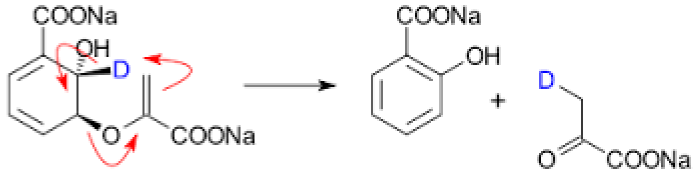
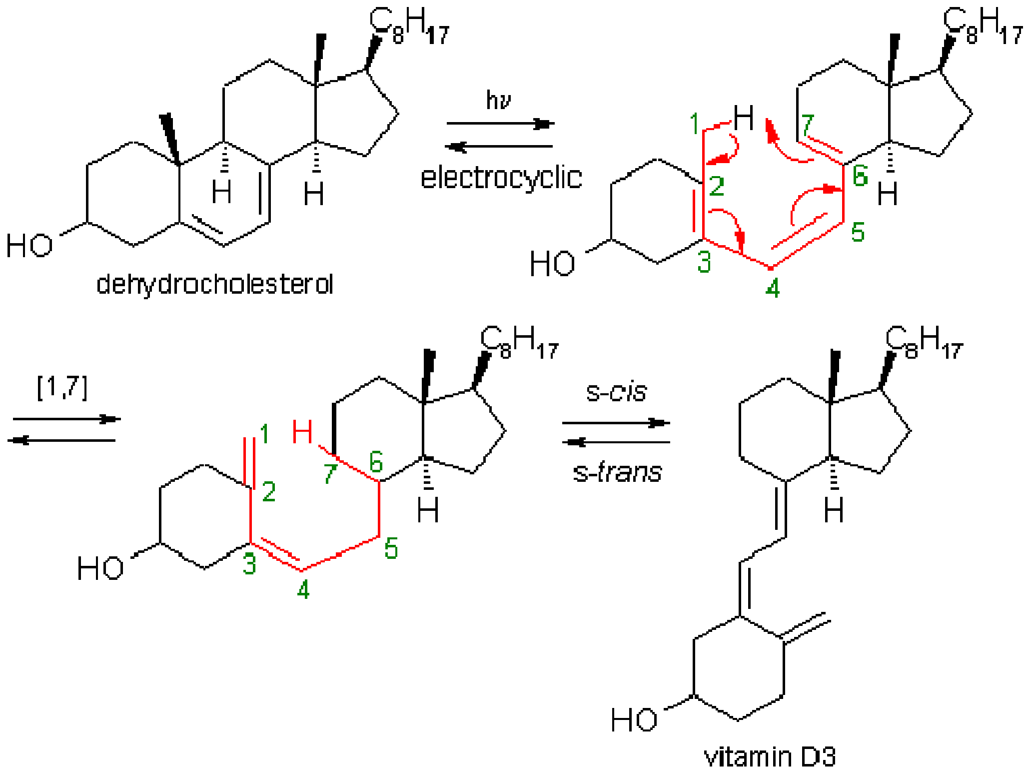
MScCH-06

Vardhman Mahaveer Open University, Kota





Reaction Mechanisms, Pericyclic Reactions, Organic Photochemistry and Stereochemistry

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Reaction Mechanisms, Pericyclic Reactions, Organic Photochemistry and Stereochemistry

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Preface

The present book entitled “Reaction Mechanisms, Pericyclic Reactions, Organic Photochemistry and Stereochemistry” has been designed so as to cover the unit-wise syllabus of MScCH-06 course for M.Sc. Chemistry (Final) students of Vardhman Mahaveer Open University, Kota. The basic principles and theory have been explained in simple, concise and lucid manner. Adequate examples, diagrammes, photographs and self-learning exercises have also been included to enable the students to grasp the subject easily. The unit writers have consulted various standard books and internet as their reference on the subject and they are thankful to the authors of these reference books.

Unit – 1

Reaction Intermediates - Formation, stability, structure, detection and reaction of carbonium ions, carbanions and free radicals

Structure of unit

1.0 Objective

An organic reaction mechanism is the detailed study of the actual steps by means of which a reaction takes place. Thus is tell us about the number of steps involved and their sequence. Actual isolation of one or more intermediates is the most concrete evidence one can obtain the mechanism of the reaction.

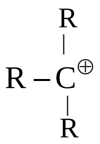
1.1 Introduction

In a chemical reaction, reactants may be converted into product in one step or in more than one step. When a reaction occurs in a single step no intermediates are formed. Intermediate lies between two highest energy states and has lower energy than both of the high energy states.

In intermediate the bonds are completely broken in the reactants and hence the system has definite geometry. It can be isolated in same cases.

1.2 Carbonium ion

An organic species which has carbon atom bearing only six electrons in its outer most shell and has a positive charge is called a carbocation or carbonium ion.



$$R-\overset{\displaystyle R}{\underset{\displaystyle R}{C^{\oplus}}}$$

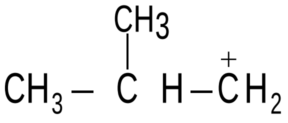
R = H or alkyl or aryl group.

Carbocations are of three types –*p*, *s* and *t* or 1^o, 2^o, 3^o. Depending upon which type of carbon atom carries the positive charge, it is correspondingly denoted as *p*, *s* or *t* carbocation. For example, if the positive charge is present on primary carbon atom it is called *p* or 1^o-carbocation, and so on. Various examples of carbocations are :

Primary-Carbocations

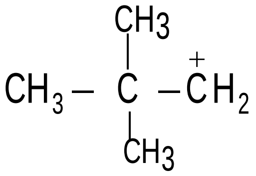
$$\overset{+}{C}H_3 \quad CH_3-\overset{+}{C}H_2 \quad CH_3-CH_2-\overset{+}{C}H_2 \quad CH_3CH_2-CH_2-\overset{+}{C}H_2$$

Methyl ethyl propyl butyl



$$CH_3-\overset{CH_3}{\overset{|}{C}}H-\overset{+}{C}H_2$$

Isobutyl



$$CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-\overset{+}{C}H_2$$

neopentyl

$$C_6H_5-\overset{+}{C}H_2$$

benzyl

$$CH_2=CH-\overset{+}{C}H_2$$

allyl

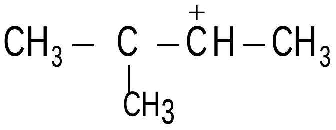
Secondary-carbocations

$$CH_3-\overset{+}{C}H-CH_3$$

Isopropyl

$$CH_3-CH_2-\overset{+}{C}H-CH_3$$

s-butyl



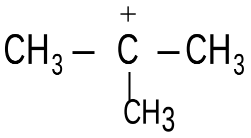
$$CH_3-\underset{\underset{CH_3}{|}}{C}-\overset{+}{C}H-CH_3$$

s-isoamyl

$$C_6H_5-\overset{+}{C}H-C_6H_5$$

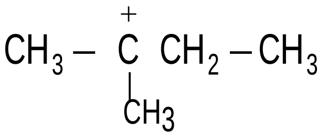
benzhydryl

Tertiary-Carbocations



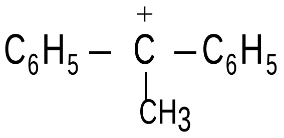
$$CH_3-\underset{\underset{CH_3}{|}}{\overset{+}{C}}-CH_3$$

t-butyl



$$CH_3-\underset{\underset{CH_3}{|}}{\overset{+}{C}}CH_2-CH_3$$

t-amyl

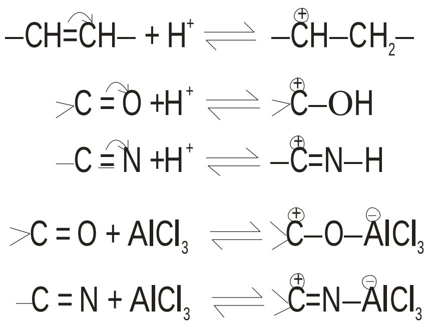


$$C_6H_5-\underset{\underset{CH_3}{|}}{\overset{+}{C}}-C_6H_5$$

trityl

1.2.1 Formation of carbonium ion

(i) **By the protonation of unsaturated compounds:** Olefins, carbonyl compounds and nitriles when dissolved (treated) with a proton-donating solvent or Lewis acid form carbonium ions.



$$-CH{=}CH- + H^{+} \rightleftharpoons -\overset{\oplus}{C}H-CH_2-$$

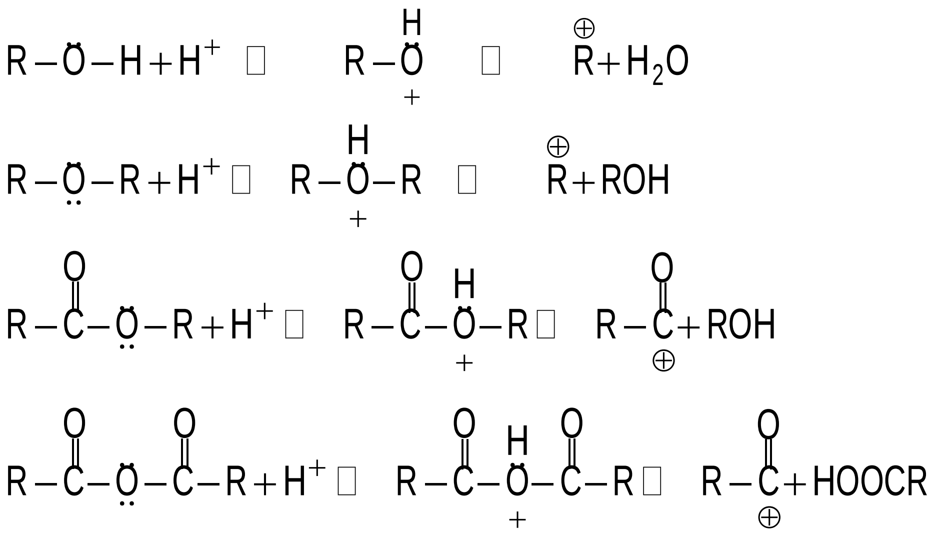
$$>C=O + H^{+} \rightleftharpoons >\overset{\oplus}{C}-OH$$

$$-C\equiv N + H^{+} \rightleftharpoons -\overset{\oplus}{C}{=}N-H$$

$$>C=O + AlCl_3 \rightleftharpoons >\overset{\oplus}{C}-O-\overset{\ominus}{A}lCl_3$$

$$-C\equiv N + AlCl_3 \rightleftharpoons >\overset{\oplus}{C}{=}N-\overset{\ominus}{A}lCl_3$$

(iii) By the protonation of an atom having long pair of electrons : Organic compounds containing lone pair of electrons on an atom, especially oxygen, form carbonium ions when treated with acid, e.g.



$$R-\ddot{O}-H+H^{+} \rightleftharpoons R-\underset{+}{\overset{H}{\ddot{O}}} \rightleftharpoons \overset{\oplus}{R}+H_2O$$

$$R-\ddot{\underset{..}{O}}-R+H^{+} \rightleftharpoons R-\underset{+}{\overset{H}{\ddot{O}}}-R \rightleftharpoons \overset{\oplus}{R}+ROH$$

$$R-\overset{O}{\overset{\|}{C}}-\underset{..}{O}-R+H^{+} \rightleftharpoons R-\overset{O}{\overset{\|}{C}}-\underset{+}{\overset{H}{\ddot{O}}}-R \rightleftharpoons R-\underset{\oplus}{\overset{O}{\overset{\|}{C}}}+ROH$$

$$R-\overset{O}{\overset{\|}{C}}-\underset{..}{\ddot{O}}-\overset{O}{\overset{\|}{C}}-R+H^{+} \rightleftharpoons R-\overset{O}{\overset{\|}{C}}-\underset{+}{\overset{H}{\ddot{O}}}-\overset{O}{\overset{\|}{C}}-R \rightleftharpoons R-\underset{\oplus}{\overset{O}{\overset{\|}{C}}}+HOOCR$$

(iii) From direct ionisation :

$$\underset{\text{t–butly chloride}}{(CH_3)_3C-Cl} \longrightarrow \underset{\text{t–butyl cation}}{(CH_3)_3\overset{+}{C}} + Cl^{-}$$

$$CH_2=CH.CH_2Cl \longrightarrow CH_2=CH-\overset{+}{C}H_2+Cl^{-}$$

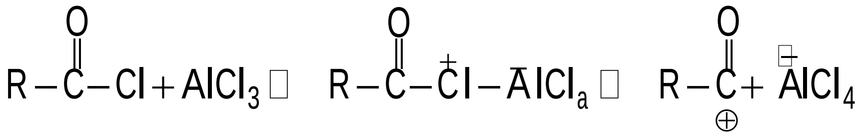
$$C_6H\ CH_2-Cl \longrightarrow C_6H_5\overset{+}{C}H_2+Cl^{-}$$

$$\underset{\substack{\text{triphenyl}\\ \text{chloride (white solid)}}}{(C_6H_6)_3C-Cl} \xrightleftharpoons{\text{liquid } SO_2} \underset{\substack{\text{Triphenylmethyl}\\ \text{cation}\\ \text{(orange solution)}}}{(C_6H_5)_3C^{+}} + Cl^{-}$$

(iv) By the protonation of alkyl or acyl halides : Alkyl or acyl halides when treated with a proton-donating solvent or Lewis acid form carbonium ions.

$$R-X+H^{+} \rightleftharpoons R-\overset{+}{X}-H \rightleftharpoons \overset{\oplus}{R}+H-X$$

$$R-Cl+AlCl_3 \rightleftharpoons R-\overset{+}{C}l-\overset{-}{A}lCl_a \rightleftharpoons \overset{\oplus}{R}+\overset{\ominus}{A}lCl_4$$



$$R-\overset{\overset{O}{\|}}{C}-Cl+AlCl_3 \rightleftharpoons R-\overset{\overset{O}{\|}}{C}-\overset{+}{C}l-\overset{-}{A}lCl_a \rightleftharpoons R-\underset{\oplus}{\overset{\overset{O}{\|}}{C}}+\overset{\ominus}{A}lCl_4$$

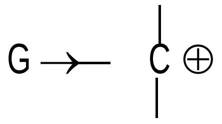
(v) By the decomposition of diazonium salts : Aliphatic and aromatic diazonium salts decompose under suitable conditions to form carbonium ions.

$$\left[R-\ddot{N}=N^{+} \rightarrow R-\overset{+}{N}\equiv N\right]Cl^{-} \rightleftharpoons \overset{\oplus}{R}+N_a+Cl^{-}$$

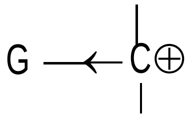
1.2.2 Stability of carbonium ion

According to laws of physics, the stability of a charged system is increased by dispersal of the charge. Therefore, any factor that tends to spread out the positive charge of the electron deficient carbon and distribute it over the rest of the ion must stabilize a carbonium ion.

Consider a substituent G, attached to an electron-deficient carbon. Following two situations may arise.



When G is electron releasing,
it disperses charge and
hence stablized cation



When G electron-withdrawing,
it intensifies charge and
destabilizes cation

An electron-releasing substituent tends to reduce the positive charge at the electron-deficient carbon; and the substituent itself becomes some what positive. This dispersal of the charge stabilizes the carbonium ion. Conversely, an electron-withdrawing group tends to intensify the positive charge on the electron deficient carbon, and hence makes the carbonium ion less stable.

Further, more that possibility for the dispersal of the charge more will be the stability of the carbonium ion. Two effects are mainly responsible for the dispersal (delocalisation) of the charge and thus stability of the carbonium ion.

(a) Hyperconjugation : This effect explains the stability of alkyl carbonium ions.

(b) Resonance : This effect explains the stability of all types of carbonium ions other than the alkyl. Since in resonance the positive charge is delocalised over adjacent atoms, carbonium ions showing resonance are far more stable than those in which resonance is not playing any part. This explains why alkyl and benzyl carbonium ions are more stable than even the t-butyl carbonium ion.

On the basis of the relative stabilities, carbonium ions may be classified into two classes, namely (i) transient (short lived) carbonium ions, and (ii) stable carbonium ions.

(i) Transient (short lived) carbonium ions :

These carbonium ions lack extensive resonance stabilization and are known only as transitory intermediates in certain organic reactions. These are very reactive and combine readily with any molecule that can give a pair of electrons. Typical examples of transient carbonium ions are alkyl (primary, secondary and tertiary). The relative stability of the alkyl carbonium ions follows the order :

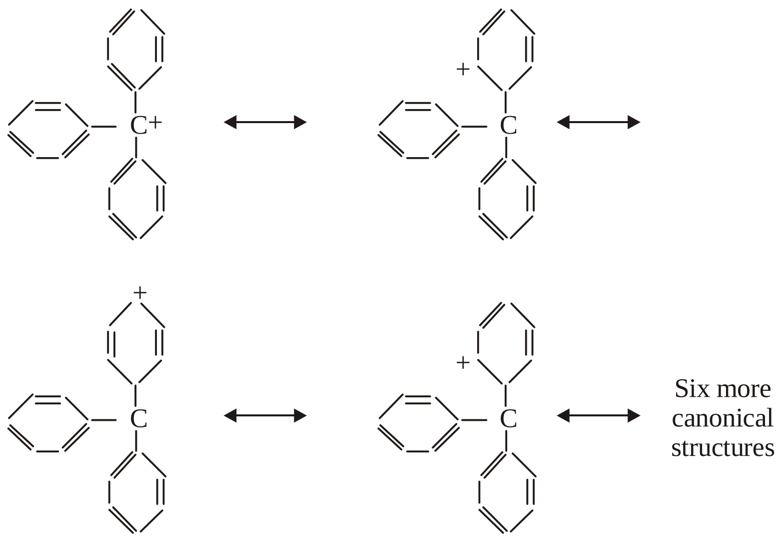
$$\text{Tertiary} > \text{Secondary} > \text{Primary}$$

i.e., $(CH_3)_3\overset{\oplus}{C} > (CH_3)_2\overset{\oplus}{C}H > CH_3\overset{\oplus}{C}H_2$

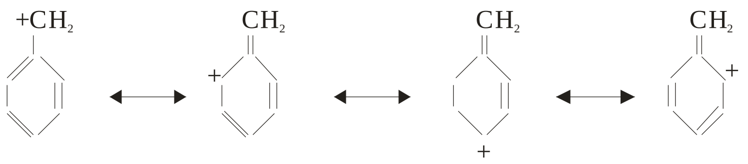
The above order of stability of the simple alkyl carbonium ions is explained in terms of hyperconjugation (no-bond resonance) which delocalizes the positive charge over ten different canonical structures in t-butyl carbonium ion, over seven in sec-isopropyl carbonium ion, and only over four in primary ethyl carbonium ion.

(ii) Stable carbonium ions :

These carbonium ions are so stable that they can be isolated and studied. The stability of these carbonium ions is explained in terms of resonance; that is, the positive charge on the ion is actually not localized on one carbon atom, but rather is distributed uniformly throughout the several possible positions (carbon atoms). For example triaryl carbonium ions, the positive charge of which is not localized on the central carbon atom, but is distributed uniformly throughout the three adjacent aromatic rings.



Benzyl and allyl cations are more stable than simple alkyl carbonium ions because of the more effective stabilization of their resonance hybrids through the following canonical structures.

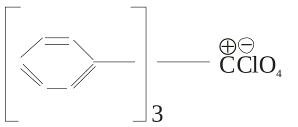


Canonical structures of the benzyl cation

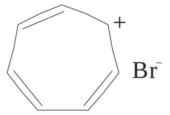
$CH_2 = CH - CH_2 \longleftrightarrow \overset{+}{C}H_2 - CH = CH_2$

Canonical Structures of the allyl cation

Some of the carbonium ions are so stable that even their solid salts are known, *e.g.*, triphenylmethyl perchlorate exists a red crystalline solid, while tropylium bromide is a yellow solid.

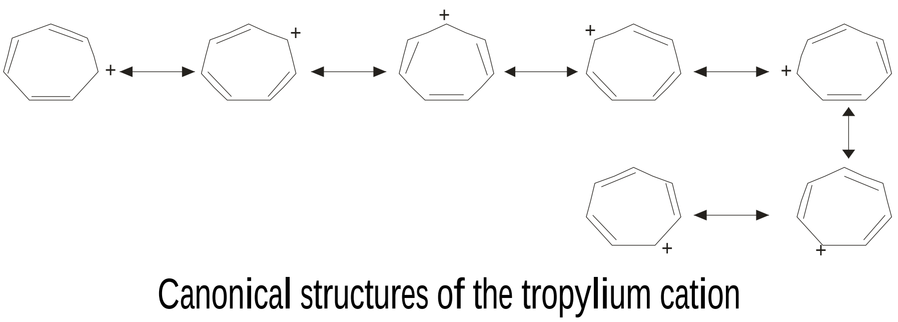


Tripheonylmethyl perchlorate



Tropylium bromide

The seven completely equivalent canonical structures for the tropylium ion hybrid are illustrated below.



Canonical structures of the tropylium cation

Actually tropylium cation is the most stable carbonium ion. It is so stable that its reaction with water, alcohols, etc. is very slow.

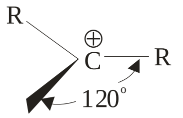
Some of the carbonium ions in their order of stability are given below.

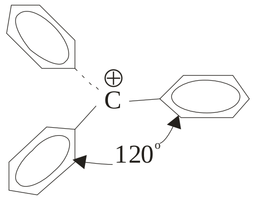
$$\text{Tropylium cation} > \underset{\substack{\text{Triphenyl}\\ \text{methyl cation}}}{(C_6H_5)_3\overset{+}{C}} > \underset{\substack{\text{Benzyl}\\ \text{cation}}}{C_6H_3\overset{+}{C}H_2} > \underset{\substack{\text{Allyl}\\ \text{cation}}}{CH_2 = CH - \overset{+}{C}H_2}$$

$$\underset{\substack{\text{tert}-\text{Butyl}\\ \text{cation}}}{(CH_3)_3\overset{+}{C}} > \underset{\substack{\text{Isopropyl}\\ \text{cation}}}{(CH_3)_2\overset{+}{C}H} > \underset{\substack{\text{Ethyl}\\ \text{cation}}}{CH_3\overset{+}{C}H_2} > \underset{\substack{\text{Methyl}\\ \text{cation}}}{\overset{+}{C}H_3}$$

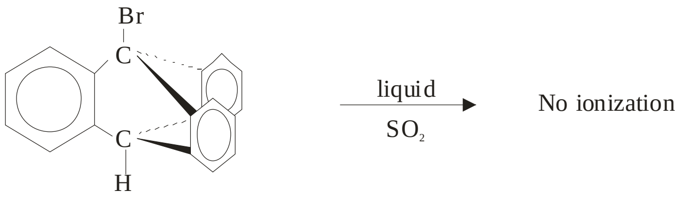
1.2.3 Structure of Carbonium ion

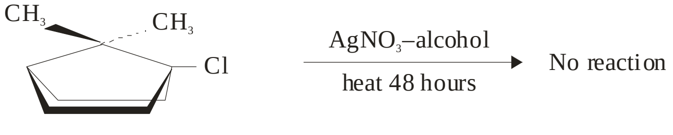
Structurally, the carbon atom of a carbonium ion is sp^2 hybridised. The three sp^2 hybrid orbital are utilized in forming bonds to the three substituents, the remaining unused *p* orbital remains vacant. The carbonium ion thus has a flat structure having all the three bonds in one plane with the bond angle of 120° between them. There is a lot of evidence to show that carbonium ions are planar structures, as illustrated below.





Such planar structure, with their 120° geometry and sp^2 hybridization are the necessary conditions for the stabilization of the carbonium ion through resonance or hyperconjugation. If anyhow the structure of a molecule is such as to preclude 120° geometry and sp^2 hybridization in the corresponding carbonium ion, the ion fails to form. This explains that the triphenylchloromethane (in liquid SO_2) and the ordinary t-alkyl halides (in presence of silver nitrate) ionize easily to form the triphenylmethyl cation and a t-butyl cation.





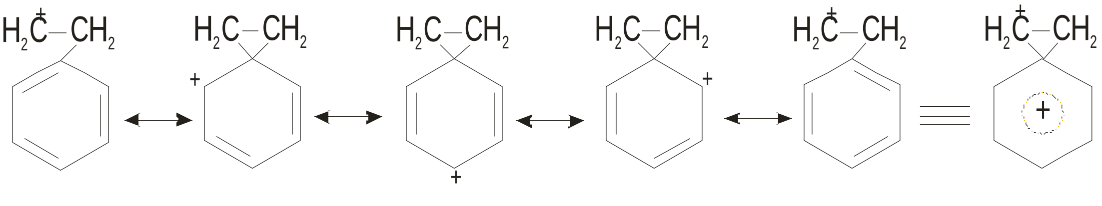
1-Chloroapocamhane

The reason why such bridged structures fail to generate carbonium ions is that the rigid structural constraint of their rings makes geometrically impossible for a resulting carbonium ion to have the planar structure required for its stabilization.

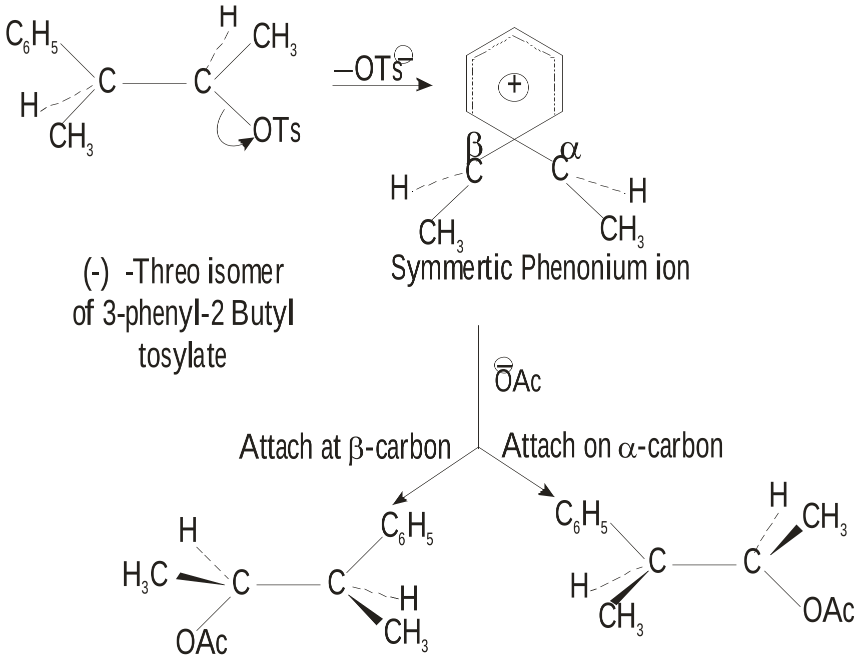
The planar nature of carbonium ion can further be proved by treating an optically active substrate (compound having asymmetric carbon atom) with a nucleophilic reagent when racemic mixture is formed. The formation of racemic mixture can be explained only when the carbonium ion (intermediate) has a planar structure. Since carbonium ion is a planar structure, the nucleophilic reagent is equally free to attack the positive carbon atom from either side of the plane (i.e., from above or below) with the result an equimolar mixture-of d and *l*-forms (racemic mixture) will be obtained.

Bridged or non-classical carbonium ions : Carbonium ions which are stabilised by the movement of either a lone pair of electrons or π–electrons, in conjugation, to the positively charged carbon atom to form a new π-bond. Such carbonium ions are called classical carbonium ions. However, formation of classical carbonium ions does not explain some reactions and thus it becomes necessary to write canonical forms involving the movement of a π-pair of electrons or even electrons to form a new σ-bond ; the carbonium ion intermediates formed in such cases are known as non-classical or bridged carbonium ions.

For example,



A strong evidence for the formation of non-classical carbonium ions is provided by the remarkable stereospecificity observed in the solvolysis of optically active threo and erythro-3-phenyl-2-butyl tosylates in glacial acetic acid medium. If (-)-threo isomer undergoes acetolysis, the product formed is a



(-) -Threo isomer of 3-phenyl-2 Butyl tosylate

Symmertic Phenonium ion

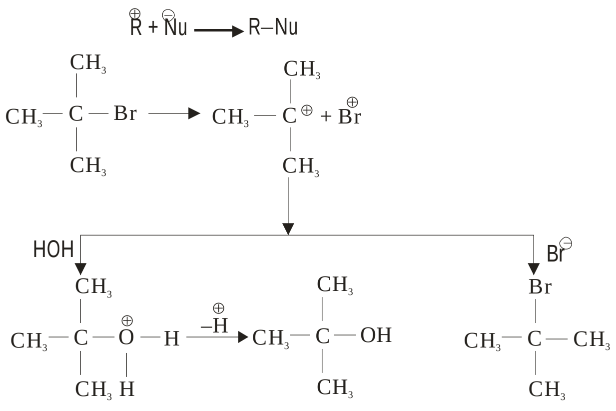
Racemic threoacetate

Racemic mixtute of threo isomer with a negligible amount of erythro isomer. The exclusive formation of threo isomer in racemic form can only be explained by the formation of bridged head or non-classical carbonium ion as intermediate. The latter may be attacked by the solvent (acetic acid) equally at either of the carbon atoms equally to form enantiomeric pair.

1.2.4 Reactions of carbonium ion

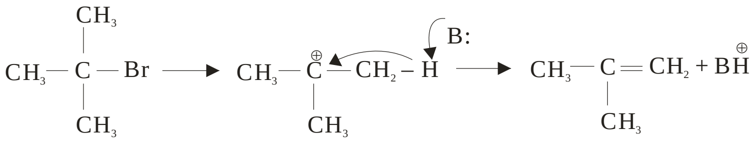
(i) Combination with a nucleophile, *i.e.,* SN^1 reaction

A carbocation may combine with a nucleophile to form a new bond. Examples are :


$\overset{\oplus}{R} + \overset{\ominus}{Nu} \longrightarrow R\text{–}Nu$

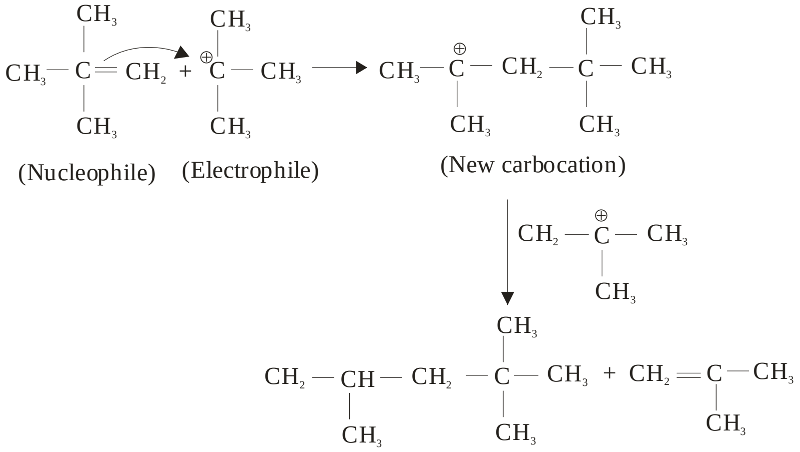
(ii) Elimination of a proton from the β-carbon (*E^1 reactions)* :

A carbocation may loss a proton form the β-carbon to form an alkene. For example the conversion of tertiary alkyl halides into alkene in the presence of base.



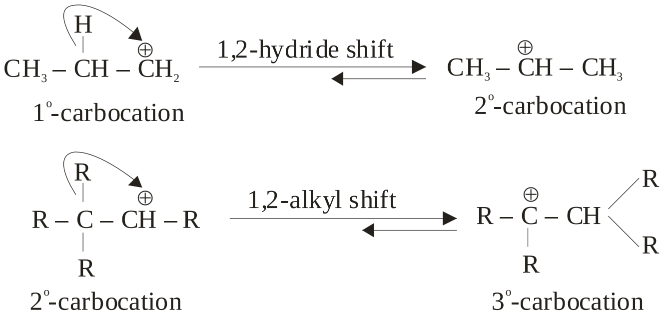
(iii) Addition to unsaturated compound :

A carbocation may react with an alkene to produce another carbocation. This reaction is mainly given by isobutene.



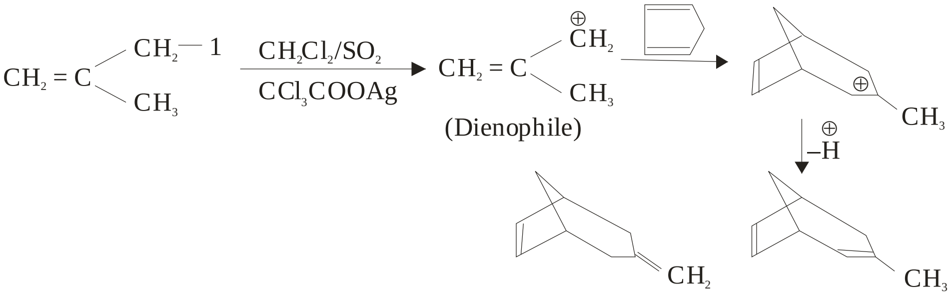
(iv) Molecular Rearrangements :

A carbocation undergoes rearrangement to produce a more stable carbocation. Rearrangements can occur by shift of an alkyl, vinyl or aryl group or hydrogen atom. Rearrangement creates a new carbon with the positive charge located on the atom from which the migration occurred. 1, 2-shifts are the most common type of rearrangements.



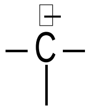
(v) Cycloaddition Reactions :

(4 + 2) cycloaddition reaction take place between diene and dienophile. In most of the cases dienophiles are neutral. For example the addition of 2-methyl allyl carbocation to cyclopentadiene .



1.3 Carbanions

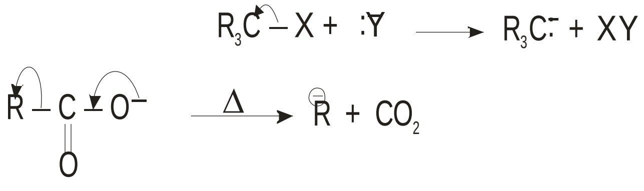
Carbanion act as nucleophiles.Carbanions are anions, i.e., negatively charged species in which a carbon carries three bonds and a lone pair of electrons, thus making the carbon atom negatively charged. So carbanion may be represented as :



$$-\overset{\ominus}{\underset{|}{C}}-$$

1.3.1 Formation of carbanions

(i) By Removal of an atom or group from carbon :



$$R_3C-X + :Y \longrightarrow R_3C:^- + XY$$

$$R-\underset{\underset{O}{\|}}{C}-O^- \xrightarrow{\Delta} \overset{\ominus}{R} + CO_2$$

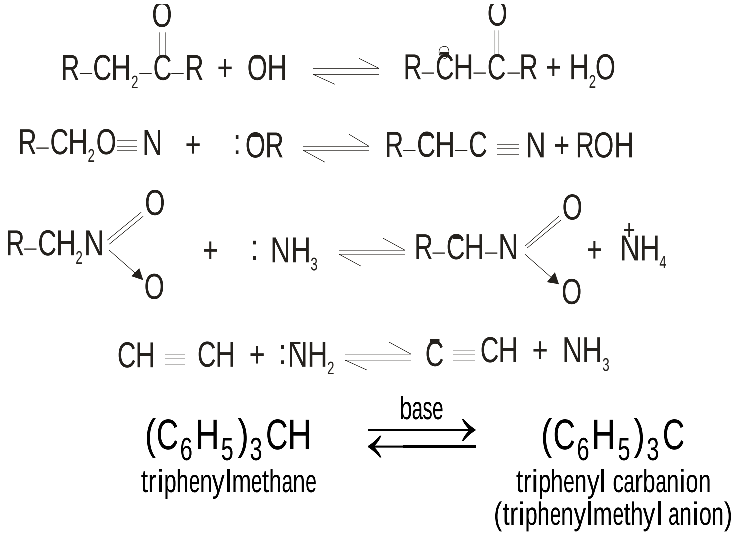
$$\underset{\text{trityl chloride}}{(C_6H_5)_3C-Cl} \xrightarrow{Na/Hg} (C_6H_5)_3\bar{C}\,\overset{+}{Na}$$

(ii) By Abstraction of a proton by a base :

$$CH_3-CHO \xrightarrow[-H^+]{NaOH} \bar{C}H_2-CHO$$

$$(C_6H_5)_3C-H \xrightarrow[-NH_2]{NaNH_2} (C_6H_5)_3\bar{C}N\overset{+}{a}$$

(iii) Miscellaneous reactions :



$$R-CH_2-\overset{\overset{O}{\|}}{C}-R + OH \rightleftharpoons R-\overset{\ominus}{C}H-\overset{\overset{O}{\|}}{C}-R + H_2O$$

$$R-CH_2O\equiv N + :OR \rightleftharpoons R-CH-C\equiv N + ROH$$

$$R-CH_2N\genfrac{}{}{0pt}{}{\nearrow O}{\searrow O} + :NH_3 \rightleftharpoons R-\bar{C}H-N\genfrac{}{}{0pt}{}{\nearrow O}{\searrow O} + \overset{+}{N}H_4$$

$$CH\equiv CH + :\bar{N}H_2 \rightleftharpoons \bar{C}\equiv CH + NH_3$$

$$(C_6H_5)_3CH \overset{base}{\rightleftharpoons} (C_6H_5)_3C$$

triphenylmethane

triphenyl carbanion
(triphenylmethyl anion)

1.3.2 Stability of carbanions

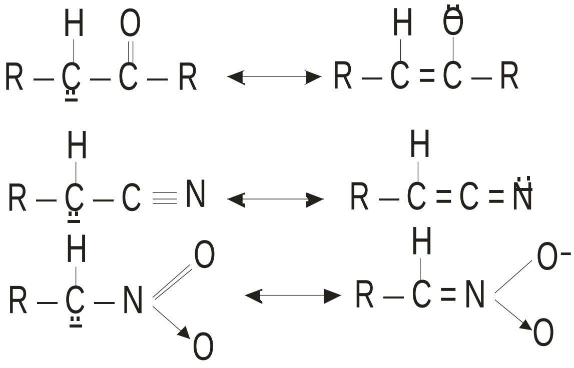
Like carbonium ion, there are two types of carbanions, *viz*. **stable and transient,** classified on the basis of their existence. Stability of carbanions are increased when the negative charge spread over a number of resonating structures. More the possibility of spreading the negative charge over more resonating structures, more the carbanion will be stable.

The possibility of resonance in a carbanion ion, in turn is due to the following two structural features.

(i) The presence of electron withdrawing (-I) group such as $-C\equiv N, -NO_2, > C=O$, etc, stabilizes a carbanion by delocalizing the negative charge. Conversely presence of electron releasing group such as an alkyl group increase the negative charge on the carbon atom of carbanion and hence carbanion becomes unstable.

(ii) The presence of double bond or an aromatic ring in conjugation with the carbon atom having negative charge stabilizes the carbanion by resonance.

The transient carbanions stabilize themselves by distributing their negative charge over a three-atom hybrid. In these examples, the resonance is possible due to the presence of –I group like $-NO_2, -C\equiv N, C=O$.

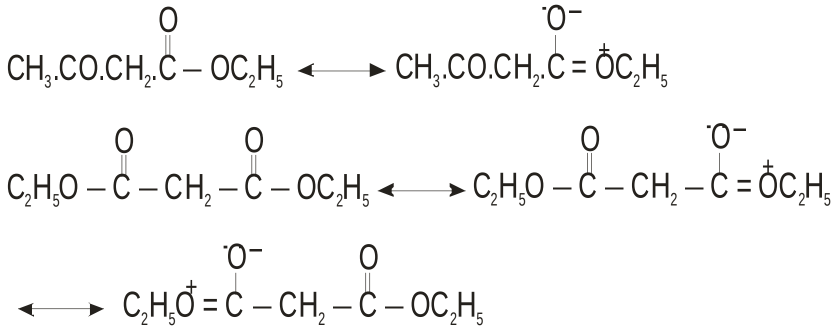


The stabilization of these carbanions *via* resonance shows the hydrogen atoms on the carbon atoms adjacent to unsaturated groups (*i.e.* α-hydrogen atoms) are more acidic in nature than those of ordinary C-H bonds.

With reference to the carbanion stability it is interesting to note that although acetylacetone, ethylacetoacetate, and ethylmalonate possess a ketonic group, their carbanion stability follows the following order

$$CH_3.CO.\overset{-}{C}H.COCH_3 > CH_3.CO-\overset{-}{C}H-COOC_2H_5$$

$$> C_2H_5O_2C.\overset{-}{C}H.CO_2C_2H_5$$

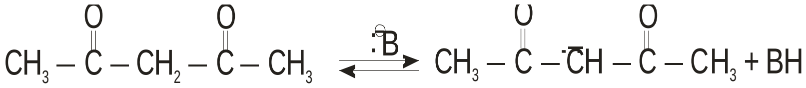


$$CH_3.CO.CH_2.\overset{\overset{O}{\|}}{C}-OC_2H_5 \longleftrightarrow CH_3.CO.CH_2.\overset{\overset{\cdot O^-}{|}}{C}=\overset{+}{O}C_2H_5$$

$$C_2H_5O-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-OC_2H_5 \longleftrightarrow C_2H_5O-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{\cdot O^-}{|}}{C}=\overset{+}{O}C_2H_5$$

$$\longleftrightarrow C_2H_5\overset{+}{O}=\overset{\overset{\cdot O^-}{|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-OC_2H_5$$

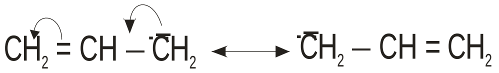
On the other hand, since there is no such stabilizing group (ester) in acetylacetone it can easily eliminate proton on approach of a Lewis base.



$$CH_3-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-CH_3 \xrightleftharpoons{:\overset{\ominus}{B}} CH_3-\overset{\overset{O}{\|}}{C}-\overset{-}{C}H-\overset{\overset{O}{\|}}{C}-CH_3+BH$$

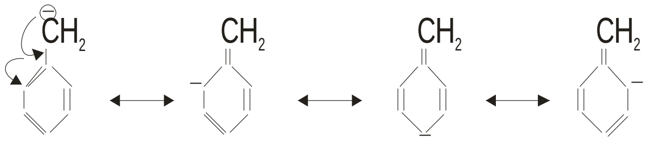
This comparison clearly exhibits the difference between the >C=O group of a ketone and an ester.

Similarly, allyl and benzyl carbanions are stabilized by means of resonance.



$$CH_2 = CH - \overset{-}{C}H_2 \longleftrightarrow \overset{-}{C}H_2 - CH = CH_2$$

Allyl carbanion

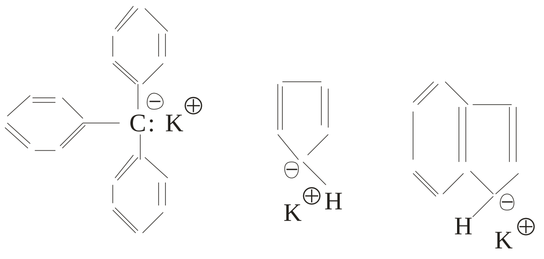


Stabilisation of benzyl carbanion

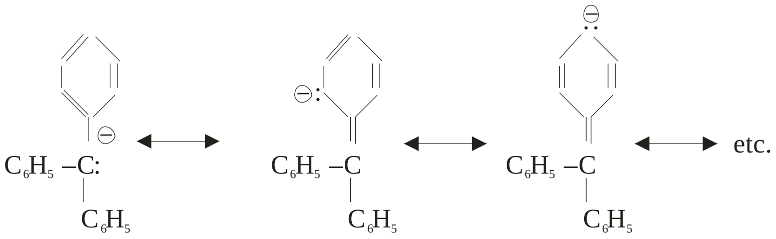
Further greater the *s* character of the carbon atom having negative charge, greater will be its stability. It is evident from the following relative stability of the carbanions.

$$\underset{\text{50\% s-character}}{R-C\equiv\bar{C}} > \underset{\text{33\% s-character}}{R_2C=\bar{C}R} > \underset{\text{25\% s-character}}{R_3C-\bar{C}H_2}$$

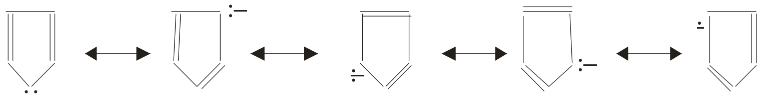
Some carbanions are so stable that their solid stable are known, *e.g.,* sodium or potassium salts of triphenylmethyl, cyclopentadienyl, and indenyl anions.



Triphenymethyl potassium　Cyclopentadienyl potassium　Indenyl postassium



Canonical structures of triphenylmethyl anion hybrid



Canonical structures of the cyclopentadienyl anion hybrid

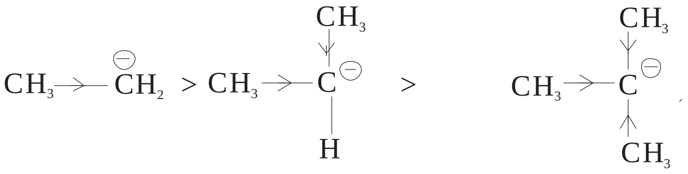
The relative order of stability of some anions is as follows.

Phenyl > Cyclopropyl > Methyl > Ethyl > *n*-Propyl > Isopropyl > Isobutyl > Cyclobutyl, etc.

The stability order of alkyl carbanion are given below :

Primary carbanion > Sec. carbanion > Tert. Carbanion

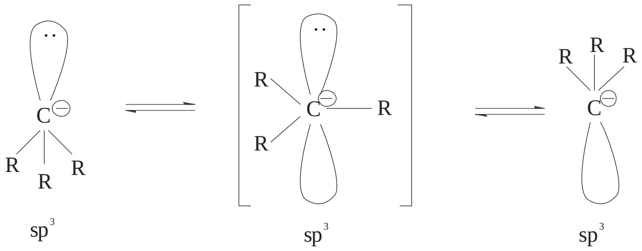
Which is reverse to the order of stability of free-radicals and carbonium ions. This can be explain on the basis of hyperconjugation. Increased number of alkyl group (+ I effect causing groups) at the carbon carrying a negative charge decreases the stability by increasing the electron density still further and thus hindering hyperconjugation.



Relative order of stability of carbanions

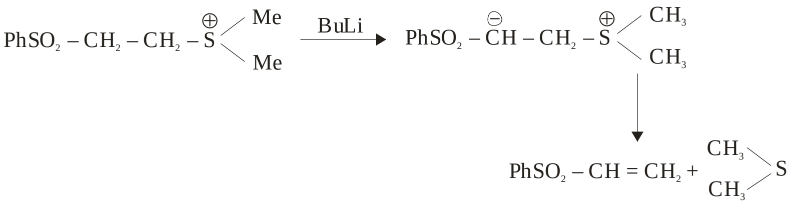
1.3.3 Structure of carbanion

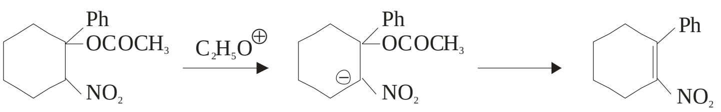
The central atom is *sp*^{3} hybridised; there *sp*^{3} orbitals forming three sigma bonds whereas the lone pair resides in the fourth *sp*^{3} orbital. Thus their geometry is tetrahedral or trigonal pyramidal like ammonia, bond angle being 109.5^o. Between these two extreme geometrical set ups, a transition state is formed in which the electron pair resides in *p*-orbital. The in transition state, the central carbon becomes *sp*^{2} hybridised.



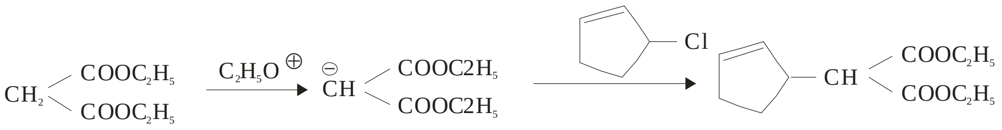
1.3.4 Reactions of carbanions :

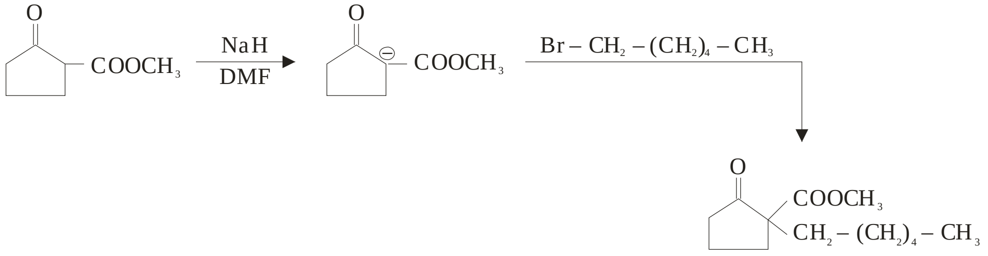
(i) Elimination reactions :

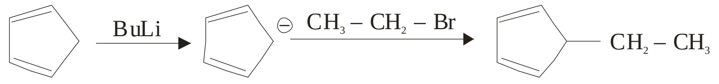




(ii) Substitution reactions :

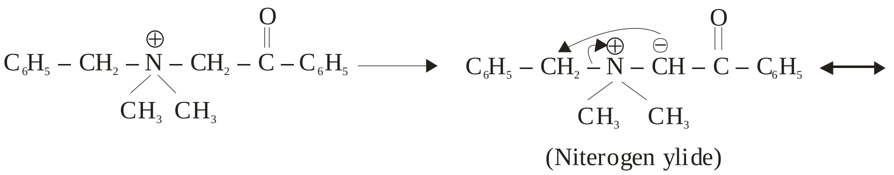


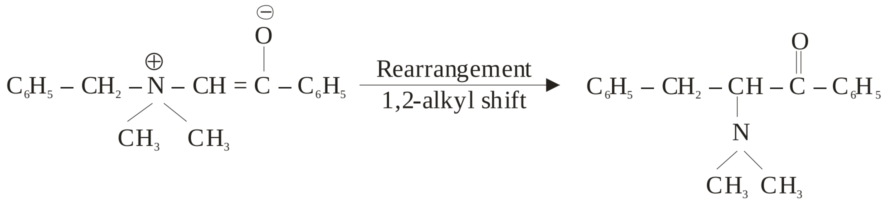




$$CH\equiv CH \xrightarrow{NaNH_2} CH\equiv \overset{\ominus}{C} \xrightarrow{CH_3-CH_2-Br} CH\equiv C-CH_2-CH_3$$

(iii) Rearrangement reaction :

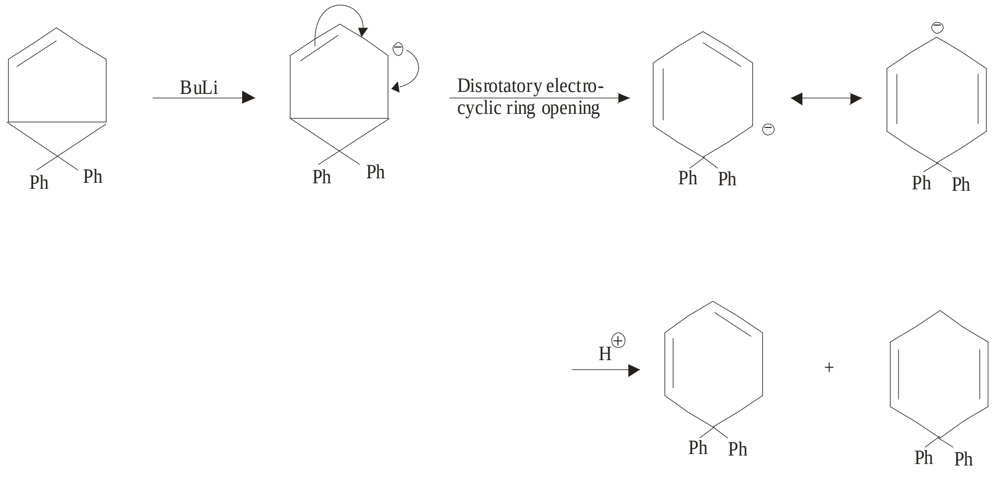




(iv) Oxidation :

$$Ph_3CH \xrightarrow{Na} Ph_3\overset{-}{C}\overset{\oplus}{N}a \xrightarrow{O_2} Ph_3C$$

(v) Electrocyclic reaction :



1.4 Free Radicals

An atom or group possessing an odd or unpaired electron is called free radical. They are paramagnetic, electrically neutral and behave like electrophiles. These are formed by hemolytic fission of the covalent bond

1.4.1 Formation of free radicals

(i) From thermal reaction :

$$(CH_3)_4Pb \xrightarrow{\Delta} 4\,\dot{C}H_3 + \underset{\text{(mirror)}}{Pb}$$

$$C_6H_5CO-O-O-COC_6H_5 \rightarrow 2C_6H_5CO\dot{O} \rightarrow 2C_6H_5 + 2CO_2$$

$$CH_3-N=N-CH_3 \xrightarrow{300^0} 2\dot{C}H_3 + N_2$$

(ii) From photochemical Reactions :

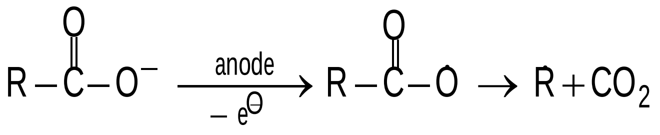
$$CH_3COCH_3 \xrightarrow{h\nu} \dot{C}H_3 + \dot{C}OCH_3$$

$$2CH_3 \rightarrow C_2H_6$$

$$CH_3CO \rightarrow \dot{C}H_3 + \dot{C}O$$

$$2CH_3\dot{C}O \rightarrow CH_3COCOCH_3$$

(iii) From Redox Reactions :

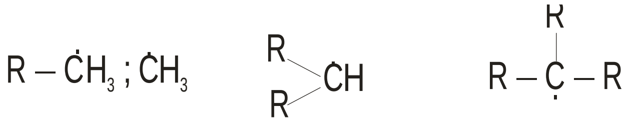


$$R-\overset{\overset{O}{\|}}{C}-O^- \xrightarrow[-\,e^{\ominus}]{\text{anode}} R-\overset{\overset{O}{\|}}{C}-\dot{O} \rightarrow \dot{R} + CO_2$$

$$2R \rightarrow R-R$$

1.4.2 Stability of Free redicals

Like the carbonium and carbanions the alkyl free-radicals are classified into three classes; primary, secondary and tertiary; depending upon whether the carbon atom carrying the odd electron is attached to two (or three), one or no hydrogen atom



Primary free radicals

Secondary free radical

Tertiary free radical

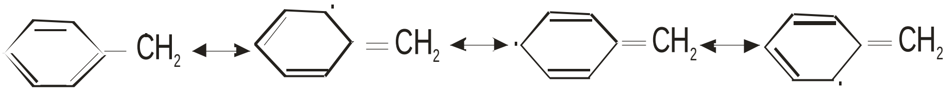
Although the alkyl radicals very much less stable than the triarylmethyl radicals, the order of stability of alkyl radicals are : tertiary > secondary > primary > methyl.

This relative stability of the three classes of free-radicals is explained on the basis of hyperconjugation or no-bond resonance. The carbon atom, carrying an unpaired electron, has a half-filled orbital that gives the radical its characteristic instability; the hyperconjugative mechanism tends to fill this orbital and thus stabilizes the radical to some extent. Tertiary free alkyl radical having more possible hyperconjugative structures or no-bond resonance than the secondary is the most stable which in turn having more possible structures than the primary is more stable and hence primary is the least stable.

In case of free radicals containing conjugated odd electron, the stability is mainly due to resonance which allows delocalization of the odd electron over several atoms. For example,

$$CH_2 = CH - \overset{\cdot}{C}H_2 \longleftrightarrow \overset{\cdot}{C}H_2 - CH = CH_2$$

Allyl free radical



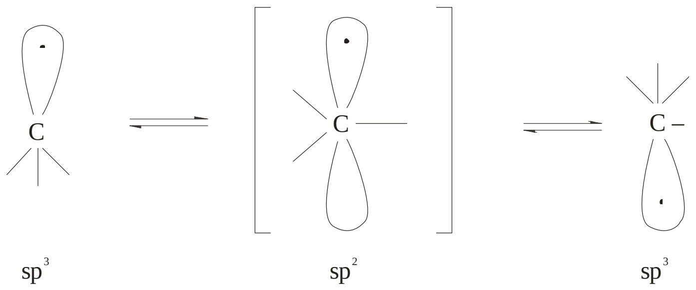
Benzyl free radical

Relative stability of free radicals.

benzyl > allyl > $3^o > 2^o > 1^o > CH_3$, vinyl

1.4.3 Structures of free radical

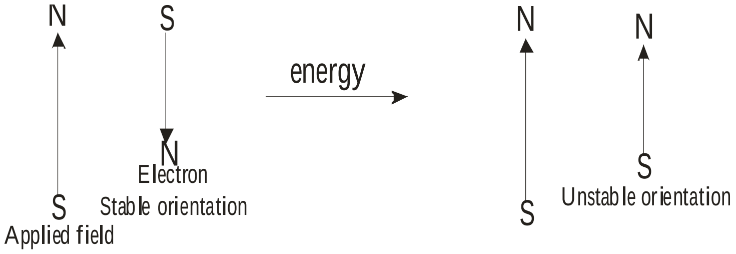
Like carbanions, generally the carbon atom is sp^3 hybridised with pyramidal or tetrahedral geometry. However, in transition state the carbon is sp^2 hybridised with trigonal planar geometry.



1.4.4. Detection of Free radical

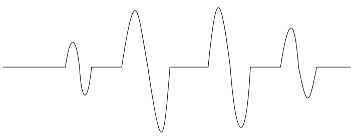
The free-radicals are detected on the basis of their magnetic property. It is a well known fact that all electrons have spin, and a spinning charge generates a magnetic field. In the ordinary molecules the electrons are paired and the magnetic field of those electrons which spin "up" is cancelled by the magnetic field of others which spin "down" and hence the molecule is, on the whole, magnetically neutral *i.e.* diamagnetic. But sine the free-radical has an odd number of electrons, one net spin will remain uncompensated and hence a free-radical generates a magnetic field, *i.e.* it will be attracted by the magnetic field (paramagnetism). So the presence of free-radical in a solution can be exhibited by the attraction towards a magnet. But unfortunately, this method is not very sensitive and only the free radical of large concentration can be detected by this method.

At present electron spin resonance (E.S.R. or E.P.R., electron paramagnetic resonance) method provides the most powerful tool for the study of free radicals. The method is based upon the fact that a free-radical in a strong magnetic field preferentially orients its odd electron spin in the more stable direction but with the absorption of light energy the spin can turn over to the unstable orientation as shown below.



Principle of E.S.R.

This method is very sensitive and can be applied to detect the free-radicals even at the concentration of 10^{-7} M. Furthermore, even very unstable radicals such as CH_3 can be detected using e.s.r.



E.S.R spectrum of methyl radical

1.4.5 Reaction free radicals

(i) Addition reaction:

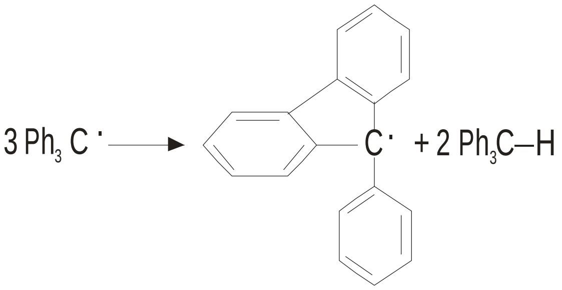
$$Ph_3C^{\cdot} + Na \quad \rightarrow \quad \underset{\text{Triphenyl methyl sodium}}{Ph_3C\ Na}$$

$$Ph_3C^{\cdot} + NO \rightarrow Ph_3CNO$$

(ii) As a reducing reagent:

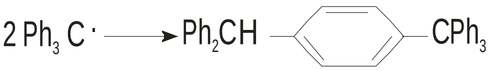
$$Ph_3C^{\cdot} + AgCl \rightarrow Ph_3CCl + Ag$$

(iii) Disproportionation:



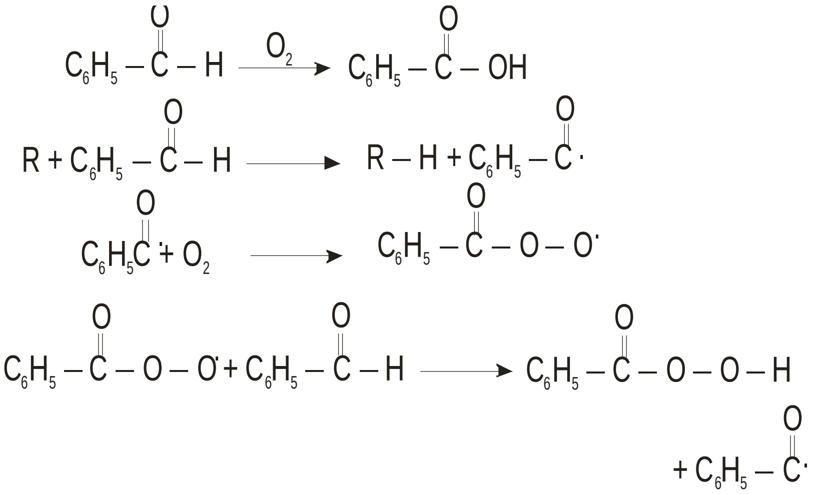
9-phenyl fluoryl

(iv) Irreversible dimerisation:



p-benzohydryl tetraphenylmethane

(v) Autoxidation : Slow oxidation of organic substances by atmospheric oxygen is known as autoxidation. The oxygen molecule frequently behaves as a biradical and it is therefore not surprising that this process involves a radical mechanism. Perhaps the most thoroughly studied example of autoxidation is the conversion of benzaldehyde to benzoic acid.



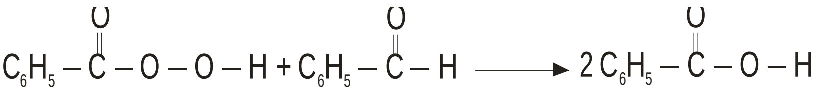
$$C_6H_5-\overset{\overset{O}{\|}}{C}-H \xrightarrow{O_2} C_6H_5-\overset{\overset{O}{\|}}{C}-OH$$

$$R + C_6H_5-\overset{\overset{O}{\|}}{C}-H \longrightarrow R-H + C_6H_5-\overset{\overset{O}{\|}}{C}\cdot$$

$$C_6H_5\overset{\overset{O}{\|}}{C}\cdot + O_2 \longrightarrow C_6H_5-\overset{\overset{O}{\|}}{C}-O-O^{\cdot}$$

$$C_6H_5-\overset{\overset{O}{\|}}{C}-O-O^{\cdot} + C_6H_5-\overset{\overset{O}{\|}}{C}-H \longrightarrow C_6H_5-\overset{\overset{O}{\|}}{C}-O-O-H + C_6H_5-\overset{\overset{O}{\|}}{C}\cdot$$

Perbenzoic acid reacts with a molecule of benzaldehyde to produce two molecules of benzoic acid.



$$C_6H_5-\overset{\overset{O}{\|}}{C}-O-O-H + C_6H_5-\overset{\overset{O}{\|}}{C}-H \longrightarrow 2\,C_6H_5-\overset{\overset{O}{\|}}{C}-O-H$$

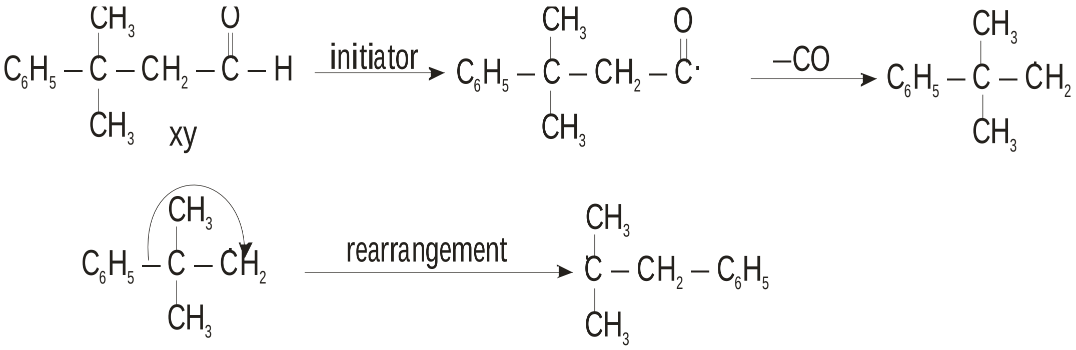
(vi) Aromatic substitution:

$$\text{Ar N} = \text{NX} \;\rightarrow\; \text{Ar}^{\cdot} + \text{N}_2 + \text{X}^{\cdot}$$

$$\text{Ar}^{\cdot} + \text{C}_6\text{H}_5 - \text{H} \;\rightarrow\; \text{Ar} - \text{C}_6\text{H}_5 + \text{H}^{\cdot}$$

[X = Cl, OCOCH$_3$, OH]

(vii) Rearrangement of Radicals:

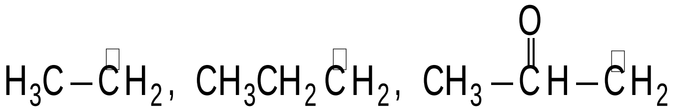


1.5 Summery

Increase in positive charge enhances the reactivity and decrease the stability of the carbocations. In contrast, decrease in positive charge lowers the reactivity and enhances the stability of carbocations.Free radicals are paramagnetic, electrically neutral and behave like electrophiles.Resonances enhances the stability of carbanions.

1.6 Review Questions

1. Explain the structure and stability of carbonium ion ?
2. Explain relative stability of primary, secondary and tertiary carbanion.
3. Arrange the following free radicals in order of decreasing stability.

1. 

$$\text{H}_3\text{C} - \overset{\square}{\text{C}}\text{H}_2,\; \text{CH}_3\text{CH}_2\overset{\square}{\text{C}}\text{H}_2,\; \text{CH}_3 - \overset{\overset{\text{O}}{\|}}{\text{C}}\text{H} - \overset{\square}{\text{C}}\text{H}_2$$

4. Write the short note on detection of free radicals.

1.7 Reference and suggested readings

- Organic Reactions and their Mechanisms IInd edition P.S. Kalsi.

- Advanced Organic Chemistry IIIrd Edition, Jagdamba Singh and L.D.S Yadav.
- Reaction Mechanism in Organic Chemistry IIIrd Edition S.M. Mukherji and S.P. Singh (Macmillan).
- Organic Chemistry Reactions and Reagents twenty six Edition O.P. Agarwal.

Unit-2

Reaction Intermediates-II

Structure of Unit

2.0 Objective

The substrate and the reagent interact, to yield the products of the reaction.

$$\text{Substrate} + \text{Reagent} \rightarrow \text{Products}$$

Some bonds in the substrate molecule are broken to give fragment. These fragments are very reactive and constitute transitory intermediate.

$$\text{Substrate} \rightarrow \underset{\text{(transitory)}}{\text{Intermediate}} \rightarrow \text{Products}$$

At once these intermediate are formed, they react with other species present in the environment to form new bonds to give the products.

The most common reaction intermediates are carbocations, carbanions, free redicals, carbenes nitrenes and benzynes. Other are ylides and enamines which are stable intermediate and can be isolated and characterized. Study of these intermediates are necessary for better understanding the reaction mechanism.

2.1 Introduction

Majority of the reactions take place through the formation of intermediates. As these intermediates are of transitory existence, so they take part in the reaction as they are formed. These cannot be isolated under normal conditions since they are very reactive. Their structures are determined by indirect means either chemically or spectroscopically or by isolating them at very low temperature. A thorough knowledge of these intermediates are necessary for clear understanding of the reaction mechanism. In this chapter we will discuss about carbene, nitrene and benzyne intermediates. Carbene and nitrene are electron deficient in nature and having only six electrons. Arynes have a one triple bond in place of one double bond in the benzene, which is differ from alkyne triple bond.

2.2 Carbenes

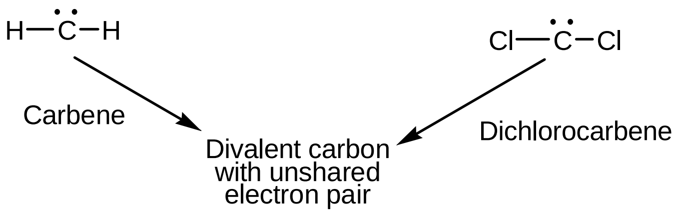
Carbenes are neutral species which have one carbon atom with two bonds and an unshared electron pair.

$$-\ddot{C}-$$

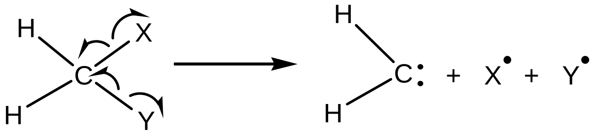
Carbenes are highly reactive species having a life time less than one second. The parent species $:CH_2$ is known as methylene. Substituted carbene are named as substituted derivative of carbene. For e.g. $:CCl_2$ is called as dichlorocarbene. However it may also called as dichloromethylene.

2.2.1 Structure of carbene

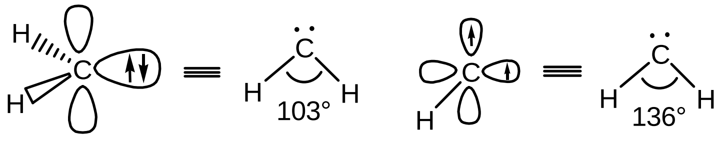
In carbenes, carbon has six electron (sextet) and hence carbenes are electron deficient in nature. The carbene carbon may be sp^2 or sp hybridized.



These two nonbonding electron of carbene are derived by the homolytic fission of two bonds. Thus carbene normally reacts as a strong electrophile.



There are two types of carbenes one is singlet and other one is triplet. In the singlet carbene both the electrons go into one orbital. On the other hand in the triplet carbene both electrons are in the different orbitals, therefore they will have parallel (unpaired) spins. In the singlet carbene electron have antiparallalel spin, so there is no magnetic moment in this state while in the triplet state, magnetic moment will be present.



Singlet state of carbene

Triplet state of carbene

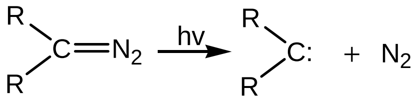
In the singlet state of carbene, carbon will have sp^2 hybridization. Two sp^2 hybrid orbitals are bonded to two hydrogen atoms and third sp^2 orbital having a lone pair electron. The unhybrid p orbital is unoccupied. Bond angle is 103° and C-H bond length is 1.12A° singlet carbene is dimagnetic.

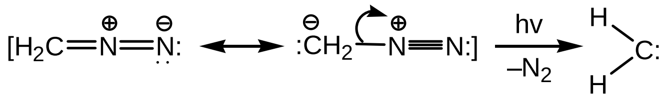
In triplet carbene, carbon atom is sp hybridized. The two sp hybridized orbitals are arrange as linear fashion and are bonded to hydrogen atom. Two unhybridized p orbitals are present each having one electron. Triplet carbene is also a bent molecule having angle of 136°. C-H bond length is 103A°. Triplet carbene is paramagnetic.

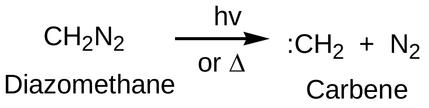
2.2.2 Formation of carbene

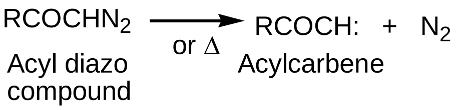
It can be prepared by following methods:

(1) By aliphatic diazo compounds: Diazocompounds easily decompose either thermally or photochemically to generate carbenes.

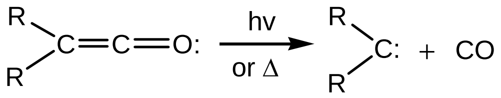




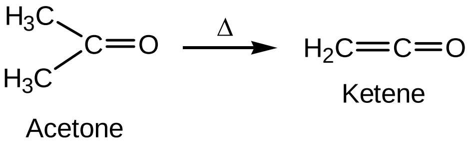




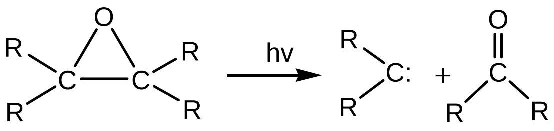
(2) By Ketenes : Ketenes can be decomposed thermally or photolytically to produce carbenes.



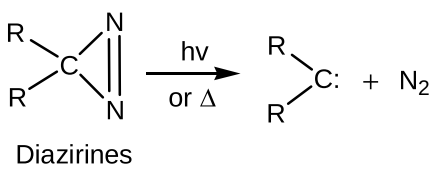
The starting ketene can be obtained by pyrolysis of acetone or from diazoketones.



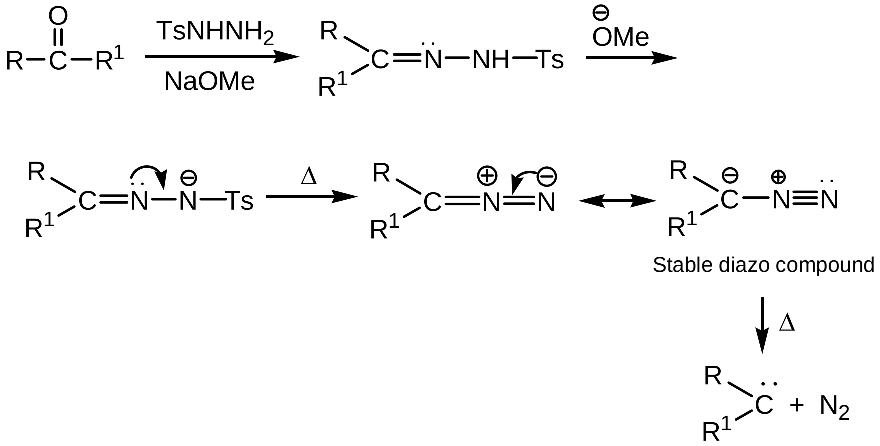
(3) **By epoxides:** Photolytic decomposition of epoxides produces carbenes.



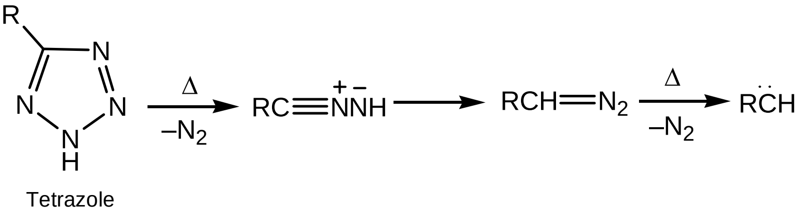
(4) **By diazirines:** Decomposition of diazirines produce carbenes.



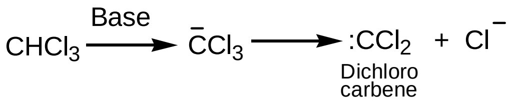
(5) **By tosylhydrazones:** Carbonyl compounds react with tosyhydrazin in the presence of alkoxide to give tosylhydrazone which on strong heating gives carbene.



(6) **By tetrazoles:** Thermal decomposition of tetrazoles produces carbenes.



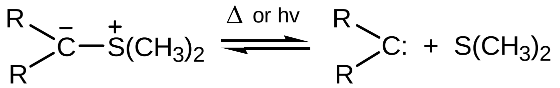
(7) **By alkyl halides:** Dichlorocarbene can be generated by loss of a proton from chloroform by a base followed by expulsion of chloride ion.



$$CHCl_3 \xrightarrow{\text{Base}} \bar{C}Cl_3 \longrightarrow \underset{\text{Dichloro carbene}}{:CCl_2} + Cl^-$$

(8) **By ylides**

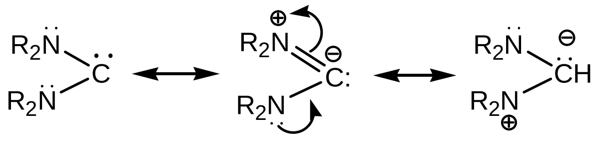
Thermal or photolytic decomposition of ylides produce carbenes.



Ylide

2.2.3 Stability of carbene

Carbenes in which the carbene carbon is attached to two atoms each bearing a lone pair of electrons, are more stable due to resonance.



2.2.4 Detection of carbenes

Since triplet carbene (multiplicity = 3) is a diradical, it has been investigated by ESR measurements. However ESR experiments cannot be made with singlet carbene.

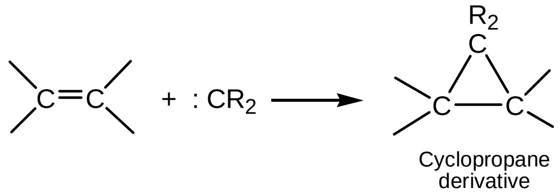
2.2.5 Reactions of carbenes

Carbenes are unstable but very reactive intermediates. Therefore, carbenes are prepared *in situ* in presence of a substrate with which it has to be reacted. Some important reactions of carbenes are as follows:

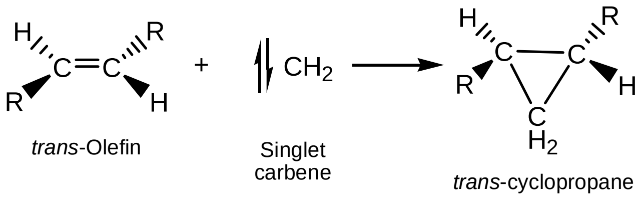
(1) Addition reaction (Cycloaddition):

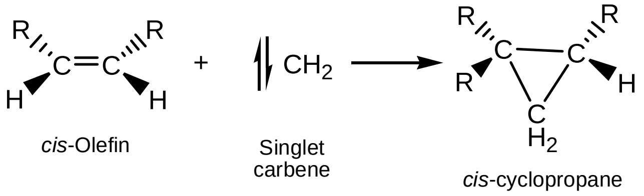
(a) With Alkenes

Carbenes add on to an olefinic double bond giving a cyclopropane derivative.

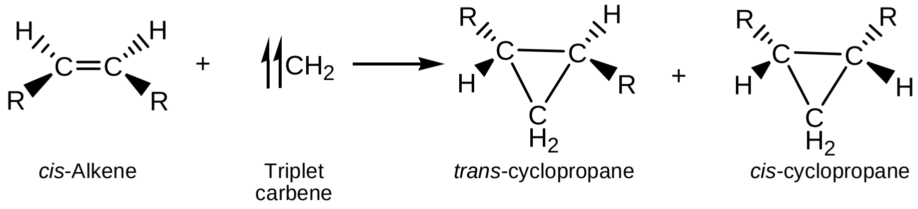


When the reaction is carried out in liquid medium singlet carbene is formed, which adds as stereospecific way. Thus, *cis*-alkene gives *cis*-cyclopropane and *trans*-alkenes gives *trans*-cyclopropane.

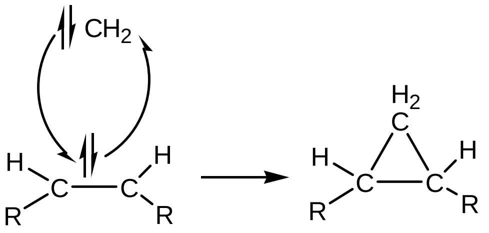




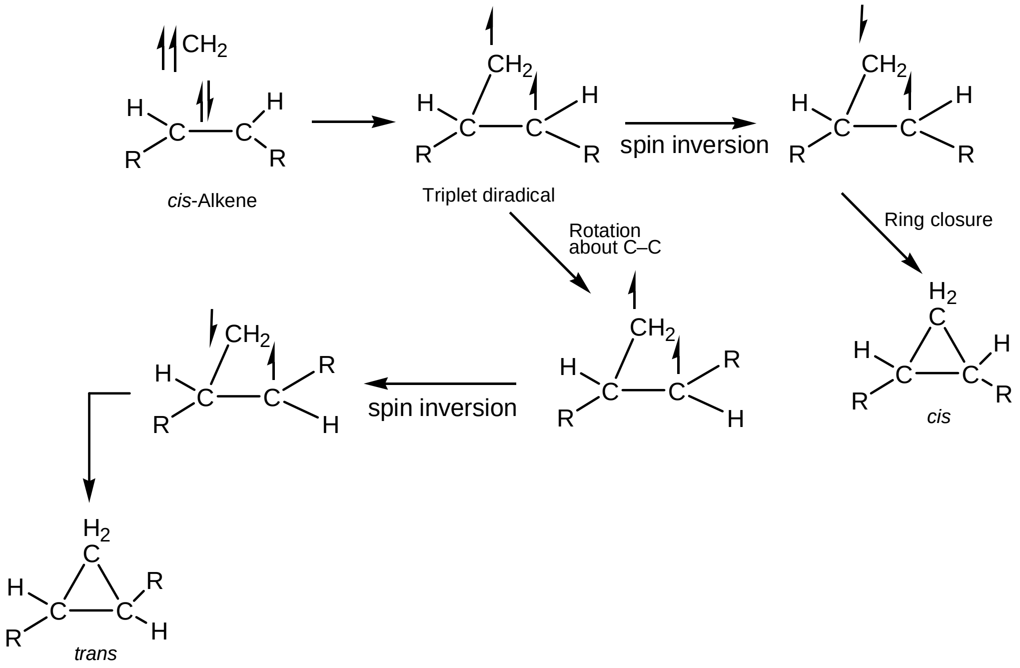
On the other hand in gaseous medium, the attacking species is triplet carbene, which does not add stereospecifically.



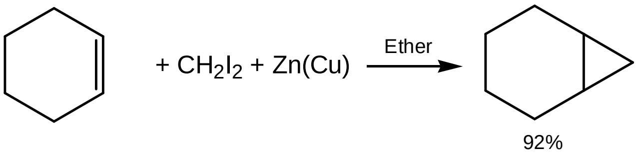
The stereochemistry of these cycloadditions is so specific that **Skell** used it as a diagnostic test for distinguishing between singlet and triplet carbenes. The addition of singlet carbene to an olefin should be in a concerted manner and therefore is stereospecific.

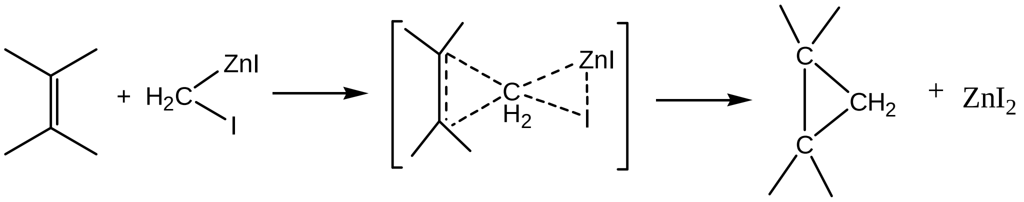


However, in case of triplet carbene, both the unpaired electrons cannot form a new covalent bond simultaneously because of their parallel spins. Hence, in this case the reaction will take place in two steps. A triplet diradical is formed In the first step, which undergoes spin inversion and then ring closure. For this the radical has to wait. During this time, there is free rotation, and a mixture of *cis* and *trans*- cyclopropane is obtained.



In the above cycloaddition reactions, carbene is generated *in situ*. A more superior procedure is to use **Simmons-Smith reagent** which transfers methylene from methylene iodide and zinc-copper couple to a carbon-carbon double bond. The attacking species is an organozinc ICH_2ZnI, a carbine like species called a carbenoid.

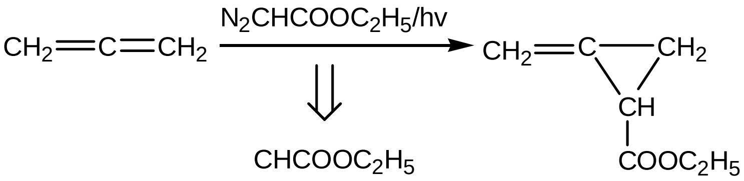




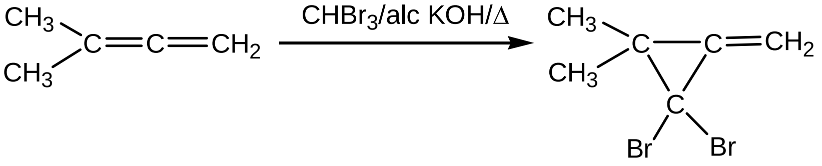
Instead of expensive methylene iodide, comparatively cheaper dibromomethane with zinc dust and curprous chloride can be used to give better yield of the adduct.

(b) With Allenes:

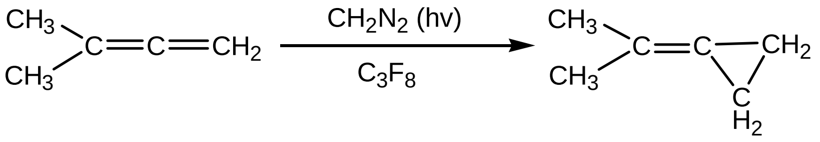
Allenes react with some carbenes to give alkylidenecyclopropane.



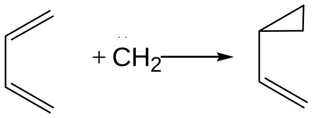
the carbene multiplicity can be determine by 3-Methyl-1,2-butadiene compound since singlet carbenes add to more substituted double bond whereas triplet carbenes add to the less substituted double bond.



1,1-Dibromo -2,2-dimethyl-
3-methylenecyclopropane
(only product)



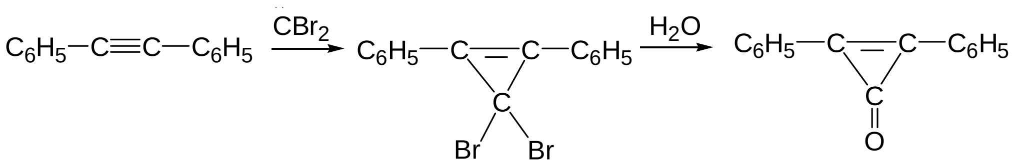
Carbene gives 1,2-addition product. Carbenes do not give 1,4-addition product with 1,3-butadienes.



1,2-Adduct

(c) By Alkynes:

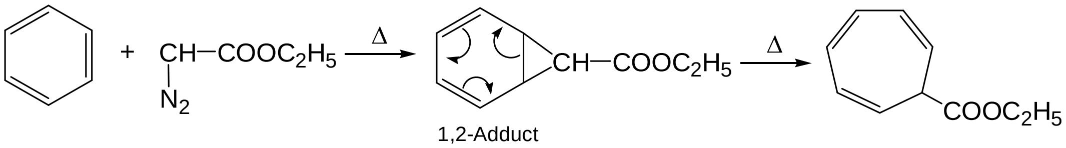
Alkynes are less reactive than alkenes towards carbenes.



3,3-Dibromo-2,2-diphenylcyclopropane

(d) By Arenes:

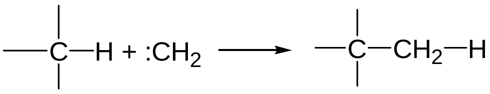
Reaction of aromatic compounds with carbenes to give 1,2 adduct which further undergoes rearrangement reaction.



1,2-Adduct

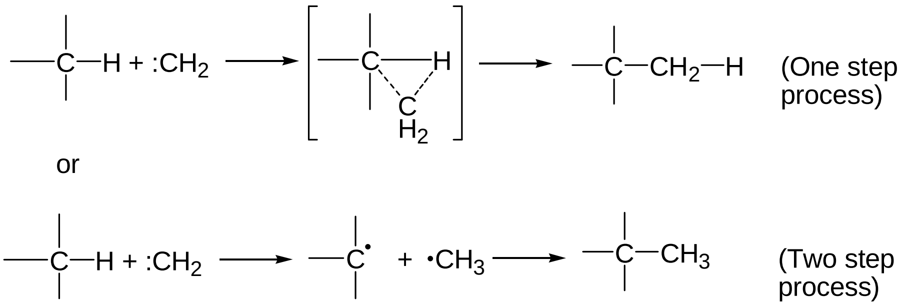
(2) Insertion reactions

Carbenes can insert into a C-H single bond.



$$-\overset{|}{\underset{|}{C}}-H + :CH_2 \longrightarrow -\overset{|}{\underset{|}{C}}-CH_2-H$$

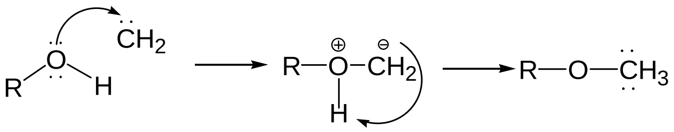
The reaction occurs in the following manner.



This insertion reaction shows that carbenes are very reactive.

In the above mentioned cycloaddition reactions, along with cyclopropane, products in which methylene is inserted into C-H single bonds are also obtained.

Insertion into X-H bonds: Carbenes can also insert into other single bonds specially O-H and N-H bonds. Reaction takes place as follows:



Ylide intermediate

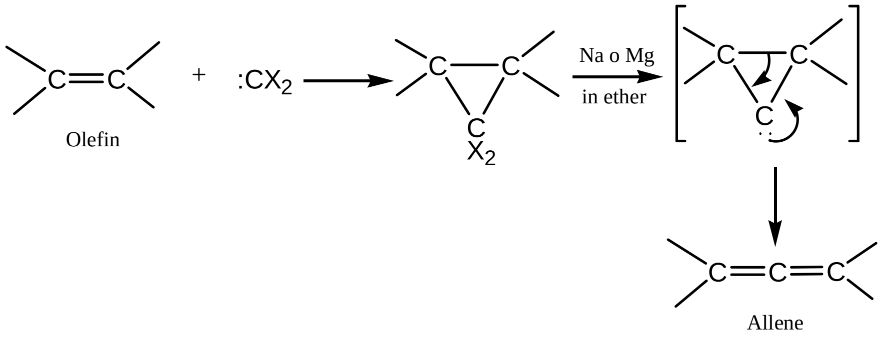
(3) Dimerization

Carbene can couple with one another forming alkenes.

$$2\,R_2C\colon \longrightarrow R_2C{=}CR_2$$

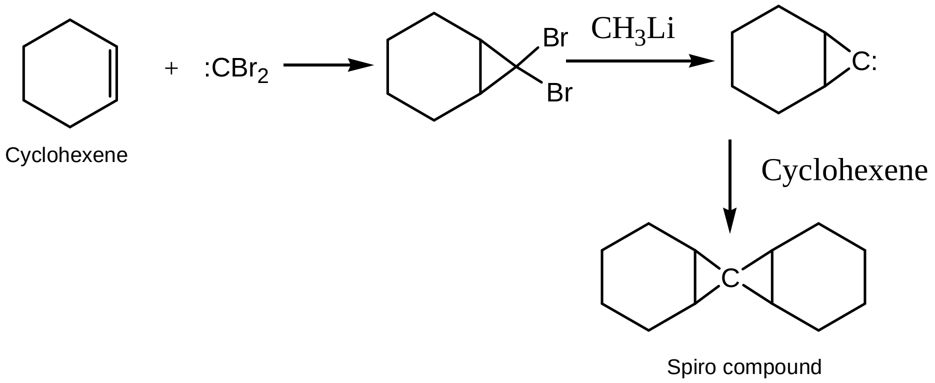
(4) Synthesis of allenes

Dihalocyclopropanes on heating with metal yield allenes.



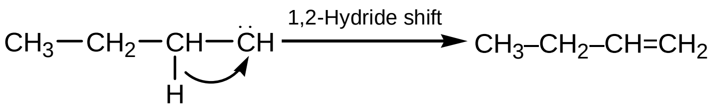
(5) Synthesis of spiro compounds

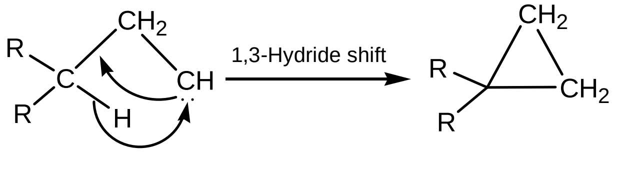
Dihalocyclopropanes, obtained from cycloalkenes and carbene, on treatment with LiMe gives spiro compound.



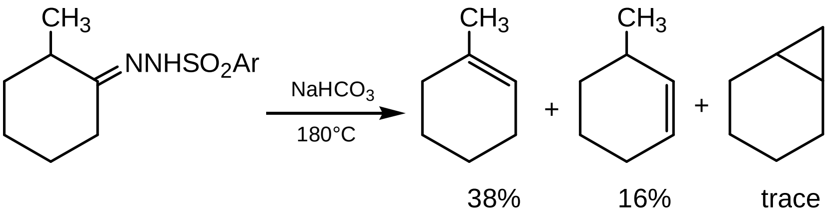
(6) Rearrangements of carbene

The most common rearrangement reaction of alkyl carbenes is the shift of hydrogen generating an alkene. This mode of stabilization predominates to the exclusion of most intermolecular reactions of aliphatic carbenes and often competes with intramolecular insertion reaction.

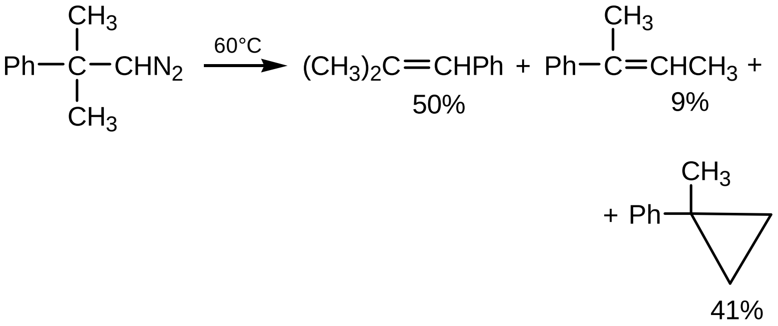




For e.g. decomposition of the tosylhydrazone of 2-methylcyclohexanone give mainly 1- and 3- methylcyclohexene rather than the intramoecular insertion product.

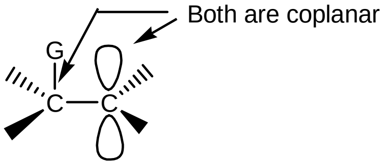


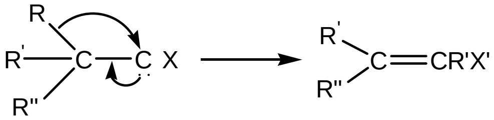
Carbenes can also be stabilized by migration of alkyl or aryl groups. In the case of 2-methyl-2-phenyl-1-diazopropane which gives the product of both methyl and phenyl migration as well as intermolecular insertion are observed.



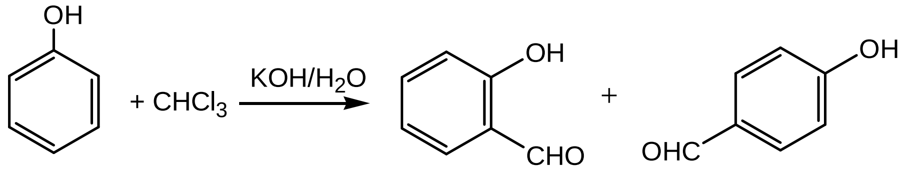
In these rearrangement migrating power of the groups in decreasing order is as follows: H > > aryl > alkyl.

The mechanism involves overlap of the migrating sigma bond with vacant p-orbital of the carbene. This can be possible if migrating group is coplanar with the vacant orbital.





Rearrangement via formation of carbene: Carbylamine reaction, Reimer Tiemann and Wolff rearrangement involves carbene intermediates. Reimer Tiemann reaction mechanism is shown below, which is involving carbene as intermediate.



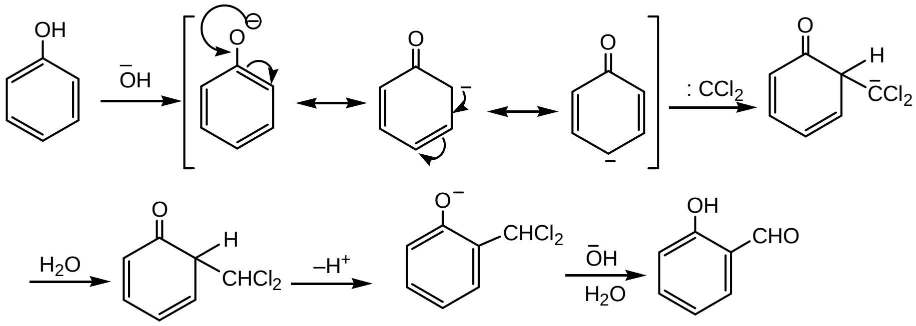
Salicylaldehyde

Mechanism:

$$CHCl_3 \xrightarrow{OH^-} \overset{\ominus}{C}Cl_3 + H_2O$$

$$\overset{\ominus}{C}Cl_2 \xrightarrow{-Cl} :CCl_2$$

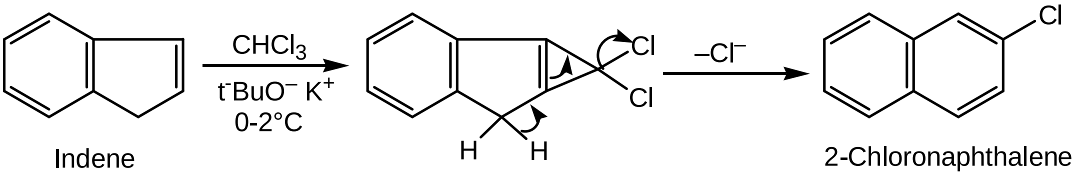
Dichlorocarbene



Salicylaldehyde

(7) Ring expansion

In certain substrates, addition of carbene involves ring expansion. For e. g. the reaction of indene with dichlorocarbene ($:CCl_2$) gives 2-chloronaphthalene.



Indene

2-Chloronaphthalene (67%)

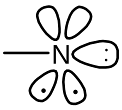
When a cyclic diazoketone is decomposed the rearrangement results in ring contraction. The reaction takes place via the intermediate carbene.

2.3 Nitrene

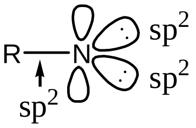
Nitrene can be considered as the nitrogen analogous of carbene. Nitrene is monovalent and has two unshared pair of electrons on nitrogen.

2.3.1 Structure of Nitrene

As with carbenes, both singlet and triplet electronic states are possible. In general nitrene obey Hund's rule and are ground state triplet with two degenerate sp orbitals containing a single electron each. Nitrene atom in the singlet is usually represented as sp^2 hybridised.



sp-triplet nitrene



sp^2-singlet nitrenes

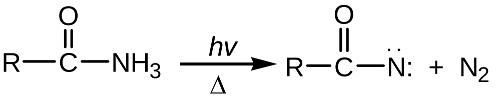
2.3.2 Formation of nitrenes

(1) By Azides:

The most common method is thermal or photolytic decomposition of azides, which gives nitrene intermediates.

$$R{-}\overset{\ominus}{N}{-}\overset{\oplus}{N}{\equiv}N \xrightarrow[hv]{\Delta \text{ or}} R{-}\ddot{N} + N_2$$

Acyl and alkyl nitrenes can be obtained by photolysis of acyl azides and isocyanates respectively.



$$R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}NH_3 \xrightarrow[\Delta]{hv} R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\ddot{N}: + N_2$$

Acyl nitrene

$$\underset{\text{isocyanate}}{R{-}N{=}C{=}O} \xrightarrow{hv} R\ddot{N} + CO$$

(2) By sulfinylamines:

Pyrolysis of sulphinylamines produce phenyl nitrene.

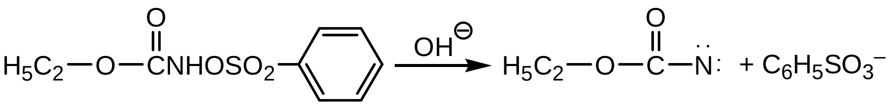
$$Ph{-}N{=}S{=}O \xrightarrow{\Delta} Ph{-}\ddot{N} + SO$$

Sulphinylamines can be readily prepared by the reaction aniline and thionyl chloride.

$$ArNH_2 \xrightarrow{SOCl_2} Ar{-}N{=}S{=}O$$

(3) By N-benzenesulfonoxy Carbamates

When N-benzenesulfonoxy carbamates reacts with a base it forms Carboalkoxynitrene by the elimination of benzenesulfonate anion.

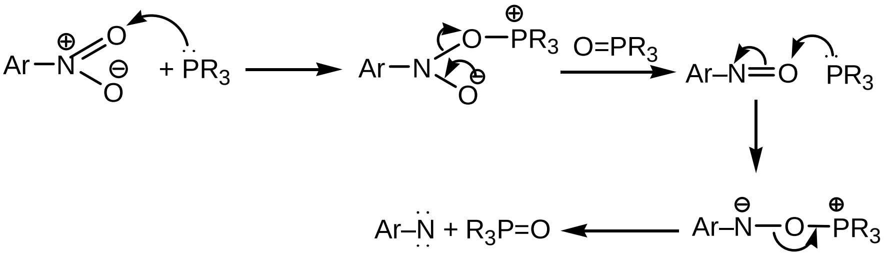


(4) By nitro and nitroso compounds: Deoxygenation of nitro and nitroso compounds may produce nitrenes. A variety of reagents can be used for deoxygenation but the best result is obtained with triethylphosphite.

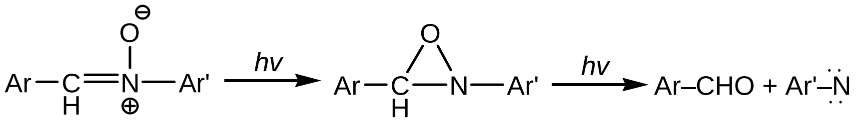
$$Ar{-}NO_2 \xrightarrow[\Delta]{(C_2H_5)_3P} Ar{-}\ddot{N}$$

$$Ar{-}NO \xrightarrow[\Delta]{(C_2H_5)_3P} Ar{-}\ddot{N}$$

Reaction takes place as follows:



(5) **By small ring compounds:** On photolysis nitrones give oxaziranes which on further photolysis give nitrene.



2.3.3 Stability of Nitrene

Nitenes are more stable than Carbenes. The energy difference between the singlet and triplet states is usually much larger for nitrenes than for carbenes, being estimated at 145 kJ/mole for nitrene itself compared with 32-42 kJ/mole carbene. The reason in energy difference is due to the difference in electronegativity of carbon and nitrogen. N is more electronegative than carbon. So nitrogen holds its electrons closer to the nucleus which decrease the energy and hence increase stability. The nature of the substituent on nitrogen affects both the multiplicity and normal electrophilic reactivity of nitrene.

2.3.4 Detection of Nitrene

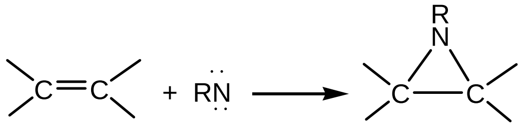
Due to triplet structure they can be detected by Electron Spin Resonance Spectroscopy (ESR). Occasionally a nitrene can be trapped by its reaction with carbon monoxide to form isocyanate.

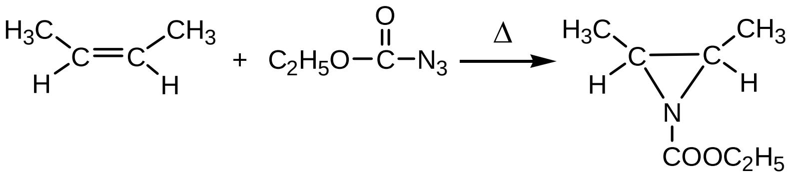
$$Ar\text{-}N_3 \xrightarrow[-N_2]{\triangle} Ar\text{-}\ddot{N} \xrightarrow{:C=O} Ar\ddot{N}=C=O$$

2.3.5 Reactions of Nitrene

(1) Addition reaction (cycloaddition):

(a) With alkenes: Nitrenes are electrophile and alkenes are nucleophile therefore addition reaction take place between alkene and nitrene. Like carbenes, the addition of nitrene to a C=C bond may be stereospecific with singlet while none stereospecific with triplet nitrenes. Mechanism is similar to the reaction of carbene with alkenes.

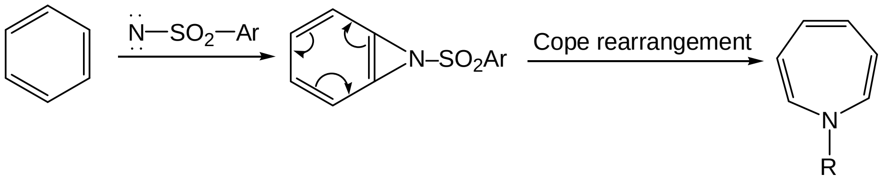




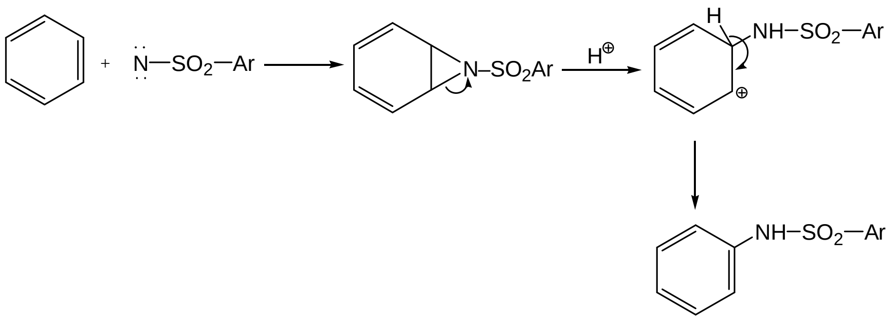
(b) With arenes

Benzene and its derivatives react with nitrenes to give ring expanded products and / or N-substituted anilines.

Ring expanded products are obtained due to rearrangement.

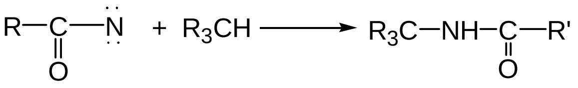


When adduct is treated with acid, this converts into N-substituted anilines.



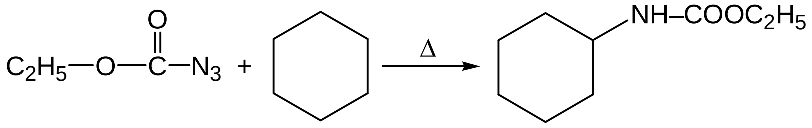
2. Insertion reaction:

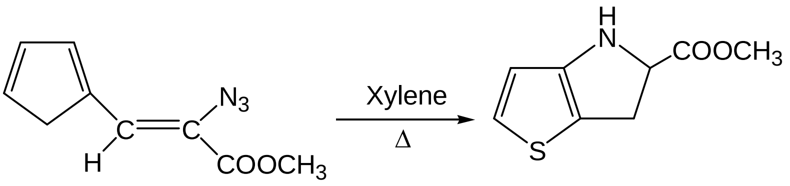
Nitrenes particularly acyl nitrene and sulfonyl nitrenes can insert into C-H bonds.



$$R-\underset{O}{\underset{\|}{C}}-\ddot{\underset{..}{N}} + R_3CH \longrightarrow R_3C-NH-\underset{O}{\underset{\|}{C}}-R'$$

Nitrene may also undergo insertion reaction with saturated hydrocarbons. Thus insertion into C-H single bonds leading to ring closure. The importance of the C-H insertion reaction of nitrene lies in the fact that it is a potential useful way of functionalizing unactivated C-H bonds, by converting hydrocarbon into amine derivatives.





Above example belongs to intramolecular C-H insertion reaction.

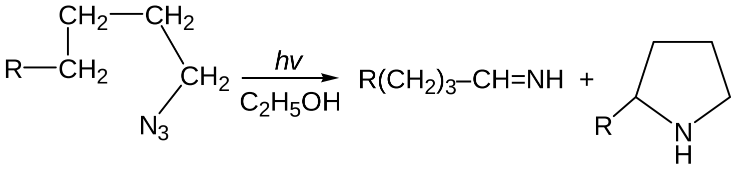
(3) Dimerization reaction:

Aryl nitrene forms azobenzene by dimerization.

$$2Ar\ddot{\underset{\cdot\cdot}{N}} \longrightarrow Ar{-}N{=}N{-}Ar$$

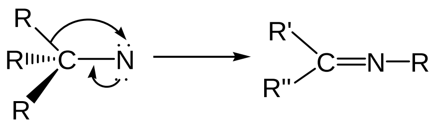
(4) Hydrogen abstraction:

If hydrogen abstraction occurs from the carbon which is α to the nitrogen then it leads to the formation of imines. This process is of considerable synthetic importance. If hydrogen abstraction takes place from 4- or 5- position which is followed by ring closure, the product formed are pyrolidines and piperidines, respectively.



(5) Rearrangements of nitrene:

Like carbene, nitrene also has vacant p orbitals so it can undergo facile rearrangement in which an atom or group on the adjacent carbon migrates to electron deficient nitrogen with simultaneous formation of new carbon nitrogen double bond. Such rearrangements are called 1,2-shifts.



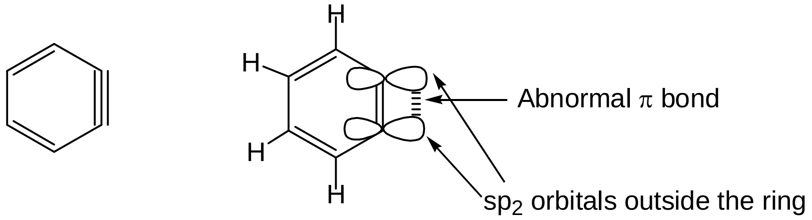
Nitrogen are also obtained as reaction intermediate in Hofmann, Schmidt and Lossen rearrangement

2.4 Arynes or Benzynes

C_6H_4 (1,2-dehydrobenzene) and its derivatives are known as benzynes. Benzynes are neutral and highly reactive reaction intermediate in which the aromatic character is not markedly disturbed. It may be obtained from benzene ring by removing two substituents at ortho position one is the form of electrophile and other in the form of nucleophile. Benzynes (arynes) contain a carbon-carbon triple bond and may be regarded as aromatic counterpart of acetylene. This triple bond is not like the triple bond of acetylene where the two carbons forms a σ bond by coaxial overlapping of sp orbital and the remaining π bonds are formed by the colateral overlapping of remaining p orbitals. Such structure is not feasible in case of benzyne, as it is associated with hexagonal geometry of benzene ring.

2.4.1 Structure of Arynes

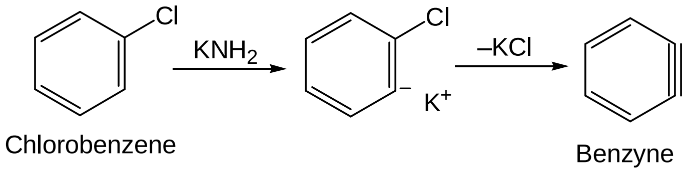
Benzyne triple bond which have two pi bonds, one is normal and the other is (new one) abnormal. This abnormal pi bond is formed by the overlapping of two sp^2 orbitals outside the ring. This pi- bond is called as external pi-bond. As the sideways overlapping is not very effective, the new bond is weak and so the benzyne is highly reactive species.

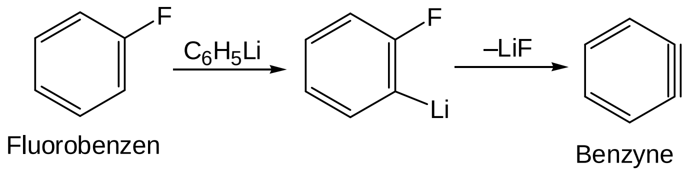


2.4.2 Formation of Arynes

(1) By aryl halides

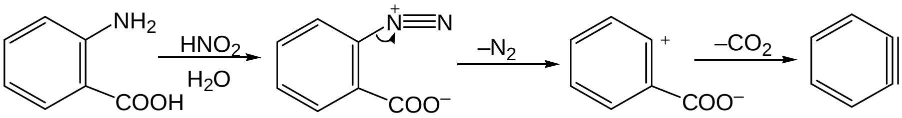
Aryl halides on treatment with strong base like KNH_2, C_6H_5Li etc., form benzyne.





(2) By *o*-aminobenzoic acid

The *o*-aminobenzoic acid on diazotization followed by decomposition of the formed diazo compound produces benzyne.



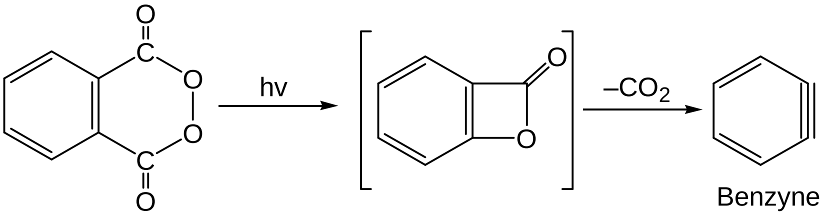
α-Aminobenzoic acid

Benzyne

This is a convenient method for the generation of benzyne.

(3) By phthaloyl peroxide

Photolytic decomposition of phthaloyl peroxide generates benzyne via lactone intermediate.

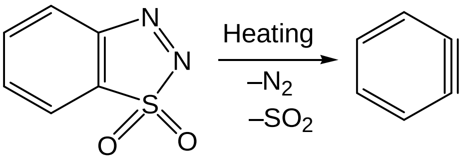


Benzyne

Phthaloyl peroxide

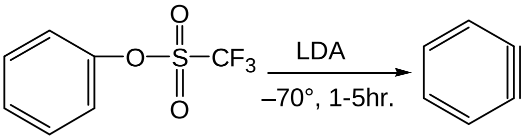
(4) By benzothidiazoate-1,1-dioxide

Thermal decomposition of benzothiadiazoate-1,1-dioxide produces benzyne.



(5) By benzenetrifluoromethane sulfonate

Benzenetrifluoromethane sulphonate on treatment with a strong base generates benzyne.

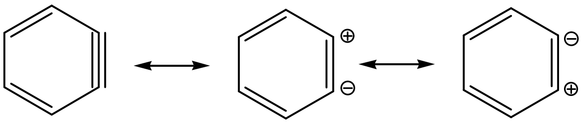


Benzene influoromethane sulphonate

Benzyne

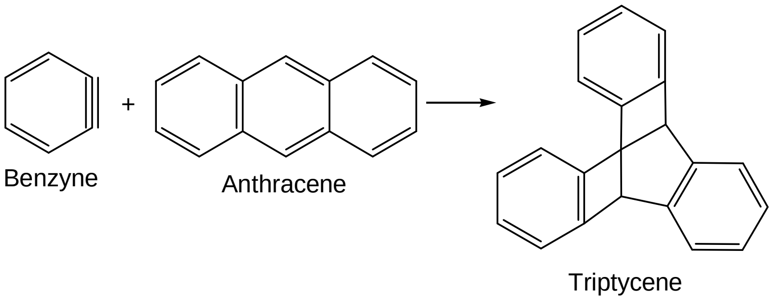
2.4.3 Stability of benzyne

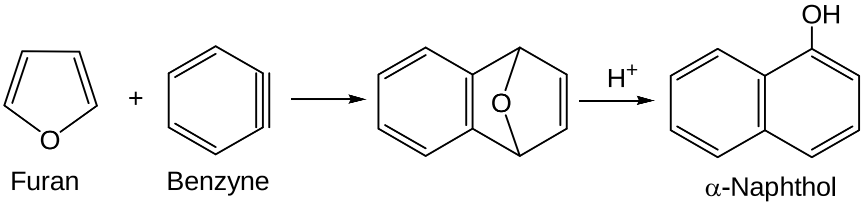
Benzyne has hexagonal planar ring structure with six delocalized pi-electrons. The additional pi-electron present in the pi-orbitals formed by the colateral overlapping of two sp^2 atomic orbitals containing one electron each. This overlapping creates deformation of the bond angle (120° to 180°). The deformation of the bond angle causes a strain which makes the species highly reactive. Some resonating structures are as follows:



2.4.4 Detection of benzyne

This intermediate can be trapped as its Diels-Alder adduct. When benzyne is formed in the presence of a diene the benzyne reacts as the dienophile. A diene often used for this purpose is anthracene which provides the structurally interesting molecule triptycene. Furan also react with benzyne to give Diels Alder addition product.





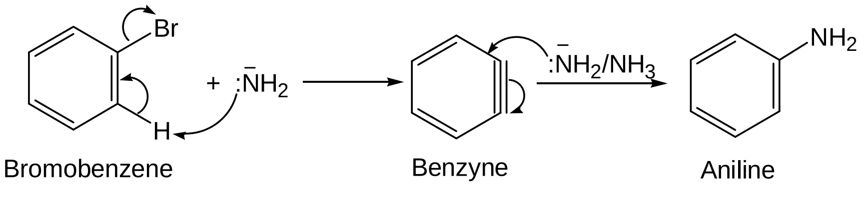
2.4.5 Reactions of benzyne

Benzyne is an extremely reactive species and is generated *in situ* for obtaining various products. In fact benzyne generated is trapped by various substrates.

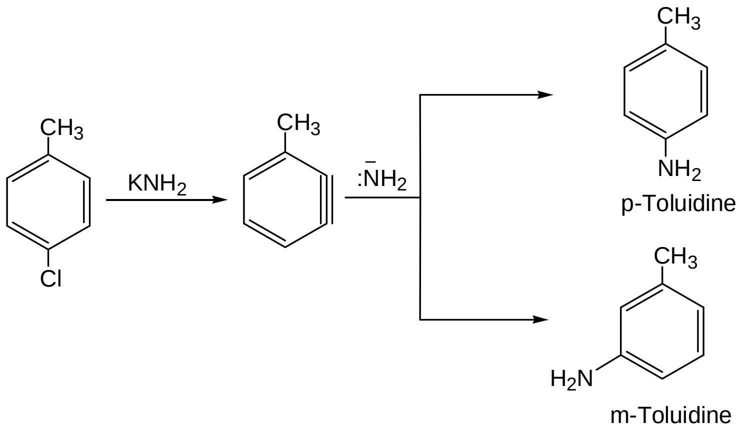
(1) Reaction with nucleoiphiles

As already discussed that aryl halides on treatment with KNH_2 (strong base) generates benzyne. When KNH_2 is used, the available nucleophile (NH_2^-) reacts with the generated benzyne to give aniline.

(i)



(ii)



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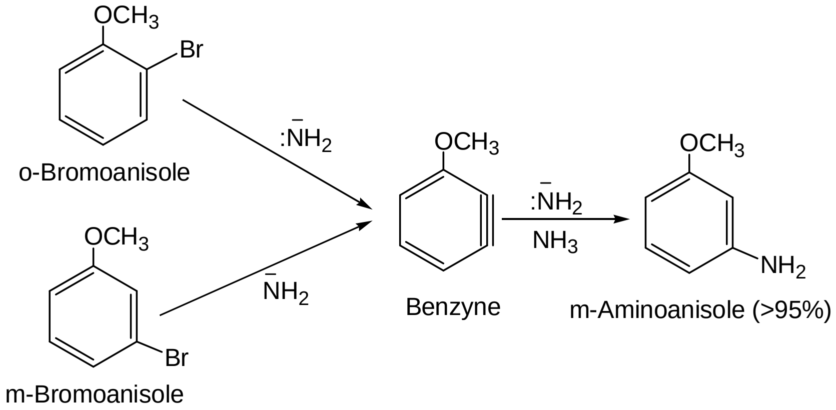
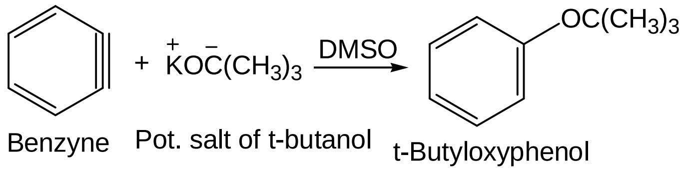
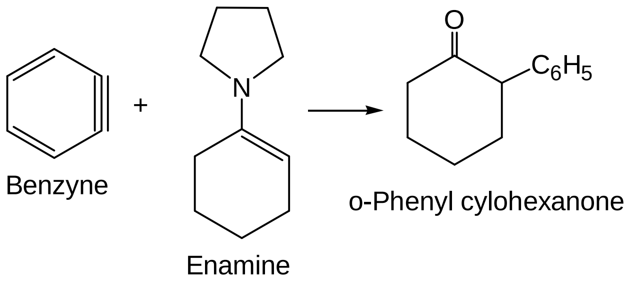


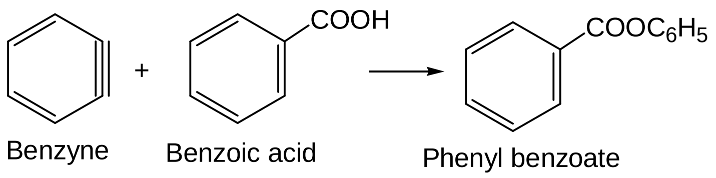
In above reactions the benzyne intermediate is obtained as a reaction intermediate. .

(2) Synthesis of simple molecules

By the reaction of a benzyne with simple reagents, a number of products can be synthesized.



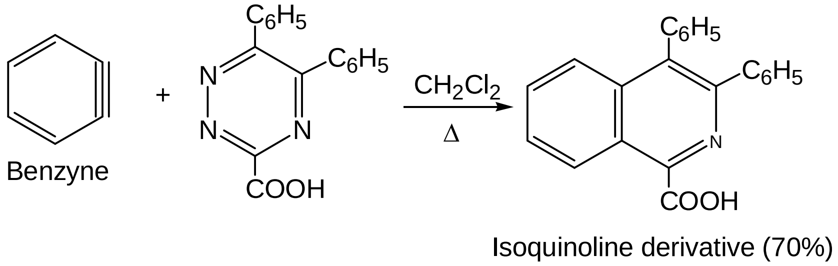




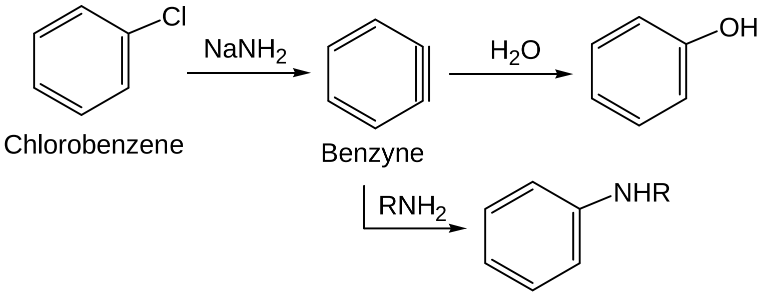
(3) Synthesis of unusual type of products

Several types of compounds which are difficult to obtain or cannot be obtained by other methods can be conveniently obtained via benzyne intermediate. Thus the generated benzyne can be trapped with anthracene, furan and their derivatives.

(i) Reaction with triazines

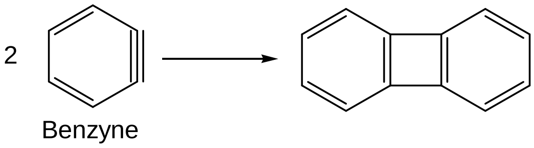


(ii) Conversion of chlorobenzene to phenol and aniline derivatives

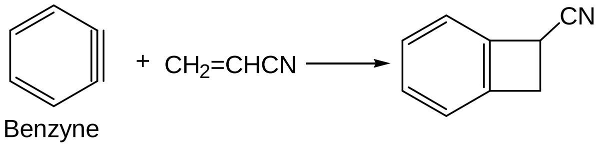


(iii) Dimerization

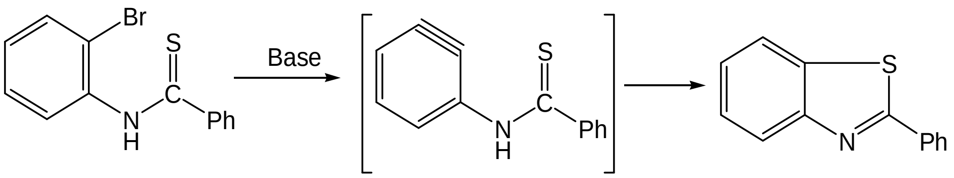
In the absence of any nucleophiles benzyne undergoes dimerization.



(iv) Reaction with olefins



(v) Synthesis of heterocyclic compounds



2.5 Summary

- In carbenes, carbon has six electron (sextet) and hence carbenes are electron deficient in nature. There are two types of carbenes one is singlet and other one is triplet
- Carbenes add on to an olefinic double bond giving a cyclopropane derivative. When the reaction is carried out in liquid medium singlet carbene is formed, which adds as stereospecific way. Thus, *cis*-alkene gives *cis*-cyclopropane and *trans*-alkenes gives *trans*-cyclopropane. In gaseous medium, the attacking species is triplet carbene, which does not add stereospecifically.
- Nitrene can be considered as the nitrogen analogous of carbene. Nitrene is monovalent and has two unshared pair of electrons on nitrogen. As with carbenes, both singlet and triplet electronic states are possible.
- Benzynes (arynes) contain a carbon-carbon triple bond and may be regarded as aromatic counterpart of acetylene. Benzyne has hexagonal planar ring structure with six delocalized pi-electrons. The additional pi-electron present in the pi-orbitals formed by the colateral overlapping of two sp^2 atomic orbitals containing one electron each.

2.6 Review Questions

1 What are carbenes? How they are generated? Give their structure.

2 Discuss the cycloaddition reactions of carbenes.

3 What are benzynes? How they are formed?

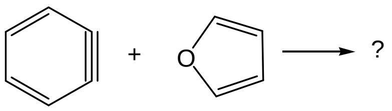
4 Discuss the rearrangement reactions involving nitrenes.

5 Write the two methods for detection of benzyne intermediate

6 Discuss the rearrangement reaction involving carbene.

7 Give the products obtained in the following reactions:

(i)



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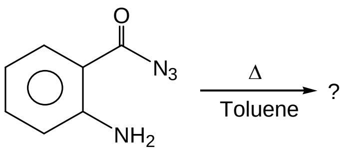

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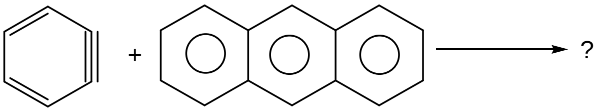

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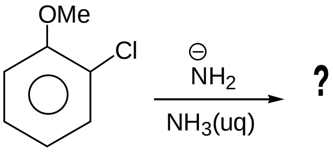


2.7 Reference and Suggested Readings

- Advanced Organic Chemistry, J. March, 6th Ed.
- Advanced Organic Chemistry Part-A, F. A. Carey and R. J. Sundberg, 5th Ed. Springer.
- Organic Reactions and their Mechanisms, P.S. Kalsi, New Age International Publishers.
- Organic Reaction Mechanism, V. K. Ahluwalia and Rakesh Kumar Parashar, Narosa Publishing House.

Unit- 3

Molecular Rearrangements-I

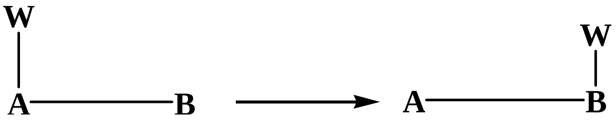
Structure of unit

3.0 Objective

The basic skeleton of the molecules remains intact in the majority of reaction of organic compounds. There are many reactions in which a skeletal rearrangement occurs. Some of these processes are of value in synthesis. In addition, however it can be a disadvantage if they occur during the course of operations designed only to effect other changes of functionality, so that it is important to be familiar with the structural features and reaction conditions which lead to rearrangement.

