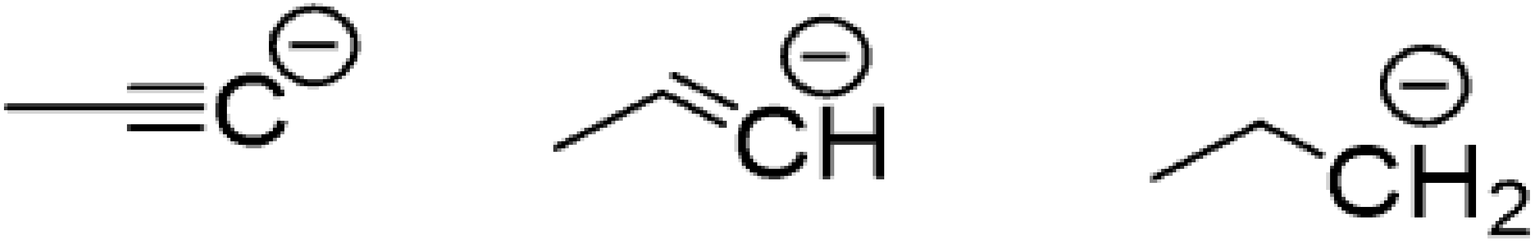


p*K*a = 44



pKa = 50

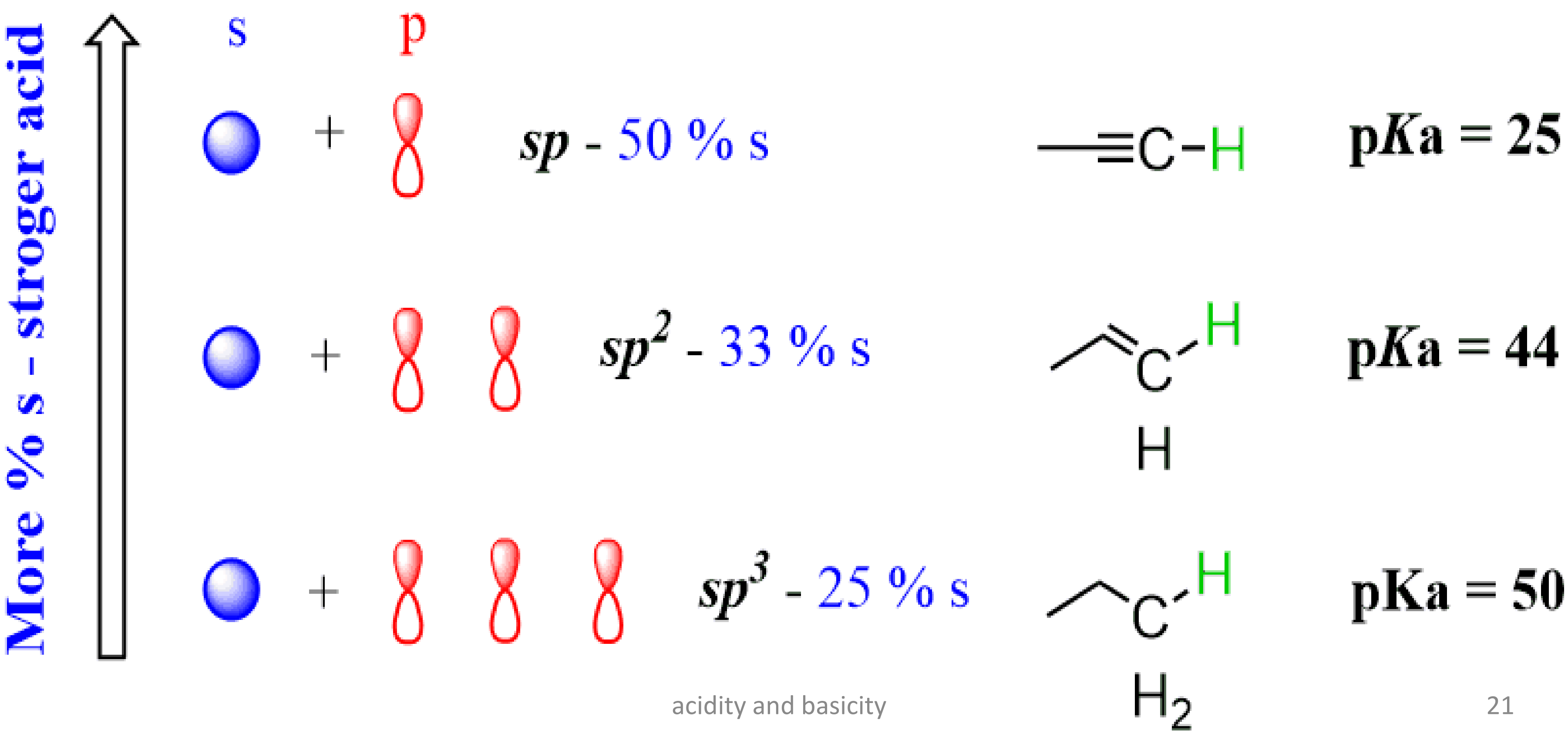
None of the factors discussed earlier can be used to explain this trend of acidity. We have the same atom (C), no resonance stabilization, and no inductive effect. Let’s put a negative charge on each carbon and to take
a closer look:



The only difference is these carbons is their hybridization state. Remember, alkanes are sp3, alkenes are sp2 and alkynes are sp-hybridized.

What you need to know is that s orbitals are more electronegative than p orbital, and the more s character the hybrid orbital has, the better it stabilizes the negative charge. These are the percentages of the s orbital (s-character) in

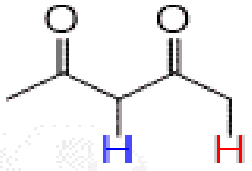
Hybridization Effect on the Acidity of Hydrocarbons



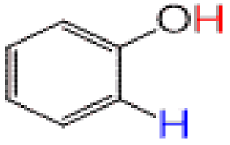
Q1] Determine if the blue- or red-colored proton is more acidic in each of the following compounds:

To summarize, whenever you need to determine the more acidic proton, visualize (or better draw) the conjugate bases and determine which one is more stable bas

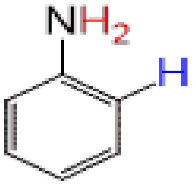
a)



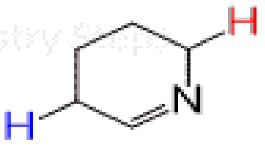
b)



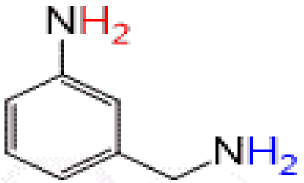
c)



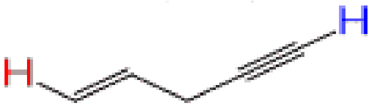
d)



e)

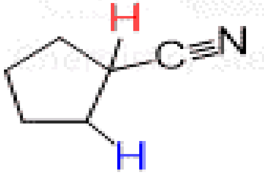


f)



