
CHEM1201: Section 2

Alex Ganose

December 26, 2012

Contents

1	Alkanes	3
1.1	Preamble	3
1.2	Reactions of Alkanes	3
1.2.1	Heterolytic Fission	3
1.2.2	Homolytic Fission	4
2	Alkenes	6
2.1	General	6
2.2	Reactions of Alkenes	6
2.2.1	Reactions of Carbocations	8
2.2.2	Summary of all Electrophilic Additions to Alkenes	10
2.2.3	Other Alkene Reactions	11
3	Alkynes	16
3.1	Reactions of Alkynes	16
4	Alkyl Halides (Haloalkanes)	21
4.1	Notes for alcohols	21
5	Nucleophilic Substitution	22
5.1	Trends in Nucleophilicity	22
5.2	Trends in leaving group ability	22
5.3	Nucleophilic Substitution Reactions	22
5.4	Bimolecular S_N2 Nucleophilic Substitution Reactions	23
5.5	Unimolecular S_N2 Nucleophilic Substitution Reactions	24
6	Elimination Reactions	27
6.1	Bimolecular E2 Eliminations	27
6.2	Unimolecular E1 Elimination	29

1 Alkanes

1.1 Preamble

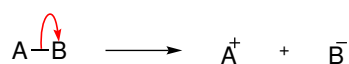
Rings, double bonds and other atoms in organic molecules introduce degrees of unsaturation or double bond equivalents. The formula for working out the degrees of unsaturation is:

$$DBE = \frac{(2 + (2 \times \#Carbons) + \#Nitrogens - \#Hydrogens - \#Halogens)}{2}$$

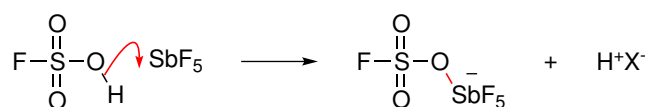
1.2 Reactions of Alkanes

The simplest saturated hydrocarbon is methane, CH_4 , which has bond angles of $109^\circ 28'$. Alkenes are made up of tetrahedral sp^3 hybridised carbon atoms covalently bonded with hydrogen. They undergo two elementary reactions:

1.2.1 Heterolytic Fission

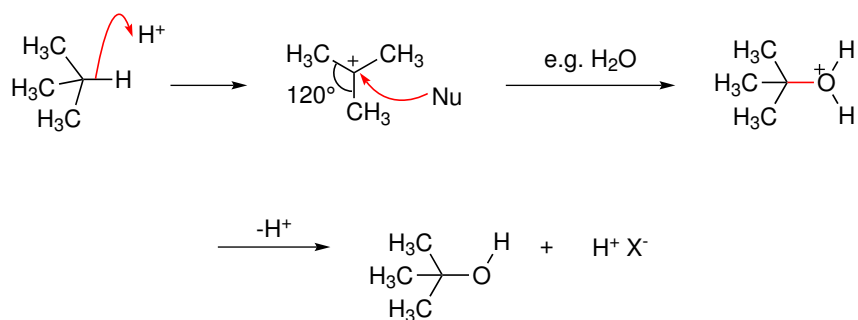


a)



"Superacid" mixture

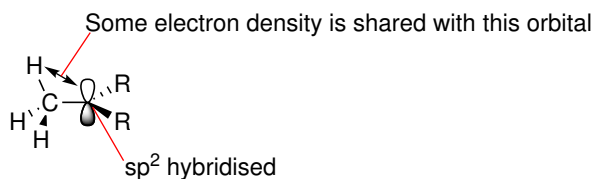
b)



A trigonal planar, carbocation is formed as the reactive intermediate

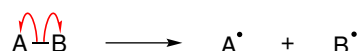
Note that charge is conserved and only the tertiary methane hydrogen is removed. This is because of the stabilisation effect from R groups. Primary carbocations ($\text{R}-\text{C}^+\text{H}_2$) are higher in energy than secondary ($\text{R}_2\text{C}^+\text{H}$) which are in turn higher than tertiary (R_3C^+) where R is an inductively electron releasing alkyl group (e.g. $\text{CH}_3\text{CH}_2\text{CH}_3$ etc). This effect can be explained by hyperconjugation, as in a carbocation there will be a sp^2 hybridised vacant p orbital that can accept electrons

coming out of the plane of the trigonal planar molecule. Electron donation occurs from the C–H bond, in the same plane as the sp^2 orbital, into the empty p orbital.

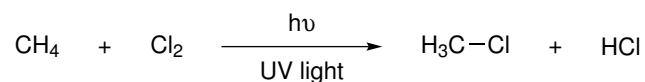


1.2.2 Homolytic Fission

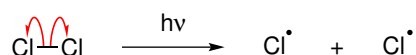
For example free radical chain reactions which are of preparative value.



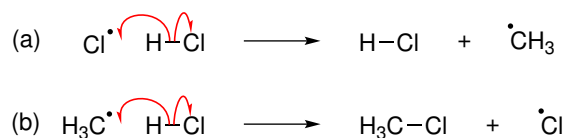
E.g. Free radical halogenation of methane:



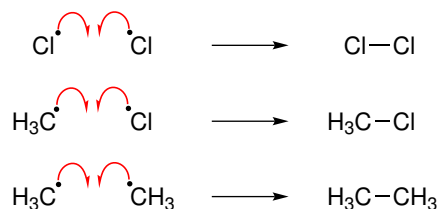
Initiation



Propagation



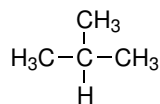
Termination



Termination reactions require another photon and account for less than 2% of the product.

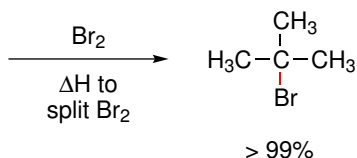
In the free radical halogenation of methane, the propagation steps take place 10^6 times for each initiation step. Additionally, other products are formed when more H's are replaced.

When using isobutane (2-methylpropane) we see interesting selectivity.

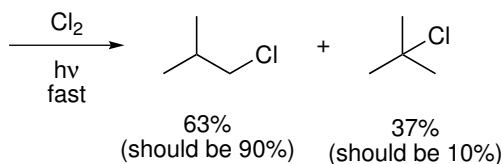


Isobutane

With Br_2 the reaction is regiospecific - a single regioisomer is formed.



With Cl_2 the reaction is regioselective meaning that there is a preference for one regioisomer rather than the others.



These regio effects occur because the chlorine is much more reactive and hence less discriminating in hydrogen abstraction than the bromine atom (more electronegative). One $\text{H}-\text{Cl}$ bond formed for Cl is -431 kJmol^{-1} and for Br is -366 kJmol^{-1} and the tertiary $\text{C}-\text{H}$ bond requires $+397 \text{ kJmol}^{-1}$ to break. Hence with Cl the reaction is exothermic and with Br it is endothermic meaning the bromine reaction requires energy, this in turn makes the reaction more discriminating.

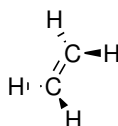
Breaking one primary bond needs $+423 \text{ kJmol}^{-1}$ and therefore, as reactions follow the path of least energy and the order of radical stability is $3^\circ > 2^\circ > 1^\circ$, the reaction proceeds above.

2 Alkenes

2.1 General

General formula: C_nH_{2n}

Ethene has a planar framework of atoms



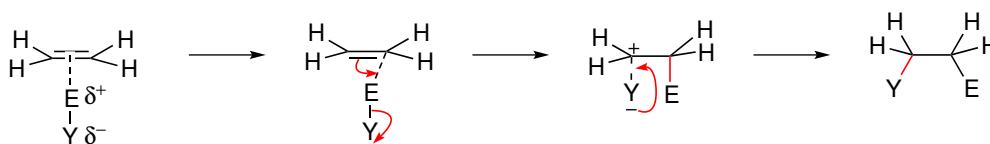
The carbon atoms have 3 sp^2 hybrid atom orbitals (using the 2s and only 2 of the 2p orbitals) which lie in the xy plane orientated at 120° relative to each other. The C–H σ bonds are formed by overlap of the sp^2 hybrids on carbon and the 1s on hydrogen, the C–C σ bond is then constructed using the remaining sp^2 orbitals. The weaker π bond is constructed using sideways overlap of the remaining 2p_z on each carbon atom.