3.1 Introduction

A rearrangement reaction involves reshuffling of the sequence of atoms to form a new structure. Migration of a group occurs from one carbon atom to another within the same molecule or from one molecule to another.



where, A - Migratory origin

B - Migration terminus

W- Migrating group

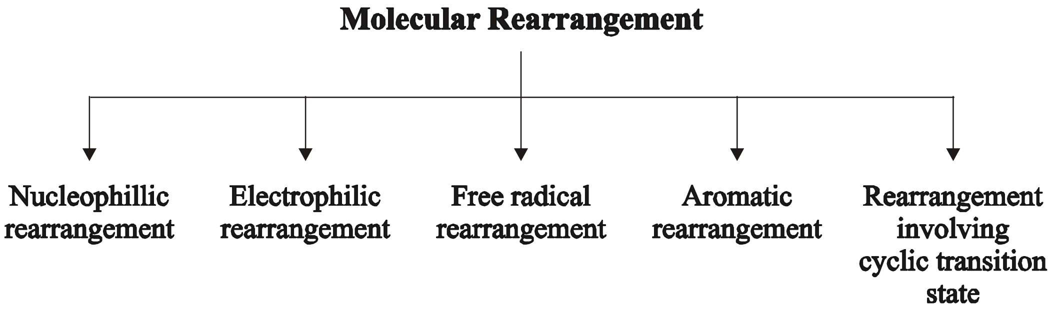
Generally, these migrations occurs from an atom to an adjacent one (called 1, 2 – shifts) also called as 'whitmore' 1,2-shifts, however longer distance migrations are also possible.

3.2 General mechanistic considerations

According to migration of migrating group to the same or another molecule, rearrangement may be classified in two types. One is intramolecular process in which migration of the migrating group 'W' occurs within the same molecule so that ‘W’ does not become completely detached from the system. Second is Intermolecular process in which migration of ‘W’ occurs between two molecules so that usually the ‘W’ group is first detached and then re-attached at another site of the second molecule.

3.2.1 Nature of Migration

According to nature of migratory group it may be of following type:

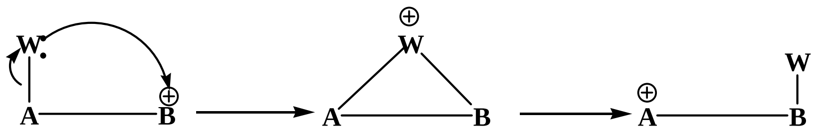


3.2.1.1 Nucleophilic Rearrangement

(Anionotropic/Carbonium ion Rearrangement)

Rearrangement in which the migration of the migratory group 'W' from a carbon atom, with its electron pair (as a nucleophilic) to an adjacent electron deficient atom takes place is known as nucleophilic rearrangement. The migratory terminus may be C, N or O. If migratory terminus is carbon, rearrangement is called as carbonium ion rearrangement. It involves carbonium ion intermediate. There may be a change of actual carbon skeleton in the product; e.g.- Pinacol-Pinacolone and Wagner- Meerwein rearrangements. If migratory terminus is nitrogen it involves nitrene intermediate. e.g. Hoffmann, Lossen and Schmidt. In Baeyer –Villiger rearrangement migratory terminus is oxygen. These are called as '1,2-shifts' where neighbouring group participation facilities the formation of the bridged carbonium ion. If the reaction rate is enhanced due to neighbouring group participation the rearrangement is said to be ‘Anchimerically assisted’. The migratory terminus atom must have an open sextet to adjust electrons of migratory group (W). It is the most common type of rearrangement.

Representation :

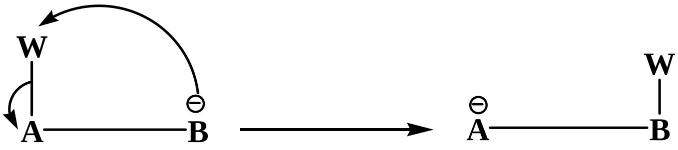


3.2.1.2 Electrophilic rearrangement

(Cationotropic/Carbanion Rearrangement)

Rearrangement in which the migration of the migratory group ‘W’ from a C atom (without bonding electrons) to an adjacent electron rich atom takes place, is known as electrophilic rearrangement. The driving force is the formation of more stable anion.

Representation :



3.2.1.3 Free-radical rearrangement

Rearrangement in which the migration of the migrating group 'W' from a C atom to the migratory terminus with a single electron takes place, is known as free radical rearrangement. It is very rare, as there is much less tendancy for a 1° or 2° carbon free radical to rearrange than the corresponding carbonium ion.

Representation :

3.2.1.4 Aromatic rearrangement

Rearrangement in which the migration of the migrating group 'W' from one position to another in an aromatic system or from a side chain to the aromatic nucleus takes place is known as aromatic rearrangement

3.2.1.5 Rearrangement involving cyclic transition state

This rearrangement belongs to pericyclic reactions in which rearrangement take place by concerted mechanism

3.3 Migratory aptitudes

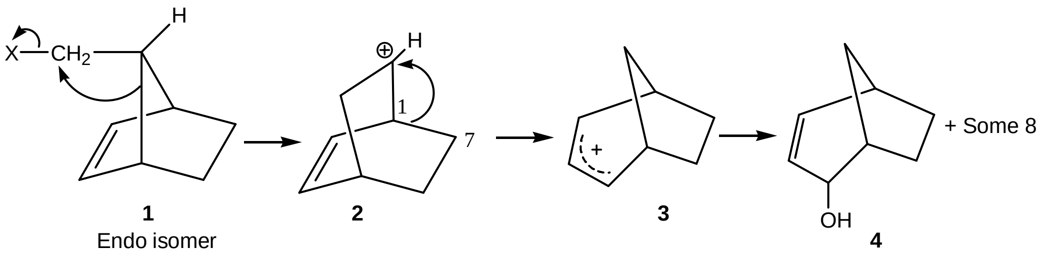
In many reactions, there is no question about which group migrates. For e.g. Hoffmann, Curtius and similar reactions were is only one possible migrating group in each molecule and migratory aptitude can be measured by comparing the relative rearrangement rates of different compounds.

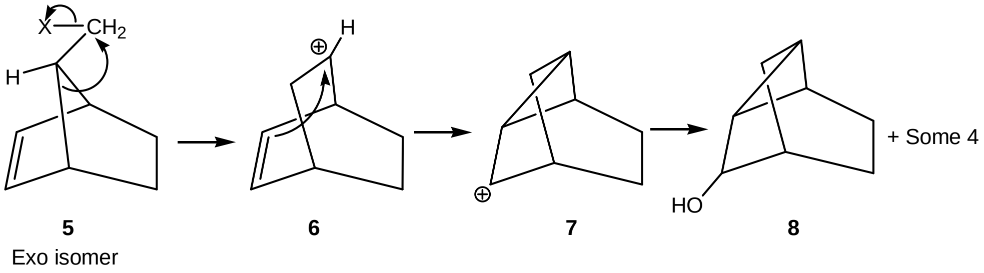
In some reactions, there are two or more potential migrating groups, but which migrates is settled by the geometry of the molecule. The ease with which any particular group migrate is known as its migratory aptitude. All groups do not migrate with equal ease in rearrangements.

Beckmann rearrangement provides an example in which only the group *trans* to the OH migrates. In compounds whose geometry is not restricted in this manner these still may be eclipsing effects so that the choice of migrating group is largely determined by which group is in the right place in the most stable conformation of molecule. In the case of Wagner-Meerwein and the Pinacol rearrangements, the molecule may contain several groups which geometrically have approximately equal chances of migrating. These reactions have often been used for the direct study of relative migratory aptitudes.

3.4 Memory effects

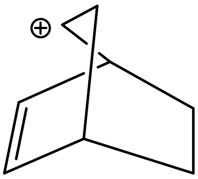
It can be explained by following reactions :



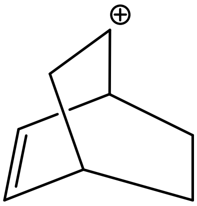


Solvolysis of the *endo* bicyclic compound **1** (X = ONs or Br) gave mostly the bicyclic allylic alcohol **4**, along with a smaller amount of the tricyclic alcohol **8**, while solvolysis of the *exo* isomer **5** gave mostly **8**, with minute amounts of **4**. Thus the two isomers gave entirely different ratios of products, though the carbocation initially formed (**2** or **6**) seems to be the same for each. In the case of **2**, a second rearrangement (a shift of 1,7 bond) follows, whereas with **6** it is an intramolecular addition of the carbocation carbon to the double bond. It seems as if **2** and **6** "remember" how they were formed before they go on to give the second step. Such effects are known as memory effects. The causes of these effects are not well known. One possible cause may be differential solvation of apparently identical carbonium ions **2** and **6.** Another possibilities are as:

(i) The ions have geometrical structures those are twisted in opposite ways (e.g., a twisted **6** might have its positive carbon closer to the double bond than a twisted **2**).



6



2

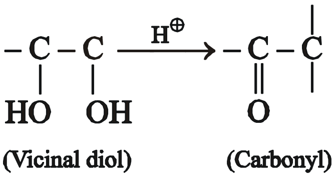
(i) Ion pairing may be responsible.
(ii) Nonclassical carbocation are involved.

One possibility that has been ruled out is that the step 1 → 2→ 3 and 5→ 6→ 7 are concerted, means **2** & **6** never exists at all. The fact which exclude this possibility is that **1** gives not only **4** but also some **8** and **5** gives **8** along with some **4**. This proves that some of **2** & **6** ions interconvert, and this phenomenon known as leakage.

3.5 Rearrangements Involving Migration to Electron-Deficient Carbon

3.5.1 Pinacol – Pinacolone rearrangement or Pinacolic rearrangement

An Acid - catalyzed conversion of polysubstituted ethylene glycols to carbonyl compounds via carbonium ion is known as pinacol-pinacolone rearrangement.



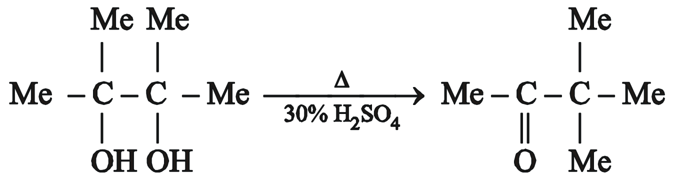
$$\underset{\text{HO}}{-\overset{}{\text{C}}}-\underset{\text{OH}}{\text{C}}\xrightarrow{\text{H}^{\oplus}}-\underset{\underset{\text{O}}{\|}}{\text{C}}-\underset{|}{\overset{|}{\text{C}}}$$

(Vicinal diol) (Carbonyl)

Characteristics:

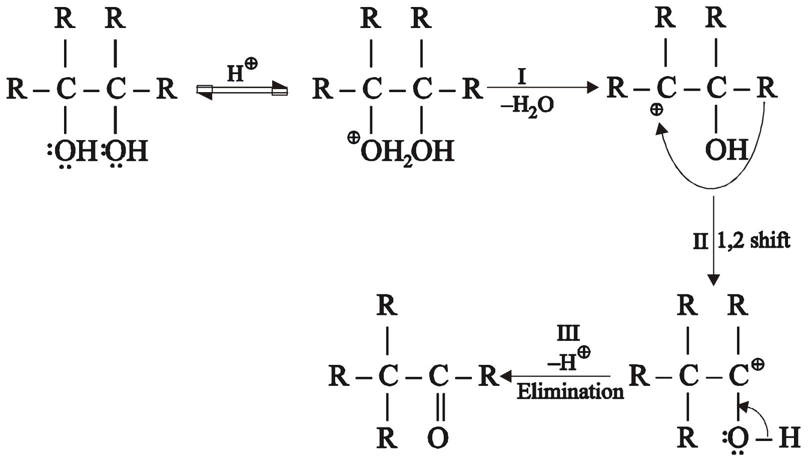
(i) Anionotropic rearrangement
(ii) Carbon to Carbon 1,2- migration
(iii) Acids used are –Mineral acids

Reaction : For example 2,3-dimethyl-2,3-butanediol (Pinacol) on treatment with H_2SO_4 generates 3,3-dimethyl-2-butanone, commonly known as pinacolone.



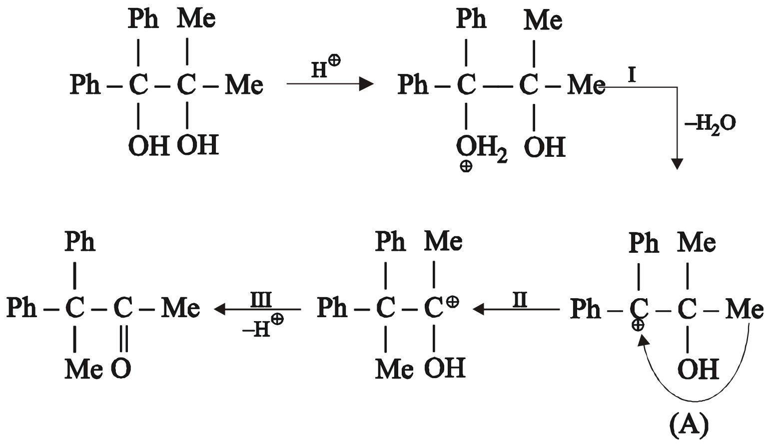
2,3-Dimethyl-2,3butanediol (Pinacol) **Methyl-t-butyl ketone (Pinacolone)**

Mechanism : The mechanism involves the loss of water from protonated diol. Then 1,2-nucleophilic shift of a group takes place (Scheme-1).



(Scheme-1)

In case of unsymmetrically substituted pinacols elimination of that OH group would occur which generates a positive charge on that C which is best able to support it i.e., where more stable carbonium ion is formed.



(Scheme-2)

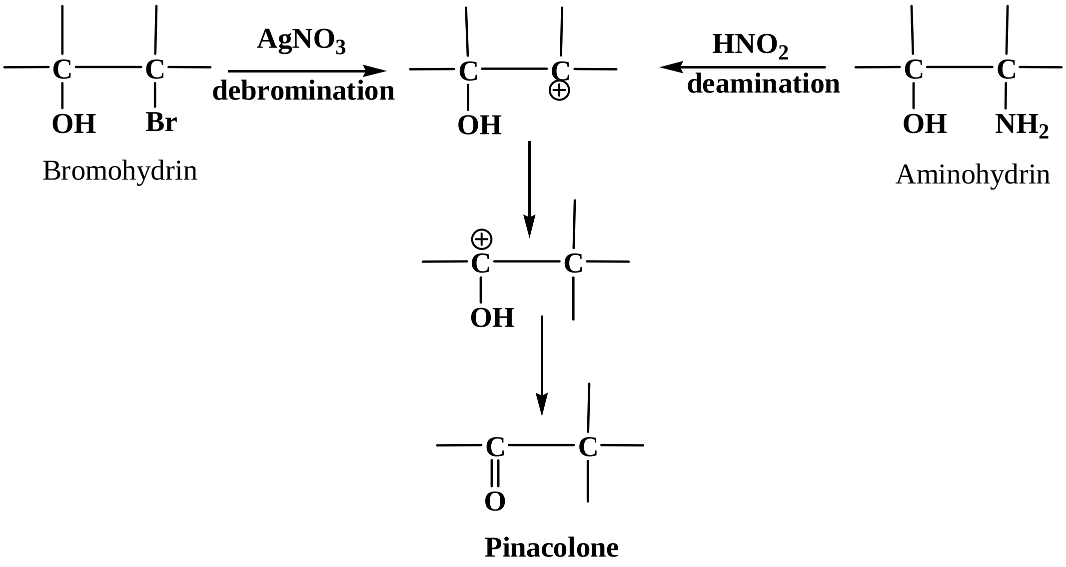
Here, initially (A) is formed which can be resonance stabilized by the presence of Ph group, and then migration of Me group occurs (scheme-2).

Detection of carbonium ion

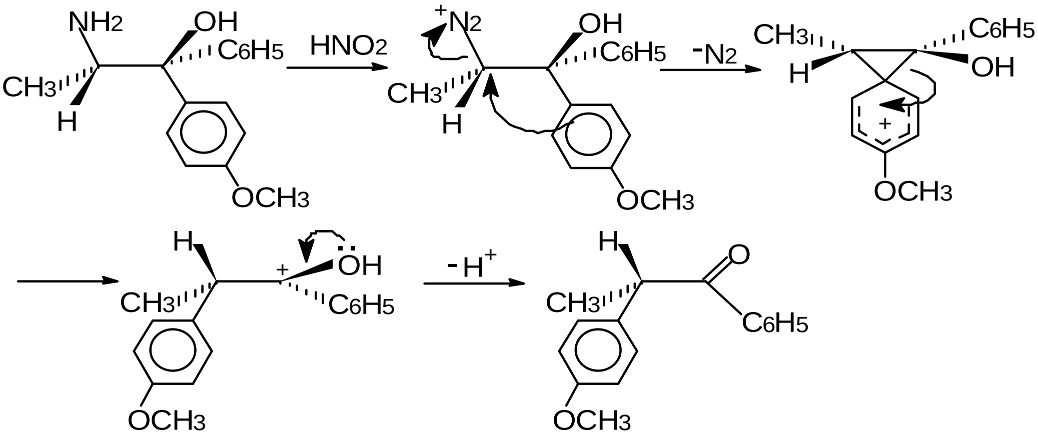
Intermediacy of carbonium ion can be demonstrated in various ways.

(i) With heavy water : Pinacol is rearranged in H_2O^{18} resulting in recovered pinacol of O^{18} isotope.

(ii) Any other reaction capable of producing the same carbonium ion results in the formation of pinacolone. Such compounds which can yield pinacolones are called Semi pinacols and the reaction is 'Semi-pinacol rearrangement'.



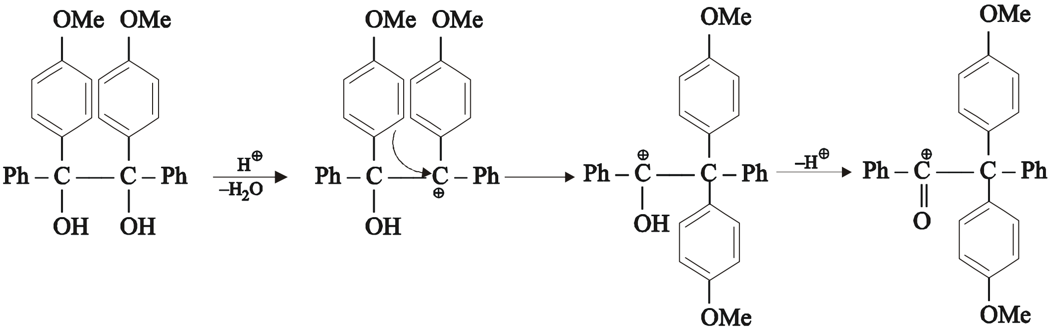
Example: Deamination of α-amino alcohols (Scheme-3) is closely related with pinacol rearrangement and is called Semipinacol rearrangement.



(Scheme-3)

Migratory Aptitude

A group which is more nucleophilic in nature on the non-ionic carbon (adjacent to positive C) will prefer to migrate.

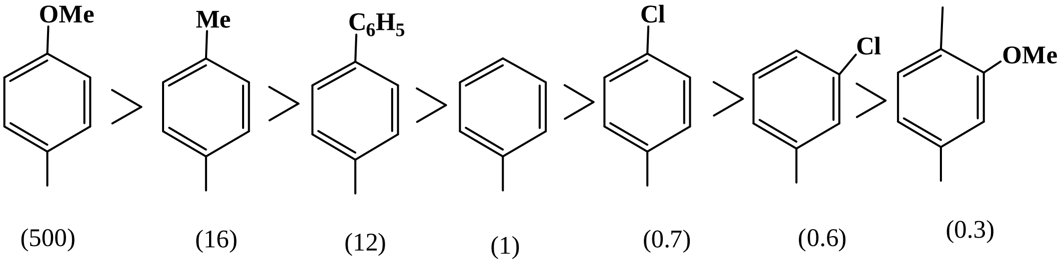


(Scheme-4)

Here, in anisyl group, the electron donating nature of –OMe group makes it a stronger nucleophile than Ph, consequently anisyl group migrates to the positively charged C preferentially (scheme-4). If All other conditions remain the same, the migratory order of group is:

Aryl > Alkyl > H

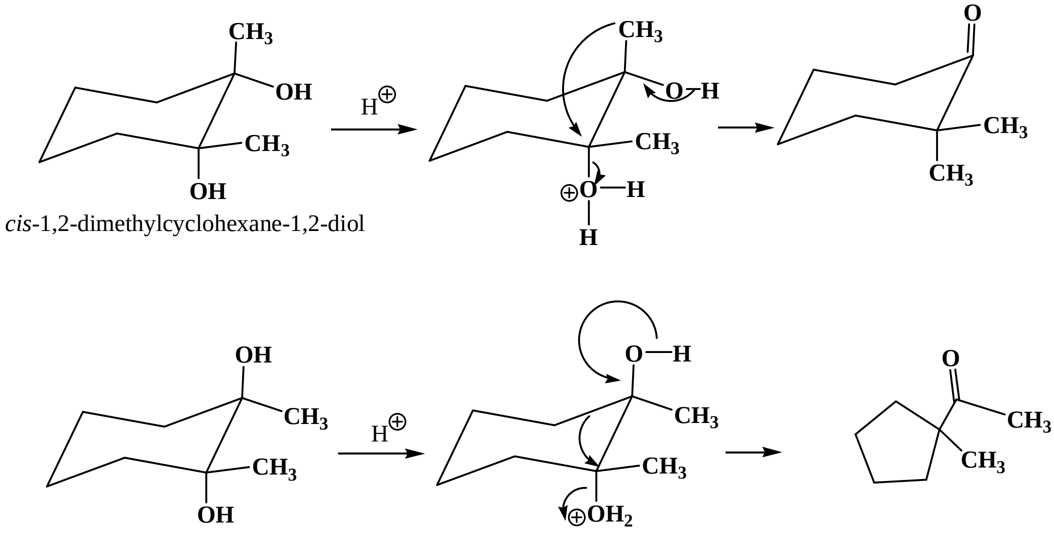
The reason is that aryl group upon migration forms an intermediate phenonium ion, which is being resonance stabilized. The relative migratory aptitude of aromatic substituents in the pinacolic rearrangement is given below, which was determined by Bachman.



These values are with reference to Ph group with migrating value of 1.

Stereochemical and Conformational Factors

The most favorable stereochemistry for pinacolic rearrangement is that the leaving group and shifting group (migrating group) must be anticoplanar. It can be explained by the example of 1,2-dimethylcyclohexane-1,2-diol. The *cis* form (having migrating group anti to the leaving group) of it undergoes the pinacolic rearrangement easily in dilute H_2SO_4 with migration of a methyl group whereas the *trans* derivative undergoes rearrangement under similar conditions with contraction of the ring (scheme-5).



cis-1,2-dimethylcyclohexane-1,2-diol

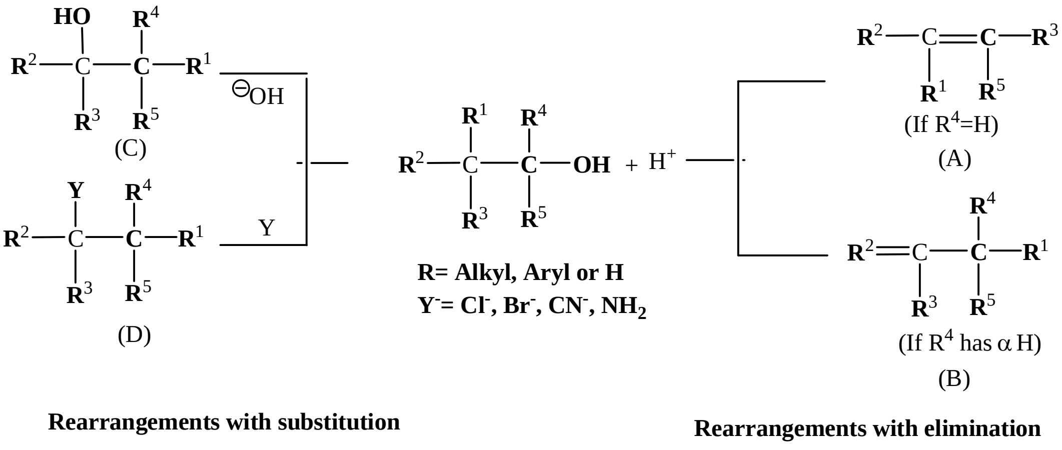
trans-1,2-dimethylcyclohexane-1,2-diol

(Scheme-5)

3.5.2 Wagner-Meerwein rearrangement

An Anionotropic rearrangement involving transformation of a lesser stable carbonium ion in to a more stable one, so that the actual carbon skeleton is changed, known as Wagner-Meerwein Rearrangement. First discovered in bicyclic terpenes.

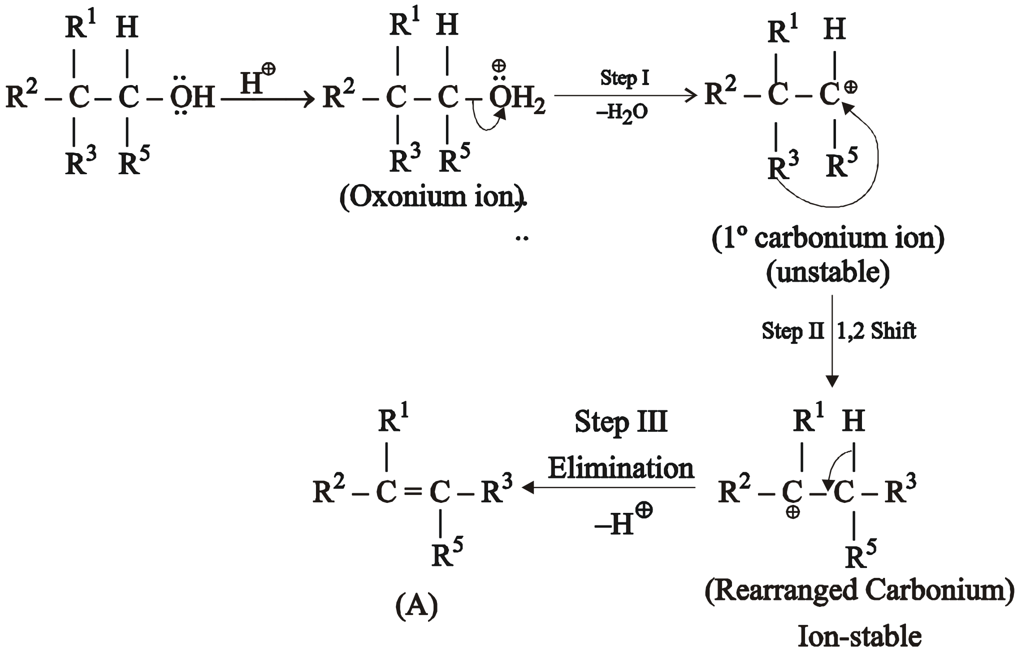
Reaction : Most common example is reaction of alcohol with conc. acid to give rearranged products with either elimination or substitution (scheme-6).



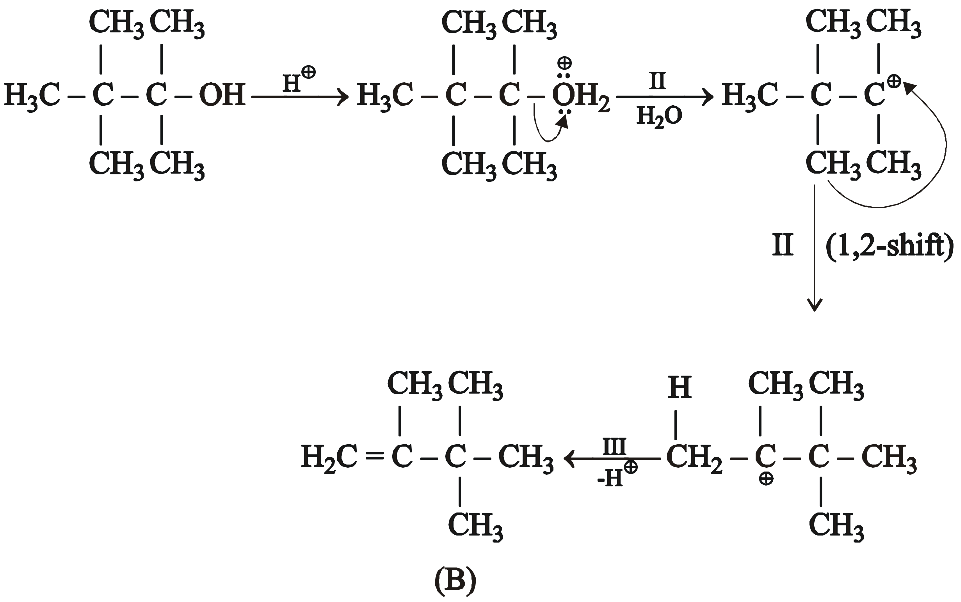
(Scheme-6)

Mechanism: The general mechanism is the generation of carbonium ion which rearranges to a more stable one followed by either substitution or elimination to yield products.

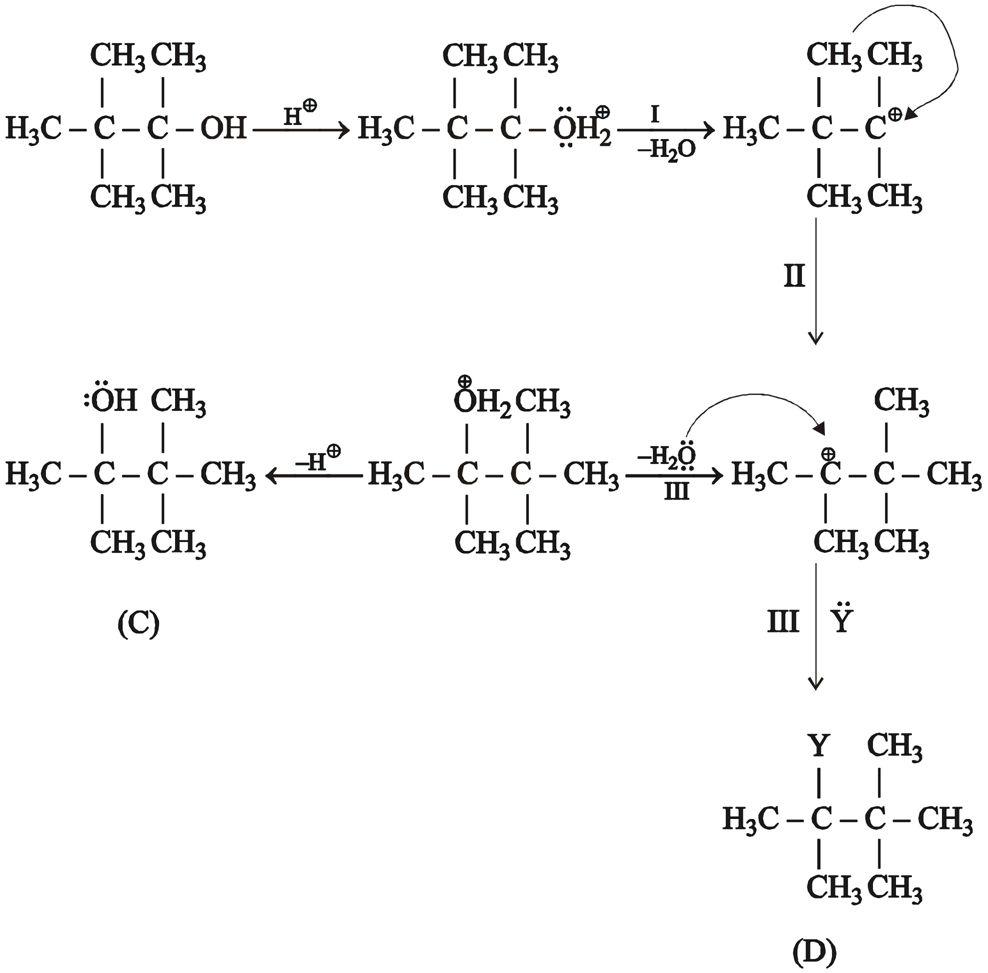
(A) If R^4 = H



(B) If R^2 has on α Hydrogen atom



(C) & (D) Rearrangements with substitution



Following reactions include Wagner Meerwein rearrangement:

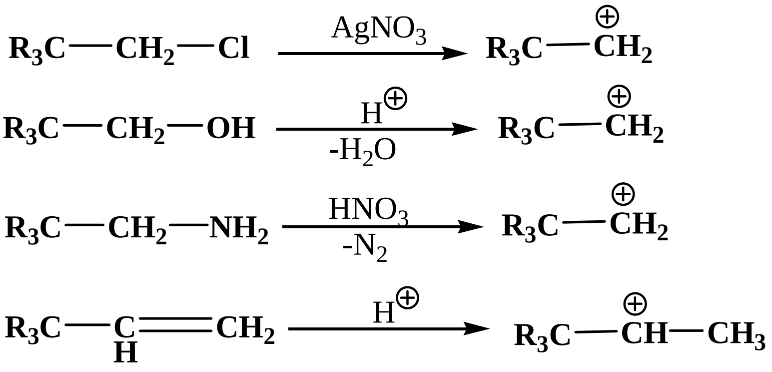
(i) Electrophilic addition of alkenes

(ii) Nucleophilic substitution (SN^1)

(iii) E^1 elimination

(iv)Friedel-Craft alkylation reactions etc.

Carbonium generation :



$$R_3C-CH_2-Cl \xrightarrow{AgNO_3} R_3C-\overset{\oplus}{C}H_2$$

$$R_3C-CH_2-OH \xrightarrow[-H_2O]{H^{\oplus}} R_3C-\overset{\oplus}{C}H_2$$

$$R_3C-CH_2-NH_2 \xrightarrow[-N_2]{HNO_3} R_3C-\overset{\oplus}{C}H_2$$

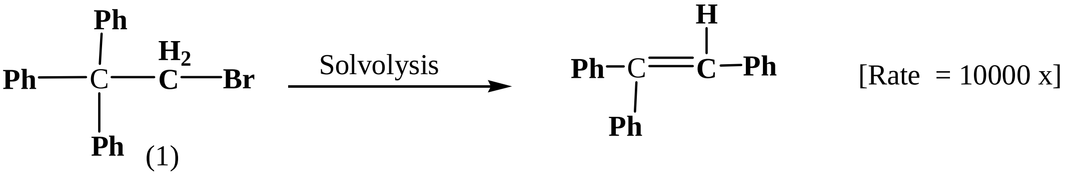
$$R_3C-\underset{H}{C}=CH_2 \xrightarrow{H^{\oplus}} R_3C-\overset{\oplus}{C}H-CH_3$$

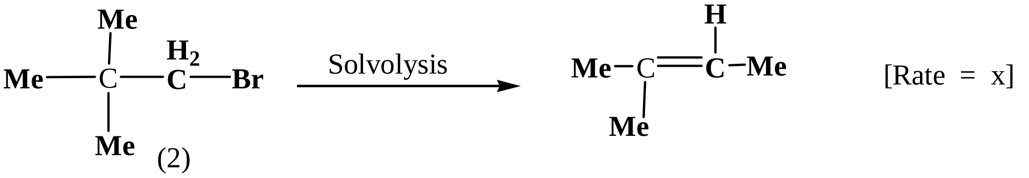
Migratory aptitude

The aryl groups has far greater migratory aptitude than alkyl groups or hydrogen

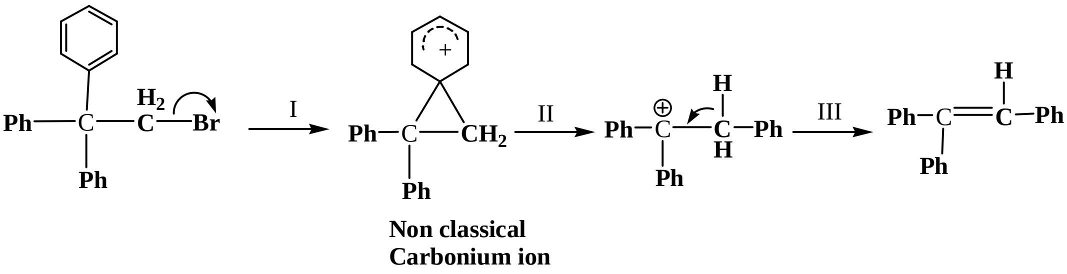
Usually Aryl > Alkyl > H, [except in deamination]

For e.g. solvolysis of neophenyl bromide is several thousand higher than solvolysis of neopentyl bromide. Why ?





The reason is that in the case of neopentyl bromide (2), during solvolysis a 1° carbonium ion is formed, which being unstable rearranges to 3° carbonium ion. While, in neophenyl bromide (1), a bridged non–classical low energy carbonium ion is formed due to neighbouring group participation of Ph group in the system and thus migration of phenyl group is favoured over Me.



Migratory aptitude is enhanced by electron rich group in the aromatic ring while electron deficient group reduces it.

Stereochemistry

The rearrangement is stereospecific i.e. the migratory group always approaches the electron deficient carbon from the direction opposite to that in which the leaving group is departing. Consequently inversion of configuration occurs at the electron deficient carbon. [In a ring system a group above the plane of the ring system moves above the plane while the group below the plane moves below the plane]

The following conversion involves Wagner-Meerwein rearrangement:-

(i) α-Pinene → Bornyl chloride

(ii) Camphene → Isobornyl chloride

(iii) Borneol → Camphene - dehydration with acids

(iv) Bornyl chloride → Camphene

3.5.3 Demjanov rearrangement

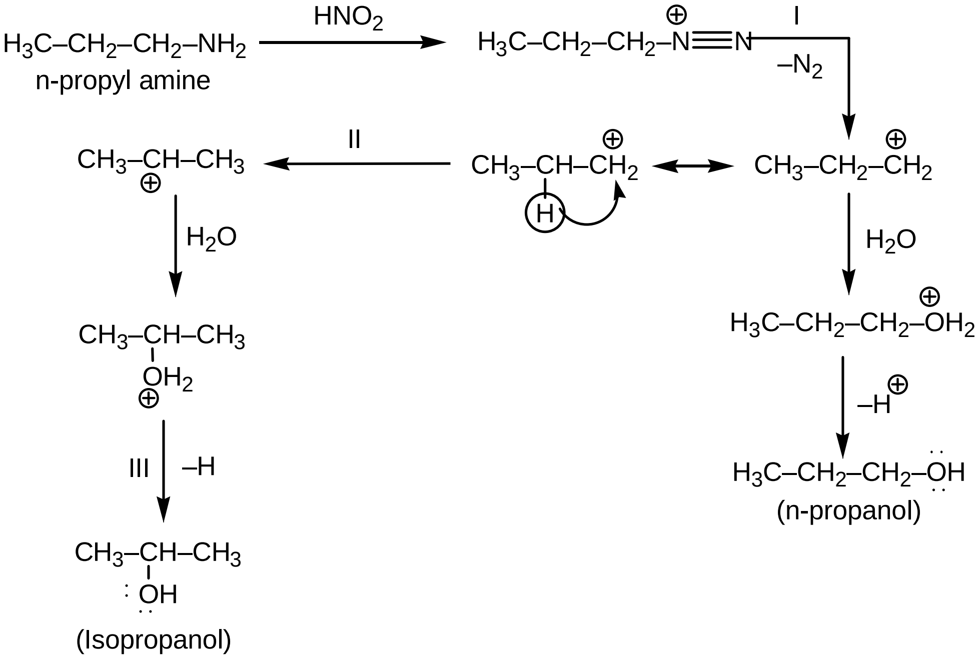
HNO_2 acid catalysed conversion of a 1° amine to form a carbonium ion which further gives rearranged products along with some elimination addition products.

Characteristics:

(iv) Anionotropic rearrangement
(v) Carbon to Carbon migration

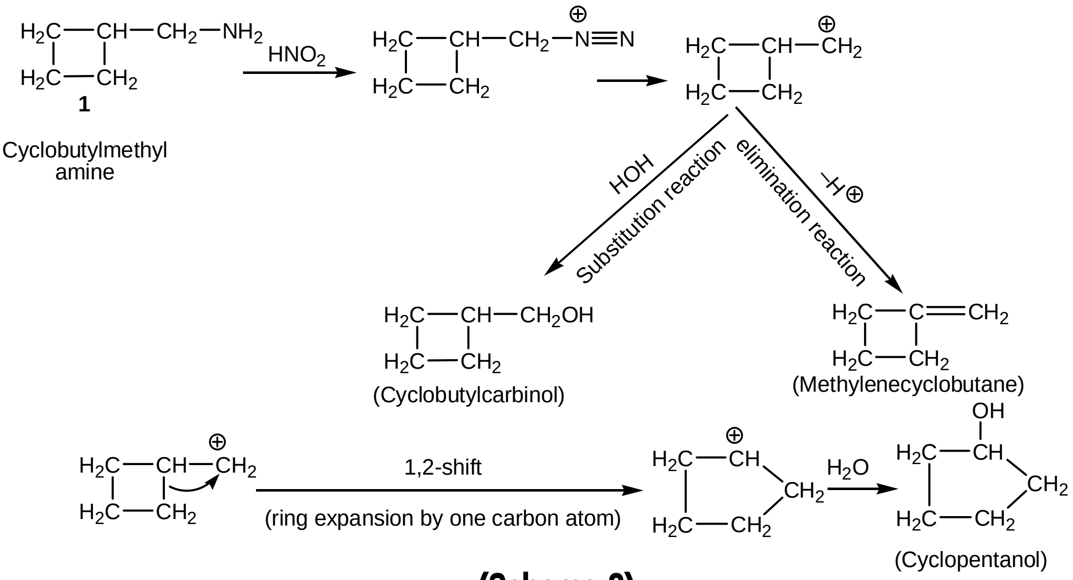
Reaction: When n-propyl amine is treated with HNO_2(scheme-7), it leads to the formation of carbonium ion, which may undergo either of the reaction to yield various products:

(a) Nucleophilic addition
(b) Rearrangement + Nucleophilic addition
(c) Elimination of proton



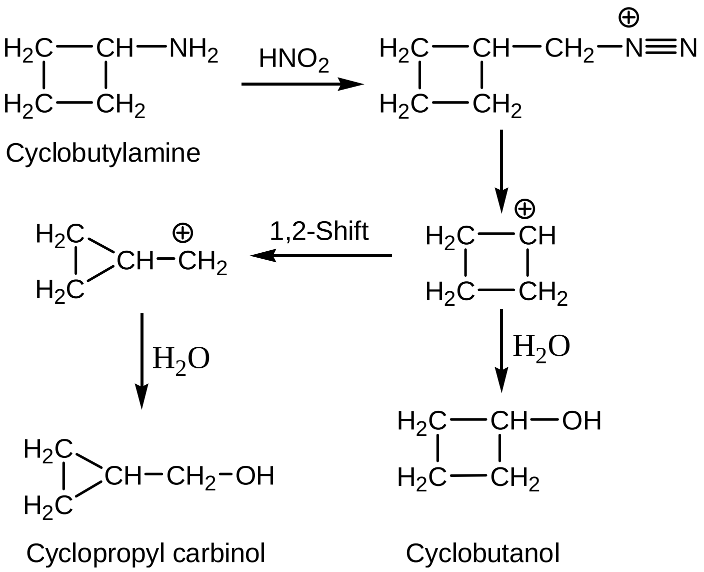
(Scheme-7)

Another example is the reaction of cyclobutylmethylamine with nitrous acid (scheme 8), which gives both cyclobutylcarbinol and cyclopentanol besides methylene cyclobutane. The formation of three products can be readily rationalized by considering all the three typical properties of carbocation, viz., addition of nucleophiles, elimination of proton and rearrangements to a more stable reaction.



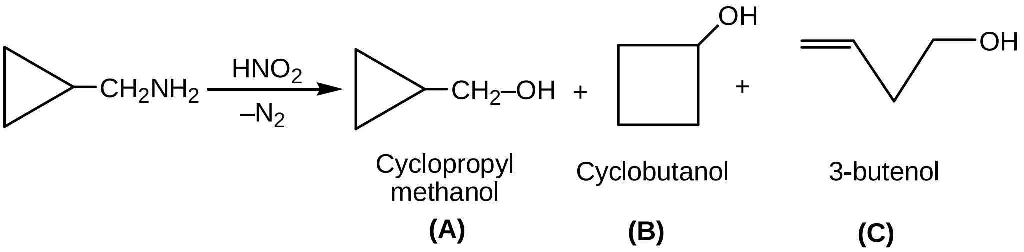
(Scheme-8)

Cyclobutylamine yields both cyclobutanol and cyclopropyl carbinol. The mechanism of these reactions are as follows (scheme 9).



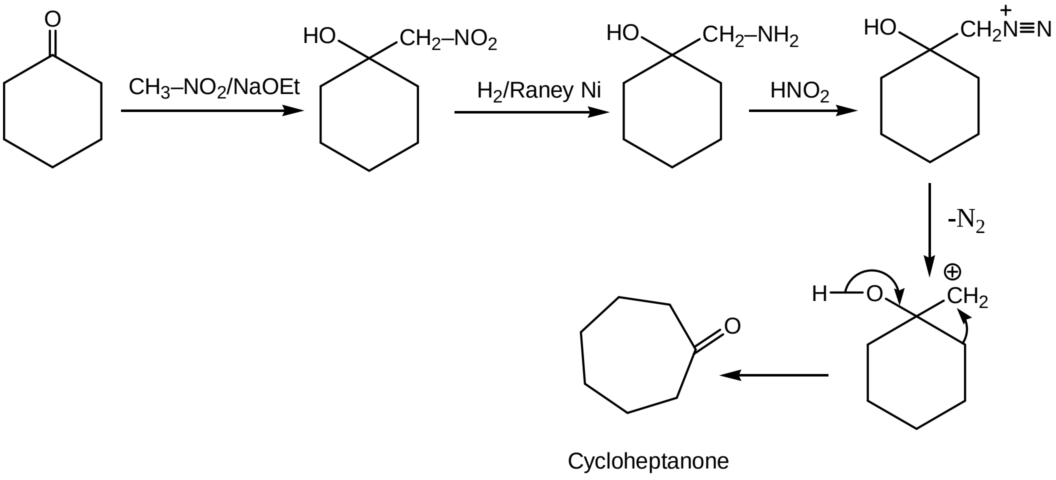
(Scheme-9)

When alicyclic amines are treated with HNO_2, various types of products are formed as shown in scheme-10.



(Scheme -10)

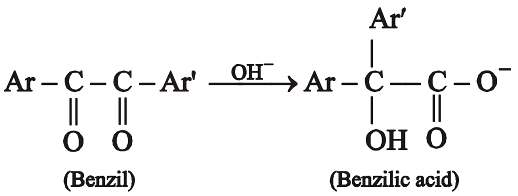
A specific variant of this reaction which leads to one carbon ring expansion is known as the Tiffeneu-Demyanov Rearrangement which is very useful for homologating cyclic ketones by the use of nitromethane or diazomethane. This reaction is used for those cyclic ketones which contain three to seven carbons in the ring of the substrate (scheme-11).



(Scheme-11)

3.5.4 Benzil-Benzilic acid rearrangement

Base catalysed rearrangement of α-diketones (usually aromatic) to yield α-hydroxy acids in their salt form is known as benzil-benzilic acid rearrangement. For example, benzil on treatment with KOH, followed by acidification yields benzilic acid.



$$\underset{\substack{\parallel \\ O}}{Ar - C} - \underset{\substack{\parallel \\ O}}{C} - Ar' \xrightarrow{OH^-} Ar - \overset{\substack{Ar' \\ |}}{\underset{\substack{| \\ OH}}{C}} — \underset{\substack{\parallel \\ O}}{C} - O^-$$

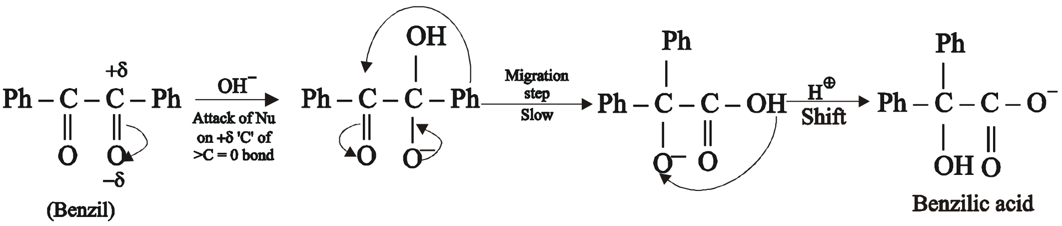
Characteristics

(i) Anionotropic rearrangement

(ii) Migration from Carbon to Carbon

(iii) Reactant are mostly aromatic α-diketones. Sometimes may aliphatic α-diketones and α-keto aldehydes.

Mechanism



Reaction begins with attack of OH$^-$ on partially positive charged carbon of > C = O group; similar to tetrahedral mechanism of nucleophilic substitution. Here, the migrating group does not move to an open sextet Carbon; but the 'carbon' makes room for it by releasing an electron pair to the 'O' of C = O group. This is a push-pull mechanism analogous to intramolecular Cannizaro reaction. The reaction is second order each in benzil and in base.

Rate α $[OH^-][Benzil]$

Migratory Aptitude

In any case if there is a choice between various aryl groups to migrate, one which is less electron releasing (electron deficient) will prefer to migrate over a more electron releasing (electron rich) group because a more electron releasing group will tend to neutralize the positive charge on the carbonyl C atom to which it is attached and hence OH$^-$ ion can attack easily on adjacent carbon of other >C=O group.

The following conversion involves benzil-benzilic acid rearrangement:

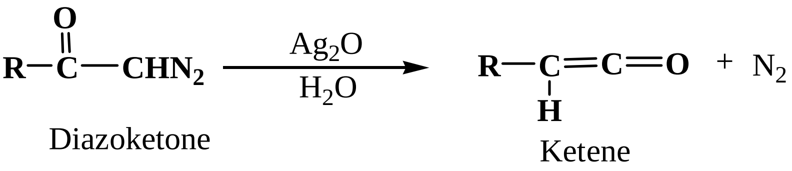
(i) Ketopinic acid → Citric acid

(ii) Furil → Furilic acid

(iii) 9,10-Phenanthraquinone→ 9-hydroxy-9-fluorenecarboxylic acid

3.5.5 Wolff rearrangement

Conversion of an α-diazoketone into a ketene and N_2 on treating with silver oxide and H_2O, is known as Wolff rearrangement.



$$R-\overset{\overset{O}{\|}}{C}-CHN_2 \xrightarrow[H_2O]{Ag_2O} R-\underset{\underset{H}{|}}{C}=C=O + N_2$$

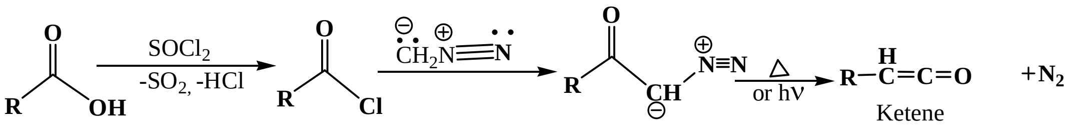
Characteristics

- (i) Anionotropic rearrangement
- (ii) Carbon to Carbon Migration
- (iii) Both thermal and photochemical rearrangements are possible

Wolff rearrangement generates ketene in the absence of any nucleophile. However, when this rearrangement is carried out in the presence of water, alcohol or amine, the ketene is converted into carboxylic acid, ester or amide, respectively. The overall reaction is known as Arndt-Eistert synthesis.

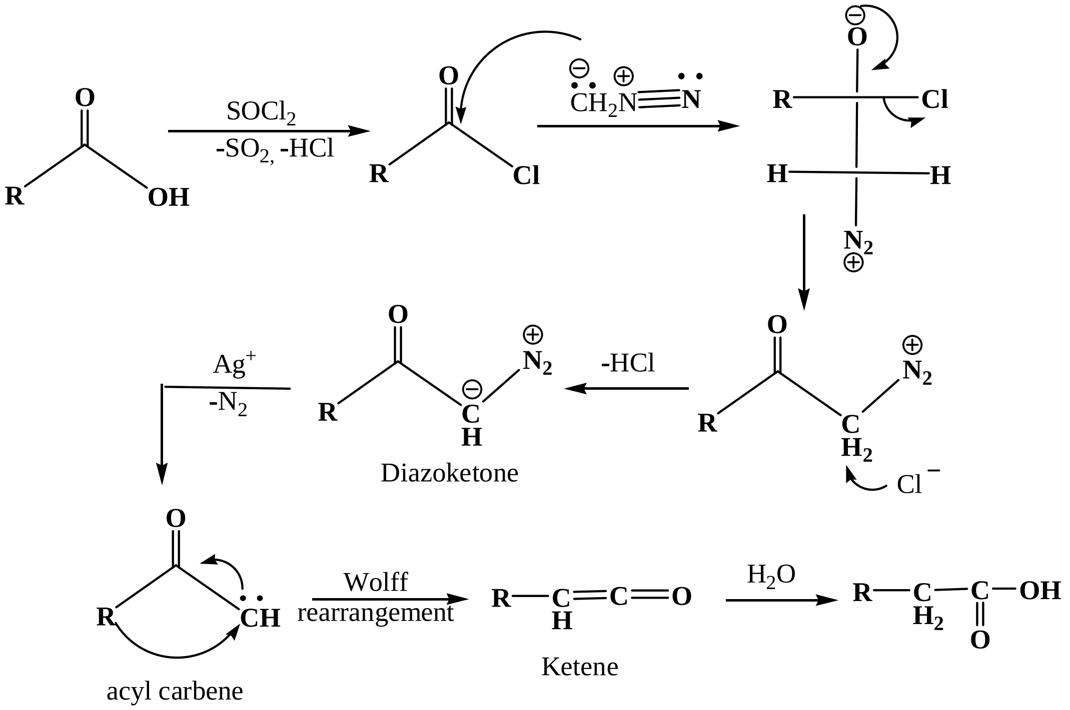
3.5.5.1 Arndt-Eistert synthesis

Arndt-Eistert reaction is a method to convert a carboxylic acid to a higher carboxylic acid homologue (i.e. contains one additional carbon atom). Acid chlorides react with diazomethane to give diazoketones, which rearranges with loss of nitrogen. In the presence of metal catalyst (Ag_2O) give ketene. The ketene is subsequently converted to its higher carboxylic acid homologue.



Mechanism :

Loss of nitrogen from the α-diazoketone is accompanied by 1,2-shift of the alkyl group with electron pair. The resulting ketene readily combines with the solvent molecule (scheme-12), which may be water to give acid, alcohol to give an ester, or amine to give an amide. If reaction is carried out by photochemically, it is believed to involve the formation of carbene.



(Scheme-12)

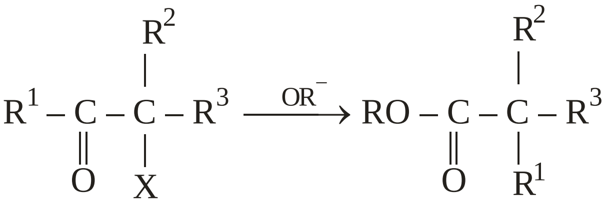
A disadvantage of this reaction is that an epoxide is formed as a by product and in some cases it may be the only product.

3.6 Rearrangements involving migration to an electron rich carbon:

These rearrangement involve electrophilic 1,2-shifts in which the migration of carbon occur from C , N, S, O to an adjacent atom bearing an unshared electron pair and negative charge.

3.6.1 Favorskii rearrangement

Base catalysed rearrangement of an α-haloketone to an ester is known as Favorskii rearrangement.



$$R^1-\underset{\underset{O}{\|}}{C}-\underset{\underset{X}{|}}{\overset{\overset{R^2}{|}}{C}}-R^3 \xrightarrow{OR^-} RO-\underset{\underset{O}{\|}}{C}-\underset{\underset{R^1}{|}}{\overset{\overset{R^2}{|}}{C}}-R^3$$

Characteristics

(i) Electrophilic, carbanion rearrangement or cationotropic rearrangement.

(ii) The product is rearranged carbon skeleton with equal number of 'C' atoms.

(iii) Carbon to Carbon migration.

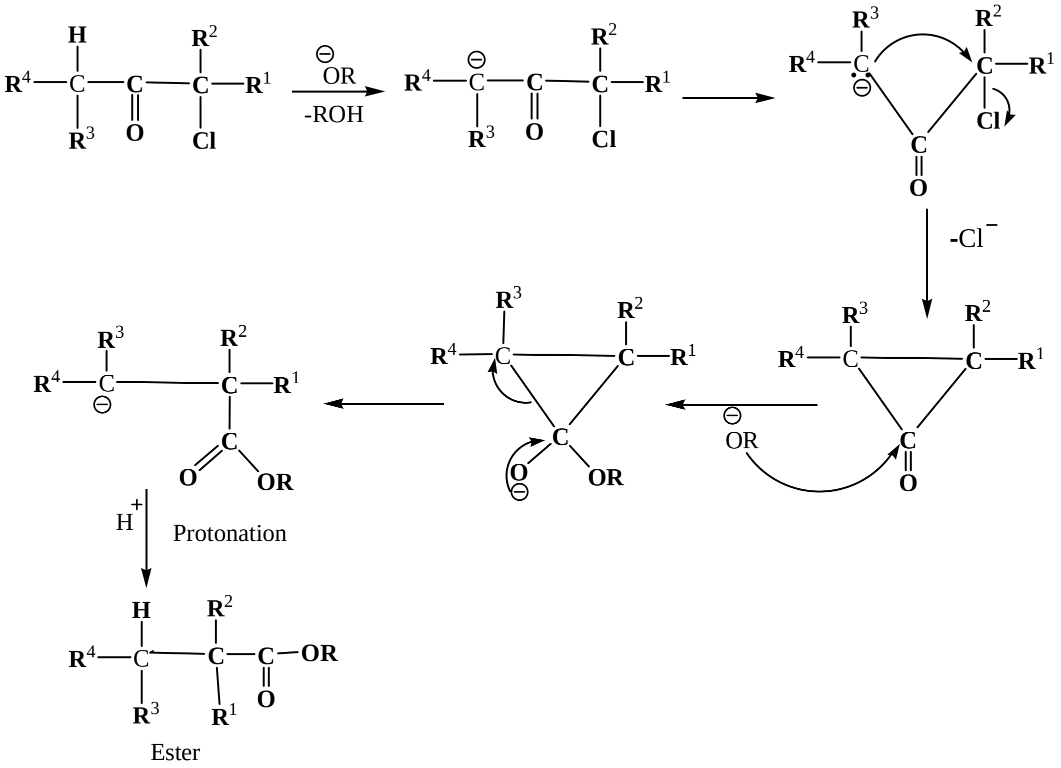
(iv) Halogen are usually Cl^-, Br^- but not I^-

(v) R^1, R^2, R^3 - Alkyl, Aryl

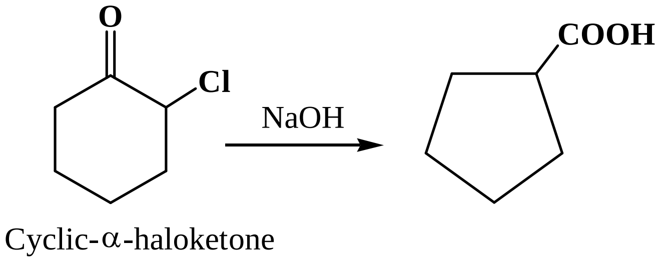
(vi) Base - Only alkoxide ions give the reaction acting as powerful base; while other bases like OH^-, amines etc. gives carboxylic acids or amides respectively.

Mechanism

The reaction proceeds via a cyclopropanone intermediate, which then undergoes rearrangement and finally gives the product ester. The overall consequence of the Favorskii rearrangement is that an alkyl group is transferred from one side of carbonyl group to the other.

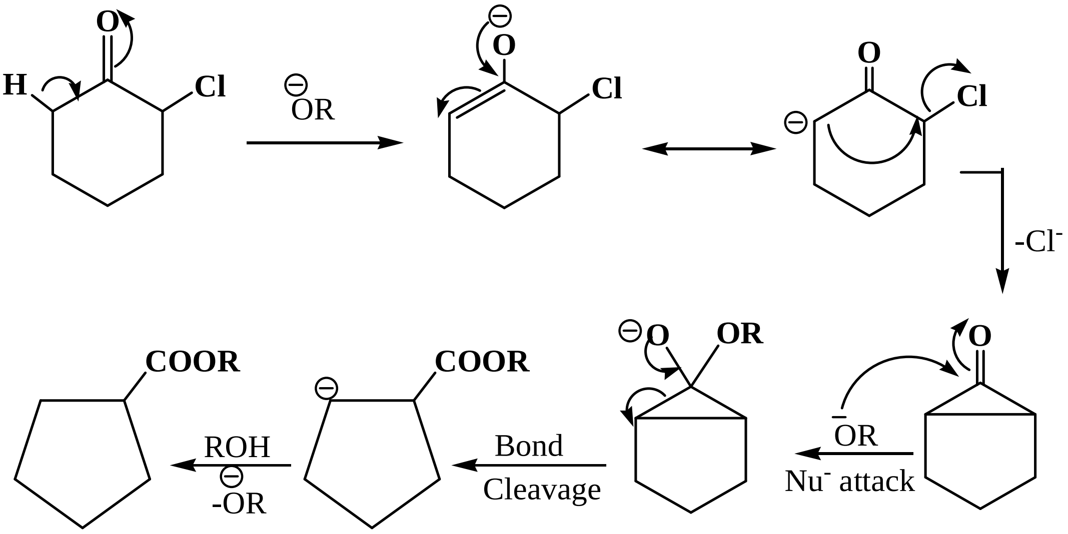


In case of cyclic α-halo ketones, the reaction with alkoxide ions results into ring contraction by the same mechanism (Scheme-13).



The mechanism again involves cyclopropanone intermediate, which as follows:

Mechanism



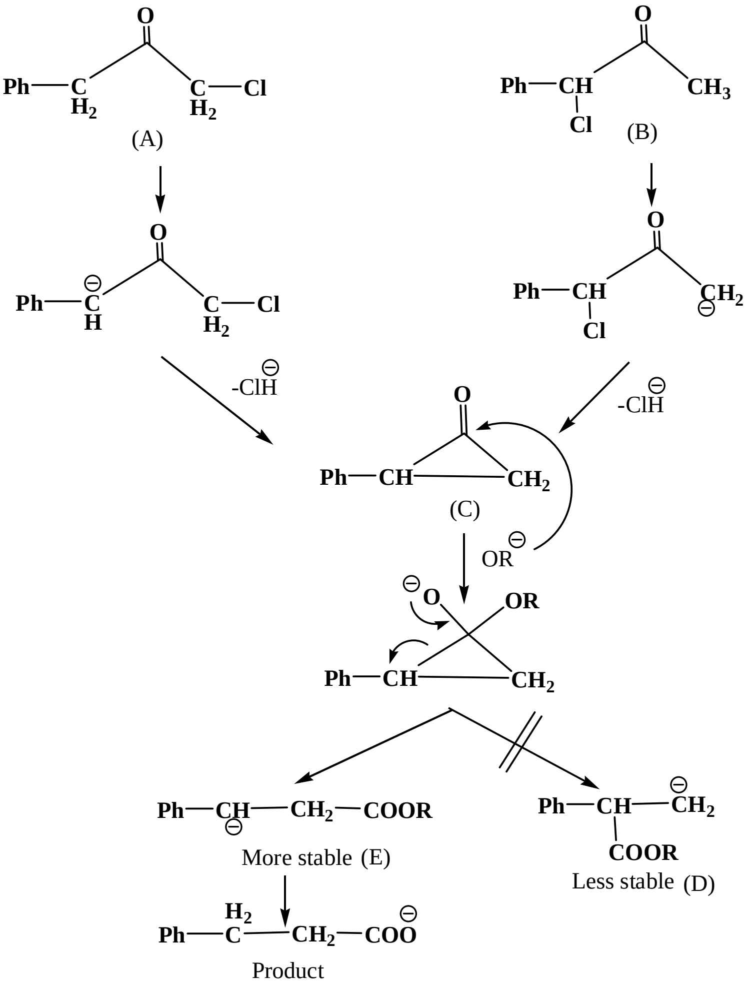
(Scheme-13)

Driving force for the reaction may be as follows:

(i) Formation of more stable carbanion.

(ii) Strain release of three membered cyclopropanone ring by ring opening and migration .

If cyclopropanone intermediate so formed is not symmetrically substituted with respect to >C=O group, then ring opening occurs from that side which leads to formation of stabler carbanion. When [A] & [B] are subjected to reaction condition (scheme-14), then intermediate [C] is formed which gives stable carbanion [E] instead of unstable [D] and ultimately the product. It can be explain by following mechanism:



(Scheme-14)

3.7 Summary

- **Rearrangement** : A rearrangement reaction involves reshuffling of the sequence of atoms to form a new structure. Migration of a group from one atom to another within the same molecule occurs.
- **Nucleophilic Rearrangement:** Migration of the migratory group 'W' from a carbon atom, with its electron pair (as a nucleophilic) to an adjacent electron deficient atom
- **Electrophilic Rearrangement**: Migration of the migratory group ‘W’ from a C atom (without bonding electrons) to an adjacent electron rich atom.

- **Pinacol–Pinacolone Rearrangement :** Acid catalyzed conversion of polysubstituted ethylene glycols to carbonyl compounds via carbonium ion.
- **Wagner-Meerwein Rearrangement:** Anionotropic rearrangement involving transformation of a lesser stable carbonium ion to a more stable one so that the actual carbon skeleton is changed.
- **Benzil-Benzilic acid Rearrangement** : Base catalysed rearrangement of α-diketones (usually aromatic) to yield α-hydroxy acids in their salt form.
- **Arndt-Eistert Reaction:** Conversion of a carboxylic acid to a higher carboxylic acid homologue.
- **Favorskii Rearrangement**: Base catalysed rearrangement of an α-halo-ketone to an ester.

3.8 Review questions

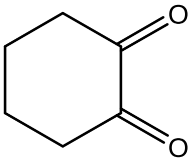
1 Write the mechanism of each of the following rearrangements.

(a) Wagner-Meerwein

(b) Benzil-Benzilic acid

(c) Pinacol-Pinacolone

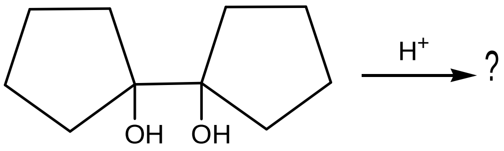
2 Identify the products formed by α-diketones

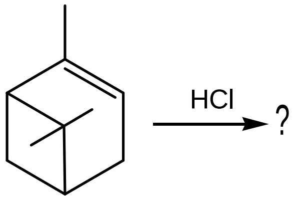
(a) 

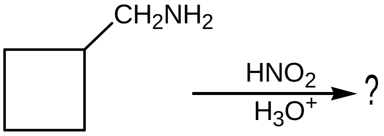
(b) $CH_3{-}COCOCOOC_2H_5$

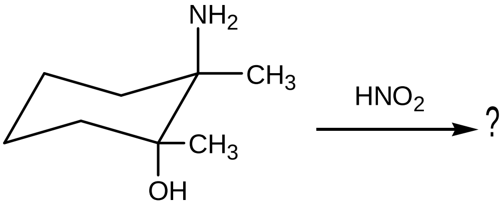
[Hint – benzil-benzilic acid rearrangements]

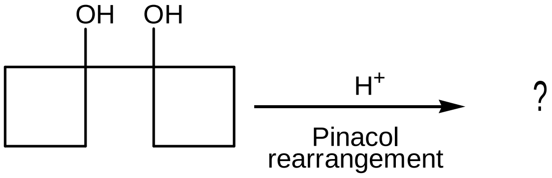
3 What products you expect from the following reactions ?

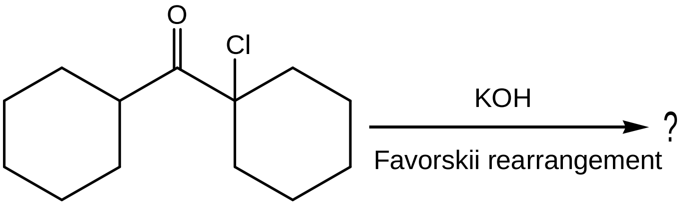
(a) 

(b) 

(c) 

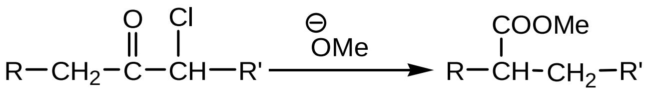
(d) 

(e) 

(f) 

4 What do you mean by migratory aptitude? Discuss its significance taking the examples of pinacol-pinacolone rearrangements.

5 Give the name and mechanism for the following reactions:



$$R-CH_2-\overset{\overset{O}{\|}}{C}-\overset{\overset{Cl}{|}}{CH}-R' \xrightarrow{\overset{\ominus}{O}Me} R-\overset{\overset{COOMe}{|}}{CH}-CH_2-R'$$

6 Give mechanism of Arndt-Eistert synthesis.

7 Explain memory effects with an example.

3.9 Reference and Suggested readings

- Advanced Organic Chemistry, J. March, 6th Ed.
- Organic Chemistry, J. Clayden, N. Greeves, S. Warren, Oxford University, Second Edition.
- Principles of Organic Synthesis, R.O.C. Norman and J. M. Coxon, CRC Press.
- Advanced Organic Chemistry Part-B, F. A. Carey and R. J. Sundberg, 5th Ed. Springer.
- Organic Reactions and their Mechanisms, P.S. Kalsi, New Age International Publishers.
- Organic Reaction Mechanism, V. K. Ahluwalia and Rakesh Kumar Parashar, Narosa Publishing House.

Unit–4

Molecular Rearrangements – II

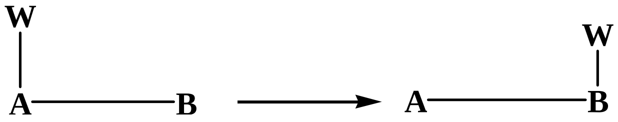
Structure of unit

4.0 Objective

There are three types of reactions: Ionic, radical and pericyclic reactions. Ionic reactions, which include addition, substitution, elimination and rearrangement. In rearrangement the molecule changes its carbon skeleton. The various rearrangements involves migration of carbon to electron-deficient carbon. Besides this there are other rearrangements which involve migration of carbon to other electron deficient atom which may be nitrogen or oxygen or to an electron rich carbon. Study of these rearrangements are important for the organic synthesis.

4.1 Introduction

Rearrangement is referred to the migration of atom or a group of atoms from one atom to another with in a molecule or from one molecule to another.



where, A - Migratory origin

B - Migration terminus

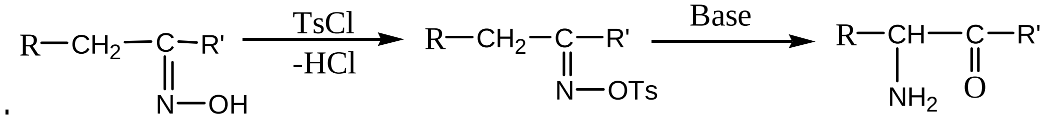
W- Migrating group

Generally, these migrations occurs from an atom to an adjacent one (called 1, 2 – shifts) also called as 'whitmore' 1,2-shifts, however longer distance migrations are also possible.

4.2 Rearrangements involving migration to an electron rich carbon

4.2.1 Neber rearrangement

Base catalysed conversion of ketoxime tosylates to α-amino ketones is known as Neber rearrangement. It is closely related to Beckmann rearrangement. The mechanism of the rearrangement involves the intermediate formation of an azirine. Aldoximes donot undergo this rearrangement.



Here, OTs is Good leaving group.

R = Mostly Ar, May also be alkyl

R^1 = Ar, R but not H

Base - Alkoxides, Pyridine

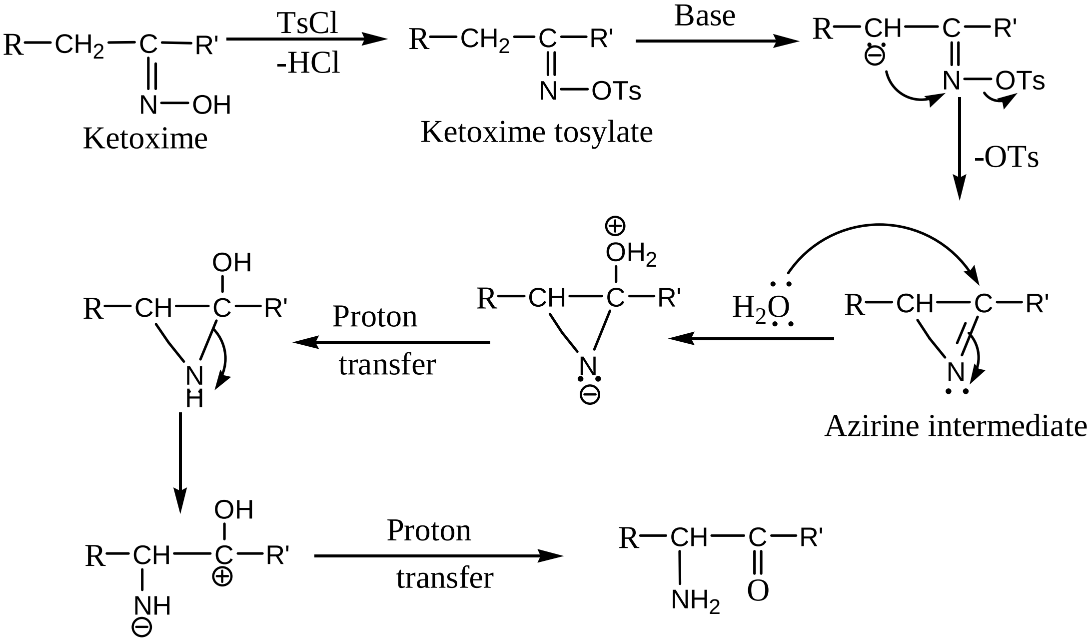
Characteristics

(i) Neber oxime tosylate-amino ketone rearrangement

(ii) Electrophilic, Carbanion rearrangement or Cationotropic rearrangement

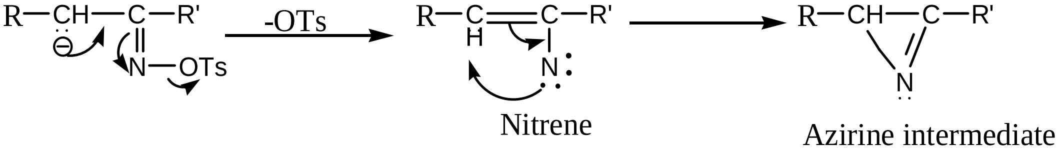
(iii) Carbon to Carbon migration of N containing group.
(iv) Product is rearranged carbon skeleton with equal number of ‘C’ atoms

Mechanism



Evidence

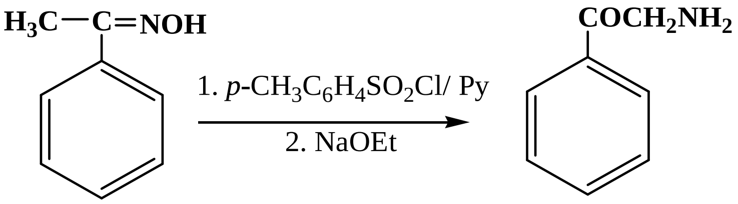
The azirine derivative formed during the reaction has been successfully isolated in various cases using mild conditions, which gives the same product when subjected to reaction conditions at the same rate. However it is also suggested that azirine formation might involve the nitrene intermediate.

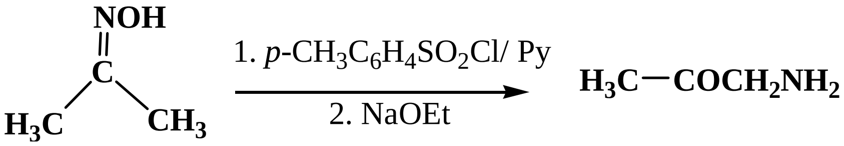


Stereochemistry:

In contrast to Beckman rearrangement, this reaction is sterically indiscriminate. As both ‘syn’ and ‘Anti’ ketoxime tosylates yield same product. This is due to the formation of a cyclic intermediate and sterospecificity is lost.

Examples:

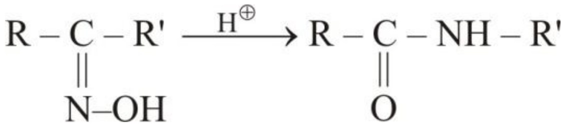




4.3 Rearrangements involving migration to electron deficient nitrogen

4.3.1 Beckmann rearrangement

Acid catalysed transformation of a ketoxime to a N-substituted amide is known as Beckmann rearrangement.

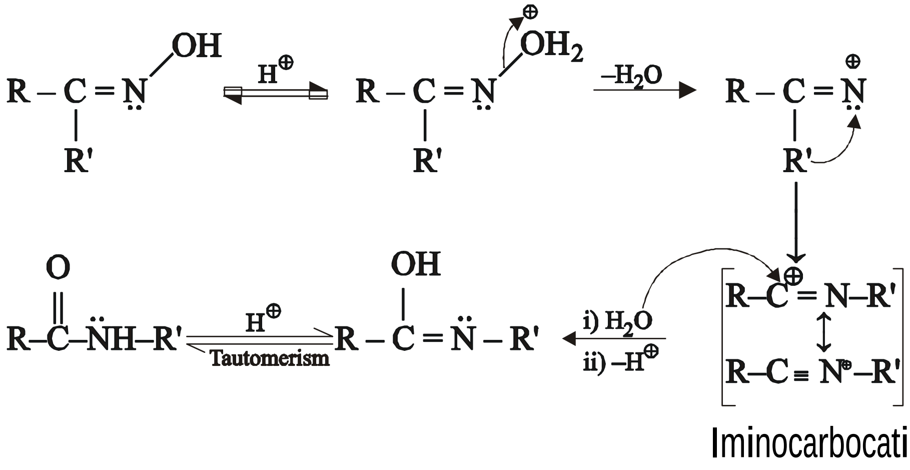


$$R-\underset{\underset{\text{N–OH}}{\|}}{C}-R' \xrightarrow{H^{\oplus}} R-\underset{\underset{O}{\|}}{C}-NH-R'$$

Characteristics

1. Anionotropic rearrangement
2. Migration Carbon to electron deficient Nitrogen
3. R & R$'$ – Alkyl, Aryl or H
    (i) R or R' = H, Migration is quite rare
    (ii) R, R' = both Alkyl, two such amides formed as R'–CO–NHR + R–CO–NHR'
4. Catalyst - Acidic reagents are Conc. H_2SO_4, HCHO, SO_2, PCl_5, $HMPA_7$, PPA, BF_3, $SOCl_2$, $PhSO_2Cl$
5. The reaction have also been carried out photochemically.

Mechanism



It involves initial attack of acidic reagent, the –OH group converts into a more easily leaving group as OH_2, $OPCl_4$, OSO_2 OH, etc. Loss of the leaving group generates an electron deficient species, which is accompanied by migration of a group from adjacent carbon to the electron deficient nitrogen. Resulting iminocarbocation reacts with water to give an amide.

Driving force

As the migration occurs via anionotropic route from C to electron deficient N, it adds stability and releases electron deficiency on the N.

Evidences

From the reaction scheme, the mechanism seems to be intramolecular while it is not so as a whole. This is evidenced by various observed factors. The rearrangement occurs under following aspects :

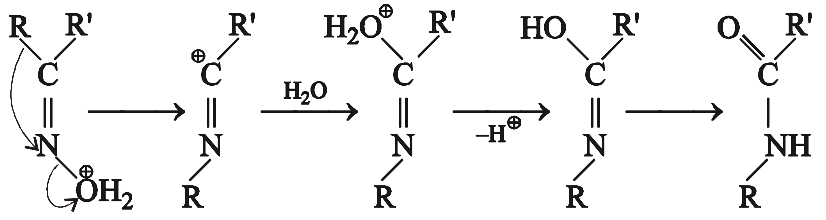
(i) The rearrangement occurs in some intermediate between oxime and amide.

(ii) Migration step is intramolecular.

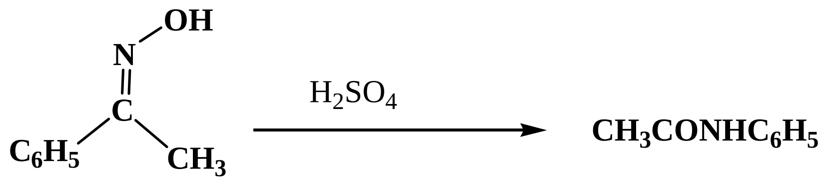
(iii) Anion (–OH or –OX) migration is intermolecular.

Stereochemistry

Reaction is stereospecific, where the migrating group is generally 'anti' to the leaving group (i.e. approaches the N atom from opposite to the 'O' atom).

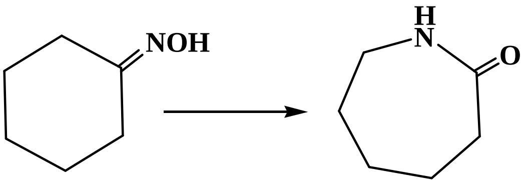


Different geometrical isomers of oximes sometimes give isomeric amides by the Beckmann rearrangement. The stereospecificity in the reaction is so well confirmed that it is used to determine the configuration of oximes. For example acetophenone oxime gives acetanilide



Acetophenone oxime Acetanilide

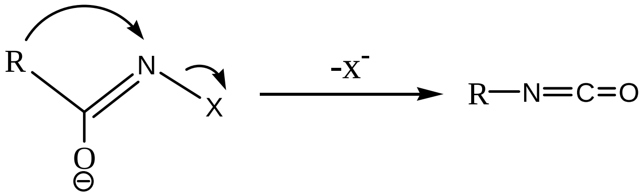
An interesting application of the rearrangement is the synthesis of caprolactam (70%) from cyclohexanone oxime and conc. H_2SO_4.



Cyclohexanone oxime Caprolactam

4.3.2 The Hofmann, Curtius, Schmidt and Lossen rearrangements:

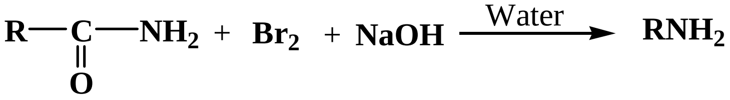
There is a group of closely related rearrangements in which carbon migrates from carbon to nitrogen. They may be formulated generally as:



Where R is an alkyl or aryl group and –X is a leaving group which may be –Br (Hofmann rearrangement), -N≡N$^+$ (Curtius and schmidt rearrangement) and -OCOR (Lossen rearrangement). In each case, if the alkyl carbon which migrates is asymmetric, it retains its configuration.

4.3.2.1 Hofmann rearrangement

Conversion of an amide into an amine with one less ‘C’ by the action of base and bromine in presence of water is known as Hofmann rearrangement.



$$R-\underset{\underset{O}{\|}}{C}-NH_2 + Br_2 + NaOH \xrightarrow{Water} RNH_2$$

Here the actual product is isocyanate, which readily hydrolyses to amine.

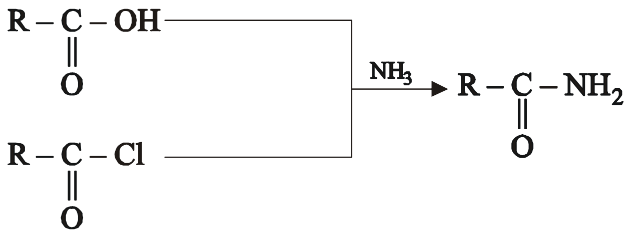
Characteristics:

(i) Hofmann degradation of amides.
(ii) Anionotropic rearrangement
(iii) ‘C’ to ‘N’ (electron deficient) migration.
(iv) Base - NaOBr acts as strong base [$NaOH + Br_2 \longrightarrow NaOBr$]
(v) R group - Aryl or Alkyl, If R = Alkyl with 6, 7 carbons then yields are quite low.

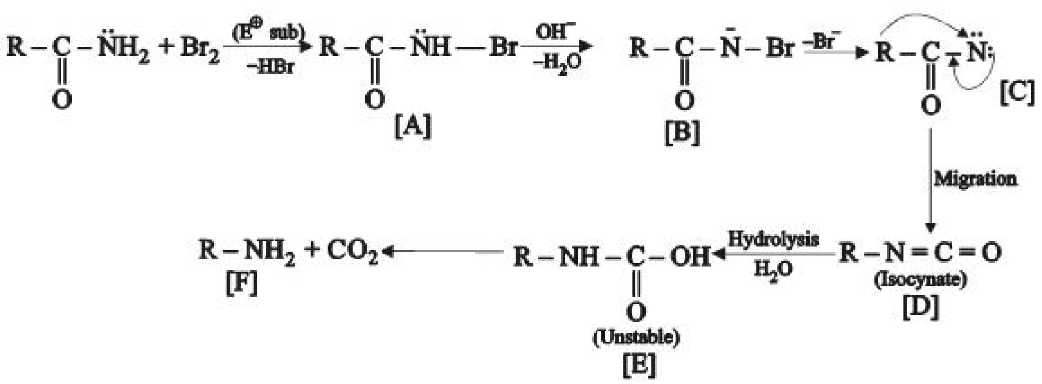
Reaction : Propanamide gives ethylamine on treatment with sodium hypobromite.

$$CH_3CH_2CONH_2 + Br_2 + 4KOH \longrightarrow CH_3CH_2NH_2 + 2KBr + K_2CO_3 + 2H_2O$$

Mechanism



Amide can be formed by the reaction of acid or acyl chloride with ammonia. Initially N-bromoamide[A] is formed by the action of alkaline hypobromite on the amide. The N-hydrogen of N-bromoamide becomes acidic and it is removed by basic OH^- ions. It give transit nitrogen anionic species [B], which is unstable and loses bromide ion with simultaneous migration of R group from adjacent C to N. The resulting isocyanate [D] is hydrolyzed under the reaction condition. It involves conversion of amide to isocyanate via probably nitrene path.



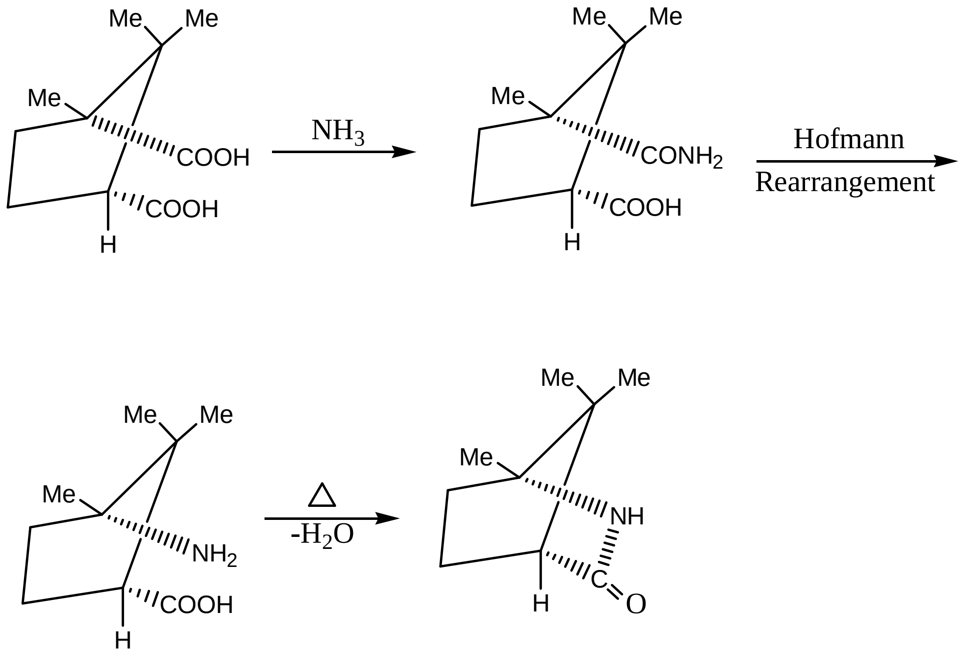
Driving Force

It is seen from mechanism that after elimination of Br^-, the nitrene formed contains an electron deficient N atom having a sextet of electrons and hence tends to gain some stability via migration of ‘R’ group from C to this electron deficient N by its pair of electron to form isocyanate. This is the probable factor which drives the reactant towards the product.

Stereochemistry

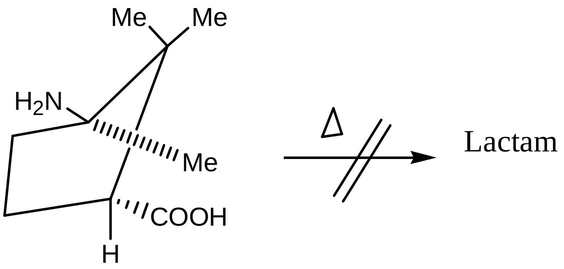
Retention of configuration occurs at migrating ‘C’ atom. This fact can easily be illustrated as follows :

When β-camphoramic acid (having both –COOH and $-CONH_2$ groups in *cis* orientation) is subjected to Hofmann rearrangement, 1-aminodihydro-α-campholytic acid [A] is formed (having both –COOH and NH_2 in cis orientation) which is evident from ready formation of lactam [B].



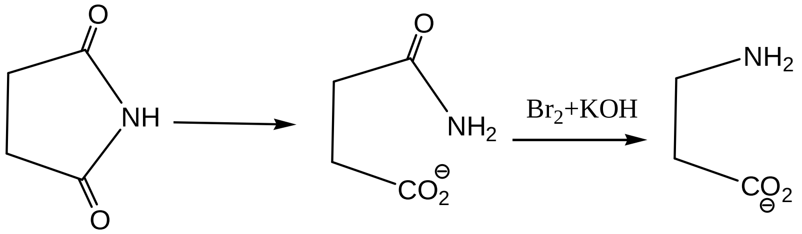
[A] [B]

If there had been inversion of configuration formation of *trans*-amino acid have been occurred which can’t form the lactam as formed above.



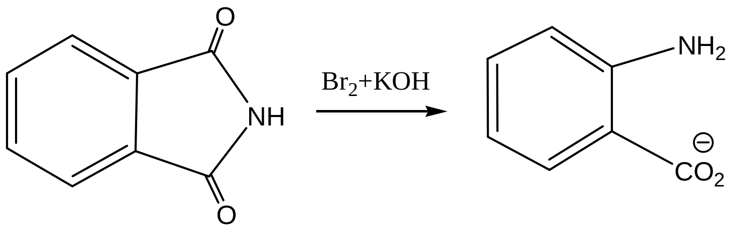
This also proves that departure of Br^- and migration of R group occurs by concerted mechanism.

This rearrangement provides an efficient route for making aliphatic and aromatic primary amines. For e.g. β-alanine can be obtained by treating succinimide with bromine and aqueous KOH; reaction occurs through the half amide of succinic acid.



Succinimide β–Alanine

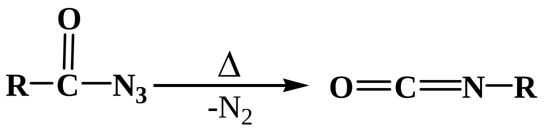
Anthranilic acid may be obtained in a similar way from phthalimide.



Phthalimide Anthranilic acid

4.3.2.2 Curtius rearrangement

Pyrolysis of acid azide to give isocynates via rearrangement is known as curtius rearrangement. Acid azides are prepared from acid chlorides on treatment with sodium azide. The reaction converts acid azide into amine with loss of a carbon.



$$\underset{\text{Acid azide}}{R-\overset{\overset{\large O}{\|}}{C}-N_3} \xrightarrow[-N_2]{\Delta} \underset{\text{Isocyanate}}{O{=}C{=}N-R}$$

Characteristics

(i) Curtius degradation of acid azide.

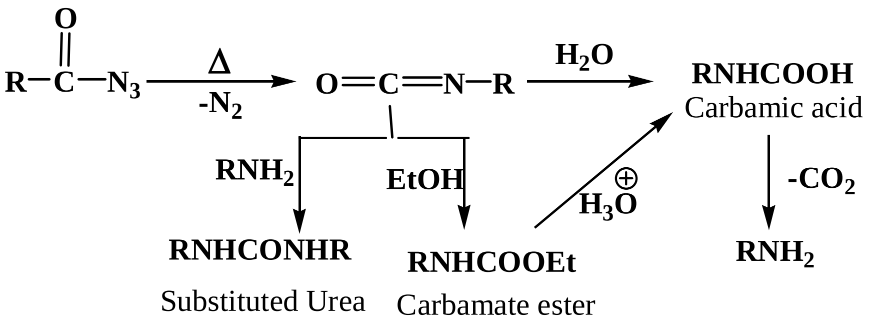
(ii) Anionotropic rearrangement

(iii) Migration from C to electron deficient N atom.

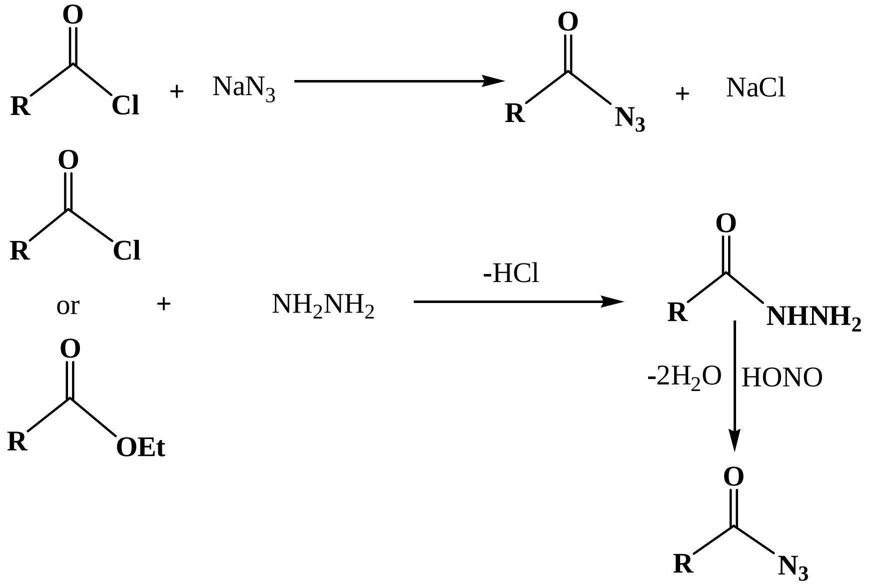
(iv) Applicable to acid azides of almost all kinds of acids - aliphatic, aromatic, alicyclic, heterocyclics etc.

(v) Isocyanate formed can be isolated in good yields in aprotic solvents.

(vi) Reaction when carried out under aqueous or alcoholic media results into amines or carbamate ester as products. e.g.

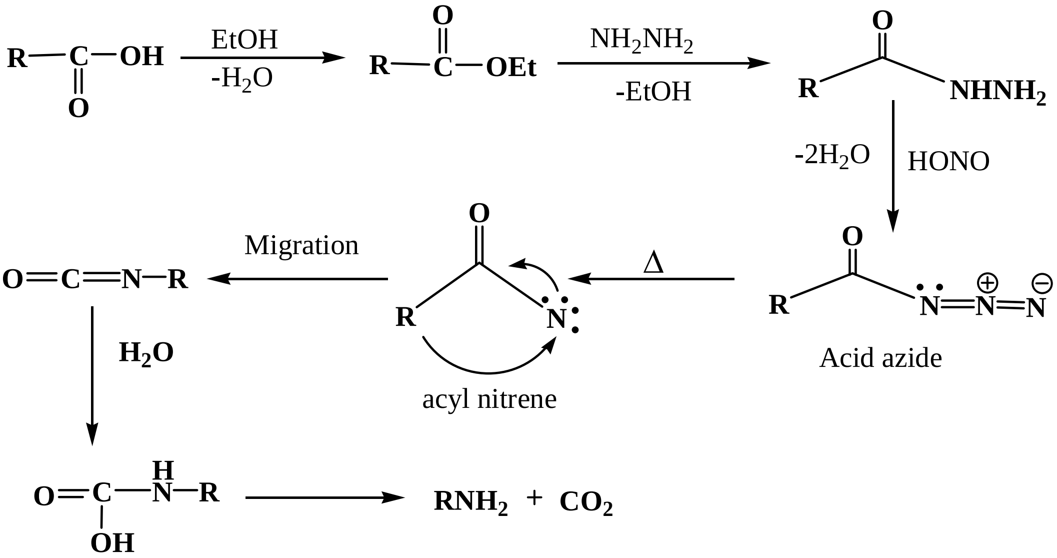


Generation of acid azide :



Acid azide

Mechanism : The rearrangement of acid azide to isocyanate is similar to Hofmann rearrangement.



Driving Force :

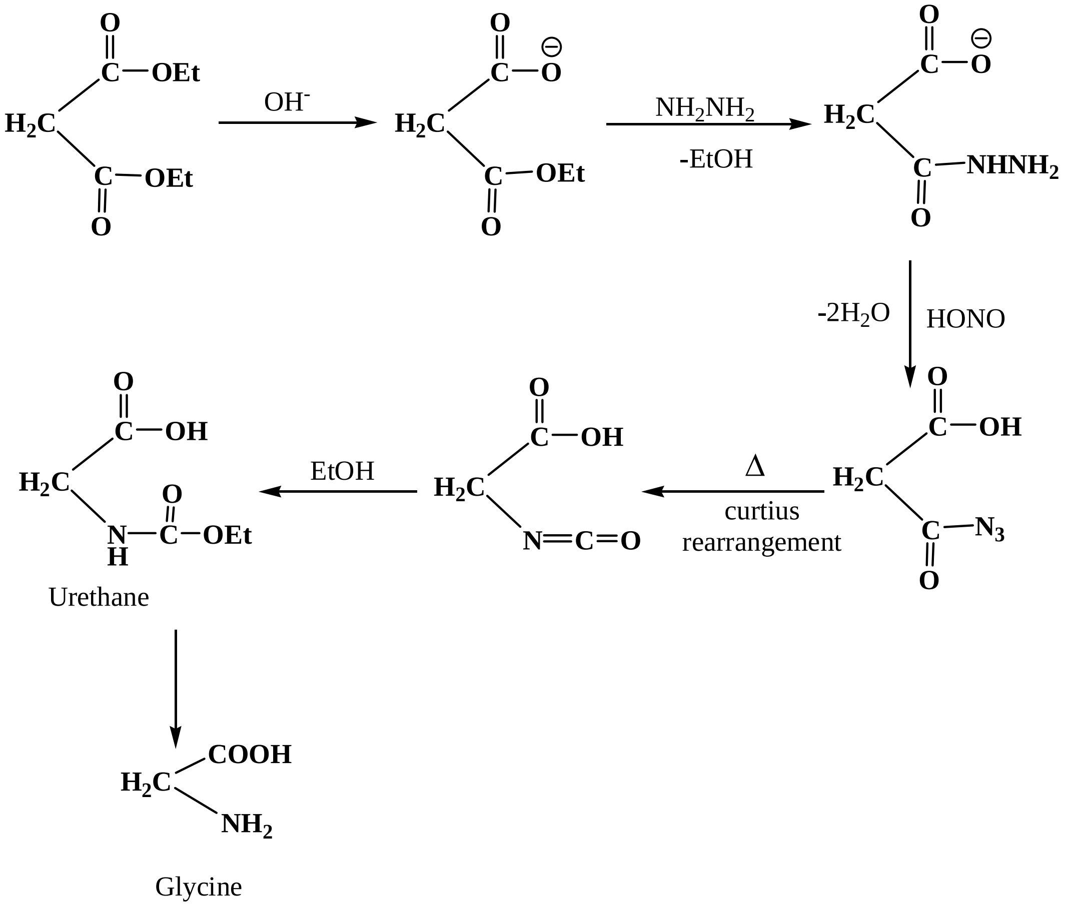
In the mechanism a nitrene is involved but yet not isolated being unstable and highly electron deficient. Hence, migration of R as with its electron pair removes the electron deficiency and in turn drives the reaction in forward direction.

Stereochemistry:

Similar to Hofmann rearrangement; retention of configuration is encountered at the migratory group ‘C’ atom.

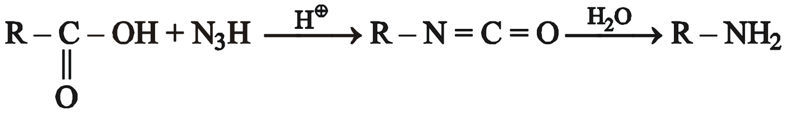
Applications:

This method is used for the synthesis of aliphatic, aromatic or heterocyclic amines. α-Amino acid may also be synthesized by this method. For e.g. synthesis of glycine is given below:



4.3.2.3 Schmidt rearrangement

Acid catalysed reaction of carboxylic acid with hydrazoic acid to give amines is known as Schmidt reaction.



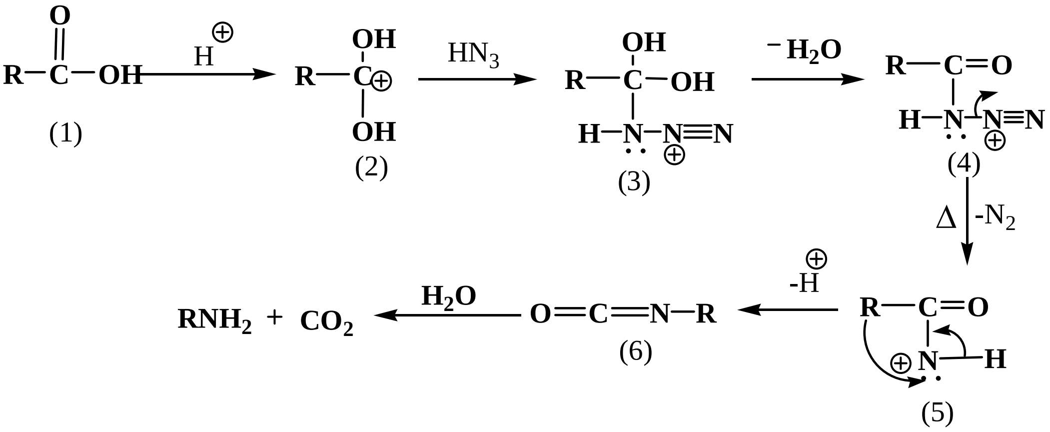
$$R-\underset{\underset{O}{\|}}{C}-OH+N_3H\xrightarrow{H^{\oplus}}R-N=C=O\xrightarrow{H_2O}R-NH_2$$

Characteristics

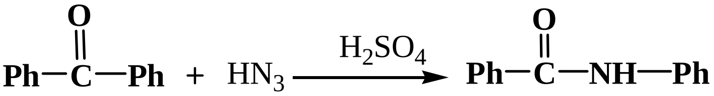
(i) Anionotropic rearrangement
(ii) Migration from C to electron deficient N
(iii) Conversion of carboxylic acid to primary amine occurs in one step
(iv) R = Alkyl, Aryl , If R = Alkyl, yields good
R = Aryl, yields variable
(v) Catalyst used commonly H_2SO_4, lewis acids can also be used.

Mechanism

Similar to Hofmann, Curtius except that here protonised acid undergoes rearrangement. Protonated carboxylic acid produces protonated acyl azide, which loses N_2 to give intermediate (5). Removal of proton and rearrangement produces isocyanate (6). Hydrolysis of isocyanate gives amine and CO_2.

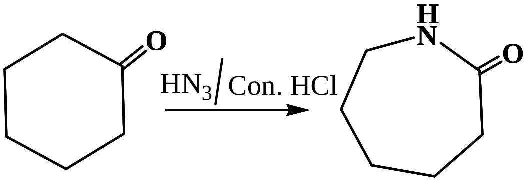


Ketones react with hydrazoic acid under strong conditions and give amides by the Schmidt reaction. For e.g. benzophenone gives benzanilide.



$$Ph-\overset{O}{\overset{\|}{C}}-Ph + HN_3 \xrightarrow{H_2SO_4} Ph-\overset{O}{\overset{\|}{C}}-NH-Ph$$

Cyclic ketones undergo ring enlargement to give lactam. It provides a synthetic alternative to the Beckmann rearrangement.



Cyclohexanone Caprolactam

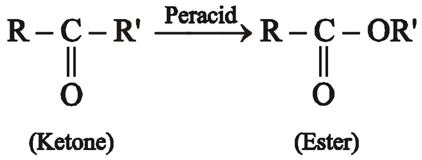
A synthetically useful example is conversion of cyclobutanecarboxylic acid in to cyclobutylamine.

4.4 Rearrangements involving migration to electron deficient oxygen

The most common rearrangement of this type is Baeyer - Villiger rearrangement.

4.4.1 Baeyer Villiger rearrangement

Oxidation of a ketone into an ester and cyclic ketones into lactones by means of a per acid is known as Baeyer Villiger rearrangement. The mechanism is closely related to that of the pinacol rearrangement.



$$\underset{\text{(Ketone)}}{R-\underset{\underset{O}{\|}}{C}-R'} \xrightarrow{\text{Peracid}} \underset{\text{(Ester)}}{R-\underset{\underset{O}{\|}}{C}-OR'}$$

Characteristics

(i) Anionotropic reaarngement

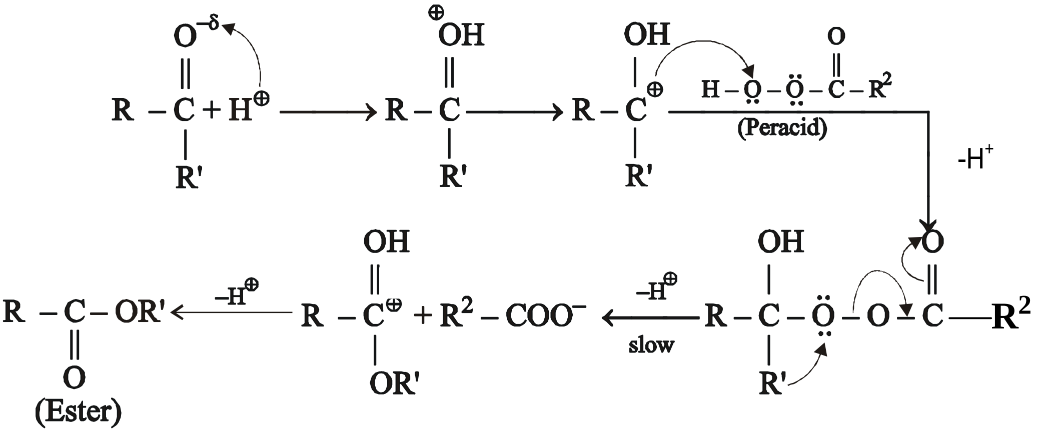
(ii) Migration from C to electron deficient 'O'.

(iii) Per acid used

(iv) Along with per acid, a buffer solution (Na_2HPO_4) must be added to prevent transesterification.

Mechanism

Involves nucleophilic attack by peracid to the electron deficient C of ketone followed by migration and ultimately by expulsion of carboxylate anion.

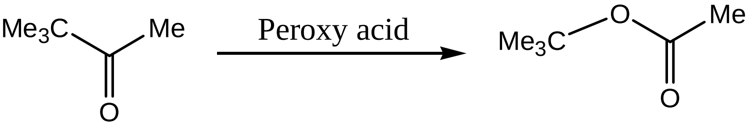


Driving Force

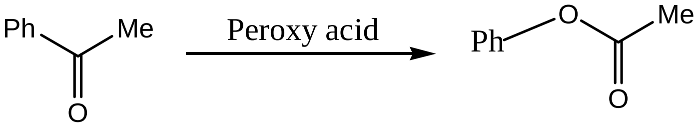
When the carbocation (protonated ketone) reacts with peracid, then due to electronegative effect the 'O' of peracid attached to 'C' of ketone becomes highly electron deficient and hence species, become unstable. Thus the migration of R' in an anionotropic way releases the electron deficiency and also ease up of the removal of R^2COO^- group which might be the probable reason for forward direction of the reaction. Acid catalyze the reaction by facilitating both addition to carbonyl and expulsion of the carboxylate.

Migratory aptitude

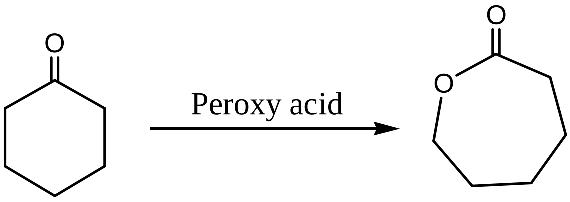
In an unsymmetrical ketone, that group migrates which is the better able to supply electrons, as in the Wagner-Meerwein and related rearrangements. Amongst alkyl group, the ease of migration is tertiary> Secondary> primary> methyl, e.g. pinacolone gives t-butyl acetate.



Amongst aryl groups, the order is, p-methoxyphenyl>p-tolyl>phenyl> chlorophenyl, etc. aryl group migrates in preference to primary alkyl groups. e.g.



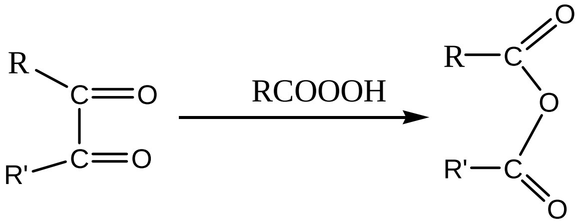
Cyclic ketones undergo ring expansion with peroxyacids. For example, cyclohexanone gives caprolactam.



Cyclohexanone Caprolactam

The lactone is hydrolysed under the reaction conditions. In an aqueous medium 6-hydroxycaproic acid is formed and undergoes condensation polymerization.

An another example is the reaction of α-Diketones with peracid which gives anhydride.

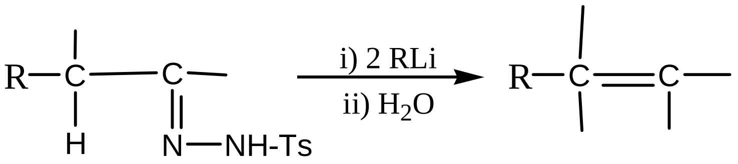


α–Diketone

4.5 Rearrangements involving migration of hydrogen to electron deficient carbon

4.5.1 Shapiro reaction

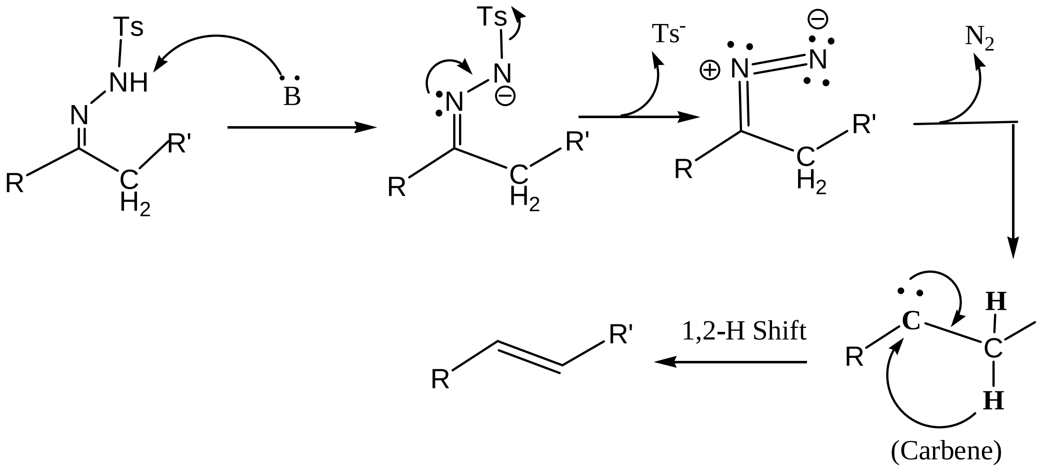
The Shapiro reaction or tosylhydrozone decomposition is an organic reaction in which a ketone p-toluenesulphonyl hydrazones is converted to an alkene in the presence of two equivalents of strong base (e.g. alkyl lithium).



Two mechanism are given for the explanation of this reaction.

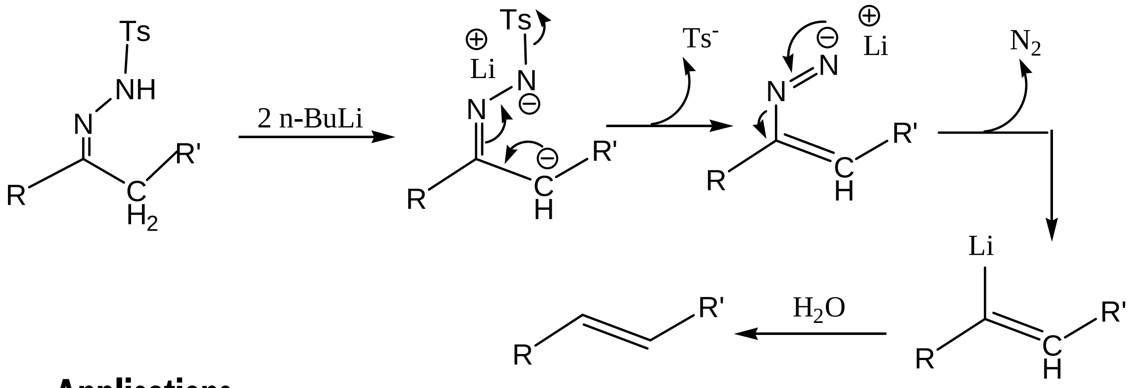
(i) Carbene mechanism

Tosylhydrazone of aldehyde or ketone on treatment with base and subsequent loss of Ts$^-$ gives the corresponding diazo compound, which produce carbene by elimination of N$_2$. Then carbene undergoes 1,2-hydrogen shift to form alkene. Migration and elimination step may be simultaneous.

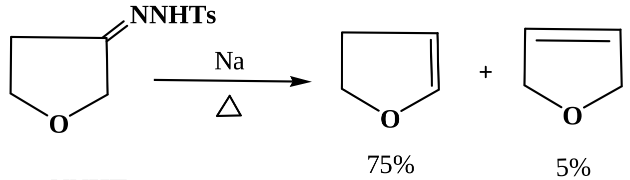


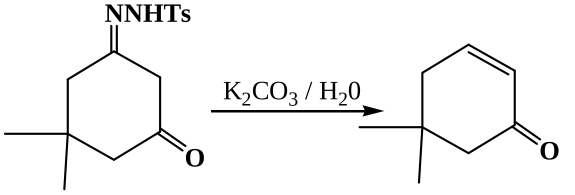
(ii) Anionic Mechanism

There is much evidence for this mechanism. Initially a ketone or an aldehyde is reacted with p-toluenesulfonylhydrazide to a p-toluenesulphonyl hydrazone (or tosylhydrazone) which is an imine or hydazone. Two equivalents of a strong base, such as n-butyllithium, then abstract first the proton from the hydrazone and then the less acidic proton α to the hydrazone carbon, leaving a carbanion. The carbanion proceeds in an elimination reaction to create the carbon-carbon double bond . This step results in expulsion of the tosyl group and formation of a diazonium anion. The anion then collapses, falling off as a neutral nitrogen molecule. The result is a vinyllithium at the position where the nitrogen had been attached. The organolithium carbon is both basic and nucleophilic. It can be reacted with various electrophiles or simply neutralized with water or an acid. The mechanism has been formulated as follows:



Applications





4.6 Summary

Neber Rearrangement

Base catalysed conversion of ketoxime tosylates to α-amino ketones.

Beckmann Rearrangement

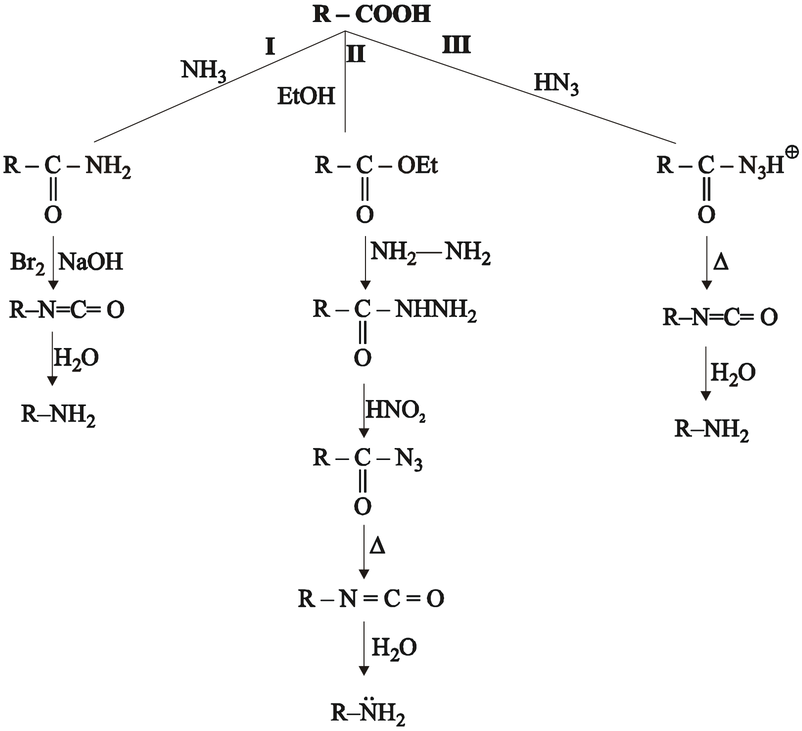
Acid catalysed transformation of a ketoxime to a N-substituted amide.

Hofmann, Curtius and Schmidt Rearrangement

I Hofmann rearrangement

II Curtius rearrangement

III Schmidt rearrangement



Conclusion : All these rearrangements are intramolecular, gives same product and have common intermediate that is isocyanate. All are anionotropic rearrangement involves retention of configuration in migrating group.

Baeyer Villiger rearrangement

Oxidation of a ketone into an ester and cyclic ketones into lactones by means of a per acid.

Shapiro Reaction

Conversion of ketone p-toluenesulphonyl hydrazones to an alkene in the presence of 2 equivalents of strong base.

4.7 Review Questions

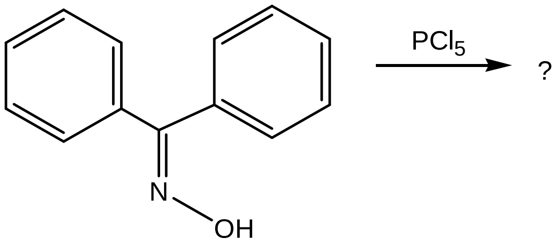
1 Write a short note on Beckmann rearrangement.

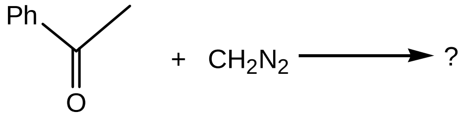
2 Give the mechanism of following reactions:

(i) Neber rearrangement

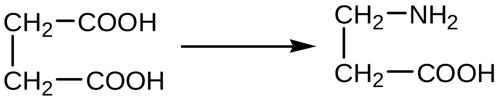
(ii) Curtius rearrangement

3 Identify the products in the following reactions:

(i) 

(ii) 

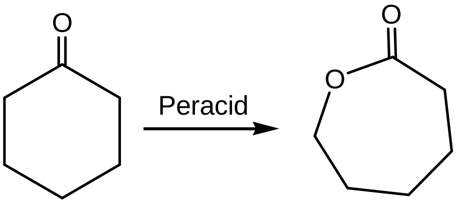
4 How can the given conversion be performed by using Hofmann rearrangement.

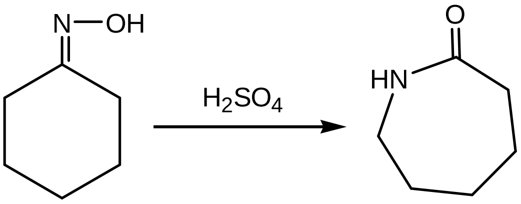


$$\begin{array}{l} CH_2-COOH \\ | \\ CH_2-COOH \end{array} \longrightarrow \begin{array}{l} CH_2-NH_2 \\ | \\ CH_2-COOH \end{array}$$

5 Write the similarities which are found in Schmidt, Curtius & Hofmann rearrangement.

6. Suggest the name and mechanism for the following rearrangement reactions:

(i) 

(ii) 

4.8 Reference and Suggested Readings

- Advanced Organic Chemistry, J. March, 6th Ed.
- Organic Chemistry, J. Clayden, N. Greeves, S. Warren, Oxford University, Second Edition.
- Principles of Organic Synthesis, R.O.C. Norman and J. M. Coxon, CRC Press.
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5th Ed. Springer (2007).

- Organic Reactions and their Mechanisms, P.S. Kalsi, New Age International Publishers.
- Organic Reaction Mechanism, V. K. Ahluwalia and Rakesh Kumar Parashar, Narosa Publishing House.

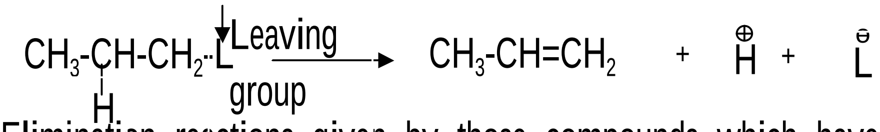
Unit - 5

Elimination Reaction

Structure of unit:

5.1 Introduction

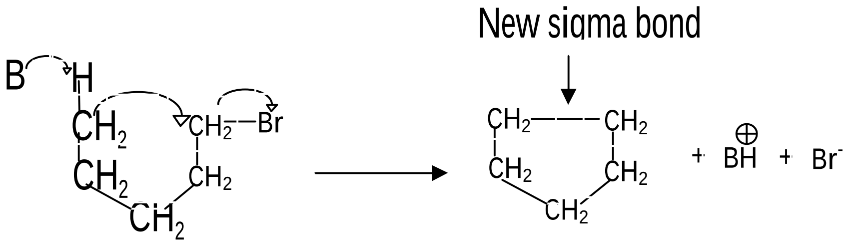
Elimination reaction is one in which two fragments are removed from a substrate to produce a modified substrate and two small units. One of these fragments is usually the leaving group of the substrate . Eliminations usually produce a new pi–bond in the modified substrate. In some elimination reactions a new sigma bond is produced instead of a pi bond.



$$CH_3\text{-}\underset{\displaystyle H}{\underset{|}{C}}H\text{-}CH_2\text{-}L \xrightarrow[\text{group}]{\text{Leaving}} CH_3\text{-}CH{=}CH_2 + \overset{\oplus}{H} + \overset{\ominus}{L}$$

Elimination reactions given by those compounds which have nucleophilic group as a leaving group. The leaving groups which are responsible for elimination reaction are: $\oplus$ $\oplus$ $\oplus$

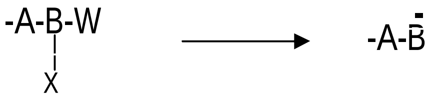
X, OH, OR, N_2, N_3, H_2O, NR_3 and $\overset{\oplus}{S}R2$



5.2 Classification of Elimination reaction

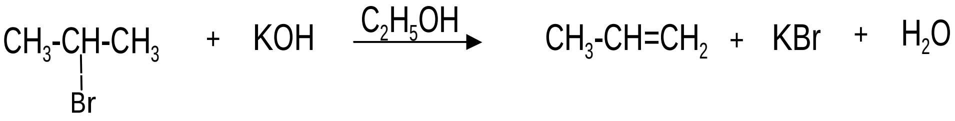
The elimination reaction can be classify into following types:

1. α-elimination- When two groups are lost from the same atom to give a carbene (or a nitrene) , the reaction is called α-elimination or 1,1 elimination.



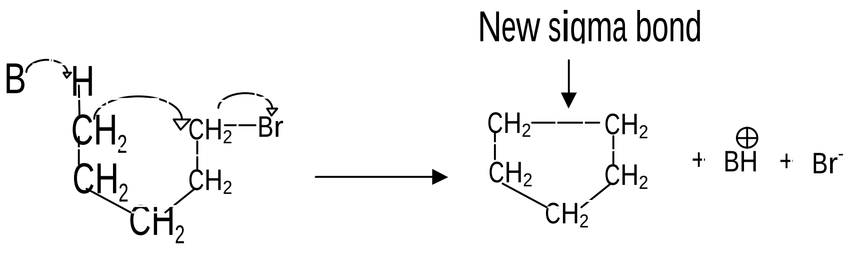
$$-A-\underset{X}{\underset{|}{B}}-W \longrightarrow -A-\bar{B}$$

2. β-elimination- When two groups are lost from adjacent atoms so that a new double (or triple) bond is formed the reaction is called β-elimination or 1,2 elimination. e.g.- dehydrohalogenation



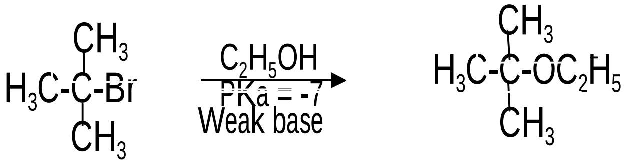
$$CH_3-\underset{Br}{\underset{|}{CH}}-CH_3 + KOH \xrightarrow{C_2H_5OH} CH_3-CH=CH_2 + KBr + H_2O$$

3. γ- elimination – In a γ- elimination , a new sigma bond is formed instead of pi-bond.



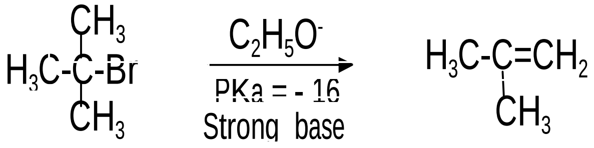
Elimination of alkyl halides

Those compounds in which leaving groups possess two electrophilic sites. The carbon to which the leaving group is attached and the hydrogen atom on the carbon adjacent to the alpha carbon. Attack of nucleophile at carbon bearing the leaving group leads to substitution reaction and attack at hydrogen leads to elimination. when nucleophile attacks on hydrogen it is known as base. Since strong base attacks on protons ,so it is true that more basic the nucleophile and it is more prone to elimination instead of substitution as the main reaction of alkyl halide.



$$H_3C-\underset{CH_3}{\overset{CH_3}{C}}-Br \xrightarrow[\text{PKa = -7} \atop \text{Weak base}]{C_2H_5OH} H_3C-\underset{CH_3}{\overset{CH_3}{C}}-OC_2H_5$$

Substitution reaction



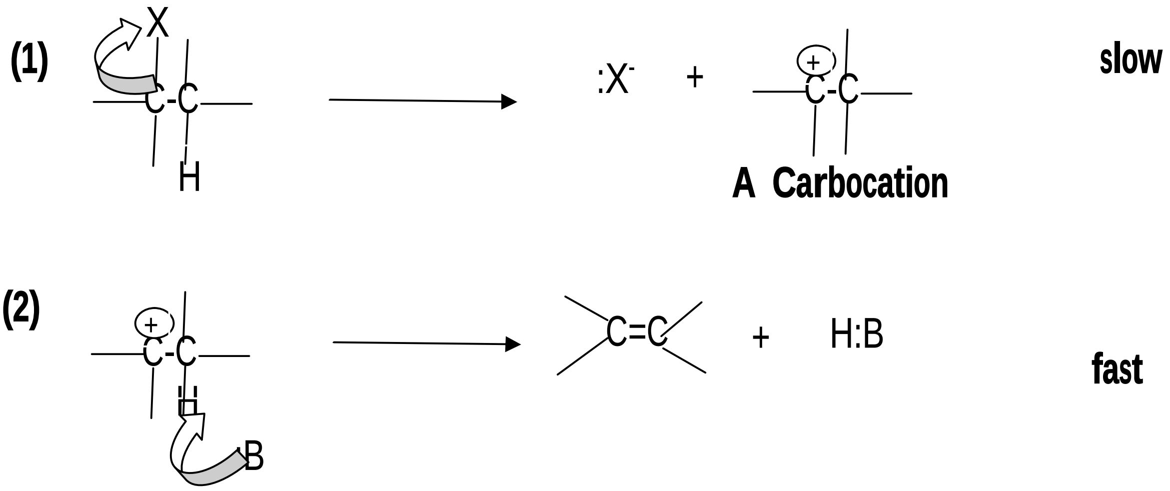
$$H_3C-\underset{CH_3}{\overset{CH_3}{C}}-Br \xrightarrow[\text{PKa = - 16} \atop \text{Strong base}]{C_2H_5O^-} H_3C-\underset{CH_3}{C}=CH_2$$

Elimination reaction

Selectivity for elimination versus subastitution can be explained on the basis of hard and soft electrophiles. In SN2 substitution , the carbon centre is a soft electrophile because it is essentially uncharged. The C-L σ* is a relatively low energy LUMO. Substitution is therefore favoured by nucleophiles whose HOMO are best able to interact with the LUMO or soft nucleophile. In contrast , the C-H σ* is higher in energy because the atoms are less electronegative. This coupled with hydrogen 's small size makes the C-H bond a hard electrophilic site and as a result hard nucleophiles favour elimination.

