

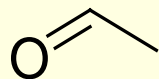
Chapter 19. Aldehydes and Ketones: Nucleophilic Addition Reactions

Aldehydes and Ketones

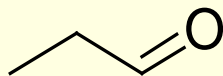
- Aldehydes and ketones are characterized by the the carbonyl functional group (C=O)
- The compounds occur widely in nature as intermediates in metabolism and biosynthesis
- They are also common as chemicals, as solvents, monomers, adhesives, agrichemicals and pharmaceuticals

Naming Aldehydes and Ketones

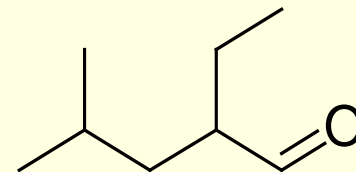
- Aldehydes are named by replacing the terminal -e of the corresponding alkane name with -al
- The parent chain must contain the —CHO group
 - The —CHO carbon is numbered as C1
- If the —CHO group is attached to a ring, use the suffix See Table 19.1 for common names



ethanal



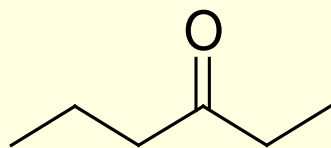
propanal



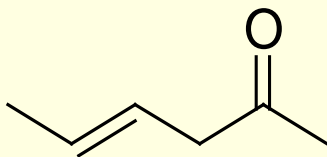
2-ethyl-4-methylpentanal

Naming Ketones

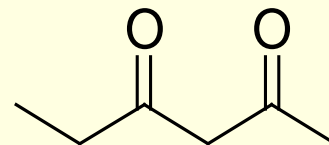
- Replace the terminal -e of the alkane name with –
one
- Parent chain is the longest one that contains the
ketone group
 - Numbering begins at the end nearer the
carbonyl carbon



3-hexanone



4-hexen-2-one



2,4-hexandione

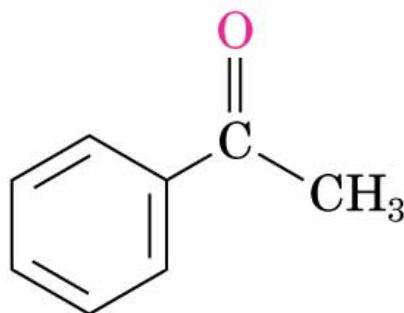
Ketones with Common Names

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

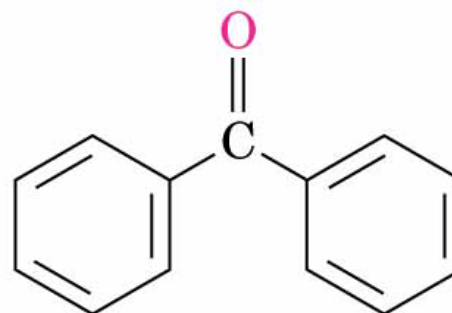


Acetone

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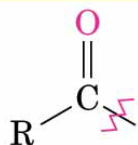
Acetophenone



Benzophenone

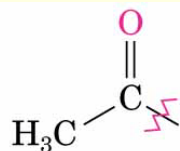
Ketones and Aldehydes as Substituents

- 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

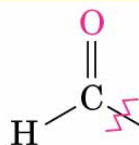


An acyl group

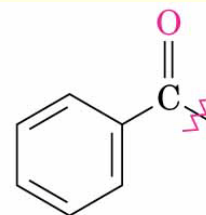
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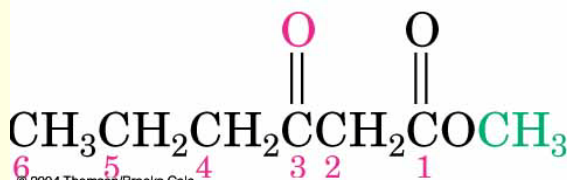
Acetyl



Formyl



Benzoyl



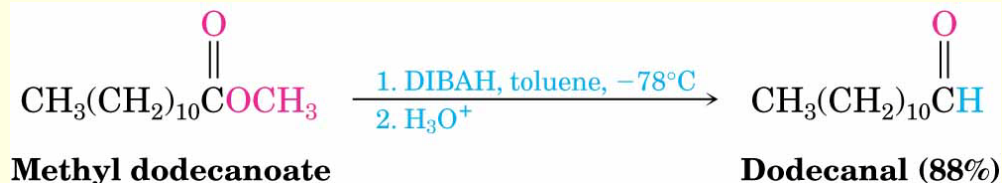
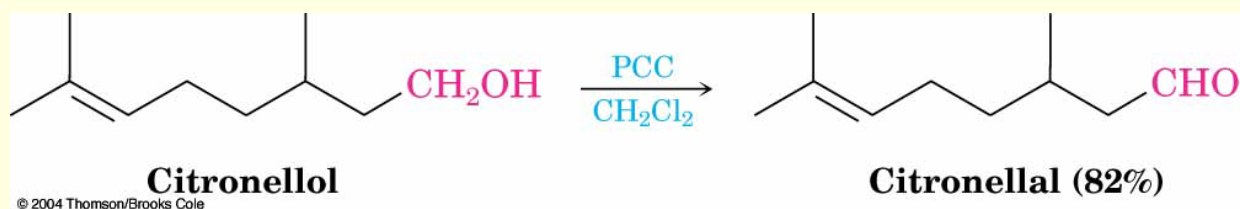
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Methyl 3-oxohexanoate

