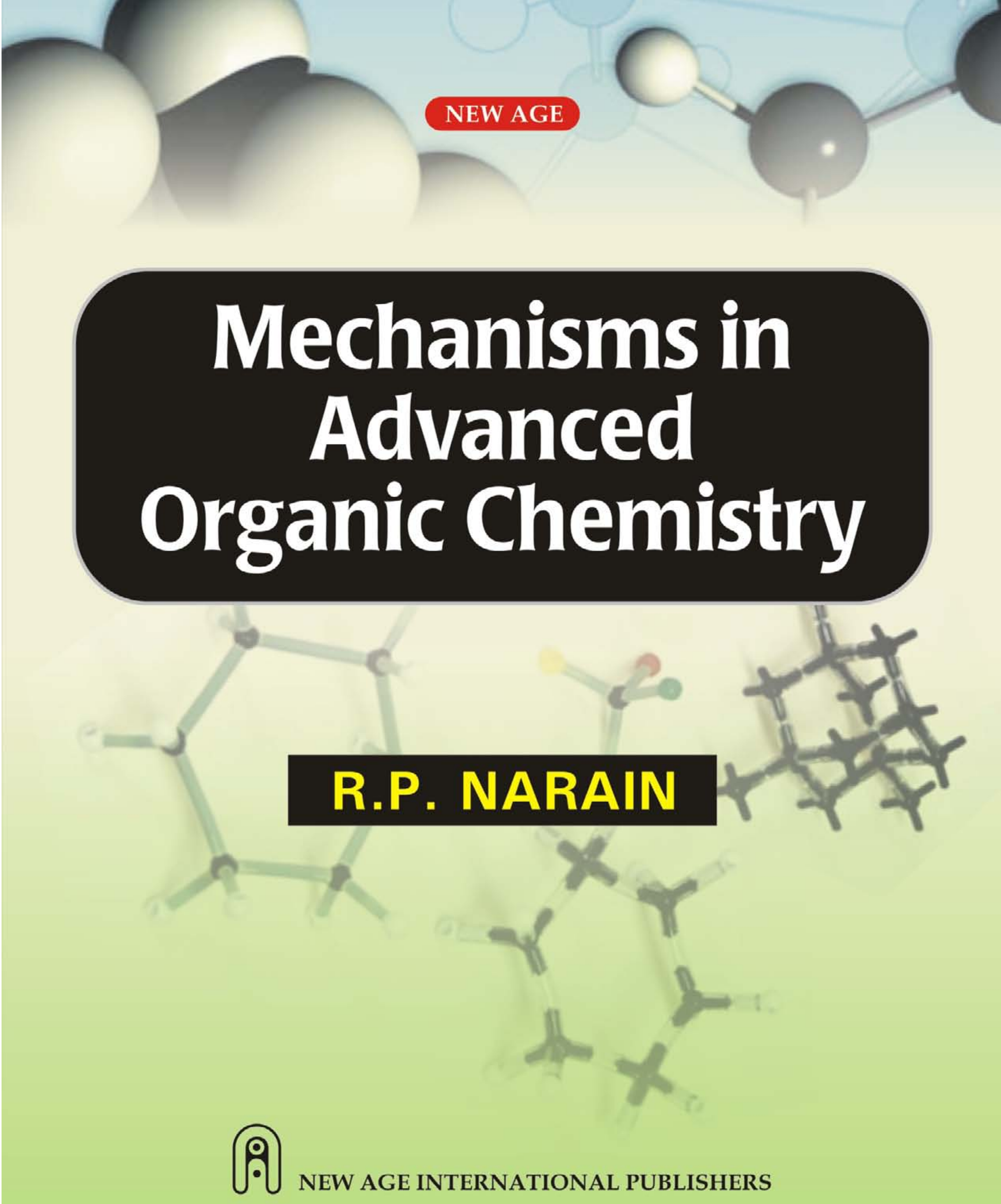

NEW AGE

Mechanisms in Advanced Organic Chemistry

R.P. NARAIN

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Mechanisms in Advanced Organic Chemistry

Mechanisms in Advanced Organic Chemistry

R.P. Narain
Formerly Reader
Chemistry Department
University of Gorakhpur
Gorakhpur (U.P.)

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PREFACE

For a very long time the need was felt by graduate and postgraduate students of Chemistry of almost all colleges and of Indian Universities for a book dealing with advanced mechanistic organic chemistry written in understandable language and with suitable examples which can be easily grasped to make their concept clear. Besides students, this has also been the requirement of teachers teaching advanced organic chemistry.

Till about 1959 there appears to be the only book by E.S. Gould (Structure and Mechanism of Organic Chemistry) but the examples mentioned in it are so difficult at several places that they elude the comprehension of even teachers, not to talk of students. Around sixties appeared the book by Jerry March (Advanced Organic Chemistry, Reactions, Mechanism and Structure). It was definitely a much better advance over that of Gould, but it has been made so bulky that its cost has become prohibitive. It adores the racks and shelves of libraries. In view of the above difficulties of teachers and students, the present book has been brought out.

Some of its special chapters are the Pericyclic Reactions, which includes Cheletropic, Electrocyclic, Sigmatropic and Cycloaddition reactions. The concept of Stereochemistry and Conformation deserve special attention not because they cater to the needs of higher students, but they are immensely useful for candidates trying for UGC and CSIR sponsored competitive examinations, but also those preparing for Union Public Service Commission and State Public Service Commission Exams. The candidates will find the chapters immensely useful and is sure to rouse interest in them in knowing more about mechanistic chemistry.

Spectroscopy is another topic, a good knowledge of which is expected from any good chemist. The spectroscopy finds immense applications in the identification of several unknown compounds in the field of research and medicine. Here one has to be very careful in elucidating the correct structure of entities. Moreover in every examination (competitive or regular) one has to show his skill in the area of spectroscopy and therefore chapters on spectroscopy giving a clear and lucid account is also noteworthy.

To the best of my knowledge, a book written by an Indian author and covering all the chapters covered in it is not known.

Part I deals with chapter involving typical complex organic reactions. Part II deals with various aspects of spectroscopy and the use of this technique in identification of compounds. Miscellaneous reagents used in organic synthesis are discussed in Part III.

The author is immensely grateful to Prof. R.P. Rastogi for writing the forward for this volume.

R.P. Narain

FOREWORD

The present book deals with mechanistic principles of organic reactions in an exhaustive and systematic manner. It would be equally useful for the study of complex reactions where inorganic reactions are also involved in the reaction network including biochemical reactions. The author had long teaching and research experience in Gorakhpur University. The subject matter has been clearly presented.

The book is divided into three parts. Part I deals with typical complex organic reactions such as (*i*) reactions involving carbocations and carbanions, (*ii*) Pericyclic and electrocyclic reactions and (*iii*) Sigmatropic and Chelotropic reactions. This part also includes material useful for characterization of products from structural point of view such as Geometrical isomerism, Stereochemistry and Conformation. Part II is concerned with spectroscopic methods of structure determination such as U.V., I.R., N.M.R. and Mass spectroscopy, which is quite useful from the angle of identification and characterization of reaction intermediates. In part III, detailed treatment of commonly used oxidizing and reducing agents along with involved reaction mechanism has been presented.

Treatment of each part is comprehensive and thorough. The book would be useful for teaching at post-graduate level and also as reference book for undergraduate level. It would be extremely useful for reference for research scientists in connection with organic synthesis, reaction mechanism of complex reactions involving inorganic and organic reactions and also bio-chemical reactions.

R.P. Rastogi

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PART-I

TYPICAL COMPLEX ORGANIC REACTIONS

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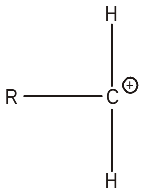
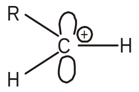
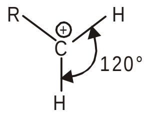
CHAPTER 1

Carbocations (Carbonium Ions)

The carbonium ions are positively charged highly reactive intermediates and have six electrons in the outer shell of central carbon. They may be represented as





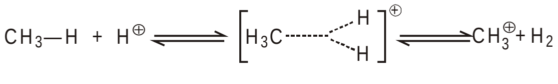


So they are very reactive toward any nucleophilic reagent *i.e.*, one that will donate a pair of electrons to carbon to form a fourth covalent bond. Being positively charged they are stabilized inductively by electron-donating substances and rendered less stable by electron-withdrawing substituents.

Since carbon of a carbonium ion is in an *sp*^{2} hybrid, the ion pair is planar with a vacant *p* orbital (as in ethylene) which is perpendicular to the plane of three covalent bonds to the carbon.

NOMENCLATURE

As early as 1902 Gomberg suggested that the word carbonium was inappropriate for such species because “onium” signifies a covalency greater than that of the neutral atom. But the nomenclature went on till about 1964 when George Olah and his coworkers found evidence by mass spectroscopy the existence of a positively charged intermediate, the CH_5^+ ion. It was supposed to have been formed by the attack of H^+ on C—H bond to give the species CH_5^+ also called the methanonium ion.



$$CH_3{-}H + H^{\oplus} \rightleftharpoons \left[H_3C \cdots \begin{matrix} H \\ H \end{matrix} \right]^{\oplus} \rightleftharpoons CH_3^{\oplus} + H_2$$

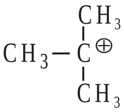
It has a three centre, two electron bond. In this the formal covalency of carbon is five rather than three.

On this basis Olah proposed that the word carbonium ion should be reserved for such pentacoordinated species, while other positively charged species originally called carbonium ions be given the name **'carbenium ions'.** Olah also suggested the nomenclature carbocations to encompass both the type of species and the IUPAC has accepted this proposal.

Although pentacovalent ions are much rarer than other positively charged ions, the general word carbocation is used for all such species. It is interesting to note that another species, the **ethanonium ion** $C_2H_5^{\oplus}$ has also been reported in the gas phase by IR spectroscopy.

So now the word carbocation is used to cover all such electron deficient and positively charged species, although some authors still prefer to use the word carbonium ions.

The difference between carbenium and carbonium ions is summarized as follows:

Carbocation property	*Carbenium ions*	*Carbonium ions*
Example	 $CH_3-\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}{}^{\oplus}$	$CH_5^{\oplus}$
Number of covalent bonds to carbon	3	5
No. of electrons in outer shell	6	8
Electron deficiency	electron deficient	not electron deficient

The simplest example of carbenium ion is $CH_3^{\oplus}$ which is so unstable that it is rarely formed even in gaseous phase. The more stable ones have been prepared in solution and in some cases even in the solid state. When in solutions they are formed in polar solvents where they get solvated. They may also be associated with a negative ion called gegenion. The ion pairs are formed in non polar solvents.

STRUCTURE AND STABILITY

The carbocations being reactive intermediates have short life and so they are unstable. But they have been rendered stable after being trapped in strongest super acids which are mixtures of fluorosulphuric and antimony pentafluoride dissolved in SO_2 or chlorofluorosulphuric acid SO_2CIF. Under these conditions their structure and stability have been correlated.

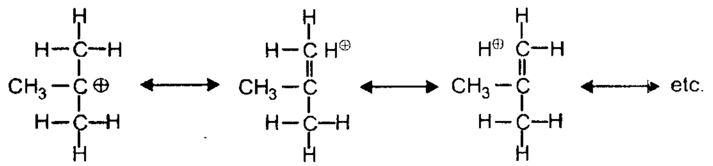
In general, the greater the resonance and hyper-conjugation the greater is the stability of carbocation. The stability also depends on the field strengths. The following examples illustrate this point.

1. Stability depending on the number of canonical forms

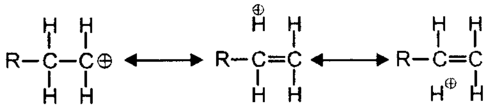
We know that among the simple carbocations the order of stability is

$$\begin{matrix}\text{tertiary} & & \text{secondary} & & \text{primary}\\ \text{carbocation} & > & \text{carbocation} & > & \text{carbocation}\end{matrix}$$

This is because the greater the number of canonical forms, the greater is the stability. Let us see the canonical forms from a tertiary and a primary carbocation.



Tertiary carbocation



Primary carbocation

Thus a tertiary carbocation like the above will give nine resonating structures while a primary will give only two hyperconjugative forms. This explains why tertiary carbocations are more stable than secondary which in turn is more stable than primary. This also explains why ethyl carbocation ($CH_3CH_2^{\oplus}$) is more stable than methyl carbocation ($CH_3^{\oplus}$).

In general the more the number of alkyl groups attached to the C, the greater is the stability. During hyperconjugation some charge delocalization occurs between the *p*-orbital of the positively charged carbon and the σ bond of the β C-H.

On the basis of hyperconjugation, among alkyl carbocations, tertiary butyl carbocation has been shown to be most stable, because in the following reaction,

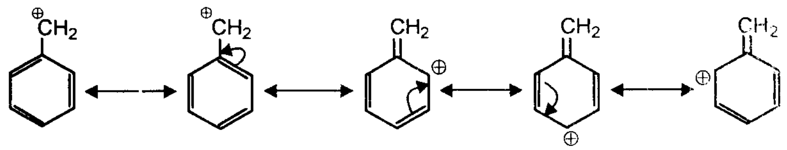
$$(CD_3)_3C^{\oplus} + (CH_3)_3CH \rightleftharpoons (CH_3)_3C^{\oplus} + (CD_3)_3CH$$

since the equilibrium constant $\kappa = 1.97$ which shows that the reaction proceeds more towards right confirming that tertiary butyl carbocation is more stable than $(CD_3)_3C^{\oplus}$. There appears to be less hyperconjugation in deuterium containing carbocation than $(CD_3)_3C^{\oplus}$. It has been shown that of all the alkyl carbocations the ter-butyl carbocation is most stable. Even the relatively stable t-pentyl and t-hexyl cations break up at higher temperatures to produce the t-butyl cation. Even methane, ethane and propane in presence of superacids produce t-butyl cation as the main product. Even paraffin wax and polyethylene give t-butyl cation.

So the order of stability among alkyl carbocations is:

$(CH_3)_3C^{\oplus}$	>	$(CH_3)_2CH^{\oplus}$	>	$CH_3CH_2^{\oplus}$	>	CH_3
t-butyl carbocation		isopropyl carbocation		ethyl carbocation		methyl carbocation

Canonical forms can also be drawn for benzylic cations and allylic cations.



Benzylic cations

allyl cations
(Two canonical structures)

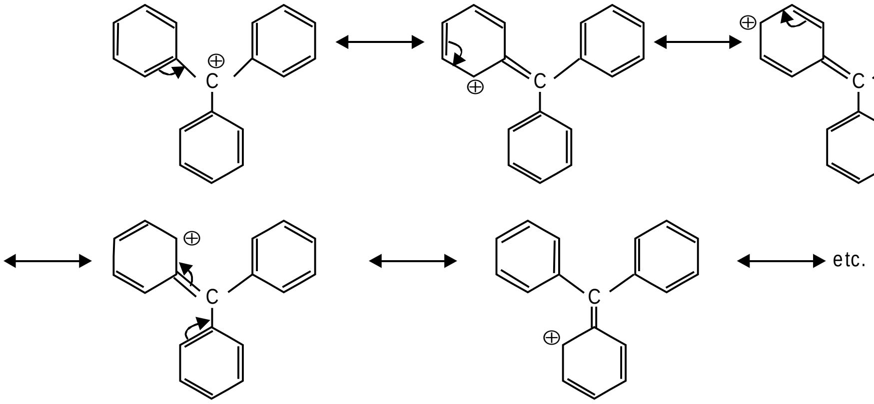
So the order of reactivity is:

$$CH_6H_5CH_2^{\oplus} > CH_2{=}CH{-}CH_2^{\oplus} > CH_3CH_2CH_2^{\oplus}$$

and the above is also their stability.

Now lest us study the stability of triphenyl and phenylalkyl cations.

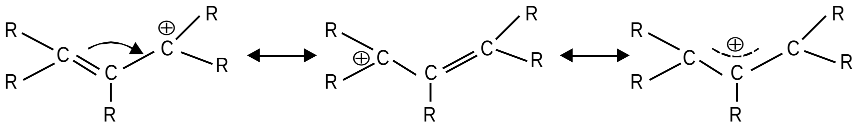
The triphenylmethyl carbocation shows its stability because the positive charge on the carbon is distributed uniformly over a number of structures.



Thus a number of canonical structures is possible. Like triphenylmethyl cation, diphenylmethyl cation is also very stable. In some cases the carbocations are so stable that their salts have been isolated in the solid state. The solid salt of triphenylmethyl cation with boron fluoride as $(C_6H_5)_3C^{\oplus}BF_4^{\ominus}$ is available commercially. Arylmethyl cations are further stabilized if they have electron-donating groups in ortho and para positions.

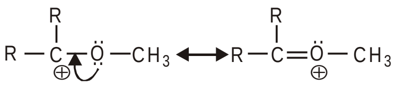
2. The stability increases when the positive charge is in conjugation with a double bond

This is due to increased delocalization of the positive charge over two atoms instead of being concentrated at one.

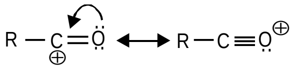


3. The presence of a heteroatom adjacent to the cationic centre and bearing an unshared pair of electrons, like nitrogen, oxygen or halogen increases stability

Such ions are stabilized by resonance



Simple acyl cations have been prepared in solution and even in the solid state. It has been found that acetyl cation $CH_3CO^{\oplus}$ is as stable as ter-butyl cation. Their canonical forms are represented as:

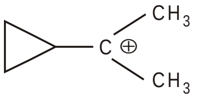


It has been shown that although the positive charge is located on cation, this structure contributes more than that containing a triple bond.

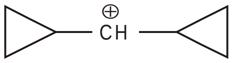
Therefore in general the carbocation stability is increased due to resonance.

4. Conjugation between the bent orbitals and p-orbitals of the cation

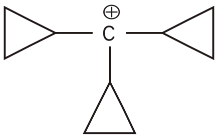
In this connection the case of cyclopropylalkyl cation and substituted cyclopropyl cations is interesting. Cyclopropylmethyl cation has been found to be more stable than benzyl cation and the stability increases with each addition of cyclopropyl groups. Thus



Dimethylcyclopropyl cation

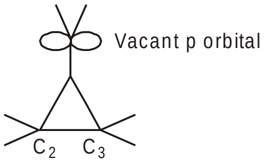


Dicyclopropyl cation



Thricyclopropyl cation

This increased stability has been explained between the bent orbitals of cyclopropyl rings and the vacant *p* orbital of the cation carbon. The vacant *p* orbital lies parallel to C_2–C_3 bond of the cyclopropane ring and not perpendicular to it. Thus the geometry becomes similar to that of a cyclopropane ring conjugated with an oblefinic bond.



The structure of carbocation has been measured by ^{13}C nmr shift of the carbon atom carrying the positive charge. The shift agrees with the electron density on this carbon.

The following table given by Olah and J. Denovan (J. Amer. Chem. Soc. 1977.90.5026) shows that substitution of an ethyl for a methyl group or a methyl for hydrogen causes a downfield shift showing that the central carbon becomes somewhat more positive.

Table 1.1

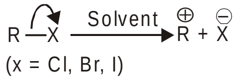
Ions	*Chemical shift*	*Temperature °C*
$(C_2H_5)_2C^{\oplus} - CH_3$	–139.4	–20°
$(CH_3)_2C^{\oplus}C_2H_5$	–139.2	–60°
$(CH_3)_3C^{\oplus}$	–135.4	–20°
$HC(OH)_2^{\oplus}$	+17.0	–30°
$C(OH)_3^{\oplus}$	+28.0	–50°

The presence of hydroxy group decreases the positive character of the central carbon.

GENERATION OF CARBOCATIONS

Following are some of the methods used to generate carbocations.

1. ***By direct ionisation:*** The direct ionisation of alkyl halides gives carbocations.

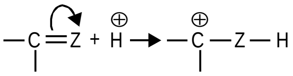


$$R-X \xrightarrow{\text{Solvent}} \overset{\oplus}{R} + \overset{\ominus}{X}$$

(x = Cl, Br, I)

The process is accelerated due to the presence of metal ions like $Ag^{\oplus}$.

2. ***Form alkenes:*** A proton or other positive species adds to one atom of an unsaturated system leaving a positive charge on the adjacent carbon.

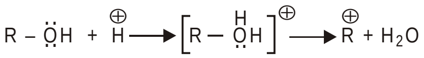


$$-\underset{|}{C}=Z + \overset{\oplus}{H} \rightarrow -\overset{\oplus}{\underset{|}{C}}-Z-H$$

3. ***Decomposition of an alkyl diazonium ions:***

$$R-\overset{\oplus}{N}\equiv N \longrightarrow \overset{\oplus}{R} + N_2$$

4. ***By protonation of alcohols:*** The protonated alcohols give carbocations on decomposition.



$$R-\ddot{\underset{..}{O}}H + \overset{\oplus}{H} \longrightarrow \left[R-\overset{H}{\underset{..}{O}}H\right]^{\oplus} \longrightarrow \overset{\oplus}{R} + H_2O$$

5. ***By reaction of acyl halides in presence of anhydrous aluminium chloride:*** The Frielel-Crafts acylation reactions came under this heading.

$$R-COCl \xrightarrow[AlCl_3]{\text{anhydrous}} \overset{\oplus}{RCO}\text{-----}\overset{\ominus}{AlCl_4} \longrightarrow \overset{\oplus}{RCO} + \overset{\ominus}{AlCl_4}$$

REACTIONS OF CARBOCATIONS

The carbocations being highly reactive intermediates of very short life react further without being isolated and give stable products. In general they give the following reactions:

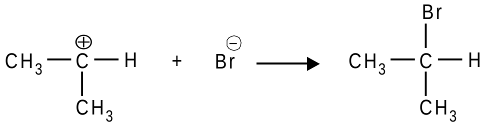
1. Reaction with nucleophiles
2. Elimination of a proton
3. Rearrangements
4. Addition to unsaturated systems.

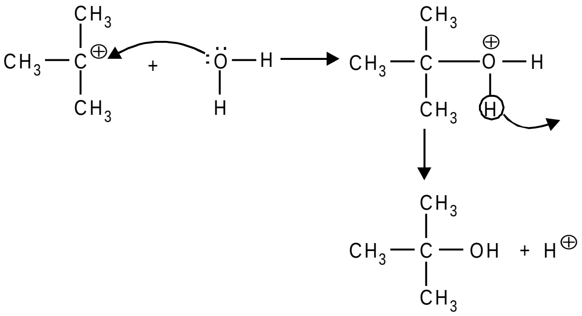
1. Reaction with nucleophiles

The carbocations react with species, the nucleophiles

$$\overset{\oplus}{R} + \overset{\ominus}{Y} \longrightarrow R-Y$$

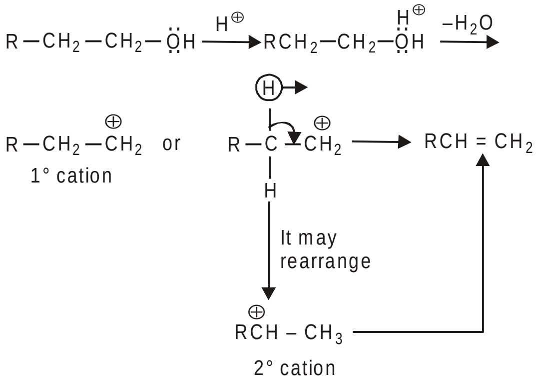
$Y = O\overset{\ominus}{H}$, halide ion or may be even a neutral species.





2. Elimination of a proton

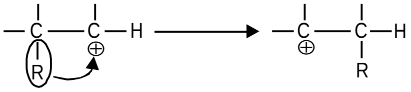
In this process the elimination of a proton results in the formation of an alkene. Thus the dehydration of alcohols gives rise to alkene in presence of conc. H_2SO_4.



So carbocations can adopt two pathways to give the stable product.

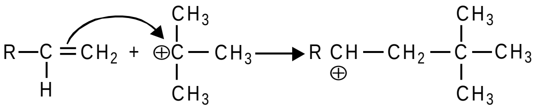
3. Rearrangements

As shown in the example due to rearrangement 1° carbocation rearranges to 2° cation. This rearrangement may involve the migration of a hydrogen with its pair of electron when it is called the **hydride shift** or it may involve the migration of an alkyl group with its bonding electrons in which case it is called the **alkyl shift.** They hydride shift is given in the above example. The alkyl shift may be represented as



4. Addition to unsaturated systems

A carbocation may add to an alkene producing a new positive charge at a new position as shown in the following example.



$$R-\underset{\displaystyle H}{\underset{|}{C}}=CH_2 + \oplus\overset{\displaystyle CH_3}{\overset{|}{\underset{\underset{\displaystyle CH_3}{|}}{C}}}-CH_3 \longrightarrow R\,\underset{\oplus}{CH}-CH_2-\overset{\displaystyle CH_3}{\overset{|}{\underset{\underset{\displaystyle CH_3}{|}}{C}}}-CH_3$$

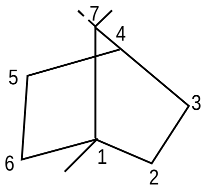
Formed by any of the two methods, the new carbocation reacts further to stabilize itself. This generally happens either by reacting with a nucleophile or by the loss of a proton.

If the new cation formed by union with an alkene further combines with an alkene, this will result in the formation of a polymer.

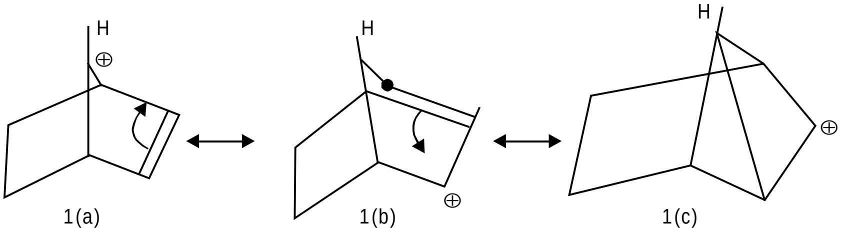
A number of reactions have been explained on the basis of generation of carbocations. The examples include the Friedel-Crafts alkylation and arylation reactions. Besides pinacol-pinacolne rearrangement, Beckmann rearrangement and Wagner-Merwein rearrangement are other examples.

NON-CLASSICAL CARBOCATIONS OR BRIDGED CARBOCATIONS

The carbocations so far studied are called classical carbocations in which the positive charge is localized on one carbon atom or delocalized by resonance **involving** an unshared pair of electrons or a double or triple bond in the allylic positions (resonance in phenols or aniline). In a non-classical carbocation the positive charged is delocalized by double or triple bond **that is not in the allylic position** or by a single bond. These carbocations are cyclic, bridged ions and possess a three centre bond in which three atoms share two electrons. The examples are 7-norbornenyl cation, norbornyl cation and cyclopropylmethyl cation.

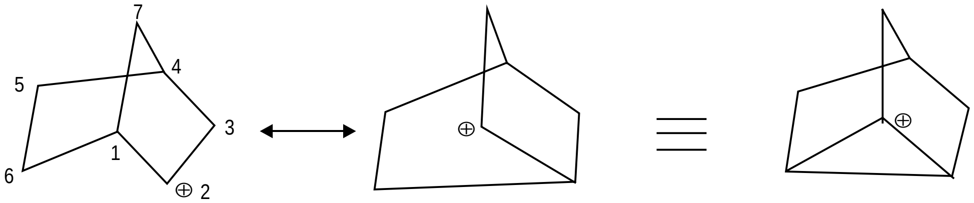


(1)



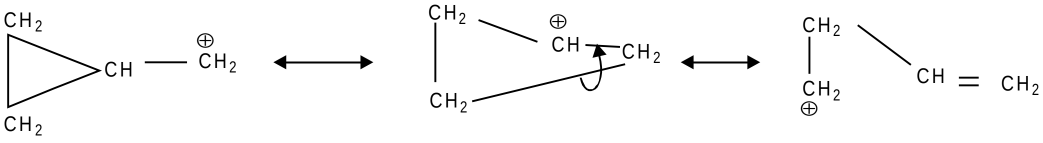
1(a) 1(b) 1(c)

7-norbornenyl cation



norbornyl
cation
2

2(a) 2(b)



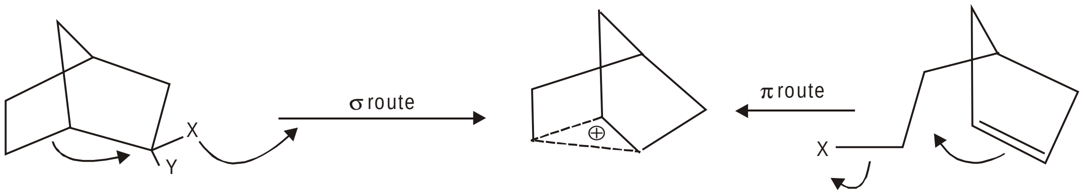
cyclopropylmethyl
cation
3

3(a) 3(b)

It we accept the existence of bridged ions, the question to be answered is why should such ions be formed in preference to classical carbocations in any particular reaction. One reasonable answer is that when several intermediates are possible, the most stable one is the one likely to be formed. Since charge is most diffuse in the bridged ion than in the classical ion, the bridged structure would be expected to be more stable than the classical structure.

GENERATION OF NON-CLASSICAL CARBOCATIONS

The non-classical carbocations can be generated if proper substrate is chosen. For example the norbornyl carbocation can be generated by the departure of a leaving group from an exosubstitued substrate



exosubstituted norbornyl compund
4

4(a)

4(b)

This is called the σ route to a **non-classical carbocation** because of the participation of a σ bond. If a π bond is involved then it is called a **π route.** Many chemists aruge that the structure written from 7-norbornenyl cation are not non-classical carbocations because they are not canonical forms but real structures and there is rapid EQUILIBRIUM between them.

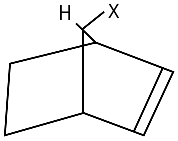
Distinction between neighbouring group participation and non-classical carbocation

It is important to distinguish between **neighbouring group participation** and non-classical carbo-cation. A non-classical carbocation can be formed due to participation of several species as a neigh-bouring group.

Some of these neighbouring groups are–

1. *C* = *C* as a neighbouring group

Here we have a *c* = *c* group attached to a carbon atom which is *adjacent* to be carbon atom where nucleophilic substitution can occur and during the course of the reaction becomes bonded of partially bonded to the reaction centre to form a *non-classical* or *bridged* ion (Fig. 1 to 1(c)). Thus the rate and/or the stereochemistry may be affected. This explains why the acetolysis of 5 is 10^{11} times faster than that of 5(a), because it involves the formation of a non-classical carbocation



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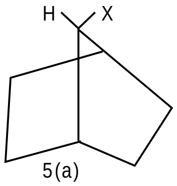


5(a)

2. The carbon-carbon single bond as a neighbouring group

This has been explained in Fig. (2 – 2(b)) and also in Fig. (3 to 3(b)).

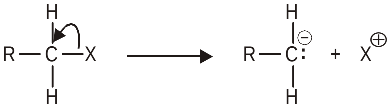
3. The 2-nor-bornyl system

This is given in Fig. (2 to 2(b)).

CHAPTER 2

The Carbanion Chemistry

The carbanions are formed during heterolytic fission of a C—X bond in which the carbon atom is more electronegative than X.

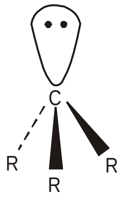


$$R-\underset{H}{\overset{H}{C}}-X \longrightarrow R-\underset{H}{\overset{H}{C}}{:}^{\ominus} + X^{\oplus}$$

The shared pair of electron goes to the carbon atom which acquires an octet with a negative charge and X goes out as a positive ion. The above species containing the carbon with the octet and a negative charge is called a carbanion.

So, it is a tricovalent carbon with a pair of electrons and the geometry has been found to be pyramidal resembling ammonia and amines in which the unshared pair occupies one apex of the tetrahedron.

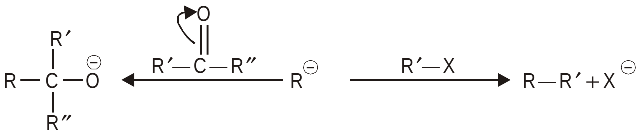
Therefore, the central carbon atom is in a state of sp^3 hybridisation, but when it is stabilized by declocatization, the hybridization becomes, sp^2 for effective resonance.



Carbanion

STABILITY

Being electron-rich it is a very reactive intermediate and forms the basis of many important organic synthesis. It can combine with a great variety of electrophiles e.g., alkyl halides and ketones and can form compounds having carbon-carbon bonds in high yields.



$$R-\underset{R''}{\overset{R'}{C}}-O^{\ominus} \xleftarrow{R'-\overset{O}{\overset{\|}{C}}-R''} R^{\ominus} \xrightarrow{R'-X} R-R'+X^{\ominus}$$

a carbanion

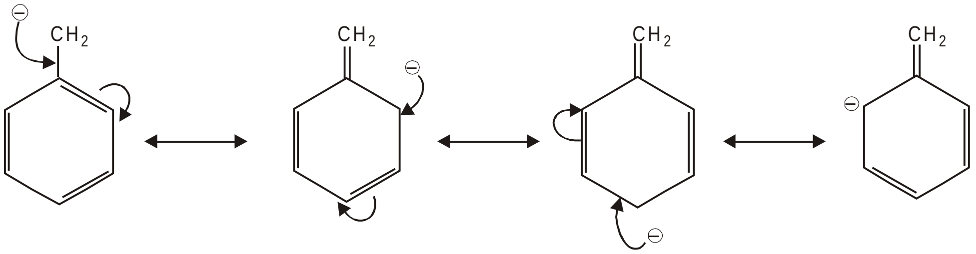
R = alkyl

X = halogen.

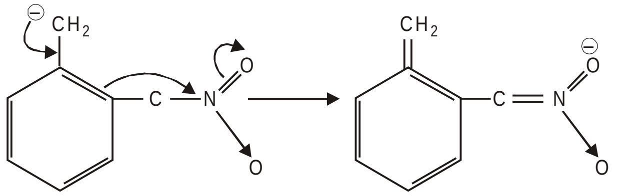
Because of the unshared electron pairs, it can also function as a base and can abstract a proton to form a conjugate acid.

$$R_3C - H \;+\; B: \rightleftharpoons R_3\overset{\ominus}{C} \;+\; \overset{\oplus}{B}H$$

The benzyl carbanion has been found to be most stable because of the extensive delocalization of the negative charge over the various resonating structures.



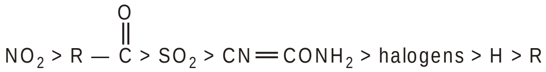
The stability becomes greater due to the presence of electron attracting groups like NO_2, – C≡N or carbonyl group in the molecule and it decreases due to electron releasing groups.



The stability of the carbanions has been found to be in the order

benzyl > vinyl > phenyl > $-C_2H_5$ > n-propyl > isobutyl > neopentyl.

The effect of groups on the stability of carbanions when present in α position is in the order.



$$NO_2 > R - \overset{\overset{\displaystyle O}{\|}}{C} > SO_2 > CN{=}CONH_2 > \text{halogens} > H > R$$

GENERATION OF CARBANIONS

The carbanions have been generated as intermediates in a large number of reactions.

In recent years new types of carbanions have been prepared which are paired with different metals and this has found the basis for the preparation of many novel organometallic compounds. Some of these metals include group IA, IIA metals besides aluminium, zinc and cadmium.

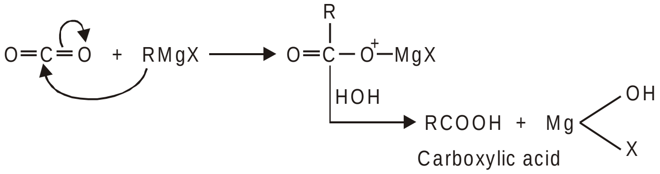
(a) Abstraction of hydrogen by a base

In organic compounds having C—H bonds, the carbon atom being more electronegative will pull the bonding electron towards itself and so hydrogen can go out as a proton. Therefore, in presence of a base this H will be attracted by the base and a carbanion will be obtained. This acidic hydrogen will be abstracted by bases like NaOH, t-BuO$^{\ominus}$ or alkyl lithium where the alkyl radical will behave like a base.

A simple example of such abstraction of proton is the formation of triphenylmethyl carbanion by $NaNH_2$ in presence of liquid ammonia.

$$Ph_3C - H + \overset{\oplus}{Na}\overset{\ominus}{NH_2} \xrightarrow{\text{liq. } NH_3} Ph_3\overset{\ominus}{C} - \overset{\oplus}{Na} + NH_3$$

In the Grignard reagent, the alkyl radical acts like a carbanion as shown by its reactions with CO_2 leading to the formation of carboxylic acids



Therefore deprotonation is a method used most often for the preparation of resonance and inductively stabilized carbanions.

$$R - H + M \rightarrow RM + ½\, H_2$$

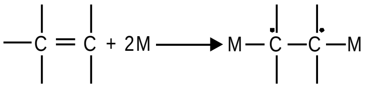
Dimethyl sulphide, Me_2S (with estimated pKa value as high as 49 in the medium of DMSO) loses proton with alkyl lithium, the idea has been put forward that any type of non-metal atom bonded to a carbon atom will make a proton attached to that carbon atom acidic to be replaced by strong bases like butyl lithium.

Deprotonation of very weakly acidic C—H acids is accomplished by metallation with organolithium and organosodium compounds.

(*b*) From Unsaturated Compounds

The carbanions can be generated from unsaturated compounds either by reduction or by addition.

(*i*) Many unsaturated compounds take up two electrons (reduction) from active metals to form **dicarbanions.** It is illustrated as follows:



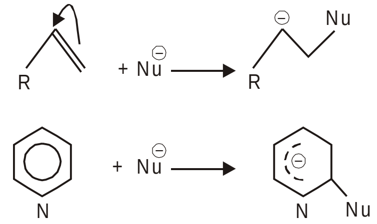
$$-\overset{|}{\underset{|}{C}} = \overset{|}{\underset{|}{C}} + 2M \longrightarrow M-\overset{|}{\underset{|}{\dot{C}}}-\overset{|}{\underset{|}{\dot{C}}}-M$$

The anion from one electron transfer is probably an intermediate. Simple alkenes do not form such stable dianions, but some conjugated derivatives do form dianions as with cyclooctatetraene forming dianion with alkali metals.

Benzene (aromatic) does not yield its antiaromatic dianion and naphthalene reduces only to its anion radical.

(*ii*) By addition:

The addition of a nucleophile to an unsaturated C = C bond generates a carbanion.



REACTIONS OF CARBANIONS WITH ELECTROPHILES

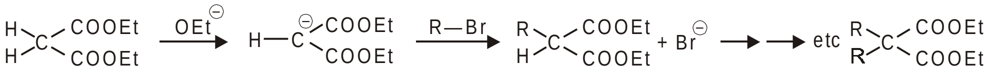
These reactions are of two types:

(*a*) Substitution, and

(*b*) Addition.

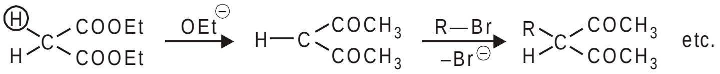
1. Substitution reactions of alkyl (sp^3) anions

The carbanions are involved in a number of substitutaion reactions. The example are the formation of mono and dialkyl malonic esters.



Carbanion intermediate

Similarly with other reactive methylene groups like β diketones we get mono and dialkylated derivatives.



diketone Carbanion intermediate

In such reactions the leaving group is a halide ion but many other groups such as sulphonates, sulphates or alkoxides have also been used. A bond is formed between R and some non-metallic or metallic element.

Virtually all elements except noble gases can be bonded to carbon.

Some substitution reaction are as follows:

(*i*) $YH \xrightarrow{R^{\ominus}} RH + \overset{\ominus}{Y}$

(*ii*) $YB(OR')2 \longrightarrow RB(OR')2 + Y^{\ominus}$

In (*i*) there is an abstraction of a proton by a strong organometallic base like BuLi because they are readily available. It is an extremely important reaction because it is used to generate other anions.

2. Addition Reactions of Alkyl (Sp^3) Anions

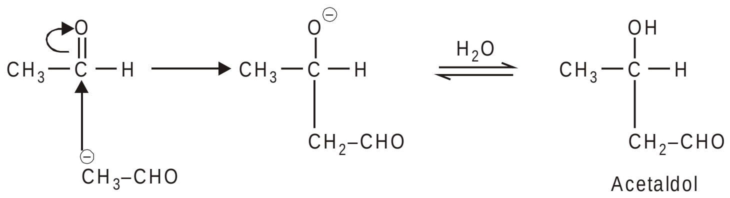
The formation of an aldol by the union of two molecules of aldehyde in presence of alkalies is an important example under this heading. The formation of acetaldol from acetaldehyde is as follows:

$$CH_3CHO \;+\; HCH_2CHO \xrightarrow{OH^{\ominus}} \underset{\beta\,\text{hydroxybutraldehyde}}{CH_3CHOH\;CH_2CHO} \xrightarrow[-H_2O]{\Delta} \underset{\text{Acetaldol}}{CH_3{-}CH{=}CH\;CHO}$$

The mechanism is as follows:

$$CH_3-CHO \xrightarrow{OH^{\ominus}} \underset{\text{a carbanion}}{{}^{\ominus}CH_2-CHO} + H_2O$$

The carbanion then attracts the second molecule of aldehyde.



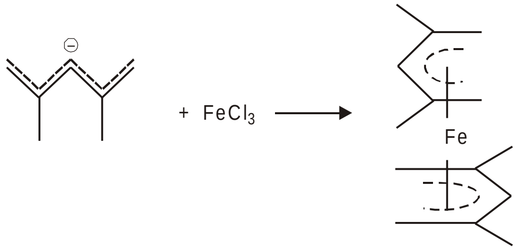
The acetaldol again having α hydrogen atom to the aldehyde repeats the process and long chain polymers are formed.

Here the carbanion obtained form the first molecule adds at the aldehydic carbon atom of the second molecule.

Other reactions involving the addition of carbanions are reactions like Perkin's reaction, Claisen condensation, benzilic acid rearrangement and Michael addition.

3. Reactions of π carbanions with Electrophiles

The π type carbanions undergo most of the reactions given by σ alkyl anions. An example is



4. Elimination Reactions of Carbanions

The elimination reactions of carbanions have been put under different classes. These are:

(*a*) α eliminations

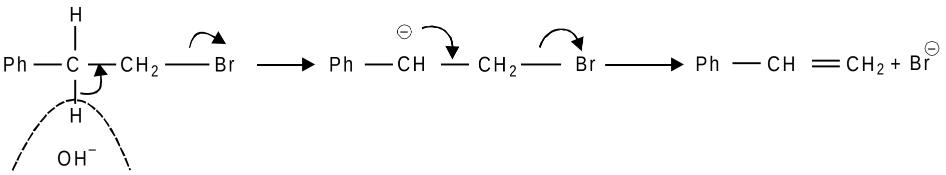
(*b*) β eliminations

(*c*) γ eliminations

(*d*) δ eliminations

Besides these cycloeliminations are also known. Many of elimination reactions proceed rapidly at room temperature but are slow at dry ice temperatures. Thus permitting carbanions containing good leaving groups to be used in substitution.

Out of the above the β elimination is most common. These eliminations result in the formation of alkenes and alkynes. When β phenylethyl bromide is heated with an alcoholic solution of an alkali first a carbanion is formed by the loss of a proton followed by the loss of a halide ion and simultaneous formation of a double bond.



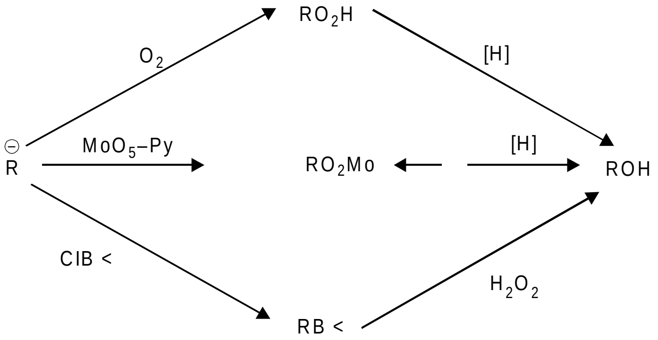
The presence of a positively charged substituent on the α carbon atom promotes the acidity of β hydrogen.

5. Oxidation Reactions of Carbanions

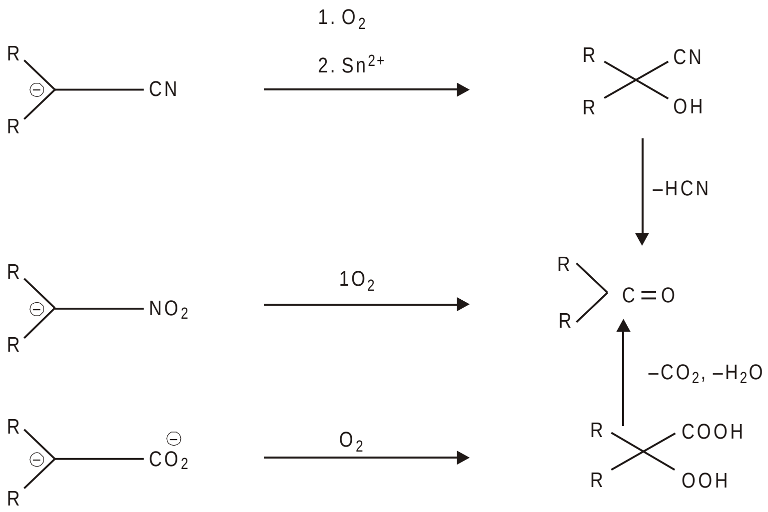
One electron oxidation of monocarbanions leads to carbon radicals and two electron oxidation gives carbocations. In most of these oxidations, the mechanism is not known, though progress is being made on some mechanisms. But there appears to be a parallelism between base strength and ease of oxidation of carbanions.

(i) Oxidation of Carbanions to Hydroperoxides, Alcohols and Ketones

The carbanions take up O_2 and these take up protons to give **hydroperoxides** in good yields. But because they are explosive in nature, they are not usually isolated and on reduction with sodium sulphite on trialkyl phosphite give alcohols. Alcohols can also be prepared via hydroperoxy molybdenum complexes and alkyl boranes. These reactions are summarized as follows:



Ketones can be prepared from special carbanions types by elimination reactions which follow oxygenation.



(ii) Oxidative Couplings

The simple coupling reaction works well in certain cases

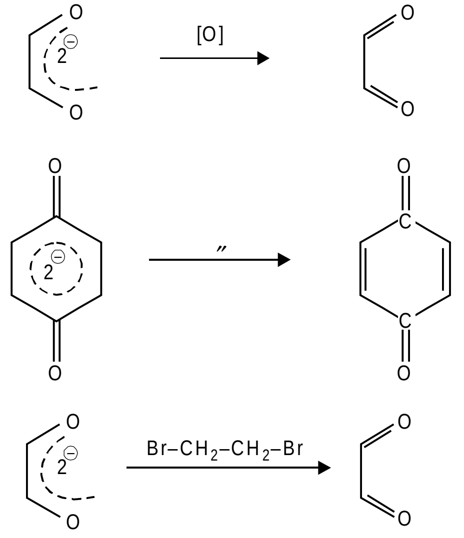
$$R^{(-)} \xrightarrow{[O]} RR$$

One of the most useful coupling reactions is the Eglintion reaction in which the oxidation of acetylene anions with ferric ion proceeds very satisfactorily.

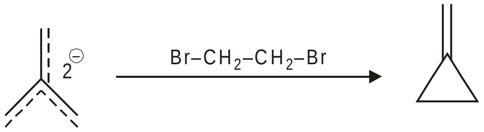
$$RC \equiv C^{\ominus} \xrightarrow{Fe^{3+}} RC \equiv C - C \equiv R$$

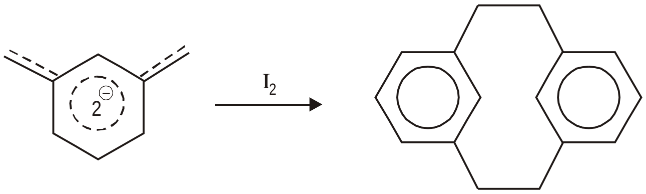
(iii) Dianion Oxidations

Oxidation of dianions, in which both the electrons are oxidized gives products which are biologically important:



When the product of two electron oxidation is a diradical, the isolated product can be thought of as being formed by intra or intermolecular coupling of this diradical.





REARRANGEMENT REACTIONS OF CARBANIONS

These rearrangement reactions are classified under different classes.

1. Intermolecular Rearrangements

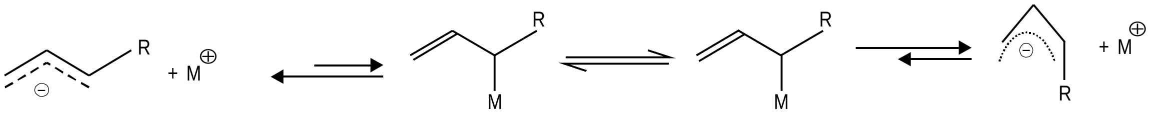
The reaction between a cation and carbanion can result in more a less tight association. Therefore stereochemical changes in the carbon species will take place.

Two conditions will arise:

(*a*) with σ carbanions no doubt a tight structure R-M will be formed, but if the carbanion R^- has a chiral centre, then due to loose form or $R^{-(n)}$, inversion of groups will take place and this will be detected by racemisation.

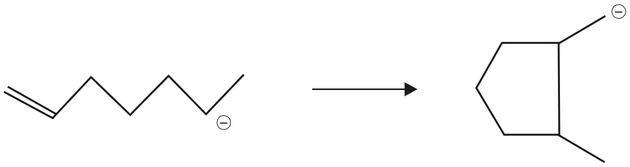
$$R^{\ominus} + M^{\oplus} \rightleftharpoons RM$$

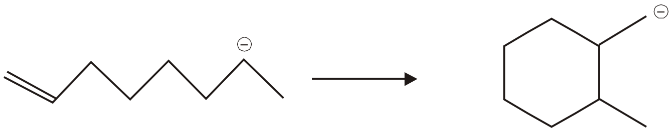
(*b*) with π carbanions geometrical isomerisation can take place either photo-chemically or thermally.



2. Intramolecular Additions

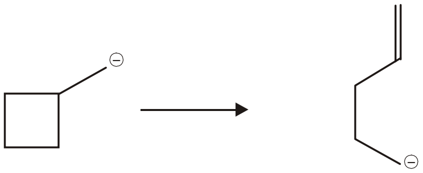
5-membered rings are kinetically formed over 6 and so a five membered ring is formed at least 2800 times faster then a six membered ring as is seen in the following and other systems

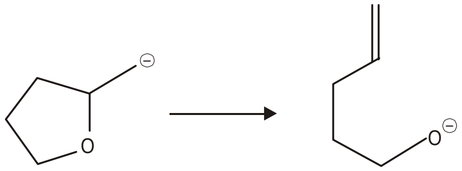




3. Intramolecular Eliminations

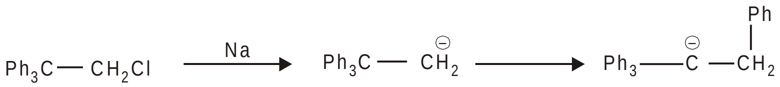
These reactions are reverse to those written in section 2 above. These reactions take place because of either release of ring strain or by elimination of groups, the species formed is more stable.





4. Sigmatropic Carbanion Rearrangement

In sharp contrast to carbonium ions, the carbanions undergo (1, 2) sigmatropic shifts very rarely if ever. An example is as given below:



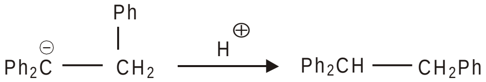
$$\mathrm{Ph_3C{-}CH_2Cl} \xrightarrow{\mathrm{Na}} \mathrm{Ph_3C{-}\overset{\ominus}{C}H_2} \longrightarrow \mathrm{Ph_3{-}\overset{\ominus}{C}{-}\overset{\overset{\textstyle Ph}{|}}{C}H_2}$$

Triphenyl ethyl chloride

Carbanion

Rearranged carbanion

It is to be noted that after the formation of the carbanion the migrating group goes to the carbanion carbon *without a electron pair*. This is in sharp contrast to re-arrangements in carbocations where the migrating group moves with the electron pairs. The above rearranged carbanion may combine with a proton to complete the reaction.



$$\mathrm{Ph_2\overset{\ominus}{C}{-}\overset{\overset{\textstyle Ph}{|}}{C}H_2} \xrightarrow{\overset{\oplus}{H}} \mathrm{Ph_2CH{-}CH_2Ph}$$

Thus the carbanion owe their importance in the synthesis of great variety of bond-forming reactions. Unlike carbocations most carbanions do not undergo rearrangements but in many cases react in substitution and addition reactions in high yields. Changing the cation and solvent can greatly affect the reaction.

CHAPTER

3

Theory of Concerted Reactions

WHAT ARE CONCERTED REACTIONS ?

Reactions in which more than one bond is broken or formed can be divided into two classes.

1. Those in which all bonds are broken and new ones are formed simultaneously so that no intermediates are involved. Such reactions are called concerted or multicentre reactions because the changes occur in concert or at the same time at more than one center. In such processes there is only one energy barrier and one transition state. (Fig. 3.1).

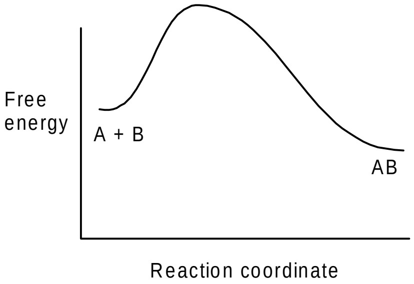


Fig. 3.1

2. This class includes reactions in which the bond forming and bond breaking processes other consecutively so that one or more intermediates are involved. These intermediates may be highly stable and capable of isolation or they may be reactive species of only transient existence. When the intermediate is stable, it is convenient to regard the entire process as consisting of two or more consecutive concerted processes. But where the intermediates are unstable, the entire process is regarded as one reaction which proceeds in a stepwise manner. The energy curve for such a reaction is as shown (Fig. 3.2).

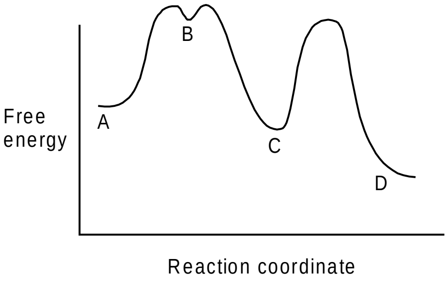


Fig. 3.2

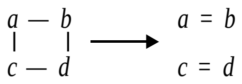
In such a reaction C is formed from A via an unstable intermediate B which has a short life time. Since B lies in a shallow energy well, it is unstable. It has a small energy barrier to surmount by which if can pass on to the products or it can revert to the reactants. The more stable an intermediate is, the deeper is the energy well, so C is relatively more stable than B.

Although C is the first isolable product to be formed it can pass to the more stable form D. C is called *kinetically controlled* product of the reaction of A. D is the product isolated after the system reaches equilibrium, it is called *thermodynamically controlled* product.

Generally thermodynamically controlled product is more stable than the kinetically controlled one although the latter is formed faster then the former from a reactant.

1. Concerted Mechanism

Let us take a reaction in which a cyclic transition state is formed.



$$\begin{array}{c} a - b \\ | \quad\;\; | \\ c - d \end{array} \longrightarrow \begin{array}{c} a = b \\ \\ c = d \end{array}$$

In the concerted fragmentation, the breaking of the *a*—*c* and *b*—*d* bond are going on at the same time. The overall reaction does not involve an intermediate. There is only one energy barrier (Fig. 1) in which both σ bonds are partially broken and new π $a = b$ and $c = d$ are partially formed.

When the two σ bonds break simultaneously and at an exactly the same rate, it is called a *synchronous process.* If, however the reactant is unsymmetrical, the two σ bonds do not break at the same rate.

In 1969 R.B. Woodward and R. Hoffmann developed a general theory of concerted reactions which proceed through a cyclic transition state process which they turned *pericyclic*. They used the concept of orbital symmetry to predict which types of cyclic transition state are energetically feasible.

2. Stepwise Mechanism

If the two σ bonds *a*—*c* and *b*—*d* break in two successive independent steps, then we have an intermediate in which only one of the σ bonds is broken and the energy profile will have two transition states as follows (Fig. 3.3).

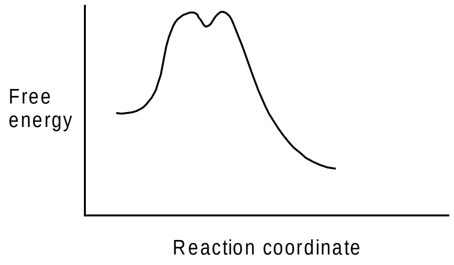
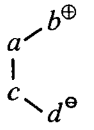


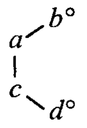
Fig. 3.3

The intermediates fall in two categories:

(*i*) Those which are highly polar.

(*ii*) Those which are essentially non-polar.





The first is called a zwitter ion while the second is a diradical.

Zwitter Ions

The zwitter ions are formed by a heterolytic cleavage of one of the bonds and the charges are stabilized by resonance. If the bond *b*—*d* is reformed, we get back the starting material.

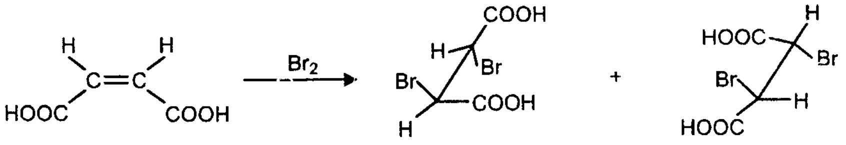
Diradicals

Homolytic cleavage of *b*—*d* bond gives a diradrical intermediate. If the centers bearing the unpaired elections in a diradical are well separated (for example by a long carbon chain) there will be little interaction between them and each will act as an independent monoradical function. Usually the centers are close enough for molecular interaction and it eliminates their reaction as separate chemical entities.

WHAT ARE STEREOSELECTIVE AND STEREOSPECIFIC REACTIONS ?

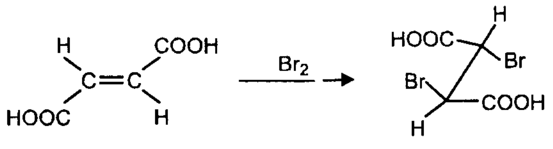
A reaction which leads to the exclusive or predominant formation of one of the several possible stereoisomeric compounds is called *stereoselective* reaction. A reaction where a given isomer leads to one product while another stereoisomer leads to opposite product is called a *stereospecific* reaction. Let us illustrate this by examples.

Maleic acid when treated with bromine gives dl pair of 2, 3 dibromosuccinic acid while fumaric acid gives the meso isomer.



Maleic acid

dl pair of 2, 3
dibromo succinic acid



Fumaric acid

Meso isomer

These are stereospecific reactions in which a given isomer gives one product (or dl pair) while another stereoisomer gives the opposite product. So the starting compounds differ only in their stereoisomerism. So we can say that all stereospecific reactions are necessarily stereoselective but the converse is not true.

However if both maleic and fumaric acid gave the dl pair or a mixture in which the dl pair predominated, the reaction would be stereoselective but not stereospecific. If more or less equal amounts of dl and meso forms were produced in each case, the reaction would be stereoselective but not stereospecific. If more or less equal amounts of dl and meso forms were produced in each case, the reaction would be non stereoselective.

This means that if a reaction is carried out on a compound that has no stereoisomers, it cannot be stereospecific but at most stereoselective. The concerted reactions, including S_N^2 displacements, E2 elimination of alkyl halides, anti and Syn addition to alkenes are all stereoselective. In the case of chiral or geometric substrates the nature of the product depends on the unique stereoelectronic requirement of the reaction. These are examples of stereospecific reactions.

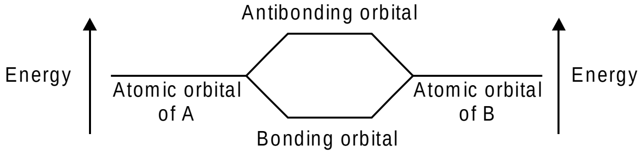
THEORY OF CONCERTED REACTIONS

Having learnt about the concerted reactions, we can now undertake the theory of these reactions. The development of the theory of concerted reactions has been due chiefly to the work of R.B. Woodward and R. Hoffmann. They have taken the basic ideas of molecular orbital theory and used them, mainly in a qualitative way, to derive selection rules which predict the stereochemical course of various types of concerted reactions. These rules are best understood in terms of symmetries of interacting molecular orbitals. Here are will see some of the most important theoretical approaches and see how they are interrelated.

Molecular Orbitals

We are familiar with *s* and *p* orbitals. The *p* orbitals are dumb-bell shaped each having a node, a region in space in which the probability of founding an election is extremely small. The lobes of a *p* orbital are labeled as + and –. These signs *do not refer to the positive and negative charges* since both lobes of an electron cloud are negatively charged. They are signs of the wave function ψ. When two parts of any orbital are separated by a node Ψ always has opposite signs on the two sides of the lobe.

We know that atomic orbitals combine to form a molecular orbital. When two atomic orbitals of comparable energy combine, they form two molecular orbitals, one of which is called the bonding molecular orbital and is of lower energy than each of the combining atomic orbitals and the other is of higher energy called the antibonding molecular orbital.



The orbitals of lower energy fill first. This means that the antibonding orbitals remain empty in the ground state. Molecular orbitals formed by the overlap of two atomic orbitals when the centers of electron density are on the axis common to the two nuclei are called σ (sigma) orbitals and the bonds are σ bonds. The corresponding anti orbitals are designated σ* or antibonding orbitals.

It is to be noted that σ orbitals are formed not only by the overlap of two *s* orbitals but by the overlap of any of the atomic orbitals (*s*, *p*, *d* or *f*) whether same or different, but the two lobes must have the same sign. A + *s* orbital can form a bond only by overlapping with another positive *s* orbital or with *a* + lobe of *a p, d* or *f* orbital.

In molecular orbital calculations, a wave function is formulated which is a linear combination of the atomic orbitals (also called LCAO) and is written as:

$$\psi = C_A\psi_A + C_B\psi_B$$

The functions ψ_A and ψ_B are functions of atomic orbitals of atoms A and B and C_AC_B are numerical coefficients which indicate the relative contributions of ψ_A and ψ_B to the molecular orbital.

HOMO and LUMO STRUCTURES

The highest occupied molecular orbital is designated as HOMO and the lowest unoccupied molecular orbital is designated as LUMO.

A positive overlap between the orbitals gives rise to the bonding orbitals while lack of overlap forms antibonding orbitals.

Now let us illustrate the HOMO and LUMO structures of same alkenes.

1. Ethylene System

We know that the parallel overlap of two *p* orbitals from two carbon atoms provides a double bond.

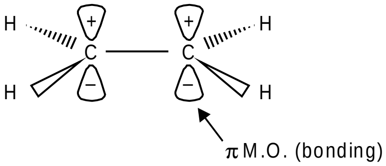
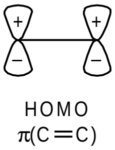
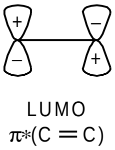


Fig. 3.4

The HOMO is that which results from the overlap of two *p* atomic orbitals of like phase, while LUMO is constructed from these two orbitals with opposite phases.

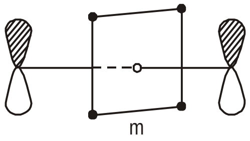




Thus in ethylene the combination of two *p* orbitals gives a π bonding orbital and a π* antibonding orbital. An important difference between the bonding and antibonding orbitals is their symmetry.

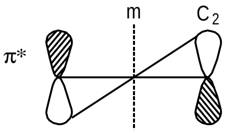
It is therefore possible to classify the various molecular orbitals according to their two independent symmetric properties which are as follows :

(*a*) Some molecular orbitals are symmetric about a mirror plane (*m*) which bisects the molecular orbitals and is perpendicular to the plane of the atoms forming the molecular orbital.



(*b*) On the other hand molecular orbitals, are known which do not have *m* symmetry as above but they show another type of symmetry about a two fold axis (called C_2) which passes at right angle in the same plane and through the centre of the framework of atoms forming the molecular orbital.

Symmetry of this type will be present if rotation of the molecule around the axis by 180° $\left(\frac{360}{2}\right)$ gives rise to a molecular orbital identical with the original.



So the picture of symmetry of orbitals of bonding and antibonding will be as follows:

Orbital	*m*	C_2
π*	A	S
π	S	A

Fig. 3.5

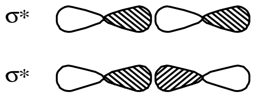
A = antisymmetric ; S = symmetric

Symmetry Properties of Ethylene

So we find that the ground state (π) orbital would be symmetric (S) with respect to the mirror plane *m* and antisymmetric (A) with respect to C_2 axis. On the other hand the antibonding orbital (π*) would be antisymmetric with respect to *m* and symmetric with respect to C_2 axis.

Symmetry Properties of Sigma Orbitals

The symmetry properties of sigma orbital of a C–C-covalent bond is having a mirror plane symmetry and because a rotation of 180° through its mind point regenerates the same σ orbital, it is also having C_2 symmetry. The σ* orbital would be antisymmetric with respect to both *m* and C_2 shown as follows:



Orbital	*m*	C_2
σ*	A	A
σ	S	S

For a linear conjugated π system the wave function ψ_n will have n–1 nodes. If n–1 is zero or an even integer ψ_n would be symmetric with respect to m and antisymmetric with respect of C_2. If n–1 is an odd integer ψ_n will be having the symmetry exactly reversed.

Table 3.1

Node (n–1)	*m*	C_2
Zero even integer	S	A
Odd integer	A	S

2. Butadiene System

The π-MO of butadiene are shown as below where the adjacent lobes of the same sign (phase) of *p* orbitals overlap while the adjacent lobes with opposite signs produce a node in the resulting MO. The 4 π electrons of butadiene are accommodated in the two bonding MO's *i.e.*, ψ_1 and ψ_2.

For ψ_1 there is zero node, and one node for ψ_2 and so on upto n–1 nodes for ψ_n.

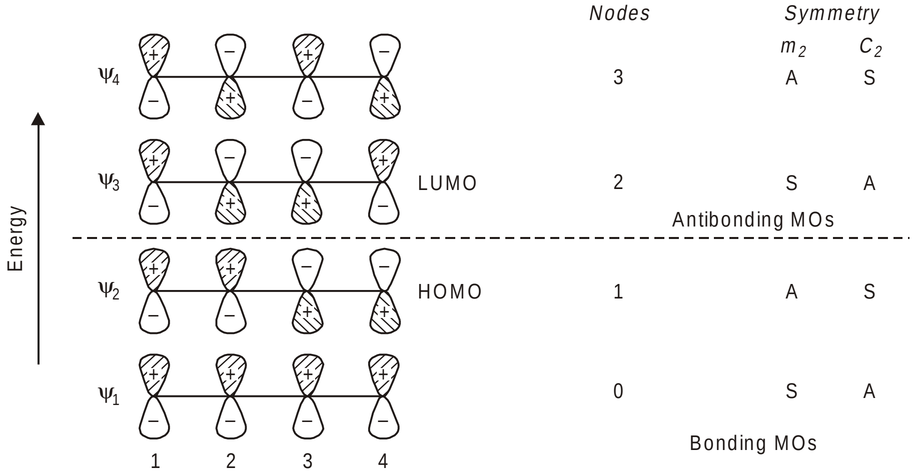


Fig. 3.6 The molecular orbitals of 1, 3 butadiene.

For polyenes *in their ground state*, the highest occupied MO (HOMO) will be symmetric with respect to m_2 for 2, 6, 10 ... π electron systems and antisymmetric for 4, 8, 12 ... π electron systems. The lowest unoccupied MO (LUMO) has the symmetry opposite to that of HOMO. In the first excited state, the LUMO of the ground state will become singly occupied because of the promotion of an electron and it will thus become the new 'highest occupied' orbital. Therefore in the circumstances the symmetry of the highest occupied orbital is opposite to that of the ground state.

	m	C_2
ψ_4	A	S
ψ_3	S	A
ψ_2	A	S
ψ_1	S	A

The coefficients of the various *p* orbitals of complex molecules containing π systems are obtained by computer programming based on approximate solutions of the Schrodinger wave equation.

FRONTIER ORBITAL APPROACH

Just as the outermost elections in an atom decides its chemistry, so the highest occupied molecular orbital (HOMO) decides its reactivity. This is called the frontier orbital.

The Frontier Molecular Orbital (FMO) approach was developed by K. Funkui for quickly predicting if a given pericyclic reaction (*i.e.*, reaction which involves a concerted reorganisation of elections within a closed loop of interacting orbitals) is allowed by examining the symmetry of the highest occupied molecular orbital (HOMO) and if the reaction is bimolecular, the interaction between the two components should be represented by interaction between suitable molecular orbitals of each. *The rule is that (for cycloaddition reaction) the reactions are allowed only when all overlaps between the highest occupied molecular orbital (HOMO) of one reactant and the lowest unoccupied molecular orbital (LUMO) of the other are such that a positive lobe overlaps only with another positive lobe and a negative lobe only with another negative lobe. Thus these HOMO-LUMO interaction are termed frontier orbital interactions.*

The extent of the interaction depends upon the geometry of approach of the components, since this affects the amounts of possible approach. It also depends upon the phase relationships of the orbitals and upon their energy separations. A small energy separation forms greater interaction.

Let us consider two ethylene molecules approaching each other in such a way that the top of one π system interacts with the bottom of the other. The HOMO of one π system must be matched with the LUMO of the other as shown. In both the cases the phase relationships at one end of the system are wrong for bond formation. So a concerted process in which both new σ bonds are formed simultaneously is not possible and the reaction will be termed a symmetry-forbidden reaction.

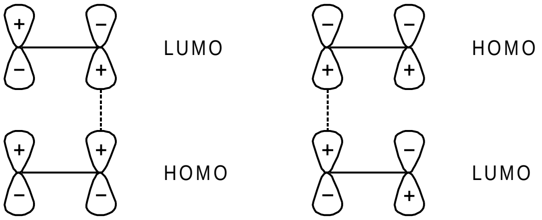


Fig. 3.7

Now let us take the case of a reaction between ethylene and an allyl anion. In both cases the HOMO-LUMO interaction leads to bonding at both terminals.

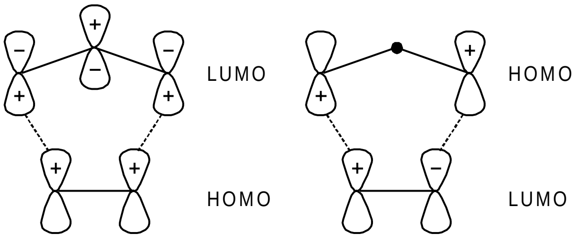


Fig. 3.8

These like phases are combining. Therefore the symmetry is allowed. It is to be noted that the terms 'symmetry allowed' and 'symmetry forbidden' only refer to the concerted processes.

Conjugated Triene

Now let us draw the molecular orbitals of a conjugated triene like 1, 3, 5 hexatriene.

$$CH_2 = CH–CH = CH–CH = CH_2.$$

The configuration of six π elections in the ground and the first excited state is as follows:

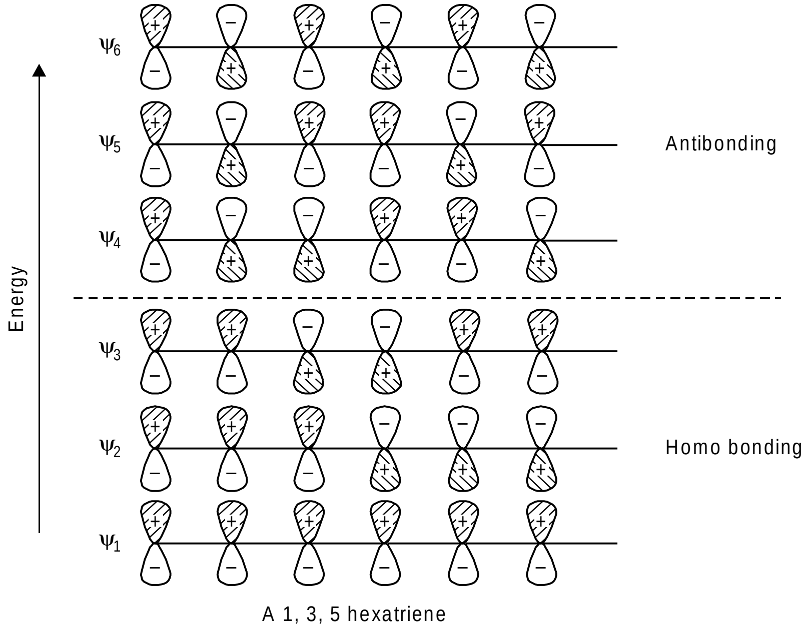


Fig. 3.9

It is to be noted that the relative symmetry about the terminal carbon atoms of HOMO of 1, 3 butadiene (ψ_2) and 1, 3, 5 hexatriene (ψ_3) is opposite.

Based on the number of π electrons in polyenes, we can predict which type of intermolecular cycloadditions will be symmetry allowed. The close in energy the frontier orbitals are, the stronger will be the interaction between them and therefore the more easily the reaction will occur. The orbital coefficients at the interacting centres can also influence the rate and the direction of addition.

Summarising we have the symmetry properties in hexatriene as follows:

	m	C_2
ψ_6	A	S
ψ_5	S	A
ψ_4	A	S
ψ_3	S	A
ψ_2	A	S
ψ_1	S	A

CHAPTER 4

Pericyclic Reactions

INTRODUCTION

It has long been known that unsaturated compounds containing a delocalized system of π electrons can rearrange into cyclic compounds or other π systems. Such reactions were only incidentally studied until 1930. O. Diels and K. Alder published their first paper on diene synthesis (which was later given the name Diels-Alder reaction) in 1928. Subsequent work of K. Alder and G. Stein (1933 and 1937) proved the generality of the reaction and its high regio and stereo selectivity. This led to the interest on thermal transformations in unsaturated compounds.

Pericyclic Reactions

In 1969 R.B. Woodward and R. Hoffmann introduced the term pericyclic reactions to differentiate those reactions which have a

(*i*) a common cyclic transition state;
(*ii*) are highly stereospecific; and
(*iii*) their stereochemistry depending on the total number of π and σ electrons involved in the formation or breaking of bonds.

Thus pericyclic reactions are intra or intermolecular processes which involve concerted reorganisation of electrons within a closed loop of interacting orbitals.

Five classes of pericyclic reactions have been recognized.

(*a*) Cycloaddition reactions
(*b*) Sigmatropic reactions
(*c*) Electrocyclic reactions
(*d*) Cheletropic reactions
(*e*) Group transfer reactions

CYCLOADDITION REACTIONS

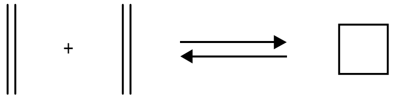
Cycloadditions form a very extensive and rapidly expanding area of chemistry, the synthetic potential and theoretical significance of which have been recognized only recently.

Carbanion reactions, reactions of alkenes with electrophiles, nucleophilic additions to carbonyl compounds, metal promoted and organomettalic reactions fall in this category. The reactions to be discussed under this heading result in the formation of a new ring from two reacting molecules. In general the cyclic transition contains four, five or six atoms. Energy required to reach the transition is provided by thermal or photochemical excitation of the reacting molecules. Other polar or radical generating reagents having high chemical potential energy are not usually involved. A concerted mechanism requires that a single transition state and therefore no intermediate lie on the reaction path between reactants and adduct. In such reactions the σ bonds are formed but not broken.

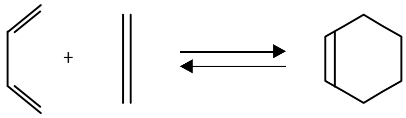
Examples

According to the above definition the examples include :

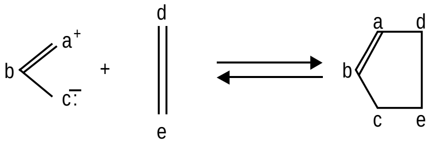
(*a*) Dimerisation of olefins



(*b*) Diels-Alder reaction

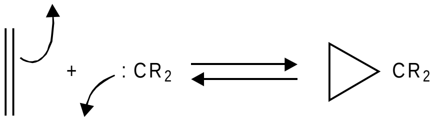


(*c*)



Reactions *b* and *c* are examples of diene synthesis:

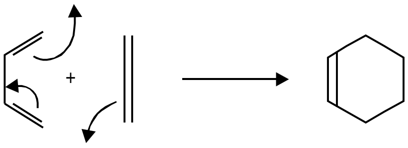
(*d*)



Classification

Cycloaddition involves the generation of a cyclic system structure at the termini of two isolated π system. The new σ bonds arise at the expense of π electrons of the reacting molecules. Thus cycloadditions are $n\ \pi \rightarrow n\ \sigma$ transformations with $n \geq 2$.

Huisgen first tried to classify cycloadditions according to the termini of one reaction partner, usually with longer chain. Thus Diels-Alder reaction is a 4 + 2 cycloaddition.

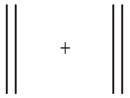
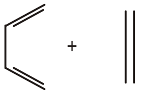
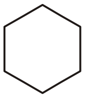
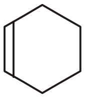
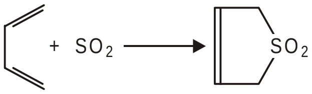
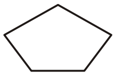
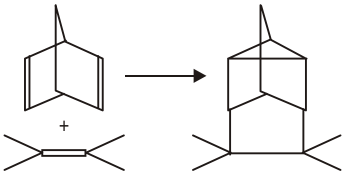
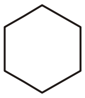


Similarly olefine dimerisation is a 2 + 2 cycloaddition. However this nomenclature is sometimes ambiguous.

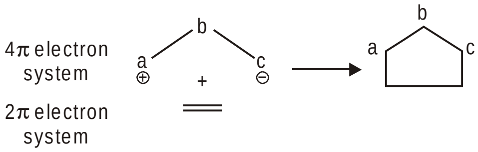
Classification based on the Number of Electrons

The system generally adopted recognized the fundamental importance of the number of electrons involved in cycloaddition and classifies the reactions on this basis.

Table 4.1. Classification of Cycloadditions

Name	*Examples*	*Type of ring involved*	*Types of transformation*
$2\pi + 2\pi$ dimerisation of olefine		(*a*) 	(1) $2\pi - 2\sigma$ cycloadditions
$4\pi + 2\pi$		(*b*) 	
4π + I fragment			(2) $2\pi - 2\sigma$ fragmentation
2 + 2 + 2 cycloaddition			(3) $3\pi - 3\sigma$ cycloaddition

In many of the above examples the number of electrons happens to be the same as the number of atoms in each component. But this is not always the case. For example in 1, 3 dipolar cycloaddition, the 1, 3 dipole has four electrons distributed on three atoms. The addition of a 1, 3 dipole to an olefine will give 3 + 2 carbon atoms in the ring but it will have $4\pi + 2\pi$ electrons according to the adopted system



Cycloadditions are usually reversible, the reverse reaction being called fragmention or cycloreversion. The latter can be designated in the same manner as for cycloaddition.

GENERAL RULE FOR PERICYCLIC REACTIONS

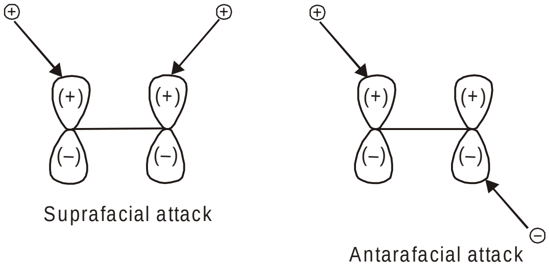
A general rule for determining the stereochemical course of concerted reactions has been put forward by R.B. Woodward and R. Hoffmann.

Let us consider a pericyclic reaction in which the electrons of a π system are used in the transition state and new bonds are being formed. The question arises in how many ways the orbitals can react? There are only two ways in which the orbitals will react.

1. When the orbitals undergoing the change lie on the same face of the molecules which are reacting (called suprafacial way).

or

2. When the overlap of the reacting orbitals or product orbitals occurs on the opposite faces of the reacting molecules (called antarafacial way).



Bonding π orbital overlap of ethene with atomic S orbital.

Fig. 4.1

The same definitions apply to longer π systems Suprafacial use of a σ bond involves bonding in the same way at both terminals. So there is retention of configuration at both ends or inversion a both ends.

Fig. 4.2

Antarafacial use of a σ bond involves retention at one end and inversion at the other.

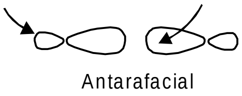


Fig. 4.3

Subscripts *s* and *a* are used to indicate a supra and an antara process respectively. Suprafacial, suprafacial (*s*, *s*) approach of two polyenes is normally sterically suitable for efficient orbital overlap. The vast majority of concerted additions involves the *s*, *s* approach.

WHAT IS SYMMETRY ALLOWED AND SYMMETRY FORBIDDEN REACTION?

A pericyclic reaction is allowed if orbital symmetry is conserved. In such reactions there is conversion of the ground (electronic) state of reactant into the ground state of the product. Such reactions are said to be thermally allowed, or there is the conversion of the first excited state of the reactant into the first excited state of the product. There are photo-chemically allowed reactions.

A pericyclic reaction is forbidden if its orbital symmetry is not conserved. In such reactions the occupied orbitals of the reactant do not transform into the occupied orbitals of the product with the same symmetry.

The details of symmetry forbidden reaction will be clear when we study the cycloaddition of ethene described later.

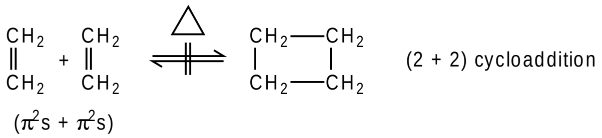
Woodward-Hoffmann Rule

It is a general rule for pericyclic reactions and predicts if a given pericyclic reaction will be allowed under a given set of conditions. The rule is as follows :

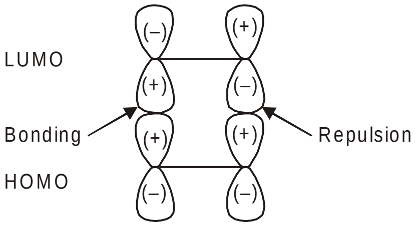
'A ground state pericyclic change is symmetry allowed when the total number of (4*q* + 2) superfacial and 4*r* antarafacial components is odd' (*q* and *r* being zero or any integer).

To apply the rule we first draw the orbital picture of the reactants and show a geometrically feasible way to achieve overlap. Then the (4*q* + 2) suprafacial electrons and 4*r* antarafacial electrons of the components is counted. If the total is an odd number, the reaction is thermally allowed.

Let us take the hypothetical cycloaddition of ethene to give cyclobutane.

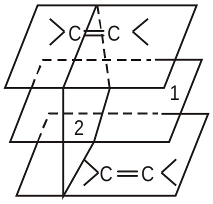


If the two molecules approach each other with their **molecular planes parallel,** the LUMO of one will react with the HOMO of the other as shown.

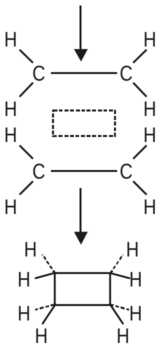


Reaction is symmetry "forbidden"

Fig. 4.4



Parallel overlap of ethylene



The reaction via a planar transition state is $\pi^2 s + \pi^2 s$. Here only one of the two new C—C bonds can be formed. This will raise its activation energy impossible to be reached. So there are two ($4q + 2$) electron suprafacial components and no antarafacial component. Since the total number of counting components is two, an even number, the reaction is thermally disallowed.

But if the approach of the **molecular planes is perpendicular,** *i.e.*, when one surface of the π orbital of one molecule interacts with both surfaces of the π orbital of the other molecule, then cycloaddition will be allowed here but the geometry of the approach will be the deciding factor and geometrically it is inaccessible.

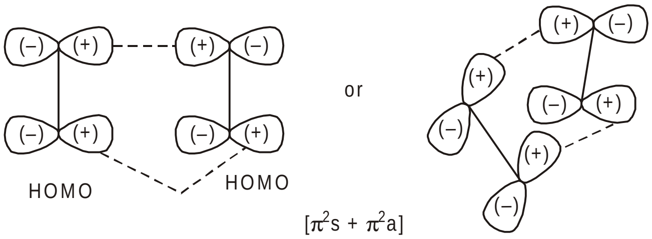
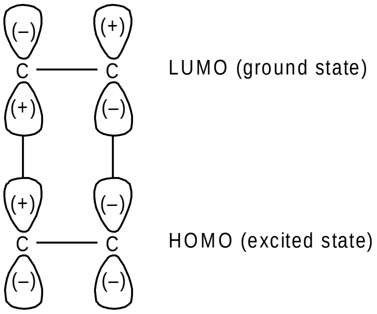


Fig. 4.5

The above interaction is suprafacial with respect to one component and antarafacial with respect to the other and is therefore a [$\pi^2 s + \pi^2 a$] process. A bonding interaction could occur between two pairs of lobes of the same sign, but the nearer alkene molecule would need to twist about its original π bond, and so it will make it geometrically inaccessible.

So summarizing we see that in thermal [2 + 2] cycloaddition, a supra-supra process is geometrically possible but symmetry forbidden. But in supra-antar process, symmetry is allowed but geometrically difficult. Now we have to explain how the photochemical formation of cyclobutane takes place from 2π components.

In photochemical process there is an excitation of an electron from the HOMO of one component to the next higher orbital which now makes this the HOMO having the opposite symmetry. This change will permit a previously forbidden reaction to become an allowed process. Thus a ($\pi^2 s + \pi^2$s) cycloaddition is symmetry allowed under photochemical conditions, which was not possible under thermal conditions.



The photochemical combination

Fig. 4.6

The flanking groups from the same lobe (suprafacially) or from opposite lobes (antarafacially).

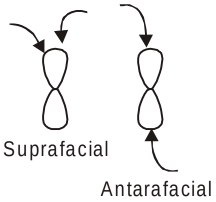
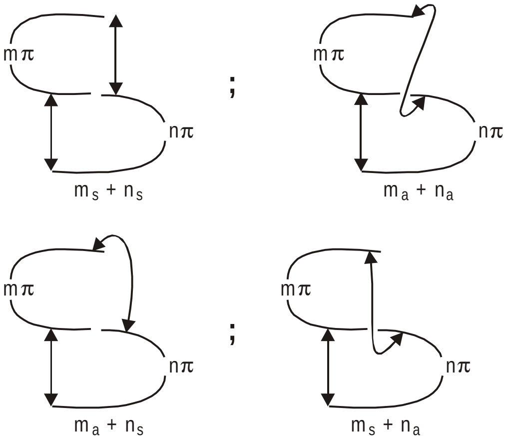


Fig. 4.6

The symbols π, σ and ω are given respectively to the π systems, σ bonds and lone *p* orbitals which participate in the transition state and the symbols (*s*) and (*a*) are indicated for their suprafacial and antarafacial use. The notation is completed by the number of electrons supplied by each component. Thus π^2s denotes a two electron π system used in a suprafacial way. wo_a indicates a vacant *p* orbital used in an antarafacial way and so on.

The cyclodimerisation of ethylene via a planar transition state is therefore a $\pi^2s + \pi^2s$ reaction. Since there are two $(4q + 2)$ electron suprafacial components and no antarafacial components, the total number of counting components is two, an even number. Hence the reaction is thermally disallowed.

In antarafacial cycloaddition new bonds develop on opposite sides of the π system. If the number of components in a cycloaddition is considered, the possible pathways become still more numerous. For m+n cycloadditions, where *m* and *n* are different, four different pathways are conceivable, distinguished by the stereochemistry of the resulted adducts : $m_s + n_s$, $m_a + n_a$ and $m_a + n_s$ and $m_s + n_a$.



$m_s + n_s$ $m_a + n_a$

$m_a + n_s$ $m_s + n_a$

Possible interactions in an m + n cycloaddition

Fig. 4.7

In this way Hoffmann and Woodward have established the following simple rule : a concerted $m + n$ cycloaddition will be symmetry allowed in the ground state and symmetry forbidden in the excited state if $m + n = 4q + 2$ (q = 0, l, 2...); if $m + n = 4q$ the reaction will be symmetry allowed in the excited state and symmetry forbidden in the ground state. This rule applies to $ms + ns$ cycloadditions and to $m_a + n_a$ processes.

The following table summerises all the rules for cycloaddition reactions.

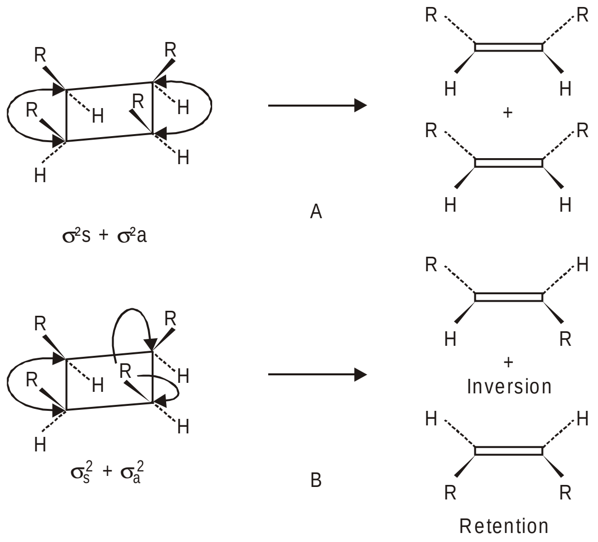
Table 4.2. Generalized rules for cycloaddition reactions

m + *n*	*Allowed in the ground state* *Forbidden in the excited state*	*Allowed in the excited state* *Forbidden in the ground state*
4q	$m_s + n_a$ $m_a + n_s$	$m_s + n_s$ $m_a + n_a$
4q + 2	$m_s + n_s$ $m_a + n_a$	$m_s + n_a$ $m_a + n_s$

The antara-supra processes, even if less studied than the more common supra-supra reactions are frequently encountered in recent works on cycloaddition reactions and confirm in their turn the utility of orbital symmetry considerations.

σ Bonds Involved in Cycloaddition Reactions

The theory of concerted cycloadditions may be extended to other reactions involving σ bonds. For instance, let us consider the cyclobutane fragmentation into two molecules of ethylene.



Fragmentation of substituted cyclobutanes into ethylenes.

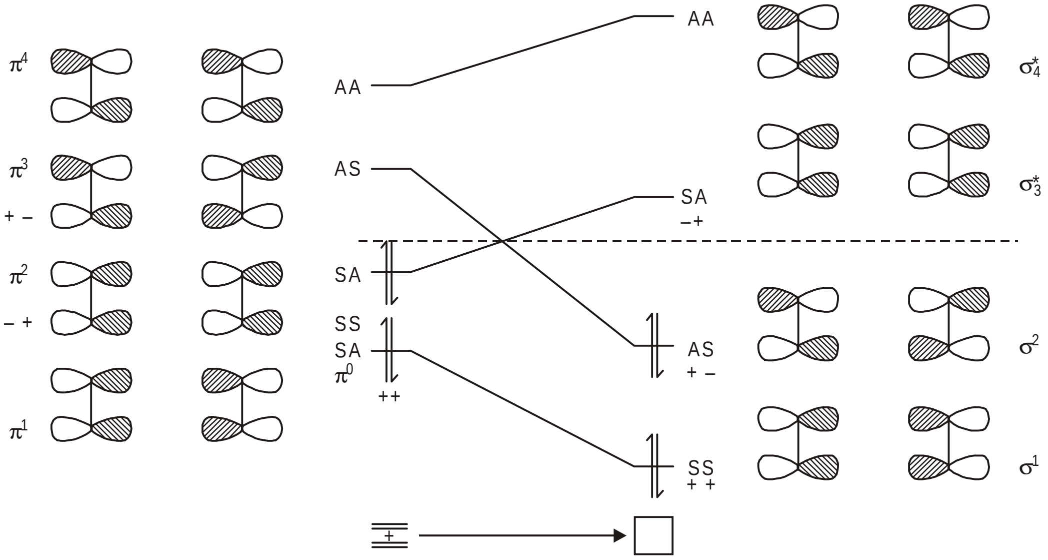
A σ bond is considered to be involved in a cycloaddition in a **supra** manner if configuration is either retained or inverted at both of its termini in the course of the reaction. The retention of the configuration at one terminus and the inversion at the other will indicate an antara addition.

The **all cis.** cyclobutane will yield only a cis alkene. Configuration is retained (or inverted) at both termini of the two σ bonds involved, the reaction is a **supra-supra** process as in A. In B a cis alkene and a trans alkene are formed. Thus at both the termini of one σ bond the configuration is retained only at one terminus and not at the other. The process will be supra-antara.

During cycloadditions (addition of π bonds to π bonds, a subscript (π or σ) preceding the number of electrons in the relevant orbital is added, for example $\pi^2 s$; $\sigma^2 s$; $\sigma^2 a$ etc.

Energy Level Diagram in Cycloaddition

The energy level diagram is constructed by placing on the left side the energy levels of the orbitals of the reactants and on the right side the energy levels of the product which indicate their symmetry. We notice that a bonding reacting level in the reactant is correlated with the antibonding level in the product.



Energy level diagram of 2 + 2 cycloaddition

Fig. 4.8

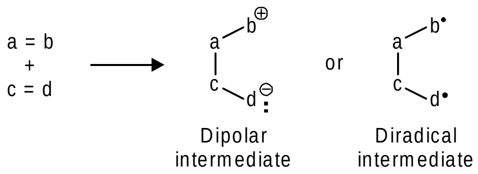
Orbitals π_1 and π_2 are combinations of the bonding π orbitals of ethylene and are therefore of equal energy. π_3 and π_4 are combinations of antibonding π orbitals and are also of equal energy. Similarly σ_1 and σ_2 are bonding σ_3^* and σ_4^* antibonding.

Thus the dimerisation of ethylene to cyclobutane involves the transformation of four π orbitals (two bonding and two antibonding) into 4σ orbitals. The orbitals of a single ethylene molecule do not relate to the symmetry of the reaction as a whole, nor does a single σ bond of the cyclobutane. We need to combine the separate orbitals in appropriately symmetrical ways. This is illustrated in the above diagram which indicates that the π_2 orbital pair of ethylene transforms into high energy σ_3 orbital pair of cyclobutane. This suggests that the ground state thermal reaction is **symmetry forbidden** and the diagram also reveals a high activation energy reaching up into the cross over region. However if the electrons are promoted to antibonding orbital, as in a photochemical reaction, the process is **symmetry allowed** in the excited state, (already discussed).

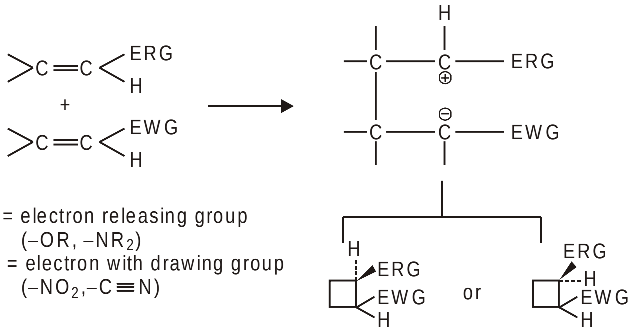
The theory again accords the observation that dimerisation is almost invariably a photochemical process. Such conclusions can also be reached qualitatively without detailed calculations, but for precise estimations of the energies involved in the more complex cases, elaborate calculations are necessary.

Some More Examples of 2 + 2 Cycloadditions

The cyclodimerisation of fluorinated alkenes and formation of cyclobutane from alkenes activated by electron withdrawing groups has formed great application in laboratory and industry recently. Either dipolar intermediate or diradicals may result in the rate determining step. The examples are afforded by the 2 + 2 cycloadditions of ketenes with alkenes.

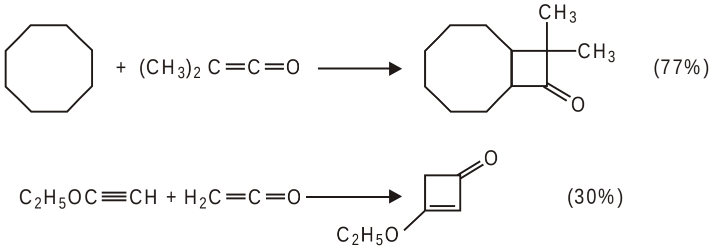


Dipolar species have been observed in the cycloaddition of polar intermediates. Thus cyclobutanes can be formed by non concerted processes involving zwitter ionic intermediates. The combination of an electron rich alkene (enamimes, enol ethers) and an alkene having electron withdrawing groups (nitro a cyano substituted alkenes) first gives a zwitter ion which can rotate about the newly formed bond before cyclization and gives both a cis and a trans adduct.



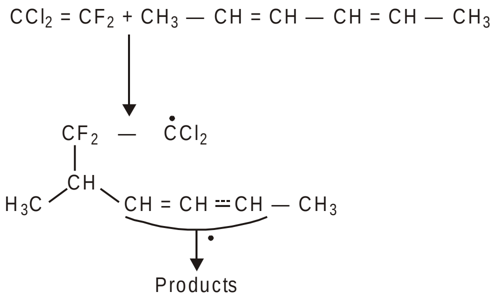
ERG = electron releasing group ($-OR$, $-NR_2$)
EWG = electron with drawing group ($-NO_2$, $-C\equiv N$)

Ketenes are especially reactive in 2 + 2 cycloadditions because they offer a low degree of steric hindrance at one center-the carbonyl group and a low energy LUMO.

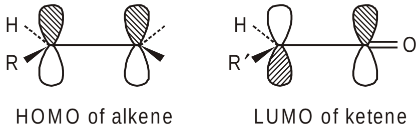


In reactions with tetracyanoethylene, the stereochemistry of the double bond of an enol ether is retained in the cyclobutane product when the reaction is carried out in non polar solvents. In polar solvents, cycloaddition is non stereospecific because of the longer life time of the zwitter ion.

Diradical intermediates are found more commonly in thermal 2 + 2 cycloadditions. The best substrates for such additions are fluoroalkenes and allenes. Thus P.D. Bartlett and his coworkers have demonstrated that the cycloaddition of 1,1-dichloro-2,2 difluroethylene to stereoisomeric hexa-2, 4 dienes yields a mixture of isomeric products in a non stereospecific way.



Thermal concerted 2 + 2 reactions are predicted to occur between an alkene and a ketene. According to Woodward-Hoffmann rules, addition must be suprafacial to one component and antarafacial to the other if the process is to be concerted.



