

## STUDY GUIDE FOR CHAPTER 15

1. Definition and Nomenclature.
  - A. Alcohols – compounds with a general formula ROH, where R is an alkyl group.
  - B. Phenols – compounds with a general formula ArOH, where Ar is an aryl group.
  - C. Diols – compounds containing two hydroxyl groups. Name based on the corresponding alkene + the suffix *diol*. Trivial names: ethylene glycol (1,2-ethanediol) and propylene glycol (1,2-propanediol).
  - D. Triols, tetraols,..., polyols – compounds with 3, 4, ..., n hydroxyl groups. Named likewise.
  - E. Thiols – compounds containing the group SH. Name based on hydrocarbon + the suffix *thiol*. When the SH group has to be considered as a substituent, then it is called a *mercapto* group.
2. Industrial sources of alcohols:
  - A. Methanol – prepared from synthesis gas, which in turn is generated from methane (natural gas).
  - B. Ethanol – prepared by hydration of ethylene (from petroleum). Also via fermentation of carbohydrates.
  - C. Isopropanol – prepared by hydration of propene (from petroleum).
3. Preparation of alcohols:
  - A. Hydration of alkenes (Chapter 6).
    - a. Acid-catalyzed hydration – obeys the *Markovnikov* rule;
    - b. Hydroboration – Oxidation – the alcohol is obtained with anti-*Markovnikov* regiochemistry;
  - B. Hydrolysis of alkyl halides (Chapter 8) – infrequently used. More valuable is the reverse process: Conversion of alcohols to alkyl halides. Also problems with elimination since hydroxide anion is both a strong nucleophile and a strong base.
  - C. Reactions of carbonyl compounds or esters with organolithium or *Grignard* reagents (Chapter 14).
  - D. Reduction of carbonyl compounds.
    - a. Catalytic – the C=O bond can be reduced (in analogy to C=C) with hydrogen in the presence of noble metal catalysts. The process requires more severe conditions than the reduction of C=C. Thus, if a molecule contains both, they are reduced unselectively.
    - b. With complex hydrides – most common are sodium borohydride (NaBH<sub>4</sub>) and lithium aluminum hydride (LiAlH<sub>4</sub>). Both react as formal donors of nucleophilic hydrogen. The reaction with an aldehyde or ketone amounts to formation of a hydrogen – carbonyl carbon bond and subsequent hydrolysis of the alkoxide. The difference between NaBH<sub>4</sub> and LiAlH<sub>4</sub> is in reactivity. Sodium borohydride is less reactive and can be used in water or alcohol solvents. Lithium aluminum hydride (LAH) is very reactive and moisture sensitive. It is used ONLY in ether solvents (ether or THF). The hydrolysis is conducted as a distinct, subsequent step.
  - E. Reduction of carboxylic acids and esters – carboxylic acids are reduced ONLY with LAH. Sodium borohydride is not reactive enough. Both LAH and NaBH<sub>4</sub> can reduce esters, but the reaction with borohydride is very slow, often not practical.
  - F. Reactions of Grignard reagents with epoxides – leads to a two carbon extension in the alcohol product.
4. Preparation of Diols.
  - A. *Via* reduction of dicarbonyl compounds.
  - B. Hydroxylation with osmium tetroxide (OsO<sub>4</sub>) – hydroxylation is a reaction of alkenes that leads to the introduction of two vicinal hydroxyl groups, i.e. leads to the preparation of a diol with 1,2-positioning of the OH groups. It occurs *via* cyclic osmate ester, which is decomposed in the presence of oxidizer (usually *t*-butyl peroxide) and base, leading to a diol and regenerated OsO<sub>4</sub>. Thus, the expensive (and highly toxic!!) osmium tetroxide can be used only in catalytic

quantity. Because of the reaction mechanism, namely the intermediate formation of a cyclic osmate ester, the overall introduction of the two hydroxyl groups is syn. In the case of cyclic alkenes it leads to the formation of *cis*-diols.