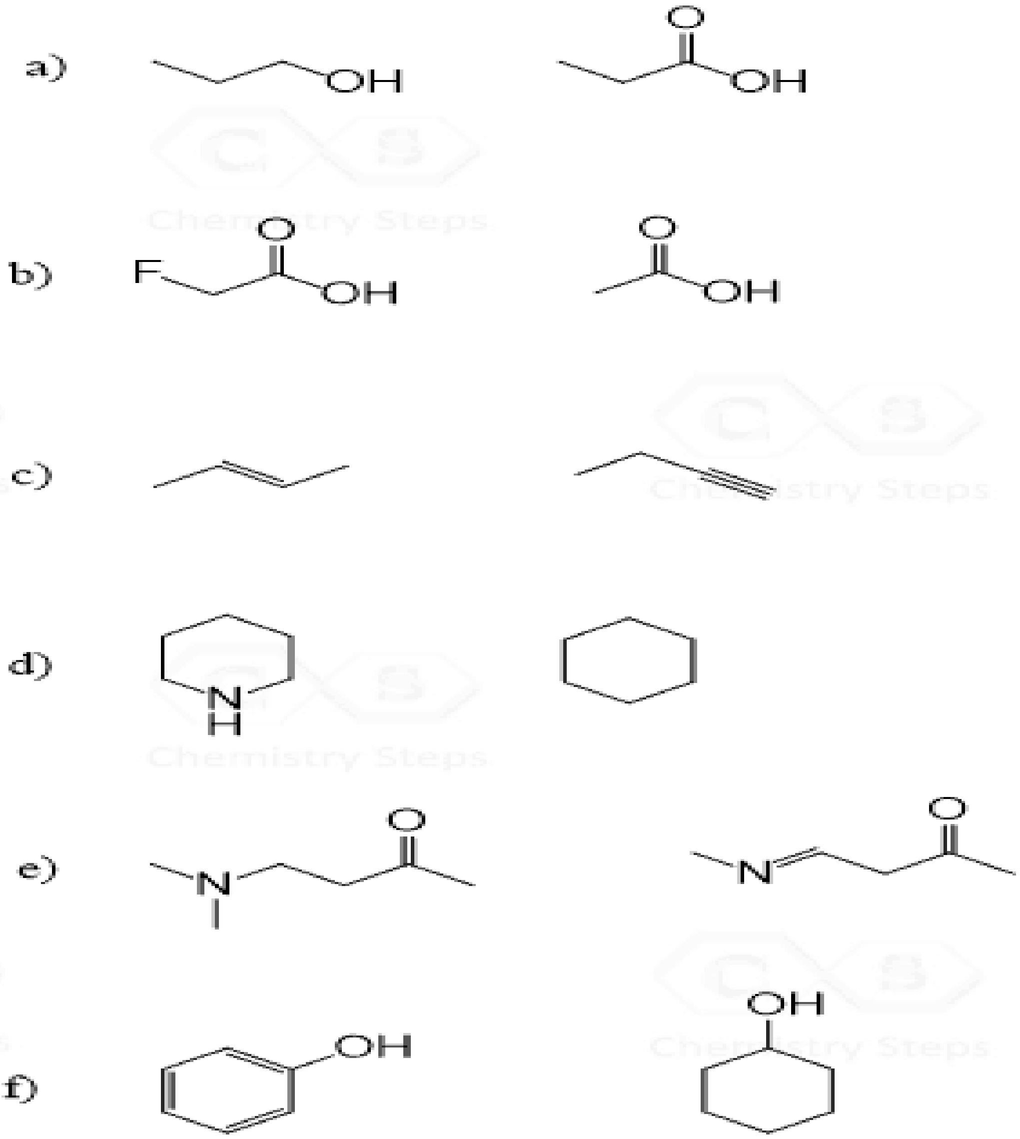
g)

h)



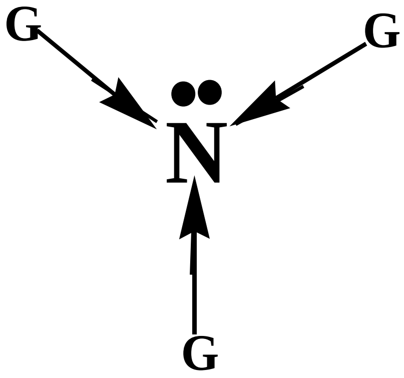
Q2] Identify the most acidic proton in each molecule

To summarize, whenever you need to determine the more acidic proton, visualize (or better draw) the conjugate bases and determine which one is more stable bas

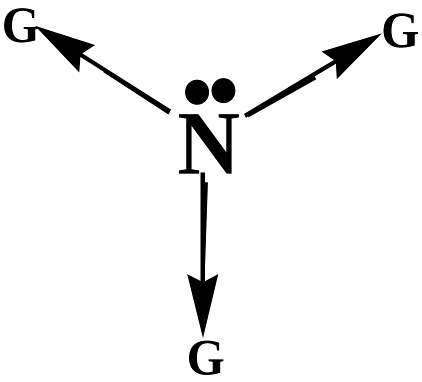


2- Basicity

We are dealing with Lewis base, and we will focus on Nitrogen as the most well known atom.



G:- is an electron donating groups such as alkyl group



G:- is an electron withdrawing groups such as NO_2,CF_3,CN ....etc

Convenient way to look at basicity is based on electron pair availability.... the more available the electrons, the more readily they can be donated to form a new bond to the proton and therefore the stronger base.

Key factors that affect electron pair availability in a base, B

Factors affecting strength of base

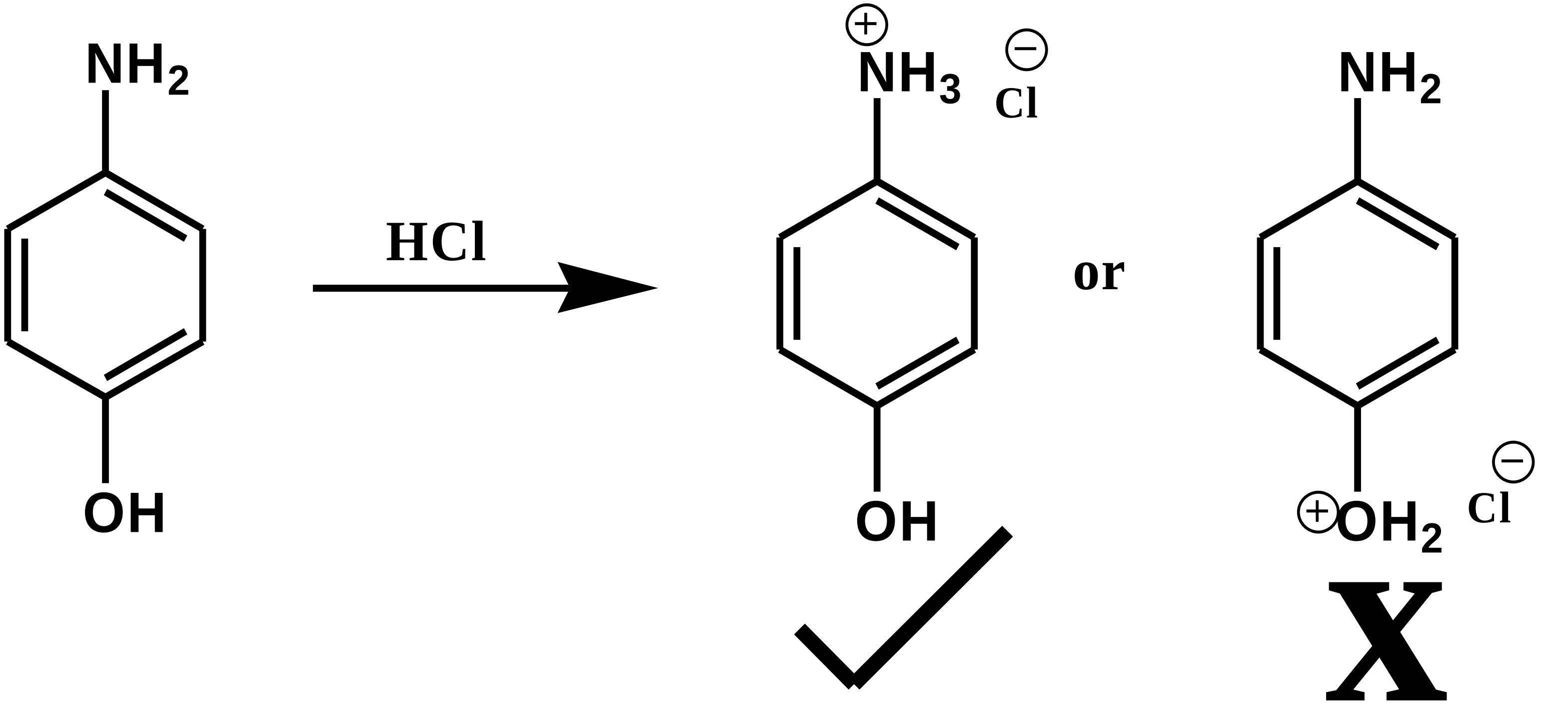
1- Electronegativity and Size

When comparing atoms within the same row of the periodic table, the more electronegative the atom donating the electrons is, the less willing it is to share those electrons with a proton, so the weaker the base.

$$CH_3^- > NH_2^- > HO^- > F^-$$

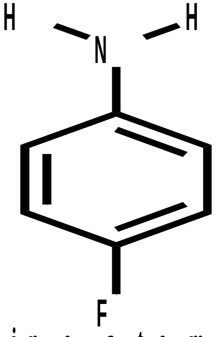
What is the evidence that oxygen is more basic nitrogen ??

