Ch 6 Overview of Organic Reactions

Reactions can be organized broadly into four types by their reactants and products.
1. Addition – Two reactants combine completely into one product with nothing left over.
    For example, ethene and HBr combine completely to make bromoethane.
    $H_2C=CH_2 + HBr \rightarrow CH_3CH_2Br$
2. Elimination – Opposite of addition, where one reactant splits into two or more products.
    For example, ethanol can decompose into ethene and water.
    $CH_3CH_2OH \rightarrow H_2C=CH_2 + H_2O$
3. Substitution – Two reactants exchange parts to become two new products.
    For example, methane and Cl_2 and exchange an H and a Cl
    to become chloromethane and HCl.
    $CH_4 + Cl_2 \rightarrow CH_3Cl + HCl$
4. Rearrangement – A single reactant rearranges its atomic bonds to become an isomer.
    For example, 1-butene can become *trans*-2-butene, where
    the two butene molecules are constitutional isomers.
    $CH_3CH_2CH=CH_2 \rightarrow CH_3CH=CHCH_3$ (trans)

Reaction Mechanism
–   Describes which bonds break and form, in what order, and the relative rates of the steps.
–   Accounts for the amounts of all reactants used and products formed.
–   Bonds can break or form symmetrically (one e^{-1} from each atom)
    or asymmetrically (both e^{-1} with one atom).
–   A symmetrical bond break is homolytic (forms two radicals). $A:B \rightarrow A\cdot + \cdot B$
–   An unsymmetrical bond break is heterolytic (polar reaction). $A:B \rightarrow A^{+1} + :B^{-1}$
–   A symmetrical bond formation is homogenic (two radical reactants). $A\cdot + \cdot B \rightarrow A:B$
–   An unsymmetrical bond formation is heterogenic (polar reaction). $A^+ + :B^- \rightarrow A:B$
–   A radical reaction is one that is both homolytic and homogenic,
    with an unpaired e^{-1} on both reactant and product sides.
        Rad$\cdot$ + A:B $\rightarrow$ Rad:A + $\cdot$B
    A species with an odd number of e^{-1} (because one e^{-1} is unpaired) is called
    a radical (Rad$\cdot$). A radical species can either be uncharged (a free radical)
    or have an ionic charge (a charged radical).
–   A polar reaction is one that is heterolytic and/or heterogenic.
    It involves only species with an even number of e^{-1} (because all e^{-1} are paired).
–   Polar reactions are much more common than radical reactions in organic chemistry.

Radical Reactions
- There are two basic types. In the first, a radical can homolytically break a single bond between two atoms, then bond with one of the two atoms, leaving the other atom with an unpaired e^{-1}.

  Rad· + A:B → Rad:A + ·B   (as seen before)
- In the other, a radical can add to a double bond by forming a bond with one atom, leaving a single bond to the other atom, which then has the unpaired e^{-1}. This creates a larger radical.
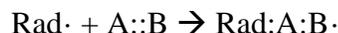
  Rad· + A::B → Rad:A:B·
- Radical reactions occur in three steps
  - Initiation – A homolytic bond break creates two radicals.
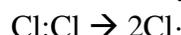
    Cl:Cl → 2Cl·
  - Propagation – A radical breaks a bond as described above to form a new radical. Typically, two radical reactions occur in a self-sustaining repeating cycle. This cycle is essentially a chain reaction, where the 2nd reaction reforms the original radical that was consumed in the 1st reaction, and vice-versa.
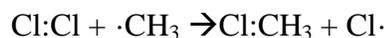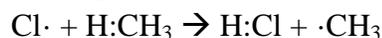
    Cl· + H:CH$_3$ → H:Cl + ·CH$_3$
    Cl:Cl + ·CH$_3$ → Cl:CH$_3$ + Cl·
  - Termination – Ends the propagation cycle by combining two radicals together.

    2 Cl· → Cl:Cl (or any other possible homogenic reaction between radicals)
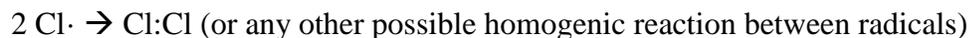
Polar Reactions
- Occur by attraction of positive and negative charges.
- A bond can be polar if the electronegativities of the two atoms are different, like O and H, and sometimes it can act polar if a solvent, acid (HA below), or base interacts with it.

