Chem Factsheet

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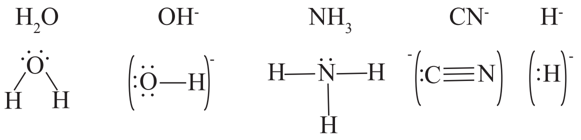
Nucleophilic Addition

The term *nucleophilic addition* refers to a chemical reaction involving a *nucleophilic species* causing an *addition reaction* of an organic molecule. More specifically it refers to the *mechanism* for such reactions.

> A *nucleophile* is a particle which is able to donate a pair of electrons (a lone pair represented by :) to an electron deficient atom (usually a $C^{\delta+}$ in a polar molecule or a C^+ atom in a carbocation) to form a new covalent bond.

Common examples of nucleophiles are water (H_2O), hydroxide ions (OH^-), ammonia (NH_3), cyanide ions (CN^-) and hydride ions (H^-).



> An *addition reaction* is one in which two or more molecules react together to form a *single* product molecule. A + B → C

Addition reactions are associated with *unsaturated* molecules – molecules which contain double bonds, triple bonds or delocalised electrons. These have "spare bonding capacity" on to which suitable reactants can "add". They include alkenes, arenes (benzene related molecules) and carbonyl compounds (aldehydes and ketones).

Alkenes and arenes are electron-rich and therefore prone to reaction with electrophiles rather than nucleophiles. It is aldehydes and ketones that are unsaturated (C=O bond) *and* have an electron deficient C ($^{\delta+}C=O^{\delta-}$) making them prone to the subject of this Factsheet, nucleophilic addition reactions.

The nucleophilic addition reactions of aldehydes and ketones

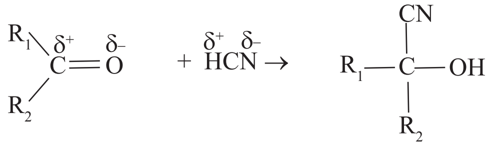
1. Addition of Hydrogen Cyanide (HCN)

Note: this applies to the Edexcel, AQA and WJEC A-level specifications. The reaction is not usually done directly with hydrogen cyanide because it is an extremely poisonous gas. Typically, an aldehyde or ketone is mixed with an aqueous solution of potassium cyanide (KCN) acidified with a little sulphuric acid. This solution will contain hydrogen cyanide from the reaction between the potassium cyanide and the sulphuric acid.

$$2KCN + H_2SO_4 \rightarrow K_2SO_4 + 2HCN$$

However, the solution still contains some free cyanide ions (CN^-) which are vital for the mechanism of the reaction – see later.

Considering the polarities of a carbonyl group ($^{\delta+}C=O^{\delta-}$) and a hydrogen cyanide molecule ($^{\delta+}H\text{-}C\equiv N^{\delta-}$), during the addition across the double bond, the δ+ H of HCN will bond to the δ- O of the C=O group to form a hydroxyl (OH) group. Similarly, δ- CN of HCN will bond to the δ+ C of the C=O group to form a nitrile (C-CN) group. In general, this can be represented as follows.

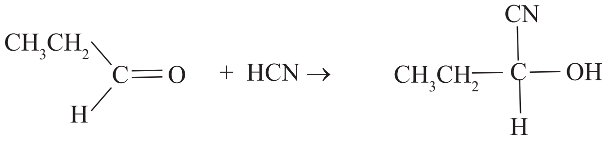


An aldehyde or keytone A 2-hydroxynitrile

In general, the product is referred to as a *2-hydroxynitrile* – the OH group is bonded to C2 where the C atom of the CN group is C1.

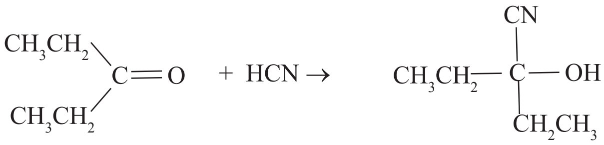
Note that this reaction involves addition of a C atom. Hence, "meth" → "eth", "eth" → "prop" and "prop" → "but" etc.