## 5. Reactions of Alcohols :

### A. Conversion to alkyl halides (Chapter 4).

- a. Alcohol + HX;
- b. Alcohol + thionyl chloride (SOCl<sub>2</sub>);
- c. Alcohol + phosphorus trihalide (PX<sub>3</sub>);

### B. Acid-catalyzed dehydration (Chapter 5).

### C. Conversion to p-toluenesulfonate esters (tosylates) (Chapter 8).

### D. Conversion to ethers via condensation – in the presence of acid two molecules of alcohol react to give a molecule of ether and a molecule of water. Diols give cyclic ethers.

### E. Conversion to carboxylic acid esters.

- a. *Fischer* esterification – it is the reaction of an alcohol with carboxylic acid, in the presence of acid catalyst, to give ester and water. The process is reversible and is driven towards ester by excess alcohol or removal of water.
- b. Reaction of alcohol with acid chloride – analogous to reaction of alcohol with sulfonyl chloride;
- c. Reaction of alcohol with acid anhydride;

### F. Conversion to esters of inorganic acids – most common are nitrates, sulfates, phosphates and phosphates. Sulfates are often used as alkylating agents.

### G. Oxidation:

#### a. Oxidation of Alcohols;

##### i. Oxidation of primary alcohols.

- a. To carboxylic acids – primary alcohols can be oxidized with a variety of reagents to produce carboxylic acids. The intermediate in these oxidations is the corresponding aldehyde, but it is usually unstable and undergoes further oxidation in the reaction conditions. Most common are dichromate/H<sub>2</sub>SO<sub>4</sub> mixture, KMnO<sub>4</sub>.
- b. To aldehydes – certain reagents are capable of stopping the oxidation at the aldehyde stage. Most widely used are pyridinium chlorochromate (PCC) and pyridinium dichromate (PDC). Both are soluble in certain organic solvents, such as methylene chloride, and this is the typical set of reaction conditions.

##### ii. Oxidation of secondary alcohols – they yield ketones as final and stable products.

##### iii. Oxidation of tertiary alcohols – they are usually resistant in conditions typical for secondary or primary alcohols. VERY extreme conditions cause breaking of the skeleton.

##### iv. Biological oxidation of alcohols – it is catalyzed by an enzyme: alcohol dehydrogenase. The role of oxidizing agent is played by the oxidized version of nicotinamide dinucleotide (NAD<sup>+</sup>), which in the process is converted to its reduced version, NADH. In fact, the entire process has to do with the formal transfer of a hydride anion to NAD<sup>+</sup>, converting ethanol to acetaldehyde.

- b. Oxidation of Diols – they undergo very characteristic cleavage with periodic acid (HIO<sub>4</sub>). It occurs via cyclic ester, which decomposes to form TWO molecules with carbonyl groups (aldehydes or ketones) and iodic acid (HIO<sub>3</sub>). Cyclic diols give dicarbonyl compounds.

## 6. Thiols.

- A. Acidity – thiols are considerably (some 100000 times) more acidic than alcohols. The reason is the weaker S – H bond and better stabilization of the resultant anion. Thiols are efficiently deprotonated by hydroxide anion.
- B. Nucleophilicity of thiolate anions – they are very strong nucleophiles and participate in various SN2 reactions.
- C. Oxidation of thiols – while alcohols are oxidized with modification at the carbon bearing the OH group, thiols are oxidized with modification of sulfur itself. It is sequential, with gradual increase of the number of oxygen atoms attached to sulfur. The stages are thiol to sulfenic acid (RSOH) to sulfinic acid (RS(O)OH) to sulfonic acid (RS(O<sub>2</sub>)OH). Another oxidation route goes through a disulfide as the first intermediate. Disulfide bonds have strength that falls between that of common covalent bonds (300 – 400 kJ/mol) and hydrogen bonds (30 kJ). The bond energy is about 220 kJ/mol. This allows for their relatively easy formation and breaking. Reversible formation of disulfide bonds (disulfide bridges) is often observed in biochemical systems.