RESONANCE AND INDUCTION TUTORIAL

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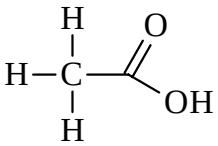
The terms "resonance" and "induction" refer to the electronic effects that atoms or functional groups may have within a compound. These effects are defined below and are dependent on the valence, bonding order and electronegativity of atoms, as well as the molecular geometry. Thus it is important that you understand these concepts prior to reviewing this tutorial.

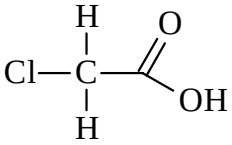
I. INDUCTION

Induction or the **inductive** effect of an atom or functional group is a function of that groups 1). electronegativity, 2). bonding order and charge and 3). position within a structure. Inductive effects refer to those electronic effects of an atom or functional group can contribute through single bonds such as saturated (sp^3) carbon atoms! This is very different from resonance effects discussed later in this section. The contribution of electronegativity, bonding order and position toward induction is as follows:

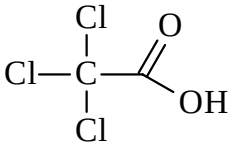
Electronegativity: Atoms or functional groups that are electronegative relative to hydrogen such as the halogens, oxygen, nitrogen, etc. may have a negative inductive effect (-I), depending on their bonding order (see the Table below). Thus these atoms withdraw electron density through the single bond structure of a compound and can assist in the stabilization of negative charge that may form in reactions. One such reaction where -I groups can have a stabilizing (enhancing) effect is the ionization of acids. Consider the case of acetic acid, chloroacetic acid and trichloroacetic acid shown below. All three of these compounds can ionize (loss of proton from the carboxyl OH). The only difference between these three structures in the degree of chloro group substitution. Chlorine atoms are electronegative (three pairs of non-bonded electrons in their valence shell) and thus have a -I effect. Thus they can help stabilize a negative charge, and enhance the ionization of an acid. Note the pKa differences between acetic acid and chloroacetic acid. Furthermore, the more Cl atoms present, the greater the total -I effect and the greater the ease of ionization (lower pKa). Again, note that the electronic effect in this example is being "induced" through single bonds; a saturated (sp^3 hybridized) carbon in this case.



Acetic acid
pKa = 4.76



Chloroacetic acid
pKa = 2.87



Trichloroacetic acid
pKa = 0.64

Atoms or functional groups that are electron donating (hydrocarbons, anions) have a positive inductive effect (+I). These groups can help stabilize positive charges in reactions such as protonation of bases.

- Bonding order and charge: As mentioned above, it is important to consider both the electronegativity and bonding order when analyzing the inductive potential of an atom. For example, oxygen in a hydroxyl group (OH) is electron withdrawing by induction (-I) because the oxygen atom is relatively electronegative and is uncharged in that bonding arrangement. However, oxygen in an "alkoxide" (O^-) structure is electron donating (+I) by induction because in this bonding order (a single bond to oxygen) it has an "excess" of electron density. Thus an OH group would help to stabilize a negative charge within a structure, while it's ionized form, the alkoxide, would stabilize a positive charge!

- Bonding position: The strength of the inductive effect produced by a particular atom or functional group is dependent on it's position within a structure. For example, the further from the site of ionization, the lower the inductive effect. This is illustrated in the example below where the acid with the chlorine atom positioned on a carbon atom nearer the reaction site (OH) is more acidic that the acid where the chlorine atom is positioned further away:

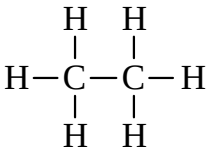
More acidic
Cl "closer" to the reaction site

Less acidic
Cl "further" from the reaction site

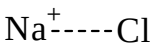
It is also important to understand the difference between inductive effects and resonance effects of a particular atom or functional group and the relationship to bonding position. For example, an oxygen atom in a hydroxy group (OH) is electron withdrawing by induction, but electron donating by resonance when placed in a position on the structure where resonance is possible This will be explained more fully below.

II. RESONANCE

Resonance may be defined as bonding or sharing of electrons between more than two atoms (nuclei). Typical covalent and ionic bonding involves sharing (covalent) or transferring (ionic) electron pairs between two atoms as shown in the examples of ethane and sodium chloride below. In these examples the bonding electrons are **localized**:



Ethane
Localized covalent bonds

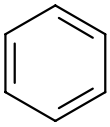


Sodium Chloride
Localized ionic bond

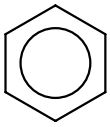
Resonance and Inductive Effects of Various Functional Groups

Inductive Effects: Electron-Withdrawing	**Inductive Effects: Electron-Donating**	**Resonance Effects Electron Withdrawing**	**Resonance Effects Electron Donating**
$-NR_3^+$ $-NH_3^+$	$-O^-$ $-COO^-$	-COOR -COOH	-OH -OR
-COOH -COOR	$-CH_3$ $-CHR_2$ $-CH_2R$ $-CR_3$	-COR -CHO	$-NH_2$ $-NR_2$
$-NO_2$ -CN		$-SO_2R$ $-SO_2NHR$	$-NHR_2$ -SH
-CHO -COR		$-NO_2$ -CN	
-F -Cl -Br -I $-CF_3$		-Ar	
-OH -OR			
$-NH_2$			
-SH $-SO_2R$			

Resonance differs from the two examples above in that it involves the sharing of electrons between more than two atoms via **delocalization**. The classical example of resonance is provided by the pi-bonding system of benzene. Benzene is a six membered ring composed of six sp^2 hybridized carbon atoms in a plane and sharing 6 pi electrons. It can be represented by the "Kekule" structure shown below which suggests and "alternating" single bond-double bond bonding pattern. This representation does not really adequately reflect the true electronic character of benzene since, in reality, all six pi electrons are shared equally by the six carbons. Thus the "inscribed" circle representation may be more accurate (although it doesn't directly indicate the number of pi electrons:



Kekule Structure of benzene

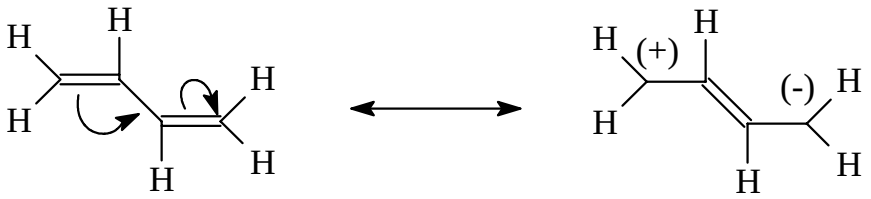


Inscribed circle structure of benzene

The Kekule structure of benzene <u>does</u> represent the electronic and structural requirements for resonance. For resonance phenomena to exist a "conjugated" electronic system must be present and the atoms involved in this system must be coplanar or capable of adopting a coplanar conformation. The type of resonance effect exerted by an atom or functional group - electron donating (+R) or withdrawing (-R) is determined by the electronic nature of the group. Each of these characteristics/requirements of resonance are defined in more detail below:

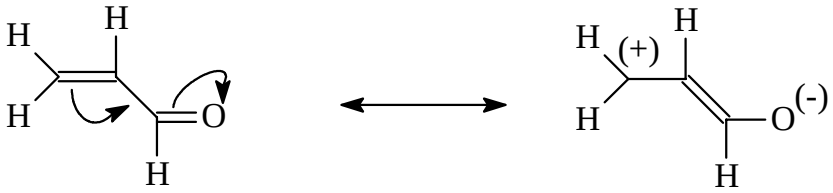
- "Conjugation": An electronic configuration in which there is an alternating single bond-double (pi) bond pattern, or an atom with non-bonded electron pairs (or lacking an electron pair) bound to a double bond system. The alternating single bond-double (pi) bond pattern

can be illustrated by butadiene. In this example the resonance structure shows that the electrons can be "shared" or delocalized (follow the arrows) creating a cationic and anionic center:



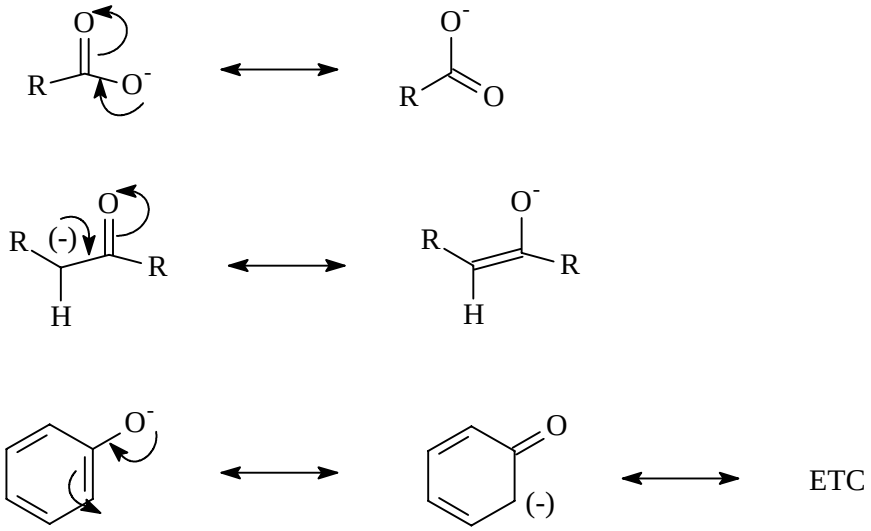
Butadiene Resonance structure

Another example of the single bond-double bond resonance pattern is in α, β-unsaturated carbonyl compounds. Here the difference in electronegativity between atoms in the pattern allows for a dipole and reactivity such as conjugate addition:

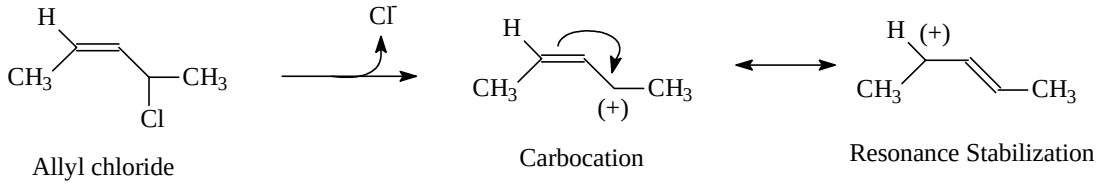


Resonance structure

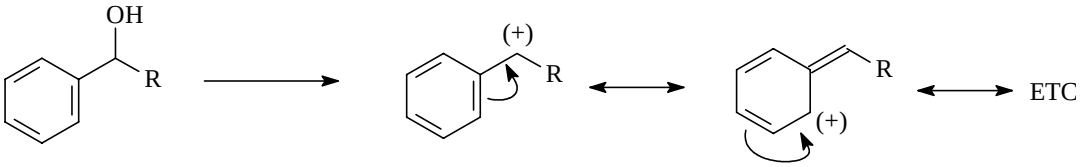
Examples of resonance resulting from atom with non-bonded electron pairs bound to a double bond system are shown below. Notice in each case below that that the "resonance phenomenon" involves an electron rich atom donating a pair of electrons to an electron deficient multiple bond system, and that in actually, the charges shown are distributed or delocalized over all of the atoms of conjugation. This resonance phenomenon is what makes carboxylic acids, and to a lesser extent phenols and protons alpha- to a carbonyl, acidic! The charged formed upon ionization can be stabilized through resonance delocalization!



Resonance can also occur in structural patterns where an atom deficient in an electron pair is bound to a double bonded system. Consider the case of the reaction of the "allyl chloride" compound below. This compound can ionize by loss of Cl^- (a good leaving group) because the charge of the resulting carbocation is stabilized by resonance delocalization of the pi (double bond) electrons. The same is true for benzyl alcohols as shown below. Benzyl alcohols can ionize because the resulting carbocation charge can be delocalized throughout the benzene ring via resonance:

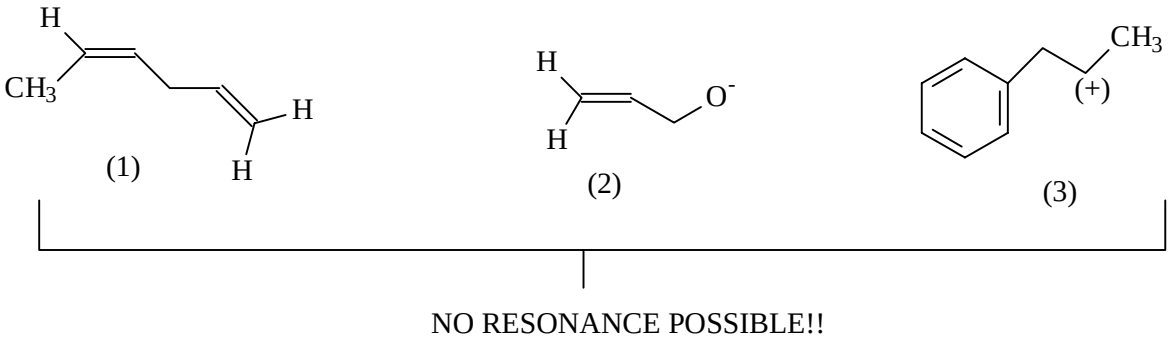


Allyl chloride Carbocation Resonance Stabilization



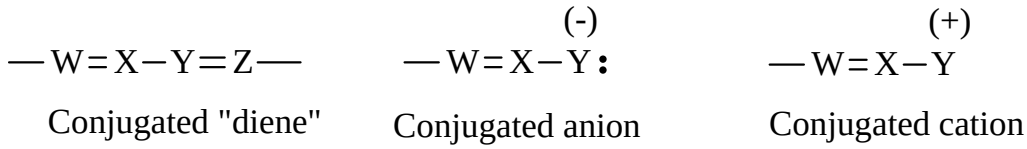
Benzyl Alcohol Carbocation Resonance Stabilization