[redacted]

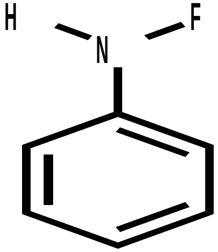


2. Inductive effect

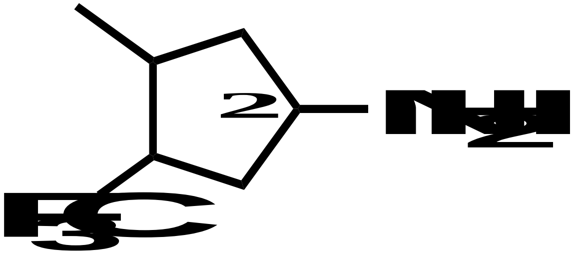
If nitrogen is directly or indirectly bonded to an EW group, this will affect negatively on basicity.

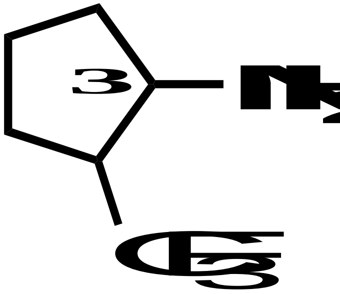


Flourine atom is bonded indirectly to the nitrogen atom

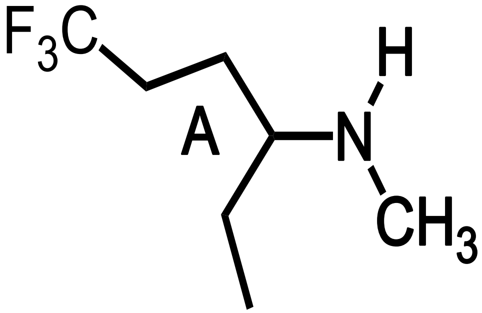


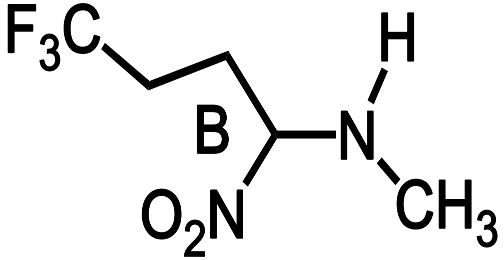
Flourine atom is bonded directly to the nitrogen atom

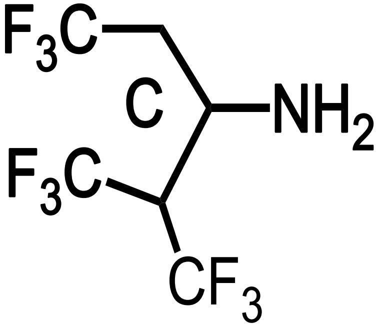




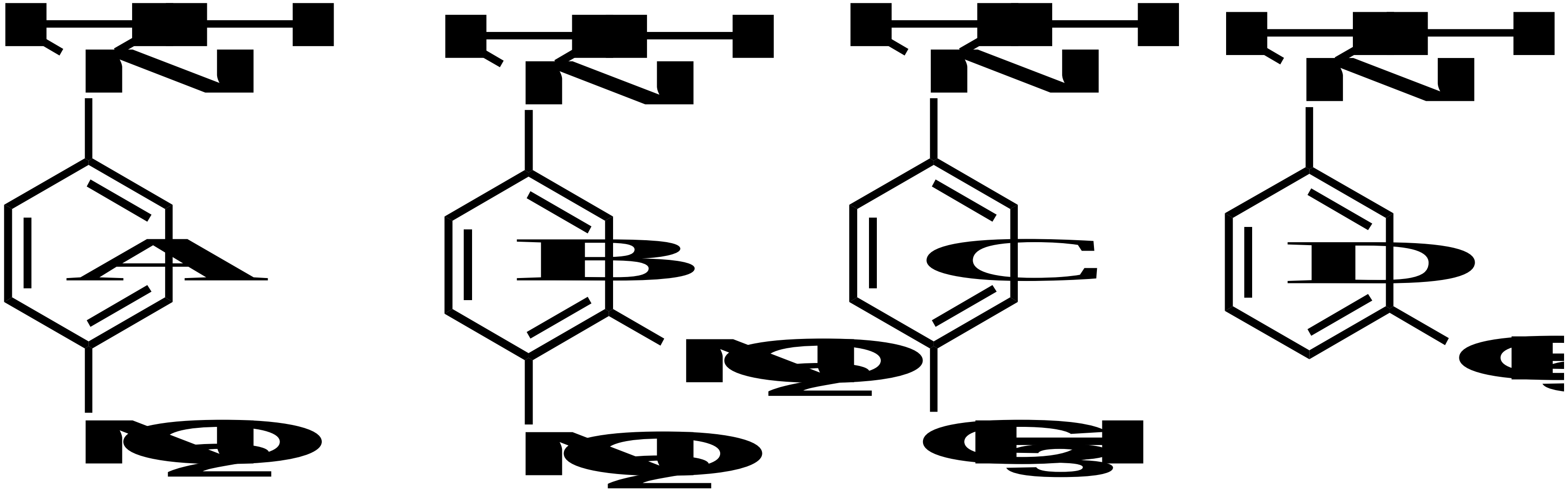
1< 3 < 2







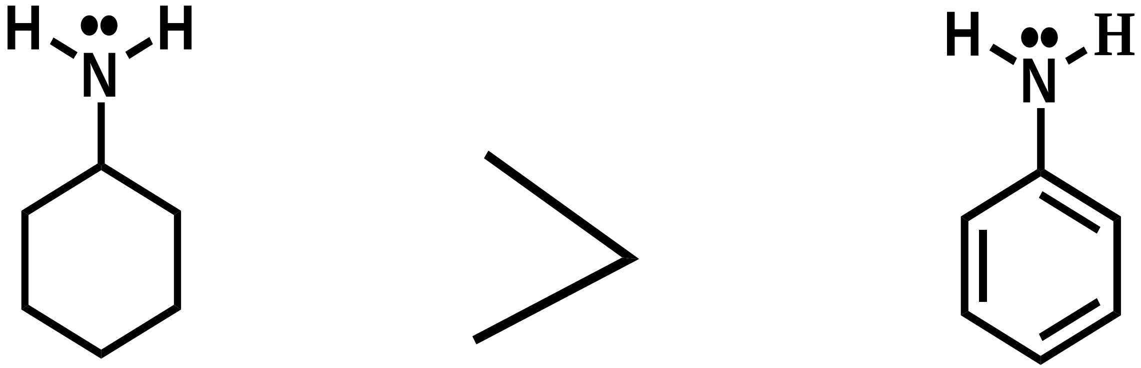
C< B < A



B< A< C < D

3. Resonance effect

Resonance is factor leads to scatter the lone pair away from nitrogen atom will minimize the basicity.



The lone pair is concentrated on nitrogen atom, so it is easy to attack the acid

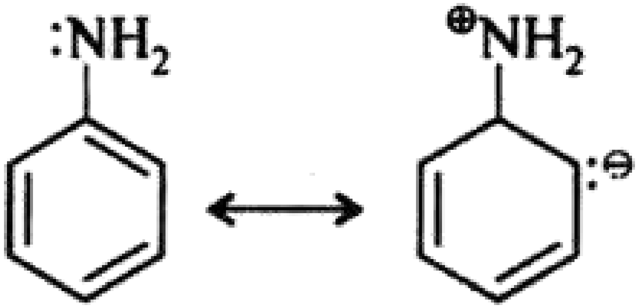
The lone pair is scattered away from nitrogen atom by resonance, so it is weak to attack the acid

For that;

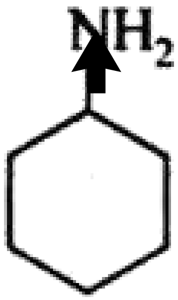
1- Aliphatic amine is more basic than aromatic amine

