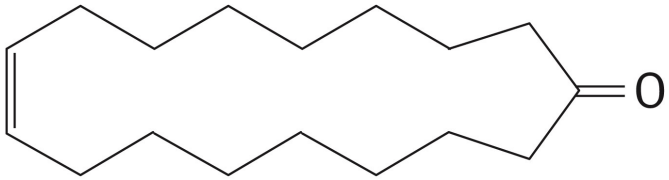
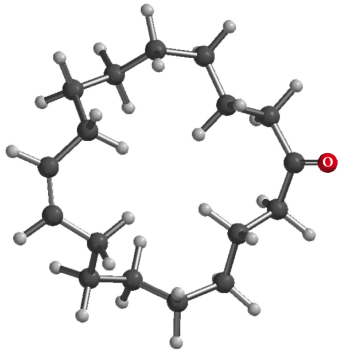
Carbonyl reactions

رح نحكي بهاد الشابتر عن أهمية carbonyl الـgroup وكيف ممكن استفيد منها في تصنيع heterocyclic system

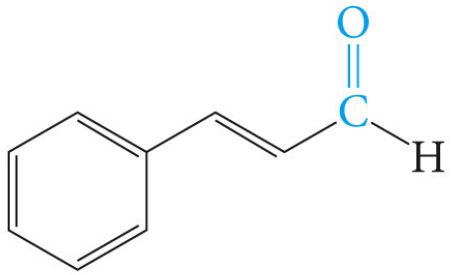


civetone

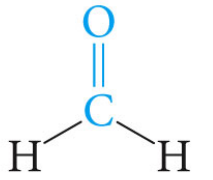


The Civet Cat is the original source of civetone, a sweet and pungent ketone used as a fixative in perfumery يستخدم كمثبت للعطور

Aldehydes and ketones are found in many fragrant odors of many fruits, fine perfumes, hormones etc. some examples are listed below.

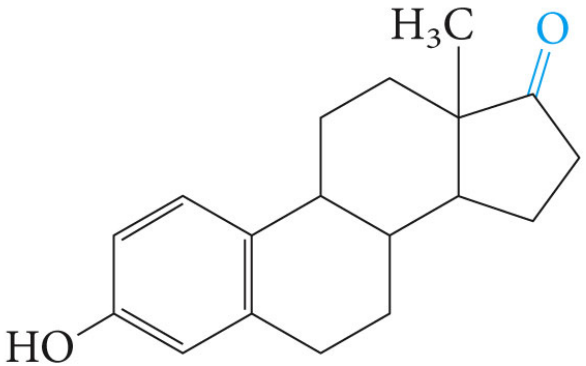


cinnamaldehyde



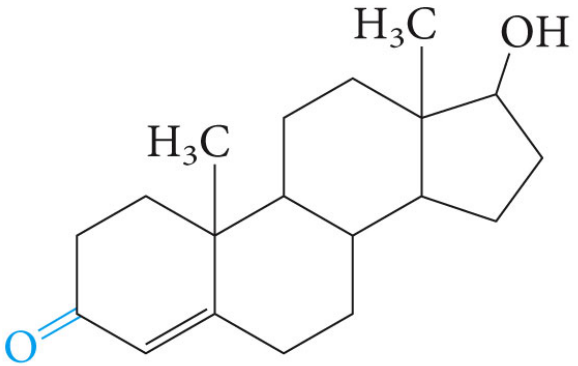
formaldehyde

cinnamaldehyde
موجود في formaldehyde
و الذي يستخدم في حفظ العينات وتخزينها للغايات الطبية ويستخدم أيضا في التحنيط



estrone

estrone + testosterone
عبارة عن sex hormone for male and female
ويوجد في substitution الخارجي
كيتون + الدهايد

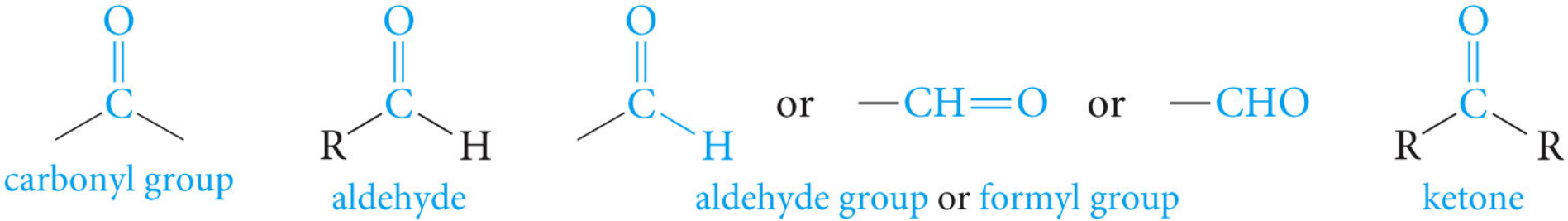


testosterone

Aldehydes and ketones are characterized by the presence of **the carbonyl group,** which is perhaps the most important functional group in organic chemistry.

Aldehydes have at least one hydrogen atom attached to the carbonyl carbon atom. The remaining group may be another hydrogen atom or any aliphatic or aromatic group. The –CH=O group characteristic of aldehydes is often called a ***formyl group***.

In ketones, the carbonyl carbon atom is connected to two other carbon atoms

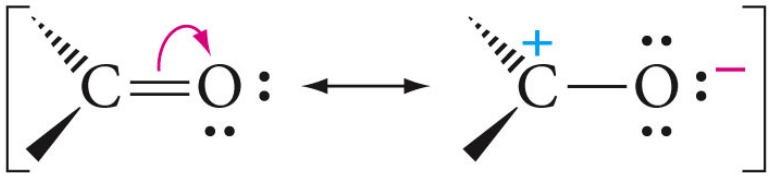


carbonyl group + H+R = aldehyde

carbonyl group + 2R = ketone

The carbonyl group is in many compounds including carboxylic acids and their derivatives.

The Carbonyl Group



resonance contributors to the carbonyl group

polarization of the carbonyl group

The carbonyl carbon is sp^2 –hybridized, the carbon-oxygen double bond consists of a sigma bond and a pi bond.

The three atoms attached to the carbonyl carbon lie on the same plane with bond angle of 120^0.

The C=O bond distance is 1.24 Å, shorter than a C-O single bond in ethers and alcohols (1.43 Å)

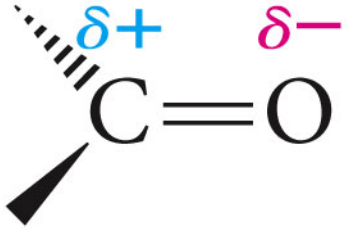
The C=O bond is polarized polariz: تعني فرق الاستقطاب وزيادة القدرة على كسب البروتونات وغيره

لما نرجع للجدول الدوري بنلاقي الكربون موجود بالمجموعة الرابعة والاكسجين موجود بالمجموعة السادسة واخدنا زمان انو لما اروح باتجاه اليمين بصير عندي more electronegativity بالتالي حب الذرة للالكترونات يزداد باتجاه المجموعة السادسة بالتالي الفرق في electronegativity بحتم على electrons الي موجودة في pi-orbital تكون متركزة اكتر عند ذرة الاكسجين يعني خلال دورانها الوقت الي رح تقضيه عند الاكسجين رح يكون اعلى من الوقت الي رح تقضيه عند الكربون وهاد الاشي بخلق عندي polarization بالتالي الكربون رح يكون partially positive والاكسجين رح يكون partially negative , لما احكي partially يعني باعتبار وزعت negative & positive بين الذرتين

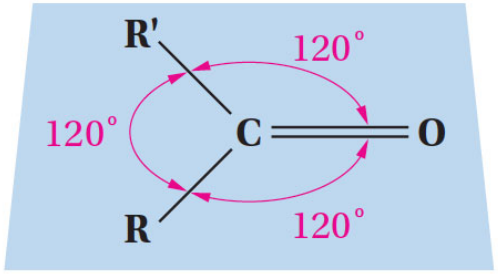
كمان عندي وجود ال double bond in any system بخلق resonation in any system

انو it is identical تمثل عندي نظام غني بالالكترونات بالتالي double bond يكون عندي long pairs of electrons