In every case above, resonance was possible because of an electronic configuration in which there is an alternating single bond-double (pi) bond pattern, or an atom with non-bonded electron pairs (or lacking an electron pair) bound to a double bond system. It is important to realize that resonance is not possible when such an electronic configuration is NOT possible. Consider the examples below. In the first example (1) resonance is <u>not</u> possible because the two double bonds are separated by MORE THAN on single bond. In the second example the negatively charged atom is separated from the double bond by more than one single bond and in example (3) the charge is separated from the C=C by more than a single double bond.

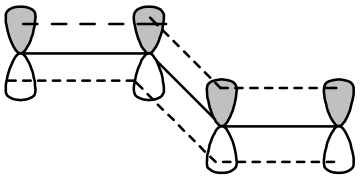


NO RESONANCE POSSIBLE!!

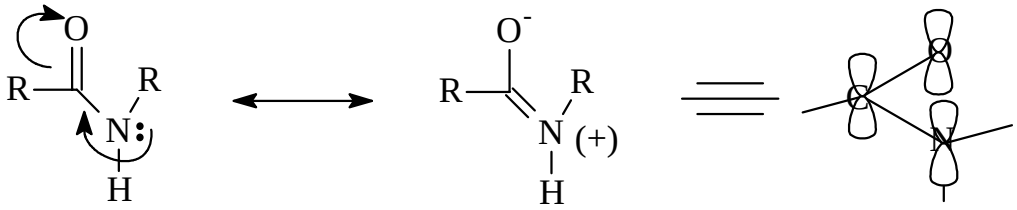
In summary, in order for resonance phenomena to occur, there must be a structural pattern characterized by the following general structures.



- Coplanarity: In order for resonance to occur, the atoms involved in "sharing" electrons (the atoms over which the electrons are delocalized) must be able to adopt a coplanar conformation. In order for electrons to be delocalized over more than two atoms, the pi orbitals of these atoms must exist in the same plane so they can overlap. This can only occur if the atoms and orbitals involved are in the same plane:

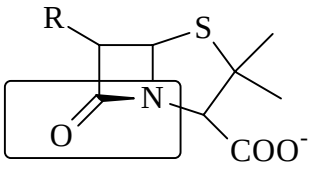


One prominent example of the requirement for coplanarity for resonance in drug science is derived from amide chemistry. Typically amides are somewhat resistant to hydrolysis because the amide nitrogen atom can donate electron density by resonance to the adjacent carbonyl and thereby reduce its electrophilicity (reactivity) toward hydrolytic nucleophiles. In order for this resonance stabilization to occur, the N-C=O atoms must be capable of existing in the same plane so their pi-orbitals can overlap:



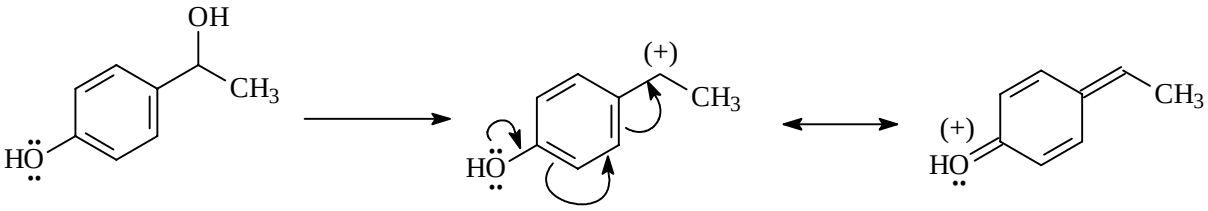
Resonance stabilization of amides

In amides where coplanarity is not possible, as in the beta-lactam antibiotics (penicillins), resonance stabilization cannot occur. In these compounds the bicyclic ring structure does not allow the amide N-C=O atoms to exist in the same plane. Thus resonance donation by N is not possible and these amides are more reactive than 'typical" amides where coplanarity allows for resonance stabilization:

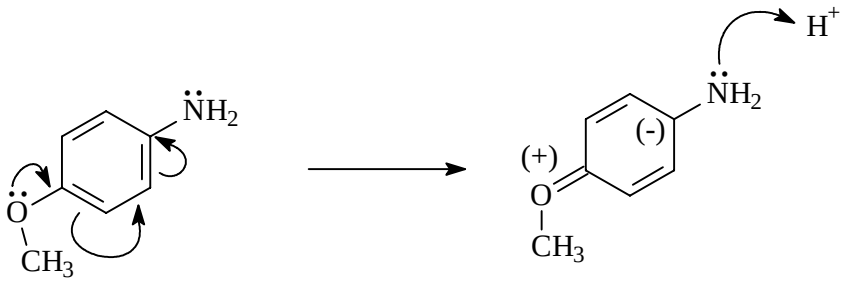


Beta-lactam amides: Non-coplanar

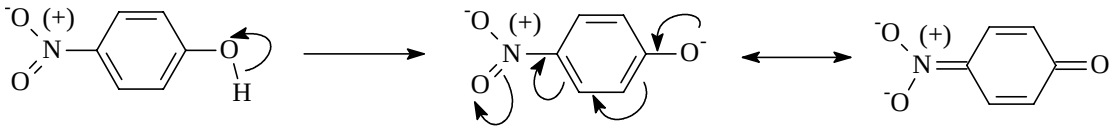
- Electron donating (+R) and Withdrawing (-R) Groups: electron donating and withdrawing groups by resonance are listed in the table on a previous page. Note that electron donors (+R) have at least one pair of non-bonded electrons on the atom involved in resonance (OH, OR, NRR, SR, etc.). As a result, +R groups can facilitate reactions that involve the formation of cations, and enhance the basicity of amines. This is illustrated in the examples below:

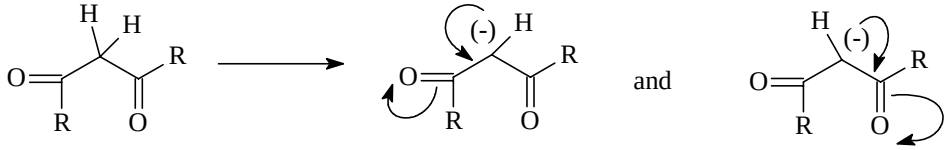


OH +R stabilization of a carbocation



- Electron withdrawing groups (-R) are characterized by electron deficient atoms linked to a site of conjugation. As a result, -R groups can facilitate reactions that involve the formation of anions, and enhance the acidic of acids. This is illustrated in the examples below:





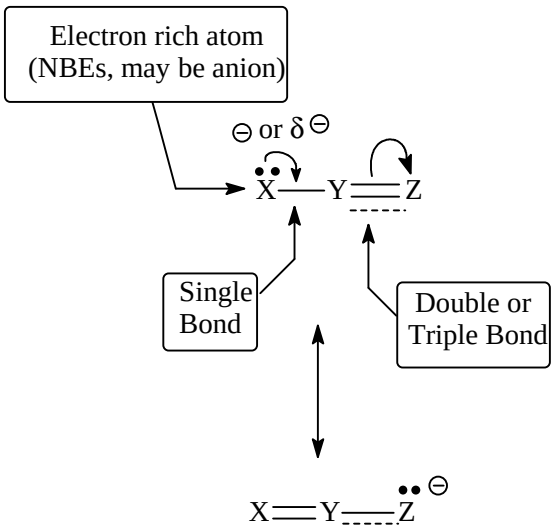
III. RESONANCE VERSUS INDUCTION:

As described above, induction involves the electronic effects of atoms and functional groups through saturated carbons, and are dependent on bond valence and position. Resonance involves the sharing or delocalization of electron pairs over more than two atoms and requires conjugation and coplanarity. To compare and contrast these two electronic effects,

consider the electronic effects of the hydroxy group (OH). This group is a withdrawer by induction (-I) and an electron donor by resonance (+R). Thus when positioned within a structure where it can participate in delocalization of pi electrons, it will function as a strong electron donor. When placed in a structure where its resonance effects are "insulated" by single bonds, only its electron withdrawing inductive effect will be felt.

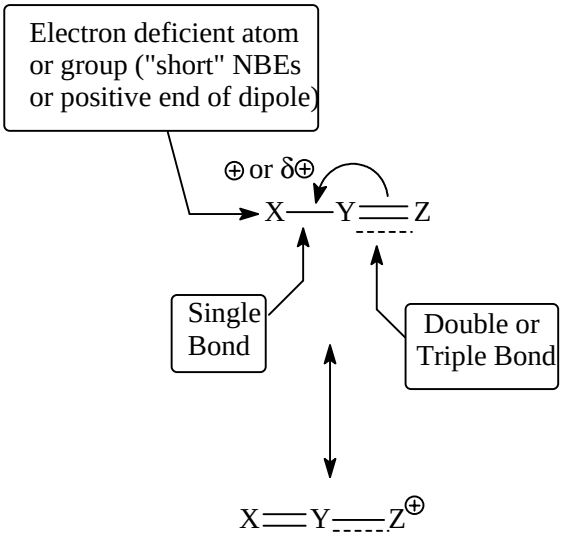
RESONANCE AND CONJUGATION

CONJUGATED SYSTEM
(X group is a donor by resonance, +R)



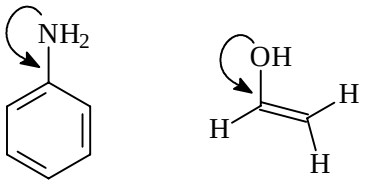
Resonance Form of Structure Above

CONJUGATED SYSTEM
(X group is a withdrawer by resonance, -R)



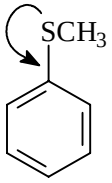
Resonance Form of Structure Above

EXAMPLES OF +R GROUPS:

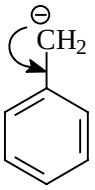


X = NH_2

X = OH

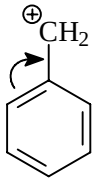


X = SCH_3

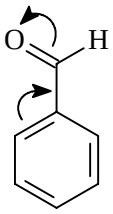


X = CH_2^-

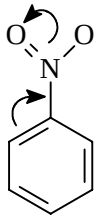
EXAMPLES OF -R GROUPS:



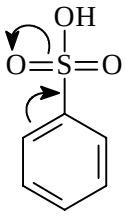
X = CH_2^+



X = CHO



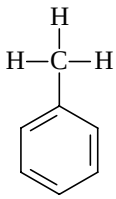
X = NO_2



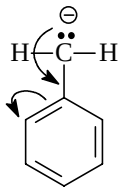
X = SO_3H

CARBON SUBSTITUENTS AND ELECTRONIC EFFECTS

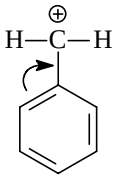
The electronic effects of an atom are a function of ionization and hybridization state as well as the nature of the structure to which they are linked (are they "in conjugation" with the structure to which they are linked):



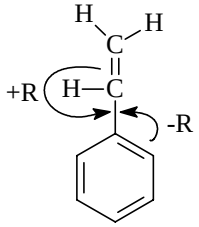
Fully saturated carbon with no NBEs. R not possible! **+I Effect**



Loss of H^+: Carbanion: NBE pair available for donation: **+R Effect**



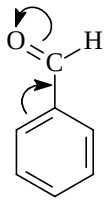
Loss of H^- Carbocation: Vacant orbital ("short" a NBE) **-R Effect**



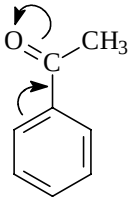
Alkene carbon: Can donate (+R) or withdraw (-R) electron density

⇓

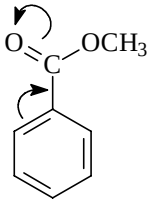
The electronic effects of an atoms are determined or modified by the nature of the functionality in which they are incorporated:



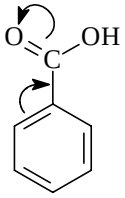
Aldehydes



Ketones



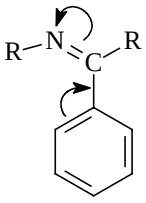
Esters



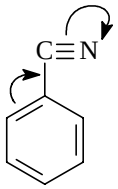
Carboxylic Acids

Carbonyl-containing functional groups (aldehydes, ketones, ester, acids) in conjugation with an aromatic ring (or other site of potential resonance) can withdraw electron density by resonance (-R) as shown above. These functional groups also withdraw electron density weakly by induction. The same is true, to a lesser degree, for analogues of the compounds above where the carbonyl oxygen is replaced by an atom of the same group (sulfur), or multiple bonded atom of the same row (as in nitrogen shown below)

⇓



Imines

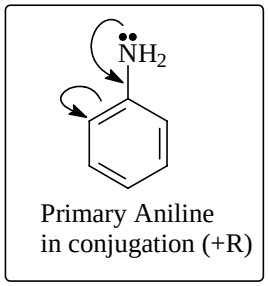


Nitriles

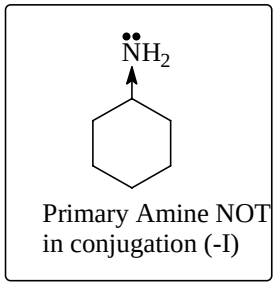
Unsaturated carbon-nitrogen functionality (imines and nitriles and similar structures) in conjugation with an aromatic system, like the carbonyl-containing functional groups can also withdraw electron density by resonance (-R) as shown above. These functional groups also withdraw electron density weakly by induction.