2- Amine is more basic than amide

1. Aliphatic amine is more basic than aromatic amine

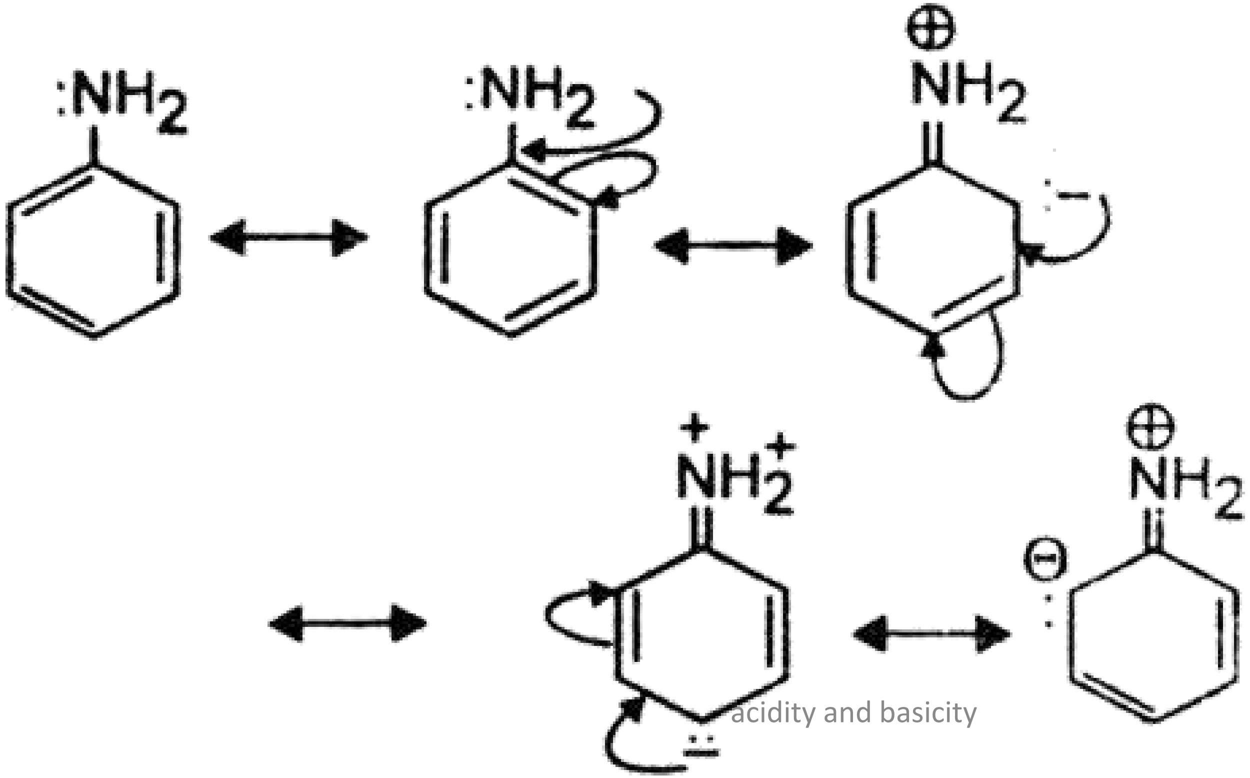


Resonating structures of aniline



Cyclohexyl amine (No resonance)

Aniline is less basic than Cyclohexylamine due to resonance effect.



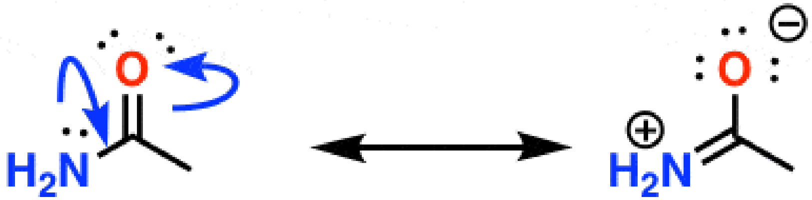
2. The basicity of amides is much lower than that of amines. Why?

Less basic **More basic**

- Oxygen is more electronegative than nitrogen, so inductive effects play a role

The Basicity Of Nitrogen Is Decreased When It Is Attached To A Pi-Acceptor

oxygen acts as a "pi acceptor" Æ *(oxygen accepts electron pair from pi bond, forming a new lone pair on oxygen)*



nitrogen acts as a "pi-donor"

Æ

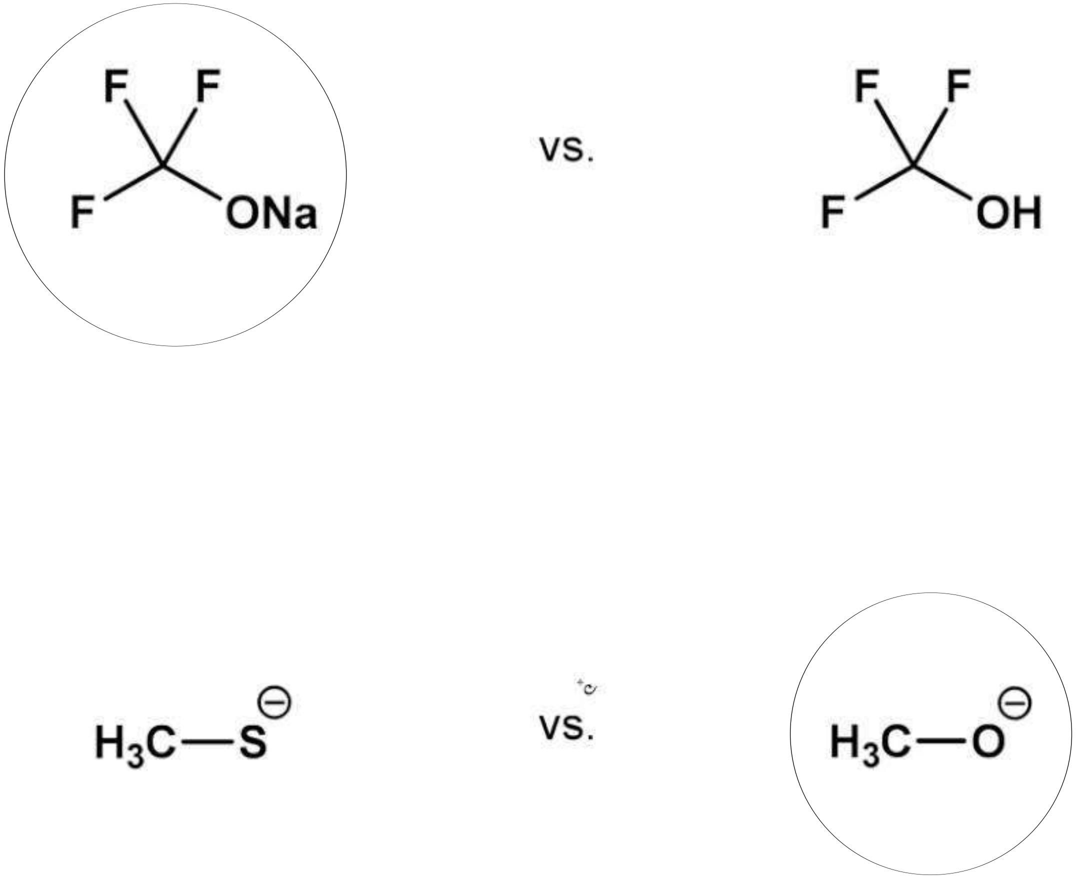
(nitrogen donates a lone pair to form a new pi-bond)

Major resonance contributor

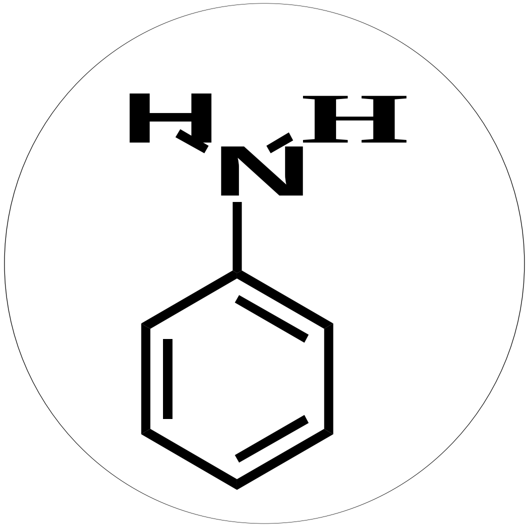
Note that nitrogen can't act as a base in this resonance form!