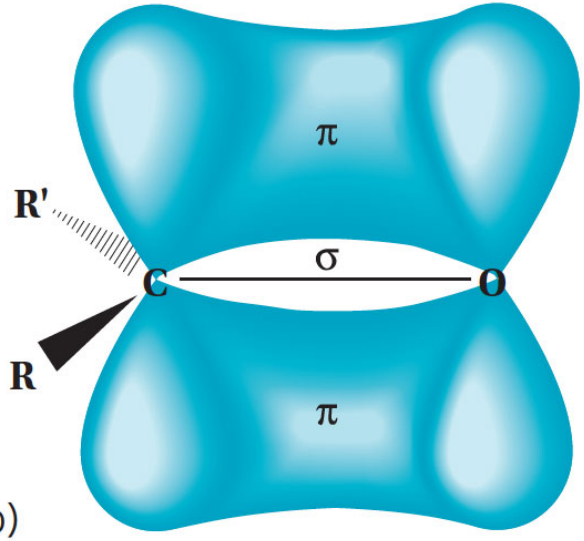
attack here by a nucleophile



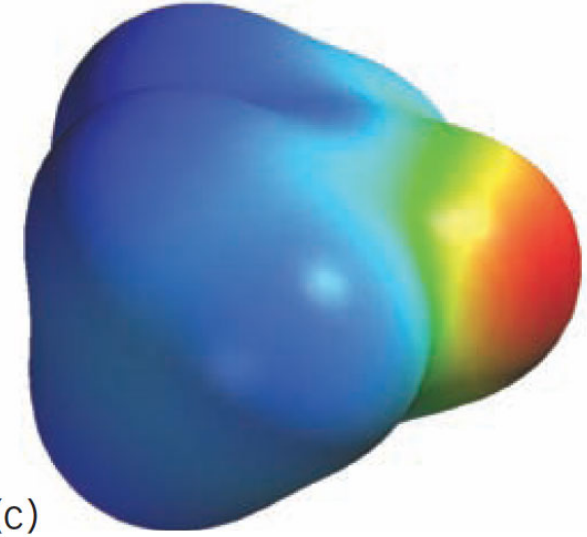
may react with a proton



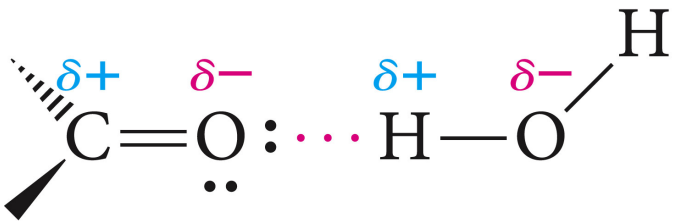
(a)



(b)



(c)



Aldehydes and ketones that have a C=O bond , but no O-H bond, cannot form hydrogen bonds with one another, as alcohols.

Aldehyde and ketones therefore have relatively higher boiling points than hydrocarbons, but less than alcohols.

Low molecular weight aldehydes and ketones are water soluble as they can for hydrogen bonds with the water molecules but not with themselves.

nucleophile they are atoms which rich in e- like :

1)long pair in electrons : O , N

2) fully negative charge شحنة سالبة واضحة

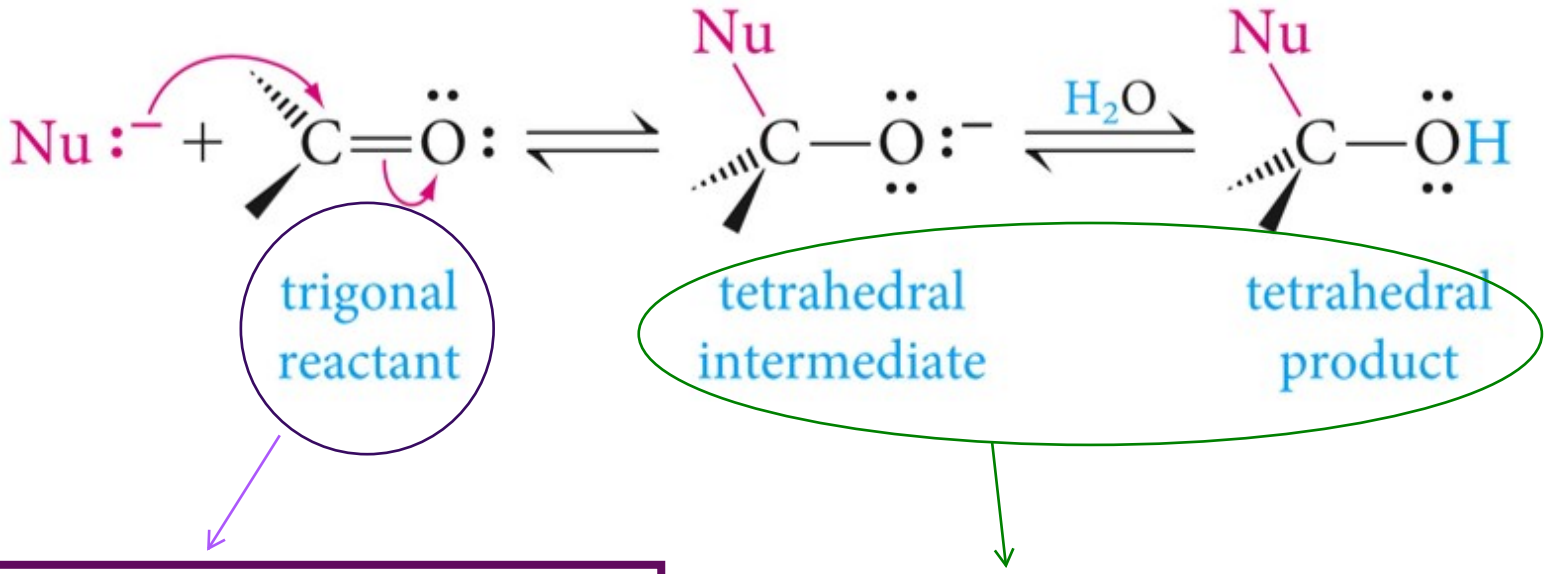
3) system have double bond

رح يهاجم عندي الـ electron deficient والي رح يكون عبارة عن carbonyl carbon

وهي من اشهر الطرق المستخدمة في تصنيع المركبات معظم الادوية ومعظم التفاعلات (biological and chemical reaction) نستغل

in order to synthesize organic وجود مجموعة الكربونيل compound

when I have a carbonyl in my system it will be attack by nucleophile : بالتالي



in this step the nucleophile forms a bond to the carbon by donating an electron pair . an electron pair shift out to the oxygen

in this step the alkoxide oxygen because it is strongly basic removes proton from H2O

جزيْ Nu الي شحنتو سالبة وكثافتو الالكترونية عالية رح يهاجم ذرة الكربون الي كثافتها الالكترونية منخفضة partial positive ونتيجة لهاد الهجوم الرابطة الثنائية الي موجودة بين الاكسجين والكربون رح تنكسر وبتصير شحنة الاكسجين سالبة و Nu برتبط ب الكربون ***الاكسجين بنفعش يكون سالب الشحنة فعشان هيك لازم نعادله وبنجيب مادة بقدر يسحب منها البروتون عشان يصير متعادل بالتالي هون الاكسجين رح تهاجم H2O و تاخد منها البروتون H