THE ELECTRONIC EFFECTS OF NITROGEN SUBSTITUENTS

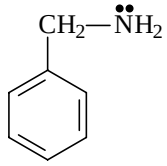
Electronic effects of an atom determined by nature of bonding <u>and</u> potential for conjugation:



Primary Aniline
in conjugation (+R)

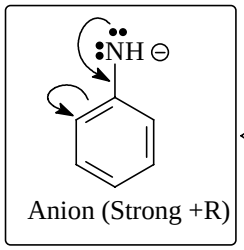


Primary Amine NOT
in conjugation (-I)



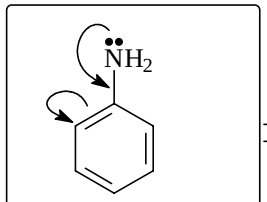
Primary Amine NOT
in conjugation (-I):
sp^3 CH_2 group "blocks"
resonance contribution

Electronic effects of an atom determined by the ionization state:



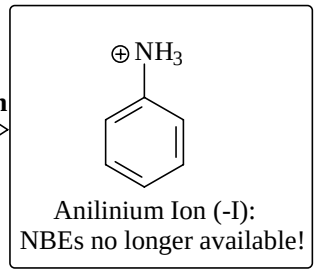
Anion (Strong +R)

Loss of H^+



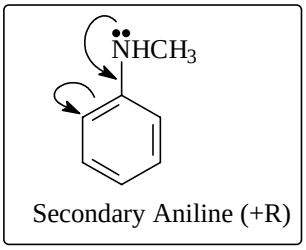
Primary Aniline (+R)

Protonation

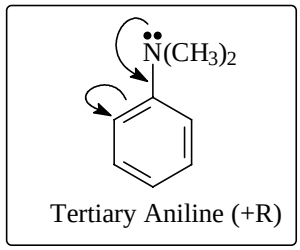


Anilinium Ion (-I):
NBEs no longer available!

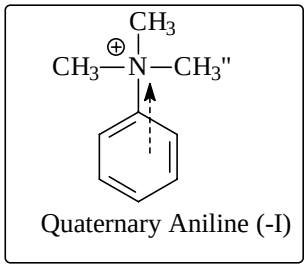
*Alkyl substitution does <u>not</u> change the nature of potential electronic effects of an atom, **<u>unless</u>** alkyl substitution changes the bonding order (i.e. "occupies" nitrogen's lone pair of NBEs):*



Secondary Aniline (+R)

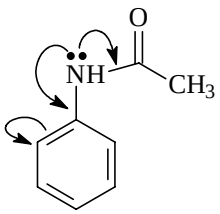


Tertiary Aniline (+R)

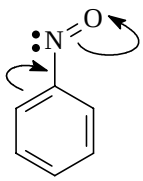


Quaternary Aniline (-I)

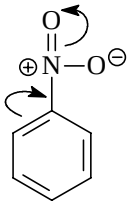
The electronic effects of an atoms are determined or modified by the nature of the functionality in which they are incorporated:



Anilide (Amides): Weak +R
due to"competing resonance"
through the bonded carbonyl



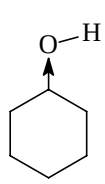
Nitroso: Electron Withdrawing (-R)
N in conjugation with electronegative
oxygen



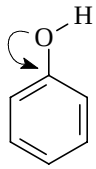
Nitro: electron Withdrawing (-R)
N in conjugation with two
electronegative oxygens

OXYGEN AND OTHER GROUP 6 ATOM SUBSTITUENTS AND ELECTRONIC EFFECTS

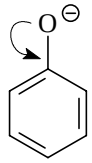
The electronic effects of an atom are a function of ionization and hybridization state <u>as well as</u> the nature of the structure to which they are linked (are they "in conjugation" with the structure to which they are linked):



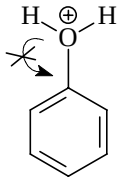
Fully saturated oxygen with <u>two pairs of NBEs</u> but not in conjugation. Only electronegative effect (**-I Effect)**



Fully saturated oxygen with <u>two pairs of NBEs</u> in conjugation. **+R Effect**



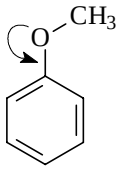
Loss of H^+: (Anion): NBEs available for donation: **+R Effect**



Loss of $H^{+\cdot}$: "Onium ion": Full valence cation (electron deficient, but R not possible): **-I Effect**

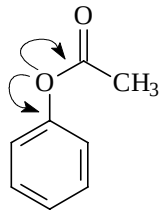
⇓

The electronic effects of an atoms are determined or modified by the nature of the functionality in which they are incorporated:



Ether

Still a +R group, but not capable of ionization

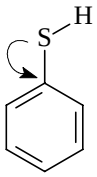


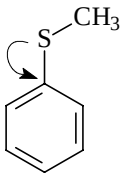
"Reverse" Ester

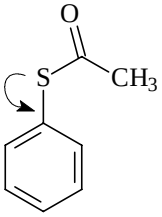
Still a +R group, but the carbonyl bonded to O (and in conjugation) reduces strength of donation by electron withdrawal

⇓

Atoms of the same group (i.e: O and S) are capable of exerting the same electronic effects (I and R), but the strength of the effect is dependent on the distance of the valence electrons from the nucleus