(Fun fact: the oxygen of amides is more basic than the nitrogen)

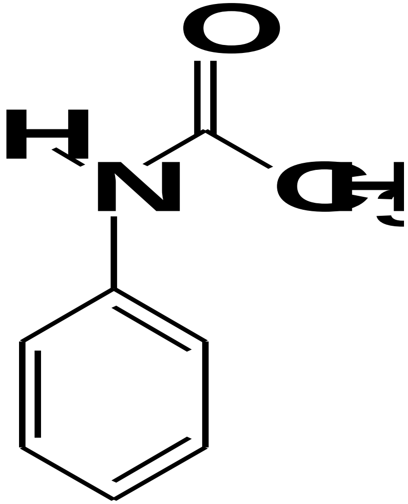
1] Which is more basic ? Why



2] Which is more basic ? why

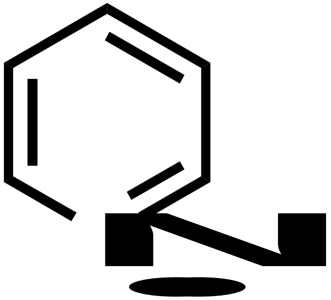


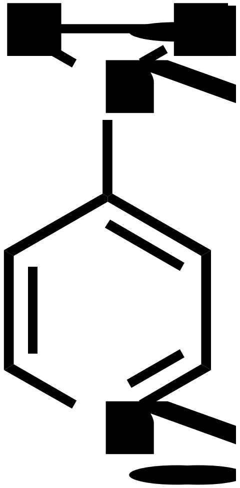
Aniline

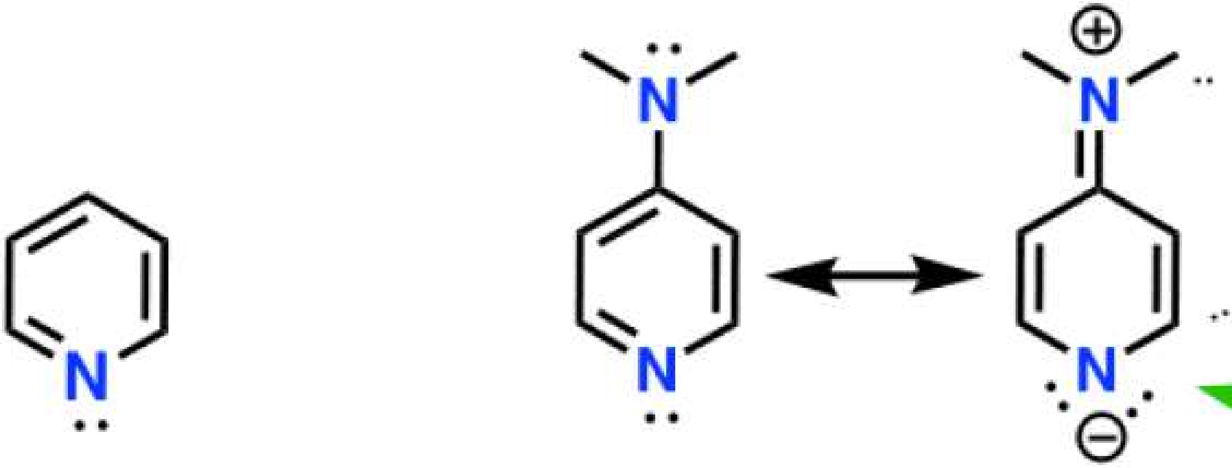


Acetanilide

3] Which is more basic ? why





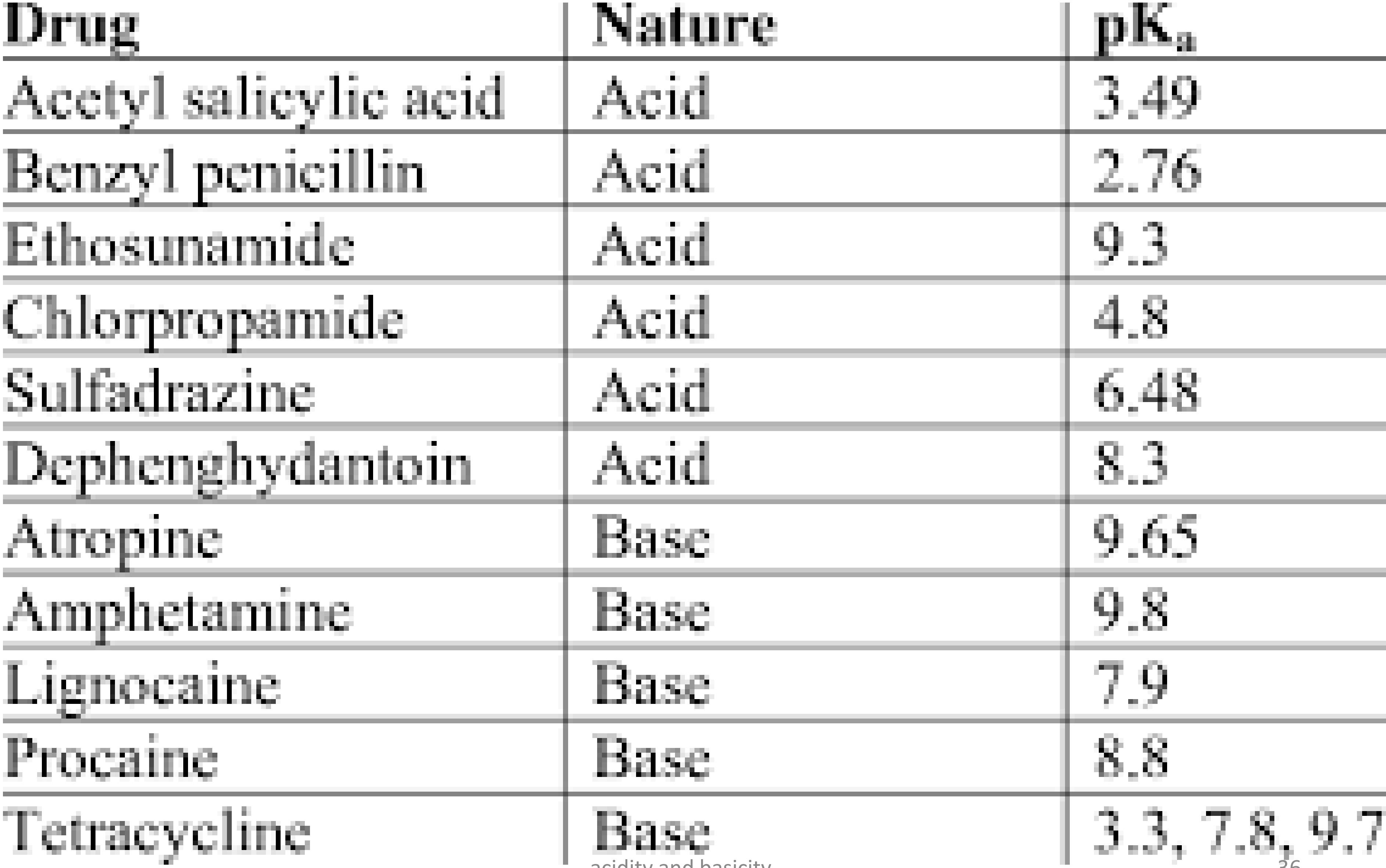


Nitrogen acts as pi-donor

Most basic nitrogen

key resonance form

Acidic and basic drugs



Drug	Nature	pK_a
Acetyl salicylic acid	Acid	3.49
Benzyl penicillin	Acid	2.76
Ethosunamide	Acid	9.3
Chlorpropamide	Acid	4.8
Sulfadrazine	Acid	6.48
Dephenghydantoin	Acid	8.3
Atropine	Base	9.65
Amphetamine	Base	9.8
Lignocaine	Base	7.9
Procaine	Base	8.8
Tetracycline	Base	3.3, 7.8, 9.7

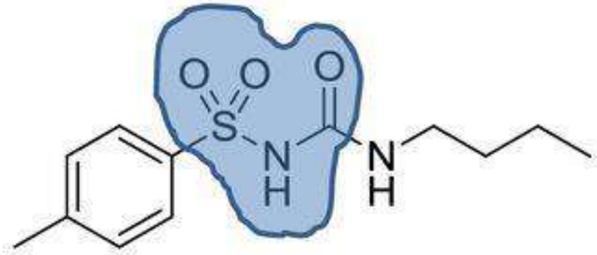
Rules

Acid drugs – become more NON ionized in acidic pH

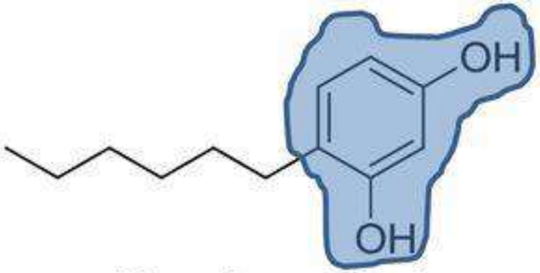
Basic drugs – become more NON ionized in basic pH (alkaline pH)

	Acid Drug	**Basic Drug**
Acid pH Environment	NON-ionized	IONIZED
Basic pH Environment		NON-ionized