Preparation of Aldehydes and Ketones

Preparing Aldehydes

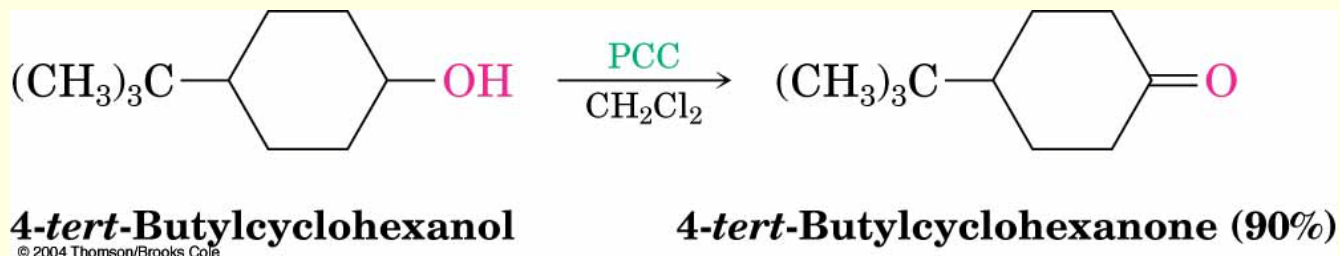
- Oxidize primary alcohols using pyridinium chlorochromate
- Reduce an ester with diisobutylaluminum hydride (DIBAH)



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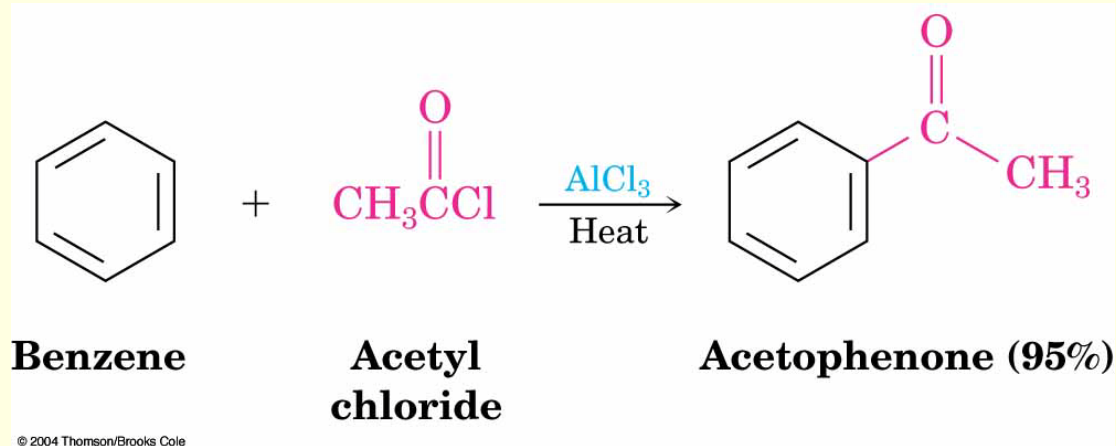
Preparing Ketones

- Oxidize a 2° alcohol (see Section 17.8)
- Many reagents possible: choose for the specific situation (scale, cost, and acid/base sensitivity)



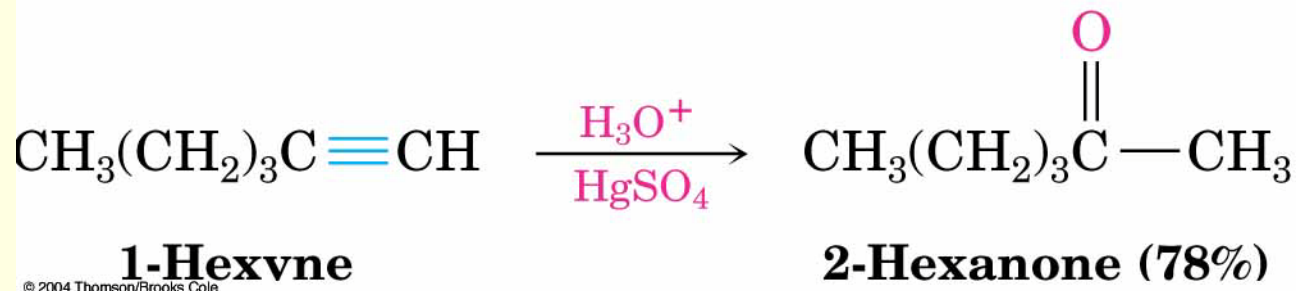
Aryl Ketones by Acylation

- Friedel–Crafts acylation of an aromatic ring with an acid chloride in the presence of AlCl_3 catalyst (see Section 16.4)