Example 1 When propanal ($R_1 = CH_3CH_2$; $R_2 = H$) reacts with hydrogen cyanide, 2-hydroxybutanenitrile is formed.



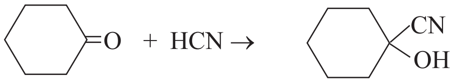
propanal 2-hydroxybutanenitrile

Example 2 When pentan-3-one ($R_1 = CH_3CH_2$; $R_2 = CH_3CH_2$) reacts with hydrogen cyanide, 2-ethyl-2-hydroxybutanenitrile is formed.



Pentan-3-one 2-Ethyl-2-hyroxybutanenitrile

Example 3 When cyclohexanone(R_1+R_2= cyclic $-CH_2CH_2CH_2CH_2CH_2-$) reacts with hydrogen cyanide, 1-cyano-cyclohexanol is formed.

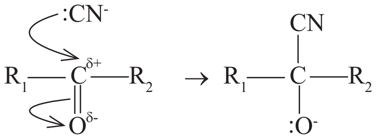


Cyclohexanone 1-cyanocyclohexanol

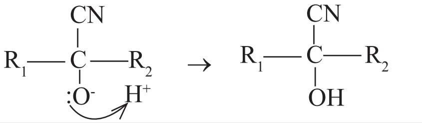
The mechanism

> Assign groups to R_1 and R_2 dependent on the example. e.g. for butan-2-one, $R_1 = CH_3CH_2$ and $R_2 = CH_3$.

Stage 1: The nucleophile ($:CN^-$) attacks $^{\delta+}C$ of C=O



Stage 2: The protonation of O^- by H^+ from H_2SO_4



2. Addition of Hydrogen using Sodium Tetrahydridoborate ($NaBH_4$)

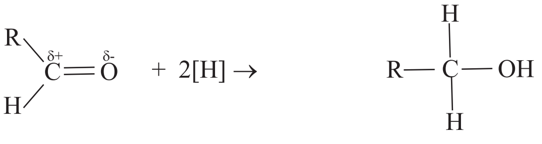
Note: this applies to the OCR and AQA specifications.

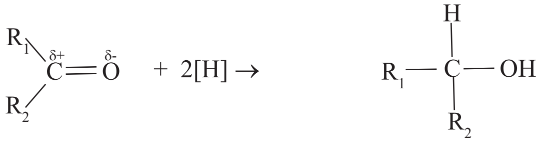
The reaction is carried out by reacting the carbonyl compound in aqueous solution to which a little sodium hydroxide has been added to make it alkaline. The reaction results in an intermediate which is converted to the final organic product by addition of a dilute acid such a sulphuric acid.

> Since this reaction involves the overall addition of hydrogen, it is often referred to as a *reduction* of the aldehyde or ketone.

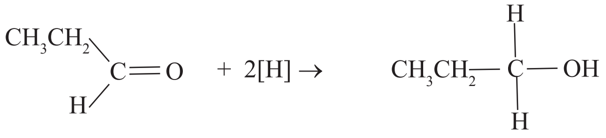
> The reactions involve addition of 2 moles of H atoms per C=O group. In simplified equations these are represented by "2[H]" but, as seen later in the mechanism, an H^- ion (the nucleophile provided by $NaBH_4$) bonds first followed by an H^+ ion.

In general, an aldehyde will produce a primary alcohol ($-CH_2OH$) whereas a ketone will produce a secondary alcohol (-CH(OH)-).

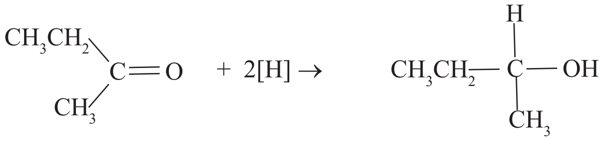

An aldehyde A primary alcohol


A keytone A secondary alcohol

Example 1 When propanal ($R_1 = CH_3CH_2$; R_2 = H) reacts with $NaBH_4$ followed by acid, propan-1-ol is formed.

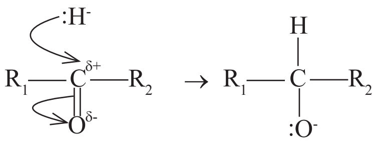

Propanal Propan-1-ol

Example 2 When butanone ($R_1 = CH_3CH_2$; $R_2 = CH_3$) reacts with $NaBH_4$ followed by acid, butan-2-ol is formed.

