ALDEHYDES AND KETONES

Objectives

Introduction

- Nomenclature of aldehydes and ketones
- Physical properties
- Preparation of aldehydes and ketones
- Chemical reactions
 - Nucleophilic reactions
 - Reduction
 - oxidation
 - **Reactions involving a-hydrogen**

Aldehydes and Ketones

Aldehydes and ketones are characterized by the the carbonyl functional group (C=O).

Some common classes of carbonyl compounds

Class	General Formula	Class	General Formula
ketones	$\mathbf{R} - \mathbf{C} - \mathbf{R}'$	aldehvdes	R-C-H
carboxylic acids	Р К−С−ОН	acid chlorides	R - C - Cl
esters	R - C - O - R'	amides	$R - C - NH_2$

Carbonyl Structure

Carbon is *sp*² **hybridized.**

C=O bond is shorter, stronger, and more polar than C=C bond in alkenes.

		length	energy
R	ketone $C = 0$ bond	1.23 Å	178 kcal/mol (745 kJ/mol)
120° CO	alkene C=C bond	1.34 Å	146 kcal/mol (611 kJ/mol)

Naming Aldehydes and Ketones

Aldehydes are named by replacing the terminal -e of the corresponding alkane name with -al

The parent chain must contain the —CHO group

The —CHO carbon is numbered possible minimum number.



Naming Ketones

Replace the terminal -*e* of the alkane name with –*one*

Parent chain is the longest one that contains the ketone group

Numbering begins at the end nearer the carbonyl carbon



Ketones with Common Names

IUPAC retains well-used but unsystematic names for a few ketones



Ketones and Aldehydes as Substituents

The R–C=O as a substituent is an acyl group is used with the suffix -yl from the root of the carboxylic acid CH₃CO: acetyl; CHO: formyl; C₆H₅CO: benzoyl

The prefix oxo- is used if other functional groups are present and the doubly bonded oxygen is labeled as a substituent on a parent chain



Boiling Points

More polar, so boiling point higher than corresponding alkane or ether.

Absence of H-bond, so boiling point lower than corresponding alcohol.



Solubility

Good solvent for alcohols.

Lone pair of electrons on oxygen of carbonyl can accept a hydrogen bond from O-H or N-H.

Acetone and acetaldehyde are miscible in water.

General methods of preparation

From alcohols by oxidation by dehydrogenation From acid chlorides **From nitriles From hydrocarbons** by ozonolysis of alkenes by hydration of alkenes by oxidation of methylbenzenes



From hydrocarbons

From Alkenes via Ozonolysis



Friedel–Crafts acylation of an aromatic ring with an acid chloride in the presence of AlCl₃ catalyst



Hydration of Alkynes

- Markovnikov Addition
- Anti-Markovnikov Addition



Hydrolysis of Geminal Dihalides

Formation of Aldehydes or Ketones

$$R - CH Cl_{2} \xrightarrow{H_{2}O} R - C - H + 2HCl$$

$$R_{2}CCl_{2} \xrightarrow{H_{2}O} R - C - R + 2HCl$$

Ketones from Nitriles

A Grignard or organolithium reagent attacks the nitrile carbon.

The imine salt is then hydrolyzed to form a ketone.



From Acid Chlorides

Aldehydes

Use a mild reducing agent to prevent reduction to primary alcohol.

$$\begin{array}{c} O \\ H_3CH_2CH_2C - Cl \end{array} \xrightarrow{\text{LiAlH}(O-t-Bu)_3} CH_3CH_2CH_2C - H \end{array}$$

Ketones

Use lithium dialkylcuprate (R₂CuLi), formed by the reaction of 2 moles of R-Li with cuprous iodide.

$$2 \operatorname{CH}_{3}\operatorname{CH}_{2}\operatorname{CH}_{2}\operatorname{CH}_{2}\operatorname{Li} \xrightarrow{\operatorname{CuI}} (\operatorname{CH}_{3}\operatorname{CH}_{2}\operatorname{CH}_{2})_{2}\operatorname{CuLi}$$

$$\overset{O}{\underset{\parallel}{\overset{\parallel}{\overset{\scriptstyle (\operatorname{CH}_{3}\operatorname{CH}_{2}\operatorname{CH}_{2})_{2}}} \operatorname{CuLi} + \operatorname{CH}_{3}\operatorname{CH}_{2}\overset{\overset{\scriptstyle (\operatorname{CH}_{3}\operatorname{CH}_{2}\operatorname{CH}_{2})_{2}}} \operatorname{CuLi} \xrightarrow{\operatorname{CH}_{3}\operatorname{CH}_{2}\operatorname{CH}_{2}} \operatorname{CH}_{2}$$

Nucleophilic Addition

A strong nucleophile attacks the carbonyl carbon, forming an alkoxide ion that is then protonated.

A weak nucleophile will attack a carbonyl if it has been protonated, thus increasing its reactivity.

Aldehydes are more reactive than ketones.



Nucleophiles

Nucleophiles can be negatively charged (: Nu⁻) or neutral (: Nu) at the reaction site

The overall charge on the nucleophilic species is not considered

Some negatively charged nucleophiles

H \ddot{Q} :- (hydroxide ion) H:- (hydride ion) R₃C:- (a carbanion) R \ddot{Q} :- (a carbanion) N \equiv C:- (cyanide ion)

Some neutral nucleophiles

 $H\ddot{O}H$ (water) $R\ddot{O}H$ (an alcohol) H_3N : (ammonia) $R\ddot{N}H_2$ (an amine)

Relative Reactivity of Aldehydes and Ketones

Aldehydes are generally more reactive than ketones in nucleophilic addition reactions.

The transition state for addition is less crowded and lower in energy for an aldehyde (a) than for a ketone (b).

Aldehydes have one large substituent bonded to the C=O: ketones have two.



Reactivity of Aromatic Aldehydes Less reactive in nucleophilic addition reactions than aliphatic aldehydes

Electron-donating resonance effect of aromatic ring makes C=O less reactive electrophilic than the carbonyl group of an aliphatic aldehyde



Addition of Water

- In acid, water is the nucleophile.
- In base, hydroxide is the nucleophile.
- Aldehydes are more electrophilic since they have fewer e⁻-donating alkyl groups.



Mechanism of addition of water





Addition of HCN

Addition of HCN is reversible and base-catalyzed, generating nucleophilic cyanide ion, CN

Addition of CN⁻ to C=O yields a tetrahedral intermediate, which is then protonated

Equilibrium favors adduct



Reactivity formaldehyde > aldehydes > ketones >> bulky ketones.

Addition of sodium bisulphite

Forms crystalline addition products.



Nucleophilic Addition of Grignard Reagents

Treatment of aldehydes or ketones with Grignard reagents yields an alcohol

Nucleophilic addition of the equivalent of a *carbon* anion, or carbanion. A carbon—magnesium bond is strongly polarized, so a Grignard reagent reacts for all practical purposes as R : [–] MgX ⁺.



Addition of Alcohol

In presence of dry HCl aldehydes and ketones react with two equivalent of alcohols to form acetals and



Formation of Acetals

Alcohols are weak nucleophiles but acid promotes addition forming the conjugate acid of C=O

- Addition yields a hydroxy ether, called a hemiacetal (reversible); further reaction can occur
- Protonation of the —OH and loss of water leads to an oxonium ion, $R_2C=OR^+$ to which a second alcohol adds to form the acetal



Cyclic Acetals Addition of a diol produces a cyclic acetal. Hydrolyze easily in acid, stable in base. Aldehydes more reactive than ketones. **Protects** aldehyde group form bases. $CH_2 - CH_2$ OHHO

 H^+

Uses of Acetals

Acetals can serve as protecting groups for aldehydes and ketones

It is convenient to use a diol, to form a *cyclic* acetal (the reaction goes even more readily)



Addition of ammonia and its derivatives

Nucleophilic addition of ammonia or primary amine, followed by elimination of water molecule.



$$C = O + H_2 \ddot{N} - Z \xrightarrow{H^+} C = \ddot{N} - Z + H_2 O$$

$$Z in Z - NH_2 \qquad Reagent \qquad Product$$

$$-H \qquad H_2 \ddot{N} - H \ ammonia \qquad C = \ddot{N} - H \ an imine$$

$$-R \qquad H_2 \ddot{N} - R \ primary \ amine \qquad C = \ddot{N} - R \ an imine \ (Schiff \ base)$$

$$-OH \qquad H_2 \ddot{N} - OH \ hydroxylamine \qquad C = \ddot{N} - OH \ an oxime$$

$$-NH_2 \qquad H_2 \ddot{N} - OH \ hydrazine \qquad C = \ddot{N} - OH \ an oxime$$

$$-NHPh \qquad H_2 \ddot{N} - NH_2 \ hydrazine \qquad C = \ddot{N} - NH_2 \ a \ hydrazone$$

$$-NHPh \qquad H_2 \ddot{N} - NHPh \ phenylhydrazine \qquad C = \ddot{N} - NHPh \ a \ phenylhydrazone$$

$$-OH \qquad H_2 \ddot{N} - NHPh \ phenylhydrazine \qquad C = \ddot{N} - NHPh \ a \ phenylhydrazone$$

$$-NHPh \qquad H_2 \ddot{N} - NHPh \ phenylhydrazine \qquad C = \ddot{N} - NHPh \ a \ phenylhydrazone$$

$$-NHPh \qquad H_2 \ddot{N} - NHPh \ phenylhydrazine \qquad C = \ddot{N} - NHPh \ a \ phenylhydrazone$$

$$-NHCNH_2 \qquad H_2 \ddot{N} - NH - C - NH_2 \ a \ semicarbazide \qquad a \ semicarbazone$$

Oxidation of Aldehydes and Ketones

CrO₃ in aqueous acid oxidizes aldehydes to carboxylic acids efficiently

Silver oxide, Ag₂O, in aqueous ammonia (Tollens' reagent) oxidizes aldehydes (no acid)



Hydration of Aldehydes

- Aldehyde oxidations occur through 1,1-diols ("hydrates")
- **Reversible addition of water to the carbonyl group**
- Aldehyde hydrate is oxidized to a carboxylic acid by usual reagents for alcohols



Ketones Oxidize with Difficulty

Undergo slow cleavage with hot, alkaline KMnO₄

C–C bond next to C=O is broken to give carboxylic acids

Reaction is practical for cleaving symmetrical ketones



Tollens Test

Add ammonia solution to AgNO₃ solution until precipitate dissolves.

Aldehyde reaction forms a silver mirror.

$$R - C - H + 2 Ag(NH_3)_2^+ + 3 OH^- - H_2O$$

$$2 Ag + R - C - O^- + 4 NH_3 + 2 H_2O$$

Reduction Reagents

Sodium borohydride, NaBH₄, reduces C=O, but not C=C.

Lithium aluminum hydride, LiAlH₄, much stronger, difficult to handle.

Hydrogen gas with catalyst also reduces the C=C bond.

Catalytic Hydrogenation

Widely used in industry.

Raney nickel, finely divided Ni powder saturated with hydrogen gas.

Pt and Rh also used as catalysts.







The Wolff–Kishner Reaction

Treatment of an aldehyde or ketone with hydrazine, H₂NNH₂ and KOH converts the compound to an alkane

Originally carried out at high temperatures but with dimethyl sulfoxide as solvent takes place near room temperature



The Cannizzaro Reaction

The adduct of an aldehyde and OH⁻ can transfer hydride ion to another aldehyde C=O resulting in a simultaneous oxidation and reduction (disproportionation)



Aldol condensation

A small amount of base is used to generate a small amount of enolate in the presence of unreacted carbonyl compound.

After the condensation, the basic catalyst is regenerated.



Dehydration of Aldol Products

The β -hydroxy carbonyl products dehydrate to yield conjugated enones

The term "condensation" refers to the net loss of water and combination of 2 molecules



Mixed Aldol Reactions

A mixed aldol reaction between two similar aldehyde or ketone partners leads to a mixture of four possible products

This is not useful



Intramolecular Aldol Reactions

Treatment of certain *di*carbonyl compounds with base produces cyclic products by intramolecular reaction



Mechanism of Intramolecular Aldol Reactions

Both the nucleophilic carbonyl anion donor and the electrophilic carbonyl acceptor are now in the same molecule.

The least strained product is formed because the reaction is reversible



The Claisen Condensation Reaction

Reaction of an ester having an α hydrogen with 1 equivalent of a base to yield a β -keto ester





Illustrative example

 $\xrightarrow{\text{Br}_2/\text{CCI}_4} (A) \xrightarrow{\text{NaNH}_2} (B) \xrightarrow{\text{Hg SO}_4/\text{H}_2\text{SO}_4} (C) \xrightarrow{\text{NH}_2\text{NHCONH}_2} (D)$

Predict (A), (B), (C) and (D).

Solution :



Illustrative example



Predict the final product.

Solution



Identification of aldehydes

 $\operatorname{RCHO} \xrightarrow{\operatorname{KMNO}_4} \operatorname{RCOOH}_{\operatorname{or} \operatorname{K}_2\operatorname{Cr}_2\operatorname{O}_7, \operatorname{H}^+} \operatorname{RCOOH}$

Tollen's test

 $\begin{array}{ll} \text{RCHO} + 2\text{Ag}\left(\text{NH}_3\right)_2^+ + 3\text{OH}^- \rightarrow \text{RCOO}^- + 2\text{Ag} + 4\text{NH}_3 + 2\text{H}_2\text{O} \\ \text{(ammonical silver nitrate solution)} & \text{(Silver mirror)} \end{array}$

Fehling's test

 $\frac{\text{RCHO} + 2\text{CuO} \rightarrow \text{RCOOH}}{\text{Blue}} + \frac{\text{Cu}_2\text{O}}{\text{Red ppt. (Cuprous oxide)}}$