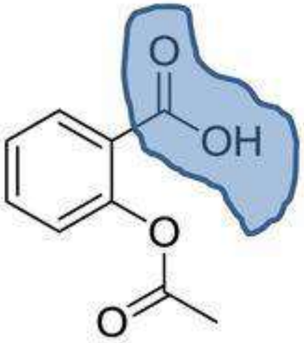
Examples of acidic drugs



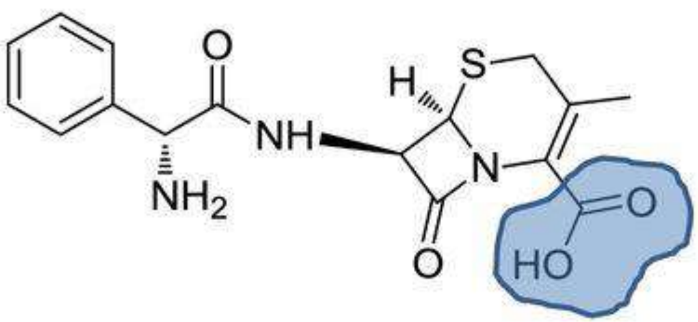
Tolbutamide
hypoglycemic agent



4-hexylresorcinol
topical anesthetic

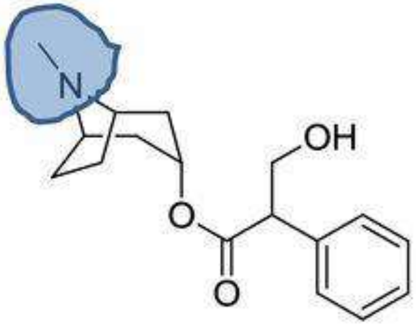


Aspirin
NSAID

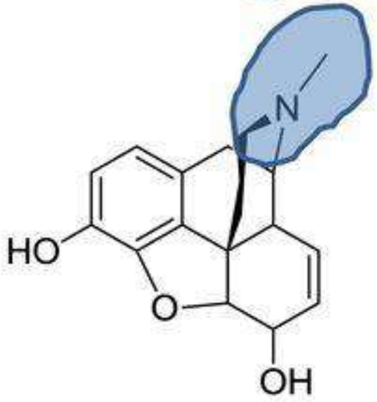


Cephalexin
Antibacterial agent

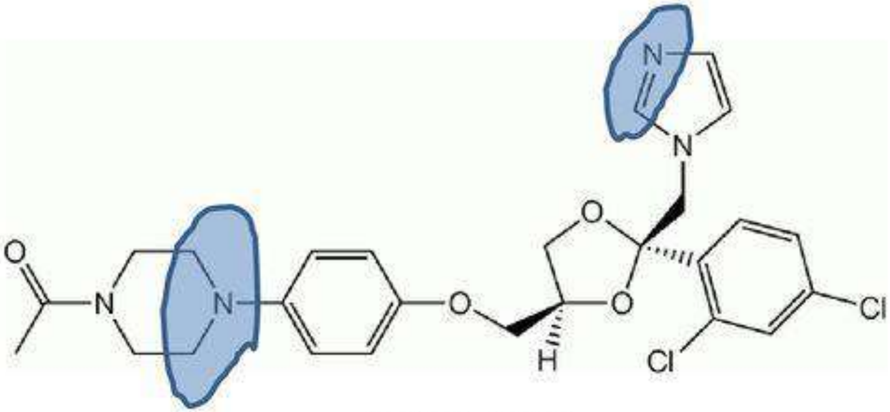
Examples of basic drugs



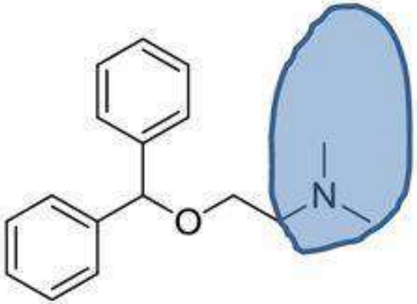
Atropine
Anticholinergic agent



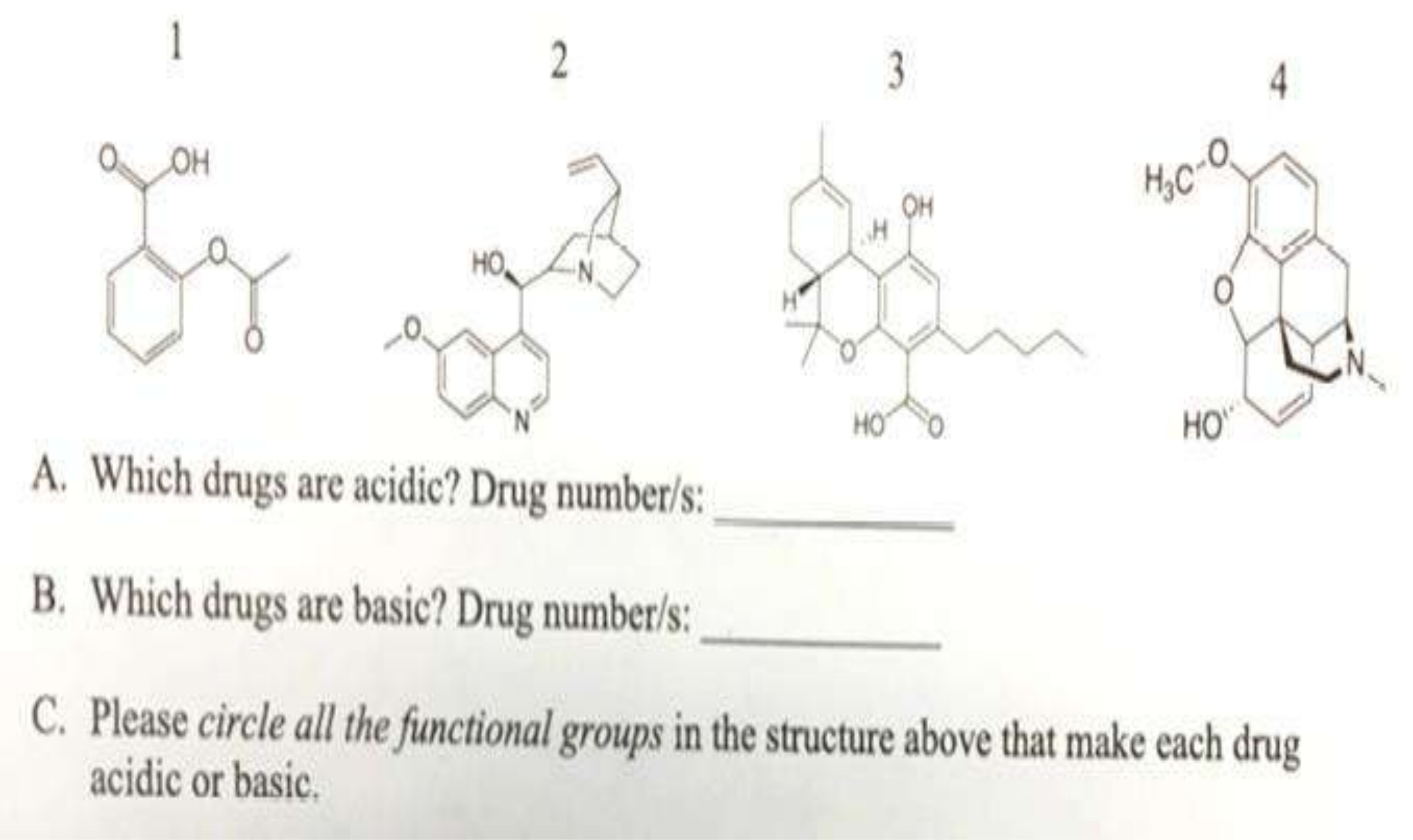
Morphine
opioid analgesic



Ketoconazole
Antifungal agent



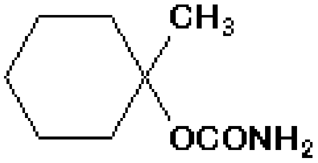
Diphenhydramine
Antihistaminic agent



A. Which drugs are acidic? Drug number/s: ______________

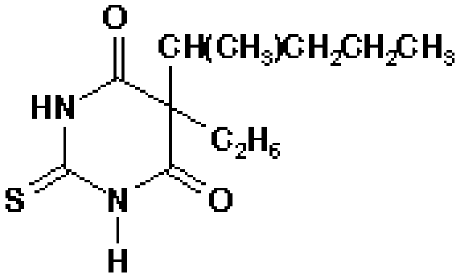
B. Which drugs are basic? Drug number/s: ______________

