

STUDY GUIDE FOR CHAPTER 6

1. Reactivity of the C=C bond.
 - A. π -bonds are weaker than σ -bonds and can undergo a relatively facile process of addition of various reagents, effectively converting them to σ -bonds. Addition, the general theme in this chapter, is the third major class of organic reactions, after *substitution* and *elimination*.
 - B. The electrons of the π -bond are relatively mobile, and can be easily donated, making the alkene a Lewis base. As such, it can react with a variety of *electrophiles*, giving rise to intermediate carbocations, which subsequently react with *nucleophiles* to give the product of addition. Since the whole process starts with the addition of the electrophile (and this is most often the rate-determining step), such reactions are generally termed as reactions of **electrophilic addition** to alkenes.
2. Hydrogenation – it is the process of addition of hydrogen (H_2) to the double bond. Leads to the conversion of an alkene to an alkane.
 - A. Heats of hydrogenation – please consult your notes from Chapter 5.
 - B. The product of this reaction is an alkane, i.e. a saturated compound. The reaction requires a catalyst, usually Pt or Pd, or Ni. It may or may not require elevated temperature.
 - C. The process occurs on the surface of the catalyst, where the H_2 -molecules are adsorbed. This adsorption is accompanied with weakening of the H – H bond. In this state the two atoms add to the double bond, one H to each carbon atom. Because of the way this happens, the addition is again a *syn*-process, with both hydrogens adding from the same side (The opposite mode of addition would be an *anti* addition).
 - D. It is often a stereoselective reaction, i.e. the two H-atoms add predominantly to one particular face, leading to the predominant (or exclusive) formation of one stereoisomer.
 - E. Since the catalyst is in the solid state, while the alkene is dissolved in some solvent, the overall process takes place in more than one phase (solid + liquid) and is therefore a process of heterogeneous catalysis.
3. Addition of HX (hydrogen halide), water or sulfuric acid.
 - A. Addition of HX – the molecule of HX is polar and a potential source of H^+ . H^+ is a common electrophile, which can add to the alkene double bond, giving rise to a carbocation. The latter reacts with the X to give the product of addition – an alkyl halide. Addition of HX is the reverse reaction of elimination of HX (dehydrohalogenation). Since acidity of HX increases in the order $HF \ll HCl < HBr < HI$, in the same order increases the rate of addition.
 - B. **Markovnikov's Rule** – if HX is added to an unsymmetrical alkene, only the product with X attached to the most substituted carbon is formed. Reason: In the rate-determining step H^+ adds to form carbocations. The most substituted carbocation has the *lowest energy* AND is formed via the *lowest energy TS*, thus making its formation the fastest reaction (Again, application of the Hammond postulate!). The next reaction with the nucleophile (X) will inevitably lead to attachment of the nucleophile to the carbocationic carbon (the most substituted one). In other words, the *Markovnikov's rule* of **regioselectivity** (i.e. where the reaction occurs, if more than one site is available) is the consequence of the stability of the resultant carbocation. We can then formulate the Markovnikov's rule in general terms: **In addition reactions, the attacking species (e.g. the electrophile) adds in such a fashion as to produce the most stable intermediate (e.g. carbocation).**
 - C. Addition of H_2O catalyzed by acid – occurs in the same fashion as addition of HX, but the nucleophile is water and the product is an alcohol. In unsymmetrical alkenes the water adds according to the Markovnikov's rule. Addition of H_2O is the reverse reaction of dehydration of alcohols.

