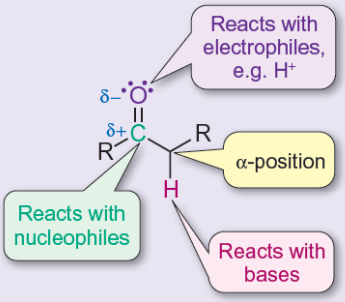
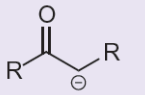
23

Aldehydes and ketones: nucleophilic addition and α-substitution reactions

23.1 The structure and reactions of aldehydes and ketones

- All aldehydes (RCHO) and ketones (RCOR) contain a C=O bond.
- The C=O bond is polar and the electrons are attracted to the oxygen atom ($^{\delta+}C{=}O^{\delta-}$)—the oxygen atom reacts with electrophiles and the carbon atom reacts with nucleophiles.

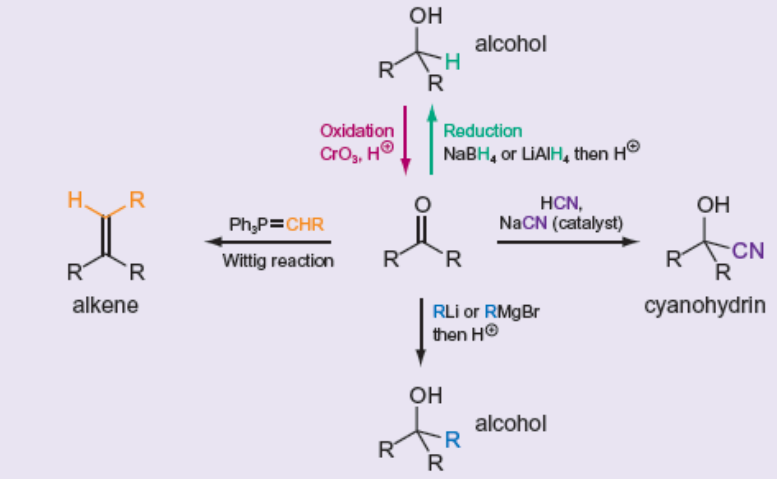




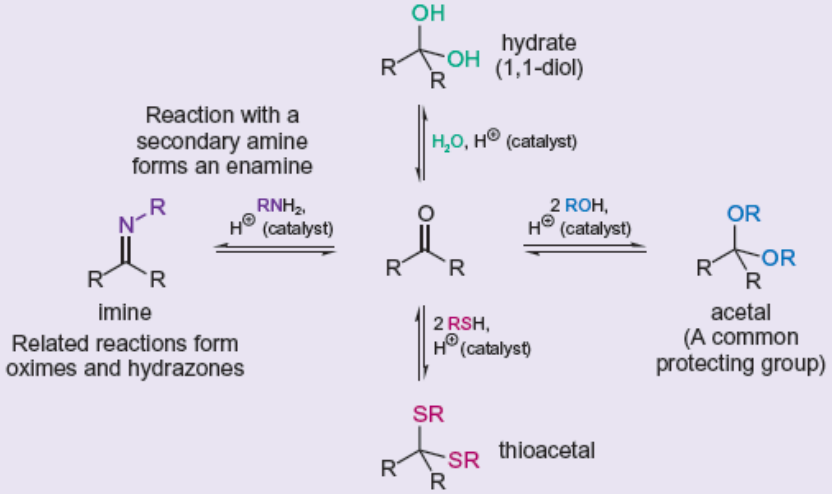
- The position of a carbon atom next to C=O is called the α-position.
- Deprotonation of an aldehyde or ketone at the α-position forms an enolate ion.
- Aldehydes and ketones undergo nucleophilic addition reactions, α-substitution reactions, and carbonyl–carbonyl condensation reactions.