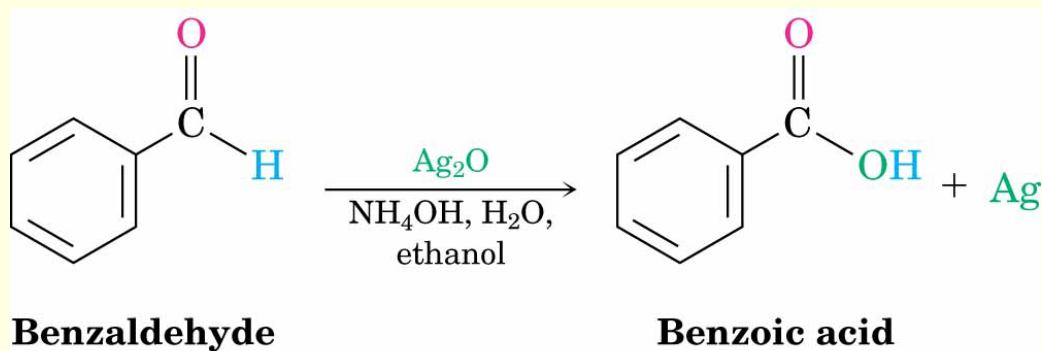
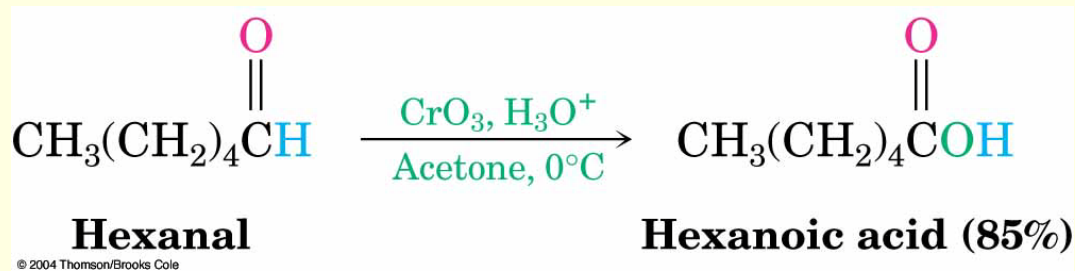
Methyl Ketones by Hydrating Alkynes

- Hydration of terminal alkynes in the presence of Hg^{2+}



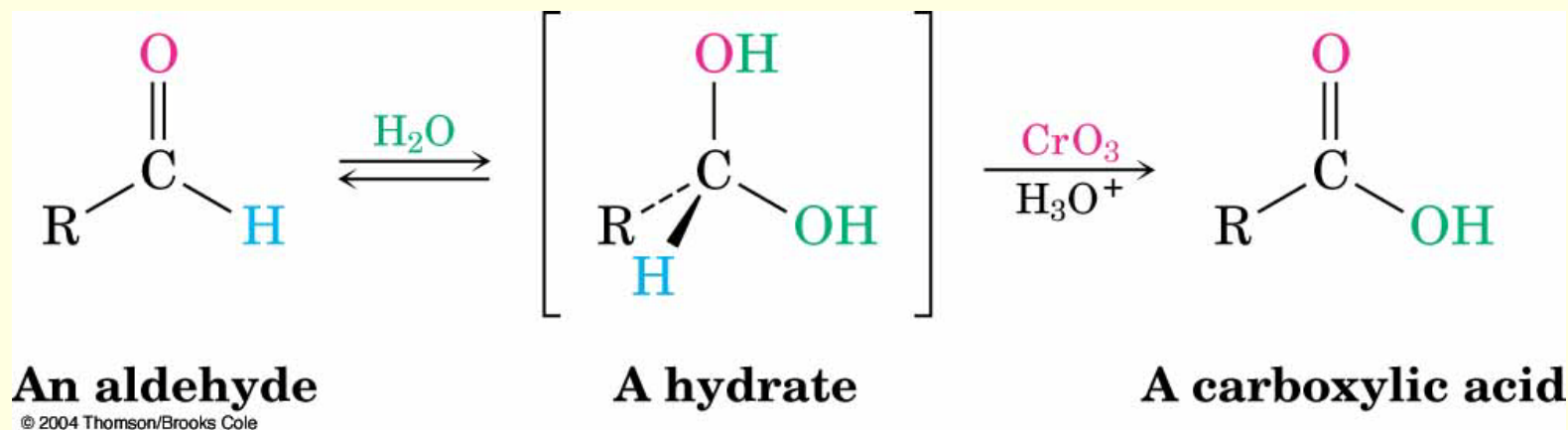
Oxidation of Aldehydes and Ketones

- CrO_3 in aqueous acid oxidizes aldehydes to carboxylic acids efficiently
- Silver oxide, Ag_2O , in aqueous ammonia (Tollens' reagent) oxidizes aldehydes (no acid)