- D. Addition of sulfuric acid, followed by hydrolysis – concentrated sulfuric acid adds in the typical fashion, giving alkyl hydrogen sulfate. Addition obeys the Markovnikov's rule. These sulfates can be hydrolyzed in boiling water to give alcohols. It is an S_N1 reaction.
4. Addition of halogen (X_2).
- A. Halogen molecules can add across the double bond to form vicinal dihalides. The reaction starts with one of the halogen atoms adding to the alkene, while the second forms a halide anion.
- B. The mechanism is peculiar, involving the formation of a cyclic halonium ion, which is a three-membered ring with a formal positive charge on the X. Halonium ions have large ring strain (they are three-membered!!) and a positive charge on an electronegative halogen atom. Both of these factors make them very reactive. They are subject to a backside attack by the halide anion (the nucleophile!!), which breaks the three-membered ring and a second halogen atom is added to the molecule. But because the nucleophile has access from only one side (the back side), the overall process gives ALWAYS the product of anti addition. The addition of halogen is STEREOSPECIFIC!
- C. If the reaction is done in nucleophilic solvents, such as water, the second step, the addition of the nucleophile, may involve other species. In the case of water, the water molecule serves as the nucleophile, and the final product contains one halogen atom and one hydroxyl group. Such materials are known as halohydrins. Halohydrins from unsymmetrical alkenes have the hydroxyl group at the most substituted carbon. Reason: In unsymmetrical cases the halonium ion is also unsymmetric, with a longer bond to and a larger positive charge at the most substituted carbon. Nucleophiles then add to this carbon. In other words, this is another version of Markovnikov's rule.
5. Reactions which Give Anti-Markovnikov Products:
- A. Free-radical Addition of HBr (Also known as *Kharasch* addition).
- 1) In presence of peroxides (molecules with O – O bonds) HBr adds to alkenes to give products with anti-Markovnikov regioselectivity, i.e. bromine is bound to the least substituted carbon. Reason: It is a free-radical process, initiated by formation of Br^{\cdot} from HBr. Br^{\cdot} then reacts with the alkene in a first propagation step, which is rate determining. If the alkene is unsymmetric, more than one radical can be formed, but among them the most highly substituted one will be the most stable, and obtained with the highest rate. This radical and the product from it will be the only one formed. So careful inspection of the mechanism shows that this reaction actually obeys the general Markovnikov's rule: The reaction's rate determining step involves the formation of the most stable intermediate. The seeming contradiction comes from the fact that bromine is the attacking species (analog of an electrophile).
- 2) HCl and HI do not add in an anti-Markovnikov fashion in presence of peroxides. Careful analysis, using BDE, shows that in case of HCl the second propagation step would be very endothermic, and the same is true for the first propagation step of a hypothetical HI addition.
- B. Hydroboration (Addition of borane, BH_3).
- 1) Borane adds to alkenes, in an anti-Markovnikov fashion, to form alkylboranes. Practically, this is carried out using borane.THF complex ($BH_3.THF$).
- 2) Borane contains a trivalent boron atom, which has an incomplete octet (only six electrons in the valence shell). This makes it a powerful electrophile, capable of adding to the double bond. The attacking species is the boron center, which adds to the less substituted carbon, thus leading to an anti-Markovnikov regioselectivity. In fact the whole process occurs in a single step. Nevertheless, in the TS, with the π -bond partially broken and electron density transferred towards the boron, the carbon atoms acquire a partial positive charge. This charge is more stabilized at the more substituted carbon and that is

why boron adds to the other, less substituted center. Thus, this reaction also follows the general principle behind the Markovnikov rule.

- 3) The resultant alkyl borane can be reacted with a mixture of H_2O_2 and NaOH, leading to the removal of the BH_2 -fragment and its replacement with a hydroxyl group. The end product is an alcohol.
- 4) Stereochemistry of hydroboration – Because of the concerted bonding of both boron and hydrogen to the double bond, via cyclic TS, the overall addition takes place to ONE side of the double bond. It is a *syn-addition*. The subsequent reaction of the alkylborane with NaOH/ H_2O_2 leads to the replacement of B with OH but the stereochemistry is not changed. Hydroboration is a STEREOSPECIFIC REACTION.
- 5) Stoichiometry of hydroboration – hydroboration actually takes place with the gradual formation of a mono-, di- and trialkylborane. Trialkylboranes are the real products of the hydroboration. The subsequent chemistry is analogous to the one described above.

6. Oxidation of Alkenes.

A. Epoxidation of Alkenes.

- 1) **Epoxides** are three-membered ring structures, also known as *oxiranes*. They are prepared by reaction of the alkene with a peroxyacid (peracid). Examples of peroxyacids.
- 2) The mechanism is concerted, leading, in one step, to the formation of the epoxide and a carboxylic acid. Since it is a single-step, concerted process, the stereochemical relationship of substituents is completely retained.

B. Oxidative Cleavage of Alkenes by Ozone.

- 1) The reaction mechanism involves the initial formation of a five-membered ring, containing the three oxygen atoms and the two carbons of the double bond – the molozonide.
- 2) The molozonide is unstable and rapidly rearranges to give another five-membered ring, the ozonide. Ozonides are more stable than molozonides.
- 3) Ozonides are further reduced by agents such as zinc or triphenylphosphine, or recently dimethyl sulfide. The products are ketones and/or aldehydes.

7. Polymerization of Alkenes – alkene molecules can join, using their π -electrons, to form long chains known as **polymers**. Because the molecules simply add to one another, it is known as addition polymerization. Polymerizations occur through intermediate active species. By nature this intermediate could be a cation, a radical or an anion, so three different types of polymerization are known:

- A. Cationic – suitable for alkenes that produce stable carbocations. The process is initiated by a Lewis acid – a proton, BF_3 , etc.
- B. Radical – suitable for a variety of alkenes, requires milder conditions if the alkene produces a more stable radical. Initiated by the thermal decomposition of peroxides.

8. Organic Synthesis. Retrosynthetic Analysis.

- A. Often one has to generate a particular product (called a target compound) from another substance, in more than one step (i.e. there is no direct, one-step method for their interconversion). The branch of organic chemistry, dealing with these issues (of designing a sequence and selecting reagents/conditions) is known as organic synthesis.
- B. A very useful way to design a synthesis is to think retrosynthetically, i.e. to start from the target and move backwards, in single steps, by asking each time the question: **How (and from which starting material) can this particular compound be obtained in a single step?** Gradually, one is capable this way to go back to the starting structure.