23.2 Nucleophilic addition reactions of aldehydes and ketones

- The C=O bond of aldehydes and ketones reacts with nucleophiles (such as H^-, an organometallic reagent, or ^-CN) in nucleophilic addition reactions.
- Nucleophiles add more rapidly to aldehydes (RCHO) than ketones (R_2CO) because of steric and electronic effects.
- Reaction of a phosphonium ylide (ylid) with an aldehyde or ketone forms an alkene in the Wittig reaction.



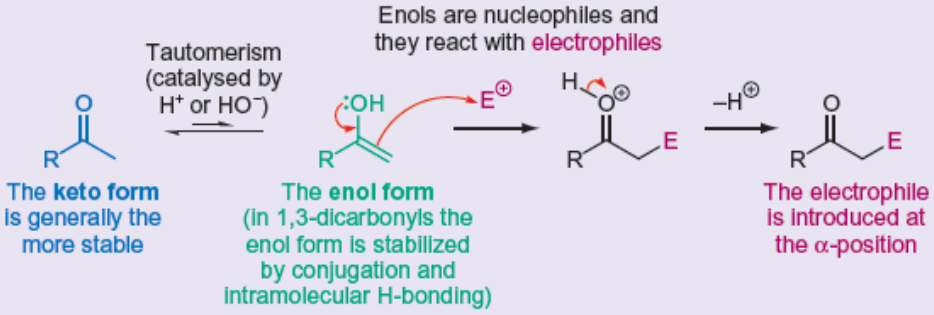
- The reactions of nucleophilic groups containing oxygen, sulfur, or nitrogen with the C=O bond are reversible and are catalysed by an acid.



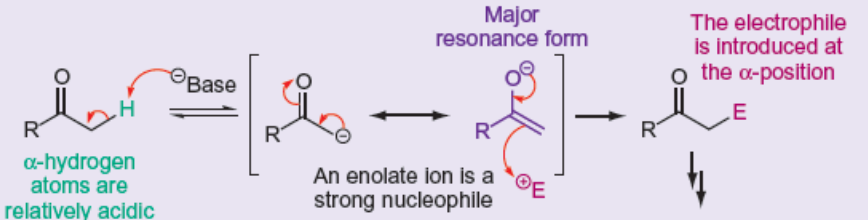
For practice questions on these topics, see questions 1–4 at the end of this chapter (pp.1095–1096).

23.3 α-Substitution reactions of aldehydes and ketones

- α-Substitution reactions involve substitution of a hydrogen atom by another group, at the carbon atom next to the C=O bond.
- α-Substitution reactions involve intermediate enols ($RC(OH)=CH_2$) or enolate ions ($RC(=O)CH_2^-$).
- The interconversion of the keto and enol forms of an aldehyde or ketone is called tautomerism.
- Formation of an enol and reaction with an electrophile (E^+):



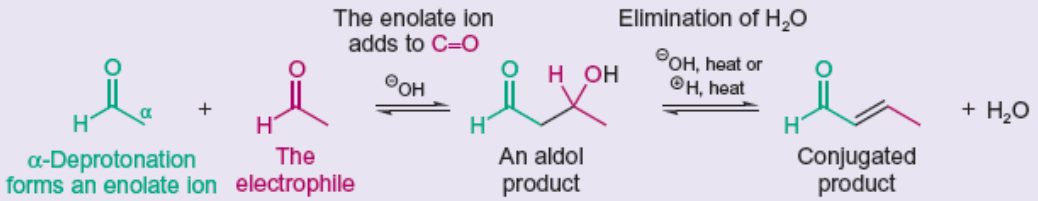
- Formation of an enolate ion and reaction with an electrophile (E^+):



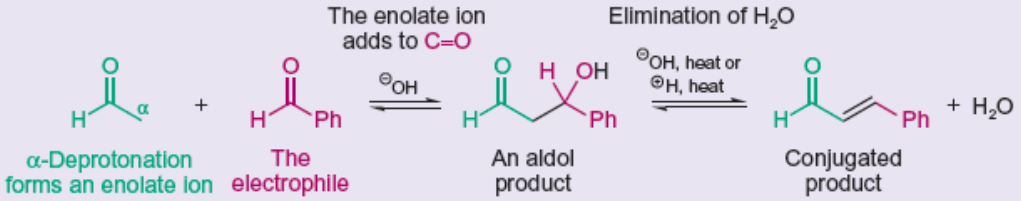
For a practice question on these topics, see question 5 at the end of this chapter (p.1097).

23.4 Carbonyl–carbonyl condensation reactions

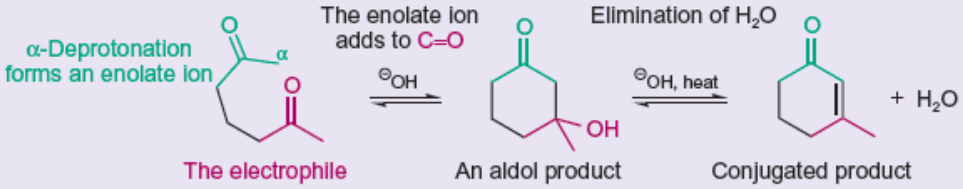
- In carbonyl–carbonyl condensation reactions, two carbonyl molecules react to form a single organic product together with a molecule of water.
- Reactions of two molecules of the *same* aldehyde or ketone are called aldol condensations.



- Reactions of two molecules of different aldehydes or ketones are called crossed (mixed) aldol condensations—a mixture of products is formed, except under certain conditions.



- When one molecule containing two C=O groups reacts with itself, this is called an intramolecular aldol condensation. This is a good method for making 5- and 6-membered rings.



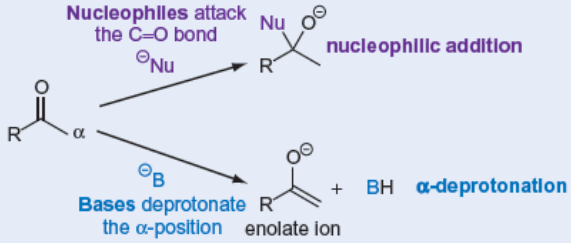
For practice questions on this topic, see questions 2, 5, and 6 at the end of this chapter (pp.1095–1097).

Concept review

By the end of this chapter, you should be able to do the following.

- For an aldehyde or ketone, describe how the C=O bond reacts with H^+.
- For an aldehyde or ketone, describe how the C=O bond reacts with a nucleophile (in a nucleophilic addition) and how enolate ions are formed by deprotonation of α-hydrogen atoms.

Nucleophilic addition versus α-deprotonation



- Draw general mechanisms for a nucleophilic addition reaction, an α-substitution reaction, and a carbonyl–carbonyl condensation reaction.
- Understand why aldehydes are more reactive to nucleophiles than ketones.
- Draw mechanisms for nucleophilic addition reactions of aldehydes and ketones using the following reagents:

$NaBH_4$ or $LiAlH_4$ then H^+	HCN, NaCN (catalyst)
RLi or RMgBr then H^+	Ph_3P=CHR
H_2O, H^+ (catalyst)	ROH, H^+ (catalyst)
RSH, H^+ (catalyst)	RNH_2, H^+ (catalyst)

- Understand how aldehydes and ketones are prepared by oxidation of alcohols.
- Recognize that addition of oxygen, sulfur, or nitrogen nucleophiles to the C=O bond is reversible and is catalysed by an acid.
- Discuss keto–enol tautomerism and understand the factors that influence the stability of keto and enol forms.
- Recognize that α-substitution reactions involve intermediate enols or enolate ions.
- Draw mechanisms for α-substitution reactions of aldehydes and ketones using the following reagents: H^+, Br_2; base, RX (where X is a good leaving group); HO^-, I_2 (both in excess).
- Draw mechanisms for aldol condensations, crossed (mixed) aldol condensations, and intramolecular aldol condensations.
- Predict the structure of a product derived from a nucleophilic addition, an α-substitution, or a carbonyl–carbonyl condensation reaction of an aldehyde or ketone.
- Propose reagents for converting an aldehyde or ketone into a product derived from a nucleophilic addition reaction, an α-substitution reaction, or a carbonyl–carbonyl condensation reaction.