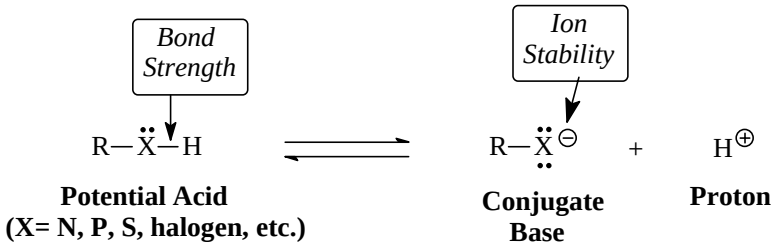






Principles of Relative Acidity

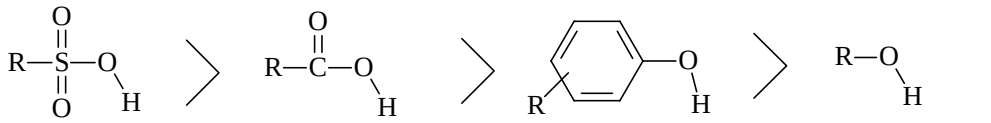
1. Acidity: Abililty of an atom to "give up" a proton and ionize (or ability of an atom to "accept" an electro
Dependent on strength of X-H bond (see below) and stability of conjugate base (X^-):



Potential Acid (X= N, P, S, halogen, etc.) | **Conjugate Base** | **Proton**

2. Relative acidities of functional groups with a "common" heteroatom (X): Example for Oxygen

When comparing functional groups with a common heteroatom, relative acidity is primarily a function c stability of the conjugate base. In the examples below, ALL of the functional groups have a common O- acidic fragment, and the O-H bonds strengths are roughly equivalent. But yet these compounds differ si cantly in acidity because of differences in the stability of the conjugate bases. Note that those O-H func groups that are most acidic are those in which the O^- charge of the conjugate base is delocalized over mo electronegative atoms (the R group is the same for all functional groups):

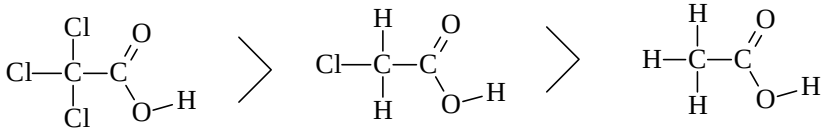


Sulfonic Acid (Charge over 3Os and S) | **Carboxylic Acid (Charge over 2Os and C)** | **Phenol (Charge over 1O and 6Cs)** | **Alcohol (Charge over 1O only!)**

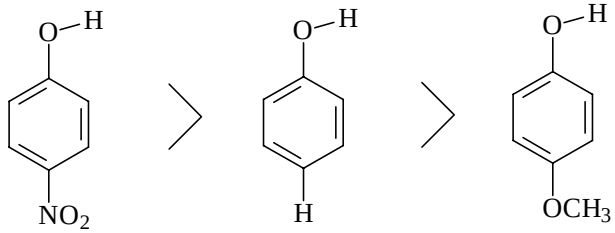
3. Relative acidities of compounds with common functional groups but different substituents: Substituent E

Compounds containing the same acidic functional group by different substituent groups may differ in the acidities based on the potential differences in electronic effects of different substitutents (see the "Resonance and Induction" chapter). For example, groups that withdraw electron density by induction or resonance will enhance acidity by stabilizing the negativecharged formed in the conjugate base. Conv those that donate electron density with decrease acidity. Consider the examples below:

Acids and an Electron Withdrawing Cl group(-I)



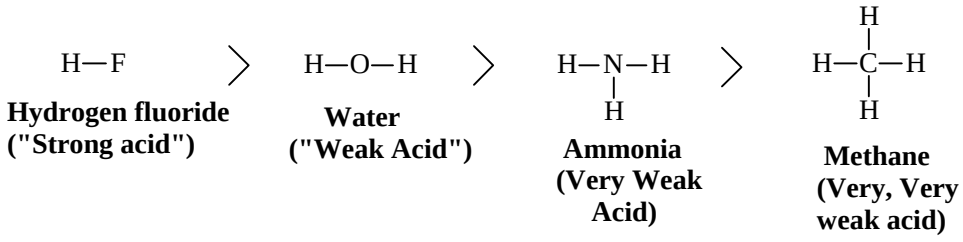
Phenols and Electron Withdrawing & Donating G groups by R

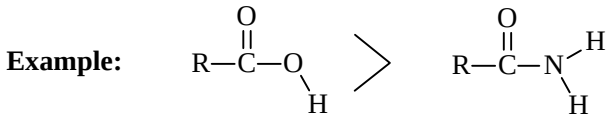


-R Group | **Electro-Neutral Group** | **+R Group**

4. Relative acidities of functional groups with "different" heteroatoms (X) with a common valence shell: The Electronegativity rationalization:

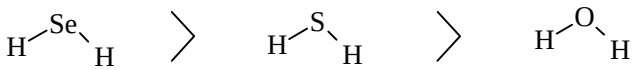
The valence electrons of atoms in the same horizontal row of the periodic table (i.e. Li, Be, B, C, N, O, F all exist in the same valence orbital (the 2s-2p orbitals for the row two atoms listed). The primary differe between the atoms of a row then is HOW MANY electrons are in the valence shell and how "electronega the atom is. As the number of valence electrons IN A COMMON VALENCE ORBITAL increases, the electronegativity increases. Thus the electronegativity trend for the row 2 atoms is F>O>N>C>B etc. Within this row of atoms, the higher the electronegativity, the greater the ability to stabilize negative cha as forms during acid ionization. It should be noted that the strength of the heteroatom-hydrogen (X-H) b also increases with the number of valence electrons in a row, but this effect is less important than the stab effect on the negative charge formed upon ionization. Thus relative acidities for functional groups with d heteroatoms of the same row (valence shell) parallels elctronegativity as illustrated below:

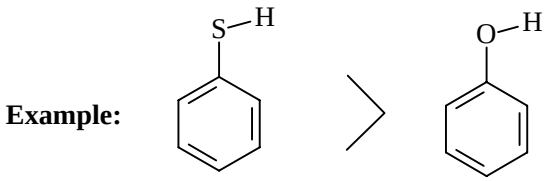




5. Relative acidities of functional groups with "different" heteroatoms (X) and a different valence shell: The "Polarizability" rationalization:

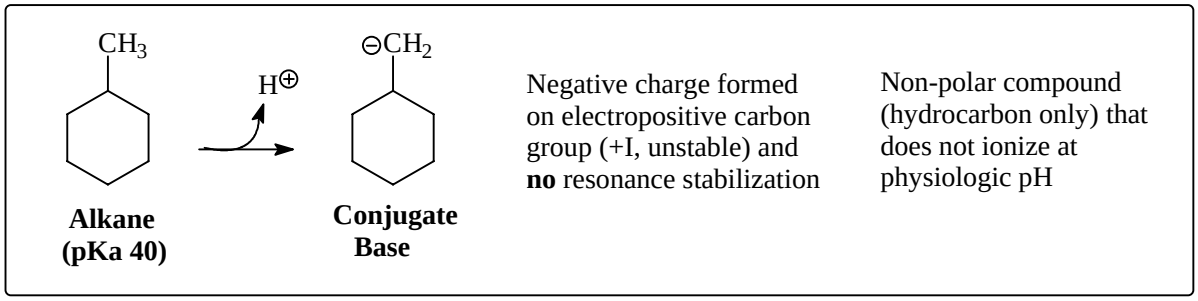
The valence electrons of atoms in the same group (column) of the periodic table (i.e. O, S, Se, Te, etc.) exist in increasing higher valence orbitals (i.e the 2s-2p for oxygen, the 3s-3p for S, etc). The primary difference between atoms (other than the obvious, the number of protons, neutrons and electrons) of the same group (column) is how far from the nucleus the valence shell is located (one shell further out for S t O). The further the valence electrons are from the nucleus, the greater the space or area over which they distributed. If charge forms in the valence shell, as in the ionization of an acid, the further this shell is fro the nucleus, the greater the area for charge distribution and the more stable the charge. Also, the further t valence shell is from the nucleus, the weaker the heteroatom-hydrogen (X-H) bond. For these reasons, atoms "further down" in a group of the periodic table are better able to stabilize charge and will therefore ionize more readily as illustrated by the examples below:





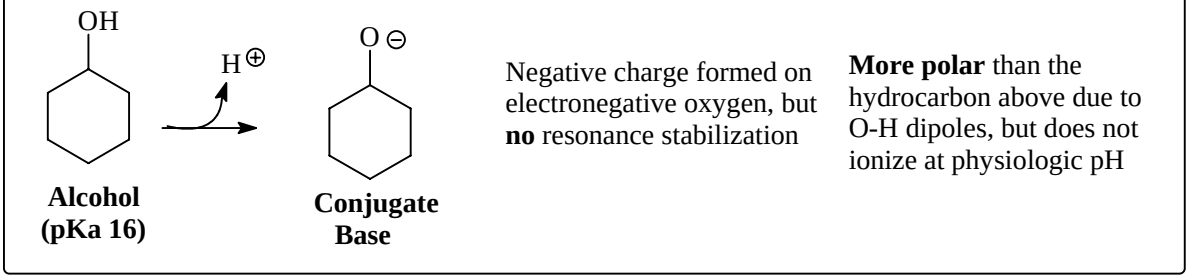
RELATIVE ACIDITIES OF ALKANES, ALCOHOLS, PHENOLS AND CARBOXYLIC ACIDS

(Increasing acidity and polarity at physiologic pH from lkanes to carboxylic acids)



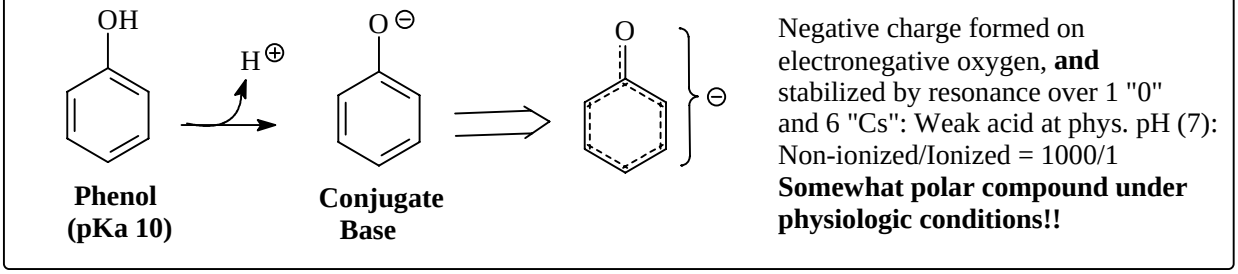
Negative charge formed on electropositive carbon group (+I, unstable) and **no** resonance stabilization

Non-polar compound (hydrocarbon only) that does not ionize at physiologic pH

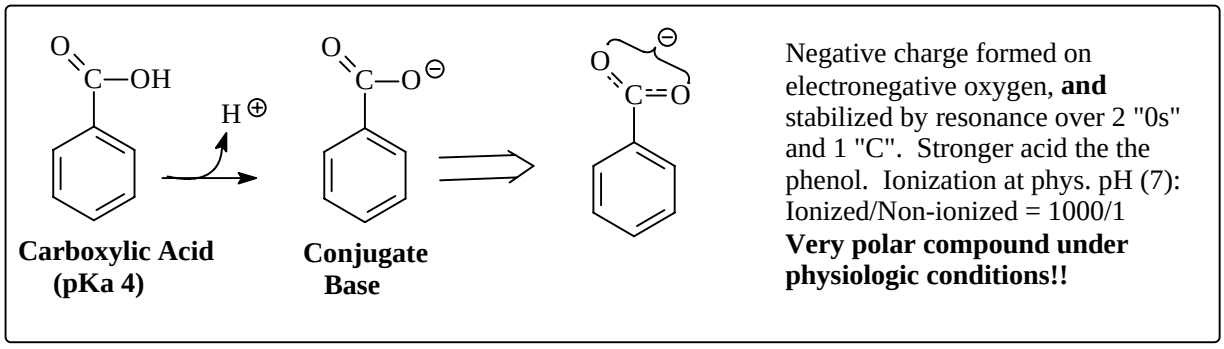


Negative charge formed on electronegative oxygen, but **no** resonance stabilization

More polar than the hydrocarbon above due to O-H dipoles, but does not ionize at physiologic pH

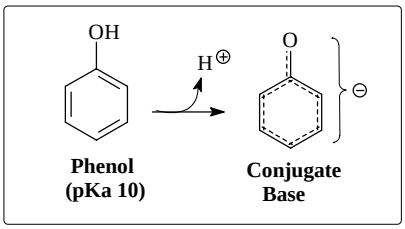


Negative charge formed on electronegative oxygen, **and** stabilized by resonance over 1 "0" and 6 "Cs": Weak acid at phys. pH (7): Non-ionized/Ionized = 1000/1
Somewhat polar compound under physiologic conditions!!



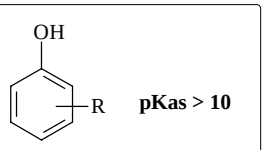
Negative charge formed on electronegative oxygen, **and** stabilized by resonance over 2 "0s" and 1 "C". Stronger acid the the phenol. Ionization at phys. pH (7): Ionized/Non-ionized = 1000/1
Very polar compound under physiologic conditions!!

