

ORGANIC SYNTHESIS

Background Chemical synthesis involves the preparation of new compounds from others. Many industrial processes involve a multi stage process where functional groups are converted into other functional groups.

When planning a synthetic route, chemists must consider...

- the reagents required to convert one functional group into another
- the presence of other functional groups - *in case also they react*
- the conditions required - *temperature, pressure, catalyst*
- the rate of the reaction
- the yield - *especially important for equilibrium reactions*
- atom economy
- safety - *toxicity and flammability of reactants and products*
- financial economy - *cost of chemicals, demand for product*
- problems of purification
- possibility of optically active products

Functional groups

Common functional groups found in organic molecules include...

C = C alkene

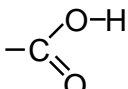
O – H hydroxyl (*alcohols*)

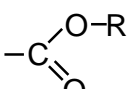
C – Cl halogenoalkane

C = O carbonyl (*aldehydes & ketones*)

C – NH₂ amine

–C≡N nitrile

 carboxylic acid

 ester

Q.1 State which of the functional groups listed above react with...

- HBr*
- H₂*
- OH⁻*
- CN⁻*
- H⁻ (as in NaBH₄ or LiAlH₄)*
- [O] (as in acidified K₂Cr₂O₇)*
- H⁺(aq)*

CHIRAL SYNTHESIS

Rationale Pharmaceutical synthesis often requires the production of just one optical isomer. This is because...

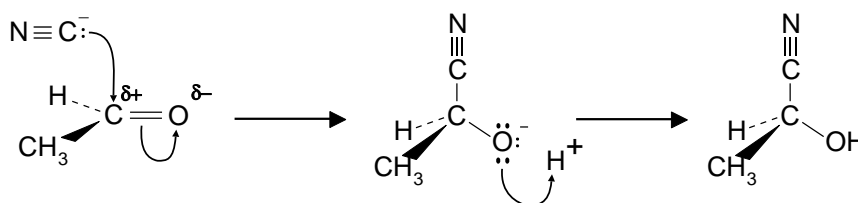
- one optical isomer usually works better than the other
- in some cases the other optical isomer may cause dangerous side effects
- laboratory reactions usually produce both optical isomers
- naturally occurring reactions usually produce just one optical isomer

Example Aldehydes and ketones undergo nucleophilic addition with cyanide (nitrile) ions

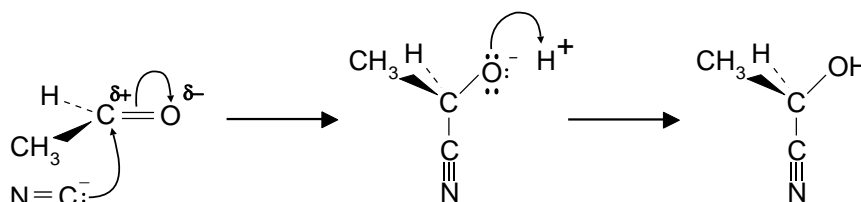


- Problem*
- the C=O bond is planar
 - the nucleophile can attack from above and below
 - there is an equal chance of each possibility
 - a mixture of optically active isomers is produced
 - only occurs if different groups are attached to the carbonyl group

CN⁻ attacks from above



CN⁻ attacks from below



Consequences

- isomers have to be separated to obtain the one that is effective
- separation can be expensive and complicated
- non-separation could lead to... **larger doses** having to be given
 possible dangerous **side effects**
 possible **legal action**

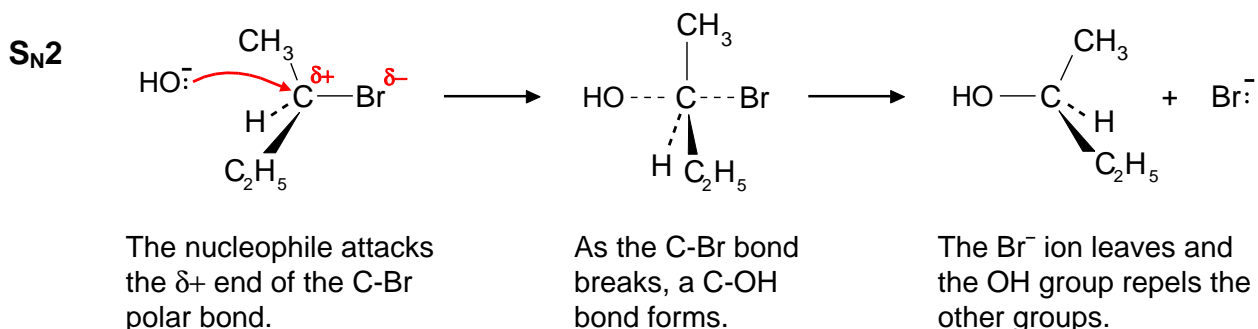
Solution

- Use
- natural chiral molecules as starting materials
 - reactions which give a specific isomer
 - catalysts which give a specific isomer
 - enzymes or bacteria which are stereoselective