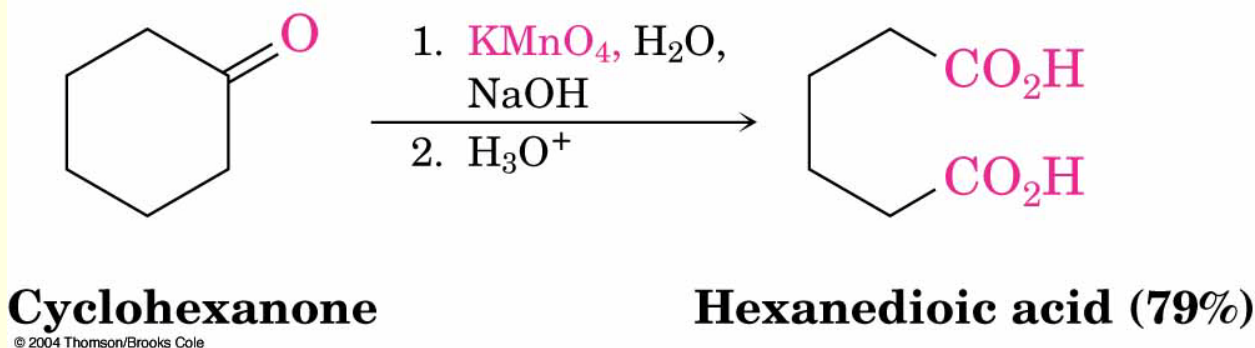
Hydration of Aldehydes

- 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

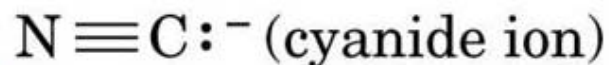
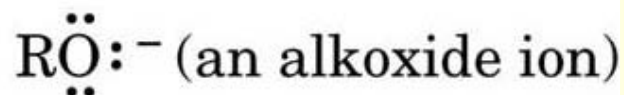
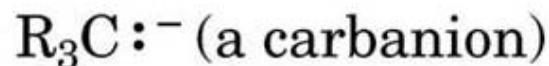
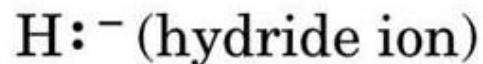
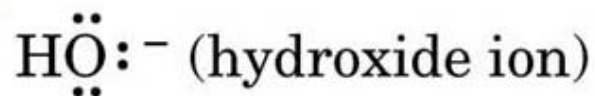
- Undergo slow cleavage with hot, alkaline KMnO_4
- C–C bond next to C=O is broken to give carboxylic acids
- Reaction is practical for cleaving symmetrical ketones



Nucleophiles

- Nucleophiles can be negatively charged ($: \text{Nu}^-$) or neutral ($: \text{Nu}$) at the reaction site

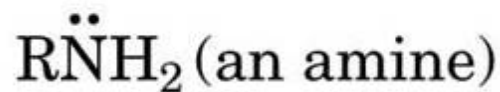
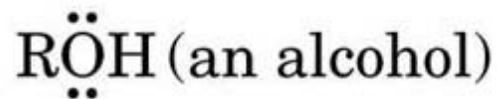
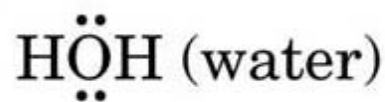
Some negatively charged nucleophiles



Other Nucleophiles

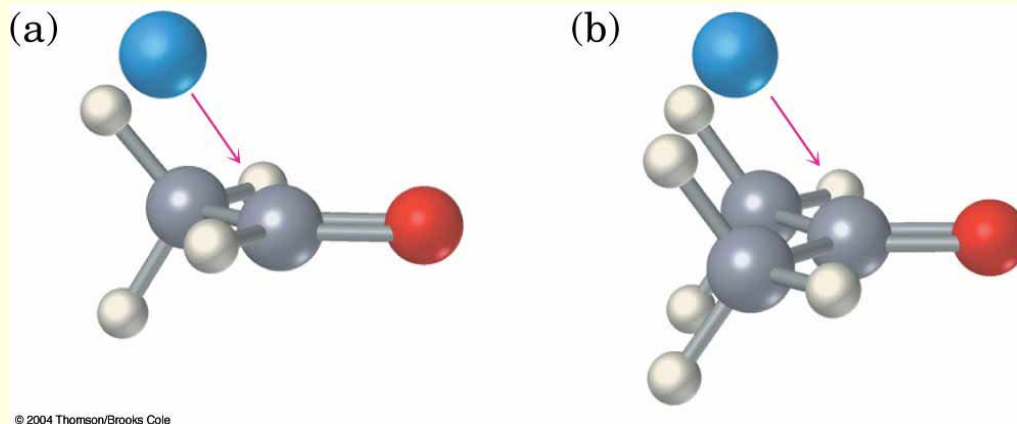
- The *overall charge* on the nucleophilic species is not considered