5.3 Mechanism of elimination reaction

If the reaction proceeds by first order kinetics, Hughes and Ingold proposed the E1 mechanism. In this mechanism the electronic changes- the bond breaking and the bond making are the same as in E2 .They are not taking place simultaneously but one after the other. Thus E1 involves two steps. In step (1) the substrate undergoes slow heterolysis to form halide ion and a carbocation. In step (2) the carbocation rapidly loses a proton to the base and forms the alkene.



Step first is identical to the first step in SN1 . In the second step of SN1 the carbocation combines with a nucleophile to yield the substitution product and in step second of E1 the carbocation reacts with the base to yield the elimination product.

The E1 reaction follows first order kinetics as in SN1 reaction . the overall rate of reaction is determined only by the slow first step. Except for the many necessary solvent molecules , this rate determining step involves only substrate and rate depends on the concentration of substrate. The rate of an E1 reaction is independent of base concentration because the reaction does not involve base.

If the rate of formation of carbocations determined how fast a reaction proceeds. Once formed the carbocation rapidly react to yield product. This mechanism was named E1 that is elimination, unimolecular, because in the rate determining step only one molecule , substrate , undergoes covalency change.

The reaction of ethyl bromide with ethoxide ion is an example of an E2 reaction. It is a second order reaction because the rate of the reaction depends on the concentration of both alkyl halide and base. It is called E2 reaction :E for elimination and 2 for bimolecular.

$$CH_3\text{-}CH_2\text{-}Br + C_2H_5O^- \longrightarrow CH_2{=}CH_2 + C_2H_5OH + Br^-$$

Rate = K [alkyl halide] [base]

The rate law tells us that ethyl bromide and ethoxide ion are both involved in the transition state of the rate determining step of the reaction. The following mechanism agree with the observed second–order kinetics.

The E2 reaction is a concerted ,one step reaction , the proton and the bromide ion are removed in the same step i.e in the rate determining step.

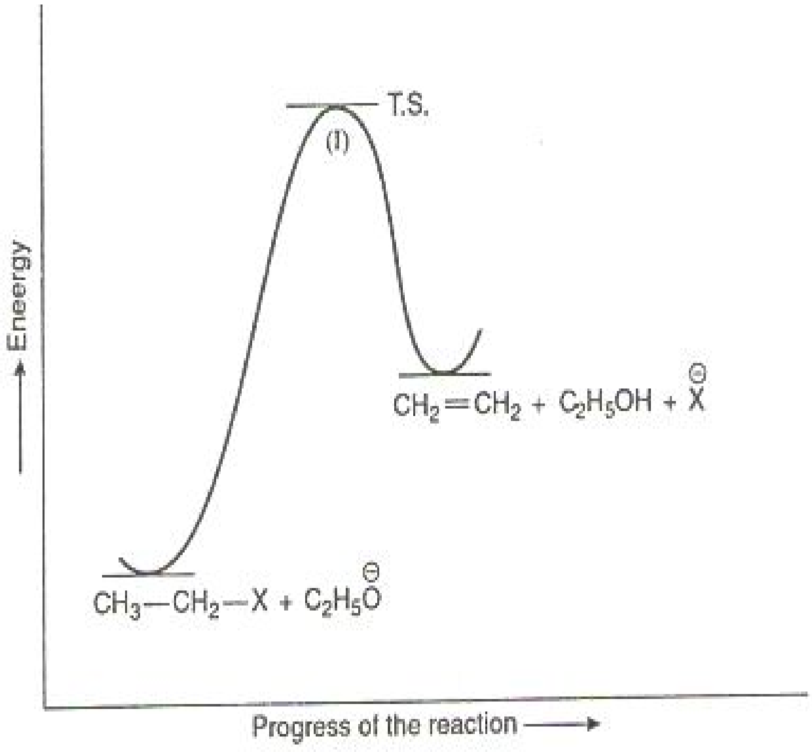


Fig.1: The E2 reaction of ethyl halide with ethoxide ion

An experimental evidence that is helpful in determining the mechanism of a reaction is a kinetic isotope effect. The kinetic isotope effect , can be used to demonstrate that a carbon –hydrogen bond is broken in the rate determining step.

When the rate constant (k_H) for elimination of H and Br from 1-bromo-2-phenylethane at 40 C is compared with the rate constant (k_D) for elimination of D and Br from 1-bromo-2, 2-dideuterio-2-phenyl ethane determined at the same temperature, k_H is found to be 7 times than k_D. So , the deuterium kinetic isotope effect is 7.1 ,which is primary kinetic isotope effect. The fact that the hydrogen–containing compound undergoes elimination faster than the deuterium-containing compound tells us that the carbon–hydrogen (or

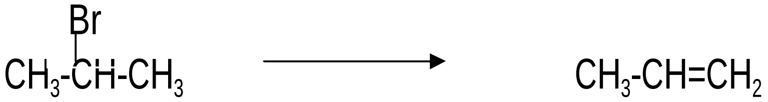
C-D) bond is broken in the rate determining step. The fact that the C-H bond is broken in the rate determining step agrees with the mechanism proposed for an E2 reaction.

$$C_6H_5\text{-}CH_2\text{-}CH_2\text{-}Br + C_2H_5O^- \xrightarrow{k_H} C_6H_5\text{-}CH{=}CH_2 + C_2H_5OH + Br^-$$

$$C_6H_5\text{-}CD_2\text{-}CH_2\text{-}Br + C_2H_5O^- \xrightarrow{K_D} C_6H_5\text{-}CD{=}CH_2 + C_2H_5OH + Br^-$$

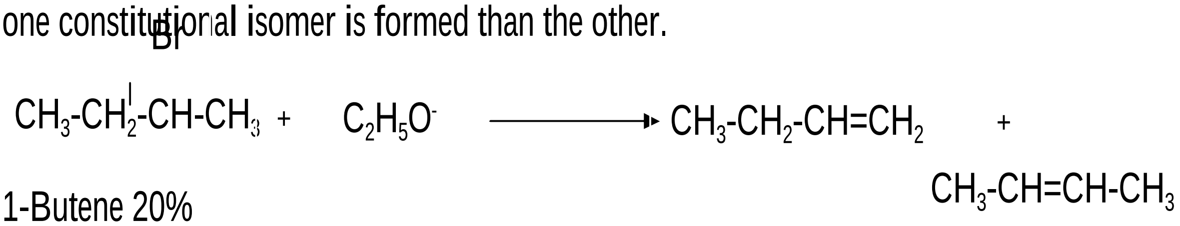
5.4 Oreintation of elimination reaction

When only one type of β-hydrogen is present the direction of elimination is certain. For example, all of the hydrogens adjacent to the carbon bearing the bromine in isopropyl bromide are equivalent. Therefore, the loss of HBr from isopropyl bromide can produce only one compound, propene.



$$CH_3\text{-}\overset{Br}{CH}\text{-}CH_3 \longrightarrow CH_3\text{-}CH{=}CH_2$$

When all β-hydrogens cannot be equal , the alkene normally produced is the most highly substituted one ,i.e.,the one with the largest number of alkyl groups bonded to the double bond. This statement is known as Satzeff rule. Satzeff pointed out that the most substituted alkene product is obtained when a proton is removed from the β-carbon that is bonded to the fewest hydrogens. Most dehydrogenation follow this rule. Thus, E2 reaction is regioselective, more of one constitutional isomer is formed than the other.



$$CH_3\text{-}\overset{Br}{CH_2}\text{-}CH\text{-}CH_3 + C_2H_5O^- \longrightarrow CH_3\text{-}CH_2\text{-}CH{=}CH_2 + CH_3\text{-}CH{=}CH\text{-}CH_3$$

1-Butene 20%

2-Butene 80%

In the above example, two alkenes are formed. The difference in the rate of formation of the two alkenes is not very great. Consequently, both products are formed but the more stable alkene is the major product of the elimination reaction.

Disubstituted alkenes are preferred over a monosubstituted alkenes and a trisubstituted alkene is preferred over a disubstituted alkene.

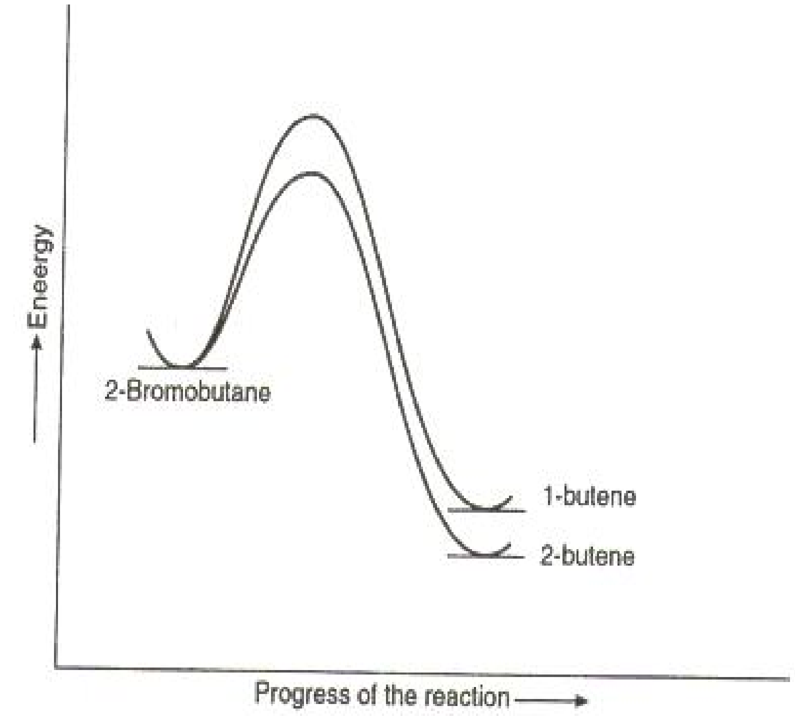
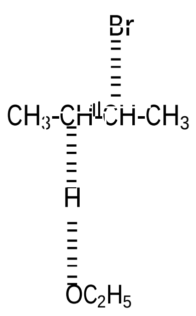
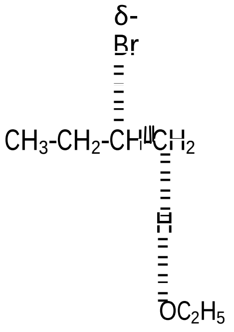


Fig. Activation energy for the formation of 1-butene and 2-butene

Formation of major product of the reaction can be explained by the mechanism as follows: We know that 2-butene is more stable than 1-butene. In the transition state leading to an alkene the C-H bond and C-Br bonds are partially broken and the double bond is partially formed, giving the transition state an alkene like structure. Because the transition state has an alkene like structure,the transition state kleading to 2-butene is more stable than the transition state leading to 1-butene. The more stable transition state allows 2-butene to be formed faster than 1-butene and 2-butene is more stable than 1-butene.



$$\begin{array}{cccc} & & \delta & \\ & & Br & \\ & & \vdots & \\ CH_3\text{-} & CH & \text{=}CH & \text{-}CH_3 \\ & \vdots & & \\ & H & & \\ & \vdots & & \\ & \bar{O}C_2H_5 & & \end{array}$$



$$\begin{array}{cc} \delta\text{-} & \\ Br & \\ \vdots & \\ CH_3\text{-}CH_2\text{-}CH & \text{=}CH_2 \\ & \vdots \\ & H \\ & \vdots \\ & \bar{O}C_2H_5 \end{array}$$

Transition state

leading to 2-butene
(more stable)

Transition state

leading to 1-butene
(less stable)

Alkyl halides have the following relative reactivitives in an E2 reaction, because elimination from a tertiary alkyl halide typically leads to a more highly substituted alkene than elimination from a secondary alkyl halide and elimination from a secondary alkyl halide leads to a more highly substituted alkene than elimination from a primary alkyl halide.

Relative reactivities of alkyl halides in an E2 reaction

Tertiary alkyl halides > sec. alkyl halides > primary alkyl halides

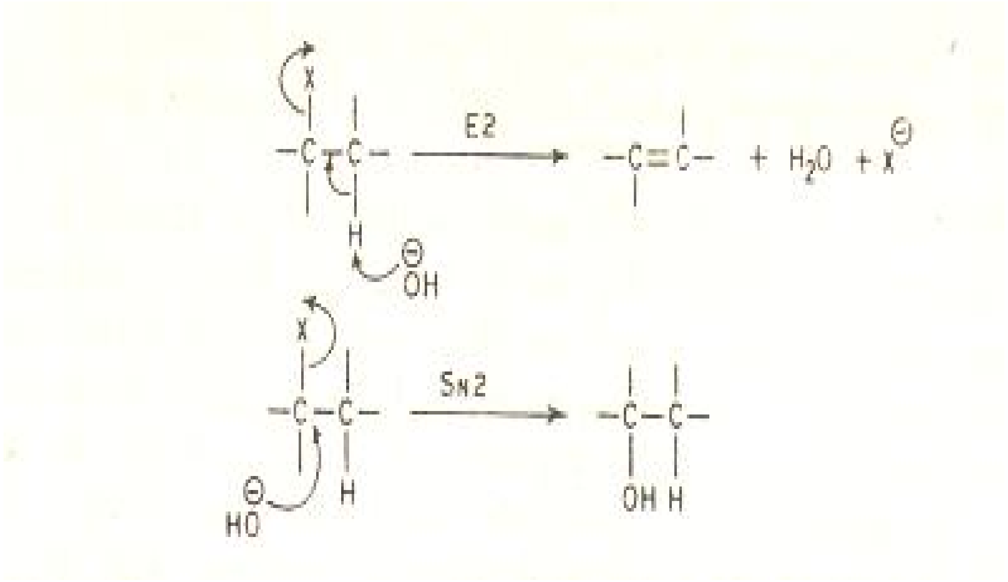
In most of the dehydrohalogenation reactions, the major products are the Satzeff product . But the most substituted alkene is not always the major product. In some cases the major alkene product is the least substituted alkene. Elimination in which least substituted alkene is the major product is known as Hofmann elimination and the rule is known as Hofmann rule.

Hofmann elimination reaction takes place in the following four cases:

- When the base is bulky.
- When the leaving group is a poor leaving group
- Steric hindrance at β-carbon
- When the alkyl halide contains one or more double bonds.

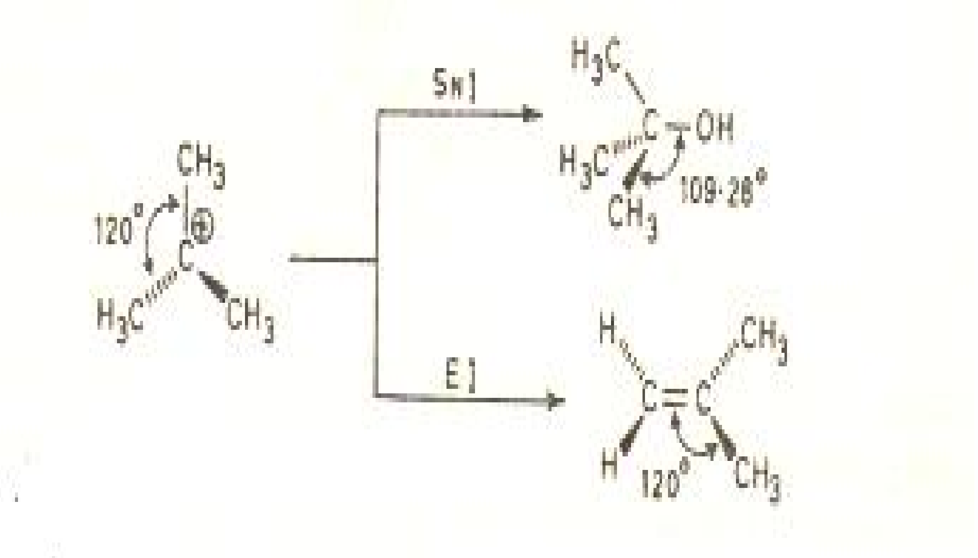
5.5 Elimination vs substitution

Like SN^1 and E-1 reactions, SN^2 and E-2 rections also occursimultaneously . If the attacking reagent is a good base , it abstracts the β-proton and causes elimination ,whereas a good nucleophile attacks the α-carbon causing substitution.The following factors influence the extent of elimination and substitution .



5.5.1 Structure of the reactant

Elimination and substitution are competing reactions, the proportion of elimination increases with increased chain branching of the reactant. One reason for this preference may be ascribed to the greater stability of highly substituted alkenes formed from substrates such as alkyl halides. The other reason is purely steric and applicable only to unimolecular reactions where carbonium ions are the common intermediates. Carbonium ions are planar structure with the bond angles of 120° and with the increase in branching they will show more resistance to the decrease in bond angles lead by substitution. On the other hand, elimination will be preferred as it does not involve any change in the bond angles.



5.5.2 Nature of base

A good nucleophile may not necessarily be a good base or vice versa. This can be demonstrated by comparing the nucleophilic and basic properties of some common reagents. The basicity of these reagents are found to be in the order H_2O, I^- , Cl^-, $CH_3COO^- < SH^- < OH^-$ whereas the nucleophilicities of the same reagents follow a different order,

$H_2O < CH_3COO^- < Cl^- < OH < I^- < SH^-$

To some extent the elimination /substitution ratio depends upon the nature of the base involved . In the bimolecular reactions (E^2 and SN^2), for example, if we have a weak base but a strong nucleophile ,e.g, I^- , there will be more substitution than elimination. On increasing the concentration and the strength of the base, the unimolecular reaction tends to bimolecularity. This change in molecularity is more pronounced in E1 than in SN1 reaction, leading to a higher proportion of the elimination product. This is precisely the reason for employing strong bases at high concentrations in the preparative methods for alkenes.

5.5.3 Nature of solvent

Change in polarity of solvent lead the change in route of reaction. In bimolecular reactions , for example, ratio of E^2/SN^2depends on the ability of solvent to solvate the two transition states of the same reactant. Less polar solvent favours E^2 reactions more than the SN^2 reactions , whereas more polar solvent favours SN2 reaction more than the elimination.

5.5.4 Effect of temperature

Generally, elimination reactions possess high activation energy than the substitution reactions. Thus, increase in temperature of the reaction mixture increases the extent of elimination reaction and the decrease in temperature of the reaction mixture increases the extent of substitution reaction.

5.5 Summary

- Elimination reaction involves the loss of fragment from the substrate and form a new modified substrate with the removal of small units.
- Elimination reaction can be classified into three types i.e- α, β and ɤ-elimination.

- In α- elimination or 1,1 elimination two groups are lost from the same atom to give carbene or nitrene.
- In β- elimination or 1,2 elimination two groups are lost from the adjacent atoms to form double or triple bond.
- In ɤ- elimination ring like structure is formed and a new sigma bond arises.
- Good base lead elimination reaction whereas good nucleophile lead substitution reaction.
- On the basis of kinetics , E1 involves two steps in which first step lead the formation of carbocation and second step involve alkene formation.
- In E2 reaction bond breaking and bond formation both take place in single step.
- In case of one type of β- hydrogen then elimination produces only one product .
- In case of different types of β- hydrogen then elimination produces more than one product but the more substituted alkene is predominantly formed (Satzeff rule).
- Disubstituted alkenes are preferred over a monosubstituted alkenes and a trisubstituted alkene is preferred over a disubstituted alkene.
- Transition state of 2-butene is more stable so it forms faster than 1-butene.
- Relative reactivities of alkyl halides in an E2 reaction Tertiary alkyl halides > sec. alkyl halides > primary alkyl halides
- Dehydrohalogenation reactions follow Satzeff rule.
- Elimination in which least substituted alkene is the major product then this is known as Hofmann rule.
- Hofmann elimination occurs when the base is bulky , poor leaving group alkyl halide possess one or more double bonds and steric hinderance at β- carbon.

- Elimination/substitution ratio depends on structure of the reactant, nature of base, polarity of solvent and temperature.
- Elimination reaction favoured by the increased chain braching in the structure of reactant, presence of good base and less polar solvent with increase in temperature.
- Substitution reaction favoured by the less chain branching in the structure of reactant, presence of good nucleophile and more polar solvent with decrease in temperature.
- Elimination reaction possess high activation energy so require increase in temperature.
- On increasing the concentration and the strength of the base, the unimolecular reaction tends to bimolecularity.

5.6 Review Questions

1 What do you understand by the term elimination reaction?

2 Discuss the various types of elimination reactions with suitable examples.

3 Explain elimination reaction with alkyl halides.

4 Write write short note on

1. Saytzeff rule
2. Hofmann elimination reaction

5 Explain the term orientation of elimination.

6 Why hydrogen containing compound undergo elimination faster than the deuterium containing compound?

7 Explain dehydrohalogenation with examples.

8 Discuss elimination reaction verses substitution reaction.

9 Discuss mechanism of elimination reaction.

10 What is essential condition required in the reactant for the elimination reaction?

11 Increase in temperature is favourable for elimination reactions or substitution reactions?

12 How the polarity of solvent effect rate of substitution?

13 Explain the factors affecting the ratio of elimination and substitution.

14 Discuss the role of nucleophile in elimination reaction.

15 How the structure of reactant affect the rate of elimination?

16 Differentiate between E1 and E2 reactions.

17 Who proposed the mechanism of E1 reaction?

5.7 References and Suggested readings

- Organic Chemistry , S.H.Pine, Tata Mc-Graw Hill, 2010 (Fifth edition)
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- Reaction Mechanism in Organic Chemistry, S.M.Mukherji and S.P.Singh, Acmillan Company of india Limited ,1976.
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Unit - 6

Molecular Orbitals and Their Symmetry Properties

Structure of unit

6.0 Objective

This chapter has been introduced to make a clear concept of molecular orbital theory. This chapter helps to answer many questions, like, how molecular orbitals are formed. How many atomic orbitals will combine to form molecular orbital? What are the bonding and antibonding molecular orbitals? What is Huckel $4n+2$ rule?

6.1 Introduction

In this chapter molecular orbital theory has been discussed in details. There is a detailed discussion of atomic and molecular orbitals. The possibilities of combination of atomic orbital to form molecular orbital has been discussed. Bonding and antibonding molecular orbitals have been discussed with various examples. Electronic configuration of many molecules has been studied.

Aromatic character of any molecule on the basis of its electronic configuration has been described in details. There is clear and detailed discussion of electrocyclic, cycloaddition and sigmatropic reactions in this chapter.

6.2 Molecular orbital theory

The structure of molecules can be easily understood through quantum mechanics. Accurate quantum mechanical calculations are enormously complicated, and so various methods of approximation have been applied to simplify the mathematics. The method that is often the most useful for the organic chemist is based on the concept of molecular orbitals.

There are various questions to answer like, what are the various molecular orbitals of a molecule like? What is their order of stability? How are electrons distributed among them? Why certain molecules are aromatic? These are things we must know if we are to understand the course of many chemical reactions: their stereochemistry, for example, and how easy or difficult they are to bring about; indeed, whether or not they will occur at all. We are not going to learn here how to make quantum mechanical calculations, but we can see what the results of some of these calculations are, and learn a little about how to use them.

In this chapter we shall discuss what is meant by the phase of an orbital, and what bonding and antibonding orbitals are. We shall see, in a non-mathematical way, what lies behind the Huckel [4n + 2] rule for aromaticity. At the end there shall be a brief look at a recent-and absolutely fundamental development in chemical theory: the application of the concept of orbital symmetry to the under- standing of organic reactions.

6.3 Wave equations. Phase

As we know that electrons show properties not only of particles but also of waves. We must examine a little more closely the wave character of electrons, and see how this is involved in chemical bonding. First, let us look at some properties of waves in general.

Let's consider the standing waves (or stationary waves) generated by the vibration of a string secured at both ends: the wave generated by, say, the plucking of a guitar string (Fig. 1).

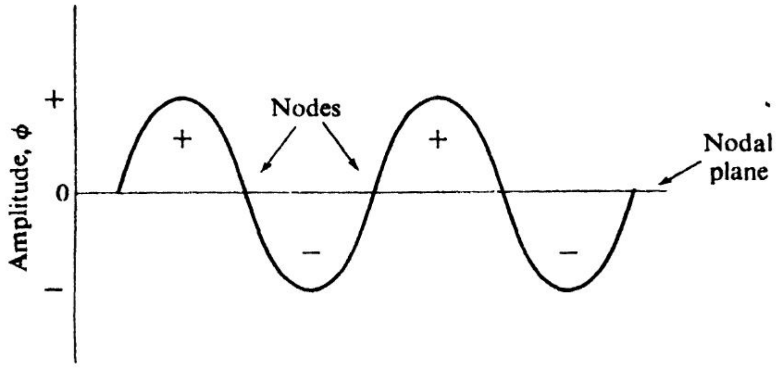


Figure 1. Standing waves. Plus and minus signs show relative phases.

As we continue horizontally along the string from left to right, we find that the vertical displacement the amplitude of the wave increases in one direction, passes through a maximum, decreases to zero, and then increases in the opposite direction. The spaces where the amplitude is zero are called nodes. In Fig. 1 they lie in aplane, the nodal plane, perpendicular to the plane of the paper. Displacement upward and displacement downward corres*pond to* oposite phases of the wave. To differentiate between phases, one can arbitrarily assign algebraic signs to the amplitude, plus for the displacement upward, and minus for displacement downward. If we were to superimpose similar waves on one another exactly out of phase-that is; with the crests of one lined up with the troughs of the other-they would cancel each other; that is to say, the sum of their amplitudes, + and -, would be zero. The differential equation that describes the wave is a wave equation. Solution of this equation gives the amplitude, ϕ, as a function, *f{x),* of the distance, x, along the wave. Such a function is a wave function.

Since, electron waves are described by a wave equation of the same general form as that for string waves. The wave functions that are acceptable solutions to this equation again give the amplitude ϕ, this time as a function, not of a single coordinate, but of the three coordinates necessary to describe motion in three dimensions. It is these electron wave functions that we call orbitals.

Any wave equation has a set of solutions-an infinity of them, actually each corresponding to a different energy level. The quantum thus comes naturally out of the mathematics.

Like a string wave, an electron wave can have nodes, where the amplitude is zero. On opposite sides of a node the amplitude has opposite signs, that is, the wave is of opposite phases. Of special interest to us is the fact that n the two lobes of a p orbital lies a nodal plane, perpendicular to the axis of the orbital

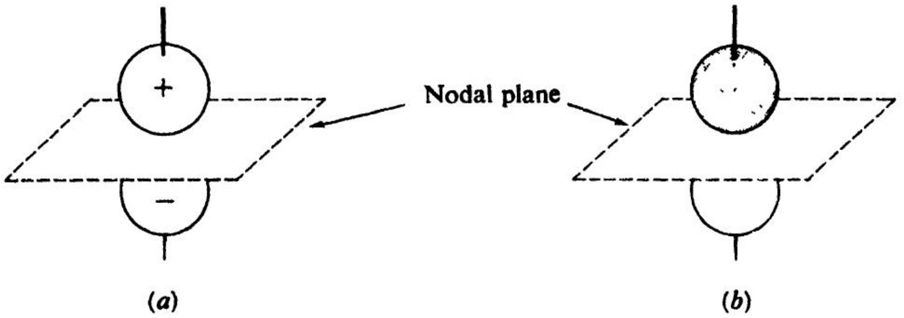


Figure 2. The two lobes are of opposite phase, and this is often indicated and signs. .

As used here, the signs do not have anything to do with charge. They simply indicate that the amplitude is of opposite algebraic sign in the two lobes.

The amplitude or wave function, ϕ is the orbital. As is generally true for waves, however, it is the square of the amplitude, ϕ^2, that has physical meaning. For electron waves, ϕ^2 represents the probability of finding an electron at any particular place. The fuzzy balls or simple spheres we draw to show the "shapes" of orbitals are crude representations of the space within which ϕ^2 has a particular value-the space within which the electron spends. say, 95% of its time. Whether ϕ is positive or negative, ϕ^2 is of course positive; this makes sense, since probability cannot be negative. The usual practice is to draw the lobes of a *p* orbital to represent ϕ^2; if + or - signs are added, or one lobe is shaded and the other unshaded, this is to show the relative signs of ϕ.

6.4 Molecular orbitals. LCAO method

Generally, molecules are the combination of atoms held together by bonds. We consider the bonds to arise from the overlap of an atomic orbital of one atom with an atomic orbital of another atom. A new orbital is formed, which is occupied by a pair of electrons of opposite spin. Each electron is attracted by both positive nuclei, and the increase in electrostatic attraction gives the bond its strength, that is, stabilizes the molecule relative to the isolated atoms.

This highly successful qualitative model parallels the most convenient quantum mechanical approach to molecular orbitals: the method of linear combination of atomic orbitals (LCAO). We have considered that the shapes and disposition bond orbitals are related in a simple way to the shapes and dispositions of atomic orbitals. The LCAO method makes the same assumption mathematically: to determine an approximate molecular orbital, ψ, one uses a linear combination (that is, a combination through addition or subtraction) of atomic orbitals.

$\psi = \phi_A + \phi_B$

ψ is the molecular orbital

ϕ_A is atomic orbital A

ϕ_B is atomic orbital B

The rationale for this assumption is simple: when the electron is near atom A, ψ resembles ϕ_A; when the electron is near atom B, ψ resembles ϕ_B.

Now this combination is effective that is, the molecular orbital is appreciably more stable than the atomic orbitals-only if the atomic orbitals ϕ_A and ϕ_B:

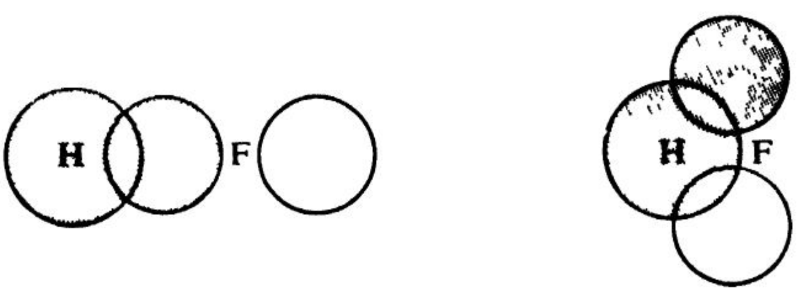
(a) overlap to a considerable extent;

(b) are of comparable energy; and

(c) have the same symmetry about the bond axis.

These necessities can be justified mathematically. Qualitatively, we can say this: if there is not considerable overlap, the energy of ψ is equal to either that of ϕ_A or that of ϕ_B; if the energies of ϕ_A and ϕ_B are quite different, the energy of ψ is essentially that of the more stable atomic orbital. 'n either case, there is no significant stabilization, and no bond formation.

When we speak of the symmetry of orbitals, we are referring to the relative phases of lobes, and their disposition in space. To see what is meant by requirement (c), that the overlapping orbitals have the same symmetry, let us look at one example: hydrogen fluoride. This molecule can be pictured as resulting from overlap of the s orbital of hydrogen with a *p* orbital of fluorine. In Fig. 3a, we use the $2p_x$ orbital, where the x coordinate is taken as the H-F axis. The s orbital overlaps the blue lobe of the *p* orbital, and a bond forms. If, however, we were to use the $2p_z$ (or $2p_y$) orbital as in Fig. 3b, overlap of both lobes-plus and minus-would occur and cancel each other. That is, the positive overlap integral would be exactly canceled by the negative overlap integral; the net effect would be no overlap, and no bond formation. The dependence of overlap on phase is fundamental to chemical bonding.



(*a*) (*b*)

Figure 3. The hydrogen fluoride molecule: dependence of overlap on orbital symmetry. (a) Overlap of lobes of the same phase leads to bonding. (b) Positive overlap and negative overlap cancel each other.

6.5 Bonding and antibonding orbitals

Quantum mechanics shows that linear combination of two functions gives, not one, but two combinations and hence two molecular orbitals: a bonding orbital, more stable than the component atomic orbitals; and an antibonding orbital stable than the component orbitals.

$\psi_+ = \phi_A + \phi_B$ Bonding orbital:

Stabilizes molecule

$\psi_- = \phi_A + \phi_B$ Antibonding orbital:

Destabilize molecule

Two *s* orbitals, for example, can be added,

We can see that why there must be two combinations. There can be as many as two electrons in each component atomic orbital, making a total of four electrons; two molecular orbitals are required to accommodate them.

Fig. 4 shows the shapes of the molecular orbitals, bonding and anti bonding, that result from overlap of various kinds of atomic orbitals. We recognize the bonding orbitals, σ and π, although until now we have not shown the two lobes of a π orbital as being of opposite phase. An anti bonding orbital, we see, has a nodal plane perpendicular to the bond axis, and cutting between the atomic nuclei. The anti bonding sigma orbital, σ^*·, thus consists of two lobes, of opposite phase. The anti bonding pi orbital, $\pi *$, consists of four lobes.

In a bonding orbital, electrons are concentrated in the region between the nuclei, where they can be attracted both nuclei. The increase in electrostatic attraction lowers the enter of the system. In an antibonding orbital, by contrast, electrons are not concentrated between the nuclei; electron charge is zero in the nodal plane. Electrons spend most of their time farther from a nucleus than in the separated atoms. There is a decrease in electrostatic attraction, and an increase in repulsion between the nuclei. The energy of the system is higher than that of e separated atoms. *Where electrons in a bonding orbital tend to hold the atoms together electrons in an antibonding orbital tend to force the atoms apart.*

It may at first seem strange that electrons in certain orbitals can actually bonding. We must remember that it is the bond dissociation energy we are concerned. We are not comparing the electrostatic attraction in an anti bond electrostatic attraction; we are comparing it with the stronger electrostatic in the separated atoms.

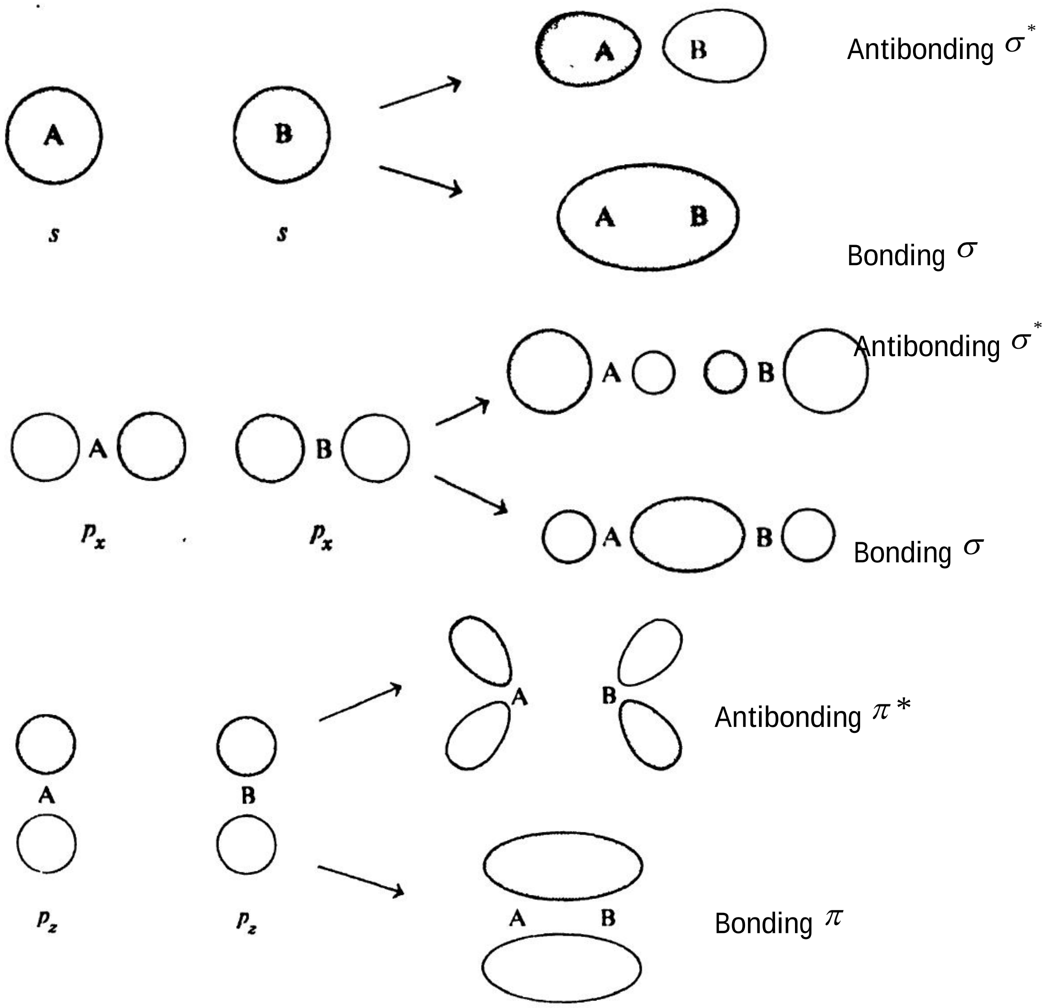


Figure 4. Bonding and anti bonding orbitals.

There are another kind of orbitals i.e. non bonding orbitals. As the name indicates, electrons in these orbitals unshared pairs, for example-neither strengthen nor weaken the bonding between atoms.

6.6 Electronic configurations of some molecules

Let us look at the electronic configurations of some familiar molecules. The shapes and relative stabilities of the various molecular orbitals are calculated by quantum mechanics, and we shall simply use the results of these calculations. Were the nuclei in place, with the molecular orbitals mapped out about them, feed electrons into the orbitals. In doing this we follow the same rules that we followed in arriving at the electronic configurations of atoms. There will be only two electrons and of opposite spin-in each orbital, with orbitals of energy being filled up first. If there are orbitals of equal energy, each gets an electron before anyone of them gets a pair of electrons. We shall limit our attention to orbitals containing π electrons, since these electrons will be the ones of chief interest to us.

For the π electrons of ethylene (Fig. 5), there are only two possibilities of molecular orbitals since there are two linear combinations of the two component *p* orbitals. The figure indicates the bonding and non bonding energy level, lower one is the bonding orbital, π, and upper one is the anti bonding orbital, π *.

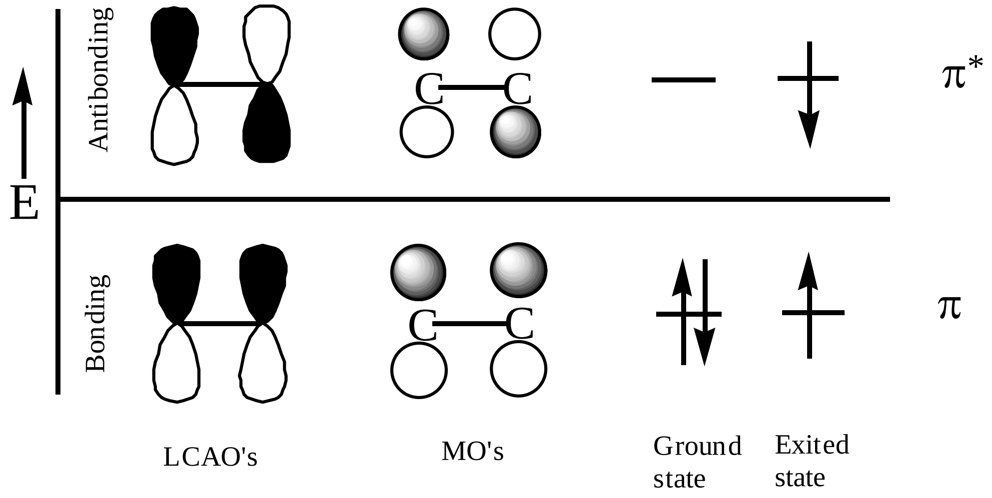


Figure 5. Ethylene. Configuration of π electrons in the ground state and the excited state.

Generally, a molecule exists in the state of lowest energy, the ground state. But it is reported that absorption of light of the right frequency (in the ultraviolet region) raises a molecule to an excited state, a state of higher energy. In the ground state of ethylene, we see, both π electrons are in the π orbital; this configuration is specified as π^2, where the superscript tells the number of electrons in that orbital. In the excited state one electron is in the π orbital and the other still of opposite spin-is in the π^* orbital; this configuration, $\pi\pi^*$*, is naturally the less stable since only one electron helps to hold the atoms together, while the other tends to force them apart.

For 1,3-butadiene, with four component *p* orbitals, there are four molecular orbitals for π electrons (Fig. 6,). The ground state has the configuration $\psi_1^2\psi_2^2$; that is, there are two electrons in each of the bonding orbitals, ψ_1 and ψ_2 .The higher of these, ψ_2 resembles two isolated π orbitals, although it is of somewhat lower energy. Orbital ψ_1 encompasses all four carbons; this delocalization provides the net stabilization of the conjugated system. Absorption of light of the right frequency raises one electron to ψ_3

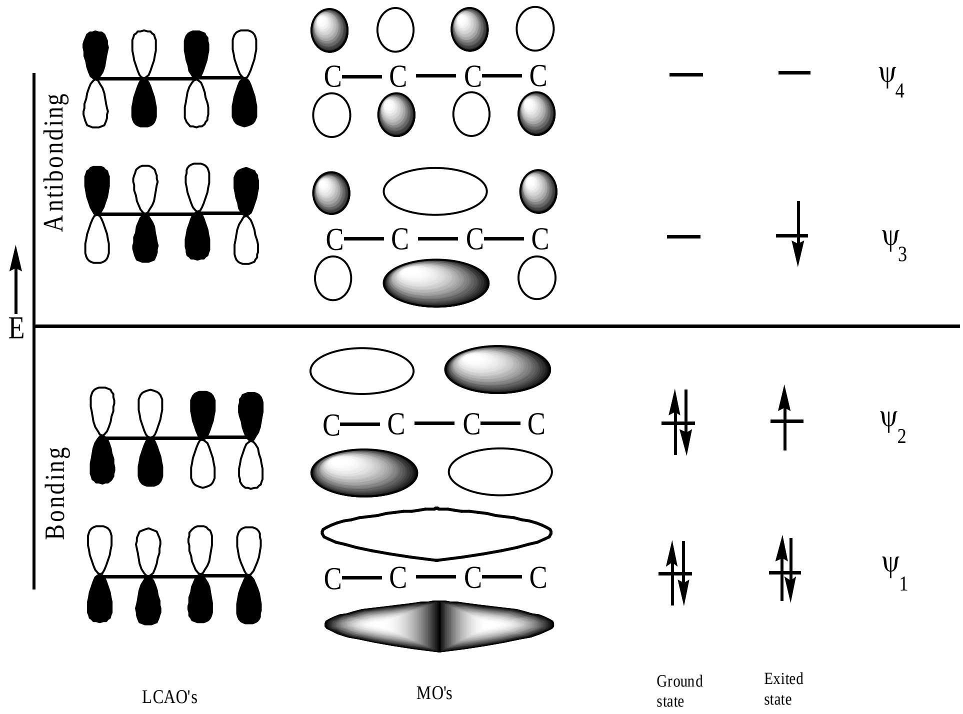


Figure 6 l,3-Butadiene. Configuration of π electrons in the ground state and the first excited state.

Now, let's have a look at the allyl system: cation, free radical, and anion. Regardless of the number of it electrons, there are three component *p* orbitals, one on each carbon, and they give rise to three molecular orbitals,

ψ_1, ψ_2 *and* ψ_3. As shown in Fig. 7, ψ_1 is bonding and ψ_3 is antibonding. Orbital ψ_2 encompasses only the end carbons (there is a node at the middle carbon) and is of the same energy as an isolated *p* orbital; it is therefore non-bonding.

The allyl cation contains π electrons only in the bonding orbital. The free radical has one electron in the non-bonding orbital as well, and the anion has two in the non-bonding orbital. The bonding orbital ψ_1 encompasses all three carbons, and is more stable than a localized π orbital involving only two carbons; it is this delocalization that gives allylic particles their special stability. We see the symmetry

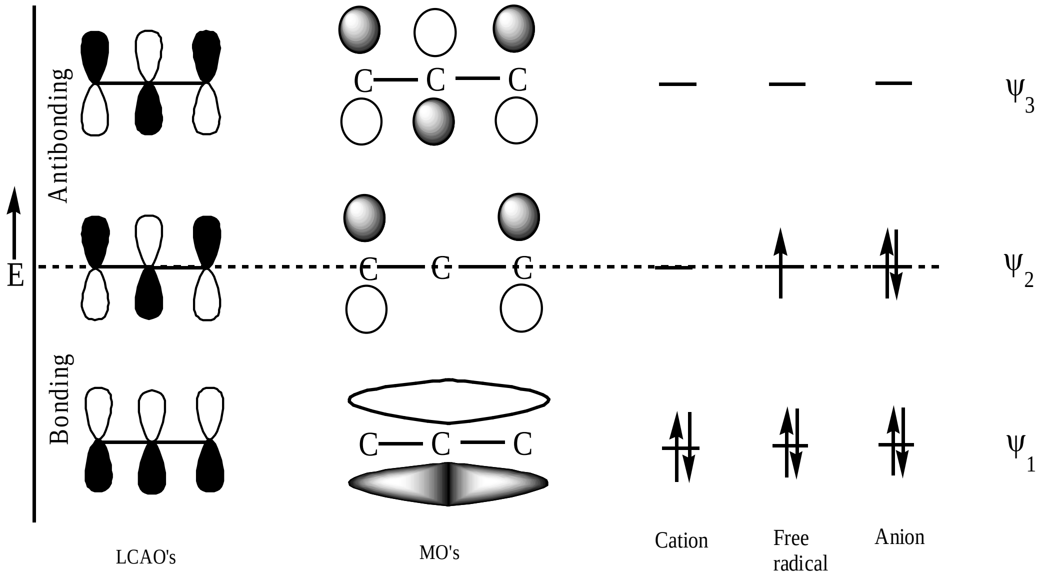
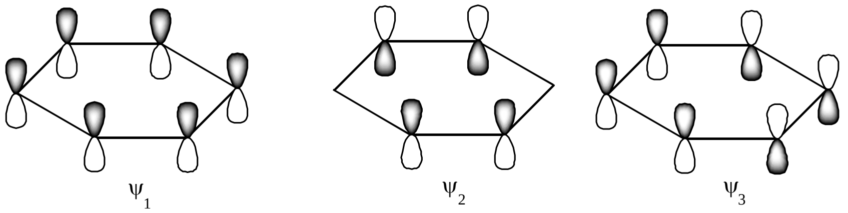


Figure 7. Allyl system. Configuration of π electrons in the cation, the free radical, and the anion.

we have attributed to allylic particles on the basis of the resonance theory; the two ends of each of these molecules are equivalent.

At last, let's see the example of benzene. There are six combinations of the six component *p* orbitals, and hence six molecular orbitals. Of these, we shall consider only three combinations, which correspond to the three most stable molecular orbitals, all bonding orbitals (Fig. 8). Each contains a pair of electrons. The lowest orbital, ψ_1 encompasses all six carbons. Orbitals ψ_2 and ψ_3 are of different shape, but equal energy; together they provide-as does ψ_1- equal electron density



Benzene: first three LCAOs

at all six carbons. The net result, then, is a highly symmetrical molecule with considerable delocalization of π: electrons.

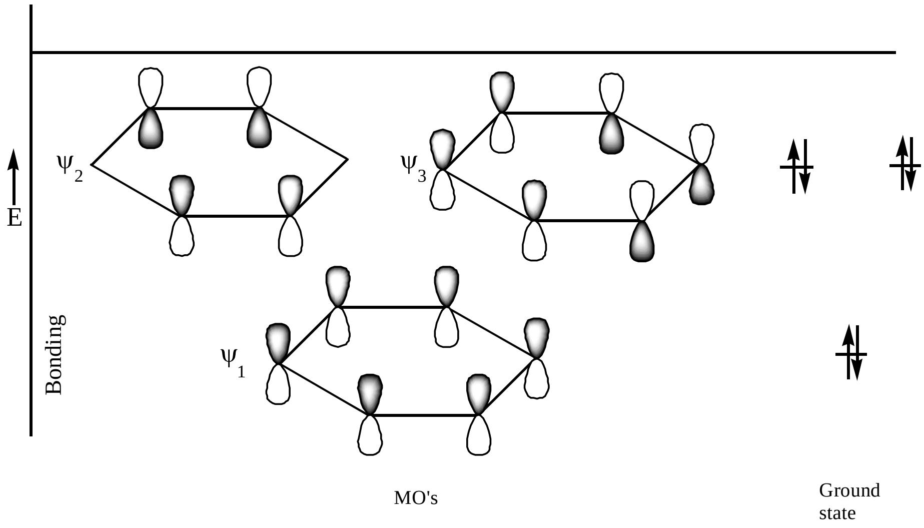
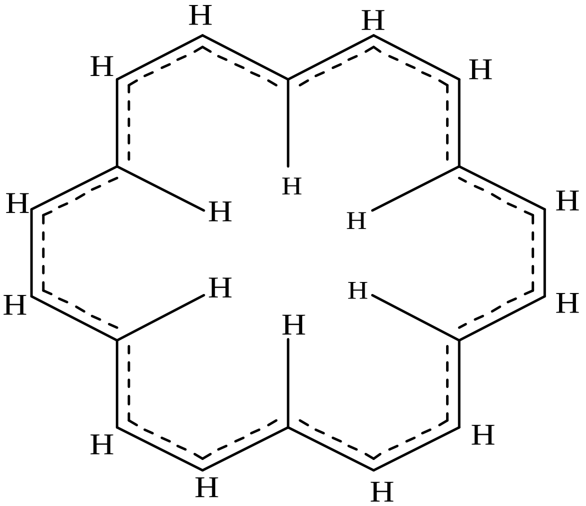


Figure 8. Benzene. Configuration of π electrons in the ground state.

6.7 Aromatic character. The Huckel 4π + 2 rule

An aromatic molecule is planner; with cyclic clouds of delocalized π electrons above and below the plane of the molecule. We have just seen, for benzene, the molecular orbitals that permit this delocalization. But delocalization alone is not enough. For that special degree of stability we call aromaticity, the number of 'It electrons must conform to Hiickel's rule: there must be a total of(4π + 2) π electrons.



Cyclooctadecanonaene

In the NMR spectrum of cyclooctadecanonaene twelve protons lie outside the ring, are deshielded, and absorb downfield; but, because of the particular geometry of the large fiat molecule, six protons lie inside the ring, are shielded and absorb upfield. The spectrum is unusual, but exactly whatwe would expect if this molecule were aromatic. Huckel was a pioneer in the field of molecular orbital theory. He developed the LCAO method in its simplest form, yet "Huckel molecular orbitals" have proved enormously successful in dealing with organic molecules. Huckel proposed the 4*n* + 2 rule in 1931. It has been tested in many ways since then, and it works. Now, what is the theoretical basis for this rule?

Now let's discuss the cyclopentadienyl system. Five sp^2-hybridized carbons have five component p orbitals, which give rise to five molecular orbitals (Fig. 9). At the lowest energy level there is a single molecular orbital. Above this, the orbitals appear as degenerate pairs, that is, pairs of orbitals of equal energy. The lowest degenerate pair are bonding, the higher ones are anti bonding.

The cyclopentadienyl cation has four electrons. Two are in the lower orbital. Of the other two electrons, one goes into each orbital of the lower degenerate pair. The cyclopentadienyl free radical has one more electron, which fills one orbital of the pair. The anion has still another electron, and with this we fill the remaining orbital of the pair. The six π electrons of the cyclopentadienyl anion are just enough to fill all the bonding orbitals. Fewer than six leaves bonding orbitals unfilled; more than six, and electrons would have to go into antibonding orbitals. Six π electrons gives maximum bonding and hence maximum stability.

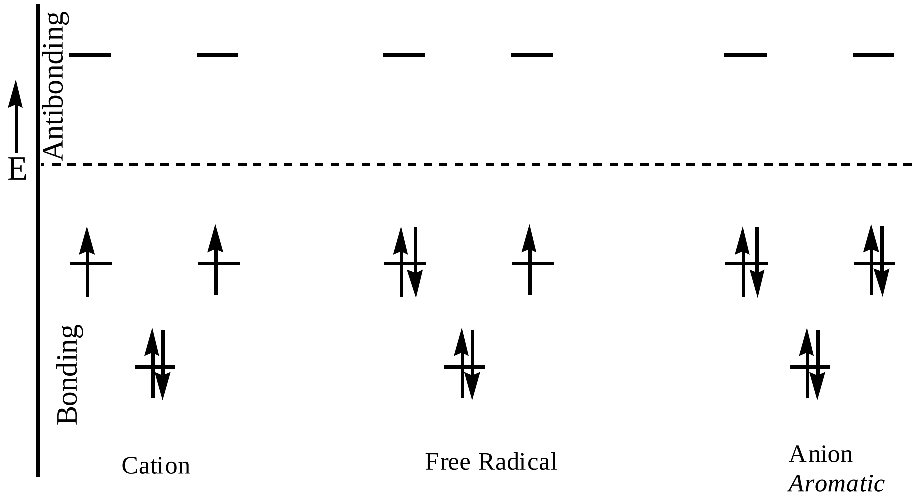


Figure 9. Cyclopentadienyl system. Configuration of π electrons in the cation, the free radical, and the anion.

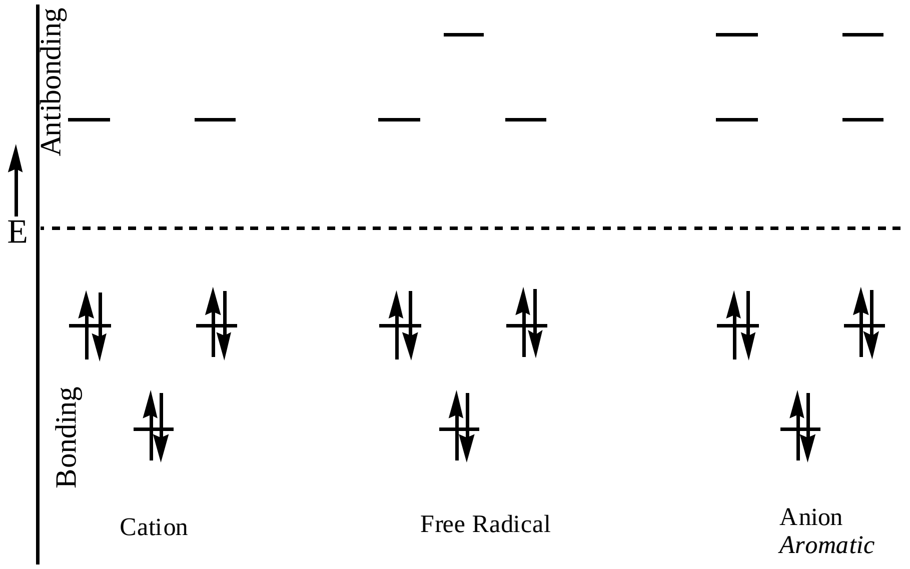
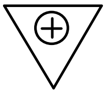
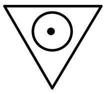


Figure 10. Aromatic compounds with six π electons. Configuration of π electrons in the cyclopentadienyl anion, benzene, and the cycloheptatrienyl cation.

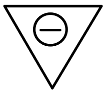
Fig. 10 displays the molecular orbitals for rings containing five, six, and seven sp^2-hybridized carbons. We see the same pattern for all of them: a single orbital at the lowest level, and above it a series of degenerate pairs. It takes ($4\pi + 2$) π electrons to fill a set of these bonding orbitals: two electrons for the lowest orbital, and four for each of n degenerate pairs. Such an electron configuration has been likened to the rare-gas configuration of an atom, with its closed shell. It is the filling of these molecular orbital shells that makes these molecules aromatic.



Cyclopropenyl
cation
Two π electrons



Cyclopropenyl
free radical
Three π electrons



Cyclopropenyl
anion
Four π electrons

The cyclopropenyl free radical and anion are not unusually stable; indeed, the anion seems to be particularly unstable. The cation has the Huckel number of two π electrons

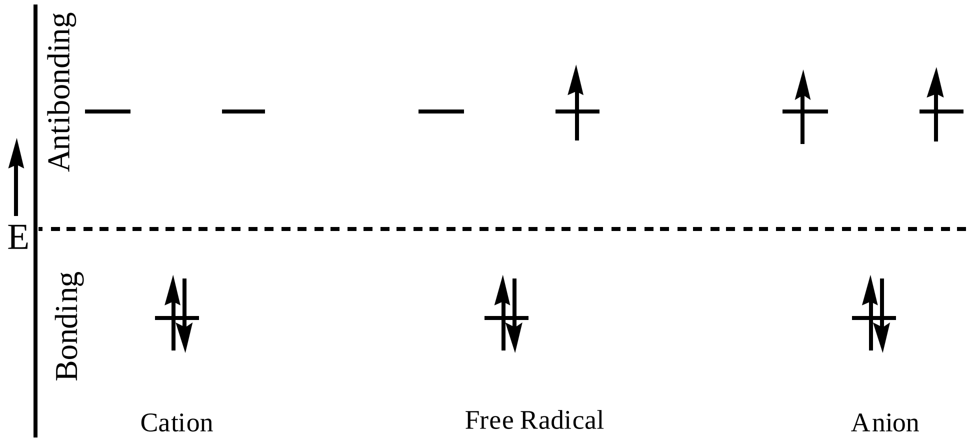


Figure 11. Cyclopropenyl system. Configuration of π electrons in the cation, the free radical, and the anion. (n is zero) and is aromatic. Here, too, aromaticity results from the filling up of a molecular orbital shell.

In the allyl system (Fig. 7) the third and fourth electrons go into a non-bonding orbital, whereas here they go into anti bonding orbitals. As a result, the cyclopropenyl free radical and anion are less stable than their open-chain counterparts. For the cyclopropenyl anion in particular, with two electrons in antibonding orbitals, simple calculations indicate no net stabilization due to delocalization, that is, zero resonance energy. Some calculations indicate that the molecule is actually less stable than if there were no conjugation at all. Such cyclic molecules, in which delocalization actually leads to destabilization, are not just non-aromatic; they are antiaromatic.

Problem 1. When 3,4-dichloro-I,2,3,4-tetramethylcyclobutene was dissolved at -78 °C in SbFs-S0$_2$, the solution obtained gave three NMRpeaks, ata δ .07, a δ .20, and b δ .68, in the ratio I : I : 2. As the solution stood, these peaks slowly disappeared and were replaced by a single peak at a 3.68. What compound is each spectrum probably due to? Of what theoretical significance are these findings?

Problem 2. (a) Cyclopropenones (I) have been made, and found to have rather unusual properties. They have very high dipole moments: about 5 D, compared with about 3 D for benzo- phenone or acetone. They are highly basic for ketones, reacting with perchloric acid to yield salts of formula (R2C30H)+C104 ". What factor may be responsible for these unusual properties?

(b) Diphenylcyclopropenone was allowed to react with phenylmagnesium bromide, and the reaction mixture was hydrolyzed with perchloric acid. There was obtained, not a tertiary alcohol, but a salt of formula $[(C_6H_5)C_3]^+Cl_4^-$ Account for the formation of this salt.

(c) The synthesis of the cyclopropenones involved the addition to alkynes of CCl_2 which was generated from $Cl_3CCOONa$. Show all steps in the most likely mechanism for the formation of CCl_2•

6.8 Orbital symmetry and the chemical reaction

A chemical reaction involves the crossing of an activation energy barrier. In crossing this barrier, the reacting molecules seek the easiest path: a low path, to avoid climbing any higher than is necessary; and a broad path, to avoid undue restrictions on the arrangement of atoms. As reaction proceeds, there is a change in bonding among the atoms, from the bonding in the reactants to the bonding in the products. Bonding is a stabilizing factor; the stronger the bonding, the more stable the system. If a reaction is to follow the easiest path, it must take place in the way that maintains maximum bonding during the reaction process. Now, bonding, as we visualize it, results from overlap of orbitals. Overlap requires that portions of different orbitals occupy the same space, and that they be of the same phase.

This line of reasoning seems perfectly straightforward. Yet the central idea, that the course of reaction can be controlled by orbital symmetry, was a revolutionary one, and represents one of the really giant steps forward in chemical theory. A number of people took part in the development of this concept: K. Fukui in Japan, H. C. Longuet-Higgins in England. But organic chemists became aware of the power of this approach chiefly through a series of papers published in 1965 by R. B. Woodward and Roald Hoffmann working at Harvard University.

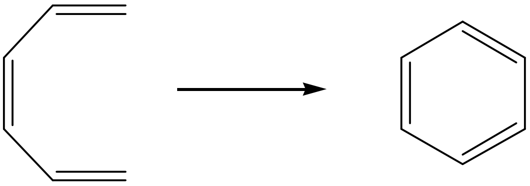
Very often in organic chemistry; many facts are accumulated, and a theory is proposed to account for them. This is a perfectly respectable process, and extremely valuable. But with orbital symmetry, just the reverse has been true.

The theory lay in the mathematics, and what was needed was the spark of genius to see the applicability to chemical reactions. Facts were sparse, and Woodward and Hoffmann made predictions, which have since been borne out by experiment. All this is the more convincing because these predictions were of the kind caned "risky": that is, the events predicted seemed unlikely on any grounds other than the theory being tested.

Orbital symmetry effects are observed in concerted reactions, that is, in reactions where several bonds are being made or broken simultaneously. Woodward and Hoffmann formulated "rules", and described certain reaction paths as sym-metry allowed and others as symmetry-forbidden. All of this applies only to concerted reactions, and refers to the relative ease with which they take place. A "symmetry- forbidden" reaction is simply one for which the concerted mechanism is very difficult, so difficult that, if reaction is to occur at all, it will probably do so in a different way: by a different concerted path that is symmetry-allowed; or, if there is none, by a stepwise, non-concerted mechanism. Even this simplified approach, we shall find, is tremendously powerful; it is highly graphic, and in some cases gives information that the more detailed treatment does not.

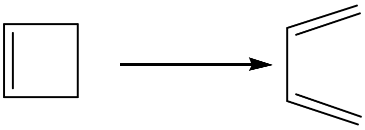
6.9 Electrocyclic reactions

Under the influence of heat or light, a conjugated polyene can undergo isomerization to form a cyclic compound with a single bond between the terminal carbons of the original conjugated system; one double bond disappears, and theremaining double bonds shift their positions. For example, 1,3,5-hexatrienes yield 1 ,3-cyclohexadienes:



1,3,5-hexatrienes   1 ,3-cyclohexadienes

The reverse process can also take place: a single bond is broken and a cyclic compound yields an open-chain polyene. For example, cyclobutenes are converted into butadienes:



Cyclobutene butadiene

Such interconversions are called electrocyclic reactions.

It is the stereochemistry of electrocyclic reactions that is of chief interest to us. To observe this, we must have suitably substituted molecules. Let us consider first the interconversion of 3,4-dimethylcyclobutene and 2,4-hexadiene (Fig. 12). The cyclobutene exists as *cis* and trans isomers. The hexadiene exists in three forms: *cis,cis; cis,trans*; and *trans,trans.* As we can see, the cis-cyclobutene yields only one of the three isomeric dienes; the trans-cyclobutene yields a

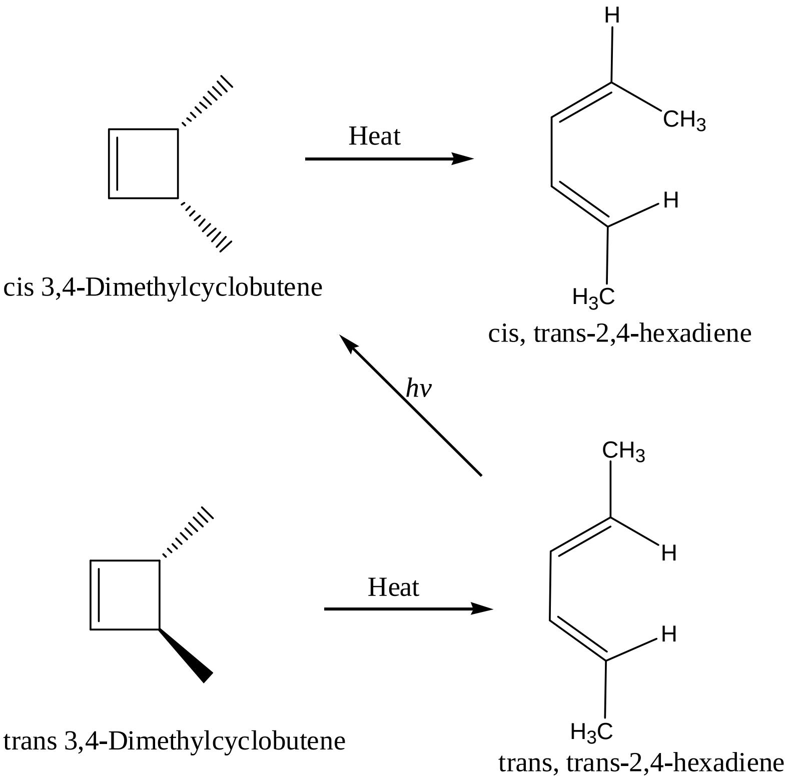


Figure 12. Interconversions of 3,4-dimethyicyclobutenes and 2,4 hexa dienes.

different isomer. Reaction is thus completely stereoselective and completely stereospecific. Furthermore, photochemical cyclization of the trans,trans diene gives a different cyclobutene from the one from which the diene is formed by the thermal (heat-promoted) ring-opening.

The interconversions of the corresponding dimethylcyclohexadienes and the 2,4,6-octatrienes are also stereoselective and stereospecific (Fig. 13). Here, too, thermal and photochemical reactions differ in stereochemistry. If we examine the

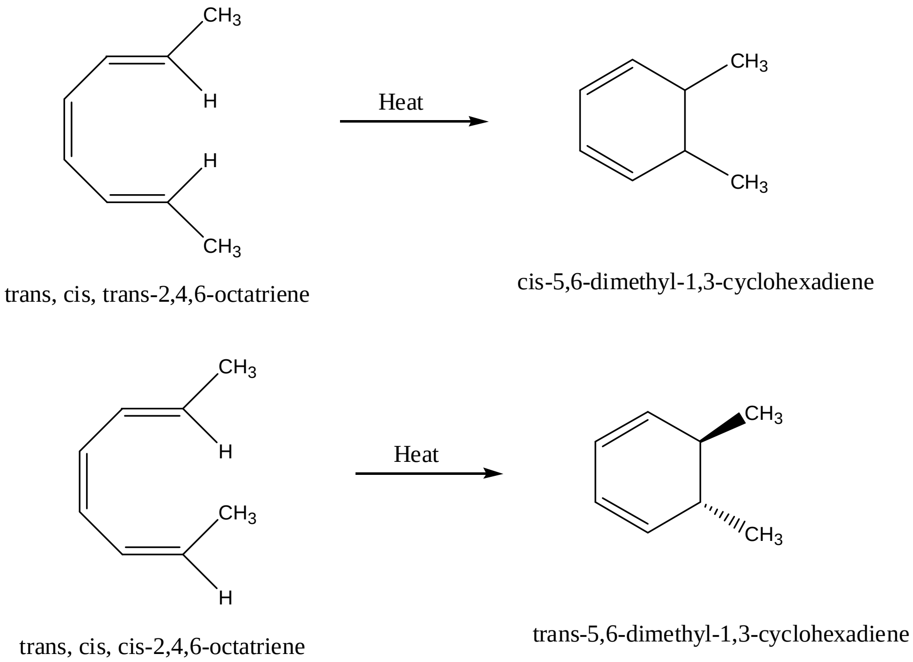


Figure 13. Interconversions of 2,4,6-octatrienes and 5,6-dimethyl- 1,3-cyclohexadienes.

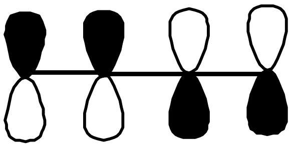
structures closely, we see something else: the stereochemistry of the triene-cyclohexadiene interconversions is opposite to that of the diene-cyclobutene interconversions. For the thermal reactions, for example, cis methyl groups in the cyclobutene *become cis* and *trans* in the diene; cis methyl groups in the cyclohexadiene are trans and trans in the related triene.

Electrocyclic reactions, then, are completely stereoselective and stereospecific.

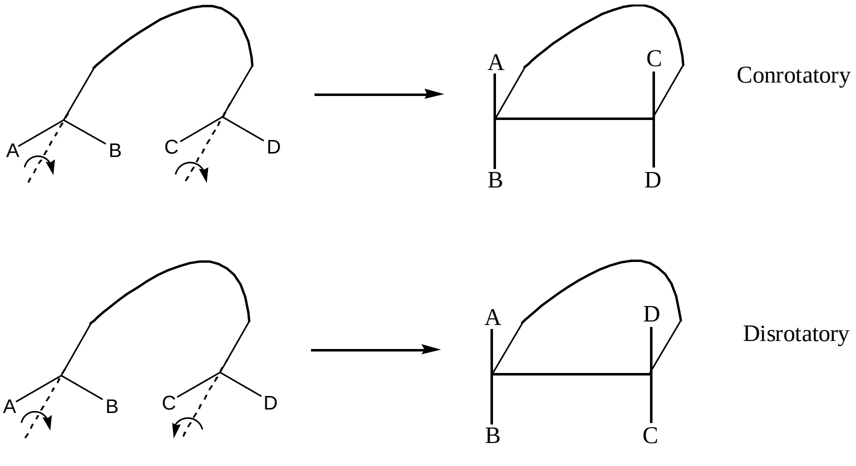
The exact stereochemistry depends upon two things: (a) the number of double bonds in the polyene, and (b) whether reaction is thermal or photochemical. It is one of the triumphs of the orbital symmetry approach that it can account for all these facts; indeed, most of the examples known today were predicted by Woodward and Hoffmann before the facts were known.

It is easier to examine these interconversions from the standpoint of cyclization; according to the principle of microscopic reversibility, whatever applies to this reaction applies equally well to the reverse process, ring-opening. In cyclization, two π electrons of the polyene form the new σ bond of the cycloalkene. But which two electrons? We focus our attention on the highest occupied molecular orbital (HOMO) of *the polyene*. Electrons in this orbital are the "valence" electrons of the molecule; they are the least tightly held, and the most easily pushed about during reaction.

Let us begin with the thermal cyclization of a disubstituted butadiene, RCH=CH-CH=CHR. As we have already seen (Fig. 6), the highest occupied molecular orbital of a conjugated diene is ψ_2. It is the electrons in this orbital that will form the bond that closes the ring. Bond formation requires overlap, in this case overlap of lobes on C-I and C-4 of the diene: the front carbons in Fig. 14. We see that to bring these lobes into position for overlap, there must be rotation about two bonds, C(1)-C(2) and C(3)-C(4). This rotation can take place in two different ways: there can be conrotatory motion, in which the bonds rotate in the same direction, or there can be disrotatory motion, in which the bonds rotate in opposite directions. Now, in this case, as we see in Fig. 14, conrotatory motion brings together lobes of the same phase; overlap occurs and a bond forms. Disrotatory motion, on the other hand, brings together lobes of opposite phase; here interaction is antibonding, and repulsive. As Fig. 15 shows, it is conrotatory motion that produces the stereochemistry actually observed. How are we to account for the opposite stereochemistry in the photochemical reaction? On absorption of light, butadiene is converted into the excited state shown in Fig. 6, in which one electron from ψ_2 has been raised to ψ_3' Now the highest occupied orbital is ψ_3' and it is the electron here that we are concerned

ψ_2  HOMO of ground state

Conjugated Diene .



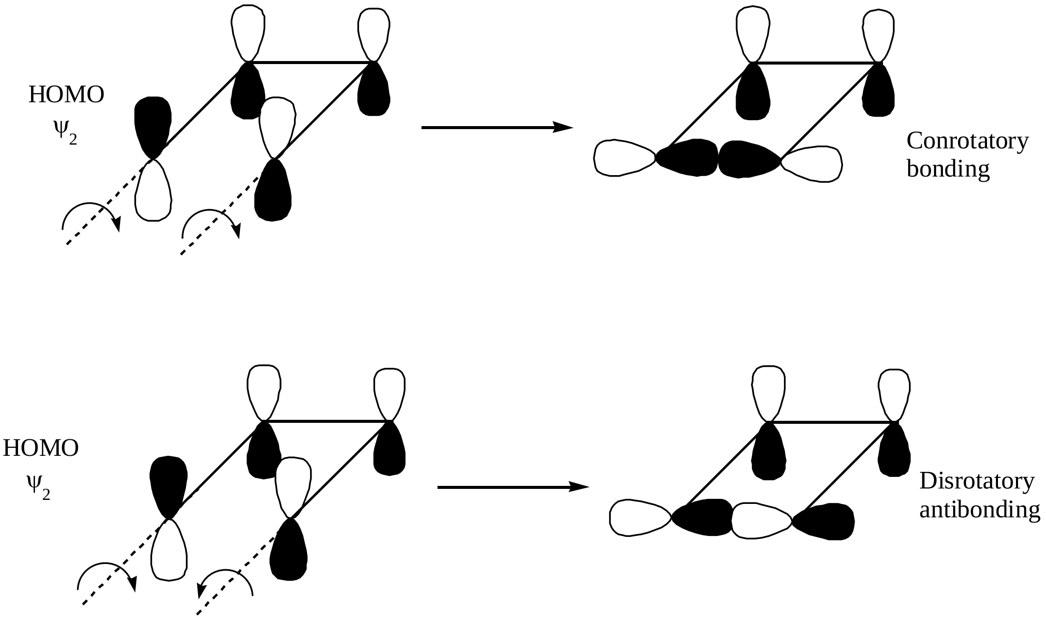
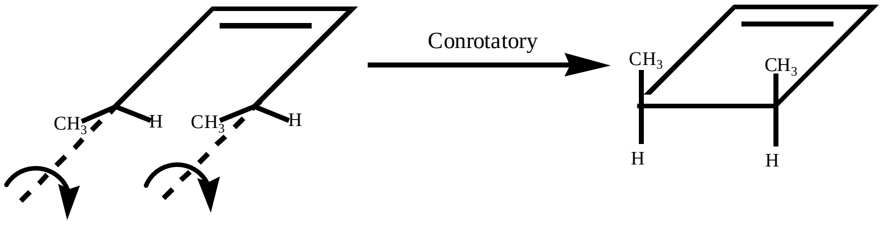
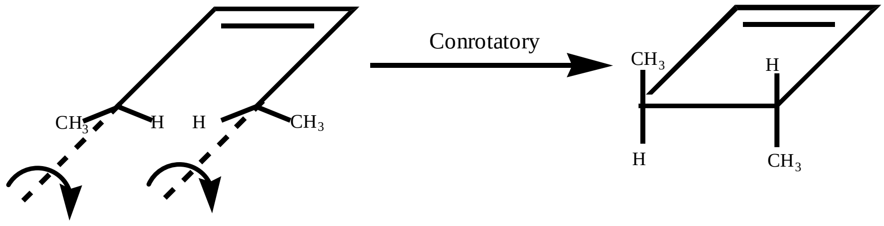


Figure 14. Thermal cyclization of a 1,3-butadiene to a cyclo Conrotatory motion leads to bonding. Disrotatory motion I bonding.



cis, trans-2,4-hexadiene

cis-3,4-dimethylcyclobutene



trans, trans-2,4-hexadiene

trans-3,4-dimethylcyclobutene

Figure 15 Thermal cyc1ization of substituted butadienes. Observed stereochemistry indicates conrotatory motion.

with. But in ψ_3 the relative symmetry of the terminal carbons is opposite to that in ψ_2 Now it is the disrotatory motion that brings together lobes of the same phase, and the stereochemistry is reversed (Fig. 16). Next, let us look at the thermal cyclization of a disubstituted hexatriene, CH=CH--cH=CH--cH=CHR, whose electronic configuration is shown in Fig. 17

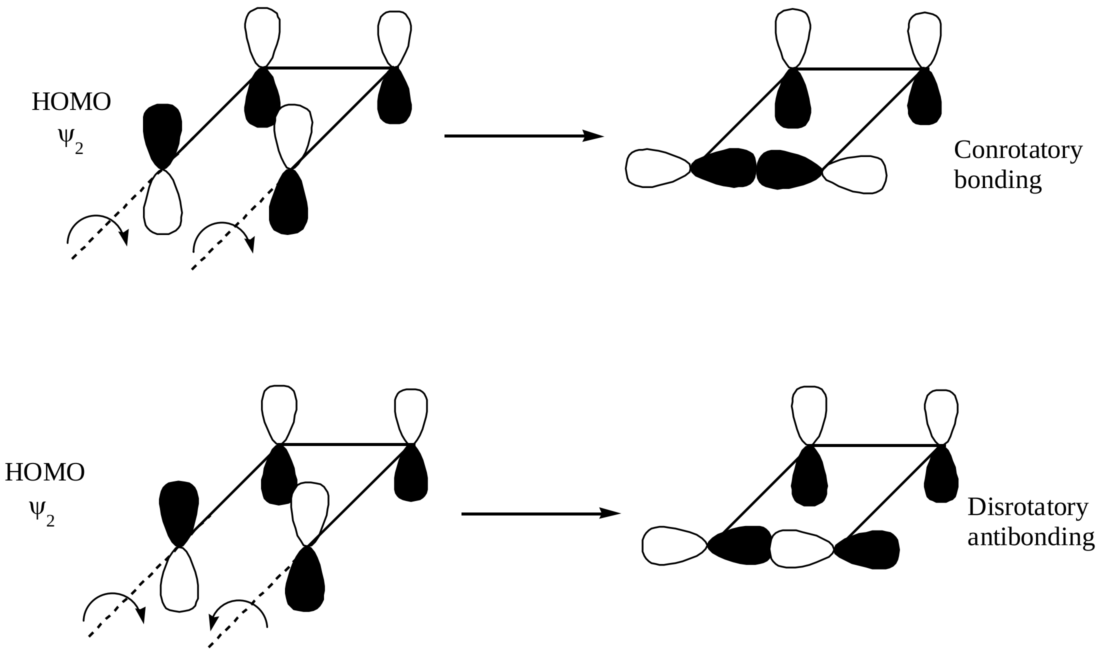
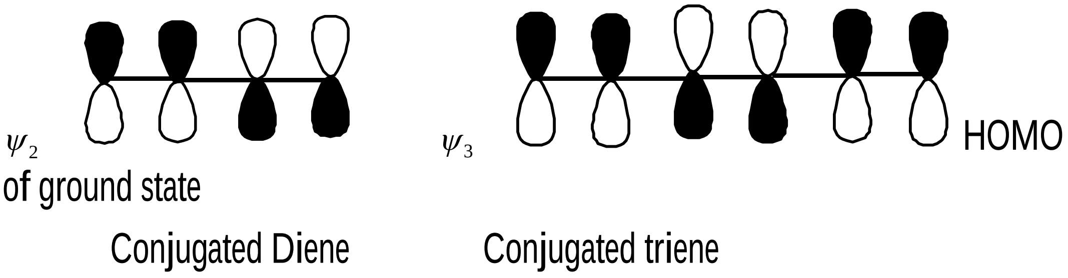


Figure 16. Photochemical cyclization of a 1 ,3-butadiene to a cyclobutene. Disrotatory motion leads to bonding. Conrotatory motion leads to antibonding.



The HOMO for the ground state of the hexatriene is ψ_3 If we compare this with the HOMO for the ground state of butadiene, we see that the relative symmetry about the terminal carbons is opposite in the two cases. For ground-state hexatriene it is disrotatory motion that leads to bonding and, as shown in Fig. 18, gives rise to the observed stereochemistry .

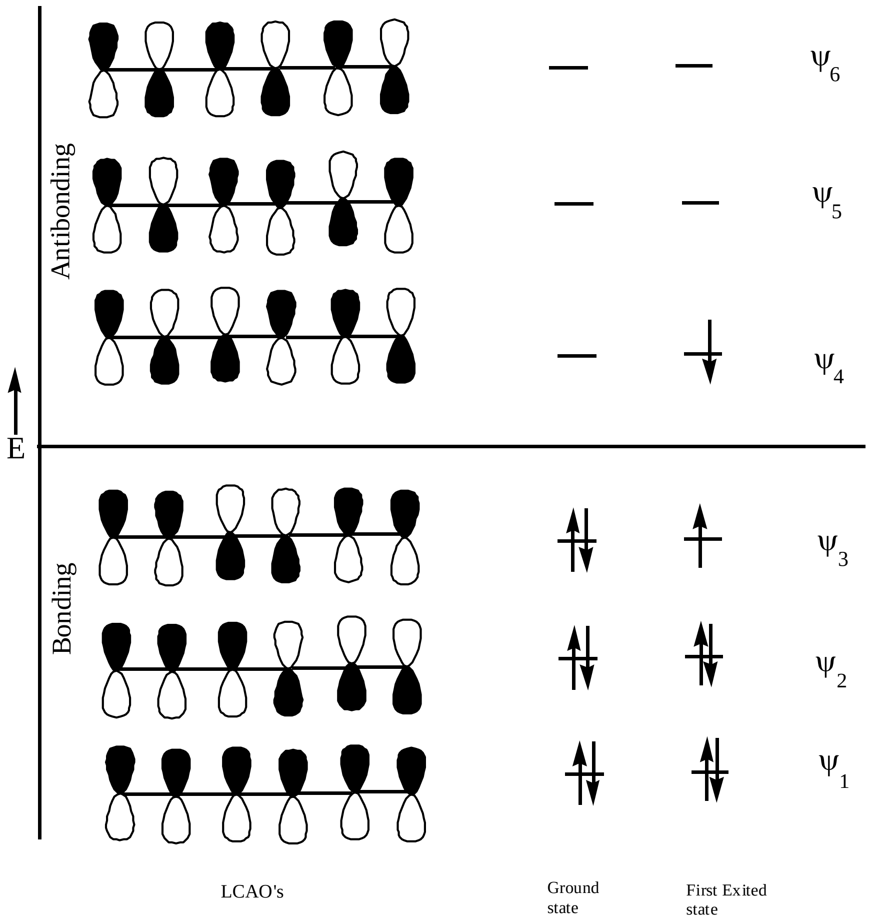


Figure 17. A 1,3,5-hexatriene. Configuration of π electrons in the ground state and the first excited state..

In the excited state of hexatriene, ψ_4 is the HOMO, and once again we see a reversal of symmetry: here, conrotatory motion is the favored process.

What we see here is part ofa regular pattern (Table 1) that emerges from the quantum mechanics. As the number of pairs of π electrons in the polyene. increases, the relative symmetry about the terminal carbons in the HOMO. alternates regularly. Furthermore, symmetry in the HOMO of the first excited state is always opposite to that in the ground state.

Table 1 WOODWARD-HOFFMANN RULES FOR ELECTROCYCLIC REACTIONS

Number of π electrons	Reaction	Motion
4π	thermal	conrotatory
4π	photochemical	disrotatory
$4\pi + 2$	thermal	disrotatory

$4\pi+2$	photochemical	conrotatory

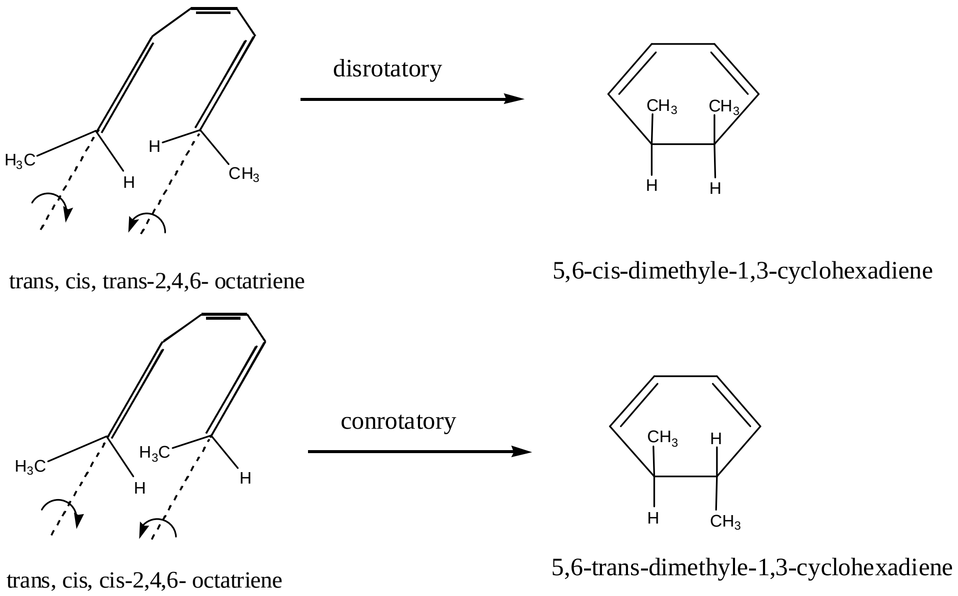
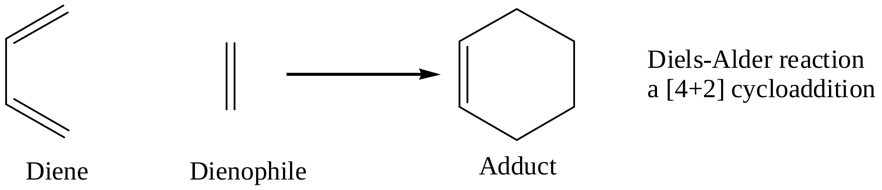


Figure 18. Thermal cyclization of substituted hexatrienes. Observed stereochemistry indicates disrotatory motion.

6.10 Cycloaddition reactions

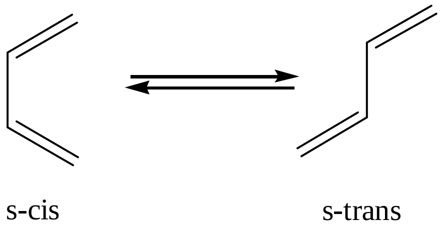
In the Diels-Alder reaction a conjugated diene and a substituted alkene-the dienophile-react to form a cyclohexene.



This is an example of cycloaddition, a reaction in which two unsaturated molecules combine to form a cyclic compound, with π electrons being used to form two new (1 bonds. The Diels-Alder reaction is a [4 + 2] cycloaddition, since it involves a system of four π electrons and a system of two π electrons. Reaction takes place very easily, often spontaneously, and at most requires moderate application of heat.

There are several aspects to the stereochemistry of the Diels-Alder reaction.

(a) First, we have taken for granted+correctly+that the diene must be in the conformation (*s-cis*) that permits the ends of the conjugated system to reach the doubly bonded carbons of the dienophile.



Required for *Diels-Alder* Reaction

(b) Next, with respect to the alkene (dienophile) addition is clearcut synthesis stereoselectivity is part of the evidence that the Diels Alder reaction is, indeed, a concerted one, that is, that both new bonds are formed in the same transition state.

(c) Finally, the Diels-Alder reaction takes place in the endo, rather than exo, sense. That is to say, any other unsaturated groups in the dienophile (for example, -CO-O-Co- in maleic anhydride) tend to lie near the developing double bond in the diene moiety (Fig. 19). For the endo preference to be seen, of course, the diene must be suitably substituted.

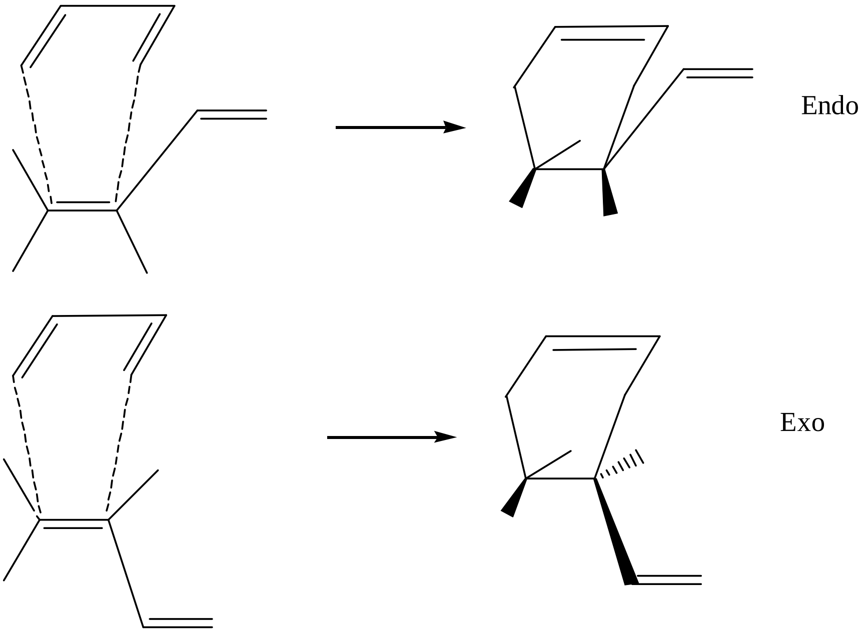
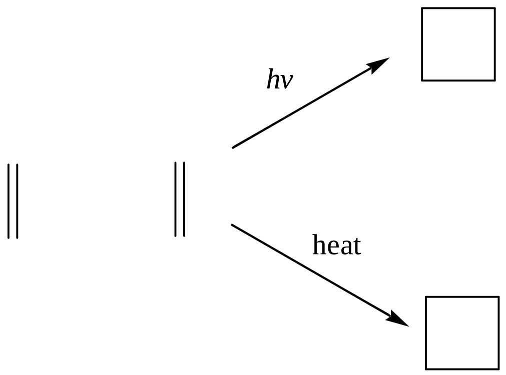


Figure 19. Stereochemistry of the Diels-Alder reaction, illustrated for the reaction between two moles of 1,3-butadiene.

Can two molecules of ethylene combine to form cyclobutane? The answer is yes, but not easily under thermal conditions. Under vigorous conditions cycloaddition may occur, but stepwise+via diradicals-and not in a concerted fashion. Photochemi cal [2 + 2] cycloadditions, on the other hand, are very common. (Although some ofthese, too, may be stepwise reactions, many are clearly concerted.)

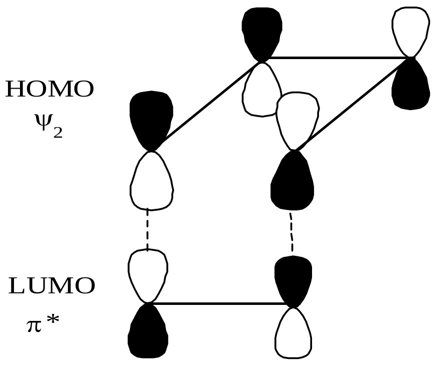
Of thermal cycloadditions, then, [4 + 2] is easy and [2 + 2] is difficult. of [2 + 2] cycloadditions, the thermal reaction is difficult and the photochemical reaction is easy.



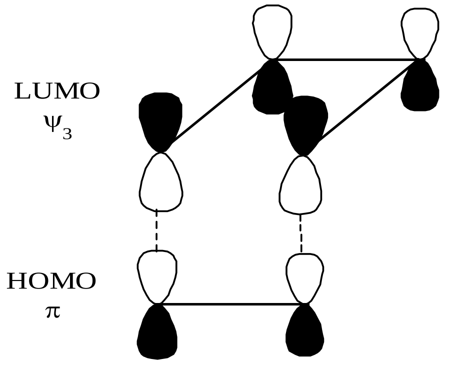
Difficult:
not a concerted reaction

In cycloaddition, two new (1 bonds are formed by use of π electrons of the reactants. The concerted reaction results from overlap of orbitals of one mciecule with orbitals of the other. As before, it is on electrons in the HOMO that we focus attention. But which orbital does the HOMO overlap? It picks an orbital into which its electrons can flow: an unoccupied orbital. And of unoccupied orbitals it picks the most stable, the lowest unoccupied molecular orbital (LUMO). In the transition state of cycloaddition, then, stabilization comes chiefly from overlap between the HOMO of one reactant and the LUMO of the other.

On this basis, let us examine the [4 + 2] cycloaddition of 1,3-butadiene and ethylene, the simplest example of the Diels-Alder reaction. The electronic configurations of these compounds-and of dienes and alkenes in general-have been given in Fig. 5 and Fig. 6. There are two combinations: overlap of the HOMO of butadiene (ψ_2) with the LUMO of ethylene (π^*); and overlap of the HOMO of ethylene (π) with the LUMO of butadiene (ψ_3) In either case, as Fig. 20 shows, overlap brings together lobes of the same phase. There is a flow of electrons from HOMO to LUMO, and bonding occurs.



Symmetry allowd (a)



Symmetry allowd (b)

Figure 20. Symmetry-allowed thermal [4 + 2] cycloaddition: 1,3-butadiene and ethylene. Overlap of (a) the HOMO of 1,3-butadiene and the LUMO of ethylene, and (b) the HOMO of ethylene and the LUMO of 1,3- butadiene.

Now, consider a thermal [2 + 2] cyclization, dimerization of ethylene. This would involve overlap of the HOMO, π, of one molecule with the LUMO, π^{*}·, of the other. But π and π^{*}· are of opposite symmetry, and, as Fig. 21 shows, lobes of opposite phase would approach each other. Interaction is antibonding and repulsive, and concerted reaction does not occur.

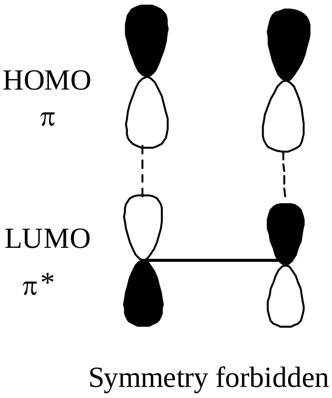


Figure 21. Symmetry-forbidden thermal [2 + 2] cycloaddition: two molecules of ethylene. Interaction is anti bonding.

Photochemical [2 + 2] cycloadditions are symmetry-allowed. Here we have (Fig. 22) overlap of the HOMO (π^{*}) of an excited molecule with the LUMO (also π^{*}) of a ground-state molecule.

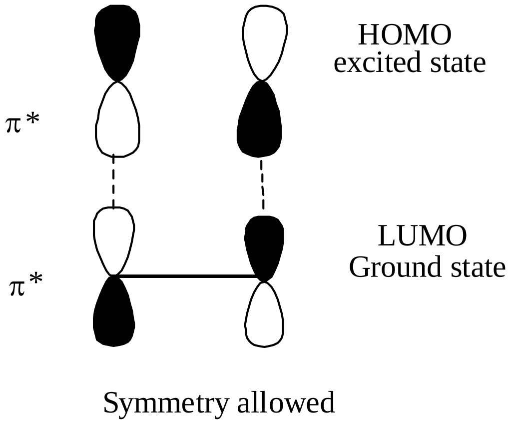
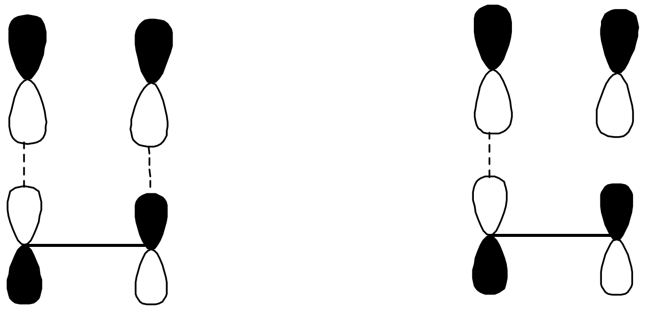


Figure 22. Symmetry-allowed photochemical [2 + 2] cycloaddition: two molecules of ethylene, one excited and one in the ground state, Interaction is bonding.

If, in a concerted reaction of this kind, both bonds to a component are being formed (or broken) on the same face, the process is said to be suprafacial. If the bonds are being. formed (or broken) on opposite faces, the process is antarafacial.

These terms resemble the familiar ones syn and anti, but with this difference. Syn andanti describe the net stereochemistry of a reaction. We have seen anti addition, for example as the overall result of a two-step mechanism. Suprafacial and antarafacial, in contrast, referto actual processes: the simultaneous making (or breaking) of two bonds on the same faceor opposite faces of a component.

So far, our discussion of cycloaddition has assumed that reaction is suprafacial with respect to both components. For [4 + 2] cycloadditions, the stereochemistry shows that this is indeed the case. Now, as far as orbital symmetry is conerned, thermal (2 + 2] cyc1oaddition could occur if it were suprafacial with respect to one component and antarafacial with respect to the other (Fig. 23). Almost certainly, such a supra,antara process is impossible here on geometric grounds.



supra, supra
symmetry forbidden

supra, antara
symmetry allowd

Figure 23. [2 + 2] Cycloaddition. Supra, supra: geometrically possible, but symmetry-forbidden. Supra, antara: symmetry-allowed, but geometrically difficult.

But if the ring being formed is big enough, both supra.supra and supra,antara processes are geometrically possible; in that case orbital symmetry determines, not whether cycloaddition occurs, but how it occurs (Table 2).

Table 2 WOODWARD-HOFFMANN RULES FOR *[i + j]* CYCLOADDITIONS

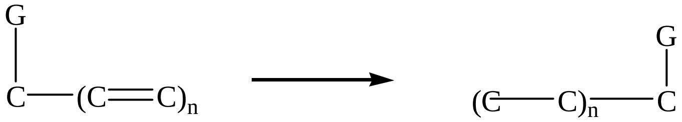
i+j	Thermal	Photochemical
4π	supra,antara	supra,supra
	antara,supra	antara,antara

$4\pi + 2$	supra,supra antara,antara	supra,antara antara,supra

Cycloadditions are reversible. These cycloreversions (for example, the retro-Diels-Alder reaction) follow the same symmetry rules as cycloadditions-as they must, of course, since they occur via the same transition states.

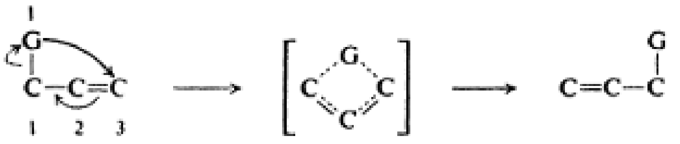
6.11 Sigmatropic reactions

A concerted reaction of the type.

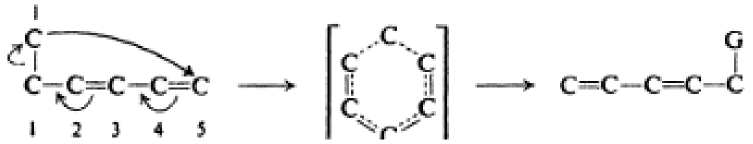


In which a group migrates with its σ bond within a π framework an one or a polyene is called a sigmatropic reaction.

The migration is accompanied by a shift in π bonds. For example.

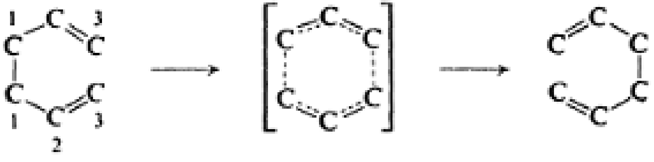


[1,3] sigmatropic reaction



[1,5] sigmatropic reaction

In the designations [1,3] and [1,5] the "3" and "5" refer to the number of the carbon to which group G is migrating (the migration terminus). The "1" does not refer to the migration source; instead, it specifies that in both reactant and product bonding is to the same atom (number 1) in the migrating group. The important *Cope rearrangment of hexa-I 5S-dienes*, for example, is a [3,3] sigmatropic reaction,



[3,3] sigmatropic reaction

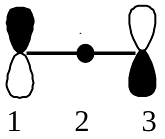
A 1,5-hexadiene

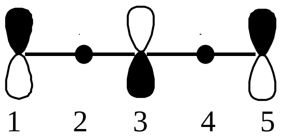
in which there is a change in position of attachment in G as well as in the π framework-indeed, G itself is a π framework. In the transition state of a sigmatropic reaction, the migrating group is bonded to both the migration source and the migration terminus; it is the nature of this transition state that we are concerned with. For convenience we considered bonding in the H_2 molecule to arise from overlap between orbitals on two hydrogen atoms. In the same way, and simply for convenience, we consider bonding in the transition state for sigmatropic reactions to arise from overlap between an orbital of an atom or free radical (G) and an orbital of an allylic free radical (the π framework).

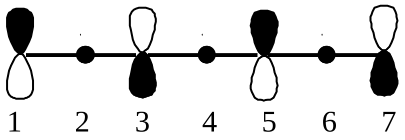
This does not mean that rearrangement actually involves the separation and reattachment of a free radical. Such a stepwise reaction would not be a concerted one, and hence is not the kind of reaction we are dealing with here. Indeed, a stepwise reaction wouldbe a (high-energy) alternative open to a system if a (concerted) sigmatropic rearrangement were symmetry-forbidden.

In the transition state, there is overlap between the HOMO of one component and the HOMO of the other. Each HOMO is singly occupied, and together they provide a pair of electrons.

The HOMO of an allylic radical depends on the number of carbons in the π framework. The migrating group is passed from one end of the aUylic radical to the other, and so it is the end carbons that we are concerned with. We see that the

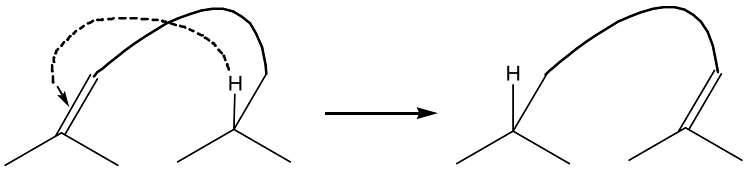




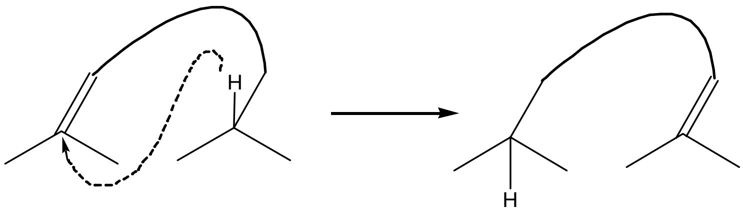


symmetry at these end carbons alternates regularly as we pass from C_3 to C_5, to C_7, and so on. The HOMO of the migrating group depends, as we shall see, on the nature of the group.

Let us consider first the simplest case: migration of hydrogen. Stereochemically, this shift can be suprafacial or antarafacial:



Suprafacial sigmatropic shift

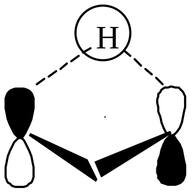


Antarafacial sigmatropic shift

In the transition state, a three-center bond is required, and this must involve overlap between the s orbital of the hydrogen and lobes of p orbitals of the two terminal carbons. Whether a suprafacial or antarafacial shift is allowed depends upon the symmetry of these terminal orbitals:

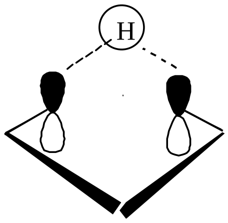
Whether a sigmatropic rearrangement actually takes place, though, depends not only on the symmetry requirements but also on the geometry of the system. In particular, [1,3] and [1,5] antara shifts should be extremely difficult, since they would require the π framework to be twisted far from the planarity that it requires for delocalization of electrons.

Practically, then, [1,3] and [1,5] sigmatropic reactions seem to be limited to supra shifts. A [1,3] supra shift of hydrogen is symmetry-forbidden; since the s orbital of hydrogen would have to overlap p lobes of opposite phase, hydrogen cannot be bonded simultaneously to both carbons. A [1,5] supra shift of hydrogen, on the other hand, is symmetry-allowed.



[1,3]

Symmetry forbidden



[1,5]

Symmetry allowed

Suprafacial migration of H

For larger π frameworks, both supra and antara shifts should be possible on geometric grounds, and here we would expect the stereochemistry to depend simply on orbital symmetry. A [1,7}H shift, for example, should be antara, a

[I,9] H shift, supra, and so on . For photochemical reactions, as before, predictions are exactly reversed.

The facts agree with the above predictions: [1,3] sigmatropic shifts of hydrogen are not known, whereas [1,5] shifts are well known.

The preference for [1,5]-H shifts over [1,3]-H shifts has been demonstrated many times. For example, the heating of 3-deuterioindene (I) causes scrambling of the label to all three non-aromatic positions. Let us examine this reaction.

We cannot account for the formation of II on the basis of [1,3] shifts: migration of D would regenerate I; migration of H would yield only III. But if we include the p orbitals of the benzene ring, and count along the edge of this ring, we see that a [1,5] shift of D would yield the unstable non-aromatic intermediate IVa, This, in turn, can transfer H or D by [1,5] shifts to yield all the observed products.

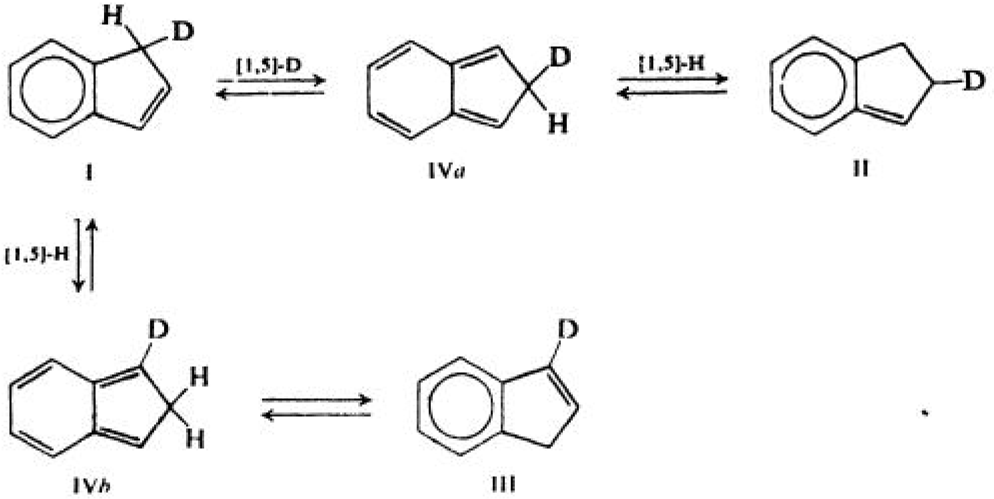
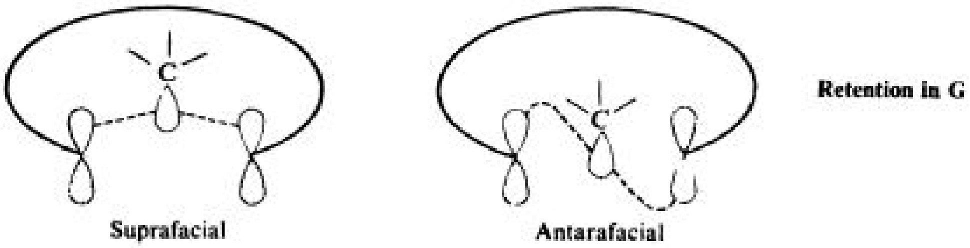


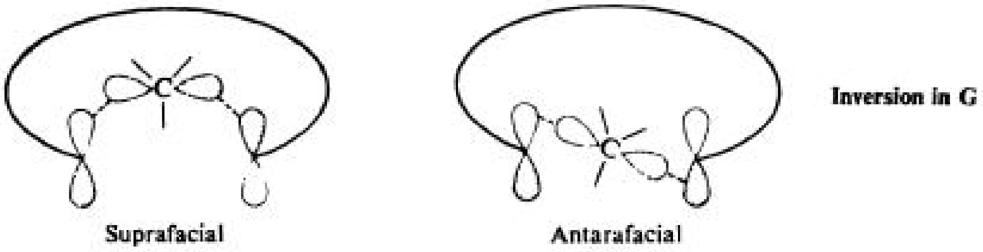
Figure 14. Deuterium scrambling in indene via unstable intermediates IVa and IVb: a series of [1,5] hydrogen shifts.

So far we have discussed only migration of hydrogen, which is necessarily limited to the overlap of an s orbital. Now let us turn to migration of carbon. Here, we have two possible kinds of bonding to the migrating group. One of these is similar to what we have just described for migration of hydrogen: bonding of both ends of the π framework to the same lobe on carbon. Depending on the symmetry of the π framework, the symmetry-allowed migration may be suprafacial or antarafacial.

With carbon, a new aspect appears: the stereochemistry in the migrating group. Bonding through the same lobe on carbon means attachment to the same face of the atom, that is to say, retention of *configuration in the migrating group.*

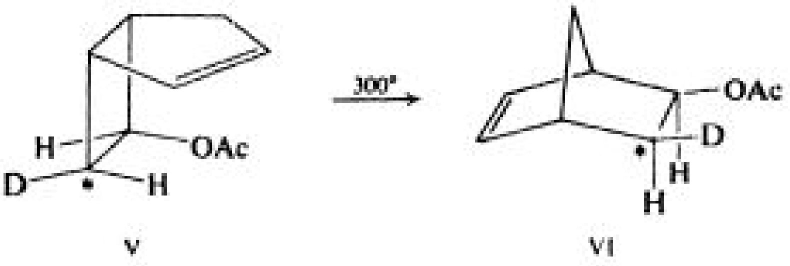


But there is a second possibility for carbon: bonding to the two ends of the π framework through different lobes of a p orbital. These lobes are on opposite faces of carbon-exactly as in an S_N2 reaction-and there is inversion of configuration in the migrating group.



For [1,3] and [1,5] shifts, the geometry pretty effectively prevents antarafacial migration. Limiting ourselves, then, to suprafacial migrations, we make these predictions: [1,3] migration with inversion; [1,5] migration with retention. These *predictions have been bome out by experiment.*

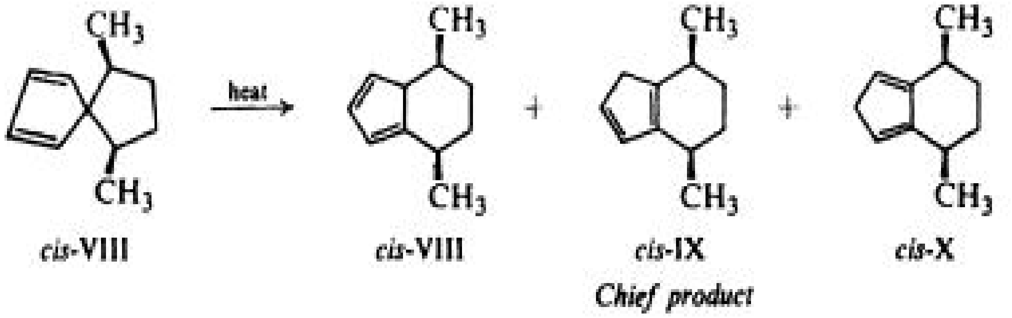
In 1968, Jerome Berson (of Yale University) reported that the deuterium-labeled bicyclo[3.2.0]heptene V is converted stereospecifically into the



V VI

exo-norbornene VI. As Fig. 25 shows, this reaction proceeds by a [1,3] migration and with complete inversion of configuration in the migrating group.

In 1970, H. Kloosterziel (of the University of Technology, Eindhoven, The Netherlands) reported a study of the rearrangement of the diastereomeric 6,9-dimethylspiro[4.4]nona-l,3-dienes (*cis*-VII and trans-VII) to the dimethyl-bicyclo-[4.3.0] nonadienes VIII, IX, and X. These reactions are completely stereo- selective and stereospecific.



As Fig.26 shows, they proceed by [1,5] migrations and with complete retention of configuration in the migrating group.

To predict a different stereochemistry between [1,3] and [1,5] migrations, and in particular to predict inversion in the [1,3] shift-certainly not the easier path on geometric grounds-is certainly "risky". The fulfillment of such predictions dem- onstrates both the validity and the power of the underlying theory.

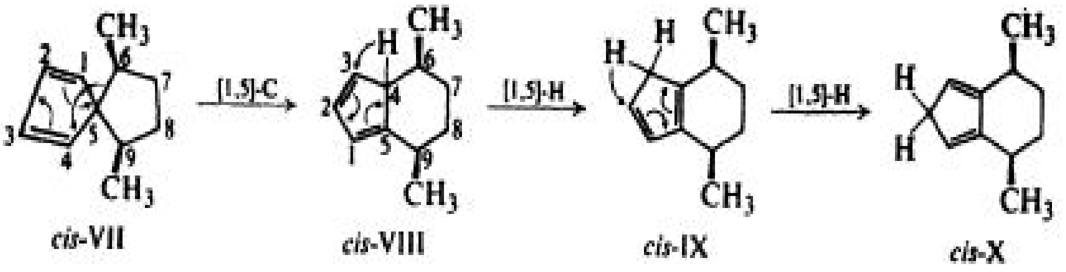


Figure 26. Rearrangement of cis-6,9-dimethylspiro[4.4]nona-1,3-diene. Migration ofC-6 from C-5 to C-4 is a [1,5]-C shift. (We count 5, 1,2,3,4.) Configuration at C-6 is retained, as shown by its relationship to configuration at C-9. Successive [1,5]-H shifts then yield the other products.

6.12 Summary

In this chapter molecular orbital theory has been discussed in details. There is a detailed discussion of atomic and molecular orbitals. The possibilities of combination of atomic orbital to form molecular orbital has been discussed. Bonding and antibonding molecular orbitals have been discussed with various examples. Electronic configuration of many molecules has been studied. Aromatic character of any molecule on the basis of its electronic configuration has been described in details. There is clear and detailed discussion of electrocyclic, cycloaddition and sigmatropic reactions in this chapter.

Unit - 7

Classification and stereochemistry of pericyclic reactions: Classification of pericyclic reactions. Woodward-Hoffmann correlation diagrams. FMO and PMO approach

Structure of Unit:

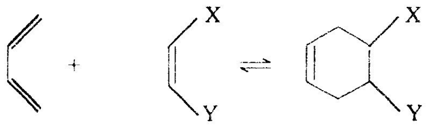
7.0 Objective

At the end of this unit learner can able to understand

- Paricyclic reactions
- There mechanism and stereochemistry
- Different types of pericyclic reactions
- Woodward-HoHmann Rule
- And various examples related to their symmetry

7.1 Introduction

The majority of organic reactions proceed either by a polar or by a radical pathway. However, there is a group (although small) of reactions that do not involve polar or radical reagents, i. e. they are substantially uninfluenced by change of polarity of solvent or by the presence of radical initiators. The most common example of this type of reactions is the Diel's - Alder reaction involving 1, 4-addition of substituted alkenes to conjugated dienes, e.g.



Such reactions are apparently concerted, i.e. the electronic rearrangements involved in bond- breaking/bond-making proceed simultaneously, i.e. it is a one step process. The transition states are cyclic and the reactions are attended by a high degree of stereoselectivity. Many of such reactions are reversible. All such concerted reactions which proceed via cyclic transition states are known as **pericyclic reactions.** As pericyclic reactions remain unaffected by polar reagents, solvent change, radical initiators, etc. these are influenced by heat or light These two influences often produce markedly different results either in terms of possibility of a reaction or in terms of the stereochemical course.

7.3 Mechanism and Stereochemistry of Perlcyclic Reactions

Diel's - Alder reaction takes place rapidly and conveniently, while simple dimerisation of olefins to cyclobutanes gives very poor results, except when photochemically induced. Woodward, Hofmann and others have shown that these contrasting results can be explained by the principle of conservation of orbital symmetry which predicts that certain reactions are symmetry allowed and others are symmetry forbidden

The orbital symmetry rules (also called the Woodward-Hofmann rules) apply only to concerted reactions. There are several ways of applying the orbital-symmetry principle of which the frontier- orbital method is the most common.

Frontier orbitals and orbital symmetry. Just as the outer shell of electrons of an atom is regarded as especially significant in determining the chemistry of that atom, so it is reasonable that, for a molecule, it is the **highest occupied molecular orbital (HOMO)** which is the key in determining reactivity. This is termed the frontier orbital. The theory is based upon two principles. -

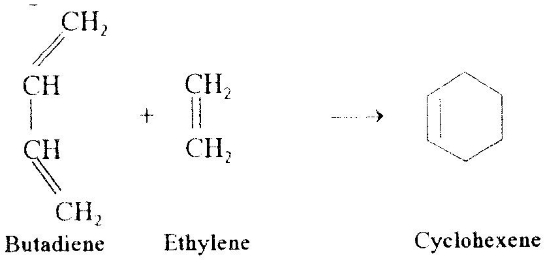
(i) Since the ground state of almost all molecules has a pair of electrons in the HOMO, bonding interaction between two molecules or between two atoms in the same molecule cannot involve only the HOMO of each because this would lead to an orbital occupancy greater than two which is contrary to Pauli's principle. The HOMO of one reactant needs to interact with an unoccupied molecular orbital of the second. Now since the bonding interaction between two orbitals increases as the energies of the two become more nearly equal, it is expected that the HOMO of one reactant would interact efficiently with the lowest unoccupied molecular orbital (LUMO) of the second.

(ii) The shaded (positive) lobe overlaps only with the shaded (positive) lobe of another orbital, and an unshaded (negative) lobe only with the un shaded (negative) lobe of another orbital. Overlap of orbitals of unlike phase results repulsion.

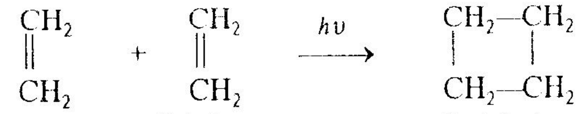
7.4 Classification of Pericyclic Reactions

Pericyclic reactions are classified into three important types which are described below.

1. Cycioadditions. A reaction in which two unsaturated molecules combine to form a cyclic compound, with π electrons being used to form two new (σ bonds is known as cycloaddition reaction. For example.



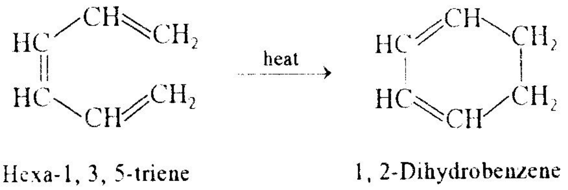
Cycloaddition reaction may again be of two types depending upon the number of π electrons in the two components.



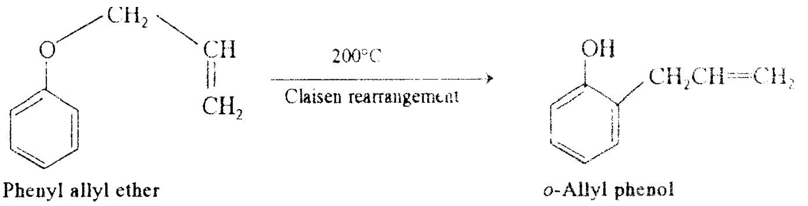
(i) (2 + 2) Cycloadditions. When both the unsaturated molecules have 2π electrons each, e.g.

(ii) (4 +2) Cycloadditions. When one ofthe systems has 4π electrons and the other has 2π electrons. Diels-Alder reactions are the most common example of this type,

2. Electrocyclic reactions. These are intramolecular pericyclic reactions which involve either the formation of a ring, with the generation of one new σ-bond and the consumption of one π-bond or the converse. For example,



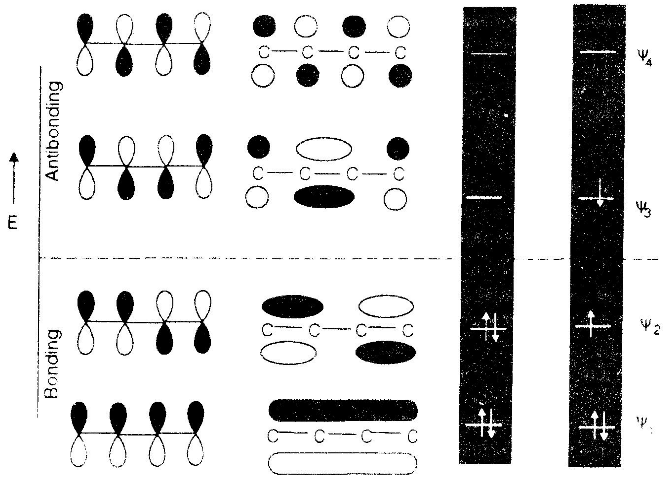
3. Sigmatropic rearrangements. In these reactions an atom or a group in a -π - electron system migrates with the σ-bond without change in the number of σ- or π-bonds. For example



7.5 (4+2) Cycloadditlons

The best known (4 π + 2π) cycloaddition is the Diel's -Alder reaction of which the simplest possible example is the reaction between butadiene and ethylene to form six-membered ring. Diels-Alder reactions take place very easily, often spontaneously, and at most requires moderate application of heat. Before considering the reaciton between butadiene and ethylene, let us first study the electronic configuration of 1, 3-butadiene and ethylene.

Electronic configuration of 1, 3-butadiene. For the four component p orbitals, there are four π MOs (two bonding and two antibonding). Thus in the ground state, butadiene has $\psi^2{}_1\psi^2{}_2$ configuration (the various possible MOs are labelled as ψ_1,ψ_2,ψ_3 etc. in the increasing order of energy), i.e. there are two electrons in each of the two bonding orbitals ($\psi_1 and\, \psi_2$). Orbital ψ_1 encompasses all four carbons, this delocalisation provides the net stabilization of the conjugated system and hence this configuration has the minimum energy. The higher ψ_2 orbital resembles two isolated π orbitals, of course it has somewhat lower energy than the isolated π orbitals. Absorption of light of the right frequency raises one electron of ψ_2 orbital to ψ_3. Thus ψ_3 has one electron in the first excited state although it is vacant in the ground state. Note that it has somewhat higher energy than the ψ_2 but less than the ψ_4 Thus the energy of the completely orbital of highest energy (HOMO) which is to participate in bond formation is near to the LUMO (lower unoccupied molecular orbital) and thus these orbitals of comparable energy can overlap.



LCAO's MO's Ground First State

Excited State

Fig. 7.1 Configuration of π electrons of 1.3-butadiene in the ground state and first excited state.

Electronic configuration of ethylene

The two π-electrons of ethylene are distributed as below.

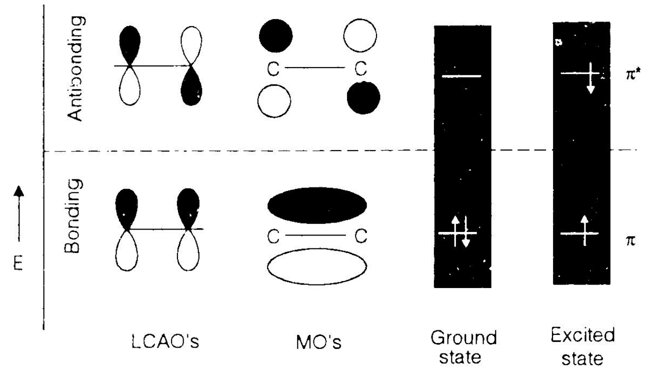


Fig. 7.2 Configuration of .electrons of ethylene in the ground state and first excited state.

From the symmetry of the MOs of butadiene and ethylene, it is apparent that the symmetries of the HOMO of butadiene (ψ_2) and the LUMO of-ethylene (π*) or LUMO of butadiene (ψ_3) and the HOMO of ethylene (π) are such that

When the reactants approach each other with their molecular planes parallel, two new C-C bonds can be formed at the same time.

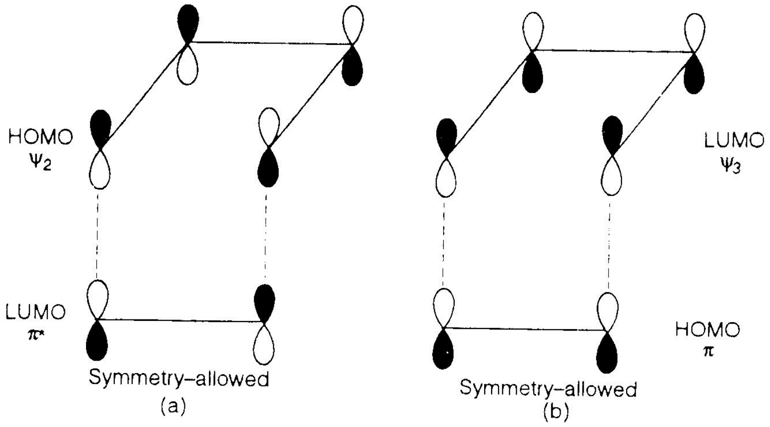


Fig. 7.3 Symmetry-allowed thermal [4 + 2] cycloaddition of I, 3-butadiene and ethylene,(a) Overlap of HOMO of I, 3-butadiene and LUMO of ethylene, (b) Overlap of LUMO of 1, 3-butadiene and HOMO of ethylene.

7.6 (2+2) Cycloadditions

The [4+2] cycloadditions are common and take place very easily and spontaneously. On the other hand, cyclodimerisation of alkenes, e.g. conversion, of ethylene to cyclobutane, is very difficult and not very common. Further, it is interesting to note that the thermal reaction is difficult while the photochemical reaction is easy.

The reason being in presence of heat, dimerization of ethylene would involve overlap of the HOMO, π_2 of one molecule with the LUMO, π^*, of the other. Now since nand π^* are of opposite symmetry, lobes of opposite phase would approach tach other. Hence interaction is antibonding and repulsive, and concerted reaction does not occur due to symmetry-forbidden overlapping.

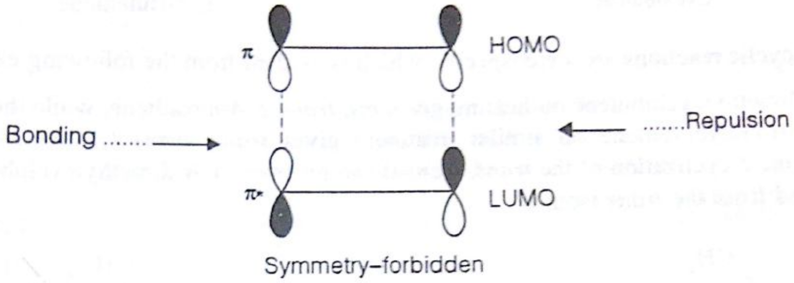
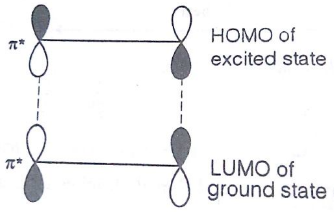


Fig. 7.4 Symmetry-forbidden thermal (2+2) cycloaddition. Interaction is anti bonding.

[2 + 2] cycloadditions are symmetry-forbidden reactions since only one of the two new C-C bonds could be formed, and the bonding energy associated with this, when offset against the loss of π-bonding of two ethylene molecules, serves to make this (two-step) process of such high activation energy that it is effectively impossible.

However, photochemical [2 + 2] cycloadditions are symmetry allowed. The simplest interpretation of this is as follows. When an olefin molecule absorbs a quantum of light, an electron is promoted from the HOMO to the LUMO, so that there are now two singly occupied molecular orbitals (SOMO). The excited HOMO therefore has the symmetry of the ground state LUMO, i.e. π^* and consequently the two can now interact.

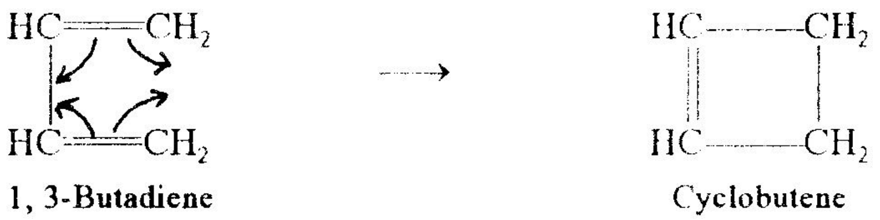


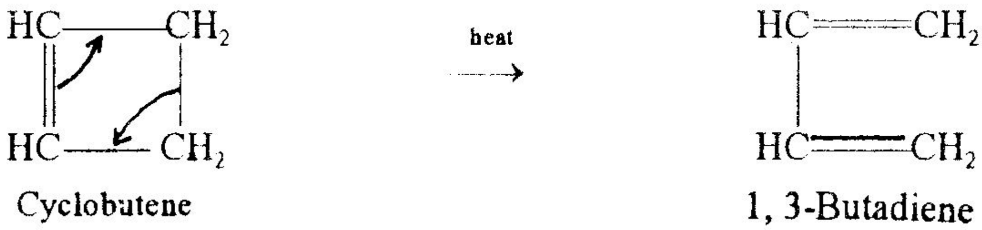
Symmetry-Allowed

Fig. 7.5 Symmetry-allowed photochemical [2 + 2] cycloaddition. Interaction is bonding

7.7 Electrocycllc Reactions

Electrocyclic reactions are those in which either a ring is formed with the generation of a new (σ - bond and the loss of a π-bond or a ring is broken with the opposite consequence, e.g.,





Electrocyclic reactions are stereospecific which is evident from the following examples.

(I) cis-3, 4-Dimethylcyclobutene on heating gives cis, trans-2, 4-hexadiene, while the trans isomer of 3, 4-dimethyl-cyclobutene on similar treatment gives trans, trans-2, 4-hexadiene. Moreover, photochemical cyclization of the trans, trans-diene gives cis-3, 4-dimethylcyclobutene although it was formed from the trans isomer.

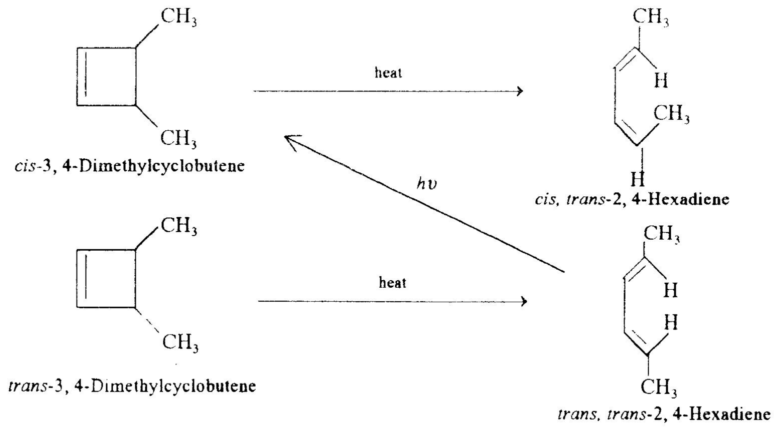


Fig. 7.6 Interconversions of 3, 4-dimethylcyclobutenes and 2, 4-hexadienes.

(ii) The interconversions of the dimetby1cyclobexadienes and 2, 4, 6-octatrienes are also stereo specific as evident from the following reactions.

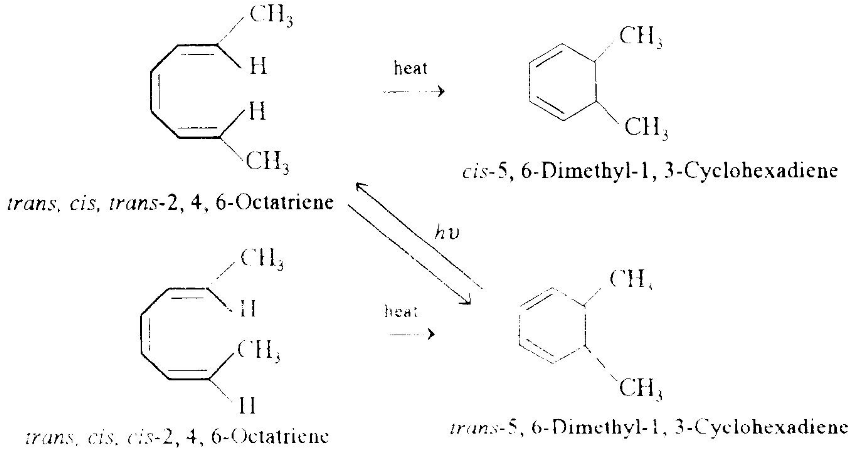


Fig. 7.7 Interconversions of 2,4,6-octatrienes and 5,6-dimethyl-1, 3-cyclohexadienes.

It is important to note that the stereochemistry of the triene-cyclohexadiene interconversions is opposite to that of the diene-cyclobutene interconversions. Thus electrocyclic reactions are completely stereospecific, and the exact stereochemistry depends upon two factors, namely

(a) The number of double bonds in the polyene.

(b) Whether the reaction is thermal or photochemical.

The orbital symmetry approach accounts all the known facts, although they were earlier predicted by Woodward and Hofmann. According to Woodward-Hofmann rule 'the orbital symmetry of the highest energy occupied molecular orbital (HOMO) must be considered, and the rotation occurs to permit overlap of two shaded (or unshaded) lobes of the p-orbitals to form the σ bond.'

7.8 Explanation of Woodward-HoHmann Rule and Orbital Symmetry

It is easier to examine these interconversions in terms of cyclisation rather than ring opening. However, whatever applies to the cyclisation may equally be applied to the reverse process, ring-opening. In cyclisation, two π -electrons ofthe HOMO of the polyene form the new σ bond, Remember that electrons in HOMO are the valence electrons, since they are the least tightly held, and the most easily pushed about during reaction. Now let us study the cyclization of a disubstituted diene as the simplest example to explain the stereospecificity of electrocyclic reactions on the basis of orbital symmetry.

Thermal cyclization of a disubstituted butadiene. As observed earlier, the HOMO of a conjugated diene which is involved in cyclisation is ψ_2.

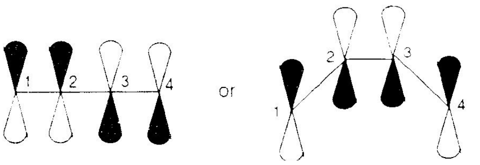


Fig. 7.8 HOMO of ground state (ψ_2) of a conjugated diene.

Bond formation between C_1 and C_4 required for cyclisation can take place only when the lobes of C_1 and C_4 are in overlapping position, i.e. when the shaded (or unshaded) lobe C_1 faces the shaded (or unshaded) lobe of C_4. We see that these lobes can come in overlapping position only when there is rotation about two bonds, C_1-C_2 and C_3-C_4. Rotation about these two bonds can take place in the same direction (conrotatory motion) or in opposite directions (disrotatory motion).

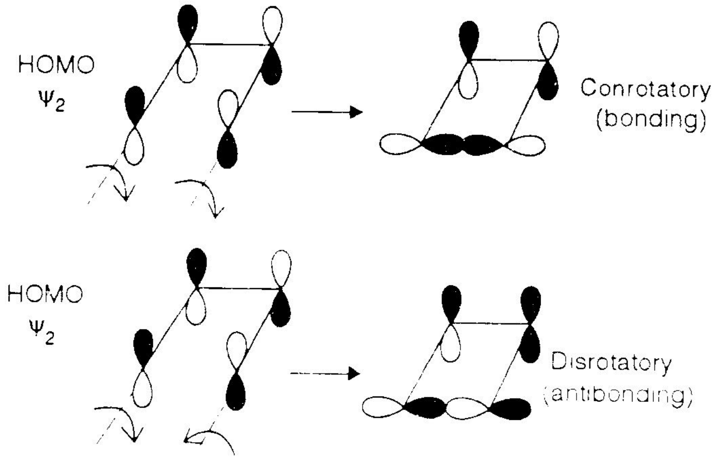


Fig. 7.9 Thermal cyclisation of 1, 3-butadiene to cyclobutene.

However, note that the conrotatory motion brings together lobes of the same phase and hence overlapping occurs and bond is formed. On the contrary, disrotatory motion brings together lobes of opposite phase leading to antibonding interaction. Thus, it is evident that in the photochemical eye/isation of conjugated dienes, conrotatory motion takes place and thus the observed stereochemistry of the product must be that which can be produced by this motion. Now let us observe the stereochemistry produced by the thermal cyclisation of the two isomeric (cis, trans and trans, trans) 2, 4-hexadiene.

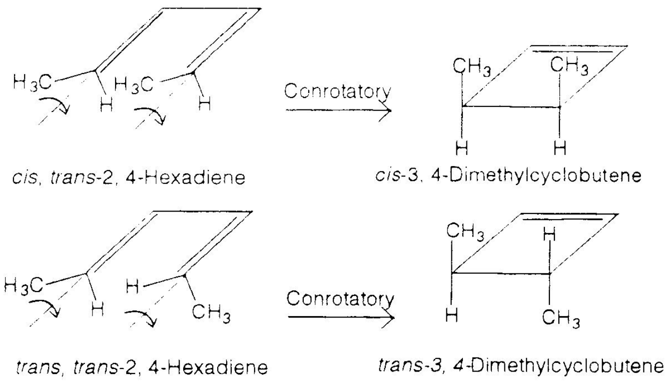
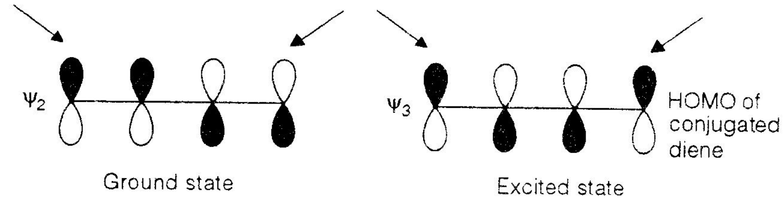


Fig. 7.10 Thermal cyclisation of substituted butadienes.

The above stereochemistry produced by conrotatory motion is in accordance with the observed stereochemistry.

Photochemical cyclisation of butadiene. It is important to note that the photochemical cyclisation of a disubstituted conjugated diene gives stereochemistry opposite to that produced during thermal cyclisation. This can be explained on the basis of the following two facts.

(a) In presence of light, butadiene absorbs light with the result one of the electrons from ψ_2 goes to ψ_3, i.e. here the HOMO is ψ_3 and not ψ_2. In other words, in excited state the HOMO is ψ_3 whose terminal carbons have symmetry opposite to that in ψ_2.



HOMO in ground state (ψ_2)
(C_1 and C_4 have different lobes on the same sides)

HOMO in excited state (ψ_3)
(C_1 and C_4 have similar lobes on the same side)

(b) In ψ_3, butadiene can undergo cyclisation only when disrotatory motion takes place (disrotatory motion brings together lobes of the same phase) and thus the stereochemistry of the product will naturally be opposite to that of thermal cyclisation.

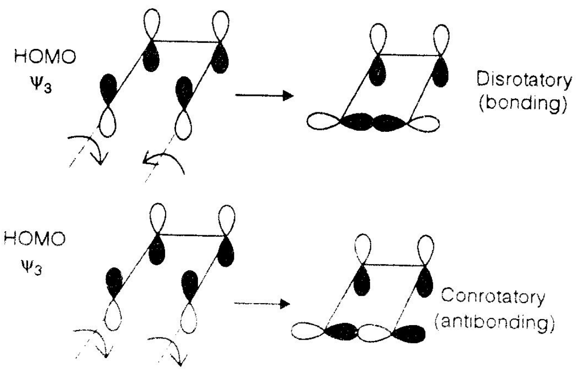


Fig. 7.11 Photochemical cyclization of 1, 3-butadiene.

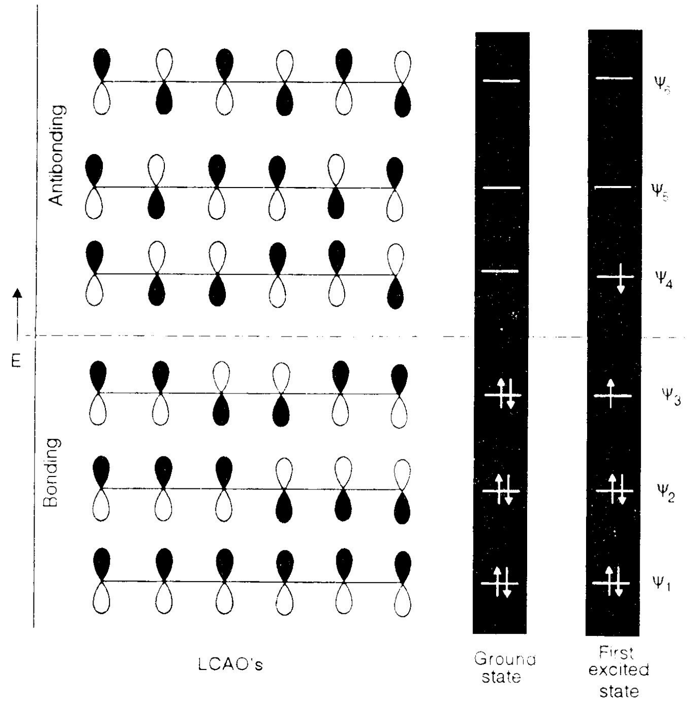
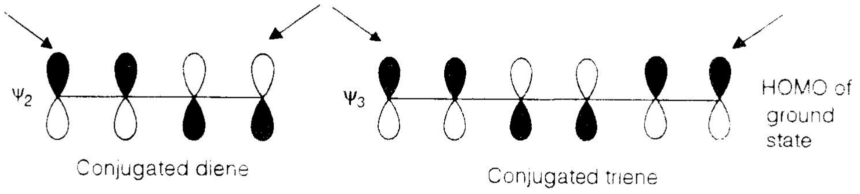


Fig. 7.12 Configuration of n electrons in ground and first excited state of 1, 3, 5-hexatriene.

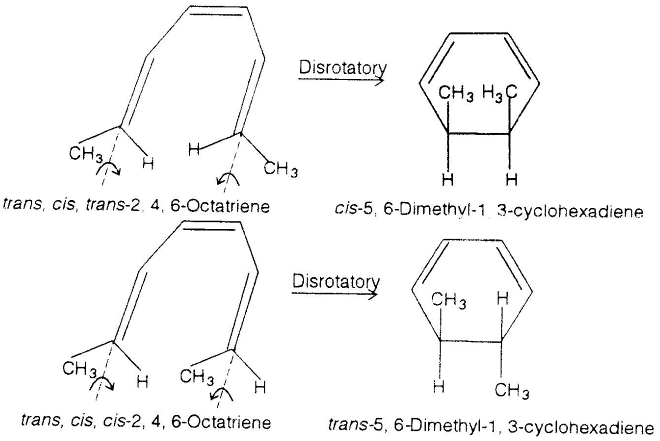
In hexatriene, the HOMO for the ground state is ψ_3 whose terminal lobes are opposite to the terminal lobes of butadiene.



HOMO of conjugated diene (ψ_2)

HOMO of conjugated triene (ψ_3)

Thus when hexatriene undergoes cyclisation in the ground state (thermal cyclisation), It is disrotatory motion that will bring together lobes of the same phase (note the difference from conjugated butadiene where conrotatory motion takes place) and produce the observed stereochemistry. In the excited state of hexatriene, ψ_4 is the HOMO in which conrotatory motion takes place during cyclisation.



trans, cis, trans-2, 4, 6-Octatriene — *cis*-5, 6-Dimethyl-1, 3-cyclohexadiene

trans, cis, cis-2, 4, 6-Octatriene — *trans*-5, 6-Dimethyl-1, 3-cyclohexadiene

In the excited state (as produced in photochemical cyclisation), ψ_4 is the HOMO. Note that the lobes of terminal carbons are opposite in ψ_4 and ψ_3 and hence photochemical cyclisation of a disubstituted hexatriene will involve conrotatory motion and thus gives products having different stereochemistry to that obtained during thermal cyclisation.

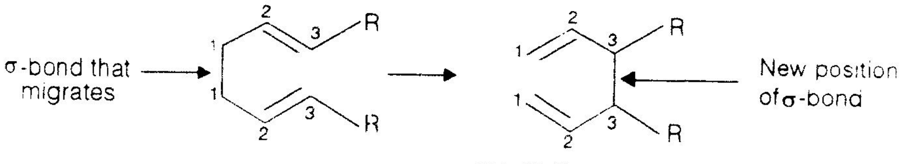
The results of such prediction can be summarised according to whether the number of electrons involved in the cyclic process is 4π or $4\pi + 2$ (where n is any integer including zero).

Woodward-Hoffmann Rules for Electrocyelle Reactions

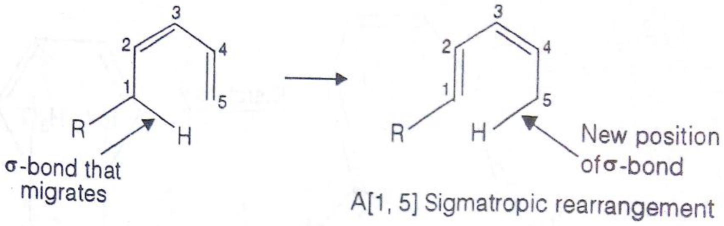
No. fo π-electrons	Reaction	Motion
4n	thermal	conrotatory
4n	photochemical	disrotatory
4n+2	thermal	conrotatory
4n+2	photochemical	disrotatory

7.9 Sigmatropic Rearrangement

A sigmatropic rearrangement is defined as an uncatalysed intramolecular process in which σ bond adjacent to one or more π systems migrates to a new position in the moecue (the overall number of π -and σ-bonds remain separately unchanged). For example,



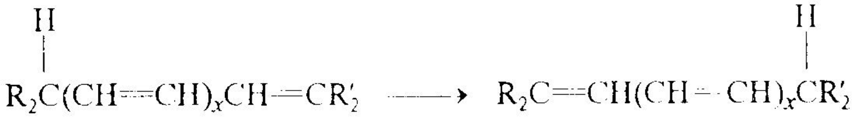
A[1, 3] Sigmatropic rearrangement



A[1, 5] Sigmatropic rearrangement

The order of a sigmatropic rearrangement is expressed by two numbers placed in bracket. These numbers can be determined by counting the atoms over which each end of the a-bond has moved. Sigrnatropic rearrangement may broadly be devided two headings.

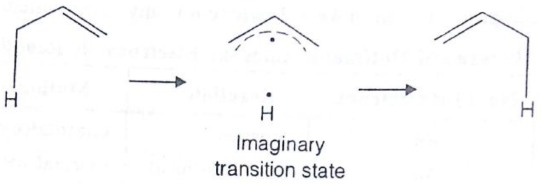
(i) Sigmatropic migrations of hydrogen: Such reactions in acyclic polyenes, can be generalised as below.



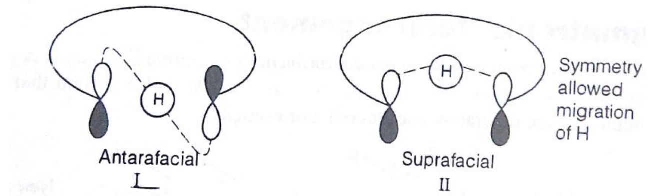
$$\overset{\displaystyle H}{\overset{|}{R_2C}}(CH{=}CH)_xCH{=}CR'_2 \longrightarrow R_2C{=}CH(CH{=}CH)_x\overset{\displaystyle H}{\overset{|}{C}}R'_2$$

Consideration of the feasibility of these shifts as concerted process, i.e. via cyclic transition states, requires as usual a consideration of the symmetry of the orbitals involved. In the transition state, a three-center bond is required, and this must involve overlap between the s orbital of the hydrogen and lobes of p orbitals of the two terminal carbons. Further, the rule governing sigma tropic migration of hydrogen is that the H must move from the shaded (or unshaded) to a shaded (or unshaded) lobe of the HOMO, it cannot move from a shaded (or unshaded) to the unshaded (or shaded) orbital.

A simplest example of this type of reaction is [1,3] sigmatropic rearrangement.

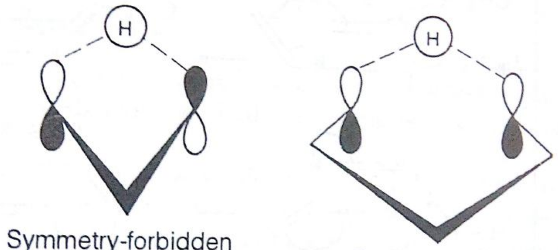


So the transition state involves the overlapping of an allyl radical and a hydrogen atom. Of the three possible molecular orbitals of allyl radical, we are concerned with the HOMO, I. In this state, overlapping between the s orbital of the hydrogen atom and lobes of p orbitals of the two terminal carbons can take place if the migration antarafacial. Consequently, the rule predicts that antarafacial" thermal [1, 3] sigmatropic rearrangements are allowed, but the suprafacial pathway is forbidden. However, in a photochemical reaction, promotion of an electron means the HOMO of allyl radical is represented by II.Now the suprafacial pathway is allowed and the antarafacial pathway is forbidden.



Whether a sigmatropic rearrangement actually takes place or not depends not only on the symmetry requirements but also on the geometry of the system. In particular, [1, 3] and [1, 5] antara migration ho be extremely difficult, since they would require the π framework to be twisted far from the planarity required for de localization of electrons.

Hence practically [1, 3] and [1, 5] sigmatropic reactions seem to be limited to supra migration. A [1, 3] supra migration of hydrogen is symmetry-forbidden since the s orbital of hydrogen would have to overlap p lobes of opposite phases which is not possible. On the other hand, a [1, 5] supra migration of hydrogen is symmetry allowed.



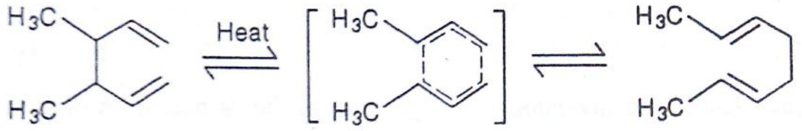
Symmetry-forbidden
[1, 3]

Symmetry–allowed
[1, 5]

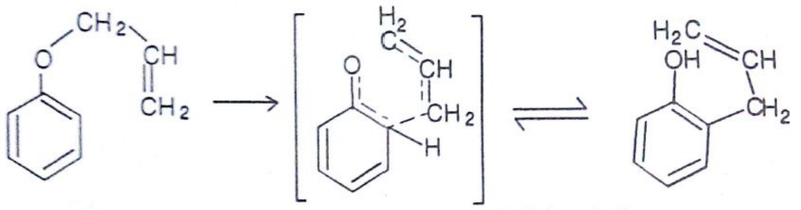
For larger π framework, both types of migrations are geometrically allowed and hence the stereochemistry of these systems depends simply on orbital symmetry. A [l, 7]- H migration should be antara, a [1,9] - H migration supra, and so on. For photochemical reactions, predictions are exactly reversed.

Sigmatropic migrations of carbon:]In migrations of carbon, unlike a hydrogen atom whose electron is in a Is orbital that has only one lobe, a carbon free radical has its odd electron in a p orbital that has two lobes of opposite phase. Thus here a new aspect appears and that is the stereochemistry in the migrating group. In a thermal suprafacial [1,5] migration, configuration is retained within the/migrating group; on the other hand, in a thermal suprafacial [1, 3] migration, configuration in the migrating group is inverted.

However, the most common examples involve a shift from carbon to carbon in the Cope rearrangement of 1, 5-dienes and a shift from oxygen to carbon in the Claisenrearrangement of allyl aryl ethers.



Cope rearrangement of 1, 5-dienes

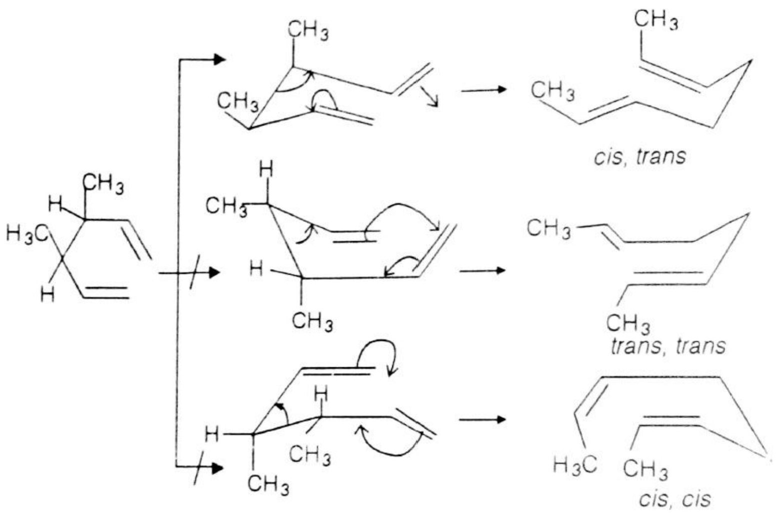


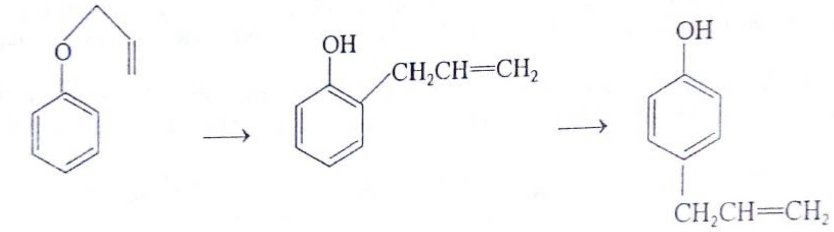
Claisen rearrangement of allyl aryl ethers

Among the thermal reactions, only those that can proceed via six -rnernbered transition states are the most common and proceed readily. Further in acyclic systems, the reaction proceeds through a chair - shaped transition state. For example, meso-3, 4-dimethyl-1, 5-hexadiene rearranges exclusively to cis, trans-E. 6- octadiene, consistent only-with a chair-shaped transition state; a boat-shaped transition state would lead to either the trans, trans- or the cis, cis-product, depending on conformation.

Formation of cis, trans-product corresponds to a shift which is suprafacial at both ends of the migrating system.

Claisen rearrangement is another example ofa [3, 3] sigmatropic rearrangement. The rearrangement of the aryl allyl ether to the o-allylphenol is the first [3,3] sigmatropic rearrangement. It may be followed by a further [3, 3] shift particularly in the absence of a para-substituent, to give p-allylphenol.





7.10 Summary

After reading this unit learner become familiar with pericyclic reaction their stereochemistry, different cycloaddition reactions, electrocyclic reactions with suitable and important examples. woodward halfmann rule and orbital symmetry is also explain clearly and then sigmatropic rearrangement is discussed very clearly and simply with examples.

7.11 Review questions

1. What are pericyclic reactions/
2. Describe HOMO and LUMO.
3. Write different types of pericyclic reactions.
4. Differentiate (4+2) and (2+2) cycloadditions.
5. Explain woodward halfmann rule and orbital symmetry.
6. Explain elecrocyclic reaction with examples.
7. Describe sigmatropic rearrangement and its types with examples.

7.12 References

- Organic Reactions Stereochemistry And Mechanism (Through Solved Problems)- P. S. Kalsi (New Age International Publisher), 2006.
- Reaction and Reagents-O. P. Agrawal (Goel Publishing House, Meerut), 2004.
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Unit - 8

Analysis of Electrocyclic Reactions

Structure of Unit

13.1 Objectives

The objective of this chapter gives an overview of electrocyclic reaction. The chapter explains the main feature of electrocyclic reaction using Frontier Molecular Orbital (FMO) approach, orbital symmetry correlation diagram and Huckel-Mobius theory or Perturbation Molecular Orbital (PMO) theory.

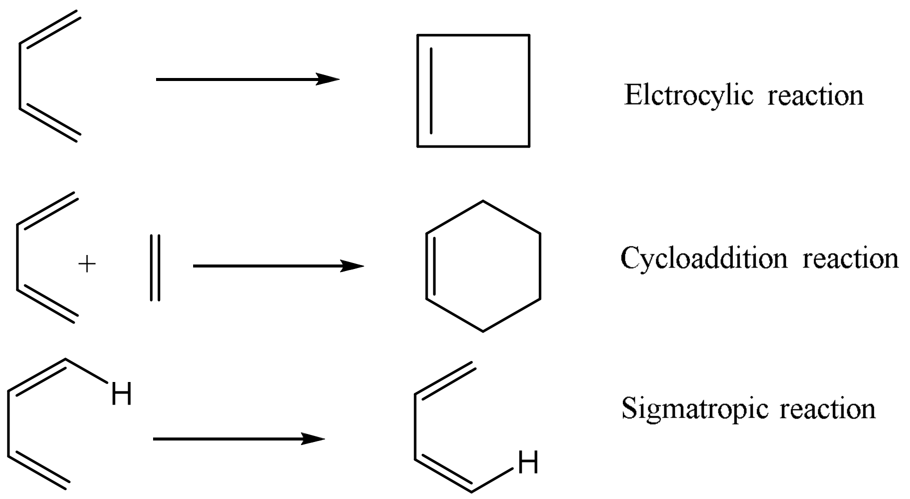
13.2 Introduction

A pericyclic reaction proceeds through concerted mechanism in which bond breaking and bond formation occur (not necessarily synchronous) through the cyclic transition structure with specific orbital alignments without ion or intermediate formation. The concerted pericyclic reactions often have characteristic and predictable stereochemistry. In many cases, the reactions also exhibit regioselectivity that can be directly related to the effect of orbital interactions on the transition state structure. Similarly, substituent effects on reactivity can be interpreted in terms of the effect of the substituents on the interacting orbitals. Pericyclic reactions are classified as

(I) Electrocyclic reactions,

(II) Cycloaddition reactions and

(III) Sigmatropic rearrangements



In this chapter Electrocyclic reactions are discussed in details.

Under the influence of heat or light, a conjugated polyene can undergo isomerisation to form a cyclic compound with a single bond between the terminal carbons of the original conjugated system; one double bond disappears, and the remaining double bonds shift their positions. The reverse process can also take place, i.e., a single bond is broken and a cyclic compound yields an open-chain polyene. These reactions are called electrocyclic reactions.

In thermal condition, the most thermodynamically stable reaction products are preferably formed, but in photochemical process, the less thermodynamically stable product is formed. The thermal and photochemical processes yield product with different stereochemistry. Stereochemistry of electrocyclic reactions is also depends on the number of double bonds in the polyenes. Electrocyclic reactions are completely stereospecific. The reason behind stereospecificity of electrocyclic reaction is that the groups bonded to the breaking bond rotate same or opposite sense during cyclisation process.

13.3 Methods of analysing pericylic reaction

There are following methods are using to analysis of pericyclic reactions,

(1) The frontier molecular orbital (FMO)

(2) Orbital symmetry correlation diagrams

(3) Huckel-Mobius theory or Perturbation Molecular Orbital (PMO)

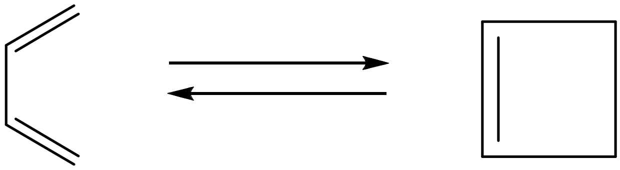
13.3.1Frontier Molecular Orbital (FMO) approach:

The mechanism of electrocyclic reactions can be understood in terms of frontier molecular orbital (FMO) theory and the outcome of reactions can be predicted using the Woodward-Hoffman rules. The pathway of such reactions is determined by the symmetry properties of the orbitals that are directly involved. The orbital symmetry must be same during overall mechanism.

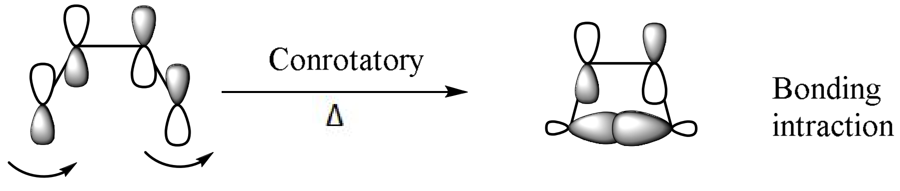
In electrocyclic reactions, only one reactant is involved and thus only the highest occupied molecular orbital (HOMO) needs to be considered. Thus, the stereochemistry of the reactions is controlled by the symmetry properties of the HOMO of the reacting system. These reactions take place thermally or photochemically. In thermal condition, the ground state HOMO is involved in the reaction, but in photochemical condition, the excited state HOMO involved.

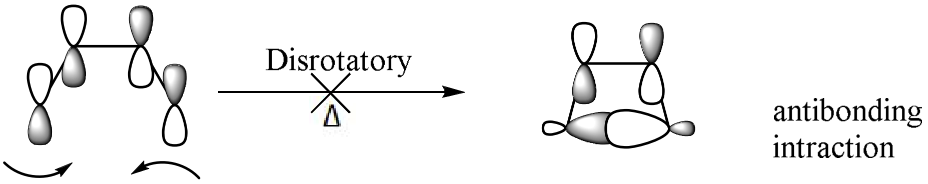
The orbitals of terminal atoms of HOMO rotate through 90^0 to allow of their potential overlap. The rotation occurs in the same direction, i.e., clockwise or counterclockwise is called conrotatory process. But rotation occurs in the opposite direction is called disrotatory process. The rotation of terminal orbital depends on the type of polyene, i.e., number of double bond and condition of reaction. It is illustrated by following system.

In 4n π-system for example interconversion of 1,3-butadiene and cyclobutene,

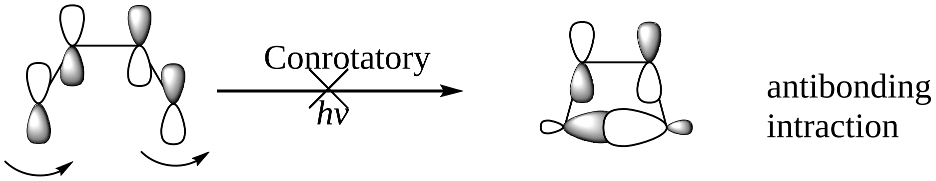


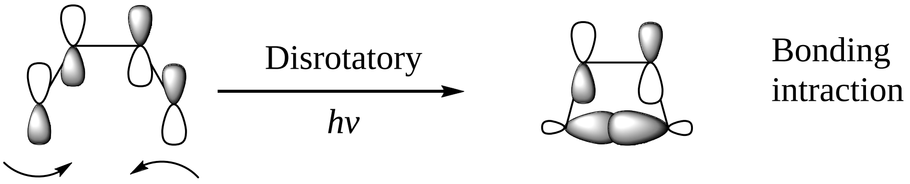
In thermal condition ground state HOMO has terminal orbital with opposite phase, conrotatory motion lead to a bonding interaction and thus to the formation of cyclobutene while disrotatory movement results in an antibonding situation. In thermal electrocyclic reaction of a 4n π-system, therefore, only conrotatory motion is allowed.



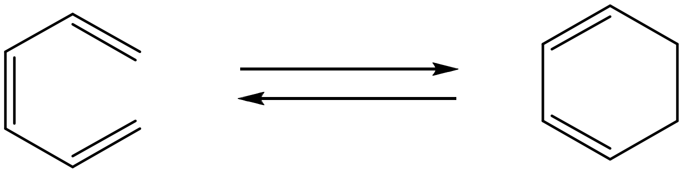


In the case of photochemical condition, irradiation of diene will result in the promotion of an electron into the orbital next higher energy level and ground state LUMO becomes the excited state HOMO which has terminal orbital with the same phase. There is conrotatory motion leading to an antibonding situation, while disrotatory motion results in a bonding interaction and the formation of cyclobutane.

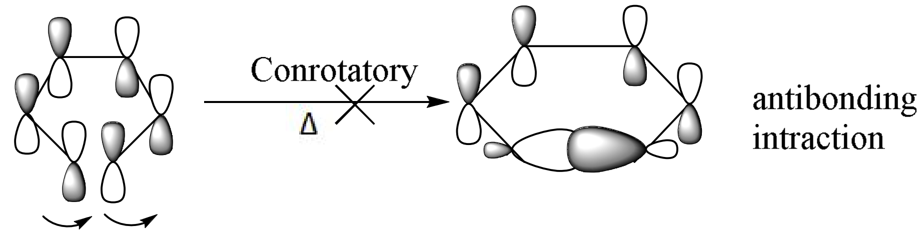


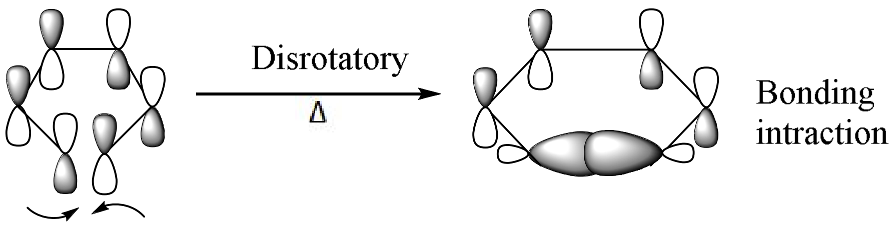


In 4n+2 π-system for example interconversion of 1,3,5-hexatriene and cyclohexadiene,

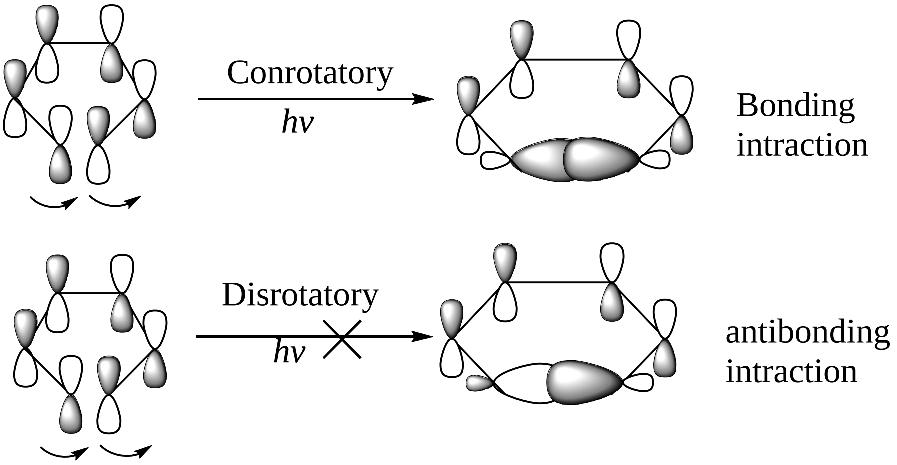


In this system, under thermal condition, conrotatory motion results in overlap of opposite phase led to an antibonding saturation while disrotatory movement results a bonding interaction due overlapping of the same phase. Hence, in thermal condition, disrotatory motion is allowed and the stereochemistry follows accordingly.





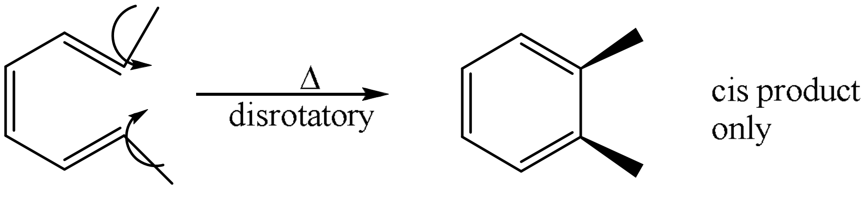
In photochemical condition, irradiation results in the excitation of electron of ground state HOMO in the next higher energy state and then LUMO become the excited HOMO which having the same phase at terminal orbital. The conrotatory motion results in overlapping of the same phase and leading to a bonding interaction, however, disrotatory motion results in antibonding interaction. In photochemical condition, therefore, conrotatory motion is allowed for 4n+2 π-systems.



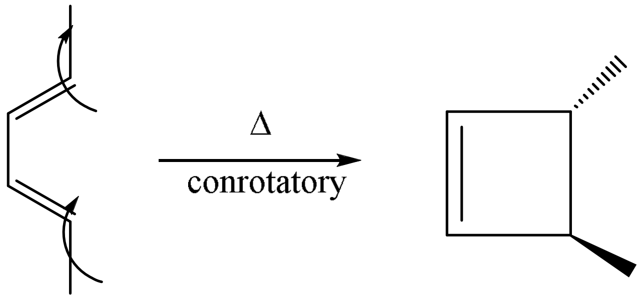
Thus, same phase of terminal orbital goes through disrotatory motion and opposite phase goes through conrotatory motion in bond formation/bond breaking. On the basis of these conclusions, Woodward and Hoffman proposed a rule for electrocyclic reaction is known as Woodward-Hoffman rules.

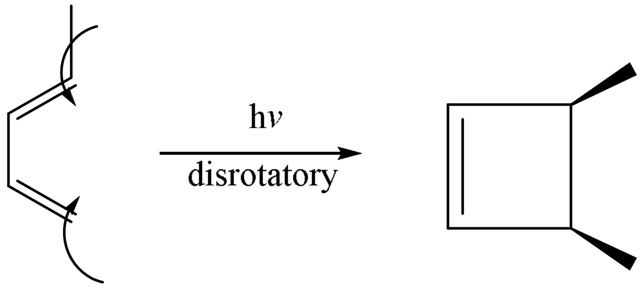
System	Reaction condition	
	Δ	hν
4n	conrotatory	disrotatory
4n+2	disrotatory	conrotatory

Electrocyclic reactions are completely stereospecific. For example ring closure of (2E,4Z,6E)-2,4,6-octatriene yields a single product with *cis* methyl groups on the ring.



Moreover, the stereochemistry of the product of an electrocyclic reaction also depends on reaction condition, i.e., thermal or photochemical reaction conditions. For example Cyclization of (2E,4E)-2,4-hexadiene with heat forms a cyclobutene with *trans* methyl groups, whereas cyclization with light forms a cyclobutene with *cis* methyl groups.

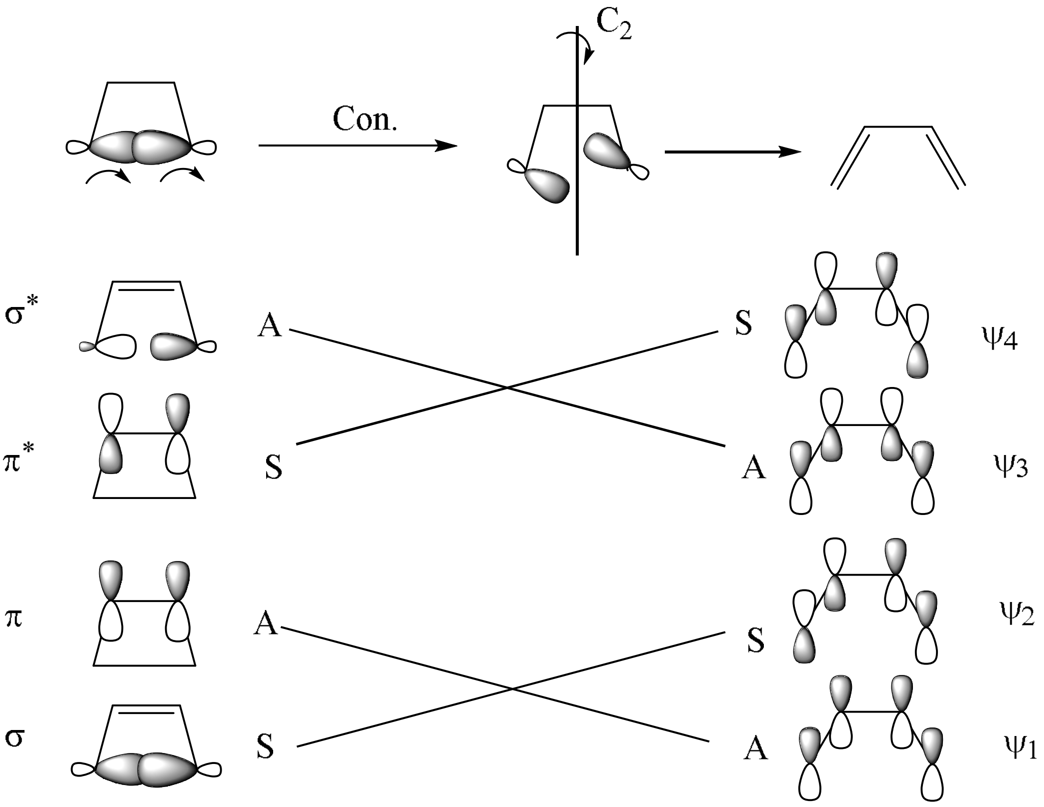




13.3.2 Orbital symmetry correlation diagrams

The analysis of electrocyclic reactions can also be done by orbital correlation diagrams. This approach focuses attention on the orbital symmetries of both reactants and products and considers the symmetry properties of all the orbitals. In any concerted process, the orbitals of the starting material must be smoothly transformed into orbitals of product through a transition state having the same symmetry. Thus, the symmetry must be conserved throughout the reaction. The orbital symmetry rules can be generalized from conjugated polyenes to any type of the conjugated system. In case of the conrotatory process, the element of symmetry that maintained throughout the reaction is the twofold rotation axis. However, in disrotatory motion, the plane of symmetry is maintained throughout the reaction.

In case of 4n π-system e.g. the cyclobutene-butadiene interconversion, the four π-orbitals of butadiene are converted into the two π- and two σ-orbitals of the ground state of cyclobutene. The π-orbitals of butadiene are designated as ψ_1, ψ_2, ψ_3, and ψ_4 and for cyclobutene, the four orbitals are π, σ, π^*, and σ^*. If the reaction takes place through conrotatory motion, then C_2 axis of symmetry is maintained throughout the reaction. The molecular orbitals must be either symmetric (S) or antisymmetric (A). Same symmetry orbitals must correlate to each other.

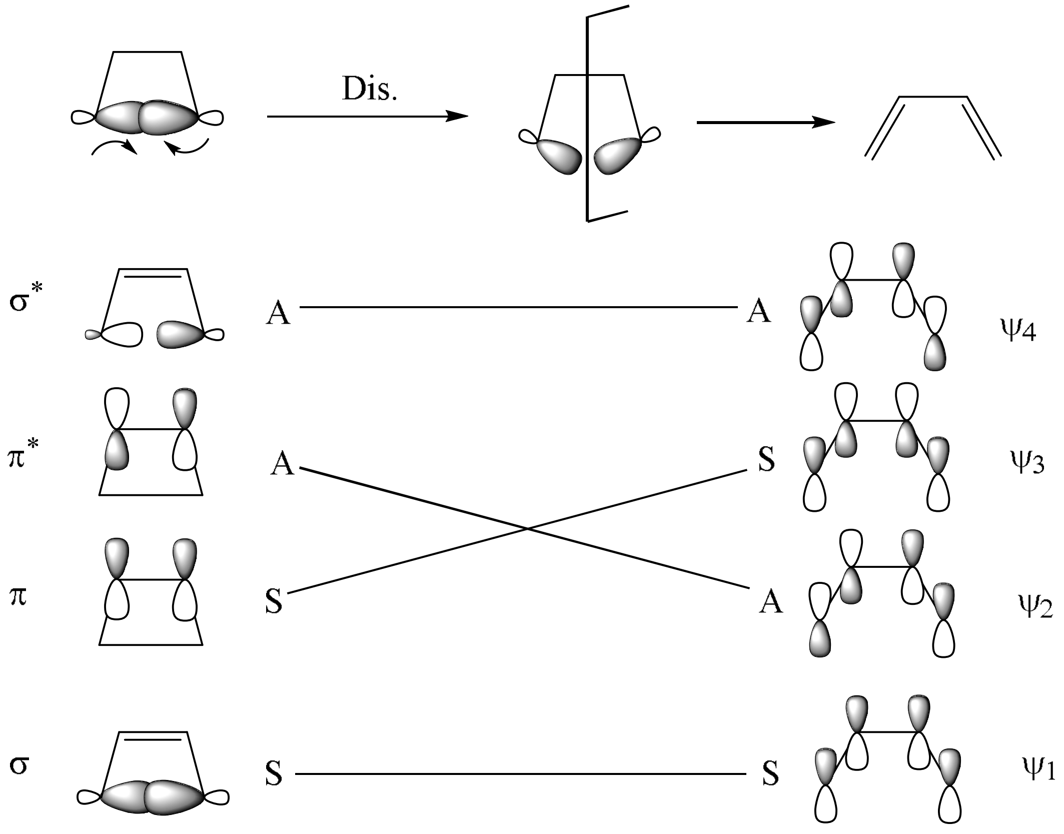


Ground state $\sigma^2\pi^2 \xrightarrow[\Delta]{\text{Con.}} \psi_1^2\psi_2^2$

Exicted state $\sigma^2\pi^1\pi*^1 \cancel{\xrightarrow[h\nu]{\text{Con.}}} \psi_1^2\psi_2^1\psi_4^1$

According to the correlation diagram of 4n π-system, when a reaction occurs through conrotatory motion, the correlation $\sigma^2\pi^2 \rightarrow \psi_1^2\psi_2^2$ is allowed under thermal conditions while correlation $\sigma^2\pi^1\pi*^1 \rightarrow \psi_1^2\psi_2^1\psi_4^1$ is forbidden under photochemical condition. In 4n π-system, therefore, conrotatory motion occurs under thermal condition.

If the reaction takes place through disrotatory motion, then the plane of symmetry is maintained throughout the reaction. The correlation diagram for conversion of cylcobutene to butadiene is illustrated as

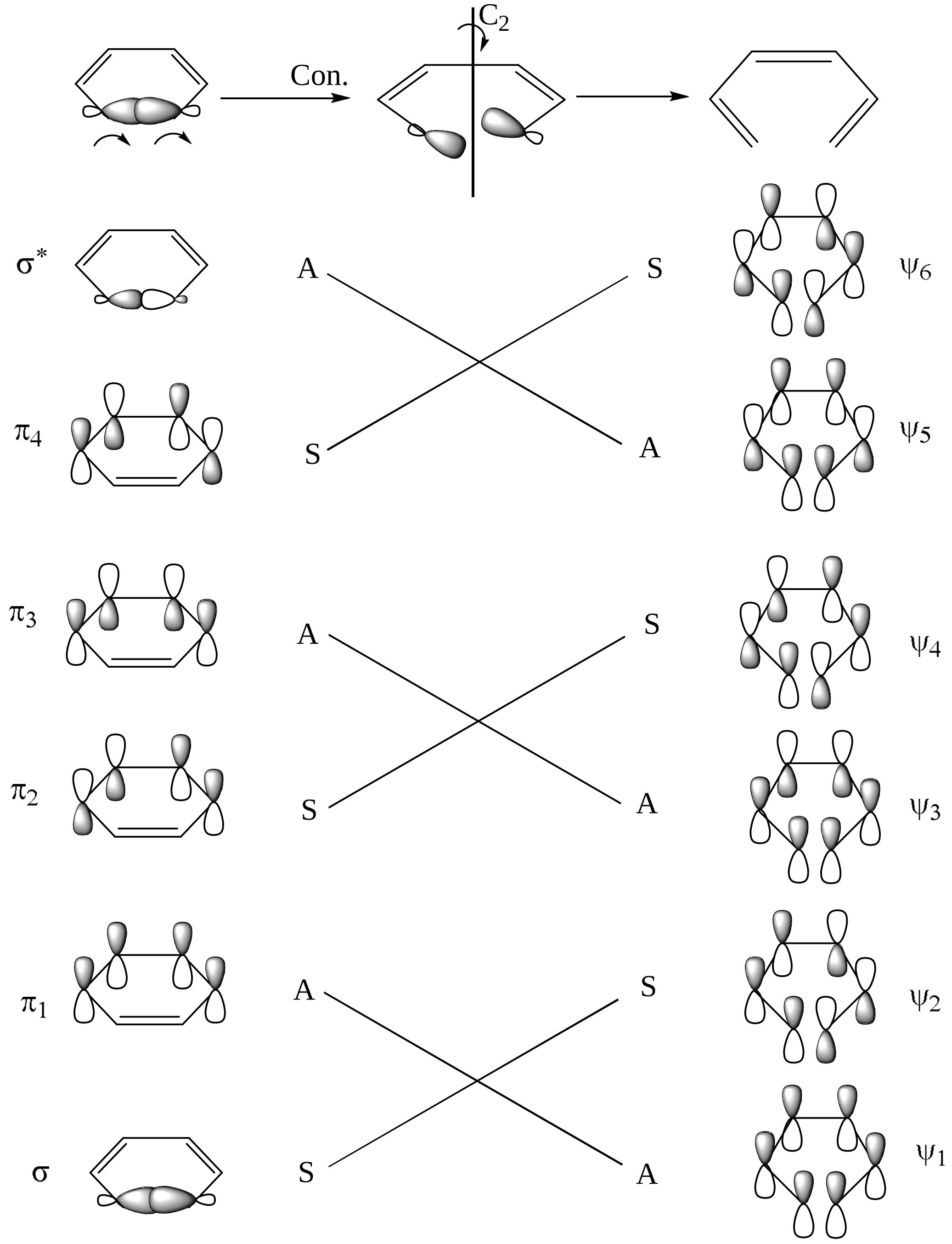


$$\text{Ground state} \quad \sigma^2\pi^2 \xrightarrow[\Delta]{\text{Dis.}} \!\!\!\!\times\;\; \psi_1{}^2\psi_3{}^2$$

$$\text{Excited state} \quad \sigma^2\pi^1\pi{*}^1 \xrightarrow[h\nu]{\text{Dis}} \psi_1{}^2\psi_2{}^1\psi_3{}^1$$

According to the correlation diagram of 4n π-system, when a reaction occurs through disrotatory motion, the correlation $\sigma^2\pi^2 \rightarrow \psi_1{}^2\psi_3{}^2$ is forbidden under thermal conditions while correlation $\sigma^2\pi^1\pi{*}^1 \rightarrow \psi_1{}^2\psi_2{}^1\psi_3{}^1$ is allowed under photochemical condition. In 4n π-system, therefore, disrotatory motion occurs under photochemical condition.

Similarly, the correlation diagrams can be constructed in analogous manner for the conrotatory and disrotatory modes for 4n+2 π-system e.g. interconversion of 1,3,5-hexatriene and cyclohexadiene. In Ring opening reaction, the four π- and two σ-orbitals of the ground state of cyclohexadiene are converted into the six π-orbitals of 1,3,5-hexatriene. The π-orbitals of 1,3,5-hexatriene are ψ_1, ψ_2, ψ_3, ψ_4, ψ_5 and ψ_6 and for cyclohexadiene, the six orbitals are π_1, π_2 π_3, π_4, σ, and σ^*. If the reaction takes place through conrotatory motion, then the plane of symmetry is maintained throughout the reaction. The correlation diagram is described as

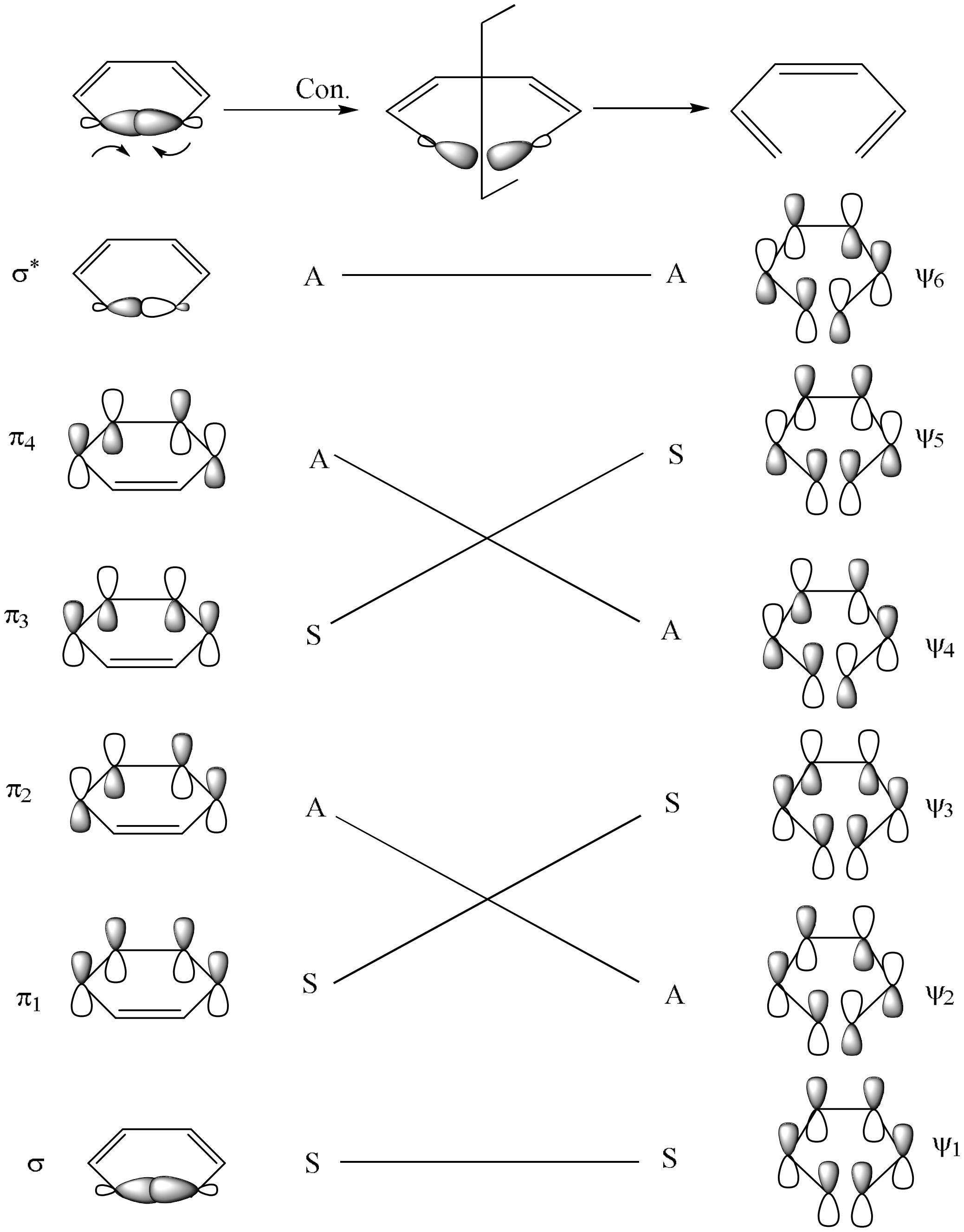


Ground state $\quad \sigma^2\pi_2^2\pi_3^2 \quad \not\xrightarrow[\Delta]{\text{Con.}} \quad \psi_1^2\psi_2^2\psi_4^2$

Exicted state $\quad \sigma^2\pi_2^2\pi_3^1\pi_4^1 \quad \xrightarrow[h\nu]{\text{Con.}} \quad \psi_1^2\psi_2^2\psi_3^1\psi_4^1$

According to the correlation diagram of 4n+2 π-system, when a reaction occurs through conrotatory motion, the correlation $\sigma^2\pi_1^2\pi_2^2 \rightarrow \psi_1^2\psi_2^2\,\psi_4^2$ is forbidden under thermal conditions while correlation $\sigma^2\pi_1^2\pi_2^1\pi_3^1 \rightarrow \psi_1^2\psi_2^1\psi_3^1\psi_4^1$ is allowed under photochemical condition. In 4n π-system, therefore, conrotatory motion occurs under photochemical condition.

If the reaction takes place through disrotatory motion, then the plane of symmetry is maintained throughout the reaction and the correlation diagram for this system is described as



Ground state $\sigma^2\pi_2^2\pi_3^2 \xrightarrow[\Delta]{\text{Dis.}} \psi_1^2\psi_2^2\psi_3^2$

Exicted state $\sigma^2\pi_2^2\pi_3^1\pi_4^1 \cancel{\xrightarrow[h\nu]{\text{Dis.}}} \psi_1^2\psi_2^2\psi_3^1\psi_5^1$

According to the correlation diagram, when a reaction occurs through disrotatory motion, the correlation $\sigma^2\pi_1^2\pi_2^2 \rightarrow \psi_1^2\psi_2^2\psi_3^2$ is allowed under thermal conditions while correlation $\sigma^2\pi_1^2\pi_2^1\pi_3^1 \rightarrow \psi_1^2\psi_2^1\psi_3^1\psi_5^1$ is forbidden under photochemical condition. In 4n π-system, therefore, disrotatory motion occurs under Thermal condition.

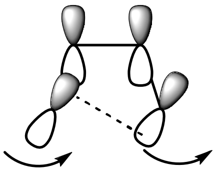
13.3.3 Huckel-Mobius theory or Perturbation Molecular Orbital (PMO) theory

Electrocyclic reactions can also be analyzed by Huckel-Mobius theory. This theory was pointed out initially by M.G. Evans in 1939, and subsequently (and independently) by H.E. Zimmerman and M.J.S. Dewar in 1966.

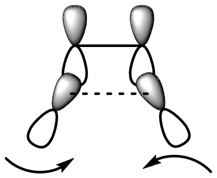
The Mobius–Huckel method provides an alternative approach to the Woodward–Hoffmann one. The basic difference in both approaches is that Mobius–Huckel method is not dependent on symmetry and only requires counting the number of plus-minus sign inversions, i.e. number of nodes in cyclic array of orbitals in transition state. The systems with zero or an even number of sign inversion are called Huckel system. While, systems with an odd number of sign inversions are called Mobius systems.

The transition states can be classified as aromatic or antiaromatic for ground state molecules. A Huckel system is aromatic when it has 4n+2 π-electrons. A Mobius system is aromatic when it has 4n π-electrons. A stabilized aromatic transitions state results in low activation energy, i.e., an allowed reaction. An antiaromatic TS has a high energy barrier and corresponds to a forbidden process.

For the 4n system, e.g., cyclobutene-butadiene transition state, the conrotatory closure results in a Mobius system, whereas a disrotatory transition state gives a Hückel system.



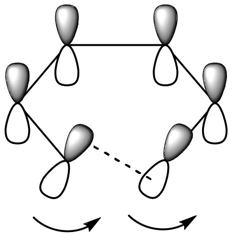
conrotatory motion,
4 π–electrons, one node
i.e. aromatic



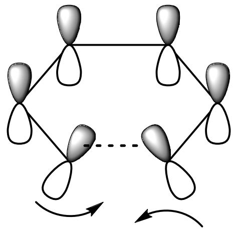
disrotatory motion,
4 π–electrons, zero node
i.e. antiaromatic

In the case of the cyclobutene-butadiene interconversion, which involves four electrons, it is the conrotatory Mobius transition state that is the favored aromatic transition state.

Similarly, the hexatriene-cyclohexadiene system leads to the conclusion that the disrotatory process will be favored because disrotatory mode gives a stabilized aromatic transition state (Huckel system).



conrotatory motion,
(4+2)π−electrons, one node
i.e. antiaromatic



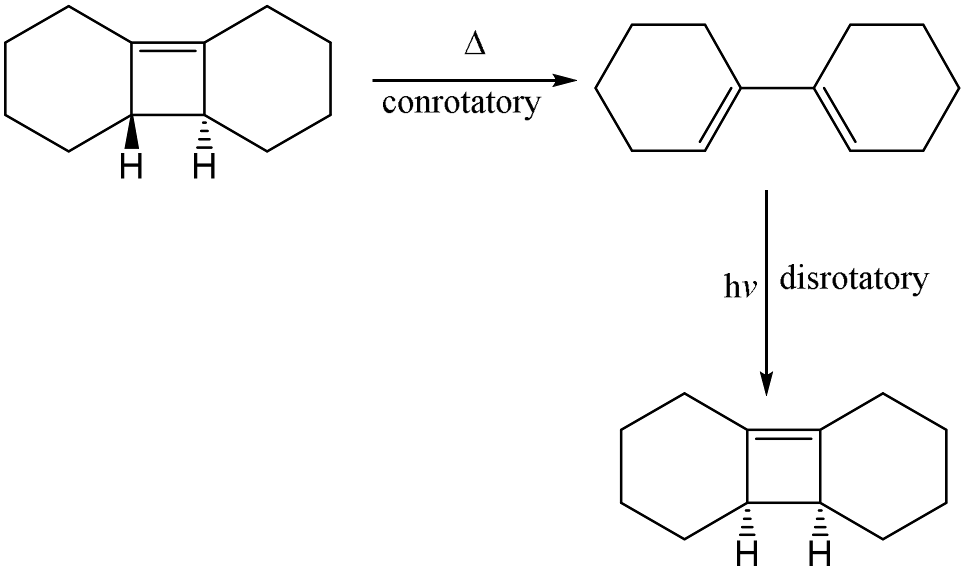
disrotatory motion,
(4+2)π−electrons, zero node
i.e. aromatic

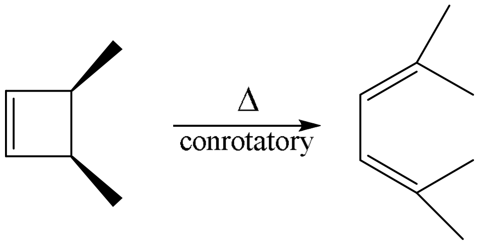
An electrocyclic reaction is thermally allowed involving a Huckel system only if the total number of electron is 4n+2. An electrocyclic reaction is thermally allowed involving a Mobius system only if total number of electron is 4n. For photochemical reactions, these rules are reversed. The conclusions of this theory are summarized in bellow table.

System	Number of sign inversion i.e. node	Aromaticity	Reaction condition	
			thermal	photochemical
4n	Zero/even	Huckel system, antiaromatic	--	Disrotatory
4n	Odd	Mobius system, aromatic	Conrotatory	--
4n+2	Zero/even	Huckel system, aromatic	Disrotatory	--
4n+2	Odd	Mobius system, antiaromatic	--	Conrotatory

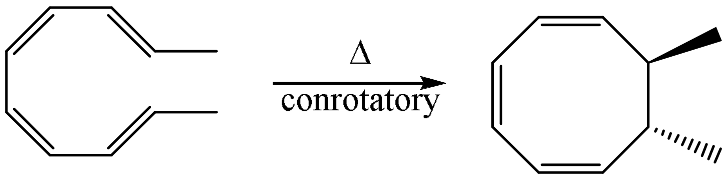
13.4 Example of electrocyclic reaction

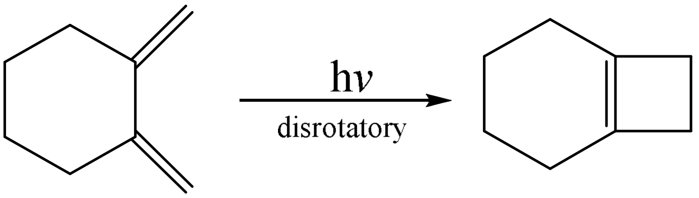
4n systems: The basic example of 4n system is interconvertion of dienes and cylcobutenes through electrocyclic reaction. However, the cylcobutenes are thermodynamically less stable than dienes and so that ring closure cannot occur due reversibility of the reaction. But, ring closure can be occurred in photochemical condition, for example

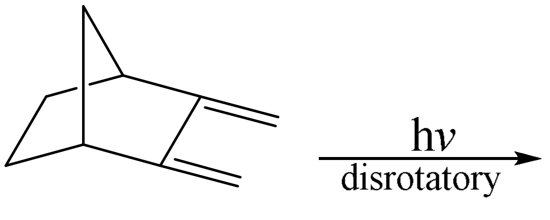


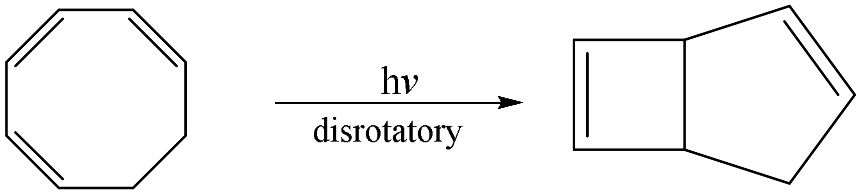


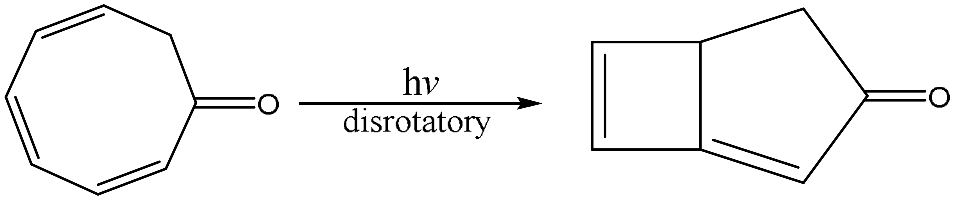
In addition to the butadiene-cyclobutene interconversion, there are many other examples of electrocyclic reaction are given in this section.

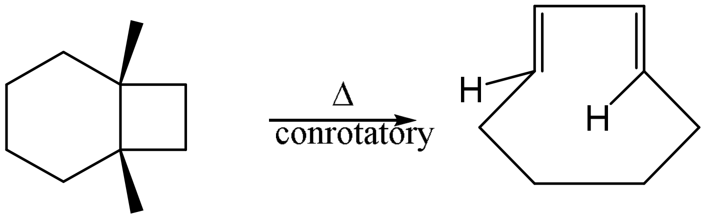






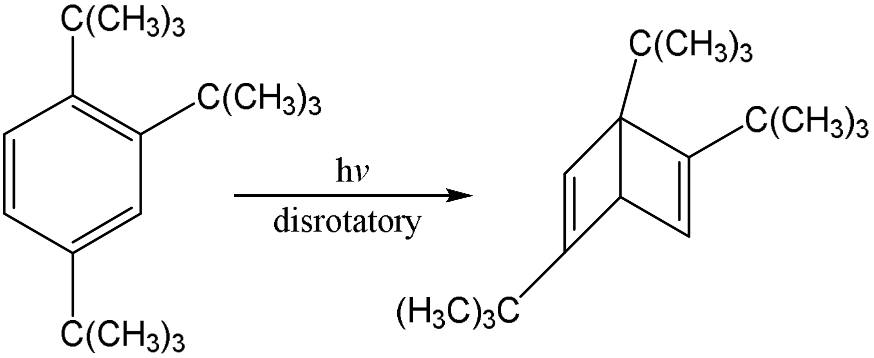


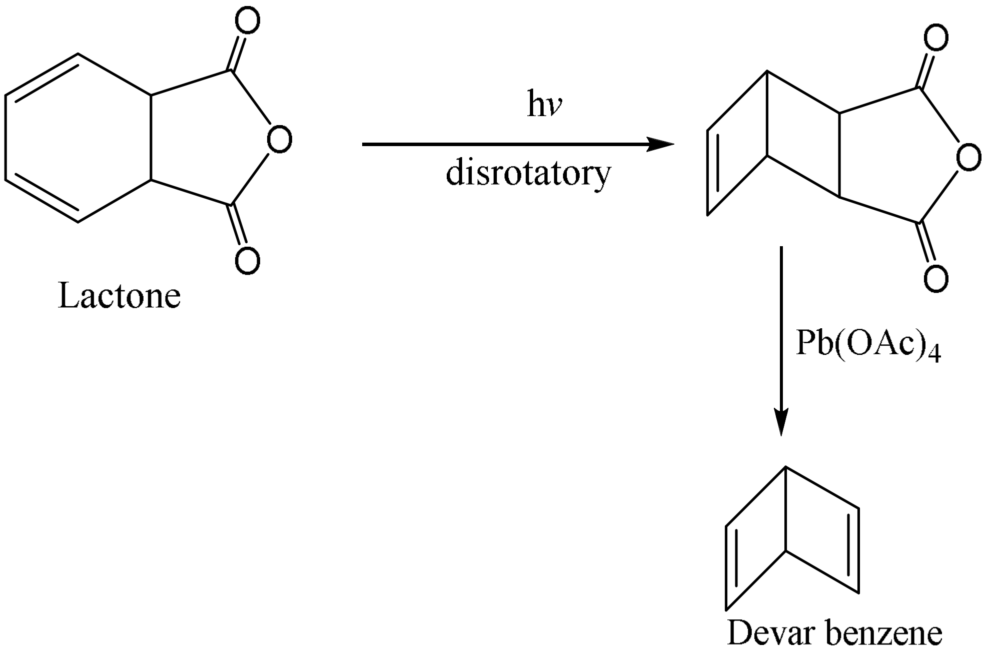




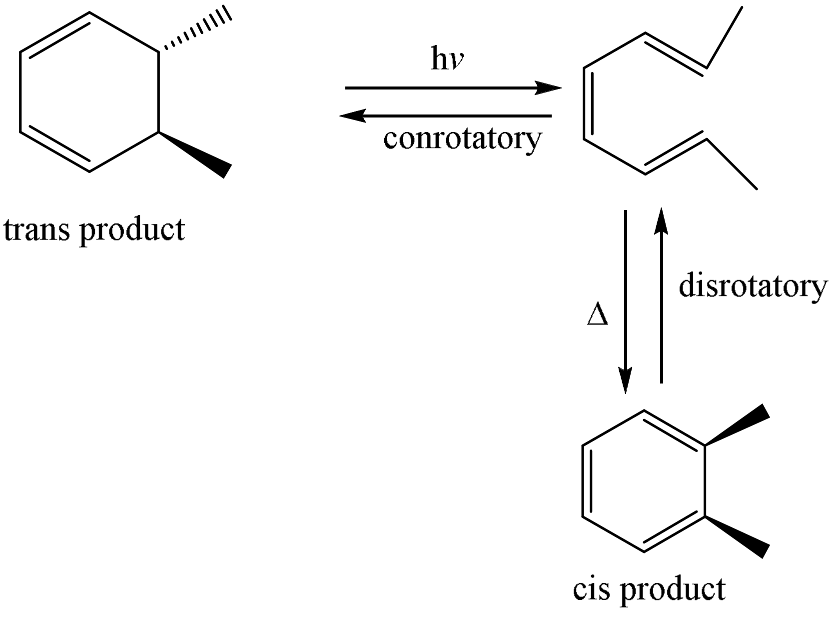
cis-bicylco [4,2,0] octa-7-ene   cis, trans cyclo octa-1,3-diene

Dewar benzene can be obtained by electrocyclic reaction, for example

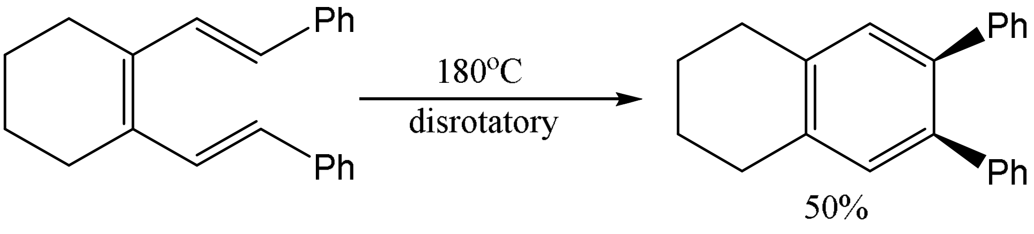


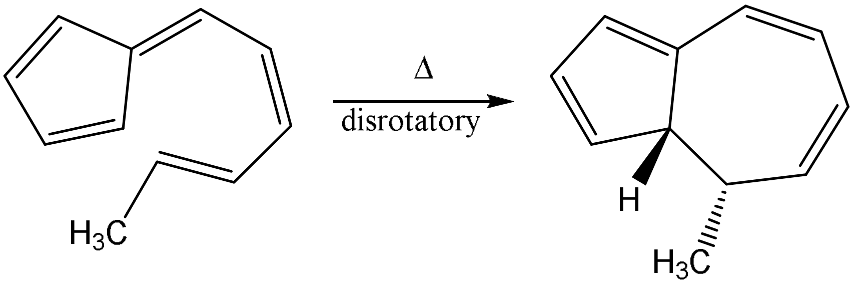


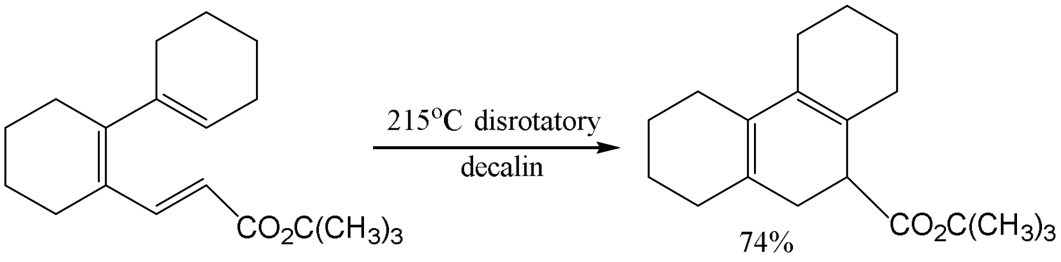
4n+2 systems: The interconversion of hexatrienes-cycloheaxadienes occurs thermally disrotatory and photochemically conrotatory. For example,

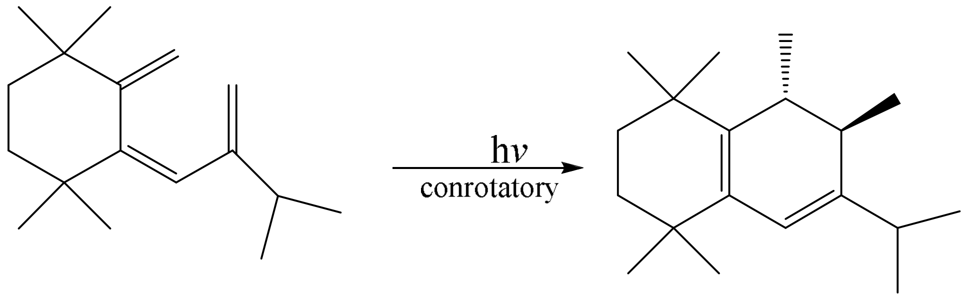


In addition to the hexatrienes-cycloheaxadienes interconversion, there are many other examples of electrocyclic reaction are given as

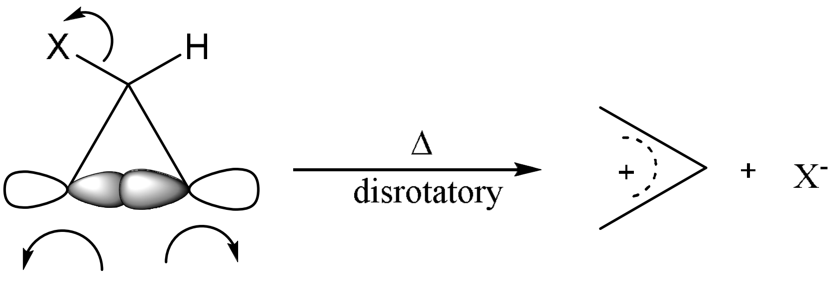




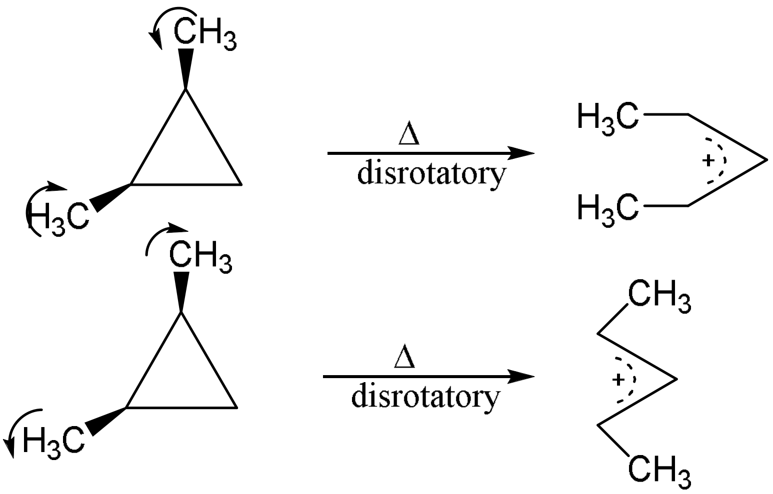




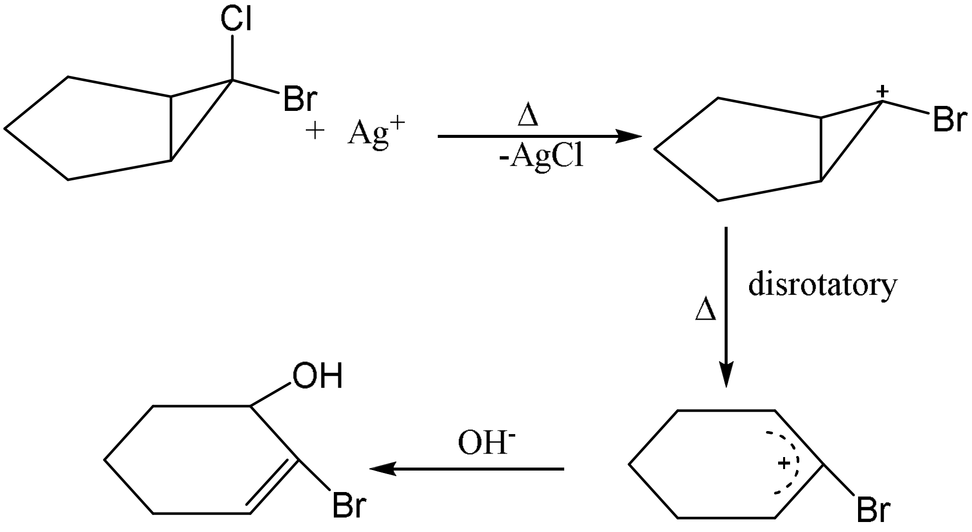
Allyl systems: Conjugated unbranched ions and radicals have an odd number of carbon atoms. For example, the allyl system (cation, anion or radical) has three carbons and three *p* orbitals, hence, three molecular orbitals. The conversion of a cyclopropyl cation to an allyl cation is the simplest possible case of an electrocyclic process because it involves only two π-electrons. The selection rules also apply to concentrated reaction of this species. In thermal condition the allyl cation follows similar Woodward-Hoffman rules according to 4n+2 π-systems (where n equals zero), i.e., in thermal condition, reaction occurs through disrotatory motion. While a cyclopropyl anion (4π-electron systems) gives rise to an allyilc anion through a thermal conrotatory mode. For example, the opening of cyclic propyl halide occurs to produce the allyl cation through disrotatory motion.



There are two possible directions for the allowed disrotation in substituted cyclopropyl cation. For example, a cis-2,3-dimethylcyclopropyl cation under goes two different disrotatory modes and leading to structurally distinct allyl cations



For example,



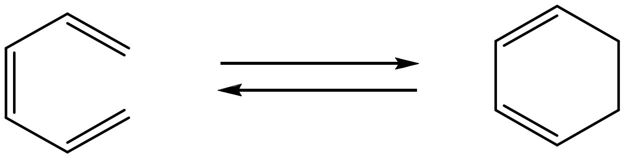
13.5 Summery

- A pericyclic reaction proceeds through concerted mechanism
- Pericyclic reactions are classified as electrocyclic reactions, cycloaddition reactions, and sigmatropic rearrangements.
- Electrocyclic reactions are ring closing and ring opening reaction
- Cyclic transition state involving either 4n electrons or 4n+2 electrons

- The thermal and photochemical processes yield product with different stereochemistry.
- The electrocyclic reaction can be analyzed using Frontier Molecular Orbital (FMO) approach Orbital correlation diagram and Huckel-Mobius theory or Perturbation Molecular Orbital (PMO) theory.
- Same phase of terminal orbital goes through disrotatory motion and opposite phase goes through conrotatory motion in bond formation/bond breaking.
- In thermal condition, disrotatory motion is allowed, while, in photochemical condition, conrotatory motion is allowed for 4n+2 π-systems.
- In thermal electrocyclic reaction of a 4n π-system, only conrotatory motion is allowed while, in photochemical condition, conrotatory motion is allowed.
- The systems with zero or an even number of sign inversion are called Huckel system. While, systems with an odd number of sign inversions are called Mobius systems.
- Thermal electrocyclic reaction occurs via aromatic transition state while photochemical reactions occur via antiaromatic transition state.

13.6 ReviewQuestions

1. What is electrocyclic reaction?
2. Write Huckel-Mobius transition state and correlation symmetry diagram for following reaction under both thermal and photochemical condition



3 Explain the following concept

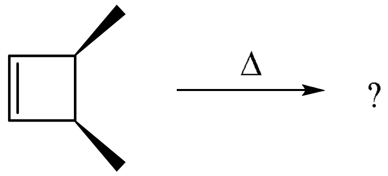
(a) Huckel-Mobius system

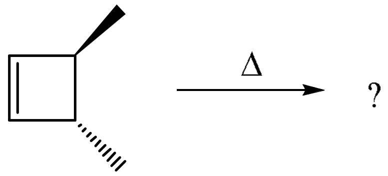
(b) FMO approach

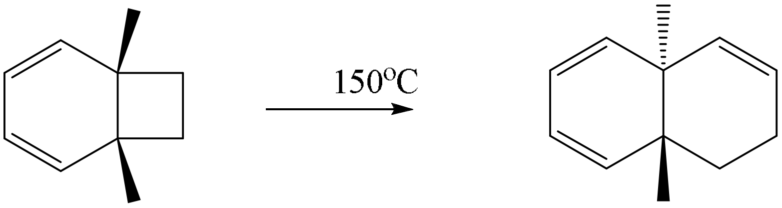
4 Why electrocyclic reaction of a 4n π-system only conrotatory motion is allowed?

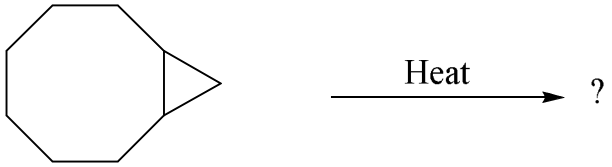
5 Explain stereochemistry of dimethyl substituted cyclohexadiene under conrotatory movement?

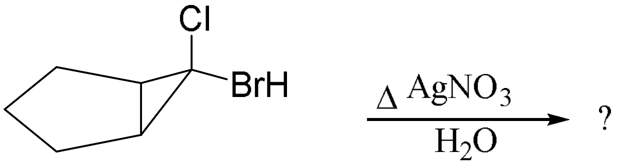
6 complete the reaction

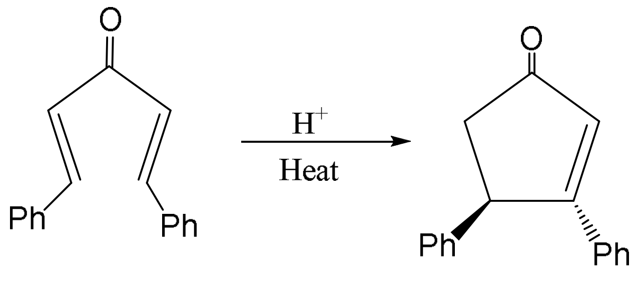




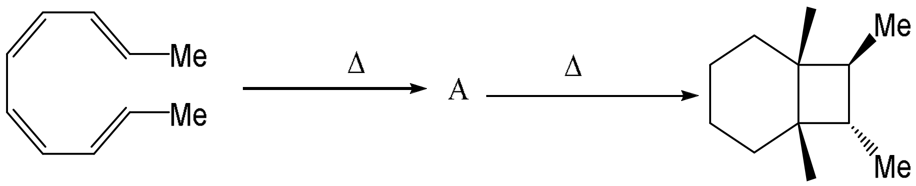


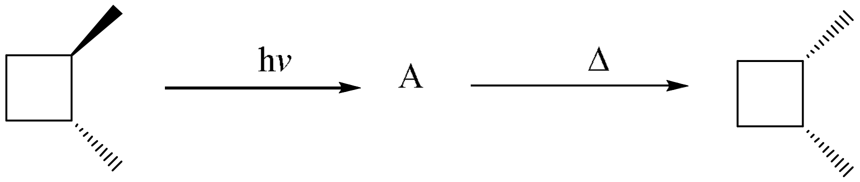


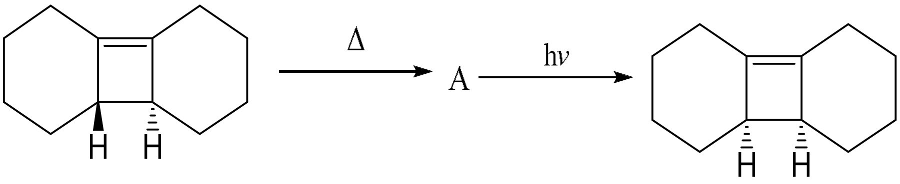




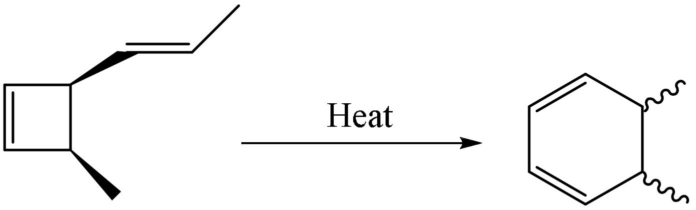
7 What is product A in following reactions and predict the conrotatory or disrotatory motion?

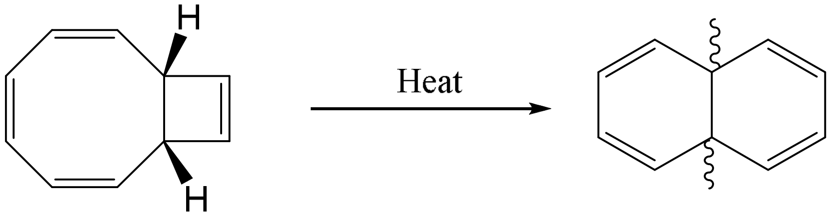






8 Predict the stereochemistry of the products of these reactions





13.7 Reference and Suggested readings

- Advanced Organic Chemistry, Part A: Structure and Mechanisms, Springer Science publication, F. Carey and R. Sundberg, 5th edition 2007
- Organic Chemistry, J. Clayden, N. Geeves, S. Warren, Oxford Publication, 2000
- Pericyclic Reactions, Ian Flaming, Oxford Science Publication, 1998
- Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, J. March, John Wiley & Sons publication, 1992.

Unit - 9

Analysis of cycloaddition: Cycloaddition, antarafacial, suprofacial additions, 4n and 4n+2 systems. 2+2 addition of Ketenes, 1,3-dipolar cycloadditions & cheletropic reactions

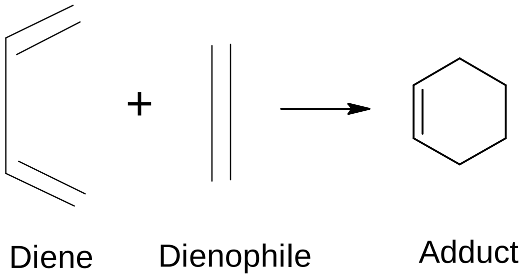
Structure of Unit:

9.0.0 Objective

The objective of this topic is the study of cycloaddition reaction which are one of the type of Pericyclic reactions which are neither effected from the solvent or catalyst which do not involve the presence of the ionic or the radical intermediate but do get affected from heat and light.the topic deals with the study of suprafacial and antarafacial addition of the diene and dienophile to have the cycloaddtion product where the cycloaddition is goverened by the conservation of the orbital symmetry rule given by woodward and Hoffman in the year 1875.

9.1 Introduction

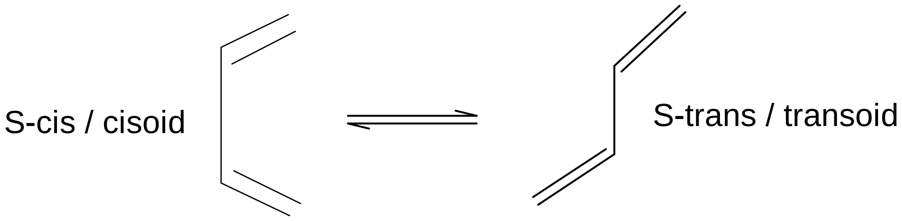
When there is combination of two unsaturated molecules to form cyclic compound, it is called as cycloaddition, wherein the formation of cyclic product π electrons are being used and two new sigma bonds are formed .these recations are classified on the basis of π electrons, involved in each component, an example of cycloaddition is Diels-Alder reaction wherein system containing 4π and 2π electrons combines to form a cyclic system.



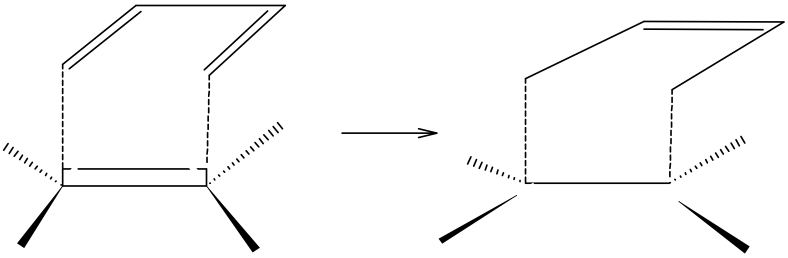
Diels-Alder reaction (4+2) cycloaddition

9.2 Stereochemical aspect of Diels-Alder reaction

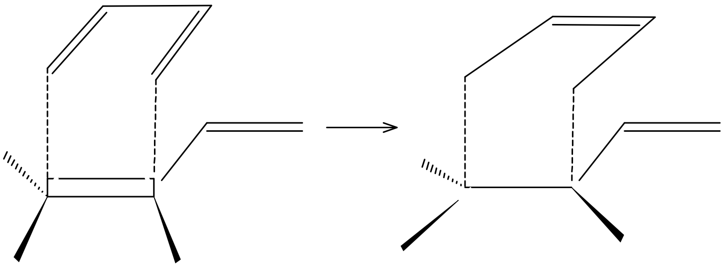
The diene should show an arrangement which allows the ends of the system to reach the doubly bonded carbons of the dienophile to reach the diene which could be achieved by s-cis or cisoid conformation of diene as shown below:



(2) The stereochemical conformation for the dienohile should also be syn which suggest that addition is concerted in nature as shown below.

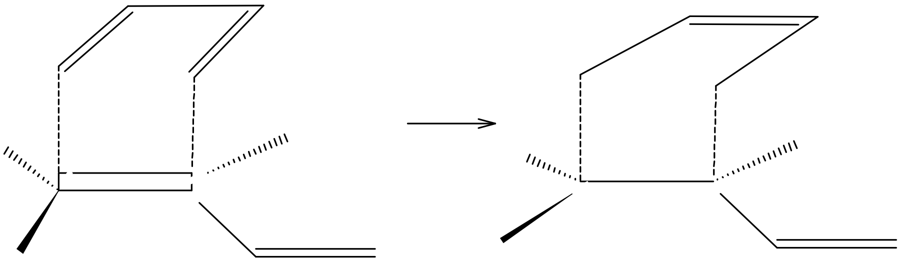


(4) Diels-Alder reactions takes place in more precisely way it is Exo addition this can be understood by the cycloadditon of diene with dienophile. If the dienophile is having any unsaturated group that should be in endo position, as seen below with refrence to developing double bond in the diene.



Endo Addition

[4+2] cycloaddition

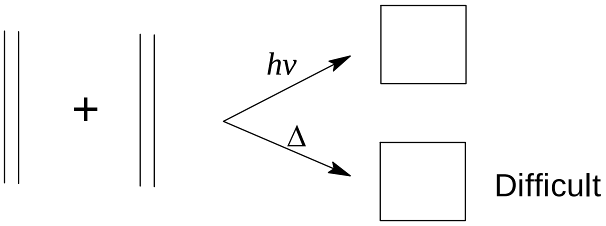


Exo Addition

[4+2] cycloaddition

Endocycloaddition is preferred over exo(4+2)cycloaddition

For [2+2] cycloadditon reactions an example can be cited of ethane (two molecules) to form cyclobutane. (4+2) cycloaddition is thermally allowed while (2+2) cycloaddition is photochemically allowed.

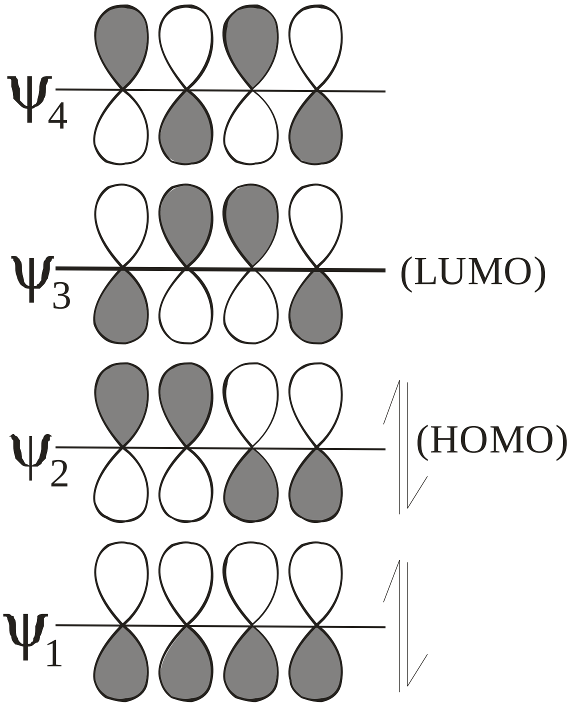


Not a concerted reaction

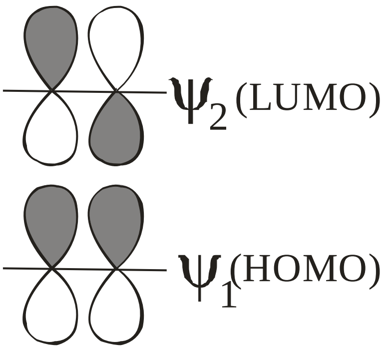
Cycloaddition can be defined as those concerted reactions wherein two σ bonds are formed by using π electrons.

Since cycloaddition is concerted in nature the stabilization of the transition state is brought about by the overlap of the HOMO (highest occupied molecular orbitals) with LUMO (lowest unoccupied molecular orbitals) of the reactants.

To understand the orbital overlapping one has to consider the orbital symmetry as shown below the molecular orbitals of diene and dienophile. For butadiene and ethane the pictorial representation of MOs is:

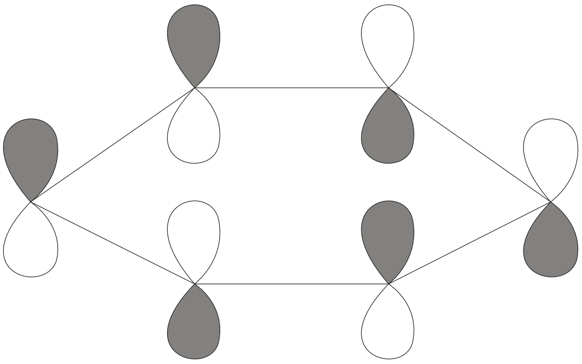


Butadiene



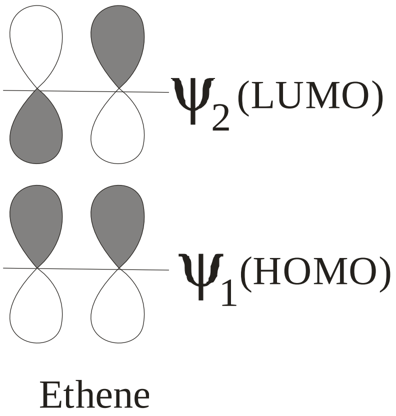
Diene

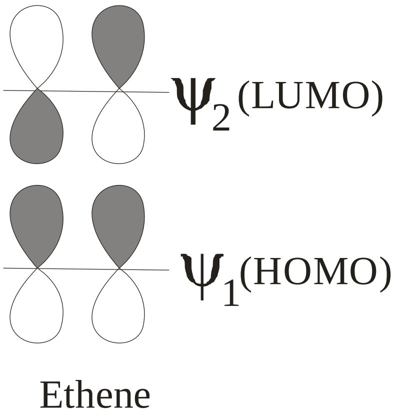
If the symmetry properties of butadiene (HOMO) and ethane (LUMO) are considered it appear that ψ_2 of butadiene and ψ_2 of ethene have same properties.



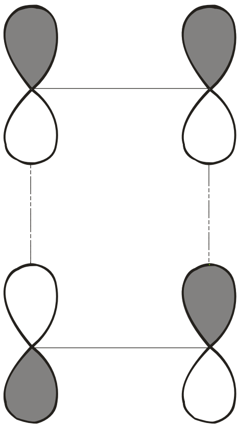
Symmetry allowed thermal (4+2) cycloaddition.

For (2+2) cycloaddition symmetry properties are studied.

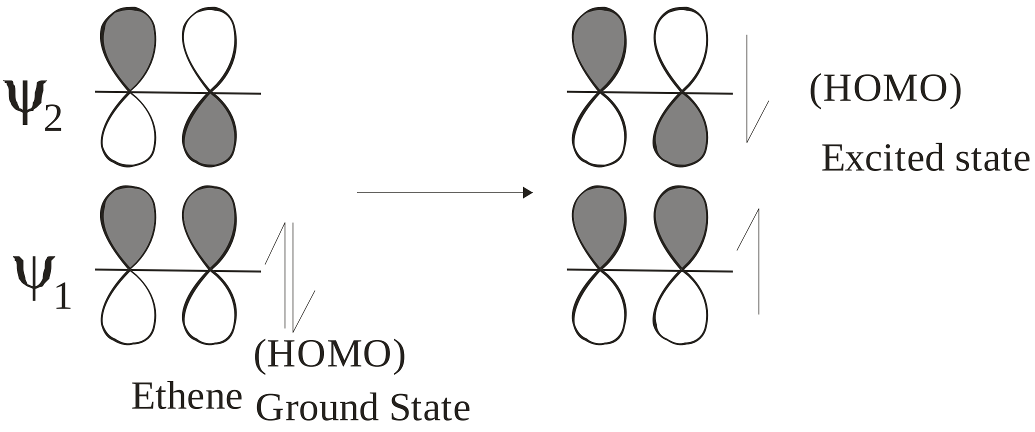




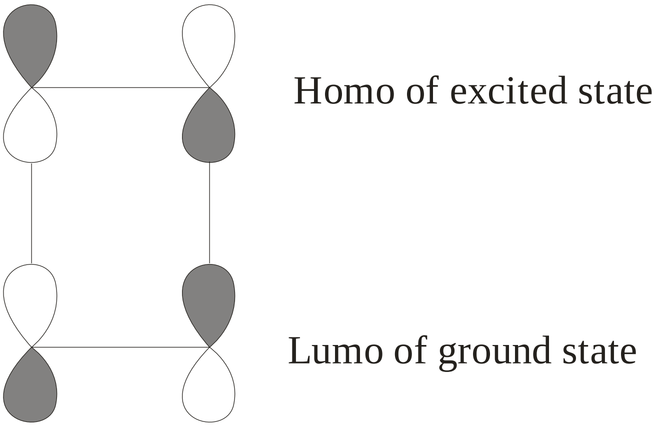
Interaction of HOMO-LUMO is considered of ethane as shown below



Symmetry forbidden thermal (2+2) cycloaddition However this (2+2) cycloaddition of ethane molecules are photochemically allowed as the symmetry properties of HOMO and LUMO is same as shown below.



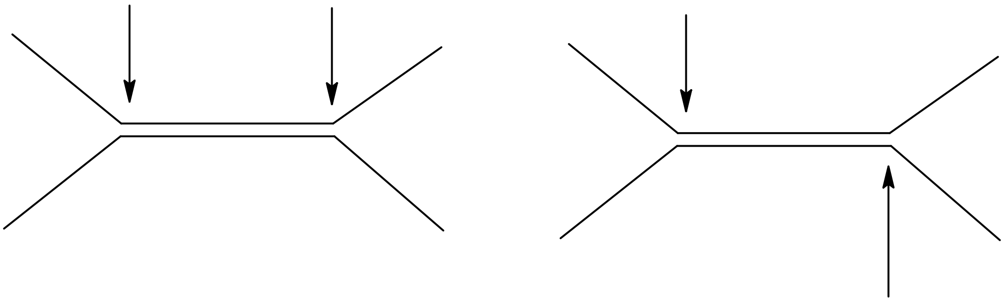
When interaction of excited HOMO of one molecule and LUMO of another is considered the symmetry properties makes cycloaddition feasible as shown below



Symmetry allowed photochemical (2+2) cycloaddition

9.2.1 Suprafacial and antarafacial additions.

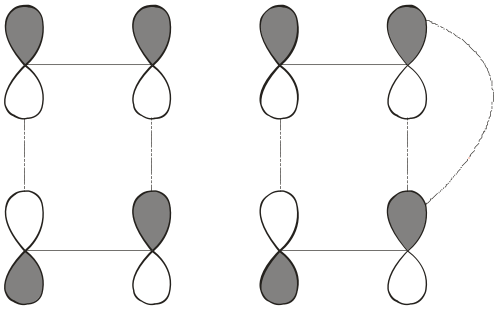
If in a concerted reaction, when bonds are broken or they are formed on the same face. It is called as suprafacial while if the same happens on the opposite sides are called as antarafacial. As shown below



Suprafacial Antarafacial

Though suprafacial and antarafacial resemble the term syn and anti however where the syn and anti describer the net stereochemistry of a reaction.Which is occurring in a two mechanism while however suprafacial and antarafacial refers to simultaneous making and breaking of bonds on the same or opposite faces.

Thermal (2+2) cycloaddition is allowed. If it is suprafacial to one and antarafacial to another component shown in fig below



Supra-supra symmetry-forbidden Supra-antara Symmetry allowed

From the symmetry properties it can be concluded that (2+2) cycloaddition supra-supra is geometrically possible but symmetry forbidden but supra-antara symmetry allowed but geometrically difficult woodward and Hoffman rules for (i+g) cycloaddition is given under.

i+j	Thermal	Photochemical
4n	supra, antara antara, supra	supra,supra antara,antara
4n+2	supra, supra antara, antara	supra,antara antara, supra

9.3 Solved Exercise

1. Give structural formula for the product expected from following reactions.

   (a) trans, trans-2,4-hexadiene+ ethylene

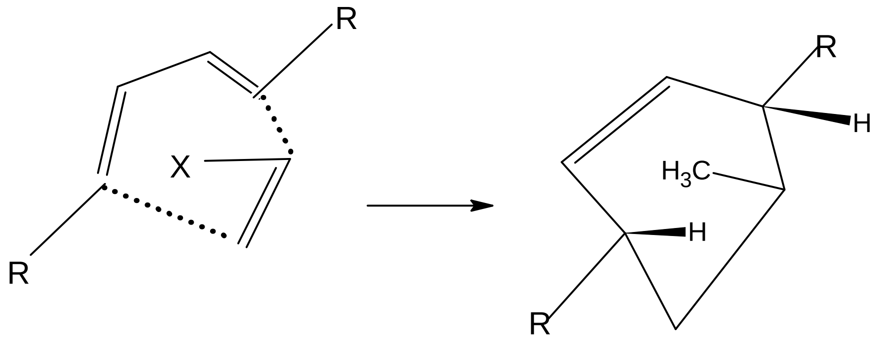
   (b) trans – 1,3-pentadiene+ maleic anhydride

   (c) cis-2-butene $\xrightarrow{hv}$ A + B

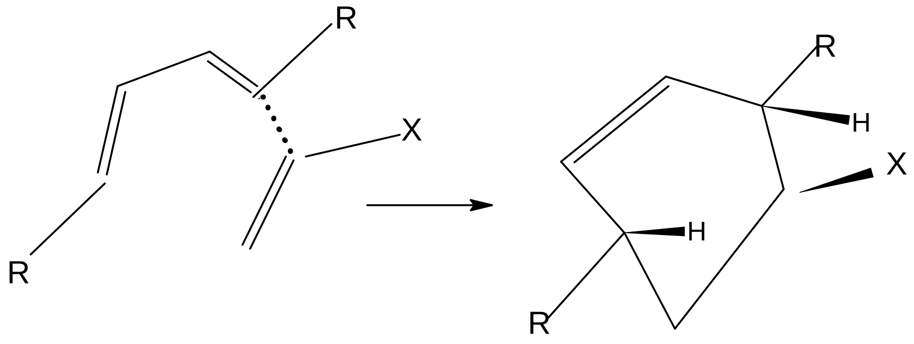
   (d) trans-2-butene $\xrightarrow{hv}$ A + B

Diels-Alder reactions are always stereopacific which means that of an intermediate exists it does not have sufficient life time to prevent rotation.

The stereochemical aspects of Diels-Alder reaction is governed by Alder rule awarding to this rule of two isomeric adducts are possible than preference is given to that adduct wherein unsaturated substituent(s) on the alkene is oriented towards the newly formed cyclohexene double bond. The transition states are called as Endo and Exo transition states.

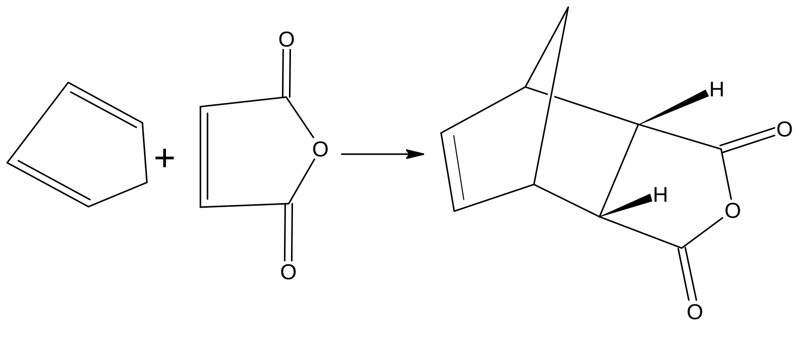


Endo addition



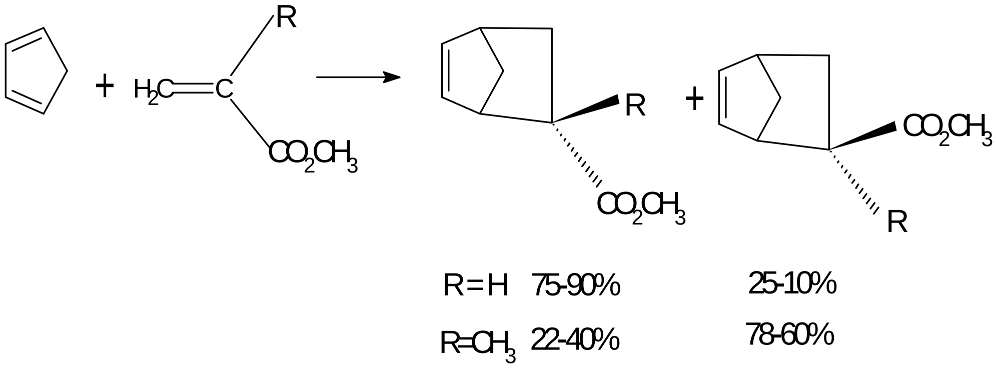
Exo addition

For the same reason the addition of dienophiles to cyclopentadiene is mainly favoured the endo stereoisomer. However sterically it is more congested case.

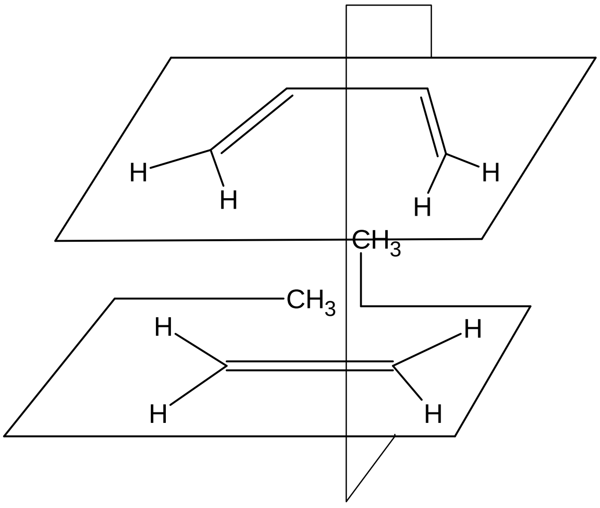


The probable several factors which determine the exo and Endo ratio includes steric effects, dipole-dipole interaction and the London dispersive forces.

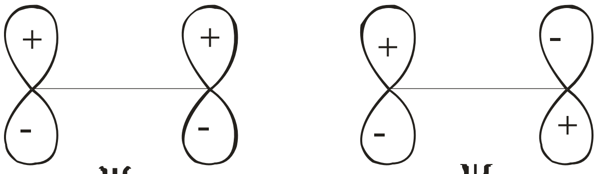
Generally most of cycloadditions follows the Alder rule but when cyclopentadiene reacts with methyl aerylate in decalin solution gives Endo adduct (75%) and Endo: Exo ratio is solvent sensitive and goes upto 90% Endo in methanol. However when methyl substituent is added to dienophile (methyl methacrylate) the exo product predominates.



For cycloadditon reactions being concerted in nature diene must opt s-cis conformation since electrons involved in diene and dienophile are π electrons so cycloaddition involves face to facee rather than edge-edge orientation. An place of symmetry perpendicular to the plane of reactants is shown below.



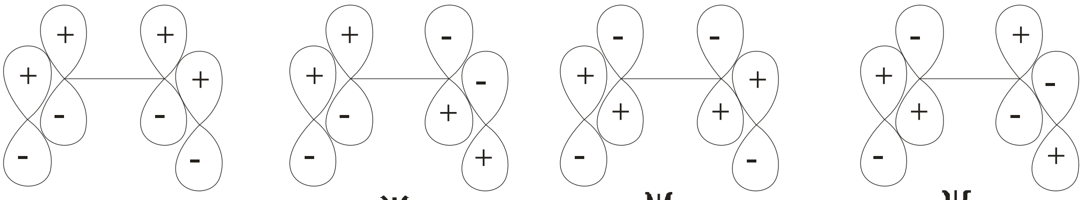
The symmetry of the orbitals are considered with respect to this plane and when are classified with respect to symmetry they can be arranged with respect to energy and the correlation lines as shown in correlation diagram below.



ψ_{1e} Symmetric (S) ψ_{2e} Antisymmetric(A)

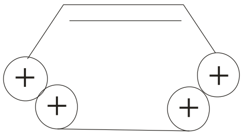
Ethylene orbitals

9.4 Orbital Symmetry

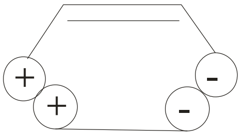


ψ_{1b} Symmetric (S) ψ_{2b} Antisymmetric(A) ψ_{3b} Symmetric (S) ψ_{4b} Antisymmetric(A)

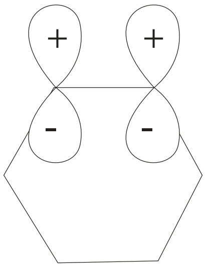
Butadiene orbitals



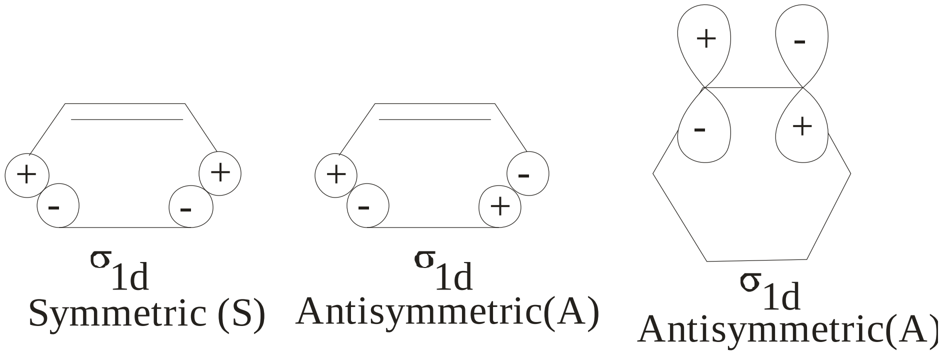
σ_{1c}
Symmetric (S)



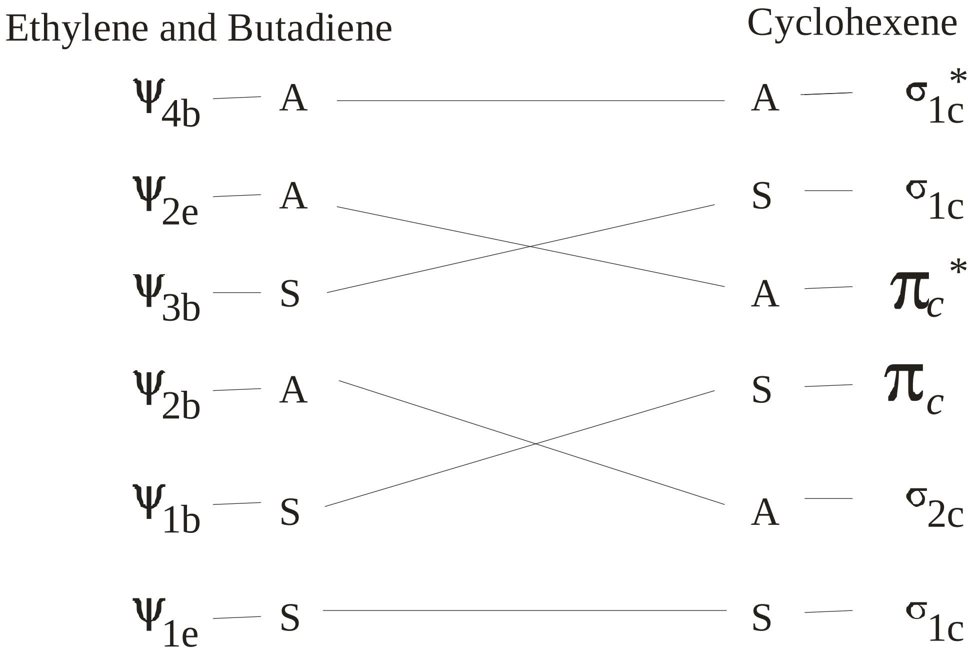
σ_{1c}
Antisymmetric(A)



σ_{1c}
Symmetric (S)



Cyclohexane orbital



Thus Diels-Alder reaction is $(4\pi_s + 2\pi_s)$ cycloaddition more precisely (2+2) cycloaddition process would be described as $(2\pi_s + 2\pi_s)$ where subscript s and a are suprafacial and antarafacial.

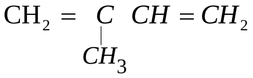
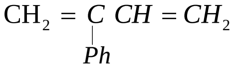
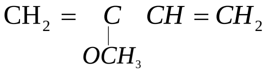
9.5 Relative ratios of Diels-Alder reactions

When dienophile contains electron with drawing/attracting group than diels-Alder reaction is more rapid and if diene contain electron releasing group the effect of substituents is given in table below

Relative reactivity toward cyclopentadiene in the Diels Alder reactions

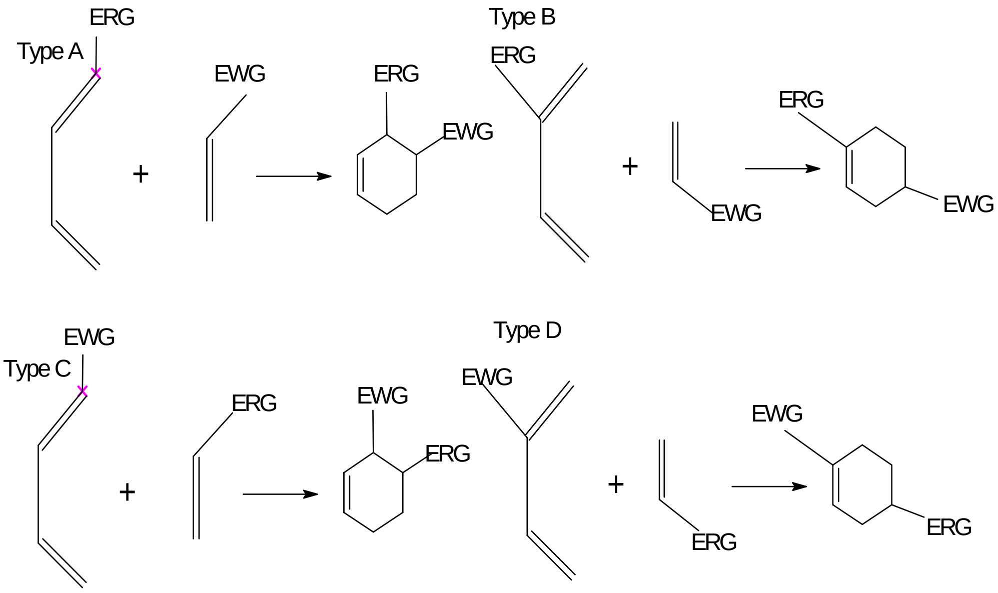
Dienophile	Relative rate*
Tetracyanoethylene	4.3×10^7
1,1 − *dicyanoethylene*	4.5×10^5
Maleicanhydride	5.6×10^4
p − *benzoquinone*	9×10^3
Maleonitrile	91
Fumaronitrile	81
Dimethylfumarate	74
Dimethylmaleate	0.6
Methylacrylate	1.2
Acrylonitrile	1.0

Relative reactivity of substituted Butadienes in the
Diels-Alder reaction

	Dienophile	
Diene	Tetracyano-ethylene	Maleic anhydride
$CH_2=CHCH=CH_2$	1	1
$CH_3CH=CHCH=CH_2$	103	3.3
 $CH_2=\underset{\underset{CH_3}{\vert}}{C}\ CH=CH_2$	45	2.3
$CH_3CH=CHCH-CHCH_3$	1.66×10^3	
$PhCH=CHCH=CH_2$	385	1.65
 $CH_2=\underset{\underset{Ph}{\vert}}{C}\ CH=CH_2$	191	8.8
$CH_3OCH=CHCH=CH_2$	5.09×10^4	12.4
 $CH_2=\underset{\underset{OCH_3}{\vert}}{C}\ CH=CH_2$	1.75×10^3	
$CH_3OCH=CHCH=CHOCH_3$	4.98×10^4	
Cyclopentadiene	2.1×10^6	1.35×10^3

The nature of substituents on dienes of dienophile effects the regiochemistry of Diels-Alder reaction.

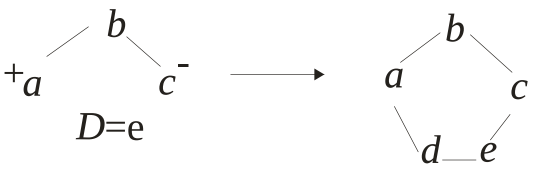
Case A and Case B as given in table shows the effect of electron donor in the diene and electron acceptor in the dienophile.



In case when substituents are reversed such that electron donor substituent on dienophile and electron accepting substituents on the diene. This is called as the INVERSE ELECTRON DEMAND Diels –Alder reaction.

9.6 [1,3]-dipolar cycloaddition

They are analogoeus to Diels –Alder reaction and concerted $(4\pi + 2\pi)$ cycloaddition. The entity a-b-c is called as 1,3-dipolar molecule and d-e is dipolarophile.



1,3-dipolar molecule have 4π electrons are isoelectronic with allyl anion. Some of 1,3-dipoles are shown below.

Some 1,3-diples

Nitrile oxide	$\text{R-C} \equiv N^{+} - \ddot{\underset{\cdot\cdot}{O}}:^{-} \leftrightarrow R - C^{+} = N - \ddot{\underset{\cdot\cdot}{O}}:^{-}$
Azides	$\text{R-}\underset{\cdot\cdot}{\ddot{\text{N}}}\text{-}\underset{\cdot\cdot}{\text{N}} = N^{+} : \leftrightarrow \text{R-}\underset{\cdot\cdot}{\ddot{\text{N}}}\text{-}N^{+} \equiv N:$
Diazomethane	$^{-}:CH_{2}\text{-}\underset{\cdot\cdot}{\text{N}} = N^{+} : \leftrightarrow {}^{-}: CH_{2} - N^{+} \equiv N:$
Nitrones	$\text{R}_{2}C = N^{+}(R) - \ddot{\underset{\cdot\cdot}{O}}:^{-} \leftrightarrow R_{2}C^{+} - \ddot{N}(R) - \ddot{\underset{\cdot\cdot}{O}}:^{-}$
Nitrilimines	$\text{R-C}^{+} = \underset{\cdot\cdot}{\text{N}}\text{-}\underset{\cdot\cdot}{\ddot{\text{N}}}\text{-}R \leftrightarrow R - C \equiv N^{+}\text{-}\underset{\cdot\cdot}{\ddot{\text{N}}}\text{-R}$

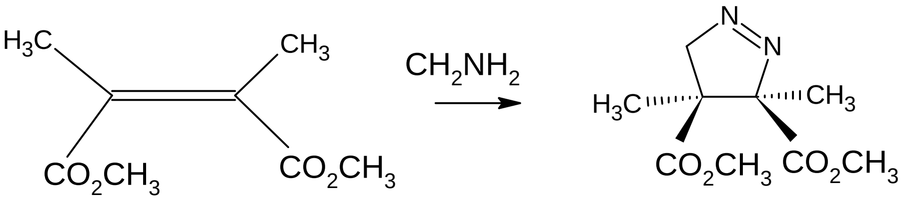
Dipolarophiles are typically alkenes or alkynes ie, essentially they should be having π bond.

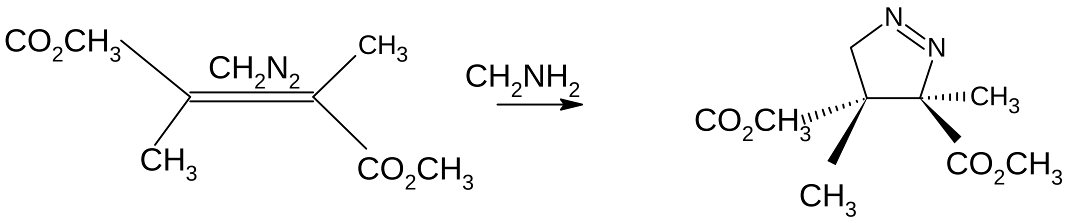
Reactivity of dipolarophiles depends on

(a) substituent present on π bond. (b) nature of 1,3-dipole

Stereochemically of 1,3 dipole cycloaddition reaction is similar to Diels-Alder reaction is stereospecific syn addition.

For eg. Additions is stereospecific for diesters with diazomethane to yield pyrazolines.





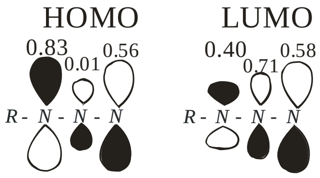
In case when 1,3 dipole and dipole are unsymmetrical addition can occurs in two possible orientation. The regioslectivity of addition is determined by steric and electronic factors the regiochemistry of dipolar cycloaddition is based on the frontier orbital concept most favourable interaction is when FMO of 1,3-dipole and dipolorophile occurs mostly LUMO of dipolarophile interacts with HOMO of 1,3-dipolar.

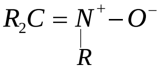
9.6.1 Regioselectivity for the 1,3 dipolar cycloaddition

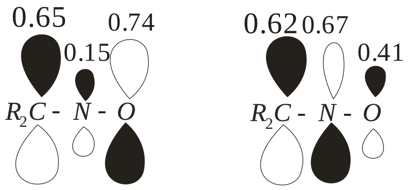
For the analysis of regioselectivity for the 1,3 dipolar cycloaddition it is mandatory to have information about the energy and atomic coefficients of frontier orbitals of both 1,3-dipole and dipolarophile.

Some results are shown below.

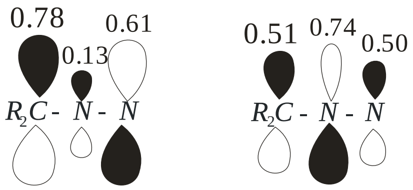
$R-N=N^{+}=N^{-}$ azide



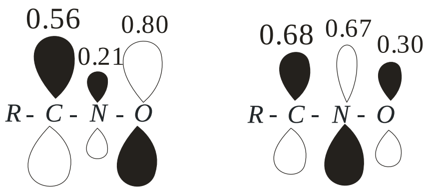

$R_2C=\underset{R}{\underset{|}{N^{+}}}-O^{-}$ Nitrone



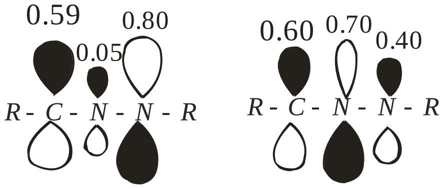
$R_2C=N^{+}-N^{-}$ diazoalkane



$RC=N^{+}-O^{-}$ Nitrile oxide



$R-C=N^{+}-N^{-}$-R Nitrile imine



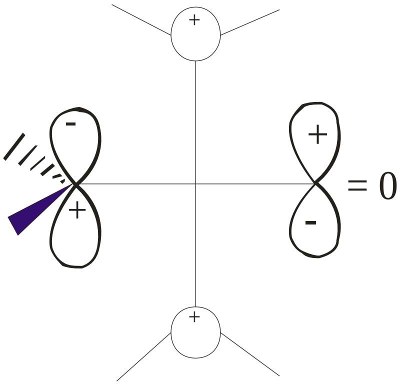
The regiochemistry of 1,3 dipolar cycloaddition can be predicted by using these orbital coefficients and by estimating relative energies of interacting orbitals.

9.7 [2+2] cycloaddition of Ketenes

$(2\pi + 2\pi)$ cycloaddition prominently taking place involes the compulsory orientation of one of the component in antarafacial mode however few reactions meets this condition. However ketenes having linear geometry with sp hybridized carbon atom give minimum steric repulsion in antarafacial transition state and fullfils this geometry restriction.

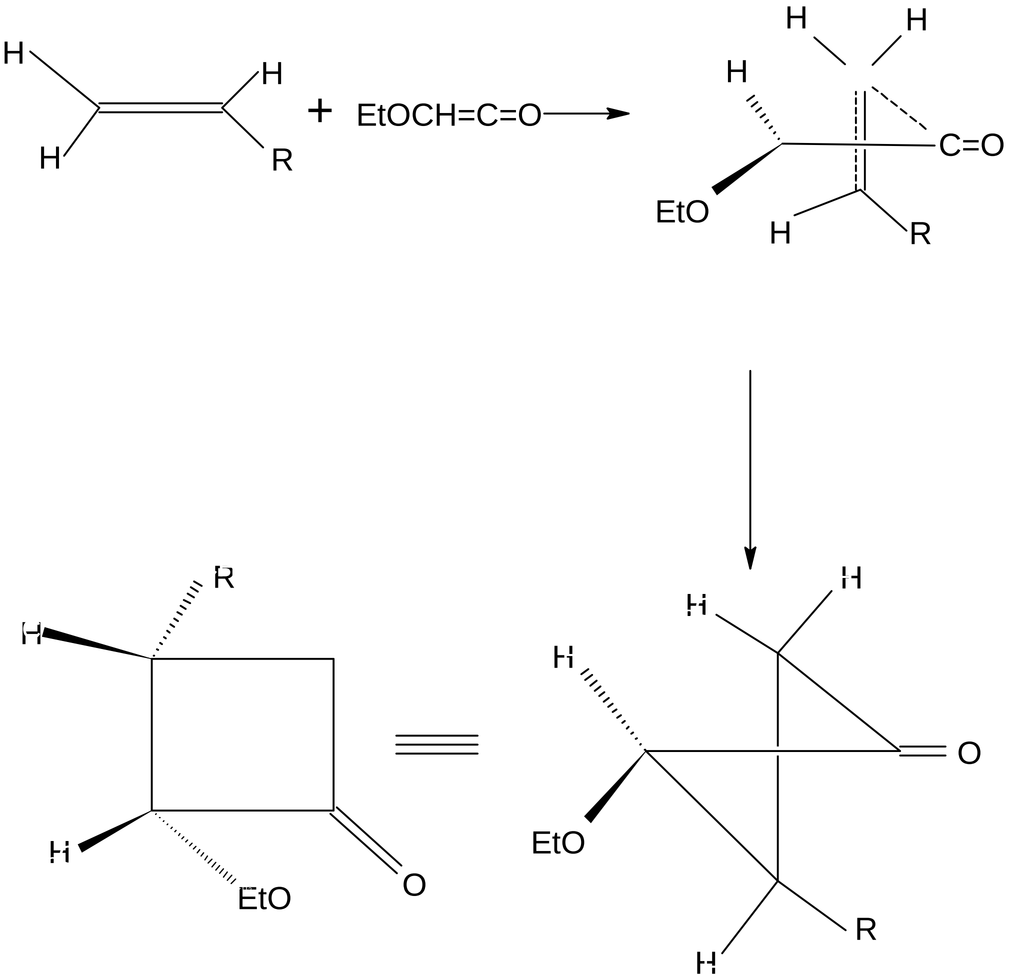
Molecular orbital modeling of the reaction concerned concerted non synchronous process which bond formation occurs at sp carbon of ketene leading to forms bond formation at terminal carbon.

The model showing concerted cycloaddition of ketene and an olefin is shown below.

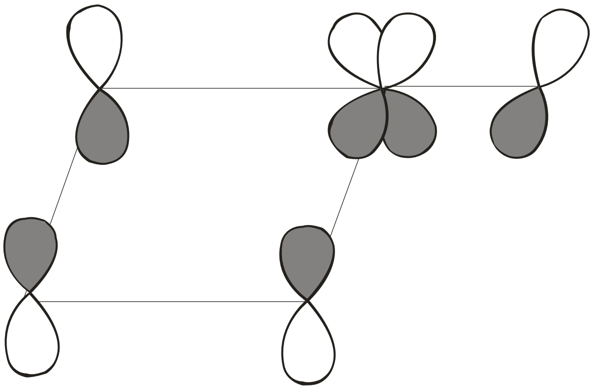


The stereochemical prediction can be made on the above mentioned model.

For example E and Z-2butene when reacts with ethoxyketone gives stereoisomeric products. In case of monosubstituted alkenes the substituent is vicinal and cis to the ethoxy group in cyclobutanone product. The reason for this is separation of alkyl and ethoxy substituent in the transition state.



There is another way to describe [2+2] cycloaddition reactions of ketone. This formulation is $\left[2\pi_s + \left(2\pi_s + 2\pi_s\right)\right]$. The basis set orbitals array is given below. The system shown below has Huckel-type topology having involvement of 6π electrons.

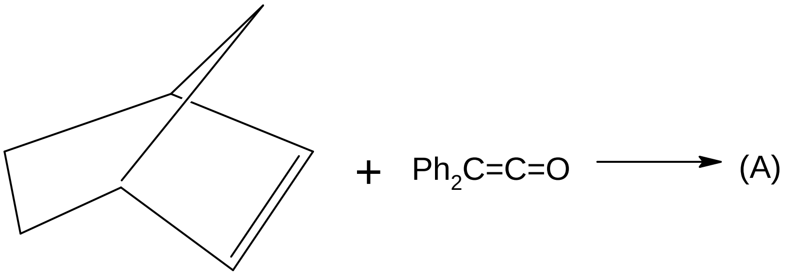


From the available data this analyse is equally compalible and the prediction made for the stereoselectivity and the reactivity on the bases of this model are in accordance with the experimental results and give better results compared to the results derived from $(2\pi_s + 2\pi_a)$ transition state.

Exercise

Q. Give structural including stereochemistry of products expected from the following reactants.

(a)



(b)

$$\left(CH_3\right)_2 C=C=O+C_2H_5OC\equiv CH \xrightarrow{O^0C} (B)$$

(c)

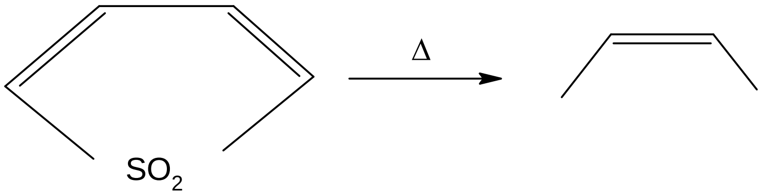
$$\left(t-but\right)_2 C=C=CH_2+CH_3CO_3H \rightarrow (C)$$

9.8 Chelotropic reactions

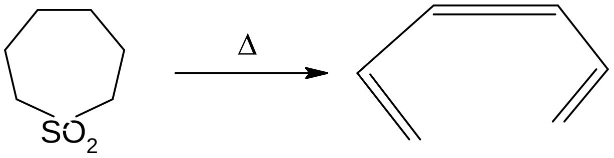
Chelotropic reactions involve those classes of reactions wherein two sigma bonds that terminate at single atom are made to broken in concerted way.

2,5-Dihydrothiophene-1,1-dioxides and 2,7-Dihydrothiepin-1,1-dioxides undergo 1,4 and 1,5 elimination respectively, both these reactions are concerted reaction. The reaction is shown below.

(A)



(B)



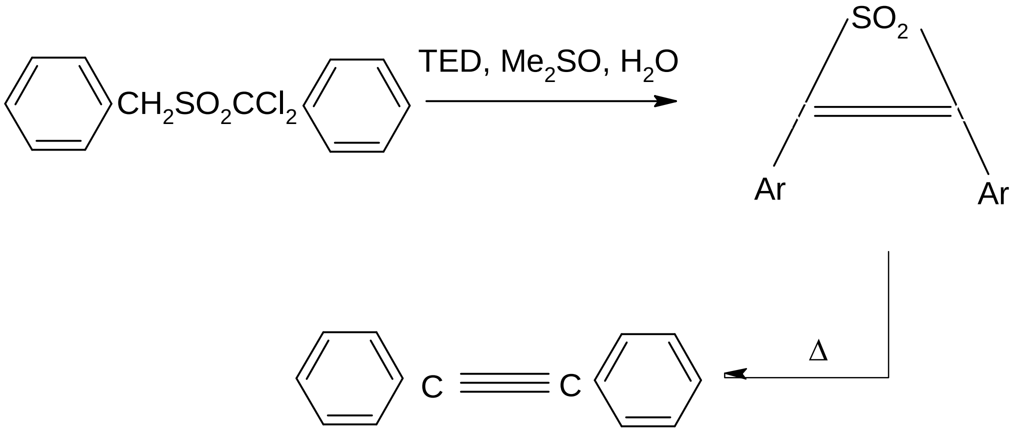
The reaction cited above is governed by orbital symmetry rules.

Reaction (A) is a suprafacial process while reaction (B) is taking by antarafacial processes.

Both the reactions ie, (A) and (B) are called as chelotropic reactions as two sigma bond connected single atom ie, sulphur are broken in a concerted way.

Elimination of SO_2 from episulfones cannot takes place in concerted way except antarafacially which is unfavourable for such a small ring. Evidances show that this reaction take place in non-concelled way.

Another example of chelotropic reaction is of $\alpha,\alpha-Dichlorobenzylsulfones$ reacts with excess of base triethylenediamine in dimethyl sulphoxide of room temperature to give 2,3-diarylthiiren-1,1-dioxides. Which are isolated and thermally decomposed as shown below.

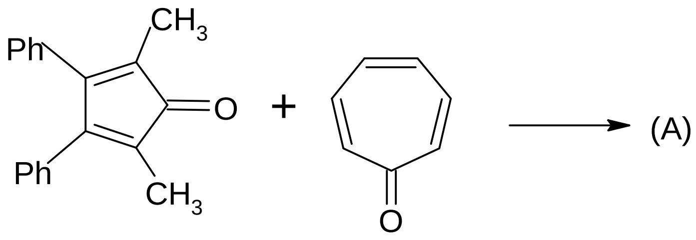


9.9 Summary

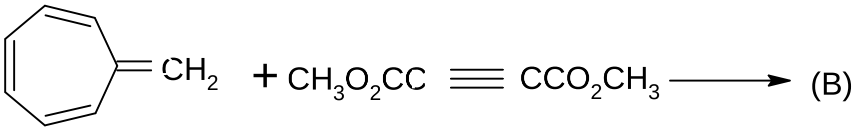
- cycloaddition reactions involve the union of diene and dienophile under thermal and photochemical conditions.
- The cycloaddition reaction involves the addition of the components either suprafacial (same side) or antarafacial (opposite sides) depending on the reaction conditions.
- Ketenes having linear geometry with sp hybridized carbon atom give minimum steric repulsion in antarafacial transition state and fullfils this geometry restriction.
- The stereochemical aspects of Diels-Alder reaction is governed by Alder rule
- In a concerted reaction, when bonds are broken or they are formed on the same face. It is called as suprafacial while if the same happens on the opposite sides are called as antarafacial.
- Chelotropic reactions involve those classes of reactions wherein two sigma bonds that terminate at single atom are made to broken in concerted way.

9.10 Review Questions

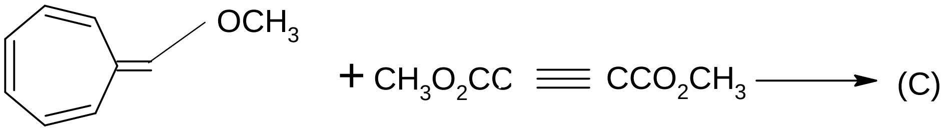
1 Predict the product of the reaction


Ph
CH$_3$
O
Ph
CH$_3$
O
(A)

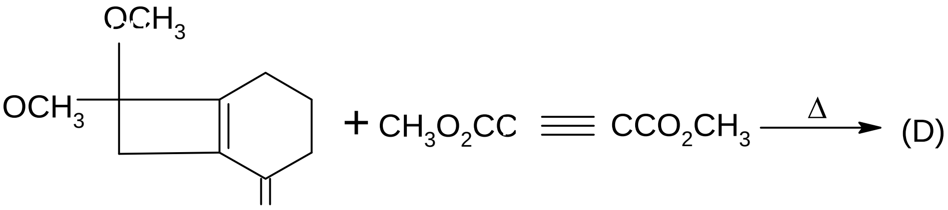
2


CH$_2$
CH$_3$O$_2$CC ≡ CCO$_2$CH$_3$
(B)

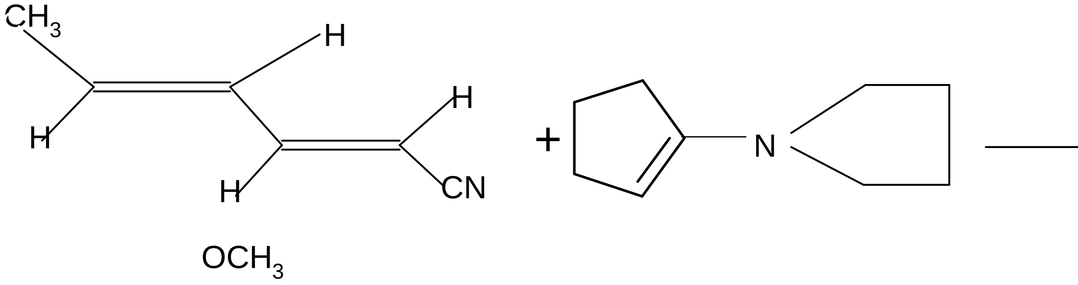
3


OCH$_3$
CH$_3$O$_2$CC ≡ CCO$_2$CH$_3$
(C)

4


OCH$_3$
OCH$_3$
CH$_3$O$_2$CC ≡ CCO$_2$CH$_3$
Δ
(D)

5


CH$_3$
H
H
H
H
CN
OCH$_3$
N

9.11 Reference Books

- Organic reaction mechanism, P.S.Kalsi, New Age International Publication.
- Organic Reaction Mechanism, Singh Mukherjee
- Organic Chemsitry, Morrison and Boyd, 6th edition,printce hall of India

Unit - 10

Analysis of Sigmatropic Reactions

Structure of Unit

10.0 Objective

Most of the organic reactions are ionic. Electrons moves from an electron rich atom towards an electron poor atom. Intermediates like cations and anions are formed. But Besides these, there is an another group of reactions where electron move round a circle and no intermediates are formed. This type of reactions is called Pericyclic reactions. These reactions go in a single step and follow concerted mechanism. For the understanding of these reactions it is necessary to know that how these reaction proceeds?

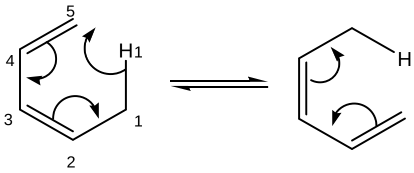
10.1 Introduction

Pericyclic reactions are concerted, do not follow any ionic or radical pathway, reamin unaffected by polar solvents, radical initiators (or inhibitors) and catalysts. These reaction take place thermally or photochemically. These are mainly classified in three classes: Electrocyclic reactions, Cycloaddition reactions and Sigmatropic rearrangements. In previous chapter you have studied electrocyclic and cycloaddition reactions. Here we will deal with only sigmatropic rearrangements.

10.2 Sigmatropic Rearrangements

Stigmatropic rearrangements involves migration of a σ bond that is flanked by one or more conjugated systems to a new position within the system. The reaction is termed [i,j] sigmatropic shift when the bond migrates from position [1,1] to position [i,j].

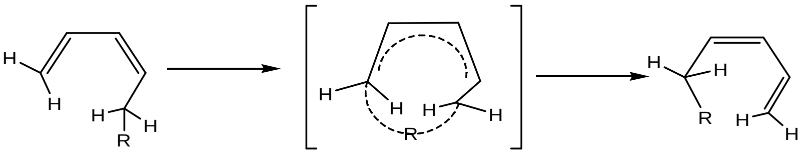
For example, a carbon hydrogen bond may move across a diene ($1\rightarrow2$). It is an example of [1,5] sigmatropic rearrangement.



(1) **(2)**

It is an uncatalysed intramolecular process. Other examples are:

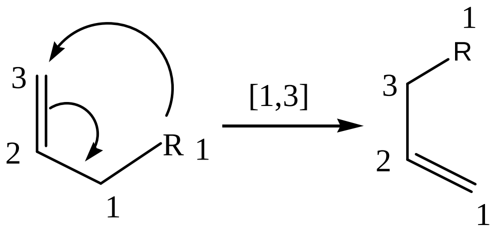
(i) Sigmatropic reaction of order [1,5]



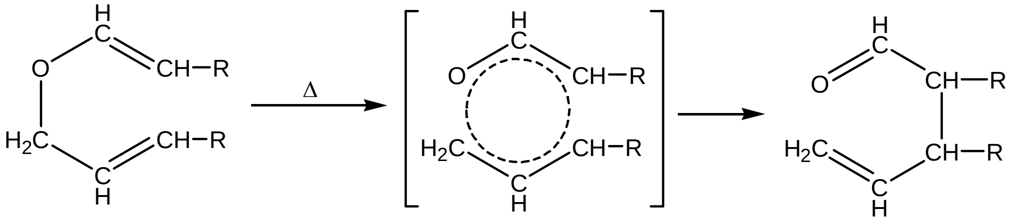
(3) **(4)** **(5)**

Transition state
(σ-symmetry)

(ii) Sigmatropic reaction of order [1,3]



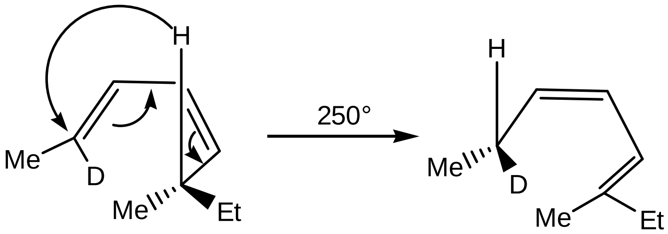
(iii) Sigmatropic reaction of order [3,3]



(6) (7) (8)

10.3 Suprafacial and Anatarafacial shift of H

Consider the system (9→10).



(9) (10)

The σ bond is made and broken on the same side of the conjugated system. This reaction can be considered as a cycloaddition of the C-H σ bond to the π-orbitals of the diene system as shown by the dotted line in Fig. 10.1. Here we see that the interaction of the HOMO of the C-H bond of (σ) and the LUMO of the butadiene (Ψ_3) is bonding if the hydrogen shifts from the top surface to the top surface. This kind of shift is known as suprafacial shift, by analogy with the suprafacial process and reaction is called a [1,5] sigmatropic rearrangement.

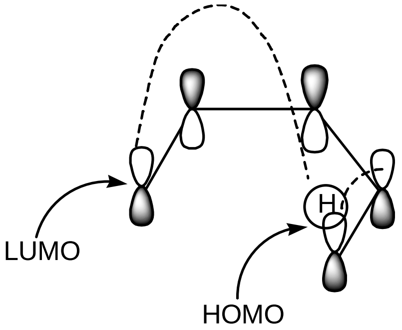


Fig. 10.1 Frontier orbitals for suprafacial [1,5] sigmatropic rearrangement of hydrogen

A similar combination of HOMO-LUMO in an allylic system (Fig. 10.2) shows that the σ orbital can have bonding interactions through lobes on opposite faces of the π-LUMO.

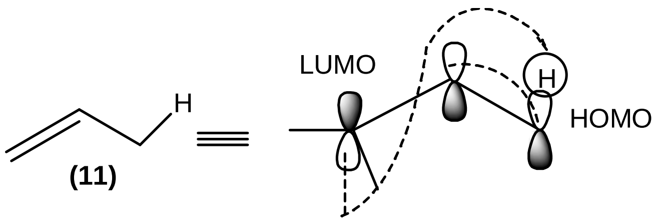
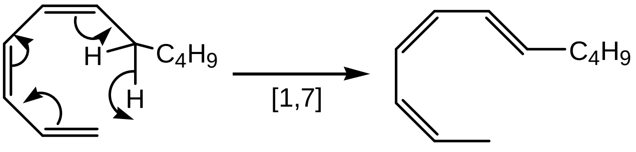


Fig.10.2. Frontier orbital for [1,3] sigmatropic rearrangement of hydrogen

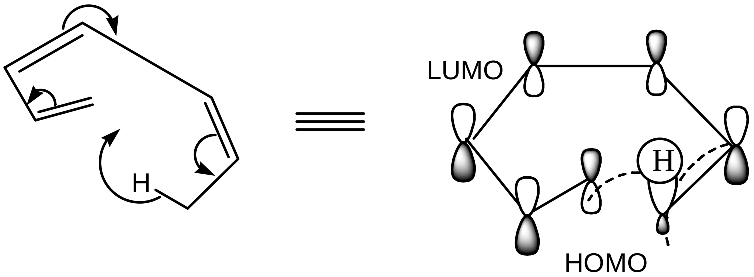
Thus the hydrogen atom leaves the upper surface and moves to the lower surface. Such a shift would be called antarafacial and the reaction is [1,3] sigmatropic rearrangement. Such rearrangements are virtually unknown in thermal reactions, although they are allowed. Geometrical requirements prevents the allowed reaction and the orbital symmetry frustrates the geometrically easy [1,3] suprafacial shift.

If we take a longer conjugated system as in the triene (12), then a [1,7] shift takes place on heating. See Fig. 10.3, we can say that this is favored when



(12)

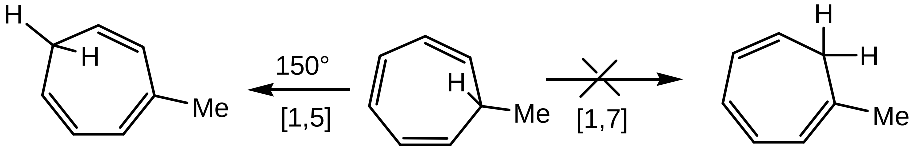
the hydrogen leaves the top surface and arrives on lower surface, in other words, in an antarafaical manner. Unlike the case of [1,3] shift there is helical shape in which continuous overlap can be maintained.



10.3. Frontier orbital for the [1,7] antarafacial shift of hydrogen

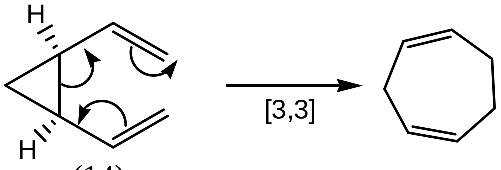
The known examples of this kind of reaction are found in open chain triene where helical geometry is possible. There is no proof that the shift is in fact antarafacial, but it is known that in cyclic trienes, like the cycloheptatriene (13), a [1,7] sigmatropic rearrangement does not take place. [at temperature above 150°], but a [1,5] sigmatropic rearrangement of the hydrogen atom occurs which is suprafacial.

In this triene, a helical transition state is impossible; thus this observation shows that [1,7] shifts occurs only in open-chain trienes strongly suggests that they are indeed antarafacial. The frontier orbital interactions as we have seen, account for this.



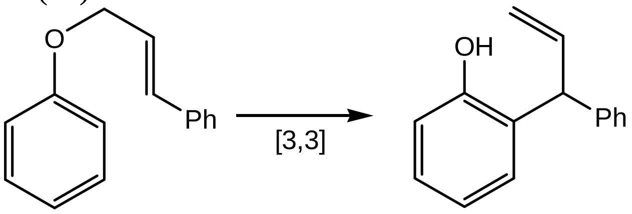
(13)

Hydrogen is not only group which can migrate, and there are therefore many other kinds of sigmatropic rearrangement. Here are some examples:



(Cope rearrangment)

(14)



(Clasien rearrangement)

(15)

Predicted stereochemical course for sigmatropic rearrangements (If hydrogen is migrating):

i,j	Thermal reaction	Photochemical reaction
1,3	Antarafacial	Suprafacial
1,5	Suprafacial	Antarafacial
1,7	Antarafacial	Suprafacial

10.4 Sigmatropic shifts involving carbon moieties

As we have seen that H atom can form bond through its 1s orbital, as it has only single lobe. It can move between two lobes of same sign. Thus H can migrate only suprafacially with respect to itself. Other atoms C, N and S, they can use their p and d orbitals having lobes of opposite signs. So they can interact either solely with one lobe i.e. suprafacially or with lobes of opposite sign i.e. antarafacially.

10.4.1 1,7-Sigmatropic shift of an alkyl group

Consider a heptatriene system in which [1,7] sigmatropic shift of an alkyl group (R = Cabc) occurs.

On the basis of frontier orbital analysis it shows two arrangement (A) and (B) [Fig 10.4] for the HOMO's of the heptatrienyl radical and the C radical. Arrangement (A) in which the π-system acts as the suprafacial component and C radical acts as the antarafacial component with two lobes of opposite signs. [Non linear π approach]. Arrangement (B) in which π system acts as antarafacial component and the orbital of C radical act as a suprafacial component interacting with single lobe [A linear σ approach].

Seven carbon chain has sufficient flexibility so it can be act as an antarafacial component.

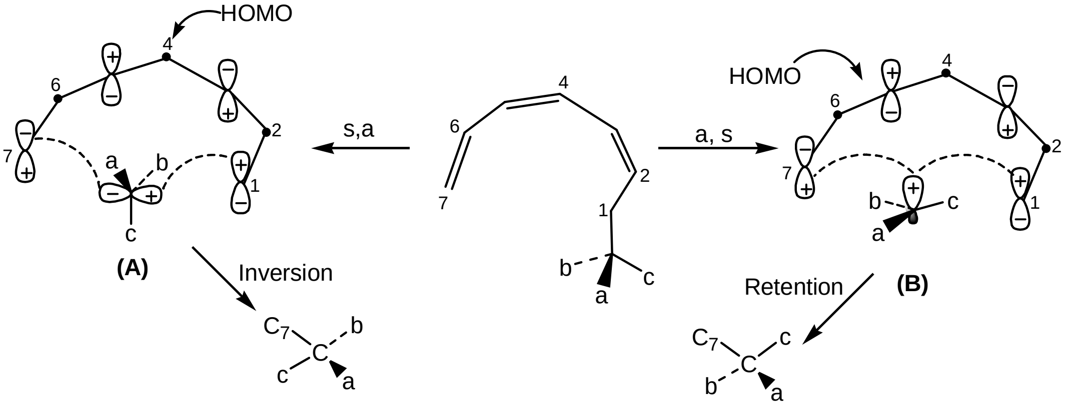


Fig. 10.4 [1,7] Sigmatropic rearrangement : (A) Suprafacial-antarafacial and (B) Antarafacial suprafacial

Rearrangement (B) which is suprafacial with respect to the migrating group will show retention of configuration but rearrangement (A) which is antarafacial with respect to the migrating group will have inversion of configuration at migrating centre. It is just like SN^2 reaction which shows walden inversion.

10.4.2 1,3-Sigmatropic shift of an alkyl group

It is just like [1,7] sigmatropic shift as explained above. A [1,3] sigmatropic [Fig 10.5] shift will occur suprafacilly on the π system and antarafacial on the alkyl group so associated with walden inversion.

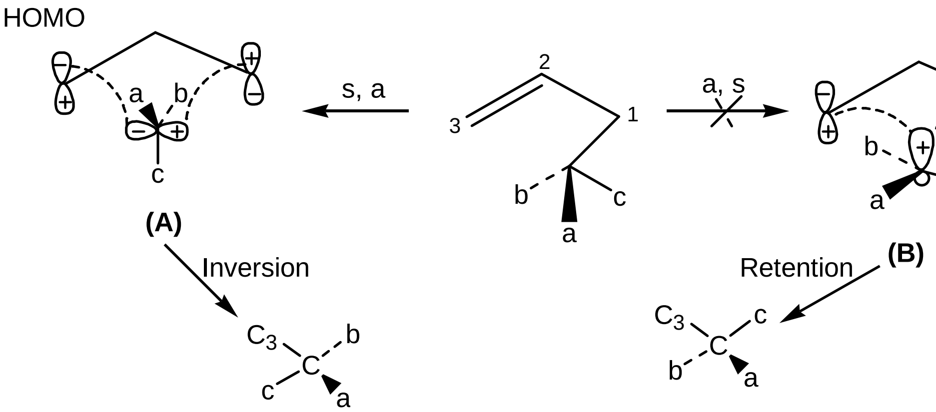


Fig 10.5 [1,3] Sigmatropic shift : (A) suprafacial antarafacial (B) antarafacial, suprafacial

10.4.3 [1,5] Sigmatropic shift of an alkyl group

We can conclude that [1,5] shift could undergo suprafacially on both the component with retention of configuration.

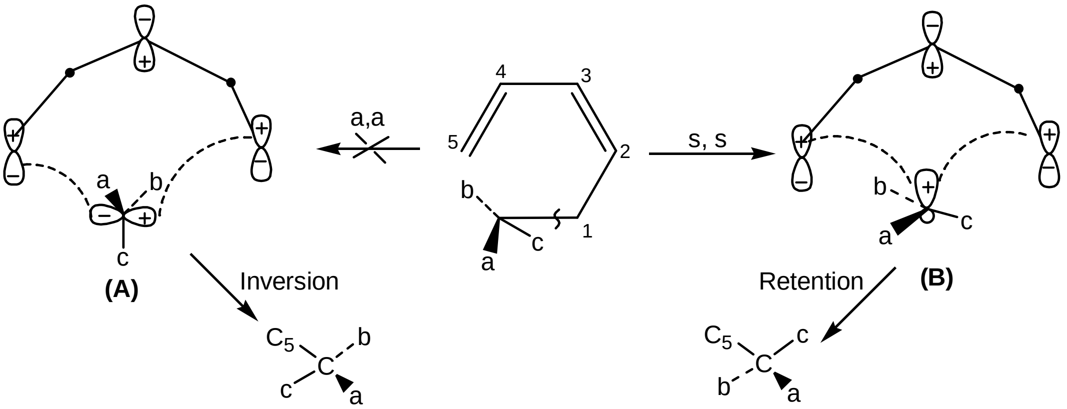
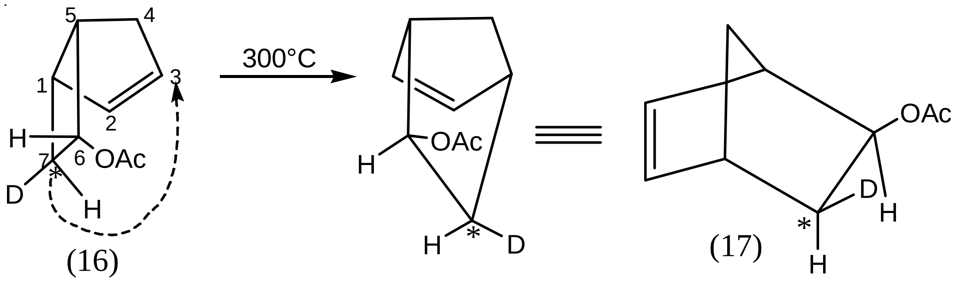


Fig 10.6 [1,5] sigmatropic shift**:** (A) antarafacial-antarafacial and (B) suprafacial-suprafacial

Thus for [i,j] sigmatropic rearrangements when both i and j greater than 1, selection rules are:

1. [i + j] = 4n : antara supra or supra antara in ground state; supra-supra or antara-antara in excited state
2. [i + j] = 4n + 2 : supra-supra or antara-antara in ground state; antara-supra or supra-antara in excited state

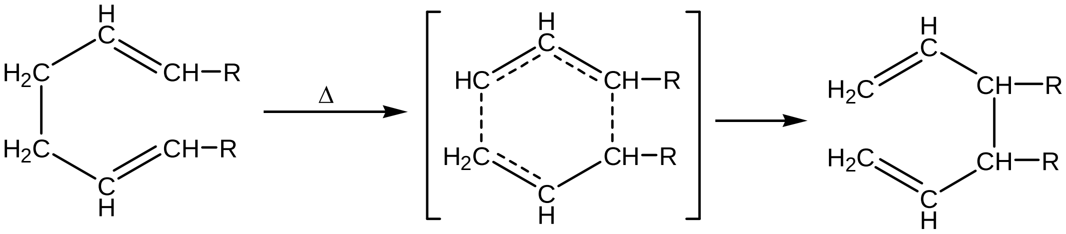
For [1,3] and [1,5] shifts, the geometry pretty effectively prevents antarafacial migration. So superfacial migrations will take place. Therefore [1,3] migration occurs with inversion, while [1,5] migration with retentions. It can be explained by following examples: Deuterium labeled bicyclo[3.2.0]heptene (16) is converted stereospecifically into the exo norbornene (17). This reaction proceeds by a [1,3] migration and with complete inversion of configuration in the migrating group.



(16) (17)

10.5 3,3-Sigmatropic rearrangements:

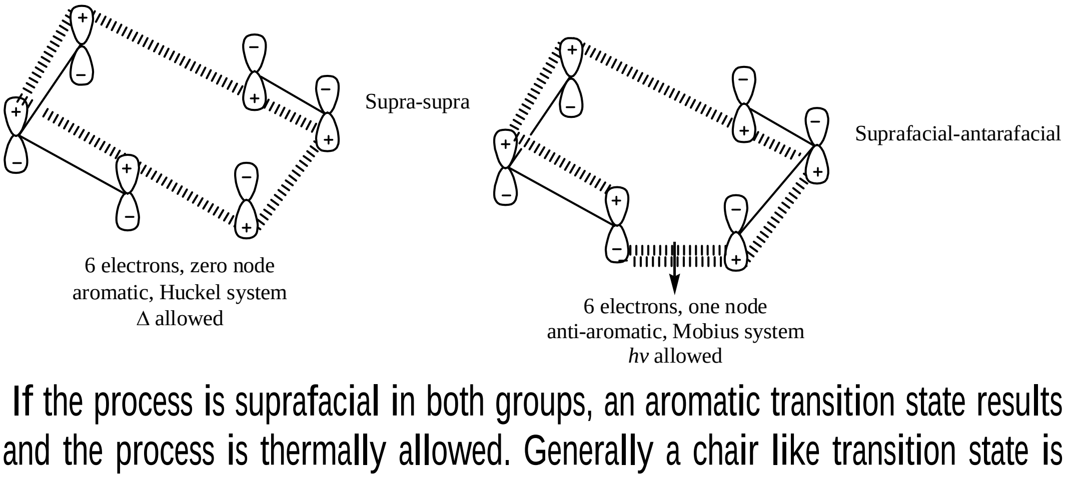
Sigmatropic rearrangements of order [3,3] are very common. Generally found in 1,5-hexadiene.



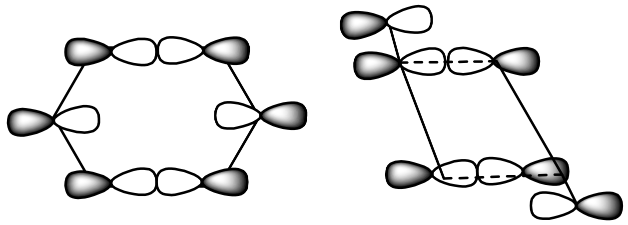
transition state

Sigmatropic Reaction of order [3,3]

For such process the transition state is represented as two interacting allyl fragments. There can be two stereochemical variations suprafacial-suprafacial (or antarafacial-antarafacial) and supra-antara as shown in the following states:

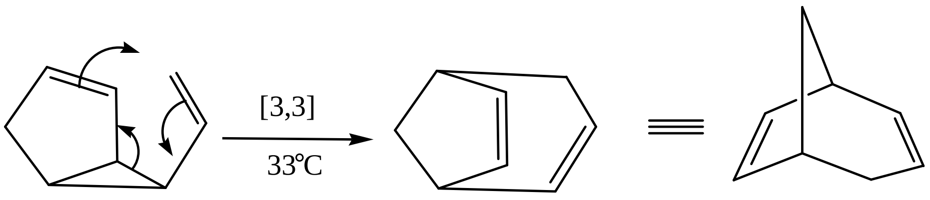


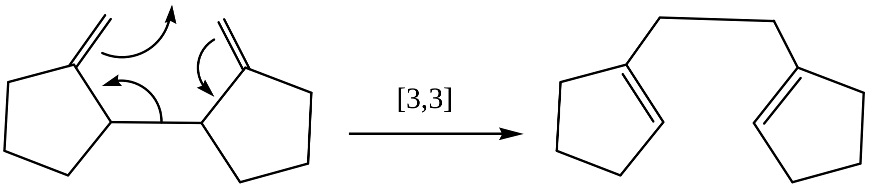
If the process is suprafacial in both groups, an aromatic transition state results and the process is thermally allowed. Generally a chair like transition state is involved, but a boat like conformation is also possible.

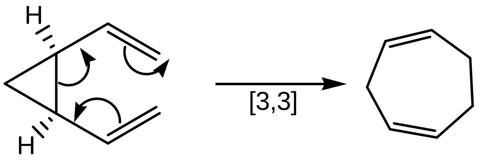


Boat transition state Chair transition state

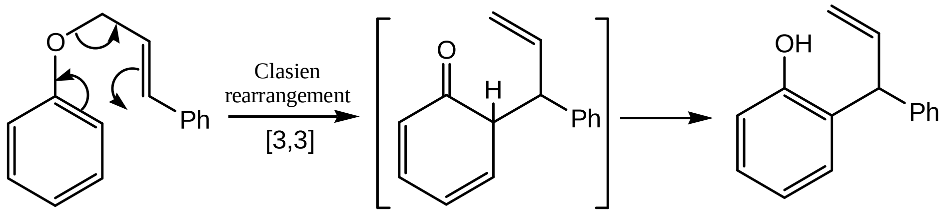
As usual, those involving a total of (4n + 2) electrons are allowed in all suprafacial mode. Here are some examples:





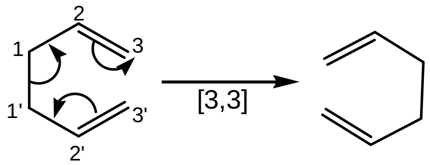


[Cope rearrangment]



10.5.1 Cope rearrangement

The thermal rearrangement of 1,5-diene through [3,3] sigmatropic shift is known as cope rearrangement. Let us take one example:



..................(i)

This example serves to illustrate the wide latitude we can allow ourselves. One way is to take to π bond between C-2 and C-3 as the 2-electron component, and the σ-bond another $2e^-$s and the other π-bond as the $2e^-$ system. Looking by the way the reaction can be regarded as a $[\sigma_s^2 + \pi_s^2 + \pi_s^2]$ cycloaddition with the participation of six electrons. On the basis of frontier orbital analysis, two imaginary transition states (A) and (B) may be envisaged both allowing supra-supra thermal interconversion.

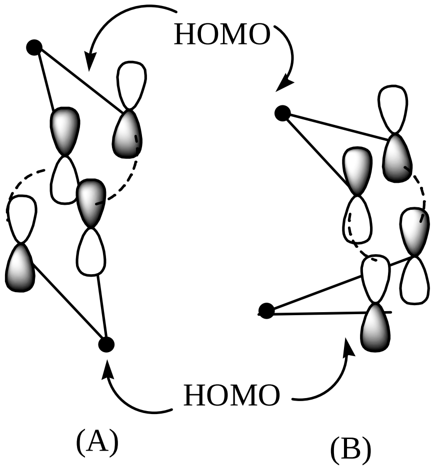
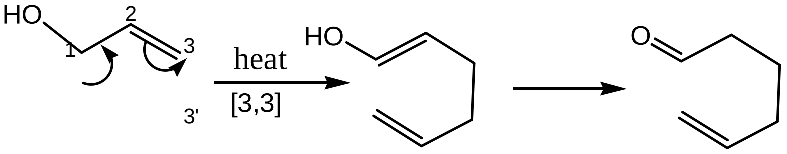


Fig 10.7 Chair like (A) and boat-like (B) transition states in the Cope rearrangement

The chair-like arrangement (A) is preferred over boat like one (B) (Fig 10.7). It has been established by stereochemistry of pyrolysis products of (±) and meso-3,4-dimethylhexa-1,5-diene (Fig 10.8). The (±) gives a mixture of E,E (90%) and ZZ (10%)dienes while the meso isomer gives selectively the E, Z isomer consistent with the chair like transition state. Predominancy of EE isomer in the pyrolysis of (±) form emphasizes that the diequatorial chair like arrangement is preferred. Chair like arrangement in the T.S. of [3,3] migration is also supported by consideration of secondary interaction in the HOMO-LUMO approach.

Directing the Cope rearrangement by formation of a carbonyl group

In its simplest version (i), it is not a reaction at all. The starting material and the product are same. We can drive this reaction too by formation of a carbonyl group if we put an OH substituent in the right place.



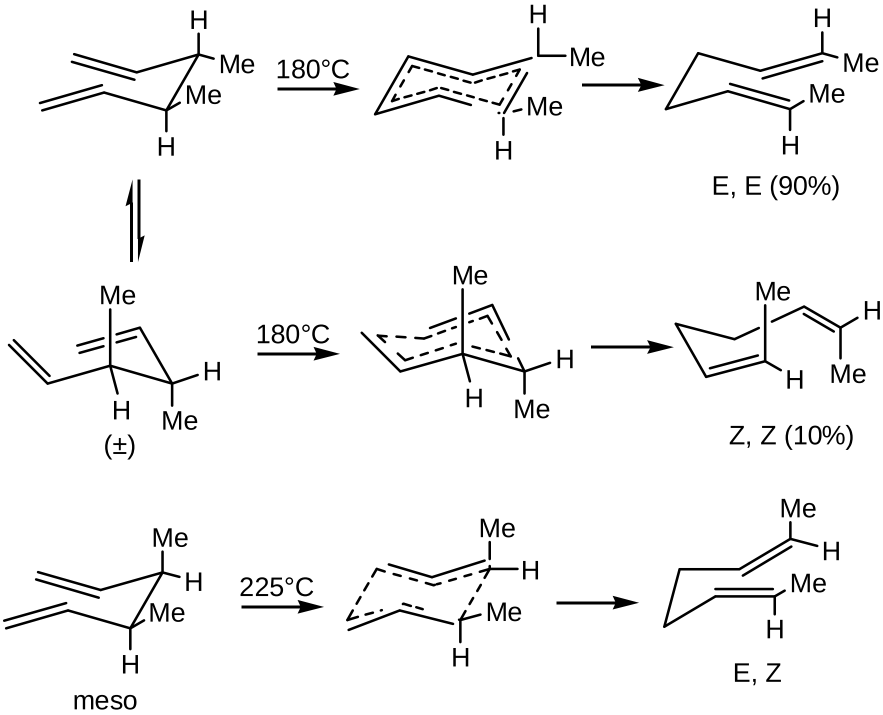
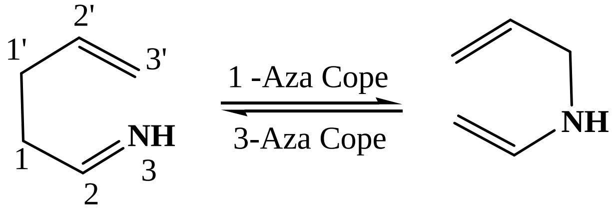


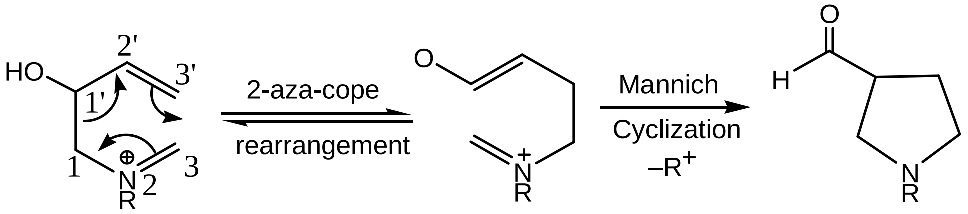
Fig 10.8 Stereoselectivity in the Cope rearrangement

10.5.2 Aza-Cope rearrangement

The Aza cope rearrangement is an example of heteroatom version of cope rearrangement which is [3,3] sigmatropic rearrangement that shifts single and double bonds between two allylic components. Aza-Cope rearrangements are generally classified by the position of the nitrogen in the molecule.



The transformation of an appropriately substituted unsaturated iminium ion to an acyl substituted pyrrolidine by [3,3] sigmatropic rearrangement followed by Mannich cyclization is an example of aza cope rearrangement (Fig 10.9). It is a synthetically powerful reaction, as it is able to create complex cyclic molecules from simple starting materials. The Mannich cyclization is irreversible and its product, an acyl substituted pyrrolidine ring, more stable than that of the rearrangement.



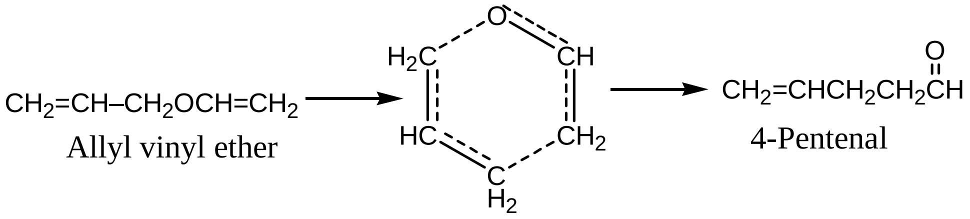
(Fig 10.9)

Transition state stereochemistry

This cationic 2-aza cope rearrangement is characterized by its high stereospecificity which arises from its high preference for a chair like transition state.

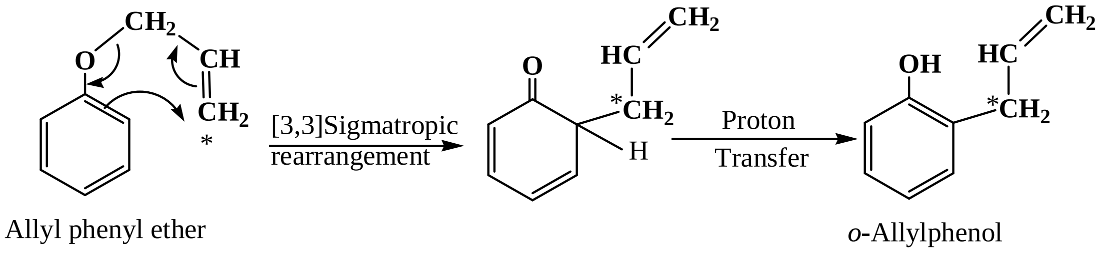
10.5.3 Clasien rearrangement

The simplest example of Claisen rearrangement is the thermal conversion of allyl vinyl ether in to 4-pentenal.



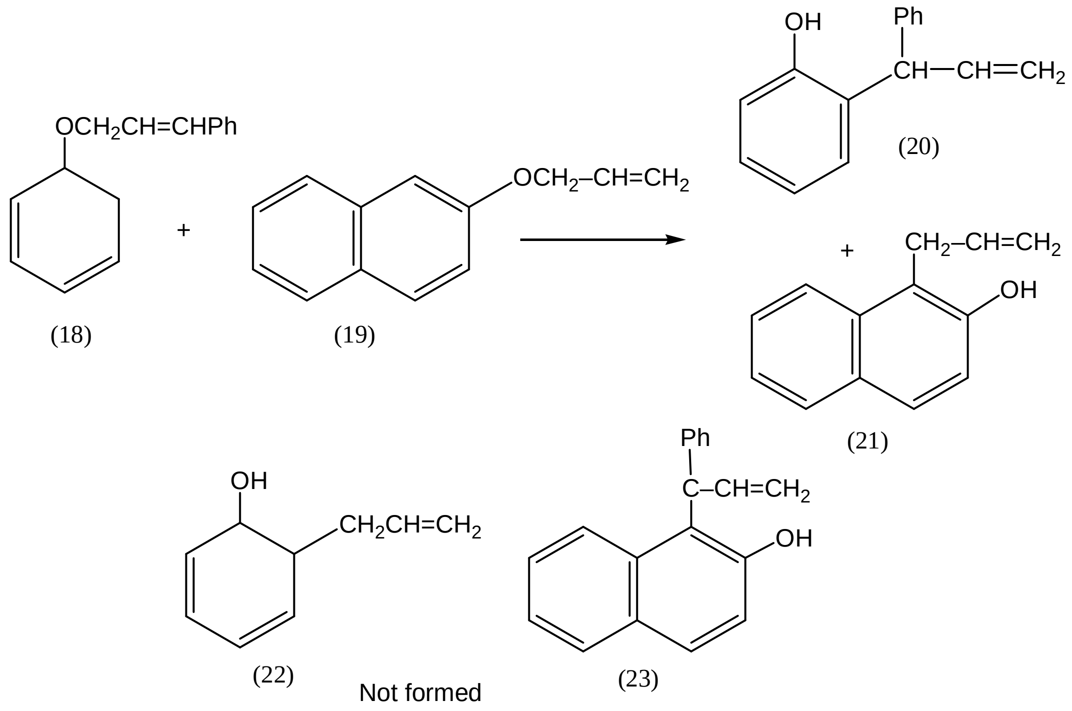
Another example is allyl ethers of phenol. The product of rearrangement is *o*-allyl phenol.This reaction proceeds via [3,3] sigmatropic rearrangement.

An important clue was obtained by the use of ^{14}C labeled allyl phenyl ether. It was noticed that the rearrangement was specific with respect to which carbon atom of the allyl group became bonded to the ring and led to the proposal of the following mechanism.

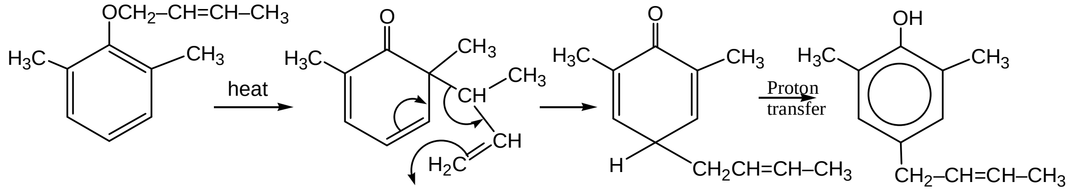


The first step in this reaction is [3,3] sigmatropic rearrangement which is one step mechanism without ionic intermediates. Second step in the reaction is simple ionic proton transfer so that aromaticity could be regenerate.

The intramolecular nature of the rearrangement was firmly established by cross over experiments in which heating of (18) & (19) simultaneously give the same product as they give separately. There is no information of the crossover product (22) & (23).



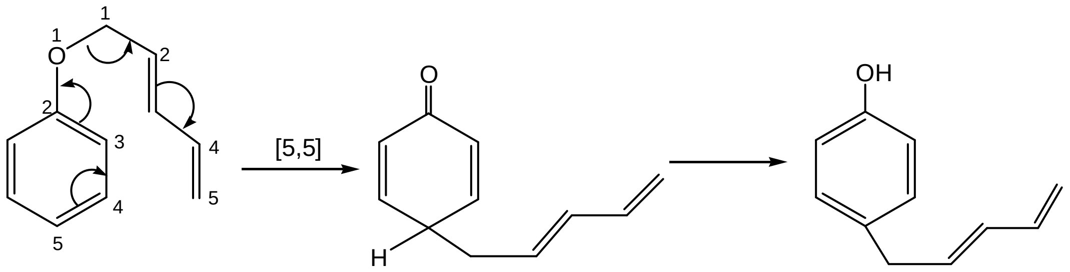
The stereochemical features are very similar to those described for the cope rearrangement. The [3,3] sigmatropic rearrangement proceeds through the chair like six memebered trasition state. The allyl group normally migrates to the ortho position of the aromatic ring. If both ortho position are blocked rearrangement take place at the para position. Initially ortho rearrangement takes place then due to non availability of ortho hydrogen a second rearrangement take place at para position (**Fig 10.10**).



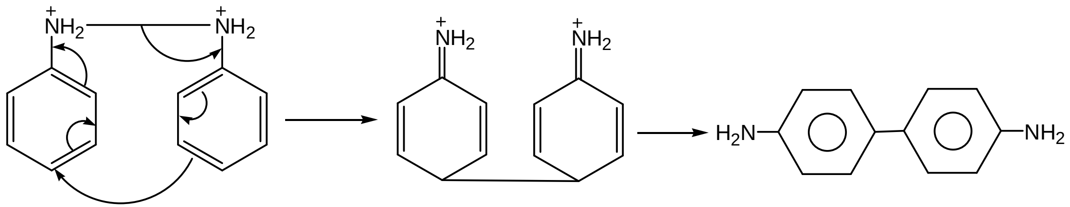
(Fig 10.10)

10.6 [5,5] Sigmatropic Rearrangement

Rearrangement of 2,4-pentadienylphenyl ethers involves [5,5] sigmatropic rearrangement. It can be considered a homologous Claisen rearrangement.



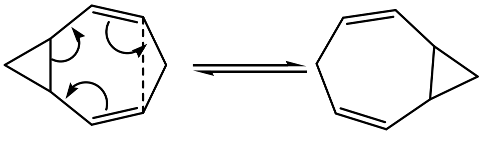
The benzidine rearrangement represents another example of a [5,5] sigmatropic rearrangement.



Benzidine

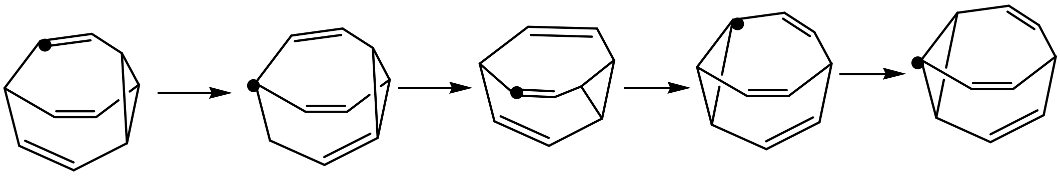
10.7 Fluxional tautomerism (Degenerate rearrangement)

A reaction process in which no overall change in structure occurs are known as degenerate rearrangement (Fluxional tautomerism). Product of rearrangement is structurally identical to the starting material. Depending on the rate at which the reaction occurs, the existence of a degenerate rearrangement can be detected by use of isotopic labels or by interpretation of the temperature dependence of NMR spectra. For e.g. homotropilidene which have dynamic equilibrium, it can be evident by NMR spectrum. The rate of interconversion is slow at low temperature and the spectrum consistent with the presence of four vinyl protons, two allylic protons and four cyclopropyl protons. As the temperature is raised the rate of rearrangement increases. It is observed that two of the vinyl protons remain essentially unchanged with respect to their chemical shift, while the signals of the other two vinyl protons coalesce with those of two of the cyclopropyl protons. Coalescence is also observed between the signals of the allylic protons and the two remaining cyclopropyl protons. It proves that set of protons whose signal coalesce are undergoing sufficiently rapid interchange with one another to result in an averaged signals.



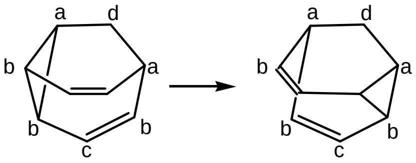
Homotropilidene

Cope rearrangement give by the 1,5-hexadiene is known as degenerate cope rearrangement. Another example is bullvalene, which is converted into itself with a first order rate constant of 3.4×10^{3} s^{-1} at 25°C. At 100°C the ^{1}H NMR spectrum of bullvalene shows a single peak at 4.22 ppm. This indicates the "fluxional" nature of the molecule.



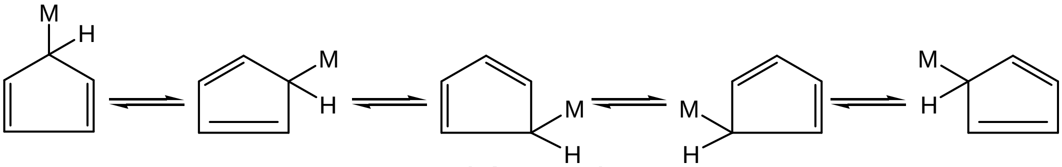
Structure indicating changing enviorment in Bullvalene

Barbaralane rearranges to itself with a rate constant 1.7×10^2 s^{-1} at 25°C. It is less symmetrical than bullvalene. It has 4 different kinds of carbon and proton in the averaged structure. Only methylene group labeled d is not affected by the degenerate rearrangement.



Barbaralane

An another example is of metal cyclopentadiene which involves fluxionality of σ bond with atom migration (Fig 10.11).

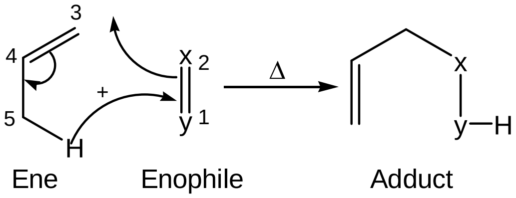


(Fig 10.11)

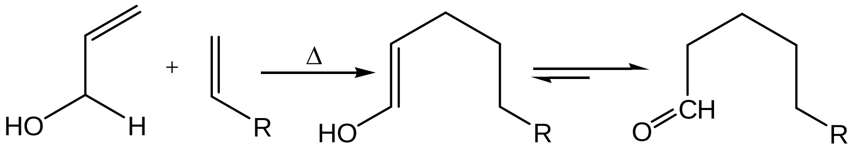
Conversion of one structure into other in fluxional molecule is known as valence isomerism and isomers are known as valence tautomers.

10.8 Ene reaction

Ene reaction is the one of the most common group transfer reaction. It involves the reaction of alkene having an allylic hydrogen (ene) with compound having multiple bond (x=y, x≡y), called enophile. The ene reaction resemble both cycloaddition and a [1,5]-sigmatropic shift of hydrogen.



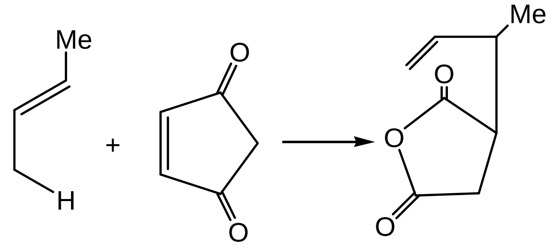
Allylic alcohol gives aldehydes



ene synthesis

During the reaction 1,5 shift of allylic hydrogen along with a shifting of allylic double bond and bonding between two unsaturated termini (one terminus of ene and other terminus of enophile) take place to give 1 : 1 adduct. This reaction is neither sigmatropic nor cycloaddition reaction. Here hydrogen moves from ene to enophile, so this reaction belongs to group transfer reactions.

The reaction involves a suprafacial interaction of all the participating orbitals as in the Diels alder reaction. Activation energy for this reaction is greater than the Diels-Alder reaction. Due to this reason ene reactions takes place at higher temperature. The reaction of trans-2-butene with Maleic anhydride to give predominantly the erythro adduct, which also implies a preference for endo addition.



trans-2-butene   Maleic anhydride

10.9 Summary

Predicted stereochemical course for [1+j] sigmatropic rearrangements in which migrating group is hydrogen

i+j	Thermal reaction	Photochemical reaction
4n	Antarafacial	Suprafacial
4n+2	Suprafacial	Antarafacial

Predicted stereochemical course for [1+j] sigmatropic rearrangements in which migrating group is Carbon (s and a refer Supra and antara; r and i refer to retention and inversion in the configuration at the migrating center)

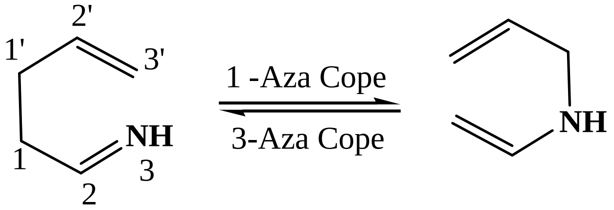
i+j	Thermal reaction	Photochemical reaction

4n	Ar si	sr ai
4n+2	Sr ai	ar si

For [i,j] sigmatropic rearrangements when both i and j greater than 1, selection rules are:

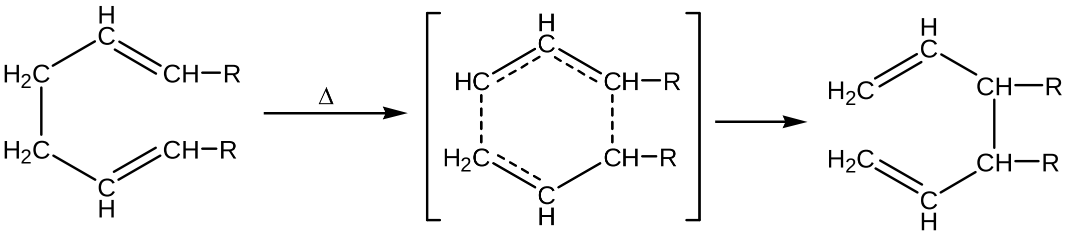
1. [i + j] = 4n : antara supra or supra antara in ground state; supra-supra or antara-antara in excited state
2. [i + j] = 4n + 2 : supra-supra or antara-antara in ground state; antara-supra or supra-antara in excited state

Aza-Cope rearrangement



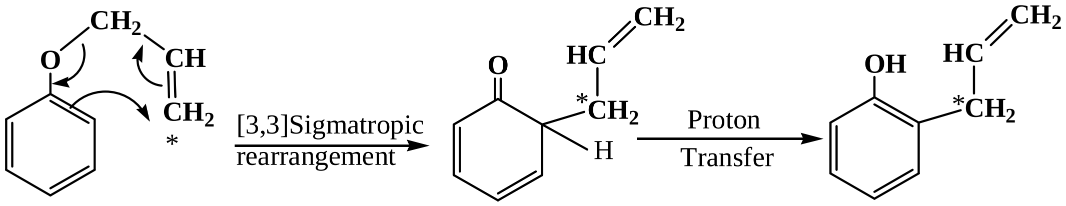
Cope rearrangement

The thermal rearrangement of 1,5-diene through [3,3] sigmatropic shift is known as cope rearrangement.



Clasien rearrangement

Claisen rearrangement is the thermal conversion of allyl phenyl ether in to *O*-allyl phenol.



Fluxional tautomerism

A reaction process in which no overall change in structure occurs are known as degenerate rearrangement (Fluxional tautomerism). Product of rearrangement is structurally identical to the starting material.

Ene reaction

Ene reaction is the one of the most common group transfer reaction. It involves the reaction of alkene having an allylic hydrogen (ene) with compound having multiple bond (x=y, x≡y), called enophile. The ene reaction resemble both cycloaddition and a [1,5]-sigmatropic shift of hydrogen.

10.10 Review Questions

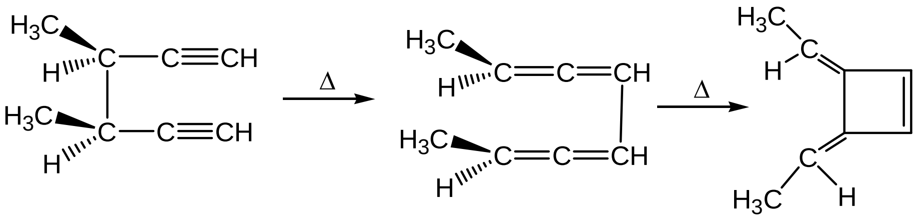
1 Give explanatory notes on the following:

(i) Fluxional tautomerism (ii) Cope rearrangement

(iii) Claisen rearrangement (iv) 1,5-Sigmatropc rearrangement

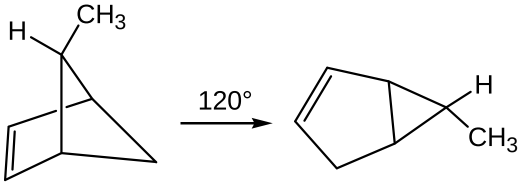
2 What are sigmatropic rearrangements. Give their stereochemistry.

3 Explain the following concerted mechanism:

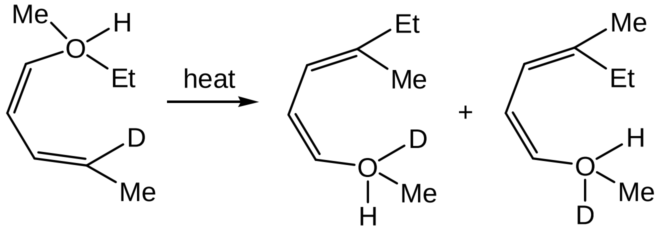


4 In each of the following, the high stereoelectivity or regioselectivity provides conformation of predictions based on the orbital symmetry. Show how this is so

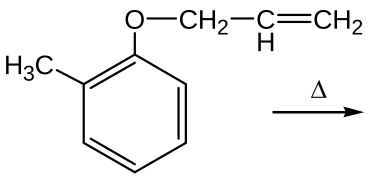
(a)

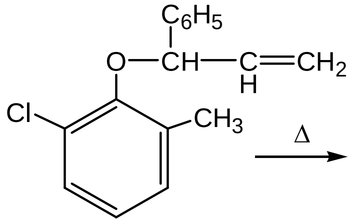


(b)

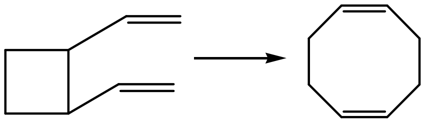


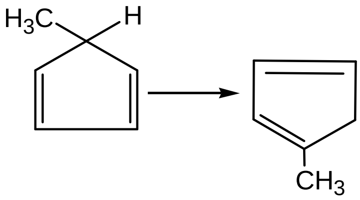
5 Complete the following reaction and give their mechanism :

(a) 

(b) 

6 Indicate the following rearrangements:

(a) 

(b) 

10.11 Reference and Suggested Readings

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- Organic Chemistry - R. T. Morrison and R. N. Boyd, Prentice Hall of India.
- Organic Chemistry, J. Clayden, N. Greeves, S. Warren, Oxford University, Second Edition.
- Principles of Organic Synthesis, R.O.C. Norman and J. M. Coxon, CRC Press.
- Advanced Organic Chemistry Part-B, F. A. Carey and R. J. Sundberg, 5th Ed. Springer.
- Organic Reactions and their Mechanisms, P.S. Kalsi, New Age International Publishers.
- Advanced Organic Chemistry, Jagdamba Singh and L.D.S. Yadav, Pragati Prakashan.

Unit - 11

Electronic Transitions

Structure of Unit

11.1 Objectives

The objective of this chapter gives an overview of basic principle of photochemical reactions of organic molecules.

11.2 Interaction of electromagnetic radiation with matter

Electromagnetic radiation is a self-propagating wave in space or through matter, which consisting of electric and magnetic waves, which are orthogonal, i.e., perpendicular to each other and shown in Fig. 1.

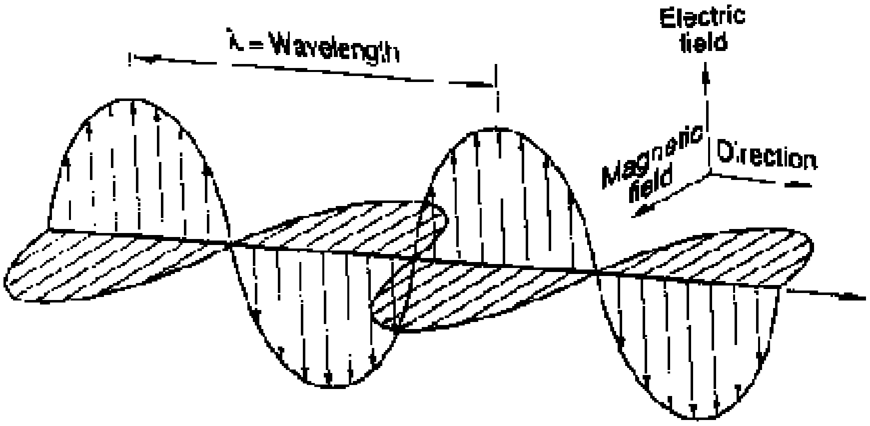


Fig.-1: Electromagnetic waves

Electromagnetic waves can be characterized by either the frequency or wavelength of their oscillations to form the electromagnetic spectrum, which includes, in order of increasing frequency and decreasing wavelength: radio waves, microwaves, infrared radiation, visible light, ultraviolet radiation, X-rays and gamma rays.

The absorption of a radiation by a matter takes it from its ground state into an excited state accompanied by change in electronic distribution, geometry and uncoupling of electron spin. Electrons can move from the ground-state energy level of a molecule to a higher level (i.e., an unoccupied orbital of higher energy) if outside energy is supplied. The reactant absorbs light emitted by the source. The light to be absorbed, the compound must have an energy level that corresponds to the energy of the radiation. Organic photochemical reactions usually involve excited electronic states. In a photochemical process, this energy is in the form of light. Light of any wavelength has associated with it an energy value given by $E = hv$, where v is the frequency of the light, and h is Planck's constant. Since the energy levels of a molecule are quantized, the amount of energy required to raise an electron in a given molecule from one level to a higher one is a fixed quantity. Only light with exactly the frequency corresponding to this amount of energy will cause the electron to move to the higher level. If light of another frequency (too high or too low) is sent through a sample, it will pass out without a loss in intensity, since the molecules will not absorb it. However, if light of the correct frequency is passed in, the energy will be used by the molecules for electron promotion, and hence the light that leaves the sample will be diminished in intensity or altogether gone. The energy of electronic transitions corresponds to light in the visible, UV, and far-UV regions of the spectrum.

In most organic molecules, all electrons in the ground state are paired, with each member of a pair possessing opposite spin as demanded by the Pauli principle. When one of a pair of electrons is promoted to an orbital of higher energy, the two electrons no longer share an orbital, and the promoted electron may, in principle, have the same spin as its former partner or the opposite spin. A molecule in which two unpaired electrons have the same spin is called a triplet, while one in which all spins are paired is a singlet. Thus, at least in principle, for every excited singlet state there is a corresponding triplet state. In most cases, the triplet state has a lower energy than the corresponding singlet, which is in accord with Hund's rule. Therefore, a different amount of energy, and hence a different wavelength is required to promote an electron from the ground state (which is almost always a singlet) to an excited singlet than to the corresponding triplet state. The designations S and T are used for singlet and triplet states, respectively. It would thus seem that promotion of a given electron in a molecule could result either in a singlet or a triplet excited state depending on the amount of energy added.

11.3 Types of excitations

Absorption of light in the ultraviolet and visible regions produces changes in the electronic energies of molecules associated with excitation of an electron from a stable to an unstable orbital. Because the energy required to excite the valence-shell electrons of molecules is comparable to the strengths of chemical bonds, absorption may lead to chemical reactions. The lower energy state is known as bonding orbital. The higher state orbital is described by antibonding orbital. The antibonding orbital are associated with the σ and π bond that are σ* and π*. The n orbital does not form bond, which is called nonbonding. The various electronic transitions are shown in Fig. 2.

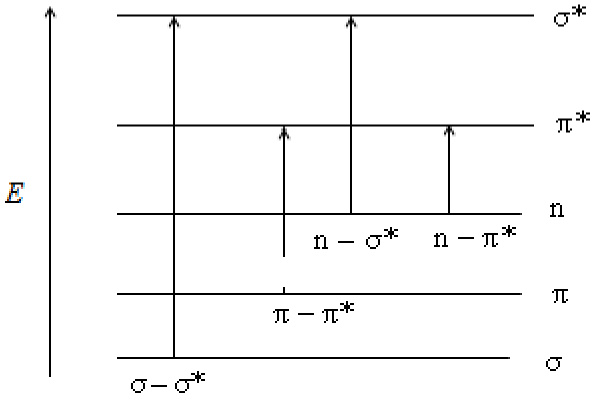


Fig. 2: Electron excitation

For most organic molecules, there are consequently four types of electronic excitation

(1) σ - σ* : Alkanes, which have no n or p electrons, can be excited only in this way.

(2) n - σ* : Alcohols, amines, ethers, and so on, can also be excited in this manner.

(3) π - π*: This pathway is open to alkenes as well as to aldehydes, carboxylic esters, and so on.

(4) n - π*: Aldehydes, ketones, carboxylic esters, and so on, can undergo this promotion as well as the other three.

The four excitation types above are listed in what is normally the order of decreasing energy. Thus light of the highest energy (in the far uv) is necessary for σ - σ* excitation, while n - π* excitations are caused by ordinary uv light. However, the order may sometimes be altered in some solvents. In 1,3-butadiene (and other compounds with two conjugated double bonds) there are two π and two π* orbitals. The energy difference between the higher π and the lower π* orbital is less than the difference between the π and π* orbitals of ethylene. Therefore 1,3-butadiene requires less energy than ethylene, and thus light of a higher wavelength, to promote an electron. This is a general phenomenon, and it may be stated that, in general, the more conjugation in a molecule, the more the absorption is displaced toward higher wavelengths.

11.5 The Fate of excited molecule: Physical Processes

When a molecule has been photochemically promoted to an excited state, it does not remain there for long. Most promotions are from the ground singlet state S_0 to the excited singlet state S_1 state. However, promotions from S_0 to triplet states are ''forbidden.'' Promotions to S_2 and higher singlet states take place, but in liquids and solids these higher states usually drop very rapidly to the S_1 state (10^{-13}– 10^{-11} s). The energy lost when an S_2 or S_3 molecule drops to S_1 is given up in small increments to the environment by collisions with neighboring molecules. Such a process is called an energy cascade. In a similar manner, the initial excitation and the decay from higher singlet states initially populate many of the vibrational levels of S_1, but these also cascade, down to the lowest vibrational level of S_1. Therefore, in most cases, the lowest Potential energy vibrational level of the S_1 state is the only important excited singlet state. This state can undergo various physical and chemical processes. In the following list, it describes the physical pathways open to molecules in the S_1 and excited triplet states. These pathways are also shown in a Jablonski diagram (Fig. 3). Following processes may take place from excited state.

1. A molecule in the S_1 state can cascade down through the vibrational levels of the S_0 state and thus return to the ground state by giving up its energy in small increments to the environment, but this is generally quite slow because the amount of energy is large. The process is called

internal conversion (IC). Because it is slow, most molecules in the S_1 state adopt other pathways.

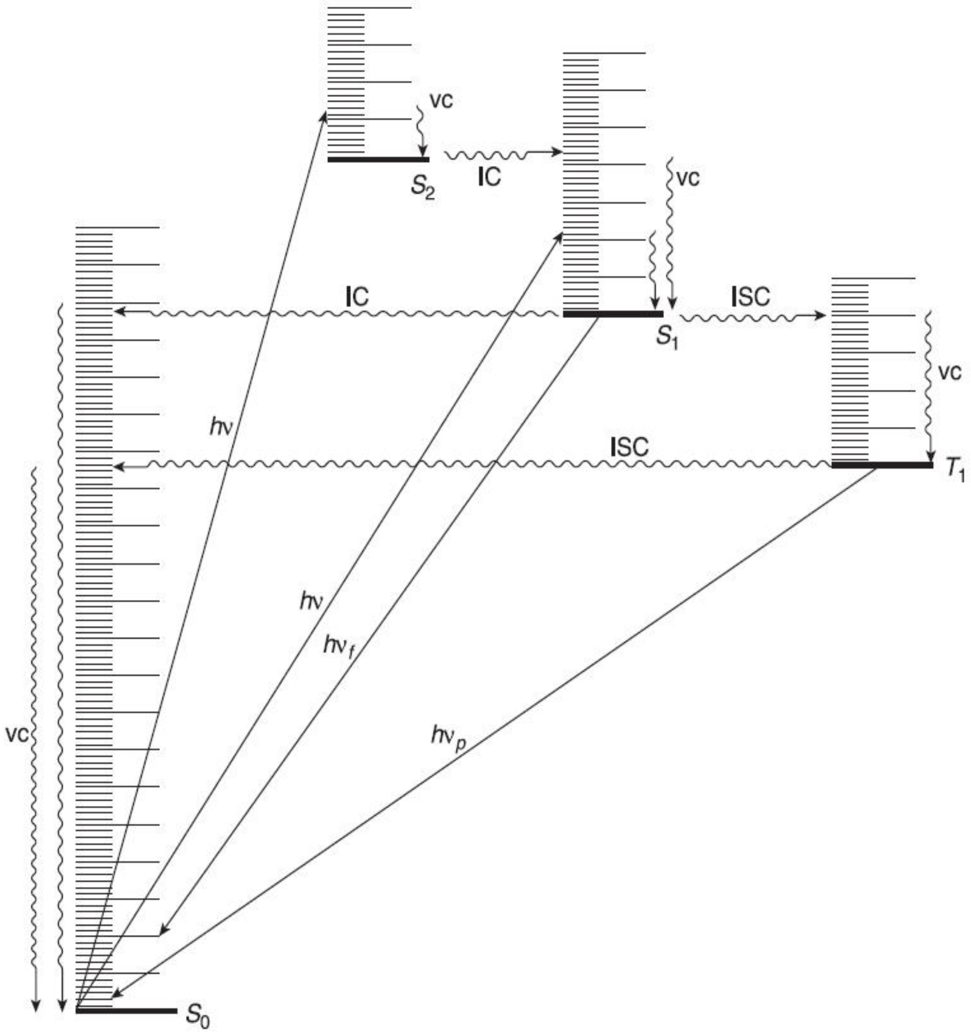


Fig. 3: Jablonski diagram

2. A molecule in the S_1 state can drop to some low vibrational level of the S_0 state all at once by giving off the energy in the form of light. This process, which generally happens within 10^{-9} s, is called fluorescence. This pathway is not very common either (because it is relatively slow), except for small molecules, for example, diatomic, and rigid molecules, for example, aromatic. For most other compounds, fluorescence is very weak or undetectable. For compounds that do fluoresce, the fluorescence emission spectra are usually the approximate mirror images of the absorption spectra. This comes about because the fluorescing

molecules all drop from the lowest vibrational level of the S_1 state to various vibrational levels of S_0, while excitation is from the lowest vibrational level of S_0 to various levels of S_1. The only peak in common is the one (called the 0–0 peak) that results from transitions between the lowest vibrational levels of the two states.

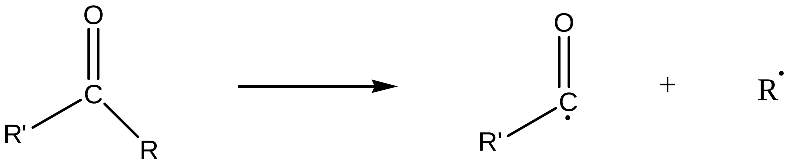
3. Most molecules (though by no means all) in the S_1 state can undergo an intersystem crossing (ISC) to the lowest triplet state T_1. An important example is benzophenone, of which ~100% of the molecules that are excited to the S_1 state cross over to the T_1. Intersystem crossing from singlet to triplet is a ''forbidden'' pathway. Intersystem crossings take place without loss of energy. Since a singlet state usually has a higher energy than the corresponding triplet, this means that energy must be given up. One way for this to happen is for the S_1 molecule to cross to a T_1 state at a high vibrational level and then for the T_1 to cascade down to its lowest vibrational level. This cascade is very rapid (10^{-12} s). When T_2 or higher states are populated, they too rapidly cascade to the lowest vibrational level of the T_1 state.
4. A molecule in the T_1 state may return to the S_0 state by giving up heat (intersystem crossing) or light (this is called phosphorescence). Both are very slow (10^3-10^1 s). This means that T_1 states generally have much longer lifetimes than S_1 states. When they occur in the same molecule, phosphorescence is found at lower frequencies than fluorescence (because of the higher difference in energy between S_1 and S_0 than between T_1 and S_0) and is longer-lived (because of the longer lifetime of the T1 state).
5. If nothing else happens to it first, a molecule in an excited state (S_1 or T_1) may transfer its excess energy all at once to another molecule in the environment, in a process called photosensitization. The excited molecule (donor) thus drops to S_0 while the other molecule (acceptor) becomes excited. Thus there are two ways for a molecule to reach an excited state: by absorption of a quantum of light or by transfer from a previously excited molecule. The donor is also called a photosensitizer. This energy transfer is subject to the Wigner spin-conservation rule, i.e., the total electron spin does not change after the energy transfer.
6. An excited species can be quenched. Qunching is the deactivation of an excited molecular entity intermolecularly by an external environmental influence (e.g., a quencher) or intramolecularly by a substituent through

a nonradiative process. When the external environmental influence (quencher) interferes with the behavior of the excited state after its formation, the process is referred to as dynamic quenching. Common mechanisms include energy transfer, charge transfer, and so on. When the environmental influence inhibits the excited state formation the process is referred to as static quenching. A quencher is defined as a molecular entity that deactivates (quenches) an excited state of another molecular entity, either by energy tranfer, electron transfer, or by a chemical mechanism. An example is the rapid triplet quenching of aromatic ketone triplets by amines, which is well known. Alkyl and aryl thiols and thioethers also serve as quenchers in this system.

11.5.1 The Fate of excited molecule: Chemical processes

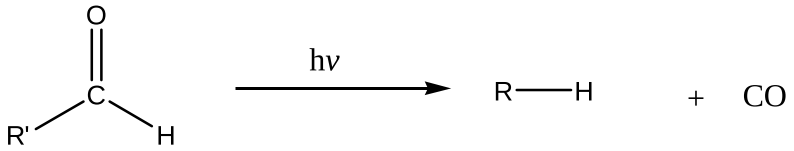
Although both excited singlet and triplet species can undergo chemical reactions, they are much more common for triplets, simply because these generally have much longer lifetimes. Excited singlet species, in most cases, have a lifetime of $<10^{-10}$ s and undergo one of the physical processes already discussed before they have a chance to react chemically. Therefore, photochemistry is largely the chemistry of triplet states. These reactions may be unimolecular or bimolecular reactions. The following possible chemical pathways can be taken by an excited molecule.

1. **Simple Cleavage into Radicals:** Aldehydes and ketones absorb in the 230–330-nm region. This is assumed to result from an n - π* singlet–singlet transition. The excited aldehyde or ketone can then cleave.

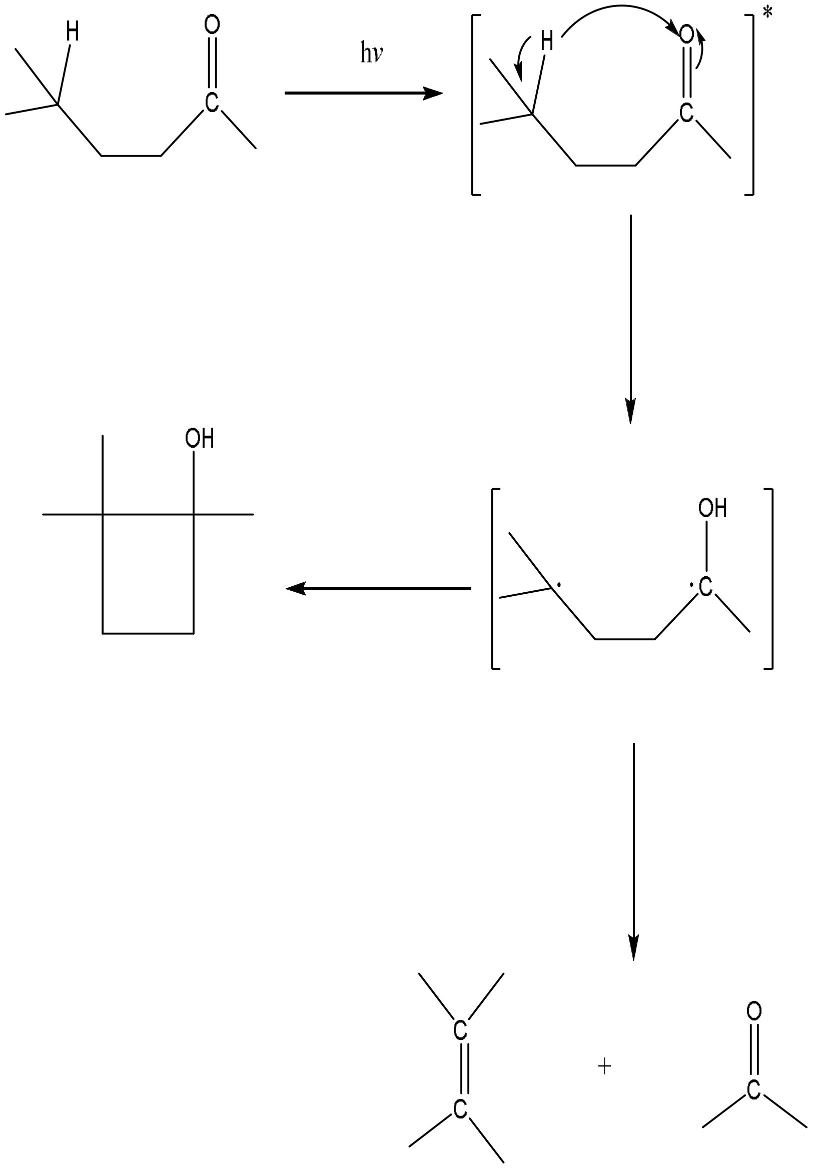


   When applied to ketones, this is called Norrish Type I cleavage or often just Type I cleavage. In a secondary process, the acyl radical can then lose CO to give alkyl radicals. Another example is cleavage of Cl_2 to give two Cl atoms.

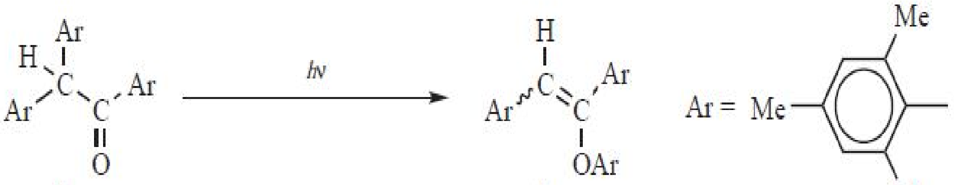
2. **Decomposition into Molecules:** Aldehydes (though not generally ketones) can also cleave in this manner,



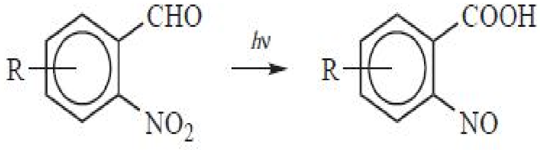
This is an extrusion reaction. In another example is Norrish Type II cleavage, involves intramolecular abstraction of the γ hydrogen followed by cleavage of the resulting diradical (a secondary reaction) to give an enol that tautomerizes to the aldehyde or ketone product. Both singlet and triplet n,π* states undergo the reaction.



3. **Intramolecular Rearrangement:** Two examples are the rearrangement of the trimesityl compound (1) to the enol ether (2), and irradiation of o-nitrobenzaldehydes (3) to give o-nitrosobenzoic acids (4).

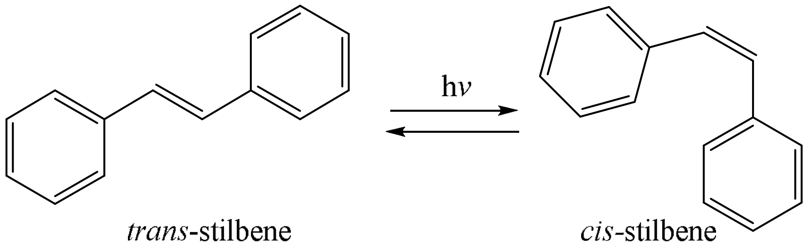


1 2



3 4

4. **Photoisomerization:** The most common reaction in this category is photochemical cis–trans isomerization. For example, cis-stilbene can be converted to the trans isomer, and the photoisomerization of O-methyl oximes is known.



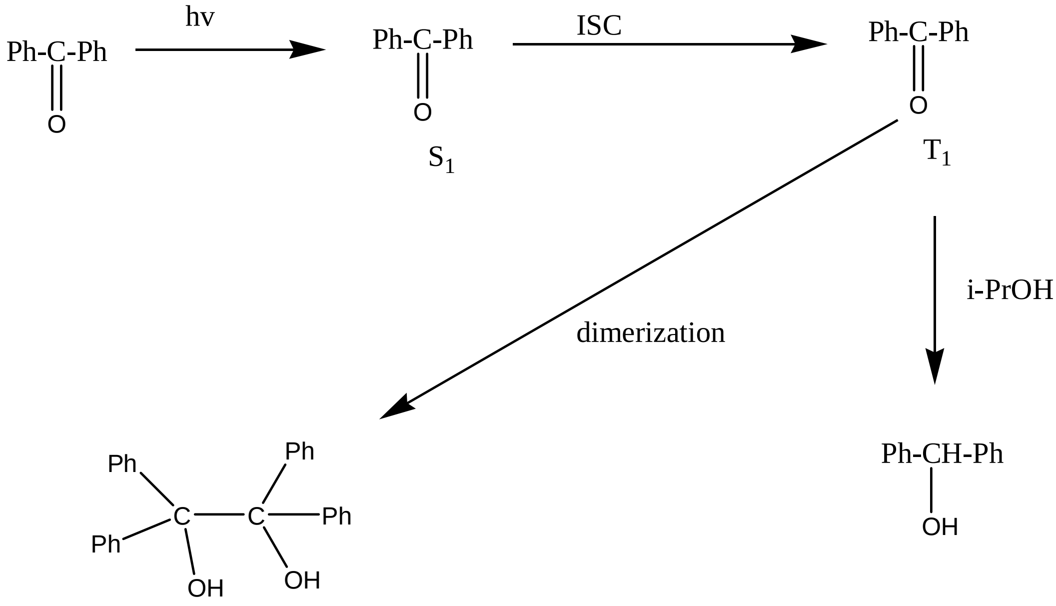
trans-stilbene
7%

cis-stilbene
93%

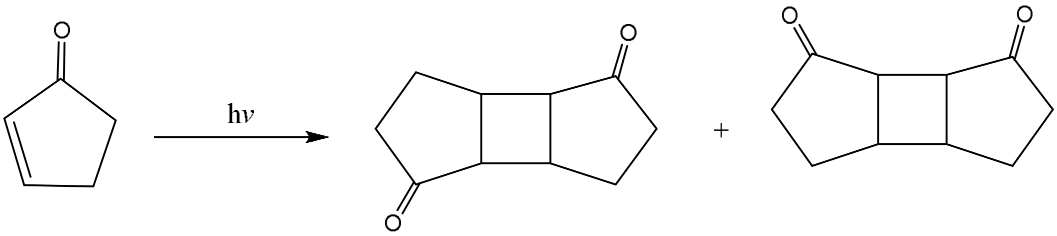
The isomerization takes place because the excited states, both S_1 and T_1, of many alkenes have a perpendicular instead of a planar geometry, so cis–trans isomerism disappears upon excitation. When the excited molecule drops back to the S_0 state, either isomer can be formed. A useful example is the photochemical conversion of cis-cyclooctene to the much less stable trans isomer. Another interesting example of this isomerization involves azo crown ethers.

5. **Hydrogen-Atom Abstraction:** When benzophenone is irradiated in isopropyl alcohol, the initially formed S_1 state crosses to the T_1 state,

which abstracts hydrogen from the solvent to give the radical. Then radical abstracts hydrogen to give benzhydrol or dimerizes to benzpinacol.



6. **Photodimerization:** An example is dimerization of cyclopentenone



11.5 Quantum Yield

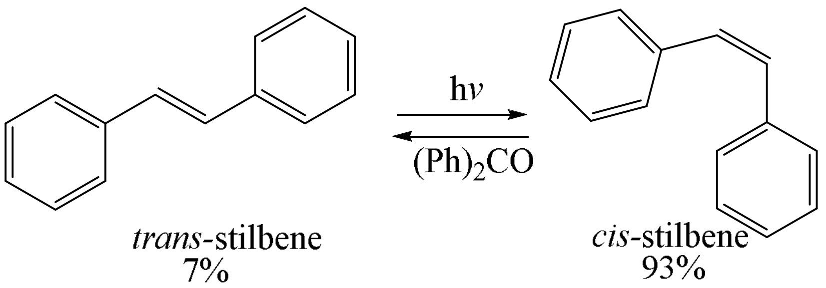
The quantum yield is the fraction of absorbed light that goes to produce a particular result. There are several types. A primary quantum yield for a particular process is the fraction of molecules absorbing light that undergo that particular process. Thus, if 10% of all the molecules that are excited to the S1 state cross over to the T1 state, the primary quantum yield for that process is 0.10. However, primary quantum yields are often difficult to measure. A product quantum yield (usually designated ϕ) for a product P that is formed from a photoreaction of an initially excited molecule A can be expressed as

$$\phi = \frac{\text{number of molecules of P formed}}{\text{Number of quanta abosrbed by A}}$$

Product quantum yields are much easier to measure. The number of quanta absorbed can be determined by an instrument called an actinometer, which is actually a standard photochemical system whose quantum yield is known. An example of the information that can be learned from quantum yields is the following. If the quantum yield of a product is finite and invariant with changes in experimental conditions, it is likely that the product is formed in a primary rate-determining process.

11.7 Energy Transfer

A triplet sensitizer absorbs the radiation undergo vibrational relaxation and intersystem crossing to its triplet state and then taking part in an energy transfer process with alkene. It is more efficient if triplet sensitizer has just a little higher in triplet state energy than one of the alkene isomer and lowers than other isomer. In such situation the alkene isomer with lower triplet energy is sensitized more efficiently than the isomer with higher triplet energy and the result is a photostationary state rich in the latter isomer. For example,



There is a ketone such as benzophenone is raised by an n - π* transition from the singlet ground state (S_0) to an excited state (S_1) by absorption of light. Intersystem crossing then occurs rapidly to give the triplet state (T_1) of the sensitizer.

$$[(C_6H_5)\ ^{1} \qquad [(C_6H_5)_2\ ^{3} \qquad [(C_6H$$

The next step is excitation of the alkene by energy transfer from the triplet state of the sensitizer.

$$[Ph - C = C -\ ^{3} \qquad [(C_6H_5)^{3} \qquad [Ph - C = C - Ph] + (C_6$$

Remember, the net electron spin is conserved during energy transfer, which means that the alkene will be excited to the triplet state. The triplet state of the alkene is most stable when the *p* orbitals, which make up the normal π-system of the double bond, are not parallel to one another. Therefore, if the energy-transfer process leads initially to a planar triplet, this is converted rapidly to the more stable nonplanar form. The excitation of either the *cis* or the *trans* isomer of the alkene appears to lead to a common triplet state.

$$^{3}[\mathrm{Ph-C=C-Ph}] \rightarrow cis-\mathrm{stilbene}\ (93\%) + trans-\mathrm{stilben}$$

11.8 Summery

- Electromagnetic radiation is a self-propagating wave in space or through matter, which consisting of electric and magnetic waves, which are orthogonal.
- The lower energy state is known as bonding orbital. The higher state orbital is described by antibonding orbital. The orbital does not form bond, which is called nonbonding.
- Fat of excited molecules describe by Jablonski diagram.
- A molecule drops from higher singlet state to lower singlet state is called internal conversion (IC).
- A molecule in the executed singlet state can undergo an intersystem crossing (ISC) to the lowest triplet state T_1.
- The quantum yield is the fraction of absorbed light that goes to produce a particular result.

11.9 Review Question

1. Explain the following concepts

(a) Quantum Yield

(b) Intersystem crossing

(c) Hydrogen-Atom Abstraction

(d) Interaction of electromagnetic radiation with matter

2. What is electron transition and explain it?

3. Explain the energy transfer process with example?

11.10 Reference and Suggested readings

- Introduction To Organic Photochemistry, John D. Coyle, John Wiley & Sons Ltd, 1986

- March's Advanced Organic Chemistry , J. March, 6th edition, John Wiley & Sons Ltd, 2007

Unit -12

Photochemistry of Carbonyl Compound

Structure of Unit :

12.1 Objectives

Photochemistry has provided a revolutionary advantage in various biological and chemical processes. It helps to explain the phenomenon of photosynthesis, phototaxis, mutagenic effects of light radiations, vision and photodynamic action. Many chemicals, which can not be synthesized by dark reactions, are produced by photochemical methods. These photosynthesized chemical have great advantage due to higher efficiency and selectivity. Photochemistry provides a phenomenon of fluorescence and phosphorescence, which is collectively known as photo physical phenomenon. For basic researches in photochemical field, the understanding of photo physical, photo biological and photo chemical process is essential.

In this chapter, our objective to explain the mechanism of various photo chemical reactions of carbonyl compound which have vast application in chemical industries.

12.2 Introduction

Photochemistry of Carbonyl Compounds:

Carbonyl compound especially ketones, undergo many interesting and versatile reaction on irradiation. Ketones exhibit mainly four band in their UV absorption spectra. The most important band is at 280 nm for the photochemistry of carbonyl compounds. The reaction is initiated by n- π^* transition. Promotion of an electron will lead to either a singlet state or a triplet state. Photochemical reaction given by carbonyl group takes place either by singlet state or by triplet or by both states.

$$\rangle C = \underset{\bullet\bullet}{\overset{\bullet\bullet}{O}} \xrightarrow{h\nu} \rangle \overset{\bullet}{C} - \underset{\bullet\bullet}{\overset{\bullet\bullet}{O}}\bullet \leftrightarrow \rangle \overset{\bullet\bullet}{C} - \underset{\bullet}{\overset{\bullet\bullet}{O}}\bullet$$

Carbonyl compounds give four type of reaction.

These are:-

(1) Norrish type I process or α-cleavage.

(2) Norrish type II process or β cleavage

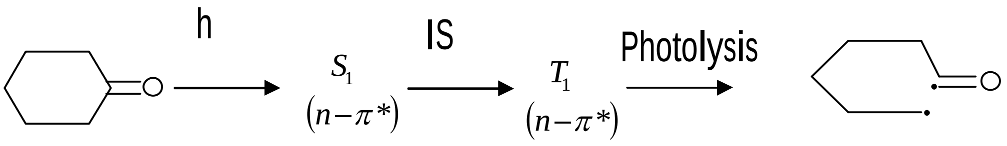
(3) Intramolecular and Intermolecular hydrogen abstraction by carbonyl Oxygen.

(4) Photocyclo addition reaction and oxetane formation.

12.3 Norrish type I process or α-cleavage

The bond dissociation energy of carbon-carbon bond adjacent to a carbonyl is comparatively small and consequently photo chemical excitation of ketones usually results in the homolytic fission of the α-cleavage or Norrish type 1 reaction. It occurs more readily in vapour phase. In the initial primary process, a diradical is formed by photolysis of cyclohexanone and their it is followed by secondary process, which result in formation of a mixture of carbon mono-oxide, cyclopentane and 5-hexenal.

Primary Process:-

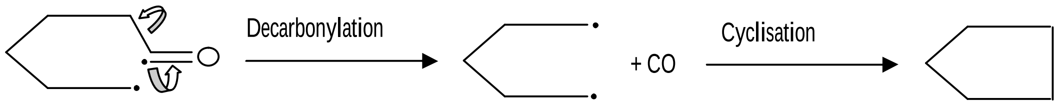


Cyclohexanone

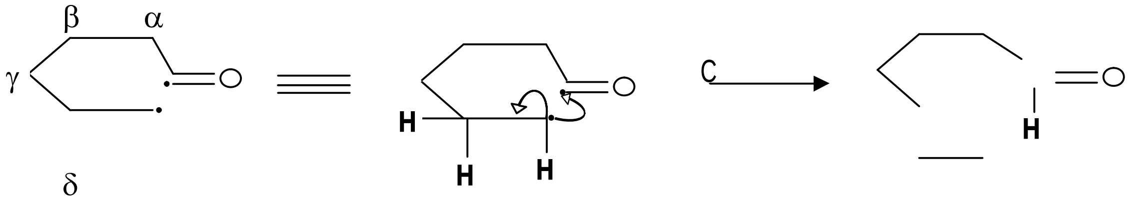
Free radical

Secondary Process:-

(i)



(ii)



Cyclohexenal

Basically Norrish type I process is given by three types of ketones :-

(I) Saturated cyclic ketones.

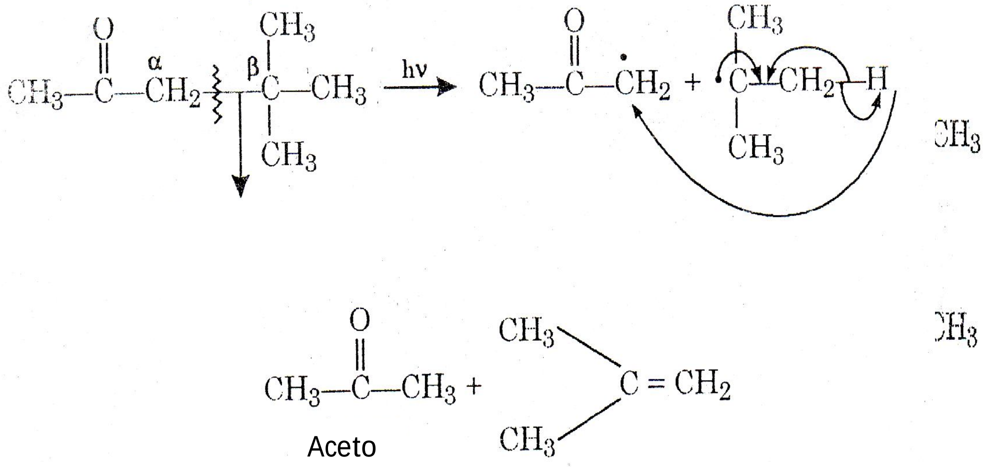
(II) Saturated acyclic ketones.

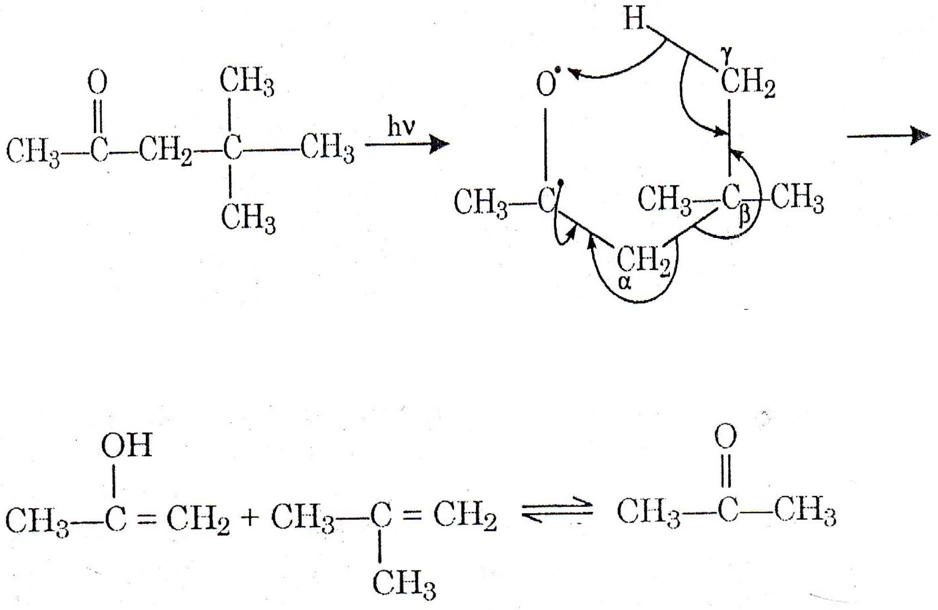
(III) β.γ unsaturated ketones

12.4 Norrish type II process or β-cleavage

Norrish type II reaction is possible If bond between α and β - carbon is weak. If reaction occurs in open chain compounds, the abstraction of hydrogen atom take place from γ - carbon atom and If system is cyclic the abstraction of hydrogen is from δ-Carbon .

In saturated acyclic compound:-





In this reaction bond breaking take place between α and β -carbon due to steric hindrance and hydrogen is abstracting from γ-carbon to carbonyl oxygen.

In saturated closed compound:

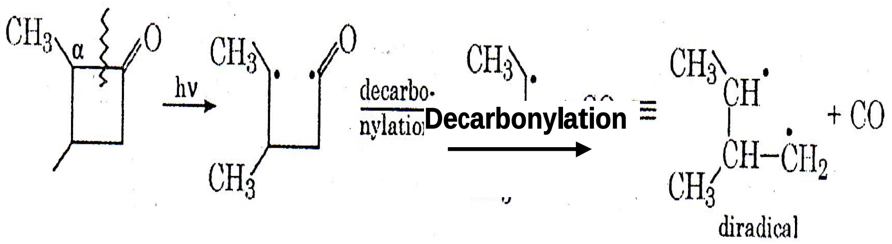
In these compound β-cleavage take place by the hydrogen abstraction from the γ-carbon.

12.5 Intramolecular reaction of Carbonyl compound by saturated cyclic ketones:-

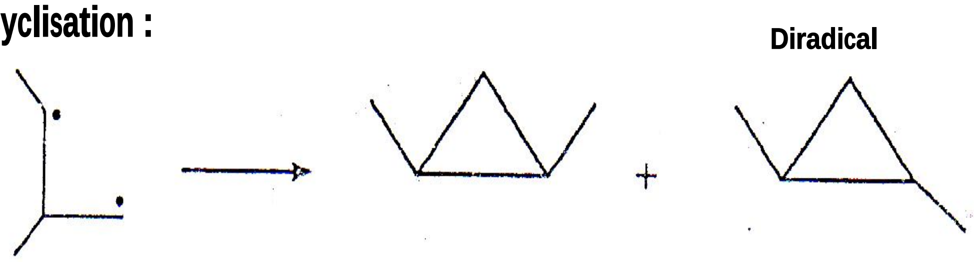
Intramolecular reaction in cyclic ketones occurs by α-cleavage. On photolysis, cyclic ketones give a biradical species. These photo reaction take place in solution or gas phase. After formation of a biradical, a hydrogen atom is abstracted from α-carbon, finally it yields hydrocarbons and olefines.

In Monocyclic Ketonic Compounds : -

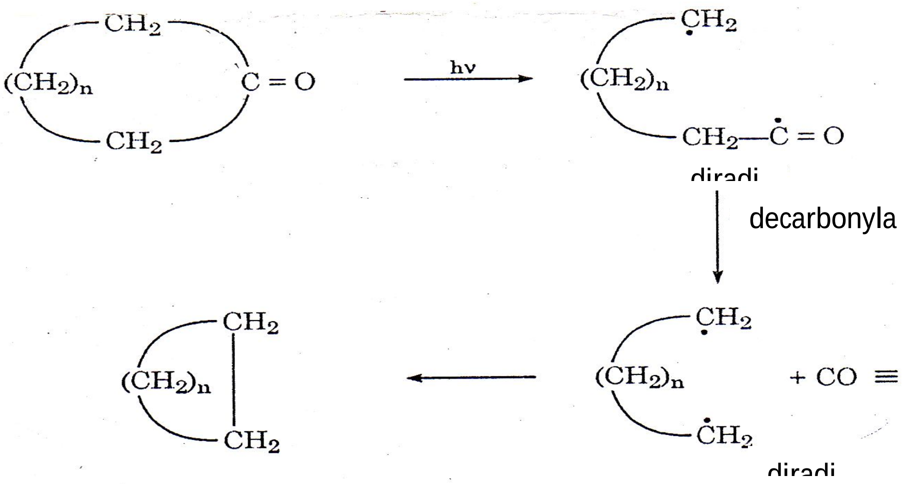
(a)

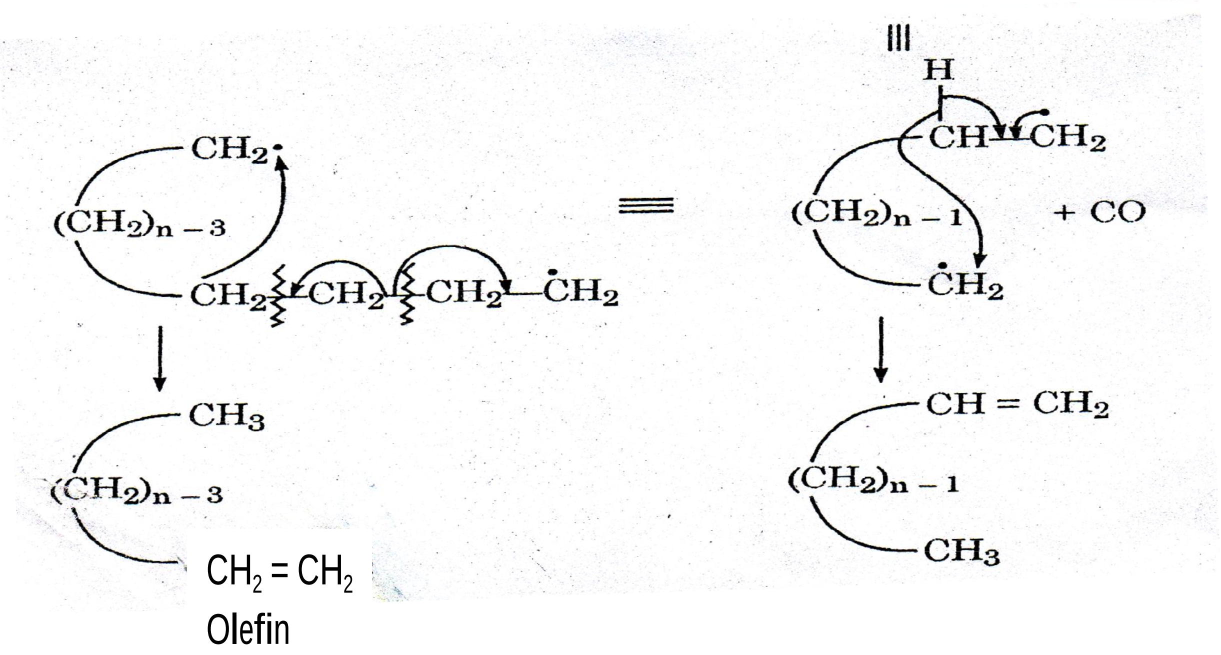


On cyclisation :



(B)

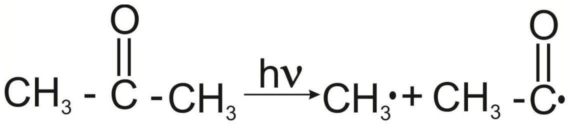




12.6 Intramolecular reaction of Carbonyls compound by saturated Acylic Ketones:

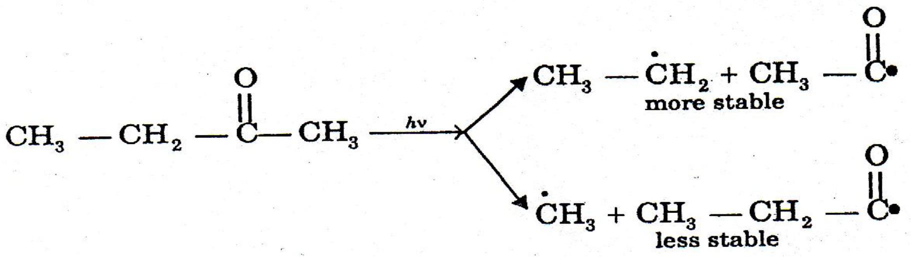
These types of reaction are carried out by all those compound which have carbonyl group, but aromatic ketones like penzophenone and acetophenone do not give these reactions. α-cleavage reaction should always be carried out in gaseous forms.

Stap (a) Acetone forms an alkyl and acyl free readical :

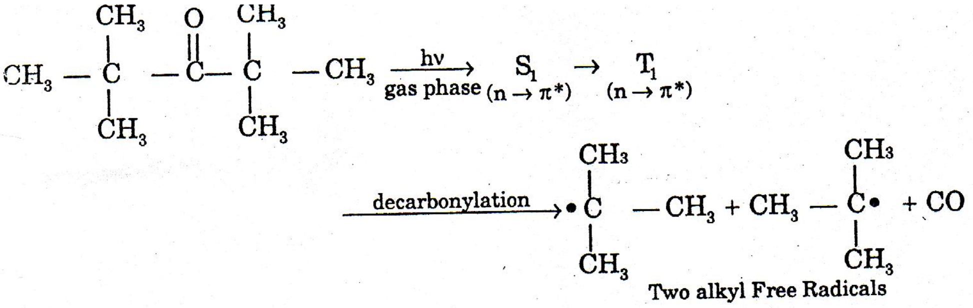


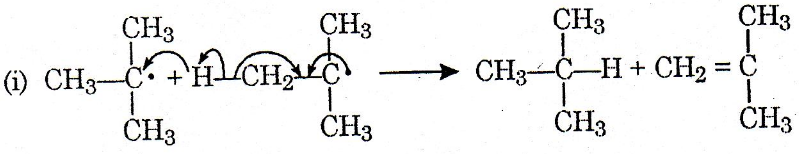
$$CH_3 - \overset{\overset{O}{\|}}{C} - CH_3 \xrightarrow{h\nu} CH_3^{\bullet} + CH_3 - \overset{\overset{O}{\|}}{C}{\bullet}$$

When two α-bonds are not identical in position, then weaker bond has to be broken

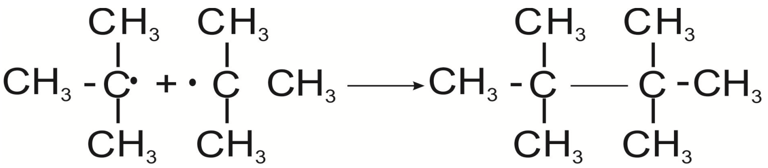


Step (b) In the secondary process of reaction, decarbonylation from acyl free radical, disproportionation, and abstraction of hydrogen atom take place.





(II) Recombination



$$CH_3-\underset{CH_3}{\overset{CH_3}{C\cdot}} + \cdot\underset{CH_3}{\overset{CH_3}{C}}\,CH_3 \longrightarrow CH_3-\underset{CH_3}{\overset{CH_3}{C}}-\underset{CH_3}{\overset{CH_3}{C}}-CH_3$$

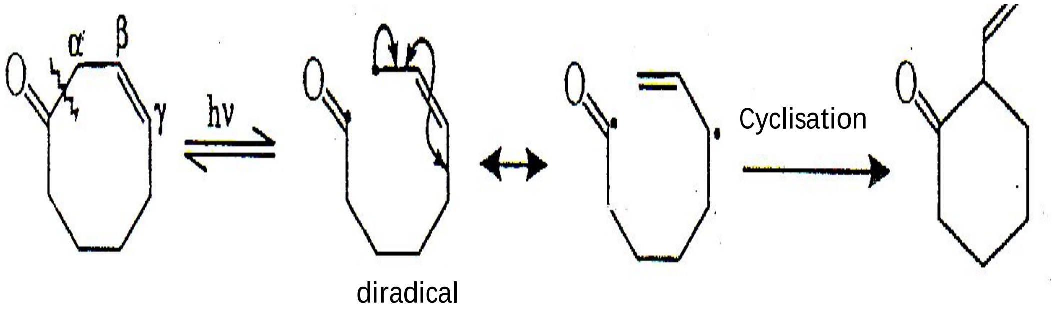
12.7 Intramolecular reaction in β,γ unsaturated Carbonyl Compound:

This reaction also consist of α-cleavage. The overall reaction follows by two steps

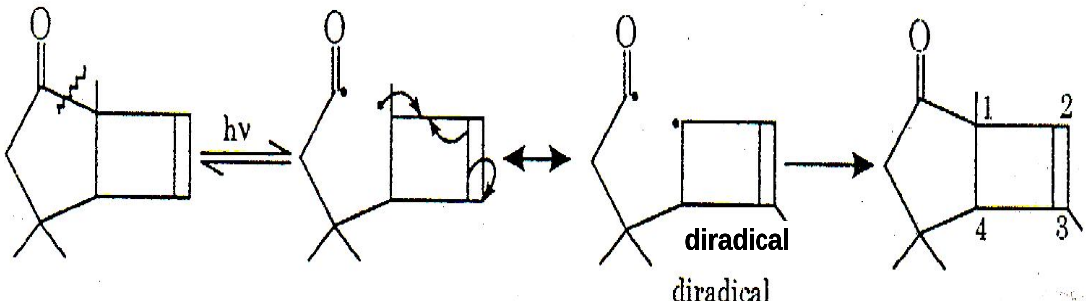
case I - 1,3-acyl shifts is involved, which form an isomeric β, γ-Unsaturated ketones.

Case II - Ring closure process take place.

(1)

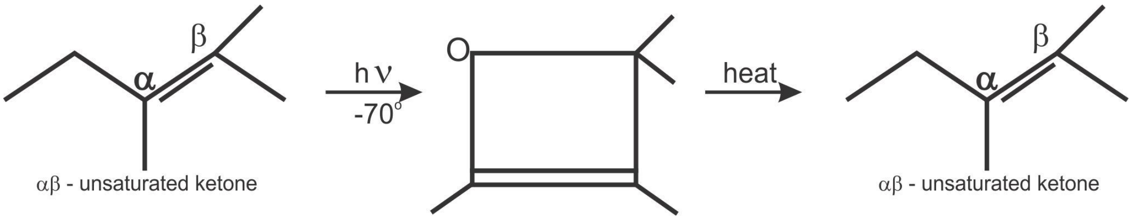


(2)



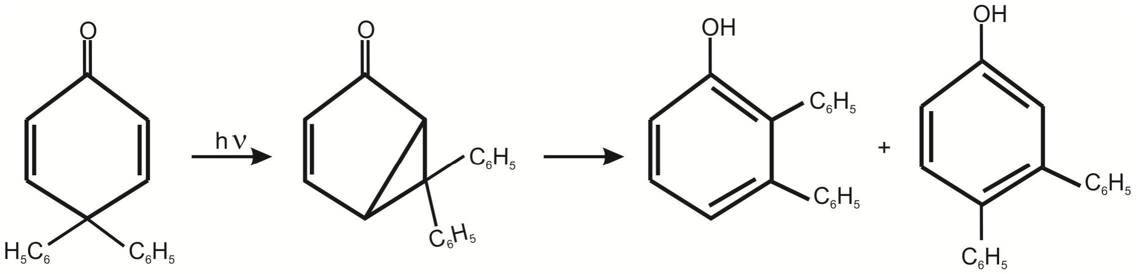
12.8 Intramolecular reaction of α-β- Unsaturated carbonyl compound

Intramolecular reaction of α, β - unsaturated carbonyl compound gives oxetene at –70^{o}C. On heating this product, it can be converted into reactant.



12.9 Intramolecular photoreaction of cyclo hexadienones

Such type of reaction is the photochemical rearrangement of compounds containing the cyclohexadienone chromophore. 4,4-Diphenylcyclo-hexadinenone (I), is rapidly isomerized to a ketone (II) and two phenols (III) and (IV) on irradiation.

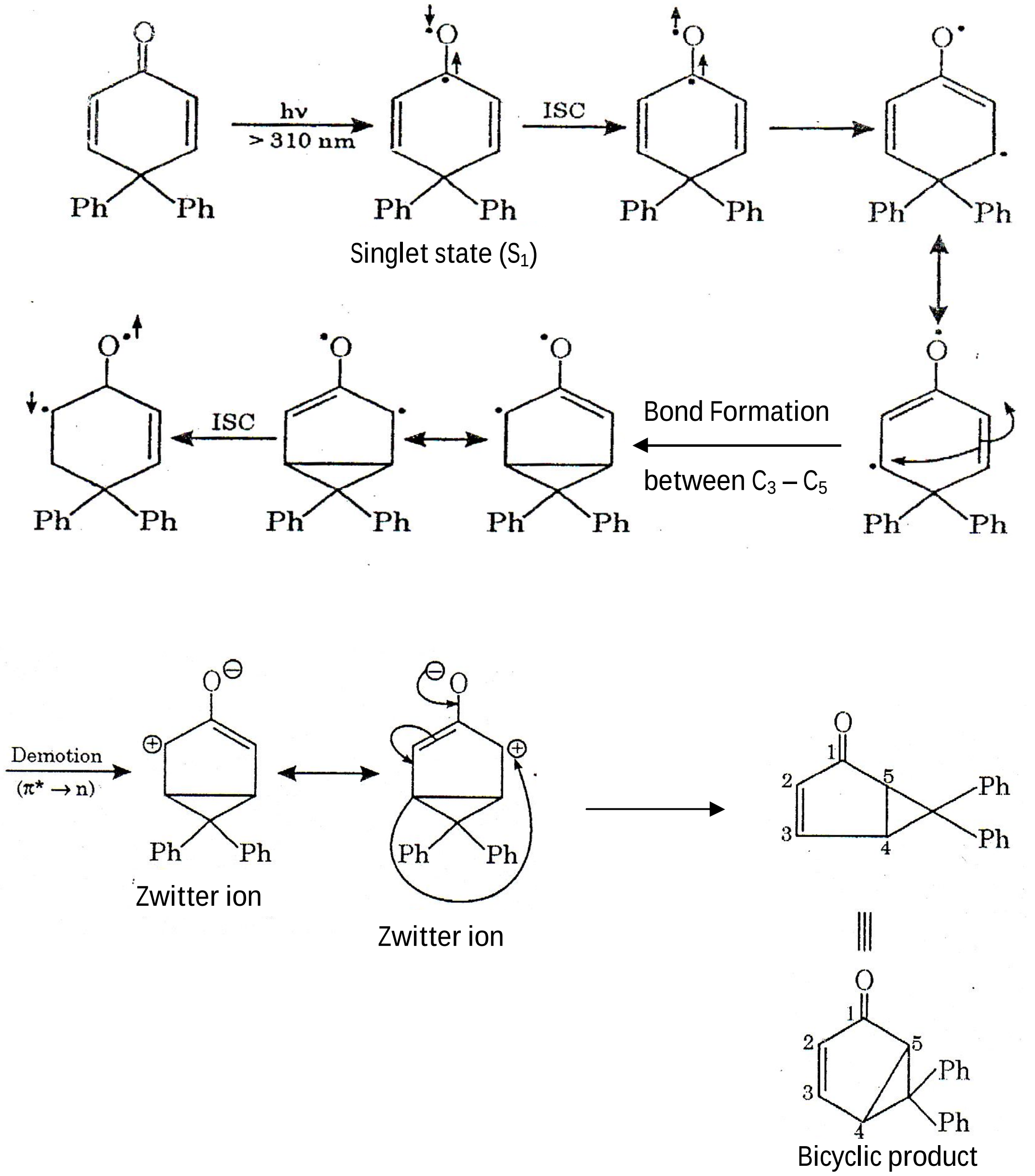


(I) (II) (III) (IV)

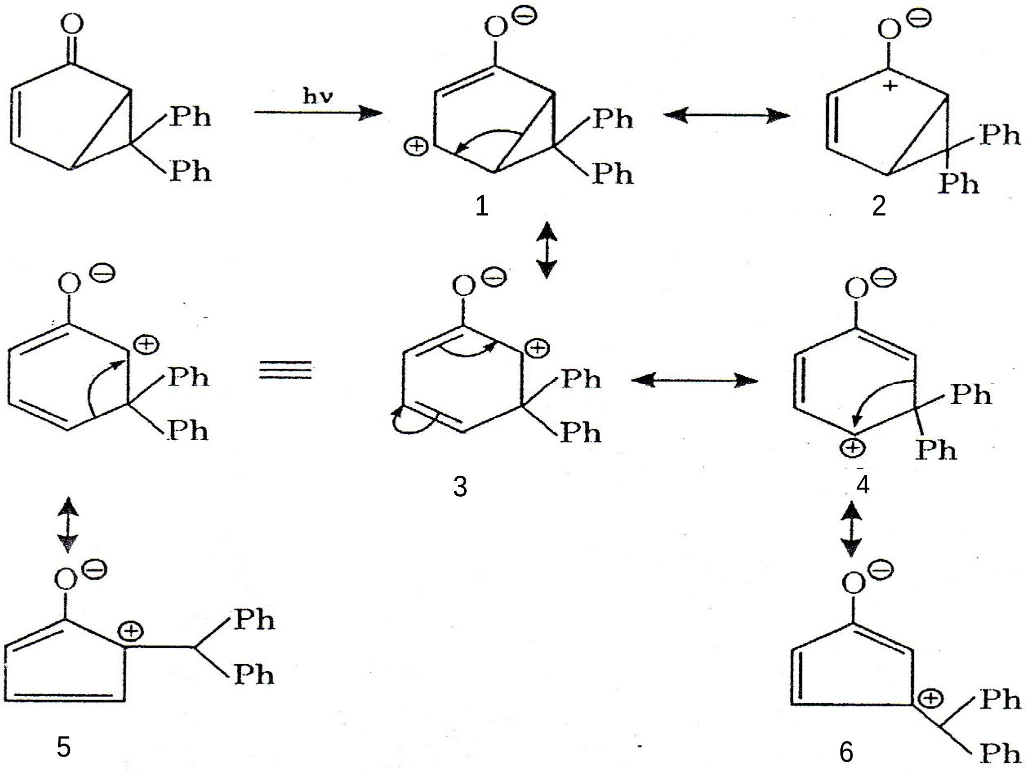
Cyclohexadienone displays absorption at about 300 nm (n-π*) and at 240 nm (π-π*).

The mechanism is given by Zimmerman. The reactive excited state is n-π* triplet state of the dionones. A new bond is formed between C_3 and C_5. After the formation of bond, the reaction is followed by ISC, i.e., intersystem crossing. Before formation of a final bicyclic product, an intermediate zwitter ion is formed. This intermediate help of manage the acyclic product.

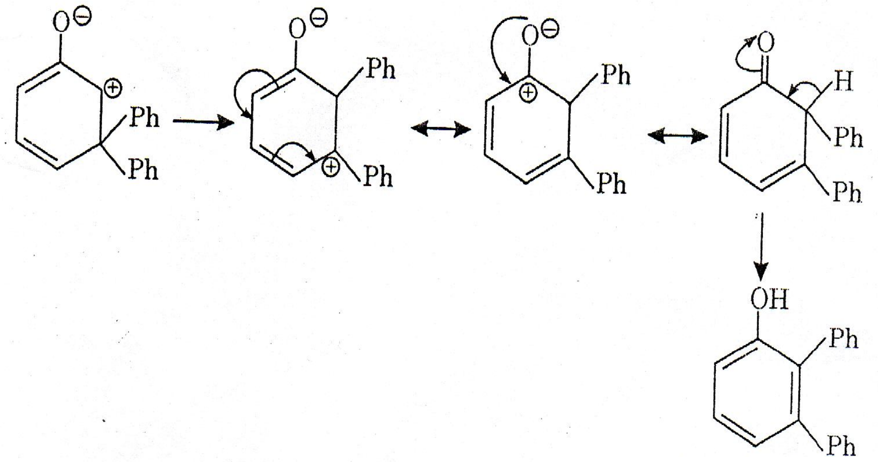
Mechanism

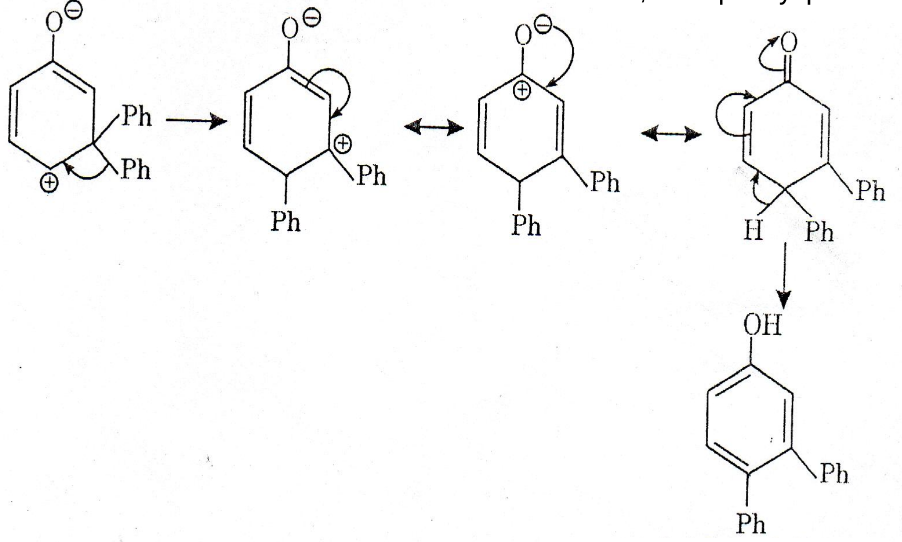


The bicyclic product can again undergo the rearrangement, because still it consists of an enone systems which may capable of undergoing to n-π* excitation.