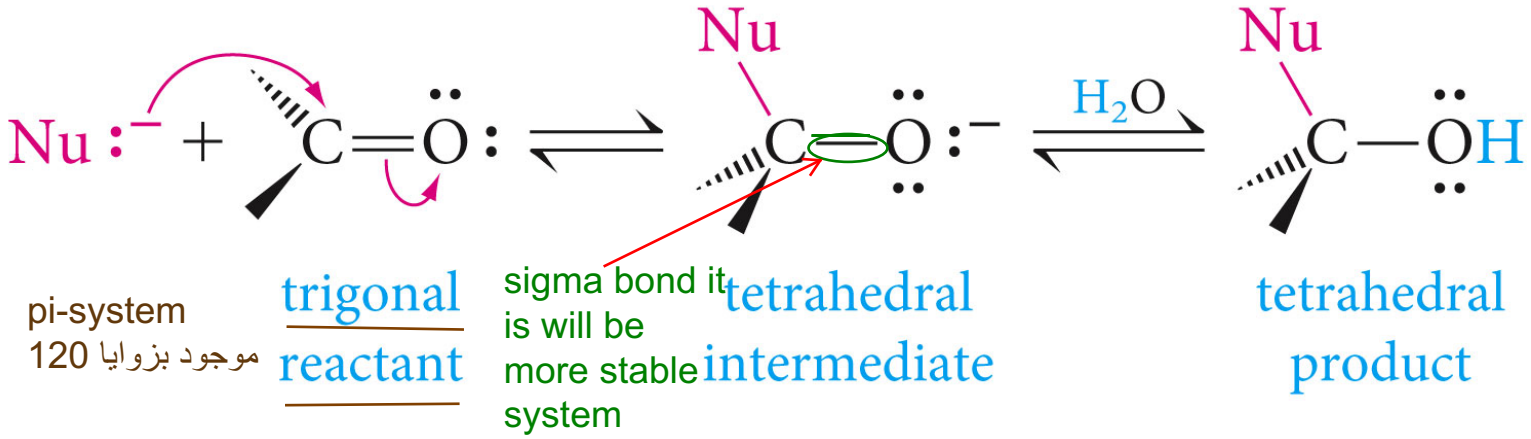
باختصار التفاعل عندي عبارة عن خطوتين

protonation for oxygen (1

attack by nucleophile of carbonyl group (2

Nucleophilic Addition to Carbonyl Groups

it is means that : system rich in e- will be added to carbonyl system in carbon because it is partially deficient in e- بتم سحبها من خلال electronegativity of O بالتالي it is susceptibile for this type of attack

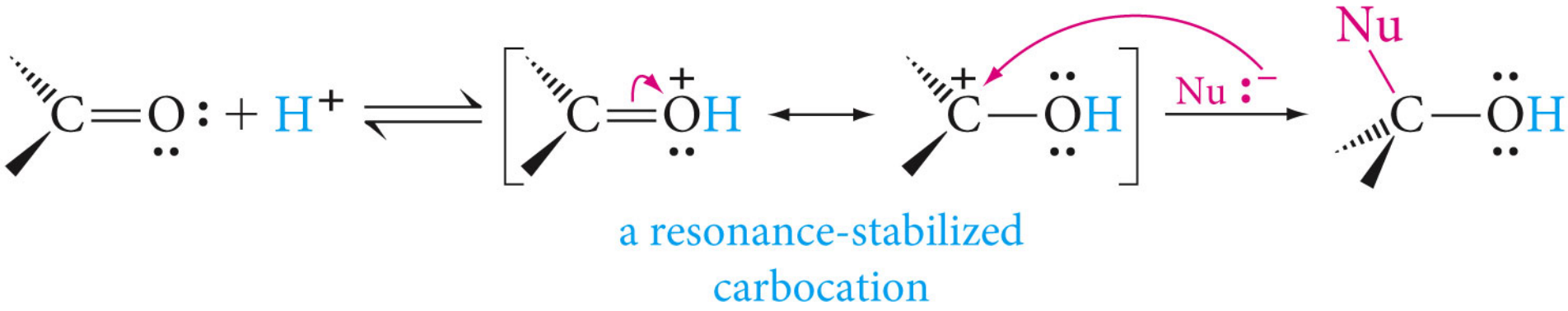


Nucleophiles attack the carbon atom of a carbon-oxygen double bond because that carbon has a partial positive charge. The pi-electrons of the C=O bond move to the oxygen atom

أي تفاعل بعملوا بالمختبر عشان يصير forward ويرتبط الـnucleophile بـ carbonyl system بدي التفاعل يتشجع forward ما بدي يتكسر مرة تانية

we add catalyst it could be basic condition acidic condition etc , all of these can make my rection go forward

Acids can catalyze the addition of weak nucleophiles to carbonyl compounds by protonating the carbonyl oxygen atom.
This makes the carbonyl carbon more electrophilic and reactive by converting it to a carbocation thereby enhancing is susceptibility to attack by nucleophiles.

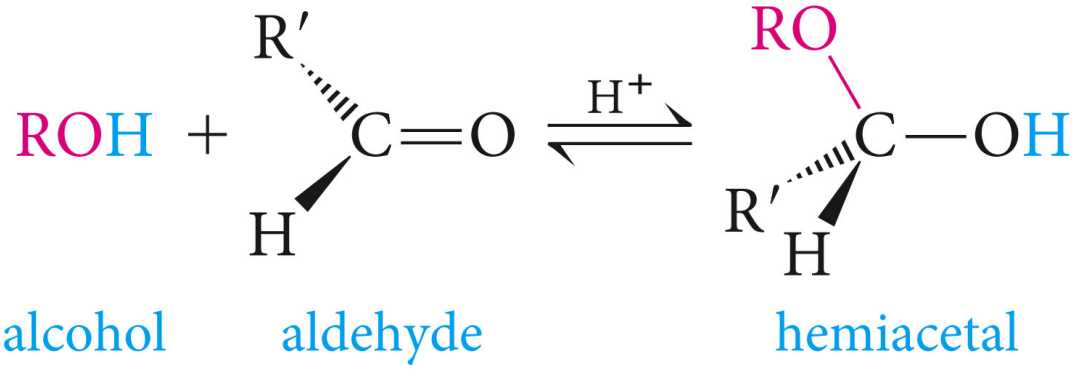


Classification of Nucleophiles;

- Those that add reversibly are also good leaving groups and are conjugate bases of relatively strong acids
- Those that add irreversibly are poor leaving groups, and are conjugate bases of weak acids.

Addition of Alcohols: Formation of Hemiacetals and Acetals

alcohols is strong nucleophile added to carbonyl group (good nucleophile)



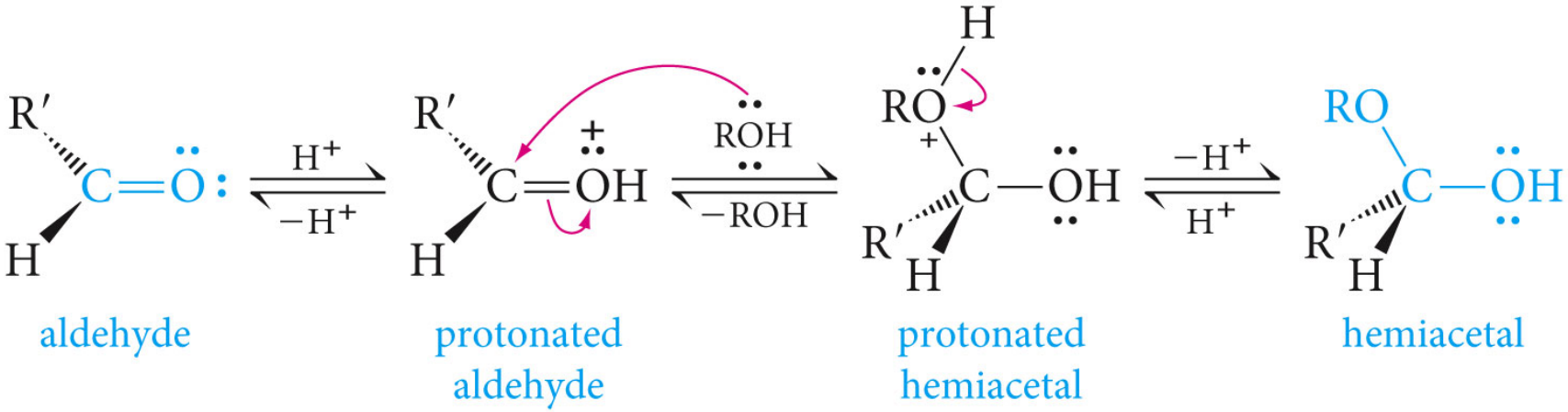
Alcohols are oxygen nucleophiles, they add to the C=O bond, the OR group becoming attached to the carbon and the proton becoming attached to the oxygen.

The product is a **hemiacetal** which contains both alcohol and ether groups on the same carbon.

The addition process is reversible

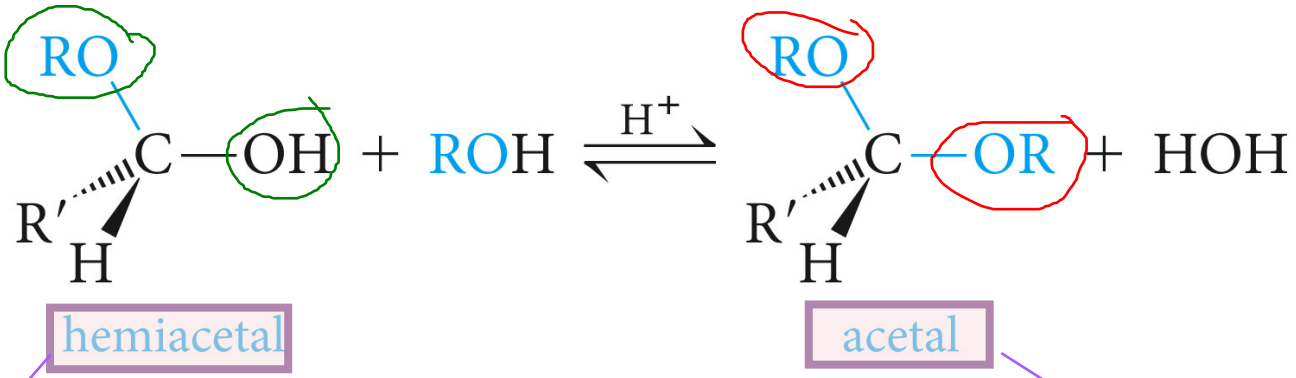
hemiacetal : has a hydroxyl (OH) and alkoxyl (OR) group on the same carbon

The mechanism of hemiacetal formation



acidic condition protonated of O :
when I get protonated to oxygen (carrying protons) >>
positive charge >>unstable>>the double bond is broken >>
يعني الاكسجين بتاخد كل الالكترونات و رح تصير شحنة الكربونة موجبة وعشان اخليها متعادلة بضيف الكحول للمركب

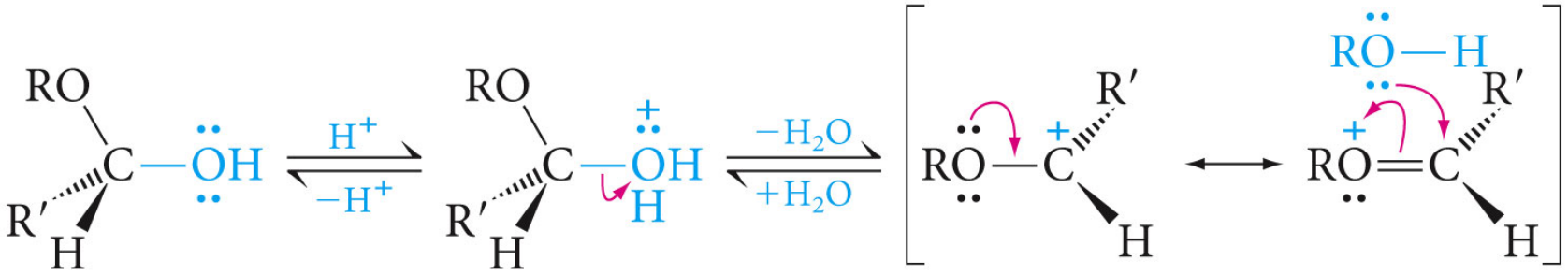
In the presence of excess alcohol, hemiacetals react to form **acetals.**
acetals have two ether functional groups at the same carbon atom.



عبارة عن كحول مع ايثر

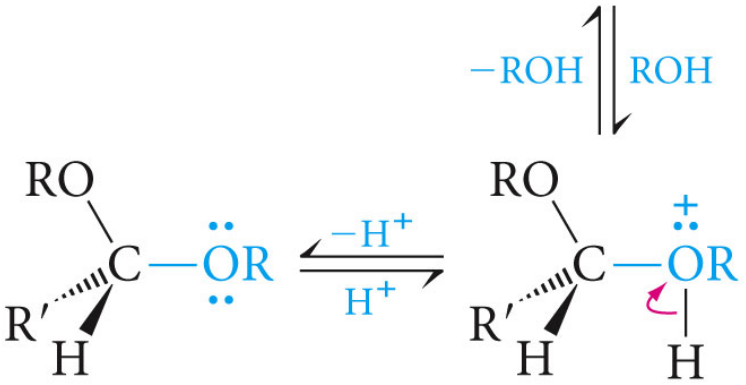
two ether عبارة عن
bond to
carbonyl carbon

Mechanism of acetal formation



هون مجموعة الهيدروكسيل رح يصرلها protonated وبتكون ماء شحنته موجبة غير مستقر بالتالي رح تنكسر عندي الرابطة الأحادية (single bond) بالتالي رح يتكون عندي intermediate مارح يصرلو isolation بالمحلول (صعب ينفصل)وبتكون عندي carbocation وذرة الكربون هاي دائما غير مستقرة وعشان اخفف من condition الي موجود عندي the oxygen give the system- بس النظام بضلو غير with it is long pair e مستقر فرح يتم مهاجمة ذرة الكربون غير المستقرة من الكحول الي موجودة بالنظام هيك بكون ضفت مجموعتين هيدروكسيل للنظام عندي

and make my hemiacetal to become an acitale



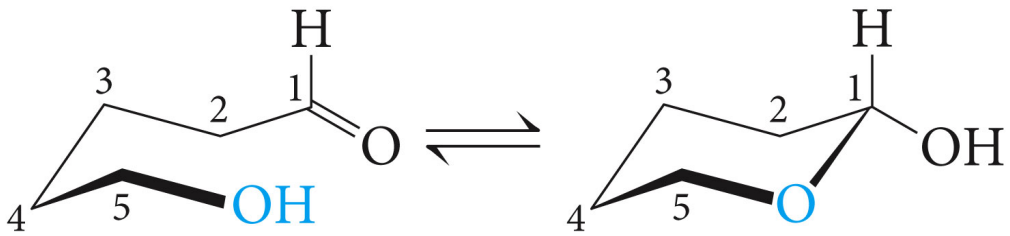
acetal

another alcohol to my compound لما اضيف

it can go farther عندي hemiacetalال

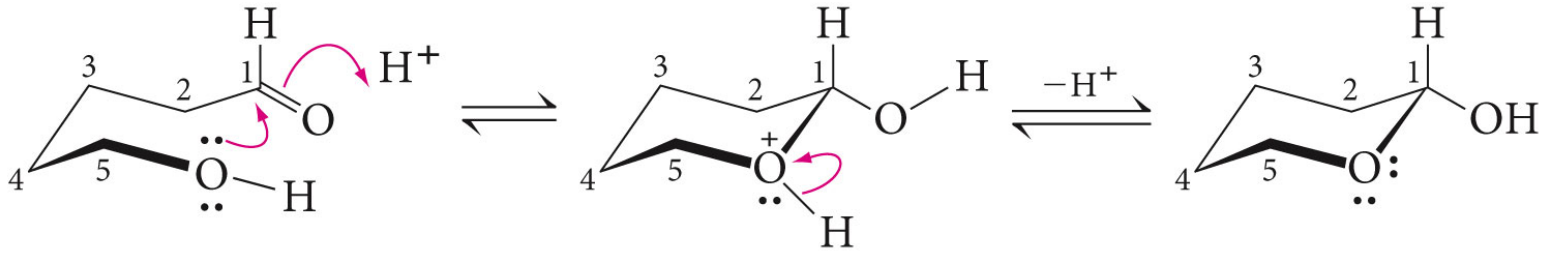
in acidic condition (same principal)

Aldehydes that have an appropriately located hydroxyl group in he same molecule may exists with cyclic hemiacetal, formed from intramolecular nucleophilic addition.

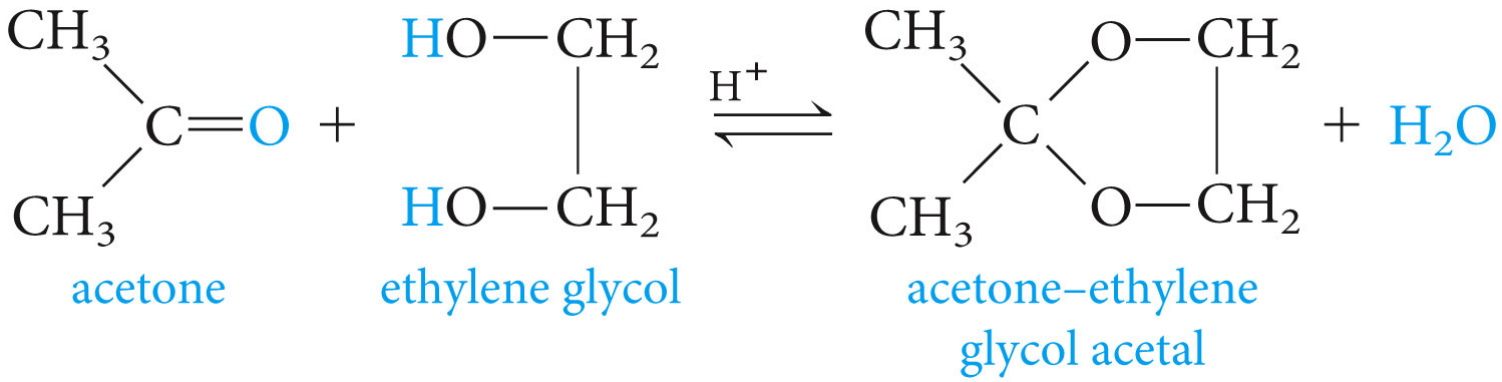


5-hydroxypentanal

hemiacetal form of 5-hydroxypentanal



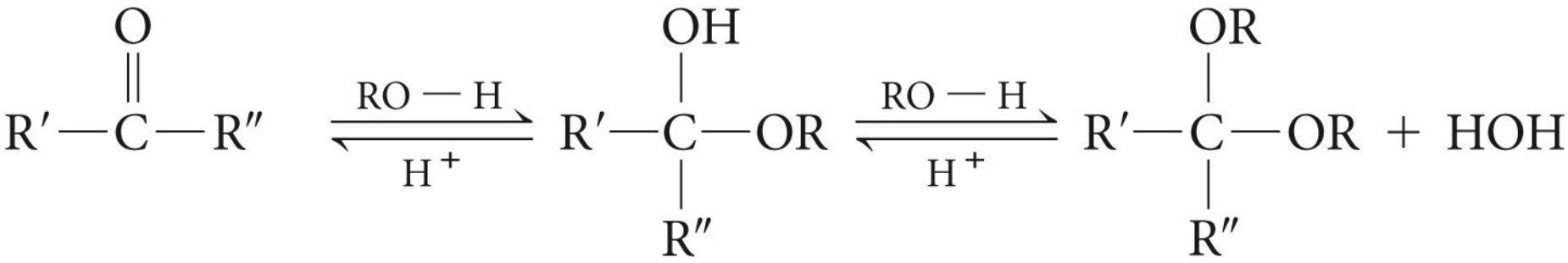
Ketones also form acetals. If glycol is used as in the example below, the product is a cyclic acetal.



-ketones they can undergo chemical reaction similar to aldehyde
-ketones can interact with alcohol and aldehyde as well to produce acetal
but the action of ketone with aldehyde is more reactive than alcohol because the aldehyde has more substitution and make the carbonyl group in ketone more deficiency of e-

the acetone it can be interact with ethylene glycol to produce acetone-ethylene (glycol acetal)

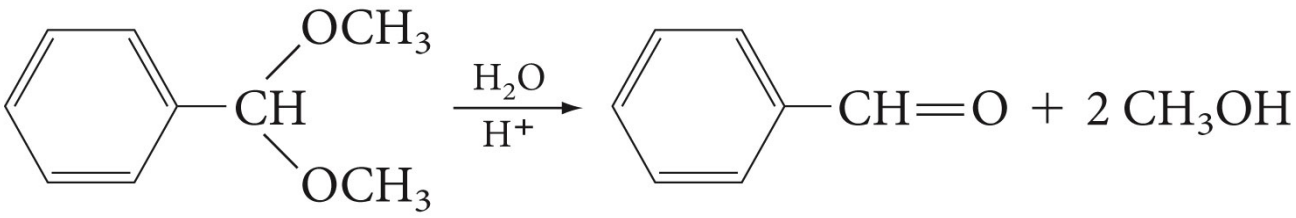
Reaction summary



Question

Write the equation for the reaction of benzaldehyde with excess methanol and an acid catalyst.

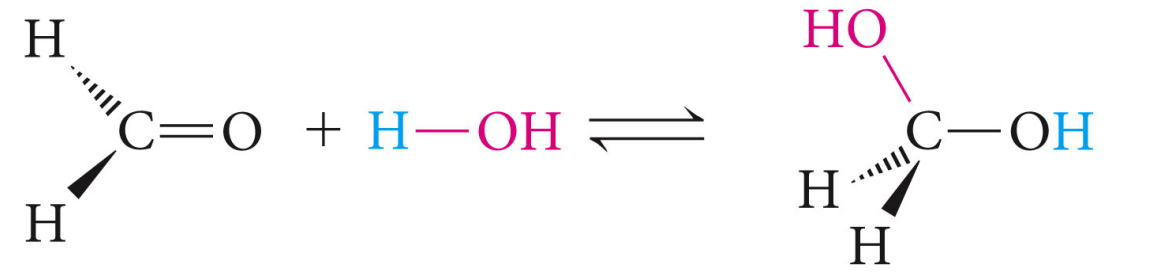
The reverse of acetal formation if acetal hydrolysis. This is achieved by excess water in the presence of an acid catalyst.



زي ما خلينا تفاعل ال acetal يصير forward in acidic condition بقدر اكسرو واخليه يرجع backward in
ضلو غير مستقر بشكل قوي acetal والسبب بهاد انو الـ acidic condition

Addition of Water: Hydration of Aldehydes and Ketones

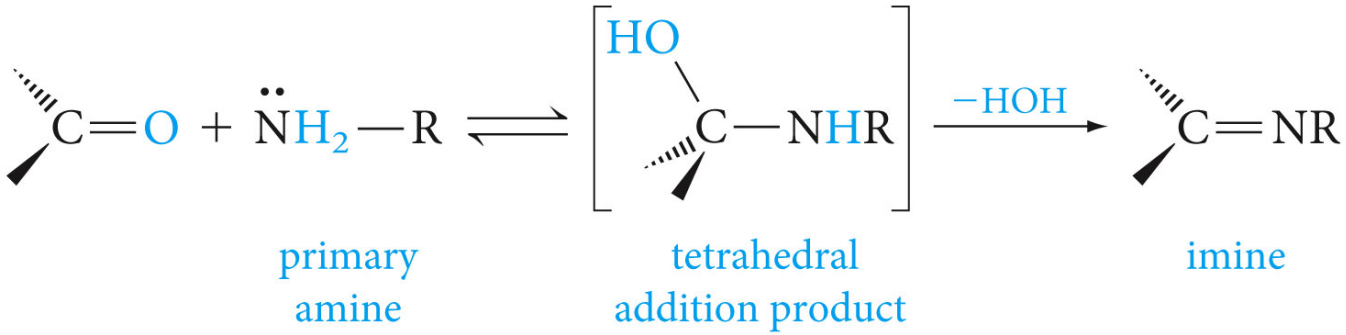
عملية إضافة الماء للتفاعل

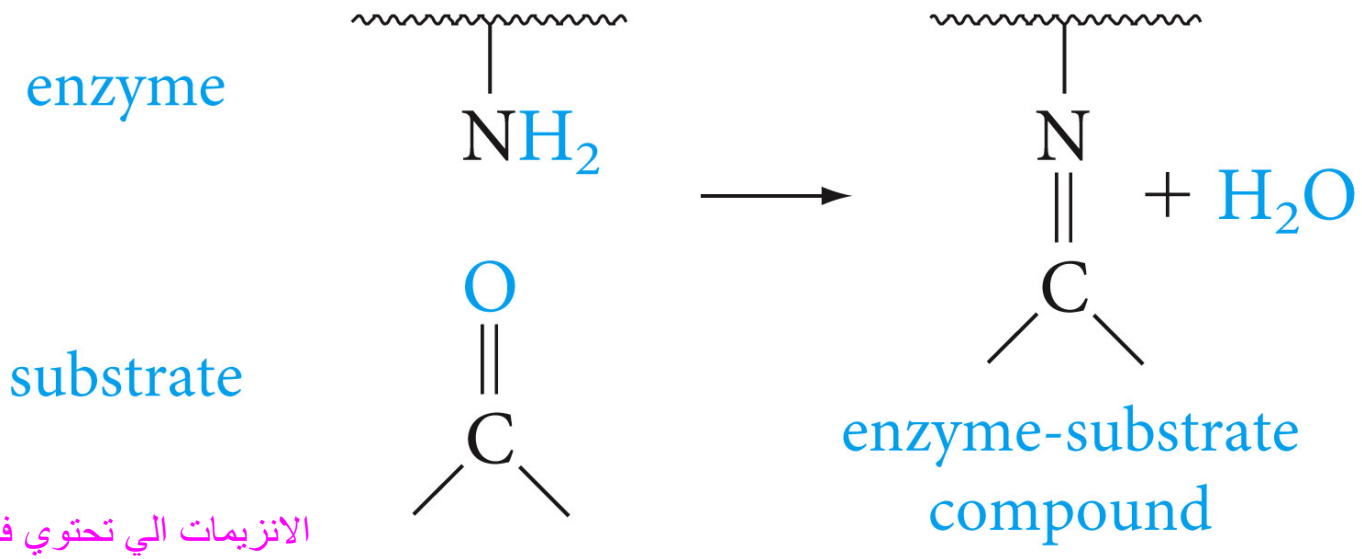


formaldehyde

formaldehyde hydrate

Addition of Nitrogen Nucleopiles





الانزيمات الي تحتوي في تركيبها على NH2 هي عبارة عن nucleophile

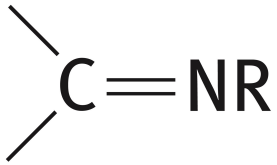
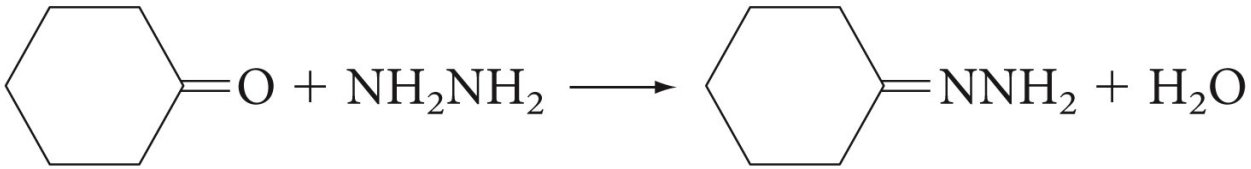


Table 9.1 Nitrogen Derivatives of Carbonyl Compounds

Formula of ammonia derivative	Name	Formula of carbonyl derivative	Name
RNH_2 or $ArNH_2$	primary amine	$>C{=}NR$ or $>C{=}NAr$	imine
NH_2OH	hydroxylamine	$>C{=}NOH$	oxime
NH_2NH_2	hydrazine	$>C{=}NNH_2$	hydrazone
$NH_2NHC_6H_5$	phenylhydrazine	$>C{=}NNHC_6H_5$	phenylhydrazone

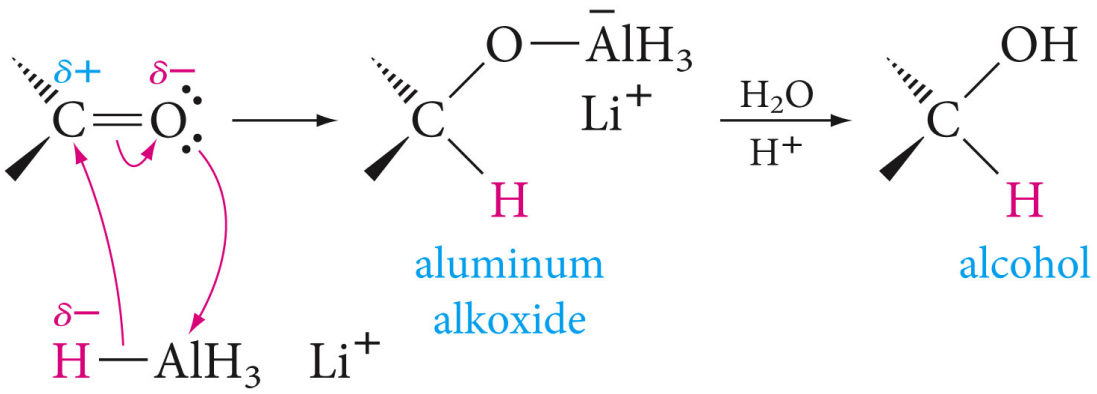
بنشوفو بمركبات antibacterial drug

موجود في mono amino oxidases enzyme inhibitor



Reduction of Carbonyl Compounds

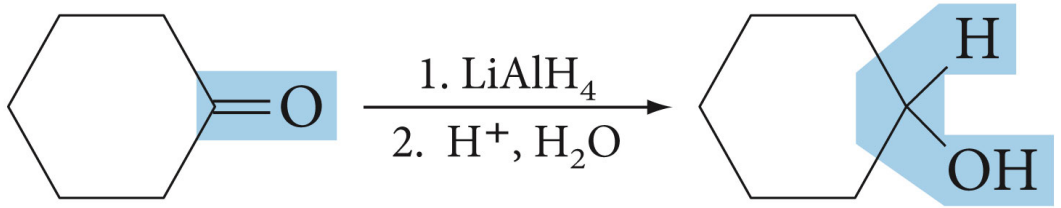
مجموعة الكاربونيل اذا صارلها reduction بتكون عندي الكحول
اما اذا صارلو oxidation بعطيني carboxylic acid



Aldehydes and ketones are easily reduced to primary and secondary alcohols respectively. Reduction can be accomplished in many ways, most commonly by metal hydrides.

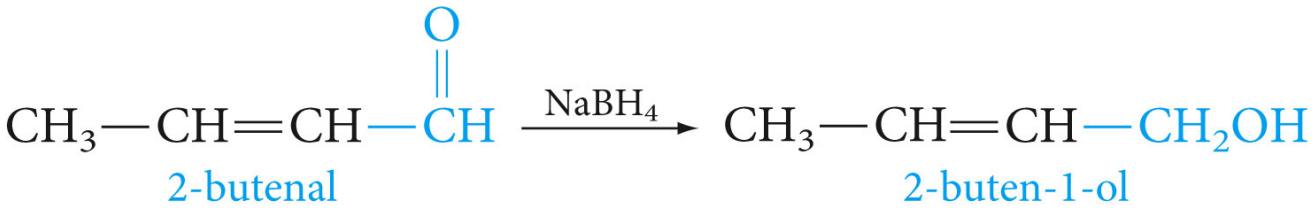
Lithium aluminum hydride ($LiAlH_4$) and sodium borohydride ($NaBH_4$) are among the commonly used.

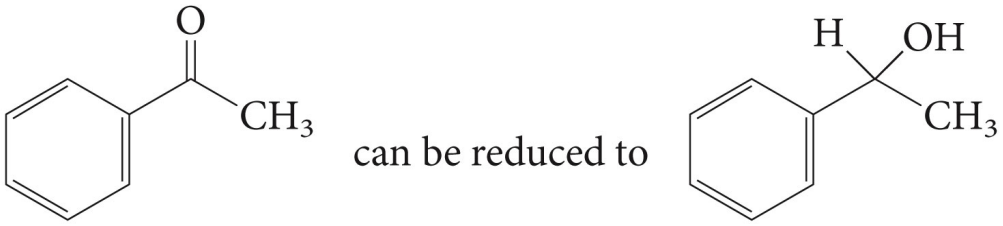
مجرد ما شفت هاي المركبات لازم اعرف انهم
عبارة عن reducing agent
they reduce the carbonyl group to alcohol



cyclohexanone cyclohexanol

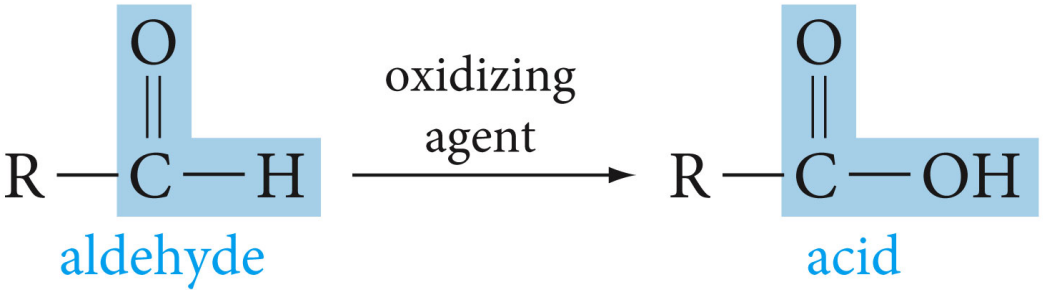
Because a carbon-carbon double bond is not readily attacked by nucleophiles, metal hydrides can be used to reduce a carbon-oxygen double bond to the corresponding alcohol without reducing the alkene.





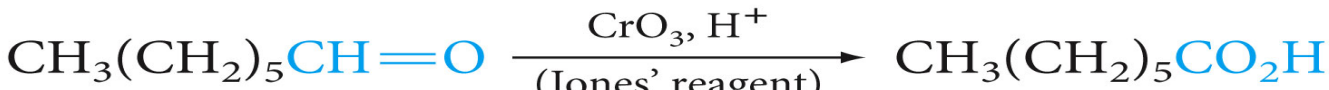
Oxidation of Carbonyl Compounds

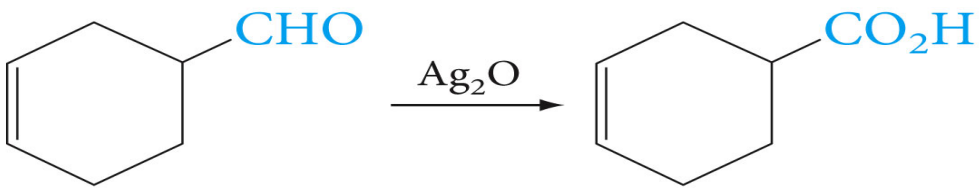
Aldehydes are more easily oxidized than ketones. Oxidation of an aldehyde gives a carboxylic acid with the same number of carbon atoms.



Oxidation may be achieved by many oxidizing agents, such as $KMnO_4$, CrO_3, Ag_2O, and peracids.

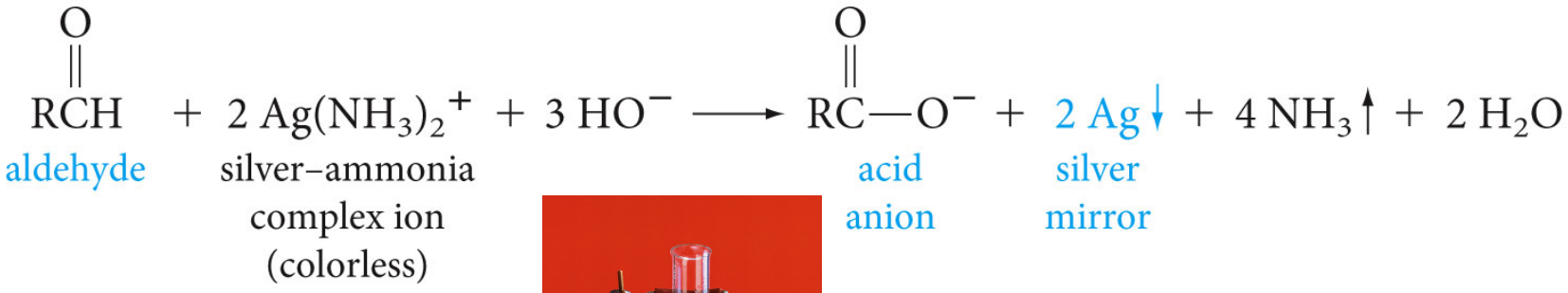
they are the most popular compound that can oxidize the carbonyl group to hydroxyl group



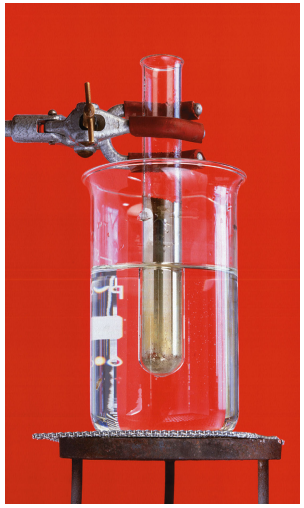


Silver ion as an oxidizing agent is expensive but has the virtue that it selectively oxidizes aldehydes to carboxylic acids in the presence of alkenes.

A laboratory test that distinguishes aldehydes from ketones takes advantage of their different ease of oxidation. In the Tollen's silver mirror test, the silver -ammonia complex ion is reduced by aldehydes (but not ketones) to metallic silver according to the equation bellow.

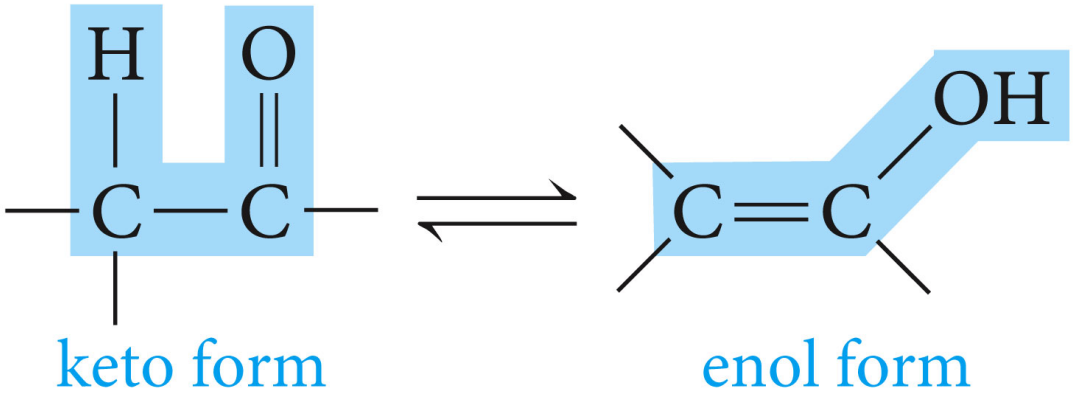


اذا كان الدهايد رح يتكون عالطرف عبارة عن مراي بينما الكيتون ما بصرلو تفاعل



If the glass vessel in which the test is performed is thoroughly clean, the silver deposits as a mirror on the glass surface

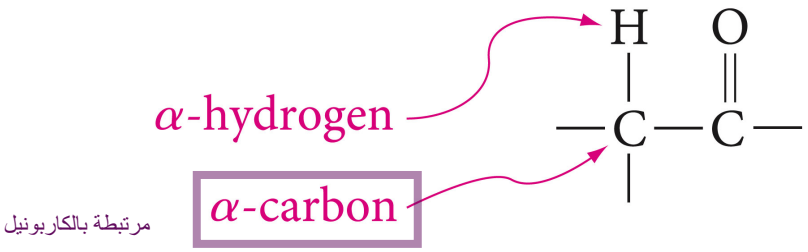
Keto-Enol Tautomerism

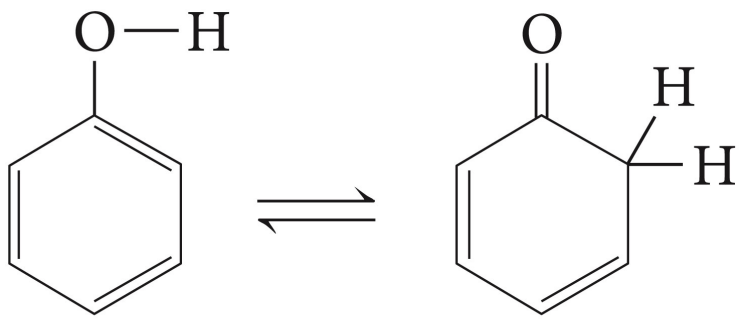


Tautomers are structural isomers that differ in the location of a proton and a double bond. The keto and enol forms of aldehyde or ketone are tautomers

carbonyl group عبارة عن

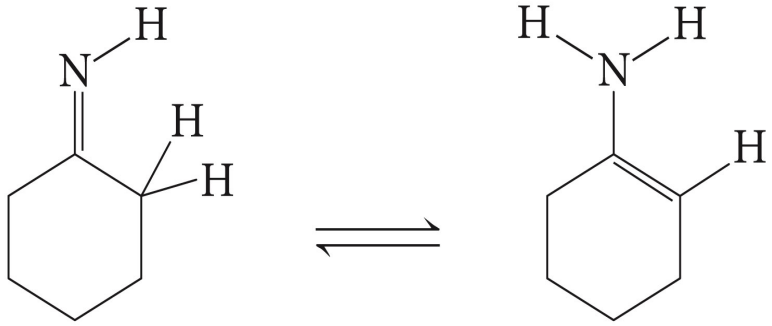
alkene + alcohol عبارة عن

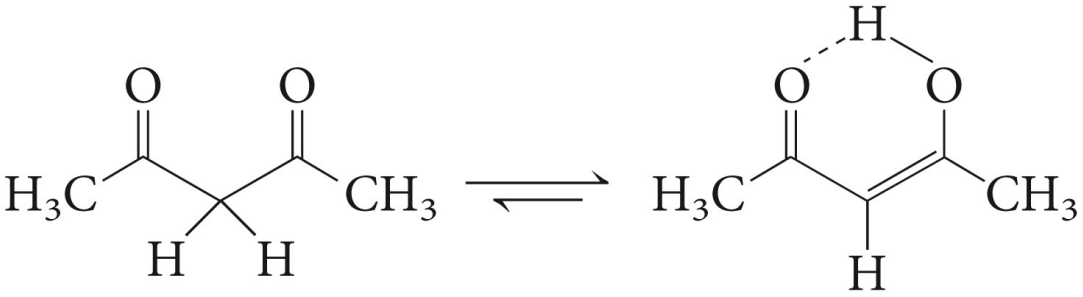




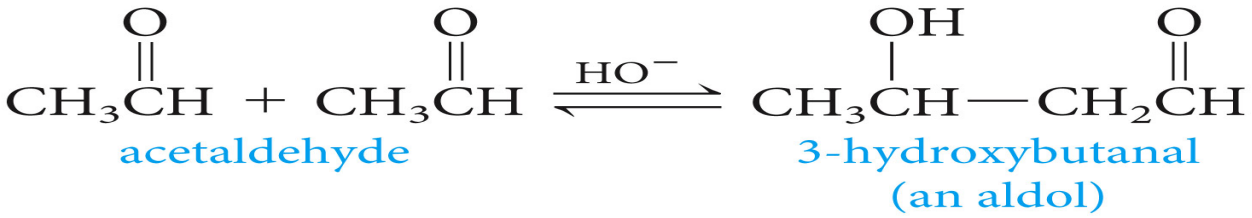
enol form of phenol

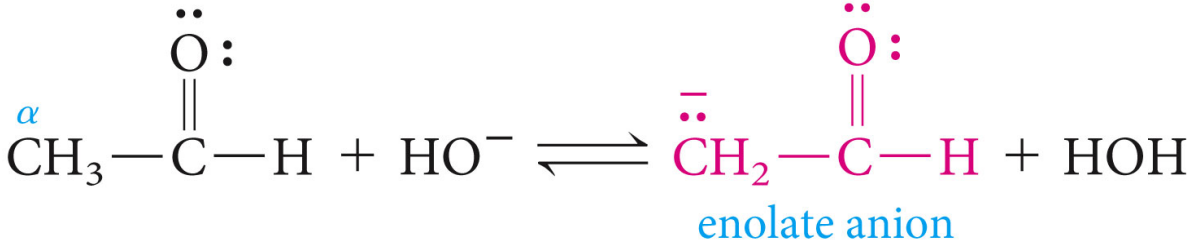
keto form of phenol

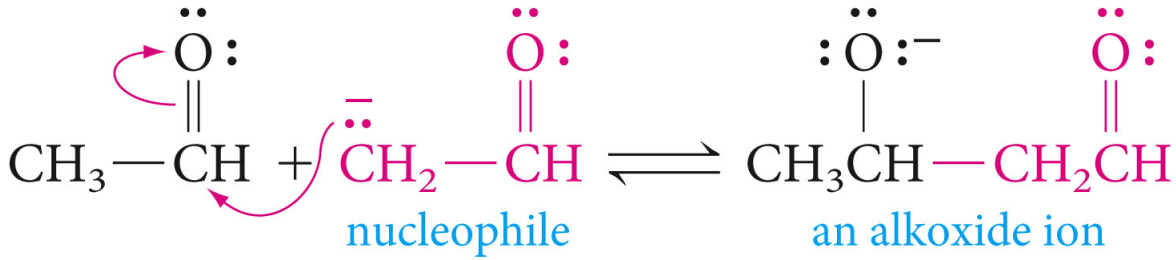


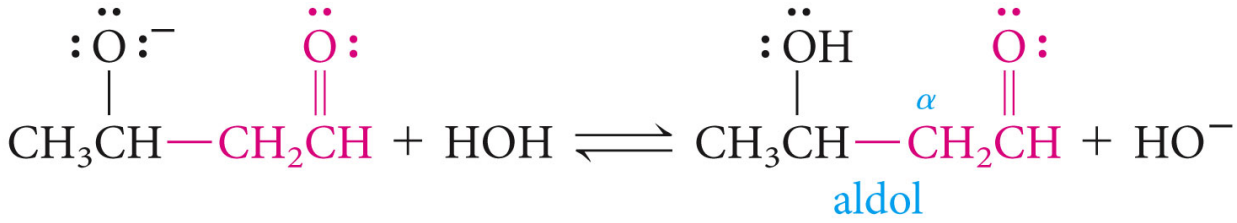


The Aldol Condensation

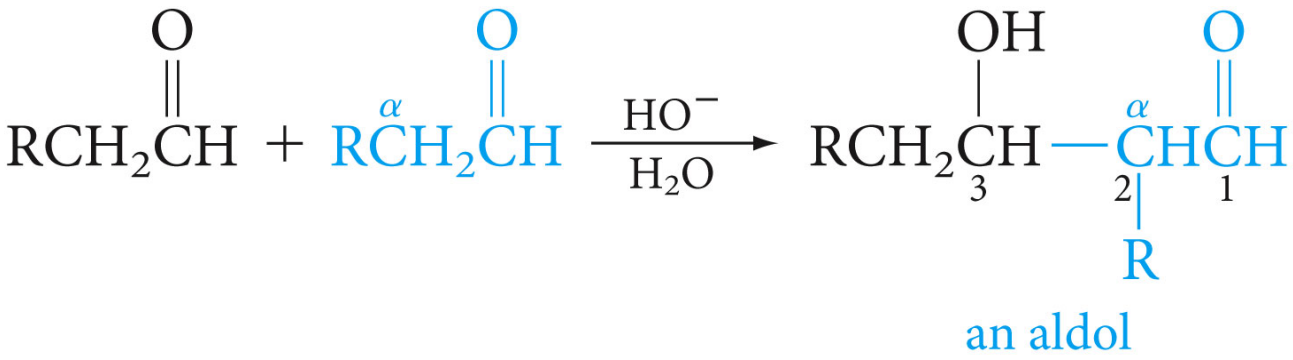








هاد السلايد والي بعدو عبارة عن أسماء تجارب رح ناخدها لقدام بالتفاعلات الكيميائية الخاصة فيهم في تصنيع الـ (hetero cyclic (system



The Mixed Aldol Condensation