Some neutral nucleophiles



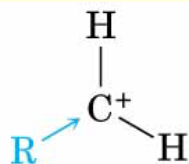
Relative Reactivity of Aldehydes and Ketones

- Aldehydes are generally more reactive than ketones in nucleophilic addition reactions
- Aldehydes have one large substituent bonded to the $C=O$; ketones have two

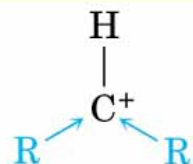


Electrophilicity of Aldehydes and Ketones

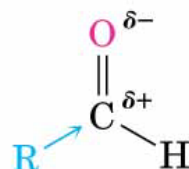
- Aldehyde C=O is more polarized than ketone C=O
- As in carbocations, more alkyl groups stabilize + character
- Ketone has more alkyl groups, stabilizing the C=O carbon inductively



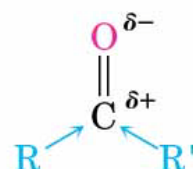
1° carbocation
(less stable, more reactive)



2° carbocation
(more stable, less reactive)



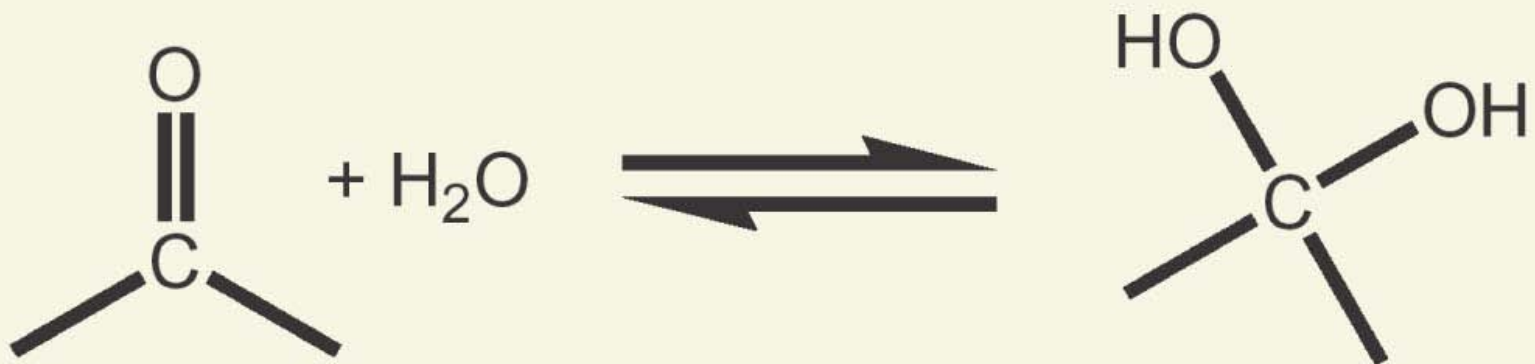
Aldehyde
(less stabilization of $\delta+$, more reactive)



Ketone
(more stabilization of $\delta+$, less reactive)

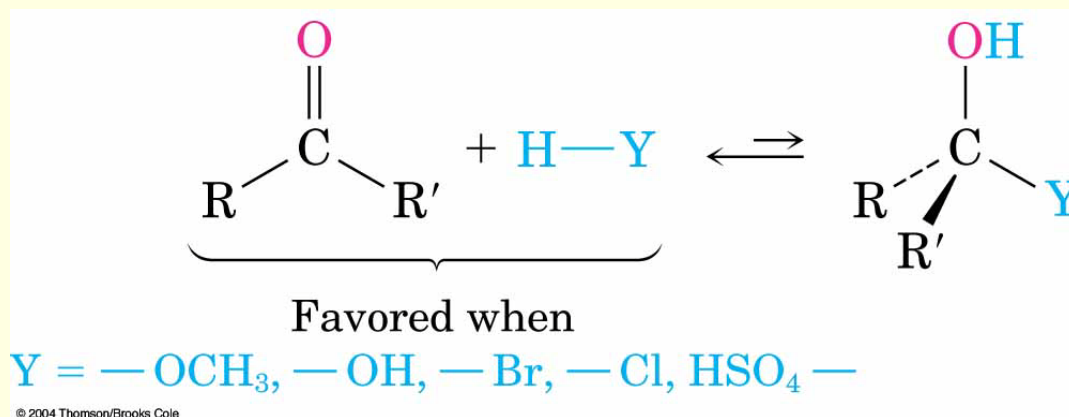
Nucleophilic Addition of H₂O: Hydration

- Aldehydes and ketones react with water to yield 1,1-diols (**geminal (gem) diols**)
- Hydration is reversible: a gem diol can eliminate water