The chemistry of alkenes is dominated by the ability of the 2π electrons to donate themselves, i.e. function as a nucleophile. Geometrical isomerism occurs due to restricted rotation about the C=C. The Z isomer is when the larger products are on the same side (cis) and E is when they are on opposite sides (trans).

2.2 Reactions of Alkenes

Due to the ability of the π cloud to donate 2 electrons, electrophilic addition to alkenes is a wide ranging and general series of reactions. For a reagent of the form $E^{\delta+}-Y^{\delta-}$ the following mechanism can be written.



First there is complex formation with the polarization and lengthening of the E–Y bond followed by the formation of the C–E bond and breakage of the E–Y bond. Finally nucleophilic capture occurs with the reactive carbocation intermediate.

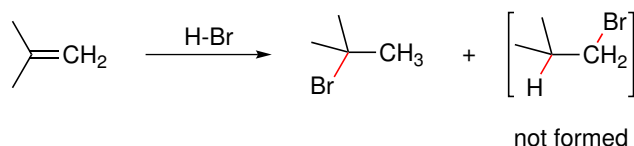
Some useful reagents are:

- Br_2
- $H-Cl$, $H-Br$, $H-X$ etc.
- H_3O^+ - acid
- $Br-OH$ - hypobromous acid (or from formation of borohydrin via H_2O/Br_2)

- $\text{Ph-S}^{\delta+}-\text{Cl}^{\delta-}$ - sulfenylation

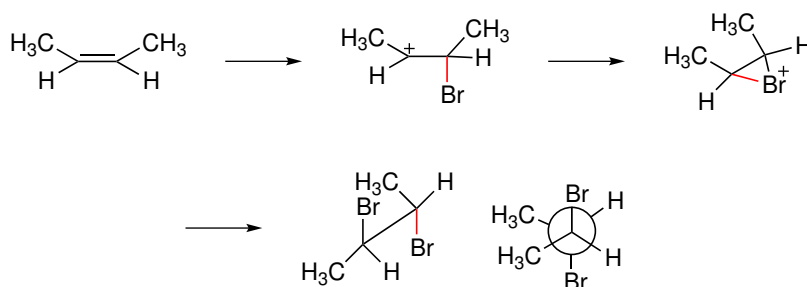
Electrophilic additions to unsymmetrical alkenes are regiospecific (only one regioisomer formed). This method of addition was first noted in 1870 by Markovnikov and is stated as an empirical rule – Markovnikov's rule. This is because addition always occurs via the lower energy carbocation.

E.g.



When the component E of the reagent $\text{E}^{\delta+}-\text{Y}^{\delta-}$ possesses lone pairs of electrons, reactions are also stereospecific (only one stereoisomer formed).

E.g. Addition of bromine to Z and E-but-2-ene.

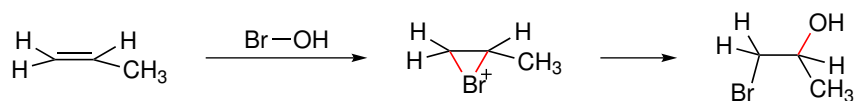


The opening of the bromonium cation occurs by nucleophilic attack from the least hindered opposite face (antiperiplanar position). Overall the reaction is a trans (or anti) electrophilic addition. Similarly the reaction of E-but-2-ene gives a different diastereoisomer.

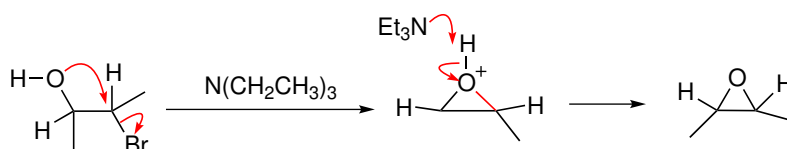
Other examples of bridged intermediates that form stereospecific compounds are:



Some reactions are both regio and stereospecific. E.g. BrOH



Bromohydrins are used in the preparation of epoxides. E.g.

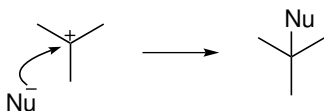


Hydration can also occur via acetomercuration to form an alcohol (see section 1) and either NaBH_4 or NaOH can be used as bases to remove the final Hg-OAc .

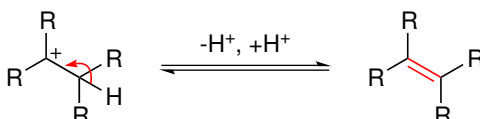
2.2.1 Reactions of Carbocations

Carbocations undergo 3 types of reaction:

- a) Capture by a nucleophile

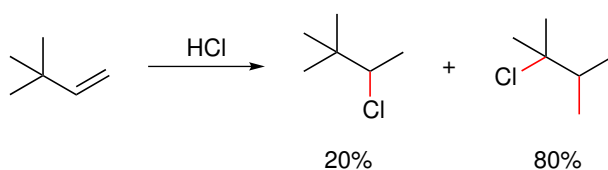


- b) Proton loss to give an alkene

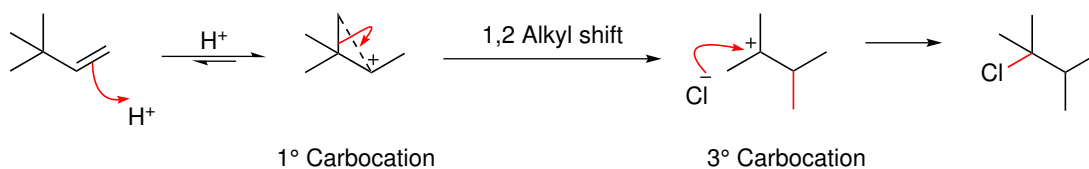


- c) Carbocation Rearrangement Rearrangement will always occur to give a lower energy carbocation. Examples of rearrangement during electrophilic addition to an alkene are:

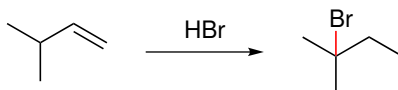
- i) Wagner–Meerwein rearrangement involving a 1,2-Alkyl shift



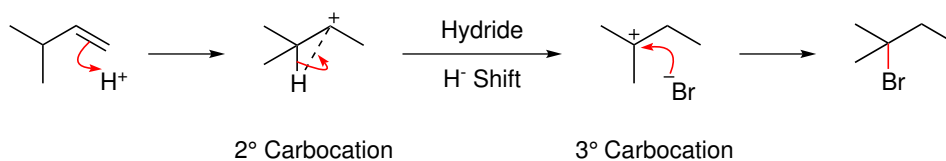
Mechanism



- ii) Hydride Shift

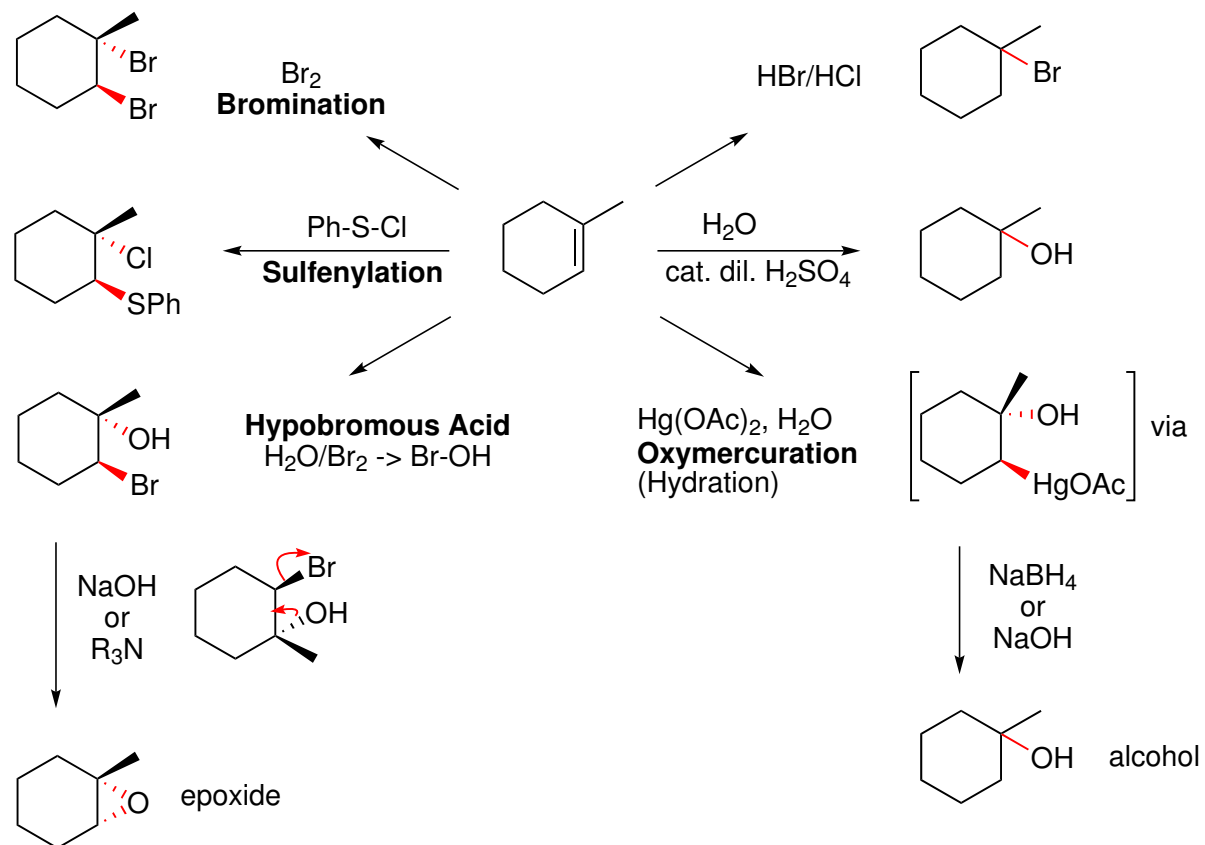


Mechanism



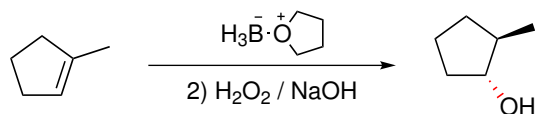
The 1,2 alkyl shift would give the same 2° carbocation and therefore would not be lower in energy.

2.2.2 Summary of all Electrophilic Additions to Alkenes



2.2.3 Other Alkene Reactions

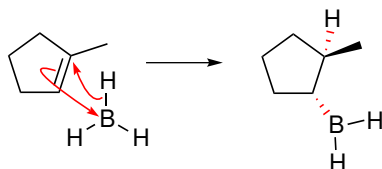
a) Hydroboration (followed by oxidation) - useful for anti-markovnikov hydration.



Mechanism

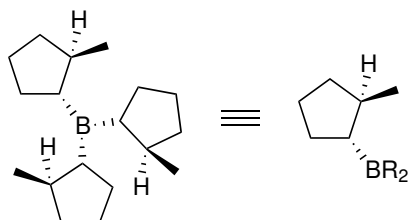


Is electron deficient but commercially available as a complex with the ether THF.

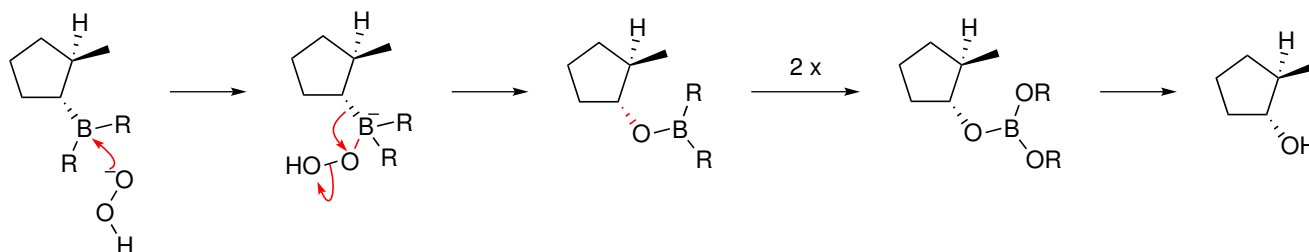


This takes place in a syn addition in a concerted way (both bonds are made in the same step). The bond to B is made slightly faster since it is the electrophilic center and the electron deficient atom. This results in the observed regiochemistry.

Each of the remaining B-H bonds also adds across an alkene to give:

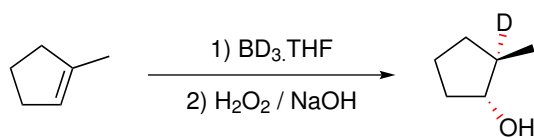


The carbon-boron bond is then replaced by a hydroxyl group with retention of configuration.

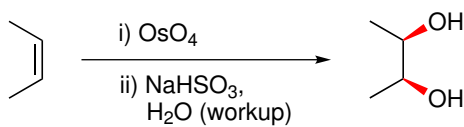


The final step occurs via borate ester hydrolysis

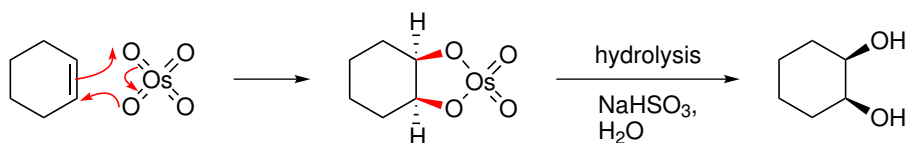
The proof of the hydroboration mechanism can be shown using deuterium labelling



b) Vicinal cis dihydroxylation



Mechanism via a concerted cycloaddition reaction.



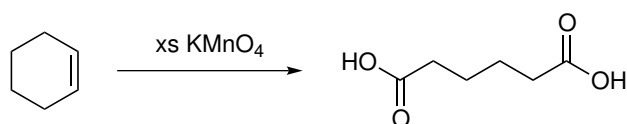
Osmate ester formed

Both the oxygen atoms are delivered from the same side (i.e. syn addition).

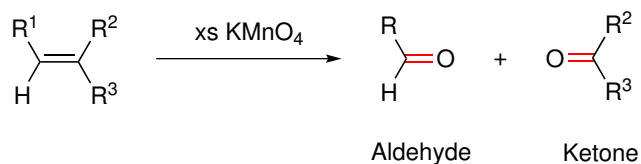
Similarly for K^+MnO_4^- under basic conditions using the ion



With excess KMnO_4 over oxidation can occur.

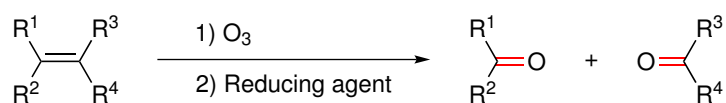


and in general for acyclic alkenes



c) Ozonolysis of alkenes

This is a milder method for oxidative cleavage of $\text{C}=\text{C}$ than KMnO_4

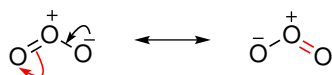


Common reducing agents are:

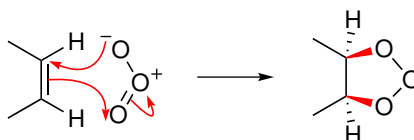
- Me_2S - Dimethyl sulfoxide
- Ph_3P - Triphenylphosphine
- $\text{Zn}/\text{H}_3\text{CCO}_2\text{H}$ - Zinc/acetic acid

Mechanism:

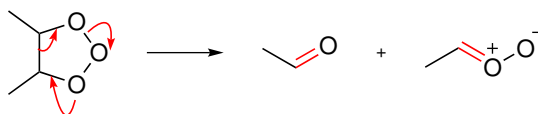
a) Formation of ozone electrophile



b) Concerted cycloaddition

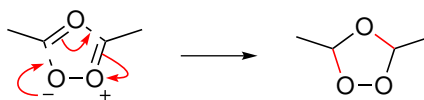


c) Fragmentation

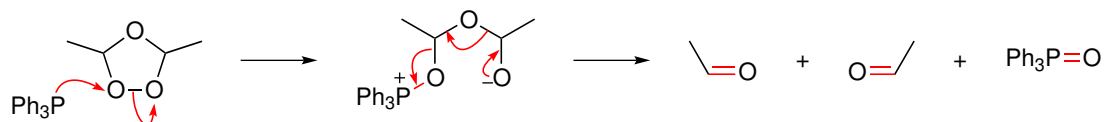


Carbonyl oxide intermediate

d) Recombination via a second cycloaddition

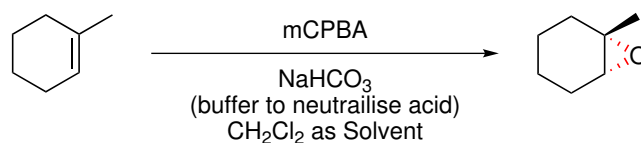


e) Reductive workup (e.g. Ph_3P)

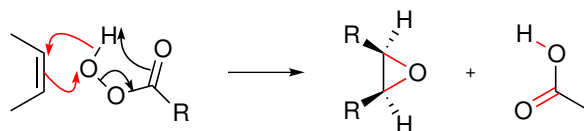


d) Preparation of epoxides using a peracid

This reaction preserves stereochemistry and preserves alkene geometry, it is stereospecific. The oxygen is delivered from the least hindered side - steric approach control.

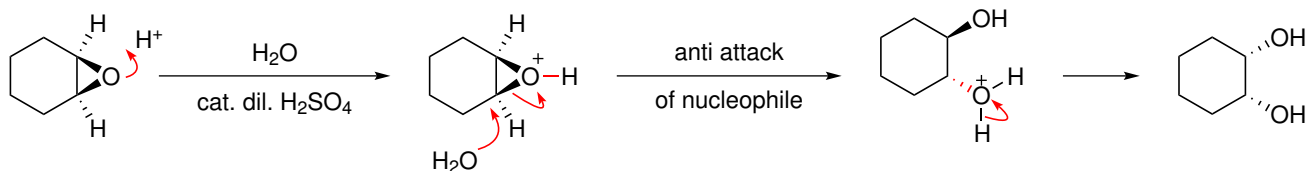


Mechanism

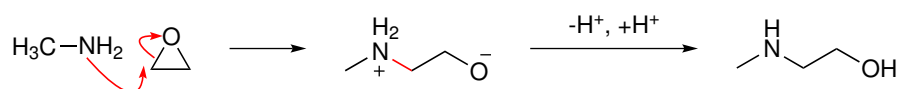


Epoxides are useful synthetic intermediates as they undergo ring opening reactions with nucleophiles and can easily be stored unlike bromium cations.

Example 1. Ring opening under acidic conditions with H_2O as a nucleophile



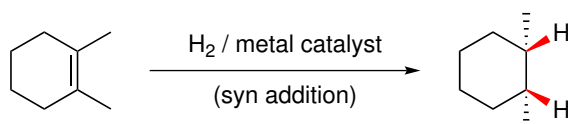
Example 2. Amines used as nucleophiles



Many other nucleophiles can be used including:

- $\text{RO}-\text{Na}^+$
- $\text{RS}-\text{Na}^+$
- R^- from RMgI

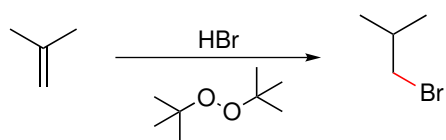
e) Catalytic hydrogenation - Synthetic route to alkanes



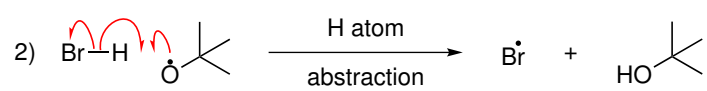
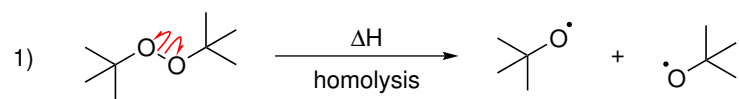
Typical metal catalysts are Pd, Pt, Ni and both hydrogen atoms are always delivered to the same side of the alkene.

f) Addition of hydrogen bromide in the presence of peroxides

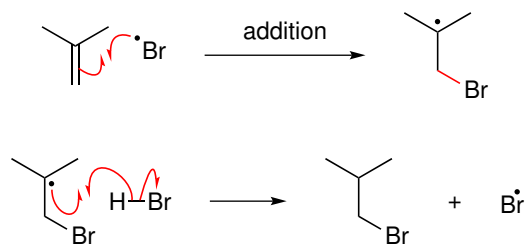
This is a free radical chain reaction that gives the anti-markovnikov product.



Initiation:



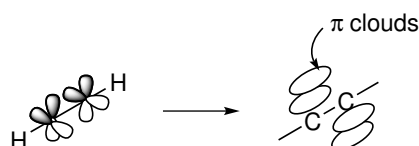
Propagation



Tertiary radical is favoured

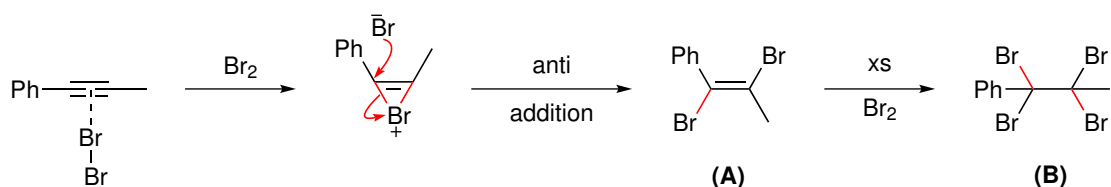
3 Alkynes

Alkynes have a single carbon-carbon triple bond and have the general formula C_nH_{2n-2} . Ethyne has a linear arrangement of the four atoms. The hybrid atomic orbitals in each carbon are constructed using the 2s orbital and only one of the 2p orbitals to give two sp hybrid atomic orbitals leaving the 2p_y and 2p_z orbitals. The two hybrid sp orbitals are constructed at 180° to each other. Each remaining p orbital contains a single electron, sideways overlap of each of these on the neighbouring carbon atoms forms two π bonds.



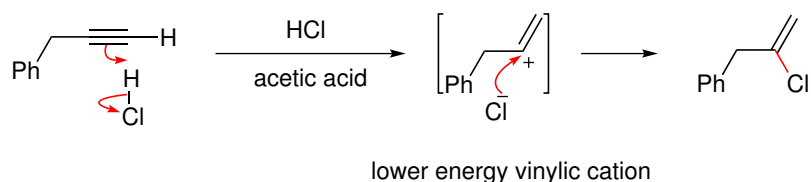
3.1 Reactions of Alkynes

a) Bromination



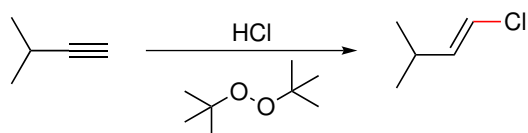
The reaction can be controlled to stop to give **(A)**. Xs reagent is needed to give **(B)**. The first anti addition is highly stereoselective to give the E (trans) isomer but it is not stereospecific.

b) Addition of Hydrogen Chloride.



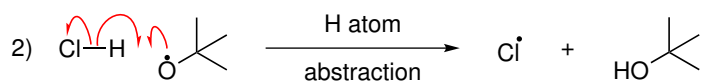
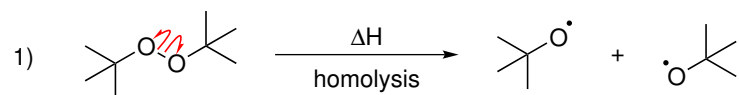
The reaction can be controlled to stop after this stage as further addition of HCl is slower. The addition is normally anti, resulting in the E (trans) isomer.

c) Addition of HCl in the presence of peroxides

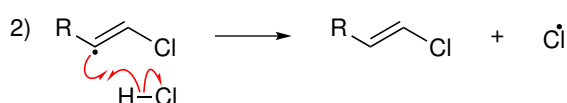
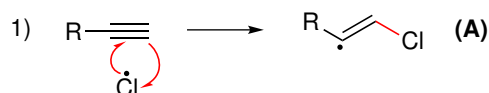


This reaction occurs by a free radical chain reaction process.

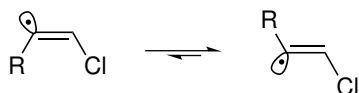
Initiation:



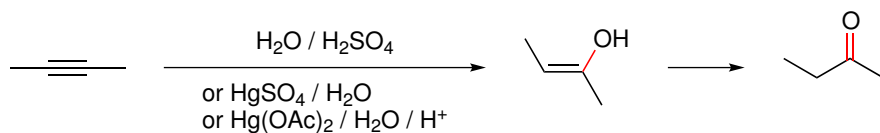
Propagation:



This reaction gives the anti-markovnikov addition as syn addition occurs to give the E isomer since the reaction occurs via the less hindered, trans form of vinylic radical. (A).

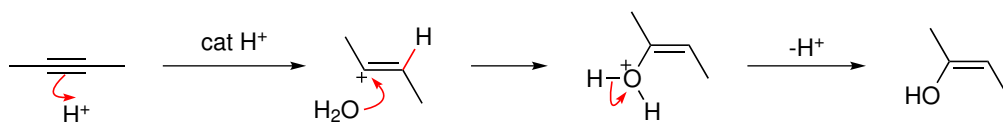


d) Hydration of alkynes by electrophilic addition of water - useful synthesis of ketones.

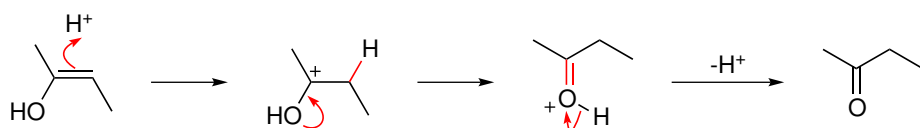


Mechanism:

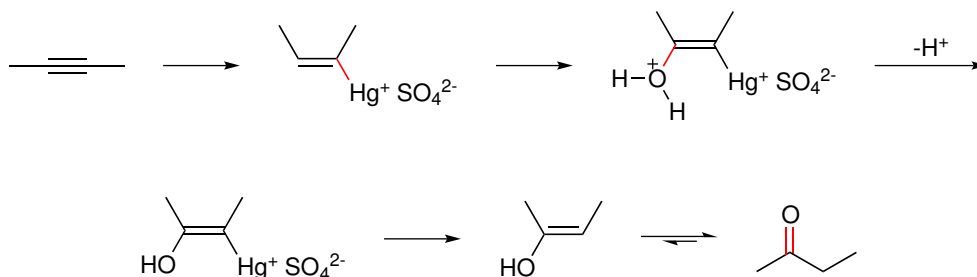
Formation of Enol:



Tautomerisation of the enol to the keto form

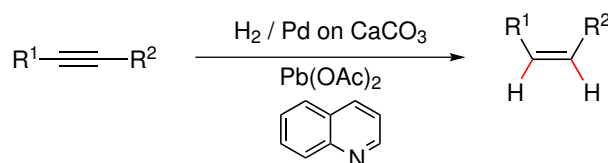


An alternate mechanism can be drawn using $\text{HgSO}_4/\text{H}_2\text{O}$:



Reduction of alkynes to alkenes takes place via 2 important reactions.

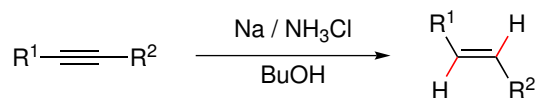
e) Catalytic hydrogenation using a Lindlar Catalyst - Forms the Z (cis) alkene



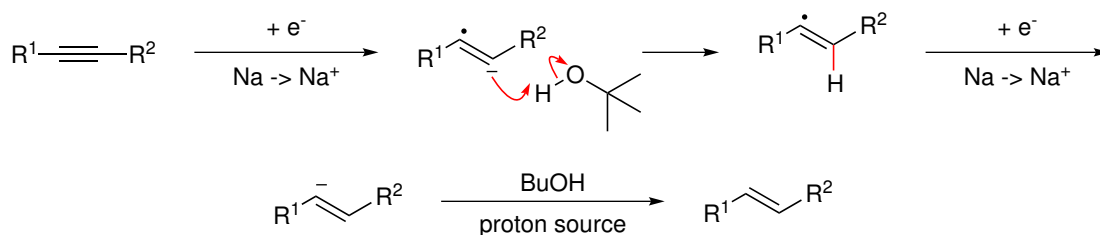
The Lindlar catalyst is a poisoned palladium catalyst, it allows syn addition. C=C is not further reduced. Another variant of the catalyst is: Pd/BaSO₄/quinoline. An industrial use of the catalyst is in making "cis" jasmine which is used in perfumery.

f) Reduction of the C ≡ C using dissolving metal reduction (Birch Reduction)

Forms the E (trans) alkene.



Mechanism: Sodium in liquid ammonia is a source of solvated electrons.



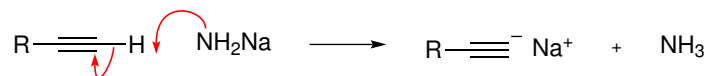
g) The deprotonation of terminal alkynes - Acetylide anions as carbon nucleophiles.

The acidity of a hydrogen atom attached to carbon varies with the degree of s character of the C atom. sp^3 (s character 25 %) < sp^2 (s character 33.3 %) < sp (s character 50 %) and consequently terminal alkynes can be deprotonated by a strong base such as:

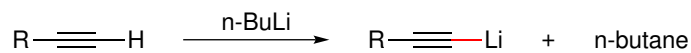
- $Na^+NH_2^-$ - sodium amide
- $nBuLi$ - n-butyl lithium

- $R-MgX$ - grignard reagent

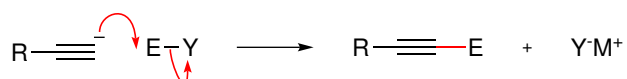
Therefore:



Or for synthesis:

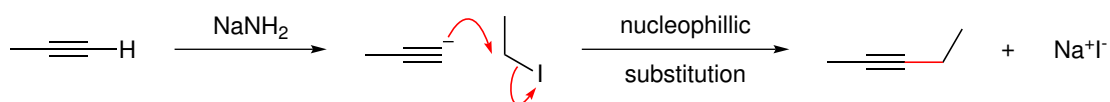


Acetylide anions are useful for making C-C bonds with electrophilic reagents.

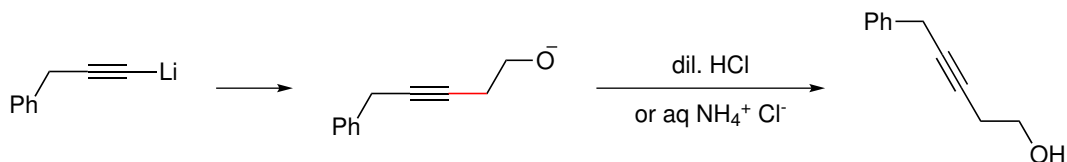


Examples of reagents:

i) Alkyl Halides

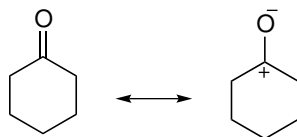


ii) Epoxide ring opening

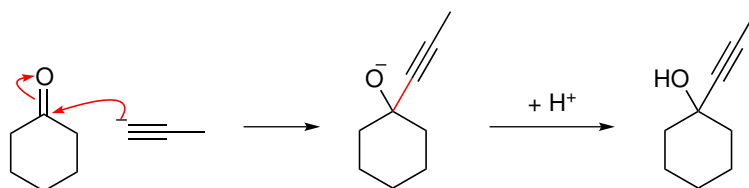


The deprotonated alkyne can then perform nucleophilic attack on the carbonyl groups of aldehydes and ketones.

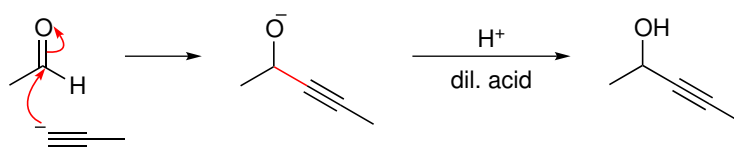
On ketones:



Therefore:

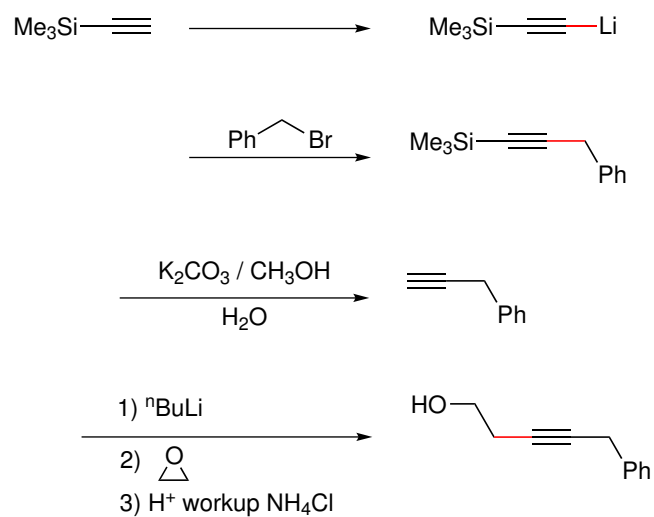


On aldehydes:



$\text{Me}_3\text{Si}-\text{C}\equiv\text{H}$ - Trimethylsilylacetylene

This is a useful compound as it allows addition on each C atom of the alkyne unit in turn.



4 Alkyl Halides (Haloalkanes)

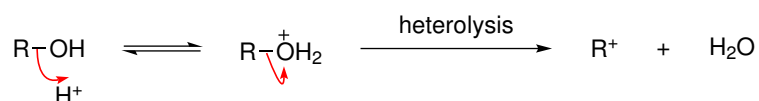
The chemistry of halogens is dominated by the nature of the halogen bond. Due to the electronegativity of the halogens, bond polarisation occurs through inductive effects $\text{H}_3\text{C}^{\delta+}-\text{X}^{\delta-}$. This means that the carbon is electropositive or electrophilic and therefore reactions involving heterolysis of the $\text{C}-\text{X}$ bond will lead to X^- . This group, X , is termed the leaving group.

Within the halides the relative abilities to function as leaving groups are: $\text{I} > \text{Br} > \text{Cl} > \text{F}$. This is because, although F is more electronegative than I (due to greater shielding), orbital overlap between C and F is very effective and forms a strong bond (teflon). The $\text{C}-\text{I}$ bond is much weaker.

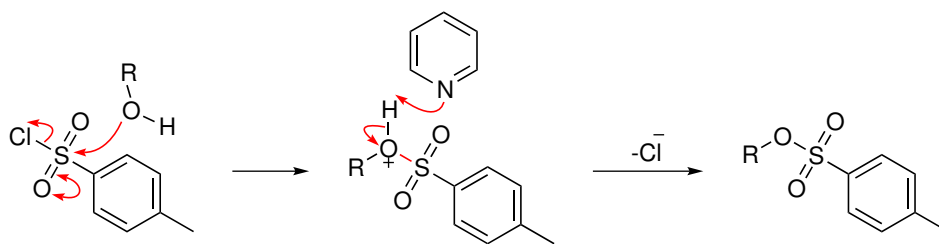
4.1 Notes for alcohols

HO^- is not a great leaving group, however it can be encouraged to leave in two ways:

- a) Protonation with an acid source ($\text{H}_2\text{SO}_4/\text{HCl}$, etc).



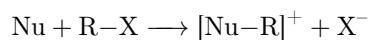
- b) Conversion to a better leaving group



TsO^- is a good leaving group (better than I^-)

5 Nucleophilic Substitution

Nucleophilic substitution involves displacement of a good leaving group X as X^- by a nucleophile Nu. The nucleophile can be neutral:



Or negatively charged:



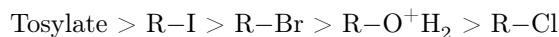
However they always possess a free lone pair of electrons to donate. Examples include:

Neutral	Negatively Charged
$\text{N}(\text{CH}_3)_3$	Cl^-
PR_3	Br^-
SR_2	I^-
OH_2	$\text{N}_3^- \equiv \text{N}^-=\text{N}^+=\text{N}^-$
$\text{H}_3\text{C-O-H}$	CN^-

5.1 Trends in Nucleophilicity

Electronegativity increases across a row of the periodic table R-NH-R is a better nucleophile than R-O-R . Additionally descending down a group, nucleophilicity increases since there are more electrons screening the nucleus, hence the valence electrons are further away and more polarisable. If a nucleophile is used as the solvent for a reaction (e.g. H_2O or $\text{H}_3\text{C-OH}$, etc), the nucleophilic substitution is called a solvolysis.

5.2 Trends in leaving group ability



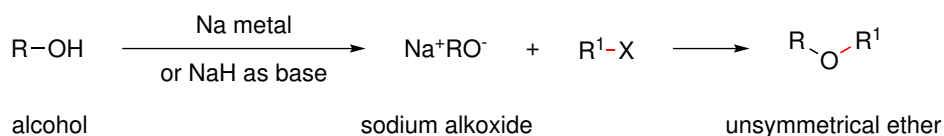
This is found by experiments measuring rates of reactions.

5.3 Nucleophilic Substitution Reactions

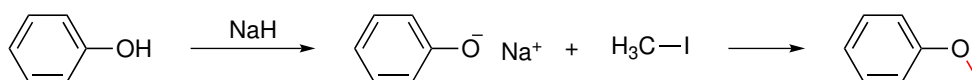
The following nucleophilic substitution reactions are particularly important for organic synthesis.

a) Williamson Ether Synthesis

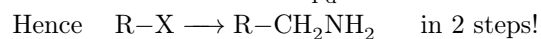
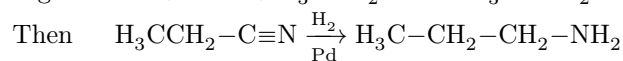
This is a good general method for the preparation of unsymmetrical ethers. It works well with primary alkyl halides ($\text{CH}_3\text{-X}$ and $\text{R-CH}_2\text{-X}$) but is problematic for hindered tertiary alkyl halides ($\text{R}_3\text{C-X}$). In general:



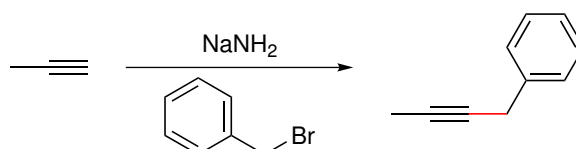
Example



b) Cyanide Anion - Very useful for making C–C bonds



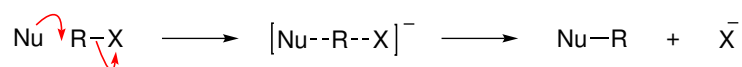
c) Acetylide Anions - Recap!



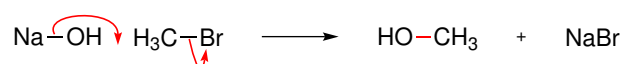
C=C bond formation!

5.4 Bimolecular S_N2 Nucleophilic Substitution Reactions

The S_N2 reaction is a one step process in which the bond to the nucleophile is being formed at the same time as the bond the leaving group is being broken.



E.g.



Kinetics

For the S_N2 reaction, we find the rate to be proportional to both the concentrations of the nucleophile [Nu] and the concentration of the alkyl halide [R–X]. Hence

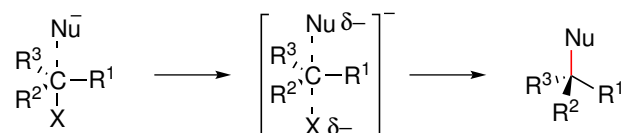
$$\text{Rate} = k[\text{Nu}][\text{R}-\text{X}]$$

2nd order kinetics.

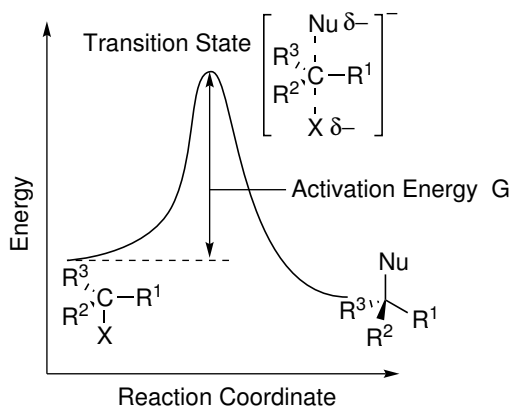
Hence two entities are involved in the rate determining step and the reaction is bimolecular.

Stereochemistry

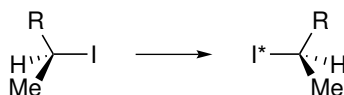
If we start with a chiral haloalkane, inversion of configuration (Walden Inversion) is observed since the new bond is being formed at 180° to the bond that is breaking.



Energy Profile Diagram



The experiment to prove that each $\text{S}_{\text{N}}2$ displacement proceeds with inversion of configuration was carried out by Hughes and Ingold using I^{*128}



The reaction gives a racemic product since the iodide anion I^{*-} reacts equally well with both enantiomers. The optical activity disappears when 50% of the starting iodide has undergone substitution. The measured rates are:

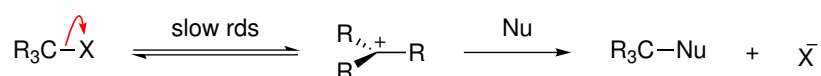
$$\text{Rate of racemisation} = 2 \times \text{rate of exchange of Iodide by } \text{I}^{*128}$$

As expected from the above analysis, $\text{S}_{\text{N}}2$ reactions are favoured by

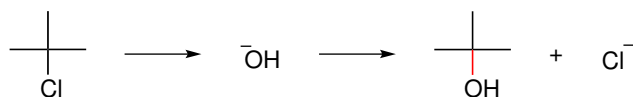
- good nucleophiles
- good leaving groups
- less hindered haloalkane substrates.

5.5 Unimolecular $\text{S}_{\text{N}}1$ Nucleophilic Substitution Reactions

The $\text{S}_{\text{N}}1$ reaction is a two step process consisting of a slow ionisation of the substrate, followed by a rapid attack of the nucleophile.



E.g.



Kinetics

The rate is proportional to the concentration of R_3CX and independent of the nucleophile:

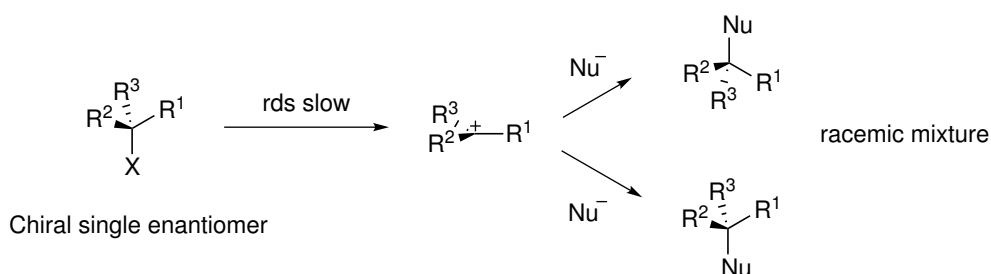
$$\text{Rate} = k[\text{R}_3\text{CX}]$$

2nd order kinetics.

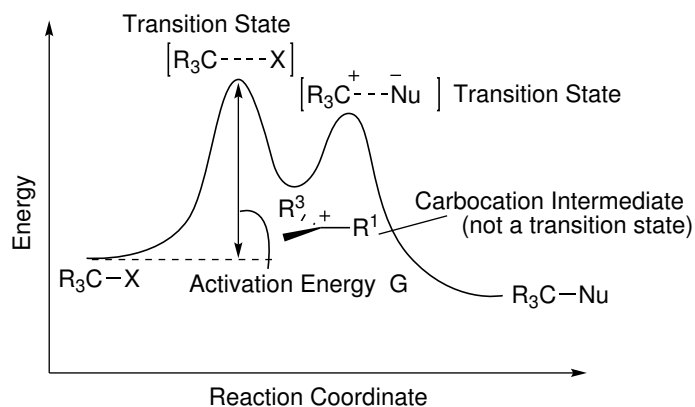
Hence only one entity is involved in the rate determining step and the reaction is unimolecular.

Stereochemistry

If we start with a chiral haloalkane and ionise it by heterolysis, a trigonal planar sp^2 hybridised carbocation intermediate is formed. Since attack of the nucleophile can occur equally from both sides of this planar intermediate, a racemic mixture of the product is formed.

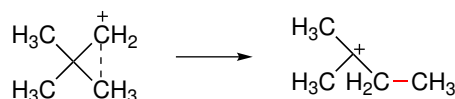


Energy Profile Diagram

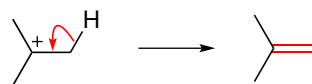


Carbocationic intermediates, unlike transition states, can undergo some competing reactions.

E.g. Rearrangement:



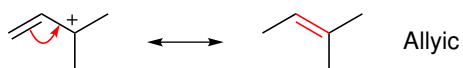
or proton loss (E_1 elimination):



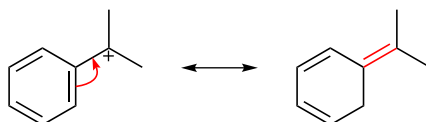
As expected from this analysis, S_N1 reactions are:

- not influenced by the nature of the nucleophile.
- favoured by good leaving groups to form the carbocation. Sometimes Ag^+ is used to favour this pathway: $R_3C-Cl + Ag^+ \longrightarrow R_3C^+ + AgCl$
- favoured by substrates that can generate low energy carbocations.

E.g. Tertiary carbocations via hyperconjugation

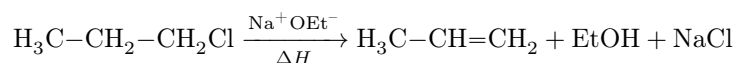


or carbocations stabilised by resonance



6 Elimination Reactions

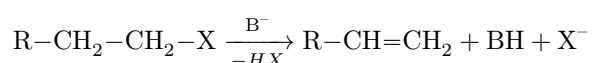
Elimination reactions of HX from haloalkanes provide a useful route for alkene synthesis.



Here, at higher temperatures, sodium ethoxide functions as a base rather than a nucleophile. If necessary more hindered and less nucleophilic bases can be used, e.g. $(\text{CH}_3)_3\text{C}-\text{O}^- + \text{K}^+$. There are many parallels with $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ reactions as there are $\text{E}1$ eliminations and $\text{E}2$ eliminations.

6.1 Bimolecular $\text{E}2$ Eliminations

For the general case of:



Kinetics

The rate is proportional to both the concentration of the haloalkane and base.

$$\text{Rate} = k[\text{RCH}_2\text{CH}_2\text{X}][\text{B}^-]$$

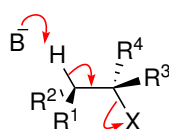
2nd order kinetics

Since both the base and the alkyl halide are involved in the RDS it is a bimolecular reaction.

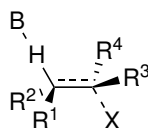
Stereochemistry

$\text{E}2$ elimination reactions are often stereospecific and lead to a single geometrical isomer of an alkene. The conformation in which the base removes the hydrogen and the leaving group is trans coplanar and is favoured in the transition state. This is called the trans anti-periplanar position.

As in $\text{S}_{\text{N}}2$, there is a transition state where bonds are broken and formed in a concerted fashion.



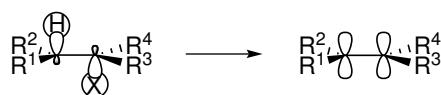
The requirement for a trans anti-periplanar reaction is:



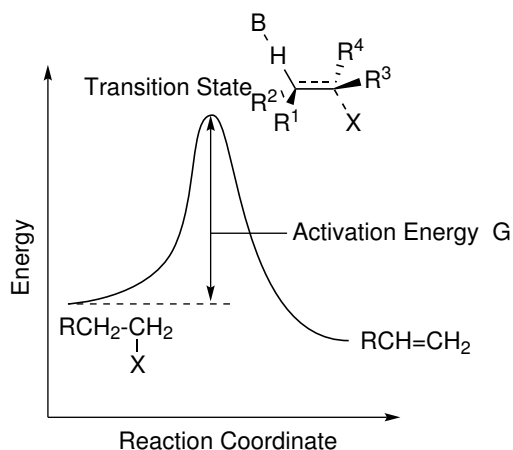
Transition state

- the trans relationship of H and X minimises steric repulsion between B^- and X.
- the coplanar relationship maximises orbital overlap leading to a π bond with perfect sideways overlap of p orbitals.

i.e.

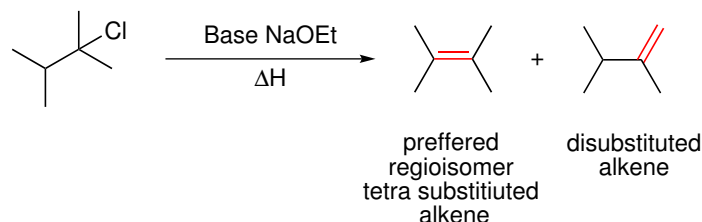


Energy Profile Diagram

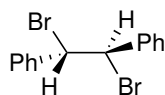


Regioselectivity

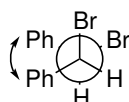
The preferred product of an alkyl halide elimination reaction is the more substituted alkene.



This is because the more substituted alkene places more of the substituents around the double bond at 120° and hence constitutes the lower energy pathway since the transition state resembles the products. The trans antiperiplanar requirement for E2 elimination allows us to predict regioselectivity as well as relative rates. For example in the conformer of:

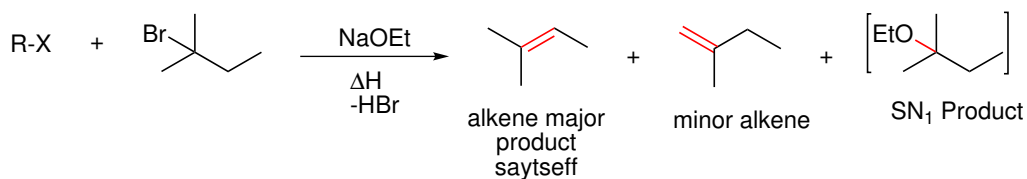


there is unfavourable syn interaction between the two phenyl groups:



This is absent in the opposite conformer and hence the transition state for E2 elimination is higher in energy and the reaction is 50 times slower.

6.2 Unimolecular E1 Elimination



Kinetics

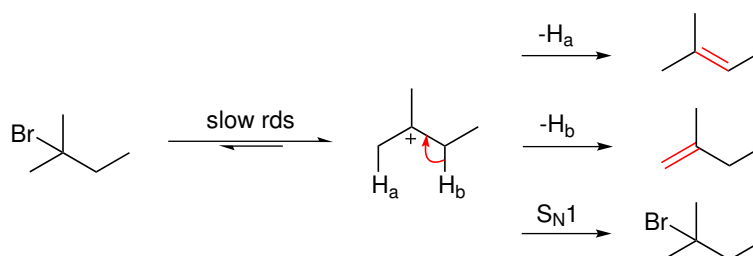
The rate is proportional to substrate concentration $[\text{RX}]$ only and is independent of $[\text{EtO}^-]$.

$$\text{Rate} = k[\text{RX}]$$

1st order kinetics.

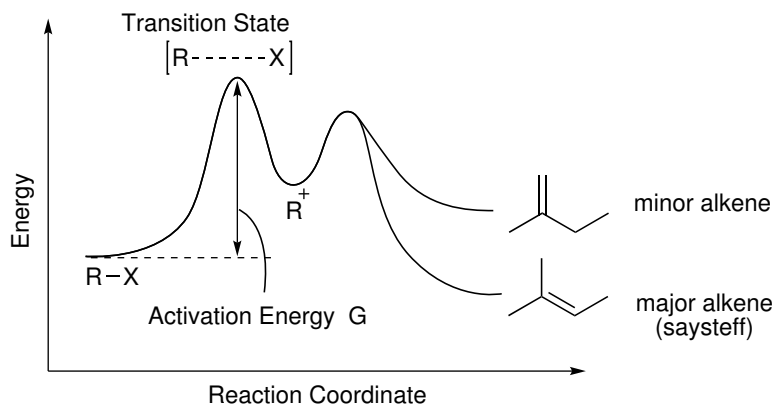
As with $\text{S}_{\text{N}}1$ we have a unimolecular reaction where ionisation of the C–X bond is the RDS.

Mechanism



The base can assist in the fast step of proton removal from the carbocation.

Energy Profile Diagram



Characteristics

E1 eliminations, like $\text{S}_{\text{N}}1$ are favoured when X is a very good leaving group, which promotes heterolysis. Additionally when R^+ is a low energy carbocation and therefore easy to form (e.g. 3° carbocation) or stabilised by delocalisation (e.g. allylic, $\text{C}=\text{C}-\text{C}^+$ or benzylic, $\text{Ph}-\text{C}^+\text{R}_2$)

Note: Nucleophilic substitution can be inhibited by use of a bulky base which is a poor nucleophile.