Other
examples

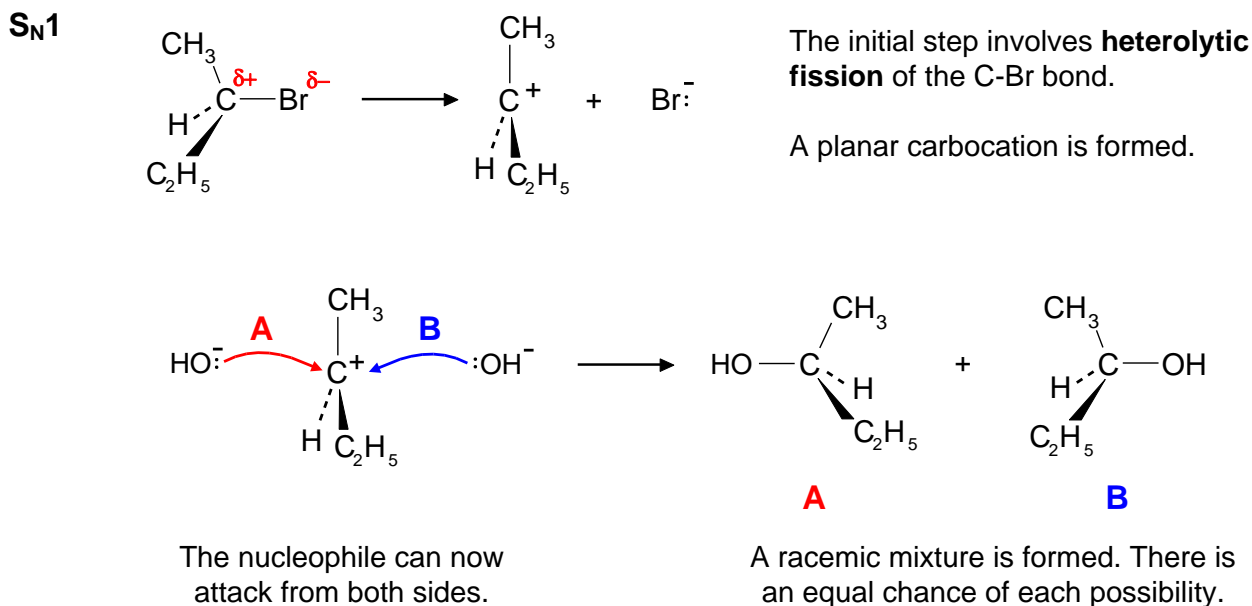
Nucleophilic substitution of halogenoalkanes

There are two possible mechanisms



This produces just one optical isomer with reversed optical activity

It is called S_N2 because two species are involved in the rate determining step.



This produces a racemic mixture of two optical isomers

It is called S_N1 because just one species is involved in the rate determining step.

S_N1 is the more likely mechanism if bulky groups are attached to the C-Br. The incoming nucleophile will have easier access.

Q.2 Which of the following produce a mixture of alcohols when treated with OH^- (aq)?



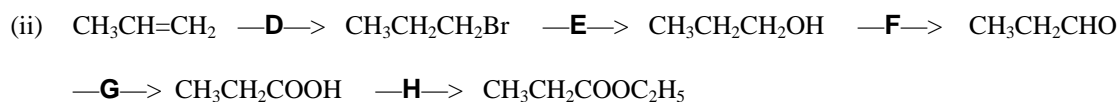
Q.3 State the reagents and conditions needed to carry out the following reaction sequences. Consider if any of the transformations give rise to isomeric (especially optical) products.



Step **A**

Step **B**

Step **C**



Step **D**

Step **E**

Step **F**

Step **G**

Step **H**

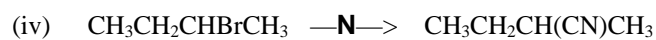


Step **J**

Step **K**

Step **L**

Step **M**



Step **N**



Step **P**

Step **Q**



Step **R**