

STUDY GUIDE FOR CHAPTER 17

- Definitions:
 - Aldehydes – compounds containing a carbonyl group bound to 1 alkyl (or aryl) group and one H-atom. The formation – CHO is called an aldehyde group.
 - Ketones – the carbonyl group is bound to 2 alkyl (or aryl) groups.
- Nomenclature.
 - Aldehydes.
 - IUPAC.
 - The longest chain, CONTAINING the aldehyde group is selected, with a suffix *-al*. The aldehyde group is a terminal group and the aldehyde carbon is ALWAYS number 1.
 - In cases when the aldehyde group is attached to a ring, the ending *-carbaldehyde* is used.
 - Common – common names for the first few members – formaldehyde, acetaldehyde, benzaldehyde.
 - As substituent – although very high ranking, in certain cases the aldehyde group is treated as a substituent, as in cases when the molecule has a carboxylic acid or ester group. In such cases the aldehyde group is named *formyl*.
 - Ketones.
 - IUPAC.
 - The longest chain CONTAINING the carbonyl group is selected, with a suffix *-one*. The numbering performed in a fashion such that the carbonyl carbon receives the lowest possible number.
 - Common
 - Names based on the word ketone + the names of the alkyl (aryl) residues. Similar to common nomenclature for ethers.
 - Trivial names for the first few members – acetone, acetophenone, benzophenone.
 - As substituents – the keto group is outranked by the aldehyde group and carboxylic acid (ester) group. In case any of those is present, the keto group is treated as a substituent and named *oxo*.
- Electronic Structure.
 - Aldehydes and ketones contain the carbonyl group, C = O, as their functional group. It resembles the C = C double bond, as it also consists of one σ - and one π -bond. The overall bond length is smaller, because of the smaller size of O.
 - Unlike the C = C bond, the C = O bond is highly polarized, because of the difference in electronegativities. This gives the carbonyl group (and often the entire molecule) a considerable dipole moment.
 - Because of the polarization, the carbon atom becomes an effective electrophilic center and is susceptible to attack by various nucleophiles.
 - The carbonyl oxygen is partially negatively charged and has unshared electron pairs, making it a Lewis base center.
- Physical Properties.
 - Boiling Points – higher than the corresponding for ethers or hydrocarbons, because of considerable dipole moment. Lower than those of alcohols, because of the lack of H-bonds.
 - Solubility – can serve as hydrogen bond acceptors, thus being very well soluble in alcohols and the first few even in water. Also very good solvents for compounds with various structures (acetone).
- Synthesis of Aldehydes and Ketones.
 - Ozonolysis of Alkenes (Chapter 6).
 - Acid-catalyzed Hydration of Alkynes – yields ketones (except for acetylene) (Chapter 9).
 - Friedel-Crafts* Acylation – gives aryl ketones (Chapter 12).
 - Gatterman-Koch* Formylation – gives aryl aldehydes.

- E. Oxidation of Primary Alcohols to Aldehydes – in oxidation of primary alcohols, in order to stop at the aldehyde stage, one has to employ specific oxidants: PCC or PDC!!).(Chapter 15).
- F. Oxidation of Secondary Alcohols to Ketones – achieved easily with a variety of oxidizing reagents (Chapter 15).
- G. Synthesis of Aldehydes from Carboxylic Acids or Esters – it is a two-step protocol, via the corresponding primary alcohol.
- H. Synthesis of Ketones from aldehydes – it is a two-step procedure, in which the aldehyde is converted to a secondary alcohol (via reaction with organolithium or *Grignard* reagent) and the latter is then oxidized to the ketone.
6. Reduction of Aldehydes and Ketones.
- A. To alcohols (C = O to CH – OH transition).
- With complex hydrides – typically NaBH₄ and LiAlH₄ are used (Chapter 15).
- B. To hydrocarbons (C = O to CH₂ transition).
- Clemmensen* reduction.
 - Wolf – Kishner* reduction – unlike the *Clemmensen* reduction, it requires basic conditions and is particularly suitable for acid-sensitive groups. Solvents with high bps are used: DMSO, ethylene glycol.
7. Nucleophilic Addition Reactions – due to the smaller number of alkyl groups attached to the carbonyl carbon, aldehydes tend to have (comparatively) larger positive charge on that carbon. This *electronic effect* is one of the reasons that aldehydes are more reactive than ketones in reactions with nucleophiles. The nucleophilic addition reactions end with (or at least go through) a tetrahedral structure of the product. Thus, the steric crowding will be expected to be larger in the product, in comparison to the starting carbonyl compound. Again, this *steric effect* is less pronounced in aldehydes, being another reason for their higher reactivity.
- A. Simple Addition Reactions – these lead to stable products with tetrahedral (*sp*³) geometry at the carbonyl carbon.
- Addition of Grignard reagents (Chapter 14).
 - Addition of water – it can be catalyzed by acid or base. The product is the corresponding *hydrate*. For some very active aldehydes and ketones the hydrate is the stable form upon dissolution in water – formaldehyde, chloral, hexafluoroacetone.
 - Addition of hydrogen cyanide – cyanide anion is a strong nucleophile, which readily attacks the carbonyl carbon. The end product, after protonation is a stable compound known as *cyanohydrin*. Some cyanohydrins (such as acetone cyanohydrin) are used in practice as sources of cyano group. Another use is their hydrolysis to α -hydroxycarboxylic acids.
 - Addition of alcohols – it is a two-stage process, whose first stage is an exact analog of the addition of water. The product is called *hemiacetal* (or *hemiketal* in case of ketones). In basic conditions *hemiacetals* (*hemiketals*) cannot undergo any further conversion, but in acid-catalyzed reactions a second stage is possible, which is a typical S_N1 process, leading to the formation of an *acetal* (*ketal*), in which two alcohol molecules are added to the carbonyl compound (Or one alcohol molecule if the alcohol is a diol, which is often the case in practice!!). *Acetals* (*ketals*) are stable in basic conditions, but fall quickly apart in acidic conditions, reverting to the starting carbonyl compound. This possibility to easily introduce and remove *acetals* makes possible their use as *protecting groups*. The protection can be very selective, since it depends on two additional factors:
 - In the presence of both an aldehyde and a keto group, the aldehyde group is protected selectively, due to its higher reactivity (True, if we do not use excess of protecting alcohol!!).
 - In the presence of two aldehyde or two keto groups, the less sterically crowded group is protected selectively (True, if we do not use excess of protecting alcohol!!).