RELATIVE ACIDITIES OF PHENOLS: SUBSTITUENT EFFECTS



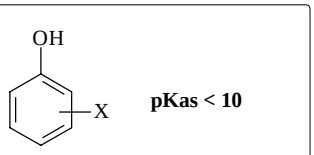
Phenol (pKa 10) **Conjugate Base**

(Be able to identify functional groups as electron donating or withdrawing by induction or resonance, and to draw resonance structure, when possible!)



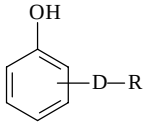
pKas > 10

Alkyl substitution at positions 2, 3 or 4 **decreases** acidity modestly due to the +I effect



pKas < 10

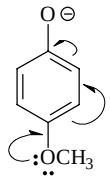
Halogen (F, Cl, Br, I) substitution at positions 2, 3 or 4 **increases** acidity modestly as a result of the -I effect of halogen (F>Cl> etc.)



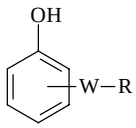
pKas >> 10

Substitution with electron donating groups by resonance (+R) at positions 2 or 4 (in conjugation) **decreases** acidity significantly (- charge destabilization). D-R Examples: $-OCH_3$, $-SCH_3$, $NHCH_3$

Example:



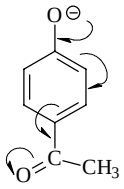
Electron donating group "destabil-izes developing negative charge in the base by +R



pKas << 10 (i.e. 7 or lower)

Substitution with electron withdrawing groups by resonance (-R) at positions 2 or 4 (in conjugation) **increases** acidity significantly (- charge stabilization). W-R Examples: $-NO_2$, $-COCH_3$, $-COOCH_3$, -CN, $-SO_2CH_3$, etc.

Example:



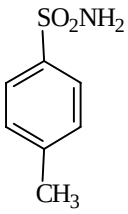
Electron withdrawing group "stabilizes" developing negative charge in the base by -R

PROBLEMS: RESONANCE AND INDUCTION (and related reactivity)

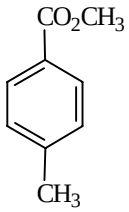
1. Why are amides less acidic than carboxylic acids?

2. Why are amides less susceptible to hydrolysis than esters?

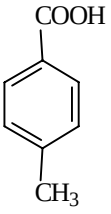
3. Answer the questions below (a-c) for the follow series of compounds:



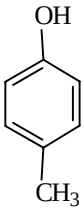
A



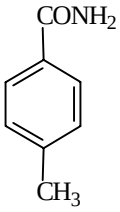
B



C



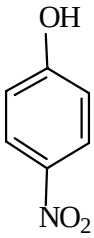
D

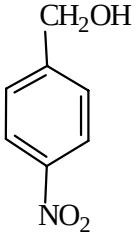


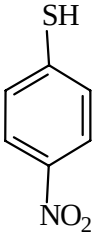
E

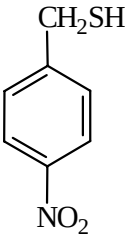
a. Which compound above is MOST acidic?
b. Which compound above is LEAST acidic?
c. Which compound above is MOST susceptible to hydrolysis?

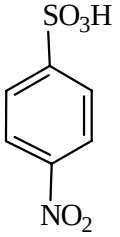
4. Rank the following set of compounds in terms of relative ACIDITY (1 = most, 5 = least):











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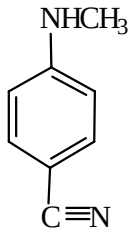
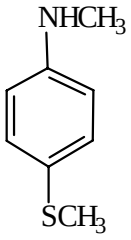
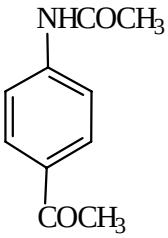
5. Rank the following set of compounds in terms of relative BASICITY (1 = most, 5 = least):



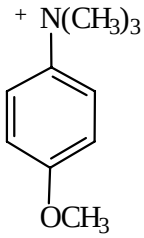
2



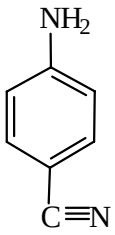
1



4

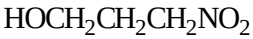


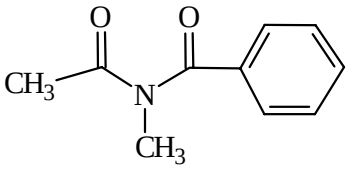
5

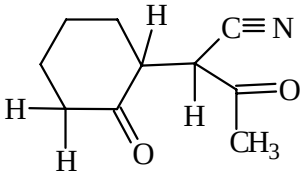


3

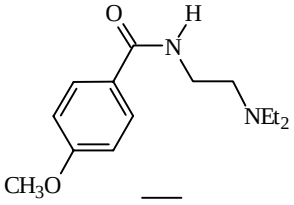
6. Circle the **MOST ACIDIC** proton(s) in each of the following compounds:







7. Rank the compounds below in terms of their relative rates of hydrolysis in vivo (1 = most rapidly hydrolyzed, 4= most slowly hydrolyzed):



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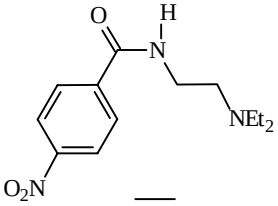

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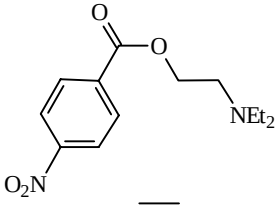

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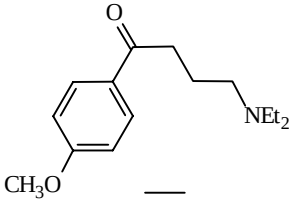

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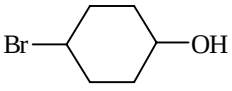
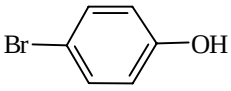
8. Answer the questions below (a-c) for the following compounds:

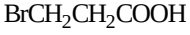


A



B

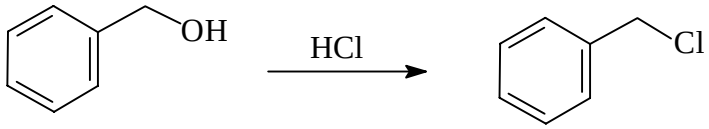
C



D

a. Circle the compound that is **most** acidic?.....A B C D
b. Circle the compound that is **least** acidic?.....A B C D
c. Circle the compound that is most **nucleophilic** (pH 2)?.....A B C D

9. Explain the difference in reactivity between the two alcohols shown below:



CH_3CH_2OH $\xrightarrow{HCl}$ NO REACTION

10. Identify the compound below that would be most likely to form an imine with a primary amine? Identify the compound below LEAST likely to form an imine: