Evidence in Optical Activity Changes
for
Nucleophilic Substitution Mechanisms

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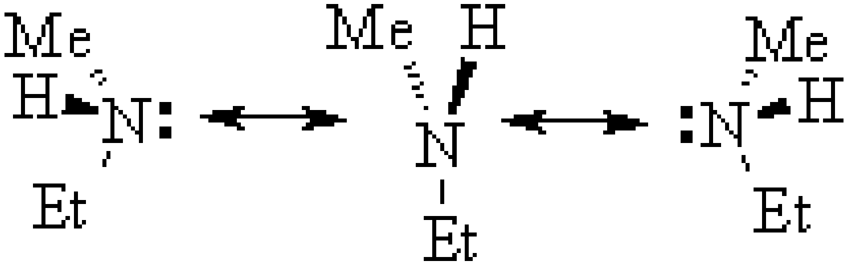
Chirality

If a molecule is non-superposable with its mirror image it is chiral.

This might occur if a molecule has no plane of symmetry

Chiral molecules must possess a chiral centre which is an atom for which if two of the groups it is bonded to are interchanged the enantiomer will result.

In general any atom with four different groups bonded to it (including lone pairs) is likely to be a chiral centre (exceptions include some trigonal pyramidal molecules – especially those with nitrogen as the central atom – which exhibit rapid pyramidal inversion).

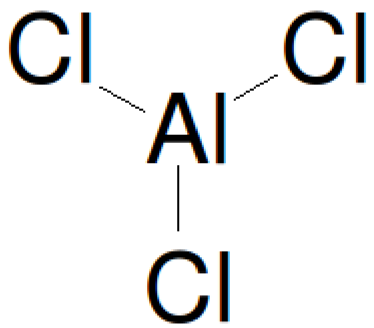


Credit: Dr. Ian Hunt
University of Calgary

Chiral

Why can no planar molecule ever be chiral?

By definition all planar molecules share a common plane which will be a plane of symmetry, hence precluding the possibility of chirality.



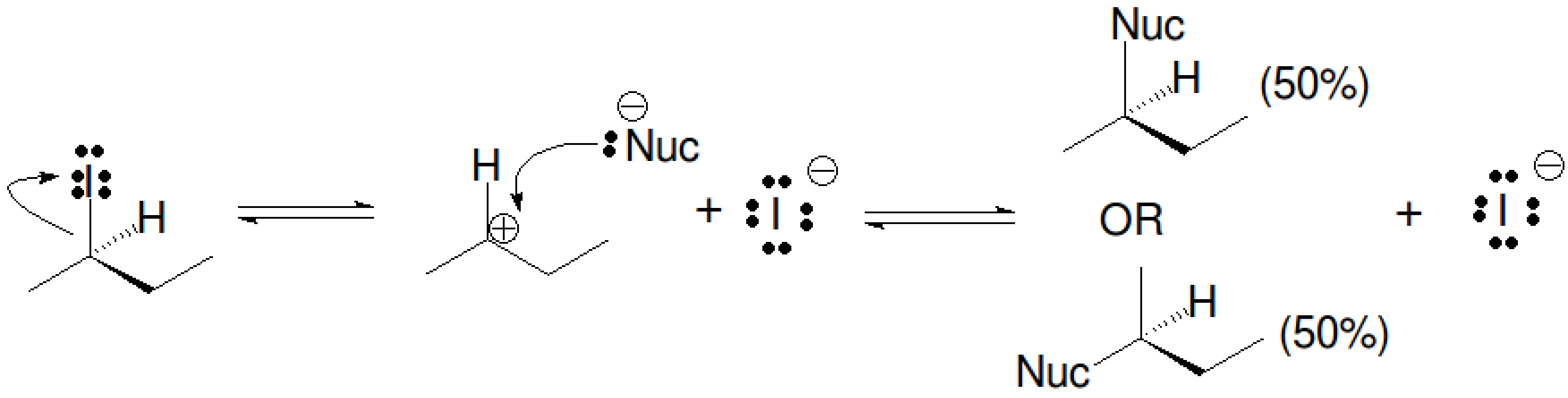
Optical Activity

Chiral molecules rotate the axis of polarisation of monochromatic (single frequency), plane polarised light.

Each of the two forms of the chiral molecule (its enantiomers) will rotate the axis of polarisation in the opposite direction by the same amount

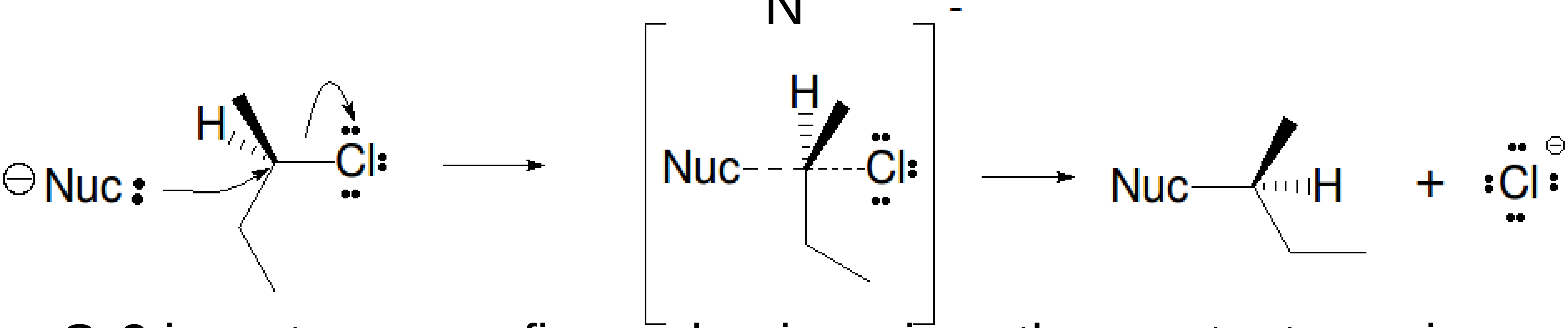
If a mixture has an equal concentration of both enantiomers there will be no net effect on the axis of polarisation. This type of mixture is a racemic mixture.

S_N1



In the second step the probability that the nucleophile will attack the carbocation from above is the same as the probability that the nucleophile will attack from below since it has a trigonal planar structure around the positively charged carbon. This thus makes the probability of forming each enantiomer the same. Due to this equal probability of attack from above or below the planar intermediate carbocation the S_N1 mechanism will always produce a racemic mixture (if the product is chiral) and thus the products will have no net effect on the axis of polarisation of plane polarised light.

S_N2



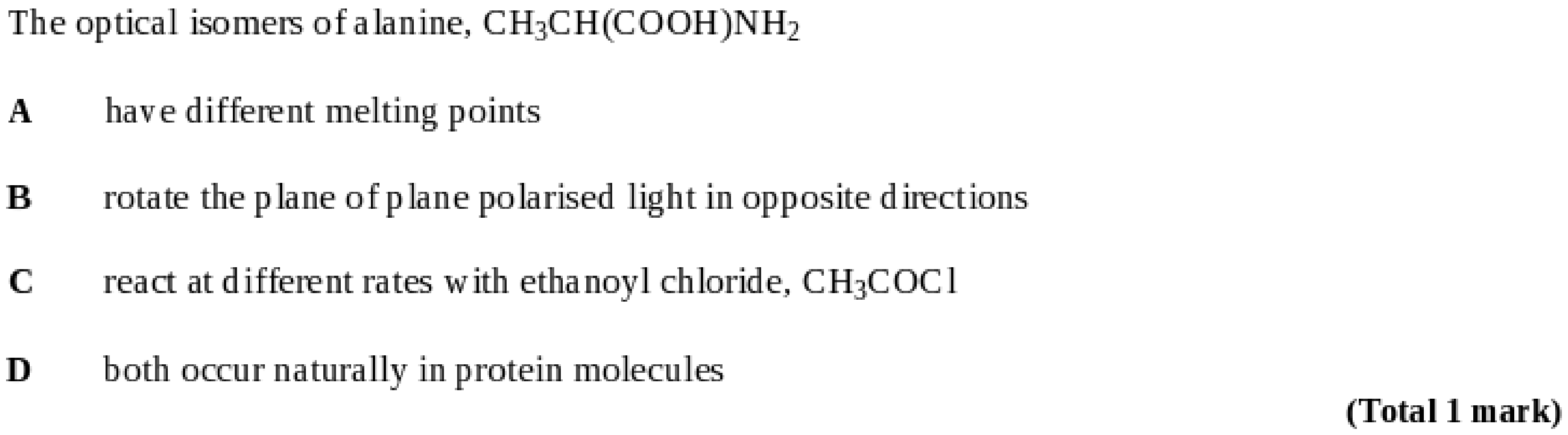
S_N2 is a stereospecfic mechanism since the reactant species undergoes an inversion of configuration.

This will thus result in the reactant molecule (if it is chiral) being converted into its opposite enantiomer during the reaction.

If the reactant solution is not racemic – and reacts via this mechanism – then the final product mixture will rotate the axis of polarisation in the opposite direction to the initial reactant mixture.

During the reaction when the mixture has no net effect on plane polarised monochromatic light may or may not be the point when a 50% conversion has occurred since the reactant and product molecules may rotate the axis of polarisation to differing degrees.

Simple Factual Question



The optical isomers of alanine, $CH_3CH(COOH)NH_2$

A have different melting points

B rotate the plane of plane polarised light in opposite directions

C react at different rates with ethanoyl chloride, CH_3COCl

D both occur naturally in protein molecules

(Total 1 mark)

B – the second carbon in the α-amino acid alanine is chiral, hence its two optical isomers will rotate the plane of plane polarised monochromatic light in opposite directions by the same degree.

All α-amino acids except for Glycine (side chain of H) are chiral.

Reactions with molecules in the body are generally stereospecific, hence generally only one enantiomer is effective.

Explanation Question

Both 2-bromobutane and butan-2-ol are chiral molecules.

If one optical isomer of 2-bromobutane is used to make butan-2-ol by reaction with aqueous hydroxide ions, the product mixture is not optically active.

The mechanism is either S_N1 or S_N2.

Explain which of these mechanisms is consistent with the lack of optical activity in the product mixture. (3)

Explanation Question

S_N1

Planar carbocation intermediate with equal chance of attack from above or below.

Produces racemic mixture of butan-2-ol, hence resulting in no net effect on the plane of polarisation of plane polarised monochromatic light thus the mixture is not optically active.

Note that if the reactant molecules were achiral then the product molecules would also be achiral and the product mixture would exhibit no optical activity.

Extended Answer Question

In the reaction between 2-iodobutane and dilute aqueous potassium hydroxide, the reaction can be followed using a polarimeter to monitor the changes in the angle of rotation of the plane of plane-polarised light as the reaction progresses. The angle of rotation is directly proportional to the concentration of 2-iodobutane.

However in the reaction between 1-fluorobutane and dilute aqueous potassium hydroxide this method will not work.

Explain why using polarimetry is ineffective with 1-fluorobutane and suggest an alternative approach to follow the reaction between 1-fluorobutane and dilute aqueous potassium hydroxide to determine the overall order of reaction. (6)

Extended Answer Question

1-fluorobutane does not have a chiral carbon hence is achiral and not optically active. Hence polarimetry is ineffective.

Use a continuous monitoring method to follow the reaction such that the overall reaction order can be easily determined.

Use quenching and titration for this: extract sample from reaction vessel at regular time intervals, quench the sodium hydroxide with an known volume of excess of dilute strong acid (e.g. dilute HCl) and record the time of the quenching after the start of the reaction. Add an suitable acid-base indicator (e.g. phenolphthalein) and titrate against a standard sodium hydroxide solution.

The volume of the titre is proportional to the excess of HCl in the reaction vessel after quenching hence is inversely proportional to the concentration of hydroxide ions, hence plot 1/(titre volume) against the time of quenching.

If the line is straight the overall reaction order is zero, if it is exponential with a constant half life the overall reaction order is one and is it is exponential with the half life doubling each time then the overall reaction order is two.