  $CH_3OH + HA → CH_3OH_2^{+1} + A^{-1}$
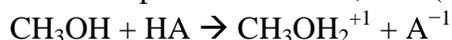
  The interaction above causes the C to become more strongly e^{-1} deficient (and more δ+).
- Polarizability can allow a molecule to act polar according to its surrounding e^{-1} field. Essentially, large anions (like I^{-1}) hold e^{-1}'s more loosely, so that the e^{-1} field can control the atom's e^{-1} distribution. As a result, C-I (and C-S) bonds can react as if they are polar in an appropriate e^{-1} field that causes the I to act δ– and the C to act δ+.
- A nucleophile (Nu) is an e^{-1} rich atom (with a negative charge or δ–), such as :NH$_3$ or Cl^{-1}, that will bond with a positive (δ+) nucleus.
- An electrophile (E+) is an e^{-1} poor atom (with a positive charge or δ+), such as H_3O^{+1}, or the δ+ C in CH$_3$Cl, that will bond with an e^{-1} rich (δ–) atom.
- In general, a polar reaction consists of a Nu donating a pair of e^{-1}'s to an E+.
- This is similar to base and acid, except bases donate e^{-1} pairs to H+ (acid), and Nu's donate e^{-1} pairs to a δ+ C (E+).

Polar Reaction Example – Addition of HBr to C_2H_4 (forms CH_3CH_2Br)
- Reaction is an electrophilic addition, where H^{+1} (the E+) is added to the double bond.
- The C-C sp^2 σ bonds are directly between nuclei, so they are strong and not very reactive.
- The Π bond is e^{-1} rich and is accessible (not directly between nuclei).
  The two lobes are above and below the molecule's plane, and the bond has high e^{-1} density.
  So, the Π bond is the Nu in the first step.
- H^{+1} is positive, and is electrophilic as a result (It is the E+).

$$H_2C{=}CH_2 \ + \ H{-}Br \ \longrightarrow \ H_2\overset{+}{C}{-}CH_3 \ + \ Br^{-} \ \longrightarrow \ BrCH_2CH_3$$
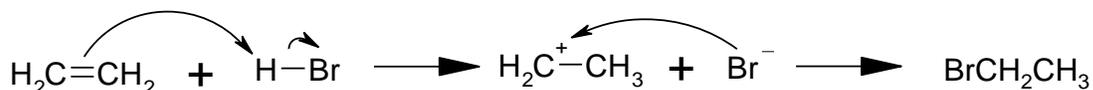
- In the 1st step, the Π e^{-1} pair forms a bond with the H^{+1}, forming a carbocation and a Br^{-1}.
- In the 2nd step, the Br^{-1} is the Nu, while the carbocation is an E+.
- All polar reactions are between an e^{-1} poor site (E+) and an e^{-1} rich site (Nu).
- The Nu always donates the e^{-1} pair to the E+.

Rules for Curved Arrows in Polar Mechanisms
1) The e^{-1}'s move from the Nu to the E+.
2) The Nu is either negatively charged or neutral.
   (Negative becomes neutral, or neutral becomes positive.)
3) E+ is either positively charged or neutral.
   (Positive becomes neutral, or neutral becomes negative.)
4) The octet rule is (almost) always followed.
   (H^{+1} leaves Br^{-1}, so that Br^{-1} keeps the 2 e^{-1}'s from the bond, and maintains its octet.)

Equilibria and Energy Changes

- For aA + bB → cC + dD, we get $Kc = \dfrac{[C]^c[D]^d}{[A]^a[B]^b}$
- If K ≫ 1, then reaction goes primarily forward,
  and if K ≪ 1, then reverse reaction is favored.
- For HBr + C_2H_4 → CH_3CH_2Br, we get $Kc = \dfrac{[CH_3CH_2Br]}{[HBr][C_2H_4]} = 7.5{\times}10^7$
- If the forward reaction is favored (spontaneous with K > 1), then $E_{products} < E_{reactants}$.
- The change in Gibb's free energy is found by: $\Delta G = \Delta H - T\Delta S$.
  A spontaneous reaction has $\Delta G < 0$ (exergonic). Nonspontaneous has $\Delta G > 0$ (endergonic).
- Heat of Reaction: $\Delta H < 0$ is exothermic and $\Delta H > 0$ is endothermic.
- $\Delta G^o = -(RT)\ln[K]$ or $K = \exp[-\Delta G^o/(RT)]$, where R = 8.314 J/mol·K.
- Entropy is a measure of randomness or disorder in a system.
  ΔS is a measure of the change in disorder for a reaction.
- The eqm constant, K, does not imply any information about reaction rates or mechanisms.