C. Please *circle all the functional groups* in the structure above that make each drug acidic or basic.



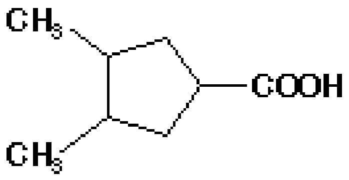
(1)

1. **Alcohol derivative**
2. **Sedative/hypnotic**
5. **Neutral**



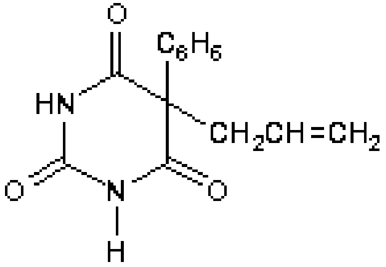
(2)

1. **Thiobarbiturate**
2. **Hypnotic**
3. **Acidic**



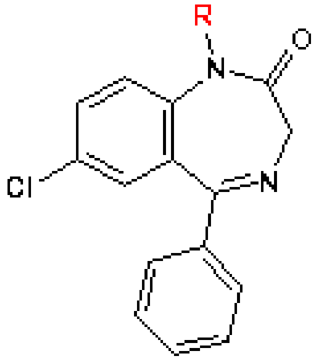
(3)

1. **Alphatic carboxylic acid**
2. **Antiepileptic (e.g. valproic acid)**
3. **Acidic**



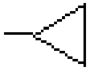
(4)

1. **Thiobarbiturate**
2. **Hypnotic**
3. **Acidic**

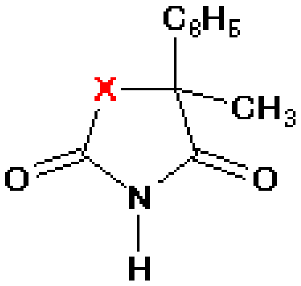


(5) R = H

(6) R = CH_2—



1. **Benzodiazepin-2-ones**
2. **Anxiolytics, sedatives**
5. **Neutral**



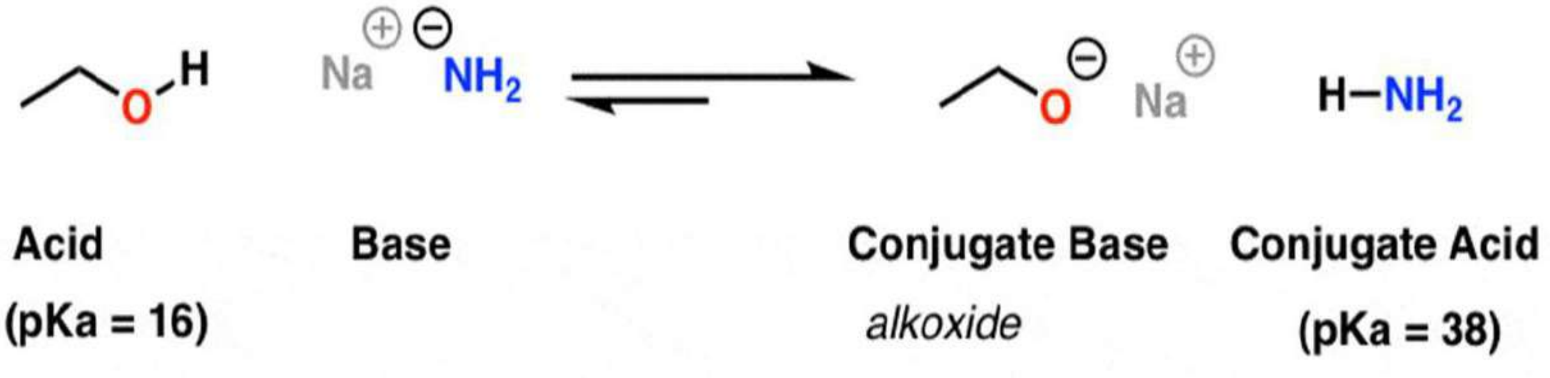
(7) X = NH

(8) X = CH_2

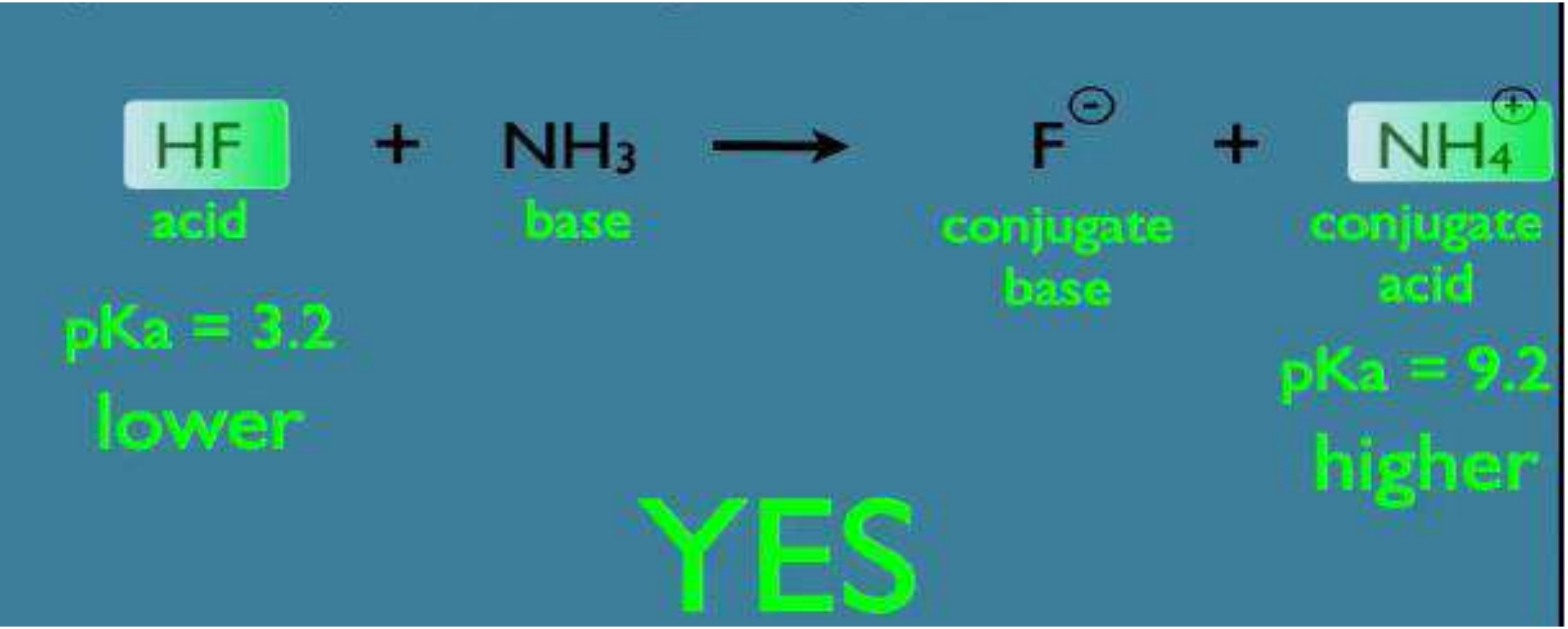
1. **Hydantoin (7)**
   Succinimide (8)
2. **Antiepileptics (7 & 8)**
3. **Acidic (7 & 8)**

Predicting Acid-Base Reactions from pKa Values

The lower the pKa value of an acid, the stronger the acid. The higher the pKa value, the weaker the acid. ... As a rule, the equilibrium of a reaction will favor the side with weaker acids.



