KARPAGAM ACADEMY OF HIGHER EDUCATION

(Deemed to be University)
(Established Under Section 3 of UGC Act, 1956)
Coimbatore – 641 021.

SYLLABUS
DEPARTMENT OF CHEMISTRY

STAFF NAME: Dr. A. THANGAMANI
SUBJECT NAME: ORGANIC CHEMISTRY-II SUB.CODE:17CHP201
SEMESTER: II CLASS: I M.Sc (CHEMISTRY)

17CHP201 ORGANIC CHEMISTRY-II: 4H 4C
REARRANGEMENTS, REACTIONS, PHOTOCHEMISTRY AND PERICYCLIC REACTIONS

Instruction Hours/week:L: 4 T:0 P:0 Marks: Internal:40 External: 60 Total:100

Scope

The course provides the knowledge about the basics of organic chemistry, which involves rearrangements, conformational analysis, stereochemistry, principles of various organic radical, concerted and photochemical reactions and outlines of the mechanism and discusses the application of reactions.

Objectives

On successful completion of the course the students should have
1. A versatile knowledge of rearrangements, different organic (radical and concerted) reactions and their applications in synthesis.
2. Understood the principles of conformational analysis and stereochemistry.
3. Mastered photochemical reactions.

Methodology
Blackboard teaching, Powerpoint presentation and group discussion.

UNIT–I
Molecular rearrangements: Intramolecular 1,2 - shifts - Wagner - Meerwein and Pinacol-Pinacolone rearrangements.
Migration to carbonyl carbon – Demyanov and Neber rearrangements.
Rearrangements to electron deficient nitrogen and oxygen – Baeyer – Villiger, Dienone - phenol, Favorskii, Fries, Wolff, Benzidine, Hoffmann Rearrangement and Stevens rearrangements.
Non-cyclic rearrangements – Chapman and Wallach rearrangements**.**

UNIT–II

Conformational analysis and stereochemistry: Stereochemistry of sulphur and nitrogen compounds, stereoselective and stereospecific reactions - R/S-notation of optically active carbon compounds. Optical isomerism of biphenyls, allenes and spiranes. Planar chirality - cyclophanes and ansa compounds - geometrical isomerism - E/Z notation-configuration in aldoximes and ketoximes. Conformation in cyclic system–decalins, perhydrophenanthrene and perhydroanthracene. Conformation and reactivity of cyclohexanes.

UNIT–III

Radical reactions: Configuration and generation of short lived free radicals-characteristics of free radical reactions – radical substitution, radical additions and rearrangement of free radicals. Typical reactions such as Sandmeyer, Gomberg, Pechmann, Ullmann, Pschorr and Hunsdiecker reactions.

Oxidation and reductions- mechanisms – aromatisation, oxidation of alcohols and glycols, ozonolysis, Sommelet reaction and selectivity in reduction-metal hydride reduction- reduction of nitro compounds and acyloin condensation.

UNIT–IV

Organic photochemistry: Introductory theory of light absorption- Jablonski diagram-photophysical processes- excimers and exciplexes - energy transfer-geometry of excited states – quantum efficiency - photochemical reaction of ketones- Norrish type-I and type-II reactions. Paterno Buchi reaction- cis and trans isomerisation-Photo-Fries rearrangement and Ene reaction and Di-pi methane rearrangement. Barton reaction.

UNIT–V

Pericyclic reactions: Definition-classification-characteristic features- the electrocyclic reaction-Woodward–Hofmann rules- orbital correlation diagram- the Frontier molecular orbital theory-electrocyclic conversion of 1,3-dienes and 1,3,5-trienes. Cycloaddition–[2+2] addition-Diel's Alder reaction- stereochemistry of Diel's Alder reaction. Sigmatropic reactions – [1,3], [1,5] and [3,3] sigmatropic shifts - Cope and Claisen rearrangements.

SUGGESTED READINGS:

Text Books:

1. Smith, M. B. (2015). *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure* (VII Edition). New Jersey: John Wiley & Sons, Inc., Hoboken.
2. Nasipuri, D. (2014). *Stereochemistry of Organic Compounds: Principles and Applications* (III Edition). New Delhi: New Age International (P) Ltd.
3. Mukherji, S. M., & Singh, S. P. (2014). *Reaction Mechanism in Organic Chemistry* (III Edition). New Delhi: Laxmi Publications Pvt. Ltd.

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2. Tewari, N. (2011). *Advanced Organic Reaction Mechanism* (III Edition). Kolkata: Books and Allied (P) Ltd.
3. Ramesh, P. (2005). *Basic Principles of Organic Stereochemistry* (I Edition). Madurai: Meenu Publications.
4. Depuy, C. H., & Chapman, O. L. (1975). *Molecular Reactions and Photochemistry* (II Edition). New Delhi: Prentice-Hall of India Private Limited.
5. Coxon, J. M., & Halton, B. (2011). Organic Photochemistry (II Edition). New Delhi: Cambridge University Press.
6. Nicholass, J. T., Scaiano J. C., & Ramamurthy, V. (2010). *Modern Molecular Photochemistry of Organic Molecules* (I Edition). United States: University Science Books.

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LECTURE PLAN
DEPARTMENT OF CHEMISTRY

STAFF NAME: Dr. A. THANGAMANI
SUBJECT NAME: ORGANIC CHEMISTRY-II SUB.CODE:17CHP201
SEMESTER: II CLASS: I M.Sc (CHEMISTRY)

S.No.	Lecture Duration Period	Topics to be Covered	Support Material/Page Nos
		UNIT-I	
1	1	**Molecular rearrangements:** Intramolecular 1,2- shifts- Wagner-Meerwein rearrangement.	R1:925-932 R2:180-182
2	1	Pinacol-Pinacolone rearrangement.	R1:933-947 R2:158-161
3	1	Migration to carbonyl carbon- Demyanov and Neber rearrangements.	R1:952-954 T1:1345-1346, 1359
4	1	Rearrangements to electron deficient nitrogen and oxygen - Baeyer-Villiger rearrangement.	R1:984-990 R2:89-91
5	1	Dienone- phenol rearrangement.	R1:961-963 R2:121-122
6	1	Favorskii rearrangement.	R1:990-1000 R2:122-125
7	1	Fries rearrangement.	R1:1000-1003 R2:131-133
8	1	Wolff rearrangement.	R1:954-957 R2:187-188
9	1	Benzidine rearrangement.	R1:1004-1008 T1:1144-1146
10	1	Hofmann and Stevens rearrangement.	T1: 1371-1373 R1:963-970 R2:136-139
11	1	Non-cyclic rearrangements- Chapman and Wallach rearrangements.	T1:1428-1430

12	1	Recapitulation and discussion of important questions.	
	Total No of Hours Planned For Unit 1=12		
		UNIT-II	
1	1	**Conformational analysis and stereochemistry:** Stereochemistry of sulphur and nitrogen compounds.	T2:300-301
2	1	Stereoselective and stereospecific reactions.	T1:173
3	1	R/S-notation of optically active carbon compounds.	T1:138-139 R3:56-62
4	1	R/S-notation of optically active carbon compounds.	T1:140-141 R3:63-66
5	1	Optical isomerism of biphenyls.	T1:130-131 R3:72-77
6	1	Optical isomerism of allenes and spiranes.	T1:132-133 R3:68-72
7	1	Planar chirality-cyclophanes and ansa compounds.	T1:134-135 R3:77-78
8	1	Geometrical isomerism-E/Z notation. Configuration in aldoximes and ketoximes.	T1:162-165 R3:137-141, 153-159
9	1	Conformation in cyclic system-decalins.	R3:228-231
10	1	Conformation of perhydrophenanthrene and perhydroanthracene.	R3:240-246
11	1	Conformation of cyclohexanes.	T1:180-185 R3:203-219
12	1	Reactivity of cyclohexanes.	R3: 257-266
13	1	Recapitulation and discussion of important questions.	
	Total No of Hours Planned For Unit II=13		
		UNIT-III	
1	1	**Radical reactions:** Configuration and generation of short lived free radicals.	T3:285-288, 291-292
2	1	Characteristics of free radical reactions – radical substitution, radical additions and rearrangement of free radicals.	T3:296-304, 308-309

3	1	Sandmeyer reaction.	T1:846-847 R2:167-170
4	1	Gomberg and Pechmann reactions.	T1:617-618, 794-796
5	1	Ullmann reaction.	R2:177-179 T1:768-769
6	1	Pschorr and Hunsdiecker reactions	T1:844-845, 854-856
7	1	Oxidation and reductions-mechanisms-aromatization. Oxidation of alcohols and glycols.	T1:1439-1440, 1442-1451, 1456-1457
8	1	Ozonolysis.	T1:1459-1463 R1:388-393
9	1	Sommelet reaction.	T1:1481-1482 R2:172-174
10	1	Selectivity in reduction-metal hydride reduction.	T1:1497-1506, 1515-1516, 1519-1522
11	1	Reduction of nitro compounds and acyloin condensation.	T1:1524-1527, 1560-1562 T3:388-401 R2:77-78
12	1	Recapitulation and discussion of important questions.	
	Total No of Hours Planned For Unit III=12		
		UNIT-IV	
1	1	**Organic photochemistry:** Introductory theory of light absorption-Jablonski diagram.	R4:29-30, 33-35
2	1	Photophysical processes-excimers and exciplexes-energy transfer-geometry of excited states- quantum efficiency.	R4:36-38, 42-43, 75-76
3	1	Photochemical reaction of ketones-Norrish type-I reaction	R4:46-47 R5:58-59, 69-71
4	1	Norrish type-II reaction.	R4:47-48 R5:59-68
5	1	Paterno Buchi reaction.	R4:49-52
6	1	Cis and trans isomerisation.	R5:20-25
7	1	Photo-Fries rearrangement and Ene reaction.	R1: 1003-1004, 1108 R4:20-21, 24-25
8	1	Di-pi methane rearrangement.	R5: 42-47

9	1	Barton reaction.	R5: 180-184
10	1	Recapitulation and discussion of important questions.	
	Total No of Hours Planned For Unit IV=10		
		UNIT-V	
1	1	**Pericyclic reactions:** Definition-classification-characteristic features.	R1:1045-1048
2	1	The electrocyclic reaction-Woodward–Hofmann rules.	R1:1045, 1051, 1064, 1101
3	1	Frontier molecular orbital theory-electrocyclic conversion of 1,3-diene and 1,3,5-triene.	R1:1049-1051
4	1	Orbital correlation diagram-electrocyclic conversion of 1,3-diene and 1,3,5-triene.	R1:1109-1113
5	1	Frontier molecular orbital theory-[2+2] cycloaddition and Diel's Alder reaction.	R1:1062-1064
6	1	Orbital correlation diagram-[2+2] cycloaddition and Diel's Alder reaction.	R1:1114-1116
7	1	Stereochemistry of Diel's Alder reaction.	R1: 1065-1067
8	1	Sigmatropic reactions–[1,3], [1,5] and [3,3] sigmatropic shifts-Frontier molecular orbital theory.	R1:1089-1093
9	1	Cope and Claisen rearrangements.	R1:1094-1101
10	1	Recapitulation and discussion of important questions.	
11	1	Discussion of previous ESE questions papers.	
12	1	Discussion of previous ESE questions papers.	
13	1	Discussion of previous ESE questions papers.	
	Total No of Hours Planned for unit V=13		
Total Planned Hours	**60**		

Text Books:

1. Smith, M. B. (2015). *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure* (VII Edition). New Jersey: John Wiley & Sons, Inc., Hoboken.
2. Nasipuri, D. (2014). *Stereochemistry of Organic Compounds: Principles and Applications* (III Edition). New Delhi: New Age International (P) Ltd.
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5. Coxon, J. M., & Halton, B. (2011). Organic Photochemistry (II Edition). New Delhi: Cambridge University Press.

UNIT-I

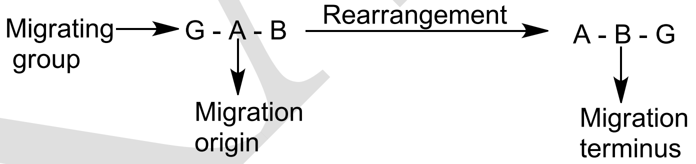
SYLLABUS

Molecular rearrangements: Intramolecular 1,2 - shifts - Wagner - Meerwein and Pinacol-Pinacolone rearrangements.
Migration to carbonyl carbon – Demyanov and Neber rearrangements.
Rearrangements to electron deficient nitrogen and oxygen – Baeyer – Villiger, Dienone - phenol, Favorskii, Fries, Wolff, Benzidine, Hoffmann Rearrangement and Stevens rearrangements.
Non-cyclic rearrangements – Chapman and Wallach rearrangements.

Rearrangement reactions

Introduction

When a chemical unit, an atom or an ion or a group of atoms, migrates from one atom to another in the same species or in another species of the same kind and thereby develops a new species, the reaction is called a **rearrangement reaction**. The atom from which the group migrates is known as migration origin and the atom to which it migrates is termed migration terminus. For example, in the conversion of G-A-B to A-B-G, the G is the migrating group, A and B are the migration origin and the migration terminus respectively.



However, the migration groups may either be an anion or a cation or a free radical, and accordingly the rearrangement reactions are broadly classified as:

1. Anionotropic rearrangement-where an anion migrates.
2. Cationotropic rearrangement-where a cation migrates.
3. Free radical rearrangement-where a free radical migrates.

When the migration of a group from an atom to another atom occurs within a molecule, it is said to be **intramolecular or molecular rearrangement**. In this case the migrating group never detaches itself completely from the rearranging species and there lies a containing tie between the migrating group and the remaining skeleton of the substrate; on the other hand, when the migration of a group from an atom of a molecule to an atom of another molecule of the same or a similar compounds takes place, the migrating group definitely detaches itself from the substrate and the reaction is termed as **intermolecular rearrangement**.

Whether a rearrangement is intramolecular or intermolecular that may be determined by **cross-over experiments**: when a mixture of two structurally related substrates, G-A-B and X-A-Y (where G is closely related to X and B to Y), is subjected to a rearrangement reaction, it is known as **cross-over experiment**. If the reaction is an intermolecular one, the product a will be a mixture of four different species: A-B-G, A-Y-X, A-B-X and A-Y-G.

$$G - A - B + X - A - Y \xrightarrow[\text{rearrangment}]{\text{Intramolecular}} \underset{\text{Intramolecular products}}{A - B - G + A - Y - X}$$

$$G - A - B + X - A - Y \xrightarrow[\text{rearrangment}]{\text{Intermolecular}} \underset{\text{Intramolecular products}}{A - B - G + A - Y - X}$$

$$\underset{\text{Cross-over products}}{A - B - X + A - Y - G}$$

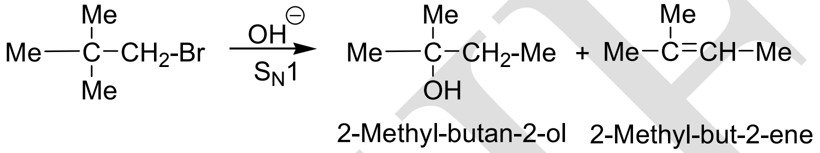
It an intermolecular reaction A-B-G and A-Y-X are the non-cross products and A-B-X and A-Y-G are called the cross-over products; whereas is an intramolecular reaction of the above cross-over products will be obtained–only A-B-G and A-Y-X, the normal intramolecular products, will form.

However, the migration may take place from an atom to the adjacent atom and this sort of migration is called the **Whitemore 1,2-shift**. The rearrangement of G-A-B to A-B-G is an example of 1,2-shift; 1,3-shift, 1,4-shift, 1,5-shift etc. which are also known. The conversion of G-A-B-D to A-B-C-G is a 1,3-shift.

Wagner-Meerwein rearrangement

Reactions involving the change in the carbon skeleton through the rearrangement of the carbocation intermediate are collectively known as Wagner-Meerwein rearrangement.

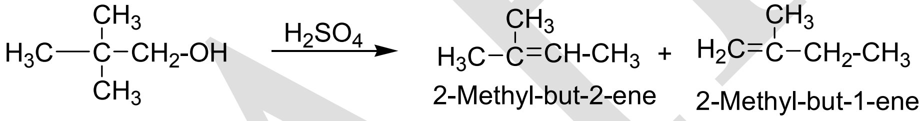
When neopentyl bromide is hydrolyzed under S_N1 condition it is found that instead of the expected neopentyl alcohol (Me_3CCH_2OH), 2-methyl-butan-2-ol and 2-methyl-but-2-ene are formed.



$$Me{-}\overset{Me}{\underset{Me}{C}}{-}CH_2{-}Br \xrightarrow[S_N1]{OH^{\ominus}} Me{-}\overset{Me}{\underset{OH}{C}}{-}CH_2{-}Me + Me{-}\overset{Me}{C}{=}CH{-}Me$$

2-Methyl-butan-2-ol 2-Methyl-but-2-ene

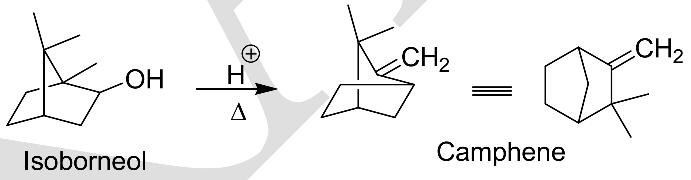
Similarly, neopentyl alcohol on dehydration gives 2-methyl-but-2-ene and 2-methyl-but-1-ene.



$$H_3C{-}\overset{CH_3}{\underset{CH_3}{C}}{-}CH_2{-}OH \xrightarrow{H_2SO_4} H_3C{-}\overset{CH_3}{C}{=}CH{-}CH_3 + H_2C{=}\overset{CH_3}{C}{-}CH_2{-}CH_3$$

2-Methyl-but-2-ene 2-Methyl-but-1-ene

In both cases, changes in the carbon skeleton are observed. Such rearrangement was first observed in bicyclic terpenes.

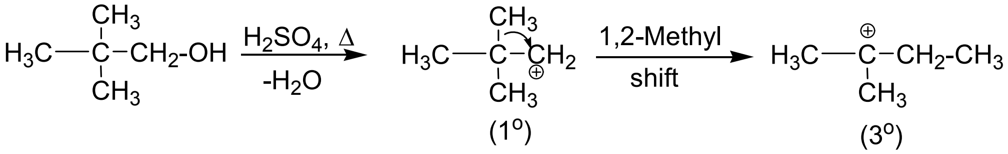


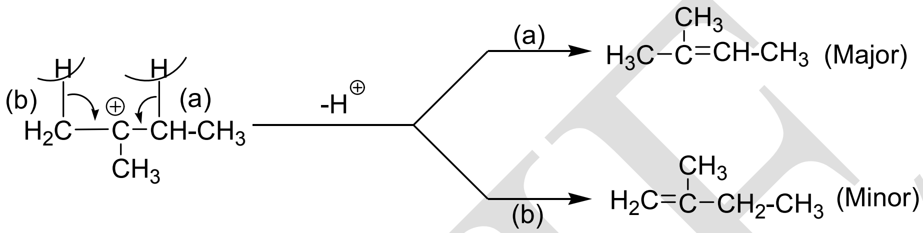
Isoborneol Camphene

Mechanism of the dehydration of alcohol is discussed below.

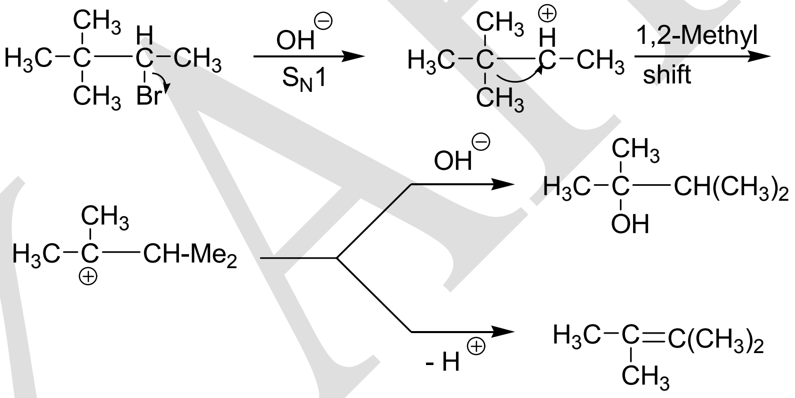
Mechanism

Protonation of the hydroxyl group of the alcohol followed by the loss of water molecule affords a 1° carbocation. The 1° carbocation then rearranges to the relatively more stable 3° carbocation by 1,2-methyl shift before the product is formed. The greater stability of the 3° carbocation provides the necessary force for the migration of the methyl group from the adjacent carbon. The rearranged carbocation then stabilizes itself by the loss of a β-hydrogen to form olefin. Zaistev's rule governs as to which of the two β-hydrogen will be eliminated.

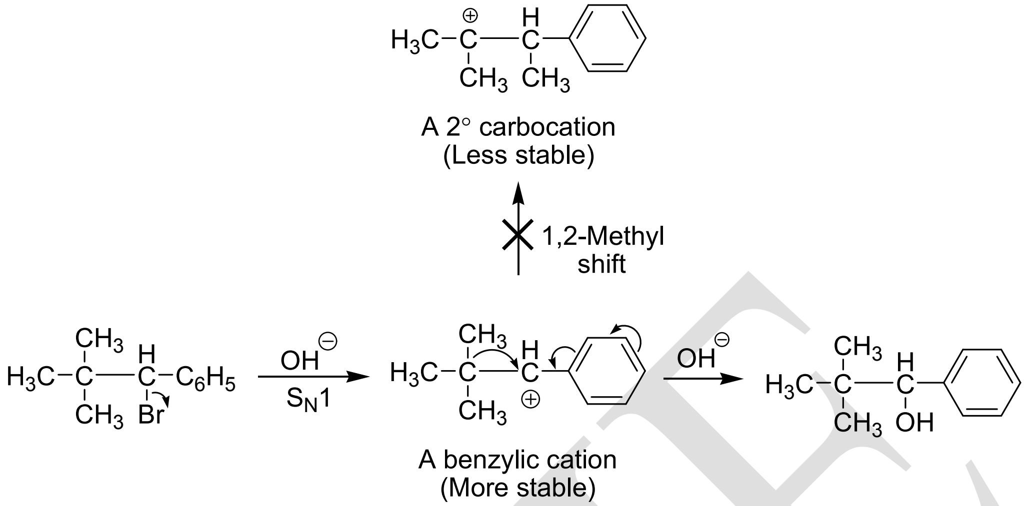




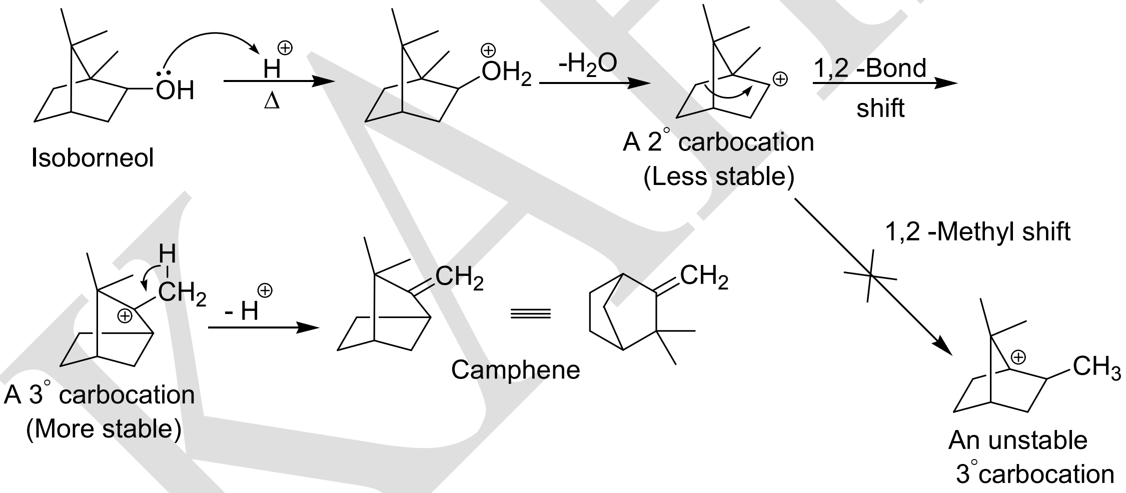
Rearrangement does not occur if the initially formed carbocation can stabilize by other factors. Thus, 3,3-dimethyl-2-bromo butane (neopentyl type) undergoes S_N1 hydrolysis with rearrangement,



while its phenyl analogue gives product without rearrangement.



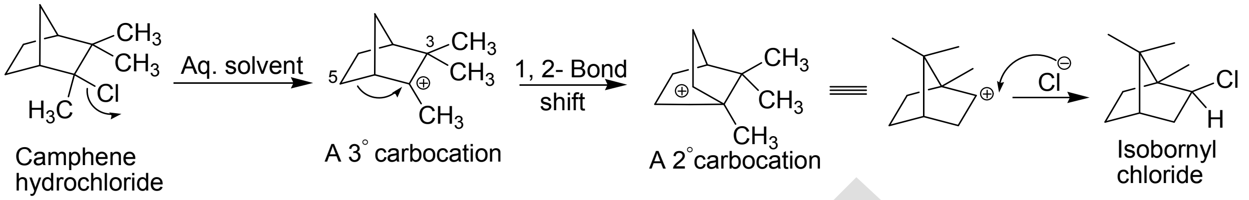
The benzylic cation is stabilized by the phenyl group through delocalization and so does not rearrange. Rearrangement in the alicyclic system may involve migration of ring methylene group resulting in the ring expansion and contraction.



The initially formed 2º carbocation rearranges not by methyl shift but by bond migration to give a relatively more stable 3º carbocation. The 3º carbocation to be obtained by 1,2-methyl shift is non-planar. So it suffers from angle strain and also, because of its rigidity, it cannot be stabilized by hyperconjugation.

Other examples are the conversion of camphene hydrochloride to isobornyl chloride, bornyl chloride to camphene, pinene hydrochloride to bornyl chloride, etc.,

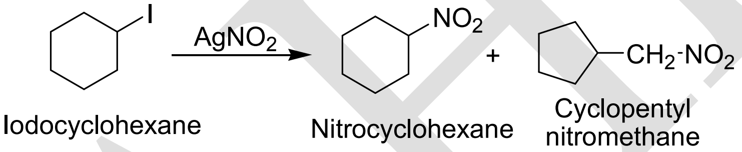
Conversion of camphene hydrochloride to isobornyl chloride



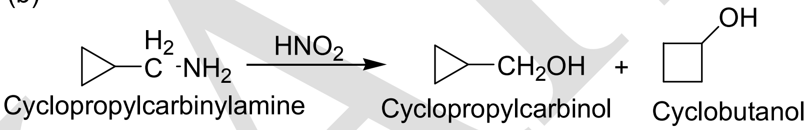
Though the rearrangement step transforms a stable 3º carbocation into a less stable 2º carbocation, relief of steric strain involving endo methyl at C-3 and endo hydrogen at C-5 makes the bond migration favourable. In the final step, the carbocation combines with a chloride ion to yield isobornyl chloride, in which chlorine is exo, due to the same steric reason.

Some simpler examples are:

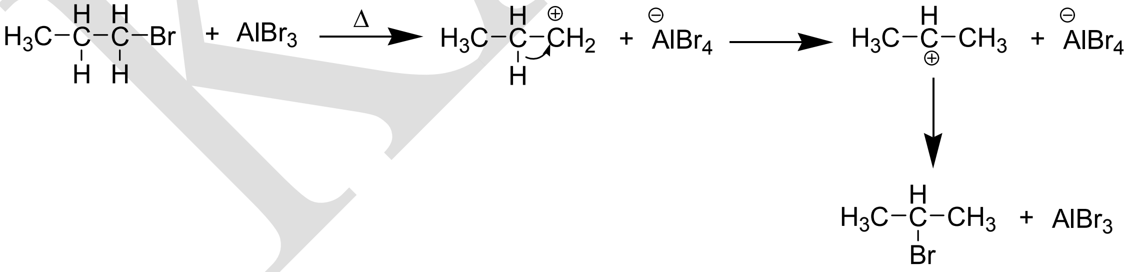
(a)



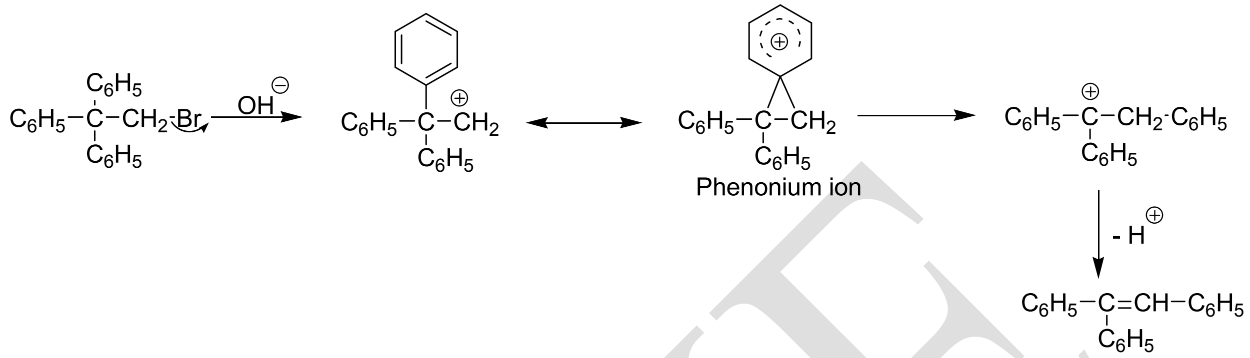
(b)



The migration group besides being alkyl and ring methylene groups may be hydride ion or aryl group.

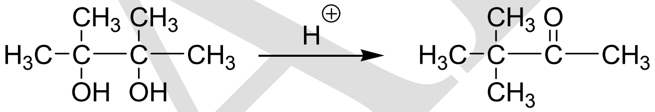


The aryl group migrates faster than alkyl group. Electron-releasing group in the aryl group increases the rate of migration while electron-withdrawing group decrease the rate of migration. Thus, elimination is many times faster in neophyl bromide than in neopentyl bromide. This is because the rearranged phenonium ion is relatively more stable due to the delocalization than the rearranged carbocation from neopentyl bromide. Hence the former has lower energy and more easily formed than the latter.



Pinacol-Pinacolone rearrangement

Pinacols are ditertiary 1,2-diols. The simplest member of the class is $Me_2C(OH).C(OH)Me_2$. When this is treated with dilute or moderately concentrated sulphuric acid (H_2SO_4), a rearrangement reaction takes place which leads to the formation of $Me_3C.COMe$ (pinacolone), and the rearrangement is known as the **pinacol-pinacolone** or **pinacol rearrangement**.

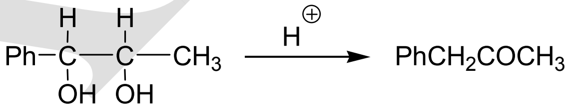


$$H_3C-\underset{OH}{\overset{CH_3}{C}}-\underset{OH}{\overset{CH_3}{C}}-CH_3 \xrightarrow{H^{\oplus}} H_3C-\underset{CH_3}{\overset{CH_3}{C}}-\overset{O}{\overset{\|}{C}}-CH_3$$

Pinacol Pinacolone

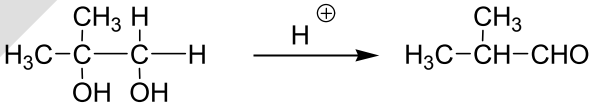
Nowadays the acid-catalyzed rearrangement reactions of 1,2-diols (*vic*-diols) to oxo compounds, aldehydes or ketones are called the pinacol-pinacolone rearrangement. For example:

(i)



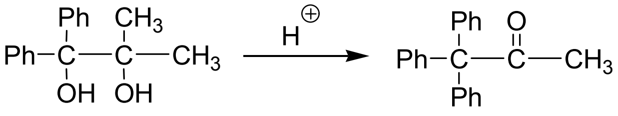
$$Ph-\underset{OH}{\overset{H}{C}}-\underset{OH}{\overset{H}{C}}-CH_3 \xrightarrow{H^{\oplus}} PhCH_2COCH_3$$

(ii)

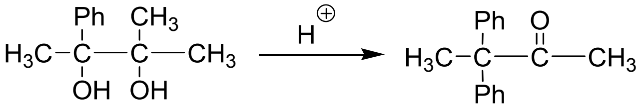


$$H_3C-\underset{OH}{\overset{CH_3}{C}}-\underset{OH}{\overset{H}{C}}-H \xrightarrow{H^{\oplus}} H_3C-\overset{CH_3}{CH}-CHO$$

(iii)



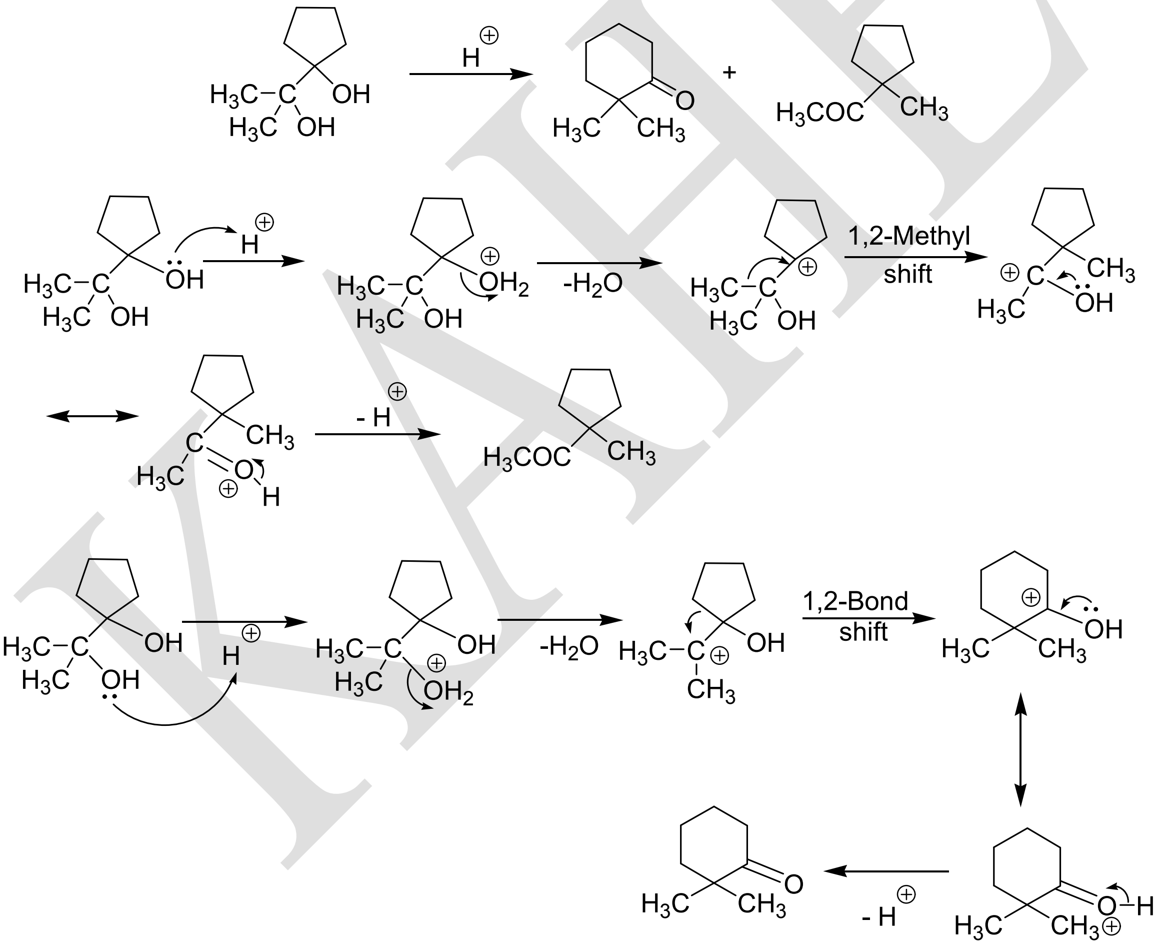
$$Ph-\underset{OH}{\overset{Ph}{C}}-\underset{OH}{\overset{CH_3}{C}}-CH_3 \xrightarrow{H^{\oplus}} Ph-\underset{Ph}{\overset{Ph}{C}}-\overset{O}{\overset{\|}{C}}-CH_3$$

(iv)


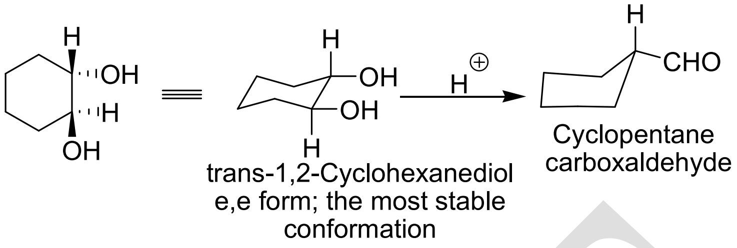
$$H_3C-\underset{OH}{\overset{Ph}{C}}-\underset{OH}{\overset{CH_3}{C}}-CH_3 \xrightarrow{H^{\oplus}} H_3C-\underset{Ph}{\overset{Ph}{C}}-\overset{O}{\overset{\|}{C}}-CH_3$$

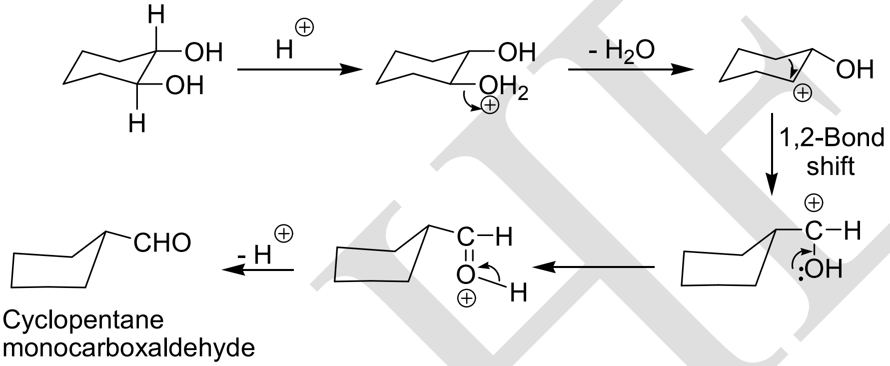
The above examples show that the migration origin and migration terminus are the two adjacent carbon atoms, and the migrating group may be an aryl or alkyl group or an H atom etc. Migration of a bond may also occur in this rearrangement whereby ring expansion and ring contraction reactions may take place.

Ring expansion

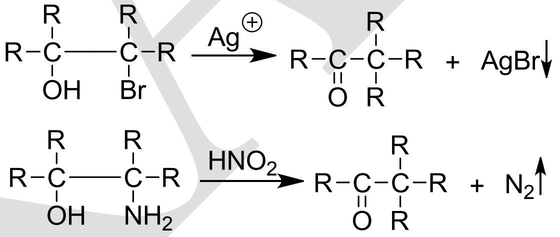


Ring contraction





Rearrangement reactions of 1,2-halohydrines and 1,2-amino-alcohols to pinacolones are analogous reactions and called the **pinacolic rearrangements**; these are carried out by treating the former compounds with Ag^+ and the latter compounds with HNO_2 ($NaNO_2/HCl$).

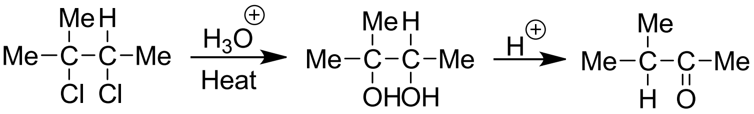


$$R-\underset{OH}{\overset{R}{C}}-\underset{Br}{\overset{R}{C}}-R \xrightarrow{Ag^{\oplus}} R-\underset{\underset{O}{\|}}{C}-\underset{R}{\overset{R}{C}}-R + AgBr\downarrow$$

$$R-\underset{OH}{\overset{R}{C}}-\underset{NH_2}{\overset{R}{C}}-R \xrightarrow{HNO_2} R-\underset{\underset{O}{\|}}{C}-\underset{R}{\overset{R}{C}}-R + N_2\uparrow$$

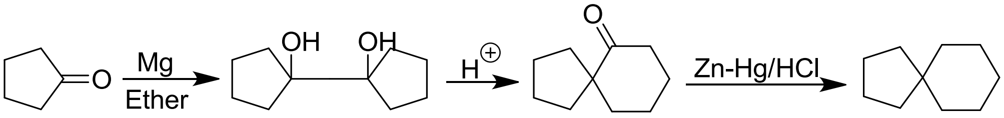
Since highly branched oxo compounds are very difficult to prepare by the other reactions, this rearrangement has interesting applications in synthesis.

For example, methyl isopropyl ketone is easily prepared from 2,3-dichloro-2-methylbutane by this rearrangement.



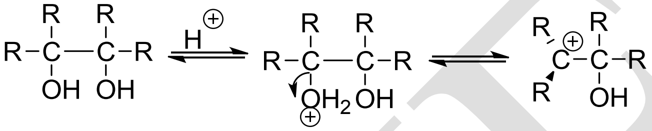
$$Me-\underset{Cl}{\overset{Me}{C}}-\underset{Cl}{\overset{H}{C}}-Me \xrightarrow[Heat]{H_3O^{\oplus}} Me-\underset{OH}{\overset{Me}{C}}-\underset{OH}{\overset{H}{C}}-Me \xrightarrow{H^{\oplus}} Me-\underset{H}{\overset{Me}{C}}-\underset{\underset{O}{\|}}{C}-Me$$

Spiranes and their derivatives can also be prepared by this reaction; e.g.,

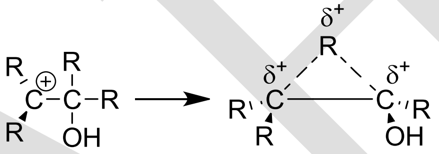


Mechanism

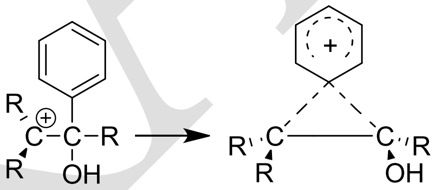
Step 1: Reversible protonation to a hydroxyl group and the elimination of water molecule; an electron-deficient carbenium ion is thus formed in this step.



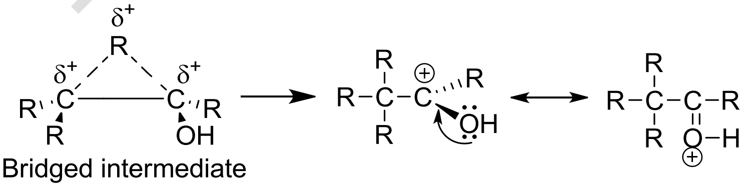
Step 2: The formation of a non-classical carbenium ion, a bridged intermediate. Here it is important to note that the migrating group never detaches itself from the substrate skeleton and thus the reaction becomes an intramolecular one.


Bridged intermediate

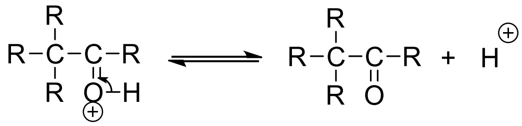
When an aryl group migrates, the bridged intermediate is an aryl cation (e.g., phenyl cation) which may be an actual compound since it is reasonably stable.


Bridged intermediate

Step 3: Actual migration of a group to form the classical carbenium ion; thus the migration origin becomes an electron-deficient atom, a resonance stabilized carbenium ion.


Bridged intermediate

Step 4: The loss of proton and the formation of axo compounds.

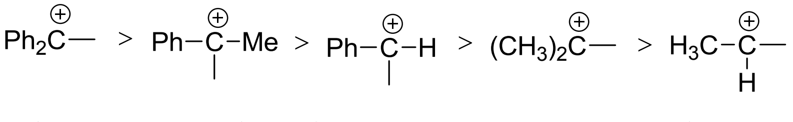


Since the mechanism involves the migration of a group with its bonded electrons to an adjacent C atom, it follows the mechanism of anionotropic 1,2-shift. It has been known from the kinetic study that the step in which elimination of water molecules occurs from the protonated 1,2-diol is the slow step and hence it is the rate-determining step.

The intramolecular nature of the reaction is supported by the cross-over experiment in which a mixture $Ph_2C(OH).C(OH)Me_2$ and $Ph_2C(OH).C(OH)Et_2$ has been treated with acid. In these reaction only intramolecular products: $Ph_2CMe.COMe$ and $Ph_2CEt.COEt$, have been obtained; $Ph_2CEt.COMe$ and $Ph_2C.MeCOEt$, the possible cross-products, have not yet been isolated. Thus cross-migration does not take place in this reaction. this shows that the reaction is essentially an intramolecular one.

However, when different groups are present on C-atoms bearing the hydroxyl groups, two questions arise: (1) which of the two OH's will be protonated and (2) which of the groups will migrate?

The answer of the first question lies with the stability order of the carbenium ions. Usually that OH receives the proton which produces the more stable carbenium ion by the elimination of water molecule. Thus in $Ph_2C(OH).C(OH)Me_2$ the OH group on the C atom holding the phenyl groups will receive the proton since the stability or diphenyl carbenium ion is greater than that of dimethyl carbenium ion. We may recall hare that the stability of a carbenium ion depends on the delocalization of the positive charge on the C atom either through resonance or through hyperconjugation. For this reason the decreasing stability order of carbenium ions is:



$$Ph_2\overset{\oplus}{C}- > Ph-\overset{\oplus}{\underset{|}{C}}-Me > Ph-\overset{\oplus}{\underset{|}{C}}-H > (CH_3)_2\overset{\oplus}{C}- > H_3C-\overset{\oplus}{\underset{H}{C}}-$$

There is no clear-cut answer in so far as **migratory preference** is concerned.

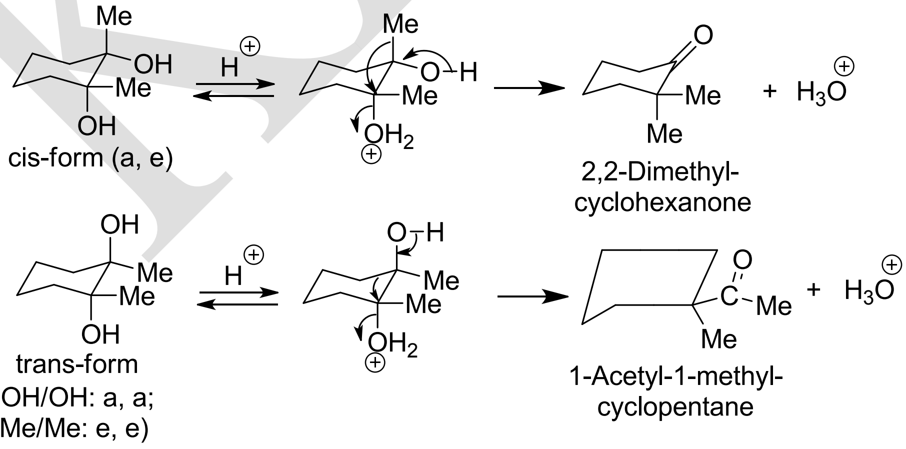
In terms of electron donating ability the usual migratory preference order is:

p-$CH_3OC_6H_4$— > *p*-$CH_3C_6H_4$— > *m*-$CH_3C_6H_4$— > *p*-ClC_6H_4— > *m*-$CH_3OC_6H_4$— > *o*-$CH_3C_6H_4$— >
o-$CH_3C_6H_4$— > alkyl, H

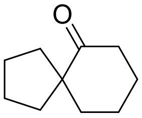
An aryl group migrates more readily than an alkyl group because the former forms a more stable bridged intermediate, the aryl cation, than the latter. The migratory aptitude of an *o*-aryl group is less than that of a *m*-aryl or a *p*-aryl because of steric hindrance.

However, there are reactions in which mere electron-donating ability does not decide which one will migrate. It has been found that a group in **anti** or **trans** position with respect to the leaving group, H_2O, in the more stable conformation of the protonated substrate migrates preferentially (for the evidence see the stereochemistry of the reaction).

It has been found in the alicyclic system that a group trans to the leaving group usually migrates in the pinacol rearrangement reaction. For example, cis-1,2-dimethylcyclohexane-1,2-diol on treatment with acid forms 2,2-dimethylcyclohexanone by the migration of the methyl group which is trans to the protonated hydroxyl group and at the same time 1-acetyl-1-methylcyclopentane also forms owing to the protonation of equatorial hydroxyl group (this has not been shown below); whereas in the same rearrangement the trans-isomer forms 1-acetyl-1-methylcyclopentane by the ring contraction reaction instead of methyl migration-this is because the methyl and hydroxyl groups are cis to each other in this configurational isomer as well as in its (e, e) form (this has not been shown below).



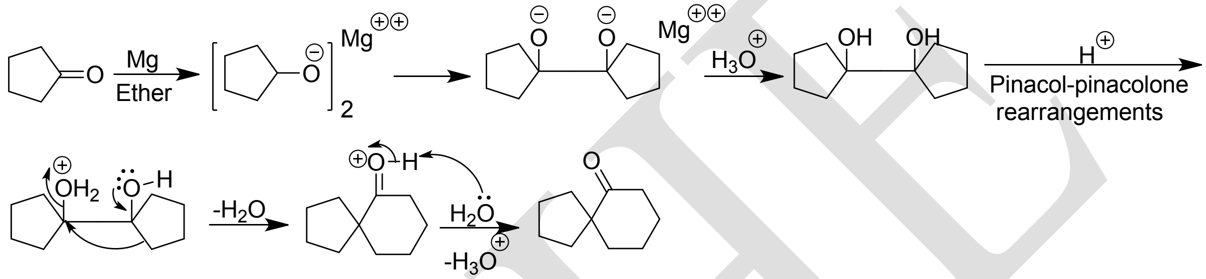
Problem 1. How can you synthesis:



from cyclopentanone

Give mechanistic steps for the synthesis.

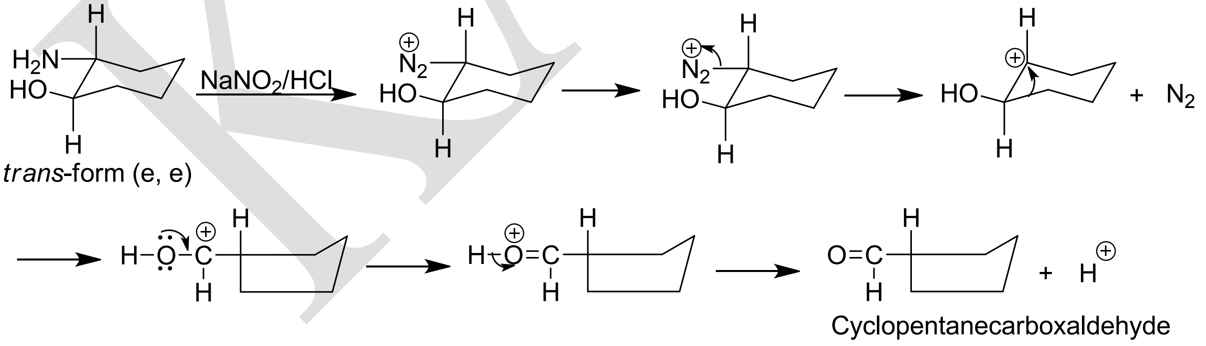
Solution:



Problem 2. What product do you expect when trans-2-amino-cyclohexanol is treated with aqueous $NaNO_2$ and dil.HCl?

Solution:

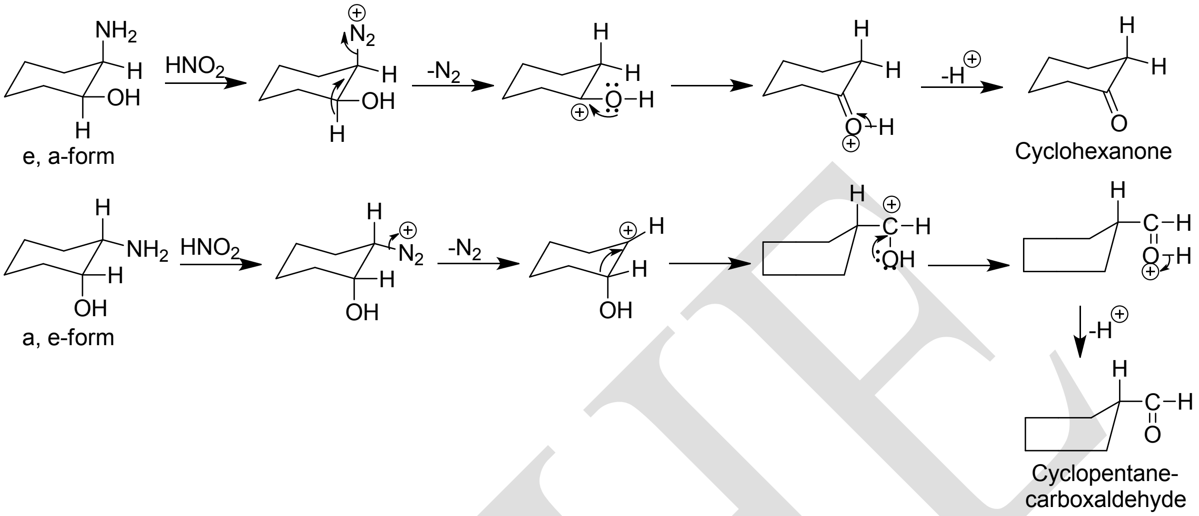
trans-2-Aminocyclohexanol will exist in diequatorial chair conformation since this is the most stable conformation among others. Since this e,e forms does not contain an H atom trans to diazonium group, ring contraction will occur to form cyclopentanecarboxaldehyde.



Problem 3. What happens when cis-2-aminocyclohexanol is subjected to pinacolic rearrangement reaction? Write down the mechanistic steps.

Solution:

cis-2-Aminocyclohexanol may exist in two chair conformation a,e and e,a as drawn below:

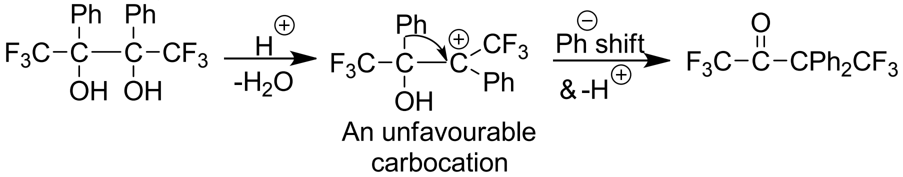


Since the trans-group migrates in a pinacolic deamination reaction, in e, a-form H will migrates and the product will be cyclohexanone; whereas in a, e-form H and NH_2 being cis to each other, ring contraction will occur to form cyclopentanecarboxaldehyde. Thus the product will be a mixture of cyclohexanone and cyclopentanecarboxaldehyde.

Problem 4. The pinacol $PhCF_3C(OH)C(OH)CF_3Ph$ is relatively unreactive under conditions which give pinacol-pinacoloane rearrangement.

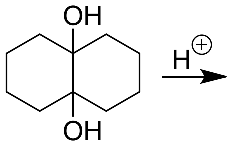
Solution:

Since the carbocation involved in the rearrangement of the pinacol $F_3CPhC(OH)C(OH)PhCF_3$ is highly stabilized by the strongly electron withdrawing $–CF_3$ group, the energy of activation for the formation of that carbocation (the rate-determining step) is very high. It is for this reason this pinacol is relatively unreactive under conditions which give pinacol-pinacolone rearrangement.

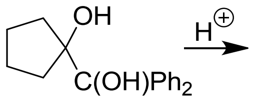


Problem 5. Predict the major product and suggest a mechanism for each of the following reactions:

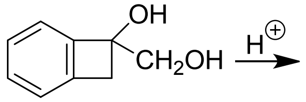
(i)



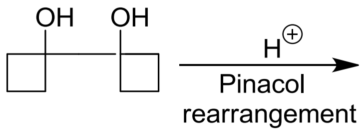
(ii)



(iii)

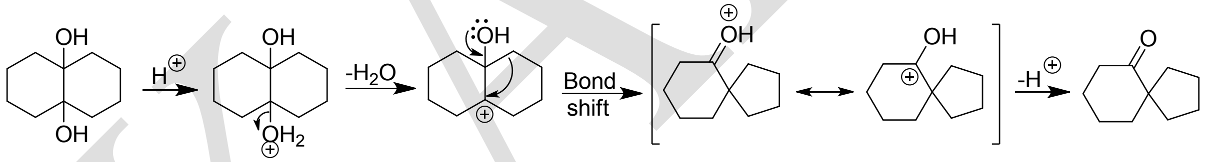


(iv)

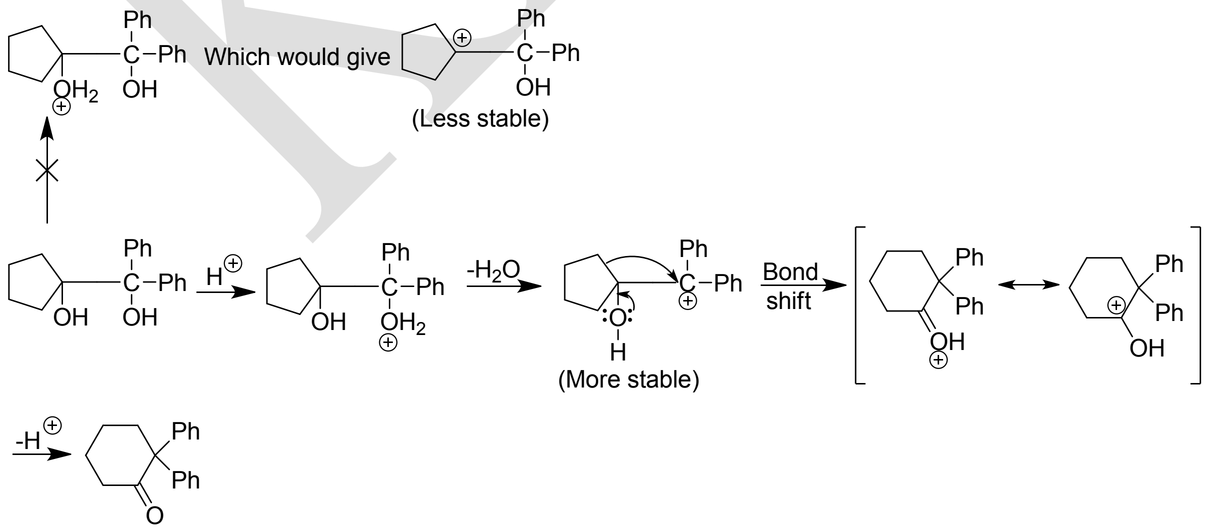


Solution:

(i)

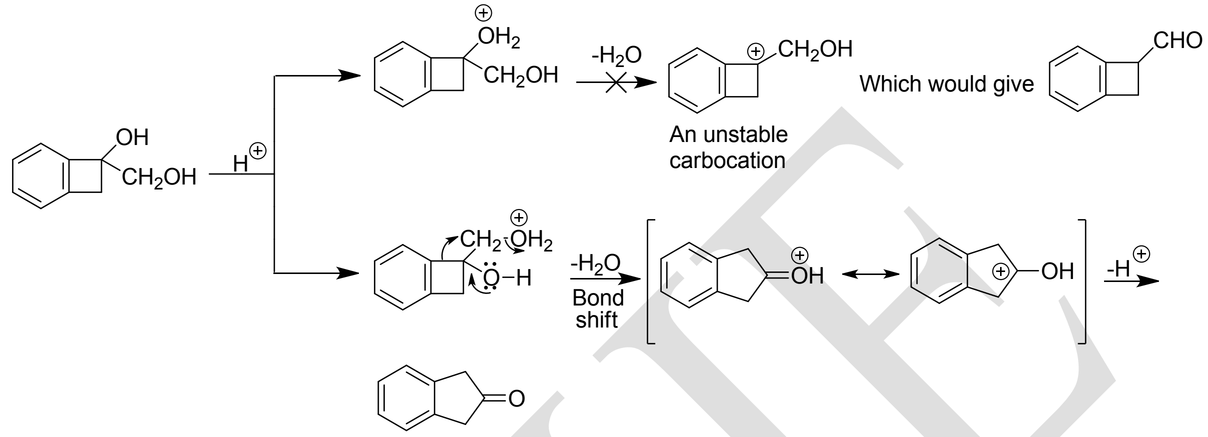


(ii)



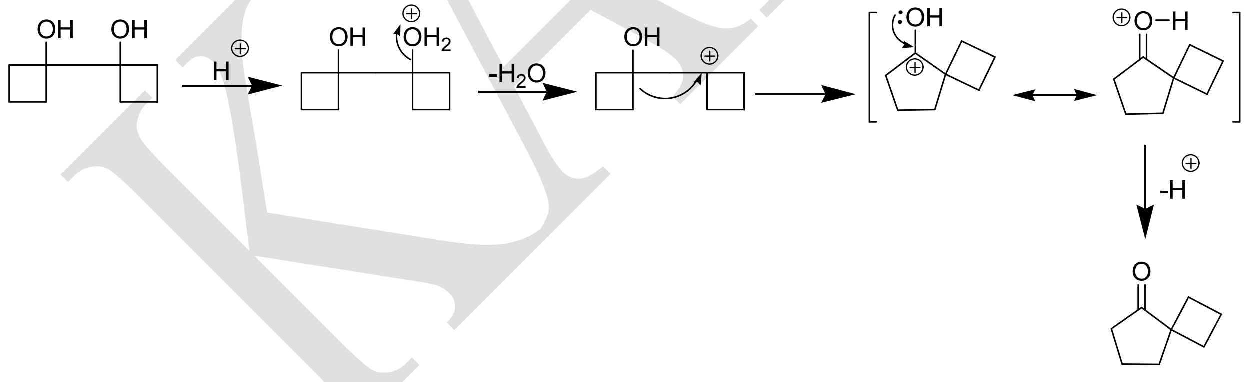
The –OH group on carbon bearing the phenyl leaves to form a relatively stable carbocation (resonance stabilized by two phenyl groups).

(iii)



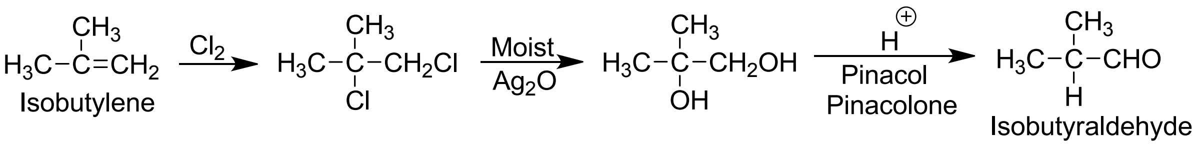
The tertiary –OH group does not leave because this leads to the formation of an unstable (due to angle strain of 120º- 90º = 30º) tertiary carbocation. As a consequence, the reaction proceeds by the loss of the primary –OH group to give a cyclopentanone derivative through ring expansion.

(iv)

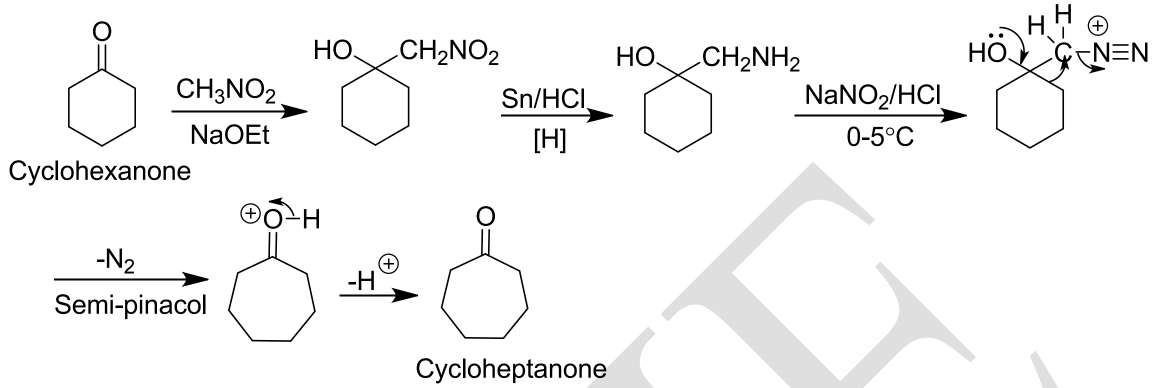


Applications

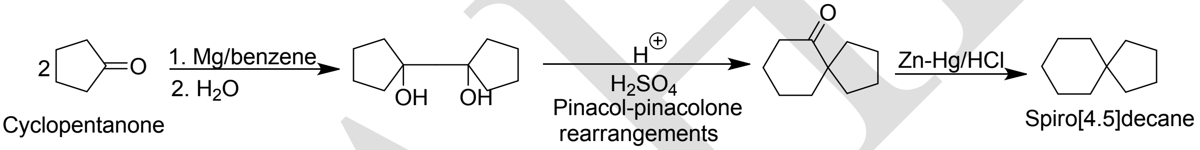
1. Carbonyl compounds may be synthesized from alkenes by using this reaction. For example, isobutyraldehyde may be prepared on a large scale from isobutylene as follows:



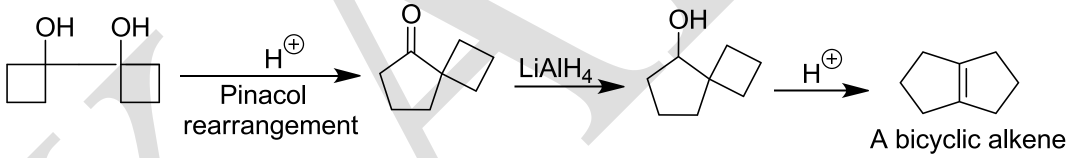
2. Ring expansion of cyclic ketone may be effected by using this reaction. For example, cyclohexanone can be converted to cycloheptanone in good yield as follows:



3. Spiro compounds may be prepared by using this reaction. For example, spiro[4.5]decane can be prepared as follows:

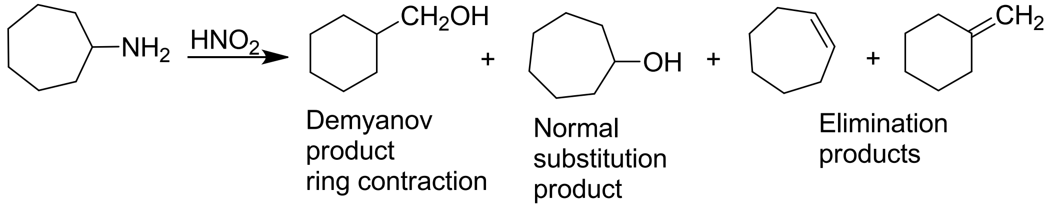


4. Bicyclic alkenes may be prepared by using this reaction. For example:

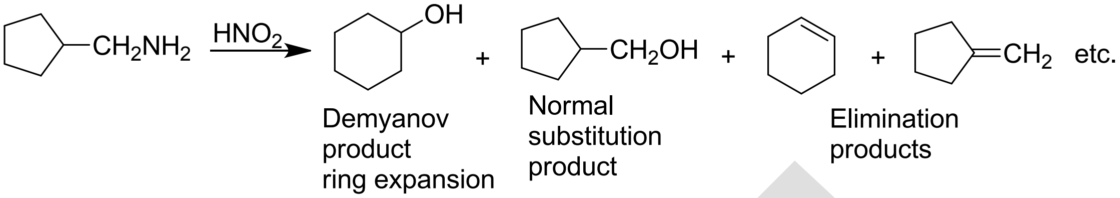


Demyanov rearrangement

The isomerisation of alicyclic rings involved ring expansion and ring contraction of cycloalkylmethylamines and cycloalkylamines respectively by the action of nitrous acid is known as the Demyanov rearrangement in the name of discover of the reaction N.Ya. Demyanov. For example, cycloheptylamine on nitrous acid treatment gives cyclohexylcarbinol, a ring contraction product along with other products.

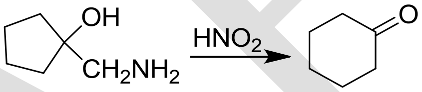


Similarly, cyclopentylmethylamine under the action of nitrous acid gives a ring expansion product amongst others.



Many side reactions may take place along with the Demyanov rearrangement; alkanols, cycloalkenes, alkenes are often the side products along with the normal substitution products, cycloalkylcarbinols and cycloalkanols.

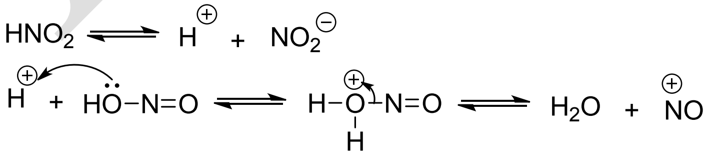
The rearrangement may be extended to alicyclic hydroxy-amines which undergo a rearrangement analogous to the pinacolic rearrangement and is known as **Tiffenev-Demyanov ring expansion**.



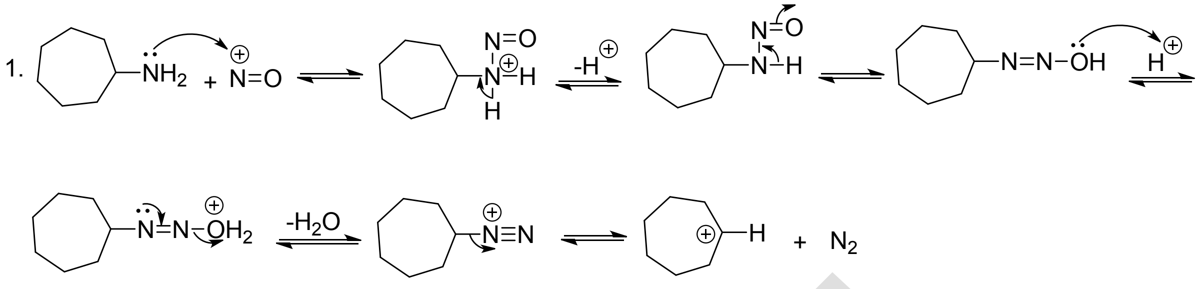
If there is any possibility of ring contraction then the seven-membered ring undergoes ring contraction readily while ring expansion occurs readily with the five-membered ring if the substrate structure favours the reaction. The three and four membered rings also undergo the rearrangement with an ease. Equatorial substituted cyclohexylamines undergo the reaction, whereas axial substituted cyclohexylamines give the products of normal substitution.

Mechanism

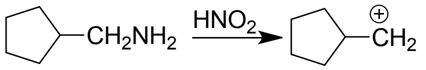
At first a carbenium ion develops by the attack of nitrosonium ion on the amino group by a series of reactions:



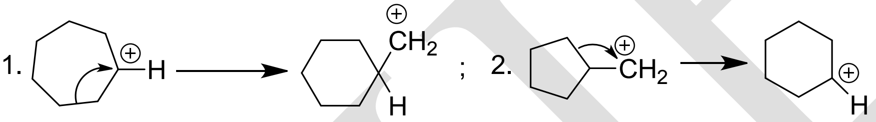
Step 1: Formation of the carbenium ion, an intermediate.



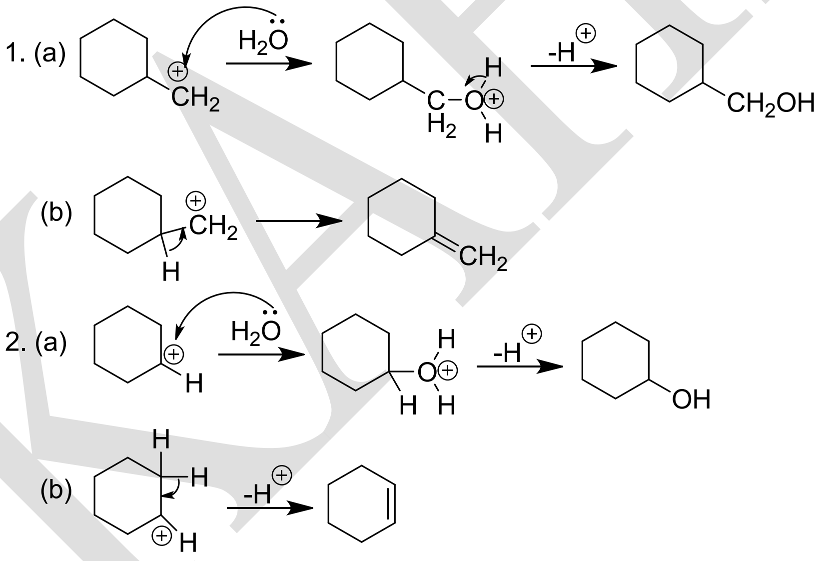
2. Similarly,



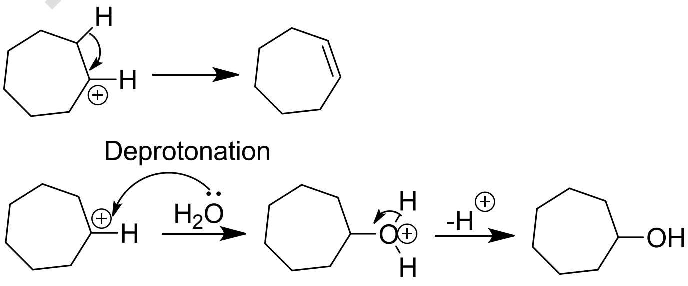
Step 2: Whitemore 1,2-shift takes place and a rearranged carbenium ion develops.

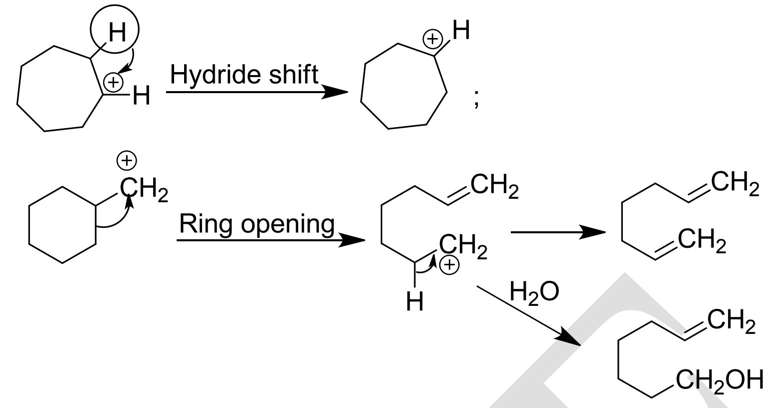


Step 3: Either the nucleophilic attack by the solvent molecule or deprotonation takes place.

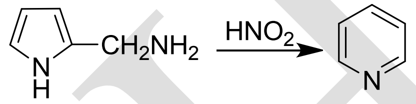


Since the carbenium ion is the intermediate, it can produce several other products:



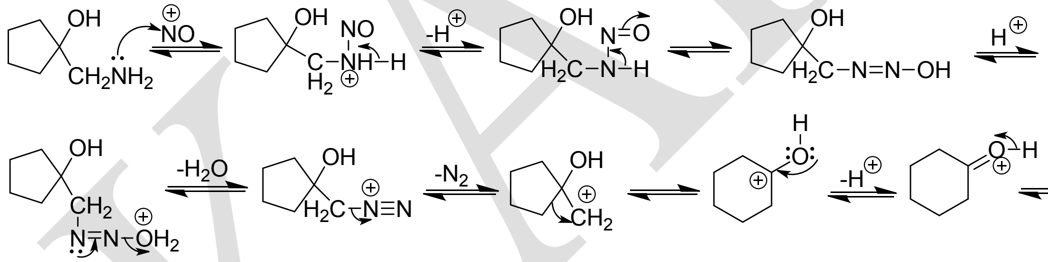


The Demyanov rearrangements are also applicable to the heterocyclic compounds. For example, 2-aminoethylpyrrole can be converted to pyridine by this rearrangement reaction:

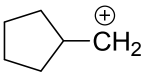


Problem 6. Give the mechanistic steps for the Tiffenev-Demjanov rearrangement.

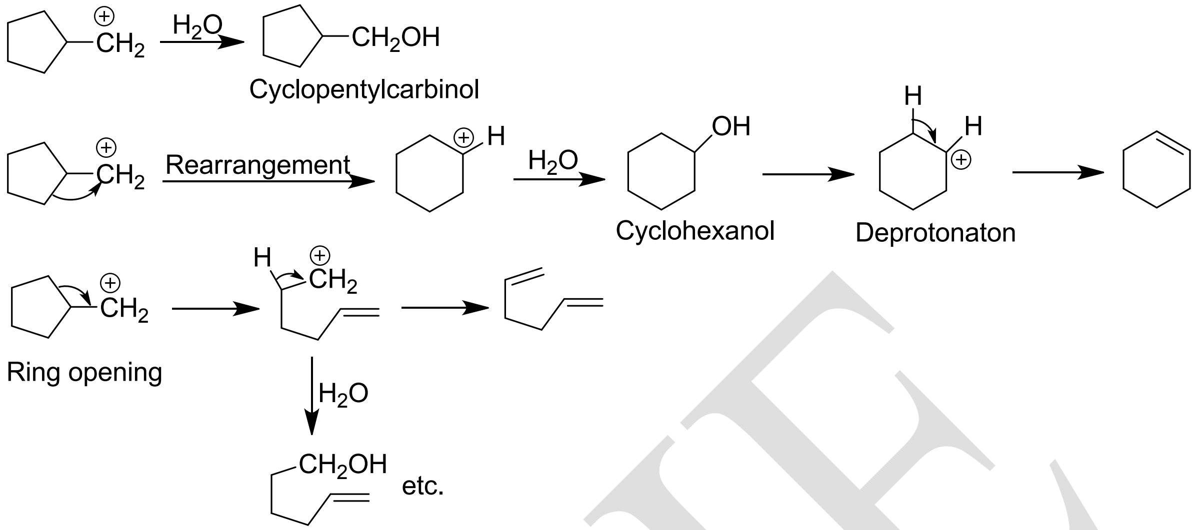
Solution:



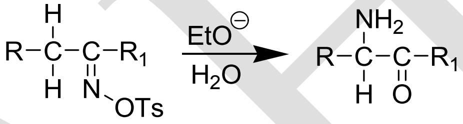
Problem 7. What products do you expect from the following carbenium ion in the aqueous medium?



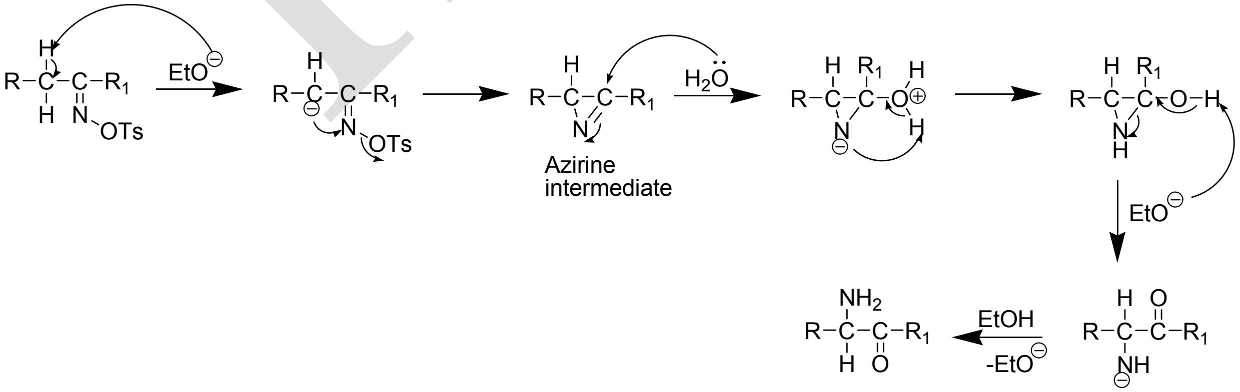
Solution:



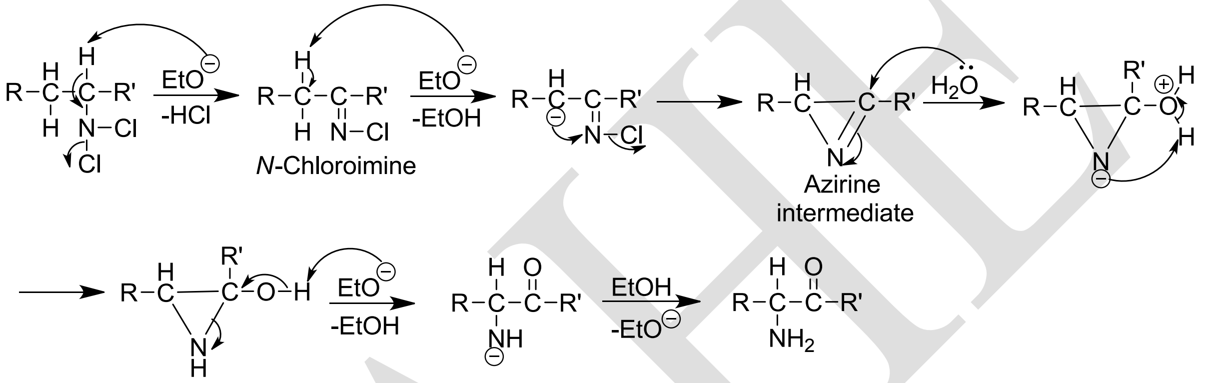
Neber rearrangement



Preparation of α-aminoketones by the treatment of ketoxime tosylates with a base such as alkoxide ion (ethoxide ion) or pyridine and subsequent hydrolysis is known as Neber rearrangement. R is usually aryl, though the reaction has been carried out with R= alkyl or hydrogen. R_1 may be alkyl or aryl but not hydrogen. The Beckmann rearrangement and the Beckmann reaction (elimination to the nitrile) may be side reactions, though these generally occur in acid media. A similar rearrangement is given by *N,N*-dichloroamines of the type $RCH_2CH(NCl_2)R^1$, where the product is also $RCH(NH_2)COR^1$. The mechanism of the Neber rearrangement is as follows:

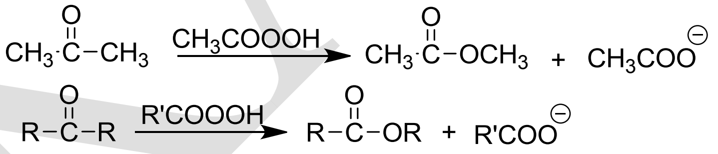


The best evidence for this mechanism is that the azirine intermediate has been isolated. In this contrast to the Beckmann rearrangement this one is sterically indiscriminate. Both a syn and an anti ketoxime give the same product. The mechanism as shown above consists of three steps. However it is possible that the first two steps are concerted and it is also possible that what is shown as the second step is actually two steps; loss of OTs to give a nitrene and formation of the azirine. In the case of the *N,N*-dichloroamines, HCl is first lost to give $RCH_2C(=NCl)R^1$ which then behaves analogously. N-chloroimines prepared in other ways also give the reaction.



Baeyer-Villiger Oxidation

The oxidation of aliphatic ketones to esters or their hydrolysed products with hydrogen peroxide or organic peroxyacids is called the **Baeyer-Villiger oxidation**. For example, when acetone is treated with peroxyacetic acid, methyl acetate forms.



$$CH_3\overset{O}{\overset{\|}{C}}-CH_3 \xrightarrow{CH_3COOOH} CH_3\overset{O}{\overset{\|}{C}}-OCH_3 + CH_3COO^{\ominus}$$

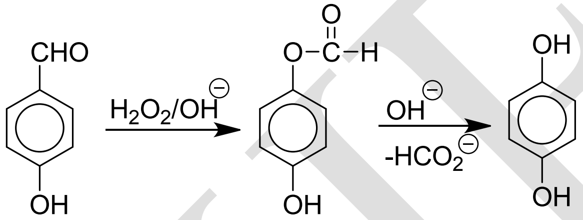
$$R-\overset{O}{\overset{\|}{C}}-R \xrightarrow{R'COOOH} R-\overset{O}{\overset{\|}{C}}-OR + R'COO^{\ominus}$$

The Baeyer-Villiger oxidation involves an intramolecular anionotropic rearrangement in which an alkyl group with its bonded electrons migrates from the carbonyl C atom (migration origin) to an electron-deficient O atom (migration terminus).

The order of migratory aptitude of the alkyl groups is 3º>2°>1º i.e., .the more nucleophilic group normally migrates.

This reaction is usually carried out in inert solvents like CH_2Cl_2 with various peroxyacids, e.g., CF_3COOOH, CH_3COOOH, C_6H_5COOOH etc.-trifluoro peracetic acid is by far the most reactive one.

A related reaction is the conversion of *o*-and *p*-hydroxybenzaldehydes or phenylketones into *o*-and *p*-dihydroxybenzenes by the action of alkaline hydrogen peroxide which is known as **Dakin oxidation**.



p-Hydroxybenzaldehyde

Quinol

The Baeyer-villiger reaction gives a good yield of esters or acids. So this may be used to prepare esters and carboxylic acids.

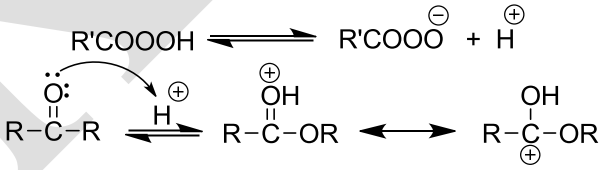
$$CH_3COCMe_3 \xrightarrow{CH_2Cl_2,\ CH_3COOOH} CH_3COOCMe_3$$

It has been found that when an alkyl with a chiral C migrates, the configuration of the chiral C does not change.

Mechanism

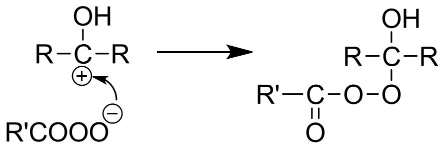
The reaction is considered to occur the following steps:

Initial step:

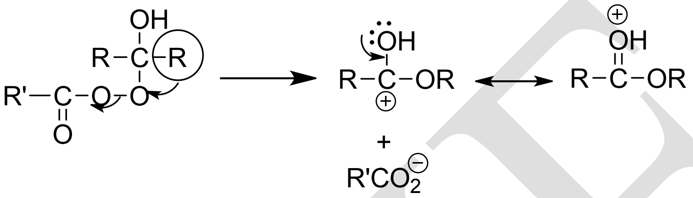


Thus, in this step the O atom of the ketone is protonated and a resonance stabilized carbenium ion forms.

Step 1: Nucleophilic attack at the carbonyl carbon by the peroxycarboxylate ion.

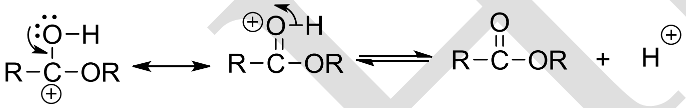


Step 2: Migration of the alkyl group and loss of R'COO$^-$ a good leaving group, in a concerted step.



This is the slower step and hence the rate-limiting step.

Final step: Loss of proton and formation of ester.



When a labeled ketone with ^{18}O is subjected to the Baeyer-Villiger rearrangement, the resulting ester contains ^{18}O. This supported the proposed mechanism.

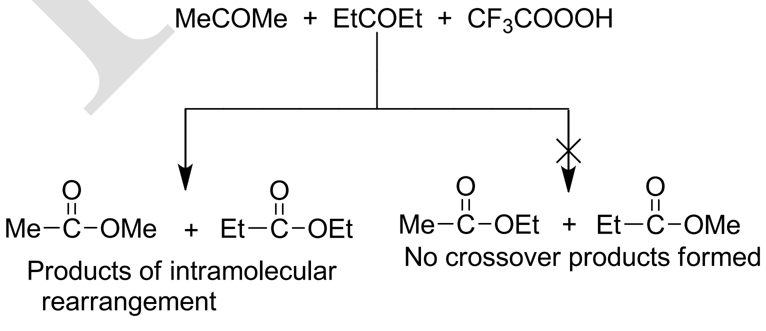
$$Ph_2C{=}{}^{18}O \xrightarrow{CF_3COOOH} Ph{-}\overset{^{18}O}{\overset{\|}{C}}{-}OPh$$

That the concerted step is the rate-limiting step is supported by the following facts:

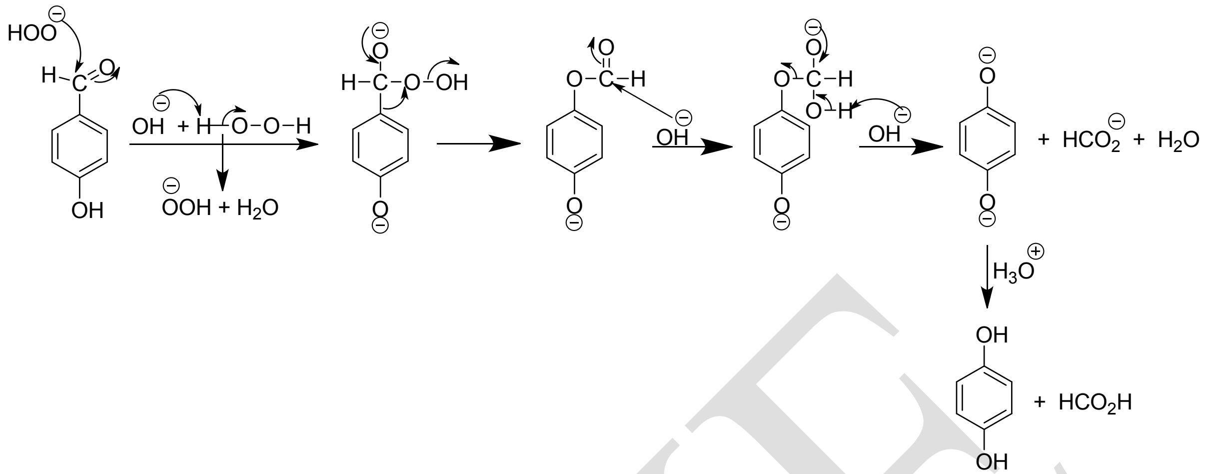
(i) An electron-withdrawing group in the R'COOO$^-$ group increases the rate of the reaction.

(ii) An electron-releasing group in the migrating alkyl group also increases the rate.

The intramolecularity of the reaction has been supported by the cross-over experiment no-cross-over product has been obtained.



However, the mechanism for the Dakin reaction may be as follows:

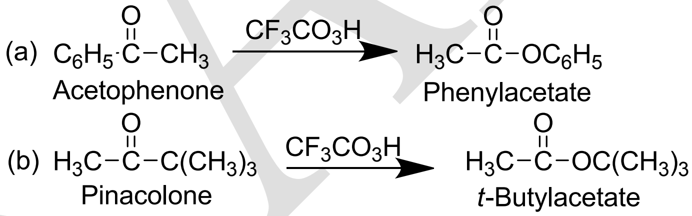


Similarly,

Applications

The reaction has valuable synthetic applications.

(i) **Esters:** Esters which are difficult to synthesize can be prepared by this method.



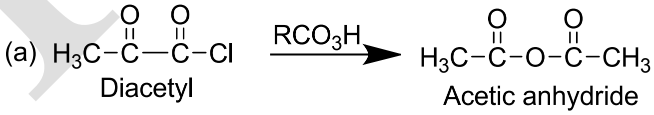
(a) $C_6H_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_3 \xrightarrow{CF_3CO_3H} H_3C\text{-}\overset{O}{\overset{\|}{C}}\text{-}OC_6H_5$

Acetophenone Phenylacetate

(b) $H_3C\text{-}\overset{O}{\overset{\|}{C}}\text{-}C(CH_3)_3 \xrightarrow{CF_3CO_3H} H_3C\text{-}\overset{O}{\overset{\|}{C}}\text{-}OC(CH_3)_3$

Pinacolone *t*-Butylacetate

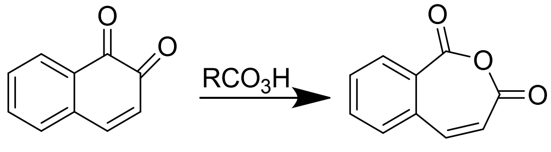
(ii) **Anhydride:** When 1,2-diketones of *o*-quinones are subjected to Baeyer-Villiger rearrangement, anhydride are produced.



(a) $H_3C\text{-}\overset{O}{\overset{\|}{C}}\text{-}\overset{O}{\overset{\|}{C}}\text{-}Cl \xrightarrow{RCO_3H} H_3C\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_3$

Diacetyl Acetic anhydride

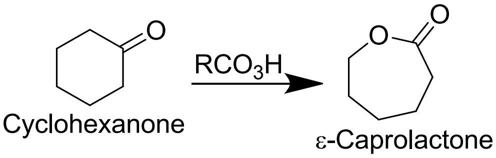
(b)



α-Naphthaquinone

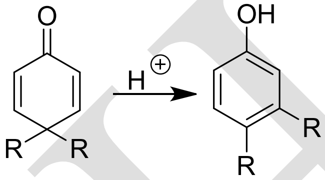
The products can be converted to various types of compounds.

(iii) **Lactones:** Cyclic ketones are converted to lactones with ring expansion.



Dienone-phenol rearrangement

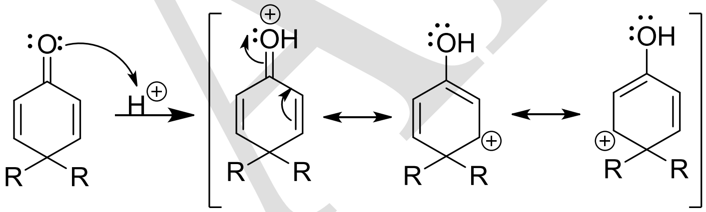
When 4,4-dialkyl cyclohexadienone is treated with acid, it is converted to phenol with migration of one of the alkyl groups to the adjacent carbon atom. This is known as the **dienone-phenol rearrangement**.



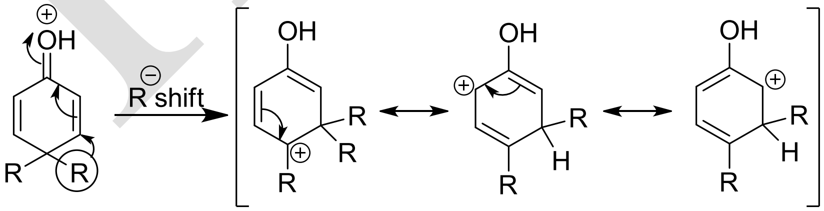
Mechanism

The mechanism of the reaction involved the following steps:

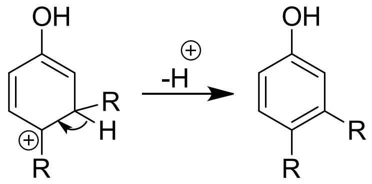
Step 1: Protonation of the dienone oxygen.



Step 2: Migration of an alkyl group to the adjacent carbon (a nucleophilic 1,2-shift) to form an arenium ion. This is the rate-determining step of the reaction.

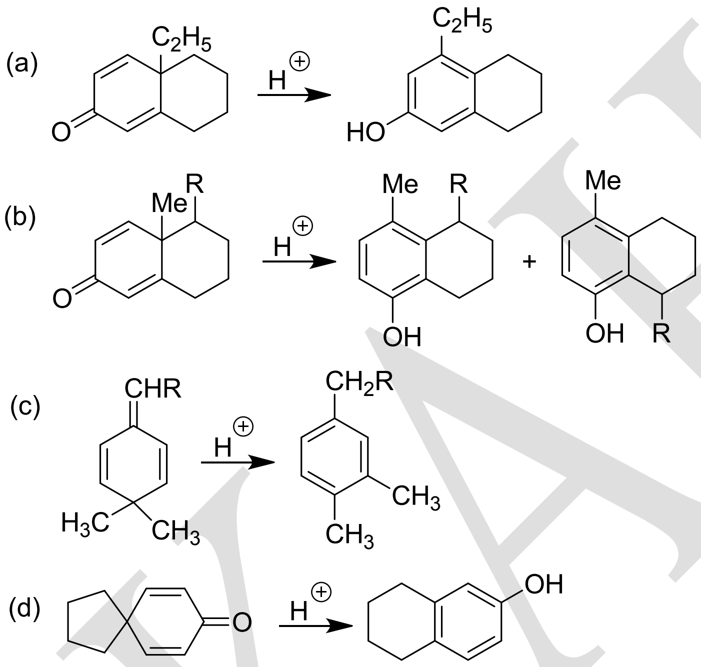


Step 3: Aromatization of the arenium ion by loss of a proton to yield the 3,4-disubstituted phenol.



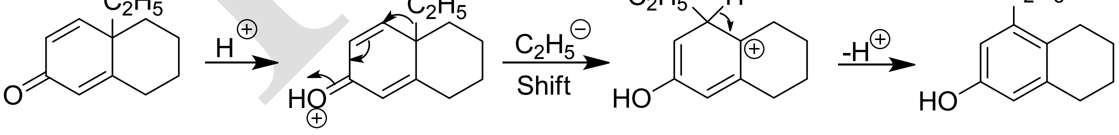
The driving force in the overall reaction is the creation of a stable aromatic system in the product.

Problem 8. Sketch a suitable mechanism for each of the following transformations:



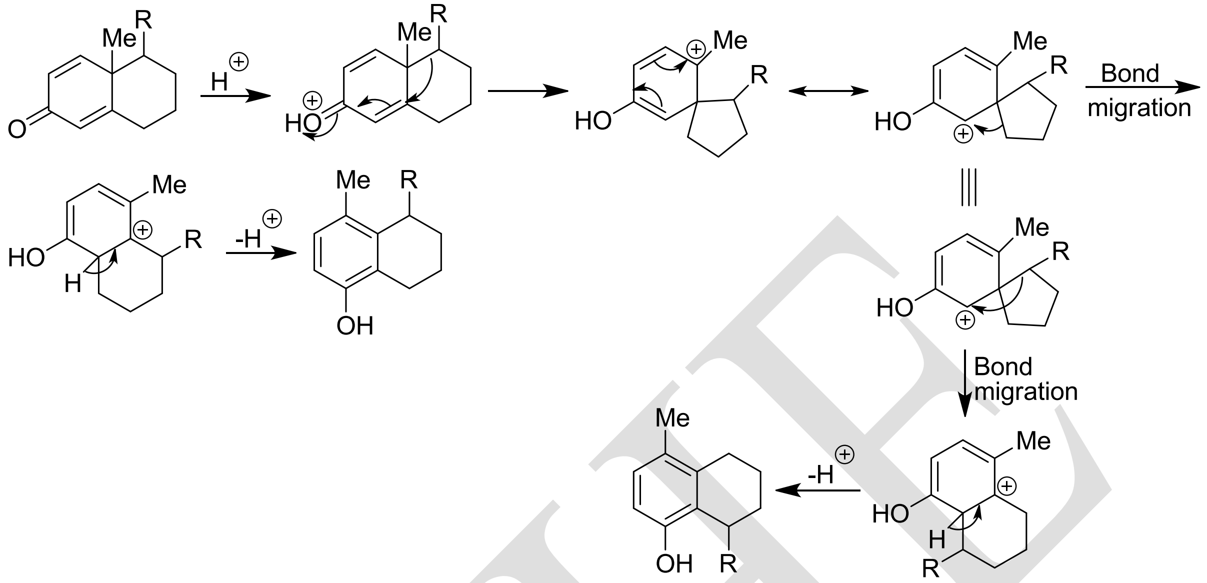
Solution:

(a)



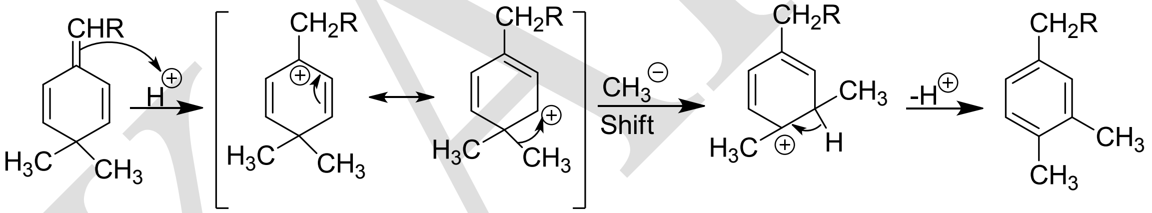
Ethyl migrates in preference to the ring methylene group to give the rearranged product.

(b)

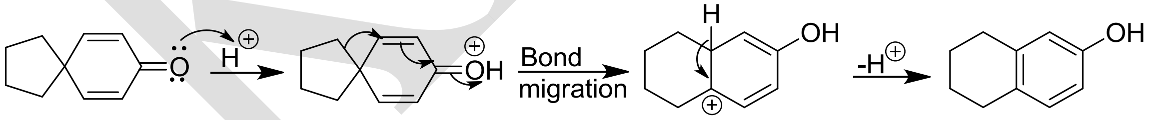


The ring bond migrates in preference to methyl to produce a carbocation which further rearranges to give isomeric products.

(c)

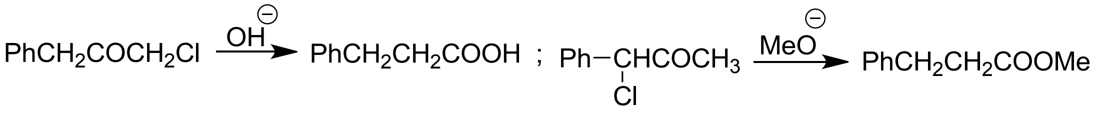


(d)

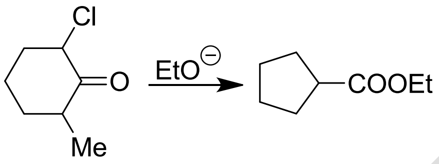


Favorskii rearrangement

The reaction of α-chloro-or α-bromoketones with a base (alkoxide, hydroxide, amines, etc.) give rearranged acids or esters and the rearrangement is called the **Favorskii rearrangement**. Cyclohexanones with α-halo group give ring contracted products while rearranged acid is the product when hydroxides or amines are used as bases.



$PhCH_2COCH_2Cl \xrightarrow{OH^{\ominus}} PhCH_2CH_2COOH$; $Ph-\underset{Cl}{CH}COCH_3 \xrightarrow{MeO^{\ominus}} PhCH_2CH_2COOMe$



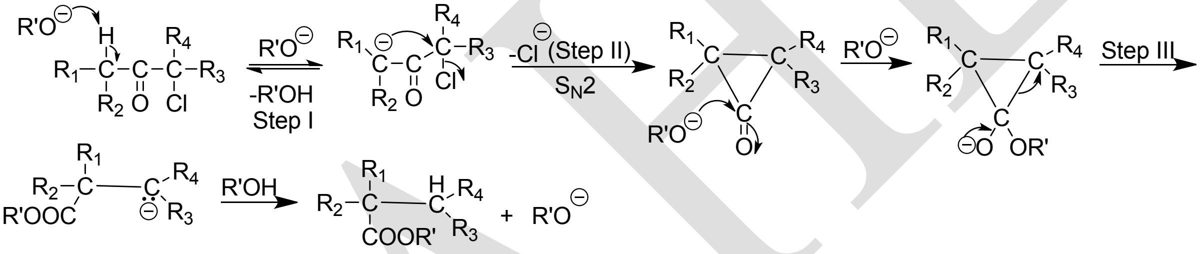
The mechanism involves the following steps:

(i) Abstraction of α-H.

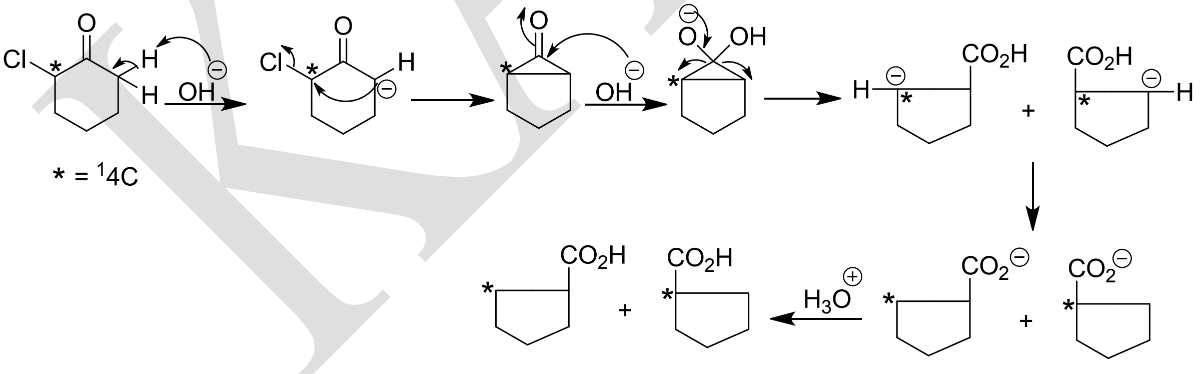
(ii) S_N2 reaction and formation of a cyclopropanone ring.

(iii) Cleavage of the cyclopropanone ring.

(iv) Abstraction of proton from the solvent.

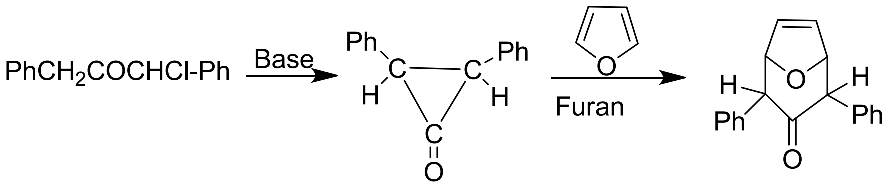


The formation of the carboxyl group both on labelled and non-labelled carbon atom is evidence in favour of the mechanism.

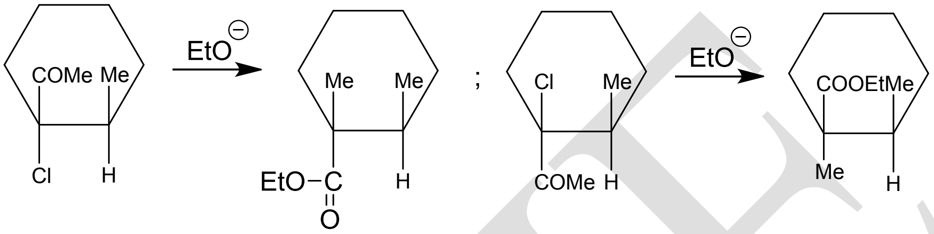


The following are further evidences in favour of the mechanism:

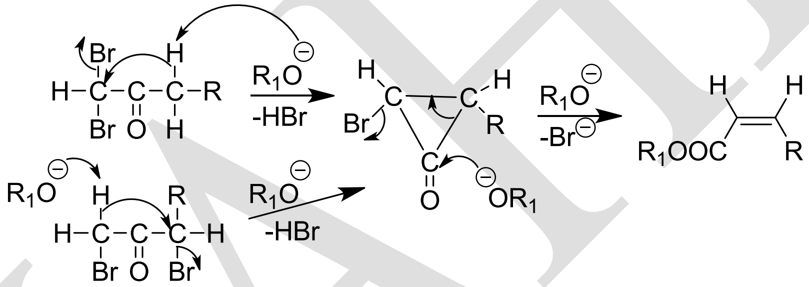
(i) Cyclopropanone intermediate has been trapped as an adduct with furan.



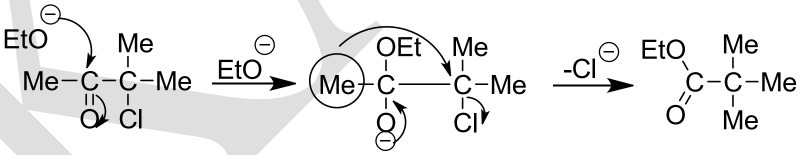
(ii) Stereospecific reactions take place in the cases of appropriate substrates.



When α,α or α,α'-dihaloketones with an α-H is subjected to the Favorskii reaction, α, β-unsaturated esters are formed.

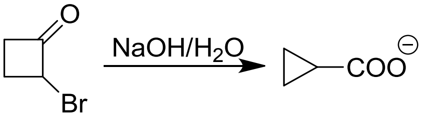


However, α-haloketones without α-H atom also undergoes the Favorskii reaction. Of course, the mechanism is quite different in this case:



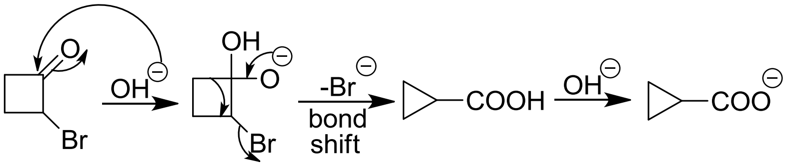
Problem 9. Suggest a reasonable mechanism for the below reaction and explain why this reaction do not proceed by the cyclopropanone mechanism.

(i)

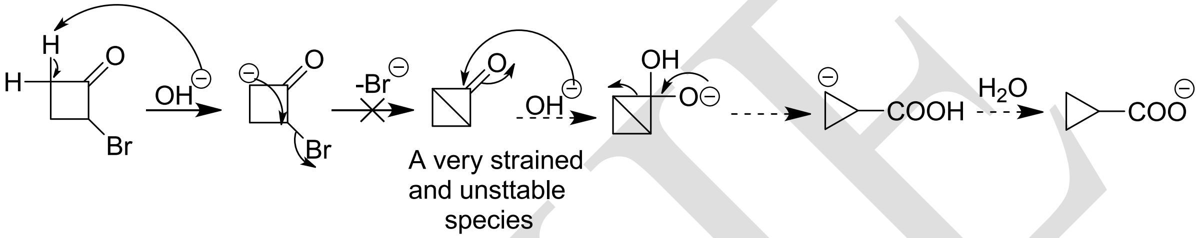


Solution:

This Favorskii reaction proceeds by the semibenzilic mechanism as shown below:

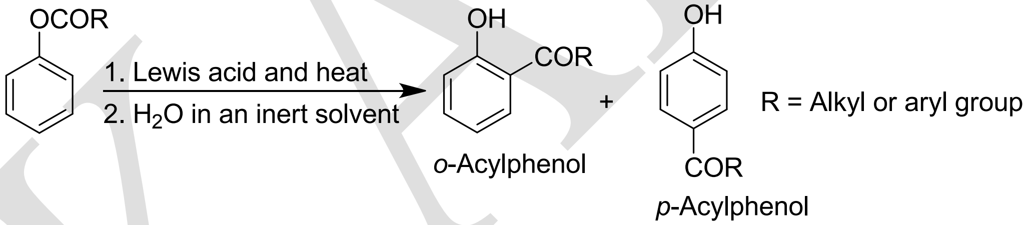


The cyclopropanone mechanism does not operate because the cyclopropanone intermediate, which is actually an extraordinarily strained bicyclobutane derivative, cannot be formed.

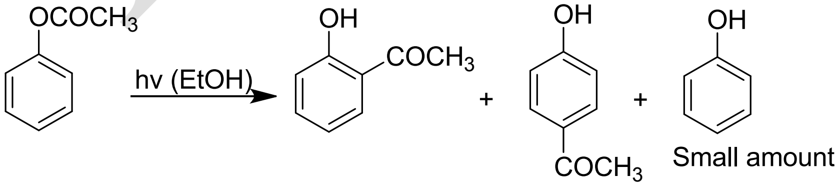


Fries rearrangement

When a phenolic ester is heated in an inert solvent in the presence of a Lewis acid as catalyst and the product is subsequently hydrolyzed, a mixture of *o*-and *p*-acylphenols is obtained and the reaction is known as the **Fries rearrangement**.

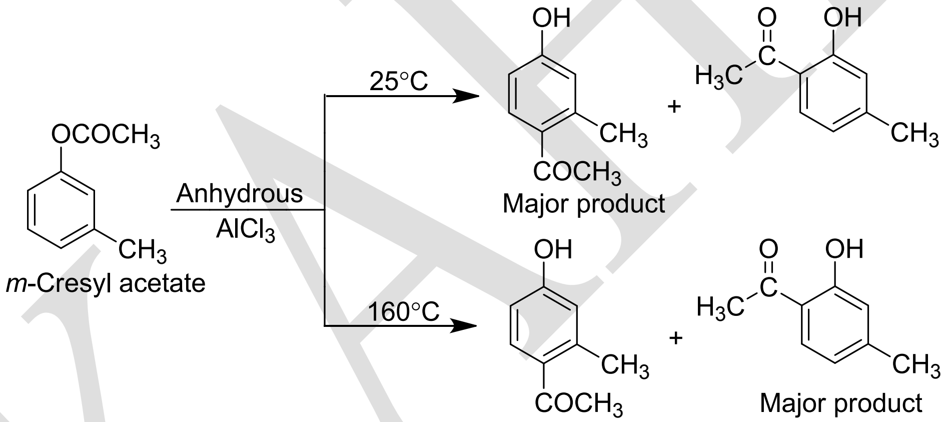


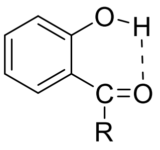
The Fries rearrangement also occurs without a catalyst in the presence of ultraviolet light and the reaction is known as **Photo Fries rearrangement**. Thus when a solution of phenyl acetate in ethyl alcohol is irradiated with ultraviolet light, *o*-and *p*-acylphenols are formed along with a small amount of phenol.



For Fries rearrangement reaction the common catalyst is anhydrous aluminium chloride and the common solvents are carbon disulphide, nitrobenzene etc. The *o*-and *p*-isomers may be separated by the process of steam distillation. Since the *o*-isomer possesses internal hydrogen bonding but the *p*-isomer does not, the former has a lower boiling point a higher volatility and a higher vapour pressure than the later. Naturally, the *o*-isomer distills out with steam while the *p*-isomer, which forms H-bonding, with water molecules, remains in the distillations flask. However, non-volatile compounds may be separated by fractional crystallization.

Of course, it is found that at a low temperature *p*-product predominate while at a higher temperature the predominating products are *o*-isomers. Solvents and concentrating of catalyst have effects on the product. The *p*-product is supposed to be kinetically controlled while the *o*-product is a thermodynamically controlled product because the latter gets extra stability through the internal hydrogen bonding. Perhaps owing to steric hindrance the *o*-isomer does not form as a major product at a low temperature.



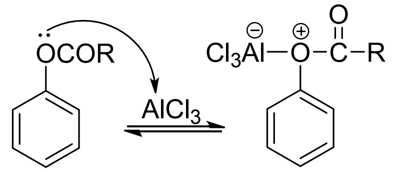


When a *m*-directing group is present in the aromatic ring, it interferes with the reaction. In some cases *m*-products are obtained in the Fries rearrangement.

Mechanism

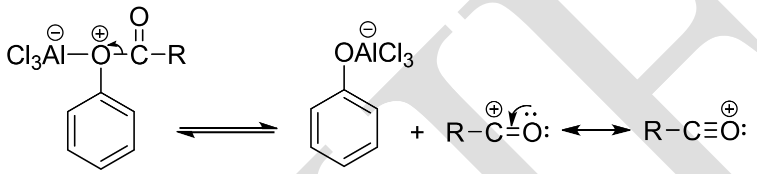
The reaction is supposed to follow both the intermolecular and intramolecular mechanisms simultaneously. However, the initial step in both the cases is the complexation of the phenolic ester with the Lewis acid.

Initial step: Complex formation:

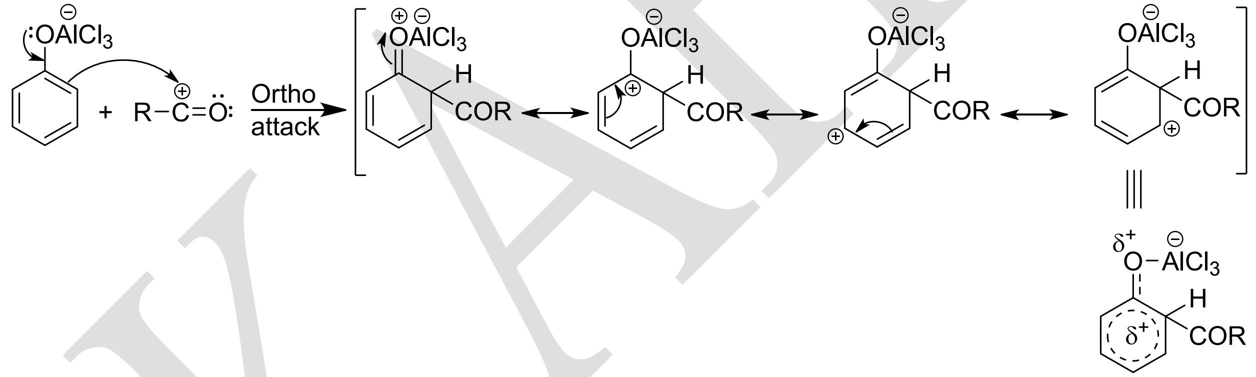


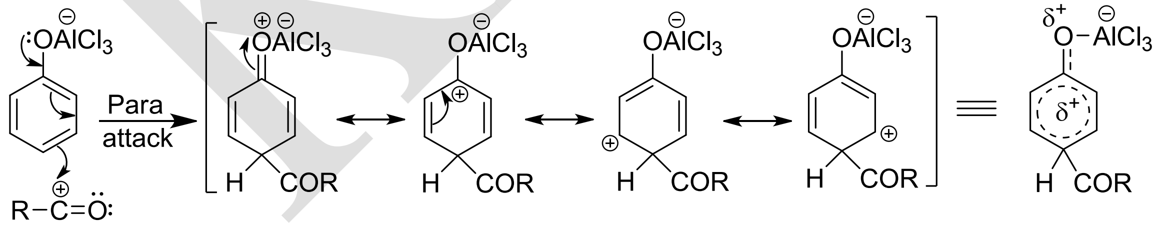
(a) Intermolecular mechanism:

Step 1: Reversible formation of the acyl cation.

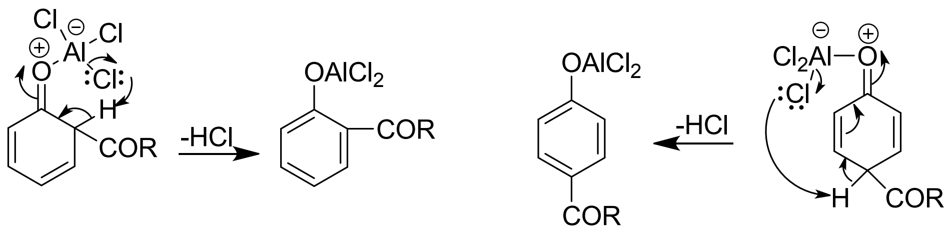


Step 2: Electrophilic attack at the *o*-and *p*-positions of the aromatic ring to form a resonance stabilized σ-complex.



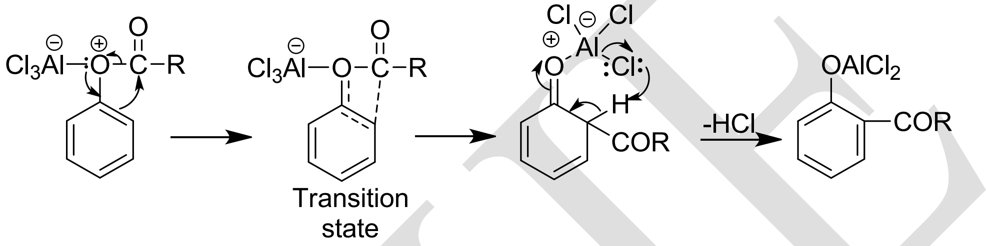


Step 3: Elimination of HCl form the σ-complex to form a more stable aromatic product.

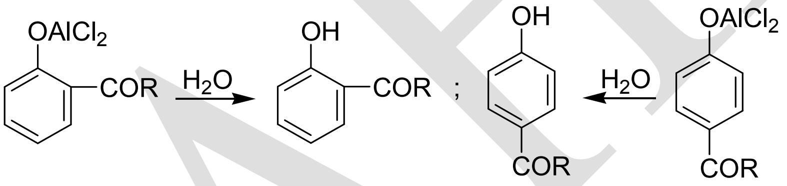


A stable product

(b) Intramolecular mechanism:



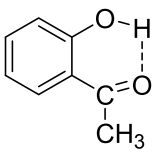
Final step: Hydrolysis of the stable product gives the acylphenol.



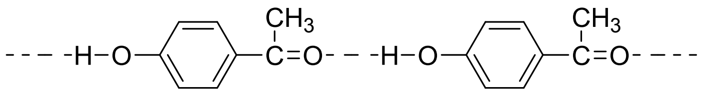
Problem 10. When a mixture of *ortho* and *para* isomers is steam distilled for separation the *ortho*-isomer distills out with steam. Account for this observation.

Solution:

The *ortho*-isomer, for example, *o*-hydroxyacetophenone is more volatile because intramolecular hydrogen bonding (chelations) causes the *o*-compound to behave as a monomer. On the other hand, the *para*-isomer, for example *p*-hydroxyacetophenone, is less volatile because intermolecular hydrogen bonding causes association among its molecules. Because of greater volatility, the *ortho*-isomer passes over with steam and the *para*-isomer remains in the distillation flask.



o-Hydroxyacetophenone (Intramolecular hydrogen bonding)

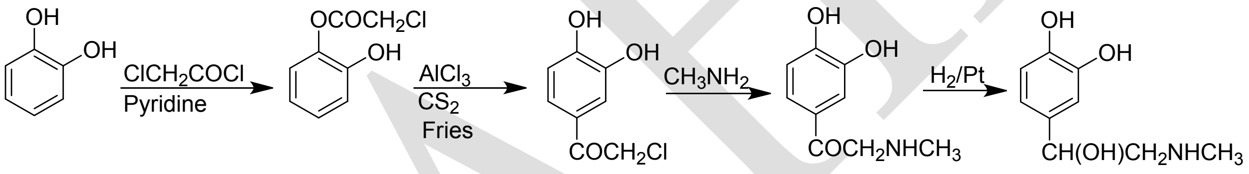


p-Hydroxyacetophenone (Intermolecular hydrogen bonding)

Applications

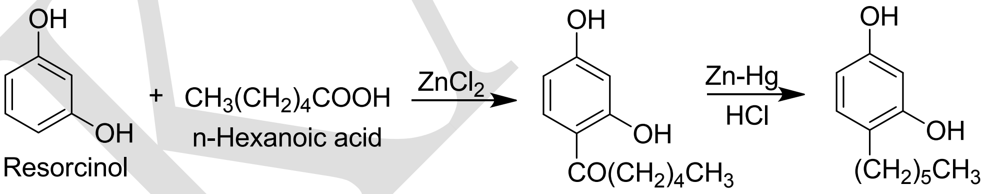
The reaction is synthetically useful because the introduction of an acyl group (RCO-) into a phenolic nucleus by the standard Friedel-Crafts procedure does not always result in acceptable yields.

i) A very useful application of this reaction is the synthesis of (±) adrenaline which is a heart stimulant.



(±)-Adrenaline

ii) The antiseptic chemical, 4-(n-hexyl)-resorcinol is synthesized by the Fries rearrangement.



Resorcinol n-Hexanoic acid 2, 4-Dihydroxyphenyl n-pentyl ketone 4-n-Hexyl-resorcinol

Wolff rearrangement and Arndt-Eistert synthesis

The thermal or photochemical or catalytic conversion of a diazoketone to a ketene with the liberation of molecular nitrogen is known as the **Wolff rearrangement**. Usually diazoketones are prepared from acyl halides by the action of diazomethane.

$$RCOCl + CH_2N_2 \longrightarrow RCOCHN_2 \longrightarrow O{=}C{=}CHR + N_2\uparrow$$

R = R or Ar

However, the reaction is usually carried out in the presence of water and silver oxide; in this case the ultimate product is a carboxylic acid having are carbon atom more than the starting acid halide.

$$\mathrm{RCOCl} + \underset{\mathrm{Excess}}{\mathrm{CH_2N_2}} \xrightarrow[\mathrm{Ag_2O}]{\mathrm{H_2O}} \mathrm{RCH_2COOH} + \mathrm{N_2}\uparrow + \mathrm{HCl}$$

So, the overall reaction is a step-up reaction and is known as the **Arndt-Eistert synthesis**. Thus the Arndt-Eistert synthesis is a step-up reaction in which a carboxylic acid is converted into its higher homologue by the reaction of its acid halide with diazomethane in the presence of water and silver oxide catalyst.

If the reaction is carried out with an alcohol or ammonia instead of water, the product will be a higher ester or amide respectively.

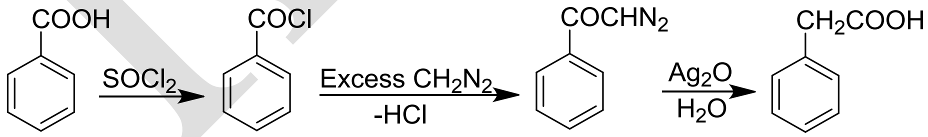
$$\mathrm{RCOCl} + \mathrm{CH_2N_2} \xrightarrow[\mathrm{Ag_2O}]{\mathrm{R'OH}} \mathrm{RCH_2COOR'} + \mathrm{N_2}\uparrow$$

$$\mathrm{RCOCl} + \mathrm{CH_2N_2} \xrightarrow[\mathrm{Ag_2O}]{\mathrm{NH_3\ (R'NH_2)}} \mathrm{RCH_2CONH_2\ (RCH_2CONHR')} + \mathrm{N_2}\uparrow$$

When the reaction is carried out in the presence of water and formic acid hydroxymethylketones are obtained.

$$\mathrm{RCOCl} + \mathrm{CH_2N_2} \xrightarrow[\mathrm{HCOOH}]{\mathrm{H_2O}} \mathrm{RCOCH_2OH} + \mathrm{N_2}\uparrow$$

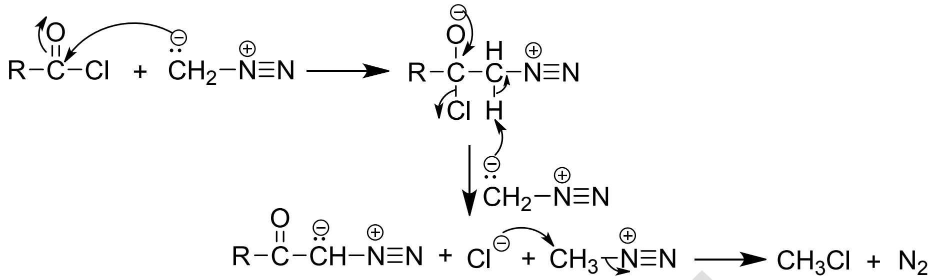
Thus the Arndt-Eistert synthesis is a good means for lengthening carbon chain and the reaction has a wide scope since alkyl, aryl and cycloalkyl diazoketones with other functions can undergo the reaction.



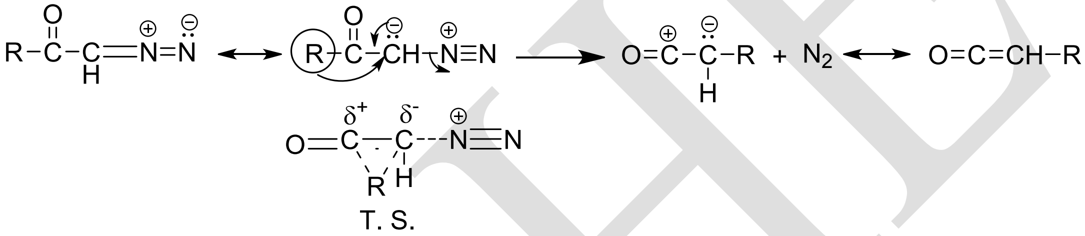
Mechanism

The possible mechanism of the Arndt-Eistert synthesis is as follows:

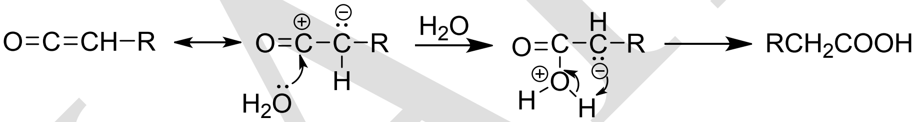
Stage 1: The conversion of the acid halide into diazoketone via a tetrahedral intermediate:



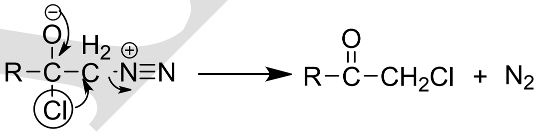
Stage 2: Wolff rearrangement: In this stage molecular nitrogen gets eliminated and the R group migrates to the anionic C more or less in a concerted step; this involves, 1,2-shift and forms an unstable compound called ketene.



Stage 3: The addition of water to the ketene and the formation of the carboxylic acid.

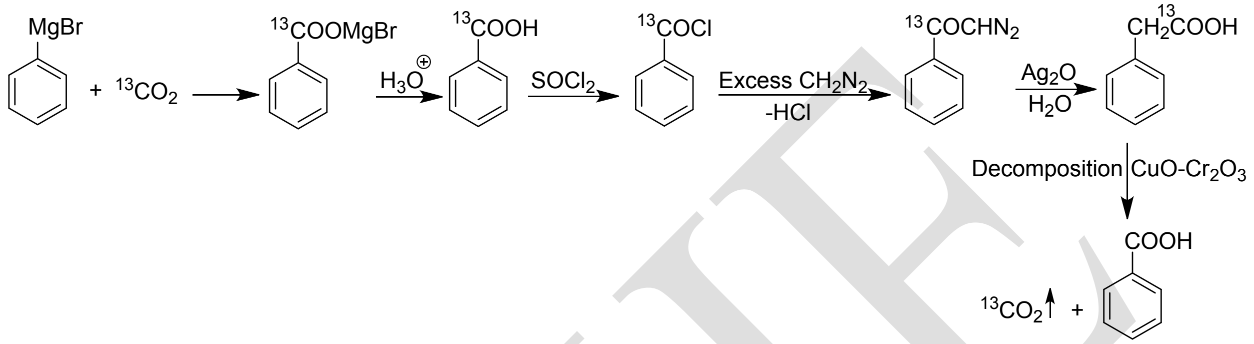


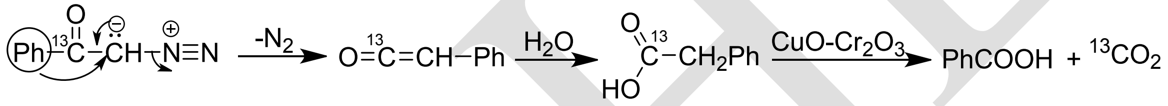
The excess use of diazomethane molecules per molecules of RCOCl is essential for the Wolff rearrangement and Arndt-Eistert synthesis. If we do not use of excess of diazomethane, $RCOCH_2Cl$ will be formed instead of diazomethane as shown below.



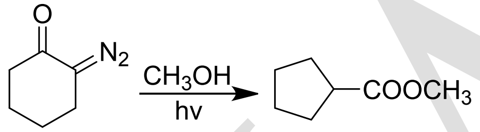
The first molecule undergoes bimolecular S_N reaction on the sp^2C of RCOCl and the second molecule abstracts the α-H; Cl^- ion gets eliminated to form the diazoketone. In the absence of excess diazomethane, molecular nitrogen evolves out and the Cl atom with its bonded electrons migrates to the N-bonded C atom to give $RCOCH_2Cl$.

That the Wolff rearrangement which takes place by the 1,2-shift has been corroborated by the fact that C=O moiety of the acid halide becomes the carboxyl group of the higher acid in the Arndt-Eistert synthesis. Huggett and his co-workers prepared phenylacetic acid from benzoic acid by the Arndt-Eistert synthesis. The carbonyl C atom of the starting benzoic acid was a radioactive carbon. They then decomposed the phenylacetic acid by CuO-Cr_2O_3 oxidation and found that the evolved carbon dioxide contains the radioactive C. If the phenyl group did not migrates from the carbonyl C atom to the α-C atom, this would not have been the result.

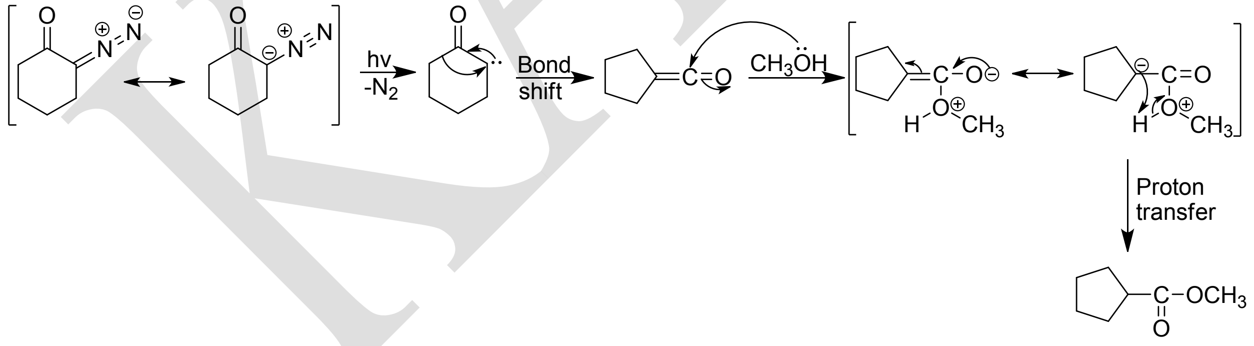




Problem 11. Sketch a mechanism for each of the following reaction:

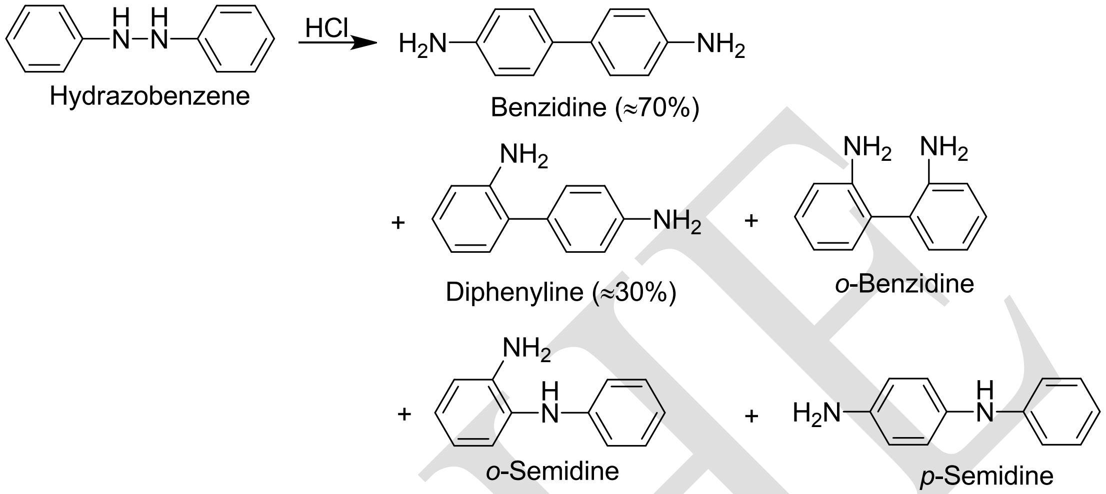


Solution:



Benzidine rearrangement

When hydrazobenzene is treated with aqueous or ethanolic hydrochloric acid or sulphuric acid, it rearranges to give about 70% 4,4'-diaminobiphenyl (benzidine) and about 30% 2,4'-diaminobiphenyl (diphenyline). This reaction, which is general for *N*,*N*'-diarylhydrazines (hydrazoarenes) is called **benzidine rearrangement**. In addition to the products already referred to, three other products 2,2’-diaminobiphenyl (*o*-benzidine), *o*-phenylaminoaniline (*o*-semidine), and *p*-phenylaminoaniline (*p*-semidine) may also be produced in smaller amounts.



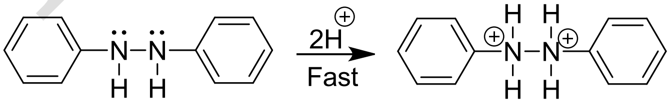
Mechanism

Several mechanisms have been proposed for this rearrangement but two of them, namely the polar transition state mechanism which follows third order kinetics (proposed by Banthorpe, Hagles, and Ingold) and the π-complex mechanism which follows second order kinetics (proposed by Dewar), deserve special mention.

Polar transition state mechanism

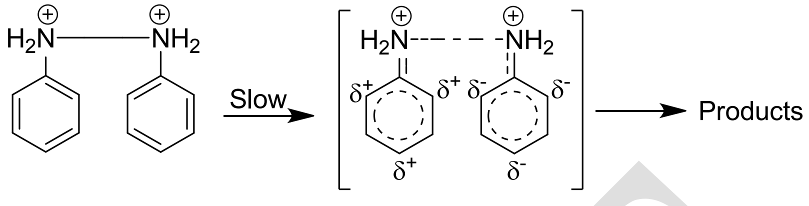
This mechanism involving a polar transition state accounts for most of the known facts. This consists of the following three steps.

Step 1: Hydrazobenzene undergoes diprotonation to give the corresponding dipositive ion. This step is fast.



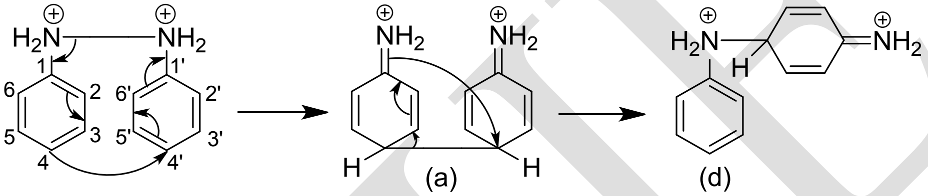
Step 2: Because of the repulsion between two positive nitrogens, the N-N bond breaks and C-C bond forms in a concerted and slow step through a polar transition state (a C-C bond is thermodynamically more stable than an N-N bond). The rings link up in the 4,4’, 2,4’ or 2,2’

manner to give the intermediate (a), (b), and (c) respectively. The intermediates (a) and (c) further rearrange to give the intermediates (d) and (e) respectively.

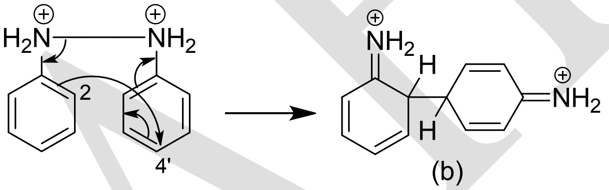


Polar transition state

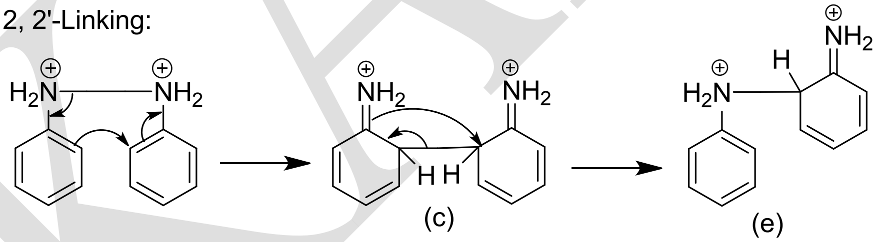
4, 4'-Linking:



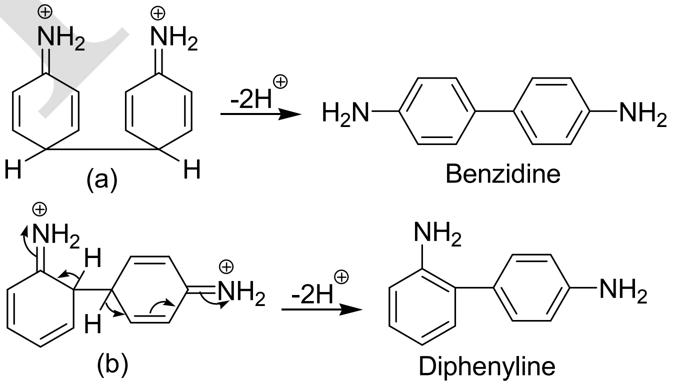
2, 4'-Linking:

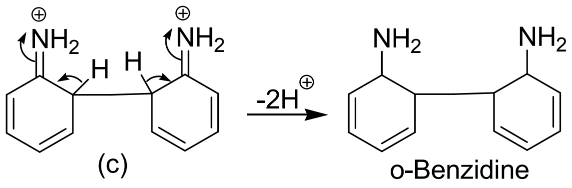


2, 2'-Linking:

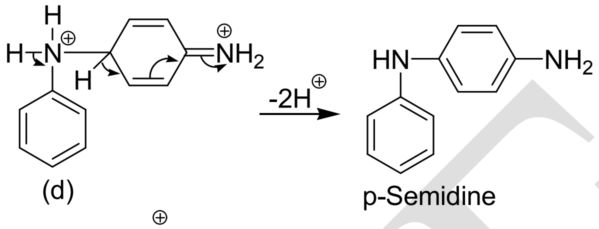


Step 3: The intermediates give rise to the products by the elimination of two protons.

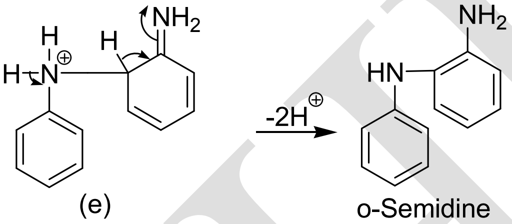




(c)



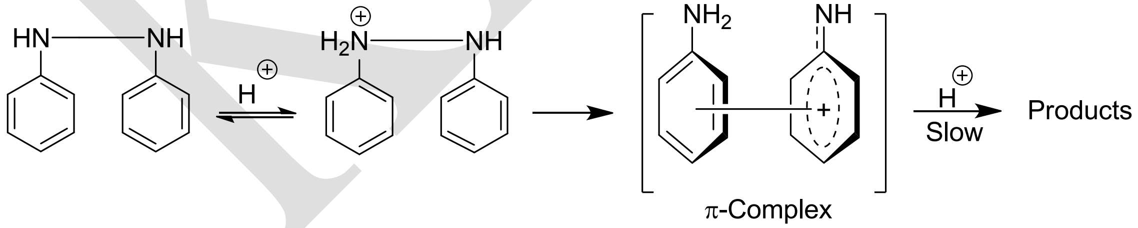
(d)



(e)

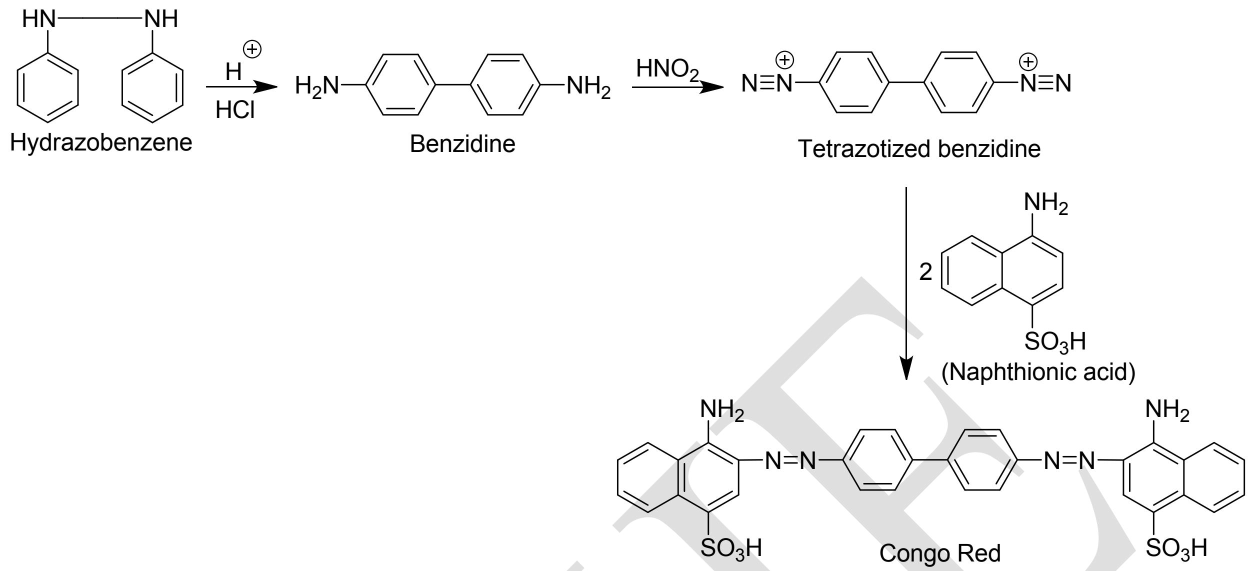
π-Complex mechanism

The first step of this mechanism involves formation of a monoprotonated intermediate. This intermediate then cleaves into two parts, aniline and a positive ion. These parts are held together by a π-orbital overlap between the filled molecular orbital of aniline and an empty molecular orbital of the other to give a sandwich like π-complex (the rings are held in parallel planes). The π-complex then gets protonated at the second nitrogen atom and finally collapses to give various products by the rotation of one of the rings.



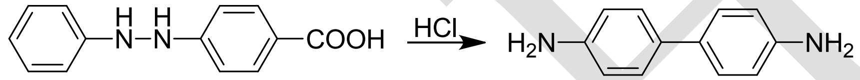
Application

An important application of the benzidine rearrangement is found in the found in the synthesis of dyes. Hydrazoarenes are first rearranged into benzidines which on diazotization followed by coupling reaction give the required diazo dyes. For example, Congo Red, which dyes cotton directly, can be synthesized as follows:

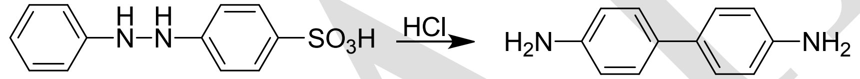


Problem 12. Sketch the mechanism of each of the following transformation:

(a)

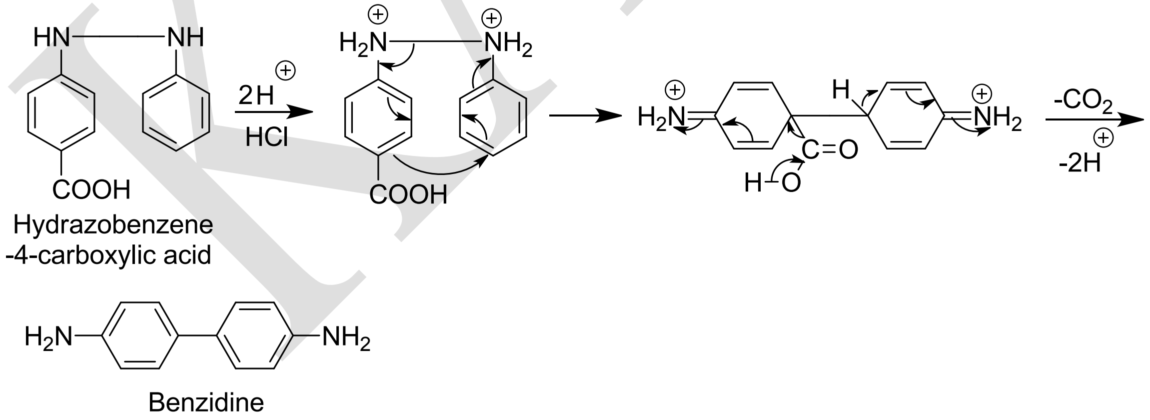


(b)

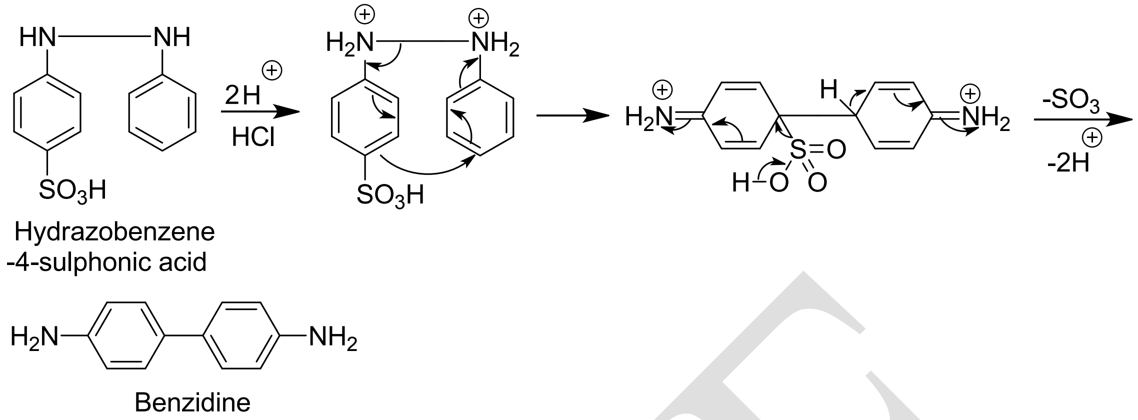


Solution:

(a) Decarboxylation occurs during the rearrangement of hydrazobenzene-4-carboxylic acid.



(b) Similarly, desulphonation occurs during the rearrangement hydrazobenzene-4-sulphonic acid.



The Hofmann rearrangement (or Degradation of Amide)

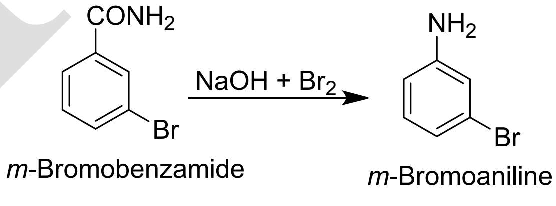
The conversion of a carboxamide to a primary amine with a C atom less by the action of alkali and halogen (chlorine or bromine) or hypohalites (NaOCl or NaOBr) is known as the **Hofmann degradation of amide**. This involves a rearrangement reaction of an *N*-haloamide into an isocyanate which hydrolyses rapidly, under the conditions of the reaction, into a primary amine and carbonate ion; because of the intermediate rearrangement, the reaction is also termed the **Hofmann haloamide rearrangement**. A few example of the reaction are given below along with the general reaction.

$$\mathrm{RCONH_2} \xrightarrow{\mathrm{NaOBr}} \mathrm{RCONHBr} \xrightarrow{\mathrm{OH^{\ominus}}} \mathrm{RCO\overset{..}{\underset{..}{N}}Br} \longrightarrow \mathrm{O{=}C{=}N{-}R} \xrightarrow[\mathrm{OH^{\ominus}}]{\mathrm{H_2O}} \mathrm{RNH_2}$$

(i)

$$\underset{\text{2-Methylbutanamide}}{\mathrm{CH_3CH_2CH(CH_3)CONH_2}} \xrightarrow{\mathrm{NaOBr}} \underset{\text{1-Methylpropanamine}}{\mathrm{CH_3CH_2CH(CH_3)NH_2}}$$

(ii)



(iii)

$$\underset{\text{Urea}}{\mathrm{NH_2CONH_2}} \xrightarrow[\text{(Not in excess)}]{\mathrm{NaOCl}} \underset{\text{Hydrazine}}{\mathrm{NH_2NH_2}}$$

The overall equation for the general reaction may be written as:

$$RCONH_2 + Br_2 + 4NaOH \longrightarrow RNH_2 + 2NaBr + Na_2CO_3 + 2H_2O$$

Here R is usually an alkyl or an aryl group. Thus in this reaction migration origin is a C atom, migration terminus is a nitrogen atom and the migration group is usually an alkyl or an aryl or a cycloalkyl group.

Since an isocyanate is one of the intermediates in the reaction, the addition of the starting amide to the isocyanate may take place to give an acyl urea specially when the base is NaOH and the reagents used are less than the requisite amounts.

$$RCONH_2 \xrightarrow{NaOBr} O{=}C{=}N{-}R \xrightarrow{RCONH_2} RCONHCONHR$$

If the primary amine formed has a 1° alkyl group ($R'CH_2$-NH_2), it may sometimes get dehydrogenated by NaOBr to give a nitrile.

$$R'CH_2NH_2 \xrightarrow{NaOBr} R'CN$$

A reaction analogous to this rearrangement is carried out by treating a carboxamide with lead tetraacetate. At first an isocyanate and then a primary amine are formed but they react with each other and the primary amine also reacts with the acetic acid, liberated from lead tetraacetate, to give ureas and acetyl derivative of the primary amine respectively.

A primary amine consisting of more than seven Cs cannot be directly prepared by the Hofmann rearrangement; a nitrile is usually formed which may then be reduced to a primary amine.

$$CH_3(CH_2)_7CONH_2 \xrightarrow{KOH + Br_2} CH_3(CH_2)_6CN \xrightarrow{[H]} CH_3(CH_2)_6CH_2NH_2$$

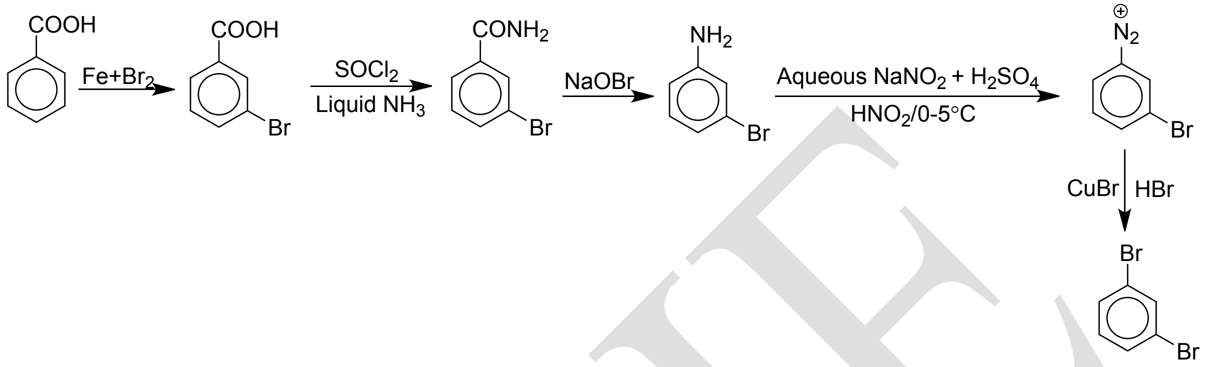
However, when a methanolic solution of such a long chain amide containing sodium methoxide as a base is treated rapidly with bromine, *N*-substituted urethan is formed which on alkaline hydrolysis produces the desired primary amine.

$$CH_3(CH_2)_nCH_2CONH_2 \xrightarrow[Br_2]{MeONa} CH_3(CH_2)_nCH_2NHCO_2CH_3 \xrightarrow{NaOH} CH_3(CH_2)_nCH_2NH_2$$

Here, $n > 5$

This reaction has a wide scope and varied application; a few are discussed below:

1. It is a good method for preparing pure primary amines; e.g., *m*-haloaniline or *m*-dihalobenzenes can be prepared in good yield by this reaction; these are difficult to prepare by other means.



2. A compound can be descended to its lower homologue by this reaction; e.g.,

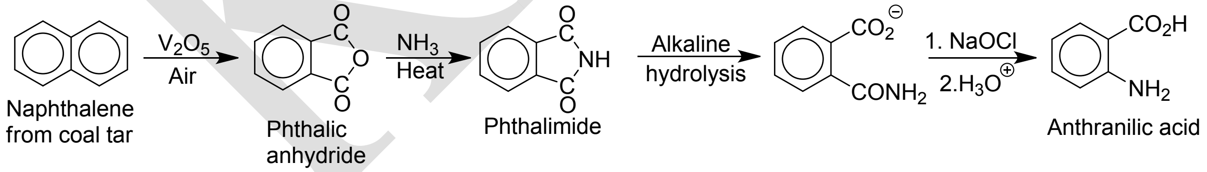
$$\begin{tikzcd}
CH_3CH_2CH_2OH \arrow[r, "{[O]}"] & CH_3CH_2COOH \arrow[r, "SOCl_2", "\text{Liquid } NH_3"'] & CH_3CH_2CONH_2 \arrow[r, "NaOH", "Br_2"'] & CH_3CH_2NH_2 \arrow[d, "HNO_2"] \\
 & & CH_3COOH & CH_3CH_2OH \arrow[l, "{[O]}"']
\end{tikzcd}$$

3. Hydrazine and anthranilic acid, the two important chemicals, are now manufactured applying the Hofmann rearrangement.

(a)

$$NH_2CONH_2 \xrightarrow[\text{Requisite amount}]{NaOCl} NH_2NH_2$$

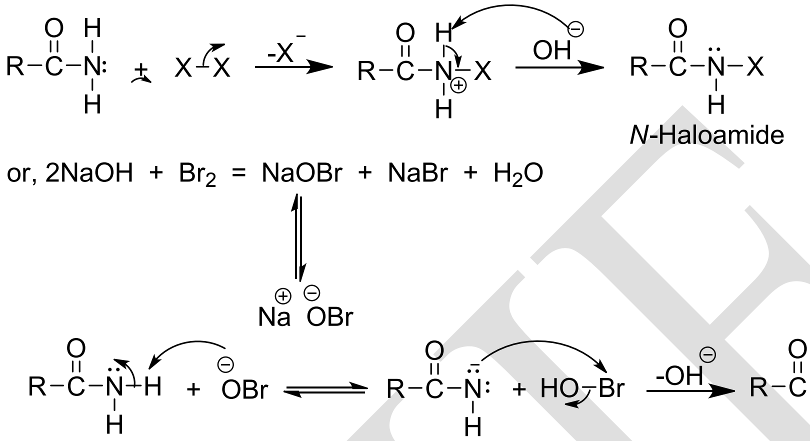
(b)



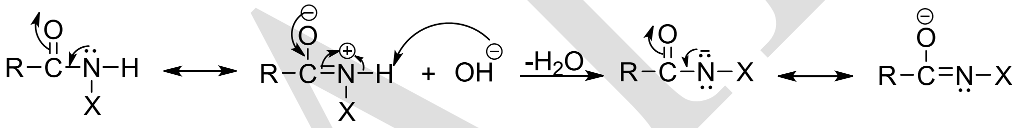
Mechanism

This is an intramolecuar anionotropic 1,2-shift rearrangement reaction involving migration of an aryl or an alkyl group from a C atom to an N atom with retention of configuration. It consists of several steps as given below:

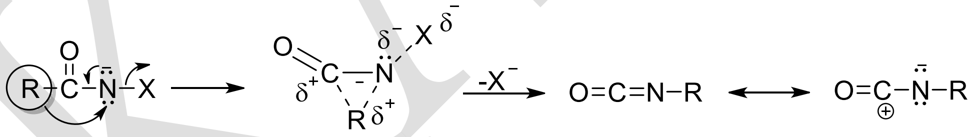
Step 1. Electrophilic substitution reaction occurs at the N atom of the amide; here a positive halogen atom attacks the N atom and a proton is abstracted by the OH^- to form *N*-haloamide.



Step 2. The H atom on the N atom is abstracted by the OH^-; the electron–withdrawing effect of the carbonyl and bromo groups makes the H highly acidic.

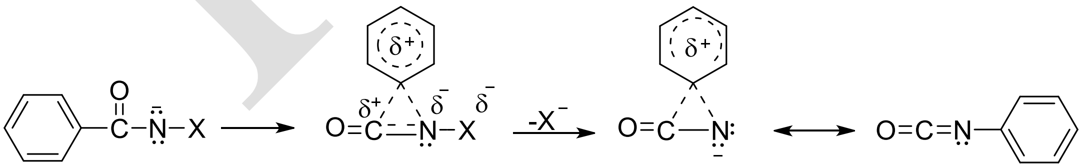


Step 3. Elimination of the halide ion and migration of the R occur in this concerted step to form isocyanate. Probably this is the rate determining step.



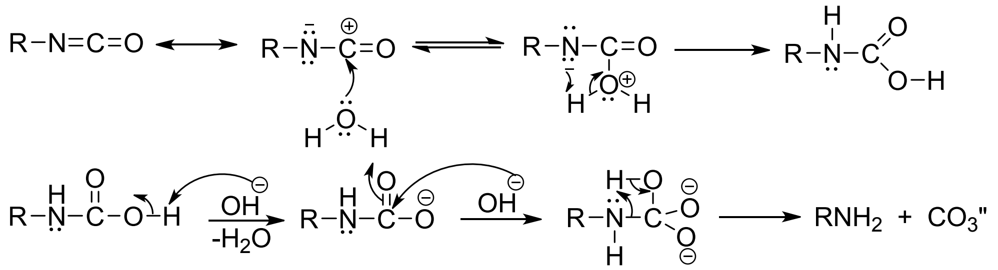
Bridged T. S.

However, when an aryl group migrates, the bridged T.S. might be a bridged intermediate.



Bridged T. S.

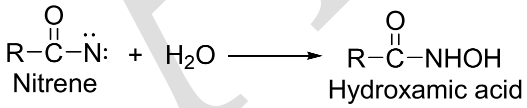
Step 4. In this step isocyanate hydrolyses to 1°amine and carbonate ion by the aqueous alkali.



Since no cross-migration is observed when two different amides are subjected to the Hofmann rearrangement simultaneously in the same solution (cross-over experiment), the reaction is undoubtedly an intramolecular one.

N-haloamides, their salts and isocyanates have been isolated. When the isolated products are separately treated with alkali, each of them forms the primary amine, the ultimate product of the Hofmann rearrangement. Thus the sequential steps as drawn for the mechanism of the reaction are quite in agreement with the experimental results.

That the elimination of the hailde ion and the migration of the R take place simultaneously in a concerted step have been supported by the fact that no hydroxamic acid has ever been isolated. If nitrene were an intermediate, hydroxamic acid would have been one of the products of the rearrangement:

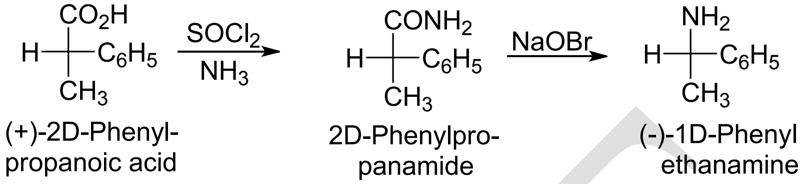


$$\underset{\text{Nitrene}}{R-\overset{O}{\overset{\|}{C}}-\ddot{N}:} + H_2O \longrightarrow \underset{\text{Hydroxamic acid}}{R-\overset{O}{\overset{\|}{C}}-NHOH}$$

The study of kinetic isotope effect on the Hofmann rearrangement of phenyl-1-C^{14} labelled *N*-bromobenzamide by Wright and Fry (1968) has ruled out the formation of nitrene as an intermediate.

Since the presence of an electron-releasing group at the *para* position of an aromatic amide accelerates the reaction while an electron-withdrawing group on the same position retards the reaction, the concerted step is the rate-determining step.

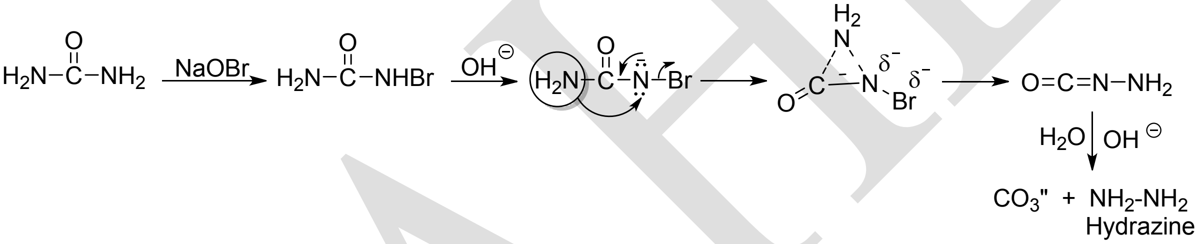
If the migrating group of an amide is chiral, the 1° amine formed shows optical activity. The question of the change in configuration about the migration terminus (N atom) or the migration origin (C atom) does not arise in the Hofmann rearrangement; what we require here is to discuss the configuration of the migrating group. The migrating group retains its configuration in this rearrangement. This has been established by the following reaction sequence:



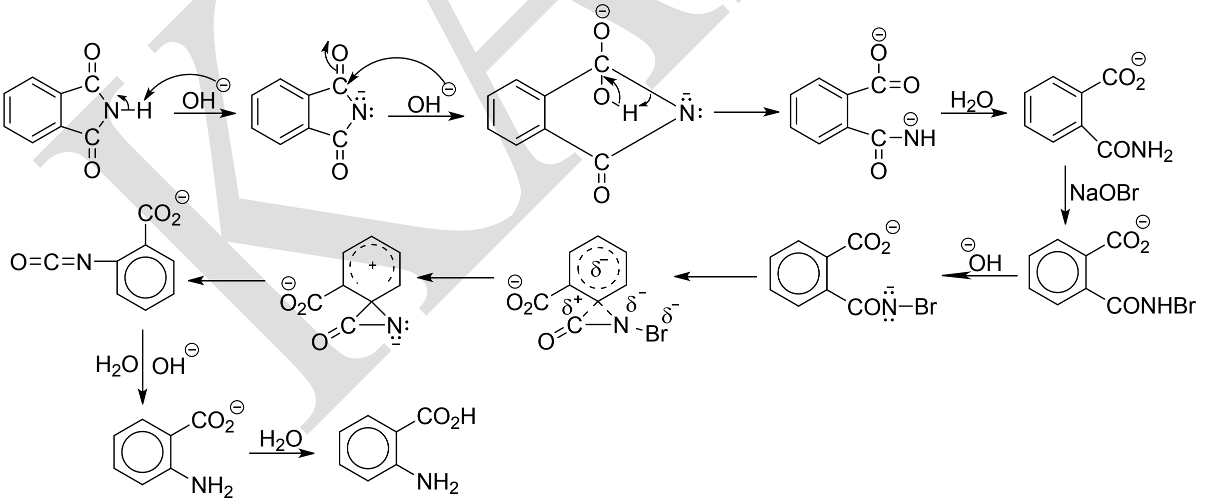
Problem 13. Give the mechanistic steps for the synthesis of (a) hydrazine and (b) anthranilic acid from urea and phthalimide respectively.

Solution:

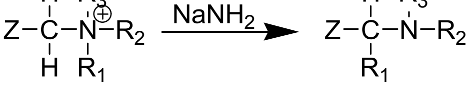
(a)



(b)

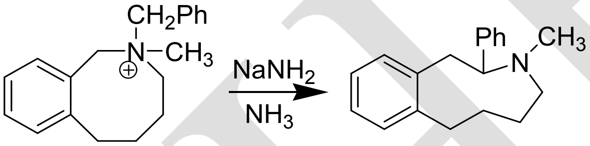


Stevens rearrangement



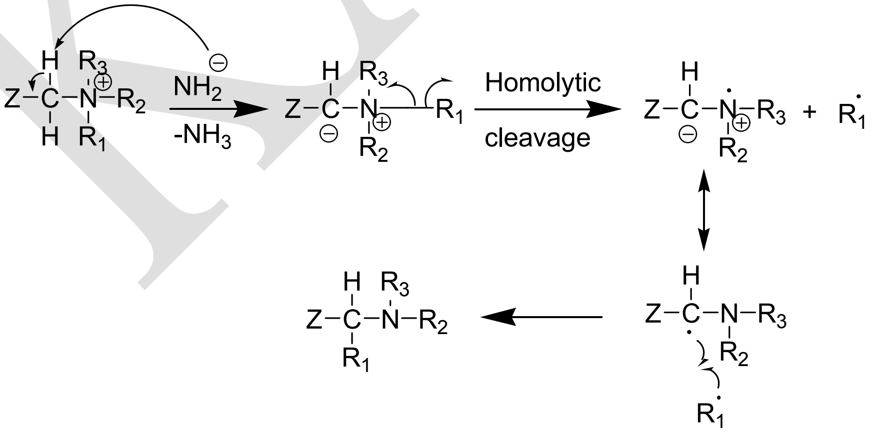
In the stevens rearrangement a quaternary ammonium salt containing an electron-withdrawing Z on one of the carbons attached to the nitrogen is treated with a strong base (such as NaOR or $NaNH_2$) to give a rearranged tertiary amine. Z is a group such as RCO, ROOC, phenyl etc.

The most common migrating groups are allylic, benzylic, benzhydryl, 3-phenylpropargyl and phenacyl though even methyl migrates to a sufficiently negative centre. When an allylic group migrates, it may or may not involve an allylic rearrangement within the migrating group, depending on the substrate and reaction conditions. The reaction has been used for ring enlargement.



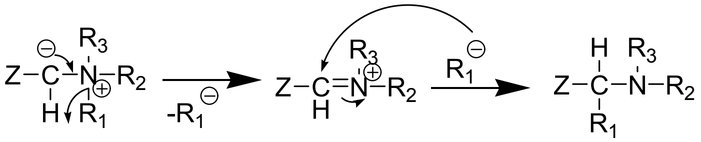
The mechanism has been the subject of much study. That the rearrangement is intramolecular was shown by cross over experiment by ^{14}C labelling and by the fact that retention of configuration is found at R_1. The first step is loss of the acidic proton to give ylide **1** which has been isolated. The finding that CIDNP spectra could be obtained in many instances shows that in these cases the product is formed directly from a free-radical precursor. The following radical pair mechanism was proposed.

Mechanism A



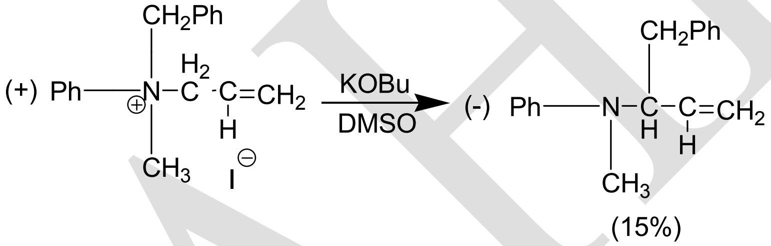
It is possible that another mechanism (b) similar to mechanism (a), but involving ion pairs in a solvent case instead of radical pairs, operates in some cases.

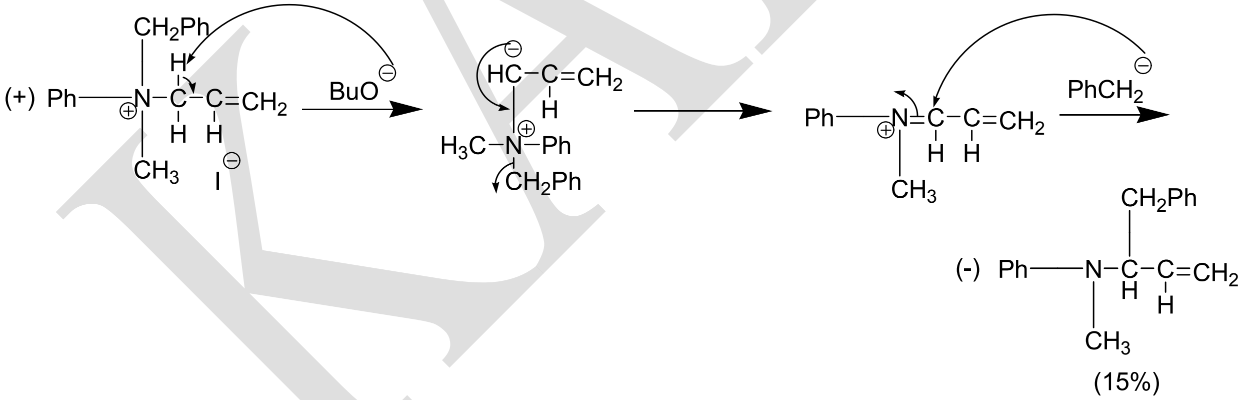
Mechanism B



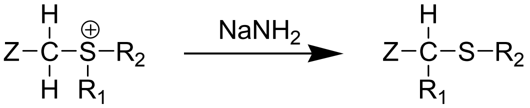
A third possible mechanism would be a concerted 1,2-shift, but the orbital symmetry principle requires that this take place with inversion at R_1. Since the actual migration takes place with retention it cannot according to this argument proceed by a concerted mechanism. However, in the case where the migrating group is allylic a concerted mechanism can also operate.

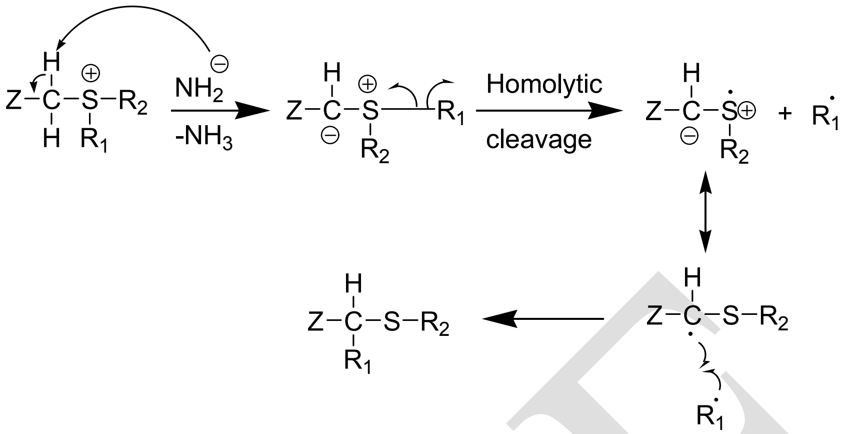
An interesting finding compatible with all three mechanisms is that optically active allyl benzylmethylphenylammonium iodide (asymmetric nitrogen) gave an optically active product.



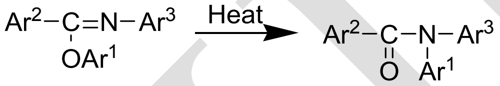


Sulfur ylides containing a Z group give an analogous rearrangement often also referred to as a Stevens rearrangement. In this case too, there is much evidence (including CIDNP) that a radical case mechanism is operating, except that when the migrating group is allylic the mechanism may be different.





Chapman rearrangement

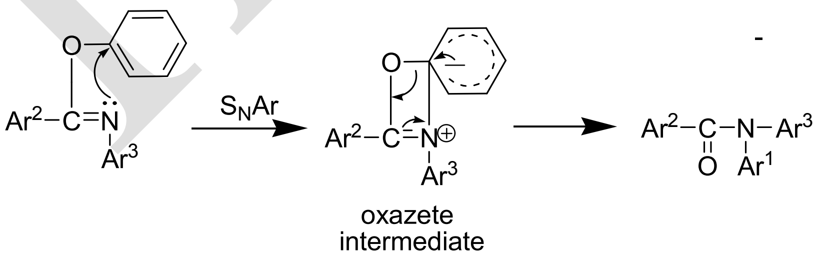


$$Ar^2-\underset{OAr^1}{C}=N-Ar^3 \xrightarrow{Heat} Ar^2-\underset{\underset{O}{\|}}{C}-\underset{Ar^1}{N}-Ar^3$$

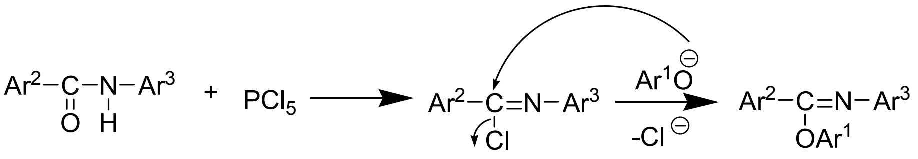
In Chapman rearrangement, N-N-diaryl amides are formed when aryl imino esters are heated. Best yields are obtained in refluxing tetraethylene glycol dimethyl ether (tetra-glyme), though the reaction can also be carried out without and solvent at all.

Many groups may be present in the rings, e.g., alkyl, halo, OR, CN, COOR, etc. Aryl migrates best when it contains electron-withdrawing groups. On the other hand, electron-withdrawing group in Ar^2 or Ar^3 decrease the reactivity. The products can be hydrolysed to diarylamines and this is a method for preparing these compounds.

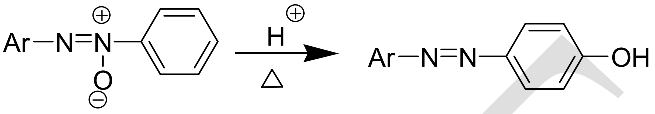
The mechanism probably involved an intramolecular aromatic nucleophilic substitution, resulting in a 1,3-oxygen-to-nitrogen shift.



Aryl imino esters can be prepared from N-aryl amides by reaction with PCl_5, followed by treatment of the resulting imino chloride with an aroxide ion.

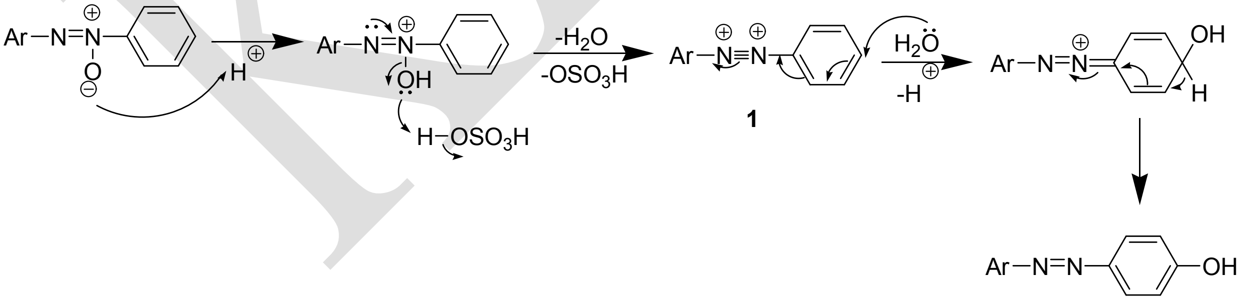


Wallach rearrangement



The conversion of azoxy compounds on acid treatment to *p*-hydroxy azo compounds (or sometimes the *o*-hydroxy isomers) is called the Wallach rearrangement. When both para positions are occupied, the *o*-hydroxy product may be obtained but ipso substitution at one of the pare positions is also possible.

Although the mechanism is not completely settled the following facts are known: (1) the para rearrangement is intermolecular. (2) When the reaction was carried out with an azoxy compounds in which the N-O nitrogen was labeled with ^{15}N both nitrogens of the product carried the label equally demonstrating that the oxygen did not have a preference for migration to either the near of the far ring. This shows that there is a symmetrical intermediate. (3) Kinetic studies show that two protons are normally required for the reaction. The following mechanism involving the symmetrical intermediate **1** has been proposed to explain the facts.



Text Book:

1. Smith, M. B. (2015). *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure* (VII Edition). New Jersey: John Wiley & Sons, Inc., Hoboken.

Reference Books:

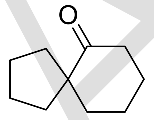
1. Tewari, N. (2011). *Advanced Organic Reaction Mechanism* (III Edition). Kolkata: Books and Allied (P) Ltd.

2. Sanyal, S. N. (2014). *Reactions, Rearrangements and Reagents* (IV Edition). New Delhi: Bharathi Bhawan (Publishers and Distributors).

POSSIBLE QUESTIONS

PART-B (Each Question Carry Two Marks)

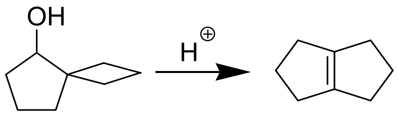
1. Define rearrangement reaction?
2. What is meant by a migration origin and migration terminus in a rearrangement reaction?
3. Define intermolecular rearrangement reaction?
4. What are the classifications of rearrangement reactions?
5. Define pinacol-pinacolone rearrangement?
6. How can you synthesize:



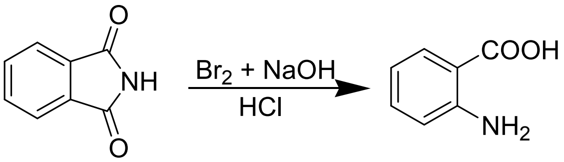
from cyclopentanone.

Give mechanistic steps for the synthesis.

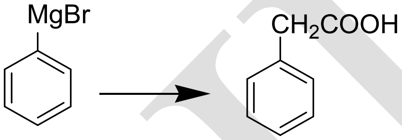
7. What happens when cis-2-aminocyclohexanol is subjected to pinacolic rearrangement reaction? Write down the mechanistic steps.
8. Why is excess diazomethane used in the Arndt-Eistert Synthesis?
9. Suggest a mechanism for the following reaction?



10. Sketch a suitable mechanism for the following transformation.



11. Give an important application of benzidine rearrangement.
12. What is photo-Fries rearrangement?
13. Define Fries rearrangement.
14. Sketch a suitable mechanism for the following conversion.

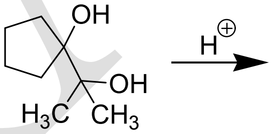


15. What product do you expect when trans-2-aminocyclohexanol is treated with aqueous $NaNO_2$ and dil. HCl?

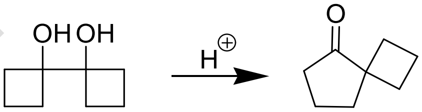
PART-C (Each Question Carry Six Marks)

1. (i) The pinacol ($PhCF_3$ C(OH) C(OH) CF_3CH_3) does not undergo pinacol-pinacolone rearrangement. Why?

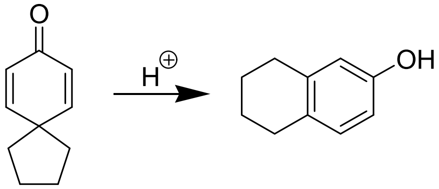
(ii) Predict the major product and suggest a mechanism for the following reaction?



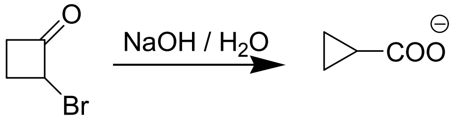
(iii) Suggest a mechanism for the following reaction?



2. (i) Sketch a suitable mechanism for the following transformation.



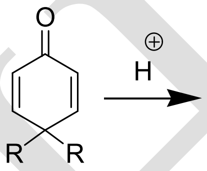
(ii) Suggest a reasonable mechanism for the below reaction and explain why this reaction do not proceed by the cyclopropanone mechanism.



(iii) Give an important application of Fries rearrangement reaction.

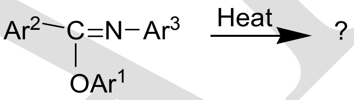
3. (i) Azoxy compounds $\xrightarrow{H^{\oplus}}$ P-hydroxy azo compounds. Name the rearrangements, give the mechanism and prove that it is intermolecular.

(ii) Predict the product, name the rearrangement and give mechanism:



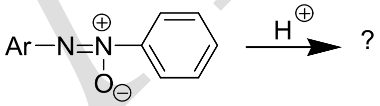
4. Predict the product, name the rearrangement and propose the mechanism for the

(a)



$$\underset{\mathrm{OAr^1}}{Ar^2-\overset{}{C}}=N-Ar^3 \xrightarrow{\text{Heat}} ?$$

(b)

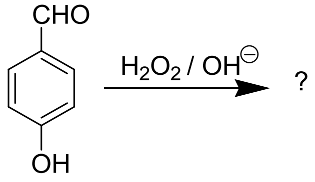


5. Explain the Wagner-Meerwein rearrangement with an example.

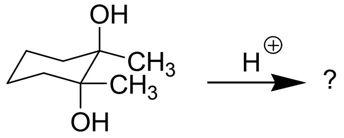
6. Explain the mechanism of Benzidine rearrangement.

7. Give the products of the following reactions with mechanism.

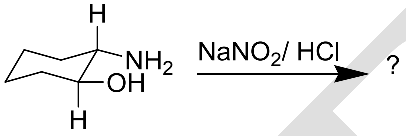
(i)



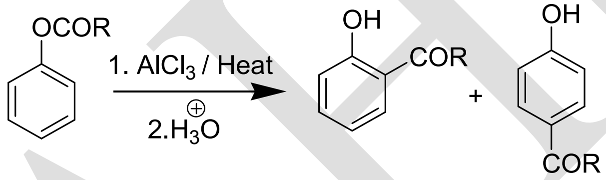
(ii)



(iii)



8. When a phenolic ester is treated with anhydrous aluminium chloride often in the absence of solvent, and the product is subsequently hydrolyzed, a mixture of o- & p- acylphenols is obtained. This synthetically useful reaction is known as the Fries rearrangement.



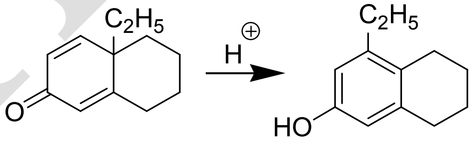
(i) Discuss the mechanism of this reaction.

(ii) Explain why low temperatures (60° C or less) generally favour the para product and high temperatures (above 160° C) favour the ortho product?

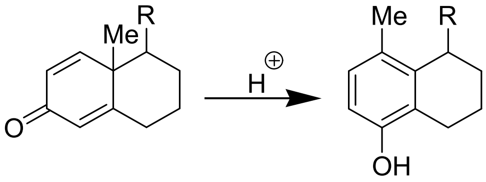
(iii) When a mixture of ortho and para isomer is steam distilled for separation, the ortho distills out with steam. Account for this observation.

9. Sketch a suitable mechanism for each of the following transformations.

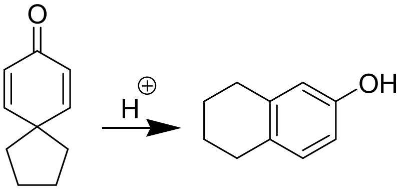
(i)



(ii)

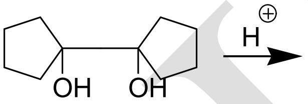


(iii)

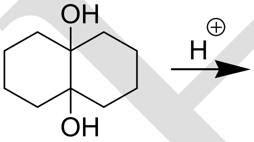


10. Predict the major product and suggest a mechanism for each of the following reactions.

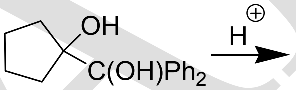
(i)



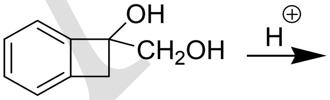
(ii)



(iii)



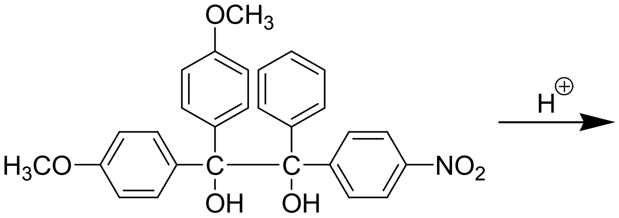
(iv)



11. Write brief notes on Chapman and Wallach rearrangements.

12. (i) The 1,2-diols containing substituents with strong –I effect does not undergo the pinacol-pinacolone rearrangement. Why?

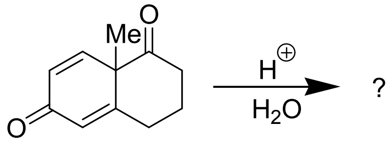
(ii) Predict the major product and suggest a mechanism for the following reaction?



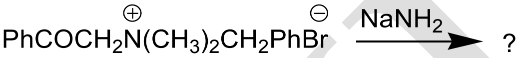
13. (i) Give some important applications of pinacol-pinacolone rearrangement.

(ii) Predict the product, name the rearrangement and propose the mechanism for the

(a)



(b)

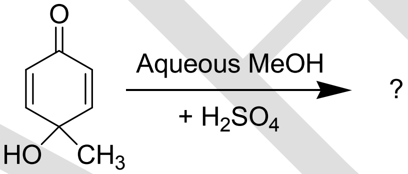


$$PhCOCH_2\overset{\oplus}{N}(CH_3)_2CH_2Ph\overset{\ominus}{Br} \xrightarrow{NaNH_2} ?$$

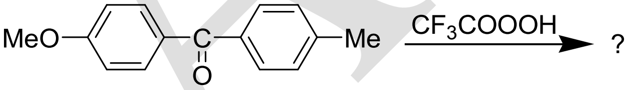
14. Write notes on Baeyer-Villiger rearrangement.

15. Give the products of the following reactions with mechanism.

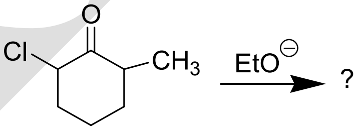
(i)



(ii)



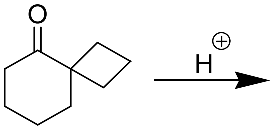
(iii)



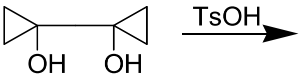
16. Explain the suitable mechanism for Wolff rearrangement with an example.

17. Predict the product and suggest a mechanism for each of the following reactions.

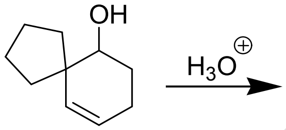
(i)



(ii)



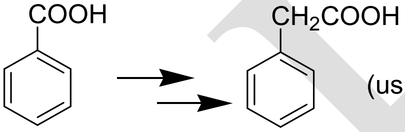
(iii)



PART-D (Each Question Carry Ten Marks)

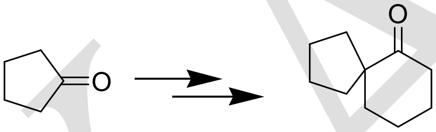
1. How will you bring about the following conversions?

(i)



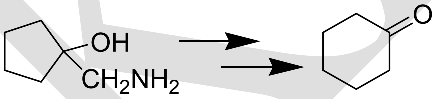
(using Wolff rearrangement)

(ii)



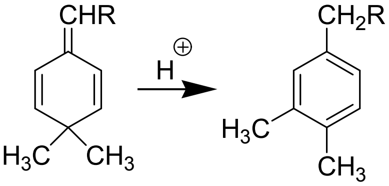
(using Pinacol-Pinacolone rearrangement)

(iii)



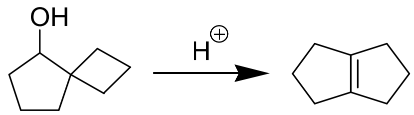
(using Tiffenev-Demyanov rearrangement)

(iv)

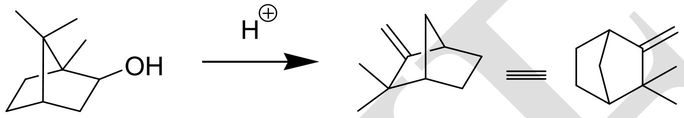


2. Suggest a mechanism for each of the following reactions.

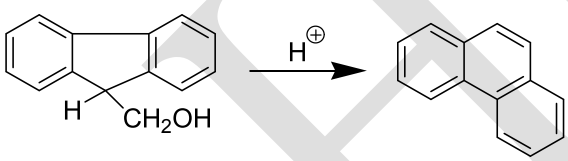
(i)



(ii)



(iii)



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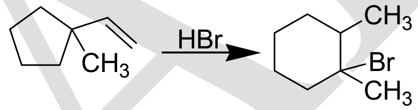


KARPAGAM ACADEMY OF HIGHER EDUCATION
(Deemed to be University)
(Established Under Section 3 of UGC Act, 1956)
Pollachi Main Road, Eachanari Post, Coimbatore–641021.

DEPARTMENT OF CHEMISTRY

UNIT-I

MOLECULAR REARRANGEMENTS

PART-A–Multiple Choice Questions
(Each Question Carry One Mark) (Online Examinations)

1. The conversion of azoxy compounds on acid treatment to *p*-hydroxy azo compounds is called the

a) Wallach rearrangement b) Stevens rearrangement

c) Chapman rearrangement d) Wolff rearrangement

2. The atom from which the group migrates is known as

a) migration terminus **b) migration origin** c) migrating group d) migration end

3. Reactions involving the change in the carbon skeleton through the rearrangement of the carbocation intermediate are collectively known as

a) Pinacol-pinacolone rearrangement **b) Wagner-Meerwein rearrangement**

c) Wollf rearrangement d) Fries rearrangement

4. Which one is a more stable carbocations?

a) methyl cation b) phenyl cation c) benzylic cation **d) dibenzylic cation**

5. In the Wollf rearrangement reactive intermediate is

a) carbene b) nitrene **c) ketene** d) alkene

6. In the Fries rearrangement the ortho isomer and para isomers may be separated by the process of

a) evaporation b) distillation c) recrystallization **d) steam distillation**

7. The conversion of ketoxime tosylates into alpha amino ketones effected by

a) Wallach rearrangement b) Wagner-Meerwein rearrangement

c) Wollf rearrangement **d) Neber rearrangement**

8. The oxidation of aliphatic ketones to esters or their hydrolyzed products with hydrogen peroxide or organic peroxyacids is called the

a) Fries rearrangement b) Wagner-Meerwein rearrangement

c) Baeyer-Villiger oxidation d) Neber rearrangement

9. The reactive intermediate in Favorskii rearrangement is

a) carbene b) nitrene c) ketene **d) cyclopropanone**

10. The thermal or photochemical or catalytic conversion of a diazoketone to a ketene with the liberation of nitrogen is known as the

a) Wolff rearrangement b) Benzidine rearrangement

c) Stevens rearrangement d) Chapman rearrangement

11. When a chemical unit, an atom or a group atoms migrates from one atom to another in the same species or in another species of the same kind and thereby develops a new species, the reaction is called a

a) rearrangement reaction b) pericyclic reaction

c) concerted reaction d) ene reaction

12. The atom to which it migrates is termed as

a) migration origin **b) migration terminus**

c) migration group d) migrating atoms

13. The conversion of G-A-B to A-B-G is an example for

a) pericyclic reaction **b) rearrangement reaction**

c) concerted reaction d) ene reaction

14. The conversion of isoborneol into camphene is effected by

a) Wolff rearrangement b) Benzidine rearrangement

c) Wagner-Meerwein rearrangement d) Wallach rearrangement

15. In the rearrangement reaction the aryl group migrates faster than

a) alkyl group b) cyclic group c) alicyclic group d) acyclic group

16. The pinacols are

a) 1,2-diols **b) ditertiary 1,2-diols** c) 1,3-diols d) ditertiary 1,3-diols

17. Bicyclic alkenes may be prepared by using

a) Wolff rearrangement b) Fries rearrangement

c) Stevens rearrangement **d) Pinacol-Pinacolone rearrangement**

18. The isomerisation of alicyclic rings involved ring expansion and ring contraction of cycloalkylmethyl amines by the action of nitrous acid is known as the

a) Pinacol-Pinacolone rearrangement **b) Demyanove rearrangement**

c) Wolff rearrangement d) Benzidine rearrangement

19. Which one is used as a base in Neber rearrangement?

a) piperidine b) NaOH **c) ethoxide ion** d) KOH

20. The conversion of ortho and para hydroxy benzaldehydes or phenylketones into ortho and para-dihydroxybenzene by the action of alkaline H_2O_2 which is known as

a) Chromic acid oxidation b) Swern oxidation c) Jones oxidation **d) Dakin oxidation**

21. The rearrangement reaction that involves nitrene intermediate is

a) Beckmann rearrangement **b) Wolff rearrangement**

c) Pinacol-Pinacolone rearrangement d) Favorskii rearrangement

22. Nitrene is an intermediate of

a) Beckmann rearrangement **b) Wolff rearrangement**

c) Pinacol-Pinacolone rearrangement d) Favorskii rearrangement

23. The product obtained in Pinacol-Pinacolone rearrangement reaction

a) ketone b) alcohol c) acid d) amide

24. Which one of the following is used as a acid catalyst in Pinacol-Pinacolone rearrangement?

a) dilute H_2SO_4 b) phosphoric acid c) acetic acid d) benzoic acid

25. The treatment of ketones with peracids or hydrogen peroxide gives esters by insertion of oxygen. The reaction is called

a) Wolff rearrangement b) Neber rearrangement

c)Baeyer-villiger oxidation d) Fries rearrangement

26.The reaction of α-haloketones (chloro or bromo) with alkoxide ion to give a rearranged ester is known as

a) Neber rearrangement b) Wolff rearrangement

c) Baeyer-Villiger oxidation **d) Favorskii rearrangement**

27. The Favorskii rearrangement with cyclo- α-haloketone gives an

a) ester b) ether c) ketone d) acid

28. The cyclo- α-haloketone undergoes Favorskii rearrangement to give

a) ring expansion product **b) ring contraction product**

c) acyclic ring product d) alicyclic ring product

29. The Favorskii rearrangement involves the formation of a ring as an intermediate

a) four membered b) five membered **c) three membered** d) six membered

30. The acid catalysed rearrangement in which vicinal 1,2,-diol is converted into ketone or aldehyde with elimination of water is called

a) Pinacol-Pinacolone rearrangement b) Wager- Meerwein rearrangement

c) Benzidine rearrangement d) Neber rearrangement

31. An example for cationotropic rearrangement is

a) Wagner-Meerwein rearrangement b) Neber rearrangement

c) Wolff rearrangement d) Photo-Fries rearrangement

32. The conversion of Pinacol into Pinacolone is an example for

a) free radical rearrangement b) anionotropic rearrangement

c) cationotropic rearrangement d) ion pair rearrangement

33. An example for free radical rearrangement is

a) Photo- Fries rearrangement b) Fries rearrangement

c) Wolff rearrangement d) Favorskii rearrangement

34. Among the following peracids which one is the most reactive?

a) permonosulphuric acid b) m-chloroperbenzoic acid

c) perbenzoic acid **d) peroxytrifluoro acetic acid**

35. The rearrangement in which phenolic esters on heating with aluminium chloride (Lewis acid) give ortho and para acyl phenol is called

a) Claisen rearrangement **b) Fries rearrangement**

c) Benzidine rearrangement d) Stevens rearrangement

36. In Fries rearrangement low temperature favours

a) ortho product b) meta product **c) para product** d) ortho and para product

37. The Pinacol- Pinacolone rearrangement is used in the preparation of

a) bicyclic alkenes b) alkanes c) alcohols d) acids

38. The diazoketones are prepared from

a) acyl halides and methane b) acid chlorides and CH_2Cl_2

c) acyl halides and diazomethane d) aryl halides and methylene dichloride

39. The reaction of acyl halides with diazomethame in the presence of water and silver oxide gives

a) alcohol **b) acid** c) amine d) dicarboxylic acid

40. The reaction of acyl halides with diazomethane in the presence of water and formic acid produces

a) methyl ketones b) alcohols **c) hydroxy methyl ketones** d) aldehydes

41. The addition of water to the ketene lead to the formation of

a) carboxylic acid b) alcohol c) ketone d) amine

42. Benzidine is also known as

a) 2,4' –diamino biphenyl b) 2,2'- diamino biphenyl

c) o-phenyl amino aniline **d) 4,4'- diamino biphenyl**

43. Fries rearrangement is useful for the preparation of

a) acid b) ketone **c) phenolic ketone** d) phenol

44. Wagner- Meerwein rearrangement follows

a) 1,2-shift b) 1,3-shift c) 1,4-shift d) 1,5-shift

45. Favorskii rearrangement can be employed to bring about

a) ring expansion **b) ring contraction**

c) ring expansion followed by ring contraction

d) ring contraction followed by ring expansion

46. An important application of the benzidine rearrangement is

a) synthesis of amines b) synthesis of acids

c) synthesis of amides **d) synthesis of dyes**

47. The catalyst used in Stevens rearrangement is

a) ferric chloride **b) soda amide** c) piperidine d) sodium hydroxide

48. Chapmann rearrangement is useful for the preparation of

a) acids b) amines **c) amides** d) phenols

49. In Chapmann rearrangement the mechanism involves an

a) aliphatic nucleophilic substitution

b) addition- elimination mechanism

c) elimination –addition mechanism

d) aromatic nucleophilic substitution

50. The spiro compounds may be prepared by using

a) Pinacol-Pinacolone rearrangement b) Benzidine rearrangement

c) Wallach rearrangement d) Chapmann rearrangement

51. In the Favorskii rearrangement the cyclopropanone intermediate has been trapped as an adduct with

a) thiophene b) pyrrole **c) furan** d) pyridine

52. When α,α- dihaloketones with an α-H is subjected to the Favorskii reaction produces

a) α,β – unsaturated acids **b) α,β- unsaturated esters**

c) β,γ – unsaturated esters d) β,γ – unsaturated acids

53. The byproduct formed in Benzidine rearrangement is

a) biphenyl b) 4-amino biphenyl c) 2-amino biphenyl **d) o-benzidine**

54. The Congo Red may be prepared from

a) Benzidine rearrangement b) Stevens rearrangement

c) Wallach rearrangement d) Fries rearrangement

55. In the presence of acidic medium the major product formed in Wallach rearrangement is

a) o-isomer b) m-isomer **c) p-isomer** d) o- and p-isomer

56. Phenyl ester reacts in the presence of anhydrous $AlCl_3$ to give

a) o- and p-hydroxy ketone b) o- p-dihydroxy ketone

c) m-hydroxy ketone d) p-hydroxy ketone

57. Cyclohexanone can be converted to cycloheptanone in good yield may effected from

a) Stevens rearrangement b) Wallach rearrangement

c) Pinacol-Pinacolone rearrangement d) Chapmann rearrangement

58. Which one is used as a solvent in Chapmann rearrangement?

a) methanol b) ethanol c) hexane **d) tetra-glyme**

59. Wallach rearrangement is

a) intermolecular b) intramolecular c) monomolecular d) bimolecular

60. Pinacol- Pinacolone rearrangement is useful for the preparation of

a) alkenes b) acids c) amines d) phenols

UNIT-II

SYLLABUS

Conformational analysis and stereochemistry: Stereochemistry of sulphur and nitrogen compounds, stereoselective and stereospecific reactions - R/S-notation of optically active carbon compounds. Optical isomerism of biphenyls, allenes and spiranes. Planar chirality - cyclophanes and ansa compounds - geometrical isomerism - E/Z notation-configuration in aldoximes and ketoximes. Conformation in cyclic system–decalins, perhydrophenanthrene and perhydroanthracene. Conformation and reactivity of cyclohexanes.

Stereochemistry of sulphur compounds

Repulsive gauche effect (hockey sticks effect)

In 1,4-dioxane (**1**), the conformer with axial X (**Figure 1**) is favoured although to a lesser extent than in related tetrahydropyran. This is due to the anomeric effect (X is an electronegative substituent). But in the corresponding 1,4-oxathiane (**2**), the equatorial conformer (**2a)** is very much favoured over the axial one (**2b**). This phenomenon previously known as the **hockey sticks effect** is now called the **repulsive gauche effect**. Both groups of workers in this field (Zefirov, Eliel) agree that the repulsive effect arises out of non-bonded repulsive between the p orbitals of the large substituents X and Y in the unit X-C-C-Y which is absent when they are antiperiplaner (as in **2a**), maximal when they are synperiplaner (as in **2b**) and medium when they are gauche. The effect is much higher in the case of S than O because of the larger size of the outer atomic orbital of the former leading to more electronic overlap.

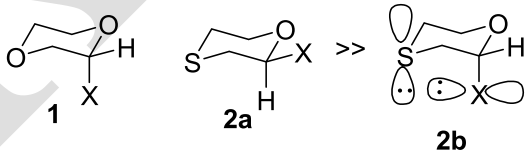


Figure 1. Hockey sticks effect.

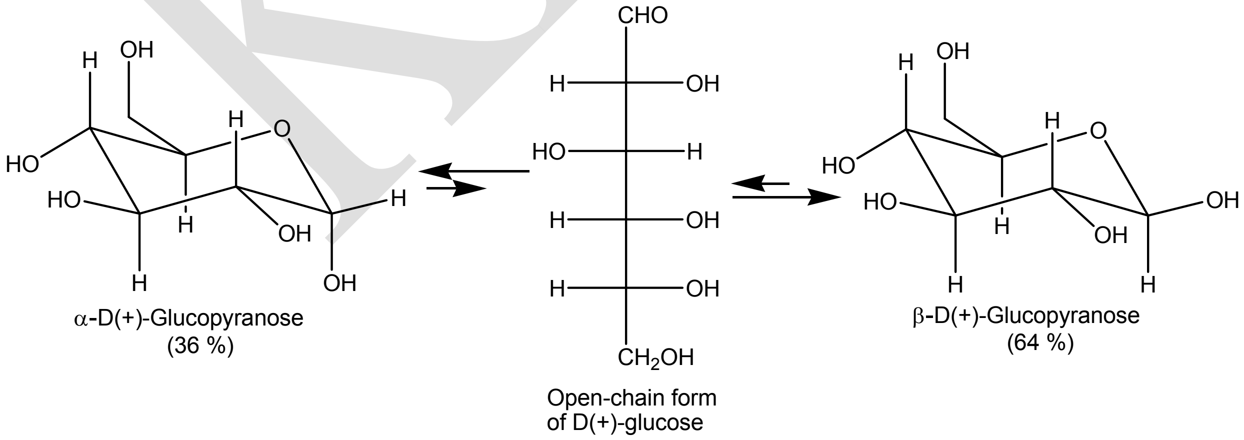
Anomeric effect

One has seen that when either pure anomer of D-glucose is dissolved in water it gives an equilibrium mixture of anomers where β-anomer (equatorial OH at C-1) predominates (**Scheme 1**). Similarly behavior is again displayed by D-mannose (*via* the corresponding open chain form) in which now, however, the α-isomer with axial hydroxyl at C-1 predominates (I, **Scheme 2**) over the β-anomer (II). This unusual favoring of the α (or the axial) orientation first observed in the case of sugars is called anomeric effect. In fact generally it is observed that during reactions which introduce oxygen or halogen atoms (e.g., OH, OCH_3, $OCOCH_3$ and Cl) at the anomeric carbon atom of a pyranose ring, the major stereoisomer is the one in which the new group occupies the axial position. The following points may be noted:

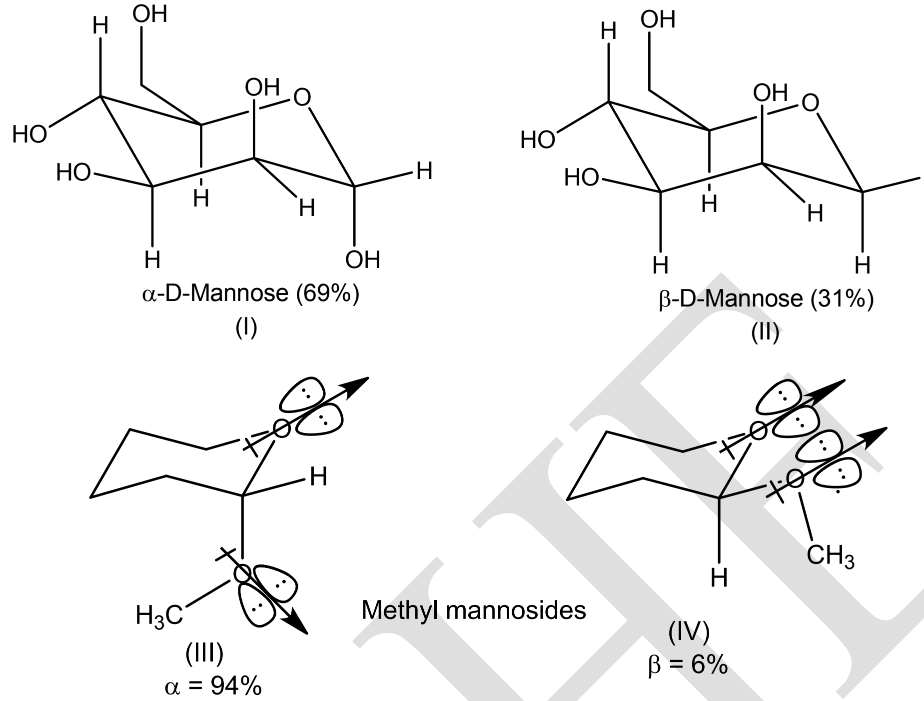
1. The preference for electronegative substituents for the axial positions at the anomeric carbon atom is called the anomeric effect.

2. This substituent (X) seems to exert two opposing effects. A steric effect which directs the substituent to the equatorial position and secondly an electronegative effect which favors the axial position. In the case of D-glucose (**Scheme 1**) the anomeric effect seems to play a secondary role to the steric difference of having the anomeric OH equatorial versus axial.

3. The methyl mannosides (III and IV, **Scheme 2**) in 1% methanolic HCl undergo equilibration to a ratio of α:β = 94:6 (**Scheme 2**). This is an operation of anomeric effect. In α-D-Mannose (or its mannosides, partial structures III and IV, **Scheme 2**) the non-bonding electrons on the oxygen of the ring and the nonbonding electrons of the substituent repel other when it is in the equatorial position (IV, **Scheme 2**). These are farther apart when the substituent is in the axial position.



Scheme 1



α-D-Mannose (69%)
(I)

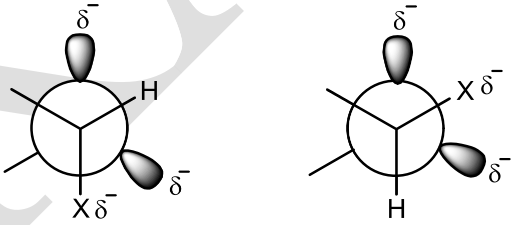
β-D-Mannose (31%)
(II)

(III)
α = 94%

(IV)
β = 6%

Scheme 2

In D-Mannose at equilibrium in water more of α-axial anomer is present than β (**Scheme 3**). This discrimination is further enhanced in methyl mannosides. In the Newman projections when the electronegative substituents (X = OH, OCH_3, Cl etc.) is axial it is *gauche* to one but *anti* to the other lobe with non-bonding electrons. When the substituent X is equatorial it is *gauche* to both lobes.



Scheme 3

Stereochemistry of nitrogen compounds

Rabbit-ear effect

In 1,3-diheterocycles such as tetrahydro-1,3-oxazine (**3**) (**Figure 2**), the conformation in which the two lone pairs are syn-1,3-diaxial (**3a**) is destabilized with respect to the other conformer (**3b**). This was known as the **"rabbit-ear-effect"** for obvious reason. This effect, however, may be regarded as nothing but an endo-anomeric effect, explained by stabilizing overlap between the p orbital of N and the antibonding orbital of the endo C-O bond which are antiperiplaner (shown in thick line) in the conformation (**3b**). This effect is lacking in the other conformer (**3a**).

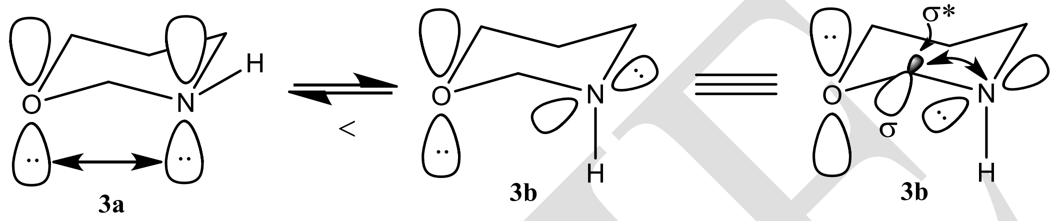


Figure 2. Rabbit-ear effect.

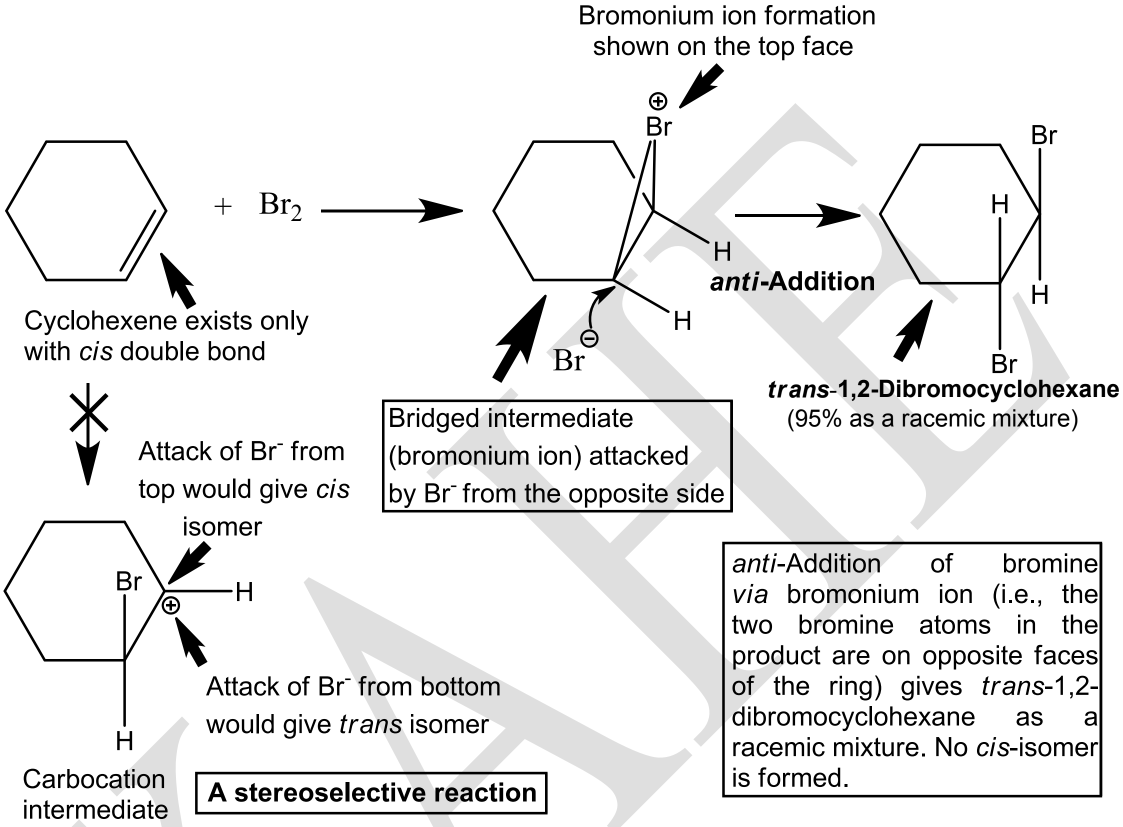
Stereoselective reaction

A stereoselective reaction is one in which the reactant is not necessarily chiral but in which the reaction produces predominantly or exclusively one stereoisomeric form of the product (or a certain subset of stereoisomers e.g., (±)-form among all those that are possible). The difference between stereoselective and stereospecific reactions may be necessary.

A stereospecific reaction is one that produces predominantly or exclusively one stereo isomers of the product when a specific stereoisomeric form of the reactant is used. Thus all stereospecific reactions are also stereoselective. All stereoselective reactions are however, not necessarily stereospecific, since there are stereoselective reactions in which the reactant cannot exist as stereoisomers e.g., in cyclohexene the double bond is only *cis*, the *trans* isomer does not exist (**Scheme 4**). Thus a stereoselective reaction is one in which stereoisomeric products are formed in unequal amounts from a single starting material.

(i) **Bromination of cyclohexene**

When cyclohexene is brominated, the product is one stereoisomeric product *trans*-1,2-dibromocyclohexane (**Scheme 4**). One may compare this stereoselective bromination of cyclohexene (cyclohexene can exist only with *cis* geometry of double bond) with stereospecific bromination of 2-butene stereoisomers. Moreover, the bromination proceeds through the cyclic bromonium ion, if the intermediate were a simple carbocation both *cis* as well as *trans*-1,2-dibromo cyclohexane would have formed.



Scheme 4

Anti-addition of bromine via bromonium ion (i.e., the two bromine atoms in the product are on opposite faces of the ring) gives *trans*-1,2-dibromocyclohexane as a recemic mixture. No *cis* isomer is formed.

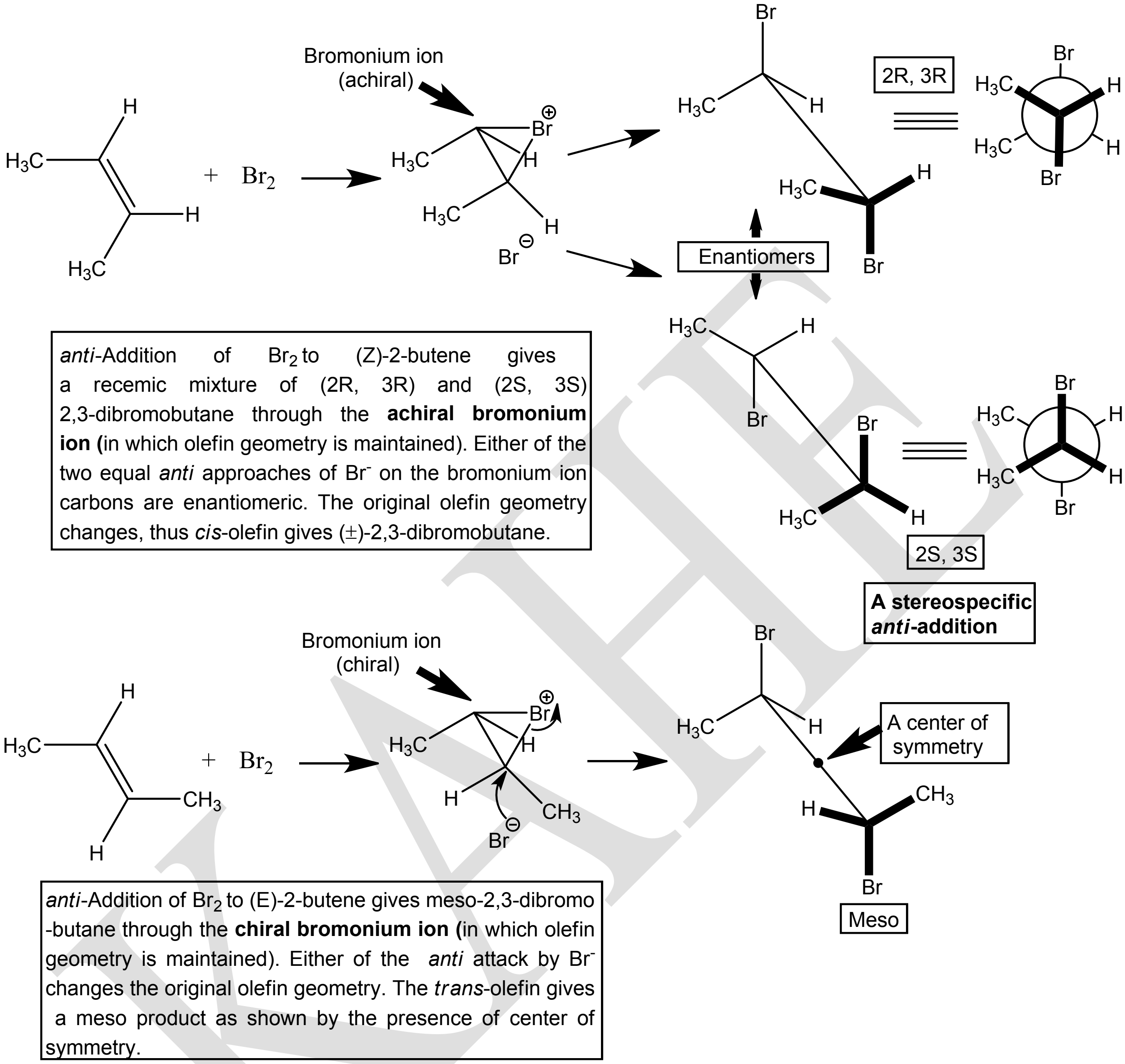
Stereospecific reaction

A reaction is stereospecific provided the reactant can exist as stereoisomers and each stereoisomeric reactant gives a different stereo isomeric product which may be (±) pair.

(i) **Bromination of (*E* and *Z*-2-Butene)**

Starting compounds differing only in their stereoisomerism must be converted into stereo chemically different products. Accordingly one says that bromine addition to (*Z*) or (*E*)-2-butene is stereospecifically *trans*. Addition to (*Z*)-2-butene gives a recemic mixture of 2,3-dibromo-butane while addition to (*E*)-2-butene gives a meso stereoisomer. Cis-2-butene (*Z*-2-butene) adds bromine e.g., from the top face (**Scheme 5**) to give the intermediate bromonium ion which is achiral i.e., it has a plane of symmetry along with bromide ion [reaction at the other face of the alkene bottom face not shown, however, would give the same bromonium ion, the two faces of (*Z*)-2-butene are overall homotopic]. The bromide ion then attacks the bromonium ion at either carbon from bottom (S_N2) types of displacement at equal rates to yield the two enantiomers in equal amounts i.e., as the racemic form.

trans-2-Butene reacts with bromine e.g., from the top face to give a chiral bromonium ion and bromide ion [reaction at the other face (bottom) would yield the enantiomer of the bromonium ion, this attack has not been shown however, the two faces of trans-2-butene are overall enantiotopic.] When the bromonium ion is opened by S_N2 type displacement at either carbon, the same achiral, meso compound is formed.



anti-Addition of Br_2 to (Z)-2-butene gives a recemic mixture of (2R, 3R) and (2S, 3S) 2,3-dibromobutane through the **achiral bromonium ion (**in which olefin geometry is maintained). Either of the two equal *anti* approaches of Br^- on the bromonium ion carbons are enantiomeric. The original olefin geometry changes, thus *cis*-olefin gives (±)-2,3-dibromobutane.

anti-Addition of Br_2 to (E)-2-butene gives meso-2,3-dibromo-butane through the **chiral bromonium ion (**in which olefin geometry is maintained). Either of the *anti* attack by Br^- changes the original olefin geometry. The *trans*-olefin gives a meso product as shown by the presence of center of symmetry.

Scheme 5

Chan, Ingold and Prelog system of nomenclature (or) R and S nomenclature

In order to circumvent of inherent disadvantages of D and L system of nomenclature, Chan, Ingold and Prelog (1955, 1966) proposed a system of nomenclature to specify the configurations of chiral molecules. According to this system, the configuration of a molecule is specified uniquely either as R (Latin: Rectus for R means right) or as S (Latin: Sinister for S meaning left) based on a set of rules: the sequence rule, ligand complementation rule and chirality rule. Like D and L, R and S are used as prefixes and have nothing to do with sign of rotation.

(i) Sequence rule

Ligands (atoms and groups) attached to the chiral elements are marked or labeled in decreasing order of priority sequence (as 1→2→3→4) based on a set of rules and sub-rules. If two or more ligands are attached to the chiral element through the same atom, then the nature of the second atom determines the order of sequence. The important set of rules and sub-rules of the sequence rule are:

(a) Higher atomic number precedes the lower.

(b) Higher mass number precedes the lower.

(c) Sequence **cis** precedes the sequence **trans**.

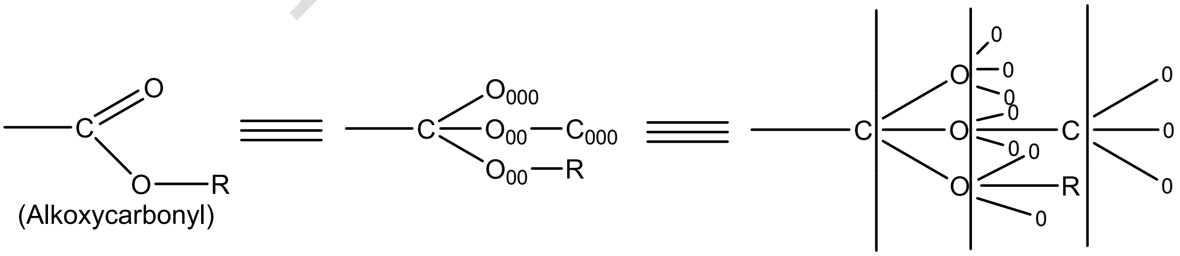
(d) Near end of the chiral axis precedes the far end.

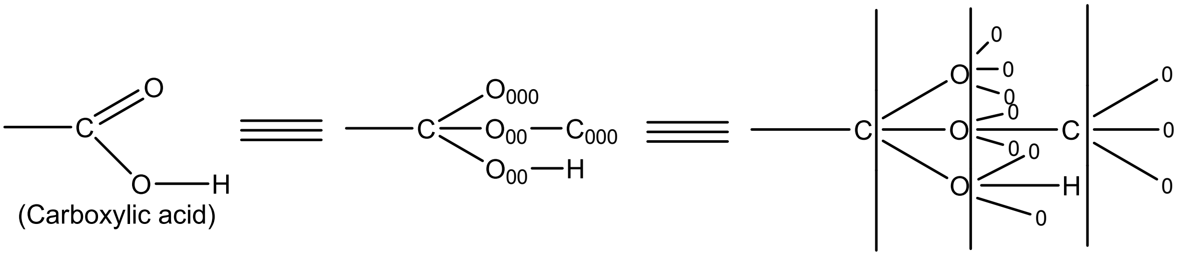
(e) R precedes S and M precedes P.

(ii) Ligand complementation rule

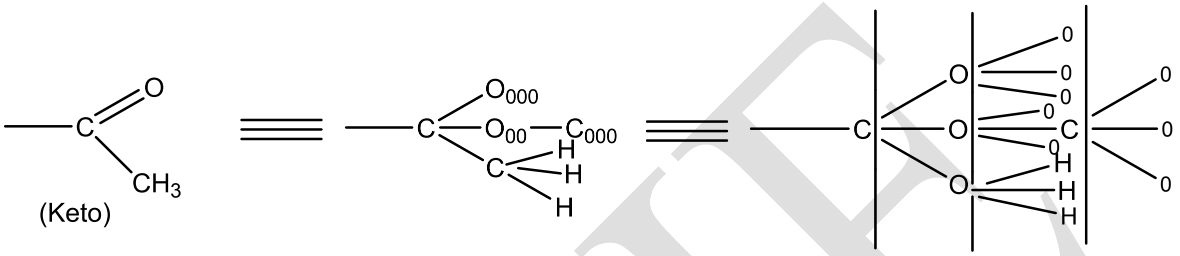
All atoms other than hydrogen are assigned a formal valence of four. When the actual valence is less than four, phantom atoms (o) are used to rise the valence to four. A phantom atom is given a formal valence of zero and necessarily ranks lowest. Triple and double bonds are counted as if they are made up of three and two single bonds.

Illustration of Ligand complementation rule (in decreasing order)

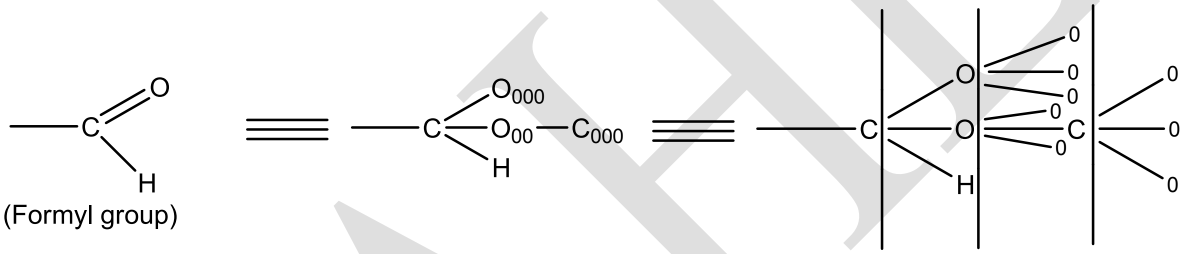




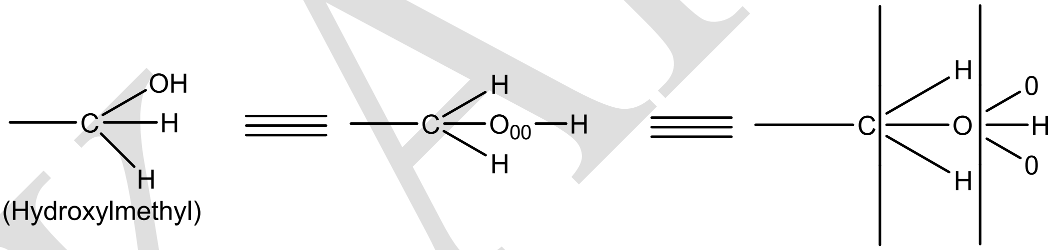
(Carboxylic acid)



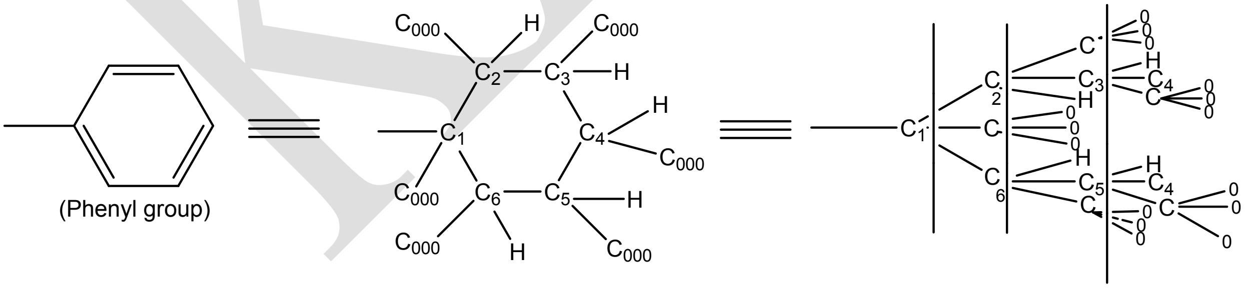
(Keto)



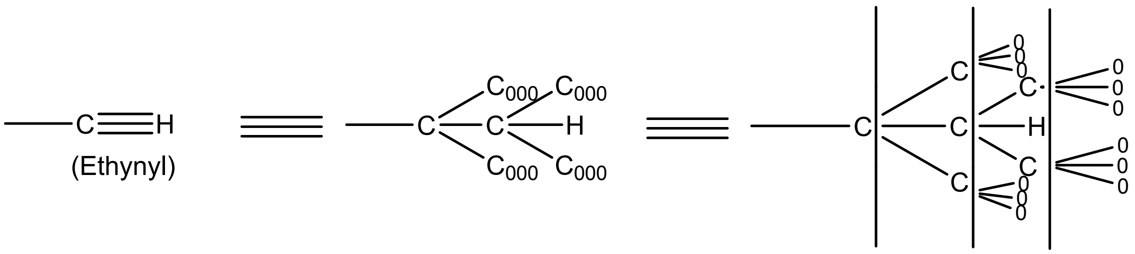
(Formyl group)

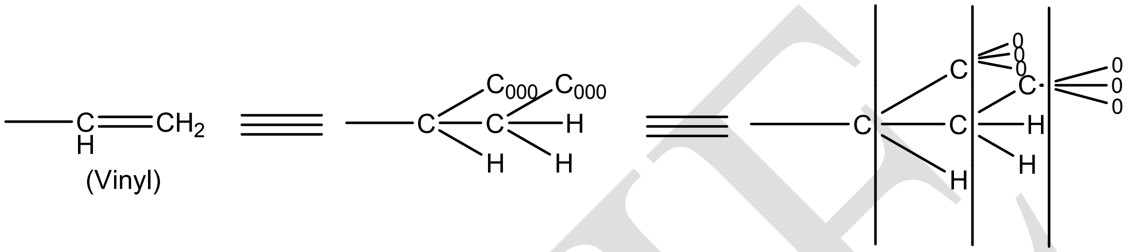


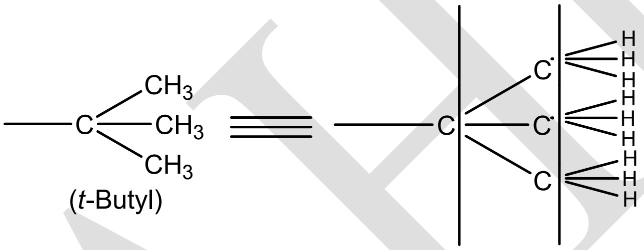
(Hydroxylmethyl)

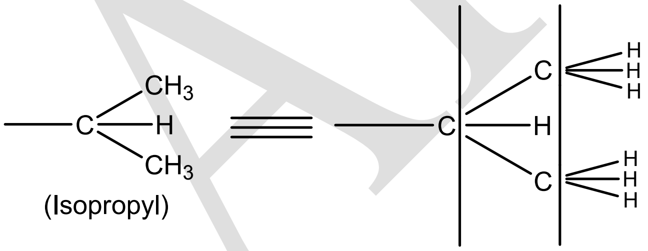


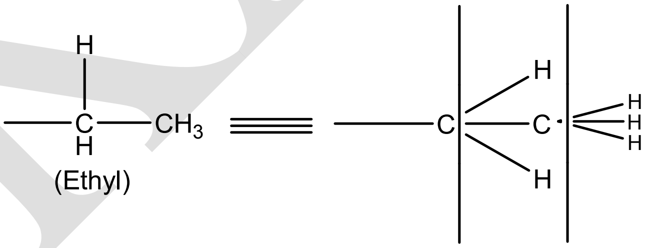
(Phenyl group)

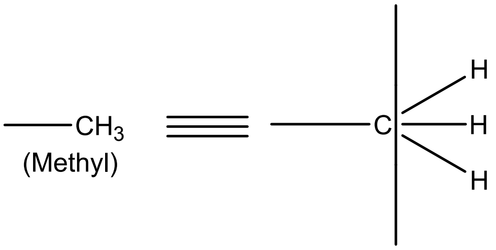

(Ethynyl)


(Vinyl)


(*t*-Butyl)

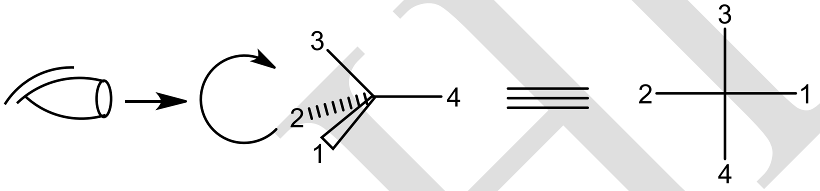

(Isopropyl)


(Ethyl)

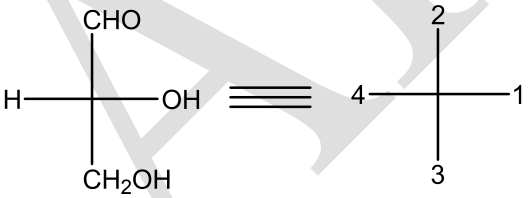

(Methyl)

(iii) Chirality rule

Once the ligands (attached to the chiral element) are ordered in decreasing order of priority by the use of sequence rule, then the molecule is viewed from a preferred side, that is from the side opposite to the least preferred group. If the remaining ligands in the decreasing order of sequence (as 1→2→3) trace a clockwise sequence, then the chiral element is given the chiral prefix R. On the other hand, if the remaining ligands in the decreasing order of priority (1→2→3) trace an anticlockwise direction, then the chiral element is designated as S. If the molecule is represented in Fischer projection, then it is so constructed that the least preferred group is at the bottom.

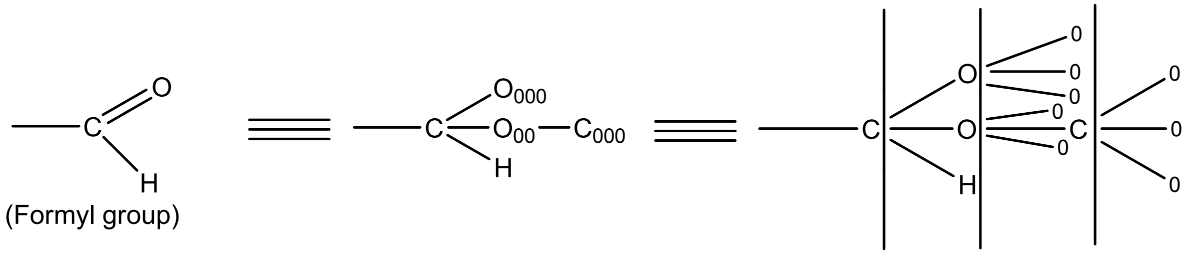


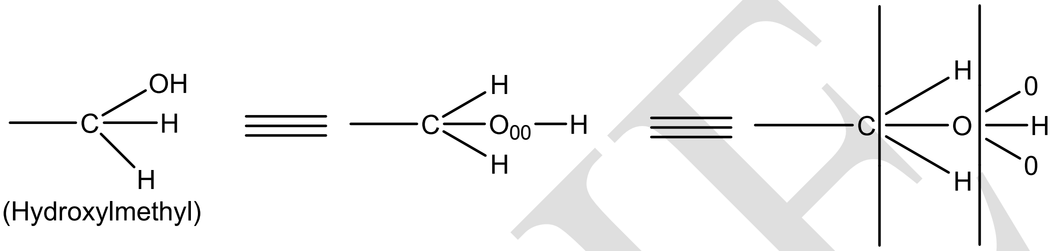
The C.I.P. notation can be illustrated with a specific example, (+)-glyceraldehyde in Fischer projection.



Step 1 (Sequence rule)

Mark the groups attached to the chiral centre in decreasing order of priority using the sequence rule. The hydroxyl group is the most prepared as it is bonded to the chiral centre through oxygen which has higher atomic number. Both formyl and hydroxymethyl groups are attached to the chiral centre through the carbon atoms. So one must move along the chain to determine the order of priority as shown.

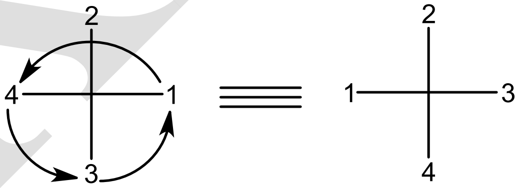

(Formyl group)


(Hydroxylmethyl)

Between formyl group and hydroxymethyl group, formyl group is preferred as the carbon atom of the formyl group is in turn attached to two oxygen atoms and one hydrogen, but in the case of hydroxymethyl, the carbon atom of hydroxymethyl is in turn attached to only one oxygen and two hydrogens. The hydrogen atom is the least preferred as it is the atom of lowest atomic number.

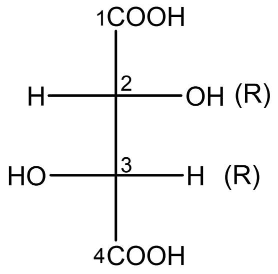
Step 2 (Chirality rule)

Since the molecule is given by Fischer projection, it must be so transformed that the lowest preferred group is at the bottom of the Fischer projection. This is done by rotating a group of three substituents, while keeping the fourth stationary as shown below.

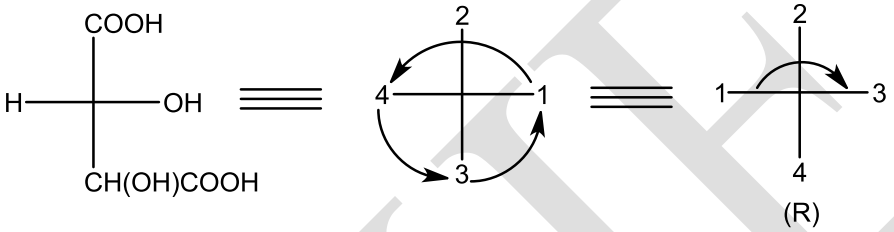


Since the remaining three substituents trace a clockwise direction, (+)-glyceraldehyde has (R)-configuration.

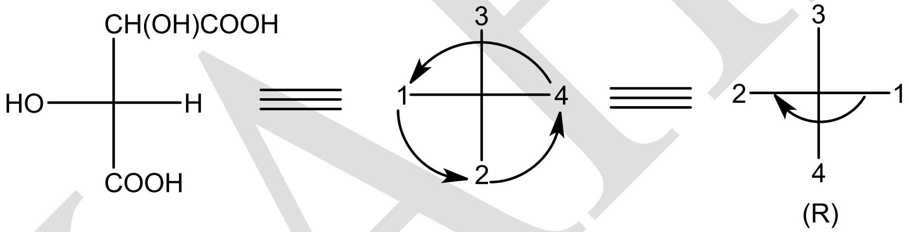
When a molecule contains two or more chiral centers, each chiral centre must be designated as R or S, illustrated with (+)-tartaric acid.



Treat the upper chiral centre (C-2) as

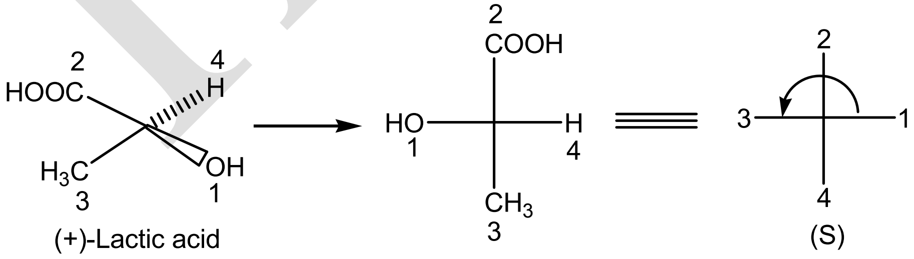


Likewise treat the lower chiral centre (C-3) as

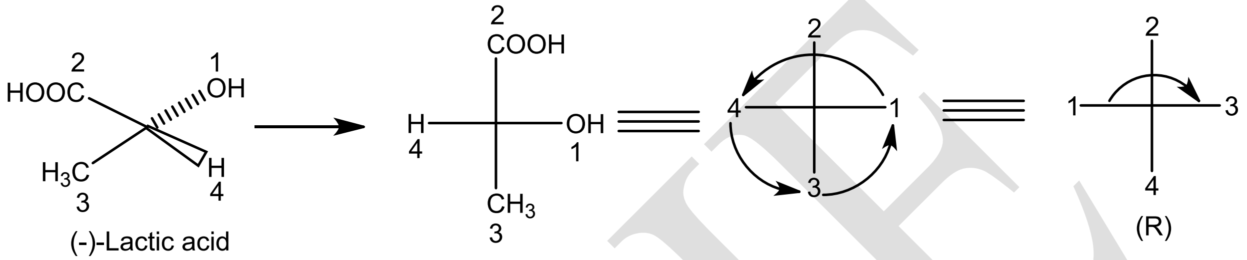


Therefore, (+)-tartaric acid is 2(R):3(R)-dihydroxysuccinic acid.

In order to designate the configuration of a chiral center of a molecule represented in wedge projection, it is first translated into Fischer projection and then modified if necessary such that the least preferred group is at the bottom of the Fischer projection.

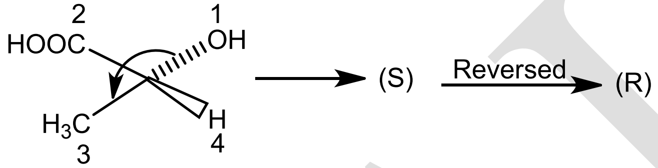


Alternatively, the wedge projection itself can be used to trace the sequence (1→2→3), if the least preferred group (4) is either above or below the plane of the molecule (or the paper). If the least preferred group (4) is below the plane of the molecule (or the paper) the sequence 1→2→3 gives correct chiral descriptor, since the least preferred group (4) is away from the observer. On the other hand, if the least preferred group (4) is above the plane of the paper, then the sequence 1→2→3 gives wrong descriptor, so the above assigned descriptor must be reversed, as illustrated below.



(-)-Lactic acid

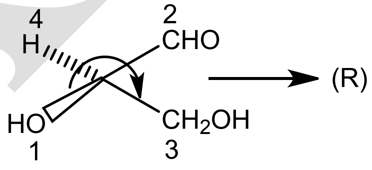
(Or)



(-)-Lactic acid

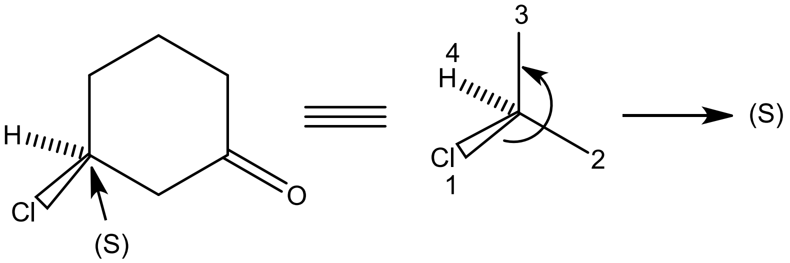
In the above example, since the least preferred group (4) namely hydrogen is above the plane of the molecule (or the paper), the assigned descriptor (S), must be reversed to R. So (-)-lactic acid has R configuration.

In the following example, since the least preferred group (hydrogen) is below the plane of the paper, the sequence 1 →2→ 3 gives correct descriptor namely R.

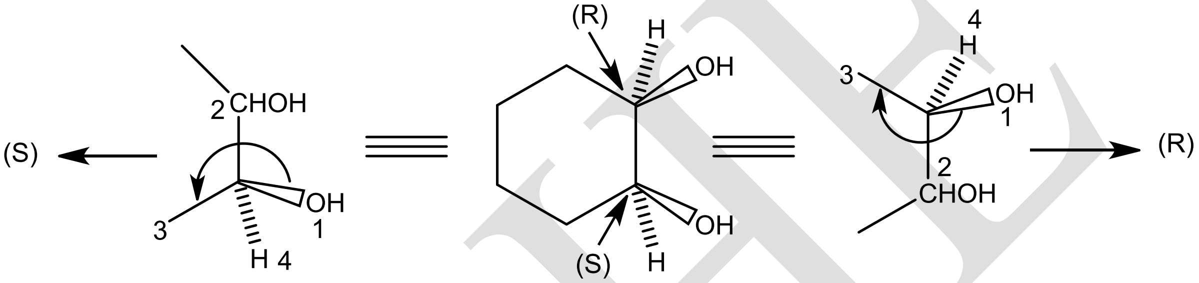


(+)-Glyceraldehyde

In order to designate the configuration of chiral centres incorporated in a planar ring system, translate the chiral unit with its four bonds into a wedge projection and treat it as described above. The following examples illustrate this procedure.



In the example given below translate the upper chiral centre into a wedge projection and treat it as described above.



Likewise, translate the lower chiral centre into a wedge projection and proceed as before. The above molecule is 1(R), 2(S) –cyclohexane-1,2-diol.

Designation of configurations of tertiary chiral centres present in steroids and terpenoids

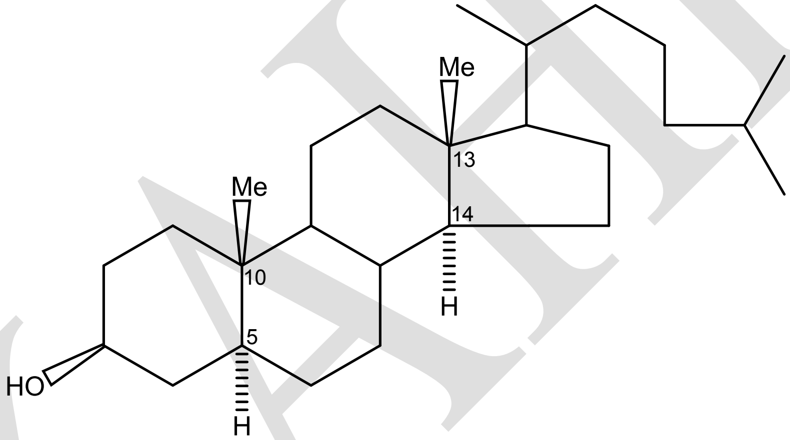
Polycyclic molecules such as steroids and terpenoids are conventionally projected on the plane of the paper such that three bonds of the tertiary asymmetric carbons lie in the plane of the paper with the fourth substituent (usually hydrogen or methyl) projecting either above or below the plane of the paper. In order to designate the absolute configuration of such tertiary asymmetric carbon atoms by C.I.P system of nomenclature, Eliel (1985) has suggested a convenient method called ligand permutation scheme. According to this method, the ligand lying out of plane (either above or below) of the molecule (or the paper) is selected as a reference ligand (fiducial). If this reference ligand is **least preferred** (4) and **is below the plane of the paper (back)**, the sequence of remaining three ligands (1 →2→ 3) gives correct descriptor (4/B+) (B refers to back and + refers to correct). On the other hand, if the least preferred ligand (4) lies above the plane of the molecule (front), the sequence of remaining ligands (1 →2→ 3) gives wrong descriptor (4/F–) and so it must be reversed (F refers to front and – sign indicates wrong). For reference ligands of other priority, the ligand permutation scheme suggested by Eliel permits easy and unambiguous assignment of R and S notation.

Ligand permutation scheme

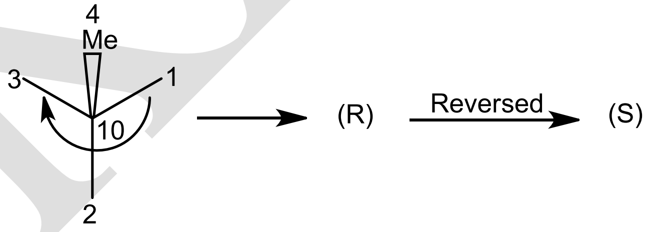
Ligands in front (above the plane)	(+)	(-)	(+)	(-)
Priority of the ligands	1	2	3	4
Ligands in the back (below the plane)	(-)	(+)	(-)	(+)

(Plus sign indicates correct assignment and
Minus sign indicates wrong assignment)

The above procedure can be illustrated with cholestanol as an example.

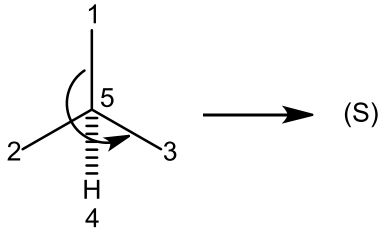


Configuration at C-10 of cholestanol



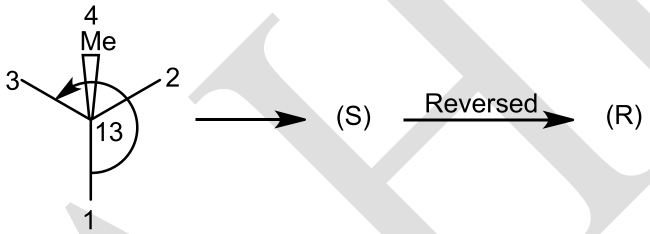
Since the least preferred group (4) namely angular methyl is above the plane of the molecule (4/F) the clockwise sequence (1 →2→ 3) leading to R descriptor must be reversed. So the configuration of C-10 is S.

Configuration at C-5

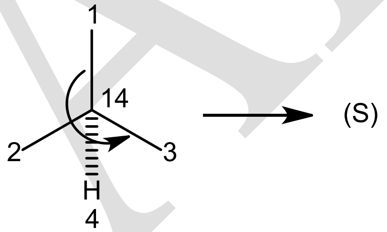


Since the least preferred group (4) namely hydrogen is below the plane of the paper (4/B) the anti-clockwise sequence (1 →2→ 3) give correct descriptor namely S. so the configuration of C-5 is S.

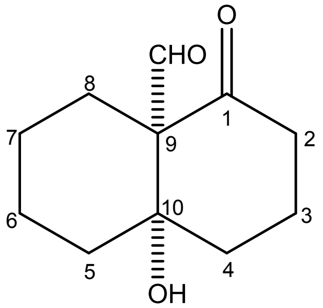
Configuration at C-13



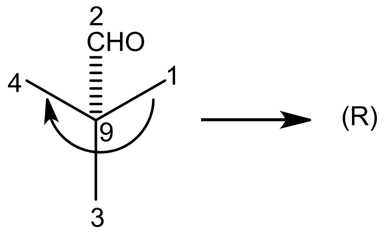
Configuration at C-14



The decalone derivative shown below illustrates an example where the reference ligands (fiducial) are of higher priority.

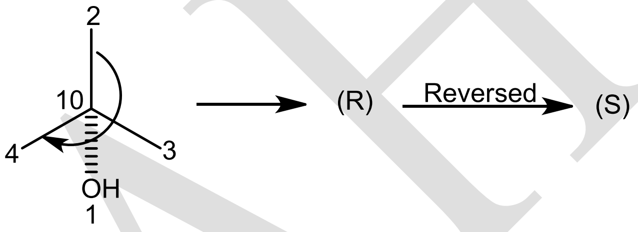


Configuration at C-9



The clockwise sequence 1→3→4 leads to R descriptor. Now the reference ligand (CHO) corresponds to second priority and is below the plane of the molecule (back) (2/B). From the ligand permutation scheme, we find that the above sequence leads to correct assignment of descriptor (positive sign) namely R.

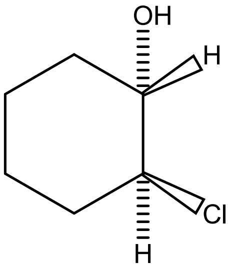
Configuration at C-10



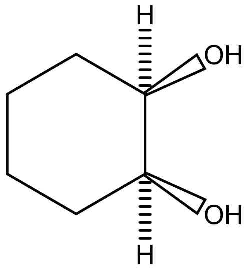
The sequence 2→3→4 (clockwise) leads to R descriptor. At C-10, the most preferred group (OH) corresponds to the reference ligand and is at the back (1/B). From the ligand permutation scheme, we find that the above sequence does not lead to correct assignment of descriptor (negative sign); hence the assignment must be reversed. So the configuration of C-10 is S. The above decalin is 9(R), 10(S)-9-formyl-1-decalone.

Problem 1. Designate the configurations of the following molecules by Cahn, Ingold and Prelog system of notation.

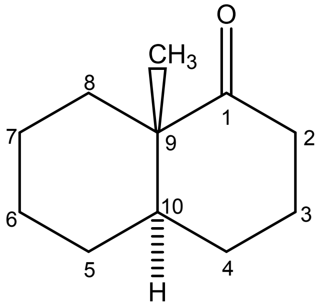
(a)



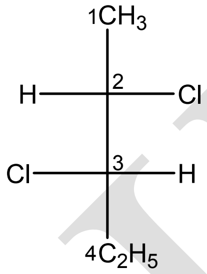
(b)


H
OH
OH
H

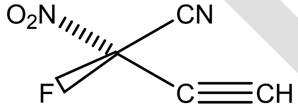
(c)


O
CH$_3$
8
1
7
9
2
10
6
3
5
4
H

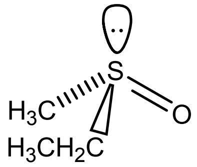
(d)


1CH$_3$
H
2
Cl
Cl
3
H
4C$_2$H$_5$

(e)

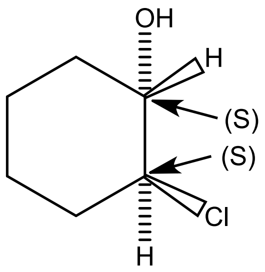

O$_2$N
CN
F
C
CH

(f)

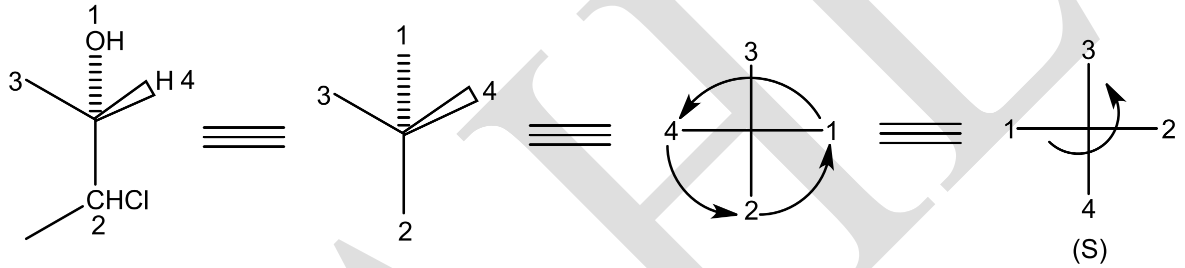

S
H$_3$C
O
H$_3$CH$_2$C

Solution:

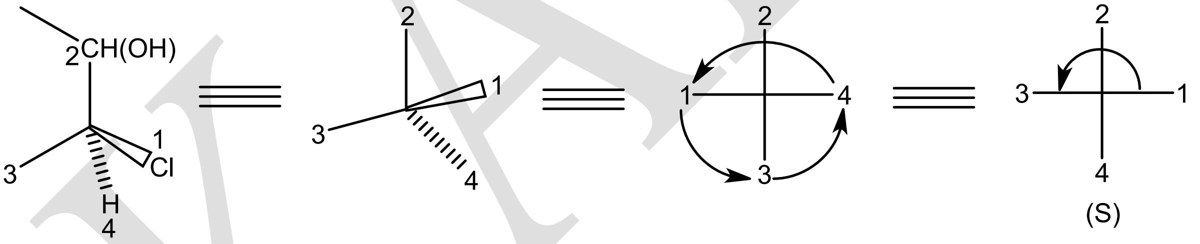
(a)



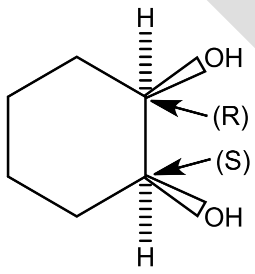
Translate the upper asymmetric carbon into a wedge projection and treat it as shown.

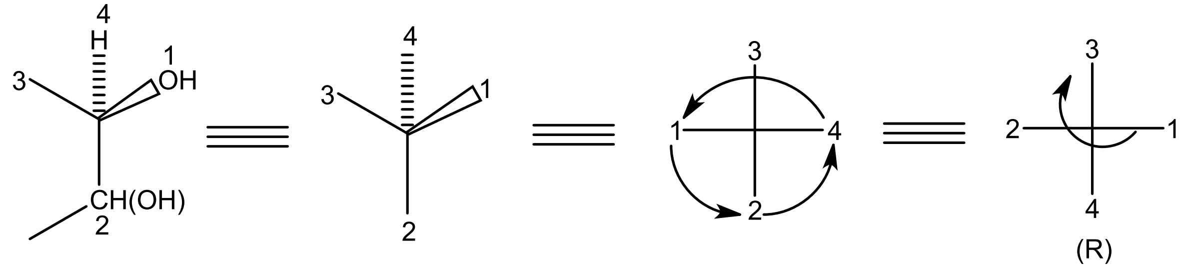


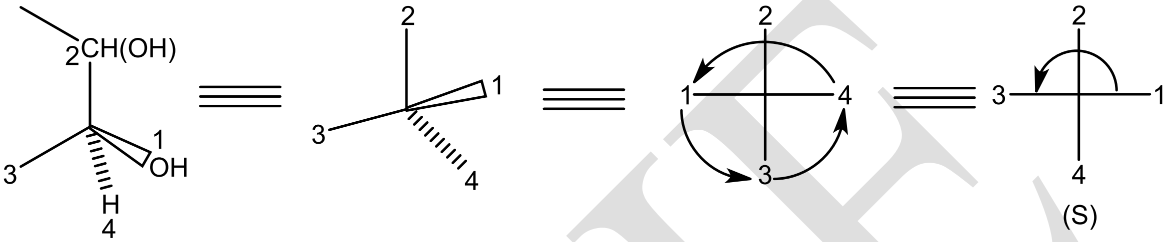
Likewise, translate the lower carbon atom into a wedge projection and treat it as shown.



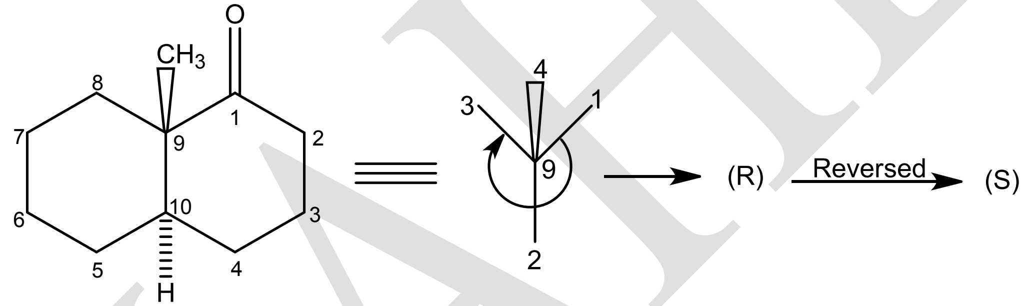
(b)



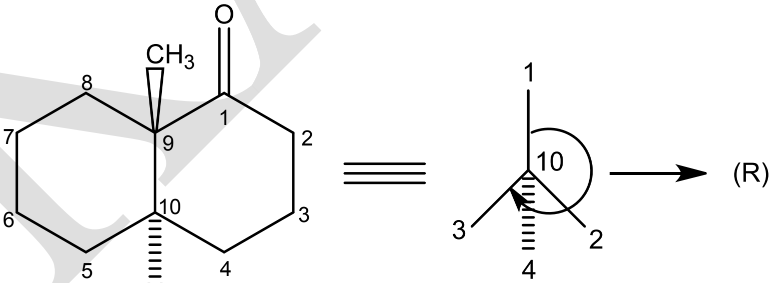




(c)

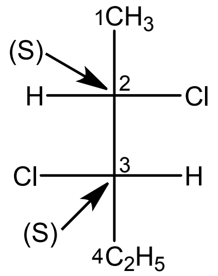


Since the least preferred group (Me) at C-9 is above the plane of the molecule, reverse the descriptor (namely R) into S [according to 4/B(+) mnemonic] (see page 15).

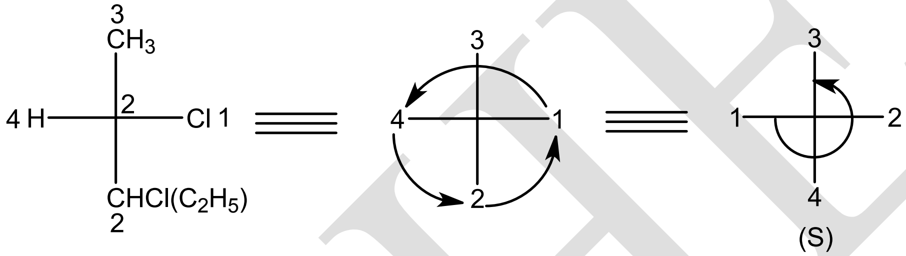


Since the least preferred group (H) at C-10 is below the plane of the ring system, molecule, according to 4/B(+) mnemonic, the sequence gives correct descriptor, namely R. Therefore, the configuration of the above compound is 9(S):10(R).

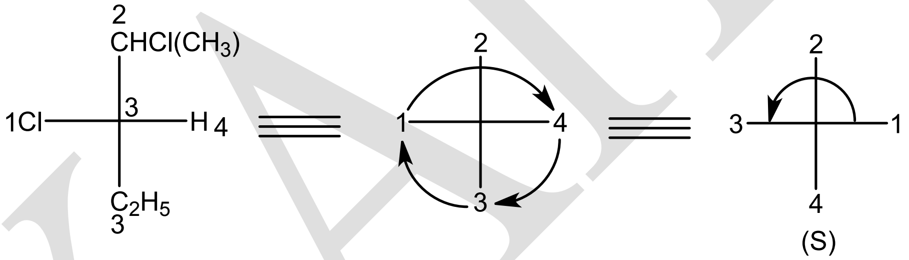
(d)



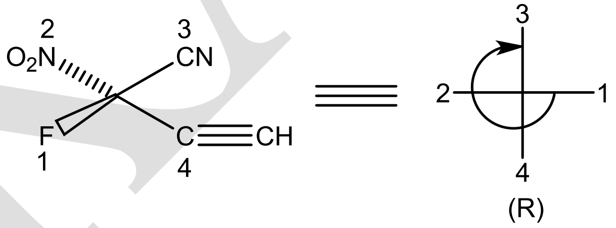
Treat the upper chiral centre (C-2) as



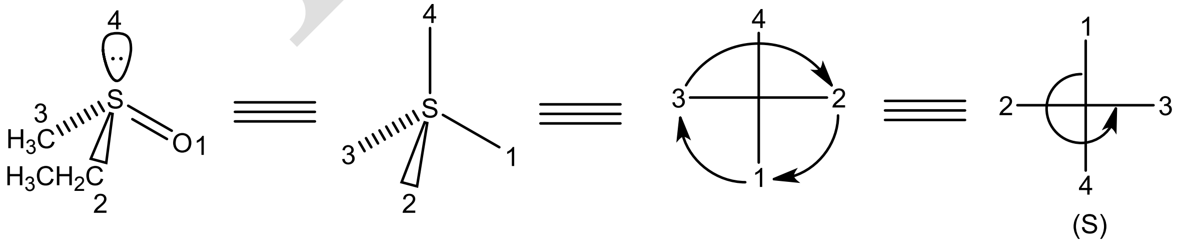
Likewise treat the upper chiral centre (C-3) as



(e)



(f)



Optical Isomerism of Biphenyls (Atropisomerism)

The term atropisomerism (meaning no rotation) covers all cases of spatial isomerism due to restricted rotation about single bonds. Optical isomerism of this kind was first detected in compounds of biphenyl series. Isolable stereoisomers resulting from restricted rotation about single bonds are called atropisomers, while rotomers are stereoisomers obtained by rotation about single bonds which cannot be isolated under ordinary conditions.

Biphenyl is represented by the structure in which two phenyl rings are joined by a single bond in their para positions (sp^2-sp^2) called pivotal bond. The distance between the **ortho**–hydrogens in adjacent rings (2, 2' and 6, 6') in the planar conformation is appreciably greater than twice the van der Walls radius of hydrogen (2 x 0.12 nm), so that the free rotation, around the pivotal bond is not impeded by steric reasons. In the crystalline state, both benzene rings of biphenyl lie in one plane. However, in solution and vapour phase, the two rings are twisted with respected to each other by an angle of 45º due to steric interaction between the 2, 2' and 6, 6' pairs of hydrogens. This interaction is further enhanced by **ortho**-substituents bulkier than hydrogen so that rotation about the pivotal bond does not occur due to steric hindrance between bulky **ortho** substituents and the two benzene rings lie perpendicular to each other and the molecule cannot adopt a planar conformation.

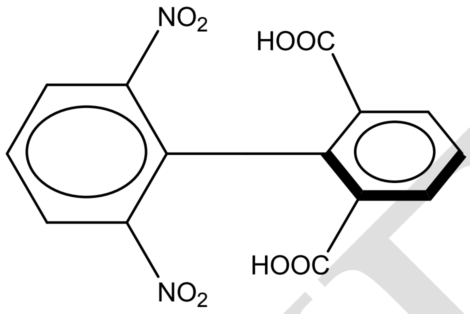
Properly substituted biphenyls are optically active (eg: 2, 2'-dinitrodiphenic acid). **Biphenyls can be chiral only when the following two conditions can be satisfied.**

(i) The **ortho** substituents must be large enough to prevent the two rings from becoming coplanar. (In such cases the plane of the molecule itself becomes the plane of symmetry of the molecule).

(ii) Neither ring can have a plane of symmetry ($\sigma \equiv S_1$) and the substituents in the **para** position cannot cause lack of symmetry. We can distinguish three different cases: both rings are symmetrical (Type i: AA……BB), one of the rings is symmetrical (Type ii: AB……BB) and neither ring is symmetrical (Type iii: AB…..AB or AB…CD).

Type i:

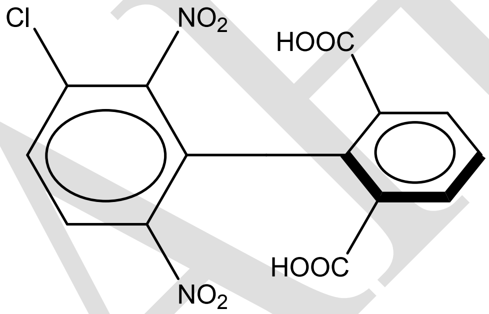
(AA…BB, both rings are symmetrical)



Achiral and optically inactive

Type ii:

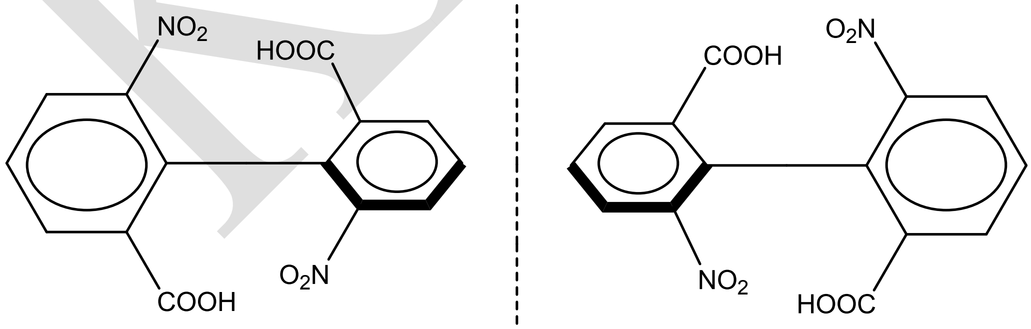
(AB…BB, one of the rings is symmetrical)



Achiral and optically inactive

Type iii:

(AB…AB or AB….CD, neither ring is symmetrical).



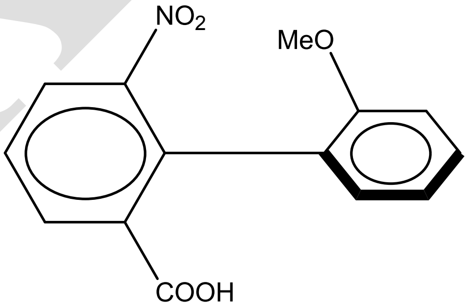
Chiral and optically active

In the first case, the molecule has two planes of symmetry. If a plane is drawn containing all atoms and groups of either ring, it becomes a symmetrical bisector of the ring. Such molecules are achiral and optically inactive.

In the second case, the plane containing the nitro groups becomes the plane of symmetry of the other ring containing COOH groups. However, one plane of symmetry is sufficient to make the molecule achiral and it is so.

In the third case, neither ring has a plane of symmetry and the molecule is chiral. Many such compounds have been resolved. It is important to note that if either ring has a plane of symmetry, the molecule is **achiral** and substituents in **para** position cannot cause lack of symmetry.

It is not always necessary that four large groups must present in **ortho** positions to prevent free rotation about the pivotal bond. Compounds with three or even two groups, if large enough can hinder the rotation and if suitably substituted can be resolved. An example is biphenyl-2,2’-bisulphonic acid. In some cases, the groups may be large enough to slow down the rotation greatly but not prevent it completely. In such cases, optically active compounds can be prepared, which slowly racemise on standing. Thus, the following compound loses optical activity with a half life of 9.4 min in ethanol at 25ºC. On the other hand, compounds with greater rotational stability can often be racemised if higher temperatures are used to supply the energy necessary to force the groups past each other.

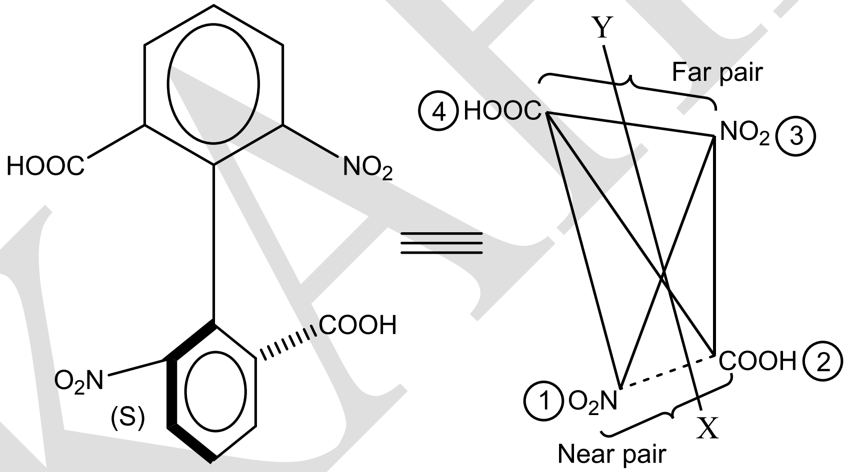


Although, the optical isomerisation of biphenyls is conventionally treated under atropisomerism, optically active biphenyl derivatives must be regarded as molecules that owe their chirality due to the presence of a chiral axis.

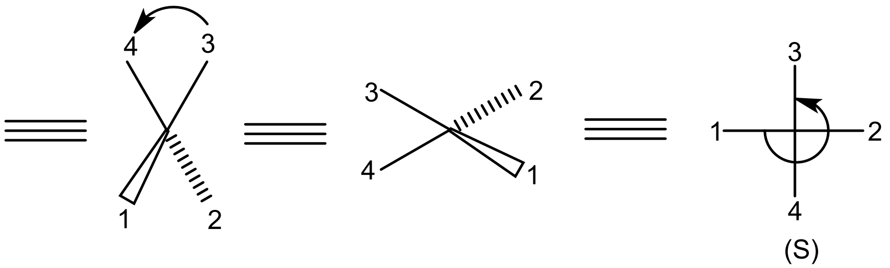
Configurational nomenclature of axially chiral molecules (Cahn, Ingold and Prelog notation or R & S system of designation of axial chirality)

In order to designate the configuration of axially chiral molecules by Cahn, Ingold and Prelog notation, an additional sub-rule is required namely, **near end of the chiral axis precedes the far end.** The terms **near** and **far** refer to the substituents as viewed from either end of the chiral axis XY. It does not matter from which end of the chiral axis the molecule is viewed.

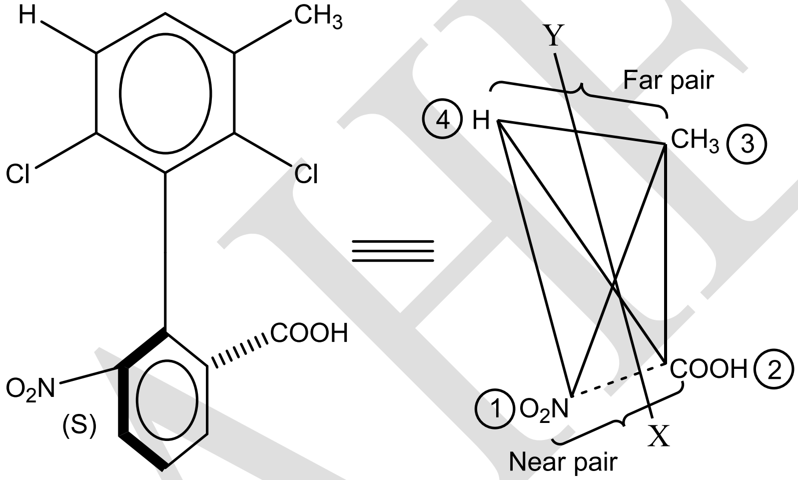
In each plane, a pair of positions is selected as near to each other as they can be such that two members of each pair can be distinguished by the sequence rule. For configurational nomenclature of biphenyls two pairs of **ortho** substituents (2,6 and 2',6') must be considered. However, when the two members of any pair of **ortho** substituents cannot be distinguished by the sequence rule, one has to consider the pair of **meta** substituents (as illustrated below).



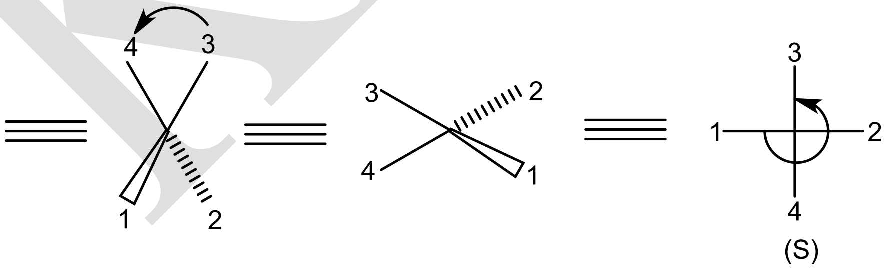
Translate the biphenyls into a disphenoid. Those **ortho** substituents of biphenyl that lie in the plane of the paper are placed at the top corners of the disphenoid and those **ortho** substituents that are perpendicular to the plane of the paper are attached to the lower corners of the disphenoid as shown. If one is looking the disphenoid from the X end of the chiral axis (XY), then O_2N/COOH becomes near pair and COOH/NO_2 becomes far pair. Label the substituents in decreasing order of priority using the sub-rule, **near groups precede far groups**. In the near pair, NO_2 group is preferred over COOH group (1→2) and in the far pair NO_2 group is preferred over COOH (3→4).



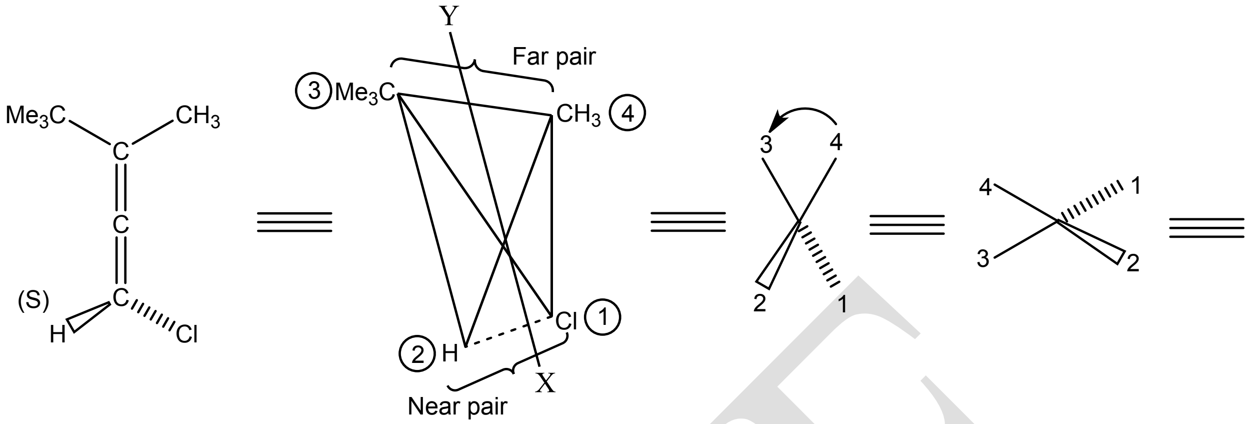
Translate the wedge projection into Fischer. Since, the least preferred group is at the bottom, it can directly be used to trace the sequence. Consider the next example.

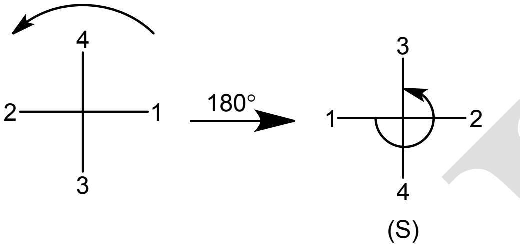


In this example, the **ortho** substituents that describe the situation are *Cl*/*Cl* in the upper ring and NO_2/COOH in the lower ring. But since two members of **ortho** pair of the upper ring namely, *Cl*/*Cl* cannot be distinguished by the sequence rule, one has to consider the **meta** pair of substituents, *viz*, H/CH_3.



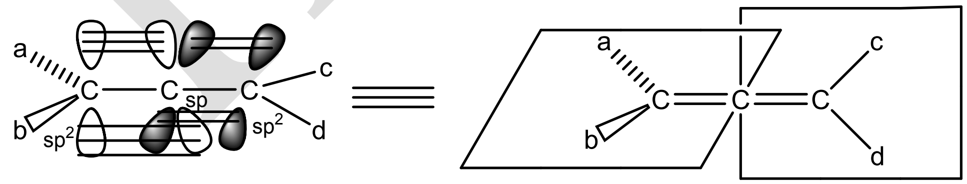
Configurational nomenclature of an allene is shown below.





Optical Isomerism of Allenes

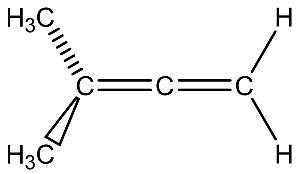
Allenes belong to a class of compounds called **cumulenes** which contain adjacent double bonds. In allene, the central carbon atom is **sp** hybridised and bonded to the two adjacent **sp^2** hybridised carbon atoms by two σ-bonds. The central **sp** carbon atom thus contains two orthogonal atomic p-orbitals, each of which can overlap with a p-orbital of the adjacent **sp^2** carbon atom thus forcing the remaining bonds of the **sp^2** carbon atoms into perpendicular planes. Suitably substituent allenes are optically active. **The necessary condition for chirality of allenes is that neither end of the molecule can have a plane of symmetry.**



Thus from the point of optical activity, allenes fall into three categories.

Type (i)

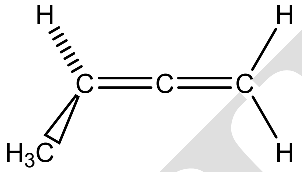
Both ends are symmetrical (AA…..BB).



Achiral and optically inactive

Type (ii)

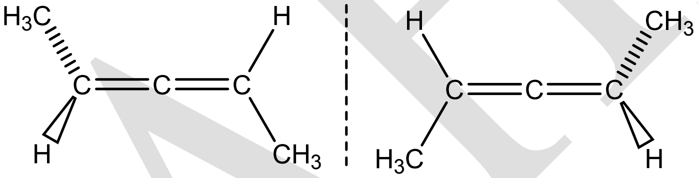
One of the ends is symmetrical (AB…..CC).



Achiral and optically inactive

Type (iii)

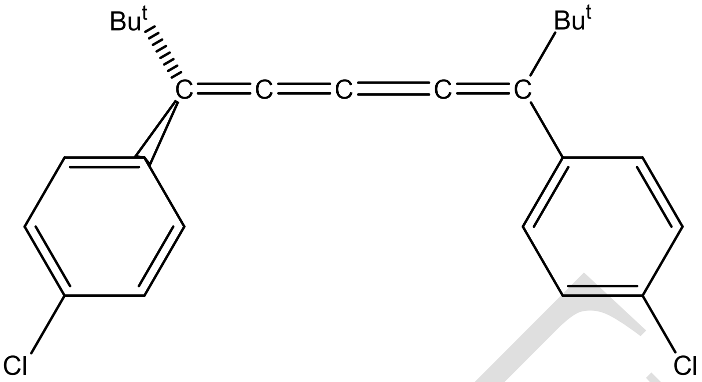
Neither end is symmetrical (AB…..AB or AB…..AC).



Chiral and optically active

These cases are completely different from **cis-trans** isomerism of compounds with one double bond. In latter cases the four groups lie in one plane and the isomers are not enantiomers and neither is chiral, while in allenes the four groups lie in two perpendicular planes and the isomers are a pair of enantiomers.

When a molecule contains three, five or any odd number of cumulative double bonds, orbital overlap causes the four groups to occupy **one** plane and **cis-trans** isomerism is observed. When four, six or any even number of cumulative double bonds are present in a molecule, the orbital overlap is such that the terminal substituents occupy perpendicular planes and the situation is analogous to that of allenens and optical activity is possible. The following compound is resolved.



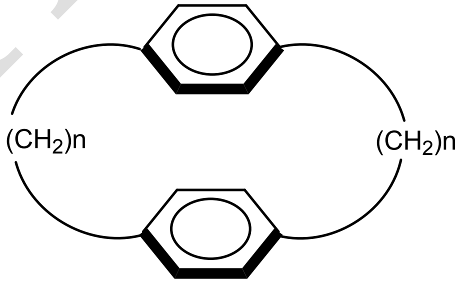
Planar chirality

Cyclophanes and Ansa compounds

Very interesting compounds are known to exist which exhibit atropisomerism; these include paracyclophanes, ansa compounds and trans-cyclooctene. All these compounds are said to owe their chirality due to the presence of a **chiral plane**. Just as in axially chiral molecules, an exchange of a pair of substituents around the chiral axis leads to an enantiomer, similarly in molecules with a **chiral plane**, an exchange of substituents across the chiral plane leads to an enantiomer.

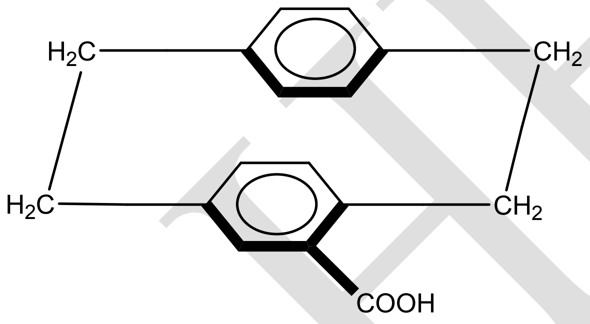
Paracyclophanes

The benzene ring in paracyclophanes with small **n** and **m** are arranged one above and other just as the shelves in a book case. Their π-electron systems are brought close together and to a certain extent are united into a single electron system. This manifests, for example, in that the acetyl group introduced into one of the rings retards the acetylation of the other ring.



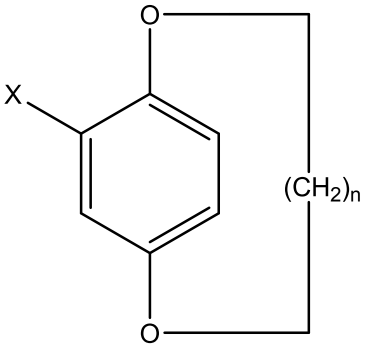
The hindrance to the free rotation of the benzene rings is also present in **paracyclophanes** with m = 3 and n = 4. But if benzene rings are linked by chains consisting of four or more methylene groups, free rotation becomes possible.

In unsymmetrically substituted rigid paracyclophanes, the presence of even one of the substituents in one of the benzene rings is enough for the structure to become chiral. This had been proved by the preparation of paracyclophanecarboxylic acid and other analogous compounds in an optically active form.



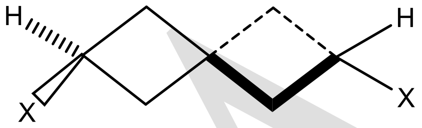
Ansa compounds

The restricted rotation of benzene ring is also responsible for the chirality of other aromatic compounds, which are called **ansa compounds** (ansa means handle in Latin). The two oxygen atoms of the hydroquinone are linked by a polymethylene chain. The number of methylene groups in the polymethylene chain of such compounds may vary. With a certain minimum number of methylene groups (n = 8 or 9), aromatic ring cannot swivel through the chain and in such cases the polymethylene chain is perpendicular to the benzene ring. Because of this restricted rotation of the benzene ring, the molecule cannot attain planar configuration. In such cases, the presence of even one ring substituent is sufficient to make the structure chiral.

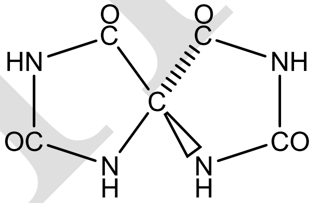


Optical Isomerism of Spiranes

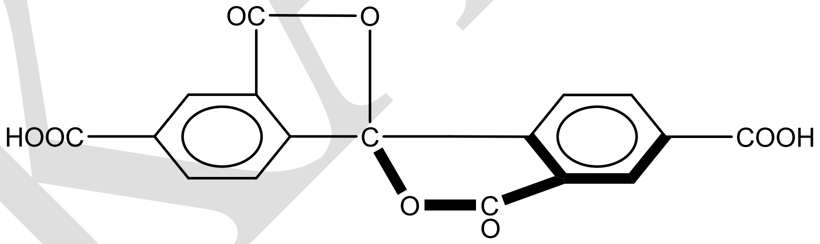
When one replaces both the double bonds of an allene by rings, one obtains a bicyclic system in which one atom is common to both the rings. Such bicyclic systems are called **spiranes**. The two rings of spirane, similar to the π-bonds of allene are orthogonal and the groups attached to the two ends define planes at right angles to the adjacent ring and to each other. Properly substituted spiranes may be resolved. **The condition for chirality is analogous to that of allene, that is, neither end of the ring can have a plane of symmetry ($\sigma \equiv S_1$).** The parent compound cannot be resolved because it contains two planes of symmetry. The planes may be removed not only by attacking two **unequal** groups at the sides of the ring but also by introducing suitable groups into the ring. Among other spiranes, quaternary ammonium salt is of interest, since it suggests that quaternary nitrogen like carbon has tetrahedral geometry.



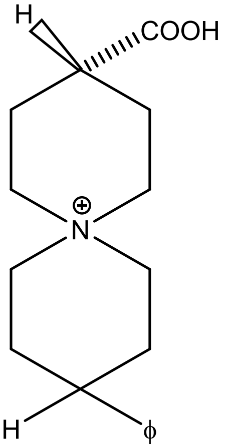
Spiro[3.3]heptane
X = H; not resolvable (achiral)
X = COOH or NH_2, resolvable



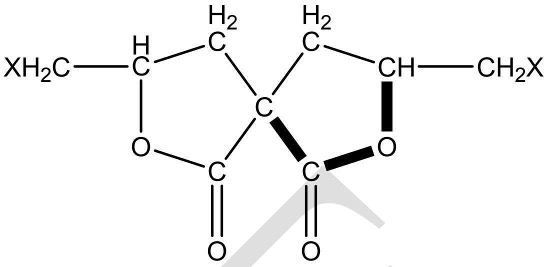
5, 5'-Spirobishydantoin



First spirane to be resolved



Spirobispiperidinium salt
(resolvable)



[This compound has been shown to exist
in three (±) forms. It is a spiran containing
asymmetric carbon atoms]

Geometrical Isomerism or Cis-Trans Isomerism

Introduction

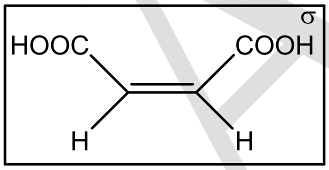
This type of isomerism was first noticed in case of maleic and fumaric acids. Maleic and fumaric acids have the same molecular formula, $C_4H_4O_4$, but differ in most of their physical and chemical properties and neither is optically active. It was originally thought that these two acids were structural isomers. It was subsequently shown that maleic acid and fumaric acid are not structural isomers but stereoisomers, eg. both are catalytically reduced to succinic acid, add one molecule of hydrogen bromide to form bromosuccinic acid, add one molecule of water to form malic acid and are oxidised by potassium permanganate to tartaric acids (the stereochemical relationships in these reactions have been ignored). Thus both acids have the same structure namely, HOOC-CH=CH-COOH, van't Hoff suggested that if there is no free rotation about the carbon-carbon double bond, the existence of two isomeric forms differing in their spatial arrangement for the formula HOOC-CH=CH-COOH would be possible.

Now we know that in case of maleic and fumaric acids, the two sp^2 carbon atoms and four substituents attached to them lie in one plane. Since the molecules are planar, they are superimposable on their mirror images. Therefore maleic acid and fumaric acid are not optically active.

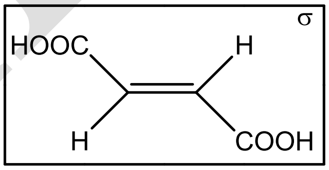
The type of isomerism exhibited by maleic and tumaric acids are known as geometrical isomerism or **cis-trans** isomerism. **It is a special case of diastereoisomerism**. Maleic acid is the **cis**-isomer (**cis**-butenedioic acid) and fumaric acid is the **trans**-isomer (**trans**–butenedioic acid). **Cis**-isomer is the one in which one set of identical groups of adjacent sp^2 carbon atoms lie on the same side of the double bond and in **trans**-compound one set of identical groups on adjacent carbon atoms lie across the double bond.

Geometrical isomerism is exhibited by a wide variety of compounds and they may be classified into three groups.

(i) Compounds containing double bonds:
C=C, C=N and N=N.
(ii) Compounds containing cyclic structures–homocyclic, heterocyclic and fused ring systems.
(iii) Compounds that may exhibit geometrical isomerism due to restricted rotation about a single bonds.



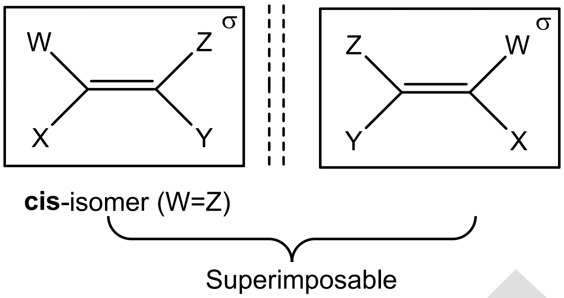
Maleic acid

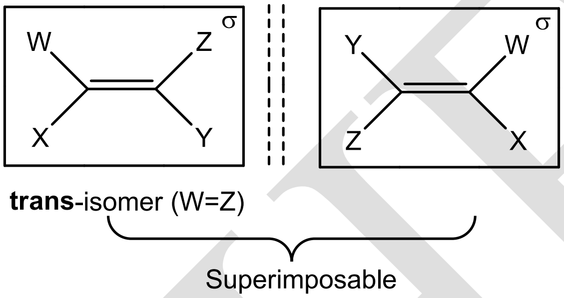


Fumaric acid

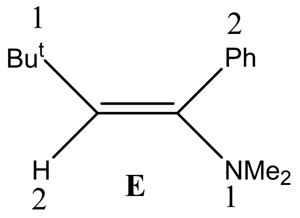
Cis-trans isomerism resulting from double bonds

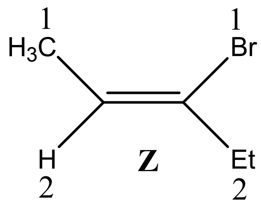
In olefinic compounds, the two sp^2 carbon atoms (C=C) and four groups attached to them lie in one plane and the free rotation around the double bond is prevented. This means in case of molecules of the type WXC=CYZ, isomerism is possible if W≠ X and Y≠ Z. In such case, they are only two isomerism **each superimposable on its mirror image** unless one of the groups happen to be chiral.



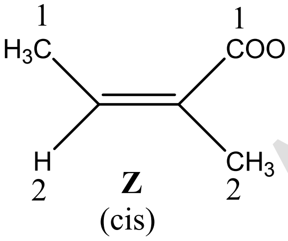


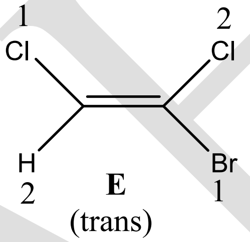
The above isomers of the formula WXC=CYZ by definition are diastereoisomers. There are two ways to name such isomers. In **older** method, one isomer is called **cis** and the other **trans**. **Cis**-isomer is the one in which **one pair of identical groups** of the adjacent olefinic carbon atoms lie on the **same** side of the double bond. In **trans**-isomer **one pair of identical groups** lie **across** the double bond. Unfortunately there is no easy way to apply this method when all the four groups are different. **Cis, trans** nomenclature is applicable only, if **at 1east one pair of substituents** on adjacent olefinic carbon atoms are **the same**. The newer method which is applicable to all cases is based on Cahn, Ingold and Prelog notation. The two groups attached to each olefinic carbon atom are ranked according to sequence rules. Then that isomer which has **two higher ranking groups** on the **same side** of the double bond is called *Z* isomer (from the German word Zusammen meaning together); that isomer in which the **two higher ranking groups** are **across** the double bond is called *E*-isomer (*E* for Entgegen meaning opposite). Note that *Z*-isomer is not necessarily the one that would be called **cis** under older system. Like **cis** and **trans**, *E* and *Z* are used as prefixes.

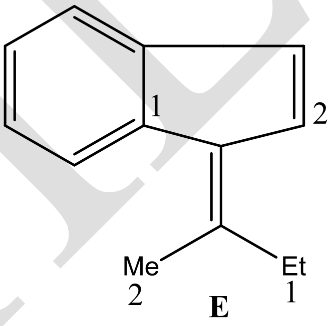


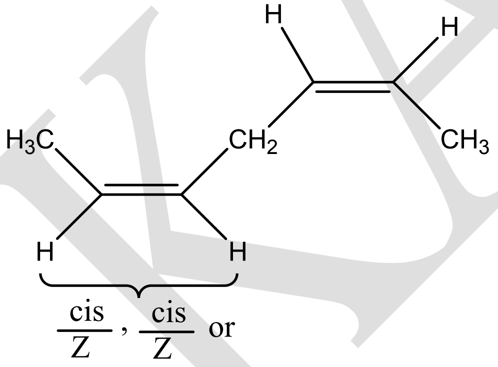


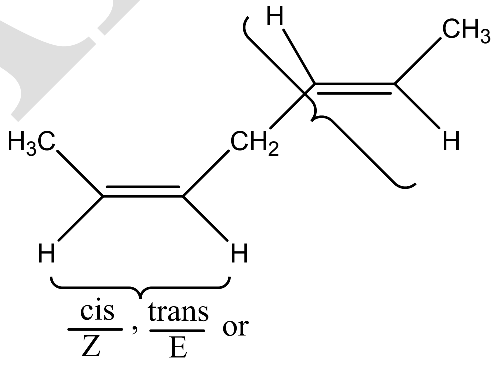
This type of isomerism is also possible with other double bonds such as C=N, N=N and even C=S, although in these cases only two or three groups are connected to the double bond atoms. In case of imines, oximes and other C=N compounds, the prefixes **syn** and **anti** are used although **cis** and **trans**, ***E*** and ***Z*** are sometimes used here also. In azo compounds there is no ambiguity.



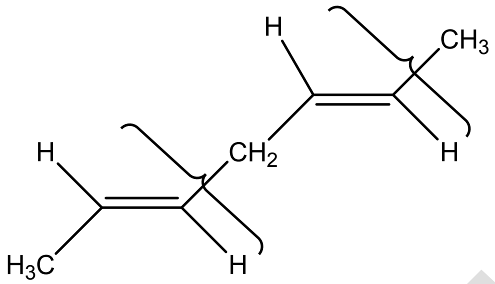






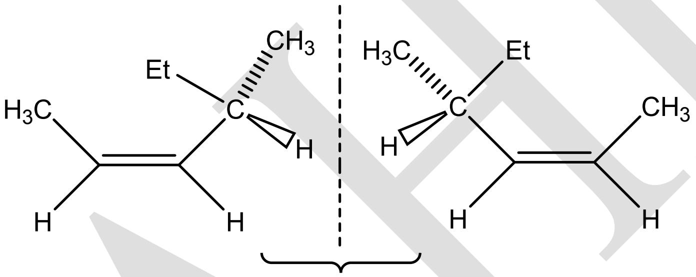


In there is more than one double bond in a molecule the number of geometrical isomers is 2^n, where n is the number of double bonds; this formula applies only to molecules in which the ends are different. If the ends are identical, eg: CHA= CH-CH=CHA, then the number of stereoisomers is $2^{n-1}+ 2^{p-1}$ where P=n/2 when n is even and P= (n+1)/2 where n is odd.

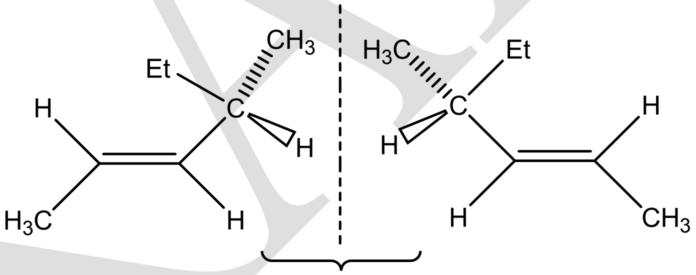


$\frac{\text{trans}}{\text{E}}, \frac{\text{trans}}{\text{E}}$

When a molecule contains a double bond and an asymmetric carbon, there are four isomers, a **cis** pair of enantiomers and a **trans** pair.



Z or cis-(±) pair

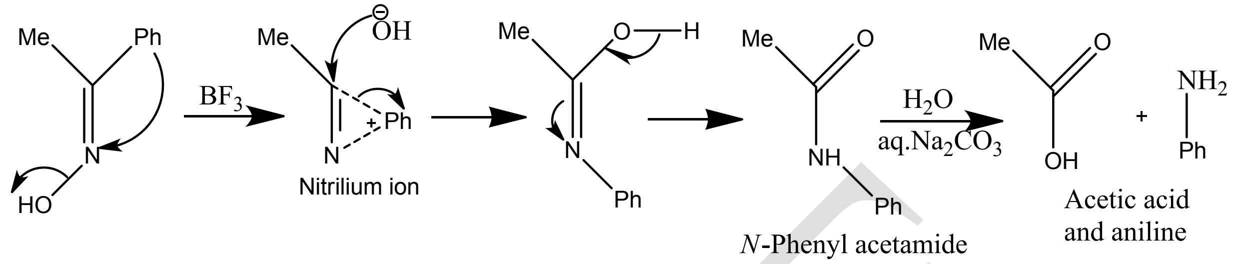


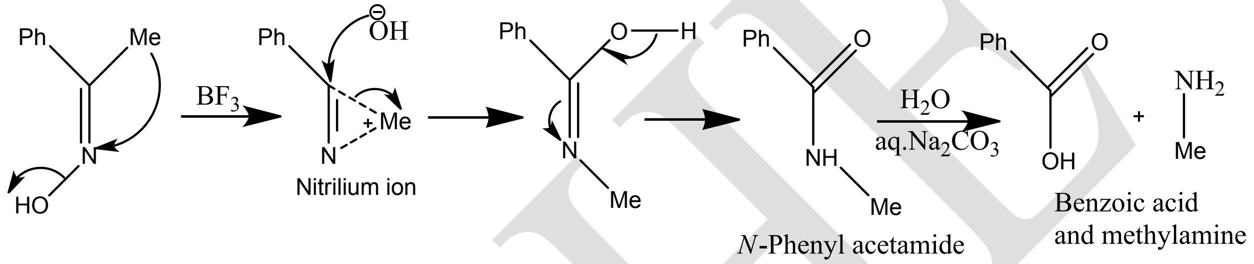
E or trans-(±) pair

Methods of determination of configuration of aldoximes and ketoximes

Beckmann Transformation: (method of determination of configuration of ketoximes)

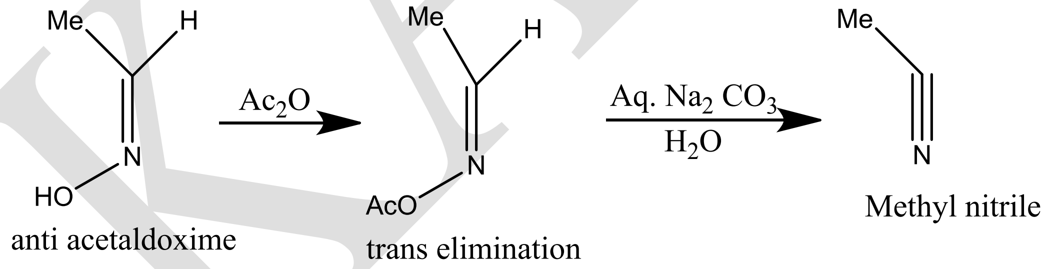
When the given ketoxime is treated with acidic reagent like $AlCl_3$, BF_3, Conc. H_2SO_4, PCl_5, $SOCl_2$, etc. the ketoxime undergoes intramolecular rearrangement to form N-substituted amide which on hydrolysis gives two compounds one acid and one amine. From the identification of amine the configuration of original oxime can be confirmed because the reaction is found to be occurred with the migration of group anti to the OH group from carbon to nitrogen.

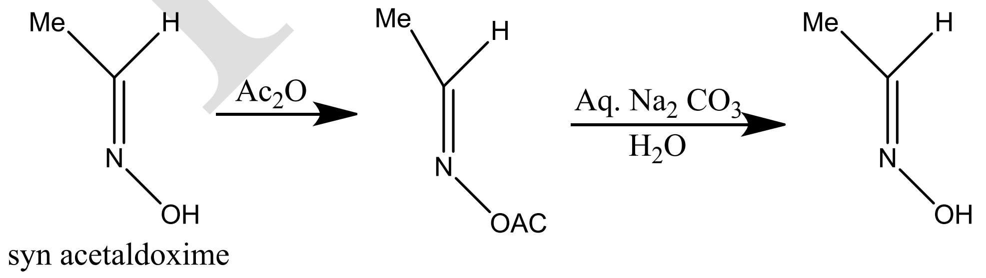




Determination of configuration of aldoximes

When the given aldoximes is acetylated with acetic anhydride and hydrolyzed we get different products for syn and anti aldoximes. Original aldoxime is obtained in **syn** isomer whereas a **nitrile** is obtained and in **anti** isomer by **trans** elimination reaction.





Conformations of cyclic system-monocyclic compounds

Conformations of cyclohexane

The cyclohexane ring system is by far the most commonly occurring of cycloalkanes in natural products doubtless because of its stability and ease of its formation. In 1980, Sachse proposed that cyclohexane ring can exist in two non-planar (puckered) forms (chair and boat) which are free from bond angle strain. Since Sachse's theory of strainless ring required the existence of two isomeric forms of cyclohexane and all attempts to isolate them failed at that time, Sachse's theory was unrecongnised for a long time. In 1918, Mohr revived Sachse's theory and explained the absence of isomeric forms of cyclohexane due to rapid interconversion of two forms. Mohr later pointed out that the union of two cyclohexane rings may result in the formation of two stereisomeric forms–the **cis** and the **trans** decalins which can no longer be interconverted without bond rupture. Later, the two isomeric forms of decalins were realised.

According to the original assumption, the boat and chair conformations were considered to be equally probable for cyclohexane. However, the 1947, Hassel established by means of electron diffraction studies that cyclohexane exists predominantly in two chair conformations.

Geometry of the cyclohexane ring system

The chair form of cyclohexane ring system is represented in the **Figure 1**, with the vertical C_3 axis. The Newman projections of chair forms of cyclohexane reveal that there are six gauche–butane interactions and consequently the enthalpy of cyclohexane chair form is estimated at 3.3 x 6=19.8 KJ/mol.

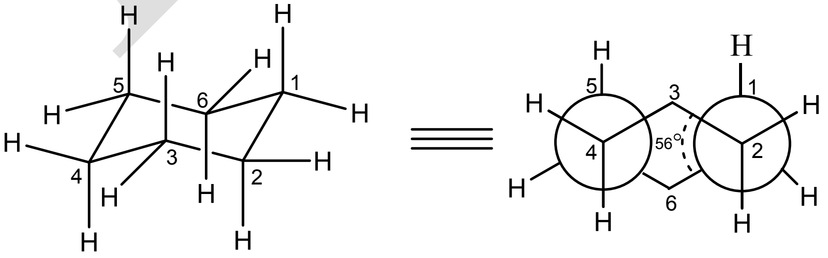
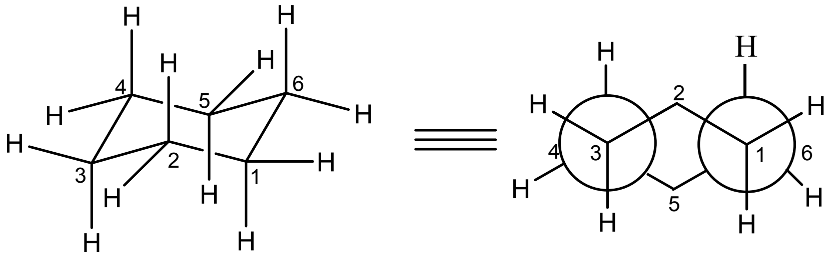
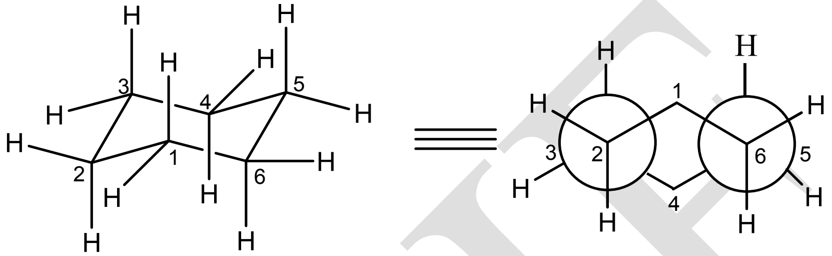


Figure 1

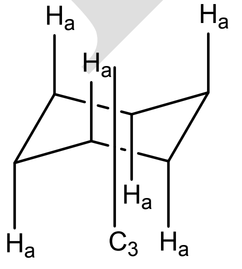




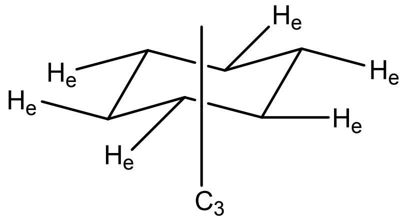
The chair form of cyclohexane belongs to D_3 point group. The principal axis is C_3 and there are three binary axes passing through the three opposite sides; three diagonal planes (σ_v) pass through the opposite corners. Its symmetry number (σ) is 6.

Equatorial and axial bonds

The twelve C-H bonds in the chair form of cyclohexane (I) are of two types. Six of the C-H bonds are called **axial** are parallel to the C_3 axis and are represented by vertical lines in the plane of the paper. These **axial** bonds are (three above and three below the plane of the molecule) alternately directed up and down on adjacent carbon atoms. The remaining six C-H bonds are inclined at an angle of 109°28′ to the C_3 axis and are described as **equatorial** bonds. The **axial** hydrogens are **homotopic** relative to each other, since they can be interchanged by rotation around C_3 and C_2 axes. The same is true of **equatorial** hydrogens relative to each other. However, the **axial** set of hydrogens is **diastereotopic** with **equatorial** set of hydrogen atoms.



(I)



Ring inversion

The cyclohexane ring is conformationally mobile. Through a process known as ring inversion or ring flipping, one chair conformation (Ia) is converted into another chair (Ib). Since the activation energy for the cyclohexane ring inversion is only 42 KJ/mol, ring inversion occurs rapidly at room temperature. In between the chair forms, there are two other notable conformations, the skew boat (III) which is less stable than the chair and the boat (II) which is 30 KJ/mol less stable than the chair (**Figure 2**).

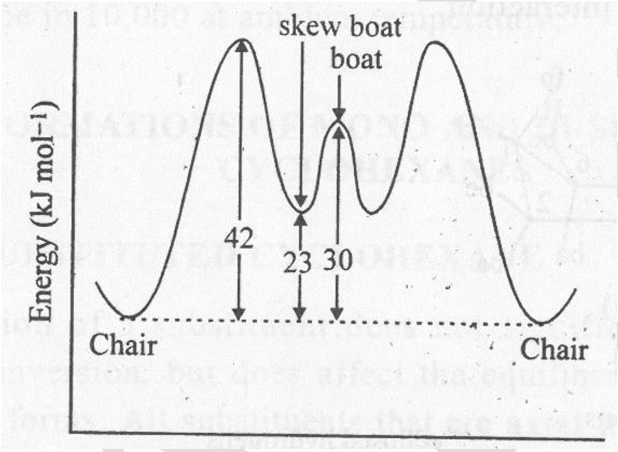
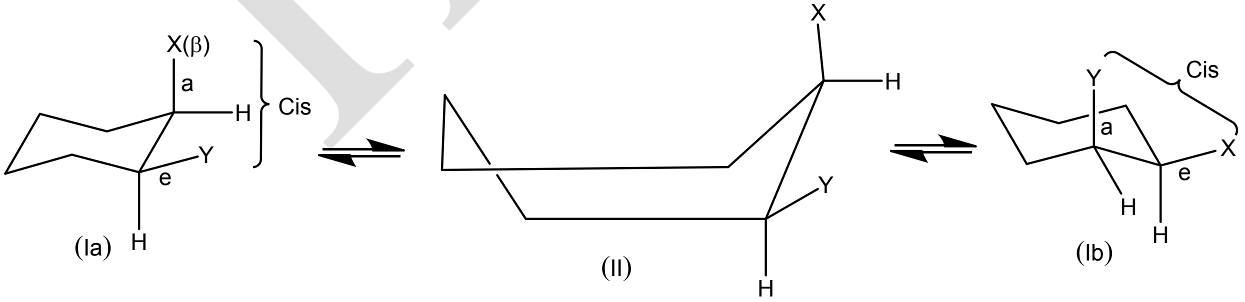


Figure 2. Energy profile and conformational of cyclohexane.

The most important consequence of ring inversion is that any substituent that is **axial** in the original chair conformation (Ia) becomes **equatorial** in the ring flipped form (Ib) and vice-versa. It should be noted that during ring inversion no change in the relative configuration ever occurs, that is, α-substituent remains α and β-substituent remains β; likewise, **cis**-remains **cis** and **trans** remains **trans;** (R) remains (R) and (S) remains (S).



Flexible conformations

The boat (II) and the twist boat (III) constitute two significant conformations of the cyclohexane (**Figure 3**). The conventional boat (II) belongs to C_{2v} point group and is free from bond angle strain but suffers from significant torsional strain due to eclipsing of four **boat equatorial** and **boat axial** hydrogens on C-2, C-3 and C-5, C-6. In addition, the hydrogens at C-1 and C-4 approach so close to each other that the distance between them (183 pm) is less than the sum of the van der Waals radii (241 pm) of hydrogen atoms. This leads to a non-bonded interaction between C-1 and C-4 hydrogen atoms, often called bowsprit-flagpole interaction.

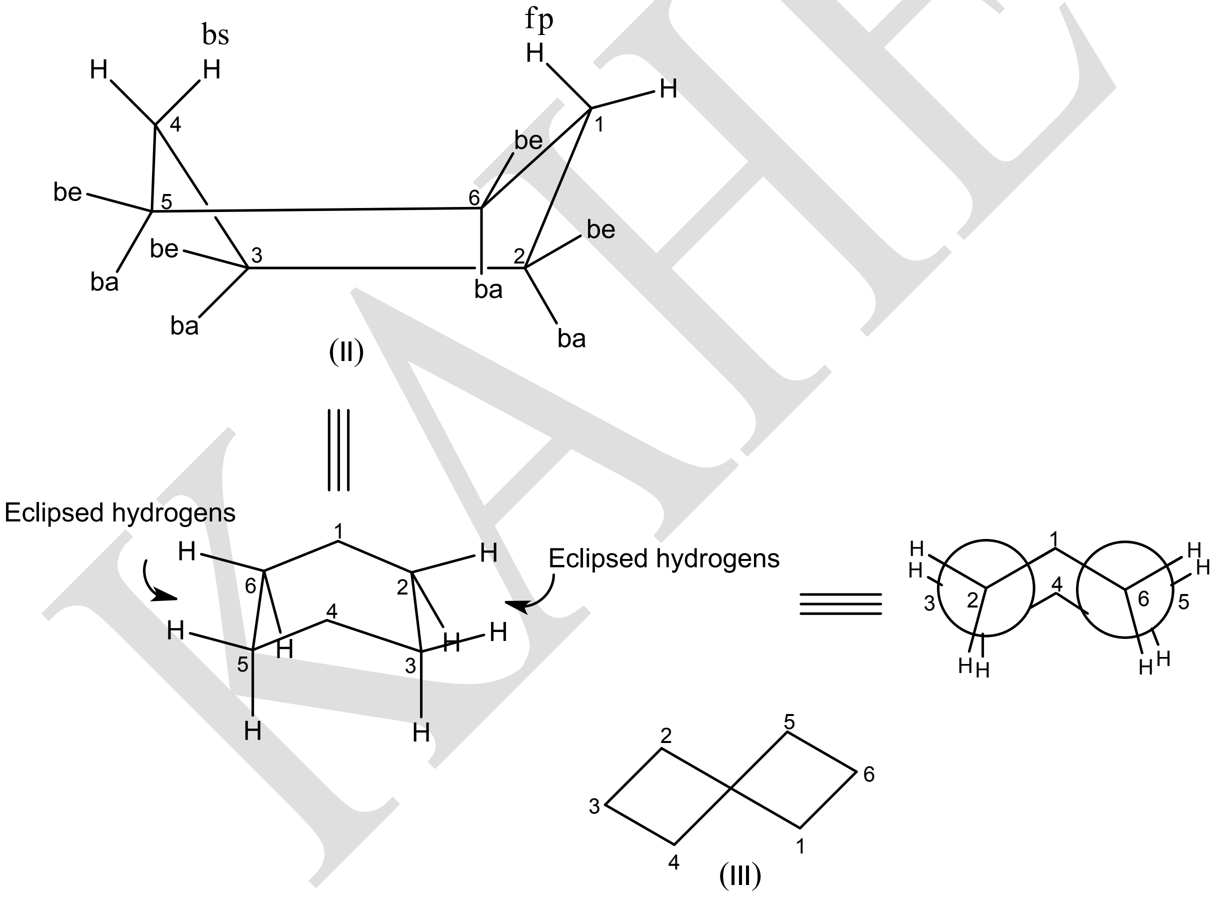


Figure 3. Extreme boat form of cyclohexane showing interfering and eclipsed hydrogens.

The boat from (II) consists of **four** gauche-butane interactions (1:2, 3:4, 4:5 and 6:1) and **two** eclipsed butane interactions (2:3 and 5:6) and the total strain may be computed as $4 \times 3.3 +$

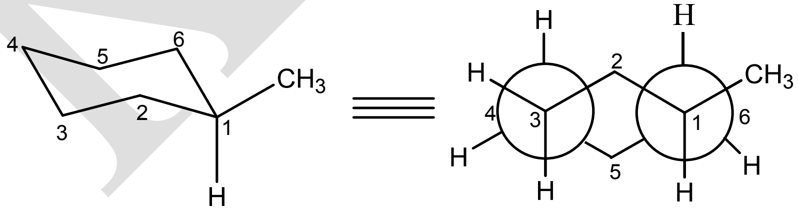
2×18 = 49.2 KJ/mol. The difference in enthalpy between the chair and boat forms is thus 29.4 KJ/mol, the enthalpy of the chair being 19.8 KJ/mol.

A modified boat conformation known as twist boat (or skew boat) (III) results when the boat (II) form is so twisted that the flagpole bowsprit hydrogens move away from each other and torsional interactions are also reduced. As a result the conformation becomes more stable. Twist boat conformation (III) belongs to D_2 point group and hence chiral. Although, the boat and twist boat conformations are of high energy, they have favourable entropy due to more degrees of freedom than chair and the population of flexible form is approximately one in 10,000 at ambient temperature.

Conformations of mono and di-substituted cyclohexanes

Monosubstituted cyclohexane

Introduction of a substituent does not significantly affect the rate of conformational inversion, but does affect the equilibrium distribution between alternative chair forms. All substituents that are **axial** in one chair conformation become **equatorial** on ring inversion and vice-versa. Monosubstituted cyclohexane (eg. methylcyclohexane) exists in two non-equivalent diastereomeric chair conformations, one with **equatorial** substitutent (IVa) and the other having the substituent in **axial** position (IVb), the former predominates at the equilibrium. For methylcyclohexane, ΔG° for the equilibrium is 7.50 KJ/mol, corresponding to a composition of 95% equatorial methylcyclohexane.



The equatorial preference of the methyl group may be related conceptually to the greater stability of the **anti** conformation of η-butane compared to **gauche** conformation. The axial methyl group of methylcyclohexane forms a part of two gauche-butane fragments (Me-C_1-C_2-C_3 and Me-C_1-C_6-C_5) while an equatorial methyl group is stereochemically similar to **anti** butane conformation. These are shown in heavy lines in the **Figure 4** and one of them can be seen clearly in Newman projection. No such interaction is present in equatorial methylcyclohexane. Since the **gauche** conformer of η-butane is 3.3 KJ/mol higher in energy than the **anti** conformer, the axial methylcyclohexane (IVb) possessing two such gauche-butane interactions is less stable than the equatorial methylcyclohexane (IVa) by 6.6 KJ/mol (2 x 3.3 KJ/mol). The potential energy diagram of methylcyclohexane as a function of conformation is given in **Figure 5**.

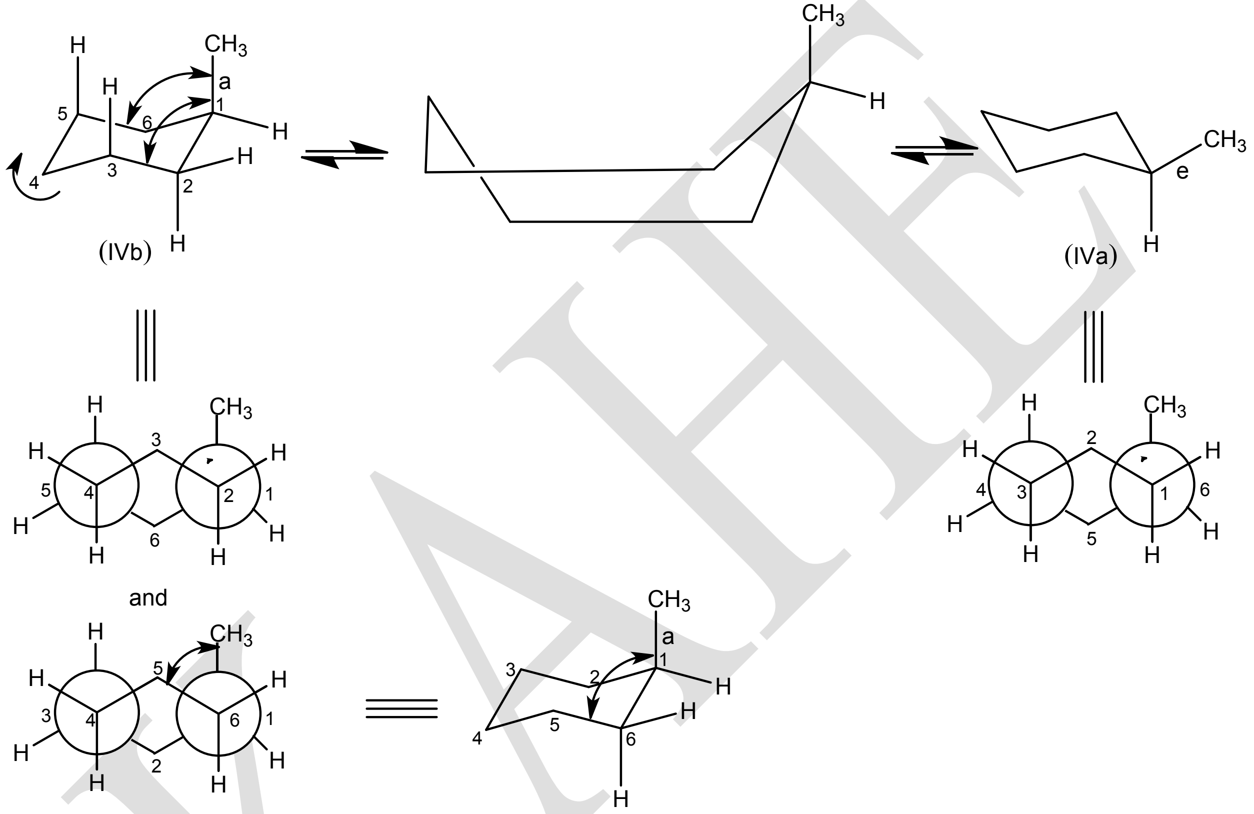


Figure 4

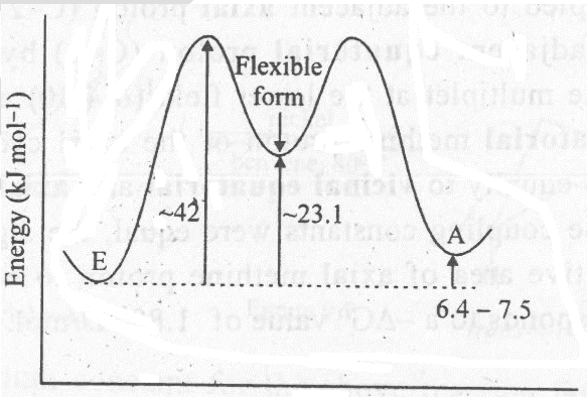


Figure 5. Potential energy of methylcyclohexane as a function of conformation.

The **axial** methyl group of methylcyclohexane (IVb) experiences van der Waals repulsion with axial hydrogens at C-3 and C-5. Interactions of this type are called **1,3-diaxial** interactions and substituents in **1,3-diaxial** orientation with respect to each other are said to be **syn** axial. The result of repulsion between **axial** methyl group and **syn** axial hydrogen leads to a slight flattening of the ring.

The free energy difference between conformers is referred as conformational free energy or sometimes A value. For substituted cyclohexanes, the equilibrium is written as

$$\text{Axial} \rightleftharpoons \text{Equatorial}$$

$$\Delta G^{\circ} = -\,RT\ln K \text{ where } K = \frac{[\text{Equatorial}]}{[\text{Axial}]}$$

Since the ΔG^{o} will be negative when equatorial conformation is more stable than the axial, the value of $-\Delta G^{o}$ is positive for substituents that favour equatorial position. The larger the $-\Delta G^{o}$ value, the greater the preference for the equatorial position.

Conformational free energy values ($-\Delta G^{o}$) for many substituents have been determined by NMR method at low temperature. At -80ºC, the NMR spectrum of cyclohexyl iodide (**Figure 6**) is well resolved and clearly indicates the presence of two conformations. In general **equatorial hydrogens** resonate at lower field than the constitutionally similar **axial hydrogens.** The multiplet at higher field (δ 3.80) is a triplet of triplet with vicinal coupling constant of 3.5 and 12 Hz. This multiplet is assigned to the axial methine proton of equatorial cyclohexyl iodide, since it is couple to the adjacent **axial** proton (C-2) by a large **trans** coupling and to the adjacent **equatorial** proton (C-2) by a small **gauche** coupling constant. The multiplet at the lower field (δ 4.50) appears as a broad peak because the **equatorial** methine proton of the axial cyclohexyl iodide is coupled approximately equally to **vicinal equatorial** and **axial** protons by small **gauche** coupling. If the coupling constants were equal, the signal would appear as a quintet. The relative area of axial methine proton to equatorial methine proton is 3.4 and corresponds to a $-\Delta G^{o}$ value of 1.88 KJ/mol.

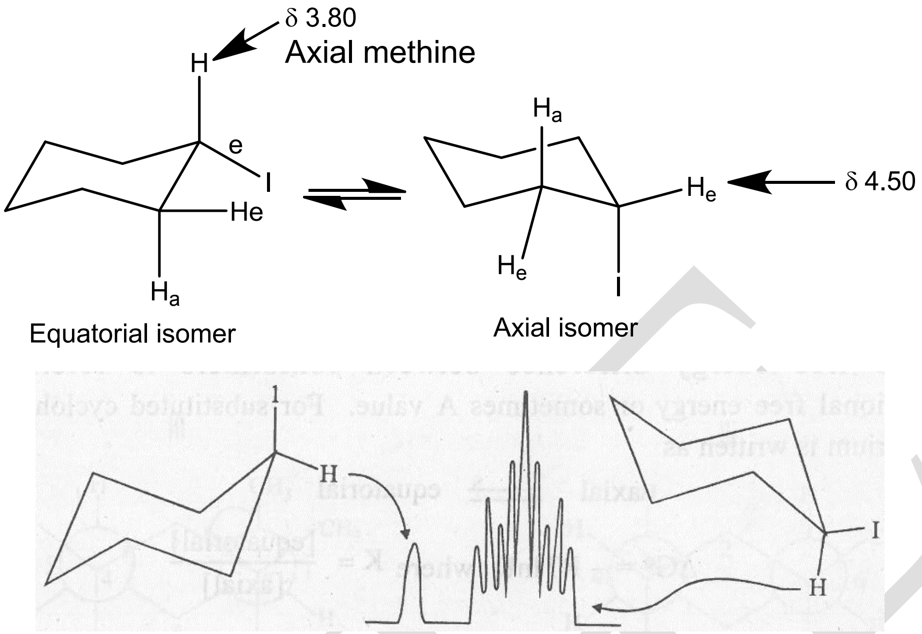


Figure 6. NMR spectrum of cyclohexyl iodide at -80°C.

A second important method for determining the conformational free energies involves establishing an equilibrium between diastereoisomers differing only in the orientation of the designated substituent. The equilibrium constant can then be determined and used to calculate the free energy difference between the diastereoisomers. For example, **cis-**and **trans-4-***t*-butylcyclohexanols can be equilibrated using a nickel catalyst in refluxing benzene to give a mixture containing 28% **cis**-4-*t*-butylcyclohexanol (axial-OH) and 72% **trans**-4-*t* butylcyclohexanol (equatorial-OH) (**Figure 7**).

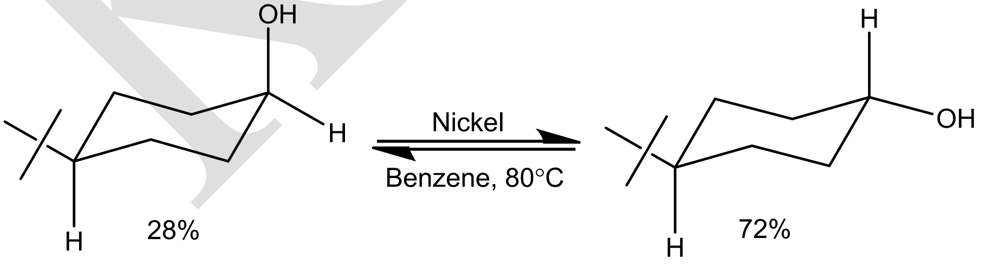
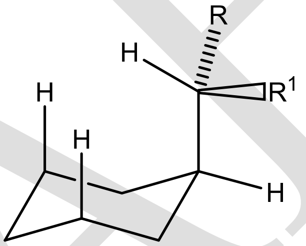


Figure 7

The equilibrium constant for the above reaction leads to a value of 2.9 KJ/mol for $-\Delta G^o$ for the hydroxyl substituent.

Among the halogen substituents, flourine is the least conformationally demanding and the preference for the equatorial orientation is nearly same for chlorine, bromine and iodine. The larger van der Waals radii of iodine and bromine relative to chlorine are compensated by the greater C-I and C-Br bond lengths, which decrease the repulsion between halogen and **syn**-axial hydrogens. The electrons of C-I and C-Br bonds are also more polarisable and lead to increased attractive interaction between halogen and other atoms.

The alkyl groups methyl, ethyl and isopropyl have similar conformational energies with isopropyl being slightly larger than methyl and ethyl. The similarity of the conformational energies of these three substituents is due to the rotation of the alkyl groups around the bond between the substituent and the ring so that the ring adopts a conformation that minimizes the effect of additional methyl substituents in ethyl and isopropyl groups.



Methyl ;R = R^1= H
Ethyl ;R = H, R^1= CH_3
Isopropyl;R = R^1 = CH_3

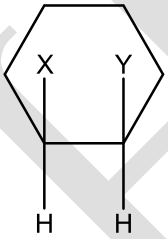
A tertiary butyl substituent experiences strong van der Waals repulsion with **syn** axial hydrogens and this strain is not relieved by rotation of tertiary butyl substituent about the bond to the ring. The conformational free energy of *t*-butyl group has been estimated as 22.5 KJ/mol. The strong preference for *t*-butyl group to occupy the equatorial orientation has made it a highly useful group for the study of conformationally biased systems.

Disubstituted cyclohexanes

Non-geminally disubstituted cyclohexanes exist as a set of three positional isomer, 1,2-, 1,3 and 1,4. Each set can exist as a pair of geometrical isomers, **cis** and **trans,** each of which in turn can exist in two interconvertible chair conformations. Depending upon symmetry, each positional isomer may exhibit enantiomerism (Each positional isomer has 2 chiral centers, so the number of stereoisomers is 4 (2^2). They are a **cis**-pair of enantiomers and **trans** pair of enantiomers. Further the **cis** and **trans** isomers exist in two interconvertible chair conformations). The stereochemical aspects of disubstituted cyclohexanes are illustrated with dimethylcyclohexanes.

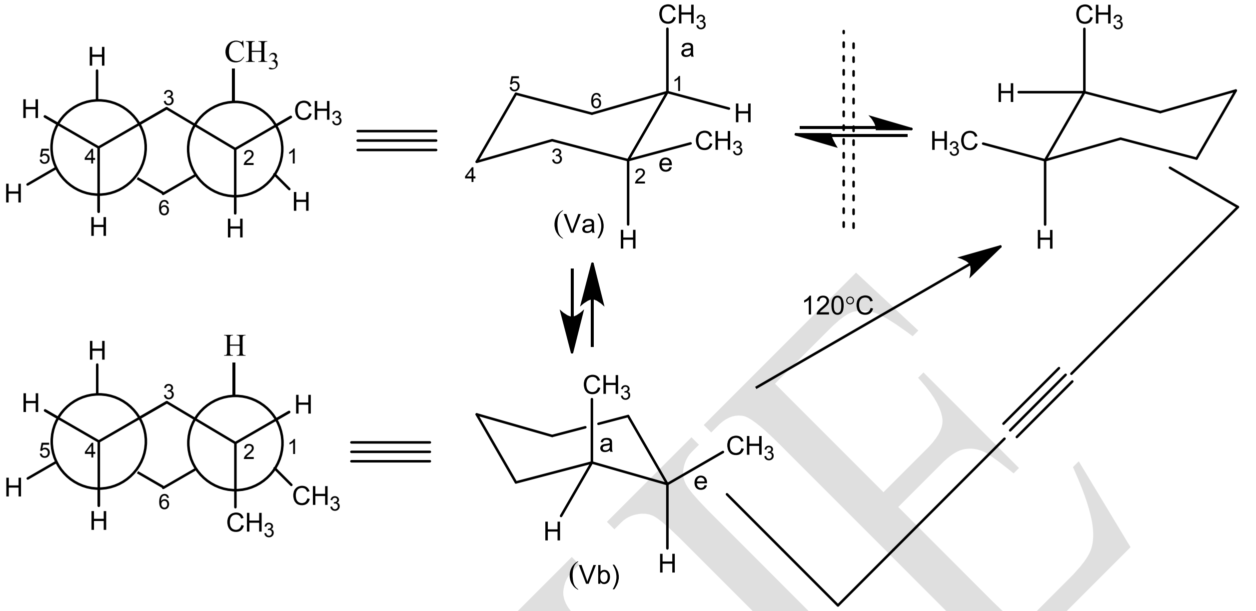
1,2-Disubtituted cyclohexane

i) **Cis –1,2-Disubtituted cyclohexane**
(eg. **cis**-1,2-dimethylcyclohexane)



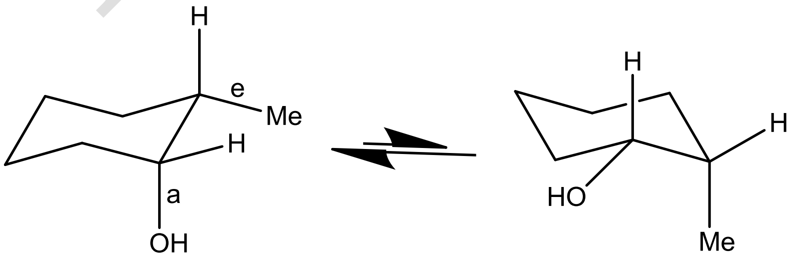
(X=Y= Me)

1,2-Substituents of a cyclohexane are said to be **cis**, if they occupy axial and equatorial orientation. **Cis**-1, 2-dimethylcyclohexane exists as two **energetically equivalent** axial–equatorial (a,e) (Va) and equatorial–axial (e,a) (Vb) chair conformations which are not superimposable on **their mirror images.** However, the classical (planar) formula of **cis-**1,2-dimethylcyclohexane has a plane of symmetry and therefore, represents a **meso** form. If the conformational representations of **cis-**1,2-dimethylcyclohexane are examined, each chair form is devoid of mirror symmetry and hence expected to be chiral. However, the two conformational isomers resulting from ring inversion are also mirror images of each other. This can readily be seen by rotating the chair form Vb by 120º around the C_3-axis. Since the two conformational isomers are equienergetic and are present in equal amounts. c**is-**1,2-dimethylcyclohexane exists as a racemate (±); since the potential energy barrier between the two conformers is too low to allow separation, the racemate is inseparable. Thus, **cis**-1,2- dimethylcyclohexane is a non-separable racemate.

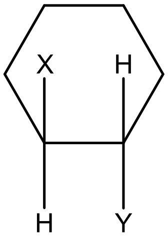


Either of the chair conformation contain three gauche-butane interactions (two for **one** axial methyl and one for a-e dimethyl) corresponding to a potential energy difference of 11.2 KJ/mol (with respect to hypothetical structure with no extra interaction). The entropy of such compounds originates from three sources (i) entropy due to symmetry number (-RTlnσ) ii) entropy due to mixing of conformers iii) entropy due to (±)-mixture. For **cis**-1,2-dimethylcyclohexane (C_1 symmetry) σ is 1 and so its contribution to the entropy is nil; the second and third factors happen to be the same. The two conformers being enantiomeric contribute an entropy of mixing, Rln2.

If the substituents are different and differ in size (X≠Y), the conformer with lower energy (the preferred conformer) is the one in which the larger group is equatorial. In **cis**-2 methyl-1-cyclohexanol (X=OH and Y=Me), the methyl group is larger than the hydroxyl and the preferred conformation is the one in which the methyl group is equatorial.

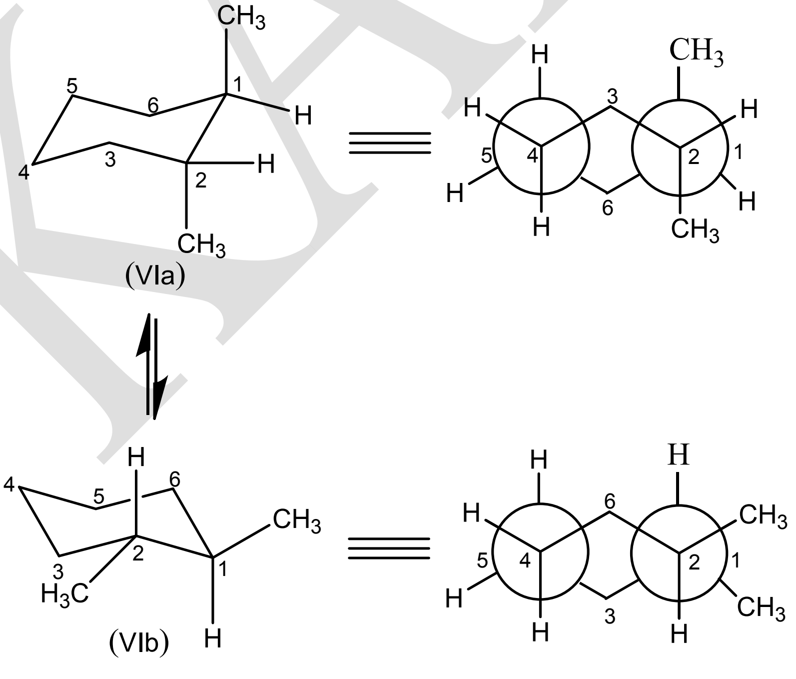


ii) Trans-1,2- Dimethylcyclohexane



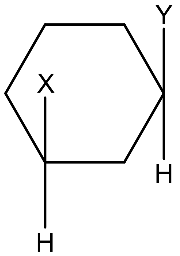
(X=Y= Me)

Two substituents on 1,2-positions of a cyclohexane are said to be **trans,** if they occupy diequatorial (e,e) or diaxial (a,a) orientation, **Trans**-1,2- dimethylcyclohexane exists in **two** energetically **non-equivalent** conformations-diaxial (a,a) (IVa) and diequatorial (e,e) (IVb) which are chiral (C_2 symmetry). Unlike 1,2-**cis**, the **trans** -1,2-dimethylcyclohexane exists as a resolvable pair of enantiomers (racemate). The diequatorial conformation contains one gauche-butane interaction (e,e-Me), while the diaxial conformer contains four gauche-butane interactions (two for each axial methyl). As a result, the diequatorial form is preferred over diaxial form by three gauche-butane interactions (11.2 KJ/mol) corresponding to 99 % of equatorial isomer.



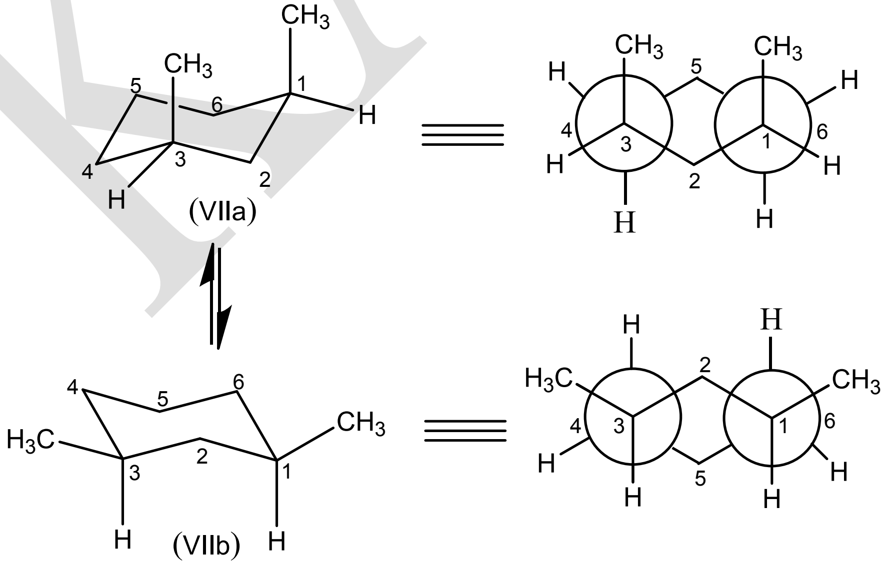
1,3-Disubstituted cyclohexane

i) Cis-1,3-Dimethylcyclohexane



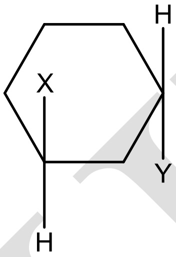
(X=Y= Me)

Two substituents occupying 1,3-positions of a cyclohexane are said to be **cis**, if they occupy diaxial (a,a) or diequatorial (e,e) orientation. **Cis**-1, 3- dimethylcyclohexane exists as two energetically **non-equivalent chair conformations** (a,a and e,e) (VIIa & VIIb) which are **achiral** due to the presence of a σ plane ($\equiv S_1$) (passing through C-2 and C-5) and so they constitute **meso** forms. The diequatorial conformer (VIIb) has no gauche-butane interactions while the diaxial form (VIIa) has two (one for each methyl) corresponding to an enthalpy of 7.5 KJ/mol and in addition a 1,3-diaxial Me/Me interaction which contributes an additional energy of 15.5 KJ/mol. The total enthalpy of diaxial isomer is thus 23.0 KJ/mol higher than that of the diequatorial one. Hence the contribution of diaxial form is almost negligible to the equilibrium.

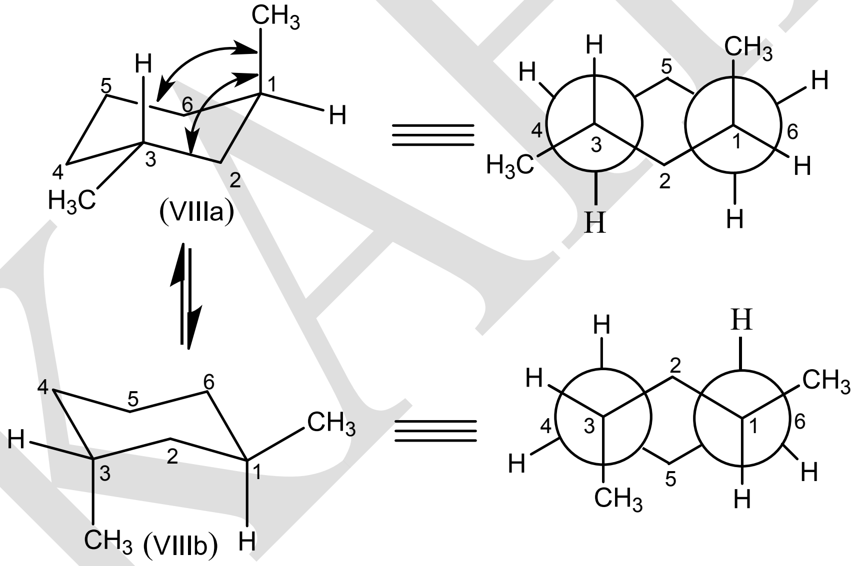


ii) Trans-1,3-Dimethylcyclohexane

Two substituents of a cyclohexane ring occupying 1,3-positions are said to be **trans,** if they bear axial-equatorial orientation. **Trans**-1,3-dimethylcyclohexane exists as two non-superimposable chair conformations (a,e) (VIIIa & VIIIb) each with two gauche-butane interactions corresponding to an enthalpy of 7.5 KJ/mol and is less stable than 1,3-**cis**-isomer (e,e) by the same amount.



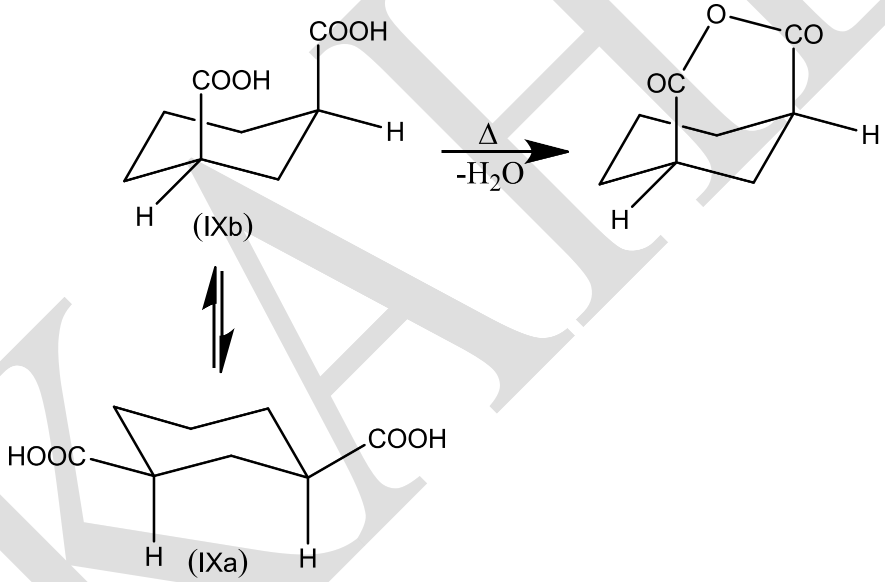
(X=Y= Me)

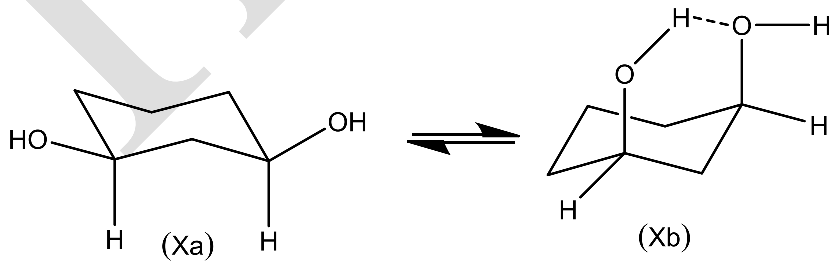


Thus, unlike the 1, 2 (also 1,4-) series, 1,3-**cis** is more stable than 1,3- **trans-** isomer. It is to be noted that **trans-**1,3-dimethylcclohexane exists as a resolvable racemate [(±)], since the chair inversion converts the molecule into an identical structure (unlike **cis**-1,2-dimethylcyclohexane where chair inversion converts the molecule into its mirror image).

When the two substituents are different (X≠Y) both **cis** and **trans** isomers are resolvable, the former (**cis**) exists in the predominantly diequatorial form and the latter (**trans**) in the equatorial–axial conformation with bulkier group occupying equatorial position.

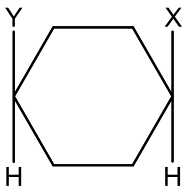
The preferred diequatorial conformation of **cis**-1,3-isomer is not suitable for certain reactions (eg. anhydride formation, hydrogen bond formation between 1,3–groups etc.) as the 1,3-groups are far apart in this conformation. However, ring inversion of the diequatorial form converts it into a diaxial conformation in which 1,3-groups are close to each other. The formation of anhydride from **cis-**1,3-cyclohexanedicarboxylic acid (IX) and the intramolecular hydrogen bond formation in **cis**-1,3-cyclohexane diol (X) takes place through the diaxial conformations (IXb & Xb) of 1,3-**cis**-isomer.





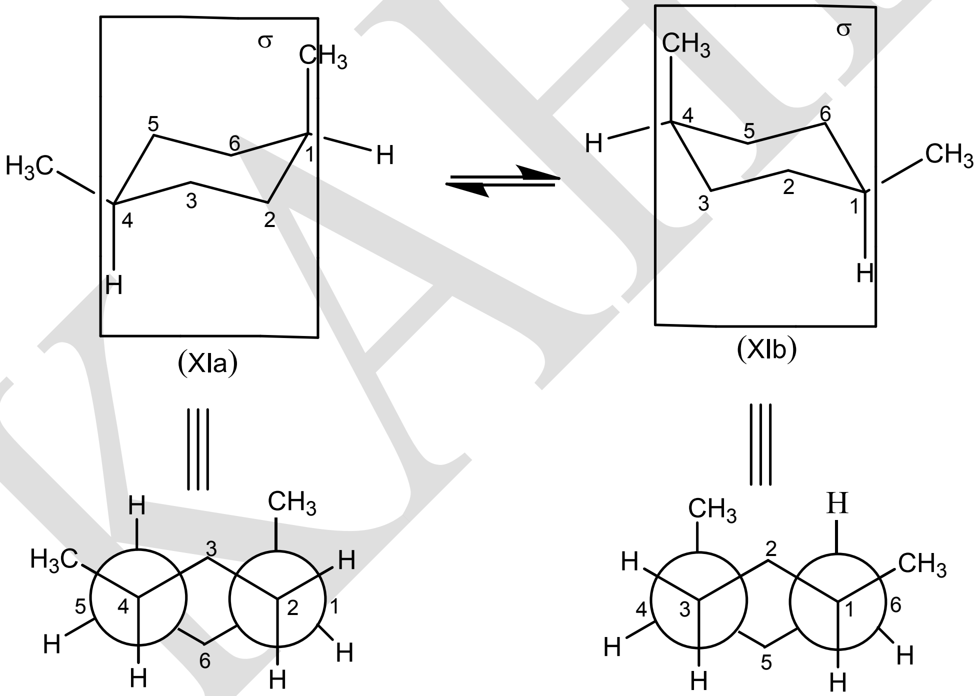
1,4-Disubstituted cyclohexanes

i) Cis-1,4-dimethylcylohexane



(X=Y= Me)

Two substituents on 1,4-position of a cyclohexane ring are said to be **cis**, if they bear axial-equatorial orientation. **Cis**-1,4-dimethylcyclohexane exists in **two identical** (a,e) and (e,a) conformations (XIa & XIb). A vertical σ-plane passes through 1,4-positions and so all conformations are **achiral** even when the two substituents are different. When both substituents are different (X≠Y), the **cis**-isomer exists in two unequally populated conformers, the preferred conformer is the one with bulkier group in equatorial position.

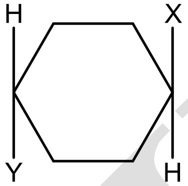


(XIa) (XIb)

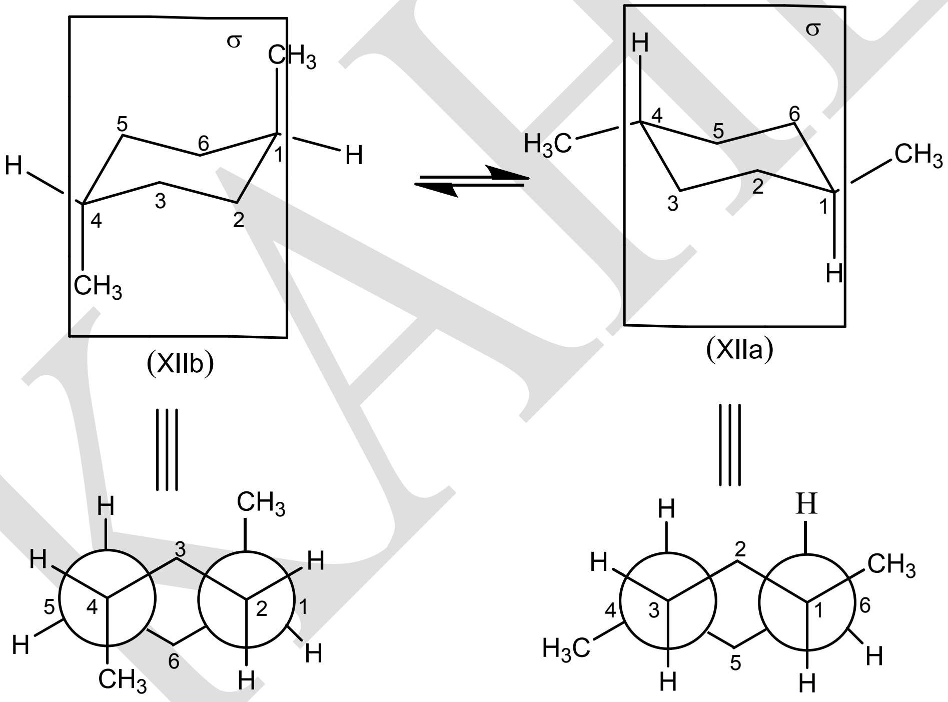
ii) Trans-1,4-dimethylcylohexane

Two substituents occupying 1,4-positions of a cyclohexane ring are said to be **trans**, if they bear diaxial or diequatorial orientation. **Trans**-1,4-dimethylcyclohexane exists in two **non-equivalent** diequatorial (XIIa) and diaxial (XIIb) conformations, of which the latter (a,a) (XII b) is destabilized by **four** gauche-butane interactions (15.0 KJ/mol). Both conformations are **achiral** as a plane of symmetry passes through 1,4-positions.

The **trans**-1,4-isomer is preferred over the **cis-**1,4 by **two** gauche-butane interactions while **trans-**1,4-has none. When both substituents are different (X≠Y), the **trans**-1,4 isomer exists predominantly in diequatorial conformation.



(X=Y= Me)

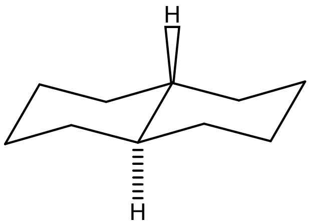


(XIIb) (XIIa)

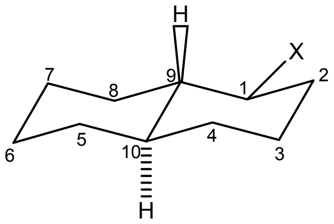
Conformation and chemical reactivity in cyclic systems

Introduction

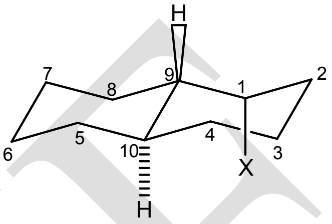
The study of relationship between conformation and chemical reactivity in cyclic systems is mainly concerned with cyclohexanoid system as this system occurs in many polycyclic natural products such as steroids, terpenoids and alkaloids. In cyclohexane ring system, axial and equatorial substituents are in different steric environment and are expected to show difference in their chemical reactivity. However, simple monosubstituted cyclohexane derivatives being conformationally mobile are not ideal molecules to study the reactivity of axial and equatorial substituents as they do not have fixed orientation; ring inversion converts an axial substituent into an equatorial and vice-versa. In order to avoid complications due to conformational inversion, most studies are carried out either on conformationally rigid systems (eg. **trans** decalin derivatives, steroids, terpenoids etc.) or on mobile ring systems that exist almost exclusively in one of the two possible conformations (**Figure 8**) (eg. menthols and **cis-**and **trans**-t-butylcyclohexanols). In **trans** decalin (I), the two cyclohexane rings are fused through their equatorial bonds and the alternative diaxial ring fusion is not possible on geometric grounds, whereas in all natural steroids, B/C ring fusion is **trans**, so that the ring system as a whole is rigid and flat. In such conformationally rigid ring systems, a given substituent has fixed orientation (either axial or equatorial) and such systems are extensively used in the study of reaction mechanisms and conformational analysis. In the latter case, the ring system though mobile, is conformationally homogeneous or biased (anancomeric) because the alternative conformation is highly strained due to bulky groups occupying axial orientation. In the most stable conformation of menthol (IIa) and neomenthol (IIIa) (epimeric alcohols, **Figure 9**), the hydroxyl group is equatorial and axial respectively. The alternative conformations (IIb & IIIb) are highly strained due to the presence of axially oriented bulky isopropyl and methyl groups and make little contribution to the conformational equilibrium.



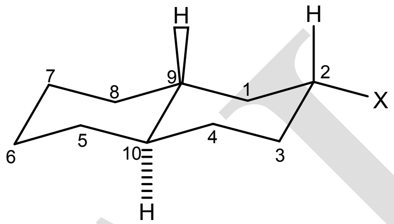
trans-decalin (I)



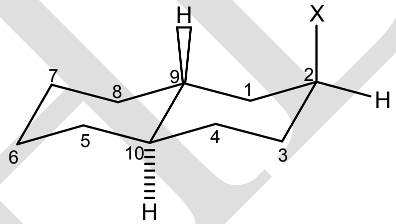
trans-1β (e-X)



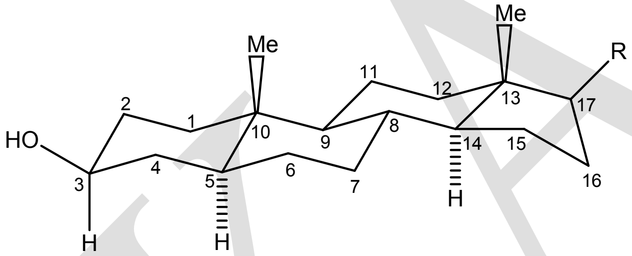
trans-1α (a-X)



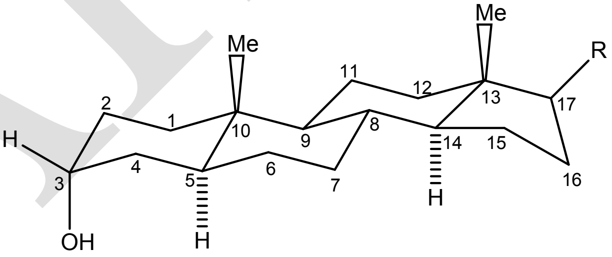
trans-2α (e-X)



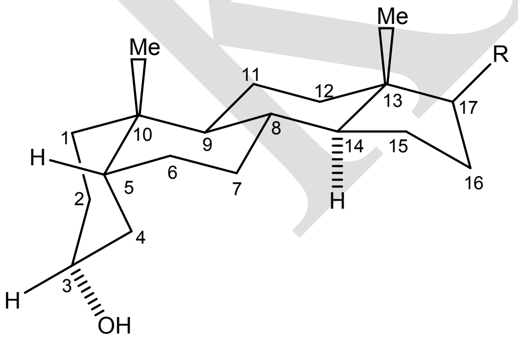
trans-2β (a-X)



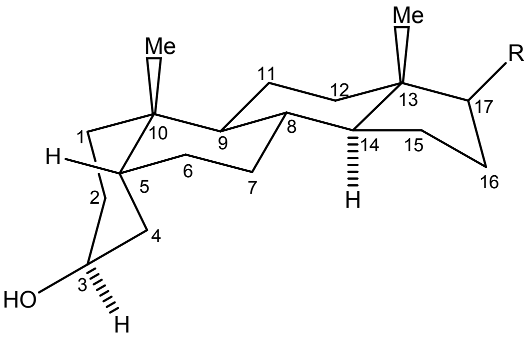
5α-Cholestan-3β-ol (e-X)



5α-Cholestan-3α-ol (a-X)

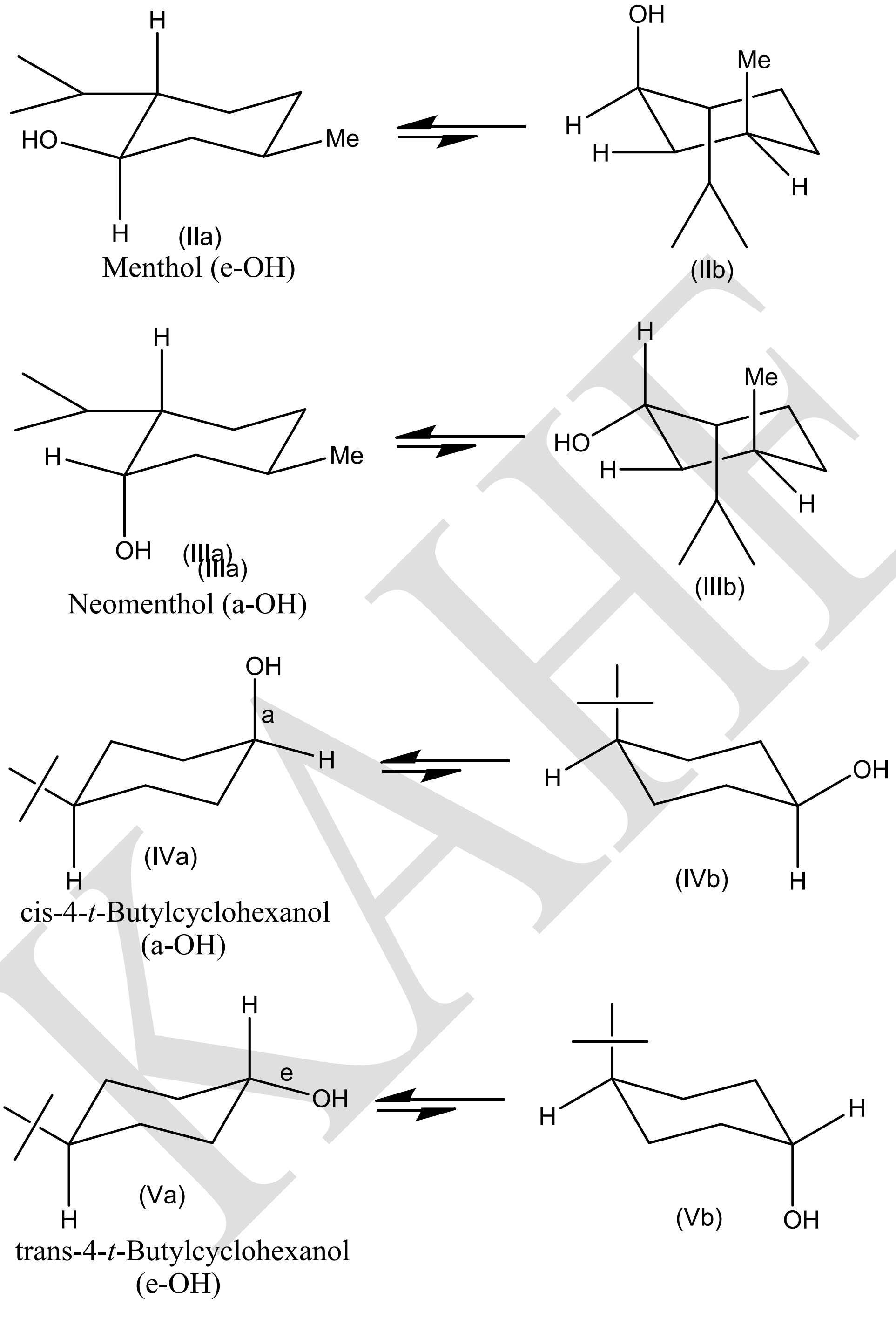


5β-Cholestan-3α-ol (e-X)



5β-Cholestan-3β-ol (a-X)

Figure 8. Conformationally rigid molecules.



(IIa)
Menthol (e-OH)

(IIb)

(IIIa)
Neomenthol (a-OH)

(IIIb)

(IVa)
cis-4-*t*-Butylcyclohexanol
(a-OH)

(IVb)

(Va)
trans-4-*t*-Butylcyclohexanol
(e-OH)

(Vb)

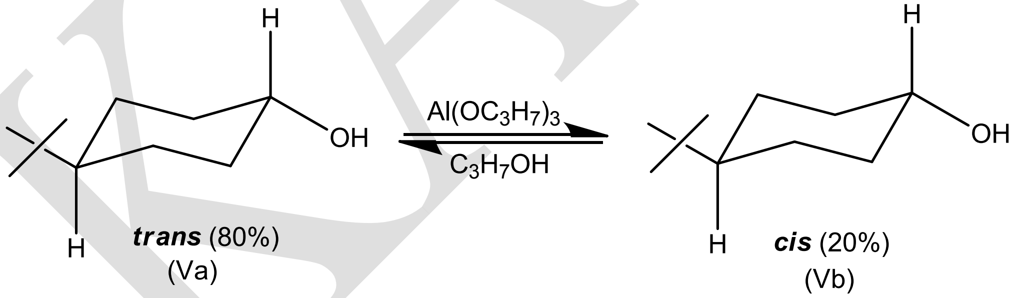
Figure 9. Conformationally biased ring systems.

A tertiary butyl is so large that *t*-butylcyclohexane exists almost entirely in that conformation in which the *t*-butyl group is equatorial. Due to this conformational preference of *t*-butyl group for equatorial orientation, the hydroxyl group in **cis**-4-*t*-butylcyclohexanol (IVa) is **axial** and in the corresponding **trans**-*t*-butylcyclohxanol (Va) the hydroxyl is **equatorial.** The alternative conformations (IVb & Vb) in which the bulky *t*-butyl group is **axial** make negligible contribution to conformational equilibrium (**Figure 9**).

Conformation and chemical equilibrium

The study of effect of conformation on chemical equilibria between configurational isomers furnishes information on the conformational preference of substituents and to predict the position of equilibrium between epimers. The results of such studies can be used to assign the configuration of unknown epimers.

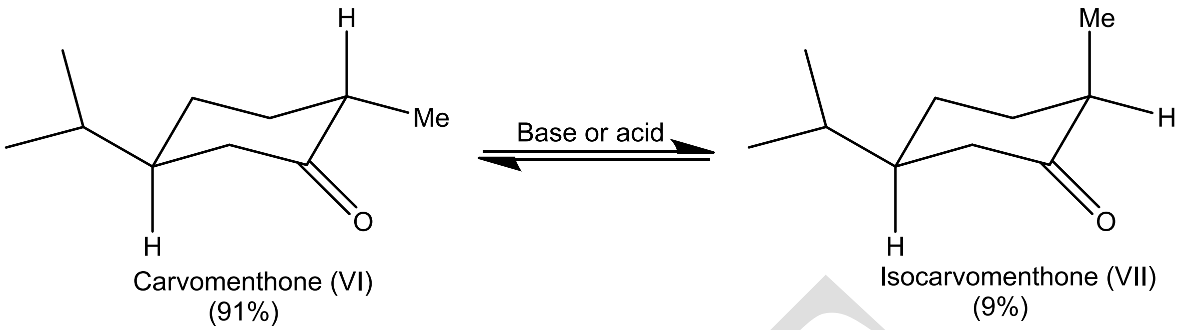
Equatorial isomers are generally more stable than axial isomers because equatorial substituents are sterically less crowded than axial substituents. When two chemically interconvertible epimers having an equatorial and axial substituent are in equilibrium, the isomer with an equatorial substituent will predominate in the equilibrium mixture. For example, the equilibrium mixture of **cis** and **trans**-4-*t*-butylcyclohexanols contained four parts of **trans** isomer (equatorial hydroxyl) (Va) to one part of **cis** isomer (axial hydroxyl) (IVa).



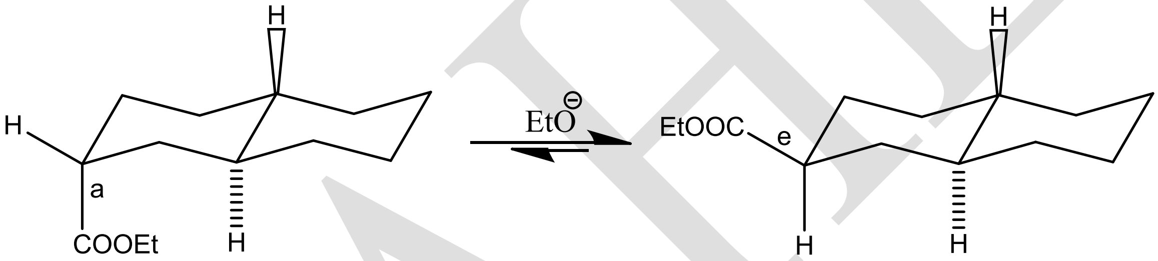
trans (80%)
(Va)

cis (20%)
(Vb)

Likewise, the equilibrium mixture of carvomenthone (VI) and isocarvomenthone (VII) contains 91% of former (methyl and isopropyl equatorial) and 9% of the latter (methyl axial and isopropyl equatorial).

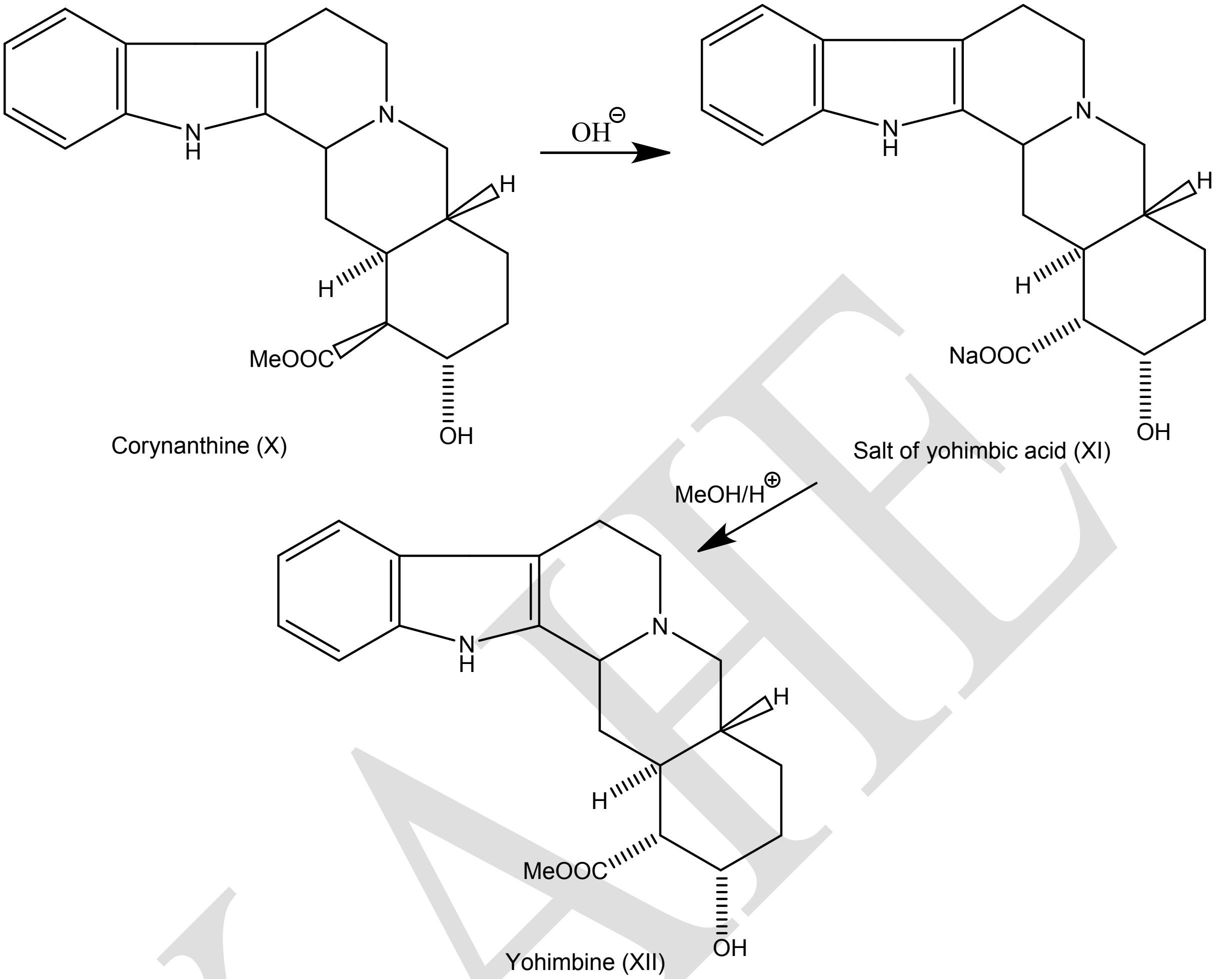


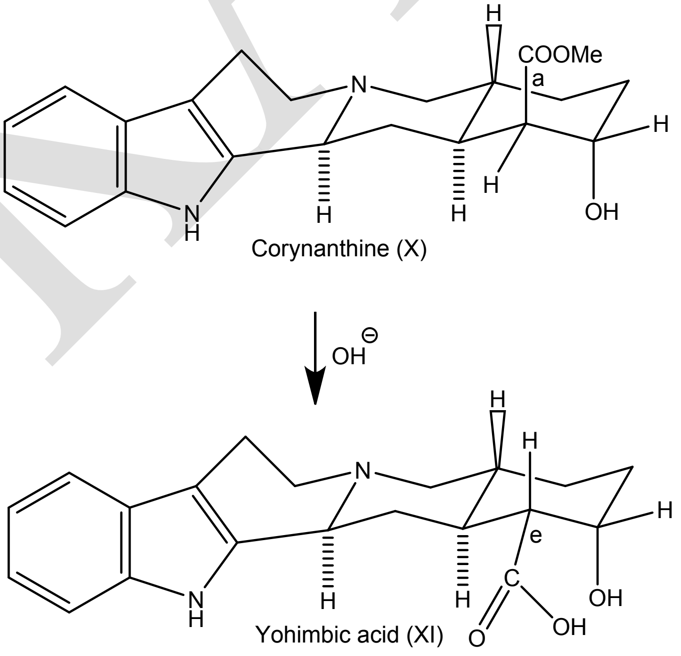
Another example is the interconversion of decalin derivatives (VIIIa & VIIIb) by the action of ethoxide ion; the equilibrium favours the isomer (VIIIb) with equatorial methoxycarbonyl group.



(VIIIa) (VIIIb)

The observation that saponification of both yohimbine (IX) and corynanthine (X) yields only yohimbic acid (XI) (which on reesterification gives only yohimbine) indicates that carbomethoxyl group is equatorial in yohimbine (IX) and axial in corynanthine (X); this change apparently involves the epimerisation of corynanthine to yohimbine under basic conditions prior to saponification of ester group.


OH⊖
MeOOC
OH
H
NaOOC
MeOH/H⊕
Corynanthine (X)
Salt of yohimbic acid (XI)
Yohimbine (XII)


COOMe
a
H
OH
Corynanthine (X)
OH⊖
e
C
O
OH
Yohimbic acid (XI)

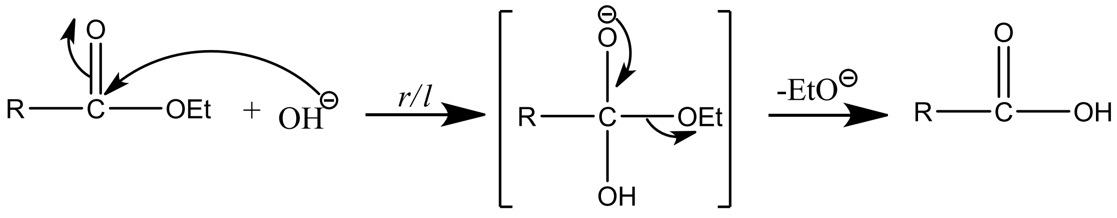
Conformation and chemical reactivity

Axial substituents are in a more crowded environment than equatorial substituents and they show difference in their reactivity. Which isomer reacts faster depends on whether the steric requirements of the transition state are less than, greater than or comparable with those of the ground state. In many reactions, the steric requirements of the transition state are greater than the steric requirements of the ground state. In such reactions, the steric crowding around the **axial** substituent produces steric hindrance and the **axial** isomer reacts slower than the **equatorial** isomer.

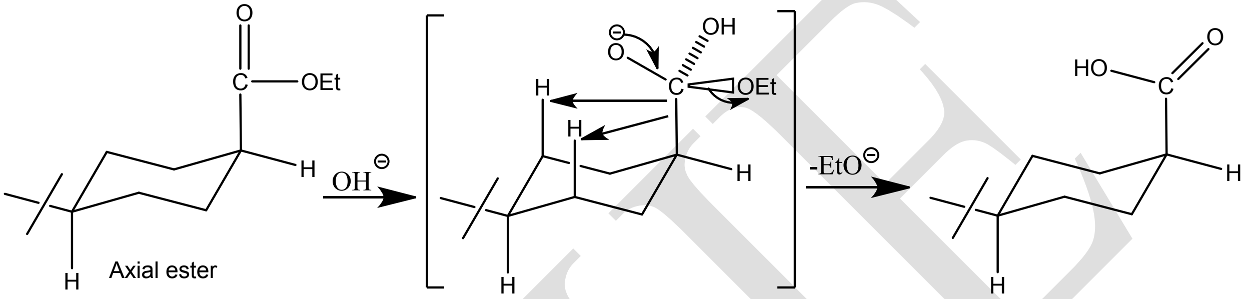
In the study of the effect of conformation on reactivity in cyclohexanoid systems, it is convenient to distinguish reactions at exocyclic atoms and reactions involving ring atoms.

Reactions involving exocyclic atoms

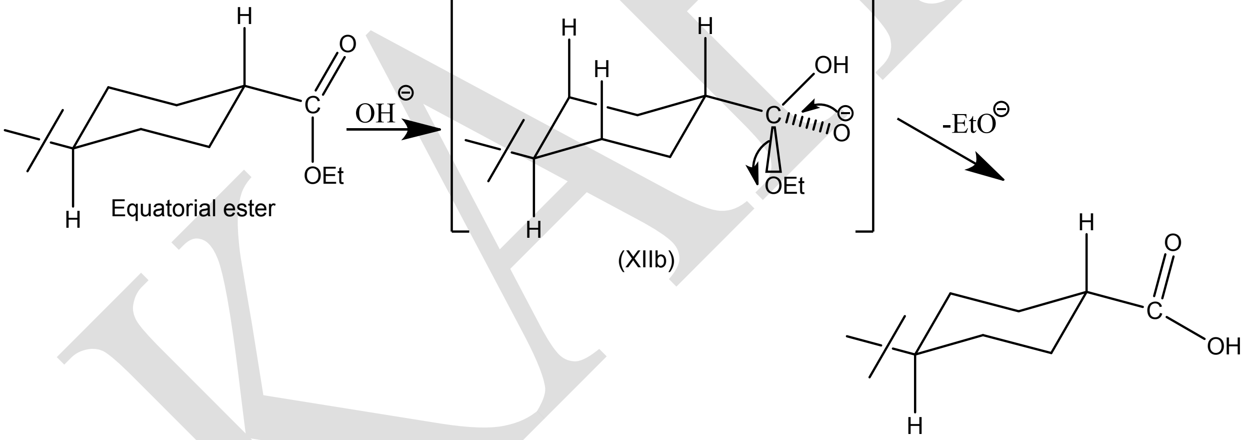
In reactions involving exocyclic positions only **steric factors** need be considered and **stereoelectronic factors** are irrelevant. Reactions such as saponification of esters and esterification of alcohols do not involve any ring atoms but are confined to exocyclic positions. The cyclohexane moiety may be either in the acid or in the alcoholic part of the ester under consideration. **In general, equatorial esters are saponified faster than axial esters and for the same reason equatorial alcohols are esterified faster than the axial alcohols.** In the ester hydrolysis (and in esterification), the rate determining step is the formation of the more space demanding tetrahedral intermediate (XII) by the nucleophilic attack on the carbonyl carbon of the ester. So in the transition state the trigonal carbon of the starting ester is converted into more space demanding tetrahedral carbon; thus the steric requirements of the transition state are greater than those of the ground state. This effect is more pronounced for an axial ester which experiences greater steric strain by virtue of **1,3-syn axial interaction.** As a result, the free energy of the transition state for an axial ester is higher than that of the equatorial ester. In other words, the activation energy for saponification (and esterification) of axial isomer is greater than that of equatorial isomer and the equatorial isomer reacts faster than the axial isomer. The situation in shown diagrammatically in **Figure 10**.



Tetrahedral intermediate
(XII)



(XIIa)



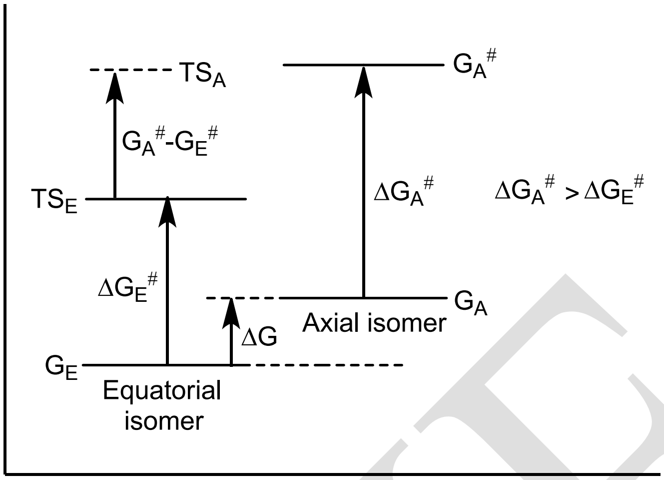
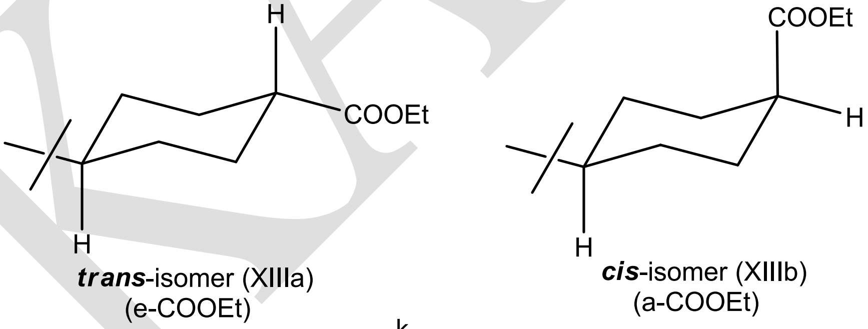


Figure 10. Energy level diagram of ground state and transition state: case of steric hindrance.

In the saponification of ethyl 4-*t*-butylcyclohexane carboxylate in 70% ethanolic sodium hydroxide, the trans-isomer (XIIIa) reacts about 20 times as fast as the cis-isomer (XIIIb) (k_{trans}/k_{cis}=20).

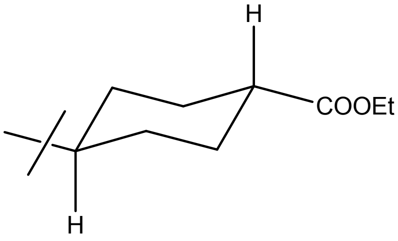
The greater rate of saponification of **trans-**isomer (XIIIa) is attributed to the greater reactivity of the equatorial ester group compared with axial ester group of **cis**-isomer (XIIIb).



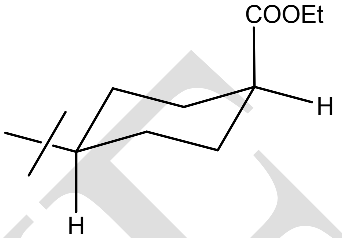
$$\frac{k_{trans}}{k_{cis}} = 20$$

The relative rates of saponification (k_{trans}/k_{cis}) of 4-*t*-butylcycohexyl-p-nitrobenzoates (XIVa & XIVb) and ethyl 4-*t*-butylcyclohexanecarboxylates (XVa & XVb) are 2.5 and 20 respectively.

The steric effect on the rate of saponification is greater when the cyclohexyl moiety is in acid part than when it is in alcoholic part. In the former case the C=O of the ester is close to the cyclohexane ring and experiences greater steric hindrance in the transition state than when it is in external acid part. Thus, the relative rate (k_{trans}/k_{cis}) for the saponification of ethyl-4-*t*-butylcyclohexanecarboxylates (XVa & XVb) and 4-*t*-butylcyclohexyl-*p*-nitrobenzotes (XIVa & XIVb) is 20 and 2.5 respectively.

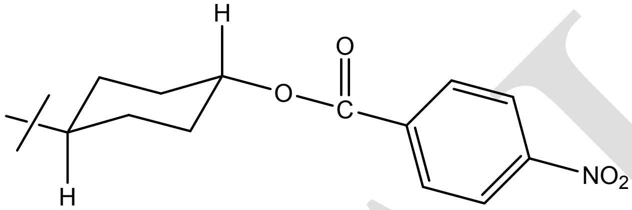


trans-isomer (XVa)
(e-COOEt)

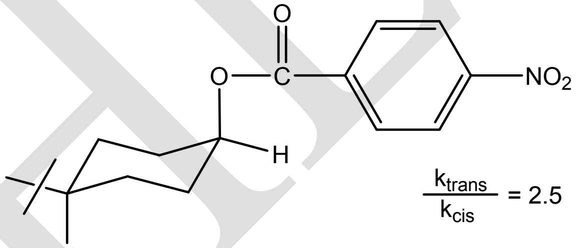


cis-isomer (XVb)
(a-COOEt)

$$\frac{k_{trans}}{k_{cis}} = 20$$



trans-isomer (XIVa)



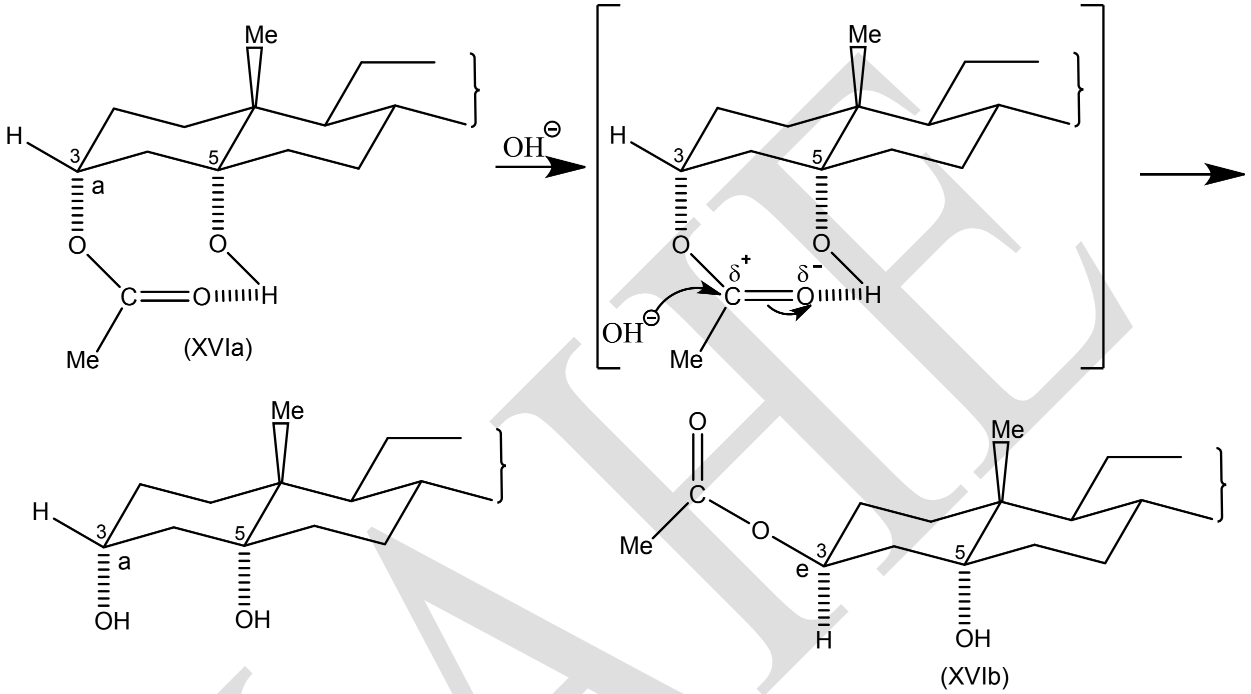
cis-isomer (XIVb)

$$\frac{k_{trans}}{k_{cis}} = 2.5$$

The observation that equatorial esters are saponified faster than the axial esters finds application in the configurational assignment of natural products. Yohimbine (IX) and coynanthine (X) are the epimers differing in the configuration of carbomethoxyl group at C-16. Experimentally, it is found that yohimbine (IX) is saponified more rapidly than coynanthine (X), therefore, the carbomethoxyl group is equatorial in yohimbine (IX) and axial in coynanthine (X). This conclusion is supported by the fact that the common product of hydrolysis (yohimbic acid) (XI) upon esterification gives only yohimbine (IX) in which the carbomethoxyl group occupies more stable equatorial position.

One exception to the general rule that equatorial esters are hydrolysed faster than axial esters in provided by the observation that the alkaline hydrolysis of 3α-acetoxycholestan-5α-ol (XVIa) proceeds faster than the corresponding 3β-isomer (XVIb). There is some evidence to show that there is intramolecular hydrogen bond interaction between the oxygen of C=O of the ester and the hydrogen of the hydroxyl at C-5, which is possible when both substituents are

axial. The intramolecular hydrogen bond formation facilitates the nucleophilic attack on the carbonyl carbon of the ester by the hydroxide ion, thereby increasing the rate of hydrolysis. On the other hand, such intramolecular hydrogen bond formation cannot occur in 3β-epimer (XVIb) in which 3-acetoxyl is equatorial.



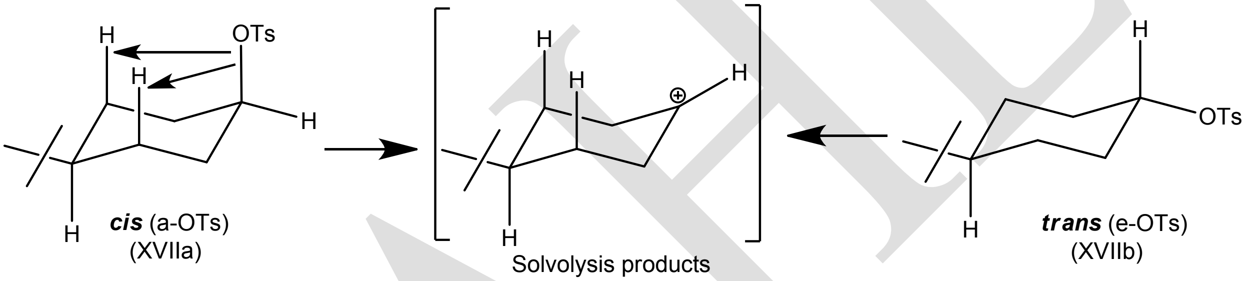
Reactions at the ring positions: steric control

There are also reactions in which the steric requirements of the ground state are greater than those of the transition state. In such cases, any steric strain by virtue of **1,3-syn axial interactions** in the ground state of the axial isomer is relieved in the transition state and the high ground state energy is reflected in a low activation energy for the reaction of the axial isomer and the axial isomer reacts faster than the equatorial isomer ($\Delta G^{\#}_{A} < \Delta G^{\#}_{E}$). The acceleration of this type is called **"steric assistance"** and manifests itself whenever, the ground state energy difference between equatorial and axial isomers is relieved in the transition state.

An example of **"steric assistance"** is provided by the solvolysis of **cis-** and **trans** 4-*t*-butylcyclohexyl tosylates (XVIIa & XVIIb). The solvolysis (S_N1) proceeds through the rate limiting formation of the carbonium ion. During this process, the space demanding sp^3

hybridised carbon atom of the ground state molecule is changed into less space demanding sp^2 carbon in the transition state. Thus the steric requirements of the transition state are less than those of the ground state.

Since the transition states for both **equatorial** and **axial** isomers must resemble the carbonium ion, the ground state energy difference (ΔG) between equatorial (**trans)** and axial (**cis**) isomers disappear in the transition states (**Figure 11**). In other words, the transition states for equatorial and axial isomers differ only slightly in their energy and high ground state energy of the axial isomer will be reflected in low activation energy and the less stable **axial** isomer (**cis**) (XVIIa) reacts faster than the equatorial isomer (**trans**) (XVIIb).



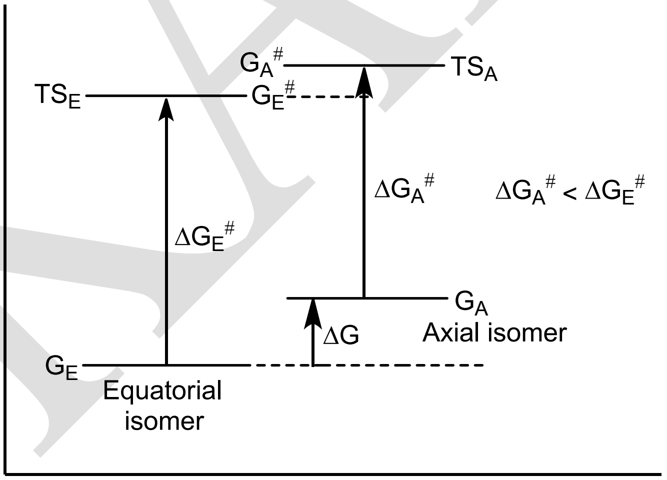
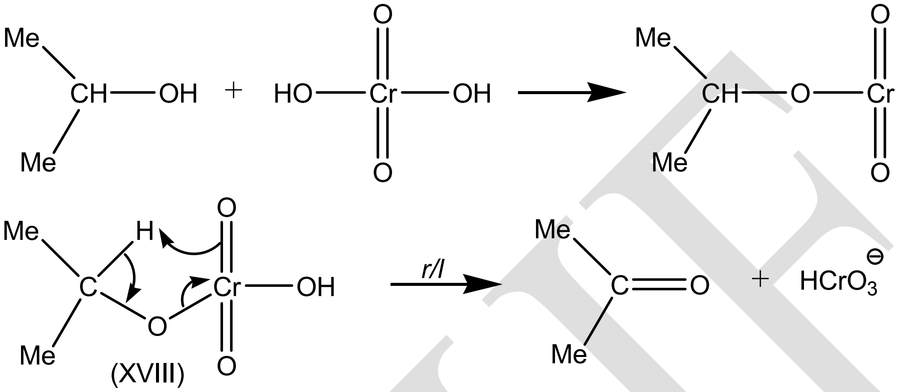


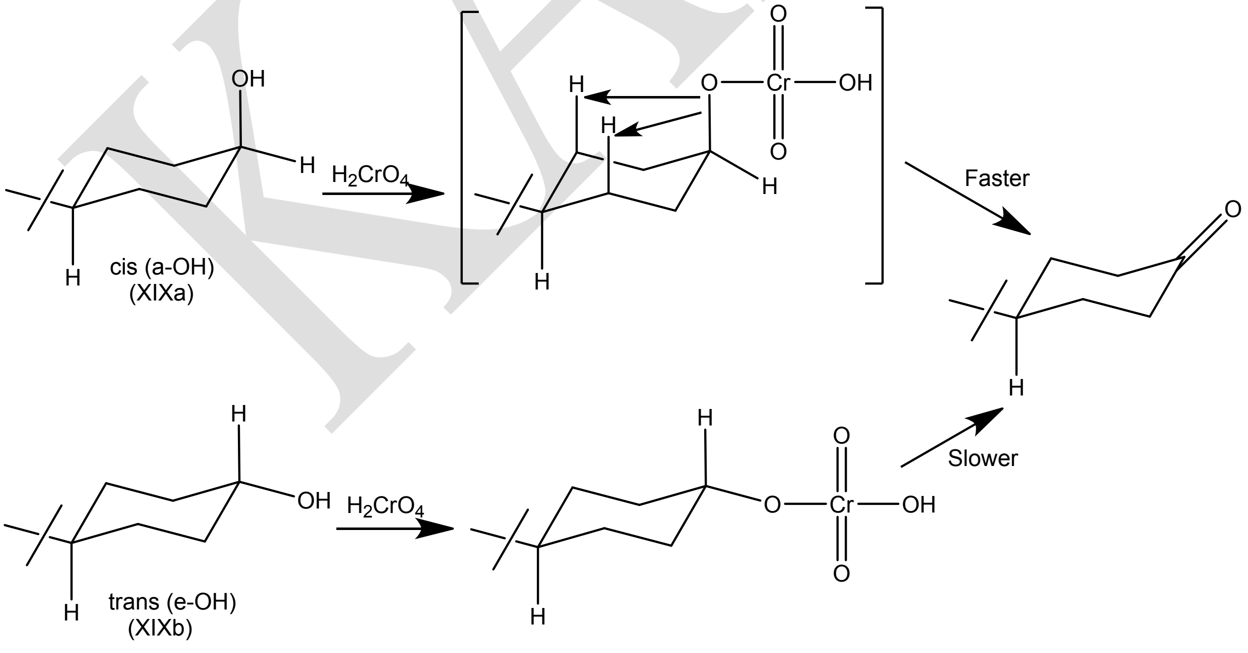
Figure 11. Energy level of ground state and transition state: case of steric assistance.

Another example of the concept of **steric assistance** is the chromic acid oxidation of secondary alcohols. **Secondary axial alcohols are more rapidly oxidised by chromic acid than secondary equatorial alcohols. Further, the more hindered the secondary axial**

alcohol, the faster the rate of oxidation. The oxidation of secondary alcohols with chromic acid has been shown to proceed through the initial formation of the chromate ester (XVIII) of the alcohol; the rate determining step involves the removal of the **alpha** hydrogen of the chromate ester with concomitant elimination of $HCrO_3^-$ group.



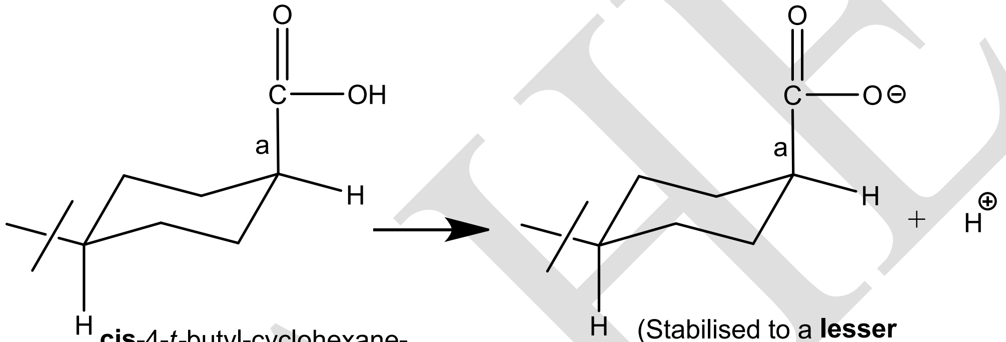
Any steric strain by virtue of 1,3-**syn axial interaction** in the axial alcohol or of its chromate ester is relieved in the transition state when the sp^3 hybridised ring carbon atom is changed into the less space demanding sp^2 carbon atom in the transition state. The high ground state energy of the **axial alcohol** is reflected in low activation energy and the less stable **axial** secondary alcohol undergoes oxidation faster than the **equatorial** secondary alcohol.



Problem 2.Of trans and cis-4-*t*-butylcarboxylic acids which is stronger and why?

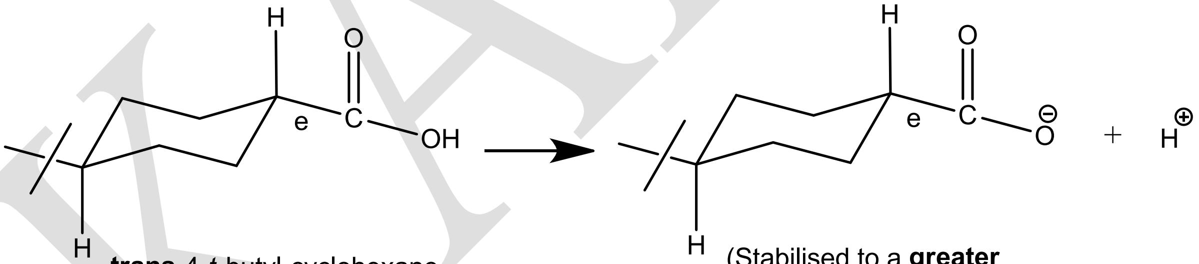
Solution:

Trans-4-*t*-butylcyclohexanecarboxylic acid is stronger than **cis**. Any factor that stabilizes the anion of the acid relative to the acid increases the acidity. **Trans**-4-*t*-butylcyclohexanecarboxylic acid is stronger because, the corresponding anion (equatorial COO^-) is solvated to a greater extent (and hence stabilized to a greater extent) than that of the **cis**-acid which, being axial, encounters some steric hindrance for solvation.



cis-4-*t*-butyl-cyclohexane-carboxylic acid
(pK_a = 8.23)

(Stabilised to a **lesser extent** by solvation)



trans-4-*t*-butyl-cyclohexane-carboxylic acid
(pK_a = 7.79)

(Stabilised to a **greater extent** by solvation)

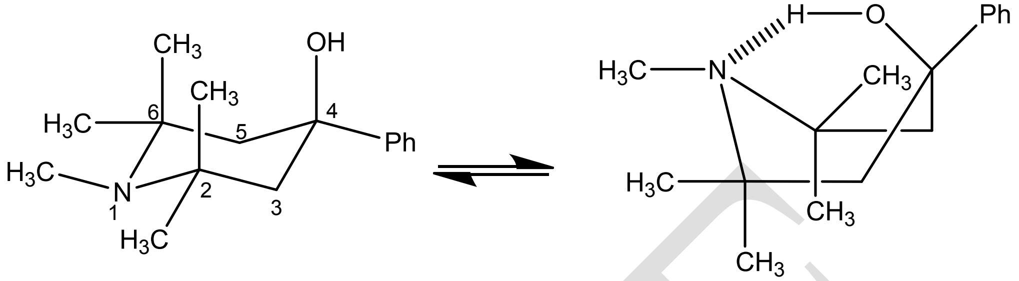
Problem 3. Sketch the preferred conformation of the following

(i) 1,2,2,6,6-pentamethyl-4-hydroxyl-4-phenylpiperidine

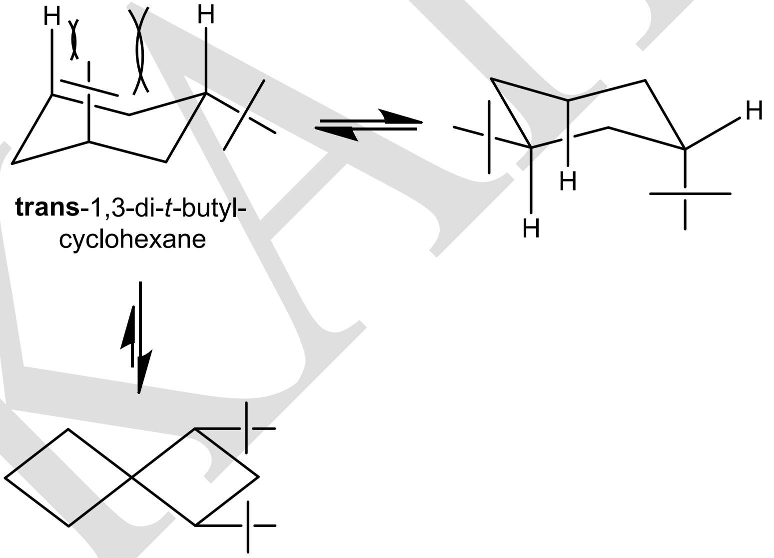
(ii) Trans-1,3-di-*t*-butylcyclohexane.

Solution:

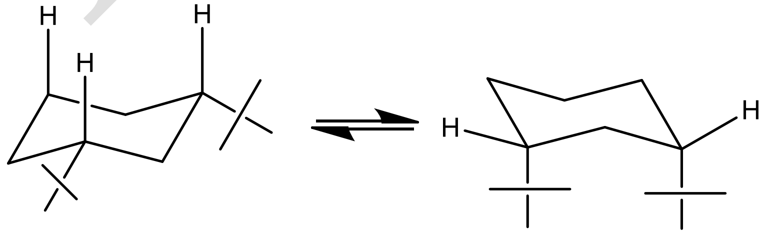
(i) This molecule exists predominantly in boat conformation. The chair conformation of this molecule is highly strained due to steric hindrance between **syn**-axial methyls (on C-2 and C-6), which is relieved in boat conformation. IR spectrum of the molecule gives evidence for intramolecular hydrogen bonding which is possible only in boat conformation.



(ii) Trans-1,3-di-*t*-butylcyclohexane exists in twist boat conformation . If this molecule were to exist in chair conformation, one of the *t*-butyl groups should occupy axial orientation. Thus, either chair conformation of the molecule is highly strained due to **syn**-axial interaction between the axial bulky *t*-butyl group and **syn**-axial hydrogens on C-3 and C-5. The steric interaction can substantially be reduced in the flexible conformations (In the chair form of **cis**-1,3-di-*t*-butylcyclohexane both *t*-butyl groups occupy equatorial position).



trans-1,3-di-*t*-butyl-cyclohexane

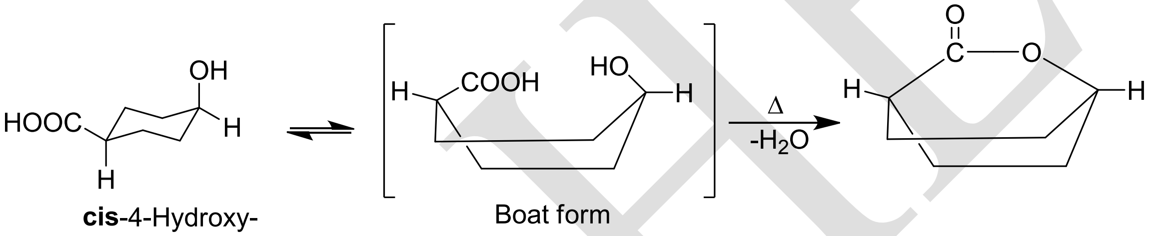


cis-1,3-di-*t*-butyl-cyclohexane

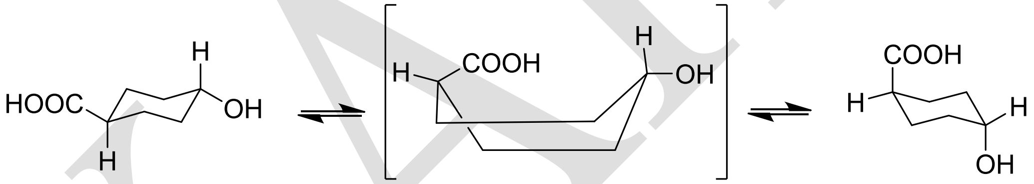
Problem 4. Account for the observation that **cis**-4-hydroxycyclohexanecarboxylic acid on heating readily lactonises, whereas under the same conditions the **trans**-isomer does not lactonise.

Solution:

Although, a given molecule exists predominantly in chair conformation, the flexible form (boat or twist boat) may be important in certain reactions. For example, in the chair conformation of **cis**-4-hydroxycyclohexanecarboxylic acid, the hydroxyl and carboxyl groups being axial and equatorial are not suitably oriented for lactonisation. However, the boat conformation permits the lactonisation by bringing the 1,4-substituents (OH and COOH) closer together.



cis-4-Hydroxy-
cyclohexanecarboxylic acid



trans-4-Hydroxy-
cyclohexanecarboxylic acid

Trans-4-hydroxycyclohexanecarboxylic acid does not lactonise because the hydroxyl and carboxylic groups being either diequatorial or diaxial (**trans**) are not suitably oriented for lactonisation.

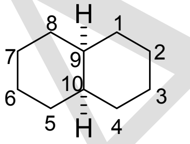
Conformations of fused ring compounds

Decalins : Bicyclo [4.4.0] decane

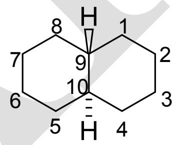
A fused ring system is one in which adjacent rings have two atoms in common. By for the most important fused ring system is the decalin which exists in two diastereoisomeric forms, the **cis** and the **trans.** If cyclohexane ring system were to be planar as suggested by Baeyer, only one form of decalin with ring junction hydrogens projecting on the same side of the molecule should exist. On the other hand, Sachse-Mohr concept of puckered rings permits the existence of two isomeric forms of decalin. In fact, Mohr predicated that two isomeric forms of decalin molecule should exist before W. Huckel succeeded in preparing them. Both isomeric forms of decalin occur in petroleum ether.

Geometry

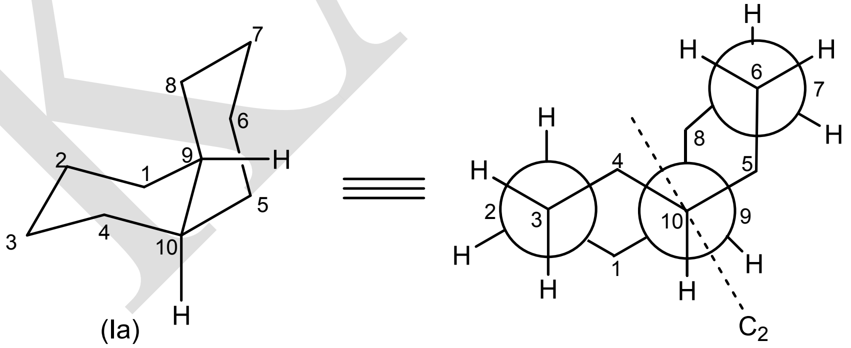
The cyclohexane rings in both **cis** and **trans**–decalins exist in chair conformation. **Cis**-decalin (I) is formed when both cyclohexane rings are joined through **axial-equatorial** bonds, whereas, the **trans**-decalin (II) is produced by joining the two cyclohexane rings through **equatorial** bonds only. **Trans**-decalin (II) has rigid geometry and cannot undergo ring inversion which would lead to a highly strained ring system with diaxial fusion. In contrast, **cis-**decalin in which two cyclohexane rings are fused through **axial-equatorial** bonds can readily undergo ring inversion by exchanging **a,e** bonds at ring junction. The two interconvertible chair conformations (Ia & Ib), similar to **cis** –1, 2-dimethylcyclohexane are equienergetic and so equally populated at room temperature. As in the case of **cis**-1, 2-dimethylcyclohexane, the ring inversion converts one conformer into its mirror image; **cis**-decalin (I) is therefore a non-resolvable recemate (±).



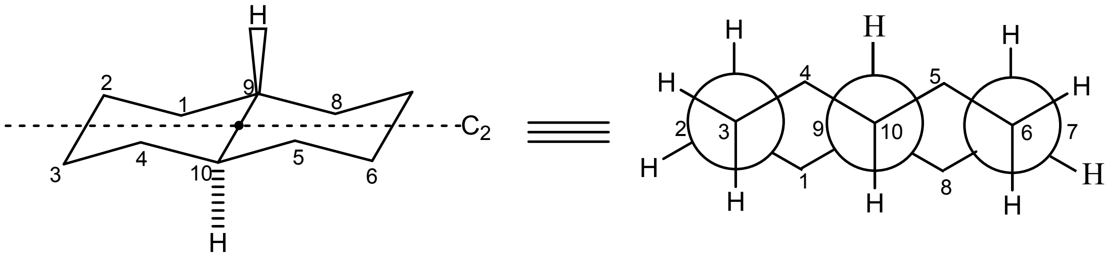
(I)



(II)



(Ia)

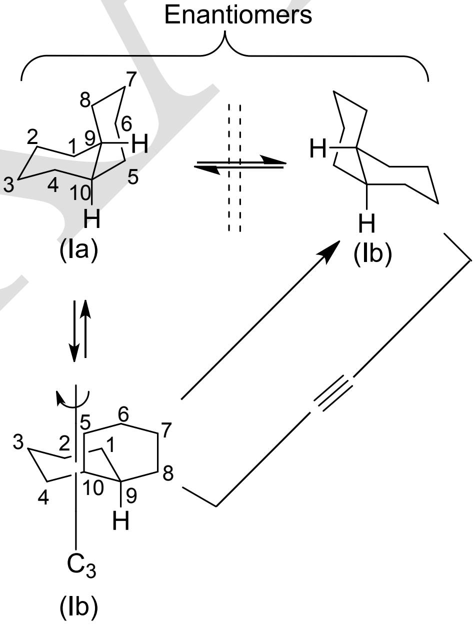


(II)

Symmetry

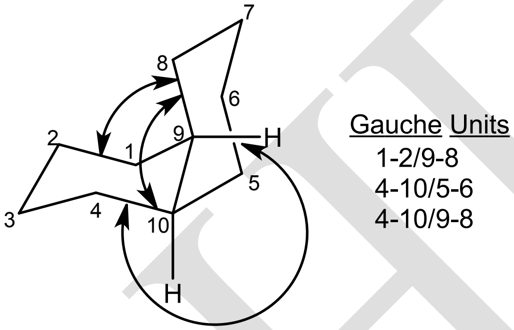
The conformation of **trans**–decalin (II) has a centre of symmetry (mid print of 9-10 bonds) and is **achiral.** In addition, it possesses a C_2 axis passing through $C_2 – C_{3,}$ $C_9 – C_{10}$ and $C_6– C_7$ bonds and a σ – plane perpendicular to C_2 axis and passing through the ring junction. It belongs to C_{2h} point group and its symmetry number is 2. On the other hand, the individual conformations of **cis**–decalin molecule are **chiral** as they are devoid of mirror symmetry. They have a C_2 axis passing through the midpoint of $C_9– C_{10}$ bond and bisecting the dihedral angle between 9-H and 10-H. Their symmetry number is also 2 and belongs to C_2 point group.

Since the two individual conformations of **cis-**declain are enantiomeric and equienergetic they are readily interconvertible at a rate too fast to separate them. So **cis**-decalin molecule is a non–separable racemate.



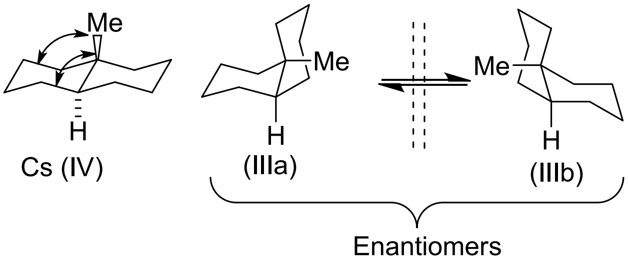
Enthalpy and free energy

The difference in enthalpy between **cis-**and **trans-**decalins can be determined by counting the number of gauche-butane interactions. In **trans-** decalin, since each ring is fused through the equatorial bonds, no gauche-butane interactions exist. In **cis-**decalin, there are **three** such interactions and the difference in enthalpy is therefore amounts to 10.5 KJ/mol (3×3.3 KJ/mol). Therefore, **trans**-decalin is more stable than **cis**.



Effect of angular methyl group

Introduction of a methyl group at one of the fused carbon atoms as in steroids (C-9 or C-10) gives rise to additional gauche- butane interactions and consequently the potential energy difference between **cis**-and **trans**-9-methyldecalin system (III & IV) is less than that of **cis**–and **trans**–decalin (I & II). The angular methyl group in **trans**-9- methlydecalin (IV) is axial and gives rise to four butane-gauche interactions (two with respect to each ring). In **cis**-9-methyldecalin (III), the 9-methyl group is axial with respect to one ring only and equatorial with respect to the other, giving rise to two gauche-butane interactions in addition to three already present in **cis-**decalin. Thus, the total number of gauche-butane interactions in the **cis-** compound is therefore five, that is one more than the **trans-** isomer. Thus, the original difference between **cis** and **trans-**decalins is reduced to one in 9-methyldecalin in farvour of the **trans**–isomer which is more stable than the **cis**-isomer by 3.35 KJ/mol.



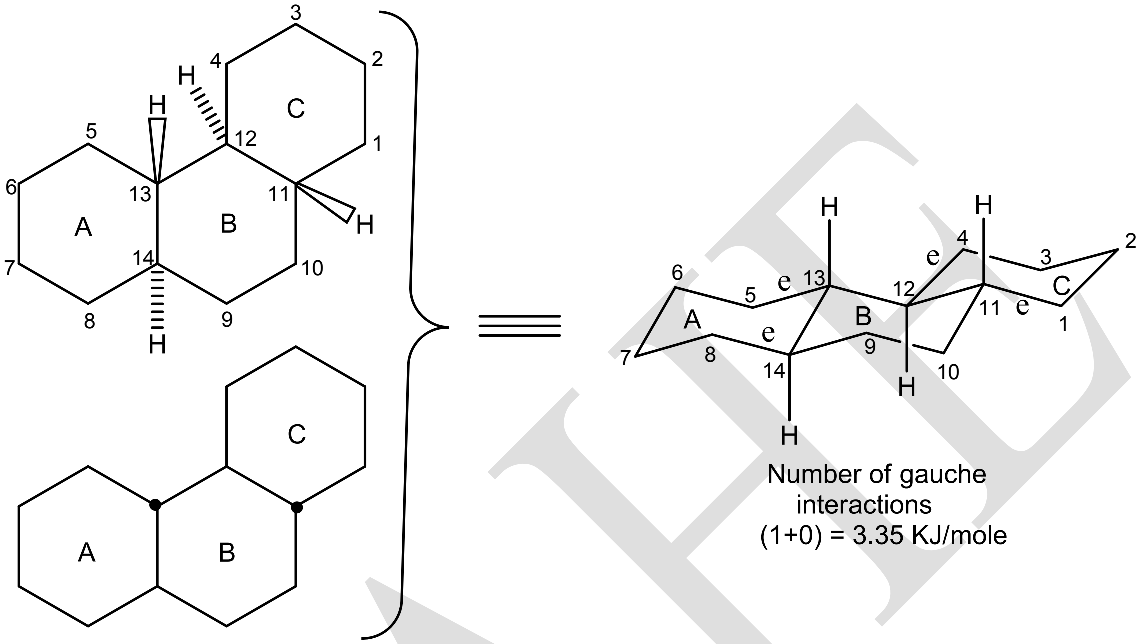
Trans-9-methyldecalin (IV) does not have any C_2-axis but possesses a plane of symmetry (σ) passing vertically along 9-10 bond and hence **achiral** (C_s point group). The individual conformations of **cis**-9-methyldecalin (IIIa & IIIb) are **chiral** as they are devoid of mirror symmetry (C_1 point group) and constitute a pair of equienergetic enantiomers. However, the two enantiomers are readily interconvertible by ring inversion and **cis**-isomer is thus a non–separable racemate (±).

Conformations of fused polycyclic ring systems

Conformations of perhydrophenanthrene

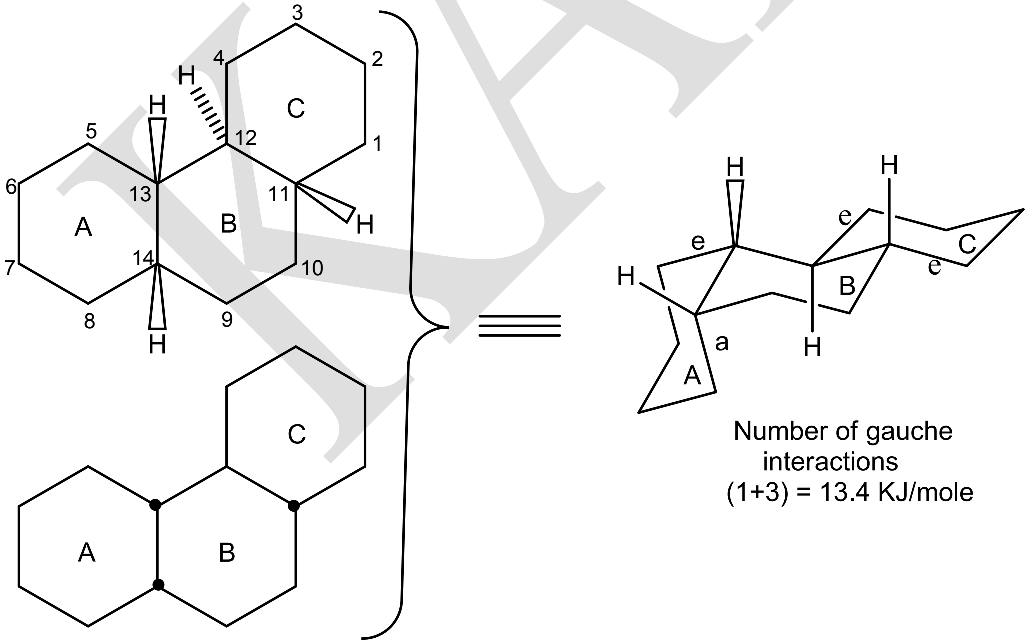
Among the fused tricyclic systems, the perhydrophenanthrene molecule is interesting in that it illustrates man stereochemical aspects of polycyclic natural products such as steroids and triterpenoids. Perhydrophenanthrene molecule contains four like chiral centres (ABAB) and so exists as **two meso** and **four racemates** (the number of like chiral centres is even and so the number of **meso** forms is $2^{(4-2)/2} = 2$ and the number of optically active forms is $2^{(4-1)} = 2^3 = 8$ which form four racemates). The six diastereoisomeric forms are shown along with their conformational representations (for chiral forms, only one enantiomer of each (±) – form is drawn).

The prefixes **cis** and **trans** are used to denote the stereochemistry of fusion of terminal rings (A and C) to the central ring (B), whereas **syn** and **anti** are used to indicate the orientation of terminal rings (A and C) with respect to each other (that is by considering the relative position of hydrogens at C-12 and C-13. The prefixes **syn** and **anti** are used when these hydrogens are on the **same** or **opposite side** respectively). A heavy dot indicates that the hydrogen atom is above the plane of the ring system whereas the absence of a dot indicates that the hydrogen is below the plane of the ring system. The relative stabilities of the six diastereoisomers have been assessed by counting butane-gauche interactions.



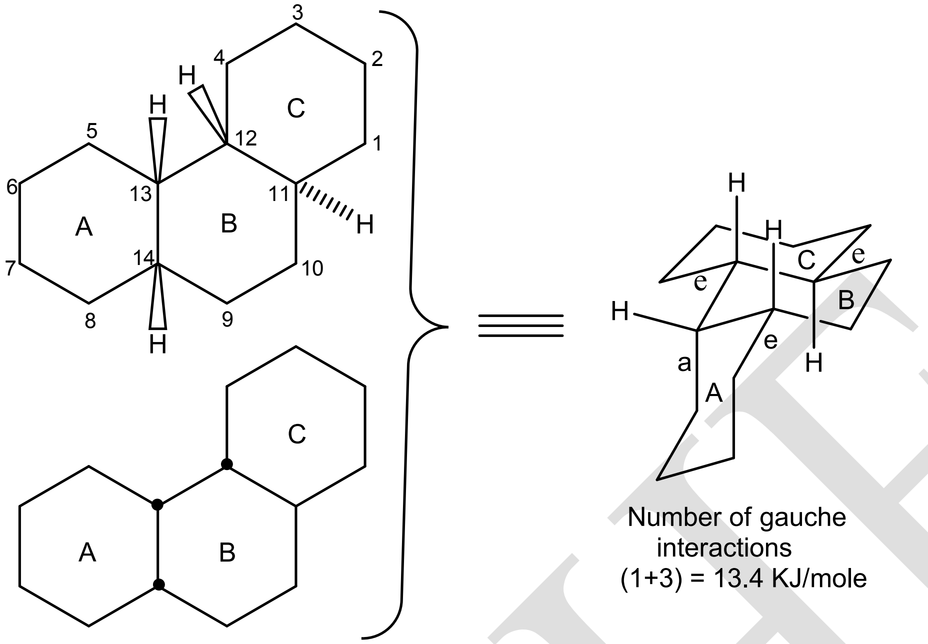
Number of gauche interactions
(1+0) = 3.35 KJ/mole

(±)-trans-anti-trans (4e) (I)



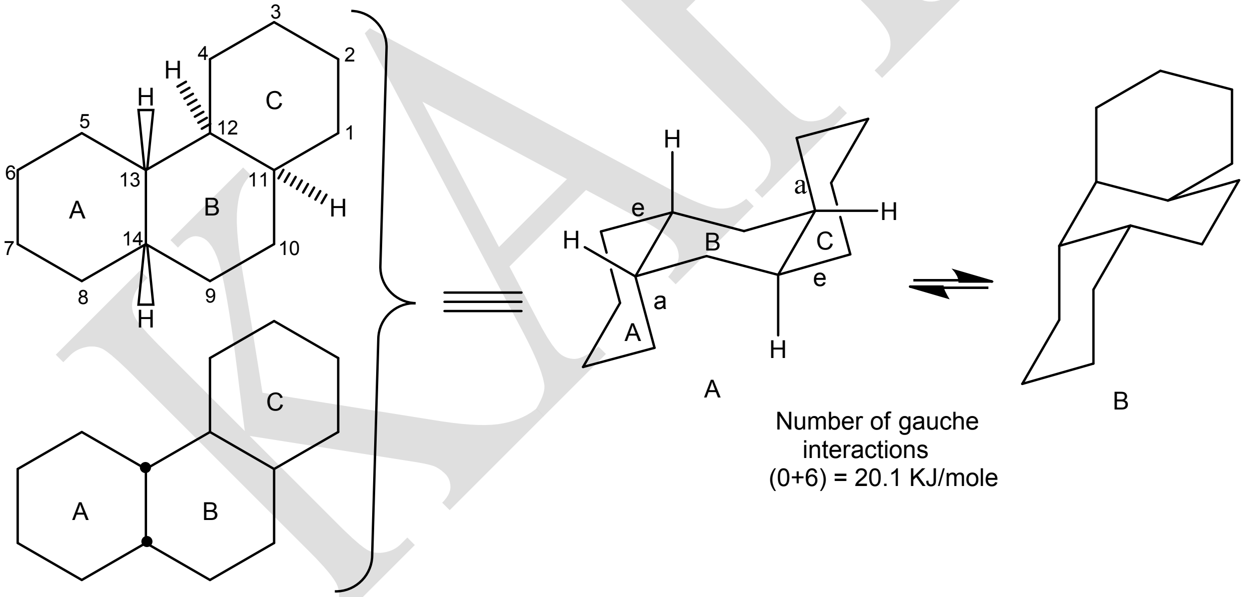
Number of gauche interactions
(1+3) = 13.4 KJ/mole

(±)-cis-anti-trans (3e + 1a) (II)



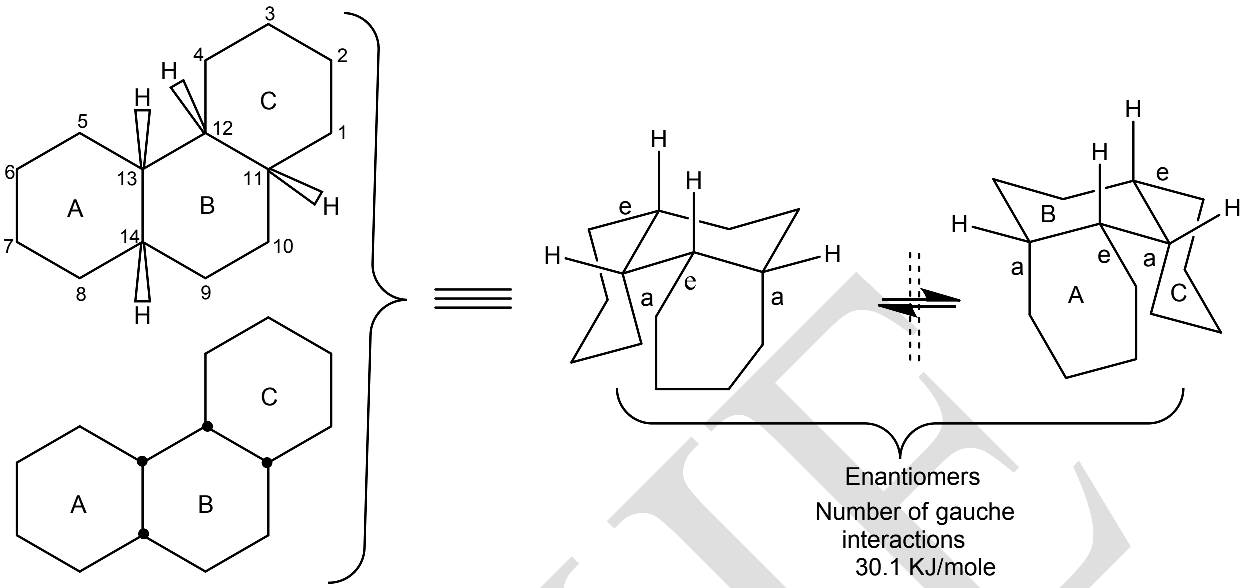
Number of gauche interactions (1+3) = 13.4 KJ/mole

(±)-cis-syn-trans (3e + 1a) (III)

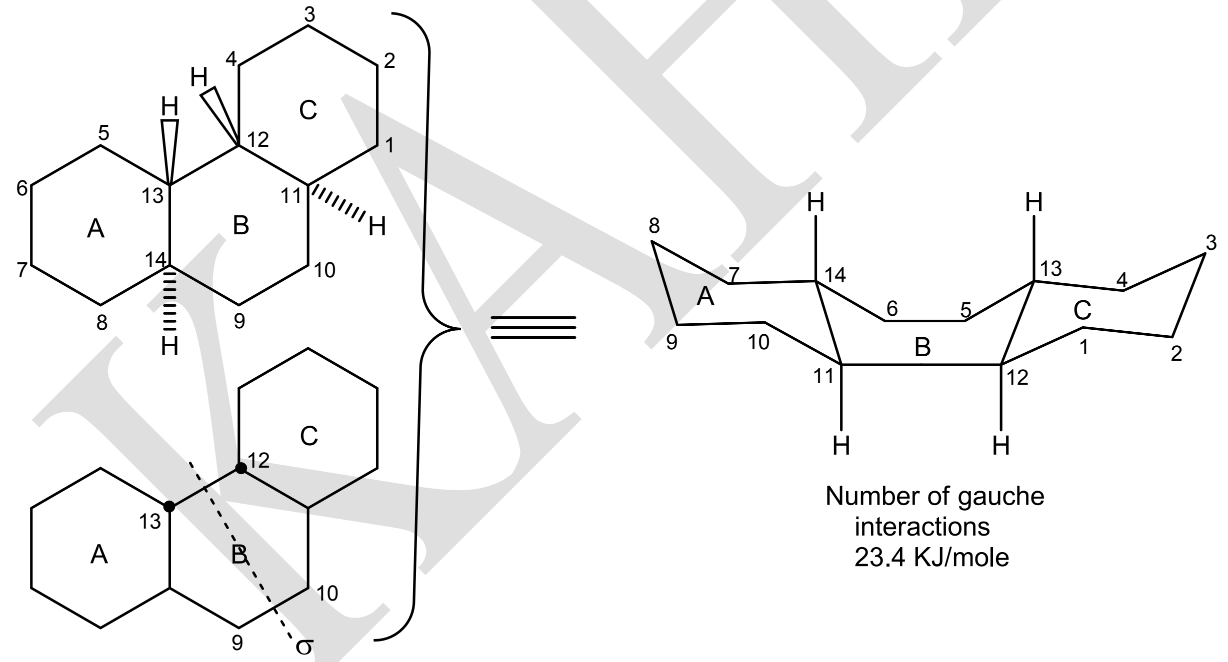


Number of gauche interactions (0+6) = 20.1 KJ/mole

(±)-cis-anti-cis (2e + 2a) (IV)



cis-syn-cis (meso) (2e + 2a) (V)



trans-syn-trans (meso) (4be) (IV)

Johnson predicated the relative stabilities of the six diastereoisomers on the basis of the following assumptions:

i) The system in which the central ring (B) is fused to other rings by **larger number of equatorial bonds** is more stable.

ii) In case when **axial bonds** of the central ring (B) are used in ring fusion, 1, 2-and 1,4-diaxial arrangements are preferred over 1,3-diaxial which suffers from a severe 1,3-diaxial methylene interaction.

iii) Regardless of the assumption 1 and 2, if the central ring junction involves two **axial** bonds either way the system is labeled, the central ring cannot exist in chair form but adopts a boat or twist-boat conformation.

Based on these assumptions, the stabilities of the six diatereoisomers are assessed.

a) The **trans-anti-trans** isomer (I) is the most stable in which the central ring (B) is fused to the other rings (A and C) by **four equatorial** bonds. However, unlike the **trans-**decalin, this system has **one gauche–butane** interaction resulting from hydrogens on C-4 and C-5 (4,5-interaction) (Although two adjacent e,e or a.e bonds of cyclohexane ring form a gauche–butane interaction, this interaction is present in all isomers).

b) The **cis-anti-trans** isomer (II) has a **cis**-decalin unit involving three gauche-butane interactions, in addition to the 4,5-interaction. So its estimated energy is 13.4 KJ/mol (4×3.5 KJ/mol).

c) The situations is same in case of **cis-syn-trans** isomer (III), the 4,5- interaction is due to a,e–substitution.

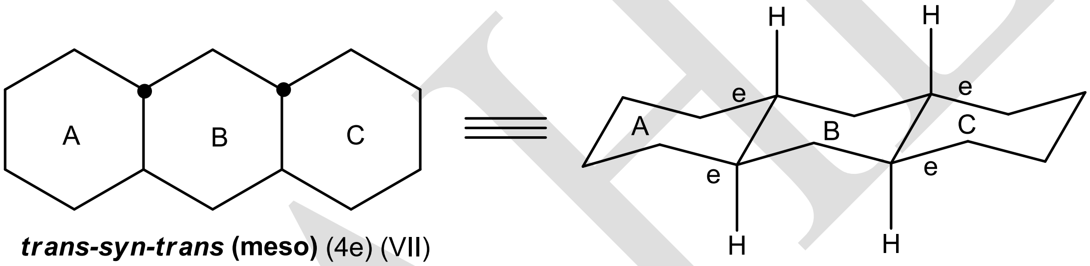
d) The **cis-anti-cis** isomer (IV) is flexible can undergo ring inversion to give energetically non-equivalent conformers A and B.

e) The **cis-syn-cis** isomer (V) also exists as a mixture of two equienergetic conformations and like **cis-**decalin is an inseparable racemate. The planar structure contains a σ- plane and hence it is designated as **meso.** In addition to the usual 4,5-interaction, this isomer has two **cis-**decalin units and a **1,3-syn diaxial** interaction (22.6 KJ/mol), so the total energy of this isomer is 29.3 KJ/mol.

f) The **trans-syn-trans** isomer (VI) cannot have both ring junctions **trans** fused with **cis-**orientation of 12-13 and 11-14. In order to achieve this geometrical requirement, the central ring (B) adopts a boat conformation with terminal rings fused through four boat equatorial (be) bonds. The estimated energy of this isomer is 23.4 KJ/mol and is **achiral.** The planar structure shows a plane of symmetry passing through 9-10 and 12-13 bonds.

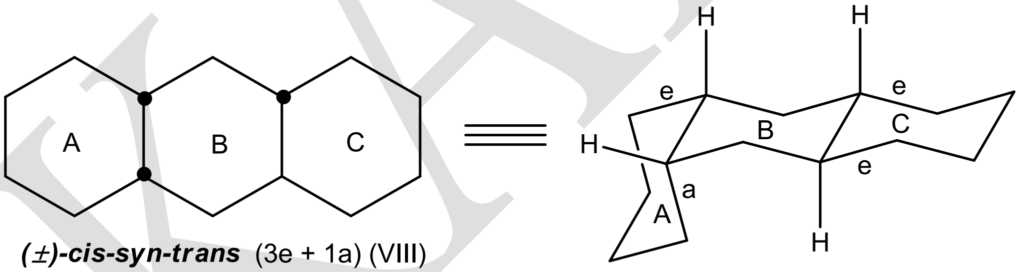
Conformations of perhydroanthracene

In perhydroanthrancene molecule, the three rings are fused in a linear manner. The four chiral centres are equivalent and correspond to AAAA type so that the number of isomers is less than predicated. Perhydroanthracene exists as **five** diastereoisomers: **trans-syn-trans(meso)** (VII), **cis-syn-trans** (VIII), **cis-anti-cis (meso)** (IX), **trans-anti-trans** (X) and **cis-syn-cis (meso)** (XI). It must be noted that the **cis-syn-trans** (VIII) may well be called **cis-anti-trans** depending on whether one looks at the bridgehead atoms in clockwise or anticlockwise direction.



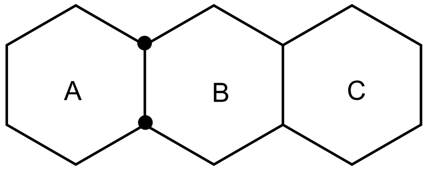
***trans-syn-trans* (meso)** (4e) (VII)

Number of gauche interactions = 0



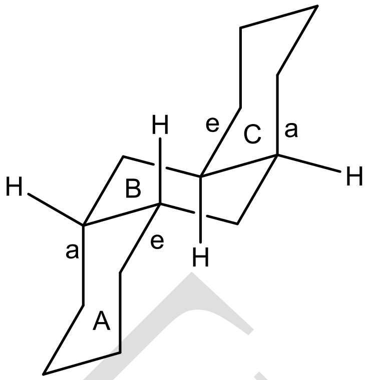
(±)-cis-syn-trans (3e + 1a) (VIII)

Number of gauche interactions = 3
(10.05 KJ/mole)

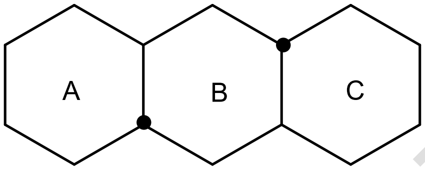


cis-anti-cis (meso) (2e + 2a) (IX)

≡

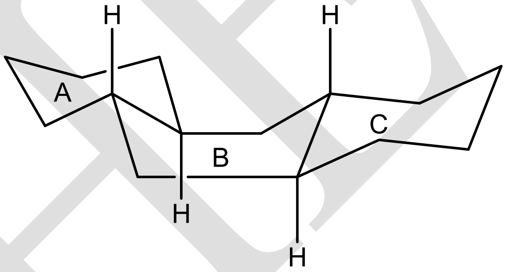


Number of gauche interactions = 6
(20.10 KJ/mole)

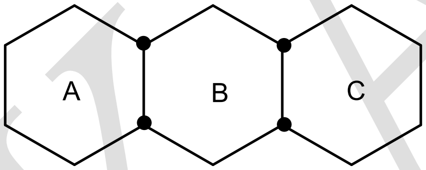


(±)-trans-anti-trans (4be) (X)

≡

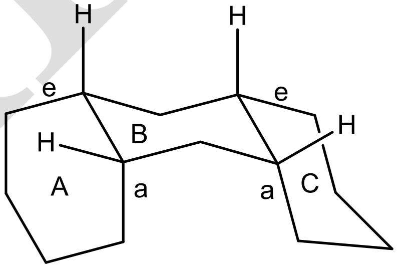


Number of gauche interactions
>23.4 KJ/mole



cis-syn-cis (meso) (2e + 2a) (IX)

≡



Number of gauche interactions
>35.0 KJ/mole

Text Books:

1. Smith, M. B. (2015). *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure* (VII Edition). New Jersey: John Wiley & Sons, Inc., Hoboken.

2. Nasipuri, D. (2014). *Stereochemistry of Organic Compounds: Principles and Applications* (III Edition). New Delhi: New Age International (P) Ltd.

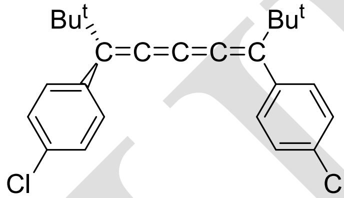
Reference Book:

1. Ramesh, P. (2005). *Basic Principles of Organic Stereochemistry* (I Edition). Madurai: Meenu Publications.

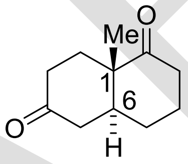
POSSIBLE QUESTIONS

PART-B (Each Question Carry Two Marks)

1. State whether the following compound is chiral or not justify your answer.

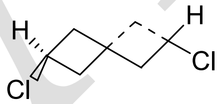


2. Give the configurations (R, S-notations) at C-1 and C-6 of the compound given below



3. Write the stable form of trans-1, 4-dimethylcyclohexane.

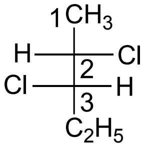
4. Comment on the chirality of the following compound.



5. Give the preferred conformations of cis-1, 2-dimethylcyclohexane and trans-1, 2-dimethylcyclohexane.

6. Write the stable forms of cis and trans-1, 3-dimethylcyclohexane.

7. The configurations (R, S notations) at C-2 and C-3 of the compound given below is



8. Give the preferred configuration of 1, 2, 2, 6, 6-pentamethyl-4-hydroxy4-phenyl piperidine.

9. Why the cis-1, 3-cyclohexanedicarboxylic acid form anhydride, where as trans-1, 3-cyclohexanedicarboxylic acid does not form anhydride?

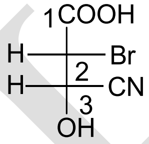
10. Why cis-1, 3-dimethylcyclohexane and cis-1, 4- dimethylcyclohexane is optically inactive?

11. The alkaline hydrolysis of 3α-acetoxy cholestane-5α-ol proceeds faster than the corresponding 3β-isomer. Why?

12. Compare the stability of cis and trans decalins.

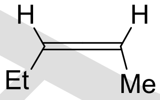
13. Define Spiranes.

14. What are the absolute configurations (R, S-notations) of the two chiral centers in the following molecule

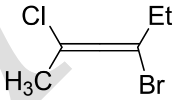


15. Indicate the configurations of the following molecules using E & Z notations.

(i)



(ii)



PART-C (Each Question Carry Six Marks)

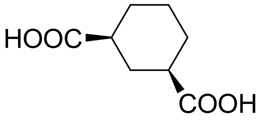
1. (i) Discusses the stereochemistry of sulphur containing compounds.
   (ii) Give the preferred conformations of
      (a) cis-1, 4-di-t-butylcyclohexane
      (b) trans-1, 3-di-t-butylcyclohexane

2. Discuss the geometry, symmetry, enthalpy and free energy of decalins.

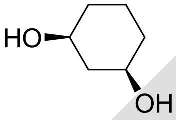
3. Write a brief note on optical isomerism exhibited by Biphenyl and Allenes.

4. (i) Discuss the stereochemistry of nitrogen compounds.
   (ii) Bring out the importance of E, Z notation in assigning the configuration of alkenes. Also discuss how the configuration of aldoximes and ketoximes can be assigned.
5. Give an account of the conformations and stability of disubstituted cyclohexane system.
6. Discuss the conformations of perhydrophenantherene.
7. Discuss the conformations of perhydroanthracene.
8. Write a brief note on planer chirality's of cyclophanes and ansa compounds.
9. Give the preferred conformations of

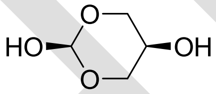
(a)



(b)



(c)

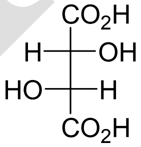


10. Explain the stereoselective and stereospecific reactions with suitable examples.
11. Discuss the effect of angular methyl group in cis and trans-9-methyldecalin.

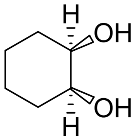
PART-D (Each Question Carry Ten Marks)

1. (i) Designate the configuration of the following molecules according to Cahn Ingold and Prelog notation.

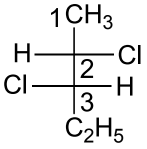
(a)



(b)

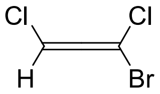


(c)

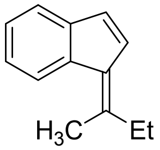


(ii) Indicate the configuration of the following molecules using E -and- Z notation.

(a)

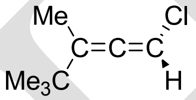


(b)



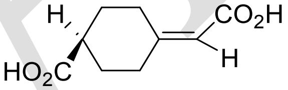
2. Designate the configuration of the following molecules according to Cahn Ingold and Prelog notation.

(a)

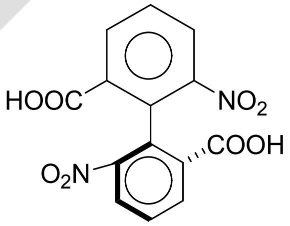


(b)

(c)



(d)



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DEPARTMENT OF CHEMISTRY

UNIT-II

CONFORMATIONAL ANALYSIS AND STEREOCHEMISTRY

PART-A–Multiple Choice Questions
(Each Question Carry One Mark) (Online Examinations)

1. The R and S nomenclature also called as

a) Cahn, Ingold and Prelog notation b) Cram's rule c) E and Z notation d) Prelog's rule

2. A phantom atom is given a formal valence of

a) 1 b) 2 **c) 0** d) 4

3. The R and S configuration of (-)-lactic acid is

a) R b) S c) E d) Z

4. The Cahn, Ingold and Prelog notation of (+)-tartaric acid is

a) S, S b) S, S **c) R, R** d) R, S

5. The term atropisomerism means

a) no rotation b) rotation c) isomer d) tautomer

6. The 2, $2'$-dinitrodiphenic acid is

a) optically active compound b) optically inactive compound

c) racemic compound d) meso compound

7. Allenes belong to a class of compounds called

a) ketene **b) cumulenes** c) carbene d) nitrene

8. In allene, the central carbon atom is

a) sp^3 hybridization b) sp^2 hybridization c) d sp^2 hybridization **d) sp hybridization**

9. The restricted rotation of benzene ring is also responsible for the chirality of other aromatic compounds, which are called

a) allenes **b) ansa compounds** c) cyclophanes d) biphenyls

10. When one replaces both the double bonds of an allene by rings, one obtains a bicyclic system in which one atom is common to both the rings. Such bicyclic systems are called

a) spiranes b) decalins c) biphenyls d) cumulenes

11. The hockey effect is also called as

a) repulsive gauche effect b) anomeric effect c) rabbit-ear effect d) epimerization

12. The bromination of cyclohexene is an example for

a) regiospecific reaction **b) stereoselective reaction**

c) stereospecific reaction d) chemoselective reaction

13. Which one is an example for anomeric effect?

a) cyclohexene b) maleic acid **c) glucose** d) cyclohexanol

14. The R and S nomenclature is mainly based on

a) Prelog’s rule b) Cram’s rule c) Fajan’s rule **d) Sequence rule**

15. The phantom atom necessarily ranks

a) lowest b) highest c) zero d) medium

16. The chair conformation of cyclohexane belongs to

a) D_2h point group **b) D_3 point group** c) C_3 point group d) D_{6h} point group

17. The most stable conformation of 1-methyl cyclohexane is

a) methyl group in axial position **b) methyl group in equatorial position**

c) methyl group in pseudo axial position d) methyl group in pseudo equatorial position

18. The preferred conformation of 1,2,2,6,6-pentamethyl-4-hydroxy-4-phenylpiperidine is

a) chair conformation b) alternate chair conformation

c) boat conformation d) twist boat conformation

19. The cis-decalin is formed when both cyclohexane rings are joined through

a) axial, axial bond b) equatorial-equatorial bond

c) axial, equatorial bond d) exo bonds

20. The conformation of trans-decalin has a

a) plane of symmetry b) rotation-reflection symmetry

c) improper- rotation symmetry **d) centre of symmetry**

21. If the group of similar priority is in the opposite side of the π-plane, the isomer is known as

a) E-isomer b) Z-isomer c) R-isomer d) S-isomer

22. The group of similar priority is in the same side of π-plane, the isomer is known as

a) E-isomer **b) Z-isomer** c) R-isomer d) S-isomer

23. The main condition for geometrical isomerism is

a) The molecule must have single bond

b) The molecule must have sigma bond

c) The molecule must have double bond

d) The molecule not has double bond

24. In German word Zusammen meaning

a) not same b) opposite c) across **d) together**

25. In German word Entgegen meaning

a) not same **b) opposite** c) together d) same

26. The meso compounds are optically inactive due to the presence of

a) plane of symmetry b) rotation-reflection symmetry

c) centre of symmetry d) alternative axis of symmetry

27. The Latin word Ansa means

a) handle b) opposite c) together d) not same

28. Racemic mixture is a mixture containing equal amount of

a) diastrereomers b) geometrical isomers

c) enantiomers d) E and Z isomers

29. If the two para positions of an aromatic ring are attached to a polymethylene chain through hetero-atoms they are called

a) ansa compounds b) cyclophanes c) allenes d) spiranes

30. An example for optical activity due to chiral axis

a) ansa compounds b) cyclophanes

c) trans-cyclooctene **d) allenes**

31. An example for chiral molecule without a chiral atom or centre

a) cyclophanes b) allenes

c) spiranes d) cumulene

32. R, S nomenclature for stereo isomers method was proposed by

a) Kekule b) Eliel

c) Cahn,Ingold and prelog d) Pauling

33. The barrier to chair-chair interconversion in cyclohexane is approximatery

a) 5 k cal mol^{-1} b) 12 k cal mol^{-1}

c) 30 k cal mol^{-1} d) 50 k cal mol^{-1}

34. Which one of the following compound cannot exhibit optical activity?

a) alanine b) sucrose **c) 1-butanol** d) 2-butanol

35. The total number of possible isomers in a compound containing 3 asymmetric centers is

a) 3 b) 6 c) 27 **d) 8**

36. The compound among the following which can exist in chiral form

a) methyl cyclohexane b) cyclopentane

c) 3- methyl pentane d) 3- methyl hexane

37. The hybridization of the central carbon atom in an allene is

a) sp^3 **b) sp** c) sp^2 d) dsp^2

38. In a cyclohexane with many groups the more stable conformation is

a) equatorial b) axial c) flagpole d) pseudo axial

39. Which of the following compound contains diastereotopic protons?

a) ethyl chloride **b) 1,2-dichloropropane**

c) 2-methyl-2-butene d) 1,2- dichloroethane

40. The most stable conformation of 1,4- dimethylcyclohexane is

a) diequatorial methyl b) equatorial methyl and axial methyl

c) diaxial methyl d) axial methyl and equatorial methyl

41. Addition of bromine to cis-2-butene yields

a) meso-2,3-dibromo butane **b) racemic 2,3-dibromo butane**

c) d-2,3- dibromo butane d) l-2,3-dibromo butane

42. The preferred conformation of cis-1,3- dihydroxy cyclohexane is

a) two OH groups are axial

b) one OH group is axial and another OH group is equatorial

c) one OH group is equatorial and another OH group is axial

d) two OH groups are equatorial

43. The most stable conformation of ethylene glycol is

a) anti **b) gauche** c) partially eclipsed d) fully eclipsed

44. When methyl group is in the axial position of methyl cyclohexane the molecule has

a) one n-butane gauche interaction

b) four n-butane gauche interaction

c) two n-butane gauche interaction

d) three -butane gauche interaction

45. In the boat conformation of cyclohexane, the most destabilizing interaction is

a) eclipsing b)1,3-diaxial c) 1,3-diequatorial **d) flagpole-flagpole**

46. Trans-decalin belongs to

a) C_{2h} point group b) D_{2h} point group c) D_{6h} point group d) C_{6h} point group

47. The cis-1,2- dimethylcyclohexane has a

a) centre of symmetry b) rotation-reflection symmetry

c) alternating axis of symmetry **d) plane of symmetry**

48. When the methyl groups are in the diaxial position in trans 1,2- dimethyl cyclohexane the molecule has

a) one butane gauche interaction b) two butane gauche interaction

c) four butane gauche interaction d) six butane gauche interaction

49. The newmann projection chair form of cyclohexane reveals a

a) six butane gauche interaction b) two butane gauche interaction

c) four butane gauche interaction d) eight butane gauche interaction

50.The one butane gauche interaction energy is approximately equal to

a) 6.6 KJ/mol b) 9.9 KJ/mol c)1500 KJ/ mol **d) 3.3 KJ/mol**

51. The cis-1,3-dimethylene cylohexane exists as two energetically non-equivalent chair conformations which are

a) chiral b) meso **c) achiral** d) optically active

52. The alkaline hydrolysis or 3α- acetoxy-cholestane – 5α-ol proceeds faster than the corresponding 3β-isomer due to

a) intramolecular hydrogen bonding b) intermolecular hydrogen bonding

c)1,3-syn diaxial interaction d) butane gauche interaction

53. Secondary axial alcohols are more rapidly oxidized by chromic acid than secondary equatorial alcohols due to

a) steric acceleration b) inductive effect

c) mesomeric effect **d) steric assistance**

54. Trans-4-t-butyl cyclohexane carboxylic acid is stronger because, the corresponding anion is

a) solvated to a lesser extent **b) solvated to a greater extent**

c) no solvation take place d) solvated to a some extent

55. The symmetry number of cis-decalin is

a) 1 b) 3 **c) 2** d) 4

56. The cis -1,4-dihydroxy cyclohexane exists predominantly in boat conformation due to

a) Vander Waals force **b) intramolecular hydrogen bonding**

c) intermolecular hydrogen bonding d) covalent bonding

57. IUPAC name of decalin is

a) bicyclo[4.4.0] decane b) cyclo[4.4.0] decane

c) bicyclo[4.4.0] undecane d) bicyclo[4.4.1] decane

58. The conformation of trans-decalin has a

a) centre of symmetry b) plane of symmetry

c) rotation–reflection symmetry d) alternating axis of symmetry

59. How many number of butane gauche interaction is possible for cis-decalin?

a) 0 b) 1 c) 4 **d) 3**

60. Which one is true for perhydroanthracene molecule?

a) It exists as five diastereoisomers b) It exists as meso compounds

c) It exists as four enantiomers d) It exixts as racemic mixtures

UNIT-III

SYLLABUS

Radical reactions: Configuration and generation of short lived free radicals-characteristics of free radical reactions – radical substitution, radical additions and rearrangement of free radicals. Typical reactions such as Sandmeyer, Gomberg, Pechmann, Ullmann, Pschorr and Hunsdiecker reactions.

Oxidation and reductions- mechanisms – aromatisation, oxidation of alcohols and glycols, ozonolysis, Sommelet reaction and selectivity in reduction-metal hydride reduction- reduction of nitro compounds and acyloin condensation.

Free radicals

The reactions that involve the production of ions by a *heterolytic cleavage* of the covalent bond. The main characteristic of such a cleavage is that the electron pair remains attached to only on of the two originally bonded atoms.

$$X{-}Y \longrightarrow X^{+} + Y^{-} \quad \text{or} \quad X^{-} + Y^{+}$$

However, rapture of the covalent bond may proceed by another way, *homolytic cleavage,* in which both the atoms possess unpaired electrons due to the symmetrical rupture of the bond.

$$X{-}Y \longrightarrow X^{\bullet} + Y^{\bullet}$$

These fragments, which are neutral species, are called *free radicals. We* thus define a free radical as an atom or group of atoms with an unpaired electron. The present chapter is devoted to the study of reactions that involve radicals as intermediates.

Free radical intermediates are often involved in reactions carried out at high temperatures or under the influence of light. Even at room temperature many reactions proceed by a free radical mechanism, particularly in non-polar solvents, and in the presence of substances known to produce radicals, such as peroxides. Most common radicals are extremely reactive species and are difficult to isolate. Such radicals are referred to as *short-lived radicals* in contrast to *stable free radicals* which are not so reactive and exist in equilibrium with the normal compounds.

Short–Lived radicals

Production of radicals

Short-lived free radicals are often produced when a molecule is supplied with sufficient energy-thermal or photochemical-to cause homolysis of a covalent bond. In addition, oxidation-reduction reactions resulting in the gain or loss of a single electron can also be used for the generation of radicals.

A. Thermal reactions

Historically, the first work to demonstrate the formation and existence of free radicals was that of Paneth and Hofeditz in 1929-31. Their procedure, often referred to as the p*aneth technique* (Figure 1), consists in passing a stream of nitrogen and the vapour of tetramethyllead, through a quartz tube. The pressure in the quartz tube is held at about 2 mm by the action of a vacuum pump.

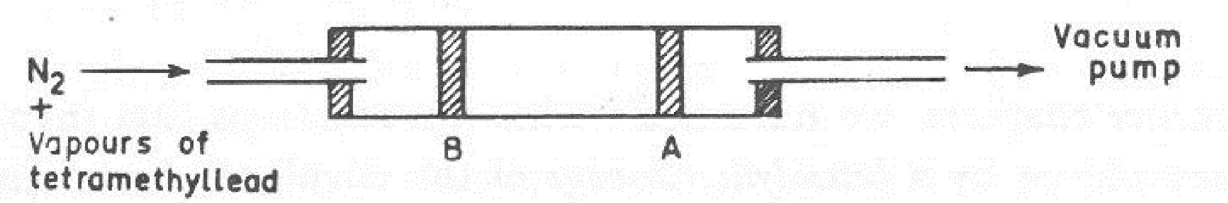


Figure 1. Production of radicals-Paneth technique.

On heating the tube strongly at any point (A), a lead mirror is deposited due to the decomposition of tetramethyllead. The gaseous product of the decomposition was found to be ethane. Subsequent heating of the tube at another point (B) on the upstream side resulted in the simultaneous disappearance and formation of mirrors at points A and B, respectively. Tetramethyllead was detected this time in the effluent gas. This unique experiment established that tetramethyllead decomposes to form lead and the methyl radical:

$$(CH_3)_4Pb \xrightarrow{\Delta} 4\,\overset{\bullet}{C}H_3 + \underset{\text{(Mirror)}}{Pb}$$

Methyl radicals, produced as a result of heating at point B, react with the mirror at point A to regenerate the volatile tetramethyllead.

$$4\,\overset{\bullet}{CH_3} + Pb \longrightarrow (CH_3)_4Pb$$

In the absence of the lead-mirror the free methyl radicals combine with each other to form ethane.

$$2\,\overset{\bullet}{CH_3} \longrightarrow CH_3-CH_3$$

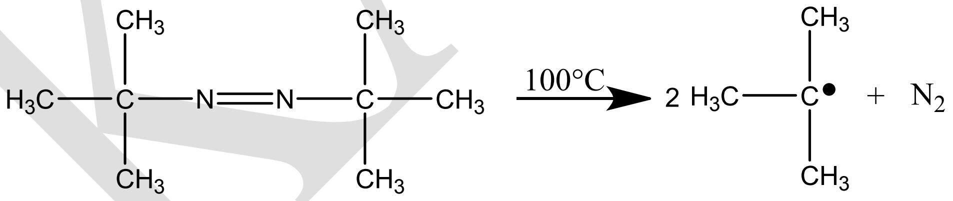
Further, the rate of the disappearance of the mirror at A was found to decrease with the increase in the distance between A and B, thereby suggesting that the methyl radicals react very rapidly to form ethane. Paneth estimated the half life of methyl radicals to be about 0.006 sec. under the above experimental conditions.

Thermal production of the radicals is not confined to the decomposition of tetramethyllead; rather they are readily generated whenever a compound having a weak covalent bond is heated. The O-O bond of a peroxide or a peracid, for example, has a strength of only 36 kcal/mole and so it undergoes rupture even at room temperature.

$$C_6H_5CO-O-O-COC_6H_5 \longrightarrow 2C_6H_5COO^\bullet \longrightarrow 2C_6H_5{}^\bullet + 2CO_2$$

Sometimes, the formation of radicals is facilitated by the simultaneous release of a very stable molecule such as nitrogen.

$$H_3C-N=N-CH_3 \xrightarrow{300°C} 2CH_3{}^\bullet + N_2$$



$$(CH_3)_3C-N=N-C(CH_3)_3 \xrightarrow{100°C} 2\,(CH_3)_3C^\bullet + N_2$$

B. Photochemical reactions

Absorption of visible or ultraviolet light provides a molecule with sufficient energy to break covalent bonds, and thus photochemical dissociation to yield radicals may occur. Very frequently photochemical dissociation is preferred to thermolysis as the former results in more selective reactions. Irradiation of gaseous acetone, for example, yields ethane, biacetyl and carbon monoxide presumably *via* free radicals.

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

$$2\,CH_3^{\bullet} \longrightarrow CH_3-CH_3$$

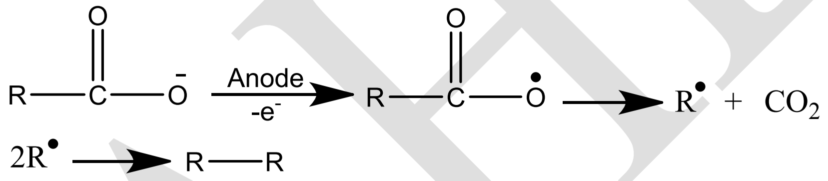
$$CH_3\overset{\bullet}{C}O \longrightarrow \overset{\bullet}{C}H_3 + CO$$

$$2\,CH_3\overset{\bullet}{C}O \longrightarrow CH_3COCOCH_3$$

Many examples of the formation of radicals by irradiation are given in the chapter dealing with photochemistry.

C. Redox reactions

One–electron oxidation-reduction reactions are very often employed to produce radicals. One such reaction that has considerable synthetic importance is the Kolbe electrolysis of the salts of organic acids.



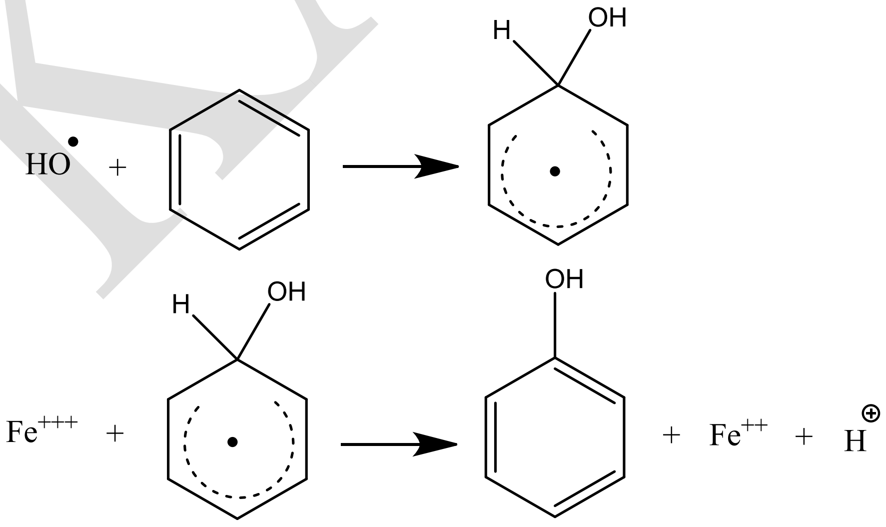
$$R-\overset{O}{\overset{\|}{C}}-O^{-} \xrightarrow[-e^{-}]{\text{Anode}} R-\overset{O}{\overset{\|}{C}}-O^{\bullet} \longrightarrow R^{\bullet} + CO_2$$

$$2R^{\bullet} \longrightarrow R-R$$

Another well-known example is that of Fenton's reagent produced by the reaction of hydrogen peroxide with ferrous ions.

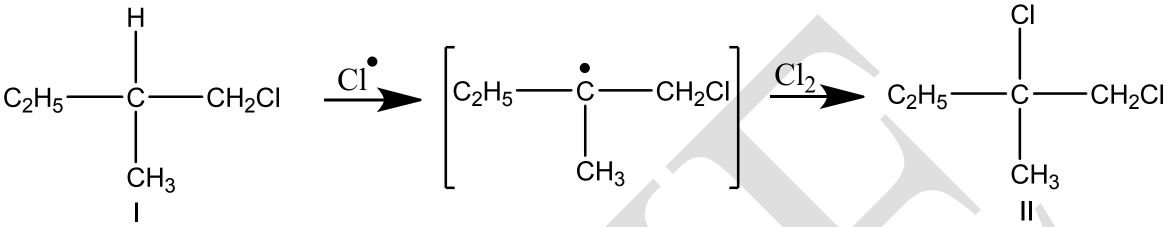
$$Fe^{++} + H_2O_2 \longrightarrow Fe^{+++} + OH^{-} + HO^{\bullet}$$

The generated hydroxyl radicals then oxidize organic substances.



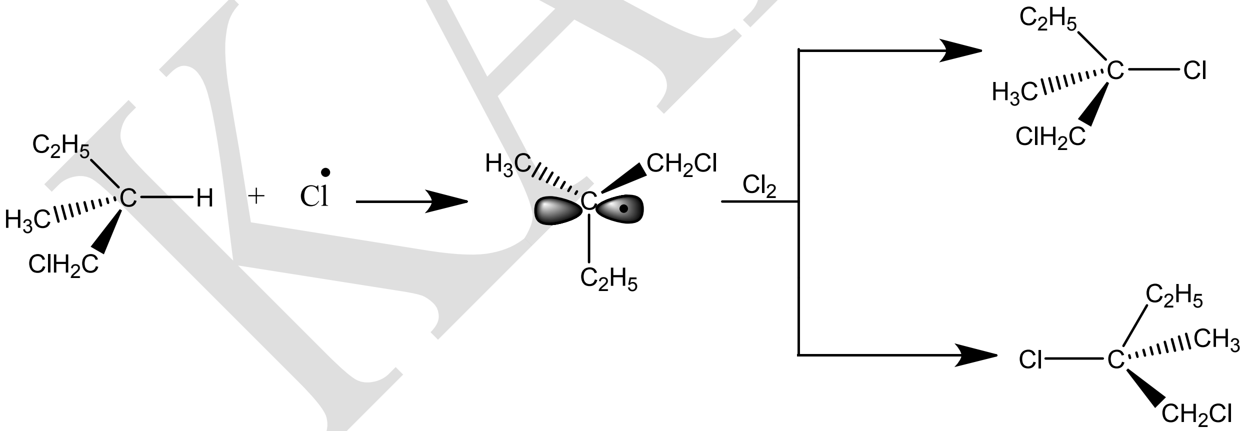
Configuration of radicals

One of the most elegant experiments to determine the configuration of free radicals is due to Brown, Kharasch and Chao who found that free radical chlorination of (+)-1-chloro-2-methylbutane (I) yields *racemic* 1,2-dichloro-2-methylbutane (II).

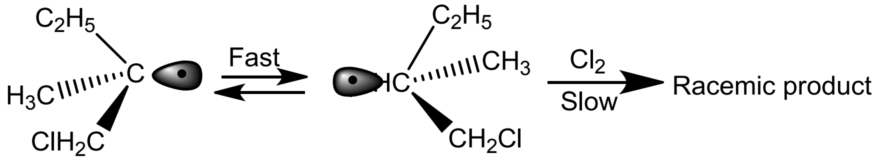


Two reasonable pictures of free radicals fit in with the above experimental data:

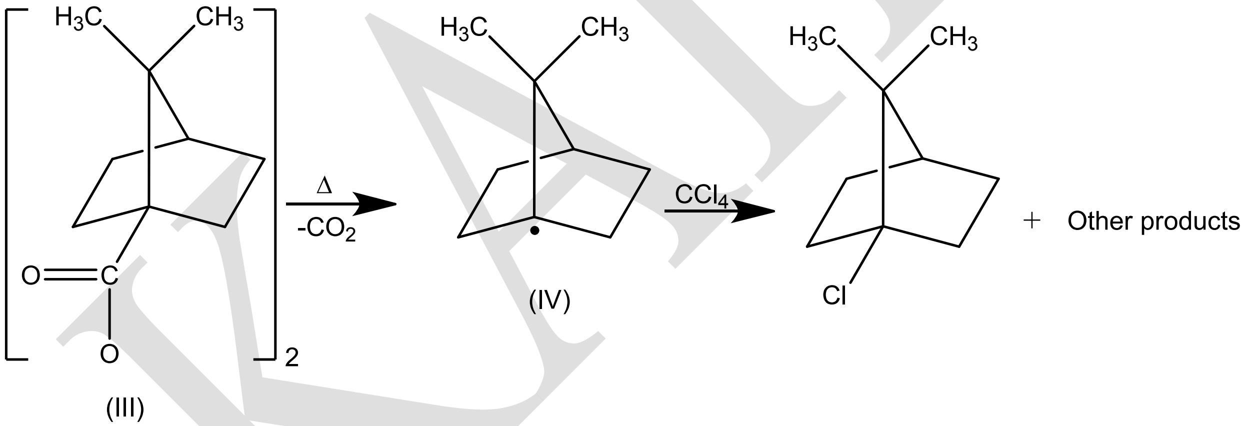
A. Either a free radical is a planar species in which the carbon atom bearing the odd electron is sp^2 hybridized (as in a carbonium ion) and the odd electron remains in the *p* orbital. Existence of such a planar radical, in which attachment of chlorine atom to either face is equally likely, explains the equal formation of the two optical isomers of 1,2-dichloro-2-methylbutane leading to racemization.



B. A free radical could also have a shape resembling a shallow pyramid which is neither planar nor tetrahedral and the orbital containing unpaired electron is some sort of hybrid between a *p* and an sp^3 orbital. If we assume that the inversion of such a pyramid is faster than the transfer reaction with chlorine molecule, we should expect a racemic product.



The question as to whether free radicals exist in a *planar* configuration or in a rapid equilibrium between the two *pyramidal* forms is difficult to answer at the moment. Since the energy barrier between the planar conformation and a shallow pyramid is rather small, ultraviolet, infrared and ESR studies have not been able to distinguish between these two configurations. However, available evidence indicates that in radicals stabilized by the unpaired electron, the three bonds of the carbon are *coplanar*. On the other hand, when the unpaired electron is situated on the carbon at a bridgehead at a bicyclic system, an *sp*^{2} configuration is completely prevented by the geometric requirements and a pyramidal configuration becomes mandatory. An interesting example is apocamphoyl peroxide (III) which readily dissociates in carbon tetrachloride yielding the apocamphyl radical (IV).

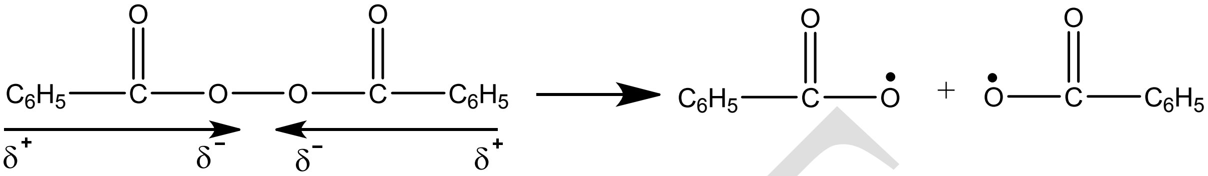


In contrast, formation of a carbonium ion at such a position is extremely sluggish due to geometric requirements of planarity.

Reactions of radicals

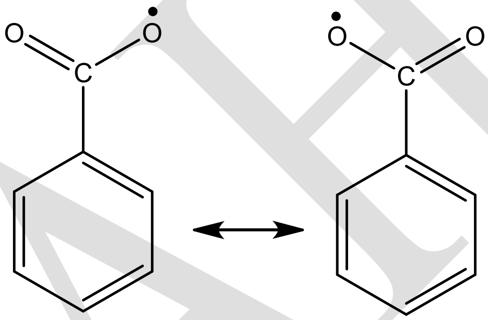
Many radical reactions are initiated by peroxides. The decomposition of one such peroxide, benzoyl peroxide, has been investigated most thoroughly and it illustrates the complexity of radical reactions.

A molecule of benzoyl peroxide may be looked upon as consisting of two dipoles joined at their negative ends. It, therefore, undergoes easy homolytic cleavage due to the repulsion between the two negative charges.

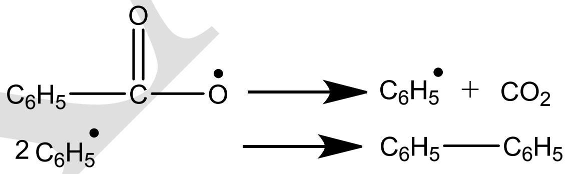


$$\underset{\delta^+ \longrightarrow \delta^-}{C_6H_5-\overset{O}{\overset{\|}{C}}-O}-\underset{\delta^- \longleftarrow \delta^+}{O-\overset{O}{\overset{\|}{C}}-C_6H_5} \longrightarrow C_6H_5-\overset{O}{\overset{\|}{C}}-\dot{O} + \dot{O}-\overset{O}{\overset{\|}{C}}-C_6H_5$$

Accordingly, substitution of the benzene ring with electron-donating groups decreases stability of benzoyl peroxide while electron-withdrawing groups slow down the rate of decomposition. Resonance stabilization of the product benzoyloxy radicals helps further in lowering the bond-dissociation energy of the already weak O-O bond.

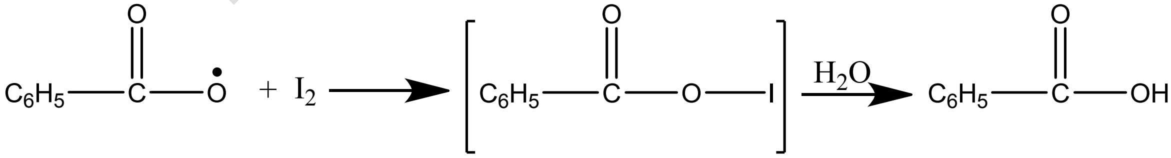


The benzoyloxy radicals may liberate carbon dioxide yielding phenyl radicals, which then combine to give biphenyl.



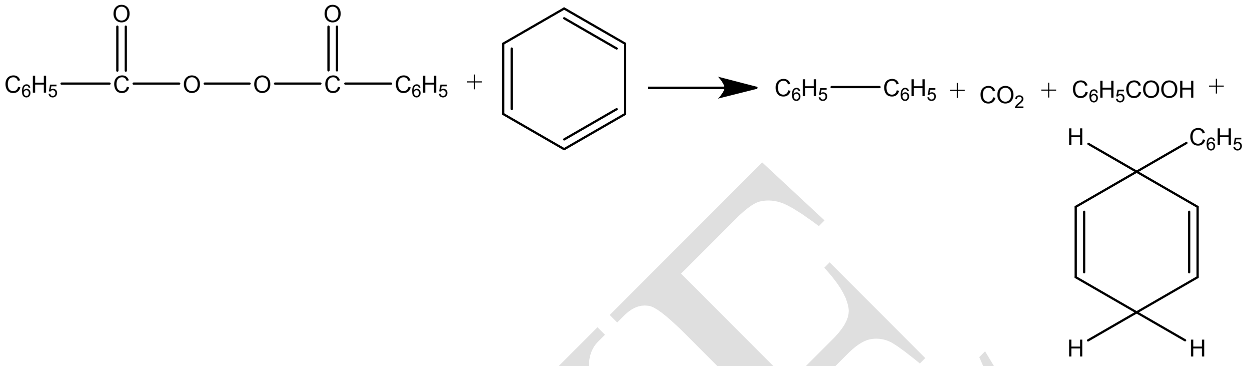
$$C_6H_5-\overset{O}{\overset{\|}{C}}-\dot{O} \longrightarrow C_6H_5^{\bullet} + CO_2$$
$$2\,C_6H_5^{\bullet} \longrightarrow C_6H_5-C_6H_5$$

The intermediacy of benzoyloxy radical is further established by the isolation of benzoic acid on carrying out the decomposition in wet carbon tetrachloride containing iodine.



$$C_6H_5-\overset{O}{\overset{\|}{C}}-\dot{O} + I_2 \longrightarrow \left[C_6H_5-\overset{O}{\overset{\|}{C}}-O-I\right] \xrightarrow{H_2O} C_6H_5-\overset{O}{\overset{\|}{C}}-OH$$

In the presence of benzene, the decomposition of benzoyl peroxide results in the formation of substitution products in addition to carbon dioxide, biphenyl and benzoic acid.



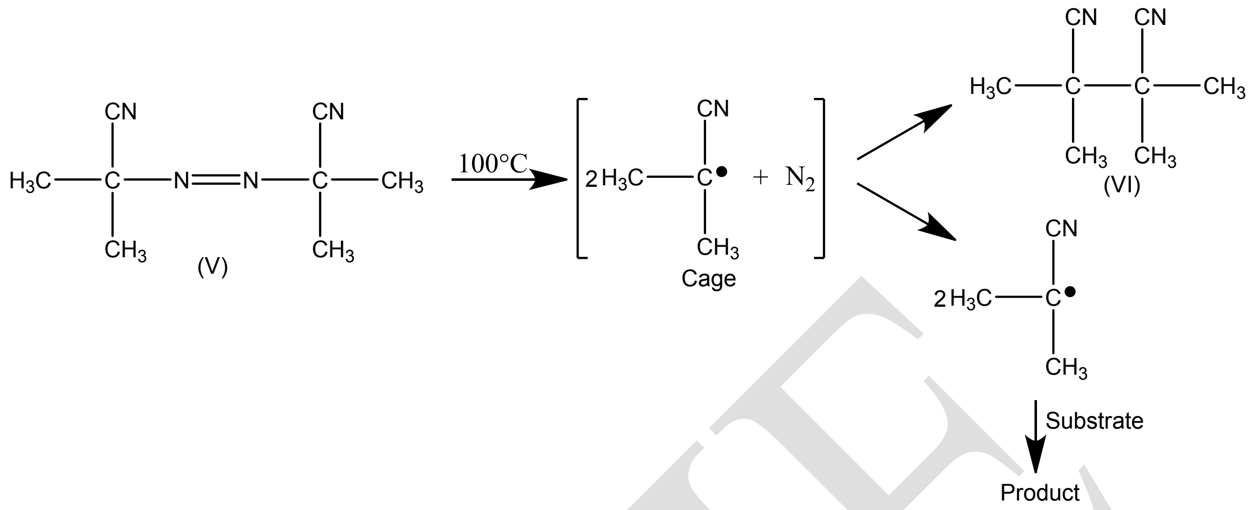
The decomposition of benzoyl peroxide is a chain reaction process in which intermediate radicals, formed by the reaction of benzoyloxy or phenyl radicals with substrates, attack the peroxide molecule to induce further decomposition.

Another class of compounds that are widely used as radical initiators are azo compounds. Azomethane, for example, decomposes to yield ethane, presumably *via* methyl radicals.

$$H_3C-N{=}N-CH_3 \longrightarrow 2CH_3^{\bullet} + N_2$$

$$2CH_3^{\bullet} \longrightarrow CH_3-CH_3$$

Even though the C-N bond in azo compounds is of normal strength (70 kcal/mole) the drive for the dissociation is provided by the nitrogen molecule whose heat of formation is 225 kcal/mole. Study of the commercially useful initiator, azoisobutyronitrile (V), has shown that unlike benzoyl peroxide, the rate of decomposition of azo compounds is independent of the nature of the solvents suggesting thereby that the generated radicals are unable to produce induced decomposition. Furthermore, these studies have revealed that after the initial decomposition the products are held in a *solvent cage* from where either they slowly diffuse out as free radicals or the two radicals combine to form tetramethylsucciononitrile (VI).



Some common reactions of the radicals are described below.

A. Halogenation

Halogenation of alkanes is again a chain-reaction consisting of initiation, propagation and termination. For the sake of clarity we shall consider halogenation by different halogens one by one.

(i) Chlorination

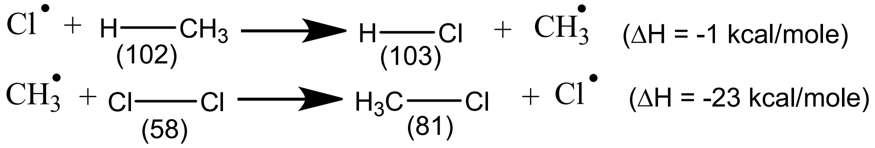
Chlorination of alkanes takes place either thermally or photochemically and it has been shown that under either of these conditions, the first step is the breaking of a chlorine molecule into two chlorine atoms. This process requires 58 kcal/mole of energy which is supplied either by heating the reaction mixture up to 250°C or irradiation it at 487.5 nm.

Initiation

$$\underset{(58)}{Cl{-}Cl} \xrightarrow[\text{or } \Delta]{h\nu} Cl^{\bullet} + Cl^{\bullet} \quad (\Delta H = +58 \text{ kcal/mole})$$

The chain-propagation step consists of the attack by the chlorine atom on the alkane molecule to abstract a hydrogen atom and thereby produce an alkyl radical. This radical, on collision with a chlorine molecule, abstracts a chlorine atom to form a molecule of alkyl chloride.

Propagation



$$Cl^{\bullet} + \underset{(102)}{H-CH_3} \longrightarrow \underset{(103)}{H-Cl} + \dot{C}H_3 \quad (\Delta H = -1 \text{ kcal/mole})$$

$$\dot{C}H_3 + \underset{(58)}{Cl-Cl} \longrightarrow \underset{(81)}{H_3C-Cl} + Cl^{\bullet} \quad (\Delta H = -23 \text{ kcal/mole})$$

The chain is finally terminated by the union of two radicals.

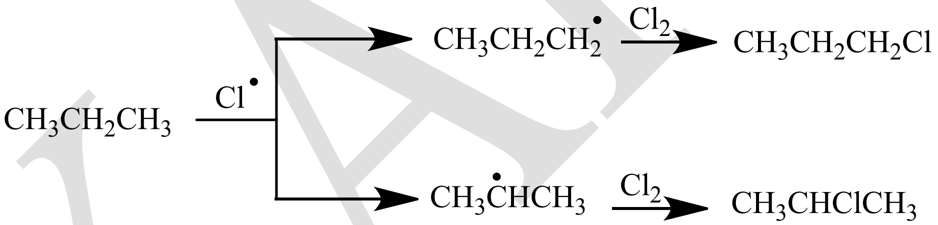
Termination

$$Cl^{\bullet} + Cl^{\bullet} \longrightarrow Cl_2$$

$$\dot{C}H_3 + \dot{C}H_3 \longrightarrow H_3C-CH_3$$

$$\dot{C}H_3 + Cl^{\bullet} \longrightarrow H_3C-Cl$$

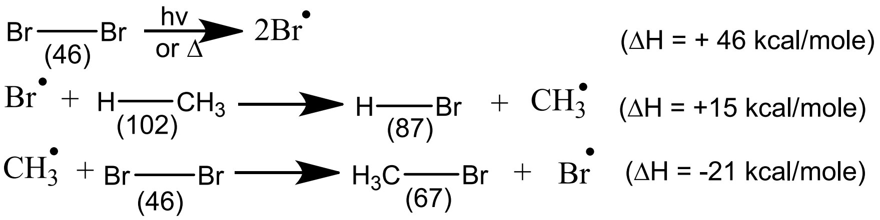
A consideration of the bond-dissociation energies (given in parentheses in the equations), makes it clear that although energy must be supplied for the initiation step, the two chain propagating steps are exothermic and hence proceed readily. As expected, the hydrogen atoms in an alkane are substituted in the general order, primary < secondary < tertiary. Thus chlorination of propane yields n–propyl and isopropyl chlorides in the ratio of 1:1.



Since there are six primary hydrogens against only two secondary hydrogens in a molecule of propane, the probability factor favours formation of a primary radical by the ratio of 3:1. The actual composition of the product mixture, however, shows that the ease of formation of a secondary radical is three times more than that of a primary radical.

(ii) Bromination

Bromination of alkanes has close similarities to chlorination except for the fact that the chain reaction initiated by bromine atoms proceeds relatively slowly. In other words, more bromine molecules are to be dissociated to produce the same yield. This difference is mainly due to different bond dissociation energies of the molecules involved in the reaction.

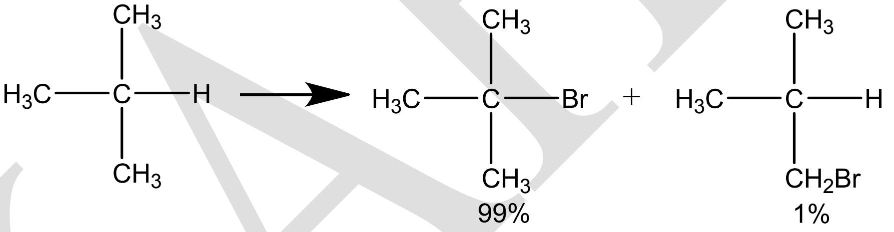


$$\underset{(46)}{Br{-}Br} \xrightarrow[\text{or } \Delta]{h\nu} 2Br^\bullet \quad (\Delta H = +46 \text{ kcal/mole})$$

$$Br^\bullet + \underset{(102)}{H{-}CH_3} \longrightarrow \underset{(87)}{H{-}Br} + CH_3^\bullet \quad (\Delta H = +15 \text{ kcal/mole})$$

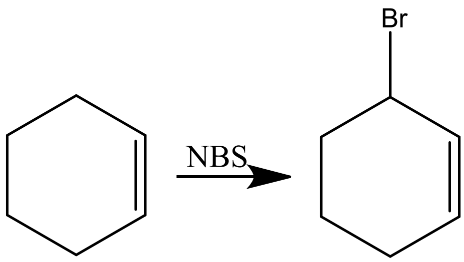
$$CH_3^\bullet + \underset{(46)}{Br{-}Br} \longrightarrow \underset{(67)}{H_3C{-}Br} + Br^\bullet \quad (\Delta H = -21 \text{ kcal/mole})$$

Although the last step of the reaction is exothermic (and therefore, occurs readily) the attack of bromine atom on the alkane is endothermic unlike the analogous step in chlorination. Thus it is somewhat difficult for a bromine atom to acquire the *activation energy* required to abstract a hydrogen atom in competition with the chain-terminating steps such as combining with another bromine atom or an alkyl radical. Overall bromination is, therefore, a slower process than chlorination. An important consequence of the low reactivity of bromine atom is its high selectivity for tertiary and secondary positions in comparison to a chlorine atom. This explains why gaseous bromination of isobutane yields mainly the tertiary bromide.



Bromination by N-Bromosuccinimide

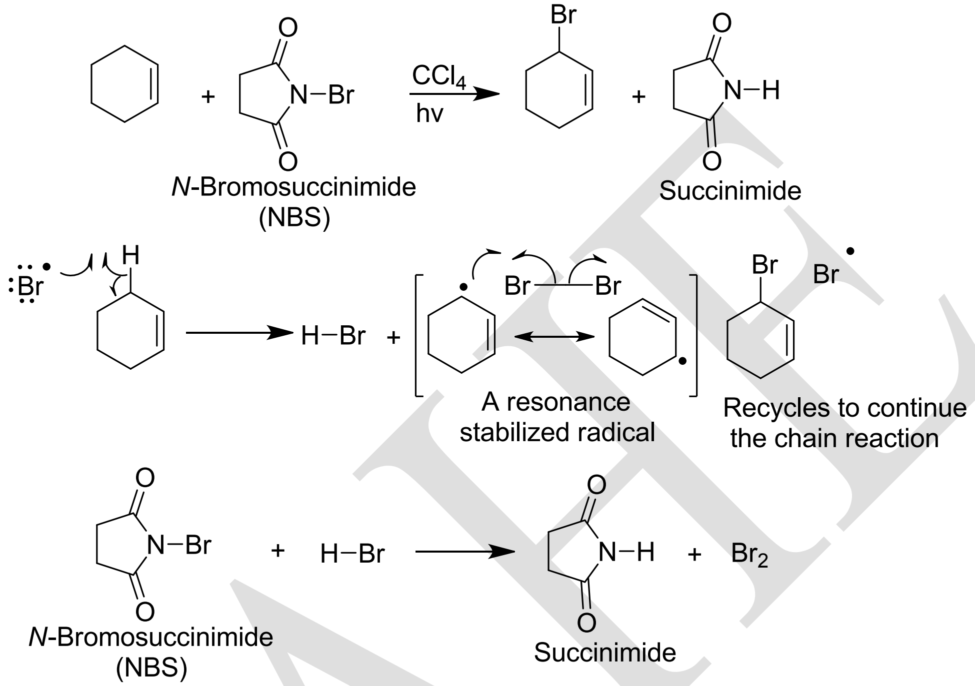
N-Bromosuccinimide (NBS) deserves a special consideration since it is a very specific reagent for allylic and benzylic bromination. The following examples illustrate the versatility of this reagent.



$$C_6H_5CH_3 \xrightarrow{\text{NBS}} C_6H_5CH_2Br$$

$$H_2C{=}CHCH_3 \xrightarrow{\text{NBS}} H_2C{=}CHCH_2Br$$

A mechanism was proposed in which the function of NBS is merely to act as a bromine reservoir maintaining a low concentration of molecular bromine by reacting with HBr that is initially formed in side reactions.

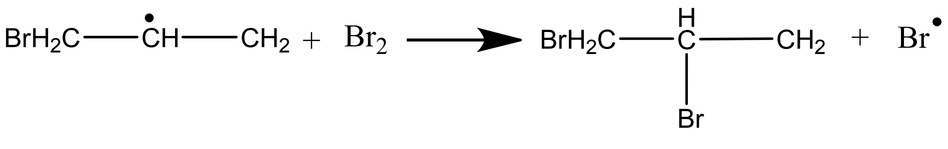


The bromine molecule dissociates into bromine atoms in presence of light or radical initiators. This explains why bromination by NBS is initiated by a peroxide or UV light. Hydrogen abstraction by bromine atom generates an allylic radical which then reacts with the molecular bromine to yield the product.

$$Br^{\bullet} + H_2C{=}CHCH_3 \longrightarrow H_2C{=}CH\dot{C}H_2 + HBr$$
$$H_2C{=}CH\dot{C}H_2 + Br_2 \longrightarrow H_2C{=}CHCH_2Br + Br^{\bullet}$$

The chain then continues with the production of HBr and bromine atoms. A low concentration of bromine favours allylic bromination over addition to the double bond since the addition of bromine atoms to the double bond is a reversible process.

$$Br^{\bullet} + H_2C{=}CH{-}CH_3 \rightleftharpoons BrH_2C{-}\dot{C}H{-}CH_3$$

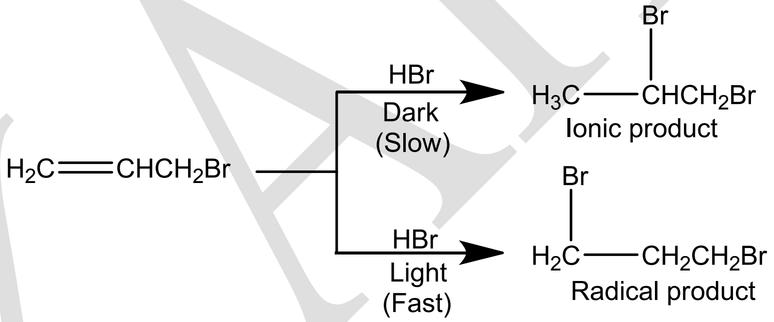


$$BrH_2C{-}\dot{C}H{-}CH_2 + Br_2 \longrightarrow BrH_2C{-}\overset{H}{\underset{Br}{C}}{-}CH_2 + Br^{\bullet}$$

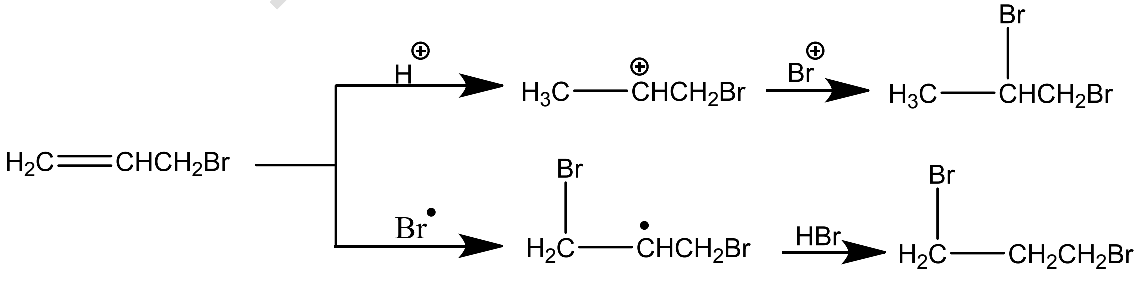
In other words, the radical formed as a result of addition of bromine will revert to the alkene if the concentration of bromine is low whereas an allylic radical is capable of waiting (since the hydrogen abstraction reaction is irreversible) till it gets a bromine molecule. Thus a low bromine concentration favours allylic bromination. This conclusion has received support from the observation that allylic bromination can also be performed by slow photolysis of molecular bromine.

B. Addition reactions

Perhaps the most celebrated example of free radical addition is the 'abnormal' addition of hydrogen bromide to olefins. This reaction was studied by Kharasch and Mayo who showed that it proceeds by either an ionic or a radical mechanism. In the dark and in the absence of radical initiators, the reaction proceeds in an ionic fashion, while in the presence of light, or a peroxide, a much faster radical addition occurs.



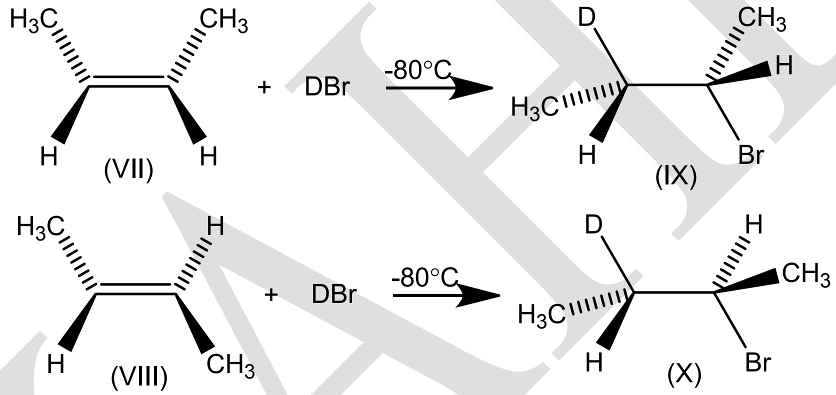
The difference in the nature of the products can be accounted for by a consideration of the stabilities of radicals and carbonium ions which follow the order primary < secondary < tertiary. Initial addition of a proton produces a relatively stable carbonium ion in the ionic reaction while a bromine atom adds first to generate the more stable secondary radical.



In the presence of oxygen, light or peroxides, hydrogen bromide dissociates to generate bromine atoms, and since radical addition is a faster process, it overtakes the addition proceeding *via* the ionic mechanism under the above conditions.

$$\begin{aligned}
&H{-}Br + O_2 \longrightarrow H\dot{O}_2 + Br^{\bullet}\\
&H{-}Br \xrightarrow{h\nu} H^{\bullet} + Br^{\bullet}\\
&\left.\begin{aligned}&ROOH \longrightarrow R\dot{O} + OH^{\bullet}\\ &R\dot{O} + HBr \longrightarrow ROH + Br^{\bullet}\end{aligned}\right\}
\end{aligned}$$

Radical addition is usually a stereospecific process yielding a **trans** product. Addition of deuterium bromide to **cis**-2-butene (VII) and **trans**-2-butene (VIII), for example, yields **threo-** (IX), and **erythro-**3-deutero-2-bromobutanes (X).

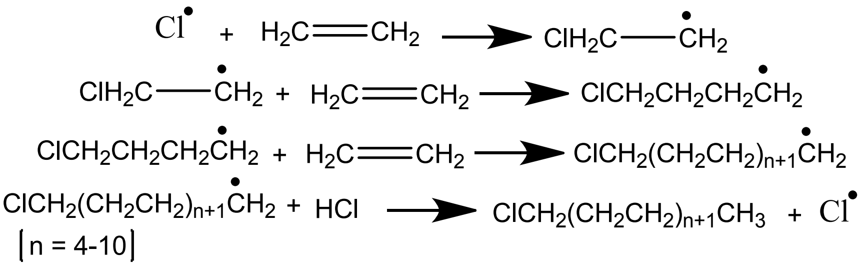


In contrast to the addition of HBr, radical addition of HI and HC1 to olefins normally does not take place. Consideration of the energy changes which would be associated with each propagating step of the radical chain process makes this absolutely clear.

$$X^{\bullet} + H_2C{=}CH_2 \longrightarrow XH_2C{-}\dot{C}H_2 \qquad \left[\begin{array}{l}X = Cl;\ \Delta H = -26\ \text{kcal/mole}\\ X = Br;\ \Delta H = -05\ \text{kcal/mole}\\ X = I\ ;\ \Delta H = +07\ \text{kcal/mole}\end{array}\right]$$

$$XH_2C{-}\dot{C}H_2 + HX \longrightarrow XH_2C{-}CH_3 + X^{\bullet} \qquad \left[\begin{array}{l}X = Cl;\ \Delta H = +05\ \text{kcal/mole}\\ X = Br;\ \Delta H = -11\ \text{kcal/mole}\\ X = I\ ;\ \Delta H = -27\ \text{kcal/mole}\end{array}\right]$$

For the addition of HC1, although the first step is exothermic–and so the addition of chlorine atom takes place readily-the second step is endothermic by 5 kcal/mole. Thus the initially formed radical is unable to decompose HC1 and polymerization begins to compete.



$$Cl^{\bullet} + H_2C{=}CH_2 \longrightarrow ClH_2C{-}\dot{C}H_2$$
$$ClH_2C{-}\dot{C}H_2 + H_2C{=}CH_2 \longrightarrow ClCH_2CH_2CH_2\dot{C}H_2$$
$$ClCH_2CH_2CH_2\dot{C}H_2 + H_2C{=}CH_2 \longrightarrow ClCH_2(CH_2CH_2)_{n+1}\dot{C}H_2$$
$$ClCH_2(CH_2CH_2)_{n+1}\dot{C}H_2 + HCl \longrightarrow ClCH_2(CH_2CH_2)_{n+1}CH_3 + Cl^{\bullet}$$
$$[n = 4\text{-}10]$$

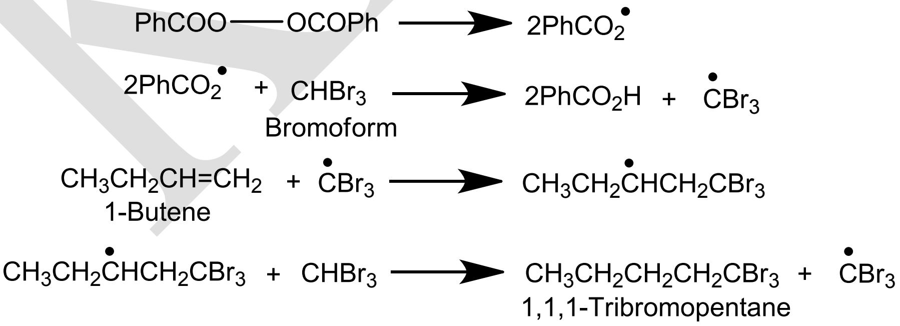
These low polymers are known as *telemers* and are produced in the addition of hydrogen chloride to ethylene in the presence of benzoyl peroxide under pressure.

For the addition of HBr, both the steps are exothermic and so the addition takes place readily.

The homolytic addition of HI to ethylene is difficult as the first step of the chain-propagating step is endothermic by 7 kcal/mole. In fact no HI has so far been added to an olefin in a free radical chain process.

Addition of Some Carbon Radicals to Alkenes-Formation of Carbon-Carbon Bonds

The addition of hydrogen bromide to C = C in radical catalysed reactions provides a good method of the formation of a carbon halogen bond. Several useful synthetic radical catalysed reactions are based on the addition of aliphatic carbon radicals to olefinic bonds. Thus a halomethane can be added to an alkene in the presence of peroxides e.g., the addition of bromoform to 1-butene.



$$PhCOO{-}OCOPh \longrightarrow 2PhCO_2^{\bullet}$$
$$\underset{}{2PhCO_2^{\bullet}} + \underset{\text{Bromoform}}{CHBr_3} \longrightarrow 2PhCO_2H + \dot{C}Br_3$$
$$\underset{\text{1-Butene}}{CH_3CH_2CH{=}CH_2} + \dot{C}Br_3 \longrightarrow CH_3CH_2\dot{C}HCH_2CBr_3$$
$$CH_3CH_2\dot{C}HCH_2CBr_3 + CHBr_3 \longrightarrow \underset{\text{1,1,1-Tribromopentane}}{CH_3CH_2CH_2CH_2CBr_3} + \dot{C}Br_3$$

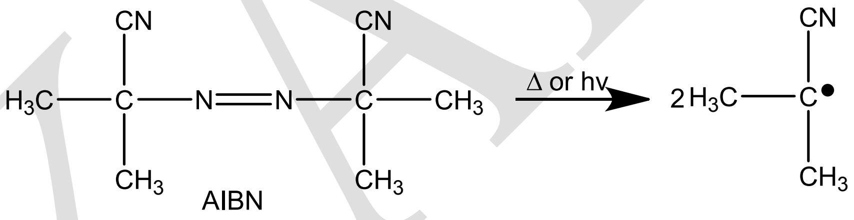
One may also use bromotrichloromethane and due to the preferential abstraction of bromine (C-Br bond is weaker than C-Cl bond), a trichloromethyl unit is added to the less substituted carbon atom of the alkene.

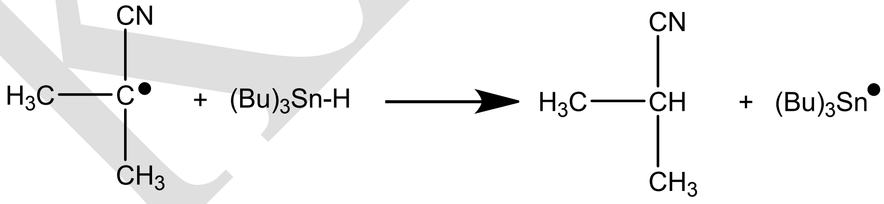
$$BrCCl_3 + H_2C{=}CHR \xrightarrow[\Delta]{Peroxide} Cl_3CCH_2CHRBr$$

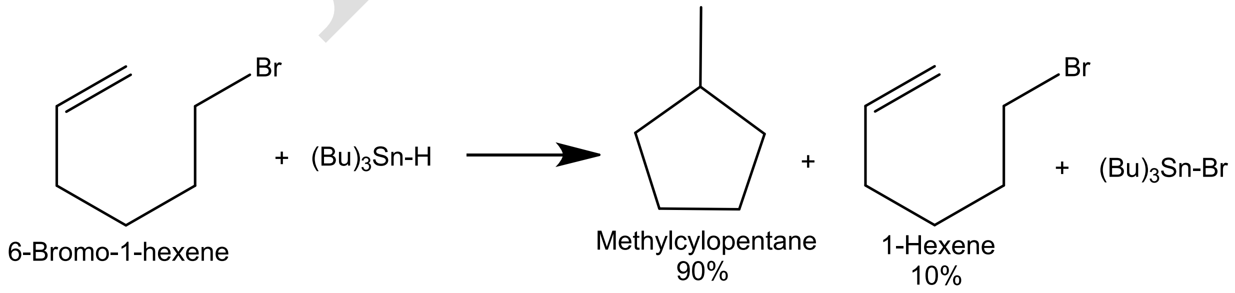
Other functional groups can also provide sufficient stabilization of radicals to permit successful chain additions to alkenes. Acyl radicals are formed by abstraction of the formyl hydrogen from aldehydes and the resulting acyl radicals (R*CO) are stabilized to some extent. The chain process results in formation of a ketone by addition of the aldehyde to an alkene.

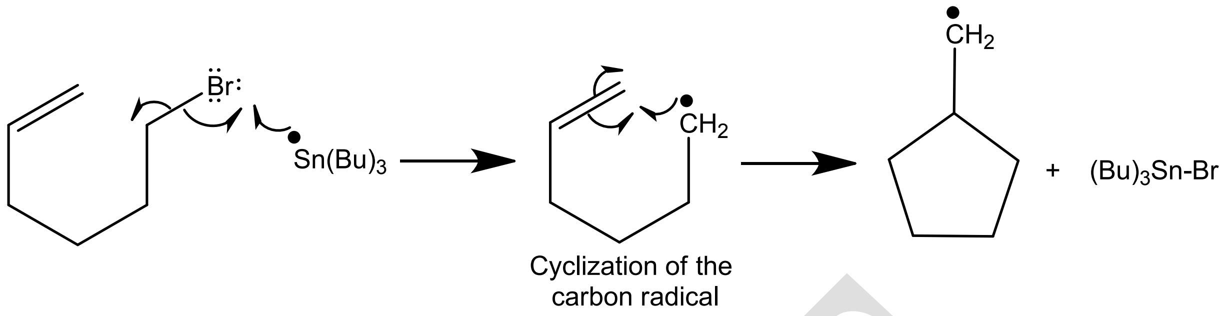
$$CH_3CHO + C_6H_{13}CH{=}CH_2 \xrightarrow{Peroxide} \underset{\text{2-Decanone}}{C_6H_{13}CH_2CH_2COCH_3}$$

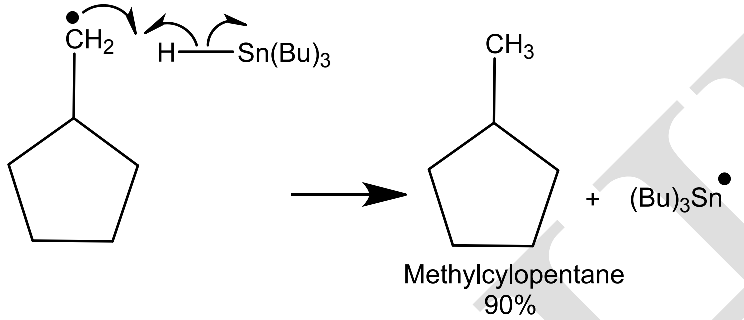
Intramolecular addition of a carbon radical to a C=C bone produces a ring. Five membered rings are greatly preferred kinetically, even when a five membered ring closure means generating a primary radical and a six membered ring closure a secondary radical (This situation may be compared with the order of ring formation in intramolecular S_N2 reactions : 5>6>3. Stability of the ring is not the only factor the probability that the ends can get together is also important). Thus five membered rings are readily formed by the tributylstannane method, i.e., on reaction of 6-brome-1-hexene with a tributyltin radical. AIBN initiates free radical formation from tributyl tin hydride.











C. Aromatic Substitution

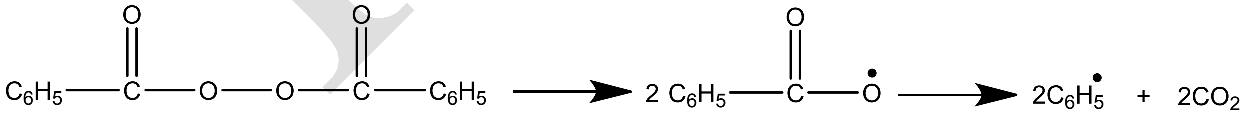
Hey observed in 1934 that the thermal decomposition of diazonium salts in aromatic solvents leads to the arylation of the aromatic rings. These results were interpreted at that time as involving *homolysis* of the ionized salts to provide aryl radicals which directly displaced a hydrogen atom in the aromatic solvent molecule.

$$\mathrm{Ar{-}N{=}N{-}X} \longrightarrow \mathrm{Ar^{\bullet}} + \mathrm{N_2} + \mathrm{X}$$

$$\mathrm{Ar^{\bullet}} + \mathrm{C_6H_5{-}H} \longrightarrow \mathrm{Ar{-}C_6H_5} + \mathrm{H}$$

$$[\mathrm{X = Cl, OCOCH_3, OH}]$$

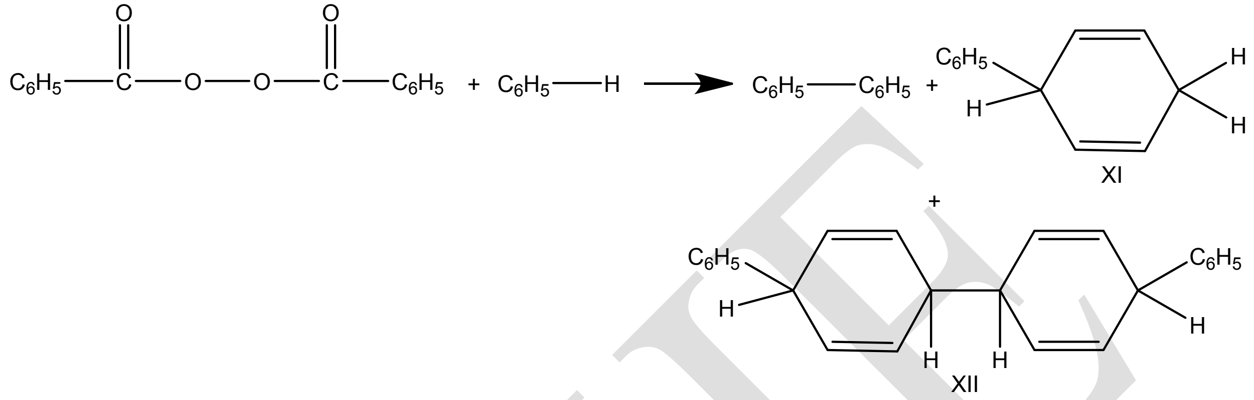
The phenyl radicals generated from others sources such as the decomposition of benzoyl peroxide in aromatic solvents also lead to similar results.



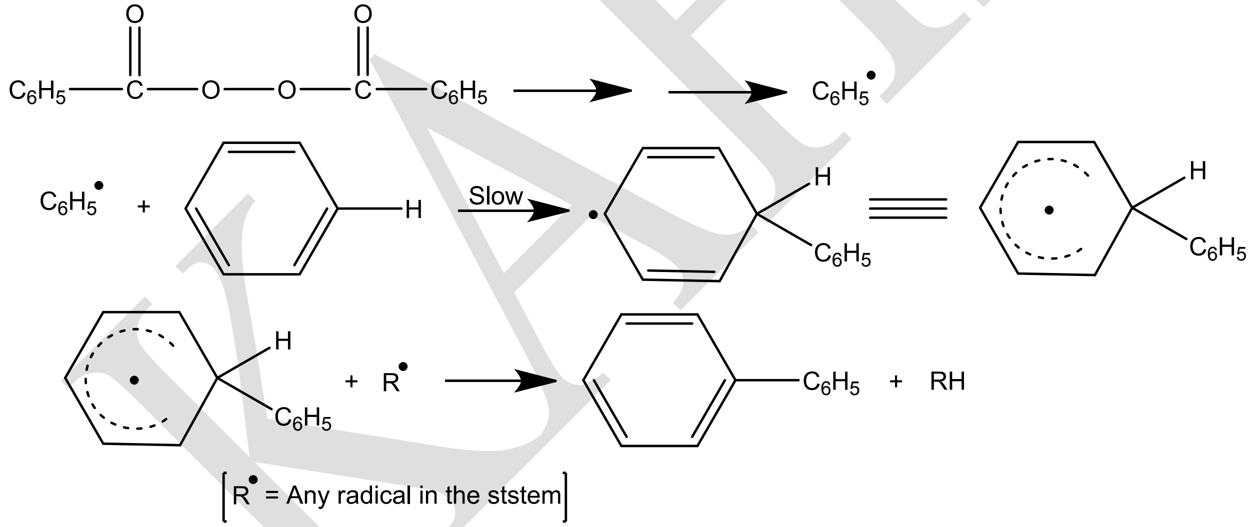
$$\mathrm{C_6H_5{-}\overset{O}{\overset{\|}{C}}{-}O{-}O{-}\overset{O}{\overset{\|}{C}}{-}C_6H_5} \longrightarrow 2\,\mathrm{C_6H_5{-}\overset{O}{\overset{\|}{C}}{-}\dot{O}} \longrightarrow 2\mathrm{C_6H_5^{\bullet}} + 2\mathrm{CO_2}$$

$$\mathrm{C_6H_5{-}H} + \mathrm{{}^{\bullet}C_6H_5} \longrightarrow \mathrm{C_6H_5{-}C_6H_5} + \mathrm{H^{\bullet}}$$

Further investigation of arylation reactions, however, resulted in the accumulation of evidence against the direct displacement mechanism. It was noted, for instance, that as the reaction involves the formation of a carbon-carbon bond at the expense of a relatively stronger carbon-hydrogen bond, it should require very high *activation* energy which is actually not the case. Furthermore, the direct displacement mechanism does not explain products such as XI and XII.

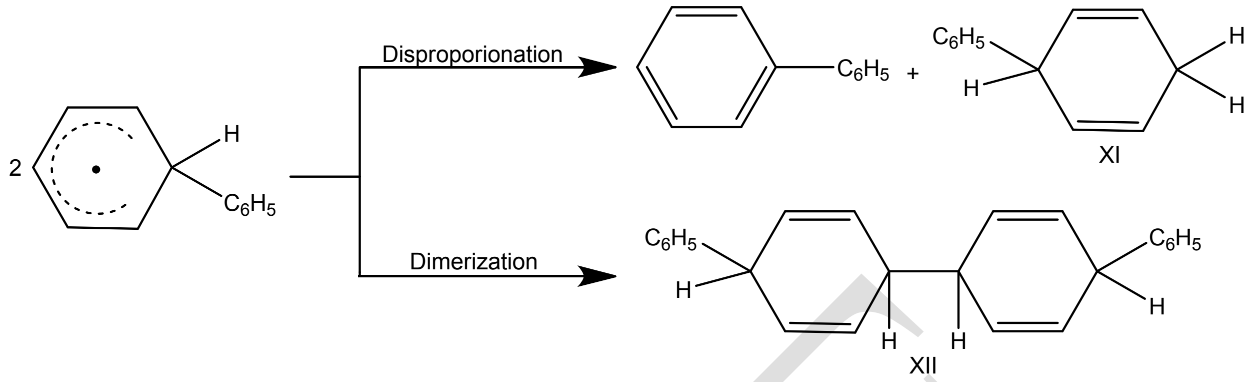


A two-step mechanism, which is not only exothermic but also explains the formation of XI and XII, was subsequently proposed.



[R• = Any radical in the ststem]

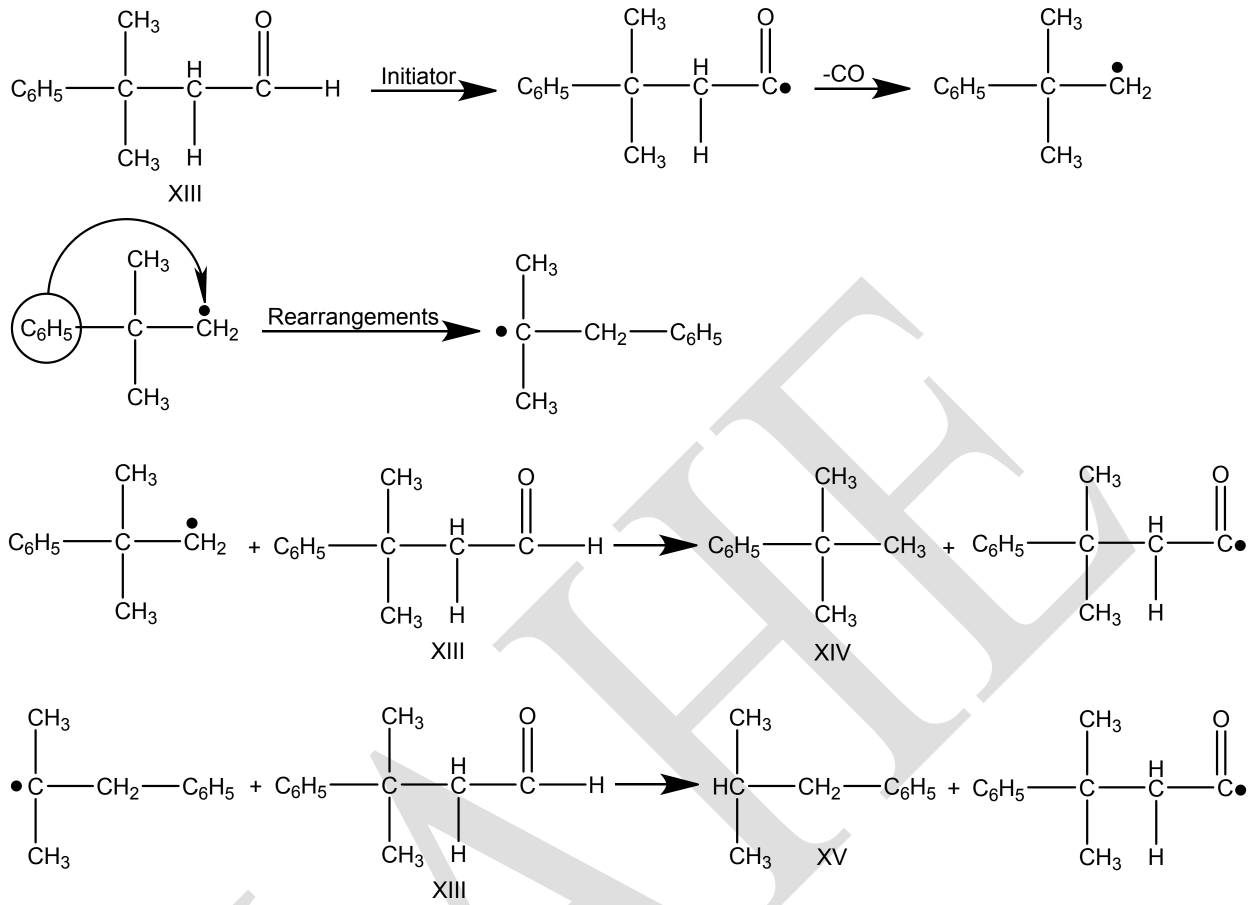
Products XIII and XIV arise due to disproportionation and dimerization of the intermediate radical, respectively.



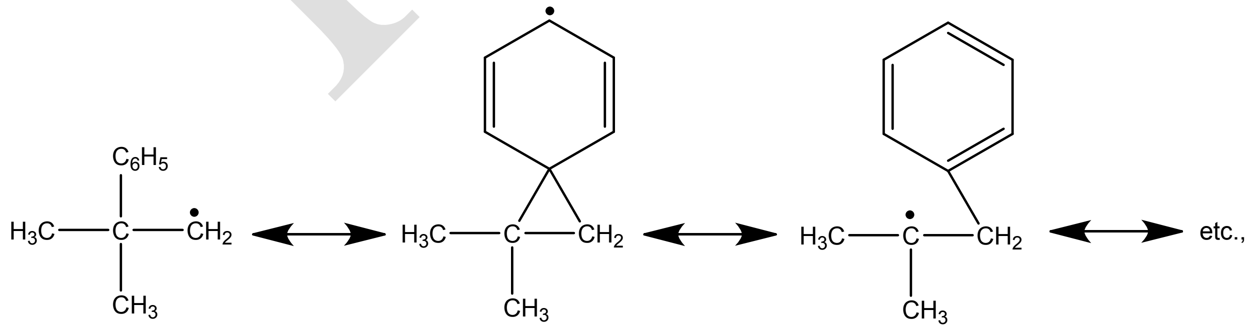
Relative rates of phenylation of different aromatic compounds have been determined by the competitive method in which a phenyl radical is generated in a solvent consisting of two substances (for example, benzene and chlorobenzene) and the proportion of each compound phenylated is then determined. Such studies have shown that nitrobenzene, chlorobenzene and toluene react faster than benzene in contrast to electrophilic aromatic substitution in which electron-donation or withdrawal by the substituents is an important factor. This is to be expected since radicals such as phenyl are neutral species and are not influenced by the polar properties of the substrate to any significant extent. Furthermore, it has been demonstrated that both electron-donating and electron-withdrawing substituents stabilize a free radical.

D. Rearrangement of radicals

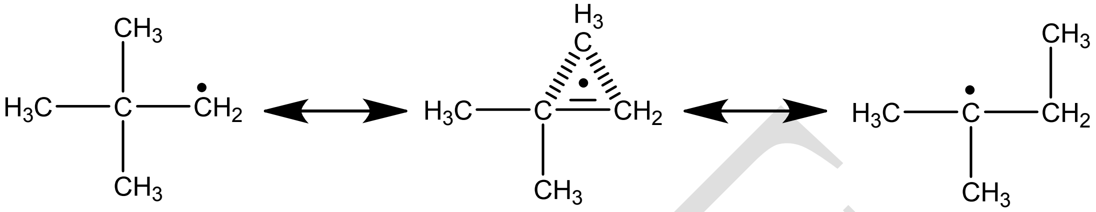
Although a primary radical may sometimes produce a tertiary radical by the migration of a substituent from the neighbouring carbon atom, in practice, radical rearrangements have been found to be distinctly less common than carbonium ion rearrangements. This diminished tendency for rearrangement is due to the fact that the difference in stability between a primary and a tertiary radical is not as much as that between a primary and a tertiary carbonium ion. Most of the reported radical rearrangements involve the shift of an aryl group from one atom to the adjacent atom. One illustrative example is the rearrangement accompanying decarbonylation of β-phenylisovaleraldehyde (XII). The reaction, which is induced by *t*-butyl peroxide, yields a product mixture consisting of almost equal amounts of isobutylbenzene (XIV) and *t*-butylbenzene (XV).



The yield of the rearranged product (XVI) increases with the dilution of the reaction mixture. This appears quite consistent with the mechanism formulated above as decrease in the concentration of the hydrogen donor (XV) would increase rearrangement at the expense of hydrogen abstraction by the radical. Further, the rate of the rearrangement is inhibited by the addition of an effective hydrogen donor such as thiophenol. The rearrangement is believed to proceed *via* the intermediate *bridged radical*.



The intermediacy of a bridged radical also explains why a methyl migration does not take place in radical rearrangements in contrast to carbonium ion rearrangements. For a hypothetical methyl migration *via* a bridged radical there will be three electrons spread over three carbons.



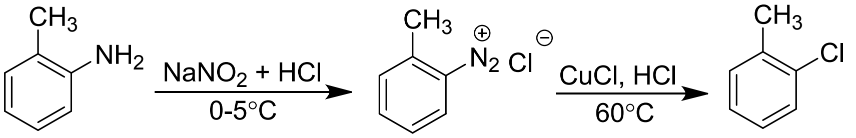
Molecular orbital calculations have shown that such a system is very unstable in comparison to a two electron system of a carbonium ion rearrangement.

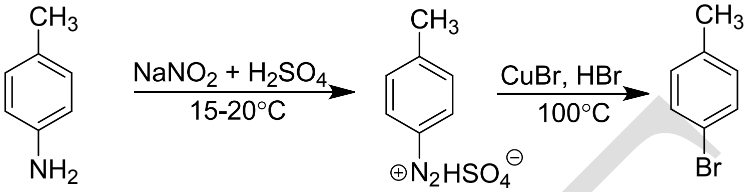
Sandmeyer reaction

Alkyl halides are more often prepared from the corresponding alcohols by reacting the alcohols with PCl_3, $SOCl_2$ or concentrated $HCl/ZnCl_2$. The aryl halides cannot be prepared from phenols by these methods. Direct halogenation of aromatic compounds yields a mixture of isomers from which it is difficult to isolate the desired isomer.

Sandmeyer reaction affords a useful method for introducing a halogen substituent at the desired position of an aromatic ring.

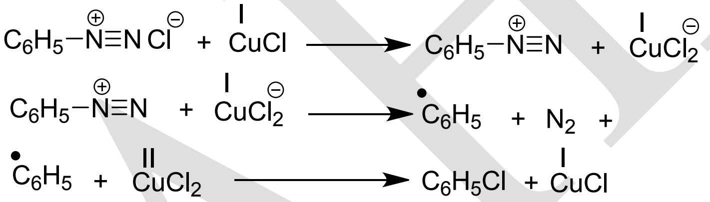
The method involves the conversion of an aromatic primary amine into an aryl diazonium salt by treatment with nitrous acid in the presence of mineral acids (usually HCl or H_2SO_4) at low temperature (0-5ºC). Subsequent decomposition of the diazonium salt by heating with cuprous chloride or bromide in the presence of an excess amount of the corresponding halogen acid gives aryl chloride or bromide. The overall reaction is, thus the replacement of the amino group of the aromatic amine by halogens.





Mechanism

It seems that cuprous copper has the power to reduce diazonium ion to aryl radical by oxidation-reduction involving one electron-transfer. The copper first acts as reducing and then as oxidizing agent.

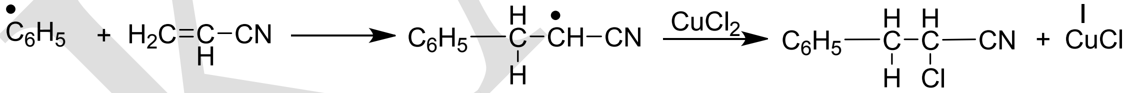


$$C_6H_5-\overset{\oplus}{N}\equiv N\,\overset{\ominus}{Cl} + \overset{I}{Cu}Cl \longrightarrow C_6H_5-\overset{\oplus}{N}\equiv N + \overset{I}{Cu}Cl_2^{\ominus}$$

$$C_6H_5-\overset{\oplus}{N}\equiv N + \overset{I}{Cu}Cl_2^{\ominus} \longrightarrow \overset{\bullet}{C}_6H_5 + N_2 +$$

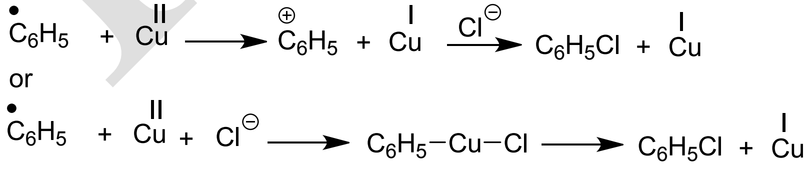
$$\overset{\bullet}{C}_6H_5 + \overset{II}{Cu}Cl_2 \longrightarrow C_6H_5Cl + \overset{I}{Cu}Cl$$

The formation of aryl radical is substantiated by the decomposition of benzene diazonium chloride in the presence of acrylonitrile when 2-chloro-3-phenylpropionitrile is obtained through free radical addition.



$$\overset{\bullet}{C}_6H_5 + H_2C=\underset{H}{C}-CN \longrightarrow C_6H_5-\overset{H}{\underset{H}{C}}-\overset{\bullet}{C}H-CN \xrightarrow{CuCl_2} C_6H_5-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{Cl}{C}}-CN + \overset{I}{Cu}Cl$$

The formation of the halide by the cupric copper may also involve a carbocation intermediate or an organo-copper compound.



$$\overset{\bullet}{C}_6H_5 + \overset{II}{Cu} \longrightarrow \overset{\oplus}{C}_6H_5 + \overset{I}{Cu} \xrightarrow{Cl^{\ominus}} C_6H_5Cl + \overset{I}{Cu}$$

or

$$\overset{\bullet}{C}_6H_5 + \overset{II}{Cu} + Cl^{\ominus} \longrightarrow C_6H_5-Cu-Cl \longrightarrow C_6H_5Cl + \overset{I}{Cu}$$

For the preparation of aryl iodide, the aryl diazonium salt is treated with potassium iodide solution. The cuprous catalyst is unnecessary because iodide ion is sufficient to decompose the diazonium salt. However, in this case also oxidation–reduction is probably involved since enough iodide is liberated in the reaction.

Aryl fluoride is prepared by treating the diazonium salt with fluoboric acid or fluoborate. Sparingly soluble diazonium fluoborate which separates is washed and dried. The dry salt is then decomposed by heating.

$$C_6H_5\overset{\oplus}{N_2}\overset{\ominus}{Cl} \xrightarrow{HBF_4} C_6H_5\overset{\oplus}{N_2}\overset{\ominus}{BF_4} \xrightarrow{150\text{-}160°C} C_6H_5F + F_2 + BF_3$$

This reaction is known as Schiemann reaction.

Applications and extension

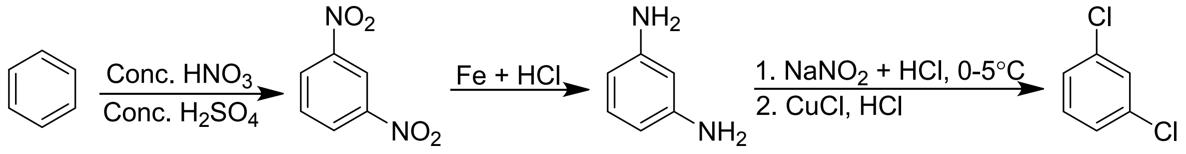
Sandmeyer reaction for the preparation of arylhalides from diazonium salt is more important and useful than direct halogenation for several reasons.

(i) Direct halogenation of aromatic compounds gives a mixture of isomers so that the yield of the desired isomer is low and difficult to separate. On the other hand, the diazonium salts gives only one halogen derivative since the halogen enters at the position previously occupied by the diazonium group.

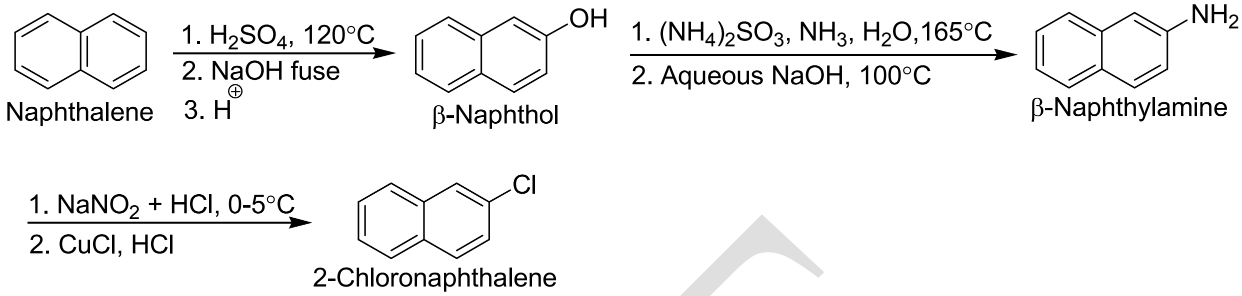
(ii) Aryl iodides and fluorides which are seldom prepared by direct halogenation can be prepared by Sandmeyer reaction and Schiemann reaction respectively.

(iii) In some cases direct halogenation at a particular position is not possible for reasons of electronic factors but this has been possible through Sandmeyer reaction, e.g.,

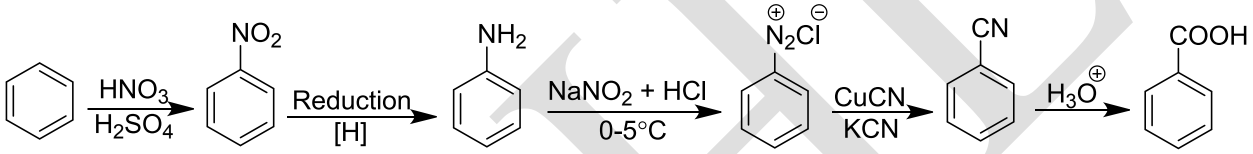
(a) Preparation of *m*-dichlorobenzene



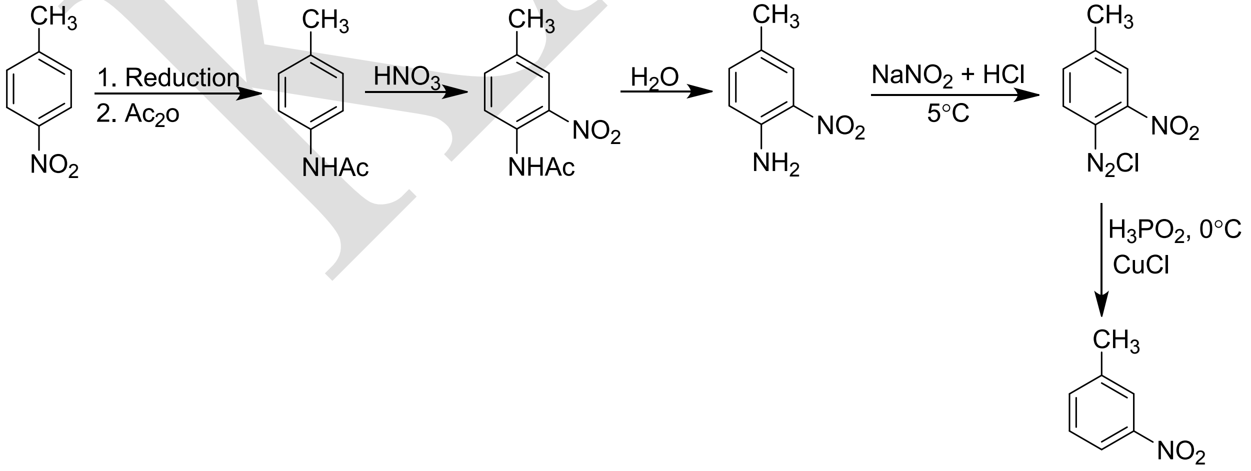
(b) Preparation of 2-chloronaphtnalene



(c) Preparation of acids-Diazonium salts on treatment with cuprous cyanide and potassium cyanide gives nitriles which on hydrolysis gives acids.

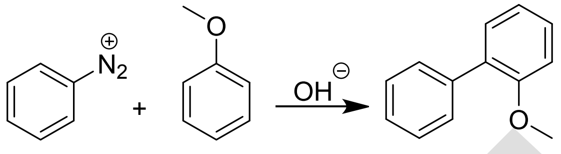


(d) Removal of amino group from aromatic rings-Amino groups of aromatic amines after conversion to the corresponding diazonium salt and treatment with hypophosphorous acid are removed from the aromatic ring. The reaction has been successfully used to prepare compounds which cannot be prepared by direct substitution. Thus, *m*-nitro toluene may be prepared from toluene. Toluene on nitration gives *o*- and *p*-nitrotoluenes. The *para*-isomer after separation is processed as below.



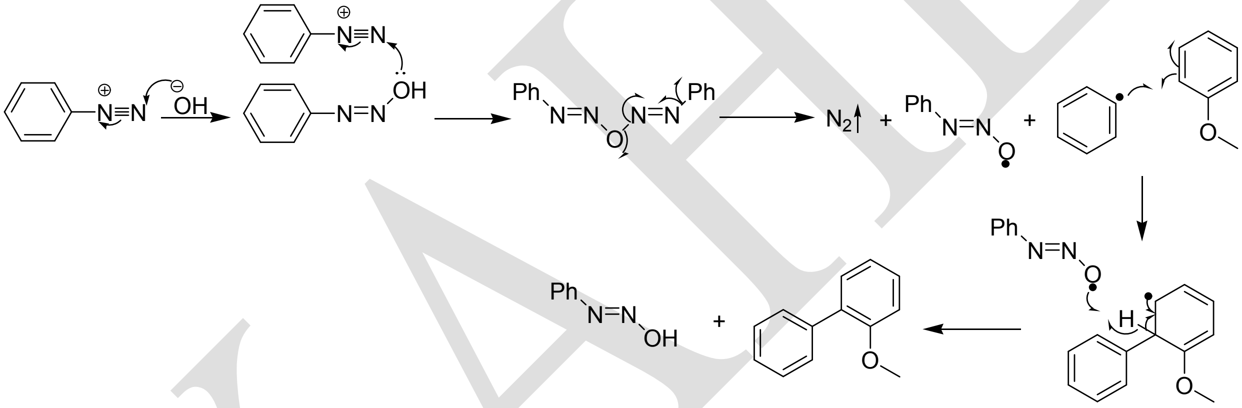
Gomberg–Bachmann reaction

$$ArH + Ar'\overset{\oplus}{N}_2X^{\ominus} \xrightarrow{OH^{\ominus}} Ar-Ar'$$



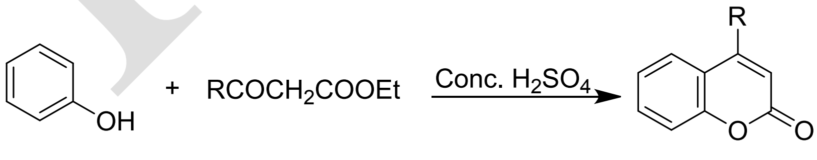
When the normally acidic solution of a diazonium salt is made alkaline, the aryl portion of the diazonium salt can couple with another aromatic ring known as Gomberg–Bachmannn reaction.

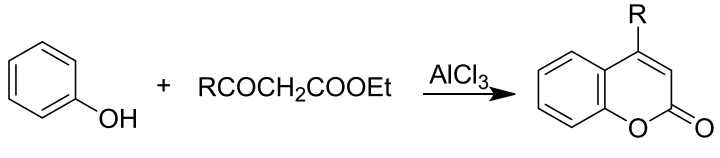
Mechanism



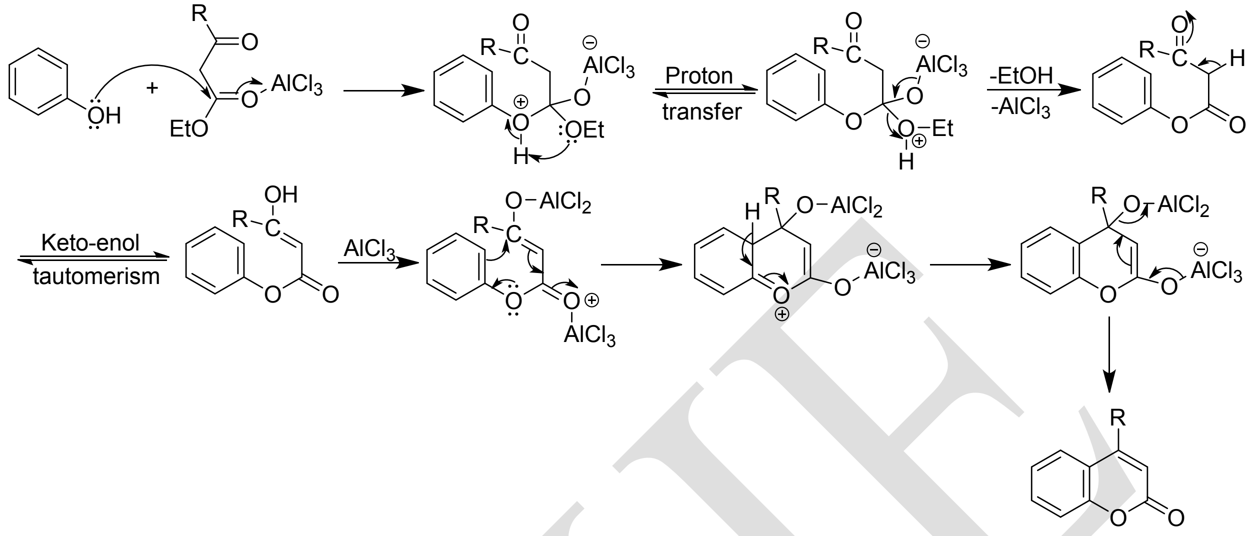
Pechmann reaction (or) condensation

The acid-catalysed condensation of phenols with β-ketoesters to produce coumarins is called the Pechmann reaction. A variety of condensing reagent such as concentrated sulphuric acid, HF, Lewis acids etc. are used.

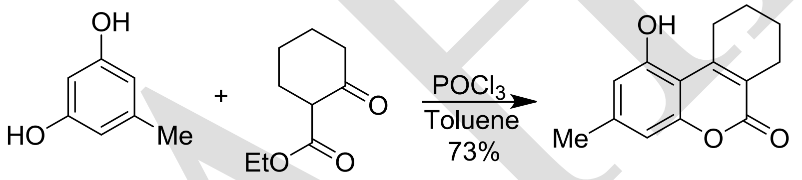


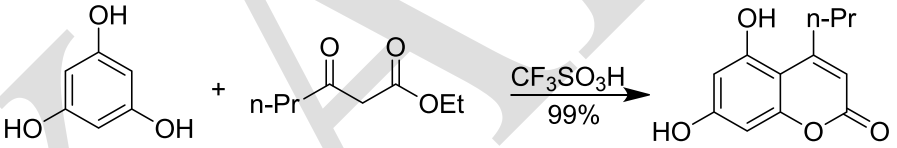


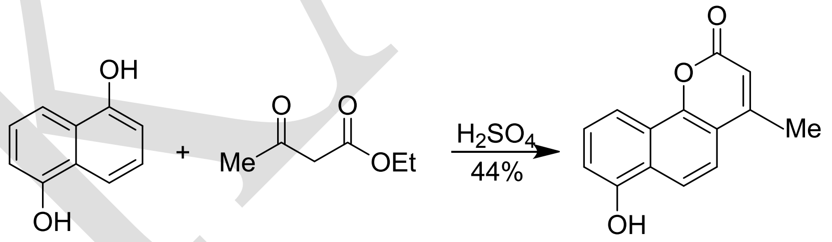
Proposed mechanism



Examples







Ullmann reaction

Ullmann reaction encompasses the synthesis of diphenyl amines, diphenyl ethers and diphenyls.

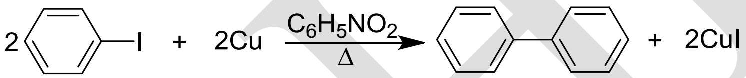
(i) $C_6H_5NHCOCH_3 + C_6H_5Br + K_2CO_3 \xrightarrow[\text{Reflux}]{\text{Cu}} (C_6H_5)_2NH + CO_2 + CH_3COOK + KBr$

(ii) $C_6H_5OH + C_6H_5Br + KOH \xrightarrow[\text{Reflux}]{\text{Cu}} (C_6H_5)_2O + KBr + H_2O$

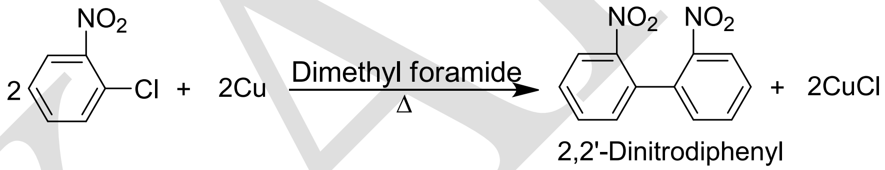
(iii) $2C_6H_5I + Cu \xrightarrow[\Delta]{C_6H_5NO_2} C_6H_5{-}C_6H_5 + CuI_2$

The preparation of diaryls (eq. iii) called Ullmann coupling reaction, is the most important reaction and is discussed below.

Ullmann coupling reaction involves the condensation of aryl halides in the presence of finely divided copper or copper bronze at an elevated temperature (100–350ºC) to yield diaryl derivatives. Thus, iodo-benzene in nitrobenzene when heated in the presence of copper powder gives diphenyl in 80% yield. Alternatively, the reactants may be heated in a sealed tube.



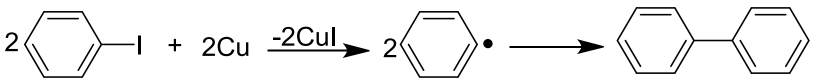
The reaction is successful with aryl iodides. However, aryl bromides and chlorides also react when electronegative substituents, which activate the halogen, are present.



A better yield is obtained on using dimethylformamide as solvent. Nitro group strongly activates the halides but only from the ortho position while alkyl (R) and alkoxy (OR) groups activate from all positions. Electron-releasing groups inhibit the reaction. The reaction is important since it is simple, straightforward and the structure of the product is known from its synthesis.

Mechanism

The mechanism of the reaction is uncertain. A radical mechanism has been suggested.



These are evidence against the radical mechanism and hence a mechanism similar to that of Wurtz reaction has been suggested.

$$C_6H_5I + Cu \longrightarrow C_6H_5CuI \quad ---(1)$$

$$C_6H_5CuI + C_6H_5I \longrightarrow C_6H_5{-}C_6H_5 + CuI_2 \quad -----(2)$$

The fact that iodide gives good results suggest that iodides undergo step (1) more readily.

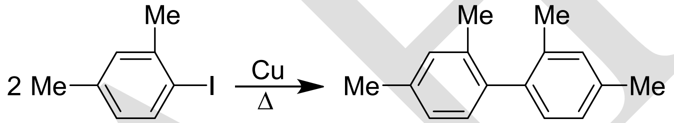
Applications

The reaction provides methods for the preparation of compounds which cannot be readily prepared by other method. The yields of the products are high in most cases.

(A) A large number of biaryls and polyaryls have been synthesized by the Ullmann coupling reaction.

(1) Symmetrical biaryls

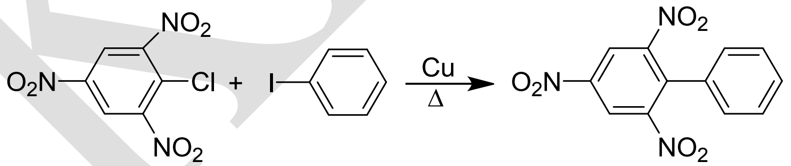
p-Iodobenzoic acid 4, 4'-Diphenic acid



2,4-Dimethyl iodobenzene 2, 2', 4, 4'-Tetramethyl biphenyl

(2) Unsymmetrical diaryls

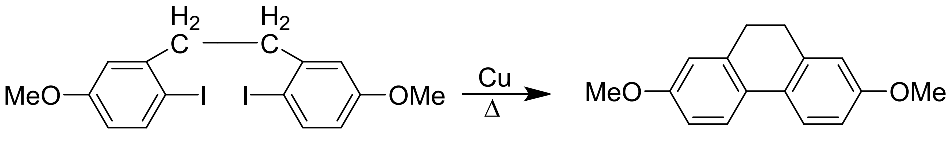
With a mixture of two different aryl halides, three products are obtained which has poor synthetic value for the yield of the desired product is low and difficult to isolate. In some cases, however, the unsymmetrical product is only formed, e.g.,



Picryl chloride 2, 4, 6-Trinitro biphenyl

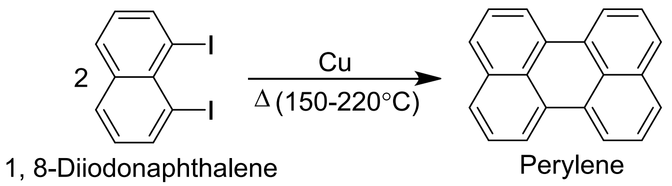
(3) Polyaryl hydrocarbons

(i)

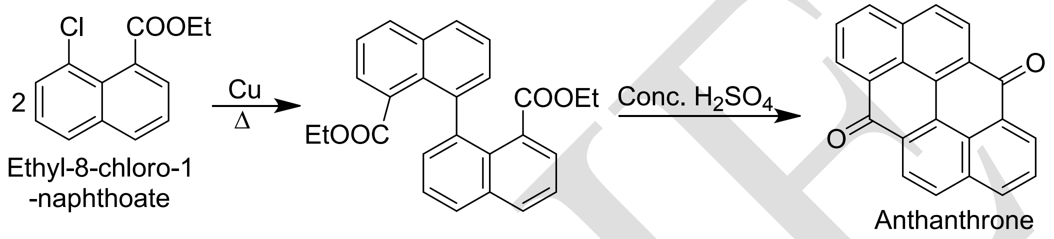


2, 2'-Diiodo-5, 5'-dimethoxy dibenzyl 2, 7-Dimethoxy-9, 10-dihydrophenanthrene

(ii)

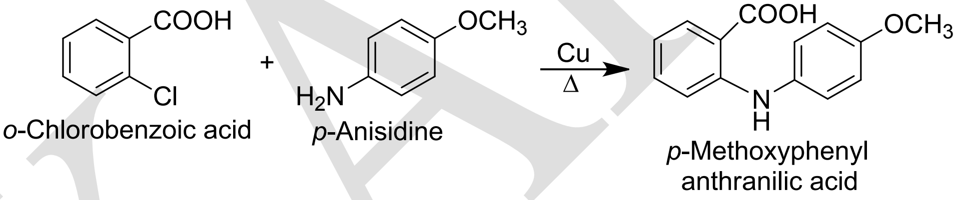


(iii)

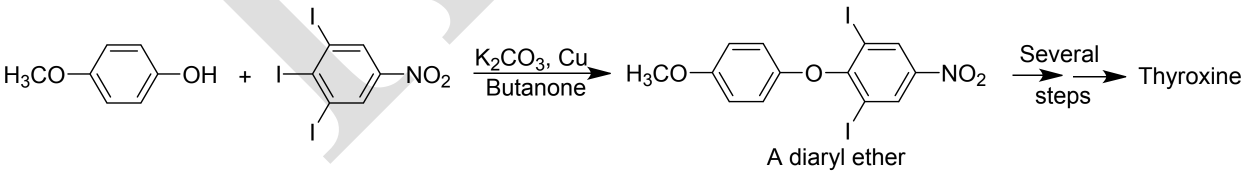


(B) Ullmann reaction also provides methods for the preparations of diarylamines and diaryl ethers

1. Diarylamines: An arylamine and an aryl halide are refluxed in the presence of anhydrous potassium carbonate and copper powder.

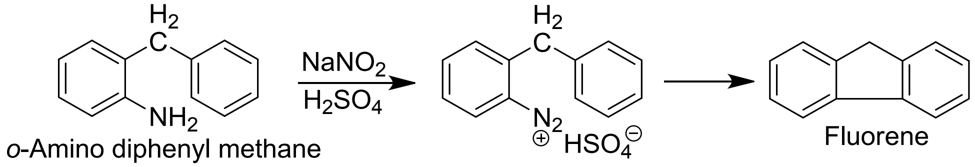


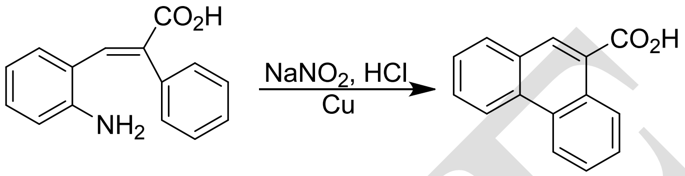
2. Diaryl ethers: A phenolic compound and an aryl halide are refluxed in the presence of potassium hydroxide or K_2CO_3 and copper. The reaction has been employed in the synthesis of thyroxine.



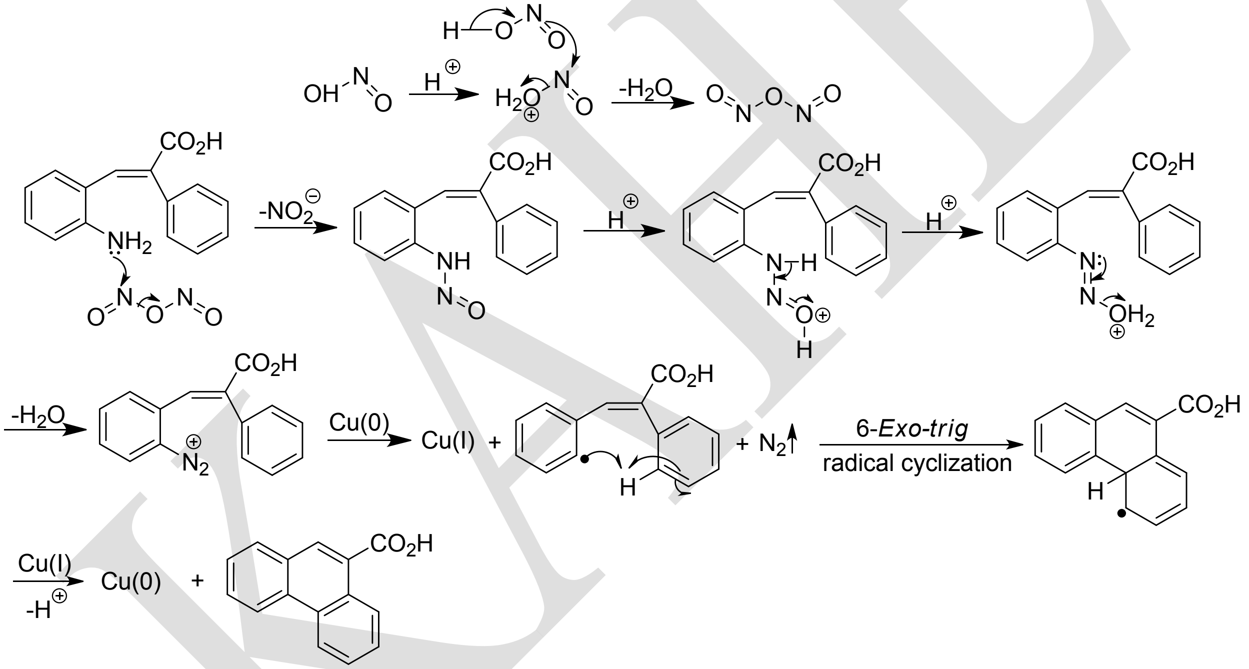
Pschorr reaction

When the Gomberg–Bachmann reaction is performed intermolecularly either by alkaline solution or with copper powder the procedure is termed Pschorr ring closure. Fluorene is prepared starting with *o*-aminodiphenyl methane.

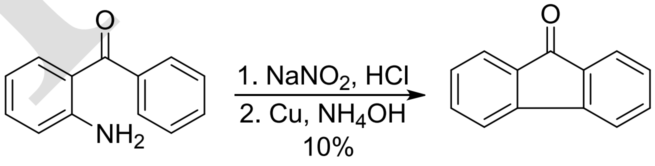


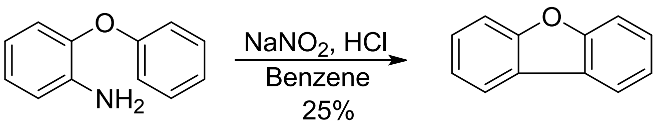


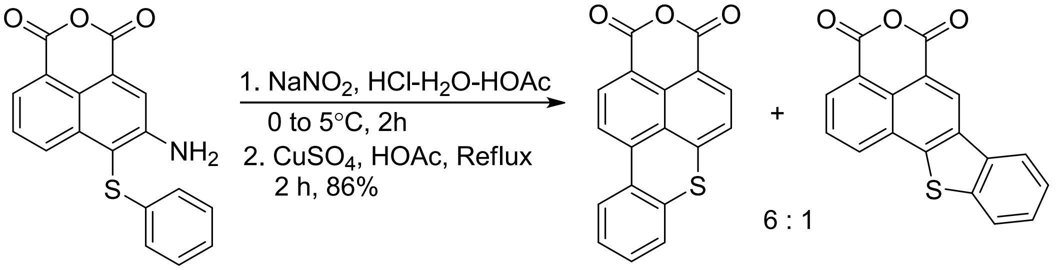
Mechanism

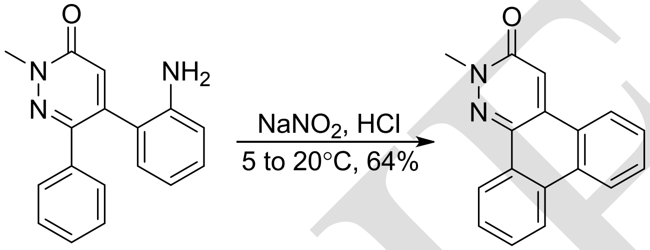


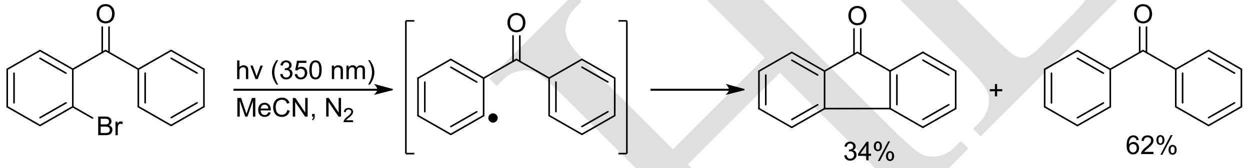
Examples





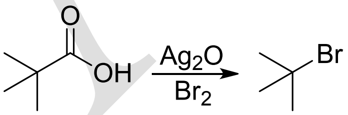






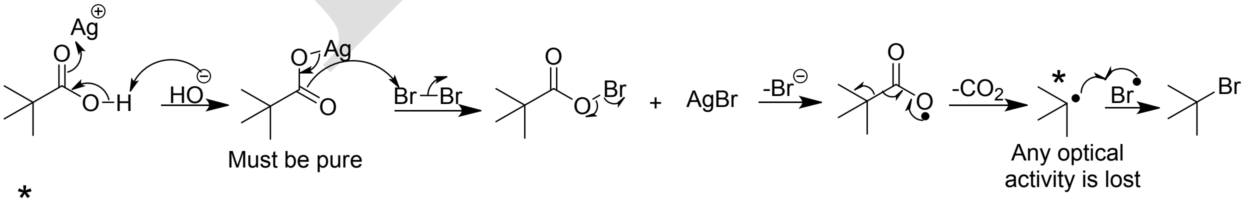
Hunsdiecker reaction (Decarboxylative bromine)

This is a free radical substitution reaction, where the reaction of a silver salt of carboxylic acid with bromine gives a bromo compound and is a method of decreasing the length of the carbon chain by one unit.

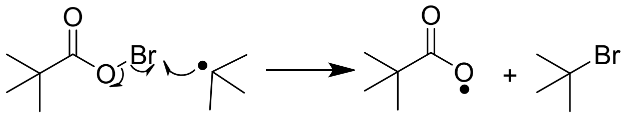


Mechanism

$$Ag_2O + H_2O \rightleftharpoons AgOH + HO^{\ominus} + Ag^{\oplus}$$



* This step can also be the propagation step:



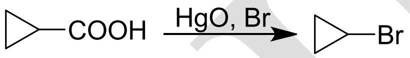
Applications

The reaction is of wide scope, producing alkyl and aryl halides.

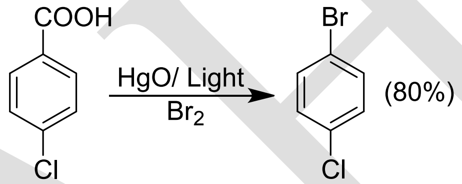
(1)

$$CH_3CO_2(CH_2)_4COOAg \xrightarrow[\substack{CCl_4\text{, Reflux} \\ \text{-AgBr}}]{Br_2} CH_3CO_2(CH_2)_3CH_2Br$$

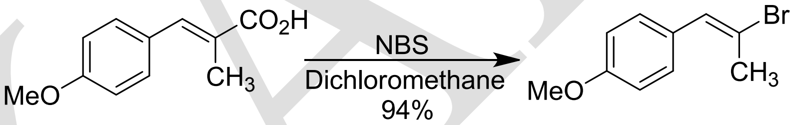
(2)



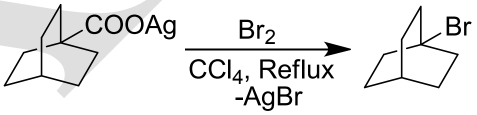
(3)



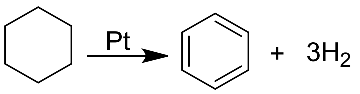
(4)



(5) A free radical has been generated at bridge head position via the Hunsdiecker reaction to show that a free radical need not be planar.



Aromatization of six-membered rings



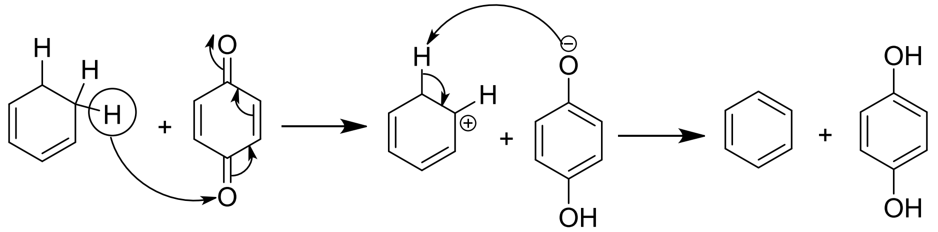
Six-membered alicyclic rings can be aromatized in a number of ways. Aromatization is accomplished most easily if there are already one or two double bonds in the ring or if the ring is fused to an aromatic ring. The reaction can also be applied to heterocyclic five-and six-membered rings. Many groups may be present on the ring without interference, and even gem-dialkyl substitution does not always prevent the reaction: In such cases one alkyl group often migrates or is eliminated. However, more drastic conditions are usually required for this. In some cases OH and COOH groups are lost from the ring. Cyclic ketones are converted to phenols. Seven-membered and larger rings often isomerized to six-membered aromatic rings, though this is not the case for partially hydrogenated azulene systems (which are frequently found in nature) ; these are converted to azulenes.

There are three types of reagents most frequently used to effect aromatization.

1. Hydrogenation catalysts, such as platinum, palladium, nickel etc. In this case the reaction is the reverse of double-bond hydrogenation, and presumably the mechanism is also the reverse, though not much is known. Cyclohexene has been detected as an intermediate in the conversion of cyclohexane to benzene, using Pt. The substrate is heated with the catalyst at about 300 to 350ºC. The reactions can often be carried out under milder conditions it a hydrogen acceptor, such as maleic acid, cyclohexene, or benzene, is present to remove hydrogen as it is formed. The acceptor is reduced to the saturated compound. It has been reported that dehydrogenation of 1-methylcyclohexene–1-^{13}C over an alumina catalyst gave toluene with the label partially scrambled throughout the aromatic ring.

2. The elements sulfur and selenium which combine with the hydrogen evolved to give respectively, H_2S and H_2Se. Little is known about this mechanism either.

3. Quinones, which become reduced to the corresponding hydroquinones. Two important quinones often used for aromatizations are chloranil (2, 3, 5, 6–tetrachloro–1,4–benzoquinone) and DDQ (2,3-dichloro–5,6–dicyano–1,4–benzoquinone). The latter is more reactive and can be used in cases where the substrate is difficult to dehydrogenate. It is likely that the mechanism involves a transfer of hydride to the quinone oxygen, followed by the transfer of a proton to the phenolate ion.



Oxidation reaction

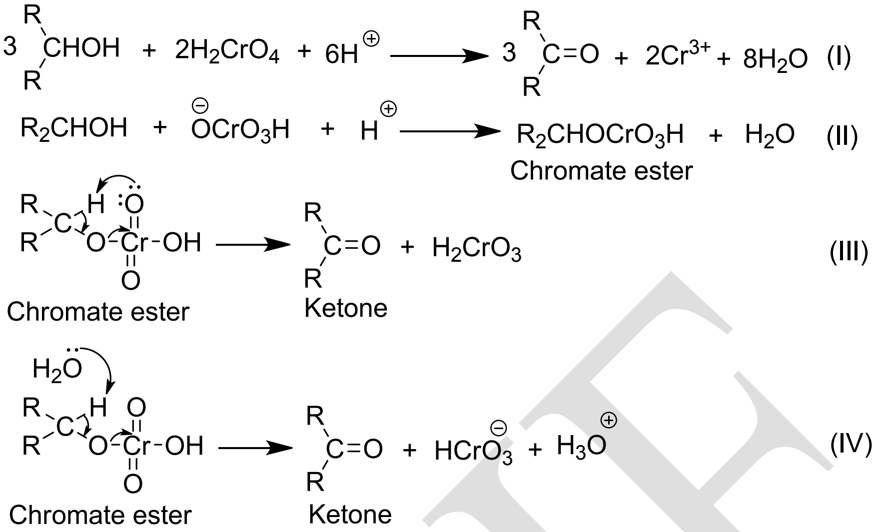
An oxidation reaction is defined as addition of oxygen to an organic compounds, removal of hydrogen or removal of electron as e.g., in the conversion of phenoxide anion to phenoxy radical.

Oxidation of alcohols to aldehydes, ketones or carboxylic acids

(A) Chromium (VI) Oxide

From among a variety of transition metal oxidants the Cr(VI)-derived reagents are highly useful. The oxidation state of Cr in these reagents is (VI), and these are powerful oxidizing species. The CrO_3 based oxidants convert an alcohol to the corresponding ketone or aldehyde and the general mechanism is given (**Scheme 1**, I balanced equation). The most commonly used reagent is chromic acid H_2CrO_4, which is usually prepared by adding chromium VI oxide (CrO_3) or sodium dichromate ($Na_2Cr_2O_7$) to sulfuric acid.

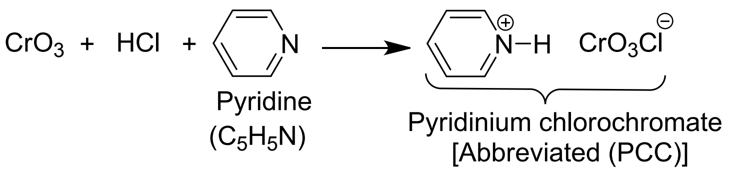
When the oxidations are carried out in aqueous acetone the process is termed Jones oxidation (or oxidation by the Jones reagent). As chromic acid oxidizes the alcohol, chromium is reduced from the +6 oxidation state (H_2CrO_4) to the +3 oxidation state (Cr^{3+}).



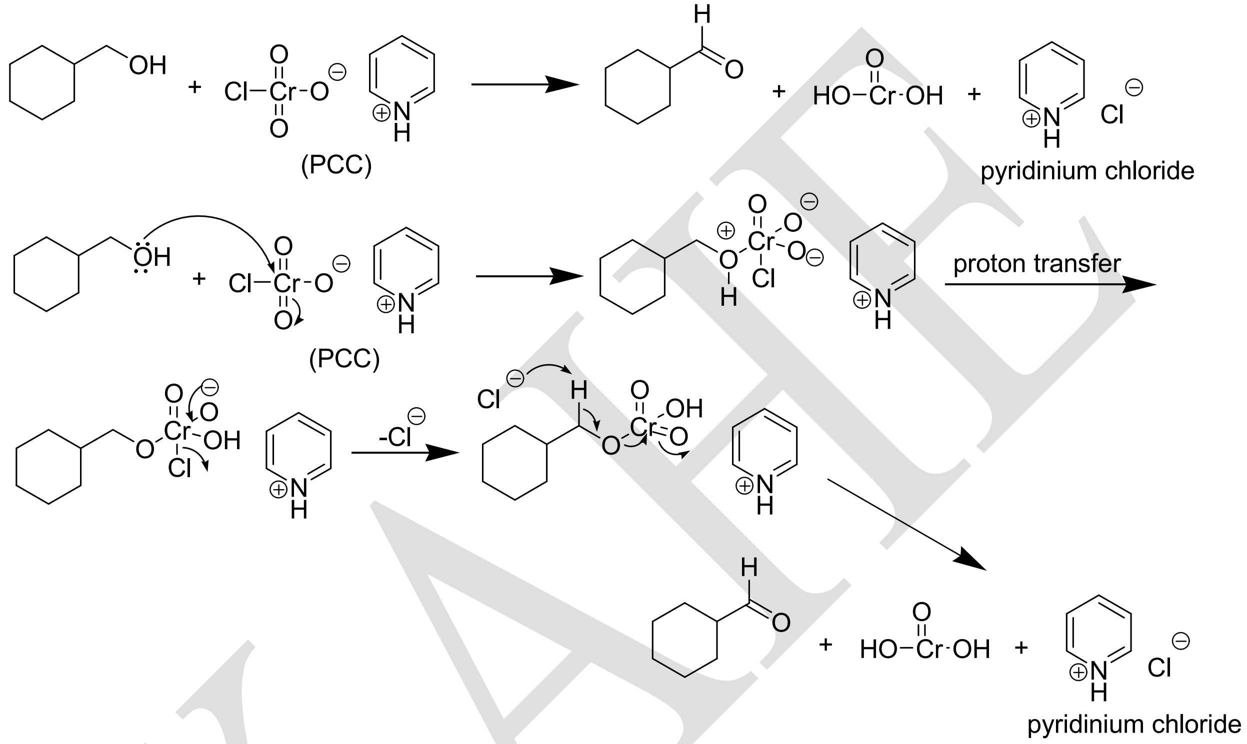
Scheme 1

The mechanism involves the initial formation of a chromate ester (eq II, **Scheme 1** and subsequent loss of a proton abstraction from the ester may take place via the cyclic (concerted) mechanism (eq III, **Scheme 1**) and $HCrO_3^-$ ion yields the ketone. The proton abstraction the ester may take place via the cyclic (concerted) mechanism (eq III, **Scheme 1**) where the proton is transferred to one of the CrO_3H oxygens. Unlike this intramolecular process, the proton loss may also be an intermolecular process (eq IV, **Scheme 1**) i.e., the α-hydrogen is abstracted by a base (usually water). Some of the most compelling evidence for either route of the mechanism i.e., the abstraction of α-hydrogen in rate determining step came from studying deuterium isotope effect. Isotope effect of about 6 was found on use of $CH_3CDOHCH_3$. Thus when chromic acid is used in the oxidation of $CH_3CDOHCH_3$ and isopropanol, $CH_3CHOHCH_3$, the deuterated compound reacted about six times slower, so that k_H/k_D is ≈ 6. The chromium trioxide pyridine complex (Collins reagent) is useful in situation when the substrate is sensitive to strong acid.

A very useful Cr (VI) reagent is pyridinium chlorochromate (abbreviated PCC), which is prepared by dissolving CrO_3 in hydrochloric acid and by subsequent treatment of the solution with pyridine (**Scheme 2**). When PCC is dissolved in DMF or is used as a suspension in CH_2C1_2, it oxidizes the secondary alcohols to ketones and allylic primary alcohols to the corresponding aldehydes. Saturated primary alcohols are oxidized to an aldehyde or the carboxylic acid depending on the conditions.

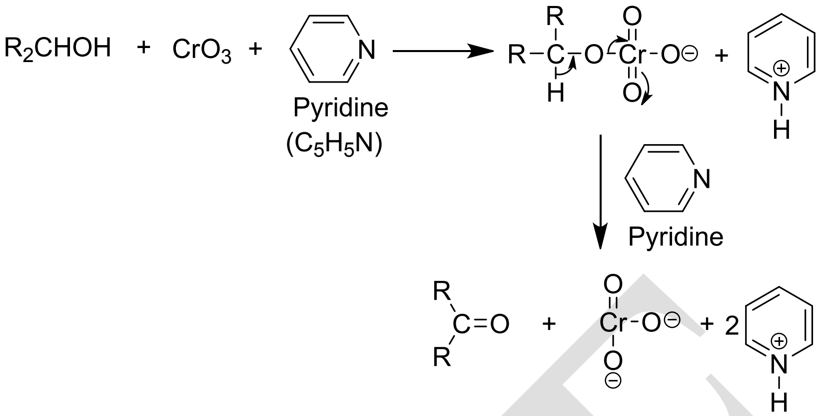


Scheme 2



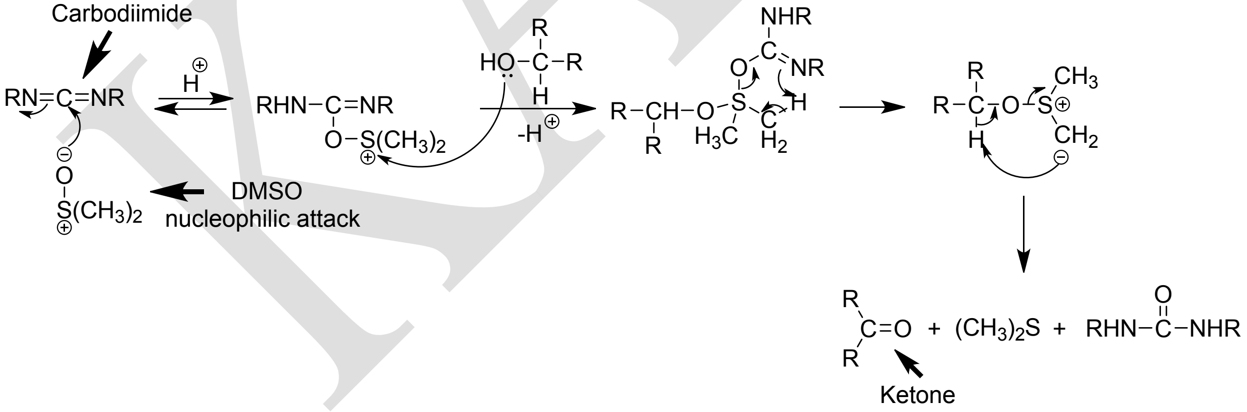
Chromium trioxide-Pyridine (Sarett's reagent)

This regent is very efficient in esterifying the alcohol because of the presence of the chromic anhydride and pyridine. Thus, an unhindered alcohol forms the ester very rapidly making the use of this mixture extremely satisfactory, particularly if the alcohol contains acid-sensitive groups in its molecule. This reagent does not oxidize double bond or thioethers and is therefore more selective than chromic acid in acetic acid or sulphuric acid. The overall mechanism is the same as discussed earlier.



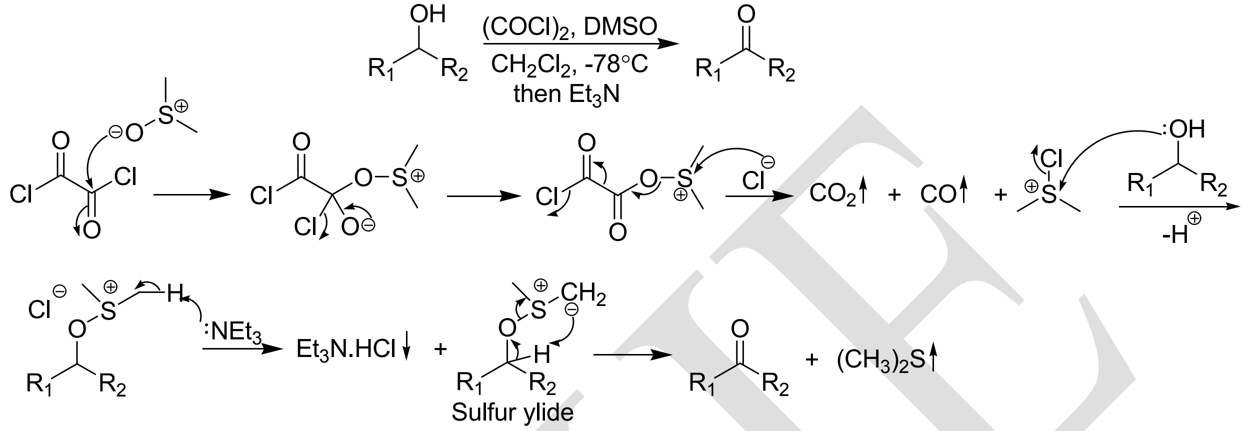
(B) Use of Dimethyl Sulfoxide (DMSO)

Dimethyl sulfoxide in combination with any one of a number of electrophilic molecules like dicyclo-hexylcarbodiimide, acetic anhydride, oxalyl chloride and sulphur trioxide brings about the oxidation of alcohols. The mechanism involves the formation of an adduct of the sulfoxide by its nucleophilic attack on the carbodiimide. This intermediate reacts with the alcohol to give an alkoxysulphonium ion which *via* the corresponding ylide, gives the carbonyl compound (**Scheme 3**, Pfitzner and Maffat method). Sulfur atoms are easily polarized, therefore, they can stabilize a negative charge on an adjacent atom. Thus the carbon atoms that are adjacent to an alkylthio group are more acidic than those adjacent to an alkoxy group.



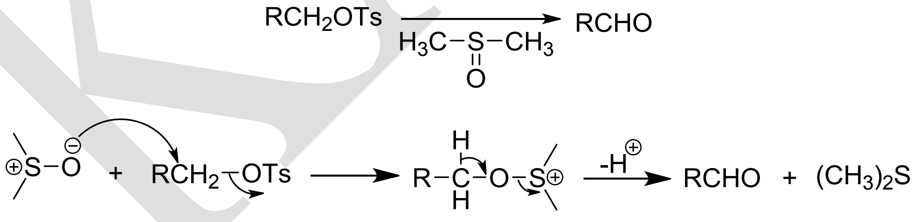
Scheme 3

Swern oxidation (**Scheme 4**) is based on the activation of DMSO toward the addition step by oxalyl chloride. The resulting alkyloxy-sulphonium salt on treatment with a base (usually triethylamine) gives the corresponding carbonyl compound in high yields under mild conditions. The oxidation proceeds *via* the activated complex formed by the loss of CO_2 and CO from the oxysulphonium salt. The carbonyl compound is then formed *via* the ylide as in the DCC method. The key step in all the oxidations with DMSO involves the addition of the alcohol and the departure of the sulfoxide oxygen as part of a leaving group.

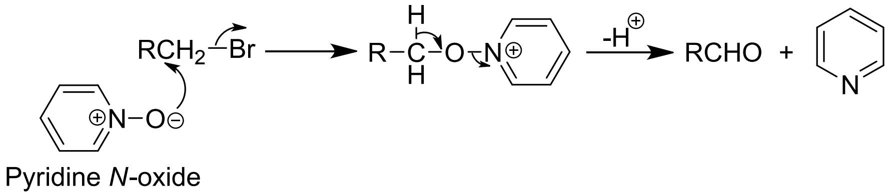


Scheme 4

Substrates with good leaving groups e.g., the alcohol toluene-*p*-sulphonates usually derived from an alcohol and the sulphonyl chloride gives the corresponding aldehydes or ketones on treatment with DMSO (**Scheme 5**). The presence of a base facilitates the reaction by removing the proton. Reaction occurs *via* an initial S_N2-displacement followed by base catalyzed elimination on the resulting sulphonium salt (**Scheme 5**). Understandably amine-oxides act in a way similar to DMSO and pyridine-*N*-oxide has been used with advantage to prepare aldehydes from halides and sulphonates (**Scheme 6**).



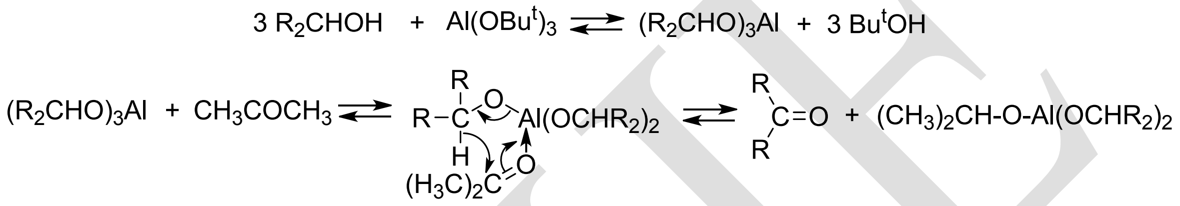
Scheme 5



Scheme 6

(C) Oppenauer method

The developments in CrO_3-pyridine and DMSO based techniques for oxidation have pushed several classical methods into background. One such method which is interesting mechanistically, is Oppenauer oxidation, this is the reverse of the Meerwein-Pondorff–Verley reduction. The technique involves heating the alcohol to be oxidised with an aluminium alkoxide in the presence of a carbonyl compound usually acetone in large excess. The carbonyl compound acts as the hydrogen acceptor within a cyclic complex (**Scheme 7**).

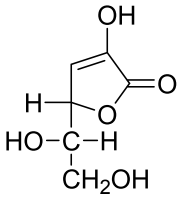


Scheme 7

(D) Catalytic oxygenation–to carboxylic acids

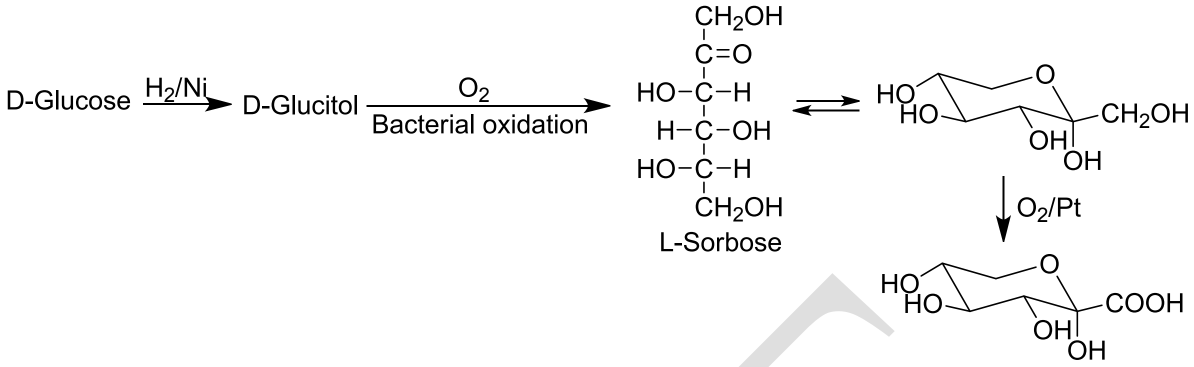
Primary alcohols can be oxidized directly to acids by reagents such as chromic (VI) acid, nitric acid, and potassium permanganate. However, in each case due to side-reactions yields are usually not high. Thus, chromic (VI) acid degrades carboxylic acids to smaller molecules, ultimately giving acetic acid (from C-methyl groups) and carbon dioxide.

A selective method using molecular oxygen on a platinum catalyst is available which generally oxidizes primary hydroxyl groups before secondary ones. This selectivity is used in an industrial method for the synthesis of vitamin C (**Scheme 8**). D-Glucose is converted into L-sorbose *via* bacterial oxidation (**Scheme 9**), which is oxidized to 2-keto-L-gulonic acid, an intermediate in the synthesis of Vitamin C.



Vitamin C

Scheme 8

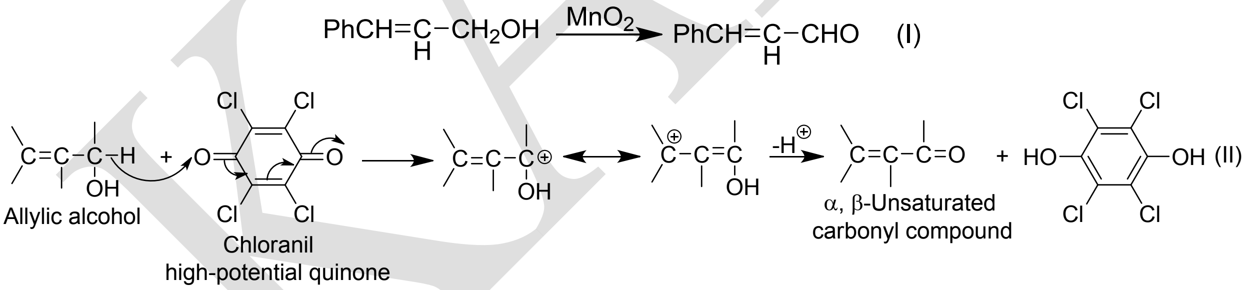


Scheme 9

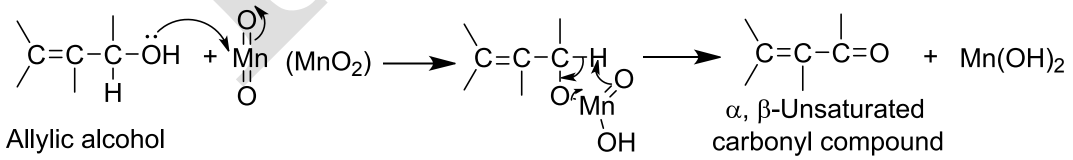
(E) Oxidation of allylic alcohols–active manganese dioxide and quinones

Manganese dioxide specifically oxidizes allylic and benzylic hydroxyl groups to give α,β-unsaturated carbonyl compounds. The reagent does not attack carbon carbon double and triple bonds and saturated hydroxyl groups (eq I, **Scheme 10**).

Several high potential quinones for example, chloranil are capable of oxidizing allylic, benzylic and propargylic alcohols. Mechanistically, the reaction proceeds *via* the formation of resonance stabilized carbocations, (eq II, **Scheme 10**).



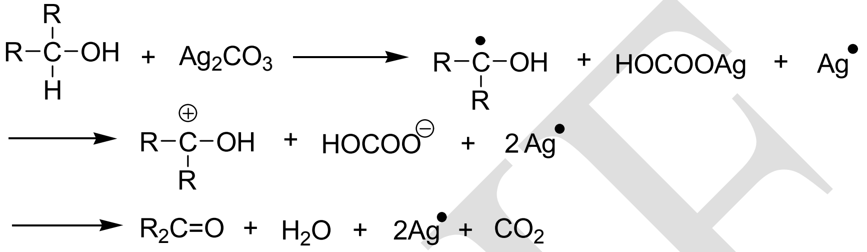
Scheme 10



Silver carbonate

This is the reagent of choice for oxidation of a sterically hindered primary or secondary alcohol in good yields, dry benzene being the usual solvent. A radical mechanism has been proposed.

$$R_2CH\text{-}OH + Ag_2CO_3 \longrightarrow R_2C{=}O + H_2O + 2Ag + CO_2$$

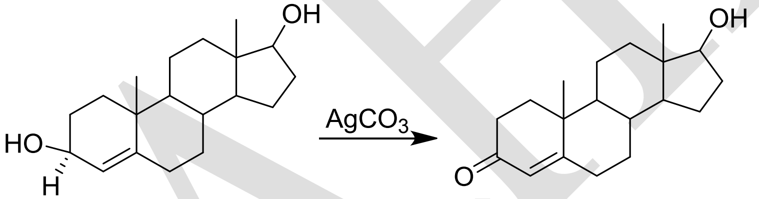


$$R-\overset{R}{\underset{H}{C}}-OH + Ag_2CO_3 \longrightarrow R-\overset{\bullet}{\underset{R}{C}}-OH + HOCOOAg + Ag^{\bullet}$$

$$\longrightarrow R-\overset{\oplus}{\underset{R}{C}}-OH + HOCOO^{\ominus} + 2\,Ag^{\bullet}$$

$$\longrightarrow R_2C{=}O + H_2O + 2Ag^{\bullet} + CO_2$$

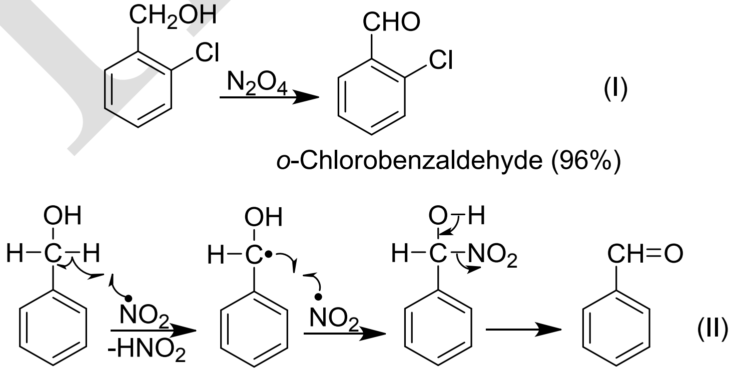
With acetone or methanol as the solvent instead of benzene, silver carbonate oxidizes an allylic alcohol selectively. For instance, testosterone is obtained in 95% yield as shown below.



Testosterone

(F) Benzylic alcohols

Primary and secondary benzyl alcohols are oxidized with dinitrogen tetroxide in chloroform at 0ºC (eq I, **Scheme 11**). Reaction is thought to proceed through (the radical) nitrogen dioxide, with the formation and decomposition of a hydroxynitro compound (eq II, **Scheme 11**).



Scheme 11

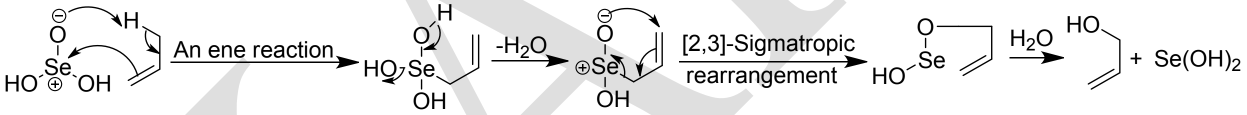
Ceric ammonium nitrate (CAN)

Ceric ammonium nitrate is the reagent of choice for the oxidation of benzylic alcohols to the corresponding aldehydes and ketones in high yields. The reaction proceeds through radical mechanism.

Allylic oxidation

Allylic oxidation of alkenes can be brought about with selenium dioxide to give carbonyl compounds, allylic alcohols, or esters depending on conditions. Essentially the mechanism of the reaction involves three steps.

1. An ene reaction between of hydrated form of selenium dioxide and an alkene.
2. The [2,3]-sigmatropic rearrangement of the resulting allylselenic acid which restores the original position of the double bond.
3. Lastly, breakdown of the selenium ester to give the product of allylic oxidation (**Scheme 12**).



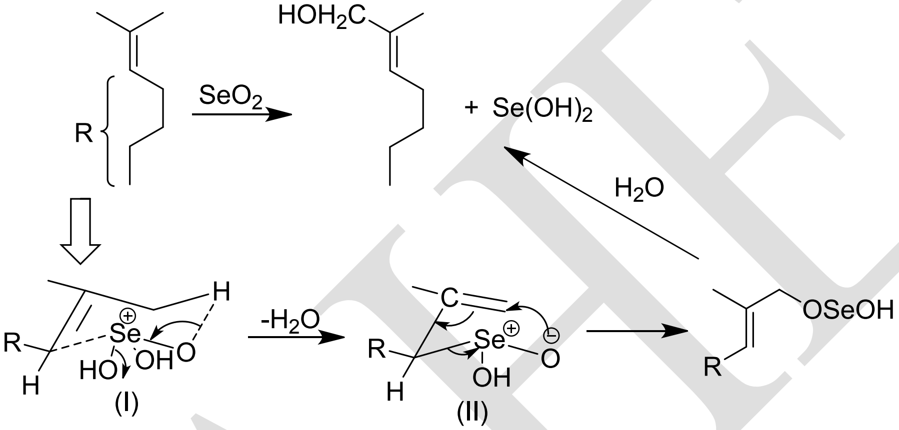
Scheme 12

Allylic alcohols are the initial products of oxidation and these are further oxidized to carbonyl groups with selenium dioxide. Normally it is the carbonyl compound that is isolated. If one wants to end up with an alcohol, the oxidation is carried out in acetic acid as the solvent and then acetate esters are formed.

Normally the oxidation is carried out with catalytic amount of selenium dioxide and *t*-butyl hydroperoxide (TBHP) which reoxidizes the spent catalyst and then the allylic alcohols is the major product.

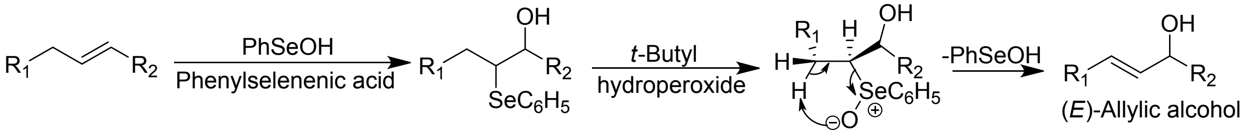
This oxidation procedure displays high selectivity in the case of trisubstituted 1,1-dimethylalkenes which give predominantly *E*-allylic alcohols or unsaturated aldehydes by selectively oxidizing the *E*-methyl group. Thus e.g., starting with 2-methyl-2-heptene

(**Scheme 13**), the major product of oxidation with selenium dioxide is the *E*-allylic alcohol. This stereoselectivity is a consequence of a cyclic transition state for the sigmatropic rearrangement step. The observed stereochemistry is the result of the reaction proceeding through the favoured transition state (I, **Scheme 13**), where the alkyl group adopts a pseudoequatorial conformation to give the selenic acid (II), the [2,3]-sigmatropic rearrangement, then enforces the observed *E*-selectivity.

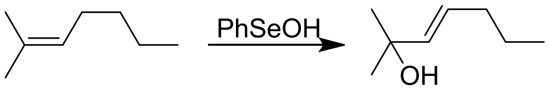


Scheme 13

An alternative method, equivalent to allylic oxidation of alkenes, but with a shift in the position of the double bond involves the intermediate formation of a β–hydroxy-selenide. The hydroxyselenide is obtained by the addition of phenyl selenenic acid to an alkene (**Scheme 14**). The hydroxyselenide is oxidised with *t*-butylhdroperoxide (TBHP) to unstable selenoxide which immediately eliminates phenylselenenic acid PhSeOH to give the *E*-allylic alcohol. With trisubstituted alkenes, the addition of phenyl selenenic acid is highly regioselective, the hydroxyl group gets attached at eh more substituted end of the carbon-carbon double bond (**Scheme 15**). Thus this addition follows Markovinkoffs rule with “Ph Se^{+}”, acting as the electrophile. The elimination always specifically proceeds away from the oxygen functionality to give the allylic alcohol.



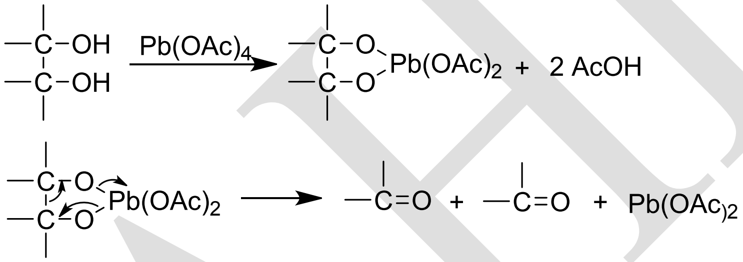
Scheme 14



Scheme 15

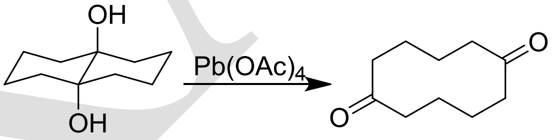
Oxidation of glycols

Carbon–carbon double bonds are cleaved *via* the glycols (1,2-diols) by reaction with lead tetra-acetate. The fragmentation is believed to occur within a cyclic adduct of the glycol and the oxidant (**Scheme 16**). This mechanism is supported by the facts that (1) the kinetics are second order (first order in each reactant); (2) added acetic acid retards the reaction (drives the equilibrium to the left) and (3) *cis* glycols react much more rapidly than *trans* glycols.

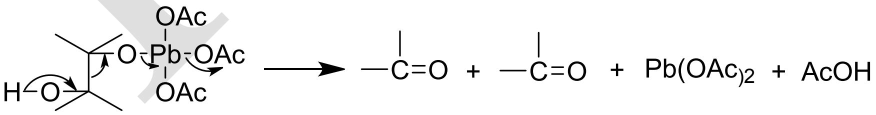


Scheme 16

The glycols that cannot form cyclic intermediates are also eventually oxidized (**Scheme 17**). The mechanism involving a cyclic transition state is the lower energy pathway, however, an acyclic path is also followed (**Scheme 18**).

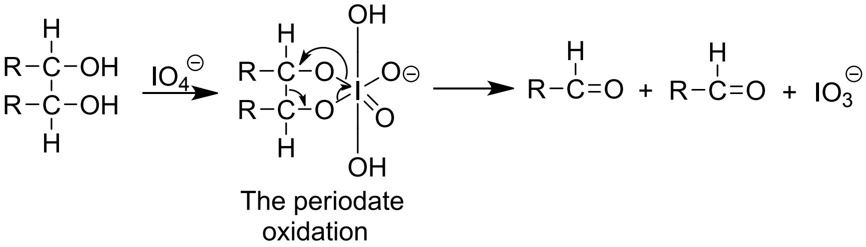


Scheme 17



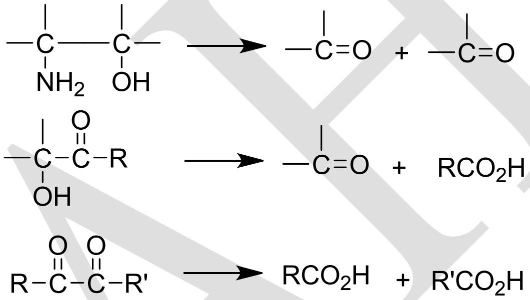
Scheme 18

Glycol cleavage with periodic acid involves a similar cyclic intermediate (**Scheme 19**).

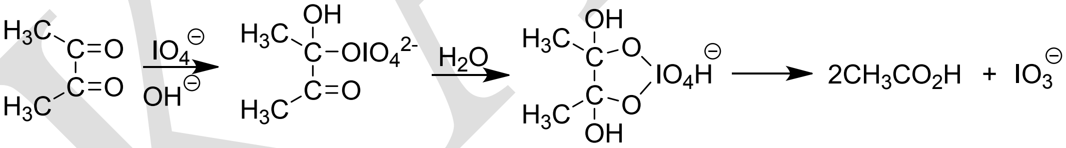


Scheme 19

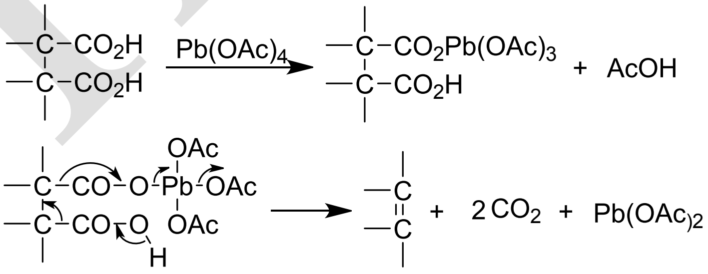
Several other combinations of adjacent functional groups are also cleaved with these reagents (**Scheme 20**). The cleavage of diketones with IO_4^- involves a reactive cyclic intermediate formed *via* the nucleophilic attack on the diketone (**Scheme 21**). Compounds with carboxyl groups on adjacent carbons (succinic acid derivatives) can be bisdecarboxylated with lead tetra-acetate (**Scheme 22**) to give alkenes.



Scheme 20



Scheme 21



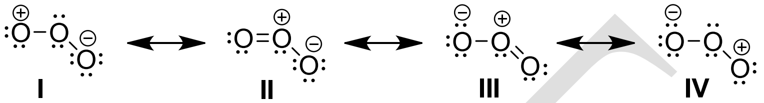
Scheme 22

Ozonolysis (O_3)

(a) Why does ozone undergo ready 1,3-dipolar addition to a carbon-carbon multiple bond?

Solution:

Ozone may represented as a hybrid of the following canonical forms:



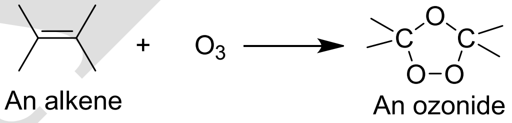
The central positive oxygen atom in structure **II** or **III** is not electrophilic because it possesses octet of electrons. However, the positive oxygen in structure **I** or **IV** possesses sextet of electrons. The other end oxygen atom is an anionic centre with a pair of electrons. Thus, the terminal atoms of ozone may function as either an electrophile or a nucleophile and because of this, ozone undergoes ready 1,3-dipolar addition to a carbon-carbon multiple bond initiated by its electrophilic end.

(b) What is called ozonolysis?

Solution:

The complete process of preparation of ozonide by adding ozone to a carbon-carbon multiple bonds, decomposition of the resulting ozonide and identification of the products formed is called ozonolysis.

(c) Discuss the mechanism of the following reaction:

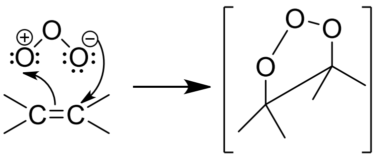


Give evidence in favour of the mechanism.

Solution:

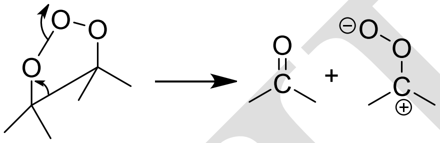
The mechanistic steps of the reaction are as follows:

Step I: 1,3- Dipolar addition of ozone to an alkene to form an unstable molozonide (**I**).



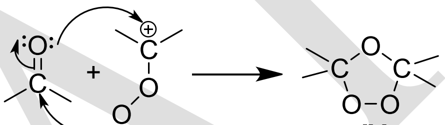
I

Step II: Decomposition of the molozonide (**I**) to form a carbonyl compound (**II**) and a zwitterion (**III**).



I II III

Step III: Recombination of the carbonyl compound (**II**) and the zwitterion (**III**) to form an ozonide (**IV**).

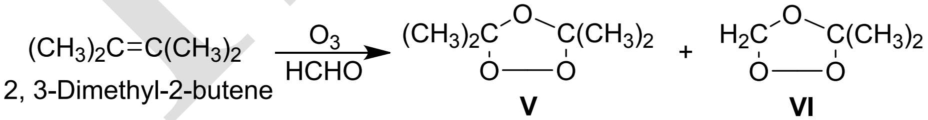


II III IV

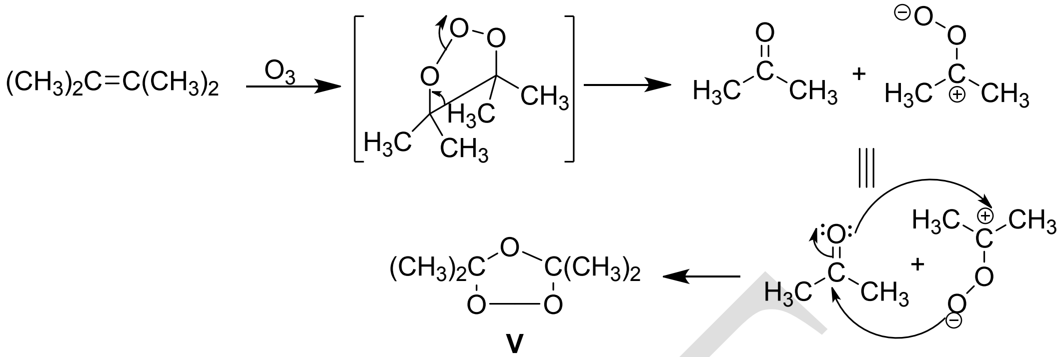
An ozonide

The mechanism is supported by the following observations:

(i) When the ozonolysis of the alkene $(CH_3)_2C=C(CH_3)_2$ is carried out in the presence of HCHO, the ozonide **VI**, in addition to the expected ozonide **V**, is isolated (a 'crossover' experiment).

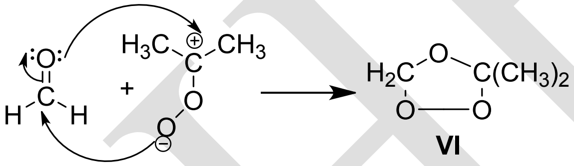


V VI



V

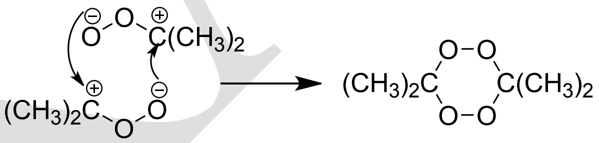
The zwitterion reacts with HCHO to form the ozonide **VI**.



VI

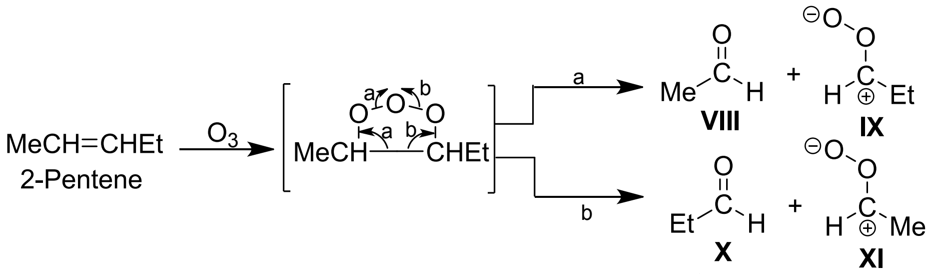
Formation of **VI** therefore confirms the generation of the zwitterion, i.e., the mechanism of fission of the molozonide followed by recombination.

(ii) The diperoxide **VII** has been isolated along with the ozonides **V** and **VI**. This also confirms the formation of the zwitterion $(\overset{\ominus}{O}-O-\overset{\oplus}{C}<)$.

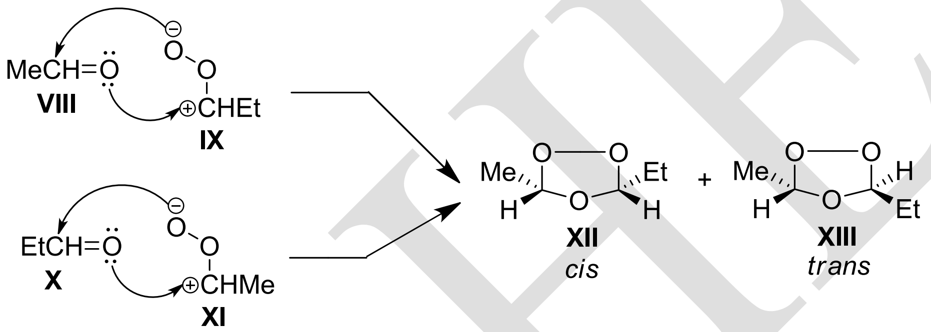


VII

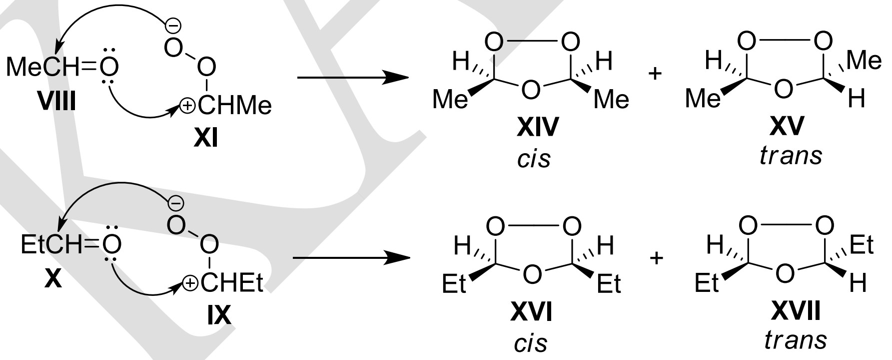
(iii) If the alkene is unsymmetrical, then two carbonyl compounds and two dipolar ions are possible and their combination can lead to three different ozonides. Also, because the ozonides have cyclic structure, each can exist in both cis-and trans-forms. Thus, six ozonides (three pairs of distereoisomers) are possible from the alkene of the type RCH = CHR'. In fact, for 2-pentene all six ozonides have been isolated which is a strong evidence in favour of the mechanism of fission followed by recombination.



Now, **VIII** and **IX** or **X** and **XI** may combine to give **XII** and **XIII**.



Again, **VIII** and **XI** may combine to give **XIV** and **XV** and **IX** and **X** may combine to give **XVI** and **XVII**.



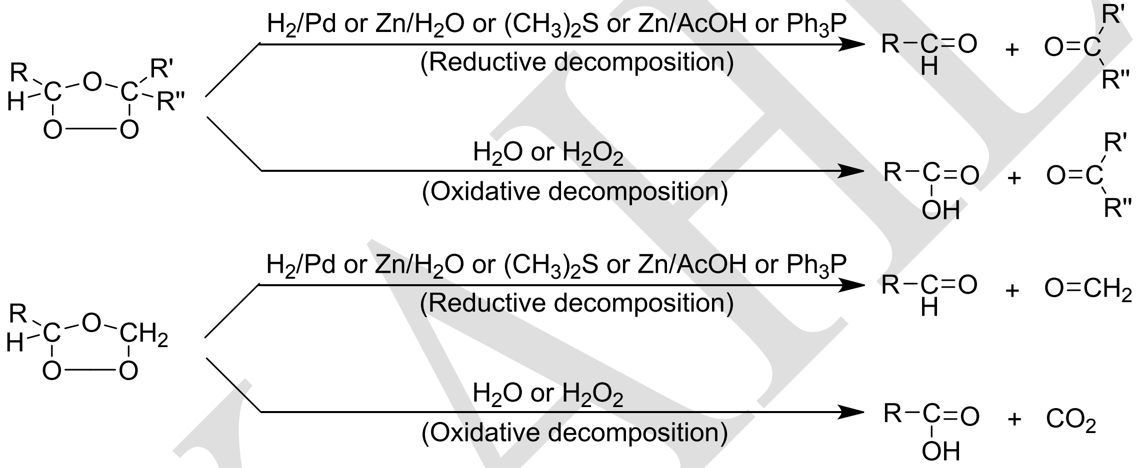
(d) How may the decomposition of an ozonide be carried out? Predict the nature of the products.

Solution:

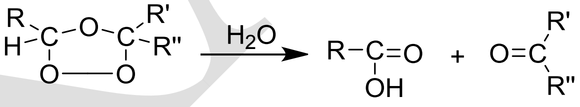
The decomposition of an ozonide may be carried out either by reductive work-up or by oxidative work-up. Reductive decomposition may be carried out by treating the ozonide with

H_2/Pd, Zn/H_2O, $(CH_3)_2S$, Zn/AcOH or triphenylphosphine. Oxidative decomposition usually occurs on simple hydrolysis but is assured by adding H_2O_2.

If a doubly-bonded carbon bears two carbon substituents, that carbon becomes a ketone after reductive or oxidative decomposition. If a doubly-bonded carbon bears hydrogen and a carbon substituent, that carbon becomes an aldehyde after reductive decomposition and a carboxylic acid after oxidative decomposition and if a doubly-bonded carbon atom bears two hydrogens, that carbon becomes formaldehyde after reductive decomposition and CO_2 after oxidative decomposition.



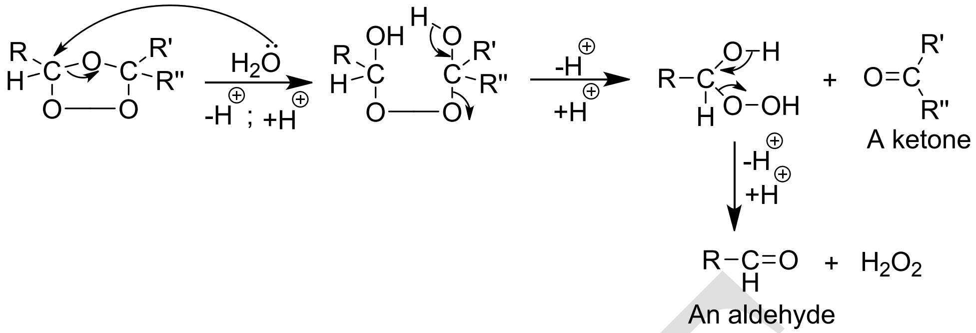
(e) (i) Give the plausible mechanism of the following reaction:



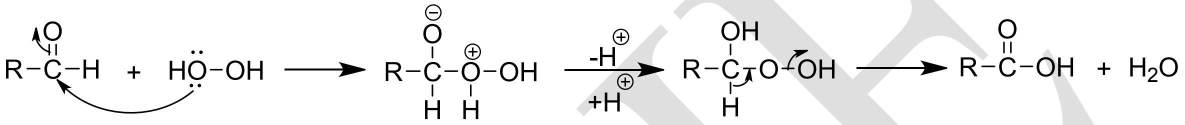
What will happen if Zn is used along with water for decomposing the ozonide?

Solution:

The mechanism of decomposition of this ozonide may be depicted as follows:



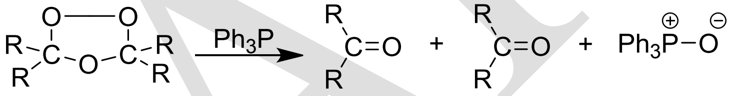
The aldehyde is further oxidised by H_2O_2 to a carboxylic acid as follows:



If Zn dust is used along with water for decomposing the ozonide, it destroys the H_2O_2 produced and prevents further oxidation of the aldehyde.

$$H_2O_2 + Zn \longrightarrow Zn(OH)_2$$

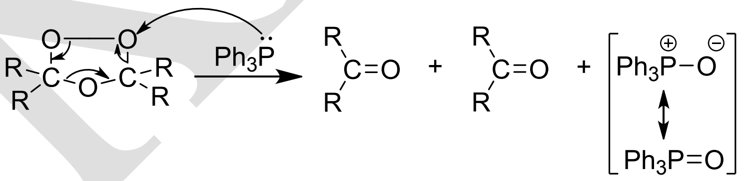
(ii) Sketch the mechanism of the following reaction:



How does dimethyl sulphide (Me_2S) react with an ozonide?

Solution:

The mechanism of decomposition of ozonide by Ph_3P is as follows:

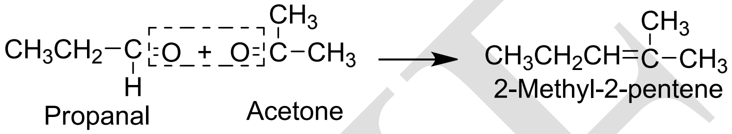


Dimethyl sulphide (Me_2S) reacts similarly and itself becomes converted to dimethyl sulphoxide ($Me_2S{=}O$).

(f) Mention some uses of ozonolysis.

Solution:

Ozonolysis is used for locating the position of a double bond in an unknown alkene. This may be worked out by dropping the carbonyl oxygen atoms of the resulting carbonyl compounds and then joining these carbonyl carbons through a double bond. For example, if an alkene produces propanal and acetone on ozonolysis, then the structure of the starting alkene will be 2-methyl-2-pentene.



Ozonolysis is also used as a means for preparing aldehydes, ketons and carboxylic acids from olefinic compounds.

Lithium aluminium hydride ($LiAlH_4$)

Lithium aluminium hydride (LAH) is one of the most important and useful reagents for the reduction of carbonyl compounds along with many other compounds.

Preparation

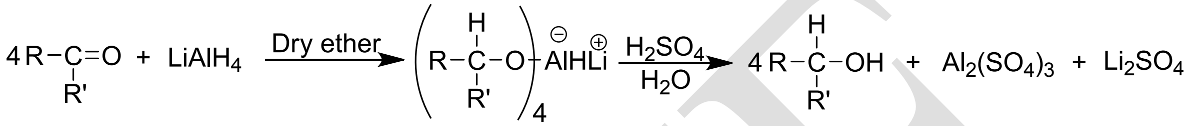
The reagent is prepared by slowly adding a calculated amount of anhydrous aluminium chloride to a paste of lithium hydride in dry ether or THF.

$$4LiH + AlCl_3 \xrightarrow[\text{or THF}]{\text{Dry ether}} \overset{\oplus\,\ominus}{LiAlH_4} + 3LiCl$$

Precipitated lithium chloride and the unreacted lithium hydride are removed by filtration. The filtrate is evaporated in the absence of air and carbon dioxide when lithium aluminium hydride is obtained as a grey solid. It is spontaneously inflammable and reacts violently with water and alcohol with the evolution of hydrogen. It is soluble in ether, tetrahydrofuran (THF) and dioxan.

Reduction procedure

Powdered $LiAlH_4$ is added to dry ether or THF and kept agitated in a flask which is fitted with a condenser and a dropping funnel. Solution of the substance in ether is then gradually run into the flask so as to maintain a gentle boiling of the mixture. The reduction product is decomposed with water and acid.



$$4\,R-\underset{R'}{C}=O + LiAlH_4 \xrightarrow{\text{Dry ether}} \left(R-\overset{H}{\underset{R'}{C}}-O\right)_4 \overset{\ominus}{Al}H\overset{\oplus}{Li} \xrightarrow[H_2O]{H_2SO_4} 4\,R-\overset{H}{\underset{R'}{C}}-OH + Al_2(SO_4)_3 + Li_2SO_4$$

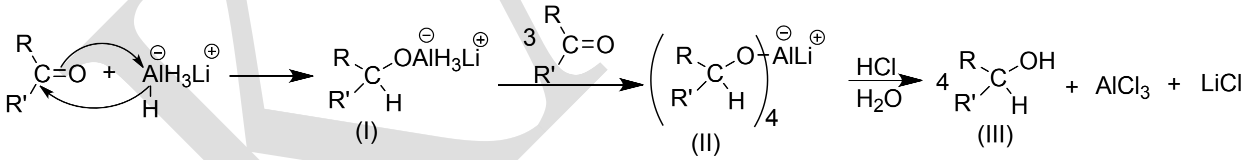
(Where R' = alkyl, OH, Cl, etc,)

Excess of $LiAlH_4$ is also decomposed by water and acid.

$$2LiAlH_4 + 4H_2SO_4 \longrightarrow Li_2SO_4 + Al_2(SO_4)_3 + 8H_2$$

Mechanism

The reagent can supply hydride ions to a large variety of compounds having groups with polarized multiple bonds such as, C=O, C=N, C=N, N=O, etc., It is suggested that as the nucleophilic hydride ion attaches the positively charged carbonyl carbon, aluminium complexes with the oxygen, i.e., the reaction is concentrated. The intermediate (I) formed in the first step has three more hydrogens which are similarly transferred to three other molecule of the substrate to yield the complex (II). The latter on hydrolysis with water and acid gives the reduced product.



The first step is fast but the subsequent steps are slow because the electron-withdrawing effect of the alkoxyl group inhibits the hydride ion transfer. It is seen that in reducing the carbonyl compound, half the hydrogen is supplied by the reagent and the other half is supplied by the solvent, i.e., water.

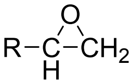
It reacts readily with acidic hydrogens. One fourth of the valuable reagent is lost in the formation of hydrogen on reacting with the hydrogens of acids.

$$RCOOH + LiAlH_4 \longrightarrow RCOO\overset{\ominus}{Al}H_3\overset{\oplus}{Li} + H_2$$

Hence acids are better converted to their esters before reduction with $LiAlH_4$.

Uses

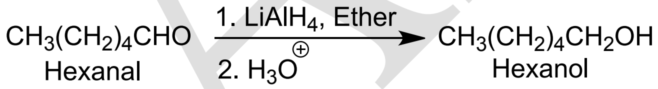
The reagent may be used to reduce aldehydes, ketones, acids and their derivatives, epoxides, etc., to alcohols. The reagent can also reduce nitriles, aliphatic nitro compounds, anilides, azides and isocyanates to amines. The substrates and their reduction products with $LiAlH_4$ are listed below.

Substrates	Reduction products	Substrates	Reduction products
RCHO	RCH_2OH	$R-C\equiv N$	RCHO or RNH_2
RCOR	RCHOHR	RNO_2	RNH_2
RCOOH	RCH_2OH	$Ar-NO_2$	ArHN=NHAr
RCOOR'	RCH_2OH + R'OH	$ArNHCOCH_3$	$ArNHCH_2CH_3$
RCOCl	RCH_2OH	R−N=C=O	$RNHCH_3$
	$RCHOHCH_3$ + RCH_2CH_2OH	RN_3	RNH_2
$(RCO)_2O$	$2RCH_2OH$		

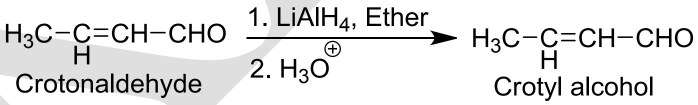
1. Reduction of carbonyl compounds

The carbonyl compounds are smoothly reduced without affecting double or triple bonds.

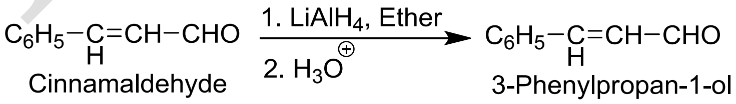
(a)



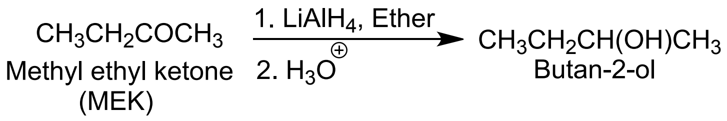
(b)



Sometimes the double bond is also reduced when a phenyl group is attached to the β-carbon.



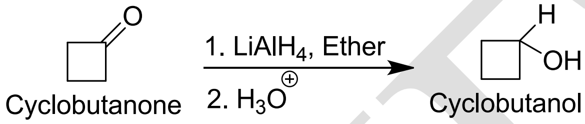
(c)



(d)

$$\underset{\text{Ethyl acetoacetate}}{CH_3COCH_2COOEt} \xrightarrow[2.\ H_3O^{\oplus}]{1.\ LiAlH_4,\ Ether} \underset{\text{Butan-1, 3-diol}}{CH_3CH(OH)CH_2CH_2OH}$$

(e) The reagent is of considerable utility for the reduction of sensitive and expensive carbonyl compounds.

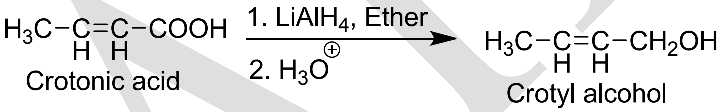


2. Reduction of acids and their derivatives

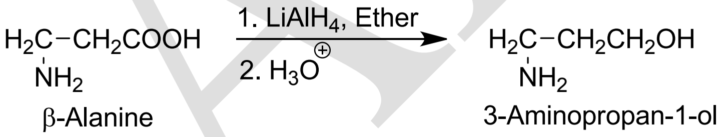
Acids are resistant to reduction by all other reagents.

Acids

$$\underset{\text{Palmitic acid}}{CH_3\text{-}(CH_2)_{14}\text{-}COOH} \xrightarrow[2.\ H_3O^{\oplus}]{1.\ LiAlH_4,\ Ether} \underset{\text{Hexadecan-1-ol (Cetyl alcohol)}}{CH_3\text{-}(CH_2)_{14}\text{-}CH_2OH}$$



$$\underset{\text{Crotonic acid}}{H_3C-\underset{H}{C}=\underset{H}{C}-COOH} \xrightarrow[2.\ H_3O^{\oplus}]{1.\ LiAlH_4,\ Ether} \underset{\text{Crotyl alcohol}}{H_3C-\underset{H}{C}=\underset{H}{C}-CH_2OH}$$



$$\underset{\beta\text{-Alanine}}{\underset{NH_2}{H_2C}-CH_2COOH} \xrightarrow[2.\ H_3O^{\oplus}]{1.\ LiAlH_4,\ Ether} \underset{\text{3-Aminopropan-1-ol}}{\underset{NH_2}{H_2C}-CH_2CH_2OH}$$

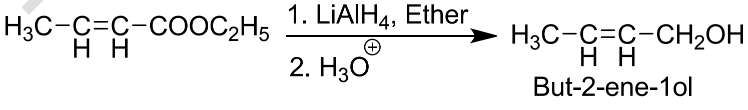
Acid chlorides

$$CH_3COCl \xrightarrow[2.\ H_3O^{\oplus}]{1.\ LiAlH_4,\ Ether} CH_3CH_2OH$$

Acid anhydrides

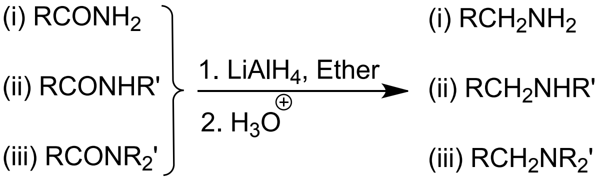
$$(CH_3CO)_2O \xrightarrow[2.\ H_3O^{\oplus}]{1.\ LiAlH_4,\ Ether} 2CH_3CH_2OH$$

Esters

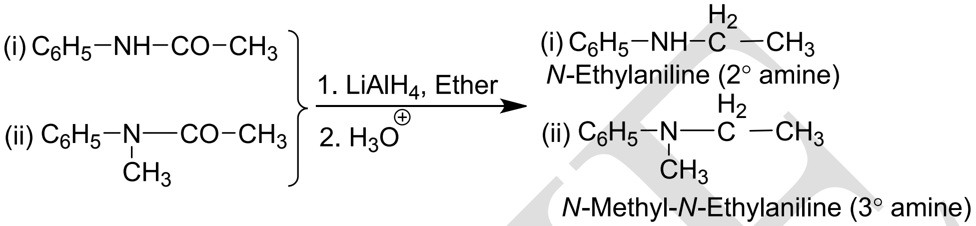


$$H_3C-\underset{H}{C}=\underset{H}{C}-COOC_2H_5 \xrightarrow[2.\ H_3O^{\oplus}]{1.\ LiAlH_4,\ Ether} \underset{\text{But-2-ene-1ol}}{H_3C-\underset{H}{C}=\underset{H}{C}-CH_2OH}$$

Amides–unsubstituted amides give 1° amines while substituted amides give 2° or 3° amines.

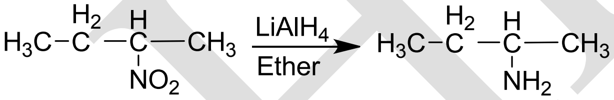


Anilides are similarly reduced to 2º or 3º amines.

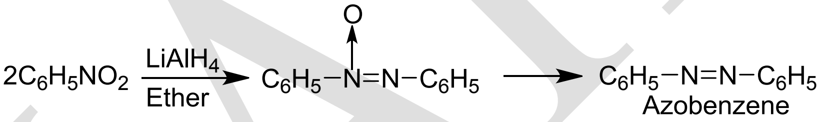


3. Reduction of nitro compounds, azides, oximes, nitriles, etc., to primary amines.

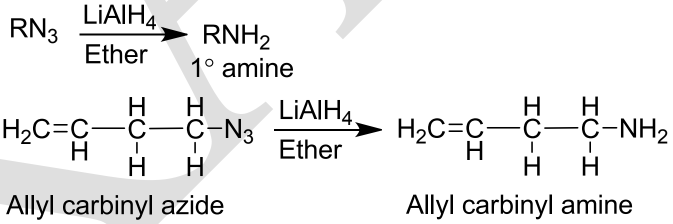
Nitro compounds



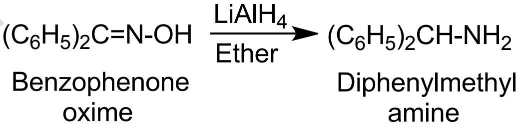
Nitrobenzene, however, gives azobenzene *via* azoxybenzene.



Azides



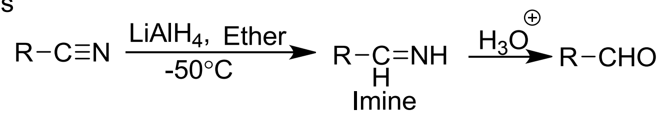
Oximes



Nitriles-Reduction of nitriles with $LiAlH_4$ may give amine or aldehyde depending on the conditions of the reaction.

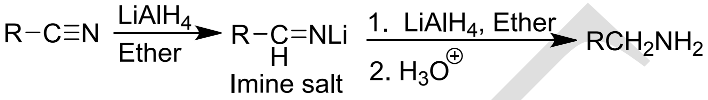
(a) Aldehydes are given when a solution of $LiAlH_4$ is added to the solution of a nitrile in dry ether or THF at low temperature.

Nitriles



$$R-C\equiv N \xrightarrow[-50^\circ C]{LiAlH_4,\ Ether} \underset{\text{Imine}}{R-\underset{H}{C}=NH} \xrightarrow{H_3O^\oplus} R-CHO$$

(b) Amines are obtained when a solution of nitrile is added to the solution of $LiAlH_4$ in ether or THF.

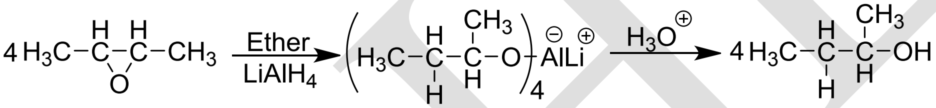


$$R-C\equiv N \xrightarrow[Ether]{LiAlH_4} \underset{\text{Imine salt}}{R-\underset{H}{C}=NLi} \xrightarrow[2.\ H_3O^\oplus]{1.\ LiAlH_4,\ Ether} RCH_2NH_2$$

4. Reduction of halides

$$4(CH_3)_2CH\text{-}CH_2Br + LiAlH_4 \xrightarrow{Ether} 4(CH_3)_3CH + LiAlBr_4$$

5. Reduction of epoxides to alcohols



6. Reaction with compounds containing active hydrogens

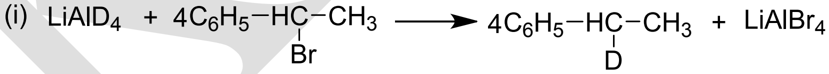
The reagent reacts with alcohols and amines to evolve hydrogen. The method can be used to estimate active hydrogen.

$$4ROH + LiAlH_4 \longrightarrow (RO)_4\overset{\ominus}{Al}\overset{\oplus}{Li} + 4H_2$$

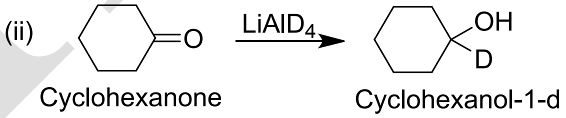
$$4RNH_2 + LiAlH_4 \longrightarrow (RNH)_4\overset{\ominus}{Al}\overset{\oplus}{Li} + 4H_2$$

7. Introduction of deuterium in organic molecules

Lithium aluminium deuteride has been used for introducing deuterium in organic compounds.



$$\text{(i)}\ LiAlD_4 + 4C_6H_5-\underset{Br}{HC}-CH_3 \longrightarrow 4C_6H_5-\underset{D}{HC}-CH_3 + LiAlBr_4$$



Sodium borohydride ($NaBH_4$)

Sodium borohydride is a reducing reagent. It reduces by transfer of hydride ions to substrates as in the case of lithium aluminium hydride.

Preparation

It is prepared by heating sodium hydride with trimethoxyborane to 250°C.

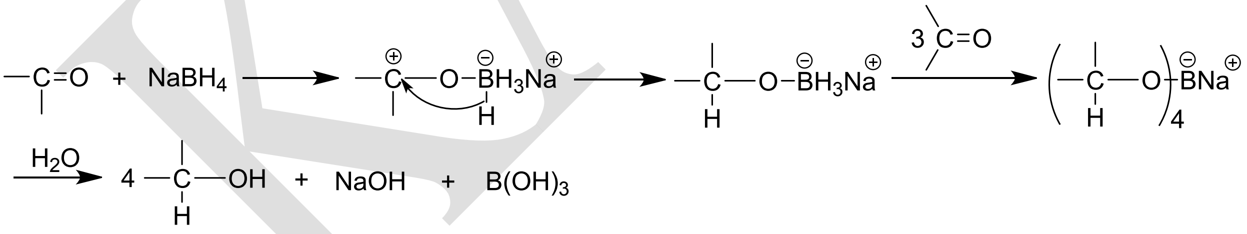
$$4NaH + B(OCH_3)_3 \xrightarrow{250°C} NaBH_4 + 3CH_3ONa$$

The reagent is insoluble in ether but soluble in water or alcohol. Hence, it can be used in hydrolytic solvents, e.g., water or alcohol. The reaction is carried out in ethanol or isopropanol.

It is a milder reducing agent than $LiAlH_4$. Reduction with $NaBH_4$ is more selective. It reduces carbonyl groups of aldehydes, ketones and acid chlorides in the presence of many reducible groups such as nitro, ester, carboxyl, epoxide, nitrile, double bond, etc., which remain unaffected. Double bonds either isolated or conjugated are not affected. The reagent is slowly hydrolysed with water. Hence, reductions which are reasonably rapid can be carried out in water without considerable hydrolysis of the reagent. Thus, water soluble sugars can be reduced in aqueous medium.

Mechanism

The mechanism of reduction is similar to that of $LiA1H_4$. The reaction proceeds by complexing the oxygen atom of the carbonyl group with boron and simultaneous transfer of the hydride ion to the carbonyl carbon. All the four hydrogens of the reagent are transferred to the four molecules of the substrate. Subsequent hydrolysis gives alcohol.



$$NaOH + B(OH)_3 \longrightarrow NaH_2BO_3 + H_2O$$

Applications

Some of its important applications are:

1. Reduction of carbonyl compounds and acid chlorides to alcohol

$$CH_3COCH_2CH_2COOC_2H_5 \xrightarrow{NaBH_4} CH_3CH(OH)CH_2CH_2COOC_2H_5$$

Ethyl-γ-ketopentanoate → Ethyl-4-hydroxypentanoate

$$C_6H_5COCH_2CH_2COOH \xrightarrow{NaBH_4} C_6H_5CH(OH)CH_2CH_2COOH$$

β-Benzoyl propanoic acid → γ-Hydroxy-4-phenylbutanoic acid

$$CH_3COCH_2CH_2COCH_3 \xrightarrow{NaBH_4} CH_3CH(OH)CH_2CH_2CH(OH)CH_3$$

Hexan-2, 5-dione → Hexan-2, 5-diol

$$CH_2OH(CHOH)_4CHO \xrightarrow{NaBH_4} CH_2OH(CHOH)_4CH_2OH$$

Glucose → Sorbitol

$$C_6H_5CH{=}CH\text{-}CHO \xrightarrow{NaBH_4} C_6H_5CH{=}CHCH_2OH$$

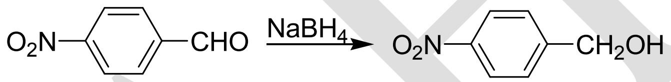
Cinnamaldehyde → Cinnamyl alcohol

$$NCCH_2CH_2CHO \xrightarrow{NaBH_4} NCCH_2CH_2CH_2OH$$

3-Cyanopropionaldehyde → 4-Hydroxybutyronitrile

$$RCOCl \xrightarrow{NaBH_4} RCH_2OH$$

Acid chloride → Alcohol



p-Nitrobenzaldehyde *p*-Nitrobenzyl alcohol

In the above compounds it will be seen that only the carbonyl group is reduced and the other function groups remain unaffected. This high selectivity of $NaBH_4$ makes it the preferred reagent for the reduction of carbonyl groups in sensitive polyfunctional molecules.

2. Reduction of carbonyl group to methylene groups

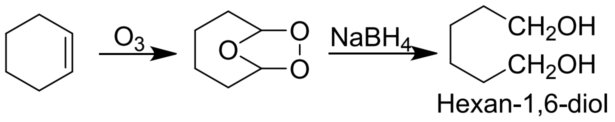
P-Toluenesulphonyl hydrazine condenses with carbonyl compounds to give to tosylhydrazones which on reduction with $NaBH_4$ give hydrocarbons.

$$R_2C{=}O + H_2N\text{-}NHTs \longrightarrow \underset{\text{Tosylhydrazone}}{R_2C{=}N\text{-}NHTs} \xrightarrow{NaBH_4} R_2CH_2$$

The method is useful in the synthesis, e.g., ketosteriods.

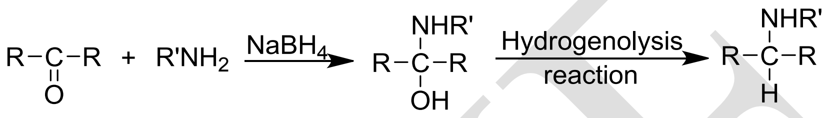
3. Reduction of ozonides

Sodium borohydride reduces ozonides to two molecules of alcohol and ozonides of cycloolefins to diols.



4. Reductive alkylation of amines

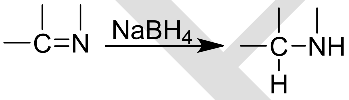
When aldehyde or ketone is treated with amines (1º or 2º) in the presence of $NaBH_4$ reductive alkylation occurs.



$$R-\overset{\displaystyle O}{\overset{\|}{C}}-R + R'NH_2 \xrightarrow{NaBH_4} R-\underset{OH}{\overset{NHR'}{C}}-R \xrightarrow[\text{reaction}]{\text{Hydrogenolysis}} R-\underset{H}{\overset{NHR'}{C}}-R$$

5. Reduction of carbon-nitrogen double bond

Although sodium borohydride does not reduce nitriles, it reduces carbon–nitrogen double bond.



$$-\overset{|}{C}=\overset{|}{N} \xrightarrow{NaBH_4} -\underset{H}{\overset{|}{C}}-\overset{|}{N}H$$

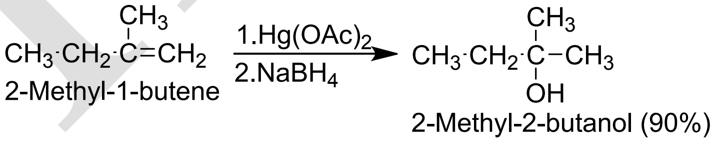
6. Reduction of ester groups

Ordinarily ester groups are unaffected by $NaBH_4$ but in the presence of LiCl or $AlCl_3$ in diglyme (diethylene glycol dimethyl ether) they are reduced to alcohols.

$$RCOOR' \xrightarrow[\text{LiCl in diglyme}]{NaBH_4} RCH_2OH + R'OH$$

7. Hydration of olefins

Olefins are hydrated under mild condition without rearrangement in high yield on treatment with mercuric acetate followed by $NaBH_4$ in situ.



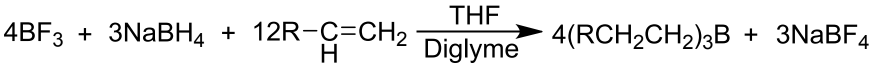
$$CH_3 \cdot CH_2 \cdot \overset{CH_3}{C}=CH_2 \xrightarrow[2.NaBH_4]{1.Hg(OAc)_2} CH_3 \cdot CH_2 \cdot \underset{OH}{\overset{CH_3}{C}}-CH_3$$

8. Preparation of diborane

Diborane which is used for the hydroboration of alkenes is prepared by reacting boron trifluoride with sodium borohydride.

$$\underset{\text{Boron trifluoride}}{4BF_3} + 3NaBH_4 \longrightarrow \underset{\text{Diborane}}{2B_2H_6} + \underset{\text{Sodium borofluoride}}{2NaBF_4}$$

Hydroboration is done in situ either in THF or in diglyme.



$$4BF_3 + 3NaBH_4 + 12R-\underset{H}{C}=CH_2 \xrightarrow[\text{Diglyme}]{\text{THF}} 4(RCH_2CH_2)_3B + 3NaBF_4$$

9. Reduction of diazonium borofluoride

Diazonium borofluoride can be reduced with $NaBH_4$ in dimethylformide or alcohol.

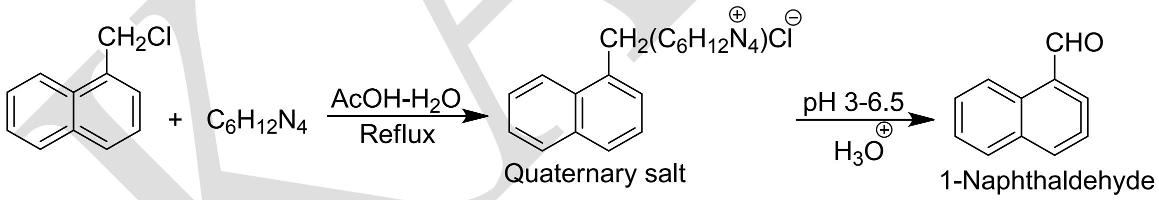
$$C_6H_5N_2Cl \xrightarrow{HBF_4} C_6H_5\overset{\oplus}{N_2}\overset{\ominus}{BF_4} \xrightarrow[CH_3OH]{NaBH_4} C_6H_6$$

10. Reduction of azides

Azides containing sulphur are not reduced to amines by the usual methods. However, sodium borohydride reduces azides to amines.

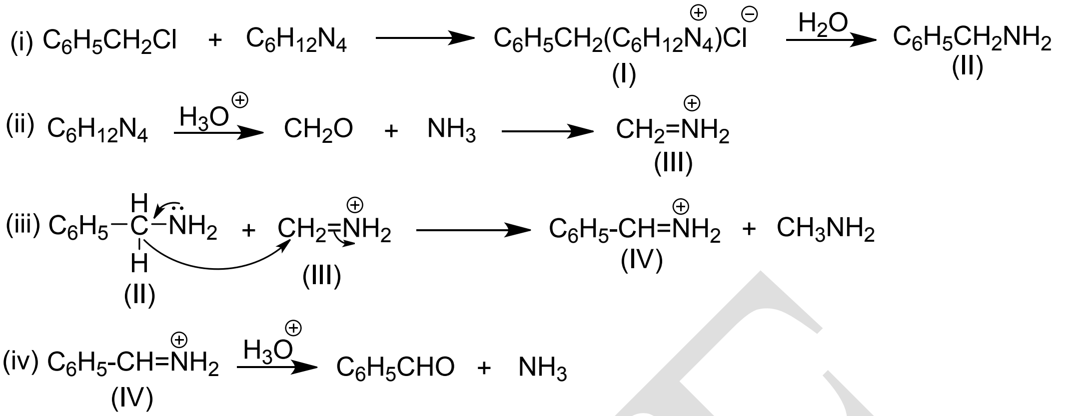
Sommelet reaction

Sommelet reaction involves the oxidation of chloromethyl group ($-CH_2Cl$) to an aldehyde group by the use of hexamethylenetetramine ($C_6H_{12}N_4$) and subsequent hydrolysis in acidic medium (pH 3-6.5). The reaction is successful with benzylic halide ($ArCH_2Cl$).



Mechanism

The mechanism is not clearly understood. According to Angyal and co-workers, the halide reacts with hexamethylenetetramine to form quaternary salt (I) which is hydrolysed to amine (II). Hexamethylenetetramine is also hydrolysed to formaldehyde and ammonia which subsequently form methylene amine (III). The amine (II) then transfers a hydride ion to methylene amine (III) to form an imine (IV), which is finally hydrolysed to aldehyde.



(i) $C_6H_5CH_2Cl + C_6H_{12}N_4 \longrightarrow \underset{(I)}{C_6H_5CH_2(C_6H_{12}\overset{\oplus}{N}_4)\overset{\ominus}{Cl}} \xrightarrow{H_2O} \underset{(II)}{C_6H_5CH_2NH_2}$

(ii) $C_6H_{12}N_4 \xrightarrow{H_3O^{\oplus}} CH_2O + NH_3 \longrightarrow \underset{(III)}{CH_2{=}\overset{\oplus}{N}H_2}$

(iii) $\underset{(II)}{C_6H_5{-}CH_2{-}\ddot{N}H_2} + \underset{(III)}{CH_2{=}\overset{\oplus}{N}H_2} \longrightarrow \underset{(IV)}{C_6H_5{-}CH{=}\overset{\oplus}{N}H_2} + CH_3NH_2$

(iv) $\underset{(IV)}{C_6H_5{-}CH{=}\overset{\oplus}{N}H_2} \xrightarrow{H_3O^{\oplus}} C_6H_5CHO + NH_3$

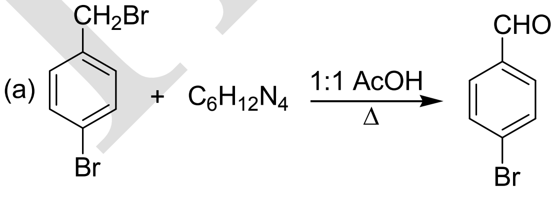
Reaction of bezylamine with excess of $C_6H_{12}N_4$ to produce aldehyde is the actual Sommelet reaction (the last three steps). When benzylamine is refluxed with hexamethylenetetramine (hexamine) in acidic medium benzaldehyde is obtained. This lends support to the above mechanism.

Strong deactivating groups as also *o*-substituents decrease the yield. When both the *o*-positions are substituted, as in 2,4-dinitrobenzylchloride, the reaction completely fails. The yield is also very poor with phenolic compounds.

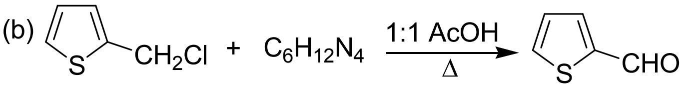
The reaction is generally useful for the preparation of aromatic aldehydes.

Applications

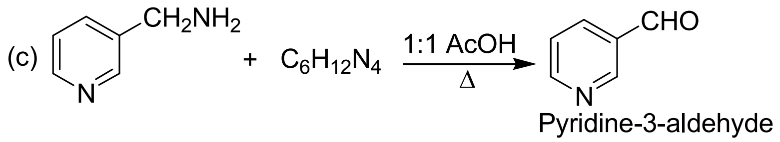
The reaction has proved useful for the preparation of aldehydes from amines and halides. Various types or aromatic, heterocyclic, some aliphatic aldehydes and amines have been prepared.



p-Bromobenzaldehyde



Thiophene-2-aldehyde



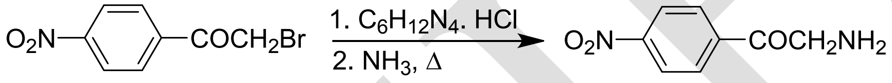
(d) $$CH_3-(CH_2)_4-CH_2-NH_2 + C_6H_{12}N_4 \xrightarrow[\Delta]{HCl} CH_3-(CH_2)_4-CHO$$

n-Hexanal

(e) $$C_6H_5CH_2Cl + C_6H_{12}N_4 \xrightarrow[\Delta]{\text{Excess } NH_3} C_6H_5CH_2NH_2$$

Benzylamine

The reaction (e) has been utilized for the preparation of an aminoketone intermediate required in the synthesis of Chloromycetin.



p-Nitro-ω-bromoacetophenone intermediate for chloromycetin

Another way to oxidize benzylic halides to aldehydes is the Krohnke reaction. The reaction consists of treatment with pyridine followed by *p*-nitrosodimethylaniline and subsequent hydrolysis.

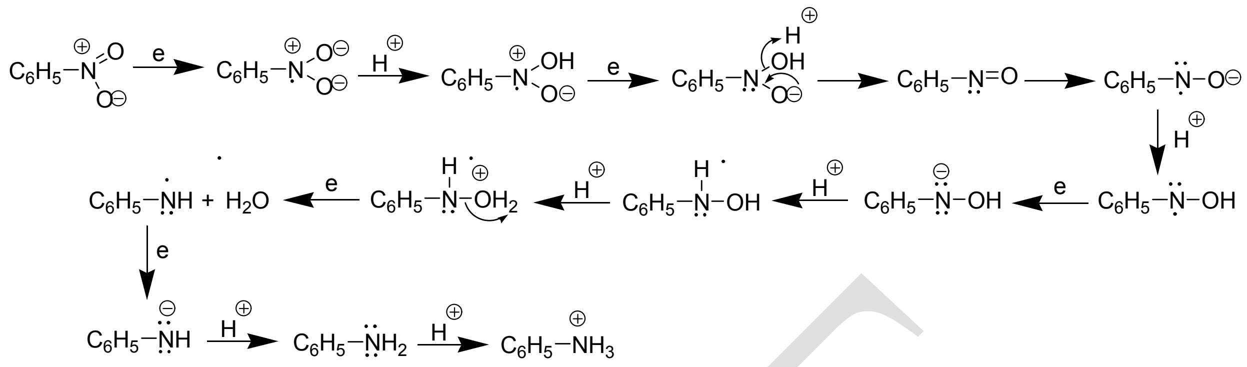
$$C_6H_5CH_2Cl + C_5H_5N \longrightarrow \left[C_6H_5CH_2\overset{\oplus}{N}C_5H_5\right]\overset{\ominus}{Cl} \xrightarrow[2.\ H_3\overset{\oplus}{O}]{1.\ p\text{-}ONC_6H_4\text{-}N(CH_3)_2,\ O\overset{\ominus}{H}} C_6H_5CHO$$

Reduction of nitro compounds

One of the most important reactions of aromatic nitro compounds is their reduction to aromatic amines. Thus a two-step reaction sequence involving nitration of aromatic substrate followed by reduction affords the simplest and most useful synthetic procedure for preparing aromatic amines. In fact, the reduction of nitro compounds to amines involves conversion of a nitrogen atom from its highest oxidation state to the lowest oxidation state.

$$Ar-H \xrightarrow{\text{Nitration}} Ar-NO_2 \xrightarrow{\text{Reduction}} Ar-NH_2$$

The reaction has been very well studied and constituents an example of a reaction whose course may be changed in a number of ways by minor changes in the nature of the reagent and reaction conditions. Following mechanistic scheme has been proposed for the overall reduction of an aromatic nitro compound with metal and acid to give the corresponding amine.



It may be noted that the exact order of addition of electrons and protons is not known. Formation of different types of compounds under different conditions has been exemplified as under:

In acidic solution with dissolving metal and acid or with hydrogen in presence of a catalyst, aromatic amine is the product.

$$C_6H_5{-}NO_2 \xrightarrow{\text{Metal/Acid}} \underset{\text{Aniline}}{C_6H_5{-}NH_2}$$

$$C_6H_5{-}NO_2 \xrightarrow{H_2\text{/Catalyst}} \underset{\text{Aniline}}{C_6H_5{-}NH_2}$$

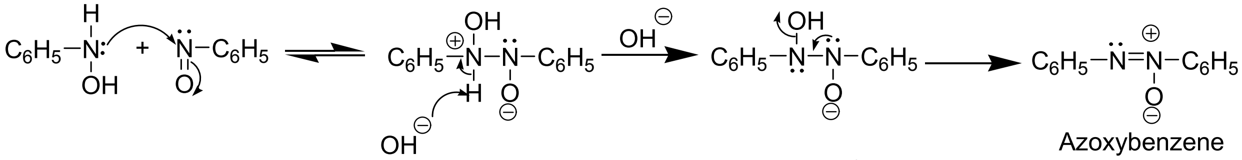
In the laboratory, aniline is usually prepared by the reduction of nitrobenzene with Sn and HCl.

In neutral solution, i.e., with zinc dust and ammonium chloride, the reaction stops at the hydroxylamine stage.

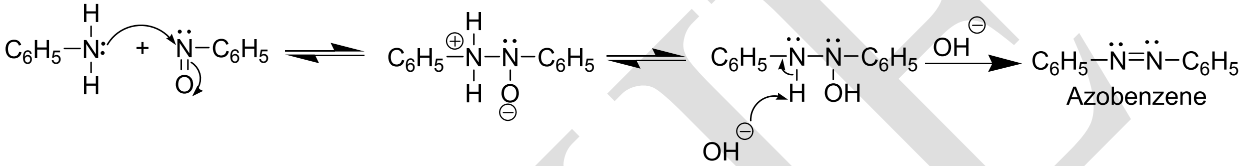
$$C_6H_5{-}NO_2 + 2\,Zn + 4\,NH_4Cl \xrightarrow{H_2O} \underset{\text{Phenylhydroxyl-amine}}{C_6H_5{-}NHOH} + 2\,Zn(NH_3)_2Cl_2 + H_2O$$

This forms the basis of Mulliken's test for nitro group. The above reaction mixture is filtered directly into Tollen's reagent when a grey precipitate or silver mirror is formed due to reducing property of phenyl hydroxylamine.

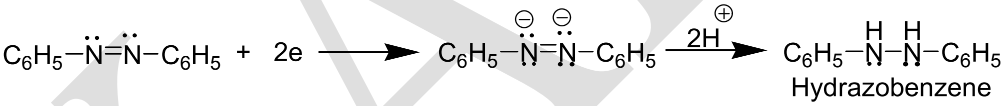
In alkaline medium different types of products are obtained depending upon the types of reagents. The final products are formed by the condensation of intermediates. When nitrobenzene is reduced with alkaline sodium arsenite the final product azoxybenzene is formed by alkali induced condensation of nitrobenzene with phenyl hydroxylamine.



With alkaline sodium stannite or iron fillings and aqueous sodium hydroxide, azobenzene is formed probably by the condensation of nitrosobenzene with aniline.

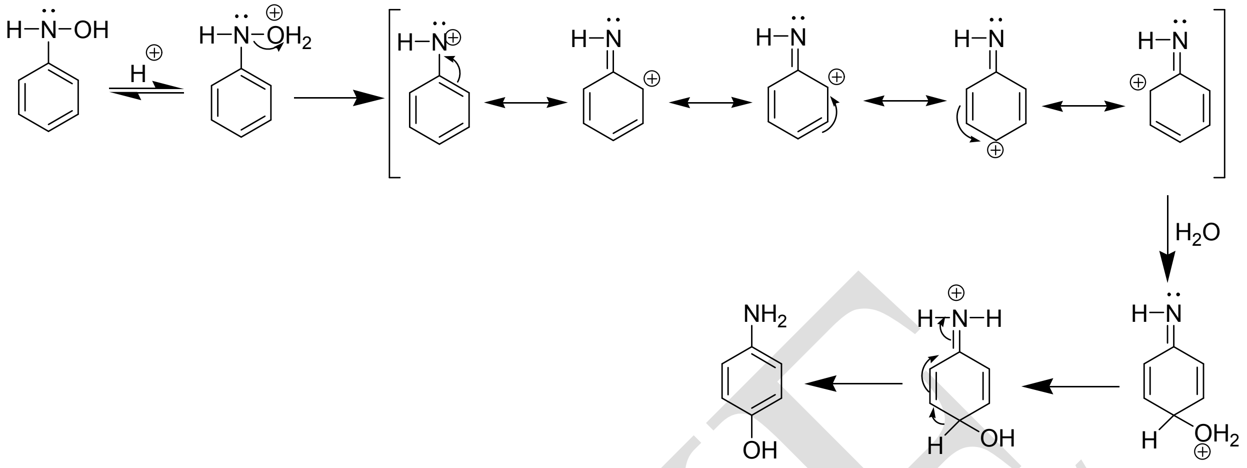


Hydrazobenzene is obtained when nitrobenzene is reduced with zinc in presence of aqueous sodium hydroxide. Since, this substrate is also obtained by the reduction of azobenzene, it can be said with certainty that the reduction of nitrobenzene under these conditions results in the formation of azobenzene which in turn gives the final product (hydrazobenzene).

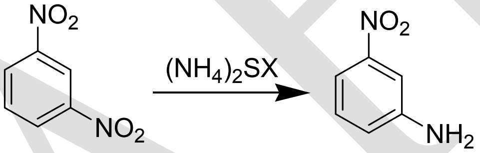


Under electrolytic conditions, the nature of products depends upon the pH of the solution used. By carefully controlling the voltage, current density and pH it has been shown that the first product of reduction is nitrosobenzene. However, this has not been isolated as it under goes further reduction to phenylhydroxylamine. In presence of a little acid the product is aniline.

It has been shown that if reduction of nitrobenzene is carried out in strongly acidic solution of *p*-aminophenol is also obtained, which is an important side product.



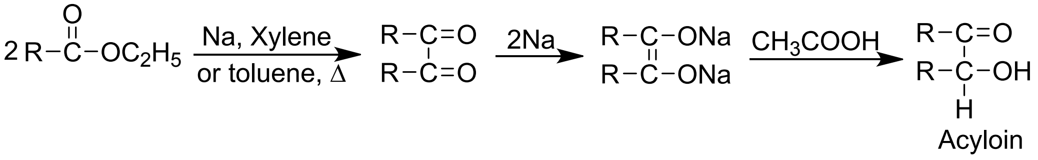
If the aromatic ring has two nitro groups, it is possible to selectively reduce one without affecting the other by taking calculated amount of stannous or titanous chloride, or by using ammonium or sodium polysulphide.



The reason for this selective reduction is not far to seek as the presence of one strong electron withdrawing group increases the ease of reduction (election acceptance) of the other nitro group. Hence, reduction of one nitro group takes place quite easily. However, after one nitro group has been reduced to an electron releasing amino group, the reduction of the other group by a week reducing agent such as ammonium polysulphide becomes relatively difficult.

Acyloin condensation

When carboxylic acid esters are refluxed with metallic sodium in aprotic solvents such as ether, benzene, toluene or xylene, free from oxygen, α-hydroxy ketones called acyloins are formed. This is called **acyloin condensation**.



$$2\,R-\overset{O}{\overset{\|}{C}}-OC_2H_5 \xrightarrow[\text{or toluene, }\Delta]{\text{Na, Xylene}} \begin{matrix} R-C=O \\ | \\ R-C=O \end{matrix} \xrightarrow{2Na} \begin{matrix} R-C-ONa \\ \| \\ R-C-ONa \end{matrix} \xrightarrow{CH_3COOH} \begin{matrix} R-C=O \\ | \\ R-C-OH \\ | \\ H \end{matrix}$$

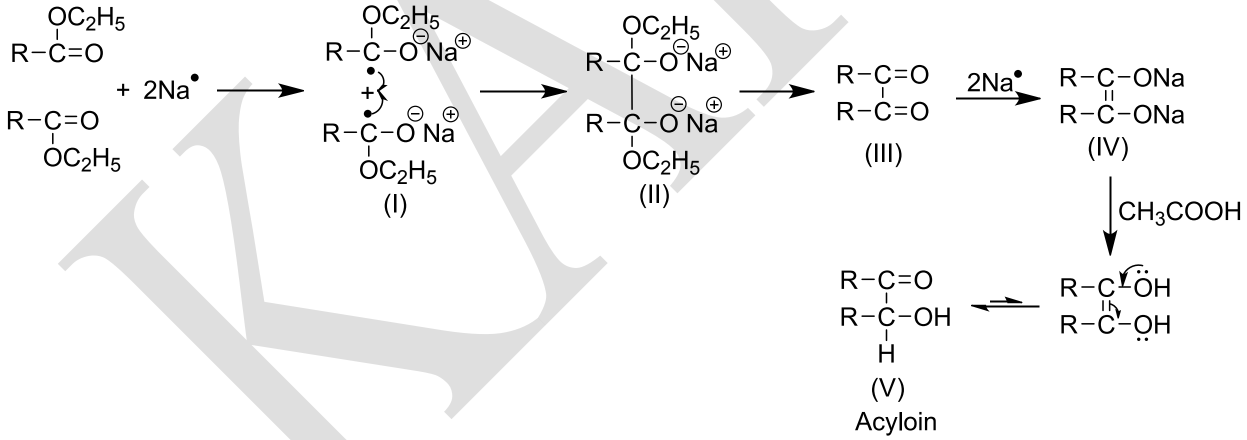
The yield of acyloin is good when R = alkyl group. With diesters, cyclic acyloins have been prepared.

Mechanism

The mechanism of the condensation is not clearly known but it is suggested that the reaction proceeds through a diketone intermediate, since diketone has been isolated in small amounts as a side product.

As the reaction occurs in the presence of metallic sodium, a direct transfer of electron, i.e., a radical mechanism is suggested.

The metallic sodium donates its electron to the carbonyl carbon to give (I) which subsequently dimerizes to yield (II). Loss of both the alkoxy groups from (II) produces 1,2-diketone (III). Further reduction gives sodium salt of enediol (IV). Finally, addition of acid yields 1,2-diol which tautomerizes to the stable acyloin (V).



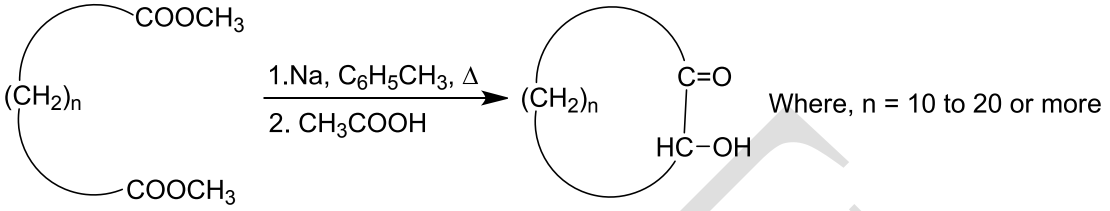
Small traces of oxygen reduce the yield. Hence the reaction is carried out in an atmosphere of oxygen-free nitrogen.

Applications

The condensation has considerable preparative value.

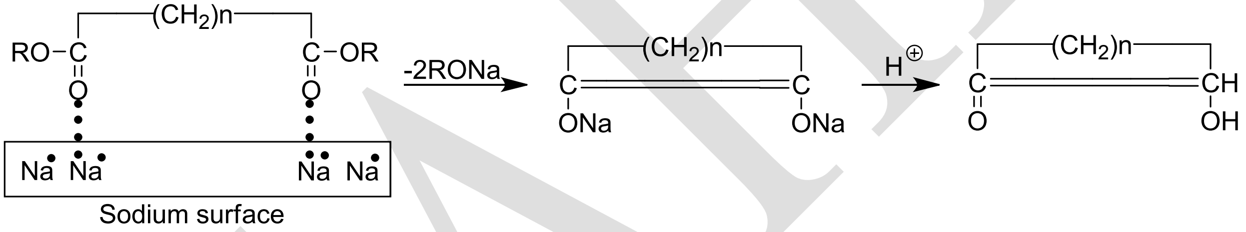
1. Preparation of cyclic acyloins

The condensation has been employed with great success for the preparation of cyclic acyloins. Long-chain dicarboxylic esters have been converted to large-ring compounds without high dilution technique. The method is the best for closing rings of ten members or more.



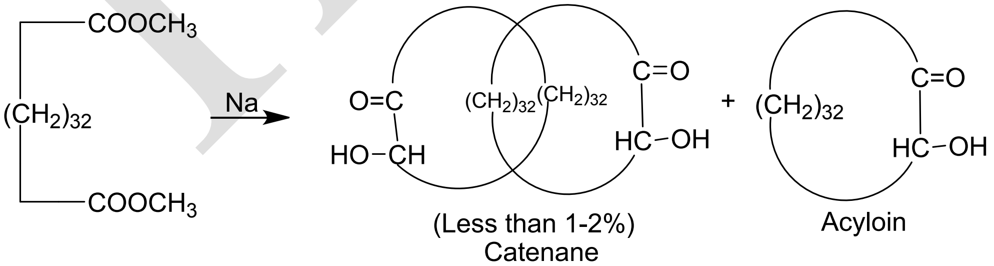
The yields are as high 60-95% for 10 to 20 membered rings.

To account for the ready formation of large rings, it is suggested that the two ends of the ester are adsorbed, albeit weakly to nearby sites on the surface of the sodium metal. Thus, the reactive ends are not available for intermolecular coupling to compete with cyclisation.



2. Preparation of catenane

An interesting and unique compound called catenane, a compound with interlocking rings, was formed when acyloin condensation was employed for ring closure with ester of 34-carbon dicarboxylic acid.



The compound has a great prospect as polymer. Unfortunately, the amount formed is very low. It is, in fact, a chance product depending upon the possibility of threading of diester molecule through the acyloin ring before it closed.

Text Books:

1. Smith, M. B. (2015). *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure* (VII Edition). New Jersey: John Wiley & Sons, Inc., Hoboken.

2. Mukherji, S. M., & Singh, S. P. (2014). *Reaction Mechanism in Organic Chemistry* (III Edition). New Delhi: Laxmi Publications Pvt. Ltd.

Reference Books:

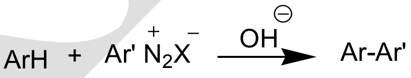
1. Tewari, N. (2011). *Advanced Organic Reaction Mechanism* (III Edition). Kolkata: Books and Allied (P) Ltd.

2. Sanyal, S. N. (2014). *Reactions, Rearrangements and Reagents* (IV Edition). New Delhi: Bharathi Bhawan (Publishers and Distributors).

POSSIBLE QUESTIONS

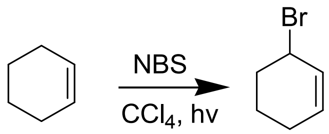
PART-B (Each Question Carry Two Marks)

1. Why does ozone undergo ready 1,3-dipolar addition to a carbon-carbon multiple bond?
2. Write the structures of benzoyl peroxide and AIBN.
3. Write the mechanism of the below reaction.

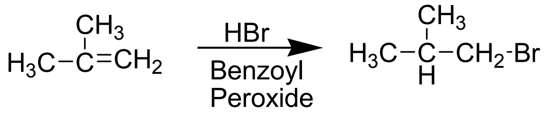


$$ArH + Ar'\overset{+}{N_2}\overset{-}{X} \xrightarrow{\overset{\ominus}{OH}} Ar\text{-}Ar'$$

4. Write the mechanism of the following conversion.



5. Write notes on radical substitution by halogen.
6. Write the mechanism of the following conversion.

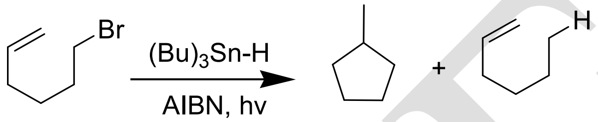


$$H_3C-\overset{CH_3}{\overset{|}{C}}=CH_2 \xrightarrow[\text{Benzoyl Peroxide}]{HBr} H_3C-\underset{H}{\overset{CH_3}{\overset{|}{C}}}-CH_2\text{-}Br$$

7. What is called ozonolysis?

8. Write the synthetic application of Ullmann reaction.

9. Write the mechanism of the following reaction.

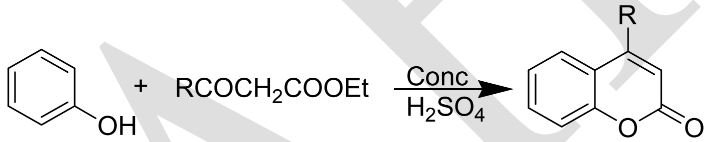


10. Write the mechanism of the below reaction.

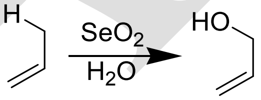
$$Ar\overset{\oplus}{N_2}\ \overset{\ominus}{Cl} + CuCl \longrightarrow ArCl$$

11. Mention some uses of ozonolysis?

12. Write the mechanism of the below reaction.



13. Write the mechanism of the following transformation?



14. What is Oppenauer oxidation method?

15. Write the synthetic applications of Hunsdiecker reaction.

PART-C (Each Question Carry Six Marks)

1. What is Sandmeyer reaction? Explain its mechanism with an example.

2. Write briefly on Acyloin condensation.

3. Explain the mechanism of Sommelet reaction.

4. Write notes on aromatization of six-membered rings.

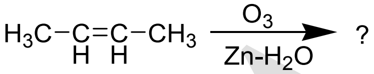
5. Choosing appropriate examples bring out the importance of any two metal hydride reductions in organic synthesis giving emphasis on selectivity.

6. Write brief notes on ozonolysis.
7. Discuss the mechanism of oxidation of alcohols and glycols.
8. Explain the mechanism of Pechmann reaction.
9. Write notes on lithium aluminum hydride and sodium borohydride.
10. Explain the rearrangement of free radicals.
11. Short note on reduction of nitro compounds.

PART-D (Each Question Carry Ten Marks)

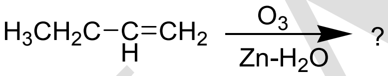
1. Explain the mechanism of
   (i) Pschorr reaction
   (ii) Hunsdiecker reaction.
   (iii) Give the products of the following.

(a)



$H_3C-\underset{H}{C}=\underset{H}{C}-CH_3 \xrightarrow[Zn\text{-}H_2O]{O_3} ?$

(b)



$H_3CH_2C-\underset{H}{C}=CH_2 \xrightarrow[Zn\text{-}H_2O]{O_3} ?$

2. (i) What is Ullmann reaction? Explain its mechanism with an example.

   (ii) Explain the mechanism of Gomberg reaction.

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DEPARTMENT OF CHEMISTRY

UNIT-III

RADICAL REACTIONS

PART-A–Multiple Choice Questions
(Each Question Carry One Mark) (Online Examinations)

1. Which reagent is used for the conversion of toluene into benzyl bromide?

a) NBS b) Br_2 c) HBr d) H_2O_2/Br_2

2. The free radicals are

a) cationic species b) anionic species c) ionic species **d) neutral species**

3. Free radicals which are extremely reactive species and difficult to isolate are referred to as

a) short lived radials b) long lived radicals

c) medium lived radicals d) prolonged lived radicals

4. Which technique is the production free radical?

a) shock tube **b) paneth** c) UV d) IR

5. The most common radical initiator is

a) tetra- methyl lead b) acetone **c) benzoyl peroxide** d) azomethane

6. Among the following which is Fenton’s reagent?

a) $Fe^{3+}+H_2O_2$ b) $Fe+H_2O_2$ c) $Fe^{1+}+H_2O_2$ **d) $Fe^{2+}+H_2O_2$**

7. Hydroxyl radical is produced by

a) Fenton’s reagent b) Tollen’s reagent

c) Fehling’s reagent d) Jones reagent

8. The conversion of benzene into phenol is effected by

a) Sandmeyer reaction **b) Fenton’s reagent** c) Gomberg reaction d) Bachmann reaction

9. The planar free radical species is

a) sp^2 hybridized b) sp hybridized c) sp^3 hybridized d) dsp^2 hybridized

10. The N-bromosuccinimide reagent is very specific reagent for

a) ring bromination b) alicyclic ring bromination

c) allylic bromination d) vinylic bromination

11. Sandmeyer reaction affords a useful method for introducing a halogen substituent at the desired position of an

a) aliphatic ring b) saturated ring c) alicyclic ring **d) aromatic ring**

12. The reactive intermediate in Sandmeyer reaction is

a) cationic b) anionic c) **radical** d) benzyne

13. When the acidic solution of a diazonium salt can couple with another aromatic ring, the reaction is known as

a) Gomberg-Bachmann reaction b) Ullmann reaction

c) Sandmeyer reaction d) Pechmann reaction

14. The acid catalyzed condensation of phenols with β-keto esters to produce coumarins is called the

a) Gomberg-Bachmann reaction b) Ullmann reaction

c) Sandmeyer reaction **d) Pechmann reaction**

15. Which one is used as a common solvent in Ullmann reaction?

a) propanol **b) nitrobenzene** c) hexane d) ethanol

16. Fluorene is prepared from

a) Pschorr ring closure reaction b) Pechmann reaction

c) Gomberg-Bachmann reaction d) Ullmann reaction

17. The main use of DDQ is

a) hydrogenation **b) de-hydrogenation** c) dehydration d) hydration

18. Among the following which one is Swern oxidation?

a) DMSO and oxalyl chloride b) CrO_3 and pyridine c) pyridine-*N*-oxide d) MnO_2

19.________ addition of ozone to an alkene to form an unstable molozonide?

a) 1,2 dipolar **b) 1,3 dipolar** c) 1,4 dipolar d) 2,3 dipolar

20. The Sommelet reaction is successful with

a) alkyl halide b) aromatic halide **c) benzylic halide** d) allylic halide

21. An atom or group atoms possessing an odd electron is called

a) ions **b) free radical** c) anion d) cation

22. A covalent bond breaks uniformity is known as

a) heterolytic fission b) nuclear fission

c) nuclear fusion **d) homolytic fission**

23. The decreasing order of the stability of free radical is

a) $1^\bullet > 2^\bullet > 3^\bullet > 4^\bullet > CH_3^\bullet$ b) $CH_3^\bullet < 1^\bullet < 2^\bullet < 3^\bullet$

c) $1^\bullet < 2^\bullet < 3^\bullet < CH_3{}^\bullet$ **d)** $\mathbf{CH_3{}^\bullet > 1^\bullet > 2^\bullet > 3^\bullet}$

24. Free radical substitution of allylic position can lead to

a) ring expansion b) molecular rearrangement

c) allylic rearrangement d) ring contration

25. The combination of radicals results in

a) rearrangement **b) radical coupling**

c) free radical reaction d) elimination

26. In redox reaction which type of free radical is formed as

a) peroxy **b) hydroxy** c) carboxyl d) carbonyl

27. The catalyst used in homolysis are formed as

a) auto catalyst b) pro catalyst **c) initiation** d) self catalyst

28. Radical addition reaction is usually a

a) complicated process **b) spontaneous process**

c) chain process d) stereospecific process

29. Radical addition reaction yield a

a) trans product b) syn product c) cis product d) meso product

30. Decomposition of benzoyl peroxide in aromatic solvent leads to the generation of

a) benzyloxy radical b) benzyl radical c) methyl radical d) phenyl radical

31. Coupling of aryl halides with copper is called

a) Ullmann reation b) Sandmeyer reaction

c) Gomberg reaction d) Phchmann reaction

32. Ullmann reaction is generally used to prepare

a) symmetrical and asymmetrical biaryls b) aryl ketone

c) aryl acid d) naphthalene

33. Intermolecular Gomberg- Bachmann reaction is called

a) Gomberg reaction **b) Pschorr ring closure**

c) Bachmann reaction d) Hunsdiecker reaction

34. Reaction of silver salt of carboxylic acid with bromine is called

a) Gomberg reaction b) Bachmann reaction

c) Ullmann reation d) Hunsdiecker reaction

35. Most convenient way to perform Hunsdiecker reaction is by the use of mixture of acid and

a) Ag salt b) I_2 c) HgO d) KI

36. In Hunsdiecker reaction the commonly used halogen is

a) Cl_2 **b) Br_2** c) I_2 d) F_2

37. In Hunsdiecker the 2:1 ratio of salt to iodine gives

a) acid b) ether c) alcohol **d) ester**

38. In which reaction the free radical has been generated at bridge head position

a) Hunsdiecker reaction b) Ullmann reation

c) sandmeyer reaction d) Pschorr ring closure

39. Hunsdiecker reaction is otherwise known as

a) hydration b) decarboxylative chlorination

c) decarboxylative oxidation **d) decarboxylative**

40. Auto oxidation is usually catalysed by

a) heat b) light **c) light and initiator** d) initiator

41. A 2° alcohol can lose two hydrogen atoms to form a

a) ester b) aldehyde c) acid **d) ketone**

42. Ozonolysis of diene yields

a) aldehyde and ketone b) ester c) ether d) acid

43. In acidic medium aromatic nitro compounds get reduced into

a) aromatic 3° amine **b) aromatic 1° amine**

c) aromatic 2° amine d) quaternary ammonium salt

44. Zinc and ammonium chloride reduce a nitro compound to

a) hydroxyl amine b) amine c) hydrazone d) oxime

45. Aniline is usually prepared by the reduction of nitrobenzene with

a) Zn b) acid c) base **d) Sn/HCl**

46. When nitrobenzene is reduced with alkaline sodium arsenite the final product is

a) hydroxylamine **b) azoxybenzene**

c) nitrosobenzene d) azobenzene

47. When nitrobenzene is reduced with alkaline sodium stannite the final product is

a) hydroxylamine b) azoxybenzene

c) nitrosobenzene **d) azobenzene**

48. Zinc and aqueous sodium hydroxide reduce a nitrobenzene compound to

a) hydrazobenzene b) azobenzene

c) azoxybenzene d) hydroxylamine

49. When nitrobenzene is reduced in strongly acidic solution it gives

a) o-aminophenol b) m-aminophenol

c) p-aminophenol d) aniline

50. The aromatic ring has two nitro groups it is possible to selectively reduce one without reacting the other by

a) Zn/HCl b) NaOH/Zn **c) $SnCl_2$** d) H_2/Pd

51. When carboxylic acid ester are refluxed with metallic zinc in an aprotic solvent such as ether, α-hydroxy ketones called acyloins are formed this is called

a) Acyloin condensation b) Pekin condensation

c) Aldol condensation d) Claisen condensation

52. Which metal is used in Acyloin Condensation?

a) K **b) Na** c) Fe d) Cu

53. The Acyloins are

a) α – hydroxy compounds b) α – dihydroxy compounds

c) α – hydroxy ketones d) α – hydroxy aldehyde

54. Which solvent is used in Acylion Condensation?

a) ether b) chloroform c) dichloromethane d) DMSO

55. Which solvent is not used in Acylion Condensation?

a) ether **b) chloroform** c) benzene d) toluene

56. Among the following which one is a metallic hydride reducing agent?

a) NaH **b) $LiAlH_4$** c) Zn d) H_2/Pd

57. In $LiAlH_4$ reduction the esters converted into

a) secondary alcohol b) tertiary alcohol

c) primary alcohol d) acid

58. Keto ester when reduced with sodium borohydride is an example for

a) regioselective reduction **b) chemoselective reduction**

c) diastereoselective reduction d) regiospecific reduction

59. Reductive decomposition may be carried out by treating the ozonide with

a) H_2O b) H_2O_2 c) Zn **d) Zn/H_2O**

60. Oxidative decomposition may be carried out by treating the ozonide with

a) H_2O_2 b) H_2/Pd c) Zn/H_2O d) Zn / AcOH

UNIT-IV

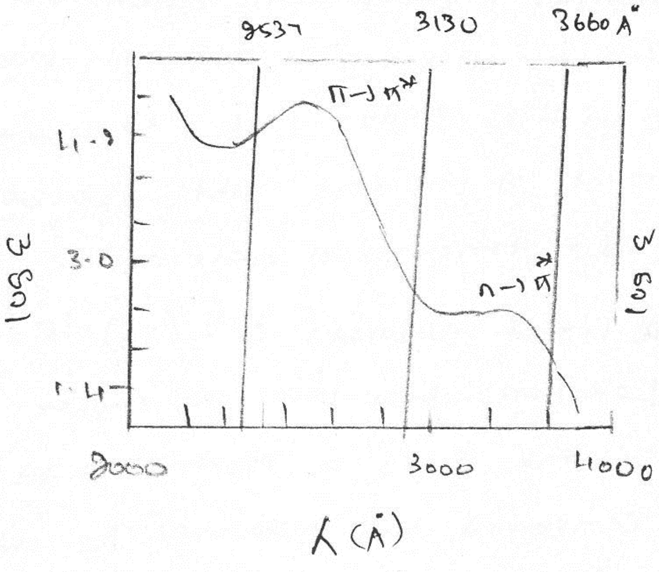
SYLLABUS

Organic photochemistry: Introductory theory of light absorption- Jablonski diagram-photophysical processes- excimers and exciplexes - energy transfer-geometry of excited states – quantum efficiency - photochemical reaction of ketones- Norrish type-I and type-II reactions. Paterno Buchi reaction- cis and trans isomerisation-Photo-Fries rearrangement and Ene reaction and Di-pi methane rearrangement. Barton reaction.

Light Absorption

Photochemistry beings with absorption of light in the 180-800 nm (1800-8000 Å) region of the spectrum, generally termed ultraviolet light. In order to know what wavelength light we should employ in a particular photochemical experiment, we must determine the ultraviolet absorption spectrum of the molecule we wish to study. Such a spectrum measures the amount of incident light absorbed by the molecule as a function of wave length.

The fraction of light absorbed (I/Io) is given by the Lambert–Bear law. The molar extinction coefficient ε is a property of the individual compound and measures the absorptivity. Ultraviolet spectra are usually plotted as ε or log ε Vs wavelength. The log ε plots are particularly useful for exhibiting weak and strong absorption bands on the same scale. **Figure 1** shows the ultraviolet spectrum of a typical aromatic ketone, benzopheneone $(C_6H_5)_2C{=}O$. the ultraviolet spectrum of 1,3-butadiene is shown in **Figure 2**. If we wish to excite these molecules, we must irradiate them with light in regions where they absorb. We must, therefore, match the emission of our source. Usually a mercury arc lamp, to the absorption of the compound. The principal emission lines of mercury arc lamps in this region are shown superimposed on the ultraviolet spectra of benzophenone and 1,3-butadiene. Low–pressure mercury arc lamps are good sources of the 2537 Å line of mercury, and high-pressure mercury are lamps are good sources of the 3130 and 3660 Å lines. Filters are available which permit selection of either of these lines.



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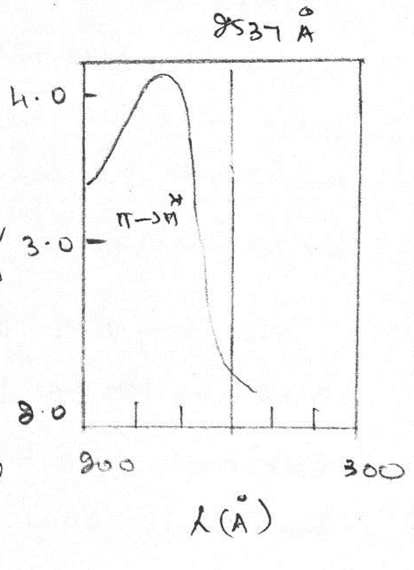


Fig 2.

$$\log I_o/I = \varepsilon Cl$$

I_o = intensity of light before entering sample

I = intensity of light after passing through sample

C = Concentration in moles per litre

l = path length of light through sample in centimeters

ε = Molar extinction co-efficient

Jablonski diagrams

Polyatomic molecules have polydimensional energy surface too complex to represent adequately by simple morse curves. Jablonski diagrams provide a useful means of representation of the excited states of such molecules. In order to appreciate a Jablonski diagram it is necessary to understand the concept of spin multiplicity. Ordinary organic molecules have an even number of electrons. In the ground state, most organic molecules have all electrons paired. Molecular states with all electrons paired are called singlet states (S_n). Absorption of light occurs without spin inversion and the initial excited state produced is a singlet excited state. Singlet excited states may undergo spin inversion, giving a new excited state with two unpaired electrons. Molecular states with two unpaired electrons are called triplet states (T_n). The singlet and triplet designations derive from the fact that singlet states do not split in a magnetic field, whereas triplet states split into three different energy levels. Free radicals that have one unpaired electron give rise to two energy levels in a magnetic field and are thus known as doublet states.

Electronic transitions between states of the same multiplicity, i.e., singlet-singlet and triplet-triplet transitions are spin-allowed, and transitions between states of different multiplicity, i.e., singlet-triplet or triplet-singlet transitions are spin-forbidden. Absorptions due to spin-forbidden transition between excited singlet and triplet states (intersystem crossing) occur in many molecules.

The major events that occur following light absorption may be summarized in terms of a Jablonski diagram. Imagine absorption of a quantum of light of sufficient energy to induce a transition from S_0 to S_2, or shown in **Figure 3**.

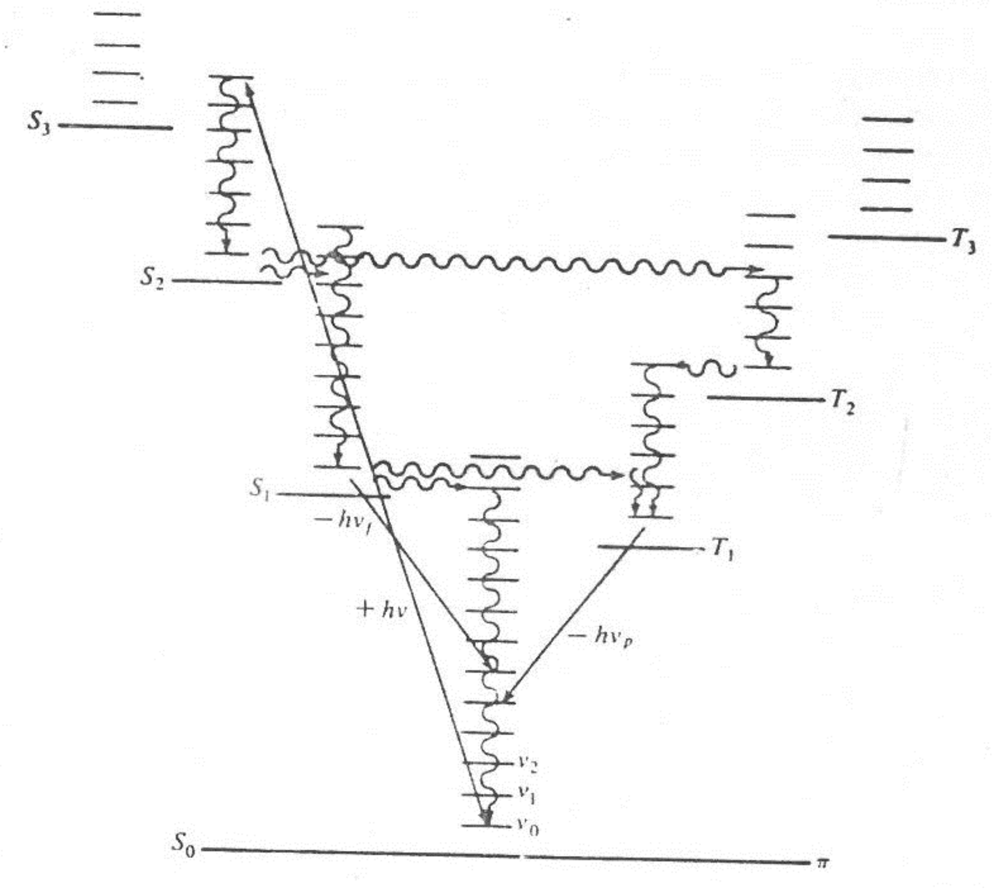


Figure 3

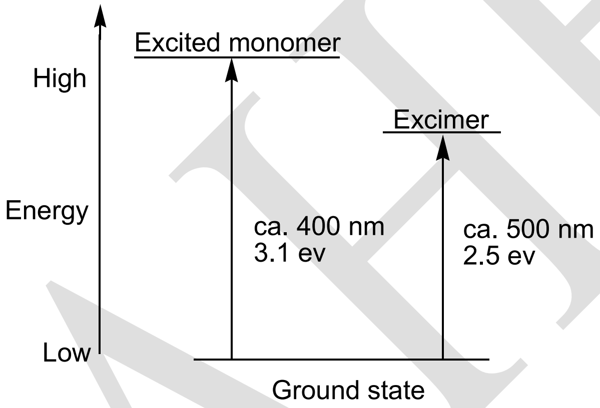
In solution, the excess vibrational energy of S_2 will be rapidly dissipated by radiation–less processes (vibrational cascade) to the solution. The S_2 state will undergo radiationless internal conversion to an upper vibrational level of S_1 which in turn will rapidly lose its excess vibrational energy to the medium. All of these processes will occur in about 10^{-11} seconds; i.e., the lifetime of upper excited singlet states is generally less than 10^{-11} sec. The thermally equilibrated low-lying singlet excited states S_1 (V_0) has a relatively long lifetime (~ 10^{-8} sec). The lifetime of this state is limited by four important processes: (1) fluorescence (2) chemical reaction (3) radiation less decay to the ground state and (4) intersystem crossing. Fluorescence is the emission of light from a singlet excited state as it returns to the ground state. Fluorescence is, in a sense, the opposite of the lowest–energy singlet-singlet light absorption process. Non-dissociative chemical reactions are more probable in long-lived excited states. For this reason, S_1 and T_1 are the major reactive states in photochemical processes. Radiationless transition from S_1 to S_0 may be thought of as internal conversion from S_1 to vibrationally excited S_0 followed by vibrational cascade to S_0 (V_0) with the medium absorbing the excess thermal energy.

Intersystem crossing involves spin inversion and gives rise to a lower-energy triplet state. This process is very important in photochemistry, because the triplet state T_1 produced is even long-lived than S_1. Low-lying triplet states in general have lifetimes greater than 10^{-6} sec and molecules with triplet lifetimes longer than one second are known. On the other hand, upper triplets excited states have very short lifetimes, just as upper singlet states do. The lifetime of the T_1 state is limited by (1) phosphorescence (2) chemical reaction and (3) radiationless decay to S_0. Phosphorescence is the emission of light from a triplet state as it returns to the ground state. Phosphorescence and internal conversion of T_1 to S_o are spin-forbidden processes, and this contributes to the relatively long lifetime or low-lying triplet excited states. Chemical reaction, especially intermolecular reaction is favoured by the longer lifetime of the T_1 state relative to the S_1 state.

Excimers and exciplexes

An excimer (originally short for excited dimer) is a short-lived dimeric or heterodimeric molecule formed from two species, at least one of which has completely filled valence shell by electrons (for example, rare gases. In this case, formation of molecule is possible only if such atom is in an electronic excited state.

Heteronuclear molecules and molecules that have more than two species are also called exciplex molecules (originally short for excited complex). Excimers are often diatomic and are composed of two atoms or molecules that would not bond it both were in the ground state. The lifetime of an excimer is very short, on the order of nanoseconds. Binding of a larger number of excited atoms form Rydberg matter clusters, the lifetime of which can exceed many seconds.



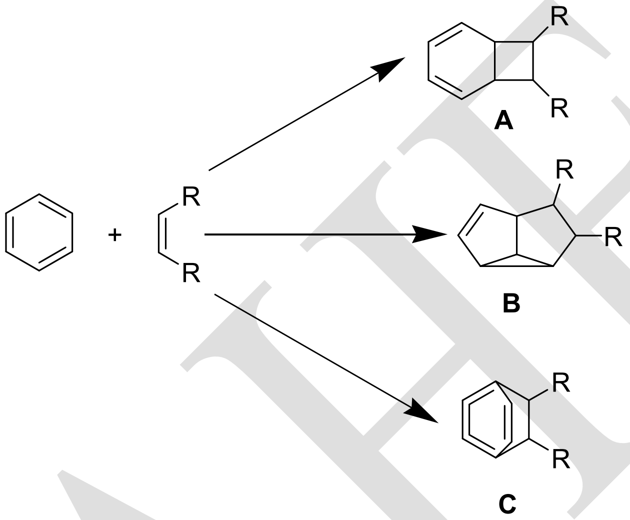
Excited atomic and molecular dimers (excimers) and complexes (exciplexes) are bound together by electronic excitation energy but are dissociated in the ground state.

Examples and use

Heterodimeric diatomic complexes involving a noble gas and a halide such as xenon chloride are common in the construction of excimer lasers, which are excimers most common application. These lasers take advantage of the fact that excimer components have attractive interactions in the excited state and repulsive interactions in the ground state. Emission of excimer molecules is also used as a source of spontaneous ultraviolet light (excimer lamps).

The molecule pyrene is another canonical example of an excimer that has found applications in biophysics to evaluate the distance between bio-molecules.

In organic chemistry many reactions occur through an exciplex for example those of simple arene compounds with alkenes: The reactions of benzene and their products depicted are a [2+2]–cycloaddition to the ortho product (A), a [2+3]–cycloaddition to the meta product (B) and the [4+2]–cycloaddition to the para product (C) with simple alkene such as the isomers of 2-butene. In these reactions it is the arene that is excited.



Energy transfer

We now need to consider a secondary means for producing electronically excited molecules. The method involves transfer of excitation energy from an electronically excited molecule to the ground state of another molecule and is generally used for producing triplet excited states. Singlet excitation energy can be transferred but the probability is limited by the lifetimes of excited singlet states (~10^{-8} sec) which are relatively short compared to the lifetimes of triplet excited states (>10^{-6} see). Triplet energy transfer in its simplest form requires that the triplet energy [$E_T = E(T_1)–E(S_0)$] of the done be 3 kcal/mole or more greater than the triplet energy of the acceptor molecule. If this condition is met, triplet energy transfer will occur at every collision between a triplet excited donor molecule and a ground state acceptor molecule. Such reactions are said to be diffusion-controlled reactions and have pseudo first-order rate constants of 10^9 to 10^{10} see^{-1}. Imagine a donor-acceptor system such that only the donor absorbs the incident light and the triplet energy of the donor is at least 3 kcal/mole greater than the triplet energy of the acceptor.

$$\mathrm{D} + h\nu \longrightarrow {}^{1}\mathrm{D}$$

$${}^{1}\mathrm{D} \xrightarrow[\text{crossing}]{\text{Intersystem}} {}^{3}\mathrm{D}$$

$${}^{3}\mathrm{D} + \mathrm{A} \longrightarrow \mathrm{D} + {}^{3}\mathrm{A}$$

$${}^{3}\mathrm{A} \longrightarrow \text{Products (Sensitization)}$$

$${}^{3}\mathrm{D} \longrightarrow \text{Products (Quenching)}$$

D = Donor, A = Acceptor

Light absorption by the donor produces singlet excited donor ^{1}D, which undergoes intersystem crossing giving triplet excited donor ^{3}D. Triplet excited donor then collides with acceptor, producing triplet excited acceptor ^{3}A and ground state donor D. The concentration of the acceptor must be kept low enough to make collisions with singlet excited donor improbable. This concentration will be determined by the singlet lifetime of the donor. It ^{3}A gives the products of interest, this is called a sensitization mechanism. It the products of interest are derived from ^{3}D, A is a quencher and this is a quenching mechanism. Sensitization and quenching are important methods for determining the spin multiplicity of excited states responsible for photochemical reaction. Sensitization is also an important method for producing the triplet states of molecules in which the efficiency of intersystem crossing is low or zero. The chemistry of singlet and triplet excited states are often quite different.

Let us consider now a specific example, which illustrates the use of sensitization in photochemistry. Direct irradiation of 1,3–butadiene in solution gives cyclobutene and bicyclobutane with minor amount of dimers. Intersystem crossing efficiency in 1,3–butadiene approaches zero and triplet derived products are not formed. Triplet–excited 1,3–butadiene produced by energy transfer from triplet–excited benzophenone gives only dimers. Comparison of the ultraviolet absorption spectra of benzophenone and 1,3–butadiene (**Figures 4 and 5**). Shows that 3660Å light will be absorbed only by benzophenone. Benzophenone with its small S_1-T_1 gap has 100% efficient intersystem crossing. The triplet energy of benzophenone (69 kcal/mole) is quite adequate for diffusion–controlled energy transfer to 1,3-butadiene (E_T = 60 kcal/mole). The energy of the $S_0 \rightarrow S_1$ transition of benzophenone is lower than that of

1,3- butadiene (**Figure 6**). Transfer of singlet energy from excited singlet benzophenone to 1,3-butadiene is thus not expected.

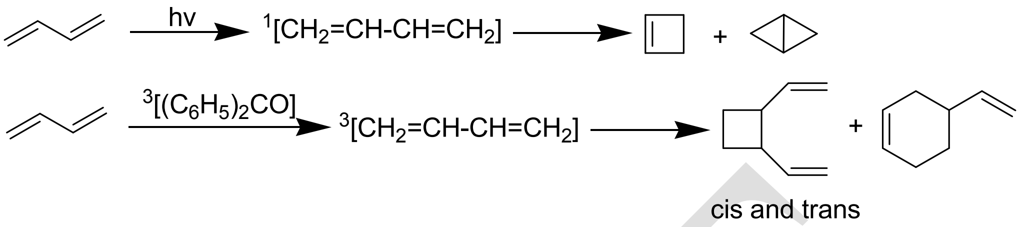


Figure 4

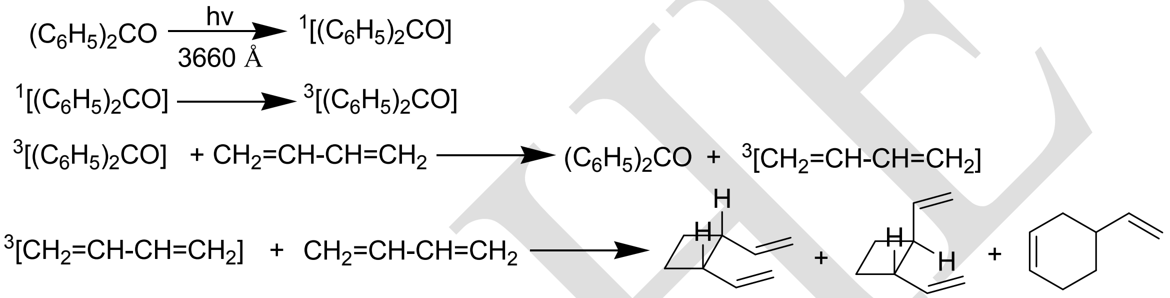


Figure 5

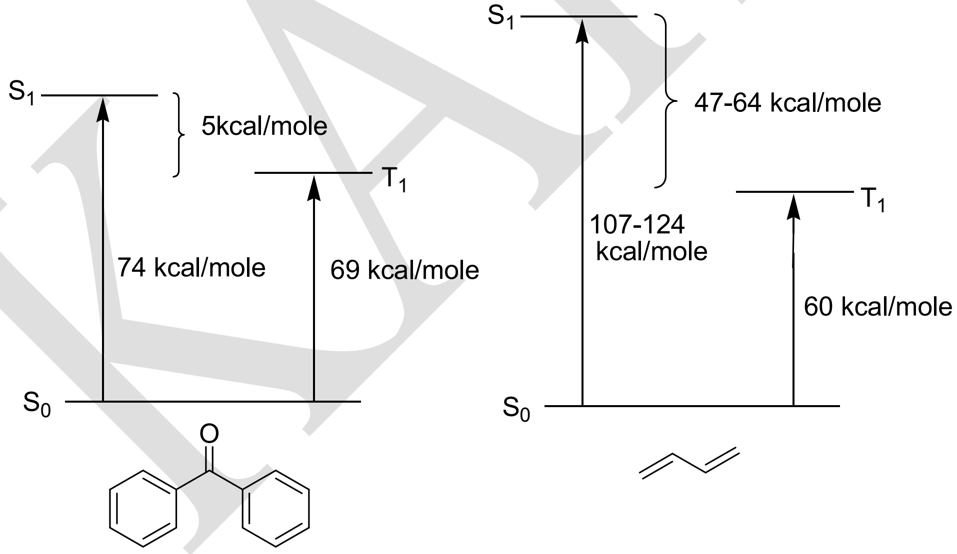
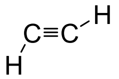


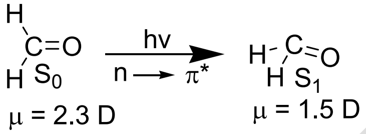
Figure 6

Geometry of excited states

The excited states will often have quite different equilibrium geometries than ground states. It is known for example that excited acetylene is bent rather than linear. Formaldehyde which is planar in its ground state, distorts slightly toward a pyramidal structure in the S_1 state.



The dipole moments of the ground state and first excited state of formaldehyde are also quite different, indicating significantly different electron distribution.



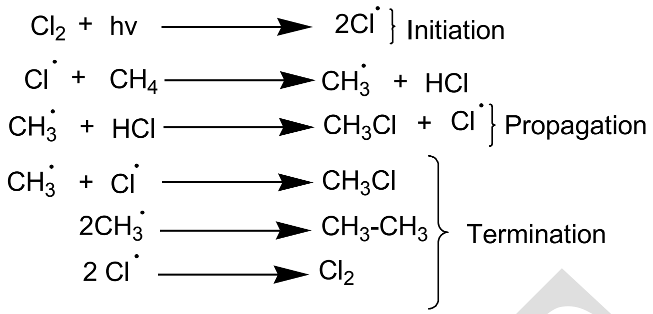
Quantum efficiency

We now need to introduce a new term, quantum efficiency which occupies a prominent place in studies of photochemical mechanisms. Quantum efficiency (or quantum yield) is a measure of the efficiency of the use of light in a photochemical reaction. The quantum efficiency for the formation of a product (ϕ_{form}) is defined as the number of molecules of product formed per quantum of light absorbed. The quantum efficiency for disappearance of starting material is defined as the number of molecules of starting material that disappear per quantum of light absorbed.

$$\Phi_{\text{form}} = \frac{\text{Number of molecues of product formed}}{\text{Number of quanta absorbed}}$$

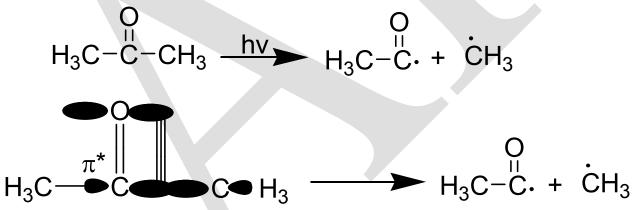
$$\Phi_{\text{dis}} = \frac{\text{Number of molecues of starting material destroyed}}{\text{Number of quanta absorbed}}$$

If a photochemical reaction gives only one product, the quantum efficiency of formation and the quantum efficiency of disappearance will be equal. If several products are formed, the sum of the quantum efficiencies of formation will be equal to the quantum efficiency of disappearance. Quantum efficiency for reactions that do not go through chain mechanisms have values of zero to one. Free radical chain processes have quantum efficiencies as high as several thousand. These high efficiencies arises from the fact that the photochemical reaction is the initiation step in a free radical chain process. The free radical chlorination of methane, for example has a high quantum efficiency, because the chain length is long. The chain propagation steps occur many times before the chain terminates.

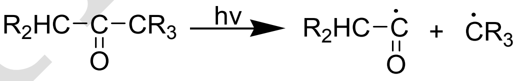


Norrish type I (or) α-cleavage

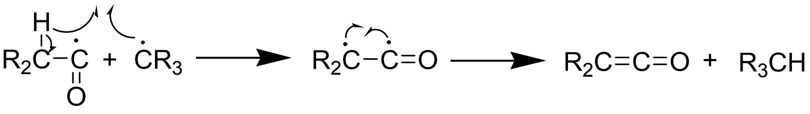
One consequence of the vacancy in the n orbital of an n, π* excited state of a ketone is the tendency to homolytic cleavage of the α carbon-carbon bond. This process is known as α–cleavage (or) Norrish type I cleavage. The half-vacant non-bonding orbital of the n, π* excited state overlaps the σ–bond orbital between the carbonyl group and the α-carbon. This overlap facilitates cleavage of the α–bond. The carbon atom of the carbonyl group undergoes rehybridization during the process of formation of the acyl radical. Both singlet and triplet n, π* states undergo α-cleavage.



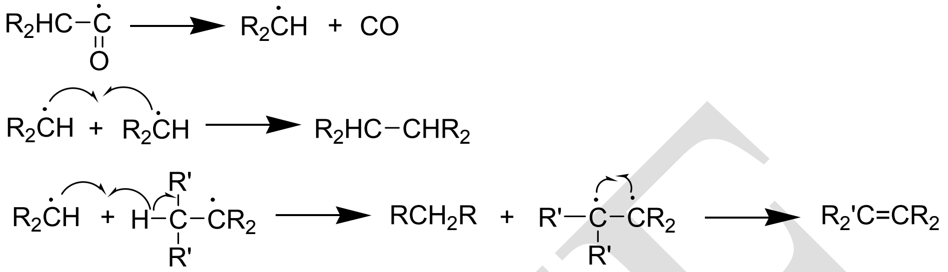
The Norrish type I process is characterized by initial cleavage of the carbonyl-carbon bond to give an acyl and alkyl radical which can undergo stabilisation by one of the routes (a-c):



(a) α–hydrogen abstraction by the alkyl radical to form a ketene and alkane. The presence of a ketene as a reactive intermediate has been demonstrated by spectroscopic method and, in the presence of a nucleophilic species such as water or methanol, it can be trapped as the carboxylic acid or ester derivative.



(b) Decarbonylation of the acyl radical to give carbon monoxide and an alkyl radical, the latter recombining to give an alkane or undergoing intermolecular hydrogen abstraction to form an alkene and an alkane.

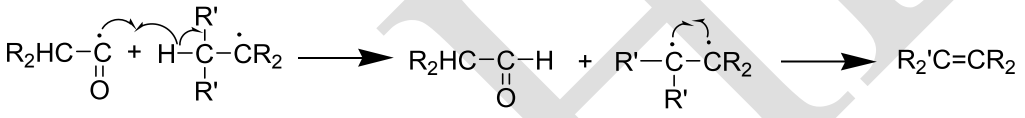


$$R_2HC-\overset{\bullet}{C}{=}O \longrightarrow R_2\dot{C}H + CO$$

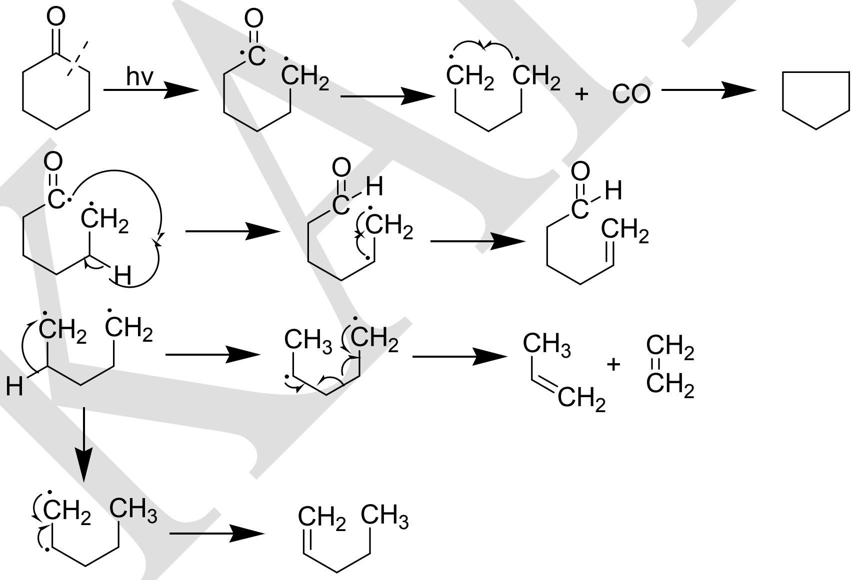
$$R_2\dot{C}H + R_2\dot{C}H \longrightarrow R_2HC-CHR_2$$

$$R_2\dot{C}H + H-C(R')_2-\dot{C}R_2 \longrightarrow RCH_2R + R'-\dot{C}(R')-\dot{C}R_2 \longrightarrow R_2'C{=}CR_2$$

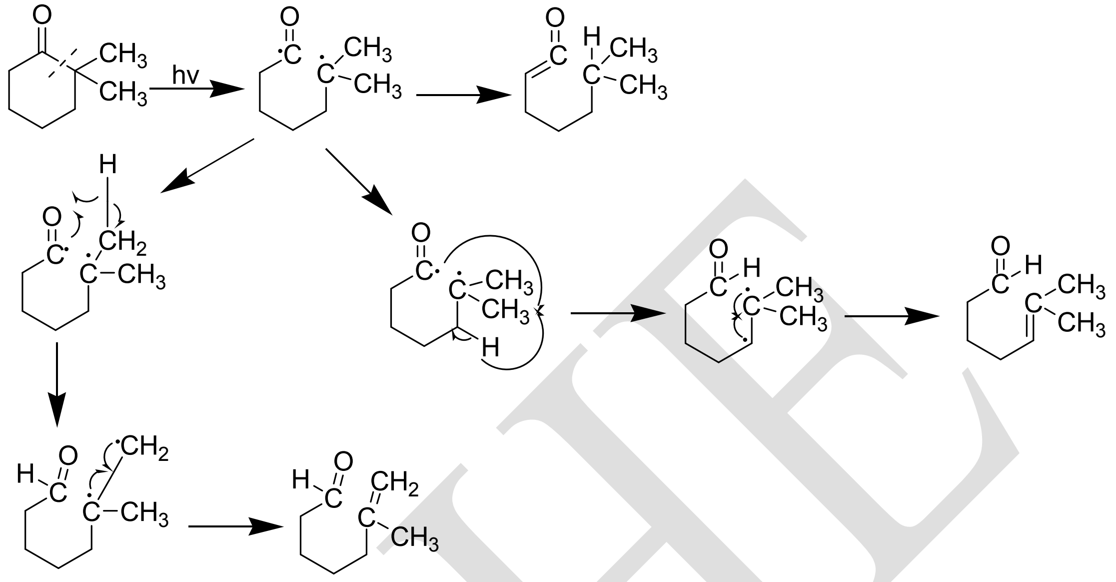
(c) Intermolecular hydrogen abstraction by the acyl radical from the alkyl radical to give an aldehyde and an alkene.



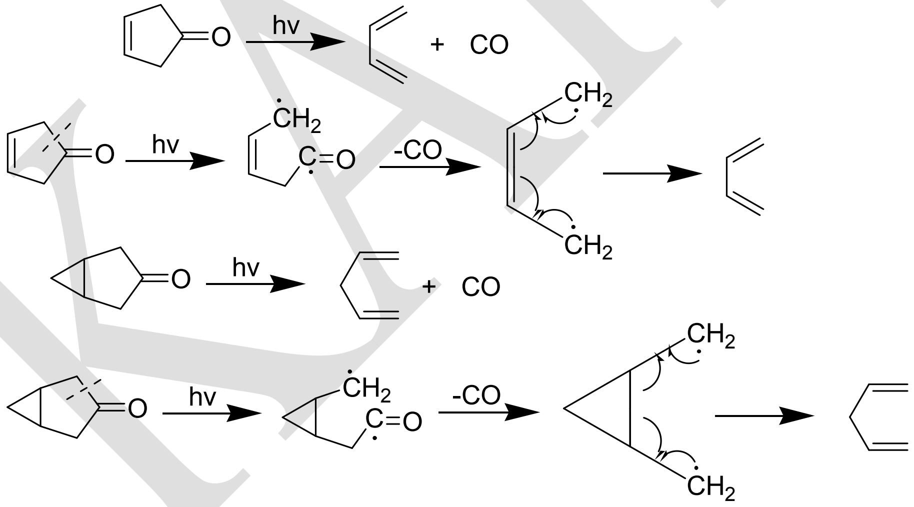
$$R_2HC-\overset{\bullet}{C}{=}O + H-C(R')_2-\dot{C}R_2 \longrightarrow R_2HC-C(=O)-H + R'-\dot{C}(R')-\dot{C}R_2 \longrightarrow R_2'C{=}CR_2$$



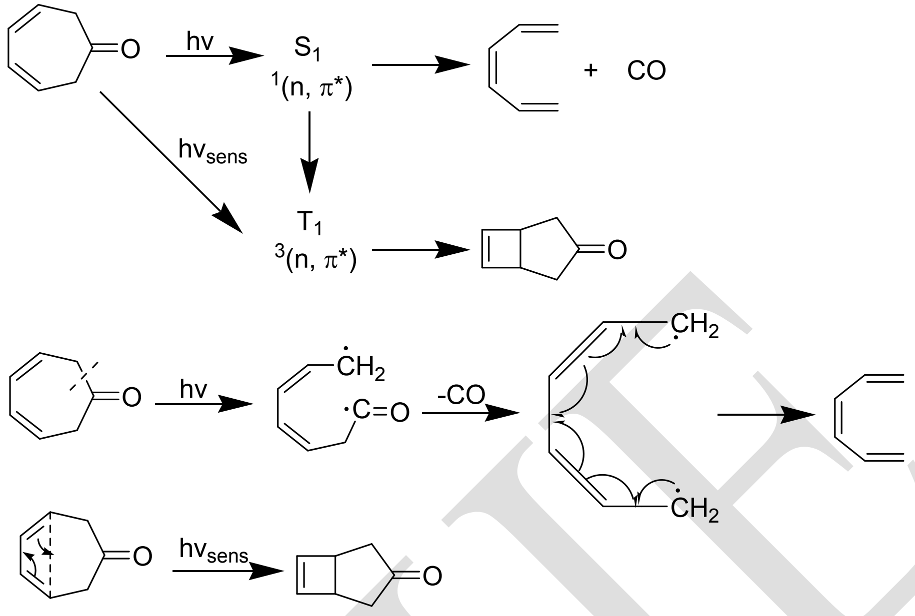
In molecules with differing degree of substitution on the α-carbons, α-cleavage will occur in such a way that the most stable alkyl radical is formed. 2,2–Dimethylcyclohexanone, for example cleaves to give the tertiary alkyl radical rather than the primary alkyl radical. The ultimate products are formed by intramolecular hydrogen transfer reactions.



Suitably placed double bounds or cyclopropane rings greatly facilitate α-cleavage.

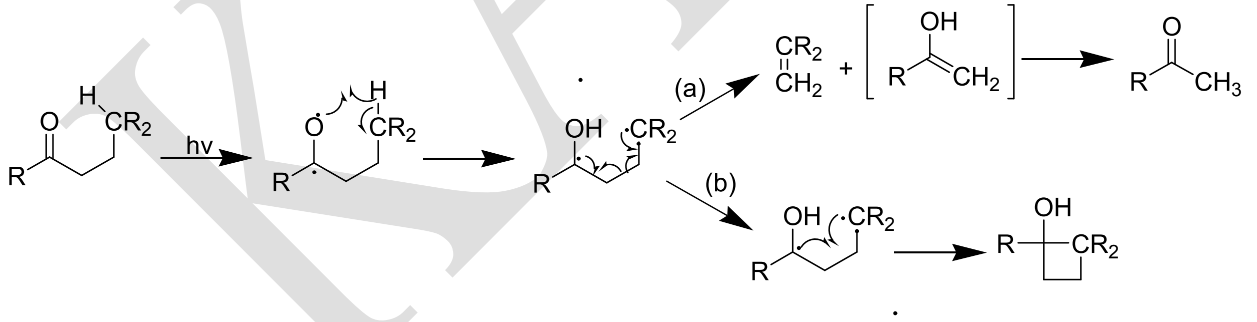


The photochemistry of 3,5-cycloheptadienone provides an instructive example. Direct irradiation gives rise to S_1 which has the $^1(n, \pi^*)$ configuration and undergoes α-cleavage, leading ultimately to decarbonylation. The T_1 state produced by energy transfer has the $^3(\pi, \pi^*)$ configuration and leads to isomerization of the diene. In the low-lying singlet-excited state energy is localized primarily on the carbonyl group, whereas in the low-lying triplet-excited state energy is localized mainly on the diene system.

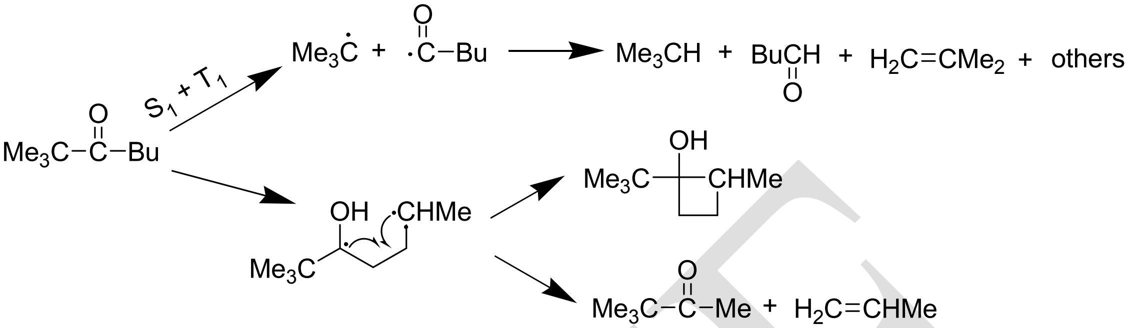


Norrish type II reaction

The Norrish type II process is characterized by intramolecular hydrogen transfer from the γ–carbon atom to the carbonyl oxygen. This often results either in the formation of a methyl ketone and an alkene, by cleavage of the α,β-carbon carbon bond (path a), or in intramolecular radical recombination to form cyclobutanols (path b below).

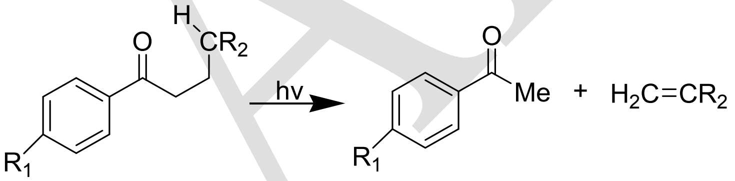


The condensed–phase photolysis of 2, 2-dimethylheptan-3-one (**Scheme 1**) illustrates both the Norrish Type I and Type II processes. The Type I process occurs from both the excited singlet and triplet states and the type II process occurs predominantly form the excited singlet state. However, many Type II reactions are known in which both the excited singlet and triplet states are involved. In the Norrish Type I process there is a preference for cleavage of the bond linking the carbonyl group to the more highly alkylated carbon. This is a result of the relative bond dissociation energies of the carbon-carbon bond and the stabilities of the resultant radicals.

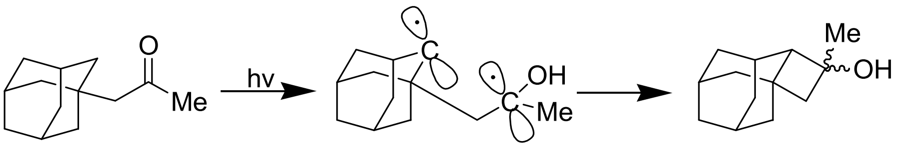


Scheme 1

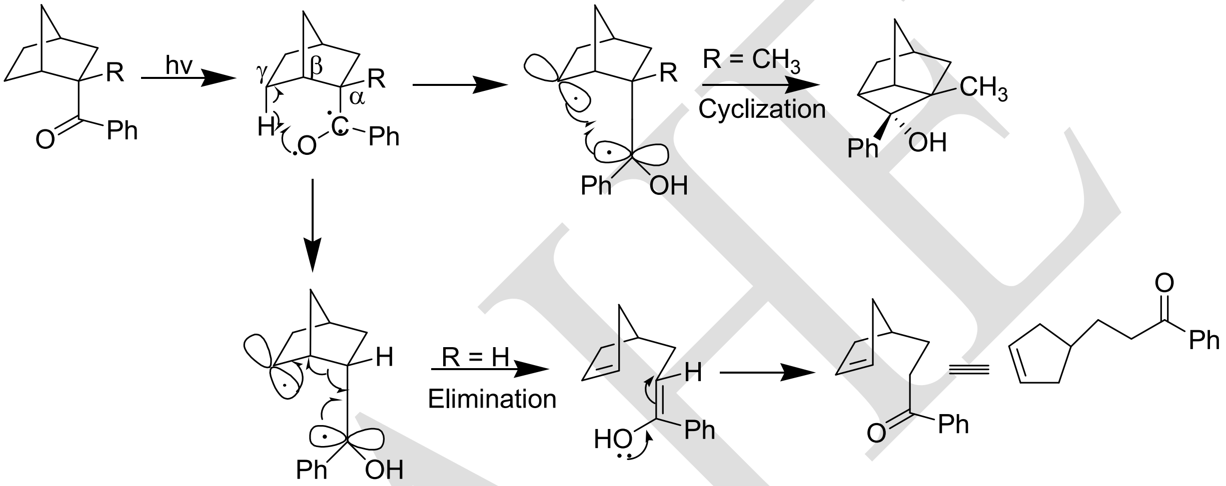
For aryl alkyl ketones the electron–releasing *p*-methyl and *p*-methoxy substituents decrease the rate constant and quantum yield for Type II cleavage. Following this trend *p*-hydroxy, *p*-amino and *p*-phenyl substituents inhibit the reaction completely. This effect is thought to be a consequence of an increases in importance of the π→π* triplet as it becomes lower in energy than the n→π* triplet state.



The adamantyl ketone is an example of a ketone in which γ–hydrogen abstraction results exclusively in cyclobutanol formation. The alternative elimination reaction path would produce a highly strained adamantene and would require overlap of the radical orbitals with the bond undergoing cleavage. This cannot be obtained for the 1,4–diradical because of the conformational restrains of the adamantane structure.



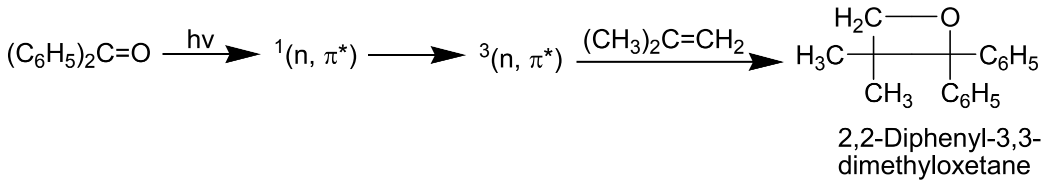
In a similar manner endo-2-benzoyl-2-methylnorboranane results in quantitative formation of the tricyclo–[3,2,1,0]octane (**Scheme 2**, R = CH_3). The presence of the 2–methyl substituent and the consequent high-energy eclipsing interaction with the phenyl group in the planar transition state required for elimination, results in cyclobutanol formation. This is in contrast with the photolysis of endo-2-benzoylnorborane where, in the absence of methyl substituent, photo–elimination is the major reaction course (**Scheme 2**, R = H).

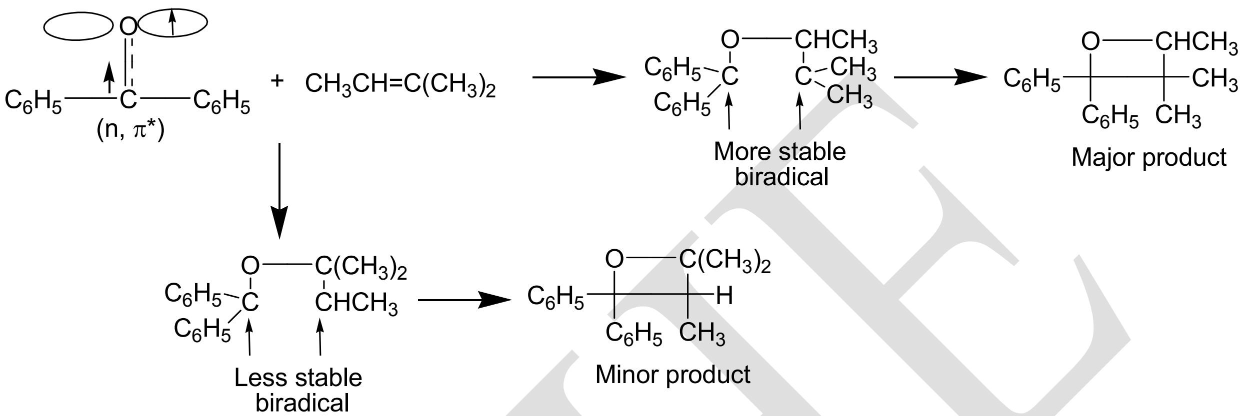


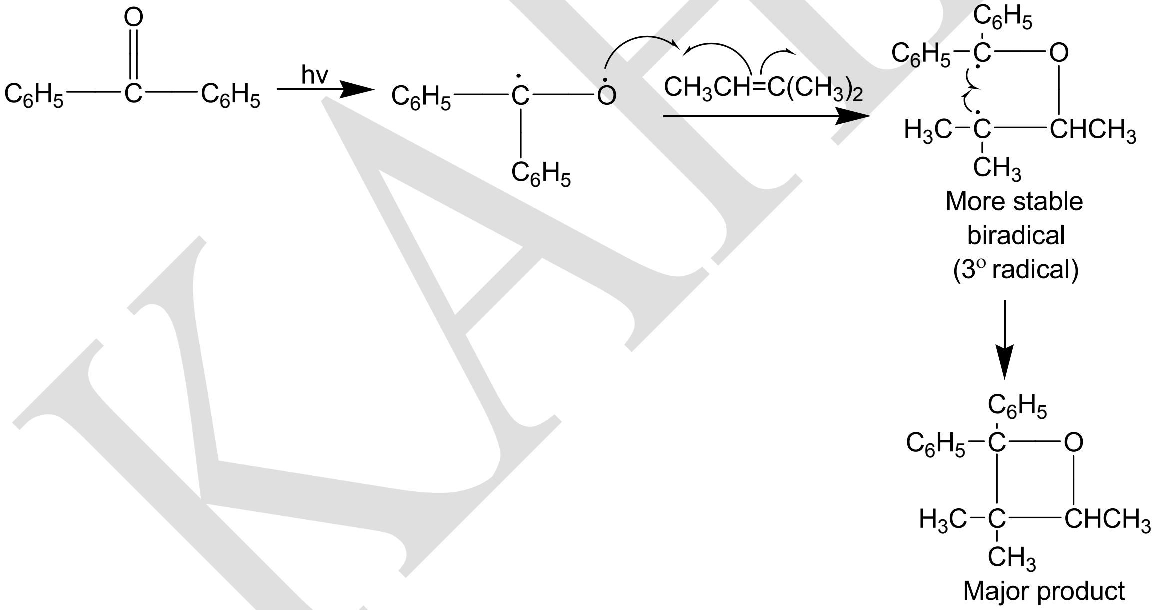
Scheme 2

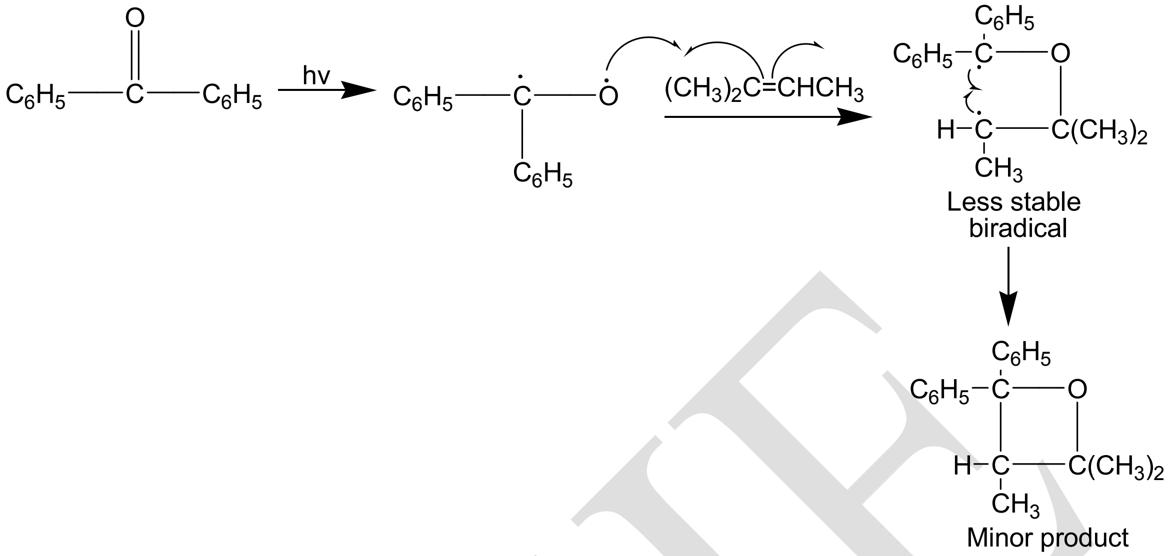
Paterno–Buchi reaction

The Paterno-Buchi reaction involves the addition of an excited ketone to an olefin to form an oxetane. Only ketones with low lying n, π* states are reactive in this process. Most of the Paterno-Buchi reactions reported involves ^{3}(n, π*) ketones. The major mode of addition can be predicted by assuming that the radical–like oxygen atom of the n, π* ketone adds to the olefin to give preferentially the most stable biradical intermediate. In the addition of ^{3}(n, π*) benzophenone to trimethylethylene the element of choice lies between a secondary radical and a tertiary radical, since both biradicals are the same in other respects. The tertiary radical is more stable and this mode of addition is preferred.


$(C_6H_5)_2C=O$
hv
$^1(n, \pi^*)$
$^3(n, \pi^*)$
$(CH_3)_2C=CH_2$
H_2C
O
H_3C
C_6H_5
CH_3
C_6H_5
2,2-Diphenyl-3,3-dimethyloxetane


O
C_6H_5
C
C_6H_5
(n, π*)
+
$CH_3CH=C(CH_3)_2$
O
CHCH$_3$
C_6H_5
C
C_6H_5
C
CH_3
CH_3
More stable biradical
O
CHCH$_3$
C_6H_5
CH_3
C_6H_5
CH_3
Major product
O
$C(CH_3)_2$
C_6H_5
C
C_6H_5
CHCH$_3$
Less stable biradical
O
$C(CH_3)_2$
C_6H_5
H
C_6H_5
CH_3
Minor product

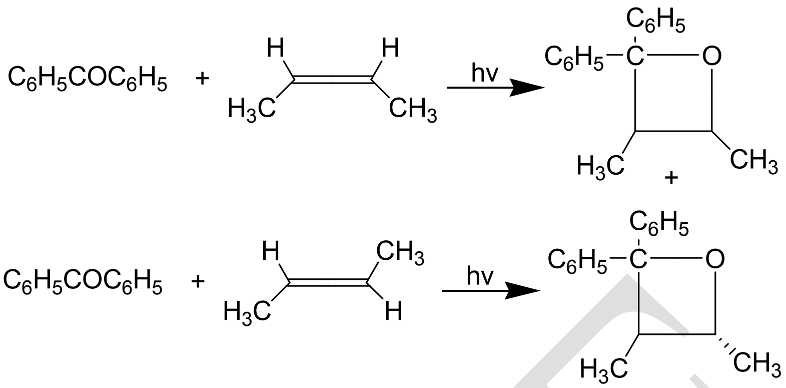

O
C_6H_5
C
C_6H_5
hv
C_6H_5
C
O
C_6H_5
$CH_3CH=C(CH_3)_2$
C_6H_5
C_6H_5
C
O
H_3C
C
CHCH$_3$
CH_3
More stable biradical
(3° radical)
C_6H_5
C_6H_5
C
O
H_3C
C
CHCH$_3$
CH_3
Major product



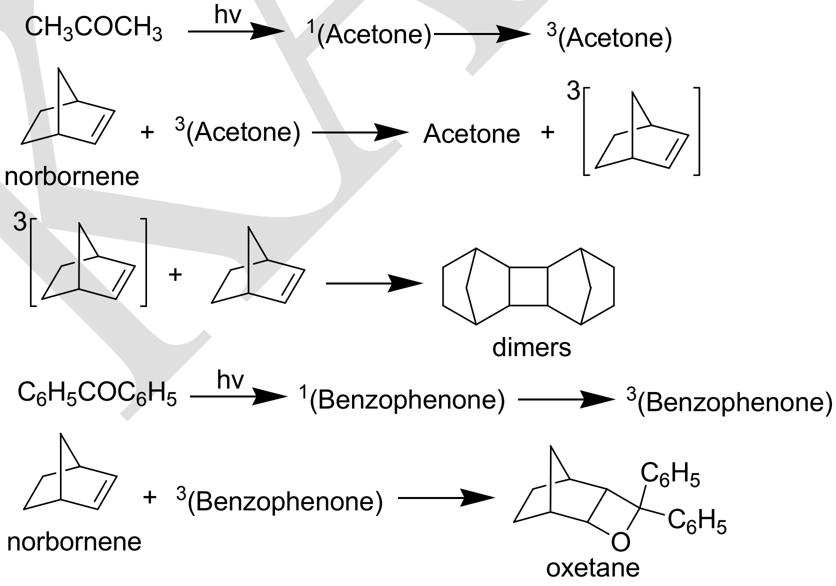
The biradical hypothesis is useful in predicting the major product in a Paterno-Buchi reaction, but it is not adequate as a mechanism. The rate constant for the reaction of excited ketone with ground state olefin is very high (~ 10^9 $mole^{-1}$ sec^{-1}) in the few cases that have been studied. This value is several orders of magnitude greater than rate constants for the addition of oxy radicals to olefins. It is probable that the reaction involves an exciplex (complex between excited ketone and olefin) that collapses to the biradical.

$$\text{ketone} \xrightarrow{hv} {}^{1}(\text{ketone})$$
$${}^{1}(\text{ketone}) \longrightarrow {}^{3}(\text{ketone})$$
$${}^{3}(\text{ketone}) + \text{olefin} \rightleftarrows \text{exciplex}$$
$$\text{exciplex} \longrightarrow \text{biradical}$$
$$\text{biradical} \longrightarrow \text{oxetane}$$
$$\text{biradical} \longrightarrow \text{ketone + olefin}$$

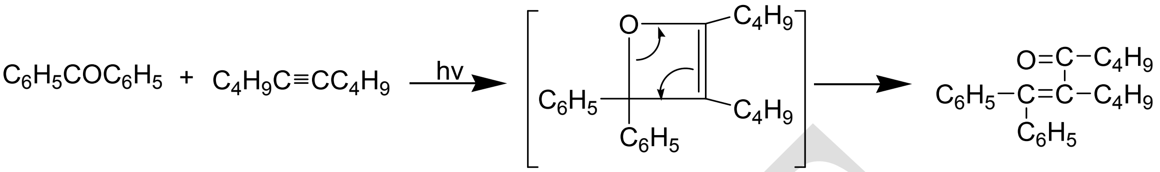
The biradical is an appearing intermediate, because addition of ${}^{3}(n, \pi^*)$ benzophenone to cis and trans-2-butene gives the same mixture of adduct in each case.



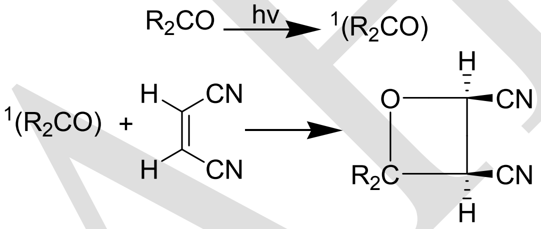
Two side reactions can limit the synthetic utility of the Paterno-Buchi reaction. If reactive hydrogen atoms (such as allylic hydrogen atoms) are present in the olefin, hydrogen abstraction by the excited ketone will compete with the Paterno-Buci reaction and complex mixtures will be formed. If the triplet energy of the ketone is comparable to, or exceeds that of the olefins, energy transfer will compete with or supplant addition. The problem is especially keen with aliphatic ketones because of their high triplet energies. Acetone (E_T ~ 78 kcal/mole), for example, transfers triplet energy to norbornene and thus produces dimers, whereas benzophenone (E_T = 69 kcal/mole) add to norbornene.



Acetylenes can replace olefins in the Paterno-Buchi reaction. The initial adducts are assumed to be oxetenes, but the only products isolated are α,β – unsaturated ketones.



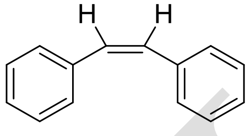
Reactions of $^1(n, \pi^*)$ excited ketones with electronegatively substituted olefins are known which also give oxetanes. These reactions differ from the usual Paterno-Buchi reaction in substituted effects on the olefin and in retention of the stereochemical integrity of the olefin. The $^1(n, \pi^*)$ excited states thus seem to be nucleophilic, and the addition probably does not involve biradical intermediate.

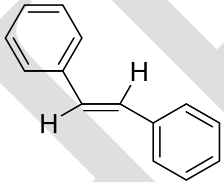


Cis and trans isomerisation (or) Geometrical isomerisation

The phenomenon of cis-trans isomerisation is well established not only for thermal ground state reactions, but also for excited state reactions. The ease with which olefins undergo geometrical isomerisation on photolysis has been known for a considerable time but the details of the reaction remain the subject of many investigation.

In a ground state isomerisation the thermal reaction proceeds by way of a non-planar transitions state common to both cis-and-trans-isomers. The transition state will collapse to give a greater proportion of the thermodynamically more stable isomer, usually the trans-isomer. However, the product composition in the photo-chemically induced isomerisation differs from that in the thermal processes and the thermodynamically less stable isomer usually predominates. The ultraviolet absorption spectra of conjugated olefins normally show that a cis-isomer absorbs at lower wavelength than the corresponding trans-isomer. In the cis-isomer, non-bonded interactions between the cis-substituents often prevent a complete overlap of the π-system and the extent of delocalisation is thereby reduced. This is well illustrated by stilbene. The trans-isomer absorbs at 294 nm (ε = 2400 m^2 mol^{-1}) whereas the cis-isomer absorbs at 278 nm (ε = 935 m^2 mol^{-1}). In cis-stilbene, steric interference between the ortho-hydrogens of the aromatic rings is relieved by rotation of the rings out of a plane with the remainder of the molecule and there is consequently a less effective overlap of the π-system. The trans-isomer is free of such interference and greater delocalisation is demonstrated by the longer wavelength of absorption.

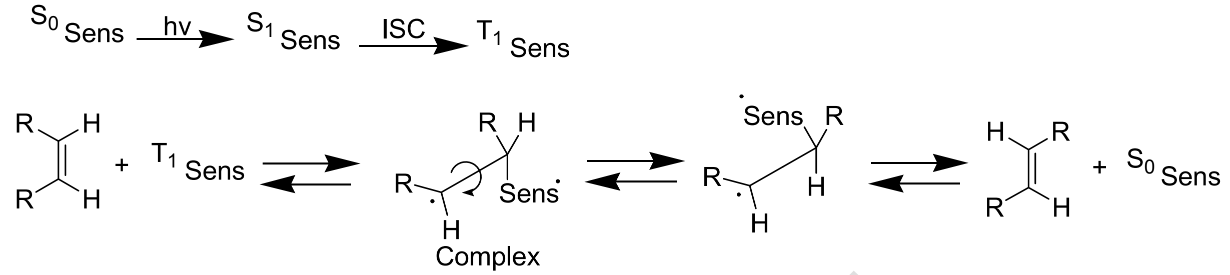

cis-stilbene


trans-stilbene

Irradiation of a trans-isomer will produce an excited species which is usually lower in energy than that of the corresponding cis-isomer. The energy of a π→π* excited species is a function of the angle of twist about the carbon-carbon σ-bond, and trans-to cis-isomerisation is believed to be effected by distortion of the trans-excited state, initially produced, to an excited state common to both cis-and trans-isomers. This excited state is termed a phantom state and for stilbene is a singlet, which for many other systems a phantom triplet is involved. A small activation energy (8 kJ mol^{-1}) is involved in producing the phantom singlet from singlet excited trans-stilbene. Collapse of the phantom state to the ground state by conventional deactivation processes will afford both cis-and trans-isomers but, nevertheless, an excited state population will be obtained from this isomer, and isomerisation from cis to trans will occur *via* the phantom state. In this way an equilibrium termed a photo-stationary state, is established and it usually contains more cis than trans-isomer. Irradiation of a pure cis or trans-isomer of a cis-trans mixture will lead to the same photo-stationary state. If the irradiation wavelength were filtered to allow only one isomer in a mixture to absorb radiation, complete conversion to the other isomer would occur a process referred to as optical pumping.

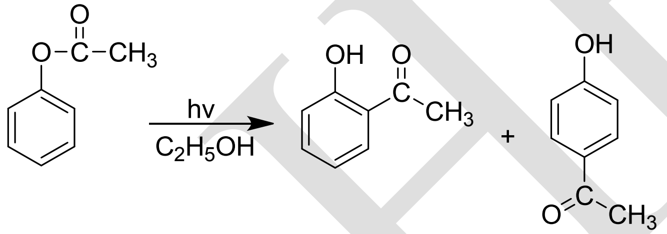
The photochemical process of geometrical isomerisation can be complicated by can current thermal isomerisation. The excited state can be deactivated by non-radiative processes, and internal conversion from S_1 can lead to a high vibrational level of the ground state. This excited ground state can undergo thermal isomerisation to the thermodynamically more stable trans-isomer. However, in general, photolysis leads to a photo-stationary state will greater than 50 percent cis-isomer in the mixture. For stilbene the photo-stationary state contains 92 percent of the cis and 8 percent of the trans-isomer.

Photochemical cis-trans isomerisation can be brought about either by direct irradiation or by triplet sensitisation. The composition of the photo-stationary states produced from the two modes of excitation is different. If, in the sensitised process, the donor species fulfills the conditions for effective sensitisation and its triplet energy is greater than that or either of the geometrical isomers, than triplet energy transfer to both the cis-and trans-isomers will occur. The initially formed cis-and trans–triplet excited species undergo distortion to a common phantom triplet which on collapsing to the ground state, affords a mixture of isomers. Because the sensitiser can excite both isomers, the proportion of cis-isomer in the photo stationary state from a sensitised reaction is lower than that obtained from direct irradiation. This is in contrast to the unsensitised isomersation where the isomer with the higher extinction coefficient undergoes preferential excitation. The cis-trans isomerisation of 1, 2-diphenylpropene has been studied for a series of sensitisers of known triplet energies. Sensitiers of high energy give photo-stationary states with approximately the same composition of isomers (55 percent cis) while direct photolysis results in a higher proportion of cis-isomer (72 percent). As the sensitiser energy is reduced anomalous results are observed. These are accounted for by non-classical energy transfer, in violation of the Frank-Condon principle, with direct production of the phantom triplet with some sensitisers an alternative mechanism may compete with or even dominate phantom triplet production in cis-trans isomerisation. This mechanism involves bonding of the oefin to the triplet sensitiser to produce a complex in which rotation about the carbon-carbon bond is more rapid than decomposition.



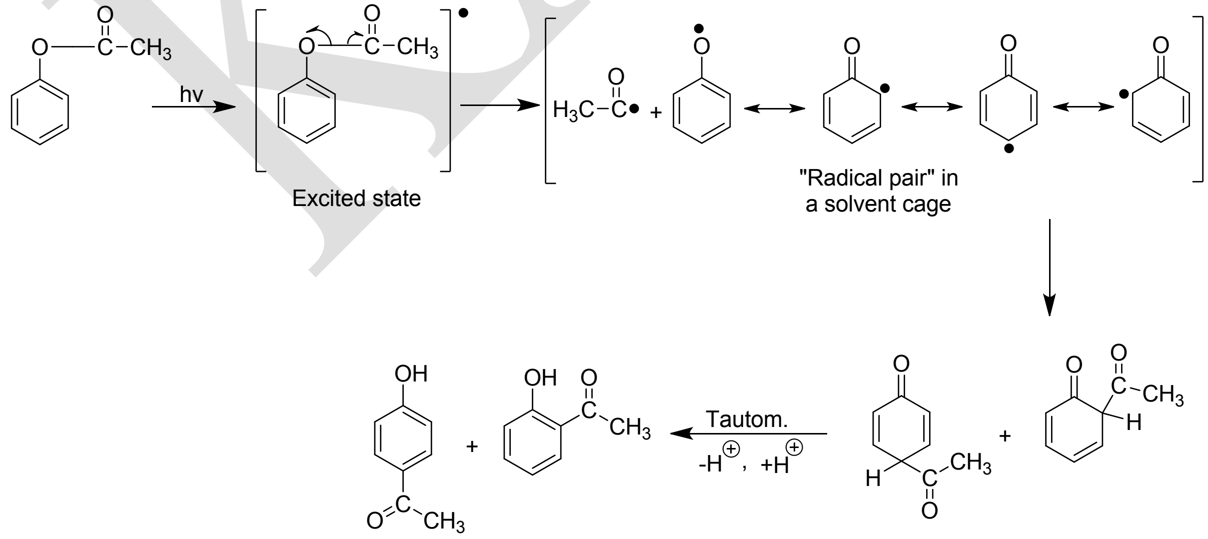
Photo–Fries rearrangement

The Fries rearrangement can also be carried out with ultraviolet light. The reaction is known as the photo-Fries rearrangement. For example:



Mechanism

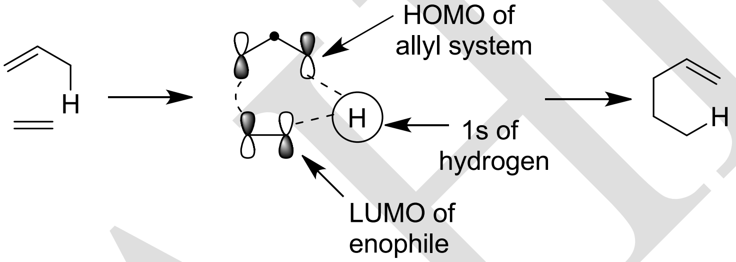
The reaction is predominantly an intramolecular free–radical process. Absorption of a photon by the ester results in its dissociation into radicals within a solvent cage. The radicals than recombine before diffusion from the solvent cage to give, after tautomerization, the rearranged products.



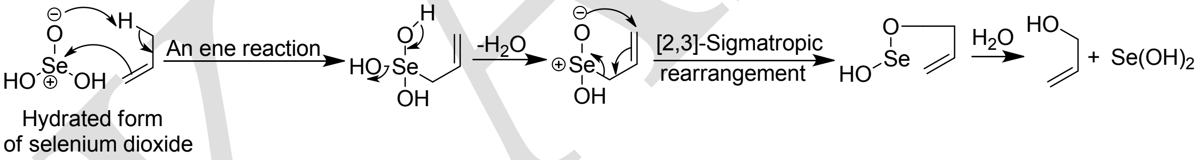
Ene reaction

An alkene having an allylic hydrogen atom reacts thermally with a dienophile (C=C, C=O, N = N etc., called enophile) with the formation of a new σ bond to the terminal carbon of allyl group followed by the [1,5] migration of the allylic hydrogen and change in the position of the allylic double bond. This reaction resembling both cycloaddition and a [1,5] sigmatropic shift of hydrogen is known as the ene reaction.

The interaction of a hydrogen atom with the HOMO of the allyl radical and LUMO of the enophile is a symmetry–allowed process. This may shown as follows.

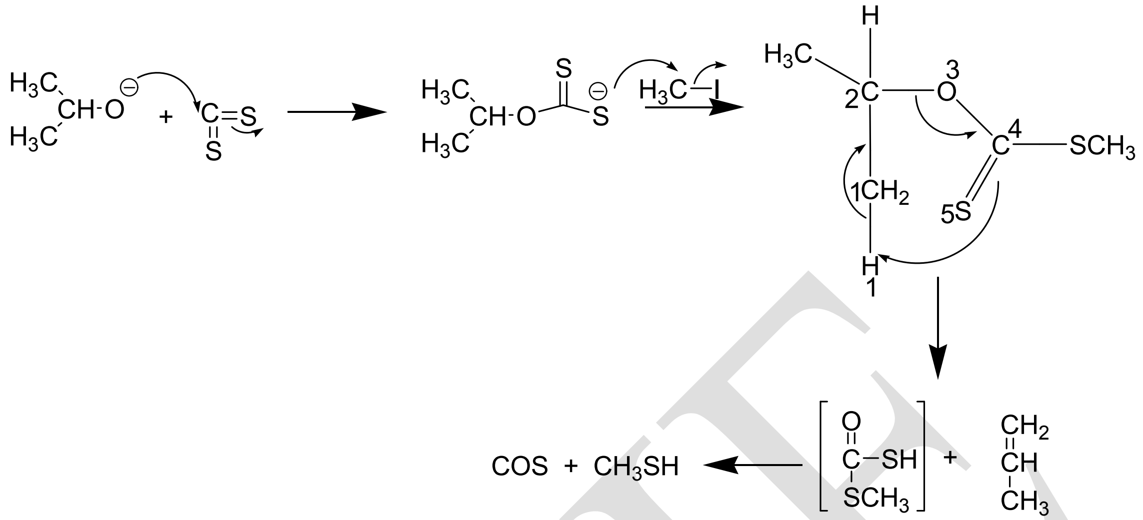


The allylic oxidation of alkenes with selenium dioxide, for example, involves an ene reaction.

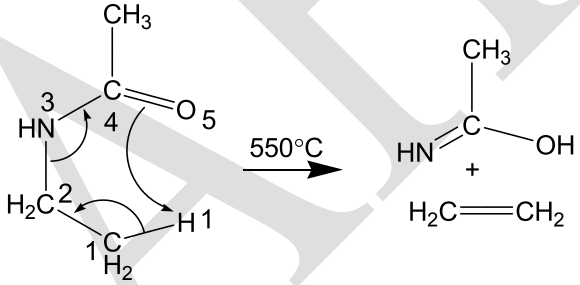


The ene reaction with sulfur and nitrogen

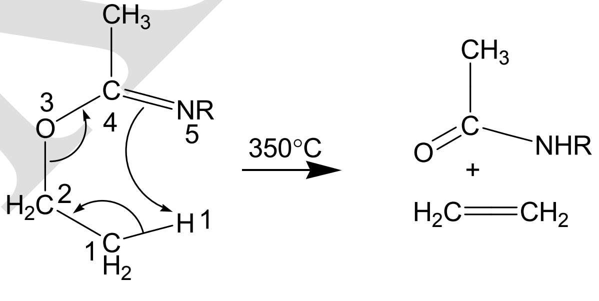
Ene reactions are not limited to systems involving carbon and oxygen; historically the Chugaev reaction preceded the acetate pyrolysis as a method for the formation of alkenes from alcohol.



Amides will also undergo pyrolytic eliminations, but the temperatures required to bring about the reaction are too high for the method to have synthetic utility. In this reaction an amide is converted into an unstable tautomer.

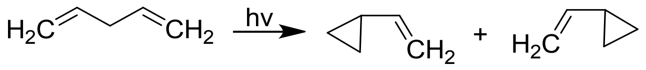


Reaction temperatures decrease markedly if the oxygen and nitrogen atoms are interchanged, since a high-energy imino ether is transformed into an amide.

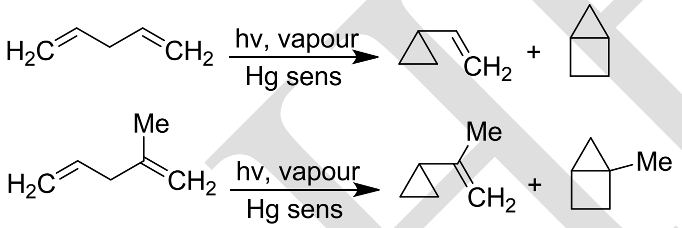


Rearrangements -1,4-dienes and the di-π-methane rearrangement

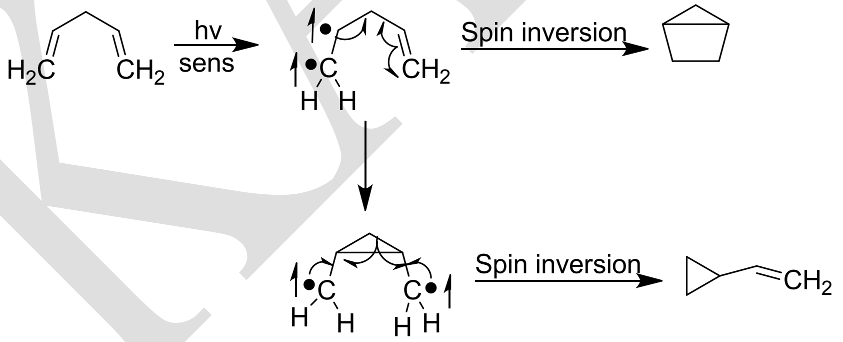
The commonest photochemical reaction of 1,4-dienes is the di-π-methane rearrangement, in which the 1,4-diene is converted into a vinylcyclopropane. A ‘di-π-methane’ units involves the saturated carbon atom directly attached to two sites of unsaturation, as exemplified by penta-1,4-dienes above. The di-π-methane rearrangement is found to be general for solution-phase photolysis of acyclic, cyclic, bi- and tricyclic 1,4-dienes.



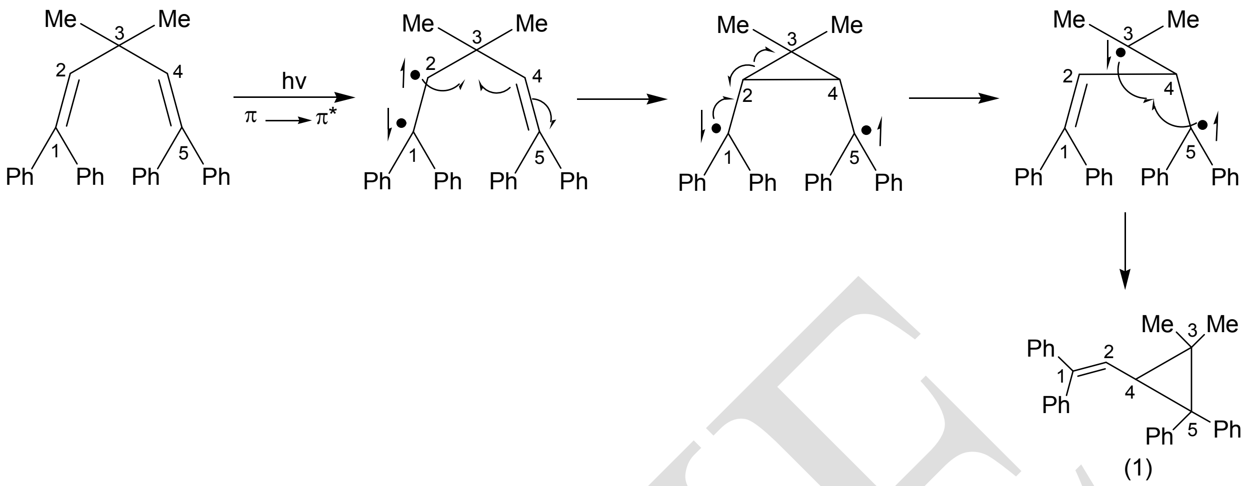
Penta-1,4-dienes above and its alkyl derivatives possess isolated olefinic chromophores and do not absorb light above 200 nm; hence only the triplet-sensitised reactions of these molecules have been examined. For all cases studied, a vinylcyclopropane is produced together with products which usually include a bicyclo[2,1,0]pentane.



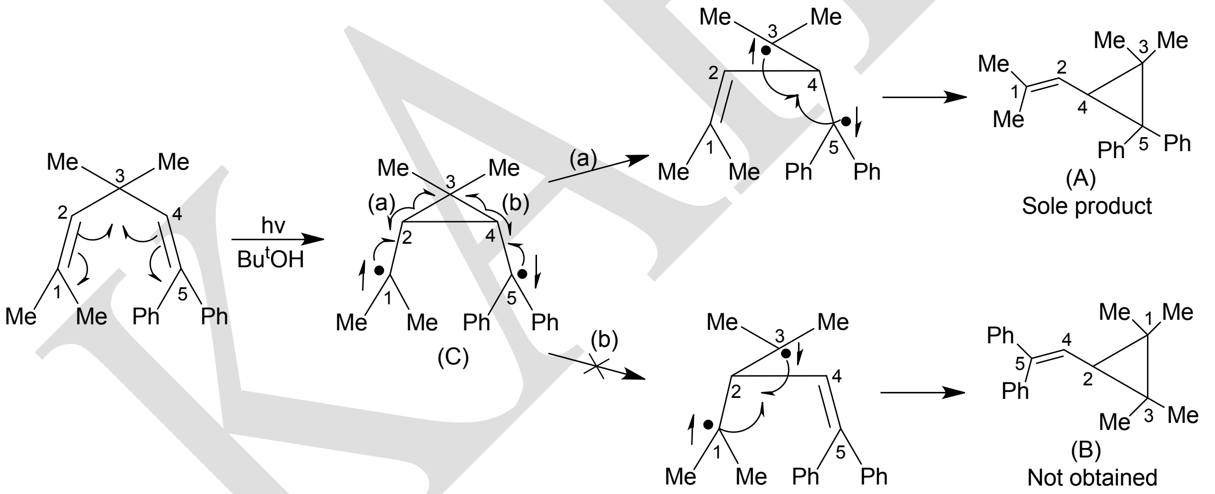
The formation of these products can be rationalised by the following mechanism, in which the unpaired electrons are shown as half-arrows which are parallel for a triplet state and antiparallel for an excited singlet state. The curved half-arrows imply singlet electron flow. The bicyclic product clearly arises by cyclo-addition of one olefinic bond on the other.



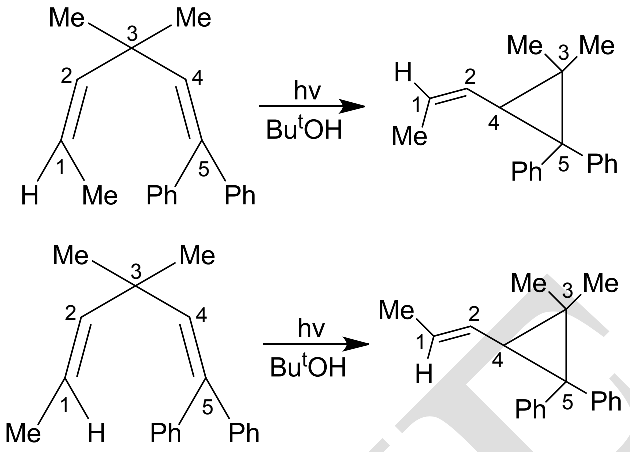
1,4-Dienes do not absorb in the accessible region of the ultraviolet. It is therefore only possible to examine the direct photolysis of a 1,4-diene if one of the double bonds has extended conjugation, shifting absorption into the accessible region of the spectrum. Direct photolysis of 3,3-dimethyl-1,1,5,5-tetraphenylpenta-1,4-diene has been found to give the vinylcyclopropane (1) as the sole primary photoproduct.



The reaction involves a rearrangement of the pentadiene skeleton with no alkyl or aryl group migration. Further electronic and stereochemical details of the reaction have been found from the related system shown in **schemes 3** and **3**. With different substituents at C_1 and C_5, two reaction routes are possible (path a and path b).



Scheme 3

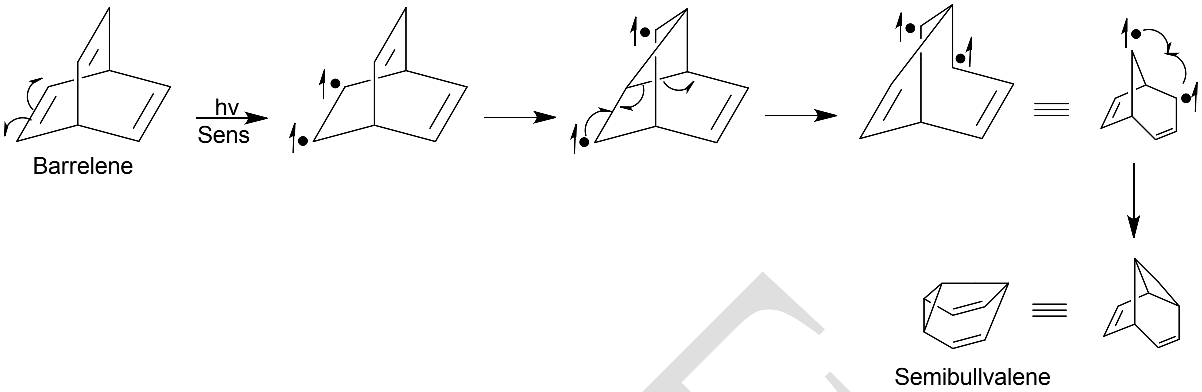


Scheme 4

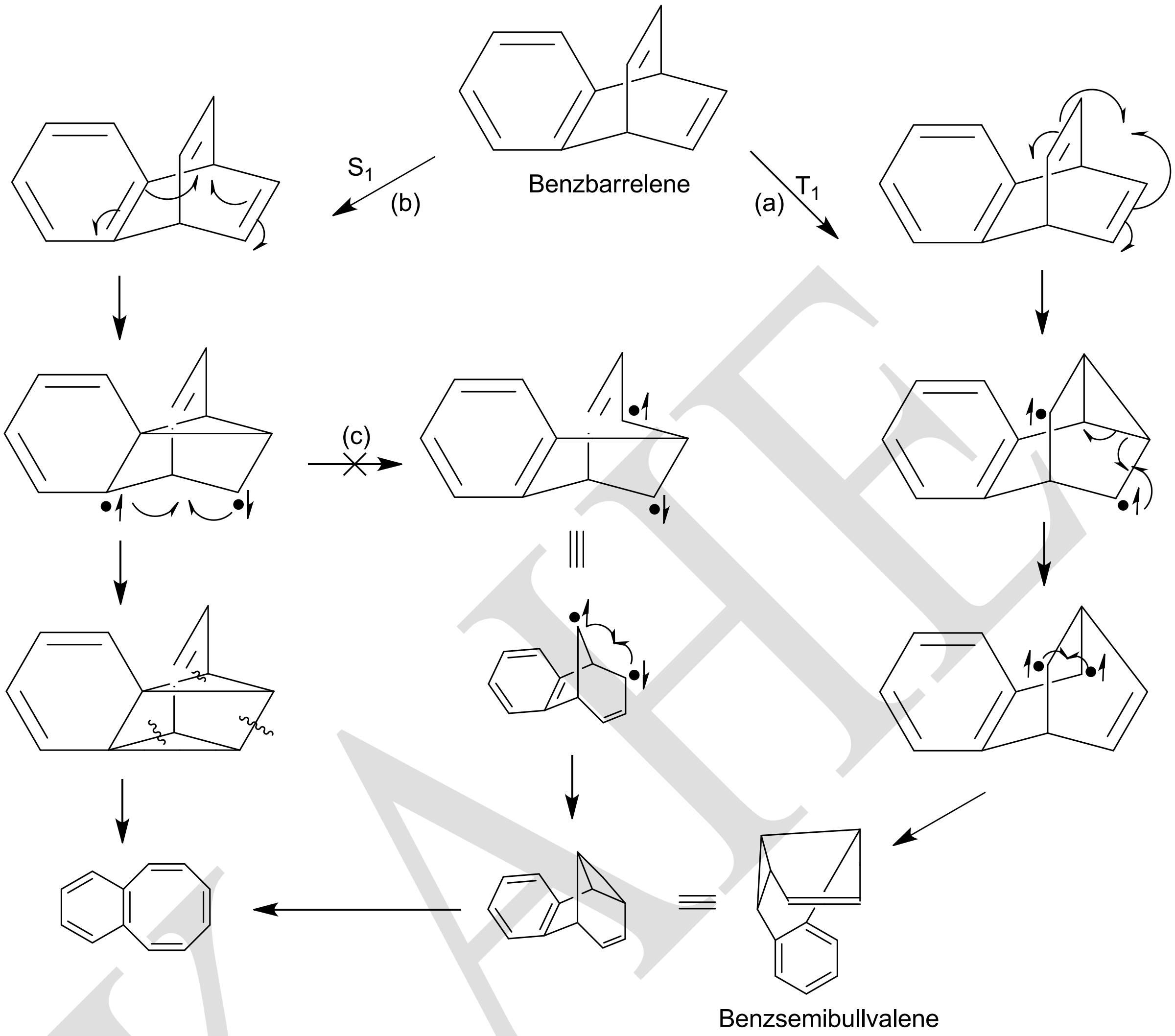
It is found that only route a **(Scheme 3)** to give 1,1-dimethyl-2,2-diphenyl-3-(2,2-dimethyl)vinylcyclopropane (A), occurs. Similar selection of reactions path is shown for reactions in **Scheme 3**. The direction of rearrangement is apparently controlled by the facility for electron delocalization during the reaction. The benzylic radical of (C), in **Scheme 3**, can be stabilized by delocalization into the aromatic ring and is not readily available for π-bond formation as required by route b; route a is therefore followed. Each rearrangement shown in involves retention of configuration at C_1 and thus cis-trans isomerisation of the C_1 and C_2 bond must be slow by comparison with formation of the cyclopropane derivative.

The extensive work of Zimmerman and his collaborators has shown that the di-π-methane rearrangement proceeds by a singlet mechanism for acyclic and monocyclic systems. The reaction is believed to be concerted and to involve inversion of configuration at C_3. The triplet-sensitised reactions of the dienes shown in **Scheme 4** do not lead to rearrangement, but rather to cis-trans isomerisation.

The di-π-methane rearrangement is not confined to acyclic and monocyclic systems. Bicyclic 1,4-dienes also rearrange but by way of a triplet mechanism ; in all probability, the in-built geometric constraint of a bicyclic molecule does not allow distortion of the triplet excited state. For example barrelene (bicycle[2,2,2]octatriene) rearranges to semibullvalene, a molecule which undergoes rapid valence bond tautomerism.



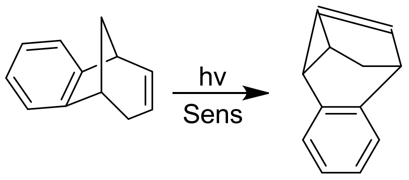
The sensitized reaction is thought by Zimmerman to proceed in a stepwise fashion unlike the acyclic singlet case. It should be noted, however, that a concentrated mechanism would be a symmetry allowed process. Differences between the singlet and triplet excited state reactions of bicyclic-1,4-dienes are known. Benzbarrelene undergoes the di-π-methane rearrangement on sensitized photolysis but gives benzcyclo-octatetraene on direct irradiation **(Scheme 5).** Deuteriation studies have shown that the benzcyclo-octatetraene is formed to an extent of 94 per cent by route b and the benzsemibullvalene entirely by route a. The reminder of the benzcyclo-octatetraene (6 per cent) comes via the benzsemibullvalene. Direct irradiation of benzbarrelene therefore proceeds almost entirely by benzo-vinyl overlap (route b).

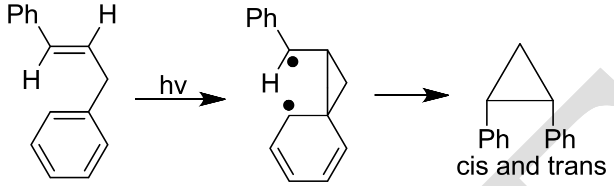


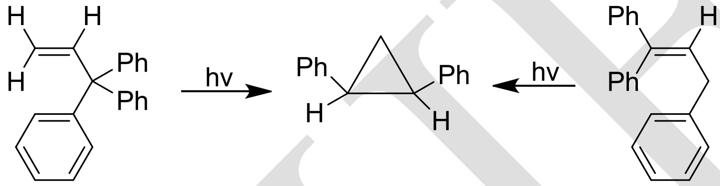
Scheme 5

The cyclo-addition of the benzo and vinyl double bonds is probably a concentrated process. The sensitized irradiation proceed by route a, which involves vinyl-vinyl overlap, with no benzsemibullvalene being formed via route c involving benzo-vinyl overlap. Where there is a choice, vinyl-vinyl bonding is preferred to benzo-vinyl bonding.

A large number of rearrangement can be classified as of di-π-methane type even through the molecules do not formally contain a 1,4-dienes unit. For example, an aryl ring may replace one of the olefinic bonds with subsequent benzo-vinyl bonding. Similarly arylcyclopropanes are formed from arylpropenes

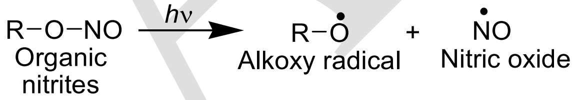




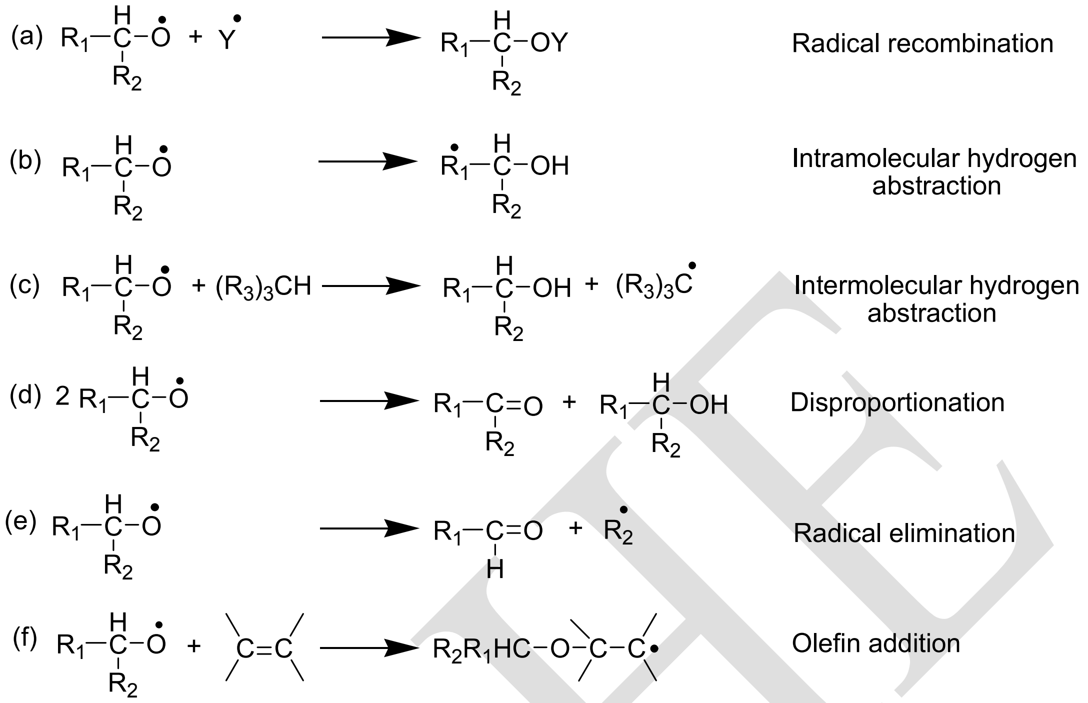


Barton reaction

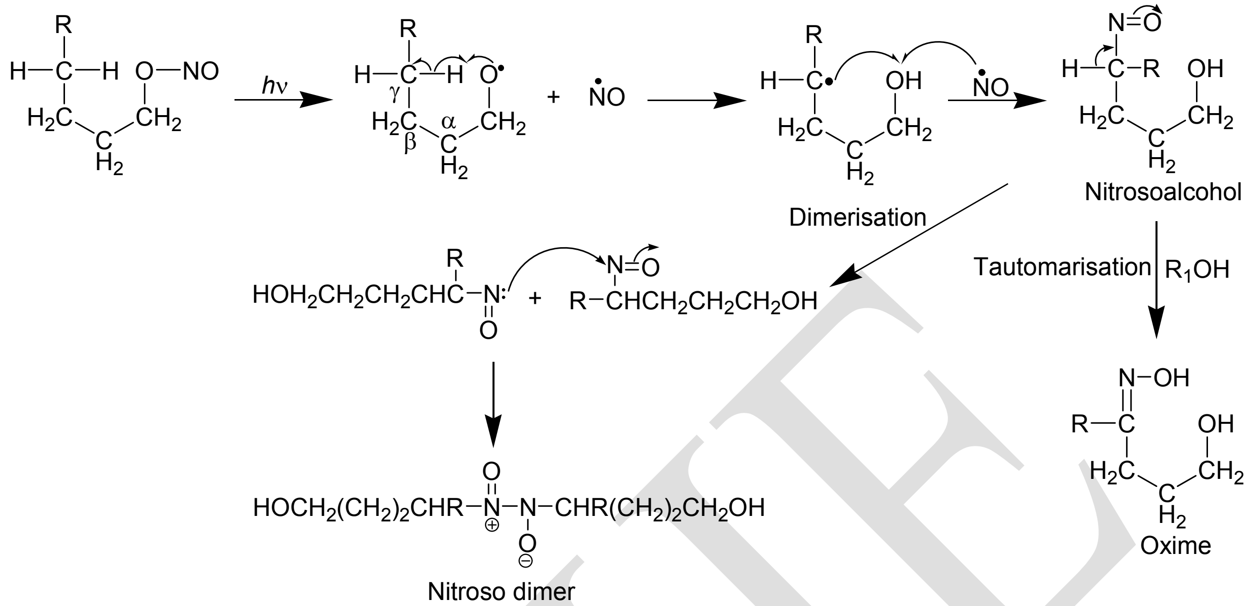
On photolysis, organic nitrites can undergo rearrangement to oximes or nitroso dimers.The reaction has received considerable attention and is of practical importance in steroid synthesis.



The O-NO bond of the nitrite is homolytically cleaved to nitric oxide and an alkoxy radical, the latter stabilising itself by one of the six routes (a-f) available to it. In the presence of a γ-hydrogen atom, intramolecular hydrogen abstraction (route b) predominates.

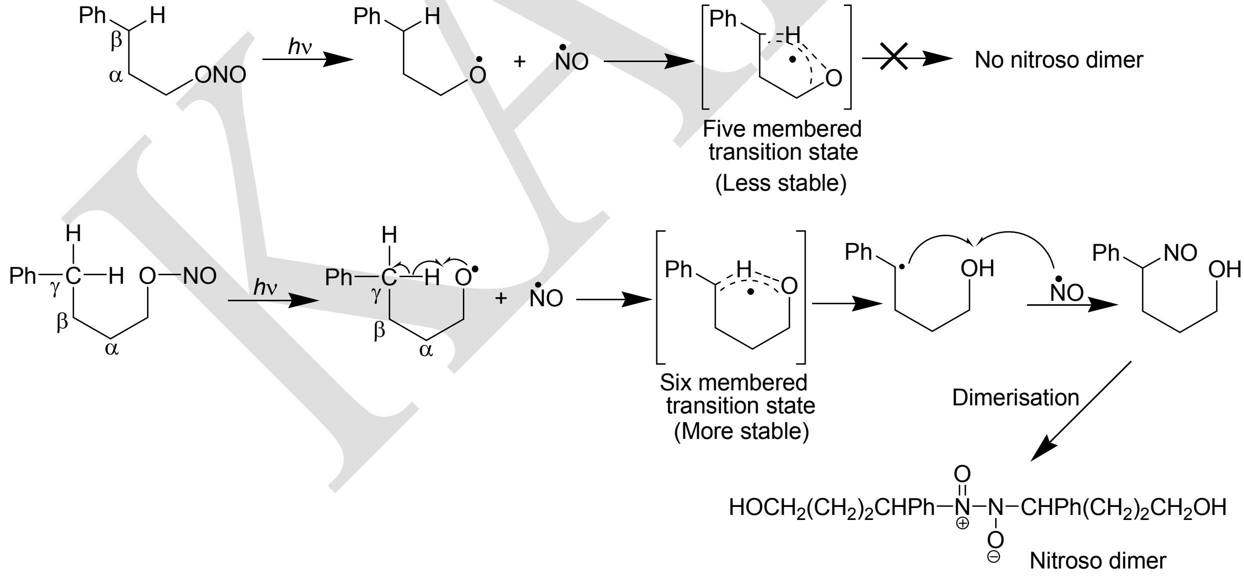


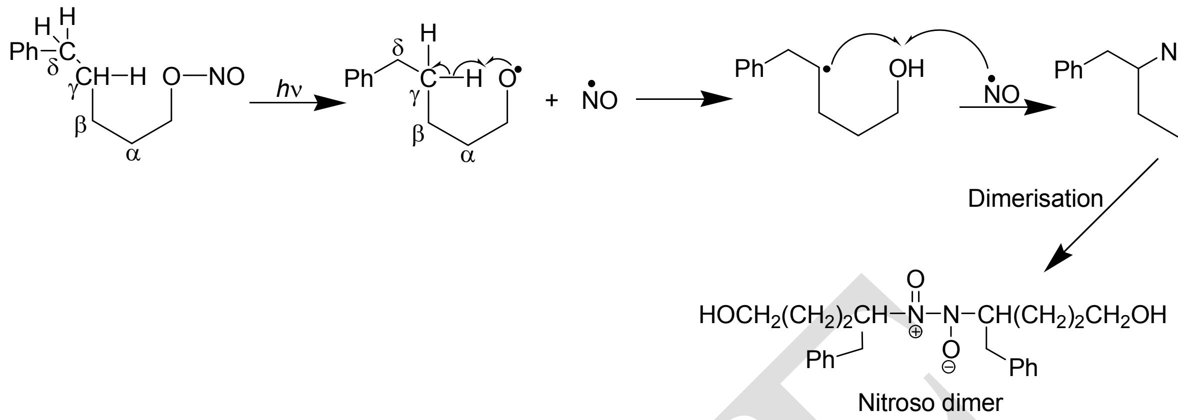
The nitric oxide generated in the photolysis step can recombine with the new alkyl readical to produce a nitroso compound which can dimerise or, in the presence of protic solvents, form an oxime (**Scheme 6**). The reaction involving nitric oxide migration is known as the **Barton reaction** and provides a useful procedure for effecting substitution γ to an oxygen function. The reaction is quite general for primary and secondary aliphatic nitrites, providing there is a γ-hydrogen atom available. Thermally generated alkoxy radicals do not possess sufficient energy to abstract such a hydrogen and therefore do not undergo this reaction.



Scheme 6

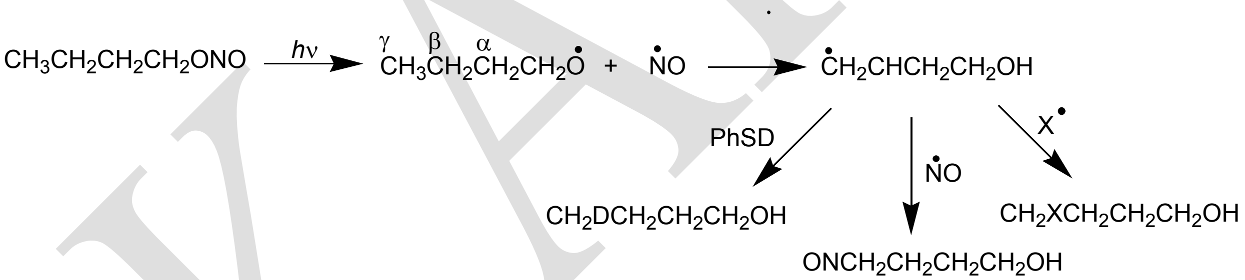
The intramolecular hydrogen transfer to the alkoxy radical involves a six-membered cyclic transition state, as demonstrated by the photolysis of a series of ω-phenylalkyl nitrites (**Scheme 7**).



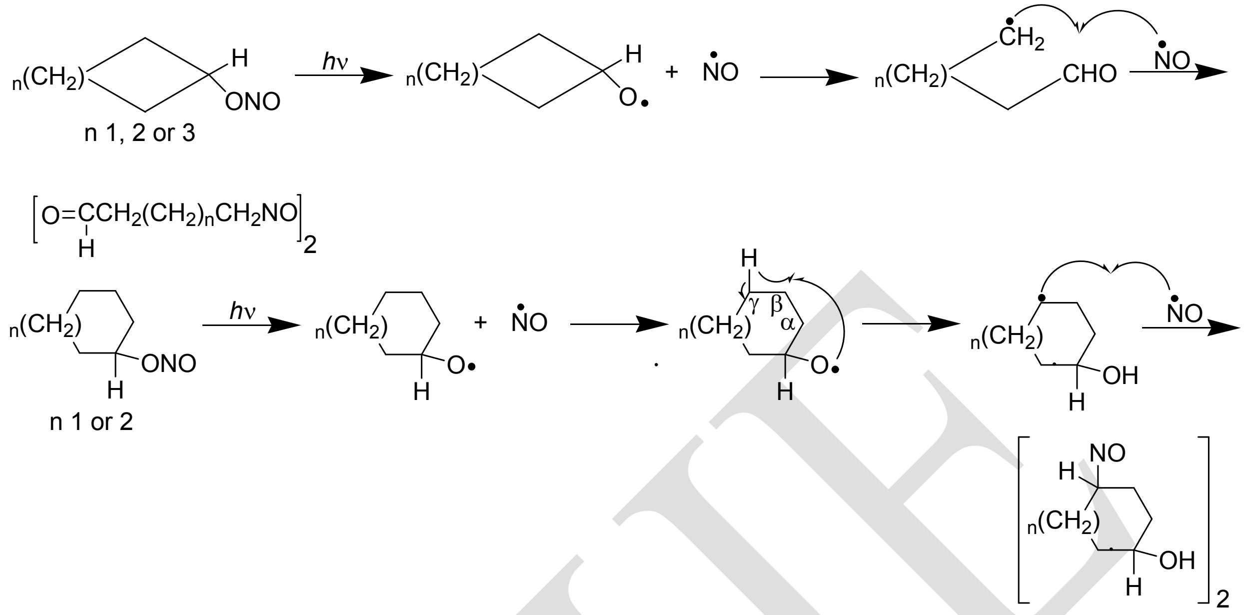


Scheme 7

The propyl and pentyl nitrites might be expected to transfer a benzylic hydrogen to the alkoxy radical through a five- and a seven-membered cyclic transition state respectively, but this is apparently not so. For the pentyl and butyl nitrites γ-hydrogen transfer occurs through a six-membered transition state. The nitric oxide produced in the homolysis is presumably not held in a solvent cage with the alkoxy radical since other free radicals can compete with nitric oxide in the final step.

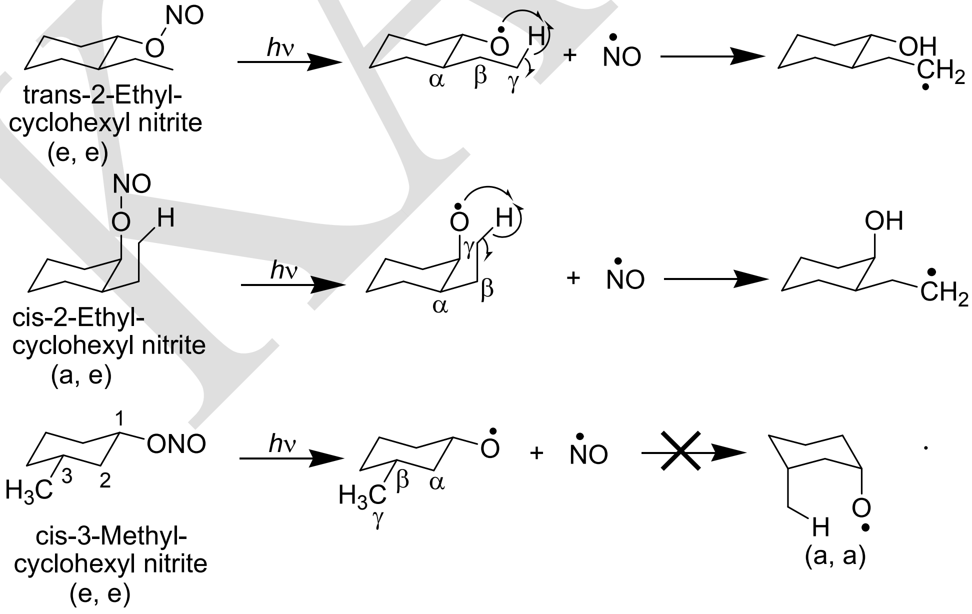


For tertiary nitrites, and primary and secondary nitrites with no γ-hydrogen, the alkoxy radical is generally stabilised by disproportionation (path d), radical elimination (path e), or intermolecular hydrogen abstration (path c). Alicyclic nitrites undergo ring cleavage with carbonyl formation on photolysis, unless the ring is large enough to accommodate the six-membered transition state for γ-hydrogen transfer (**Scheme 8**).



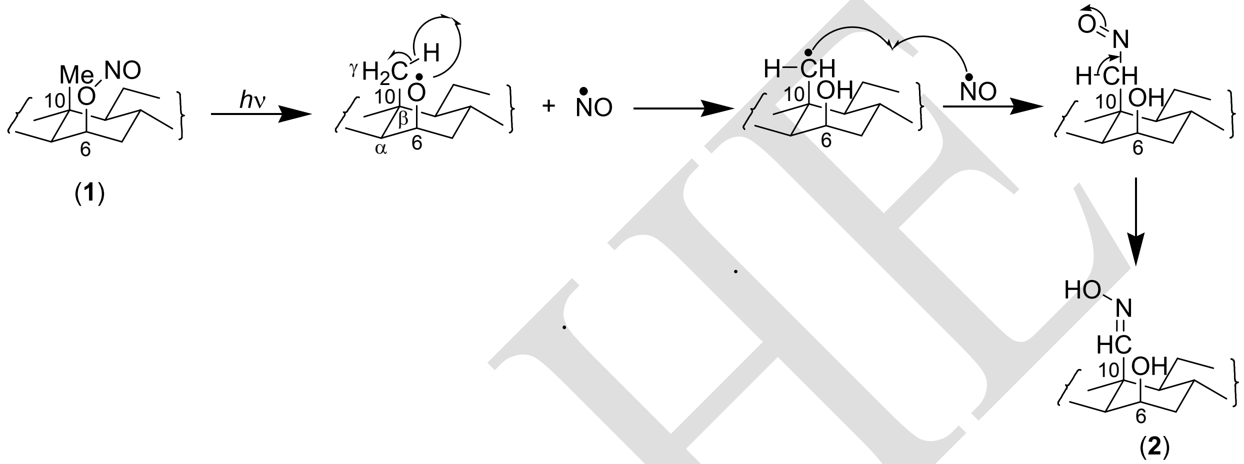
Scheme 8

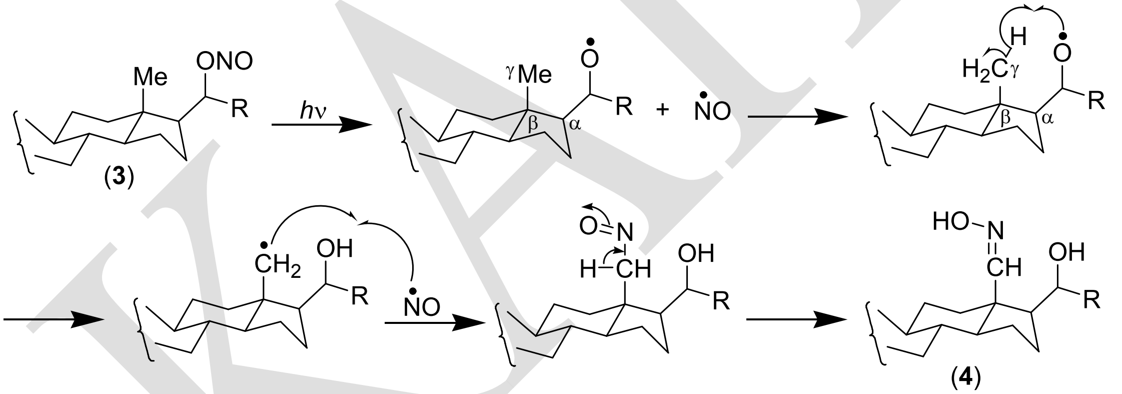
For this latter reaction to occur, the substituents must be suitably oriented. While *cis*- and *trans*-2-ethylcyclohexyl nitrite undergo γ-hydrogen transfer reactions, *cis*-3-methylcyclohexyl nitrite does not. The alkoxy radical, for this latter compound is too far removed from the γ-hydrogen, and ring inversion to the di-axial conformer is unfavourable (**Scheme 9**).



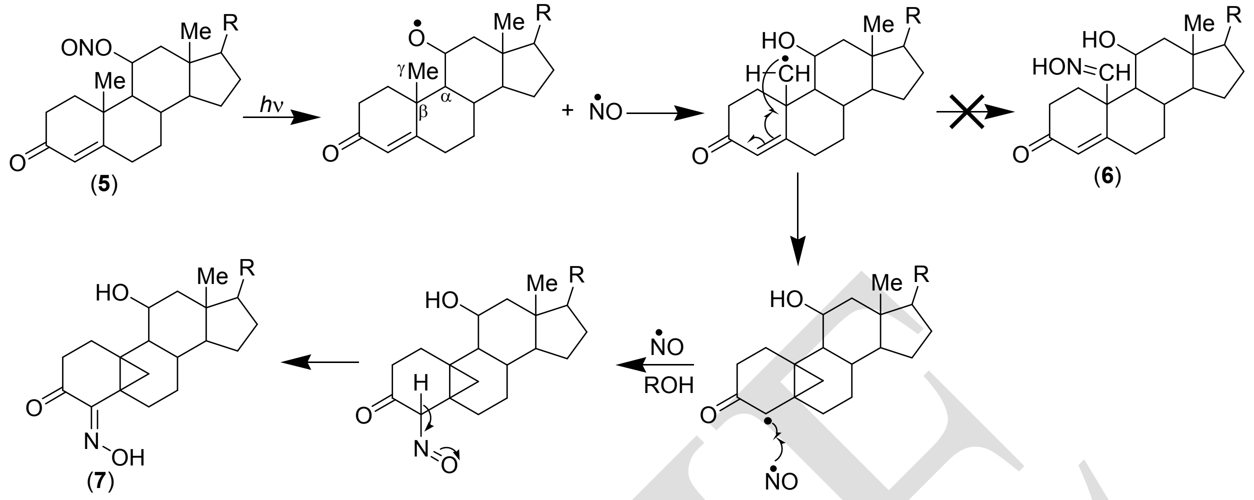
Scheme 9

The reaction finds use in functionalising the C_{13} and C_{10} steroid methyl groups. The angular methyl at C_{13} can be attacked by axial alkoxy radicals at C_{20}, C_{15}, C_{11} and C_8; that at C_{10} may react with axial alkoxy radicals at C_{11}, C_8, C_6, C_4 and C_2. For example, 3β-acetoxy-cholestan-6β-ol nitrite (**1**) and 3β-acetoxy-5α-pregnan-20β-ol nitrite (**2**) in protic solvents give the C_{19} and C_{18} aldoximes (**3**) and (**4**) respectively.





The combination of the intermediate alkyl radical with nitric oxide can be regarded as an intermolecular process (a solvent cage is not involved) and alternative lower energy stabilisation paths may result. Thus photolysis of the corticosterone derivative (**5**) does not give the 19-aldoxime (**6**) but rather the 4-ketoxime (**7**).



The photochemistry of hypochlorites parallels that of the nitrites. Intramolecular γ-hydrogen transfer, involving a six-membered transition state, is again the preferred reaction course. The alkyl radical so formed can undergo radical recombination to give the γ-chlorohydrin.

$$RCH_2(CH_2)_2CH_2OCl \xrightarrow{h\nu} RCH_2(CH_2)_2CH_2O^{\bullet} + Cl^{\bullet} \longrightarrow R\overset{\bullet}{C}H(CH_2)_2CH_2OH \xrightarrow{Cl^{\bullet}} RCHCl(CH_2)_2CH_2OH$$

Reference Books:

1. Tewari, N. (2011). *Advanced Organic Reaction Mechanism* (III Edition). Kolkata: Books and Allied (P) Ltd.

2. Depuy, C. H., & Chapman, O. L. (1975). *Molecular Reactions and Photochemistry* (II Edition). New Delhi: Prentice-Hall of India Private Limited.

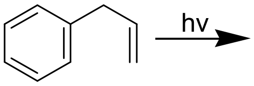
3. Coxon, J. M., & Halton, B. (2011). Organic Photochemistry (II Edition). New Delhi: Cambridge University Press.

POSSIBLE QUESTIONS

PART-B (Each Question Carry Two Marks)

1. Define fluorescence and mention its lifetime.
2. Define excimer.

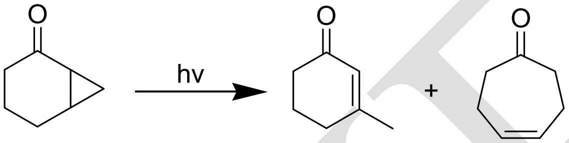
3. Predict the product in the below reaction.



4. Define phosphorescence.

5. Write the names of the two non-radiative processes in organic photochemistry.

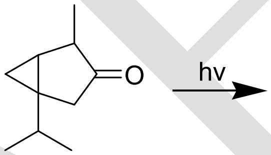
6. Suggest reasonable mechanism for the following reaction.



7. Define the following terms (a) singlet states and (b) triplet states.

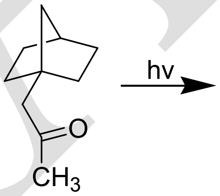
8. What is oxa-di-π-methane rearrangement?

9. Predict the product in the following reaction.

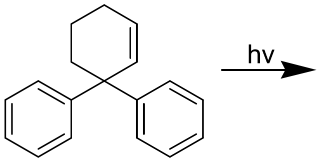


10. Define exciplex.

11. Predict the product in the following reaction.

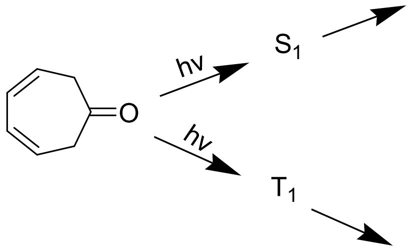


12. Write the product formed in the following photochemical transformation.

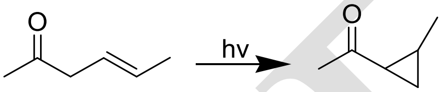


13. Define quantum efficiency.

14. Predict the product in the following reaction.



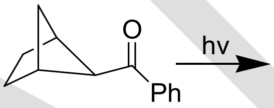
15. Suggest a reasonable mechanism for the below reaction?



PART-C (Each Question Carry Six Marks)

1. (i) Explain the various photochemical processes in electronically excited molecules with a diagram.

(ii) The major product formed in the following photochemical reaction is



2. Explain the following photochemical reactions.

(i) Norrish Type I

(ii) Norrish Type II

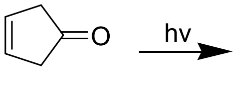
3. Draw Jablonski diagram and explain the various energy transition process.

4. Explain the Paterno Buchi reaction.

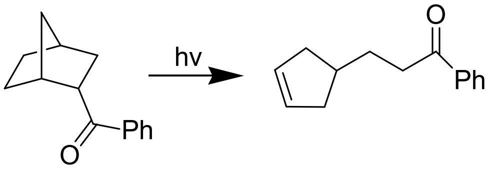
5. Discuss the mechanism of ene reaction with suitable examples.

6. Explain the di-π-methane rearrangement with an example.

7. (i) Predict the product in the below reaction.

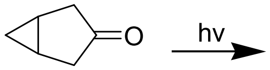


(ii) Suggest reasonable mechanism for the following reaction.

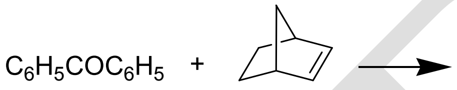


(iii) Why acetone reacts with norbornene give dimers whereas benzophenone adds to norbornene give oxetane?

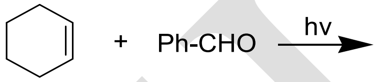
8. (i) Predict the product in the following reaction.



(ii) Predict the product in the following reaction.



(iii) Write the product formed in the following photochemical transformation.



9. Explain the mechanism of Photo Fries rearrangement

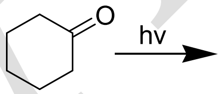
10. Discuss the mechanism of cis and trans isomerisation and quantum efficiency.

11. Write notes on Barton reaction?

PART-D (Each Question Carry Ten Marks)

1. i) Predict the products in the following reactions.

(a)



(b)

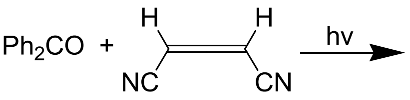
$$\text{Benzaldehyde} + \text{2-methyl but-2-ene} \xrightarrow{hv}$$

ii) Complete the following equation.

(a)

$$PhC\equiv CPh + PhCHO \xrightarrow{hv}$$

(b)



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DEPARTMENT OF CHEMISTRY

UNIT-IV

ORGANIC PHOTOCHEMISTRY

PART-A–Multiple Choice Questions
(Each Question Carry One Mark) (Online Examinations)

1. Which type of electronic transition can be seen in saturated aldehydes and ketones?

a) $\sigma \rightarrow \sigma^*$ b) $n \rightarrow \sigma^*$ **c) $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$** d) only $\pi \rightarrow \pi^*$

2. Which of the following decay with change in multiplicity is known as ISC?

a) $S_1 \rightarrow S_0$ b) $S_2 \rightarrow S_1$ c) $T_2 \rightarrow T_1$ **d) $S_1 \rightarrow T_1$**

3. In fluorescene which one of the following decay of excited state takes place?

a) $S_1 \rightarrow S_0$ b) $T_1 \rightarrow S_0$ c) $T_2 \rightarrow T_1$ d) $T_1 \rightarrow S_0$

4. Which one of the following excited state has a long life?

a) S_1 b) S_2 **c) T_1** d) T_2

5. Which one of the following electronic titrations is not allowed?

a) $\pi \rightarrow \pi^*$ b) $\sigma \rightarrow \sigma^*$ c) $n \rightarrow \pi^*$ **d) $\delta \rightarrow \delta^*$**

6. Photochemical Paterno-Buchi reaction is a cyclo-addition between

a) two >C=C< groups **b) a >C=O and >C=C< groups**

c) a >C=N–R and >C=C< groups d) a >C=S and >C=C< groups

7. Which one of the following decay takes place in phosphorescence?

a) $S_1 \rightarrow S_0$ **b) $T_1 \rightarrow S_0$** c) $T_2 \rightarrow T_1$ d) $T_1 \rightarrow S_1$

8. If a photochemical reaction has higher quantum yield than unity, it indicates

a) reversible reaction b) elementary reaction **c) chain reaction** d) radical reaction

9. Oxetanes can be prepared by photochemical reaction between

a) carbonyl compounds and olefins b) carbonyl compounds and alkanes

c) alcohols and olefins d) alcohols and alkanes

10. During the photolysis of ketones in Norrish type II cleavage

a) a homolytic scission leads to the formation of a radical intermediate

b) CO is produced

c) photoexcited carbonyl group abstracts a gamma hydrogen in the primary step

d) radicals formed dimerize

11. When toluene is refluxed with Br_2 in the presence of light it mainly gives

a) o-bromotoluene b) p–bromotoluene

c) mixture of o- and p-bromotoluene **d) benzyl bromide**

12. Which one of the following molecules will have n → π* transition at the longest wavelength?

a) HCHO b) $CH_3COC_2H_5$ **c) $C_6H_5COC_6H_5$** d) $CH_3COC_6H_5$

13. Photolytic conversion of organic nitrites into nitroso alcohols is known as

a) Ritter reaction b) Birch reduction

c) Barton reaction d) Paterno–Buchi reaction

14. Photolysis of carbonyl compound in which intramolecular abstraction of γ–H–atom followed by cleavage takes place, is known as

a) Norrish type III process b) Norrish type I process

c) Norrish type II process d) Norrish type IV process

15. How many types of electronic transitions are taking place in visible and UV regions?

a) two types b) three types c) five types **d) four types**

16. Norrish type I cleavage is also called as

a) α-cleavage b) β-cleavage c) γ-cleavage d) δ-cleavage

17. In the Paterno–Buchi reaction the addition of an excited ketone to an olefin forms an

a) oxetane b) azirine c) biradical d) oxetene

18. In the Paterno–Buchi reaction the acetylenes can replace olefins to produce an

a) ketones b) oxetanes **c) α, β–unsaturated ketone** d) β,γ –unsaturated ketones

19. The conversion of acetic acid phenyl ester into *o*-hydroxyacetophenone and *p*-hydroxyacetophenone is effected by

a) Sandmeyer reaction b) Ullmann reaction

c) Pechmann reaction **d) Photo–Fries rearrangement**

20. The allylic oxidation of alkenes with selenium dioxide is an example for

a) Photo-Fries reaction **b) ene reaction**

c) electrocyclic reaction d) cycloaddition reaction

21. A common example for photochemical reaction

a) ferrodxidin **b) photo synthesis**

c) hemoglobin d) hemocyanin

22. The relationship of energy of radiation to frequency and wavelength is

a) E = h/v b) E = v/h **c) E = hv** d) E = h

23. The efficiency of photochemical reaction is usually expressed as

a) percentage b) photochemical yield

c) quantum yield d) point scale

24. Life time of phosphorescence is

a) 10^{-5} to 10^{-2} s **b) 10^{-3} to 10 s** c)10^{3} to 10 s d) 10^{-5} to 10^{-3} s

25. Conversion of carbonyl compounds to oxetanes by irradiation in the presence of olefin is

a) Mannich reaction **b) Paterno – Buchi reaction**

c) Norrish type I reaction d) Norrish type II reaction

26. Conversion of carbonyl compounds into oxetanes is effected by

a) Paterno–Buchi reaction b) di – π – methane rearrangement

c) Norrish type I reaction d) photo reduction

27. Phosphorescence is due

a) internal conversion b) inter system crossing

c) $T_1 \rightarrow S_0$ d) inter system conversion

28. Which one of the following occurs during Norrish type II reaction?

a) intramolecular hydrogen abstraction

b) α – cleavage intermolecular hydrogen abstraction

c) α – cleavage

d) photo dimarization

29. Life time of upper excited state is

a) 10^{-10} s b)10^{-9} s **c)10^{-11} s** d)10^{-12} s

30. The α, β-unsaturated ketone prepared by

a) di – π – methane rearrangement b) photo reduction

c) Paterno – Buchi reaction d) Norrish type I reaction

31. The Paterno – Buchi reaction is used for preparation of

a) ketone b) acid c) alcohols **d) α, β – unsaturated ketones**

32. Which one of the transition refers to internal clear conversion?

a) S_1 to T_1 **b) S_2 to S_1** c) S_1 to S_0 d) T_1 to S_0

33. Which refers to phosphorescence?

a) S_1 to S_0 b) T_2 to S_0 c) S_0 to S_1 **d) T_1 to S_0**

34. Which is correct regarding fluorescences?

a) spin allowed transition b) spin – forbidden

c) due to intersystem crossing d) internal conversion

35. Which is true regarding phosphorescence?

a) spin allowed transition **b) spin–forbidden**

c) due to ISC d) IC

36. The commonest photochemical reaction of 1,4-dienes is the

a) di – π – methane rearrangement b) Barton reaction

c) Paterno – Buchi reaction d) Photo-Fries rearrangement

37. Paterno – Buchi reaction is an example for

a) electrophilic addition **b) photo cycloaddition**

c) electrophilic substitution d) nucleophilic substitution

38. An example for photosensitizer is

a) butadiene b) butane **c) benzophenone** d) acetophenone

39. The cleavage of acetone with light to give acetyl radical and methyl radical is called

a) Norrish type I reaction b) Norrish type II reaction

c) Beta – cleavage d) Grob fragmentation

40. Molecular states with all electrons paired are called

a) triplet states **b) singlet states** c) doublet states d) quartet states

41. Molecular states with two unpaired electrons are called

a) triplet states b) singlet states c) doublet states d) quartet states

42. Which states do not spilt in a magnetic field?

a) doublet states **b) singlet states** c) triplet states d) quartet states

43. In the presence of magnetic field, triplet states spilt into

a) two different energy levels b) one energy levels

c) two same energy levels **d) three different energy levels**

44. Free radicals with one unpaired electron give rise to two energy levels in a magnetic field and this known as

a) singlet states **b) doublet states** c) triplet states d) quartet states

45. Electronic transitions between states of the same multiplicities are

a) spin allowed b) spin – forbidden

c) geometrical allowed d) geometrical forbidden

46. Which one of the following electronic states are spin allowed?

a) singlet - triplet b) singlet - doublet

c) doublet - triplet **d) triplet – triplet**

47. Which one of the following electronic states are spin forbidden?

a) singlet - triplet b) singlet - singlet

c) doublet - doublet d) triplet – triplet

48. The singlet states are represented as

a) T_n b) D_n **c) S_n** d) Q_n

49. The triplet states are represented as

a) T_n b) D_n c) S_n d) Q_n

50. Non – dissociative chemical reactions are most probable in

a) long – lived ground states b) short – lived ground states

c) long – lived excited states d) short – lived excited states

51. Low –lying triplet states life times is

a) $<10^{-6}$ s **b) $>10^{-6}$** c) 1 d) 0

52.The example for excimers is

a) benzene b) acetophenone c) benzophenone **d) rare gases**

53. Which one is an example for excimers?

a) alcohol b) acid **c) pyrene** d) ketone

54. An example for exciplex is

a) benzene with alkenes b) benzene with ketones

c) benzene with α, β – unsaturated ketone d) ketones

55. The life time for excited singlet states is

a) 10^{-6} s b) 10^{-2} s c)10^{-10} s **d)10^{-8} s**

56. Intersystem crossing efficiency in 1,3- butadiene is

a) 1 **b) 0** c) 3 d) 2

57. Quantum efficiency are also called as

a) quantum yield b) percentage yield

c) reaction yield d) product yield

58. Quantum efficiency is generally used for

a) thermal reaction **b) photochemical reaction**

c) ionic reaction d) free radical reaction

59. The free radical chlorination of methane has a

a) low quantum efficiency b) no quantum efficiency

c) high quantum efficiency d) medium quantum efficiency

60. Decarbonylation of the acyl radical gives

a) CO and alkyl radical b) CO_2 and alkyl radical c) CO d) CO_2

UNIT-V

SYLLABUS

Pericyclic reactions: Definition-classification-characteristic features- the electrocyclic reaction- Woodward–Hofmann rules- orbital correlation diagram- the Frontier molecular orbital theory- electrocyclic conversion of 1,3-dienes and 1,3,5-trienes. Cycloaddition– [2+2] addition-Diel's Alder reaction- stereochemistry of Diel's Alder reaction. Sigmatropic reactions – [1,3], [1,5] and [3,3] sigmatropic shifts - Cope and Claisen rearrangements.

Pericyclic reactions

1) What are pericyclic reactions? Why are they so called?

Solution:

There is an important class of chemical reactions which are insensitive to the presence of polar solvents and catalysts and do not involve ionic or free radical intermediates. Such reactions following a concerted mechanism involving simultaneous bond breaking and bond making and proceeding via a cyclic transition state are called pericyclic reactions.

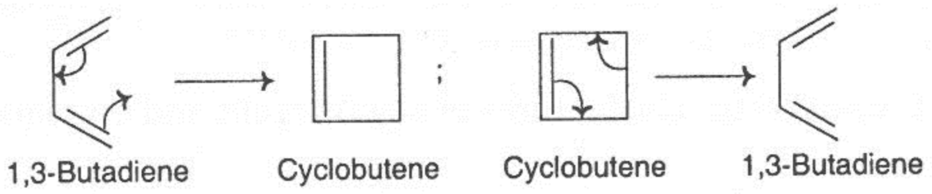
These reactions are so called because they take place through cyclic transition states.

2) What are the principal classes of pericyclic reactions? Define and explain them with examples.

Solution:

These are three principal classes of pericyclic reactions. They are (i) electrocyclic reactions, (ii) cycloaddition reactions and (iii) sigmatropic reactions (rearrangements).

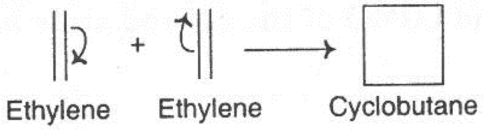
(i) Electrocyclic reactions: In a number of reactions concerted ring closing of conjugated polyenes takes place to form cycloalkenes and in many other reactions the ring of a cycloalkene opens to form a conjugated polyene. For example:



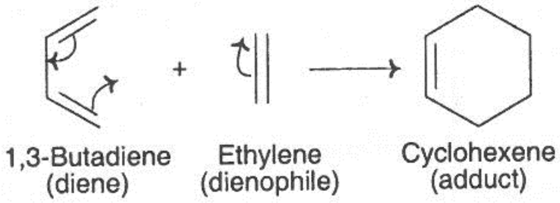
Such interconversions between a conjugated polyene and a cycloalkene are called electrocyclic reactions.

In electrocyclic reactions σ and π bonds are interconverted. In the first example, one π bond of 1,3-butadiene becomes a σ bond in cyclobutene and in the second example, a σ bond of cyclobutene becomes a π bond in 1,3-butadiene. In both the cases the remaining π bond shifts its position.

ii) Cycloaddition reactions: There are a number of reactions of alkenes and polyenes in which two molecules (same or different) combine concertedly to form a cyclic product having two new σ bonds and two fewer π bonds. These reactions are called cycloaddition reactions. For example:



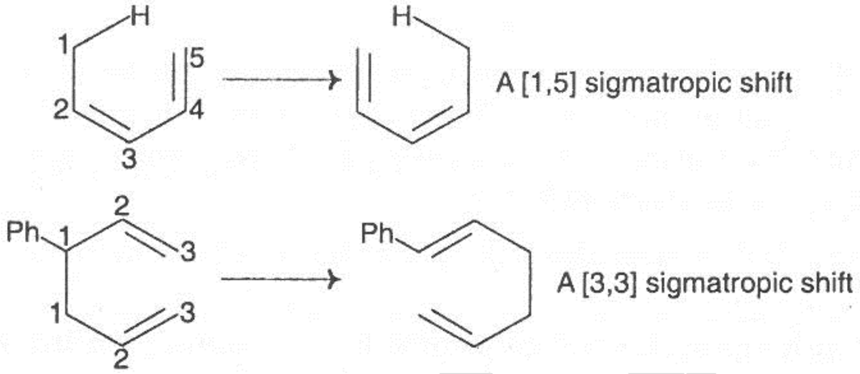
A [2 + 2] cycloaddition



A [4 + 2] cycloaddition
(familarly known as Diels-Alder reaction)

On the basis of the number of π electrons involved in each component, the first example is classified as a [2+2] cycloaddition and the second example is classified as a [4+2] cycloaddition.

(iii) Sigmatropic reactions (rearrangements): In some concerted uncatalyzed reactions a σ bond migrates along with the atom or group attached to it to a new position within a π framework (an ene or a polyene) i.e., one end of a σ bond migrates. In some other reactions both ends of a σ bond migrates. Reactions of either type are called sigmatropic reactions (rearrangements). For example:



In the first example one end of the σ bond moves over five atoms and in the second example both ends of a σ bond migrate over three atoms.

3) How many approaches have been made to explain the stereochemical results of pericyclic reactions?

Solution:

There are three approaches by which the stereochemical aspects of pericyclic reactions can be explained. They are (i) conservation of orbital symmetry (correlation diagram), (ii) Frontier molecular orbital approach (FMO) and (iii) the aromatic transition state concept (HMO).

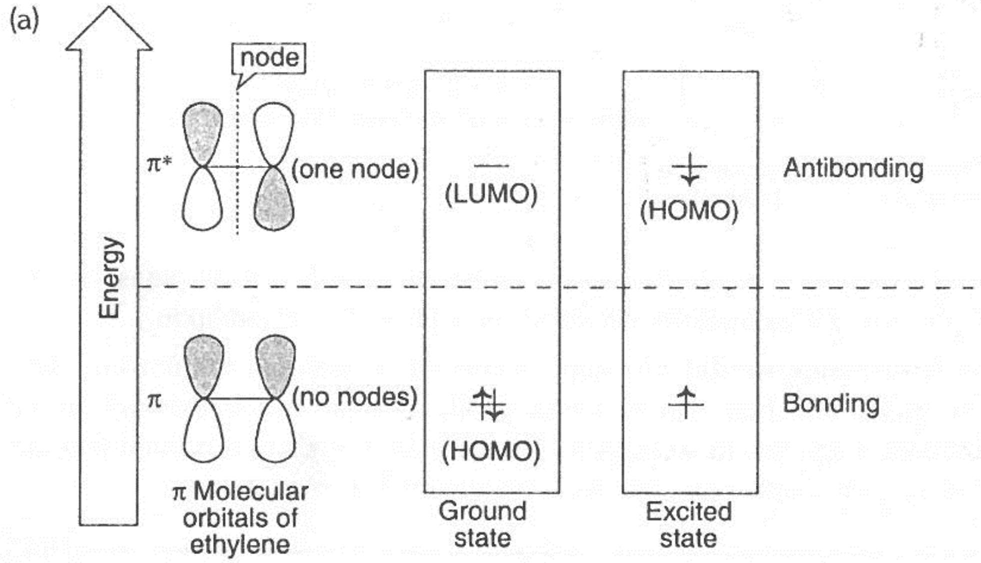
4) Write down the characteristic features of electrocyclic and cycloaddition reactions?

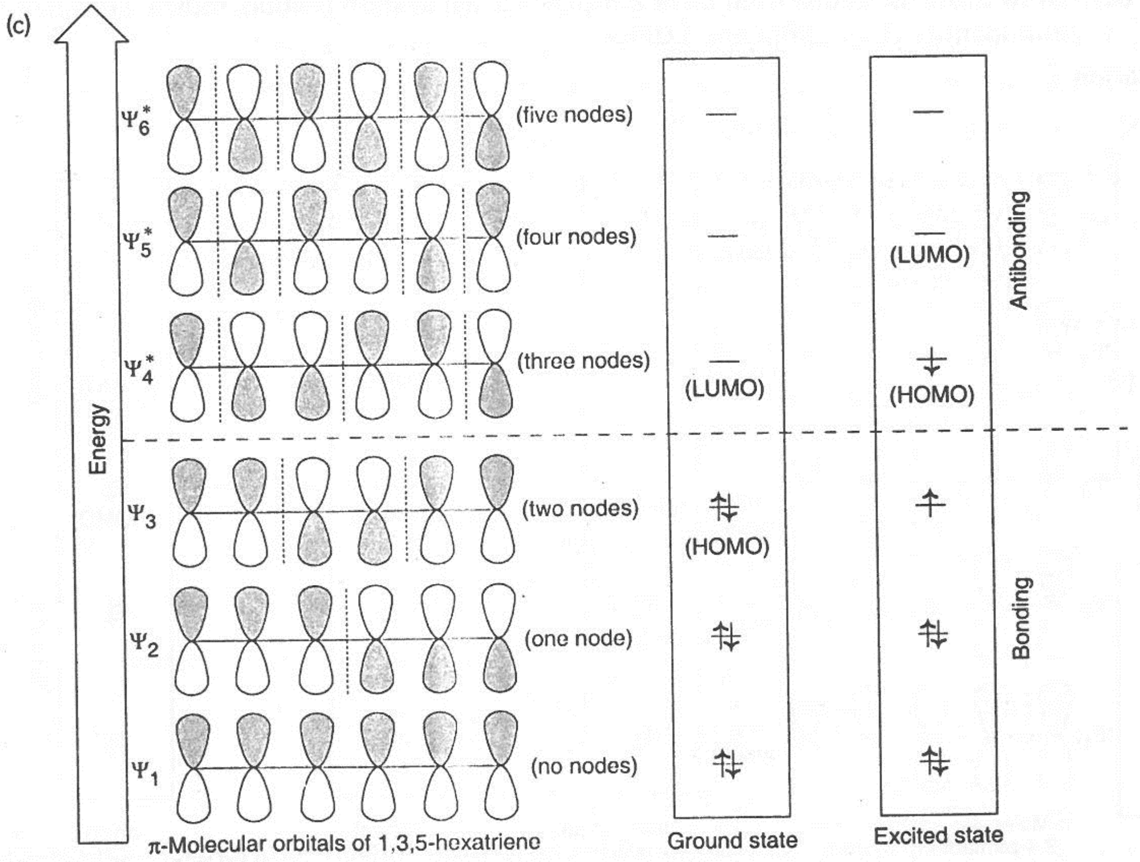
Solution:

i) They involve interconversion of π and σ bonds.
ii) They require only heat or light for initiation.
iii) Their mechanisms do not involve free radical or ionic intermediates.
iv) Bonds are made or broken in a single concerted step involving a cyclic transition state.
v) The reactions are highly stereospecific.

5) Draw the π-molecular orbital of (a) ethylene (b) 1,3-butadiene and (c) 1,3,5-hexatriene show the configuration of π electrons in the ground state and the first excited state and identify the HOMO and LUMO of the ground state and the first excited state.

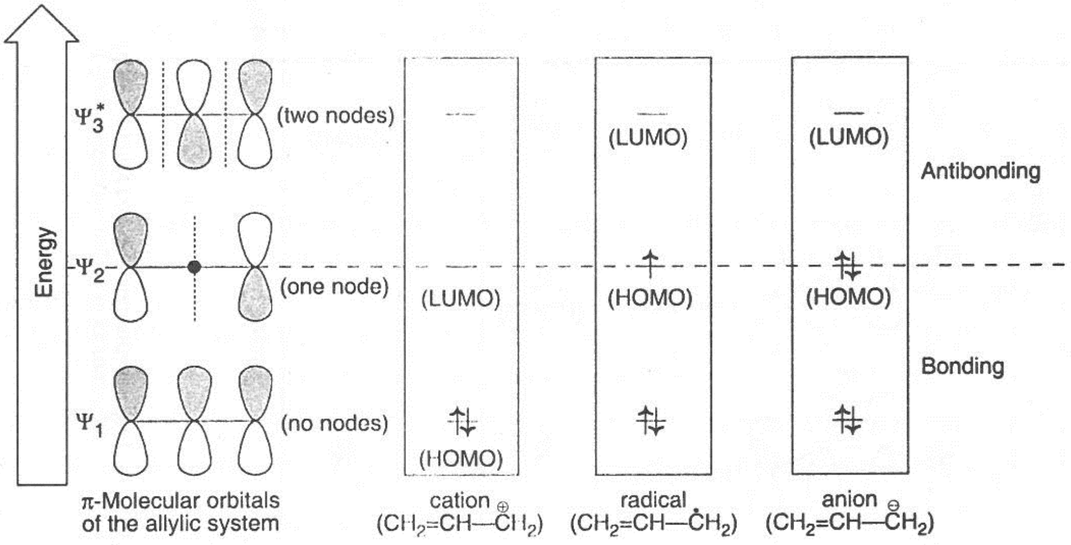
Solution:





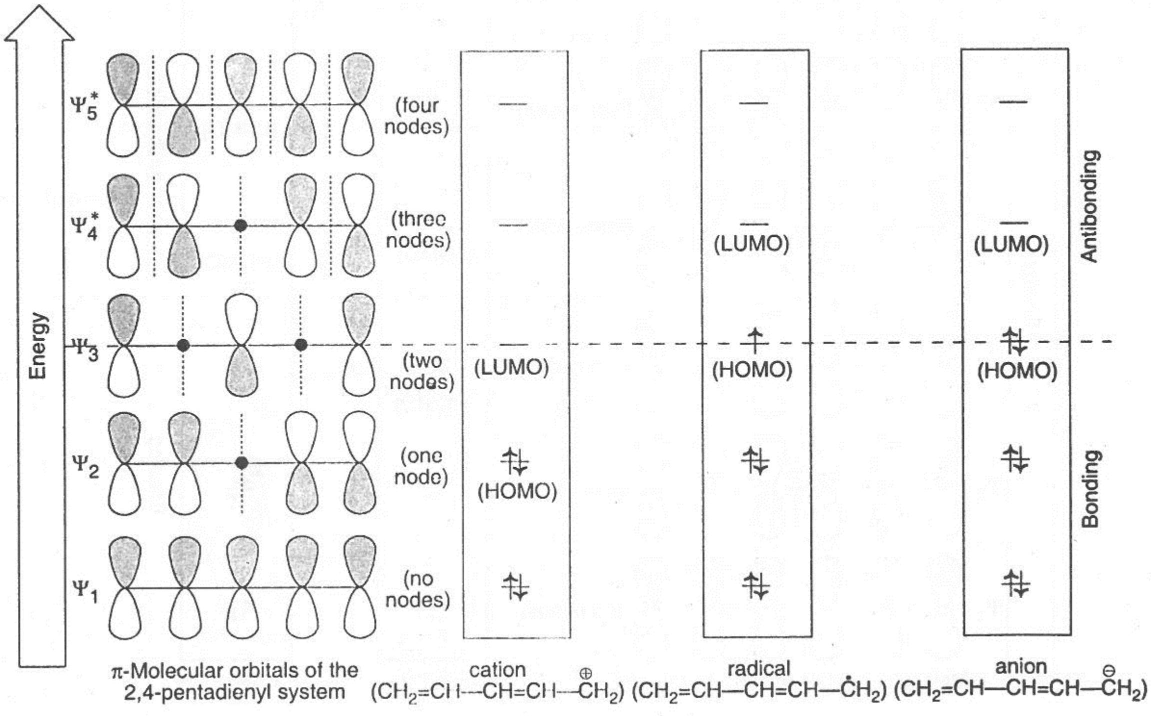
6) Draw the π-molecular orbitals of the allyl system (cation, radical and anion) and identity the HOMO and LUMO.

Solution:



7) Draw the π-molecular orbitals of 2,4-pentadienyl system (cation, radical and anion) and identify the HOMO and LUMO.

Solution:



8) What do you understand by bonding and antibonding molecular orbitals?

Solution:

Half of the molecular orbitals having lower energies than the isolated p orbitals are called bonding molecular orbitals and the other half of the molecular orbitals having higher energies than the isolated p orbitals are called antibonding molecular orbitals.

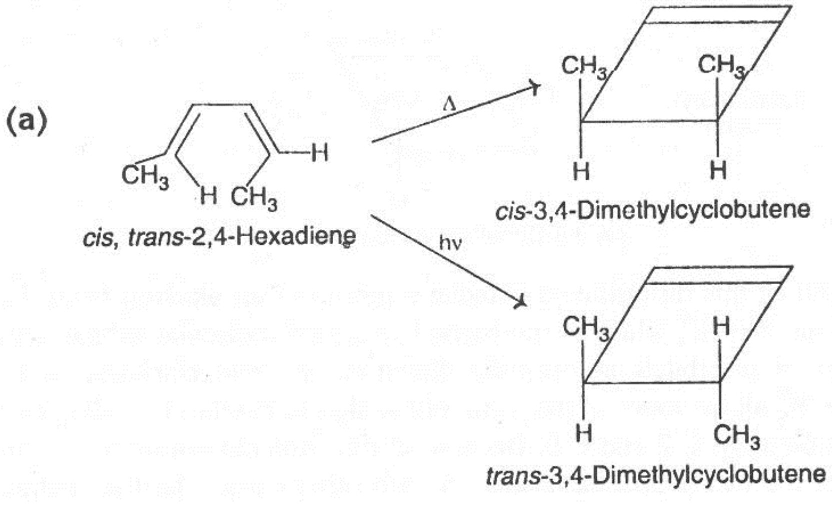
9) Two molecular orbitals of particular importance in understanding pericyclic reactions. What are these orbitals? Why are they termed frontier orbitals?

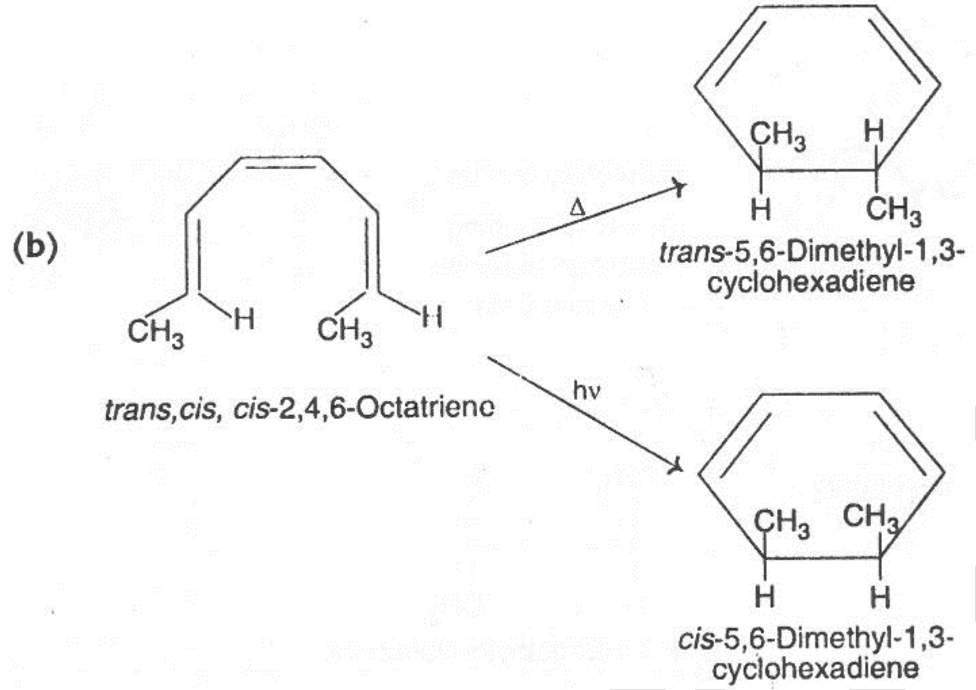
Solution:

The two molecular orbitals which are of particular importance in understanding pericyclic reactions are (i) the occupied molecular orbital of highest energy, termed the **highest occupied molecular orbital (HOMO)** and (ii) the unoccupied molecular orbital of lowest energy, termed the **lowest unoccupied molecular orbital (LUMO)**.

The HOMO and LUMO are termed frontier orbitals because they are the molecular orbitals of the energy extremes: the HOMO is the occupied molecular orbital of highest energy, and the LUMO is the unoccupied molecular orbital of lowest energy.

10) Explain the results of the following electrocyclic reactions by Frontier Molecular Orbital (FNO) approach.



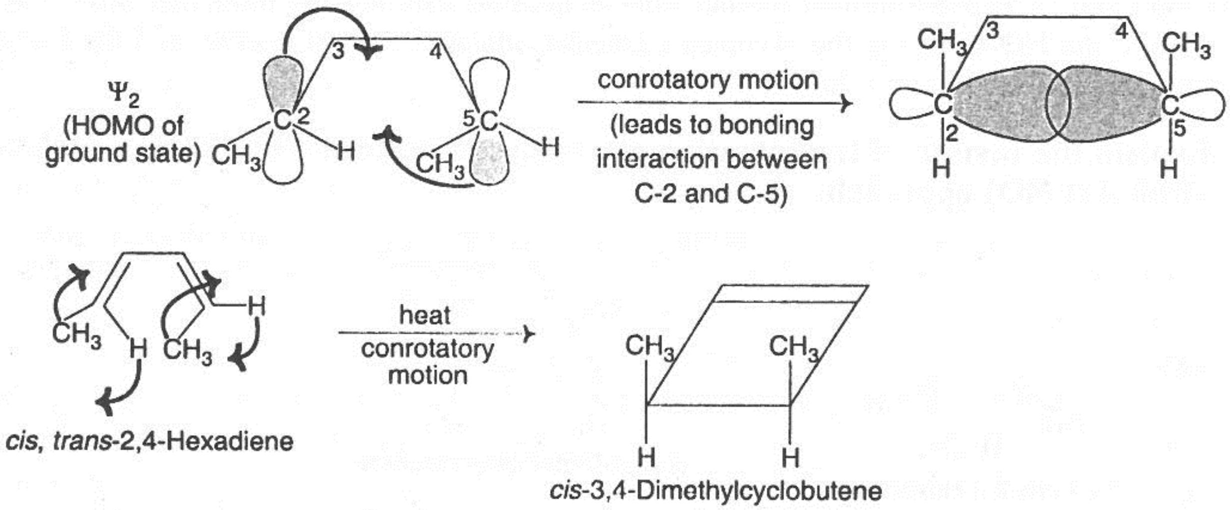


Solution:

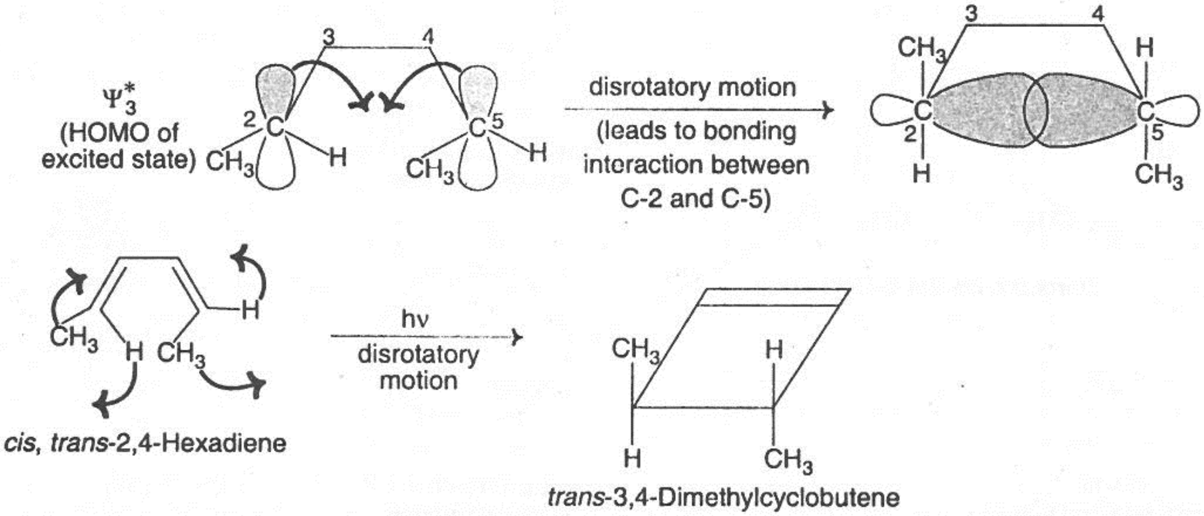
a) cis, trans-2,4-Hexadiene undergoes thermal and photochemical cyclisation to give cis and trans–3,4-dimethylcyclobutene respectively. These observations may be explained by FMO approach as follows.

For concerted cyclization to occur the symmetry of the highest occupied molecular orbital (HOMO) of the polyene system is to be considered. When the ring closure take place, the two terminal p orbitals must overlap and the overlapping lobes must have same phase sign.

In the ground state it is Ψ_2 which is the HOMO of this disubstituted butadiene system. The conrotatory motion of orbitals (rotation of p orbitals in the same direction, i.e., both clockwise or both anticlockwise) at C-2 and C-5 of Ψ_2 allows lobes of the same phase sign to overlap i.e., allows formation of a bonding σ-molecular orbital between C-2 and C-5. Because of this, ring closure occurs in conrotatory mode and this type of motion of the two p orbitals relative to each other causes the two methyl groups to be placed on the same side of the product molecule, that is, in the cis configuration.

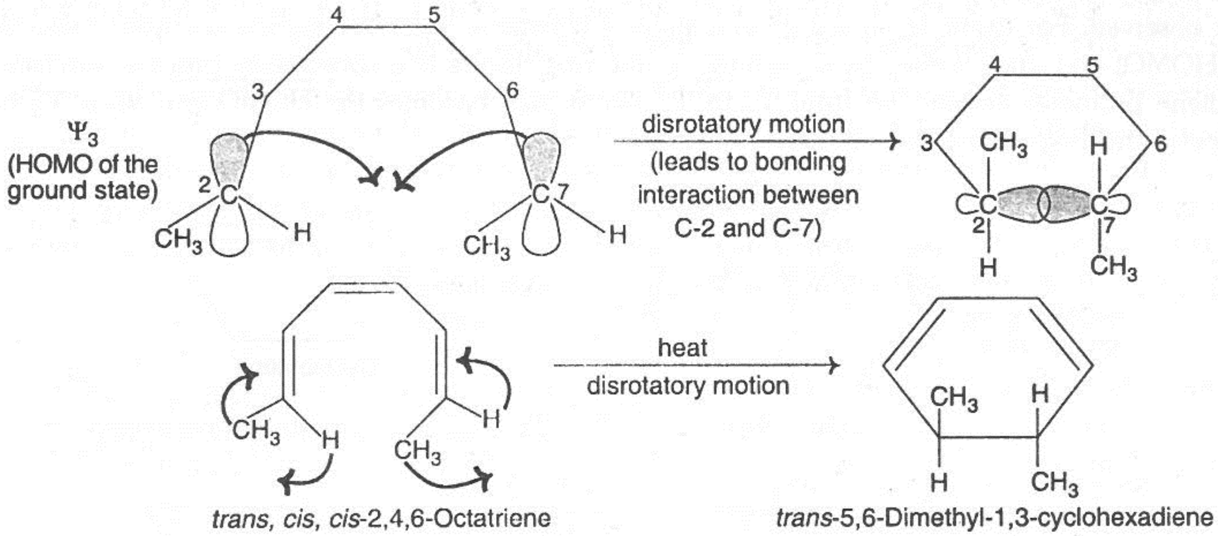


Irradiation (absorption of light) of this disubstituted butadiene promotes an electron from Ψ_2 to Ψ_3^*. Therefore, in the first excited state it is to Ψ_3^* which is the highest occupied molecular orbital. Disrotatory motion of the orbitals (rotation of p orbitals in opposite direction i.e., one clockwise and another anticlockwise) at C-2 and C-5 of Ψ_3^* allows lobes of the same phase sign to overlap i.e., allows formation of a bonding σ-molecular orbital between C-2 and C-5. Because of this, ring closure occurs in disrotatory mode and this type of motion of the two p orbitals relative to each other causes the two methyl groups to be placed on the opposite sides of the product molecule, that is, in the trans configuration.

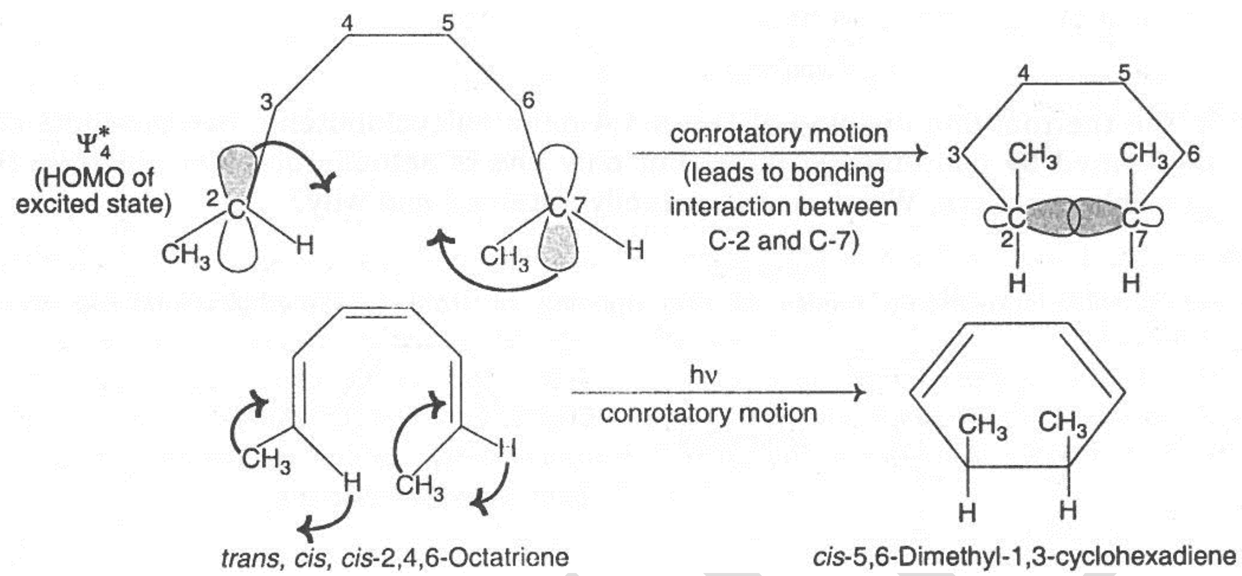


(b) trans, cis, cis-2,4,6-octatriene undergoes thermal and photochemical cyclization to give trans and cis-5,6-dimethyl-1,3-cyclohexadiene respectively.

In the ground state Ψ_3 is the HOMO of this octatriene and so, disrotatory motion of the orbitals leading to bonding interaction between C-2 and C-7 occurs and as a result of this, trans-5,6-dimethyl-1,3-cyclohexadiene is obtained by thermal cyclization.



In the excited state Ψ_4^* is the HOMO of this octatriene and so, conrotatory motion of the orbitals leading to bonding interaction between C-2 and C-7 occurs and as a result of this, cis-5,6-dimethyl-1,3-cyclohexadiene is obtained by photochemical cyclisation.



11) Write down the Woodward-Hoffmann rules (selection rules) for electrocyclic reactions.

Solution:

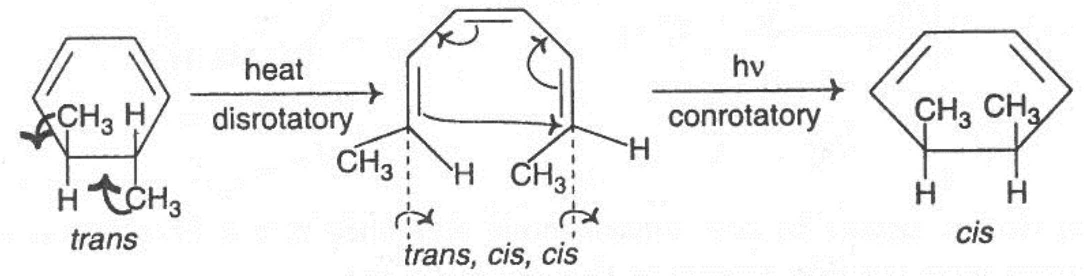
Woodward-Hoffmann rules (selection rules) for electrocyclic reactions may be given as follows:

Number of electrons involved	Mode of Activation	Allowed Stereochemistry
4n n = 1, 2, 3…	Thermal Photochemical	Conrotatory Disrotatory
4n+2 n = 0, 1, 2, 3,…	Thermal Photochemical	Disrotatory Conrotatory

12) Can you suggest a stereospecific method for converting trans-5,6-dimethyl-1,3-cyclohexadiene into cis-5,6-dimethyl-1,3-cyclohexadiene?

Solution:

When heated, trans-5,6-dimethyl-1,3-cyclohexadiene, a 6π electron system [(4n+2) π, where n=1], undergoes disrotatory ring opening to give trans, cis, cis-2,4,6-octatriene. This, when irradiated undergoes conrotatory ring closure to give cis-5,6-dimethyl-1,3-cyclohexadiene.



13. Discuss the feasibility of thermal/photochemical electrocyclic reactions using correlation diagram.

Solution:

A correction diagram is simply a diagram showing the possible transformation of reactant orbitals to product orbitals. An electrocyclic of a cycloaddition reaction can easily be analyzed by constructing a correlation diagram.

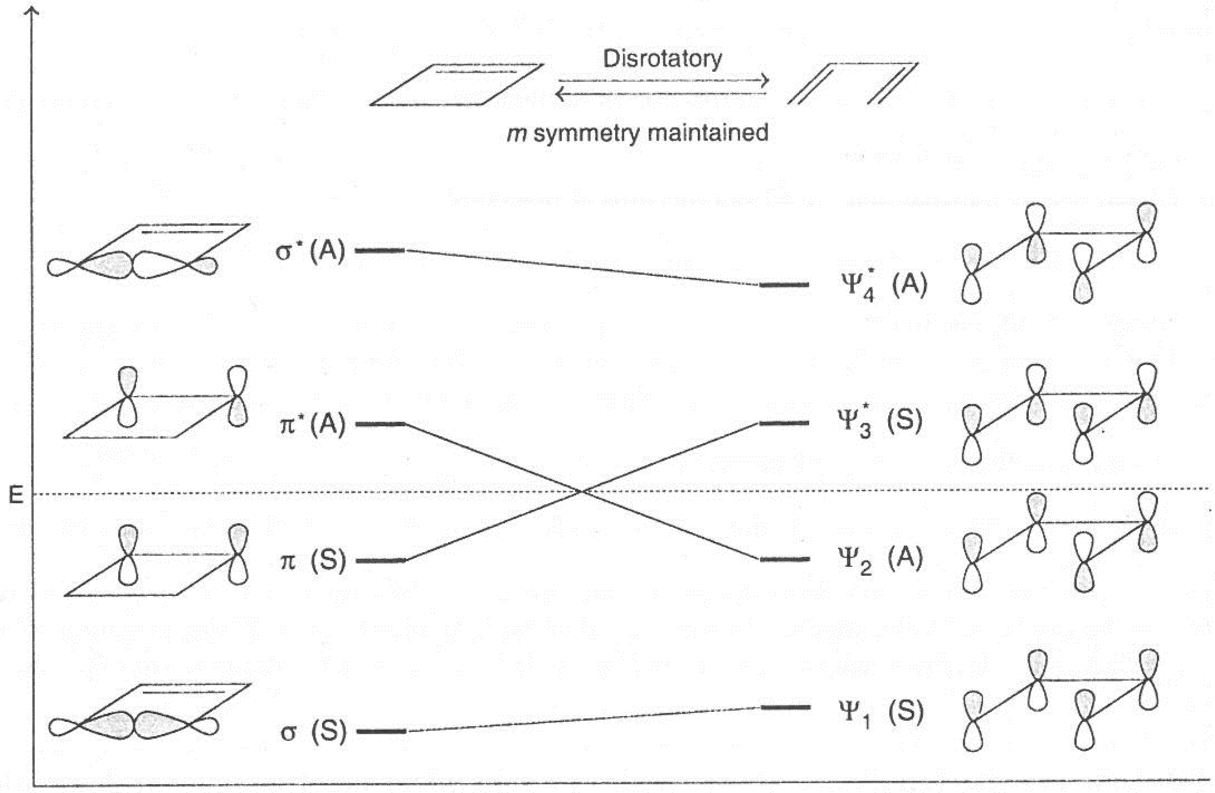
Concerted reactions occur with conservation of orbital symmetry. This implies that concerted reactions occur readily when the orbital symmetry characteristics of reactants and products are identical, but with difficulty when the symmetry characteristics differ. Therefore, in order to determine whether a reaction is allowed or not, it is necessary to determine the symmetry of the requisite orbitals of the reactants and products and then to connect orbitals of like symmetry, having minimum energy differences. If the occupied orbitals of the reactant can be converted to the occupied orbitals of the products, the reaction is symmetry allowed and if not, the reaction is symmetry forbidden.

Electrocyclic reactions

(a) Cyclobutene $\rightleftarrows$ butadiene transformation:

The orbitals of cyclobutene which are directly involved are σ and π and the related antibonding orbitals σ^* and π^*. These four orbitals pass on to the four π orbitals, Ψ_1, Ψ_2, Ψ_3^* and $\Psi_4^*$of 1,3-butadiene.

The ring-opening (or ring-closing) may be a disrotatory process or a conrotatory process. In the case of disrotatory ring opening, cyclobutene preserves a plane of symmetry (m or σ) throughout the transformation, while a two-fold axis of symmetry (C_2) is maintained at all times in conrotatory mode of ring closure. The correlation diagram for disrotatory interconversion of cyclobutene-butadiene system in which m symmetry is maintained in as follows:

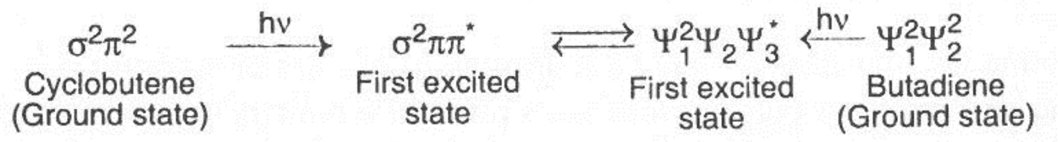


The following two conclusions can be drawn from such a diagram:

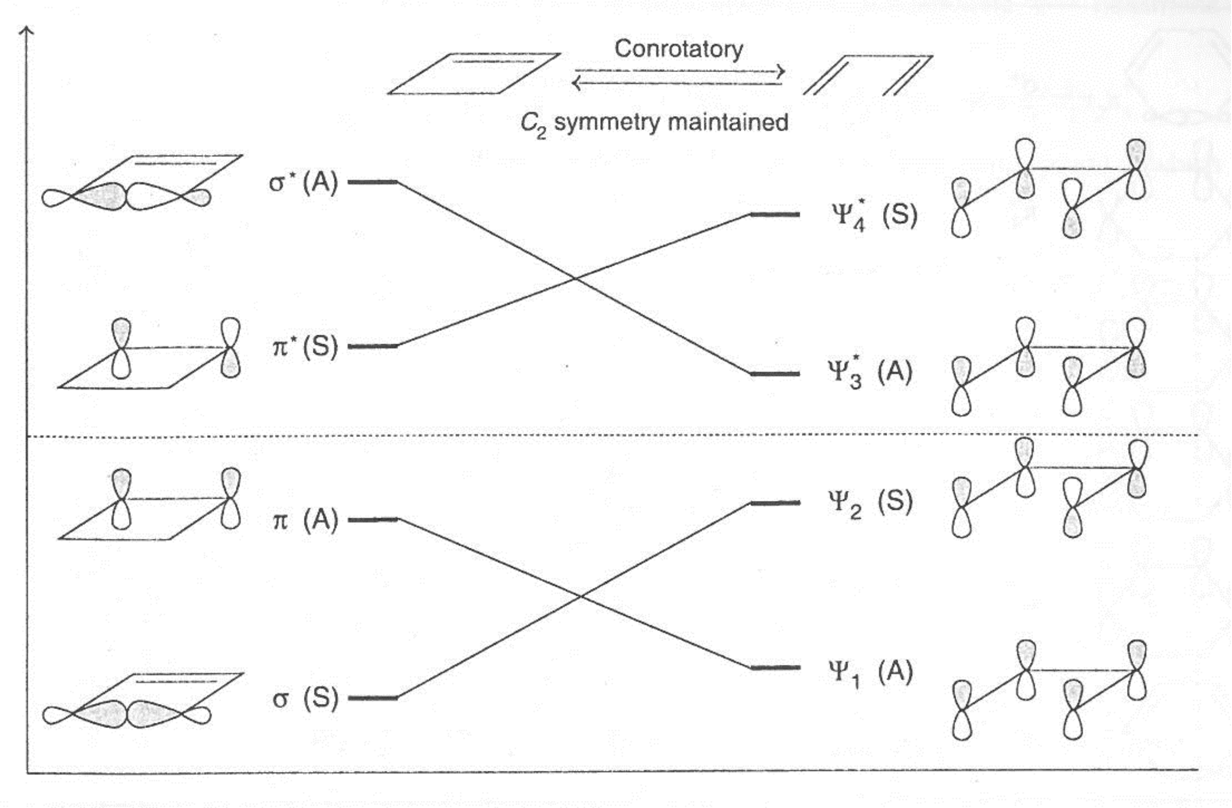
(i) Thermal transformation takes place only when the ground state orbitals of the reactants correlate with the ground state orbitals of the products. In the above diagram the cyclobutene ground state orbital, σ, correlates with the 1,3-butadiene ground state orbital, Ψ_1, but the π orbital of the former does not correlates with Ψ_2 of the latter. Instead it correlates with Ψ_3^* which is an excited state and an antibonding orbital. Thermal transformation of cyclobutene $\rightleftarrows$ 1, 3-butadiene system by disrotatory process is, therefore, symmetry-forbidden.

$$\sigma^2\pi^2 \xrightarrow[\times]{\Delta\ \text{(disrotatory)}} \Psi_1^2\Psi_3^{*2}\ ;\quad \Psi_1^2\Psi_2^2 \xrightarrow[\times]{\Delta\ \text{(disrotatory)}} \sigma^2\pi^{*2}$$

ii) Photochemical transformation takes place only when the first excited state orbitals of the reactants correlate with the first excited state orbitals of the products. In this case, σ, π and π^* orbitals of cyclobutene correlates with Ψ_1, Ψ_2 and Ψ_3^* orbitals of 1,3 butadiene. In other words, the first excited state of cyclobutene correlates with the first excited state of 1,3 butadiene and therefore, disrotatory ring-opening (and ring-closure) is photochemically a symmetry-allowed process.



The correlation diagram for conrotatory interconversion of cyclobutene-1,3-butediene system in which a C_2 symmetry is maintained is as follows.



The following two conclusions may be drawn from the above correlation diagram:

(i) Since the ground state orbitals of cyclobutene ($\sigma^2\ \pi^2$) correlate with the ground state orbitals of 1,3-butadiene ($\Psi_1^2\ \Psi_2^2$), a thermal conrotatory process in either direction is a symmetry-allowed process.

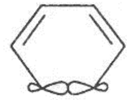
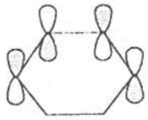
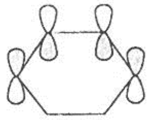
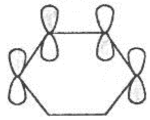
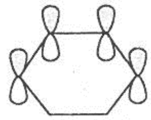
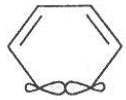
$$\sigma^2\pi^2 \xrightleftharpoons{\Delta(\text{con})} \Psi_1^2\Psi_2^2$$

(ii) The first excited state of cyclobutene ($\sigma^2\pi\pi^*$) correlates with the upper excited state ($\Psi_1^2\ \Psi_2\ \Psi_4^*$) of 1,3-butadiene and the first excited state of 1,3-butadiene ($\Psi_1^2\ \Psi_2\ \Psi_3^*$) correlates with a high energy upper excited state of cyclobutene ($\sigma^2\pi\sigma^*$). Therefore, a photochemical conrotatory process in either direction is symmetry-forbidden.

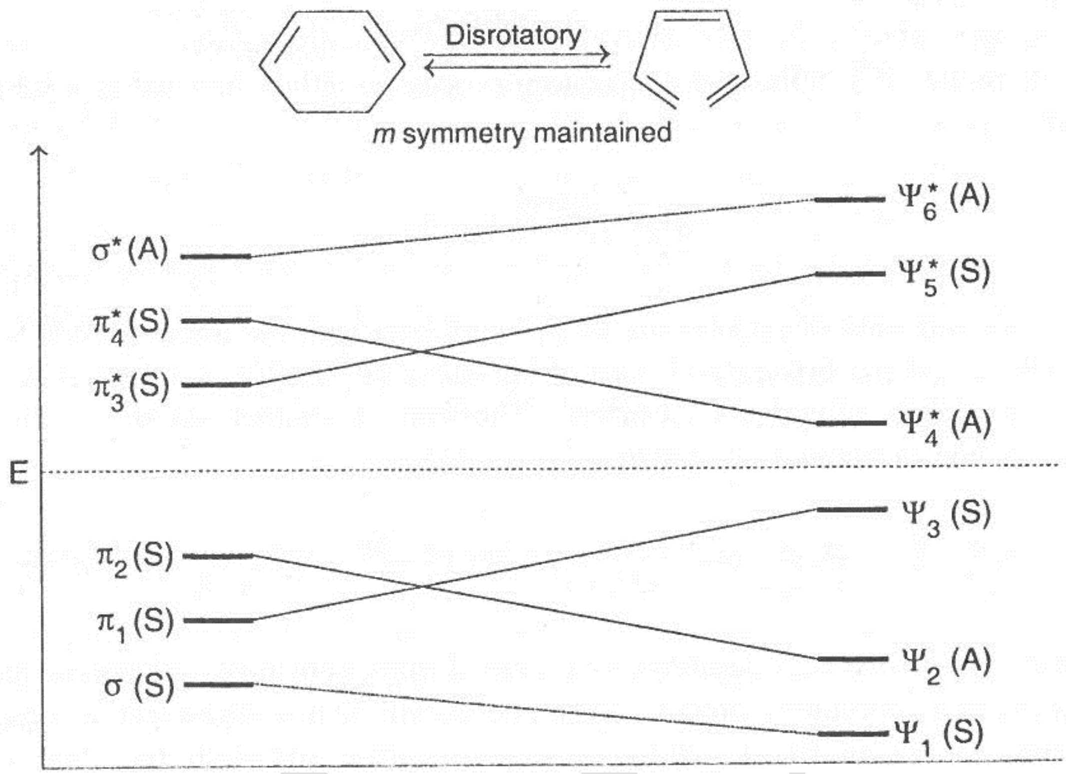
$$\sigma^2\pi^2 \xrightleftharpoons{h\nu} \sigma^2\pi\pi^* \not\longrightarrow \Psi_1^2\Psi_2\Psi_4^* \ ; \ \Psi_1^2\Psi_2^2 \xrightarrow{h\nu} \Psi_1^2\Psi_2\Psi_3^* \not\longrightarrow \sigma^2\pi\sigma^*$$

It is evident from the above considerations that thermal ring-opening of cyclobutene and ring-closure of 1,3-butadiene proceed in a conrotatory process, while photochemical inter conversion involves a disrotatory mode. These generalizations are true for all the systems containing 4nπ electrons, where n = 0,1,2, etc.

(b) Cyclohexadiene ⇌ 1,3,5-hexatriene transformation. For system containing (4n+2) π electron the theoretical prediction is completely different. Cyclohexadiene-1,3,5-hexatriene interconversion is a typical example of this type. In this case six molecular orbitals (Ψ_1 to Ψ_6^*) of 1,3,5-hexatriene and six molecular orbitals (σ to σ^*) cyclohexadiene are involved and therefore, to be considered. The symmetry properties of the six molecular orbitals of cyclohexadiene are as follows.

		m	C_2
	σ^*	A	A
	π_4^*	A	S
	π_3^*	S	A
	π_2	A	S
	π_1	S	A
	σ	S	S

The correction diagram for disrotatory interconversion of cyclohexadiene- hexatriene system in which m symmetry is maintained is as follows.



The following two conclusions can be drawn from this correlation diagram:

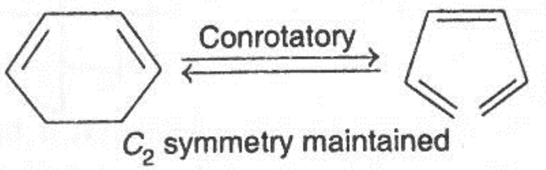
(i) Since the ground state bonding orbitals of cyclohexadiene correlate with the ground state bonding orbitals of hexatriene, a thermal disrotatory process in either direction is symmetry allowed.

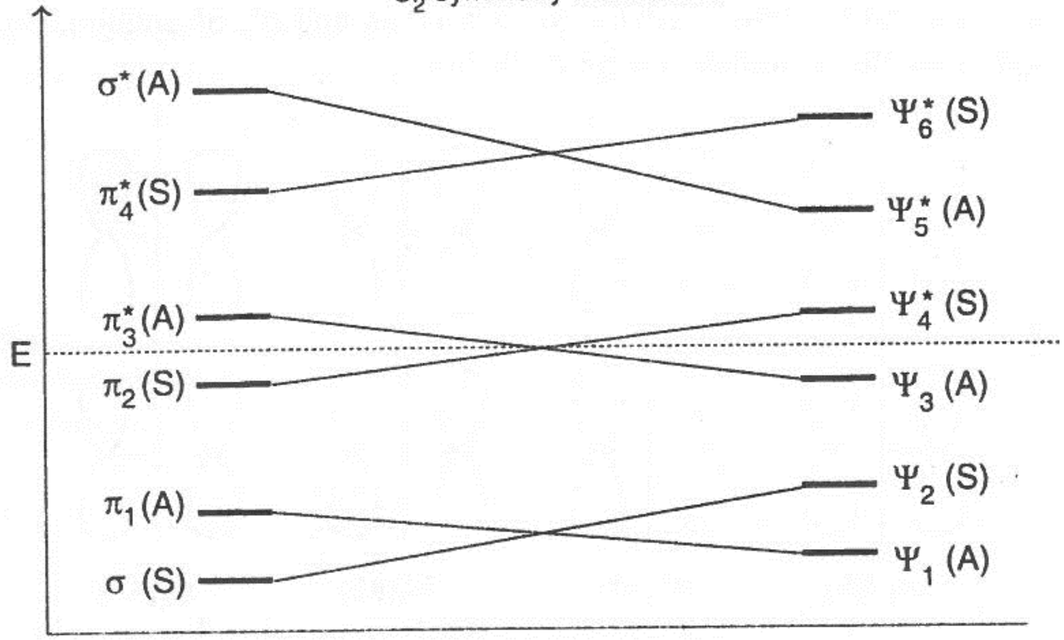
$$\sigma^2\pi_1^2\pi_2^2 \xrightleftharpoons{\Delta(\text{dis})} \Psi_1^2\Psi_2^2\Psi_2^3$$

(ii) Since the first excited states of both cyclohexadiene and hexatriene correlate with the upper excited state of the other, photochemical transformation of cyclohexadiene $\rightleftarrows$ hexatriene system by disrotatory mode is symmetry-forbidden.

$$\sigma^2\pi_1^2\pi_2^2 \xrightarrow{h\nu} \sigma^2\pi_1^2\pi_2\pi_3^* \nleftrightarrow \Psi_1^2\Psi_2^2\Psi_3\Psi_5^* ; \quad \Psi_1^2\Psi_2^2\Psi_3^2 \xrightarrow{h\nu} \Psi_1^2\Psi_2^2\Psi_3\Psi_4^* \nleftrightarrow \sigma^2\pi_1^2\pi_2\pi_4^*$$

The correlation diagram for conrotatory interconversion of cyclohexadiene- hexatriene system in which a C_2 symmetry is maintained is as follows.





The following two conclusions can be drawn from this correlation diagram:

(i) Since the ground state orbitals of cyclohexadiene correlate with the first excited state orbitals of hexatriene, a thermal conrotatory process in either direction is symmetry-forbidden.

$$\sigma^2\pi_1^2\pi_2^2 \xrightarrow[\times]{\Delta\text{ (con)}} \Psi_1^2\Psi_2^2\Psi_4^{2*} \; ; \; \Psi_1^2\Psi_2^2\Psi_3^2 \xrightarrow[\times]{\Delta\text{ (con)}} \sigma^2\pi_1^2\pi_3^{2*}$$

(ii) Since the first excited state of cyclohexadiene correlate with the first excited state of hexatriene, a photochemical conrotatory process in either direction is symmetry-allowed.

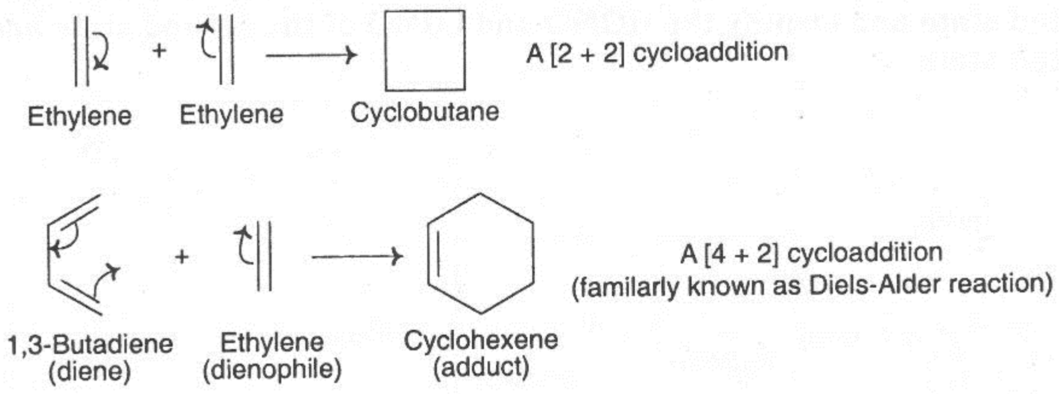
$$\underset{\substack{\text{Cyclohexadiene}\\\text{(ground state)}}}{\sigma^2\pi_1^2\pi_2^2} \xrightarrow{h\nu} \underset{\substack{\text{First excited}\\\text{state}}}{\sigma^2\pi_1^2\pi_2\pi_3^*} \rightleftharpoons \underset{\substack{\text{First excited}\\\text{state}}}{\Psi_1^2\Psi_2^2\Psi_3\Psi_4^*} \xleftarrow{h\nu} \underset{\substack{\text{Hexatriene}\\\text{(ground state)}}}{\Psi_1^2\Psi_2^2\Psi_3^2}$$

It is evident from the above considerations that thermal ring-opening of cyclohexadiene and ring closure of hexatriene proceed in a disrotatory process, while photochemical interconversion involves a conrotatory mode. There generalizations are true for all the systems containing (4n+2) π electrons, where n = 0,1,2,3,etc.

Thus Woodward-Hoffmann rules (selection rules) for electrocyclic reactions may be summed up as follows:

Number of electrons	Thermal	Photochemical
4n	Con	Dis
4n+2	Dis	Con

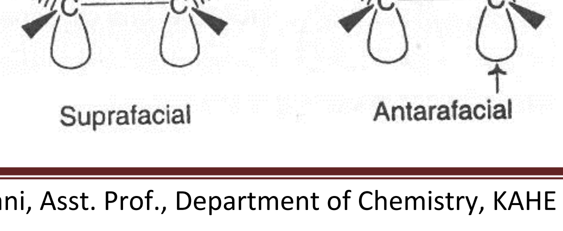
Cycloaddition reactions



14). How may a cycloaddition reaction be classified by its stereochemistry with respect to the plane of each reacting molecule?

Solution:

A cycloaddition reaction may take place either across the same face, or across opposite faces of the plane in each reacting component. It the reaction occurs across the same face of a π system, the reaction is said to be suprafacial with respect to that π system. If the reaction occurs at opposite faces of a π system, it is said to be antarafacial with respect to that π system.

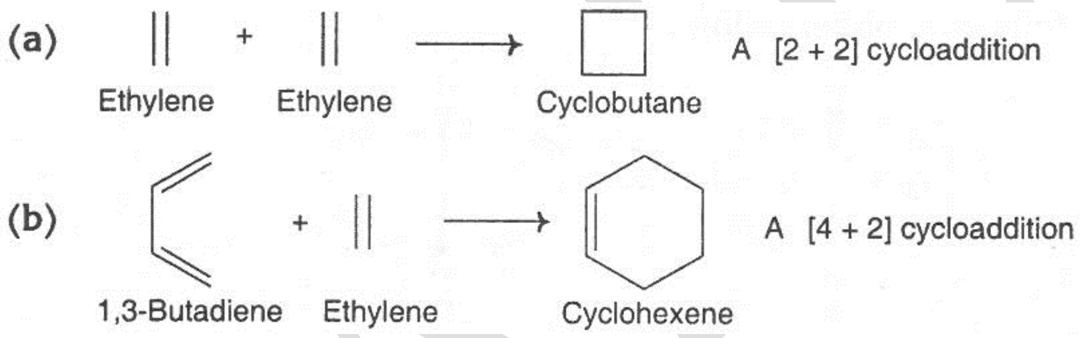


15) What do you understand by symmetry allowed and symmetry forbidden reactions?

Solution:

In case of FMO approach to a pericyclic reaction when the HOMO of one component and LUMO of other component overlap in the same phase leading to bonding interaction then it is called a symmetry allowed reaction but when HOMO and LUMO overlap in the different phase leading to anti-bonding interaction, then it is called a symmetry forbidden.

16) Discuss the Frontier Molecular Orbital (FMO) method of predicting viability of the following two cycloaddition reactions:



Solution:

For a cylcoaddition reaction between two unsaturated molecules to occur there must be bonding overlap (same phase overlap) between the p-orbitals at the terminal carbons of the frontier orbitals i.e., the highest occupied molecular orbital (HOMO) of one reactant and lowest unoccupied molecular orbital (LUMO) of the other. Therefore, a symmetry allowed reaction is that in which HOMO-LUMO overlap is a bonding interaction and a symmetry forbidden reaction is that in which HOMO-LUMO overlap is an antibonding interaction.

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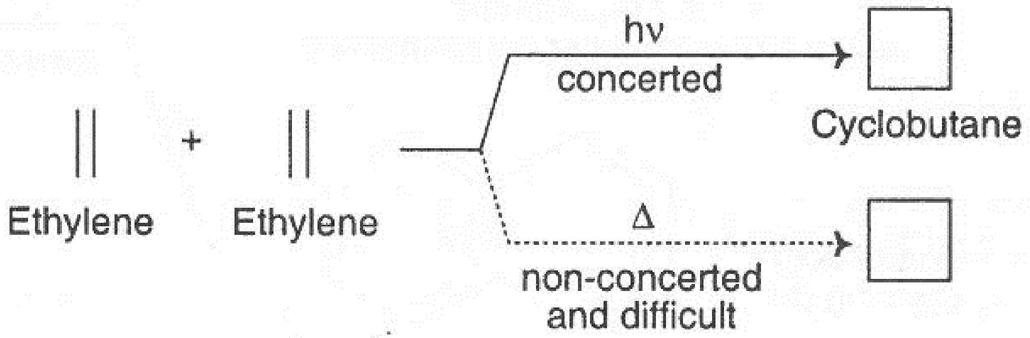
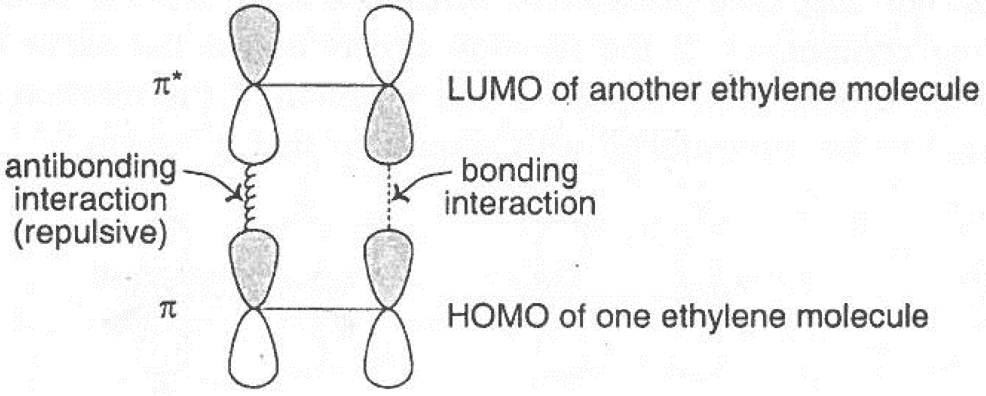
(a) The [2+2] cycloaddition of two ethylene molecules to form a molecule of cyclobutane is photochemically allowed but thermally forbidden (i.e., unlikely to take place in a concerted process).

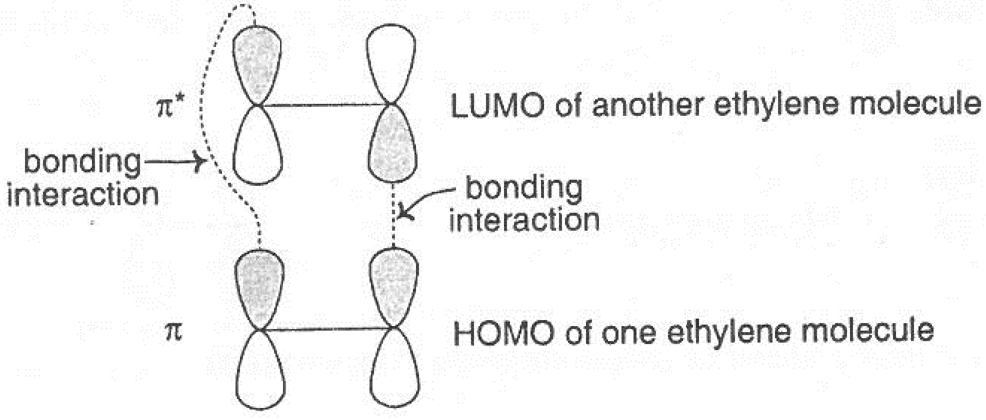


Thermal reactions involve molecules reacting in the ground state. In [2+2] cycloaddition of ethylene, lobes of HOMO (π molecular orbital) in one molecule and that of LUMO (π* molecular orbital) of the other does not overlap in a fashion leading to bonding interaction between both set of carbon atoms. Therefore, the reaction, which is suprafacial with respect to both components ($\pi^2s + \pi^2s$) is thermally forbidden. It means that a thermal (ground state) cycloaddition of ethylene is unlikely to occur in a concerted process. In fact, thermal cycloaddition of two ethylene molecules takes place through non-concerted, free radical mechanism.



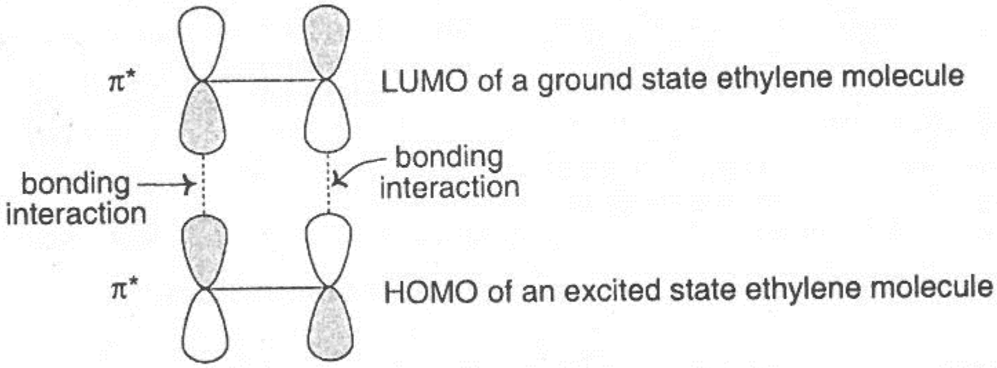
(Thermally forbidden *supra-supra* interaction)

However a thermal [2+2] cycloaddition could occur provided it is suprafacial with respect to one component and antarafacial with respect to the other i.e., it is $\pi^2s + \pi^2a$. This process, though symmetry allowed, is geometrically very difficult (the T.S. energy is very high).



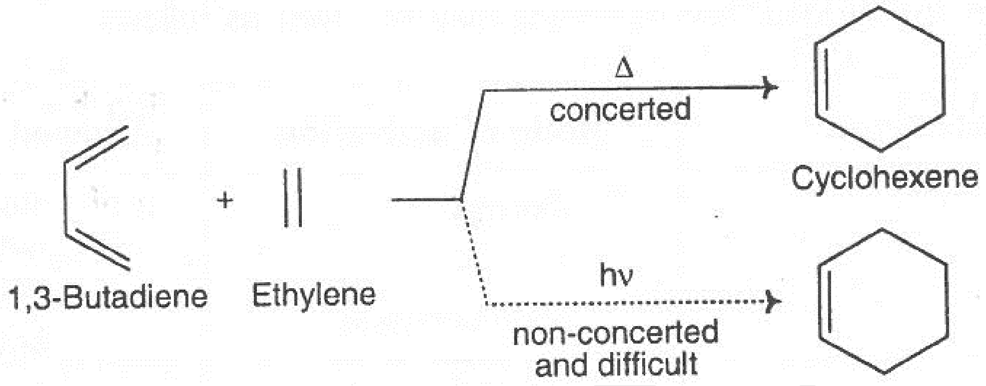
(Symmetry allowed, but geometrically difficult *supra-antara* interaction)

On irradiation of ethylene one electron is promoted to the antibonding molecular orbital, i.e., from π to π^*. Therefore, in the excited state the HOMO of ethylene molecule is π^*. In this case we find that a bonding interaction occurs between the HOMO of an excited state ethylene molecule and the LUMO of a ground state ethylene molecule. Hence the reaction which is suprafacial with respect to both the components ($\pi^2s + \pi^2s$) is photochemically allowed and occurs readily through a concerted process.

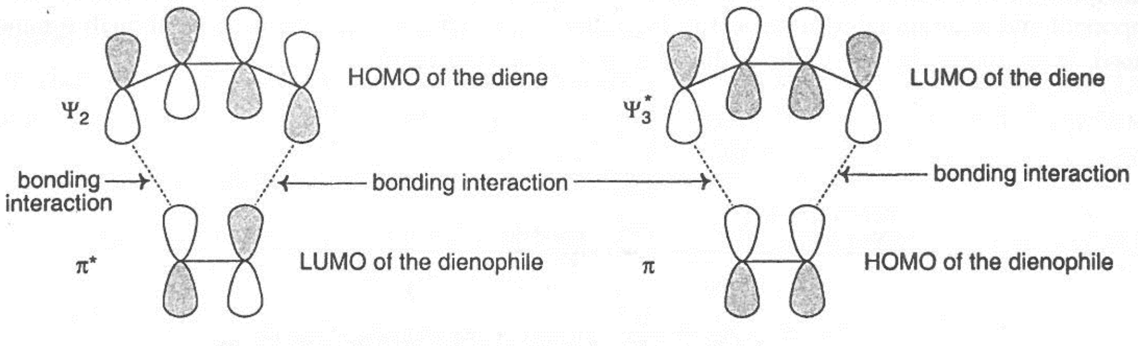


(Photochemically allowed *supra-supra* interaction)

(b) The [4+2] cycloaddition of 1,3-butadiene and ethylene to form a molecule of cyclohexene (the simplest example of Diels-Alder reaction) is thermally allowed but photochemically forbidden i.e., unlikely to take place in a concerted process.

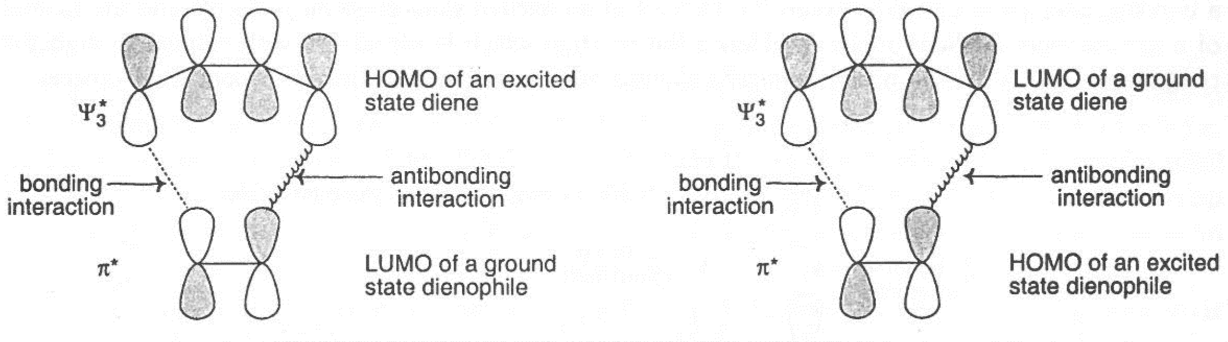


There are two combinations of orbital interactions: the overlap of the HOMO of butadiene (Ψ_2) with the LUMO of ethylene (π^*) and the overlap of the HOMO of ethylene (π) with the LUMO of butadiene (Ψ_3^*). In either case, the overlap brings together lobes of the same phase. There is a flow of electrons from HOMO to LUMO and bonding interaction occurs. This thermal reaction which is suprafacial with respect to both the components ($\pi^4s + \pi^2s$) is, therefore, symmetry allowed and occurs readily through a concerted process. Although ($\pi^4a + \pi^2a$) mode of cycloaddition is symmetry allowed, it is geometrically not possible.



(Symmetry allowed *supra-supra* mode of interactions)

On irradiation, one electron of HOMO (bonding) is promoted to HOMO (anti-bonding). Under this conditions ($\pi^4s + \pi^2s$) cycloaddition is symmetry forbidden because the HOMO of the excited state of one component and LUMO of the other have no proper orbital symmetry to interact in a bonding way.



(Symmetry forbidden *supra-supra* mode of interactions)

Although ($\pi^4a + \pi^2s$) and ($\pi^4s + \pi^2a$) modes of cycloaddition are symmetry allowed, they are geometrically very difficult.

17) Write down the selection rules for cycloaddition reactions.

Solution:

The selection rules for cycloaddition reactions may be given as follows:

Number of electrons	**Mode of activation**	**Allowed stereochemistry**
4n	Thermal	Supra–antara Antara-supra
	Photochemical	Supra–supra Antara-antara
4n+2	Thermal	Supra–supra Antara-antaraantara
	Photochemical	Supra–antara Antara-supra

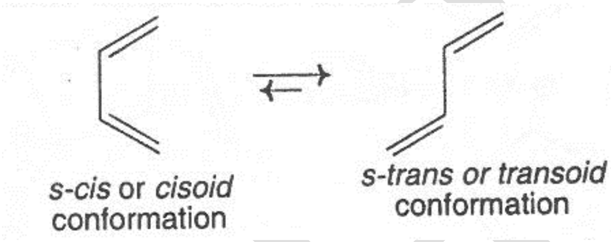
n = 1,2,3,…etc.

18) Discuss the important aspects to the stereochemistry of the Diels-Alder reaction.

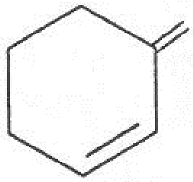
Solution:

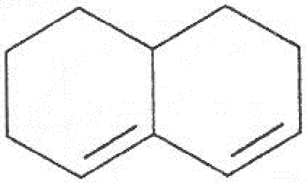
The important aspects to the stereochemistry of the Diels-Alder reaction are as follows:

(i) In this reaction the diene must be in the s-cis conformation that permits the ends of the conjugated system to reach the doubly bonded carbon atoms of the dienophile.



That the cisoid geometry of the diene is essential is shown by the fact that the fixed transoid diene I and II and the linear diyne III do not undergo the Diels–Alder reaction.

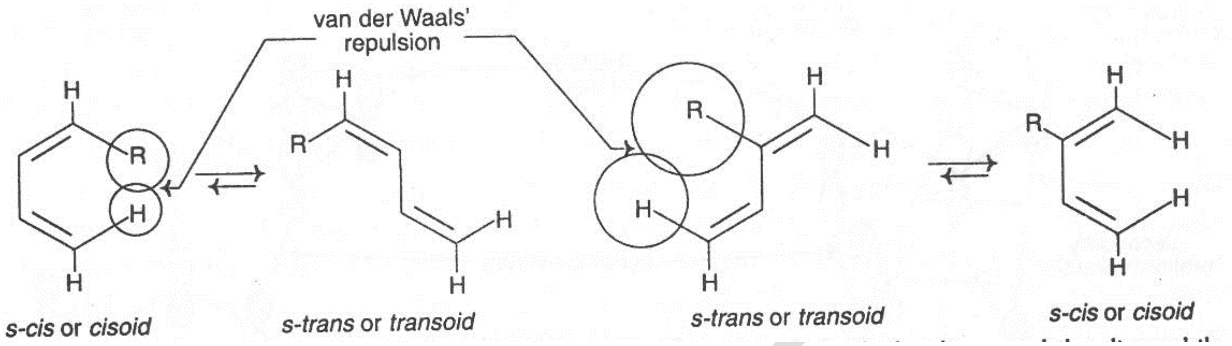

I


II

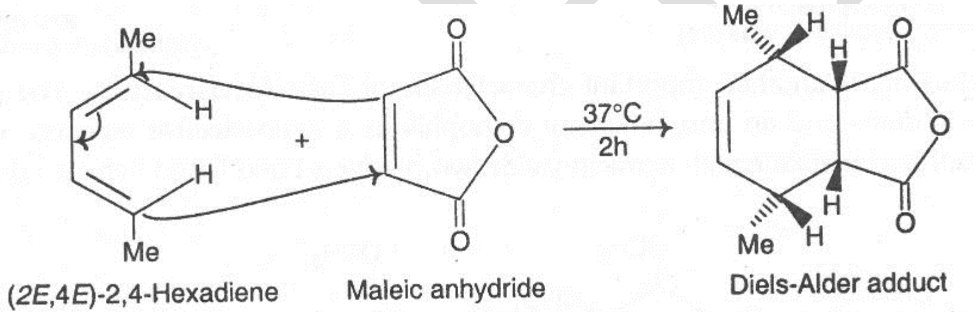
$H-C\equiv C-C\equiv C-H$

III

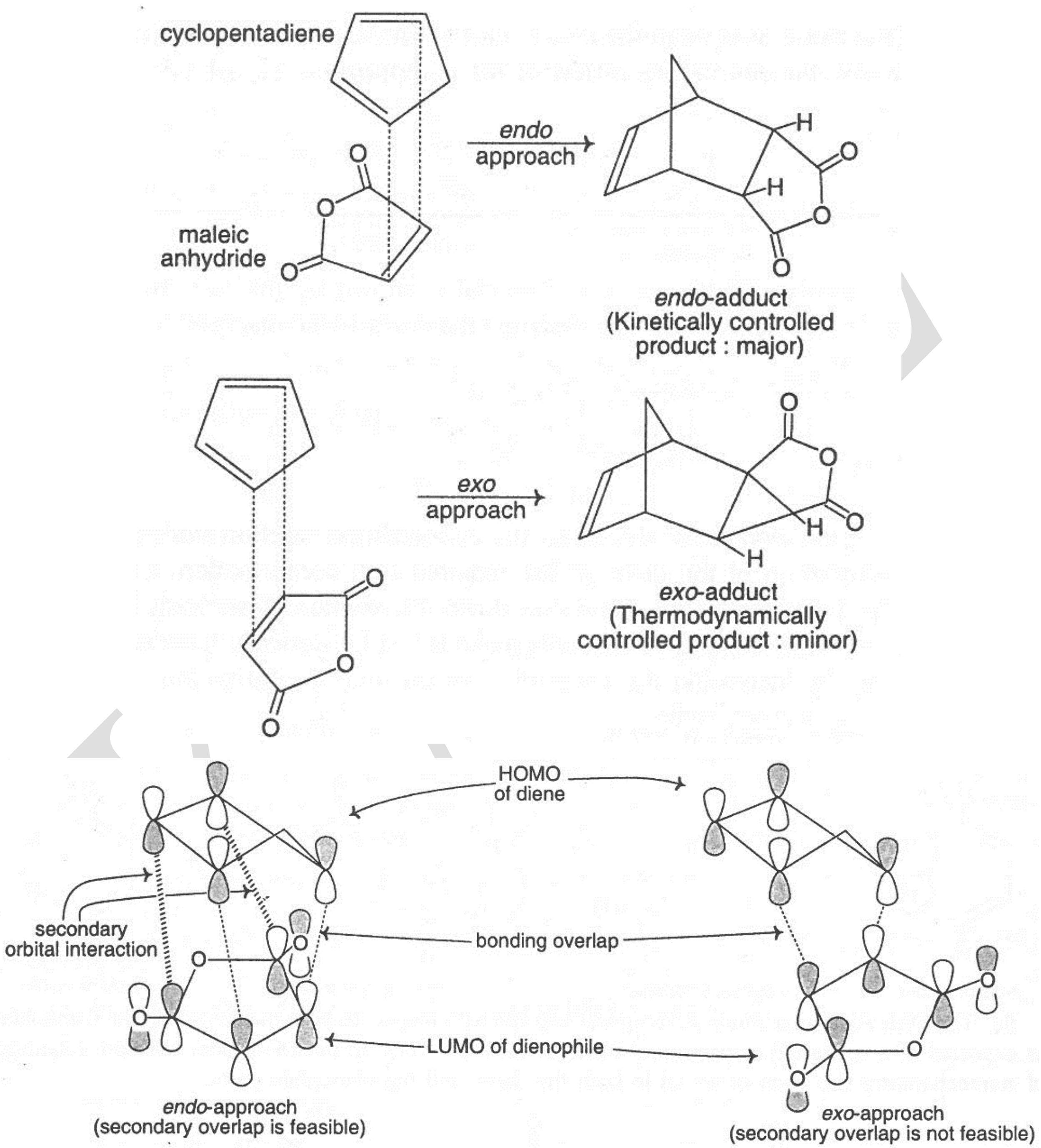
The substituents in the diene may also effect the cycloaddition reaction sterically. The substituents effect the equilibrium proportion of the diene in the required s-cis conformation. Consequently, Z alkyl or aryl substituents in the 1-position of the diene slow down the reaction by sterically hindering formation of the s-cis conformation, while bulky 2-substituents make it fast by sterically hindering formation of the s-trans conformation i.e., by increasing the proportion of the s-cis conformation.



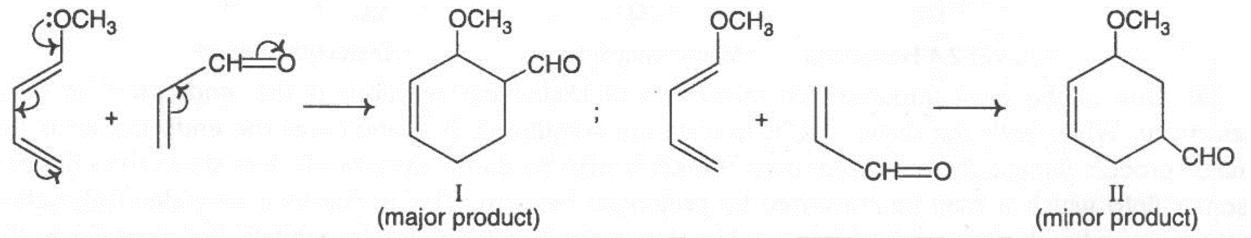
(ii) The Diels-Alder reaction is stereospecifically syn with respect to both the diene and the dienophile as expected of a concerted (supra-supra) mode of addition. Thus in the Diels-Alder reaction, retention of stereochemistry has been observed in both the diene and the dienophile parts.



(iii) One of the most important characteristics of Diels-Alder reaction is the 'endo rule' or endo selectivity. When both the diene and dienophile are substituted, in many cases the endo isomer is the major product (kinetically controlled) even though it may be thermodynamically less stable than the exo isomer (into which it may be converted by prolonged heating). This is due to a secondary interaction between non-bond forming orbital lobes of like sign in the frontier molecular orbitals. For example in the reaction between cyclopentadiene and maleic anhydride the transition state for the endo addition is stabilized through secondary interactions involving lobes of HOMO and LUMO of the same phase. There secondary interactions are not possible in the transition state for exo addition since the relevant set of centres in the diene and the dienophile are now far apart from each other. The endo addition, therefore, occurs at a faster rate to give the endo adduct as the major product (the kinetically controlled product).



(iv) Regioselectivity is another important characteristic of Diels-Alder reaction. The reaction between an unsymmetrical diene and an unsymmetrical dienophile is a regioselective reaction. For example, the reaction of 1-methoxybutadiene with acrolein yields two products I and II and between them I is the major product.



I
(major product)

II
(minor product)

Although it is more appropriate to explain the regioselectivity in terms of the coefficient of terminal orbitals of HOMO and LUMO in many cases it may be determined from the consideration of electrophilic and nuclcophilic centres at the two components. Because of the +R effect of the –OMe group, the 4-position of 1-methoxybutadiene is more nucleophilic compared to 2-position and because of the –R effect of the -CHO group, the 3-position of acrolein is more electrophilic compared to 2-position. For this reason, C-4 of the diene adds to C-3 of the dienophile to give the major product I.

19) Furan acts as a diene in the Diels-Alder reaction but pyrrole normally does not. Explain

Solution:

Furan being less aromatic than pyrrole it takes part in the Diels-Alder reaction.

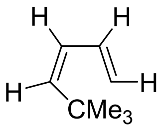
20) Why does anthracene undergo the Diels-Alder reaction but naphthalene does not?

Solution:

The energy gained by the cycloaddition reaction being less than the energy lost by the naphthalene molecule owing to the loss of aromaticity by one of the two benzene rings, naphthalene does not take part in the Diels-Alder reaction. In the case of anthracene, the energy gained by the reaction is more than the energy lost by the loss of aromaticity of the middle ring and so the reaction occurs.

21) Explain why the following compounds do not undergo Diels-Alder reaction:

(i)



(ii)

$H-C\equiv C-C\equiv C-H$

Solution:

(i)

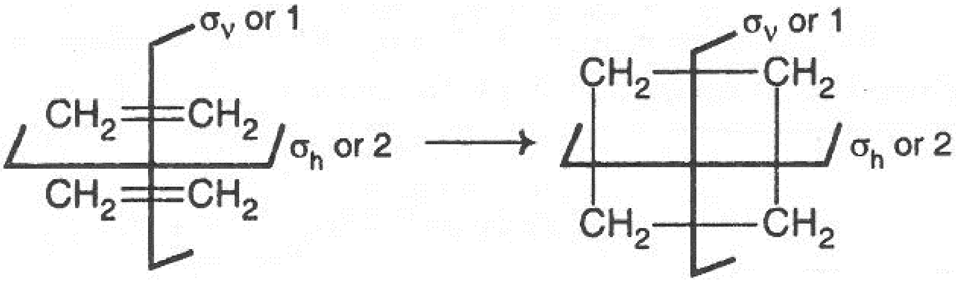
Dienes in the cisoid form undergo the Diels-Alder reaction. Transoid forms do not undergo the reaction because this form leads to a highly strained six-membered transition state whose energy content is very high. Compound (i) experience high strain in the cisoid form and the remain in the transoid form. So, compound (i) do not undergo the reaction.

(ii)

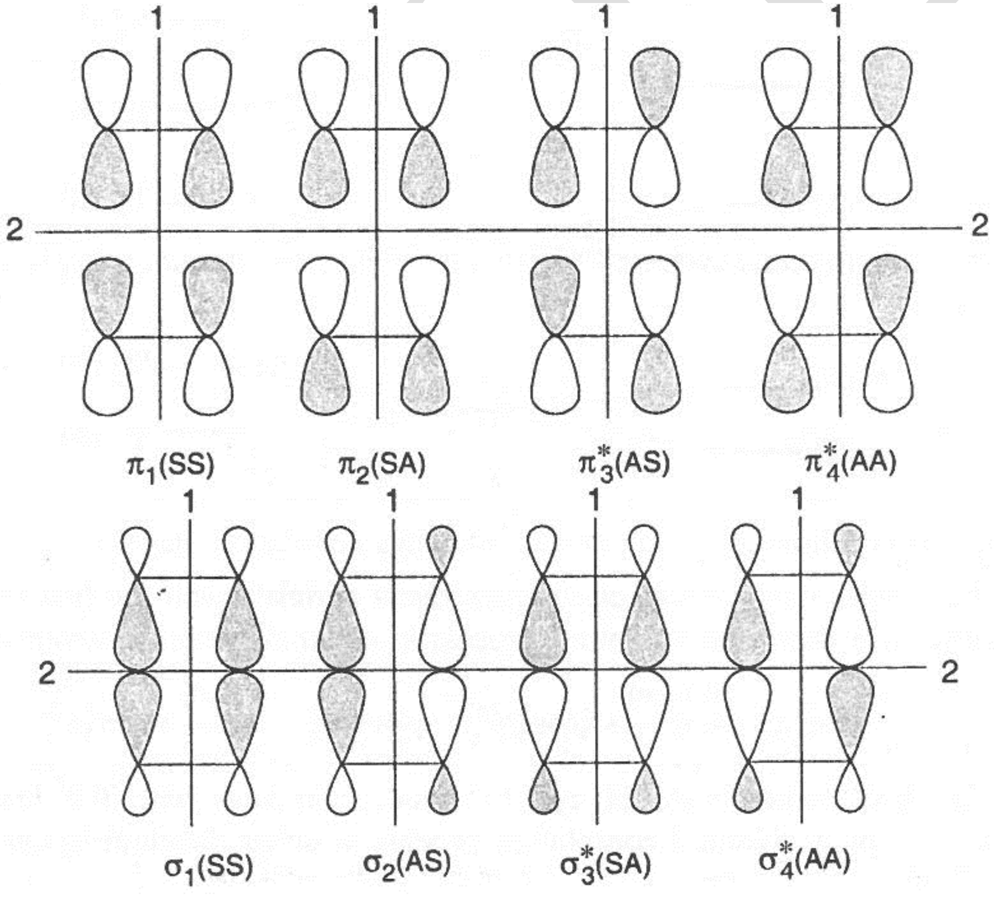
Compound (ii), 1,3-butadiyne is a linear molecule. Hence all the carbons are in the sp-hybridised state. The p atomic orbitals (AOs) on end carbons of the compound when overlap the p atomic orbitals (AOs) of the dienophile, a highly strained 1,3-cyclohexadiene will be formed. The corresponding transition state will have trienyl-like linear moiety with high strain and energy. It is difficult to overcome the energy barrier of the transition state. So the reaction does not occur.

Correlation diagram for cycloaddition reactions

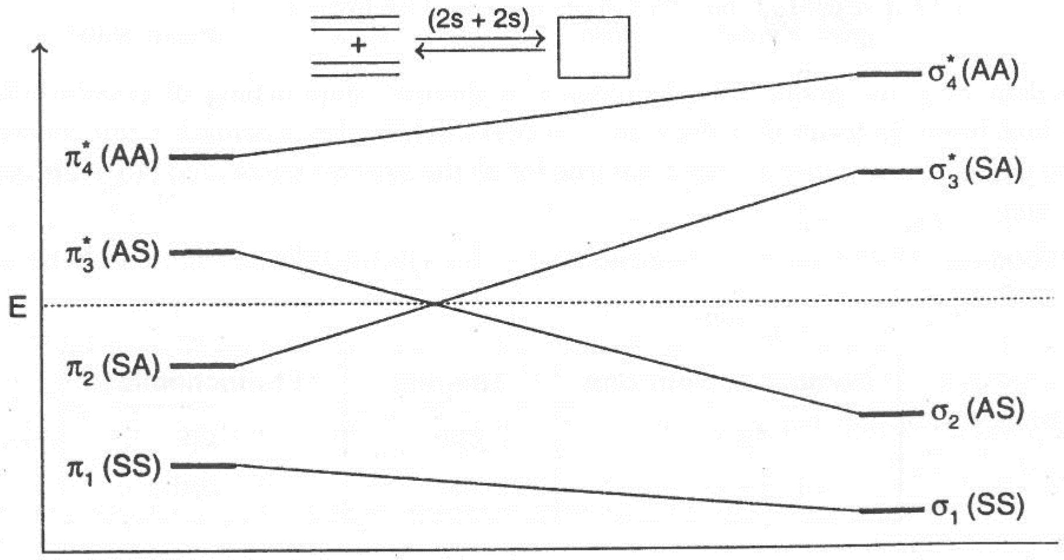
a) [2+2] cycloaddition reaction: The control of orbital symmetry in this cycloaddition may be illustrated by the cycloaddition of two ethylene molecules approaching each other vertically (2s+2s) to form a molecule of cyclobutane. Such a system has vertical and horizontal planes of symmetry which shall be referred to as 1 and 2 respectively.



In this reaction we are concerned with the four π orbitals (π, π bonding and π*, π* antibonding) of the two ethylene molecules and the four σ orbitals (σ, σ bonding and σ*, σ* antibonding) of cyclobutane. The symmetry properties of these orbitals are given below.



The correction diagram may now constructed by joining the reactant orbitals with the product orbitals of the same symmetry.



The following two conclusions can be drawn from this correlation diagram:

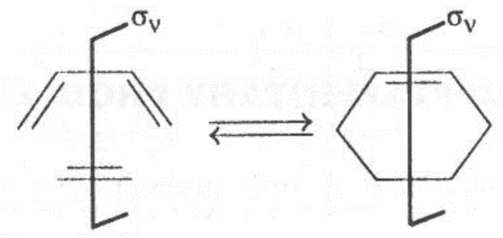
(i) The combination of two ground state ethylene molecules cannot result in the formation of ground state cyclobutane while conserving the orbital symmetry. Hence the thermal cycloaddition is symmetry-forbidden.

$$\pi_1^2\pi_2^2 \nleftrightarrow \sigma_1^2\sigma_3^{2*} \; ; \; \sigma_1^2\sigma_2^2 \nleftrightarrow \pi_1^2\pi_3^{2*}$$

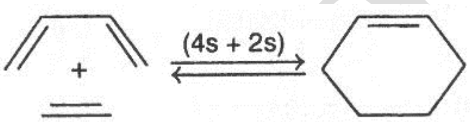
(ii) Since the first excited state of ethylene systems correlates with the first excited state of cyclobutane, the photochemical process (in either direction) is symmetry allowed.

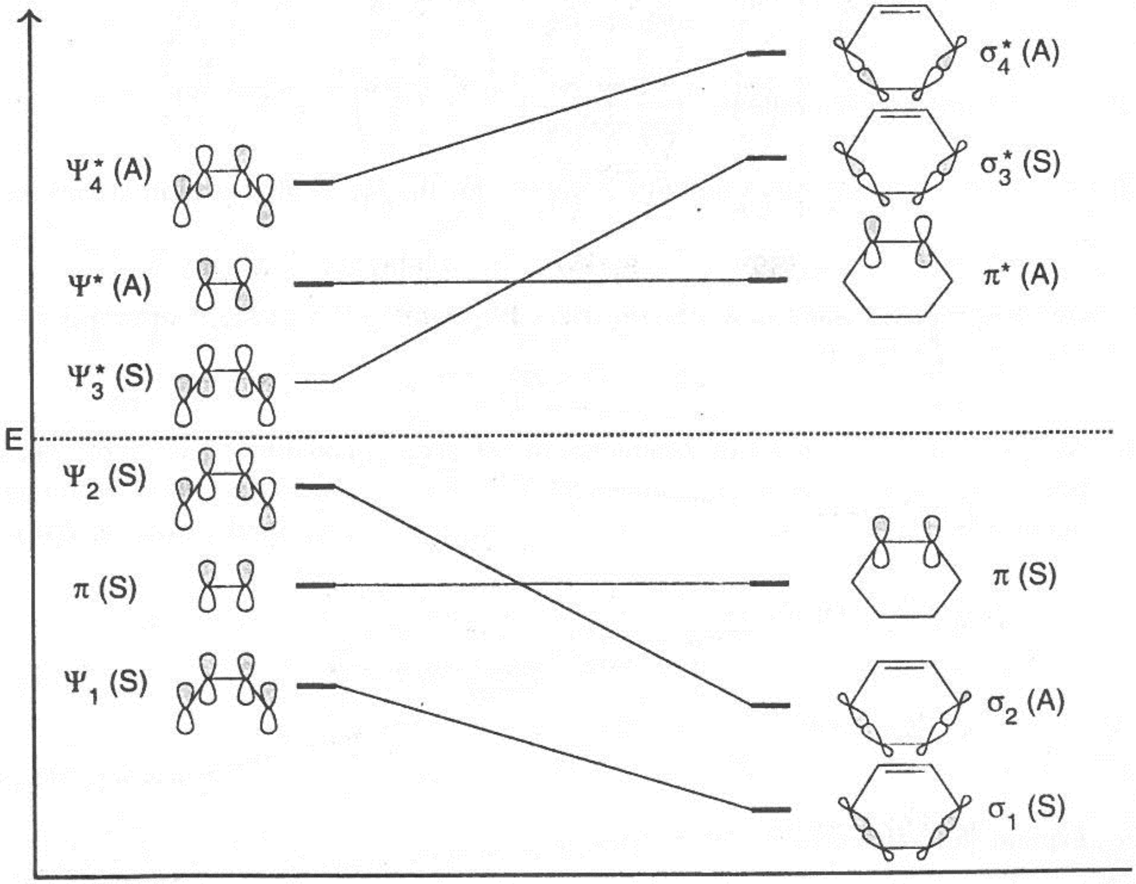
$$\pi_1^2\pi_2^2 \xrightarrow{h\nu} \pi_1^2\pi_2\pi_3^* \rightleftharpoons \sigma_1^2\sigma_2\sigma_3^* \xrightarrow{h\nu} \sigma_1^2\sigma_2^2$$

b) [4+2] cycloaddition reaction: The control of orbital symmetry in this cycloaddition reaction may be illustrated by the cycloaddition of one ethylene and one butadiene molecule approaching each other vertically (4s+2s) to form a molecule of cyclohexene. In this case, there is only a single vertical plane of symmetry.



The correlation diagram may now be constructed by joining the reactant orbitals with product orbitals of the same symmetry.





The following two conclusions can be drawn from this correlation diagram:

(i) Since the ground state orbitals of reactants correlate with the ground state orbitals of the product the thermal (4+2) cycloaddition (the Diels-Alder reaction) and cyclo reversion are symmetry-allowed processes.

$$\Psi_1^2\pi^2\Psi_2^2 \rightleftarrows \sigma_1^2\sigma_2^2\pi^2$$

(ii) Photochemical transformation is not possible because the first excited state of the reactants do not correlate with the first excited state of the product. Rather it correlates with the upper excited state of the product.

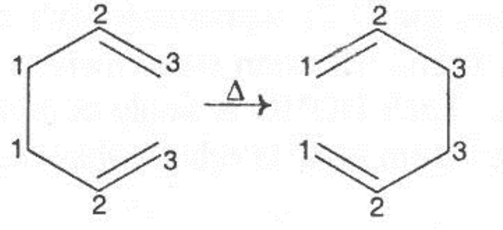
$$\Psi_1^2\pi_2\Psi_2^2 \xrightarrow{h\nu} \Psi_1^2\pi^2\Psi_2\Psi_3^* \not\leftrightarrow \sigma_1^2\sigma_2^2\pi\sigma_3^* ;\ \sigma_1^2\sigma_2^2\pi^2 \xrightarrow{h\nu} \sigma_1^2\sigma_2^2\pi\pi^* \not\leftrightarrow \Psi_1^2\pi^2\Psi_2\pi^*$$

22) What are sigmatropic rearrangements? What do you mean by the order [i, j] or [1, j] of a sigmatropic rearrangement? Give examples.

Solution:

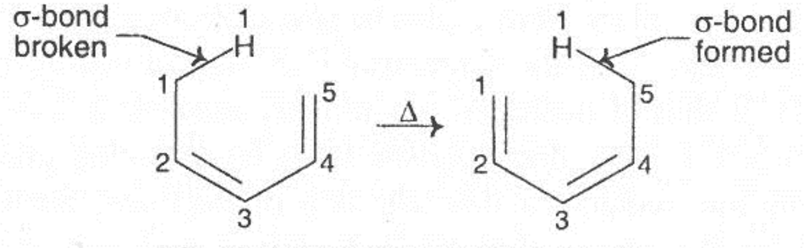
Pericyclic reactions in which a σ-bonded atom or group migrates from one end of a π-system to the other (equivalent to the migration of a σ-bond) or a σ-bond flanked by two π electron systems migrates to a new position within the molecule in an uncatalyzed intramolecular process are known as sigmatropic rearrangements.

When both the termini of a σ bond move, say one from C-1 to C-i and other from C-1 to C-j, it is referred to as [i, j] order of sigmatropic rearrangement. For example, in the following reaction, a σ-bond migrates from C-1 to C-3 position. It is, therefore, a sigmatropic change of the order [3+3] since i and j both correspond to 3.



A [3, 3] sigmatropic rearrangement

When an atom or group migrates unchanged through a π system, it is referred to as [1, j] order of sigmatropic rearrangement and this is because one end of the σ bond moves from C-1 to a carbon numbered j, but the other end remains attached to the migrating atom. For example, the following sigmatropic rearrangement is of the order [1,5] because hydrogen is migrated from C-1 to C-5 (j = 5); the other end of the σ-bond is still attached to hydrogen (i = 1).

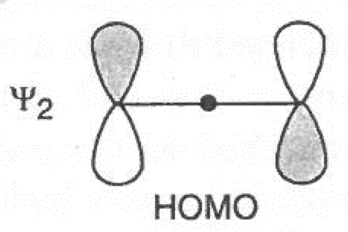


A [1, 5] sigmatropic rearrangement

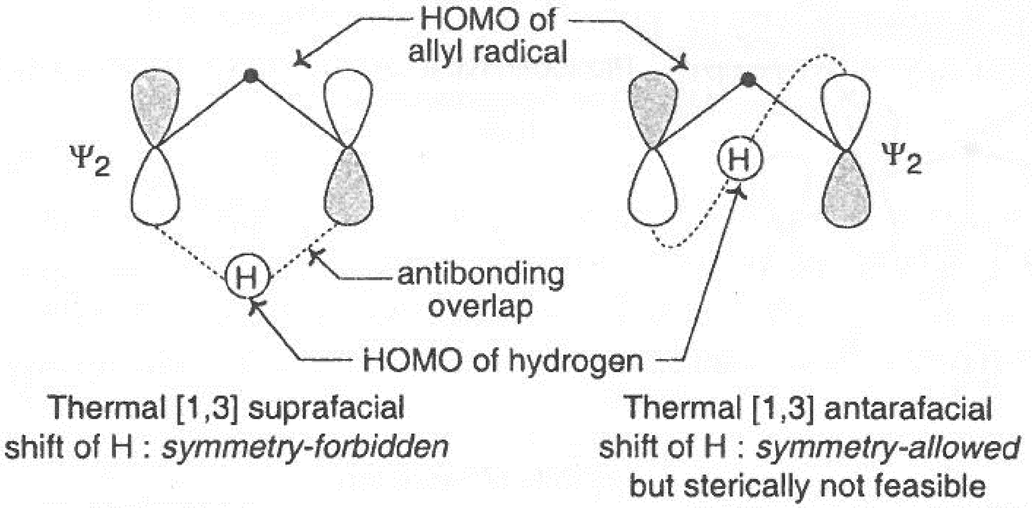
23) Thermal [1,3]–sigmatropic shift of hydrogen is not observed but photochemical [1,3] shift of hydrogen is facile. On the other hand, thermal [1,5] sigmatropic shift of hydrogen is facile but photochemical [1,5] shift of hydrogen is seldom observed. Explain these observations by FMO approach.

Solution:

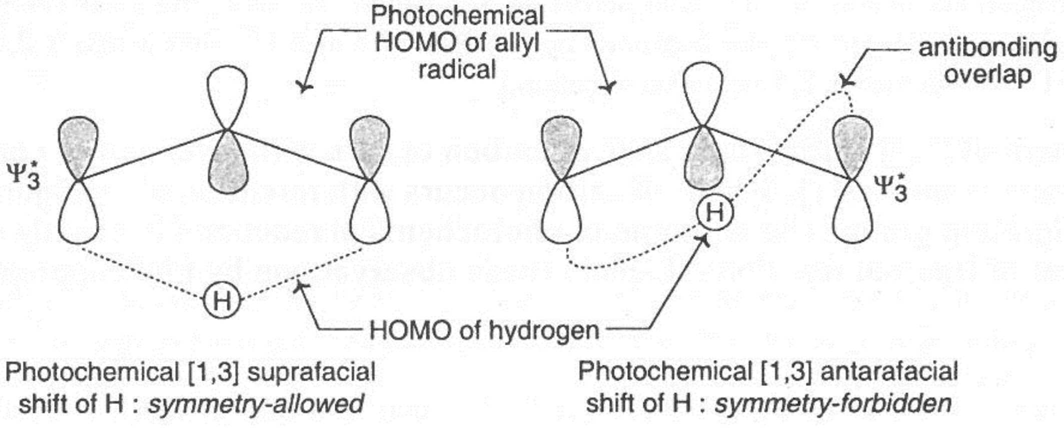
The frontier orbital analysis treats the [1,3] sigmatropic shift of hydrogen as the interaction of a hydrogen atom with an allyl radical. In the transition state, there is overlap between the HOMO of one component and HOMO of the other. Each HOMO is singly occupied and together they provide a pair of electrons. The HOMO of hydrogen atom is its 1s orbital which has only one lobe. The HOMO of allyl radical is as follows:



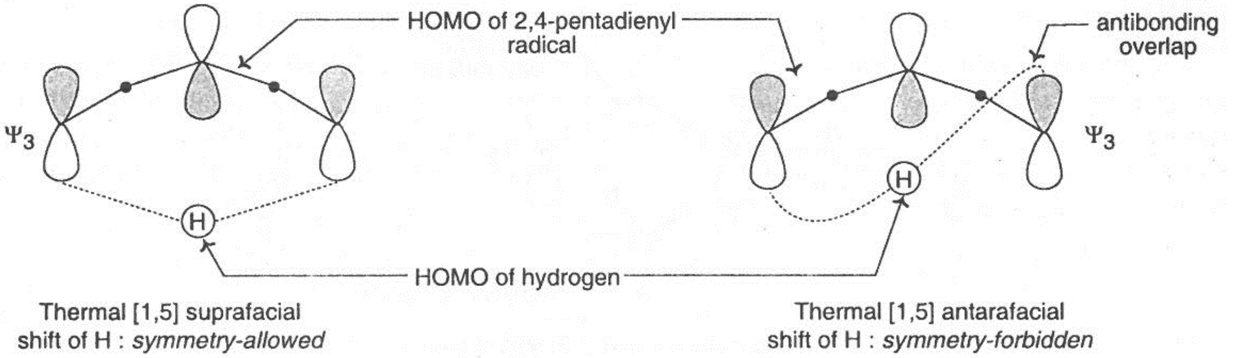
Migration of H atom must take place from a plus or from a minus to minus lobe, i.e., it must move to a lobe of same phase sign. Thus the suprafacial [1,3] shift of hydrogen is not symmetry-allowed. Although the antarafacial [1,3] shift of hydrogen is symmetry-allowed, it does not take place because it is sterically very difficult. In fact, for bridging opposite lobes by migrating proton the π framework is to be twisted far from planarity that requires for delocalization of electrons. Such a transition state is likely to be highly strained. It is for this reason thermal [1,3] shift of hydrogen is not at all observed.



In photochemical reaction promotion of an electron from Ψ_2 to Ψ_3^* takes place and now it is Ψ_3^* which is HOMO of the allyl radical. Suprafacial pathway for [1,3] shift is now symmetry-allowed and antarafacial pathway is symmetry-forbidden. Since suprafacial migration does not involve any distortion of strain in the concerted transition state, photochemical [1,3] shift of hydrogen is facile.

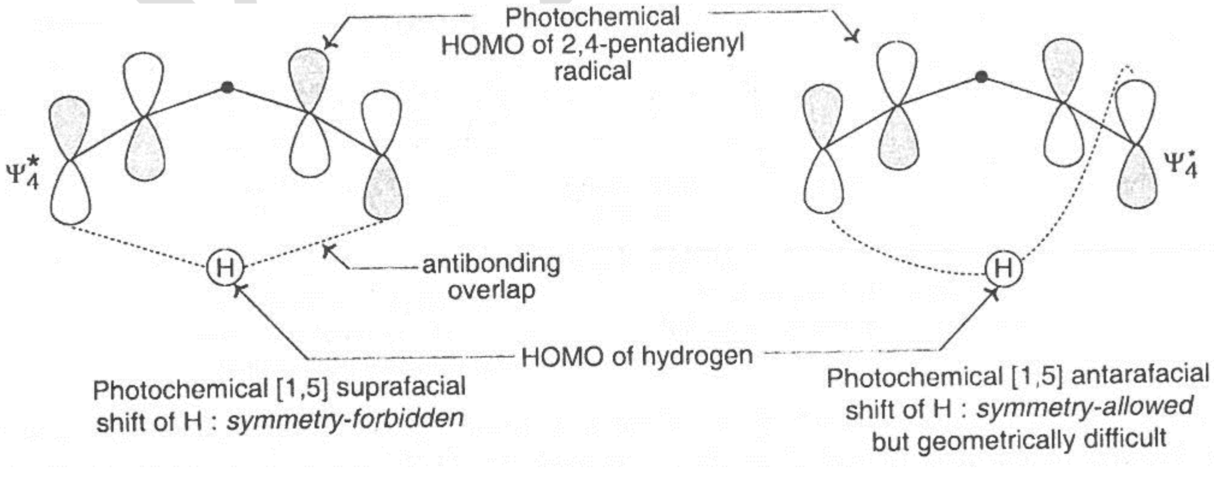


[1,5] shift of hydrogen is considered as the interaction of a hydrogen atom with 2,4-pentadienyl radical. Thermal [1,5] suprafacial shift of hydrogen is symmetry-allowed because in this reaction hydrogen moves to a lobe of same phase sign suprafacially. However, the antarafacial shift is symmetry-forbidden.



Since suprafacial migration does not involve any distortion or strain in the transition state, thermal [1,5] shift of hydrogen is facile and very common.

In photochemical reaction, it is Ψ_4^* which is the HOMO of the pentadienyl radical and in this case antarafacial shift of hydrogen is symmetry-allowed but suprafacial shift of hydrogen is symmetry-forbidden. Although symmetry-allowed, the antarafacial shift is extremely difficult from steric point of view and for this reason, photochemical [1,5] shift of hydrogen is seldom observed.

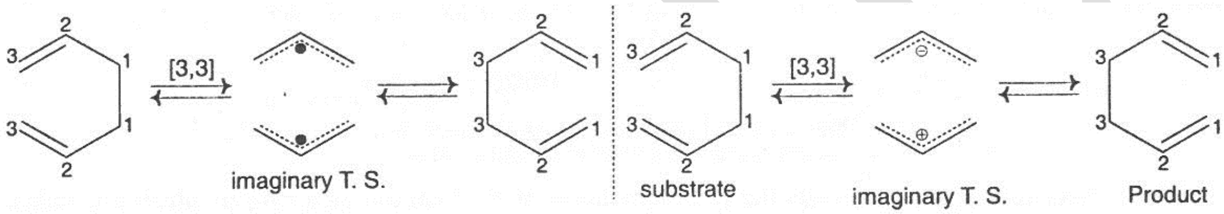


Cope rearrangement

1,5-Dienes isomerizes in a [3,3] sigmatropic rearrangement known as cope rearrangement. Explain by orbital symmetry analysis why this rearrangement is a relatively facile thermal process but not commonly observed on photochemical activation.

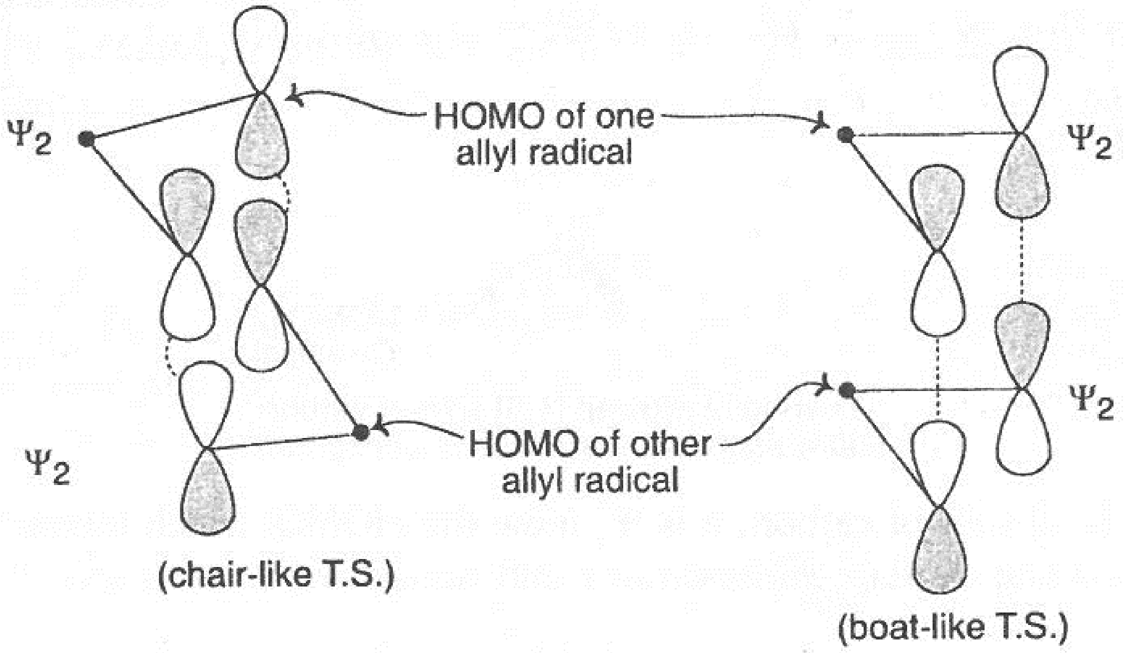
Solution:

The transition state for [3,3] sigmatropic rearrangement can be visualized as the interaction of two allyl free radical of a cation and an anion.



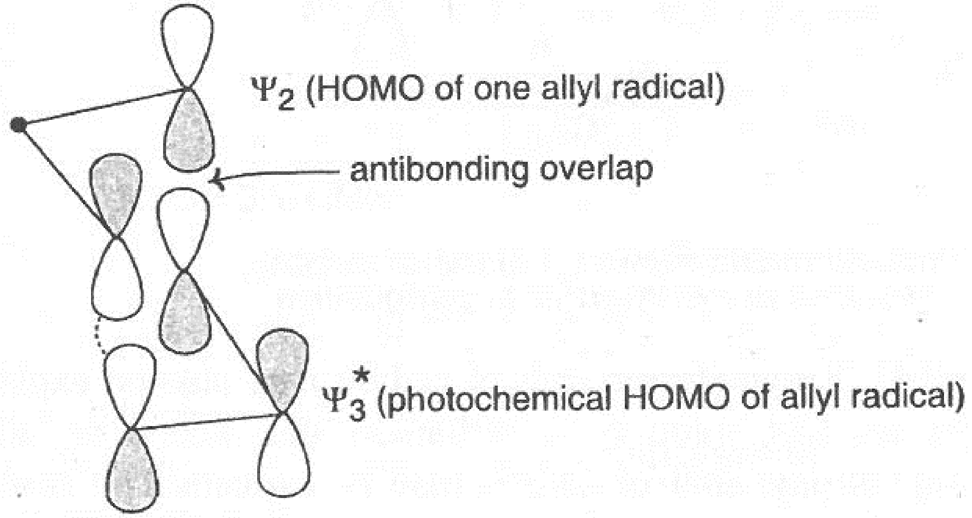
The frontier orbitals involved are the HOMOs of two free radicals or the HOMO of the anion and LUMO of the cation, which are the same orbital (Ψ_2) of the allyl system. The two MOs involved achieve bonding overlap when the [3,3] sigmatropic rearrangement occurs suprafacially on both the components. (The antarafacial interaction with respect to any of the component is not energetically feasible and so does not occur even when there is bonding interaction). Because of symmetry allowed supra-supra interaction, this rearrangement is relatively facile thermally.

Although a chair-like as well as a boat-like transition state may be envisaged allowing supra-supra interaction, the reaction takes place through the more stable chair-like transition state preferably.



Thermally allowed *supra-supra* interaction

When irradiated, promotion of one electron from the HOMO to the LUMO of allyl radical takes place. Therefore, Ψ_3^* is the HOMO of one component and this interacts with Ψ_2 of the other. Now an orbital analysis shows that there is one antibonding interaction. Thus the reaction is photochemically forbidden.

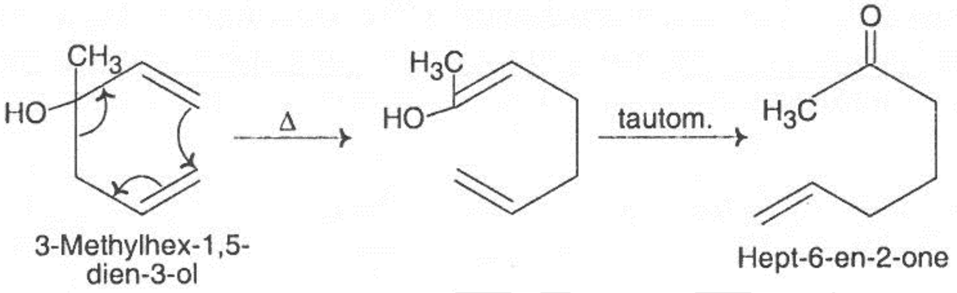


Photochemically forbidden *supra-supra* interaction

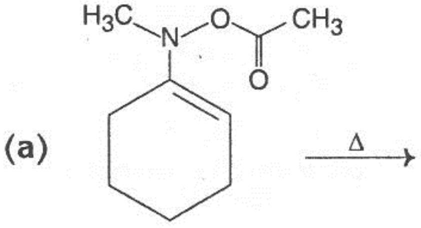
24) What is an oxy-cope rearrangement? Give an example.

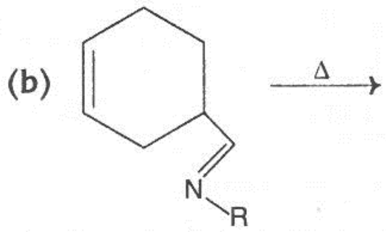
Solution:

It a hydroxyl group is present at C-3 position of a 1,5-diene system, then it undergoes cope rearrangement to give an enol which readily tautomerizes to a ketone. This is known as the oxy-cope rearrangement. For example, 3-methylhex-1,5-diene-3-ol undergoes oxy-cope rearrangement to give hept-6-en-2-one.



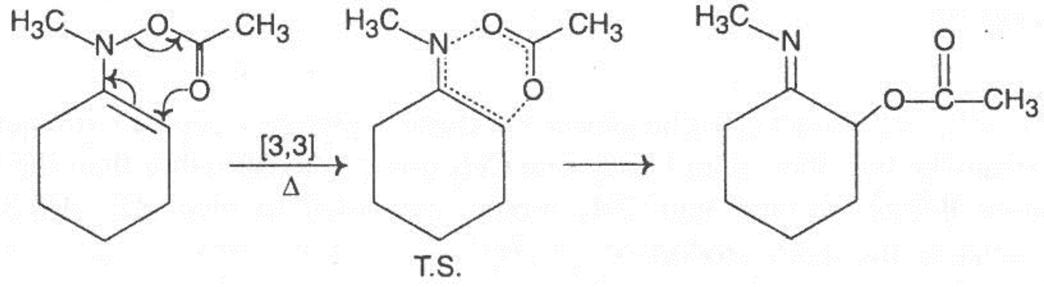
25) Predict the product and suggest a mechanism of each of the following variants of Cope rearrangement:



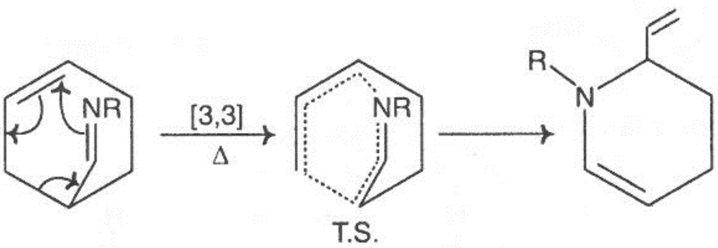


Solution:

(a) This variant of Cope rearrangement occurs as follows:

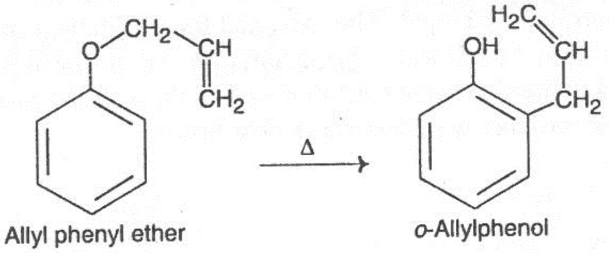


(b) This aza-Cope rearrangement occurs as follows:



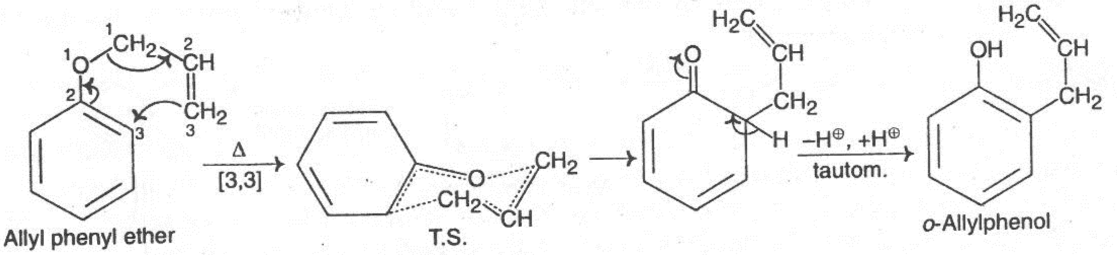
Claisen rearrangement

One of the oldest [3,3]-sigmatropic rearrangements was discovered by Claisen and is known as the Claisen rearrangement. It is a thermally induced transformation of allyl phenyl ethers to phenolic derivatives. Give the mechanism of the following reaction and offer an experiment to prove that the allyl chain undergoes an inversion.

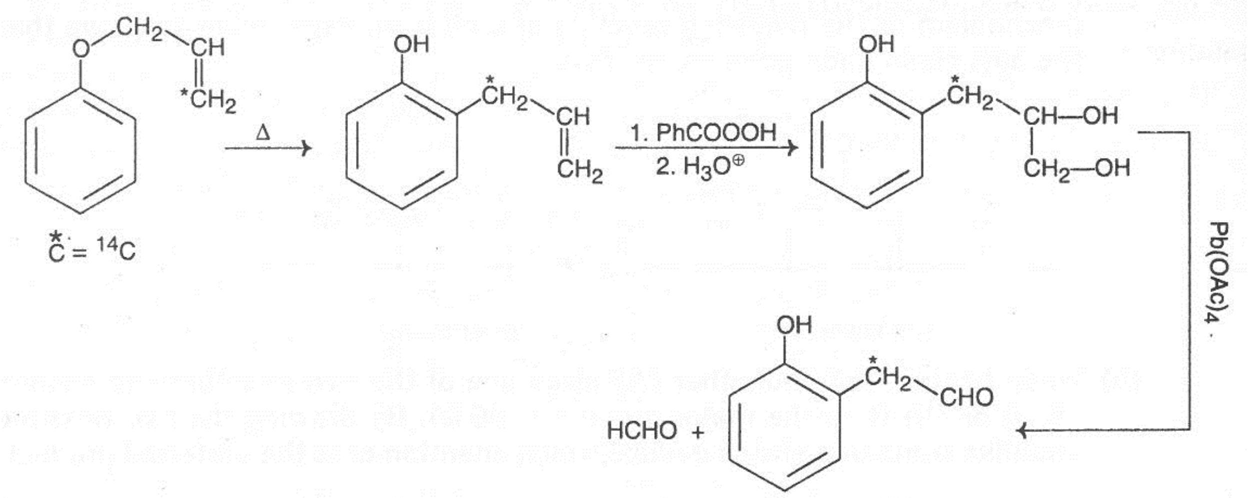


Solution:

Allyl phenyl ether undergoes Claisen rearrangement *via* a chair-like transition state to give an intermediate ortho-dienone which rapidly tautomerizes to give the more stable *o*-allyl phenol.



That the allyl chain undergoes an inversion has been proved by ^{14}C labelling experiment. When the following ^{14}C labelled allyl phenyl ether is heated and the rearranged ortho-allylphenol is subjected to hydroxylation with peracid-dilute acid and then oxidised with lead tetraacetate, HCHO is obtained without ^{14}C. This observation suggests that the allyl chain must undergo an inversion during migration.



26) Write down the selection rules for sigmatropic reactions.

Solution:

The selection rules for sigmatropic reactions may be gives as follows:

(a) Rules for the migration of a H-atom:

Number of electrons (1+j)	**Mode of Activation**	**Allowed Stereochemistry**
4n	Thermal Photochemical	Antarafacial Suprafacial
4n+2	Thermal Photochemical	Suprafacial Antarafacial

n = 1,2,3,… etc.

(b) Rules for other thermal sigmatropic reactions:

Number of electrons	**Allowed Stereochemistry**	
	Generalized stereochemistry	**Stereochemistry of single-atom migrations**
4n	Supra-antara Antara-supra	Supra-inversion Antara-retention

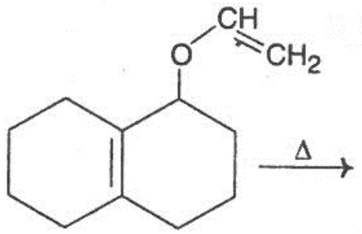
4n+2	Supra-supra Antara-antara	Supra- retention Antara- inversion

n = 1,2,3,… etc.

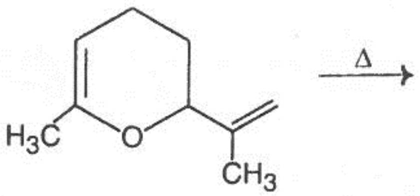
27) Predict the product and suggest a mechanism for each of the following reactions:

(a) $(CH_3)_2C = CH—CH_2—O—CH = CH_2 \xrightarrow{\Delta}$

(b)

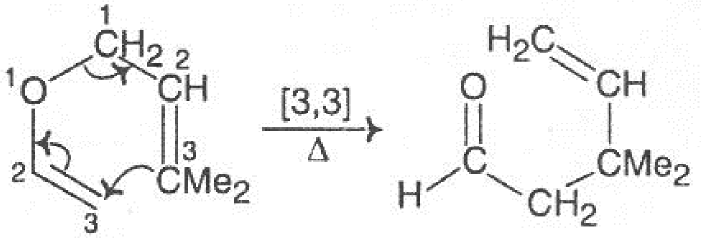


(c)

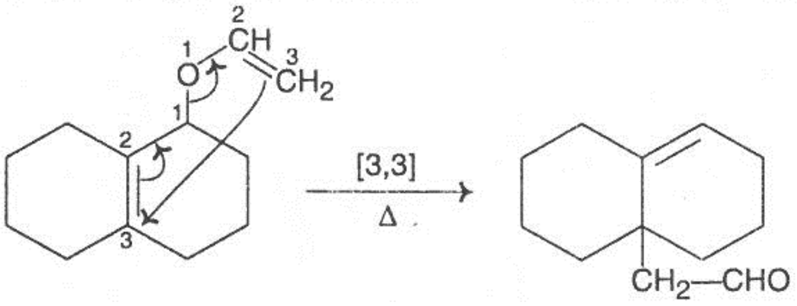


Solution:

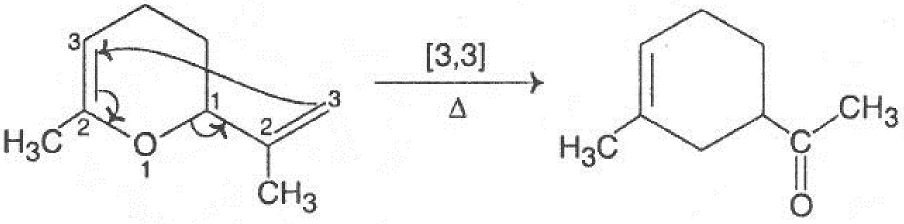
(a) This aliphatic allylic vinylic ether undergoes Claisen rearrangement (a [3,3] sigmatropic shift) to an unsaturated aldehyde.



(b) This allylic vinylic ether also gives an unsaturated aldehyde by Claisen rearrangement.

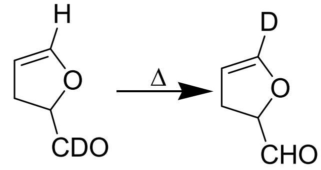


(c) This allylic vinylic ether undergoes Claisen rearrangement to give an unsaturated ketone.

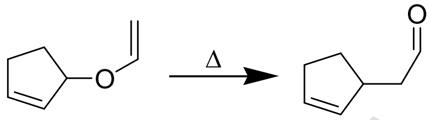


28) Provide mechanism for the following transformations.

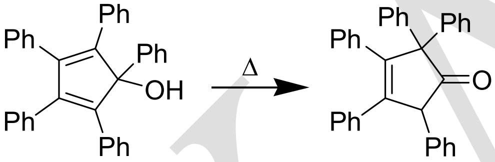
(a)



(b)

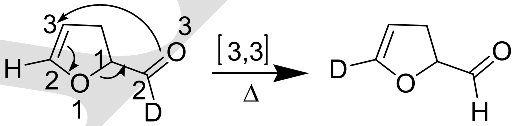


(c)

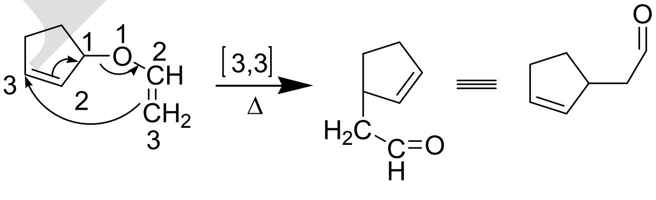


Solution:

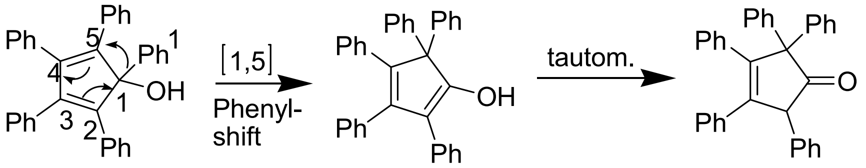
(a)



(b)

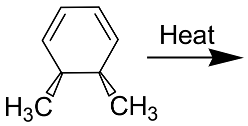


(c)

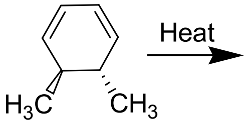


29) Predict the products in the following reactions and account.

(i)

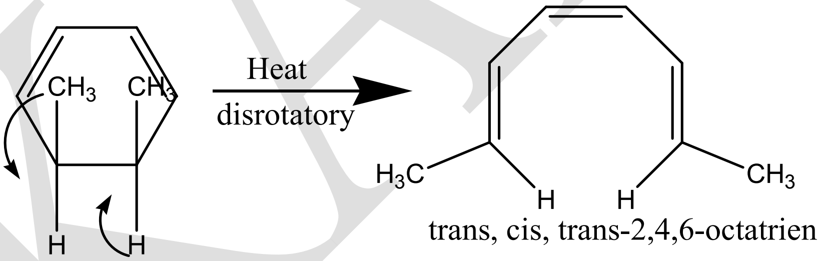


(ii)



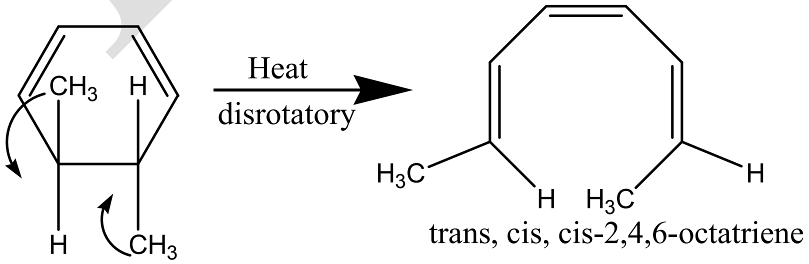
Solution:

(i) When heated cis-5,6-dinethyl-1,3-cyclohexadiene, a 6π electron system [(4n+2)π, where n=1], undergo disrotatory ring opening to give trans, cis, trans-2,4,6-octatriene.



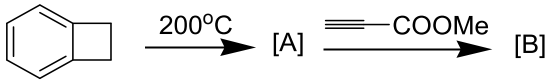
trans, cis, trans-2,4,6-octatriene

(ii) When heated trans-5,6-dimethyl-1,3-cyclohexadiene, a 6π electron system [(4n+2)π, where n=1], undergo disrotatory ring opening to give trans, cis, cis-2,4,6-octatriene.

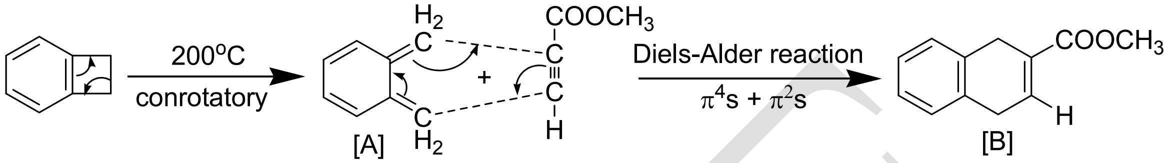


trans, cis, cis-2,4,6-octatriene

30) Identify the products/reagents (A-B) in the following sequence.

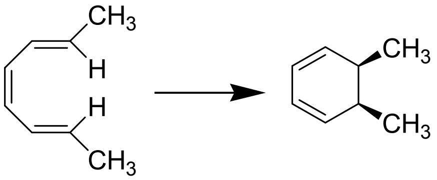


Solution:

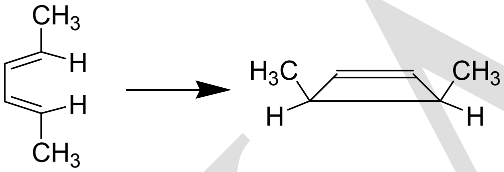


31) For each of the following concerted reactions, specify the conditions and mode of rotation.

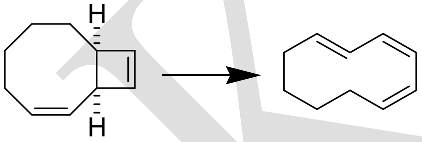
(i)



(ii)

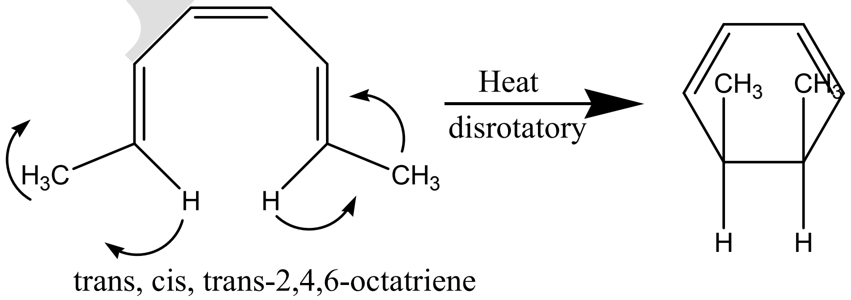


(iii)

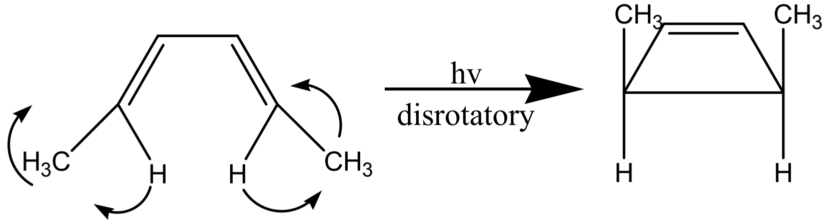


Solution:

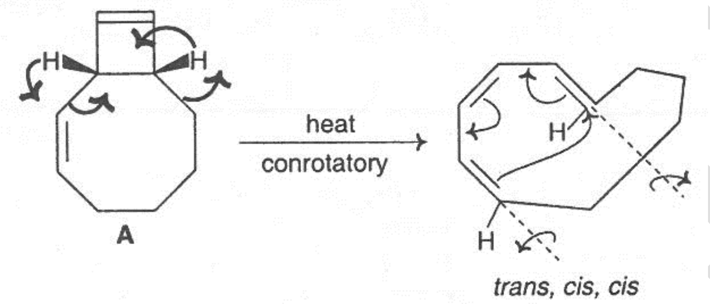
(i)



(ii)



(iii) When heated, the compound A, a 4π electron system (4nπ, where n=1), undergoes conrotatory ring opening to form trans, cis, cis-1,3,5-cyclodecatriene.



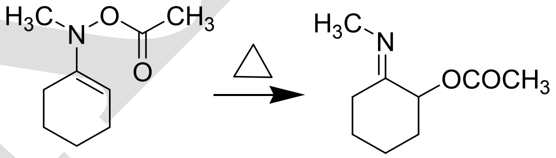
Reference:

1. Tewari, N. (2011). *Advanced Organic Reaction Mechanism* (III Edition). Kolkata: Books and Allied (P) Ltd.

POSSIBLE QUESTIONS

PART-B (Each Question Carry Two Marks)

1. What are pericyclic reactions? Why are they called so?
2. Define cycloaddition reactions.
3. Draw the π-molecular orbitals of the allyl system (cation, radical and anion) and identify the HOMO and LUMO.
4. Define electrocyclic reactions.
5. Write down the characteristic features of electrocyclic and cycloaddition reactions.
6. What do you understand by bonding and antibonding molecular orbitals?
7. Can you suggest a stereospecific method for converting trans-5, 6-dimethyl-1, 3-cyclohexadiene into cis-5,6-dimethyl-1,3-cyclohexadiene?
8. Draw the л-molecular orbitals of 2,4-pentadienyl system (cation, radical and anion) and identify the HOMO and LUMO.
9. Write down the selection rules for cycloaddition reaction.
10. Write down the Woodword-Hoffmann rules (selection rules) for electrocyclic reactions.
11. How cycloaddition reactions are classified by its stereochemistry with respect to the plane of each reacting molecules?
12. Predict the product and suggest a mechanism of the following variant of Cope rearrangement.



13. Define sigmatropic reactions.
14. How many approaches have been made to explain the stereochemical results of pericyclic reactions?
15. Two molecular orbitals are of particular importance in understanding pericyclic reactions. What are these orbitals? Why are they termed Frontier orbitals?

PART-C (Each Question Carry Six Marks)

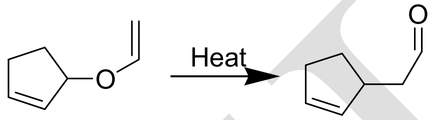
1. (i) Discuss the important features of pericyclic reactions.

   (ii) In electrocyclic reactions for 4π electron systems Con rotation is thermally allowed and Dis rotation is photochemically allowed. Illustrate with examples.

2. Draw the orbital correlation diagram for the π2s+ π2s cycloaddition reaction and find out whether the reaction is thermally allowed or not.

3. (i) Write notes on Cope rearrangement.

   (ii) Indicate the migrating bond and assign [i, j] value for the following conversion.

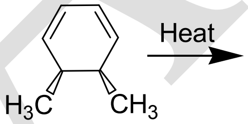


   (iii) Illustrate a 1, 3 –sigmatropic rearrangement with an example.

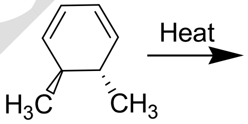
4. Explain how the correlation diagram approach is useful in predicting the mechanism of electrocyclic reactions considering the Con rotary ring closure of 1, 3, 5-hehatriene as an example.

5. Predict the products in the following reactions and account.

   (i)

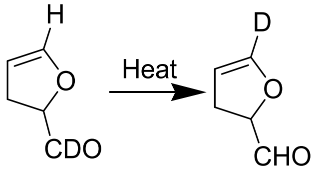


   (ii)

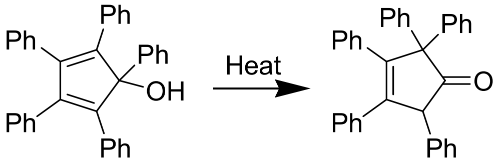


   (iii) Indicate the mechanism for the following conversions.

   (a)



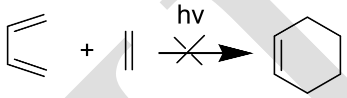
(b)



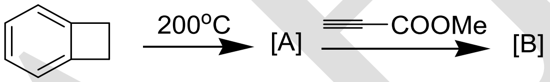
6. Construct the orbital correlation diagrams for the π4s + π2s cycloaddition and based on that state whether the reaction is allowed under thermal or photochemical condition.

7. (i) Draw π orbitals of buta-1,3-diene and ethylene and identify their HOMO and LUMO.

(ii) Using "Frontier orbital concept" explain why the $\pi^{4s} + \pi^{2s}$ cycloaddition given below is photo chemically not allowed?



(iii) Identify the products/reagents (A-B) in the following sequence.

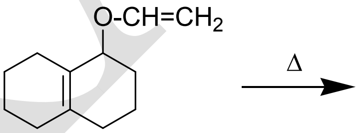


8. Predict the product and suggest a mechanism for each of the following reactions.

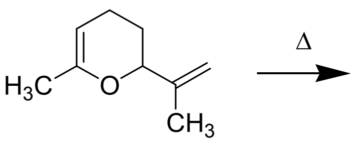
(i)

$$(CH3)_2C=CH-CH_2-O-CH=CH_2 \xrightarrow{\Delta}$$

(ii)



(iii)

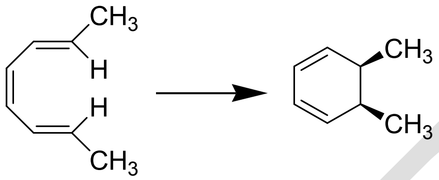


9. Discuss the important aspects to the stereochemistry of the Diels-Alder reaction.

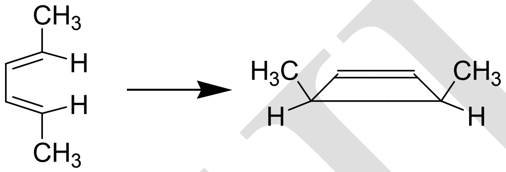
PART-D (Each Question Carry Ten Marks)

1. For each of the following concerted reactions, specify the conditions and mode of rotation.

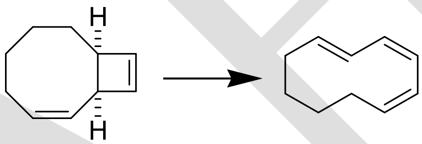
(i)



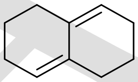
(ii)



(iii)



(iv) The diene,



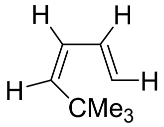
does not undergo Diels-Alder reaction.

2. (a) Furan acts as a diene in the Diels-Alder reaction but pyrrole normally does not. Explain

(b) Why does anthracene undergo the Diels-Alder reaction but naphthalene does not?

(c) Explain why the following compounds do not undergo Diels-Alder reaction:

(i)



(ii)

$H-C\equiv C-C\equiv C-H$

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DEPARTMENT OF CHEMISTRY

UNIT-V

PERICYCLIC REACTIONS

PART-A–Multiple Choice Questions
(Each Question Carry One Mark) (Online Examinations)

1. The electrocyclic reaction for the ground state of hexatrienes?

a) conrotatory **b) disrotatory**

c) conrotatory or disrotatory depending on the temperature at which reaction is carried out

d) cannot be predicted

2. The thermal ring opening reactions of cyclobutenes are

a**) conrotatory** b) disrotatory

c) conrotatory or disrotatory depending on the temperature at which reaction is carried out

d) cannot be predicted

3. Claisen rearrangement is an example for

a) [2,3] sigmatropic rearrangement b) [1,3] sigmatropic rearrangement

c) [1,5] sigmatropic rearrangement **d) [3,3] sigmatropic rearrangement**

4. The π-molecular orbitals of allyl anion, the LUMO ground state is

a) ψ_1 b) ψ_2 c) ψ_3 **d)** ψ_3^*

5. In the reaction of cyclopentadiene with acrylate ester giving Diels-Alder reaction products, the interacting frontier orbitals are

a) HOMO of a diene and LUMO of a dienophile

b) HOMO of a dienophile and LUMO of a diene

c) HOMO of a diene and HOMO of a dienophile

d) LUMO of a diene and LUMO of a dienophile

6. Diels-Alder reaction normally yields endo-adduct as a major product. This is due to

a) higher stability of the products b) faster rate of formation of the endo product

c) steric hindrance **d) secondary orbital interactions between a diene and a dienophile**

7. The conversion of vinylcyclopropane to cyclopentene upon heating is an example of

a) [3,3] -sigmatropic rearrangements **b) [1,3]-sigmatropic rearrangements**

c) [1,5]- sigmatropic rearrangements d) [1,2] -sigmatropic rearrangements

8. Diels-Alder reaction is a

a) [2+2] thermal cyclization b) [4+2] photoaddition

c) [4+2] cycloaddition d) [3+3] cycloaddition

9. In the [4+2] cycloaddition of 1,3-butadiene and ethylene

a) overlap of the HOMO of butadiene with the LUMO of ethylene

b) overlap of the HOMO of ethylene with the LUMO of butadiene

c) overlap of the HOMO of butadiene and ethylene with the LUMO of ethylene and butadiene

d) overlap of the LUMO of butadiene with the LUMO of ethylene

10. Select the incorrect statement from the given statements.

a) HOMO is the highest occupied molecular orbital

b) in conrotatory motion bonds rotate in the same direction

c) Diels-Alder reaction is a [4+2] cycloaddition

d) in the suprafacial reaction both bonds are formed on the opposite face of the component

11. Cope rearrangement is

a) [2,3] sigmatropic rearrangement b) [3,2] sigmatropic rearrangement

c) [3,3] sigmatropic rearrangement d) [1,3] sigmatropic rearrangement

12. Thermolysis of allyl phenyl ether generate

a) o-allylphenol only b) o-and p-allylphenol only

c) o-,m- and p-allylphenols d) m-allylphenol only

13. The concerted photochemical reaction between two olefins leading to a cyclobutane ring is

a) $\pi 2s+\pi 2a$ cycloaddition b**) $\pi 2s+\pi 2s$ cycloaddition**

c) $\sigma 2s+\sigma 2s$ cycloaddition d) $\pi 2s+\sigma 2a$ cycloaddition

14. How many approaches have been made to explain the stereochemical results of pericyclic reaction?

a) one b) two **c) three** d) four

15. The π-molecular orbitals of 1,3,5-hexatriene the HOMO of ground state is

a) ψ_1 b) ψ_2 c) ψ_3* **d) ψ_3**

16. The ground state HOMO of 1, 3, 5-hexatriene is

a) bonding molecular orbital b) anti bonding molecular orbital

c) non- bonding molecular orbital d) sigma bonding molecular orbital

17. The half of the molecular orbitals having lower energies then the isolated p-orbitals are called

a) bonding molecular orbital b) anti bonding molecular orbital

c) non- bonding molecular orbital d) sigma bonding molecular orbital

18. When HOMO and LUMO overlap in the different phases leading to antibonding interaction, then it is called a

a) symmetry allowed **b) symmetry forbidden**

c) geometrically allowed d) geometrically forbidden

19. A thermal [1,3]-suprafacial shift of hydrogen is

a) symmetry forbidden b) symmetry allowed

c) geometrically allowed d) geometrically forbidden

20. 1,5-diene isomerizes in a [3,3] sigmatropic rearrangement known as

a) Claisen rearrangement b) Ene reaction

c) Fries rearrangement **d) Cope rearrangement**

21. The anti-bonding orbitals corresponding to sigma bonds are called

a) σ* b) σ c) π* d) π

22. A typical example for the π-π* transition is

a) butane **b) 1,3- butadiene** c) butyl alcohol d) ethane

23. A concerted reaction does not involve the formation of

a) intermediates b) free radicals c) complex d) ions

24. Pericyclic reactions are_______in nature.

a) strereospecific b) radioactive c) optically active d) additive

25. Electrocyclic reactions are

a) irreversible **b) reversible** c) spontaneous d) non-spontaneous

26. Electrocyclic reaction is

a) intermolecular reaction **b) intramoleculer reaction**

c) electrophilic reaction d) nucleophilic reaction

27. In electrocyclic reaction both the orbitals rotate in the opposite direction ring closure is

a) conrotatory **b) disrotatory** c) bisrotatory d) birotatory

28. In electrocyclic reaction both the orbitals rotate in same direction ring closure is

a) conrotatory b) disrotatory c) bisrotatory d) birotatory

29. Example for cycloaddition reaction is

a) Wittig reaction b) Ene reaction **c) Diels-Alder reaction** d) Kolbs reaction

30. A cycloaddition reaction occurs across the same face of the π system, the reaction is said to be

a) suprafacial b) antarafacial c) heterofacial d) homofacial

31. A cycloaddition reaction occurs across the opposite face of the π system, the reaction is said to be

a) suprafacial **b) antarafacial** c) heterofacial d) homofacial

32. Cope rearrangement is a [3,3] sigmatropic rearrangement of a

a) 1,3- diene **b) 1,5 diene** c) 1,4-diene d)2 ,5-diene

33.Claisen rearrangement is a [3,3] sigmatropic rearrangement of a

a) allyl phenyl ether b) vinyl ether

c) allyl ether d) acetylenic ether

34. Pericyclic reaction can be promoted by

a) light b) heat **c) light and heat** d) UV rays

35. In node region the probability of finding an electron is

a) 0 b) 1 c) -1 d) 0.5

36. Selection rules for pericyclic reactions are known as

a) Hofmann rule b) Bredtis rule

c) Saytzeff rule **d) Woodward- Hofmann rule**

37. A sigma bond is broken, a new sigma bond is formed and the π electron rearranges and it is known as

a) electrocyclic reaction b) cycloaddtion reaction

c) sigmatropic reaction d) chelotropic reaction

38. sigmatropic rearrangement have_____transistion state

a) cyclic b) acyclic c) non-cyclic d) alicyclic

39. Conrotatory ring closure of 2E, 4Z- hexadiene leads to the

a) cis product b) trans product c) anti product d) syn product

40. Cis, trans-2,4- hexadiene undergoes thermal cyclization to give

a) trans-3,4- dimethyl cyclo butane **b) cis- 3,4- dimethyl cyclo butane**

c) cis- 5,6- dimethyl-1,3-cycrohexadiene d) trans-5,6- dimethyl-1,3- cyclohexadiene

41. Pericylic reactions are divided into_______categories

a) 3 b) 4 **c) 5** d) 6

42. According to Woodward-Hofmann rules 4nπ electrons under cyclization allowed stereochemistry is

a) conrotatory b) disrotatory c) suprafacial d) antarafacial

43. How many nodes are possible for ground state, HOMO of 1, 3,5-hexatriene is

a) 1 **b) 2** c) 3 d) 4

44. How many nodes are possible for excited state, HOMO of 1, 3,5-hexatriene is

a) 0 b) 1 c) 2 **d) 3**

45. The π-molecular orbitals of 1,3,5- hexatriene the HOMO of excited state is

a) ψ_1 b) ψ_2 c) ψ_3^* **d) ψ_4^***

46. The π-molecular orbitals of 1,3,5-hexatrine the LUMO of ground state is

a) ψ_3 b) ψ_4 **c) ψ_4^*** d) ψ_2^*

47. The π-molecular orbitals of 1,3,5-hexatrine the LUMO of excites stage is

a) ψ_2 b) ψ_4^* **c) ψ_5^*** d) ψ_6^*

48. The π-molecular orbitals of 2,4-pentadienyl cation the HOMO of ground stage is

a) ψ_1 **b) ψ_2** c) ψ_3 d) ψ_4^*

49. The π-molecular orbitals of 2,4-pentadienyl cation the LUMO of ground stage is

a) ψ_1 b) ψ_2 **c) ψ_3** d) ψ_4^*

50. The half of the molecular orbital having higher energies than the isolated p-orbitals are called

a) bonding molecular orbitals **b) anti-bonding molecular orbitals**

c) non-bonding molecular orbital d) sigma bonding molecular orbital

51. The π-molecular orbitals of allyl cation the HOMO of ground state is

a) ψ_1 b) ψ_2 c) ψ_3^* d) ψ_2^*

52. The π-molecular orbitals of allyl cation the LUMO of ground state is

a) ψ_2 **b) ψ_2** c) ψ_4^* d) ψ_5^*

53. The π-molecular orbitals of 2,4-pentedienyl radical the HOMO of ground state is

a) ψ_2 **b) ψ_3** c) ψ_4^* d) ψ_5^*

54. The π-molecular orbitals of 2,4-pentedienyl radical the LUMO of ground state is

a) ψ_2 b) ψ_3^* **c) ψ_4^*** d) ψ_5^*

55. Which transition state is more stable in cope rearrangement?

a) chair like transition state b) boat like transition state

c) twist boat like transition state d) half chair like transition state

56. The transition state for [3,3]–sigmatropic reaction can be visualized as the interaction of

a) two cations b) two anions

c) two allyl free radical d) one allyl free radical

57. The oxy-cope rearrangement which position of 1,5-diene system having hydroxyl group?

a) C-1 position b) C-2 position

c) C-3 position d) C-4-position

58. The 3-methyl hex-1,5-diene-3-ol undergoes oxy-cope rearrangement to give

a) hept-6-en-2-one b) hept-5-en-2-one

c) hept-4-ene-1-one d) hept-3-ene-3-one

59. Thermal [1,5]- suprafacial shift of hydrogen is

a) symmetry allowed b) symmetry-forbidden

c) geometrically allowed d) geometrically forbidden

60. The π- molecular orbitals of allyl anion, the HOMO of ground state is

a) ψ_1 **b) ψ_2** c) ψ_3 d) ψ_2^*

Reg. No……………….

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(For the candidates admitted from 2017 & onwards)

PG DEGREE EXAMINATION, JANUARY 2018

SECOND SEMESTER

INTERNAL TEST-I

CHEMISTRY

ORGANIC CHEMISTRY-II
(Rearrangements, Reactions, Photochemistry and Pericyclic Reactions)

Time: 2 hours **Maximum: 50 marks**
Date: 29-01-2018 **Subject code: 17CHP201**

PART- A (20 x 1=20 Marks)
Answer All the Questions

1. Reactions involving the change in the carbon skeleton through the rearrangement of the carbocation intermediate are collectively known as

a) Pinacol-pinacolone rearrangement b) Wagner-Meerwein rearrangement
c) Wolff rearrangement d) Fries rearrangement

2. Bicyclic alkenes may be prepared by using

a) Wolff rearrangement b) Fries rearrangement
c) Stevens rearrangement d) Pinacol-Pinacolone rearrangement

3. The rearrangement reaction that involves nitrene intermediate is

a) Beckmann rearrangement b) Wolff rearrangement
c) Pinacol-Pinacolone rearrangement d) Favorskii rearrangement

4. The Favorskii rearrangement involves the formation of which ring as an intermediate

a) four membered b) five membered c) three membered d) six membered

5. The example for free radical rearrangement is

a) Photo- Fries rearrangement b) Fries rearrangement
c) Wolff rearrangement d) Favorskii rearrangement

6. An important application of the benzidine rearrangement is

a) synthesis of amines b) synthesis of acids
c) synthesis of amides d) synthesis of dyes

7. The Favorskii rearrangement cyclopropanone intermediate has been trapped as an adduct with

a) thiophene b) pyrrole c) furan d) pyridine

8. Which one is used as a solvent in Chapmann rearrangement?

a) methanol b) ethanol c) hexane d) tetra-glyme

9. Allenes belong to a class of compounds called

a) ketene b) cumulenes c) carbene d) nitrene

10. The restricted rotation of benzene ring is also responsible for the chirality of other aromatic compounds, which are called

a) allenes b) ansa compounds c) cyclophanes d) biphenyls

11. The R and S nomenclature is mainly based on

a) Prelog's rule b) Cram's rule c) Fajan's rule d) Sequence rule

12. The preferred conformation of 1,2,2,6,6-pentamethyl-4-hydroxy-4-phenylpiperidine is

a) chair conformation b) alternate chair conformation
c) boat conformation d) twist boat conformation

13. The meso compounds are optically inactive due to presence of the

a) plane of symmetry b) rotation-reflection symmetry
c) centre of symmetry d) alternative axis of symmetry

14. In the boat conformation of cyclohexane, the most destabilizing interaction is

a) eclipsing b)1,3-diaxial c) 1,3-diequatorial d) flagpole-flagpole

15. IUPAC name of decalin is

a) bicyclo[4.4.0] decane b) cyclo[4.4.0] decane
c) bicyclo[4.4.0] undecane d) bicyclo[4.4.1] decane

16. Which one is true for perhydroanthracene molecule?

a) It exists as five diastereoisomers b) It exists as meso compounds

c) It exists as four enantiomers d) It exixts as racemic mixtures

17. When the acidic solution of a diazonium salt can couple with another aromatic ring known as

a) Gomberg-Bachmann reaction b) Ullmann reaction

c) Sandmeyer reaction d) Pechmann reaction

18. Among the following which one is Fenton's reagent?

a) $Fe^{3+}+H_2O_2$ b) $Fe+H_2O_2$ c) $Fe^{1+}+H_2O_2$ d) $Fe^{2+}+H_2O_2$

19. The N-bromosuccinimide reagent is very specific reagent for

a) ring bromination b) alicyclic ring bromination

c) allylic bromination d) vinylic bromination

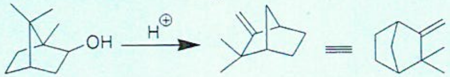
20. Decomposition of benzoyl peroxide in aromatic solvent leads to the generation of

a) benzyloxy radical b) benzyl radical

c) methyl radical d) phenyl radical

PART- B (3 x 2= 6 Marks)
Answer All the Questions

21. Suggest the mechanism for the following reaction?

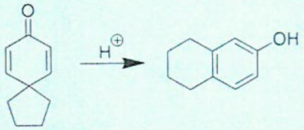


22. The alkaline hydrolysis of 3α-acetoxy cholestane-5α-ol proceeds faster than the corresponding 3β-isomer. Why?

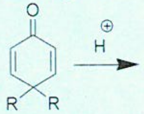
23. Write the structures of benzoyl peroxide and AIBN.

PART- C (3 x 8= 24 Marks)
Answer All the Questions

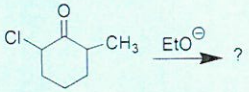
24. (a) (i) Sketch a suitable mechanism for the following transformation.



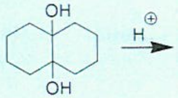
(ii) Predict the product, name the rearrangement and give mechanism:



(iii) Give the product of the following reaction with mechanism.



(iv) Predict the major product and suggest a mechanism for each of the following reaction.



(Or)

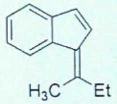
(b) Write brief notes on Stevens and Wallach rearrangements.

25. (a) Discuss the Fries rearrangement.

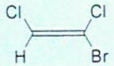
(Or)

(b) (i) Indicate the configuration of the following molecules using E-and- Z notation.

(a)

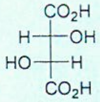


(b)

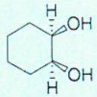


(ii) Designate the configuration of the following molecules according to Cahn Ingold and Prelog notation.

(a)



(b)



26. (a) Write a brief note on optical isomerism exhibited by biphenyl and allenes.

(Or)

(b) What is Ullmann reaction? Explain its mechanism with an example.

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PG DEGREE EXAMINATION, MARCH 2018

SECOND SEMESTER

INTERNAL TEST-II

CHEMISTRY

ORGANIC CHEMISTRY-II
(Rearrangements, Reactions, Photochemistry and Pericyclic Reactions)

Time: 2 hours
Date: 19-03-2018

Maximum: 50 marks
Subject code: 17CHP201

PART- A (20 x 1=20 Marks)
Answer All the Questions

1. Reductive decomposition may be carried out by treating the ozonide with

a) H_2O b) H_2O_2 c) Zn d) Zn/H_2O

2. Keto ester when reduced with sodium borohydride is an example for

a) regioselective reduction b) chemoselective reduction

c) diastereoselective reduction d) regiospecific reduction

3. The aromatic ring has two nitro groups it is possible to selectively reduce one without reacting the other by

a) Zn/HCl b) NaOH/Zn c) $SnCl_2$ d) H_2/Pd

4. Which solvent is used in Acylion Condensation?

a) ether b) chloroform c) dichloromethane d) DMSO

5. Which one of the following excited state has a long life?

a) S_1 b) S_2 c) T_1 d) T_2

6. Which one of the following decay takes place in phosphorescence?

a) $S_1 \rightarrow S_0$ b) $T_1 \rightarrow S_0$ c) $T_2 \rightarrow T_1$ d) $T_1 \rightarrow S_1$

7. If a photochemical reaction has higher quantum yield than unity, it indicates

a) reversible reaction b) elementary reaction

c) chain reaction d) radical reaction

8. Photolytic conversion of organic nitrites into nitroso alcohols is known as

a) Ritter reaction b) Birch reduction

c) Barton reaction d) Paterno–Buchi reaction

9. In the Paterno–Buchi reaction the acetylenes can replace olefins to produce an

a) ketones b) oxetanes c) α, β–unsaturated ketone d) β,γ –unsaturated ketones

10. The allylic oxidation of alkenes with selenium dioxide is an example for

a) Photo-Fries reaction b) ene reaction

c) electrocyclic reaction d) cycloaddition reaction

11. Conversion of carbonyl compounds into oxetanes is effected by

a) Paterno–Buchi reaction b) di – π – methane rearrangement

c) Norrish type I reaction d) photo reduction

12. Which one is an example for excimers?

a) alcohol b) acid c) pyrene d) ketone

13. In the reaction of cyclopentadiene with acrylate ester giving Diels-Alder reaction products, the interacting frontier orbitals are

a) HOMO of a diene and LUMO of a dienophile

b) HOMO of a dienophile and LUMO of a diene

c) HOMO of a diene and HOMO of a dienophile

d) LUMO of a diene and LUMO of a dienophile

14. The conversion of vinylcyclopropane to cyclopentene upon heating is an example of

a) [3,3] -sigmatropic rearrangements b) [1,3]-sigmatropic rearrangements

c) [1,5]- sigmatropic rearrangements d) [1,2] -sigmatropic rearrangements

15. The π-molecular orbitals of 1,3,5-hexatriene the HOMO of ground state is

a) ψ_1 b) ψ_2 c) ψ_3^* d) ψ_3

16. 1,5-diene isomerizes in a [3,3] sigmatropic rearrangement known as

a) Claisen rearrangement b) Ene reaction

c) Fries rearrangement d) Cope rearrangement

17. A cycloaddition reaction occurs across the same face of the π system, the reaction is said to be

a) suprafacial b) antarafacial c) heterofacial d) homofacial

18. According to Woodward-Hofmann rules $4n\pi$ electrons under cyclization allowed stereochemistry is

a) conrotatory b) disrotatory c) suprafacial d) antarafacial

19. Which transition state is more stable in cope rearrangement?

a) chair like transition state b) boat like transition state

c) twist boat like transition state d) half chair like transition state

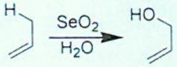
20. The transition state for [3,3]–sigmatropic reaction can be visualized as the interaction of

a) two cations b) two anions

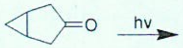
c) two allyl free radical d) one allyl free radical

PART- B (3 x 2= 6 Marks)
Answer All the Questions

21. Write the mechanism of the following transformation?



22. Predict the product in the following reaction.



23. What are pericyclic reactions? Why are they called so?

PART- C (3 x 8= 24 Marks)
Answer All the Questions

24. (a) Explain the mechanism of Sommelet reaction.

(Or)

(b) Explain the Paterno Buchi reaction.

25. (a) Explain the following photochemical reactions.

(i) Norrish Type I

(ii) Norrish Type II

(Or)

(b) (i) Draw π orbitals of buta-1,3-diene and ethylene and identify their HOMO and LUMO.

(ii) Using Frontier orbital overlap, explain why the $\pi 4s + \pi 2s$ reaction between butadiene and ethylene is thermally allowed but not photochemically.

26. (a) Construct the orbital correlation diagrams for the $\pi 4s + \pi 2s$ cycloaddition and based on that state whether the reaction is allowed under thermal or photochemical condition.

(Or)

(b) Explain how the correlation diagram approach is useful in predicting the mechanism of electrocyclic reactions considering the Con rotary ring closure of 1, 3, 5-hehatriene as an example.