Frontier orbitals of alkene and ketene

Minimizing the steric interations in the transition state (between R and R′), it leads to a cyclobutanone product in which these substituents are cis

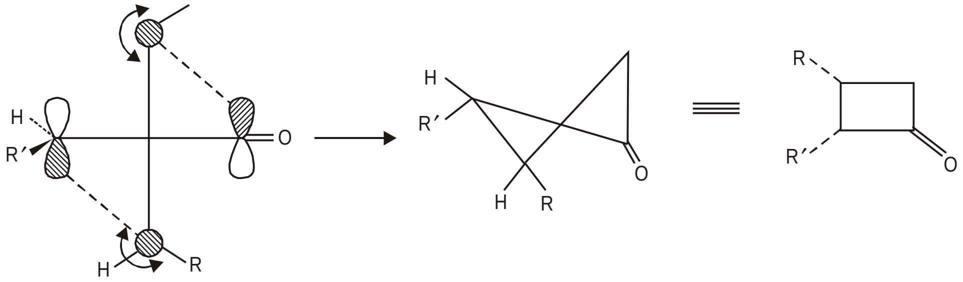
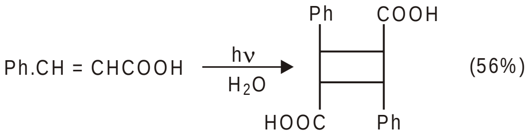


Fig. 4.9

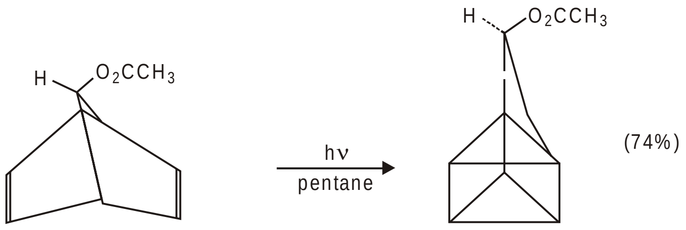
Ketenes are especially reactive in 2 + 2 cycloaddition because they offer a low degree of steric hindrance at one center-the carbonyl group and a low energy LUMO.

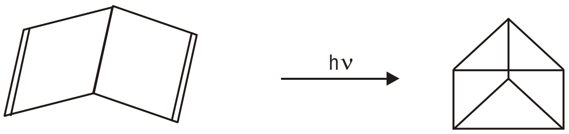
Photochemical Cycloadditions

The reaction types which includes 2 + 2 cycloaddition and carried out by photochemical means have also great synthetic potentiality. The photodimerisation of cinnamic acids were among the earliest photochemical reactions to be studied. These compounds give good yield of dimers when irradiated in the crystalline state. In solution, cis-trans isomerisation is the dominent reaction.

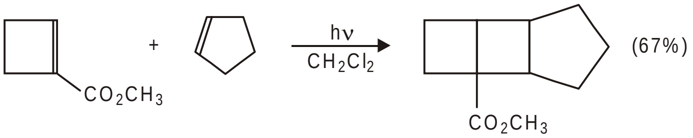


Cycloaddition of carbon-carbon double bonds can also occur intramolecularly. If the two double bonds are in the same molecule, the concerted reaction may have high yields as in the following examples.





Yields are best for aromatic ketones and aldehydes.



Such 2 + 2 cycloadditions also confirm the generality of Woodward-Hoffmann rule.

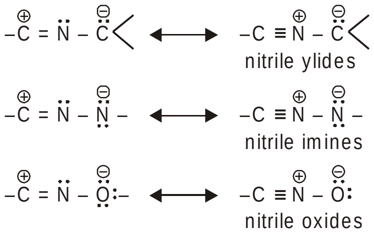
2 + 3 Cycloadditions (1, 3 dipolar cycloadditions)

The 2 + 3 cycloaddition implies a reaction between 1, 3 dipole and an unsaturated compound called dipolarophile. The product of the reaction is a five membered heterocycle. Its theory has been develoed by R. Huisgen. According to him there are four classes of dipoles distinguished by their bonds and the way they are stabilized by conjugation.

(*a*) Dipoles with double bond in which the electron deficient atom acquires the octet by conjugation with unshared electrons from the adjacent atom.

$$\overset{\oplus}{a}=\ddot{b}-\overset{\ominus}{\ddot{c}}: \longleftrightarrow a\equiv\overset{\oplus}{b}-\overset{\ominus}{\ddot{c}}:$$

The central atom must have a lone pair of electrons and must be able to develop for bonds. It can therefore be only a nitrogen atom. Atoms *a* and *c* can be carbon, nitrogen or oxygen.



$$-\overset{\oplus}{C}=\ddot{N}-\overset{\ominus}{\ddot{C}}\!< \longleftrightarrow -C\equiv\overset{\oplus}{N}-\overset{\ominus}{\ddot{C}}\!<$$

nitrile ylides

$$-\overset{\oplus}{C}=\ddot{N}-\overset{\ominus}{\ddot{N}}- \longleftrightarrow -C\equiv\overset{\oplus}{N}-\overset{\ominus}{\ddot{N}}-$$

nitrile imines

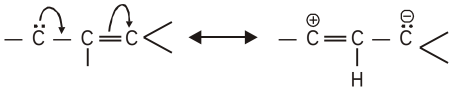
$$-\overset{\oplus}{C}=\ddot{N}-\overset{\ominus}{\ddot{O}}:- \longleftrightarrow -C\equiv\overset{\oplus}{N}-\overset{\ominus}{\ddot{O}}:$$

nitrile oxides

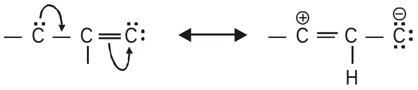
(*b*) Dipoles with double bonds and without octet stabilization. Such dipoles are similar to vinyl carbons.

$$\ddot{a}-b=c \longleftrightarrow \overset{\oplus}{a}=b-\overset{\ominus}{\ddot{c}}:$$

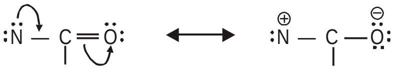
The examples are vinyl carbenes, keto carbenes or ketoimines.



vinyl carbenes

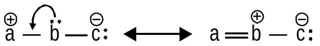


keto carbenes



keto imines

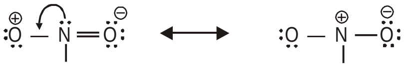
(*c*) Dipoles without double bond and with octet stabilization. The central atom can be either nitrogen or oxygen, where as the marginal atom may be carbon, nitrogen or oxygen.



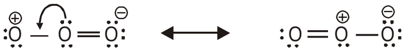
The electron deficient atom is stabilized by conjugation with the unshared electrons of the adjacent atom.

The examples are azoxy compounds, nitro compounds or ozone.

azoxy compounds

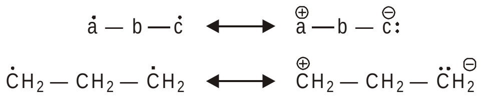


nitro compounds



ozone

(*d*) Dipoles without double bond and without octet stabilization. An example of this class is trimethylene.

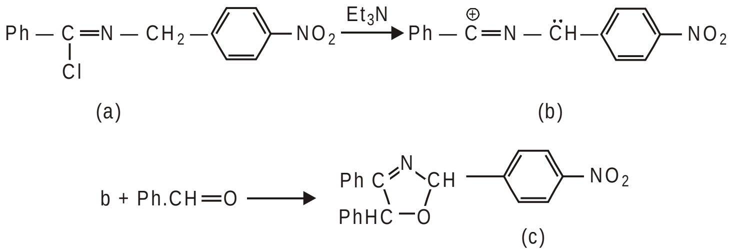


Such 1, 3 dipolar additions show a striking similarity with diene additions. If the 1, 3 dipolar species is a stable compound, the reaction takes place just by mixing the components with or without heating. They take place in absence of any catalyst or light.

Kinetic measurements have shown that the reaction is a second order (first order in each component), the rate constant is slightly affected by polarity of the solvent.

The 1, 3 cycloadditions are highly stereospecific and the concertedness of the reaction is demonstrated by the orientation of the reagents in the transition state.

The formation of the adduct (*c*) can be explained by the steric demands in the two components as in the diene addition, the reagents must approach each other from the least hindered side.



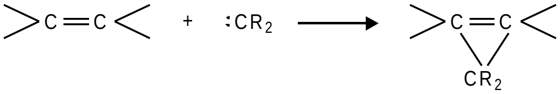
There also appears to be great similarity between 1, 3 dipolar addition and the Diels-Alder reaction (which is 4 + 2 cycloaddition) described in the later pages.

Some Other Examples of Cycloadditions

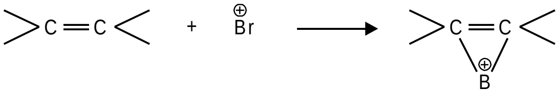
Before describing 4 + 2 cycloaddition, we also have examples of 2 + 1 cycloaddition.

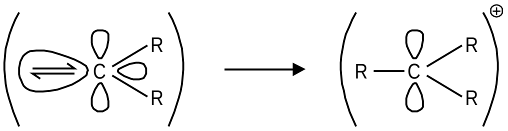
2, 1 cycloaddition

These cycloadditions lead to the formation of three membered rings commonly seen in the carbene addition to double bonds.



We know that carbenes have either a singlet or triplet structure. The addition of singlet carbene gives a halogenium ion and is therefore stereospecific.

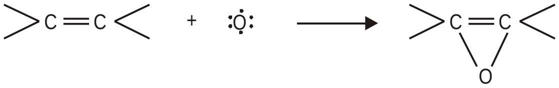


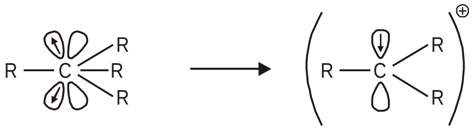


singlet carbene

It leads to the formation of carbenium ions which is trigonal.

The addition of a triplet carbene is similar to the addition of atomic oxygen.

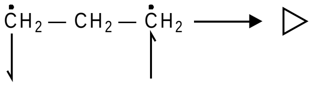




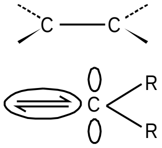
triplet carbene

It is non stereospecific. So the stereochemistry of the product reveals us whether the carbene was singlet a triplet.

The cycloaddition of methylene :CH_2 to ethylene has indicated that the components can be correlated in the ground state with the ground state trimethylene. The reaction is thus symmetry allowed in the ground state.



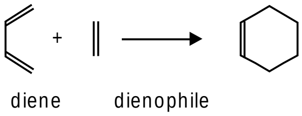
In the transition state, the reagents should approach each other in a non-symmetric way as proposed by P.S. Skell and A.Y. Garner.



4 + 2 Cycloadditions Diels-Alder Reaction

General Features

The reaction between a conjugated diene with a monoene to give a six membered ring compound is the best known example of 4 + 2 cycloaddition and bears the name of two workers Diels-Alder who first recognized the scope of the reaction and began investigating into its mechanism. Most of the evidence goes to show that it is a concerted reaction which involves simultaneous formation of two new σ bonds.



Diels-Alder reaction

The reaction is carried out simply by heating a diene or another conjugated system of π bonds with a reactive unsaturated compound (dienophile). Usually the reaction is not sensible to catalysts and light does not affect the course. Depending on the specific components, either carboxylic or heterocyclic products can be obtained. The stereospecificity of the reaction was firmly established even before the importance of orbital symmetry was recognized. In terms of orbital symmetry classification, the Diels-Alder reaction is a $\pi^4s + \pi^2s$ cycloaddition, an allowed process.

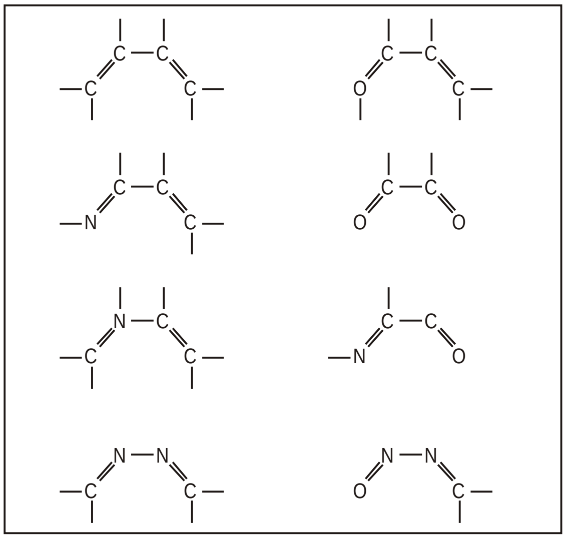
SCOPE OF DIELS ALDER REACTION

The great advantage of Diels Alder reaction in organic synthesis lies in its high stereoselectivity. Examples of Diels-Alder reactions are known for almost all types of π bonds acting as dienophiles. The diene system may be all carbon or there may be many variations as shown in the following tables.

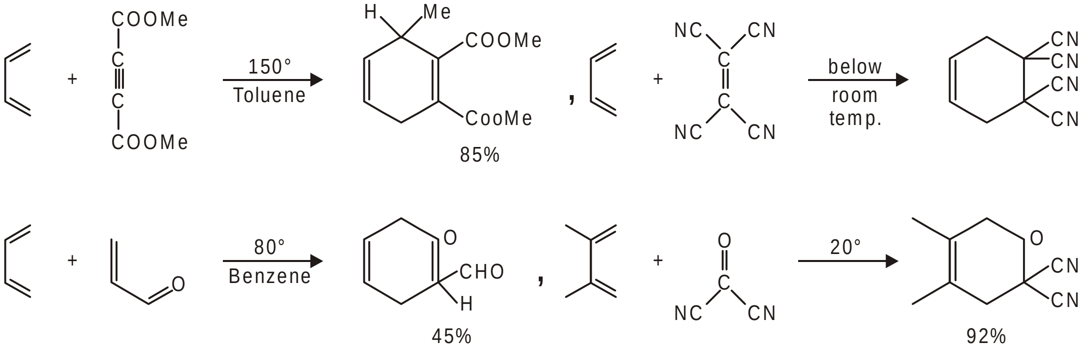
Table 4.3 Examples of Dienophiles

>C=C<	O=O (singlet O_2)
–C≡C–	–N=S
>C=N–	>Si=C<
>C=O	>C=S
–N=N	

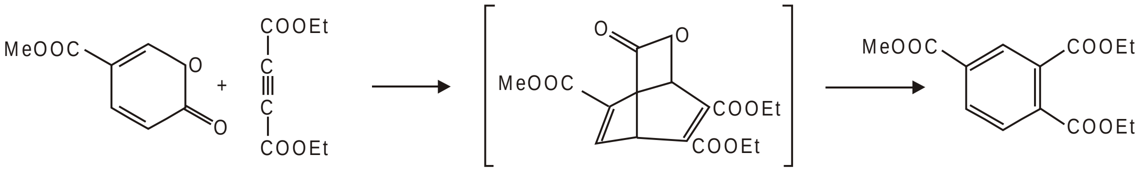
Table 4.4 Systems acting as dienes



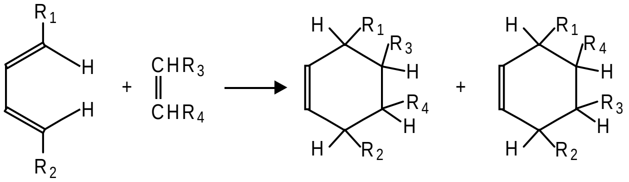
Thus the considerable variation possible in the structures of both diene and dienophile makes the Diels-Alder reaction a very versatile synthetic route to both carboxylic and heterocyclic compounds. Some examples are:



The synthetic utility of Diels-Alder reaction becomes still greater when an adduct gives components different from those from which it was formed. This is called **retro-Diels-Alder reaction** an example of which is an follows :



If in the reactions of a substituted diene with an alkene, if chiral centers developed in the reaction are considered, then the number of isomers developed becomes very large. For example in the following case, four chiral centers are developing and so the number of isomers formed becomes 32 depending upon different orientations.



Actually one orientation predominates (called high regioselectivity) and only one diastereoisomer is produced (called high stereoselectivity). The Diels-Alder reaction is reversible and may be carried out under thermodynamic or kinetic controlled conditions.

Kinetic Studies

The Diels-Alder reaction is a second order reaction, first order in each component.

$$\text{Rate} = k_2 \text{ [diene] [dienophile]}$$

The presence of Lewis acids, through not necessary may accelerate the reaction rate and affect regioselectivity.

The reverse reaction, the retro-Diels-Alder reaction is a clean first order reaction, both in the gaseous and condensed phase.

$$\text{Rate} = k_1 \text{ [adduct]}$$

The above two rate reactions are in agreement with a concerted reaction.

Stereochemistry and Endo and Exo Addition

A normal Diels-Alder reaction is a ($\pi^4 s + \pi^2 s$) cycloaddtion and the stereochemistry of both the diene and alkene is retained in the cyclization process. The diene and alkene approach each other in parallel planes. The bonding ineraction involves between C_1 and C_4 of the diene and carbon atoms of the dienophilic double bond are in a six center arrangement as illustrated below :

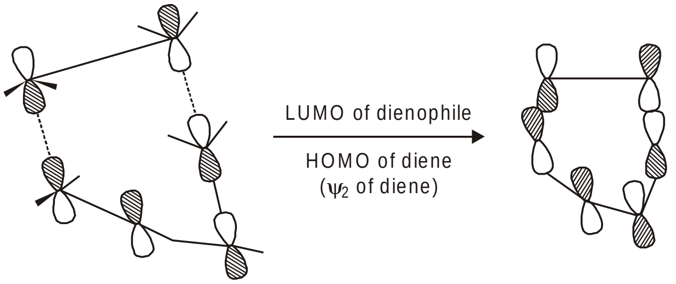
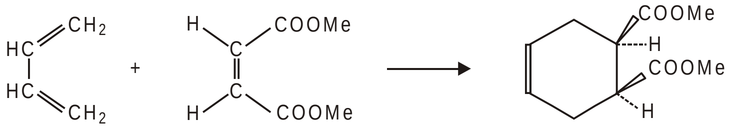


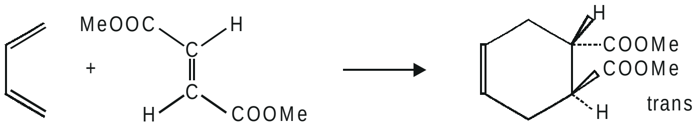
Fig. 4.10 A normal Diels-Alder reaction, cycloaddition of ethane and 1,3 butadiene.

Thus we find that the reaction is a syn (suprafacial) addition with respect to both the diene and dienophile. The frontier orbitals involved shows that the reaction occurs by interaction of HOMO and LUMO. So there is no possibility of substituents to change their position. Substituents which are on the same side of the diene or dienophile will be cis on the newly formed ring as is seen between the reaction of dimethyl maleate (a cis dienophile) with 1,3 butadiene. The product formed is cis 4,5 dicarbomethoxy cyclohexane.

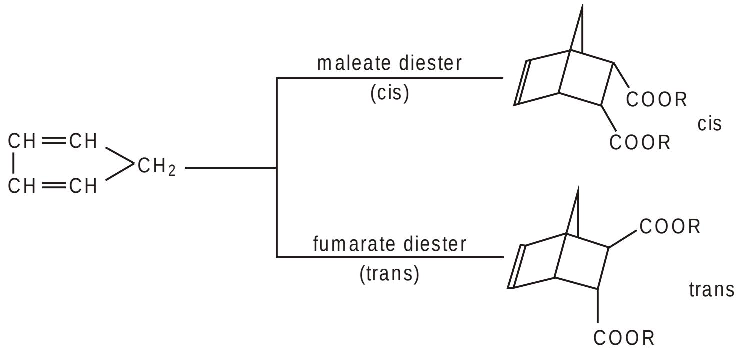


Cis 4, 5 dicarbomethoxy cyclohexane.
No trans isomer is formed

But 1, 3 butadiene with dimethyl fumarate gives a trans product



How the relative orientation of substituents is preserved in the adduct is also illustrated by the combination of cyclopentadiene with the two isomers of 1, 2 disubstituted dienophile. Here the cis isomer gives the cis product and the trans isomer, the trans adduct.



Cis-addition is the normal result of a synchronous bond formation in a $\pi^4 s + \pi^2 s$ cycloaddition and needs no further comments.

Variations to the cis addition have been found in the transtition state in some cases and a mixture of products has been reported. Two possible stereochemical variations have been reported because of **endo and exo addition**. Thus in the dimerisation of butadiene Hoffmann and Woodward have shown that besides the primary orbital interactions between C_1 and C_4 of the diene and C_1 and C_2 of the dienophile, there are also secondary interactions (shown by dotted lines and also called endo addition) between C-2 of the dieno and C-3 of the dienophile. Such orientations are only possible in endo orientation and this will stabilize the transition state.

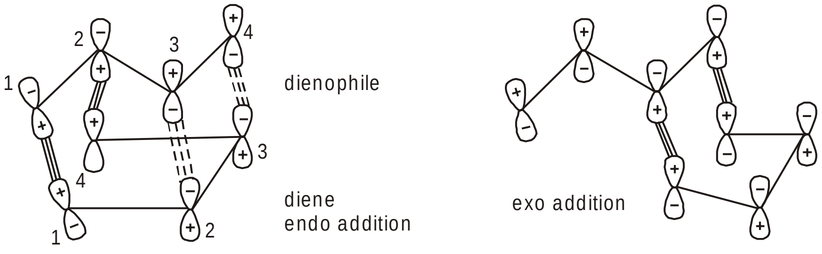


Fig. 4.11

Such addition will not be possible in exo-orientation.

These secondary interactions play an important role in cycloadditions having highly electron deficient dienophiles.

The indimerization of cyclopentadiene again two products are formed, the major being formed by the endo addition. Here also there are secondary bonding interactions.

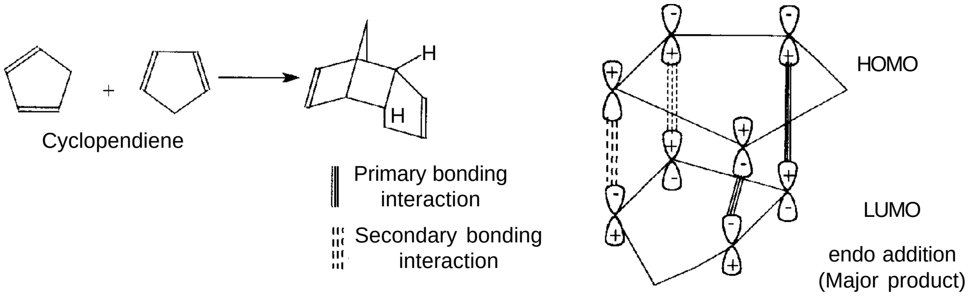


Fig. 4.12

The exoaddition will be as follows :

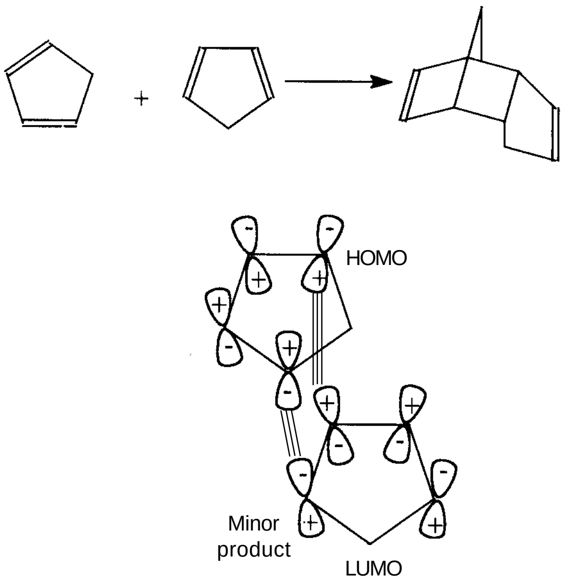


Fig. 4.13

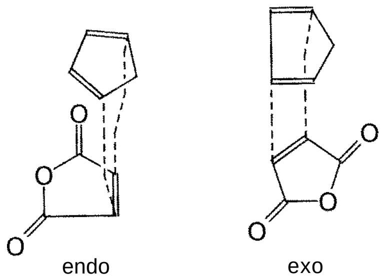
In these dimerisations one molecule acts as a diene and the other as the dienophile. The endo product is thermodynamically less stable and secondary interactions tend to reduce the activation energy. No such interactions are possible for the exo transition state.

Some more examples of endo addition

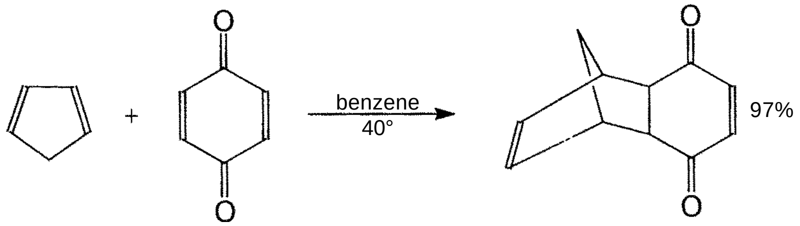
(1) Addition of maleic anhydride to cyclopentadiene.

Here also two orientations are possible and the endo product predominates. Sometimes the exo adducts are completely excluded.

Sometimes the initially formed endo adduct may isomerise to the less sterically hindered and more stable exo adducts followed by a retro Diels-Alder reaction followed by recombination.



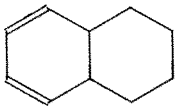
(2)

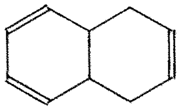


Whatever may be the explanation of actual stereochemistry, the endo orientation is consistent with a concerted mechanism.

It is to be noted that the endo addition rule is not as universal as the cis-addition rule. It can be finished by the more general rule according to which the reagents approach each **other from the less hindered side.** If that side appears to correspond to an exo-orientation, then exoaddition will occur both under and thermodynamic conditions.

The attack from the less-hindered side and in which how the products formed by exo or endo additions vary has attracted great attention and a very interesting case of the reaction between naphthalene derivatives and 4 phenyl-1, 2, 4 triazoline 3, 5 dione (d) acting as dienophile has been reported by B.M. Jacobson in 1973.


a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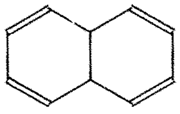
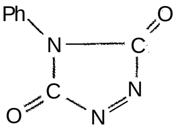
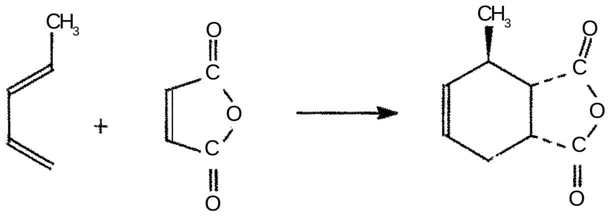

c

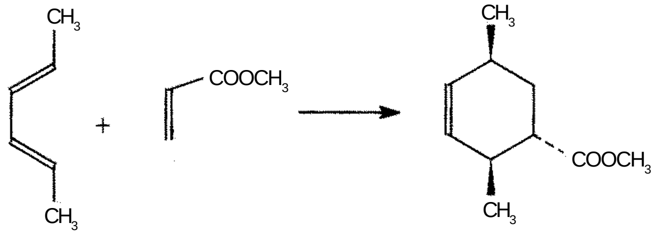


d

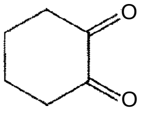
In all the above cases the attack from the less-hindered side (exo-orientation) was preferred and the ratio exo/endo varied from 19 (for *a*) to 4 (for *c*). The increase in weight of endo-orientation for *c* cannot be explained only on secondary overlap interactions. But they are accounted for by decrease of geometrical constraints. The steric requirements of saturated cyclohexane ring are higher than the steric requirements of sp^2 carbon atoms in C.

While studying the stereochemistry of the endo addition, it has been found that the bulky side of the olefine is normally under the ring as in the following examples :

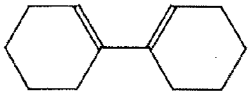




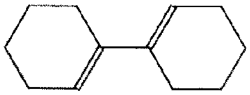
Steric factors have also been studied in several cases. It has been found that dienes which easily adopt the *s*-cis confirmation undergo Diels-Alder reaction readily. The cyclic dienes undergo the reaction if they have cis conformation. If they are frozen into a trans-conformation, the reaction does not occur. This explains why *e* and *f* undergo the reaction easily but *g* fails to react.



e

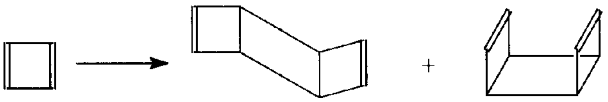


f

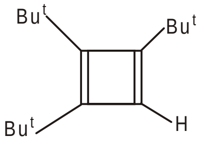


g

Besides the above configurational and steric factors electronic effects of substituents have also been studied on Diels-Alder reaction. How the electronic and steric factors both operate is best afforded by cyclobutadiene which is a highly reactive species and undergoes Diels-Alder reaction even at very low temperature to give a mixture of the following two products.

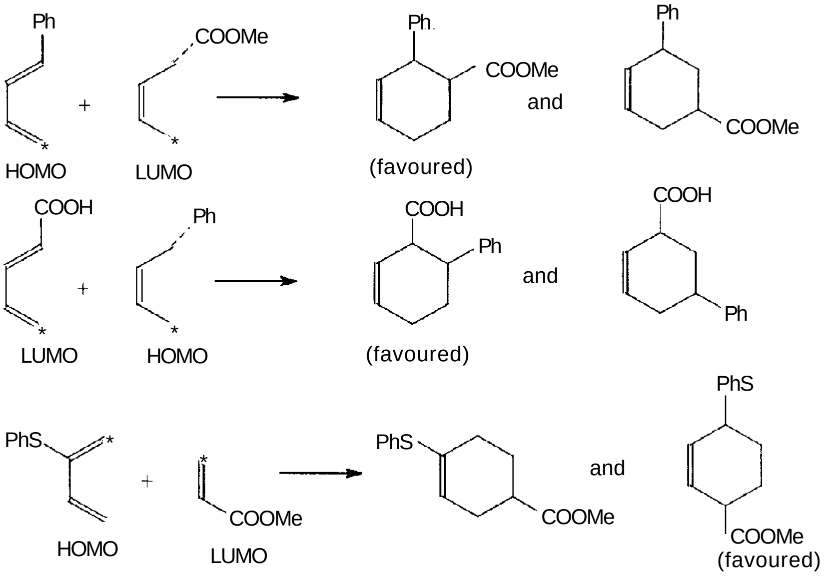


The case of this dimerisation can be related to the closeness in energy of cyclobutadiene HOMO and LUMO. In contrast, the tritertiary butyl cyclobutadiene in which the bulky t-butyl groups hinder dimerisation can be isolated at room temperature.



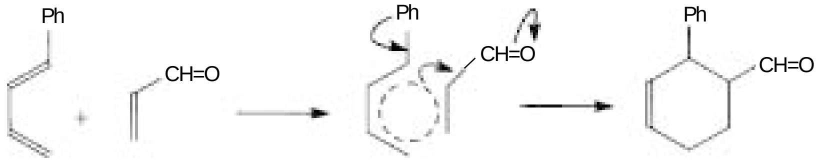
Orientation (Regioselectivity)

A question of regioselectivity arises when both the diene and alkene are unsymmetrically substituted and two different orientations are possible. Thus a 1-substituted diene with a mono substituted dienophile may form an ortho and a meta adduct. The same dienophile with a 2-substituted diene can yield a meta and a para product. Actually it has been observed that 1 sustituted dienes preferentially form ortho adducts whereas with 2-substituted derivatives para adducts are formed.



This regioselectivity was originally one of the greatest unsolved problems in Diels-Alder reaction but with the application of FMO theory, it has now been solved satisfactorily. Calculations made on systems containing heteroatoms give a set of coefficients which account for the observed orientation.

The regioselectivity of a diene addition has also been explained on a concerted mechanism. The transition state involves a six π-electron system similar to benzene except for the fact that besides a *p*-π overlap, *p*-σ overlap must also be considered.



As in benzene, the substituents in ortho and para will be better conjugated than those in meta. These qualitative aspects of regioselectivity have been studied quantitatively by quantum mechanical studies. Further the molecular orbital considerations have shown that the favoured transition state will be that in which there is strongest interaction between the HOMO of the diene and LUMO of the dienophile. In the most common cases the dienophile bears an electron withdrawing substituent and the diene an electron releasing one. Here the interation is between the LUMO of the dienophile and the HOMO of diene.

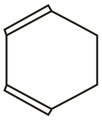
Diene Reactivity

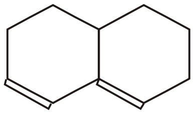
In a synchronous Diels-Alder reaction, the following facts have come to light about dienes :

1. Simple dienes react readily with good dienophiles and they must adopt a cisoid geometry about the bond (*s*-cis).

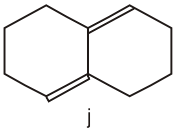
   But in the substituted dienes like cis-1-substituted dienes, the *s*-cis conformation is disfavoured with respect to the *s*-cis form of corresponding transform due to the non-bonding interactions between the substituent and the 4-hydrogen. In a concerted reaction the trans isomer should be therefore more reactive than the cis-derivative.

2. The conformation of cyclic and polycyclic dienes is frozen either in the cisoid or in the transoid form (*i*).

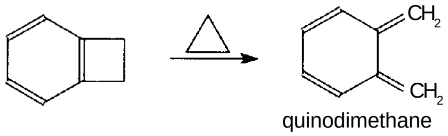

h


i

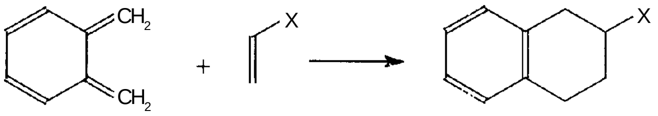
   But irrespective of the mechanism (concerted or stepwise) the reaction is only possible from cisoid forms. In the frozen transoid conformation, the reaction does not occur. This is why the following does not react.


j

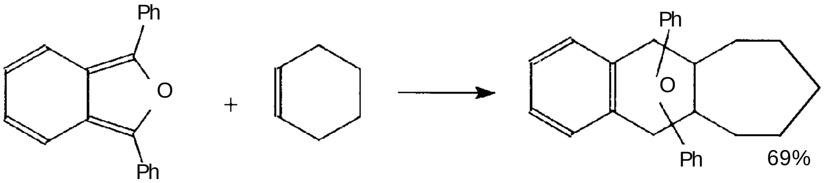
3. Dienes can also be generated under the conditions of Diels-Alder reaction from precursors. An example of exceeding reactive diene is quinodimethane which has been synthesized from the pyrolysis of benzocyclobutene.



In a Diels-Alder reaction from it a benzenoid ring has been established having aromatic stabilization.



Another example of a diene with extra ordinarily high reactivity is diphenyl benzo (c) furan (diphenyl isobenzofuran)



Here again the high reactivity is due to the gain of aromatic stabilization in the adduct. Polycyclic aromatics are moderately reactive as the diene component in Diels-Alder reactions. Anthracene forms adducts with a number of dienophiles. The addition occurs at the centre ring. The naphthalene ring system is much less reactive.

4. The formation of Diels-Alder adducts is now used in the determination of the position of double bonds in polycyclic hydrocarbons.
5. Polar substituents also have a marked effect on cycloaddition.

The diene component is electron rich whereas the dienophile is electron deficient. Electron releasing substituents favour the reaction, while the electron with drawing groups decrease the rate. This may be due to their effect in raising the energy of the dienes HOMO to make it more compatible with the dienophiles LUMO.

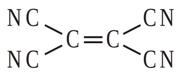
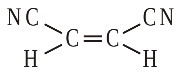
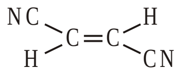
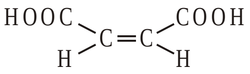
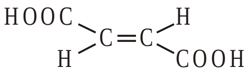
This explains why 2 methyl butadiene reacts with maleic anhydride (the dienophile) at 30°C in the medium of dioxane with twice the speed as compared with butadiene. But under the same conditions butadiene reacts 10 times faster as compared with 2-chlorobutadiene which has an electron withdrawing group. Thermodynamically unstable compounds are the most reactive dienes.

Dienophile Reactivity

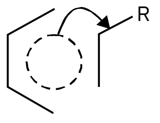
The reactivity of the dienophile depends on the electron demand of the reaction. Electron-withdrawing groups in the dienophile will accelerate the reaction rate. Simple alkenes and alkynes such as ethylene and acetylene are poor dienophiles. In the following table some representative dienophiles have been tabulated along with their reaction with cyclopentadiene.

All of these compounds bear at least one strongly electron withdrawing substituent or a double or a triple bond. Thus tetra cyanoethylene is about 4.6×10^8 times as reactive as cyclopentadiene. As a result of sensual studies, the following conclusions have been obtained.

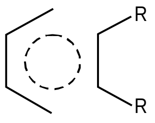
Table 4.5. Reactivity of some representative dienophiles towards cyclopentadiene in dioxane at 20°C

No.	*Dienophiles*	*Rate*
A.	*Substituted Alkenes*	
1.	 $(NC)_2C=C(CN)_2$	460000000
2.	 $NC(H)C=C(H)CN$	910
3.	 $NC(H)C=C(H)CN$	806
4.	 $HOOC(H)C=C(H)COOH$	628
5.	 $HOOC(H)C=C(H)COOH$	742
B.	*Substituted Alkyne*	
6.	$F_3CC\equiv CCF_3$ Hexafluro-2 butyne	

1. A disubstitutd derivative, R–CH = CH–R should react twice as fast as a monosubstituted compound R–CH = CH_2.
2. If a reaction proceeds through a cyclic transtion state *k* and *l* respectively, two substituents should be more efficient in stabilizing it than a single substituent.

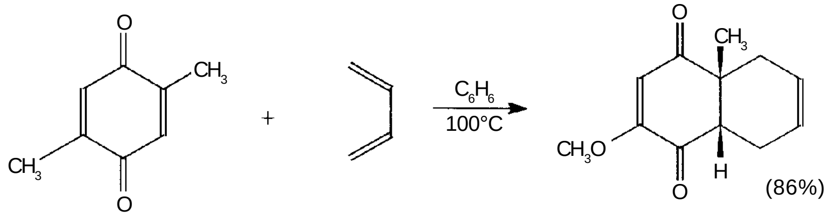


k



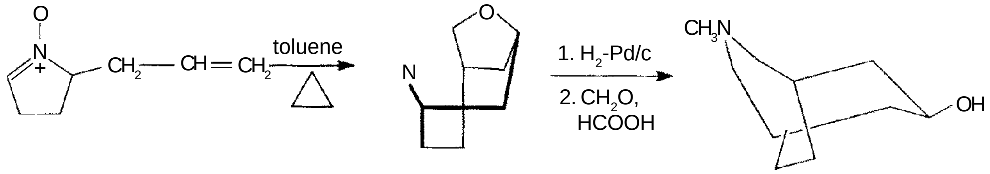
l

3. Substituted trans ethylenes react at least 50–100 times as fast as the corresponding monoderivatives which indicates a concerted mechanism.
4. Transient intermediates like benzynes or cyclobutadiene are extremely reactive dienophile.
5. In diene reactions with inverse electron demands simple alkenes are most reactive. This is why these reactions have been used to identify simple alkenes.
6. Functionalized dienophiles have long been used in synthetic organic chemistry. For example a substituted benzoquinone (a dienophile) underwent cycloaddition with 1,3 butadiene and was the first step in the early synthesis of steroids.

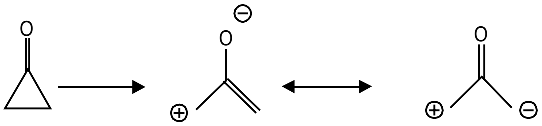


Intramolecular Diels-Alder Reactions

An area of Diels-Alder Chemistry that has received a good deal of attention recently is in the synthesis of polycyclic natural products. This involves intramolecular variant. Thus a pseudotropine has been synthesized. The oxygen-nitrogen bond of isoxazoline can be cleaved by reduction.



Cyclopropanones are also reactive toward cycloadditions of various types. Probably a dipolar species is first formed from reversible cleavage of cyclopropanone ring.



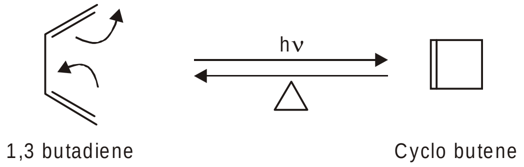
CHAPTER 5

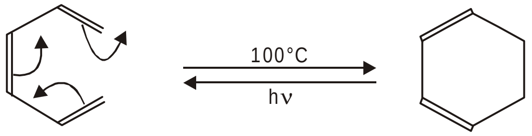
Electrocyclic Reactions

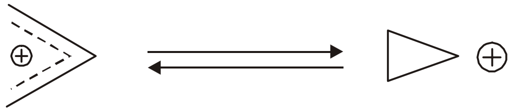
INTRODUCTION

An electrocyclic reaction is defined as a concerted closure of a ring starting from a conjugated open system in which a π orbital is converted into a σ orbital. It is therefore an example of intramolecular cycloaddition or retroaddition.

Some examples are:

1. 

2. 

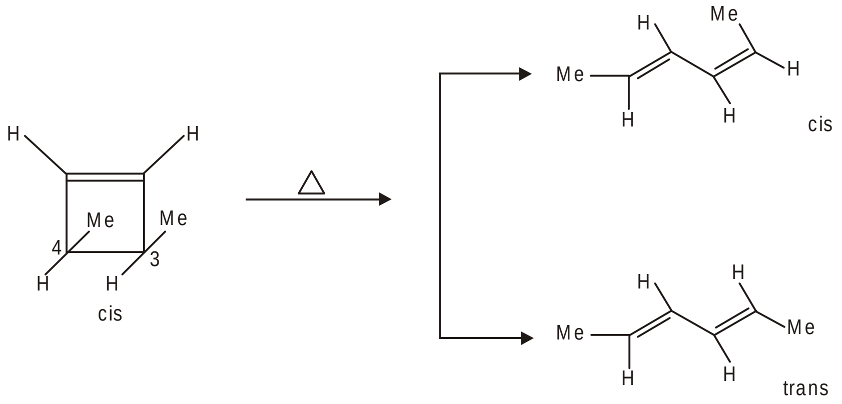
3. 

So if the π system of the open chain partner is having *n*π electrons, the cyclic partner will have (*n* – 2) π electrons and one additional σ bond.

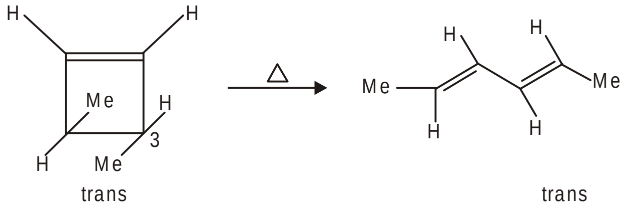
Electrocyclic reactions can be brought about by heat, by ultraviolet irradiation and sometimes by use of metal catalysts. The thermal reaction is generally not reversible and as written above cyclobutenes have been converted to 1, 3 dienes by heating between 100° and 200°C. But the photochemical conversion can be carried out in either direction. Generally 1, 3 dienes can be converted to cyclobutenes rather than the reverse because the dienes because of π electrons are strong absorbers of light at the used wavelengths.

These reactions are nearly always stereospecific and the stereospecificity in the product has been confirmed by n.m.r. studies. The interest in these reactions has grown during the last about two decades; firstly because of their many synthetic uses and secondly they have paved the way for the confirmation of the theory of orbital symmetry.

The highly stereospecific nature of the reaction is illustrated in the thermal conversion of cis 3, 4 dimethylcyclobutene into cis-trans, 2, 4 hexadiene



But the trans isomer gave only the trans-trans diene.



In the following disrotatory motion, the movement can be in any of the ways, either by inward or outer ward rotation. (Opening by movements in different directions).

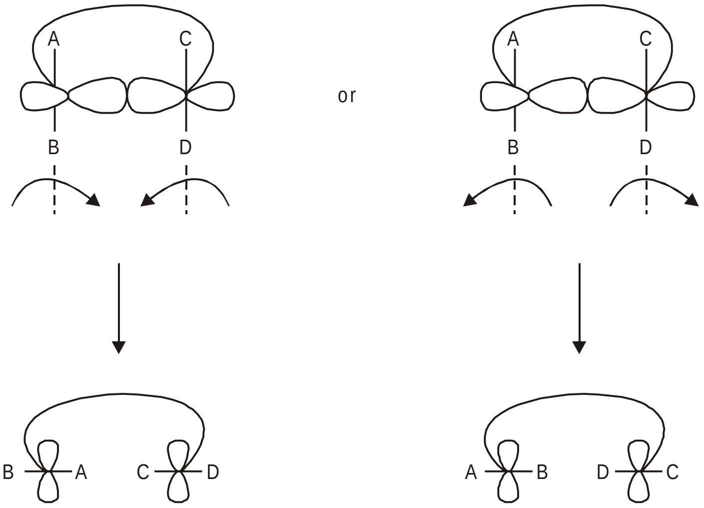


Fig. 5.1

For conrotatory motions, the picture will be as follows:

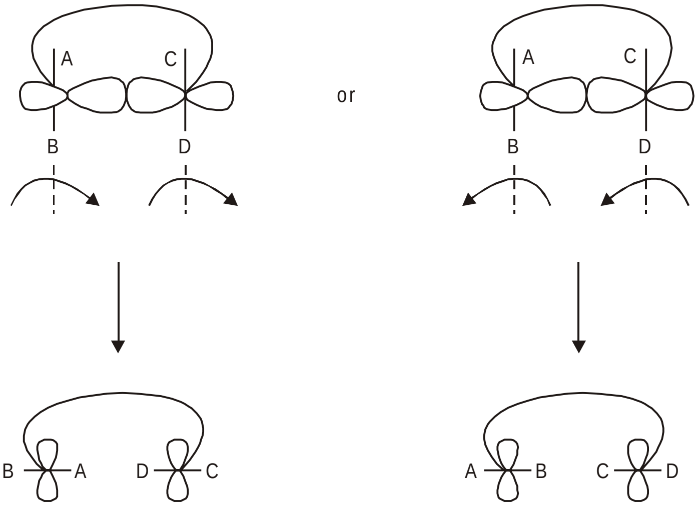


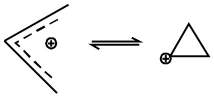
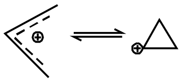
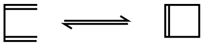
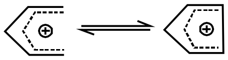
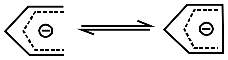
Fig. 5.2

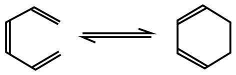
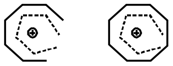
If A, B, C and D are all identical, then there will be only one possible product, but if they are all different, then there are four possible products. Basically the theory distinguishes only the disrotatory modes or conrotatory modes. But predictions can be made on the basis of steric effects.

Electrocyclic processes are also observed with ionic systems, both cationic and anionic. The decisive factor in the stereochemistry is the number of electrons in the delocalized polyenic system. Thus the mode of ring opening or ring closure depends on the π electrons in the open polyene.

THERMAL ELECTROCYCLIC REACTIONS

Table 5.1. Electrocyclic reactions

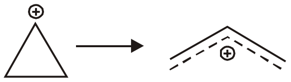
No. of electrons in the relevant M.O. of polyene	*Reaction type*	*Examples*	*Ground State*	*Excited State*
2	[1, 3]		D	C
4	[1, 3]		C	D
4	[1, 4]		C	D
4	[1, 5]		C	D
6	[1, 5]		D	C

6	[1, 6]		D	C
6	[1, 7]		D	C

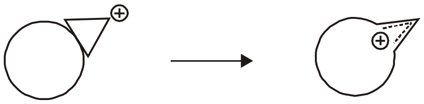
C = Conrotatory; D = Disrotatory

2π System

The most simple electrocyclic reaction involving a 2π electron system is the formation of an alkyl cation from a cyclopropyl cation

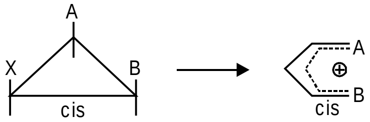


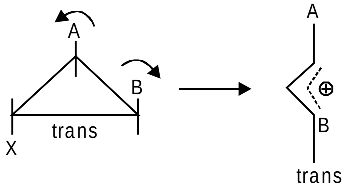
The reaction is an important one, especially in bicyclic system where it leads to ring expansion



The change of cyclopropyl cation to allyl cation is an irreversible reaction because only the ring opening is observed. It is irreversible cyclopropyl cation, is thermodynamically unstable with respect to allyl cation and also because the ring is under strain.

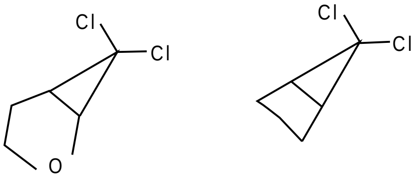
Other factors which affect the case of electrocyclic ring opening include the nature of substituents which can stabilize or destabilize the development of possible charge and the release of strain in small cyclic systems. Thus different stereochemistries have been observed in the ring opening of cyclopropyl derivatives. All cis derivatives generate an all-cis allyl cation but the anti derivatives will form the all trans cation.





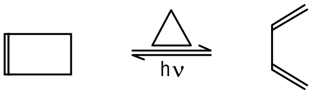
Thus outward disrotatory reaction is favoured over the inward process, if A and B are bulky groups. P.R. Schleyer et al [J.Amer.Chem. Soc 88, 2868 (1966)] have confirmed this experimentally showing that the anti derivatives solvolyse faster than the syn derivatives. But the outward motion will be disfavoured over the inward process if A and B form a medium-sized ring.

The effect of substituents and the relief of strain is also visible in certain cyclic ethers. The presence of adjacent oxygen in the following cyclic ether assists ring opening smoothly at 60°C and the strained bicyclopentane is unstable even at 0°C. The ring opening has been facilitated by the relief of strain.



4π System

The simplest example of an electrocyclic reaction involving 4π electron system is the thermal opening of cyclobutenes to 1,3 butadienes. The reaction can be done thermally or photochemically and under either conditions, it is stereospecific.



The two reactions can be separately carried out. The cyclobutene must be thermodynamically unstable with respect to the diene. Therefore in a thermal process only a ring opening of cyclobutene is observed. But under photochemical conditions dienes are more efficient in absorbing radiant energy than are simple alkenes. This is why ring closure of dienes can be carried out in high yields photochemically.

A σ bond of cyclobutene breaks to form the open chain diene. This breaking will be either con –or disrotatory. The conrotatory thermal opening will be as follows :

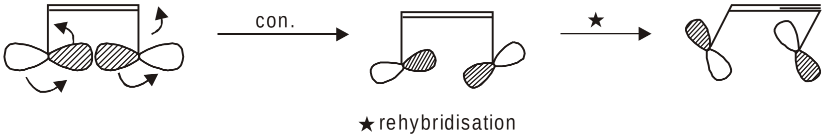


Fig. 5.3

After the ring opening, rehybridisation will occur to give the product.

In disrotatory motion one *p* orbital will rotate in clockwise and the other in anticlockwise direction.

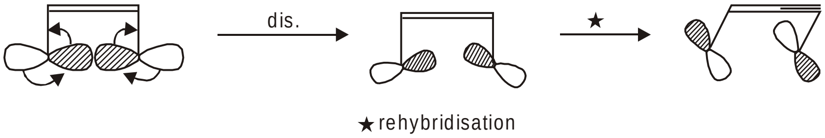
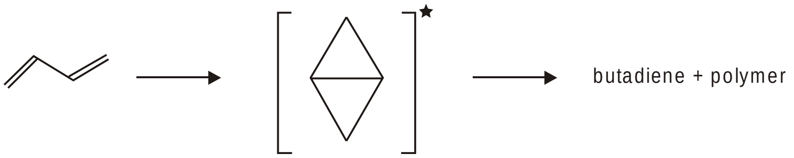


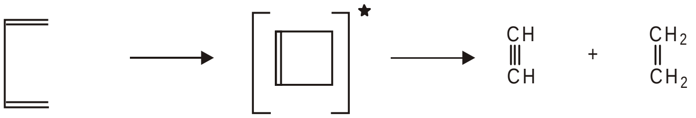
Fig. 5.4

The stereochemical significance of ring opening or ring closure becomes marked by taking substituted reactants. The identification of the product will indicate whether the reaction has taken place in con or disrotatory manner.

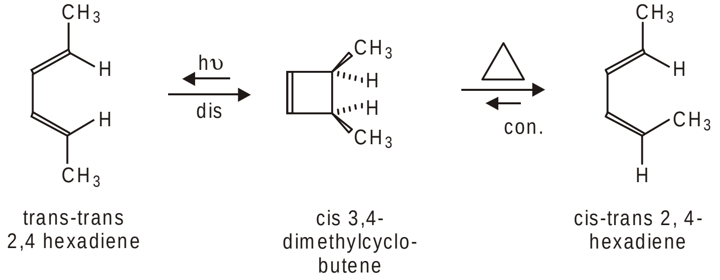
In most cases the ring opening goes to completion and there are very few examples of the reverse reaction i.e., the thermal cyclisation of butadienes. The ring opening takes place smoothly in solution or in the gas phase at temperatures between 120° and 200°C.

In attempts to carry out cyclisation from butadiene 1,3 in the gaseous phase and under photochemical conditions R.Srinivasan (J.Amer.Chem.Soc. 88, 3765 (1966) showed that irradiation yields a complex mixture of ethylene, acetylene, but-l ene, hydrogen and polymers. The quantum yields of acetylene and ethylene formation increase with pressure.





The effect of substituents on ring opening is marked in the following examples:



This is because that in thermal reaction, the change is conrotatory while in photochemical process, it is disrotatory, illustrated as follows:

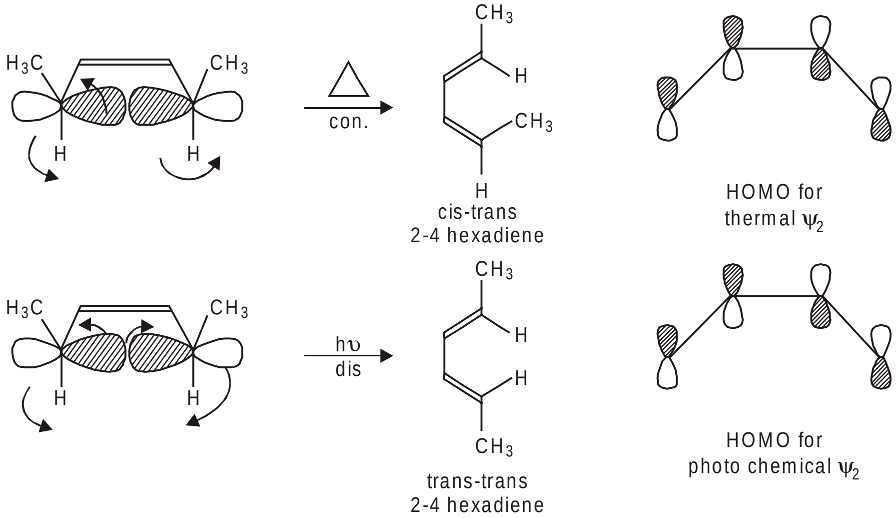
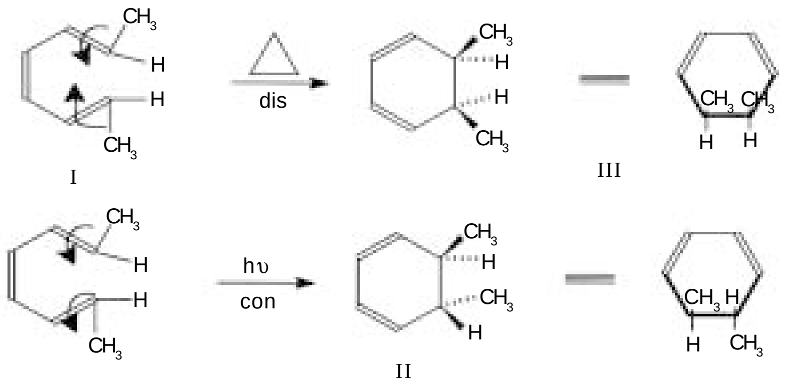


Fig. 5.5

For photochemical reaction ψ_3 is the first excited state and the two shaded lobes being on the same side of the plane are forced to undergo disrotatory change.

From this it should not be inferred that all electrocyclic reactions under thermal conditions proceed in a conrotatory manner and under irradiation they proceed in a disrotatory fashion. This is clear from the following example:

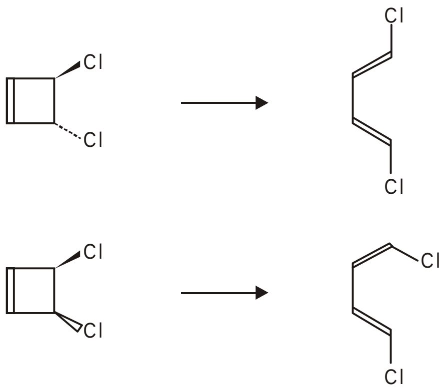
Irradiation of trans, cis, trans 1,6 dimethylhexa-l,3,5 triene (I) gives rise to trans-5, 6 dimethylcyclohexa 1,3 diene (II) while thermal ring closure gives rise to cis 5, 6 dimethyl cyclohexa 1,3 diene III.



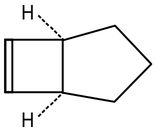
I III

II

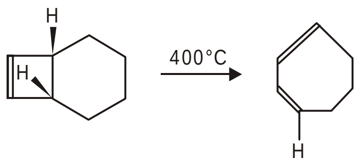
Typical examples occur with the trans and cis 3,4 dichlorocyclobutenes which open stereo specifically to trans, trans and cis, trans-1,4-dichlorobutadiene respectively.



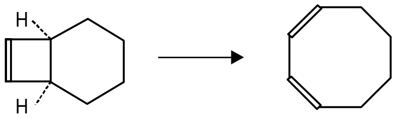
Fused cyclobutenes are thermally rather stable, specially those in which the second ring is five or six membered. For example the following cyclobutene does not isomerise below 380°C.



This appears to be surprising because the fusion of a second ring should increase the strain and make the ring opening easier. However the allowed ring opening is conrotatory which would required the formation of dienes containing a trans fused double bond under drastic conditions.



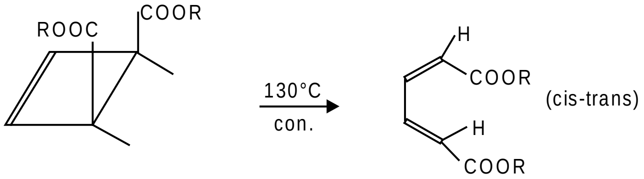
The fused cyclobutenes prefer a path which leads to disallowed cis, cis cyclic diene. Thus bicyclo-octane(IV) opens at 230°–260°C to give cis, cis 1,3 cyclooctadiene and not cis-trans diene.



(IV)

The activation energy 180 K J mole^{-1} is much higher than for opening of simple cyclobutenes.

Cyclobutenes are thermally converted into butadienes and the ring opening corresponds to a conrotatory process.



So in electrocyclic processes the reactant orbitals change into product orbitals through an intermediate transition state and in the most stable transition state the symmetry of the reactant orbitals is conserved while passing to product orbitals. Thus a symmetrical orbital in the reactant must change into an antisymmetric orbital.

The transformation cyclobutene $\rightleftharpoons$ butadiene can be either con- or disrotatory (see Fig. above).

In con-rotatory motion C_2 symmetry is maintained throughout while in disrotatory motion *m* symmentry is maintained.

The directly involved orbitals of cyclobutene are σ and π and their related antibonding orbitals σ* and π*. The corresponding π molecular orbitals are represented by ψ_1, ψ_2, ψ_3 and ψ_4. The picture in a disrotatory change will be as follows:

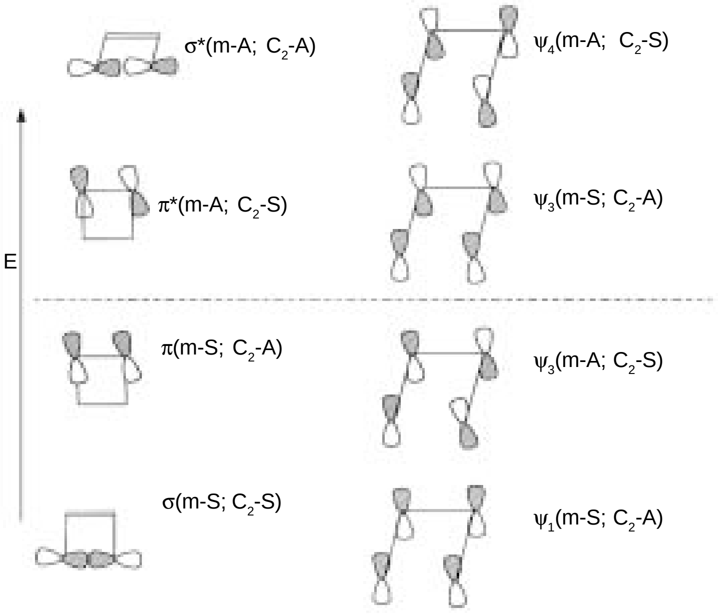
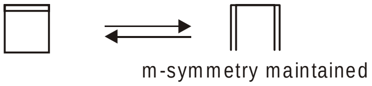


Fig. 5.6 Symmetry properties of M.Os of cyclobutene and butadiene.

On the basis of the above the following correlation diagram can be constructed showing correlation between orbitals of the same symmetry having minimal differences in a disrotatory interconversion. The lines connecting the orbitals show similar symmetry.



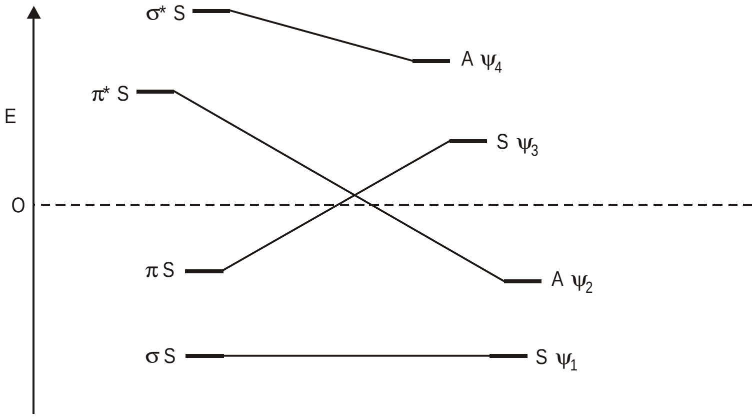


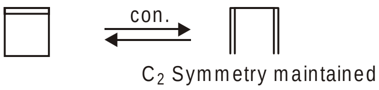
Fig. 5.7 Correlation diagram between cyclobutene-cyclobutadiene system in a disrotatory interconversion.

A thermal transformation will be expected when the ground state orbitals of the reactants will correlate with the ground state orbitals of the product.

In the above example although the ground state orbital of cyclobutene, σ, correlates with the ground state orbitals of butadiene ψ_1, the π orbital of the former does not correlate the ψ_2 orbital of the latter, but rather it correlates with the ψ_3 which is an excited state. So in such a case the thermal transformation by disrotatory processes will be a symmetry forbidden reaction.

On the other hand in a photochemical transformation by a disrotatory process, one electron is promoted from π to π^* orbital and so the σ, π and π^* orbitals of cyclobutene would correlate with ψ_1, ψ_2 and ψ_3 orbitals of butadiene. Thus the first excited state of cyclobutene, since it correlates with the first excited state of butadiene, therefore, the process would be a photochemically symmetry allowed process.

The same arguments can be applied to construct the correlation diagram for the conrotatory process in the transformation of cyclobutene $\rightleftharpoons$ butadiene system. In such a case, as we have seen, a C_2 symmetry is maintained throughout.



Here two things are clear:

1. There is a correlation between the ground state orbitals of cyclobutene and butadiene *i.e.* $\sigma^2\pi^2 \rightleftharpoons \psi_1^2\psi_2^2$. Therefore a thermal conrotatory process would be a symmetry allowed process.

2. The first excited state of cyclobutene ($\sigma^2\pi^*$) is correlated with the upper excited state $(\psi_1^2\psi_2\psi_3)$ of butadiene making it a high energy symmetry forbidden process.

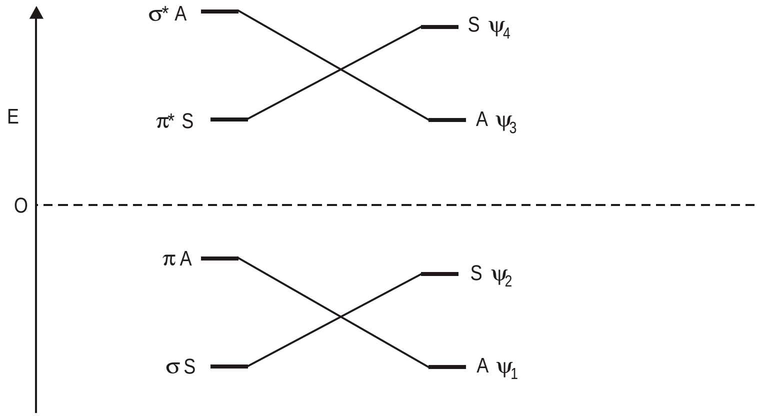


Fig. 5.8 Correlation diagram between cyclobutene-butadiene system in a conrotatory interconversion

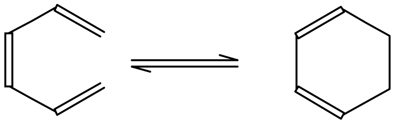
Similarly the first excited state of butadiene $\psi_1^2\psi_2\psi_3$ is correlated with a high energy upper excited state $\sigma^2\pi\sigma^*$ of cyclobutene. Thus a photochemical conrotatory process in either direction would be a symmetry forbidden reaction.

So a thermal opening of cyclobutene takes place in a conrotatory fashion while photochemical inter conversion involves a disrotatory fashion. **These generalizations hold good for all systems having 4q π electrons where q is any integer like 0, 1, 2 etc.**

For systems having (4*q* + 2) π electrons theoretical predictions are entirely different and they are in conformity with the experimental facts.

6π System

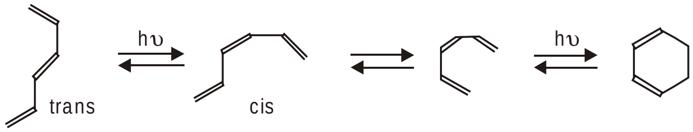
The equilibration of a hexa-1,3,5 triene with a cyclohexa-1,3 diene differs in some respects from the electrocyclic processes discussed above.



To study the above reaction, besides knowing their symmetry, we have to look into the geometry of the acyclic triene. The following facts have come to light.

A. Cyclization in the ground state is possible only from the cis isomer.

B. Under photochemical conditions and in excited state, the trans changes to cis rapidly and it is then followed by cyclization.

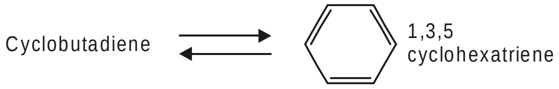


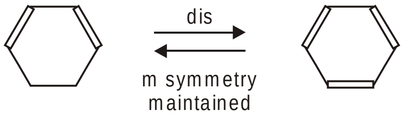
There seems to be no great difference in the free energy between acyclic triene and the cyclic diene. This is because of smaller strain in the six-membered ring as compared with the four-membered one. On the other hand in 6π electron system in electrocyclic process there is more efficient absorption in the near regions of *u.v.* spectrum. This is why under both thermal and photochemical conditions, the (1, 6) electrocyclic reactions are reversible. Side reactions are more frequent in reversible. Side reactions are more frequent in reversible transformations of trienes than in dienes. The dehydrogenation of cyclic dienes to aromatic compounds may also occur in the thermal process. On heating cyclohexadiene yields benzene and hydrogen.

The electrocyclic ring opening is prevented by the energetically more favourable process, the aromatisation. The cis-hexa-l,3 diene is stable at 100°C but undergoes electrocyclic closure at higher temperature.

Hexa-l,3,5 triene gives on irradiation benzene, hydrogen and hexa 1,2,4-triene. The process is conrotatory in both the directions.

It is possible to construct the correlation diagram of



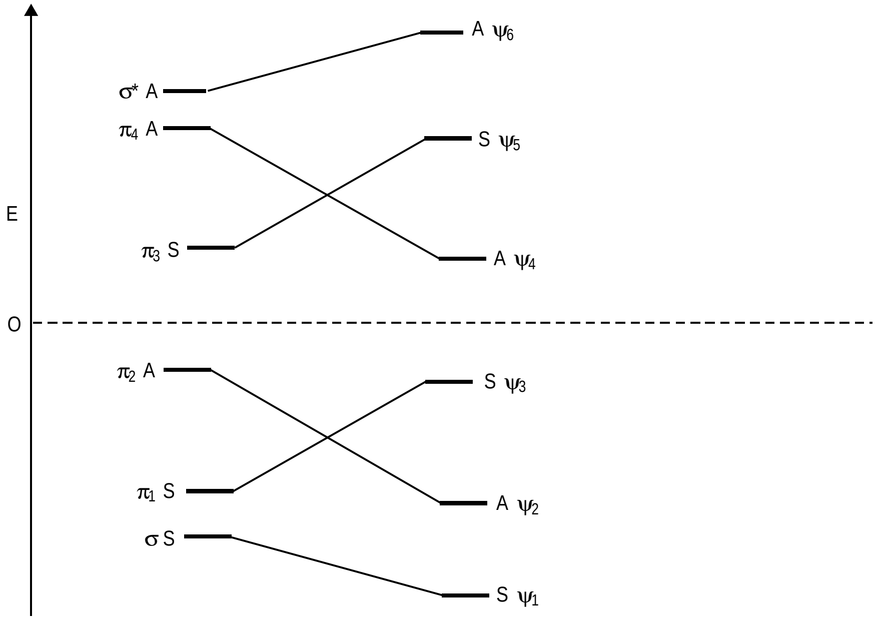


The symmetry properties of molecular orbitals of cyclohexadiene are given in the following table.

Table 5.2

	M	*C2*
σ^*	A	A
π_4	A	S
π_3	S	A
π_2	A	S
π_1	S	A
σ	S	S

Correlation diagram for disrotatory motion of cyclohexadiene-hexatriene system symmetry maintained.



From the correlation diagram we find that in disrotatory fashion:

1. The ground state bonding orbitals of cyclohexadiene is correlated with the ground state bonding orbitals of hexatriene and so it will be a thermally allowed reaction.
2. For a 1,3,5-triene the symmetry of the HOMO is ψ_3. Therefore a thermal cleavage of cyclohexadiene should be such that the positive lobes must lie on the same side of the plane which requires a disrotatory motion.

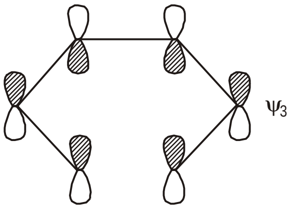


Fig. 5.9 HOMO for thermal reaction

3. In the photochemical process the lobes of the same sign must overlap and this is possible by conrotatory motion.

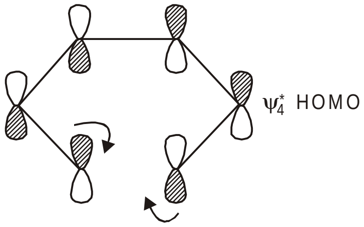
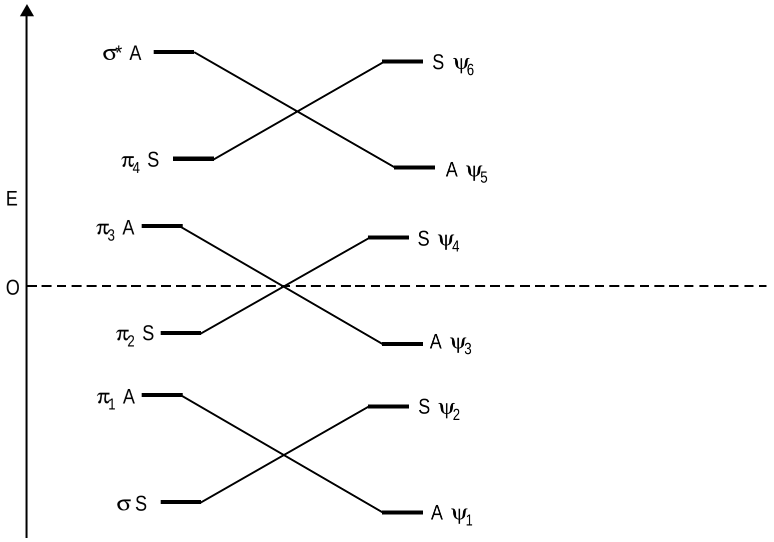


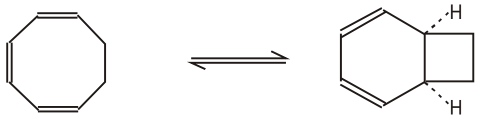
Fig. 5.10 HOMO for photochemical reaction

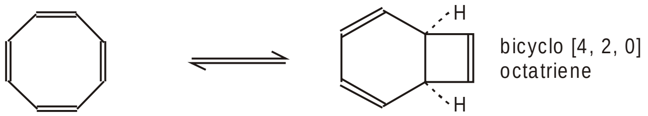
Here the electron gets promoted to π_3 in cyclohexadiene.

The correlation of the conrotatory diagram of interconversion of cyclohexadiene-hexatriene is as follows where C_2 symmetry is maintained.



Although a few other acyclic examples of stereospecific isomerisation of hexatrienes are known, specially in the field of natural product like steroid chemistry, the commonest reactions of this type are in cyclic hexatrienes. Cyclooctatriene and cyclooctatetraene are systems in which the electrocyclic reaction goes very readily and they show an interesting trend.





The reverse reaction is more favourable for the cyclooctatriene equilibrium.

For cyclooctatetraene and its product, so the equilibrium strongly favours the former to such an extent that the half life of the bicycloisomer is only a few minutes at 0°C. Thus as the bicyclic system becomes very strained, the equilibrium lies more in favour of the reverse reaction.

ELECTROCYCLIC REACTIONS OF RADICALS

The electrocyclic reactions of π systems containing an impaired electron are difficult to interpret using the above simple theories. The symmetry of the HOMO of the radical system corresponds to that of the corresponding anion. Thus the allyl radical would be expected to cyclize in the same manner as the alkyl anion i.e., in a conrotatory manner. In fact the interconversion takes place in a disrotatory manner. Theoretical calculations based on Huckets theory also give ambiguous or incorrect predictions. And therefore more sophisticated calculations are required to obtain reliable results.

For example in cyclopropyl cations, it can be seen that groups situated on the same side of the ring as the leaving group will move inwardly. The same process will impose an ontoward disrotatory motion to the groups situated in anti as follows.

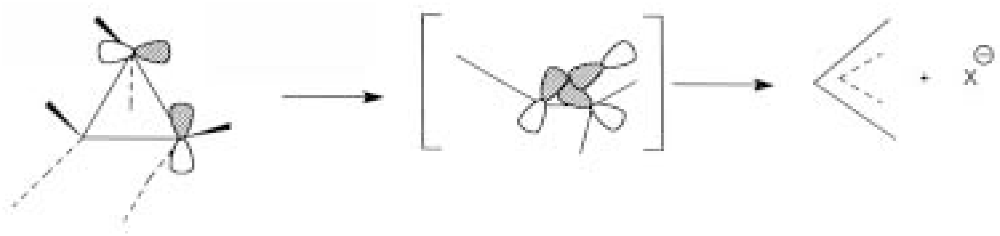


Fig. 5.11

METAL-CATALYSED ELECTROCYCLIC REACTIONS

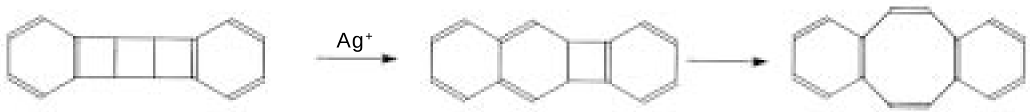
Transition metal catalysts can alter the normal thermal reactions of a polyene system in several ways.

(*a*) First the catalysed reaction can give products which are not related to any pericyclic process.

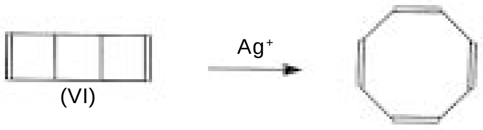
(*b*) Catalysts can also give a product resulting from a formally disallowed thermal reaction: the catalysed ring opening of strained cyclobutene provides examples.

(*c*) Finally there are a few examples of preformed transition metal complexes which follow the same course as the thermal reactions of the ligand, but with different rate.

The disrotatory opening of fused cyclobutenes (V) and (VI) is catalysed by Ag^+.



(V) (not isolated) dibenzocyclo-octatetraene



(VI)

The conversion of (V) to dibenzocyclochatetraene is an instantaneous reaction at room temperature in presence of Ag ions.

Various suggestions have been put forward to explain how a catalyst operates. Some of these are as follows:

(*a*) In presence of metal, a completely different mechanism operates, which is a root of low energy involving one or more intermediates. This happens in some metal catalysed sigmatropic and cycloaddition reactions.

(*b*) The metal supplies filled and empty orbitals of right symmetry to interact with the LUMO and HOMO of the diene. This provides a good mechanism for the transfer of electron density from the HOMO to the LUMO. By this a forbidden disrotatory reaction becomes an allowed one.

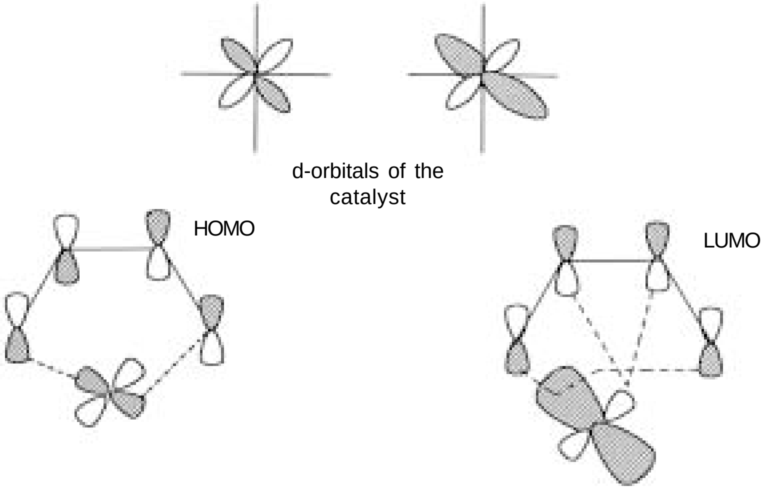


Fig. 5.12 Interaction of d orbitals with diene π orbitals

(*c*) Another theory given by van der Lugt and coworkers (Tetrahedron Lett., 1970, 2281) says that the reaction remains forbidden in presence of metal. The activation energy is lowered because the excited electronic configurations of the metal substrate complex are much lower in energy than those of the substrate alone.

PHOTOCHEMICAL ELECTROCYCLIC REACTIONS

It has already been pointed out that if a thermal reaction is disrotatory, then the photochemical reaction would be conrotating and vice-versa. This has been utilized in synthetic organic chemistry, because by choosing the appropriate conditions, the stereochemistry of the product can be selected.

The LUMO of a conjugated linear polyene has a symmetry opposite to that of HOMO. Thus the excitation of an electron into the LUMO will reverse the direction of ring closure or ring opening compared with that of ground state system. **For 2,6, ... $(4n + 2)$ π systems, photochemically induced ring closure should be conrotatory and for 4, 8, ... $4n\pi$ systems it should be disrotatory.**

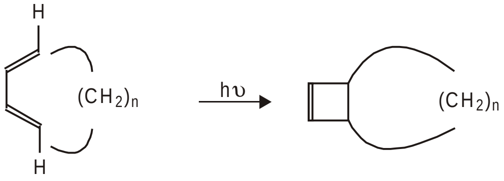
Table 5.3. Woodward-Hoffmann Rules for Electrocyclic Reactions

No. of electrons	*Motion Thermal*	*Photochemical*	
$4n$	con	*d* is	Thermally allowed but photochemically forbidden
$4n + 2$	dis	con	Thermally allowed but photochemically forbidden

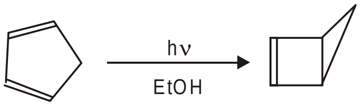
The simple picture given above agrees remarkably well with the observed experimental facts; but it has raised certain problems. For example, let us consider butadiene-cyclobutene ring closure

$$\text{butadiene} \xrightarrow[\text{ring closure disrotatory}]{h\upsilon} \text{cyclobutene}$$

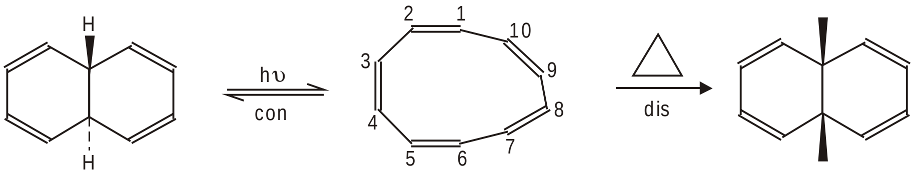
But the reverse conversion does not proceed smoothly. This is because the diene is a stronger absorber of light at wave lengths used in the reaction. So it is the diene which is excited. The most instructive examples are those where the diene forms part of a ring so that a fused cyclobutene is formed.



Since the reverse reaction is thermally disallowed, the products may be unexpectedly stable. Thus cyclopentadiene can be partially converted photochemically into bicyclo [2,1,0] pentene, which in spite of having a strained structure has a half life of about two hours at room temperature.



Many other examples of contrasting behaviour have been discovered. For example all-cis-cyclodecapentaene (VII) photochemically equilibrate at low temperatures with trans 9, 10 dihydronapthalene by a conrotatory six electron electrocyclic reaction but it is converted thermally into cis-9, 10 dihydronaphthalene by disrotatory closure.



VII

CHAPTER

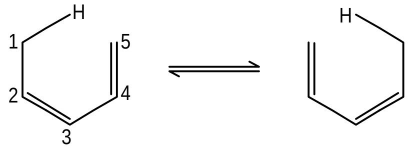
6

Sigmatropic Re-arrangements

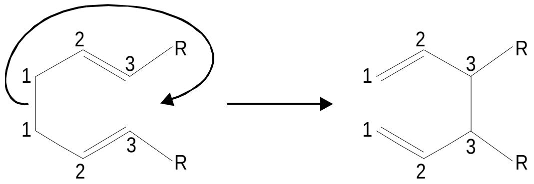
INTRODUCTION

Rearrangements in which a sigma bonded group is transferred from one end of a conjugated π system to the other are called sigma bond rearrangements. Some examples are:

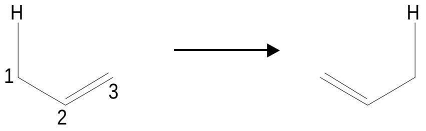
1. 1, 5 hydrogen shift in a conjugated diene



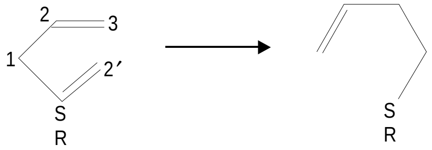
2. Cope rearrangement. This is a 3, 3 sigma-tropic rearrangement. Here there is an interaction between a pair of allyl radicals.



3. The migration of hydrogen through an allyl system is rearrangement of order 1, 3 because the univalent hydrogen move from C-1 to C-3.



4. The ylide rearrangement is a sigmatropic change of the order (3, 2) since the new σ bond is two and one atoms away from the original position.



All these rearrangements are uncatalysed thermal rearrangements and occur intra-molecularly and include a large variety of structural types.

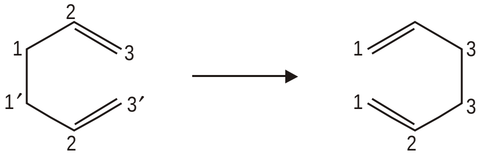
Woodward and Hoffmann have given the name of *sigmatropic rearrangements* to such reactions because they involve the movement of a sigma bond which is adjacent to one or more π system.

Originally very few types of such rearrangements were known *e.g.*, Copes rearrangement, Claisen rearrangement and some 1, 5 hydrogen shift in some dienes, but now many others have been discovered. The common feature of such reactions is that they are concerted, uncatalysed and involve a bond migration through a cyclic transition state.

Nomenclature

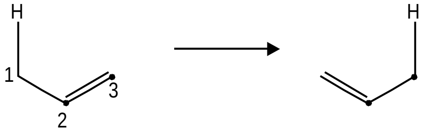
There is a well defined formal system of nomenclature given by R.B. Woodward and R. Hoffmann (J.Amer.Chem.Soc, 87, 4389 (1965) and this is widely used.

The numbering is written by the order [*i*, *j*] written in a bracket. The letter *i* and *j* denote the number of atoms across which the σ bond migrates. Let us take the case of cope-rearrangement of 1, 5 hexadiene.



In this case the σ bond which has migrated is to carbon atom 3 and 3′ and the original bond was between C-1 and C-1'. Therefore, this shift is represented as [3, 3]. So here *i* = 1 and *j* = 1. The numbering always starts from the original termini of the σ bond. Each of the original termini is given the number 1.

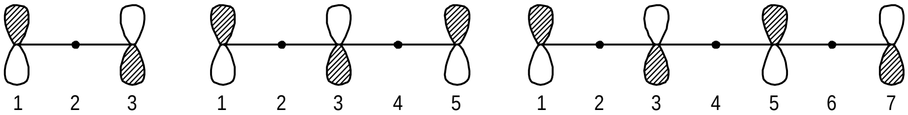
In the (1, 3) shift of the inivalent hydrogen *i* = 1 and *j* = 3.



Thus the termini of the original σ bond are labelled first and this is followed by numbering the chain subsequently.

THE HOMO OF ALLYLIC RADICALS

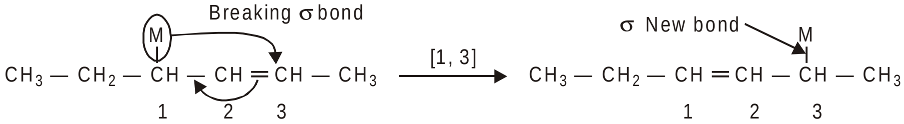
The homo of allylic radicals with several carbon atoms can be depicted as follows:



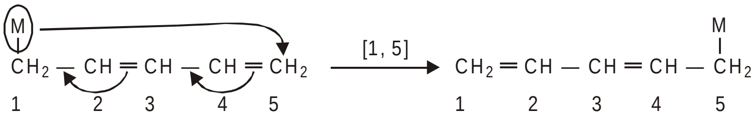
Let us see the migration of a hydrogen atom and how the selection rules have been put forward to explain the formation of an imaginary transition state in a sigmatropic reaction.

Hydrogen migrations

Let there be the migration of hydrogen (or deuterium atom or an alkyl radical) in an alkene of the type.



This is called (1, 3) shift because the original σ bond attached at carbon 1 has been broken and it has attached itself at the carbon 3. But in a petadiene of the type given below (1, 5) sigmatropic rearrangement can take place.

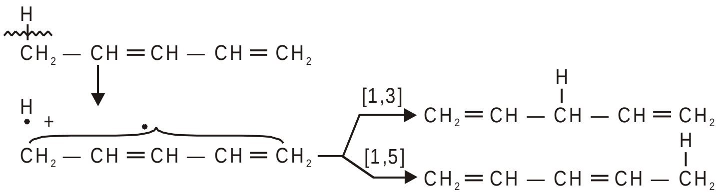


Thus in the rearrangement, in the transition state, there will be an overlap between the orbital of the atom or free radical (R) of the group which is migrating and the orbital of an allylic free radical. So there will be an overlap between the HOMO of one component and the HOMO of the other.

It will be in the following steps :

1. There will be the homolytic cleavage of the σ bond giving two free radicals. So one electron remains with the original migrating group and the other is associated with the π framework.

   It is necessary that the π framework must have the correct symmetry to give an interaction.
2. For a [1, 5] shift of hydrogen or deuterium the pentadienyl system must accommodate the six electrons, four from already two π bonds and one each obtained during homolytic cleavage.
3. In pentadienyl the Homo will be that which have ψ_3 function.
4. Thus the 1*s* orbital of hydrogen or any other species will simultaneously interact with C-1 or C-5 of the allyl system.
5. Bonding interaction will be by suprafacial mode.



How [1, 5] rearrangement will be favoured is clear from the following arrangement of *p* orbitals in pentadiene in which the HOMO of one component will react with the HOMO of the other suprafacially. ψ_3 will be the highest HOMO orbital in pentadiene and the reaction will be facilitated easily.

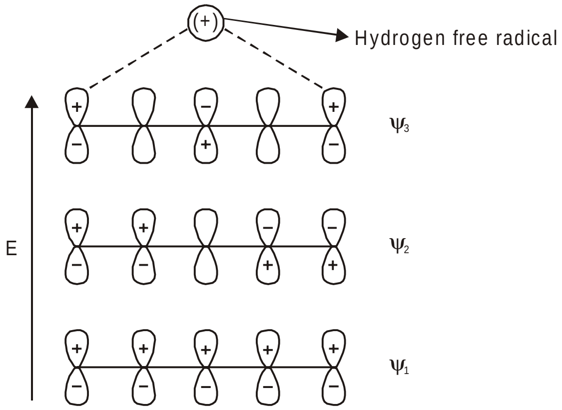


Fig. 6.1 [1, 5] sigmatropic reaction

In some π molecular orbitals the phase at a given carbon atom may be zero and hence the *p* orbital in such a case is left unmarked.

This view also explains satisfactorily why a [1, 3] sigmatropic shift of a hydrogen in 1, 3 pentadiene will not be possible. In this case, a [1, 3] shift would have to be antarafacial and such a rearrangement would be structurally prohibited.

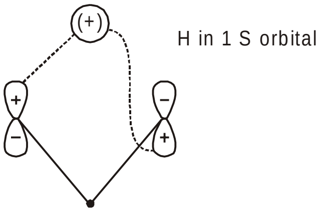


Fig. 6.2 [1, 3] sigmatropic migration of hydrogen

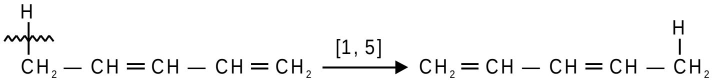
So a [1, 5] or larger rearrangements suprafacial shift is symmetry allowed but a [1, 3] shift would be structurally prohibited, because geometrically it will not be feasible. This would require the hydrogen to migrate to the opposite side of the allyl system and this is sterically difficult.

Another advantage of this approach is that it allows the possibility of introducing substituent effects. Substituents which alter the energies of allyl π orbitals relative to the S orbital will increase the chances of interaction either with ψ_1 or with ψ_3.

OTHER VIEWS ABOUT SIGMATROPIC TRANSITION STATE

1. Formation of a cyclic transition state structure

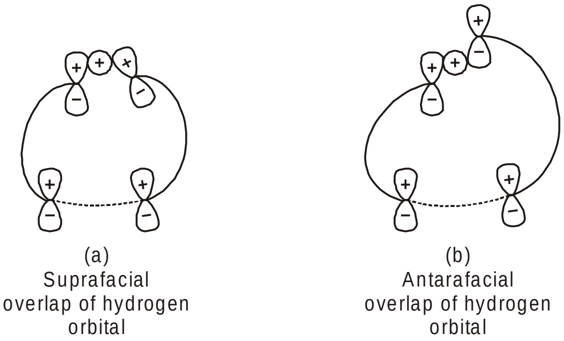
Let us take again a [l, 5] shift of a hydrogen atom on a pentadiene, studied earlier.



$$\overset{H}{CH_2}-CH=CH-CH=CH_2 \xrightarrow{[1,5]} CH_2=CH-CH=CH-\overset{H}{CH_2}$$

The bonding hydrogen orbital overlaps simultaneously with the *p*-orbitals on both the terminal carbon atoms and a cyclic transition structure is formed in which the C-1 becomes a *p*-orbital and

C *j* becomes sp^3 hybridised bonding orbital. These terminal *p* orbitals also overlap the other *p* orbitals coming in between. Thus these are two stereochemically different ways in which the overlap can take place in the formation of a cyclic structure.


(a) Suprafacial overlap of hydrogen orbital

(b) Antarafacial overlap of hydrogen orbital

Fig. 6.3

In structure (*a*) the hydrogen orbital overlaps suprafacially with the terminal *p* orbitals of the π system while in structure (*b*) the overlap is antarafacially. Therefore the geometry of the two transition systems becomes different. While the suprafacial overlap has a plane of symmetry, the antarafacial migration has two fold axis.

The transition state in suprafacial attack is designated as of Huckel type in which *no sign inversion of the cycle has taken place*. The other type of migration involves *one sign* inversion. This is called mobius type inversion. The Huckel type of inversion occurs when the total number of electrons is 2, 6, ... , ($4n + 2$). This is also called aromatic transition state. In mobius type the participating electrons is 4, 8, ... *i.e.* $4n$.

The advantage of the method in this system is that it does not require a knowledge of the symmetries of HOMO and LUMO of the reactants.

So it is the number of electrons and not the number of atoms which determines the selection rule. Therefore, the selection rules for hydrogen migration in thermal sigmatropic shifts can be summarized as follows; as given in the table:

Table 6.1 Selection rules for sigmatropic hydrogen migration

No. of electrons	*Sigmatropic migration*	*Nature of attack*
Neutral compound		
4	(1, 3)	Antarafacial
6	(1, 5)	Suprafacial
$4n$	(1, ($4n$–1))	Antarafacial
$4n + 2$	(1, ($4n + 1$))	Suprafacial
Cation Polyene		
4	(1, 4)	Antarafacial
6	(1, 6)	Suprafacial
$4n$	[1, $4n$]	Antarafacial

Contd...

Anion Polyene		
4	[1, 2]	Antarafacial
6	(1, 4)	Suprafacial
4*n*	(1, (4*n* – 2))	Antarafacial

2. Frontier orbital approach

The above selection rules can also be derived from frontier orbital theory.

For transitions involving 4*n* + 2 and 4*n* electron systems, the pictures will be as fallows. The First leads to Suprafacial overlap while the second to antarafacial overlap.

Fig. 6.4

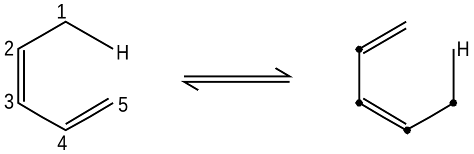
FMO approach for 4*n* + 2 electrons showing suprafacial overlaop.

Fig. 6.5

FMO approach for 4*n* electrons showing antarafacial overlap.

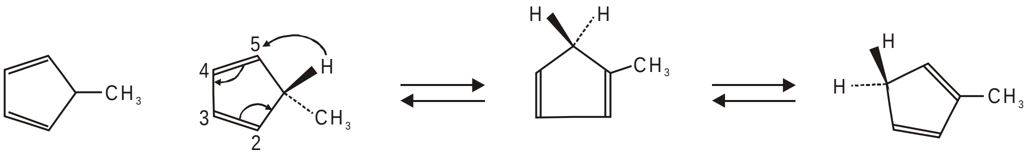
Some other examples of hydrogen shifts

The above selection rules, therefore, predict that [l, 5] hydrogen shifts in neutral polyenes would be thermally allowed and the reaction would be facile, but thermal [1, 3] and [l, 7] shifts must go by an antarafacial process and they will be difficult to attain because of the geometric strain. This is also confirmed by many experimental observations. Thus concerted uncatalysed [1, 3] hydrogen shifts have not been seen in the diene of the following type, [1, 5] shifts are well known.

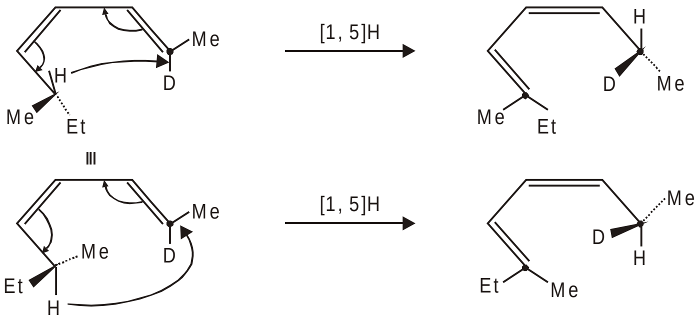


This also explains why in a thermal reaction a cyclopentadiene derivative shows only a singlet for the methyl group in PMR spectrum.

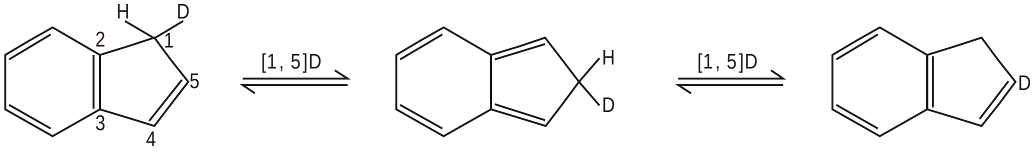
This is also a [l, 5] thermal migration of hydrogen. The hydrogen migrates so fast in preference to the methyl group that at room temperature one sees a singlet for the methyl group.



In acyclic dienes [1, 5] suprafacial nature of hydrogen shift has also been demonstrated. In acyclic 1, 3 diene with a chiral group at one terminal gave two isomers expected from a suprafacial [1, 5] shift but gave neither of isomers that would result from an antarafacial migration. In this reaction chirality is first transferred from one terminal to the other.

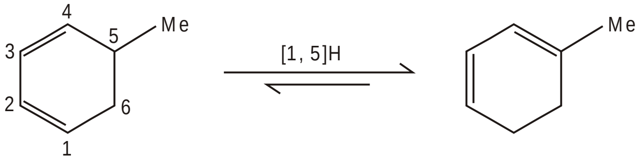


In both cyclic and acyclic dienes which can achieve the necessary geometry the [1, 5] shift is commonly observed because the activation energy is lowest for the transition states involving minimal distortion. This is particularly so in cyclopentadienes and indenes. The preference for [1, 5] over [1, 3] shifts is demonstrated by thermal rearrangement of 1-duterioindene. At 200°C, deuterium became 'scrambled' over all three non-benzenoid carbons.



As a result of the movement of hydrogen to an adjacent carbon atom, the activation energy becomes lower by about 40 k Jmol^{-1} than in open system.

The substituents also considerably affect the activation of the rearrangement. In cyclohexa-1, 3-diene, the [l, 5] hydrogen migration takes place on a non adjacent carbon atom so that activation energies become comparable with those of acyclic dienes. Thus the activation energy for rearrangement of 5 methyl-cyclohexa, 1, 3-diene is 143 kJ mol^{-1}.



With seven membered rings, because the ring size becomes flexible, the activation energy becomes slightly less. Thus for 2 methyl cycloheptadiene, the value is 124 k J mol^{-1}.

Migrations in cyclopropane rings

Since cyclopropane rings can often participate in place of double bonds, pericyclic reactions have been extended to them also. Atleast they show olefine–like character and in their ability to transmit conjugation.