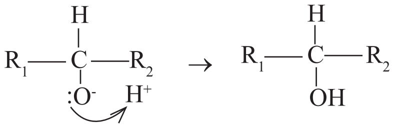

Butanone Butan-2-ol

The mechanism

Stage 1: The nucleophile (:H from $NaBH_4$) attacks $^{\delta+}C$ of C=O



Stage 2: The protonation of O^- by H^+ from H_2SO_4



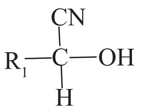
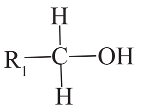
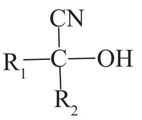
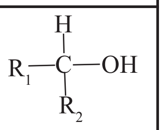
> AQA students! Compare the mechanisms for the addition of HCN and reduction. They are exactly parallel to each other with CN and H interchanging.

Racemisation during nucleophilic addition

A molecule will exist as a pair of *optical isomers* (also called *enantiomers*) if it contains a carbon atom bonded to 4 different groups. Such a carbon atom is referred to as a *chiral carbon* or *chiral centre*.

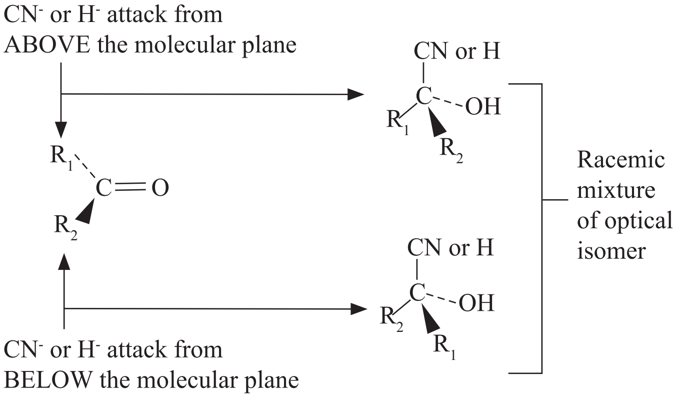
The pair of optical isomers are *non-superimposable mirror images of each other* and differ only in their effects on plane-polarised light. One isomer will rotate the plane of the polarised light in a clockwise direction while the other will rotate it ant-clockwise.

Depending on the structure of the reacting aldehyde or ketone, it is *possible* to form optical isomers in both the HCN and the $NaBH_4$ reactions. This is summarised in the following table.

General product of ALDEHYDE with:		General product of KETONE with:	
(a) HCN	(b) $NaBH_4$	(a) HCN	(b) $NaBH_4$
			
Optical isomers occur provided R_1 not an H atom.	Optical isomers not produced because 2 H atoms bonded to C atom.	Optical isomers occur provided R_1 and R_2 are not the same.	Optical isomers occur provided R_1 and R_2 are not the same.

> In those cases where optical isomers *are* formed, the product is an equimolar mixture of the 2 optical isomers, not an individual isomer. This is called a *racemic mixture* (or *racemate*) and shows zero optical activity because the opposite rotational effects of the 2 isomers cancel each other out. *Racemisation* is said to have occurred during the nucleophilic addition reaction.

Racemisation occurs because the carbonyl region (>C=O) of an aldehyde or ketone is *planar*. When the CN^- or H^- nucleophile attacks the $C^{\delta+}$ atom of the C=O group (see mechanism), there is a *50:50 chance of attack above or below this plane*. Attack above or below produces a different optical isomer as shown in the following diagram resulting in a 50:50 mixture of the optical isomers.



Practice Questions

Select the questions which are appropriate for your specification.