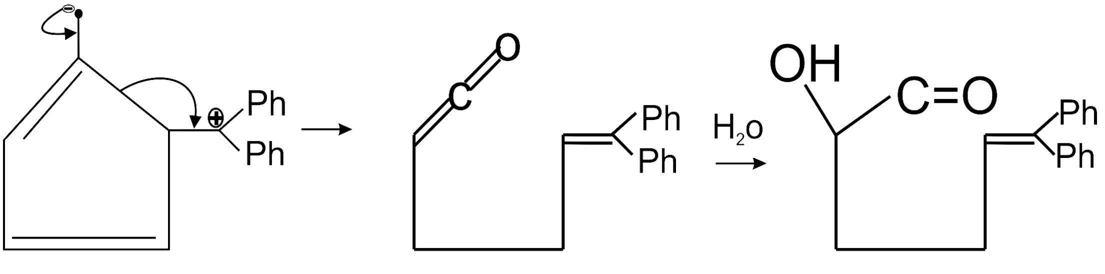


In cyclohexaclienones, the π*-n electron demotion state comes due to electron rich π system in n-π* state. But the observed rearrangements are characteristic of migration of electron deficient centres. Out of above (1) to (6) products, product (3) and (4) can undergo phenyl migration and form 2, 3 and 3,4-diphenyl phenol, respectively.


2, 3 – diphenyl phenol


3,4 – diphenyl phenol

If medium is aqueous, than the structure no (5) can rearrange and gives a ketones and then form an acid.

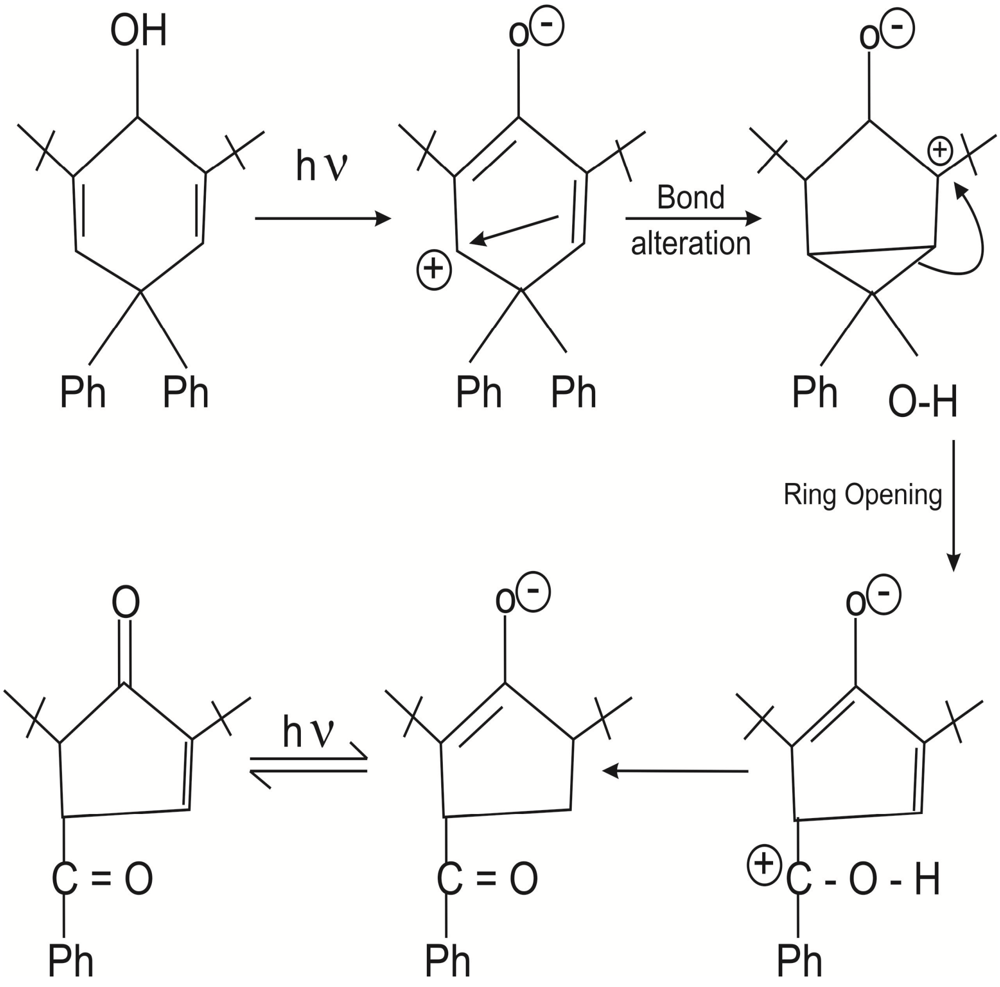


Ketene

Acid

(5)

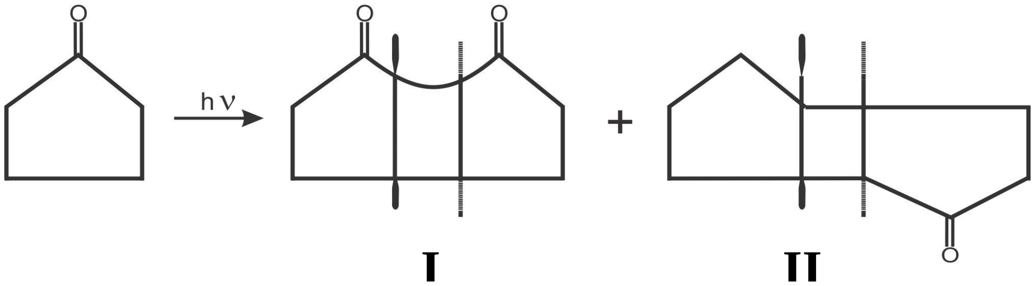
If one of the phenyl group is replaced by an hedroxy group, ring opening takes place rather than phenyl group migration.



12.10 Intermolecular Cycloaddition reaction

Photocyclodimerization

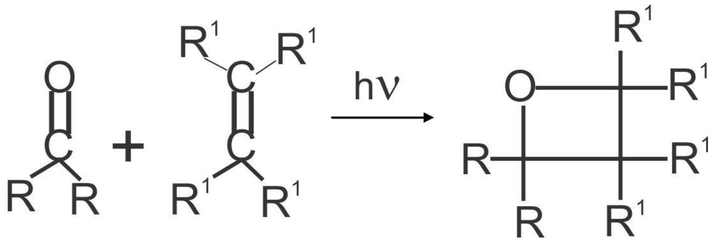
Intermolecular photodimerization of α, β-unsaturated ketones occur most readily in cyclic systems. on irradiation, it gives two photo dimers undergoing across the carbon-carbon double bond by π-π*state. For example Irradiation of cyclopentenone yields head-to-head (I) and head-to-tail(II) dimers. head-to-head dimers are preferred in polar solvent, while non-polar solvent favour had to tail dimers.



I II

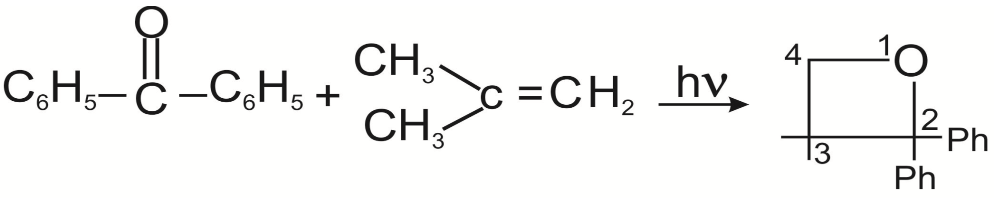
Intermolecular cycloaddition Reaction: (Formation of oxetane)

Carbonyl compounds yield oxetane on irradiation in the presence of olefin. This photocycloaddition reaction of carbonyl compound is known as paterno-Buchi reaction.

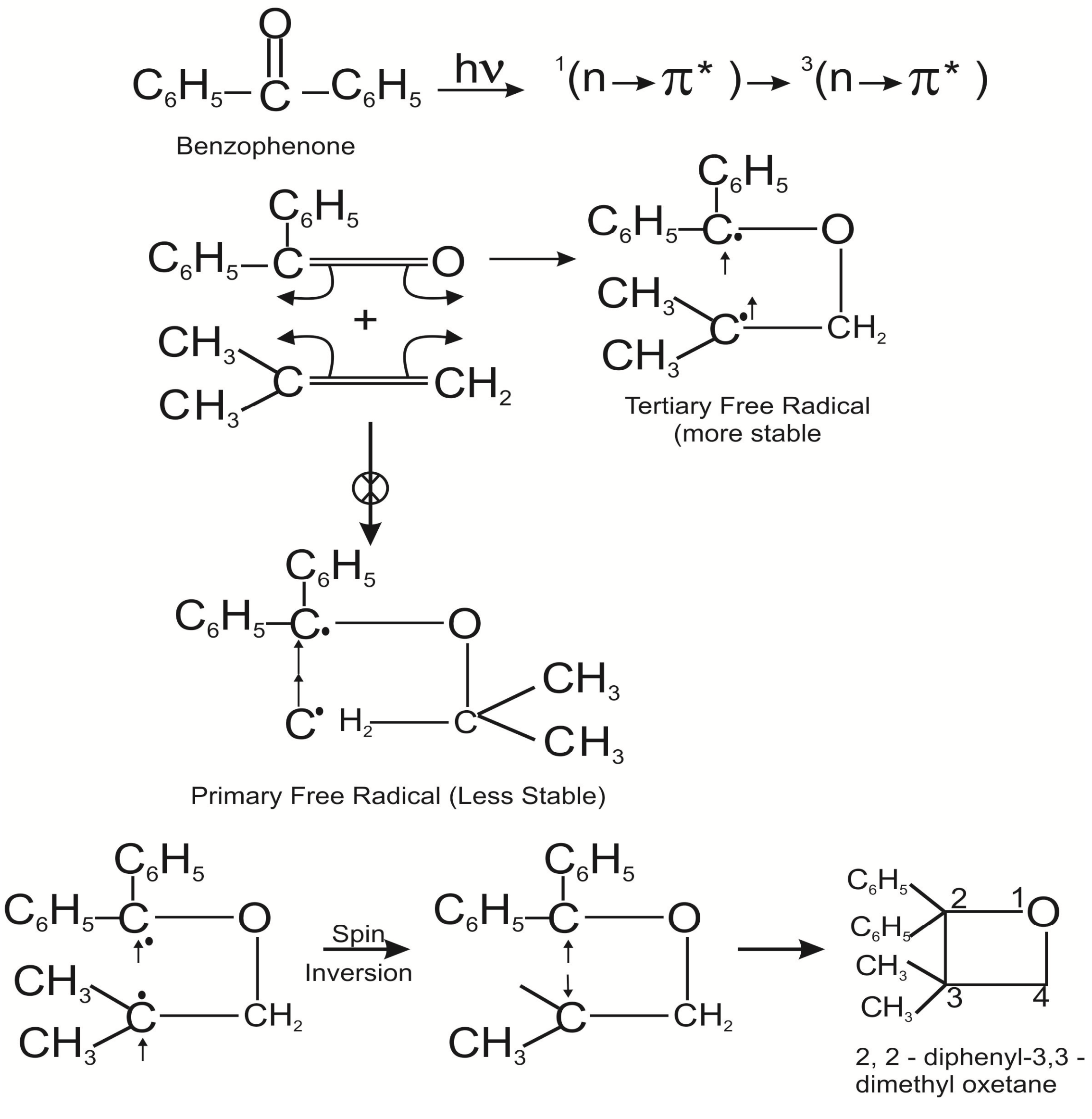


The addition is usually performed by irradiation with the light and it involve the excited state of carbonyl compounds rather than that of the olefin. The light energy required for the n-π^* transition initiated the reaction in simple carbonyl compounds.

In this reaction oxygen atom of the ketone ^{3}(n-π^*) add to an unsaturated compound and form a stable diradical Intermediate followed by a final product, called oxetane, on irradiation.



Reaction-Mechanism



Other example of patern Buchi reaction in which reaction of Benzophenone with Cis and trans 2-butene, yields the same mixture of both isomeric oxetone.

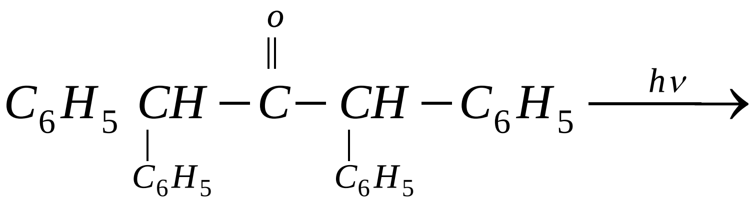
Drawback of the paterno-Buchi reaction is the competing energy transfer process from the excited ketone to the olefine, in cases where the triplet energy of the former exceed that of the latter. For example irradiation of acetone with norbornene, yields dimers of norbornene rather than oxetanes.

12.11 Summary

We know that carbonyl groups adsorb light from 230-330 nm region. In the photochemistry of ketone, each of primary reaction occurs from the n-π^* triplet state and final product can be formed after the secondary process. Here we concluded that photochemical reaction of carbonyl compound are found in four basic photochemical processes. These are as follows – (1) α cleavage or Norrish type – I Process which carried out for those substrate having two α bonds. It is the week bond which will break first. (2) β cleavage or Norrish type II reaction. If a β bond to the carbonyl group has to be cleavaged during a photochemical reaction, an abstraction of intramolecular hydrogen bond in take place (3) If the reaction is intermolecular, the hydrogen atom will abstract from the oxygen of carbonyl group. (4) Addition of carbonyl oxygen occurred to a carbon-carbon double bond means cycloaddition and cyclodimerisation reaction.

12.12 Review questions/Comprehensive questions

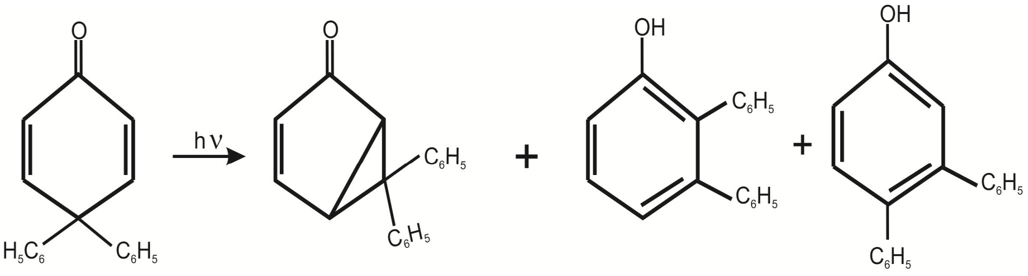
1. Carbonyl compound give mainly four types of photochemical reaction. Give name of the reaction with one example each?
2. What type of excitation are possible in a compound containing carbonal group on irradiation with UV light?
3. Give meehauism of Nanish time I process how many types of combining compound times this reaction?
4. Write note on photodimerisation of α, β unsaturated ketones?
5. What is paterno-Buchi reaction? Discuss its mechanism along with the stereochemical consequences?
6. Irradiation of norbornene with benzophenone leads to the formation of the corresponding oxetane? However dimer of norbornehe is obtained on the Irradiation of narbornene with acetophenone. How do you explain these results?
7. Complete the following norrish type I reaction : -



$$C_6H_5\underset{\underset{C_6H_5}{|}}{CH}-\overset{\overset{o}{\|}}{C}-\underset{\underset{C_6H_5}{|}}{CH}-C_6H_5\xrightarrow{h\nu}$$

8. What will the product of the reaction when carvone camphor is irradiated with UV light in the presence of MeOH?

9. Irradiation of 4, 4 – diphenyl cyclohexadienone (1) yields a mixture of three products (2), (3), & (4). Explain a suitable mechanism for this transformation.



(I) (II) (III) (IV)

0 Explain the following

(1) photochemistry of cyclic ketone

(2) Photochemistry of acyclic ketone

11. Discus the mechanism of intramalecular photoreactions in β, γ-unsaturated carbonly.

12.13 References and suggested reading :

- "Advanced organic chemistry" structure and mechanism, A.Carey, Richard J.Sundberg, fifth edition, francies, Springer 2007.
- "Reaction mechanism in organic chemistry" S.M. Mukherji, S.P. Singh, Macmillan India Limited, 1996
- "Photochemistry and pericyclic reaction" Jagdamba Singh & Jaya Singh, New age international publishers, 2012.

- "Essential of molecular photochemistry" A. Gilbert and J. Baggott, CRC Press, Boca Raton, Florida, 1991
- Organic Photochemistry, J.M. Coxon, B. Halton, Cambridge University press, Cambridge 1974.

Unit–13

Photochemistry of Alkenes and Dienes

Structure of Unit

13.1 Objectives

This chapter gives an overview of photochemical reactions of alkenes and dienes including geometrical isomerism, electrocyclic reactions and rearrangement of 1,4- and 1,5-dienes. From a synthetic point of view, the photochemical reactions are might be useful to synthesize of particular product. These reactions are also having importance in biological processes.

13.2 Introduction

The absorption of a radiation by an organic molecule takes it from its ground state into an excited state accompanied by change in electronic distribution, geometry and uncoupling of electron spin. Although electronically excited molecules are normally very short lived, their high reactivity is frequently sufficient for photochemical reaction occur.

Electronic structure of alkenes can be described in term of π and σ bonding orbitals, with corresponding of π^* and σ^* anit-bonding orbitals. There are generally two type of transitions occur given as

(i) π - π^* transition (π, π^* excited state) is the more intense absorption with λ_{max} of around 180nm ($\varepsilon \sim 10^4$ Mol^{-1} dm^3cm^{-1})

(ii) π - σ^* transition (π, σ^* excited state) is weak.

However, gas phase spectra show an evidence of Rydberg absorption leading to a Rydberg state (π, 3s).

Simplest alkenes absorb UV light with λ_{max} of around 180nm, but conjugated systems such as diene and polyenes or aryl-substituted alkenes absorb at λ_{max} > 200nm with increment of around 35 nm per successive double bond. So that for simple alkene, direct irradiation must be carried out with vacuum UV sources. However, a medium-pressure mercury lamp with a quartz filter can be applied for highly substituted alkenes, possessing wavelength over 200 nm.

A feature of alkenes photochemistry is that singlet and triplet state reactions are more distinct. There is a large energy difference between singlet (π, π^*) and corresponding triplet state for alkenes, so intersystem crossing is very inefficient and a triplet sensitizer is needed to populate the triplet state. Thus, The large energy difference between singlet and triplet state, and different spin characteristics lead to different reaction from singlet (direct irradiation) and triplet state (sensitizer irradiation) in many alkenes.

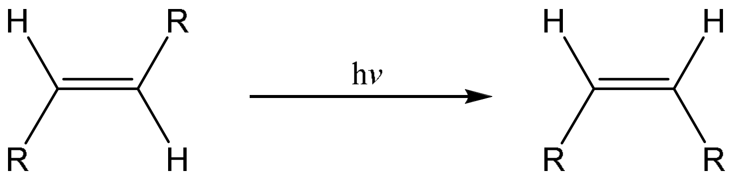
The reactions of alkenes and dienes are grouped into geometrical isomerization about carbon-carbon double bond, concerted reaction like electrocyclic, shifts (usually hydrogen) along π-system, di-π-methane reaction and photoaddition reactions.

13.3 Intramolecular reactions of the olefinic bond

In this heading, intramolecular reaction like geometrical isomerization, di-π-methane reaction and cyclisation reaction of alkenes are discussed in details .

13.3.1 Geometrical isomerism

Alkenes with suitably substitute display geometrical isomerism due to restriction rotation about carbon-carbon double bond, which exist in two isomeric forms are called *cis* and *trans* form.



cis form *trans* form

Usually, the *trans* isomer is thermodynamically more stable because of the less steric hindrance. Interconversion of geometrical isomer of alkenes can be carried out by thermally, catalytically or photochemically. When thermally and catalytic methods are used, we get a thermodynamically more stable isomer, i.e., *trans* isomer in large proportion. But photochemical can establish a mixture that is richer in the *cis* isomer. Irradiation therefore provides a means of converting a *trans* alkene to the *cis* isomer. Photoisomerization in alkenes can be occured through direct radiation, photosensitizer and catalysis process.

13.3.1.1 Direct radiation

On the direct irradiation of an alkene with suitable radiation, the (π, π^*) excited state is formed initially in a conformation that retains the geometry of the ground state from which it is formed, is called a vertical excited state (Fig. 13.1). However, there is no net π - bonding in the (π, π^*) excited state and little barrier to rotation about the former double bond, with the result that relaxation can take place rapidly to give non-vertical (π, π^*) state, this has lower energy and a different geometry with an angle of twist of around 90^o compared with the planar geometry of vertical state (scheme 13.1). This twisted geometry is believed to be the minimum energy geometry for both the singlet and triplet excited states. But the twisted geometry is an energy maximum on the ground state surface. The non-vertical state can relax to either cis or trans configuration of the ground state by radiationless decay. The return from the singlet excited state to the ground state involves re-pairing of the electrons by a nonradiative process. Return from the triplet state requires intersystem crossing.

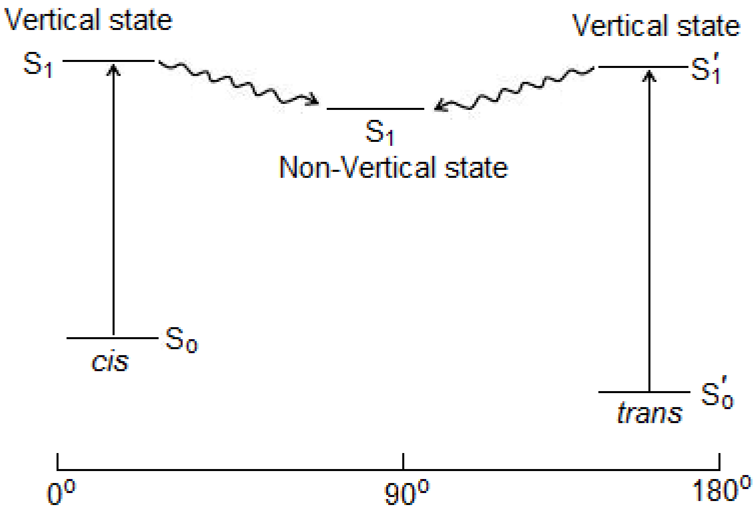
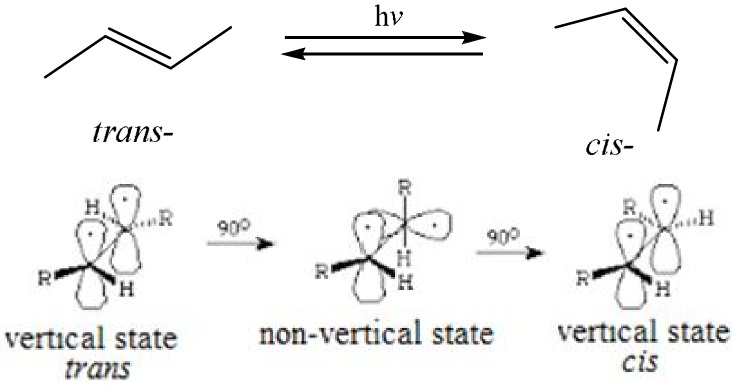


Fig. 13.1 Energy diagram of an alkene showing vertical and non-vertical state



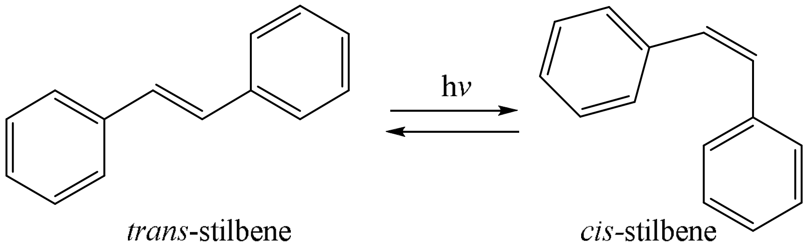
Scheme 13.1

There is an approximately equal probability of forming *cis* and *trans* isomer. However, it has been found that these geometrical isomers are obtained in different proportion at phtostationary state. The composition of the photostationary state depends upon the ratio of the trans→cis and cis→trans isomerization quantum yields (and   ) and the molar absorption coefficients ε of the corresponding isomers. The relationship can be expressed quantitatively as alkene

$$\frac{[trans]}{[cis]} = \frac{\varepsilon_c}{\varepsilon_t}\left(\frac{\emptyset_{c\to t}}{\emptyset_{t\to c}}\right)$$

The *trans* isomer absorbs significantly more light than the *cis* isomer because of absorption occurs toward longer wavelengths and higher extinction coefficients than *cis* isomer. If the quantum yields for both conversions are approximately equal, then the conversion of *trans* to *cis* will occur faster than the converse process when the two isomers are in equal concentrations. A photostationary state will be achieved when the rates of formation (from the non-vertical state) and disappearance (by absorption of light) for each isomer become equal and at this point the concentration of the *cis* isomer will be greater than that of the *trans* isomer.

It is possible that one particular geometrical isomer can be obtained by photoisomerization reaction. A typical example of photoisomerization reaction is the conversion of *trans*-l,2-diphenylethene(stilbene) to *cis*-form. The *trans*-stilbene absorbs a 313nm (= 2300 and = 16,300 l mol^{-1} cm^{-1}) of wavelength strongly than *cis* form and gives a photostationay state mixture containing 93% *cis*-stilbene and 7% *trans*-stilbene. Hence, photoisomerization is provided a route to obtain thermodynamically less stable isomer which is otherwise difficult to obtain by other method.



trans-stilbene
7%

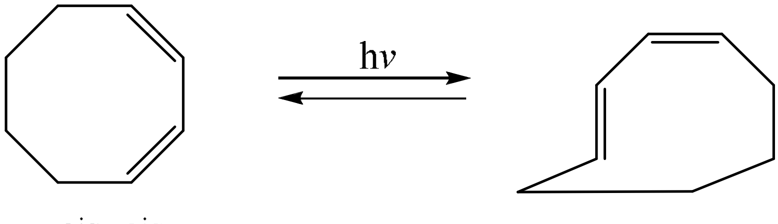
cis-stilbene
93%

Although dienes and polyenes show similar behaviour as monoalkene, but there are two complicating factor are considered in the geometrical isomerization.

(i) The central single bond of diene has substantial double bond character in an excited state, so that the rapid ground state interconversion does not occur in the excited state.

(ii) The relaxed, non-vertical excited state of the conjugated system may have an angle of twist less than 90°.

Thus, conjugated systems do not exhibit a wavelength-dependent composition for their photostationary states, the theoretical basis for understanding the variation is quite complex. For example, The cis, cis cycloocta-1,3-diene at 248nm is converted into a mixture with high amount of less stable cis, trans (67%) isomer.

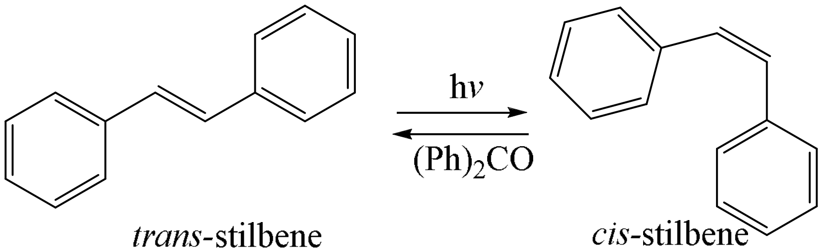


cis, cis-

cis,trans-

13.3.1.2 Photosensitized Isomerization

Photochemical isomerization also occurs through triplet excited state using photosensitizers. A triplet sensitizer absorbs the radiation undergo vibrational relaxation and intersystem crossing to its triplet state and then taking part in an energy transfer process with alkene. It is more efficient if triplet sensitizer has just a little higher in triplet state energy than one of the alkene isomer and lowers than other isomer. In such situation the alkene isomer with lower triplet energy is sensitized more efficiently than the isomer with higher triplet energy and the result is a photostationary state rich in the latter isomer. For example,



trans-stilbene
7%

cis-stilbene
93%

There is a ketone such as benzophenone is raised by an n - π* transition from the singlet ground state (S_0) to an excited state (S_1) by absorption of light. Intersystem crossing then occurs rapidly to give the triplet state (T_1) of the sensitizer.

$$[(C_6H_5)\ ^1 \qquad [(C_6H_5)_2\ ^3 \qquad [(C_6H$$

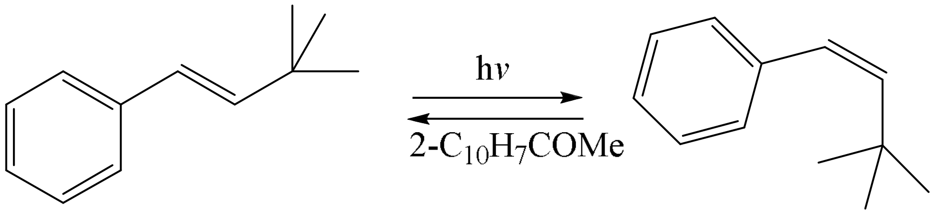
The next step is excitation of the alkene by energy transfer from the triplet state of the sensitizer.

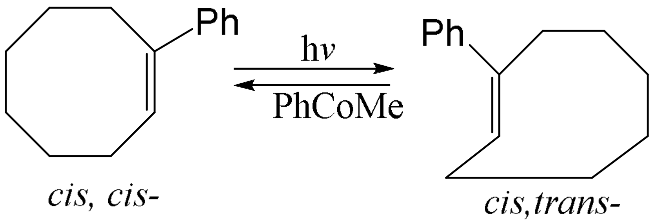
$$[Ph - C = C -\ ^3 \qquad [(C_6H_5)^3 \qquad [Ph - C = C - Ph] + (C_6$$

Remember, the net electron spin is conserved during energy transfer, which means that the alkene will be excited to the triplet state. The triplet state of the alkene is most stable when the *p* orbitals, which make up the normal π-system of the double bond, are not parallel to one another. Therefore, if the energy-transfer process leads initially to a planar triplet, this is converted rapidly to the more stable nonplanar form. The excitation of either the *cis* or the *trans* isomer of the alkene appears to lead to a common triplet state.

$$^3 \qquad [Ph - C = C - Ph] \rightarrow cis - \text{stilbene}\ (93\%) + trans - \text{stilben}$$

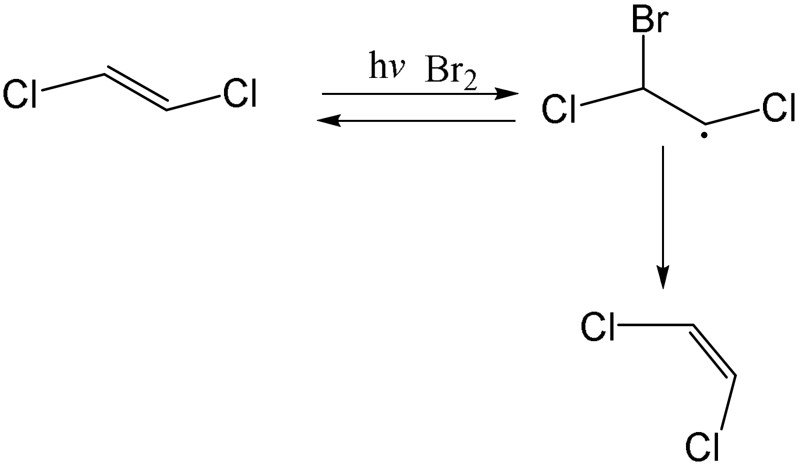
For example,





13.3.1.3 Catalyzed method

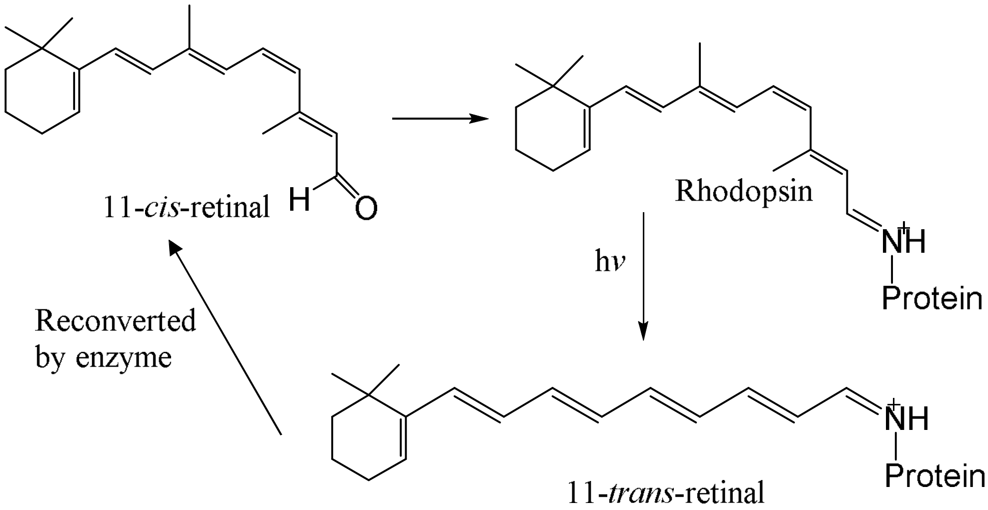
Photoiosmerization of alkenes are also achieved in the presence of catalysis, e.g., Bromine. Halogen atom absorbs the photon and gives radical, then radical adds to alkene forming the intermediate radical where bonds can rotate. So that the alkene excited state does not take part.



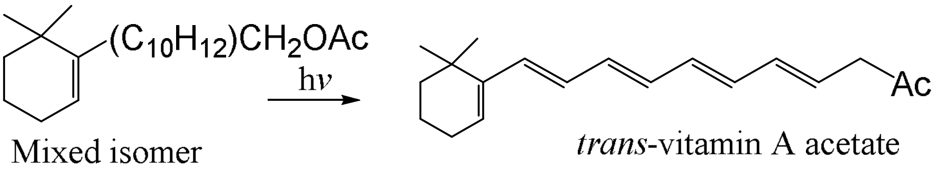
13.3.1.4 Biological importance

Photochemcial geometrical isomerization is impotent in biological system, for example,

(i) The retina of the eye consists of a number of photoreceptor cells containing the visual pigment rhodopsin, which is derived from 11-*cis* retinal by the reaction of the aldehyde group with an amino substituent in a protein (opsin). The *cis*-Rhodopsin absorbs photon in the visible region and isomerization of the double bond occurs to afford *the trans*-rhodopsin. This change in geometry of bound retinal leads to changes in protein structure that trigger a nerve impulse, which is interpreted by the brain leading to vision. The *trans* form of retinal reconverted into *cis* form by an enzyme present in the eye and visual cycle again begins.

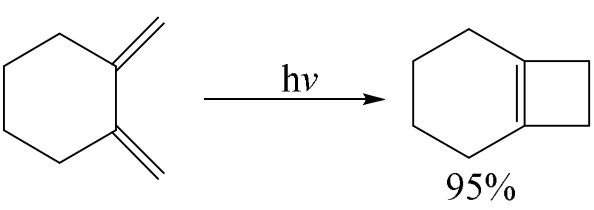


(ii) The chlorophyll-sensitized isomerization vitamin A acetate which is used commercially to obtain the required all *trans* isomer from the mixture of isomer resulting from the synthesis. There photoinduced electron transfer occurs and rotation of Carbon-Carbon bond in the most stable isomer unlike triplet sensitized reaction.

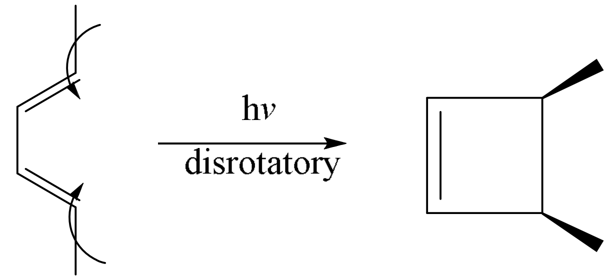


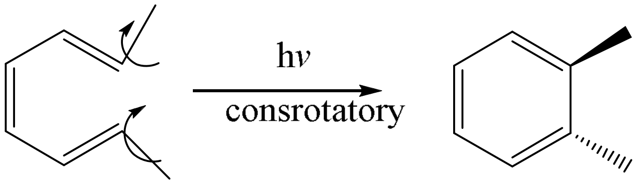
13.3.2 Cyclisation reactions:

An electrocyclic ring closure, i.e. cyclisation reaction is an intramolecular reaction that forms a cyclic product containing one more σ bond and one fewer π bond than the reactant. These reactions occur through the concerted pericyclic reaction in which bond making and bond breaking occur in a single step. Such reactions occur thermally or photochemically. In thermal reaction, thermodynamically stable compound is favored, but in photochemical reactions, the molecule absorbs a radiation with suitable wavelength and the direction change will be toward a photostationary state that favors the compound with lower absorption coefficient at the wavelength of radiation, for example,

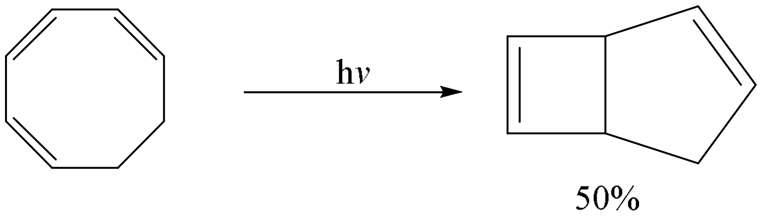


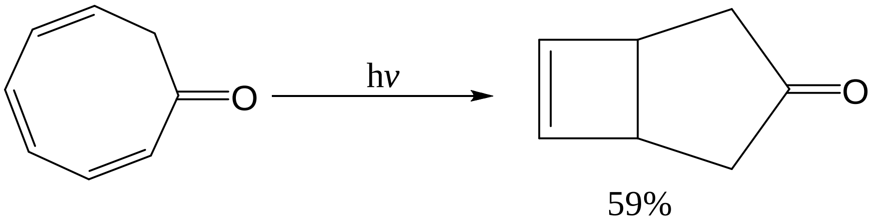
In these reactions involve a change of the π- and σ-bond positions within a conjugated system in a cyclic transition state. According to the Woodward–Hoffmann orbital symmetry rules, the 4n electron systems in the excited state react through a disrotatory mode in which rotations occur in the same direction (clockwise or anticlockwise) about the axes of double bonds. Whereas those reactions with 4n+2 electrons react through a conrotatory pathway in which rotations occur in the opposite direction (one clockwise and the other anticlockwise) about these axes.

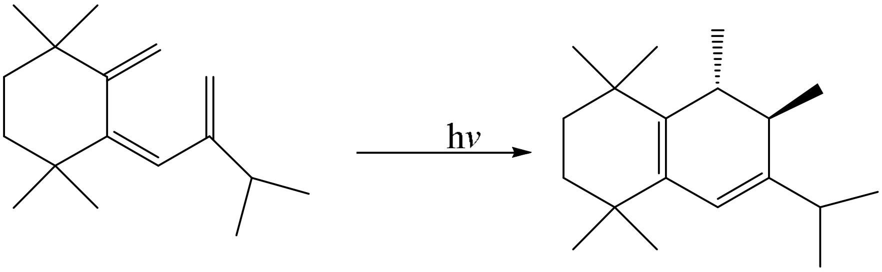


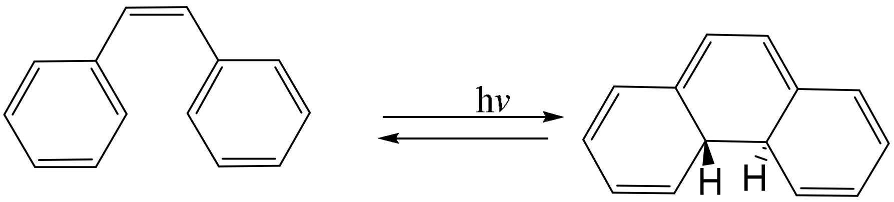


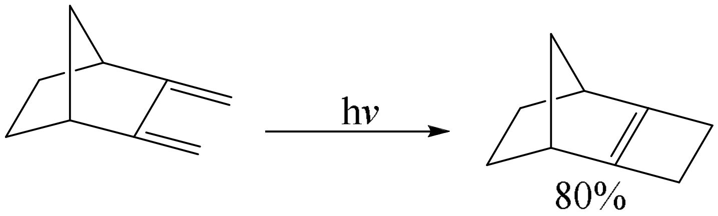
Example,



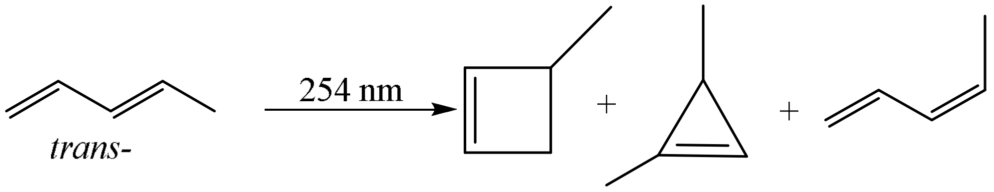


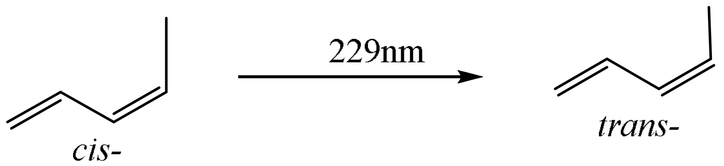




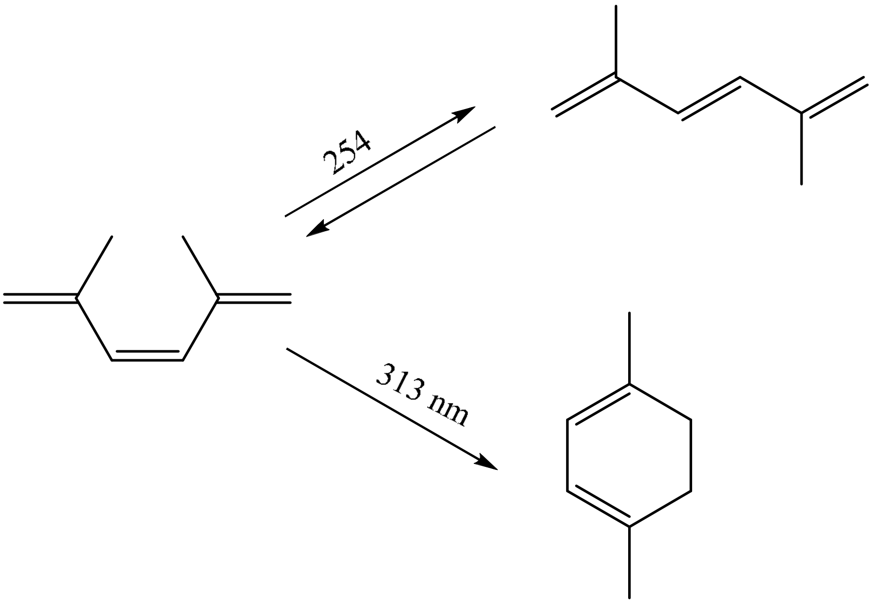


Electrocyclic reactions of conjugated dienes take place through the vertical singlet state. The triplet state is generally not involved in this process. There are two important factors that affect electro cyclization, (i) reaction efficiency is usually lowered by a simultaneous geometrical isomerization along the double bond and (ii) *cis*-diene conformation must be achieved before cyclization proceeds. Direct irradiation of dienes may result in wavelength-dependent photoproduct formation, which is related to different absorption properties of the diene conformers. For example, trans-penta-1,3-diene, irradiated at 254 nm, gives cyclic product in low quantum yield with two other products; however, when it is irradiated at 229 nm, where the *trans*-conformation absorbs predominantly, mostly *trans–cis* isomerization is observed.

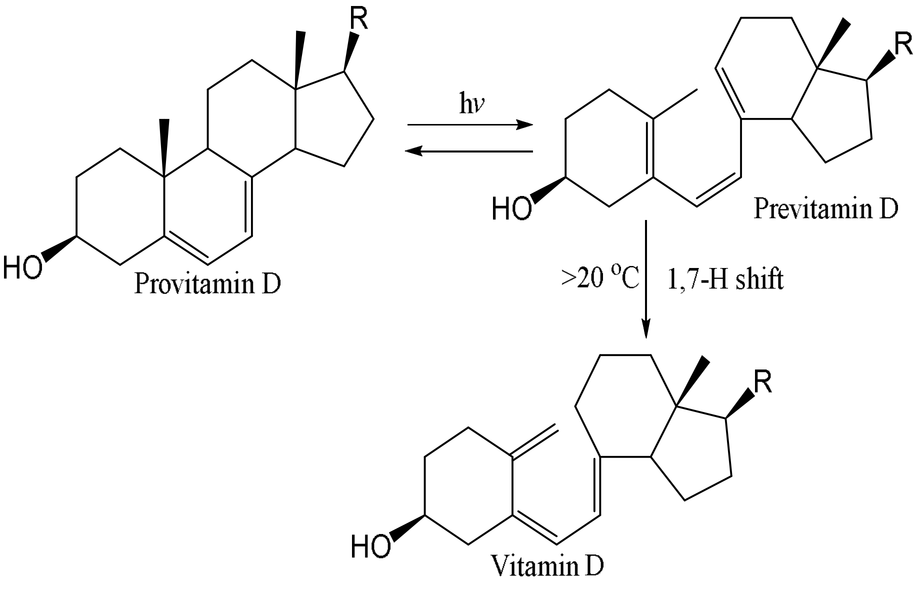




The conjugated triene, e.g., 2,5-dimethylhexa-1,3,5-trine undergoes efficient *cis*-*trans* isomerization at 254nm, but it cyclizes to a cyclohexadiene using 313 nm radiation.

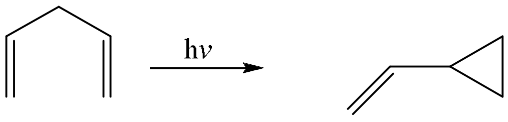


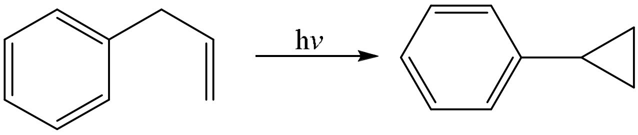
Electrocyclic process is a key reaction in the synthesis of vitamin D which is useful in bone formation, immune system responses, cell defences and anti-tumor activity. Vitamin D comes in two closely related forms, vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol), and their metabolites. Both vitamin D2 and D3 occur naturally in some foods. However, vitamin D3 can also be synthesized in skin cells called keratinocytes from 7-dehydrocholesterol (provitamin D), which undergoes a photochemical six electron conrotatory electrocyclic ring opening at 280 nm to previtamin D3, which spontaneously isomerizes to vitamin D in a thermal antarafacial hydride [1,7]-sigmatropic shift.



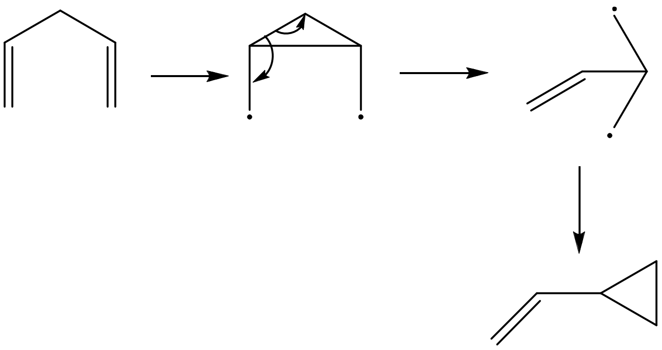
13.3.3 Rearrangement of 1,4- and 1,5-dienes

Irradiation of 1,4-diene or 3-phenyl alkenes often lead to vinylcyclo propane or phenyl cyclo propanes through of an 1,2-shift of vinyl or phenyl group accompanied by ring closure lead to an photoproduct that is usually not obtainable by another route. These reactions are termed the di-π-methane rearrangement, also known as the Zimmerman reaction.

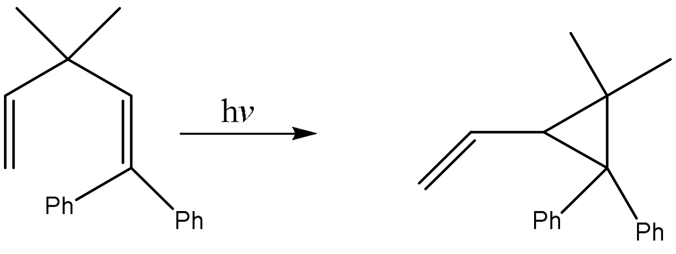


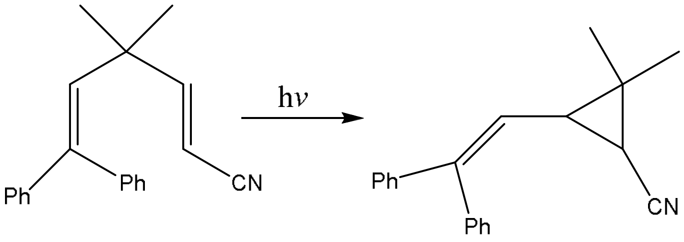


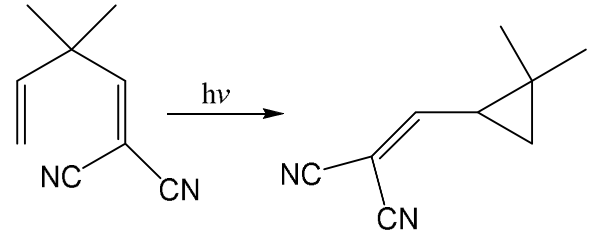
According to the proposed stepwise biradical mechanism, 1,3- and 1,4-biradical intermediates and also the second π-bond may be involved. The mechanism starts with formation a bonding between atom 2 and 4 of 1,4-diene unit, then cleavage of 2,3-bond and formation of a 3,5-bond.

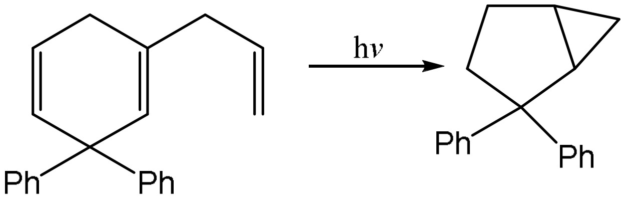


The di-π-methane reaction generally occurs through the excited singlet state obtained by direct irradiation, whereas the triplet pathway is accessible only using triplet sensitizers due to the poor intersystem crossing efficiencies of alkenes. The di-π-methane rearrangements often show a high degree of diastereoselectivity and/or regioselectivity, for example,

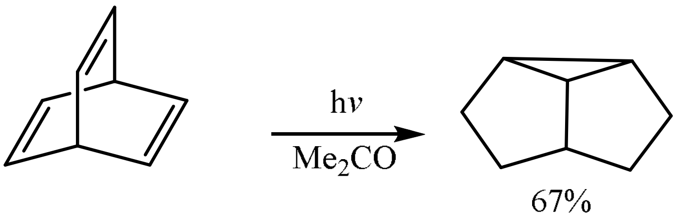


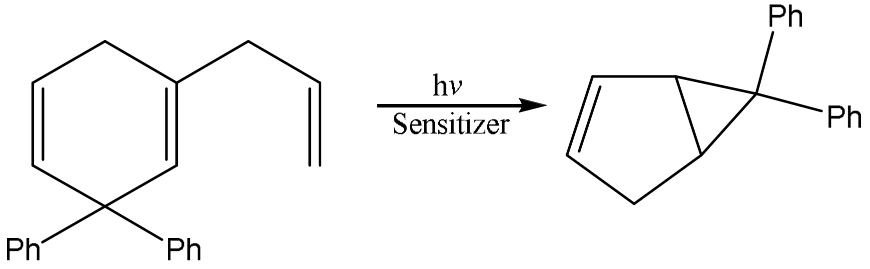




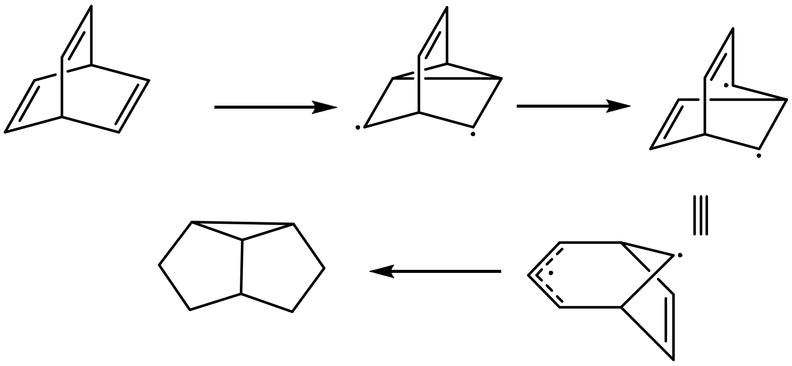


In contrast, cyclic di-π-methane systems rearrange from the triplet state. For example, triplet sensitization of bicyclo[2.2.2]octa-2,5,7-triene provides semibullvalene.

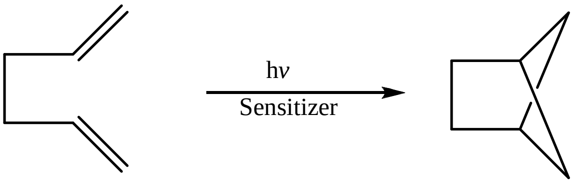




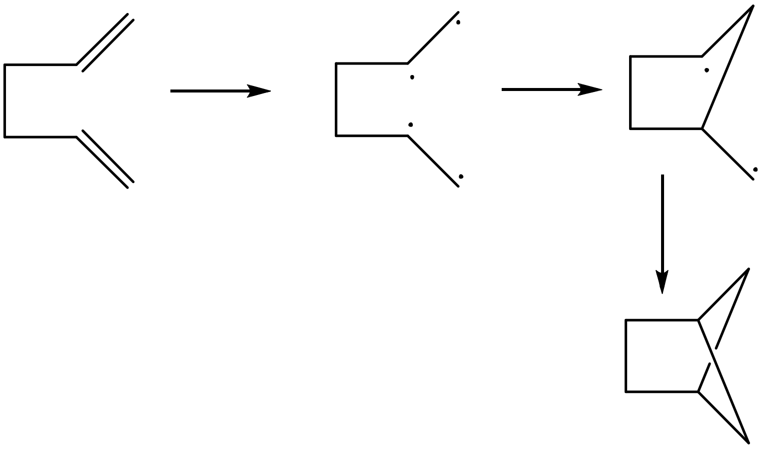
Mechanism:



In 1,5 diene, a rearrangement occurs by irradiation and bicycle product is formed. It is sensitized by Hg (gas phase). The mechanism of this reaction involves biradical formation in which initially 1,5-bond is formed, then 2,6-bond is formed.



Mechanism:



13.4 Summery

- Photochemical reaction of alkenes take place generally through signlet or triplet π - π^* state.
- Photoisomerization reaction gives less thermally stable geometrical isomer.
- Photoisomerization in alkenes can be occured through direct radiation, photosensitizer and catalysis process.

- The ratio of both geometrical isomers in the photostationary state depends upon the ratio of the quantum yields of both isomer and the molar absorption coefficients of the corresponding isomers.
- Photochemcial geometrical isomerization is impotent in biological system like vision.
- Photocyclisation reactions occur through the concerted pericyclic reaction via a disrotatory or conrotatory mode.
- Electrocyclic process is a key reaction in the synthesis of vitamin D.
- The di-π-methane rearrangement occurs through biradical mechanism.

13.5 Review Question

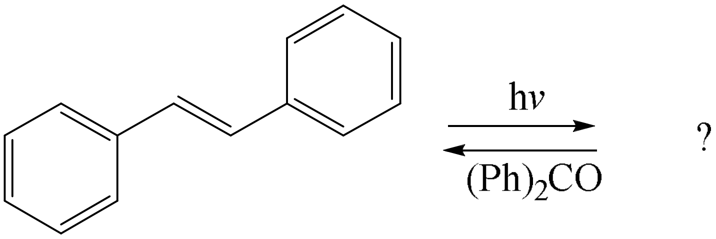
1. Explain the following concepts

(a) photosensitizer isomerization

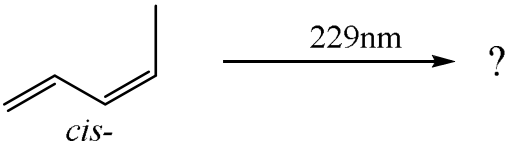
(b) Non-vertical excited state

2. Write the mechanism of Di-π-methane reaction?
3. Why geometrical reaction gives cis isomer in large amount?
4. Predict the photoproduct

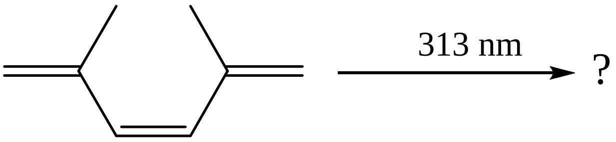
(a)



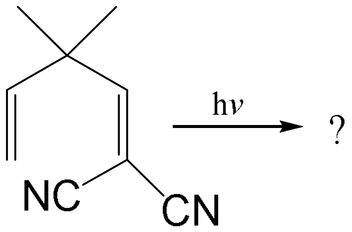
(b)



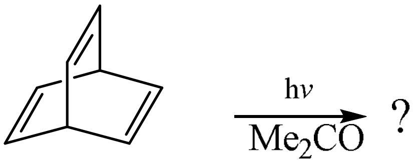
(c)



(d)



(e)



5. What is role photoisomerization in Vision?
6. Explain r**earrangement of 1,5-dienes** with mechanism?
7. Give three example of 1,6-triene cyclisation reaction?

13.6 Reference and Suggested readings

- Introduction To Organic Photochemistry, John D. Coyle, John Wiley & Sons Ltd, 1986
- Photochemistry of organic compounds from concepts to practice, Petr Klan and Jakob Wirz, John Wiley & Sons Ltd, 2009

Unit -14

Photochemistry of Aromatic Compounds: Isomerisation, additions and substitutions

Structure of Unit

14.0 Objective

14.1 Introduction

14.2 Benzene and its various excited states

- 14.3.1 Isomerisation of Aromatic compounds
- 14.3.2 Mechanism of 1,2-shift by benzvalene intermediate
- 14.3.3. Mechanism of 1,2-alkyl shift through prismane intermediate
- 14.3.4 Mechanism of 1,3 alkyl shift through prismane
- 14.3.5. Photochemical Isomerisation of trisubstituted benzene
- 14.3.6 Photochemical isomerisation of tetrasubstituted benzene

14.4 Photochemical addition reactions of aromatic compounds

- 14.4.1 1,2-photochemical addition reactions of aromatic compounds
- 14.4.2 1,3]-Photochemical addition reactions of aromaticcompounds
- 14.4.3 [1, 4]-Photochemical addition reaction of aromatic compounds
- 14.4.4 Photochemical addition of oxygen
- 14.4.5 Photochemical dimerisation reactions of aromatic hydrocarbons

14.5 Application of photochemical addition reaction of aromatic compounds

14.6 Photochemical substitution reaction of aromatic compounds

- 14.6.1 Nucleohilic substitution
- 14.6.2 Electrophillic substitutions
- 14.6.3 Other type of substitutions
- 14.6.4 Photochemical radical substitution reactions

14.0 Objective

Photochemistry is the chemistry of electronic excited states of organic molecules these states are generated by irradiating the molecules by Uv or Visible light .this unit comprises the detailed study of the singlet and triplet state of organic molecule these have different physical properties and chemical reactivity the product obtained at the end of photochemical reactions unexpected and entirely different from those obtained in thermal reactions, typical photochemical reactions include isonmerisation around carbon-carbon double bonds molecular rearrangements and fragmentations, inter and intera molecular hydrogen abstractions, cycloadditions and dimerisations.

14.1 Introduction

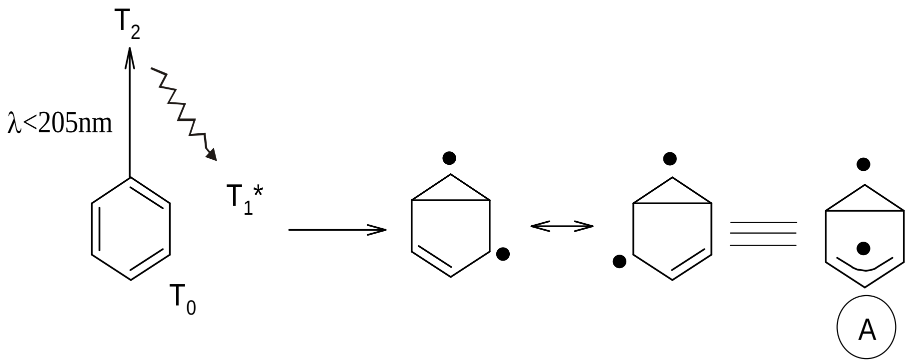
The usual chemical reaction shown by benzene and its derivatives has been studied in detail for a long time. Later is observed by experiments that benzene is prove to photochemical reactions also. It is known that the electronic transition in benzene occurs at 230-270nm which corresponds to a energy value of approximately 448.0kJmol^{-1} and since this value exceeds the resonance energy of benzene (36kcals or 151.2kJ mol^{-1}). it appears that when benzene is irradiated with electrmagnetic radiations of above mentioned wavelength, a photo chemical reaction will result with the formation of products that shall not be aromatic in nature. In fact aromatic compounds undergo transfromations of various derrivatives of benzene shows surprising results which are in contrast to the thermal stability of aromatic compounds. In addition to this the photochemical rearrangements of benzene derrivatives provide direct routes several highly strained molecules.

14.2 Benzene and its various excited states

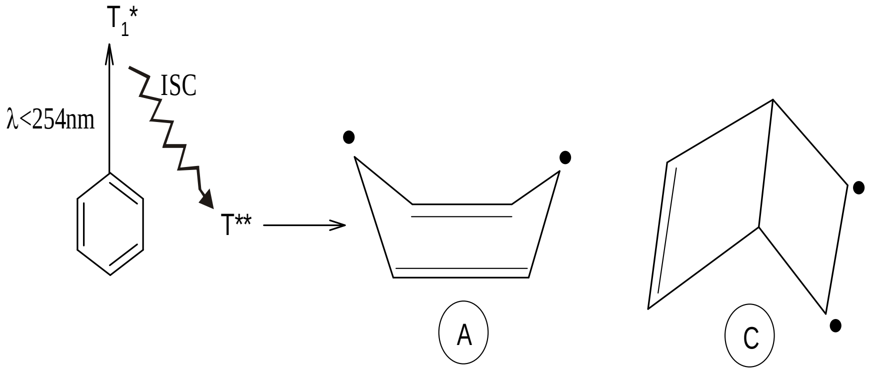
To have a better look let us consider the exited states of benzene.

(1) When liquid benzene is irradiated with electromagnetic radiation of wavelength lower than 205 x 10^{-9} meter, the state T_2 is produced. This is then converted to a different vibrationally excited state

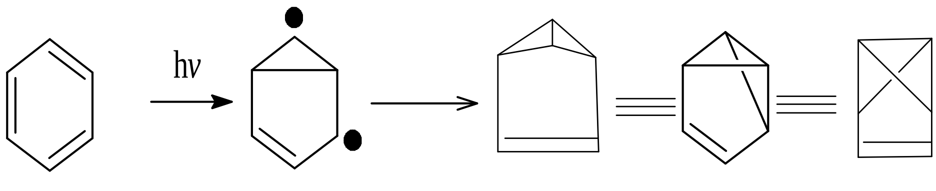
singlet state T_1. This state produces bicyclo [31.0] hexenyl biradical (A) digramatically it is shown below.



(2) If the liquid benzene is irradiated with radiations having $\lambda = 254 \times 10^{-9} m$. It transits directly into the excited state T_1^*. Intersystem crossing (ISC) process converts T_1 state to another state T^{**} which produces 1,4-biradical (B) and [2,2,0] hexenyl biradical (c) which is a bicyclic system. This is shown below

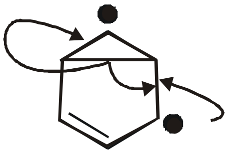


The biradical produces benzvalene and fulvene viz-

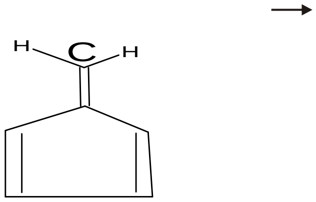


Benzvalene

Fulvene is obtained from prefulvene C-C bond cleavage and 1,2-hydrogen shift viz-

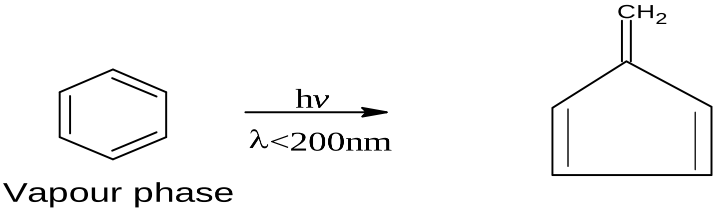


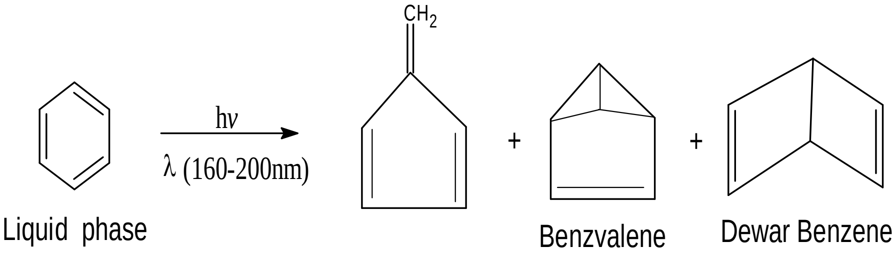
Prefulvene

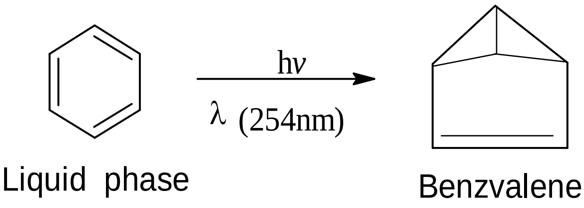


Fulvene

Similarly several highly strained molecules (Dewar benzene, prismane etc) have been obtained by when substituted benzenes are irradiated. The strained systems are reaction intermediates of photochemical isomerisation of substituted benzene. The nature of these intermediates depends upon the state of the aromatic starting material and also upon the wavelength of the light used in photochemical processes. Thus



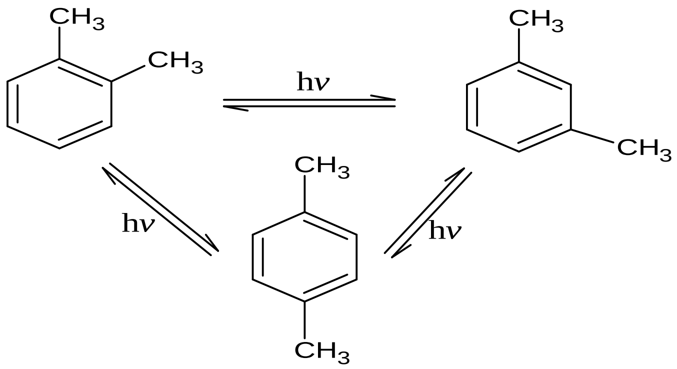




Thus it is seen that the above photochemical rearrangements of benzene molecule provides routes to many highly strained molecules which are in contrast to thermal stability of aromatic compounds.

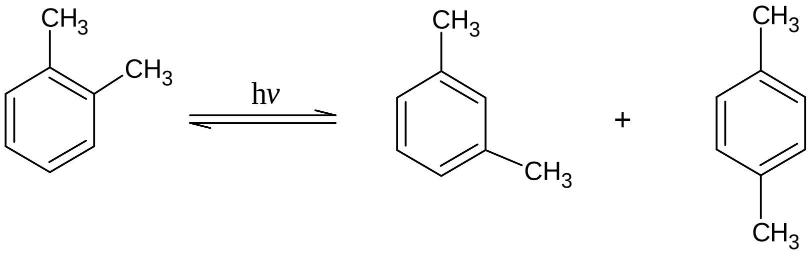
14.3 Isomerisation of Aromatic compounds

Aromatic compounds containing one ring show various photochemical rearrangements leading to the formation of various isomers. For example O-xylene is irradiated, a mixture of 1,2, 1,3 and 1,4 dimethylbenzene is obtained eg



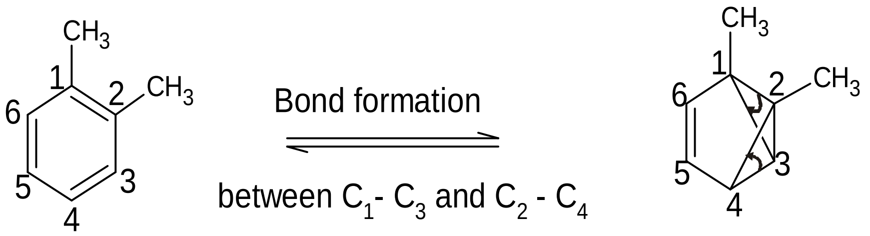
It can be seen that conversion of O - xylene into m - xylene and conversion of m - xylene to p- xylene occurs through 1,2 -xylene group ($-CH_3$) shift. However conversion of o -xylene to p -xylene and vice versa involves 1,3 - shift of $-CH_3$ group.

It is observed that 1,2 alkyl shift occurs through benzvalene as well as prismane as intermediates for example.



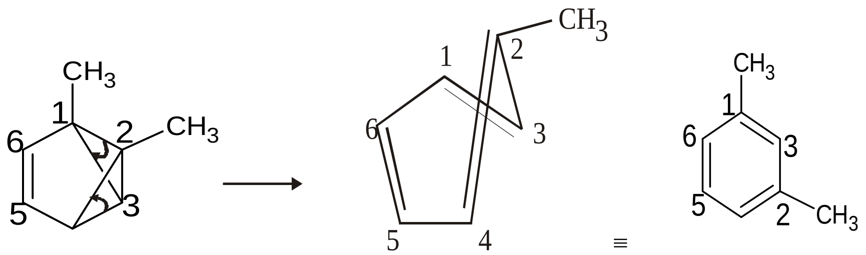
14.3.1 Mechanism of 1,2-shift by benzvalene intermediate

Mechanism



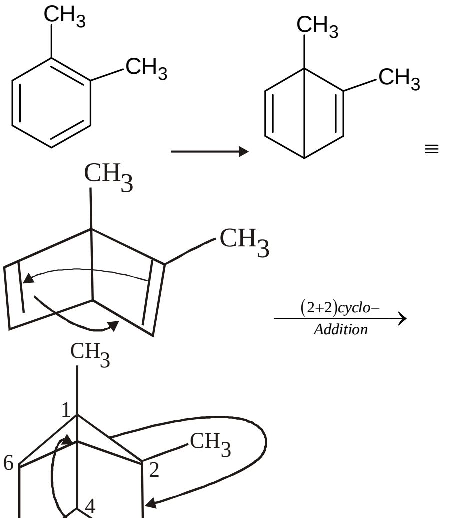
Benzvalene

Now benzvalene undergoes reorganisation of carbons of the ring by bond cleavage between C_1 - C_2 and C_3-C_4 followed by the bond formation between C_1-C_3 and C_2 - C_4 viz.



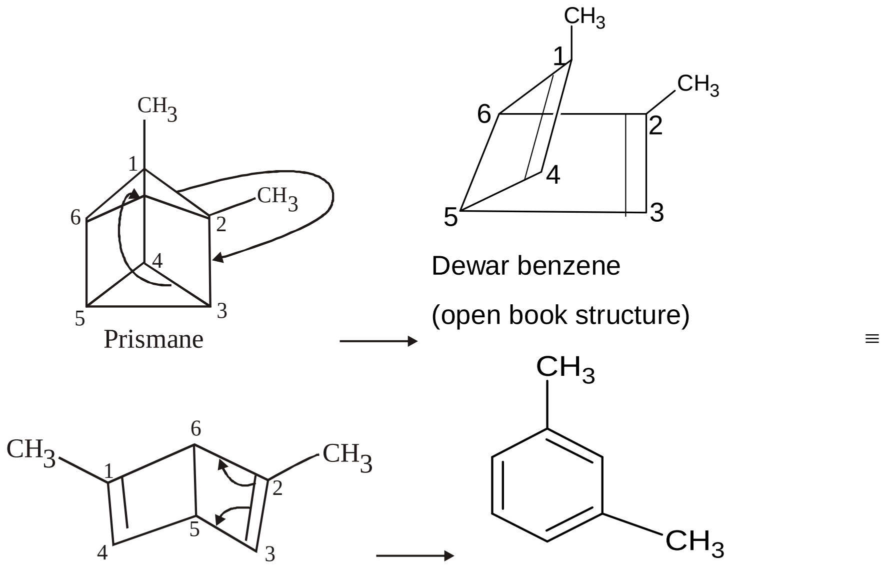
14.3.2. Mechanism of 1,2-alkyl shift through prismane intermediate

This mechanism can be depicted as below.



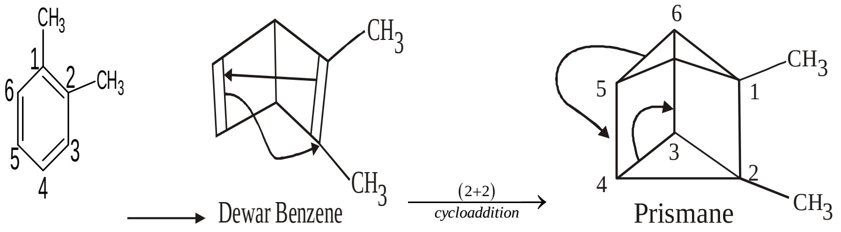
Prismane

Now this prismane so formed undergoes reorganisation of the ring by breaking the bonds between C_1 - C_2 and C_3 - C_4 followed by the bond formation between C_2 - C_3 and C_1 - C_4 as shown below.

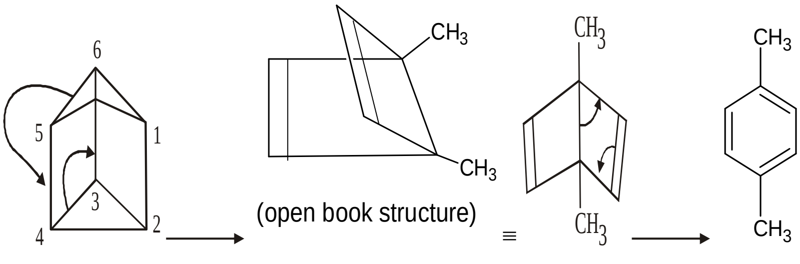


14.3.3 Mechanism of 1,3 alkyl shift through prismane

It is known that 1, 3-alkyl shift takes place through the formation of prismane as an intermediate. This is shown below.



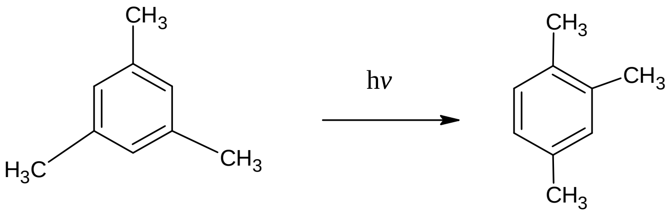
Now the substituted prismane undergoes reorganisation of the carbon of the ring by breaking the bonds between C_3-C_4 and C_5 - C_6 followed by bond formation between C_3 - C_6 and C_4 - C_3 atoms as shown below.



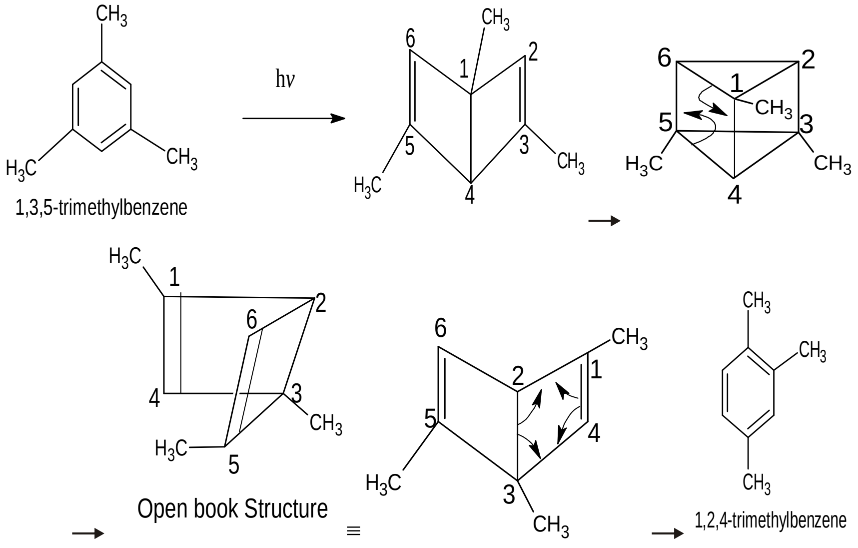
14.3.4. Photochemical Isomerisation of trisubstituted benzene

Photochemical isomerisation of 1, 3,5-trimethylbenzene to 1,2,4-trimethylbenzene is an interesting photochemical reaction occuring through 1,2-alkyl group shift. The process has been throughly investiated by tracer technique using C^{14} labelling.

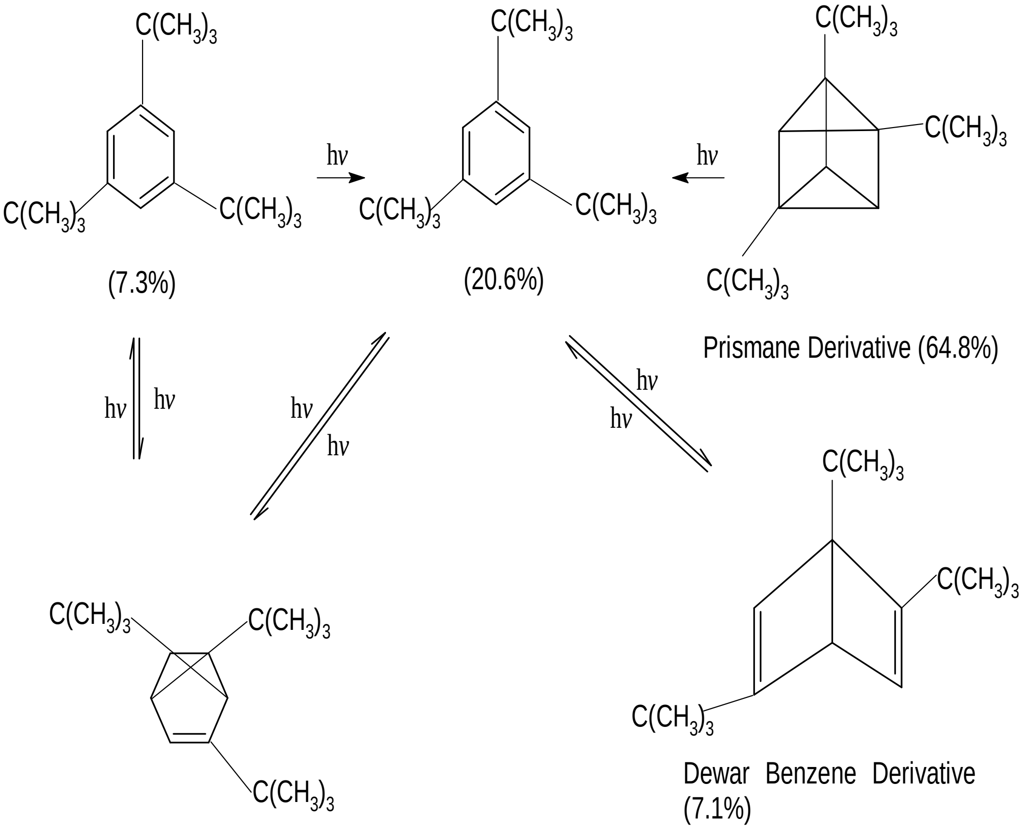
The overall reaction is



The mechanism of the reaction follws the following route.



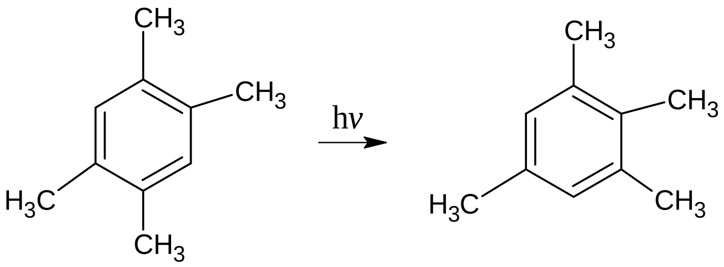
The photochemical conversion of 1, 3,5- tri-t-butyl benzene into 1,2,4-tri-t-butyl benzene involves a lot of complications. It is shown below



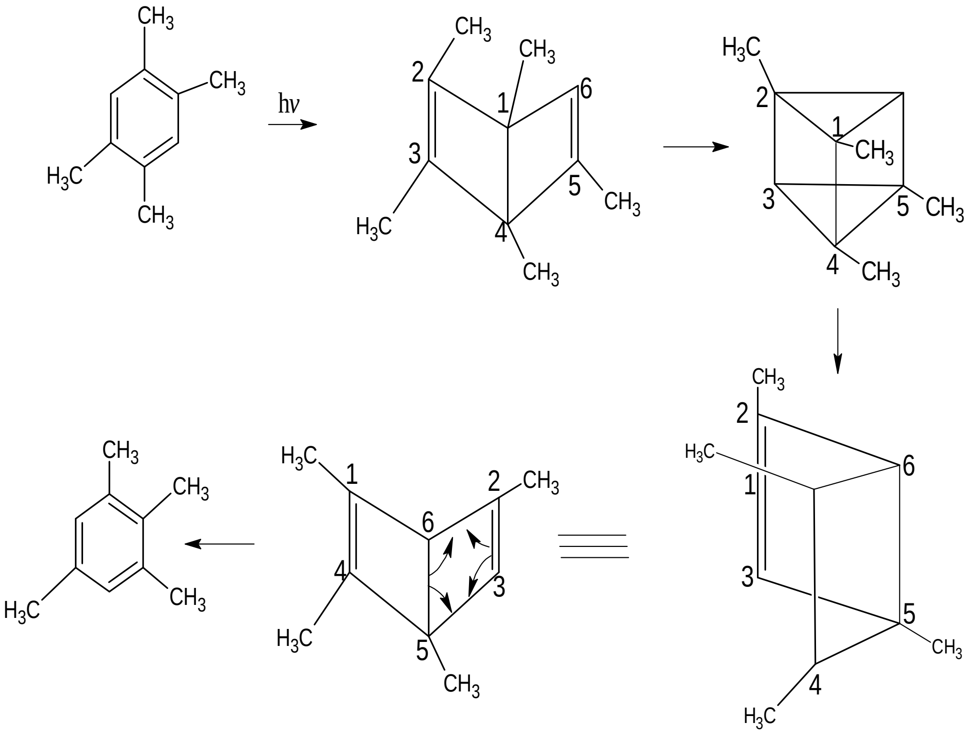
It is evident that in this process a photostationary state (a type of pseudo equilibrium) is established. This equilibrium involves all the species present in the reaction namely the two tri-t-butyl which are reactant and product and also the intermediate in benzene derivative, prismane derivative and a dewar benzene derivative. The percentage of vaious species are written below them.

14.3.5 Photochemical isomerisation of tetrasubstituted benzene

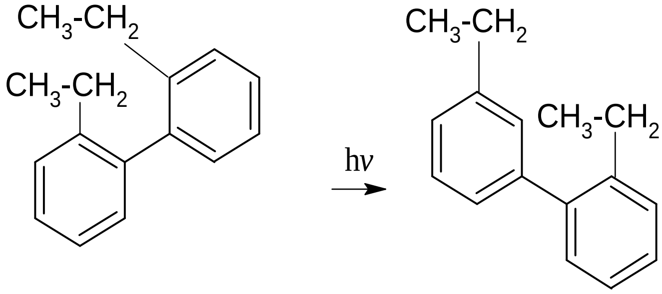
Tetrasusbtituted benzene namely 1, 2, 4, 5-tetramethyl benzene also exhibits photochemical isomerisation and is converted into 1,2,3,5-tetramethylbenzene. The overall reaction is as follows

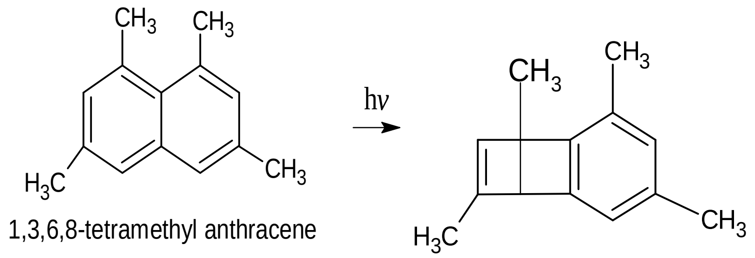


The mechanism of the above photochemical reaction can be shown by following route.



It is clear that this isomerisation envolves prismane and Dewar benzene derivatives. Some other examples of isomerisation are given below.





1,3,6,8-tetramethyl anthracene

14.4 Photochemical addition reactions of aromatic compounds

Photochemical addition reactions are found to be reversible in nature. These reactions are also termed as cycloaddition reactions as a cyclic compound is formed as a last product. when a mixture of olefin is irradiated with light of apporopriate wavelength, large variety of products are obtained The addition takes place at 1,2-1,3 and 1,4 position of benzene ring. Four types of mechanisms have been suggested for these reactions viz. -

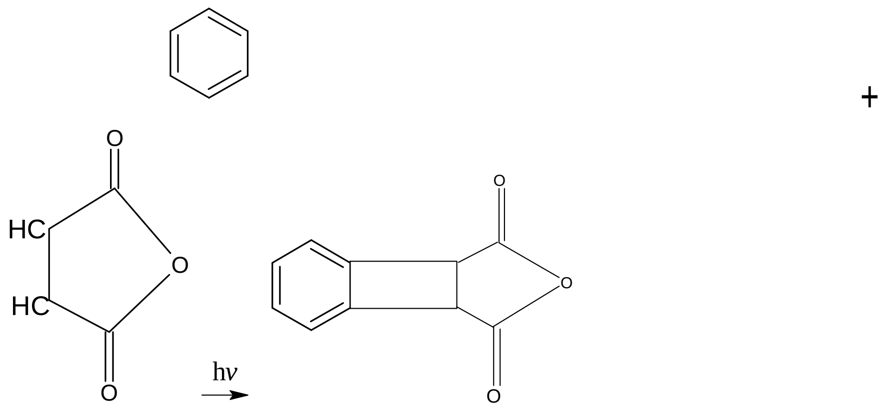
(a) Reaction of aromatic compound excited state with ground state of alkene.

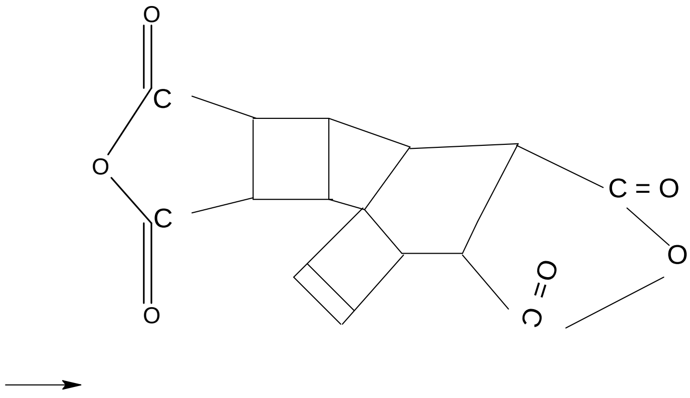
(b) Reaction of olefin in excited state with ground state of aromatic participant.

(c) Conversion of excited aromatic compound to form a biradical intermediate which in fun reacts with olefin to give the final product.

(d) Reaction between polar species obtained either by charge-transfer complexes or by electron transfer.

It is observed that benzene undergoes photochemical addition with maleic anhydride. The composition of the product shows that it contains benzene and maleic anhydride in the ratio of 1:2 viz.

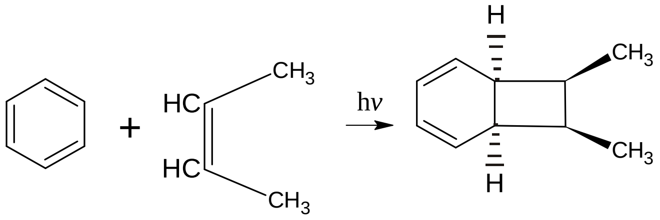


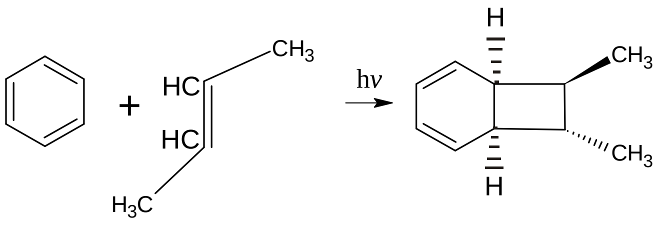


The above reaction is found to proceed via a charge transfer complex involving benzene and the maleic anhydride with mono and disubstituted benzenes a similar reaction is found to occur with a slow kinetics due to steric hindrance by substituent (S) present on benzene ring. With highly substituted benzenes however no reaction takes place.

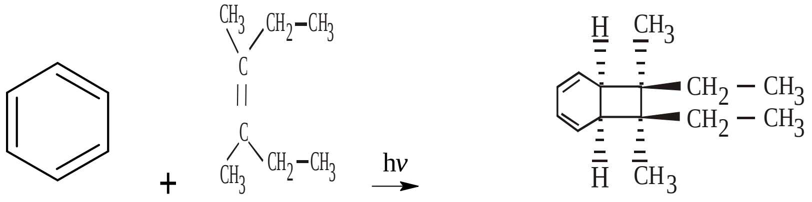
14.4.1 [1,2-]photochemical addition reactions of aromatic compounds

When benzene (liquid) and 2-butane (Cis or Trans) are irradiated with light, 1,2 photoaddition takes place. It is interesting to note that in this reaction the stereochemistry of 2-butene is retained. This shows that the reaction is stereospecific and concerted.

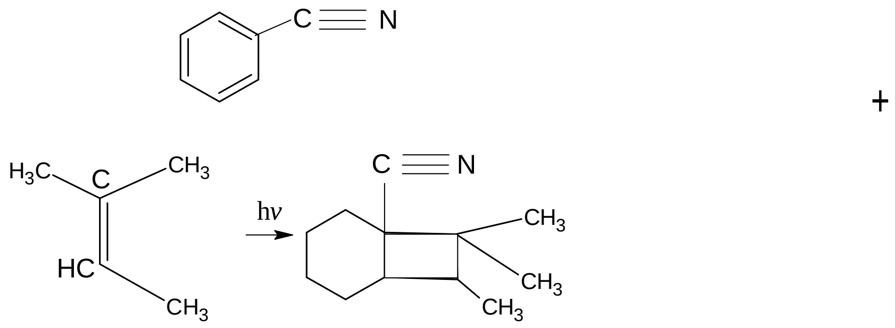


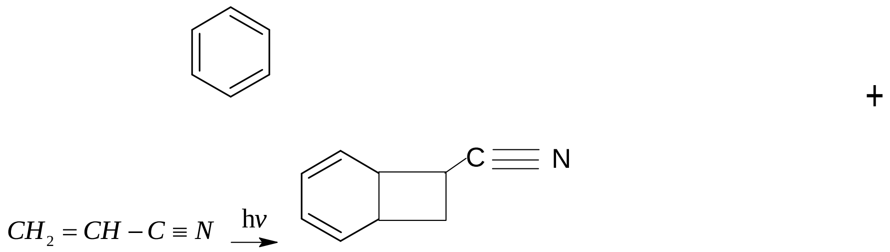


Benzene reacts with alkenes to give bicyclo [4.2.0] octa-2,4-diene type of products ie,

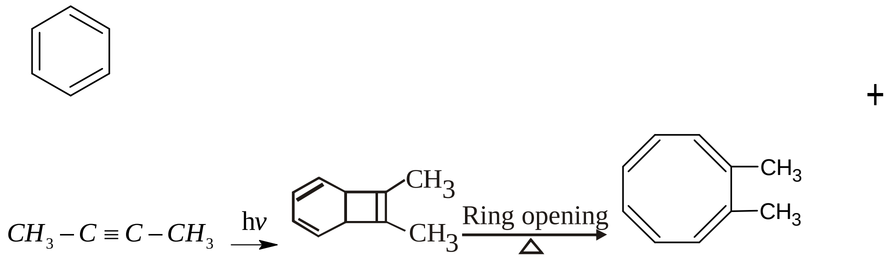


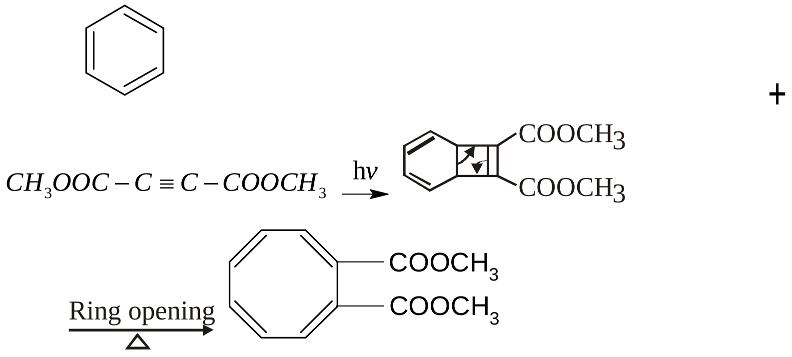
In the above reaction it is suggested that photo-excited alkene reacts with ground state benzene and because the stereochemistry of alkene is found to be retained the process must be concerted. Similarly we have the following photochemical addition.





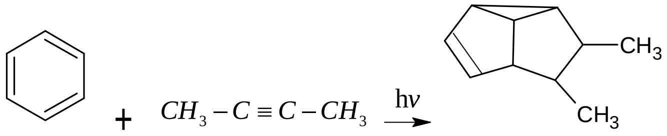
A number of acetylene and its derivatives react photochemically with benzene to produce cyclooctatetraene derivatives via intermediate 1,2-photo addition product viz-



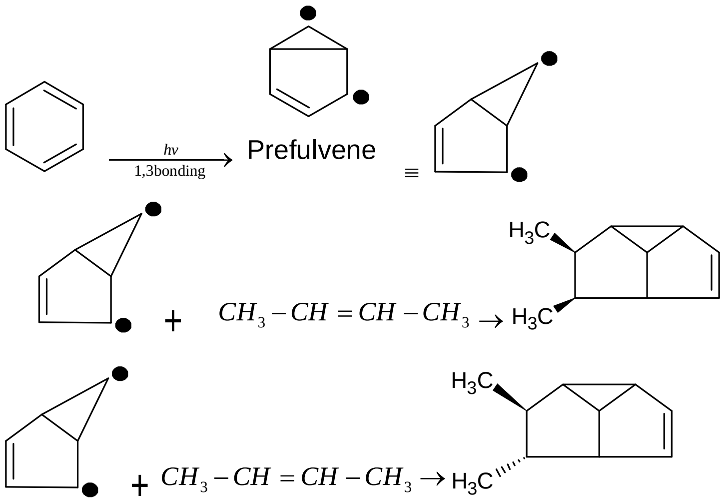


14.4.2 [1,3]-Photochemical addition reactions of aromatic compounds

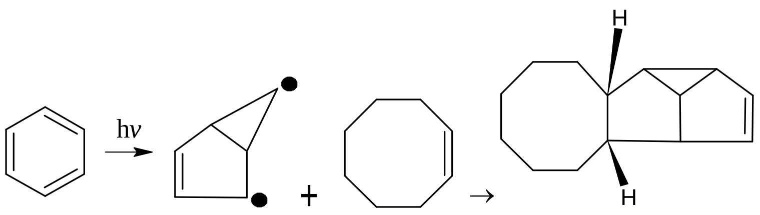
The 1,3 addition leads to the formation of a tricyclic system and involves the addition of olefinic double bond across the meta position of benzene. Viz-



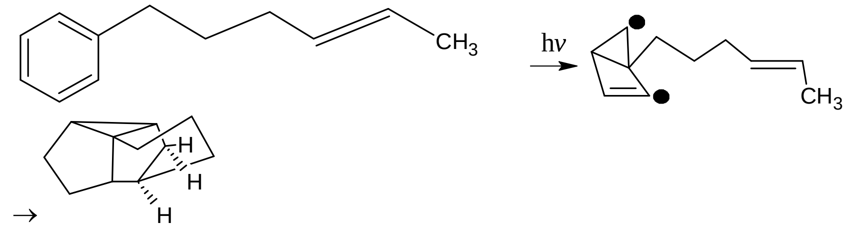
Above reaction occurs only when alkyl substituents are present across the double bond in olefin ie with 2-butene (as shown above), norbornene, cyclobutene, allene etc. It occurs both in liquid and vapour phases at. The stereochemistry of olefin is retained and signlet excited state of benzene is involved. It is interesting to note that the reaction proceeds vice the formation of prefulvene biradical and fulvene and benzvalene are not involved. The mechanistic route can be best shown by following way.



Benzene also adds to cyclooctene in the following way.

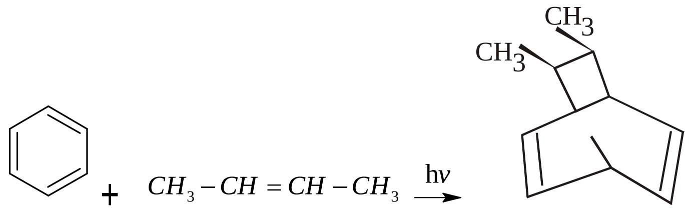


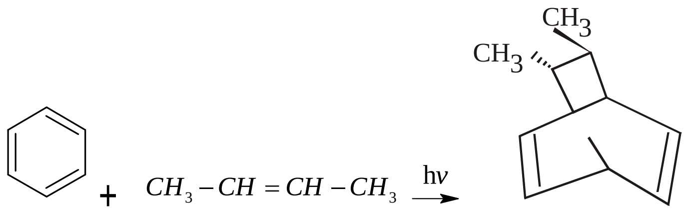
Sometimes it is observed that an intramolecular addition takes place when an olefinic side-chain is present on benzene ring as substituent. For example when 6-phenylhex-2ene is irradiated the following product is obtained.



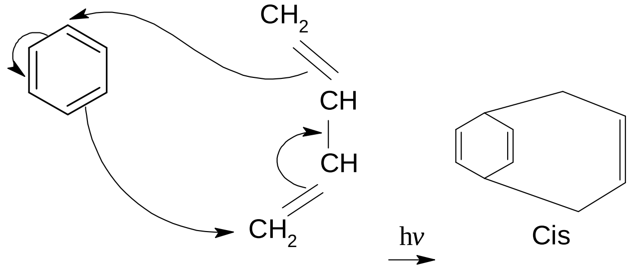
14.4.3 [1, 4]-Photochemical addition reaction of aromatic compounds

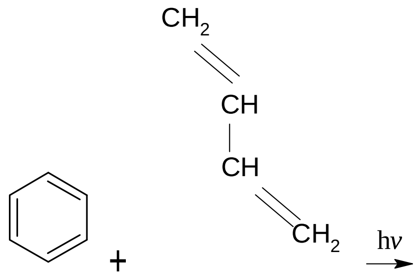
In these types of photochemical reactions the addition of olefin takes place in the para position of benzene. The reaction involves the singlet excited state of benzene and is stereospecific ie the stereochemistry of the olefin is retained. The reactions are analogous to Diels-Alder reaction as benzene acts as diene in this case. Viz-

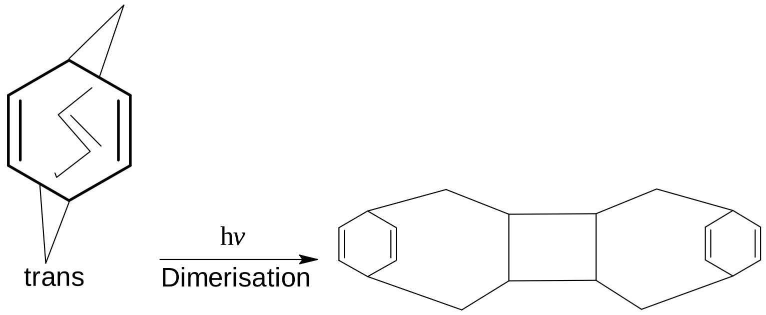




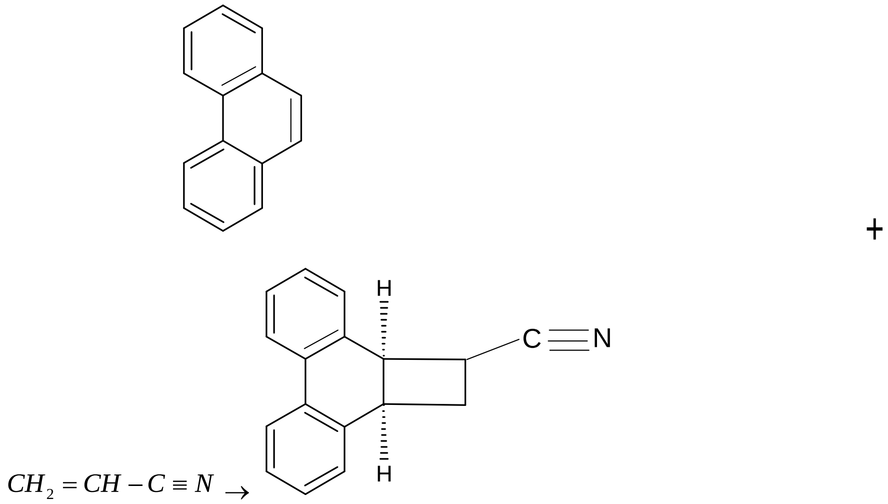
Similarly butadiene when irradiated with benzene it undergoes [4+4] cycloaddition and the reaction is found to be stereospecific in nature Viz-

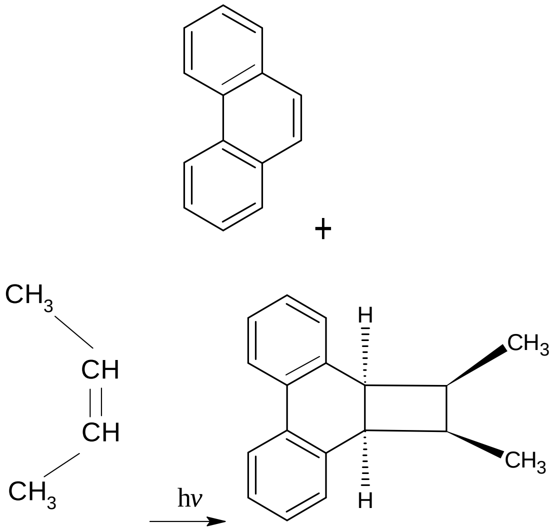


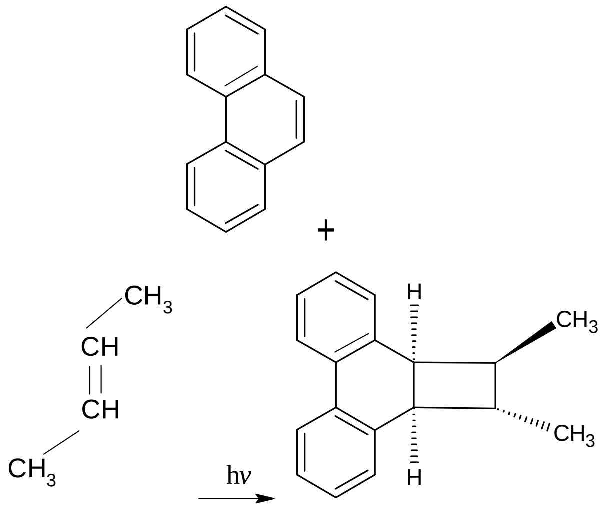


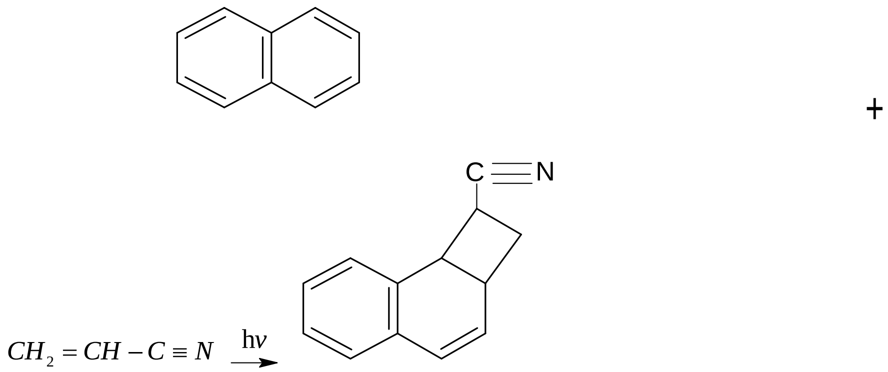


Not only benzene but condensed aromatic system napthalene, Anthracene and Phenanthrene also undergo photochemical addition reaction. It is to be noted that in case of nepthalene and phenanthrene. It is [2+2] cycloaddition whereas in case of anthracene. It is [4+2] cycloaddition. These are shown below.

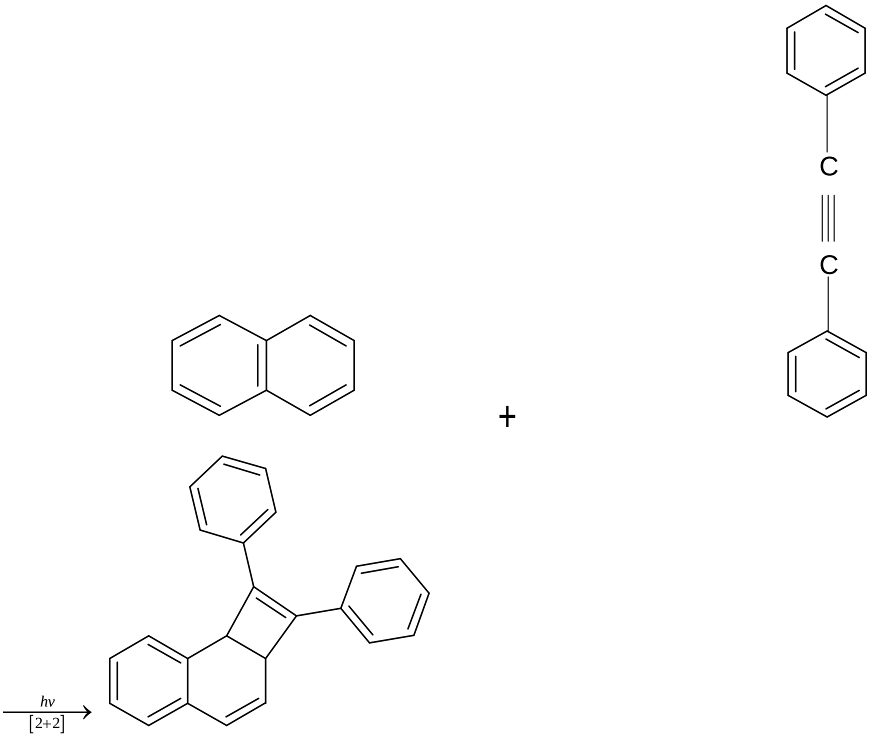


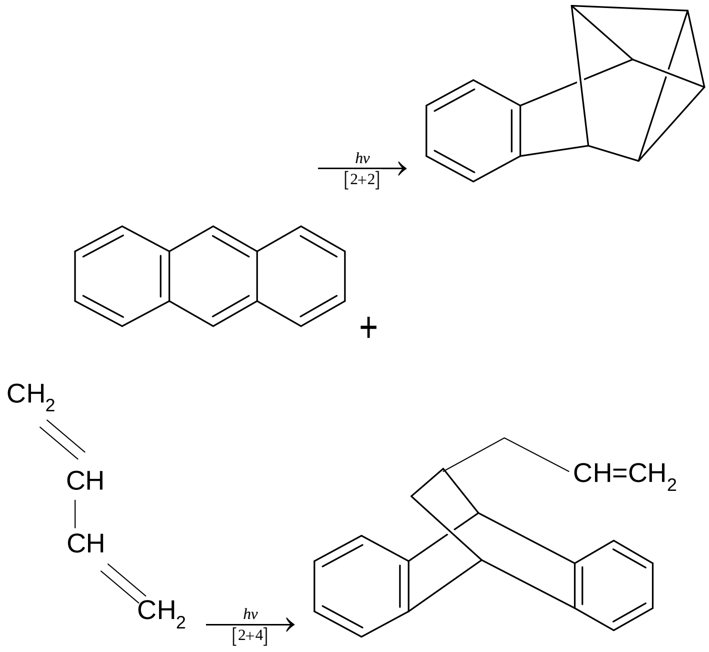






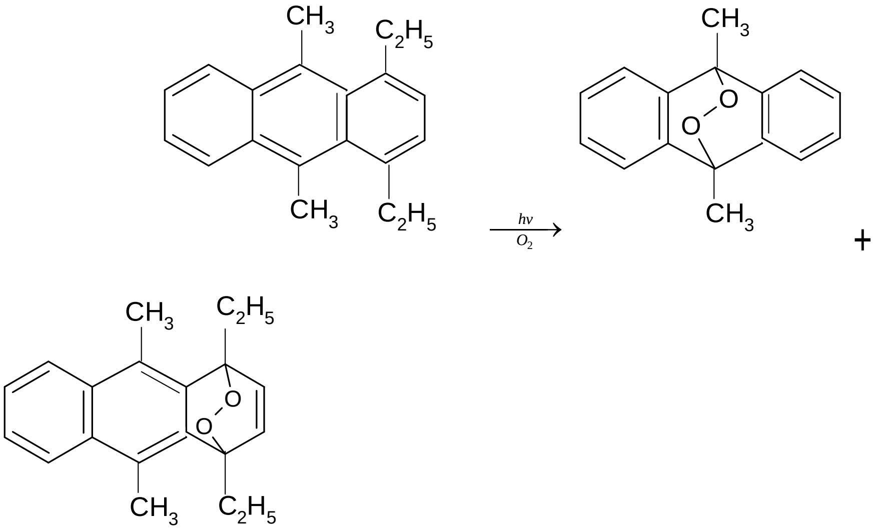
$CH_2 = CH - C \equiv N$

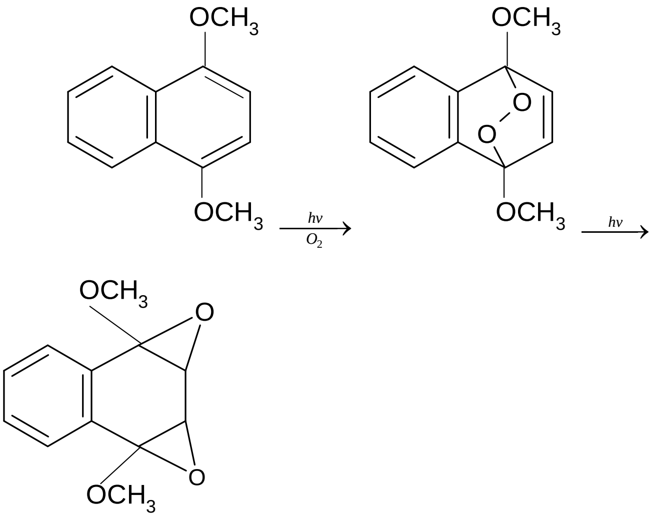




14.4.4 Photochemical addition of oxygen

Condensed ring systems such as nepthalene and anthracene undergo photochemical addition with oxygen to form peroxides. The nature of the final product depends upon the nature of the substituents presents on aromatic system for example.



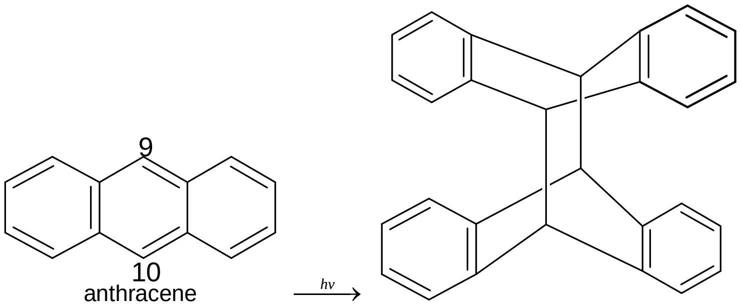


The mechanical studies of this photochemical reaction have shown that triplet excited state of aromatic hydrocarbon first excites oxygen molecule by the process of energy transfer as a result of this singlet oxygen is produced. This singlet oxygen now adds thermally with the ground state of aromatic hydrocarbon. Thus the reaction is a [4+2] cycloaddition type.

14.4.5 Photochemical dimerisation reactions of aromatic hydrocarbons

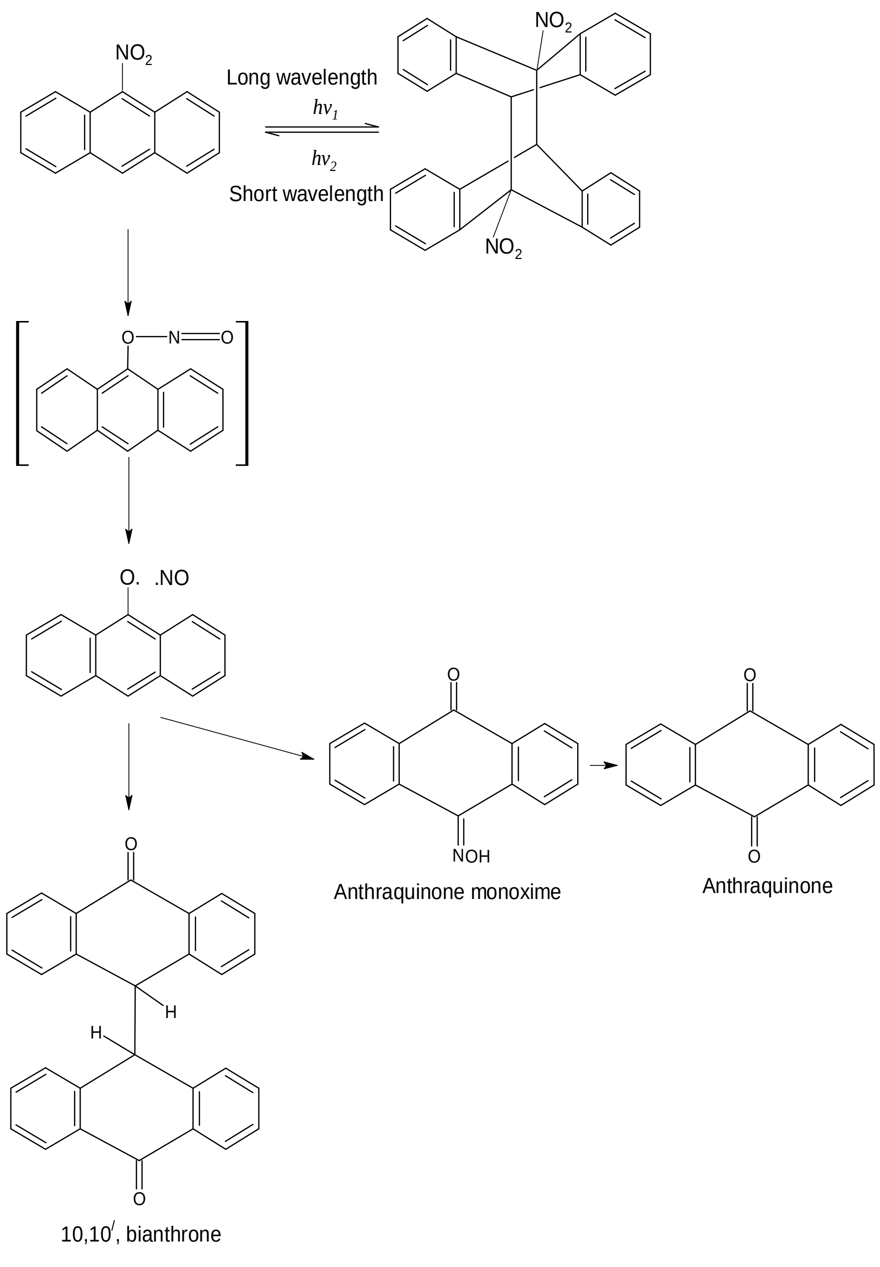
It has been observed that under the conditions of high concentration of aromatic compound, some typical photochemical dimerisation reactions take place.

Napthalene and Anthracene undergophotodimerisation consider the following reaction of Anthracene.



Here two molecules of anthracene undergo addition at 9, 10-positions. If a substituent is present at 9- position of anthracene than a head to tail dimer is obtained. This dimerisation has been found to be dependent upon the wavelength of the light used in the photochemical process. In general irradiation with longer wavelength results in dimerisation whereas shorter wavelengths cause other processes to occur because shorter wavelength radiation are associated with high energy and so cause the photochemical cleavage of the dimer formed.

For example when 9-nitroanthracene is irradiated with long wavelength light produces the dimer on the other hand when the same process is carried out by irradiation with shorter wavelength the products formed are nitric oxide (NO), anthraquinone, anthraquinone monoxime, and $10,10^{/}$-bianthrone. It is supposed that these products are produced through 9-anthryl nitrile intermediate. The reaction is shown below

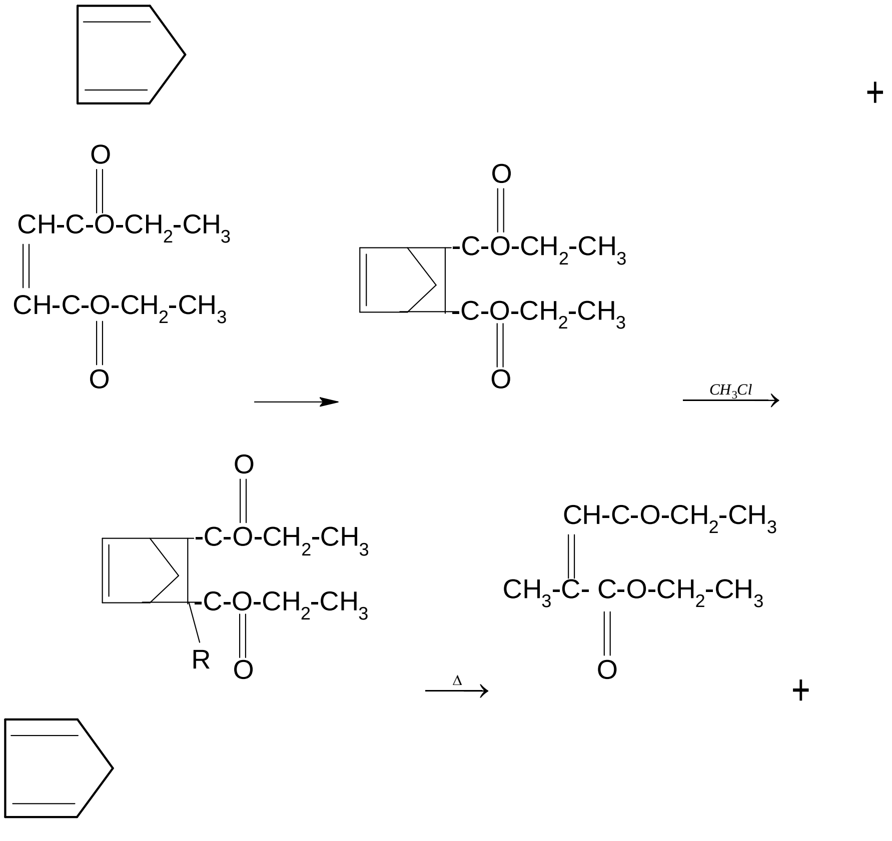


It is interesting to note that the electron distribution in excited and ground state of an aromatic compound is quite different. This can be illustrated by comparing the dissociation constants of phenyl in its excited and ground state. The following table shows the pK_a values for 2-nepthol and 2-nepthylamine. It can be noted that the difference in the values in S_0 and S_1 state indicate a major change in electron density in these state .

Compound	pK_a		
	S_0	S_1	T_1
2-naphthol	9.5	3.1	8.1
2-naphthylamine	4.1	-2	3.3

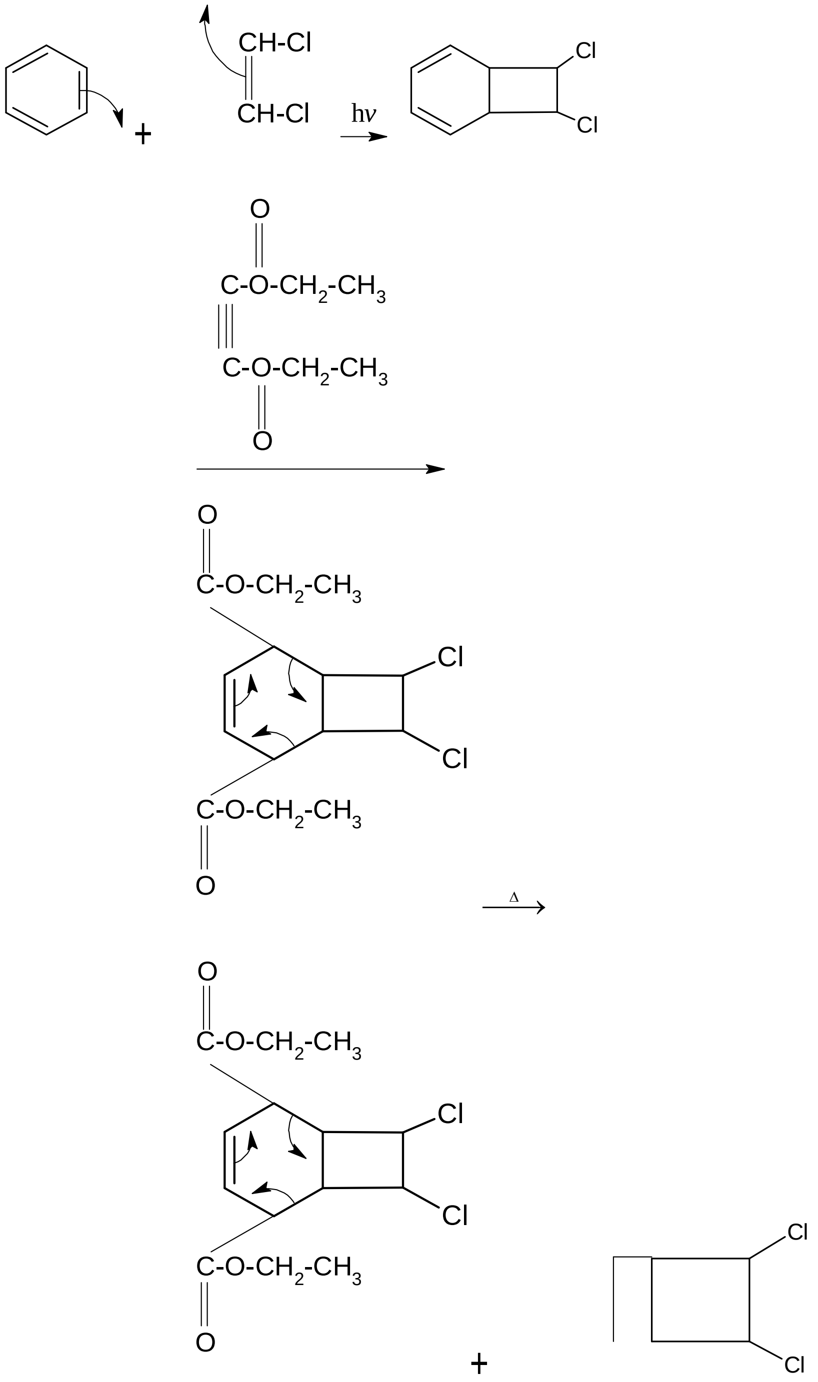
14.5 Application of photochemical addition reaction of aromatic compounds

(1) In photochemical addition the most common is cycloreversion which is also know as retro-Diels-Alder's reaction. By the use of this reaction new type of chemically modified dienophile can be synthesise. This is shown below



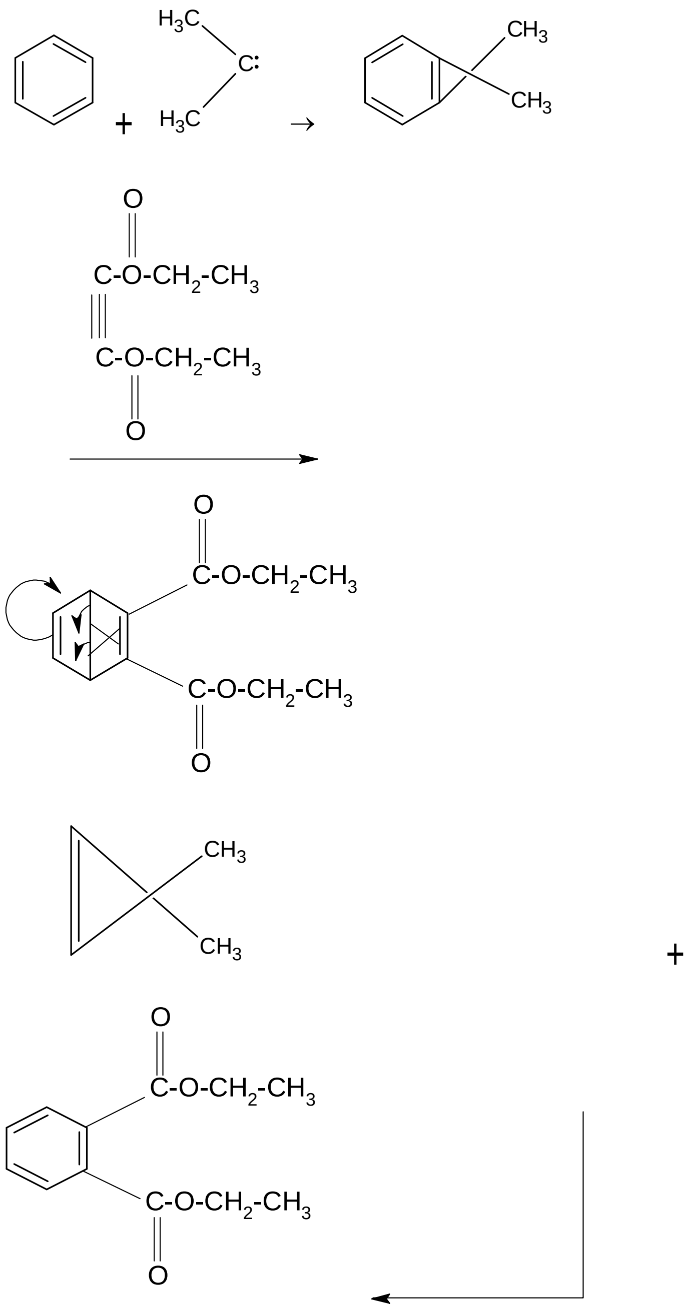
(2) It is possible to produce highly reactive compounds which cannot be prepared by conventional methods. These are then used as reagents for preparing various other organic compounds. This can be illustrated by following examples

(a)



(highly reactive compound)

(b)



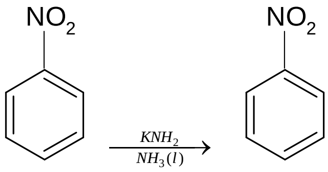
14.6 Photochemical substitution reaction of aromatic compounds

Substitiution reactions either in aromatic ring or in side chain of the ring can be carried out photochemically. These reactions can occur with homolytic or heterolytic cleavage of the bond in the substrate molcule. The quantum yield of such reaction is found to be very high and they involves the lowest singlet state.

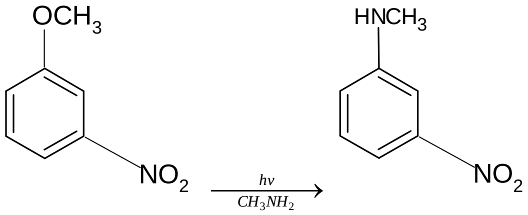
It has been mentioned earlier that there is a great difference in the distribution of charge in ground and excited state of the molecule. Thus in photochemical reactions it is possible to control the position of the nucleophile deriving substitution reactions in the following pages it is discussed in detail.

16.6.1 Nucleohilic substitution

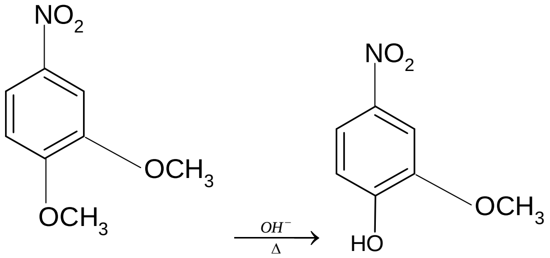
It is known in general chemistry that if $-NO_2$ group is seated on benzene ring it activates the attacking nucleophile at ortho and para position Viz-



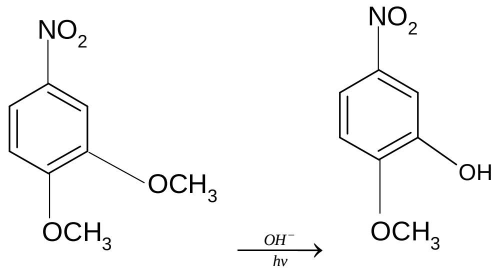
But it is observed that during photochemical reaction which involves excited state the $-NO_2$ group behaves as meta directing group.



Similarly the compound 3,4-dimethoxynitrobenzene when heated with OH^- ions produces 4-hydroxy-3-methoxynitrobenzene ie the $-OCH_3$ group at 4 position is replaced by -OH group.



On the otherhand when the same reaction is carried out photochemically ie by irradiating with UV light the $-OCH_3$ group present at 3-position is replaced by OH^- group. ie



The reason of this behaviour is that under the influence of heat, the -NO_2 group makes ortho and para position of the ring positive due to its -I and -M effect but under photochemical conditions ortho and meta positive become positive compared to para position.

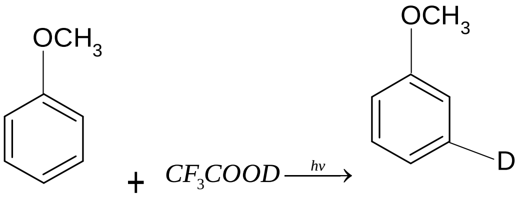
Similar reactions are observed with cyano group when it is present on nepthalenes and substituted nepthalenes.

16.6.2 Electrophillic substitutions

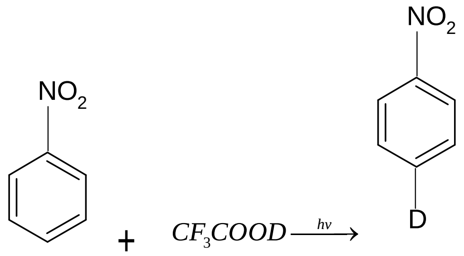
Unexpected products can be obtained by photochemical electrophonic substitution of substituted benzene. For examples,

Usually the -CH_3 group is ortho and para directing under thermal conditions but when toluene is irradiated in the presence of CF_3COOD, m-deuterio substituted toluene is obtained as a major product Viz-

The same reactions when carried out with Anisole and nitrobenzene we get unexpected product as shown below.



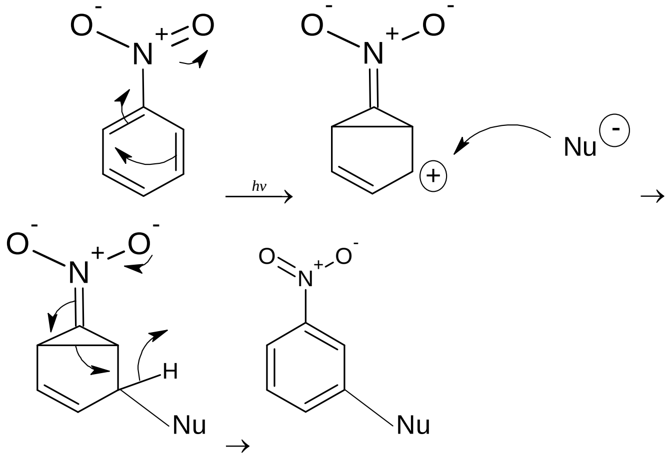
m -deuterio anisol



p-deuteri o nitrobenzene

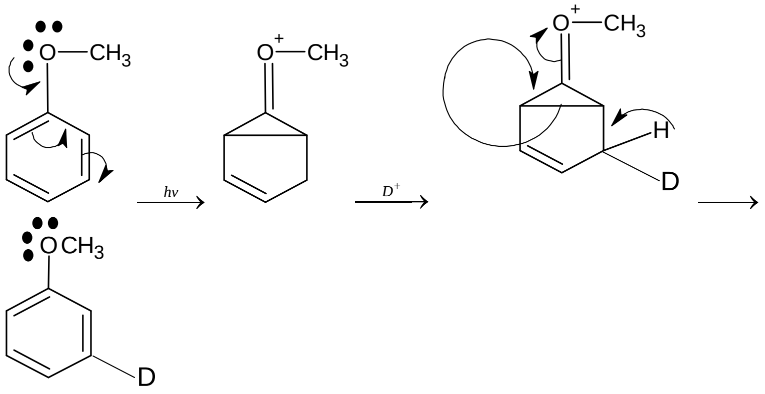
Thus it can be concluded that orientation of various groups becomes different in photochemical processes. Here nitro group activates the paraposition and methoxy group activates Meta position.

These results can be explained by reorganising the orientation rules for electrophillic and nucleophillic susbtitution by considering the change in the change distribution in ground and excited state ie S_0 S_1. of the ring of the point of attack. An electron withdrawing substituent decreases the electron density at m-position so it acts as a m-directing group for the incoming nucleophilic substituent



Mechanism of photonucleophilic substitution

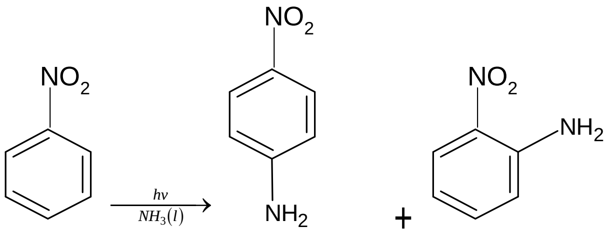
On the parallel lines an electron donating group causes an increase in the electron density at m-position so behaves as a m-director for in coming electrophilic substituent Viz-



Mechanism of Photoelectric Substitution

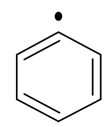
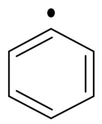
14.6.3 Other type of substitutions

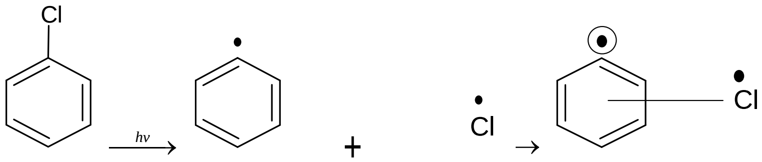
These types of photochemical substitution follow the orientation rules characteristic of the ground state of the benzene ring. The detailed mechanism of these types of photochemical substitution is still a matter of investigation. For example



14.6.4 Photochemical radical substitution reactions

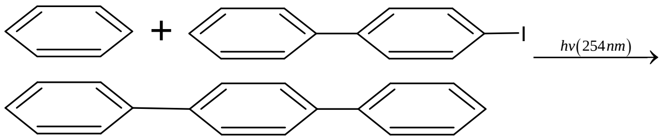
Sometimes it so happens in photochemical reaction that when subjected to exposure of light, the aromatic compound undergoes homolytic cleavage in its ground state resulting in the production of free radicals which then give rise to the final products. It is to be noted that in such cases the products obtained are those characteristic of reactions. $Ar + X \xrightarrow{hv} \dot{Ar} + \dot{X}$

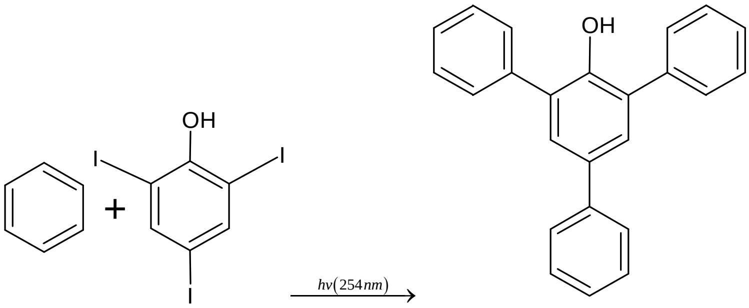
When Chlorobenzene is irradiated in liquid phase the  + $\overset{\bullet}{Cl}$ radical combine to generate transient $\pi-$chlorobenzene and an isomer of chlorobenzene in which the chorine forms a $\pi-$complex with  radical Viz-



($\pi-$complex)

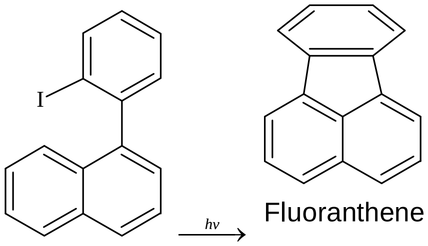
This type of photochemical homolytic cleavage of a bond between carbon atom of aromatic ring and halogen has been used to produce phenyl substituted aromatic compounds. For example



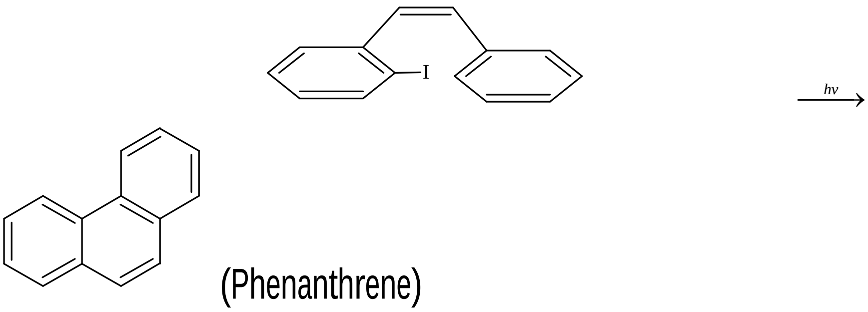


It is to be noted that the Yield of these compounds is very high.

Similarly polynuclear compounds can also be produced by these photochemical processes in good amount.

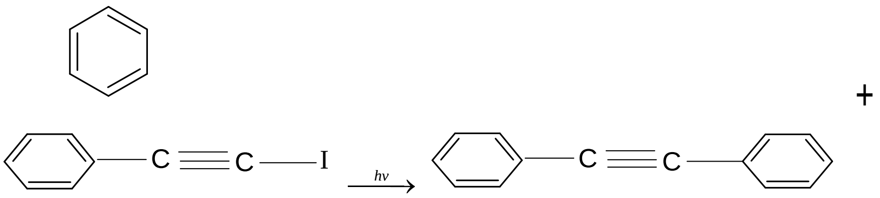


Fluoranthene



(Phenanthrene)

Similar reactions are also given by iodoacetylenes also.



14.7 Summary

- In excited state benzene yields benzvalene, fulven, prismane,most of the photochemical isomerisation reactions of benzene involve 1-2 shift by benzvalen intermediate.
- some mechanistic path involves prismane intermediate during 1-2,1-3 alkyl shifts
- Tracer technique using 14C has been used to investigate the mechanical pathway.
- Photochemical addition reactions of aromatic system produce unexpected products through the charge transfer process.
- During substitution reaction in photochemistry the orientation rule are entirely changed.

14.8 Review Questions

1. Discuss in detail various excited state of benzene.
2 Discussss the mechanism of 1-2 Alkyl shift by benzavalene intermediate. (2) by primane intermediate
3 write an expainatory note on photochemical isomerisation of the tetra substituted benzene.
4 write short notes on
    (a)1,2 photochemical addition reaction
    (b)1,2 photochemical addition reaction
    (c) Photochemical addition reaction
5 what are the various applications of the photochemical reaction of the aromatic compounds.

14.9 Refrence Books

- Organic Photochemistry,Gurdeep R Chatwal,Himalya Publication House.
- Fundamental of hotochemstry,K.K rohatgi-Mukherjee, New age international.
- Organic Photochemistry,R.C Ameta

Unit - 15

Miscellaneous Photochemical Reactions

Structure of unit:

15.0 Photo fries rearrangements

This reaction involves migration of a group across a double bond (1,3 migration) in structure of the following type:

Such rearrangements in aromatic systems lead to 1,3 and 1,5 migration of an R group.

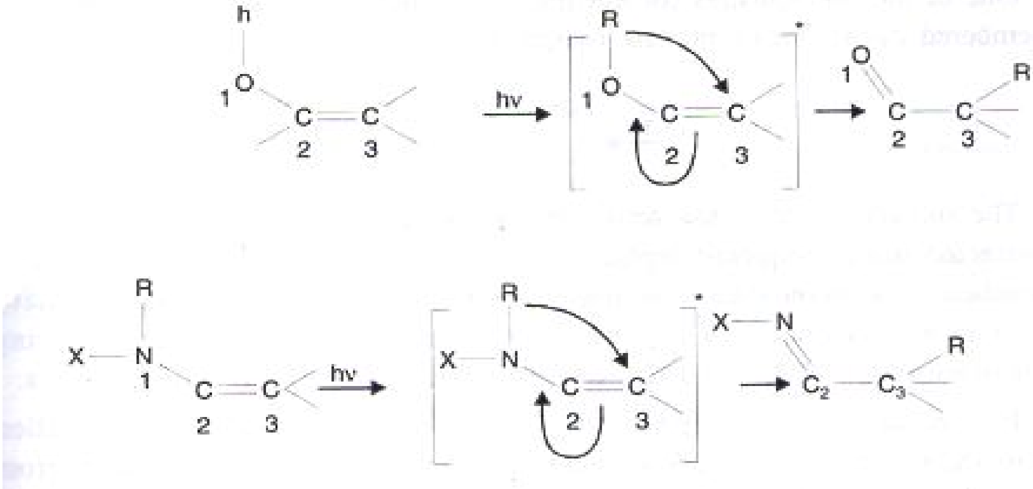


Fig.1: Mechanism of Photo fries rearrangement reaction

Photofries rearrangement is an intramolecular rearrangement, where acyl and alkyl groups migrate to ortho- and para- positions on irradiation. In this rearrangement , the substrate dissociates into phenoxy and acyl radicals, which recombine within the solvent cage to give intermediates on aromatization to the product.

When photofries rearrangement is carried out in gaseous phase, only phenol is obtained, which confirms the formation of solvent cage.

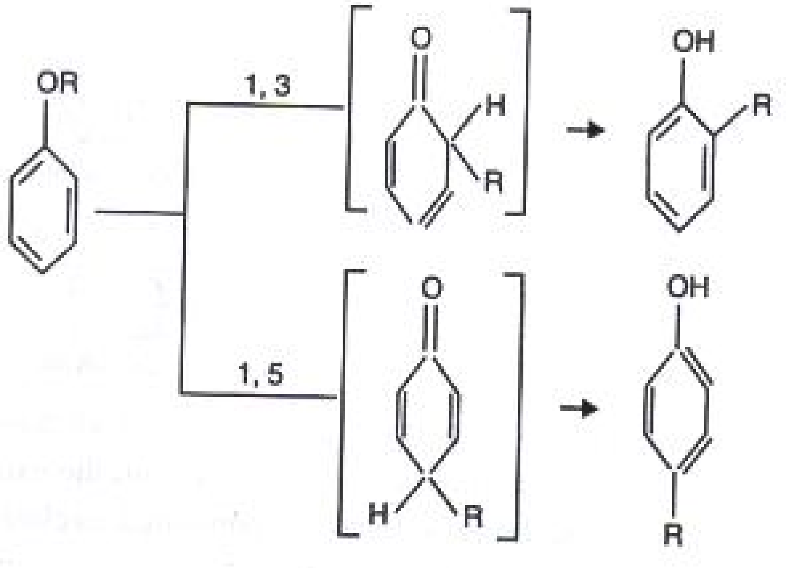


Fig.2: Photo fries rearrangement reaction

15.1 Photo Fries reaction of anilides

The corresponding reaction for anilides is as follows:

These rearrangements occurs through intermediate formation of free radicals.

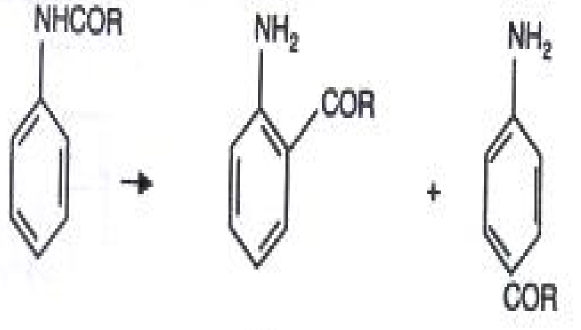


Fig.3: Photo fries reaction of anilides

15.2 Barton reaction

Photolytic conversion of organic nitrites into nitroso alcohols is known as Barton reaction. When a compound consists of the C-O-NO group and a C-H bond is brought into close proximity (generally 1,5-position), the alkoxyl radicals are formed by photolysis of nitrites, in the solution phase , which have suffficient energy to bring about selective intramolecular abstraction of hydrogen atom and produce a carbon radical.

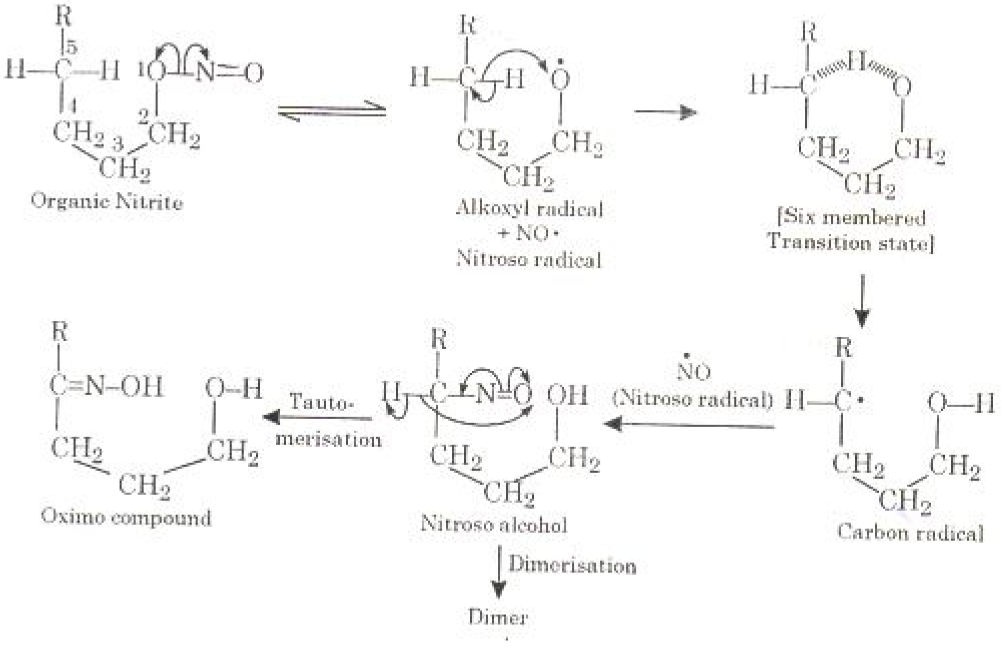
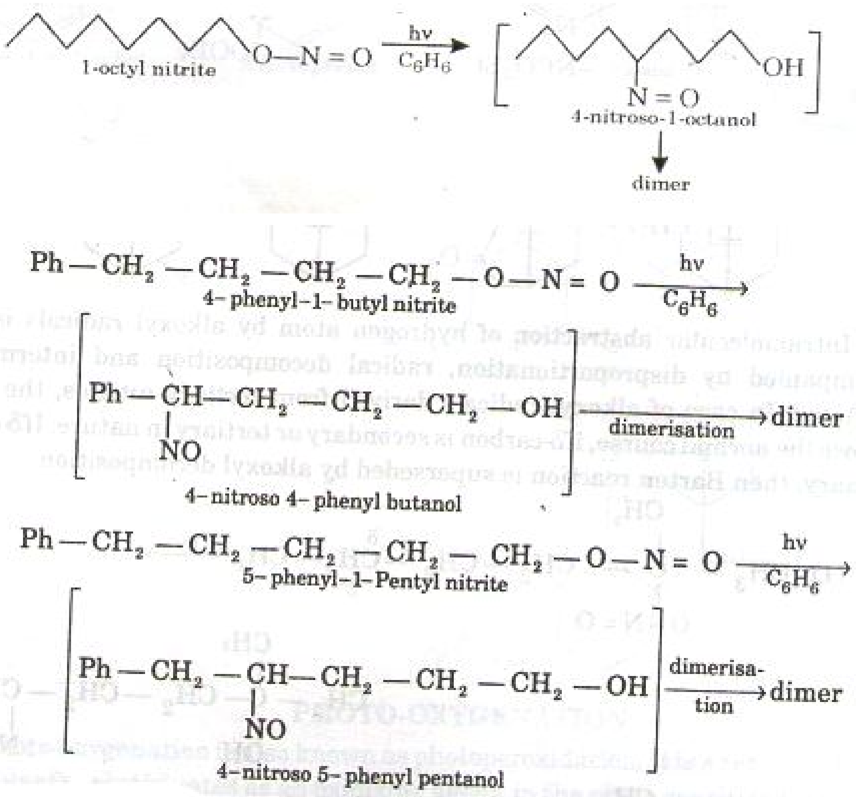


Fig. 4: Mechanism of Barton reaction

Some examples of Barton reaction are given below:



The produced carbon radical reacts with nitrogen monoxide (NO) and gives nitroso alcohol. The nitroso alcohol can be isolated from the solution by process of dimerisation.

One of the prerequisities for the Barton reaction is the availability of a six membered cyclic transition state.

As the Barton reaction consists of great selectivity in the hydrogen abstraction step , it has found application mainly in the field of steroids.

15.3 Singlet molecular oxygen reaction

Kautsky discovered the reactivity of singlet oxygen in 1930, to explain sensitized oxidation of substrates when absorbed on silica gel.

15.3.1 Configuration of molecular oxygen

Molecular oxygen has a unique electronic configuration in that the electronic character of ground state oxygen is triplet.

$O_2 = \sigma(1s)^2, \sigma^*(1s)^2, \sigma(2s)^2, \sigma^*(2s)^2, \sigma(2px)^2, \pi(2py)^2, \pi(2pz)^2, \pi^*(2py)^1, \pi^*(2pz)^1$

It has two unpaired electrons , one in π*(2py) and other in π*(2pz). Therefore ,it has triplet multiplicity i.e., 2s + 1 = (2 × 1 +1) = 3 .

15.3.2 Types of Singlet oxygen

Two types of singlet oxygen can be generated photochemicallly:

1. $^1\Delta g$ singlet oxygen
2. $^{1}\Sigma g^{+}$ singlet oxygen

15.3.3 Electronic configuration of $^1\Delta g$ singlet oxygen

It is $\sigma(1s)^2$, $\sigma^*(1s)^2$, $\sigma(2s)^2$, $\sigma^*(2s)^2$, $\sigma(2px)^2$, $\pi(2py)2 = \pi^*(2py)^2$, $\pi(2pz)^2$, $\pi^*(2pz)^0$

Vacant orbital

$^1\Delta g$ singlet oxygen is mostly responsible for usual photo-oxygenation reaction.

15.3.4 Electronic configuration of $^1\Sigma g^+$ singlet oxygen

It is $\sigma(1s)^2$, $\sigma^*(1s)^2$, $\sigma(2s)^2$, $\sigma^*(2s)^2$, $\sigma(2px)^2$, $\pi(2py)2 = \pi(2pz)^2$, $\pi^*(2py)^1\uparrow$, $\pi^*(2pz)^1\downarrow$

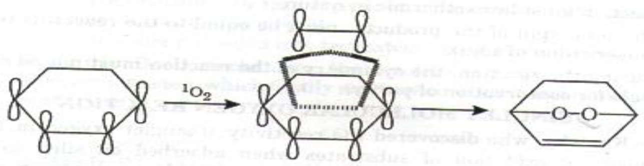
Half filled orbital

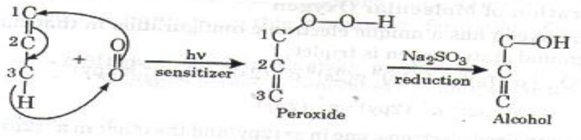
Half filled orbital with opposite spin

15.3.5 Photo-Oxygenation Reaction.

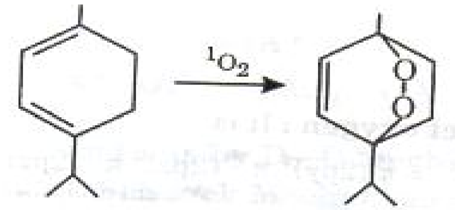
a. Cisoid Dienes – Singlet oxygen gives addition reactions with cisoid dienes. This reaction proceeds in concerted manner by formation of six membered transition state.

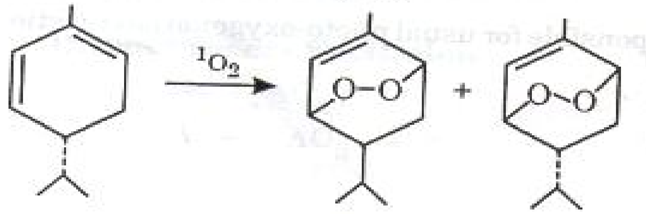
   Monoalkenes give 1,4- cycloadddition reaction with singlet oxygen:

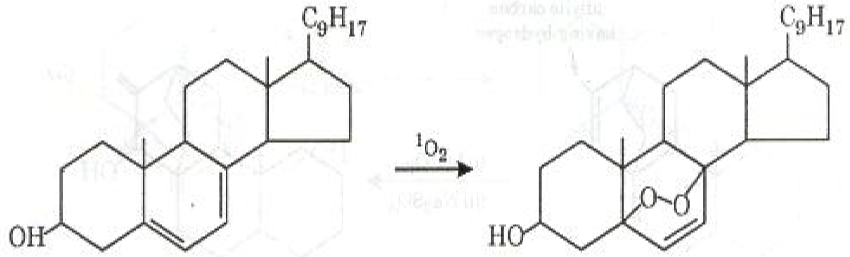


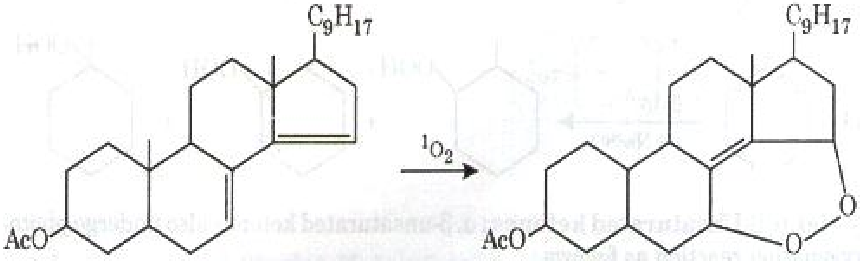


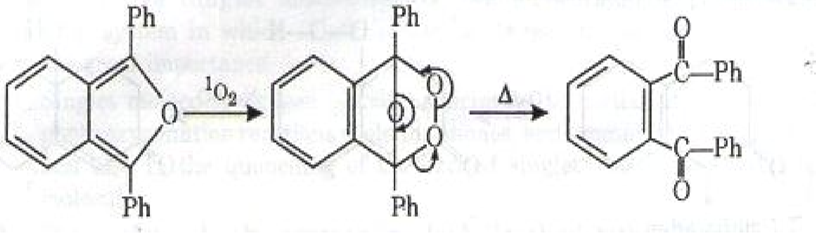
Some more examples of photo-oxygenation are given below:







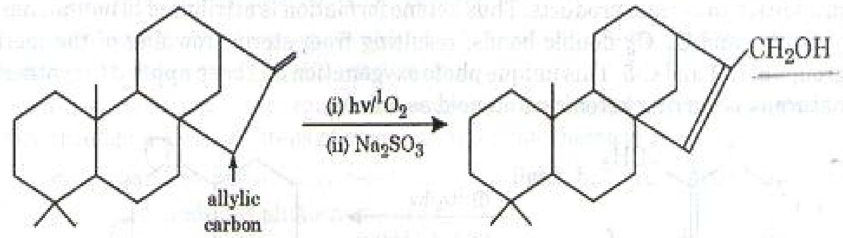




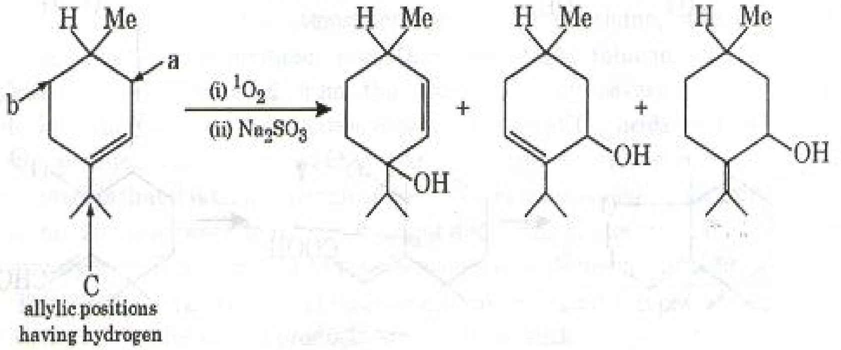
b. Mono-olefines

Olefins give hydroperoxy compounds and the reaction is called an ‘ene’ reaction. Some examples of the photo-oxygenation of mono-olefines are given below:

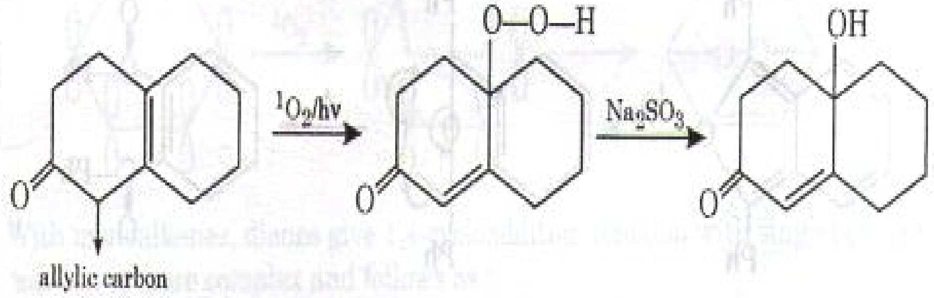
(1)



(2)



c. β-ɣ unsaturated ketones - β-ɣ unsaturated ketones also undergoes photooxygenation reaction as folllows:



d. Caratenoids and related terpenoids- Photo oxygenation of carotenoid and terpenoids give ketene derivatives in addition to normal products.

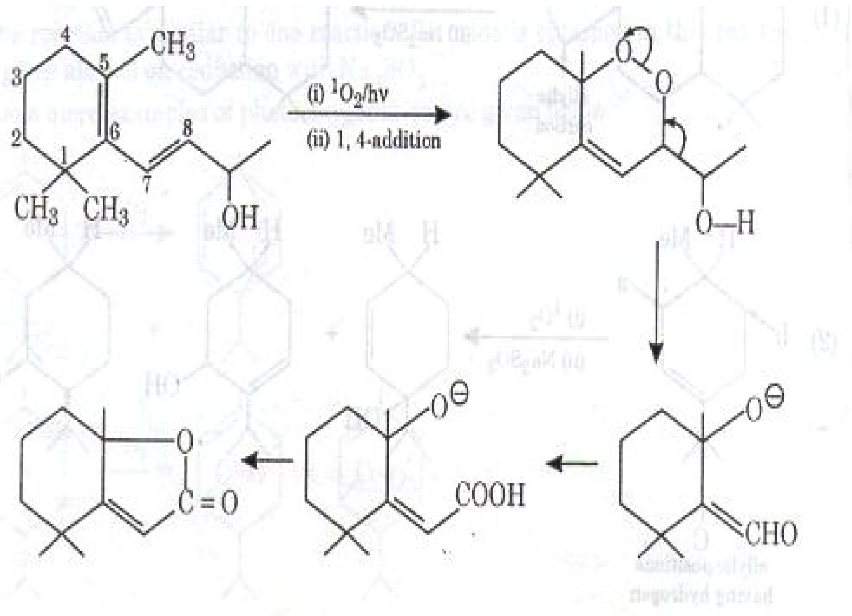


Fig.5: The unique Photooxygenation reaction to synthesized naturally occurring ketenic carotenoids.

15.3.6 Importance of singlet molecular oxygen

1. Singlet molecular oxygen participates in various dye sensitized photo oxygenation reactions of olefins , dienes and aromatic hydrocarbons.
2. It is used in the quenching of the excited singlet and triplet states of molecules.
3. It is involved in the chemiluminescent phenomena , photo dynamic reactions, photocarcinogenicity and in metal catalyzed oxygenation reactions.

15.4 Photochemical formation of smog

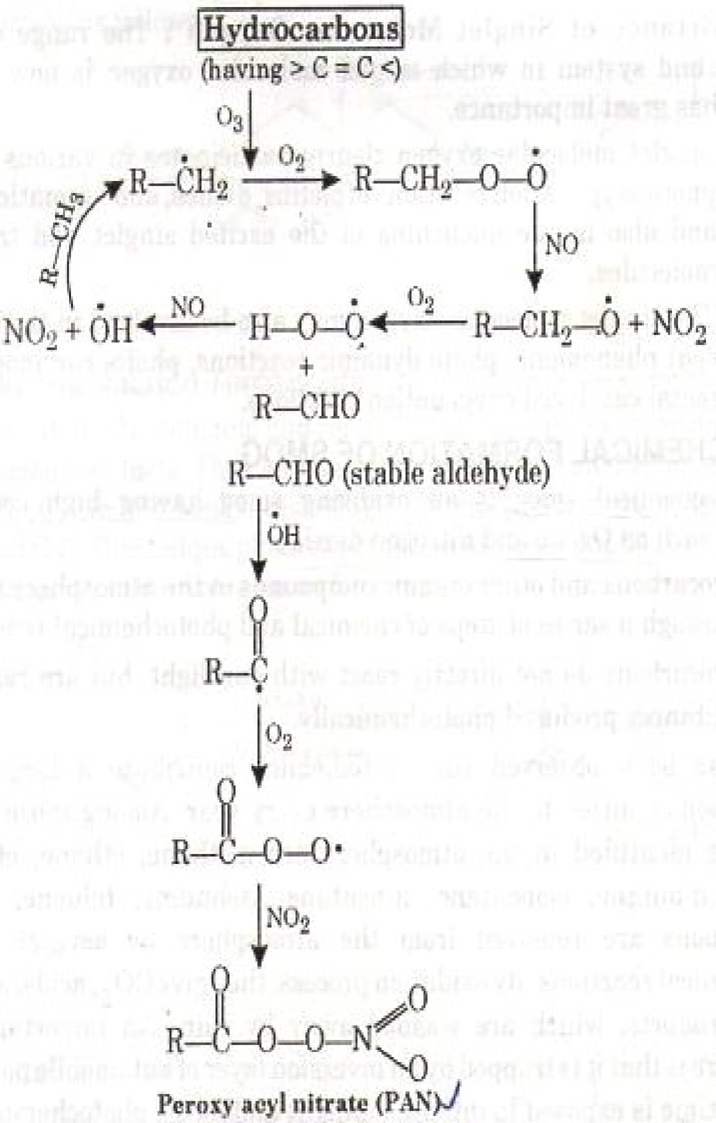
Photochemical smog is an oxidizing smog having high concentration of oxidants like ozone and nitrogen dioxide.

Hydrocarbons and other organic compounds in the atmosphere are assumed to oxidize through a series of steps of chemical and photochemical reactions. After oxidation processs, they give CO_2, acids and aldehydes as end products and washed away by rain.

An important property of atmosphere is that it is trapped by an inversion layer of automobile pollutants and at the same time it is exposed to intense sunlight and form photochemical oxidants in the atmosphere. This give rise to the phenomenon of photo chemical smog.

15.4.1 Reaction of smog formation

The probable reaction of smog formation with its mechanism is given below:



In the formation of smog, a brown haze is found in the atmosphere. It is due to the heavy concentration of particles in the atmosphere.

15.4.2 Effect of smog on life

1. Damage to materials like rubber , vegetation etc. and alse lead respiratory disorders.
2. Peroxyl acyl nitrate (PAN) is produced in the atmosphere which is a phototoxic substance.
3. PAN , acrolein and formaldehyde also caused eye irritation.

15.5 Photochemistry of vision

The eye of vertebrae consists of lens and retina . The retina is made up of two types of light sensitive cells , rods and cones. The rods and cones present in the retina act as the receptors of the eye. The rods are sensitive for low light intensity and responsible for vision in dim light . The cones are responsible for colour selector .

15.5.1 Photosensitive pigment

The photosensitive pigment present in rods is called rhodopsin or visual purple pigment. Its opsin is scotopsin and retinal is 11-cis retinal. Rhodopsin is present in the membrane of the rod disks as shown in diagram given below.

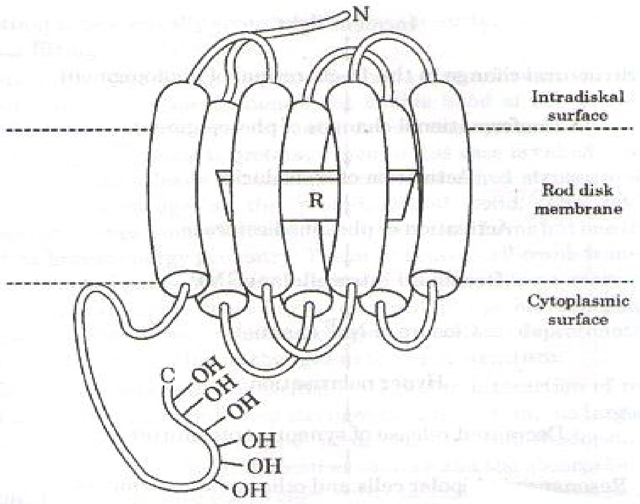


Fig.6: Diagramatic representation of the structure of rhodopsin.

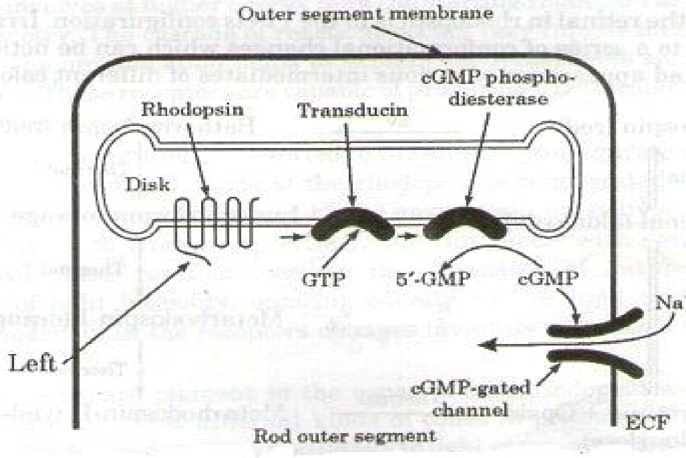


Fig.7: Steps in phototransduction in rods.

Rhodopsin is very sensitive light receptor and coupled with G-proteins. Complexation between the opsin and the 11-cis retinal takes place by imine formation between the primary amino group of lysine in the side chain of the protein and the aldehyde group of 11-cis retinal to form rhodopsin. This protein retinal complex absorbs light energy of a visible photon and undergoes a stereomutation of the 11-cis C=C to 11-trans C=C .This change in the molecular geometry of retinal separates it from the protein surface. This is due to the fact that the all-trans structure of retinal cannot be sterically accommodated on the opsin surface , only 11-cis form can be accommodated. This detachment of the two components of the complex is called bleaching of rhodopsin. Such bleaching causes an electrical signal to be sent to the brain where it is translated into a visual image.

The photosensitive pigment in the cone cells is called iodopsin. The protein part is photopsin. There are three different kinds of cones in man. These respond maximally at wavelengths 455nm (blue), 535nm (green) and 622nm (red). Each contains 11-cis-retinal and photopsin. The photons of these three wavelengths cause a change in the configuration of the 11-cis form to all trans form of retinal in each type of cone cell, causing an electric signal to the brain, which translates it to the respective colours.

The time taken for such changes in configuration in retinal and sending the electric signal to the brain and its perception is of order of a few picoseconds. The chemical changes taking place in the chemistry of vision are very fast(10^{-12}s).

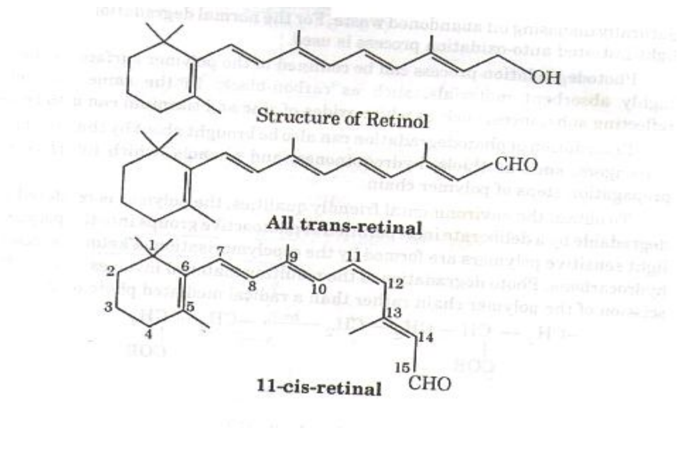


Fig. 8: Structure of retinol, 11-cis-retinal and all trans-retinal

Irradiation of rhodopsin leads to a series of conformational changes which can be noticed by the disappearance and appearance of various intermediates of different colours. In the dark the retinal in rhodopsin is in the 11-cis configuration .

hv

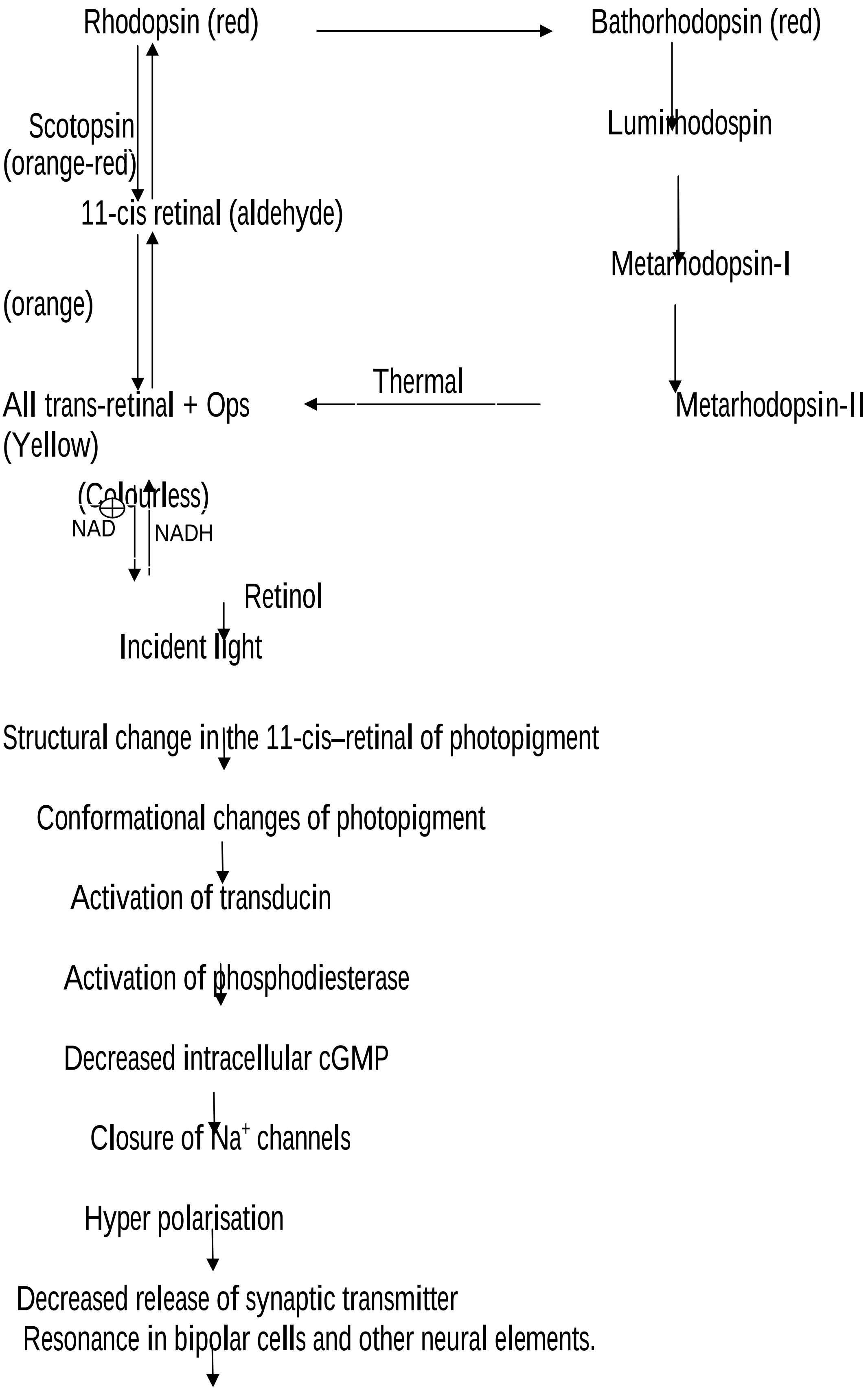


Fig. Sequence of events involved in phototransduction in rods and cones of eye.

15.6 Summary

- When Photofries rearrangement is carried out in gaseous phase , only phenol is obtained.
- The prerequisities for the Barton reaction is the availability of a six-membered cyclic transition state.
- Generally, $^1\Delta g$ singlet oxygen is responsible for photo oxygenation reaction.
- Singlet oxygen gives addition reaction with cisoid dienes and mono-olefines.
- During the formation of photochemical smog, various types of secondary pollutant intermediates and products are formed.
- Eyes contain two types of light sensitive cells rods and cones. The eyes possess photosensitive protein which is of two types, opsin and retinal.
- Photosensitive pigment in rods is rhodopsin and in cones is iodopsin.
- Light activates 11-cis retinal and this activates Gt_2 which activates phosphodiesterase, catalyzing the conversion of cGMP to 5’GMP.

15.7 Review questions

1 Explain Photofries rearrangement.

2 What is Barton’s reaction ? Give its mechanism.

3 Why cyclohexyl nitrite on photolysis does not give a product typical of Barton reaction while cyclooctyl nitrite (II) reacts in this manner ?

4 Why in a Barton reaction from a long chain alcohol , the alkoxy radical formed in the reaction abstracts a hydrogen from its own chain exclusively from the δ -position and not from the γ-position ?

5 Write the electronic configuration of the following:

a. Molecular oxygen b. $^1\Delta g$ singlet oxygen

c. $^1\Sigma g^+$ singlet oxygen

6 How many types of singlet oxygen can be generated photochemicallly?

7 Discuss the addition reactions of singlet oxygen with –

1. Cisoid dienes 2. Mono-olefines

3. β-ɣ unsaturated ketones 4. Carotenoids

8 Give the importance of singlet molecular oxygen.

9 Discuss the role of hydrocarbons in photochemical formation of smog.

10 Explain the effects of photochemical smog on life.

11 Describe the various reactions involved in smog formation .

12 Explain photochemistry of vision.

13 Discuss the role of photosensitive pigment in vision.

14 Which photosensitive pigment present in rods and cones?

15 Describe the sequence of events involved in phototransduction in rods and cones of eye.

15.8 References and Suggested readings

- Modern Molecular Photochemistry ,N. J. Turro ,Springer ,1991.
- Fundamentals of Photochemistry, K.K. Rohatgi-Mukherjee, New Age International Publishers, 2014 (Third Edition).
- Organic Reactions and their Mechanisms, P.S.Kalsi, New Age International Publishers, 2000 (Second Edition).
- Organic Chemistry, R. T. Morrison, R.N.Boyd and S.K.Bhattacharjee, Pearson, 2011 (Seventh edition).

Unit -16

Conformations of Some Acyclic Molecules

Structure of unit:

16.0 Meaning of conformation

The term conformation is used to denote any one of the infinite number of momentary arrangements of the atoms in space that results from rotation about single bond.

Conformation can be defined as the different spatial arrangements of atoms in a molecule which are readily interconvertible by rotation about single bonds are called.

Conformers / rotamers / conformational isomers are readily interconvertible and nonseparable.

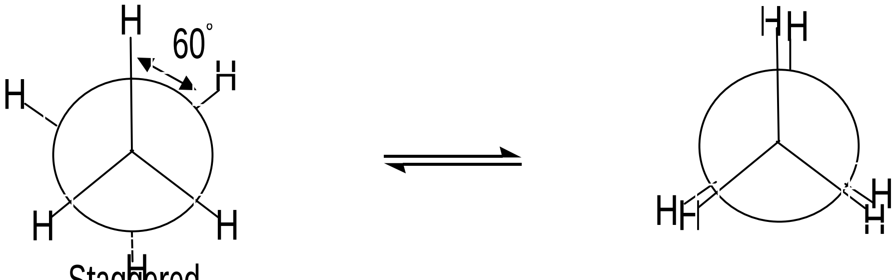
A study of physicochemical properties of a compound in terms of its conformations in the ground and transition state, is called conformational analysis.

Conformation and configuration are the terms related to energy barrier for interconversion of different spatial arrangements of atoms in a molecule.

In case of conformers energy barrier for conversion of different spatial arrangements is in between >0.6 and < 16 Kcal/mole but in configuration it is > 16 Kcal / mole.

16.1 Conformation of ethane

When an ethane molecule rotates about its carbon-carbon single bond, then two extreme conformations are found i.e. staggered and eclipsed conformation. An infinite number of conformations between these two extreme conformations are also possible. The Newman projections for staggered and eclipsed conformations of ethane are given below.



Staggered

Eclipsed

Fig. 1 : Conformations of ethane

Staggered conformation: A conformation with a 60° dihedral / torsional angle (angle between the atoms attached to the front and the rear carbon atoms) is known as staggered conformation. It is the most stable conformation because the carbon-hydrogen bonds are as far away from each other as possible. In staggered conformation the distance between hydrogen nuclei is 2.55 Å.

Eclipsed conformation: A conformation with a 0° torsional angle is known as eclipsed conformation. It is the least stable conformation because the carbon-hydrogen bonds are closest. In eclipsed conformation the distance between hydrogen nuclei is 2.29 Å. The rotational energy barrier in ethane is 2.9 kcal / mole.

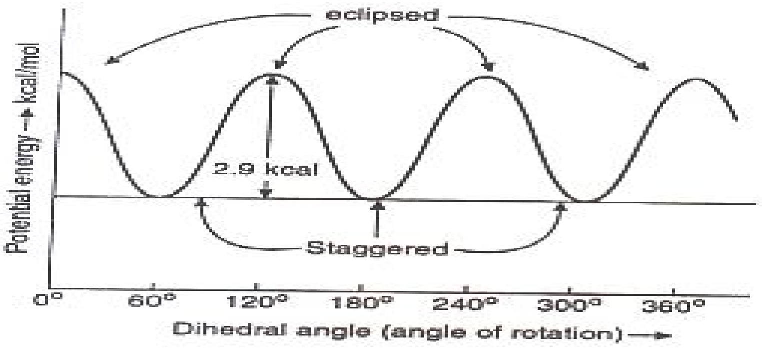


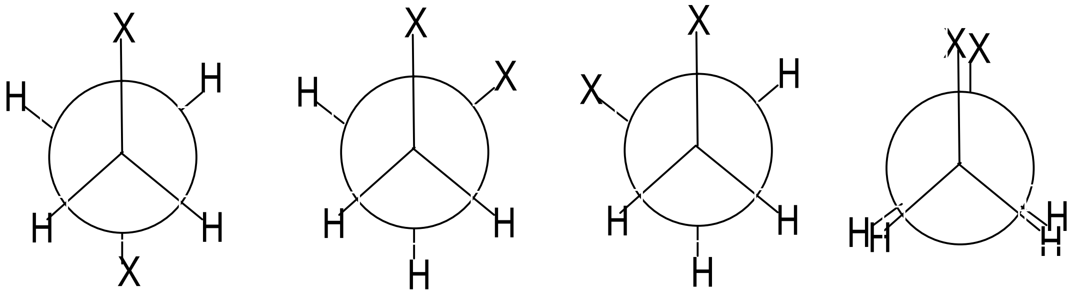
Fig.2: Rotational energy profile for ethane

16.2 Conformation of 1,2-dihaloethanes

The conformations of 1, 2-dihaloethanes have been extensively studied by various physical methods. The energy differences between conformational isomers of 1,2-dihaloethanes can be obtained by thermodynamic properties, dipole moment measurement, infrared, Raman and microwave studies. The energy differences between the different conformational isomers of 1,2 dihaloethane are as follows:

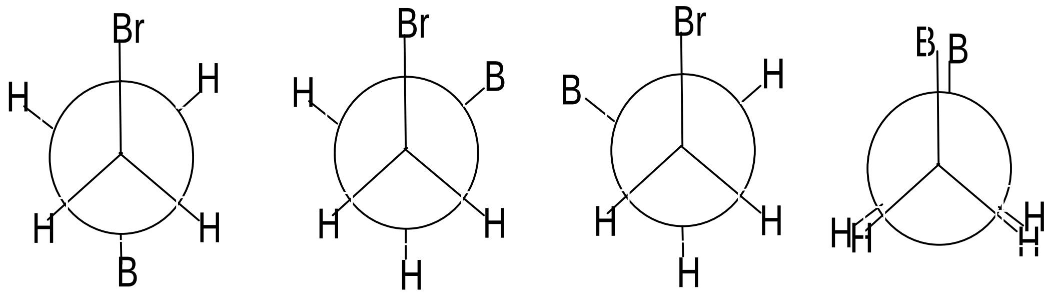
a.1,2 dibromoethane – 1.4 to 1.8 kcal./mole in gas and 0.73 to 0.76 kcal./mole in liquid. In gaseous state (at 22°C) 1,2 dibromoethane contain 85% anti conformers due to steric factor and electronic interaction (dipole-dipole repulsion).

b. 1, 2 dichloroethane – 1.0 to 1.3 kcal./mole in gas and 0.0 kcal./mole in liquid. In gaseous state (at 22°C) 1,2 dichloroethane contain 73% anti conformers. In 1,2 dichloroethane the two conformers, anti and gauche are equally populated in the liquid state.



Ant P- M- Cis

Fig. 3: Various conformations of 1, 2 dihaloethane

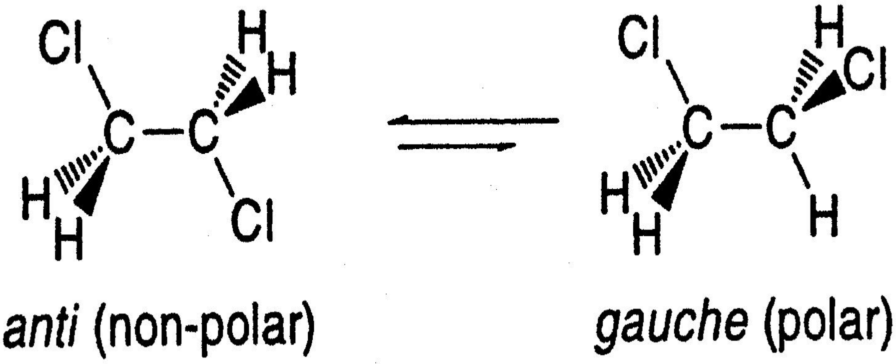


Ant P- M- Cis

Fig. 4: Various conformations of 1, 2 dibromoethane

The anti and gauche forms of 1, 2 dibromoethane possess different dipole moments. In anti form, the C-Br bond dipoles are antiparallel so its dipole moment is zero whereas in the gauche form it possesses finite value. 1,2 chlorofluoro, 1,2-bromofluoro and 1,2 fluoroiodoethane possess predominantly anti form in gaseous state and gauche form in liquid state.

Effect of polarity of solvent on conformation: In the presence of polar solvents, the electrostatic repulsion decreases due to high dielectric constant of the medium and the ratio of gauche conformers increases. Gauche form possesses considerable dipole moment, so it is preferably found in polar solvents.



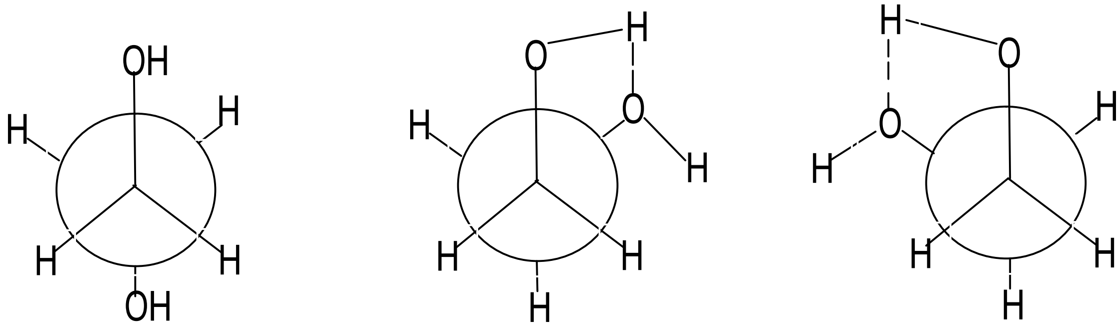
On increasing the number of halogen substituents , the barrier energy increases gradually from 15.5 KJ/mol in ethyl chloride to 50- 60 KJ/mol in hexachloroethane. Tetrabromo derivatives and tetrachloro derivatives exhibit preference for gauche conformer over the anti.

The maximum possible number of vibrations (IR and Raman lines) in a non-linear molecule like 1, 2 dibromoethane exhibit (3N - 6) where N is the number of atoms in the molecule. 1,2 dibromoethane in liquid and gaseous state show more than the allowed number of lines but in solid state it does not shows any additional line. The reason behind this is that solid 1,2 dibromoethane possess exclusively antiform whereas on liquefaction some molecule convert into gauche form so liquid material show more spectral lines than the solid one.

Cis form of 1, 2 dibromoethane devoid centre of symmetry whereas gauche form possess centre of symmetry. Population of the gauche conformation is greater in liquid than in gaseous state.

16.3 Conformation of ethylene glycol

Ethylene glycol exists in two stable conformations- anti and gauche conformations. Gauche conformation possess have two enantiomers. In the gauche conformation two hydroxyl groups are close enough to give rise to an intramolecular bond. A strong absorption due to this intramolecular bond is found in the spectrum of ethylene glycol, it means that a considerable fraction of the molecules are in the gauche form, despite of steric and dipolar repulsion of the hydroxyl groups.

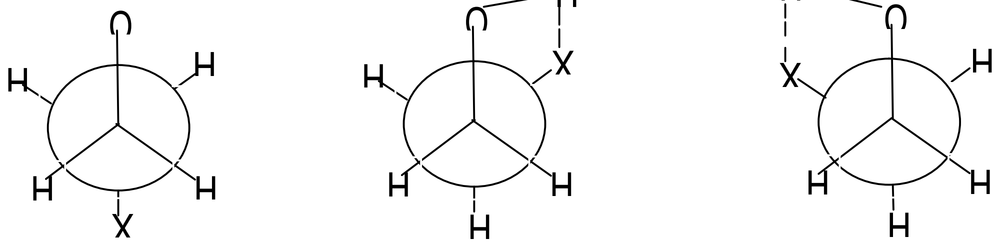


Anti P- Gauche M- Gauche

Fig. 5: Conformations of ethylene glycol and H- bonding

Generally , 2-substituted ethanols of the type, X-CH_2-CH_2-OH where X = OH, NH_2, F, Cl, Br, OCH_3, $NHCH_3$, $N(CH_3)_2$ etc. all have the preferred gauche conformations with OH and X forming intramolecular H-bonds. Their dihedral angle is slightly greater than 60°.

In solid state 2-chloroethanol exists exclusively in H-bonded gauche form but in liquid and gaseous state an equilibrium is developed between 15% anti and 85% gauche form.



Ant P- M-

Fig. 6: Conformations of 2-substituted ethanols and H- bonding

(Where X = OH, NH_2, F, Cl, Br, OCH_3, $NHCH_3$, $N(CH_3)_2$ etc.)

Intramolecular H-bonding between two vicinal groups gives an appreciable amount of stability about 8-20 KJ/mol to a conformer. The essential condition for an effective intramolecular H-bonding to occur is that the donor and acceptor groups must be in close proximity which is possible only in eclipsed or gauche conformation.

In the eclipsed conformation the atoms are present nearby due to which vanderwaals repulsive forces becomes dominant and makes this conformation unstable. The gauche conformation is best suited for intramolecular H-bonding having a torsion angle of 60-70° between the interacting groups. In case of anti conformer two hydroxyl groups are oppositely placed which does not permit the formation of intramolecular H-bonding.

The IR spectrum of ethylene glycol is recorded in dilute carbon tetrachloride solution using a lithium floride prism. In the IR spectrum of ethylene glycol, two bands appear at 3644 cm^{-1} and 3612 cm^{-1}. The former band shows the OH stretching frequency of unbounded hydroxyl group in dilute solutions of monohydric alcohols and the later OH stretching frequency can be assigned for the intramolecularly bonded hydroxyl group. Thus, we can conclude that IR in CCl_4 shows a frequency difference of 32 cm^{-1}.

The vibrational frequencies of the free and bonded OH are sufficiently different ($\Delta\nu =$ 40 cm^{-1}) to permit their separate detection in dilute solution. Ethylene glycol exists exclusively in H-bonded gauche forms as shown in fig. 5.

16.4 Conformation of n-butane

In case of n-butane, for conformational analysis butane may be treated as derivative of ethane where one hydrogen on each carbon is replaced by a methyl group. Different conformations of butane can be obtained by rotation about its middle carbon-carbon bond as shown below.

Butane possess three staggered conformers (I, III and V) out of these three conformers, conformer III (known as anti conformer) is more stable in which two methyl groups are far apart. Conformers (I and V) are called gauche conformers in which the largest substituents are adjacent.

Anti and gauche form have different energies due to steric strain or steric hindrance (strain on a molecule due to repulsion between electrons of large atoms or groups which lie too close to each other).

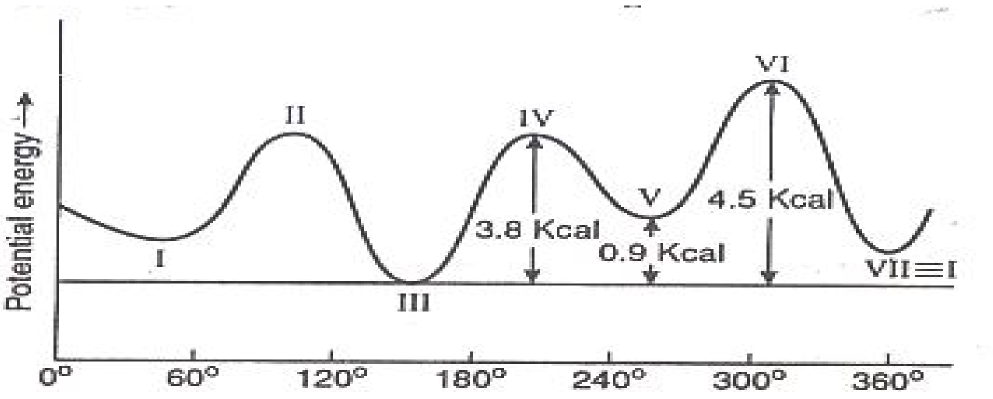


Fig.7: Rotational energy barrier of n-butane in terms of change in potential energy and dihedral angle

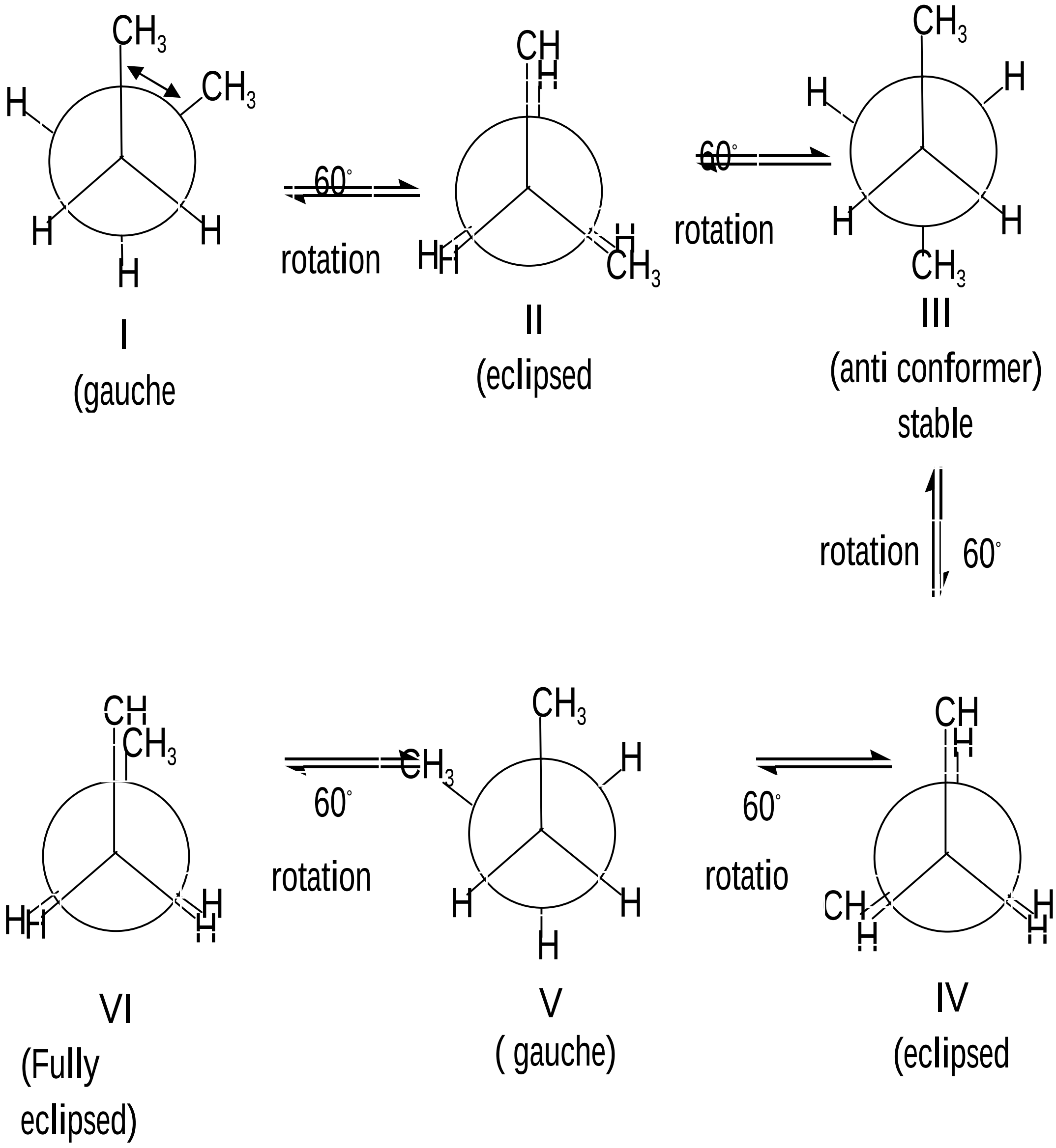


Fig. 8: Various conformations of n-butane

Butane possess three eclipsed conformers (II, IV and VI) out of these three conformers, conformer VI (fully eclipsed conformer) is least stable in which the two methyl groups are closest to each other. All these eclipsed conformers have both torsional and steric strain . Conformers (II and IV) are called eclipsed conformers.

Relative stabilities of six conformers of n-butane in decreasing order is as follows:

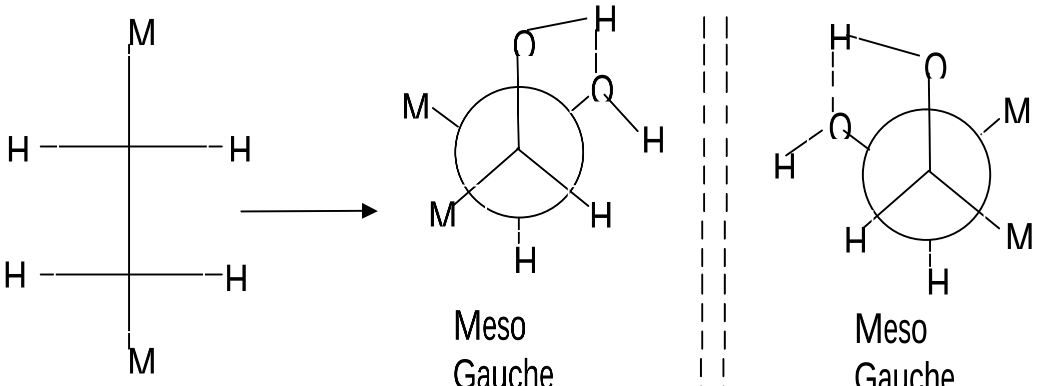
Anti (III) > Gauche (I and V) > Eclipsed (II and IV) > Fully eclipsed(VI)

16.5 Conformations of butane-2, 3-diols

Butane 2,3 diol and a series of glycol having general formula RCHOHCHOHR exists in two diastereomeric forms, the meso and the dl isomer. In butane 2,3 diol both the meso and dl forms are gauche conformers predominately as they permit H-bond formation. The two meso gauche conformers are enantiomeric and equally populated . The active isomer of butane 2,3 diol also consists of two H-bonded gauche conformers (as shown in fig.9) which are unequally populated in one form two methyl groups are anti and is more preferable than the other.

The I.R spectra of two diastereomers exhibit that the intramolecular H-bonding in the meso is weaker than the racemic or dl form. The strength of the H-bonding can be measured by the difference in the free and H-bonded OH stretching frequencies ($\Delta\nu$) which is 42 cm^{-1} for the meso and 49 cm^{-1} for the racemic. The two hydroxyl groups are lying nearby for the formation of intramolecular H-bond and increases of torsion angle between the two methyl groups which is sterically unfavourable in the enantiomeric conformers. In case of diastereomeric conformers it lead two gauche methyls closer which increases the torsional angle between the methyl group and hydroxyl group.

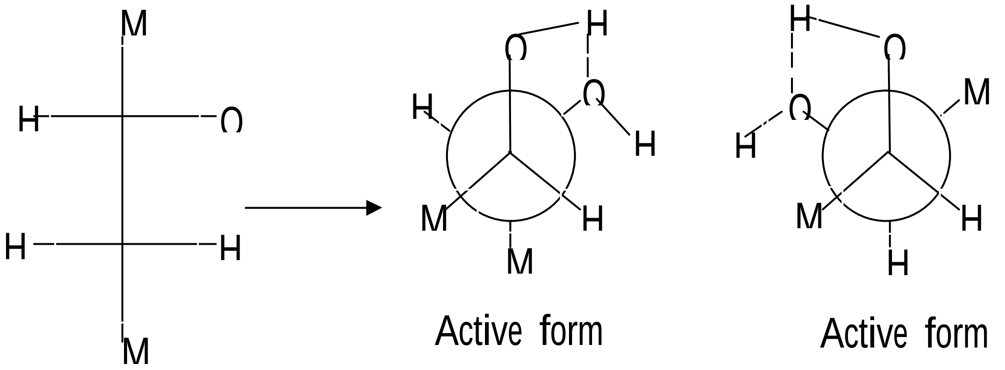
It has been observed that if methyl groups are replaced by bulkier alkyl groups, $\Delta\nu$ increases for both the diastereomers but the increase of $\Delta\nu$ is more for racemic than the meso form. Thus intramolecular H-bonding is more stronger in the active / racemic form rather than the meso isomers .Consequently, active / racemic form is more stable than the meso isomers.



Meso- butane 2,3

Meso Gauche enantiomeri

Meso Gauche enantiomeri



Racemic - butane 2,3

Active form diastereomeric conformer

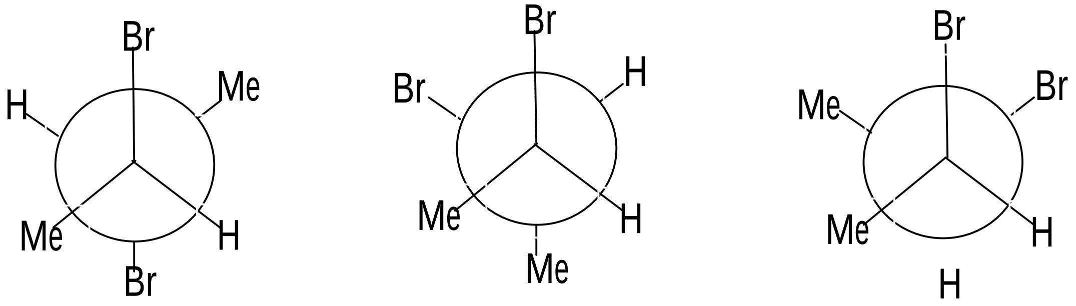
Active form diastereomeric conformer

Fig. 9 : Various conformations of butane 2,3 diol

Racemic butane 2,3 diol enhances the conductivity of boric acid more than the meso isomer. In case of racemic butane 2,3 diol the two methyl groups are anti but in meso form the two methyl groups are gauche . Due to intermolecular H-bonding with the solvent meso glycol is more stable than the racemic one. Free energy change for the conversion of the active diol to the borate complex is more favourable than the meso isomer.

16.6 Conformations of 2, 3 dibromobutanes

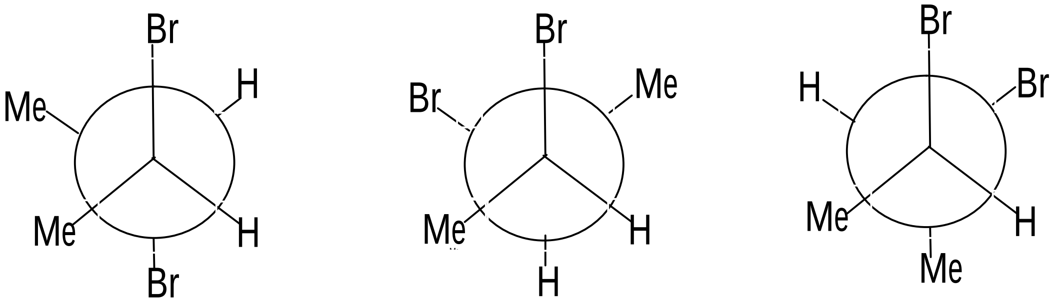
The meso form of 2,3 dibromobutane predominantly exists in the anti conformation [fig.10 (a)]. The two gauche conformers [fig.10 (b) and (c)] with three consecutive gauche interactions are relatively unstable. The three conformers of the active form [fig.10 (d), (e) and (f)] are all substantially populated. For the calculation of enthalpies of different conformers the following values of gauche interactions are used- Me / Me = 3.3 KJ /mol , Me / Br = 0.8 KJ /mol , Br / Br = 3.0 KJ /mol (in the liquid state).



(a) Anti -80%
1.6 KJ /mol

(b) Gauche-10%
7.1 KJ /mol

(c) Gauche-10%
7.1 KJ /mol



(d) Active - 36%
4.9 KJ /mol

(e) Active - 42%
4.9 KJ /mol

(f) Active - 22%
6.3 KJ /mol

Fig. 11 : Various conformations of 2,3 dibromobutane

For each conformer one can estimate the relative enthalpy and respective population (assuming $\Delta S = 0$) from the gauche interactions. Meso isomer contains predominantly near about 80% of the anti conformer and this form is energetically more preferred over the other forms. Meso form is more stable than the active form despite of the fact that active form contains two almost equienergetic gauche conformers [fig.10 (e) and (f)].

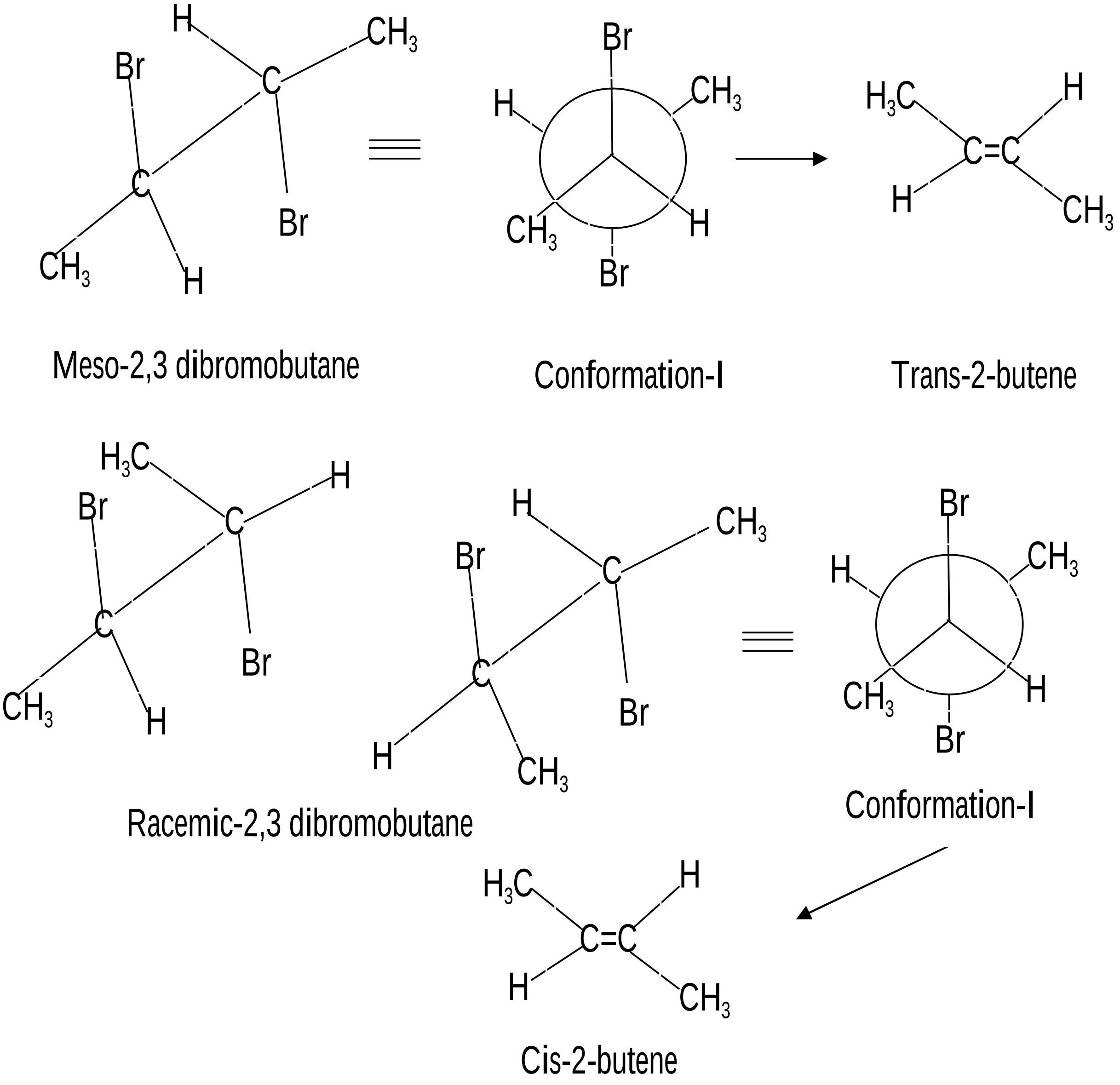


Fig.10: Conformation effect on debromination of 2,3 dibromobutane

Effect of conformation on reactivity can be demonstrated by the debromination of 2,3 dibromobutane with a metal like zinc. The meso -2,3 dibromobutane can eliminate bromine from conformation I to give trans-2-butene whereas racemic -2,3 dibromobutane gives cis-2-butene. The racemic isomer involves a less stable transition state as compared to the meso isomer.

16.7 Summary

- The different spatial arrangements of atoms in a molecule which are readily interconvertible by rotation around single bond is called conformations.

- Conformers / rotamers / conformational isomers are interconvertible and non separable.
- Energy difference between various conformers is in between > 0.6 and < 16 Kcal/mole.
- Two extreme conformations of ethane are staggered and eclipsed conformations. Energy barrier in ethane is 2.9 Kcal/mole.
- Butane possess three staggered (one anti and two gauche) and three eclipsed (one fully eclipsed and two partially eclipsed) conformations.
- Staggered conformations possess steric strain whereas eclipsed conformers possess both torsional and steric strain.
- Relative stability of six conformers of n-butane are- Anti > Gauche > Eclipsed > Fully eclipsed.
- By various physical methods like thermodynamic properties, dipole moment measurements, IR, Raman and microwave studies energies of different conformational isomers of 1,2 dihaloethane can be obtained.
- 1, 2 dibromoethane contain 85% anti conformer and 1, 2 dichloroethane contain 73% anti conformer in gaseous state at 22°C temperature.
- Due to the presence of polar solvents the ratio of gauche conformers increases.
- In case of haloethane, if number of halogen substituents increases, barrier energy increases gradually from 15.5 KJ/mol in ethyl chloride to 50-60 KJ/mol in hexachloroethane.
- In the IR and Raman spectrum of 1,2 dibromoethane in liquid and gaseous states exhibit more than the allowed number of lines due to the presence of both anti and gauche form. But in solid state it contains only anti form thus it shows allowed number of lines in the spectrum.
- Ethylene glycol exists in two stable conformations anti and gauche forms.

- In ethylene glycol maximum fraction of molecule remains in gauche form, as this form lead the two hydroxyl groups are close enough to give rise to an intramolecular H-bond.

- Substituted ethanol preferred gauche conformation due to the formation of intramolecular H-bond.

- In the IR spectrum of ethylene glycol two bands appear at 3644 cm^{-1} and 3612 cm^{-1}. The vibrational frequencies of the free and bonded OH are sufficiently different (Δv = 40 cm^{-1}) which permit its detection in dilute solution.

- Butane 2,3 diol exist in the meso form and dl isomer and these two forms are gauche conformers , which permits H-bonding.

- The IR spectra indicates that the intramolecular H-bonding in meso form is weaker than the racemic.

- Racemic butane 2,3 diol enhances the conductivity of boric acid more than the meso form.

- The meso form of 2,3 dibromobutane exists in the anti conformation and the three conformers of the racemic form are all substantially populated.

16.8 Review Questions

1. What do you understand by the terms conformation and configuration?
2. Discuss conformations of ethane. Which conformation is more stable and why?
3. Write short note on the following-
    1. Conformations of dihaloethane
    2. Conformations of ethylene glycol
4. How can we study various conformations of different compounds?
5. Discuss the energy difference of 1, 2 dichloroethane in gaseous and liquid state.
6. How polarity of solvent affects the ratio of conformers in dihaloethane?
7. How energy barrier effects with the number of halogen substitutents in ethyl chloride?

8. IR spectrum of solid 1,2 dibromoethane is different from the liquid and gaseous 1,2 dibromoethane. Why?
9. Which conformer of dihaloethane is more stable in polar solvent and why?
10. Which conformer of ethylene glycol is more preferable and why?
11. Discuss the various conformers of n-butane and their relative stability.
12. Discuss the IR spectra of two diastereomeric forms of butane-2,3 diol.
13. Which form of butane-2,3 diol possess more stability and why?
14. Write in short about the application of racemic butane-2,3 diol.
15. Explain the details of various conformations of 2,3 dibromobutane with suitable diagram.
16. How conformation of 2,3 dibromobutane affect the reactivity in case of debromination?

16.9 References and Suggested Readings

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Unit -17

Confirmation of some cyclic molecules Cyclobutanes, Cyclopentane and Cyclohexane and Monosubsituted Cyclohexane

Structure of Unit

17.0 Objective

The stabilty of the molecule i8s a function of the various parameters the objective of this unit is to study the effect of internal strain on the stability of the molecule. the origin of the strain comes from the steric strain, dipole –dipole interaction ,bond angle strain and bond apposition strain.all these factors shows the a coupled impact on the molecule when it aquires some preferred confirmation .the physical and the chemi8cal properties of the molecule under examination ,depends mainly upon its confirmation in the present unit all the above mentioned factors have been discussed in detail for the cyclic systems so as to reach a conclusive idea of the structure of the molecule .

17.1 Introduction

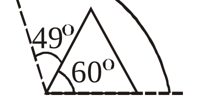
It was known in earlier times of development of chemically that cyclic molecules exist in nature.

A number of cyclic compounds containing five and six membered rings were known. It was observed by the chemists that compound containing - three or four carbon atoms were difficult to prepare. Many efforts were made from tuire to tuire, to prepare these compounds but these were not successful.

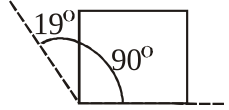
In 1885 Adolf Von Baeyer a pioneer worker in the field proposed a theoretical interpretation of the difficulties associated with the instability of cyclic molecules like cyclopropanes and cyclobutanes.

According to Baeyer view in cyclic compound carbon prefers to have tetrahedral geometry with a bond angle of $109^{0}28^{/}$. Thus it is obvious that in the compounds other than cyclopentane the carbon atom will experience a strain. Baeyer's work was based upon a simple, geometrical notion- that in three membered ring being a equilateral triangle (Cyclopropane) the angle is 60^{0} whereas in a four membered ring (cyclobutane) being square the bond angle should be 90^{0} and in five membered ring (Cyclopentane) being a pentagonal in shape, the bond angle should be 108 and so on.

According to Baeyer in cyclopropane the bond angle is 90^{0} so it should be under an angular strain of $(109^{0} - 60^{0})$ 49^{0} and thus must be highly reactive . In cyclobutane this strain is $19^{0}(109^{0}- 90^{0})$ So it must also be reactive. If we look to cyclopentane the strain is 1^{0} $(109^{0} - 108^{0})$ so it is almost strain free whereas cyclohexane $(109^{0} - 128^{0}$; strain - $19^{0})$ and other higher cycloalkanes seem to be suggested that very large rings are highly strained and so shall be incapable of existance.



Cyclopropane



Cyclobutane

Cyclopentane

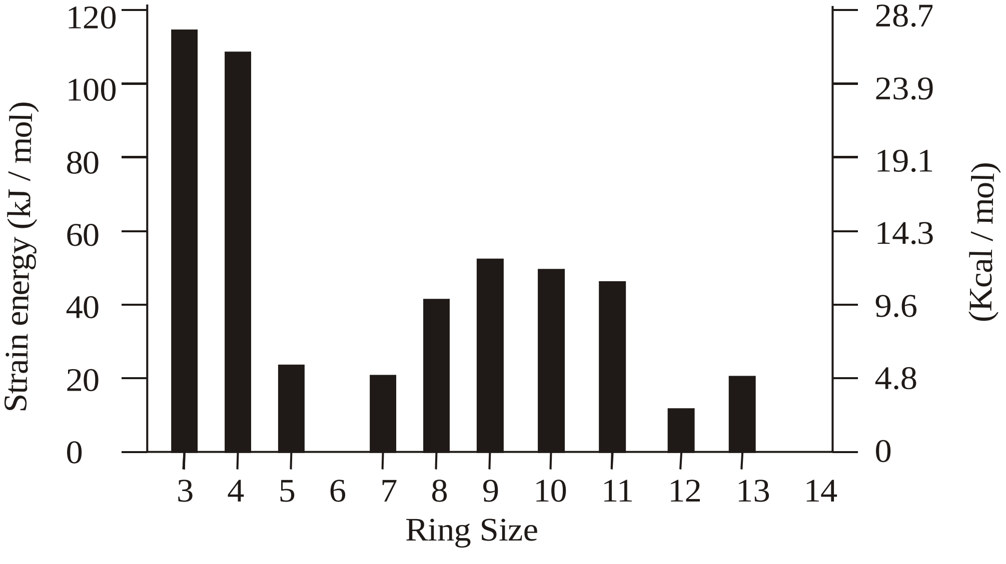
Although the suggestion of Baeyer carries some truth about the angular strain in saml rings however rings having three carbon atoms to thirty carbon atoms can easily be prepared. Let us look to the facts.

17.2 Heat of Combustion of Cycloalkanes

In order to measure the amount of first strain in a given organic compound, we first measure the total energy of the compound and then substract the energy of a strain free reference compound. The difference between the two values gives us the amount of extra energy of the molecule due to strain.

The simplest way to evaluate the strain energy of cycloalkanes is to measure their heat of combustion (i.e, the amount of heat evolved when the compound burns completely with oxygen.) The more energy (strain) a compound contains, the more energy (as heat) it will release during combustion.

Now because the heat of combustion of a hydrocarbon depends upon it size, it is determined per -CH_2 unit. Subtracting a reference value derived from a strain - free acyclic alkane and then multiplying by the number of CH_2 unit in the ring gives overall strain energies. The results of show calculations are given below in the table.



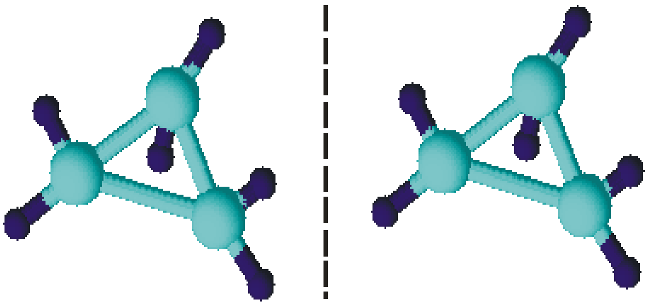
Cycloalkane strain energies, calculate by taking the difference between cycloalkane heat of cobustion per CH_2 and acyclic alkane heat of combustion per CH_2 and multiplying by the number of CH_2 units in a ring. Small and medium rings are strained, but cyclohexane rings are strain free.

The data show that Baeyer's theory is incorrect cyclopropane and cyclobutane are indeed quite strained, but cyclopentane is more strained than predicted and cyclohexane is strained. For cycloalkanes of still larger size, there is no regular increase in strain and rings of more than 14 carbon atoms are strain - free.

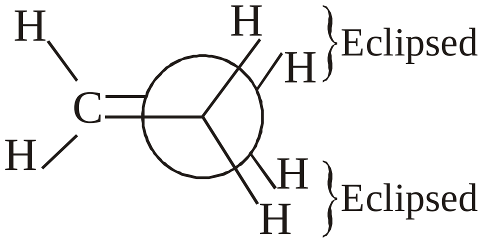
17.3 The Nature of Ring Strain

Baeyer during his submission of angular strain assumed that ring are flat and this assumption appears to be wrong. Actually most of the cycloalkanes are not flat but adopt puckered three dimensional conformation which allow the bond angle to acquire nearly a tetrahedral value so it appears that the concept of Baeyer must hold for three and four membered ring in cycloalkanes.

In addition to angle strain, sevveral other factors are incorporated in the determination of shapes of cycloalkanes. One such factor is the barrier to bond rotation. This is also refered as torsional strain. It is known that these open chain alkanes are most stable which have Staggered conformation and these having eclipsed conformation are least stable. This conclusion is extended for cycloalkanes also. In a cycloalkane if the neighbouring C - H bond eclipse each other a torsinal strain is created for example in cyclopropane there is a considerable torsional strain, in addition to angle strain since C - H bonds on neighbouring carbon atoms are eclipsed. It is shown below.



Stereo View



It is seen that larger cycloalkane adopt puckered non planar conformations to minimize their torsional strain.

In addition two types of above discussed strains i.e. anagle strain and torsional strain, the third factor is steric strain which also contributes to the overall strain energy of cycloalkane. In a molecule two non bonded atoms repel each other when they are in close approach. When these non bonded atoms approach two closely, they attempt to occupy the same positions in space.Such none bonding steric interactions play an important role in deciding the minimum energy conformations of cycloalkanes having medium size rings molecules containing seven carbon atoms to eleven carbon atoms.

Thus it can be concluded that cycloalkane adopt their minimum energy conformations by involving following three types of strains

(a) **Angle strains** the strain due to expension or compression of bond angle.

(b) **Torsional strain:** The strain due to eclipsing of bond present on neighbouring atoms and

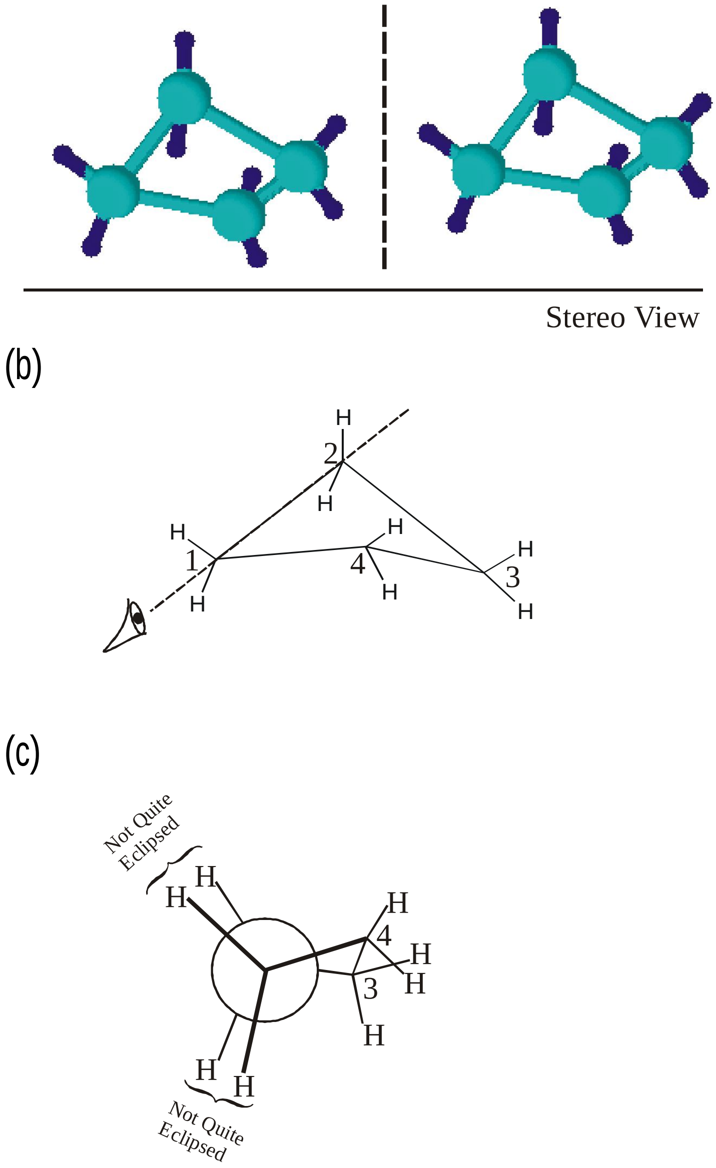
(c) **Steric strain:** The strain due to repulsive interactions when atoms approach each other very closely.

17.3.1 conformations of cyclobutane

Cyclobutane has less angle strain than cyclopropane but here the magnitude of torsional strain is more because it contains larger number ring hydrogens than in cyclopropane. The result is that the total strain for these two compounds is nearly the same 110.4 KJ mol^{-1} (26.4 KCal mol^{-1}) for cyclobutane and 115.0KJ mol^{-1} (27.5Kcal mol^{-1}) for cyclopropane.

It has been show experimentally that the ring in cyclobutane is not quite flat but is slightly bent such that one carbon atom lies about 25^0 above the plane of other three remaining carbon atoms. This is shown below

(a)

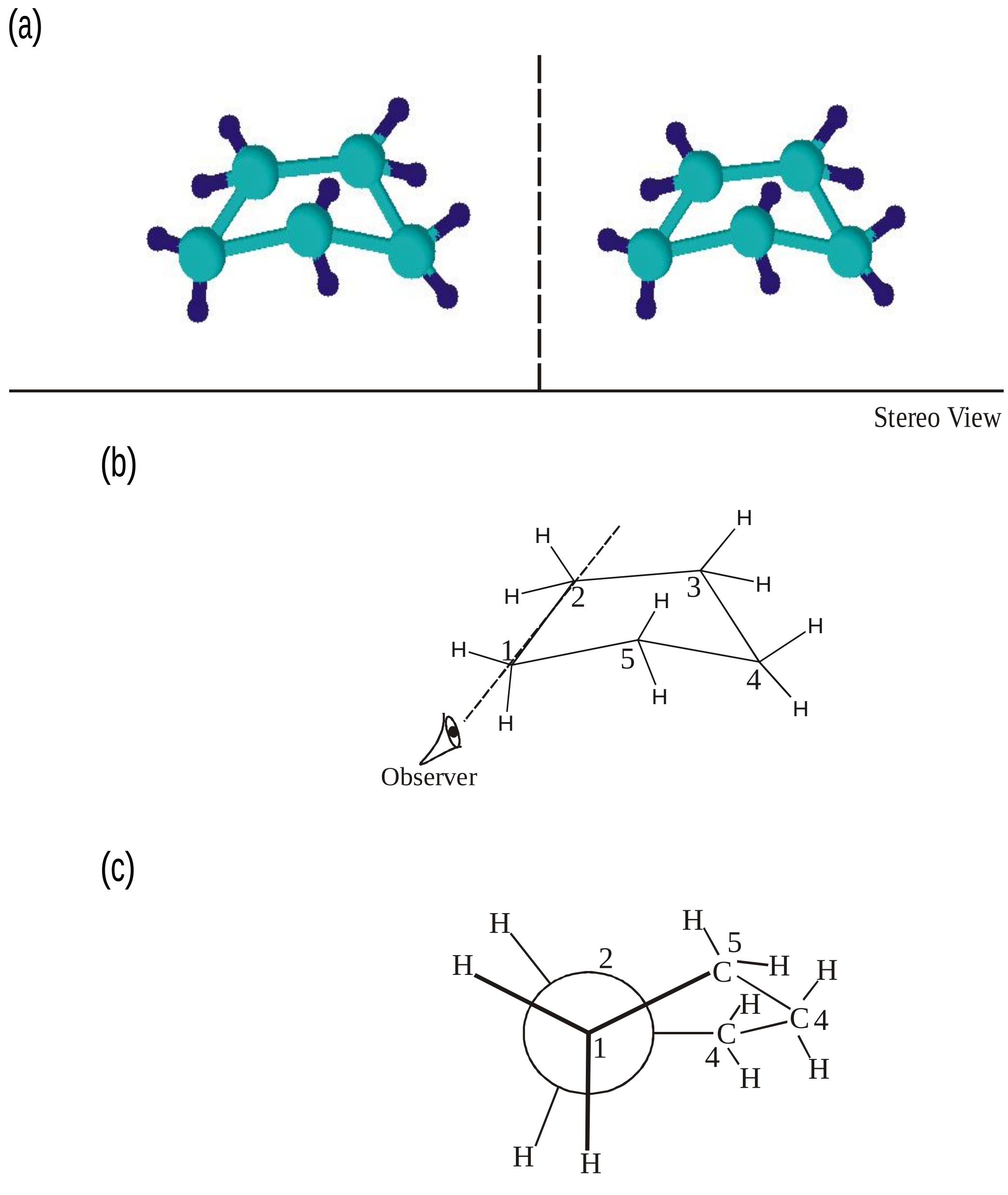


The conformation of cyclobutane

The overall effect of this slight bend results in an increases in the angle strain but in a decrease in the torsional strain, until a minimum energy balance between the two opposing effect is achieved.

17.3.2 Conformations of Cyclopentane

Baeyer predicted that cyclopentane ring is nearly strain free but its combustion data indicate that it has a total strain energy of about 26.0 kJmol^{-1} (6.2Kcal mol^{-1}). The planar cyclopentane has practically no angle strain but it has a larger magnitude of torsional strain. Due to this reason the ring of cyclopentane twists to acquire a puckered, non planar conformation which causes a balance by increasing its angle strain and decreasing the torsional strain. Four carbon atoms of cyclopentane lies approximately in the same plane but the fifth carbond atom bent out of the plane. Most of the hydrogens become nearly staggered with respect to their neigghbours as is depicted in the diagram below



Conformation of Cyclopentane

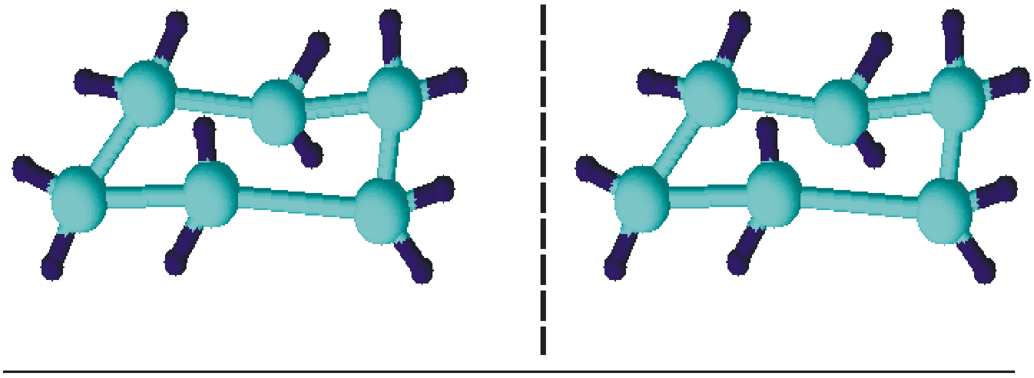
17.3.3 Conformations of Cyclohexanes

Susbstituted cyclohexanes occur widely in nature. A large varity of chemical compounds, used as important pharmaceutical agents contain cyclohexane ring.

Experimental data collected by the study of combustion enthalpy of cyclohexane data suggest that cyclohexane ring is strain - free, with neither angle strain nor torsional strain.

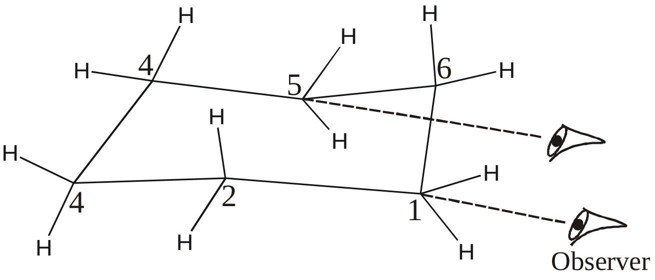
The explanation to the above fact was first suggested by Hermann sachse in 1890 and was then extended by Ernst Mohr. Conrarory to Baeyer's assumption, the cyclohexane ring is puckered into a three dimensional conformation which releives its all type of strains. The angle C-C-C reaches the strain free tetrahedral value (109^{0}) when the ring adopts a CHAIR-CONFORMATION (So called becuase of its similarity to a lounge chair having a back, seat and a footrest). This is shown below in the figure. Furthermore if the molecule is sighted along any one of the C-C bond in a ''Newman projection" formula it is found that chain cyclohexane has no torsional strain because all neighbouring C-H bonds are in staggered positon.

(a)

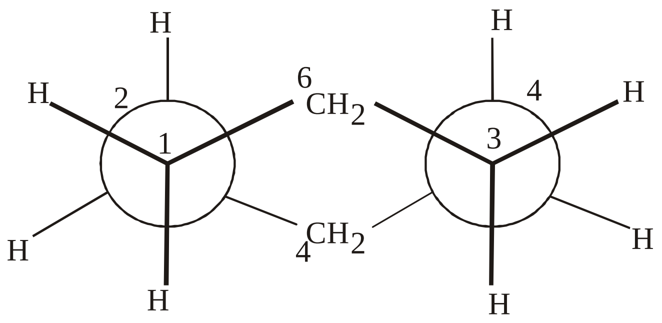


Stereo View

(b)



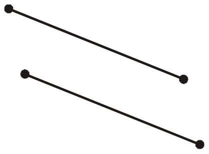
(c)



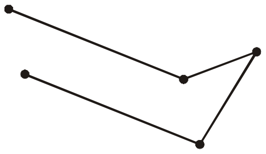
Conformation of Cyclohexane

A Convinient way to visualize chair cyclohexane is through its molecular model. This can be done in the following three steps.

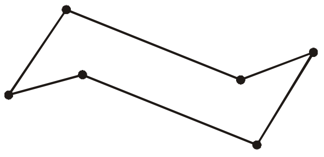
step I : Two parallel, slanted downward lines are drawn which are slightly offset from each other. This is to show that four of the cyclohexane carbon atoms lie in one plane.



Step II : The topmost carbon atom is located above and to the sight of the plane of the other four and these are connected to show the bonds.

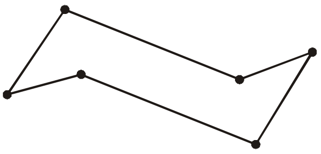


Step III : The bottommost carbon atom is shown below and to the left of the plane of the middle four carbon atoms and is connected with bonds.



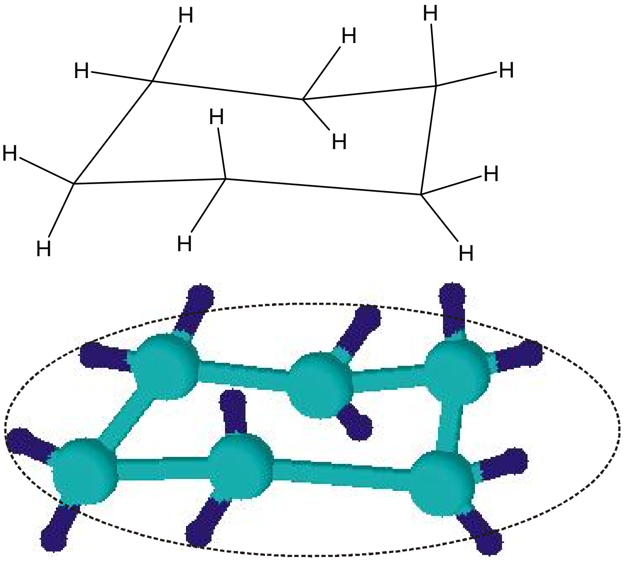
It is to be noted that the bonds of topmost and bottomost carbon atoms must be parallel.

When the chain of cyclohexane is viewed the lower bond is infornt and the upper bond is in the back. This is done to eliminate the optical illusion. This is depicted below



17.4 Axial and Equatorial Bonds in Cyclohexane

The chair conformation of cyclohexane exhibits importants effect on its chemical behaviour. For example the chemical properties of substituted cyclohexanes is significantly controlled by their conformations. There are two types of positions for substituents on the ring. These are “axial” and “equatorial” positions. The chair cyclohexane has six axial hydrogens which are perpendicular to the ring (i.e., parallel to ring axis) and six equatorial hydrogen which lie in the plane of ring (i.e., around the ring equator). This is shown below in the figure.

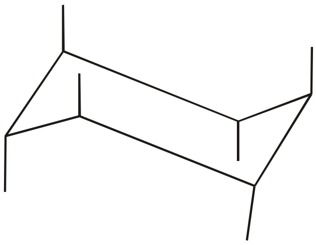


Axial and equatorial hydrogen atoms in chair cyclohexane

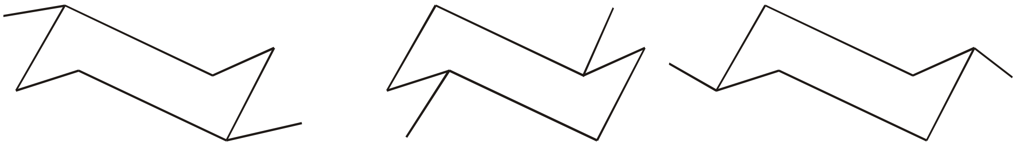
It is evident from the above diagram that each carbon atom in cyclohexane has one axial and one equatorial hydrogen. Thus each side of the ring has three axial and three equatorial hydrogens arranged alternately. For example, if the top side of the ring has axial hydrogens on carbon atom 1,3 and 5 then there will be equatorial hydrogens on carbon atoms 2,4 and 6. The reverse will be true for bottom side of the ring.

It is to be noted that here the terminology ‘cis’ and ‘trans’ is not used. Two hydrogens on the same side of the ring are always cis, regardless of the fact that they are axial or equatorial or adjacent. In the same way two hydrogens on opposite sides of the ring are always trans regardless of whether they are axial or equatorial.

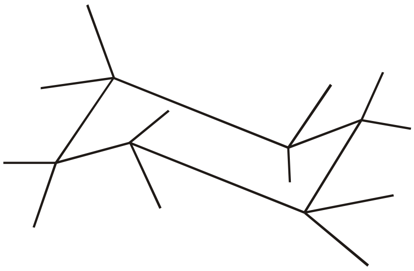
The procedure for drawing axial and equatorial bonds is outline in the following diagram.



Axial bonds : The six bonds, one on each carbon, are parallel and alternate up down.



Equatorial Bonds : The six equatorial bonds, one on each carbon, come in three sets of two parallel lines. Each set is also parallel to two ring bonds. Equatorial bonds alternate between sides around the ring.

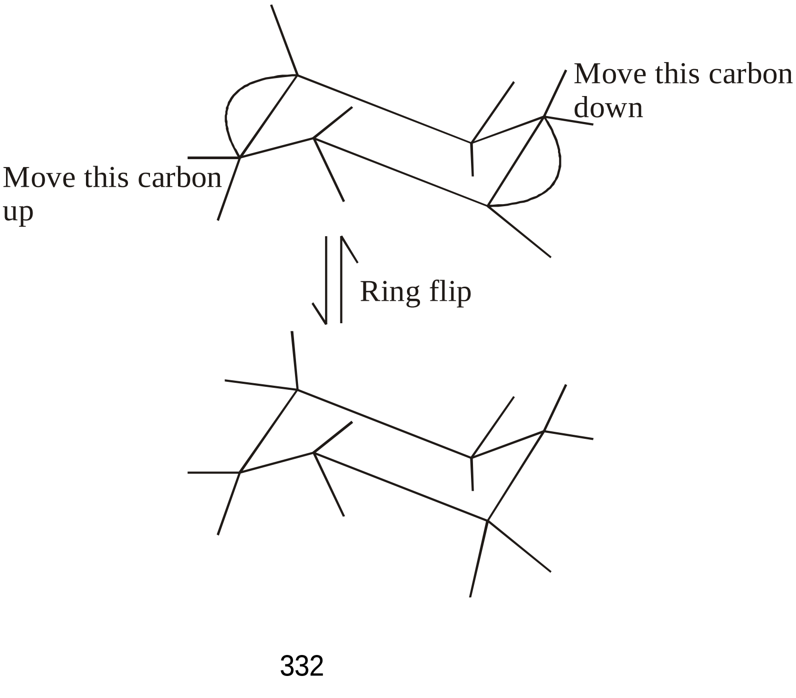


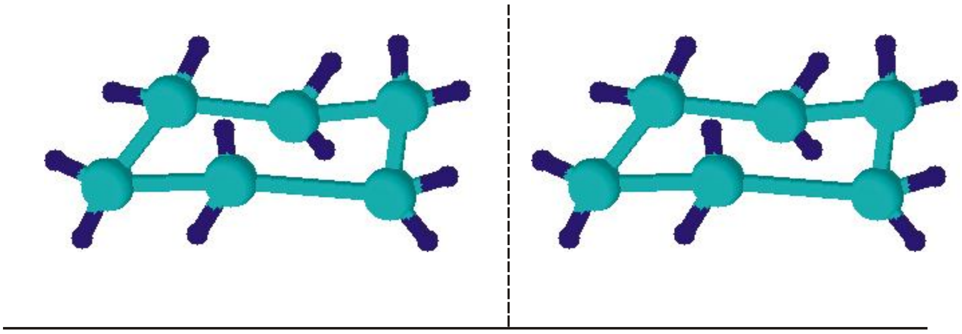
Completed Cyclohexane

17.5 Conformational Mobility of Cyclohexane

As chair cyclohexane has two kinds of positions, ie axial and equatorial we can expect that a monosubstituted cyclohexane will exist in two isomeric forms. In fact there is only one methylcyclohexane, one bromocyclohexane, one cyclohexane etc and the reason for this is that cyclohexane ring are conformationally mobile at room temperature.

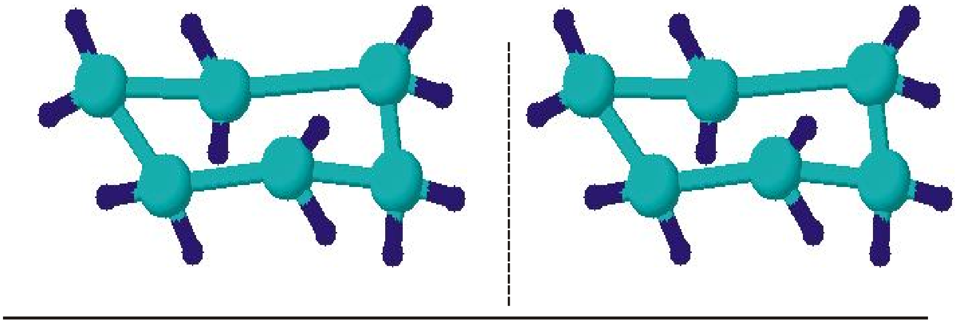
Different chain conformations are easily and readily interconvertible and this results in the exchange of axial and equatorial positions. This type of interconversion is called as a “ring - flip” and is shown below as the result of this flipping those positions which were prevalently occupied by the axial hydrogen are now occupied with the hydrogens by the equatorial hydrogens and vice versa this ring flipping takes place by approximately by 100000 per second at 25 degree centigrade





Stereo View

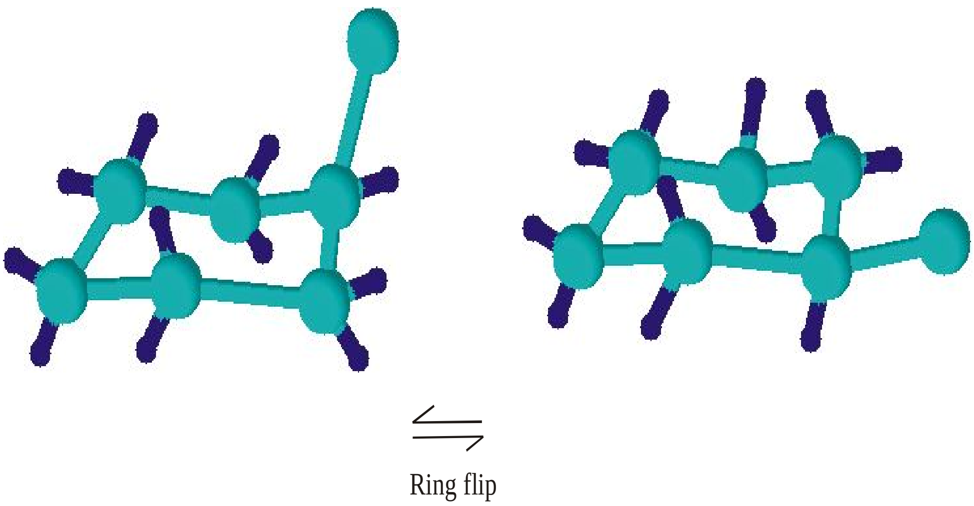
Ring flip

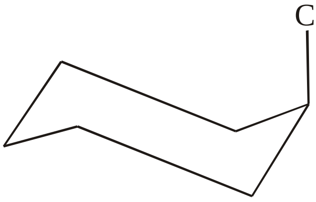


Stereo View

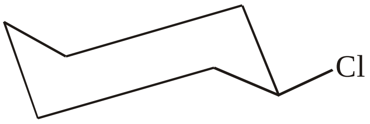
The chair conformation of the cyclohexane can undergo ring flipping by keeping the middle four carbon atoms in place and folding the two ends of the conformation in opposite directions. In this process the axial substituent in original chair form becomes an equatorial subsituent in the ring flipped chair form and vice versa. for example an axial chlorocyclohexane becomes equatorial chlorocyclohexane after the ring flip.

The energy required for this process of chair - chair interconversion is only about 45kJmol^{-1} (10.8 Kcal mol^{-1}) consequently the process of ring flib occurs at very rapid rate at room temperature. Thus we observe only a single structure rather than distinct axial and equatorial isomers. This is shown below.it can be seen from the data of interconversion of the chair to boat form and vice versa that spectroscopic methods are the only alternative to have the correct tool for the assignement of the relative positions of the groups.however in case of the reaction nature the spatial arrangement of the groups changes as the elimination involving of the hydrogen has to be at the transequitorial to the halogen atom for the antiperiplanar arrangement of the groups done through the flipping of the conformations.



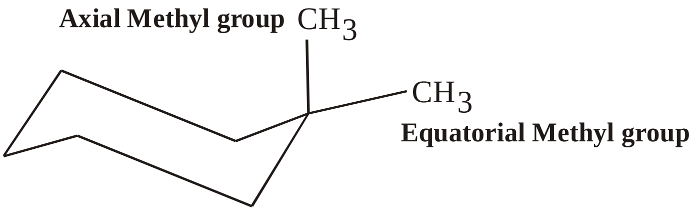


Axial chlorocyclohexane



Equatorial chlorocyclohexane

For a better understanding let us draw 1,1-dimethyl cyclohexane to indicate which methyl group is axial and which is equatorial. For this we draw a chair cyclohexane ring and then we put two methyl group at the same carbon atom. The methyl group whichlies in the rough plane of the ring is always equatorial and the other is axial. It is depicted below



17.6 Conformations of Monosubsituted Cyclohexanes

Although cyclohexane rings rapidly flip between conformations at room temperature, the two conformations of a monosubsituted cyclohexane are not equally stable. For example in methyl cyclohexane the equatorial conformer is more stable than axial conformer by an amount of 7.6kJmol^{-1} (1.8Kcal mol^{-1}). This stability criteria extends for other monosubsituted cyclohexanes also. In general a substituent is more stable in equatorial conformation than in axial conformation.

It is known that in such situations the percentage of two isomers at equilibrium can be evaluated by using the equation. $\Delta E = -RT \ln K$

where ΔE = Energy difference between two isomers,

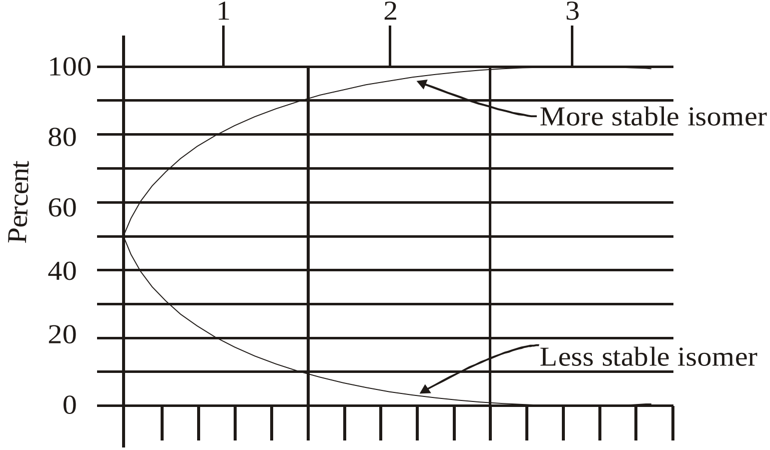
R = Universal gas contant (8.315JK^{-1}mol^{-1})

T = Temperature in Kelvin

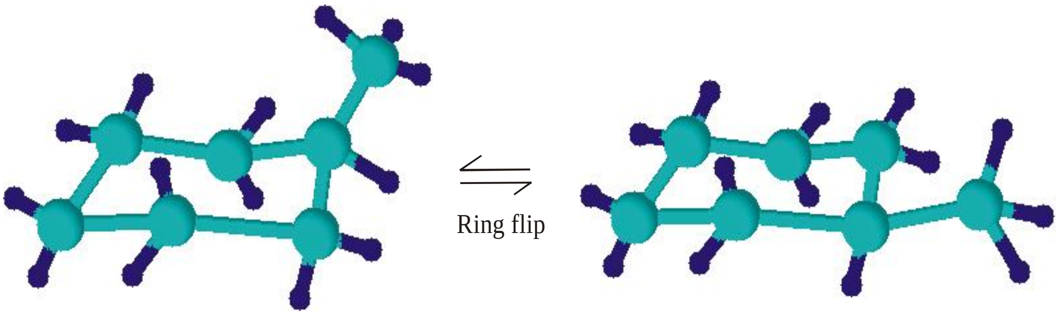
K = Equilibrium constant between two isomers.

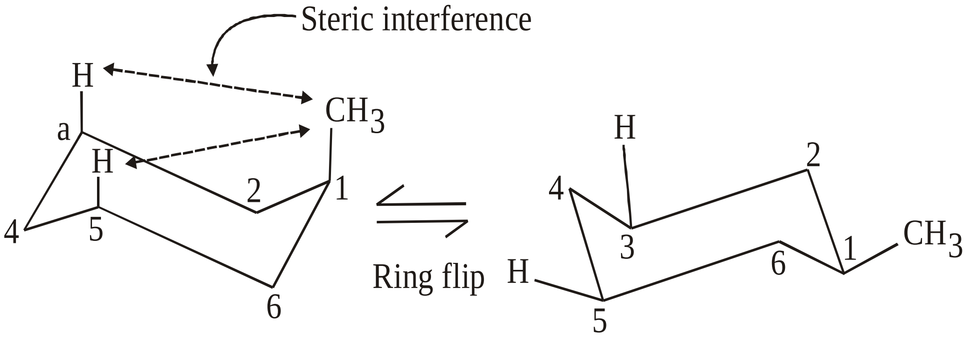
If the above equation is applied for the equilibrium equatorial methylcyclohexane $\rightleftharpoons$ axial methylcyclohexane (with value = 7.6 kJmol^{-1})

It is found that about 95% of methylcyclohexane molecules have the methyl group at equatorial position at any given instant and only 5% have methyl group at axial positions. Following figure depicts the relationship between energy and isomer percentage

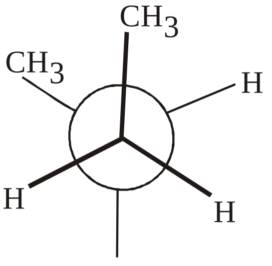


Cause of the energy difference between axial and equatorial conformers is the steric strain which is caused by " 1,3 - diaxial interaction". That is the axial methyl group at C, is very close to axial hydrogenous on C_3 and C_5 (three carbon atoms away) and this results in a steric strain of about 7.6kJmol^{-1}. This is shown in the figure below

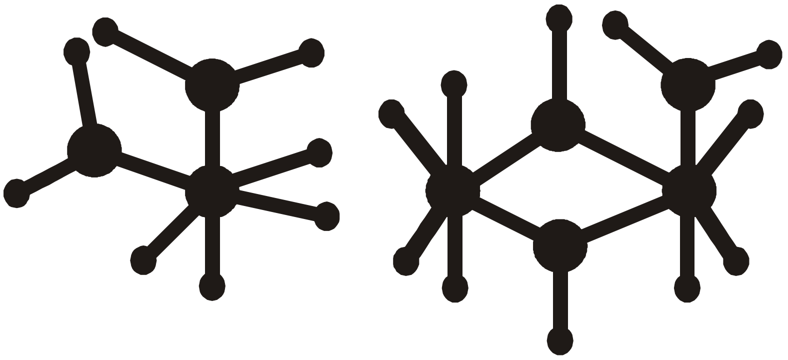


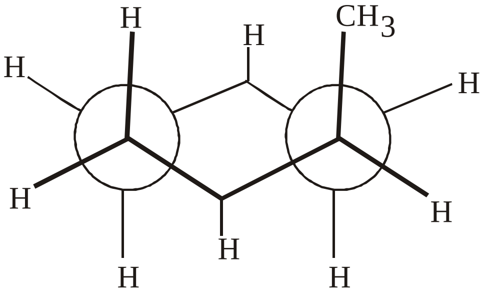


This 1,3 diaxial steric strain is very common in cycloalkanes. In cyclobutane the steric strain between methyl group in gauche butane makes it less stable than anti butane by 3.8KJmol^{-1} (0.9Kcal mol^{-1}) because of steric interference between hydrogen atoms on the two methyl group. If we compare the four carbon fragment of axial methylcyclohexane with gauche butane. It is observed that steric interactions is same in both the cases this cases this depicted below.



Gauche butane
(3.8kJ / mol)



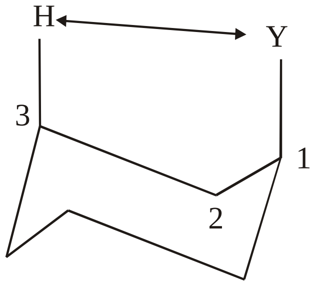


Axial methylcyclohexane
(7.6 kJ / mol strain)

If we look along the C_1 - C2 bond of axial methylcyclohexane we see that axial hydrogen at C_3 has a gauche butane interaction with the axial methyl group at C_1. Similarity along C_1- C_6 bond shows that the axial hydrogen at C_5 also has a gauche butane interaction with the axial methyl group at C_1. Both interactions are absent in equatorial methylcyclohexane and thus we find an energy difference of 7.6 $KJmol^{-1}$ between the two forms.

The criterion for methylcyclohexane is also true for other monosubsituted cyclohexane. A subsituent when seated at equatorial position is more stable than when it is at axial position. The exact amount of 1,3-diaxial steric strain in a specific compound depends on the nature and size of the subsituent.

This is clear from the data given in the table below.



Strain of one H-Y 1, 3-diaxial interaction

Y	**(kJ / mol)**	**(Kcal / mol)**
-F	0.5	0.12
-Cl	1.0	0.25
-Br	1.0	0.25
-OH	2.1	0.5
$-CH_3$	3.8	0.9
$-CH_2CH_3$	4.0	0.95
$-CH(CH_3)_2$	4.6	1.1
$-C(CH_3)_3$	11.4	2.7
$-C_6H_5$	6.3	1.5
-COOH	2.9	0.7

-CN	0.4	0.1

Steric strain in monosubstituted cyclohexanes

The data in the above table indicated that the amount of steric strain increases in the order

$$-CH_3 < -CH_2-CH_3 < \left(CH_3\right)_2 CH- << \left(CH_3\right)_3 C-$$

And it is accordance with the increasing bulk of these alkyl groups. It is also to be noted that the values in the above table are for 1,3 -diaxial interactions of the subsituent with one hydrogen atom. These values if doubled will give the amount of strain in monosubsituted cyclohexane.

17.7 Summary

- 1885 Adolf von Baeyer was the first person to theoreticsl formulation to ease thedifficulties associated with instability of the cyclic molecules viz cyclopropane ,cyclobutanes and others.
- Baeyer strain theory was based on the simple calculation that cyclopropane has the angle of 60 deg. cyclobutane has the angle of 90 deg. and cyclopentane has 108 degree and so on.
- Among the staggered and eclipsed conformers of the cycloalkane the most stable is the staggered confirmation as it involves leats repulsion interaction.
- the stereochemical arrangements of the bonds in the cyclohexane are such that they are axial and equatorial, wherein the equatorial are along the plane of the ring while axial are orthogonal to the plane of the ring.
- For the process of the elimination the hydrogen of the cyclohexane have to be in the anti periplanar conformation so in the presence of the base the hydrogen arranges in the way that they are Trans to the halogen atom.
- Flipping frequency of the axial and equatorial hydrogen are at the rate of one lakh times per second as the energy required for flipping is provide at the room temperature.
- 1,3 positions of the cyclohexanes suffers a great repulsive interaction when the nature of the groups is changes from less bulky to more bulky

- Energy required for the chair –chair flipping is very less around 45 kJ/mol.
- The presence or the absence of the optical activity of the confermers of cyclic compounds can be sorted out by the use of the polarimeter, wherein the optically active compounds looses the centre of symmetry.

17.8 Problems

1. Cyclopropane is more strained than cyclohexane by 115kJ/mol. Which has the higher heat of combustion on a per gram basis, cyclopropane or cyclohexane?
2. Draw 1,1-dimethylcyclohexane, indicating which methyl group is axial and which is equatorial.
3. Each hydrogen - hydrogen eclipsing interaction in ethane costs about 4.0kJ/ mol. How many such interactions are present in cyclopropane? What fraction of the over all 115kJ/ mol (27.5kcal / mol) strain energy of cyclopropane is due to torsional strain?
4. Cis - 1,2 - dimethylcyclopropane has a larger heat of combustion than trans - 1,2-dimethylcyclopropane. How can you account for this difference? Which of the two compounds is more stable?
5. How many hydrogen-hydrogen elipsing interactions would be present if cyclopentane were planar? Assuming an energy cost of 4.0kJ/mol for each eclipsing interaction, how much torsional strain would planar cyclopentane have? How much of this strain is relieved by puckering if the measured total strain of cyclopentane in 26.0kJ/mol ?
6. Draw the most stable conformation of cis-1,3-dimethylcyclobutane. Draw the least stable conformation.
7. Draw two different chair conformations of cyclohexanol (hydroxycyclohexane), showing all hydrogen atoms. Identify each position as axial or equatorial.
8. A cis-1,2-disubstituted cyclohexane, such as cis-1,2-dichlorocyclohexane, must have one group axial and one group equatorial. Explain.
9. A trans-1,2-disubstituted cyclohexane must either have both groups axial or both groups equatorial. Explain.

10. Draw two different chair conformations of trans-1,4-dimethylcyclohexane, and label all positions as axial or equatorial.
11. How can you account for the fact that an axial tert-butyl substituent has much larger 1,3-diaxial interaction than isopropyl, but isopropyl is fairly similar to ethyl and methyl? Use molecular models to help with your answer.
12. Why do you suppose an axial cyano substituent causes practically no 1,3-diaxial steric strain (0.4kJ/mol)? Use molecular models to help with your answer.
13. Estimate the percentage of axial and equatorial conformer present at equilbrium in bromocyclohexane.
14. what is the stereochemical requirement of the elimination reaction of the halosubstituted cycloalkanes.

17.9 Refrence Books

- Stereochemistry of organic compounds ,D.Nassipuri
- Stereochemsitry of the organic compounds , P.S.kalsi,New age Publication.
- Organic chemistry , I.L Finar.

Unit-18

Conformations of Di-Substituted Cyclohexanes

Structure of Unit:

18.0 Objetcive

it is known that tree dimension nature of compound and the rotation around carbon-carbon single bond leads to different spatial orientation of molecule these are called rotamers in this unit a complete discussion of the results obtained by the analysis of spatial relationship of various substituent present in cyclic a system main emphasis has been laid down upon various types of strain produced in the molecule this in turn have an effect on the thermodynamically and kinetic stability of the molecule during a chemical synthesis of a complex molecule the study of and the knowledge of the confirmations of the all the species involved appears to9 be prime factor in thi8s unit the cyclic systems having two substituent has been studied in detail the problem becomes more complicated when a functional group is also present in addition to the substituent .

18.1 Introduction

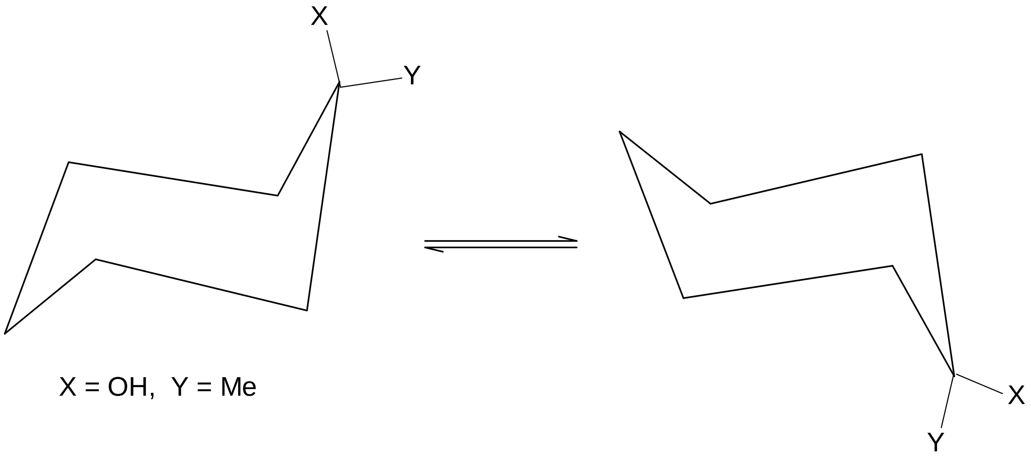
The principle of conformational analysis of monosubstituted cyclohexanes. However, two additional points have to be taken into consideration. These are:

(1) Disubstituted cyclohexanes generally exist in two or more diastereomeric forms and each of them is capabel of existing in two (sometimes even more) conformers. Thus it is desirable to examine each pair of conformers of a diastereomer on the basis of, symmetry, enthalpy, entropy and free energy basis to evaluate the preferred conformation. Then a comparison is made between the diastereomers through the preferred conformer of conformers of each.

(2) The substituted present may interact among themselves sterically or otherwise and these interactions must also be included in the analysis.

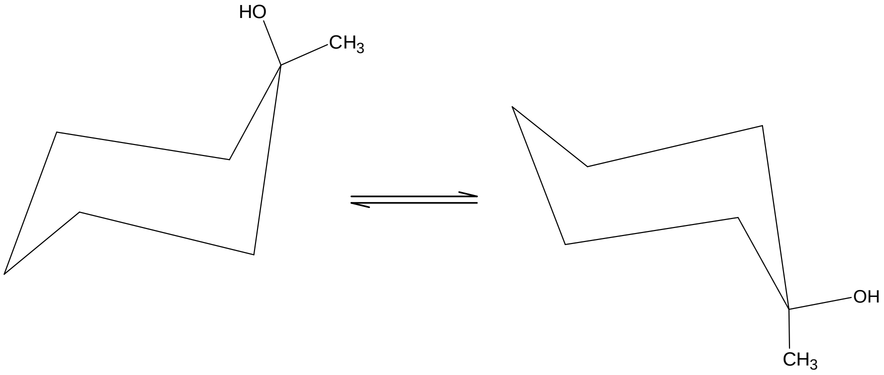
18.2 1,1-Disusbstituted Cyclohexanes

1,1-disubstituted cyclohexanes are also called as geminally substituted. They donot exhibit any configurationals isomerism but exist in two interconvertible conformers is given in the following figure.

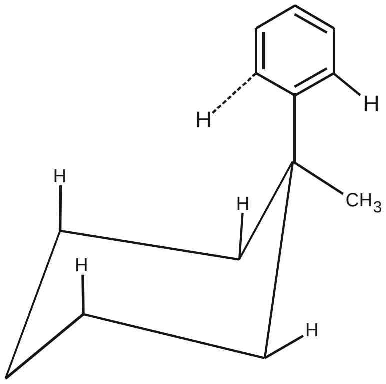


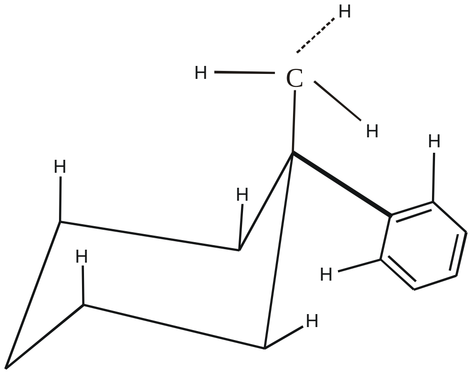
These forms are separated by each other by an energy barrier which is usually of the same order of magnitude as the cyclohexane ring inversion. When the subsituents X and Y are same as in 1,1-dimethyl cyclohexane, the two conformers are identical and are known as topomers. On the other hand when the subsituents X and Y are different for example I 1-methylcyclohexanol, the two conformers are diastereomers and are present in unequal amounts. In principle, in such cases the ratio of the two conformers should correspond to the difference in the conformational free eenrgies of the two substituents.

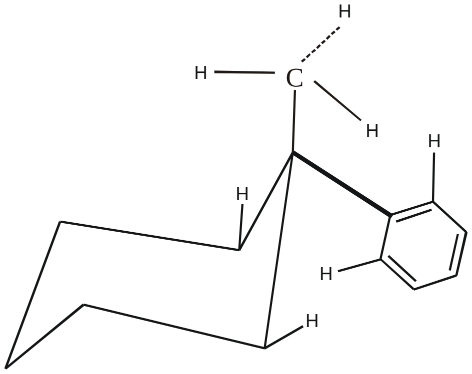
Sometime it is also found that although the conformer with the bulkier substituents in the equatorial position generally predominates but there exists a levelling effect , i.e the preferred conformer is less populated than expected. Thus it is observed that 1-methylcyclohexanol exists as a 70:30 mixture of axial and equatorial conformers in dimethyl sulphoxide (DMSO) at 35^{0}C corresponding to a free energy difference of 2kJmol^{-1} whereas the actual difference between $-\Delta G^0$ values of methyl and hydroxyl groups is around 3.5kJmol^{-1}. This is shown in the figure



In some situation, the opposite conformer predominates. Thus in case of 1-methyl-1-phenyl cyclohexane, the conformer with axial phenyl and equatorial methyl is preferred over the other with equatorial phenyl and axial methyl by 1.33kJmol^{-1} in spite of the appriciable difference of $-\Delta G^0$ values of phenyl and methyl group which are 12.6 and 7.5kJmol^{-1} respectively. This can be explained on the basis of the fact that phenyl ring in one conformer is so oriented that its interactions with axial 3-H and 5-H are minimum. There may be some interactions between the ortho hydrogens and adjacent equatorial hydrogens. On the other hand in another conformer the phenyl group is in its usual bisecting orientation and interacts strongly with the hydrogen atoms of methyl group. This is diagramatically shown below:



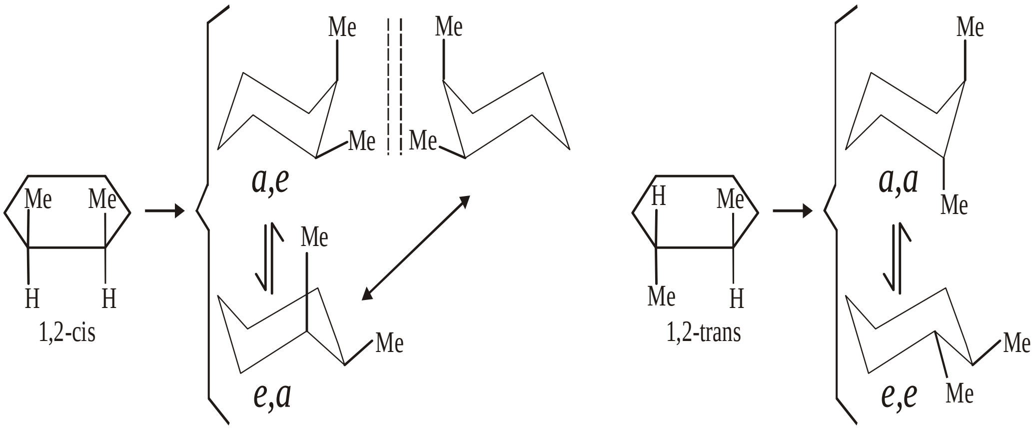




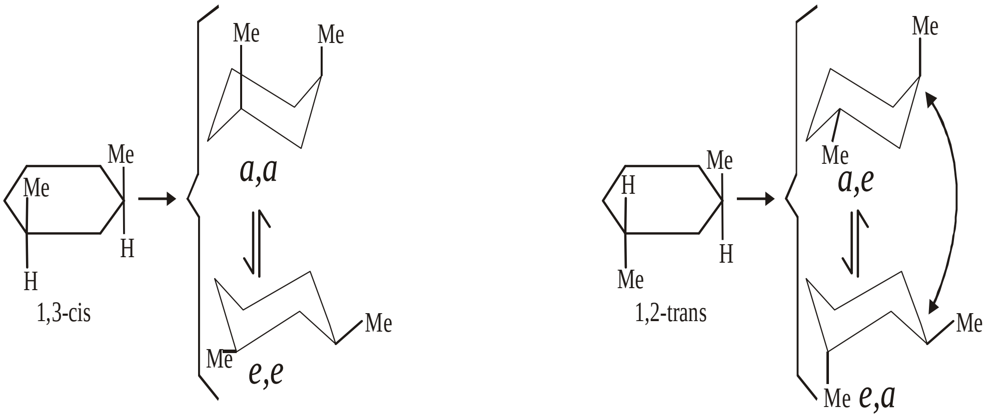
18.2.1 Disubstituted Cyclohexanes

It is observed that non-geminally disubstituted cyclohexane exist in three sets of positional isomers which are 1,2-, 1,3- and 1,4- isomers. Each of them constitutes a pair of cis-trans diastereomers which in turn exists in two interconvertible chain conformers. In addition to this, depending upon symmetry property, a particular isomer may exhibit eneantiomerism also. These all situation are shown diagramatically also. These all situation are shown diagramtically in the diagram below

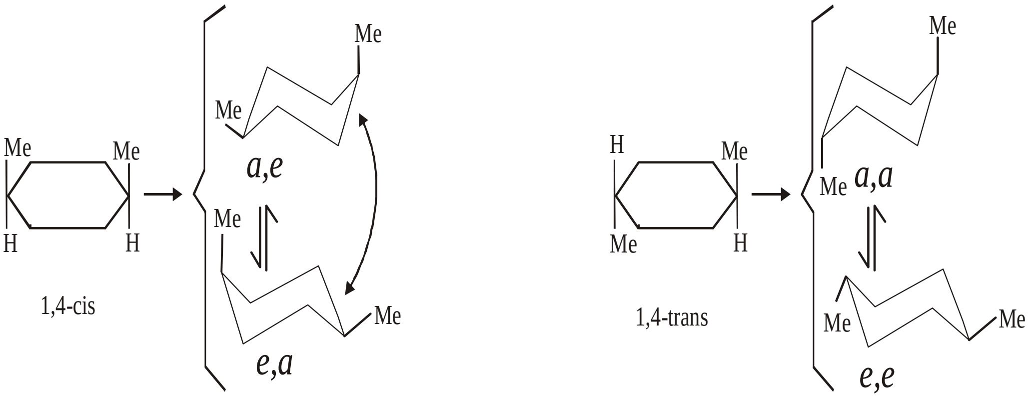
1.



2.



3.

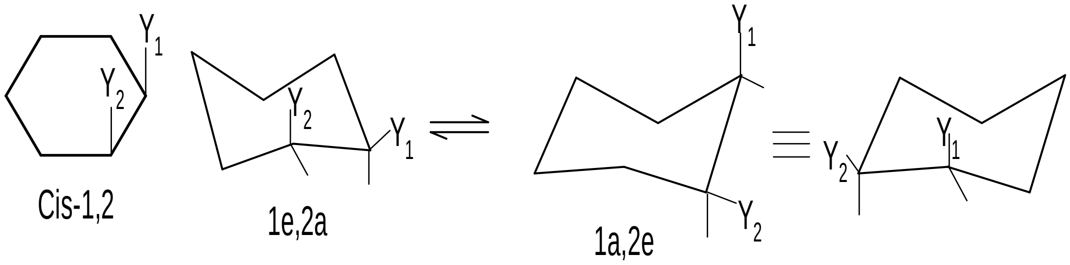


Configuration and conformations of dimethylcyclohexanes (the double-headed arrows indicate identity and the reversible arrows ring inversion)These disubstituted cyclohexanes are discussed below systematically.

18.2.2 (A) 1,2-disubstituted cyclohexane

It is important to note that in case of cis-compounds of this category, one substituent must be in the axial position whereas the other should be at equatorial position. If there is a difference in the size of the substituents the 1, 3-interactions will become dominant particularly when the larger group is in axial position.

So it is evident that the conformation, with larger group in equatorial position, will be of lower energy.

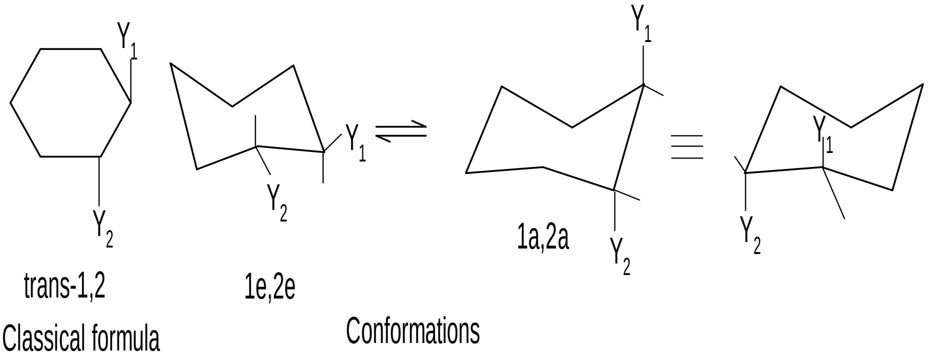


Classical formula Conformations

To illustrate it we can sight the example of cis-2-methyl cyclohexanol. In this compound because methyl group is larger in size than hydroxyl group, thus the preferred conformer shall be one in which the methyl group is equatorial ie, 1a-hydroxyl, 2e-methyl. This has been found true as a general rule; we can say that, greater the difference in the size of two substituent, larger will be the dominancy of the conformer which has larger group in the equatorial position.

In Cis compounds having two substituents identical there occurs a plane of symmetry and hence resolution is not possible. On the otherhand if we look to the conformational representation then for the cis compounds with $Y_1 = Y_2$, there are no elements of symmetry and consequently the two forms are non-superimposible. When this type of conformation undergoes flipping, the resulting conformation is the mirror image of the original conformation and that obtained after flipping, their populations are equal and so this type of 1,2-disubstituted cyclohexane having $Y_1 = Y_2$ is optically inactive.The absence of optical activity is due to external compensation. However such type of compounds has never been resolved and the reason is being that the two enantiomers are readily interconvertible. In actual practise each eneantiomer undergoes very rapid autoracemisation.

Whether the substituents Y_1 and Y_2 are identical or different, the two conformations are not same and because of the 1,3-interactions the e,e form will be more stable than the cis-isomer (a,e form). An example of this situation is of the compound 2-methylcyclohexanol. The transform of this compound if found to be more stable than the cis. The cis form converts readily into tranform when heated with sodium moreover on reduction of 2-methyl-cyclohexane with sodium and ethyl alcohol, Trans form is produced.

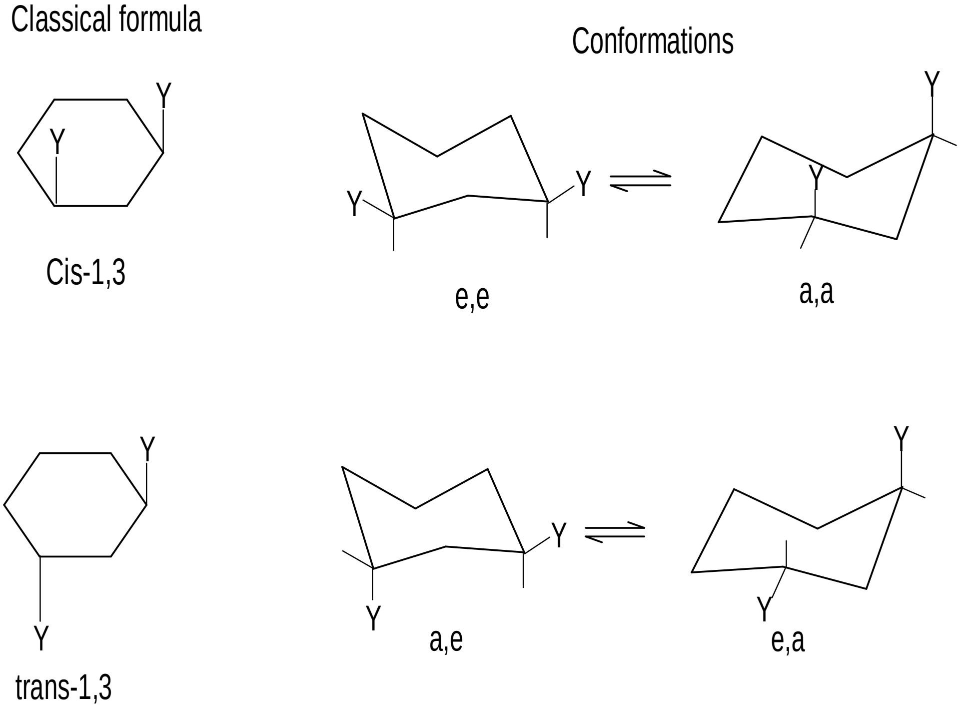


Both the classical formula and the e,e (and a,a) conformation of trans 1,2-disubstituted cyclohexane (whether Y_1 and Y_2 are same of different) and non superimposible on their mirror images. None of the conformation can be converted into its mirror image by flipping. Hence it can be concluded that trans 1,2-disubstituted cyclohexanes substituents are identical or not.

18.2.3 1,3-Disubstituted Cyclohexanes

In 1, 3-disubstituted compounds the two trans conformations are identical when the two substituents are same. The cis e,e form is more stable than cis a,a form and also their trans-e,a-conformation. For example in case of 1,3-dimethylcyclohexane the cis 1,3-e,e form is the most stable conformation. It is to be noted that this situation is reverse of that of the 1,2-dimethylcyclohexane. According to a rule the isomer which has higher boiling point, refractive index and density is the one with less stable configuration. Thus the trans-1, 3-disubstituted cyclohexane have the higher physical properties (the Trans form has more axial substituents than more stable cis form)

18.2.4 1,4-Disubstituted Cyclohexanes



In these compounds the cis isomer exists in two identical e,a- and a,e conformations. On the other hand the trans isomer is found to exist in two different e,e- and a,a-conformations of these the a,a conformation is unstable because of four gauche interactions by an amount 15kJmol^{-1}. During symmetry operations it is observed that the vertical plane passing through C-1 and C-4 is a σ plane and thus all conformers are achiral even if the two substituents are different.

When both the susbstituents are different the 1,4-trans isomer has diequatorial conformation but the cis isomer is found to exist in two differently populated e,a-conformations of these the conformer having bulkier group in equatorial position is found to dominate.

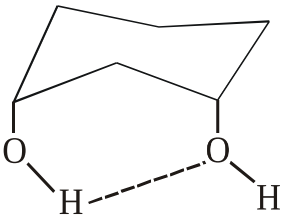
It is seen that arguments used for the disubstituted cyclohexane can also be applied to the higher substituted cyclohexane. To sum up the following generalisation many be helpful.

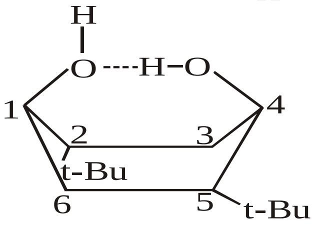
(i) In cyclohexane systems, mono-di-tri and poly substituted derrivatives always have a tendency to adopt chain conformation as far as possible

(ii) The chain conformation with maximum number of equatorial substituents is always preferred. This is true only when the internal forces due to dipole interactions or hydrogen bonding do not exist. When these interactions are present, it is necessary to determine the dominating interaction before finalising the conformation for the molecule under study.

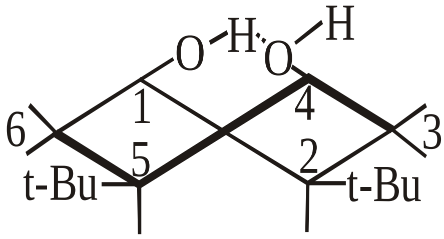
(iii) The energy barriers between various conformations are so small that their mutual interconverstions cannot be prevented.

To illustrate the above generalisations let us consider the case of cyclohexane -1,3-diol. This compound is known to have diaxial rather than diequatorial orientation. The reason for this is that there is interamolecular hydrogen bonding (shown by its infrared spectra) which stabilises the diaxial but not the diequatorial form. The conformation of the ring is in the chair form. This is shown below.





Boat

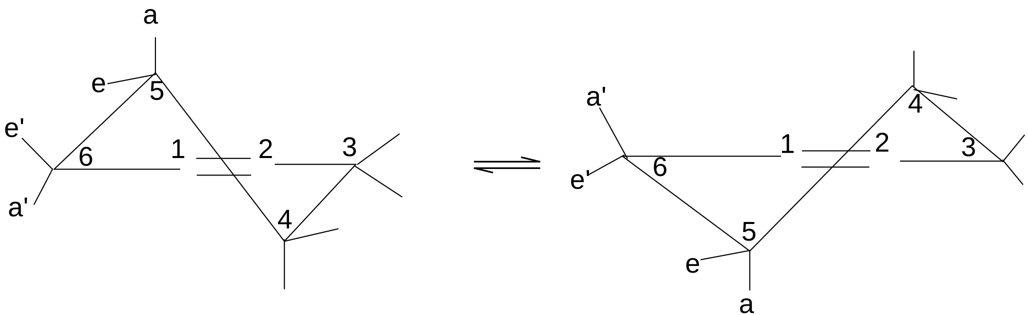


Twist Boat

When intramolecular hydrogen bonding is possible between the substituents at 1 and 4 positions, the molecule may assumed a boat conformation, rather than the chair in which the hydrogen bonding is not possible. However the boat conformation may be a twist boat form.

18.3 Disubstituted Cyclohexenes

Cyclohexane contains two sp^2 hybridised carbon atoms. The conformation has been studied by X-ray crystallography and also by its electron diffraction studies in vapour phase. The presence of a double bond in the ring causes the ring to assume the half chair conformation in which atoms 1, 2,3 and 6 lie in one plane. This is shown below.

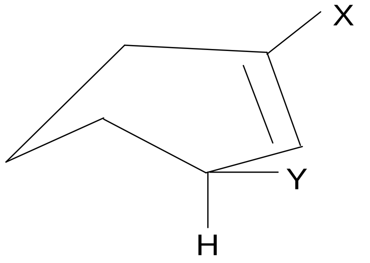


Cyclohexane

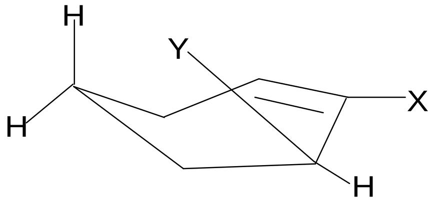
The hydrogen atoms present at C_4 and C_5 are axial and equatorial types but the hydrogen atoms present at C_3 and C_6 are present in quasi-axial (or pseudo-axial)(a') and quasi- equatorial (or pseudo equatorial) (e') as shown above.

The addition of halogen and halogen acids proceeds through polar mechanism and results in the formation of trans product, so it can be anticipated that the preferred product will be a diaxial one, in a rigid system. However, in mobile system if the diaxial form is less stable than the diequatorial form then the equilibrium will shift towards diequatorial form. It has been found true experimentally also. For example when cyclohexane is allowed to react with bromine the product obtained is trans 1,2-dibromocyclohexane and the diaxial and diequatorial forms exist in about equal amounts. The two C-Br bonds, being polar, exert strong dipole-dipole interactions and thus partly offset the 1,3-interactions. It is interesting to note that when the addition of bromine is carried out in the presence of cinchonine or cinchonidine, the product obtained is trans -1, 2-dibromocyclohexane and it is optically active.

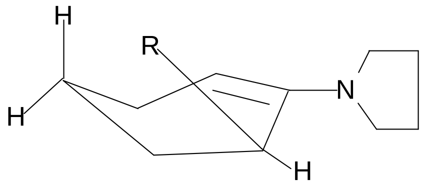
In disubstituted cyclohexanes, allylic 1,2 strain is found to exist. For example if the two substituents X and Y are sufficiently large, then in case of equatorial conformer these substituents will interfere sterically and so the axial conformer will dominate. in case of 6-e and *l*-susbtituent the dihedral angle is lower than its normal value. If both the substituents are methyl the axial conformer is preferred and it has been proved by their thermodynamical studies. It has also been found that allylic 1,2 strain is considerable when the substituents present are bulky. It is confirmed by the fact that the compound enamine fig(III) and 1-phenyl-6-t-butylcyclohexane (fig IV) exist in axial conformations. This fact has also been supported by their NMR studies. These compounds are shown in the figure below.



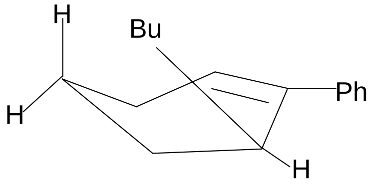
I



II



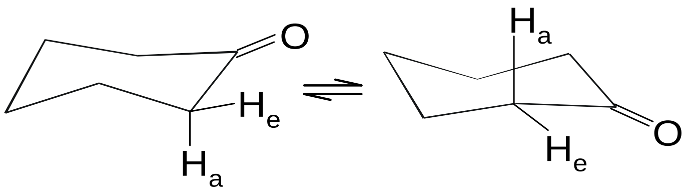
III

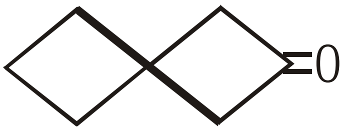


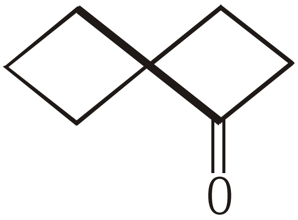
IV

18.4 Di Substituted Cyclohexanones

Cyclohexanone molecule exists in the chair form. This chair form produces a topomer. Sometimes two flexible forms are also notices. All these forms are shown diagramatically in the diagrams below.







Conformation and geoemtry of cyclohexanone

The dominating chain form of the cyclohexanone molecule differs from that of cyclohexane in the following points

18.4.1 (1) Geometry

in case of cyclohexanone the ring is found to be flattened at the side of carbonyl group . In the chair form there is a vertical plane involving C-1 and C-4 and from the symmetry point of view it falls in Cs point group. On the other hand the two flexible forms belong to chiral point groups which are C_1 and C_2. The dominanacy of angular and torsional strains causes some instability in cyclohexanone as compared to parental compound cyclohexane.

The flexible forms are more stabilised due to their twist boat structures. Thus it appears that in case of bulky substituents the flexible forms will be more populated.

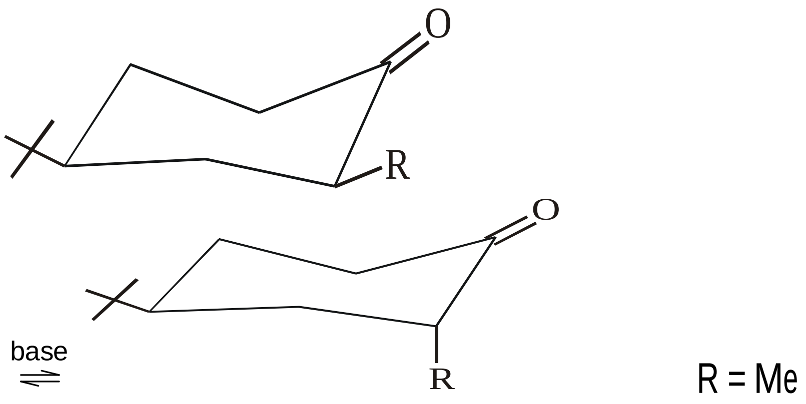
18.4.2 (2) Ring inversion

The value of free energy of activation for the ring inversion in cyclohexanone is found to be comparatively lower and the reason for this is due to the different status of hybridisation of ring carbon atoms in cyclohexanone. Moreover due pseudorotation among the flexible forms is more frequent thus making the transition states unidentical.

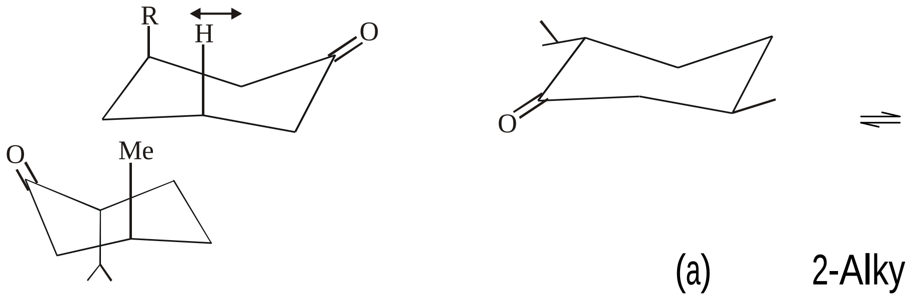
18.4.3 **(3) 2-alkyl-and -3-alkylketone effect(say an alkyl group)**

In cyclohexanone if a substituent (say an alkyl group) is present at C-2 or C-6 it interacts with the oxygen atom of $>C=O$ group and produces a destabilising effect of equatorial conformer. This is known as 2-alkyl ketone effect. In 3-alkylcyclohexanone, the axial conformer is more stable than equatorial conformer and this is known as 3 alkylketone effect diagramatically these effects are shown below.

(a)



(b)

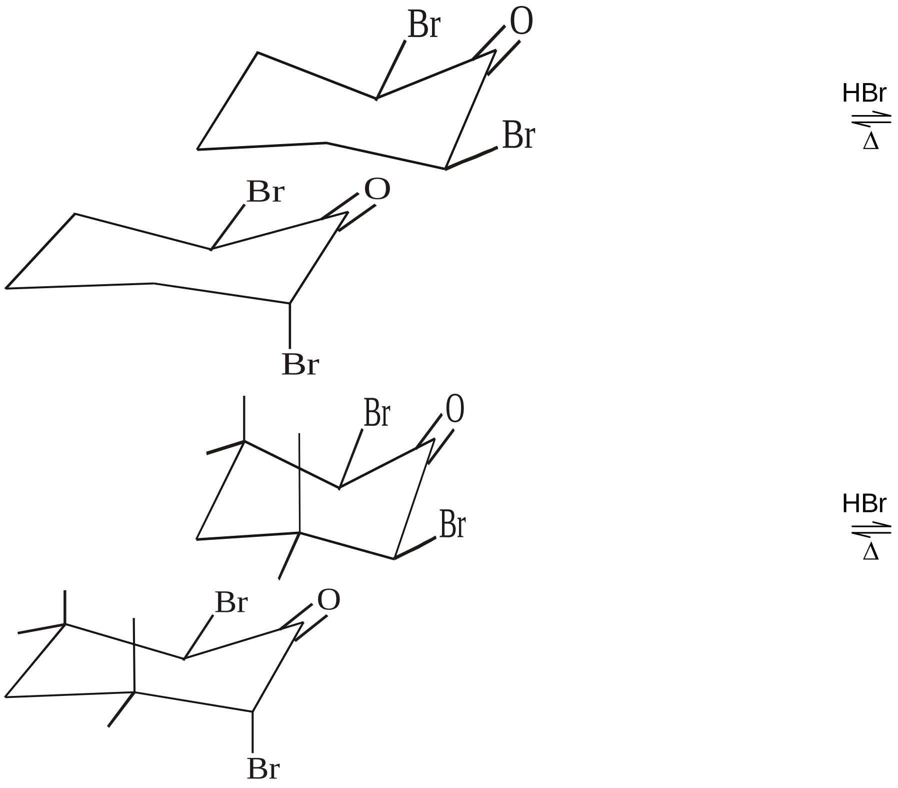


(a) 2-Alkyl Ketone effect (b) 3 - Alkylketone effect

Among disubstituted cyclohexanones, 2,6- dibromo-cyclohexanone has been studied in detail. When cy. The trans isomer is found to predominate. There occurs a repulsion between the polar bonds ie C = O and C-Br and an orthogonal arrangement is obtained.

On the other hand in 3,3,5,5 tetramethyl-2,6-dibromocyclohexanone the cis isomer is formed although it involves considerable dipole-dipole interactions in it. This can be explained on the basis of the well known reflex effect.

According to this if the bulky groups are present in axial positions on one side of the ring, the axial bonds open and causes some deformation in the ring ie the axial groups are pinched on the other side of the ring. Thus the axial bromine have severe synaxial interaction with four hydrogen atoms present in the axial position. Thus the stability order is reversed than expected by other considerations.



Reflex effect in bromocyclohexanones

It is observed that carbonyl group interacts with - substituents in substituted cyclohexanones and some change in sectroscopic properties is produced.

The IR stretching frequency of $>C=O$ group in equatorial conformer is slightly increased. On the other hand this frequency is not changed if axial halogens are present. Thus this fact can be used to differentiate between the isomers containing axial and equatorial halogens on the carbon atom next to $>C=O$ group in the disubstituted cyclohexanones.

On theother hand the presence of polar axial bond in disubstituted cyclohexanone causes a bathochromic shift in $n \rightarrow \pi^*$ transition of carbonyl group. The cause of this shift is assumed to be due to delocalisation of σ and π electrons. In equatorial isomer some hypsochromic shift is seen which is of lower value than bathochromic shift.

It has also been found that the hydrogen atom at axial position present at the -carbon atom can easily be removed by between the electrons of C-H bond and electrons of the $>C=O$ group. This favours the formation of enolate anion. The same reason can be offered for the protonation of the enolate anion form the axial side.

18.5 Molecular Mechanics

Molecular mechanics , which sometimes also known as faced field calculation , is a mathematical procedure which is used for the purpose of calculating conformational geometries this methods used to calculate the following the parameters in the conformations of molecule

1 Bond angles

2 Bond distances

3. Total potential energy

the above parameters are computed for each conformation of molecule under examination to provide above information we also have another approach known as Molecular orbital calculations but it is observed that molecular mechanics is easier less cumbersome and is more is more accurate in molecular orbital calculations position of the nuclei of the atoms are assumed and wave equations are used for the purpose o9f electrons .on the other hand molecular mechanics calculations ignore the electrons and concentrate to study the position of the nuclei .there is another difference in the two approaches . in molecular orbital calculations each molecule is analyzed as an individual unit whereas in molecular mechanics firstly parameters are calculated for the small molecules and their data are than used in the calculations for the larger and complicated molecules.

in molecular mechanics some empirically device set of equations are used for the purpose of calculating rhe potential energy of the molecules tehse equations include terms like vibrational bond stretching , bond angle bending and other interaction terms between various atoms present in the molecule ,all these terms are than summed up as shown below

$$V=\sum V_{stretch} + \sum V_{bend} + \sum V_{torsion} + \sum V_{VDW}$$

in the above equation the last term ($\sum V_{VDW}$) includes vanderwaal interaction between non bonded atoms present in the molecule the various sets of the functions ,called the forced field are collected. They contain adjustable parameters .these parameters are treated for the condition of the optimization in order to get the best fit of known properties of the molecules.Now a tacit assumption is made that the corresponding parameters and the force constants calculated for one conformer can be transferred to the another with theproper mathematical modifications . thus it appears that molecular mechanics is solely based on experimentl data

in typical molecular mechanics calculations for molecule a hy6pothetical geometrical structure is assumed .different parameters like bond distances ,angles ,torsion angles for this trial geometrical structure are given different values in this procedure hydrogen atoms are usually nt considered because their positions are calculated latter from the standard geometrical parameters . now a list of interractons are written for this trial structure of the molecule these terms include bond distances , atoms attached to a common atom (bond angle) , atoms attached to the adjacent atoms ,(Torsion angle) , and non bonding interaction these second step includes the selection of forced field parameters for these interactions bya computerized method . the potential energy of the trial structure is than calculated through the above equation. the next step is the energy minimization process this done by the plotting a graph between small changes in geometrical coordinates abnd the energy of the molecule .on this graph various points are located where the first derivative of potential energy that is V are equal to Zeothis means that the total energy of the molecule will be mnimum, this process is repeated sepeartely for each of the stable conformations because there is no known method for finding the lowest energy for a molecule .

molecular mechanics can also be employed for the study of enrgy maxima but it is found that it furnishes much less details in this field for this purpose a number of forced field computer programmes are available .

molecular mechanics calculations give the total potential energy of each conformations .now if the mole fraction of all the conformations are known or can be calculated it is evident that enthalpy of formation of a compound can be calculated by this approach with a high degree of accuracy these data can be helpfukl in calculating other thermodynamical properties of the molecules.

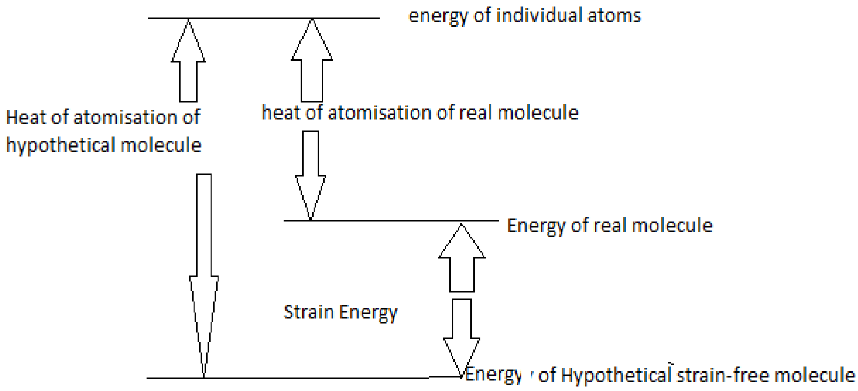
Although the results furnished by the molecular mechanics are satisfactory and show a comfortable agreement with the experimental measurements yet it is no totally reliable, the reason for this is that it does fail in certain cases.

The second limitation of molecular mechanics approach lies in its mathematical implementation. This is to say that it can be used only in those cases of molecules for which the parameters are transferrable; this is the condition of the simple molecules only. it is interesting to note that molecular orbital calculations do not have this limitations .

18.6 Strain

a molecule is set to be under steric strin when bonds are forced to make abnormal angles this results in an increase in the energy of the molecule and the cause is angular distortion .the cause of abnormal bond angles lies in the structural feature of the mo9lecule on eof these is found in ssmall ring compounds when the aangle is less than normal orbital overlap this strain is called as the small angle starin the other reason is the that non bonded atoms are forced to remain in closed proximity because it is demanded by the geometry of the molecule these are called as the non bonded interracrions

thus a molecule in strain possess strain energy the value of this energy in a particular molecule cann be calculated from thermochemical data the strain energies cannot be known exactly because the energy of real moleculecan be measuresd but that of a hypothetical unstrained molecule can not be it is possible to strain energy calculation can be depicted by the following scheme .



18.7 Summary

- in di substituted cyclic system various interactions are operative

- main interaction are a-a,e-e,a-e
- the interactions not only depends on the relative positions of the substituent but there bulk also plays a vital role in deciding the energy content of the cyclic molecule
- if the cycli8c system has a functional group or instauration the chemical properties of the molecule are comprehensively influenced by the spatial position of the substituent
- the molecule prefers to acquire that confirmation in which it has dissipated most of its energy and acquires the lowest energy state
- in case of the confirmers with the bulkier substituent it has been found that the equatorial position generally predominates but the leveling effect also operates
- The leveling effect makes the population of the preferred conformer less than expected.
- In case of 1,2 disubstituted cyclic system it is not only the relatige position but the size of the substituent also plays an important role in deciding the total energy content of the molecule .
- It is general observation that the conformations with the lager groups in the equatorial position have the lower energy.
- When the two conformers having the identical substituent are non superimpooable the optical property are also becomes inclusive.

18.8 Review Questions

1. what are the various types of the internal strain in a molecule
2. what is the significance of the word rotamer
3. Explain the sterechemical aspect of the molecule with reference to the elimination of the alkyl substituted cyclohexane.
4. what is flipping explain with the example.
5. what is the significance of Free Energy of formation of a conformer.
6. how the values of the enthalpies of hydrogenation decides the stability of the organic molecule
7. What is leveling effect?

8. what is Quasi – Axial and Quasi –equatorial position support your ans with example .
9. what is a TOPOMER give an example
10. Explain the term ring Inversion with example
11. what are two alkyl and three alkyl effects
12. what is the effect of stretching IR frequency of carbonyl group in the following compounds
    a. Cyclohexanones
    b. mono substituted cyclohexanone
    c disubstituted cyclohexanone
13. what causes the bath chromic shift in n- π* transition o carbonyl compound illustrate with examole
14. how is the acidity of axial hydrogen is affected in disubstituted cyclohexanes.

18.9 Refrence books

- Advance dorganic Chemistry ,Jery March,4th edition,johnwiley and sons.
- Organic synthesi ,Michael B smith,2nd edition ,Mac Grah hill.
- Organic Chmistry ,I.L Finar Volume II,ELBS

Unit - 19

Conformations of A Few Other Monocyclic and Bicyclic Systems

Structure of Unit

19.0 Objective

As we know that we can find out the structures of molecules by various techniques like : X-ray, NMR, IR. X-ray reveal exactly where the atoms are in crystals. IR spectroscopy gives the information about the bonds in the molecule. NMR spectroscopy gives us information about the atoms themselves and how they are joined up. Upto now; we have mainly been interested in determining which atoms are bonded to which other atoms and also the shapes of small localized groups of atoms. But on a slightly larger scale, shape is not usually so well defined. Since rotation is possible about single bonds and this rotation means that while the localized arrangement of atoms stays the same, the molecule as a whole can adopt a number of different shapes. But the arrangement about the double bonds always remains the same because double bonds can't rotate. All the single bonds in the molecule are constantly rotating at the room temperature.

The chances that two molecules will have exactly the same shape at any one time are quite small. Even though no two molecules have exactly the same shape at any one time, they are still all the same chemical compound – they have all the same atoms attached in the same way, these different shape of molecules of the same compound are called as conformations.

In this unit we will deal with conformation of a few other monocyclic and bicyclic systems.

19.1 Introduction

Conformation of a molecule are defined as the various arrangement of its atoms in space which differ only in rotation around single bond or bonds (i.e. in dihedral angles) and are easily interconvertible.

If we rotate about as many single bonds as we like then we get one conformation to another. It cannot be done by breaking any bonds. That's the reason why we can't rotate about a double bond – to do so we need to break the π bond.

Example:

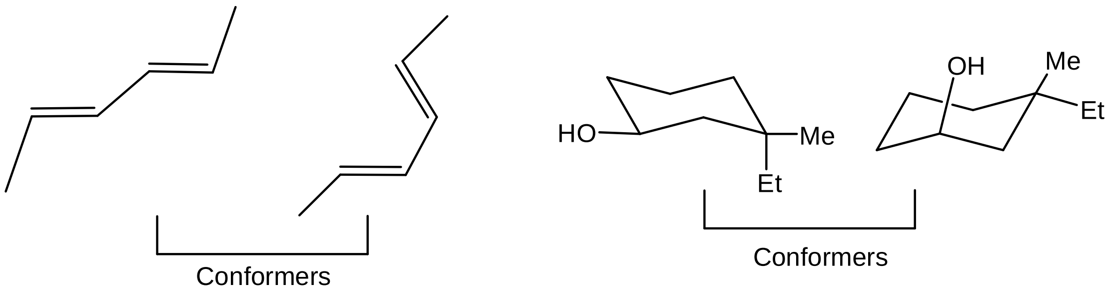


Fig. 1

Figure 1: shows compound each showing conformation.

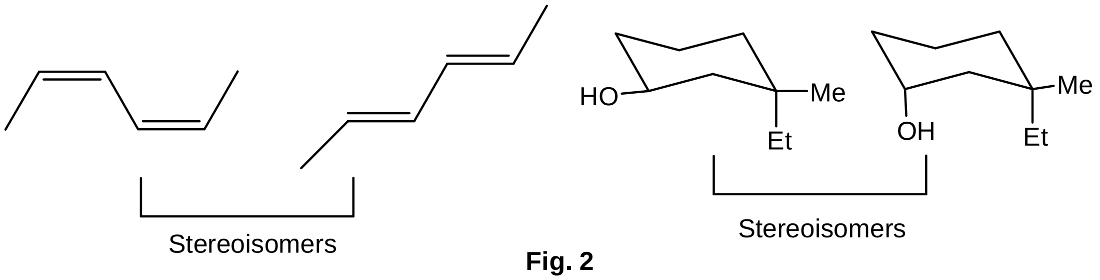


Fig. 2

Figure 2: shows compounds with different configuration. Since these pairs can only be interconvert by breaking a bond. Compounds with different configuration are called stereoisomers.

Rotation or bond breaking:

- Structure that can be interconverted simply by rotation about single bonds are conformations of the same molecule.
- Structures that can be interconverted only by breaking one or more bonds have differ configuration and are stereoisomers.

19.2 Conformational effects in six membered rings containing unsaturation

When we introduce sp^2-hybridized atoms into open chain molecules, torsional barriers becomes less for e.g. torsional barrier in 1-alkenes and aldehyde are somewhat smaller than in alkanes. Similar effects are noted when sp^2 centers are incorporated into six membered rings. The free energy barrier for ring inversion in cyclohexane is 10.3 kcal /mol; while it has been reduced to 7.7 kcal /mol in methylene-cyclohexane and to 4.9 kcal /mol in cyclohexanone. The following changes occurs by the introduction of an sp^2 hybridised carbon into cyclohexane ring:

One or more valence angles are increased, the ring slightly flattens in the vicinity of the sp^2 carbon decreasing torsion angles and increasing torsional strain and finally the steric interactions among the substituents and between the substituents and the ring change perceptibly. Consequently there is an overall increase in enthalpy of cyclohexanes with an sp^2 hybridized ring atom relative to simple cyclohexanes. Now in this reference we will discuss cyclohexene as it is the simplest six membered ring containing unsaturation.

19.2.1 Cyclohexene

The conformation of cyclohexene is described as a half chair (1). It is confirmed by X-ray crystallographic data of cyclohexene derivatives and on the basis of electron diffraction and microwave spectroscopy. The torsion angles as shown in supported by theoretical calculations and show considerable flattening of the ring near the double bond. Cyclohexene geometry have following characteristic features:

1. The C-1, C-2, C-3, and C-6 atoms are in a plane as are the two vinylic hydrogens. The other two ring carbons C-4 and C-5 are disposed alternately up and down (or down and up) with respect to this plane.
2. The structure (I) has a C_2 axis bisecting the double bond (no σ plane) and belongs to point group C_2 (chiral). The two enantiomeric structure (**1**) and (1') are however, interconvertible by inversion of the ring* and so form an inseparable (±) pair. They are shown in a different perspective by the structures (2) and (2').
3. The C(1) – C(2) bond length is 1.335A°, and the C(1) – C(2) – C(3) bond angle is 123°. The substituents at C-3 and C-6 are tilted from the usual axial and equatorial directions and are referred to as pseudoaxial and pseudoequatorial. The activation energy for ring inversion is 5.3 kcal / mol.
4. The interconversion of the two half-chair forms probably goes through a transition state which may be represented by the boat conformation (3).

   The experimental barrier energy is 22.2 kJ mol^{-1} (ΔG^{++} as determined by

^{1}H NMR from the coalescene of 4-H and 5-H of cyclohexene-d_6 at –164°C). The calculated value of enthalpy for the boat (3) is 25.0 kJ mol^{-1}. The barrier energy is very sensitive to substituents at C-4 and C-5 which is consistent with the boat as the transition state.

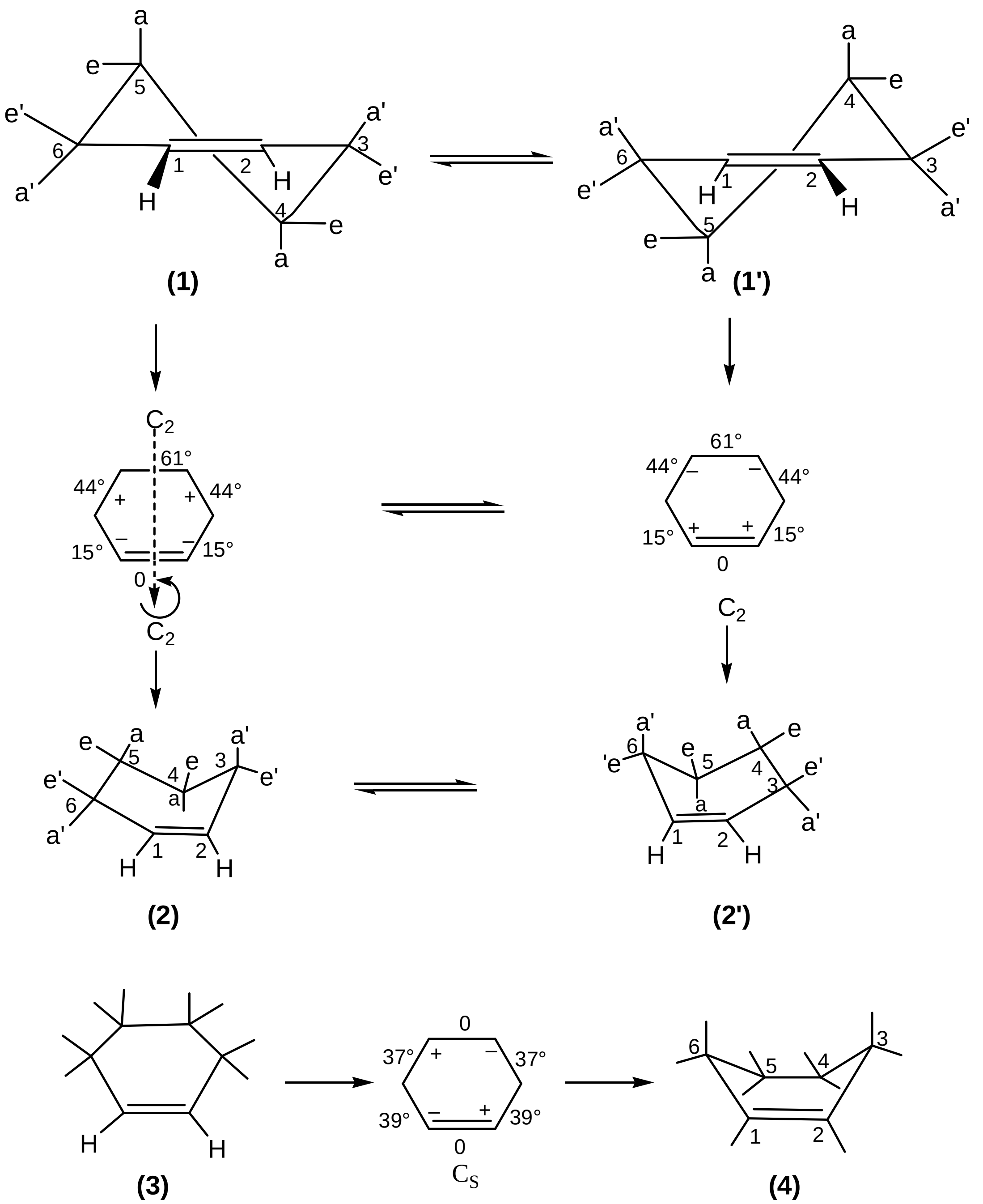
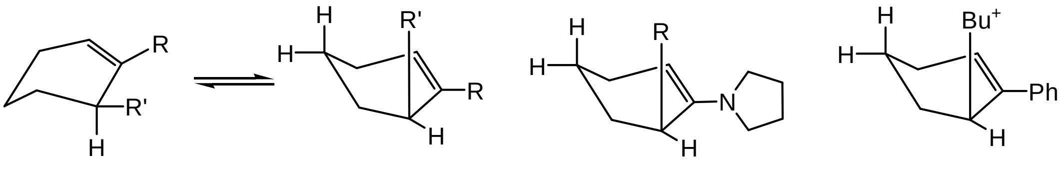


Figure 3. Conformation of Cyclohexene

5. A^{1,2} Strain (allylic 1,2-strain): Johnson and Malhotra have postulated a second theorem which states that in a cyclohexene (5) which have (Figure 4) R and R' are of moderate size, they will interfere sterically with each other in the equatorial conformer (5) to such an extent that the axial conformer (5') will be preferred. As already stated the dihedral angle between 6-e-substituent and 1-substituent is considerably less than the normal value of 60°. When both the substituent are Me, an enthalpy difference of 1.5 KJ mol^{-1} has been calculated in favour of the axial conformer (which contains a 1,3-diaxial Me/H interaction) corresponding to a mixture of 64:36 at ambient temp. When the groups are bulky, A^{1,2}-strain becomes manifest otherwise it is not a powerful effect and e.g., Ph. Thus the enamine (6) and 1-phenyl-6-t-butylcyclohexene (7) exist predominantly in the axial conformers.



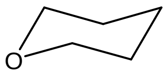
5 5' 6 7

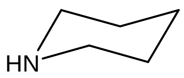
Figure-4: Allylic 1,2-strain

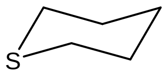
19.3 Conformational effects in six membered heterocyclic ring

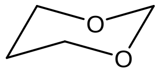
The replacement of carbon by other element produces changes in several structural parameters and consequently affects the conformational characteristic of the molecule.

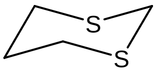
The changes which are most obvious on introduction of a heteroatom into six membered rings have to do with bond angles and bond length. Both the C-O and C-N bond length (1.43 & 1.47A$^{\circ}$ respectively) are shorter than the C-C bond length of 1.54 A$^{\circ}$, while the C-S bond length (1.82 A$^{\circ}$) is longer. The normal valence angle are somewhat smaller than tetrahedral at oxygen and nitrogen and significantly so for sulphur for which the C-S-C angle value is 100°. The six membered heterocycles containing oxygen (tetrahydropyran), nitrogen (piperidine) and sulfur (thiane), all resemble the chair conformation of cyclohexane but are modified so as to accommodate the bond lengths and bond angles characteristic of the heteroatom. The rings are all somewhat more puckered than cyclohexane.


tetrahydropyran


Piperidine


Thiane


1,3-dioxane


1,3-dithiane

The conformation of six membered heterocycles, specially those containing N and O atoms is of special interest as existence of these ring systems in natural products : piperidine in alkaloids and tetrahydropyran in sugars. Oxygen in tetrahydropyran and nitrogen in piperidine are considered to be sp^3 hybridised. The important conformational features of these two ring systems along with a few related heterocycles are discussed here.

19.3.1 Molecular geometry:

The six-membered N, O or S heterocycles exist almost exclusively in chair conformation. It has been proved for piperidine derivatives by X-ray crystallography and for tetrahydropyran derivatives by microwave spectroscopy.

The ring torsion angles (53-56°) of piperidine are very similar to those in cyclohexane. C-O and C-N bonds are shorter than C-C bonds, so the chair conformation of piperidine and tetrahydropyran are expected to be slightly more puckered than cyclohexane. It is also true for thiane since the effect of the longer C-S is compensated by the smaller C-S-C bond angle (100°).

On the basis of Karplus equation, Lambert has developed a method; which indicates the nature of the ring structure (chair or deformed chair) of six membered heterocycles.

$$J_{(\text{cis or trans})} = A\cos^2\theta_c \text{ or } A\cos^2\theta_t$$

$$R = \frac{J\ trans}{J\ \text{cis}} = \frac{A\ \cos^2\theta_t}{A\,cos^2\,\theta_c} = \frac{\cos^2\theta_t}{\cos^2\theta_c}$$

For six membered heterocycles if value of R = 2, it indicates perfect chair. As the value decreases (approaching 1, R < 2) , then ring chair is assumed to be flatter. On the other hand if R - > 2 indicates a more puckered chair conformation.

It is difficult to use Karplus equation on heterocyclic system owing to unknown value of A which is differ for different H-C-X-H or H-X-Y-H segments and also depends on substituents.

R value around 2 provide additional support to the chair conformation for piperidine and tetrahydropyran. Boat conformation is approximately 20 kJ mol^{-1} higher for piperdine and 16 kJ mol^{-1} higher for tetrahydropyran.

19.3.2 Barrier to ring inversion:

The Order of torsional interaction for the C-X, X-X or C-C bonds are:

C-X > X-X or X-Y > C-C

The effect is reflected in the free energy of activation for inversion of different heterocyclic ring systems (Table 1). As in the case of cyclohexane, ring inversion takes place through the intermediate twist boat forms and as this conversion involves torsion along bonds, the higher the torsional interaction, the higher is the activation energy.

Table 1 : Free energy of activation for ring inversion of six membered heterocycles

Ring system	**ΔG (kJ mol^{-1})**
Cyclohexane	43.2
Piperidine	43.6
Tetrahydropyrane (Oxane)	39.8
Thiane	37.7
1,3-Dioxane	40.6
1,2,4,5-Tetraoxane	62.8

19.3.3 Pyramidal inversion:

The conformational analysis of six-membered heterocycles is complicated by the fact that pyramidal inversion and ring inversion occur side by side and are often competitive. Generally ring inversion is slower than pyramidal inversion. For piperidine itself, the two inversions bring about the same conformational changes: N-H_e to N-H_a and vice versa. For tetrahydropyran, both the processes are degenerate isomerisation (as in cyclohexane). Inversion at O is inconsequential in any case since it interchanges the positions of the two lone pairs of electrons only. The difference in ring inversion and pyramidal inversion can be seen in 1,3-dimethylpiperidine (Figure 5). Ring inversion (RI) leads to conformational isomers, the configuration (cis and trans) remains unaltered. While pyramidal inversion (PI) converts a cis isomer into a trans isomer and trans into cis. Since both RI and PI occur concomitantly at ambient temperature, an equilibrium is reached among the four conformers shown.

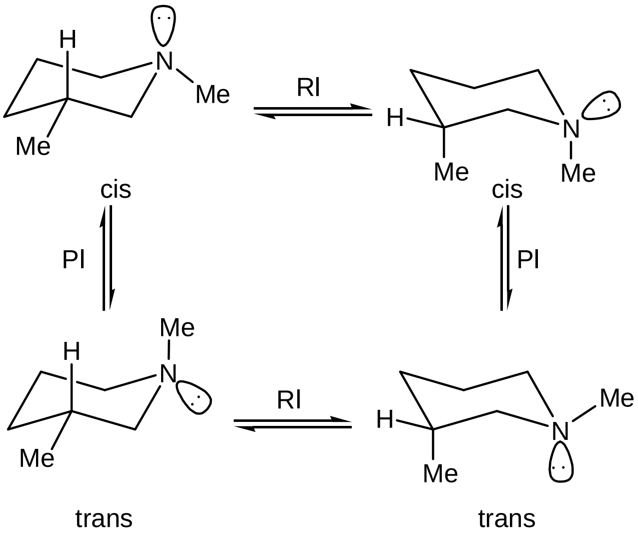
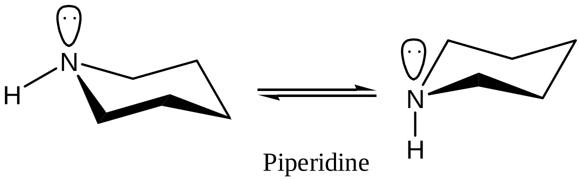
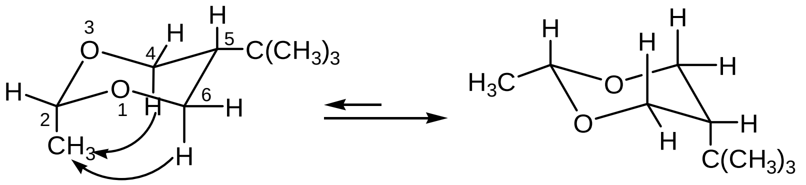


Figure –5 : Ring inversion and pyramidal inversion in piperidine

19.3.4. 1,3-Synaxial interactions:

In heterocyclic ring the steric repulsions for axial substituents are reduced due to the replacement of methylene groups of cyclohexane by oxygen or nitrogen. It is seen in cis-2-methyl-5-tert-butyl-1,3-dioxane (Fig-6) in which the preferred conformation has the bulky t-butyl group axial and the methyl group equatorial. As the divalent oxygen has no substituent, therefore 1,3-diaxial interactions which are the main unfavourable interactions for axial substituents in cyclohexane are absent.





(1,3-Diaxial interactions below the ring)

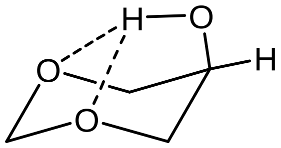
Preferred conformation
(No 1,3-diaxial interactions below the ring)

Figure-6: Cis-2-methyl-5-tert-butyl-1,3-dioxane

If we take 2-alkyl substituent, however it will have a greater preference for the equatorial orientation in a 1,3-dioxane than in cyclohexane presumably because the decreased C-O bond length 1.43A° (C-C bond length 1.54 A°) brings an alkyl group closer to the syn-axial hydrogens at C(4) and C(6) to results in increased Vanderwaals repulsion.

19.3.5 Intramolecular H-bonding:

The heteroatom of the ring may formed intramolecular H-bond with one or more OH (or NH_2) group present in the molecule thereby affecting the conformational situation.



5-Hydroxy-1,3-dioxane

Thus 5-hydroxy-1,3-dioxane exists in the preferred conformation in which OH is in axial position in order to form H-bond with the ring O atoms.

19.3.6 Nitrogen lone pair in piperidine:

There is controversy regarding the conformational preference of the lone electron pair and H at N in piperidine. The dipole moment of 4-chlorophenylpiperidine suggests that NH_e conformer is more stable by approximately 2.2 kJ mol^{-1}. NMR spectral measurements at low temperature exhibit two conformers at -172°C for piperidine with $\Delta G°$ of 1.5 kJ mol^{-1} in favour of the N-H_e form. When NH in piperidine is replaced by N-R the conformer with equatorial R and axial lone pair is always preferred.

19.4 Stereoelectronic effects in heterocycles

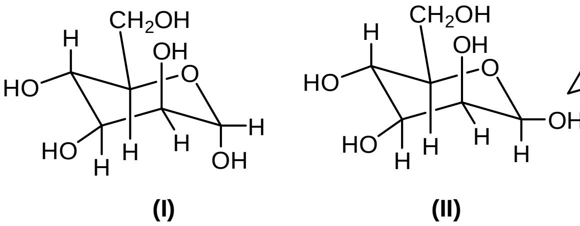
If one or more heteroatoms are present in the ring, they give rise to stereoelectronic effect in many cases which considerably affects the conformational situation in heterocyclic compounds. One of the such effect is anomeric effect which is found in pyranose sugars and their derivatives.

19.4.1 Anomeric effect:

The incorporation of heteroatoms can result in stereoelectronic effects that have a pronounced effect on conformation and ultimately on relactivity. Pyranose sugars substituted with an electron withdrawing group such as halogen or alkoxy at C-1 are often more stable when the substituent has an axial rather than equatorial orientation. This tendency is not limited to carbohydrates but carries over the simpler ring systems such as 2-substituted tetrahydropyrans. This phenomenon is known as Anomeric effect, it involves a substituent at the anomeric position in carbohydrate pyranose rings.

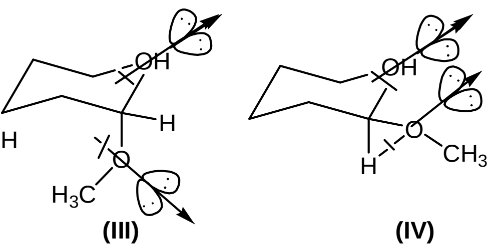
This substituent (X) seems to exert two opposing effects. A steric effect which directs the substituent to the equatorial position and secondly an electronegativity effect which favour the axial position.

The methyl mannosides (II and III, Figure-8) in 1% methanolic HCl undergo equilibration to a ratio of $\alpha : \beta = 64 : 6$ (Figure-8). This is an operation of anomeric effect. In α-D-Mannose (or its mannosides, partial structures III and IV, Figure 8, when $-OCH_3$ is in the equatorial position (IV, Figure-8), the non-bonding electrons on the oxygen of the ring and the nonbonding electrons of the substituent repel to each other. These are farther apart when the substituent is in the axial position.



(I) α -D-Mannose (69%)

(II) β-D-Mannose (31%)



(III) α = 94%

(IV) β = 6%

Methyl mannosides

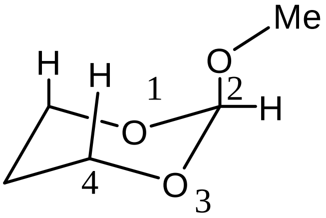
Figure-7

Figure-8

Other two related effects are double anomeric effect and rabbit ear effects.

19.4.2 Double anomeric effects:

1,3-dioxanes which is substituted at C-2 with electronegative groups show a double anomeric effect. The axial methoxy derivative (v) is very much preferred over the equatorial isomer in spite of the fact that the synaxial interaction of the axial OMe with 6H & 4-H are very high due to a puckered chair form of 1,3-dioxane.



(V)

19.4.3 Rabbit ear effect:

In tetrahydro-1,3-oxazine (1,3-diheterocycles) the conformation in which the two lone pairs are syn-1,3-diaxial (VIa) is destablised with respect to other conformer (VIb). This is known as the rabbit ear effect. The reason is that the conformer (VIb)) has stabilized overlapping between the p orbital of N and the antibonding orbital of the endo C-O bond which is antiperiplanar (shown by thick line) so it is endo anomeric effect. This effect is lacking in the other conformer (VIa).

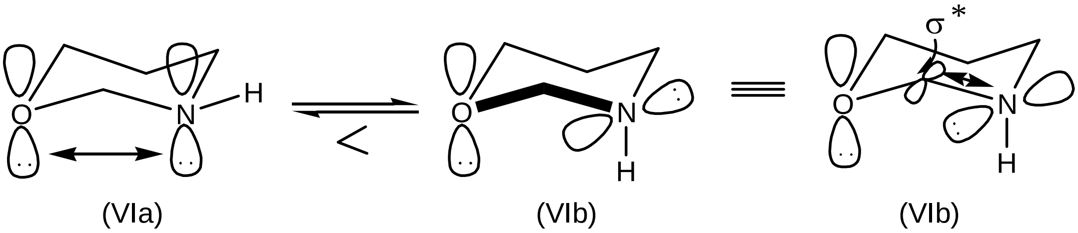
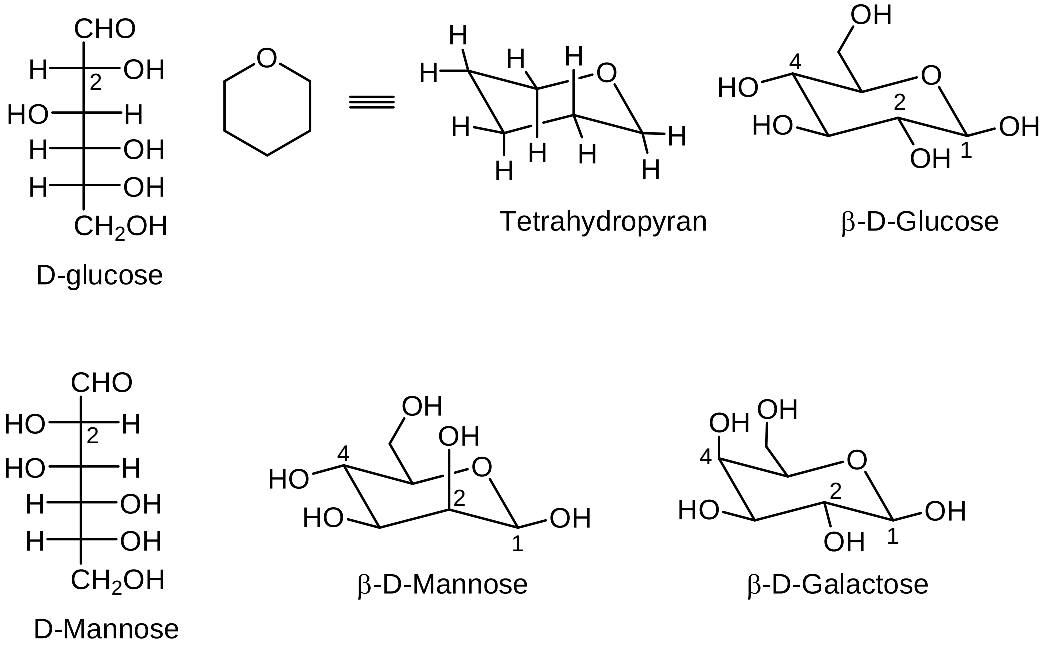


Figure- 8 Rabbit ear effect

19.5 Conformations of common sugars

The conversion of Haworth formula of α-D-glucose to chair formula is shown below. The following points may be consider regarding conformations of some sugars.



D-glucose Tetrahydropyran β-D-Glucose

D-Mannose β-D-Mannose β-D-Galactose

Figure-9

- The six membered ring which includes an oxygen atom is related to the heterocyclic ring tetrahydropyran (Fig 9). A saccharide in its six membered form is called pyranose.
- Hexoses like D-glucose shows that it has four stereoconters. There are sixteen stereoisomers – the total number of naturally occurring stereoisomers being eight.
- Only the three of these namely D-glucose, D-mannose and D-galactose are the most widely occurring.
- Introducing an oxygen atom into a six membered ring has marked effect on the conformation depending on the position and nature of the substituent. As we have discussed the C-O bonds in tetrahydropyran are shorter than the C-C bonds in cyclohexane, there can be more severe 1,3-diaxial interactions if a group is in the position can predominate.
- The 1,3-diaxial interactions are less severe if the substituents is removed two atoms away from the oxygen atom. In these compounds a conformation with the larger group in the axial position can predominant.
- Moreover, an oxygen atom in the ring provides an opportunity for hydrogen bonding when the substitutent is an OH group and an axial OH group can also be stabilized.

- At first draw β-D-glucose in which all the hydroxyl group are equatorial. To draw other common sugars, notice as to how these differ from D-glucose and make appropriate changes.

19.6. The shape of rings other than six membered ring

19.6.1 Conformation of Bicyclic System:

A molecule with two rings that share two or more carbon atoms is called a bicyclic system. The rings of such a system are called fused and the carbons at which the two rings are fused are called 'bridgehead carbons'. Decalin is an important bicyclic alkane formed by the fusion of two cyclohexane rings at 1,2-positions. The structure of decalin and the mode of numbering of its carbons have been shown below. The IUPAC name of decalin is bicycle[4.4.0]decane.

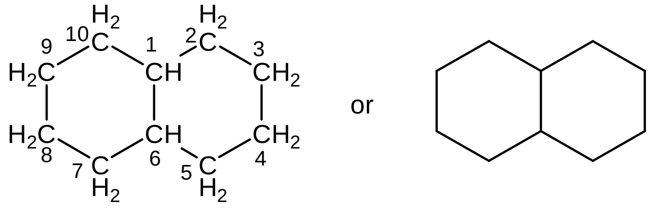


Fig. 10: Structure of decalin

(1 and 6 carbons are bridgehead carbons)

19.6.1.1 Cis-trans isomerism of decalin

As we have described the decalin molecule is formed by the fusion of two cyclohexane rings. As we know that the chair form of cyclohexane is most stable. Hence the decalin is, expected to be formed by fusion of the chair forms of two cyclohexane rings. If we make the model of the chair form of cyclohexane, it can observed that two chairs can be connected in two manners. As decline contains ten carbons only, two carbons will be removed from a chair model of cyclohexane ring before connecting it to the model of the other cyclohexane ring. Now, we find that these two systems can be connected in two manners. If two equatorial bonds of cyclohexane ring are used to connect it to the four carbon system, a decalin molecule results in which the two hydrogens on bridgehead carbons are on the opposite sides. It is *trans*-decalin (Fig.11).

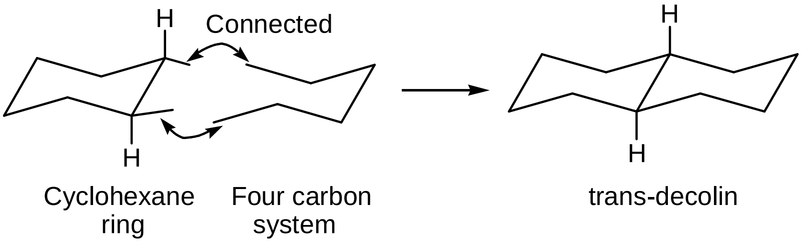


Figure 11: *trans*-Decalin

If one equatorial and one axial bonds of cyclohexane ring are used for connecting it to the four carbon system, a decalin molecule results which has two hydrogens on the same side of the bridgehead carbons. It is *cis* decalin.

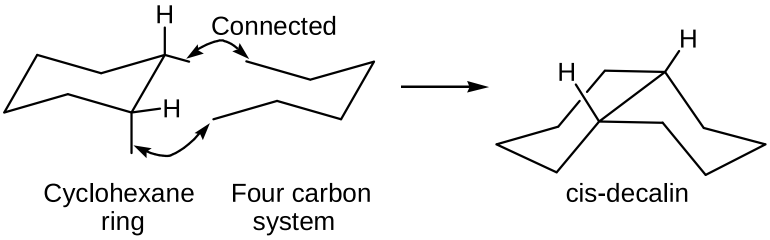


Figure-12: *cis*-Decalin

The *cis*-and *trans*-decalins can be separated. *cis*-Decalin boils at 195° while *trans*-decalin boils at 185.5°. With the help of models, it can be shown that *cis*- and *trans*-decalins cannot be interconverted by rotation about carbon-carbon bonds and therefore they are configurational diastereomers. The *cis*- and *trans*-decalins can be represented in the following manner (Fig 13):

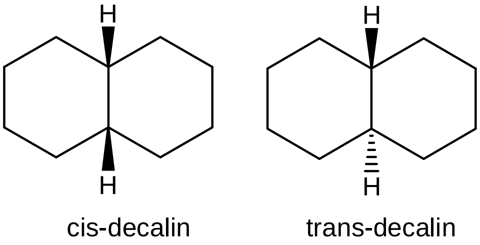


Figure-13

19.6.1.2 Relative stabilities of *cis*- and *trans*- decalins

The results indicate that *trans*-decalin is more stable than its *cis*-isomer by about 2 Kcal/mole. Why?

The relative stabilities of these two isomers can be easily explained, if their structures are correlated with the structures of *cis*- and *trans*- 1,2-dimethylcyclohexanes. We can see that *trans*-1,2-dimethylcyclohexane (in which both methyl groups are present in equatorial positions) is more stable than *cis*-1,2-dimethylcyclohexane (in which one methyl group is present in axial position whereas the other occupies the equatorial position) by about 1.87 Kcal/mole.

The *trans*- decalin may be considered as diequatorial 1.2-disubstituted cyclohexane in which the 1,2-substituents are the two ends of a four carbon-bridge , -$CH_2CH_2.CH_2CH_2$-. In this case, the two cyclohexane rings are present in uncrowded positions, as expected in diequatorial positions. Like *trans*-1,2-dimethylcyclohexane, *trans*-decalin will be expected to be more stable.

The *cis*- decalin may be considered as *eq, ax*-1,2-disubstituted cyclohexane in which the 1,2-substituents are the two ends of a four carbon-bridge, –$CH_2CH_2.CH_2CH_2$-. In this case, there will be appreciable non-bonded interactions within the concave area (Figure-14) . Thus, *cis*-decalin will be less stable than *trans*-decalin.

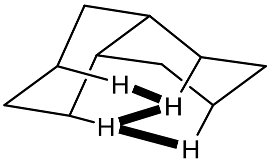


Figure-14 : Non bonded interactions in *cis*-decalin

It is interesting to know that although there is a difference of only 2 Kcal/mole between the stabilities of *trans*- and *cis*-decalins, the conversion of one into the other takes place under only vigorous conditions. As the conversion of *cis*-decalin into *trans*-decalin and vice-versa requires the cleavage of one carbon-carbon bond and one carbon bond. This can be seen with the help of the models of *cis*- and *trans*- decalins. Thus, although there is only a small difference between the stabilities of *cis*- and *trans*- decalins, their interconversion is very difficult.

If we introduce an heteratom in the decalin ring then barrier to interconversion of *cis* and *trans* decalin can be decreased in some cases. For e.g. in azadecalin. (Fig. 15) If a nitrogen atom occupies a bridgehead position in cis and trans form of decalin cannot be isolated. The rapid interconversion of these form is due to the easy inversion of configuration at nitrogen which eliminated the need for a trans-diaxial tranisition state.

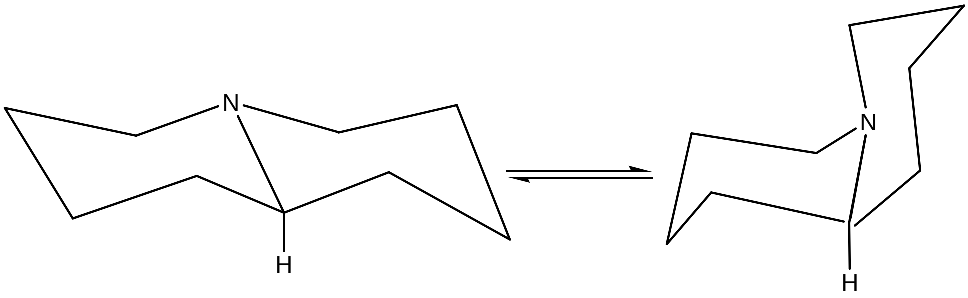
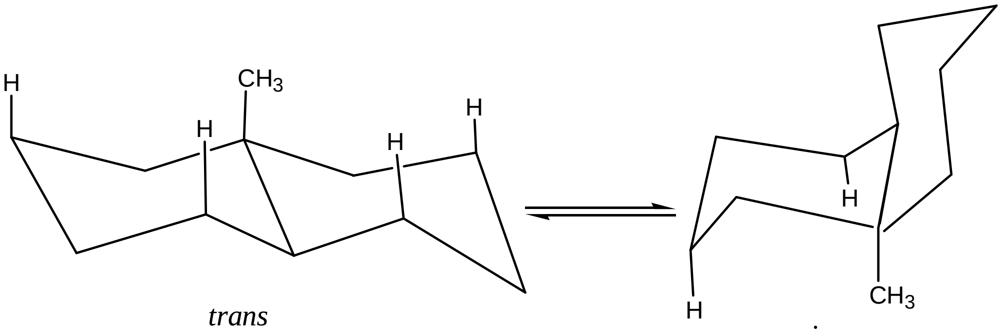


Figure 15: Azadecalin

When an angular methyl group is introduced, the *cis* form becomes slightly more stable than the *trans* form (Figure 16). The methyl group is sterically compressed by four axial hydrogen atoms and by only two (C_2 and C_4) in the case of *cis*-isomer, so the introduction of methyl groups reduces the difference in energy between the decalin.



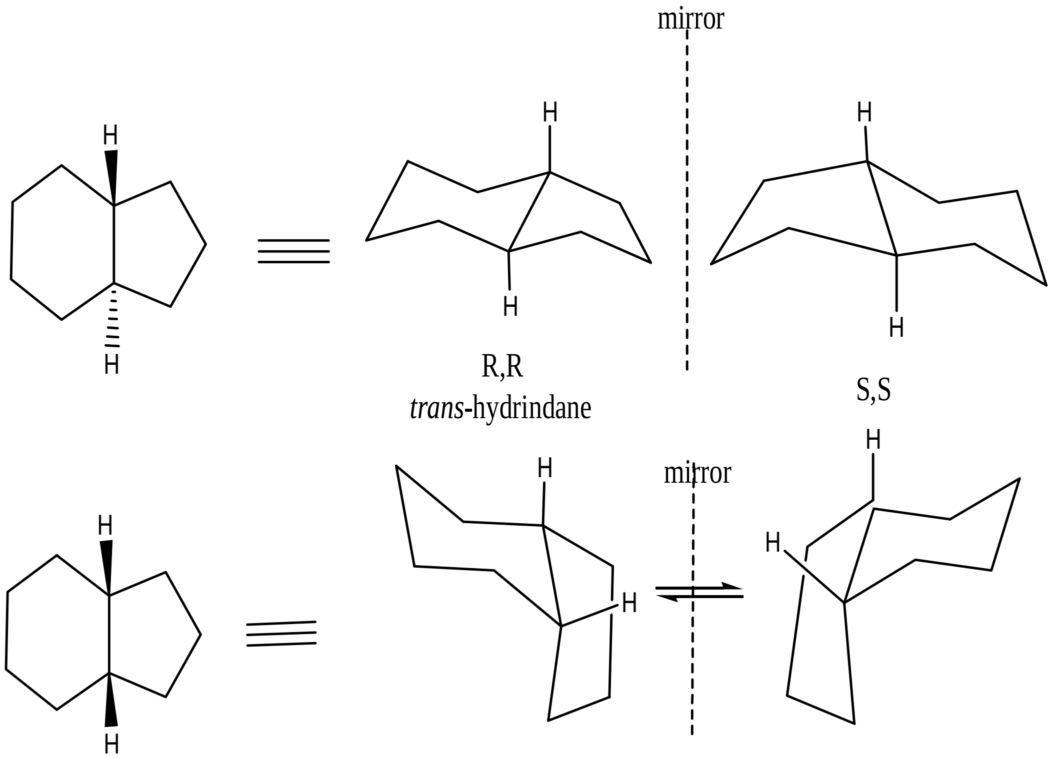
trans

cis

Figure 16: 9-Methyldecalin

19.6.2 Bicyclic system: The Hydrindanes (Bicyclo[4.3.0]Nonane):

In this system different size of rings are fused. The dissimilarity of the two rings makes the ring-fused carbon atoms stereocenters. It clearly shows the presence of two stereocenters and predicts the trans isomer as a (±) pair i.e. two stable trans isomers whereas cis-isomer as a meso compound.



cis-hydrindane

Figure 17

Trans hydrindanes are conformationally rigid molecule, whereas cis-hydrindane is flexible and exists as a (dl)-pair of conformers. The free energy of activation of this conformational inversion is considerably smaller than the inversion barrier of *cis*-decalin. This is due to the more planar structure of the five membered ring and as a result there is less strain in the fused system.

19.7 Summary

- Conformation of a molecule are defined as the various arrangement of its atoms in space which differ only in rotation around single bond or bonds (i.e. in dihedral angles) and are easily interconvertible.
- When one or more sp^2 carbon atoms are introduced in a cyclohexane ring, a few changes in the conformations take place. The molecules become flatter near the trigonal atoms increasing the angle strain and torsional strain. These molecules such as cyclohexanone and cyclohexane are, therefore, thermodynamically and kinetically less stable with respect to cyclohexane.

- The changes which are most obvious on introduction of a heteroatom into six membered rings have to do with bond angles and bond length. Both the C-O and C-N bond length are shorter than the C-C bond length, while the C-S bond length is longer. The normal valence angle are somewhat smaller than tetrahedral at oxygen and nitrogen and significantly so for sulphur for which the C-S-C angle value is 100°. The six membered heterocycles containing oxygen (tetrahydropyran), nitrogen (piperidine) and sulfur (thiane), all resemble the chair conformation of cyclohexane but are modified so as to accommodate the bond lengths and bond angles characteristic of the heteroatom. The rings are all somewhat more puckered than cyclohexane.
- *trans*-Decalin is more stable than its *cis*-isomer by about 2 Kcal/mole.

19.8 Review Questions

1 Comment on the conformational effects in six memebered rings containing unsaturation.

2 Write a short note on conformational effects in six membered heterocyclic rings.

3 Explain why 5-hydroxy-1,3-dioxane exists in the conformation in which OH is in axial position?

4 Show the preferred conformation of cis-2-methyl-5-tert-butyl-1,3-dioxane.

5 Explain why trans decalin is more stable than *cis* decalin by 2.7 Kcal/mole?

6 Comment on the conformation of decalin.

19.9 Reference and Suggested Readings

- Stereochemistry of Organic Compounds, D. Nasipuri, New Age International Publishers.
- Organic Chemistry, J. Clayden, N. Greeves, S. Warren, Oxford University, Second Edition.
- Advanced Organic Chemistry Part-B, F. A. Carey and R. J. Sundberg, 5th Ed. Springer.
- Stereochemistry conformation and Mechanism, P.S. Kalsi, New Age

International Publishers.

- Advanced Organic Chemistry, Jagdamba Singh and L.D.S. Yadav, Pragati Prakashan.

Unit -20

Conformation and Reactivity

Structure of unit:

20.0 Introduction

The different spatial arrangements of atoms in a molecule which are readily interconvertible by rotation about single bonds are called conformations.

Conformers / rotamers / conformational isomers are readily interconvertible and nonseparable.

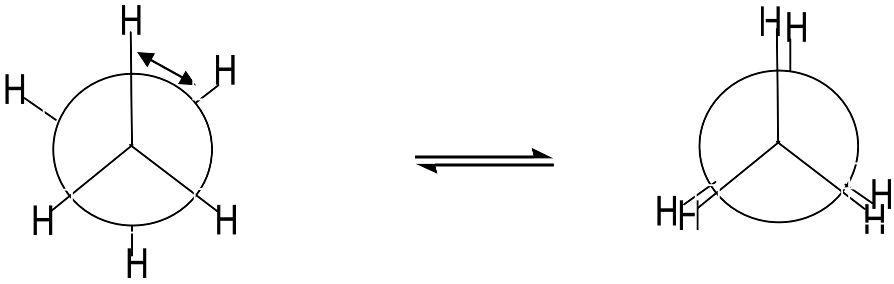
Conformation and configuration are the terms related to energy barrier for interconversion of different spatial arrangements of atoms in a molecule.

In case of conformers energy barrier for conversion of different spatial arrangements is in between >0.6 and < 16 Kcal/mole but in configuration it is > 16 Kcal / mole.

20.1 Conformations of acyclic systems

20.1.1 Conformations of ethane

When an ethane molecule rotates about its carbon-carbon single bond, then two extreme conformations are found i.e staggered and eclipsed conformation. An infinite number of conformations between these two extreme conformations is also possible. The Newmann projections for staggered and eclipsed conformations of ethane are given below.



Staggered

Eclipsed

Fig. 1 : Conformations of ethane

Staggered conformation: A conformation with a 60° dihedral / torsional angle (angle between the atoms attached to the front and the rear carbon atoms) is known as staggered conformation. It is the most stable conformation because the carbon-hydrogen bonds are as far away from each other as possible. In staggered conformation the distance between hydrogen nuclei is 2.55 Å.

Eclipsed conformation : A conformation with a 0° torsional angle is known as eclipsed conformation. It is the least stable conformation because the carbon-hydrogen bonds are closest. In eclipsed conformation the distance between hydrogen nuclei is 2.29 Å. The rotational energy barrier in ethane is 2.9 kcal / mole.

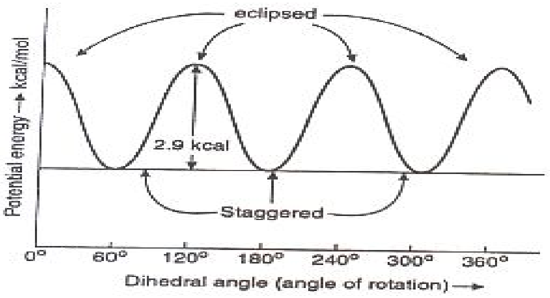


Fig.2: Rotational energy barrier of ethane in terms of change in potential energy and dihedral angle

20.1.2 Conformations of propane

Like ethane , propane also has the following two extreme conformations- staggered and eclipsed.

20.1.3 Conformations of n-butane

In case of n-butane, for conformational analysis butane may be treated as derivative of ethane where one hydrogen on each carbon is replaced by a methyl group. Different conformations of butane can be obtained by rotation about its middle carbon-carbon bond as shown below.

Butane possess three staggered conformers (I, III and V) out of these three conformers, conformer III(known as anti conformer) is more stable in which two methyl groups are far apart. Conformers (I and V) are called gauche conformers in which the largest substituents are adjacent.

Anti and gauche form have different energies due to steric strain or steric hindrance (strain on a molecule due to repulsion between electrons of large atoms or groups which lie too close to each other.

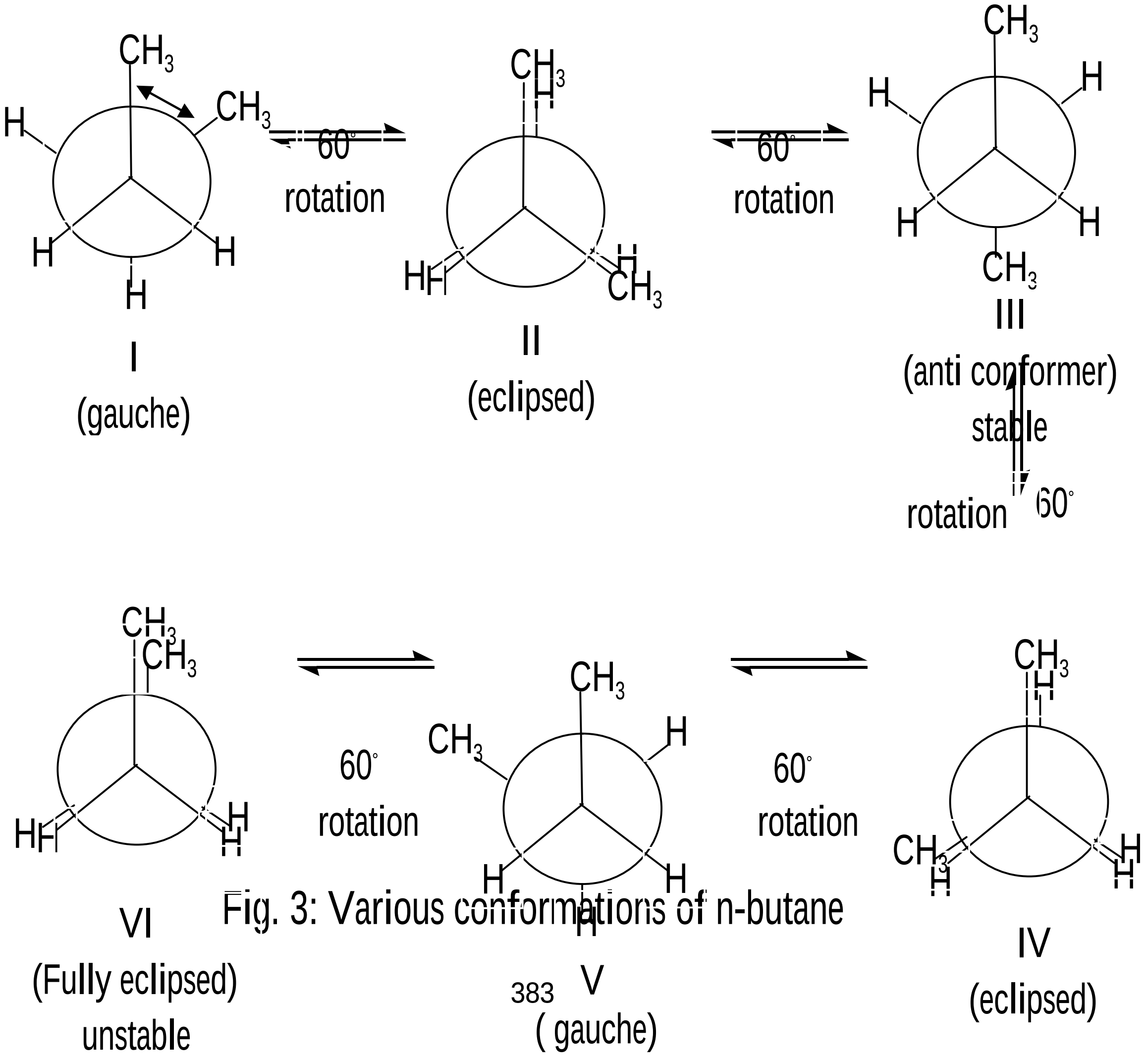


Fig. 3: Various conformations of n-butane

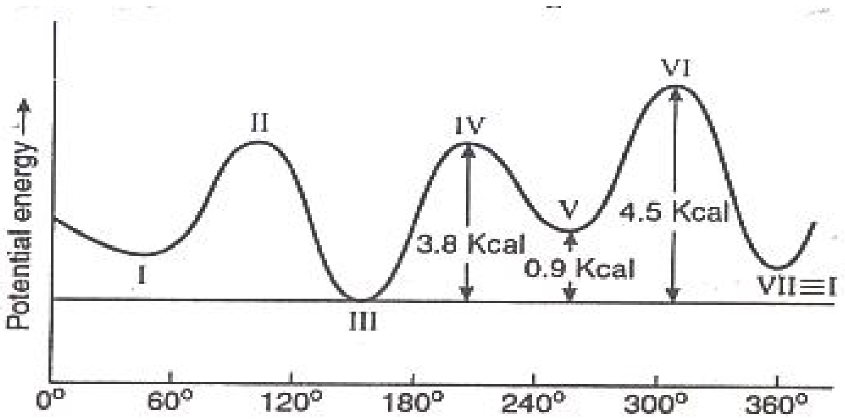


Fig.4: Rotational energy barrier of n-butane in terms of change in potential energy and dihedral angle

Butane possess three eclipsed conformers (II, IV and VI) out of these three conformers, conformer VI (fully eclipsed conformer) is least stable in which the two methyl groups are closest to each other. All these eclipsed conformers have both torsional and steric strain . Conformers (II and IV) are called eclipsed conformers.

Relative stabilities of six conformers of n-butane in decreasing order is as follows:

Anti (III) > Gauche (I and V) > Eclipsed (II and IV) > Fully eclipsed(VI)

20.2 Conformation of cycloalkanes

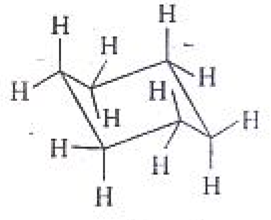
Compounds having five and six membered rings are more stable than three and four membered rings. Cyclic compounds twist and bend in order to achieve a final structure which minimizes the following three kinds of strain that can destabilize a cyclic compound:

1. Angle strain (Baeyer strain) - This results when the bond angle is different from the desired tetrahedral bond angle of 109.5°.
2. Torsional strain (Pitzer strain) - This is caused by repulsion of the bonding electrons of one substituent with bonding electrons of another substituent on the adjacent atom.
3. Steric strain (Vander Waals strain) - This is caused by atoms or groups approaching each other too closely.

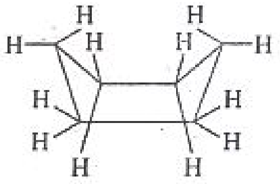
According to Sachse, cyclohexane and larger rings are not planar. These rings possess puckered structure in which all the angles are tetrahedral so they are strainless. Cyclohexane exists in two forms i.e chair and boat conformations .

Chair is the staggered form and boat is eclipsed. Both these forms are free from angle strain. Boat form possess steric repulsion between flagpole hydrogens pointing towards each other at $C_1$and C_4 (1.83Å apart).

Chair form is more stable than the boat form as boat conformation possess both torsional and steric strains. Energy barrier for interconvetrsion of the chair and boat conformations is 10.8 kcal/ mole.



Chair conformation
of cyclohexane



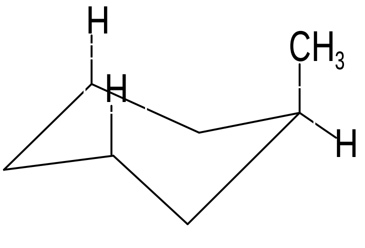
Boat conformation
of cyclohexane

Chair form is rigid but boat form is flexible and readily convert into twist boat (1.5 kcal/mole lower energy than boat form). In chair conformation of cyclohexane there are two kinds of positions occupied by the hydrogen atom. Six hydrogens are axial which are perpendicular to the average plane of the ring and the other six are equatorial hydrogens present in the average plane of the ring.

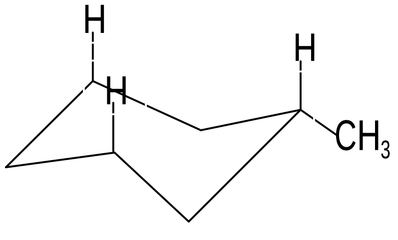
Conformations of monosubstituted cyclohexanes

In case if one hydrogen of cyclohexane is replaced by a larger atom / group,crowding occurs. The most severe crowding occurs by the three axial bonds of the same side resulting 1,3 diaxial interaction which lead steric strain in the molecule.

Monosubstituted cyclohexane possess chair conformation in which the substituent occupy equatorial position as e-Me conformation is more stable than a-Me by energy barrier 1.8 kcal/ mole.



axial –methyl
(a-Me)

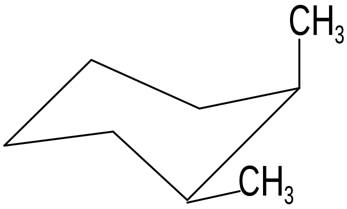


equatorial –methyl
(e-Me)
Preferred conformation

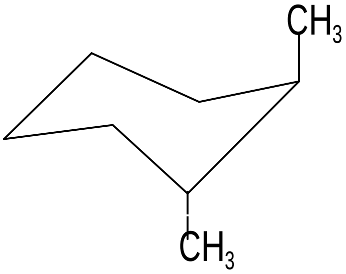
Conformations of disubstituted cyclohexanes

In case if two substitutents are present on a cyclohexane ring either cis or trans to each other or 1,2-, 1,3- or 1,4- with respect to each other. In disubstituted cyclohexane the chair form is the most preferred conformation which contains both substitutents at equatorial positions.

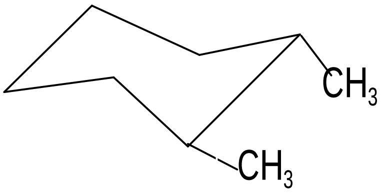
In 1,2 dimethyl cyclohexane two forms are possible i.e cis and trans. Cis form (ae or ea) contain one substituent axial and another is equatorial . Trans form (ee or aa) contain either both substituents axial or equatorial. In 1,2 dimethyl cyclohexane ee-1,2 dimethyl cyclohexane is more stable than ae or ea 1,2 dimethyl cyclohexane as there is no 1,3 diaxial interaction causing strain. Stability order ee > ae > aa



Cis-1,2-dimethylcyclohexane (a.e or e.a)



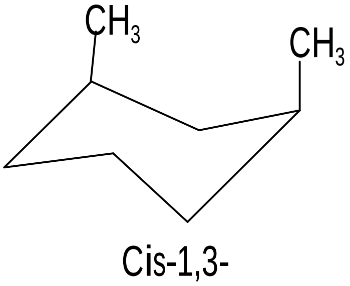
Trans -1,2-dimethylcyclohexane (a.a) less stable



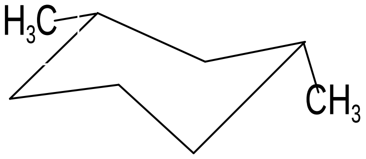
Trans -1,2-dimethylcyclohexane (e.e) more stable

1,2 dimethyl cyclohexane exists as a pair of configurational distereomers –cis and trans isomers. Cis and trans isomers exists with a pair of conformational enantiomers and configurational enantiomers, respectively. These cis and trans forms also exists as two conformational diastereomers.

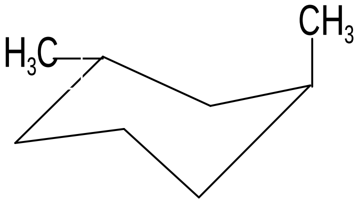
In 1,3 dimethylcyclohexane the maximum number of equatorial substitutents give the preferred conformation in which dipole interaction like forces are absent. 1,3 dimethylcyclohexane possess two cis and one trans chair conformations. Stability order - ee > ae > aa



Cis-1,3-dimethylcyclohexane (a.a) less stable

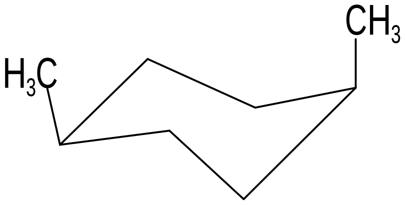


cis -1,3-dimethylcyclohexane (e.e) more stable

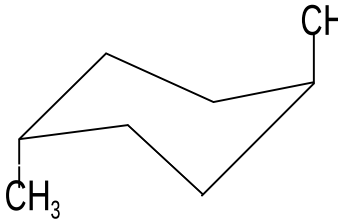


Trans -1,3-dimethylcyclohexane (a.e or e.a)

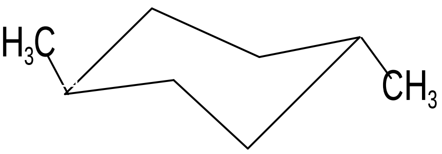
1,4 dimethylcyclohexane possess one cis and two trans chair conformations. Stability order - ee > ae > aa. 1,4 dimethylcyclohexane not contain any chiral centre. It exists as cis-trans diastereomers. Cis and trans both forms contain plane of symmetry.



Cis-1,4-dimethylcyclohexane (a.e or e.a)



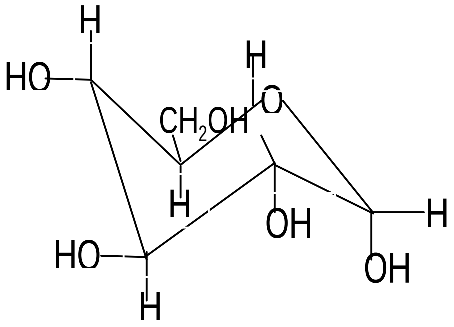
Trans -1,4-dimethylcyclohexane (a.a) less stable



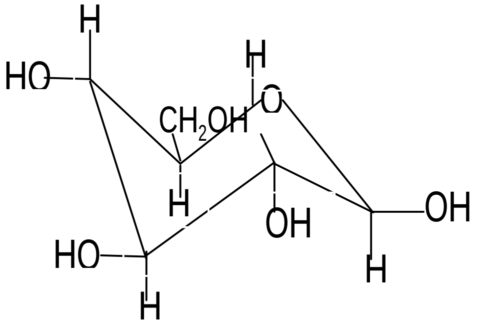
Trans -1,4-dimethylcyclohexane (e.e) more stable

20.3 Conformations of sugars

It has been found that, in α-D (+) glucopyranose the glycosidic hydroxyl is axial and in β- anomer it is equatorial. Conformation which possess greater number of larger groups in equatorial position is more stable. Thus, β- anomer is more stable than the α- anomer and it predominates in the equatorial mixture.



α- D (+) glucopyranose less stable



β - D (+) glucopyranose more stable

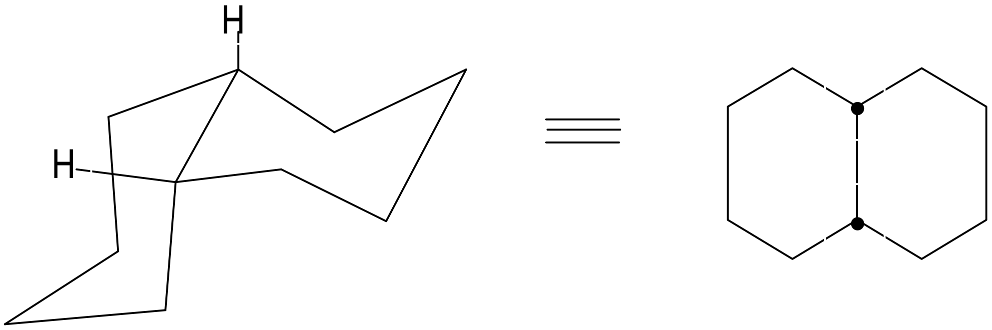
20.4 Conformations of fused rings

Decalin is a well known example of fused ring system. It exist in two diastereoisomeric forms cis and trans which depends on the way of fusion of two cyclohexane rings.

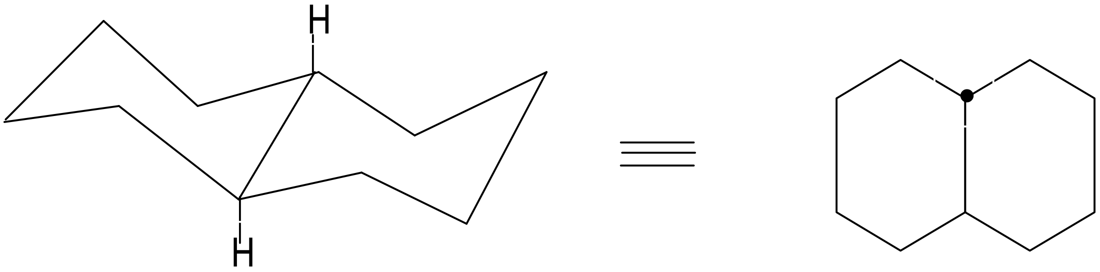
Cis- form (ea or ae) - In cis form two cyclohexane rings are fused in such a manner that the equatorial bond of one ring is fused with the axial bond of the other.

Trans- form (ee)- In trans form two cyclohexane rings are fused in such a manner that the equatorial bond of one ring is fused with the equatorial bond of the other.Trans form is more stable than the cis by 2.7 kcal/mole.

Cis form is flexible so undergo conformational flipping like chair conformation of cyclohexane. Trans form is rigid so it does not undergo conformational flipping .



Cis decalin
less stable



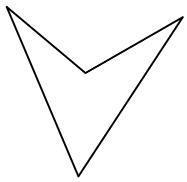
Trans decalin
More stable

Cis decalin is chiral and its both conformations are nonsuperimposable mirror images of each other (nonresolvable enantiomeric pairs). Trans decalin is optically inactive due to presence of centre of symmetry.

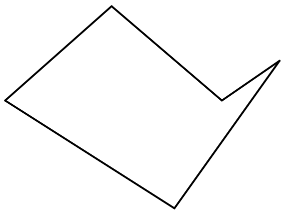
In substituted decalin substituents occupy fusion points of the two rings . In cis decalin substitutent is axial with one ring and equatorial with respect to other. In trans decalin substitutents are axial with respect to both the rings.

20.5 Conformations of other rings

Different rings possess different conformations to minimize strain of substitutents. Like three membered ring is planar but cyclobutane exists with an angle of about 35° between the planes. Cyclopentane exists in two puckered conformations-envelope and half chair . Among these two conformations envelope form predominates.

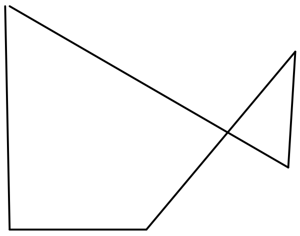


cyclobutane



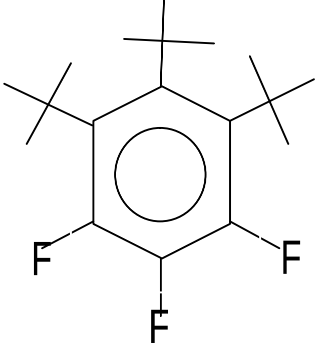
envelope conformation

more stable

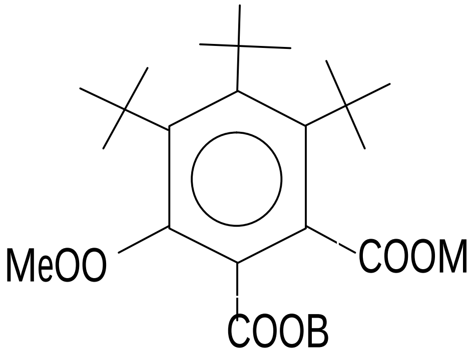


Half chair conformation

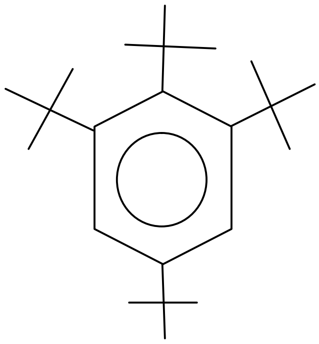
Larger rings always found in puckered structure but higher rings like cycloheptane, cyclooctane etc possess small instabilities due to torsional strain and vanderwaal repulsion. In some sterically hindered compounds ring not becomes planar due to high degree of strain e.g- 1,2,4 –tri-t-butylbenzene compounds (as shown below in I to III). In these molecules large substitutent groups cannot fit into the available space and are not able to maintain normal bond angles.



I



I



III

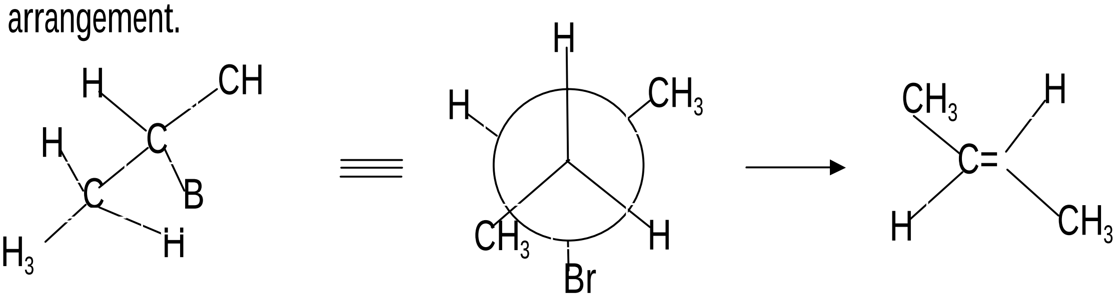
20.6 Effect of conformations on reactivity

Due to stereoelectronic and steric factors chemical reactivity is affected by conformations. There are some examples given below which explain the effect of conformation on reactivity.

20.6.1 Acyclic compounds

E2 reactions are stereospecific and most of these reactions are anti elimination. In anti elimination the five atoms involved including the base must be in same plane and the eliminating groups must be trans to each other, this conformation is called anti-periplanar.

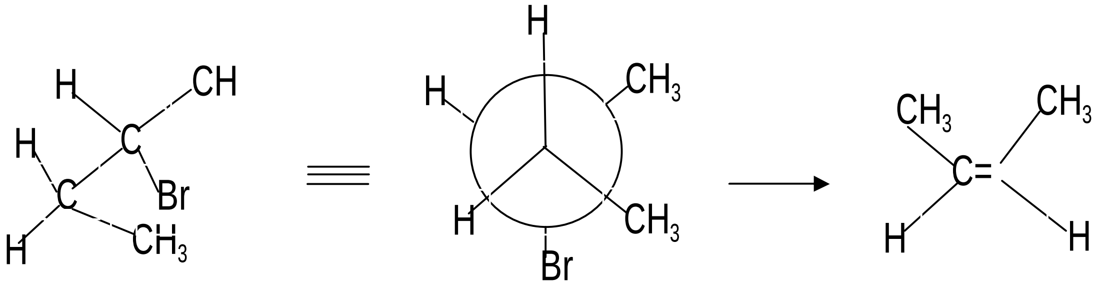
e.g–2-bromobutane can give either cis or trans-2-butene. The stereoelectronic requirement of the reaction must involve only those conformations of 2-bromobutane in which the eliminating groups attain anti-periplanar arrangement.



2-

Favoured

Trans-2-butene



2-

Less favoured

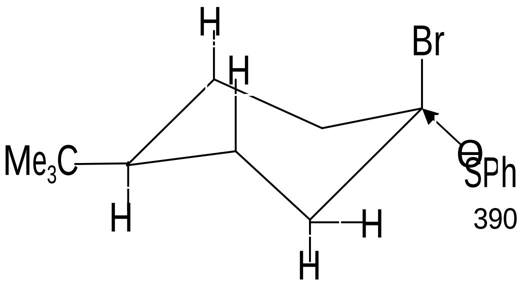
Cis-2-

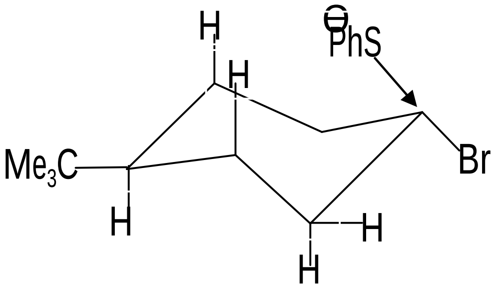
In pyrolytic eliminations , the two eliminating groups lie cis to each other. Like pyrolysis of xanthates, acetates and amine oxide are syn elimination.

20.6.2 Cyclic compounds

The reactivity of axial and equatorial groups of cyclohexane which is mostly found in natural products depends on conformation. Mostly equatorial substitutents shows high reactivity than axial one .

1. Substitution reaction- SN2 and SN1 reactions occur more frequently with axial substitutents than the equatorial one. e.g -4-t-butylcyclohexyl bromide

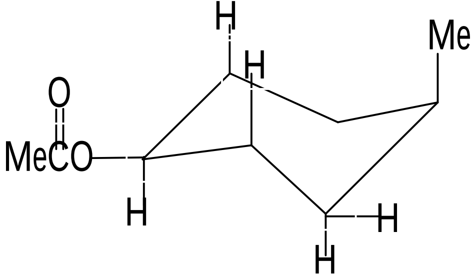




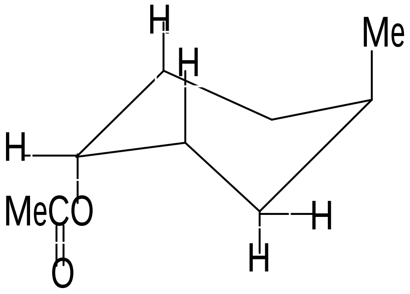
Axial Br show 60 times

equatorial Br show slower

2. Esterification and hydrolysis- Equatorial isomer exhibits esterification and hydrolysis reactions more frequently than the axial one as axial isomer possess 1,3 diaxial interaction. e.g- cholestanyl acetate possess acetate group on equatorial position undergo saponification more readily than the axial one.

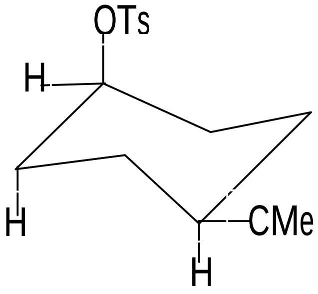


Equatorial ester gives saponification reaction more readily

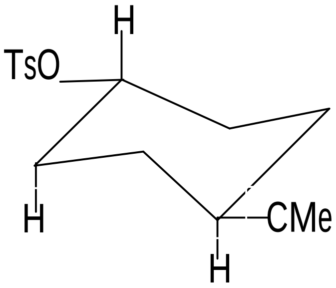


Axial ester gives saponification reaction

3. Elimination reactions- Eliminating groups should be in antiperiplanar arrangement this is the stereoelectronic requirement for E2 reaction. e.g- 4-t-butylcyclohexyl tosylate

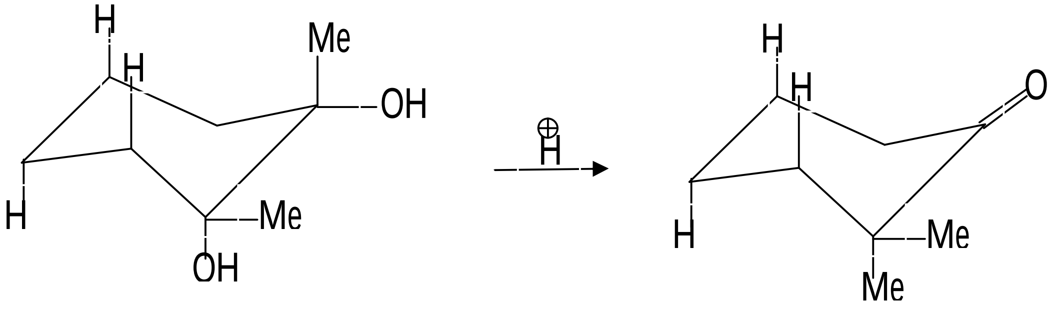


cis isomer is 100 times faster



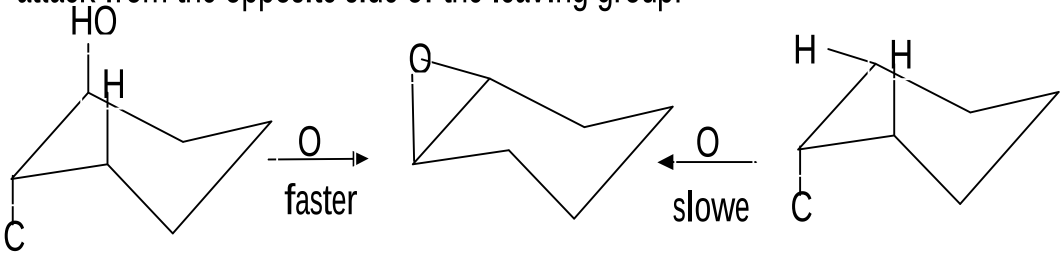
trans isomer give slow reaction

4. Molecular rearrangements- Conformation governs the product formation in various molecular rearrangement reactions. e.g- Pinacol-pinacolone rearrangement of 1,2-dimethyl-1,2-cyclohexanediol, its cis isomer gives 2,2-dimethylcyclohexanone and trans gives cyclopentane derivative.



cis isomer

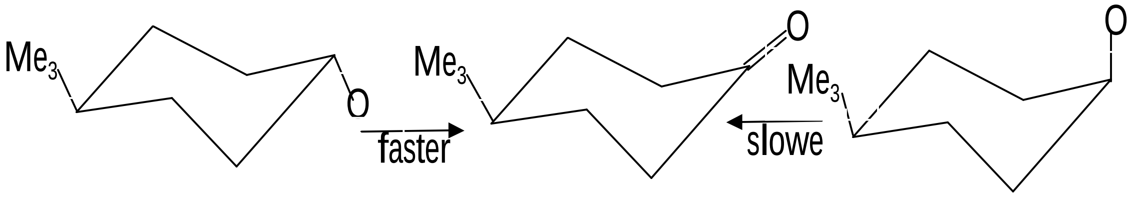
5. Neighbouring group participation- Neighbouring group participation involve the presence of neighbouring group which must be in a position to attack from the opposite side of the leaving group.



trans isomer

cis isomer

6. Oxidation –Substituents on axial position removed more frequently during oxidation to remove 1,3 diaxial interaction, than the equatorial one.



Trans

Cis

20.7 Curtin-Hammett Principle

According to the Curtin-hammett principle the relative amounts of products formed from two pertinent conformers are completely independent of the relative populations of the conformers and depend only on the difference in the free energy of the transition states.Rate of reaction is slower than the rate of conformational interconversion.

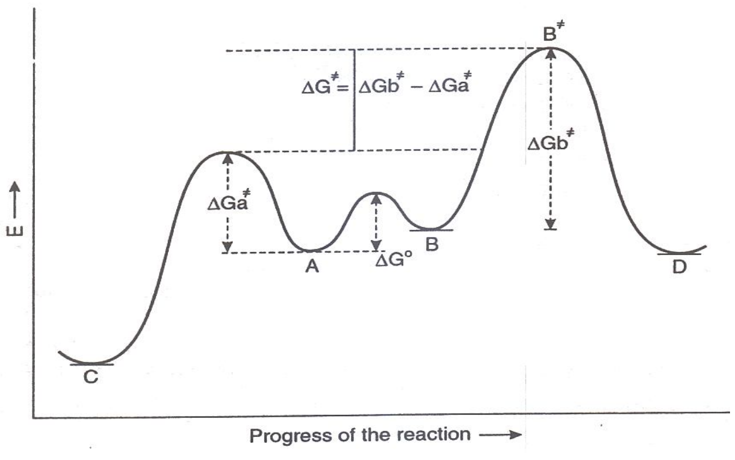


Fig. 5 : Energy diagram for different C and D products.

Suppose A and B are conformational isomers and both are in rapid equilibrium.

$$A \rightleftharpoons B$$

In chemical reaction may be elimination , addition or substitution A gives product C and B gives product D . Product C and D may be different substances or they may be conformers of the same substances.

$$C \xleftarrow{K_c} A \underset{K_A}{\overset{K_B}{\rightleftharpoons}} B \xrightarrow{K_D} D$$

In most cases, the energy of activation for a chemical reaction will be greater than that for a conformational equilibrium. If this is the case , $\Delta G_a^{\#}$ and $\Delta G_b^{\#}$ $>>\Delta G^{\circ}$. The conformers of the reactant are in equilibrium and are interconverted at a rate much faster than that at which the competing reactions occur ($K_AK_B >> K_CK_D$).

In this case equilibrium is maintained,
$$K = \frac{[B]}{[A]}$$

$$\frac{dC}{dt} = K_C[A]$$

$$\frac{dD}{dt} = K_D[B]$$

In case the reaction is first order or pseudo first order then product ratio is-

$$\frac{dD}{dC} = K_D[B] / K_C[A]$$

$$= \frac{K_D[B]}{K_C[A]}$$

$$= \frac{K_D}{K_C} K$$

$$K = \frac{[B]}{[A]} = e^{-\Delta G^{\circ}/RT}$$

$$K_C = e^{-\Delta Ga^{\#} / RT}$$

$$K_D = e^{-\Delta Gb^{\#} / RT}$$

$$\text{Product ratio} = e^{-\Delta G^{\#} / RT}$$

20.8 Summary

- The different spatial arrangements of atoms in a molecule which are readily interconvertible by rotation around single bond is called conformations.
- Conformers / rotamers / conformational isomers are interconvertible and non separable.
- Energy difference between various conformers is in between > 0.6 and < 16 Kcal/mole.
- Two extreme conformations of ethane and propane are staggered and eclipsed conformations. Energy barrier in ethane is 2.9 Kcal/mole.
- Butane possess three staggered (one anti and two gauche) and three eclipsed (one fully eclipsed and two partially eclipsed) conformations.
- Staggered conformations possess steric strain whereas eclipsed conformers possess torsional and steric strain.
- Relative stability of six conformers of n-butane are- Anti > Gauche > Eclipsed > Fully eclipsed.
- Cyclic compounds possess three kinds of strains- angle strain (Baeyer strain), torsional strain (Pitzer strain) and steric strain (Vander Waals strain).
- Cyclohexane occurs in two forms- chair and boat conformations. Energy difference between these two forms is 10.8 Kcal/mole.
- Chair form is more stable than the boat form as boat conformation possess torsional and steric strains.
- Monosubstituted cyclohexane possess chair conformation in which the substituent occupy equatorial position as e-Me conformation is more stable than a-Me by energy barrier 1.8 kcal/ mole.
- In 1,2 dimethyl cyclohexane two forms are possible i.e cis and trans. Stability order is ee > ae > aa.

- 1,3 dimethylcyclohexane possess two cis and one trans chair conformations. Stability order - ee > ae > aa.
- 1,4 dimethylcyclohexane possess one cis and two trans chair conformations. Stability order - ee > ae > aa.
- In α-D (+) glucopyranose the glycosidic hydroxyl is axial and in β-anomer it is equatorial so β-anomer is more stable than the α-anomer .
- Decalin is exist in two diastereoisomeric forms cis and trans which depends on the way of fusion of two cyclohexane rings. Trans form is more stable than cis form by energy 2.7 kcal/mole.
- Larger rings always found in puckered structure but higher rings like cycloheptane, cyclooctane etc possess small instabilities due to torsinal strain and vanderwaal repulsion.
- Conformation effects the chemical reactivity due to stereoelectronic and steric factors. Like in acyclic compounds rate of elimination reactions and in cyclic compounds rate of substitution (SN1 and SN2) , esterification, elimination, neighbouring group participation and oxidation reactions depends on the conformation of the compound.
- In molecular rearrangements, the type of product formation depends on the conformation of the compound.
- Curtin-hammett principle give the relative amounts of products formed from two pertinent conformers are completely independent of the relative populations of the conformers and depends only on the difference in the free energy of transition states.

20.9 Review Questions

1. What do you understand by the terms conformation and configuration?
2. Discuss conformations of cis- and trans –decalins.
3. Write short note on the following-
    1. Conformations of sugar
    2. Conformations of various rings

4. Discuss the effect of conformation on chemical reactivity by giving some examples of cyclohexane derivatives.
5. Discuss the conformations of cis-trans Decalin.
6. With suitable examples, discuss the effect of angle strain, torsional strain and intramolecular hydrogen bonding on the stability of conformations.
7. Discuss the effect of conformation on reactivity of various compounds by given an examples of acyclic and cyclic compounds.
8. Why chair conformation of cyclohexane is rigid ? Is chair conformation can be converted into boat form?
9. How many strains are present in cyclic compounds ?
10. Discuss the conformations of ethane and butane.
11. Explain steric strain by giving an example of 1,2,3 tributyl compounds.
12. How conformations effect the product formation in molecular rearrangement reactions ?
13. Discuss the various conformations of disubstituted cyclohexane.

14 Explain Curtin-Hammett principle. Also give derivation for Curtin-Hammett principle.

15 Which conformation of cyclohexane – boat or twist boat is more stable and why?

16 How substitution in case of Decalin affect the stability of its conformations?

20.10 References and Suggested Readings

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