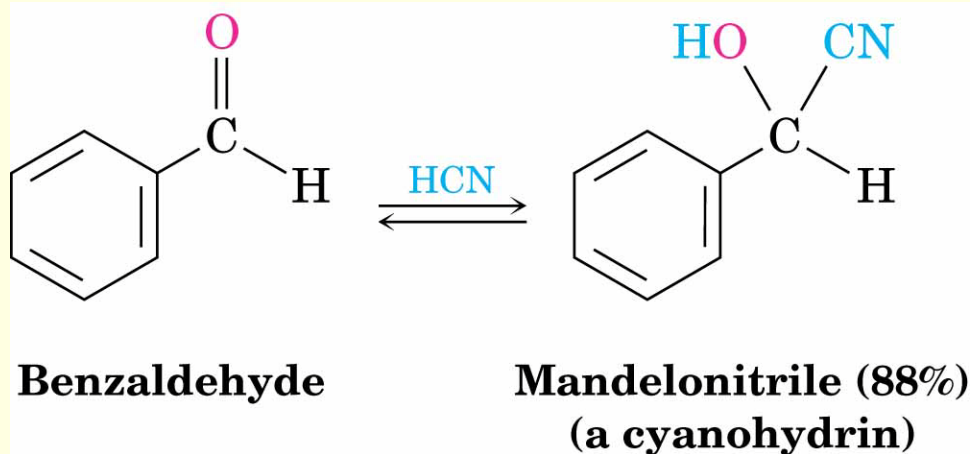
Addition of H-Y to C=O

- Reaction of C=O with H-Y, where Y is electronegative, gives an addition product (“adduct”)
- Formation is readily reversible



Nucleophilic Addition of HCN: Cyanohydrin Formation

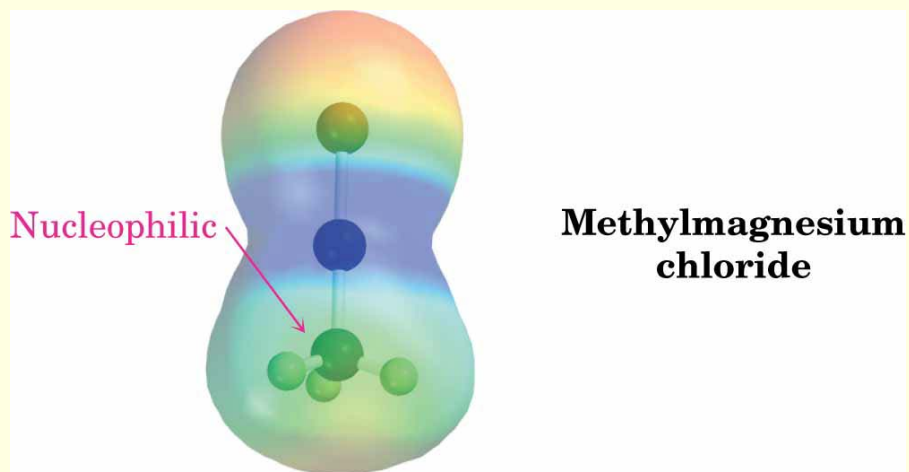
- Aldehydes and unhindered ketones react with HCN to yield cyanohydrins, $\text{RCH(OH)C}\equiv\text{N}$



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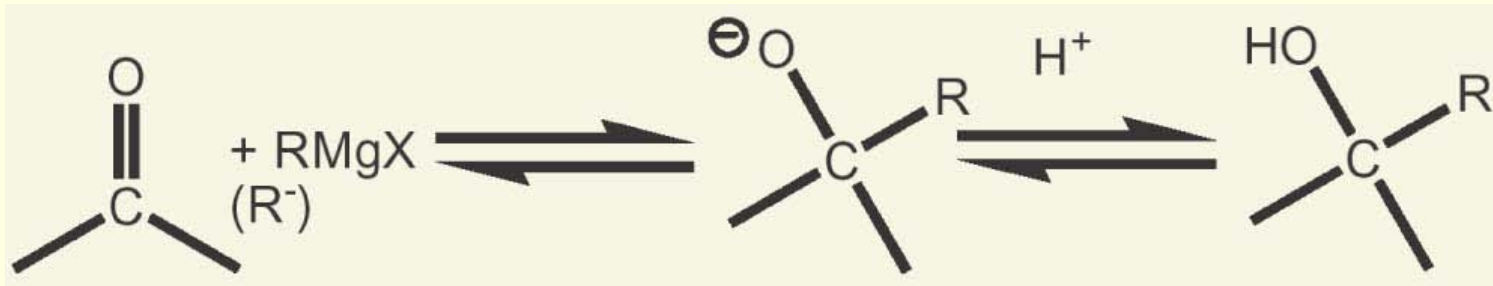
Nucleophilic Addition of Grignard Reagents and Hydride Reagents: Alcohol Formation

- 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 $R : ^- MgX ^+$.



