CHEMISTRY 2500

Topic #7: Reaction Mechanisms, Kinetics and Operational Species

Fall 2014

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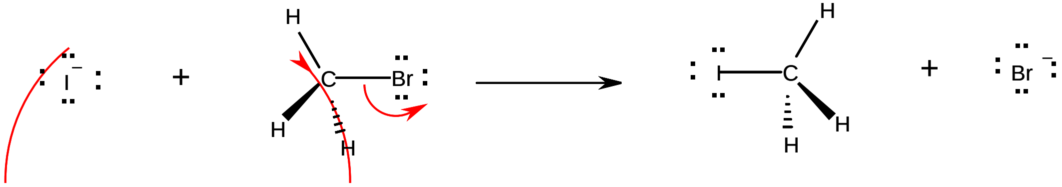
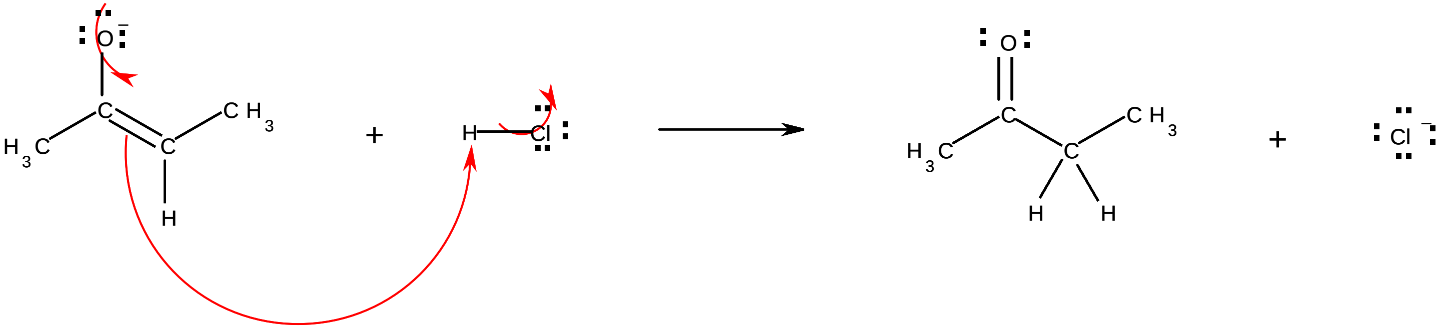
Reaction Mechanisms and Kinetics

- A reaction mechanism is a series of step(s) describing how a reaction proceeds. The movement of electrons in each step are shown using arrows commonly referred to as “curly arrows”:



- Each step in a reaction mechanism is referred to as an **elementary process** and can be imagined to proceed as the result of one collision between molecules (or as a single step involving only one molecule). As such, the electrons will appear to “flow” from one part of the system to another:



Things That Are Essential to Remember!!!

- CURLY ARROWS **ALWAYS** SHOW MOVEMENT OF **ELECTRONS**. NEVER ATOMS OR IONS!

- Electrons flow in **ONE DIRECTION** – from electron-rich to electron-poor; from Lewis base to Lewis acid; from **NUCLEOPHILE TO ELECTROPHILE**.

- Don’t push multiple arrows into the same atom. One in; one out. (Often just “one in” or “one out”.)

- Each arrow represents the movement of a **PAIR**[*] of electrons.

- When pushing electrons, remember that period 2 elements (including C, N and O) can **NEVER** have more than 8 electrons!!!

[*] To show movement of single electrons, chemists use half-arrows.

Reaction Mechanisms and Kinetics

- We can “map out” an elementary process using a **reaction profile diagram** which shows the energy of the system throughout the elementary process:
- The highest energy point on the reaction profile diagram occurs at the **transition state** for the reaction. A transition state is highly unstable and short-lived. It cannot be observed directly.