1. Write equations for the nucleophilic addition of HCN to
   (a) ethanal
   (b) hexan-3-one. Name the organic product in each case and decide whether it will be produced as a racemic mixture or not.
2. Write equations for the nucleophilic addition of hydrogen using $NaBH_4$ to
   (a) ethanal
   (b) hexan-3-one. Name the organic product in each case and decide whether it will be produced as a racemic mixture or not.
3. Outline the mechanism for the nucleophilic addition of HCN to propanal.
4. Outline the mechanism for the nucleophilic addition of hydrogen using $NaBH_4$ to pentan-3-one.
5. Explain why the reaction of propanal with HCN results in a racemic mixture.
6. Explain why the reaction of pentan-3-one with $NaBH_4$ does not result in a racemic mixture.

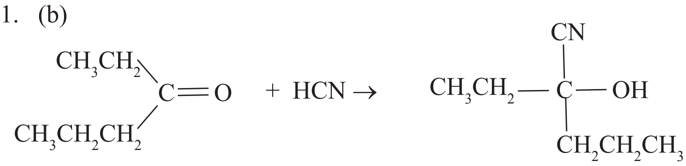
Answers to questions

1. (a)

2-hydroxypropanitrile

Racemic – C2 has 4 different groups bonded to it

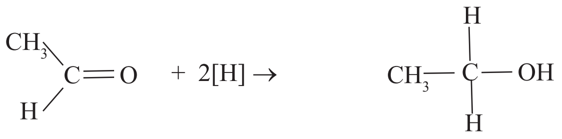
1. (b)



2-ethyl-2-hydroxypentanenitrile

Racemic – C2 has 4 different groups bonded to it

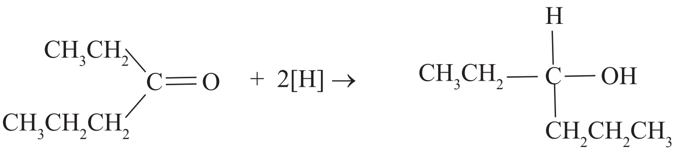
2. (a)



ethanol

Not racemic

2. (b)

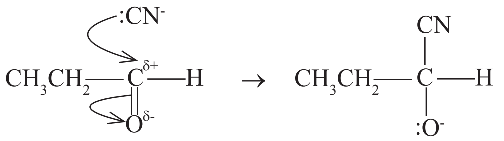


Hexan-3-ol

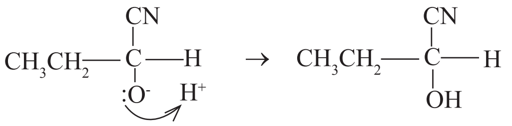
Racemic – C2 has 4 different groups bonded to it

3 $R_1 = CH_3CH_2$ and $R_2 = H$

Stage 1: The nucleophile (:CN) attacks $^{\delta+}$C of C=O

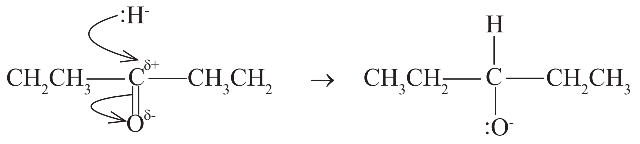


Stage 2: The protonation of O^- by H^+ from H_2SO_4

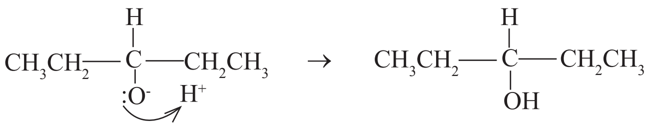


4 R_1 and $R_2 = CH_3CH_2$

Stage 1: The nucleophile (:H from $NaBH_4$) attacks $^{\delta+}$C of C=O



Stage 2: The protonation of O^- by H^+ from H_2SO_4



5. As seen in the answer to question 3, propanal reacts with HCN to produce 2-hydroxybutanenitrile which can exist as optical isomers because C2 is bonded to 4 different groups. The CN^- nucleophile can attack above or below the planar >C=O group in propanal with equal probability. Hence the 2 optical isomers are produced in equal amounts.

6. As seen in the answer to question 4, pentan-3-one reacts with $NaBH_4$ to produce pentan-3-ol which cannot exist as optical isomers because none of its carbons is bonded to 4 different groups. The CN^- nucleophile can still attack above or below the planar >C=O group in pentan-3-one with equal probability but each produces the same non-optically active pentan-3-ol.

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