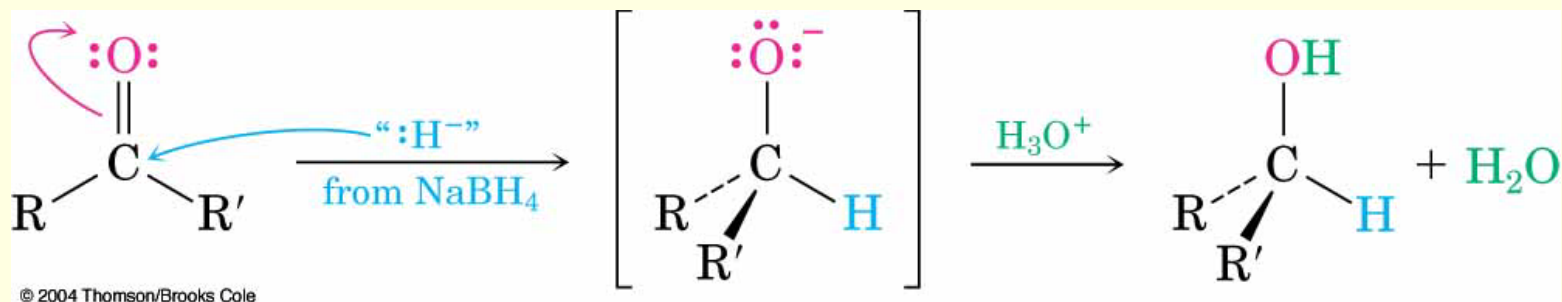
Mechanism of Addition of Grignard Reagents

- Complexation of C=O by Mg^{2+} , Nucleophilic addition of R^- , protonation by dilute acid yields the neutral alcohol
- Grignard additions are irreversible because a carbanion is not a leaving group



Hydride Addition

- Convert C=O to CH-OH
- LiAlH_4 and NaBH_4 react as donors of hydride ion
- Protonation after addition yields the alcohol

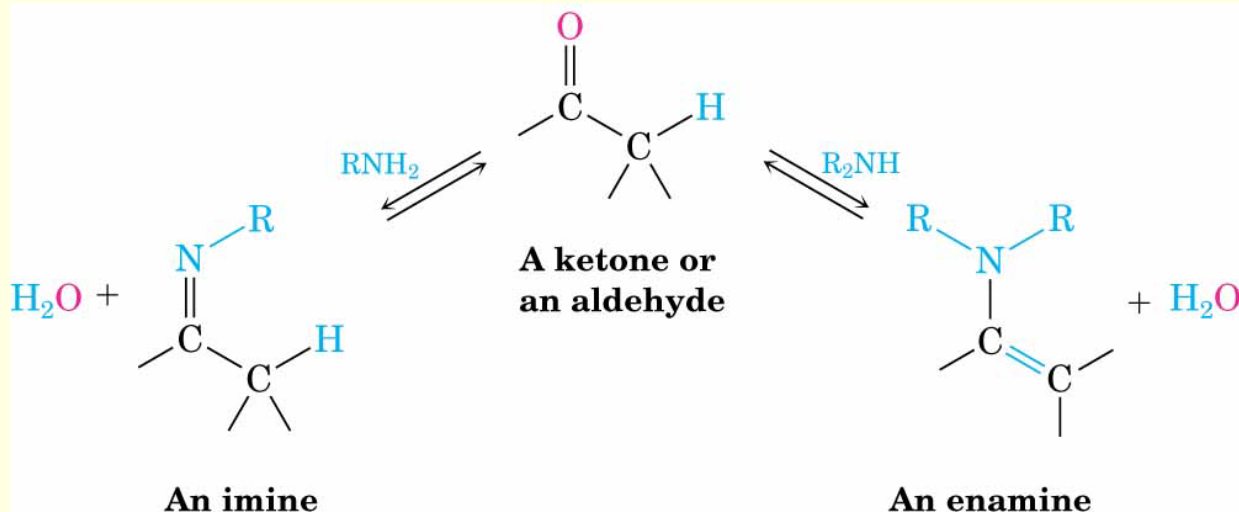


Nucleophilic Addition of Amines: Imine and Enamine Formation

RNH_2 adds to $\text{C}=\text{O}$ to form imines, $\text{R}_2\text{C}=\text{NR}$ (after loss of HOH)