Reaction Mechanisms and Kinetics

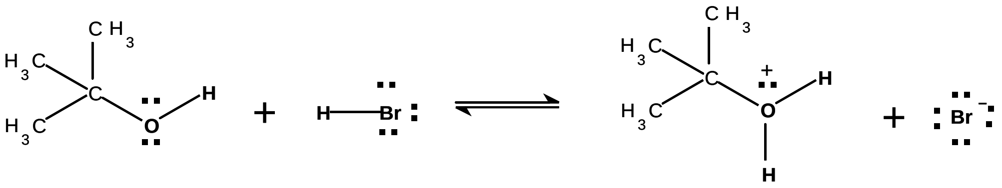
- An elementary process may involve the movement of several electron pairs, but the movements will all be connected and in the same direction. If an electron pair makes a new bond to an atom, either another pair breaks a bond from that same atom (the weakest bond!) or it was the last electron pair to move:

Reaction Mechanisms and Kinetics

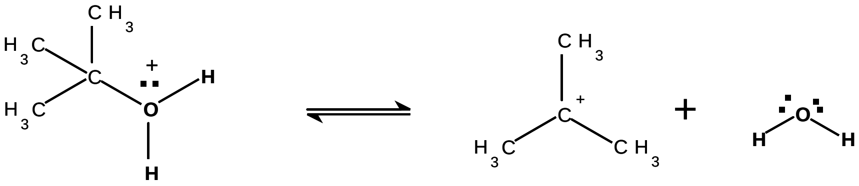
- Some reaction mechanisms have a single elementary process; however, it is more common to see multi-step mechanisms.

  e.g.

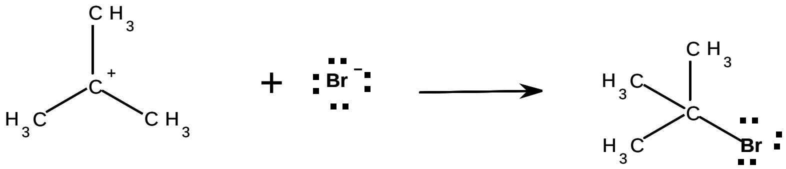
Step 1:



Step 2:



Step 3:



Overall:

Reaction Mechanisms and Kinetics

- Each elementary process within a multi-step mechanism will have its own transition state (which is *not* drawn as part of the mechanism).

- In addition, a multi-step mechanism will have **intermediates**. (the products of all elementary processes except the last one).

- Intermediates are semi-stable molecules or ions that often exist long enough to be observed. An intermediate for a spontaneous reaction will never be more stable than the final product (if it was, the reaction would stop at the intermediate).

- *Label the intermediates on the reaction mechanism on the previous page.*

Reaction Mechanisms and Kinetics

- Reactions involving **catalysts** usually have intermediates since a catalyst increases the rate of a reaction by providing an alternate mechanism (which usually has more steps, each having a smaller activation energy than the catalyst-free mechanism). *Note that the reverse is not necessarily true; a reaction can have intermediates without a catalyst.*

- Catalysts are neither created nor consumed during a reaction. Since they are neither reactants nor products – but are often necessary for the reaction to proceed – they are drawn above the reaction arrow:

- In order for a catalyst to affect the rate of a reaction, it must speed up the reaction's **rate determining step** (the slowest elementary process). This step serves as a kind of "bottleneck" to the overall rate of reaction and is therefore the only step affecting the overall rate of reaction.

Acidity (pK_a)

- A Brønsted acid is a molecule that loses H^+ to a Brønsted base. The **acidic site** is the hydrogen atom:
- A Brønsted base is a molecule that makes a bond to the hydrogen atom of a Brønsted acid. The **basic site** is the atom/bond donating the electrons used to make this bond:

Acidity (pK_a)

- Brønsted acidity is measured using K_a values or pK_a values.
    - K_a is the equilibrium constant for the dissociation of an acid into H^+ and its conjugate base. Where possible, K_a values are measured using water as the solvent.

$$\mathbf{HA} \rightleftharpoons \mathbf{H^+} + \mathbf{A^-} \qquad K_a = \frac{a_{H^+} \cdot a_{A^-}}{a_{HA}}$$

Strong acids react more strongly with water, giving larger K_a values.

- pK_a is derived from K_a:

$$pK_a = -\log K_a$$

Acids with large values for K_a (strong acids) will therefore have low, or even negative, values for pK_a

An acid's strength is determined by the stability of its conjugate base!!!
As the stability of A^- increases, so does the strength of HA.