In the Walash model each carbon atom has an sp^2 orbital which is directed towards the centre of the ring and a *p* orbital the lobes of which overlap with the *p* orbitals of the adjacent carbons. These *p* lobes can overlap with other *p* lobes in a conjugated π system. So the plane of the ring becomes parallel to the plane in which the rest of the π system lies.

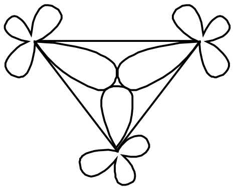
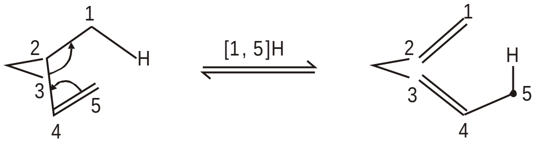


Fig. 6.6

[1, 5] H shifts have been observed in such systems. Such reactions have been called *homodienyl* [1, 5] hydrogen shifts and selection rules for them have been applied as in other dienyl shifts.



Homodienyl [1, 5] shift

Migrations of atoms or groups other than hydrogen

Sigmatropic migrations are not confined to hydrogen atoms only. Groups of nearly every type have been found to migrate. These include alkyl, aryl, vinyl, acyl or alkoxy carbonyl groups. Organometallic functions, such as trialkylsilyl groups R_3Si– also migrate readily.

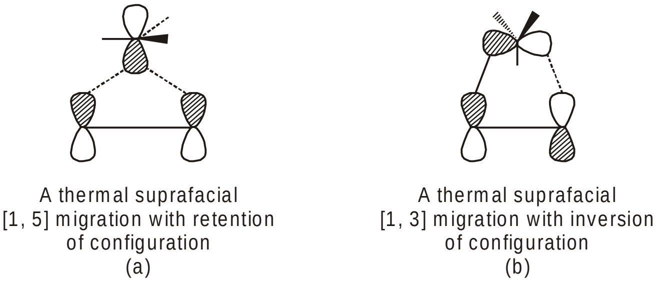
But in attempting to explain such migrations, we have to take into consideration several factors. For example while considering the migration of an alkyl group, we have to consider whether the configuration is retained or inverted in the product. There is also the question of speed of migration, why should they migrate at different rates and whether the relative rates are likely to be the same in all cases. Answers to some of these problems have started to come.

SELECTION RULES

We have seen that in the migration of a hydrogen atom in pentadiene, the IS orbital of hydrogen overlaps the *p* orbitals in pentadiene suprafacially in a [1, 5] shift. If in place of hydrogen one has a carbon of an alkyl radical, then a carbon free radical will have is odd electron in a *p* orbital which has two lobes of opposite sign. In such a condition during a thermal [1, 5] suprafacial process, symmetry will be conserved if the migrating carbon moves in a manner that the lobe which was originally attached to the π system remains attached to it.

Thus the configuration of the migrating group will be retained. But in a [1, 3] thermal suprafacial migration the process would involve opposite lobes. So if the migrating carbon was originally bonded via its positive lobe it must now use its negative lobe to form the new C-C bond. This will mean an inversion of configuration in the migrating group.

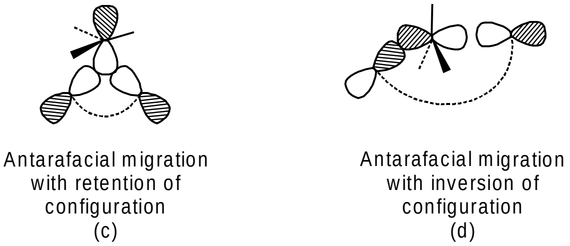
So in a [1, 5] suprafacial thermal rearrangement, there is retention of configuration but in a [1, 3] suprafacial process, there is inversion of configuration.


A thermal suprafacial [1, 5] migration with retention of configuration (a)

A thermal suprafacial [1, 3] migration with inversion of configuration (b)

Fig. 6.7

In general four types of transition states can be envisaged for sigmatropic migrations of the order (*i*, *j*), two in which the migrating group moves suprafacially (*a*) and (*b*) and two in which it means antarafacially (*c*) and (*d*)


Antarafacial migration with retention of configuration (c)

Antarafacial migration with inversion of configuration (d)

Fig. 6.8

These selection rules based on their classification as aromatic or antiaronatic transition state are given in the following table.

Table 6.2 Selection rules for sigmatropic group migration

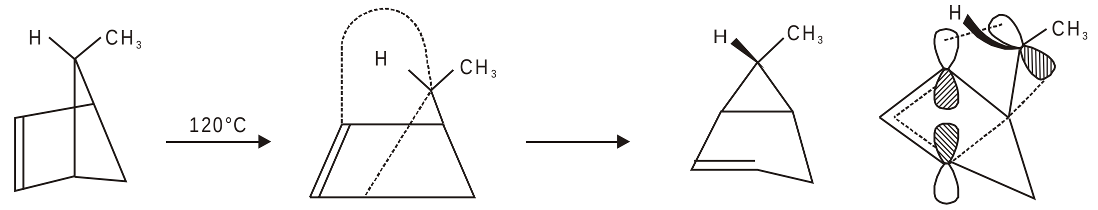
No. of electrons	*Shift*	*Thermally allowed migrations*
Neutral compound		
4	(1, 3)	(Suprafacial with inversion) (Antarafacial with retention)
6	(1, 5)	(Suprafacial with ratention) (Antarafacial with inversion)
4*n*	(1, (4n–l))	(Suprafacial with inversion) (Antarafacial with retention)
4*n* + 2	(1, 4*n* + 1)	(Suprafacial with retention) (Antarafacial with inversion)
Cation		
4	(1, 4)	Same as in neutral
6.	(1, 6)	Same as in neutral
Anaion		
4	(1, 2)	Same as in neutral
6	(1, 4)	Same as in neutral

The predictions of the orbital rules are straightforward when applied to migrations in which transition states involve relatively little strain. Difficulty arises when the allowed states are difficult to achieve.

Shifts in neutral species

[1, 3] shifts

These are not common. An example of a suprafacial shift with inversion of configuration is the thermal rearrangements of bicyclo-hexene, studied by W.R. Roth and A. Friedrich (Tetrahedron Letters 1969, 2607).

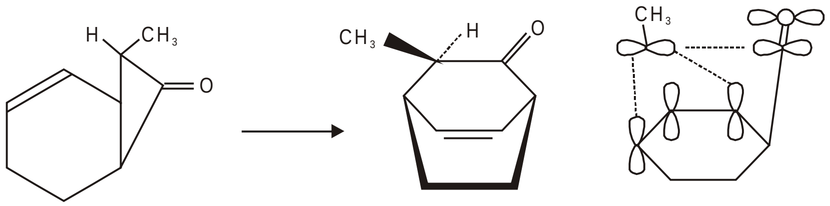


bicyclo (2.1.1) hexene

bicyclo (3.1.0) hexene

The substituted methylene bridge migrates in such a way that the methyl group is almost exclusively *exo* in the product.

Another example of suprafacial migration with inversion is the rearrangement of bicyclo octenone to give again a ketone and reported by J.A. Berson (1972).



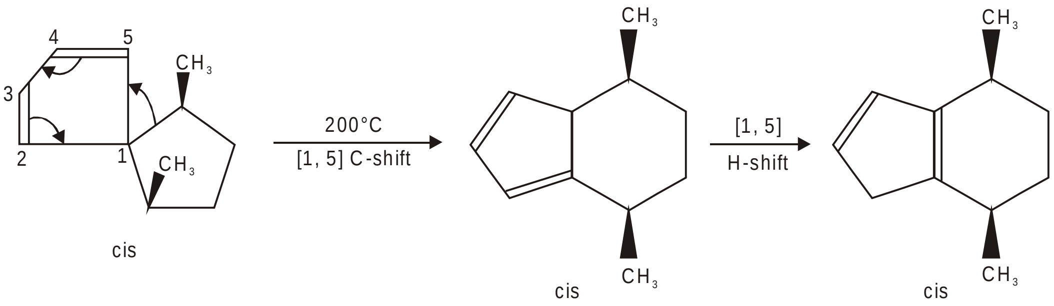
less stable ketone

The ketone which is formed as a result of [1, 3] rearrangement is due to the interaction between the methyl group and a hydrogen atom in a bridging methylene group. The migration with inversion is particularly favoured by overlap with the carbonyl π orbital.

(1, 5) shifts

We have already seen that in [l, 5] alkyl shifts with symmetry allowed will lead to retention of configuration. Another such example with retention of configuration in a [1, 5] alkyl shift is the rearrangement of spirodienes.

Thus the conversion of cis-6, 9 dimethylspiro [4, 4] nona-1, 3 diene to dimethyl bicyclo nonadiene is an example. The first product is a suprafacial [1, 5] carbon shift with retention of configuration at the migrating carbon. This is then followed by a [l, 5] hydrogen shift which becomes the major product.



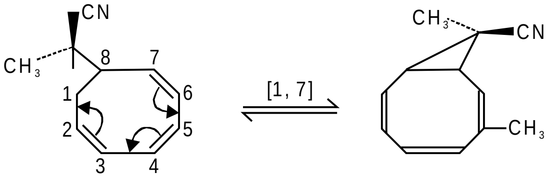
Generally [1, 5] alkyl shifts are followed by migration of hydrogen or other groups, the hydrogen migrates much more readily than an alkyl group. Now results have been obtained which show that the relative ease of migration differs with different groups. The groups which migrate readily are those in which the carbon atom is sp^2 hybidised *i.e.*, acyl, aryl and vinyl and so on. In the indene system the order in which the groups migrate is CHO > COMe > H > CH = CH_2 > CO_2 Me > CN > Me. It is likely that similar order is followed in other ring systems. The other groups which undergo [1, 5] shifts readily include Me_3 Sn, Me_3Si and NO_2.

[1, 5] shifts occur most readily in five membered rings, both carbocyclic and heterocyclic, because these arrangements require movement of groups to an adjacent atom in the ring. Migrations in cyclohexadienes require about 40–60 KJ mol-^{1} more activation energy then in cyclopenadienes and this makes migration of alkyl and similar groups difficult in six membered rings. Activation energy is also influenced on whether aramatic character is created or destroyed by migration.

[1, 7] and higher order shifts

This has been brought out by C.W. Spangler in chem. Reviews 76, 187 (1976).

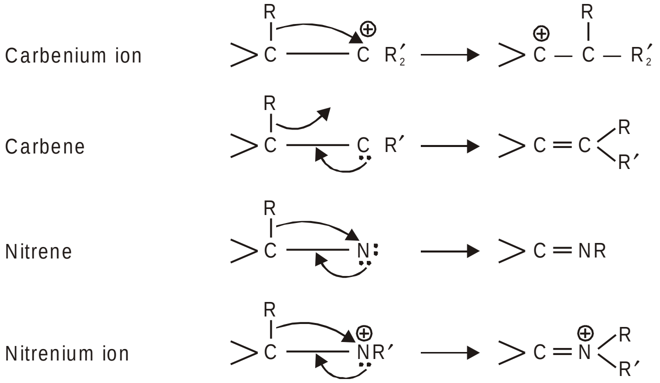
Examples of shifts of higher order than [1, 5] are relatively rare. But an example of a thermal suprafacial process involving [1, 7' shift and inversion of the migrating group is afforded by bicyclononatrienes.



Shifts in charged species

Many important molecular rearrangements show alkyl or aryl shifts in carbocations and other electron deficient species. Thus in this group we have examples of Wagner-Meerwein rearrangement, pinacol-pinacolone rearrangement and expansion and ring contraction of small rings. They proceed by a carbocation rearrangement. The electron deficient centre need not be a carbenium ion. The only requirement is that it has a vacant *p* orbital. The [l, 2] shifts in singlet carbenes, nitrenes and nitrenium ions are of the same general type.

Molecular orbital calculations have shown that in all these electron-deficient centres suprafacial [1, 2] shift occurs with retention of configuration through a two electron Huekel type transition state:



[1, 2] shifts to electron deficient centres

In all these reactions the migrating group moves with retention of configuration. It also explains why concerted [1, 2] shifts to electron rich centres will be unfavourable or why 1, 2 shifts of hydrogen or alkyl groups in radicals or anions are rare.

[1, 4] shifts in cationic polyenes are allowed either by antarafacial process when the configuration of the migrating group will be maintained or as suprafacial when inversion in the migrating group will occur.

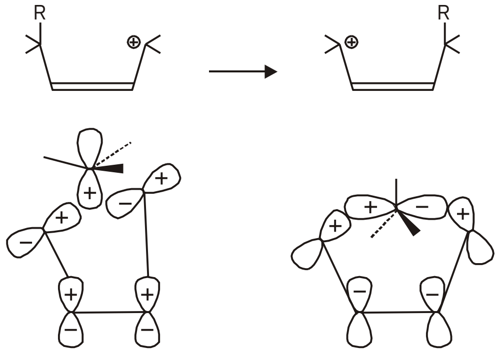


Fig. 6.7

Application of FMO method

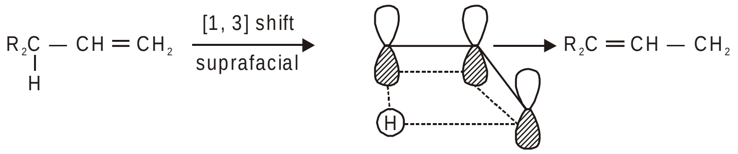
According to Huckel’s rule a monocyclic planer conjugated system having $(4n + 2)\pi$ electrons is aromatic and hence stable in the ground state. A system having $4n$ π electrons is unstable and will be antiaromatic.

But these rules are reversed by the presence of a node in the arrangement of atomic orbitals. Thus a system having $(4n + 2)\pi$ electrons and a node would be antiaromatic while that with $4n$ π electrons and a node would be aromatic and hence stable in the ground state.

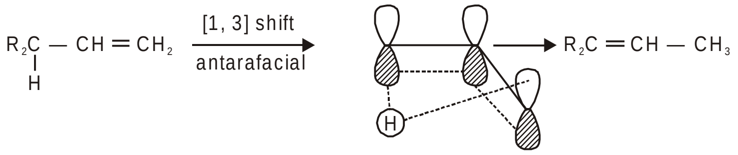
Applying these rules in pericyclic reactions it has been shown and a generalization given that *thermal reactions occur via aromatic transition states while photochemical reactions proceed via antiaromatic transition state.* A cyclic transition state is considered to be aromatic or isoconjugate with the corresponding aromatic system if the member of conjugated atoms and that of the π

electrons involved happen to be the same as in the corresponding aromatic system. On the other hand a cyclic transition state will be regarded to be antiaromatic or isoconjugate with the corresponding antiaromatic system if the member of conjugated atoms and that of the π electrons involved happen to be the same as in the corresponding antiaromatic system.

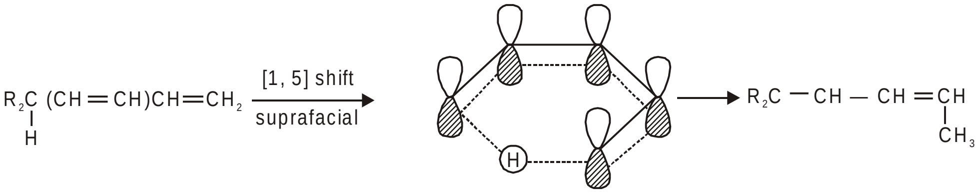
Let us apply the rules in some cases:



0 node. Total 4 electrons
(3 from *p* and one from H)
hence antiaromatic and *hv* allowed



0 node. Total 4 electrons
hence aromatic Δ allowed



0 node. Total 6 electrons
(5 from *p* orbitals and 1 from H)
hence aromatic Δ allowed

Summary of all these is given in the following table:

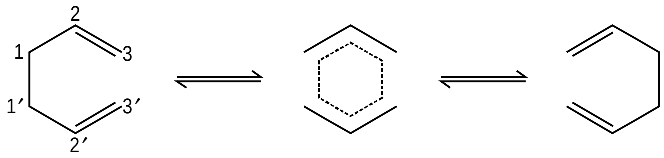
Table 6.3 Selection rules for sigmatropic change by FMO method

No. of electrons	*No. of nodes*	*Aromaticity*	*Shift mode*
4*n*	0 or even	Antiaromatic	Supra, hV
4*n*	Odd	Aromatic	Antara, Δ
4*n* + 2	0 or even	Aromatic	Supra, Δ
4*n* + 2	Odd	Antiaronatic	Antara, hV

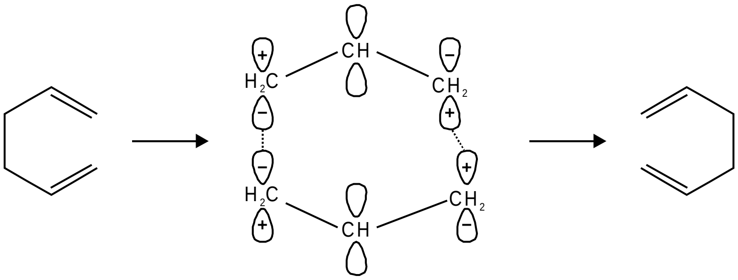
These selection rules have been found to be remarkably successful in thermolytic reactions (symmetry allowed ones) photolytic reactions have been found to be more complex.

[3, 3] SIGMATROPIC CHANGES : THE COPE AND CLAISEN REARRANGEMENTS

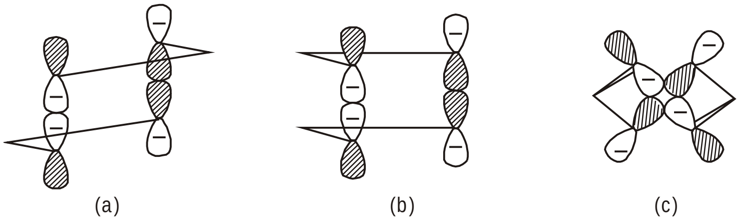
(3, 3) sigmatropic changes are an important group of thermal rearrangements which involve a six membered cyclic transition state. The transition state can be considered as two interacting allyl systems.



The principles of orbital symmetry conservation establish that concerted suprafacial [3, 3]-sigmatropic arrangements are allowed processes. Based on these principles and the results of numerous experiments their stereochemistry is highly predictable.



Various geometries are possible for the transition state and they can be classified on whether each of the allyl systems interacts with lobes of the other system on the same side (suprafacially) or on opposite sides (antarafacially). Three transition states have been given. All have been classed on Huckels system, on the basis of 'aromatic transition state' approach and so all are thermally allowed. The following picture gives the allowed transition state for thermal [3, 3] shifts.


(a) (b) (c)

(*a*) Represents suprafacial, suprafacial chair form.

(*b*) Represents suprafacial, suprafacial boat form.

(*c*) Represents antarafacial, antarafacial twisted form.

Of all these (*c*) is much less likely to be formed because it involves twisting of the allyl system while (*a*) and (*b*) are strain free. Again of these (*a*) is more favoured because the six *p* lobes are in a quasi planar arrangement. Moreover the molecular orbital calculations made by Dewar have shown that the central *p* lobes of the two allyl systems in the boat form appear to have a slight destabilizing effect and this has also been confirmed by Woodward and Hoffmann with the aid of correlation diagrams. But both the chair and boat forms have been found in practice.

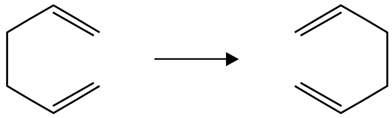
Therefore, the [3, 3] sigmatropic rearrangement has become a useful tool in synthetic organic chemistry. The following are some examples which include Cope and Claisen rearrangement.

The Cope Rearrangement

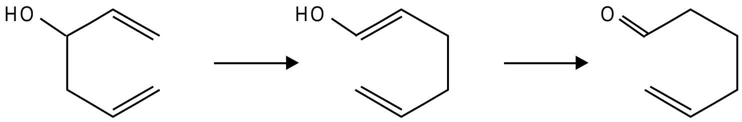
The 1, 5 dienes isomerise on heating up to 300°. The reaction is normally reversible and gives an equilibrium mixture of starting material and the product. The temperature needed to bring about depends on the substituents. If the substituent R is a conjugate group (*i.e.*, consisting of double bonds) then they lower the energy of the transition state and rearrangement goes at 165–185°C.

Some examples are:

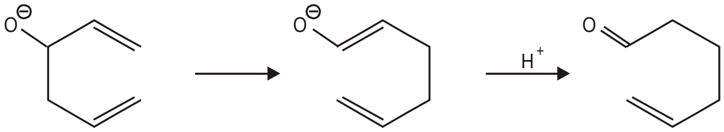
1. Cope rearrangement



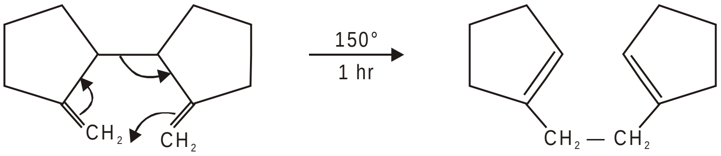
2. Oxy. Cope rearrangement



3. Anionic oxy. Cope rearrangement,

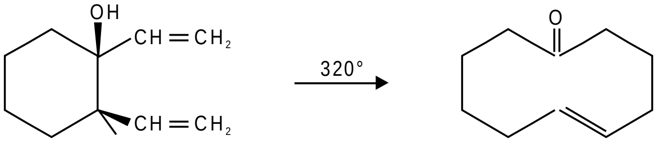


4.



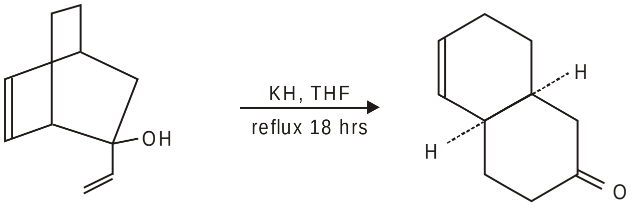
100%

5.



90%

6.

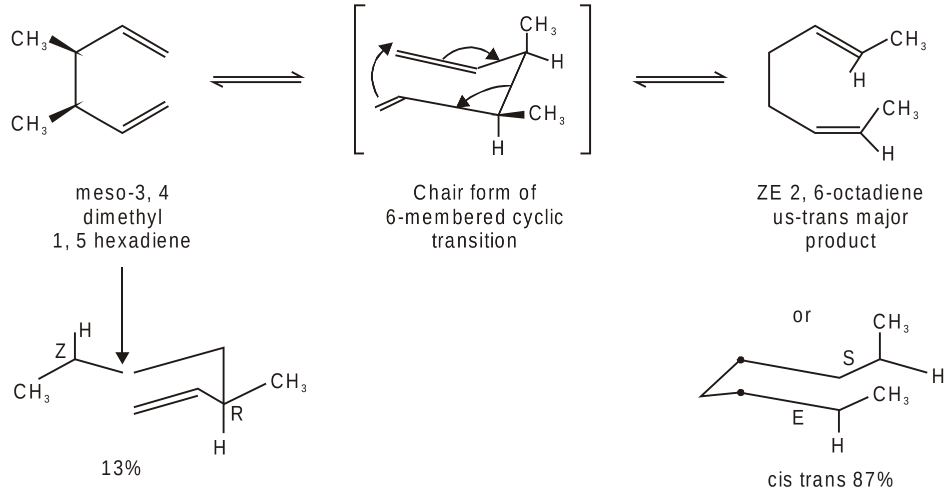


98%

Cope rearrangements are generally reversible processes and there are no changes in the number of single and double bonds as a result of the reaction, so roughly the total bond energy is unchanged. The position of the final equilibrium is governed by the relative stability of the starting materials and the products.

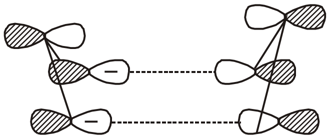
When the ring strain is relieved, Cope rearrangements occur at much lower temperatures and there is complete conversion to ring opened products.

A common example of Cope rearrangement involving [3, 3] sigmatropic rearrangement in a 1, 5 diene is the pyrolysis of meso 3, 4 dimethyl hexa-1, 5 diene giving exclusively cis, trans isomer of 2, 6 octadiene. The process involves a six electron transition state which has a chair like configuration and substituents occupy equatorial sites.



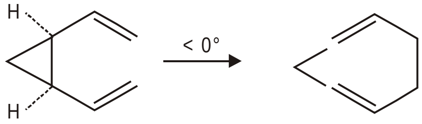
The preferred double bond geometry in the product usually has the more bulky substituent trans to the main carbon chain since this is the sterochemistry which arises from an equatorial-like orientation in the transition state.

In some cyclic system the chair transition is sterically impossible to attain, and the Cope reaction still goes but by a boat transition state.

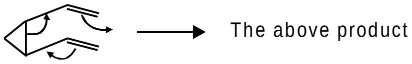


a boat like geometry

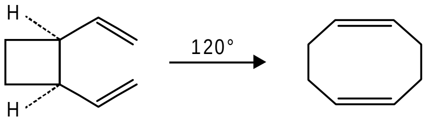
Thus a Cope rearrangement proceeding through a boat-like transition state is the rearrangement of cis 1, 2 divinyl cyclo-propane.



The structure of the molecule is such that it does not allow the attainment of a chair shaped transition state.



Similarly the conversion of cis 1, 2 divinylcyclobutane also involves a boat transition state.



In both the above examples the conversion takes place easily because of the release of strain in small rings.

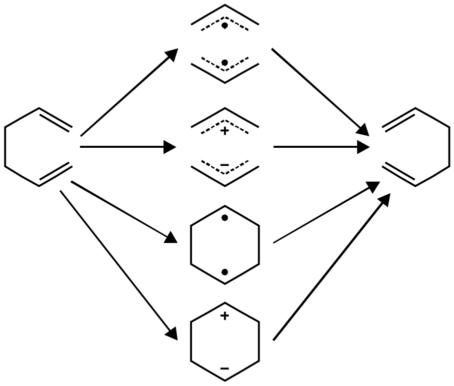
The rearrangement of divinyl cyclopropane may also be regarded as an electrocyclic ring closure in which the cyclopropane ring takes the place of a double bond. But reactions of this type have been regarded as Cope rearrangement. Therefore the course of most Cope rearrangements can thus be regarded as a concerted [3, 3] shift with the chair transition state being more favourable than the boat.

There are also instances where a system undergoes Cope rearrangement through different possibilities. This is afforded by the examples of hexadiene. The alternatives are of two types.

(*a*) Dissociation into a pair of allylic radicals or into a cation-anion pairs followed by recombination

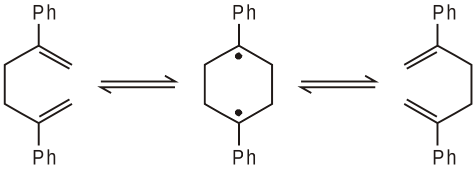
or

(*b*) Formation of a new σ bond before the first has started to cleave giving a diradical or a zwitter ion intermediate.



Stepwise alternatives for the Cope rearrangement

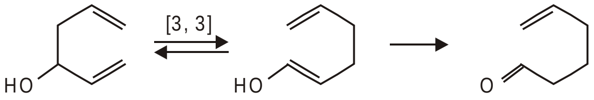
A diradical intermediate appears to be formed in the rearrangement of 2, 5 diphenyl-1, 5-hexadiene probably due to the phenyl groups stabilizing the radical centres.



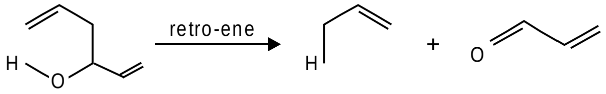
The Oxy-Cope rearrangement

If the diene has a 3-hydroxy substituent (C–3) the rearrangement is called the Oxy-Cope rearrangement. It is different from the normal Cope rearrangement, in two respects:

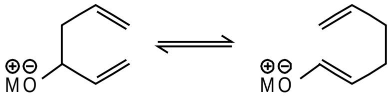
(*a*) The primary product an enol, is not isolated because it rapidly undergoes a tautomeric change to give the corresponding ketone and



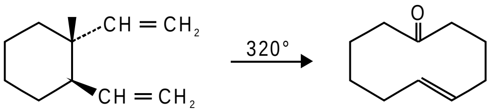
(*b*) The [3, 3] shift competes with a retro-ene reaction (described later) so that the products of both reactions are normally isolated.



The Cope rearrangement of alkoxide ions is much faster ($10^{10} - 10^{17}$ times) compared with the normal oxy-Cope rearrangement. This is also called anionic oxy-Cope rearrangement and occurs under mild conditions.

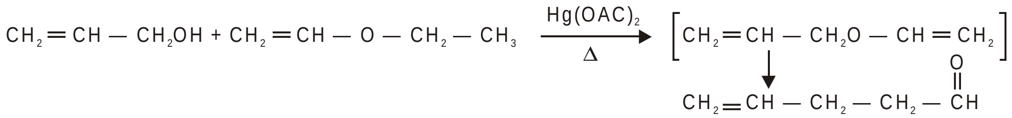


The oxy-Cope rearrangements have found use in the synthesis of medium sized rings as in the following example.



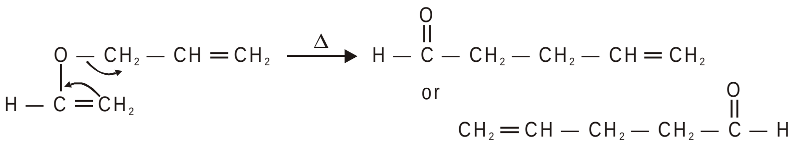
The claisen rearrangements

The [3, 3] sigmatropic rearrangement of allyl vinyl ethers is known as Claisen rearrangement. Allylic alcohols can be converted to allyl vinyl ethers by mercuric acetate catalysed exchange with ethyl vinyl ether. The allyl vinyl ether need not be isolated because it undergoes rearrangement to 4-pentenal.



$$CH_2{=}CH-CH_2OH + CH_2{=}CH-O-CH_2-CH_3 \xrightarrow[\Delta]{Hg(OAC)_2} \left[CH_2{=}CH-CH_2O-CH{=}CH_2\right] \downarrow CH_2{=}CH-CH_2-CH_2-\overset{\overset{O}{\|}}{C}H$$

So basically the Claisen rearrangement is a thermal [3, 3] sigmatropic rearrangement of allyl vinyl ether. The mechanism is probably as follows:

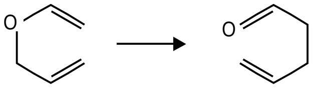


$$\xrightarrow{\Delta} H-\overset{\overset{O}{\|}}{C}-CH_2-CH_2-CH{=}CH_2 \quad \text{or} \quad CH_2{=}CH-CH_2-CH_2-\overset{\overset{O}{\|}}{C}-H$$

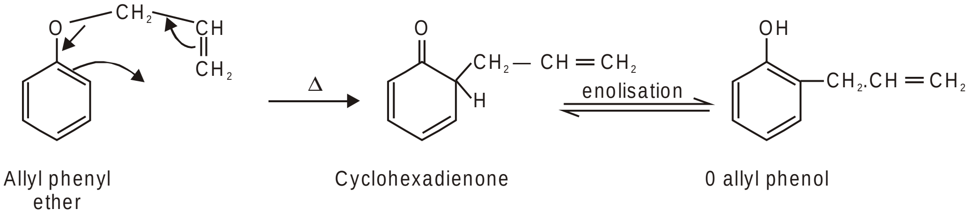
4 pentenal

Some other examples

1. Claisen rearrangement of allyl vinyl ethers.

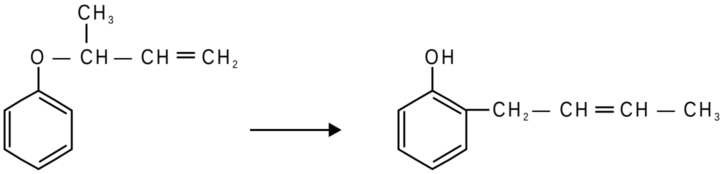


2. Claisen rearrangement of allyl phenyl ethers. These were thoroughly studied before the rearrangement of allyl vinyl ethers

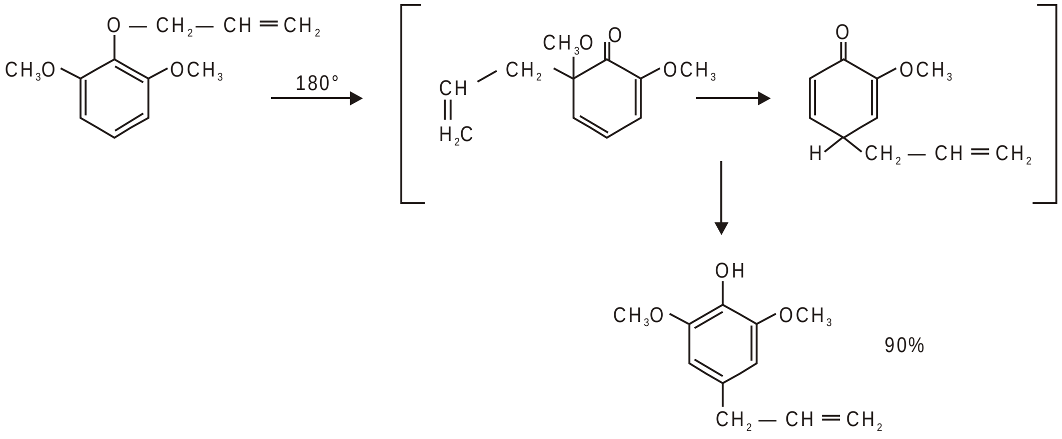


The allyl group migrates to the ortho position and using C^{14} the allylic group is end interchanged.

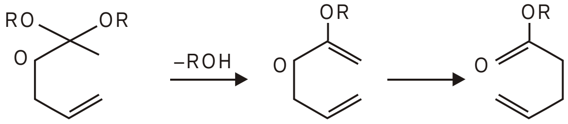
3.



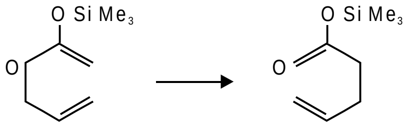
In unsubstituted phenyl ethers, the enolisation is faster than the Cope reaction. This is why the product is predominantly ortho isomer. When both the ortho positions are substituted, the allyl group undergoes a second migration via a concerted sigmatropic mechanism giving a para substituted phenol. This is called para Claisen condensation.



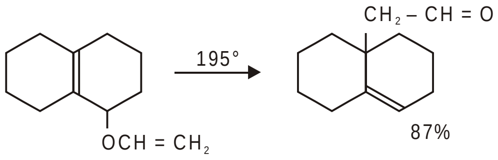
4. Orthoester Claisen rearrangement.



5. Claisen rearrangement of O-Allyl-O′ trimethyl silylketene acetals.

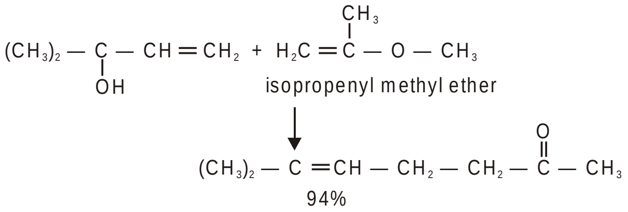


6.



This is an application of Claisen rearrangement and introduces a substituent at the angular position at the junction of two six membered rings. This type of introduction becomes necessary in the synthesis of steroids and terpenes.

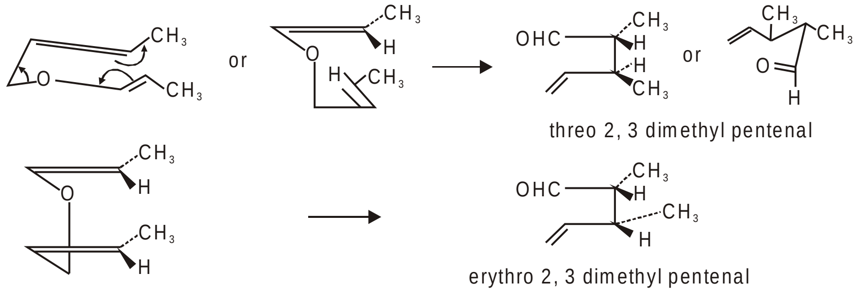
By changing the groups the process has increased the versatility of Claisen rearrangements and has made it a powerful synthetic tool. Thus long chain unsaturated ketones can be prepared in good yields by the following reaction.



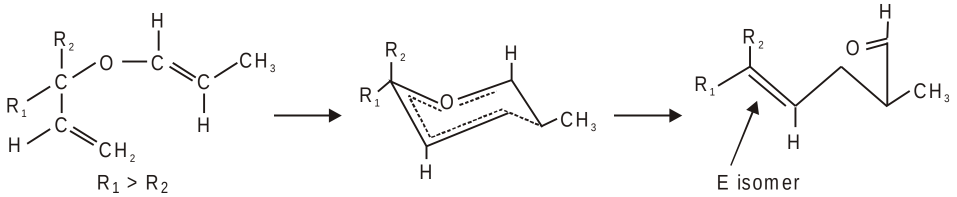
$$(CH_3)_2-\underset{OH}{C}-CH=CH_2 + \underset{\text{isopropenyl methyl ether}}{H_2C=\overset{CH_3}{C}-O-CH_3} \longrightarrow \underset{94\%}{(CH_3)_2-C=CH-CH_2-CH_2-\overset{O}{\overset{\|}{C}}-CH_3}$$

Both in the alkyl and aryl series, the reactions show characteristics of concerted processes. They are first order and have large negative entropies of activation, because of the cyclic transition state. The allylic group is inverted in the rearrangement and optical activity is retained if starting ether is optically active. Polar solvents increase the rate and the rate becomes 100 times as fast as in a non-polar solvent. The substituents appear to have little effect. Electron releasing groups increase the rate when present in the para position and electron withdrawing groups retard the process.

The Claisen rearrangement goes through a transition state in the chair conformation. This is the supported by the fact that trans, trans-crotyl propenyl ether gave more than 97% of the threo aldehyde showing a preference for the chair form while reaction in the boat gave mainly erythro aldehyde.



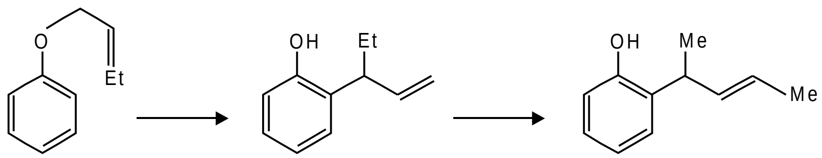
It is to be noted that in the allyl vinyl ether (where $R_1 > R_2$) the newly formed double bond has the E configuration. This is because that in the chair–like transition state, there is preference for placing the larger group in the pseudoequatorial position.



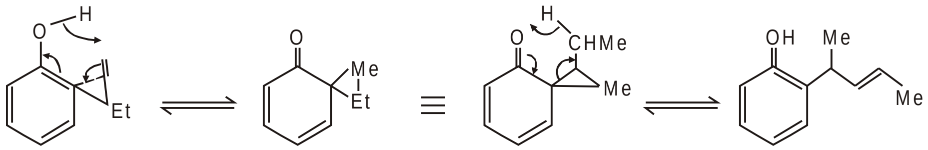
So we find that both Cope and Claisen rearrangements are [3, 3] sigmatropic rearrangements and proceed by suprafacial-suprafacial pathway.

ABNORMAL CLAISEN REARRANGEMENTS

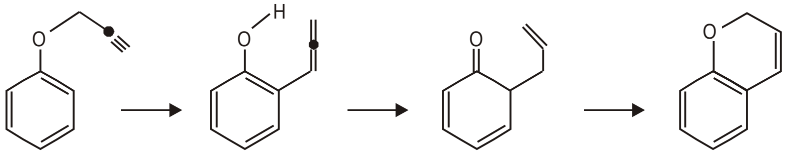
Some allyl phenyl ethers with an alkyl substituent on the end carbon of the allyl group rearrange to give the normal ortho-Claisen product together with another isomeric O-allyl phenol. The latter, formed by the rearrangement of the normal product, has been established. This is called abnormal Claisen rearrangement, is illustrated by the following example.



The mechanism is as follows:

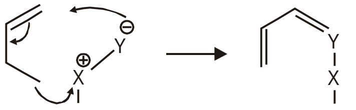


Another abnormal Claisen rearrangement is the product formed on heating phenyl propargyl ether. The normal product O-allenyl phenol rearranges by a [l, 5] hydrogen shift and then there is an electrocylic ring closure to give chromene which is the observed product.

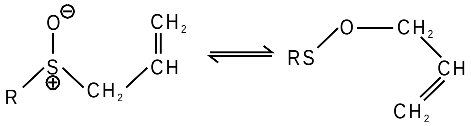


[2, 3] sigmatropic rearrangements

A class of [2, 3] sigmatropic rearrangements may be represented as



Where X is S or Se and Y is oxygen or a carbanionic site. The rearrangement of allyl sulphoxides to allyl sulphenates is an example.



This reaction was discovered while studying the mechanism of racemisation of optically active of aryl sulphoxides.

Other sigmatropic shifts

There are few examples of other allowed sigmatropic shifts involving six ten electron transition states, but these are not common reactions. A [3, 4] shift is observed in competition with a [1, 2] shift in cations derived from cyclohexane diols. This is a cationic equivalent of the Cope rearrangement,

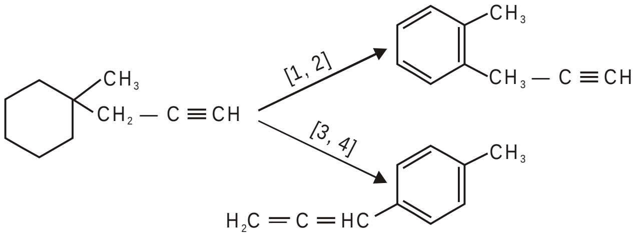


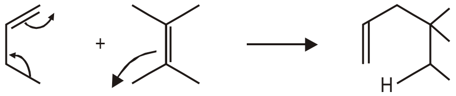
PHOTO CHEMICAL REARRANGEMENTS

Sigmatropic shifts which are unfavourable in the ground state become favourable in the first excited state under photo-chemical conditions and vice versa.

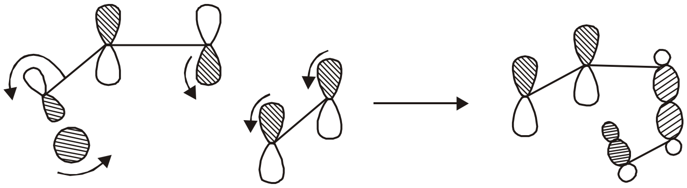
A suprafacial alkyl [1, 3] shift with retention of configuration and already discussed provides an example. The transition state contains four electrons and is of Huckel type and makes the reaction unfavourable in the ground state but many photo-chemical [1, 3] shifts do occur in the four numbered ring structure.

The ene reaction

A reaction of an allylic compound containing a hydrogen to an alkene function is an ene reaction. Thus a reaction between propene and ethylene is an example of an ene reaction.



It resembles both a cycloaddition and a [1, 5] sigmatropic shift of hydrogen. It is a symmetry allowed process shown as follows:

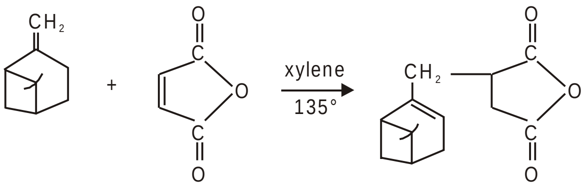


As the name implies it is related to the diene cycloaddition reaction, the Diels-Alder reaction. The 'ene' component the olefin with the allylic hydrogen, takes much the same part as the diene in the Diels-Alder reaction.

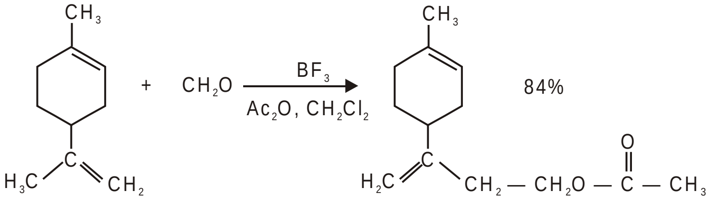
In the transition state a boat like structure appears and there will be a suprafacial cis addition to the termini of the π bond. The ene reaction does not have a symmetrical transition state and it is a thermally allowed concerted reaction. Its transition state involves a suprafacial interaction of six electrons (4 from the π bonds and two from the σ bond) So it is a Huckel system and transition state is aromatic. In the terminatlogy of Woodward and Hoffmann it can be regarded as $\sigma^2 s + \pi^2 s + \pi^2 s$ reaction.

Some examples

1. β-pinene is particularly prone to ene reactions and reacts with maleic anhydride in refluxing xylene.



2. Alkenes can react with formaldehyde under conditions of acid catalysis in an ene process where protonated formaldehyde ($CH_2 = OH$) or its equivalent acts a highly electrophilic enophile.



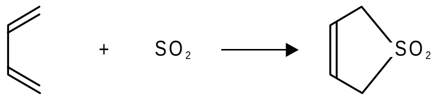
Many ene reactions can be catalysed by lewis acids, particularly $AlCl_3$ and ethyl aluminium chloride.

CHAPTER 7

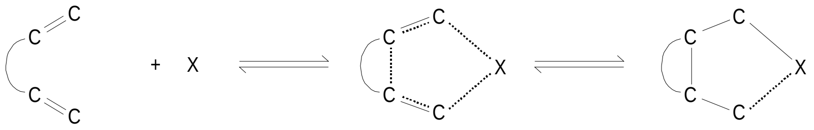
Cheletropic Reactions

INTRODUCTION

Reactions in which two σ bonds terminate at a single atom or made or broken in a concerted chemical reaction are called cheletropic reactions:



Thus in general, the reaction can be represented as



Some small molecules have a filled and vacant orbital available on the same atom for bonding to other atoms. Sulphur dioxide, carbon monoxide and singlet carbenes are examples. In each case one atom (sulphur or carbon) has a lone pair electrons in the plane of the molecule and a vacant *p* orbital orthogonal to it.

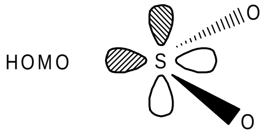
S atom in the ground state

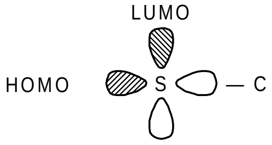
$1s^2\ 2s^2\ 2p^6\ 3s^2\ \overset{3p}{\boxed{\uparrow\downarrow}\boxed{\uparrow}\boxed{\uparrow}}$

C atom in the ground state

$1s^2\ 2s^2\ \overset{2p}{\boxed{\uparrow\downarrow}\boxed{\uparrow}\boxed{\uparrow}}$

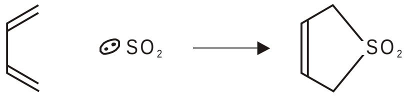
The HOMO and LUMO in the case of SO_2 and CO are shown below in which the HOMO is that which has a lone pair of electrons in the plane having the atoms while the LUMO represents the *p* orbital perpendicular to this plane.





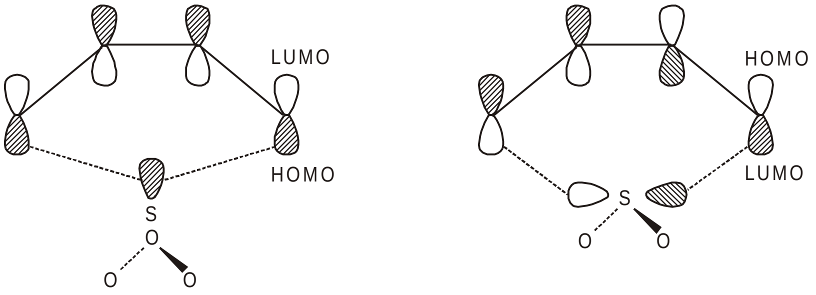
Symmetry allowed Cycloaddition of SO_2 to a diene

In cycloaddition or eliminations involving of such molecules of σ bonds which are formed or broken are to the same atom. For example the addition of butadiene to SO_2 is as follows:

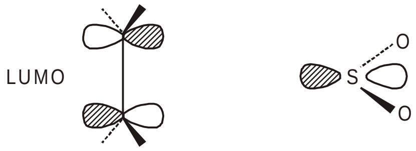


Woodward has proposed the word cheletropic (from the Greek Chele-meaning claw) for such reactions.

The molecule of SO_2 must lie in a plane which bisects the suprafacial cis conformation of the diene. This attack of SO_2 will be from below, so that a concerted suprafacial, suprafacial addition is allowed. Such reactions are called *linear* cheletropic processes.



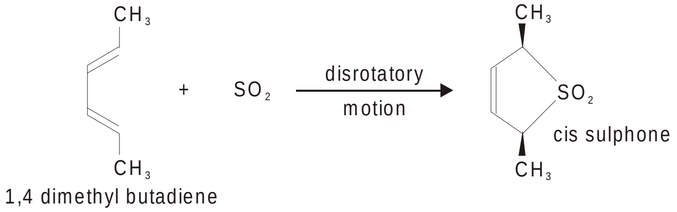
Linear cheletropic addition of SO_2 to butadiene



Concerted suprafacial, suprafacial addition to an alkene

The concerted suprafacial, suprafacial addition to an alkene as shown above is a disallowed process. So in linear cheletropic process the interaction is suprafacial for both orbitals of the diene and also for HOMO of SO_2, but it is antarafacial for the LUMO of SO_2.

So in the transition state, the terminal carbon atoms of the diene must move in the disrotatory manner so that the HOMO of SO_2 can interact with the LUMO of diene or the LUMO of SO_2 with the HOMO of diene. This is why trans, trans 1, 4 disubstituted dienes give 3 substituted sulphones.



But in photochemical reactions, the stereochemistry becomes opposite.

As a result of several experiments, the following conclusions have been arrived at:

The linear cheletropic reactions in which the polyene is a suprafacial component (*i.e.*, involving disrotatory motion of the termini) will be allowed if it has a total of (4*n* + 2) electrons. But linear cheletropic reactions in which the polyene is an antarafacial component (*i.e.*, involving conrotatory movement of the termini) are allowed if it has a system of 4*n* electrons.

These rules are reversed for a non-linear cheletropic change

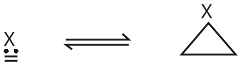
Cheletropic reactions include both addition and elimination reaction. The number of elimination reactions that have been studied in detail is not large but there is sufficient information to establish that orbital symmetry controls are operating.

Various Cheletropic reactions

Cheletropic reactions can be studied under different heads.

Cheletropic reactions involving 4 electrons

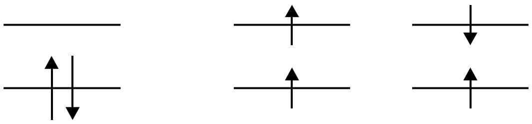
The cycloaddition of an atom or group X to an olefine to form a three-membered ring and the reverse process constitutes an example of four electron cycloaddition or elimination and if the reaction is concerted it becomes an example of cheletropic reaction.



The forward reaction is limited to the addition of high energy species such as carbenes or nitrenes.

Addition of carbenes or nitrenes

Carbenes ($:CR_2$) and nitrenes ($:\ddot{N}R$) are short lined reactive intermediates which are electron deficient. They contain a carbon or nitrogen atom with two non-bonding orbitals between which are distributed 2 electrons. These two electrons can be in the same orbital or one electron may be in each.



Singlet ground state

Triplet structures after excitation

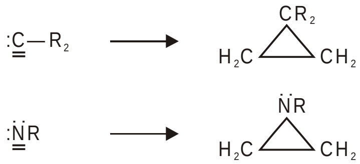
The carbenes can have a non-linear or linear structure as follows:

Non linear structure

Linear structure

The bent structure, increases the difference in energy of non-bonding orbitals and is likely to be formed for the singlet ground configuration whereas the excited configurations are likely in a linear or nearly linear structures.

Carbenes and nitrenes add to olefines to give cyclopropanes and aziridines respectively.



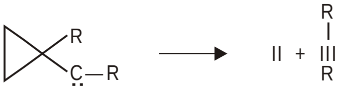
These are 4 electron reactions and synthetically very useful. These additions are not given by all carbenes and nitrenes. Many preferentially undergo rearrangement, fragmentation, insertion or hydrogen abstraction. Sometimes these reactions can be avoided by using metal catalysts in the decomposition of carbene precursors or by using organometallic sources of the intermediates.

The following table given carbenes and nitrenes which commonly add to olefines.

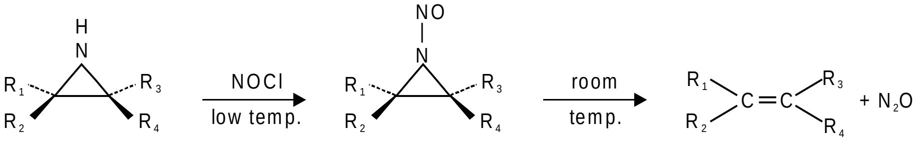
Table 7.1

Carbenes	
methylene	: CH_2
dihalogenocarbene	: CX_2 (X = F, Cl, Br)
vinylidene carbenes	: $C = CR_2$
diaryl carbenes	: CAr_2
atomic carbon	: C :
Nitrenes	
cyanonitrene	: $\ddot{N}CN$
amino nitrenes	: $\ddot{N}NR_2$

Some fragmentation reactions from cyclopropyl carbenes and aziridine derivatives are as follows:

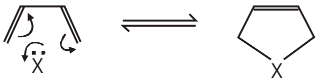


N-Nitrosoaziridines are unstable compounds formed from aziridines and nitrosyl chloride at low temperatures. At room temperature they decompose stereospecifically giving nitrous oxide and the olefine.



Cheletropic reactions involving 6π electrons

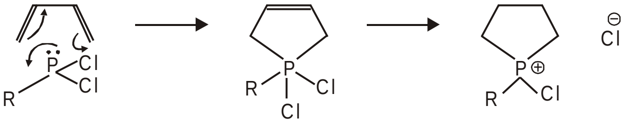
Six electron cycloaddition of the type shown below where both sigma bonds are formed to the same atom of one component are quite limited



This is because of retro-cycloaddition. In retro-cycloadditions, the reverse reactions are more favoured and the same selection rules apply. This is also because that X is normally a small inorganic molecule and of high thermodynamic stability.

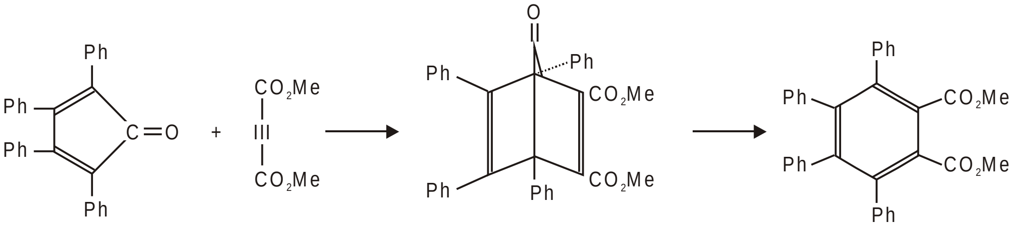
The forward reaction is only well known for SO_2, but even in this case the reverse reaction takes place readily and this property has been applied in the separation and purification of dienes. The addition of sulphur monoxide has also been reported by R.M. Dodson and R.F. Sauers (Chem. Comm. 1967, 1189). SeO_2 also adds to dienes in a Diels-Alder manner in which Se = O acts as dienophile.

Another example of 6 electron cheletropic reaction is the addition of trivalent phosphorus compounds with the dienes



These 6π electron additions and eliminations are apparently concerted and thus come in the category of linear cheletropic process ($\pi^4s + \omega^2s$ cycloaddition and $\pi^2s + \sigma^2s + \sigma^2s$ cycloelimination).

The loss of carbon monoxide from cyclopent-3-enones proceeds much more readily than the loss of carbon monoxide from cyclopropanones and cyclopentanones.

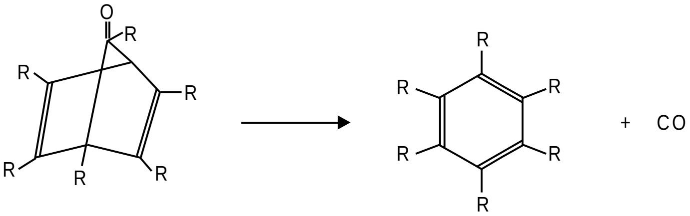


Although a detailed stereochemical study is not available, the generality and the ease of the reaction suggest that the process is concerted. The loss of carbon monoxide becomes particularly easy when an aromatic product is formed.

The extrusion of CO becomes so easy because it is thermodynamically stable.

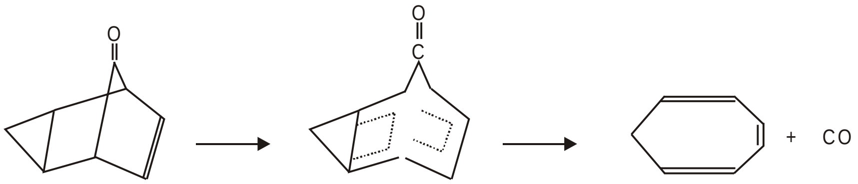
Facile thermal expulsion of CO occurs only in molecules which permit a concerted bond making and bond breaking.

The generation of bicyclo [2.2.1]-heptadiene-7-one is accompanied by the elimination of CO spontaneously

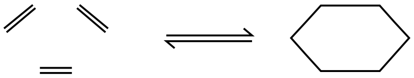


This reaction is utilised for the synthesis of highly substituted benzene rings. Higher temperatures are required to eliminate CO from related systems that cannot lead directly to an aromatic ring.

Exceptionally facile elimination of CO also takes place from the following structure in which monoaromaticity can stabilize the transition state.

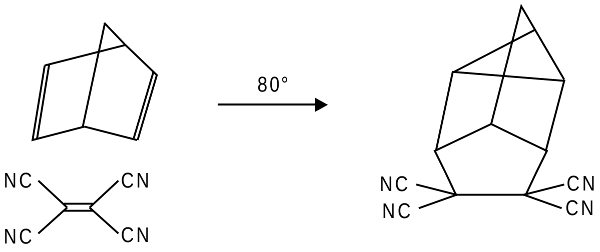


2 + 2 + 2 Cycloadditions and eliminations



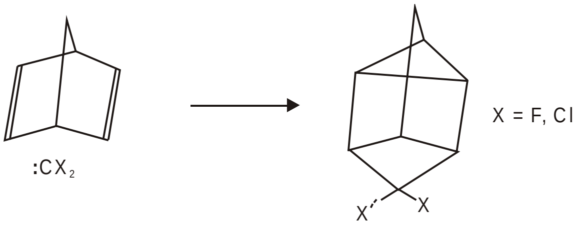
Concerted 2 + 2 + 2 cycloadditions are thermally allowed as $\pi^2 s + \pi^2 s + \pi^2 s$ or $\pi^2 s + \pi^2 a + \pi^2 a$ processes. The termolecular collisions necessary for these cycloadditions are very unlikely and the only examples known are those where at least two of the component π bonds are held together in one reactant.

An example of such $\pi^2 + \pi^2 + \pi^2$ addition is the cycloaddition of tetracyanoethylene and other dienophile to nor bornadiene.

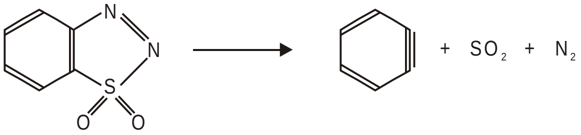


The geometry of the molecule favours the process. This reaction is also called **homo-Diels-Alder** reaction because a cyclopropane ring is formed rather than a π bond.

A possible 2 + 2 + 2 addition involving a cheletropic component is the addition of dihalocarbenes to norbonadiene.

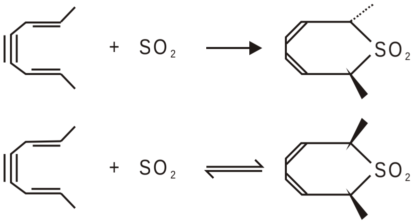


There are several examples of fragmentation involving cheletropic components. Some of these are:

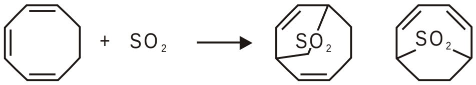


Cheletropic reactions involving 8π electrons

SO_2 adds readily to cisoid hexatrienes by a linear cheletropic $\pi^6 s$ and $\omega^2 s$ process.



The reverse reaction is a linear cheletropic extrusion of SO_2 with conrotatory twisting of the terminal methylenes. With cyclic triene SO_2 forms only the 1,4 adduct. In this case the antarafacial addition to the triene is geometrically impossible and the alternative non-linear $\pi^6 s + \omega^2 s$ process does not compete with the concerted $\pi^4 s + \omega^2 s$ linear cheletropic addition to a diene component. So a non-linear cheletropic addition containing eight electrons becomes highly unfavourable. This is illustrated by the fact that SO_2 is eliminated 60,000 times more slowly (even at 180°) from (*c*) than from (*b*). In (*b*) $\pi^4 s + \omega^2 s$, retro process is allowed.



(a) (b) (c)

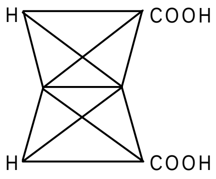
The geometry of (*c*) makes conrotatory twisting of the two methylene groups (6 retro $\pi^6 s + \omega^2 s$) impossible. So if it has to be concerted, the elimination would have to be non-linear cheletropic.

CHAPTER 8

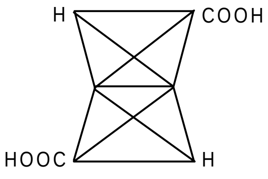
Geometrical Isomerism

GENERAL INTRODUCTION

Maleic and fumaric acids both having the molecular formula $C_4H_4O_4$ were originally regarded as structural isomers and this is why different names were given to them. But because on reduction and several addition reactions both gave the same products, they were later recognized to be examples of spatial isomers. For example., reduction with hydrogen over nickel or platinum catalyst gives succinic acid in both the cases. Both add a molecule of water or hydrogen chloride and give malic acid or chlorosuccinic acid respectively. When it was realized that they were examples of spatial isomers, van't Hoff gave the following structures to them in which the two tetrahedra are placed edge to edge.

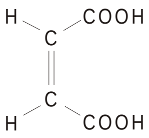


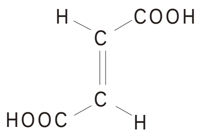
maleic acid
(cis)



fumaric acid
(trans)

In one similar groups are situated on the same side while in the other they are present on different sides. The former is called the cis and latter the trans form. This is why this type of spatial isomerism is called the cis-trans isomerism and was the first to be studied in olefinic compounds. It has occurred because of the different geometric forms of the isomerisms. Writing the same thing on the plane of paper, the forms become





The cis form is the maleic acid while the trans form is the fumaric acid.

Now we know that since maleic acid on heating gives the anhydride by cyclization easily which is not possible from fumaric acid, the two carboxyl groups are much closer to each other in maleic than in fumaric acid and hence the above two different configurations have been given.

The term configuration signifies the spatial arrangement of atoms in stereoisomers which differ from one another because their atoms are arranged differently in space. Therefore this term is different from constitution or conformation.

In the above arrangement the two hydrogen atoms and the two carboxyl groups are all in one plane, or the molecule is flat. The cis-trans isomerism is also called geometrical isomerism and we know that this isomerism is shown not only by olefines but by a large variety of compounds which may be broadly classified as follows:

1. Compounds having double bonds.
2. Compounds with cyclic structures. This includes homocyclic, heterocyclic and fused ring systems.
3. Compounds with restricted rotation about a sigma bond.

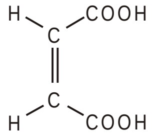
Compounds having Double Bonds

The type of compounds containing double bond and showing geometrical isomerism includes those having C=C, C=N and N=N structures.

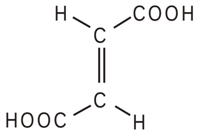
The second important condition in C=C group is that each of the doubly linked carbon atoms is attached to two different univalent atoms or groups.

Thus the following type of compounds exhibit geometrical isomerism

(a)

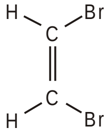


maleic acid (m.p. 130°)

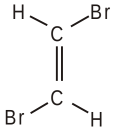


fumaric acid (m.p. 286°)

(b) The two acetylene dibromides

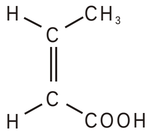


cis (m.p. 53°)

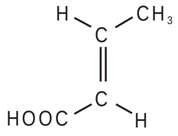


trans (m.p. 6.5°)

(c) Crotonic and isocrotonic acids.

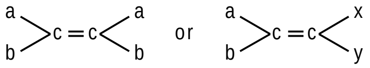


isocrotonic acid cis
(m.p. –15°)

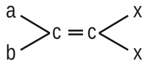


crontonic acid trans
(m.p. –72°)

Thus the isomers in these cases have the same molecular and structural formulae but slightly different physical and chemical properties. So in general it can be said that all olefinic compounds having the formula



may be expected to show geometrical isomerism while compounds of the general type

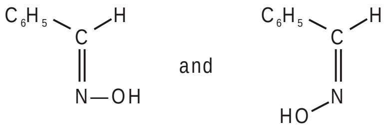


will not show the isomerism because one carbon atom is linked to similar groups.

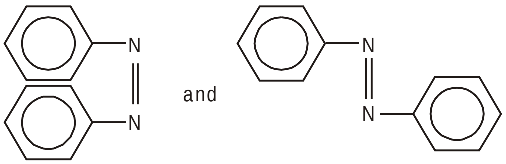
The examples of compounds showing geometrical isomerism and having >C=N- structure are afforded by the oximes of aldehydes and ketones. Benzaldoxime, prepared by the action of hydroxylamine or benzaldehyde exists in the two forms.

$$C_6H_5 - CH = O + H_2\ NOH \longrightarrow C_6H_5CH = NOH$$

benzaldoxime



An example of a compound of the –N=N– structure and showing geometrical isomerism is the syn and anti form of the azobenzene.



syn anti

Isomerism in all these compounds is due to the different spatial arrangement of the atoms within the molecule. The difference in properties between the two forms is sometimes so marked, that it constitutes a method for the determination of configuration of the cis-trans isomeric forms.

Why this isomerism is found in double bond compounds?

We have seen that this isomerism is found in alkenes provided some structural conditions are fulfilled. The question is why this isomerism is found in such type of alkenes?

We know that in alkenes a double bond consists of a σ and a π bond. The *p*-orbital tends to overlap as much as possible to make the bond strong because the greater the overlap of the two *p* orbitals, the stronger would be the bond. Maximum overlap occurs when the molecule becomes planar because in this condition the two *p* orbitals are parallel. Any distortion from the planar structure leads to decreasing overlap of the orbitals and a consequence of the weakening of the bond. The picture is represented as follows:

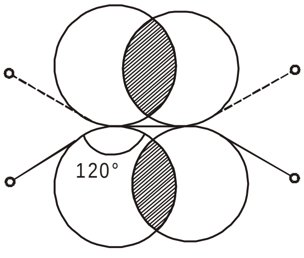


Fig. 8.1

On account of this overlap there is considerable resistance to rotation about a double bond and it produces a rigid molecule. In other words the disposition of groups attached to the carbon atom can be shown in different ways in space, giving rise to isomers. Therefore geometrical isomerism is a consequence of restricted rotation about double bonds.

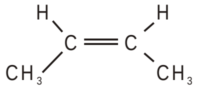
We have already seen that geometrical isomers exist in cis and trans forms provided at either end of the double bond, the carbon atoms carry different groups. However the number of geometrical isomers increases with the number of double bonds provided the above conditions are fulfilled and the number is obtained by the relation:

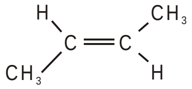
Number of geometrical isomers = 2^n

where *n* is the number of such double bonds which have different substituents at each end.

Relative stabilities of isomers

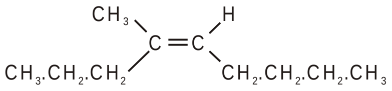
The relative stabilities of the two forms depend on the nature of groups present on the carbon atoms. Since in the cis form the groups are close enough to each other, they suffer a sort of strain due to crowding which does not occur in the trans form. Consequently the cis becomes less stable of the two. This is why cis-2 butene is slightly less stable than the trans.



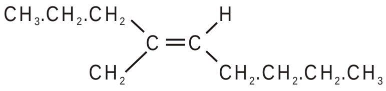


However when bulkier phenyl groups are present as in 1,2 diphenyl ethylene (also called stilbene) the equilibrium mixture at room temperature contains several thousand times the trans form as compared to the cis. This is because of the energy difference between the two. But these empirical generalizations hold good only when the groups in question are alkyl radicals. For example the cis 1,2 dichloroethylene is more stable than trans. This is not very well understood at present.

It is easy to describe cis and trans forms in simple molecules. When four different groups are attached to a carbon-carbon double bond the cis form is that which contains the longest carbon chains on the same side of the double bond.



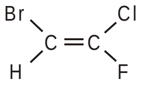
cis



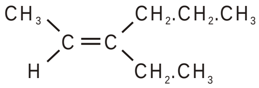
trans

NOMENCLATURE OF GEOMETRICAL ISOMERS

When geometrical isomerism is due to the presence of one double bond where only two substituents are present it is easy to designate the isomers by the terms cis and trans. But if the alkene is a tri- or tetrasubstituted one, the terms cis and trans become ambiguous and do not apply at all as in the following examples.



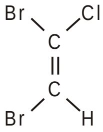
I



II

It becomes difficult to decide whether, for example 1 is cis or trans isomer No. two groups are the same and the same is true for the compound II. The Chemical Abstracts Service has proposed an unambiguous system that has been adopted by IUPAC and is based on the preferences of groups. It is also called the E-Z system and applies to alkene diastereomers of all types.

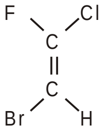
In the E-Z system we first examine the two groups attached to one carbon atom of the double bond and then arrange them in order of preference of atomic number. Then we repeat this operation at the other carbon. When the two groups of higher priority number are on the same side of the molecule, the compound is the Z isomer (from the German word zusammen, meaning together) But if the two groups of higher priority number are on opposite sides of the double bond, the compound is the E form (from the German word entgegen, meaning opposite). The following examples would illustrate the point clearly.



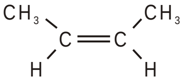
Z

$Cl > F$

$Br > H$

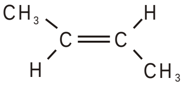


E



(Z)-2-butene
cis-2-butene

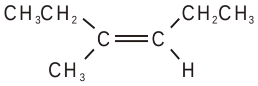
$CH_3 > H$ $CH_3 > H$



(E)-2-butene
trans-2-butene

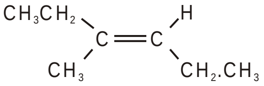
$CH_3 > H$

$CH_3CH_2 > CH_3$



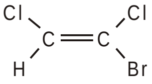
(Z)-3-methyl-3-hexene

$CH_3CH_2 > H$



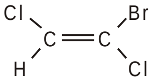
(E)-3-methyl-3-hexene

There are exceptions also:



$Cl > H$

$Br > Cl$



(E) 1 bromo 1:2 dichloroethane (Z) 1. bromo, 1,2 dichloro ethan

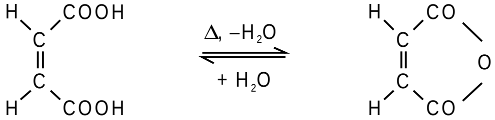
Sometimes the prefix iso is used to signify the less stable isomer as in isocrotonic acid which is cis and it is less stable. Similarly the prefix allo is also used to signify the less stable isomer; e.g., allocinnamic acid.

It is to be noted that geometrical isomers are now also classified as diastereoisomers. Therefore diastereomers are any stereoisomers which are not enantiomers of each other and the term is not restricted to optical isomers only.

DETERMINATION OF CONFIGURATION OF GEOMETRICAL ISOMERS

There is no general method for determining the configuration of cis-trans isomers. A number of methods are employed to get reliable results. The methods employed depend on the nature of the compound. The following are some of the methods employed.

(*i*) ***Method of cyclisation:*** Wislicenus was the first to suggest that an intramolecular reaction would take place easily if the reacting groups are on the same side of the double bond. Thus to find out the configuration of maleic and fumaric acids, we heat the two acids. Since the former forms the anhydride easily and not the latter, the former is cis while fumaric acid is trans. Also since the anhydride adds on water even at room temperature and is transformed back into maleic acid, there can be no doubt about the maleic acid being cis.



Note that during the cyclization process, the bonds between the unsaturated carbon atoms and their nearest substituent remain intact and on this basis the configurations have been determined. If, however this center, also called steric center, is disturbed, then the results of configurations may become erroneous.

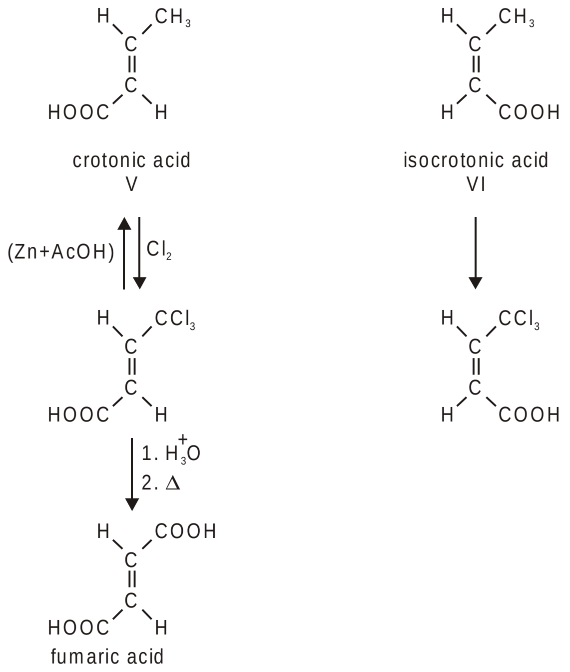
On similar reasonings the configuration of citraconic acid is cis because it forms the anhydride while its isomer mesaconic acid is trans.

citraconic acid
III

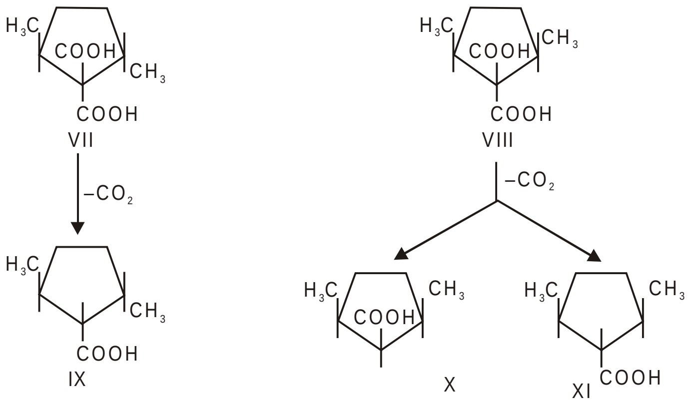
mesaconic acid
IV

(*ii*) ***By converting the compounds into compounds of known configuration:*** In this method a compound of unknown configuration is converted into a compound having known configuration. Naturally here also the steric center must be left intact.

We know that crotonic acid exists in cis and trans forms and to find their configurations we take the two trichlorocrotonic acids and carry out their hydrolyses. One gives fumaric acid and so crotonic (V) acid becomes the trans forms while isocrotonic acid (VI) is thus the cis form.



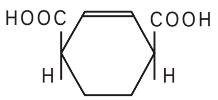
(*iii*) ***By converting the compound into less symmetrical compounds:*** It is a peculiar method of determining the configuration of cyclic compounds which involves converting the compound into a compound of lower symmetry. For example there are two 2, 5 dimethylcyclopentane 1, 1-dicarboxylic acids, one is the cis and the other is trans. Each one of them on decarboxylation forms 2, 5 dimethyl cyclopentane-1-carboxylic acid. The trans isomer VII gives only one monocarboxylic acid (IX), while the cis isomer (VIII) forms two stereoisomeric monocarboxylic acid X and XI depending on which of the carboxyl group is eliminated.



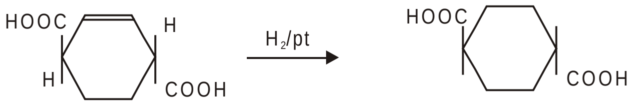
Therefore in one case the number of geometrical isomers increases and so the configurations of dicarboxylic acids are determined.

(*iv*) ***Method of optical activity:*** **Many geometrical isomers having cyclic structures are optically active and so are resolvable and their configurations can be established.**

For example, cyclohexene dicarboxylic acid exists in cis and trans forms XII and XIII.



cis
XII



trans
XIII

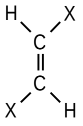
hexahydrophthalic acid
trans
optically active
XIV

The trans form, since it has no plane of symmetry is optically active and is resolvable and since on catalytic reduction it gives hexahydrophthalic acid (m.p. 309°C) and whose trans configuration is unambiguously established, therefore the trans configuration of XIII is also established.

Some physical methods for the determination of configurations

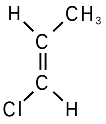
A number of physical methods are also employed to determine the configurations of cis-trans isomers. Some of these are described below.

(*i*) ***Method of dipole moments.*** Many cis-trans isomers show characteristic differences in the magnitude of their dipole moments. Compounds of the type XCH=CHX where X is a single atom or a simple group with cylindrical symmetry, the dipole moment of the trans form is zero:

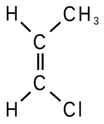


$\mu = 0$

But if there are different substituents at the double bond, the dipole moment of the trans form will not be zero but the differences for the cis-trans isomers of such compounds in many cases are characteristic as in the following example:



$\mu = 1.97$ D
XV



$\mu = 1.71$ D
XVI

In 1 chloro-1-propene XV the trans has a greater dipole than the cis XVI. Because the methyl group has electron donor and chlorine electron-acceptor properties and in the trans form there is vectorial addition of dipole moments of both polar bonds, therefore, the view that the cis form has always a dipole moment higher than the trans is erroneous. Still in other cases the differences in the dipole moments of cis and trans isomers may be too small to assign the configuration with any confidence. This is why the method of dipole moments of assigning configurations to geometrical isomers must be used with caution.

(*ii*) ***Melting point, boiling point, solubility etc.*** Most geometrical isomers show characteristic differences in melting point and solubility in various media and from a number of observations, the following generalizations have been arrived at :

(*a*) The trans form has a higher melting point and a lower solubility than the cis form.

(*b*) The boiling point, heat of combustion, heat of hydrogenation, density, refractive index of the cis isomer are greater than the trans.

	m.p.	*density*
Maleic acid (cis)	130°	
Fumanoic acid (trans)	286°	
Acetylene dibromide (cis)	–53°	2.2846
Acetylene dibromide (trans)	–6.5°	2.2667

Exceptions are also known where the higher melting form is more soluble.

(*c*) A determination of the dissociation constant of the cis-trans isomer also helps in establishing the configuration of the isomers.

Let us take maleic and fumaric acids. The values of the first and second dissociation constants are as follows:

	Maleic acid (cis)	*Fumaric acid (trans)*
Dissociation constant		
Ist	1.2×10^{-2}	1×10^{-3}
IInd	3×10^{-7}	3×10^{-5}

Because of the two carboxyl groups to be nearer each other due to spatial arrangement, the tendency of the hydrogen to go off as H^+ is greater in the cis than in the trans form. This is why the first dissociation constant of cis is greater than the trans. But once the hydrogen has gone off as proton, it becomes difficult for the second proton to overcome the attraction of the two closely spaced COO^- groups in the cis form. This explains why the second dissociation constant of the cis is lower than the trans form.

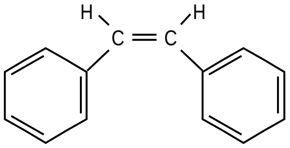
(*d*) Because of greater symmetry, the trans forms are thermodynamically more stable than the cis forms. This is why the heat of combustion of maleic acid is higher (1370 kJ/mole) than that of fumaric acid (1340 kJ/mole). This is also the reason why cis forms often spontaneously turn into the energetically more favourable trans forms. The reverse conversion is possible when a certain quantity of energy is consumed in the form of ultraviolet radiation.

Based on these generalizations is the Auwers-Skita rule according to which; in a pair of cis-trans isomers, the cis has a higher boiling point, density and refractive index. Thus in general the trans form usually the stabler of the two isomers.

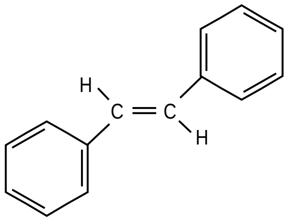
SPECTROSCOPIC METHODS OF DETERMINING THE CONFIGURATIONS

1. Ultraviolet spectra. The absorption in compounds containing conjugation is due to π-π transition and the longer the conjugation the longer is the wavelength of absorption.

Let us take the case of cis and trans stilbenes. (diphenylethylene).



cis-stilbene
λ_{max} = 280 nm
(ε = 10,500)



trans-stilbene
λ_{max} = 296 nm
(ε = 29000)

In the cis form because of the proximity of two large benzene rings, they cannot be arranged in the same plane and there will be decreased overlap of the π electrons. This results in shorter wave lengths and lower extinction coefficient as composed with trans, which is planer, has larger λ_{max} and extinction coefficient. So is also the case with cinnnamic acid where the values are :

	cis-isomer	trans-isomer
Cinnanic acid	λ_{max} = 280 nm	λ_{max} = 295 nm
	(ε = 13,500)	(ε = 27000)

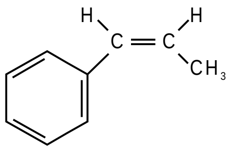
2. Infrared and Raman spectra. The infrared spectra of cis-trans isomers of unsymmetrical alkenes of the type R-CH=CH-R′ show characteristic differences

	cis-isomer	trans-isomer
Stretching frequency of C=C	1660 (medium)	1675 (weak)
Deformation vibrations of	C-730-675 (strong)	965 (strong)

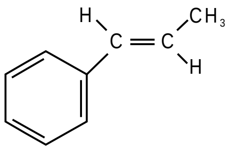
Absorption brought about by C-H bending is much more intense than that brought about by C=C stretching. The vibration band of C=C for cis forms is more intense than that for transforms.

In the trans isomers of symmetrically substituted olefins there is no absorption in the region of 1600 cm^{-1} in the IR spectra.

In the Raman spectra in cis-olefins the stretching vibrations of the C=C is at lower frequencies (1654-1657 cm^{-1}) than in trans olefins (1668-1671 cm^{-1}). For example



1653 cm^{-1}



1668 cm^{-1}

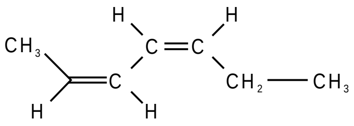
3. NMR spectra. The use of NMR spectroscopy for distinguishing between the cis and trans isomers is based on the fact that the spin-spin coupling constants of olefine protons in disubstituted alkenes are as a rule different. The spin-spin coupling constant is usually 4-12 cps (7 cps on the average) with cis protons as the double bond and 12-18 cps (15 cps on the average) with the trans isomer and so can be distinguished.

4. Mass spectrometry. The technique of mass spectrometry has also been employed to characterize the cis-trans isomers. Generally the trans isomers give molecular ions of higher intensity than the cis and the greater the steric effects in the molecule, the greater is this diference in intensities.

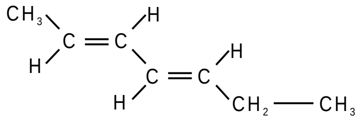
For fragment ions also it has been found that the intensity is greater for trans than for cis isomer.

Number of Geometric Isomers

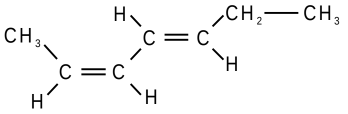
We have seen that provided other conditions of geometrical isomerism are satisfied, a compound exists in its cis or trans forms. But a question arises as to how many isomers will be obtained if a molecule contains more than one double bond? Naturally the possibility of geometrical isomerism and the formation of more isomers increases with the increase of double bonds. Each additional and **different double bond** having proper requisites **doubles the number** of geometric isomers. For example 2,4-heptadiene exists in the following four geometric forms. The different forms have been named depending on the presence of similar or dissimilar groups on the same side of double bonds.



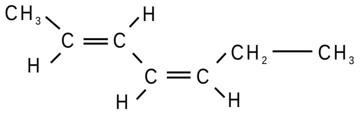
cis-cis



trans-trans



cis-trans



trans-cis

Like the rule for optical isomers, if *n* represents different double bonds, each satisfying the requirements of geometric isomerism, the number of geometric isomers will be given by 2^n.

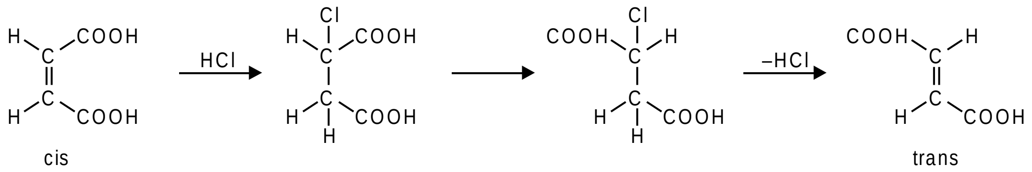
STABILITY AND INTERCONVERSIONS OF CIS-TRANS ISOMERS

The cis and trans forms differ greatly in energy and the cis form, being generally less stable, is readily converted into the trans form in presence of suitable reagents like halogens, halogen acids or nitrous acid e.g.,

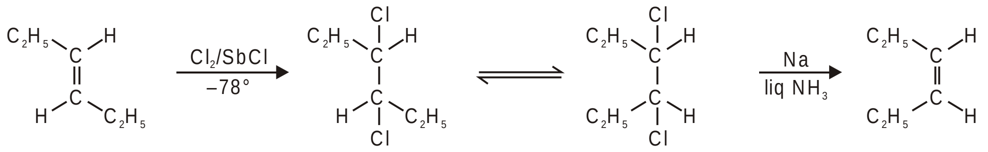
$$\text{maleic acid} \xrightarrow{Br_2,\ I_2 \text{ or } HX} \text{fumaric acid}$$

Other methods such as prolonged heating above the melting point or in presence of catalysts have also converted cis into trans forms. Thus in the pair of maleic-fumanic acid, the transform appears to be more stable and the same situation exists in cinnamic acids, stilbenes, 2-butenes and many other compounds. **However it cannot be generalized that trans forms are always invariably more stable than the cis forms,** because Viche found that in l-bromo-2-fluroethylene or 1,2-dibromoethylene the cis is more stable than the trans.

The reverse change of the conversion of trans into cis involves an increase of energy and is brought about by sunlight or best by ultraviolet light in presence of a trace of bromine. Wislicenus suggested that an alternative addition and elimination of the reagent took place during such a change. After the addition has occurred, the carbon atoms become singly bound and consequently free to rotate around their common axis. Assuming that a certain rotation has taken place, the subsequent elimination of the reagent would give the stereoisomer of the original substance. The conversion of maleic into furanic in presence of HCl is represented as follows:



Similarly the conversion of trans 1,2 diethyl ethylene into its cis isomer is represented as follows:



However in certain cases no reagent is used shows that the mechanism is not so simple. Further in the conversion of cis glutaconic acid into the trans form has thrown light that unexpected phenomena may occur in what seem to be very simple reactions and may sometimes lead to erroneous conclusions.

Preparation of cis-trans isomers

The methods to prepare cis-trans isomers are broadly put in two categories.

1. Physical Methods
2. Chemical Methods

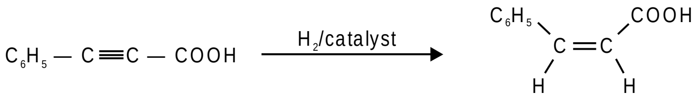
1. *Physical Methods*

Since the isomers differ in their physical properties, techniques of distillation, crystallization or chromatography have been employed.

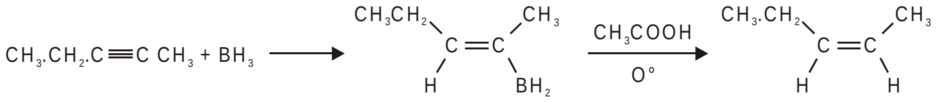
2. *Chemical Methods*

The chemical methods are more interesting and involve the formation of double bond in the molecule. In the process one stereoisomer is formed in larger amounts than the other. The methods generally are of two types

(*i*) **Additions at the triple bond.** The catalytic hydrogenation of acetylenes gives predominantly the cis isomer. The reason is obvious. Both the hydrogen atoms approach the double bond from the same side from the side of the catalyst. The hydrogenation of phenyl propiolic acid is an example.



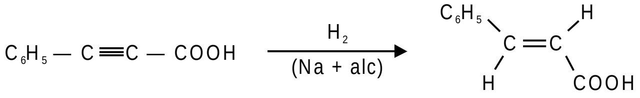
The hydroboration of alkynes gives predominantly cis isomer, as in the following example. Diborane adds as BH_3 to alkynes in a cis isomer and forms vinyl boranes which react with acetic acid at low temperature to give cis-alkenes.



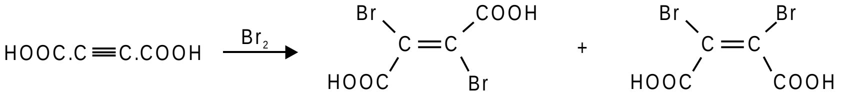
(a vinyl borane) cis-2-pentene

It is an example of stereoselective reaction as it leads predominantly one form.

The reduction with nasdcent hydrogen (sodium in alcohol or zinc in acetic acid) leads to the more stable, often the trans isomers.

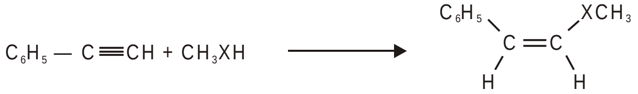


But catalytic reduction of the same phenyl propionic acid gives cis cinnamic acid. Therefore by adding hydrogen under various conditions, one can obtain a desired isomer. The conversion of acetylene into olefinic compounds has been carried out not only for the sake of obtaining the adduct, but Michael studied the various addition reactions for the sake of obtaining a desired product cis or trans. For example, he found that the addition of bromine to acetylene-dicarboxylic acid leads predominantly to the formation of trans isomer.



trans (70%) cis (30%)

The nucleophilic addition of anions CH_3O^-, RS^- or ArS^- also proceeds by trans scheme.



(X = 0, S)

(*ii*) ***Elimination reactions.*** We know that Elimination Reactions proceed by E1 or E2 mechanisms. Reactions involving the elimination of halogens, halogen acids, water or amines etc. usually proceed by the scheme of trans elimination and from a number of studies it has been shown that trans eliminations occur more readily than cis.

Direct experimental evidence for the trans elimination in E2 reactions has been obtained from deuterated -2-bromobutane (the deuterium atom occupies position 3). This compound on dehydrobromination forms trans and cis butene-2 in the ratio of 6:1

CH_3-CHBr-CHD-CH_3

Deuterated 2-bromobutane

The fact that the trans compound contains no deuterium, while the cis compound contains it, shows that the reaction proceeds by trans mechanism.

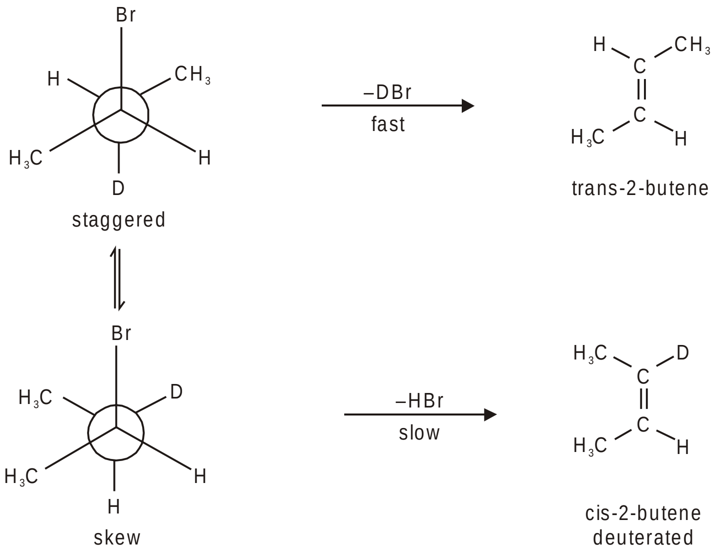


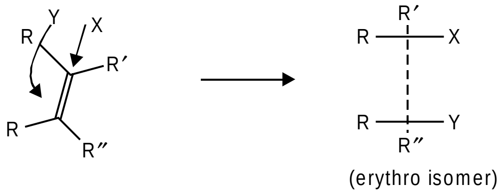
Fig. 3

The formation of the desired product depends on the nature of the substituents present in the starting compound, particularly its volume, the electronic properties of the substituents, their ability to form hydrogen bonds and other factors. Then the conformation of the original compound may be favourable or unfavourable for the reaction. The steric factors may also come into play in 1,2 elimination reactions.

STEREOCHEMISTRY OF ADDITIONS TO DOUBLE BONDS

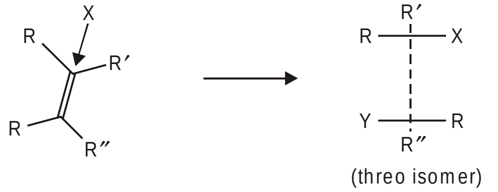
An important question that has been attracting the attention of chemists since the end of the last century was about the approach of the attacking species on the double bond whether the attacking species approach the double bond from the same side (cis-addition) or from opposite sides (trans addition)? Now it has been established that it all depends on the type of the reagent and also on the configuration of the olefine. To illustrate the point various cases may arise.

1. cis-Addition to cis olefines



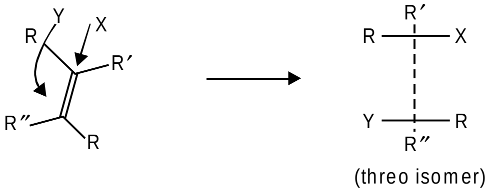
If R′=R″ and X=Y, then a meso compound is formed

2. trans-Addition to a cis olefine

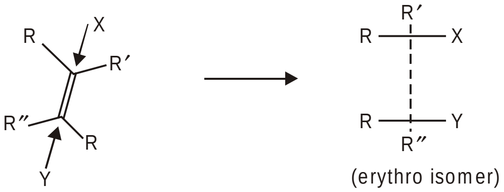


If R′=R″ and X=Y, then a recemic mixture is likely to be the product.

3. cis-Addition to a trans olefine

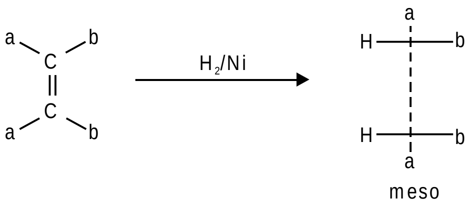


4. trans-Addition to a trans olefine

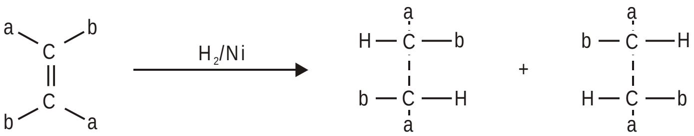


cis-Addition Reactions

Let us take the hydrogenation of a cis alkene in presence of a catalyst. Because the attacking particle on both the carbon atoms is the same and the alkene is also cis, as expected we get a meso compound.



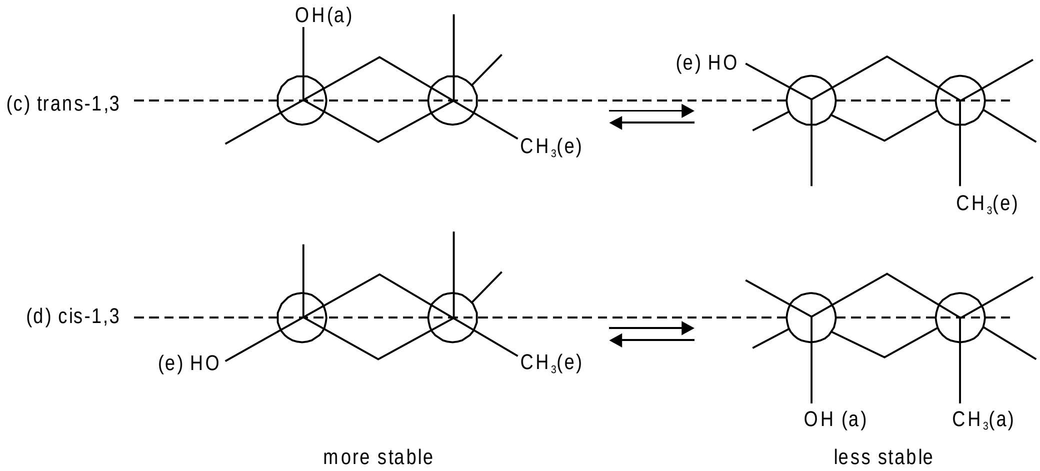
But if the alkene is a trans one, the same hydrogenation will give a racemate.



The above rule of catalytic hydrogenation on cis alkenes operates in a large number of cases, but there are also some exceptions.

Another familiar example of the reaction proceeding in cis fashion is the hydroxylation of alkenes which occurs by osmium tetroxide or by the action of $KMnO_4$.

Its Neuman's projection formula would be



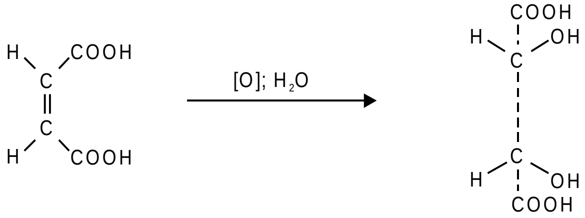
When the two substituents are identical, then the cis-e, e-isomer is more stable than the cis-a, a and is also more stable than the trans-e, a-conformation and it has been shown that the cis-l,3-e, e-form is the most stable one.

Allinger has concluded that for cyclohexanes, the isomer which has the higher boiling point, refractive index and density is the one which has less stable configuration.

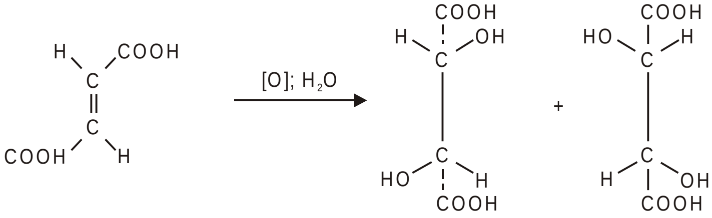
It is observed that the 1,3 isomer exists in distereoisomeric cis and transforms. One more thing becomes obvious in the cis form and that is that either both the substituents are equatorial or both are axial. In either case there is a plane of symmetry passing through carbon atoms 2 and 5, if both the substituents are identical, e.g., in 1,3 dimethyl cyclohexane.

In the above example, the transform does not have a plane of symmetry and so has discrete existence. This is why the trans isomer, whether having similar or dissimilar substituents is resolvable.

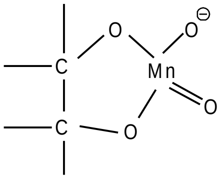
The oxidation of maleic acid by $KMnO_4$ gives mesotartaric acid.



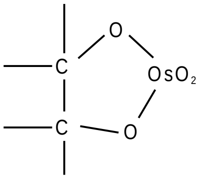
But similar oxidation of fumaric acid gives a raceime mixture



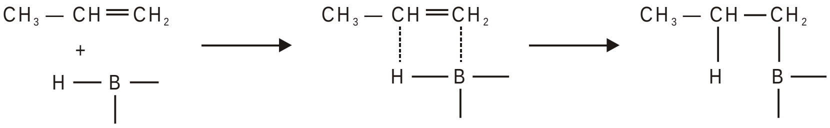
Now it has been established that cis hydroxylation occurs because the following intermediate products of cyclic structure are first formed.



and



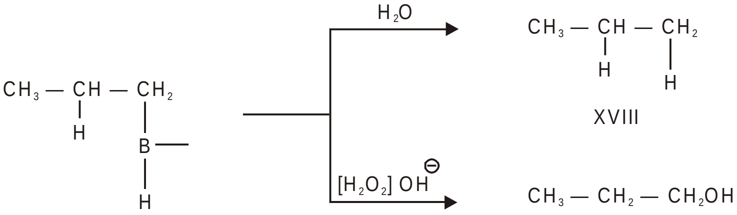
The **hydroboration** (addition of >B-H linkage across a double bond) reaction discovered in the sixties follows a single step mechanism, involving a cyclic transition state and the addition of diborane to the double bond proceeds in cis manner. The boron atom generally gets attached to the less substituted carbon atom of the alkene, but this is probably because of steric factors- the bulky boron-containing group can approach the less substituted carbon more easily. The addition proceeding through a four-centre transition on propene is as follows:



four centre transition state

XVII

The reaction product XVII on decomposition with water exchanges the boron atom for hydrogen and gives a saturated hydrocarbon XVIII and on oxidation by H_2O_2 in alkaline medium forms an alcohol XIX.



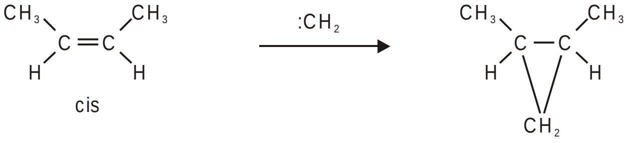
XVIII

XIX

The four centre transition state requires the addition of both boron and hydrogen to the same face of the molecule.

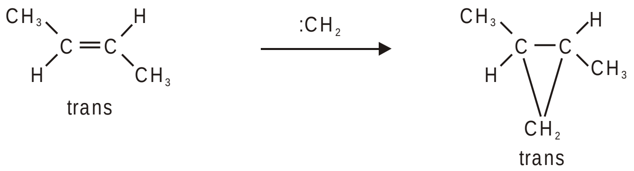
Therefore addition of boron hydride becomes necessarily a cis addition.

The addition of **carbenes** is also a stereospecific reaction, each geometrical isomer forms the cis addition product. Thus carbene generated from the photolysis of diazomethane adds in a cis manner to both cis and trans butene-2.

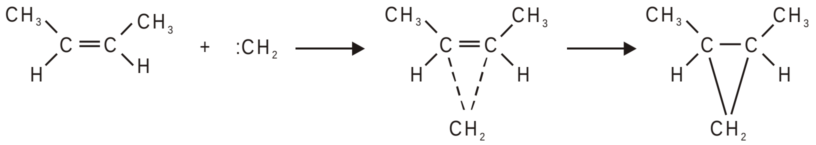


cis

cis

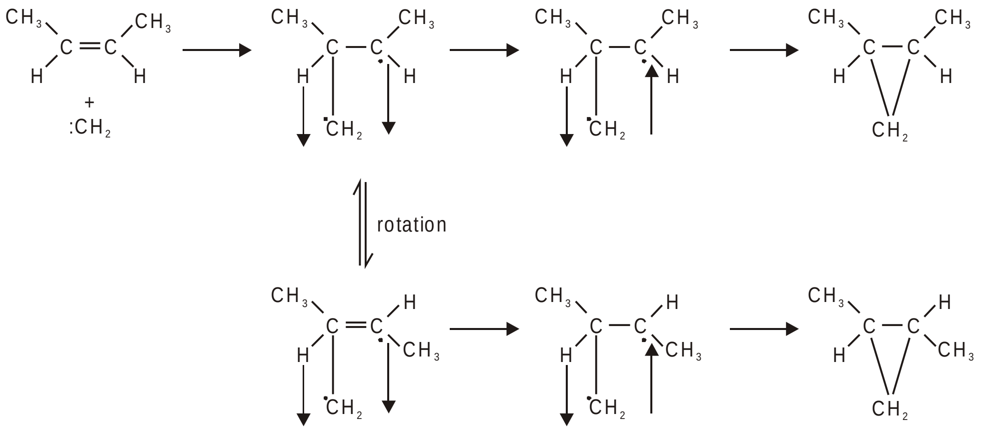


The stereospecificity of the above reaction is due to the addition of singlet methylene as follows in which case both the bonds are formed simultaneously.



However the stereospecificity is lost when the reaction is carried out in presence of an inert gas like nitrogen.

In this state the addition of methylene occurs in the triplet state and starting from each a mixture of cis and trans products is obtained. This is because in the triplet state, the two electrons have parallel spins and carbene behaves as diradical. To explain non stereospecificity it is assumed that rotation about the single bond occurs more rapidly than spin inversion. The entire mechanism can be written in the following manner:



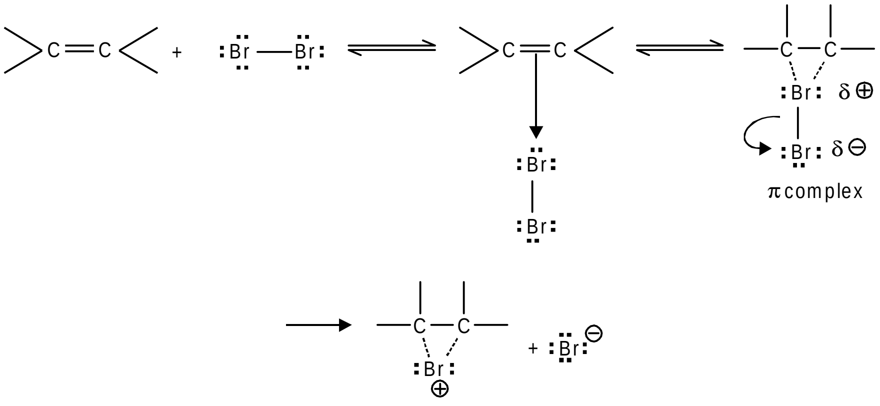
Much also depends on how the carbene is generated. Duncan et al showed that carbene generated by the photolysis of ketone adds to the above substrate in a non-stereospecific manner.

trans-Addition Reactions

The addition of halogens, halogen acids, water and hypohalides proceeds according to the trans scheme. As an example we take the addition of bromine to an alkene which proceeds in the following steps.

1. As the mobile π electrons of the alkene approach the bromine molecule, the electrons of the bromine-bromine bond are drifted in the direction of that bromine which is more distant from the alkene..Thus the bromine molecule becomes **polarized** and a partial

negative charge develops on this farthest bromine atom. Polarization weakens the bromine-bromine bond and results in its heterolytic fission. A bromide ion departs and a cyclic brominium ion is formed.

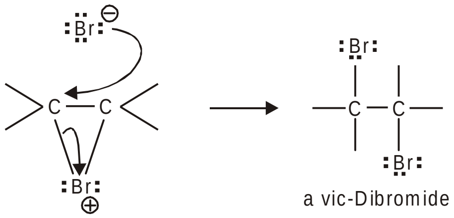


Brominium ion

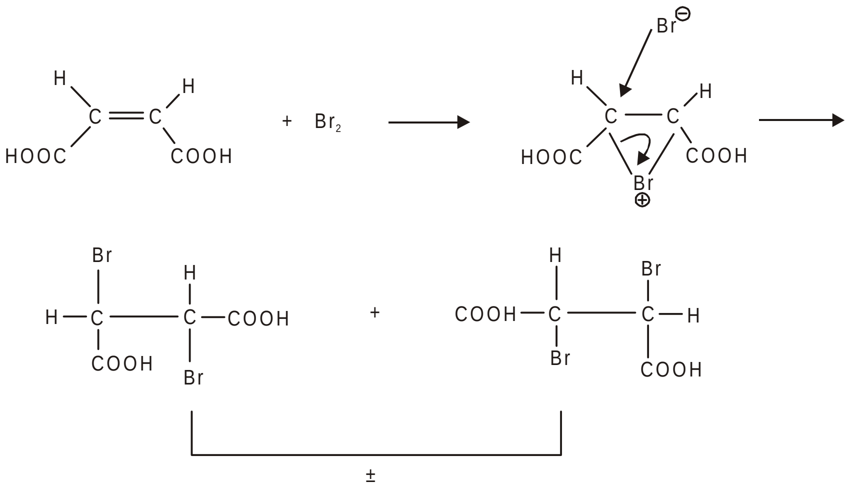
It is to be noted that in the brominium ion the bromine atom is bonded to the two carbon atoms by **two pairs of electrons.** This is possible through the enhanced electron pairs present on bromine.

2. In the next step one of the bromide ions attacks one of the carbon atoms of the brominium ion. This nucleophilic attack results in the formation of a vicinal dibromide by opening the three membered ring.

   The ring opening may be considered as an S_N^2 reaction.



Similarly the addition of bromine to maleic acid giving a racemic mixture of dibromosuccinic acid is again a trans addition. Here also there is first the formation of a bridged (or a non-classical) carbocation followed by the attack of the bromide ion. The various steps are as follows:



The bromide ion attacks from the rear and it involves the breaking of the bonds of the asymmetric atom and so a Walden inversion is possible. Further since the brominium ion is symmetrical, there are chances for each carbon atom to be attacked equally well. This is why **equal** amounts of active isomers is obtained and the product is a racemic mixture. So starting from the cis acid, the trans addition gives a mixture of racemate.

The existence of brominium ion has been confirmed by N.M.R. studies also.

The addition of halogens and halogen acids to alkenes has been shown to be predominantly trans and where the results do not agree, explanations have been given in terms of steric factors. Dewar has proposed that in all electrophilic addition reactions where a classical carbocation is formed, cis addition is the rule and where there is the preponderance of the trans product, the effect is due to steric factors.

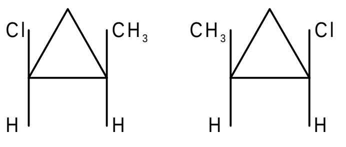
Therefore summarizing, the problem of addition reactions to alkenes is not so simple and is more complicated than what it looks. It depends on so many factors, e.g., the nature of alkene, the addendum and on the reaction conditions. If the addition proceeds through the formation of bridged ions, then trans addition is the rule. But if it involves a classical carbocation, then cis addition is the mechanism.

One factor that increases the stability of the bridged ion is the nature of the addendum and in this respect the order is I > Br > Cl > F. This is why with iodine we always get the trans addition and the order has been established experimentally. But where the addendum is not an iodine atom and the classical carbocation is stabilized by resonance, then cis addition takes up which may later on by **rearrangement** give the trans isomer. **It has also been formed that the nature of the solvent also affects the amounts of cis and trans products.**

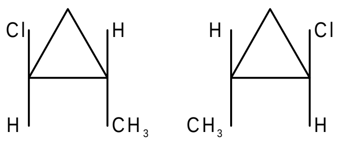
STEREOCHEMISTRY OF CYCLIC COMPOUNDS

Cyclic compounds also exist in stereoisomeric forms, *i.e.*, they may show geometrical and optical isomerism at the same time. While considering them, the saturated rings are regarded as rigid flat structures and the groups attached to the carbon atoms are regarded as being above or below the plane of the ring. For example since it is not possible to have free rotation about the carbon-carbon single bonds of cyclopropane, geometric isomers are possible. But because the carbon atoms of the ring are tetrahedral, so the cyclic molecules may have optical isomers as well.

An example is l-Methyl-2-chlorocyclopropane which exists as a pair of geometric isomers and since each isomer has a non superimposable mirror image, it has a pair of enantiomers. Thus its forms are



cis isomers
(pair of enantiomers)



trans isomers
(pair of enantiomers)

Further details are given in the next chapter 9 on optical isomerism an chapter 10 on conformation.

CHAPTER

9

Basic Concepts of Stereochemistry

IMPORTANCE OF STEREOCHEMISTRY

The stereochemistry deals with the study of spatial structure of molecules and its effect on the physical and chemical properties of the compound. Until recently stereochemistry was thought to be purely a theoretical area of study but since it not only affects the properties but also controls the rate of reaction, it has assumed great practical importance. Now stereochemistry is applied to study physiological properties, biochemistry, molecular biology, pharmacy and even in medicine. So the scope of the subject has become enormous. Stereoisomerism is classified into two types.

1. Optical isomerism
2. Geometrical isomerism

Optical Isomerism

Optical isomerism is shown by compounds which are capable of rotating the plane of polarized light. The phenomenon is called optical activity and the substances possessing this property are called optically active substances. The optical activity is observed and measured by an instrument called polarimeter.*

Optical Activity

The polarimeter essentially consists of two Nicol prisms, one the polarizer and the other the analyser with a sample tube kept in between them which contains the substance (a liquid or a solution) to be examined.

When a ray of light from some light source is passed through a polarizer, the transmitted light is plane-polarized light. If this light is passed through the sample tube, its plane gets rotated. If the analyser has to be turned to the right (clockwise) to restore the original field, the substance is said to be *dextrorotatory*, if to the left (anti clockwise) it is *laevorotatory*.

Since the degree of rotation depends on the wave length, monochromatic light (light of a single wave length) is necessary and the common polarimeters use the sodium D line (5890°) or the

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* All standard text books on practical physical chemistry describe the construction and working of a polarimeter.

mercury green line. Now modern spectropolarimeters use photocells because they give more accurate value (up to 0.001°) or even less.

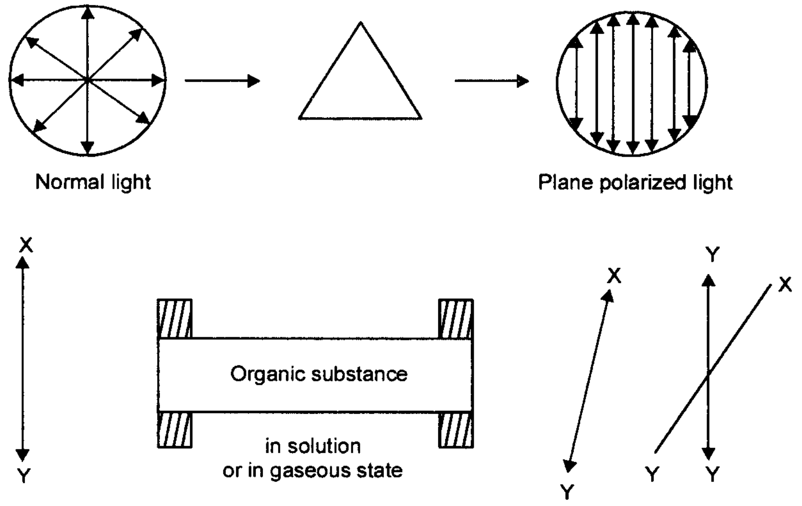


Fig. 9.1 Schematic diagram of the polarimeter

The extent of rotation depends on :

1. The nature of the compound.
2. Concentration of the solution.
3. Length of the solution in the observation tube.
4. Wave length of light used.
5. Temperature of the solution.
6. Nature of medium (*i.e.*, solvent).

For comparison a standard is kept by fixing the conditions of temperature and concentration. The specific rotation [α] D, which is practically constant and is characteristic of a substance is defined by the expression.

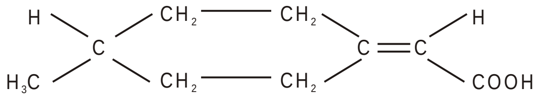
$$[\alpha]_D^t = \frac{100 \times \alpha\ obs}{l \times c}$$

where α is the observed angle of rotation, l is the length of the solution in decimetres and C represents the gram of the substance in 100 CC of the solution. The determination is carried out at temperature using sodium light, the D line. Since rotation depends on solvent, this should also be stated. The value of $[\alpha]_D$ varies with the wave length of light and is generally measured with sodium light. When the temperature is not mentioned, it is supposed to have been measured at room temperature.

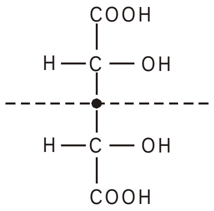
Now we know that all asymmetric molecules have shown optical activity.

ASYMMETRY AND CHIRALITY

Compounds containing a carbon atom united with four different atoms or groups are called asymmetric compounds and this carbon atom is called an asymmetric carbon atom. Originally the presence of an asymmetric carbon atom was regarded to impart optical activity. But later compounds were discovered which showed optical activity but were devoid of asymmetric carbon atoms, e.g., methyl cyclo-hexylidence acetic acid.



This compound is optically active because of *molecular asymmetry.* Of course, the presence of an asymmetric carbon atom lends asymmetry to the molecule and hence gives rise to optical activity but it is not always essential. The presence of an asymmetric carbon atom may or may not give rise to optical activity. The case of meso. tartaric acid is worth mentioning in this connectiar. Although the molecule has two asymmetric carbon atoms but it is optically inactive.



$$\begin{array}{c} COOH \\ | \\ H-C-OH \\ | \\ H-C-OH \\ | \\ COOH \end{array}$$

The inactivity in the molecule is due to the fact that it is perfectly symmetric as shown by the dotted line, the upper half exactly coinciding with the lower half. Therefore, molecular asymmetry and not the presence of asymmetric carbon atoms is responsible for optical activity. Since the term asymmetric has been found to be inadequate, now the term chirality has been introduced. The word chiral (the Greek word *cheir* means hand; pronounced kiral) signifies, the property of ‘‘Handedness’’. An object that in not superimposable upon its mirror image is chiral and this mirror-image relationship is the same as left hand has with the right. If an object and its mirror image can be made to coincide in space, they are said to be *achiral*.

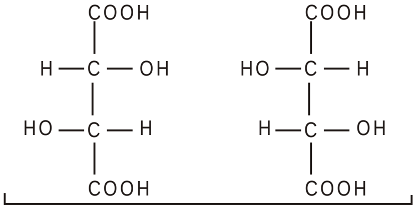
Eliel has used the term *dissymmetric* but this term is used in different connotation by other authors.

At present it is suffice to say that optically active substances are always chiral molecules but they must not necessarily be asymmetric.

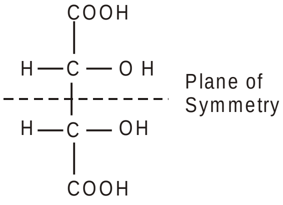
Let us now differentiate between structures which are asymmetric and dissymmetric. The word asymmetric conveys the idea that the molecule is completely devoid of the elements of symmetry. Dissymmetric on the other hand means not completely devoid of elements of symmetry but possessing so few elements of symmetry that on the whole it will posses two structures which will be the mirror images of each other. Therefore to avoid confusion the term asymmetric is used to cover examples which rotate the plane polarized light. The two forms of an optically active compound are called *enantiometers* or *enantiomorphs* or *optical antipodes.* They are also said to have enantiomeric relationship to each other.

Compounds with Asymmetric Carbon Atoms, Diasteroisomers

In general, the maximum number of optically active isomers is given by 2^n where n represents the number of asymmetric carbon atoms. Thus for a compound where $n = 1$, as in lactic acid, there would be two stereoisomers, one the dextro and the other the laevo. For a compound with two asymmetric carbon atoms, there would be $2^2 = 4$ stereoisomers. But if the two asymmetric carbon atoms carry exactly identical groups, as in tartaric acid, the number would be fewer than four and we know that it exists in three forms, the *d* the *1* and the meso.



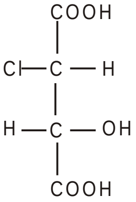
dl pair



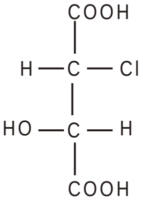
meso

The meso form is inactive although it has two asymmetric carbon atoms. This is because it has a plane of symmetry and the molecule is internally compensated *i.e.*, the rotation of the upper half is balanced by the rotation of the lower half.

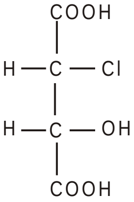
On the other hand let us study the case of 2 chloro 3 hydroxy succinic acid which has two asymmetric carbon atoms and which are not identical. This compound exists in four stereoisomeric forms as predicted by 2^2 formula. The various projection formula are:



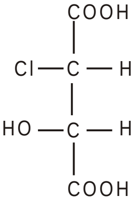
(i)



(ii)



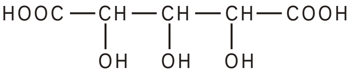
(iii)



(iv)

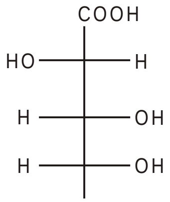
Since all the molecules are asymmetric and have no plane of symmetry, all are optically active. Further structures I and II are enantiomorphs and so are structures III and IV. But structures III and I or IV and I are although stereoisomers but are not enantiomorphs. *Such pairs of steroisomers which possess chirality but are not the mirror images of each other are called diastereomers.* Thus III and IV are diastereomers of 1. So diastereomers will always be formed when the compound contains two dissimilar asymmetric carbon atoms and will exist in four stereoisomeric forms.

The number of spatial isomers increases with increasing number of asymmetric carbon centres with the addition of each new asymmetric centre, the number of isomers doubles. The trihydroxy glutaric acid molecule has three identical asymmetric carbon atoms.



$$HOOC-\underset{OH}{\underset{|}{CH}}-\underset{OH}{\underset{|}{CH}}-\underset{OH}{\underset{|}{CH}}-COOH$$

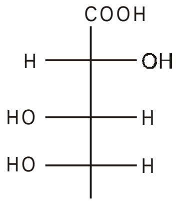
Therefore it should exist in eight stereoisomeric form according to 2^3. But since the asymmetric carbon atoms are identical, the number of active forms would be less than eight. It exists in two active and two meso forms.



(V)

Dextro

m.p 128°C

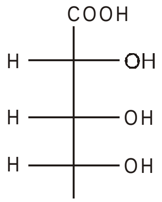


(VI)

Laevo

m.p 128°

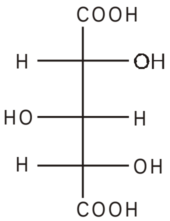
mp. dl mixure 155°C



(VII)

Meso-Form A

mp unknown



(VIII)

Meso-Form B

mp 152°C

The two meso forms, although optically inactive differ in chemical properties. For example, on heating the meso form A, readily forms a lactone, whereas the meso form B does not. In such an example the central carbon atom is said to be pseudoasymmetric. But if one of the carboxyl groups is esterified so that the top and bottom parts of the molecule become structually different, then the central carbon atom becomes truly asymmetric and the molecule would have three true asymmetric atoms and it will exist in eight stereoisomeric forms.

Properties of Diastereomers

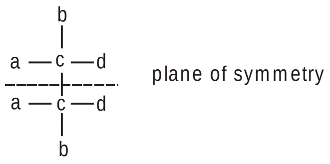
1. *The diastereoisomers have different physical properties.* They have different melting and boiling points, solubilities, densities, refractive indices or adsorption coefficients. They can be easily separated, most often by fractional crystallization and adsorption. The enantiomers are not separated by these techniques.
2. *They may or may not be optically active.* The geometric isomers are not optically active, but diastereomers other than geometric isomers are optically active.
3. Unlike enantiomers, *diastereoisomers have similar but not identical chemical properties.* The enantiomers have identical properties except the reactions with dissymmetric reagents.

WHAT TYPE OF COMPOUNDS DON'T SHOW OPTICAL ACTIVITY?

We have already seen that mesotartaric acid is optically inactive because of internal compensation, although, it contains two asymmetric carbon atoms. We have also seen that the molecule as a whole must be asymmetric for being optically active. Therefore, the best criterion to judge optical activity would be whether molecule is superimposable on its mirror image or not. Now superimposability would lead to optical activity and vice-versa and non-symmetrical molecules are non superimposable. To decide whether a molecule is symmetrical or not, we should first try to know whether it has a plane of symmetry, a centre of symmetry or an alternating axis of symmetry. *The presence of any one of these would lead the molecule to be symmetrical and hence to optical inactivity.*

A Plane of Symmetry

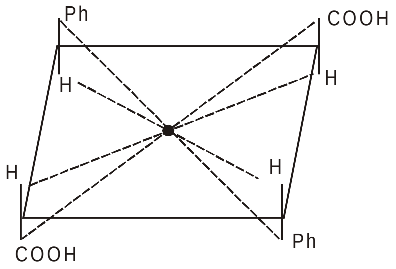
Let us consider a molecule of the type C abd – C abd (exemplified by mesotartaric acid) which has got a plane of symmetry shown by the dotted line.



The line divides the molecule is such a way that the upper half becomes the mirror image of the lower half. Therefore, the plane of symmetry is that which divides the molecule into two such parts so that each becomes the mirror image of the other. Compounds possessing this plane of symmetry would always be optically inactive.

A Centre of Symmetry

Compounds containing a centre of symmetry are exemplified by those which have three dimensional structures, particularly of ring systems. Let us concentrate on a derivative 2 : 4 diphenylcyclobutane 1, 3 dicarboxylic acid (IX).



IX

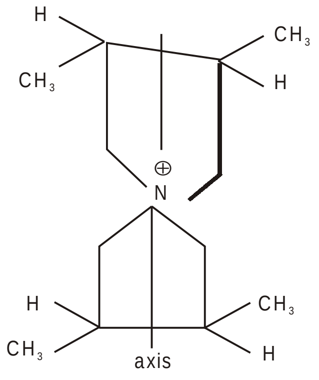
The centre of the molecule (shown by a thick dot) is the centre of symmetry, because lines drawn on the side and produced an equal distance on the other meet similar points in the molecule. In this connection, it can be mentioned that compounds possessing even numbered rings will have a possibility of having a centre of symmetry and would lead to optical inactivity.

An Alternating Axis of Symmetry

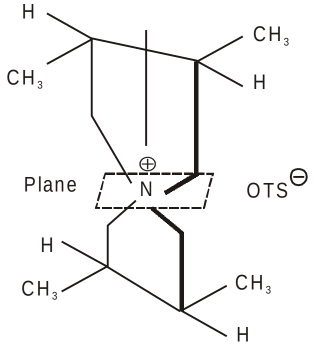
In 1956 McCasland and Proskow prepared the p.toluenesulphonate of the compound X and found that it has neither a plane nor an centre of symmetry and yet the molecule was superimposable on its mirror image and hence inactive. The molecule owes its symmetry due to the presence of what has been called an alternating axis of symmetry. Rotation of the molecule through 90° along the axis shown produces XI. Observing the latter through a central plane perpendicular to the axis shows that it is identical with X and also coincides with it.

Therefore a molecule will be said to have an *n* fold alternating axis of symmetry if rotation through 360°/*n* along an axis produces a structure, observing which in a plane perpendicular to the axis, which is identical with and coincides with the original.

Having seen the ideas of chirality and the elements of symmetry we are now in a better position to classify the optically active compounds into various categories. The following generalization has been very useful.



X

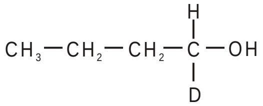


XI

1. Compounds with asymmetric carbon atoms

Compounds with one asymmetric carbon atom would be active because of a tetrahedral structure. When there are two or more such asymmetric carbon centres, we will have to take into consideration the concepts of the plane of symmetry.

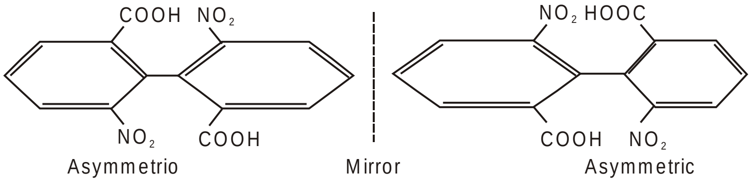
Replacement of a hydrogen atom by deuterium in 1 butanol by 1D has created optical activity.



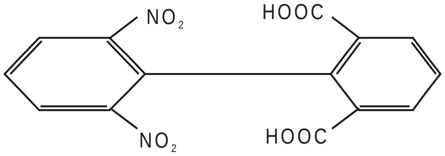
$$CH_3-CH_2-CH_2-\underset{D}{\overset{H}{\underset{|}{\overset{|}{C}}}}-OH$$

2. Restricted Rotation Leading to Perpendicular Dissymmetric Planes

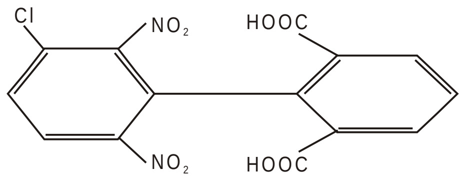
This is best illustrated by taking hindered biphenyls as example. If the two ortho positions on each ring be differently substituted and that too with groups large enough to cause steric hindrance, then due to restricted rotation along the central bond, two asymmetric isomers come to exist which become the mirror images of each other with equal and opposite rotations.



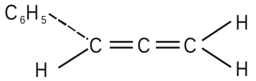
In the above example there is no plane of symmetry in either rings and hence the molecule is active. On the other hand in molecule of the type given below although there is restricted rotation along the central axis but, the molecule has two planes of symmetry on either rings and hence it is inactive.



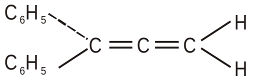
In the first example both the rings had no plane of symmetry while in the second both had planes of symmetry. There is yet a third case where only one ring is symmetric as in the following and this one plane is sufficient to make the compound inactive, because if either ring is symmetrical, the molecule would be inactive. It is important to note that groups in para positions cannot cause dissymmetry. Finally it is equally important to note that the presence of four large groups in ortho position is essential for restricted rotation. Cases of optical activity have been observed in biphenyls containing three or even two balky groups present on either ring as in biphenyl 2, 2′–bisulphonic acid.



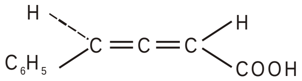
The allenes are another example of compounds which show molecular asymmetry if both ends are dissymmetric.



Inactive



Inactive

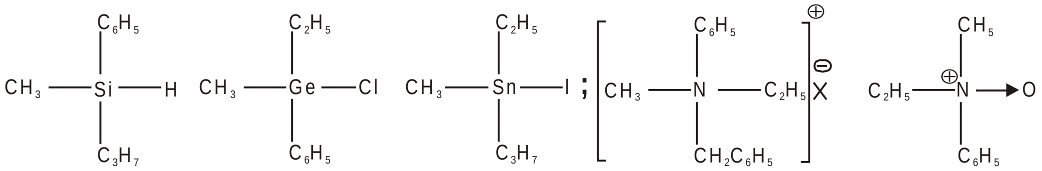


Active

Rotation here is restricted due to the double bond and the groups at the end are in two perpendicular planes.

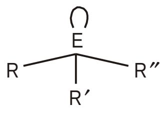
3. Compounds with other asymmetric atoms

The carbon atom is not the only atom which produces chiral centres in organic compounds. Silicon, germanium, tin, or N (in quaternary salts or N-oxides) whose bonds point towards the corners of a tetrahedron also form optically active compounds provided the groups are different.



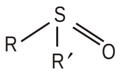
Even metals like Cu, Pt, or Pd which form tetrahedral coordination compounds also from asymmetric compounds. In all these cases, therefore, the centre of asymmetry has a tetrahedral configuration just like an asymmetric carbon atom.

Elements which form *pyramidal* bonding also form optically active compounds provided the groups are different. To this class belong derivatives of trivalent nitrogen, phosphines, arsines or stibines.

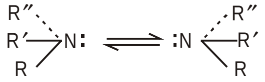


E = N, P, As, Sb

The sulphoxides are also active because of a pyramidal configuration.

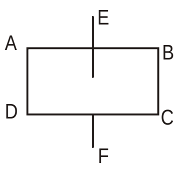


The optical activity in above type of pyramidal compounds is explained on the basis that the unshared pair of electrons is analogous to a fourth group and is therefore different from others. Their structure approaches a tetrahedral configuration with different groups. The case of tertiary amines is interesting. Although the arrangement of bonds approaches a tetrahedral configuration no ordinary tertiary amine has been resolved. This is explained on the basis that in such molecules the nitrogen with the unshared pair rapidly oscillates from one side of the RR′ R″ plane to the other resulting in very rapid interconversion. It can be imagined as the molecule flipping inside out, just like an umbrella in a gale.

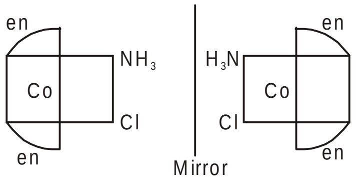


The interconversion is so rapid that it can be of the order of millions of times per second and so resolution becomes extremely difficult.

Many metals form co-ordination compounds with six legands. For example Co, Cr, Fe, Ru, Rh and Pt are known to form such complexes and if the legands are sufficiently different, the configuration is an octahedral one and this configuration is characteristic of optically active compounds. No complex with six different groups (XII) has been resolved, although theoretically it is possible. The optically active complex of cobalt with ethylene diamine (designated as ‘en’) is as follows (XIII) with its mirror image.



XII

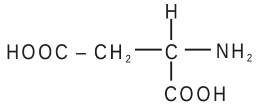


XIII

Sign of Rotation and Configuration

Usually polarimetric measurements are carried out to find out a given optical antipode and the result is reliable, but the sign of rotation, is not always a direct expression of configuration because rotation, as already stated, depends on nature of solvent, concentration of solution and temperature etc. as the following example shows:-

Aspartic acid at 20°C rotates the plane of polarization to the right, $[\alpha]\ D^{20} = +\ 4.36°$ but with the increase in temperature, the plane of polarization is rotated to the left, $[\alpha]\ D^{90} = -1.86°$ although the configuration of the antipode remains unchanged. Therefore, determination of the configuration of the isomers is a specific area of stereochemistry. The reader at this state must understand the logic to tackle this problems, the experimental techniques employed have been given later.

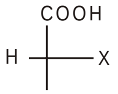


$$\mathrm{HOOC-CH_2-\overset{\displaystyle H}{\underset{\displaystyle COOH}{C}}-NH_2}$$

NOMENCLATURE OF OPTICAL ISOMERS

In optical isomerism it becomes essential to give name to the enantiomers, because the formulas can not be employed in oral speech. Therefore, the following systems were evolved.

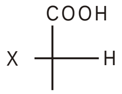
1. In the simplest and oldest system the formula of the compound *is compared with a standard substance taken as the key compound. In the series of* α *amino or* α *–hydroxy acid, the key is the top part of the projection* formulas (Fischer projection formulas).



D-Series

D – Hydroxy acid (X = OH)

D – Amino acid (X = NH_2)

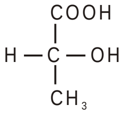


L Series

L – Hydroxy acid (X = OH)

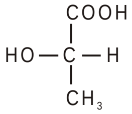
L – Amino acid (X = NH_2)

If the OH or NH_2 group in the top part is towards the right, it is called D-Acid, if towards the left then it is L-acid. Thus D-lactic acid and its antipode will be



$$\begin{array}{c} COOH \\ | \\ H-C-OH \\ | \\ CH_3 \end{array}$$

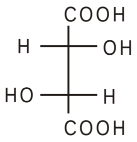
D – (–) Lactic acid



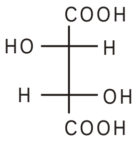
$$\begin{array}{c} COOH \\ | \\ HO-C-H \\ | \\ CH_3 \end{array}$$

L (+) Lactic acid

The letter D and L are always written in capital and the sign of rotation is then represented in brackets. This means that these letters have nothing to do with rotation. On similar reasoning, tartaric acid would be

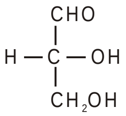


D (+) Tartaric acid



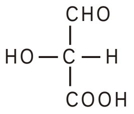
L (–) Tartaric acid

In the case of sugars the reference substance is glyceraldehyde and according to a suggestions by Rosonoff the OH group present on the right be designated as D-configuration.



$$\begin{array}{c} CHO \\ | \\ H-C-OH \\ | \\ CH_2OH \end{array}$$

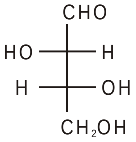
D (+) Glyceraldehyde



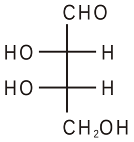
$$\begin{array}{c} CHO \\ | \\ HO-C-H \\ | \\ COOH \end{array}$$

L (–) Glyceraldehyde

In sugars the designations D or L refer to the configuration of the bottom asymmetric centre.



D (–) threose

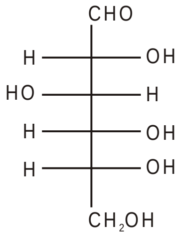


L (+) erythrose

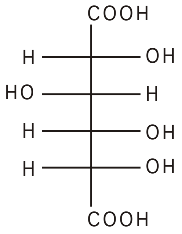
Therefore all forms in which the bottom asymmetric carbon atom possesses the same configuration as *D-glyceraldehyde are said to belong to the* D–series and their enantiomorphs to the L–series.

The shortcoming of the system is that the configuration of *only one* (bottom) asymmetric carbon is specified while the configurations of the remaining ones remain hidden.

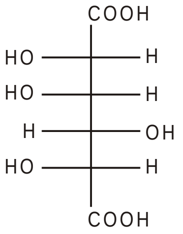
The second draw back is if we consider the following cases:



D (+) glucose

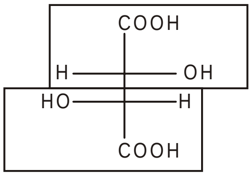


XIV



XV
Saccharic acid

Glucose on oxidation gives saccharic acid and on the basis of D-glucose structure, XIV would be D and XV, L on the account of the bottom asymmetric carbon atom. But if XV is rotated in the plane of paper through 180° if becomes exactly identical with XIV. Dispute like this and tartaric acid have raised great interest in improving the system of nomenclature.



D with respect to hydroxy acid

L – with respect to glyceraldehyde

In view of these shortcomings, *the system has been limited to only three classes of optically active organic compounds, the Sugars, amino acids and hydroxy acids.*

2. The rho-sigma (ρ –σ) system. It was proposed by the Russian, A.P. Terentiev and coworkers around 1955 and takes into consideration *a three dimensional model* instead of the projection formula, because of simplicity. Even a compound with one asymmetric carbon atom can be represented by an many as twelve projection formulae. Therefore, we proceed in the following manner—

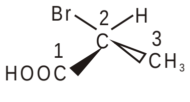
(*i*) First the main chain is determined and its atoms are numbered.

(*ii*) A perspective projection is then drawn so that the beginning of the chain projects forward towards the observer and the end is behind the plane of the paper.

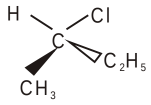
(*iii*) A priority sequence is determined for substituents at the asymmetric centre.

(iv) The substituent present on the left of the asymmetric carbon is denoted by the symbol ρ (rho) and if present on the right, then by the symbol σ (sigma).

(*v*) The notation is written before the numeral which indicates the position of the substituent. For example.

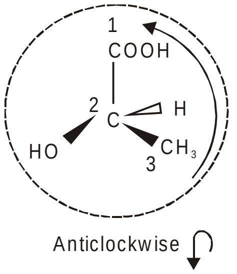


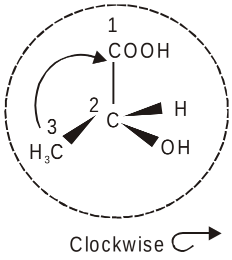
ρ-2 Bromopropionic acid



σ2 – Chlorobutane

Again concentrating our attention on one asymmetric carbon compound, lactic acid and viewing the projection based on C asym-H bond, the optical antipodes can be written as follows, like Neuman's projection formulae:





It is to be noted that in these structures the priority groups are present respectively on the left and right side of the asymmetric carbon and hence designated as ρ and σ. But for such projections based on C asym –H bond, the following convention is also adopted.

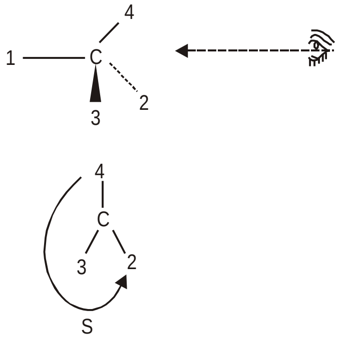
If while moving from the atom of the main chain with higher atomic number to the atom of the main chain with the lower atomic number (from the end of the chain to the beginning, from CH_3 to COOH group in the above example), we go in an anticlockwise direction, it will represent the rho (ρ) configuration. If movement is in clockwise direction, it will be the sigma (σ) form.

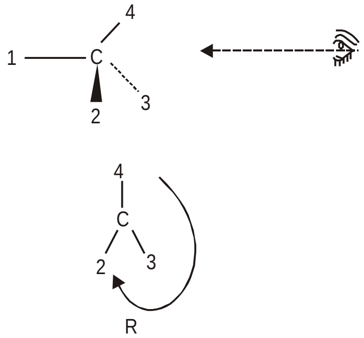
For additional rules involving more complicated cases, the readers is referred to *Tetrahedron*, 1, 1, 119-128 (1957).

3. The R, S, convention, proposed by R.S. Cahn, C ingold and V Prelog in 1956 is also based on a three dimensional model rather than on the projection formula and has been adopted by the IUPAC. It has also been called the ‘‘Sequence rule’’ is quite straightforward and involves the following simple steps.

Step

1. First the atoms or groups attached to the asymmetric or chiral carbon are identified and assigned *priorities* by numerals. Such that the numbers 4, 3, 2, 1 signify the order of decreasing priority, 4 > 3 > 2 > 1.



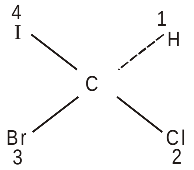


2. The molecule is then visualized so that the substituent of lowest priority is directed away from us and is below the plane of the paper.
3. Looking along the bond of lowest priority, one will see the *asymmetric carbon atom with the three attached substituents* radiating out like the spokes of a wheel. Now moving along the path 4 to 3 to 2 if the motion is clockwise then the asymmetric carbon atom is called R (from the latin word Rectus–right). It the eye moves in anticlockwise direction, the configuration is specified as S (from the latin word sinister meaning left. Sometimes, this

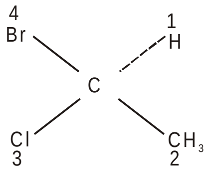
convention has also been referred as Rectus and Sinister system but the shortened from R, S are more common.

The priorities of the substituents are judged according to the following *sequence rules*–

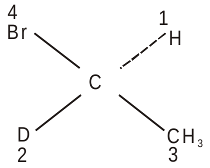
1. When all the four atoms attached to the asymmetric carbon atom are different, priority depends on the atomic number. *The atoms of higher atomic number precede the lower one.* Thus in compound bromo-chloroiodomethane,



The priority is I, Br, Cl, H. Similarly in 1 bromo 1 chloroethane, the priorities would be Br, Cl, C and H.

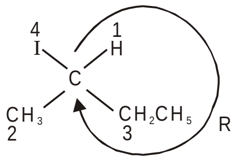


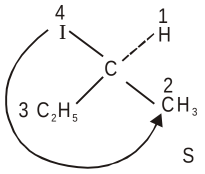
2. When the two atoms are isotopes of each other, *the isotope of higher atomic mass preceds the lower one.* For example, in 1 deutero 1 bromoethane, the priorities would be Br, C, D and H.



3. When the two atoms directly attached to the asymmetric carbon are same, as in C_2H_5 and CH_3, *priority is determined by comparing the next atom in the group using the considerations of atomic number and atomic mass. If it still becomes difficult to decide the priority, the comparison is extended to the next atom and so on.*

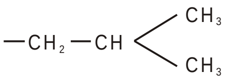
   For example, when the groups are ethyl-CH_2–CH_3 and methyl–CH_2-H, the asymmetric carbon is united with a carbon carrying two hydrogen atoms and no distinction can be made. Going to the next atom which is C in ethyl and H in methyl, this constitutes the first point of difference and so ethyl gets precedence over methyl, because carbon has higher atomic number than hydrogen. On this basis the R and S configurations of 2 iodobutane would be.



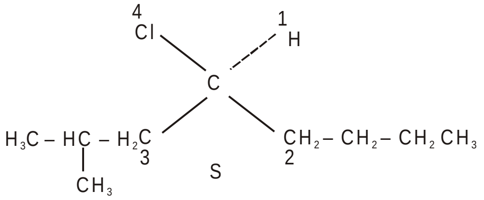


Complications may arise when the alkyl radicals are straight or branched chain as in normal and isobutyl attached to the asymmetric carbon atom.

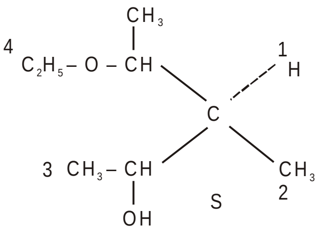
$-CH_2-CH_2-CH_2-CH_3$



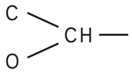
The first carbon atom in both the cases is exactly identical and difference arises from the second carbon. This carbon has two other carbon atoms attached to it in isobutyl whereas the analogous carbon in normal butyl has only one attached carbon. Therefore, isobutyl gets precedence over normal butyl. On this basis, the following configuration of 4-chloro 2 methyl octane would be S

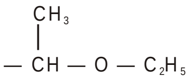
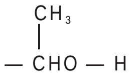


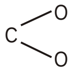
Cases where two substituents are branched, the branch of higher priority gets the precedence as in the following example:

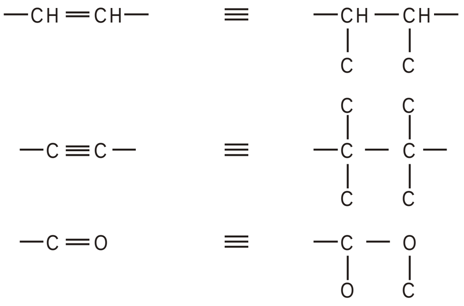


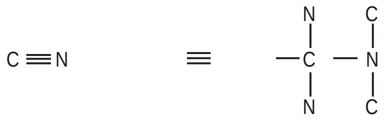
The asymmetric carbon atom is attached with two branched groups which have the structure.

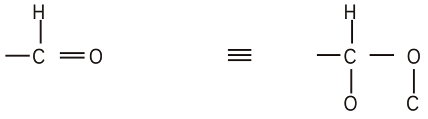


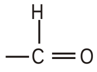
But  $-\overset{\overset{CH_3}{|}}{CH}-O-C_2H_5$ gets precedence over  $-\overset{\overset{CH_3}{|}}{CH}O-H$ since carbon atom has higher atomic number than H and so the molecule is S.

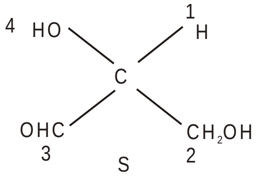
4. *The atoms attached to the multiple bound are considered to be duplicated (for a double bond) and triplicated (for a triple bond)* Thus a C = O is counted as if it were  For example:



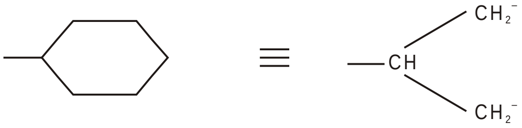


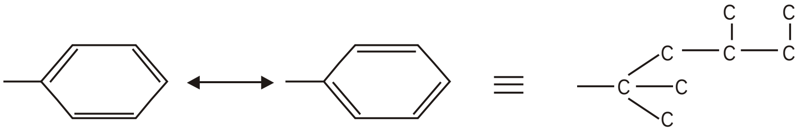


Between the groups  $-\overset{\displaystyle H}{\overset{|}{C}}=O$ and $-CH_2OH$, the former will get the priority as in glyceraldehyde.

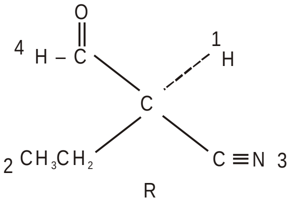


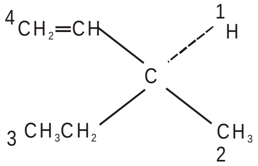
The ring systems are treated as branched chains and phenyl group is treated for the purpose of determining its priority as though it had one of the Kekule's structures





Some examples of compounds containing multiple bonds are as follows–

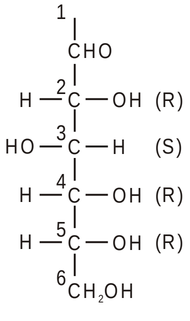




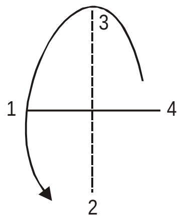
The prefix (RS) is used to denote a racemic modification. For example, (RS)–Sec butyl chloride. The symbols R and S are applied to compounds whose absolute stereochemistry has been determined. However, while applying the nomenclature to projection formulae of compounds containing several asymmetric centres Cahn, Ingold. Prelog procedures are supplemented by the following conversion rule.

Where the substituent of lowest priority is to the left or right, the clockwise sequence of decreasing priority is denoted by S and the anticlockwise by R.

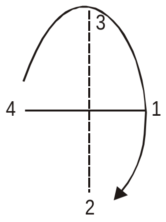
Applying it to glucose, whose absolute configuration has been determined, the molecule is represented as follows with the symbols R and S specified at various asymmetric carbon atoms.



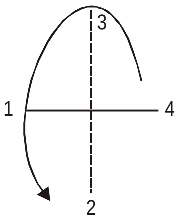
D-gluose



R at C – 2

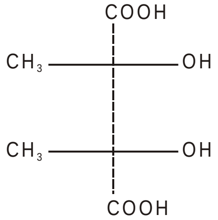


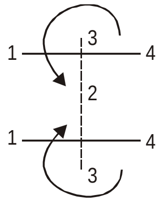
S at C – 3



at C – 4 and C – 5

So is the case with 2,3 – dimethyl tartaric acid.

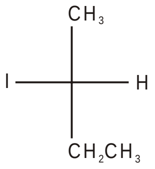


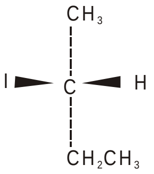


R, S-2,3 dimethyl tartaric acid.

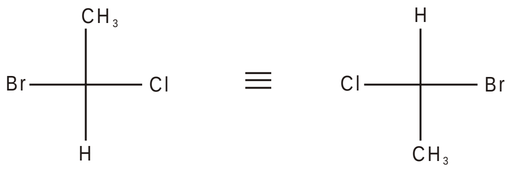
Fischer Projections

In a Fischer projection of representing an optically active compound, an asymmetric atom is shown at the intersection point of two lines of a cross. The horizontal lines going to left and right of this point are the bonds extending forward from the plane of paper. The two vertical lines going to top and bottom are those going back away from the plane of paper. For example 2-iodobutane can be represented as:

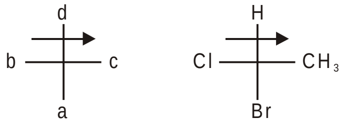




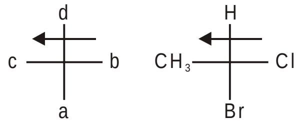
The Fischer projections are two-dimensional representations of three dimensional objects. Further a Fischer projection may be rotated in the plane of paper by 180°, but not by 90° as illustrated in the following examples—



In order to ascertain the R and S forms in Fischer's projection, the guideline is that the lowest priority group is put at the top and the highest at the bottom. Now if while moving from priority group *b* to *c* the motion is towards right, it represents the R configuration; if to the left, then it is the S form. It is illustrated again by taking 1 chloro 1 bromo-ethane.



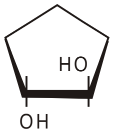
(R)



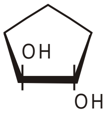
(S)

STEREOISOMERISM IN CYCLIC COMPOUNDS

Cyclic compounds also exist in stereoisomeric forms. Let us now study the case of cyclopentane, 1, 2 diol. It has two chiral carbons and exists in three stereoisomeric forms.

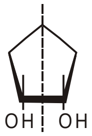


XVI



XVII

enantiomers

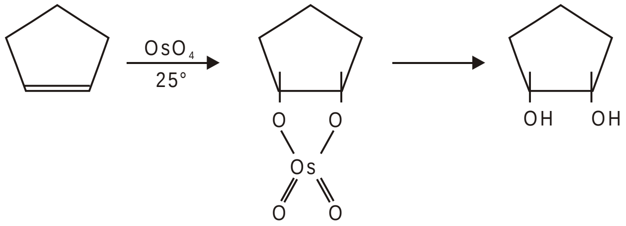


XVIII

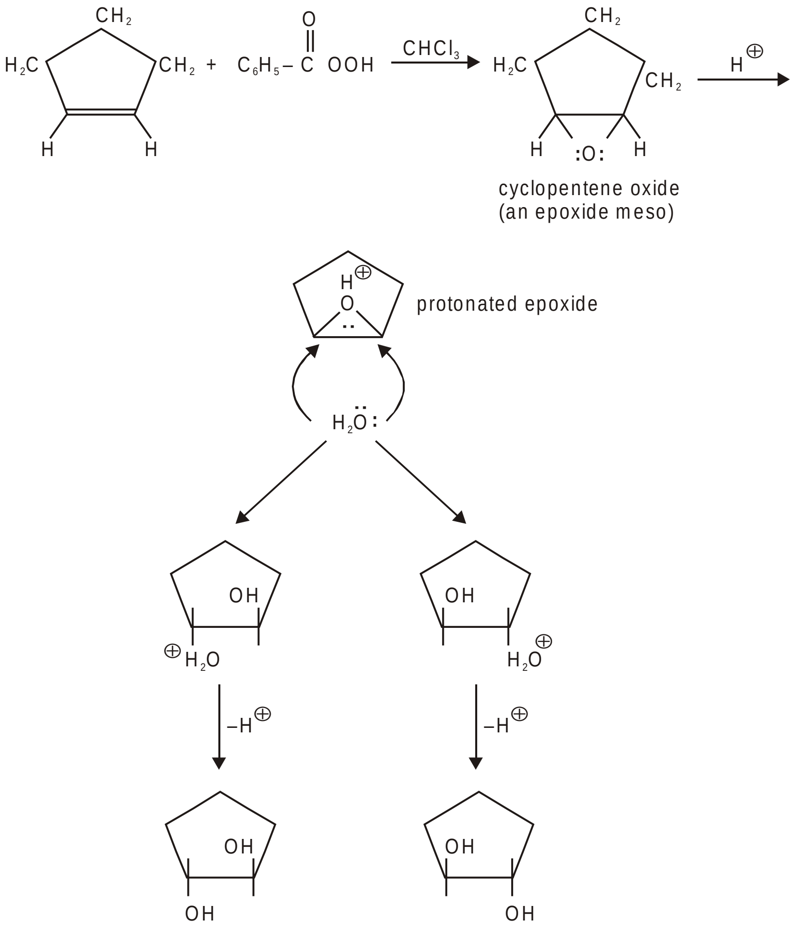
meso form

The forms XVI and XVII represent the trans forms and are a pair of enantiomers while XVIII is the cis form and is the meso compound because it has a plane of symmetry which is perpendicular to the plane of the ring, shown by dotted line.

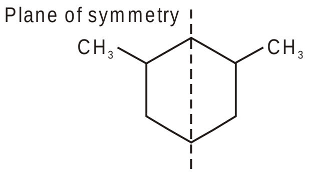
The cis form has been prepared by the syn hydroxylation of cyclopentene by osmium tetroxide as follows:



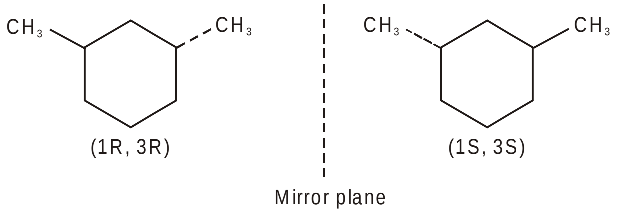
The attack of OsO_4 whether from the above or below the plane of the ring will give the same cis compound. On the other hand hydroxylation with per-oxybenzoic acid (resulting in antihydroxylation) will given a mixture of trans enantiomers, first an epoxide ring is formed which is highly strained and itself is a meso compound. On treatment with aqueous acid, the ring gets protonated and the attack of water necleophile on the ring will then be at two points given a mixture of products. The various steps are shown below.



Since the rate of opening of the two paths are equal, the enantiomorphs are formed in equal amount. Let us now take another interesting example of 1, 3 dimethyl cyclohexane. It exists in the cis and trans forms. Since the cis form has a plane of symmetry, it is the meso compound.

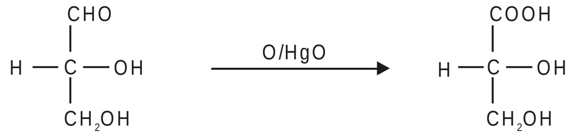


However since no such symmetry exists in the trans form it exists in two enantiomorphs.



METHODS FOR DETERMINING ABSOLUTE CONFIGURATION

Till recently there was no method of determining the absolute configuration of molecules. Therefore Rosanoff had proposed that one compound be chosen as standard and an arbitrary configuration be assigned to it. For this he chose D(+) glyceraldehyde because of its relation to sugars and other compounds could then be related to it. On this basis the relative configuration of glyceric acid was established.

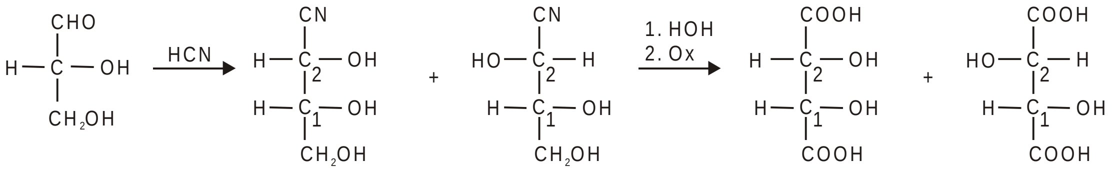


It is now possible to assign the absolute configurations to many compounds having the configurations of glyceraldehyde. The change in rotation does not necessarily affect configuration. The same compound may rotate the plane in opposite directions under different conditions. The following methods have been employed for correlating the configurations.

1. By carrying out chemical reactions without disturbing the asymmetric centre

The method has been employed for glyceraldehyde-glyceric acid example. The process can be repeated further and the configurations of many other compounds can be correlated with either glyceraldehyde or glyceric acid.

Thus tartaric acid can be be synthesized from glyceraldehyde via cyanohydrin reaction.

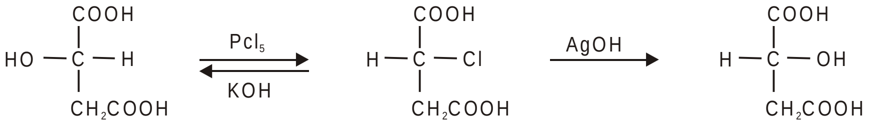


In this conversion the original asymmetric carbon of glyceraldehyde is left intact and another asymmetric centre has been created and it can exist in both possible configurations. Therefore, starting from dextrorotatory glyceraldehyde, laevorotatory tartaric acid is obtained along with the meso form. This establishes the configuration of XIX and from this the configuration of its antipode can be written.

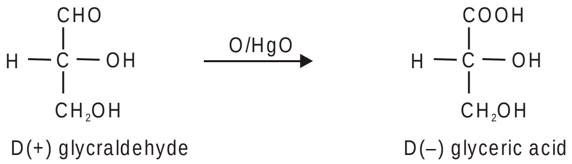
In these conversions it is a rule that the bonds about the asymmetric centre remain intact.

2. Reactions which involve displacements, at asymmetric centres

When an atom or group directly linked to an asymmetric carbon atom is replaced, the configuration of the new compound may be opposite to that of the original. Thus L(–) malic acid can be converted into D–(+) malic acid as follows:



This curious phenomenon of inversion of groups about the asymmetric carbon atom, first studied by Walden (1893, 1985) is called *Walden Inversion.* In a number of other reactions, the inversion was so quantitative that the yield of the opitcal isomer was 100%; while in others the product was a mixture of the (+) and (–) forms in unequal amounts signifying that the inversion was partial. The above conversion has been shown to occur in two steps. The step in which the actual inversion occurs constitutes a Walden inversion. Change in the sign of rotation does not necessarily mean that an inversion of configuration has occurred as is clear from the oxidation of D(+) glyceraldehyde to D(–) glyceric acid.

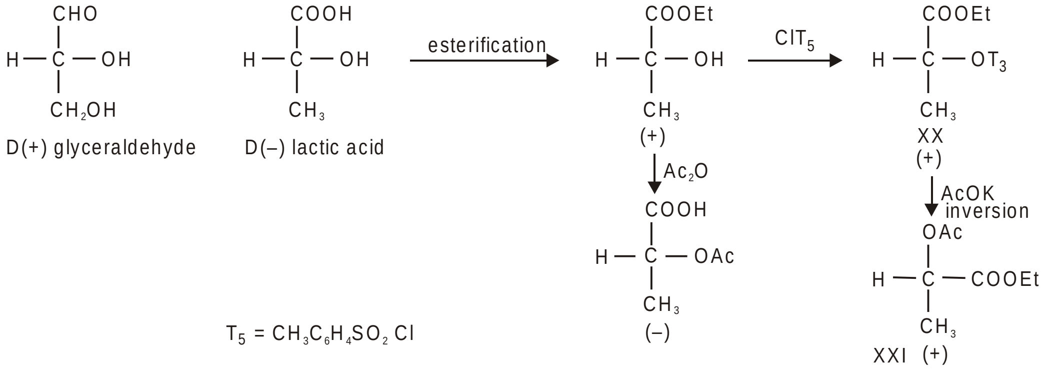


Thus although the rotation changes, configurations remains the same in the starting material and the product. This is because the asymmetric carbon atom is not involved in the reaction and so configuration can be determined without any difficulty.

But the determination of configuration becomes difficult when the asymmetric carbon atom is involved in the reactions. In such cases relative configurations are determined on the basis of the nature of starting material and the product and Kenyon et al. on the basis of studies of a number of optically active hydroxy compounds gave a basis for determining relative configurations. Since the esterification of a monocarboxylic acid by an optically active alcohol involves the following mechanism in which there is fission of acyl-oxygen bond,

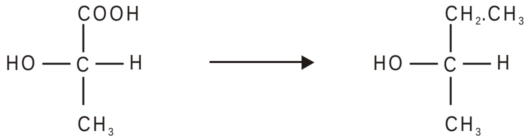
$$R-\overset{O}{\overset{\|}{C}}-OH \quad H-OR^{*} \longrightarrow R-\overset{O}{\overset{\|}{C}}-OR^{*} + H_2O$$

Kenyon assumed that in all such esterifications the O–R* bond remains intact and so no inversion of the alcohol occurs. The following transformations show-how the products can be assigned configurations on the basis of D (+) Glyceraldehyde.



At the stage where inversion occurs there is removal of the complete group attached to asymmetric carbon atom and so the configurations of XX and XXI can be correlated with glyceraldehyde.

Acids of established configurations have been used to correlate the configurations of other oxygen-containing optically active compounds. Thus on the basis of lactic acid, the configuration of the simplest optically active alcohol, 2 butanol has been assigned as follows—



$$\mathrm{HO-\overset{\displaystyle COOH}{\underset{\displaystyle CH_3}{C}}-H} \longrightarrow \mathrm{HO-\overset{\displaystyle CH_2.CH_3}{\underset{\displaystyle CH_3}{C}}-H}$$

S(+) Lactic acid S(+) 2 Butanol

3. X-ray diffraction

The X-ray diffraction studies have not only helped in elucidating the complete structure of a compound in its crystalline state but also in establishing its configuration. The noteworthy feature of the method is that no recourse is taken to chemical work. Thus the structure of the alkaloid thelepogine, C_{20} $H_{31}NO$ has been settled without chemical work. For the last two decades the method has been widely employed because it takes less time due to the use of automatic diffractometers and electronic computers.

The method, also called heavy atom method, consists in introducing a heavy atom in the molecule. Then X-rays with a wave length close to the X-ray absorption of the heavy atom is introduced. As a result a phase shift is superimposed on the ordinary diffraction pattern and configuration is then deduced. The method was first employed in 1951 by Bijvoet et al. to examine sodium rubidium tartrate who concluded that it is possible to differentiate between the two optically active forms. In other words it was possible to determine the *absolute* configuration of the enantiomers. Since then the absolute configurations of about two hundred optically active compounds have been elucidated by their *correlation* with other substances of known configuration.

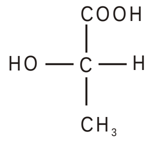
4. Method of Opitcal Rotation

Some times the sign and extent of rotation help in determining which isomer has which configuration. This happens because rotation of structurally related compounds of identical configuration undergoes analogous changes under the influence of temperature, solvent or other factors. Let us study the molecular rotations of L(+) lactic acid and alanine.

Table 9.1

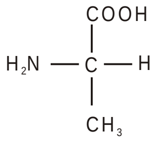
Substituent at OH or NH_2 groups	*Substituent at COOH group*	*L(+) lactic acid*	*(+) – alanine*	*(–) –alanine*
C_6H_5 CO–	– NH_2 (Amide)	+ 135°	+ 93°	– 93°
C_6H_5 CO–	– C_2H_5	+ 59.5°	+ 107°	– 107°
C_6H_5 CO–	– CH_3	+ 43.5°	+ 15°	– 15°
CH_3 CO–	– C_2H_5	– 80.9°	– 84°	–84°

Since the same shift is observed in (+) lactic acid and (+) – alanine, hence the configurations of the two are identical and so the following formulas have been assigned to alanine.



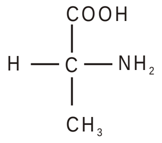
$$\begin{array}{c} \mathrm{COOH} \\ | \\ \mathrm{HO} - \mathrm{C} - \mathrm{H} \\ | \\ \mathrm{CH_3} \end{array}$$

L(+) lactic acid



$$\begin{array}{c} \mathrm{COOH} \\ | \\ \mathrm{H_2N} - \mathrm{C} - \mathrm{H} \\ | \\ \mathrm{CH_3} \end{array}$$

(+) alanine



$$\begin{array}{c} \mathrm{COOH} \\ | \\ \mathrm{H} - \mathrm{C} - \mathrm{NH_2} \\ | \\ \mathrm{CH_3} \end{array}$$

(–) alanine

In the strict sense of the term, it is not the coincidence of rotations in signs or their increase or decrease but the *direction of the shift.* In both the case the directions are the same.

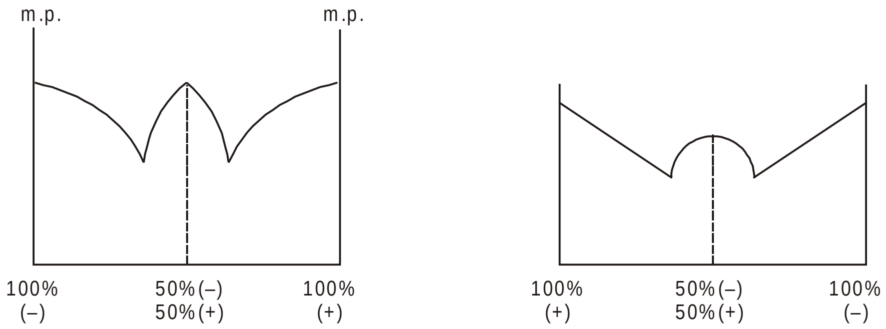
The method is quite reliable and has been used for the correlation of configurations of various tertiary butyl alcohol. In this connection some empirical rules have been formulated for certain type of deviatives.

The *Amide Rule* as formulated by Freudenberg states. The rotation of amides of α hydroxy acids of the D–series is always shifted to the right as compared with the rotation of corresponding hydroxy acids.

The Ester Rule states that in the esterification of hydroxy acids of D-series with methanol, the shift takes place to right but in esterification with ethanol the shift to the right increases.

5. The Method of quasi-racemates

Most of us appear to have the notion that a racemate consists of equal amounts of their antipodes, but the racemates are not simple mixtures. Actually they are molecular compounds of their antipodes. They have their own physical constants like melting point, density or solubility which is different from their antipodes. Their melting points may be higher or lower than that of their antipodes as illustrated diagramatically in Fig.



melting point diagram of a racemate

Fig. 9.2

A *quasi-racemate or pseudo-racemate* is a true racemate like molecular compound formed between optical antipode of different (but related) compounds. The quasi-racemate also has a melting point curve resembling the curve of a true racemate but with quasi-racemic compounds the curves are unsymmetrical, because the melting points of the components are different as shown in Fig. (9.3). The curve A represents the melting point of a true-racemate formed by mixing (+) mandelic acid XXII and (–) hexahydromandelic acid XXIII while B represents that of a mixture of (+) XXII and (+) hexa hydro-mandelic acid XXIII.

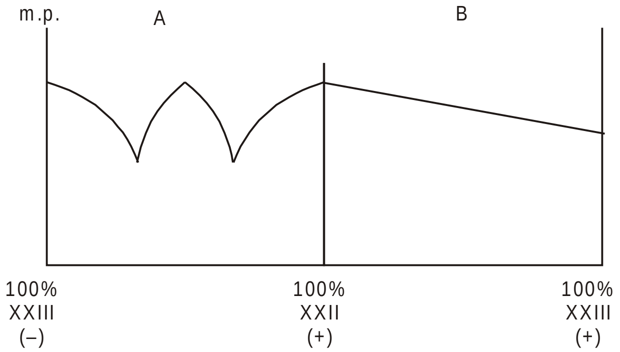


Fig. 9.3

A. melting point curve of a true racemate.

B. melting point curve of (+) mandelic and (+) hexahydro-mandelic acid.

In B the straight line is inclined and so is different from A. Since according to a general rule, the configurations of compounds forming a quasi-racemate must be opposite, in the above example, the acids with the same sign of rotation have the same configuration.

Therefore, the conditions essential for quasi-racemic mixtures are that:

(*i*) The substances must be chemically related.

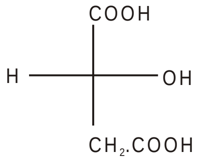
(*ii*) They have only one asymmetric carbon atom of opposite configuration and

(*iii*) Whose crystals are isomorphones.

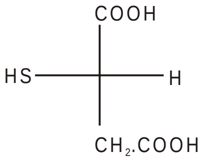
Fredga believes that substances capable of forming true racemates are also liable to form quasi-racemates.

Quasi racemates are formed by members of a homologous series and also by pairs of compounds which differ in that the hydrogen is replaced by a chlorine, bromine or iodine atom (but the molecule must not be too small).

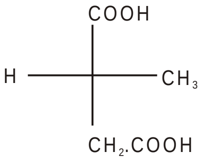
It has been established that by mixing derivatives of acids having opposite rotation, the compounds had opposite, configurations. The (+) malic acid (XXIV) and (–) mercaptosuccinic acid (XXV) had opposite configurations.



XXIV



XXV



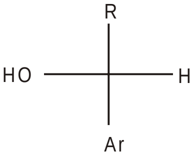
XXVI

Further since XXV formed a quasi racemic compound with (+) methyl succinic acid XXVI, they have opposite configurations and so XXIV and XXVI have the same configuration.

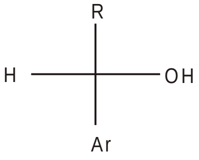
The quasi-racemate method is most interesting in the sense that it may be applied to compounds that can not be correlated by direct chemical reactions.

6. N-M.R. Studies

The behaviour of enantiomers towards chiral solvents shows different N.M.R. spectra. Thus enantiotopic protons can be detected by measuring N.M.R. spectra in chiral solvents. The relative position of signals depends on the configuration of the compounds. It has been found that for alcohol of the following configuration dissolved in an active base, the signal of the methine proton of R configuration has stronger field than that of S–. Another use of N.M.R. spectra for configuration determination is based on the formation of diastereomers and then comparing the chemical shift of the groups.

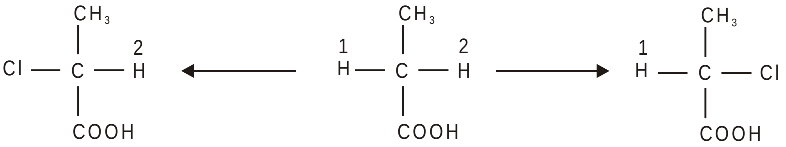


R^-



S^-

Laboratory synthesis yields a racemic mixture. When a compound containing an asymmetric carbon atom is synthesised in the laboratory from a compound that has none, the product is always a racemic mixture. Thus if α chloropropionic acid is prepared from propionic acid a racemic mixture results:



As shown from the above formula, the two hydrogen atoms (H^1 and H^2) in propionic acid are identical. There is, therefore, an equal chance of either H atom being replaced by the Cl. atom. Hence there results equal number of molecules of laevo and dextro isomers and the product is a racemic mixture. It may be noted that the two chloropropionic acids are the mirror images of each other.

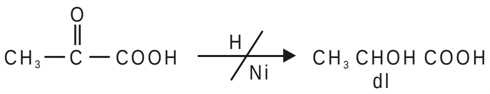
On the other hand, according to E. Fischer, the asymmetric compounds produced with the mediation of living organisms are almost invariably active. We now proceed to find the reasons for this.

ASYMMETRIC SYNTHESIS (ASYMMETRIC INDUCTION)

Therefore, as we have seen, we can not prepare an optically active compound from an inactive one by the ordinary laboratory methods. Such a synthesis however, can be accomplished by attaching an optically active molecule or groups to the original compound and then removing it after the new asymmetric atom has been produced.

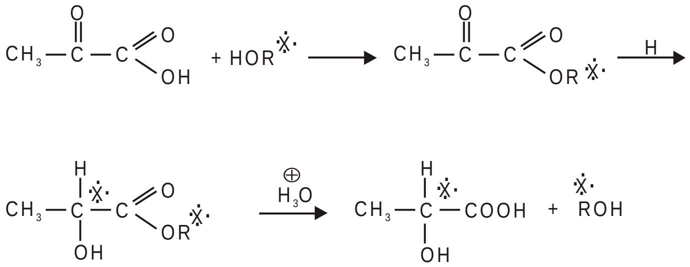
The synthesis of an asymmetric compound carried under the influence of an optically active molecule or group is termed asymmetric synthesis.

For example, pyruvic acid on reduction yields a dl mixture of lactic acid.



$$CH_3-\overset{\overset{O}{\|}}{C}-COOH \;\overset{H}{\underset{Ni}{\not\longrightarrow}}\; \underset{dl}{CH_3\,CHOH\,COOH}$$

But if it is esterified with some optically active alcohol (ROH*) and then reduced, the resulting ester on hydrolysis yields an optically active lactic acid.



In such synthesis the two *d* and *1* forms are not produced in equal quantities.

The asymmetric synthesis explains why most asymmetric compounds obtained from natural sources are optically active. In nature, the syntheses are carried out under the influence of optically active enzymes. The enzymes unite with the substance and when the synthesis is complete, they separate from the product and are again free to combine with fresh molecules of the original substance.

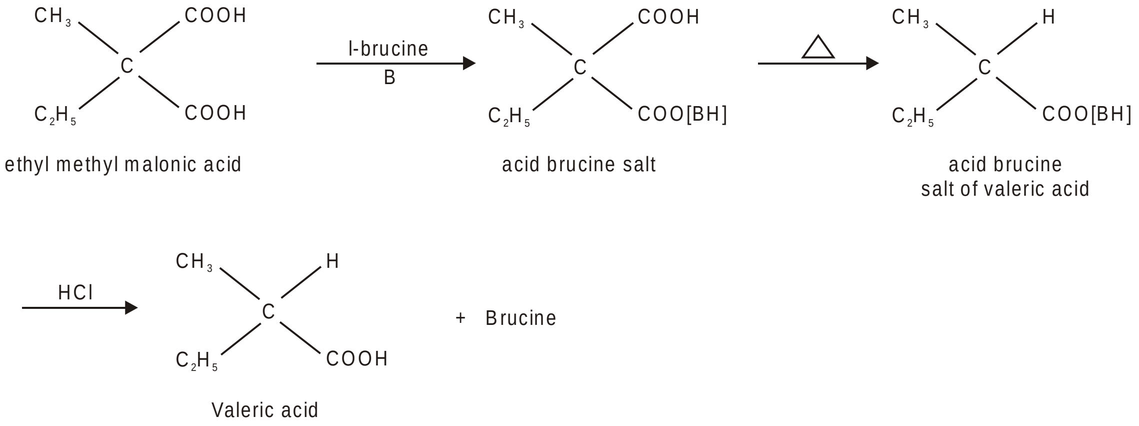
Thus there exists a radical difference between the reactions that go on in the animal and vegetable world on the one hand and those in the laboratory on the other.

In the reduction of the > C = 0 group of pyruvic acid by hydrogen in presence of nickel catalyst, the reaction rate by the two paths is the same and so the *d* and *1* forms are obtained in equal amounts.

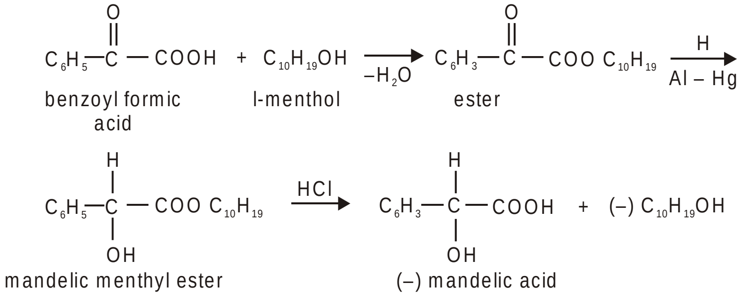
But since the enzyme catalysed reductions are *steroselective* signifying that *it gives only one of a set of stereoisomers*, the two isomers are not formed in equal amounts.

The asymmetric synthesis thus carried out is also known as *partial asymmetric synthesis* and to distinguish it from that where no optically active compound is used but in its place circularly polarized light is used, we use the term *absolute asymmetric synthesis.*

The first successful attempt in asymmetric synthesis was made by Marckwald in 1904 who prepared an active (–) –valeric acid by heating the half brucine salt of ethyl methyl malonic acid at 170°C.



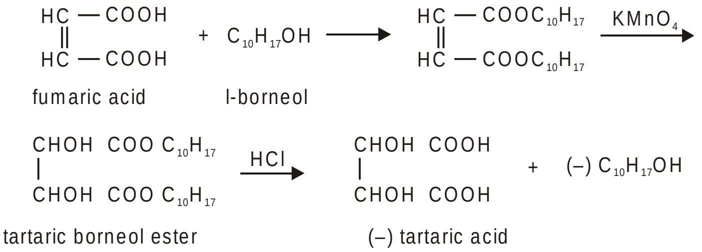
Mckenzie carried out a number of asymmetric synthesis by reducing the keto groups in several ketoesters in which the ester group contained a chiral group. Thus he synthesized l-mandelic acid from benzoyl formic acid by the following steps using l-menthol



$$C_6H_5-\overset{\overset{O}{\|}}{C}-COOH + C_{10}H_{19}OH \xrightarrow[-H_2O]{} C_6H_3-\overset{\overset{O}{\|}}{C}-COO\,C_{10}H_{19} \xrightarrow[Al-Hg]{H}$$

$$C_6H_5-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-COO\,C_{10}H_{19} \xrightarrow{HCl} C_6H_3-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-COOH + (-)\,C_{10}H_{19}OH$$

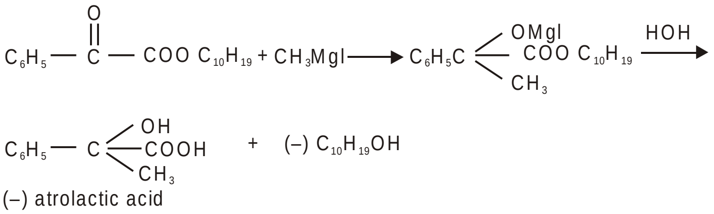
Mckenzie and Wren have synthesized l tartaric acid from fumaric acid using l-borneol.



$$\begin{array}{l}HC-COOH\\ \|\\ HC-COOH\end{array} + C_{10}H_{17}OH \longrightarrow \begin{array}{l}HC-COOC_{10}H_{17}\\ \|\\ HC-COOC_{10}H_{17}\end{array} \xrightarrow{KMnO_4}$$

$$\begin{array}{l}CHOH\;\;COO\,C_{10}H_{17}\\ |\\ CHOH\;\;COO\,C_{10}H_{17}\end{array} \xrightarrow{HCl} \begin{array}{l}CHOH\;\;COOH\\ |\\ CHOH\;\;COOH\end{array} + (-)\,C_{10}H_{17}OH$$

Mckenzie prepared (–) atrolactic acid using Grignard reagents.



$$C_6H_5-\overset{\overset{O}{\|}}{C}-COO\,C_{10}H_{19} + CH_3MgI \longrightarrow C_6H_5C\left<\begin{array}{l}OMgI\\ COO\,C_{10}H_{19}\\ CH_3\end{array}\right. \xrightarrow{HOH}$$

$$C_6H_5-C\left<\begin{array}{l}OH\\ COOH\\ CH_3\end{array}\right. + (-)\,C_{10}H_{19}OH$$

Asymmetric transformation

In racemisation we have the formation of an equimolecular mixture of optical antipodes, represented as:

$$\underset{100\%}{(+)\,A} \longrightarrow \underset{50\%\quad 50\%}{(+)\,A.\,(-)\,A} \longleftarrow \underset{100\%}{(-)-A}$$

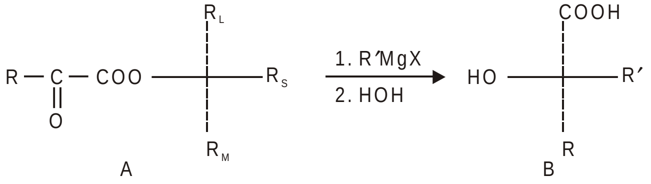
and in certain cases there may be a change in the spatial arrangement of the substituents about an asymmetric centre. But if this change occurs under the influence of other elements of chirality present in the substance or in its environment (solvent, catalyst) then the moment of attainment of equilibrium may not coincide with the formation of an equimolecular mixture of both enantiomers. The result, one of the forms may prove more favourable than the other. Thus in this case starting from a racemate we can obtain mixtures of such enantiomers which have a preponderance of one of them. Such processes are termed *asymmetric transformations.*

Mechanism of Asymmetric Syntheses

Various concepts of asymmetric synthesis have been put forward.

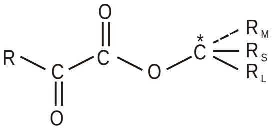
1. Erlenmeyer suggested that the asymmetric reagent exerts an influence on the achiral molecule and converts it from a distance into a chiral species. Of course in such conversions the stearic factors play an important part. This concept is called *asymmetric induction*.
2. First there appears equal amounts of dextro and laevo forms in equilibrium with each other, but due to the presence of asymmetric reagent, the equilibrium gets displaced. This is actually asymmetric transformations.
3. The asymmetric reagent combines with the molecule and a new asymmetric centre is created. Diastereomers are always first formed which have different energy reserves and so they are formed with different rates.

All these explanations though provide an answer to the question *why* asymmetric synthesis takes place but do not throw any clue on the *course* of asymmetric synthesis. Now the concept of the mechanism is entirely based on conformational analysis. This idea was developed by Prelog in 1953-1956 while studying the asymmetric synthesis effected by the interaction of Grignards reagent with α ketoesters. *Prelogs* rule states that if an optically active alcohol used as an asymmetric reagent has the configuration A, a hydroxy acid having the configuration B will be formed in bulk:



The symbols RL, R_M and R_S represent the large medium-sized and small groups of the directing reagent; R is the radical of the keto acid and R' that of the Grignard reagent.

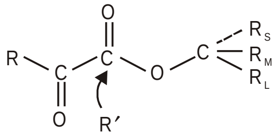
According to Prelog et al. the most stable conformation of the ester was that in which the two oxo groups are planner and *trans* to each other.



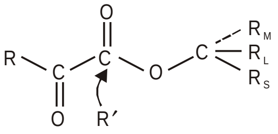
As a result of the rotation about the O–C* bond, the optically active asymmetric alcohol may arrange itself in three ways. So three conformations should be considered for the starting ester, the formation of which was equally probable for all. Those in which the groups R_S, R_M and R_L in turn (*i*) lie in the plane (*ii*) in front of the plane and (*iii*) behind the plane.

Prelog originally proposed that the most populated conformation, was that in which R_S lay in the plane, but later proposed that it was that in which R_L lay in the plane and groups R_S and R_M were skew. The third energetically favourable conformation was that in which R_M group lies in the plane.

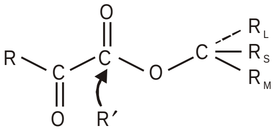
(i)



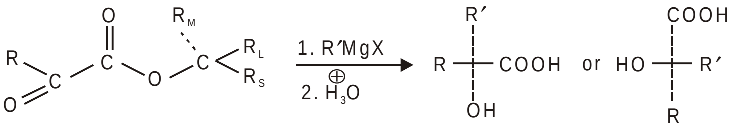
(ii)



(iii)



The thick arrow shows when the attack is from the front face and the thin arrow when attack is from the back. The directions of the approach of R′ from the front or behind are not equivalent. In (*i*) the more favourable approach will be from behind because R′ is sterically hindered. The same will be true for (*ii*) whereas for conformation (*iii*) the preferential attack will be from the front. Taking all the three into account, the attack from behind will be preferential which leads to the configuration given by the rule. The rearward attack for (*ii*) can be schemetically shown as:



The application of the rule to various asymmetric synthesis has helped in elucidating the configuration of a number of molecules.

Absolute Asymmetric Synthesis

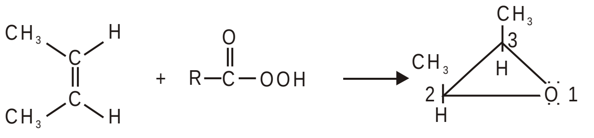
The right and left circularly polarized light having a wave length in the neighbourhood of the absorption band of the substrate is unequally absorbed by some enantiomers. So some racemic compounds were irradiated with right and left circularly polarized light and the product was found to be active. This afforded the possibility of preparing optically active products from inactive one without the intermediate use of optically active reagents. This is called absolute asymmetric synthesis or absolute asymmetric decomposition (or destruction) because one enantiomer is decomposed or destroyed preferentially.

STEREOSELECTIVE AND STEREOSPECIFIC REACTIONS

As we have seen a stereoselective reaction is one in which there is a preponderance of one isomer *irrespective* of the stereochemistry of the reactant. The enzymatic reduction of pyruvic acid is stereoselective when the chiral molecules of the enzyme complexes with achiral pyruvic acid, they given a preponderance of one form of pyruvic acid-enzyme complex which then gives a single form of lactic acid.

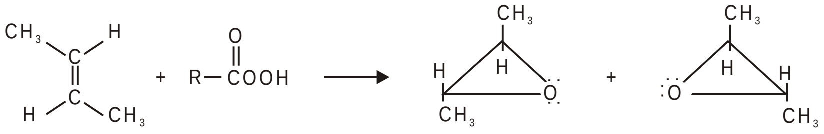
On the other hand a stereospecific reaction is one in which *a particular stereoisomeric form of the reactant reacts to give a stereoisomeric form of the product.* The enzymatic reduction of pyruvic acid is not stereospecific because the reactant can not existin stereoisomeric form. Therefore, all reactions that are stereospecific are necessarily stereoselective but not all stereoselective reactions are stereospecific.

Let us take the example of 2–butene to make the point clear. Since it exists in cis and trans forms, it reacts with peroxy acids in a stereospecific way. The cis form gives only cis-2, 3 dimethyl oxirane while the trans. form gives only trans-2, 3 dimethyl oxiranes.



cis 2 buntene

cis 2, 3 dimethyl oxirane
(a meso compound)



trans 2-buntene

trans 2, 3, dimethyl oxiranes
(enantromrs)

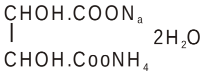
Since the two reactants cis and trans butenes are stereoisomers, being diastereomers, the product from cis is a meso compound and that from the trans give a pair of enantiomers, by definition both the reactions are stereospecific.

RESOLUTION OF RACEMIC MIXTURES

Resolution is the process of separating the enantiomers from a mixture. The process may not be quantitative or the enantiomer may not be optically pure. Although a number of methods are available for resolution, they largely depend on the chemical nature of the compound under consideration. The following are some of the methods commonly employed.

1. Mechanical Separation

The method is applicable to only solid substances which form well defined crystals. Thus in 1848 Pasteur separated for the first time the active forms of sodium ammonium tartate by evaporating a recemic solution below 27°. Two type of crystals were obtained, which had different shapes and were the mirror images of each other. The crystals were separated under a microscope with the help of forceps. Since the crystals of one type were all *d* isomer and the crystals of the other type were 1 isomer, their separation led to a separation of the recemic mixture. On dissolving in solution they showed opposite rotation.



$$\begin{array}{l} \text{CHOH.COON}_a \\ | \\ \text{CHOH.CooNH}_4 \end{array} \; 2H_2O$$

It should be noted that the isomers crystallize separately below a certain temperature known as transition temperature, while above that temperature they crystallize as the recemic variety.

The method although simple is very limited in its application because it is difficult to find conditions under which well defined and separate crystals are formed. Further the method is too tedious and time consuming and is now only of historical importance because it was first employed by Pasteur for resolution while he was still 26 years of age. Therefore, it was the first experiment in the history of science that gave optically active compound from an inactive one.

2. Preferential crystallization by inoculation

In this method a supersaturated aqueous solution of the racemate is inoculated with a crystal of one enantiomer of any other isomorphous crystal of a foreign substance, when this form of the isomer is precipitated. The resolution of glutamic acid by inoculation is now an industrial process.

The method is limited in the scope as it has been successfully tried only in two amino acids, glutamic acid and aspartic acid. In others it has resulted only in partial resolution. Harada has now (1965) succeded in resolving free amino acids by inoculation.

3. Biochemical Method

The method is based on the fact that certain bacteria, fungi, mould or yeast when allowed to grow in a racemic solution, assimilate or consume one of the enantiomers faster than the other. This is why the method is also known as *selective assimilation or preferential decomposition.* Thus Penicillium glaucum a species of green mould when allowed to grow in ammonium racemate solution consumes the *d* θ tartaric acid and leaves the *l* form, but in a racemic lactic acid it assimilates the *l* form leaving behind the *d* form.

A complete separation of the isomers is not possible by this method because it is not always easy to find a suitable mould or bacterium for each and every racemic compound. Therefore, the method suffers from the following defects:

(*a*) It is a slow process.

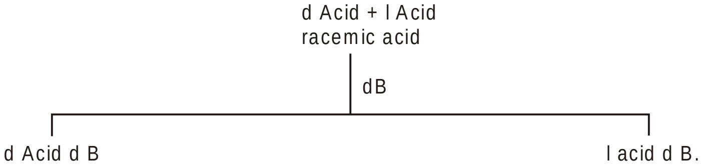
(*b*) It is not economical since one half of the substances is destroyed.

(*c*) It can not be applied to all mixtures of poisonous substances in which the bacteria themselves will finish.

4. Salt formation with an active acid or base

This method is most general and frequently employed. It depends on the use of an optically active substance in the resolution of a recemic mixture.

To separate a racemic acid, we take the help of an active base say *d* B (B = Base), which combines with the two forms of the acid forming two type of salts which are not enantiomorphs, but are distereoisomers. It is schematically represented as:



Since the two salts will have different solubilities or other physical properties, they can be separated by fractional crystallization. The *d* and *l* acids are then set free from the salts by treatment with HCl. Generally it is easy to obtain the less soluble isomer in a pure state, but it may be very difficult to obtain the more soluble isomer.

The recemic mixture of an acid is separated by an optically active alkaloid like brucine, quinine or morphine.

A racemic mixture of a base can be resolved by an active acid which is easily available like *d* or *l* tartaric acid. A racemic mixture of alcohols is resolved by esterification with an active acid. The recemic aldehydes have been resolved by using optically active hydrazines e.g., *d* amyl, phenylhydrozine and separating the resulting hydrozones.

Therefore, summing up the entire process involved three successive operations; the formation of a pair of diastereomers, then separation and finally the destruction of each of the diastereomers resulting in resolution.

To achieve these objectives, several conditions have to be fulfilled which are described in a general way as follows:

The formation of the diastereomer is possible only if the compound to be resolved has a chemically active group which can react with the active resolving agent. Then the bonds of the asymmetric centre must remain intact during the reaction so that the possibility of racemisation is reduced to the minimum.

Since the most resolving agents are expensive, tartaric acid and others having low cost are preferred while choosing an asymmetric reagent. Care should be taken to see that the diastereomers formed should differ as strongly as possible in their solubility.

The solvent used is also important and the success of reasolutiar depends much on the proper selection of the solvent. There is no hard and fast rule in the selection of the solvent. Generally water, alcohols, acetone and ethyl oxalates have been chosen as solvents. In some cases the selection of the solvent becomes very difficult and the diastereomers are then separated by several fractional crystallizations.

The temperature may also play an essential role in the process of resolution.

Cases are also there where only partial resolution has been accomplished through diastereomer formation. In such cases additional purification is required through recrystallization of the impure enantiomer from a suitable solvent.

5. Resolution via molecular compounds

This method is closely related with the one just described. In both the cases the racemate is converted into a pair of diastereomers, the only difference is that resolution via diastereomers involves the formation of stable chemical compounds, while resolution via molecular complexes gives readily decomposable molecular compounds only. The latter method is advantageous in that the preparation and decomposition of molecular compounds take place under mild conditions which reduce the possibility of racemisation to a minimum.

Thus Pasteur noted that the amide of (–) malic acid forms molecular compounds of different properties with the enantiomeric amides of tartaric acid. With amide of (+) tartaric acid large transparent crystals are formed whose solubility is 18% at 20°C, while with the amide of (–) tartaric acid, thin needles are formed with solubility almost two times higher. Free malic and tartaric acids also form diastereomeric molecular compounds.

6. Chromatography

Optically active substances are preferentially adsorbed by some optically active adsorbent. Thus Broadly and Easty (1951) found wool and casein to adsorb (+) mandelic acid from its aqueous solution. Some workers also successfully carried out resolution without using an active adsorbent. The alumina was found to be suitable for resolving diastereoisomers of (–) menthyl (±) mandelate.

This chromalographic method is convenient and useful in a number of cases. Crystals of quartz which are chiral exhibit different adbsoptive power for several antipodes and so also starch has been employed. Gas-liquid chromatography (GIC) is also employed to resolve racemates. For example to separate racemic α amino acids they are converted into esters with optically active alcohols like (–)2 butanol or trifluroracetyl devivatives, which are then separated by GLC.

Paper Chromatography too has been employed. The paper was impregnated with a solution of (+) camphor sulphonic acid or it was used as such unimpregnated, because paper itself is optically active.

7. Kinetic method of resolution

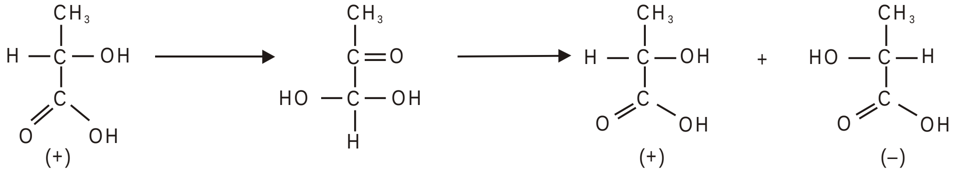
Starting from a racemate, it is possible to prepare mixtures of enantionmers with a preponderance of one form in them. We have described this in asymmetric transformations, consequently we have *first* and *second* order asymmetric transformations. In a first order there is a shift of the equilibrium to the side of formation of one of the enantiomers in solution while in a second order there is a complete conversion of the racemate into one of the optically active forms.

RACEMISATION

The conversion of an optically active compound into an optically inactive mixture (dl mixture) is known as racemisation. The (+) and (–) forms of most compounds are capable of racemisation under the influence of heat, light or chemical reagents. Which agent can bring about racemisation, depends on the nature of the compound. For example (+) tartaric acid when heated strongly with water to 175° is transformed into a mixture of racemic and mesotartaric acids.

It is important to note that racemisation is not accompanied by the breakdown of the substance. In fact the composition, structure and chemical properties are retained. Only its optical activity is lost.

Sometimes intramolecular change may bring about recemisation as depicted in lactic acid:



But when a molecule contains two or more asymmetric carbon atoms and the configuration of only *one* is inverted, the process is called *epimerisation.*

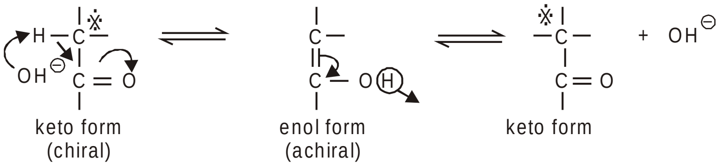
It the original compound loses all of its optical activity in the course of reaction, it is called *complete* racemisation, but if only a part of its optical activity is lost which occurs when an enantiomer is partly converted into its racemic form, then it is called partial racemisation.

Mechanism of racemisation

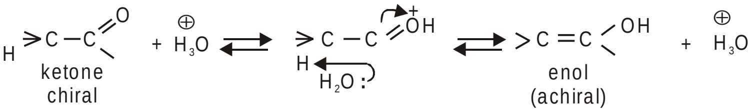
A number of hypotheses have been put forward to account for racemisation and a single theory cannot explain the racemisation of all types.

1. Enolisation

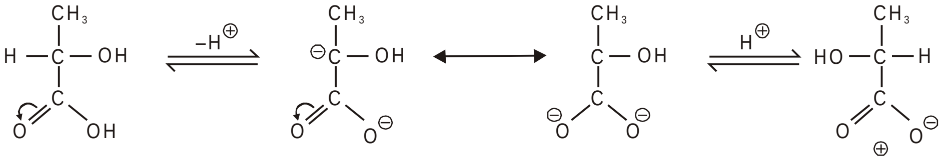
One of the most widespread theories is the theory of enolisation mechanism put forward by Beckmans in the last century and explains beautifully racemisation in compounds containing a carbonyl group next to the chiral centre:



The original asymmetric carbon(*) in the keto form loses its asymmetry and is changed to the enol form. But owing to its symmetry the enol form can produce another keto form in which the configuration about the asymmetric carbon would be the mirror image of the original and hence would lead to racemisation. This type of enolization is a case of keto-end tautamerism and it has also been found that in such cases the change is catalysed acids or bases. The acid-catalysed enolization is as follows:



The racemisation of (–) lactic acid in an aqueous sodium hydroxide is believed to proceed through an intermediate carbanion which through a mesomeric change gives the other form:



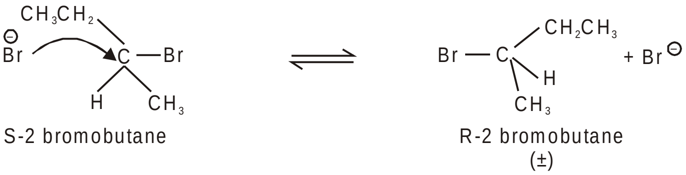
It is obvious that any factor which prevents tautomerism would hinder racemisation and this happens when the hydrogen atom attached to the asymmetric carbon atom is replaced by some other group. Thus while mandelic acid, C_6H_5–CH(OH). COOH having the structure resembling lactic acid is racemised by warming with aqueous aodium hydroxide, atrolactic acid C_6H_5–C (CH_3) (OH) COOH is not racemised under the same conditions.

A good deal of evidence has been collected to support this tautameric mechanism.

This means that if racemisation proceeds via enolization then the rates of racemisation and enolization should be the same and kinetic studies have established this.

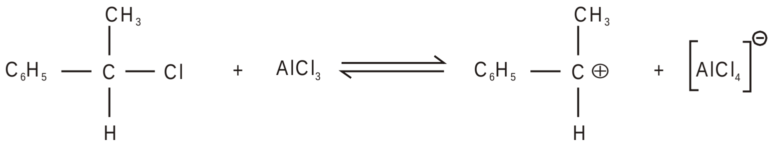
Therefore, these reactions in which the chiral molecules are first converted into an achiral intermediate are examples of S_N1 reactions because the leaving group departs from a chiral carbon and they lead to complete recemisation.

These are also reactions in which inversion of configuration occurs signifying the reaction to be of S_N2 type. For example racemisation of S–2–bromobutane on heating with bromide ions in acetone results in inversion.



2. By heating (Thermal racemisation)

There are cases where racemisation takes place under the influence of heat. Under such conditions there is homolytic fission of the bond between the asymmetric carbon atom and one of the substituents. The radical formed may assume either of the two enantiomeric configurations with equal possibility of recombination, giving a racemate. For example α chloroethyl benzene during distillation undergoes thermal racemisation, but in presence of lewis acids it undergoes racemisation with the intermediate formation of a carbocation.



$$C_6H_5-\overset{\displaystyle CH_3}{\underset{\displaystyle H}{C}}-Cl + AlCl_3 \rightleftharpoons C_6H_5-\overset{\displaystyle CH_3}{\underset{\displaystyle H}{C}}\oplus + [AlCl_4]^{\ominus}$$

Again the same compound (+) or (–) form when dissolved in liquid SO_2 undergoes spontaneous recemisation even at room temperature. Again the same carbocation is supposed to be formed as the intermediate which then gives the other isomer. The carbocation being planar and symmetric recombines with the chloride ion giving the other form. The basis of this machanism is that alkyl halides in liquid SO_2 exhibit electrical conductivity thus supporting isnisation.

3. By time

In many cases optical activity disappears after prolonged storage and the process is described as *autoracemisation.*

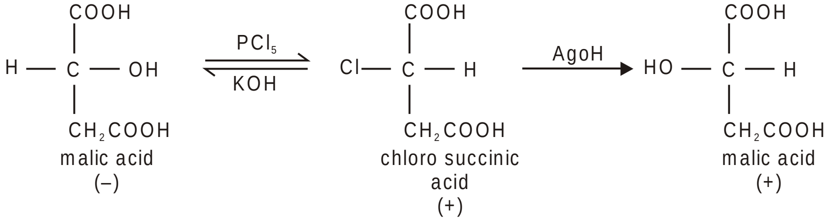
Antoracemisation has been observed with substances not only in solid or liquid states but also in their solutions, For Example (+)–phenyl bromoacetic acid after three years of storage becomes inactive, in its solid state. A liquid showing antoracemisation is the ethyl ester of bromosuccinic acid.

Generally antoracemisation occurs with substances which have a halogen atom attached to a chiral centre.

Walden Inversion (Optical inversion)

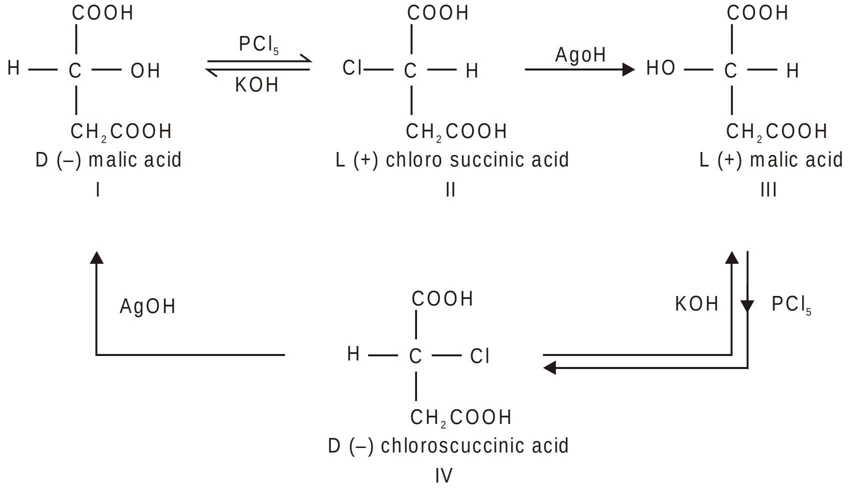
When an atom or group directly linked to an asymmetric carbon atom is replaced, the configuration of the new compound may be opposite that of the original. Thus (+)–malic acid can be converted into (–)–form as follows in the next parea.

This curious phenomenon of the ‘inversion’ of groups about the asymmetric carbon atom first studied by Paul Walden is called *Walden inversion* or *Optical inversion.* This was the first study of the influence of spatial structure on the reactivity of compounds and by a series of reactions Walden changed an optically active compound into its enantiomer. The interesting feature is that in some cases the inversion is so quantitative that the enantiomer is 100% optically pure, in other a mixture of (+)-and (–)-forms is obtained in unequal amounts.

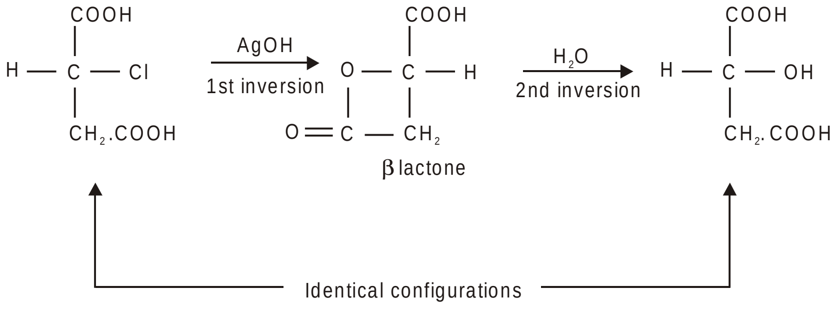


In the above inversion, we find the change has occured in two steps and Walden inversion is actually that step in which the inversion of configuration occurs and it is to be noted that the change in the sign of rotation does not necessarily convey the inversion of configuration. We have a number of methods of correlating configurations. In general it has been found that when inversion is going to take place, there is a complete removal of the group attached to the achiral centre, but the removal of a complete group will not always lead to inversion.

Some further peculiar observations have been made regarding optically active malic acid. Since at that time, 1896 X-ray analysis was not available, Walden suggested the change to be taking place through the following cycle, based on the sign of rotation.



But the fact that a change of configuration occur on the path II → III → IV or III → IV → I is clear since by a two stage process an optically active compound (+)–. chlorosuccinic acid in

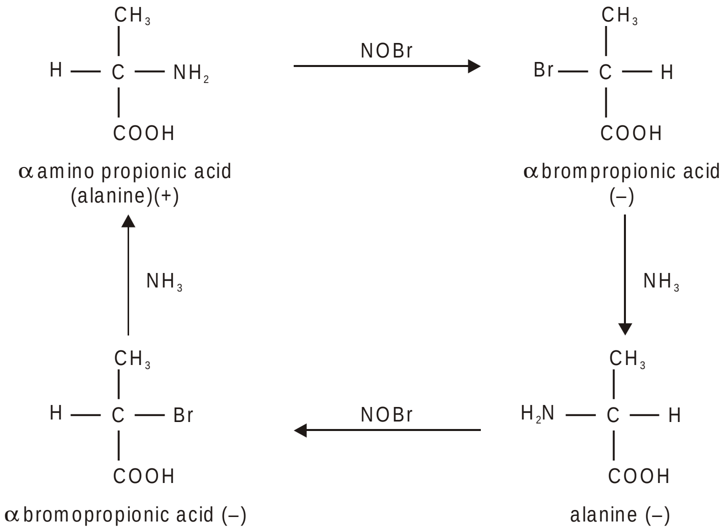


the first case and (+)–malic acid in the second is converted into its antipode. Thus one reaction proceeds with and the other without the inversion of configuration. So reagents like PCl_5 and KOH etc. produce a change in the direction of optical rotation but moist Ag_2O does not.

More exactly according to the hypothesis put forward by Hughes and Winstem the second reaction proceeds with two inversions of configuration:

Walden inversion is a rule for S_N2 reactions except in reactions where there is a participation of the neighbouring atom as in the above reaction involving the intermediate cyclization into the lactone.

E. Fisher noted such an inversion in the following

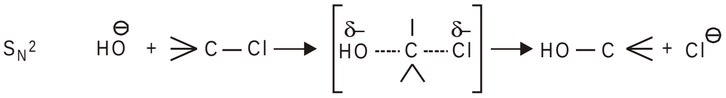


Mechanism of Walden Inversion

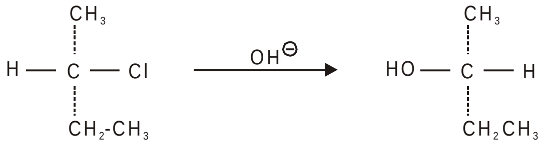
After extensive studies it has been found that three factors influence Walden inversion. These are:

1. the nature of the reagent.
2. the nature of the substrate and
3. the nature of the solvent.

Many theories have been put forward to explain the mechanism of inversion. According to the accepted Hugles, Ingold theory aliphatic nucleophilic substitution reactions occur eigher by S_N2 or S_N1 mechanism. In the S_N2 mechanism the backside attack reduces electrostatic repulsion in the transition state to a minimum when the leaving meleophile leaves the asymmetric carbon, naturally an inversion of configuration occurs at the central carbon atom.



Thus D–(+)–2 chlorobutane is converted to 2. butanol by aqueous base and the product has inverted configuration:

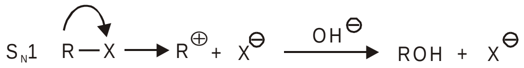


D(+) L(–)

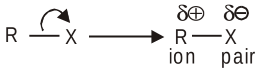
Therefore inversion always occurs in S_N2 mechanisms except when there is a participation of the nighbouring atom.

Since S_N2 mechanism operates in primary alkyl halides, this proves that the nature of the substrate is important for inversion. The is also known as *stereokinetic rule* for S_N2 reactions.

We have seen that substitution in secondary and tertiary alkyl halides proceeds by an S_N1 mechanism in which there is first slow ionisation resulting in the formation of a flat carbocation and hence the attack by the nucleophilic reagent can take place equally well from either side, *i.e.*, equal amounts of (+) and (–)– forms are likely to be produced giving a racemic product:



In case there is not complete dissociation into the ions and there is an ion-pair formed first, then the picture will be different. The leaving group will protect its side from attack by the nucleophile. In that case inversion will occur exclusively or will predominate:



Only when there is complete dissociation of the ion pair, complete recemisation can be expected.

So we see that the nature of the substrate is again of importance in inversion.

From a number of experiments it has been concluded that with short life carbocations (obtained from secondary and tertiary alkyl deviatives) inversion is generally observed. But in long life carbocation where there is spreading of the charge, the product is a racemic one, as in diphenyl methyl carbocation Ph_2CHX. Therefore it also affords a means of estimating the relative stability of carbocations.

CHAPTER 10

Conformation

The subject of conformation has gained importance since our knowledge of three dimensional structure of organic molecules has become quite detailed.

The landmark in the history of conformation started in 1874 when van't Hoff and Le Bel gave the tetrahedral structure of the carbon atom in which the angle between the valency bonds was 109°29'.

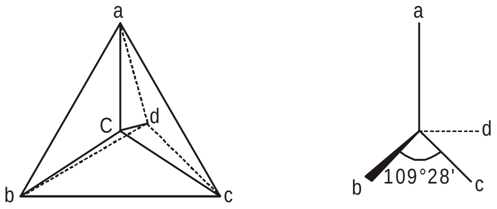


Fig. 10.1

If this carbon holds in different atoms, the bond angles are somewhat (a little) changed and the tetrahedron ceases to be regular. But the real foundation for conformational study was laid in 1935 when it was observed that there was discrepancy between the entropy of ethane as found from the heat capacity measurements and as calculated from spectral data. From this the physical chemists concluded that there must be hindrance to rotation about the carbon bond in ethane. Later it was found that there was tortional barrier to free rotation to the extent of about 2.8 K cals per mole.

CONFORMATION AND CONFORMATIONAL ANALYSIS

The word conformation means the different arrangement of atoms in space that result from rotations of groups about a single bond and an analysis of energy changes that a molecule undergoes when groups rotate about single bonds is called a **conformational analysis**.

Conformational analysis is largely due to the work of O. Hassel of Norway and D.H.R. Barton of Britain and both were awarded Nobel prize in 1969 mainly for their contribution in this field.

It will be proper at this stage to understand the difference between configuration and conformation. Isomers made up of same atoms and bonded by same bonds but having different three dimensional structures which are not inter-changeable are called configurations. Therefore, configuration represents isomers which can be separated. On the other hand conformation represents conformers which are rapidly inter convertible and thus are non separable. But instead of the word 'Conformer', the term conformational isomer is often used.

Conformational Analysis

We know that the rotation about a double bond is impossible without disturbing the π bond, which requires a large amount of energy (about 60 K cals/mole). This restricted rotation gives rise to cis-trans isomerism in olefines and their derivatives.

For a long time the idea was prevailing that rotation about a single bond was completely free. It was only in 1936 that it was suggested that this rotation was hindered and this bindrance was different for different saturated compounds (Kemp and Pitzer).

Let us consider when two non bonded atoms come close to each other and are at a distance which is only slightly less than the sum of their van der Waals radii. This will result in repulsion between electron shells of these atoms. This repulsion, called *steric repulsion*, will increase upon further approach of the atoms. Naturally it should affect the energy of the molecule and so while correlating the energy of the molecule with its reactivity one should not only take into account, the bond energy and the polar effects etc. but also the steric repulsion between non-bonded atoms. So when a bond is being formed between two atoms, the groups attached to these atoms approach each other in space as well and even if they are not large, a steric interaction between them is possible (*The bond lengths are always considerably smaller than the sum of the van der Waals radii of the corresponding atoms*).

Let us now consider the conformations in some open chain system.

Conformation of Ethane

The simplest molecule where we can discuss rotation armed a carbon-carbon single bond is ethane.

Using the ball and stick model, the ethane molecule can be represented as:

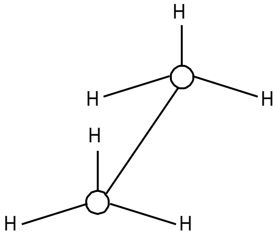
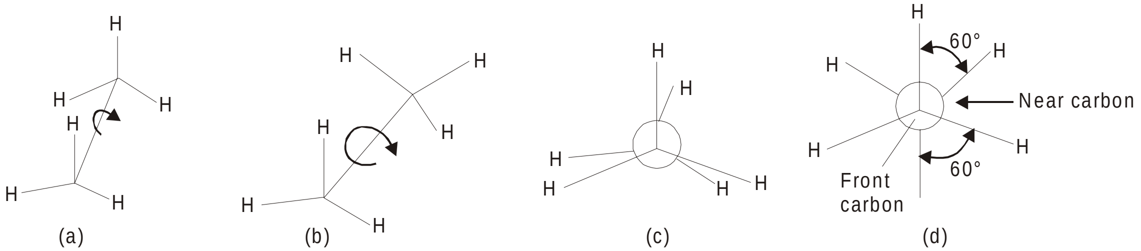


Fig. 10.2

Where the circle represents the two carbon and sticks the bonds. Now, if we allow the stick joining the two carbon nuclei to rotate freely in the holes, then an infinite number of different atomic arrangements becomes possible.



(a) Eclipsed (b) Staggered (c) Eclipsed (d) Staggered

The structures (*a*) and (*b*) are called perspective formulae. In this the bonds projecting forward are towards the observer, while these going backward are away from the observer. The above perspective formulae are represented by another type of diagram, Figs. (*c*) and (*d*) called the *Neuman projection formula*. The noteworthy point is that in (*a*), the hydrogen atoms of one carbon lie exactly opposite the hydrogen atom of the other. This arrangement is called the *eclipsed* form of ethane. Here, the hydrogen atoms are crowded together. It is, therefore, of highest energy due to repulsion between protons and so has the *least stability*. In Fig. (*d*), the hydrogen atoms are as far apart as possible and this arrangement is called the *staggered* form of ethane. This is the *most stable* conformation (*i.e.* it is the conformation of *lowest potential energy*).

In both the conformations, the bond angles and bond lengths are maintained intact. The above prospective formulae are represented by another type of diagram Figs. (*c*) and (*d*) called the Neuman projection formula. The observer is looking at the C—C bond head on. The three lines going from the centre of the circle represent the valencies of the front carbon as shown in Fig. (*c*) with respect to the observer. The rear carbon atom is represented by a circle to which three bonds attach. The Neuman projection formula shows quite clearly that in the staggered conformation two bonds on the two adjacent carbons are separated by an angle of 60°. These elipsed and the staggered conformations of ethane have been obtained by the rotation along the carbon-carbon sigma bond axis. In between these two extreme conformations, we have skew conformations. These have stabilities between that of the staggered and that of the eclipsed conformation. So the relative stabilities are in the order : staggered > skew > eclipsed.

Now the question arises : Which of these is the actual structure of ethane molecule? The answer is all of them. The eclipsed and staggered conformations posses identical physical character but differ only in energy content. So we find that because in the eclipsed form, the hydrogen atoms are clear together, they exert repulsive forces on one another and due to which their potential energy becomes very high resulting in their least stability. On the other hand in the staggered form, since the hydrogen atoms are farther from each other, the repulsive forces are very much reduced and the molecule comes to posses minimum energy giving it greater stability. The energy difference between the staggered and the eclipsed form is shown in Fig. 10.3.

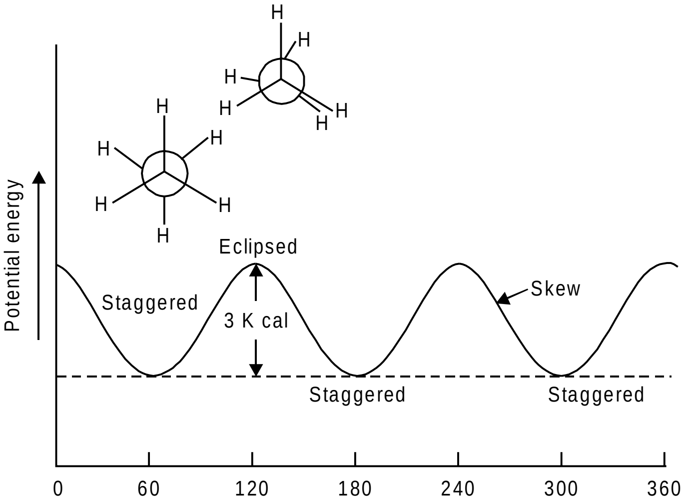


Fig. 10.3 Potential energy changes during rotation about C—C single bond of ethane.

As the bond rotates the energy gradually increases, reaches a maximum when the eclipsed form is reached. Further rotation, as seen from the above graph, decreases the energy again till it comes to a minimum when the staggered conformation is reached. The energy difference between the staggered and eclipsed form is 3 Kcals/mole. This is called the energy barrier. Although ethane exists in all the forms, but it spends most of its time in the staggered form because, it is very stable.

Further, if the energy difference between the two forms is so small even at room temperature, the friction of the molecular collisions with sufficient energy is large enough to bring about a rapid interconversion between the various forms. This is why this small energy difference will not permit the isolation of the two forms so easily.

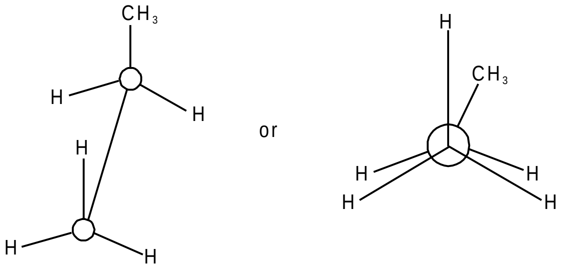
Actually this energy barrier creates hindrance in free rotation in the molecule. Therefore, strictly speaking there is not free rotation in ethane. But since this value is small we, may neglect it and regard that there is free rotation about C—C single bond in ethane.

The nature of the rotational barrier in ethane is not easily explained. It is too high to be due to van der Waal's forces. It is considered to arise by interactions among the electron clouds of C—H bonds and quantum mechanical calculations show that the barrier should exist.

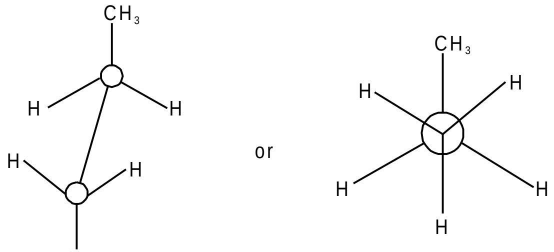
The energy required to rotate the ethane molecule about the C—C bond is called *torsional energy* and the relative instability of ethane is due to the torsional strain. When the energy barrier is large due to substitution of hydrogen by larger groups, as in substituted diphenyls, rotation at room or temperature is completely prevented and then we speak of configuration and not conformation.

Conformation of Propane

By replacing a hydrogen of ethane by methyl group, we obtain propane and the picture is like the same as in ethane and the eclipsed and staggered forms are as follows:



Eclipsed

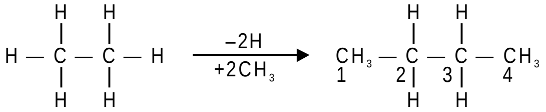


Staggered

Here also the rotation can occur about the two carbon bonds and is almost free. The energy difference between the eclipsed and staggered forms is 3.3 K gals/mole. This is also too low and permits ready interconversion.

Conformation of Butane

Butane may be regarded as ethane in which one hydrogen atom on each carbon atom is replaced by a methyl group



$$\mathrm{H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H} \xrightarrow[+2CH_3]{-2H} \mathrm{\underset{1}{CH_3}-\underset{H}{\overset{H}{\underset{2}{C}}}-\underset{H}{\overset{H}{\underset{3}{C}}}-\underset{4}{CH_3}}$$

If we consider rotation along C_2—C_3 bond, we get the staggered forms. Due to the presence of two methyl groups there are two eclipsed and two staggered forms.

Eclipsed Forms

1. That in which one methyl group is eclipsed by the other methyl group.
2. That in which the methyl group is eclipsed by a hydrogen atom.

Staggered Forms

1. That in which the two methyl groups are as far apart as possible. These are called *anti*- or *transoid* conformation.
2. That in which the two methyl groups are at an angle of 60° to each other and are called *skew or gauche* form.

The energy changes between the different forms arising from the rotation of C_2–C_3 bonds are shown in Fig. 10.4.

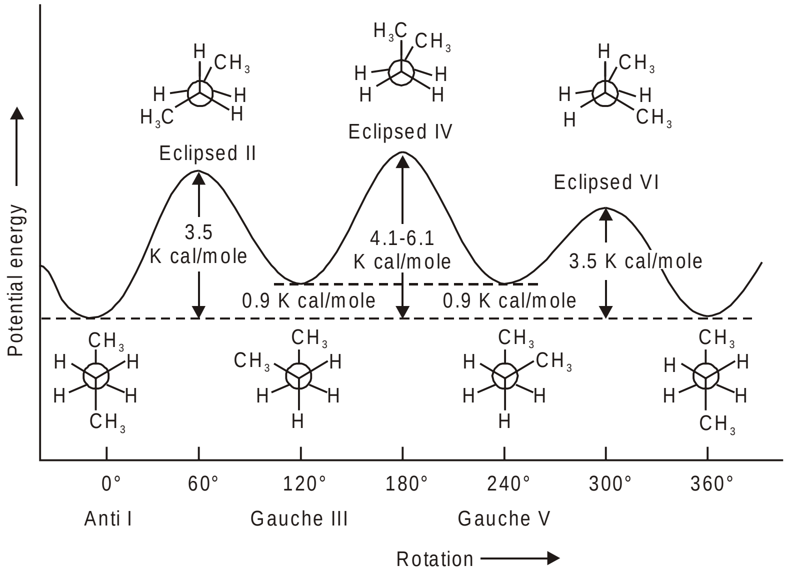


Fig. 10.4

The high energy barrier estimated at 4.4–6.1 K cal/mole corresponds to that eclipsed form where one CH_3 group is eclipsing the other CH_3 (IV). A second eclipsed form is that (II and VI) where a hydrogen atom is eclipsing the CH_3 group and there is also Hydrogen—hydrogen eclipsing. The energy maxima in these is only 3.5 K cals/mole, which is only slightly greater than ethane. The eclipsed form IV has the greatest repulsive force than forms II and VI. There forms II and VI being of lower energy than IV are more stable and so the conformation II and VI is more favoured– Eclipsed conformation IV has the greatest energy of all because there is large van der Waals repulsive force between the eclipsed methyl groups.

In the staggered anti conformation I, the two methyl groups are as far apart as they can be and so this system is most stable. When the CH_3 groups are rotated 60° with respect to each other, some van der Waals interaction occurs and we get the gauche forms III and V which are less stable than the anti form by about 0.8 to 0.9 K cals/mole, but the conformation still corresponds to a potential energy minimum. This small value of 0.9 K cals/mole is due to the van der Waals repulsive force between the two CH_3 groups. While barriers to rotation in butane are larger than those of ethane, they are still too small to permit the isolation of gauche and anti conformations. Such conformations of minimum energy (namely anti and the two gauche) are sometimes, called *conformational isomers or conformers*. Of these three, the two gauche forms are the mirror images of each other. In spite of this, the molecule is inactive. This is because the two forms are present in equal amounts and interconvert too rapidly for separation.

Why there is energy difference between the staggered and the eclipsed form is not completely understood. It is not simply due to the van der Waals repulsive forces, because such forces are too small to account for the observed differences in potential energy. Now it is known that the differences are in some way due to interaction of electron clouds in C—H or C—C bonds and various causes for such interactions are known.

So butane molecule has a higher population of the anti-conformer and the population of the two gauche conformers is equal.

It is interesting to note that the different conformers can be separated, if the energy difference between them is about 14 K cals/mole.

Ring Strains in Cycloalkanes

While the conformation of cycloalkanes has been discussed in detail later, it will be worth while to see how the ring strain in such compounds is calculated as this will give us a broad picture about their relative stability.

We know that all cycloalkanes do not have the same relative stability. Cyclohexane is most stable while cyclopropane and cyclobutane are much less stable, because they have a ring strain in their molecules.

To find the ring strain, we must first know the relative heats of combustrain of these compounds,

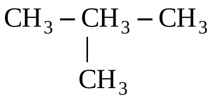
The heat combustion of a compound is the enthalpy change for the complete oxidation of the compound. Thus for CH_4, it is of the order of 192 K cals/mole.

$$CH_4 + 2O_2 \longrightarrow CO_2 + 2H_2O \qquad H = -192 \text{ K cals/mole.}$$

Since the complete oxidation of two isomeric hydrocarbons will give the same number of moles of CO_2 and H_2O, using the same moles of oxygen, we can find their heats of combustain. For butane and isobutane, the values determined experimentally are:

$$CH_3. - CH_2.CH_3 + 6\tfrac{1}{2}O_2 \longrightarrow 4CO_2 + 5H_2O \qquad \Delta H = -687$$

n-butane



$$\underset{\displaystyle CH_3}{CH_3 - \overset{}{\underset{|}{CH_3}} - CH_3} + 6\tfrac{1}{2}O_2 \longrightarrow 4CO_2 + 5H_2O \qquad \Delta H = -685$$

isobutane.

Thus *n*-butane which liberates more heat than isobutane must have more potential energy and so is less stable than isobutane. Similarly the heat of combustion of cycloalkanes can be written in the following form:

$$(CH_2)_n + \frac{3}{2}nO_2 \longrightarrow nCO_2 + nH_2O + \text{heat}$$

Since cycloalkanes do not have isomers, the heat evolved has been calculated per CH_2 group. First we find the heat of combustion of cyclohexane which is most stable and then the heat of combustion per CH_2 group. It comes to 157.4 K cals/mole. Now to calculate the ring strain for other cycloalkanes, we multiply 157.4 K cal/mole by *n* and then subtract it from the heat of combustion of cycloalkane.

As an illustration, the ring strain in cyclopropane, cyclobutane and cyclohexane and cyclodecane has been calculated:

Table 10.1

Cycloalkane	*n*	*Heat of* combustion K cal/mole*	*Heat of combustion/ CH_2 group K cals/mole*	*Ring strain K cals/mole*
1. Cyclopropane	3	499.8	166.6	(166.6 – 157.4) × 3 = 27.6
2. Cyclobutane	4	655.9	164.0	(164 – 157.4) × 4 = 26.4
3. Cyclohexane	6	944.5	157.4	(157.4 – 157.4) × 6 = 0
4. Cyclodecane	10	1586.0	158.6	(158.6 – 157.4) × 10 = 12

(*From fundamentals of Organic Chemistry by I.W. solomons. 1982 Edition. John Wiley and Sons, New York)

Since the heat of combustion per CH_2 grmp in cyclohexane is 157.4, it does not differ much from that of *n* alkanes. (In butane, it is 687/4 = 171.7) This leads to the conclusion that butane can have no ring strain. Cyclopropane has greatest ring strain and hence is least stable. It can also be said that ring strain is a form of potential energy that a cyclic molecule contains and the greater is the ring strain the greater is the potential energy and hence lesser the stability.

Cyclopentane and cycloheptane have almost equal ring strains (6.5 and 6.4) and a 15 membered cycloalkane again has a very slight amount of ring strain.

PRINCIPLES OF CONFORMATION

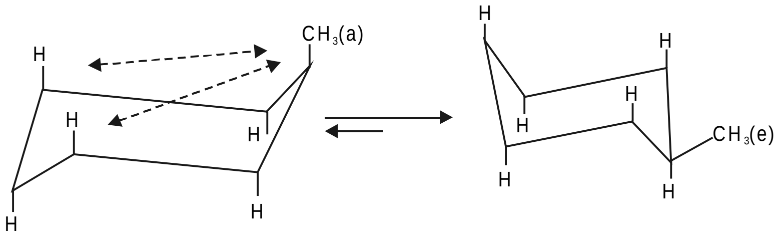
We know that rotation along a single bond in a molecule allows it to assume a conformation with minimum strain energy. This strain energy is a sum total of so many factors like angle bending, rotational and steric strain, steric hindrance and bond bending and so the geometry of the molecule becomes such that the strain energy comes minimum.

The angle bending arises due to the deviation of each bond angle from the normal. The rotational strain is a function of torsion and arises due to restricted rotation along a C–C axis. Steric strain is due to non bonded interaction of groups for each other. It is said to arise due to close crowding of groups and their mutual compression. It increases as the distance between the non bonded atoms decreases. In view of other strain, the bond stretching strain is of minor importance. To study the various combined effects of all the strain and then to arrive which conformer will have minimum energy is now done by means of a computer.

The process of assessing the preferred conformation has become of importance of cyclic compounds, at least in six-membered rings because in their formation, almost all the strains are involved. We have seen that cyclohexane exists mostly in the chair conformation and the boat form occurs in negligible proportion because of higher energy which is of the order of ≥6 K cals/mole.

When we study the case of cyclodecane, we find that x-ray crystallographic studies reveal that the most stable conformation has C—C bond angles of 117° which indicates some angle strain from the normal 109°28'. So the wide bond angles allow the molecule to expand and minimise unfavourable repulsions between hydrogens across the ring.

The case becomes interesting when one studies mono substituted cyclohexanes. For example, methyl cyclohexane exists in two forms, one in which the methyl group is axial and the other in which it is equatorial. The latter is more stable than the former by 1.6 K cals/mole and in an equilibrium mixture, it is present to the extent of 98%. This is because that when the CH_3 group is axial, it is so close to the two axial hydrogens on the same side of the molecule, that the van der Waals, forces between them are repulsive:



In fact any group has considerably more room when it occupies an equatorial position. This effect becomes more pronounced when the group becomes bulky. For example the conformation of tertiary butyl cyclohexane. With the tertiary butyl group in the equatorial position is about 5 K cals/mole more stable than when it is in the axial position and so at room temperature the conformation with the substituent in the equatorial position is virtually present to the extent of 100%. In this matter alkyl groups appear to have greater conformational preference than the polar groups.

Also the preference appears to increase with the size of the alkyl radical. But if the substituent is a polar group, this preference appears to be un-important.

In disubstituted compounds, the conformation with the least axial substituent is most favoured. Therefore the non-polar groups as far as possible adopt equatorial positions. But this also very much depends on the configuration and the generalization is that:

(*i*) in cis, 1, 2 disubstituted cyclohexane, one substituent is axial and the other is equatorial.

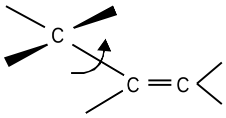
(*ii*) in trans 1, 2 compounds, both substituents may be axial or equatorial.

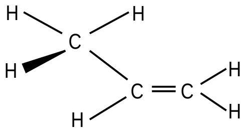
This is also true for 1,4 disubstituted cyclohexanes, but for 1,3 compounds, the reverse is true, the trans must have a *e* and cis either *aa* or *ee* conformation. But if the substituents are alkyl groups, the diequatorial predominates the diaxial. The trans 1, 2-*e e* conformations are thermodynamically more stable than cis 1, 2 isomers which therefore occurs as a *e* form.

Finally since the eclipsed conformation has increased internal energy, it can not be adopted by molecules without distortion of the normal angles and bond length and are therefore, unfavourable conformations. This is why the molecules always try to assume a staggered conformation.

Rotation about Bonds involving Carbon Atoms in a State of sp^2 Hybridisation

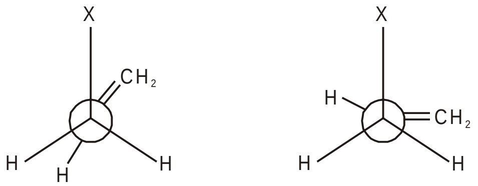
So far we have discussed conformations of a molecule obtained by rotation along sp^3–sp^3 bond *i.e.*, between two tetrahedral carbon atoms. But there are many compounds in which one carbon is in a state of sp^2 hybridisation. Examples are substituted alkenes where one carbon atom is tetrahedral and the other trigonal, for example propene:





Its stable conformation would be that in which one of the hydrogens of the CH_3 group would be eclipsed by the ethylenic system.

Microwave, spectral studies have shown that allylhalides exist in two forms, of which the skew form is more stable.



Fully eclipsed Skew

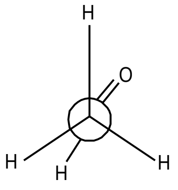
Conformations of $CH_2 = CH—CH_2X$

In cis and trans –1, 3 dichloropropenes, the skew form is again more stable (In the Newman formula for this compound, the CHCl group would be in place of CH_2 group).

The carbonyl compounds and carboxylic acids would be other examples of conformations involving sp^3–sp^2 hybridisatram.

Acetaldehyde

It exists in a conformation where the oxygen atom is eclipsed by a hydrogen atom. This is due to the result of the development of partial charges. $O^{\delta\ominus}$ and $H^{\delta\oplus}$ and consequent attraction between them.



Acetaldehyde

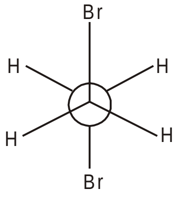
METHODS FOR DETERMINING CONFORMATION

A number of methods are employed to determine the conformations. These include the measurement of dipole moment or the study of spectral properties like I.R. studies or N.M.R. or electron diffraction or X-ray diffraction studies. Some of these methods are discussed below :

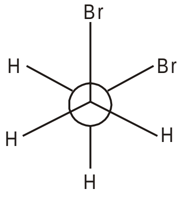
1. Dipole Moments

As an illustration, let us take the case of 1,2 dibromoethane and see how far the calculated value of dipole agrees with the observed value.

If we assume the molecule to exist in the staggered and gauche forms,



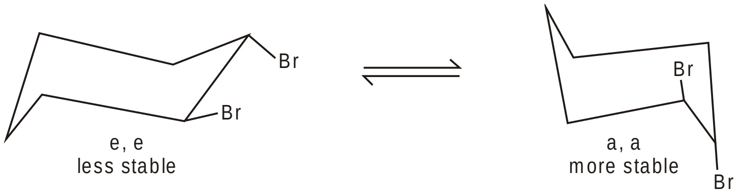
Staggered or
anti



Gauche

then in the staggered form, the dipole moment should be zero because the C–Br bonds are anti parallel and in the gauche form it should have a finite value. The actual dipole moment measured experimentally is approximately I D (Debye unit). This value shows that the molecule can not exist entirely in the staggered or anti form. Further since on cooling, the dipole moment varies with temperature, the molecule does not exist entirely in the gauche form either. This leads to conclusion that probably there is an equilibrium between the two forms and this arises due to the twisting to and fro about the bond between the two carbon atoms and as the twisting varies with temperature, so would the dipole moment vary. It has been concluded on the basis of dipole moments and polarizabilities that 89% of the molecules are in anti and 11% in the gauche conformations.

The case is interesting in 1,2 dibromocyclohexane. The moment for the diaxial isomer is assumed to be zero, while the calculated and observed values for the diequatorial form are respectively 3.09 D and 3.12 D. The trans diaxial form is more stable than the trans diequatorial, although the latter is favoured sterically. The reason for the lesser stability of the trans diequatorial form is that it is destabilized by dipole repulsion.

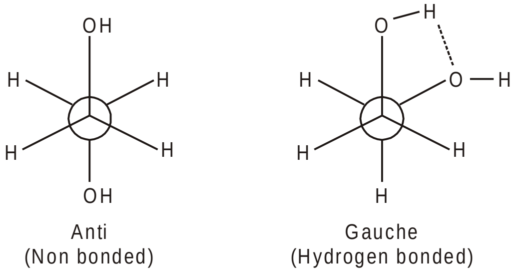


1, 2 dibromocyclohexanes

2. Infrared Spectra

More evidence for the existence of several conformational isomers, at least in liquid and gaseous substances comes from infrared and also Raman spectra. For example each conformer has its own I.R. spectrum, but the peak positions are often different. Thus the C–F bond in equatorial fluorocyclohexane absorbs at 1062 Cm^{-1}, the axial C–F bonds absorbes at 1129 Cm^{-1}. So the study of infrared spectrum tells, which conformation a molecule has. Not only this, it also helps to tell what percentage of each conformation is present in a mixture and since there is relationship between configuration and conformation in cyclic compounds the configuration can also be frequently determined.

When there are chances for the presence of both anti and gauche forms in an equilibrium, the anti isomer is preferred, because the steric and dipole repulsion come into play in the latter, as is illustrated from the example of ethylene glycol. The two forms of this glycol are:



Conformational isomers of ethylene glycol

But on account of the intramolecular hydrogen bonding as manifested by the I.R. spectrum, in the gauche form, it also exerts a considerable influence. Since the absorption due to this hydrogen bond is strong in the spectrum of ethylene glycol, it shows that a considerable fraction of the molecules are in the gauche form despite the steric and dipolar repulsion of the hydroxyl groups. This means that the repulsion is more than balanced in the formation of hydrogen bond. Since the hydrogen bonds may be as strong as 5 Kg cal/mole.

From the studies made by I.R. and Raman spectra on 1,2-dihaloethanes, the conclusion has been that the gauche form is more important in polar than in non polar solvents. This is because that the gauche form has a considerable dipole moment while the anti has nearly none. Solvation by polar solvents reduces the potential energy of a dipole and so makes the gauche form more stable relative to the anti.

3. Nuclear Magnetic Resonance Spectra

Valuable information on conformational equilibrium can be obtained particularly by N.M.R. technique. When a molecule can exist in several conformations which rapidly interchange, then any proton which assumes all possible positions in a very short time, the n.m.r. spectrum would show only one peak. This happens in most open chain compounds and even in cyclohexanes where the interconversion is very rapid. But if the interconversion is slowed or prevented, either by cooling or due to the inherent structure in the molecule, the hydrogens of each conformer appear separately and so more than one peak would appear. For example by cooling cyclohexane to –110°C, two peaks appear, one due to equatorial and the other to the axial hydrogens.

Generally the axial protons absorb at higher field than the equatorials, but this is not always the case. As an example, the n.m.r. spectrum of 1,1-diflurocyclohexane at different temperatures (for fluroine nuclei) has been taken. At +30°C a single peak appears which means that both fluorine atoms, the axial and equatorial—are practically equivalent because of the rapid interconversions of the two conformations. At low temperatures, the life time of each conformation becomes longer. As the temperature decreases, the signal widens and splits into two peaks and finally at –100°C, two signals appear corresponding to two different dispositions of the fluorine nuclei. This has been illustrated in the figure 10.5.

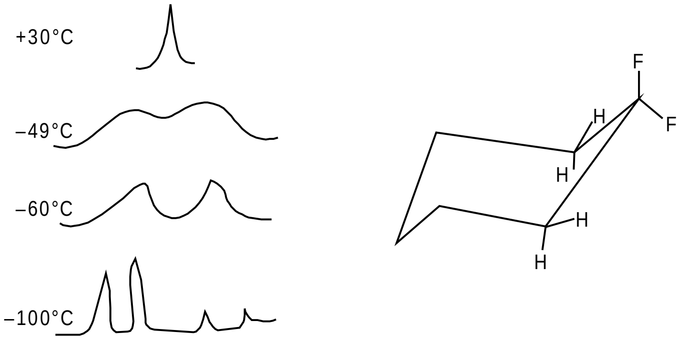


Fig. 10.5 NMR spectra of 1, 1-diflurocyclohexane

From the spectral data the life time τ of an individual conformer has been calculated and the results are as follows:

C°	τ, Sec.
+30	1.0×10^{-6}
–49	6.5×10^{-4}
–60	1.2×10^{-3}
–100	2.0×10^{-2}

After having found the peaks due to axial and equatorial protons, the proportions of the conformers can also be established by measuring the area under the peaks. The rate of conversion from one conformer to another has been obtained from the shape of the peaks.

So we find that the n.m.r. spectra not only help in elucidating the conformation, but have also been used to calculate the life time of the conformers, their proportions in an equilibrium mixture and finally the rate of interconversion.

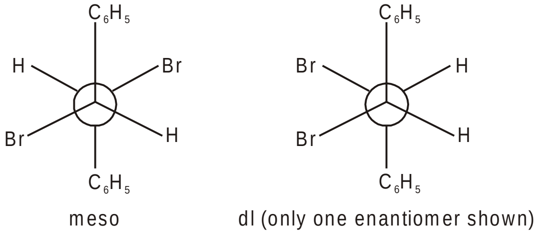
4. X-ray and Electron Diffraction Studies

X-ray and electron diffraction studies which are used to measure bond distances and bond angles give valuable information about conformation too.

X-ray diffraction has been used to indicate conformation in the solid state and this has been helpful because all molecules in a crystal have the same conformation. But there is one drawback that the conformation of the solid is not necessarily the same as that of the molecules in other phases. So this coupled with other methods should be employed for conformational elucidation.

The principle of the method is that once a substance crystallizes, the interconversion of the various conformers stops and so the crystals correspond to one discrete conformation or another. This has established, that 1,2-dichloroethane crystallises exclusively in the anti form, while ethylene chlorohydrin crystallizes in a gauche form because of intra molecular hydrogen bonding. But when the molecule crystallizes in two or more conformations, we say that it shows polymorphism.

X-ray diffraction has settled the conformation of stilbene dibromide. The meso form is that when both phenyl groups and bromine atoms are anti so that steric and dipolar repulsions are at a minimum. The dl form crystallizes in conformation in which the bromines are approximately gauche, and thus the steric repulsion of the bulky phenyl groups is at a minimum, even though there is steric and dipolar repulsions of the bromine atoms.



Conformations of meso and dl forms of stillene dibromides.

5. Optical Rotatory Dispersion

We know that when an asymmetric compound rotates the plane of polarized light, the amount of rotation also depends on the wave length of light used. In optical rotatory dispersion, the rotations are measured not at a single wave length, but over a range of wave lengths cohering the ultraviolet and the visible region. The instruments used are called *spectropolarimeters* and the results are expressed in the form of *optical rotatory dispersion* curves (ORD curves). In such experiments, the sodium vapour lamps are used as light source, which radiate light a wave length 589 nm (5893A). The curves obtained are shown in Fig. 10.6 and 10.7. Some compounds give what is called a *plain curve* while others illustrate the *Cotton effect*.

In a *positive* Cotton effect, as the wave length decreases, the rotation increases reaches a peak and then sinks to a trough (after which it rises again) (Fig. 10.6) while descending the curve crosses the zero axis at a wave length at which the compound absorbs light. In a *negative* Cotton effect, the phenomenon is just the reverse. As the wave length decreases, there is first a drop and then a sharp rise. *If any compound shows a positive Cotton effect, its enantiomer must show a negative one*. The curves which ascend or descend monotonically are called *plain curves*.

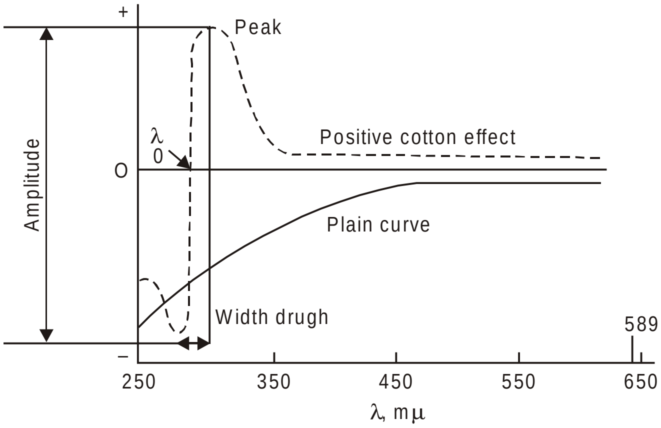


Fig. 10.6 Plain and positive Cotton effect curves.

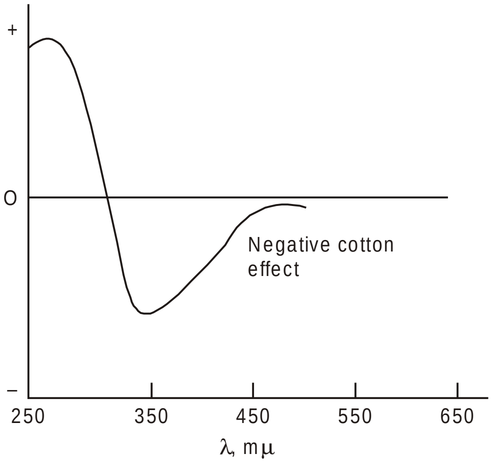


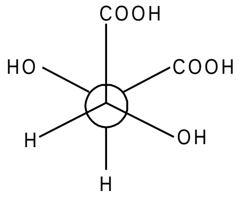
Fig. 10.7 Curve showing negative Cotton effect.

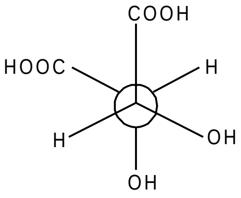
In Cotton effect curves, we use the terms *peaks* and *troughs.* The use of maxima and minima is not recommended because of the confusion that may arise. Since these terms are employed to describe ultra violet spectra, the sign of rotation is unimportant. Sometimes we also use the terminology amplitudes and widths of Cotton effects. The meanings of these terms are clear from Fig. (10.6). The plain curves are much less useful than Cotton effect curves.

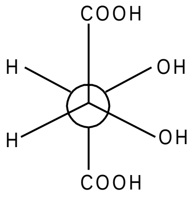
The character of ORD curves depends on the structure, configuration and conformation of optically active substances and also on the nature of choromophores present and their position relative to asymmetric centre. In many cases the curves depend on solvent and temperature. This is why spectropolarimetry becomes an important physico-chemical method (for investigating organic compounds). By introducing an optically active radial into organic compounds that do not possess optical activity, it is possible to extend the range of investigation by spectropolarimetric methods.

Two enantiomers of a compound exhibit mirror image curves, one showing, positive and the other negative Cotton effect. Structural information is also available from measuring the light absorption using asymmetric light which is circularly rather than plane polarized. Such techniques are called *circular dichroism*. The circular dichroism curves, generally provide the same information as ORD curves, but the former are simpler and more convenient for interpretation and theoretical calculations. This is because that each absorption peak in the molecule gives rise to a CD peak and this is relatively uninfluenced by other parts of the molecule, while in an ORD peak the given absorption is often complicated by background effects from other regions. The net result is an overlapping of effects. But this some times, becomes advantageous because a more complicated curve gives more information.

Let us now apply the technique in some specific cases. The existence of optical activity of several compounds in solution has been explained due to the presence of several active forms of the compound in equilibrium with each other and various assumptions about the forms were also put forward. The equilibrium between the different forms depended on external conditions. But a definite explanation was put forward in 1930 about tartaric acid and it was said that the molecule exists in the following three conformations and each of which makes a certain contribution to the rotation observed.





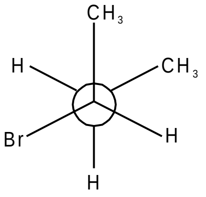


These conceptions of the nature of 'dynamic isomers' were later confirmed by physicists. Calculations have also shown that the rotation value must depend on the conformation of the molecule.

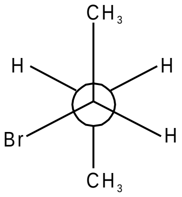
How conformation is related with optical rotation is brought out by the fact that with decreasing temperature there is an increase of rotation of conformationally mobile compounds. This is explained that at ordinary temperatures, several conformations occur at equilibrium, the rotation of which may be opposite in sign and so the total rotation is small. With the decreasing temperature the equilibrium is displaced in favour of the most preferred conformation with a characteristic rotation. An example of this is butanol-2.

Conformational Asymmetry

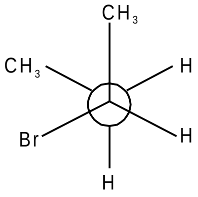
We should also be familiar with the meaning of the term conformational asymmetry. We know that different conformations of the same compound have different symmetry and different statistical contribution (*i.e.*, their percentage content is different). Therefore, the total effect on the polarization of light depends on the arrangement of atoms in different conformations and also on the statistical contribution of each conformation. This is called conformational asymmetry. The compound CH_3–CH_2–CH (CH_3)Cl has conformational asymmetry because two identical atoms (*c*) are situated at the asymmetric centre. This compound has three staggered conformations.



(1)



(2)

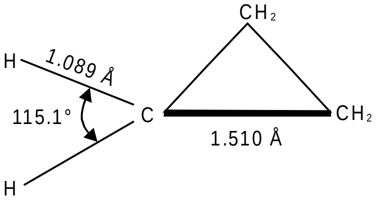


(3)

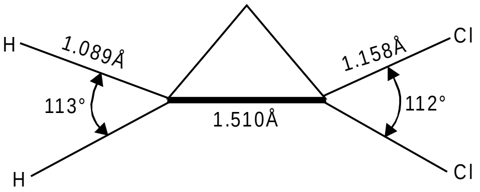
Of these the third one is excluded because it is unfavourable and all the three substituents in it are in the skew position. If the chain of carbon atoms is longer, the number of conformations also increases sharply and according to Bremster the calculations of such compounds also becomes complicated and requires the building up of the dimensional models, a discussion of this is beyond the scope of the present text.

Conformations of Three to Five Membered Rings

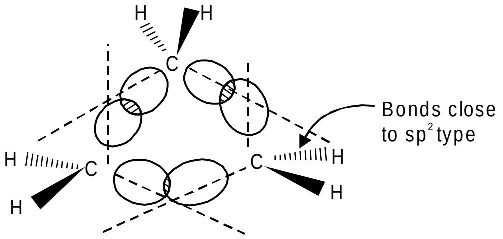
As already stated earlier cyclopropane is the only planar alicyclic compound in which the three points lie in a single plane and on the basis of X-Ray diffraction studies the following structure has been assigned to the molecule.



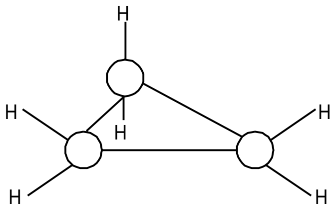
The electron diffraction studies of 1, 1-dichlorocyclopropane has given the following values for bond distances and bond angles.



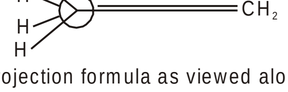
The noteworthy point is a shortening of C–C bond distance as compared to the aliphatic C–C bond distance which is 1.54 Å. This shortening manifests itself in the development of special character of the bonds. Since the *sp*^{3} orbitals of carbon now cannot overlap as effectively as they do in alkanes where perfect end-on overlap occurs the bonds in cyclopropane becomes bent and weak and also lead to an angle strain and so the molecule has greater potential energy. So this bent or banana bond accounts for the most of the ring strain.



Overlap of p orbitals in cyclopropane



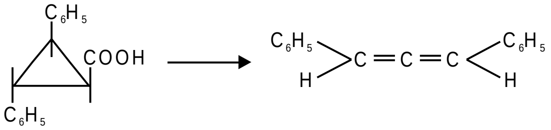
A line and circle drawing



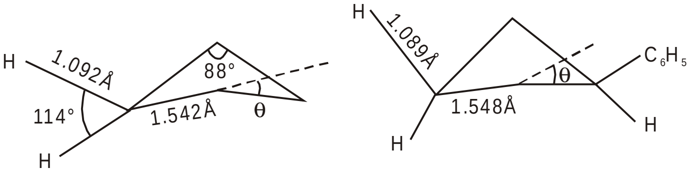
Neuman projection formula as viewed along one C–C bond shows the elipsed hydrogens.

Because the ring is planar the hydrogen atoms of the ring are all *eclipsed*.

The specific feature of the bonds also affects its chemical behaviour and the stereochemistry of substitution reactions. For example in the conversion of (–) trans –2, 3 diphenyl cyclopropane carboxylic acid into (+) 1, 3 diphenylallene the optical activity is retained.



Cyclobutane has no planar structure. The bond angle and bond distances in cyclobutane and phenyl cyclobutane are as follows:



The internal angles are 88°, a departure of more than 21° from the normal tetrahedral bond angle. The molecule is slightly 'folded' and the nonplanar structure has been established by X-ray, electron diffraction methods from dipole moment measurements and from NMR spectra. If the molecule were planar, the internal angle would be 90° instead of 88° and torsional strain would be considerably longer because all the eight hydrogens would be eclipsed by folding or bending, the ring relieves more of its torsional strain than it would cost in the slight increase in its angle strain.

Cyclopentane. The internal angles of a regular pentagon are 108°, a value very close to the normal tetrahedral bond angle, 109°28'. Therefore, departure of the valence bonds from their normal direction is 109°28'–108°2 = 44 and no Baeyer strain is present here if the molecule is planar. But planarity would introduce considerable torsional strain because all 10 hydrogen atoms would be elipsed. Thus like cyclobutane, cyclopentane assumes a slightly bent conformation in which one or two atoms of the ring are out of the plane of the others. This would relieve the torsional strain. So the slight twisting of the carbon-carbon bonds makes the molecule non planar as shown below (Fig. 10.8).

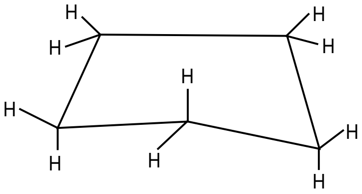
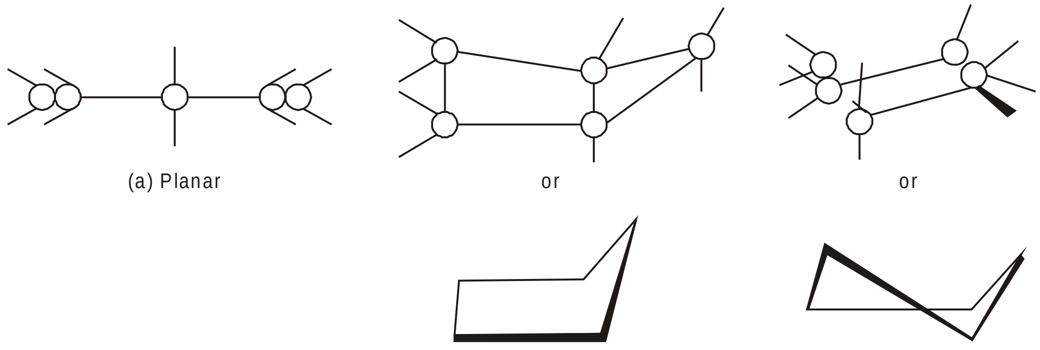


Fig. 10.8

In this structure the front carbon atom is bent upwards.

Two non-planar conformations are believed to exist for cyclopentane which is the envelope form 10.9(*b*), and half chair form 10.9(*c*).



(a) Planar or or

(b) Envelope (c) Half chair

Puckered forms

Fig. 10.9 Cyclopentane.

Thus cyclopentane molecule is flexible and shifts from one conformation to another constantly. With little torsional strain the molecule is as stable as cyclohexane.

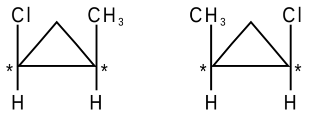
In the envelope form four carbon atoms are in one plane and the remaining one outside, while in the half chair, three are in one plane and the other two outside and the electron diffraction studies have confirmed the puckered nature of the molecule. Actually this puckering is not fixed but the individual carbon atoms move up and down at right angles to the average plane of the ring *i.e.*, no *particular* carbon atom is *always* out of the plane, but each one takes up this conformation. So the ring is in a sort of constant wave like motion. This effect was been termed *pseudo rotation* by Pitzer. Pseudo rotation occurs in cyclopentane because the potential energy barriers are very low but if one or more substituents are present in the ring, the energy barrier may become high to prevent pseudorotation.

But where the addendum is not an iodine atom and the classical carbocation is stabilised by resonance, then cis addition takes up which may later on by *rearrangement* give the trans isomer. It has also been found that the *nature of the solvent also affects the amounts of cis and trans products.*

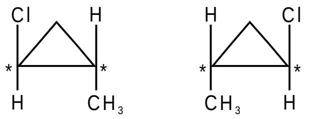
STEREOCHEMISTRY OF CYCLIC COMPOUNDS

Cyclic compounds also exist in stereoisomeric forms, *i.e.*, they may show geometrical and optical isomerism at the same time. While considering them, the saturated rings are regarded as rigid flat structures and the groups attached to the carbon atoms are regarded as being above or below the plane of the ring. For example, since it is not possible to have free rotation about the carbon-carbon single bonds of cyclopropane, geometric isomers are possible. But because the carbon atoms of the ring are tetrahedral, so the cyclic molecules may have optical isomers as well.

An example is 1-methyl-2-chlorocyclopropane which exists as a pair of geometric isomers and since each isomer has a nonsuperimposable mirror image, it has a pair of enantiomers. Thus its forms are:

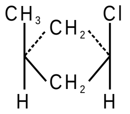


cis isomers
(pair of enantiomers)

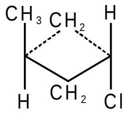


trans isomers
(pair of enantiomers)

So for a molecule with two different asymmetric carbon atoms we will have not more than four stereoisomeric forms. Similarly other cyclic molecules show a similar stereoisomerism. However, with even-numbered rings certain molecules show only geometrical isomerism as in 1-methyl-3-chlorocyclobutane.



cis isomers
(optically inactive)



trans isomers
(optically inactive)

The above example shows that geometric isomerism may occur without optical isomerism.

Classification of Monocyclic Ring Systems

Monocyclic ring systems are usually classified according to the number of carbon atoms in the ring and thus we have:

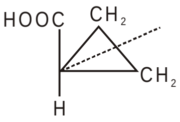
1. Small rings—which are 3 and 4 membered.
2. Common rings—5, 6 and 7 membered.
3. Medium rings—8, –11 membered.
4. Large or macro rings—12 membered and larger.

Small and common rings are jointly classed as classical rings and medium and large rings as many membered rings.

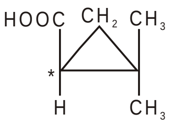
Of great interest are also the various bi and polycyclic (multiring) structures.

Cyclopropane Rings

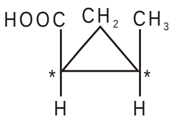
Cyclopropane is the only planar cis alicyclic compound and the three points lie in the single plane. Its monosubstituted derivative also has a plane of symmetry and the substituted carbon atom is not asymmetric. Let us take the case of cyclopropane-monocarboxylic acid. It has a plane of symmetry shown by the dotted line and hence the molecule is inactive (*xx*).



(xx)

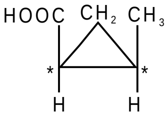


(xxi)

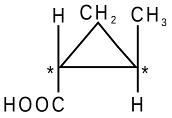


(xxii)

But if we examine 2, 2 dimethyl cyclopropane-monocarboxylic acid (*xxi*) it has no plane of symmetry. The molecule contains an asymmetric carbon atom (*) and exists in (+) and (–) forms and one racemic form. However, a non-geminally disubstituted odd-membered ring provides an interesting example. An example is 2-methyl cyclopropane monocarboxylic acid (*xxii*). It has no plane of symmetry and contains two asymmetric carbon atoms. It exhibits both geometrical and optical isomerism.



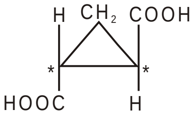
(active) cis
(xxii)



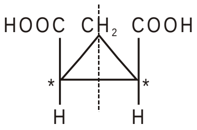
(active) trans
(xxiii)

The geometrical isomers are xxii and xxiii. The cis and trans both will exist in two optically active forms along with their one racemic modification. Therefore, the optically active forms of cis and trans will all be different and we will have two pairs of enantiomers. This is also according to the rule of 2^n optically active forms where *n* represents the number of different chiral centres.

However, when the two substitutes are same as in cyclopropane 1, 2-dicarboxylic acid (xxiv), we will again have two geometrical isomers cis and trans, but because the molecule contains two similar chiral centres (*), we will have (+) and (–) forms coming from the trans only along with its racemic variety. The cis form, having a (vertical) plane of symmetry will represent the mesovariety. Therefore, the condition is the same as in tartaric acid.



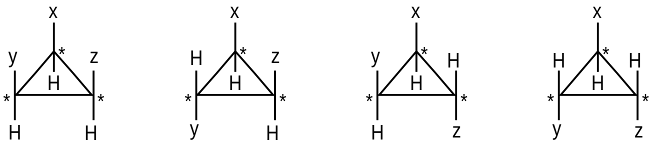
(xxiv) (a)
trans
(will exist as (+) and (–)
and a racemic form)



(xxiv) (b)
cis
meso (inactive)

So with two similar substituents put in vicinal positions in cyclopropane, there will be a (+), a (–), a dl mixture and a meso variety. The configurations of xxiv (*a*) must be specified by R and S. It is not true for xxiv (*b*). It is sufficient to say that it is meso.

Now, let us examine the case where all three carbon atoms of cyclopropane become asymmetric and satisfied by different groups. In such a case because the molecule contains three different chiral centres, therefore, there will be $2^3 = 8$ optically active forms (four pairs of enantiomers) and there will be four geometrical isomers. The different forms are (xxv) *a*–*d*).

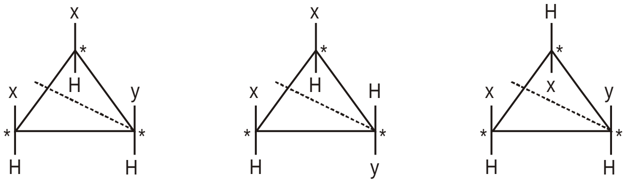


(a) (b) (c) (d)

(xxv)

Since all of them do not have any plane of symmetry, all will exist in their (+) and (–) forms.

If, of the three asymmetric carbon atoms, two are similar, then there will be three geometrical isomers (*xxvi a–c*).

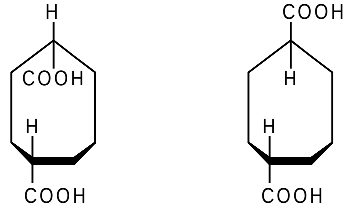


(a) (b) (c)

(xxvi)

Of these *a* and *b* have a (vertical) plane of symmetry shown by dotted line and therefore they represent the meso variety. Only *c* does not have a plane of symmetry and this will exist as (+) and (–) along with its racemic variety.

Similar considerations apply to all odd-membered rings, no matter whether the substitutes are 1, 2, 1:3, 1:4 or in any other position relative to each other. It can be illustrated by taking the example of cycloheptane 1, 4-dicarboxylic acid, the ring of which is not planar. The cis form is meso while the trans exists in (+) and (–) forms along with its dl form.



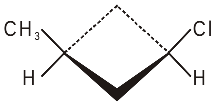
cis (meso) trans

Fig. 10.10. Stereoisomers of cycloheptane 1, 4-dicarboxylic acid

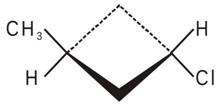
Cyclobutane Rings

With even-membered rings certain molecules show only geometric isomerism. Examples are afforded by 1, 3 disubstituted cyclobutanes.

1 methyl-3-chlorocyclobutane shows only geometric isomerism and its cis and trans forms are:



cis
(Optically inactive)



trans
(Optically inactive)

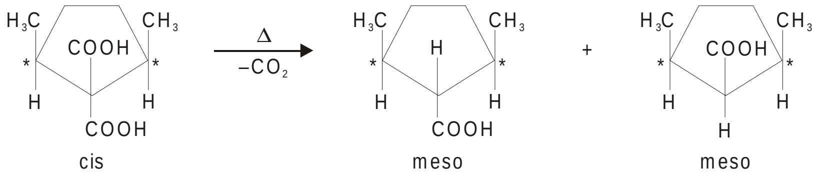
They are not the optical isomers. If two similar substituent are present in 1, 3 positions, then still we will have only geometrical but not the optical isomers as in cyclobutanes 1, 3-dicarboxylic acid.

cis trans

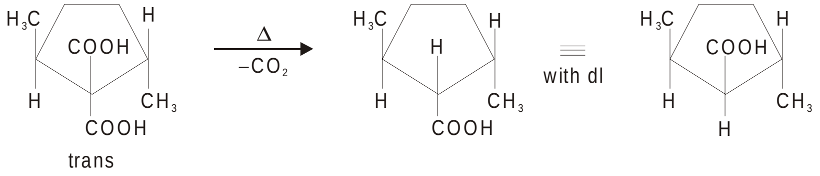
Fig. 10.11 Inactive 1, 3-cyclobutane dicarboxylic acid

Cyclopentane Rings

A number of examples involving the stereochemistry of five membered rings are met in furanose sugars. An interesting example is that of 2, 5 dimethylcyclopentane 1, 1 dicarboxylic acid. This acid can exist in two geometrically isomeric forms which can be distinguished by decarboxylation. The cis xxvii isomer forms two monocarboxylic acids which are meso because they possess a vertical plane of symmetry. The trans isomer xxviii forms only one monocarboxylic acid and since it possesses no elements of symmetry, therefore, exists in optically active forms and a meso variety.



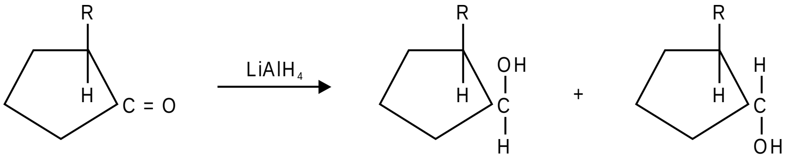
(xxvii)



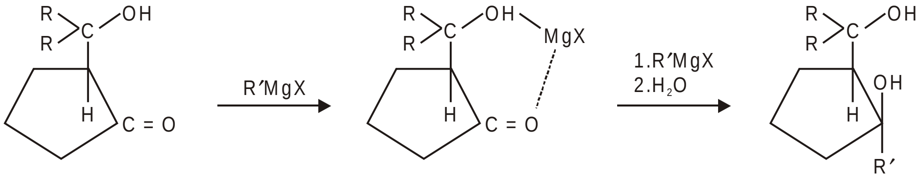
(xxviii)

Further it is to be noted that all the three acids from the cis contain two asymmetric carbon atoms.

However, the reactions of monosubstituted cyclopentanone sometimes becomes so much stereodirected that a mixture of cis and trans isomers is obtained. For example the reduction of 2-alkyl cyclopentanone by $LiAlH_4$ gives a mixture of cis-trans isomeric alkyl cyclopentanols.



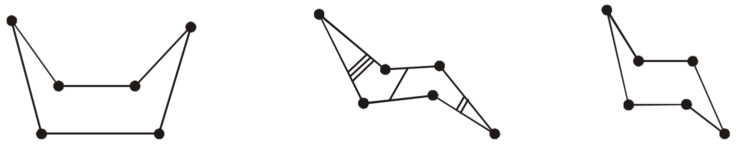
But high stereospecificity is observed when the substituent contains a hydroxyl group.



Owing to chelation the radical approaches from the side opposite to the substituent and the reaction becomes completely stereospecific.

Cyclohexane Rings

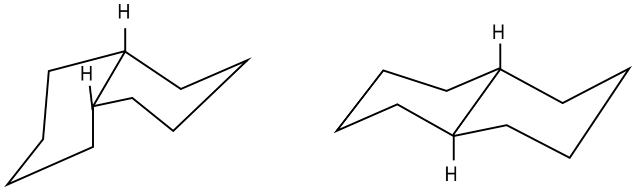
Generally six-membered rings are more stable than five-membered ones and on the basis of the tetrahedral theory Sachse in 1890 pointed out that cyclohexane could exist in two forms known as *boat* and *chair conformations* and neither of which is planar. They are actually puckered *i.e.,* non-planar and are free of angle strain and so are called strainless rings.



Boat form

Chair form

Since the theory of strainless ring put forward by Sachse required the existence of two isomeric forms and since all attempts to find them had failed the theory was not given much importance till 1918 when Mohr explained the absence of the two forms because of their rapid interconversion. This rapid interconversion can be beautifully illustrated on models where no considerable effort will be needed. Mohr also pointed out that the union of two cyclohexane rings may result in the formation of cis and trans decalins.



cis-decalin

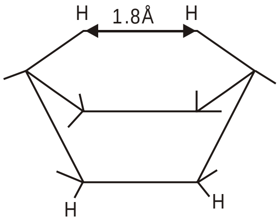
trans-decalin

Both the isomers are formed by the union of the rings in the chair forms.

The energy barrier between the chair and boat form of cyclohexane is about 35 k J/mole and this is not large enough to prevent their rapid interconversion at room temperature. This is why it is not possible to isolate each conformation.

The chair and boat forms are both free from angle strain, but while there is no bond opposition (eclipsing) strain in the chair form and due to which its potential energy is at a minimum, there is bond opposition strain (of the type found in the eclipsed form of ethane) in the boat form and due to which its potential energy becomes high. This accounts for the energy difference in the two forms and also ensures that the two conformations are discrete entities. But the difference is not high enough to prevent their rapid interconversion at room temperature and to make their isolation easy.

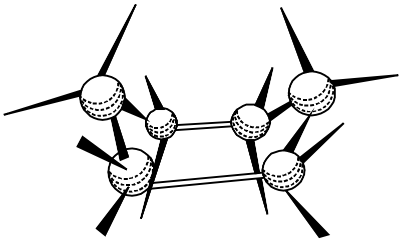
Apart from these considerations, there is also repulsion of the pair of hydrogen atoms that are at the top of the boat.



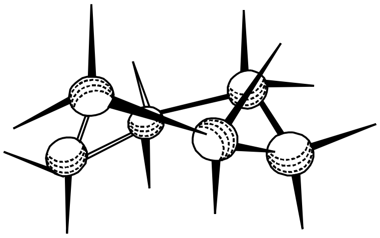
The distance between their centres at normal tetrahedral angles should have been only about 1.8 Å, but the sum of the van der Waals radii of the two hydrogen atoms is 2.4Å. This is sometimes called “bowsprit-flagpole interaction’ and this too makes its contribution to the increased energy of the boat form.

As a result of these unfavourable interactions, *i.e.,* opposition to bond strain (*i.e.,* between the pair of hydrogens shown at the bottom) and also due to bowsprit interaction, the potential energy of the boat form becomes high and this is why the boat conformation is not the preferred one. Hassel in 1947 established by means of electron diffraction studies that cyclohexane exists predominantly in the chair form. This has also been confirmed by electron diffraction studies and results obtained from Raman and I.R. spectra. Calculations made on the basis of entropy show that only about one molecule in a thousand will be in the boat form.

While considering the conformation of the cyclohexane ring one has to note that the boat form while it is flexible, but in distorting the model one obtains forms in which both the bowsprit flagpole interaction and the bond opposition strain due to eclipsing of the adjacent hydrogen atoms are alleviated. These forms are called “*skew-boat*” or “*twist boat*” forms and have lower energy than the boat forms. The flexing causes the twist conformation to have lower energy than the boat conformation. But this is not sufficient to cause the twisted form to be more stable than the chair form.



Boat



Skew boat

The potential energy values of the various forms is shown in Fig. 10.12.

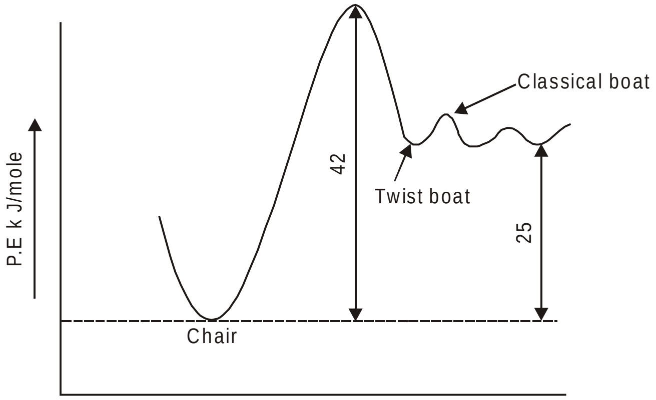


Fig. 10.12 Potential energy of cyclohexane as a function of conformation.

The potential barrier that separates the chair and boat forms from one another is 42 k J/mole while the energy difference between the two conformations is 21-25 k J/mole.

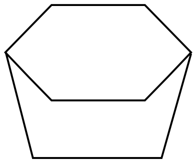
The various energy characteristics given apply to unsubstituted cyclohexane ring, the pressure of substituents can change the energy relations between the conformations and may even render the boat conformation more preferred, but the number of such examples is small.

The potential barrier that separates the chair and boat forms from one another is 42 kJ/mole while the energy difference between the two conformations is 21-25 kJ/mole.

The various energy characteristics given apply to unsubstituted cyclohexane ring, the presence of substituents can change the energy relations between the conformations and may even render the boat conformation more preferred, but the number of such examples is small.

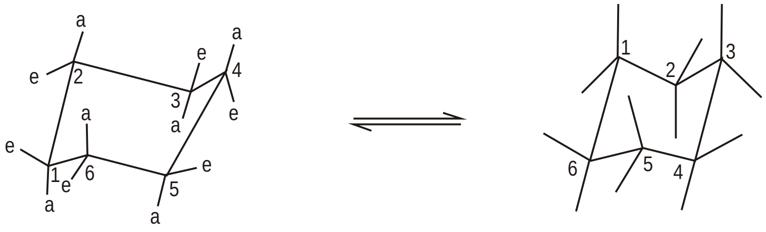
The true boat actually lies at the energy maximum between two skew-boats and has been found to be 1.6 kcal/mole less stable than the latter.

An example of a compound having a preferred boat conformation is that of [2.2.2] bicyclooctane. This compound must necessarily exist as a boat because its cis-4 hydroxy cyclohexane-carboxylic acid easily forms lactose and the water elimination must proceed through the boat conformation. The trans isomer will not lactonize.



[2.2.2] Bicyclooctane

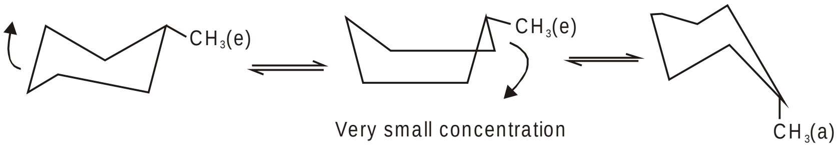
In chair form of cyclohexane ring, there are two possible kinds of bonds, those pointing up and down are called axial and those pointing sideways are called equatorial. Since they are commonly represented by letters *a* or *e*, this is why the substituents attached to these bonds are called axial or equatorial substituents respectively.



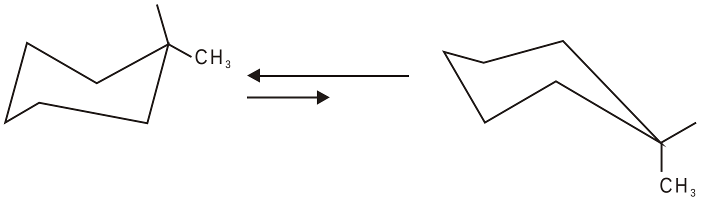
During change in conformation, the ‘raised’ carbon atoms are lowered and the ‘lowered’ ones are raised and at the same time the axial bonds become equatorial and vice-versa. This transformation is called interconversion as shown above.

Monosubstituted Cyclohexanes

Since in chair form, the bonds are axial or equatorial, therefore monosubstituted cyclohexane exists in two isomeric forms-the axial or equatorial. So while considering a reaction with a monosubstituted cyclohexane, one must consider the reaction of both the species, just as while writing the reactions of acetoacetic ester we take into account its reactions with the keto or enol forms. Thus an equatorially substituted chair readily changes into a boat form and this in turn changes into another chair in which the substituent now is axial.



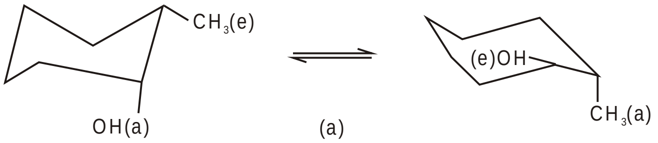
In general in such transformations, the equatorially oriented substituent is energetically more favourable and it can be represented as follows:



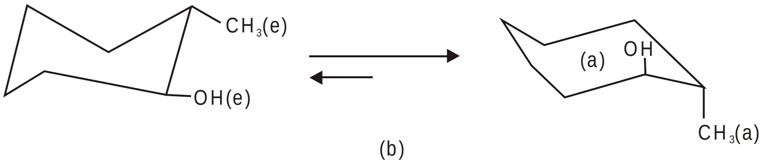
Such interconversions with monosubstituted cyclohexanes and also with disubstituted ones do not involve any "rearrangement" *i.e.*, no chemical bonds are broken nor reformed, only their conformation changes and this has been confirmed by NMR studies e.g., methyl cyclohexane at –110°C gives separate signals for equatorially or axially oriented methyl groups.

Disubstituted Cyclohexanes

Depending on the orientation of substituents, the disubstituted cyclohexanes can be either equatorial-axial or diequatorial. This is illustrated with 2-methyl cyclohexanol. It exists in two stereoisomeric forms and each of which has two conformations which are readily interconvertible.



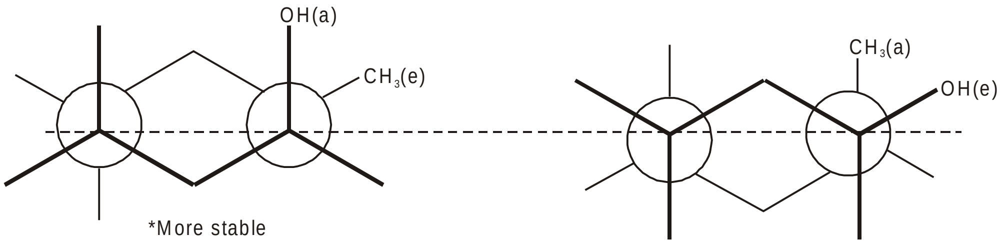
(a)



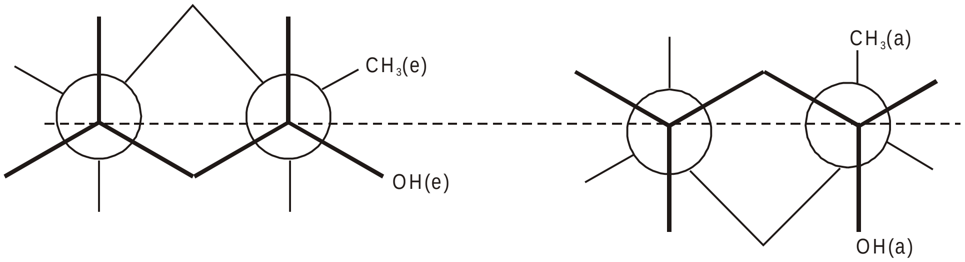
(b)

Writing the above (*a*) and (*b*) forms in Newman projection formula, the picture will be as follows:

(a) (cis)



(b) (trans)



The dotted line divides the projection into an upper and a lower half. The isomers in which the substituents are on the same side of the dotted line are cis while those in which they are on the opposite side are trans. Both the isomers *a* and *b*, sine they have no plane of symmetry, they can be resolved into their optical antipodes.

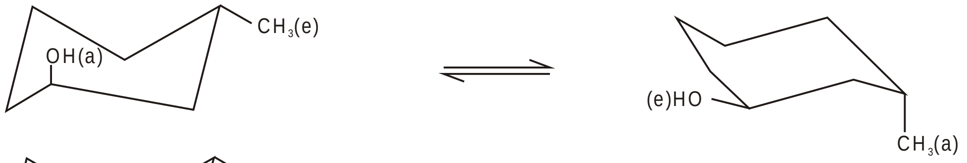
If however, the two substituents are identical, the chance of the formation of optical antipodes becomes reduced. Of the isomers the conformation with lower energy will be that in which the larger group is equatorial. In the above cis-2-methyl cyclohexanol, since the methyl group is larger than the hydroxyl and therefore the preferred form will be 1 a—hydroxyl 2e methyl Ẋ· isomer and the greater the difference in size between the two substituents, the greater will be the predominance of the form with the larger group in equatorial position.

Whether the two substituents are identical or not, but if both are present in equatorial position, the ee form will be the preferred one. This form will be more stable than the cis isomer (*a*, *e* form) and this has also been established in the above example. The cis is readily converted into the trans on heating with sodium.

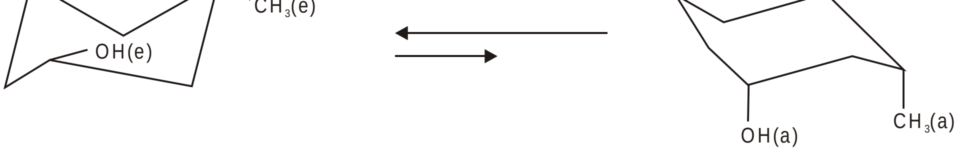
Disubstituted Cyclohexanes with Substituents in 1-3 Positions

Let us again take the case of methyl cyclohexanol, but with substituents in 1, 3 positions. Two stereoisomers of this compound are known.

(c)



(d)



With identical substituents, the cis e, e is more stable than cis a, a or trans e, a and so cis 1, 3 e, e is the most stable one.

So 1, 3 isomer exists in diastreoisomeric cis and trans forms and both may be equatorial or both axial.

CONFORMATIONAL ENERGIES OF SUBSTITUENTS

We have seen that equatorial conformation of substituents is more preferred than the axial conformation. The energy difference between molecules with substituents in the equatorial and axial positions is called conformational energy. This energy depends on the nature of substituents and the greater the difference, the greater is the chance of substituents occupying the axial position.

The conformational free energies of some substituents in substituted cyclohexanes is given in the following table:

Table 10.2 (From book Topics in Stereochemistry by J. Hirsch, Interscience Publishers, New York) Conformational free energies of substituents in substituted cyclohexanes.

Substituent	*ΔG kJ/mole*
CH_3	7.1
C_2H_5	7.3
C_6H_5	13.0
Cl, Br, I	1.7
OH, in an aprotic solvent	2.2
In a protic solvent	3.7
$–OCH_3$	2.5
$–OC_2H_5$	3.8
COOH	5.7
NO_2	4.6

It is significant that the conformational energy does not simply depend on the size of the substituent, it also depends on the volume. Let us see the OH group and that where hydrogen of the OH is replaced by other groups e.g., $–OCH_3$, OC_2H_5. There is not much difference. It remains practically constant. This happens because the key atom is that attached with the ring (oxygen) remains the same in all cases. It also depends upon the electric charge, the negative charge considerably increases the conformational energy, as in carboxyl and phenyl group.

Physical Properties of Substituted Cyclohexanes

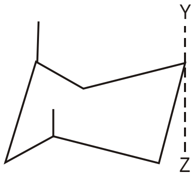
The relationship between certain physical properties and conformation was first given by Von Auwers and A. Skita and is generally known as **Auwers-Skita rule or conformational rule**. Since the rule was first given in 1920 by Auwers and in 1923 by Skita, it has undergone many modifications by Allinger 1957 (J.Amer. Chem. Soc., 79, 3443, 1957) and Wepster in 1961. It states that among alicyclic epimers not differing in dipole moment, the isomer of highest heat content (enthalpy) has higher density, higher refractive index and higher boiling point.

CONFORMATION AND CHEMICAL REACTIVITY

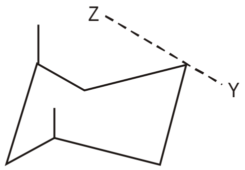
Compounds with axial and equatorial orientation of substitutents not only differ in physical properties but in reactivity as well, because the rates of formation of equatorial and axial isomers and rates of substituion and elimination reactions are different.

The relationship between conformation and chemical reactivity was first pointed out by D.H.R. Barton in 1950. In a paper he drew attention to the difference in chemical behavior when substituents were placed in equatorial and axial properties in cyclohexanes. This will become clear from some of the following examples:

We know that in S_N^2 reactions the attacking group approaches from the rear. Therefore if the geometry of the molecule in such that it hinders the approach of the attacking group(z) along the line remote from the group to be expelled (Y), then S_N^2 reaction will be slowed down. In the following conformations, it is clear that the transition state for the S_N^2 reactions will be formed more readily when Y is axial (I) than when it is equatorial (II).



(I)



(II)

In (I) the approach of Z is unhindered, but in II it is hindered by the rest of the ring. So S_N^2 reaction will occur more readily when the substituent is axial than when it is equatorial.

The study of S_N^1 reaction in cyclohexane becomes difficult because of the ease with which the elimination reactions occur at the same time. However it has been shown that S_N^1 reaction will be sterically accelerated for an axial substituent, because the formation of carbocation will relieve the steric strain due to 1, 3 interactions which is absent with equatorial substituent.

The concept of internal strain (1 strain) has also been employed to explain some reactions.

Changes in I strain bring about changes in the hybridization of the carbon atom during the reaction. Thus in the reduction of the ketones the trigonal sp^2 hybridized carbon changes to tetrahedral carbon atom.

$$>C=O \xrightarrow{NaBH_4} >CHOH$$

Depending on the nature of ketone, the reaction proceeds at different rates as shown.

	Relative rate
Aliphatic ketone	1
Cyclobutanone	581
Cyclopentanone	154
Cyclohexanone	355

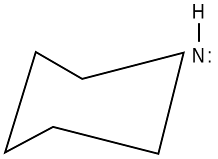
Barton put forward the following ideas on the reduction of alkyl cycloalkanones on the basis of conformation.

1. Catalytic hydrogenation in neutral medium gives an axial alcohol from sterically hindered ketone and an equatorial alcohol from sterically unhindered ketones.
2. Catalytic hydrogenation in acid medium gives predominantly an axial alcohol.
3. Reduction with $LiAlH_4$ proceeds according to rule 1.

4. Reduction with $Al(OP^i_r)_3$ gives also axial alcohol.
5. Reduction with sodium gives an equatorial isomer.

SIX-MEMBERED HETEROCYCLIC RINGS

Because of the similarity of bond lengths and bond angles, the stereochemistry of six membered rings containing nitrogen and oxygen is similar to that of cyclohexane. The bond lengths C–C, C–N and C–O are almost same and so also the bond angles C–C–C, C–N–C and C–P–C. This fact has thrown light on the stereochemistry of nitrogen containing alkaloid like piperidine and others. On this basis the hydrogen atom attached to piperidine is axial.



Piperidine X = CH_2

Medium Rings

Three types of studies have been employed to establish the conformation of rings larger than six carbon atoms. These are

1. Studies based on physical measurements. These include X-ray analysis, infrared analysis and measurement of dipole moments.
2. Calculations of torsional potential functions, and
3. Chemical studies

The infrared studies have shown that the conformation in such cycloalkanes is little temperature dependent and so these molecules have a fixed conformation. While common and large rings differ little in chemical behaviour, the medium rings have specific features that are not found in other class of organic compounds. The medium rings (8-10C) are characterized by high energy content as shown by the following Fig. (10.13) of energy diagrams.

From the Fig. (10.13) it is seen that compounds with 8-11 carbon atoms have increased energy content. The reason for this is formation of intramolecular overcrowding of atoms and consequent production of strain due to non bonded atoms, also called Prelog strain. It increases the energy of the system.

Another interesting feature of such rings is that there is no definite conformational relationship between the cis and trans configurations. The reason is that we have a large number of degrees of freedom in such rings and they become more similar to open chains. So the cis substituents can be so rotated on adjacent carbons that they become trans to each other.

Let us take the case of an eight membered ring, the cyclooctane.

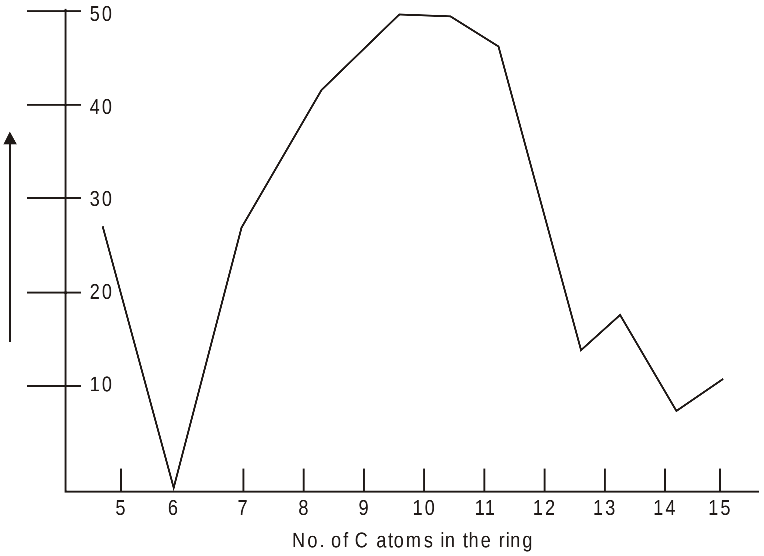
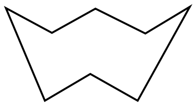


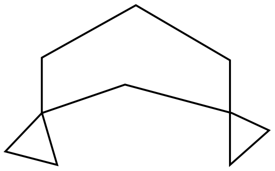
Fig. 10.13 Enthalpy of cyclic compounds as a function of the number of carbon atoms in the ring.

Cyclooctane

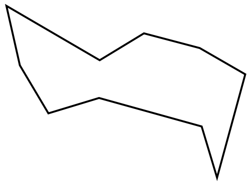
At one time it was believed that cyclooctane occurs in the extended crown form and the saddle conformation as shown below but on the basis of calculations of minimum energy strain, Hendrickson (1964) and Wiberg (1965) suggested that neither of the above two forms is the correct picture. R. Srinivasav and T. Srikrishnan (Tetrahedron 27, 5, 1009-1012, 1971) showed that the molecule exists as the boat-chair form in a number of crystalline derivatives.



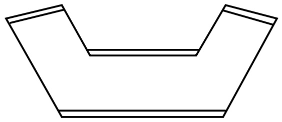
Extended
crown form



Saddle form



Boat-chair
form



Cyclooctateraene
tub form

Similar conformation is believed to exist for cycloheptane. Another eight remembered ring, cyclooctatetraene exists in the tub form as shown.

Cyclononane

The conformations of cyclononane are combinations of chair and twist-boat forms as follows:

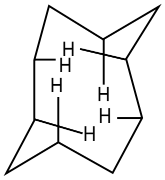
Cyclononane

Cyclodecane

Cyclodecane molecule is a typical representative of the medium ring. While in cyclohexane all carbon atoms are equivalent, in cyclodecane we have three types of carbon atoms and hydrogen atoms occupy six different positions unlike cyclohexane where we have only two positions, axial and equatorial.

In medium size rings some of the bonds of the carbon atoms are directed **into the ring**. Such bonds and therefore the substituents attached to them are called **intra-annular bonds** and the bonds going outside the ring and therefore the sustituents attached to them are called **extraannular** or **peripheral**.

X-ray analysis has shown that cyclodecane in its most preferred conformation exists as shown below in which the two chain forms of cyclohexane are joined by 1,3 axial bonds and six hydrogen atoms are intraannular and 14 peripheral.



Cyclodecane

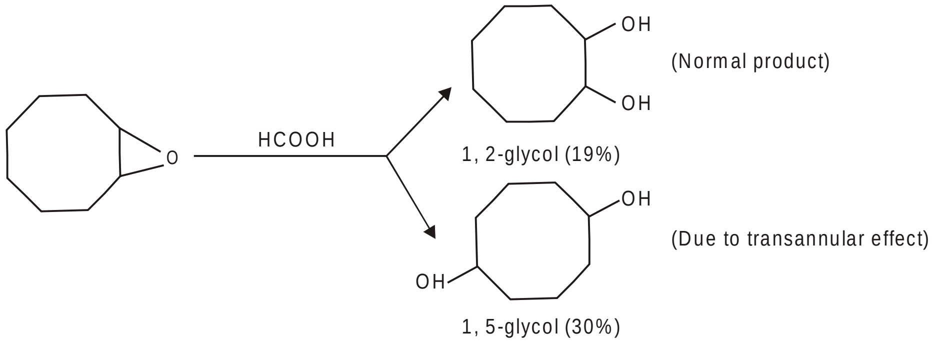
Therefore the CH_2 groups in cyclodecane are stereochemically non equivalent. There are CH_2 groups in which both the hydrogen atoms are peripheral, there are those in which one hydrogen is peripheral and the other is intraannular. The last two types differ from each other in that in one case the peripheral hydrogen is equatorial and in other axial.

Due to these more complicated conformations the medium rings are so different from the large rings in many physical and chemical properties. This has been explained on the basis of bond opposition strain, angle strain and steric strain and so on. Since the intraannular hydrogen atoms are arranged in two layers (the upper and lower), they cause intramolecular overcrowding of hydrogen atoms and this is also responsible for the increased energy of cyclodecane. Reactions taking place with hydrogen atoms on **opposite sides** of the ring are called **transannular interaction** and it also produces **transannular strain**. The net result is that they all increase the energy of the system.

Substituents larger than hydrogen atoms cannot generally occupy intraannular positions. We have seen about transannular reactions which are special distinctive feature of medium-sized rings. The transannular reactions do not occur at the carbon atom of the chain and they also do not involve the neighbouring atoms. They take place between atoms on opposite sides of the ring.

Transannular reactions have also been described in cyclooctane series. For example, cyclooctane oxide combines with formic acid to form two glycols by such reaction.

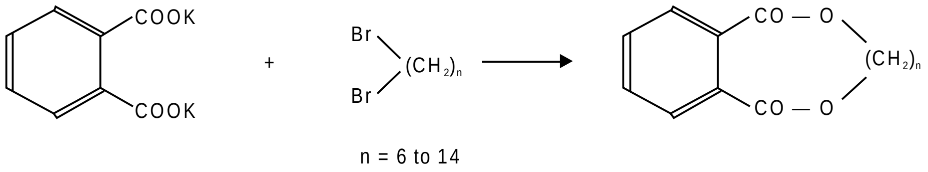
Another characteristic feature of such transannular reactions is their stereospecificity. Thus if the starting material is a certain spatial stereoisomer, the product will also be a certain stereoisomer and not a mixture of isomers. This is because of the spatial form of the ring.



Large Rings

Alicyclic ring compounds having carbon atoms greater than 12 are highly flexible. They do not have cis-trans forms because they have nearly free rotation along C-C bonds. It is generally believed such compounds exist as extended rectangles with zig-zag conformations. Their square form is less preferred because no intramolecular close packing is possible in it.

Their structural feature plays an important part in their synthesis. The approach of the two ends of a long aliphatic chain is impossible. But if the fragments are suitably oriented, then large ring can be synthesized.



Concept of I-strain

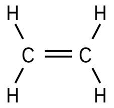
We have already seen about the I-strain (internal strain) in medium rings. It will be interesting to mention here that the reactions of medium rings are either faster or slower than other ring systems, e.g., the rate of hydrolysis of medium ring chlorides is faster but the reducion of medium ring ketones by $NaBH_4$ is slower. Such differences can be explained in terms of total ring strain, called I-strain in them. They are caused by many factors, like steric repulsion, bond opposition forces, and angle deformation and so on. But the difficulty is that we cannot quantitatively measure such forces.

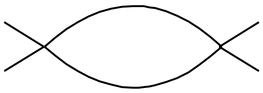
Changes in I-strain may be considered in terms of changes in hybridization from Sp^2 to Sp^3 or arise vice versa. If the change from Sp^2 to Sp^3 is accompanied by an increase in I-strain, the reaction would be hindered and those from Sp^3 to Sp^2 would be facilitated.

Baeyer's Strain Theory

While correlating the stability of the ring with their size Adolf von Baeyer advanced in 1885 his famous strain theory. We know that the four valencies of a carbon atom go to the four corners of a regular tetrahedron with carbon atom as the center and the angle between any two bonds is 109°28'. Baeyer postulated that if this angle is varied in the formation of a certain compound, a strain is set up in the resulting molecule and the greater the variation from the normal angle, the greater is the strain. When two carbon atoms are joined by a single bond, the normal angle of 109°28' is maintained and hence no strain is set up.

But union between two carbon atoms by a double bond, as in ethylene results in considerable displacement of valency bonds, which become parallel and therefore the bond angle is reduced to zero.

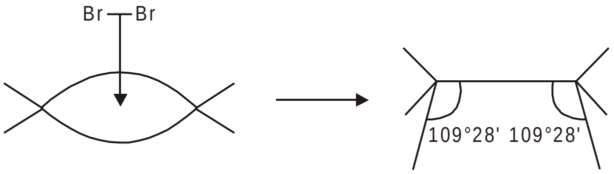




The angle through which each bond has been displaced is now therefore

$$\frac{109°\,28'-0}{2} = 54°44'$$

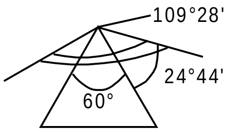
The factor half shows that the strain is spread over two bonds. This means that in the formation of double bond, there is a very heavy strain in the molecule and this will be relieved when C=C bond is converted into C-C bond. This is why the olefines have a strong tendency to open up and form addition products, when the normal angle will be restored and the molecule will be free of strain.



In ring compounds also, the 4C valencies are not in their normal state. The amount of distortion produced in different cases can be calculated as follows:

In a 3-membered ring, as in cyclopropane, the 3C atoms may be considered at the three corners of an equilateral triangle and the distortion will be

$$\frac{109°\,28'-60}{2} = 24°44'$$



Evidently the strain in cyclopropane is less than in ethylene and hence it is comparatively more stable.

In a four-membered ring, the four carbon atoms are at the corners of a rectangle and the angle of strain is

$$\frac{109°\,28'-90°}{2} = 9°44'$$

In a similar manner, the strains in 5, 6, 7 and 8 membered rings would be

5-membered $$\frac{109°28'-108°}{2} = 44'$$

6-membered $$\frac{109°28'-12°}{2} = -5°16'$$

7-membered $$\frac{109°28'-128°34}{2} = -9°33'$$

8-membered $$\frac{109°28'-135}{2} = -12°48'$$

A positive angle of strain means that the bonds are bent inwards while a negative sign shows that the bonds are bent outwards. But in either case the magnitude of the angle and not its sign measures the strain in the molecule. Therefore we find that the strain in the ring decreases upto 5-carbon atoms and again begins to increase thereafter. The double bond is under maximum strain. These conclusions arrived at by Baeyer are in agreement with the fact that cyclopentane in which the strain is minimum is the most stable of all cycloparaffins and has the least tendency to open up to form addition products. Ethylene in which the strain is maximum is the least stable and forms addition products most readily.

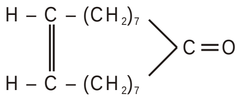
The strain theory agrees reasonably well with small ring compounds containing six or less carbon atoms, e.g.,

1. it beautifully explains the easy formation of cyclic anhydrides from 1:4 and 1:5 dicarboxylic acids and why
2. only γ and δ hydroxy acids readily form lactones. But the theory has been found to be insufficient in several ways.

Limitations of the Strain Theory

Some of the limitations of the theory are:

1. According to the theory a heavy strain is involved in the formation of a double bond. Therefore such compounds should be difficult to be prepared. The results are however contradictory. **In fact the double bond is formed so easily that there is little evidence for a heavy strain.**
2. Baeyer had the idea that the rings were planar and so rings of 10 to 30 C atoms would have low stability. But now we know that the rings need not be planar. They would be puckered and would retain the natural valence angle and be free from strain. **Therefore the strain theory does not apply to rings of six-members and larger.** Cyclohexane, as we have seen is completely strain-free in its chair form. Compounds like civetone, a musk base of perfumery and consisting of 17 C atoms should be difficult to prepare in the laboratory, but once obtained has the same degree of stabilizing as most other organic compounds.



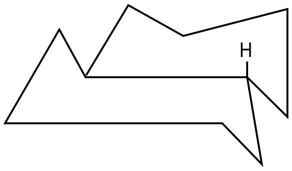
Civetone

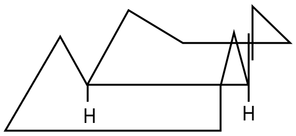
3. When four identical groups are attached to a carbon atom, the four carbon valencies are equivalent and the valency angle is 109°28'. But when the groups are different, the valencies are no longer equivalent but point towards the four corners of an **irregular** tetrahedron. If the configuration of cyclopropane were an equilateral triangle, the four valency angle of each carbon atom would be 60°. But this value is impossible and it can be never less than 90°. Further calculations made by Coulson (1949) have shown that the smallest carbon valency angle is 104°. This results in a loss of overlap of *p* orbitals and produces a state of 'strain' due to bent bonds.
4. Finally Baeyer's theory is based on a mechanical concept of valency and served its purpose in stimulating research in the field of cyclic compounds. Now we have the electronic theory and the reactivity of olefines has been attributed to the π electrons and not on the basis of strains.

   Therefore the concept of puckered rings was introduced and the existence of boat and chair forms in cyclohexane.

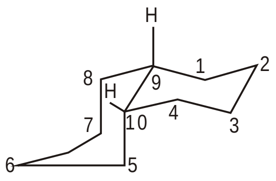
Fused Ring System

Among the fused ring systems, the most important compound is decalin. This compound exists as the cis and trans forms and the existence of these two forms on the basis of non-planar structures was predicted by Mohr. He thought that the two decalins were formed by the fusion of two chair forms or two boat forms of cyclohexane and so he assigned, the following structures.

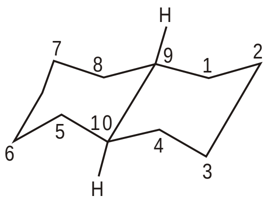




Later it was proved that the two isomers were built of rings in the chair form as follows and Huckel actually isolated the two forms.



cis-Decatin

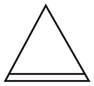


trans-Decatin

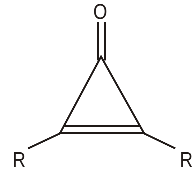
The trans-decation has a center of symmetry, midway between C_9 and C_{10} and is therefore an optically inactive molecule. The cis-decation is dissymmetric and has two interconvertible conformations, but the trans-decalin is a rigid molecule.

Therefore summarizing the stability of rings depends on a number of factors.

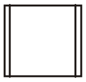
1. **Ring Size.** The stability of rings has been correlated with its size and the greater the ease of ring closure, the greater is the stability and the probability of ring closure decreases with the increasing size of the ring. The ring closure depends on two facts:
   (*i*) The ease of having the ends meeting and
   (*ii*) The strain factor which becomes more favourable to closure as the ring size increases from 3 to 6 and then again becomes less favourable upto 9 members and then again becomes more favourable to larger rings.
2. **Nature of Ring.** So far we have studied the stability of saturated alicyclic rings, but interesting results, though not systematic and uniform have been obtained by introducing heteroatoms, phenyl rings or unsaturation in such compounds. Some of the compounds thus synthesized are:



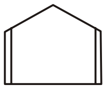
Cyclopropene
(i)



R = C_6H_5 or $C_3H_7^n$
(ii)



Cyclobutadiene
(iii)



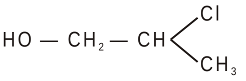
Cyclopentadiene
(iv)

Cyclopropene and a number of its derivatives have been synthesized, although this is a highly strained compound. Simply because we cannot synthesize a compound, we should not conclude that it would be highly strained and too unstable to exist. The compound cyclopropenone derivative would be too highly strained to exist but it is stabilized by having aromatic rings. The next compound cyclobutadiene is too unstable to be isolated. It has been isolated as a silver nitrate complex. Greater stability has been noticed in cyclopentadiene although this forms a dimer on standing.

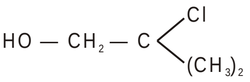
3. **Nature and Degree of Substitution in the Ring.** Little is known about the effect of introducing hetero atoms into the ring and the ease of ring closure. Ring closure with *w*-bromoalkylamines $Br(CH_2)_nNH_2$ is extremely slow for n = 9 or 11.

The alkyl groups generally favour ring closure, atleast in small and common rings as will be clear from epoxide formation from chlorohydrins in basic medium; as illustrated below:

$HO—CH_2—CH_2—Cl$ 1



$HO—CH_2—CH(Cl)(CH_3)$ 5



$HO—CH_2—C(Cl)(CH_3)_2$ 248

CHAPTER

11

Some Novel Reactions in Organosilicon Chemistry

Although carbon and silicon both belong to the same group of periodic table, the group IV, also called the group of bridge elements, the differences between the two are so wide that silicon chemistry is being given an altogether separate treatment different from the carbon chemistry. Just as carbon is the main element of organic chemistry, the element silicon has been rightly called the central atom of the inorganic world.

The difference in the properties of the silicon atom from that of the carbon is because of its comparatively bigger size, less electronegative nature and the presence of the available vacant *d* orbitals.

The elemental silicon itself has attracted great attention during the recent years because in its 99.9% purity it is very effective in absorbing solar energy and hence it has proved of tremendous applications in the manufacture of solar batteries and semi conductors. Once the solar batteries have trapped the solar energies, it an be transformed into electrical energy and so it is going to solve the energy problem of the country. Moreover, the production of this type of energy will rid the country of the pollution problem besides saving the exchequer spent on the purchase of various liquid fuels.

During the last three decades, a number of organosilicon compounds have been prepared which have opened new vistas in the synthesis of numerous organic compounds and have brought to light many fascinating reactions.

EXPEDITED ORGANIC SYNTHESIS WITH ORGANOSILICON COMPOUNDS

Designed synthesis of organic compounds whether in the pharmaceutical, macromolecular, biological or pure chemical field is an art as well as a science. Of all branches of chemistry, synthesis is today the most vibrant with new techniques and methodologies and is most rapidly developing. The techniques used a decade ago have become outmoded today.

One such technique is the use of organosilicon compounds which besides shortening multistep syntheses, gives improved yields and facilitates the isolation and purification of the product.

The wide spectrum of Organosilicon Reagents now available can be used to:

(*a*) form bonds which were not possible till recently.

(*b*) shield functional groups from undesired reactions *i.e.*, in the protection of groups.

(*c*) to increase the rate of bond-forming reactions *i.e.*, to activate certain reactions and finally.

(*d*) to exclude the less favoured modes *i.e.*, in the direction of a certain reaction.

Some of the basic principles differentiating the silicon chemistry from the carbon chemistry are:

(*a*) Nucleophilic substitution at silicon is easier than substitution at carbon.

(*b*) The corresponding bond energies of Si–O, Si–Cl and Si–F are larger than C–O, C–Cl or C–F.

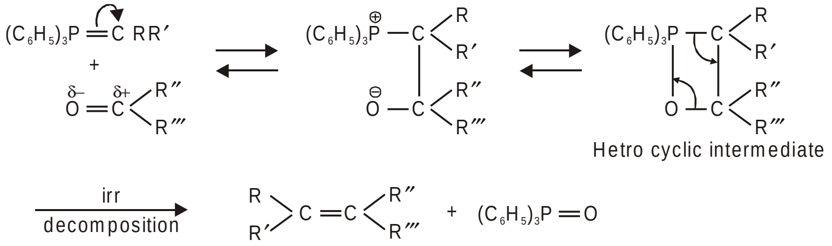
(*c*) The rates of nucleophilic substitution at silicon are comparable to those of deprotonation, *i.e.*, base will attack Me_3Si as readily or more readily, as H.

(*d*) If the bond is polarized in the direction $Si^{\oplus}$ and $H^{\ominus}$ then addition to olefines takes place in anti Markownikeff's fashion under a variety of catalysts.

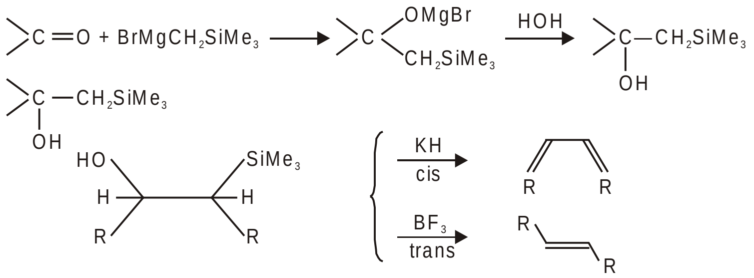
CREATION OF A BOND

One of the earliest synthetic uses of organosilicon reagents was the silicon equivalent of writing reaction called Peterson Reaction.

The Wittig reaction consists in the replacement of carbonyl oxygen of aldehydes and ketones by a methylene group with the aid of phosphine-methylenes resulting in the formation of cis or trans olefines. The reaction proceeds through the nucleophilic addition of Wittig reagent (phosphine methylene) across the > C = O bond and formation of an intermediate cyclic.



The Peterson reaction utilizes a metal derivative of chloromethyltrimethylsilane and the yields are better than the Wittig reaction. The intermediate β-hydroxysilanes can undergo either cis or trans elimination depending on reagent choice.



Significantly, trimethylsilyl azide is an excellent substitute for hydrazoic acid in many reactions– such as curtius rearrangement of acid chlorides to isocyanates which proceeds with Me_3SiN_3 in one pot process and in higher yields.

$$RCOCl + Me_3SiN_3 \longrightarrow RNCO + N_2 + Me_3SiCl$$
$$R = CF_3–, EtO_2C – CH_2 – CH_2 – etc.$$

Trimethylsilyl azide is also a specific for conversion of maleic anhydrides to the biologically active oxazinedione ring systems.

PROTECTION OF GROUPS

The concept of the protecting group to shield a sensitive function while synthetic operations take place at another molecular site is an age old technique. Several silanes: trimethylchloro (Me_3SiCl), triethylchloro (Et_3SiCl), phenyldimethylchloro (Ph Me_2SiCl) and ter butyldimethylchloro (Bu^+ Me_2SiCl) have found numerous applications in protecting O–H, N–H, C≡CH and SH bonds. This protecting function can be utilized in both reagents as well as substrates.

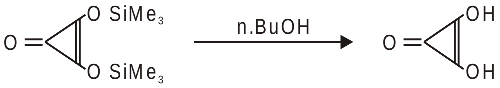
The advantages of silicon protection are: (1) Easy preparation (2) Stability, and (3) case of removal.

(1) Nearly any OH or NH can be easily silylated.

(2) The thermal stability of silyl ethers (protected hydroxyl functions) is good. Hydrolytically, silylethers are less stable but the rate of hydrolysis of $R_3Si–OR'$ changes with R, *i.e.*, ter. butyldimethylsilyl ethers hydrolyse about 10,000 times slower than trimethylsilyl ethers.

(3) For removal, or desilylation, typically 2 ethanolie NaOH on the basic side or 50% aqueous acetic acid on the acidic side will cleave Si–O to Si–O–H and H–O with variation depending on the R group of R_3Si but the reagent of choice is flouride ion, since E.J. Corey's observation that fluoride is highly selective for removal of silyl groups especially ter. $BuMe_2Si$. Since Si–F bonds are strong, fluoride is very nucleophilic towards silicon.

Many laboratories have turned to CsF. R. West found that butanol removed Me_3Si from a bis-silyloxy ethene. For selective protection of primary OH, ter-butyldiphenylsilyl has been suggested, as it is inert to 80% acetic acid.

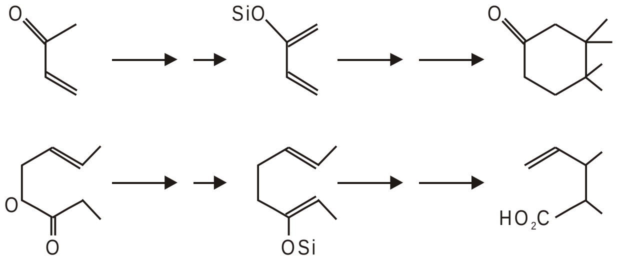


Sometimes, the removal can be turned to good advantage synthetically. Thus, phenoxysilanes can be expected to be cleaved more readily than alkoxysilanes because – OPh is more basic than – OR, hence a better leaving group.

ACTIVATION

Silicon substitution often increases the rates of reactions which proceed quite slowly with the unsubstituted compound.

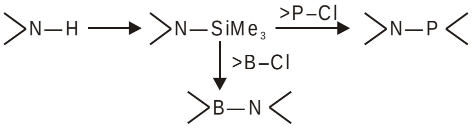
The silylative conversion of a ketone or aldehyde to silylenol ether developed by Marshall, Ireland and Danishevsky produces a reactive diene which can participate in Diel-Alder or Claisen rearrangements.



The work of M.E. Jung, A.B. Mossman and M.A. Lyster (J. Org. Chem., 43, 3698, 1978) has beautifully demostrated the utility of trimethylsilyl iodide in the cleavage of carbon-oxygen bonds under mild conditions.

$$\left.\begin{array}{r} Ar—O—CH_3 \\ R—CO_2CH_3 \\ ArCH = O \end{array}\right\} \xrightarrow{Me_3SiI} \left\{\begin{array}{l} Ar—OH \\ RCO_2H \\ ArCHI_2 \end{array}\right.$$

Activation of H–N for formation of P–N and B–N bonds by silylation is a well known technique illustrated as

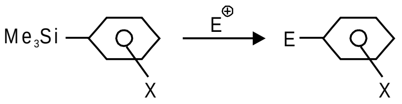


By analogous methods S–N bonds have also been created and these compounds have shown promise of super conductivity.

Direction

The ability of silicon to direct the stereochemistry is a technique just beginning to be appreciated.

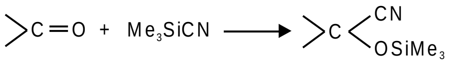
Careful studies by C. Eaborn have shown that electrophilic aromatic substitution of silicon is faster than substitution of hydrogen. Thus a silicon in an aromatic ring directs substitution with hardly any rearrangement. This technique is particularly useful for preparation of specifically deuterated arenes as protolysis (deuterolysis) or aryl silanes is rapid.



SOME APPLICATIONS OF ORGANOSILICON COMPOUNDS TO ORGANIC SYNTHESIS

As already seen the use of organosilicon reagents for organic synthesis and as intermediates to be discussed later is now becoming a field of great importance.

Although carbon and silicon both belong to the same group of periodic table and many of the silicon compounds resemble carbon compounds, but the chemical reactivity of silicon in organosilicon compounds is more comparable to that of hydrogen because many nucleophilic displacements at silicon, hydrosilylation of multiple bonds, carboxyl addition reactions of Me_3SiCN and other silicon pseudohalides, electrophilic substitution reactions of unsaturated silanes and β-elimination reactions have analogous reactions in proton systems. But the organosilicon system is more reactive than the analogous proton system. For example addition of Me_3SiCN to carboxyl groups occurs with compounds which do not form stable cyanoydrins and cleavage of silicon in electrophilic substitution and β-elimination reactions generally takes place in preference to the cleavage of hydrogen.



Why Silicon Compounds are Reactive ?

The electro positive nature of silicon, coupled with its larger size and availability of the empty '*d*' orbital affects its reactivity.

S_N2 nucleophilic displacements at the silicon atom are much more facile, particularly with elements which are more electronegative. Compounds of the type R_3SiX (X = leaving group) hydrolyse rapidly in aqueous solutions.

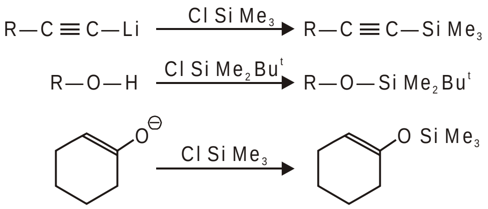
Formation and Cleavage of Bonds to Silicon

The reactivity of organosilicon compounds is influenced by the more electropositive nature of the silicon atom as compared to carbon and hydrogen and also by the availability of empty *d* orbitals, although the latter point has now become controversial. On this basis Si–O and Si–F bonds are stronger than the C–O and C–F bonds. The Si–H bonds are weaker than C–C and H–C bonds.

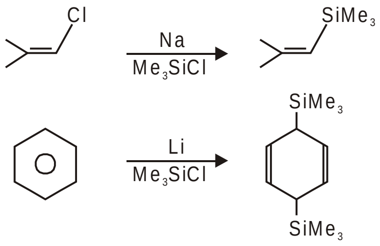
This is why S_N2 type of displacements are more facile at the silicon atom than at the carbon. This is particularly so with nucleophiles derived from the more electronegative element. In compounds of the type of R_3SiX (where X = leaving group), the nucleophilic displacements and hydrolysis in aqueous media occur rapidly.

Formation

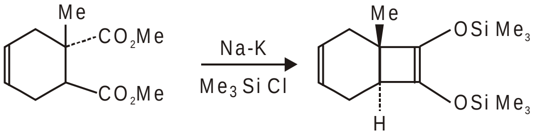
1. Nucleophilic displacement reactions at silicon are very useful for formation of bonds from silicon to carbon and to electronegative elements. Some examples are:



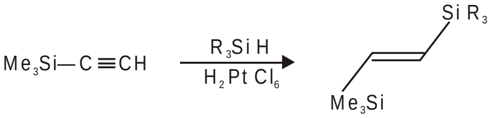
2. *Reductive Silylation.* This is a novel method of preparing organosilicon compounds and has been largely employed by R. Calas and J. Dunogues in 1976. Here a reducing agent (*e.g.,* Na, Li or Mg) is used in presence of a silylating agent (*e.g.,* Me_3SiCl). The reactions presumably proceed by trapping nucleophilic intermediates as soon as they are generated.



Reductive silylation is preferred because it is less expensive than other methods, is adaptable to large scale work and promises to be of much synthetic value. This technique has not only improved the yields of acylain reactions but has led to the preparation of small rings also.



3. *Hydrosilylation.* The word hydrosilylation, signifying the addition of Si–H to organic molecules is another suitable method of creating Si–C bond. This addition of Si–H across multiple bonds (*e.g.*, C = C, C≡C, C = O) is generally accomplished in the presence of a catalyst such as H_2PtCl_6. The hydrosilylation of simple olefines and acetylenes generally proceeds to place the silicon predominantly at the less substituted carbon atom. Although the cause of reaction depends on the catalyst and conditions, stereospecific cis addition of Si–H to the multiple bond can be achieved.



In 1976 W.C. Still (J. Org. Chem. 41, 3063-41) discovered Me_3SiLi and in the same year P.B. Dervan and MA Shippey (J. Awer Chem. Soe, 98, 1265-1267, 1976) discovered Me_3SiK which are silicon nucleophiles and both of which promised to be very useful for preparing organosilicon compounds.

Cleavage of Bonds to Silicon

The cleavage of bonds to silicon atom in organosilicon compounds is accomplished by nucleophilic displacement reactions at silicon. If a group attached to silicon can be considered to be a “leaving group” (*e.g.,* in silyl ethers or silyl acetylenes) cleavage occurs readily under nucleophilic conditions, especially with nucelophiles from the more electronegative elements. Fluoride and oxygen nucleophiles are frequently used.

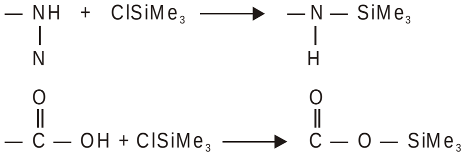
An organic group attached to silicon can sometimes be converted to a good leaving group by reaction with an electrophile (*e.g.,* by protonation) if a positive change is generated β to silicon. Thus under acidic or electrophilic conditions a variety of unsaturated organosilicon compounds undergo electrophilic substitution reactions.

Organosilicon Protecting Groups

1. *Protection of Alcohols.* Trimethylsilyl ethers, readily prepared from alcohols by treatment with a variety of silylating agents have found considerable use for the protection of alcohols. They are thermally stable and reasonably stable to many organometallic reagents and they are easily cleaved by hydrolysis in acid or base or by treatment with fluoride ion. *t*, Butyl dimethylsilyl ethers have considerably greater hydrolytic stability and are easier to work with than trimethylsilyl ethers. They are prepared from alcohols by treatment with *t*. butyl dimethylsilyl chloride.

$$t.\ BuMe_2SiCl + HOR \longrightarrow Bu^t\ Me_2\ Si{-}OR + HCl.$$

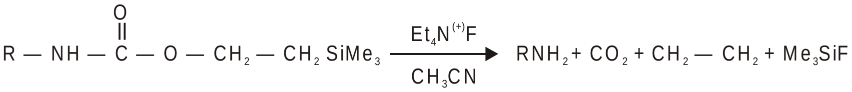
2. Protection of Amines and Carboxylic Acids Amines and carboxylic acids can also be converted to trimethylsilyl derivatives. A general reaction is



$$-\underset{\underset{N}{|}}{NH} + ClSiMe_3 \longrightarrow -\underset{\underset{H}{|}}{N}-SiMe_3$$

$$-\overset{\overset{O}{\|}}{C}-OH + ClSiMe_3 \longrightarrow \overset{\overset{O}{\|}}{C}-O-SiMe_3$$

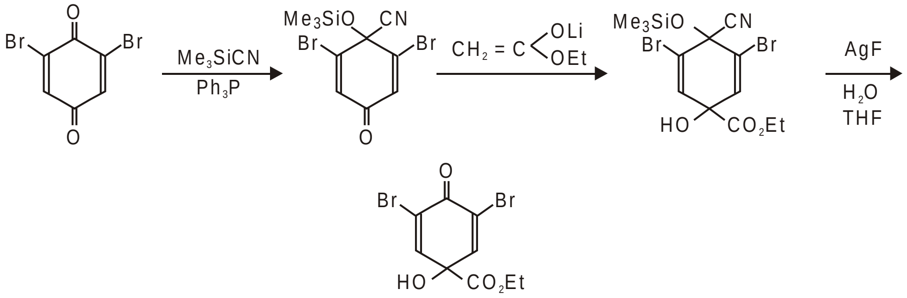
These desiratives have been useful for gas chromatographic and mass spectral analyses, but since they are very sensitive to hydrolysis, their use as protecting group in multistep organic synthesis become limited. But since trimethylsilyl ethyl derivatives are more stable towards hydrolysis and can be easily removed under very mild conditions, they are more useful for protection of amines and carboxylic acids.



$$R-NH-\overset{\overset{O}{\|}}{C}-O-CH_2-CH_2\,SiMe_3 \xrightarrow[CH_3CN]{Et_4N^{(+)}F} RNH_2+CO_2+CH_2-CH_2+Me_3SiF$$

3. *Protection of carbonyl groups.* A number of organosilicon pseudohalides (*e.g.*, Me_3SiX; X–CH, SR, N_3 etc.) have been shown to add to carbonyl groups, especially in the presence of suitable catalysts.

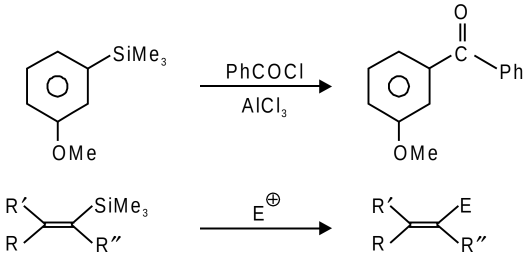
Me_3SiCN reacts with both saturated and unsaturated aldehydes and ketones to given silylated cyanohydrines. This reaction has been particularly useful for the regioselective protection of a carbonyl in *p*. quinones and *p*. quinol antibiotic metabolite has been prepared.



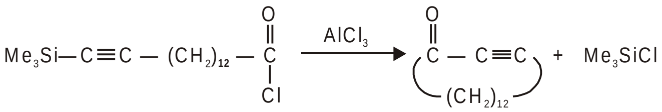
Silylated cyanohydrins of ketones have been shown to be useful precursors to aminomethyl carbinols, which are useful in ring expansion of cyclic ketones (Tiffenean-Demjanov ring expansion).

Electrophilic Substitution Reactions

Many unsaturated organosilicon compounds undergo facile electrophilic substitution reactions. The arylsilanes also appear to be activated towards electrophilic substitution. Substitution normally takes place exclusively at the site of silicon atom.



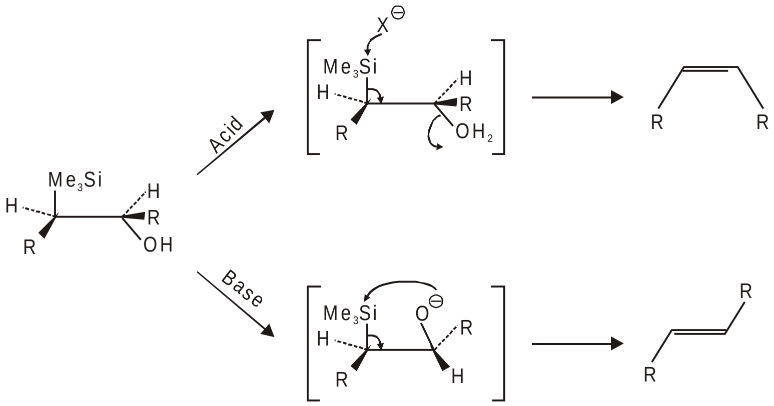
Electrophilic substitution reactions on alkynylsilanes are also known. In 1978 K. Ultimootd, M. Tanaka and coworkers by an intramolecular reaction carried out the synthesis of a macrocyclic ketone.



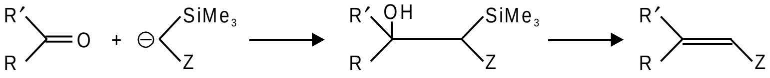
Allylsilanes have been found to be more reactive than vinyl silanes toward electrophiles and they are being studied more intensively in recent years because they hold considerable promise in organic synthesis. In allylsilanes, the geometry of carbon-silicon bond can be more favourably be oriented for efficient stabilization of a developing positive change β to silicon.

Synthesis of Olefines

Recently organosilicon compounds are being used for the synthesis of olefines by elimination reactions both in acidic and basic conditions. Thus β hydroxysilanes give elefines. These reactions have been shown to be highly stereospecific. The acid catalysed elimination taking place by an anti pathway and the base induced elimination taking place by a syn pathway.



These β elimination reactions have been used in an olefine synthesis called the Peterson olefination reaction which is analogous (and sometimes superior) to the Wittig reaction. The Peterson olefination reaction involves the addition of an α-silyl carbanion to an aldehyde or ketone to give β-hydroxysilane, followed by β-elimination to give the olefine.



—Z = —H, —R, —CH = CH_2, —Ar, —CN, —COOR, —$SiMe_3$ — PPh_2 etc.

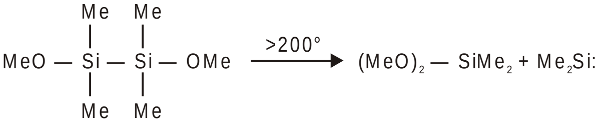
Reactive Intermediates in Organosilicon Chemistry

Till about 1978 not much was known about the reactive intermediates in organosilicon chemistry but after that an almost explosion has taken place and now the vast amount of literature has shown their importance in the synthetic organic chemistry and in a way they are more important than purely organic reactive intermediates like carbenes, benzynes or nitrenes.

In the present heading, their generation and utility in some synthetic reactions have been described.

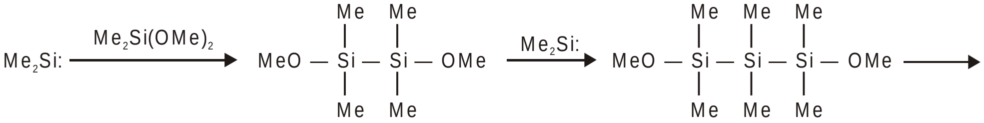
Silylenes (R_2Si:)

The silicon analogue of carbene is now called silylene and it was discovered by the thermally–induced alpha elimination of methoxydisilanes. The most common method of silylene generation is:



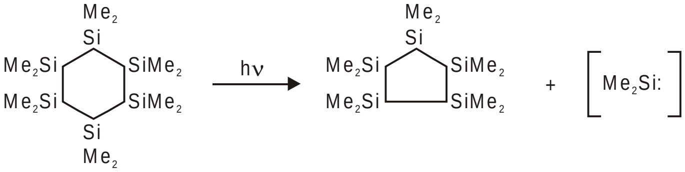
$$\mathrm{MeO-\underset{Me}{\overset{Me}{Si}}-\underset{Me}{\overset{Me}{Si}}-OMe \xrightarrow{>200^\circ} (MeO)_2-SiMe_2 + Me_2Si{:}}$$

(*a*) However this method is limited by the fact that the silylene generated by the above thermolysis readily inserts into the Si–O bond as follows:

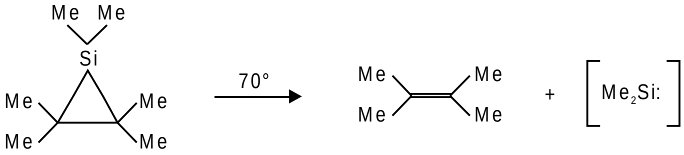


$$\mathrm{Me_2Si{:} \xrightarrow{Me_2Si(OMe)_2} MeO-\underset{Me}{\overset{Me}{Si}}-\underset{Me}{\overset{Me}{Si}}-OMe \xrightarrow{Me_2Si{:}} MeO-\underset{Me}{\overset{Me}{Si}}-\underset{Me}{\overset{Me}{Si}}-\underset{Me}{\overset{Me}{Si}}-OMe \longrightarrow}$$

(*b*) Some other methods of silylene generation are by the photolysis of polysilanes.

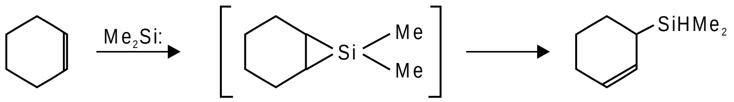


(*c*) and theromolysis of the only recently available silacyclopropanes.

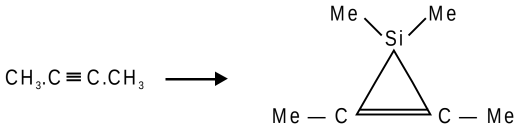


The important chemical behaviour of silylene is the insertion reaction like carbenes. Some insertion reactions which have come to light are:

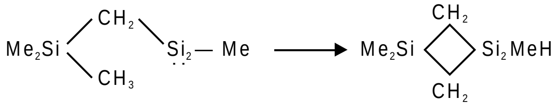
(*i*) Insertion into the π bond of olefines :



(*ii*) Insertion into π bond of acetylenes



(*iii*) Insertion into C–H bonds.

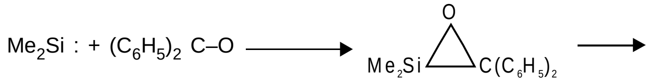


(*iv*) Insertion into Si–H bonds.

$$Me_2Si: + Et_3SiH \longrightarrow Et_3Si\text{–}SiMe_2H$$

This insertion is so efficient that silyl hydrides are used for silylene detection.

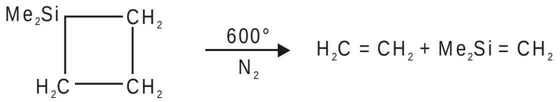
(*v*) Recently it has been shown that silylenes can insert into the π bond of a carbonyl group to form an unstable oxasilacyclopropane intermediate.

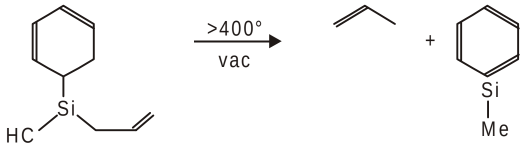


Silenes $R_2Si\text{–}CR'_2$

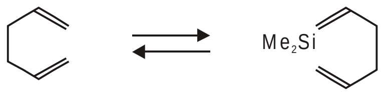
For a long time it was thought that a (*p–p*) π bonding between a silicon and carbon atom was not possible because of the greater size of the silicon atom, the bond distance between Si and carbon becomes great and so an effective parallel overlap of the *p–p* orbitals was not possible. This is why silenes, analogous to alkenes were not possible. But now (*p–p*) π bonding to silicon has become accepted and the last few years have seen a flood of reactions which are explained on the basis of the formation of silene intermediates. The formation of these intermediates and the π bonded silicon was supported by various studies. The following are some of the methods for silene generation:

(*a*) By flow pyrolysis of various precursors.

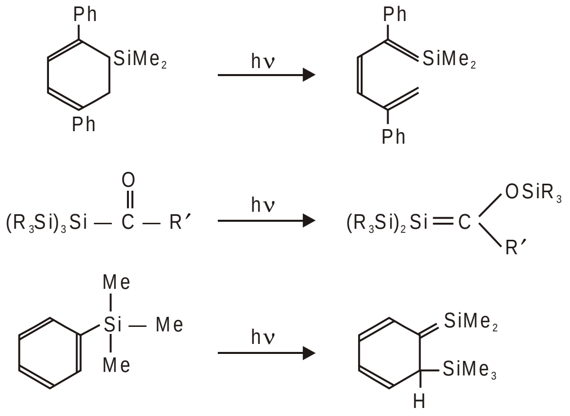




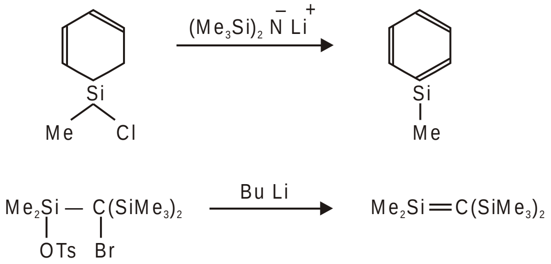
(*b*) By thermal rearrangements.



(*c*) By photo chemical rearrangements.

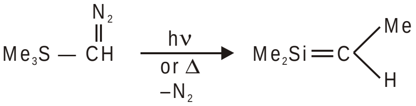


(*d*) Elimination from silyl halides or esters.



$$\underset{\text{OTs}}{\mathrm{Me_2Si}} - \underset{\text{Br}}{\mathrm{C}}(\mathrm{SiMe_3})_2 \xrightarrow{\text{Bu Li}} \mathrm{Me_2Si{=}C(SiMe_3)_2}$$

(*e*) and rearrangement of silyl carbenes.

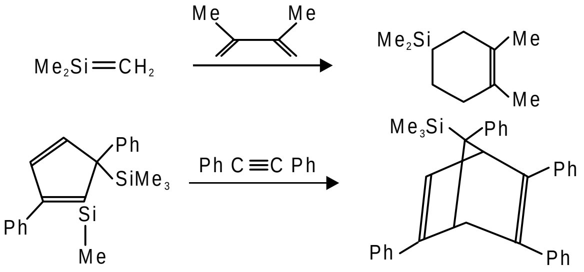


$$\mathrm{Me_3S} - \overset{\overset{\mathrm{N_2}}{\|}}{\mathrm{CH}} \xrightarrow[\substack{\text{or } \Delta \\ -\mathrm{N_2}}]{h\nu} \mathrm{Me_2Si{=}C(Me)(H)}$$

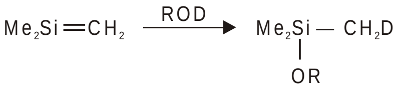
Although still remains much to be done in the chemistry of silenes, some general reactions are as follows:

(*i*) Dimerisation:

(*ii*) Diel's-Alder reactions:

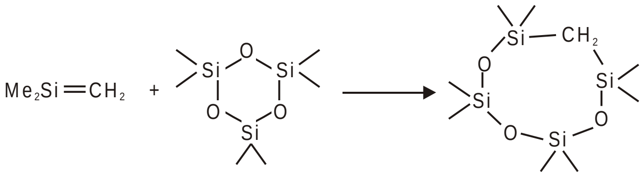


(*iii*) Alcohol additions

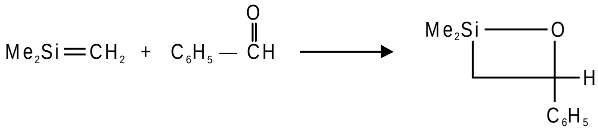


$$Me_2Si{=}CH_2 \xrightarrow{ROD} \underset{\displaystyle OR}{\underset{|}{Me_2Si}}-CH_2D$$

(*iv*) Insertion into Si–O bonds.

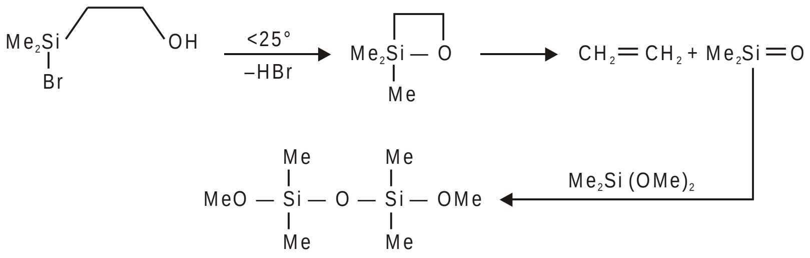


(*v*) and addition to carbonyls.



This last reaction is interesting because a four membered ring, a silaoxetane, has never actually been observed. It thermally decomposes to a molecule of olefine and a molecule of silanone $R_2Si{=}O$.

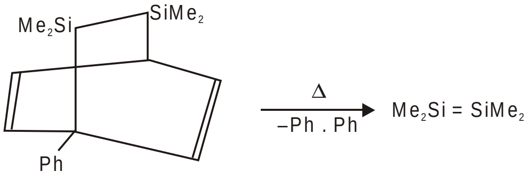
Silanones ($R_2Si{=}O$). As already written above, an attempt to prepare a four membered silaoxetane ring has not been very successful because of its instability but these reactions have been used conveniently to generate silanone S.



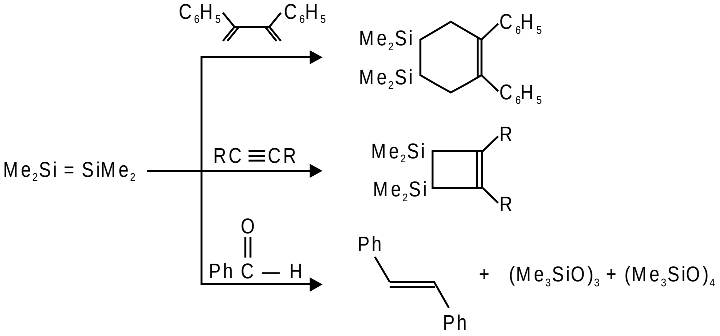
One reaction of silanone is the insertion reaction as exemplified above.

Disilenes ($R_2Si{=}SiR_2$). Now that (*p–p*) π bonding in silicon chemistry has become an established fact, compounds having multiple bonding beween silicon atoms have been prepared. Such compounds having a double bond between two silicon atoms are called disilene.

The first evidence for the formation of compounds having a silicon-silicon double bond first appeared in 1969 when it was formed that disilebicyclo [2.2.2] octadienes on heating extruded tetramethyldisilene.



This disilene undergoes Diels. Alder reaction with 1, 3 diene addition to acetylene and a single example of reaction with a carbonyl system.



Silyl Anions (R_3Si:). They have been generated by the following methods:

(*a*) By the anionic cleavage of disilanes

$$Ph_3Si - SiPh_3 \xrightarrow[THF]{Li} Ph_3SiLi$$

$$Me_3Si - SiMe_3 \xrightarrow[HM\ PA]{Na\ O\ Me} Me_3SiNa + Me_3Si\ OMe$$

$$Me_3Si - SiMe_3 \xrightarrow[HMPA]{MeLi} Me_3SiLi + Me_4Si$$

HMPA: Hexamethylphosphoramide

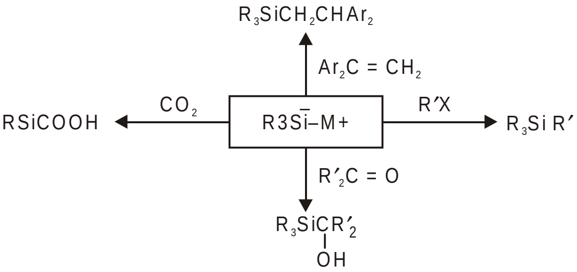
(*b*) *From silyl halides.* Since disilanes are usually prepared from Wurtz coupling of chlorosilanes, so metallation of silyl halides is accomplished with potassium or lithium in ether solvent.

$$Ph_2MeSiCl \xrightarrow[THF]{Li} Ph_2MeSiLi\ (66\%)$$

(*c*) From silyl mercury compounds by transmetallation reactions.

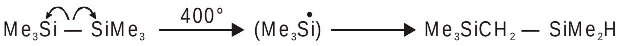
$$(Me_3Si)_2\ Hg \xrightarrow{Li} 2Me_2SiLi + Hg$$

Some important reactions of silyl anions are as follows and they have emerged on the basis of the carbanion chemistry.



Silyl Radicals ($R_3\dot{Si}$). Much is known about the chemistry of silyl radicals. They can be produced from thermolysis, photolysis and electron transfer reactions. With the exception of disproportionation and degradation to silenes, most of the reactions known for the carbon radicals are also known for silyl radicals.

Thermolysis. Hexaphenyldisilene does not undergo thermolysis to $Ph_3\dot{Si}$. This might probably be due to a long Si–Si bond. However, hexamethyldisilane is believed to dissociate homolytically. If true, the end product is an isomer of the starting disilane and formed in quantitative yield.



$$Me_3Si-SiMe_3 \xrightarrow{400°} (Me_3\dot{Si}) \longrightarrow Me_3SiCH_2-SiMe_2H$$

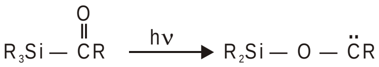
Photolysis. The photolysis of silyl mercurials is one of the most useful methods for the production of silyl radicals:

$$(Me_3Si)_2\ Hg \xrightarrow{h\nu} 2Me_3\dot{Si} + Hg$$

Photolysis of silyl ketones can produce silyl radicals quite clearly.

$$Me_3Si\overset{\overset{O}{\|}}{C}-Me \xrightarrow{h\nu} Me_3\dot{Si} \xrightarrow{CCl_4} Me_3SiCl$$

But the method suffers from the difficulty of obtaining starting materials and photo induced rearrangement of silyl ketones



$$R_3Si-\overset{\overset{O}{\|}}{C}R \xrightarrow{h\nu} R_2Si-O-\ddot{C}R$$

Electron transfer. The conversion of silylhydrides to silyl radicals is through hydrogen abstraction by various other radicals.

$$Cl_3SiH \xrightarrow[R-O-O-R]{\Delta} Cl_3\dot{Si}$$

PART-II

SPECTROSCOPY

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CHAPTER 12

Spectroscopy

SOME GENERAL CONSIDERATION

The word *radiant energy* is the energy transmitted from one body to another in the form of radiations. This energy has wave nature and because it is associated with electric and magnetic fields, it is also called *electro-magnetic radiations*. The visible light, ultraviolet, infrared, X-rays, radio-waves and microwaves are all different forms of electromagnetic radiations.

It is well known that when a beam of white light is passed through a prism, it is split into seven colours splitting from the violet range to the red end and is called spectrum, each having its own wave length. By arranging these waves in increasing or decreasing order, the spectrum obtained is called *electromagnetic spectrum*. So the spectrum obtained by white light is called *continuous spectrum* and it lies in the range of 3800Å-7600Å and this is subdivided into a number of regions which corresponds to different colours. These are given in the following table 12.1:

Table 12.1

Radiation	*Wave length* *Å*	*Frequency* *Sec^{-1}*	*Energy* *KJ/mole*
Radiowaves	3×10^{13}	10^5	4×10^{-8}
Microwaves	3×10^9	10^9	4×10^{-4}
Infrared	6×10^6	5×10^{11}	2×10^{-1}
Visible	7600	4×10^{14}	1.60×10^2
Ultraviolet	3800	8×10^{14}	3.16×10^2
X-rays	150	2×10^{16}	9×10^3
Y-rays	1	3×10^{18}	1.20×10^6
Cosmic rays	1×10^{-3}	3×10^{21}	1.20×10^9

The region of 3800Å corresponds to the violet colour and 7600Å wave length corresponds to red colour. A region of wave length lesser then 3800Å is called the *ultraviolet light* and that greater than 7600Å is called the *infrared radiation.*

The infrared and ultraviolet radiations are not visible to the eye and so they are know as *invisible radiations*. The energy of white light is least while the energy of cosmic rays is very large.

Far UV		*Ultraviolet (U.V.)*			*Visible light*			*Infrared*
1	1.5	2	3	4	5	6	7	8×10^{-8} cm
	150	200	300	400	500	600	700	800 m/n
	1500	2000	3000	4000	5000	6000	7000	8000Å

Range of electronic spectra.

The increasing order of wave length of different electromagnetic radiations is as follows:

Cosmic rays < Y rays < X rays < uv rays < visible rays < i.r. rays < micro waves < radio waves and the increasing order of different energies are

Radiowaves < microwaves < i.r. < visible < u.v. < x-rays < y rays < comic rays.

SPECTROSCOPY

In spectroscopy we study the effect of interaction of electromagnetic radiation on matter. For examples *X-rays* are produced by bombandment of metal targets with high speed electrons. So the different types of electromagnetic radiation interact with the matter and give different types of spectroscopy.

In ultraviolet and visible region, electronic transition of atoms and molecules are observed. This is why it is called *electronic spectroscopy*. In infrared region the absorption of radiation by an organic compound causes *molecular vibrations* and so it is called *vibrational spectroscopy.*

The absorption of electromagnetic radiation by the matter in the radio frequency region gives rise to *nuclear magnetic resonance (NMR) or electron spin resonance (ESR) spectroscopy*. The radio-waves and microwaves originate from alternating electric current and the energy change involved is due to the reversal of spin of nucleus of electron.

The science of spectroscopy has become the most powerful tool available for the determination of atomic and molecular structures and can be applied on a wide range of samples.

The study of spectroscopy can be carried out under two heads:

1. *Atomic spectroscopy.* This spectroscopy gives results of interaction of electromagnetic radiation with atoms which are in their lowest energy state or ground state.
2. *Molecular spectroscopy.* This spectroscopy deals with the interaction of electromagnetic radiation with molecules. This results in transition between rotational and vibrational energy levels besides electronic transitions.

The following table gives the effect of various spectra on different properties.

1.	X Ray	K and L shell electrons
2.	Far u.v.	Middle shell electrons
3.	Visible	Valency electrons
4.	i.r.	Molecular vibrations.
5.	Far i.r.	Molecular rotations and low lying vibrations.

The spectra of molecules are much more complicated than those of atoms. Molecular spectroscopy has become much more important now because of the large number of complicated molecules being synthesized.

In electromagnetic radiation, since there is the production of an electrical field, it is this field that interacts with the electrons in the matter.

Types of Molecular Spectra

When a molecule absorbs or emits a photon, its energy is increased or decreased and the following possibilities may occurs:

(*a*) *Electron spin resonance (e.s.r.)* may occur which involves a change in the resultant spin of the electron.

(*b*) *Nuclear magnetic resonance (n.m.r.)* may occur which involves a change in the direction of nuclear spin quantum number.

(*c*) *Rotational spectra arise* and there is change in the rotational quantum number. But this occurs in the far infra red and microwave regions.

(*d*) *Vibrational-Rotational spectra arise*. Here there is change in both the vibrational quantum number (v) and rotational quantum number (j). These occur in the near infrared region.

(*e*) *Raman spectra.* This is concerned with the change in the vibrational and rotational quantum numbers.

LASERS

A laser is a source of monochromatic radiation available principally in the visible and infra red regions. Light from a laser has several properties

(*a*) It is highly monochromatic.

(*b*) The light emitted is *coherent i.e.*, the waves originating from all the atoms or molecules are in same phase with each other.

Importance of lasers

(*a*) It has high degree of localized heating.

(*b*) It can give high power levels.

Use of lasers

They are mainly used for:

(*a*) Localized heating.

(*b*) As an exciter for Raman spectroscopy.

CHAPTER 13

Ultraviolet Spectroscopy

ULTRAVIOLET AND VISIBLE SPECTROSCOPY

As already stated earlier the visible light has electromagnetic radiations varying in the wavelength region 3800Å-7600Å. This ordinary light can be divided into 3 parts:

(*a*) Ultraviolet light (1000-4000 Å)

(*b*) Visible or white light (3800-7600Å)

(*c*) Infrared light (7500°-upwards)

Radiations below 4000Å and above 8000Å are invisible and lie in the *ultra violet and infra red regions respectively. Therefore, visible region gives a colour to a particular substance*. In the visible region the light is composed of seven colours called VIBGYOR.

A number of colours appear when the visible or white light falls on a compound. The colour produced depends or how the white light reacts with the compound. A number of cases may arise:

(*a*) The substance will appear black, if the white light is completely absorbed.

(*b*) The substance will appear white if the white light is reflected completely.

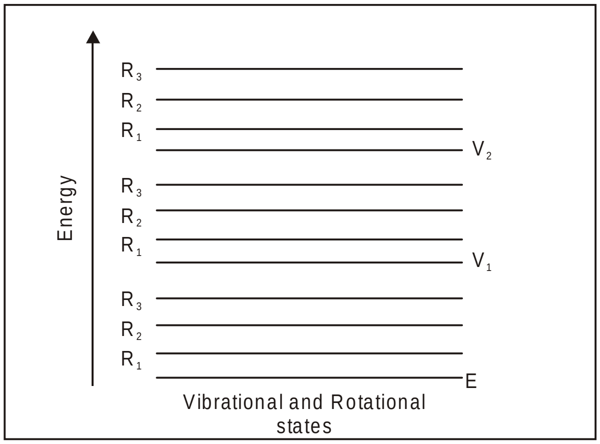
(*c*) If all the wave lengths of white light are absorbed except a single narrow band, which is reflected, the colour of the substance will be the colour of the reflected band.

Spectra of Liquids

In the electronic transitions in visible and ultraviolet region with liquids or solutions, we do not get vibrational bands along with rotational fine structure, but we get a continuous broad electronic band and hence such curves do not give much valuable information. This is because the vibrational fine structure gets suppressed due to overlapping of vibrational spacings.

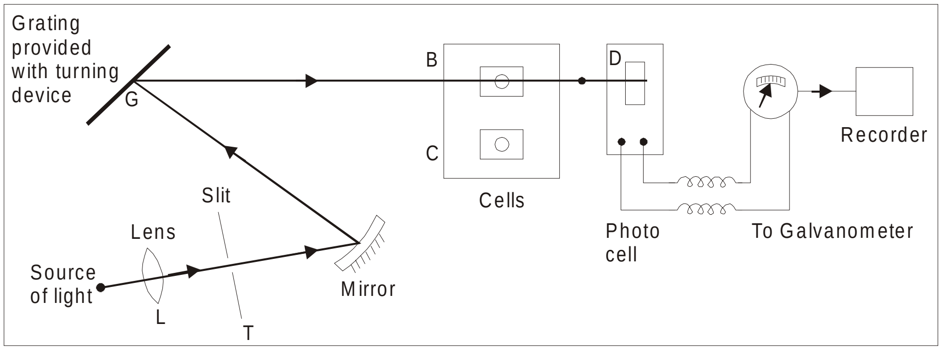
Spectrophotometer

A spectrophotometer is a combination of *spectrometer* and *photometer*. A photometer is an instrument which is used for the production of light of selected colour or wavelength. The spectrometry involves the determination of the light absorptive capacity of a chemical. So spectrophotometric analysis provides a significant method of determining minute quantities of a substance.



So spectroscopy has a wide range of applications and may be employed to determine a constituent constituting a major part of sample.

First let us see how the absorption spectra of liquids is recorded in a spectrophotometer.

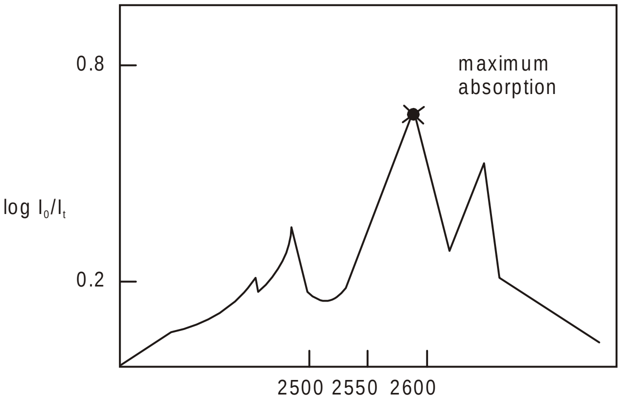


Spectrophotometer (Diagramatic)

For visible region the lenses and prisms of ordinary glass can be used but since glass is opaque to radiation of shorter wave lengths in ultraviolet spectrophotometers they are made of quartz. In infra red spectrophotometers they are made of large crystals of NaCl, CsF or KBr.

The source of light is the hydrogen discharge tube in the ultraviolet region. The light after passing through lens and slit, gets reflected from the mirror and falls on the optical grating. Here it is divided into narrow spectral region of different wave lengths. The light of desired wave length is then passed through the cell B containing the solution under examination. From here it goes to the galvanometer via photo cell. The photo-electric cells gives the intensity of light. The cell B is now replaced by cell C containing pure solvent and the same light is passed again through it and then to the photo cell. The intensity of light is again measured by the galvanometer.

It I_0 is the intensity of light which passes through the solution and I_t the intensity of the same light which passes through the solvent, then I_0/I_t is called *transmittance*. From the thickness of the cell and I_0/I_t, absorption co-efficient or extinction co-efficient is calculated. Then log I_0/I_t is plotted against λ. The maximum absorbance will be given by the maxima in the curve.



Spectrophotometers are of two types:

(*a*) Manual or Non-recording.

(*b*) Automatic a Recording.

The latter are more convenient and since they give reliable results, they are mostly used.

ULTRA VIOLET SPECTROSCOPY

The fundamental principles of spectroscopy which are applied for visible spectroscopy are also applicable to ultraviolet region.

Origin of u.v. Absorption Spectra

Ultraviolet absorption spectra appear when outer electrons of atoms or molecules absorb radiant energy and undergo transition to higher energy levels. These transitions are quantised and depends on the compound under examination.

The measurement of absorption of ultraviolet and visible radiation, therefore, provides a convenient means of analysis of numerous inorganic and organic species. Radiation in these regions is of sufficient energy to cause electronic transition of outer valency electrons. We have seen that spectra of molecules in solution or their ions represent a continuous broad band due to the superposition of vibrational and sometimes rotational energy changes upon electronic transitions. But if the sample is composed of atoms or simple molecules in the gaseous state, then its absorption spectrum will consist of a series of sharp, well defined lines corresponding to the permitted electronic transition.

Both organic and inorganic species show electronic transitions in which outermost bonding electrons are promoted to higher energy levels. The main function of the absorbed energy is to raise the molecules from the ground state energy level E_0 to the higher excited anergy level and the difference of the energy levels ΔE is given by:

$$\begin{aligned}\Delta E &= E_1 - E_0\\ &= h\nu\\ &= h\frac{c}{\lambda}\end{aligned}$$

where *h* is Planck's constant, C = velocity of light and λ is the wave length of the absorbed radiation.

The value of Δ E depends upon how tightly the electrons are bound and so the absorption will occur in the U.V. Two conditions arise:

(*a*) If the electrons are tightly bound by sigma bonds as in saturated compounds like CH_4, C_2H_6 etc. no light of visible range will be absorbed. The light of U.V. region will only be absorbed and the compound will appear colourless.

(*b*) If the electrons are loosely bound as in unsaturated compounds like C_2H_4, C_3H_6, the absorption will occur in the visible region and the substance will appear coloured. For a coloured substance, the value of ΔE lies between 71.0 and 35.5 K cals/mole. So if the organic compound is be coloured, it must have mobile electrons which can be raised from the ground state to the excited state and the values of ΔE being 71.0 and 35.5 K cals/mole.

Because the electrons lie in definite orbitals the value of ΔE and the frequency of light absorbed will also have definite values. The frequency of the absorbed light will be associated with a particular line in the spectrum. So the spectrum of the compound will have a large number of lines corresponding to the large number of excited states. *So the lines will appear as a band and they will give colour to the definite parts of the spectrum.*

It is to be noted that *the total energy of a molecule is the sum of its electronic energy, its vibrational energy and its rotational energy*. This is why each energy brings about a corresponding change. These energies decrease in the order:

$$E \text{ electronic} > E \text{ vibrational} > E \text{ rotational}$$

Because of electronic excitation ultraviolet spectroscopy is also known as *electronic spectroscopy*.

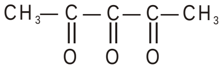
Colour in Organic Compounds

The colour depends upon spectral range in which the substance absorbs light. *A substance which absorbs only in ultraviolet will transmit all white light and it will appear colourless*. When a substance shows a colour in white light, it indicates light which is absorbed. NaCl solution is colourless because it does not absorb selectively any light in the visible region. Copper sulphate solution is blue because out of the white light it absorbs yellow and red leaving the blue to be transmitted.

Therefore, only coloured substances can be studied in the visible region. Colourless substances do not absorbs white light appreciably and hence they are studied in ultraviolet.

If unsaturated linkages like –C = C–, –N = N–C–O, –N = O etc. (also called chromophores) are present in the molecule, less energy is required for the excitation of π electrons and so the absorption bands occur *in the near ultraviolet region and some times in the visible spectrum.*

Two or more unsaturated groupings e.g., dimethyl ketene $(CH_3)_2 = C = O$ often enhance one another and so visible colour is produced. Similar is the case of triketones.



$$CH_3-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-CH_3$$

which is more deeply coloured. *Conjugation of the double bond also intensifies colour due to bathochromic effect*.

Benzene with its six π electrons is an exception and it shows appreciable absorption in the *near ultraviolet*. If the *conjugation is destroyed say by the introduction of a–CH$_2$ group, in the unsaturated chain then a shift of the absorption band towards the shorter wave length appears*. This produces a lessening in the intensity of the colour, also called hypsochromic effect. This is why C_6H_5 (CH = CH)$_4$ C_6H_5 is greenish yellow but $C_6H_5CH_2$ (CH = CH)$_4$ C_6H_5 is colourless. This explains that the colour in the dyes is due to the presence of chromophoric structure and of an auxochromic group.

Let us take the case of phenols and nitro-phenols. The phenoxide ion $C_6\ H_5O^{\ominus}$ is colourless, but *p* nitro phenol is yellow, because the $-NO_2$ group in *p*–position produces a yellow ion—p.NO_2–$C_6H_4O^{\ominus}$. Similarly triphenylmethyl cation is colourless or pale yellow or pale yellow in acidic solution, but the corresponding ion containing two or three OH groups in para position produces deep red colour.

Colour in organic compounds is also due to resonance. This also explains why a system of open conjugate double bonds containing two or more double bonds imparts colour to it.

Absorption in Organic Molecules

All organic compounds are capable of absorbing electromagnetic radiations in which the electrons are excited to the next higher energy level.

These electrons are of three different types in organic molecules.

(*a*) *Sigma (σ) electrons*. These electrons are associated with saturated bonds. They remain localized between internuclear axis and because they are tightly held, the energy of ultraviolet or visible region is not sufficient to overcome this attraction and can not excite these σ electrons. *This is why compounds containing σ bonds do not absorbs in U.V. region and they remain transparent in the near U.V. region and they are used as solvents.* This explains why hexane is used as a solvent in U.V. spectroscopy.

(*b*) *Pi (π) electrons.* Since π bonds are weak bonds the energy produced by U.V. radiation can excite these electrons to the next higher level.

(*c*) *Non-bonding (n) electrons*. These electrons are held less firmly and are present on nitrogen, oxygen, sulphur and halogen atoms. They are not involved in bonding and can be excited by U.V. radiation. These are also called *n*-electrons and they require lesser energy for excitation than the π electrons. Thus the energy needed for promoting an electron is in the order.

$$\sigma > \pi > n$$

The non boding (*n*) electron can undergo two types of transition.

(*i*) $n \longrightarrow \pi^*$ (antibonding π orbital)

An example of this is found in carbonyl compounds.

$$>C=\underset{..}{\ddot{O}} \longrightarrow >C=\underset{..}{\dot{O}}^{\ominus}$$

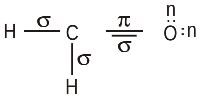
(*ii*) $n \longrightarrow \sigma^*$ (antibonding π orbital)

An example of this transition is found in ethers.

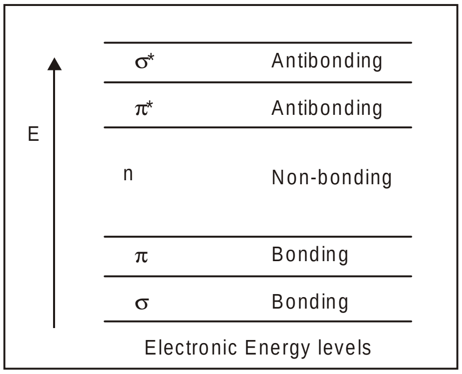
$$R-\underset{..}{\ddot{O}}-R \longrightarrow R-\underset{..}{\dot{O}}^{\ominus}-R$$

An electron in the circle is called the excited electron. Absorption, although at a longer wave length than saturated hydrocarbons occurs below 9.4×10^1 K cal/mole. Therefore, *ethers, disulphides, alkyl halides and alkyl amines are transparent to ultraviolet light*.

The case of formaldehyde is interesting because it contains all the three types of electrons and the energies for the various types of molecular orbitals differ significantly.



Energy Levels in Different Molecular Orbitals



Electronic Energy levels

Based on electronic energy levels, there are four important types of transitions.

These are :

(*a*) $\sigma \longrightarrow \sigma^*$

(*b*) $n \longrightarrow \sigma^*$

(*c*) $\pi \longrightarrow \pi^*$

(*d*) $n \longrightarrow \pi^*$

The energies required for various transitions are in the order.

$$\sigma \longrightarrow \sigma^* > n \longrightarrow \sigma^* > \pi \longrightarrow \pi^* > n \longrightarrow \pi^*$$

As shown from the table $n \longrightarrow \pi^*$ requires less energy than a $\pi \longrightarrow \pi^*$ or $\sigma \longrightarrow \sigma^*$ transition.

(1) σ – σ* *Transition*. This transition requires greatest energy because of strong σ bonds and these transitions occur in alkanes or saturated hydrocarbons in which outermost electrons are involved in single bonds. This is the only transition available and requires high energy ultraviolet light between 150 – 200 nm. Below 200 nm oxygen present in the air begins to absorb and hence such transitions are studied in vacuum ultraviolet region.

The following figures involving $\sigma \longrightarrow \sigma^*$ transitions give the absorption peaks.

Compound	Absorption peak (τ_{max})
CH_4	125 nm
C_2H_6	135 nm

In ethane because the C–C bond strength is less than C–H bond, this is why it requires less energy for excitation.

(2) $n \longrightarrow \sigma^*$ *Transition*. This transition occurs on compounds having atoms with *unshared electron pairs* besides σ electrons. The $n \longrightarrow \sigma^*$ transitions requires less energy than $\sigma \longrightarrow \sigma^*$ transition.

Such transitions are brought about by radiation in the region of 150–250 nm with most peaks appearing below 200 nm.

Compound	*Absorption peak* (τ_{max}) *nm*	*Molar extinction co-efficient* τ_{max}
H_2O	167	
CH_3OH	184	
$CH_3–O–CH_3$	184	
$C_2H_5–O–C_2H_5$	188	
CH_3Cl	173	200
CH_3l	259	400

Alcohols and ether absorbs at wave length shorter than 185 nm, therefore, they are commonly used for work in near ultraviolet region.

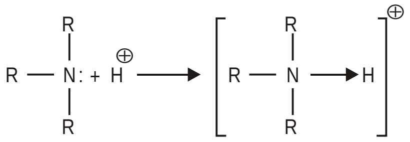
The case is interesting in CH_3Cl and CH_3I. The *n*-electons of chlorine are difficult to excite because of the great electronegativity of chlorine than iodine. The n- electrons of iodine are loosely bound. Hence τ_{max} for CH_3Cl is 173 while that for CH_3I it is 259. *This is the reason why less energy is required for* $n \longrightarrow \sigma^*$ *in* CH_3I *than in* CH_3Cl *and the molar extinction co-efficient* τ_{max} *for a particular absorption is directly proportional to the probability of the particular electronic transition.*

The dipole moment also plays a significant role in the transition of a molecule because a molecule can absorb radiation only when its dipole changes. In *general the more symmetrical a molecule, the light will be absorbed very slowly. Greater the transition dipole, greater is the absorption intensity. The ease of excitation is of the following order:*

$$N = O > C = S > N = N > C = O > C = C$$

Hydrogen bonding. The $n \longrightarrow \sigma^*$ is also sensitive to hydrogen bonding. *In general the hydrogen bonding shifts the absorption towards shorter wave length*. Since *n*-electrons on nitrogen in amines is loosely bound as compared to that in oxygen so $n \longrightarrow \sigma^*$ transition is more probable in amines than alcohols.

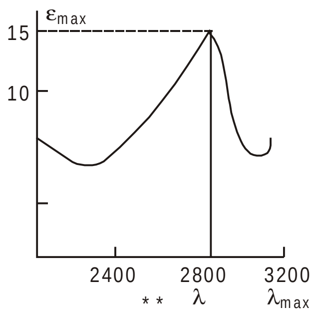
The protonated amine, because it does not have any *n*-electron, hence the spectrum of such an amine does not show any absorption due to $n \longrightarrow \sigma^*$ transition.



(3) π ⟶ π* *Transition*. In this transition there is the promotion of an electron from a bonding π orbital to an anitbonding π* orbital and is found in simple alkenes, *aromatic and carbonyl compounds*. Since this excitation requires less energy, *this transition occurs at longer wave lengths*. Compounds containing double or triple on like alkenes, alkynes, carbonyl compounds, aldehydes, ketones cyanides and azo compounds undergo π ⟶ π* transition (also *called K-bonds*)

(4) *n* ⟶ π* *Transition*. These transitions are also called *R. Bonds* (German, Radical). Here the *n*-electron of the heteroatom is excited to the π* antibonding orbital. This transition requires least energy than all other transitions for excitation *hence this transition gives rise to absorption bonds at longer wavelengths.*

The *n* ⟶ π* Transition exhibit a weak bond in their absorption spectrum is found in saturated aldehydes and ketones *i.e.*, carbonyl compounds (>C = $\underset{\cdot\cdot}{\ddot{O}}$) Schiff bases (>S = $\ddot{N}$–) or azo compounds $(-\ddot{N}=\ddot{N}-)$.



Electronic spectrum of aectone

This transition is best studied by noting the spectrum of the substance in an acid solution. The bonds due to *n* ⟶ π* transition in pyridine disappear in acid solution because of the formation of bond between acidic proton and *n*-electrons

$$C_6H_5N: + H^{\oplus} \longrightarrow C_6H_5\overset{\oplus}{N}H$$

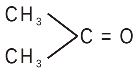
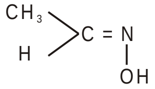
Difference between *n* ⟶ π* and π ⟶ π* transition

The most important difference between the two transitions is the effect of solvent on the wave length of the peak.

n ⟶ π*	π ⟶ π*
Here the peak is shifted to the shorter wave length (also called hypochromic or blue shift) with increase in solvent polarity.	Here the peak is shifted to the longer wave length (also called bathochromic or red shift)

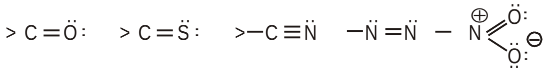
Electronic transition of simple organic molecules and the corresponding absorptions

Table 13.1

Transition	*Compound*	*Formula*	*Absorption*		*Solvent used*
			λ_{max}	ε_{max}	
$\sigma \to \sigma^*$	Methane	CH_4	1250	Strong	Vapour
	Ethane	C_2H_6	1350	Strong	Vapour
$n \to \sigma^*$	Methyl bromide	CH_3Br	2040	200	Vapour
	Dimethyl ether	$CH_3–O–CH_3$	1838	25520	Vapour
	Trimethylamine	$(CH_3)_3N$	2273	900	Vapour
$\pi \to \pi^*$	Ethylene	$CH_2 = CH_2$	1620	10000	Vapour
	1, 3 Butadiene	$CH_2 = CH–CH = CH_2$	2170	20900	Hexane
$n \to \pi^*$	Acetone		2800	15	Cyclohexane
	Acetaldehyde oxime		2790	15	Cyclohexane

Structural elements causing near ultraviolet and visible absorption and colour are called *chromophores*. There kinds of chromophores exist.

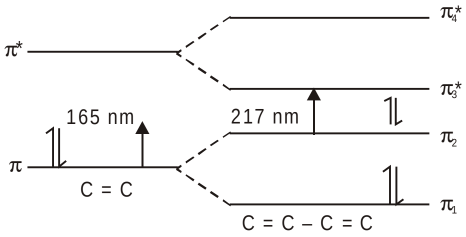
1. Groups containing π electrons and capable of undergoing $\pi \to \pi^*$ transitions e.g. $CH_2 = CH_2$ which has one chromophore, having τ_{max} 1850 in ethanol solvent.
2. Groups containing both π and *n* electrons and capable of undergoing $\pi \to \pi^*$ and $n \to \pi^*$ transitions.



3. Groups containing *n* electrons only and capable of undergoing $n \to \pi^*$ transitions.

Chromophores containing *n* electrons only are called auxochromes.

In conjugated dienes, the π orbitals of separate alkene groups combine to give two bonding orbitals (π_1 and π_2) and two antibonding orbitals (π_3* and π_4*). The $\pi_2 \to \pi_3^*$ transition in a conjugated diene is of very low energy than $\pi \to \pi^*$ or an unconjugated alkene. So $\pi_2 \to \pi_3^*$ transition of butadiene (λ_{max} = 217 nm) suffers red shift relative to $\pi \to \pi^*$ transition in ethylene (τ_{max} 171 nm).



Creation of two energy levels in 1,3 butadiene

Choice of Solvent and Solvent Effects

It has already been pointed out that the absorption bands in ultraviolet spectrum are very broad as compared with infrared or NMR spectrum.

Ultraviolet spectra of compounds are usually determined in the vapour phase or in very dilute solution. The most commonly used solvents in u.v. studies are cyclohexane, 95% ethanol and 1:4 dioxane. The most widely used is 95% ethanol because it is cheap, good solvent and is transparent down to about 210 nm. It is also a good choice when a more polar solvent is required. The most useful solvent would be that which would not absorb within the region under investigation.

So the most important point in choosing a solvent would be its absorbing effect. *Generally polar solvents like water, alcohol, esters and ketones tend to obliterate the spectral fine structure arising from vibrational effects. Further the position of* λ_{max} *is also influenced by the nature of solvent.*

APPLICATIONS OF ULTRAVIOLET SPECTROSCOPY

1. *In qualitative analysis*. The study provides an evidence in the elucidation of structures of organic compounds. For example, if there is no appreciable absorption in the region 270 to 280 nm, then the compound does not contain a benzene ring.

   Similarly if there is no absorption from 210 nm to the visible, the compound does not have conjugated unsaturation.

   If there is transparency down to 180 nm this also shows absence of isolated double bonds.

2. *In quantitative analysis.* A large number of reagents react with nm absorbing species to yield products that absorb strongly in u.v. and visible regions. Therefore, these reagents are frequently used for the determination of an absorbing species.

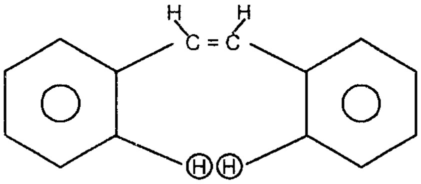
   So substances which do not show useful absorption can be determined by adding a reagent to form an absorbing complex.

3. *Analysis of organic compounds.* Large number of organic molecules absorb radiation in ultraviolet and visible region. So molecules having high molecular absorptivities can be determined directly.

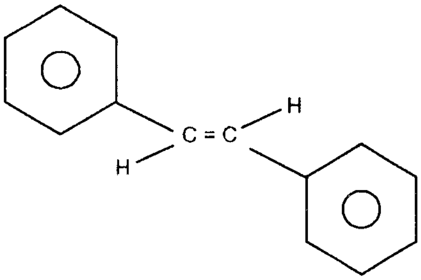
   On this basis the drug tetracycline hydrochloride has been identified. Its percentage in a tablet has also been established.

4. *Analysis of inorganic complexes.* Valuable information has been arrived at by proper choice of a chelating agent and confirmation of the structure of complexes has been arrived.
5. Besides the above, this ultraviolet spectroscopy has also helped in identifying the ortho and para forms of hydrogen molecule.
6. Absence or presence of chromophores can be detected by electronic spectra.
7. Due to the presence of conjugation, the cis and transforms can be identified.

   Due to steric hindrance by cis substituents, coplanarity and conjugation of cis polymers is hindered. As a result the absorption of trans polyenes occurs at higher wave lengths compared with the absorption of cis polyenes. The same effect is observed in cis trans stilbenes.



cis stilbene λ_{max} 1850Å



trans stilbene λ_{max} 2955 Å

CHAPTER 14

Infrared Spectroscopy

INTRODUCTION

The infra red region has been divided into three parts:

(*a*) The near infra red

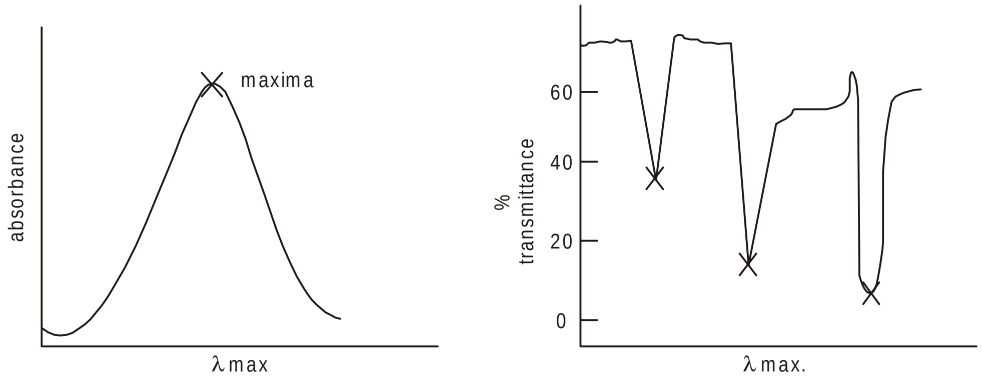
(*b*) The middle infra red

(*c*) Far infra red.

Near infra red region	Middle infra red region	Far infra red region
14400-4000 cm^{-1}	4000-667 cm^{-1} wave lenghts or	700-200 cm^{-1}
37-10 K cal per mole	10-1 K cal per mole	1-0.1 K cal per mole

The large majority of analytical applications are limited to middle infrared region. But in recent years interest has developed in near infra red and far infrared regions.

In ultraviolet spectroscopy the absorption bands appeared as maxima but in infrared spectroscopy the wave length is plotted against transmittance and hence the peaks appear as dips. In ultraviolet the absorbance is plotted against wave length while in the infrared transmittance is plotted wave length.



Curve in u.v. spectroscopy

Curve in i.r. spectroscopy

Fig. 14.1

Each dip in the spectrum is called a band or peak. The transmittance is 0 % if all the radiation is absorbed and with no absorption the transmittance is 100%. The absorption of infrared radiations can be expressed either in terms of wave length (λ) or in wave number ($\bar{\nu}$). Mostly infra red spectra of organic compounds are plotted as percentage transmittance against wave number. The relationship between wave length and wave number is as follows:

$$\text{Wave number} = \frac{1}{\text{wave length in centimeters}}$$

If $\quad$ wave length (λ) $= 2.5\ \mu, \quad \mu$ = micron

$$= 2.5 \times 10^{-4}\ \text{cm} \quad (\because\ 1\mu = 10^{-4}\ \text{cm})$$

then, $\quad$ wave number ($\bar{\nu}$) $= \dfrac{1}{2.5 \times 10^{-4}\,\text{cm}}$

$$= 4000\ \text{cm}^{-1}$$

The wave length 15μ corresponds to wave number equal to 667 cm^{-1}. Thus in terms of wave number, the ordinary infrared region cover 4000 cm^{-1} to 667 cm^{-1}.

Bond intensity is either expressed in terms of absorbance (A) or Transmittance (T)

$$A = \log_{10}\left(\frac{1}{T}\right)$$

In ultraviolet spectroscopy we have seen that there is not much difference between the vibrational and rotational levels in the energy of the molecule but i.r. spectroscopy is confined to molecules having some difference between the two energy levels. *This is why i.r. absorption spectra are often referred to as rotation-vibration spectra.*

Origin of Infrared Spectra

It has to be noted that atoms in a molecule do not always remain in fixed relative positions but when energy is supplied, three changes take place in the molecule.

(1) It may be lead to electronic transition from one orbit to another in which a line spectrum is obtained as we get in atoms.

(2) It may result in the rotation of the molecule AB as a whole or

(3) It may change the energy of vibrations of the atoms A and B in the molecule.

The following figure shows energy levels for two different vibrational states of a diatomic molecule. (Fig. 14.2)

The rotational levels are sketched for two lowest vibrational levels, $v = 0$ and $v = 1$. Since vibrational and rotational levels are quantized just like electrons, therefore, for a given molecular species these energy changes will have certain definite values.

From the figure, it is evident that the energy required for exciting emission will be least for rotation and higher for vibrational and still greater for electronic transitions. So if the excitation energy is kept so small so that it produces transition from one rotational quantum level to another within a given vibrational level, the spectrum obtained will be called **rotational spectrum**. Since the energy involved is small, these spectra are found in far infrared.

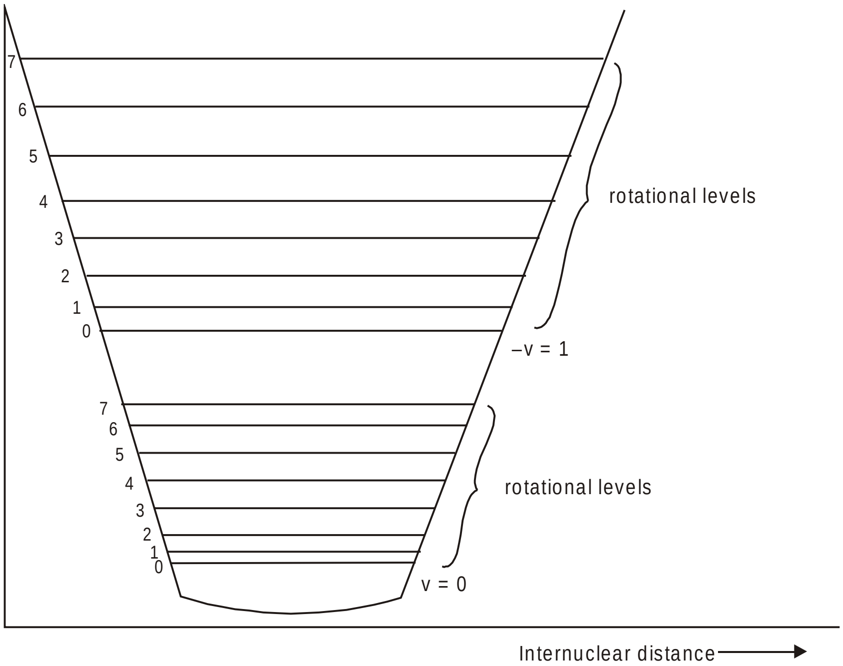


Fig. 14.2

So when energy is supplied three types of band spectra are possible.

(1) Vibrational. (2) Rotational and (3) Electronic band spectra.

Molecular vibrations

It has already been pointed earlier that atoms in a molecule are not held rigidly and absorption in the infra red region brings changes in the vibrational and rotational levels. Molecular vibrations occur when more energetic radiation in the region 10^4 to 10^2 cm^{-1} are passed through the sample of the substance. So a single vibrational energy change is accompanied by a large number of rotational energy changes. This is why the vibrational spectra appear as **vibrational-rotational bands**. The absorbed energy brings about predominant changes in the vibrational energy which depends upon:

(1) Masses of atoms present in the molecule.

(2) Strength of the bonds, and

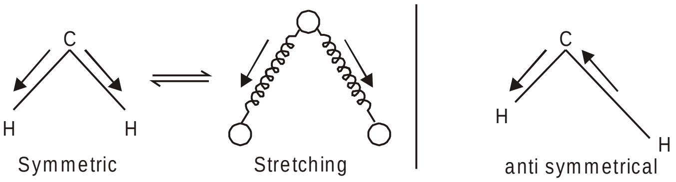
(3) The arrangement of atoms in the molecule.

It has been found that no two compounds except the enantioners have similar infra red spectra.

When infrared light is passed through the sample, vibrational and rotational energies increase..

Two kinds of fundamental vibrations are:

(*a*) **Stretching.** If the molecule is visualized as consisting of balls of different sizes tied with springs (the balls corresponding to the atoms and the springs to the bonds), the stretching will be represented as follows in which the distance between the two atoms increases or decreases but the atoms remain in the same bond axis.

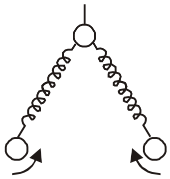


Stretching vibrations are due to stretching and contracting bonds with no change in bond angles. This stretching can be symmetric or anti symmetric. In symmetric it is in the same direction. In anti symmetric stretching, one atom approaches the central atom while the other departs from it.

This type of spectra is given by diatomic molecules with permanent dipole moments, i.e. in heteronuclear diatomic molecules and polyatomic molecules with and without permanent dipole moment.

The vibrational-rotational spectra are not exhibited by homonuclear molecules because they have no permanent dipoles.

(*b*) ***Bending.*** In this type of vibration, the position :



of the atoms change with respect to the original bond axis. Since more energy is required to stretch a spring than that required to bend it, so stretching absorptions of a bond appear at higher frequencies (higher energy) as compared to the bending absorption of the same bond.

When infrared radiation is passed through the substance energy is absorbed and amplitude of that vibration is increased when the molecule returns to its ground state by releasing the extra energy by vibrational collision a transitional processes. By absorption the temperature of the substance also increases.

The vibrational spectra of molecules gives us an information about the flexibility of the molecule i.e., the ease with which the bond length and bond angles can be distorted from their normal positions. These changes produce a change in the dipole moment of a heteronuclear molecule and an exchange of energy occurs between oscillating dipoles and the electrical field of radiation of suitable frequency. No such phenomenon occurs in homonuclear species.

TYPES OF VIBRATIONS IN POLYATOMIC MOLECULES

The infrared spectra of polyatomic molecules are very complex because of number of vibrations that can occur in a molecule containing several atoms and several bonds.

Types of Bending Vibrations (Deformations)

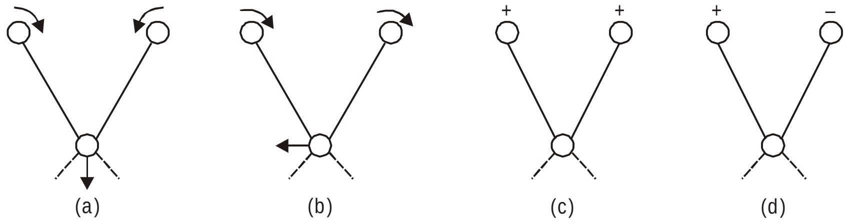
Bending operations are of four types:

(*a*) *Scissoring*. Here two atoms approach each other.

(*b*) *Rocking*. Here the movement of atoms takes place in the same direction.

(*c*) *Wagging*. Two atoms move up and below the plane with respect to the central atom.

(*d*) *Twisting*. In this type, one of the atoms moves up the plane while the other moves down the plane with respect to the central atom.



Type of bending vibrations

(a) Scissoring (b) Rocking (c) Wagging (d) Twisting

Scissoring and rocking are called in *Plane Bending* while wagging and twisting are called *out of plane Bending*.

Therefore the motion of a molecule is described in terms of

(*a*) The motion of the entire molecule.

(*b*) Rotational motion and

(c) Individual vibrations of each of its atoms.

Vibrations of Polyatomic Molecules

The value of stretching vibrational frequency can be calculated fairly easily by application of HOOK's law which may be represented as :

$$\bar{\nu} = \frac{1}{2\pi c}\left\{\frac{K}{\frac{m_1\ m_2}{m_1 + m_2}}\right\}^{\frac{1}{2}}$$

where $\bar{\nu}$ = Vibrational frequency in cm^{-1} (Wave number)

C = velocity of light cm sec^{-1} $(2.998 \times 10\ \text{cm sec}^{-1})$

m_1 = mass of one atom in *g*

m_2 = mass of second atom in *g*

K = Force constant of the band in dynes cm^{-1} $(g.\ \text{sec}^{-2})$

or

$$\bar{\nu} = \frac{1}{2\pi c}\sqrt{\frac{k}{\mu}}$$

where μ = reduced mass.

The force constant K relates with the strength of the bond. For a single bond, it is approximately 5×10^5 dynes cm^{-1}. It becomes double and triple for double and triple bonds respectively.

Thus the value of vibrational frequency of wave number depends upon :

(*i*) Bond strength, and

(*ii*) Reduced mass.

So if the bond strength increases or reduced mass decreases, the value of vibrational frequency increases. Polyatomic molecules may exhibit more than one fundamental vibrational absorption bands. The number of these fundamental bands, is related to the *degree of freedom* in a molecule and the number of degrees of freedom is equal to the number of coordinates necessary to locate all atoms of a molecules in space.

Consider a molecule containing N atoms. We can refer to the position of each atom by specifying three coordinates (*e.g.*, X, Y and Z Cartesian coordinates): Thus the total number of coordinate values is 3 N and we say that the molecule has 3 N *degrees of freedom* since each coordinate value may be specified quite independently of the others. Once all 3 N coordinates have been fixed, the bond distances and bond angles of the molecules are also fixed and no further orbitrary specification can be made. So a molecule which is of finite dimension will thus be made of rotational, vibrational and translational degrees of freedom.

3 N degrees of freedom = translational + rotational + Vibrational. C = C is expected to absorb at higher frequency than C–C because of the greater bond strength in former than in the latter. Similarly O–H stretching absorbes at higher frequency than C–C because of the smaller value of reduced mass for O–H as compared with C–C bond. The O–H should absorb at higher frequency, than F–H. But this is not true. Actually F–H bond absorbs at higher frequency because of higher electronegativity of fluorine as compared to oxygen.

Rotational degrees of freedom result from the rotation of a molecule about an axis through the centre of gravity.

Calculation of the Number of Vibrational Degrees of Freedom

Since only three coordinates are necessary to locate a molecule in space, *the molecule has always three translational degrees of freedom.*

Let us take the case of CO_2 which is a linear triatomic molecule. In general in a molecule containing more than two atoms all the four types of vibrations are possible and the addition interaction of vibrations called *coupling* occur.

In CO_2 one coupled vibration is symmetric and the other is asymmetric.

In the symmetric one, since there is no change in the dipole moment, it is not seen in the infra red spectra but there is also an asymmetric vibration, one oxygen atom approaches the carbon atom and the other moves away. Thus this asymmetrical stretching appears in the infrared spectrum in the region 2330 cm^{-1}.

The remaining two vibrational modes studied under *bending vibrations* involves scissoring. This is due to the bending motion in all possible planes around the bond axis. Since turning the plane of vibrations can not alter the energy it leads to deformation vibration to produce a peak in the region 667 cm^{-1}. This is why *CO_2 shows two absorption peaks*, one at 2330 cm^{-1} and the other at 667 cm^{-1}.

So in CO_2 the number of vibrational degree of freedom (which is 4) is calculated as follows:

Number of atoms (N) = 3

Total degrees of freedom = 3 N

= 3 × 3 = 9

Translational = 3

Rotational = 2

Vibrational degrees of freedom = 9 – 3 – 2 = 4

In general for a linear molecule, there would be two degree of rotational freedom and the degree of freedom can be calculated as follows :

Total number of atoms = N

Total degree of freedom = 3 N

Translational degree of freedom = 3

Rotational degree of freedom = 2

Vibrational degree of freedom = 3N – 3 – 2

= 9 – 5 = 4

Non-Linear Triatomic Molecules

This includes compounds like H_2O, SO_2 or N_2O. There will be three degrees of rotation because rotation about all the axis X, Y and Z will result in a change in the position of atoms and so the vibrational degree of freedom can be calculated as follows :

Total number of atoms (N) = 3

Total degree of freedom = 3N

= 3 × 3 = 9

Translational degree of freedom = 3

Rotational degree of freedom = 3

Vibrational degree of freedom = 9 – 3 – 3

= 9 – 6 = 3

So there will be 3 vibration modes.

∴ For linear triatomic molecules there will be

3 N – 5 fundamental vibrations

and for non linear triatomic molecules there will be 3 N – 6 Fundamental vibrations.

Let us apply the 3 N – 5 rule to a diatomic molecule (per force linear)

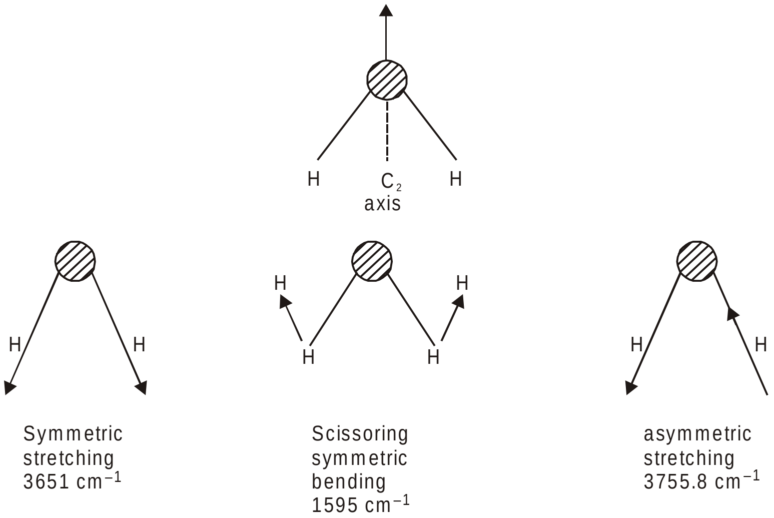
N = 2

3 N – 5 = 1

and there will be only one fundamental vibration.

Water molecule H_2O

Since the central atom is not in line with other two atoms, a symmetric vibration produces a change in dipole and this will be responsible for the infra red absorption.



This is why a stretching peak appears at 3651 cm^{-1} and due to symmetric stretching and another at 3755.8 cm^{-1} due to asymmetric stretching. A bending vibration causes an absorption at 1595 cm^{-1}.

In water since we have 3N–6 = 3 allowed vibrational modes, these are referred as normal mode of vibration (*or normal vibrations*) of the molecule. *A normal vibration is defined as a molecular motion in which all the atoms move in phase and with the same frequency*.

The normal vibrations for a linear triatomic molecule CO_2 is as follows:

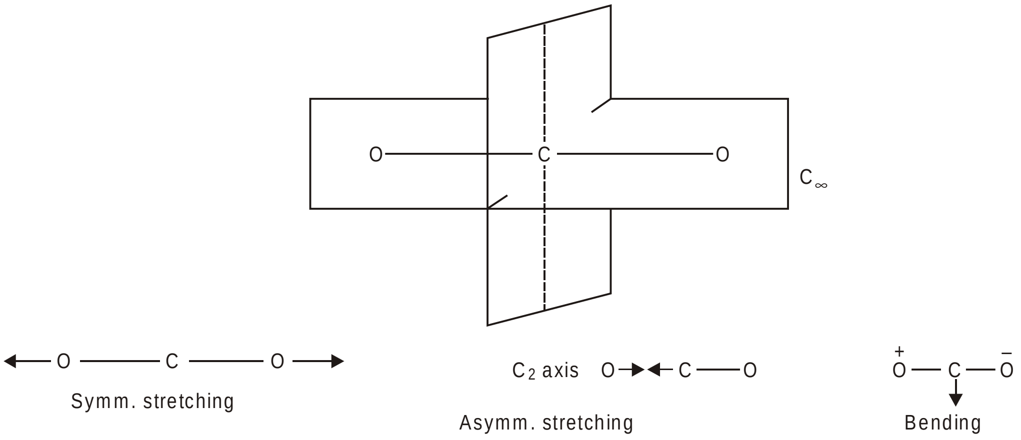


Fig. 14.3

This molecule has two different sets of symmetry axes. There is a C_2 axis passing through the carbon atom at right angles to the bond direction and there is an ∞ fold axix (C_∞) passing through the bond axis itself. The names symmetric stretch and anti symmetric stretch are self evident. The symmetric stretch produces no dipole which remains zero. So this *vibration is not infra red active*.

For linear triatomic molecules 3 N – 5 = 4 and we expect four vibrational modes instead of three as shown in the fig. Out of the four there are *two* vibrations, one in the plane of the paper and the other in which the oxygen atoms move simultaneously into and out of the plane. The two sorts of motion are termed degenerate and so we have only three vibrations.

Vibrational degree of freedom in C_6H_6

This is a non linear molecule and vibrational degree of freedom can be calculated as follows:

Number of atoms (N) = 12

Total degree of freedom = 3 × 12 = 36

Translational = 3

Rotational = 3

Vibrational degree of freedom = 36 – 3 – 3

= 30

So theoretically there should be 30 fundamental bands in the infrared spectrum. But this theoretical number is seldom obtained, because of the following reasons:

(*a*) Some fundamental vibrations might fall outside the region.

(*b*) Some are two weak to be observed as bands.

(*c*) Some are so close that they overlap (called degenerate vibrations).

(*d*) Some do not appear for want of a change in dipole moment.

(*e*) There may appear some additional bands called combination bands, difference bands and overtones.

It is to be noted that absorptions due to bending vibrations occur at frequencies below 1500 cm^{-1}. *This region below 1500* cm^{-1} *is called finger print region and in this region, bands are observed due to combination or overtones.*

Some polyatomic molecules like CO_2 CS_2 or $SnCl_4$ which do not possess a permanent dipole, but develop a fluctuating dipole due to certain modes of vibrations also respond to infrared region of electro magnetic radiation.

Factors Influencing Vibrational Frequencies

We know that the probable frequency or wave number of absorption can be calculated by the application of Hook's law. But this calculated value is never equal to the observed experimental value. The difference is due to the structure of the molecule in the immediate neighbourhood of the band and since the force constant of the band changes with electronic structure, the absorption frequency is also shifted.

Following are some of the factors responsible for shifting the vibrational frequencies from their normal value:

1. *Bond strength:* Stretching vibrations occur in order of bond strength and stronger the bond, greater is the amount of energy required to stretch it and since the bond strength of some bonds is in the order as shown below, their stretching frequencies are also shown with them.

   $C\equiv C$ > $C=C$ > $C-C$

   $-2200\ \text{cm}^{-1}$ $-1650\ \text{cm}^{-1}$ $-1200\ \text{cm}^{-1}$

   Similarly

   $C-H$ > $C-C$

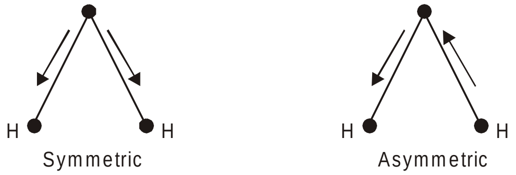
   $-3000\ \text{cm}^{-1}$ $1200\ \text{cm}^{-1}$

   Since the mass of C–H bond is much less than that of C–C bond, this factor is also accounted for in observed frequencies.

   Therefore (*a*) vibrational frequency increases with the strength of the bond and

   (*b*) C–H and O–H stretchings occur at higher frequencies than C–C or C–O stretchings.

2. *Coupled vibrations*. For an isolated C–H bond there will be one stretching absorption frequency but in case of a methylene group, two absorptions will occur depending on symmetric and asymmetric vibrations.



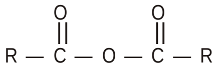
The asymmetric vibration will occur at higher wave number compared with the symmetric vibration. *These are called coupled vibrations because they occur at different frequencies than required for an isolated C–H stretching*.

Similarly coupled vibrations of CH_3 group take place at different frequencies compared to CH_2 group.

For methyl group symmetric and asymmetric vibrations are as follows :

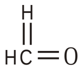
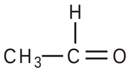
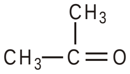
Fig. 14.4 Vibrations in methyl group

Sometimes the two vibrational levels have the same energy.

Acid anhydrides having the structure  $R-\overset{\overset{O}{\|}}{C}-O-\overset{\overset{O}{\|}}{C}-R$ and having two C = O groups show absorptions between 1850-1800 and 1790-1745 cm^{-1}. So there is a difference of about 65 cm^{-1}. This is due to difference between symmetric and asymmetric stretching.

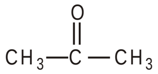
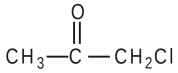
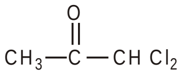
3. *Electronic effects*: Changes in the absorption frequency for a particular group take place when the substituents in the neighbourhood are changed. The frequency shifts, in these cases may be due to inductive, mesomeric or due to field effects and there will be combined effect due to all. The effect of one can only be estimated approximately.

Let us consider the case of the presence of alkyl group on the stretching frequency of C = O group. The alkyl group exerts a + I effect. It lengthenes or weakens the bond and lowers the force constant and wave number of absorption decreases. This is marked in the following compounds, having as C = O group.

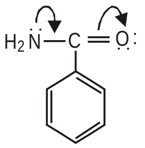
Compound	*No. of alkyl group*	*Stretching frequency*
 $H\overset{\overset{H}{\|}}{C}=O$	NIL	1750 cm^{-1}
 $CH_3-\overset{\overset{H}{\vert}}{C}=O$	One	1745 cm^{-1}
 $CH_3-\overset{\overset{CH_3}{\vert}}{C}=O$	Two	1715 cm^{-1}

It is to be noted that the aldehydes absorbs at higher wave number than ketones.

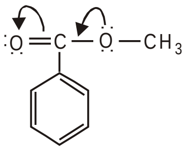
If the compound has an electronegative atom or group which exerts a - I effect, this increases the force constant or bond order and the wave number of absorption rises, as is clear from the following :

Compound	*Atom having -I effect*	*Stretching frequency*
 $CH_3-\overset{\overset{O}{\|}}{C}-CH_3$	NIL	1715 cm^{-1}
 $CH_3-\overset{\overset{O}{\|}}{C}-CH_2Cl$	One	1725 cm^{-1}
 $CH_3-\overset{\overset{O}{\|}}{C}-CH\,Cl_2$	Tow	1740 cm^{-1}

In some cases where the lone pair of electrons present on an atom is in conjugation with the double bond of a group, like carbonyl, the mobility of the lone pair matters, as in the following :



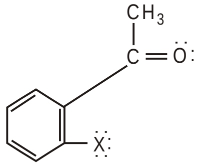
Benzamide
νc = 0 1663 cm^{-1}



Phenyl acetate
νc = 0 1730 cm^{-1}

Since nitrogen atom is less electronegative than oxygen, the electron pair of nitrogen on the amide is more mobile and participates more in conjugation. Due to this greater degree of conjugation to νC = O absorption in amides is much less than in esters.

In ortho substituted compounds, the lone pairs of electrons on two atoms influence each other through space interactions and change the vibrational frequencies of both the groups. This is *called field effect*.



The non bonding electrons on oxygen and halogen atom cause electrostatic repulsions. This makes it to go out of the plane of the double bond. The conjugation is diminished and absorption occurs at higher wave number.

4. *Hydrogen bonding:* Hydrogen bonding *brings about downward frequency shifts*. In general, the *stronger the hydrogen bonding greater is the absorption towards lower wave number than the normal value*.

Two types of hydrogen bonding can be readily distinguished in infra red spectroscopy. The intermolecular hydrogen bonds give rise to broad bands whereas bonds arising from intramolecular H bonds are sharp and well defined.

Intermolecular hydrogen bonds are concentration dependent. On dilution, the intensities of such bonds decrease and finally disappear. Intramolecular hydrogen bonds are independent of concentrations.

Hydrogen bonding in O–H and N–H compounds, deserve special mention. Mostly non-associating solvents like CS_2, $CHCl_3$ or CCl_4 are used, with them because some solvents like benzene, acetone etc. influence O–H and N–H compounds to a considerable extent. As nitrogen is less electro negative than oxygen hydrogen bonding in amines is weaker than in a alcohols. Thus ν N–H is 3500 cm^{-1} in but in aliphatic alcohols a sharp band appears at 3650 cm^{-1}.

Intramolecular hydrogen bonding can be observed in dilute solutions of di and poly hydroxy compounds in CCl_4, where no intermolecular hydrogen bonds are formed. Under these conditions a number of cyclic and acyclic diols have two bonds and others have single band in the O-H stretching mode region.

INSTRUMENTS

The IR spectrophotometers are of two types:

1. Single beam or
2. Double beam

The single beam instrument measures directly the amount of energy transmitted by the sample. They give the most accurate transmittance measurements and is particularly helpful for quantitative analysis. It has simpler and more reliable systems than double beam.

The double beam is particularly useful in qualitative analysis and most IR spectrophotometers operate on the double beam principle. A simplified double beam IR spectrophotometer has been given in the following figure with its essential units and functions.

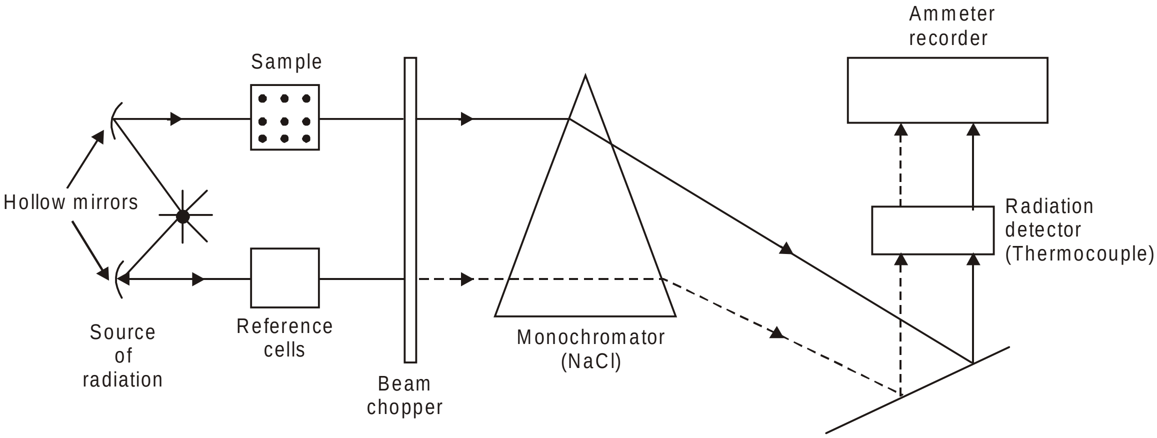


Fig. 145 A double beam IR spectrophotometer

SOURCE OF RADIATION

This is usually an electrically heated filament whose rays are separated by hollow mirrors into two beams, one for sample and the other for reference cell.

Cells

These are either containers one containing the sample dissolved in an NaCl inert solvent and the other with the solvent only.

One cell containing the sample embedded in KBr add the other containing only pure KBr for reference.

Beam chopper

The beam chopper forces radiation to come alternately from the sample and the reference cell.

Monochromator

It consists of a prism of NaCl which varies the wave length, controlled by the recorder.

Radiation detector

A thermocouple as radiation detector converts the alternating IR beams from the sample and reference cell into an alternating electric current.

Ammeter recorder

It records the intensities of current from the sample.

Since glass is opaque for IR spectroscopy, alkali halide optics must be used.

Sampling techniques

Various techniques can be employed for placing the sample in the path of infrared beam depending on whether the sample is a gas, liquid or solid, since the inter molecular forces of abtractions are most operative in solids and least in gases, and since this affects the frequencies of absorption therefore, it is important to state the physical state of the sample for correct interpretation.

Solids

The solids may be examined as alkali halide mixture and usually NaCl is used because it is transparent throughout the infra red region. Potassium bromide also serves the purpose well. The substance under examination should also be perfectly dry because water absorbs strongly at about 3710 cm^{-1} and also at 1630 cm^{-1}.

The solid sample is then ground with KBr and is then made into a disc after drying under elevated temperature at high pressures. A blank disc of KBr is prepared which may be put in the path of a reference beam. Discs obtained from a poorly ground mixture scatter more light than they disperse.

Spectrum of solid can also be obtained from a mull or paste. Some commonly used mulling reagents are (*i*) nujol (*ii*) hexachlorobutadiene or (*iii*) chlroflurocarbon oil etc. *Nujol is the most commonly used reagent which is a mixture of liquid paraffinic hydrocarbons of high molecular weights*. Solid samples can also be examined in solutions

Liquids

The liquid whose spectrum is to be recorded is squeezed between two sodium chloride plates which are transparent to infrared light. For samples that contain water, plates may be constructed with calcium fluoride.

The pair of sodium chloride plates enclosing the liquid is then placed in the path of the sample beam and spectra recorded.

Gases

Very few organic compounds can be examined as gases. The gaseous sample is introduced into a gas cell having the walls made up of sodium chloride. This cell can be directly put in the path of sample beam. The gas cell is usually 10 cm long.

Solutions

It is most convenient to determine the spectrum in solutions. Excellent solvents are those that have poor absorptions of their own. These solvents absorbs in one region or the other. Some important solvents are (*i*) Chloroform (*ii*) carbon tetrachloride or (*iii*) carbon disulphide.

Water can not be used as solvent as it absorbs in several regions of the IR spectrum.

The sample is dissolved in 1-5 % of the solvent and it is then placed in a solution cell consisting of transparent windows of alkali metal halides. A second cell containing pure solvent is then placed in the path of reference beam to cancel out solvent interferences.

Finger print region

One of the important functions of the infrared spectroscopy is to determine the identity of two compounds. The infrared region 4000 cm^{-1} –650 cm^{-1} is of great importance in studying an organic compound. Since IR spectra contain a number of bands no two compounds will have the same IR spectrum (except optical isomers). Thus IR spectra may be regarded as finger print of a molecule.

Finger print can be sub divided into three regions:

(*i*) Region : 1500-1350 cm^{-1}

It includes gem. dimethyl near 1380 cm^{-1}

NO_2 at 1350 cm^{-1}

(*ii*) Region 1350-1000 cm^{-1}

It includes alcohols, esters, lactones and acid anhydrides.

Phenols absorbs at 1200 cm^{-1}

Esters lu 1380. 1050 cm^{-1}

(*iii*) Region : below 1000 cm^{-1}

It distinguishes between cis and trans forms in alkenes. The higher value in alkenes shows that hydrogen atoms are trans with respect to each other.

Table 14.1 Characteristic group Absorptions in IR spectra of organic molecules.

Position of absorption	*Vibrations Group*	*Type*	*Occurrence in organic compounds*
3700-3200	$O^{\delta-}$-$H^{\delta+}$	Stretching	Alcohols, phenols, carbocyclic acids.
	$N^{\delta-}$-$H^{\delta-}$	Stretching	Primary and secondary amines, amides.
3220-3300	$\equiv$C-H	Stretching	Terminal alkynes
3100-3000	$=\underset{\vert}{C}-H$	Stretching	Alkenes
3100-3000	>C-H	Stretching	Aromatics
3000-2700	$-\overset{\vert}{\underset{\vert}{C}}-H$	Stretching	Compounds with CH_3 and CH_2 groups.
2300-2100	$C\equiv C$	Stretching	Alkynes
1820-1000	$>C^{\delta+}=O^{\delta-}$	Stretching	Carboxylic acids, aldehydes and ketones
1680-1500	>C = C<	Stretching	Aromatics, alkenes
1550-1500	$-N\begin{smallmatrix}\nearrow O\\ \searrow\!\!\searrow O\end{smallmatrix}$	Stretching	Nitro compounds

1470-570	$=\overset{\mid}{C}-H$	Bending	Aromatics, alkenes
	$\geqslant\overset{\mid}{C}-H$	Bending	Alkanes
1360-1030	$\geqslant\overset{\delta+}{C}-\overset{\delta-}{H}<$	Stretching	Amines, amides
780-500	$\geqslant\overset{\delta+}{C}-\overset{\delta-}{X}$	Stretching	Alkyl and aryl halides
700-550	$\geqslant\overset{\delta+}{C}-\overset{\delta-}{S}$	Stretching	Thioethers and disulphides.

In very small molecules such as CH_4 or C_2H_2 the molecule vibrates as a whole and all atoms are involved equally in vibrational excitation and not all vibrations can be seen. Generally different groups of large molecules are not excited to the same extent. Polar groups takes preference and as a result the IR spectra of large molecules show IR bands of *group vibration* rather than of molecular vibration.

Structural influences such as conjugation or configuration and intra and inter molecular attractions hydrogen bonding in particular shift the IR bands of the groups involved.

APPLICATIONS OF SPECTROSCOPY

Infrared spectrum of a compound gives more information than is normally available from the electronic spectra.

1. It is used for rapid detection of functional groups.

   In this technique almost all groups absorbs characteristically within a definite range. Thus a strong IR band at 1800 to 1600 cm^{-1} in the IR spectrum of an unknown compound indicates that a carbonyl group is present. Identical compounds have identical IR spectra. Molecules with identical or similar shapes of their IR spectra in the finger print region have the same or a similar skeleton of atoms.

   The shift in the position of absorption for a particular group may change with the change in the structure of the molecules. Thus conjugation of multiple bonds shifts the IR absorption to lower wave numbers.

   Thus

$CH_3–CH_2\ C\equiv N$ Propionitrile.	$–C\equiv N$	Stretch at 2250 cm^{-1} no conjugation.

   But

$CH_2–CH\text{-}C\equiv N$ Acrylonitrile	$–C\equiv N$	Stretch at 2230 cm^{-1} due to conjugation.

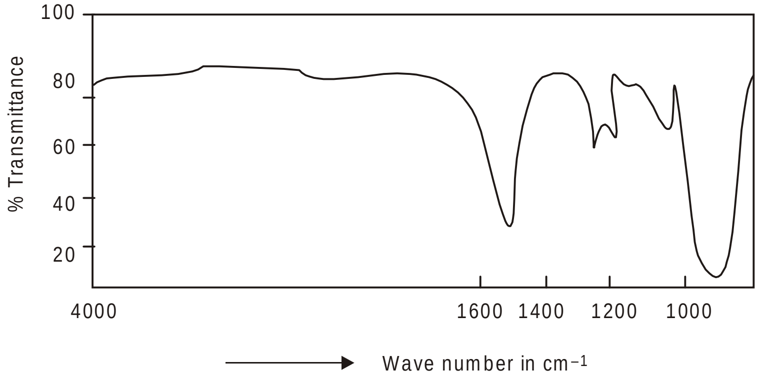
2. Presence of hydrogen bonds. Shift of IR bonds to lower wave numbers indicates the presence of hydrogen bonds. This is absorbed in alcohols, animes, carboxylic acids and amides

   e.g. -OH stretch band of free alcohols is between 3650 and 3600 cm^{-1} in vapour phase but -OH stretch band of alcohols in liquid phase is between 3600 and 3200 cm^{-1}.

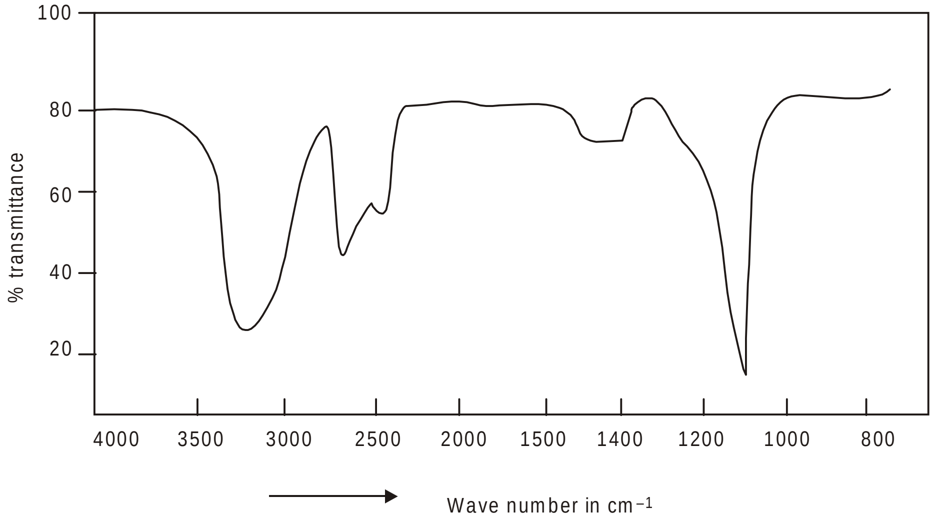
The shift in the absorption position helps in predicting this factors which cause this shift. Some of the factors which cause this shift from its characteristic wave number are inductive effect, conjugation, angle or strain and hydrogen bonding etc. Therefore, it is a very reliable technique for disclosing the identity of compound.

3. Impurities in a compound can be detected from the nature of bands which no longer remain sharp and well defined.
4. When the presence of a carbonyl group (> O = O) has been established further study will reveal whether the carbonyl group is aldehyde, ketonic, ester or samide etc. Aldehydes can be recognised by its characteristics C-H stretching, esters from its C-O stretching and amides for N-H stretching.

IR Spectra of Some Compounds



I.R. spectra of carbon tetrachloride



I.R. spectra of methanol

CHAPTER 15

Nuclear Magnetic Resonance Spectroscopy

INTRODUCTION

Nuclei of atoms with odd numbered masses or with even masses but odd atomic numbers possess a nuclear spin. Atoms with even masses and even atomic numbers do not have nuclear spins. These spinning nuclei behave as tiny magnets.

So the magnetic properties occur with those nuclei, the examples of which are:

1. Odd mass number and odd atomic number:

   $_{1}H^{1}$, $_{7}N^{15}$ $_{15}P^{31}$

2. Even masses and odd atomic number: $_{7}N^{14}$
3. Odd mass numbers and even atomic number: $_{6}C^{13}$

The spin numbers l have values 0, 1/2, 3/2, or 5/2 and so forth. If 1 = 0 the nucleus represents no spin.

If the sum of the protons and neutrons is odd, the spin number l is half integral. For example H^{1}, C^{13} and P^{31} have $l = 1/2$ and a uniform charge distribution.

B^{11}, Cl^{35}, Br^{81} have $l = 3/2$.

If both protons and neutrons are even numbered l = zero. C^{12} and O^{16} are examples and they give no NMR signals.

The best example of NMR spectroscopy is protons $_{1}H^{1}$ where $l = 1/2$

Since magnets line up when influenced by magnetic field, so when placed in an external magnetic field with the direction ↑ and strength H, the magnetic moment of a spinning nucleus will line up *with* ↑ or *against* the external field H. Alignment with the field H is more stable and is characterised by a lower potential energy E′ relative to the energy E″ required for the alignment against the field. (Fig. 15.1)

Consequently the stronger the magnetic field H, the greater will be the energy difference ΔE between both alignments and

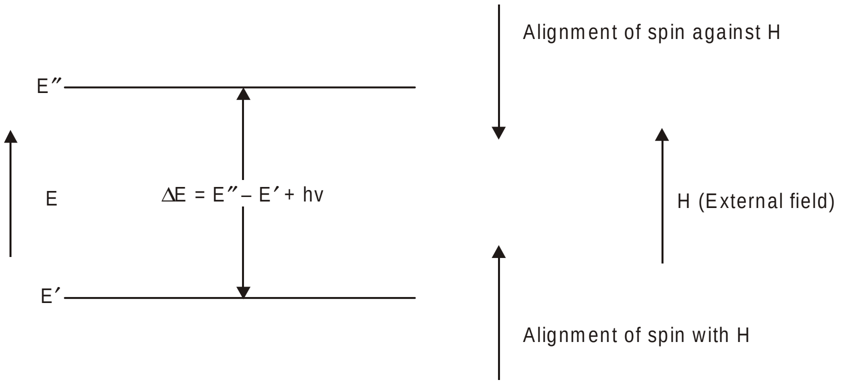


Fig. 15.1 Alignment of nuclear spin in the magnetic field

$$\Delta E = \text{const} \times H$$

$$= \frac{\nu h}{2\pi} \times H$$

where H = external magnetic field strength (in gauss)

h = Planck's constant (6.62×10^{-27} erg^{-s})

v = gyromagnetic ratio (26.75 for protons specific for each nucleus)

v = gyromagnetic ratio = $\frac{2\pi\mu}{h\text{I}}$

here μ = magnetic moment of the spinning bar magnet.

I = spin quantum number of the spinning magnet.

Absorption of energy $\Delta E = \frac{vh}{2\pi} \times H$ by a spinning nuclens, flips the nuclear magnet over from the more stable alignment with the field to the less stable one against it. **This event is called nuclear amagnetic resonance (NMR). Quantitatively NMR takes place when the energy quanta hv of electromagnetic radiation make up the energy difference between both alignments (↑ and ↓) at field strength H**

$$hv = \frac{vh}{2\pi} H$$

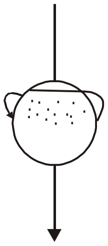
$$= \Delta E$$

As a result the frequency of the absorbed radiation is proportional to the strength of the external field H.

$$v = \frac{v}{2\pi} \times H$$

$$= \text{const.} \times H$$

Processional motion. Consider a spinning top. It also performs a slower waltz like motion in which the spinning axis of the top moves slowly around the vertical.



This is processional motion and the top is said to be processing around the vertical axis of earth's gravitational field.

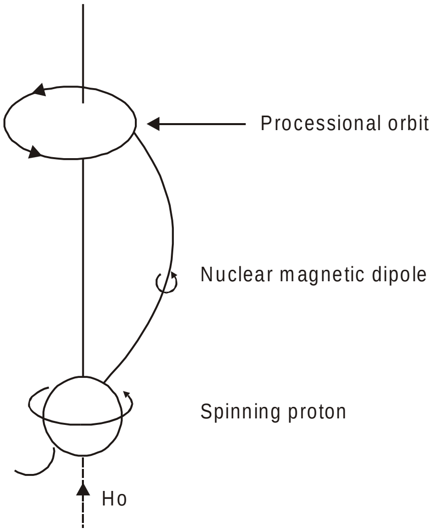


Fig. 15.2 Proton processing in a magnetic field Ho

It has been found that

$$\omega = v\text{Ho}$$

where W = angular processional velocity and

Ho = applied field in gauss and

v = gyromagnetic ratio.

A relationship which correlates electromagnetic frequencies with the magnetic field is

$$v \text{ Ho} = 2\pi v$$

where v is the frequency of electomagnetic radiation. The value of this frequency (v) is called *processional frequency*.

The processional frequency may be defined as the number of revolutions per second made by the magnetic moment vector of the nucleus around the external field, Ho. Alternatively, the processional frequency of the spinning bar magnet (nucleus) may be defined as equal to the frequency of electromagnetic radiations in megacycles per second necessary to induce a transition from one spin state to another. The main atom of organic molecules ${}^{12}_{6}C$ does not have a nuclear spin. But protons present in most organic molecules and proton magnetic resonance can be observed in such compounds. At a field strength of about 10^4G, the frequency required to flip the spinning hydrogen nucleus is of the order of 10^8Hz (1 Hz = 1 cps)

NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY: HYDROGEN NUCLEI

If a substance is placed in a magnetic field of variable strength and exposed to radiation with constant frequency and the field strength is then varied, the energy differene ΔE between both alignments of the nuclear magnets changes accordingly. At H_i absorption of radiation takes place and a resonance signal is observed. Usually the field is kept constant and absorption is observed at a certain frequency (Fig. 15.3)

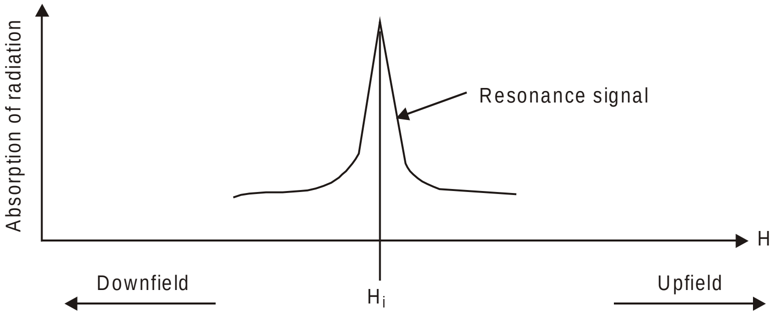


Fig. 15.3 NMR spectrum of a spinning nucleus

For one kind of base nuclei e.g., protons, the resonance signal always appears it the same field strength Fig. 15.3. But in atoms and nuclei the hydrogens and protons are enveloped by atomic orbitals e.g. S orbitals. Therefore, when placed in a strong magnetic field of an NMR spectrometer, the electrons circulate and this circulation of electrons induces a secondary field. This induced field with strength Hind opposes the external one at the nucleus. Therefore, the nucleus feels a weaker field H_{actual} relative to the external field H

$$H_{actual} = H - H_{ind.}$$

Therefore, the nucleus is *shielded* by the electronic orbitals with the result that the hydrogen atoms require a higher field strength for NMR relative to protons by themselves.

CHEMICAL SHIFTS AND NUMBER OF SIGNALS

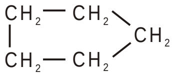
The difference in position of NMR signals due to different intramolecular environment is called *chemical shift*.

Signal positions is NMR spectra are referred relative to the signal of a standard, which in organic molecules is usually tetramethylsilane (TMS), $(CH_3)_4$ Si. It has 12 equivalent methyl protons and shows one signal at an extremely high field. The NMR signal of most organic compounds appears at a lower field.

So the number of signals in the NMR spectrum tell the number of different sets of equivalent protons in a molecule. Each signal corresponds to a set of equivalent protons. Therefore, protons with identical electronic environments are identical and have *the same chemical shift. Protons with different electronic environment (different adjacent atoms, different types of bond) are non equivalent and have different chemical shifts*.

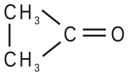
Let us find out the equivalent protons (signals) in the following type of compounds:

(a)



Cyclopentane
(One signal)

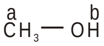
(b)



acetone
(One signal)

In cyclopentane all the ten protons are in similar environment. Therefore, only one signal is observed. Similarly we have only one signal for acetone.

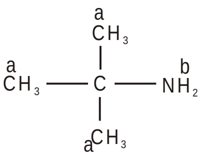
(b)



$$\overset{a}{CH_3}-\overset{b}{OH}$$

2 NMR
Signals

(b)



ter-butylamine.
2 NMR signals

In the above examples two NMR signals will be observed because they have two sets of non-equivalent one with methyl protons and the other marked with *b*.

(*c*) Compounds having more than two signals are as follows:

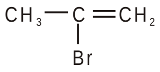
$$\overset{a}{CH_3}-\overset{b}{CH_2}-\overset{c}{NH_2}$$

3 signals

$$\overset{c}{CH_3}-\overset{b}{CH_2}-\overset{a}{CH_2}-Cl$$

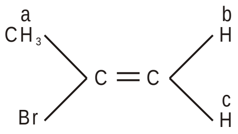
3 signals

So we can say that a particular set of protons are chemically equivalent if they remain in exactly similar environment. The case of 2 bromo propene affords another interesting example:

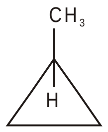


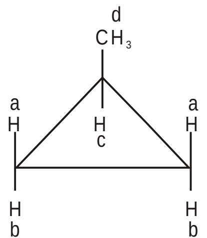
$$CH_3-\underset{Br}{\underset{|}{C}}=CH_2$$

It appears that it will have two sets of equivalent protons or two signals. But actually it has three sets of protons in it because the H^b and H^c are not in exactly similar environment.



Similar considerations apply in case of substituted cycloalkanes, e.g., methyl cyclopropane



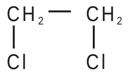


4 NMR signals

Although it has three sets of protons but actually 4 signals are observed from its stercochemical structure.

The following are some examples to further clarify the above point. The compound with the stereochemical structure along with the number of NMR signals is given:

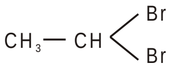
(*i*)


$\underset{Cl}{CH_2}-\underset{Cl}{CH_2}$

1, 2 dichlorethane

One signal

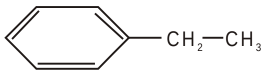
(*ii*)



1, 1 dibromoethane

Two signals

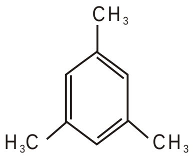
(*iii*)



Ethyl benzene

Three signals

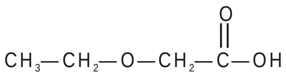
(*iv*)



Mesitylene

Two signals

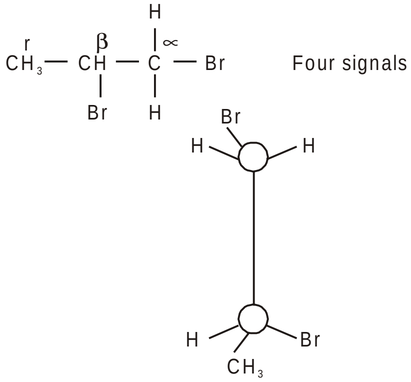
(*v*)


$CH_3-CH_2-O-CH_2-\overset{\overset{O}{\|}}{C}-OH$

Ethoxy acetic acid

Four signals

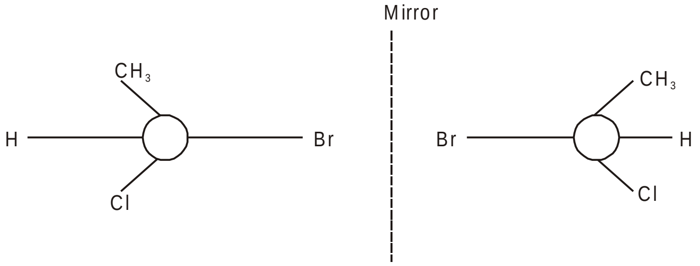
(*vi*) Let us consider the structure of α, β, dibromo propane



$$\overset{r}{CH_3}-\underset{Br}{\overset{\beta}{CH}}-\underset{H}{\overset{H\ \propto}{C}}-Br$$

An examination of the above stereochemical formula or its model would easily show that the two hydrogens attached to the α carbon are stereochemically different. So its NMR spectrum will have 4 signals and this is actually so.

NMR spectra do not distinguish between mirror images. The two enantiomeric forms of 1, 1 - bromo chloroethane contain *enantiotopic protons* which are magnetically equivalent and only one NMR signal of this pair of enantiomeric protons is observed. In contract *distereotopic protons* (e.g. the two protons attached to 2-bromopropane) are magnetically non equivalent and each proton gives a separate signal.



Instrumentation

NMR spectrophotometer makes use of

1. A magnet
2. The magnetic field sweep
3. Radiofrequency source
4. A signal detector and recording system
5. The sample holder

The detector system is used to note that energy is being transferred from the radiofrequency beam to the nucleus radio frequency.

The sample is taken in a glass tube which is placed between pole faces of a magnet. A radio frequency source (v = 60 mega cycles sec^{-1}) is made to fall on the sample. It is done by feeding energy into a coil wound round the sample tube. A signal is detected if the nuclei in the sample resonates with the source. The energy is thus transferred from the source via nuclei to the detector coil.

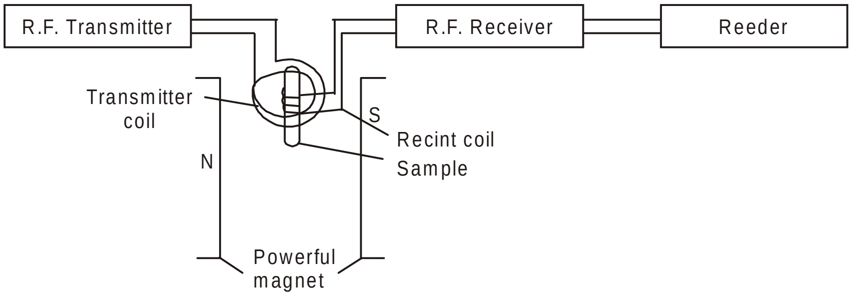


Fig. 15.4 Schematic diagram of an NMR spectrometer

The protons being in different electronic environment in a molecule do not resonate at exactly 60 mega cycles sec^{-1}. Therefore, radio frequency source is held steady and field strength is varied by placing small electromagnet to the pole faces of the main magnet. Thus as the field strength increases the processional frequency of each proton increases until resonance with radio frequency source takes place and due to proton resonance a peak appears on the chart paper. Thus a series of peaks corresponding to different applied field strengths are obtained. Each peak means a set of protons.

Fig. 15.3 represents the simplest NMR spectrum. When there are more than one kind of protons in a molecule, a more complex NMR is obtained. Toluene for example has two resonance signals suggesting that toluene contains two types of protons.

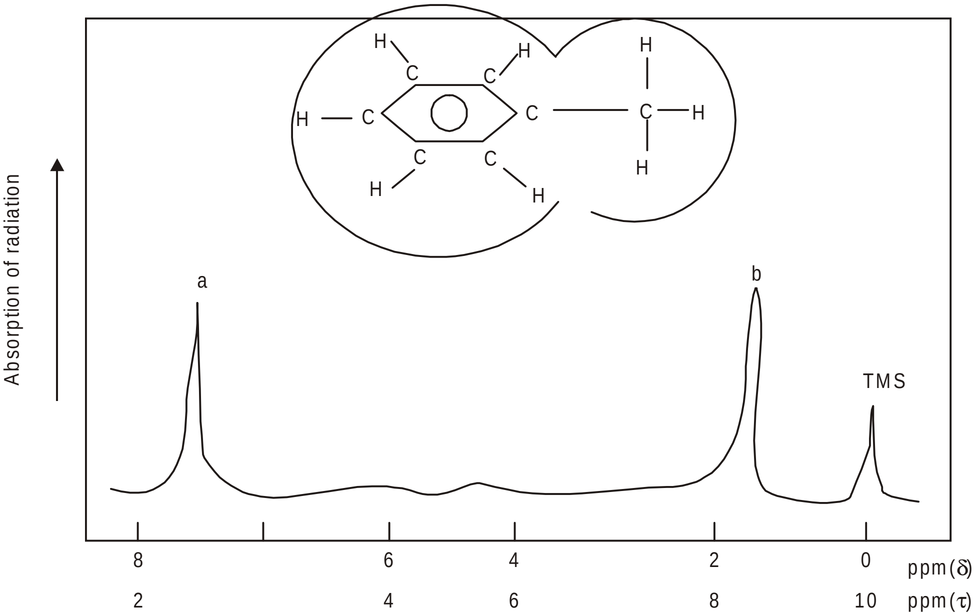


Fig. 15.5 NMR spectrum of toluene

A compound for NMR spectroscopy must be a liquid or solid which can be put in a solution. The usual solvents are deuterochloroform ($CDCl_3$), deuteroacetone (CD_3-CO-CD_3) or deuterium oxide (D_2O).

In the above examples we have been dealing with molecules containing protons (^1H) as nuclei with magnetic properties. This specialized NMR spectroscopy is often referred to as *proton magnetic resource (PMR) spectroscopy.* We have already seen that when an organic molecule is placed in a magnetic field, its elections are made to circulate and in so doing they induce secondary magnetic field. This circulation of electrons about the protons itself generates a magnetic field which opposes the applied field, with the result that the field felt by the protons is diminished. This is called the shielding of the proton. So the proton is shielded when the induced field opposes the applied field but when the induced field reinforces the applied field the proton is deshielded and the field felt by the proton is increased. So a shielded proton requires a stronger field and a deshielded proton requires a weaker field to give effective strength at which absorption will occur. This is expressed by saying that:

Deshielded proton would give the resonance signal upfield and a shielded proton would absorb down field. These shifts in the NMR signals are what are known as *Chemical shifts*. These shifts are measured with reference to a standard which is tetramethylsilane (TMS).

It has been noted that electron-withdrawing substituents (e.g., halogens) on the carbon bearing the proton deshield the proton, while electron releasing substituents (e.g. alkyl group) *shield* the protons.

Tetramethylsilane (TMS) is referred as the standard because of the low electronegativity of silicon, the shielding of equivalent protons in tetramethylsilane is greater than most of the organic compounds. Therefore, the NMR signal for a particular proton in a molecule will appear at different field strengths compared with a signal for TMS:

Tetramethylsilane has some other advantages which are:

(*i*) It is miscible with almost all organic substances.

(*ii*) It has no intermolecular association with the sample.

(*iii*) It is highly volatile and therefore can be easily recovered from the system.

(*iv*) Its resonance is sharp and intense since all twelve hydrogen nuclei are equivalent (*i.e.*, have the same chemical environment) and hence absorb at exactly the same position.

Thus if about 5% of TMS is added to a sample and the complete NMR spectrum produced, the sharp high field resonance of the TMS is easily recognised and can be used as a standard from which to calibrate the spectrum and to measure the chemical shift positions of other molecular groupings.

EXPRESSION OF CHEMICAL SHIFTS

We have seen that the NMR signal for a particular proton in a molecule appears at different field strengths compared with a signal from TMS difference, called the chemical shift, expressed by δ is obtained by dividing the differences in field strength or frequencies by the field strength or frequency at which the signal appears for the standard.

$$\delta = \frac{\text{H sample} - \text{H}_{\text{TMS}}}{\text{H}_{\text{TMS}}}$$

or

$$\delta = \frac{v\ \text{sample} - v_{\text{TMS}}}{v_{\text{TMS}}}$$

It is not measured in gauss

So protons with the same chemical shift are called equivalent protons. Non equivalent protons have different chemical shifts expressed by δ (Delta) pr τ (Tau) scales. Since majority of organic compounds have protons resonating at lower fields than the protons of tetramethylsilane, δ for chemical shift for TMS has been given a value zero, a scale has been given in which most proton resonances are of the same sign and any protons or set of protons absorbing at a field lower than TMS is given a positive value for δ.

The value of δ is expressed in parts per million (ppm) and most chemical shifts have δ values between 0 and 10. In the tau or τ scale, the signal for TMS is taken as 10 ppm. The two scales are related by the expression:

$$\tau = 10 - \delta$$

and shown diagrammatically as follows:

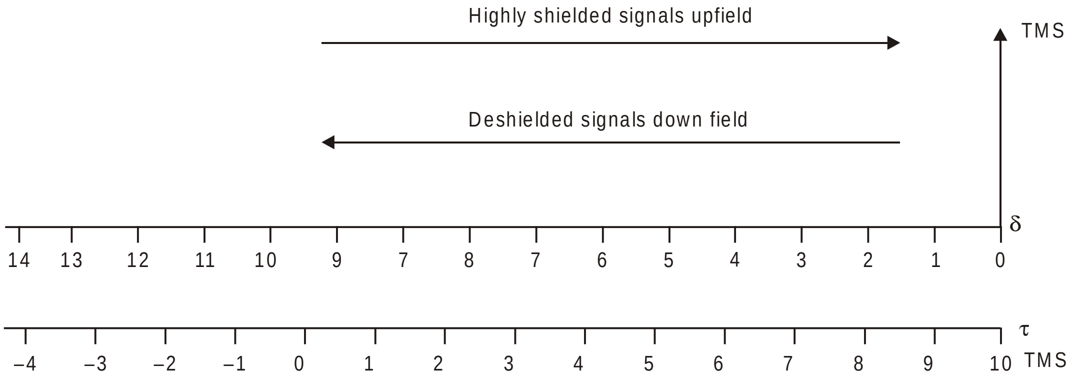
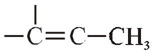
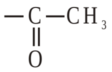


Fig. 15.6 Diagrammatic representation of tau and delta signals

NMR signal for TMS (highly shielded) appears at the extreme right of spectrum with δ = 0 ppm. Greater the deshielding of protons, larger will be the value of δ.

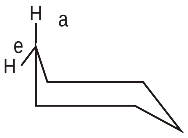
The types of protons with different chemical shifts in ppm for some organic species are given in the following table.

Table 15.1

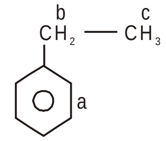
Group and type of protons	*Chemical shifts of* $^{1}_{1}H$		*Compund*
	τ	δ	
$(CH_3)_4$ Si	10	0	Tetramethylsilane (standard)
$\geqslant C-CH_3$	9	1	
$\geqslant C-CH_2-C\leftarrow$	8–9	2 to 1	Alkanes
$\geqslant CH$	8	2	
 $-\overset{\vert}{C}=C-CH_3$	8.2	1.8	Alkenes
Acetylenic	8–6.5	2–3.5	Alkynes
$C\equiv C-H$			
$H-C-OH$	6.6 – 6	3.4 – 4	Alcohols
$H-C-OR$	6.7 – 6	3.3 – 4	Ethers
$H-C-COOR$	8 – 7.8	2 – 2.2	Esters
 $-\underset{\underset{O}{\Vert}}{C}-CH_3$	7.7	2.3	Ketones
$H-C-COOH$	8 – 7.5	2 – 2.5	Acids
RCHO	1 – 0	9 – 10	Aldehydic
ArOH	6 – 2	4 – 12	Phenolic
$H-C-F$	6 – 5.5	4 – 4.5	Fluorides
$H-C-Cl$	7 – 6	3 – 4	Chlorides

In olefines, acetylenes, aldehydes, ketones, acids and esters, etc. if the proton is present in the positive region, it will be shielded and absorption occurs upfield. On the other hand if the proton is in the negative region, its absorption is downfield.

In saturated cyclic hydrocarbons, diamagnetic currents are induced due to circulating bond electrons. Although, the effect is weak, but this is sufficient to distinguish between axial and equatorial protons is cyclohexane. The axial protons are shielded and they absorb 0.5 ppm upfield as compared to the equatorial.



The deshielding effect also depends on the distance from the absorbing protons. As this distance increases the deshielding effect decreases. Thus in the compound the τ value of absorption decrease is in the order $c > b > a$.



Acetylene in magnetic field

It should be noted that electron density is not the only factor determining the value of shielding constant. Another frequently very important contribution to shielding arises from the field induced circulation of electrons in neighboring parts of a molecule which gives rise to a small magnetic field acting in opposition to the applied field. For example circulation of the cylindrical charge cloud comprising and acetylenic triple bond *reduces* the effect of the applied field at a hydrogen nucleus or the axis of the circulating charge. The nucleus is thus shielded and resonates to a high applied field.

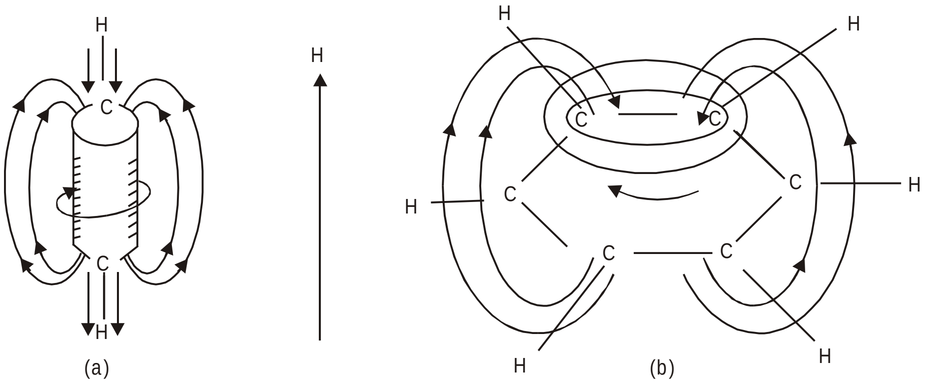


Fig. 15.7 The field induced electronic circulation in (*a*) acetylene and (*b*) benzene showing shielding and dishielding respectively at nearby hydrogen nuclei.

Benzene in magnetic field

In benzene the circulation of the annular cloud of π orbital electrons around the benzene ring (only the top angular) is shown to simplify the diagram, but the identical annulus beneath the ring circulates in the same direction. The induced field is here *in the same direction* as the applied field in the vicinity of the hydrogen nuclei and these nuclei are consequently deshielded and resonate to low applied field.

In toluene, the methyl protons resonate at 2.34 δ where as a methyl group attached to an acyclic alkane appears at 1.95δ. This is due to the greater deshielding influence of the ring current in aromatic compound as compared to the other.

Thus NMR spectrum helps us in deciding whether a particular compound has substantial aromatic character in it or not.

Factors influencing chemical shift

These are:

1. Anisotropic effects

2. Inductive effect
3. Hydrogen bonding
4. van der Waals deshielding

1. *Anisotropic effect:* (Also called space effect). The δ value (chemical shift) in each case can be justified by explaining the manner in which π electrons circulate under the influence of the applied.

This has been explained above by taking acetylene and benzene as examples. The deshielding effect of protons attached to C = C is higher than can be accounted for by the inductive effect alone.

2. *Inductive effect:* A proton is deshielded if it is attached with an electronegative atom or group and greater the electronegativity, greater is the deshielding caused to the proton and so if the deshielding is more, then the δ value will also be more:

τ values for CH_3 protons

Compound	*λ value*
CH_3F	5.75
CH_3Cl	6.90
CH_3Br	7.36

3. *Hydrogen bonding:* A hydrogen atom showing the properties of hydrogen bonding absorbs at a lower field in comparison to the one which does not. Being less shielded the field felt by such a proton will be more and hence resonance will occur at downfield.

4. *Van der Waals deshielding:* In big molecules where there is overcrowding, it is possible that some proton may be occupying sterically hindered position. Thus such a proton will be deshielded and will resonate at a higher value of δ than expected.

Solvents used

There should be a proper selection for the choice of a solvent in NMR measurements. The solvent should be such that it does not give its own absorption and it should *dissolve at least 10% of the substance under investigation*. The commonly used solvents in NMR spectroscopy are:

(*i*) Carbon disulphide – CS_2
(*ii*) Carbon tetrachloride – CCl_4
(*iii*) Deutero chloroform – $CDC1_3$
(*iv*) Hexa chloroacetone – CCl_3 – CO–CCl_3
(v) Dimethyl sulphoxide – DMSO which is highly polar

The NMR spectrum measured in one solvent may be slightly different from that measured in another solvent. This difference arises due to difference in polarity of the solvent. This is why recording an NMR spectrum, the solvent is mentioned in the spectrum.

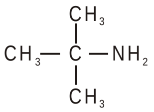
So the solvent should be

(*i*) Devoid of hydrogen atom
(*ii*) Chemically inert and
(*iii*) It should dissolve the sample to fairly good extent

Splitting of signals and spin-spin coupling

It has ‘already been pointed out that each set of protons in a molecule gives one signal or each signal corresponds to one set of protons. It is found that in certain molecules, a single peak is not observed, But a group of peaks is observed.

Generally, splitting of NMR signals to multiplets (doublet, triplet, quartet) is found for compounds *containing two or more adjacent sets of unequivalent protons*. But no multiplet structure of signals is observed when non-equivalent protons are separated by a proton free atom as seen in case of ter. butylamine.



$$CH_3-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}-NH_2$$

Each spinning proton carries a magnetic field aligned with ↑ or against ↓ the applied field H ↑. The same is true for all adjacent protons. *Their individual magnetic fields combine to a resultant field. This is called spin-spin coupling.*

As a general conclusion, n non equivalent protons adjacent to one or more protons produce an NMR signal effect an (n + 1) splitting of that signal.

Let us consider the molecule of ethyl bromide $CH_3^a\ CH_2^b$ Br. It has two kinds of protons *a* and *b* hence two signals are expected in NMR spectrum. It is to be noted that for each kind of proton, we do not get singlets but a group of peaks. For a protons a triplet is observed and so *a* group of three peaks is absenced. The *b* protons give a group of four peaks *i.e.*, a quartet.

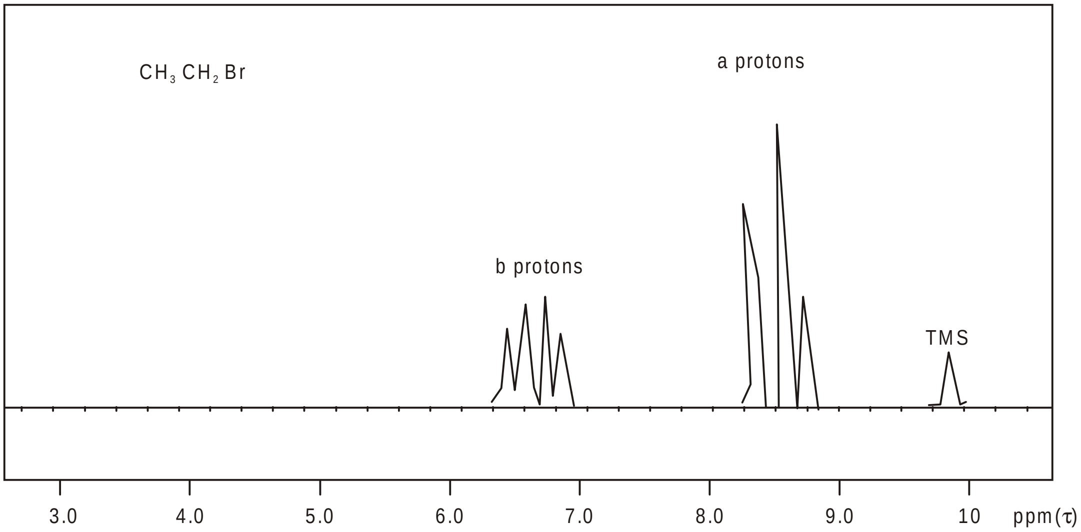
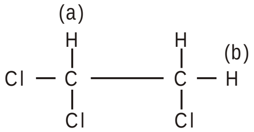


Fig. 15.8 NMR spectrum of ethylbromide

Similarly, 1, 1, 2, trichloroethane has two sets of non equivalent protons *a* and *b*.



$$\mathrm{Cl-\underset{Cl}{\overset{H}{C}}-\underset{Cl}{\overset{H}{C}}-H}$$

Two signals are therefore expected in the NMR spectrum. The signals of proton *a* should appear at lower field to that of proton *b* due to the stronger deshielding action of two chlorine atom adjacent to proton *a*. The intensity ratio of the signals should be

Signal *a* : signal *b* = 1.2

(1 CH and 2 CH_2 protons)

But the NMR spectrum does not show two signal peaks. Instead *a* triplet of peaks at *a* lower field ($\tau = 4.23$) and a doublet of peaks at a higher field ($\tau \perp 6.05$) are observed.

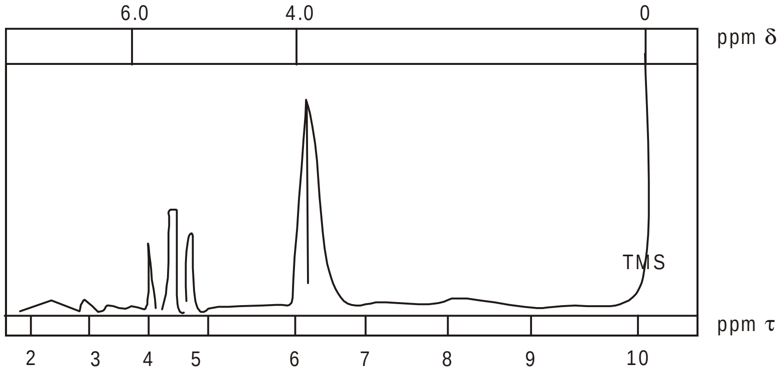


Fig. 15.9 NMR spectrum of 1 : 1 ; 2 trichloroethane

So the NMR spectrum shows a *doublet* for the methylene protons due to one adjacent non equivalent CH proton. There is a triplet for CH proton due to spin-spin coupling of *two* adjacent non equivalent CH_2 protons.

Origin of Multiplet Peaks

This is due to spin-spin coupling. It should be noted that *chemically equivalent protons do not show spin-spin coupling due to interactions among themselves.*

If there is one adjacent proton, it may align with or against the applied external field. In that case the external field will either be strengthened or weakend. Therefore two peaks will appear:

1. downfield due to alignment with the field and
2. upfield due to alignment against the field.

Both fields will make a doublet and the ratio of the alignments is 1 : 1 (Fig. 15.9)

The NMR spectrum of 1, 1, 2, trichloroethane shares a doublet for the methylene protons due to *one* adjacent non-equivalent CH protons. The spins of two protons adjacent to the one considered couple in three different manners relative to the external field, reinforcing not affecting and opposing the external field.

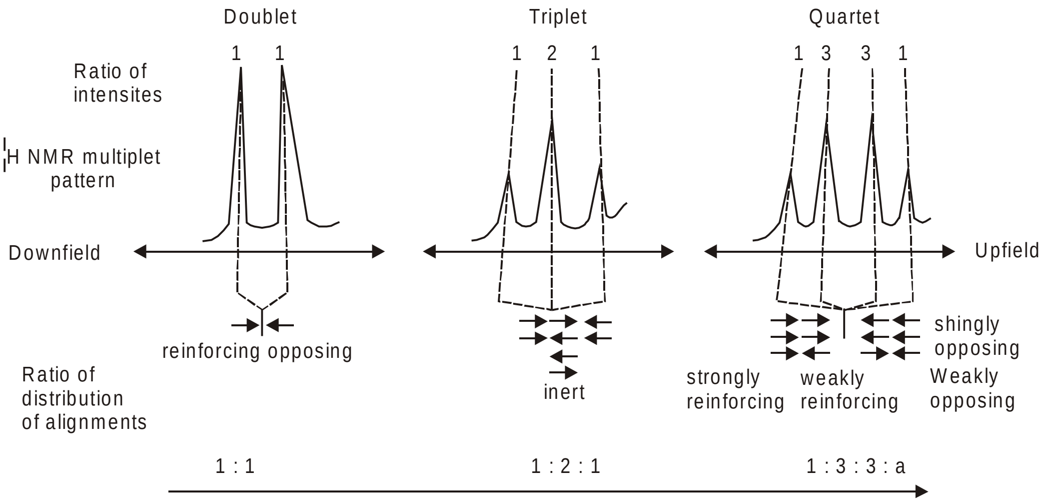
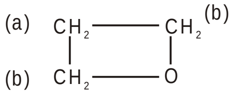


Fig. 15.10 Pattern of simplet multiplets.

Fig. 15.10 from organic chemistry by Alhert Zlutkins and Gunther Jung. (Mc Graw-Hill Ltd. p. 524)

Similarly spins of three protons adjacent to one considered couple gives four different splits relatives to the external field which will be strongly reinforcing weakly re-inforcing, weakly opposing and strongly opposing. Therefore a guartet of peaks will appear which will be in the ratio of 1 : 3 : 3 : 1.

Let us now study the NMR spectrum of trimethylene oxide.



It has two sets of non-equivalent protons, *a* and *b*. The signal of *a* is influenced by four (n = 4) protons of set *b*. Therefore, it will split into five (n + 1 = 5) peaks forming a quintet with centre τ = 7.28. The signal of set *b* is influenced by (n = 2) protons of set *a* therefore, it will split into a triplet (n + 1 = 3) of peaks with centre at τ = 5.27. The downward shift of the triplet due to set *b* results from the deshielding influence of the electron-withdrawing oxygen (Fig. 15.11).

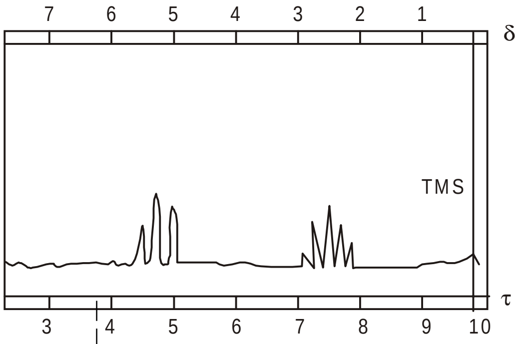


Fig. 15.11 ^{1}H NMR spectrum of trimethylene oxide

Thus the relative intensities of the individual lines of a multiplet correspond to the numerical coefficient of the lines in the binomial expression:

$$(1 + X)^n = 1 + 1 \text{ if } n = 1$$

If n =2 then $(1 + X)^2 = 1 + 2x + x^2$, so the lines of the triplet will have relative intensities 1:2:1.

Similarly if $n = 3$ then $(1 + x)^3 = 1 + 3x^2 + 3x + x^2$, the relative intensities of the quartet will be = 1 : 3 : 3 : 1

For quintet the relative intensities will be 1 : 4 : 6 : 4 : 1.

Therefore, the splitting of a signal is due to the different environment of the absorbing proton with respect to the nearby protons.

Coupling Constants

The distance J between the peaks of a multiplet, measured in hertz is called *coupling constant.* The separation of peaks in a triplet is exactly the same as that observed in a doublet. From this a conclusion has been derived that the *spin-spin coupling is a reciprocal affair*, *i.e.*, the effect of '*a*' kind of proton on '*b*' proton is exactly the same as the effect of '*b*' proton on '*a*' type of protons as in 1, 1, 2 trichloropropane (Fig. 15.12). In general it can be said that the coupling constants are measures of efficiency of spin-spin, coupling.

But things are not so simple, because the heights, of peaks in a particular multiplet are not always symmetrical. For example in a doublet, the intensity should be 1 : 1, but some times it is not exactly so. Same is the case with triplet and other multiplets.

The coupling constants generally lies between 0 and 20 Hz and depend on the structural relationship between the protons as demonstrated for those of vinyl group.

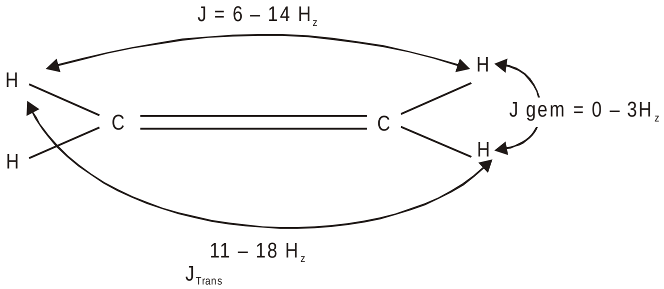


Fig. 15.12

In a compound having the structure > $CH^b – CH^a_2$ – two signals will be expected in the NMR spectrum because of the influence of two equivalent protons, the signal for the proton '*b*' will appear as *a* triplet and the distance between any two adjacent peaks will be the same as shown (Fig. 15.13)

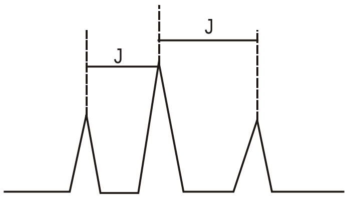


Fig. 15.13 Splitting of proton '*b*' into triplet

Geminal coupling. In case of protons attached to the same carbon atom having different chemical environment, the value of J depends upon the bond angle and it can have any sign.

A few points of geminal coupling have been noted :

(*i*) The value of J increases with increase in bond angle (increase in *s* character). Thus J gem for :

Methane = –12.4 cps

and for ethylene = + 2.5 cps.

(*ii*) The value of J decreases if any electo-negative substituent withdraws electrons from the π bonds as shown below :

Compound	J–gem
Methane	–12.2 cps
Methyl choride	– 10.8 cps
Methyl fluroide	– 9.4 cps

(*iii*) The increase- in the electro-negativity of the atom also increase the value of J as seen from the example of CH_3C1 and CH_3F.

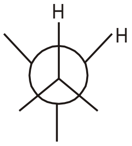
(iv) For alkenes, the value of J is in the order

$$J_{trans} > J\ cis > J\ gem$$

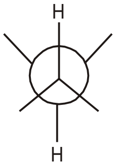
Vicinal coupling

Vicinal protons are those which are separated by three bonds and in such compounds the value of J varies with the dihedral angle.

For gauche protons the value of J varies from 2–4 cps and for anti protons J varies from 5–12 cps



Gauche



Anti

For vicinal protons (*i*) the values of J are always positive and for olefines (*ii*) J trans > J_{cis}.

Interpretation of NMR spectra

(A) *To interpret an NMR spectrum first we should see the peaks and then tau values. In this connection, the following points are kept in mind about the* τ *values :*

(*i*) The Tau values of methyl > methylene > methine.

(*ii*) Then we should concentrate on the nature of groups because the greater the electro-negativity of the substituent, lower is the value of tau.

(*iii*) The orbitals holding the various protons are then considered and in this connection, the tau values present on different orbitals are as follows:

$$Sp^3 > SP^2 > SP$$

(*iv*) The tau values of aromatic protons is always less than 4 ppm.

(*v*) The cyclic protons always have or higher values of tau than other protons.

(*vi*) The tau values of aldehydic protons are generally 0.8 ppm or less.

(*vii*) The absorption due to –COOH group appear at –0.5 to –2.0 t.

(*viii*) The chemical shifts of protons in O-H group and in $–NH_2$ group depends on temperature, solvent, concentration and the neighbouring groups.

(B) *The number of signals indicates the number of sets of protons in different chemical environments.*

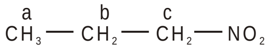
(C) *Point B above also tells the number of equivalent protons causing the splitting of a signal.*

APPLICATIONS OF NMR SPECTROSCOPY

NMR spectroscopy is widely used for the detailed determination of the structure of an unknown compound. Some of these are:

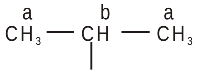
(1) Identification of structural isomers

Let us take example of 1-and 2-nitro propane



$$\overset{a}{CH_3}—\overset{b}{CH_2}—\overset{c}{CH_2}—NO_2$$

1–nitropropane



$$\overset{a}{CH_3}—\underset{NO_2}{\overset{b}{CH}}—\overset{a}{CH_3}$$

2–nitropropane

1–nitroproane has three sets of non equivalent protons and so three multiplet signals as a result:

Set *a* : CH_3 triple at τ = 8.97

Set *b* : CH_2 septet at τ = 7.93

Set *c* : CH_2 triplet at τ = 5.62

2-Nitropropane has only two sets of non-equivalent protons showing therefore two signals with pattern different from those of 1-nitroporpane.

Set *a* CH_3 doublet at τ = 8.45

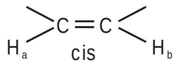
CH septet at τ = 5.33

(2) Detection of hydrogen bonding

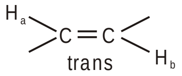
Intermolecular hydrogen bonding shifts the signal of the involved protons to a lower field increasing the bond width. The extent of hydrogen bonding varies with the solvent, concentration of the solution and the temperature. Intramolecular hydrogen bonding also shifts the signal of the involved proton downfield but the chemical shift of an intramolecular hydrogen bonded proton is independent of concentration. Thus the two types of hydrogen bonding can be distinguished.

(3) Distinction between cis-Trans Isomers and conformation can be made

Cis - and trans isomers can be easily distinguished by NMR spectroscopy because cis and trans protons have different chemical shifts and coupling constant.



J cis = 7 – 12 cps



J trans = 13 – 18 cps

The conformations and the axial and equatorial positions of the proton or group carrying a proton can be distinguished from the different values of coupling constants.

(4) Detection of aromaticity

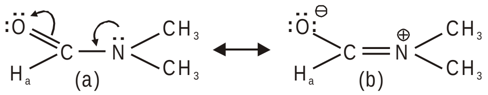
We know that aromatic compounds, polynuclear and heterocyclic compounds follow Huckel’s rule in which they have a $(4n + 2)$ system of π electrons and the protons attached to such systems are extremely deshielded due to the circulating sextet of π electrons. As a result, the signals of aromatic protons appear at a very low’field than those observed even for benzene. The tau value of benzene is $\tau = 2.63$. From this the aromaticity of a compound can be verified.

(5) Detection of electronegative atom a group

It has already been described earlier that the presence of an electronegative atom or group in the neighbourhood of a proton causes deshielding and the signal is shifted downfield. The greater the electronegativity of the adjacent atom, smaller is the tau value of absorption. Thus electronegativities and inductive substituent effects can be studied by NMR.

(6) Detection of the double bond due to hindered rotation

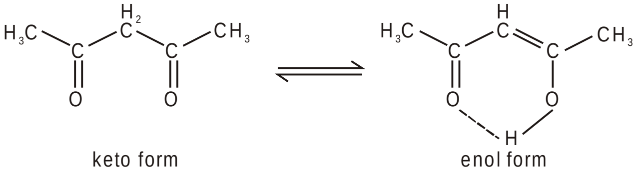
Hindered rotation can separate the NMR signals of apparently equivalent protons. This causes changes in the geometry of the molecule. This fact is illustrated by C – N bond if N, N dimethyl - formamide which has partial double bond character due to resonance stabilization of the molecule:



The $> C = N^{\oplus} <$ double bond hinders free rotation. The methyl protons are ‘no longer equivalent and so (b) shows two signals in the NMR spectrum.

(7) In quantitative analysis

NMR spectroscopy has been utilized in the quantitative analysis of the racemic mixtures. The important condition is that the proton signals of the components are well separated. Ketoenol tautomerism has been studied in this manner. This is illustrated by acetyl acetone.



The NMR spectrum of pure acetylacetone shows signals of the following kinds of non-equivalent protons.

$-CH_2$ – protons at $\tau = 6.35$ Due to keto form.

$= C - OH$ proton at $\tau = -4.3$ Due to enol form

$= C - H$ proton at $\tau = 4.4$

$-CH_3$ protons at $\tau = 7.78$ Due to enol and keto compund.

and = 7.79

The number of enol protons (= C – H and = C – OH) relative to the keto protons yields the ratio.

$$\frac{\text{Enol protons}}{\text{Keto CH}_2\text{ protons}} = 8 : 2$$

So 80% of the enol and 20% of the ketone are present in the equilibrium mixture of acetylacetone.

^{13}C-NMR SPECTROSCOPY (CMR)

So far we have studied the NMR (or PMR) spectroscopy and its applications. In recent years a new technique called the ^{13}C – NMR or CMR technique has been developed. ^{12}C nucleus is not magnetically active because its $l = 0$ and does not give any NMR signal. ^{13}C like ^{1}H has a spin number $l = \frac{1}{2}$ and so it has been developed.

There is considerable difference between the ^{1}H and ^{13}C NMR because the latter are difficult to record then ^{1}H due to the following reasons.

(*i*) The natural abundance of ^{13}C is only 1.11% that of ^{12}C which is not detectable by NMR. Further the sensitivity of ^{13}C is only about 1.6 % that on ^{1}H. It is 1/5700 that of ^{1}H. This value of sensitivity is so low that unaided standard NMR spectrometers are not adequate for its study.

The availability of *Fourier Transform instrumentation* which permits the irradiation of all ^{13}C nuclei has given impetus to ^{13}C spectroscopy.

(*ii*) The magnetic resonance of ^{13}C is much weaker and weak signals are obtained which are therefore, scanned by a computer.

(*iii*) ^{13}C spectra show chemical shifts that are more sensitive to details of structure than proton shifts.

(*iv*) In compounds having ^{13}C - ^{1}H spin – spin interactions become pronounced and hence *spin decoupling* becomes essential, This has been achieved with a wide band oscillator which decouplets all protons simultaneously and allows all 13 C multiplets to singlets. This is why special methods of recording have been employed.

In spite of the above *limitations* ^{13}C NMR or (CMR) spectra are more easily interpreted and give the following important information :

(*a*) Many of the functional groups containing carbons are directly observable.

(*b*) It gives the total number of protons

(*c*) The total number of carbon atoms and the

(*d*) presence of carbonyl group in the compound.

(*e*) It gives much idea about substitution and molecular geometry.

Phosphorus – 31

^{31}P shows magnetic properties similar to ^{1}H and ^{19}F ^{31}P with $l = 1/2$ exhibits sharp NMR peaks with chemical shifts extending over range of 700 ppm, ^{31}P NMR has been used in the quantitative analysis of condensed phosphates, hydroxymethyl phosphines and thiophosphates.

The resonance signal of $P^{(III)}$ compounds occur at much lower field than $P^{(V)}$ compounds.

^{ll}Boron

^{11}B resonance spectra have been used to analyse the complex boron hydrides.

CHAPTER

16

Mass Spectrometry and Lasers

INTRODUCTION

Mass spectroscopy is an outstanding analytical technique and is more important than infrared and nuclear magnetic resonance spectroscopy.

In obtaining a mass spectrum of a compound, a small sample (0.1 – 1 mg) is vaporized at high vacuum (10^{-4} mm Hg) and is then bombarded by a beam of medium energy electrons. The molecules are fragmented to positively and negatively charged ions. Positively charged $M^{(+)}$ is called molecular ion

$$M + e^{\ominus} \longrightarrow M^{\oplus} + 2e^{\ominus}$$

The charged species are then passed through electric and magnetic fields. The fragment ions are separated into ion groups of equal mass to charge ratio, the *m/e* value (*m* is the mass of ion and *e*, the electronic charge). After this the beam reaches a counter which registers the number of ions for each *m/e* group. A recorder then plots the number of ions due to each *m/e* group versus the mass. A mass spectrum is obtained, representing a series of peaks, each having a particular height and each corresponding to *m/e* ratio.

The peak clue to molecular ion is referred as M^+ peak and its mass corresponds to the molecular weight. The first analytical application of mass spectrometry was described in 1940 when mass spectrometers of good quality became commercially available.

APPLICATIONS OF MASS SPECTROSCOPY

l. It provides a very reliable method for molecular weight determination.
2. Since it is extremely sensitive, very small quantities of the sample are needed and purity of a sample can be established because of high precision. Materials present in concentrations .of less than 1 ppm can be easily detected.
3. It provides information about the mode of fragmentation process and so becomes helpful in investigating a reaction mechanism and in tracer work.
4. It has been used for the identification and structural analysis of complex compounds.
5. It is also being used widely in petroleum industry.

Some Important points in mass spectroscopy

1. ***The sample :*** The substance should have, higher vapour pressure. For organic compounds the vapour pressure should not be near about 10^{-7} mm Hg. The general rule is that the higher the vapour pressure, the more easily the mass spectrum is obtained.
2. ***Ions :*** Since ionisation is achieved by electron bombardment, hence the electrons should have sufficient energy (50 – 100 eV) to induce rupture of any bond in the molecule.
3. ***Positive Ions :*** The positive ions are used because they are more abundant than the negative ions.

Mass spectrometer

The mass spectrometer is an instrument which produces charged ions from the parent substance and also ions obtained by the fragmentation of the original molecule.

It is one of the most costly and complex electronic devices now employed by chemists. A number of mass spectrometers have been devised.

The following represents the flowsheet and the working of a mass spectrometer.

Sample.

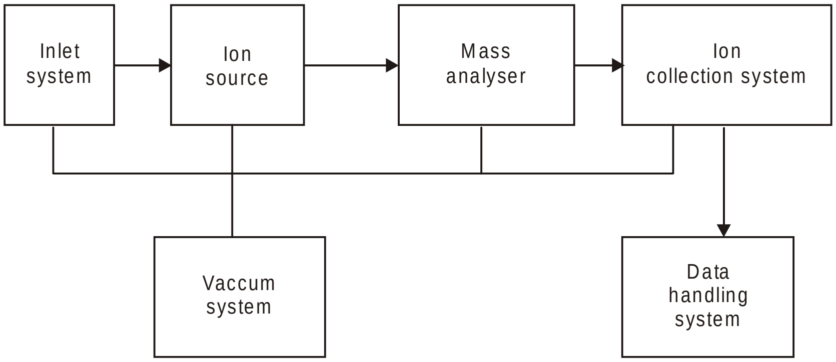


Fig. 16.1

In the removal of electron, it is the electron of lowest ionisation potential which goes out and the following order has been found

$$\text{Lone pair} < \text{Conjugated } \pi < \text{Non conjugated } \pi < \sigma$$

In alkanes the ionisation of C–C sigma bond is easier than C – H sigma bond.

Principle of operation of mass spectrometer

A diagram of a simple mass spectrometer is shown in the Fig. 16.2.

Positive ions are produced by bombarding neutral atoms or molecules in the vapour phase with a high energy electron beam in the ionisation chamber. One (or sometimes two) electron are ejected from the outer most shells.

$$M + e^{(-)} \rightarrow M^{(+)} + 2e^{(-)}$$

or

$$M + e^{(-)} \rightarrow M^{2(+)} + 3e^{(-)}$$

Gases, liquids and moderately volatile solids can be injected directly into the ioinisation chamber. The solids (about 1mg) is heated and vaporized. A relatively low vapour pressure is required, because the apparatus itself works at 10^{-7} mm Hg.

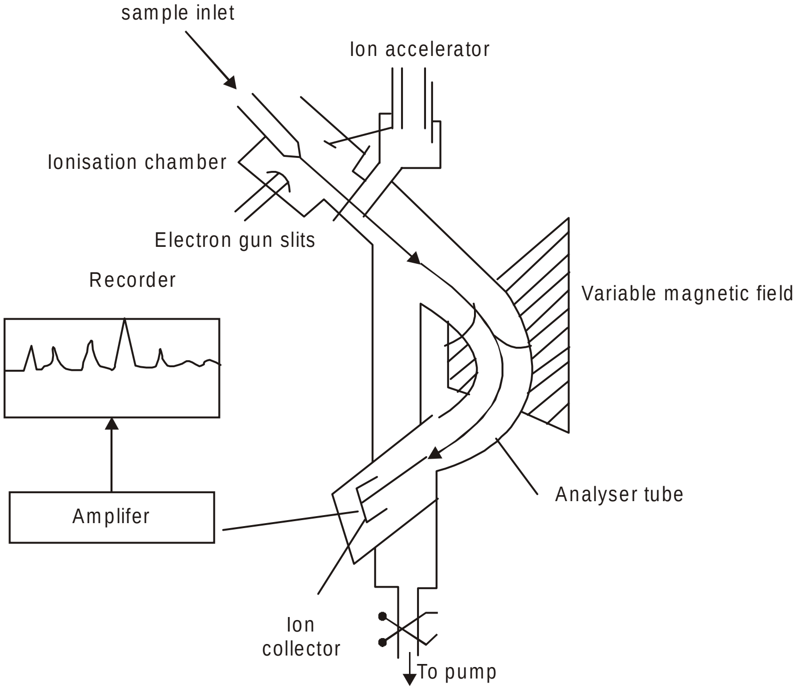


Fig. 16.2 Simple mass spectrometer

The stream of positive ions is accelerated by an electric field. Then it passes through a variable magnetic field which deflects the ions in the beam according to their mass. For fixed values of electric and magnetic fields, only ions of a particular mass reach the ion collector. Other ions collide with the walls of the instrument. The ion collector is linked through amplifying circuits to a recorder. This is then coupled with the variable magnetic field and as the strength of the field is gradually increased, ions of increasing mass enter the collector and a mass spectrum is obtained. The relative height of the peaks gives a measure of the relative members of the different ions from the sample.

The resolving power of modern mass spectrometers is very high and this has been achieved by using a combination of magnetic and electric fields to separate the ions. This gives sharper lines in mass spectra and these are called "double focussing" mass spectrometers. They can distinguish between masses differing by only 1 part in 33,000.

In 1935 A.O. Nier designed a relatively simple but accurate mass spectrometer employing the principle of double focussing. The essential features are the same as described above but some improvements have been made which are:

1. The positive rays are produced by the ionisation of the vapour of the element.
2. The temperature of the tube is controlled with the help of an electric furnace surrounding it.
3. The analyser is a semi circular tube. This analyser is not heated except by conduction.

A.O. Neir analysed a great number of elements such as Ar, Kr, Xe, K, Rb, Zn, Cd and Hg and determined the relative abundances of isotopes with high degree of accuracy.

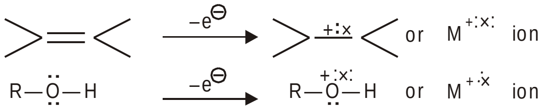
The mass spectrometer bombards an organic molecule (M) with high energy electrons of about 8 – 13 eV (or 185 – 330K cal per mole) In actual pracice the beam of electrons is accelerated to 70 eV which is greater than the bond energy met in organic molecules. This fragments the molecule, ejects an electron and leads to the formation of radical cation represented as M^{+-} or generally written as M^{+} for simplicity. This is also known as molecular ion or parent ion. This molecular ion has the same weight as the starting molecule because the lost electron has negligible mass.

The formation of some molecular ions is represented as follows:

$$M + e^{\ominus}(70\text{ eV}) \longrightarrow M^{+} + 2e^{\ominus}$$

normal molecule

radical ion.



Interpretation of some spectra

The peak obtained in the spectrum is referred to as M^{+} peak and the intensity of this highest peak is called the *base peak and it corresponds to the molecular weight of the substance and the intensities of all other peaks are expressed relative to the base peak. The base peak is caused by the fragment ion which is most stable and whose formation requires least energy.* Mass spectrum of methane is given on page 268.

The most intense peak, the base peak represents the M^{+} and represents the molecular weight as 16. Another small peak representing about 1.1% appears at m/e = 17. Since a molecule of methane can not take up a proton, the formation of this species shows that carbon was in the form of ^{13}C. So it is an isotopic peak and is present in about 1.1%.

In addition to this there are some additional peaks which is unusual in the typical organic compounds, The mass spectrum of methane shows m/e values of 14, 13, 12, 2 and 1. This is explained as due to the formation of cationic fragments as follows:

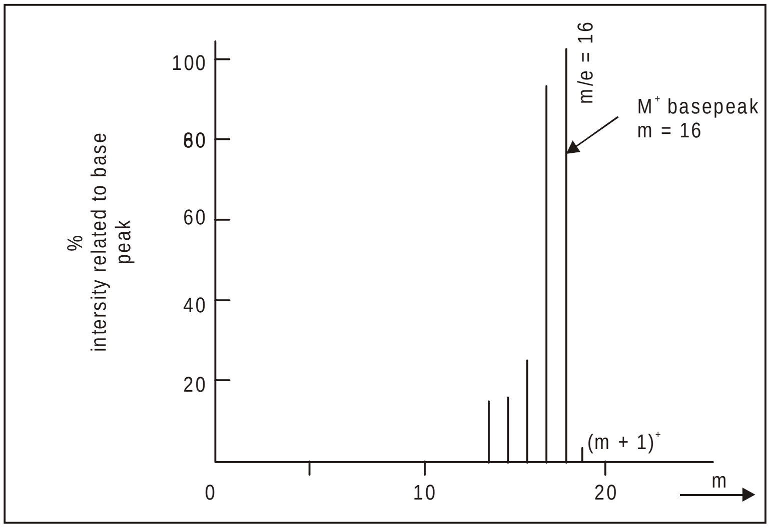
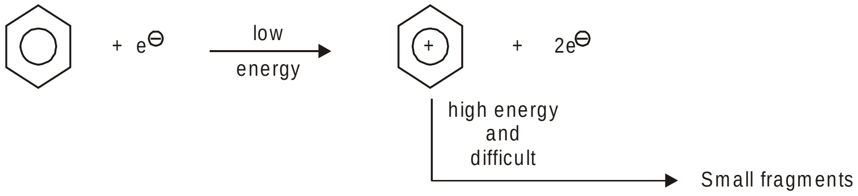


Fig. 16.3

$$
\begin{aligned}
CH_4 + e^{\bullet} &\rightarrow (CH_4)^{+\bullet} + 2e^{\bullet}\\
&\quad m = 16\\
(CH_4)^{+\bullet} &\rightarrow CH_3^{+} + H^{\bullet}\\
&\quad m/e = 15\\
CH_3^{+} &\rightarrow (CH_2)^{+(-)} + H^{\bullet}\\
&\quad m/e = 14\\
(CH_2)^{+\bullet} &\rightarrow CH^{+} + H^{\bullet}\\
&\quad m/e = 13\\
CH_4^{+} &\rightarrow (C)^{+\bullet} + H^{\bullet}\\
&\quad m/e = 12
\end{aligned}
$$

Mass Spectrum of benzene

The benzene molecule is a system of rich π electrons. Removal of π electron requires low energy and benzene cation is formed easily. Its positive charge is delocalized by the π molecular orbitals. Due to this resonance stabilization, further fragmentation of benzene cation requires considerable energy and therefore occurs with low probability.



So the molecular ion of benzene has m/e = 78 and the peak base also confirms this.

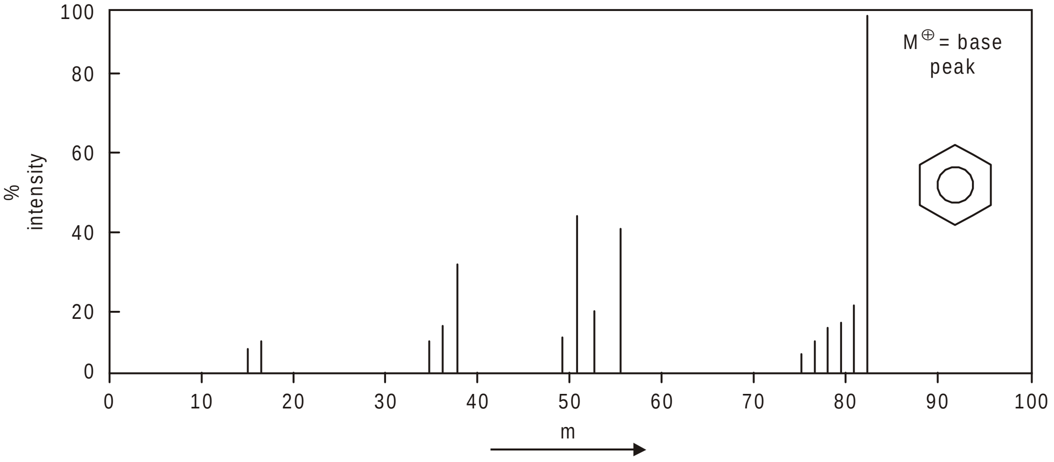
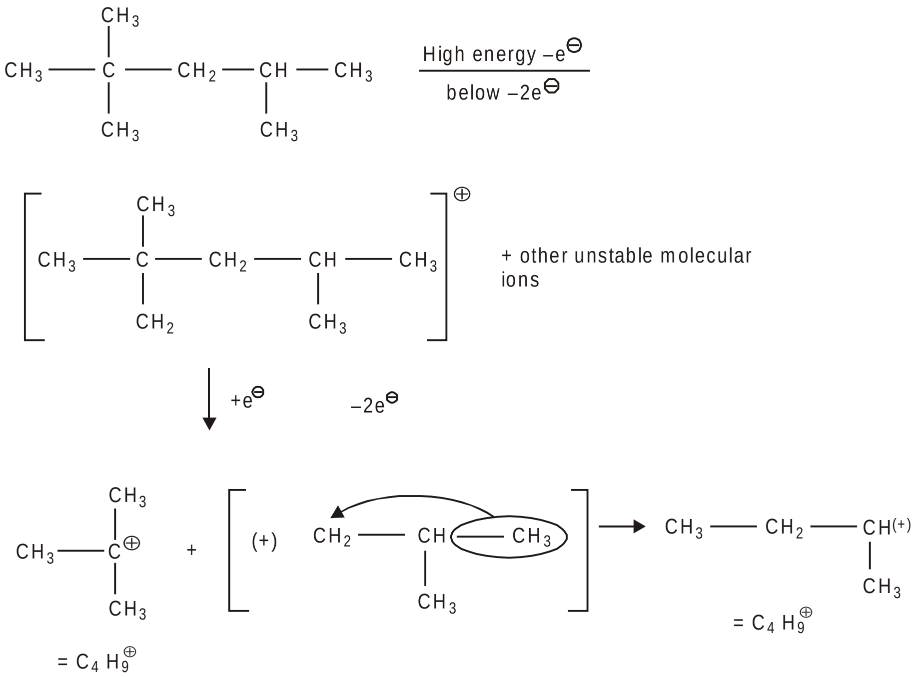


Fig. 16.4

Mass Spectrum, of 2, 2, 4 trimethyl pentane

Saturated aliphatic compounds represent the other extreme. Since they do not have π electrons ionisation, the molecular ion requires removal of electrons from σ orbitals and so high energies. Therefore the formation of molecular ion is difficult. Further, since, the formation of molecular ion is difficult and since this is quite unstable, it cleaves easily into more stable carbocations.

For example, the molecular ion of 2, 2, 4 trimethylpentane shows a high tendency to cleave and more stable terbutyl-carbocation results:



So the peak due to the formation of molecular ion m/e = 114 is very weak and $C_4H_9^{\oplus}$ peak with m = 57 is the lease peak. Other peaks appearing in the spectra may be due to further fragmentation or to isotopes present in the molecule.

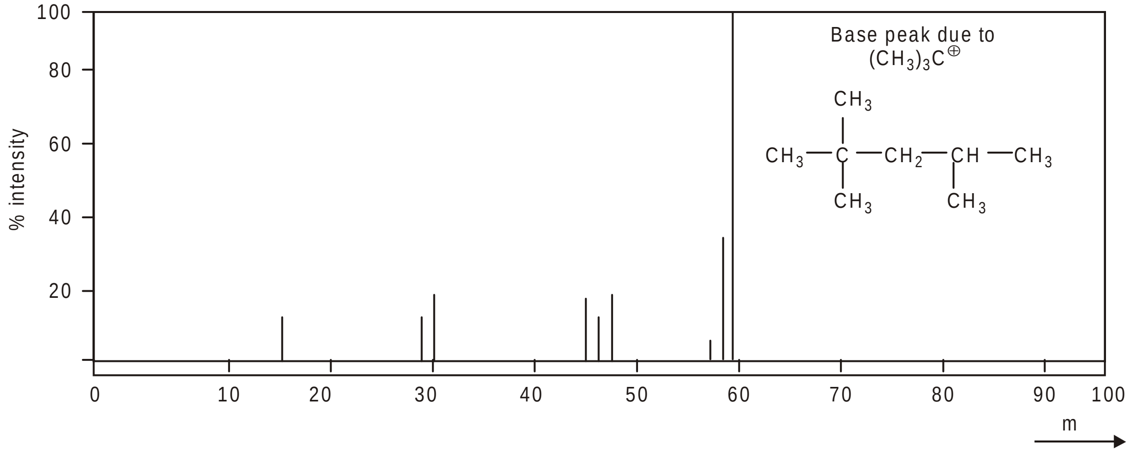


Fig. 16.5

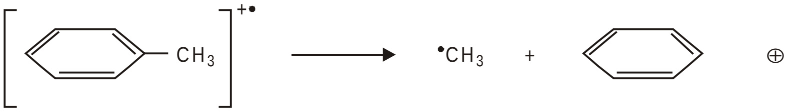
SOME GUIDING PRINCIPLES FOR FINDING THE BASE PEAKS

The following guiding principles have been put forward for finding the base peaks:

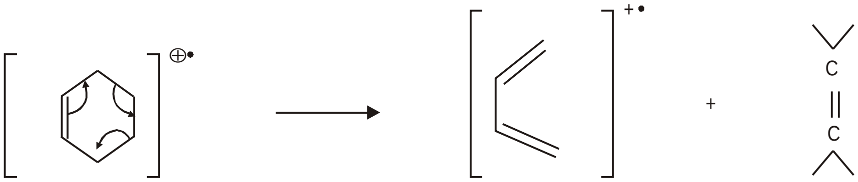
1. The height of the base peak of the molecular ion is greatest for straight chain and decreases with the degree of branching.
2. The relative height decreases with increasing molecular weight in a homologous series.
3. Since in the series of carbocations, the order of stability is

   tertiary > secondary > primary > CH_3

   hence cleavage is favoured at the tertiary carbon atom.
4. Ring compounds contain highest intensity and it is 100% in benzene
5. Saturated rings with side chain lose side chain at the alpha carbon atom and positive charge remains with the ring.

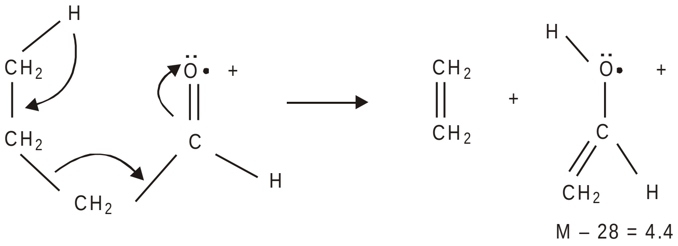


But the unsaturated rings undergo retro Diels-Alder reaction.



For some molecules no molecular ion is visible in the mass spectrum as in ter. butyl alcohol, $(CH_3)_3$ COH in which the heaviest ion occurs at mass 59. corresponding to $M^+ - CH_3$ (74 – 15). So in such cases care must be taken in the interpretation of the spectra.

The fragmentation processes of many molecules are very complex. For example normal butraldehyde, $CH_3 - CH_2 - CH_2 - CHO$ has its most intense spectral peak at 44. This has been explained by the following molecular rearrangement.



Use of a Spark Source

A recent modification of mass spectrometric technique involves the use of a spark source. A spark is struck by means of a high voltage between two rods of the material under examination. Under this drastic treatment many substances decompose completely into their elements and give positive ions. The ion detector is usually a photographic plate which shows a line mass spectrum. A number of exposures are taken for each sample and a quantitative estimate of the presence of an element in the sample can be made from the exposure time.

This technique is rapid and has an enormous potential. Its sensitivity is such that impurities present as one part in 10^9 can be recorded. The complete analysis takes about 4 hours.

Its uses are chiefly confined to investigations on inorganic solids where detection of minute impurities is required as in the analysis of alloys rock material and semi conductors.

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PART-III

MISCELLANEOUS REAGENTS USED IN ORGANIC SYNTHESIS

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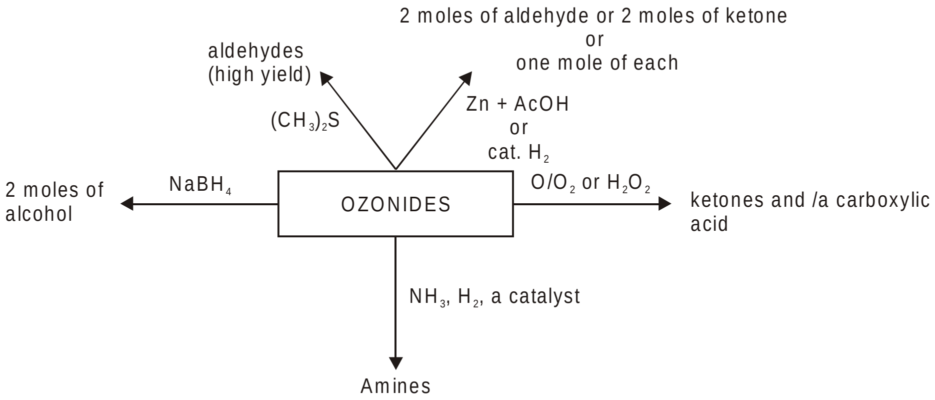
CHAPTER 17

Oxidising Agents and Their Mechanism

OZONE (O_3) $\overset{\ominus}{O}-\overset{\oplus}{O}=O$

It is a well known reaction that compounds containing double bonds react with ozone and form ozonides which on decomposition form carbonyl compounds. Various reagents have been used to decompose these ozonides. With zinc and acetic acid or by catalytic hydrogenation, the ozonides give two moles of aldehyde or two moles of ketone or one mole of each, depending on the nature of groups attached to the olefinic carbon atom. Dimethyl sulphide gives high yields of aldehydes. Oxidation of the ozonide by oxygen of H_2O_2 gives ketones and/or carboxylic acids. The hydride reagents like $NaBH_4$ give two moles of alcohol. Treatment with ammonia, hydrogen and a catalyst gives amines.



The triple bond compounds can also be ozonised but the reaction is much slower.

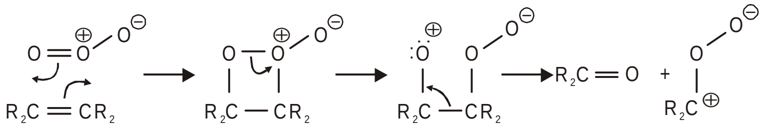
Ozonolysis has been a very important reaction in locating the position of the double bonds in the molecule. From the nature of products obtained after decomposing the ozonide, it becomes possible to locate the double bonds. If the molecule contains more than one double bond, generally ozone adds at all the bonds and so all the bonds are cleaved.

Mechanism of Ozonolysis

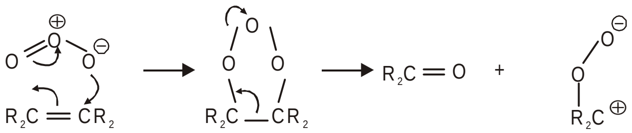
How the initial electrophilic addition of ozone to alkene takes place is not completely known, but it is thought that in the first step of addition the bond connecting the two carbons remains intact.

Two possible courses have been proposed. In one case the intermediate is a four-membered ring, while in the other it is a five membered ring. Both the intermediates decompose to give a carbonyl compound and zwitter ion.

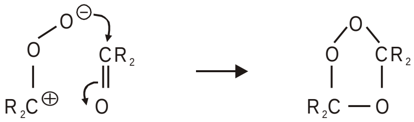
(a)



(b)



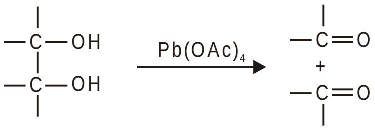
The carbonyl compound and the zwitter ion can recombine to give the normal ozonide.



These are only the suggested mechanisms. Less is known about how the ozonides are decomposed, at least in case of triple bonds. The knowledge about ozonolysis at present available is largely due to the work of R.C. Criegee (in Peroxide Reaction Mechanisms, interscience, New York, 1962, p. 29.).

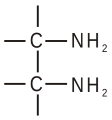
LEAD TETRA-ACETATE Pb(OAc)$_4$

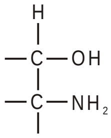
It is an important reagent for the oxidative cleavage of vicinal glycols which are oxidised at room temperatures to aldehydes, ketones or both depending on the nature of glycol.

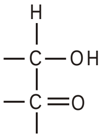


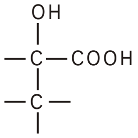
$$\begin{matrix} | \\ -C-OH \\ | \\ -C-OH \\ | \end{matrix} \xrightarrow{Pb(OAc)_4} \begin{matrix} | \\ -C{=}O \\ + \\ -C{=}O \\ | \end{matrix}$$

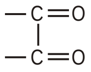
The reaction takes place in the medium of acetic acid and yields are generally good. This is why the route to obtain aldehydes or ketones from alkenes via glycol formation is preferred over that of ozonolysis. Other compounds which are readily cleaved include those with the groups:


α, β diamines


α, amino alcohols

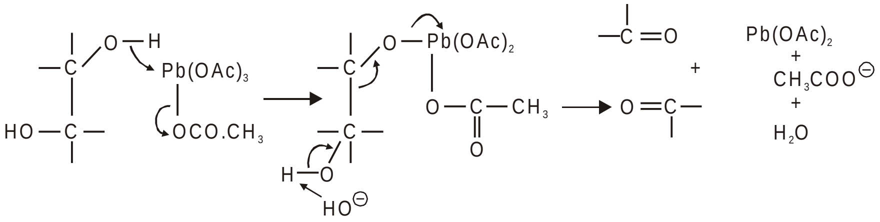

α, hydroxy-aldehydes or ketones


α, hydroxy acids


α, diketones

Mechanism of Cleavage

Since the cleavage of vicinal glycols is acid or base catalysed, the following ionic mechanism has been proposed:

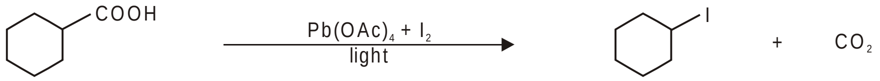


Criegee had earlier postulated the formation of an intermediate cyclic ester, but this was later ruled out and now the above mechanism has been established.

The glycol cleavage has also been useful in the determination of structure and configuration of a natural octulose and a natural nonulose.

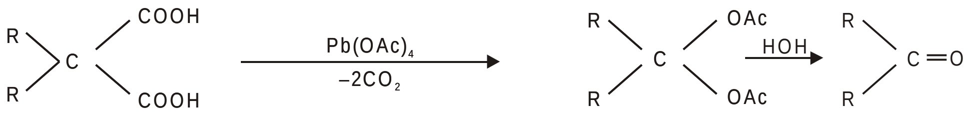
(ii) Oxidative Decarboxylation

Lead tetra-acetate has also been used to cleave acids. The carboxyl group is replaced by halide or acetoxy.



$$Pb(OAc)_4 \;+\; 2\ RCOOH \rightarrow (AcO)_2 - Pb - (OCOR)_2 \;+\; 2\ AcOH.$$

If, however, the two carboxyl groups are present on the same carbon e.g., malonic acid series, then also decarboxylation takes place and gem. diacetate (acylals) are produced.



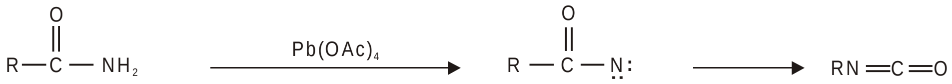
The hydrolysis of the ester gives ketones and therefore the reaction becomes of special significance.

(ii) Oxidative CleavaGe of Diamines

O. Diamines are oxidised to dicyanides:

(iii) Oxidative Rearrangement

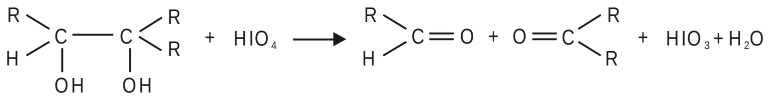
The amides undergo a rearrangement resembling Hofmann rearrangement and give isocyanate.



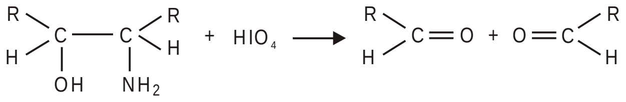
$$R-\overset{\displaystyle O}{\overset{\|}{C}}-NH_2 \xrightarrow{Pb(OAc)_4} R-\overset{\displaystyle O}{\overset{\|}{C}}-\ddot{N}: \longrightarrow RN{=}C{=}O$$

PERIODIC ACID HIO_4

Like lead tetra acetate, periodic and also cleaves vicinal glycols very smoothly and forms carbonyl compounds. The reaction introduced by Malaprade in 1928 may be represented as:

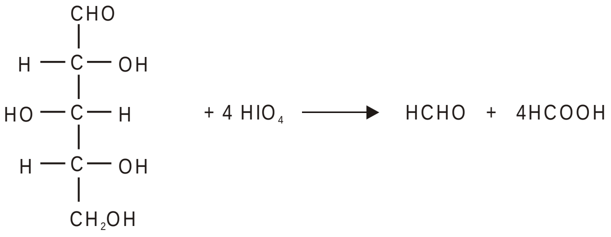


Compounds containing hydroxyl and amino group in adjacent positions are also cleaved to give carbonyl compounds:



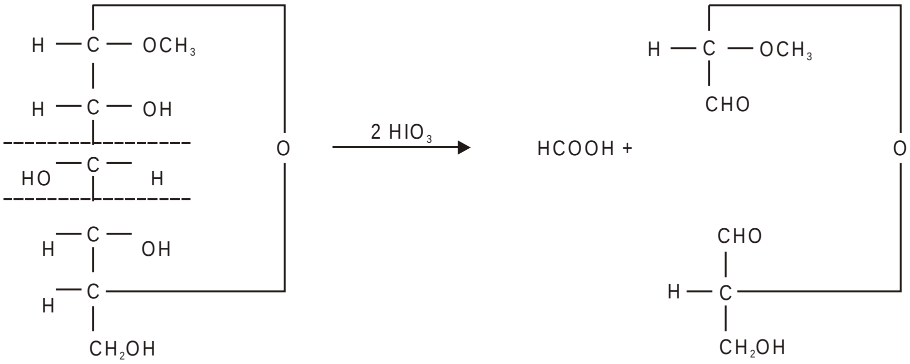
However, unlike lead tetra acetate, it fails to oxidise oxalic acid. Such oxidation reactions are best carried out in aqueous solutions and at room temperatures.

If the compound contains three or more OH groups in adjacent positions, the middle one usually goes out as formic acid and this oxidation has helped much in the determination of the size of rings in sugars. For example, a free sugar is oxidised completely to formaldehyde and formic acid.



xylose

One molecule of periodic acid is used for each pair of adjacent hydroxyl groups. Thus by estimating formaldehyde and formic acid and the amount of periodic acid consumed, it is possible to know the number of free adjacent hydroxyl groups. However, if the sugar is in the form of a glycoside ring complete oxidation does not take place as is illustrated by the following example:



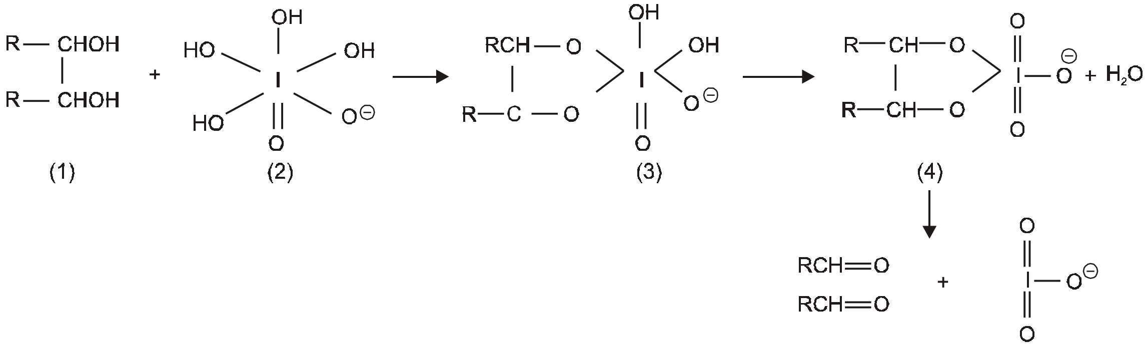
α methyl glycoside diglycolaldehyde

The asymmetric centres at C_2, C_3 and C_4 have been destroyed.

The mechanism of oxidation of vicinal glycols by HIO_4 has been studied by G.J. Buisst and C.A. Bunton (J. Chem. Soc., 1406, (1954). According to these workers, the reactive species is the para form of periodic acid (H_5IO_6) which is formed by the action of water on HIO_4.

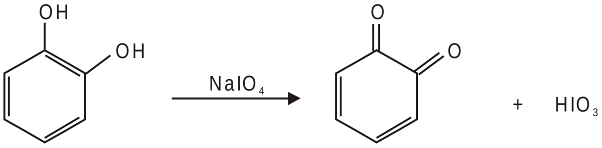
$$2\ HIO_4 + 4H_2O = 2H_5IO_6$$

The anion of this para form forms a cyclic intermediate with the glycol which may get hydrated (3) or dehydrated. (4) These then give the final oxidation product and liberate the anion.



Oxidation Of Phenols

Periodic acid also oxidises phenols, particularly the ortho compounds. Thus catechol gives o. benzyoquione on oxidation with sodium periodate.



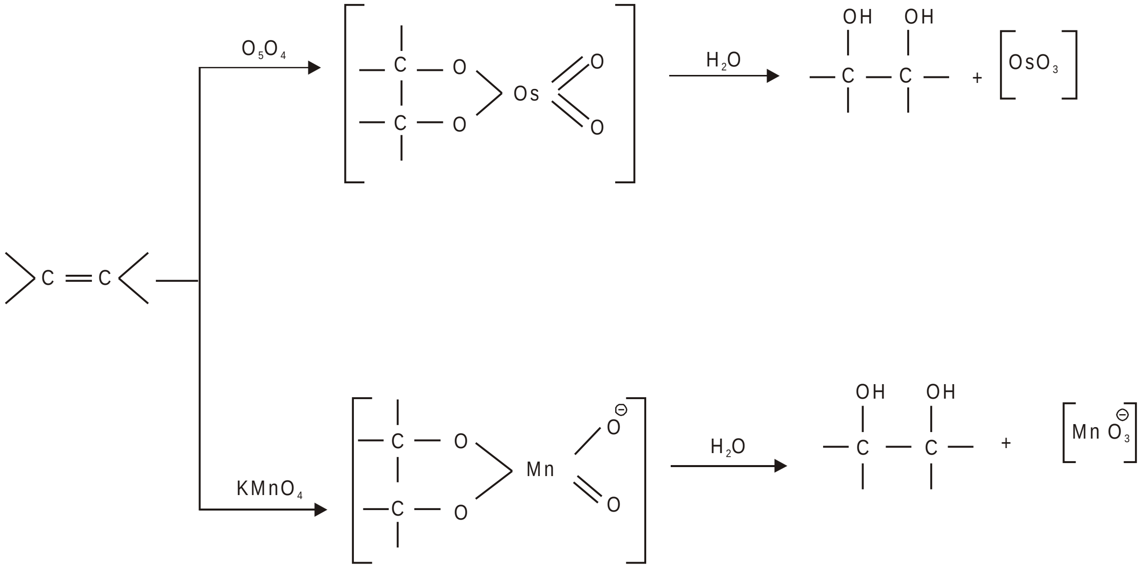
OSMIUM TETROXIDE OSO_4

Osmium tetroxide is a crystalline solid, (m.p. 40°, b.p. 135°) soluble in ether and benzene but little in water (about 5.7 g/100g.)

Like Baeyer's reagent, it oxidises alkenes forming cis glycols and the addition takes from the less hindered side of the double bond.

Such reactions have also been called hydroxylation reactions and the nature of the product formed depends on the nature of the hydroxylating agent. Thus while $KMnO_4$ and OsO_4 give cis products, hydroxylation of an alkene carried out by H_2O_2 catalysed by SeO_2 results in trans addition.

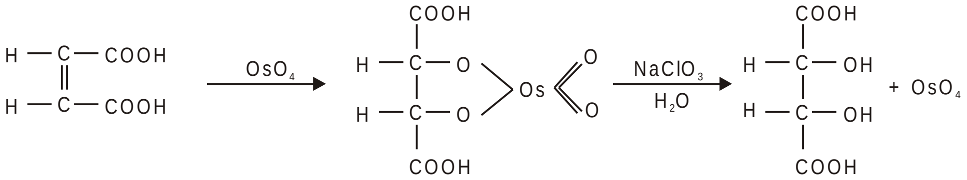
The cis addition by $KMnO_4$ and OsO_4 is explained by the formulation of a cyclic organometallic intermediate, which although isolable is usually decomposed in solution by sodium sulphite in ethanol or other reagents.



The cyclic intermediate, also called the osmate ester has been definitely known, in case of OsO_4. Wiberg using isotopic oxygen in $KMnO_4$ has shown that both the glycol oxygens come from the permanganate ion and on the anology with the osmate ester, has given a cyclic structure to the permanganate intermediate also. This shows that fission takes place between oxygen and the metal atom without disturbing the C–O bond.

The glycols are formed in high yields with OsO_4 but the chief drawback is its high cost and toxic nature. This is why its use is limited to small scale preparation of fine chemicals like pharmaceuticals and for degradative studies. When used as a catalyst, OsO_4 is used with H_2O_2, which reoxidises Os to OsO_4.

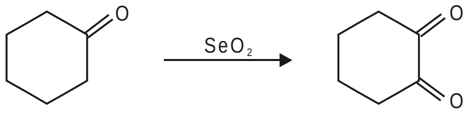
Oxidation of maleic acid by $NaClO_3$–OsO_4 in aqueous solution involves the formation of the cyclic osmate ester, the oxidative clevage of which by chlorate gives mesotartaric acid with the regeneration of OsO_4.



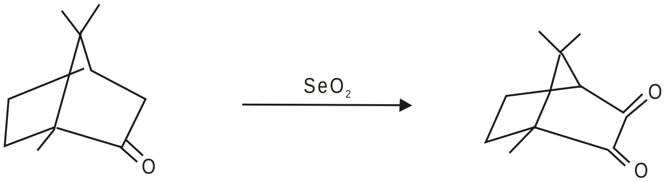
SELENIUM DIOXIDE SeO_2

Selenious Acid H_2SeO_3

1. Selenium dioxide has been used to oxidise reactive methylene group to carbonyl compound. This methylene group is in α-position to a carbonyl group. Thus cyclohexanone has been oxidised to cyclohexane –1, 2 dione.



Camphor has been oxidised to camphor quinone which is an intermediate in the preparation of Horner’s acid.

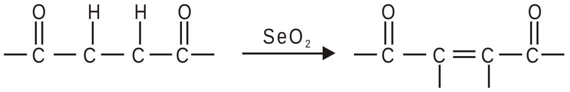


Since SeO_2 is an extremely poisonous substance, so proper care is taken in its handling. The double and triple bonds and the aromatic rings appear to activate the methylene group.

2. Another important use of SeO_2 is in the oxidation of CH_3 groups to CHO, but not to COOH group. But such CH_3 group must be activated by a carbonyl or other group. Thus phenyl glyoxal has been prepared in about 72% yield by refluxing a solution of acetophenone in the medium of dioxane for about 4 hours.

$$C_6H_5COCH_3 + H_2SeO_3 \xrightarrow[4\ hrs]{reflux} C_6H_5COCHO$$

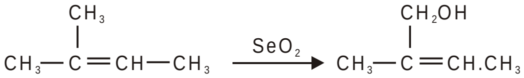
3. Barnes and Barton have dehydrogenated triterpenoid 1, 4 diketones to enediones by SeO_2 if the two hydrogens to be eliminated are cis, but not if they are in trans position.



$$-\overset{O}{\overset{\|}{C}}-\overset{H}{\overset{|}{C}}-\overset{H}{\overset{|}{C}}-\overset{O}{\overset{\|}{C}}- \xrightarrow{SeO_2} -\overset{O}{\overset{\|}{C}}-\underset{|}{C}=\underset{|}{C}-\overset{O}{\overset{\|}{C}}-$$

4. SeO_2 has also been used to carry out allylic hydroxylation of olefines and in this connection the following points are guiding factors.

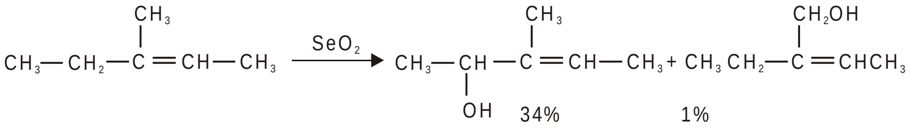
   (*a*) Hydroxylation occurs α to the more highly substituted end of the double bond.



$$CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CH_3 \xrightarrow{SeO_2} CH_3-\overset{CH_2OH}{\overset{|}{C}}=CH.CH_3$$

(*b*) If the molecule contains primary, secondary and tertiary hydrogens, the order of attack is:

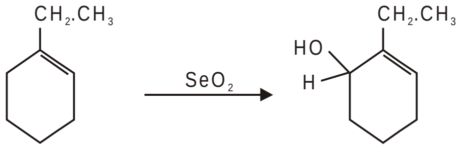
$$CH_2 > CH_3 > CH=$$



$$CH_3-CH_2-\overset{CH_3}{\overset{|}{C}}=CH-CH_3 \xrightarrow{SeO_2} CH_3-\underset{\underset{OH}{|}}{CH}-\overset{CH_3}{\overset{|}{C}}=CH-CH_3 + CH_3CH_2-\overset{CH_2OH}{\overset{|}{C}}=CHCH_3$$

34% 1%

(*c*) When a double bond is in a ring, oxidation occurs within the ring and again at the α to the more branched end of the chain.



(*d*) If the double bond is the terminal end of the molecule, an allylic rearrangement of the double bond takes place and a primary alcohol is the product.

$$CH_3.CH_2.CH_2.CH=CH_2 \xrightarrow{SeO_2} CH_3.CH_2.CH=CH-CH_2OH$$

Organic Peracids

The organic peracids like per carboxylic acids are important reagents because they are used to:

1. convert isolated double bonds to epoxides, also called epoxidation of alkenes.
2. oxidise ketones to esters and.
3. to convert α diketones and α-ketoesters to anhydrides.

Some of the important per acids are perbenzoic acid, m-chloroperbenzoic acid, peracetic acid and the powerful trifluoroperacetic acid. Here we shall deal with only perbenzoic acid.

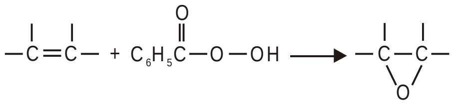
PERBENZOIC ACID $C_6H_5.CO_2.OH$

It is prepared by dropwise addition of 70% H_2O_2 to a solution of benzoic acid dissolved in methane solphonic acid and keeping the temperature around 25–30°. After the addition the solution is cooled to 15°, diluted with ice and cold saturated $(NH_4)_2SO_4$ solution to decrease the solubility. It is finally extracted with benzene. The solution is directly used for epoxidation and other reactions.

$$C_6H_5COOH + H_2O_2 \xrightarrow{CH_3SO_3H} \underset{\sim 90\%}{C_6H_5CO_2OH + H_2O}$$

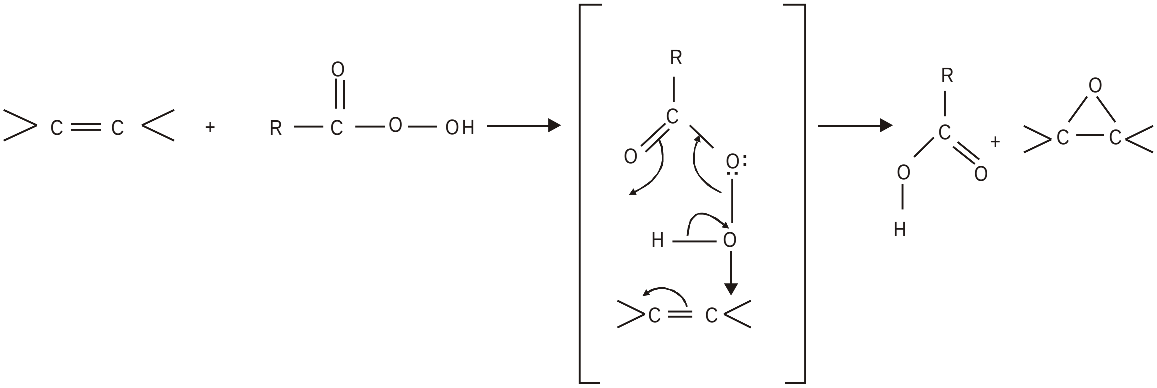
1. Epoxidation of Alkenes

Perbenzoic acid reacts with alkenes at low-temperatures (0–25°) to give high yields of epoxides.



$$-\overset{|}{C}=\overset{|}{C}- + C_6H_5\overset{\overset{O}{\|}}{C}-O-OH \longrightarrow -\overset{|}{C}-\overset{|}{C}- \text{ (with O bridging)}$$

The electron-donating groups, if present in the alkene enhance the rate of the reaction. This is why the reaction is particularly rapid with tetraalkyl olefines. The electron-withdrawing groups in the peracids also increases the reaction rate. The following suggested mechanisms has been accepted for the conversions.

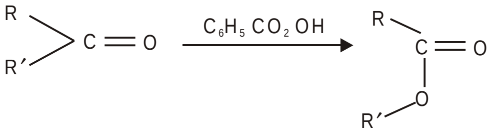


The evidence for the mechanism is that it is a second order reaction. Further, since the reaction proceeds readily in nonpolar solvents, hence the formation of ions from perbenzoic acid, as postulated earlier, is inhibited. The final evidence is that the reaction is stereospecific and proceeds with the retention of cis or trans configurations present in the initial olefine.

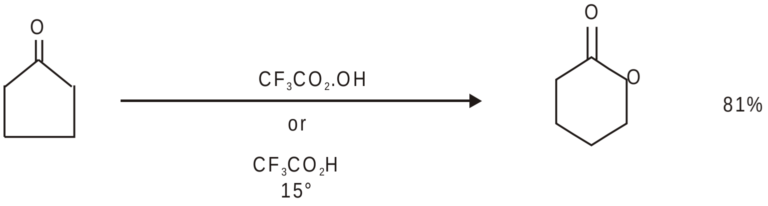
The formation of epoxides from oxygen appears to be a free radical process.

2. Oxidation of Ketones to Esters (Baeyer-Villiger rearrangement)

The conversion of ketones to esters by perbenzoic acid involves an "insertion" of an oxygen atom.



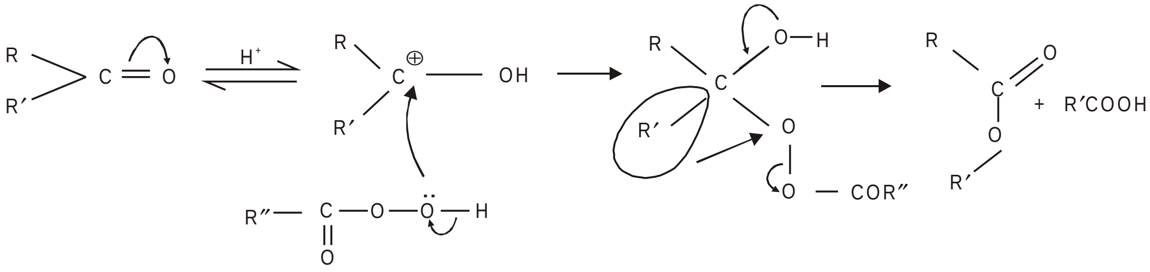
If the ketone is cyclic, a lactone is the product, but this reaction is practical only with 3–6 membered ring ketones:



These relations are called Baeyer-Villiger rearrangement and in such reactions peroxytrifluoroacetic acid is used as an oxidising agent.

Mechanism

The reaction is catalysed by acids which first protonate the ketone. This is followed by the nucleophilic attack of peracid and the final stage is the elimination-migration to give the product.



Syrkin suggested that the elimination-migration is a concerted process.

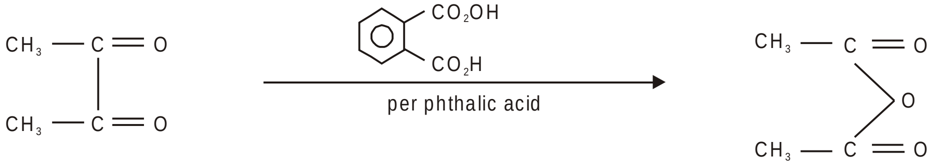
Electron-donating groups in the ketone and electron-withdrawing groups in the per acid accelerate the reaction. The case of migration of some common groups decreases in the order.

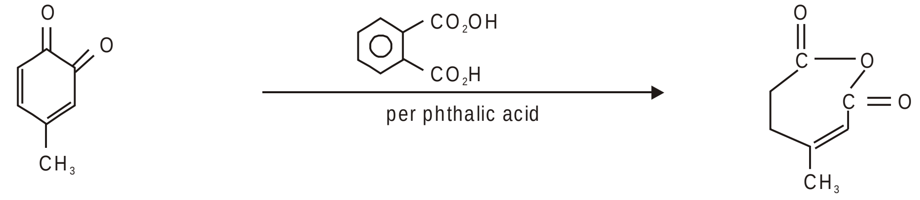
ter. alkyl > sec. alkyl – cyclohexyl > benzyl – phenyl > primary alkyl > methyl.

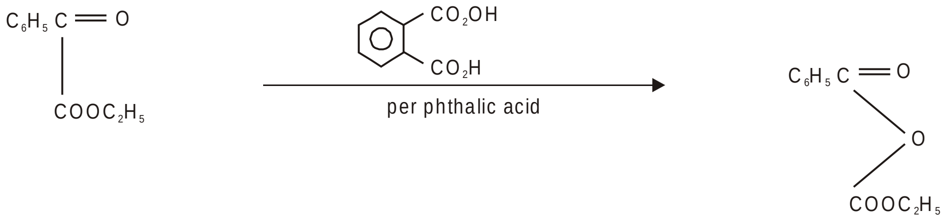
In case the migration group is optically active, the activity is retained in the product.

3. Oxidation of α-Diketones, o-quinones and α keto-esters

In such oxidations peracetic acid and perphthalic acids are reagents of choice and the following are some of the examples:







CHAPTER

18

Some Reducing Agents and Their Mechanism

LITHIUM ALUMINIUM HYDRIDE $LiAlH_4$

The discovery of the reagent was announced in 1947 by A.E. Finholt, A.C. Bond and H.I. Schleesinger.

It is prepared by the gradual addition of aluminium chloride to a slurry of lithium hydride in ether. The precipitated LiCl and unreacted LiH are filtered off.

$$4LiH + ALCl_3 \longrightarrow LiAlH_4 + 3LiCl.$$

It is a highly reactive reagent and great care must be taken in its handling because it rapidly reacts with moisture or protic solvents liberating hydrogen and accompanied by a danger of explosion. In direct contact with liquid water, it may cause ignition. Vigorous grinding or a sharp mechanised shock may result in fire or explosion . This is why specially dried solvents are not required, because the use of a slight excess of the reagent serves as a convenient and effective drying agent.

Although the reagent is written as $LiAlH_4$ but interpreted as $Li^{\oplus}[AlH_4]^-$ or Li^+ AlH_4^-. In ether solution, it exists as aggregates of solvated lithium ions and aluminus-hydride ions.

Functions

Among the complex hydrides, lithium aluminium hydride is the most versatile reducing agent.

It reduces:

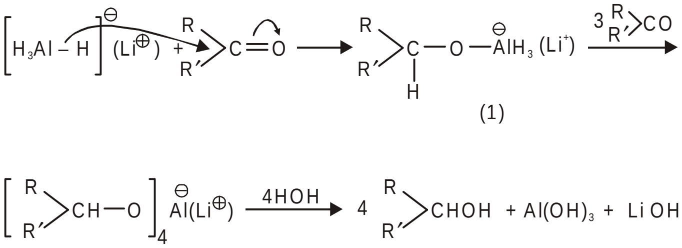
1. Aldehydes, ketones, carboxylic acids, acids chlorides, esters and epoxides to the corresponding alcohols.
2. Cyclic anhydrides to lactones.
3. Amides, nitriles and oximes to amines.
4. Alkyl halides and tosylates to their corresponding hydrocarbons.
5. Double bonds in conjugation to a carbonyl group and allylic and propargylic alcohols. But the isolated double and triple bonds are inert.

Not only this, another important feature of the reduction is the extent to which the geometry of the product can be controlled. For examples by the appropriate choice of the conditions pure axial and equatorial isomers of cyclohexyl derivatives can be prepared.

Mechanism or Reduction

(i) Reduction of Carbonyl Group

In the reduction of a carbonyl group, there is an initial transfer of a hydride ion by an S_N^2 mechanism when the complex (1) is formed. Since it has still three more hydrogen atoms, it reacts with three more molecules of ketone to give the alkoxide (2) Hydrolysis of the latter gives secondary alcohol, along with aluminium and lithium hydroxides.

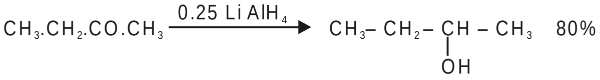


(1)

(2)

Because of its low molecular weight (37.95) and because each molecule reduces four moles of an aldehyde or a ketone, small amounts of $LiAlH_4$ give very good yields of the reduction products. This is apparent from the following reductions in which only 0.25 mole of the reagent gives good yields of the corresponding reduction products.

$$CH_3(CH_2)_5CHO \xrightarrow{0.25\ LiAlH_4} CH_3(CH_2)_5CH_2OH \quad 86\%$$



$$CH_3.CH_2.CO.CH_3 \xrightarrow{0.25\ LiAlH_4} CH_3-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_3 \quad 80\%$$

$$CH_3.CH{=}CHCHO \xrightarrow{0.25\ LiAlH_4} CH_3.CH{=}CH.CH_2OH \quad 70\%$$

Two factors control the course of reduction of cyclic ketones :

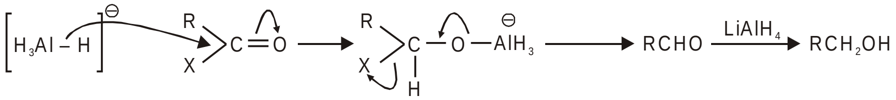
(*a*) Steric hindrance to the approach of the hydride ion called the steric approach control.

(*b*) Stability of the final product – called the product development control.

Since the equatorial substituents are more stable than axial substituent, the product development control gives mainly the equatorial alcohol unless the steric hindrance to the approach of the reagent is very severe.

(ii) Reduction of Carboxylic Acids and Derivatives

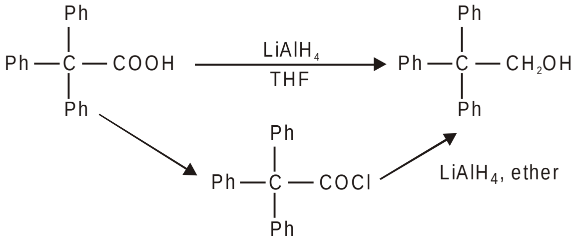
A particularly interesting property of lithium aluminium hydride is its ability to reduce carboxylic acids and its derivatives to primary alcohol.



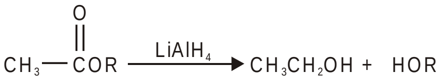
(1)

where X = OH, OR, halogen or OCOR’.

Triphenylacetic acid is not reduced under ordinary conditions in the medium of ether. But it is converted into a primary alcohol in good yield either by reduction in higher boiling solvent like THF or by first converting it into an acid chloride which is then readily reduced in ether.



Since an acetyl derivative of an alcohol is easily cleaved by $LiAlH_4$, the reagent is often used in the deacetylation of compounds sensitive to acids or bases.



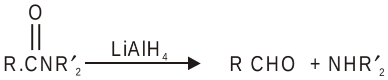
$$CH_3-\overset{O}{\overset{\|}{C}}OR \xrightarrow{LiAlH_4} CH_3CH_2OH + HOR$$

(iii) Reduction of Amids, Nitriles and Oximes

An amide on reduction is changed to the corresponding amine and the order of the reactivity is $RCONR_2 > RCONHR > RCONH_2$.

$$R\,\overset{O}{\overset{\|}{C}}-NH_2 \xrightarrow{LiAlH_4} R\,CH_2NH_2$$

Sometimes other groups may also be reduced without disturbing an amide function. If the amide is in excess, an aldehyde is the main product rather than an amine.

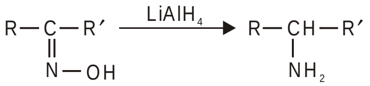


$$R.\overset{O}{\overset{\|}{C}}NR'_2 \xrightarrow{LiAlH_4} R\,CHO + NHR'_2$$

The nitriles have been reduced to primary amines and the reaction has been found to be of wide scope.

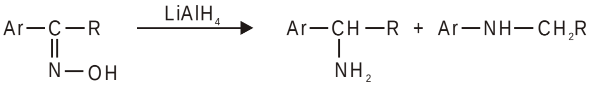
$$R-C\equiv N \xrightarrow{LiAlH_4} R\,CH_2-NH_2$$

Similarly the reduction of both aldoxime and ketoxime gives again primary amines.



$$R-\underset{\underset{N-OH}{\|}}{C}-R' \xrightarrow{LiAlH_4} R-\underset{\underset{NH_2}{|}}{CH}-R'$$

The aromatic oximes usually give secondary amines from rearrangement, sometimes as side products and sometimes as main products.



$$Ar-\underset{\underset{N-OH}{\|}}{C}-R \xrightarrow{LiAlH_4} Ar-\underset{\underset{NH_2}{|}}{CH}-R + Ar-NH-CH_2R$$

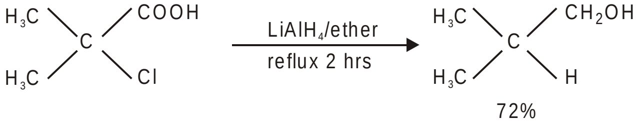
(iv) Reduction of Alkyl Halides and Tosylates

Being a versatile reducing agent, lithium aluminium hydride reduces both alkyl and aryl halides to hydrocarbons.

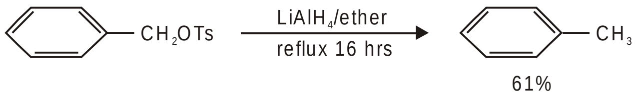
$$RX \xrightarrow{LiAlH_4} RH$$

Trevoy and W.G. Brown reported in 1949 that $LiAlH_4$ reduced both benzyl iodide and benzyl bromide at 35° in high yields. The solvents were either ether or THF. The products were toluene.

It has been shown that not all the four hydrogen atoms are reactive in reducing alkyl halides. If however, a compound possesses two reducible groups, both are reduced as in the following example:



The tosylates resemble alkyl halides and are also reduced to hydrocarbons.



(v) Reduction of Allylic and Propargylic Alcohols

Although lithium aluminium hydride does not reduce alkenes or acetylene hydrocarbons, it reduces allylic alcohols and their acetylenic counterparts. Thus cinnamic acid is reduced to dihydrocinnamyl alcohol.

$$C_6H_5CH{=}CH.COOH \xrightarrow[\text{reflux 15 min.}]{\text{Li Al }H_4\text{/ether}} \underset{85\%}{C_6H_5CH_2.CH_2OH}$$

In the above reduction cinnamyl alcohol is first formed which then changes to the saturated alcohol.

Similarly phenyl propiolic acid is first reduced to phenyl propargyl alcohol which then forms a complex with $LiA1H_4$ and decomposition of the latter with water gives cinnamyl alcohol.

$$\underset{\text{Phenyl propiolic acid}}{C_6H_5C{\equiv}C.COOH} \xrightarrow[-70°]{\text{Li Al }H_4} \underset{\text{Phenyl propargyl alcohol}}{C_6H_5C{\equiv}C.CH_2OH} \xrightarrow{LiAlH_4} \underset{\text{Cinnamyl alcohol}}{C_6H_5CH{=}CH.CH_2OH}$$

SODIUM BOROHYDRIDE : NABH$_4$

Sodium borohydride was discovered by H.I. Schlesinger and H.C. Brown in 1943 and was prepared by heating methyl borate with sodium hydride.

$$4NaH + B(OCH_3)_3 \longrightarrow NaBH_4 + 3NaOCH_3$$

Sodium borohydride is a much milder reducing agent than lithium aluminium hydride and like the latter is used for the reduction of carbonyl compounds like aldehydes and ketones. However, under normal conditions it does not readily reduce epoxides, esters, lactones, acids, nitriles or nitro groups.

The aldehydes are reduced so rapidly that condensation reactions promoted by alkali do not interfere.

While ether is the common solvent for $LiAlH_4$, in which it is soluble, hydroxylic solvents like water, methanol and ethanol are preferred for $NaBH_4$, It is more soluble in methanol than in ethanol, but since it reacts with the former at an appreciable rate than the latter, hence ethanol is the preferred solvent. Isopropanol, in which $NaBH_4$ is stable, is used for kinetic studies of the reduction of aldehydes and ketones.

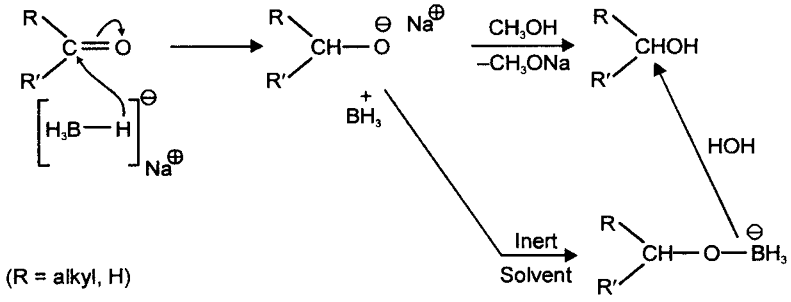
Functions

1. The aldehydes, ketones and acid chlorides are reduced to alcohol.
2. Cyclic anhydrides are reduced to lactones.
3. The esters and lactones are reduced to ethers.
4. The alkyl halides and tosylates are reduced to hydrocarbons.
5. In presence of boron trifluoride, the reagent is used to obtain diborane in situ.

Mechanism of Reduction

The mechanism of reduction is analogous to that for lithium aluminium hydride.

(i) Reduction of Carbonyl Compounds



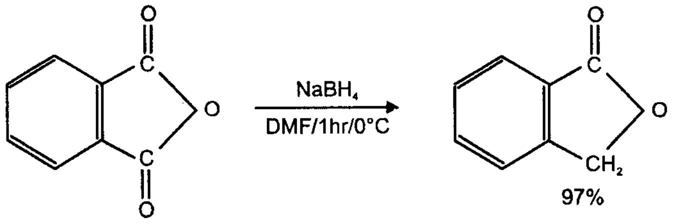
(R = alkyl, H)

The acid chlorides are reduced to alcohols.

$$RCOCl \xrightarrow{NaBH_4} RCH_2OH$$

(ii) Reduction of Cyclic Anhydrides

The cyclic anhydrides are reduced to lactones just by keeping the compound in contact with $NaBH_4$, at 0° for 1 hour in the medium of dimethyl formamide.



(iii) Reduction of Esters and Lactones

Normally the carboxylic esters are not reduced by sodium borohydride, but in presence of the large amount of the reagent in methanol, the ester may be reduced in varying degree to alcohols.

In presence of inert solvents like dioxane or THF, sodium borohydride can catalyse ester exchange.

$$\mathrm{RCOOMe} \xrightleftharpoons{\mathrm{NaBH_4/EtOH}} \mathrm{RCOOEt} + \mathrm{MeOH}$$

The lactones are reduced to cyclic ethers.

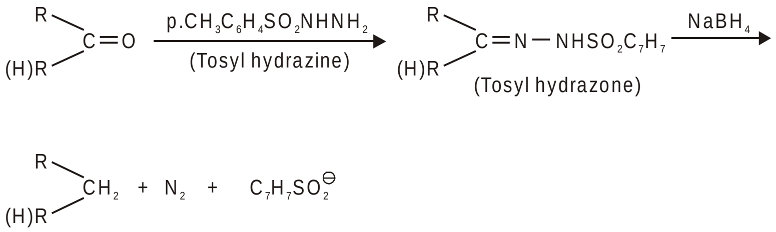
(iv) Reduction of Alkyl Halides and Tosylates

The secondary and tertiary alkyl halides, which generally form stable carbocations, are reduced to hydrocarbons.

$$(C_6H_5)_2\,CHCl \xrightarrow{OH^{\ominus}} (C_6H_5)_2\,CH^{\oplus} \xrightarrow{NaBH_4} (C_6H_5)_2\,CH_2 \qquad 94\%$$

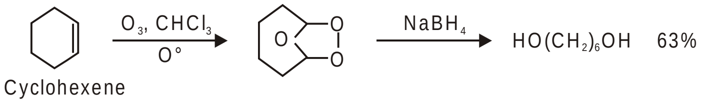
$$(C_6H_5)_3\,CCl \xrightarrow{OH^{\ominus}} (C_6H_5)_3\,C^{\oplus} \xrightarrow{NaBH_4} (C_6H_5)_3\,CH \qquad 90\%$$

The tosyl hydrazones are reduced to R_2CH_2. Since the reduction proceeds smoothly, it constitutes a valuable method of removing carbonyl groups in organic synthesis.



(v) Some other Reductions

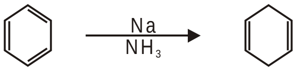
As already written earlier sodium borohydride in presence of BF_3 can generate diborance in situ. The ozonides can be reduced to alcohols.



METAL/LIQUID AMMONIA

(Birch Reduction)

A solution of lithium, sodium, potassium or calcium in liquid ammonia can reduce a wide variety of unsaturated groups. Thus when aromatic rings are reduced by such metals in liquid ammonia, non-conjugated cyclohexadienes are produced. The reaction is called Birch reduction.



Functions

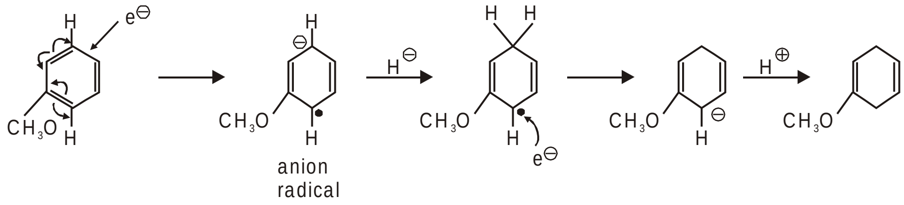
Metal/ammonia reduction is employed in the :

1. reduction of aromatic rings.
2. reduction of aryl ethers and phosphites.
3. conversion of disubstituted acetylenes to trans olefines.
4. conversion of conjugated dienes to mono olefines.

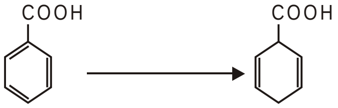
(i) Reduction of Aromatic rings

As already stated above, the aromatic rings are changed to non conjugated cyclohexadienes.

The alkali metals in liquid ammonia give deep coloured solutions which have been shown to contain solvated electrons. The unsaturated system takes up an electron to give an anion radical. There is evidence for this species from electron spin resonance studies. It accepts a proton from the solvent to give a radical; which is reduced to a carbanion by another sodium atom. Finally the addition of a proton gives the reduced product. This proton is supplied by a protic solvent like enthanol and not from NH_3.



From the above mechanism, it becomes obvious that the presence of electron withdrawing groups on the ring would accelerate the reaction, while electron-donating groups would retard it. The former give 1, 4-dihydrobenzenes, while the latter give 2, 5-dihydrobenzenes.

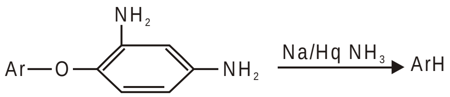


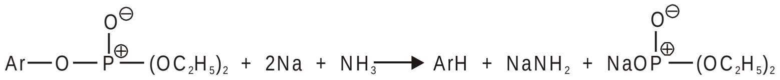
The ordinary olefines are not reduced under these conditions. But sodium in liquid ammonia reduces double bonds if they are conjugated to aromatic systems or other multiple bonds.

Another question that has come up is : why the addition of proton to carbanion occurs only at position 6 to give 1,4 diene and not at 2 or 4 to give a 1,3 diene ? This has been answered on the “principle of least motion” advanced by Hine according to which those reactions are favoured which involve the least change in atomic position and electronic configuration.

(ii) Reduction of Aryl Ethers and Phosphites

The aryl ethers and phosphites of the following type are reduced by Na/liq NH_3 to the corresponding aromatic hydrocarbons.

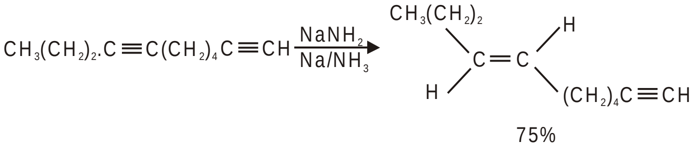




$$Ar{-}O{-}\overset{O^{\ominus}}{\overset{|}{P}}{}^{\oplus}{-}(OC_2H_5)_2 + 2Na + NH_3 \longrightarrow ArH + NaNH_2 + NaO\overset{O^{\ominus}}{\overset{|}{P}}{}^{\oplus}{-}(OC_2H_5)_2$$

(iii) Conversion of Disubstituted Acetylenes to trans Olefines

The following is the best example:



SOME METAL CATALYSTS USED IN HYDROGENATION

Nearly all unsaturated compounds react rapidly with hydrogen at low temperatures and pressures in presence of finely divided metal catalysts such as nickel, platinum and palladium. For maximum catalytic effect, the metal is taken in the finely divided state. This is achieved for platinum and palladium by reducing the metal oxide with hydrogen. A specially active form of nickel is the "Raney nickel".

Such heterogeneous reactions are extremely difficult to study in detail. It is thought that the reaction occurs on the surface of the catalyst. The reacting substances may be held loosely by van der Waals forces or more tightly by chemical bonds. The mode of action probably involves a bonding of hydrogen atoms to the metal surface first. Then this activated hydrogen is transferred to the π electrons giving the reduced product. The hydrogenated compound is then replaced by a fresh molecule of unsaturated compound. The scheme may be represented as:

It implies that the addition of the hydrogen should always be cis and should be from the less hindered side of the molecule and this is actually the result.

The experiment is carried out by stirring a solution of the compound with the catalyst power in an atomsphere of hydrogen gas. The rate of decrease in the volume of hydrogen, measured manometrically, gives the reaction rate. It is supposed to be complete when the stoichiometric quantity of hydrogen has been used up. The rates of reduction of different functions are different and the order of rates for different unsaturated groups is as follows:

ORDER OF REACTIVITY FOR HYDROGENATION

Group reduced	*Product*
RCOC1	RCHO.
R-NO_2	RNH_2
alkynes	alkenes (cis)
R–CHO	R–CH_2OH
alkenes	alkanes.
R–CN	R–CH_2NH_2
Ketones	sec.alcohols.

RANEY NICKEL CATALYSTS

As already stated it is a specially active form of nickel and is prepared from a nickel-aluminium alloy : sodium hydroxide is added to dissolve the aluminium and nickel is left as a black pyrophoric powder.

$$2Ni - Al + 2OH^- + 2H_2O \rightarrow 2Ni + 2AlO_2^- + 3H_2$$

The literated hydrogen gets adsorbed on the nickel surface. The method was developed by Raney and hence the name.

Highly active nickel, platinum and palladium catalysts can also be prepared by reducing the metal salts with sodium borohydride.

Reductions done by Raney-Nickel Catalysts

(i) Reduction of Aromatic Ethers

The aromatic ethers are reduced to hydrocarbons.

$$Ar - OR \xrightarrow[\Delta]{\text{Raney Ni}} ArH + RH.$$

If R is aromatic, it is reduced to a cyclohexane ring unless degassed catalyst is used.

The mechanism involves probably the formation of an arylion which takes up a proton from the solvent to complete the reduction :

$$Ar - O - R \xrightarrow[\text{from catalyst}]{+H^-} Ar^- + ROH$$

The ROH is then also reduced.

(ii) Reduction of C = C and C ≡ C Compounds

Hydrogenation of double and triple bonds has already been discussed. If the compound contains reducible functional groups, they may also be reduced; but selective reduction of double bonds has been possible under suitable conditions.

Of the various catalysts used for the reduction of multiple bonds, Raney nickel is very effective.

Raney nickel deactivated with piperidine and zinc acetate has been used for semihydrogenation of acetylenic compounds.

(iii) Reduction of Nitriles

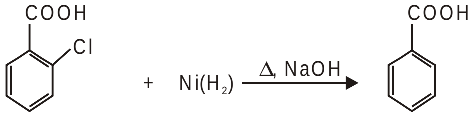
Raney nickel hydrogenation of aromatic and aliphatic nitriles in ethanol containing 4 equivalents of phenyl hydrazine gives 90% of aldehydes.

$$R - C \equiv N \longrightarrow RCHO$$

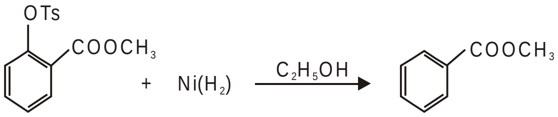
This reduction has also been achieved by treating the nitrile with sodium hypophosphite (NaH_2PO_2) and Raney nickel in aqueous acetic acid – pyridine or formic acid.

(iv) Reduction of Halides and Tosylates

In aromatic or aliphatic acids, containing fluoro, chloro, bromo or iodo substituents Raney nickel in alkaline solutions displaces the halogens.

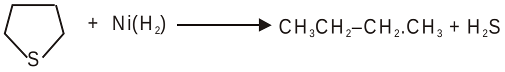


Similarly phenyl tosylates are changed to corresponding hydrocarbons at room temperature and pressure.



(v) Desulphurization

Hydrogenolysis of carbon-sulphur bonds (desulphurization) is carried out with Raney nickel.



Other catalysts are poisoned and inactivated by sulphur compounds.

PLATINUM

When NH_4Cl is added to a solution of platinum tetrachloride, sparingly soluble ammonium chloroplatinate is obtained, which on ignition gives spongy platinum.

$$PtCl_4 + 2NH_4Cl \longrightarrow (NH_4)_2\, PtCl_6$$

$$(NH_4)_2PtCl_6 \xrightarrow{\Delta} 2NH_4Cl + 2Cl_2 + Pt.$$

It is commonly considered to be an inert element, but this is not quite correct. In the fused state it absorbs oxygen and in the finely divided state it absorbs appreciable amount of hydrogen. It has been shown that at 80° and under a pressure of 1 atmosphere, it absorbs about 900 times of as much hydrogen as its own volume. This is why it is used as a catalyst in several hydrogenation reactions.

Platinum Black

When a solution of chloroplatinic acid, $PtCl_4$. 2HCl. $6H_2O$ is reduced by alkaline formaldehyde, platinum black is obtained.

This catalyst is useful for the destruction of excess hydrogen peroxide. The mixture containing H_2O_2 and the catalyst is stirred in the medium of alcohol-water, till the evolution of oxygen ceases.

Platinum oxide, PtO_2, is used in the selective reduction of an unsatruated aldehyde to an unsaturated alcohol.

$$\underset{\text{cinnamaldehyde}}{C_6H_5CH = CHCHO} + H_2 \xrightarrow{PtO_2} \underset{\text{cinnamyl alcohol.}}{C_6H_5CH = CHCH_2OH}$$

PALLADIUM

On strongly heating crystals of tetrammine palladium chloride, $[Pd(NH_3)_4]Cl_2 . H_2O$, palladium in the form of a sponge or fine powder is obtained.

Like platinum, it is used as a catalyst in several hydrogenation reactions. It absorbs hydrogen to a much greater extent than platinum. When heated to dull redness, it absorbs about 1000 times its own volume of hydrogen. If the temperature is raised further, the hydrogen is expelled. In the process probably the hydrogen molecules are broken into hydrogen atoms which then fit into the palladium lattice.

Coupled with various substances, several palladium catalysts have been prepared some of which are :

1. 5% Pd on $BaSO_4$.
2. 5% Pd on C.
3. $PdCl_2$ on C containing 5% Pd.
4. 10% Pd on C.

Cram and Allinger have shown that Pd-$BaSO_4$ catalyst partially poisoned with quinoline is very suitable for the partial reduction of the triple bond.

(i) Dehydrogenation

Linstead has reported that several hydroaromatic hydrocarbons undergo dehydrogenation when heated with palladium charcoal in liquid phase. The process is accelerated by passing CO_2 into the liquid to remove hydrogen. Vigorous heating also removes hydrogen from the active surface of the catalyst. The course of the reaction can be studied by measuring the hydrogen.

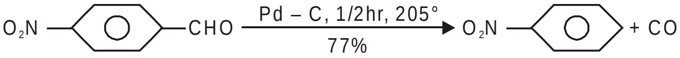
Thus tetralin (b.p.208°) is dehydrogenated only when it is boiling.

(ii) Decarbonylation of Aldehydes

A 5% palladium on charcoal when heated with some aromatic aldehydes brings about its decarbonylation.

For example:

$$C_6H_5CHO \xrightarrow[78\%]{Pd - C,\ 1hr,\ 179^\circ} C_6H_6 + CO$$



The reaction does not appear to be satisfactory with aliphatic aldehydes and also with some aryl aldehydes. Like platinum, coupled with various substances, palladium is also used to catalyse several organic reactions. One such combination is known as Lindlar's catalyst.

Lindlar Catalyst

It is a combination of Pd-$CaCO_3$- Pbo and has been prepared from palladium chloride.

Lindlar catalyst is highly effective in preferential hydrogenation of triple bonds to cis double bonds.

ALUMINIUM ISOPROPOXIDE $Al(OCHMe_2)_3$

(Meerwein-Pondrof-Verley Reagent)

Aluminium isopropoxide is a specific reagent for the reduction of carbonyl group to hydroxyl group. Since it reduces the carbonyl group in presence of other reducible groups like nitro or a double bond which remain unaffected, aluminium isopropoxide is largely employed for the reduction of unsaturated aldehydes and ketones.

The reaction which is carried out in presence of isopropyl alcohol is also called Meerwein-Pondorf-Verley reduction. An example is the reduction of crotonaldehyde to crotyl alcohol.

$$\underset{\text{Crotonaldehyde}}{CH_3.CH{=}CHCHO} + (CH_3)_2\,CHOH \xrightarrow[110^\circ,\ 8 - 9\ hrs]{Al(OPri)_3} \underset{\text{crotyl alcohol}}{CH_3.CH{=}CH.CH_2OH} + (CH_3)_2\,C{=}O$$

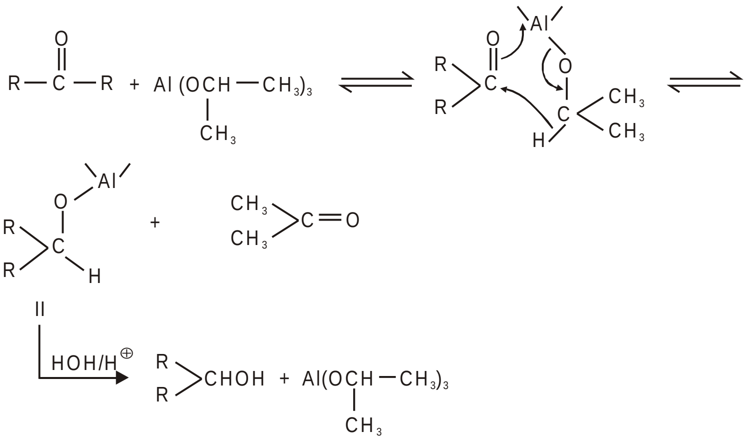
Since the reaction is reversible and the reverse reaction is called Oppenauer oxidation, the equilibrium is shifted to right by removing the acetone by distillation.

Mechanism

The mechanism involves three stages:

1. the initial formation of a cyclic coordination complex (I)
2. Which then forms a mixed alkoxide II by hydrogen transfer.
3. Finally the hydrolysis of II gives the alcohol and regenerates aluminium isoproxide by combining with the acetone.

Using deuterium labelling technique, it has been shown that it is the α –H atom of II which goes to the carbonyl carbon of the starting aldehyde or ketone.



In the above mechanism $Al(OP_r^i)_3$ has been shown to be reacting as a monomer, but actually it is not so because it exists as trimer or tetramer and it is in these forms that it reacts.

CHAPTER 19

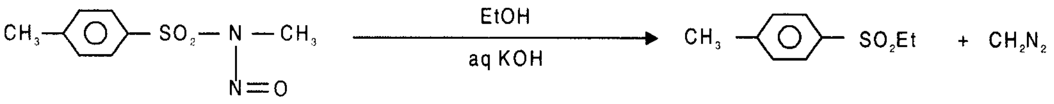
Miscellaneous Compounds

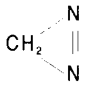
SOME MISCELLANEOUS REAGENTS AND THEIR APPLICATIONS

Diazomethane $CH_2=\overset{\oplus}{N}=\overset{\ominus}{\ddot{N}}: \longleftrightarrow \overset{\ominus}{\ddot{C}}H_2-\overset{\oplus}{N}\equiv N:$

Diazomethane is one of the most versatile and useful reagents in organic chemistry in spite of the fact that it is very highly toxic and dangerously explosive and can not be stored without decomposition.

All reactions employing diazomethane must be carried out in a well-ventilated hood behind a safety screen. After observing the appropriate precautions, diazomethane is safely prepared by the base treatment of N-methyl-N nitroso-p-toluene sulphonamide ('Diazald').



Diazomethane is an intensely yellow gas at room temperature and is handled in ether or methylene chloride solution. It has an unusual structure and the molecule is linear. Its cyclic isomer, called diazirine  is also known.

Diazomethane finds great applications in synthetic organic chemistry.

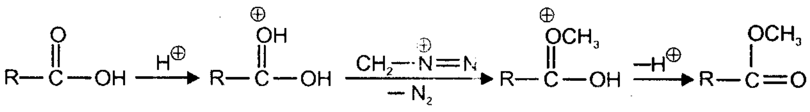
Applications

1. Esterification of Acids

Diazomethane is extensively used to prepare methyl esters of acids on a small scale. The method is simple and proceeds, without a catalyst. The evolved nitrogen poses no problem of separation and yields are quantitative. Because of its colour and bubbles of nitrogen gas coming out, it acts as its own indicator to show when the reaction is complete.

$$C_6H_5COOH + CH_2N_2 \xrightarrow[\text{ether}]{\text{Room temp.}} C_6H_5COOCH_3 + N_2.$$

The acid supplies proton which catalyses esterification.



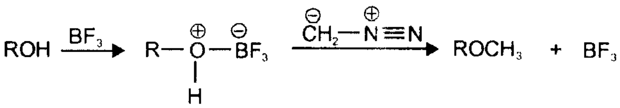
$$R-\overset{O}{\overset{\|}{C}}-OH \xrightarrow{H^{\oplus}} R-\overset{\overset{\oplus}{OH}}{\overset{\|}{C}}-OH \xrightarrow[-N_2]{CH_2-\overset{\oplus}{N}=N} R-\overset{\overset{\oplus}{OCH_3}}{\overset{\|}{C}}-OH \xrightarrow{-H^{\oplus}} R-\overset{OCH_3}{\overset{|}{C}}=O$$

2. Methylation of Alcohols

An alcohol itself is inert towards diazomethane but it can be methylated in presence of boron trifluoride etherate or fluoroboric acid. A mineral acid cannot be used because it will react itself with CH_2N_2.

$$\phi CH_2OH + CH_2N_2 \longrightarrow \phi CH_2OCH_3 + N_2$$

The mechanism appears to be as follows:



$$ROH \xrightarrow{BF_3} R-\underset{\underset{H}{|}}{\overset{\oplus}{O}}-\overset{\ominus}{B}F_3 \xrightarrow{\overset{\ominus}{C}H_2-\overset{\oplus}{N}\equiv N} ROCH_3 + BF_3$$

The method has also been used to methylate phenols, at least those, which are expensive because the yields are quantitative. The more acidic phenols react very well in absence of a catalyst.

3. Methylation of Amines

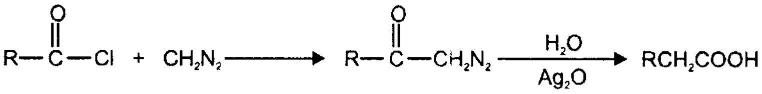
When ammonia is used as the amine, mixtures of primary, secondary and tertiary amines are the products. The primary aliphatic amines give mixtures of secondary and tertiary amine. Best results are obtained with secondary amines which give tertiary amines.

$$CH_2N_2 + R_2NH \longrightarrow CH_3NR_2 + N_2$$

The reaction proceeds also with primary aromatic amines but diaryl and benzylamine react poorly.

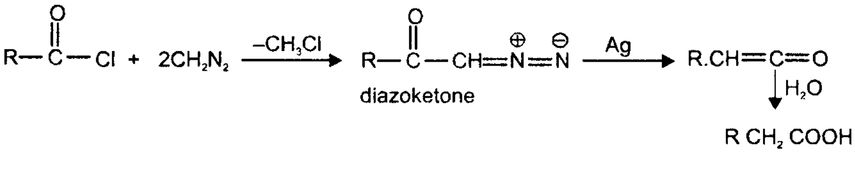
4. Arndt-Eistert Synthesis

In Arndt-Eistert synthesis, and acyl chloride is converted to a carboxylic acid with one additional carbon atom.



$$R-\overset{O}{\overset{\|}{C}}-Cl + CH_2N_2 \longrightarrow R-\overset{O}{\overset{\|}{C}}-CH_2N_2 \xrightarrow[Ag_2O]{H_2O} RCH_2COOH$$

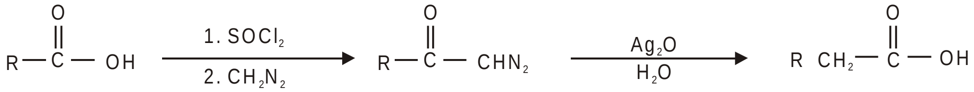
The reactions appears to proceed in two stages which are:



$$R-\overset{O}{\overset{\|}{C}}-Cl + 2CH_2N_2 \xrightarrow{-CH_3Cl} \underset{\text{diazoketone}}{R-\overset{O}{\overset{\|}{C}}-CH=\overset{\oplus}{N}=\overset{\ominus}{N}} \xrightarrow{Ag} R.CH=C=O \xrightarrow{H_2O} R\,CH_2\,COOH$$

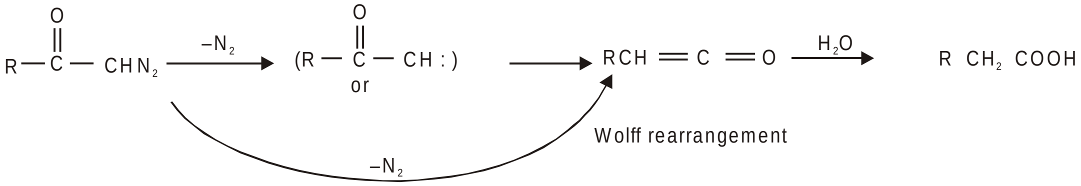
The diazoketone first formed is decomposed in a high-boiling solvent (benzyl alcohol or octanol 2) at 160°-180°. Although no catalyst is required, but the addition of a collidine base improves the yield. The second step is the rearrangement of the diazoketone which is also called Wolff rearrangement.

The Arudt-Eistert reaction is the best method of increasing the length by one carbon atom; not only in acid chlorides but also in carboxylic acid or ketones. With acids the reactions is:



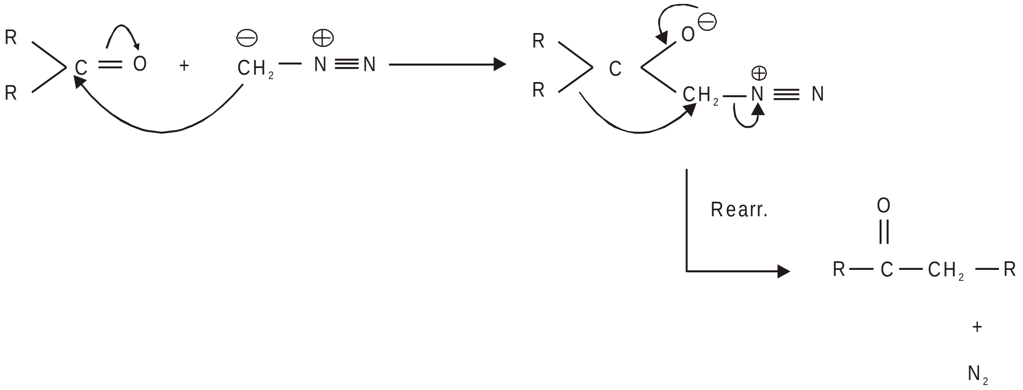
$$R-\overset{O}{\overset{\|}{C}}-OH \xrightarrow[2.\ CH_2N_2]{1.\ SOCl_2} R-\overset{O}{\overset{\|}{C}}-CHN_2 \xrightarrow[H_2O]{Ag_2O} R\ CH_2-\overset{O}{\overset{\|}{C}}-OH$$

and the mechanism is:



$$R-\overset{O}{\overset{\|}{C}}-CHN_2 \xrightarrow{-N_2} (R-\overset{O}{\overset{\|}{C}}-CH:) \longrightarrow RCH=C=O \xrightarrow{H_2O} R\ CH_2\ COOH$$

With ketones the mechanism is as follows:



LIQUID AMMONIA

Ammonia liquefies at atmospheric pressure only when cooled to –33° but at moderate pressures it can be liquefied at ordinary temperatures. There is considerable intermolecular hydrogen bonding in liquid ammonia, which is a colourless mobile liquid but is troublesome to handle because the fumes are noxious. This is why great care is required in its handling.

Liquid ammonia is largely used as a solvent not only for many inorganic salts but also for most organic compounds (except most saturated hydrocarbons).

Phosphorus, iodine and sulphur which are all insoluble in water are soluble in liquid ammonia. Since the amide ion, NH_2^-, is a very strong base, liquid ammonia is a good solvent to obtain a strongly basic medium.

An unusual and very important property of liquid ammonia is its ability to dissolve the alkali and alkaline earth metals reversibly. The solutions obtained are dark blue and the colour is independent of the metal. Such solutions have strong reducing power and high electrical conductivity. This is why solutions of metals in liquid ammonia are used as strong reducing agents and it is believed that an anionic species describable as solvated electron is responsible for these properties.

However, liquid ammonia does not necessarily dissolve all salts which are soluble in water. $BaCl_2$, for example, is soluble in water but insoluble in liquid ammonia. Thus on adding a saturated solution of $Ba(NO_3)_2$ in ammonia to a solution of AgCl in ammonia, a precipitate of $BaCl_2$ is obtained.

$$Ba^{++} + 2NO_3^- + 2Ag^+ + 2Cl^- \longrightarrow 2AgNO_3 + BaCl_2 \downarrow$$

While sodium, potassium and calcium react immediately with water liberating hydrogen, these metals simply dissolve in ammonia without evolving hydrogen. The solutions contain the metal, metal ion and solvated electrons and act as powerful reducing agents. However, in presence of catalysts these metals react with ammonia and evolve hydrogen.

$$Na + NH_3 \xrightarrow{\text{Catalyst}} NaNH_2 + \frac{1}{2}H_2$$

Solutions of metals in liquid ammonia conduct electricity better than any salt in any liquid and the main current carrier is the *solvated electron*. This implies that the electron gets free from the parent metal atom sodium and occupy cavities in the liquid. At higher alkali metal concentrations the solutions are copper coloured and have a metallic lustre and all electrical conductivity studies indicate that they are very similar to liquid metals.

Liquid ammonia is used in the synthesis of the following type of compounds:

1. Ammonolysis of halogen compounds

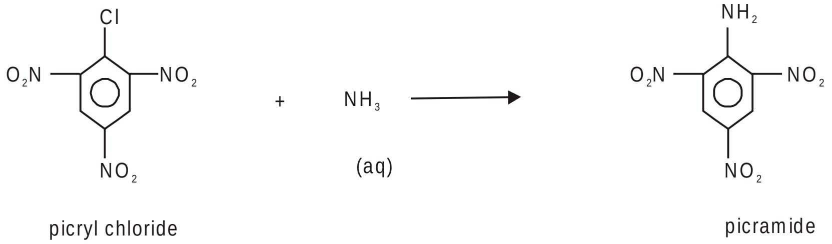
We know that nuclear halogens can be replaced by amine groups but with difficulty. Yet aniline has been manufactured from chlorobenzene by heating it with excess aqueous ammonia in presence of Cu_2O at about 250° under pressure.

$$2C_6H_5Cl + 2NH_3 + Cu_2O \longrightarrow \underset{90\%}{2C_6H_5NH_2} + 2CuCl + H_2O$$

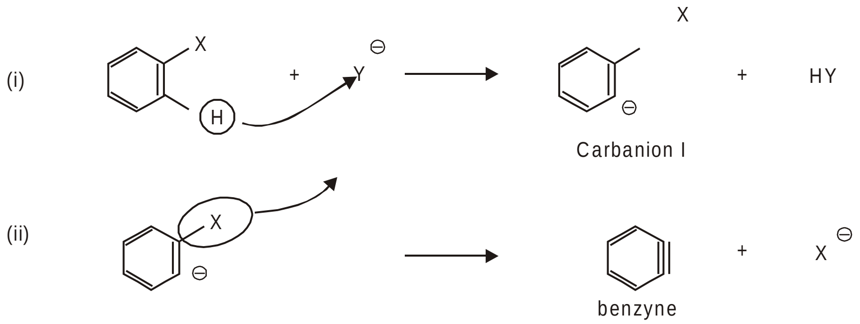
The Cu_2O renders the reaction irreversible by decomposing the NH_4Cl formed in the reaction.

In general the method is not as useful for the preparation of arylamines as for aliphatic amines. But the method becomes of preparative interest when the nuclear halogenated compound contains in addition some electron withdrawing substituents *e.g.*, $-NO_2$, –CN etc. in ortho and para positions. Thus, 2, 4, 6 trinitroaniline (picramide) is readily prepared by the action of aqueous ammonia on 2, 4, 6 trinitrochlorobenzene (picryl choloride).

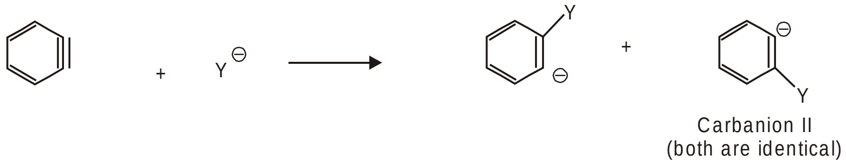
The ammonolysis of C_6H_5Cl is not a simple replacement reaction as it appears to be. The reaction involves two stages, elimination and then addition. An intermediate benzyne is formed.



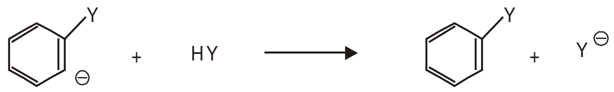
(*a*) Elimination



(*b*) Addition

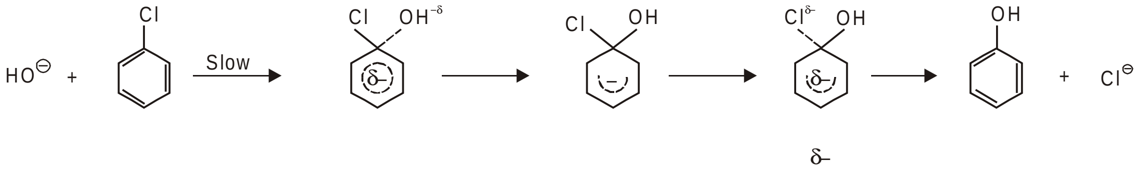


Carbanion II then takes proton from HY to form the required product.

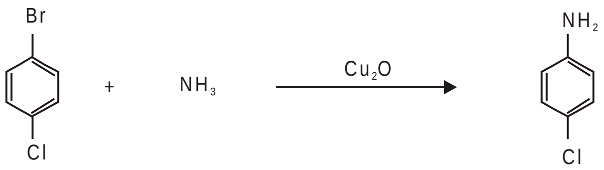


X is any halogen atom attached to the aryl nucleus or is any nucleophile *i.e.*, $-OH^{\ominus}$, $-OR^{\ominus}$, $-NH_2^{\ominus}$, $CN^{\ominus}$ and $SH^{\ominus}$. The order of reactivity of the halogen atom is Br > I > Cl > F when the reaction is carried out with KNH_2 in liquid ammonia.

Another view is that these nucleophilic reactions proceed via intermediate σ complex (S_N2).



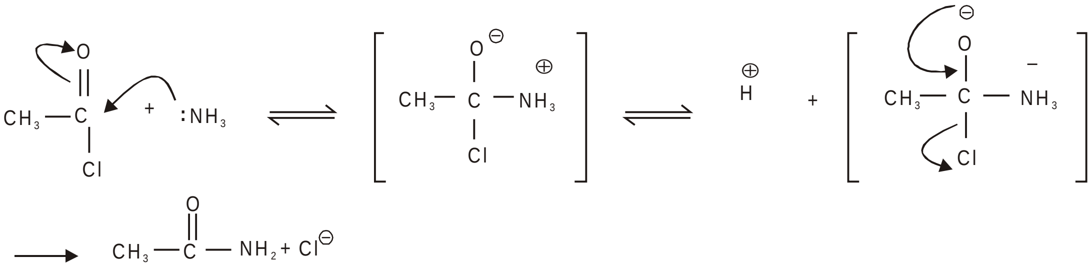
Similarly



In both the above examples, the Cu_2O renders the reaction irreversible by decomposing the NH_4C1 formed in the reaction.

2. Preparation of acid amides

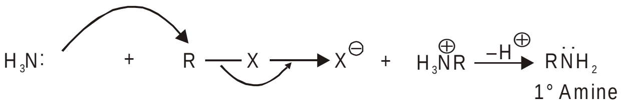
By the action of concentrated NH_3 solution on acid chlorides, acid anhydrides or esters, acid amides can be synthesized.



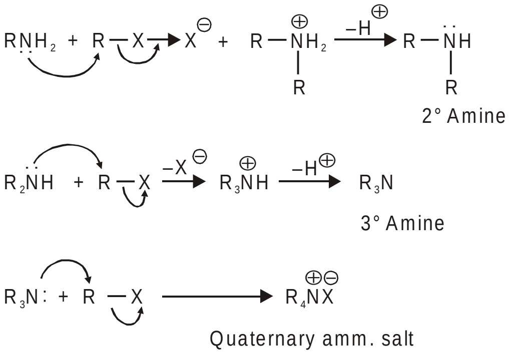
The other moieties will also give acid amides with ammonia.

3. Preparation of amines by ammonolysis

By heating an alkyl halide with an alcoholic solution of ammonia in a sealed tube, a mixture of amines is formed by nucleophilic substitution reaction.



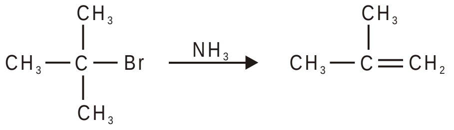
The primary amine formed will react further with alkyl halide giving a secondary amine and by repeating the process a tertiary and finally a quaternary ammonium salt will be formed.



Good yields of 1° amines are obtained by using large excess of ammonia. The ammonolysis proceeds best by using primary alkyl halides. The tertiary alkyl halides tend to form alkenes due to the dominance of the competing elimination reaction.

$$CH_3.CH_2-CH_2-Br \xrightarrow{NH_3} CH_3.CH_2.CH_2.NH_2 \quad \text{(Substitution dominates)}$$

n.propyl brmide (1°) n.propyl amine



$$CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-Br \xrightarrow{NH_3} CH_3-\overset{\overset{CH_3}{|}}{C}=CH_2$$

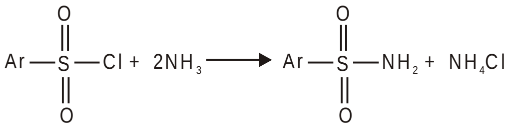
(Elimination dominates)

tsr. lentyl bromide 2 methyl propene

The secondary alkyl halides occupy on intermediate position and both substitution and elimination take place.

4. Sulphonamides

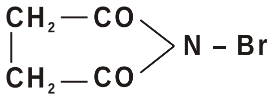
The sulphonamides are prepared by the action of concentrated aqueous solution of NH_3 on sulphonyl chlorides.



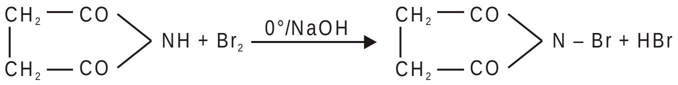
$$Ar-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-Cl + 2NH_3 \longrightarrow Ar-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-NH_2 + NH_4Cl$$

The sulphonamides are used in the preparation of chloramines which are good disinfectants. Ring substituted sulphonamides are used in the preparation of sulphadrugs.

N-BROMOSUCCINIMIDE (NBS)



It is a very important derivative of succinimide and is easily prepared by the action of bromine on succinimide at 0°C in presence of NaOH.



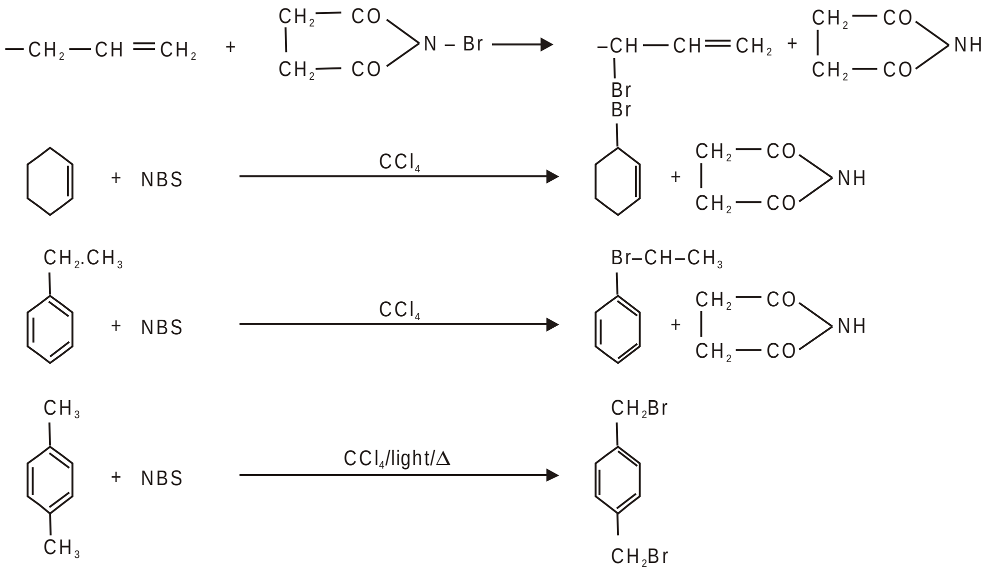
The sample gets coloured due to the occlusion of bromine. It is recrystallized from 10 times its weight of water to obtain the pure form. It is always necessary to use the pure form by eliminating inorganic impurities which tend to increase the addition of bromine in reactions.

Functions

Since NBS is conveniently handled and since it is unreactive towards a variety of other functional groups, it is a valuable reagent for brominating in allylic position in olefines, acetylenes or even aromatic compounds.

Examples:

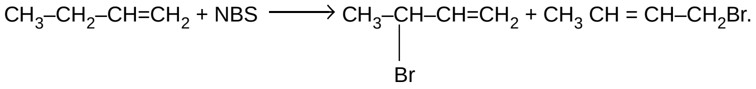
Whereas pure NBS effects side chain bromination of aromatic hydrocarbons, aged material effects bromination of aromatic ring.



Allylic Bromination

Bromination of olefines by NBS is also known as Wohl-Ziegler bromination and as already written, the reaction is specific at allylic position and good yields are obtained.

In unsymmetrical olefines, a mixture of products is obtained probably due to allylic shift in the molecule



$$CH_3–CH_2–CH=CH_2 + NBS \longrightarrow CH_3–\underset{\overset{|}{Br}}{C}H–CH=CH_2 + CH_3\;CH = CH–CH_2Br.$$

If the molecule contains both the primary and secondary carbons carrying hydrogens in α-positions, as $CH_3–CH=CH–CH_2–CH_3$, then a secondary position is substituted more readily than the primary, some allylic substitution at tertiary carbon has also been reported. In case the molecule contains both the double and triple bonds, the preferred position of substitution is α to the triple bond.

Mechanism of Bromination

That the mechanism of bromination by NBS was a free radical one was first suggested by Goldfinger et al (1953, 1956) and later supported by Dauben and Mc Coy in 1959 and also by Tedder et al in 1960 and 1961. The strongest point in favour of the reaction being a free radical one is that it is catalysed by free radical initiators like peroxides and is also promoted by light. Indeed new substitution at the allyl position is often used to detect free radicals. Like free radical reactions, it is also retarded by inhibitors.

The various steps of the reactions are:

(*a*) Initiation: $Br_2 \rightleftharpoons 2Br^{\bullet}$

(*b*) Propagation: (*i*) $Br^{\bullet} + RH \longrightarrow R^{\bullet} + HBr$

(*ii*) $R^{\bullet} + Br_2 \longrightarrow RBr + Br^{\bullet}$

The function of N-bromosuccinimide is, therefore, to provide molecular bromine at a *very low concentration* by reacting with HBr produced in the propagation step.

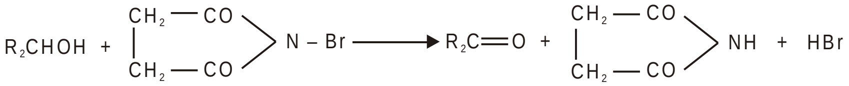
An important question now arises here. If bromine is the reacting species why does it not react with the double bond either by ionic or free radical mechanism ? The answer is that its concentration is too low and this slows the rate of addition and in the circumstances only allylic substitution successfully takes place. This means that if there is regular, slow and steady supply of bromine and if somehow HBr formed, be removed to check addition, then it should be possible to brominate an olefine in allylic position even in absence of NBS and this has been demonstrated by Tedder *et al.*

Tanuer (1964) has shown that in polar solvents the mechanism of bromination is not free radical but involves an electrophilic attack by $Br^{\oplus}$.

Some Other Applications

1. Oxidising reactions

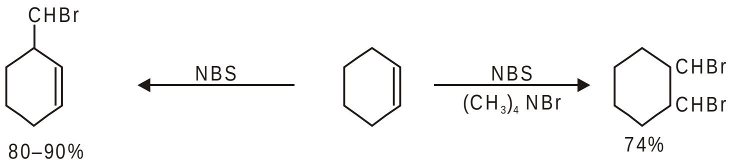
N-bromosuccinimide is a selective oxidising agent and oxidises OH groups without disturbing other oxidisable groups. Thus while it does not oxidise aliphatic primary alcohols; in presence of water it is highly selective for the oxidation of secondary alcohols to ketones.



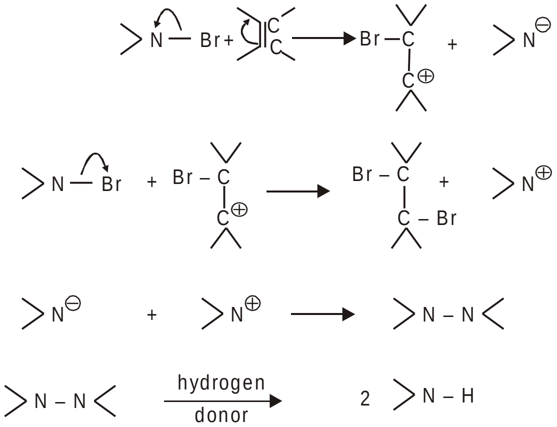
The aliphatic primary alcohols are oxidised by N-Chlorosuccinimide, but the mechanism is not clear.

2. Formation of addition compounds

In addition to substitution N-bromosuccinimide also forms addition compounds although in small amounts. Such addition reactions are catalysed by tetra-alkyl ammonium salts. Thus while with cyclohexene allylic substitution occurs, in presence of tetramethylammonium bromide, 1:2 dibromocyclohexane is obtained as the main product.

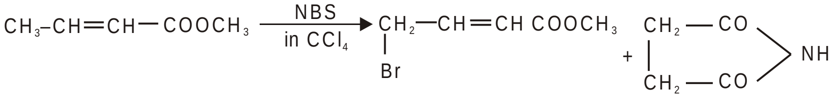


The mechanism involves the attack of Br$^{\oplus}$ ions over the double bond followed by other steps.



3. Synthesis of Methyl 3 Bromocrotonate

Methyl crotonate reacts with NBS and brominates is allylic position giving methyl 3-bromocrotonate, a valuable synthetic reagent used in Reformatsky reaction.

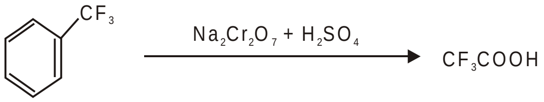


$$CH_3–CH{=}CH—COOCH_3 \xrightarrow[\text{in } CCl_4]{NBS} \underset{Br}{\underset{|}{C}}H_2—CH{=}CH\ COOCH_3 + \begin{matrix} CH_2—CO \\ | \\ CH_2—CO \end{matrix}\!\!>NH$$

CCl_4 is advantageous to use because succinimide is insoluble in this solvent and hence can be easily removed.

TRIFLUOROACETIC ACID CF_3COOH

Trifluoroacetic acid is prepared by treating ααα trifluorotoluene with sodium dichromate and sulphuric acid for 15 days.



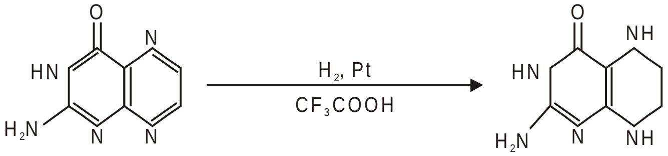
It is colourless liquid (B.P. 72.4°) and is strongly acidic. It is infinitely soluble in water.

Applications

1. Hydrogenation Solvent

Trifluoroacetic acid is the best solvent for several platinum-catalysed hydrogenation processes. For example the rate of reduction of ketones to secondary alcohols is about three times faster than in acetic acid. The ketones are taken in concentrated solutions to keep the reactions faster.

In the reduction of pterines, there is selective and complete reduction of the pyrazine nucleus.

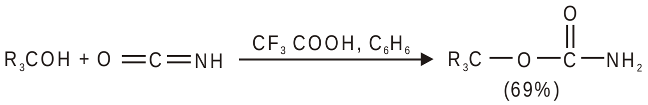


2. Solvent for Kinetic Studies

It is a good solvent for kinetic studies of aromatic electrophilic substitution.

3. Preparation of Carbamates

The carbamates of alcohols, even those of tertiary alcohols can be prepared in good yields. The alcohol is stirred with 2 equivalents of sodium cyanates and trifluoroacetic acid at room temperature for few hours.



$$R_3COH + O{=}C{=}NH \xrightarrow{CF_3COOH,\ C_6H_6} R_3C-O-\overset{\overset{O}{\|}}{C}-NH_2 \quad (69\%)$$

This method has general applicability.

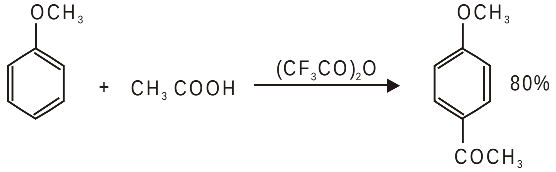
TRIFLUOROACETIC ANHYDRIDE $(CF_3CO)_2O$

Trifluoroacetic anhydride is prepared by the dehydration of trifluroacetic acid with P_2O_5.

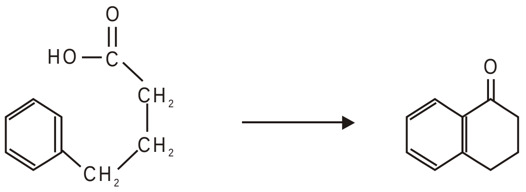
It is a colourless liquid (b.p. 39.5°).

Applications

1. ***Acylation:*** The reagent catalyses the arylation of activated aromatic compounds by reaction with carboxylic acids. Thus methyl phenyl ether can be acylated with acetic acid in presence of trifluoroacetic anhydride in good yields.



γ-phenyl butyric acid can be cyclized to α tetralone in good yields on being warmed with trifluoroacetic anhydride at 60-70° for 3 hours.

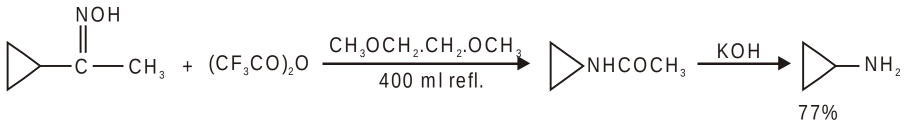


α-tetralone

2. *Esterification:* An alcohol reacts with an acid as per following scheme in presence of trifluoroacetic anhydride.

$$R'COOH + HOR + (CF_3CO)_2O \longrightarrow R'COOR + 2CF_3COOH$$

3. *Rearrangements:* Emmons found the reagent suitable for Beckmann rearrangements giving water soluble amides. Thus methyl cyclopropyl ketoxime in the medium of 1, 2-dimethoyethane was treated under reflux with stirring with trifluoroacetic anhydride in 1 hr. and refluxed for 1 hr. more. The cyclopropylamine was obtained.



SODIUM AMIDE $NaNH_2$ (SODAMIDE)

Sodium amide is prepared by passing a stream of dry ammonia over metallic sodium at 300-400° taken in an iron vessel.

$$2Na + 2NH_3 \longrightarrow 2NaNH_2 + H_2$$

Sodium amide is a waxy solid (m.p. 210°) and turns yellow in contact with moist air when it becomes explosive. The explosive material is destroyed by reaction with NH_4C1.

$$NaNH_2 + NH_4Cl \longrightarrow NaCl + 2NH_3$$

It is also hydrolysed on coming in contact with water.

$$NaNH_2 + HOH \longrightarrow NaOH + NH_3$$

Applications

1. Synthesis of Acetylenic Compounds by Dehydrohalogenation

Sodium amide has been extensively used in the synthesis of a large number of acetylenic compounds by dehydrohalogenation. An example is:

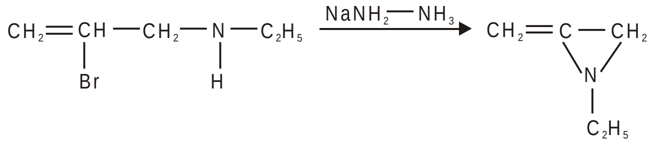
Phenyl-acetylene has been obtained in good yields by adding 1 mole of β bromostyrene to a well-cooled (–33°) suspension of 2 moles of sodium amide in liquid ammonia. After the vigorous reaction has subsided, the compound is separated by adding plenty of water.

$$C_6H_5CH{=}CHBr \xrightarrow{NaNH_2} C_6H_5C{\equiv}CNa \xrightarrow{H_2O} \underset{75\%}{C_6H_5C{\equiv}CH}$$

By starting with styrene dibromide, the yield of phenyl acetylene is reduced to about 64%.

2. Synthesis of Ring Compounds

Dehydrohalogenation has been utilised successfully for certain ring closure reactions.



N-ethyl allenimine

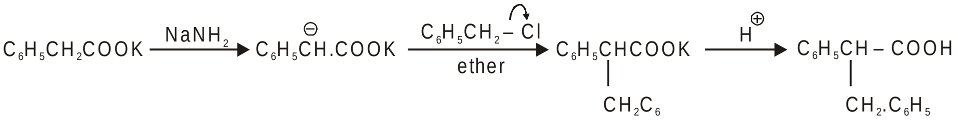
3. Generation of Reactive Anions

With the help of sodamide it is possible to generate reactive anions which then add on to unsaturated compounds forming higher alkylated derivatives.

$$CH_3COOK \xrightarrow{NaNH_2} \overset{\ominus}{C}H_2COOK + CH_2{=}CH_2 \longrightarrow \overset{\ominus}{C}H_2{-}CH_2{-}COOK$$

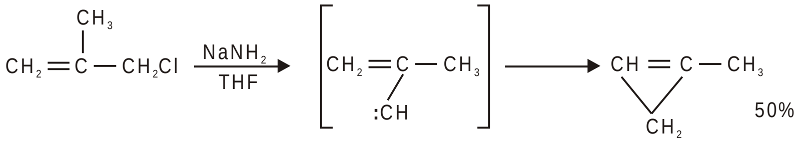
The process can repeat itself once or twice.

The reactive anion can also combine with some other saturated species as in the following example of phenyl acetic acid:



4. Synthesis of Cyclopropenes

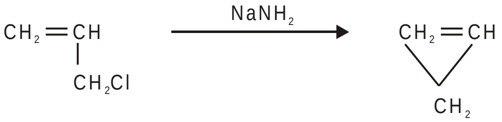
Some cyclopropenes have been synthesized by refluxing methallyl chloride with sodium amide in the medium of THF.



1-methyl cyclopropene

The reaction appears to proceed through a carbene intermediate.

Starting with allyl chloride, cyclopropene has been synthesized conveniently although in about 10% yield



RC ≡ CNa and derived compounds. Sodium acetylides have been used for the synthesis of a large number of organic compounds containing triple bonds.

Thus sodio derivative of propyne can be converted into tetrolic acid as per following scheme:

$$CH_3-C\equiv CH \xrightarrow{NaNH_2} CH_3C\equiv CNa \xrightarrow{CO_2} CH_3C\equiv C\ COONa \xrightarrow{HCl}$$

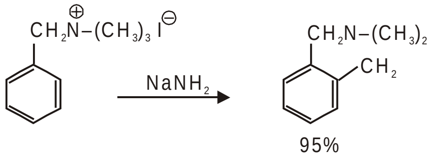
$$CH_3C\equiv C\text{–}COOH \text{ tetrolic acid.}$$

$$\sim 55\%$$

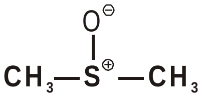
Similarly 1-hexyne has been synthesised as follows from acetylene:

$$HC\equiv CH + Na \xrightarrow[-H_2]{\text{Liq. } NH_3} HC\equiv C\,Na \xrightarrow{n.\ C_4H_9Br} n.C_4H_9C\equiv CH \quad 80\%$$

Other reactions: The reductive rearrangement of benzyl trimethylammonium iodide to tertiary amine has been achieved as follows :



DIMETHYL SULPHOXIDE (DMSO)



$$CH_3-\overset{\overset{\displaystyle O^{\ominus}}{|}}{S^{\oplus}}-CH_3$$

Dimethyl sulphoxide is a highly hygroscopic liquid and is miscible with water. Its m.p. is 18.5° and b.p. 189°C. It is one of those versatile compounds which is a solvent not only for many organic compounds but many inorganic salts as well.

It is interesting to note that non-ionisable substances such as alkyl halides undergo dissociation in the medium of DMSO.

Applications Involving DMSO as Solvent

1. For Study of Molecular Rotations

The molecular rotations of various lactones are studied in the medium of DMSO which has been found to be superior to pyridine.

2. Conversion of Alkyl Chlorides to Cyanides in DMSO

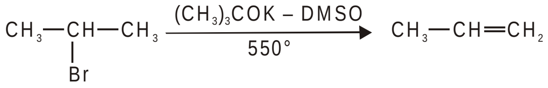
The alkyl halides react with cyanide to produce alkyl cyanides. But this reaction has rarely been employed to obtain the increased length of the chain because of the long reaction times and poor yields. However, the use of DMSO as a solvent has simplified the procedure and improved the yields for the conversion of primary and secondary alkyl chlorides into cyanides, without any rearrangement.

$$R\text{–}Cl + NaCN \xrightarrow{\text{DMSO}} R\text{–}CN + NaCl$$

The results are better with bromides or iodides DMSO not only enhances bimolecular nucleophilic displacements at carbon atoms but also increases electrophilic substitution.

3. Dehydrohalogenation

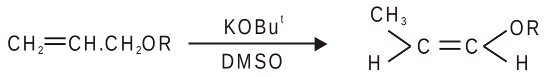
Several dehydrohalogenation reactions have been carried out with the help of DMSO. Thus isopropyl bromide has been successfully converted to propene by heating with potassium tertiary butoxide-DMSO mixture at 550°.



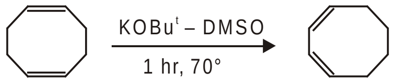
$$CH_3-\underset{\underset{\displaystyle Br}{|}}{CH}-CH_3 \xrightarrow[550^\circ]{(CH_3)_3COK\,-\,DMSO} CH_3-CH=CH_2$$

4. Double Bond Migration

In presence of the basic catalyst potassium t-butoxide, the solvent DMSO accelerates some rearrangement reactions. For example, allyl ethers are rearranged to cis-propenyl ethers.



Cyclooctadiene 1,5 is isomerised even under mild conditions to cyclooctadiene 1, 3.

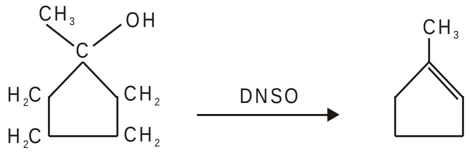


Applications Involving Reactions with DMSO

Dimethyl sulphoxide brings about the dehydration and oxidation reactions in some alcohols.

1. Dehydration

The secondary and tertiary benylic alcohols and tertiary aliphatic alcohols undergo dehydration when refluxed with DMSO at 160-185° for about 9-16 hours. 1-methyl cyclopentanol 1 is dehydrated to 1 methyl cyclopentene.

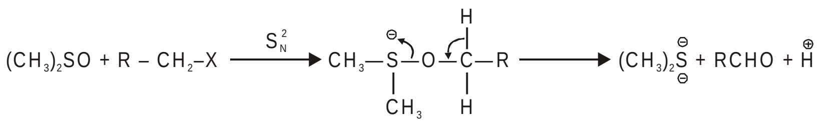


2. Oxidation

The primary alkyl halides (chlorides, bromides and iodides) are oxidised to aldehydes in good yields.

$RCH_2Cl \xrightarrow{\text{DMSO (air)}} RCHO$ (R = aliphatic or aromatic)

The secondary alcohols are oxidized to ketones. In such oxidations, although air facilitates the process, but there is no oxygen uptake and since $(CH_3)_2S$ has been isolated from the reaction products, it shows that DMSO is the oxidant. The mechanism in these oxidations is proabably as follows:



$$(CH_3)_2SO + R-CH_2-X \xrightarrow{S_N^2} CH_3-\underset{CH_3}{\overset{\ominus}{S}}-O-\underset{H}{\overset{H}{C}}-R \longrightarrow (CH_3)_2\overset{\ominus}{\underset{\ominus}{S}} + RCHO + \overset{\oplus}{H}$$

Ketenes on treatment with DMSO in presence of conc. HCl undergo oxidative hydrolysis.

$$(C_6H_5)_2C = C = O \xrightarrow{HCl\text{-}DMSO} (C_6H_5)_2-\overset{OH}{C}-COOH$$

3. Thermal Decomposition

The usual method of carrying out of Wolff-Kishner reduction is to heat a hydrzone in presence of a base at about 200°. But by using DMSO as solvent and potassium t.butoxide as base, the reduction can be carried at room temperature.

Thus by adding about 2.0 g of benzophenone hydrozone to a mixing of 2.0 g of a mixing of sublimed potassium t.butoxide in 5 ml of DMSO, with constant stirring the reaction was complete in 8 hrs.

$$(C_6H_5)_2C = NNH_2 \xrightarrow{KOBu^t\text{-}DMSO} (C_6H_5)_2CH_2 + N_2$$

BORON TRIFLUORIDE

Boron trifluoride is most important of all the halides of boron and is obtained as a colourless highly pungent gas by heating boron trioxide with CaF_2 and Conc. H_2SO_4.

$$B_2O_3 + 3CaF_2 + 3H_2SO_4 \longrightarrow 3CaSO_4 + 3H_2O + 2BF_3.$$

Since the gas is extremely soluble in water forming the hydrates $BF_3.H_2O$ and $BF_3.2H_2O$, it is collected over mercury.

It is mainly used as a Lewis acid catalyst for many organic reactions. The most common Lewis acids in the descending order of activity are $AlCl_3 > BF_3 > SnCl_4 > ZnCl_2$.

Applications

1. Acylations

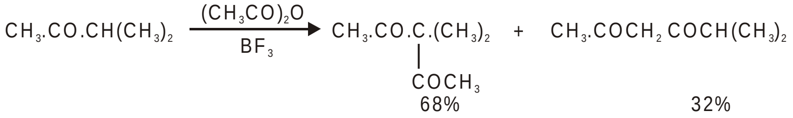
Although most acylations of active methylene compounds are base catalysed, the acylations of ketones carried out with acetic anhydride take place best in presence of BF_3. Acetone is converted to acetylacetone.

$$CH_3COCH_3 + (CH_3CO)_2O \xrightarrow{BF_3} CH_3COCH_2COCH_3$$

It is supposed that first there is complexation between the acid anhydride and BF_3 and then there is electrophilic attack by the acylinm ion.

$$(CH_3CO)_2O + BF_3 \longrightarrow \underbrace{\left[CH_3C\equiv O\right]^{\oplus}}_{\text{acylium ion}} \left[CH_3COOBF_3\right]^{\ominus}$$

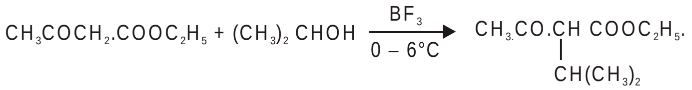
The acylation of asymmetrical ketones takes place mainly at the more unsubstituted position.



$$CH_3.CO.CH(CH_3)_2 \xrightarrow[BF_3]{(CH_3CO)_2O} \underset{68\%}{CH_3.CO.\underset{COCH_3}{\overset{|}{C}}.(CH_3)_2} + \underset{32\%}{CH_3.COCH_2COCH(CH_3)_2}$$

2. Alkylations

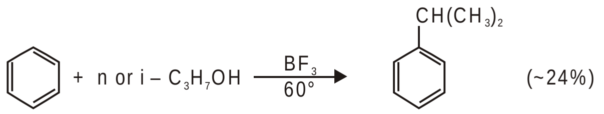
Acetoacetic ester can be alkylated by isopropyl group if BF_3 is saturated at low temperatures in the reaction mixture.



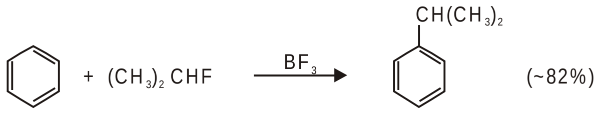
$$CH_3COCH_2.COOC_2H_5 + (CH_3)_2\,CHOH \xrightarrow[0-6°C]{BF_3} CH_3.CO.\underset{\displaystyle CH(CH_3)_2}{\underset{|}{CH}}\,COOC_2H_5.$$

3. Friedel-Crafts Reactions

Friedel-Crafts alkylations can be carried out with isopropanol using anhydrous BF_3 as an active catalyst.



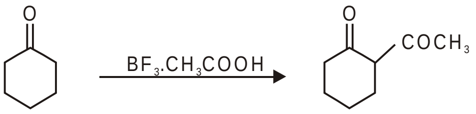
Using isopropyl fluoride and BF_3, the yield of isopropyl benzene can be raised to about 82%.



Coupled with acids or alcohols, boron trifluoride has again found great importance.

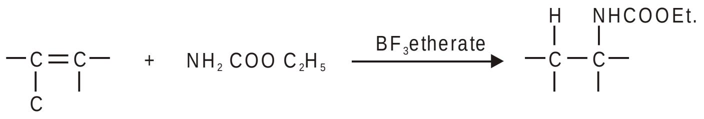
4. Boron Trifluoride-Acetic Acid Complexes. $BF_3.CH_3COOH$

It is a hygroscopic solid and is recommended for the acetylation of a ketone, such as cyclohexanone.



5. Boron Trifluoride Etherate Complex $BF_3(C_2H_5)_2O$

It is a colourless liquid and carbamates add to olefines in presence of BF_3-etherate to give N-substituted urethanes.



$$-\underset{\displaystyle C}{\underset{|}{C}}=\underset{|}{C}- \quad + \quad NH_2\,COO\,C_2H_5 \xrightarrow{BF_3\text{etherate}} -\underset{|}{\overset{\overset{\displaystyle H}{|}}{C}}-\underset{|}{\overset{\overset{\displaystyle NHCOOEt.}{|}}{C}}-$$

6. Reduction of Esters to Ethers

Esters have been reduced to ethers by BF_3. etherate complex.

$$RCOOR' \xrightarrow{BF_3\text{-etherate}} RCH_2OR'$$

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