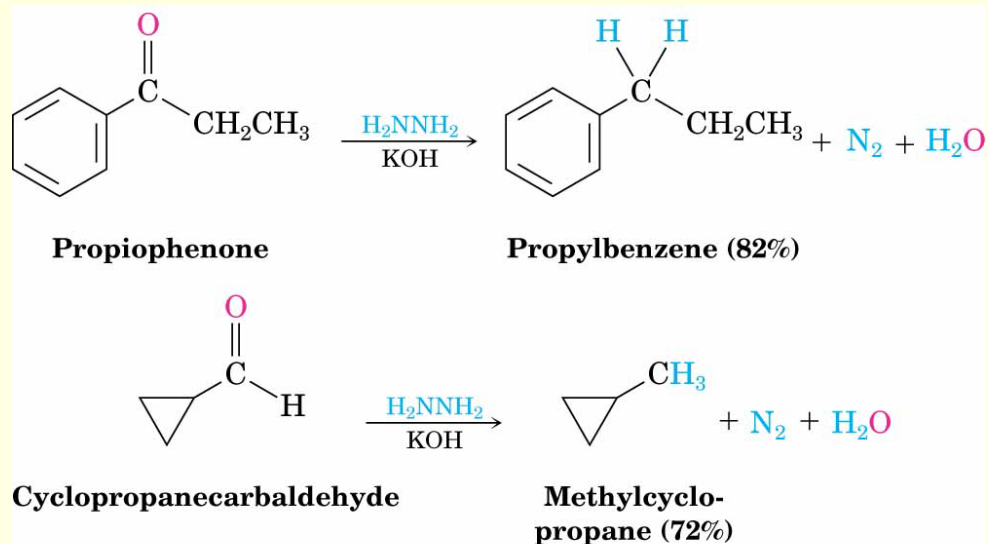
R_2NH yields enamines, $\text{R}_2\text{N}-\text{CR}=\text{CR}_2$ (after loss of HOH)

(*ene* + *amine* = unsaturated amine)



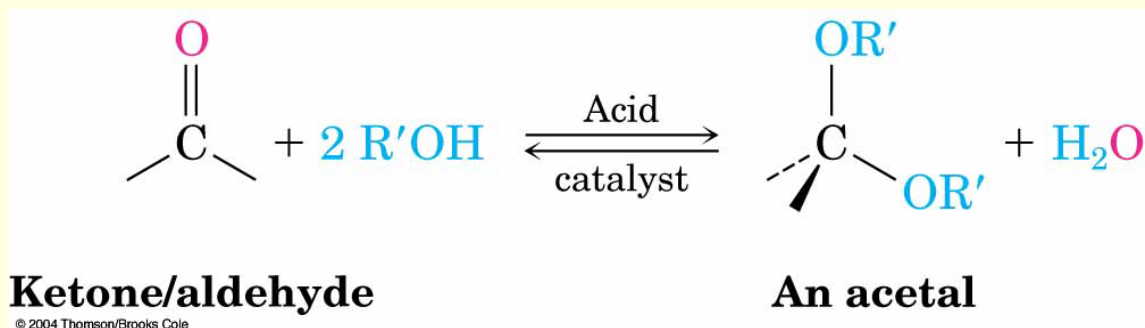
Nucleophilic Addition of Hydrazine: The Wolff–Kishner Reaction

- Treatment of an aldehyde or ketone with hydrazine, H_2NNH_2 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



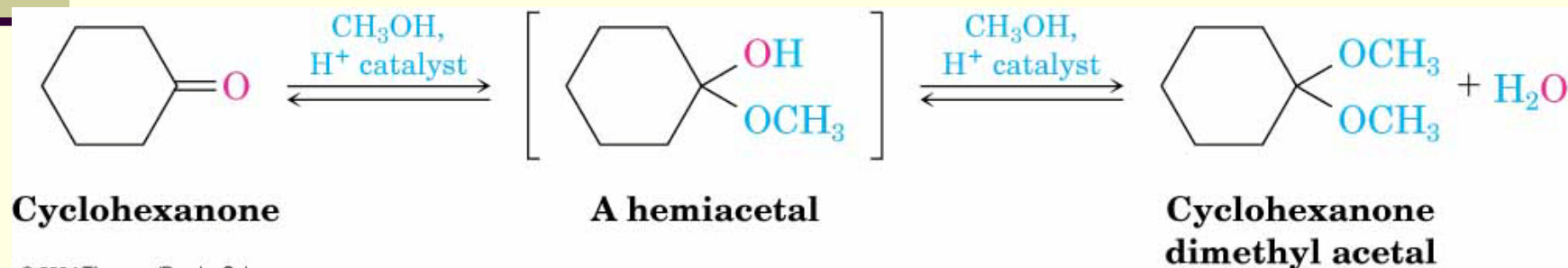
Nucleophilic Addition of Alcohols: Acetal Formation

- Two equivalents of ROH in the presence of an acid catalyst add to C=O to yield acetals, $R_2C(OR')_2$
- These can be called *ketals* if derived from a ketone



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



Summary

- Aldehydes are from oxidative cleavage of alkenes, oxidation of 1° alcohols, or partial reduction of esters
- Ketones are from oxidative cleavage of alkenes, oxidation of 2° alcohols, or by addition of diorganocopper reagents to acid chlorides.
- Aldehydes and ketones are reduced to yield 1° and 2° alcohols , respectively
- Grignard reagents also gives alcohols
- Addition of HCN yields cyanohydrins
- 1° amines add to form imines, and 2° amines yield enamines
- Reaction of an aldehyde or ketone with hydrazine and base yields an alkane
- Alcohols add to yield acetals