This equilibrium is favorable by about 22 pKa units [K - 10^{22}] since we are going from a stronger acid (ethanol, pKa 16) to a weaker acid (NH_3, pKa 38)



$$HF + NH_3 \longrightarrow F^{\ominus} + NH_4^{\oplus}$$

acid — base — conjugate base — conjugate acid

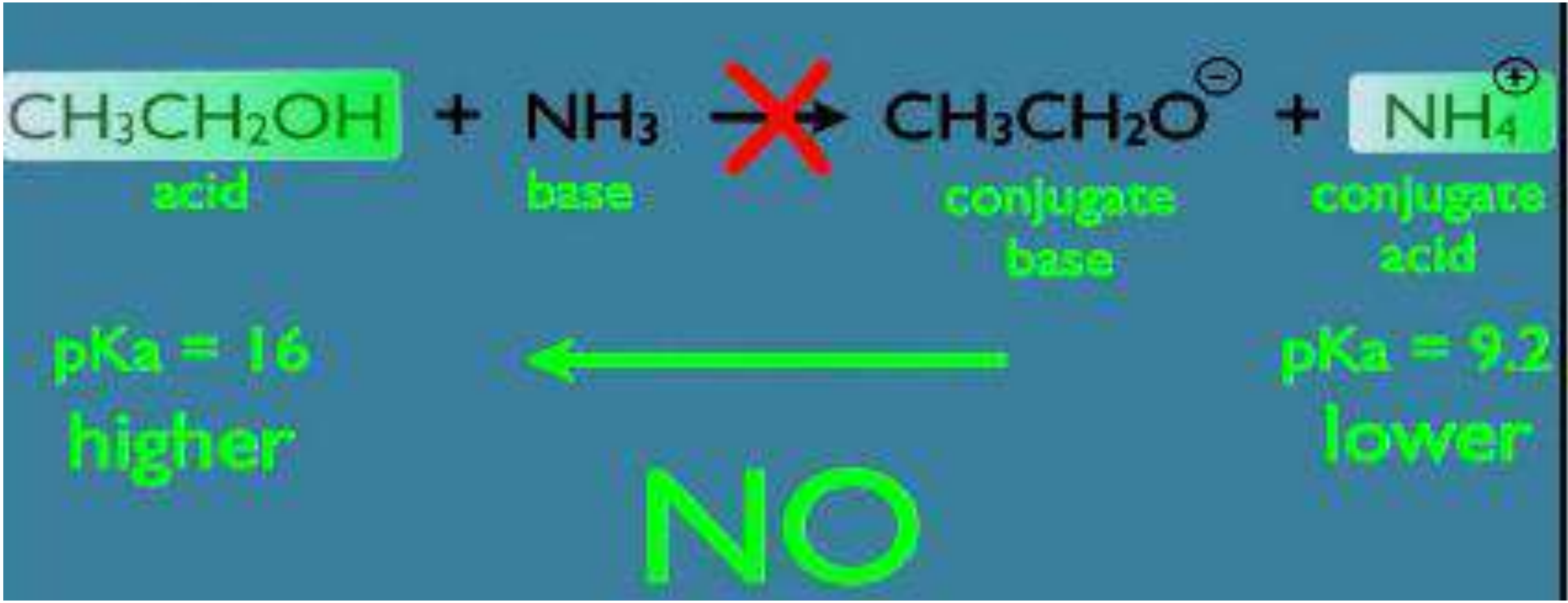
pKa = 3.2

lower

pKa = 9.2

higher

YES



$$CH_3CH_2OH + NH_3 \cancel{\longrightarrow} CH_3CH_2O^{\ominus} + NH_4^{\oplus}$$

Strong acid
(pKa = –8)

Weak acid
(pKa = 14)

Difference: ~24 pKa units

This acid-base reaction is favored by a factor of ~10^{22}
(essentially irreversible)

Acid

Base

Conjugate Base

Conjugate Acid

p*K*a = 4.75

p*K*a = 15.7

$$H_3C{-}C{\equiv}C{-}H \;+\; Na^+NH_2^- \overset{?}{\rightleftharpoons} H_3C{-}C{\equiv}\bar{C}\;Na^+ \;+\; NH_3$$

$$\underset{pKa\,=\,25}{H_3C{-}C{\equiv}C{-}H} \;+\; Na^+NH_2^- \rightleftharpoons H_3C{-}C{\equiv}\bar{C}\;Na^+ \;+\; \underset{pKa\,=\,38}{NH_2{-}H}$$

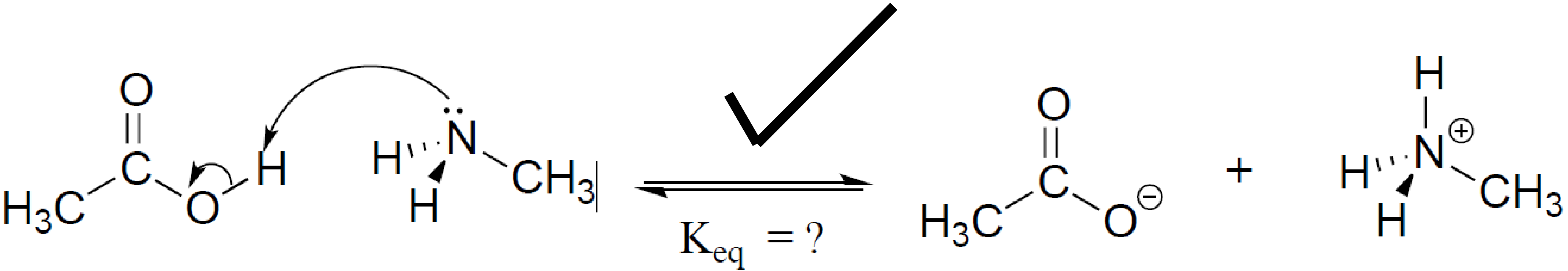
✓

more stable
weaker base

X

less stable
stronger base

Oxygen is more electronegative than nitrogen

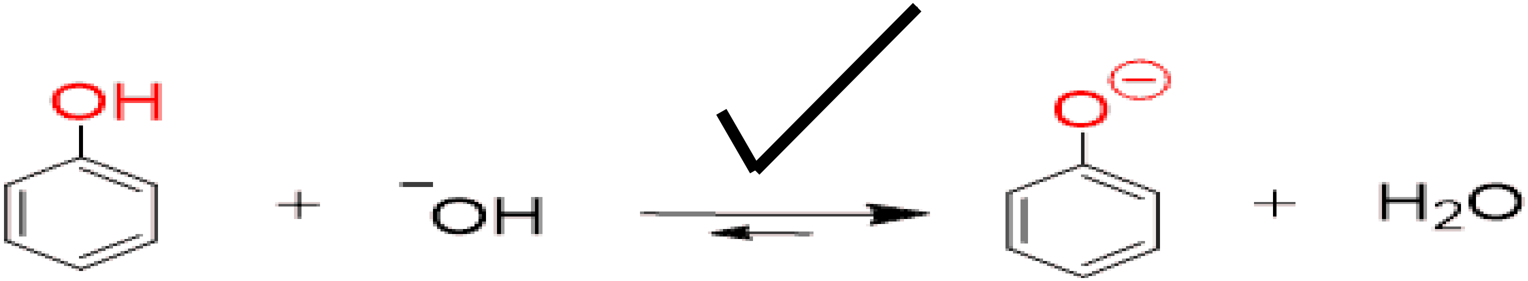


$pK_a = 4.8$

(stronger acid)

$K_{eq} = ?$

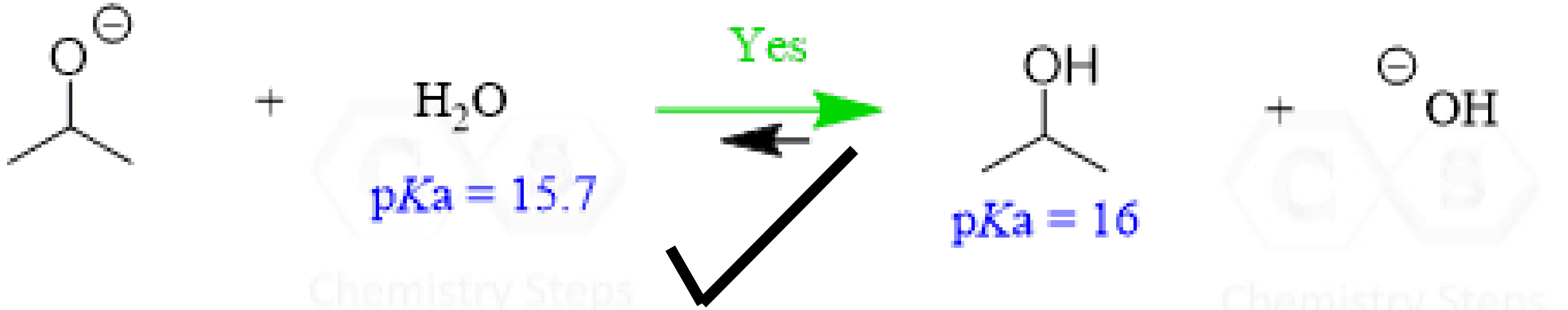
$pK_a = 10.6$



less stable
stronger base

more stable
weaker base

Oxygen in phenol is resonance-stabilized a)



b)