Acidity (pK_a)

- The following table, taken from Sorrell p.144, shows typical pK_a values (rounded to the nearest 5) for different types of hydrogen atoms typically found in organic molecules:

pKa	**Type of Compound**
-10	mineral acids: H_2SO_4, HI, HBr, HCl, sulfonic acids RSO_3H
0	H_3O^+, H_3PO_4
5	Carboxylic acids, HF, thiophenols ArSH, HN_3
10	Weak inorganic acids (H_2S, HCN, NH_4^+), amine salts (RNH_3^+), phenols (ArOH), thiols (RSH), aromatic amides ($ArCONH_2$)
15	H_2O, alcohols, thiols (RSH), amides $RCONH_2$
20	ketones (the alpha proton $H\text{-}CH_2COR$)
25	Esters (the alpha proton $H\text{-}CH_2CO_2R$), alkynes RCCH, nitriles ($H\text{-}CH_2CN$)
30	Anilines ($ArNH_2$)
40	Ammonia (NH_3), amines (RNH_2), benzylic protons ($ArCH_3$)
45	Arenes (ArH) and alkenes ($RCH{=}CH_2$)
50	Alkanes

- A more detailed pK_a table can be found on the inside cover of Sorrell.

Acidity (Trends)

- Acidity tends to increase left-to-right across a period:

Acid	Conjugate Base	pK_a
H_3C-H		48
H_2N-H		38
HO-H		15.7
F-H		3.1

- Acidity tends to increase top-to-bottom down a group:

Acid	Conjugate Base	pK_a
HO-H		15.7
HS-H		7

Acidity (Trends)

- Acidity tends to increase with the number of π bonds (a measure of the s-character of the MO containing the lone pair in the conjugate base – more ‘s’ = more stable):

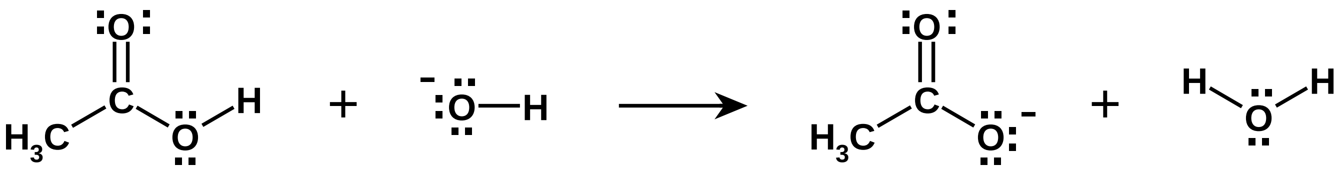
Acid	Conjugate Base	pK_a
$H_3C\text{-}H$		48
$=CH_2$		44
$\equiv CH$		25
$R\text{-}OH_2^+$		~0
$R=OH^+$		-4 to -10

- Acidity increases with resonance-stabilization of the conjugate base.

Acidity

- In order for a proton transfer reaction to be product favoured, it is necessary to use a base whose conjugate acid is weaker than the acid to be deprotonated:

e.g.



- Here, the products are more stable than the reactants. Hydroxide is a stronger base than acetate because acetic acid (pK_a=4.7) is a stronger acid than water (pK_a=14).
- Why is the acetate anion more stable than the hydroxide anion?

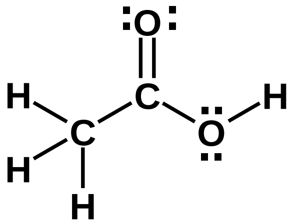
Acidity

- Phenol is “just an alcohol with a benzene ring”. Why is phenol more acidic than most non-aromatic alcohols?
- Sulfur and nitrogen are both less electronegative than oxygen. Why are thiols more acidic than alcohols, but amines less acidic?

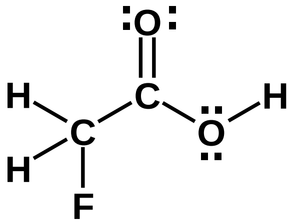
Acidity (Inductive Effect)

- We can increase the strength of an acid by adding electron-withdrawing groups, further stabilizing its conjugate base.