Bond Dissociation Energy (D)
- Defined as the E input in gas phase at 25 ^{o}C needed to break a bond into two radicals.
- Can be used to calculate ΔH^o (not ΔG^o or ΔS^o) for the gas phase reaction.
- Does not apply to molecules in liquid solution, because solvent molecules interact with the solute to change ΔH^o, ΔS^o, and ΔG^o. This interaction is called solvation. For instance, if the solvent molecules order the orientation of the solute molecules, then the solute molecules have less disorder, which is less entropy.
- The D values (in kJ/mol) for various bonds are listed in Table 6.3.
- To find ΔH^o, add up values for the reactant bonds that are broken (E input), then subtract the sum of the product bonds that are formed (E released).
    $\Delta H^o = \Sigma$(D for reactant bonds) $- \Sigma$(D for product bonds)
- We can use $Br_2 + CH_4 \rightarrow CH_3Br + HBr$ as an example.
  Br-Br and CH_3-H bonds will break, and H-Br and CH_3-Br bonds will form.
  So, the enthalpy is found as $\Delta H^o = (194 + 439) - (294 + 366) = -27$ kJ/mol

Energy Diagrams and Transition States
- Reactions occur when reactants collide and bonds reorganize.
- The process can be graphed with Energy (Gibb's free energy or G) on the y-axis and the progress of reaction (called the Reaction Coordinate) on the x-axis.
- This graph progressively shows the energy of each substance involved.
- At collision (between reactant and product), the reactant molecules are stuck together, old bonds are partially broken, and new bonds are partially formed.
- This is called the transition state (or activated complex), and uses this symbol: $\ddagger$
- The activation energy is needed to convert the reactants into $\ddagger$,
  $Ea_{fwd} = (G^{\ddagger}) - (G_{reactants}) = \Delta G^{\ddagger}_{fwd}$ (See Fig 6.4)
- The energy that is released when $\ddagger$ forms the products is equivalent to the Ea of the reverse reaction.
  $Ea_{rev} = (G^{\ddagger}) - (G_{products}) = \Delta G^{\ddagger}_{rev}$
- This gives us $\Delta G_{rxn} = (G_{products}) - (G_{reactants}) = \Delta G^{\ddagger}_{fwd} - \Delta G^{\ddagger}_{rev} = Ea_{fwd} - Ea_{rev}$
- A high $\Delta G^{\ddagger}$ means a lot of energy is needed to create $\ddagger$, and a low $\Delta G^{\ddagger}$ means that $\ddagger$ is easy to form.
- If $\Delta G^{\ddagger} < 80$ kJ/mol, then the reaction can proceed at 25 ^{o}C.
- Also, $\Delta G^{\ddagger}$ is related to k, the rate constant in the reaction's rate law.

Intermediates
- Intermediates are formed during one step of a reaction's mechanism, but are consumed in another subsequent step.
- So, intermediates do not appear in the net chemical equation.
- For instance, the carbocation and the bromide are the intermediates in the reaction between HBr and C_2H_4.
- In the two-step reaction between HBr and C_2H_4, both steps have a $\Delta G^{\ddagger}$ and a ΔG^o. (See Fig 6.7)
- The energy diagram for the 1st step of the reaction has an Ea for step 1, then E goes back down to convert $\ddagger$1 into the intermediates.
- The 2nd step has an Ea to convert the intermediates into $\ddagger$2, then E goes back down to convert $\ddagger$2 into the products.
- The resulting graph has two "humps", which are the two $\ddagger$'s. The carbocation intermediate at the low point between the two humps.
- The 1st step is endergonic ($\Delta G_{rxn} > 0$ and the step is not spontaneous), because the intermediate has a relatively high energy. But, the 2nd step is exergonic ($\Delta G_{rxn} < 0$ and the step is spontaneous), because E is released when the intermediate becomes the product.
- Also, the 1st step is slow because its Ea is large, while the 2nd step is fast because its Ea is small,
- Metabolism is catalyzed by enzymes, and takes place with many small steps, rather than one large curve. This not only allows energy to be released in small steps, rather than all at once, but also lowers the Ea requirements so that the reactions can occur at normal body temperatures. See Figure 6.8.