- B. Addition-Elimination Reactions – the first stage is still attack of the nucleophile and formation of a tetrahedral compound, which however is an intermediate that eliminates some small molecule, to give the final stable product. Such reactions (particularly when the small eliminated molecule is water) are known as condensation reactions or *condensations*.
- Addition of ammonia and primary amines – these are good nucleophiles that react by attacking the carbonyl carbon and forming (after protonation) tetrahedral intermediates known as *aminols* (or *carbinolamines*). The latter, in presence of acid catalyst, lose water and are converted to molecules with a C = N bond, known as *imines*. The entire process is acid-catalyzed, but pH needs to be carefully adjusted since too high or too low pH both lead to decrease of the reaction rate. Imines' stability depends on the type of amine used in the reaction. Ammonia gives very unstable imines; primary alkyl amines give relatively stable compounds; primary aryl amines give completely stable materials. Imines (particularly when an aryl group is present) are also known as *Schiff Bases*.
 - Addition of Hydroxylamine and Hydrazines – these compounds also possess an NH₂ group, like primary amines, and are also capable (and even more reactive) to react with aldehydes and ketones. The corresponding stable product after condensation is *oxime* (in the case of hydroxylamine) or various *hydrazones* (in the case of hydrazines). A particular type of substituted hydrazine is *semicarbazide*, which also gives stable products, *semicarbazones*. These materials often have well defined solid crystalline properties, and are used to characterize various aldehydes and ketones, thus facilitating the elucidation of unknown structures.
 - Addition of Phosphorus Ylides (Wittig reaction) – phosphorus ylides are another example of compounds with a carbanionic carbon (i.e. nucleophilic carbon). The latter can attack the carbonyl carbon to form *betaine*, which forms an *oxaphosphetane ring*. The latter undergoes elimination of triphenylphosphine oxide, to give an *alkene* as a final and stable product. The Wittig reaction is a very important practical method for synthesis of alkenes.
8. Oxidation Reactions.
- Oxidation of Aldehydes – aldehydes are unstable towards oxidation and are easily transformed into the corresponding carboxylic acids, even with relatively weak oxidants, such as silver oxide or soluble versions of Ag⁺, particularly [Ag(NH₃)₂]⁺ (*Tollens Test!!*).
 - Baeyer – Villiger* Oxidation of Ketones – achieved upon reaction of ketones with peracids. Involves a step of nucleophilic attack of the peracid on the carbonyl carbon of the ketone, followed by rearrangement. The product is an ester with one-atom increase of the chain length (compared to the starting ketone). In the case of cyclic ketones, the product is an ester with one-atom increase of the ring size.
9. Spectroscopy of Aldehydes and Ketones.
- IR – very strong band (C = O stretch) in the region of 1700 cm⁻¹. Aldehyde hydrogen has characteristic C – H stretches at 2700 and 2800 cm⁻¹.
 - NMR.
 - ¹H NMR – the aldehyde hydrogen has a very characteristic signal at 9 – 10 ppm. The signals for hydrogens at carbons directly adjacent to the C = O group appear at 2 – 2.5 ppm.
 - ¹³C NMR – the carbonyl carbon is very far downfield shifted, typically in the region 190 – 220 ppm. Nothing else but aldehyde and ketone carbonyl groups appear in this region.
 - Mass Spectrometry – there are two characteristic fragmentations:
 - Alpha*-cleavage – the breaking of the bond between the carbonyl carbon and the carbon immediately adjacent. The driving force is the stability of the so obtained *acylium* cation.
 - The *McLafferty* rearrangement – requires the presence of hydrogen at the γ -carbon atom. Occurs through a cyclic transition state, gives an alkene and another carbonyl compound.
 - UV – there are two types of electronic transitions, which fall into the typical UV region:

- i. The $\pi - \pi^*$ transition – as in the case of alkenes, it is observable only if the C = O group is conjugated to at least one more multiple bond (or benzene ring).
- ii. The $n - \pi^*$ transition – the promotion of an electron from the oxygen's lone pair to a π^* orbital. It is “forbidden” (i.e. it has a very low extinction coefficient), but it requires less energy and is observable regardless of the environment within a particular molecule (i.e. whether the C = O is conjugated or not!). For non-conjugated compounds it appears in the region 280 – 300 nm.