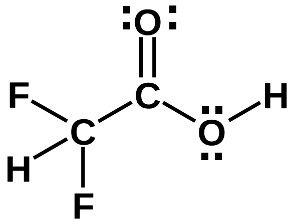
  e.g. To increase the acidity of acetic acid, replace one or more hydrogen atoms of the methyl group with halogens:



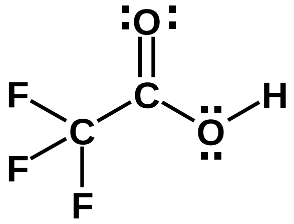
pK_a = 4.74



pK_a = 2.66



pK_a = 1.24



pK_a = 0.23

- This stabilization through σ bonds is called an **inductive effect**.
  - Inductive effects are strongest when close to the acidic hydrogen. *($CF_3CH_2CH_2CH_2CO_2H$ is not significantly more acidic than $CH_3CH_2CH_2CH_2CO_2H$)*
  - We saw inductive effects in CHEM 1000 when we looked at the strength of the oxoacids (e.g. $HClO_2$ vs. $HClO_3$ vs. $HClO_4$)
- Physical proximity of electronegative atoms can also slightly affect pK_a. This is known as a **field effect**.

Acidity (Solvent Leveling)

- We know that a strong acid ($pK_a < 0$) dissociates fully in water because it is a stronger acid than H_3O^+ ($pK_a = 0$) so reacts fully with H_2O to generate H_3O^+ and its conjugate base. This effect is known as **solvent leveling**:
    - No acid stronger than the conjugate acid of the solvent can exist in any solution.
    - No base stronger than the conjugate base of the solvent can exist in any solution. *(Hydroxide isn't the strongest base – not by a long shot! It's just the strongest base that can exist in water. When we use stronger bases than hydroxide, we will use non-aqueous solvents.)*

Reaction Mechanisms: Operational Species

- In most organic reactions, electrons flow from electron-rich atoms to electron-poor atoms, making and breaking bonds as they go.
- The electron donors are termed **nucleophiles** (“nucleus lovers” or “positive charge lovers”) and the electron-rich parts of them are the **nucleophilic sites**.
  - A nucleophile provides an electron pair to make a new bond to any non-hydrogen atom. As such, nucleophilic sites are either:
    - atoms that have one or more lone pair of electrons, or
    - π bonds
  - Nucleophiles often have negative charges since anions are, by definition, electron-rich. Any carbon atom with a negative charge will be a good nucleophile! An anion is always more nucleophilic than its conjugate acid (even when that conjugate acid is also a nucleophile):

Reaction Mechanisms: Operational Species

- The factors that contribute to making a good base tend to be the same factors that make a good nucleophile. As such, in most cases we can estimate relative nucleophilicity by comparing relative basicity:

- One notable exception to this trend is the series of halide ions:
    - Basicity: $F^- > Cl^- > Br^- > I^-$
    - Nucleophilicity: $I^- > Br^- > Cl^- > F^-$

This same logic applies when comparing other groups going down the periodic table (e.g. R_3P is more nucleophilic than R_3N)

Reaction Mechanisms: Operational Species

- Finally, it is worth noting that steric bulk will make a molecule/ion less nucleophilic as it makes it more difficult for it to access an electrophilic site.

Reaction Mechanisms: Operational Species

- The electron acceptors are termed **electrophiles** (“electron lovers”) and the electron-poor parts of them are the **electrophilic sites**.
  - Electrophilic sites are atoms that have either a full or partial positive charge and some way to accept electrons:
    - an incomplete octet (i.e. an “electron-deficient” atom),
    - a π bond to break, or
    - a good **leaving group**
  - Incomplete octets are easy to recognize. Look for atoms with three bonds and no lone pairs. When a nucleophile attacks this type of electrophile, the octet rule is fulfilled:

Reaction Mechanisms: Operational Species

- When deciding if one end of a π bond is an electrophilic site, imagine a nucleophile attacking and breaking that bond, pushing the electrons from the π bond onto the other atom as a lone pair. Is the charge stabilized?
  - If yes, you have found an electrophilic site:
  - If no, the site is not electrophilic:
- Leaving groups are discussed on the next pages. If a partially positive atom has a good leaving group attached, that will also be an electrophilic site.

Reaction Mechanisms: Operational Species

- Some reactions involve a **leaving group** which is an atom (or group of atoms) which breaks away from a molecule during a reaction, taking a pair of electrons with it.
  - When discussing a leaving group, we refer to the molecule/ion after it has left. A good leaving group is stable after leaving. This is often measured by referencing the strength of its conjugate acid. A good leaving group has a strong conjugate acid. This is more often stated as “a good leaving group is the conjugate base of a strong acid”.
    - In R-Cl, the leaving group is Cl^- (conjugate acid = HCl)
    - In $R\text{-}OH_2^+$, the leaving group is H_2O (conjugate acid = H_3O^+)
    - In R-OH, the leaving group is HO^- (conjugate acid = H_2O)

Reaction Mechanisms: Operational Species

A few common leaving groups:

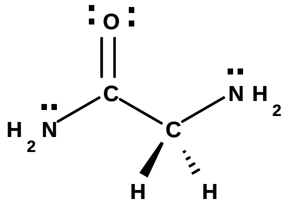
Generic Molecule	Leaving Group	Conjugate Acid	pK_a of Conjugate Acid
R-I	I^-	HI	-11
R-Br	Br^-	HBr	-9
R-Cl	Cl^-	HCl	-7
R-OTs	TsO^-	HOTs	-7
$R\text{-}OH_2^+$	H_2O	H_3O^+	0

Note that F^- and HO^- are not on this list. They're not *horrible* leaving groups, but they're not very good either. We saw why HO^- isn't a very good leaving group on the previous page. Why not F^-?

Reaction Mechanisms: Operational Species

- You will encounter many acidic and basic sites in organic chemistry that do not conform to the “HX is an acid, HO^- is a base” model that is prevalent in general chemistry.

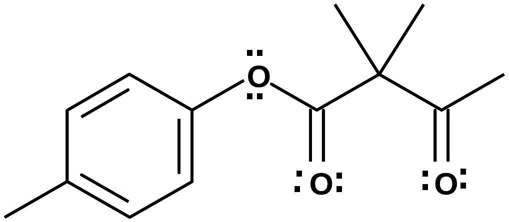
  e.g. There are three basic sites on the molecule below, the oxygen atom and the two nitrogen atoms. Usually, nitrogen atoms are considered more basic than oxygen atoms, but which of the two nitrogen atoms is more basic?



Reaction Mechanisms: Operational Species

e.g. The molecule below has three basic sites and one acidic site (two if you're very generous in defining "acidic"). Identify them and rank them in terms of reactivity (by category; don't compare acid to base).

Rationalize your rankings.

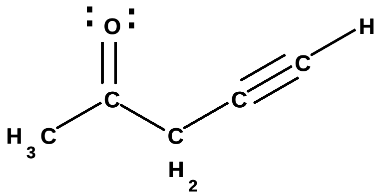


Reaction Mechanisms: Operational Species

Reaction Mechanisms: Operational Species

e.g. The molecule below has two basic sites, three acidic sites, two nucleophilic sites and one electrophilic site. Identify them and rank them in terms of reactivity (by category).

Rationalize your rankings.



Reaction Mechanisms: Operational Species

Reaction Mechanisms: Operational Species

- It is incorrect to mix-and-match the terms acid and electrophile, or base and nucleophile. They are not interchangeable.

  e.g. I^- is a good nucleophile but not a good base

- It is, however, entirely possible for a molecule to be both an acid and an electrophile – or both a base and a nucleophile. It is even possible for the same molecule to be an acid, a base, a nucleophile and an electrophile all at the same time. In that case, how it reacts will depend on the other species in the reaction flask (since usually the most nucleophilic site reacts with the most electrophilic site – assuming it can reach).

Reaction Mechanisms: Operational Species

- When solving a mechanism, we can use the different kinds of sites (A, B, E, Nu) to help us.

  e.g. How can we rationalize the following reaction?